Cancer Research in Switzerland

A publication of the Swiss Cancer Research foundation, the Swiss Cancer League and the cantonal cancer leagues on their funded research projects 2019

Imprint

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Ester Vonplon (*1980 in Schlieren) lives in Castrisch in the Grisons' Surselva. Her artistic projects are often inspired by the landscape and nature there. Thus, many of the pictures in this report were taken on hikes during which Ester Vonplon laid plants by the wayside on photographic paper more than a hundred years old. The often blurred shadows (white in the brown negative, dark blue in the inverted positive) bear witness to the wind that moved the fine plants, while the stains in the background are due to ageing processes that bring unexpected disturbing effects to light. These pictures taken without a camera have at least two things in common with cancer research: the experimental approach – and the fact that the results are often unpredictable.

estervonplon.com

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Edition 2020

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Editorial

The SARS-CoV-2 virus has conquested the globe. And with its rapid spread around the world, many patients with cancer are especially worried. Because they are receiving treatment that not only kills cancer cells but also often weakens the immune system, patients with cancer are susceptible to all kinds of infections, and thus also to Covid-19, the disease caused by the new coronavirus.

The immune system plays a decisive role in this disease: Its response to the virus determines whether we survive the disease without threatening complications. Covid-19 progresses to a much more difficult process if inflammatory responses become exacerbated and the body's own immune system damages especially the lungs and the heart muscle. There are antibodies that can disrupt the inflammation process, as they block the receptors for the pro-inflammatory protein Interleukin-6. Such antibodies are also used in oncology, when strong, life-threatening inflammatory responses occur during treatment.

Thomas Cerny

Gilbert Zulian

"Thanks to cancer research, we know how our immune system works – and how we can use antibodies and immune cells in a targeted manner against cancer and other diseases."

Evidently, knowledge of the immune system is highly important also in the fight against the new coronavirus. And here, cancer research has made a significant contribution: It developed the bases for our understanding of the immune system. Thanks to cancer research, we know how our immune system works – and how we can use antibodies and immune cells in a targeted manner against cancer and other diseases.

Unfortunately, it is likely that there will always be pandemics. We all hope that the current crisis is soon over. It is important to survive it with as little damage as possible – and to utilize the opportunity to learn from the present experiences, so that we will be better armed in the future: We must find national and international solutions that are crisis-resistant.

Prof. em. Thomas Cerny, MD
President of the Swiss Cancer Research foundation

PD Gilbert Zulian, MD
President of the Swiss Cancer League

Research promotion of the Swiss Cancer League and Swiss Cancer Research foundation

Researching means looking very carefully – and pointing the way to progress

In 2019 the Swiss Cancer Research foundation, the Swiss Cancer League, and the cantonal and regional leagues gave nearly 26.5 million francs in funding to 183 research projects and research institutions. We express our heartfelt thanks to the charitable donors for their support. And we regret that 35 high-quality research proposals could not be funded.

A recently published study conducted by a research team headed by Andrea Alimonti, a member of the Scientific Committee, found that male patients with cancer had a 1.8-fold increased risk of Covid-19 infection among the whole male population. On average, they also tended to develop more severe disease. Unexpectedly, however, the researchers found an exception: Patients with prostate cancer receiving androgen-deprivation therapies appear to be better protected against SARS-CoV-2 infections – the virus causing Covid-19. Naturally, the study has provided only initial findings. It is not yet known whether these treatments lowering testosterone levels could, for example, also protect healthy men against Covid-19. Whether a reliable Covid-19 preventive treatment can be developed form the prostate cancer treatment must be investigated in further studies.

This example shows that research results are often not predictable or foreseeable. And it makes it clear that diligent observation is worth it and pays off. For if researchers not only have their planned aim in their line of sight but also keep their eyes open and look very carefully, they discover unexpected things – and point the way to progress. It is for this reason that the two partner organizations Swiss Cancer League (SCL) and Swiss Cancer Research foundation (SCR) as well as the cantonal and regional cancer leagues (CCL) are committed to funding research. Each research success – even unplanned and unexpected – increases our knowledge. And a broader knowledge base opens up more chances to improve patients' survival rates and quality of life.

A broad spectrum of research

We fund research projects along the entire range of cancer research, which can be divided into four areas: basic, clinical, psychosocial, and epidemiologic cancer research. *Basic research* studies how cancer cells develop, multiply, and spread in the body. *Clinical* research, for one, works with cancer cells and tumour tissue to identify, for instance, new weak points and targets. For another, clinical research also consists in conducting clinical trials with patients to test new treatments or optimize existing treatments. *Psychosocial research* studies the psychological and social effects of cancer. The goal is to improve the quality of life of patients with cancer and their family members. *Epidemiologic research* investigates the incidence of cancer in the population, for example, or examines the role played by smoking, lack of exercise, or unfavourable environmental conditions, among other things, in the development of cancer.

Rolf Marti, PhD
Head of the Research, Innovation & Development department, Swiss Cancer League, and director of the Swiss Cancer Research foundation

In addition, in the framework of a programme to strengthen *health services research* in oncology and cancer care, the SCR also funds research projects that weigh the costs and benefits of medical services and demonstrate new ways of organizing health services in oncology as efficiently as possible. Unlike in other areas, research project proposals in the area of health services research are not reviewed by the Scientific Committee but instead by an expert panel expressly set up for the health services research programme; the panel members include also persons with demonstrated expertise in fields such as health economics or nursing sciences (see p. 26).

Many thanks for the generous funding amount

In 2019 the SCR, SCL, and the CCL gave nearly 26.5 million francs in funding to 183 research projects and research institutions (Figure 1; Table 1). A good three quarters of all funds granted came from the SCR; the SCL contributed nearly 15 % and the CCL 8 %. The SCR and SCL used somewhat over 1 million francs to directly support young researchers: They made it possible for a total of nine bursary recipients to study their research questions in Switzerland or also abroad using up-to-date research methods. Here we would like to extend heartfelt thanks to the charitable donors.

Figure 1
Cancer research funding by SCR, SCL, and CCL since the founding of SCR in 1990

Research funding by the CCL has been recorded centrally and published only since 2009.

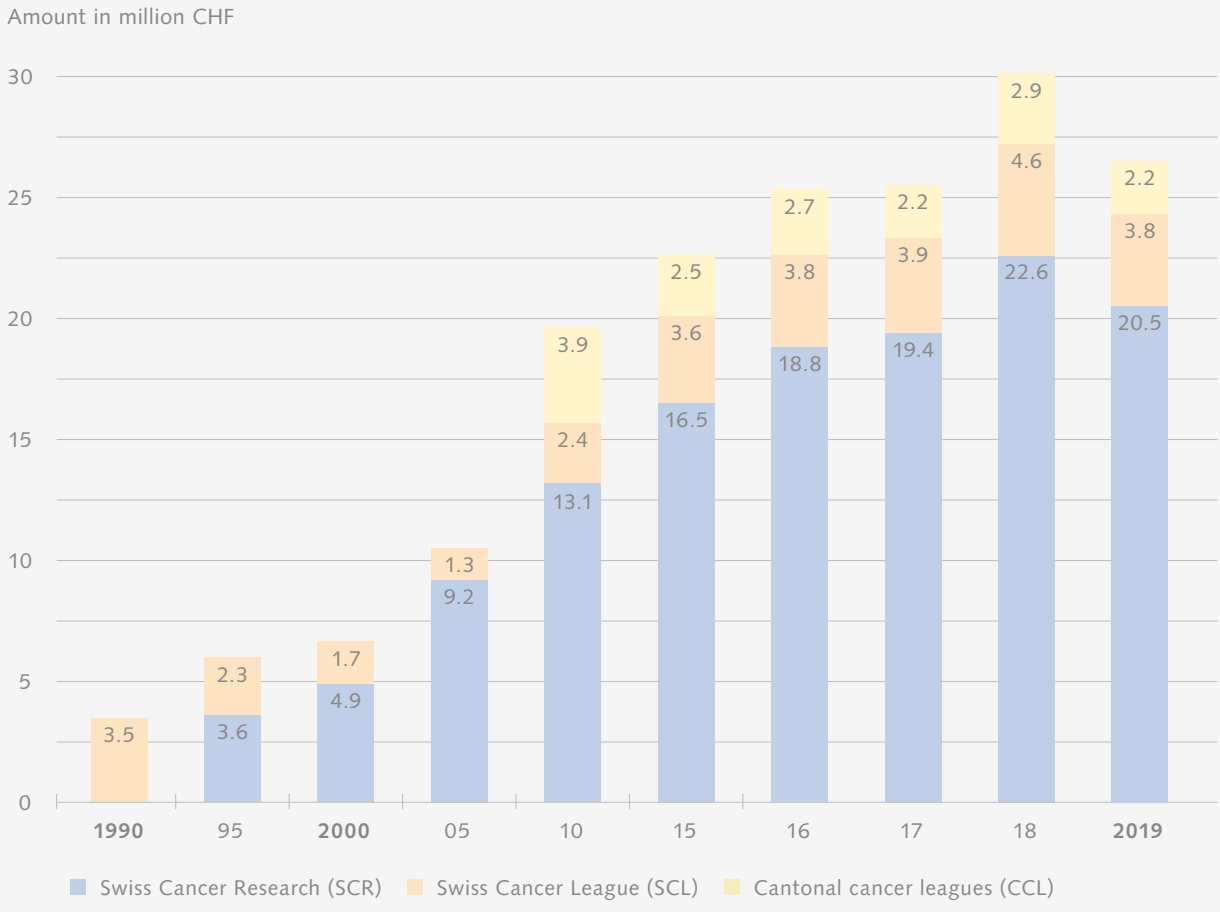
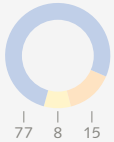


Table 1
Research funding by SCR, SCL, and CCL in overview

Number of grants approved and amount granted in 2019 (all funding areas)

	Number of grants approved	Amount granted in kCHF	Proportion of total funding in %
Total SCR, SCL, and CCL			
Independent research projects	94	20 729	78
Bursaries	9	1 084	4
Programme for health services research	8	983	4
Research organizations and institutions	6	2 450	9
Programmes, organizations and conferences	66	1 249	5
Total	**183**	**26 495**	**100**
SCR			
Independent research projects	51	15 573	76
Bursaries	6	825	4
Programme for health services research	8	983	5
Research organizations and institutions	6	2 450	12
Programmes, organizations and conferences	26	661	3
Total	**97**	**20 492**	**100**
SCL			
Independent research projects	11	2 982	78
Bursaries	3	259	7
Programmes, organizations and conferences	40	588	15
Total	**54**	**3 829**	**100**
CCL			
Independent research projects	32	2 174	100
Programmes, organizations and conferences	n. s.	n. s.	–
Total	**32**	**2 174**	**100**

n. s. = not specified



(percentage of funds)

As in previous years, the most successful cancer research centres in the competition for funding were the universities and university hospitals in Zurich, Lausanne, Bern, and Basel (Table 2). Researchers in the Canton of Zurich (including ETHZ) received in total nearly 5.8 million francs, which is more than one fourth of the funding nationwide. Researchers in Bellinzona were also successful, together they were granted nearly 1.5 million francs.

35 high-quality research proposals unfortunately not funded

With the largest part of the funding, the SCR and the SCL supported independent research projects, where the researchers alone determine what research questions they will investigate. In 2019 a total of 170 research proposals were submitted to the two partner organizations (Table 3). After careful review of all proposals, the Scientific Committee responsible for evaluating them rated 103 research projects as high in quality and promising – and recommended them for funding. However, due to the limited funding available, the SCR foundation board and the board of the SCL could approve grants for only 68 research projects. Unfortunately, 35 research projects that were also recommended by the Scientific Committee for grants could not be funded, as there was not enough funding for independent research available

Table 2
Distribution of competitive cancer research funding by SCR and SCL to the research institutions in 2019

Research institutions	Number of projects	Amount in kCHF	Proportion in %
Universität/Inselspital Bern	16	3 868	19.0
Universität/Universitätsspital Basel	8	2 336	11.5
EOC Bellinzona	1	375	1.8
IOSI Bellinzona	1	362	1.8
IOR Bellinzona	4	740	3.6
Université/HUG Genève	2	466	2.3
EPF Lausanne	5	1 759	8.7
Université/CHUV Lausanne	11	3 426	16.9
Kantonsspital St. Gallen	3	524	2.6
PSI Villigen	3	692	3.4
Kantonsspital Winterthur	2	375	1.9
ETH Zürich	4	1 226	6.0
Universität/Universitätsspital Zürich	19	4 171	20.5
Total	**79**	**20 320**	**100**

Abbreviations

CHUV	Centre Hospitalier Universitaire Vaudois
EOC	Ente Ospedaliero Cantonale
EPF	Ecole Polytechnique Fédérale
ETH	Eidgenössische Technische Hochschule
FMI	Friedrich-Miescher-Institut
HUG	Hôpitaux Universitaires de Genève
IOSI	Istituto Oncologico della Svizzera Italiana
IRO	Institute of Oncology Research
PSI	Paul Scherrer Institut

Table 3
Distribution of funds by SCR and SCL and success rates of the independent research projects in the different domains

	2018		2019	
	Grant applications	Amount in kCHF	Grant applications	Amount in kCHF
All projects				
Received/applied for	218	62 633	170	50 778
Recommended	118		103	
Approved	81	22 677	68	19 058
Success rate	37 %	36 %	40 %	38 %
Basic research				
Received/applied for	98	32 880	81	27 652
Recommended	67		55	
Approved	39	12 534	32	10 317
Success rate	40 %	38 %	40 %	37 %
Clinical research				
Received/applied for	71	20 581	53	15 889
Recommended	33		29	
Approved	26	7 714	17	5 017
Success rate	37 %	37 %	32 %	32 %
Psychosocial research				
Received/applied for	8	1 808	8	1 666
Recommended	7		4	
Approved	6	1 227	4	480
Success rate	75 %	68 %	50 %	29 %
Epidemiologic research				
Received/applied for	8	2 382	7	2 378
Recommended	3		7	
Approved	2	521	7	2 261
Success rate	25 %	22 %	100 %	95 %

	2018/2019		2019/2020	
	Grant applications	Amount in kCHF	Grant applications	Amount in kCHF
Health services research				
Received (letter of intent)/applied for	33	4 982	21	3 193
Invited (full proposal)/applied for	10	1 066	10	1 376
Recommended	8		8	
Approved	8	681	8	983
Success rate	80 %	64 %	80 %	71 %

for all of the high-quality research proposals submitted (see also the interview with Nancy Hynes, president of the Scientific Committee on page 23 below).

In 2019 the competition for the limited funds available was about as high as in the previous year, as can be seen in the comparable success rates (Table 3). But that was not the case in all areas of research: Epidemiologic research stands out particularly, where all of the proposals submitted met the quality criteria of the Scientific Committee and could be funded.

Financing of indispensable services that benefit research

In addition to funding independent research projects, the SCR and the SCL also supported six different research organizations (Table 4). The funds finance central and indispensable services provided by these organizations that benefit clinical and epidemiologic research in Switzerland. The services include, for example in clinical research, administrative tasks such as submitting the necessary documents to the ethics committees and Swissmedic, the authorization authority, for the study approval process. In the area of cancer prevalence statistics in Switzerland, the organizations supported by the SCR provide researchers with their know-how and their resources for collecting, managing, and analysing data (see box). For their expenditures, the six organizations receive compensation based on performance agreements. The performance agreements define in a clear and binding way

Table 4
Supported research organizations

Funding in the years 2013–2019

Amount in kCHF

	2013	2014	2015	2016	2017	2018	2019
Swiss Group for Clinical Cancer Research (SAKK)	*900	*1 050	*1 100	*1 150	*1 300	*1 300	1 100
International Breast Cancer Study Group (IBCSG)	500	450	400	350	350	350	350
National Institute for Cancer Epidemiology and Registration (NICER)	250	250	250	250	250	250	250
International Extranodal Lymphoma Study Group (IELSG)	200	200	250	250	350	350	350
Swiss Paediatric Oncology Group (SPOG)	150	150	150	200	250	250	300
Swiss Childhood Cancer Registry (SCCR)	75	75	100	100	100	100	100
Total	**2 075**	**2 175**	**2 250**	**2 300**	**2 600**	**2 600**	**2 450**

*of wich 200 000 CHF funded by SCL

The research organizations supported, in brief

Swiss Group for Clinical Cancer Research (SAKK)
SAKK is a decentralized academic research institute that has conducted clinical studies on cancer treatment in all larger hospitals in Switzerland since 1965. SAKK encompasses a network of about 20 Swiss research groups and a coordination centre in Bern. In particular for rare cancers SAKK works together with selected collaborative groups in other countries. SAKK aims to improve existing cancer treatments, study the effectiveness and tolerability of new treatments (chemotherapy, medications, surgery), and establish new treatment standards. → www.sakk.ch/en

International Breast Cancer Study Group (IBCSG)
Since 1977 the IBCSG has conducted academic clinical trials with the aim to improve treatment for women with breast cancer. The IBCSG is a multicentre study group with a coordination centre located in Bern, a data management centre and a statistics centre in the United States, and a pathology reference laboratory in Italy that serves the entire organization. In Switzerland, all university clinics, numerous cantonal hospitals, and oncologists in private practices participate in IBCSG studies. → www.ibcsg.org

National Institute for Cancer Epidemiology and Registration (NICER)
As a national coordination centre, NICER collects and aggregates the data from the cantonal and regional cancer registries, harmonizes their work, and assures the quality of the data. Since the start of 2020, NICER has also been assigned the tasks of the National Agency for Cancer Registration (NACR), which was foreseen by the new Cancer Registration Act. The data collected in the network are utilized to determine national statistics on cancer incidence. For health care policy, the data enable evidence-based decision making that benefits the population as well as individual patients with cancer. → www.nicer.org

International Extranodal Lymphoma Study Group (IELSG)
The IELSG is a multicentre study group that was created in 1998 in Ascona, with a coordination and data management centre in Bellinzona. It aims to coordinate international research activities in the area of extranodal lymphomas. As these lymphomas are rare and moreover develop in all organs in the body, different treatments are required. To jointly test and optimize the treatments, more than 200 international institutes participate in the IELSG network. → www.ielsg.org

Swiss Paediatric Oncology Group (SPOG)
SPOG has been conducting clinical cancer research in paediatric oncology and haematology since 1977, with the aim to improve treatment and quality of life of children and adolescents with cancer. SPOG is a national, independent association with headquarters in Bern. The members are all paediatric oncology departments at Swiss hospitals and the Swiss Childhood Cancer Registry. As childhood cancers are relatively rare, research in childhood cancer is possible only in the framework of international collaborations. At present, SPOG is taking part in more than 20 clinical trials in which approximately 150 young patients in Switzerland are participating. → www.spog.ch

Swiss Childhood Cancer Registry (SCCR)
The SCCR is the national cancer registry for children and adolescents in Switzerland. Since 1976 it has captured all new cases of cancer in young persons up to the age of 20. It also documents treatments and conducts longitudinal studies on the health and quality of life of childhood cancer survivors. In this way it contributes towards research on the causes of childhood cancer, improvement of cancer treatment, and prevention of late effects in cancer survivors. The SCCR, which is funded from several sources, is located at the Institute of Social and Preventive Medicine at the University of Bern. At the start of 2020, the SCCR was transferred to a national registry, the Childhood Cancer Registry, funded by the federal government. → www.kinderkrebsregister.ch

the requirements regarding reporting and evaluation as well as the targets for research. In addition, there is the condition that the research organizations must secure independent and long-term financing that guarantees their continuing existence independently of the contributions from the SCR. In 2019, the SCR paid out a total of 2.45 million francs to the six research organizations (Table 4).

Rolf Marti, PhD
Rolf Marti is the head of the Research, Innovation & Development department (formerly, the Scientific Office) and is a member of the Managing Board at the Swiss Cancer League (SCL). Marti is also the director of the Swiss Cancer Research (SCR) foundation.
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Partner organizations and committees

Swiss Cancer Research foundation (SCR)

In existence since 1990, the Swiss Cancer Research foundation, with the help of donations, provides funding for all areas of cancer research: basic, clinical, epidemiologic, and psychosocial research. A special focus is the funding of patient-centred research projects that result as far as possible in direct patient benefit. The SCR foundation board is responsible for distributing the funds to researchers. The board's funding decisions are based on the recommendations made by the Scientific Committee, which reviews the grant applications according to clearly defined criteria. The SCR also supports the development and implementation of measures to fight cancer in Switzerland – namely, the National Strategy Against Cancer 2014–2020.

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Swiss Cancer League (SCL)

The Swiss Cancer League (SCL) works towards a world where fewer persons get cancer, fewer persons suffer from the consequences and die of cancer, and more persons are cured of cancer. Persons with cancer and their families should receive care and support in all phases of cancer. The SCL, headquartered in Bern, is the national umbrella organization of the cantonal and regional cancer leagues. The SCL supports the cantonal cancer leagues through information brochures and services. It operates the cancer support helpline (0800 11 88 11) and advises persons with cancer also per e-mail, chat, or Skype. The SCL is also active in the area of health policy and informs the wider public on risk factors and cancer screening measures. It also offers specific continuing education courses for a variety of professionals and funds cancer research.

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Cantonal cancer leagues (CCL)

The 18 cantonal and regional cancer leagues provide persons with cancer and their family members with individual counselling by experts on treatment and financial and organizational questions. The CCL staff often advise persons over a longer time period and support them in difficult situations. They provide information on legal and insurance issues and provide contacts to other support institutions, such as home care organizations. If persons with cancer experience financial difficulties as a result of their illness, they can apply for support payments. The CCL also organize group meetings and courses where persons with cancer can talk about their fears and experiences and discuss ways to cope with their illness. Some cancer leagues offer specialized psycho-oncology support for children of adults with cancer. And in some cantons, there are outpatient oncology care services that support persons with cancer at home. The CCL do not all offer the same services. The type and extent of services depend greatly on the financial and human resources as well as on the services provided by other providers in the region.

Cantonal and regional cancer leagues in the German-speaking part of Switzerland and in Liechtenstein

- Aargau Cancer League
- Basel Cancer League
- Bern Cancer League
- Central Switzerland Cancer League
- Eastern Switzerland Cancer League
- Grisons Cancer League
- Liechtenstein Cancer League
- Schaffhausen Cancer League
- Solothurn Cancer League
- Thurgau Cancer League
- Zurich Cancer League

Cantonal cancer leagues in the French-speaking part of Switzerland and in Ticino

- Fribourg Cancer League
- Geneva Cancer League
- Jura Cancer League
- Neuchâtel Cancer League
- Ticino Cancer League
- Valais Cancer League
- Vaud Cancer League

The board of the Swiss Cancer Research foundation

The board is the highest body of the Swiss Cancer Research foundation (SCR).
It monitors adherence to the foundation goals and manages the foundation's assets.
The board of the SCR meets two to four times a year. Based on the recommendations
of the Scientific Committee, it decides on the granting of funds to researchers.

The members of the SCR foundation board serve on a voluntary basis.
The members are:

President

Prof. em. Thomas Cerny, MD
Kantonsspital St. Gallen

Prof. Daniel E. Speiser, MD
Université de Lausanne
Basic research representative

Prof. Martin F. Fey, MD
Inselspital Bern
Clinical research representative

Prof. Beat Thürlimann, MD
Kantonsspital St. Gallen
Clinical research representative

Prof. Murielle Bochud, MD
Unisanté Lausanne
Epidemiologic research
representative

Up to March 2020

Prof. Nicolas von der Weid, MD
Universitäts-Kinderspital beider Basel
Paediatric research representative

Since April 2020

Nicolas Gerber, MD
Universitäts-Kinderspital Zürich
Paediatric research representative

Christine Egerszegi-Obrist
Former member of
the Swiss Council of States
Mellingen

Silvio Inderbitzin, PhD
St. Niklausen

Treasurer

Gallus Mayer
Former Banking specialist
St. Gallen

The board of the Swiss Cancer League

The board members represent different specialties in the fight against cancer and also the different regions of Switzerland. The board is responsible for strategic management of the Swiss Cancer League – and in this role they make the decisions on the granting of the funds.

The members of the board are:

President

PD Gilbert Bernard Zulian, MD
Former head physician of Palliative Medicine
Hôpital de Bellerive, Hôpitaux universitaires de Genève (HUG)

Vice president

PD Georg Stüssi, MD
Head, Department of Haematology
Istituto Oncologico della Svizzera Italiana (IOSI)

Prof. Solange Peters, MD
Head physician of medical oncology
Centre hospitalier universitaire vaudois (CHUV)

Up to April 2019

Lucienne Bigler-Perrotin
Manager
Geneva Cancer League

Since May 2019

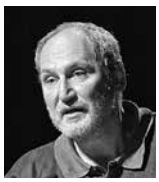
Franck Moos
Manager
Valais Cancer League

Christoph Kurze
Managing director
Grisons Cancer League

Treasurer

Gallus Mayer
Former Banking specialist
St. Gallen

Hans Neuenschwander, MD
Former head physician of Palliative Care
Ospedale regionale di Lugano



Markus Notter, MD
Radiation Oncology
Lindenhofspital Bern

Brigitta Wössmer, PhD
Head psychologist of Psychosomatics
Universitätsspital Basel

Karin Zimmermann, PhD
Registered nurse / scientific staff
Inselspital Bern

The Scientific Committee

The Scientific Committee reviews the research proposals submitted to the SCR and the SCL by researchers requesting funds for their research projects and ideas. In the evaluation of research grant applications, the main criterion is always whether a research project can generate important new findings. The Scientific Committee also rates the originality and feasibility of the research projects (see box, "Criteria for high-quality cancer research").

Each research grant application is reviewed carefully by several experts. (see box, "The research grant application review process"). At two meetings of the Scientific Committee per year, the grant applications are discussed in depth and ranked on a list. Only the best projects are recommended for funding. Based on the recommendations, the board of the SCR or the SCL decide which projects will be granted financial support.

Criteria for high-quality cancer research

The quality of research grant applications is evaluated according to the following criteria:

- Cancer relevance: Is the proposed research project expected to contribute important new observations or knowledge on the causes, prevention, or treatment of cancer?
- Originality or socioeconomic significance: Is the proposed research project original, innovative (basic research projects), or of socioeconomic importance (clinical or epidemiologic projects)?
- Choice of methodology: Have the most appropriate methods for realization of the project been chosen?
- Feasibility: Is the project feasible in terms of finances, human resources, and organization?
- Track record: What are the applicant's (or the project group's) previous research achievements?

The Scientific Committee receives operational support from the Research, Innovation & Development department of the SCL. The department organizes the calls for and the peer review of research grant applications, makes the grant payments in annual increments, and receives the interim and final research reports of the funded projects.

The research grant application review process

The grant application is submitted online.
↓
The grant application is sent to two members of the Scientific Committee for review.
↓
The two Scientific Committee members recommend external reviewers.
↓
The Research, Innovation & Development department of the SCL asks the external reviewers to review the grant application.
↓
The grant application is reviewed. Four to six reviews are obtained for each grant application, two of which are by Scientific Committee members.
↓
The grant application and the reviews are discussed in detail at the biannual meeting of the Scientific Committee.
↓
After the meeting, the Research, Innovation & Development department writes up detailed minutes and creates a ranking list of all grant applications discussed, following the Scientific Committee's recommendations.
↓
The ranking list is forwarded to the boards of the SCR and SCL. The boards make the final funding decision.
↓
The grant applicant is informed of the decision by the Research, Innovation & Development department. Reviewer comments are fed back to the applicant anonymously.

"We award the limited funds to the best projects"

Today, about 200 research proposals are submitted each year to the Swiss Cancer League (SCL) and its partner organization, the Swiss Cancer Research foundation (SCR) – about twice as many as were received 20 years ago. Many are high-quality grant proposals for which there is unfortunately not enough funding available, says Nancy Hynes, president of the Scientific Committee.

Nancy Hynes, what motivates you to work on a voluntary basis on the Scientific Committee of the SCL and SCR?
The work is very diverse and exciting. Reading so many research grant applications keeps you abreast of the latest scientific developments. Besides that, after having received funding so often for my own research projects, I want to give something back – and do the research community a service.

You are the president of the Scientific Committee. Are your tasks different than the tasks of the other members of the Scientific Committee?
Yes, as president I look at all of the research proposals – and then assign them to individual members of the Committee. Here the content of the proposal naturally plays a role. For instance, if the research proposal addresses psychosocial questions, different knowledge is required than for projects that examine the molecular mechanisms of a cancer. But I also try to distribute the workload – that is, the number of research proposals that we review and evaluate – as fairly as possible among the members. Today, about twice as many research proposals are submitted to us than were submitted 20 years ago. This naturally increases the effort required for evaluation of the proposals.

How are the members of the Scientific Committee chosen?
When a member's term of office is up, which is the case after nine years (maximum), we look for a successor with similar expertise. Sometimes, the member leaving the Committee points us towards good people. We then look at the candidates' publications. With candidates from Switzerland, we also check whether the person was awarded grants from us in the past for their research proposals. A person who writes good research proposals also tends to be able to assess others' proposals. Often, someone will stand out who has been an external reviewer: When an expert always sends us high-quality and well-thought-out evaluations on time, we know that we can rely on that person.

Each research proposal is reviewed by at least two members of the Scientific Committee and in addition by external reviewers. How often do the reviewers disagree on the quality of a proposal?
It almost never happens that one reviewer finds a research proposal great and another finds it of little value. Of course, there are diverging assessments, but when you look more closely it mostly turns out that they concern nuances, a different weighting of details or different evaluations regarding how important the proposed cancer topic is.

Is a lack of importance of the cancer topic the most frequent reason for not selecting a research project for funding?
No, that is rarely the case. It is much more often that we find a research proposal good but cannot fund it because we must award the limited funds available to the best research projects. That is why we unfortunately have to turn down many projects that do not make it to the top.

The members of the Scientific Committee are recognized experts with an excellent scientific track record. Together they cover all scientific areas relevant to cancer research.

The members of the Scientific Committee are:

President

Prof. Nancy Hynes, PhD
Friedrich-Miescher-Institut für biomedizinische Forschung (FMI)
Basel

Basic research

Prof. Andrea Alimonti, MD
Istituto Oncologico della Svizzera Italiana (IOSI)
Bellinzona

Prof. Joerg Huelsken, PhD
Institut suisse de recherche expérimentale sur le cancer (ISREC)
Ecole Polytechnique Fédérale de Lausanne (EPFL)
Lausanne

Prof. Tatiana Petrova, PhD
Département d'oncologie fondamentale
Université de Lausanne
Epalinges

Prof. Pedro Romero, MD
Département d'oncologie
Université de Lausanne
Epalinges

Up to December 2019

Prof. Primo Schär, PhD
Departement Biomedizin
Universität Basel
Basel

Prof. Jürg Schwaller, MD
Departement Biomedizin
Universitätsspital Basel
Basel

Since January 2020

Prof. Manuel Stucki, PhD
Klinik für Gynäkologie
Universitätsspital Zürich
Schlieren

Prof. Sabine Werner, MD
Institute of Molecular Health Sciences
ETH Zürich
Zürich

Clinical research

Prof. Jörg Beyer, MD
Klinik für Onkologie
Universitätsspital Zürich
Zürich

Since January 2020

Prof. Andreas Boss, MD
Institut für diagnostische und
interventionelle Radiologie
Universitätsspital Zürich
Zürich

Prof. Markus Joerger, MD, PhD
Onkologie/Hämatologie
Kantonsspital St. Gallen
St. Gallen

Prof. Aurel Perren, MD
Institut für Pathologie
Universität Bern
Bern

Up to December 2019

Prof. Martin Pruschy, PhD
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Research (DBMR)
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Prof. Beat W. Schäfer, PhD
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Universitäts-Kinderspital Zürich
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Prof. Emanuele Zucca, MD
Istituto Oncologico della Svizzera
Italiana (IOSI)
Ospedale San Giovanni
Bellinzona

Psychosocial research

Sarah Dauchy, MD
Département interdisciplinaire
de soins de support
Gustave Roussy
Villejuif, France

Prof. Sophie Pautex, MD
Unité de gériatrie et
de soins palliatifs communautaires
Hôpitaux universitaires de
Genève (HUG)
Chêne-Bougeries

Epidemiologic research

Prof. Simone Benhamou, PhD
Institut national de la santé et
de la recherche médicale (INSERM)
Paris, France

Milena Maria Maule, PhD
Dipartimento di Scienze Mediche
Università di Torino
Torino, Italy

Panel of experts for health services research

The panel of experts for oncological health services research (from left): Rolf Marti (Swiss Cancer Research foundation office), Isabelle Peytremann-Bridevaux, Urs Brügger, Corinna Bergelt, Thomas Perneger, Marcel Zwahlen, Sabina De Geest, Cinzia Brunelli, Oliver Gautschi, Thomas Rosemann, Thomas Ruhstaller, Peggy Janich (Swiss Cancer Research foundation office)

For evaluation of the grant applications submitted to the Health Services Research in Oncology and Cancer Care programme, the Swiss Cancer Research foundation brought together a panel of experts. The members of the panel cover a wide range of disciplines – and have proven knowledge in health economics or nursing sciences, for example.

The submitted research project proposals are evaluated and selected in a two-step process. The following persons make up the members of the expert panel:

- **Prof. Marcel Zwahlen, PhD** (president)
  Institut für Sozial- und Präventivmedizin, Universität Bern, Bern
- **Prof. Corinna Bergelt, PhD**
  Institut und Poliklinik für Medizinische Psychologie, Universitätsklinikum Hamburg-Eppendorf, Germany
- **Prof. Urs Brügger, PhD**
  Berner Fachhochschule für Gesundheit, Bern
- **Cinzia Brunelli, PhD**
  Fondazione IRCCS Istituto Nazionale Tumori, Milano, Italy
- **Prof. Sabina De Geest, PhD**
  Institut für Pflegewissenschaften, Universität Basel, Basel
- **Prof. Oliver Gautschi, MD**
  Medizinische Onkologie, Luzerner Kantonsspital and Universität Bern, Luzern and Bern
- **Prof. Thomas Perneger, MD**
  Service qualité des soins, Hôpitaux universitaires de Genève, Genève
- **Prof. Isabelle Peytremann-Bridevaux, MD**
  Institut universitaire de médecine sociale et préventive, Université de Lausanne, Lausanne
- **Prof. Thomas Rosemann, MD**
  Institut für Hausarztmedizin, Universitätsspital Zürich, Zürich
- **Prof. Thomas Ruhstaller, MD**
  Brustzentrum Ostschweiz, St. Gallen

Prizes for outstanding achievements in cancer research and the fight against cancer

In 2019, the Swiss Cancer League awarded the Robert Wenner Prize to Andrea Alimonti. Through his research, Alimonti discovered how cancer cells age – and how this senescence can be utilized therapeutically. The Recognition Award was given to the Voltigo Palliative Care Team in Fribourg and to the Swiss Society of Psycho-Oncology. The Cancer Medal 2019 was awarded to former Federal Councillor Ruth Dreifuss. And the Swiss Bridge Award 2019 went to dual recipients, a research team in Germany and a research team in Switzerland – for further development of cellular immunotherapies.

From left to right: Gilbert Zulian, president of the Swiss Cancer League; Nancy Hynes, president of the Scientific Committee; Andrea Alimonti, winner of the Robert Wenner Prize; Franco Cavalli, scientific director of the Oncology Institute of Southern Switzerland, Bellinzona; Daniela de la Cruz, CEO of the Swiss Cancer League.

Robert Wenner Prize

The 2019 Robert Wenner Prize of 100 000 francs for researchers under the age of 45 was awarded to Andrea Alimonti. Italian-born Alimonti is a physician scientist, an oncologist who does the greater part of his work not at the patient's bedside but in the research laboratory. Alimonti discovered that under certain conditions, cancer cells (which were thought for a long time to stay forever young and immortal) age – and that this ageing, or senescence, can be triggered and increased in order to keep cancer development at bay. For these ground-breaking findings, the Swiss Cancer League awarded the prize to Alimonti, who is head of the molecular oncology group at the Institute of Oncology Research in Bellinzona.

Pro-senescence therapy

After receiving his MD degree from the University of Rome and completing medical training in oncology in Rome, Alimonti completed a postdoctoral fellowship in cancer biology at Memorial Sloan-Kettering Cancer Center in New York, where he studied the PTEN gene. PTEN is a tumour suppressor gene that stops cells from degenerating and proliferating uncontrollably. Reduced PTEN activity can be sufficient to trigger development of a tumour. But if the gene is completely absent, the cancer cells paradoxically become senescent – and stop multiplying, as Alimonti was the first to discover. The fact that the cancer cells can also be made senescent through pharmacological substances made the researchers hopeful: "We believe that a pro-senescence therapeutic approach to cancer is a very promising new strategy", wrote Alimonti and his colleagues in their paper in 2010.

When Alimonti returned to Switzerland in 2011 and started his own research group, his team made another discovery: The researchers noticed that a certain subset of immune cells can infiltrate the tumour – and oppose senescence of the cancer cells. These cells, called myeloid-derived suppressor cells, MDSCs, in addition secrete signal molecules that cause prostate cancer cells to proliferate even in the absence of male hormones, which they normally need for their growth.

Clinical trials have begun

In experiments with mice, Alimonti's team demonstrated how the harmful effect of these immune cells can be neutralized and tumour growth pushed back by means of pro-senescence therapy. Alimonti – in collaboration with a group at Royal Marsden Hospital in London – has now started two clinical trials to test whether pro-senescence therapy in combination with immunotherapy approaches can also help patients. As prostate cancer continues to be the second most common cause of cancer-related death in men in Switzerland, there is a great need for new treatments that improve the prospects of patients with prostate cancer.

Robert Wenner Prize

The Robert Wenner Prize to support outstanding young researchers in cancer research was established by bequest of Robert Wenner, a gynaecologist from Basel who died in 1979. The Swiss Cancer League has awarded the Robert Wenner Prize annually or every second year since 1983. The prize winners, all under the age of 45, receive 100 000 francs, with 80 000 francs earmarked for an ongoing research project and 20 000 francs as discretionary funds.

→ www.krebsliga.ch/rwp

Recognition Award and Cancer Medal

Member of the board Solange Peters (second from left) and Swiss Cancer League president Gilbert Zulian (fourth from left) present the Recognition Award to the Voltigo team: Daniel Betticher (Hôpital fribourgeois, left), Frédéric Fournier (Voltigo, third from left), Rose-Marie Rittener, and Corinne Uginet (Fribourg Cancer League, right).

Members of the board of the Swiss Cancer League Solange Peters (left) and Gilbert Zulian (second from left) present Judith Alder (third from left) and Ruedi Schweizer (right) the Recognition Award for the Swiss Society of Psycho-Oncology (SGPO).

The Recognition Award with 5000 francs prize money was given to two winners in 2019: to the Voltigo Palliative Care Team in Fribourg and to the Swiss Society of Psycho-Oncology.

High-quality service for support and palliative care of patients with cancer

In the Canton of Fribourg, persons with cancer and their families have been able to depend on Voltigo for ten years. During those years, the high-quality service developed into one of the main pillars of the cantonal network for support, rehabilitation, and palliative care of patients with cancer in Fribourg. Voltigo, a mobile palliative care team, eases the suffering of and cares for patients at the location of their choice, including at their home. With this, Voltigo makes an important contribution to the best possible quality of life for the patients.

Successful interdisciplinary model of biopsycho-social medicine

The Swiss Society of Psycho-Oncology (SGPO) was founded in 2003 and may be regarded as a successful interdisciplinary model of biopsychosocial medicine. The SGPO has institutionalized and professionalized psycho-oncological support and care of patients with cancer and their families – and in this way made a decisive contribution to the development, improvement, networking, and promotion of psychosocial support services.

The Recognition Award

With the Recognition Award the Swiss Cancer League honours persons or organizations for their committed work towards improving the situation of patients. The award goes in particular to innovative projects or inventions that aid persons with cancer.
→ www.krebsliga.ch/anerkennungspreis

Former Federal Councillor Ruth Dreifuss receives the Cancer Medal from Gilbert Zulian, president of the Swiss Cancer League.

Former Federal Councillor Ruth Dreifuss was awarded the Cancer Medal 2019. During her term in office and continuing thereafter, Dreifuss stood up for affordable medications and equal access in health care. With the award, the Swiss Cancer League also honoured her committed efforts towards prevention and screening and improvement of palliative care in Switzerland.

The Cancer Medal

The Cancer Medal was designed by iron sculptor Bernhard Luginbühl. It is awarded by the Swiss Cancer League every one to two years and recognizes outstanding services in the areas of prevention, early detection, and the fight against cancer and its consequences.
→ www.krebsliga.ch/krebsmedaille

Swiss Bridge Award

From left to right: Philipp Lücke, CEO of the Swiss Bridge Foundation, Lukas Bunse, prize winner, Gordon McVie, Chairman of the Jury, Denis Migliorini, prize winner, Jakob Passweg, president of the Swiss Bridge Foundation

The Swiss Bridge Award 2019 was shared by a research team in Germany and a research team in Switzerland. Presented with prize money of 250 000 francs each, the teams are pursuing approaches that aim at alleviating side effects and expanding the use of cellular immunotherapies.

"Living drugs"

New cellular immunotherapies cannot be compared with classical drugs. Drugs are clearly defined chemical substances. The new immunotherapies, however, are "living drugs", as they consist of patients' own immune cells to fight cancer at the cellular level. A patient's cells are genetically modified and multiplied in a laboratory. They are then transferred back into the patient's body, where thanks to genetic upgrading, the cells can act with increased strength against degenerated tumour cells. For some patients, cellular immunotherapies lead to spectacular successes; for other patients, these therapies fail. Therefore, more research is needed to further develop this new and promising treatment so that more patients can benefit from it.

Europe-wide competition

That is why for the 2019 Swiss Bridge Award, the Swiss Bridge Foundation called for research projects focusing on cellular immunotherapies. A total of 52 young researchers from all over Europe competed for the award. In a two-stage evaluation process, the jury of renowned experts chose two research projects in their final selection: The two project leaders, Denis Migliorini at the University Hospital of Geneva, and Lukas Bunse at the German Cancer Research Center in Heidelberg, Germany, each received 250 000 francs for implementation of their research projects.

Reduce neurotoxic side effects

Migliorini and his team want to reduce the considerable neurotoxic side effects of currently approved immunotherapies. Nerve damage occurs in 30 to 50% of patients, with the spectrum ranging from temporary neurological deficits (such as disorders when walking or speaking) to severe seizures and comatose states, which can be fatal in some cases. The researchers recently discovered that the target molecule of the genetically modified immune cells is found not only on the surface of cancer cells but also on the surface of what are called pericytes. Pericytes form the blood vessel walls in the brain and play a central role in the blood-brain barrier. In their research project, Migliorini and his team plan to equip the patients' immune cells with an additional gene that enables the genetically modified cells to distinguish between cancer cells and pericytes – and in this way only kill the cancer cells.

Immunotherapies for brain tumours

Up to now, cellular immunotherapies have mainly been successful in combating various types of blood cancer. Bunse and his team are trying to extend this treatment method to gliomas. Gliomas are tumours that infiltrate the brain – and due to their invasive growth, they cannot be cured today, even by surgical removal. In previous studies, the researchers identified promising target molecules in glioma cells. Bunse and his team are now planning to produce new genetically modified immune cells in their new research project and then to test – first with animal models and then with patients – whether these immune cells are able to prevent the growth of gliomas.

Swiss Bridge Award

The Swiss Bridge Foundation was founded in 1997 at the initiative of Thomas Hoepli, foundation board member, with the support of the Swiss Cancer League. The foundation's aim is to fund high-quality cancer research projects in Switzerland and other countries with support from private donors and foundations. Since its beginnings, the Swiss Bridge Foundation has awarded more than 25 million francs for research work in Belgium, Brazil, England, France, Germany, Israel, Italy, Norway, Spain, Sweden, and Switzerland.
→ www.krebsliga.ch/swissbridgeaward

Insights into research policy

Review of the programme to strengthen health services research in oncology and cancer care

Coming to an end this year is the funding programme through which the Swiss Cancer Research foundation – in the framework of the National Strategy Against Cancer – has strengthened oncological health services research. In this interview, the president of the panel of experts that has evaluated grant applications to the programme provides a preliminary assessment.

Marcel Zwahlen, you are the president of the panel of experts for the programme for strengthening health services research in oncology and cancer care. What is health services research exactly?
That is a difficult question, a controversial issue that often leads to debate by the panel. The broadest denominator is perhaps that health services research is concerned with studying health services in real life. In the world of practice – under real life conditions – a lot of things are less clear than in theory. For instance, in many cases guidelines or policies set down what the ideal treatment looks like. But in everyday clinical practice, there are always deviations from that treatment. Health services research can describe how often – and why – clinical practice deviates from recommended treatments.

Why is health services research important?
With our programme we do not fund research projects that are interested in a single molecule XY or that are strongly oriented towards the biomedical clinical picture. Instead, the focus is often on the patient experience: Cancer treatment is a complex matter; patients are usually seeing a number of different specialists, who often give too little thought to the fact that they are not the only actors in the treatment process – and who therefore do not always coordinate their work optimally. Research projects in health services research can reveal, for example, which interfaces function well and which not as well.

What is special about health services research?
Health services research is distinguished especially by its interdisciplinarity. In Switzerland it is a relatively new branch of research that often also uses different methods than those traditionally used in the life sciences. In our programme, there are research projects working with qualitative interviews or focus

"I hope that the systematic and continuous learning process will continue"

groups, a concept that originally comes from marketing. For this reason, the Swiss Cancer Research foundation, which funds the programme, brought together a panel of experts covering a wide range of disciplines – with specialists in medicine, the economy, statistics, nursing sciences, and other areas.

What is also special about health services research is that the findings are usually context specific. In theory, a medication is equally effective anywhere in the world, but in practice, local conditions play an important role. Because the health system in Switzerland is set up differently than, say, in Great Britain, the results of a study there are not directly transferable to our conditions here.

The research programme will soon come to an end. Are you satisfied with it?

We have not yet conducted a thorough review; that task still lies ahead. At the conclusion we will hold a meeting together with National Research Programme (NRP) 74. NRP 74 is the Swiss National Science Foundation's programme "Smarter Health Care", which focuses mainly on optimal care of patients with chronic conditions. Actually, the meeting was originally planned to be held in April. But due to the coronavirus, it has been rescheduled for the end of October. The goals of the meeting are, for one, scientific exchange: It will be an opportunity for the persons involved in the different research projects to get together and network. For another, the aim is to draft scenarios showing what – after completion of the two research programmes – the future of health services research in Switzerland could look like.

What could it look like?

I hope that the systematic and continuous learning process that our research programme has initiated will continue. For that to happen, however, better organized data will be needed in the future. For instance, it is very difficult for researchers to obtain access to anonymized claims and billing data from health insurers. That set of data should be made more readily accessible – following clear regulations, naturally. After all, here in Switzerland we are all required to obtain health insurance. The data therefore do not belong to the companies but to society.

Research-related activities in the National Strategy Against Cancer

The National Strategy Against Cancer (NSC) brings together, in 28 projects, more than 50 actors who are jointly planning and implementing activities at the national level. Although the NSC is not a research-specific initiative, research has an important place in it. The following describes advances in three selected research-related projects and takes a look at the period after 2020 – and thus after conclusion of the NSC.

Reimbursement by compulsory basic insurance for therapies used in clinical trials

There were increasing reports from oncologists that health insurers refused to cover a treatment if it was prescribed within a clinical trial. The insurers based their refusal on the argument that a medical treatment in a clinical trial is not a mandatory benefit to be reimbursed by the insurance but is instead "research". This argument is highly problematic, as it means that for example in trials on optimal use, drugs on the list of pharmaceutical specialties, which are standard treatments, are not reimbursed by health insurers – and this pushes up the cost of clinical trials unreasonably.

The insurers based their argument on Article 49 of the Federal Act on Health Insurance, which provides that reimbursements may not contain cost components for public services obligations, to which research belongs. The Swiss Group for Clinical Cancer Research (SAKK) brought this problem to the attention of the NSC and the Swiss Cancer Research foundation (SCR), and it was then decided to intervene in this matter at the federal level. As a discussion basis, an expert was commissioned to write a legal opinion[1]. The legal opinion provides a firm conclusion: "If a medical service is recognized by the Federal Act on Health Insurance as a mandatory benefit to be paid by the insurers, it retains the character of a mandatory benefit also when it is prescribed in the framework of a clinical trial that is conducted in the context of a hospital. The insurer's refusal to pay the mandatory benefit because it was prescribed in a research context is against the Federal Health Insurance Act, and is therefore contrary to federal law."

On this basis, representatives of SAKK, SCR, and the NSC entered into discussion with the Health and Accident Insurance Directorate of the Federal Office of Public Health. Fortunately, the results of the legal opinion were not called into question by the FOPH. On the contrary, the representatives of the FOPH confirmed that a therapy in the framework of the list of pharmaceutical specialties (as a mandatory benefit to be paid by insurers) must be reimbursed in every case, independently of whether it is prescribed in a clinical trial or not. To be able to respond to any deviations from this by individual insurers, the SAKK asks all health care providers to document and report such cases to SAKK (please report to: sabine.bucher@sakk.ch).

Strengthening health services research in Switzerland

Health services research is still a young field of research, especially in Switzerland. Other countries have had professional societies for decades as well as state-funded institutions[2], but there has been nothing comparable in Switzerland up to now. For this reason, the Swiss Academy of Medical Sciences (SAMS) undertook first efforts to strengthen health services research in 2012 and launched a research funding programme,

Michael Röthlisberger, PhD
Co-director of the National Strategy Against Cancer

providing 4.4 million francs in funding to 46 research projects[3]. Subsequent to this, starting in 2017, research project funding has been ensured by the SCR, with the Health Services Research in Oncology and Cancer Care programme, and by the Swiss National Science Foundation, with its National Research Programme "Smarter Health Care" (NRP 74). Nevertheless, not much has been done in the area of institutionalizing cooperation among researchers. This lack of networking can, for example, have effects on the quality of the research proposals. In addition, institutionalized networks would be important for sustainable establishment of this branch of research in Switzerland. Therefore, the SCR in cooperation with the NSC and NRP 74 held a conference on the future of health services research in Switzerland (hsrconference.ch). The primary goal of the conference was to sustainably strengthen and interconnect the health services research community. However, to firmly anchor health services research in Switzerland, there is also a need in the future for measures for targeted research funding and for institutionalization.

Networking the clinical oncology registries in Switzerland

The Swiss Personalized Health Network (SPHN) was set up in 2017 and is now an important and central structure in the Swiss health care system. The aim is to interconnect in a decentralized fashion interoperable health data – that is, data that can be linked and evaluated – from the different actors (in a first step, university hospitals, and later on, further producers of data), so that the data is utilizable for research. The largest oncology-related project, which is being implemented in the framework of the SPHN Initiative, is called Swiss Personalized Oncology (SPO). The goal is nationwide interoperability of the clinical and laboratory-based data on patients with cancer.

Another large project in this area (but outside the SPHN Initiative) is the Swiss Real World Data (RWD) Registry of the Swiss Group for Clinical Cancer Research (SAKK). This is a centralized data warehouse that stores data from the SAKK centres in a structured and standardized form and links it closely with the Onconavigator project. The Onconavigator is planned to generate treatment recommendations based on molecular patient data and using artificial intelligence methods. Further clinical registries in Switzerland are, for example, the Alpine Tumor Immunology Registry (Alpine TIR: a registry recording immune-oncological treatments in Swiss and Austrian hospitals), the Swiss Urology Registry, and the Swiss Breast Center Database.

To obtain the greatest benefit from these registry projects, it is absolutely essential to network them with each other and to make the data combinable. Here, great progress has already been made, for instance in the compatibility of the data in the SPO and RWD and through technical integration of the Alpine TIR in the RWD project. To discuss further possibilities and challenges, the NSC conducted a mini-symposium on clinical cancer registries at the semi-annual SAKK meeting, to bring the actors together and to initiate further cooperation*. In view of the further development of the health care system – and especially of the highly developed cancer area – and looking towards precision medicine based on large quantities of data, the automatic evaluation and networking of these data collections will be very important.

* www.nsk-krebsstrategie.ch/projekte/klinische-register

Outlook

The NSC ends in December 2020. However, the tasks that the NSC took over remain: It will still be important to support and coordinate the actors in the projects at the national level – and to combine their voices vis-à-vis political and administrative authorities. As the successor to the NSC, Oncosuisse – the group of currently seven large cancer organizations in Switzerland (www.oncosuisse.ch) – will take over the tasks. This accords with the wishes of the actors in the field of cancer in Switzerland, as a stakeholder survey conducted in 2019/2020 identified*. Along the same lines as the distribution of the NSC projects, Oncosuisse, too, will in future promote activities in the following areas: Prevention & Screening, Treatment & Aftercare, Data, Registries & Quality, and Research. The plan is to bring together a broader group of actors than previously and to strengthen their common voice vis-à-vis political and administrative authorities regarding both health services issues and research policy issues.

Michael Röthlisberger, PhD
Michael Röthlisberger completed a PhD in basic cancer research. He then headed the research department of the Swiss Academy of Medical Sciences and co-headed the NSC. Starting 2021, Röthlisberger will take over the management of Oncosuisse.
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* www.nsk-krebsstrategie.ch/projekte/begleitaktivitaet-aufbau-cancer-community

Six months since enactment of the Cancer Registration Act: An initial review of the Childhood Cancer Registry

The Cancer Registration Act (Krebsregistrierungsgesetz [KRG]) came into force on 1 January 2020.

What does that mean, actually?
There is now a new reporting obligation for all cancer cases in Switzerland, so that there will be uniform and complete registration in cancer registries.

Wasn't that the case prior to the new law coming into effect?
For children and adolescents, data on cancer cases has been collected since 1976 in the Swiss Childhood Cancer Registry (SCCR). At the start of this year, the SCCR was transferred to a national registry, the Childhood Cancer Registry. Also, most of the cantons have set up cantonal cancer registries over the past decades, but previously, reporting was voluntary.

What changes with the Cancer Registration Act?
Now,
- there is an obligation to report, and cancer cases are registered nationwide by means of a clearly defined process
- it is uniformly established what cancers and precancerous conditions are registered
- the data set collected across Switzerland is uniform and standardized
- cooperation between the parties involved (cancer registries, persons with a reporting obligation, Federal Statistical Office, and Federal Office of Public Health) is clearly defined.

Why is that important?
From a health policy perspective, it is important to know, for example, how many people are diagnosed with various cancers; how many people are currently being treated in Switzerland for cancer; what the survival rates are for different cancers; what comorbidities foster the development of cancer or affect survival. To answer these questions, we are dependent upon long-year, complete, uniform, and valid data from the whole country. That is exactly what the Cancer Registration Act provides.

Cancer registration makes it possible to answer questions that are relevant for health policy in a timely manner. And the data – in anonymized form – can also be used in research. A broad range of research approaches (basic research, clinical research, and epidemiologic research) leads to continuous improvement of prevention measures, screening methods, and effective but safe therapies, with the aim to prevent cancers when possible or, if they occur, to treat them successfully with as few side effects and late effects as possible.

If cancer registration is so important, do all patients agree with registration?
The Cancer Registration Act protects the rights of patients and defines the process of how they are informed: The medical specialist that makes the diagnosis informs the patient both orally and through providing a patient information brochure. Patients with cancer and their legal representatives have a right to withhold consent to registration. As in the past, withholding of consent is rare with the Childhood Cancer Registry. Most patients are aware that today's good

Verena Pfeiffer, PhD, and Prof. Claudia Kuehni, MD
Co-heads of the Childhood Cancer Registry in Bern

prognoses are thanks to previous patients who participated in clinical trials and allowed their cancer-related data to be recorded in the registries. For this reason, they are glad to make their own contribution to increasing knowledge.

With the new law in effect, what has changed for the Childhood Cancer Registry?

Up to 2019 the Swiss Childhood Cancer Registry (SCCR) was conducted as a research project under the Human Research Act. The data were primarily reported by the nine paediatric oncology clinics in Switzerland. Although all cancers were recorded for children under the age of 16 years, there were gaps in the data for 16- to 20-year-olds because patients in this age group are no longer treated in paediatric oncology but rather at a large number of different clinics. The SCCR made the data accessible in a timely manner and utilized it intensively to identify the causes of childhood cancers, to optimize therapies, and to evaluate quality of life and possible late effects in childhood cancer survivors. Here, cancer registration as well as research in the SCCR was funded by third parties.

Now, from the start of 2020 onwards, the Childhood Cancer Registry is funded by the federal government. It pays for the collection and registration of data on children and adolescents with cancer. All persons with a reporting obligation (physicians, laboratories, hospitals, and other private or public institutions in the health care system that are involved in the diagnosis or treatment of childhood cancers) must report the data on children and adolescents up to age 19, as defined by the Cancer Registration Act, to the Childhood Cancer Registry. The Childhood Cancer Registry completes the data by comparing it with the hospitals' medical statistics and the Federal Statistical Office's causes of death statistics. Who must report what data to whom, and what happens with the data, is regulated in detail in the Cancer Registration Act and the associated ordinance. Detailed information on the data collected and information for patients can be found on the website of the Childhood Cancer Registry (kinderkrebsregister.ch). The website also provides a contact form for further questions from children and adolescents with cancer, their parents, and persons with a reporting obligation.

What is currently the greatest challenge?

The Childhood Cancer Registry receives a lot of inquiries from researchers, physicians, and health authorities. They may want to clarify the feasibility of a clinical trial or find out how many diagnoses were made of a certain type of cancer in a particular time period or whether there are regional clusters of cancer diagnoses, for instance. This shows the great interest in the registered data for research purposes or to make valid statements in the area of health policy. The ordinance associated with the Cancer Registration Act has provisions regulating the sharing of cancer registry data. In general, requested data may only be shared in anonymized form, so that no individuals can be identified. Concerning use of the data for research purposes, the ordinance goes even a bit further: Here, data are only considered anonymized if 20 data sets have been aggregated. The reasoning behind this provision was to prevent the theoretical danger that with

very rare cancers, individuals could be identifiable despite data anonymization. In practice, however, this means that only evaluated tables may be made available to researchers and no anonymized data sets on individual patients. For example, the ordinance requires aggregation for research purposes also where the personal characteristics do not permit identification of any individuals. This makes it impossible to carry out state-of-the-art analyses with modern statistical methods. Especially for rare cancers, there is still very little known about the causes or about the course of the disease over the long term. These data are therefore essential for research. The fact that we are now collecting standardized data since January 2020 but can utilize it for research only with great restrictions seems absurd and does not serve patients with cancer. We therefore hope that with evaluation of the Cancer Registration Act and its ordinance by the responsible federal authorities, the legal provisions will be adapted quickly to achieve a sensible relation between data protection and research, so that the collected information can be used – as before – to increase medical knowledge.

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The new Cancer Registration Act:

On the way to optimized data bases and their use

Due to the short period of time since the Cancer Registration Act (KRG) came into force on 1 January 2020, the new framework has not yet had an effect on the epidemiologic data that are available for monitoring, reports, and research.

For this reason, these data still reflect the strengths and weaknesses of the old system: One of the strengths is that almost all diagnosed cases are recorded through the registration. This works well mainly due to the voluntary cooperation of the physicians in the regional networks that the cantonal cancer registries actively developed. Another strength is the quality of a large part of the registered data.

Legal uncertainty adjusted

A weakness of the old system is that the legal uncertainty affected all parties (patients, reporting office, cancer registry, authorities): There were no specific legal regulations at either the federal or cantonal level (with the exception of FR, LU, SO, TI, ZG, and ZH). Probably as a side effect of the political discussions on the KRG, some hospitals and pathology institutes even refused to participate in the registration – an untenable situation. Furthermore, restrictions on access to the data in the communal and cantonal register of residents varied greatly. This access is important, for one, in order to clarify responsibility depending on the place of residence of the patient (and thus in order to avoid duplication) and, for another, in order to annually update the vital status (living or deceased). The last weakness mentioned here is the heterogeneity of the coding, which is problematic for nationwide evaluation. For this reason, the Association of Swiss Cancer Registries (VSKR) and Oncosuisse founded the National Institute for Cancer Epidemiology and Registration (NICER) in May 2007 as an independent foundation to coordinate at the national level the harmonization, data processing, quality assurance, and use of the data collected by the cantonal cancer registries. NICER was successful in all of these areas but could not eliminate the basic problems.

The new KRG now provides for use of data that is registered uniformly nationwide. This database is defined and administered by the newly created National Agency for Cancer Registration (NACR), the tasks of which have been assigned to NICER. The law sets out the rights and obligations of all of the parties mentioned above and ensures that both clinical information and also the necessary official information in the register of residents and at the Federal Statistical Office can come together in the cancer registry. This has been made much easier through the new allowed use of the AHV (social security) number as a unique personal identifier. Through this, many of the weaknesses of the old system mentioned above are eliminated. Not least, the new KRG also achieves full coverage of the Swiss population. A strong intervention set out by the

Ulrich Wagner, PhD, and Matthias Lorez, PhD
National Institute for Cancer Epidemiology and Registration (NICER) in Zurich

new KRG is that physicians have an active duty to report; this therefore supersedes the active acquisition of data by the cancer registries. The primary reason for this is to protect sensitive personal data, so that registries can only view information as per the provisions in the law. The effects of these new regulations on completeness and quality of the data will be carefully examined by the NACR.

Uniform and expanded data

The data, which will be available for monitoring, health reporting, and (health services) research, have been expanded to include some important information, such as stage information for lymphomas, leukaemia, and gynaecological tumours; prognosis factors for breast, prostate, colon, testicular, head and neck cancers, and melanoma; prognostic treatment-related factors; somewhat more in-depth information on the initial course of treatment than in the past; and information on recurrence. For breast, prostate, and colon cancer only, there will also be information available on previous diseases and comorbidities; this limitation does not hold for cancers in children and adolescents. Childhood cancers will continue to be registered in far greater detail than cancers in adults. The new KRG thus provides for substantial improvements of the data on cancer at the population level. However, fully recorded and quality-tested data will be available at the earliest in 2023.

On the other hand, the new KRG presents us with new challenges. It upholds data protection – and therefore sets out a very narrow framework for data disclosure and reporting. For example, the new regulations only allow NICER/NACR to publish incidence data in a reduced form. Moreover, the available data, for example the data in our popular and much visited Stat-Atlas on our website* only go up to incidence year 2015. For anonymization reasons, newer data can no longer be published in this form, as the case numbers are often too small. With small numbers, even though identification of individual persons is in fact hardly possible, it cannot be excluded theoretically. And what holds for the federal level also holds (and to an even greater extent) for the cantons, mainly for the cantons with a small population, because the number of cases is even lower. This jeopardizes transparency, openness, and traceability as the bases for policy decisions and for voter empowerment. It is certainly desirable and necessary to protect sensitive disease data well from misuse. However, this should not lead to excessive restrictions on what is aimed for: informing the public on the cancer situation in Switzerland.

Enable the use of collected data

The KRG aims specially to strengthen patient rights. This is achieved through the right to information, the right to withhold consent to registration, and the right of access that goes further than the right to inspect in the data protection law up to now. Data protection in the storing and processing of data is also ensured. But in addition to facilitating regulations, sufficient trust must be placed in the data-processing public institutions and they must be adequately equipped in a way that a protected data processing and publication process at the individual case level is possible – also for researchers. The body of individual cases then forms the basis for epidemiologic findings that can bring the benefit that is anchored in the law. Data protection in publication can also be ensured for protection level 3 data (patient data), as other federal departments, such as the Federal Statistical Office, show.

* www.nkrs.ch/NicerReportFiles2018/EN/report/atlas.html

Together with our partners, we are not limiting ourselves to identifying and describing problems that arise with the coming into force of the KRG – that is, problems only arising now. Rather, we are generating solution options that then feed into further development and interpretation of the legal bases. The solution options take aim at the data structure, the coding guidelines, the information, and also the rules in the ordinance. Regarding disclosure and publication of data, there is no need to immediately add, to the three patient rights mentioned above, a fourth right to use the data made available (that would only be possible through law). Nonetheless, the following is clear: Optimal use of the collected data under reasonable consideration of data protection is an ethical and economic imperative! The leverage necessary to meet this demand exists within the law and the ordinance.

Ulrich Wagner, PhD

Ulrich Wagner studied law and public administration at the University of Konstanz and then continued his studies at the University of St. Gallen and University of Bielefeld, where he completed a doctorate in Public Health in the area of health economics and management. Wagner is associated professor at the UNESCO chair at the University of Bucharest and visiting professor at the University of Applied Sciences and Arts in Northwestern Switzerland (FHNW). He had leadership positions at teaching and research institutions and was head of population-based national health statistics at the Swiss Federal Statistical Office. Today, as director of the NICER foundation he also heads the newly created National Agency for Cancer Registration (NACR).

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Matthias Lorez, PhD

Matthias Lorez completed a PhD in neuroscience at the University of Zurich and then worked in the pharmaceutical industry as head of a laboratory in safety pharmacology. Lorez completed a postgraduate programme in applied statistics. Today, as scientific collaborator and senior biostatistician at the foundation National Institute for Cancer Epidemiology and Registration (NICER) he is responsible for data quality and health monitoring, as well as the definition and further development of cancer data structure conforming to the Cancer Registration Act.

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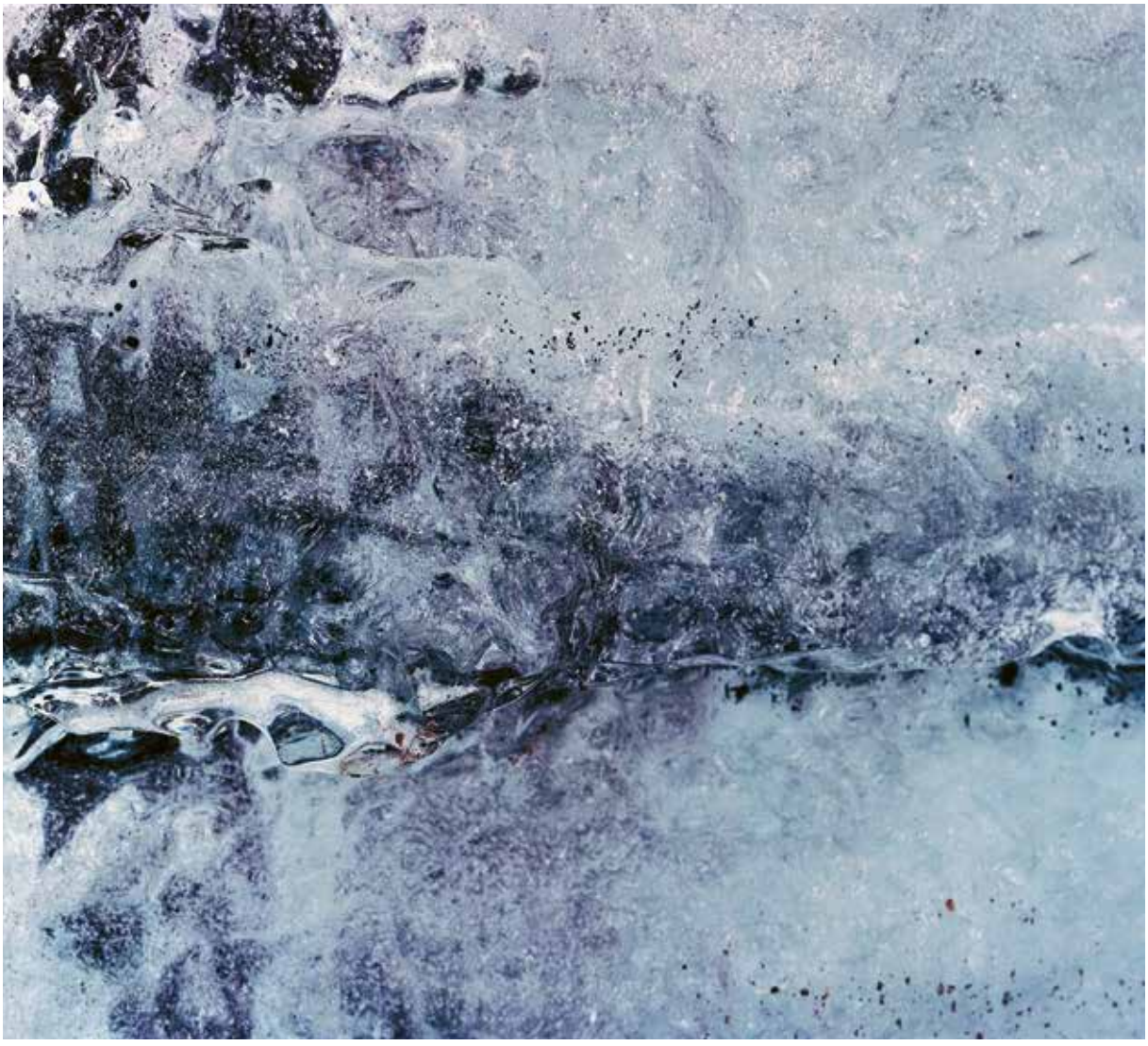

Research funding by the cantonal and regional cancer leagues

Overview of the many-sided efforts

The Cancer League is organized as a federation and unites, in addition to the national umbrella organization, the Swiss Cancer League, 18 cantonal and regional leagues that also support research – and in this way facilitate medical advances in their canton.

In 2019, eight cantonal and regional cancer leagues (CCL) provided almost 2.2 million francs' funding to a total of 32 different cancer research projects. Compared to the previous year, the CCL thus supported 16 fewer research projects (see table). As in previous years, the largest sum was invested by the Ligue genevoise contre le cancer, followed by the cancer leagues of Basel and Zurich.

The CCL handle evaluation of research proposals differently. Some leagues, such as the Basel Cancer League and the Bern Cancer League, have their own scientific committees. At other leagues, the research grant applications are rated by their board members, or they delegate the task to the Scientific Committee, which also evaluates the research proposals submitted to the Swiss Cancer League and its partner organization, the Swiss Cancer Research foundation.

Although the evaluation procedures differ from league to league, all of the CCL follow a common goal: to fund the best cancer research projects and institutions in their region. With this, the CCL pave the way for progress in cancer treatment – and make it possible not only for patients today but also for patients in the future to benefit from the findings of the funded research projects.

Table

Research funding by the cantonal and regional cancer leagues in overview

	Number of projects and institutions supported		Amount granted in kCHF	
Cancer League	2018	2019	2018	2019
Aargau	2	2	90	90
Basel	16	9	711	585
Bern	2	2	100	142
Central Switzerland	1	1	30	25
Geneva	11	8	1 496	866
Grisons	1	2	15	25
Ticino	n. s.	3	n. s.	190
Thurgau	3	0	50	0
Vaud	3	n. s.	30	n. s.
Zurich	9	5	419	251
Total	**48**	**32**	**2 941**	**2 174**

n. s. = not specified

List of funded research projects and institutions

Listed below are the funding contributions that were paid out in 2019.

Aargau Cancer League

Bodis Stephan | Clinical cancer research on hyperthermia
Radio-Onkologie-Zentrum KSA-KSB, Kantonsspital Aarau, Aarau
CHF 50 000.– | Duration: 1. 3. 2019 – 1. 3. 2020

Pica Alessia | High-resolution ophthalmic magnetic resonance imaging at 1.5T: towards a non-invasive method to assist proton therapy planning for uveal melanoma
Paul Scherrer Institut (PSI), Villigen
CHF 40 000.– | Duration: 16. 1. 2017 – 15. 1. 2020

Basel Cancer League

Aceto Nicola | Genome-wide CRISPR screen in vivo to identify genes involved in the generation of circulating tumour cell clusters and organ-specific metastasis
Departement Biomedizin, Universität Basel, Basel
CHF 60 000.– | Duration: 1. 10. 2019 – 31. 3. 2021

Bentires-Alj Mohamed | Effects of glucocorticoids in metastatic breast cancer
Departement Biomedizin, Universitätsspital Basel, Basel
CHF 70 000.– | Duration: 1. 7. 2019 – 30. 6. 2021

De Libero Gennaro | MR1T cell recognition of solid tumours
Departement Biomedizin, Universität Basel, Basel
CHF 65 000.– | Duration: 1. 9. 2019 – 30. 8. 2021

Kurzeder Christian | Effect of digoxin on clusters of circulating tumour cells (CTCs) in breast cancer patients
Gynäkologische Onkologie, Universitätsspital Basel, Basel
CHF 51 000.– | Duration: 1. 6. 2019 – 30. 5. 2021

Matter Matthias | Molecular analysis of hepatocellular adenomas with atypical features
Institut für Pathologie, Universitätsspital Basel, Basel
CHF 12 280.– | Duration: 1. 10. 2019 – 30. 9. 2020

Meyer Sara Christina | Characterization of resistance to tyrosine kinase inhibition as a basis for novel therapeutic approaches in myeloid malignancies
Departement Biomedizin, Universitätsspital Basel, Basel
CHF 91 880.– | Duration: 1. 7. 2019 – 30. 6. 2020

Pfister Marc | Observational pilot study to evaluate blood and urine kidney injury markers with the goal to facilitate early detection of renal adverse drug events in paediatric cancer patients treated with nephrotoxic chemotherapy
Pädiatrische Pharmakologie, Universitäts-Kinderspital beider Basel, Basel
CHF 80 000.– | Duration: 2. 12. 2019 – 1. 12. 2021

Rentsch Cyrill | SAKK 09/18: Extended pelvic lymph node dissection vs. no pelvic lymph node dissection at radical prostatectomy for intermediate- and high-risk prostate cancer: An international, multicenter, randomized phase III trial
Urologische Klinik, Universitätsspital Basel, Basel
CHF 75 000.– | Duration: 1. 6. 2019 – 30. 5. 2022

Zippelius Alfred | Modelling T cell dysfunction to explore novel targets for cancer immunotherapy
Departement Biomedizin, Universitätsspital Basel, Basel
CHF 80 000.– | Duration: 1. 5. 2019 – 30. 4. 2020

Bern Cancer League

Arambasic Miroslav | Whole-exome sequencing analysis of familial lymphoma cases in Switzerland
Universitätsklinik für medizinische Onkologie, Inselspital Bern, Bern
CHF 93 115.– | Duration: 1. 5. 2019 – 31. 10. 2020

Daskalakis Michael | Translational study on viral mimicry: Marker for prediction of epigenetic treatment response or prognosis in patients with AML or MDS
Universitätsklinik für Hämatologie und Hämatologisches Zentrallabor, Inselspital Bern, Bern
CHF 49 250.– | Duration: 1. 9. 2019 – 31. 8. 2020

Central Switzerland Cancer League

Roser Katharina | Cancer in adolescents and young adults: latest information
Departement für Gesundheitswissenschaften und Medizin, Universität Luzern, Luzern
CHF 25 000.– | Duration: 7. 11. 2019 – 1. 1. 2022

Geneva Cancer League

Bouchardy Christine | Importance of oncological family history in the occurrence and evolution of colorectal cancer: a population study in the canton of Vaud
Registre genevois des tumeurs, Université de Genève, Genève
CHF 100 000.– | Duration: 1. 1. 2019 – 31. 12. 2019

Cohen Marie | Targeted delivery of the PEDF gene into ovarian cancer cells: a promising therapeutic approach in ovarian cancer
Centre de recherche translationnelle en onco-hématologie et maternité, Hôpitaux universitaires de Genève, Genève
CHF 124 309.– | Duration: 1. 1. 2018 – 31. 12. 2020

Hugues Stéphanie | Impact of the tumour microenvironment on lymphatic vessel features and immunomodulatory functions
Département de pathologie et d'immunologie, Université de Genève, Genève
CHF 100 675.– | Duration: 1. 1. 2019 – 31. 12. 2021

Labidi-Gali Intidhar | Impact of ovariectomy in patients with germline BRCA1 mutated breast cancer
Département d'oncologie et division de pathologie clinique, Hôpitaux universitaires de Genève, Genève
CHF 93 147.– | Duration: 1. 1. 2018 – 31. 12. 2020

Merat Rastine | RNA-binding protein mediated post-transcriptional modification of genetic expression: a strategy to overcome tumour plasticity and the heterogeneous melanoma cell response to targeted therapies
Division de dermatologie, unité d'oncodermatologie, Hôpitaux universitaires de Genève, Genève
CHF 142 885.– | Duration: 1. 1. 2018 – 31. 12. 2019

Senn Pascal | Prevention of cisplatin-induced deafness in an animal model
Département des neurosciences cliniques, Université de Genève, Genève
CHF 95 545.– | Duration: 1. 1. 2018 – 31. 12. 2020

Sobolewski Cyril | Role of TIA1 and stress granules in hepatocellular carcinoma
Département de physiologie et métabolisme, Université de Genève, Genève
CHF 92 284.– | Duration: 1. 1. 2018 – 31. 12. 2019

Walter Martin A. | A nanohydrogel polymer serving as a platform for optimal delivery of an advanced prostate cancer drug
Département de radiologie et informatique médicale, Hôpitaux universitaires de Genève, Genève
CHF 116 713.– | Duration: 1. 1. 2019 – 31. 12. 2020

Grisons Cancer League

Hohloch Karin | Prospective multicentre study on the use of complementary medicine during cancer treatment
Onkologie/Hämatologie, Kantonsspital Graubünden, Chur
CHF 20 000.– | Duration: 1. 1. 2020 – 31. 12. 2021

Metaxas Yannis | Outcome of pembrolizumab as palliative immunotherapy in malignant mesothelioma: a retrospective analysis in a real-world population
Onkologie/Hämatologie, Kantonsspital Graubünden, Chur
CHF 5000.– | Duration: 1. 8. 2016 – 28. 2. 2017

Ticino Cancer League (Fondazione ticinese ricerca sul cancro)

Alimonti Andrea | The role of the microbiota in driving castration-resistant prostate cancer
Institute of Oncology Research, Università della Svizzera Italiana, Bellinzona
CHF 60 000.– | Duration: 1. 1. 2019 – 31. 12. 2019

Bertoni Francesco | Finding a way to by-pass the resistance to PI3K inhibitors in marginal zone lymphomas
Institute of Oncology Research, Università della Svizzera Italiana, Bellinzona
CHF 60 000.– | Duration: 1. 8. 2019 – 31. 7. 2020

Catapano Carlo | Preclinical modelling of cancer stem cells directed therapies
Institute of Oncology Research, Università della Svizzera Italiana, Bellinzona
CHF 70 000.– | Duration: 1. 4. 2019 – 31. 3. 2020

Zurich Cancer League

Britschgi Christian | A high-throughput kinase modulator screen to identify novel therapeutic options and cellular in clear cell sarcoma
Medizinische Onkologie, Universitätsspital Zürich, Zürich
CHF 70 140.– | Duration: 1. 1. 2019 – 31. 12. 2019

Freiberger-Rupp Sandra, Morand Grégoire B., Rupp Niels J. | Investigation of novel marker combinations to predict response to immunotherapy in mucosal melanoma
Institut für Pathologie und Molekularpathologie, Universitätsspital Zürich, Zürich
CHF 39 554.– | Duration: 1. 1. 2019 – 31. 12. 2019

Jae-Hwi Jang | Targeting lung cancer by CD26/DPP4 inhibition in combination with anti-PD-L1 antibody
Klinik für Thoraxchirurgie, Universitätsspital Zürich, Zürich
CHF 71 600.– | Duration: 1. 1. 2019 – 31. 12. 2019

Kahraman Abdullah | Genome-wide identification of drugable non-coding cancer driver mutations via aberrant alternative splicing in prostate and pan-cancer
Institut für Pathologie und Molekularpathologie, Universitätsspital Zürich, Zürich
CHF 59 821.– | Duration: 1. 1. 2019 – 31. 12. 2019

Morand Grégoire B., Rupp Niels J. | Investigation of the prognostic importance of tumour hypoxia in oral squamous cell carcinoma by immunohistochemical and metabolic molecular tumour imaging
Klinik für Ohren-, Nasen-, Halskrankheiten, Universitätsspital Zürich, Zürich
CHF 10 000.– | Duration: 1. 1. 2019 – 31. 12. 2019

Heterogeneity of tumour cells: What is it, and why does it make successful treatment of cancers difficult?

We know that cancer is a common disease – approximately one in three people will have cancer in their lifetime. It still remains a feared diagnosis, and when people are diagnosed, they are deeply shocked: We do not normally expect that it will happen to us, here and right now. Thoughts crowd the mind, along with memories of situations and others diagnosed with cancer, and a feverish search for information begins. On the Internet there are reports of new drugs and treatments that promise miraculous cures. However, besides the question of availability, it must be carefully examined for which cancer the different treatment approaches can be implemented with a promise of success.

That is because cancers are very heterogeneous. Consultations with physicians can provide a framework, but in the end, reliable predictions are often not possible. Why is this so? Why, despite precision medicine and exact genetic analyses, can we not just as precisely predict the course of the cancer and how it should best be treated?

A partial answer is that we still lack medications for targeted treatment of all specific genetic errors that a cancer cell can show. Medications of that kind with targeted effects are used especially successfully in chronic myeloid leukaemia: They have simply revolutionized the treatment of these patients[1]. However, the special feature of this subtype of leukaemia is that it is driven mainly by a single genetic mutation. When tumours become more complex genetically, it becomes more difficult to treat them[2].

Prof. Claudia Lengerke, MD
Attending physician at the Department of Hematology, University Hospital Basel, and professor of hematology and stem cell research at the University of Basel

Accumulation of genetic alterations

Another important part of the answer, in my opinion, is heterogeneity. What does that mean? It is not only about heterogeneity regarding the affected organs or the cause of the cancer. It is certainly easy to see that colon cancer and leukaemia are very different diseases, for example. But it is also about heterogeneity within the same type of cancer.

In the vast majority of cases, cancer is caused by the accumulation of genetic alterations, which are present in the cells long before cancer develops (often years before). A distinction must be made between mutations that occur at the beginning of this process and mutations that additionally occur later on. Whereas the first mutations are present in all tumour cells, the later mutations are found in only a part of the tumour cells: That is why tumours are composed of several clones, which are more or less genetically related and which, due to their different genetic make-up, behave heterogeneously. Some clones like to settle in the liver, lungs, or blood marrow; others survive cancer therapies better. Depending on from which part of a tumour and thus from which clones a sample is taken for genetic analysis, the findings will differ.

Science is aware of this heterogeneity. Through complicated investigations on the frequency of genetic alterations in certain tumours and their significance for the functionality of cancer cells, researchers can (at least in part) determine which genetic errors are most likely driver mutations that exist in all cancer cells of the patient and drive the cancer. Treatments must address this type of mutations in order to sustainably fight the cancer. Despite this scientific advancement, however, it is often difficult to select an appropriate treatment, because in many cases no specific therapies exist and because in the same patient there can also be several genetic mutations that are cancer drivers. It therefore often remains unclear in what combination and in what time sequence the cancer should be treated.

Immature cancer stem cells

And as if all this were not complex enough, there is also another kind of heterogeneity that further limits our successes in treating cancer. As we and other research teams have found in recent years, there are also major differences between cancer cells with identical genetic make-up that are related to the maturity of the tumour cells. Research studies on leukaemia but also on solid tumours have shown that small, especially immature subpopulations of cells within a tumour – called cancer stem cells – are solely responsible for the occurrence of cancers, whereas the many other tumour cells play hardly any role at all.

These cancer stem cells have, for example, a special affinity for protected areas in the body – such as niches in the bone marrow – and thus survive cancer therapies much better than more mature cancer cells with the same genetics[3,4]. These protective environments weaken the effectiveness of not only classic

chemotherapies but also targeted molecular therapies[5]. As we demonstrated recently in a paper published in Nature[4], cancer stem cells in niches even survive attacks from the body's own immune system better and are also better armed against immunotherapies. These connections also explain, among other things, why cancers sometimes recur after apparently successful treatment.

To be able to treat cancer more effectively, we have to accept these complexities and with this awareness face the resulting challenges. Researchers and medical experts, regardless of their location, should pool their expertise and strengths and exchange their knowledge for a better understanding of these multiple facets of the heterogeneity in cancer and to be able to counter them with the right answers. Targeted therapies for driver mutations, immunotherapies, and treatments for cancer stem cells (that, for example, eliminate the protective environmental influences and/or make them visible again to the immune system) in combination and applied at the right points in time[6] show promise for the greatest successes, I believe. They are thus the way into the future.

Prof. Claudia Lengerke, MD
Claudia Lengerke studied medicine at the University of Tübingen (Germany), where she also completed her training as a specialist in internal medicine, haematology, and medical oncology. She was a postdoc research fellow at Harvard Medical School in Boston (USA), working on pluripotent stem cells; she then founded her own research group in Tübingen. In 2013 she was appointed professor at the University of Basel and University Hospital Basel. In Basel she conducts research on the emergence and therapy resistance of tumours, with the aim to develop better treatment concepts for patients. As vice dean of the Faculty of Medicine at the University of Basel, Lengerke also promotes the education and training of young scientists. In May 2020, Lengerke accepted an appointment as professor at the University of Tübingen and medical director of the Tübingen University Clinic. She will continue as a professor at the University of Basel up to 2021, however.
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Selected results

Project
The ATP-gated ionotropic P2X7 receptor as a possible target to enhance the efficacy of cancer immunotherapy
Istituto di Ricerca in Biomedicina, Bellinzona
CHF 235 600.– | Duration: 1.7.2017 – 31.10.2019 | KFS-4110-02-2017

Project coordinator
Prof. Fabio Grassi, MD | fabio.grassi@irb.usi.ch

Strengthening the immune responses of T-cells

Solid tumours change their surrounding tissue: This causes the T-cells responsible for fighting the tumour cells to age prematurely and lose their defensive power. But in a research project funded by the Swiss Cancer Research foundation, researchers have demonstrated a way to possibly rejuvenate T-cells and enhance their healing effects.

In the fight against blood cancers, T-cells sometimes bring about spectacular results. But up to now, there has been no success against solid tumours. This is also due to the fact that tumours change their microenvironment, or niche, as the findings of a research study funded by the Swiss Cancer Research foundation suggest: "We have shown that in the tumour microenvironment molecules accumulate that cause premature ageing of T-cells – and thus make the T-cells, which are specifically responsible for fighting tumour cells, unable to do their job," reports Fabio Grassi, research group leader at the Institute for Research in Biomedicine in Bellinzona.

Together with his team, Grassi decoded the molecular processes of this premature ageing. A protein with a name worthy of Star Wars, P2X7, plays a central role. It sits on the surface of the T-cells and is on the lookout for a molecule called ATP. ATP is known as the source of chemical energy for biochemical processes in the cells. "But ATP also plays an important role outside the cells as a danger signal: It is present in injured or inflamed tissue and is also found in high concentrations in the microenvironment of tumours," Grassi explains. In a first phase of the defensive response (which is dictated by innate immunity), the immune cells need P2X7 in order to recognize where ATP is present – and thus where the injury or tumour is. But later, when the specific (or adaptive) immune response takes the lead, P2X7 is to blame for accumulation of genetic damage in the T-cells and for premature T-cell exhaustion in the fight to suppress cancer cells.

In experiments with mice, the researchers in the Grassi group turned off the P2X7 gene in the T-cells. As a result, the tumours grew more slowly, and the mice lived longer. It still remains to be seen whether the findings can be applied to humans. But should it be possible to inhibit P2X7? For example by using substances to provide the T-cells with a reconstitution signal that maintains their response against tumour cells? Then T-cell therapies will finally also have a chance, in the fight against solid tumours, to build on the successes that they have had with leukaemia and lymphomas.

Reference

Romagnani A, Rottoli E, Mazza EMC, Rezzonico-Jost T, De Ponte Conti B, Proietti M, et al. P2X7 receptor activity limits accumulation of T cells within tumor. *Cancer Res.* 2020;80:3906-19. doi: 10.1158/0008-5472.CAN-19-3807.

Project
Effect of exercise and exercise factors on cancer cachexia
Biozentrum, Universität Basel, Basel
CHF 255 500.– | Duration: 1. 1. 2016 – 30. 6. 2019 | KFS-3733-08-2015

Project coordinator
Prof. Christoph Handschin, PhD | christoph.handschin@unibas.ch

Exercise prevents muscle wasting and anaemia

Many patients with cancer experience cancer-induced muscle loss. Often, muscle strength is additionally limited due to anaemia: A reduced number of red blood cells cannot transport enough oxygen. However, a study funded by the Swiss Cancer Research foundation has shown that exercise improves both muscle wasting and anaemia.

Many cancers remain undetected for a long time. The first sign is often noticeable weight loss that cannot be reversed by increasing caloric intake. The medical term for disease-induced muscle wasting and accompanying loss of body fat is cachexia (from the Ancient Greek word for 'bad condition'). But very little is known about what exactly triggers and drives this harmful development. As cachexia, and not the tumour itself, is estimated to constitute the actual cause of death in up to 40% of all patients with cancer, a better understanding is sorely needed. Christoph Handschin, full professor of pharmacology at the University of Basel, reports, "In our research project, we investigated the molecular mechanisms of cachexia."

In their experiments, Handschin's research group compared tumour development in mice kept in cages with and without a running wheel. In mice with cancer that were sedentary, the concentration of fatty acids in the blood increased. "The blood plasma was milky; this was very apparent," Handschin says. The researchers were surprised to find that the changes in the metabolic blood profile led to a shortened lifespan of red blood cells – and red blood cells also became scarce. As this scarcity entails a reduction in the transport capacity for oxygen in the blood (which muscles need to do their work), this anaemia, just like the muscle wasting, leads to a general weakening.

In contrast, in tumour-bearing mice that exercised on a running wheel, the blood plasma was clear. "Apparently, muscle activity can normalize the metabolic blood profile at least in part," says Handschin. In the mice with sufficient exercise, the red blood cell count was also higher. On endurance tests, these mice performed much better than the sedentary mice. Does exercise also have a positive effect in humans? Handschin is now working with the Oncology Department at the University Hospital of Basel – and plans next to examine blood samples of patients participating in an exercise study.

List of approved research projects in 2019

More information about the funded projects can be found on www.krebsliga.ch/researchprojects

Total funds allocated: CHF 10 657 352.–

Allam Ramanjaneyulu | Investigating ribonuclease inhibitor (RNH1) mediated myelopoiesis to resolve myeloid differentiation blockade in myeloid malignancies
Department for Biomedical Research, Universität Bern, Bern
CHF 134 300.– | Duration: 1.1.2020 – 31.12.2021 | KFS-4896-08-2019

Barth Patrick | Rewiring adenosine signalling to enhance engineered T-cell therapies
Laboratory of Protein and Cell Engineering, EPF de Lausanne, Lausanne
CHF 354 800.– | Duration: 1.8.2019 – 31.7.2022 | KFS-4687-02-2019

Basler Konrad | Elucidating the Toll pathway's role in cancer progression and metastases formation
Institut für Molekulare Biologie, Universität Zürich, Zürich
CHF 334 900.– | Duration: 1.12.2019 – 30.11.2022 | KFS-4835-08-2019

Baumgartner Martin | Restricting cell invasion and tumour expansion by combinatorial targeting of FGFR signalling in malignant paediatric tumours
Abteilung Onkologie, Universitäts-Kinderspital Zürich, Zürich
CHF 366 900.– | Duration: 1.1.2020 – 31.12.2022 | KFS-4853-08-2019

Böttcher Steffen | Elucidating and harnessing the molecular mechanism of the dominant-negative effect of TP53 missense mutations in premalignancy and overt cancer
Klinik für Medizinische Onkologie und Hämatologie, Universitätsspital Zürich, Zürich
CHF 283 750.– | Duration: 1.1.2020 – 30.6.2023 | KFS-4885-08-2019

Brisken Cathrin | Different facets of estrogen receptor alpha (ER) signalling during ER+ breast carcinogenesis
Institut suisse de recherche expérimentale sur le cancer, EPF de Lausanne, Lausanne
CHF 375 000.– | Duration: 1.9.2019 – 31.8.2022 | KFS-4738-02-2019

Cascione Luciano | Ultra-conserved long non-coding RNAs in B-cell lymphoma
Institute of Oncology Research (IOR), Bellinzona
CHF 180 600.– | Duration: 1.7.2019 – 30.6.2021 | KFS-4713-02-2019

Catapano Carlo | Mitochondrial dynamics at the crossroad between stemness and treatment resistance in prostate cancer
Laboratory of Experimental Therapeutics, Institute of Oncology Research (IOR), Bellinzona
CHF 362 300.– | Duration: 1.1.2020 – 31.12.2022 | KLS-4899-08-2019

De Libero Gennaro | A novel population of human MR1-restricted T-cells in anti-tumour immunity
Departement Biomedizin, Universität Basel, Basel
CHF 374 800.– | Duration: 1.7.2019 – 30.6.2022 | KFS-4707-02-2019

Dotto Gian-Paolo | Androgen receptor signalling in melanoma development
Département de biochimie, Université de Lausanne, Lausanne
CHF 361 750.– | Duration: 1.7.2019 – 30.6.2022 | KFS-4709-02-2019

Herrmann Inge | Rationally designed high-z metal oxides for precision radiotherapy
Departement Maschinenbau und Verfahrenstechnik, ETH Zürich, Zürich
CHF 238 900.– | Duration: 1.2.2020 – 31.1.2023 | KFS-4868-08-2019

Hess Christoph | Kynurenine pathway activation during EBV infection of B-cells: molecular metabolism, immune modulation and development of lymphoproliferation
Departement Biomedizin, Universität Basel, Basel
CHF 375 000.– | Duration: 1.8.2019 – 31.7.2022 | KFS-4729-02-2019

Ho Ping-Chih | CD36-mediated metabolic adaptation supports metabolic fitness and epigenome required for intratumoural Tregs
Oncologie fondamentale, Université de Lausanne, Epalinges
CHF 323 450.– | Duration: 1. 2. 2020 – 31. 1. 2024 | KFS-4865-08-2019

Kovacs Werner | Exploring the role of pexophagy and peroxisomal metabolism in clear cell renal cell carcinoma (ccRCC) tumourigenesis
Institut für Molekulare Gesundheitswissenschaften, ETH Zürich, Zürich
CHF 243 900.– | Duration: 1. 7. 2019 – 30. 6. 2022 | KFS-4735-02-2019

Krämer Stefanie | Assessing the immune state of the tumour and its microenvironment by imaging Legumain and CD80 by positron emission tomography (PET)
Institut für Pharmazeutische Wissenschaften, ETH Zürich, Zürich
CHF 374 950.– | Duration: 12. 1. 2020 – 11. 1. 2024 | KFS-4900-08-2019

Lengerke Claudia | An unrecognized protein function adds a novel perspective to SOX2 driven cancer
Experimentelle Hämatologie, Universitätsspital Basel, Basel
CHF 353 650.– | Duration: 1. 12. 2019 – 30. 11. 2022 | KFS-4852-08-2019

Ludewig Burkhard | Deciphering the molecular landscape of cancer-associated fibroblasts in pancreatic cancer at single cell resolution
Medizinisches Forschungszentrum, Kantonsspital St. Gallen, St. Gallen
CHF 245 300.– | Duration: 1. 7. 2019 – 30. 6. 2021 | KFS-4701-02-2019

Meylan Etienne | Characterization of lamellar body-like organelles and leucine-rich repeat kinase 2 in lung adenocarcinoma
Institut suisse de recherche expérimentale sur le cancer, EPF de Lausanne, Lausanne
CHF 326 950.– | Duration: 1. 7. 2020 – 30. 6. 2024 | KFS-4839-08-2019

Mitsiadis Thimios | Single-cell analysis of human head and neck squamous cell carcinoma: clonality, microenvironment, and cell-cell communication
Zentrum für Zahnmedizin, Universität Zürich, Zürich
CHF 367 450.– | Duration: 6. 1. 2020 – 5. 1. 2023 | KFS-4890-08-2019

Mueller Cristina | Design and application of a new class of PSMA ligands in combination with terbium radioisotopes
Zentrum für Radiopharmazeutische Wissenschaften, Paul Scherrer Institut (PSI), Villigen
CHF 350 800.– | Duration: 1. 8. 2019 – 31. 7. 2022 | KFS-4678-02-2019

Orts Julien | Structural investigation of the mechanism of inhibition of KRas by small molecules
Laboratorium für Physikalische Chemie, ETH Zürich, Zürich
CHF 284 950.– | Duration: 1. 2. 2020 – 31. 7. 2023 | KFS-4903-08-2019

Peng Ren-Wang | Integrative molecular characterization uncovers new therapeutic rationales for malignant pleural mesothelioma (MPM)
Universitätsklinik für Thoraxchirurgie, Inselspital, Bern
CHF 374 450.– | Duration: 1. 2. 2020 – 31. 1. 2023 | KFS-4851-08-2019

Perentes Jean Yannis | Harnessing the power of intravital microscopy to explore how the tumour vasculature modulates immune cell infiltration of malignant mesotheliomas and dissemination of cancer cells
Service de chirurgie thoracique, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 141 100.– | Duration: 1. 10. 2020 – 30. 9. 2023 | KLS-4862-08-2019

Pertz Olivier | Imaging breast cancer oncogenic signalling and its response to targeted therapy at the single cell level
Institut für Zellbiologie, Universität Bern, Bern
CHF 368 700.– | Duration: 1. 1. 2020 – 31. 12. 2022 | KFS-4867-08-2019

Petrova Tatiana | Overcoming chemoresistance and immune exclusion in colorectal cancer
Oncologie fondamentale, Université de Lausanne, Epalinges
CHF 375 000.– | Duration: 1. 1. 2020 – 31. 12. 2022 | KFS-4895-08-2019

Platt Randall | Development of a high-throughput CRISPR-Cas9 in vivo platform for rapid modelling of human cancers and biomarker discovery
Department of Biosystems Science and Engineering, ETH Zürich, Basel
CHF 375 000.– | Duration: 1. 1. 2020 – 31. 12. 2022 | KFS-4863-08-2019

Riggi Nicolò | An integrative model of oncogenic epigenetic drivers in human translocated sarcomas
Institut de pathologie, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 369 800.– | Duration: 1. 1. 2020 – 31. 12. 2022 | KFS-4859-08-2019

Sartori Alessandro A. | Towards novel inhibitors targeting homologous recombination: from innovative research tools to cancer therapy
Institut für Molekulare Krebsforschung, Universität Zürich, Zürich
CHF 328 000.– | Duration: 1. 8. 2019 – 31. 7. 2023 | KFS-4702-02-2019

Scheiermann Christoph | Characterization of the effect of time-of-day in the immune response on tumour engraftment and growth
Département de Pathologie et d'Immunologie, Université de Genève, Genève
CHF 340 650.– | Duration: 1. 2. 2020 – 31. 1. 2024 | KLS-4836-08-2019

Suter David | Role of mitotic bookmarking by TEAD transcription factors in self-renewal of cancer stem cells
Institute of Bioengineering, EPF de Lausanne, Lausanne
CHF 326 950.– | Duration: 1. 3. 2020 – 29. 2. 2024 | KLS-4832-08-2019

Tolstonog Genrich | Lymphovascular invasion as a source of residual disease and a potential treatment target following surgery in head and neck cancer
Service d'oto-rhino-laryngologie, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 332 600.– | Duration: 1. 1. 2020 – 31. 12. 2022 | KFS-4726-02-2019

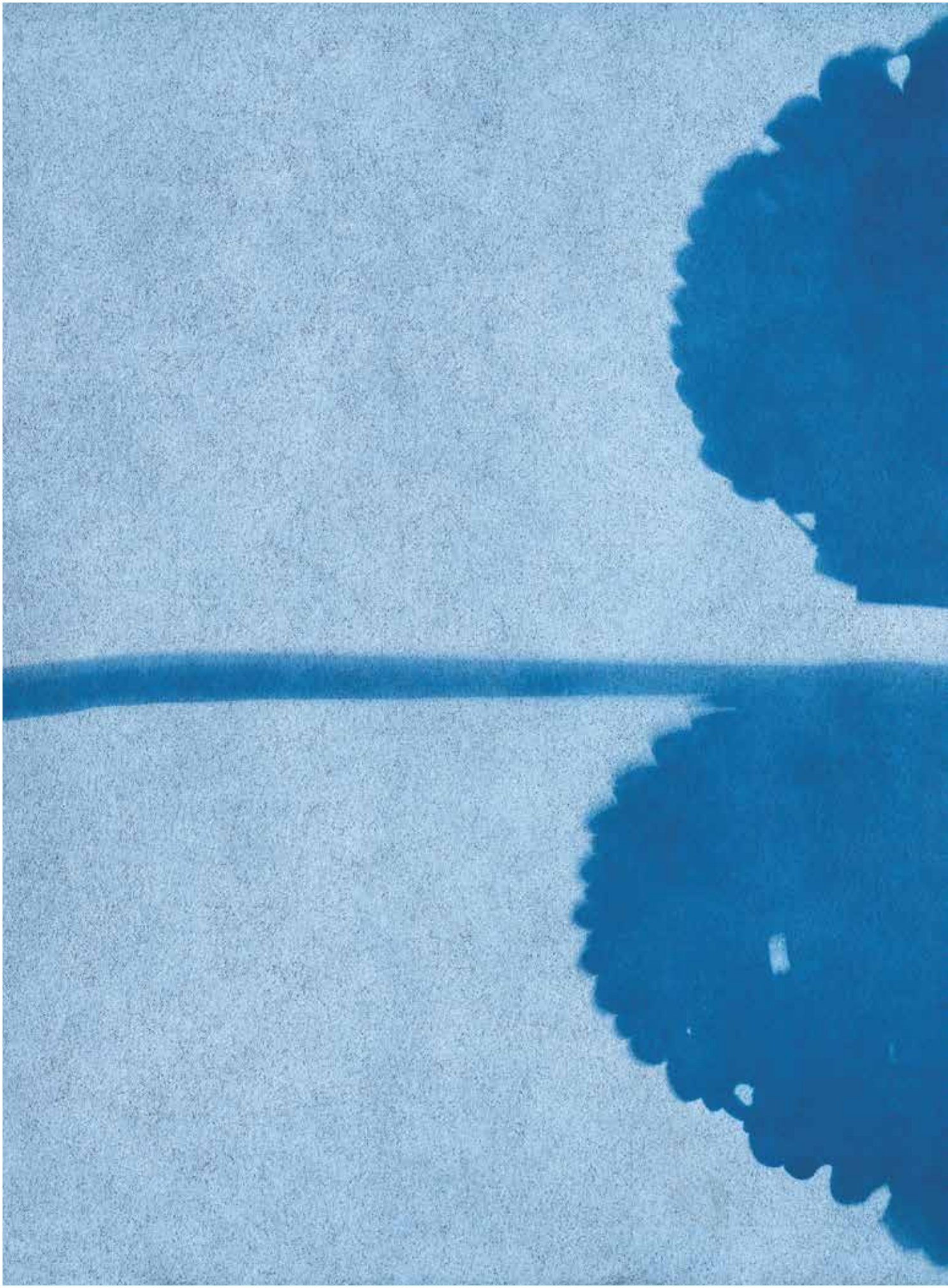
Verdeil Gregory | Identifying immune mechanisms in muscle invasive bladder cancer and improving current immunotherapy
Oncologie fondamentale, Université de Lausanne, Epalinges
CHF 370 100.– | Duration: 1. 1. 2020 – 31. 12. 2022 | KFS-4840-08-2019

Approved bursaries in 2019

Scheidegger Nastassja | Functional genomic approach to exploit dependencies on anti-apoptotic BCL2 family members for targeted combinatorial therapy in acute myeloid leukaemia
Destination: Department of Pediatric Oncology, Dana-Farber Cancer Institute, Boston (USA)
CHF 98 700.– | Duration: 1. 2. 2020 – 31. 1. 2022 | BIL-KLS-4857-08-2019

Telarovic Irma | Radiotherapy treatment volume and its role for the tumour-oriented immune response
Destination: Klinik für Radio-Onkologie, Universitätsspital Zürich, Zürich
CHF 189 902.– | Duration: 1. 9. 2019 – 31. 8. 2022 | MD-PhD-4820-06-2019

Wilk Christian Matthias | ERK signalling pathway activity in dendritic cell development and disease
Destination: Icahn School of Medicine at Mount Sinai, Hess Center for Science and Medicine, New York (USA)
CHF 52 000.– | Duration: 1. 3. 2020 – 28. 2. 2022 | BIL-KFS-4724-02-2019



Onconavigator and integration of real-world data (RWD) into the clinical evidence

In the last 20 years knowledge in medical oncology has advanced very rapidly. New findings from clinical research are generated at increasingly shorter time intervals. Contributing to this acceleration is increased in-depth knowledge on the molecular structure and control of tumour cells. Today, cancer is no longer understood as a single, fixed, histopathologically defined disease but rather as a myriad of diseases having individual characteristics that also change over the course of the disease. More precise diagnosis is combined with personalized forms of treatment that extend traditional therapies and in part even replace them. Innovations of this kind are highly selective for ever smaller groups of tumour patients. As a basic principle in oncology, "splitting" is replacing "lumping". Innovation is overtrumping validation by far. This development cascade culminates in complex diversity of treatment choices, which is increasingly challenging the human factor as the determining element today.

Broad collective learning

For patients, these advancements mostly bring benefits: More and more patients with cancer can be treated successfully. For physicians, however, there are increasing challenges of many kinds. From the clinical perspective, a main difficulty is evaluating the numerous and steadily growing number of treatment options. The basis of decision making are the findings of clinical trials with comparatively small numbers of patients and strict inclusion and exclusion criteria,

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Prof. Michael Krauthammer, MD, PhD
Chair of medical informatics at the University of Zurich and managing director of biomedical informatics at University Hospital Zurich

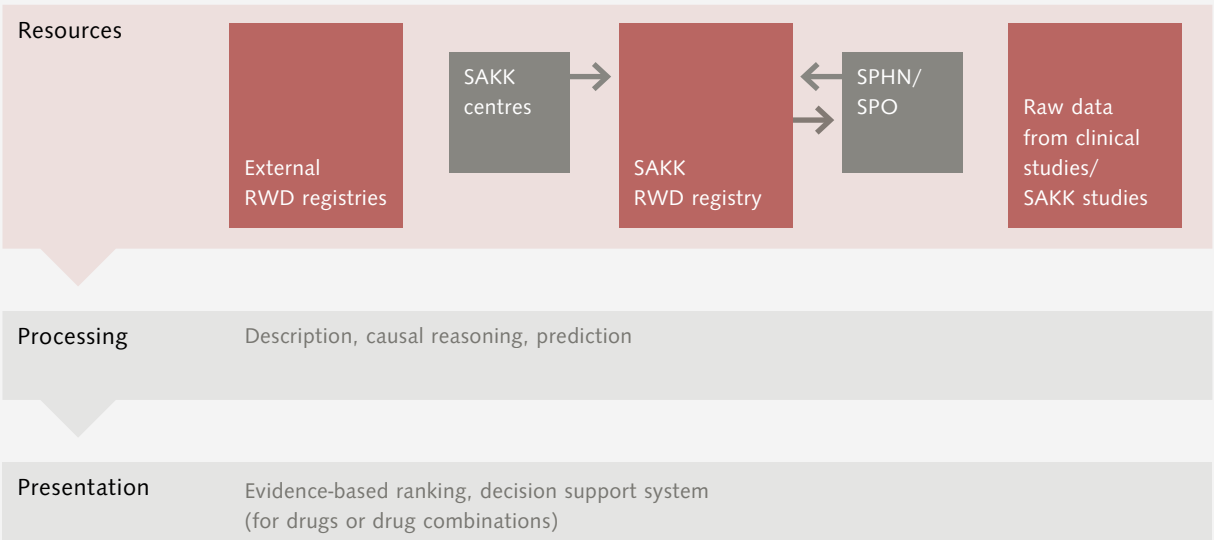
which most patients in everyday clinical practice do not meet. In addition, in oncology more and more drugs are used off-label. Although this is strictly regulated, it also opens up possibilities for early use of new medications and widens the range of treatments. There is only limited accompanying utilization research for oncological therapies on the market in the real world, and it does not cover whole populations worldwide. Up to now, for broad collective learning from successes and failures in oncology, there has been a lack of the following: impetus, a platform, quality standards, stamina, funding basis, and suitable instruments.

Onconavigator is based on the view that up to now, we have not been utilizing important resources for rational decision making in the selection of treatments for patients with metastatic solid tumours. Decisions become complex, when established standard treatments were used with great benefit but then unfortunately failed. Such situations happen regularly in oncology. Depending on the cancer, there are on average one to two established palliative therapies that are recommended as standard treatments by medical associations. However, in most cases, three to five palliative therapies are used sequentially. The selection of treatments with little or questionable benefit also applies to the off-label mode (in accordance with Article 71 a-d of the Health Insurance Ordinance). Off-label use is more and more often based on evidence of mutations found by molecular genetic analyses using next generation sequencing (NGS) technologies. In practice, technically well-established NSG panel tests are in use that cover practically all cancer-associated genes today. These are the biological basis for targeted therapy (genomic therapy) approaches and thus expand the potential therapy options sometimes many times over.

The treatment decision lies in the hands of the treating oncologist. The decision is based on individual weighing of benefit and risk of all eligible therapy options and taking into consideration the published evidence and guidelines from medical associations. In addition, ideally the decision also considers the patient's goals and values and is guided by the availability and affordability of the therapies.

Figure 1
Onconavigator (1st step)

Development of a system to support the choice of therapy.
Using methods of artificial intelligence, Onconavigator will sift through data from tumour registers and raw data from clinical studies – and describe and evaluate possible therapy options for patients with metastasized solid tumours.



Decision support

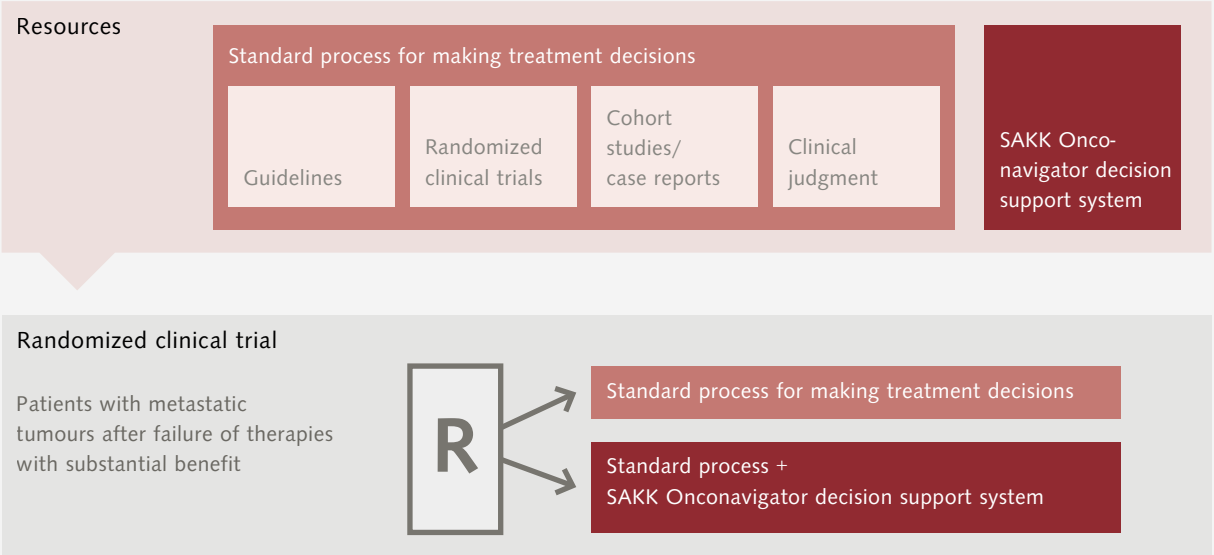
A prerequisite for the use of therapies is the authorization and determination of therapeutic indications by Swissmedic, the Swiss Agency for Therapeutic Products, as well as cost coverage (insurance reimbursement) based on the authorized list of drugs and special therapies (list of pharmaceutical specialties). The list forms the input filter for all registered therapeutic products. Up to now, however, there has been no possibility for collective learning regarding how the many registered therapies affect individual patients. There has been no systematic examination of oncological therapies used in the real world outside of the trial criteria.

In addition to registration as the first filter, there is a need for a review filter that evaluates and ranks the benefit of the therapies used in the real world (Figure 1). Onconavigator aims to use this data source and other primary data sources from further tumour registries as well as raw data from randomized oncological studies for ranking purposes in order to build a patient-specific decision support system. The analysis instruments for this are traditional statistical methods but also artificial intelligence technology methods[1]. In a further step, Onconavigator aims to test the value of its decision support system in a randomized controlled trial (RCT) (Figure 2), and if it proves its worth, to further develop it. It will then be available to all oncologists seeking support for their decisions.

The basis for a real-world analysis is a systematically structured, national, prospective, comprehensive, and high-quality registry that encompasses all cancer therapies for metastatic tumours. The Swiss Group for

Figure 2
Onconavigator (2nd step)

Randomized clinical trial to determine if the therapies chosen with the support by Onconavigator achieve better results.



Clinical Cancer Research (SAKK) is setting up such a real-world data (RWD) registry. SAKK is coordinating and is integrating input from several working groups; participating in the working groups are, among others, the Swiss Personalized Health Network (SPHN), Swiss Personalized Oncology (SPO), Swiss Molecular Pathology and Tumor Immunology Breakthrough Platform (SOCIBP), the Onconavigator working group, a clinical registry for immunotherapy studies (Alpine TIR), and a SAKK registry for SARS-CoV-2 infections in patients with cancer (CaSA study). The goal is to build a harmonized, electronic infrastructure for central collection of health-related RWD from SAKK-network hospitals in Switzerland. The minimum data set contains demographic, clinical, pathological (including comprehensive NGS panel test as an obligatory inclusion criterion), and outcome data. A framework protocol for the first 2000 patients has been developed. Data collection is planned to begin in October 2020.

Mutually supportive cooperation in a national network

Today, numerous RWD registries are being set up in oncology and also in other fields of medicine[2]. In oncology, the focus is mainly on national cancer registration, which is anchored in national law and managed by NICER (National Institute for Cancer Epidemiology and Registration). It centres on epidemiologic data, which is primarily made available to the federal authorities. Scientific projects like Onconavigator, however, require considerably broader clinical data with a focus on specific records on tumour biology, therapy, and outcomes. Moreover, the majority of the existing registries were developed as locally isolated projects, so that frequently, the data are not exchangeable with other registries. One of the biggest challenges is to collect data for national research projects from the hospitals' many different and fragmented IT systems, which mostly contain unstructured data. Having found a common language (minimum data set) in the SAKK RWD registry, further challenges are now new routes of access for at least partially automatable data transfer into the SAKK central data warehouse.

We will be successful if we continue to follow a joint national approach and if we prepare, early on, for international collaboration with other scientific projects and registries. Today, RWD registries are not a replacement for randomized controlled trials. Instead, they build a basis for collective learning from daily clinical practice and for deriving hypotheses for prospective studies[3,4]. They are a primary instrument of research but have interfaces with many stakeholders in the health care system. The SAKK RWD registry project and also Onconavigator are doubtless ambitious. They build on mutually supportive cooperation in a national network.

Prof. Dieter Köberle, MD

Dieter Köberle studied medicine in Innsbruck (Austria) and completed his training in internal medicine and medical oncology at Cantonal Hospital St. Gallen, where he worked up to 2012. Köberle's main research area is gastrointestinal oncology. He has conducted research with SAKK for over 20 years and teaches at the University of Bern as an adjunct professor. Since 2013 he has headed the Medical Clinic and Tumor Centre at St. Claraspital in Basel.

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Prof. Michael Krauthammer, MD, PhD

Michael Krauthammer studied medicine in Zurich and biomedical informatics at Columbia University in New York (USA). After heading a research group at Yale University for 14 years, Krauthammer was appointed full professor of medical informatics at the University of Zurich in 2018. His research areas are cancer genetics and the use of artificial intelligence in biomedicine.

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krauthammerlab.ch

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1. Lindsell CJ, Stead WW, Johnson KB. Action-informed artificial intelligence – matching the algorithm to the problem. *JAMA*. 2020;323:2141-2. doi: 10.1001/jama.2020.5035.
2. Booth CM, Karim S, Mackillop WJ. Real-world data: towards achieving the achievable in cancer care. *Nat Rev Clin Oncol*. 2019;16:312-25. doi: 10.1038/s41571-019-0167-7.
3. Panagiotou OA, Hoffman Högg L, Hricak H, Khleif SN, Levy MA, Magnus D, et al. Clinical application of computational methods in precision oncology: a review. *JAMA Oncol*. Published online May 14, 2020. doi: 10.1001/jamaoncol.2020.1247.
4. Bertagnolli MM, Anderson B, Norsworthy K, Piantadosi S, Quina A, Schilsky RL, et al. Status update on data required to build a learning health system. *J Clin Oncol*. 2020;38:1602-7. doi: 10.1200/JCO.19.03094.

Selected results

Project
Is early palliative care associated with a reduction in intensity and costs of care at the end of life in patients with advanced cancer? A randomised trial
Universitäres Zentrum für Palliative Care, Inselspital, Bern
CHF 192 600.– | Duration: 1. 11. 2016 – 30. 4. 2019 | KFS-3725-08-2015

Project coordinator
Prof. Steffen Eychmüller, MD | Steffen.Eychmueller@insel.ch

A better and less costly kind of care at the end of life

On average, patients who clarify in a palliative care consultation where the priorities lie for their remaining lifetime cope better with their situation. The number of emergency centre visits deceases. But how much the costs are reduced cannot be determined with certainty because in Switzerland it is very difficult to evaluate health insurance company data.

That is not what Steffen Eychmüller, head of the University Centre for Palliative Care at Bern University Hospital, had actually imagined. Together with his research group, he obtained permission from 99 patients with advanced cancer to have their health insurance billing statements evaluated in the context of a cost-effectiveness analysis. But some of the health insurers resisted. Up to now, the researchers have obtained the data for only 54 patients. "We are still hunting the records down," says Eychmüller, even though after almost three years' duration, the study should have already been completed.

Added to this, each health insurer structures the cost data differently. With a lot of patience, the researchers unified and merged the data to examine their research question in a project funded by the Swiss Cancer Research foundation: What is the effect of early palliative care consultation and advance planning on the costs of care at the end of life? Due to the small sample size, the study has only limited significance.

Nevertheless, the study found that on average, patients who had a palliative care consultation utilized less cost-intensive health care services in the last month of life – and, for example, had fewer emergency centre visits – than patients who had no palliative care consultation. Together with questionnaire responses from relatives who were caring for the patients at home, the results revealed a clear picture: Patients who define the priorities in their remaining time of life retain control and, on average, cope with their situation better.

The average duration of the palliative care consultation was 52 minutes and the cost, with preparation and postprocessing, was 380 francs. In the study, this additional expense was more than compensated for: In the group of patients with no palliative care consultation, the average care costs in the last month of life were 7649 francs, and in the group with a palliative care consultation the costs were 7033 francs. "The cost analyses and the feelings of the persons involved point in the same direction. They show that palliative advice can improve the quality of treatment at the end of life without making it more costly," says Eychmüller.

Reference

Fliedner M, Zambrano SC, Schols JMGA, Bakitas M, Lohrmann C, Halfens RJG, et al. An early palliative care intervention can be confronting but reassuring: A qualitative study on the experiences of patients with advanced cancer. *Palliat Med.* 2019;33:783-92. doi: 10.1177/0269216319847884.

Project
Lobular carcinoma of the breast: insights from a new PDX model
Institut suisse de recherche expérimentale sur le cancer (ISREC), Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne
CHF 357 750.– | Duration: 1. 5. 2016 – 30. 4. 2019 | KFS-3701-08-2015

Project coordinator
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Model for invasive lobular carcinoma

Invasive lobular carcinoma belongs to the oestrogen receptor-positive subtypes of breast cancer, but it does not respond to the treatments available today. In a research project funded by the Swiss Cancer Research foundation, researchers have now characterized the molecular properties of this type of breast cancer and as a result have identified new therapeutic targets.

Some decades ago, breast cancer was viewed as a single disease, but today the term breast cancer covers many different diseases that can be distinguished from each other and treated in a targeted manner. But scientific progress is not linear and takes winding paths: "With breast cancer, there are several parallel classifications, and this causes confusion," says Cathrin Brisken, professor at the Swiss Federal Institute of Technology Lausanne (EPFL).

In the clinic, for instance, classification by receptor status plays an important role, as patients whose cancer cells do not have oestrogen receptors receive different treatments than patients with hormone receptor-positive (ER+) breast cancer: "The differentiation is therapeutically relevant," explains Brisken. But less attention is paid to other findings. For example, pathology looks at the appearance of the cancer cells under the microscope. In most cases, approximately 70%, nothing special is found. These are what are called the non-specific types of tumours.

But around 30% look different. "For the specific tumours there are flowery descriptions, but they often do not help us draw conclusions regarding selection of an appropriate treatment," Brisken says. Around half of these specific tumours are invasive lobular carcinomas. "Although it belongs to the hormone receptor-positive breast cancers, invasive lobular carcinoma does not respond well to tamoxifen, which is the normally used endocrine therapy," Brisken says.

With the aim to improve the prognosis of patients with invasive lobular carcinoma, Brisken and her team – in a research project funded by the Swiss Cancer Research foundation – isolated cancer cells from biopsies. They injected the tumour cells through the nipples into the milk ducts of mice. Then Brisken and her team found that these xenotransplantation models were in many ways similar to human cancer and, for instance, also showed typical development of metastases in the ovaries and the meninges.

Detailed investigation of these models also revealed special molecular characteristics of this type of breast cancer: "We discovered that the tumour cells grow along collagen fibres – and that a chemical blockade of the enzyme that plays a central role in the production of these collagen fibres inhibits tumour growth and metastasis," says Brisken. The researchers used a molecule in their experiments that, however, could never be used as a therapeutic agent, as it causes severe side effects. Brisken and her team are now working together with a research group in Great Britain to find a substance with more specific effects.

Reference

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List of approved research projects in 2019

More information about the funded projects can be found on www.krebsliga.ch/researchprojects

Total funds allocated: CHF 5 525 553.–

Aceto Nicola | Individualized therapy prediction from the analysis of circulating tumour cells
Departement Biomedizin, Universität Basel, Basel
CHF 359 500.– | Duration: 1. 2. 2020 – 31. 7. 2023 | KLS-4834-08-2019

Afshar-Oromieh Ali | Development of deep learning algorithms for detection, quantification and characterization of prostate cancer lesions in PSMA-ligand PET/CT
Universitätsklinik für Nuklearmedizin, Inselspital, Bern
CHF 153 850.– | Duration: 1. 8. 2019 – 31. 7. 2021 | KFS-4723-02-2019

Andratschke Nicolaus | PRophylactic cerebral Irradiation or active MAgnetic resonance imaging surveillance in small-cell Lung cancer patients (PRIMALung study)
Klinik für Radio-Onkologie, Universitätsspital Zürich, Zürich
CHF 197 900.– | Duration: 1. 10. 2020 – 30. 9. 2024 | KLS-4841-08-2019

Bassani-Sternberg Michal | Deciphering the antigenic landscape of immunologically 'hot' and 'cold' tumours for optimal design of personalized cancer immunotherapy
Département d'oncologie, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 374 300.– | Duration: 1. 9. 2019 – 31. 8. 2022 | KFS-4680-02-2019

Bertoni Francesco | An integrated approach to identify the mechanism of resistance to copanlisib and venetoclax in marginal zone lymphoma
Lymphoma Genomics, Institute of Oncology Research (IOR), Bellinzona
CHF 360 350.– | Duration: 2. 8. 2019 – 1. 8. 2022 | KFS-4727-02-2019

Bürgler Simone | Epstein-Barr virus- and malaria-associated Burkitt's lymphoma: AID/APOBEC enzymes as key molecules and future therapeutic targets?
Experimentelle Infektiologie und Krebsforschung, Universitäts-Kinderspital Zürich, Zürich
CHF 247 000.– | Duration: 1. 1. 2020 – 31. 12. 2023 | KLS-4883-08-2019

De Bock Katrien | Metabolic and neurodevelopmental programmes regulating angiogenesis and the neurovascular unit in brain tumours
Departement Gesundheitswissenschaften und Technologie, ETH Zürich, Zürich
CHF 322 500.– | Duration: 1. 7. 2019 – 30. 6. 2023 | KFS-4758-02-2019

Grünberg Jürgen | Development of ovarian cancer stem cell-directed radioimmunotherapy using auger-electron and alpha-particle emitters
Zentrum für Radiopharmazeutische Wissenschaften, Paul Scherrer Institut (PSI), Villigen
CHF 266 950.– | Duration: 10. 1. 2020 – 9. 7. 2023 | KFS-4876-08-2019

Huelsken Joerg | Targeting cancer plasticity mechanisms for an enhanced efficacy of immunotherapy
Institut suisse de recherche expérimentale sur le cancer, EPF de Lausanne, Lausanne
CHF 375 000.– | Duration: 1. 2. 2020 – 31. 1. 2023 | KFS-4830-08-2019

Iezzi Giandomenica | Role of bacteria-specific T-lymphocytes in immune responses against human colorectal cancer
Ente Ospedaliero Cantonale, Dipartimento di Chirurgia, Università della Svizzera Italiana, Lugano
CHF 374 650.– | Duration: 1. 11. 2019 – 31. 10. 2022 | KFS-4751-02-2019

Neidert Marian | Dissecting the heterogeneity of T-cell antigens in glioblastoma – mapping natural HLA ligands and characterizing tumour-infiltrating lymphocytes
Klinik für Neurochirurgie, Universitätsspital Zürich, Zürich
CHF 325 000.– | Duration: 1. 7. 2019 – 30. 6. 2023 | KFS-4754-02-2019

Pless Miklos | Influence of a home-based nutrition and exercise programme including an application for monitoring quality of life in cancer outpatients
Medizinische Onkologie, Kantonsspital Winterthur, Winterthur
CHF 310 600.– | Duration: 1. 3. 2020 – 28. 2. 2023 | KFS-4821-08-2019

Rossi Davide | Molecular subtypes of splenic marginal zone lymphoma
Lymphoma & Genomics Research Program, Institute of Oncology Research (IOR), Bellinzona
CHF 125 000.– | Duration: 1. 7. 2019 – 30. 6. 2021 | KFS-4705-02-2019

Seiler-Blarer Roland | Determining predictors of response to a combination of checkpoint inhibitors (anti-PD-L1 and anti-CTLA-4) by single-cell tumour profiling and monitoring of immune cell populations in liquid biopsies in bladder cancers within the NITIMIB trial
Universitätsklinik für Urologie, Inselspital, Bern
CHF 365 750.– | Duration: 1. 9. 2019 – 31. 8. 2022 | KFS-4718-02-2019

Theocharides Alexandre | Linking function and genomics of myelofibrosis stem cells
Klinik für Medizinische Onkologie und Hämatologie, Universitätsspital Zürich, Zürich
CHF 357 000.– | Duration: 1. 1. 2020 – 31. 12. 2023 | KFS-4875-08-2019

Wirsching Hans-Georg | Overcoming immune evasion of hypermutated glioblastoma
Klinik für Neurologie, Universitätsspital Zürich, Zürich
CHF 375 000.– | Duration: 1. 1. 2020 – 31. 12. 2022 | KLS-4870-08-2019

Worni Mathias | A phase II study to assess efficacy, safety and immunologic response of irreversible electroporation (IRE) followed by checkpoint inhibition (nivolumab) in metastatic pancreatic cancer
Viszeralchirurgie, Lindenhofspital, Bern
CHF 126 900.– | Duration: 11. 1. 2019 – 31. 10. 2021 | KFS-4682-02-2019

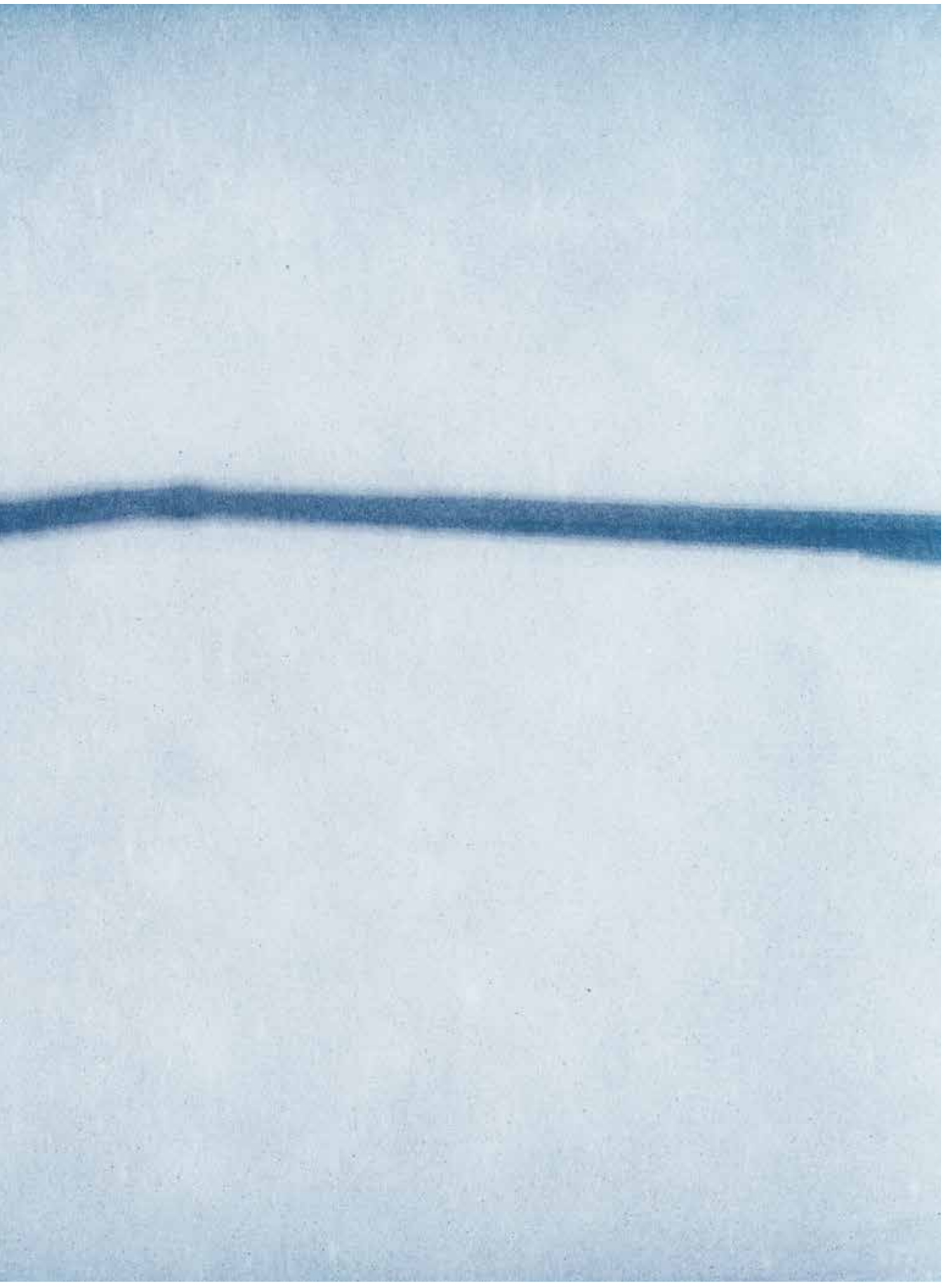
Approved bursaries in 2019

Bögeholz Jan Lukas | Discovery of minor histocompatibility antigens for post allogeneic blood stem cell transplantation immunotherapy
Destination: Stanford Comprehensive Cancer Center, USA
CHF 104 000.– | Duration: 1. 10. 2019 – 30. 9. 2021 | BIL-KFS-4733-02-2019

De Paula Costa Monteiro Inês | Engineering T-cell for adoptive cell transfer therapy of cancer
Destination: Département d'oncologie, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 191 553.– | Duration: 1. 11. 2019 – 31. 10. 2022 | MD-PhD-4819-06-2019

Schawkat Khoschy | Assessment of solid pancreatic lesions: can radiomics and functional MRI differentiate focal pancreatitis from pancreatic cancer?
Destination: Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, USA
CHF 24 500.– | Duration: 1. 4. 2020 – 30. 9. 2020 | BIL-KLS-4854-08-2019

Schmassmann Philip | Synergistic activation of microglia by targeting CD47 and siglecs
Destination: Departement Biomedizin, Universität Basel, Basel
CHF 188 250.– | Duration: 1. 9. 2019 – 31. 8. 2022 | MD-PhD-4818-06-2019



Psycho-oncological support – yes, no, maybe later

A cancer diagnosis is very stressful for the patients and for their families and friends. People with cancer often experience great psychological and social burdens that can have a negative effect on their treatment and on their quality of life. International professional associations therefore recommend screening for psychosocial distress in patients with cancer using short questionnaires. The aim is to identify patients with high psychosocial distress quickly so that psycho-oncological support services can be offered early on. Distress screening is also a criterion for cancer centre accreditation.

Different types of support needs

Patients with higher distress scores on a screening instrument tend to have a need for psycho-oncological support, as research evidence has shown that they are at increased risk for developing psychological disorders during the course of the disease. Despite this, only a small percentage of patients utilize psycho-oncological support services, and this, surprisingly, is independent of how they themselves rate their distress.

Diana Zwahlen, PhD
Head psychologist at University Hospital Basel

Following Salmon[1], we can describe three types of need for support:

1. need for psycho-oncological support due to higher levels of distress,
2. patients' own desire for support, without them necessarily attending a support services appointment, and
3. actual uptake of psycho-oncological support services (Figure).

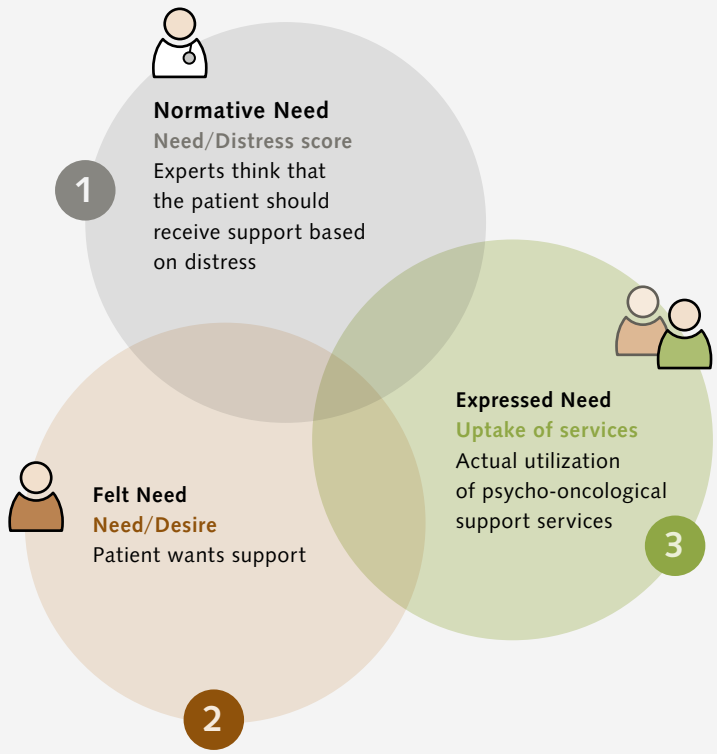
From clinical experience to systematic examination

These clinical experiences were a central starting point for our own research project. In a study (from 2013 to 2017) funded by the Swiss Cancer League, the study group on psychosomatic medicine and medical oncology at University Hospital Basel examined the relation between high scores on a distress screening (namely, the Distress Thermometer) and actual uptake of psycho-oncological support services as well as patients' reasons for and against utilizing psycho-oncological support[2].

In our study, we evaluated the responses of 333 patients at the oncology clinic. During the first outpatient consultation at the Medical Oncology Department at University Hospital Basel, when the planned oncological treatment was discussed in detail, about half of the study participants had elevated scores on subjective distress on the Distress Thermometer (score 5 or higher). With these scores, experts recommend psycho-oncological support.

In our study we divided the patient group with elevated distress into three groups of approximately the same size: One group stated that they wanted a psycho-oncological support services appointment.

Figure
Need for support services from different perspectives, adapted from Salmon et al. (2015)



The two other groups had either no desire for support or were ambivalent about support: Of the patients in these two groups, "no desire" or "ambivalent", only few patients attended a support services appointment within the observation period of four months. In the group of patients that had expressed a desire for support, two thirds of the patients attended a psycho-oncological support services appointment within the four-month period[3].

The ambivalent group

Our study identified a group of patients to which little attention has been paid: Patients with cancer who, despite scoring high on distress, do not accept oncological support and do not have a negative attitude but rather ambivalent feelings towards psycho-oncological support. This group can be described as vulnerable, as they had on average high subjective distress but did not utilize psycho-oncological support services in the four-month period.

Four overarching topics

In a further step, we wanted to learn more about why patients turn down, accept, or are ambivalent about psycho-oncological support services. We were particularly interested in the ambivalent group, which had not been studied previously. To this purpose we captured patients' reasons qualitatively and evaluated them[3].

In semi-standardized interviews we recorded patients' reasons for and against utilizing psycho-oncological support services. In all, 734 arguments for or against psycho-oncological support were collected (multiple answers were possible). From these we defined 32 overarching categories, which we then grouped into four overarching central categories, regardless of whether the participants were for or against or ambivalent about psycho-oncological support.

A first central topic was *general attitude* towards psychological support. This describes both negative and positive attitudes on the part of patients with cancer towards psycho-oncology (for example: "I do not view psychologists as relevant for my treatment"). Further central topics were *experienced distress* in the current situation (for example: "At the moment I feel fine physically and psychologically"), *handling of the disease,* or subjective coping strategies (for example: "In my life I have always gotten through everything on my own"), and finally, *experienced formal and informal support* (for example: "My family gives me the support I need").

The pattern of the reasons

The ambivalent group and the groups with a definite yes or no to psycho-oncological support mentioned different reasons: As expected, the ambivalent group offered arguments both for and against psycho-oncological support. In this group, playing an important role in the decision were especially their current situation with all uncertainties and fears but also their available resources. The group of ambivalent patients was basically open to psycho-oncological support,

however. Another feature was that fewer persons in this group than in the groups with a definite yes or no expressed reasons based on a positive or negative attitude or based on a clear idea about how they wanted to deal with the cancer situation.

The ambivalent group had an open attitude and made the decision on support services based on how they were currently feeling. In contrast, for the patients with a clear yes or no to psycho-oncological support services, attitude was an important factor in utilization. This explains why a considerable group of patients with low distress scores utilized psycho-oncological support. This group of patients viewed psycho-oncological support as one of the parts of their treatment, or had already had good experience with psychosocial services.

But why are ambivalent patients reserved about accepting psycho-oncological support, even though they often experience elevated distress? We suspect that at the start of treatment, patients are overwhelmed and first of all need to come to terms with their new life situation. In addition, there are many medical appointments to attend, so that a psycho-oncological support services appointment in addition can quickly seem like too much: "Maybe later" was a frequent statement. Our findings led us to assume that whether or not they attend a psycho-oncological support session depends on how patients are doing during the course of the treatment and on whether they are reminded about the availability of psycho-oncological support services at a later time point as well. Our study also found that a physician's recommendation was one of the most important predictors of uptake of psycho-oncological support services[4]!

Recommendations for daily clinical practice

Based on our findings, we recommend that in clinical practice we pay attention not only to distress scores but also to the patient's subjective desire and motivation for support. The patient's desire may or may not agree with the expert's perspective. If the patient's desire for support is captured on the questionnaire with the item "Would you like to have a psycho-oncological support services appointment – yes or no?", this falls short and, on the whole, conceals ambivalent motivation. With this item, questions regarding psycho-oncological support have too little room. Patients' reasons for or against utilization are complex and should be taken up in a conversation. In addition, patients with cancer should be asked about their distress and need for support several times throughout the course of treatment. This is particularly important for patients who show ambivalence. They are a vulnerable group with higher levels of distress on average and low uptake, even though they have an open attitude towards psycho-oncological support. Our finding that a physician's recommendation was a main predictor of psycho-oncological support services uptake underlines how important the personal conversation with the physician is and how central an explicit recommendation is for uptake of support services. Physicians can use screening questionnaires (such as the frequently used Distress Thermometer) in order to have a personal conversation about distress and the patient's support needs. Physicians' assessments and advice are important to make access easier for underserved patient groups – and to optimize psycho-oncological care.

Diana Zwahlen, PhD

Diana Zwahlen studied psychology at the University of Bern and completed a doctorate in the area of psycho-oncology in 2009. She worked for some years at the university hospitals of Zurich, Basel, and Bern. In addition to her scientific work, she also completed clinical training. Today Zwahlen is head psychologist at the Department of Psychosomatic Medicine, a federally recognized psychotherapist and a psycho-oncologist at the Medical Oncology Department at University Hospital Basel. Her teaching and research interests focus on optimization of psycho-oncological services and on family burdens (systemic perspective). She is co-president of the Swiss Society of Psycho-Oncology.

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Selected results

Project
Communication in cancer care: what is good for the patient? – The cancer patient perspective
Service de psychiatrie de liaison, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 239 400.– | Duration: 1. 1. 2015 – 30. 9. 2019 | KFS-3459-08-2014

Project coordinator
Prof. Friedrich Stiefel, MD | frederic.stiefel@chuv.ch

New insights on physician-patient communication

Researchers used qualitative research methods to examine audiotapes of physician-patient consultations. They uncovered new mechanisms that play an important role in communication between patients and specialists.

In the specialist training of oncologists, communication skills training has been mandatory in Switzerland since 2006. In the communication course, cancer specialists practice several communication techniques and reflect upon their personal communication behaviour. The goal is to meet the high communication demands of the profession to the best possible extent. A cancer diagnosis triggers existential questions and thoughts in the persons concerned, and they in turn expect their treatment team to show willingness to empathize with others – and to have the ability to explain complex things in a comprehensible way.

However, precisely how it matters that a patient is satisfied with a consultation is difficult to grasp. Up to now, communication research has focused mainly on individual aspects of consultations and, for example, recorded how many open questions are asked in a consultation, says psychiatrist and psycho-oncologist Friedrich Stiefel. Together with his colleague Céline Bourquin at Centre hospitalier universitaire vaudois (CHUV) in Lausanne, he looked beyond this narrow perspective: In a research project funded by the Swiss Cancer Research foundation, the researchers examined audiotapes of 24 randomly selected physician-patient consultations in depth using qualitative social research methods.

They found new patterns in physician-patient consultations. For instance, whether, and how often, patients express their feelings depends also on how they are responding to treatment: "Patterns of this kind show that a holistic analysis of consultations is necessary in order to capture the various factors that ultimately determine the atmosphere of a consultation," explains Stiefel. The atmosphere plays an important role in how satisfied a patient is with the consultation. And that in turn has an effect on trust and willingness to cooperate – and also on treatment adherence. Thus, good communication increases the effectiveness of treatment.

List of approved research projects in 2019

More information about the funded projects can be found on www.krebsliga.ch/researchprojects

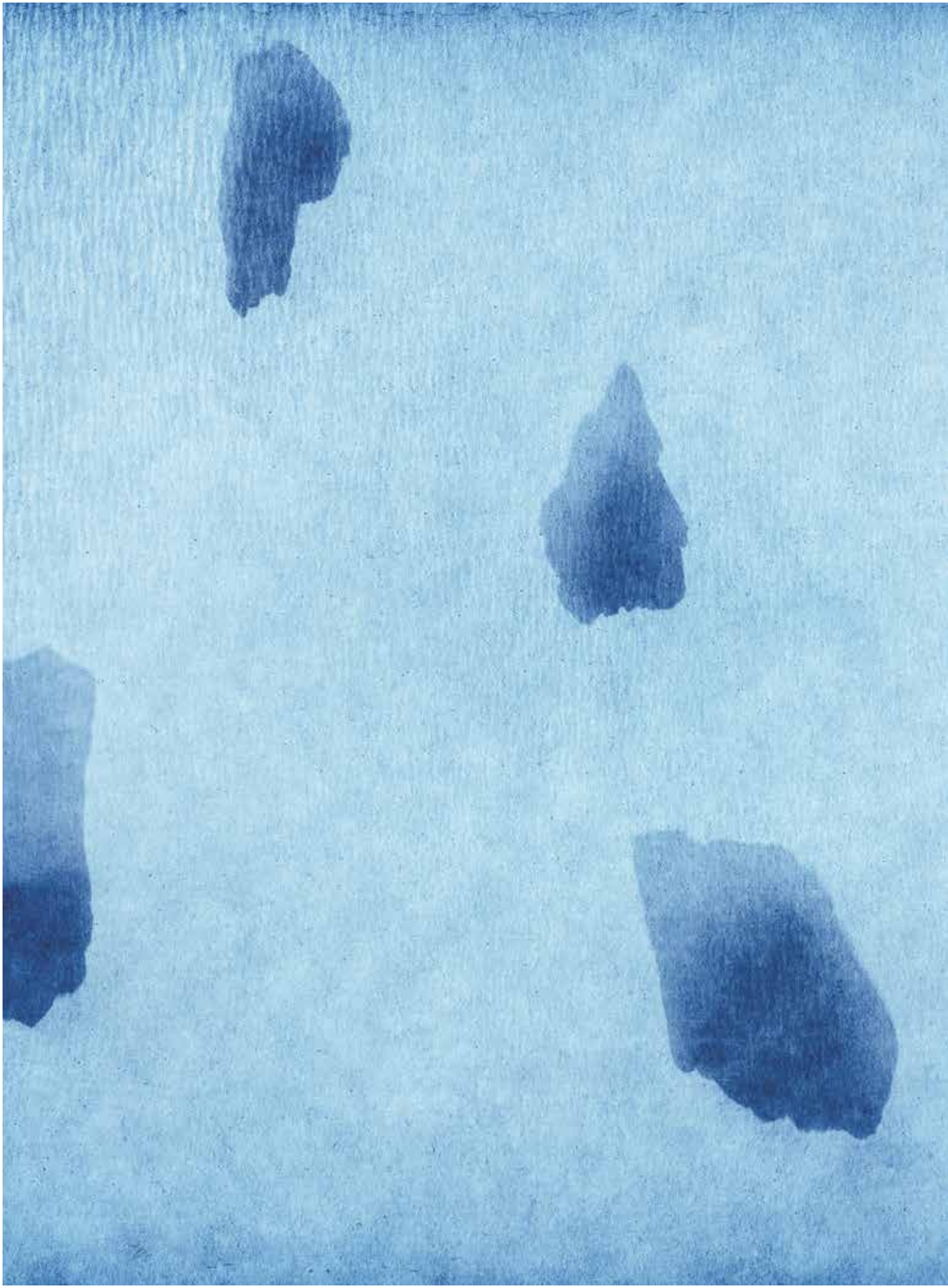
Total funds allocated: CHF 479 300.–

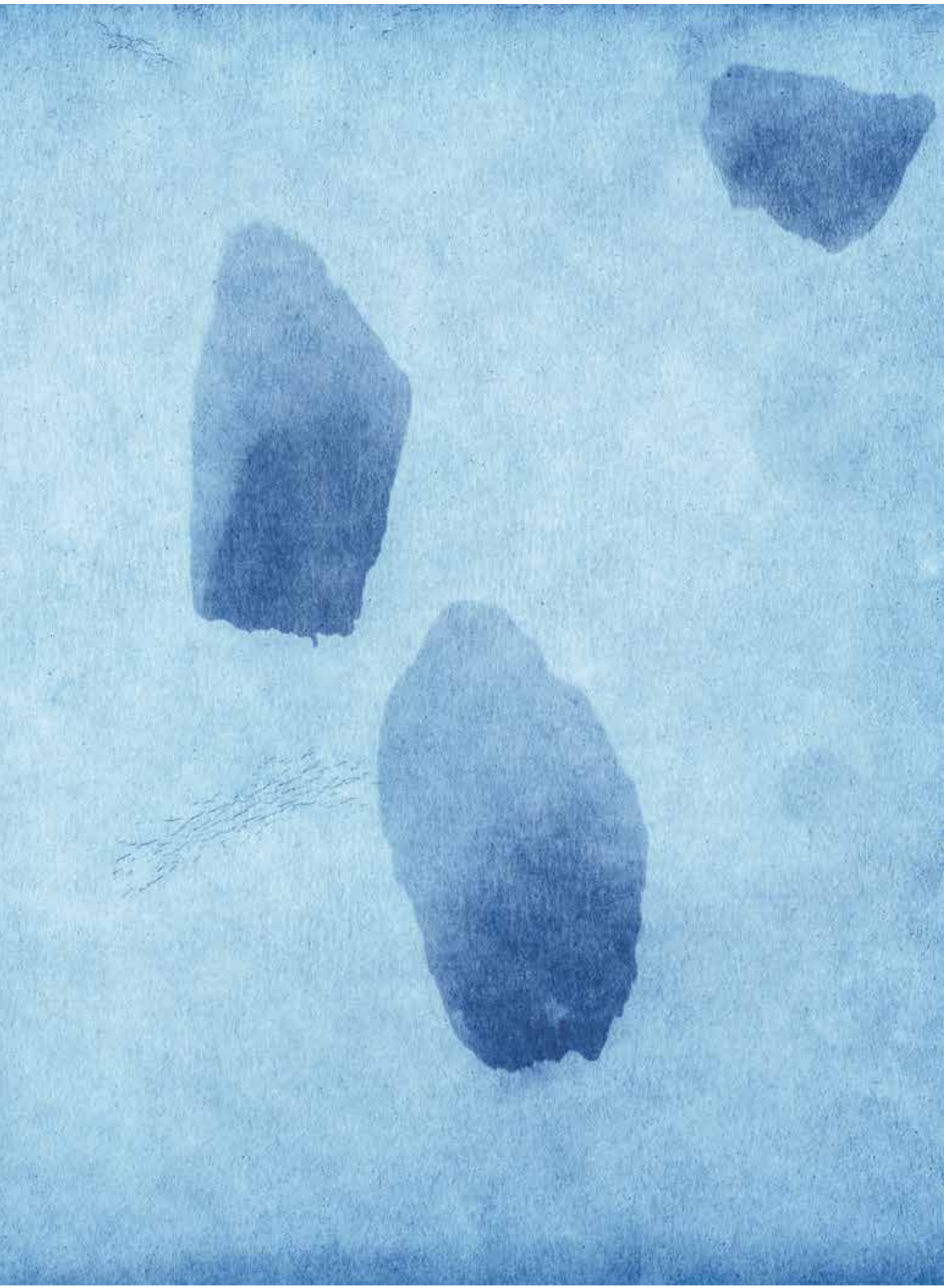
Biller-Andorno Nikola | Autonomy and relations. Investigating the role of shared decision-making in young haemato-oncological patients
Institut für Biomedizinische Ethik und Medizingeschichte, Universität Zürich, Zürich
CHF 181 150.– | Duration: 1. 7. 2019 – 31. 12. 2021 | KFS-4690-02-2019

Bondolfi Guido | Mindfulness-based cancer recovery programme for patients living with a gynaecological cancer: a randomized controlled pilot study (SERENITY)
Département de psychiatrie, Université de Genève, Genève
CHF 125 750.– | Duration: 1. 8. 2019 – 31. 7. 2022 | KFS-4696-02-2019

Elger Bernice | Towards culturally equitable paediatric oncology care – providers' cross-cultural competences and accessibility of care for cultural minorities
Institut für Bio- und Medizinethik, Universität Basel, Basel
CHF 76 600.– | Duration: 1. 5. 2020 – 31. 10. 2021 | KLS-4822-08-2019

Leibundgut Kurt | Efficacy of physical training and cognitive training in children and adolescents after cancer – the brainfit-study
Universitätsklinik für Kinderheilkunde, Inselspital, Bern
CHF 95 800.– | Duration: 1. 9. 2019 – 31. 8. 2021 | KFS-4708-02-2019





Investigation of reimbursement for off-label use of drug treatments

Off-label use (OLU) is the use of approved pharmaceutical drugs for other than their registered indications. This practice is very common in the treatment of patients with cancer[1–3]: OLU is mainly found in situations where there are only a few or no established therapies. OLU is also common when, for instance, a new study finds that an already approved medication also shows benefit in another type of cancer. A prominent example of this is trastuzumab, which was originally approved for treatment of a certain type of breast cancer. It is firmly established in the treatment for this indication[4]. A randomized controlled trial showed that trastuzumab improves survival also for patients with a subtype of gastric (stomach) cancer, when prescribed additionally to what was then the standard treatment[5]. However, it took another year until the authorities granted approval of the medication for treating stomach cancer as well.

The results of such trials are announced at medical conferences and published in medical journals. The information on the demonstrated benefit of such treatments is therefore available, and physicians want to treat their patients based on the latest developments in medicine. But the problem is that the process of authorization of drugs by the authorities (in Switzerland by Swissmedic) takes time – and that is why there is always OLU in such situations. The medications are therefore also not on the list of drugs and special therapies (list of pharmaceutical specialties, LS) of the Federal Office of Public Health for this indication, and the health insurance companies are not required to reimburse the cost of the treatment.

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PD Lars G. Hemkens, MD, MPH
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Differing appraisals of the clinical benefits

However, according to Article 71 of the Ordinance on Health Insurance, in some situations basic insurance reimburses the cost for medicinal products in off-label use: Namely, if the use of the drug is expected to result in a significant treatment benefit against an illness that may be fatal for the insured person and if furthermore, there is no other effective and authorized treatment option available that is included in the LS. For OLU, the treating physician must submit a request for cost reimbursement to the insurance provider before the start of treatment. To back up the application for reimbursement, the applicant often refers to findings from studies that demonstrate the clinical benefit of the planned OLU. The reimbursement decision lies with the insurance provider alone. One of the main problems with this process is the appraisal and interpretation of the therapeutic benefit. Medical examiners working for the insurance companies use various tools – such as the 9-field model[6] – to guide their appraisal of therapeutic benefit based on the available studies, and they are also supposed to consider the individual clinical circumstances of the patients. However, the models used are not validated, and the health insurers are also not obligated to use them.

A 2013 report commissioned by the Swiss Cancer League was the first to point to the growing importance of OLU in Switzerland and to describe the various problem areas[7]. The physicians interviewed for the report mainly criticized the lack of transparency in the health insurers' decision processes on reimbursement of OLU: When and why a request for reimbursement was turned down was not clear. In addition, the report emphasized that little data was available on the reality and prevalence of OLU in Switzerland. And the factors that could affect the cost reimbursement decisions by the health insurers could not be investigated, since there was no systematic and empirical investigation of the problem.

Lack of relationship between demonstrated benefit and cost reimbursement

In view of this, in 2017 we launched a multicentre research project funded by the Swiss Cancer Research foundation to investigate how often OLU is actually requested in Switzerland and how often the cost is actually reimbursed by the health insurers. In addition, we examined whether there is a relationship between the available clinical evidence for demonstrated therapeutic benefit of the treatment (for example, better survival) and the reimbursement decisions[8]. In principle, we would assume that there is a relationship – OLU requests should actually be approved more frequently by health insurers if randomized controlled trials demonstrate a survival benefit for the drug.

To answer these important questions in daily oncological and haematological care, we analysed the records of nearly 6000 patients with cancer that were treated at three large centres for haematology and oncology in Switzerland: Basel, Bern, and St. Gallen. In addition, we searched the literature for the most frequent OLU indications in order to gather the available evidence from randomized controlled trials. Our findings so

far show that for approximately 20% of the patients examined, at least one request for cost reimbursement was submitted during the course of their treatment. Two out of three reimbursement requests were approved, but one third of the requests were rejected by the health insurers. Astonishingly, we found no association between the available clinical evidence on the benefit of an OLU treatment for the particular indication and the probability of cost reimbursement by the health insurers. Some reimbursement requests for treatments with demonstrated improvement in overall survival were turned down, whereas in other cases, reimbursement was approved even though there were no data demonstrating a survival benefit of the treatment in the particular indication. It is interesting that sometimes different decisions were made within one and the same health insurance company.

Having the possibility to receive treatment based on the latest scientific findings

In sum, we can say that a large part of patients with cancer in Switzerland have access to OLU treatments. But our results so far also show that the decision making by the health insurers is still characterized by inconsistency and a lack of transparency. All too often the health insurers' reimbursement decisions do not reflect the available clinical evidence. The rapid development in medical research, especially in molecular diagnostics and classification of tumours, presents challenges to the worldwide health care systems not only in terms of administration but also financially. Cancer drugs belong to the most expensive medications used in daily medical practice. That makes it all the more important to assess new treatment developments in accordance with high scientific standards. In view of the abundance of literature, however, it is indispensable that in case of doubt the available evidence for OLU be reviewed by independent experts, who are able to interpret also the results of trials with complex designs. All patients with cancer in the Swiss health care system should have the possibility to receive the best possible care and treatment based on the latest scientific findings. There are technologies available that can aid standardized and transparent decision making. For this to actually happen, however, prompt and concerted efforts are needed on the part of everyone involved: health insurers, patient advocacy groups, policy makers, and the medical profession.

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Selected results

Project
Breast cancer and young women: tumor profile, treatment, outcome and effect of pregnancies
Registre genevois des tumeurs, Université de Genève, Genève
CHF 268 650.– | Duration: 1.1.2016 – 31.3.2020 | KFS-3713-08-2015

Project coordinator
Prof. Elisabetta Rapiti Aylward, MD | elisabetta.rapiti@unige.ch

Evaluating characteristics of breast cancer in young women

For young women, the risk of breast cancer recurrence, even 20 years after treatment, is higher than for women diagnosed with breast cancer at age 40 and older. This means it is important to monitor young patients with breast cancer for a longer time than has been done in the past, as a study funded by the Swiss Cancer Research foundation has discovered.

Breast cancer is more frequent after the age of 50, but since the turn of this century, breast cancer among young women has increased in Europe. "We do not know the reason for this. There are probably many factors involved – such as overweight, birth control pills, and the ever-earlier onset of menstruation," says Elisabetta Rapiti, director of the Geneva Cancer Registry. As women under age 45 are not invited to breast cancer screening programs, they are more likely to be diagnosed with an advanced stage. In addition, breast cancer in young patients more frequently shows aggressive biological characteristics than breast cancer in older women.

Despite these worrying signs, up to now there has been no systematic overview available on the epidemiologic situation of young women patients with breast cancer, says Rapiti. For this reason, she and her team examined data stored in the Geneva Cancer Registry and evaluated the data on a total of 1586 patients who were aged 45 and younger when their first breast cancer was diagnosed in the years from 1970 to 2012. Two thirds (1051) of the patients did not have a recurrence, but 265 patients had local recurrences, and 403 patients had distant metastases. A comparison of the patients younger than age 40 with patients who were diagnosed between 40 and 45 years of age revealed the following: "The younger the women, the higher the risk of recurrence," Rapiti explains.

According to the research team, the strengths of this study include the high accuracy and reliability of data available at the Geneva Cancer Registry. "Thanks to the strong, high-quality network of experts that operates in this geographically restricted area, we are confident that all available information was captured," note the researchers in their final report on this research project funded by the Swiss Cancer Research foundation. From the fact that breast cancer recurs in some women only after 20 or 25 years, the researchers conclude that for this group of patients, follow-ups should not end after ten years but should continue, if possible.

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List of approved research projects in 2019

More information about the funded projects can be found on www.krebsliga.ch/researchprojects

Total funds allocated: CHF 2 465 300.–

Auer Reto | Effects of electronic nicotine delivery systems (ENDS) for smoking cessation on cancer-related health outcomes: 12-, 24-months follow-up of the efficacy, safety and toxicology of ENDS (ESTxENDS) randomized controlled trial
Berner Institut für Hausarztmedizin, Universität Bern, Bern
CHF 372 300.– | Duration: 1. 6. 2019 – 31. 5. 2022 | KFS-4744-02-2019

Berezowska Sabina Anna | Molecular epidemiology of lung cancer brain metastases
Institut für Pathologie, Universität Bern, Bern
CHF 365 500.– | Duration: 1. 10. 2019 – 30. 9. 2022 | KFS-4694-02-2019

Bochud Murielle | Dietary intake, overweight, and late effects development in childhood cancer survivors
Département Epidémiologie et Systèmes de Santé, Unisanté – Centre universitaire de médecine générale et santé publique, Lausanne
CHF 359 450.– | Duration: 1. 7. 2019 – 30. 6. 2022 | KFS-4722-02-2019

Guseva Canu Irina | Examining cancers and labour indicators to assess the burden (ExCaLIBur)
Département Santé au travail et environnement, Unisanté – Centre universitaire de médecine générale et santé publique, Lausanne
CHF 226 800.– | Duration: 2. 9. 2019 – 1. 1. 2023 | KFS-4699-02-2019

Hemkens Lars | Emerging trends and developments in cancer treatment innovation: expansion of the CEIT-cancer project (exCEIT)
Departement Klinische Forschung, Universitätsspital Basel, Basel
CHF 233 500.– | Duration: 1. 4. 2020 – 31. 3. 2022 | KFS-4842-08-2019

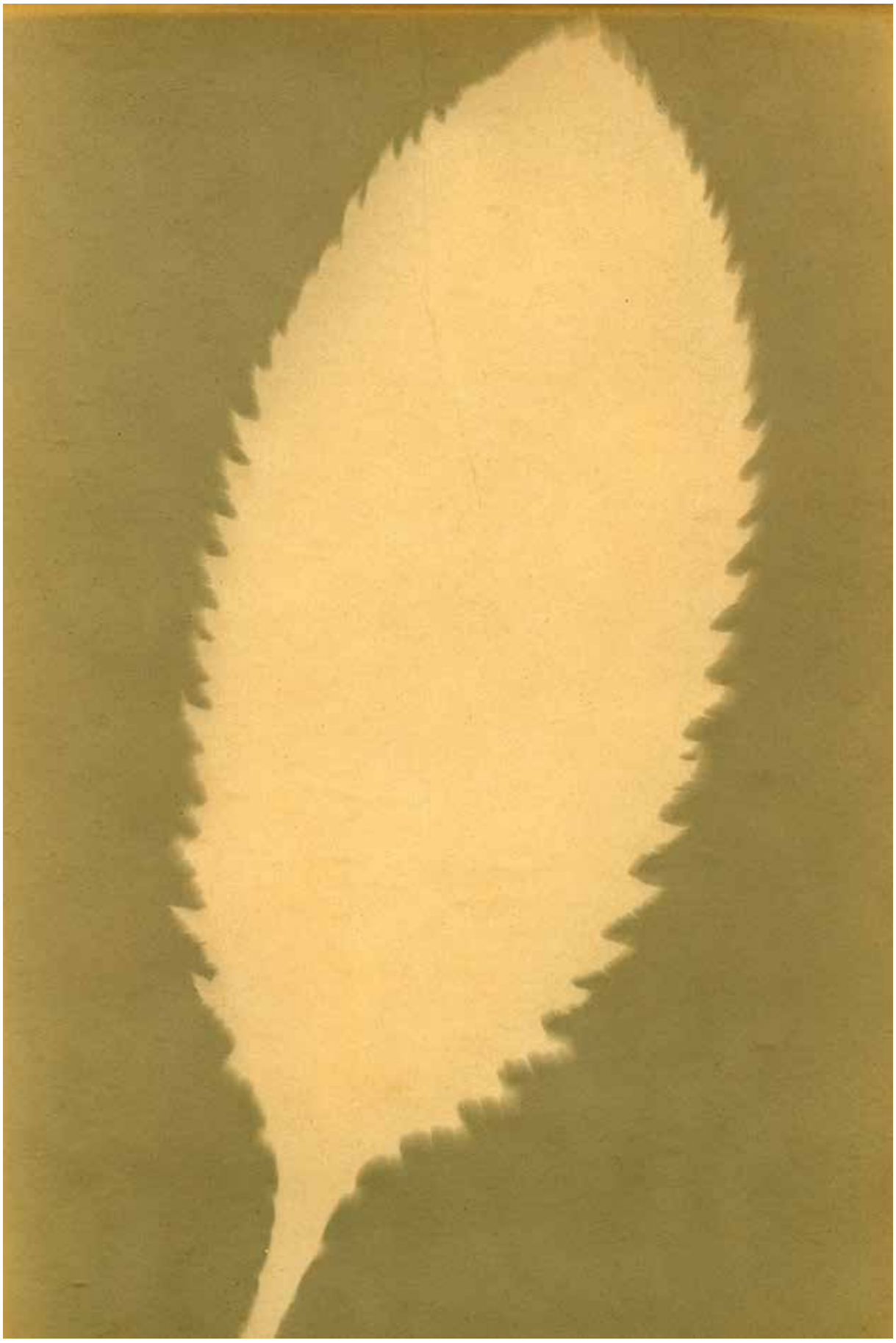
Kaderli Reto Martin | Distant metastases and long-term survival after complete resection of neuroendocrine tumours of the appendix: an international multicentre study (SurvivApp)
Universitätsklinik für Viszerale Chirurgie und Medizin, Inselspital, Bern
CHF 329 500.– | Duration: 1. 7. 2019 – 31. 12. 2022 | KFS-4741-02-2019

Wandeler Gilles | Hepatocellular carcinoma surveillance in people living with chronic hepatitis B infection in Senegal and Zambia
Universitätsklinik für Infektiologie, Inselspital, Bern
CHF 374 500.– | Duration: 1. 9. 2020 – 31. 8. 2024 | KLS-4879-08-2019

Approved bursaries in 2019

Correia Dora | Practice pattern impact in cancer outcome in the paediatric proton consortium registry prospective cohort
Destination: Massachusetts General Hospital, Boston, USA
CHF 98 750.– | Duration: 1. 1. 2020 – 30. 6. 2021 | BIL-KFS-4755-02-2019

Tinguely Pascale | Local thermal ablation as alternative to surgical resection for colorectal cancer liver metastases – population-based analyses on survival, local recurrence prediction and health economic relevance
Destination: Karolinska Institute, Stockholm, Sweden
CHF 105 000.– | Duration: 1. 1. 2020 – 31. 12. 2021 | BIL-KLS-4894-08-2019



Cost-benefit ratio of cancer drugs

Introduction and research question

The number of cancer drugs approved in Switzerland has risen steadily in recent years[1]. Health costs in general have increased at the same time[2]. To ensure access to the most important cancer drugs, there has been an increasing demand for a real and consistent relationship between the cost of a drug and its clinical benefit. That means that for drugs with high clinical benefit, a higher price is justified, whereas for drugs with low clinical benefit, a lower price is indicated. This accords also with Swiss law, based on which the Federal Office of Public Health must set the price of the drug taking into equal account price comparisons with other countries and a therapeutic cross-comparison (Art. 65b of the Health Insurance Ordinance of 27 June 1995, SR 832.102).

Two internationally recognized oncology associations, the European Society for Medical Oncology (ESMO) and the American Society of Clinical Oncology (ASCO), developed frameworks that aid in the evaluation of the clinical value of cancer drugs: the ESMO Magnitude of Clinical Benefit Scale (ESMO-MCBS) and the ASCO Value Framework (ASCO-VF)[3,4]. These frameworks include, for example, assessment of clinical trial endpoints like overall survival, progression free survival, and also quality of life and toxicity. Although the two frameworks for assessing clinical value take different approaches, they usually produce comparable findings: A drug will show a high or low clinical value in both systems[5].

In our study, which was published this year in The Lancet Oncology[6], we examined whether there is an association between cancer drug prices and their clinical benefit. We assessed this association for five countries: Switzerland, Germany, England, France, and the United States.

Prof. Kerstin Noëlle Vokinger, PhD, MD, LL.M.
Assistant professor at the University of Zurich

No relation between cost and benefit

First, we identified all new cancer drugs that were approved between 2009 and 2019 by the US Food and Drug Administration (FDA), the regulatory authority for food and drugs in the United States, and the European Medicines Agency (EMA), the regulatory authority for drugs in the European Union. We included a total of 47 cancer drugs for solid tumours to assess the association between cost and clinical benefit. Most of the indications were for melanoma (malignant skin cancer, 8 medications), breast cancer (7 medications), lung cancer (7 medications), and prostate cancer (4 medications).

We then calculated the monthly drug treatment costs in the five countries. We chose monthly drug treatment cost (and not the package price, for instance) for better comparability of the costs. After all, it is possible that a medication is taken only once a month, whereas others are taken several times a month.

The highest drug prices were found for the United States, followed by England, Switzerland, Germany, and France. Whether or not England is really in second place (or whether Switzerland is) cannot be assessed conclusively, as England internally grants rebates on numerous medications that are not publicly known, and thus the prices actually paid for the drugs are lower than the official prices (which we used in our study).

We assessed clinical benefit using both ASCO-VF and ESMO-MCBS. If a drug was available in several different packages with different prices, we took the lowest priced package as a reference. We then analysed whether there was an association between the calculated monthly treatment costs and clinical benefit.

Using the ESMO-MCBS, there were no significant associations between monthly drug treatment cost and clinical benefit of the cancer drugs in all five countries. Using the ASCO-VF, there was a significant association only for France (and not for Switzerland, Germany, England, or the United States).

An example is cabazitaxel, a drug approved for treatment of prostate cancer. In comparison, it shows lower clinical benefit than abirateron (ESMO-MCBS 2 versus 4), but it costs the same as or more than abirateron (Switzerland: $5292 versus $3475, Germany: $3311 versus $3340, England: $4554 versus $3568, USA: $10 531 versus $10 887).

The findings for the United States are not very surprising, as drug prices in the United States are not regulated. For the European countries, however, the findings are unexpected, as the laws provide that in price setting, the clinical benefit of the drug must also be taken into account.

Implications for Switzerland

The results of our study show that in Switzerland among other countries, the clinical benefit of cancer drugs is not sufficiently reflected in the price of the drugs. This must change. It can be assumed that in the near future, more cancer drugs will come on the market. That makes it all the more important that the clinical benefit of a drug is considered in the price. As a clinical value assessment system for use in price negotiations between the Federal Office of Public Health and the pharmaceutical manufacturer, the ESMO-MCBS (or the ASCO-VF) could be a good basis.

Considering the rising health costs, it is essential that cancer drugs with high clinical benefit have a higher price and cancer drugs with low clinical benefit have a lower price. This can also create the right incentives within drug development, which serves patient well-being.

Acknowledgement

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Prof. Kerstin Noëlle Vokinger, PhD, MD, LL.M.
Kerstin Noëlle Vokinger studied law and medicine jointly at the University of Zurich and completed doctorates in both fields. She completed the Master of Laws program (LL.M.) at Harvard Law School, and she was a post-doctoral research fellow at Harvard Medical School. Since May 2019, Vokinger has been an assistant professor at the Institute of Law at the University of Zurich as well as affiliated faculty at Harvard Medical School. In her research, she works in the area of regulatory sciences at the intersection of medicine, law, and technology, with a focus on assessment of clinical value, price setting, and regulation of cancer drugs.
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Selected results

Project
Harnessing social media in adolescent and young adult (AYA) oncology.
The views of AYA and healthcare providers: an exploratory study
Institut für Bio- und Medizinethik, Universität Basel, Basel
CHF 74 750.– | Duration: 1.1.2019 – 1.5.2020 | HSR-4361-11-2017

Project coordinator
Eva de Clercq, PhD | eva.declercq@unibas.ch

Seeing not only the risks but also the opportunities in social media use

Many health care professionals are reluctant to interact with their young patients online. For good reason, as it is difficult to maintain the necessary professional distance on social media channels such as Instagram or Facebook. But that should not keep nurses and physicians from speaking with their patients about how they use social media, concludes a research project funded by the Swiss Cancer Research foundation.

Referred to as "digital natives", most adolescents and young adults with cancer use Instagram, Facebook, TikTok, or Twitter to learn more about their cancer and to find mutual support in exchanges with friends, family, or other patients with cancer. With this possibility of self-empowerment, social media are contributing to a paradigm change in the health care system, where the traditional paternalistic doctor-patient relationship is giving way more and more to a modern and patient-centred model, says bioethicist Eva de Clercq at the University of Basel.

In her research project, which was funded within the Swiss Cancer Research foundation's programme to strengthen health services research in oncology, de Clercq and her colleague Michael Rost interviewed young people with cancer and spoke with health care professionals in Switzerland. In addition, they took a critical look at the research literature on new means of communication in oncology. On that basis, the researchers can now draw a differentiated picture of the use of digital networking.

"Many nurses and physicians hesitate to enter the social media sphere of their patients," explains de Clercq. That is because in virtual space, worlds that are separate in analog life flow seamlessly into each other. This "context collapse" makes it difficult to maintain professional boundaries. It is also not very helpful that current guidelines and recommendations focus on behaviour that should be avoided and disregard constructive uses of social media.

"In training courses, health care professionals should learn more about trends in technology and media, so that in their conversations with young patients they can point out benefits and risks," says de Clercq. In her view, it would be desirable for medical institutions and self-help groups for young people with cancer to be more connected online.

Unfortunately, the needs and preferences of this group of patients are too often underestimated and misjudged, reports de Clercq. For this reason, social media has a great and up-to-now unexploited potential to improve health services for young patients with cancer on many levels: "Social media can be important allies, not only in providing access to information but also in psychosocial care and cancer treatment adherence."

List of approved research projects in 2019/2020

More information about the funded projects can be found on www.krebsliga.ch/researchprojects

Total funds allocated: CHF 982 650.–

Arditi Chantal | The Swiss Cancer Patient Experiences-2 (SCAPE-2) study: a national survey
Département Epidémiologie et Systèmes de Santé, Unisanté – Centre universitaire de médecine générale et santé publique, Lausanne
CHF 220 000.– | Duration: 1. 7. 2020 – 30. 6. 2022 | HSR-4946-11-2019

Bähler Caroline | Primary care continuity in Swiss cancer patients and its impact on avoidable hospitalisations and intensity of treatment at the end of life: a follow-up project
Abteilung Gesundheitswissenschaften, Helsana-Gruppe, Zürich
CHF 69 000.– | Duration: 1. 11. 2020 – 31. 10. 2021 | HSR-4944-11-2019

Beyer Jörg | Improving outcomes for men with germ-cell cancer through a supra-regional second-opinion online portal and national expert advice
Universitätsklinik für Medizinische Onkologie, Inselspital, Bern
CHF 178 000.– | Duration: 1. 6. 2020 – 31. 5. 2023 | HSR-4947-11-2019

Kuehni Claudia E. | Improving access to screening for hearing loss after childhood cancer – a novel community-based approach
Institut für Sozial- und Präventivmedizin, Universität Bern, Bern
CHF 247 850.– | Duration: 1. 5. 2020 – 30. 4. 2023 | HSR-4951-11-2019

Maillard Julien | Changes of health-related quality of life after high-risk abdominal surgical oncology; a prospective observational study; ChangeQol study
Service d'anesthésie, Hôpitaux universitaires de Genève, Genève
CHF 73 750.– | Duration: 1. 6. 2020 – 30. 11. 2022 | HSR-4949-11-2019

Puhan Milo | Patient preferences regarding benefits and harms of advanced prostate cancer treatments in Switzerland
Institut für Epidemiologie, Biostatistik und Prävention, Universität Zürich, Zürich
CHF 49 650.– | Duration: 1. 5. 2020 – 30. 4. 2021 | HSR-4950-11-2019

Struja Tristan | PrevenT ReAdmissions of Cancer patients at the KSA – The TRACK Project: A retrospective, case-control, single-center study
Onkologie/Hämatologie, Kantonsspital Aarau, Aarau
CHF 58 700.– | Duration: 1. 4. 2020 – 30. 9. 2020 | HSR-4955-11-2019

Tschudin Sibil | Oncofertility after-care in Switzerland: assessment of the current state and the needs of cancer survivors and health care professionals and preparation of a model of care
Gynäkologische Sozialmedizin und Psychosomatik, Frauenklinik, Universitätsspital Basel, Basel
CHF 85 700.– | Duration: 1. 4. 2020 – 31. 3. 2023 | HSR-4945-11-2019

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