SAKK

Schweizerische Arbeitsgemeinschaft für Klinische Krebsforschung
Groupe Suisse de Recherche Clinique sur le Cancer
Swiss Group for Clinical Cancer Research
Gruppo Svizzero di Ricerca Clinica sul Cancro

Jahresbericht

18

Der Jahresbericht 2008 ist auch als PDF-Datei auf unserer Webseite
http://sakk.ch publiziert.

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Editorial

Aktualitäten 2008

Von Prof. Richard Herrmann | Präsident SAKK

Das Jahr 2008 war ein gutes Jahr für die SAKK. Verschiedene Ziele, die wir uns gesetzt hatten, konnten wir erreichen. Darüber wird in diesem Jahresbericht zu lesen sein. 2008 war das erste Jahr, in dem die SAKK wieder ihre volle Selbständigkeit erreicht hat. Das äusserte sich nicht nur darin positiv, dass die Beteiligten mit weniger Sitzungen auskamen. Man spürt auch im Umfeld, dass die SAKK und die Arbeit sowohl des Koordinationszentrums als auch der Mitglieder mehr Anerkennung erfahren. Unsere Arbeit wird als wichtig angesehen.

Wie schwierig es ist, klinische Forschung zu organisieren, erleben jetzt die neu gegründeten Clinical Trial Units (CTU). Dabei agieren sie noch im Wesentlichen auf lokaler Ebene. Der Weitsicht der SAKK-Gründergeneration ist es zu verdanken, dass wir auf diesem Gebiet viele Schritte voraus sind.

Worin besteht das «Geheimnis», das uns erlaubt, in dieser Weise gut zu funktionieren? Es ist das Zusammenspiel verschiedener Kräfte,

– einerseits der Mitglieder in allen Regionen der Schweiz sowie der assoziierten Mitglieder im Ausland
– andererseits des Koordinationszentrums der SAKK in Bern.

Damit diese Kräfte zusammenwirken können, brauchen wir

– gemeinsame Ziele,
– Verständnis für die Arbeitsweise und Probleme des anderen und
– eine offene Kommunikation.

Allen für die SAKK Verantwortlichen ist es ein grosses Anliegen, eine gute Balance zwischen allen Interessen zu finden. Wir müssen unseren Auftraggebern und ihren Forderungen gerecht werden, unseren Mitgliedern, aber auch dem Koordinationszentrum selbst. Dessen Arbeitslast muss sich in einem Rahmen bewegen, der sich bewältigen lässt, mit dem wir unsere Ziele aber auch weiterhin erreichen. Wir möchten beschlossene Projekte zügig voranbringen, aber haben auch hohe Ansprüche an die Qualität der Arbeit und das Wohlergehen unserer Mitarbeiterinnen und Mitarbeiter.

Es ist erfreulich, dass im vergangenen Jahr in einigen Projektgruppen mehrere jüngere Kolleginnen und Kollegen bei der Konzeption und der Durchführung klinischer Studien Verantwortung übernommen haben. Diese Tendenz sollte sich fortsetzen. Ich rufe daher die jungen Kolleginnen und Kollegen auf, neue Ideen in ihren Projektgruppen zu diskutieren und neue Projekte zu lancieren. Für Besuche spezieller Kurse über klinische Forschung und kürzere Aufenthalte an ausländischen Forschungszentren stehen weiterhin Mittel zur Verfügung.

Damit wir weiterhin qualitativ hochstehende klinische Forschung betreiben können, hat der Vorstand den Projektgruppen vorgeschlagen, eine/n internationale/n Experten/in ihres Gebietes als Diskussionspartner einzuladen. Wir sind der Auffassung, dass damit neue Ideen rascher und besser abgestützt in unsere Projekte übernommen werden können.

Wir haben im vergangenen Jahr wieder mehrere sehr konstruktive Gespräche mit Behörden und Organisationen geführt, die uns entweder fördern (Staatssekretariat für Bildung und Forschung) oder mit denen wir an der Optimierung der klinischen Forschung in der Schweiz arbeiten (Swissmedic, Arbeitsgemeinschaft der Ethikkommissionen der Schweiz [AGEK]). Ich bin zuversichtlich, dass wir gemeinsam die anstehenden Probleme lösen können.

Unsere Ziele 2009 sind unverändert: Wir möchten international kompetitive klinische Studien von exzellenter Qualität bei Krebserkrankungen durchführen. Wir wollen den Krebspatienten in der Schweiz Zugang zu neuen, hoffnungsvollen Therapien verschaffen, und wir wollen international einen Beitrag zur Verbesserung der Ergebnisse von Krebsbehandlungen leisten.

Ich wünsche mir, dass alle Beteiligten so tatkräftig und engagiert an diesen Zielen mitarbeiten wie im vergangenen Jahr. Es lohnt sich. Wir konnten die Ergebnisse unserer Arbeit in bedeutenden, international angesehenen Fachzeitschriften wie z. B. mehrfach im Journal of Clinical Oncology und Lancet Oncology publizieren. Insgesamt erschienen 44 Publikationen über abgeschlossene SAKK Studien oder Studien, an denen die SAKK namhaft beteiligt war. Dies widerspiegelt die Leistungsfähigkeit der SAKK und ihren Einfluss in der Krebsforschung.

Dass das Jahr 2008 ein gutes Jahr für die SAKK war, verdanken wir dem Einsatz aller Beteiligten, sowohl der Mitarbeiterinnen und Mitarbeiter des Koordinationszentrums als auch jeder/s Einzelnen in unseren Mitgliedsinstitutionen. Diesen allen möchte ich hier meinen ganz persönlichen Dank aussprechen.

Aktivitäten am Koordinationszentrum

Von Dr. Peter Brauchli | Direktor SAKK

Nach einer Restrukturierung fragt man sich oft, ob sich der Aufwand gelohnt hat. Diese Frage können wir mit einem klaren Ja beantworten. Die vorher herrschenden Doppelspurigkeiten waren zeitaufwendig und unnötig. Die Fusion zwischen dem SIAK und der SAKK hat in den Jahren der Planung und der Umsetzung viele Ressourcen in Anspruch genommen. Jetzt haben wir wieder mehr Zeit, produktiv zu arbeiten. Dennoch sind weitere Verbesserungen in unserer täglichen Arbeit möglich und nötig, damit wir unsere Vorgaben schneller erreichen. Dabei ist es wichtig, sich in Erinnerung zu rufen, was unser Hauptziel ist: Aufgabe der SAKK ist die Ausarbeitung und Durchführung qualitativ hochstehender klinischer Studien in onkologischen Indikationen, deren Ergebnisse den Patienten sobald als möglich zugute kommen.

Einige wichtige Aufgaben wurden schon in Angriff genommen und gewisse zukunftsträchtige Projekte weiterentwickelt. Dazu gehören die Überarbeitung der Standard Operating Procedures (SOPs), der Aufbau der Abteilung Regulatory Affairs und der Ausbau unseres Electronic Data Capturing-Systems SINATRAS. Diese Veränderungen, Anpassungen und Verbesserungen sind für eine erfolgreiche Zukunft notwendig. Ausserdem ist es im sich rasch wandelnden Feld der klinischen Forschung in der Schweiz für die SAKK unerlässlich, sich klar zu positionieren und ihre Ansprüche geltend zu machen. Daher haben wir im Laufe des Jahres einige Aussagen über die SAKK und ihre Tätigkeiten festgehalten, die kommuniziert werden sollen, wenn von der SAKK die Rede ist. Damit hoffen wir auch, in den Zentren ein Wir-Gefühl erzeugen zu können.

SAKK-Positionierung

Was wir tun und wer wir sind

Die SAKK ist eine gemeinnützige Organisation, die sich seit 1965 als kooperative Gruppe der multizentrischen klinischen Krebsforschung verpflichtet.

Gestützt auf eine Leistungsvereinbarung mit dem Bund, führt die SAKK im Sinne eines akademischen, dezentralen Forschungsinstituts klinische Studien an allen grösseren Spitälern in der Schweiz durch und arbeitet auf internationaler Ebene mit ausländischen kooperativen Gruppen zusammen.

Ziel ist es, bestehende Krebsbehandlungen für erwachsene Patienten und Patientinnen weiterzuentwickeln und die Wirksamkeit und Verträglichkeit neuer Therapien zu untersuchen.

Die SAKK ist mit ihrem Netzwerk die primäre Ansprechpartnerin für sämtliche Fragen der klinischen Krebsforschung für Behörden, Verbände und pharmazeutische Unternehmen in der Schweiz.

In der nationalen Krebsbekämpfung arbeitet die SAKK mit allen Akteuren zusammen.

Der SAKK-Vorstand

Der SAKK-Vorstand hat im Vergleich zum ehemaligen Executive Committee mehr Verantwortung und neue Aufgaben, die er unter Berücksichtigung der NPO-Corporate Governance-Prinzipien wahrnimmt. Damit die Studienauswahl in der SAKK gemäss international anerkannter Kriterien erfolgen kann, haben die Projektgruppen und anderen Fachorgane ein Antragsrecht.

Im Laufe des Jahres hat der Vorstand den Prozess zur Studienauswahl weiter verbessert. Der Vorstand entscheidet im Plenum über die Durchführung neuer Studienprojekte anhand folgender Kriterien:

a) wissenschaftliche Relevanz,
b) Durchführbarkeit (inkl. Rekrutierungsschätzung),
c) Konformität mit der SAKK-Strategie,
d) Finanzierbarkeit.

Diese Auswahl wird umso schwieriger, je mehr engagierte Studienleiter hochwertige Projekte ausarbeiten und dem Vorstand einreichen. Vier Studien, die 2008 das finale Assessment erreichten, wurden schliesslich nicht durchgeführt. Gründe dafür waren meist eine Ablehnung durch den SAKK-Vorstand und mangelnde Unterstützung durch die beteiligten Firmen. Um die Vorgehensweise bei der immer komplexeren Entscheidungsfindung besser zu regeln, wurde ein Organisationsreglement ausgearbeitet.

Zudem wurden die Vorstandsmitglieder mit der Verantwortung für ein oder mehrere Ressorts beauftragt. Die wichtigsten Kontakte zwischen dem Vorstand und den Projektgruppen werden durch eine sogenannte Verbindungsperson (Liaison Person) hergestellt. Deren Hauptaufgabe ist es, die Sicht des Vorstandes in den Projektgruppen zu vertreten und die Empfehlungen des wissenschaftlichen Beirats über den Vorstand an die Projektgruppen zu übermitteln. So sollen auch internationale Berater und Experten vermehrt an den Sitzungen der Projektgruppen teilnehmen, und Mitglieder sollen ermutigt werden, Abstracts von SAKK-Studien an Kongressen zu präsentieren.

Strategie

Im April fand die Retraite des SAKK-Vorstands statt, die dazu diente, die strategische Ausrichtung zu überprüfen und die Empfehlungen des wissenschaftlichen Beirats umzusetzen. Die auf Empfehlung des Beirats gegründete Projektgruppe Urogenitale Tumoren konnte 2008 eine erste Studie eröffnen, und mindestens zwei weitere werden 2009 folgen. An der Retraite wurde auch besprochen, dass Prüfärzte ermutigt werden sollen, vermehrt Phase-III-Studien in den wichtigsten Indikationen durchzuführen und auch Überlegungen zu übergreifender Forschung (translational research), Ergebnisforschung (outcomes research), Lebensqualität und Nachbehandlung miteinzubeziehen. Mehrere vielversprechende Phase-II-Studien sollten uns dabei die Möglichkeit eröffnen, die getesteten Therapien bei entsprechend guten Ergebnissen anschliessend auch in einer Phase-III-Studie zu evaluieren.

Zusammenarbeit mit ausländischen Zentren

Die Zusammenarbeit mit ausländischen Zentren erweist sich oft als schwierig. Dafür sind mehrere Gründe verantwortlich. Ein Zentrum im Ausland zu eröffnen, ist aufwendig und verzögert die Studienaktivierung, meist weil die Firma im entsprechenden Land das Studienmedikament oft nicht ohne weiteres zur Verfügung stellt. Um diese Probleme besser anzugehen, wurde eine Stelle Regulatory Affairs am SAKK-Koordinationszentrum geschaffen und besetzt. Von den ausländischen Zentren bleibt das EIO Milano weiterhin unser wichtigster Partner. Auch mit dem Zentrum in Budapest konnte die Zusammenarbeit erfolgreich fortgeführt werden. Freiburg im Breisgau schloss einen ersten Patienten in eine SAKK-Studie ein. Im Laufe des Jahres 2009 werden Treffen mit Vertretern der ausländischen Zentren stattfinden, damit im Ausland mehr Patienten eingeschlossen werden können.

Die Studientätigkeit

Die SAKK hat letztes Jahr 817 Patienten in 44 klinische Studien eingeschlossen, die höchste Anzahl in fünf Jahren. Davon wurden 532 Patienten in eigene Studien rekrutiert. 2008 haben wir eine noch nie da gewesene Anzahl von neuen Protokollen betreut. Insgesamt wurden vom Vorstand sechs SAKK- und fünf Studien von ausländischen kooperativen Gruppen akzeptiert. Die SAKK hat 2008 fünf neue Studien aktiviert.

Letztes Jahr wurden 44 Manuskripte veröffentlicht, an denen die SAKK entweder federführend oder massgeblich beteiligt war. Dies ist die höchste Anzahl in der mehr als 40-jährigen Geschichte der SAKK. Zudem sind wir stolz, dass die SAKK an zwei Studien teilgenommen hat, deren Resultate nun von einem unabhängigen Gremium der American Society of Oncology (ASCO) als wichtiger Fortschritt und für die Behandlung relevant angesehen wurden (Adjuvante Brustkrebstherapie (NCIC CTG MA.17. IBCSG Trial 17-98) und adjuvante Melanomtherapie (EORTC 18991)).

Kooperationen

Mit der Clinical Trial Unit (CTU) Bern führte die SAKK 2008 ihre erste gemeinsame Fortbildung für Prüfärzte durch. Ausserdem organisierte die Statistikabteilung der SAKK gemeinsam mit der Universität Zürich am Institut für Sozial- und Präventivmedizin (ISPM) der Universität Zürich ein Symposium mit dem Titel «Standardisierung und Individualisierung». Beide Veranstaltungen stiessen auf ein reges Interesse und wurden von verschiedenen Berufsgruppen gut besucht.

Des Weiteren wurde für ein Projekt zur Datenanalyse von Tumormarkern eine Kooperation mit dem Swiss Institute of Bioinformatics (SIB) in Lausanne ausgearbeitet. Mit der Swiss Clinical Trial Organization (Swiss-CTO) fanden konstruktive Gespräche statt.

Die Schweizerische Pädiatrische Onkologie Gruppe (SPOG) hat mit einem eigenen Sekretariat am SAKK-Koordinationszentrum und der Ernennung einer Geschäftsführerin ihre Strukturen gestärkt und kann damit noch besser als eigenständige Organisation auftreten. Gleichzeitig arbeitet die Schweizerische Pädiatrische Onkologie Gruppe (SPOG) insbesondere im Umgang mit externen Institutionen weiter mit der SAKK zusammen.

Koordinationszentrum

Um die wachsende Menge an zu entwickelnden Studien und die damit zusammenhängende Arbeit zu bewältigen, wurde die Anzahl der von der SAKK festangestellten Mitarbeitenden auf Ende 2008 um acht Personen auf 41 (3395 Stellenprozente) erhöht. Vor allem für ihr Haupttätigkeitsfeld (Studienentwicklung und -durchführung) wurden bei der SAKK mehr Personen eingestellt und zusätzliche Räumlichkeiten dazugemietet. Neben der Studienkoordination wurden auch die Abteilungen Statistik und Informatik ausgebaut. Die neue Stelle Leitung Regulatory Affairs konnte mit Pascale Wenger besetzt werden, und Edith Rickenbacher konnte als neue Leiterin der Abteilung Administration, Finanzen und Personalwesen gewonnen werden.

Vorstand

Präsident
Prof. Richard Herrmann
Universitätsspital Basel

Vize-Präsident
Prof. Beat Thürlimann
Kantonsspital St.Gallen

Prof. Daniel Betticher
Kantonsspital Freiburg

Prof. Stephan Bodis
Kantonsspital Aarau

PD Dr. Yves Chalandon
Hôpital Universitaire
de Genève

Prof. Martin Fey
Inselspital Bern

Prof. Michele Ghielmini
Ospedale Regionale
Lugano

Prof. Holger Moch
Universitätsspital Zürich

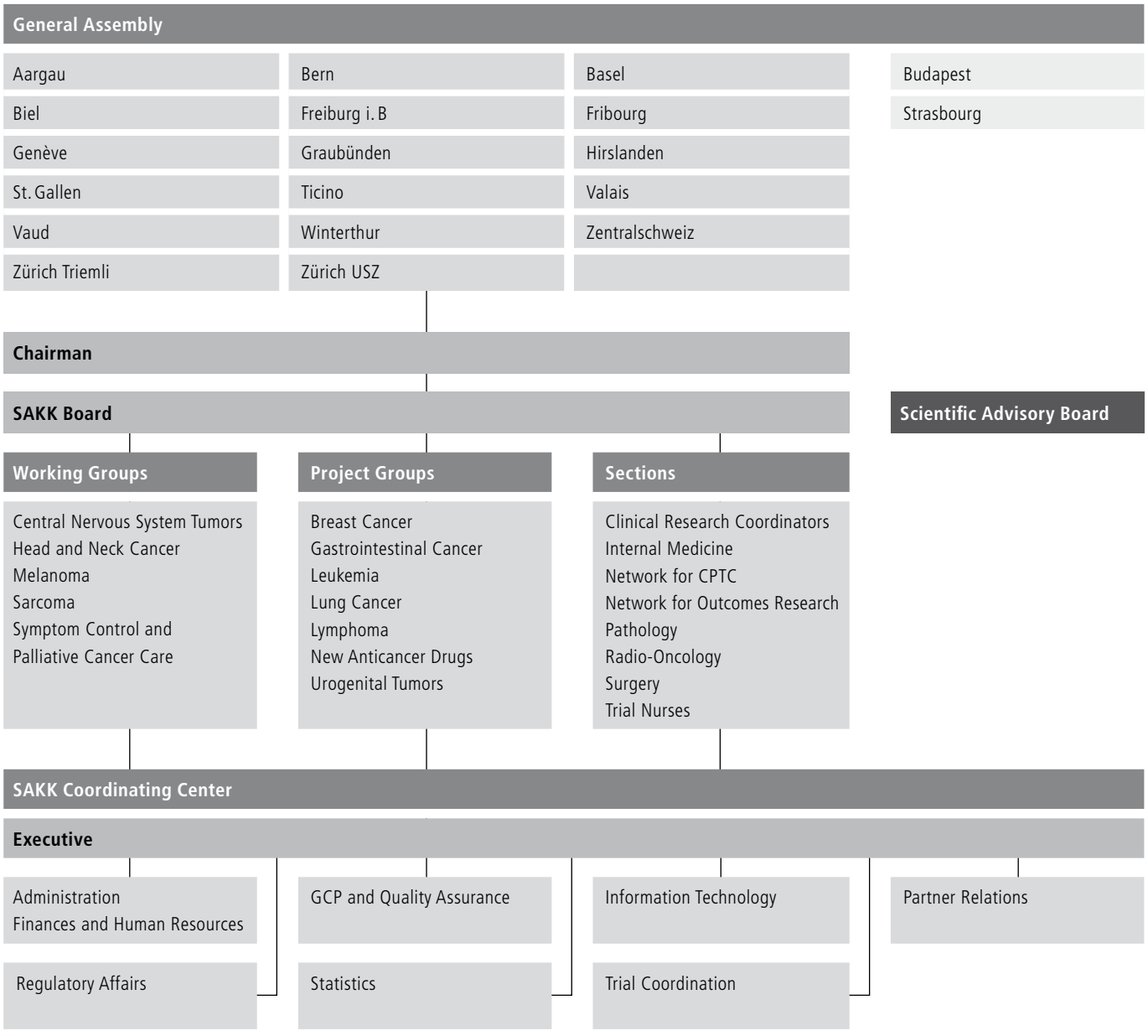
Prof. Christoph Renner
Universitätsspital Zürich

PD Dr. Arnaud Roth
Hôpital Cantonal
Universitaire Genève

Dr. Roger von Moos
Kantonsspital Chur

Prof. Walter Richard Marti
Universitätsspital Basel

Organigram Swiss Group for Clinical Cancer Research (SAKK)



SAKK Führungskräfte, Ehrungen, Beförderungen, Ernennungen

Chefärzte
- Prof. Dr. Thürlimann, Chefarzt Brustzentrum, Kantonsspital St. Gallen
- PD Dr. Abdelkarim S. Allal, Chefarzt Radio-Onkologie, Kantonsspital Freiburg
- PD Dr. Emanuele Zucca, Stv. Chefarzt der Forschungsabteilung, IOSI, Oncology Institute of South. Switzerland, Ospedale San Giovanni, Bellinzona

Leitende Ärzte
- Dr. Thomas Ruhstaller, Leitender Arzt, Brustzentrum, Kantonsspital St. Gallen: ab 1. 1. 2009
- Prof. Dr. Jens Huober, Oberarzt mit besonderer Funktion, Brustzentrum, Kantonsspital St. Gallen: ab 1. 1. 2009
- Prof. Dr. Bernhard Pestalozzi, Leitender Arzt a. i., Klinik und Poliklinik für Onkologie, Universitätsspital Zürich

Privatdozent
- Dr. Florian Strasser, Oberarzt Onkologie und Palliativmedizin, Dept. Innere Medizin, Kantonsspital, St. Gallen
- Dr. Viviane Hess, Klinik für Medizinische Onkologie, Universitätsspital Basel

Professur
- PD Dr. Bernhard Pestalozzi, Titularprofessor, Klinik und Poliklinik für Onkologie, Universitätsspital Zürich
- PD Dr. Christoph Driessen, Leiter Klinische Forschungsabteilung, Kantonsspital St. Gallen
- PD Dr. Martin H. Brutsche, Chefarzt Pneumologie, Kantonsspital St. Gallen

SAKK Vorstand
- Prof. Dr. Walter Richard Marti, Leitender Arzt Allg. Chirurgie, Universitätsspital Basel
- Prof. Dr. Michele Ghielmini, Oncology Institute of South. Switzerland, IOSI, Ospedale San Giovanni, Bellinzona

SAKK Projektgruppen
- Prof. Dr. Christoph Rochlitz, Abteilung Onkologie, Universitätsspital Basel: Co-Präsident der Projektgruppe Brustkrebs (Nachfolger von Prof. Dr. Stefan Aebi)

SAKK Sektionen
- Prof. Dr. Paul M. Schneider, Klinik für Viszeral- u. Transplantationschirurgie, Universitätsspital Zürich: Präsident der SAKK Sektion Chirurgie (Nachfolger von Prof. Walter R. Marti)
- Prof. Dr. Bernhard Pestalozzi, Klinik und Poliklinik für Onkologie, Universitätsspital Zürich: Präsident Network for Outcomes Research
- Prof. Dr. Thomas Szucs, Institut für Sozial- und Präventivmedizin, Universität Zürich: Vize-Präsident Network for Outcomes Research

Ernennungen
- PD Dr. Markus Manz: Vize-Direktor des IRB (Institute for Research in Biomedicine), Bellinzona

Preisverleihungen
- Prof. Dr. Franco Cavalli, Direktor Oncology Institute of South. Switzerland, IOSI, Ospedale San Giovanni, Bellinzona: Krebspreis der Krebsliga Schweiz
- PD Dr. Emanuele Zucca, Stv. Chefarzt der Forschungsabteilung, Oncology Institute of South. Switzerland, IOSI, Ospedale San Giovanni, Bellinzona: SAKK/Pfizer Preis
- Dr. Roger von Moos, Medizinische Onkologie, Kantonsspital Chur: SAKK/Pfizer Preis

SAKK Halbjahresversammlungen 2008

Halbjahresversammlung Juni

Die Sommer-Halbjahresversammlung der SAKK fand am 19. Juni im Tagungszentrum Blumenberg in Bern statt. Etwa 150 Onkologiespezialisten, 50 Vertreter der Pharmaindustrie und 30 Mitarbeiterinnen und – mitarbeiter des SAKK-Koordinationszentrums nahmen an dem Treffen teil. Die Sitzungen der Projektgruppen wurden rege besucht. Die Arbeitsgruppen und Sektionen trafen sich auch im Rahmen der Versammlung.

Das Netzwerk Outcomes Research wählte einen neuen Präsidenten, Prof. Bernhard Pestalozzi, und einen neuen Vize-Präsidenten, Prof. Thomas Szucs.

Prof. Walter Richard Marti vom Universitätsspital Basel wurde von der SAKK-Mitgliederversammlung als neues Vorstandsmitglied gewählt. Er ersetzt Prof. Markus Zuber vom Kantonsspital Olten, der nach zwei Amtszeiten zurücktritt.

Halbjahresversammlung November

Am 20. und 21. November trafen sich fast 200 Mediziner und SAKK-Mitarbeiterinnen und Vertreter der Pharmaindustrie zur Winter-Halbjahresversammlung in Basel. Während des Treffens fanden zwei Symposien mit interessanten Vorträgen statt. Die Sessionen der SAKK-Projektgruppen, Arbeitsgruppen und Sektionen, an denen die laufenden und geplanten Forschungsprojekte diskutiert wurden, stiessen auf grosses Interesse.

Am SAKK-Symposium sprach Prof. Ruggero De Maria vom Istituto Superiore di Sanità in Rom über Krebsstammzellen und ihre Rolle in der zielgerichteten Krebstherapie. Danach fand die Übergabe des mit 20 000.– Schweizer Franken dotierten SAKK/Pfizer Preis 2008 statt. Die Auszeichnung, die Projekte kürt, welche die Qualität der klinischen Forschung in der Schweiz verbessern, wurde von SAKK-Präsident Prof. Richard Herrmann und Dr. Thomas Schaller der Firma Pfizer an Dr. Roger von Moos und PD Dr. Emanuele Zucca vergeben.

Zucca, Chef der Lymphomabteilung am IOSI, erhielt seinen Anteil des Preises für die Errichtung einer Lymphom-Datenbank. Von Moos, leitender Arzt für Onkologie und Hämatologie am Kantonsspital Graubünden, wurde für den Aufbau der klinisch-onkologischen Forschung im Kanton Graubünden geehrt.

Prof. Bernhard Pestalozzi

Prof. Thomas Szucs

Prof. Walter Richard Marti

Prof. Michele Ghielmini

Die SAKK-Mitglieder stimmten an ihrer Versammlung dem Vorschlag zu, die Anzahl der Vorstandsmitglieder von 11 auf 12 zu erhöhen. Einstimmig wurde Prof. Michele Ghielmini, Chef der Medizinischen Onkologie am Istituto Oncologico della Svizzera Italiana (IOSI), als Vertreter der italienischen Schweiz in den Vorstand gewählt.

Dr. Thomas Schaller, PD Dr. Emanuele Zucca,
Dr. Roger von Moos, Prof. Richard Herrmann (von links)

Verleihung des SAKK/Amgen Research Grant 2009
Der mit CHF 50 000.– dotierte Preis für translationale Forschung, innovative und praxisorientierte Krebsforschung, die das Leben von Patienten verbessert, wird an der Halbjahresversammlung der SAKK am 26./27. November in Basel verliehen.

Das Teilnahmereglement zur Preisvergabe des SAKK/Amgen Research Grant 2009 kann angefordert werden bei:

Prof. Richard Herrmann, Präsident SAKK
SAKK Koordinationszentrum
Effingerstrasse 40, 3008 Bern

By Dr Stefanie Lerch I Head of Trial Coordination

Summary of Activities

In 2008, a total of 817 patients (632 in 2007) were included in 44 clinical trials coordinated by SAKK*:

	2008	2007
Total patients from Switzerland	773	584
Total patients from foreign countries	44	48
Total	**817**	**632**

	2008	No. of trials
Total patients in SAKK trials	532	21
Total patients in trials of cooperative groups (without IBCSG)	139	13
Total patients in IBCSG trials	100	6
Total patients in Sendo trials	46	4
Total	**817**	**44**

* SAKK 21/07 and SAKK 63/03 are not included

Trials open for accrual in 2008

Urogenital Cancer

SAKK 08/07 | Docetaxel and cetuximab in patients with docetaxel-resistant hormone-refractory prostate cancer (HRPC). A multicenter phase II trial

Lung Cancer

SAKK 16/00 | Preoperative radiochemotherapy vs. chemotherapy alone in non-small cell lung cancer patients with mediastinal lymph node metastases (stage IIIA, N2). A randomized phase III trial

SAKK 17/04 | Neoadjuvant chemotherapy and extrapleural pneumonectomy of malignant pleural mesothelioma (MPM) with or without hemithoracic radiotherapy. A randomized multicenter phase II trial

SAKK 19/05 | Bevacizumab and erlotinib first-line therapy in advanced non-squamous non-small cell lung cancer (stage IIIB/IV) followed by platinum-based chemotherapy at disease progression. A multicenter phase II trial

Breast Cancer

SAKK 22/99 | Randomized phase III trial of Herceptin® followed by chemotherapy plus Herceptin® versus the combination of Herceptin® and chemotherapy as palliative treatment in patients with HER2-overexpressing advanced/metastatic breast cancer

SAKK 23/03 | Trastuzumab monotherapy followed by the combination of trastuzumab and letrozole in postmenopausal women with ER-positive, HER-2 positive advanced breast cancer resistant to a nonsteroidal aromatase inhibitor. A multicenter two-step phase II trial

SAKK 24/06 | Bevacizumab (Avastin®) and pegylated liposomal doxorubicin (Caelyx®) as first-line therapy for locally recurrent or metastatic breast cancer. A multicenter, open-label phase II trial

IBCSG 22-00 | Low-dose Cytotoxics as «Anti-angiogenesis Treatment» following Adjuvant Induction Chemotherapy for Patients with ER-negative and PgR-negative Breast Cancer

IBCSG 23-01 | A randomized trial of axillary dissection vs. no axillary dissection for patients with clinically node negative breast cancer and micro-metastases in the sentinel node

IBCSG 24-02 | BIG 2-02/SOFT Suppression of Ovarian Function Trial (SOFT). A Phase III Trial Evaluating the Role of Ovarian Function Suppression and the Role of Exemestane as Adjuvant Therapies for Premenopausal Women with Endocrine Responsive Breast Cancer

IBCSG 27-02 | BIG 1-02/NSABP Trial B-37 A randomized clinical trial of adjuvant chemotherapy for radically resected loco-regional relapse of breast cancer

IBCSG 35-07 | BIG 1-07 SOLE Study of Letrozole Extension. A phase III trial evaluating the role of continuous letrozole versus intermittent letrozole following 4 to 6 years of prior adjuvant endocrine therapy for postmenopausal women with hormone-receptor positive, node positive early stage breast cancer

IBCSG 36-07 | ALTTO (Adjuvant Lapatinib and/or Trastuzumab Treatment Optimisation) study. A randomised, multi-centre, open-label, phase III study of adjuvant, lapatinib, trastuzumab their sequence and their combination in patients with HER2/ErbB2 positive primary breast cancer

IBIS II | International Breast Cancer Intervention Study. A randomised double blind control trial divided into two strata

Leukemia

SAKK 30/00/HOVON42 | Randomized induction concerning the value of G-CSF priming in adult patients ($\leq$ 60 yrs of age) with acute myelocytic leukemia (AML) or refractory anemia with excess of blasts (RAEB, RAEB-t) with IPSS score $\geq$ 1.5

SAKK 30/07 | 5-Azacytidine to treat acute myeloid leukemia in elderly or frail patients not suitable for intensive chemotherapy. A multicenter phase II trial

APL 2006 | A randomized trial assessing the role of arsenic trioxide and/or ATRA during consolidation course in newly diagnosed acute promyelocytic leukemia (APL)

CLL7 | Randomized phase III trial comparing early treatment with fludarabine, cyclophosphamide+rituximab versus deferred treatment in untreated Binet stage A patients with high risk of progression

CML IV | Randomized controlled comparison of Imatinib vs Imatinib/IFN-α vs Imatinib high-dose (800 mg) and determination of the role of allografting in newly diagnosed CML

GRAALL 2005 | Randomized phase III trial assessing the value of intensive vs standard induction and intensification in a randomized comparison and for B-ALL in a second randomization the benefit of rituximab in addition to chemotherapy and for Ph^+ ALL in a randomized comparison the non-inferiority of an imatinib based induction therapy vs a chemotherapy based induction combined with imatinib

HOVON 81 | A Phase II multicenter study to assess the tolerability and efficacy of the addition of Bevacizumab to standard induction therapy in AML and high risk MDS above 60 years

Lymphoma

SAKK 36/06 | A multicenter phase II trial testing Everolimus (RAD001) for the treatment of patients with relapsed or therapy resistant mantle cell lymphoma

SAKK 37/05 | Ibritumomab tiuxetan and high-dose melphalan as conditioning regimen before autologous stem cell transplantation for elderly patients with lymphoma in relapse or resistant to chemotherapy. A multicenter phase I trial

SAKK 38/07 | Prospective evaluation of the predictive value of PET in patients with diffuse large B-cell-lymphoma under R-CHOP-14. A multicenter study

CORAL 50-03B | GELARC-CORAL Collaborative Trial in Relapse/Refractory Aggressive Lymphoma Randomized study of ICE plus rituximab (R-ICE) versus DHAP plus rituximab (R-DHAP) in previously treated patients with CD 20 positive diffuse large B-cell lymphoma, eligible for transplantation followed by randomized maintenance treatment with Rituximab

EBMT MMVAR | A Randomized controlled study of Velcade (Bortezomib) plus Thalidomide plus Dexamethasone compared to Thalidomide plus Dexamethasone for the treatment of myeloma patients progressing or relapsing after autologous transplantation

HD13 | Morbus Hodgkin in adults, limited stages

HD14 | Morbus Hodgkin in adults, intermediate stages

HD15 | Morbus Hodgkin in adults, advanced stages

IFM 2005-02 | Relevance of maintenance therapy using Lenalidomide (REVLIMID®) after autologous stem cell transplantation in myeloma patiens under the age of 65 (Open, randomised, multi-centric trial versus placebo)

Gastrointestinal Cancer

SAKK 40/04 | Clinical function after total mesorectal excision and rectal replacement. A prospective randomized trial comparing side-to-end anastomosis, colon-J-pouch and straight coloanal anastomosis

SAKK 41/06 | Bevacizumab maintenance versus no maintenance after stop of first-line chemotherapy in patients with metastatic colorectal cancer. A randomized multicenter phase III non-inferiority trial

SAKK 56/07 | Dasatinib first-line treatment in gastrointestinal stromal tumors. A multicenter phase II trial

SAKK 75/06 | Cetuximab in combination with radiation therapy and chemotherapy prior to surgery in patients with resectable, locally advanced esophageal carcinoma. A multicenter phase Ib-II trial

SAKK 77/06 | Continuous sunitinib treatment in patients with unresectable hepatocellular carcinoma. A multicenter phase II trial

SAKK 77/07 | External beam radiotherapy for unresectable hepatocellular carcinoma. A multicenter phase I/II trial

Melanoma

SAKK 50/07 | Temozolomide combined with bevacizumab in metastatic melanoma. A multicenter phase II trial

Sarcoma

EuroEwing 99 | Studie zur Behandlung des Tumors der Ewing-Gruppe

Supportive Care

SAKK 95/06 | A multicenter randomized controlled phase III study of longitudinal electronic monitoring of symptoms and syndromes associated with advanced cancer in patients receiving anticancer treatment in palliative intention

Central Nervous System Cancer

SAKK 70/03 | Whole brain radiotherapy in combination with gefitinib (Iressa) or temozolomide (Temodal) for brain metastases from non-small cell lung cancer (NSCLC). A randomized phase II trial

New Drugs

S065APOX01 | Phase I dose finding and pharmacokinetic study of intravenous APO010, a recombinant form of human Fas ligand, in patients with solid tumors

S065ST1901 | Phase I dose finding and pharmacokinetic study of the intravenous camptothecin ST1968 in patients with solid tumors

SKSD00701 | Dose-finding study of satraplatin in combination with oral vinorelbine in patients with advanced solid tumors. A SAKK-SENDO phase Ib study

SKSD00702 | A phase IB study of the histone deacetylase inhibitor Panobinostat (LBH589) given orally in combination with Carboplatin and Paclitaxel in patients with advanced solid tumors. A SAKK-SENDO phase Ib study

Trials Activated in 2008

Breast Cancer

SAKK 21/07 | Swiss Observational Bone Study: a substudy of BIG 1-98

Leukemia

SAKK 30/07 | 5-Azacytidine to treat acute myeloid leukemia in elderly or frail patients not suitable for extensive chemotherapy. A multicenter phase II trial

Gastrointestinal Cancer

SAKK 56/07 | Dasatinib first-line treatment in gastrointestinal stromal tumors. A multicenter phase II trial

SAKK 77/07 | External beam radiotherapy for unresectable hepatocellular carcinoma. A multicenter phase I/II trial

Urogenital Cancer

SAKK 08/07 | Docetaxel and cetuximab in patients with docetaxel-resistant hormone-refractory prostate cancer (HRPC). A multicenter phase II trial

Trials closed in 2008

Breast Cancer

SAKK 24/06 | Bevacizumab and pegylated liposomal doxorubicin as first-line therapy for locally recurrent or metastatic breast cancer. A multicenter, single-arm phase II trial
Closed for accrual on 05. 09. 2008

Gastrointestinal Cancer

SAKK 75/06 | Cetuximab in combination with radiation therapy and chemotherapy prior to surgery in patients with resectable, locally advanced esophageal carcinoma; a multicenter phase Ib-II trial
Closed for accrual on 28. 11. 2008

SAKK 76/02 | Docetaxel and cisplatin chemotherapy followed by radiochemotherapy in patients with inoperable, locally advanced esophageal cancer
Closed for accrual on 21. 02. 2008

SAKK 77/06 | Continuous sunitinib treatment in patients with unresectable hepatocellular carcinoma. A multicenter phase II trial
Closed for accrual on 07. 08. 2008

Leukemias

SAKK 30/00/HOVON 42 | Randomized induction and post induction therapy in adult patients with acute myelocytic leukemia or refractory anemia with excess of blasts (RAEB, RAEB-t) with IPSS score >/= 1.5
Closed for accrual on 26. 08. 2008

Lymphomas

CORAL 50-03B | Randomized study of ICE plus rituximab versus DHAP plus rituximab in previously treated patients with CD20 positive diffuse large B-cell lymphoma, eligible for transplantation followed by randomized maintenance treatment with rituximab
Closed for accrual on 01. 07. 2008

HD15 | Morbus Hodgkin in adults, advanced stages
Closed for accrual on 18. 04. 2008

IFM 2005-02 | Relevance of maintenance therapy using Lenalidomide (REVLIMID®) after autologous stem cell transplantation in myeloma patiens under the age of 65 (Open, randomised, multi-centric trial versus placebo)
Closed for accrual on 25. 08. 2008

Project Group Breast Cancer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Presidents:

1 Prof. Dr Stefan Aebi, Department of Medical Oncology, Inselspital, University Hospital Bern (until end of 2008)
2 PD Dr Georges Vlastos, Department of Gynecology, Breast Unit, University Hospital Geneva (HUG)
3 Prof. Dr Christoph Rochlitz, Department of Medical Oncology, University Hospital Basel (starting January 2009)

Objectives

The Breast Cancer Project Group (BCPG) aims to facilitate and conduct clinical and translational research in breast cancer and to collaborate with international research groups (i. e. IBCSG, BIG, EORTC). In the trials SAKK 22/99, 23/03, 24/06, 21/07, and IBCSG 22, 23, 24, 25, 27, 35, 36 and IBIS II, these objectives have been reached. In addition, the BCPG keeps its members updated on clinical trials of IBCSG and BIG, and has reached a high visibility of members of the project group in the breast cancer community, it also cultivates excellent international relations.

The reintegration of the gynecologists, an important objective for the BCPG, is still ongoing. As of 2008, a gynecologist is co-president of the BCPG. The «Arbeitsgemeinschaft für Onkologie», AGO, has agreed not to develop projects in breast cancer and to focus on gynecologic malignancies. Several gynecologists are members of the BCPG.

With the trial SAKK 92/08 the BCPG develops a project in supportive care to prevent PPE (palmar-plantar erythrodysesthesia) in patients indicated for treatment with pegylated liposomal doxorubicin.

Activities

Trial Activated in 2008

SAKK 21/07 | *Swiss Observational Bone Study: a substudy of BIG 1-98*

The primary objective was to construct a statistical model that describes the evolution of bone mineral density in patients treated in each arm of the BIG 1-98 trial.

This model could generate data about BMD modifications over time and potentially be applicable to all patients, rather than a selected substudy population. This will increase the knowledge about the patients who are most «bone-fragile».

The study was activated on June 16, 2008. An abstract has been submitted to ASCO 2009.

Closed Trials

SAKK 24/06 | *Bevacizumab (Avastin®) and pegylated liposomal doxorubicin (Caelyx®) as first-line therapy for locally recurrent or metastatic breast cancer. A multicenter, open-label phase II trial*

The main objective of this trial was to evaluate the safety and tolerability of pegylated liposomal doxorubicin in combination with bevacizumab in patients with inoperable locally recurrent or metastatic breast cancer.

After all patients (43) registered had reached the required observation time of 6 months, the evaluation of the primary endpoint had failed to demonstrate sufficient tolerability of the combined treatment. Therefore, and according to the requirements of the trial protocol, the trial was definitively and permanently closed as of September 5th 2008.

The trial is not yet published, the preparation of the manuscript is planned in 2009.

Strategic Elements for the Next Two Years

In the next two years the group will focus its activities on the following strategic elements:

- To facilitate and conduct clinical and translational research in breast cancer
- To focus on metastatic breast cancer
- To develop non-drug trials
- To collaborate with international research groups
- To define membership in terms of collaboration and responsibilities
- To create team spirit (at least in a core group of active members)
- To provide opportunities for the professional development of young researchers
- To consider the integration of a patient advocate

Portfolio Plan

The portfolio plan for the next years contains the following trials:

SAKK 92/08 PPE trial | *Local antiperspirans for prevention of palmar-plantar erythrodysesthesia (PPE) in patients treated with pegylated liposomal doxorubicin: A randomized, multicenter, double blinded, phase III trial*

The aim of this trial is to evaluate the effects of F511 cream on the occurrence of palmar-plantar erythrodysesthesia (PPE) in patients with breast cancer treated with pegylated liposomal doxorubicin.

The trial was accepted by the SAKK Board on October 21, 2008, and is being developed.

SAKK 21/08 | *Fulvestrant with or without AZD6244, a mitogen-activated protein kinase kinase (MEK) 1/2 inhibitor, in advanced stage breast cancer progressing after first-line aromatase inhibitor: a randomized phase II trial*

The primary objective of the trial is to assess the activity of the combination fulvestrant + AZD6244 in patients progressing after first-line AI.

Project Group Gastrointestinal Cancer

President:
Prof. Dr Markus M. Borner, Clinical Research Unit of the Oncology Department, Inselspital, University Hospital Bern and Oncology Unit, Hospital Biel

Objectives

The main objectives of the project group reached since 2007 have been to cover as many clinical situations in Gastrointestinal cancer as possible with interesting protocols, to avoid competition with registration studies of the industry, as well as to promote the international collaboration.

Activities

Trials Activated in 2008

SAKK 56/07 | *Dasatinib first-line treatment in gastrointestinal stromal tumors. A multicenter phase II trial*

The primary objective is to assess the efficacy of dasatinib treatment by fusion PET/CT-scan.

Secondary objectives are to assess the efficacy and safety of dasatinib in GIST, to correlate efficacy of dasatinib with KIT and PDGRF mutation status, the efficacy and safety with dasatinib drug exposure, and to assess the efficacy of second-line treatment with another TK-inhibitor.

The trial was activated on January 18, 2008.

SAKK 77/07 and SASL 26 | *External beam radiotherapy for unresectable hepatocellular carcinoma. A multicenter phase I/II trial*

HCC is the fifth most common cancer worldwide with increasing incidence rates in Europe and high mortality rates. The standard care for non-resectable liver cancer is TACE. Alternative methods are radiofrequency ablation (RFA), nuclear therapy with intra-arterial radioactive beads and ionizing radiation. Ionizing radiation is a highly effective single agent against HCC. Radiotherapy has been underused in the past due to technical inadequacy. More recent technical developments such as image-guided radiotherapy, CT-based RT planning, and 3D-

conformal dose delivery allow minimizing the dose to non-target tissue such as non-affected liver tissue, kidneys and the gut. Thus, less collateral dose delivery to healthy neighboring tissue allows dose escalation to the diseased segments. The present trial is the first to investigate and define the potential role of high-dose external beam RT for non-resectable HCC in Switzerland and a few centers abroad, seeking to establish RT as a potential experimental arm in a subsequent phase III trial.

The trial was activated on November 7, 2008.

Closed Trials

SAKK 75/06 | *Cetuximab in combination with radiation therapy and chemotherapy prior to surgery in patients with resectable, locally advanced esophageal carcinoma. A multicenter phase Ib-II trial*

The trial was closed on November 28, 2008. There was no unexpected toxicity observed. In 12 centers 28 patients were enrolled.

SAKK 76/02 | *Docetaxel and cisplatin chemotherapy followed by radiochemotherapy in patients with inoperable, locally advanced esophageal cancer. A multicenter phase II trial*

At the interim analysis 21 patients were evaluated, of which four had local control, instead of the eight required for the trial continuation. Some patients were not evaluated according to protocol, since distant progression was documented and endoscopy and biopsies were not considered clinically relevant. The trial thus is formally negative. The therapy schedule was however well tolerated, with only 3/21 patients having e. g. grade III dysphagia under RCT. The outcome in this rather poor patient group was acceptable, particularly since some patients with residual tumor cells on biopsy had clinically meaningful long-term control. The results were presented in a poster at the ESMO 2008 meeting.

In seven centers 21 patients were enrolled. The trial was closed on February 21, 2008.

SAKK 77/06 | *Continuous sunitinib treatment in patients with unresectable hepatocellular carcinoma. A multicenter phase II trial*

The interim analysis included the first 24 of the total 45 patients required for this trial as stated in the trial protocol. No protocol violations were committed regarding trial inclusion/exclusion for the first 24 patients. The primary endpoint was progression-free survival 12 weeks after trial enrollment. The observed number of patients who were alive and progression-free at 12 weeks satisfied the criterion for trial continuation. No cause for concern was raised with regard to (serious) adverse events.

Due to a fast accrual, this trial was closed earlier than expected on August 7, 2008. In nine Swiss centers 31 patients were enrolled, in one center in Budapest 14 patients.

Strategic Elements for the Next Two Years

In interdisciplinary trials the focus will be brought on

- the treatment sequence in synchronous CRC
- Intraperitoneal chemotherapy
- Radiation vs other options in HCC
- Favor clear-cut translational questions over therapeutic fishing expeditions

Each trial should

- have one major translational endpoint
- consider aspects of quality, infrastructure and available resources in Switzerland

Portfolio Plan

The following trials are in the process of discussion or activation:

SAKK 41/07 | *Neoadjuvant treatment with radiotherapy and capecitabine with or without panitumumab in patients with advanced, K-ras unmutated rectal cancer. A randomized multicenter phase II trial*

The objectives of this trial are to assess the efficacy and safety of the neoadjuvant regimen of capecitabine and external beam radiotherapy (RT) in combination with panitumumab in patients with advanced K-ras unmutated rectal cancer.

SAKK 41/08 | *Neoadjuvant radiotherapy combined with capecitabine and sorafenib in patients with advanced, K-ras mutated rectal cancer. A multicenter phase I/IIa trial*

The objective of the phase I part is to determine the recommended dose of the neoadjuvant regimen of capecitabine, sorafenib and external beam radiotherapy (RT) in patients with advanced K-ras mutated rectal cancer.

The objectives of the phase IIa part are to assess the efficacy and safety of the neoadjuvant regimen of capecitabine, sorafenib and external beam RT in patients with advanced K-ras mutated rectal cancer.

SAKK 77/08 | *Sorafenib alone or in combination with everolimus in patients with unresectable hepatocellular carcinoma. A randomized multicenter phase II trial*

The objective of the trial is to investigate if the combination of sorafenib plus everolimus can stop tumor progression, with a sorafenib monotherapy group used to control selection bias.

SAKK 77/09 | *A phase I open label/Phase II randomized, double-blind, multicenter trial investigating the combination of Everolimus and TransArterial ChemoEmbolisation (TACE) with doxorubicin in patients with hepatocellular carcinoma eligible for TACE*

The objective of the phase I part is to determine the maximum tolerated (MTD) dose and dose limiting toxicities of the administration of daily everolimus in patients with HCC treated with TACE.

The objective of the phase II part is to determine the efficacy and tolerability of the administration of daily everolimus in patients with HCC treated with TACE as compared to TACE alone.

NCIC BI | *A phase III study of gemcitabine plus capecitabine (GEMCAP) versus gemcitabine alone in advanced biliary cancer*

The primary objective of this study is to compare the overall survival in patients with histologically or cytologically proven adenocarcinoma of the biliary tree that are either unresectable or metastatic and randomized in a 1:1 fashion to receive either gemcitabine and capecitabine (GEMCAP) or gemcitabine alone (GEM) as first-line chemotherapy. The progression-free survival, response rate, duration of response, rate of stable disease, rate of disease control, toxicity and quality of life between the two treatment arms will also be compared. The relationship between the expression of baseline tumor molecular marker (at diagnosis) with outcomes and response to treatment will also be explored.

SAKK 75/08 | *Multimodal therapy with and without cetuximab in patients with locally advanced esophageal carcinoma. Unblinded, prospectively randomized phase III trial*

The primary objective of the trial is to determine the efficacy of neoadjuvant chemoradiotherapy (CRT) combined with immunotherapy followed by adjuvant immunotherapy compared with the same schedule without immunotherapy (neoadjuvant and adjuvant).

Secondary objectives of the trial are to compare the toxicity of the two therapy arms and to determine duration of response and patterns of failure.

EORTC 40071 | An EORTC trial on the role of lapatinib in advanced gastric cancer is in development in the Gastrointestinal Group under the lead of PD Dr Arnaud Roth.

Collaboration with/Participation in Other Groups

The Project Group Gastrointestinal Cancer maintains the collaboration with other SAKK groups. The established collaboration with foreign Groups/Centers e. g. the German esophageal cancer group, EORTC, NCIC and Italian centers (EIO) is continued.

Project Group Leukemia

President:
PD Dr Yves Chalandon, Hematology Service,
University Hospital Geneva (HUG)

Objectives

We offer clinical studies covering the main topics in acute and chronic leukemia, however not myelodysplasia (MDS) low risk and Myeloproliferative Disorders (MPD). The project group collaborates with international study groups in developing and performing phase III trials. But still, more participation of Swiss members in international cooperative groups is desirable. Phase I–II trials testing new compounds and combinations are being developed. The project group also participates in international working groups. We have established a platform for younger clinical researchers, and some younger investigators are now involved in SAKK trials. Furthermore, the project group plans the foundation of a Swiss registry for acute leukemia, and will check to take over the lead in Phase III trials. The objective to have active membership working in the field of acute and chronic leukemia has been partially achieved as still too few members are active (around 10–15). With the smaller centers participating in SAKK we are hoping to have more success in including patients particularly in chronic leukemia trials (partially achieved) in all Swiss centers.

Activities

Trials Activated in 2008

Phase III trials:

APL 2006 (Acute Promyelocytic Leukemia) | *Randomized phase III trial assessing the role of arsenic trioxide and/or ATRA during consolidation course in newly diagnosed acute promyelocytic leukemia (APL)*

We hope that the event-free survival at two years will further increase at the investigational arms with reduced toxicity and without increasing the relapse rate by comparison with a classical anthracycline-AraC consolidation regimen. The total accrual target is 895 patients. The trial was activated on April 8, 2008.

Phase II trials:

AML (Acute Myeolid Leukemia)

SAKK 30/07 | *5-Azacytidine to treat acute myeloid leukemia in elderly or frail patients not suitable for intensive chemotherapy. A multicenter phase II trial*

The main objective of the trial is to evaluate the efficacy of 5-azacytidine in a population of patients with AML not suitable for induction type chemotherapy because of age or relevant comorbidities. Secondary objectives are to evaluate survival and adverse events. The trial was activated on September 23, 2008.

Translational research

SAKK 63/03 | *Blood and bone marrow banking in SAKK leukemia trials*

The main objective of the trial is to preserve material for later use in biological studies which will be submitted to SAKK in the future. The members of the SAKK Leukemia Project Group have decided to bank the material centrally in Aarau. It will be collected at the time of inclusion of a patient into one of the ongoing trials. The project is supervised by a banking committee. The database documenting the collection and central storage of material resides at the SAKK Coordinating Center. A remote data entry facility has been developed to this effect. It will also provide to the researchers an overview of the banked material, thus enabling them to check if enough material is available for a potential future study. 61 samples have been collected.

Closed Trials

Acute Myeolid Leukemia, AML/high risk MDS

SAKK 30/00 | *Randomized induction concerning the value of G-CSF priming in adult patients (≤ 60 yrs of age) with acute myelocytic leukemia (AML) or refractory anemia with excess of blasts (RAEB, RAEB-t) with IPSS score ≥ 1.5*

The trial was testing the value of priming leukemic cells with G-CSF during induction and post-induction chemotherapy in patients ≤ 60 years. Remarkable for such a long-term trial, the accrual continued to be as planned.

The trial was closed on August 26, 2008, after having recruited a total of 154 AML patients among the Swiss centers. No major protocol violations have been reported.

Strategic Elements for the Next Two Years

- to develop phase II trials for patients with acute leukemia unfit for intensive chemotherapy or for elderly patients with new drugs targeted therapy (in combination with low-dose sequential chemotherapy) or vaccines
- to stimulate translational research projects (prognostic MRD (Minimal Residual Disease) as well as study of leukemic stem cells, leukemogenesis, genomic and proteomic) as this was poorly done for the last two years. We need to have more collaboration with research laboratories.
- to improve the input of SAKK in the collaboration with international study groups as far as clinical phase III trials are concerned
- to create a Swiss registry for acute leukemia

Portfolio Plan

Trials

Phase III:

CLL 10 protocol of the German CLL Study Group (GCLLSG) | *Phase III trial of combined immunochemotherapy with Fludarabine, Cyclophosphamide and Rituximab (FCR) versus Bendamustine and Rituximab (BR) in patients with previously untreated chronic lymphocytic leukemia*

The trial will be activated in 2009.

EBMT RIC-MUD AML | *A Randomized Phase III study comparing conventional chemotherapy to low-dose total body irradiation-based conditioning and hematopoietic cell transplantation from related and unrelated donors as consolidation therapy for older patients with AML in first Complete Remission*

The trial will be activated in 2009.

Phase II:

SAKK 32/09 | *Phase II trial of sequential administration of Rituximab and Cladribine in the treatment of patients with newly diagnosed, relapsed and refractory hairy cell leukemia and variant forms.*

The SAKK Board will decide about the conduct of the trial in the final assessment in 2009.

Phase I:

SAKK 65/08 | In collaboration with the Phase I project group and the lymphoma project group *Nelfinavir and Bortezomib in patients with hematological malignancies who are not eligible for intensive cytotoxic therapy*

The trial proposal is being discussed and has to be approved by the SAKK Board.

Follow-up Trials

HOVON 92/SAKK 30/08 (follow-up HOVON 42/SAKK 30/00) | *A phase II-III randomized study to assess the added value of Laromustine in combination with standard remission-induction chemotherapy in patients aged 18-65 years with previously untreated acute myeloid leukemia (AML) or myelodysplasia (MDS) (RAEB with IPSS $\geq$ 1.5)*

The trial will be activated in 2009.

CML V, Chronic Myeloid Leukemia with the German Study Group, which should follow the CML IV protocol

The trial is under discussion in the project group.

A follow-up trial of the SAKK 30/07 AML trial for frail elderly AML patients.

Primary objective: to test the feasibility and efficacy of combination therapy of 5-Azacytidine with another new drug (AML targeted therapy)

The trial is under discussion in the project group.

Collaboration with/Participation in Other Groups

The Leukemia Project Group collaborates with the Lymphoma Project Group within the SAKK and with the following other groups:

- Project Group New Anticancer Drugs
- Laboratory group (molecular diagnostic), Swiss Molecular Hematology/Oncology Working Group
- The Dutch HOVON group in AML
- The collaborative group GRAALL (Group for Research in Adult Acute Lymphoblastic Leukemia) including the French groups GOELAMS-LALA, Belgium in ALL
- The German CLL Study Group (GCLLSG) in CLL
- The German CML Study Group (GCMLSG) in CML
- The European APL group
- The European Leukemia Network
- The European Group for Blood and Marrow Transplantation (EBMT)

Project Group Lung Cancer


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Presidents:

1 PD Dr Miklos Pless, Department of Medical Oncology and Tumor Center, Kantonsspital Winterthur

2 Prof. Dr Walter Weder, Division of Thoracic Surgery, University Hospital Zurich

Objectives of the Lung Cancer Project Group

- The Lung Cancer Project Group offers interesting studies to Swiss cancer centers to treat as many Non-Small Cell Lung Cancer (NSCLC) patients as possible in trials (stage IV).
- It establishes a network of Swiss lung cancer centers with multidisciplinary thoracic capacity (stage IIIB/IIIA), and a solid basis for translational research (tissue banking).
- The group has become an attractive partner for pharmaceutical companies with interesting compounds, and helps to advance the career of young oncologists.

Activities

Open Trials in 2008

There were no new trials activated in lung cancer in 2008, but we made important progress in SAKK 16/00, SAKK 17/04, and SAKK 19/05.

Strategic Elements for the Next Two Years

- to establish follow-up studies for stage IV (SAKK 19/09), stage IIIB (SAKK 16/08) and also open a new Small-Cell Lung Cancer trial (SAKK 15/08)
- to establish a cooperation with other cooperative groups, e. g. the Belgian group in Leuven
- to support the ETOP platform
- to publish translational research data on our phase II trials

Portfolio Plan

SAKK 15/08 SCLC, Small-Cell Lung Cancer | *Carboplatin and Paclitaxel plus ASA404 as first-line chemotherapy for extensive-stage small-cell lung cancer (SCLC). A phase II trial*

The main objective is the efficacy and feasibility of this combination in SCLC.

The trial is resubmitted to the SAKK Board.

SAKK 16/08, NSCLC | *Preoperative chemo-radiotherapy combined with concomitant Cetuximab in non-small cell lung cancer (NSCLC) patients with IIIB disease. A multicenter phase II trial*

The objective of this trial is to evaluate activity and safety of sequential neoadjuvant chemo-radiotherapy with concomitant targeted therapy of cetuximab in operable stage IIIB NSCLC patients.

The protocol is being developed and will be submitted to the SAKK Board.

SAKK 19/09, NSCLC | *Pemetrexed, cisplatin and bevacizumab, or erlotinib and bevacizumab for metastatic adenocarcinoma of the lung according to EGFR mutation status: a multicenter phase II study including biopsy at progression (BIOPRO trial)*

The trial proposal has to be approved by the SAKK Board.

Collaborations with Working Groups, Sections and Other Groups:

- Leuven (Belgium)
- Novi Sad (Serbia)

Project Group Lymphoma

President:
PD Dr Nicolas Ketterer, Centre Pluridisciplinaire d'Oncologie, University Hospital Lausanne (CHUV)

Objectives

The Lymphoma Project Group's main objectives are to bring together onco-hematologists and other specialists involved and interested in the management of lymphoma/myeloma patients, to ameliorate the management and the treatment of patients with lymphoma, by developing and leading some original clinical trials. The project group stimulates and promotes translational research for a better understanding of lymphoid malignancies, with the aim to improve the treatment of the patients in the following projects:

- Minimal Residual Disease, MRD and other ancillary studies in follicular lymphoma (FL) trials
- MRD + Ig-VH status in mantle cell lymphoma trials
- Participation to the pathological subprojects in the CORAL trial

Activities

Open Trials in 2008

There were no new trials activated in lymphoma in 2008, but we made important progress in SAKK 36/06, SAKK 37/05, SAKK 38/07 and HD13, HD14, and EBMT MMVAR.

Closed Trials

IFM 2005-02 | Intergroupe Francophone du Myélome (maintenance after Autologus Stem Cell Transplantation, ASCT)

Relevance of maintenance therapy using Lenalidomide (REVLIMID®) after autologous stem cell transplantation in myeloma patients under the age of 65 (Open, randomised, multi-centric trial versus placebo)

International, open, phase III trial (Revlimid® versus placebo) comparing the direct clinical benefit.

The trial has been closed for accrual in August 2008 after the planned sample size had been reached. Twenty-five patients have been enrolled in eight centers in Switzerland.

HD15 | *Morbus Hodgkin in adults, advanced stages*

Reducing toxicity by de-escalation, while maintaining efficacy

This trial has been activated in 13 centers in Switzerland.

CORAL study (ASCT for DLBCL in 1st relapse) | GELARC-CORAL Collaborative Trial in Relapse/Refractory Aggressive Lymphoma. *Randomized study of ICE plus rituximab (R-ICE) versus DHAP plus rituximab (R-DHAP) in previously treated patients with CD20 positive diffuse large B-cell lymphoma, eligible for transplantation followed by randomized maintenance treatment with Rituximab*

The trial has been closed last summer. Twenty-four patients have been enrolled in 10 centers in Switzerland. The second randomization of the last patient has been foreseen in December 2008. The end of maintenance for the last patient should be reached in December 2009. An analysis for R-ICE versus R-DHAP on the first 400 patients is in preparation.

Strategic Elements for the Next Two Years

The project group adjusts its activities to comply with the objectives requested by the Scientific Advisory Board in 2007. The group concentrates on key trials and therefore, will build on pre-existing collaborations and launch a key clinical trial under SAKK's guidance. Furthermore it plans to participate as SAKK member in major European trials.

Portfolio Plan

Diffuse Large B-Cell-Lymphoma, DLBCL

SAKK 38/08 (relapsed elderly) | *Rituximab, bendamustine and lenalidomide in elderly and/or frail patients with relapsed or refractory aggressive non-Hodgkin's Lymphoma. A phase I/II trial*

The objective of the phase I part is to determine the MTD (The highest dose of a drug treatment that does not cause unacceptable side effects) of the combination of rituximab, bendamustine and lenalidomide in patients with relapsed refractory aggressive Non-Hodgkin Lymphoma, NHL, not eligible for high-dose therapy with ASCT.

The objective of the phase II part is to determine the efficacy and safety of the combination of rituximab, bendamustine and lenalidomide in patients with refractory or relapsed aggressive NHL not eligible for high-dose therapy with ASCT.

The trial has been accepted by the SAKK Board and is being developed.

Follicular Lymphoma, FL

SAKK 35/09 | *GA 101 versus Rituximab for untreated follicular lymphoma. An intergroup randomized phase II trial*

The primary objective of this trial is to investigate if GA 101 is more effective than rituximab. The trial will be developed in collaboration with the Nordic Lymphoma Group.

Multiple Myeloma, MM

IFM 2009 trial | *Randomized phase III study comparing conventional dose treatment using a combination of Bortezomib, Lenalidomide and Dexamethasone to high-dose treatment with peripheral stem cell transplant in the initial management of myeloma in patients under 65 years of age*

The aim of the protocol is to determine if, in the era of new drugs, high-dose treatment is still necessary in the initial management of myeloma in young patients. The primary objective is to compare event-free survival in the two arms. The trial will be activated in France at the end of 2009.

SAKK 65/08 | *Synergistic targeting of the ER stress response with Nelfinavir and Bortezomib: a phase I dose escalation trial in advanced hematologic malignancies*

The aim of the trial is to establish tolerability and toxicity of the induction of UPR (unfolded protein response) activity and/or the inhibition of akt-phosphorylation by nelfinavir in combination with bortezomib in patients with advanced hematopoetic malignancies, and to establish a recommended dose for a phase II trial.

This trial will be developed and conducted in collaboration with the Project Group Leukemia and with the Phase I Project Group. Patients will be accrued in selected centers. The trial has to be approved by the SAKK Board in 2009.

HD18 | *Treatment optimization in the first-line treatment of advanced stage Hodgkin lymphoma; treatment stratification by means of FDG-PET*

The aim of the trial is to individualize treatment for each patient by adapting it to early response and thus to continue intensive treatment only with those patients who show an inadequate treatment response.

The trial has been activated in Germany on May 13, 2008 and is open for accrual in Germany. The trial will be activated 2009 in Switzerland.

Collaborations

The Project Group seeks to have an active role in selected large international collaborative projects, allowing a reinforcement of our collaboration with other large cooperative international groups as:

- German Hodgkin Study Group (HD trials)
- Intergroupe Francophone du Myélome (IFM trials)
- GELA, (CORAL study)
- European Mantle Cell Lymphoma Network

Project Group New Anticancer Drugs/ Phase I Trials

President:
PD Dr Cristiana Sessa, Oncology Institute of Southern Switzerland (IOSI) Bellinzona

Objectives

The primary aim of the project group is to increase the active participation in Phase I trials and to get new drugs to be tested by SAKK in Phase II trials; the group also aims to increase experience and set up a central coordination for early drug development.
SAKK and SENDO have established a collaboration in order to increase and improve the involvement of selected SAKK centers in early clinical trials, and to provide SAKK with a constant flow of new drugs for Phase II trials.

Activities

Trial Activated in 2008

SKSD00702 | *A phase Ib study of the histone deacetylase inhibitor Panobinostat (LBH589) given orally in combination with Carboplatin and Paclitaxel in patients with advanced solid tumors. A SAKK-SENDO phase Ib study*

The primary objective of the trial is to determine the Maximum Tolerated Dose (MTD) of panobinostat (LBH589) when administered in combination with carboplatin and paclitaxel in patients with advanced solid malignancies and to identify the Recommended Dose (RD) for a subsequent phase II trial.
The trial was activated on May 20, 2008.
Participating centers: Bellinzona (IOSI), Lausanne (CHUV), Basel (USB)

Portfolio Plan

SAKK 65/08 | *Synergistic targeting of the ER stress response with Nelfinavir and Bortezomib: a phase I dose escalation trial in advanced hematologic malignancies*

This trial is developed in collaboration with the Project Group Leukemia and the Project Group Lymphoma. Patients will be accrued in selected centers. The trial is still in discussion and has to be approved by the SAKK Board in 2009.

Collaboration with/Participation in Other Groups

- Project Group Breast Cancer
- Project Group Leukemia
- Project Group Lymphoma
- SENDO Southern Europe New Drugs Organization

Project Group Urogenital Tumors


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Presidents:

1 PD Dr Silke Gillessen, Department of Medical Oncology, Kantonsspital St. Gallen
2 Prof. Dr George Thalmann, Department of Urology, Inselspital, University Hospital Bern

Objectives

Since the group was promoted from a working group to a project group, it has reached a better attendance from urologists, pathologists, and oncologists, and recently also from radio-oncologists.

A new culture of collaboration with the urologists was developed and is ongoing, especially in the STAMPEDE trial and a planned bladder cancer trial.

Ongoing, good translational research opportunities with Prof. Holger Moch, University Hospital Zurich, and Prof. Lukas Bubendorf, University Basel, and Prof. Wilhelm Krek, ETH Zurich, are realized in the development of projects in prostate cancer.

Activities

Trial Activated in 2008

SAKK 08/07 | *Docetaxel and cetuximab in patients with docetaxel-resistant hormone-refractory prostate cancer (HRPC). A multicenter phase II trial*

The main objectives of this trial are to assess the efficacy and safety of the chemo-immunotherapy treatment with docetaxel and cetuximab in docetaxel-resistant patients with HRPC (second-line therapy in prostate cancer).

The trial was activated on June 17, 2008.

Closed Trials

None

Strategic Elements for the Next Two Years

The Project Group Urogenital Cancer aims

- to pursue trials in prostate cancer as main topic
- to involve more centers
- to develop second-line therapies
- to develop therapies in indolent PSA (Prostate-Specific Antigen) rising conditions (metastatic or not) despite androgen ablation
- to conduct trials in palliative care
- to strengthen the collaboration between oncologists, radio-oncologists and urologists

Portfolio Plan

Trials:

SAKK 08/08 | *RAD001 in Hormone Refractory Prostate Cancer as first-line treatment*

The main objectives of this trial are to assess the efficacy and safety of everolimus as first-line therapy in non-rapidly progressive CRPC (Castration-Resistant Prostate Cancer).

SAKK 08/08 is in a protocol finalizing state.

STAMPEDE | *Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy. A 5-stage multi-arm randomised controlled trial*

The trial will be activated in Swiss centers in 2009.

Follow-up Trials:

- A second-line trial in prostate cancer is planned.
- If SAKK 08/07 is successful, a Phase III trial in first-line HRPC (Docetaxel/Cetuximab) will be planned.

Collaboration with/Participation in Other Groups

- Collaboration with other SAKK groups such as PG New Anticancer Drugs
- Collaboration with foreign Groups/Centers like MRC (Medical Research Council)
- Collaboration with other Cooperative Groups such as EORTC (European Organisation for Research and Treatment of Cancer)

Section Clinical Research Coordinators (CRC)


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Presidents:

1 Christine Biaggi Rudolf, SAKK Coordinating Center Bern
2 Julia Rengier-Styles, Centre Pluridisciplinaire d'Oncologie, University Hospital Lausanne (CHUV)

Short introduction

From the very beginning the skills required for a position as a Clinical Research Coordinator (CRC) could only be learned on the job. Most people applying for such a position had some background in the medical field since they came from nursing or had worked as a receptionist in a doctor's office before. Nowadays, this position is more and more filled by new PhD graduates who want to acquire their first work experience outside academia after successfully finishing their thesis. Either way, very few have previous experience as a CRC. That is why many years ago the Section of Clinical Research Coordinators was founded, which in the early days was called the Data Managers Section. The goal was to form an interactive group with participants from all the various SAKK centers in Switzerland and from SAKK affiliate centers in the neighboring EU countries that would meet on a regular basis to exchange ideas and experiences on how to run and coordinate data management in clinical trials.

Activities 2008

In January we had our two-day annual meeting for CRCs at the SAKK Coordinating Center in Bern. It was a very intense program with a lot of interesting presentations in various fields of cancer research as well as some excursions into Good Clinical Practice (GCP). The first morning of those two days was particularly intended for new section members who had only recently started their work as a CRC at a center. Overall 45 certificates were handed out indicating the presence of the attendees.

In November the Section met at the semi-annual meeting in Basel. This meeting focused mainly on new procedures (such as: changes regarding documentation of adverse events reported on case report forms, availability of a new pregnancy reporting form) and updates (e. g. on certain aspects of GCP, announcement of introduction of electronic data capturing for SAKK trials in 2009, activation and closure of SAKK trials throughout 2008) presented by SAKK staff on one hand, on the other hand the Clinical Trial Unit (CTU) Basel introduced its educational program for clinical research professionals which is planned to start in fall 2009.

Outlook

In 2009 the section intends to concentrate on finding ways in which we can improve sharing professional knowledge. There are quite a few medium-sized centers, which employ only one CRC – the CRCs working in such a center need support from well organized CRC personnel.

Further, we hope to strengthen the collaboration and discussions between the SAKK and the CTU Bern in order to launch our own educational program for clinical research professional training tailored especially towards CRCs.

In 2009 we will again organize our two-day annual meeting (January 26/27) as well as a section meeting in Basel on November 26 as part of the SAKK semi-annual meeting.

Section Internal Medicine

President:
Dr Rudolf Morant, Department of Internal Medicine, Tumorzentrum ZeTuP, St. Gallen

Activities 2008

The Section Internal Medicine was working on a new proposal for a phase III trial concentrating on the effect of low-molecular weight heparin (LMWH) on survival in cancer patients with a high risk for thromboembolism.

SAKK 91/08 | *The effect of low-molecular weight heparin (e. g. Enoxaparin) on survival and thromboembolism in a high-risk subgroup of cancer patients.*

The primary objective of this multicenter phase III trial is to demonstrate that LMWH prophylaxis over six months will result in a significantly reduced death rate (25 % relative risk reduction) in a subcategory of cancer patients with a high risk of venous thromboembolism, or VTE.

Secondary objectives are to evaluate the VTE rate and bleeding complications.

SAKK 91/08 would be the first proof of principle trial with LMWH in a high-risk cancer population with a simple, safe and easily available intervention and a hard single endpoint (mortality).

Principal investigators of SAKK 91/08 are Dr Stefanie Pederiva and Prof. Jürg Beer, both at the Kantonsspital Baden, who presented their trial proposal to the project groups Lung Cancer, Gastrointestinal Cancer and Breast Cancer as well as to the section meeting Internal Medicine during SAKK's last semi-annual meeting in Bern.

Currently, the centers have to indicate their interest and prospective accrual for this trial. The trial proposal has been re-submitted to the SAKK Board. So far, no pharmaceutical company is willing to provide the drug for this interesting project.

Section Pathology

President:
Prof. Dr Holger Moch, Institute of Surgical Pathology, Department Pathology, University Hospital Zurich

Short Introduction

The Section Pathology is active in the following areas:

- The quality and the outcome of many clinical trials frequently require input by pathologists.
- Some trials need a review of the initial pathological diagnosis. The goal of such a review is quality assurance and control. Such reviews have become crucial, particularly with targeted therapy, where the most accurate determination of both the tumor type and the selected target is mandatory.
- Most predictive parameters of clinical responses to novel drugs are performed on tumor tissues. Such predictive tests, e. g. k-RAS testing in colorectal cancer are frequently performed in oncological trials. Quality assurance is mandatory in such predictive tests.
- Translational research consists of exploratory investigations of the fundamental mechanisms, which may yield new evidence on predictive or prognostic factors. It may involve clinical and laboratory investigations on clinical material collected during clinical trials. Translational researchers in pathology may screen patients' tissue samples for markers and correlate them with clinical findings with the aim to identify new therapy modalities and novel diagnostics for tumor diseases.
- For translational research projects, the collection of biomaterial is necessary. Pathologists are involved in prospective and retrospective collection of biomaterial and the establishment of biobanks.

Activities 2008

The Section Pathology is involved in many SAKK trials. The section members also play an important role in the activities of the IBCSG, both on a practical level by contributing patients and on an intellectual and leadership level. Fur-

ther, section members continue to enroll patient material in earlier studies and in new SAKK trials. There are many activities in collaboration with the groups Lung Cancer (SAKK 16/00, SAKK 17/04 etc.), Lymphoma (SAKK 38/07), Melanoma (SAKK 50/07) and others. These activities include the collection of biomaterial, translational research and predictive tests. The completion of patient forms (p-form) requires the engagement of many pathologists.

Outlook

The new strategy of SAKK aims to improve the activities of pathologists in different oncology trials. Pathologists will be involved in the early phases of protocol development. In these phases, laboratory tests can be discussed and implemented in the protocols. From an administrative and logistic point of view, improvement of budgeting, implementation and monitoring of pathology activities in clinical trials are the main objectives for 2009. Costs for biomarker research are only partly paid by the SAKK. Therefore, pathologists should perform more extensive exploratory laboratory-based translational research covered by other, third party funding (e. g. from Oncosuisse or the Swiss National Science Foundation SNF). In the last year, the first SNF grant application has been funded on the basis of material collected in a SAKK trial.

Section Radio-Oncology

Presidents:

1 PD Dr Ludwig Plasswilm, Department of Radiation Oncology, Kantonsspital St. Gallen
2 Dr Sabine Balmer Majno, Division Radio-Oncology, University Hospital Geneva (HUG)

Activities 2008

In 2008 the members of the SAKK Section Radio-Oncology focused on possibilities to increase the activities and participation of radiation-oncology within SAKK protocols.

During the meeting of the Section Radio-Oncology in November 2007 the idea of a new protocol panel of Swiss Radiation Oncology was introduced (Swiss Trials in Radiation Oncology «SWITRO»). This panel should become a platform of cooperation between the Scientific Association of Swiss Radiation Oncology (SASRO) and the Section Radio-Oncology. A detailed proposal for the generation of such a platform to boost clinical research in radiation-oncology in Switzerland has been discussed within the SASRO executive committee and at the semi-annual meetings in 2008. Finally, the majority of the members of the Radio-Oncology Section agreed to accept SWITRO being the new protocol panel of the Radio-Oncology Section. The start-up meeting of the new panel was held on November 11, 2008, and was attended by D. Aebersold, S. Bodis, L. Plasswilm, D. Weber, K. Zaugg, F. Zimmermann (in the future a representative of the Swiss Society of Radiobiology and Medical Physics will also be invited to join the panel). At that meeting 17 proposals of new protocols were discussed and preliminarily ranked by priority for further discussions and activities within SAKK.

Proposals of new trials

- Intensity-modulated radiation therapy (IMRT) + chemotherapy in anal cancer
- Adjuvant radiation therapy in node positive prostate cancer
- Radiochemotherapy plus EGFR-antibody therapy in unresectable recurrent head and neck cancer
- Postoperative radiochemotherapy plus EGFR-antibody therapy in resectable recurrent head and neck cancer
- FET-PET based planning in primary glioblastoma
- Dose escalation in radiation therapy of biochemically relapsed prostate cancer

In addition and as a complementary effort to «SWITRO» members of our section are also involved in proposals of new protocols which are under discussion within the different SAKK project groups and working groups. Besides these activities members of the Radio-Oncology Section are involved in several ongoing or recently finished protocols.

SAKK – Ongoing trials with strong links to the Radio-Oncology Section

SAKK 70/03 | *Whole brain radiotherapy in combination with gefitinib (Iressa®) or temozolomide (Temodal®) for brain metastases from non-small cell lung cancer (NSCLC). A randomized phase II trial*

SAKK 76/02 | *Docetaxel and cisplatin chemotherapy followed by radiochemotherapy in patients with inoperable, locally advanced esophageal cancer. A multicenter phase II trial*

SAKK 75/06 | *Cetuximab in combination with radiation therapy and chemotherapy prior to surgery in patients with resectable, locally advanced esophageal carcinoma. A multicenter phase Ib-II trial*

SAKK 77/07 and SASL 26 | *External beam radiotherapy for unresectable hepatocellular carcinoma. A multicenter phase I/II trial*

SAKK 16/00 | *Preoperative chemoradiotherapy vs. chemotherapy alone in non-small cell lung cancer (NSCLC) patients with mediastinal lymph node metastases (stage IIIA, N2): A randomized prospective phase III trial*

SAKK 17/04 | *Neoadjuvant chemotherapy and extrapleural pneumonectomy of malignant pleural mesothelioma (MPM) with or without hemithoracic radiotherapy. A randomized multicenter phase II trial*

SAKK Trials in cooperation with the German Hodgkin Lymphoma Study Group

HD13, Limited stages | *Qualitätssicherungsprotokoll zur Toxizitätsreduktion in der Primärtherapie des frühen Morbus Hodgkin*

HD14, Intermediate stages | *Qualitätssicherungsprotokoll zur Effektivitätssteigerung in der Primärtherapie des intermediären Morbus Hodgkin*

Outlook

In 2009 the Radio-Oncology Section will mainly focus on the initiation of new SAKK protocols, based on our current proposals, and to support the ongoing SAKK 77/07 trial. Also the cooperation of the Radio-Oncology Section and SASRO will be advanced. Special thanks go to Daniel Aebersold, Inselspital Bern, and president of SASRO, who strongly supports this cooperation. Daniel Aebersold and Ludwig Plasswilm together were personally strongly involved into the set-up and organization of our new joint protocol panel «SWITRO».

Section Surgery


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Presidents:

1 Prof. Dr Walter Richard Marti, Department of Surgery, University Hospital Basel (until end of January 2009)
2 Prof. Dr Paul M. Schneider, Department of Surgery, University Hospital Zurich (starting February 2009)

Short Introduction

The Section Surgery aims to design and conduct clinical and translational research in the field of surgically treated cancers and functions as a platform to promote other multicenter trials in the surgical community.

Activities 2008

The Section Surgery has held its annual meeting on November 20, 2008, in Basel. The main focus of activities in 2008 was to continuously work on the SAKK 40/04 trial. The primary objective of this trial is to compare a 5 cm colon-J-pouch, side-to-side anastomosis and straight coloanal anastomosis as reconstruction techniques after rectal cancer surgery with respect to defecation quality (evacuation problems, fragmentation of stools), stool frequency, mortality and morbidity. As secondary objectives, the three different reconstruction techniques are compared in respect of short and mid-term quality of life and long-term clinical outcome. As the patient accrual is favorable (~50/year) but not as high as expected (94/year), we still encourage new clinics to participate in this trial. Lately, the Department of Surgery, Kantonsspital Bruderholz, led by PD Dr Igor Langer, has joined in to help us to reach the goal to include 282 patients in the trial. So far over 125 patients have entered the trial.

Furthermore, in collaboration with SAKK project groups we participate as surgeons in other trials, currently in the ongoing lung cancer trials SAKK 16/00 and SAKK 17/04.

Outlook

Prof. Dr Markus Zuber has discontinued his position as vice-chairman of the SAKK Board after two full election periods. All his great achievements are acknowledged. Prof. Walter Marti has been elected as member of the SAKK Board in June 2008 by the General Assembly.
This was the moment to renew the presidency of the SAKK Section Surgery. Prof. Paul Schneider, Professor of Surgery, working at the University Hospital of Zurich, being proposed for this position at the annual meeting of the section and elected by the SAKK Board, will take over this position in February 2009. For sure, Prof. Paul Schneider with his vast clinical and research experience will help to boost scientific activities at the Section Surgery.

Section Trial Nurses

President: vacant
Contact person: Christel Böhme, oncology nurse, head of trial coordinators, Oncology/Hematology, Kantonsspital St. Gallen

Short introduction
We are a group of nurses who evaluate draft protocols for their practical and nursing implications and patient considerations, as well as CRF comprehensibility.
In this function we serve as a part of the SAKK internal protocol review process.
Additionally, on each SAKK protocol with a medical treatment a trial nurse is assigned as a contact person for nursing issues.
The group members, with a multifaceted nursing background hold different positions in Swiss hospitals. All work with patients treated in SAKK clinical trials.
Our goal is to make a contribution to assure high-quality clinical trial performance.

Activities 2008
- Review of several SAKK protocols
- Meeting at the semi-annual meeting in Basel
- Exchange of knowledge throughout the year

Outlook
- Continue our work within the Internal Review Board
- Acquire new colleagues to maintain and strengthen our group
- Provide support for nursing issues in ongoing SAKK trials

Network for Cancer Predisposition Testing and Counseling (CPTC)


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Presidents:

1 PD Dr Pierre O. Chappuis, Unité d'oncogénétique et de prévention des cancers, Service d'Oncologie, University Hospital Geneva (HUG)
2 Prof. Dr André-Pascal R. Sappino, Unité d'identification des prédispositions génétiques aux cancers, University Hospital Geneva (HUG)

Short introduction

The main goals of the Network for CPTC are:

– to harmonize the clinical practice of counseling and management of at-risk individuals;
– to consolidate the activity of several Swiss reference molecular laboratories for cancer predisposition testing and the network with basic researchers;
– to collect clinical data and mutation screening results of families with inherited cancer predisposing syndromes that are managed in the network counseling centers;
– to participate in trials evaluating the impact of surveillance and risk reduction strategies;
– to inform and educate health professionals and the lay community on predictive oncology.

Activities 2008

There are 17 centers located in 10 cities throughout Switzerland providing genetic counseling and evaluation for cancer predisposition testing according to the Swiss regulation (KVL/OPAS/OPre art. 12, let. v). More than 400 new families have been managed by network oncogenetic centers this year.

Swiss referral guidelines for genetic counseling and evaluation for BRCA1/BRCA2 testing have been established by the network. These guidelines have been prepared to help clinicians identify the situations where a familial aggregation or a syndrome of hereditary breast/ovarian cancer should be suspected, and an adequate management could be proposed. These guidelines have been approved by the Swiss Society of Medical Genetics, the Swiss Society of Senology, the Swiss Society of Medical Oncology and the Swiss Society of Gynecology and Obstetrics.

Up to now, complete BRCA1/BRCA2 mutation screening has been performed in 850 distinct families. Members of the network have provided counseling to these families outlining features of the hereditary breast/ovarian cancer syndrome or familial aggregation of breast cancer. Pathogenic mutations have been identified in 20 % of these families and unclassified variants were characterized in 13 % of the index cases tested. We collected clinical and socio-demographic data on families screened for BRCA1/BRCA2 modifications for future research projects.

The IBIS II-Prevention randomized double blind control trial is designed to evaluate anastrozole vs. placebo as an effective method of preventing breast cancer in postmenopausal women at increased risk of the disease. The IBIS II-DCIS trial compares anastrozole vs. tamoxifen as an effective preventive breast cancer drug for postmenopausal women with conservatively-treated ductal in situ cancer. Thirty-two women have already been included in these preventive trials in St. Gallen, Bern, Geneva, Ticino and Lausanne.

Outlook

– to manage individuals identified at high-cancer risk according to standard clinical practice in Switzerland;
– to publish the Swiss guidelines for genetic counseling and evaluation for BRCA1/BRCA2 testing;
– to evaluate the prediction models of germ-line mutations based on the series of families already screened for BRCA1/BRCA2 mutations;
– to initiate a collaborative group to establish guidelines in genetic counseling and testing for patients with multiple colorectal polyps.

Network for Outcomes Research


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President:

1 Prof. Dr Bernhard Pestalozzi, Department of Oncology, University Hospital Zurich

Vice-President:

2 Prof. Dr Thomas Szucs, Institute of Social and Preventive Medicine, University of Zurich

Objectives of the Network

To establish a network of experts and interested researchers and to further promote interdisciplinary outcomes research in oncology. The network may be called in by any SAKK project or working group to provide advice on outcomes research relevant questions in ongoing or planned trials.

Furthermore, the network will collect ideas on outcomes research which can be implemented in oncology trials in Switzerland. One of the important aims of the network is to anchor outcomes research as a part of the clinical trials performed by SAKK. In addition, the network tries to perform other non-randomized controlled trials related outcomes research studies in accordance with the SAKK mission.

Activities 2008 and Outlook

The primary activity is to perform health-economic evaluations (HEA) alongside the clinical trials to provide an incremental cost-effectiveness ratio for a new treatment in question. Although, Switzerland has no institution like the National Institute for Health and Clinical Excellence (NICE) in the U.K. to evaluate cost-effectiveness of drugs, it becomes more and more important to collect health economic information on newly introduced treatments. Sooner or later, this information will be important for health-care decisions.

The Network for Outcomes Research focuses only on direct medical resource usage and its costs. It takes into consideration the perspective of the statutory health insurance or the health system.

For two ongoing SAKK trials the network has evaluated the resource usage and costs of several different data providers. Data from patient records, insurance companies as well as case report forms were evaluated. The evaluation showed that a lot of data are available, but that it is extremely difficult to obtain and combine them in a useful way. Therefore, we decided to use only data from insurance companies in trials where no changes in case report forms are possible anymore. For future trials only case report forms will be used as the primary source to collect data on resource use. Costs are then calculated according to Tarmed or laboratory lists of the Swiss health-care system.

We try to perform cost-effectiveness analyses in different ways. If possible, we will take patient-level costs as they are and perform analyses in line with state of the art methodology, e. g. by using bootstrapping methods to calculate confidence intervals for incremental cost-effectiveness ratios.

For trials with long overall survival times, where it is impossible to record all the cumulated costs and effects over a very long period, costs and effects will have to be modeled.

Trials

SAKK 16/00 (open) | *Preoperative chemoradiotherapy vs. chemotherapy alone in non-small cell lung cancer (NSCLC) patients with mediastinal lymph node metastases (stage IIIA, N2). A randomized prospective phase III trial*

This trial is ongoing and will be considered under a statutory health-insurance perspective, cost data coming from the insurance companies.

SAKK 35/03 (closed) | *Comparing two schedules of rituximab maintenance in rituximab-responding patients with untreated, chemotherapy resistant or relapsed follicular lymphoma. A randomized phase III trial*

This trial has a long-time overall survival and therefore a two-step economic analysis is planned by partially using insurance claim data and modeling cost and effects for long-term survival.

Health-economic analyses for some recently developed trials are planned. For these we will prospectively implement necessary health economic variables into the case report forms to avoid having to collect data from external providers. Although, it is clear that within these forms one cannot

report all resources used, at least the most cost-driving factors such as hospitalizations or expensive treatments can be reported.

We especially want to draw your attention to the trial SAKK 77/08 and SASL 29 *Sorafenib alone or in combination with everolimus in patients with unresectable hepatocellular carcinoma. A randomized multicenter phase II trial* This trial will be the first in which the resource usage data collection for the HEA, will be completely implemented within the case report forms. Due to the expected short duration of this trial, it serves well as «pilot project» performing HEA this way.

The network is not only involved in SAKK trials but also aims at performing studies in the field of outcomes research in cooperation with third parties, for example studies which are literature-based. Last year, the network performed together with Konstantin Dedes, University of Zurich, a health economic modeling study for the treatment of breast cancer with bevacizumab. This study has been published in the European Journal of Cancer. Similar studies are planned.

Another project in cooperation with the health insurance company Helsana will be a study of end-of-life care in cancer patients in Switzerland. So far, no such study has been performed and therefore, it is unique and has an explorative character. The primary objectives of the study are to evaluate the therapy intensity and hospitalization rates of end-of-life care. Therapy intensity may be defined differently according to literature but we will primarily focus on the percentage of patients (all or sub-groups) receiving any chemo- and/or radiotherapy and/or cancer related surgery during the last month before death. The secondary objective is to assess the magnitude and significance of the effects of insurance coverage, demographic, geographic or treating hospital-related items on the delivery of care.

Depending on the results of this study we hope to initiate a discussion among Swiss oncologists and other cancer treating physicians to reflect on the treatment situation of Swiss cancer patients.

The study will include all identified deceased cancer patients of the years 2006–2008 from the Helsana cohort, but depending on the available number of patients, subgroup analyses for certain cancer types such as lung, colon, breast or prostate are planned.

At the semi-annual SAKK meeting in November 2008 Prof. James Raftery, Director of NETSCC and The Wessex Institute, gave a very interesting talk on «Evidence based decision making: NICE, oncology and health economics.»

Portfolio Plan

SAKK 77/08 and SASL 29 | *Sorafenib alone or in combination with everolimus in patients with unresectable hepatocellular carcinoma. A randomized multicenter phase II trial*

SAKK 77/09 and SASL 30 | *A phase I open label/phase II randomized, double-blind, multicenter trial investigating the combination of everolimus and TransArterial ChemoEmbolisation (TACE) with doxorubicin in patients with hepatocellular carcinoma eligible for TACE. HEA in Phase II*

SAKK 75/08 | *Multimodal therapy with and without cetuximab in patients with locally advanced esophageal carcinoma. An unblinded, prospectively randomized phase III trial*

Collaboration with/Participation in Other Groups

The network initiates project-level cooperation with different institutes active in the field of cancer, e. g. with insurance companies, National Institute for Cancer Epidemiology and Registration (NICER), and the Children's Cancer Registry.

SAKK and Collaborating Groups

Urogenital Tumors

SAKK 08/91, 08/93, 08/95, 08/97, 08/00 Munger-Beyeler, C., Bernhard, J., Rufibach, K., Morant, R., and Schmid, H.P. (2008). *Quality of analgesic treatment in patients with advanced prostate cancer: do we do a better job now? The Swiss Group for Clinical Cancer Research (SAKK) experience.* Support Care Cancer, 16(5), 461–467. (Journal Impact Factor 2.21)

EORTC 30891 Studer, U.E., Collette, L., Whelan, P., Albrecht, W., Casselman, J., de Reijke, T., Knonagel, H., Loidl, W., Isorna, S., Sundaram, S.K., and Debois, M. (2008). *Using PSA to guide timing of androgen deprivation in patients with T0-4 N0-2 M0 prostate cancer not suitable for local curative treatment (EORTC 30891).* Eur Urol, 53(5), 941–949. (Journal Impact Factor 5.63)

Lung Cancer

SAKK 17/00 Ribi, K., Bernhard, J., Schuller, J.C., Weder, W., Bodis, S., Jorger, M., Betticher, D., Schmid, R.A., Stupp, R., Ris, H.B., and Stahel, R.A. (2008). *Individual versus standard qualit y of life assessment in a phase II clinical trial in mesothelioma patients: feasibility and responsiveness to clinical changes.* Lung Cancer, 61(3), 398–404. (Journal Impact Factor 3.46)

SAKK 19/03 D'Addario, G., Rauch, D., Stupp, R., Pless, M., Stahel, R., Mach, N., Jost, L., Widmer, L., Tapia, C., Bihl, M., Mayer, M., Ribi, K., Lerch, S., Bubendorf, L., and Betticher, D.C. (2008). *Multicenter phase II trial of gefitinib first-line therapy followed by chemotherapy in advanced non-small-cell lung cancer (NSCLC): SAKK protocol 19/03.* Ann Oncol, 19(4), 739–745. (Journal Impact Factor 4.88)

EORTC 08971 SILVA Bottomley, A., Debruyne, C., Felip, E., Millward, M., Thiberville, L., D'Addario, G., Rome, L., Zatloukal, P., Coens, C., and Giaccone, G. (2008). *Symptom and quality of life results of an international randomised phase III study of adjuvant vaccination with Bec2/BCG in responding patients with limited disease small-cell lung cancer.* Eur J Cancer, 44(15), 2178–2184. (Journal Impact Factor 4.45)

Breast Cancer

SAKK 24/06 Greuter S, Schmid F, Ruhstaller T, Thuerlimann B. *Bevacizumab-associated osteonecrosis of the jaw.* Ann Oncol. Letter to the editor. 2008 Dec;19(12):2091–2. Epub 2008 Oct 31. (Journal Impact Factor 4.88)

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Betriebsrechnung 1. Januar bis 31. Dezember (in CHF)	**2008**	**2007**
Betriebsertrag		
Forschungsbeiträge Bund[1]	3 930 520.00	5 266 800.00
Forschungsbeiträge diverse[2]	1 427 794.58	765 860.89
Erträge Industriekooperationen	2 268 112.60	2 319 453.15
Industrieeinnahmen Krebsbulletin	281 885.00	352 655.00
Spenden, Legate und Erbschaften	40 720.00	0.00
Diverse Erträge	484 918.85	211 564.60
Total Betriebsertrag	**8 433 951.03**	**8 916 333.64**
Betriebsaufwand		
Diverser studienbezogener Aufwand	– 529 278.75	– 311 799.90
Forschungsbeiträge SPOG[3]	0.00	– 449 460.00
Forschungsbeiträge VSKR (NICER)[4]	0.00	– 900 900.00
Forschungsbeiträge IBCSG[5]	– 250 000.00	– 250 000.00
Forschungsbeiträge Zentren	– 2 699 123.95	– 2 198 918.25
Reise- und Repräsentationsaufwand	– 241 480.75	– 199 901.50
Sonstiger Betriebsaufwand	– 63 649.62	– 154 901.55
Total Betriebsaufwand	**– 3 783 533.07**	**– 4 465 881.20**
Zwischenergebnis 1	4 650 417.96	4 450 452.44
Koordinativer Aufwand		
Personalaufwand	– 4 080 476.39	– 3 160 505.11
Sonstiger Koordinationsaufwand	– 831 077.70	– 975 575.25
Total koordinativer Aufwand	**– 4 911 554.09**	**– 4 136 080.36**
Zwischenergebnis 2	– 261 136.13	314 372.08
Finanzergebnis		
Finanzertrag	131 068.35	50 618.64
Finanzaufwand	– 117 838.11	– 2 194.80
Total Finanzergebnis	**13 230.24**	**48 423.84**
Zwischenergebnis 3	– 247 905.89	362 795.92
Periodenfremder Erfolg		
Periodenfremder Ertrag	58 024.39	0.00
Auflösung nicht benötigter Rückstellungen	154 628.40	77 900.00
Total periodenfremder Erfolg	**212 652.79**	**77 900.00**
Vereinsergebnis	**– 35 253.10**	**440 695.92**

1 2007: Staatssekretariat für Bildung und Forschung SBF (die Gelder flossen via SIAK zu den entsprechenden Vereinen, gemäss Leistungsvereinbarung mit dem Bund); ab 2008 flossen die Gelder direkt vom SBF zu SAKK, SPOG und VSKR (NICER)
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3 Schweizerische Pädiatrische Onkologie Gruppe SPOG
4 Verein Schweizerischer Krebsregister VSKR
5 International Breast Cancer Study Group IBCSG

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