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 2018

Imprint

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Michael Sieber (*1976 in Kandersteg) has been working as a freelance photographer since 2005. Part of the pictures in this report come from the series "Centovalli", in which Sieber looks out of the moving train through rainy windows at remote landscapes and the untouched gorges of the Melezza. "As a passenger and spectator, I recognize an aesthetic in the chaos of the wilderness," Sieber notes.

The photographs in the "Botanical Prisoners" series are at least as astounding: they surprise with the contrasts that result from the collision of the irrepressible organic growth forms of plants with the rigid constructions of glass and metal greenhouses.

michaelsieber.com

Some of the pictures in the "Botanical Prisoners" series were created with the kind permission of the Succulent Collection of Grün Stadt Zürich, the Botanical Garden of the University of Zurich, and the Botanical Garden of the University of Bern.

Cancer Research in Switzerland

Edition 2019

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Editorial

We live in interesting times, especially when it comes to advances in the treatment of cancer. The latest development is a treatment – only recently approved – that in many ways is no longer comparable to conventional medications. A classic drug is a chemically clearly defined substance. But the new treatment takes the patient's own immune cells, genetically modifies and multiplies them in the laboratory, and then reintroduces them to the patient, where – thanks to the new gene that was added to the cells in the laboratory – they can fight the degenerated tumour cells with renewed strength.

For some patients, this treatment brings about spectacular successes. But almost equally impressive is the price that the manufacturers demand for the modified patient cells: several hundred thousand francs! And that although the modified cells are a medical service that was developed with public funding at academic research institutions. Many hospitals in Switzerland are able to take patients' immune cells and modify them genetically. We need to pool this highly specialized knowledge, now spread over several hospitals, and commit to common goals: The aim is to investigate and develop further treatments as a complement to the commercial products, so as to better exploit the great potential of cell therapies.

Thomas Cerny

Gilbert Zulian

The time is ripe for a new national platform for cell therapies: Together with a number of other organizations, the Swiss Cancer Research foundation has started a nationwide network for research and development of new cell therapy approaches. We are committed to contributing towards improved collaboration and to financing a coordination centre. We are convinced that if we join forces, this will not only strengthen Switzerland as a research centre but also benefit people with cancer in the future. Thanks to the new treatment methods that will be developed jointly, we will be able to treat more patients more successfully.

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

PD Gilbert Zulian, MD
President of the Swiss Cancer League

Drawing on the wealth of experience to improve treatments

In 2018 the Swiss Cancer Research foundation, the Swiss Cancer League, and the cantonal and regional leagues gave 30.1 million francs in funding to 175 research institutions and research projects. This sum is a new record that was made possible only by the trust and support of the charitable donors, to whom we express our heartfelt thanks.

What the Swiss Paediatric Oncology Group (SPOG) accomplished in 1976 was a pioneering achievement. At a time when only isolated regional cancer registries were being established for adults, the childhood cancer specialists set up the nationwide collection of information on diagnosis, treatment, and disease progression of cancer in children and adolescents. Today, this collection – the Swiss Childhood Cancer Registry (SCCR) – contains data on more than 12 000 persons. The SCCR has received financial support from the Swiss Cancer Research foundation from its beginnings.

The data allow physicians to learn from the well-documented cases. This store of knowledge aids the continuous improvement of treatment and the obtaining of insights on the causes of the disease. Recently, for instance, SCCR researchers demonstrated for the first time that children who reside less than 100 meters' distance from motorways have a higher risk of leukaemia.

Analyses of that kind are all the more meaningful the more reliable and complete the data are. According to Claudia Kühni and Verena Pfeiffer, the two co-heads of the SCCR, "for children up to age 15, more than 95 % of cases are documented in the registry. This shows that the nine childhood cancer centres in Switzerland work very closely and well with the SCCR". Coverage is not as high for young people aged 16 to 19. They are often too old for paediatric oncology but too young for adult oncology. For this reason, "in research especially they are at risk of not being included in either one," says Kühni.

New Cancer Registration Act

But the new Cancer Registration Act, which comes into force on 1 January 2020, provides for a reporting obligation for all new cancers in Switzerland. Pfeiffer and Kühni hope that with the new law, the data on young people aged 16 to 19 will soon approach complete coverage. However, "with the new Cancer Registration Act there are not only advantages," explains Pfeiffer. The disadvantage is that the Swiss Confederation will cover only the costs connected with collecting and

Rolf Marti, PhD
Head of Research, Innovation & Development, Swiss Cancer League

counting the cancers, or in other words, only the costs for monitoring. Funds will have to be raised separately for the research activities based on the data. And here you sense Kühni and Pfeiffer's great commitment: They want to continue to make the constantly growing wealth of experience available to researchers. This is also to the benefit of the young patients.

"For many families affected by cancer, there is some consolation in knowing that with their story, they are contributing to better treatments in the future," says Kühni. And indeed, medicine has made spectacular progress in the treatment of childhood cancer. As the data in the SCCR demonstrate, the cancer survival rate in the 1980s was about 60 %. Today, a child with cancer has, statistically, a ten-year survival rate of 85 % to 90 %.

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.

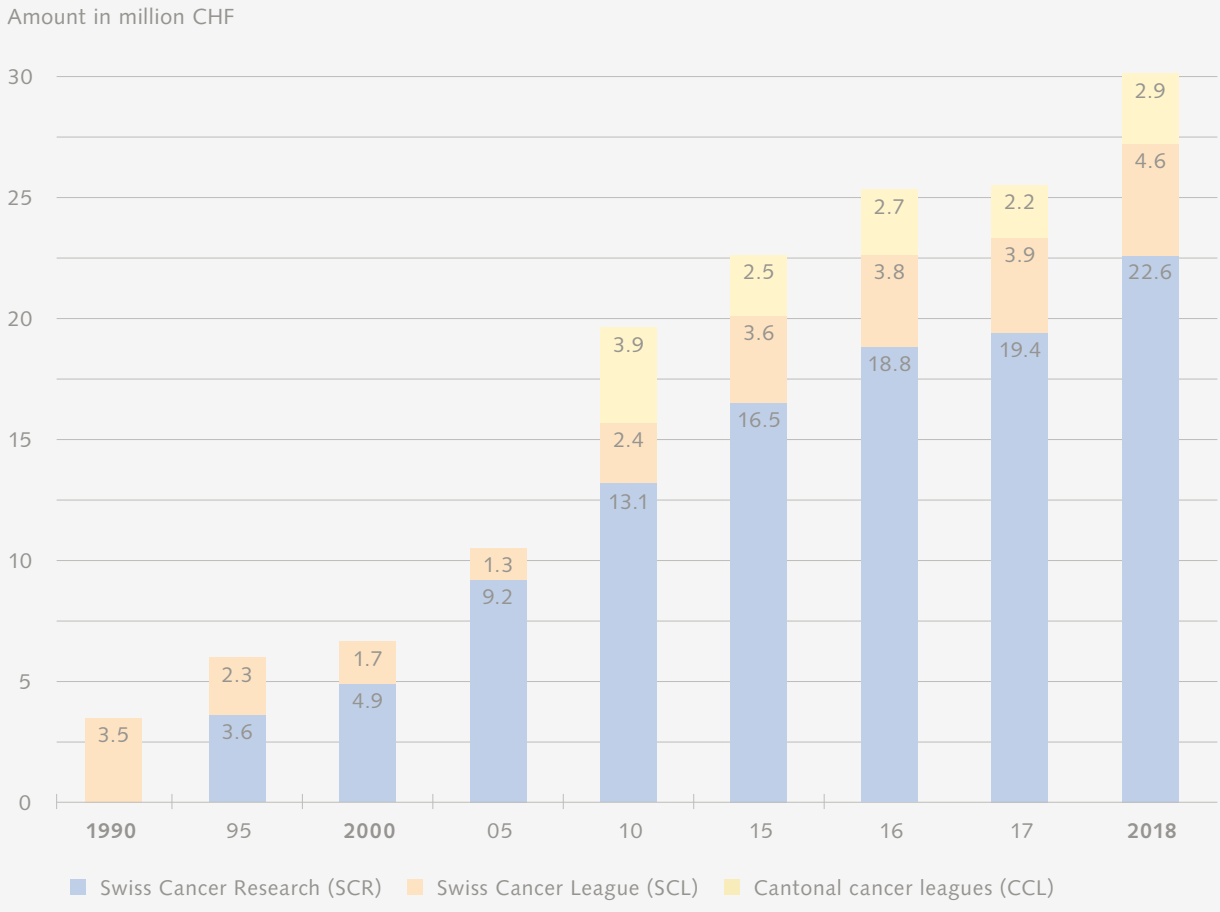
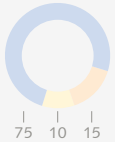


Table 1
Research funding by SCR, SCL, and CCL in overview

Number of grants approved and amount granted in 2018 (all funding areas)

	Number of grants approved	Amount granted in kCHF	Proportion of total funding in %
Total SCR, SCL, and CCL			
Independent research projects	112	24 117	80
Bursaries	8	924	3
Programme for health services research	7	1 393	5
Research organizations and institutions	12	3 340	11
Programmes, organizations and conferences	36	371	1
Total	**175**	**30 145**	**100**
SCR			
Independent research projects	59	18 124	80
Bursaries	5	566	2
Programme for health services research	7	1 393	6
Research organizations	6	2 400	11
Programmes, organizations and conferences	13	180	1
Total	**90**	**22 663**	**100**
SCL			
Independent research projects	14	3 872	85
Bursaries	2	308	7
Research organizations	1	200	4
Programmes, organizations and conferences	23	191	4
Total	**40**	**4 571**	**100**
CCL			
Independent research projects	39	2 121	73
Bursaries	1	50	2
Research institutions	5	740	25
Programmes, organizations and conferences	n. s.	n. s.	–
Total	**45**	**2 911**	**100**

n. s. = not specified



(percentage of funds)

The other side of the success story

However, as the registry documents the long-term course of the disease, the data also show the other side of this success story: Successfully treated young patients often pay for their survival with health problems later on. Even decades after treatment, the aggressive therapies can have late effects, including hearing impairments, infertility, and sometimes fatal cardiovascular problems and secondary tumours.

"Our data show that many childhood cancer survivors should receive aftercare for the rest of their lives," Kühni says. However, the reality in Switzerland is different. Problematic is mainly the transition from paediatrics to adult medicine. As long as the former patients are under the care of their paediatric oncology department, their aftercare is ensured. But when they reach the age of majority, they are discharged, often without having found for them an appropriate long-term care option with regular follow-ups.

The SCCR is committed to improving this situation. It is involved in the introduction of a 'Survivorship Passport' or 'Passport for Care'. This is a document that contains individual recommendations for aftercare. It is meant to be given to former patients so that they can take over a part of the control of their aftercare.

The Swiss Cancer League (SCL), too, feels it is very important that people with cancer become able to deal with their disease in a self-determined way. For instance, the SCL promotes further development and recognition of oncological rehabilitation in Switzerland and supports people with cancer in finding their way back to the world of work after treatment, when possible. Together with the cantonal and regional cancer leagues (CCL) and the Swiss Cancer Research foundation (SCR), the SCL also supports cancer research projects that will generate results that benefit patients with cancer.

More than 30 million francs

In 2018, the SCR, the SCL, and the CCL together provided support in the total amount of 30.1 million francs (Figure 1; Table 1) for 175 different research institutions and research projects. This funding sum for the year is a new record. Three quarters of all funds granted came from the SCR; the SCL contributed 15 % and the CCL 10 %.

As in previous years, universities and university hospitals in Zurich, Lausanne, Basel, and Bern were the most successful cancer research centres in the competition for funding (Table 2). Researchers in the research location Zurich (including ETHZ) received in total over 7 million francs, which is more than one fourth of the

Table 2
Distribution of cancer research funding by SCR and SCL to the research institutions in 2018

Research institutions	Number of projects	Amount in kCHF	Proportion in %
Kantonsspital Aarau	1	105	0.4
Universität/Inselspital Bern	17	2 713	11.2
Universität/Universitätsspital Basel	15	3 799	15.6
IOSI Bellinzona	2	577	2.4
IRB Bellinzona	2	691	2.8
Université de Fribourg	2	704	2.9
Université/HUG Genève	6	1 135	4.7
EPF Lausanne	4	1 046	4.3
Université/CHUV Lausanne	17	4 661	19.2
Kantonsspital Luzern	1	351	1.4
Kantonsspital St. Gallen	4	649	2.7
PSI Villigen	2	569	2.3
Kantonsspital Winterthur	1	32	0.1
ETH Zürich	4	1 053	4.3
Universität/Universitätsspital Zürich	21	5 870	24.1
Brustzentrum Zürich	1	370	1.5
Total	**100**	**24 325**	**100**

Abbreviations

CHUV	Centre Hospitalier Universitaire Vaudois
EPF	Ecole Polytechnique Fédérale
ETH	Eidgenössische Technische Hochschule
HUG	Hôpitaux Universitaires de Genève
IOSI	Istituto Oncologico della Svizzera Italiana
IRB	Istituto di Ricerca in Biomedicina
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

	2017		2018	
	Grant applications	Amount in kCHF	Grant applications	Amount in kCHF
All projects				
Received/applied for	183	48 745	218	62 633
Recommended	89		118	
Approved	70	18 995	81	22 677
Success rate	38 %	39 %	37 %	36 %
Basic research				
Received/applied for	92	30 635	98	32 880
Recommended	51		67	
Approved	33	10 212	39	12 534
Success rate	36 %	33 %	40 %	38 %
Clinical research				
Received/applied for	44	11 666	71	20 581
Recommended	19		33	
Approved	18	4 495	26	7 714
Success rate	41 %	38 %	37 %	37 %
Psychosocial research				
Received/applied for	6	1 335	8	1 808
Recommended	4		7	
Approved	4	829	6	1 227
Success rate	67 %	62 %	75 %	68 %
Epidemiologic research				
Received/applied for	12	2 920	8	2 382
Recommended	8		3	
Approved	8	2 066	2	521
Success rate	67 %	71 %	25 %	22 %

	2017/2018		2018/2019	
	Grant applications	Amount in kCHF	Grant applications	Amount in kCHF
Health services research				
Received (letter of intent)/applied for	29	4 231	33	4 982
Invited (full proposal)/applied for	13	2 189	10	1 066
Recommended	7		8	
Approved	7	1 393	8	681
Success rate	54 %	63 %	80 %	64 %

total funding nationwide. Researchers in Lausanne (including EPFL) received over 5.6 million francs for 21 research projects, and researchers in Basel were granted almost 3.8 million francs for 15 research projects.

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 2018, a total of 185 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 110 research projects as solid and promising – and recommended them for funding. However, due to the limited funding available, the SCR foundation board could approve only 73 research projects for funding, which is not quite 40 % of all proposals submitted. For the other 37 high-quality research projects, there was unfortunately not enough funding for independent research available: Even though these projects were rated highly by the Scientific Committee, the SCR and the SCL had to inform the project heads that they would not receive a grant.

Competition for the limited funds available was about as high as in 2017. One noticeable difference in the success rates for grant applications was in the area of epidemiological research: In 2017, two thirds of all research proposals submitted received funding; in 2018, however, this was only one fourth of the research projects.

Unlike in all other areas, research projects 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 research programme; the panel members include also persons with demonstrated expertise in, for example, health economics or nursing sciences (see p. 28).

Performance agreements for financing services

In the strategy of the two funding organizations SCR and SCL, approximately 60 % of the funds is earmarked for what is called patient-centred research, the aim of which is to produce results that as far as possible directly benefit patients and their families. In the area of independent research projects, this target is not achieved. However, the SCR and the SCL also support six different research organizations (Table 4). The funds compensate the organizations for central and indispensable services that benefit clinical and epidemiological research in Switzerland.

These 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 figures on the prevalence of cancer 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 expenditure, these organizations receive compensation based on performance agreements. The performance agreements define in a clear and binding way the requirements regarding

Table 4
Supported research organizations

Funding in the years 2012–2018

Amount in kCHF

	2012	2013	2014	2015	2016	2017	2018
Swiss Group for Clinical Cancer Research (SAKK)	600	*900	*1 050	*1 100	*1 150	*1 300	*1 300
International Breast Cancer Study Group (IBCSG)	560	500	450	400	350	350	350
National Institute for Cancer Epidemiology and Registration (NICER)	200	250	250	250	250	250	250
International Extranodal Lymphoma Study Group (IELSG)	200	200	200	250	250	350	350
Swiss Paediatric Oncology Group (SPOG)	150	150	150	150	200	250	250
Swiss Childhood Cancer Registry (SCCR)	50	75	75	100	100	100	100
Total	**1 760**	**2 075**	**2 175**	**2 250**	**2 300**	**2 600**	**2 600**

*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 (radiotherapy, chemotherapy, surgery), and establish new treatment standards. → www.sakk.ch

International Breast Cancer Study Group (IBCSG)
Since 1977 the IBCSG has conducted academic clinical trials with the aim to improve treatment of 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 harmonizes the work of the 14 cantonal and regional cancer registries. It compiles the cancer data collected in the cantons, assures the quality of the data, and analyses the data at the national level. These 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 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 (SKKR)
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 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. → www.kinderkrebsregister.ch

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 2018, the SCR paid out a total of 2.4 million francs to the six research organizations. Another 200 000 francs were provided by the SCL (Table 4).

Rolf Marti, PhD
Rolf Marti has headed the Research, Innovation & Development department (formerly: Scientific Office) since 2003. He is a member of the managing board of the Swiss Cancer League and director of the Swiss Cancer Research foundation office.
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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 works towards a world where fewer persons get cancer, fewer persons suffer the consequences and die of cancer, more persons are cured of cancer, and persons with cancer and their families receive care and support in all phases of cancer and in dying. The Cancer League brings together the national umbrella organization headquartered in Bern and 19 cantonal and regional cancer leagues. The SCL supports the cantonal cancer leagues through knowledge transfer, provision of services, developments, and coordination at the national level. It provides information on risk factors and early detection measures and runs national cancer prevention programmes. It offers specific continuing education courses for a variety of occupational groups and funds cancer research.

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Cantonal cancer leagues (CCL)

The 19 cantonal and regional cancer leagues provide persons with cancer and their family members with individual advice from 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 help with the reorganization of the clients' social and financial situation. The CCL also 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 organize group meetings and courses where persons with cancer can talk about their fears and experiences and learn ways to deal 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 are at work in Switzerland and in Liechtenstein. The CCL do not all offer the same services. The type and extent of services depends heavily on the financial and human resources of the individual cancer league as well as on the services made available by other providers.

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

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

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

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

Silvio Inderbitzin, PhD
St. Niklausen

Prof. Murielle Bochud, MD
Unisanté Lausanne
Epidemiologic research
representative

Treasurer

Gallus Mayer
Former Banking specialist
St.Gallen

The board of the Swiss Cancer League

The highest body of the Swiss Cancer League (SCL) is the delegates' assembly, to which the representatives of the cantonal and regional cancer leagues belong. Strategic management of the SCL is the responsibility of the board. Board members represent different specialties in the fight against cancer and also the different regions of Switzerland.

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)

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

Lucienne Bigler-Perrotin
Managing director
Ligue genevoise contre le cancer

Markus Notter, MD
Radiation Oncology
Lindenhofspital Bern

Christoph Kurze
Managing director
Krebsliga Graubünden

Brigitta Wössmer, PhD
Head psychologist of Psychosomatics
Universitätsspital Basel

Treasurer

Gallus Mayer
Former Banking specialist
St. Gallen

Karin Zimmermann, PhD
Registered nurse / scientific staff
Inselspital Bern

The Scientific Committee

Members of the Scientific Committee in April 2018 (from left to right): Pedro Romero, Sarah Dauchy, Jürg Schwaller, Mark Rubin, Primo Schär, Joerg Huelsken, Maria Blettner, Andrea Alimonti, Simone Benhamou, Aurel Perren, Emanuele Zucca, Jörg Beyer, Nancy Hynes (president), Beat Schäfer, Martin Pruschy, Sabine Werner, Silke Gillessen, Rolf Marti (head of Research, Innovation & Development department), Tatiana Petrova, Peggy Janich (head of Research Funding), Sophie Pautex.

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 members of the Scientific Committee are recognized experts with outstanding performance and achievements. Together they cover all areas relevant to cancer research. The members of the Scientific Committee represent the following disciplines:

- Basic research: 7 members
- Clinical research: 7 members
- Psychosocial research: 2 members
- Epidemiologic research: 2 members

The Scientific Committee reviews research grant applications according to clear criteria (see box, "Criteria for high-quality cancer research"). In the evaluation of research grant applications, the main criterion is always whether a research project can generate important new findings that will contribute towards improving the prevention or treatment of cancer. The Scientific Committee also rates the originality and feasibility of the research projects – and recommends only the best projects for approval. It attaches particular importance to patient-centred research.

Each research grant application is reviewed carefully by several experts. In addition to two members of the Scientific Committee, also international reviewers evaluate the quality of the grant application (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. Based on the ranking list the boards of the SCR and SCL decide which projects will be approved for funding. As the financial means are limited, not all high-quality grant applications can be funded, unfortunately. Funding goes exclusively to industry-independent research projects.

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.

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.

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

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

Clinical research

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

until June 2018

Prof. Silke Gillessen, MD
Onkologie/Hämatologie
Kantonsspital St. Gallen
St. Gallen

since July 2018

Prof. Markus Joerger, MD
Onkologie/Hämatologie
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Prof. Aurel Perren, MD
Institut für Pathologie
Universität Bern
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Prof. Martin Pruschy, PhD
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Prof. Mark A. Rubin, MD
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Research (DBMR)
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Prof. Beat W. Schäfer, PhD
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Prof. Emanuele Zucca, MD
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Psychosocial research

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Gustave Roussy
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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

until December 2018

Prof. Maria Blettner, PhD
Institut für Medizinische Biometrie,
Epidemiologie und Informatik (IMBEI)
Johannes Gutenberg-Universität Mainz
Mainz, Germany

since January 2019

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 2018 the Swiss Cancer League awarded the Cancer Prize to George Thalmann for his valuable support and his donating of his expertise on prostate cancer and testicular cancer for many years. The Recognition Award 2018 was given to Pirmin Schwegler, footballer, for his efforts on behalf of children and adolescents with cancer. The Swiss Cancer League awarded the Cancer Medal to Bea Heim, health policymaker. And finally two recipients, a research group in Spain and a research group in Switzerland, have won the Swiss Bridge Award.

In its advice and support work the Swiss Cancer League relies on the expertise of specialists. George Thalmann, since 2010 chairman and director of the Department of Urology, University Hospital of Bern (Inselspital), has contributed his knowledge on male reproductive cancers and on the effects of cancer on sexuality and fertility as a specialist editor of several brochures. The brochures and publications of the Swiss Cancer League are aimed at persons with cancer, family members, interested persons, and professionals.

In addition, George Thalmann has provided his expertise directly to persons with cancer who turn to him with questions and concerns in online consultations through the *Krebsforum* offered by the counselling and information service of the Swiss Cancer League. Thanks to Thalmann's donation of his time and advice, many affected persons benefit from his huge wealth of experience in the areas of prostate cancer and testicular cancer.

Kathrin Kramis (CEO of the Swiss Cancer League, left) and Jakob Passweg (former president of the Swiss Cancer League, right) present the Cancer Prize 2018 to George Thalmann (centre).

Ori Schipper, PhD
Communication officer, Swiss Cancer League

Bea Heim, health policymaker from the Social Democratic Party (centre) holds the Cancer Medal presented to her by Kathrin Kramis (CEO of the Swiss Cancer League, left) and Gilbert Zulian (president of the Swiss Cancer League, right).

The Swiss Cancer League is grateful that with George Thalmann, it can rely on a competent consultant. Thalmann's vast expertise and selfless and generous donation of his knowledge and experience are an enormous enrichment.

Bea Heim was awarded the Cancer Medal 2018, in honour of her efforts in health policy also benefitting patients with cancer. Heim, Social Democratic Party member of the National Council, makes the voices of persons with cancer heard at the political level. For many years, she has unceasingly called attention to the urgent need for action in the area of care. In addition, Heim actively supports many concerns that are key issues for the Swiss Cancer League. For example, Heim demands affordable prescription drugs – and thus fights side by side with the Swiss Cancer League against a two-tier system of health care and for equal access to medical treatments for all persons, poor or rich.

Cancer Prize
With the Cancer Prize the Swiss Cancer League recognizes persons who have made outstanding contributions to cancer research or committed efforts to promote research activities in service of prevention, early detection, and treatment of cancer. The prize also serves as recognition for services to the Swiss Cancer League and its goals. The 10 000-franc prize is usually awarded each year.
→ www.krebsliga.ch/krebspreis

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

With the Recognition Award 2018, the Swiss Cancer League honoured Pirmin Schwegler, footballer, for his efforts on behalf of children and adolescents with cancer. As a young child, Schwegler had leukaemia, which he survived thanks to treatment and his stamina. Later, as a young man, he realized his childhood dream: He became a professional footballer, at first with FC Luzern and the Young Boys in Switzerland. He then continued in the German Football League, and he also plays for the Swiss national football team.

Schwegler uses his fame and his influence to draw public attention to childhood cancer. He regularly visits young patients in oncology units in hospitals. He supports fundraising projects for children with cancer, whose situation he is well familiar with based on his own experience. Through his own fundraising campaign, *Mein Klub – meine Hilfe* (my club – my support), also using his contacts in the world of football, he raised more than 100 000 francs for the *Berner Stiftung für krebskranke Kinder und Jugendliche* (Bern foundation for children and adolescents with cancer).

"I am committed to giving something back to the clinic that saved my life," writes Schwegler on his website. Schwegler also donated the Recognition Award prize money of 5000 francs to the Bern foundation.

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. The award comes with 5000 francs prize money.
→ www.krebsliga.ch/anerkennungspreis

Pirmin Schwegler (centre) receives the Recognition Award 2018. Kathrin Kramis (CEO of the Swiss Cancer League, left) and Gilbert Zulian (president of the Swiss Cancer League, right) congratulate him.

The Swiss Bridge Award 2018 was given to joint recipients, a research group in Spain and a research group in Switzerland. With the prize money of 250 000 francs that each research group received, they will investigate characteristics of cancers that can predict the treatment success of immune therapies.

Immune therapies – such as checkpoint inhibitor therapy, for which the discoverers recently received the Nobel Prize in Physiology or Medicine – are encouraging, for they can sometimes cure also patients with advanced cancer. But immunotherapy treatments are also frustrating, because they often fail to induce responses; only one out of five patients benefits. Researchers and doctors cannot predict in advance whether a patient will respond to the immunotherapy drug.

Two-step evaluation process

For the 2018 award the Swiss Bridge Foundation had called for proposals from researchers under the age of 45 to help close this knowledge gap. The foundation received proposals from 111 researchers from all over Europe. In a two-step evaluation process the jury of renowned experts selected projects submitted by two project heads: Ping-Chih Ho at the Department of Fundamental Oncology at the University of Lausanne / Ludwig Lausanne Branch (Switzerland) and Rodrigo de Almeida Toledo at the Vall d'Hebron Institute of Oncology in Barcelona were each awarded 250 000 francs for realization of their research projects.

Cold and hot tumours, immunologically speaking

Ping-Chih Ho's team is interested in differences between what are called cold and hot tumours. Immunotherapies mostly work well with hot tumours, but they do not work with cold tumours, as the microenvironment of the tumour apparently keeps the immune cells from infiltrating into the tumour tissue and attacking the tumour. Ho and his team recently discovered a gene that is active only in hot tumours. Using mice experiments, the researchers even succeeded in activating the gene in cold tumours and thus in making the tumour microenvironment accessible again for the immune system's cells that attack cancer. The researchers now aim to find out whether the gene plays such a crucial role also in humans and to possibly develop a test that can predict response to immunotherapy.

Genomic analyses

Rodrigo de Almeida Toledo and his team will take samples of tumours from patients who are being treated with a number of different immunotherapeutics in Barcelona. The genomic analysis – comparison of the whole tumour DNA in tumours that respond

well to the immunotherapy and the DNA in tumours that do not respond and continue to grow – aims to reveal differences that could be used in the future not only for prediction of immunotherapy response in patients but also for identification of possible new cancer immunotherapy targets.

Swiss Bridge Award

The Swiss Bridge Foundation was founded in 1997 at the initiative of Thomas Hoepli, foundation board member, and with the support of the Swiss Cancer League. The aim of the foundation is to financially support high-quality cancer research projects in Switzerland and other countries. 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

Ori Schipper, PhD
Ori Schipper graduated in plant molecular biology and followed a postgraduate course in science journalism.
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National Strategy Against Cancer

Overview of the programme for strengthening oncological health services research

For five years, the Swiss Cancer Research foundation's Health Services Research in Oncology and Cancer Care programme provides approximately one million francs annually in funding for projects in health services research. Three funding rounds are complete, and the fourth is underway. The last opportunity for researchers to submit convincing research proposals is in 2020.

The health care system faces great challenges, among them the growing need for economic and also personnel resources. To avoid underprovision, overprovision, and misprovision and to ensure good health services provision in the long term, present-day processes in the health care system have to be analysed and new concepts developed. Health services research makes a significant contribution here. It studies how people are provided with health products and services, focusing mainly on the quality, benefits, and costs of medical care. Care refers not only to patients but to the entire healthy population as well, such as in the area of prevention.

Health services research differs in this way from basic research and clinical research. Basic biomedical research is often called the first pillar and produces new findings on biological processes using cell cultures, tissue, and animal models. Clinical research is called the second pillar; it studies the effectiveness of treatments in clearly defined and selected groups of patients. Following this logic, health services research can be called the third pillar of health research (Figure 1).

The findings of health services research are intended to serve patients, service providers, and decision makers in the government and the economy and to make a significant contribution towards needed restructuring and further development of the health care system. Researchers in the field differentiate three different levels: the macro, meso-, and microlevel. Research at the microlevel focuses on individual interactions between service providers and recipients. Research at the mesolevel analyses the organization and delivery of health services and products under everyday conditions. The macrolevel analyses the health care system at the regional, national, and international level; for this, the data analysed are usually already available, highly aggregated data. But for studies at the meso- and microlevel, researchers do not only use already existing data and instead generate data themselves.

Alexandra Uster
Scientific collaborator at the Research, Innovation & Development department, Swiss Cancer League

Peggy Janich, PhD
Head of Research Funding, Swiss Cancer League

In Switzerland, the Swiss Academy of Medical Sciences (SAMS) together with the Gottfried and Julia Bangerter-Rhyner foundation undertook first efforts to strengthen health services research in 2012 and launched a five-year research funding programme. Since 2015, the Swiss National Science Foundation is promoting research projects in the framework of the's National Research Programme 'Smarter Health Care' (NRP 74). However, neither of these two funding programmes has a primary focus on oncology. For this reason, the Swiss Cancer Research foundation (SCR), with financial support from the Accentus Foundation (Marlies-Engeler-Fonds), launched a research programme that is incorporated in the National Strategy Against Cancer 2014–2020 and that funds studies in health services research in oncology. Since 2016, each year the programme has funded up to four larger research projects (funding up to 250 000 francs) and several smaller pilot projects (funding up to 75 000 francs). The funding programme aims to point up the need for improvement in service provision to people with cancer and to help to meet the challenges in the area of oncology.

Figure 1
Position of health services research in the research landscape in medicine and health care system

The three-pillar model (taken from: Schweizerische Akademie der Medizinischen Wissenschaften. Stärkung der Versorgungsforschung in der Schweiz. *Swiss Academies Reports*. 2014;9).

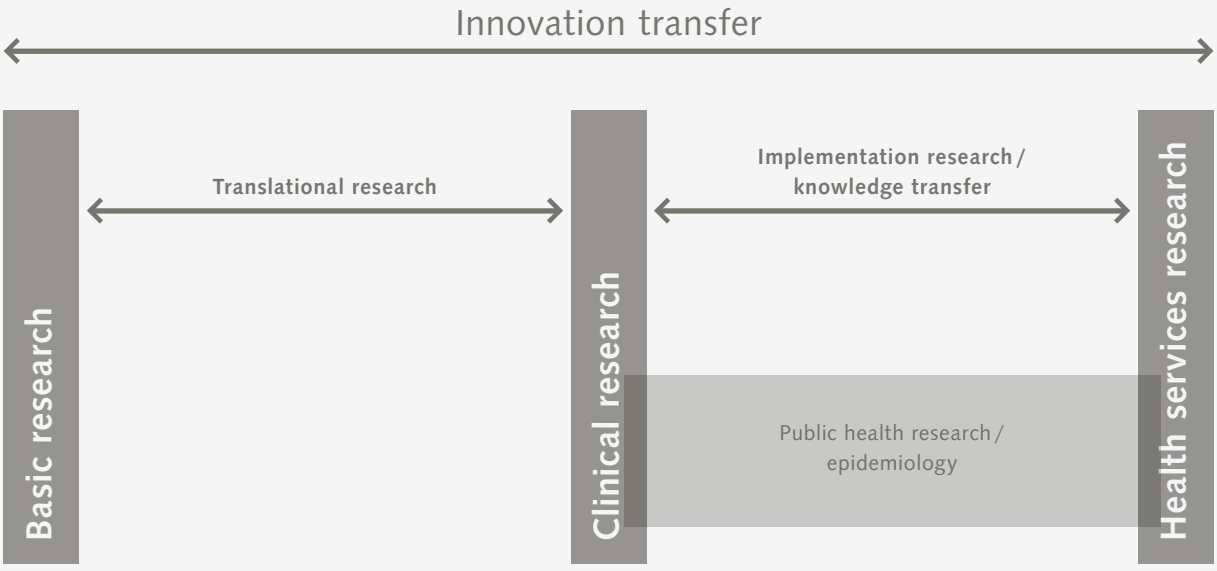


Table 1
The 22 health services research projects funded up to now

Topic of the research project	Organizations involved	Disciplines involved
1 Continuity of care in patients with cancer in Switzerland	Health insurance	Public health
2 Effect of adherence to guidelines on healthcare provision for patients with myelodysplastic syndrome in Switzerland	Hospital University	Haematology Public health
3 Mammography screening programmes and demographic and socioeconomic inequalities in utilization of screenings	Hospital University	Socioeconomics Sociology General internal medicine
4 Need for psychosocial aftercare of childhood cancer survivors	University	Public health Psychology
5 Evaluation of quality of care for young women with breast cancer in Switzerland	Hospital Cancer registry	Public health Gynaecology Medical oncology
6 Optimization of targeted cancer therapies: for better self-management by the patient	Hospital	Clinical pharmacology Pharmaceutics Medical oncology
7 Security problems in the utilization of information technologies in care for patients with cancer	Foundation	Quality management
8 Changes in rates of colon cancer screening from 2012 to 2017 in Switzerland	Hospital Health insurance University	General practice / family medicine General internal medicine Public health
9 Social media use in adolescents and young adults during and after cancer: views of patients and views of oncologists	University	Bioethics and medical ethics
10 Development and testing of a healthcare provision model for promoting self-management with allogeneic stem cell transplantation	University Hospital Higher education institution	Public health Nursing science Haematology General internal medicine Computer science Biostatistics
11 Comparison of two tumour aftercare strategies for patients with treated oral, throat, and laryngeal cancer	University Hospital	Oral and maxillofacial surgery Radiation oncology Radiology Biostatistics
12 Experience of patients with cancer with treatment and care: a multicentre cross-sectional study in the French-speaking part of Switzerland	University Hospital	Public health Nursing science

Topic of the research project	Organizations involved	Disciplines involved
13 Aftercare for childhood cancer survivors in Switzerland	University Hospital	Paediatric oncology-haematology Public health
14 Can an exercise training programme during chemotherapy reduce the undesirable side effects on heart function in patients with breast cancer?	Hospital	Cardiology Medical oncology
15 Differences in the use of radiation therapy in women whose entire breast was removed due to breast cancer	Hospital Cancer registry	Radiation oncology Public health
16 Better identification of psychological stress in patients with cancer using a mobile phone app	Hospital	Medical oncology Psychology
17 Individual prediction of progression risk in patients with chronic lymphocytic leukaemia at an early stage	Hospital	Haematology
18 Burden on patients with cancer and their families from the cost of proton therapy	Research institute Hospital	Radiation oncology Public health
19 Is it cost effective to test every patient with breast cancer for hereditary breast cancer?	Hospital University	Gynaecology Medical oncology Nursing science Medical genetics Economics Biostatistics
20 What is the association between case numbers of abdominal surgery for cancer and the treatment results?	Health insurance	Public health
21 Clinical benefit, pricing, and cost coverage of oncology medications: a comparative study of Switzerland, England, Germany, France, and the United States	Hospital	General practice / family medicine Medical oncology Health law
22 Health economic analyses of postoperative treatment of stage 0 cancer/precancerous breast lesions	Hospital University	Radiation oncology Gynaecology Economics

Macrolevel Health care system
Mesolevel Institutions providing health services
Microlevel Interactions between providers and recipients

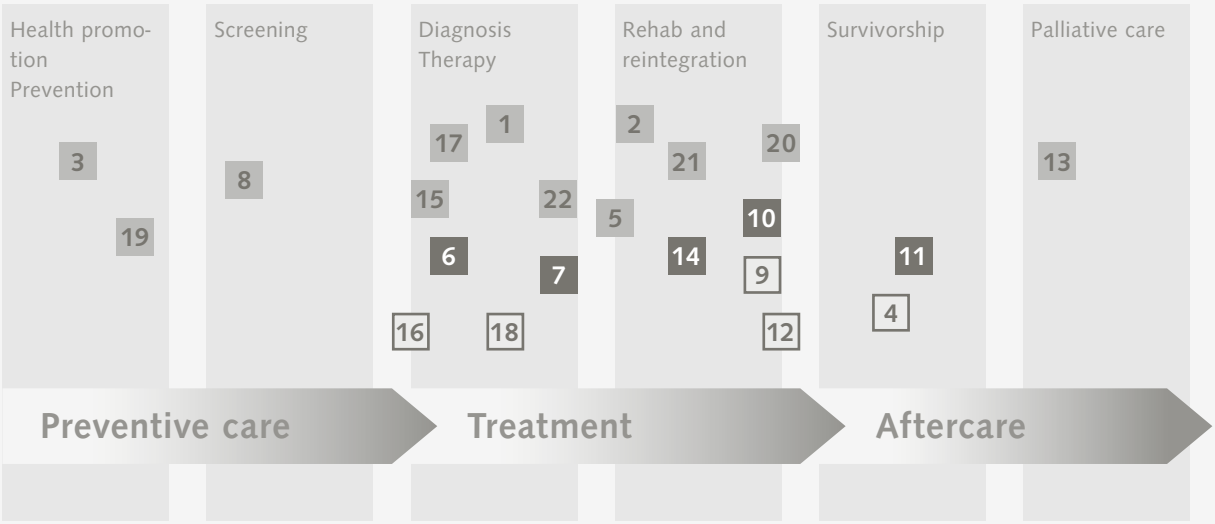
In 2019 the SCR issued a fourth call for grant applications for the Health Services Research in Oncology and Cancer Care programme. In the first three, already completed funding rounds, a total of 106 research proposals were submitted. The total funding requested by the applicants was nearly 16 million francs. In a two-step process, a panel of experts brought together for this programme evaluated the research proposals. The experts, who represent all relevant topic areas in health services research, rated all of the submitted research projects on their importance for oncological care, scientific quality and appropriateness of the chosen research methods, feasibility, and the applicants' previous scientific track record.

Up to the present time, the panel of experts has approved 22 grant applications with a total funding amount of somewhat more than three million francs (Table 1). Most of the projects funded were submitted by researchers working at hospitals and universities or universities of applied sciences but were also submitted by researchers at cancer registries, health insurance companies, and foundations. An initial analysis of the principal applicants' and co-applicants' fields of study and institutes shows that, as expected, the scientific disciplines represented are widely spread. In the area of clinical medicine, especially the fields medical oncology, radiation oncology, haematology, general internal medicine, and gynaecology are represented. In the area of non-clinical medicine, the main scientific discipline represented is public health. The group of other scientific disciplines is very heterogeneous: Represented here are the fields pharmacy, ethics, biostatistics, information technology, nursing sciences, economics, sociology, psychology, and information sciences.

Regarding the research topic, the funded research projects are spread across all levels (macro-, meso-, and microlevel) and across the entire patient (care) pathway (Figure 2). The patient pathway starts out at cancer prevention and describes the long pathway from diagnosis to treatment to palliative care or survivorship. As Figure 2 and Table 1 show, in the area of prevention, the funded research projects are studying

Figure 2
Health services research along the patient care pathway

The funded health services research projects, shown along the patient pathway and shown in colors indicating the three levels of health services research.



Macrolevel Health care system
Mesolevel Institutions providing health services
Microlevel Interactions between providers and recipients

research questions on screening programmes and genetics tests. In the area of treatment, the research topics deal mainly with medical care and care quality, but health economics and legal aspects are also being examined. Four projects are investigating research questions that cross treatment and survivorship and have therefore been placed at the intersection. Important research topics in the area of aftercare are health services provision and the needs of persons who had childhood cancer.

The 22 research projects being funded are diverse and investigate important topics. The Health Services Research in Oncology and Cancer Care programme is thus underway in a very positive manner. Next year, researchers will have another opportunity to submit grant applications. It is not yet clear whether the funding programme will continue after its official duration outside of the National Strategy Against Cancer. However, it is certain that the SCR together with the Swiss Cancer League and other relevant actors will organize a community-building conference. The aim of the meeting will be to promote collaboration between researchers in health services research in Switzerland and in this way to strengthen health services research in Switzerland on a long-term basis.

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Alexandra Uster studied food science at ETH Zurich. Uster then worked as scientific staff at the Laboratory of Biotechnology at ETH Zurich and at Cantonal Hospital Winterthur. She joined the Swiss Cancer League in March 2018.
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Peggy Janich, PhD
After studying biotechnology at Brandenburg University of Technology Cottbus-Senftenberg and Technische Universität Dresden, Janich completed a PhD at the Centre for Genomic Regulation in Barcelona. She then worked as a researcher at the University of Lausanne before joining the Swiss Cancer League in February 2016. She has been the head of Research Funding since January 2017.
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Clinical research 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. The co-directorate of the NSC provides the actors with targeted and need-specific support. Although the NSC is not a research-specific initiative, research has an important place in it, and clinical research in particular. Here the main actors are the Swiss Cancer Research foundation (SCR) and the Swiss Group for Clinical Cancer Research (SAKK). Two clinical research projects are described in the following: Regional Networks (NSC project 6.2.3) and Legal Opinions on Reimbursement for Research Services (NSC project 6.2.2). Information on all of the other NSC projects is available at www.nsk-krebsstrategie.ch.

The Regional Networks project is being conducted by the SAKK and is funded to a large extent by the Swiss Cancer League. It deals with the issue that clinical trials are conducted mainly at university and cantonal hospitals and that in order to participate, patients must travel to these centres. The aim of the project is to make it possible for more patients to join clinical trials, because clinical trials, as a part of standard care, play an important role in the treatment of patients with cancer. The SAKK conducts clinical trials in 20 hospitals, which each have a catchment area of 300 000 to 400 000 people, which is a rather low number for clinical trials. Smaller hospitals, which focus mainly on optimal local patient care and aftercare, do not conduct clinical research, even though they care for patients who sometimes qualify for clinical trials and could benefit from them. In line with the goal of equal access, the project aims to decouple participation in clinical trials from close proximity to central hospitals. But there are hurdles; in addition to quantity structure, other obstacles are administrative effort and costs, regulatory requirements, data management, travel costs, and additional time required on the part of the trial personnel. Because of these obstacles, patients who are well served in local care must switch to a university hospital or cantonal hospital to be able to join a clinical trial. Prof. Roger von Moos, MD, president of the SAKK, believes (freely quoted here) that the data should travel and not the patients.

In view of the differing cantonal framework conditions, any regional networks will have to be organized somewhat differently. For example, a central hospital can collaborate with cooperating smaller hospitals/oncology practices. Or individual sub-investigators at network locations can work with principal investigators at central hospitals. It can also be that a network location becomes a trial centre itself and the SAKK provides only expertise and training for the setting up of the centre.

In June 2018, seven regions were chosen for supporting the building of regional networks; the actual implementation will take place in 2019 to 2020. The participants are seven SAKK members – with a total of 22 networked hospitals:

- **Centre hospitalier universitaire vaudois**
  with: Clinique de Genolier
- **Hôpital du Valais Sion**
  with: Hôpital de Sierre / Hôpital de Martigny

Michael Röthlisberger, PhD, and Catherine Gasser, Dr. iur
Co-directors of the National Strategy Against Cancer

- **Hôpital Fribourgeois**
  with: Hôpital intercantonal de la Broye / Hôpital de Riaz / Spital Murten / Spital Tafers
- **Solothurner Spitäler AG**
  with: Kantonsspital Olten / Bürgerspital Solothurn / Spital Dornach
- **Kantonsspital St. Gallen**
  with: Spital Flawil / Spital Rorschach / Spital Grabs / Spital Herisau / Spital Linth / Spital Wil / Spital Wattwil
- **Kantonsspital Winterthur**
  with: TUCARE Bülach / GZO Wetzikon / Spital Limmattal / Spital Uster
- **Kantonsspital Luzern**
  with: Kantonsspital Zug

The multitude of participating institutions as well as their diversity in structure, organization, and volume create significant challenges for implementation of the project. In line with the goal of equal access, however, the Regional Networks initiative is an extremely important component that should be incorporated into the framework of coordinated and integrated care. Besides the institutions, ultimately it is primarily patients who can benefit greatly from networking and expansion of clinical cancer research.

On the issue of reimbursement for medical treatment delivered within academic clinical trials, the SAKK and SCR, with the support of the NSC, have started talks with the Federal Office of Public Health (FOPH). The basis is a legal opinion that states clearly that (inpatient) treatment should not lose its status as covered by the health insurance due to the fact that it is delivered within a clinical trial and being considered as 'research'. It simply does not do for health insurers to exclude coverage not only for trial-specific (such as additional imaging examinations and laboratory tests or costs for treatment of possible side effects in the investigational treatment arm) but also for not-trial-specific measures (such as drugs on the special medications list that belong to the standard treatment) or even for the entire standard treatment arm (which is completely identical to the standard treatment) based on Federal Act on Health Insurance (KVG), Art. 49 Paragraph 3.

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Michael Röthlisberger completed a PhD in basic cancer research. Röthlisberger then headed the research department of the Swiss Academy of Medical Sciences and worked in the Innovation & Health Services Quality department at the Swiss Cancer League.
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Catherine Gasser, Dr. iur.
Before taking on the co-directorate of the National Strategy Against Cancer together with Michael Röthlisberger, Catherine Gasser was head of the Aftercare section at the Swiss Cancer League. Gasser had previously worked as general project manager for the Medical Professions Act and was head of the health professions division of the Federal Office of Public Health.
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Research funding by the cantonal and regional cancer leagues

Supporting cancer research projects in the Canton of Aargau

The Swiss Cancer League focuses on three areas in the field of cancer: It is actively involved in prevention and early detection, in counselling and supporting persons affected by cancer and their families, and in funding research. Specific tasks are carried out in the association by the 18 cantonal and regional cancer leagues and by the Swiss Cancer League according to the existing competencies and possibilities.

The Aargau Cancer League sees as its main role the direct support of persons affected by cancer in the canton. The league's affirmation, "We have time, space, and advice," describes the way that it sees itself. As a complement to other service providers in the health care system, the league assists patients and also all residents of the canton by providing information, advice, and support.

Nevertheless, funding research is important to the Aargau Cancer League as well. For one, the league receives earmarked donations and legacies that are expressly appropriated for realization of research projects. For another, there are several specialized institutes and centres located in Aargau that play an innovative and leading role in cancer research. The Aargau Cancer League gives priority to projects that have a connection with the canton.

When submitting research grant applications to the Aargau Cancer League, researchers are not restricted regarding the research topic. Evaluation of the scientific quality of the research proposals submitted is done by the Scientific Committee of the Swiss Cancer League and the Swiss Cancer Research foundation. The Aargau Cancer League considers it appropriate and reasonable to delegate this important task to the specialized committee. The results of the evaluation give the board of the Aargau Cancer League a basis for funding a submitted research project. Depending on the funds available, projects are funded in full or in part. In recent years, several grant applications could be approved for funding.

The Centre for Proton Therapy at the Paul Scherrer Institute in Villigen is the worldwide leader in the treatment of ocular tumours. In this highly specialized area, the Aargau Cancer League is supporting the project 'High resolution ophthalmic magnetic resonance imaging at 1.5T: towards a non-invasive method to assist proton therapy planning for uveal melanoma' with a multiyear financial commitment. Also for the Centre for Proton Therapy, the Aargau Cancer League provides financial support for analysis of late effects of irradiation of tumours in children.

At the KSA-KSB Radiation Oncology Department at the Cantonal Hospital in Aarau, the Aargau Cancer League supports the evidence-based further development of superficial hyperthermia and deep tissue hyperthermia, combined with radiotherapy, as a form of treatment of different tumour entities. The Aargau

Martin Wernli, MD
Head of association development at the Swiss Cancer League and former president of the Aargau Cancer League

Cancer League also provided financial support in the initial phase of the establishment of the Swiss Radionuclide Centre at PARK innovAARE in Villigen, one of the five sites nationwide of the Switzerland Innovation foundation. The Radionuclide Centre aims to develop new methods for diagnosis and treatment of different cancers using radio-pharmaceuticals.

Through this diverse research support, the Aargau Cancer League seeks to fulfil the task entrusted to the league by many charitable donors and to actively pursue the vision that more people with cancer can be treated successfully.

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Martin Wernli, MD
From 1993 to 2018 Martin Wernli was a member of the board of the Aargau Cancer League, for the last 18 years serving as president. Since retiring in 2016 as head of the Department of Oncology, Haematology, and Transfusion Medicine at the Cantonal Hospital in Aarau, Wernli has headed development of the association of all cancer leagues in Switzerland. Up to 2015, he headed the regional Swiss Red Cross (SRC) Blood Donor Service in Aargau-Solothurn for about 20 years. In addition, he helped create the Cancer Registry of the Canton of Aargau and has served as president of that foundation since its beginnings in 2011.
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Overview of the many-sided efforts

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

In 2018, nine cantonal and regional cancer leagues (CCL) provided almost 3 million francs' funding to a total of 45 different cancer research projects and institutes. Compared to the previous year, the CCL thus supported nine more research projects (see table). The largest sum was invested by the Ligue genevoise contre le cancer, followed by the cancer leagues of Basel, Zurich, and Bern.

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 grant applications are rated by their board members, or they delegate the task to the Scientific Committee that 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 make possible new approaches in treatment and in cancer research: The findings of the funded projects benefit not only patients with cancer today but also patients in the future.

Ori Schipper, PhD
Communication officer, Swiss Cancer League

Table

Research funding by the cantonal and regional cancer leagues in overview

	Number of projects and institutions supported		Amount granted in kCHF	
Cancer League	2017	2018	2017	2018
Aargau	1	2	40	90
Basel	11	16	560	711
Bern	6	2	400	100
Central Switzerland	2	1	65	30
Eastern Switzerland	1	0	100	0
Geneva	7	11	534	1 496
Grisons	0	1	0	15
Thurgau	1	3	10	50
Ticino	3	n. s.	228	n. s.
Zurich	4	9	271	419
Total	**36**	**45**	**2 208**	**2 911**

n. s. = not specified

List of funded research projects and institutions

The list shows the financial contributions granted in 2018.

Aargau Cancer League

Bodis Stephan | Clinical cancer research on hyperthermia
Radio-Onkologie-Zentrum KSA-KSB, Kantonsspital Aarau, Aarau
CHF 50 000.– | Duration: 1. 1. 2018 – 31. 12. 2018

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

Christofori Gerhard | Single cell analysis of invasive, metastatic and chemoresistant breast cancer cells
Departement Biomedizin, Universität Basel, Basel
CHF 66 250.– | Duration: 1. 9. 2018 – 31. 8. 2019

Diesch Tamara | Pregnancy rates and pregnancy outcome after haematopoietic stem cell transplantation in childhood
Pädiatrische Onkologie und Hämatologie, Universitäts-Kinderspital beider Basel, Basel
CHF 15 000.– | Duration: 1. 1. 2018 – 31. 12. 2018

Finazzi Tobias | Evaluating the benefit of stereotactic MRI-guided adaptive radiotherapy for early-stage non-small cell lung cancer
Klinik für Radioonkologie, Universitätsspital Basel, Basel
CHF 50 000.– | Duration: 1. 9. 2018 – 28. 2. 2020

Höller Sylvia | Comparative methylation profiles as a diagnostic tool in differentiating osteoblastomas from special variants of osteosarcomas
Institut für Pathologie, Universitätsspital Basel, Basel
CHF 30 000.– | Duration: 1. 4. 2018 – 31. 3. 2020

Kashyap Abhishek | Dissecting the role of GEFH1 in induction of anti-tumour immunity upon treatment with microtubule-targeting chemotherapy in tumour models and cancer patients
Departement Biomedizin, Universitätsspital Basel, Basel
CHF 60 000.– | Duration: 1. 6. 2018 – 31. 5. 2019

Kovac Michal | A nanopore-based detection of TP53 gene rearrangements in paediatric osteosarcoma and Li-Fraumeni families
Institut für Pathologie, Universitätsspital Basel, Basel
CHF 30 000.– | Duration: 1. 9. 2018 – 31. 8. 2020

Le Magnen Clémentine | Towards the development of clinically-relevant ex vivo models of prostate cancer
Institut für Pathologie, Universitätsspital Basel, Basel
CHF 40 000.– | Duration: 1. 4. 2018 – 31. 3. 2019

Maas Ole Christopher | Decision making in radio-iodine ablation
Klinik für Radiologie und Nuklearmedizin, Kantonsspital St. Gallen, St. Gallen
CHF 20 000.– | Duration: 1. 5. 2018 – 30. 4. 2019

Matter Matthias | Regulation of metastasis formation by miRNAs in hepatocellular carcinoma patient
Institut für Pathologie, Universitätsspital Basel, Basel
CHF 21 421.– | Duration: 1. 10. 2018 – 30. 9. 2019

Nageswara Rao Tata | Assessing the role of GDF15 in the pathogenesis of myeloproliferative neoplasms
Departement Biomedizin, Universitätsspital Basel, Basel
CHF 40 000.– | Duration: 1. 8. 2018 – 31. 7. 2019

Papachristofilou Alexandros | SAKK 01/18: reduced intensity radiochemotherapy for stage IIA/B seminoma
Klinik für Radioonkologie, Universitätsspital Basel, Basel
CHF 75 000.– | Duration: 1. 7. 2018 – 30. 6. 2022

Piscuoglio Salvatore | Disease monitoring of hepatocellular carcinoma undergoing sorafenib treatment using plasma-derived cell-free DNA
Institut für Pathologie, Universitätsspital Basel, Basel
CHF 43 245.– | Duration: 1. 9. 2018 – 31. 8. 2019

Rass Ulrich W. | Assessment of the anti-tumour potential of targeting DNA2 replication stress response factor in vivo
Friedrich Miescher Institut für biomedizinische Forschung, Basel
CHF 127 000.– | Duration: 1. 6. 2018 – 31. 5. 2020

Scheinemann Katrin | Evaluation of rehabilitation programs in Swiss childhood cancer survivors (Rehab SCCS)
Pädiatrische Onkologie und Hämatologie, Universitäts-Kinderspital beider Basel, Basel
CHF 18 900.– | Duration: 1. 7. 2018 – 30. 6. 2019

Vlajnic Tatjana | Predictive biomarker profiling for immune checkpoint inhibition in advanced urothelial carcinoma: A pilot study
Institut für Pathologie, Universitätsspital Basel, Basel
CHF 36 000.– | Duration: 2. 4. 2018 – 1. 4. 2019

Zanetti Dällenbach Rosanna | Comparison of accuracy and reproducibility of breast lesion characterization between real-time elastography and shear wave elastography
Gynäkologische Onkologie, St. Claraspital, Basel
CHF 38 565.– | Duration: 3. 11. 2017 – 2. 11. 2020

Bern Cancer League

Francica Paola | Identification of novel synthetic lethal interactions with radiotherapy
Institut für Tierpathologie, Universität Bern, Bern
CHF 60 000.– | Duration: 1. 9. 2018 – 1. 3. 2020

Marinoni Ilaria | Chromatin accessibility landscapes in DAXX/ATRX mutant pancreatic neuroendocrine tumours
Institut für Pathologie, Universität Bern, Bern
CHF 40 000.– | Duration: 1. 10. 2018 – 1. 10. 2019

Central Switzerland Cancer League

Winterhalder Ralph | SAKK 24/14: Anti-EGFR-immunoliposomes loaded with doxorubicin in patients with advanced triple negative EGFR positive breast cancer – a multicentre single arm phase II trial
Medizinische Onkologie, Luzerner Kantonsspital, Luzern
CHF 30 000.– | Duration: 1. 1. 2017 – 31. 12. 2018

Geneva Cancer League

Bounameaux Henri | Support for the creation of a translational research centre in onco-haematology
Centre de recherche translationnelle en onco-hématologie, Université de Genève, Genève
CHF 400 000.– | Duration: 1.1.2018 – 31.12.2022

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

Institut en Science Infirmière | Medical research project in nursing science
Fondation Webster, Bellevue, Genève
CHF 100 000.– | Duration: 1.1.2018 – 31.12.2021

Labidi-Gali Intidhar and Tille Jean Christophe | 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

Legal Frédérique Anne and Wrobel Ludovic | Histopathological and molecular evaluation of the effect of beta-blockers in patients with melanoma
Division de dermatologie, Hôpitaux universitaires de Genève, Genève
CHF 77 695.– | Duration: 1.1.2018 – 31.12.2018

Mandriota Stefano | Role of aluminium in the development of breast cancer
Fondation des Grangettes, Genève
CHF 60 000.– | Duration: 1.7.2016 – 30.6.2018

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

Toso Christian | Surgical treatment of patients with hepatocellular carcinoma
Service de chirurgie viscérale, Hôpitaux universitaires de Genève, Genève
CHF 109 675.– | Duration: 1.7.2016 – 30.6.2018

Tsantoulis Petros | Support for the translational research centre in onco-haematology – precision oncology
Centre de recherche translationnelle en onco-hématologie, Université de Genève, Genève
CHF 200 000.– | Duration: 1.1.2018 – 31.12.2021

Grisons Cancer League

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 15 000.– | Duration: 1.8.2016 – 28.2.2017

Thurgau Cancer League

Legler Daniel | Co-financing for a total internal reflection fluorescence (TIRF) microscope
Biotechnologie Institut Thurgau, Kreuzlingen
CHF 30 000.– | Duration: 1.1.2018 – 31.12.2018

Rainer Fritz | Project to assess the need for psycho-oncological support in the canton of Thurgau
Spital Thurgau AG, Kantonsspital Münsterlingen, Münsterlingen
CHF 10 000.– | Duration: 1.1.2018 – 31.12.2018

Schmidt Anne | Support Cancer Registry Thurgau
Krebsregister Thurgau, Kreuzlingen
CHF 10 000.– | Duration: 1.1.2018 – 31.12.2018

Zurich Cancer League

Bourquin Jean-Pierre | Exploring the genomic landscape of myeloid and stem cell marker VNN2 positive unfavorable acute lymphoblastic leukaemia
Abteilung Onkologie, Universitäts-Kinderspital Zürich, Zürich
CHF 57 546.– | Duration: 1.1.2018 – 31.12.2018

Dieterich Lothar | Tumour-derived extracellular vesicles – messengers that shape the lymph node microenvironment and control tumour immunity in melanoma
Pharmazeutische Wissenschaften, ETH Zürich, Zürich
CHF 39 370.– | Duration: 1.1.2018 – 31.12.2018

Gari Kerstin | Cancer-associated up-regulation of an alternatively spliced DNA polymerase
Institut für Molekulare Krebsforschung, Universität Zürich, Zürich
CHF 40 000.– | Duration: 1.1.2018 – 31.12.2018

Kirschner Michaela | The role of microRNAs in malignant pleural mesothelioma progression and resistance to chemo- and immunotherapy
Klinik für Thoraxchirurgie, Universitätsspital Zürich, Zürich
CHF 50 000.– | Duration: 1.1.2018 – 31.12.2018

Knobel Philip | Exploring the interactome of ADAM17 in the tumour microenvironment and its role for radiation resistance
Klinik für Radio-Onkologie, Universitätsspital Zürich, Zürich
CHF 25 970.– | Duration: 1.1.2018 – 31.12.2018

Meier-Abt Fabienne and Theocharides Alexandre | Identification of new therapeutic targets against haematopoietic malignancies by proteomic analysis of (pre)leukaemic stem cells
Klinik für Hämatologie, Universitätsspital Zürich, Zürich
CHF 37 000.– | Duration: 1.1.2018 – 31.12.2018

Pruschy Martin and Unkelbach Jan | Radiotherapy treatment volume and its role for the tumour-oriented immune response
Klinik für Radio-Onkologie, Universitätsspital Zürich, Zürich
CHF 35 000.– | Duration: 1.1.2018 – 31.12.2018

Shakhova Olga | Delineating the molecular and cellular basis of therapy resistance in metastatic melanoma
Departement Onkologie und Hämatologie, Universitätsspital Zürich, Zürich
CHF 57 045.– | Duration: 1.1.2018 – 31.12.2018

Wälchli Thomas and Hoerstrup Simon P. | Nogo-A is a negative regulator of CNS angiogenesis – molecular mechanisms and applications in brain tumours
Klinik für Neurochirurgie und Neurowissenschaften, Universitätsspital Zürich, Institut für Regenerative Medizin, Universität Zürich, Zürich
CHF 57 546.– | Duration: 1.1.2018 – 31.12.2018

The promises and challenges of T cell immunotherapy

In recent years, immunotherapy has revolutionized the landscape of cancer care. Two key disruptive principles have been demonstrated that are presently driving clinical development. For one, immune checkpoint blocking antibodies have definitively shown that in principle any solid tumour can be naturally recognized and attacked by the immune system. The immune checkpoint antibodies can effectively enhance the immune system and drive a T cell mediated clinical response. For another, adoptive T cell therapy using T cells engineered with a synthetic chimeric antigen receptor (CAR) has definitively demonstrated that synthetic biology and cell engineering can lead to the development of T cells with redirected specificity against specific cancer-associated antigens and with supernatural properties that can lead to eradication of metastatic tumours. These two principles were not obvious at all less than a decade ago. The race is now on to capitalize on the successes of recombinant technology and cell engineering, to defeat cancer in its many facets.

Adoptive cell transfer (ACT) is a promising therapeutic approach in which patients receive lymphocyte infusions targeting cancer cells. Several ACT approaches are presently in development, using naturally occurring tumour-specific T cells, most commonly tumour-infiltrating lymphocytes (TILs), as well as T cells engineered with a synthetic CAR or a T cell receptor (TCR). TILs are obtained directly from an autologous tumour sample and are naturally enriched in tumour-reactive lymphocytes, which are expanded ex vivo in the presence of high dose interleukin-2 prior to reinfusion into the patient. A review has shown that TIL induce enduring complete responses in up to 25 % of treated patients with metastatic melanoma in different clinical trials[1]. In addition, preliminary clinical data from recent studies show promising results in other indications than melanoma[2].

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TCRs and CARs, unlike TILs, are transgenic cells produced by gene transfer technology applied to bulk or subsets of peripheral blood T lymphocytes, thus creating a cell product where the majority of T cells are effectively redirected to tumours by virtue of expressing an exogenous receptor. The T cell receptor consists of two chains (α and β), not covalently connected with the CD3 complex on the T cell surface of natural lymphocytes[3]. The TCR recognizes specific immunogenic peptides noncovalently linked to major histocompatibility complex (MHC) molecules on the surface of antigen-presenting cells or tumour cells[4], leading to T cell activation. Synthetic TCRs used to engineer T cells may be structurally modified to boost affinity to the cognate antigen. Several TCR-transduced T cells have been tested in the clinic against shared tumour antigens, such as a melanocytic differentiation antigen MART-1 or MAGE-3. Increasing affinity of the TCR can enhance tumour identification and response rate but may also lead to recognition of normal tissues from the same lineage containing the targeted antigen at lower levels (on-target toxicity) or to cross-reactivity against molecularly related epitopes present in unrelated normal tissues (off-target toxicity)[5]. Nevertheless, promising results without noticeable toxicity have been reported in the clinic with T cells expressing an affinity-enhanced TCR specific for the cancer-testis antigen NY-ESO-1[6]. Additionally, TCR-transduced T cell therapies specific to defined tumour mutated antigens (neoantigens) are likely to be safe, although this requires confirmation in the clinical setting.

CARs were designed to overcome several possible limitations of TCR-based therapy, such as the requirement of MHC expression by target tumour cells, MHC restrictions, and T cell anergy due to lack of costimulation. CARs' independence from MHC-expression is a significant biological benefit, as tumour cell loss of MHC is a basic mechanism for immune escape[7]. In essence, CARs consist of antibody-binding domains (generally a single-chain variable fragment, or scFv) fused to T cell signalling domains from cell surface receptors[8]. First generation CARs contained only the activation domain of CD3-zeta, the signalling domain of the TCR, without costimulatory endodomains, and the results from the initial clinical studies in patients with different types of cancer were disappointing[9]. Second generation CARs including costimulatory domains (such as CD28 or 4-1BB) became the leading paradigm for engineered T cell therapies in cancer[10-13]. Targeting $CD19^{+}$ aggressive B cell lymphomas and B cell precursor acute lymphoblastic leukaemia (B-ALL) with CAR T cells has been a breakthrough and clearly changed clinical practice. CD19 is a B cell lineage restricted surface molecule that is required for B cell growth and expressed at high levels in B cell malignancies[14], but also on normal B cells, leading to on-target toxicity and hypogammaglobulinemia. Because CAR T cells are a living medicine capable of self-amplification and persistence in treated patients, it has been demonstrated that their benefits can last for many years.

Based on dramatic response rates in clinical trials[15, 16], the US Food and Drug Administration (FDA) and the European Medical Agency (EMA) approved the first CD19-targeted CAR T cell products – tisagenlecleucel (Kymriah®, Novartis) and axicabtagene ciloleucel (Yescarta®, Gilead) – for haematological neoplasms in

the United States and Europe, respectively, between September 2017 and August 2018[17,18]. Swissmedic also approved both products in 2018 to 2019. A third product, lisocabtagene maraleucel (JCAR017), has shown interesting results in recurrent/refractory CD19$^+$ non-Hodgkin lymphoma[19]. Although most young people with recurrent B-ALL are expected to experience complete remission after therapy with second-generation CD19-specific CARs, therapeutic resistance may emerge, mainly due to the loss of the CAR-targeted antigenic epitope[8]. The frequency of recurrence with CD19-negative versions was 28 % in the global study for young adults and paediatric patients with ALL[20]. This important challenge may be overcome by co-targeting a second epitope on malignant B cells to enhance clinical efficacy.

The emergence of CAR T cells for leukaemia and lymphoma is noteworthy from a number of angles. CAR T cells, for example, are the first form of gene transfer therapy to be commercially approved by the US FDA. Furthermore, CAR T cells provide a tangible demonstration that carefully designed T cells can eradicate metastatic cancers and thus deserve further clinical development. Significant attempts are presently being made to expand CAR technology beyond haematological malignancies. Clinical trials of CARs targeting shared antigens present in solid tumours have focused on a variety of targets expressed by solid tumours but also by normal tissues, betting on different expression levels or different topologic distribution of antigens, for example polarized expression restricted to luminal surface of organs. Targets have included carcinoembryonic antigen (CEA), carbonic anhydrase 9 (CA-IX), mesothelin, ErbB2/Her-2, epidermal growth factor receptor (EGFR), EGFR-viii, GD2 disialoganglioside, glypican 3 (GPC3), prostate specific membrane antigen (PSMA), folate receptor, interleukin-13 receptor a2 (IL-13Ra2), fibroblast activation protein (FAP), and others. Although most studies with CARs in solid tumours have not reported significant toxicity, the doses used to date have been low, and reported antitumor activity was also low[21]. Third generation CARs have enhanced effector features and in vivo persistence relative to CARs of the second generation, whereas CARs of the fourth generation (called TRUCKs or armoured CARs) combine the expression of a second generation CAR with gene inserts that improve anti-tumour activity such as cytokines, costimulatory ligands or enzymes that degrade the extracellular matrix of solid tumours. Additionally, 'smart T cells' equipped with a suicide gene or synthetic control devices are under nonclinical and clinical investigation[22].

CAR T cell therapies have achieved extraordinary milestones, but significant challenges remain in clinical practice. First, treatment-related toxicities continue to be a major issue. Preventing or managing unwanted toxicity therefore emerges as a key component in the efficient clinical application of these methods[23]. CD19 CAR therapy toxicities include transient myelotoxicity from conditioning lymphodepleting chemotherapy, which is commonly short-lived. Importantly, the most concerning toxicities derive from immune cell hyperactivation and include cytokine release syndrome (CRS, indeed the most commonly observed toxicity) and CAR-related encephalopathy syndrome (CRES, the most dangerous toxicity). These latter toxicities are new to the medical teams trained to manage patients

with haematologic malignancies, including expert transplant teams, and require intensive monitoring and timely toxicity management by newly assembled dedicated interdisciplinary teams, including intensive care and neurological intensive care specialists, to minimize the morbidity and mortality associated with this potentially curative therapeutic approach. Thus, owing to the threat of CRS and neurological toxicity, the FDA conditionally supported CAR T cells with a risk evaluation and mitigation strategy. A number of engineering options have also been suggested to limit toxicity associated with CAR T cells[24].

The original development of ACT was conducted in academic settings, mostly in the United States, generally within multidisciplinary centres of excellence with highly qualified staff. The transition to commercial product distribution model by pharmaceutical and biotechnology firms[25,26] requires careful preparation of medical centres for the clinical challenge. An active debate is presently ongoing in our country as to which centres should be allowed to handle CAR T cell products. Restriction to highly specialized centres that can assemble interdisciplinary teams with expertise not only in haematology and transplantation but also in intensive care medicine and intensive neurology care seems necessary to ensure high-quality care and optimal outcomes. A leading international expert immune effector cell (IEC) taskforce developed standards within the international FACT/JACIE organization (FACT: Foundation for the Accreditation of Cellular Therapy; JACIE: Joint Accreditation Committee ISCT-Europe & EBMT) that assures quality of cell therapy programs throughout the world[27]. According to these standards, cell therapy centres have the option to integrate IEC programs into existing autologous or allogeneic hematopoietic stem cell transplant (HSCT) programs or to perform IEC accreditation independently of HSCT activities.

An additional challenge relates to the costs of therapy. For the foreseeable future, CAR T cell therapy will be mostly an autologous product. Autologous products have a complex value chain, based on a service business model. Clinicians and producers must work closely to procure the patient's blood T cells and ship them to a centralized processing and expansion centre, which then assumes the responsibility of returning the modified cells to the initial point of care and the specific patient in strictly regulated physical environments[28]. Cost of product is a significant challenge for clinical development of cellular immunotherapy, with sector projections of up to US $150 000 or even 500 000 per dose[29]. Managing severe adverse reactions in an intensive hospital setting adds significantly to the costs. The important cost associated with these therapies has driven new reimbursement models, such as "pay-for-performance", i. e. payment is made upon ascertaining clinical benefit.

What is the role of Swiss academic centres in this complex environment? Academic centres remain a key engine for innovation. First, research and development at academic centres continue to produce novel therapies, to address major areas of need not covered presently by commercial products. A large fraction of patients with haematological malignancies as well as nearly all patients with solid tumours who fail standard therapies presently have no commercial CAR product options available and would be candidates for

novel T cell therapy approaches. CAR or TCR-transduced T cells and especially TILs could be very promising for many of these patients. Based on important successes reported with TCR-transduced T cells targeting NY-ESO-1, bulk TILs in cervical cancer, or neoantigen targeted TILs in solid tumours, important therapeutic opportunities for personalized T cell therapy are foreseen, and testing these interventions is urgently needed. T cell manufacturing in an academic environment could also greatly reduce the cost of products. Furthermore, academic environments are far more prone to develop personalized approaches such as those based on targeting private neoantigens, which require customization on a single-patient basis. However, the advancement of cell therapy in academic centres relies on adequate recruiting capacity for clinical trials to be completed. A national network that includes the major Swiss centres certified to deliver T cell therapy would greatly accelerate the testing and application of novel therapies such as TILs and engineered T cells for numerous solid tumour and haematological indications. Recognizing such a network as a national priority could greatly benefit patients and advance the translational agenda in Switzerland.

George Coukos, MD, PhD

George Coukos received his medical degree and PhD from the University Hospital of Modena and the University of Pennsylvania. Coukos and his team made critical contributions to our understanding of how tumours exploit regulatory T cells to suppress immune responses and of the role that tumour-feeding blood vessels play in such immunosuppression. In parallel, Coukos has been very involved in the development of novel immunotherapies. He is a member of many professional societies and has received more than 20 awards for his work. In addition to being the director of Ludwig Lausanne, he also co-directs the Swiss Cancer Center Léman and is a full professor at the University of Lausanne.

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Selected results

Project
A tumour on a chip approach to understand signalling networks mediating melanoma drug resistance at the single-cell level
Institut für Zellbiologie, Universität Bern, Bern
CHF 363 200.– | Duration: 1. 6. 2016 – 30. 9. 2019 | KFS-3727-08-2015

Project coordinator
Prof. Olivier Pertz, PhD | olivier.pertz@izb.unibe.ch

Analysing single cancer cells

Today, how well a drug works against cancer cells is still being measured using methods that determine the average response of a cluster of cells. But cancer cells are diverse: Even when most of the cells die, a few cells are resistant to the treatment. To discover these first signs of resistance, researchers – supported by the Swiss Cancer Research foundation – are developing the technology for single-cell analyses.

Cells are highly complex systems with thousands of different proteins, the concentrations of which change depending on the current state of the cell. In this light, it is not surprising that the response to a treatment can vary. This apparently also applies to the new, targeted therapies that aim at a particular genetic mutation of cancer cells. "Even when 99 % of the cells die due to the treatment and only 1% survive, resistance can develop from that," says Olivier Pertz, professor of cell biology at the University of Bern.

Together with his research group, Pertz is developing new methods for analysis of what happens in single cells in a tumour cell group. For this purpose, they transfer fluorescent molecules – called biosensors – into the cells. When illuminated by a certain light source, the biosensors glow more or less intensively, depending on how strong certain signalling pathways are activated in the cell. A computer with image recognition software connected to the microscope then analyses automatically whether the cell is resting or – driven by the activated signalling pathway – is proliferating rapidly and uncontrolledly.

The researchers initially tested their method on melanoma cells that show the BRAF mutation that is typical of malignant melanomas. BRAF inhibitors can actually neutralize the effect of this mutation and in this way halt the development of the cancer. Unfortunately, however, cancer cells are robust. As the Pertz team has demonstrated in their experiments, a few cells resist the inhibition. "Using our dynamic single-cell analysis, we hope to derive simple rules that will show how we can tackle the robustness of cancer cells," says Pertz.

Project
EMT – an escape mechanism of cancer (stem) cells from therapy?
Departement Biomedizin, Universität Basel, Basel
CHF 348 000.– | Duration: 1. 3. 2015 – 28. 2. 2018 | KFS-3479-08-2014

Project coordinator
Prof. Gerhard M. Christofori, PhD | gerhard.christofori@unibas.ch

Making invasive cells harmless

A tumour becomes deadly mostly only when cancer cells spread to new areas of the body and form metastases. Metastasizing cancer cells often resist traditional chemotherapy. But a research project supported by the Swiss Cancer Research foundation has developed a new idea: The dangerous invasive cells can be converted into harmless fat cells.

Tumours are made up primarily of rapidly growing and dividing cells. Their intensive metabolism makes them responsive to chemotherapeutic agents. Unfortunately, however, tumours are more than merely a mass of proliferating cells. A small minority of the cancer cells are less active – but all the more adaptable and resistant. Precisely these cells play the main role in the formation of metastases.

The invasive cells originate in the rapidly multiplying cells but in their development go through a process called epithelial-mesenchymal transition (EMT). Cells on the surface of organs (the epithelium) undergoing an EMT lose their previous function and identity. But along with this loss of identity, there is a gain in development possibilities and plasticity. For this reason, cells transformed through EMT can not only survive chemotherapy but also detach from their sister cells in the tumour, enter the bloodstream, and travel to different parts of the body, where they form new tumours.

Up to now, the great plasticity of cancer cells was seen as a challenge. Now, the researchers also see an opportunity in cancer cell plasticity: EMT-transformed cells can be differentiated at least in the laboratory into practically any cells, as Gerhard Christofori's research group at the University of Basel has demonstrated in a research study funded by the Swiss Cancer Research foundation. The researchers converted dangerous invasive cancer cells into harmless fat cells using the anti-diabetic drug rosiglitazone combined with the cancer drug trametinib. "Fat cells no longer divide, so that this conversion neutralizes also the effect of the many mutations that otherwise drive the cancer cells to multiply rapidly," Christofori says.

As a next step, the researchers want to examine whether the drugs that they used can be combined with conventional chemotherapy. "The result would be an approach that targets both the invasively disseminating cells and the rapidly multiplying cancer cells," says Christofori. If these tests also show positive results, investors will be needed for financing the costly clinical trials with humans.

Reference

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List of approved research projects in 2018

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

Total funds allocated: CHF 12 533 775.–

Altmeyer Matthias | PARP inhibitor sensitization by deregulated PARP1 turnover in cancer
Institut für Molekulare Mechanismen bei Krankheiten, Universität Zürich, Zürich
CHF 361 300.– | Duration: 1. 7. 2018 – 30. 6. 2021 | KFS-4406-02-2018

Arber Caroline | Engineering T-cells to target multiple myeloma
Département d'oncologie, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 375 000.– | Duration: 1. 2. 2019 – 31. 1. 2022 | KFS-4542-08-2018

Becher Burkhard | Harnessing innate lymphoid cell surveillance of cancer metastasis
Institut für Experimentelle Immunologie, Universität Zürich, Zürich
CHF 334 900.– | Duration: 15. 10. 2018 – 14. 10. 2021 | KFS-4431-02-2018

Bentires-Alj Mohamed | Assessing the effects of protein tyrosine phosphatase SHP2 on immune cells in models of metastatic breast cancer
Departement Biomedizin, Universitätsspital Basel, Basel
CHF 375 000.– | Duration: 1. 3. 2019 – 28. 2. 2022 | KFS-4414-02-2018

Carbone Giuseppina | Biological and clinical impact of epigenetic cross-talks in ERG fusion positive prostate cancers
Laboratory of Experimental Oncology, Istituto Oncologico della Svizzera Italiana (IOSI), Bellinzona
CHF 246 500.– | Duration: 29. 12. 2018 – 29. 12. 2020 | KLS-4569-08-2018

Cejka Petr | Investigating the mechanisms of chemoresistance in BRCA-deficient cells
Istituto di Ricerca in Biomedicina (IRB), Bellinzona
CHF 326 950.– | Duration: 1. 8. 2018 – 31. 7. 2022 | KLS-4370-02-2018

Chijioke Obinna | NK cells driving CARs
Institut für Experimentelle Immunologie, Universität Zürich, Zürich
CHF 372 000.– | Duration: 1. 6. 2018 – 31. 5. 2021 | KFS-4371-02-2018

Constam Daniel | Melanoma immune surveillance by activin-A and its role in anti-PD-1 immune checkpoint therapy
Institut Suisse de Recherche Expérimentale sur le Cancer (ISREC), EPF de Lausanne (EPFL), Lausanne
CHF 371 050.– | Duration: 1. 8. 2018 – 31. 7. 2022 | KFS-4454-02-2018

Cosset Erika | A new role for Galectin-3 in glioblastoma aggressiveness
Département de Médecine, Université de Genève, Genève
CHF 367 500.– | Duration: 1. 1. 2019 – 31. 12. 2021 | KFS-4554-08-2018

Curioni Alessandra | Development of new immunotherapies for mesothelioma: learning from pre-clinical models to design clinical trials
Hämatologie und Onkologie, Universitätsspital Zürich, Zürich
CHF 238 450.– | Duration: 1. 2. 2019 – 31. 1. 2022 | KLS-4538-08-2018

De Palma Michele | Engineered dendritic cell vaccines for melanoma immunotherapy
Institut Suisse de Recherche Expérimentale sur le Cancer (ISREC), EPF de Lausanne (EPFL), Lausanne
CHF 355 350.– | Duration: 1. 7. 2019 – 30. 6. 2023 | KLS-4505-08-2018

Geiger Roger | The role of fatty acid metabolism in the anti-tumour T-cell response
Istituto di Ricerca in Biomedicina (IRB), Bellinzona
CHF 363 750.– | Duration: 1. 1. 2019 – 31. 12. 2021 | KFS-4593-08-2018

Giachino Claudio | Molecular mechanisms of oncogenesis versus tumour suppression by Notch in glioma subsets
Departement Biomedizin, Universität Basel, Basel
CHF 363 300.– | Duration: 1. 5. 2019 – 30. 4. 2022 | KLS-4518-08-2018

Hajnal Alex | Studying developmental cell invasion in the nematode C. elegans to understand tumour cell metastasis
Institut für Molekulare Biologie, Universität Zürich, Zürich
CHF 324 800.– | Duration: 1. 9. 2018 – 31. 8. 2021 | KFS-4377-02-2018

Hegi Monika | Targeting the epigenome of glioblastoma
Centre de recherche en neurosciences, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 272 750.– | Duration: 1. 9. 2018 – 31. 8. 2021 | KFS-4461-02-2018

Held Werner | Exploiting memory-like CD8 T-cells to improve tumour immunotherapy
Département d'oncologie, Université de Lausanne, Lausanne
CHF 361 750.– | Duration: 1. 9. 2018 – 31. 8. 2021 | KFS-4407-02-2018

Hutter Gregor | The role of microglia and its modulation in glioblastoma
Neurochirurgische Klinik, Universitätsspital Basel, Basel
CHF 323 050.– | Duration: 1. 8. 2018 – 31. 7. 2022 | KFS-4386-02-2018

Jandus Camilla | Innate lymphoid cells (ILCs) as novel, targetable immune regulators in bladder cancer patients
Département d'oncologie, Université de Lausanne, Lausanne
CHF 374 950.– | Duration: 1. 7. 2018 – 30. 6. 2021 | KFS-4402-02-2018

Johnson Rory | Multi-phenotype genome-engineering screens for long intergenic non-coding RNAs driving non-small cell lung cancer
Department for BioMedical Research, Universität Bern, Bern
CHF 359 350.– | Duration: 1. 1. 2019 – 31. 12. 2021 | KFS-4534-08-2018

Jungraithmayr Wolfgang | A new therapeutic concept against lung cancer by inhibition of CD26/DPP4
Klinik für Thoraxchirurgie, Universitätsspital Zürich, Zürich
CHF 251 600.– | Duration: 1. 6. 2018 – 30. 5. 2020 | KFS-4144-02-2017

Katanaev Vladimir | Cancer as 'information disease': application of the principles of information theory to signal transduction in cancer cells
Département de physiologie cellulaire et métabolisme, Université de Genève, Genève
CHF 360 350.– | Duration: 1. 10. 2018 – 30. 9. 2021 | KFS-4379-02-2018

Levesque Mitchell | Multi-omic, single-cell profiling of melanoma for predictive biomarker identification in check-point blockade
Dermatologische Klinik, Universitätsspital Zürich, Zürich
CHF 250 000.– | Duration: 1. 10. 2018 – 30. 9. 2020 | KFS-4459-02-2018

Martinou Jean-Claude | Genetic and pharmacological inhibition of the mitochondrial pyruvate carrier: effects on tumour growth and metastasis
Département de biologie cellulaire, Université de Genève, Genève
CHF 160 150.– | Duration: 1.1.2019 – 29.6.2020 | KFS-4434-02-2018

Nevado Cristina | Optimization of bromodomain blockers for the treatment of castration-resistant prostate cancer
Institut für Chemie, Universität Zürich, Zürich
CHF 249 300.– | Duration: 1.9.2019 – 31.8.2021 | KFS-4585-08-2018

Penengo Lorenza | High DNA replication speed promoted by the interferon stimulated gene 15 as a novel strategy for chemosensitization
Institut für Molekulare Krebsforschung, Universität Zürich, Zürich
CHF 375 000.– | Duration: 4.2.2019 – 3.2.2022 | KFS-4577-08-2018

Peter Matthias | Tumour growth and invasion – cellular mechanisms underlying the oncogenic properties of the novel multi-subunit E3 ubiquitin ligase GID in breast cancer development
Institut für Biochemie, ETH Zürich, Zürich
CHF 312 500.– | Duration: 1.10.2019 – 31.3.2022 | KLS-4574-08-2018

Petrausch Ulf | Optimizing CAR-T cells with PD-1/PD-L1 blockade for the treatment of malignant pleural mesothelioma
Institut für Experimentelle Immunologie, Universität Zürich, Zürich
CHF 47 775.– | Duration: 1.1.2018 – 30.6.2018 | KFS-4231-08-2017

Roth Patrick | Integrins as targets for advanced chimeric antigen receptor (CAR) T cell treatment of glioblastoma
Klinik für Neurologie, Universitätsspital Zürich, Zürich
CHF 352 300.– | Duration: 1.3.2019 – 28.2.2022 | KFS-4544-08-2018

Rüegg Curzio | Mechanisms and therapeutic targets of breast cancer metastatic colonization
Département d'oncologie, de microbiologie et d'immunologie, Université de Fribourg, Fribourg
CHF 357 800.– | Duration: 1.10.2018 – 30.9.2021 | KFS-4400-02-2018

Rufer Nathalie | Impact of TCR-ligand avidity on cell function, memory/survival, persistence and migration to tumour lesions of anti-cancer CD8 T-cell clonotypes
Département d'oncologie, Université de Lausanne, Lausanne
CHF 370 100.– | Duration: 1.9.2018 – 31.8.2021 | KFS-4368-02-2018

Santoro Raffaella | Towards personalized medicine of prostate cancer: modelling of prostate cancer heterogeneity through organoid technology
Institut für Molekulare Mechanismen bei Krankheiten, Universität Zürich, Zürich
CHF 306 950.– | Duration: 1.1.2019 – 31.12.2021 | KFS-4527-08-2018

Skoda Radek C. | Targeting metabolic alterations and extra-medullary haematopoiesis to treat myeloproliferative neoplasms
Departement Biomedizin, Universitätsspital Basel, Basel
CHF 374 250.– | Duration: 1.10.2018 – 30.9.2021 | KFS-4462-02-2018

Sommer Lukas | Mechanisms governing melanoma initiation, progression, and therapy resistance
Anatomisches Institut, Universität Zürich, Zürich
CHF 375 000.– | Duration: 1.1.2019 – 31.12.2021 | KFS-4570-08-2018

Stockmann Christian | Tuning of oxygen sensing in adoptive NK cell transfer for cancer therapy
Anatomisches Institut, Universität Zürich, Zürich
CHF 366 000.– | Duration: 1.1.2019 – 31.12.2021 | KFS-4397-02-2018

Sturla Shana | A molecular basis for stratifying patients with acute lymphoblastic leukaemia for personalized pro-drug therapy
Departement Gesundheitswissenschaften und Technologie, ETH Zürich, Zürich
CHF 368 300.– | Duration: 1. 9. 2018 – 31. 8. 2022 | KFS-4443-02-2018

Tang Li | Delivery of cancer neoantigen vaccine with a carrier-free nanogel for personalized immunotherapy
Laboratory of Biomaterials for Immunoengineering, EPF de Lausanne (EPFL), Lausanne
CHF 313 950.– | Duration: 1. 7. 2019 – 30. 6. 2023 | KFS-4600-08-2018

Vozenin Marie-Catherine | Phase III clinical trial: therapeutic efficacy of FLASH-RT in domestic cats with superficial carcinoma of the nasal planum
Service de Radio-Oncologie, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 186 750.– | Duration: 1. 10. 2018 – 30. 9. 2022 | KFS-4438-02-2018

Werner Sabine | Roles and mechanisms of action of the growth and differentiation factor activin in skin carcinogenesis
Institut für Molekulare Gesundheitswissenschaften, ETH Zürich, Zürich
CHF 366 900.– | Duration: 1. 1. 2019 – 31. 12. 2021 | KFS-4510-08-2018

Zhang Ye | Towards online MRI guided scanned proton therapy
Zentrum für Protonentherapie, Paul Scherrer Institut (PSI), Villigen
CHF 321 100.– | Duration: 1. 8. 2019 – 31. 7. 2023 | KFS-4517-08-2018

Mesothelioma real-time data from Europe: the Mesoscape database and virtual tumour bank

Introduction

Malignant pleural mesothelioma (MPM) is an aggressive tumour with heterogeneous behaviour arising from the mesothelial cells lining the thoracic cavity and lung surface. MPM is a rare cancer that is difficult to treat and is commonly associated with asbestos exposure[1]. Based on data from the Italian mesothelioma registry, the median latency from exposure to onset of the disease is 44.6 years[2]. In Europe, the incidence is about 20 per million[3]. The incidence rate is still rising; the peak is expected around 2020 and beyond[2,4]. Moreover, asbestos is still being used in many developing countries[5]. Prognosis of MPM remains dismal, with a median survival of around 12 months for patients receiving chemotherapy only[6] and around 23 months for patients receiving multimodality treatment[7,8].

To allow further refinement of the available treatment modalities, markers predicting therapy response and prognosticating patients' progression free survival (PFS) and overall survival (OS) are of great interest in order to select subgroups of patients benefitting from multimodal treatment or not. Further studies may provide knowledge about the pathways involved in MPM carcinogenesis, and genes within the identified pathways could be used as new therapeutic targets.

The multicentric collection of clinical as well as pathological data submitted to a database and virtual tumour bank allows researchers to improve knowledge and facilitate decision making in patients with MPM. Mesoscape is a multi-institutional European tissue bank, built under the umbrella of the European Thoracic Oncology Platform (ETOP) and chaired by Isabelle Schmitt-Opitz (Switzerland) and Paul Baas (The Netherlands). Mesoscape aims to harmonize and raise standards of translational research in MPM.

Prof. Isabelle Schmitt-Opitz, MD
Senior attending surgeon at the Department of Thoracic Surgery at University Hospital Zurich

The ETOP Mesoscape project is designed to address clinical, pathological, and molecular characteristics of mesothelioma and their impact on outcome. The analysis of the database is a unique approach to real-time data, reflecting the reality of mesothelioma characteristics, treatment, and prognosis in Europe.

Materials and methods

A decentralized biobank with fully annotated tissue samples was established. Selection criteria for participating centres included sufficient number of cases and documented ethical approval. Patient selection was based on availability of comprehensive clinical data with adequate follow-up and on adequate quantity and quality of formalin-fixed paraffin-embedded (FFPE) tumour tissue.

Following a stringent data quality review, participating centres were informed as to which cases qualified, and thereafter they retrieved respective tissue blocks and proceeded with either tissue microarray (TMA) construction on-site or shipment of the block for TMA construction at the Institute of Pathology at University Hospital Zurich. Inclusion criteria for FFPE blocks for TMA construction were:

a. A diagnosis of mesothelioma according to the 2004 WHO classification.
b. Tumour samples should be fixed in buffered formalin 4%.
c. Optimal donor blocks are defined by the presence of adequate quantity (at least 0.5 cm^2) of tumour tissue in one or more blocks of FFPE tissue. Note that 0.5 cm^2 of tumour tissue will be adequate to generate one TMA but insufficient for creating a replicate block.
d. The donor blocks have to be at least 3 mm thick to enable TMA construction. Thicker tissue blocks are preferred, since they allow more stability during TMA construction and increase section number from each TMA block.

Results

At the end of May 2019, the ETOP Mesoscape contained information on 497 patients from ten centres, diagnosed between 1999 and 2018. The following centres are participating in the Mesoscape project:

- Sotiria General Hospital, Athens, Greece (17 cases)
- Netherlands Cancer Institute, Amsterdam, The Netherlands (50 cases)
- University Hospital Zagreb, Zagreb, Croatia (28 cases)
- University Hospital Leuven, Leuven, Belgium (40 cases)
- University Hospital of Parma, Parma, Italy (33 cases)
- University Hospital Zurich, Zurich, Switzerland (255 cases)
- Institut Català d'Oncologia (Bellvitge), Barcelona, Spain (28 cases)
- Erasmus MC, Rotterdam, The Netherlands (5 cases)
- St. James's Hospital, Dublin, Ireland (10 cases)
- University Health Network, Toronto, Canada (31 cases)

The following results are a preliminary report. A more detailed analysis including also pathological data is planned in the future. Patients were primarily men (84%) with an ECOG Performance status of 0 or 1 (each 46%); 75% of the patients had known previous exposure to asbestos. The median age was 64 years. The primary histology of patients was epithelioid (72%), followed by biphasic (22%) and sarcomatoid (6%). Clinical staging was available for 77% of the

patients. The stage distribution (I/II/III/IV) was 14%/29%/42%/15%. Among the biomarkers common in both data sources, calretinin and WT1 were detected in the vast majority of patients tested (calretinin: 97%, WT1: 89%). 90% of the tested cases were CK5/6 positive, 91% were D2-40 positive, and 97% were Pan-CK positive.

Palliative treatment was administered in 41% of the cases. Of these patients, 84% received palliative chemotherapy (mostly using multiple agents). Palliative surgery was undertaken in 32% (62 of 194 patients with available information) and palliative radiotherapy in 13% of the patients. Complete resection was performed in 59% of the Mesoscape patients. This was combined with induction chemotherapy (81%), and adjuvant chemotherapy and radiotherapy were administered in 4% and 37% of the patients, respectively.

Conclusion and outlook

Mesoscape is one of the largest databases, allowing reports on mesothelioma epidemiology and treatment. As tissue from all Mesoscape patients is preserved locally and is available for detailed molecular investigations, Mesoscape provides an excellent basis for evaluating the influence of molecular parameters on the disease outcome, as well as providing an overview of the molecular landscape. Besides these epidemiological analyses, several biomarkers will be assessed for their clinical significance. Currently, clinical data will be matched with the ESTS (European Society of Thoracic Surgery) registry of more than 2000 mesothelioma cases for a relevant epidemiological study of MPM treatment in Europe. The Mesoscape virtual biobank will be a detailed clinical database coupled to a state of the art pathological (and molecular) database, which will allow us and other clinical researchers to analyse larger numbers of cases than currently possible in single institution studies. This will accelerate the translation of biomarker knowledge obtained through Mesoscape projects to the clinic. In addition, procedures used by groups of mesothelioma specialists working in translational research across Europe will be coordinated and harmonized. Furthermore, the collaborative work will raise the standards of translational research and result in the development of diagnostic or prognostic algorithms for personalized medicine in mesothelioma care. Ultimately, Mesoscape will bring together specialists from all fields of mesothelioma research. This will result in more coordinated and harmonized research efforts towards personalized treatment of a devastating cancer.

Acknowledgment

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Prof. Isabelle Schmitt-Opitz, MD

Isabelle Schmitt-Opitz studied at the University of Cologne Medical School and then entered a clinical and research residency at the Department of General-, Visceral-, Vascular- and Thoracic Surgery of the Charité in Berlin. Since 2004, she has worked at the Division of Thoracic Surgery at University Hospital Zurich. She won a Swiss National Science Foundation Professorship in 2011 and is a member of the medical faculty of the University of Zurich. Her research interests focus on improving treatment outcomes of patients with mesothelioma.

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Selected results

Project
How physical activity influences carcinogenesis: the case of HCC
Department for BioMedical Research, Universität Bern, Bern
CHF 234 750.– | Duration: 2. 2. 2015 – 31. 7. 2018 | KFS-3506-08-2014

Project coordinator
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Exercise is medicine for liver cancer

Regular physical exercise has anti-tumour effects and reduces the growth and progression of liver cancer, as researchers have discovered in studies funded by the Swiss Cancer Research foundation. In addition, the anti-diabetic drug metformin was shown to have a similar effect.

It has been known for some time that regular physical exercise promotes health and helps prevent overweight, diabetes, chronic inflammation, and even several types of cancer. But whether exercise is also beneficial to a person with cancer has been little studied up to now. A research team headed by Jean-François Dufour at Inselspital and the University of Bern has now reduced this gap in knowledge through experiments with rats.

The researchers implanted tumours in the livers of the rats and then divided the animals into different treatment groups. Compared to tumours in rats in the sedentary group, tumours in rats in the exercise group, which ran on a treadmill for 60 minutes a day, grew more slowly. The anti-tumour effect of active muscle power was also found when exercise was combined with sorafenib. At present, sorafenib is the only approved drug for first-line treatment of liver cancer.

The researchers discuss two reasons for the additive effect of regular physical activity with sorafenib. First, sorafenib and physical activity affect different signalling pathways in the cancer cells. The simultaneous effects work like a combination therapy. Second, based on their analyses, the researchers also discovered that regular physical activity changed the behaviour not only of the cancer cells but also of the healthy liver cells in the vicinity of the tumour. The researchers deem this finding important, because liver cancer (more so than other types of cancer) is dependent on the tumour environment.

Many patients are weakened by liver cancer to the extent that they cannot be expected to engage in intensive physical activity. For this reason, Dufour and his group also tested whether the cancer-inhibiting effect of physical activity can also be achieved through medication. They knew that the anti-diabetic drug metformin has an effect on the same molecular pathways as does physical activity. But they are the first to demonstrate through their findings that metformin can be combined with sorafenib and that the combination (like the combination with physical activity) can provide additional anti-tumour effects. It remains to be shown whether these new findings can apply to human patients and clinical practice.

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Project

Clinical decision-making with novel cancer treatments: a meta-epidemiological study on the post-approval generation of clinical evidence

Basel Institut für Klinische Epidemiologie & Biostatistik, Universitätsspital Basel, Basel

CHF 166 000.– | Duration: 1. 10. 2015 – 30. 9. 2018 | KLS-3587-02-2015

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Uncertainty when treating with novel cancer drugs

The knowledge documented in clinical trials on the benefits of new cancer drugs is much more limited than previously assumed. Often, one single trial is the basis for the decision to approve a substance for the market. This conclusion was reached by a research project supported by the Swiss Cancer League.

In the period from 2000 to 2016, 92 novel drugs were approved by the US Food and Drug Administration (FDA). With such a large number of new drugs, it becomes more and more difficult to maintain an overview. But now, in a research project funded by the Swiss Cancer League, Lars Hemkens and his research group have conducted a systematic examination of the complex and often hundreds-of-pages-long approval documents of the FDA, also extracting the relevant information for assessing the benefit and entering the information into a novel database.

This database is intended to be made available to the international research community, so that the existing evidence will be better utilizable in the future: The database should help physicians and their patients to make well-founded treatment decisions. However, when creating the database, Hemkens and his team noticed that the evidence basis is often rather thin. In contrast to other areas of medicine, such as cardiology or diabetology, where for every substance there are several approval trials, the requirements for cancer drugs are less stringent.

Especially since the FDA began assessing novel drugs according to its Accelerated Approval Program, it seems to be increasingly finding also single, often not randomized clinical trials with fewer than 200 patients to be a sufficient basis for decision making on approval. "The approval authorities are working in an area with conflicting expectations and demands," says Hemkens. On the one hand, there is a sense of urgency to make new substances available as quickly as possible to patients facing the risk of death. But this argument loses some of its power, if the fact that the new substances often increase patient survival by only a few months is taken into account. On the other hand, the FDA should make certain that it has received sufficient data to be able to correctly judge the benefit and side effects of a substance. "If a therapy is approved based on evidence from a single trial only, there is uncertainty about its actual benefit: A second or third study could change the assessment of the drug's effects considerably. To be sure that patients receive good treatment, today and in the future, we need more clinical trials – not fewer," says Hemkens.

References

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Ladanie A, Speich B, Naudet F, Agarwal A, Pereira TV, Sclafani F, et al. The Comparative Effectiveness of Innovative Treatments for Cancer (CEIT-Cancer) project: Rationale and design of the database and the collection of evidence available at approval of novel drugs. *Trials.* 2018;19:505.

Ladanie A, Speich B, Briel M, Sclafani F, Bucher HC, Agarwal A, et al. Single pivotal trials with few corroborating characteristics were used for FDA approval of cancer therapies. *J Clin Epidemiol.* 2019. pii: S0895-4356(19)30008-3. [Epub ahead of print]

List of approved research projects in 2018

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

Total funds allocated: CHF 7 714 000.–

Ansari Marc | The children's hepatic international collaboration (CHIC)
Unité d'onco-hématologie pédiatrique, Hôpitaux universitaires de Genève (HUG), Genève
CHF 45 400.– | Duration: 1. 1. 2019 – 31. 12. 2020 | KLS-4540-08-2018

Blum Sabine | A randomized phase II multicentre study to assess the tolerability and efficacy of the addition of midostaurin to 10-day decitabine in UNFIT (i.e. HCT-CI ≥ 3) adult AML and high risk myelodysplasia (MDS) (IPSS-R > 4.5) patients
Oncologie, Service d'hématologie, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 191 900.– | Duration: 1. 7. 2018 – 31. 1. 2020 | KFS-4412-02-2018

Bornhauser Beat | RIPping off novel cell death pathways to eradicate drug resistant leukaemia
Experimentelle Infektiologie und Krebsforschung, Universitäts-Kinderspital Zürich, Zürich
CHF 375 000.– | Duration: 1. 10. 2018 – 30. 9. 2021 | KFS-4384-02-2018

Bourquin Carole | Impact of obesity on anti-tumour response to immunotherapy
Section des Sciences Pharmaceutiques, Université de Genève, Genève
CHF 368 850.– | Duration: 1. 3. 2019 – 28. 2. 2022 | KFS-4535-08-2018

Elicin Olgun | VoiceS: voice quality after transoral CO_2-laser surgery versus single vocal cord irradiation for unilateral stage 0 & I glottic larynx cancer – a randomized phase III trial
Universitätsklinik für Radio-Onkologie, Inselspital Bern, Bern
CHF 160 700.– | Duration: 1. 10. 2019 – 30. 9. 2023 | KLS-4567-08-2018

Flatz Lukas | Deciphering anti-PD1-induced autoimmune skin toxicity in non-small cell lung cancer
Institut für Immunbiologie, Kantonsspital St. Gallen (KSSG), St. Gallen
CHF 358 800.– | Duration: 1. 9. 2018 – 31. 8. 2021 | KLS-4409-02-2018

Ghielmini Michele | Multilayer model for personalized risk stratification of follicular lymphoma patients
Ospedale Regionale Bellinzona e Valli, Istituto Oncologico della Svizzera Italiana (IOSI), Bellinzona
CHF 330 800.– | Duration: 1. 9. 2018 – 31. 8. 2021 | KFS-4395-02-2018

Heinzelmann-Schwarz Viola | Maintenance therapy with aromatase inhibitor in epithelial ovarian cancer: a phase III randomized double-blind placebo-controlled trial (MATAO trial)
Frauenklinik, Universitätsspital Basel, Basel
CHF 375 000.– | Duration: 1. 2. 2019 – 31. 1. 2023 | KFS-4586-08-2018

Hrbacek Jan | Clip-free ocular proton therapy
Zentrum für Protonentherapie, Paul Scherrer Institut (PSI), Villigen
CHF 247 700.– | Duration: 1. 7. 2018 – 30. 6. 2021 | KFS-4447-02-2018

Moeckli Raphaël | Multi-criteria decision making in radiotherapy: robustness and clinical regions of interest of pareto fronts
Institut de Radiophysique, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 232 950.– | Duration: 1. 3. 2019 – 28. 2. 2023 | KFS-4399-02-2018

Ng Charlotte | Single-cell dissection of the cellular ecosystem in hepatocellular carcinoma
Department for BioMedical Research, Universität Bern, Bern
CHF 250 350.– | Duration: 1. 9. 2019 – 31. 8. 2023 | KFS-4543-08-2018

Papachristofilou Alexandros | SAKK 01/18: reduced intensity radiochemotherapy for stage IIA/B seminoma
Klinik für Strahlentherapie und Radioonkologie, Universitätsspital Basel, Basel
CHF 356 700.– | Duration: 1. 1. 2019 – 31. 12. 2022 | KLS-4511-08-2018

Peters Solange | Characterization of sugar usage by pro-tumour neutrophils in lung cancer
Centre Pluridisciplinaire d'Oncologie, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 340 350.– | Duration: 1. 1. 2019 – 31. 12. 2021 | KFS-4555-08-2018

Pless Miklos | Comparison of PD-L1 expression before and after neoadjuvant chemoradiation or chemotherapy in stage III non-small cell lung cancer. A retrospective analysis
Medizinische Onkologie, Kantonsspital Winterthur, Winterthur
CHF 31 650.– | Duration: 1. 3. 2018 – 28. 2. 2020 | KFS-4381-02-2018

Radtke Freddy | Neutrophil mediated immune-suppression in colorectal cancer
Institut Suisse de Recherche Expérimentale sur le Cancer (ISREC), EPF de Lausanne (EPFL), Lausanne
CHF 365 200.– | Duration: 1. 1. 2019 – 31. 12. 2021 | KFS-4513-08-2018

Rentsch Cyrill A. | Extended pelvic lymph node dissection vs. no pelvic lymph node dissection at radical prostatectomy for intermediate- and high-risk prostate cancer
Abteilung Urologie, Universitätsspital Basel, Basel
CHF 365 950.– | Duration: 1. 9. 2019 – 31. 8. 2022 | KLS-4436-02-2018

Riether Carsten | IL-21/IL-21R signalling in leukaemia stem cells
Department of BioMedical Research, Universität Bern, Bern
CHF 325 000.– | Duration: 1. 10. 2018 – 30. 9. 2022 | KFS-4389-02-2018

Romero Pedro | Translating insights on murine T-cell metabolic intervention to the clinical theater
Département d'oncologie, Université de Lausanne, Lausanne
CHF 361 750.– | Duration: 1. 6. 2018 – 31. 5. 2021 | KFS-4404-02-2018

Soysal Savas Deniz | Stromal gene expression signatures: a predictive marker for associated malignancy in breast biopsies of uncertain malignant potential to reduce open surgical excisions
Clarunis Universitäres Bauchzentrum Basel, Universitätsspital Basel, Basel
CHF 318 400.– | Duration: 1. 10. 2018 – 30. 9. 2021 | KFS-4375-02-2018

Szabo Csaba | Delineation of the molecular mechanisms responsible for the upregulation of H2S biosynthesis in colon cancer cells
Département d'oncologie, de microbiologie et d'immunologie, Université de Fribourg, Fribourg
CHF 346 550.– | Duration: 1. 4. 2019 – 31. 3. 2023 | KLS-4504-08-2018

Tausch Christoph | VISION I: vacuum assisted biopsy immediately before surgery as an intra- or peri-operative comparison for patients who underwent neoadjuvant chemotherapy for breast cancer
Chirurgie, Brust-Zentrum Zürich, Zürich
CHF 370 550.– | Duration: 1. 9. 2018 – 31. 8. 2022 | KFS-4426-02-2018

Unkelbach Jan | Combined proton-photon radiotherapy
Klinik für Radio-Onkologie, Universitätsspital Zürich, Zürich
CHF 336 400.– | Duration: 1. 4. 2019 – 31. 3. 2022 | KFS-4528-08-2018

Velin Dominique | Role of helicobacter pylori infection in the response to cancer immunotherapies
Service de gastro-entérologie et d'hépatologie, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 300 050.– | Duration: 1. 7. 2018 – 30. 6. 2021 | KFS-4452-02-2018

Zander Thilo | SAKK 39/16 – OptiPOM: alternate day dosing of pomalidomide in patients with refractory multiple myeloma. A multicentre, single arm phase II trial
Innere Medizin/Onkologie, Luzerner Kantonsspital, Luzern
CHF 351 300.– | Duration: 1. 11. 2018 – 31. 10. 2021 | KFS-4564-08-2018

Zenz Thorsten | The landscape of drug combination effects in leukaemia & lymphoma
Hämatologie, Universitätsspital Zürich, Zürich
CHF 245 450.– | Duration: 1. 7. 2018 – 30. 6. 2021 | KFS-4439-02-2018

Zlobec Inti | Refining risk-stratification for colorectal cancer patients: convolutional neural network analysis of histological images to predict outcome and molecular subtyping
Institut für Pathologie, Universität Bern, Bern
CHF 361 250.– | Duration: 1. 8. 2018 – 30. 4. 2022 | KFS-4427-02-2018

Approved bursaries in 2018

Total funds allocated: CHF 562 000.–

Finazzi Tobias | Evaluating the benefit of stereotactic MRI-guided adaptive radiotherapy for early-stage non-small cell lung cancer
Destination: Department of Radiation Oncology, VU University Medical Center, Amsterdam (NL)
CHF 19 000.– | Duration: 1. 9. 2018 – 29. 2. 2020 | BIL KFS-4380-02-2018

Fischer Stefanie | Metastatic prostate cancer and innate immunity: finding a predictive biomarker for response to taxanes
Destination: Academic Health Science Centre, University of Manchester, and The Christie NHS Foundation Trust, Manchester (GB)
CHF 102 000.– | Duration: 1. 11. 2018 – 31. 10. 2020 | BIL KLS-4502-08-2018

Kienzler Jenny Christine | Improvement in treatment of brain metastases – timing of radiosurgery in relation to surgery and immunotherapy for best local control – comparison of endogenous immune response and genetic signature of the tumour microenvironment between primary tumours and brain metastases
Destination: David Geffen School of Medicine, Department of Neuro-surgery, Brain Tumor Center, University of Los Angeles (USA)
CHF 105 000.– | Duration: 1. 1. 2019 – 31. 12. 2020 | BIL KFS-4563-08-2018

Mortezavi Ashkan | Cell-free circulating tumour DNA profiling of localized prostate cancer for improved disease detection and classification
Destination: Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm (S)
CHF 182 000.– | Duration: 1. 9. 2018 – 31. 8. 2020 | BIL KLS-4558-08-2018

Schmid Sabine | Lung cancer early detection and classification using methylome analysis of plasma cell-free DNA
Destination: Medical Oncology, Kantonsspital St. Gallen (KSSG)
CHF 154 000.– | Duration: 1. 7. 2019 – 30. 6. 2021 | BIL KFS-4393-02-2018

From the struggle against the disease to the return to normal life: Stress and adjustment in breast cancer survivors and their partners

The stress associated with breast cancer may have enduring negative consequences on the affected women and their partners even several years after the end of oncological treatment, when women are considered as cancer survivors (five years after diagnosis according to the American Cancer Society[1]). This lasting impact has long been underestimated; consequently, the "forgotten needs of survivors" have been emphasized in the literature (e. g. Holzner et al.[2]). Studies are thus needed to better understand the variables playing a role in survivors' and partners' adjustment when returning to a life without illness. To this end, with the support of the Swiss Cancer League we are currently conducting a follow-up study (Phase II) of a previous study made at the Breast Centre of the CHUV in Lausanne (Phase I study, supported by SNSF/NCCR LIVES and the Swiss Cancer League). In Phase I, we interviewed and surveyed more than 120 women with non-metastatic breast cancer four times across the two years following breast surgery. The ongoing Phase II study is focused on the women's needs; in parallel, we have also conducted another study on partners' needs.

Breast cancer and stress associated with the disease in women

Breast cancer is a major stressful event. Women have to cope not only with the somatic symptoms (such as extreme fatigue) related to the disease and its treatment but also with its emotional consequences. The announcement of the diagnosis may be experienced as a traumatic event: Women face fear of death and

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uncertainty about the future. In addition, they have to reorganize their daily life to deal with the practical constraints of treatment. Unsuccessful coping with this situation may result in elevated levels of psychological distress; evidence is strong that elevated distress at the beginning of treatment is predictive of psychological problems (such as depression and anxiety), independently of the evolution of the cancer[3]. There are, however, large individual differences; some women are able to cope with this situation more efficiently than others. Several psychosocial variables have been found to explain this variability in the immediate post-surgery period[4-7]: the quality of social support, the quality of the couple relationship, the ability to trust others and to perceive the help given by caregivers, and privileged coping strategies, to name a few.

Whereas some studies have shown that survivorship induces immediate relief and a significant improvement in quality of life over a period of five years, in the long term the women have to face several other challenges, including the fear of recurrence, the aftermath of the stress experienced during the acute phase of the disease, the integration of a new body image, the return to being a regular couple with a regular sexual life, and enduring pain (e. g. in the breast area where the surgery was performed and the arm/shoulder region, or phantom breast pain). For these reasons, stress and emotional distress may remain elevated even in the long term, with possible implications such as depression, relational distress, and diminished engagement in work[8]. The aim of our Phase II study is thus to identify the needs of the women and to evaluate the extent to which the psychosocial variables assessed during the treatment phase may explain individual variability and which variables buffer or, on the contrary, aggravate the impact of the stress associated with the illness. In this new Phase, 41 women agreed to participate, five to seven years after the breast surgery. The methodology is mainly qualitative, relying on in-depth interviews, but some variables are also being assessed via questionnaires (e. g. psychological distress, posttraumatic stress, sexual functioning). The study is in progress. Elements of the first interviews highlight the feeling of some women of having been left on their own at the end of the treatment, when there was no more support from the medical staff, persistent concerns about body image, and the necessity to make sense of the illness by integrating it in an autobiographical narrative.

Psychological distress in partners

Like patients, partners may also report a high level of psychological distress during the acute phase of the illness as well as in a long-term perspective. During the treatment period, they have to cope with the fear of losing their loved one and uncertainty about the couple's future. Moreover, they assume increased responsibility for daily tasks (i. e. take over the tasks that the women cannot do and take care of the women). This has been referred to as the "caregiver burden", which is a condition associated with risk of the development of psychological distress[4,9]. The return to normal life is a challenge as well. In another

study led by our team (Sarah Cairo Notari as principal investigator) and supported by the University Fund Maurice Chalumeau and the Swiss National Science Foundation, we specifically examined the experiences of male partners of breast cancer survivors, by focusing on the long-term impact of the illness on their intimate and sexual life. Preliminary analyses revealed that most partners reported changes in their sexuality long after the end of treatments. There is great individual variability in the way that changes were experienced, especially depending on the meaning and expectancies that men have regarding their own sexuality. A lack of information and support from health professionals was also reported. These findings reinforce the necessity for health professionals to acknowledge the needs of partners, especially regarding sexuality[10].

Conclusion

Women and their partners may still be affected by the emotional aftermath of the disease, at a time when support is dramatically reduced, however, as the end of medical treatment is often considered as the end of the women's needs – not to mention the needs of partners, which are often not acknowledged even at the time of treatment. Getting back to 'normal' life is a challenge in cancer, and tailor-made interventions must be designed by taking into account the needs expressed by the patients and their partners.

Prof. Nicolas Favez, PhD

Nicolas Favez is a full professor at the Faculty of Psychology and Educational Sciences of the University of Geneva. Favez heads the Clinical Psychology of Interpersonal Relationships Unit (UPCRI). He is also co-director of the research unit of the Centre for Family Study (IUP, Lausanne University Hospital). He is specialized in couple, family, and interpersonal relationships. His research activities and teaching relate to family and couple relationships, observation and assessment methodology, and therapeutic work with couples and families. He has published a variety of books and papers on couple and family interactions.

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Sarah Cairo Notari, PhD

Sarah Cairo Notari is a research and teaching fellow and senior lecturer at the Faculty of Psychology and Educational Sciences of the University of Geneva. Notari completed undergraduate studies at the University of Lausanne and a PhD in psychology at the University of Geneva in 2016. She has worked in the Clinical Psychology of Interpersonal Relationships Unit (UPCRI) since 2010. Her teaching and research interests lie in the area of psycho-oncology, clinical health psychology, couple relationships and sexology.

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10. Cairo Notari S, Medico D, Zaman K, Favez N. Sexuality after women's breast cancer: The experiences of survivors' male partners. *Psycho-Oncology.* 2018;27 Suppl 3:178.

Selected results

Project
Web-based stress management for newly diagnosed cancer patients (STREAM-1): a randomized, wait-list controlled intervention study
Frauenklinik, Universitätsspital Basel, Basel
CHF 267 340.– | Duration: 1. 1. 2014 – 30. 4. 2018 | KFS-3260-08-2013

Project coordinator
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Online help improves quality of life in patients with cancer

For many patients, a cancer diagnosis causes psychological distress. An online stress management program can provide relief, as shown by a study supported by the Swiss Cancer Research foundation.

Most patients report that the period immediately after the cancer diagnosis is difficult. Suddenly, their world is turned upside down. They need to regain their footing despite all their worries. Professional psychological support can help, but only a minority of patients with newly diagnosed cancer receive psycho-oncological care. That is mainly because psycho-oncological services have busy workloads and cannot accept and provide services to an unlimited number of new patients.

Supported by the Swiss Cancer Research foundation, a team of researchers has developed an online stress management programme for newly diagnosed patients with cancer called STREAM (Stress aktiv mindern). STREAM offers patients with cancer a low-threshold option for help in dealing with their stressful situation. In a study with 129 patients in Switzerland, Germany, and Austria, the researchers found that this web-based programme providing online guidance is very feasible – and effective in improving quality of life.

For eight weeks, the online guidance intervention gave participants practical exercises and specific information on managing the stress that many patients experience most keenly at the start of their illness. In addition, therapists provided weekly written feedback via e-mail. For Viviane Hess, a senior physician in oncology at University Hospital Basel and one of the researchers, the results of the study reveal not only that helping patients to help themselves and regular e-mail contact support patients efficiently but also that patients who get through the initial shock well usually also tolerate the therapy better and improve their prospects of successful treatment.

Reference

Urech C, Grossert A, Alder J, Scherer S, Handschin B, Kasenda B, et al. Web-Based Stress Management for Newly Diagnosed Patients With Cancer (STREAM): A Randomized, Wait-List Controlled Intervention Study. *J Clin Oncol.* 2018;36:780-8.

List of approved research projects in 2018

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

Total funds allocated: CHF 1 227 350.–

Barth Jürgen | Effectiveness of a mindfulness and relaxation self-care app for cancer patients: a randomized controlled multicentre study
Institut für komplementäre und integrative Medizin, Universitätsspital Zürich, Zürich
CHF 359 400.– | Duration: 1. 10. 2019 – 30. 9. 2022 | KFS-4556-08-2018

Bourquin Sachse Céline | Towards "second generation" communication trainings in cancer care: in search of meaningful outcome measures
Service de Psychiatrie de Liaison, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 152 350.– | Duration: 1. 3. 2019 – 29. 8. 2020 | KFS-4401-02-2018

Favez Nicolas | From the struggle against the disease to the return to normal life: stress and adjustment in breast cancer survivors
Faculté de psychologie et des sciences de l'éducation, Université de Genève, Genève
CHF 58 450.– | Duration: 1. 3. 2019 – 29. 2. 2020 | KLS-4507-08-2018

Guttormsen Sissel | Communication with cancer patients and their families about approaching death: scaffolding conceptual and practical learning for health professionals
Institut für Medizinische Lehre, Universität Bern, Bern
CHF 374 950.– | Duration: 1. 4. 2019 – 31. 3. 2022 | KFS-4522-08-2018

Jenewein Josef | Dignity therapy+: a brief psychological and existential intervention for dying patients and their families
Klinik für Psychiatrie und Psychotherapie, Universitätsspital Zürich, Zürich
CHF 147 500.– | Duration: 1. 11. 2018 – 31. 10. 2020 | KFS-4413-02-2018

Pautex Sophie | "Revie ⊕" Impact of a resource-based life review intervention on advanced cancer patients in an oncological outpatient centre: a waitlist randomized controlled trial
Unité de soins palliatifs communautaires, Hôpitaux universitaires de Genève (HUG), Genève
CHF 134 700.– | Duration: 1. 9. 2018 – 31. 8. 2021 | KFS-4390-02-2018

Measuring regional difference in cancer care: Trends in breast cancer surgical procedures and their relation to socioeconomic disparities and screening patterns

Much debated in the discussion of social inequalities in health has been the role of medical care. Inequal access to early detection, appropriate care, and state of the art management as well as differences in tumour biology are possible explanations for survival differences between socio economic classes. Regional disparities have been described for Switzerland that affect income, access to services including access to health care services, education, and other socio economic factors[1].

There is a high availability of public or private resources to be allocated to health. Switzerland is one of the richest countries in the world and its expenditure per person on health is among the highest[2]. This applies also to the per person costs for cancer, even when adjusting for direct purchasing power. In Switzerland, the standard of care is high, uptake of new drugs is above average compared to other countries in Europe[3], and life expectancy is one of the highest in the world. However, since health care policies are mainly developed at the cantonal level, there is a considerable amount of geographical variation in health expenditures, control programmes, and treatment procedures.

Wealth of information in the hospital discharge dataset

In cantons with cancer registration, detailed analyses can be made. Ess et al.[4] found important regional disparities in the state of the art management of breast cancer among regions covered by cancer registration. Disparities included surgical as well as non-surgical management issues. Predictors of guideline compliance on the patient level were treatment by a surgeon

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with high caseload, residence, and age of the patient but not socio economic factors. There were pronounced differences in mastectomy rates from 24 % in Geneva to 38 % in St. Gallen in 2003–2005. The differences persisted after adjustment for age and tumour size. However, it was unclear where the other cantons would fit into this picture.

In cantons without cancer registration, consistent measurement of quality of care is not easily possible. Beginning in 2020, all cantons are mandated to collect data under the new Cancer Registration Act, so that results may be available in a few years. In a recent study[5], we showed an alternative way to measure by using the nationwide hospital discharge dataset. We assessed whether the differences in breast cancer care described above persisted over time and how the results relate to the situation in the whole country.

In Switzerland, geo-referenced data on hospitalizations including socio economic characteristics of the patient, diagnosis, and procedures have been collected yearly by the Federal Statistical Office since 1998 and cover the whole country. The wealth of information provided in the database has the potential to assess space-time patterns and trends of cancer health care-related procedures for control and health planning purposes, but it has only been used occasionally.

In our study, we applied Bayesian negative-binomial spatio-temporal models. We adjusted for influencing factors and took time and geographical correlation into account. Covariates were patient characteristics and regional surgeon and gynaecologist density. We included women with invasive breast cancer as the main reason for hospitalization who had at least one breast cancer-related surgery and did not present with distant metastases at first visit.

Reduced mastectomy rates in regions with mammography screening programmes

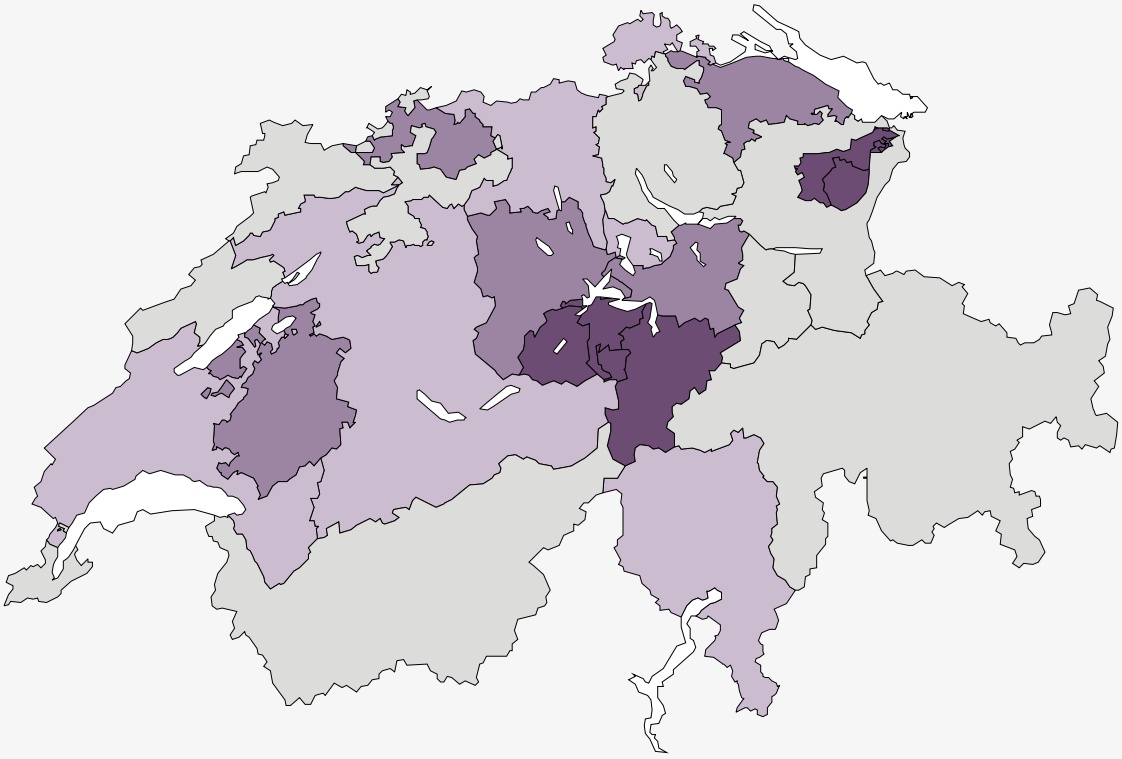
We analysed more than 70 000 patients with breast cancer. Mastectomy rates declined from 43 % to 30 % from 2000 to 2012 for patients aged 50–69 and from 61 % to 43 % for patients above the age of 70. Mastectomy rates remained stable for patients under 50. At all ages we found important geographical differences. Compared to the German-speaking part of Switzerland, mastectomy rates in the French-speaking region were significantly lower (relative risk ratio (RR): 0.72). The French-speaking region was the first to establish mammography screening programmes (MSPs). However, the existence of MSPs correlated with an additional significantly reduced rate of mastectomies of about 13 % (RR: 0.87). Rates were also significantly influenced by age (RR 50–69: 0.92, RR 70+: 1.25), differences in co-morbidity (RR one co-morbidity: 1.17, RR more than one: 1.35), and higher surgeon or gynaecologist density (RR: 1.01 and 1.06). No differences were found for patients in different socio economic groups or with different insurance types.

It is important to note that higher or lower than average rates are not the same as ‘too high’ or ‘too low’, since this study did not evaluate individual cases but rather compared populations (ecological study). The decision to undergo mastectomy or breast-conserving surgery is ideally made on an individual level by a

well-informed patient, based on medical reasons and personal preferences. Both types of surgery have their advantages and disadvantages, but analysing the differences in rates and trends may help us to gain clearer insights into the decision-making process in the surgical treatment of breast cancer.

For the discussion of inequalities in cancer care, it is a very important and positive message that patients – regardless of their socio economic background or their having basic/half-private/private insurance – are treated the same regarding breast cancer surgical treatment. However, there are some pronounced differences among the cantons. Some of this is explained by the existence or absence of organized screening programmes. The study revealed that mammography screening programmes have a positive effect on mastectomy rates. The rate reduction is partly due to the fact that screening participants have lower stages of invasive breast cancer compared to non-participants and that breast cancer patients with lower stages are significantly less likely to receive a mastectomy in

Figure
Regional differences in mastectomy rates in the years 2009–2012



- Significantly (between 20 % and 45 %) higher than average
- Slightly (between 5 % and 20 %) higher than average
- Swiss average (+/- 5 %)
- (Between 5 % and 20 %) lower than average

Switzerland. Lower mastectomy rates coincide with more women receiving breast-conserving surgery – and hence with an overall higher quality of life for many of those patients.

Showing and highlighting the differences and contributing factors in cancer care is the first step in reducing inequalities for patients with cancer. Equally important is the subsequent communication of these differences to the public, health professionals, and policy makers.

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Selected results

Project
Dietary habits, nutrition and risk of late effects after childhood cancer
Unisanté, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 290 200.– | Duration: 1. 7. 2015 – 30. 6. 2018 | KFS-3644-02-2015

Project coordinator
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Overweight in childhood cancer survivors

Childhood cancer survivors have an increased risk of cardiovascular disease and other late effects. For this reason, healthy eating habits are especially important for them. However, childhood cancer survivors adhere as poorly to current dietary recommendations as the general population does, as a study supported by the Swiss Cancer Research foundation discovered.

Thanks to advances in medicine, childhood cancer can be cured in more than eight out of ten cases. But the disease and the aggressive treatment often leave lasting traces. Even decades later, childhood cancer survivors have an elevated risk of health problems such as diabetes, high blood pressure, and cardiovascular disease. In the general population, overweight and poor eating patterns are well-known risk factors for these diseases. Do these factors also play a role for childhood cancer survivors?

To answer this question, Murielle Bochud and her research team at Lausanne University Hospital (CHUV) sent questionnaires to more than 2500 childhood cancer survivors and compared their responses with those of their siblings as well as with data from the Swiss Health Survey. Of the childhood cancer survivors, 43 % ate meat one to three times a week (and thus adhered to recommended amounts), but only 7% ate sufficient fruits and vegetables. Just like their siblings and also the sample of the general population, childhood cancer survivors apparently pay little attention to the recommendations for a healthy diet.

A comparison of body weight also revealed no significant differences between the general population, childhood cancer survivors, and childhood cancer survivors' siblings: In all three study populations, approximately 25 % of the persons are overweight. The only exception were childhood cancer survivors who had had direct radiation to the brain, skull, or both (cranial radiation therapy): They were found to have a much higher risk of weight gain after treatment. To prevent overweight, the researchers recommend that particular attention be paid to this group of patients in the future.

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List of approved research projects in 2018

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

Total funds allocated: CHF 520 650.–

Locatelli Isabella | Predicting cancer incidence and annual number of new cancer cases in Switzerland up to 2025
Unisanté, Centre hospitalier universitaire vaudois (CHUV), Lausanne
CHF 184 400.– | Duration: 1. 1. 2019 – 31. 12. 2021 | KFS-4385-02-2018

Spycher Ben D. | Residential and occupational exposure to UV radiation and haematological malignancies
Institut für Sozial- und Präventivmedizin, Universität Bern, Bern
CHF 336 250.– | Duration: 3. 1. 2019 – 2. 1. 2022 | KLS-4592-08-2018

Approved bursaries in 2018

Total funds allocated: CHF 99 600.–

Rohner Eliane | Urine-based HPV testing: evaluation of a novel cervical cancer screening method
Institut für Sozial- und Präventivmedizin (ISPM), Universität Bern, Bern
CHF 99 600.– | Duration: 1. 10. 2018 – 30. 9. 2020 | BIL KFS-4423-02-2018

The dilemma of optimal treatment of precancerous breast disease

In Switzerland, about 6000 new cases of breast cancer are diagnosed each year. Ductal carcinoma in situ (DCIS) is a non-invasive Stage 0 breast cancer, or precancerous condition, and it accounts for approximately 20 % of all types of breast cancer[1]. With the introduction of mammography screening, the incidence of DCIS has risen in Switzerland, as in other countries[2]. Clinical diagnosis of DCIS based on a lump that can be felt has become seldom. Today, stage 0 DCIS is usually found through detection of microcalcifications on mammograms and histological confirmation. Patients with correctly treated DCIS have an excellent prognosis: The risk that surgically removed DCIS will develop metastases or that the patient will die of breast cancer is practically non-existent[3].

For the affected patients, who have the examination for the sake of breast cancer prevention and then find themselves diagnosed with DCIS, there is, however, a thin line between Stage 0 breast cancer with an excellent prognosis and a potentially fatal malignant disease. Despite receiving detailed information, the anxiety and upset experienced by women with a DCIS diagnosis are often similar in intensity to that of women diagnosed with invasive breast cancer[4]. This also happens partly because today, DCIS is treated the same way that an invasive carcinoma is treated: Either mastectomy or breast-conserving lumpectomy with radiation treatment[5]. More frequently than with invasive breast cancer, due to local recurrence, further operations are necessary because of incomplete removal after breast-conserving therapy or even mastectomies. Consequently, the surgical treatment is then more extensive than with an invasive carcinoma.

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It is understandable that reassuring words from the physician about the good prognosis are not heard: How can the disease be seen as harmless if there is a need for immediate surgical excision followed by five weeks of radiation, during which the patient often sits next to terminally ill patients in the waiting room?

Proven effectiveness

For us as treating physicians following evidence-based guidelines, the optimal treatment of DCIS represents a dilemma. The effectiveness of post-operative radiotherapy has been well demonstrated: A meta-analysis of four randomized trials with a total of nearly 4000 patients found clearly that radiotherapy cut the risk of recurrence in the affected breast by half – for both DCIS recurrences and also for invasive carcinoma[6]. This effect, reduction of the recurrence risk in the affected breast from 28 % to 13 % after ten years in the total patients, was found for all subgroups, and was thus independent of age, size of tumour, histology, or other therapy. And a more recent American study found that even with good-risk DCIS, radiotherapy can significantly cut the risk of recurrence even further, from 11 % to less than 3 %[7, 8]!

Besides radiotherapy, also endocrine therapy as adjuvant therapy of DCIS has been studied in analogy to the invasive carcinoma. An American study found that the selective oestrogen receptor modulator tamoxifen – additionally to lumpectomy and radiotherapy – can reduce the ipsilateral but also the contralateral recurrence risk, at least in women with oestrogen receptor-positive DCIS[9]. An Australian study looked at long-term results concerning the effect of tamoxifen in women with DCIS[10]. Here again, tamoxifen was found to reduce the incidence of all new breast events, reducing recurrent ipsilateral DCIS and contralateral tumours but having no effect on ipsilateral invasive disease.

Danger of 'over-treatment'

None of the adjuvant therapies can improve patient survival, however, which is probably also due to the fact that invasive recurrences are relatively rare and can be treated with a view to full recovery (curative). In addition, the patients for the most part do not have any symptoms with DCIS, of which they are not even aware until their screening results. For this reason, the danger of 'over-treatment' of DCIS with the current standard treatment has been discussed in the scientific literature in recent years[11]. The discussion has since been taken up in the media as well, such as in an article in the *Neue Zürcher Zeitung*[12] or in a television report by *Schweizer Radio und Fernsehen SRF*[13].

However, it is difficult to know what is appropriate treatment and what is over-treatment, since there are no established criteria for determining this. It is a matter of weighing up improving the prognosis through therapy versus the burden and possible side effects of the treatment. Another point is the cost of treatment. Adjuvant radiotherapy or endocrine therapy do not improve survival, but they spare some patients the necessary treatment if there is recurrence. For patients, it is especially important to avoid invasive

breast cancer and to avoid mastectomy[14]. Also, with an invasive recurrence, chemotherapy can be necessary. Then again, the adjuvant therapies are expensive and are associated with possible acute and late side effects. In the worst case, radiotherapy can increase the risk of secondary malignancies, and radiation on the left side of the body can cause radiation heart disease, although modern techniques minimize this risk[15]. Endocrine therapy with tamoxifen for several years can lead to side effects, such as fatigue or hot flashes, which reduce quality of life, and raises the risk of endometrial cancer[16].

Scientific approach: cost effectiveness

The decision as to whether the potential benefit of a therapy justifies the risks is ultimately up to the patient, with whom we treating physicians weigh up in detail the advantages and disadvantages in a person-to-person discussion. A scientific approach to quantifying the value of a treatment involves determining its cost effectiveness. Here the direct costs as well as the subsequent costs of various treatment strategies are set in relation to the quality-adjusted life year (QALY) gained. This approach takes into account not only the number of years that the treatment extends life but also quality of life and its reduction due to side effects or required subsequent therapies. In some countries, such as Great Britain, these health economics analyses are used to determine which treatments to approve. In Switzerland, the federal law on health insurance requires approval of new therapies to be based on three criteria: they must be effective, appropriate, and also efficient.

However, the cost effectiveness is currently not decisive for approval and for coverage by the health insurance scheme[17]. Nevertheless, the examination of the cost effectiveness of adjuvant therapies for DCIS that we are conducting in a research study supported by the Swiss Cancer Research foundation is important: It can have an effect on the perception of the value of these treatments in the whole field of oncology. The advantages of adjuvant radiotherapy and endocrine therapy demonstrated in the trials may seem small, but compared to other oncological treatments, such as immunotherapies, the costs of these therapies are relatively low. If our analysis should reveal that the therapies are not cost effective, these findings could provide further arguments for de-escalation in the treatment of DCIS, particularly for patient groups with a favourable risk profile.

Ongoing studies on treatment de-escalation

At present, the guidelines in most cases recommend surgical excision and adjuvant radiotherapy, although adjuvant radiotherapy is not mandatory, depending on the patient's individual risk profile[5]. A more definite treatment de-escalation in DCIS is being investigated in some ongoing research studies: The LORD study in the Netherlands is comparing the current standard treatment for low-risk DCIS with regular active surveillance using mammography with no primary surgery and radiation. The primary endpoint is new diagnosis of ipsilateral invasive breast tumours. Similar studies on treatment strategies without primary surgery are being conducted in Great Britain (LORIS) and in the United States (COMET). In the COMET study, patients in the surveillance group can also receive endocrine therapy[11]. Until the results of these studies become available, the treatment standard will remain lumpectomy or mastectomy. Until then, any adjuvant therapy should be guided by the individual risk of the patient and examined critically in discussion – also regarding its cost effectiveness.

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Selected results

Project
Continuity of care in Swiss cancer patients
Abteilung Gesundheitswissenschaften, Helsana, Zürich
CHF 65 000.– | Duration: 1. 7. 2017 – 30. 6. 2018 | HSR-4083-11-2016

Project coordinator
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Continuity of care provided by general practitioners is beneficial

Based on anonymized claims data, a research study supported by the Swiss Cancer Research foundation found that on average, patients with cancer who see their general practitioner regularly not only generate fewer costs than patients seen at irregular intervals by their physician but also have a lower risk of death.

In the health sciences, cancer is seen as a classic example of a complex disease: Treatment, which often consists in several phases, requires interdisciplinary cooperation between numerous specialists. Here, the transitions and interfaces – such as between inpatient and outpatient care in a hospital – are the most delicate moments in the care of the patient: If the health care specialists do not coordinate their work well, there is a risk of fragmented and uncoordinated care – with high costs and poor outcomes.

To what degree are patients with cancer in Switzerland affected by this problem? In a programme started by the Swiss Cancer Research foundation for strengthening oncological health services research, Eva Blozik and her team investigated the effects of continuity of care on treatment costs and also on risk of hospitalization and death in Switzerland. "Continuity sounds very abstract, but we have shown that it can in fact be measured," says Blozik.

Blozik and her co-authors examined claims data from the Helsana health insurance group, their employer. From 2014 to 2017, of the approximately 1.2 million insured, 23 515 persons were newly diagnosed with cancer. On average, they had 14 appointments with their general practitioner in a year and 18 appointments with various specialists. Using a number of statistical methods, the researchers found that continuity of care in Switzerland is basically very high – in rural regions somewhat higher than in large urban areas.

"The main finding of our study is that continuity of care mainly provided by general practitioners plays an important role and leads to better results in every respect," says Blozik. Patients who see their physician regularly not only generate reduced costs. In addition, patients provided with continuity of care have a lower risk of hospitalizations or death within the next year.

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List of approved research projects in 2018/2019

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

Total funds allocated: CHF 680 900.–

Bachtiary Barbara | Evaluation of financial toxicity in cancer patients undergoing proton therapy in Switzerland
Zentrum für Protonentherapie, Paul Scherrer Institut (PSI), Villigen
CHF 74 200.– | Duration: 1. 4. 2019 – 31. 1. 2021 | HSR-4668-11-2018

Blozik Eva | Does hospital volume affect long-term outcomes after abdominal cancer surgery: analysis of Swiss health insurance claims data
Gesundheitswissenschaften, Helsana, Zürich
CHF 69 000.– | Duration: 1. 11. 2019 – 31. 10. 2020 | HSR-4665-11-2018

Dedes Konstantin J. | Are we offering BRCA1/BRCA2 testing to the right women in Switzerland? Cost-effectiveness of the BRCA mutation testing threshold
Klinik für Gynäkologie, Universitätsspital Zürich, Zürich
CHF 172 100.– | Duration: 1. 7. 2019 – 30. 6. 2021 | HSR-4671-11-2018

Panje Cédric | De-escalation strategies versus standard adjuvant therapy in DCIS of the breast – a cost-effectiveness analysis
Klinik für Radio-Onkologie, Kantonsspital St. Gallen (KSSG), St. Gallen
CHF 38 900.– | Duration: 1. 5. 2019 – 30. 4. 2020 | HSR-4667-11-2018

Ribi Karin | Improving screening and referral for psychological distress in adult cancer patients: a feasibility study
Quality of Life Office, International Breast Cancer Study Group (IBCSG), Bern
CHF 91 600.– | Duration: 1. 5. 2019 – 31. 12. 2021 | HSR-4669-11-2018

Rossi Davide | Medical resource savings by individualized watch and wait strategy in early stage chronic lymphocytic leukaemia
Lymphoma & Genomics Research Program, IOR Institute of Oncology Research, Bellinzona
CHF 73 800.– | Duration: 1. 7. 2019 – 30. 6. 2020 | HSR-4660-11-2018

Vokinger Kerstin Noëlle | Clinical benefit, prices, and reimbursement of cancer drugs: a comparative study between Switzerland, England, Germany, France and the US
Institut für Hausarztmedizin, Universitätsspital Zürich, Zürich
CHF 97 150.– | Duration: 1. 7. 2019 – 30. 6. 2021 | HSR-4670-11-2018

Zwahlen Daniel Rudolf | Disparities in the application of postmastectomy radiotherapy in breast cancer patients in Switzerland: a pooled analysis of 7 cancer registries in 2003–2005 and a comparing analysis with the data of 2013–2015
Institut für Radio-Onkologie, Kantonsspital Winterthur, Winterthur
CHF 64 150.– | Duration: 1. 5. 2019 – 30. 4. 2021 | HSR-4663-11-2018

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