Report 2017

Investigator Initiated Clinical Trials Programme (IICT)

SWISS NATIONAL SCIENCE FOUNDATION

1. IICT programme

Since 2015, the IICT programme has been offering targeted support for industry-independent, comprehensive clinical studies with the aim of meeting major scientific and societal needs. The studies go beyond the scope of project funding in terms of their research questions, comprehensive nature, duration, complexity and costs. The programme concerns prospective, randomised, interventional, multicentre studies of new or existing treatments. Studies have to be outside the industry focus and their topics must be under-researched. There is one call each year, up to and including 2020.

2. Funded proposals

The first two IICT calls resulted in 16 projects being supported by the SNSF with a total funding budget of CHF 22.3 million. In both calls, all proposals rated as outstanding or excellent received funding. This corresponded to success rates of 12% in the 2015 call and 20% in the 2016 call.

Women are principal investigators in two of the 16 funded projects. In the 2015 call, the success rate for female principal investigators was 8% compared to 13% for male principal investigators. The success rate of principal investigators was 20% for both genders in the 2016 call. Of all 45 members of the funded study consortia, 8 are women.

The highest number of grants were awarded for studies in internal medicine, followed by neurology/psychiatry and cardiovascular diseases. Annex 1 provides a detailed overview of the funded trials.

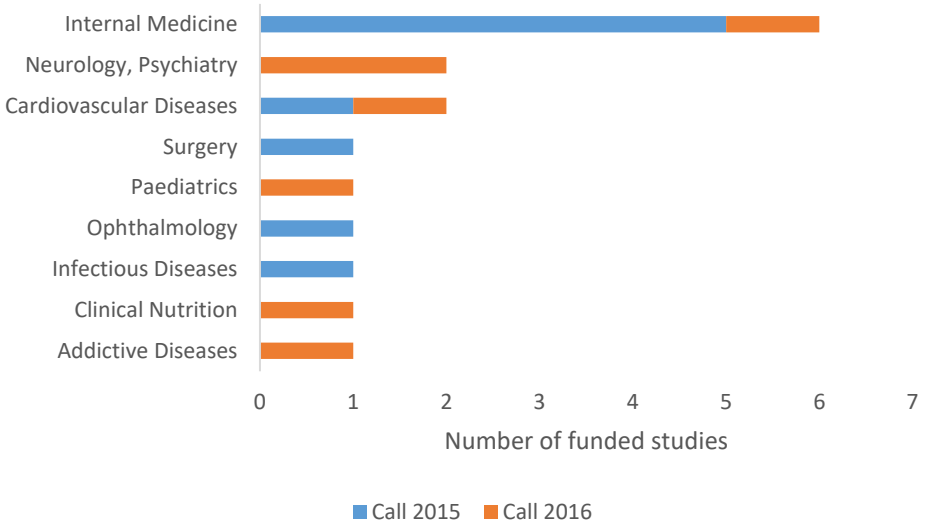

Figure 1. Medical areas of the funded studies as declared by the applicants.

Funded projects are based at the University Hospitals of Basel, Bern (Inselspital), Geneva, Lausanne and Zurich, University Children's Hospitals of Basel and Zurich, University Hospital of Psychiatry Zurich, University Psychiatry Clinic Basel, University of Bern (Institute of Family Medicine), Institute for Work and Health in Epalinges (Institut universitaire romand de santé au travail), Cantonal Hospital St. Gallen, Hospital Felix Platter Basel and City Hospital Triemli Zurich.

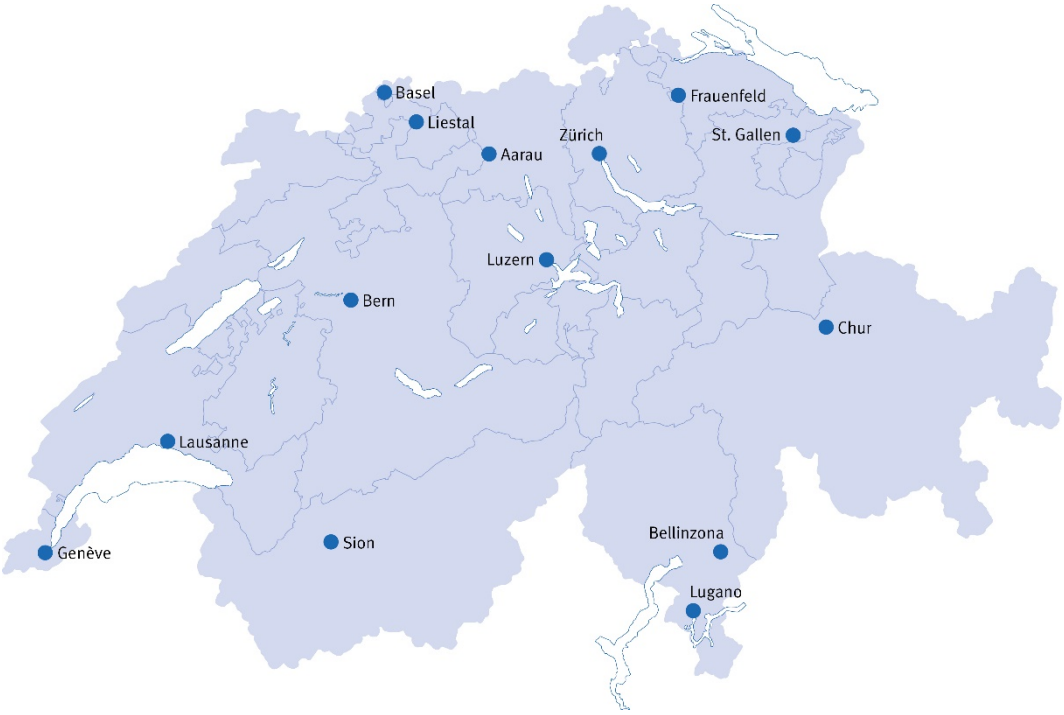

Figure 2. Location of IICT recruitment sites in Switzerland

7300 patients are planned to be enrolled in the 16 funded studies, varying between 98 and 2000 patients per trial (average: 456, median: 216). The trials are conducted with 3 to 13 recruiting sites (average: 7.3 sites). A total of 116 sites are involved in the projects, 93 of which are based in Switzerland. The Swiss recruiting sites are located at all five university hospitals, 3 children's university hospitals, 9 cantonal hospitals, 2 private practices and 17 other institutions. Five of the 16 studies involve patient recruitment outside Switzerland. 23 foreign recruiting sites in Germany (11), France (3), United Kingdom (2), Netherlands (2), Belgium (2), Austria (1), Spain (1) and Romania (1) are participating in the studies.

Investigators of the 9 projects funded as a result of the first IICT call planned a preparation period of 8 months on average (varying from 1 to 12 months; median: 9 months) before starting the clinical trial. Only two of the 9 research teams reached all milestones set for the preparation phase as initially planned, one in nine months and one in twelve months. The reasons for the delays in the other projects were manifold and included the absence of key persons due to illness, problems with the supply or formulation of the study drug or placebo, delayed finalisation of documents for submission to Swissmedic, complexities in establishing collaboration with recruiting sites in Switzerland and abroad, missing proof of feasibility of patient recruitment and

other unexpected difficulties in starting the study. At the time of publishing the report (March 2018), eight out of nine study teams have achieved all milestones of the preparation phase and started recruiting patients. For these projects, the average time needed to reach the milestones of the preparatory phase was 12.4 months (median: 12 months, minimum: 9 months, maximum: 16 months).

3. IICT applications in the 2015 and 2016 calls

The IICT programme has attracted considerable attention from the clinical research community. In response to the call in 2015, 112 research groups expressed their intention to apply and 75 of them went on to submit an application, with the total funding request amounting to CHF 116 million. For the second call, the SNSF received 55 letters of intent and 35 full proposals, with a total funding request of CHF 51 million.

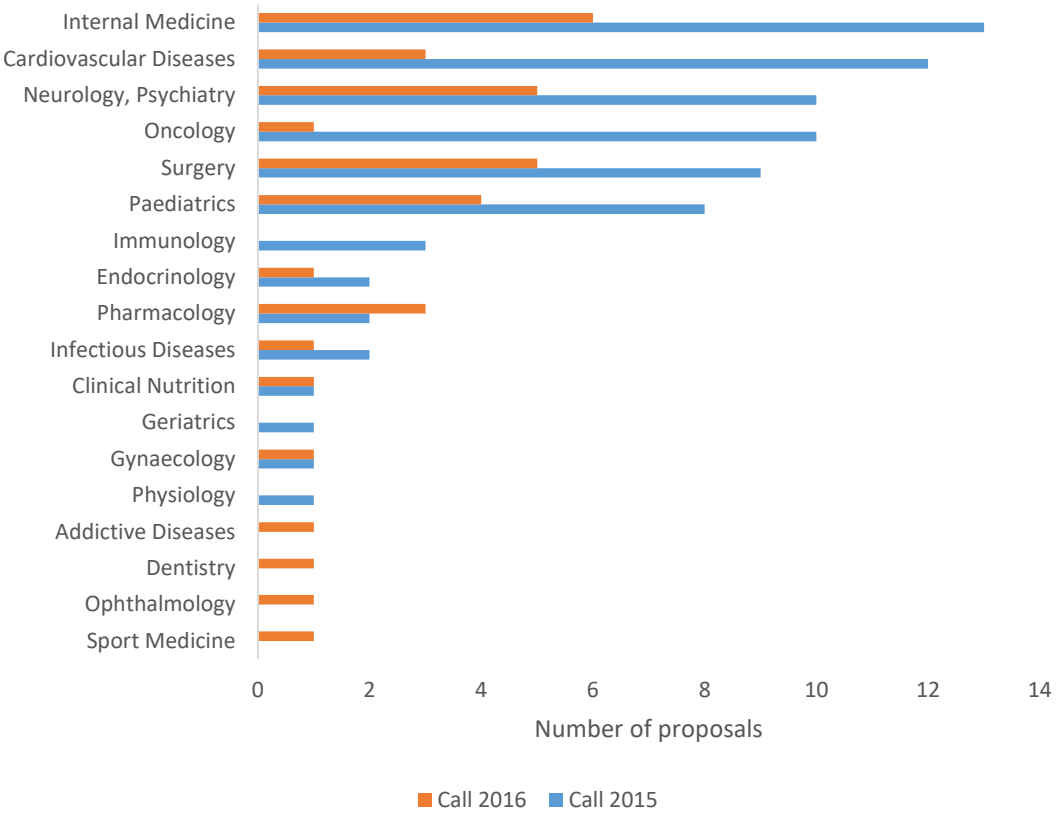

Figure 3. Submitted proposals by medical speciality as declared by the applicants.

Proposals were submitted by researchers from a wide range of medical areas. The SNSF received the highest number of applications from researchers in internal medicine, cardiovascular diseases, oncology, surgery and paediatrics.

In the 2015 call, 26% of the submitted applications did not satisfy the formal call specifications. A similar percentage (23%) was observed in the 2016 call. The SNSF did not consider them for evaluation. Lack of randomisation was the main reason for a non-consideration decision in the 2015 call. In the second call, the main reason was

that principal investigators did not fulfil the personal eligibility criteria for applicants in the IICT programme.

Reason for non-consideration	Percentage of submitted proposals	
	Call 2015	Call 2016
Trial is not randomised	9%	0%
Application for an observational study	5%	0%
Application for an exploratory study	4%	0%
Requested study duration is too long	3%	6%
Application to develop technology for a novel treatment	3%	0%
No intervention in patients	3%	0%
Origin of study is outside Switzerland	3%	0%
Unjustified single centre study	1%	3%
Late resubmission of required documents	1%	0%
Personal eligibility criteria of applicant not fulfilled	1%	11%
Applicant with submission of more than 1 application in the same call	0%	3%

Table 1. Reasons for non-consideration decisions.

9 of the 35 proposals (26%) submitted in response to the 2016 call were resubmissions of projects which had not received funding in the year before. Four of them were successful with the second, revised proposal.

The average funding request per clinical study in the 2015 and 2016 calls was CHF 1'640'770 (median CHF 1'641'190), ranging from CHF 267'215 to CHF 3'725'413). On a per year basis this corresponds to CHF 89’071 to CHF 745’082 per study.

45% of the studies were planned for a duration of 60 months, of which 12 months were dedicated to a preparation period and 48 months were planned for the study itself. The requested average duration was 53 months.

The intended number of patients per trial was 258 (median), ranging from 18 to 6624 patients. In 10% of the evaluated applications, the planned patient number was more than 1000, and in 25% less than 100.

IICT Call		Funding request (CHF)	Duration (months)	Number of patients	Number of recruiting sites
2015	Average	1'702'398	53	703	8
	Median	1'630'713	60	212	6
	Minimum	506'504	24	18	1
	Maximum	3725413	60	6624	33
2016	Average	1'515'232	52	476	6
	Median	1'651'666	54	330	6
	Minimum	267'215	24	40	2
	Maximum	2'696'829	60	2'000	16
OVERALL	Average	1'640'770	53	628	8
	Median	1'641'190	60	258	6
	Minimum	267'215	24	18	1
	Maximum	3'725'413	60	6'624	33

Table 2. Summary of evaluated proposals.

4. Evaluation of proposals

Of the 55 proposals evaluated following the 2015 call, two were rated A (outstanding) and seven AB (excellent). After the second call, one of the 27 evaluated proposals was given a rating of A and six an AB rating. The SNSF funded all projects rated either A or AB.

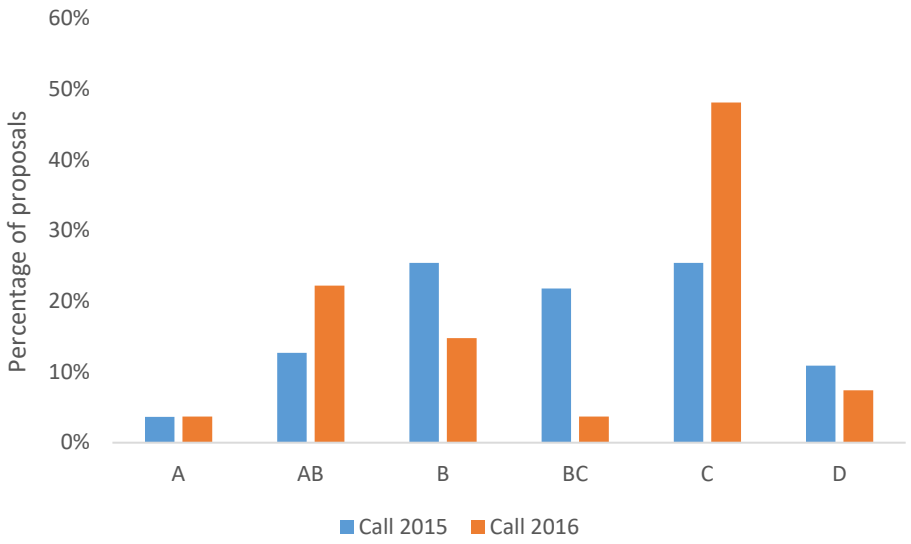

Figure 4. Ratings of the evaluated proposals.

In one third of the proposals that were neither funded after call 2015 nor after call 2016, the international evaluation panel and the external reviewers criticised the fact that the planned study was of limited clinical relevance or would not have a significant impact on clinical practice. In 15% of the proposals, limitations in respect of originality and innovation or the expected low knowledge gain led to a lower rating.

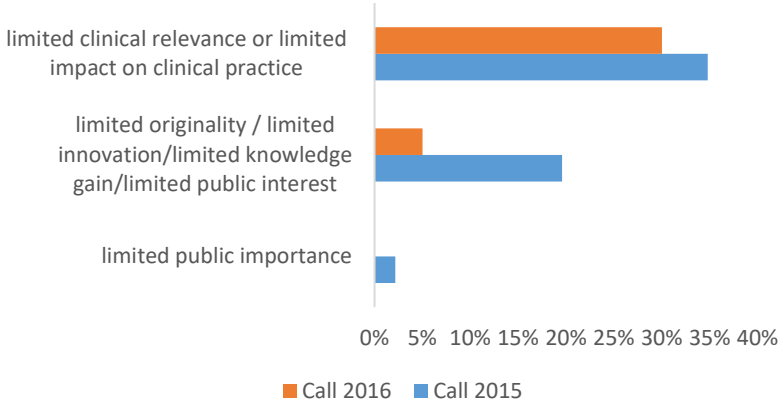

Figure 5. Reasons for lower ratings as regards the evaluation criteria 'clinical relevance', 'impact on clinical practice', 'originality' and 'public importance'.

Regarding the suitability of the methodological approach and the feasibility of the project, the most common criticism for projects submitted for the 2015 call was that the proposed hypothesis was not convincing, the rationale for medical intervention was not well justified or the study design was inadequate. In the second call, however, the most common reasons for a lower rating were an incomplete or insufficient sample size and/or power calculation, feasibility issues and criticism with regard to the primary endpoint.

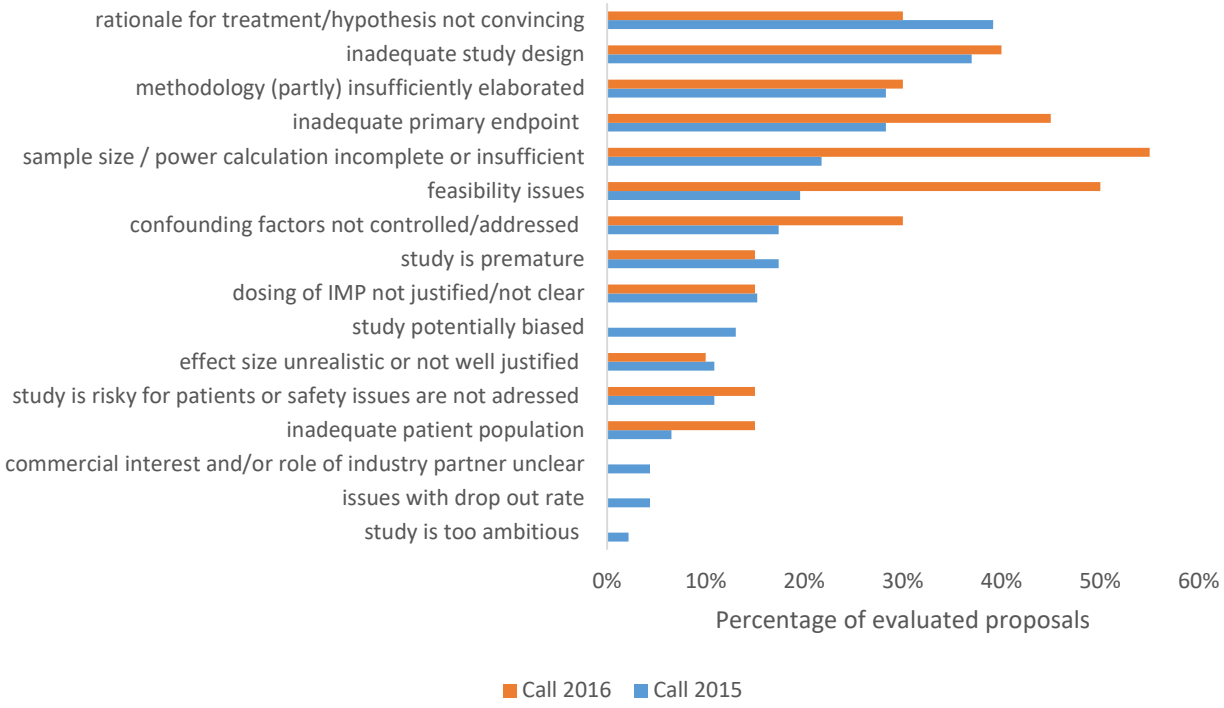

Figure 6. Reasons for lower ratings in regard to the evaluation criteria of feasibility and methodology.

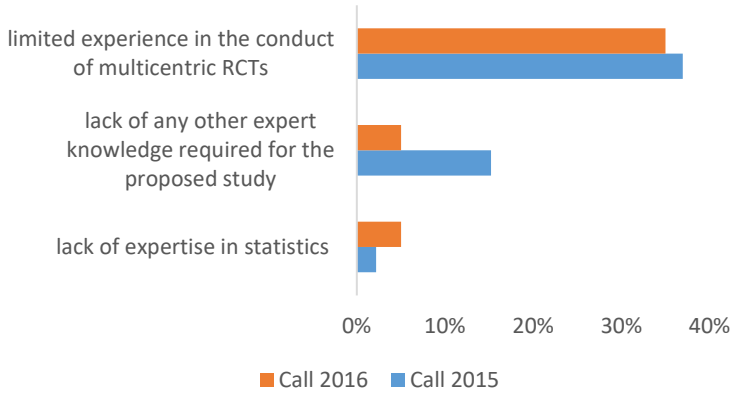

Figure 7. Reasons for lower rating as regards the track record of the applicants and their expertise in relation to conducting the proposed clinical study.

Concerning the scientific track record and the applicants' expertise in relation to the project, in 36% of the rejected proposals the evaluators criticised the applicants' limited experience in conducting multicentre randomised controlled trials. In 12% of the applications, the lack of a specialist on the research team with the expert knowledge needed to cover a specific aspect of the study was criticised and in 3% explicitly the lack of expertise in trial statistics.

Annex 1: List of funded trials

SNF number **Principal investigator, institution** **Further applicants, institution**	**Title**	**IICT call**	**Total duration (months)**	**Number of patients**	**Number of recruiting sites**	**Funding (CHF)**
33IC30_173533 Abegg Matthias, Inselspital Bern	A pragmatic, randomized, non-inferiority trial comparing the effectiveness of Botulinum toxin-based treatment with conventional strabismus surgery in acquired esotropia	2016	60	142	9	520,000
33IC30_173552 Auer Reto, University of Bern Cornuz Jacques, University Hospital Lausanne Hopf Nancy, Institut Universitaire Romand de Santé au Travail Rodondi Nicolas, Inselspital Bern	Efficacy, Safety and Toxicology of Electronic Nicotine Delivery Systems as an aid for smoking cessation: The ESTxENS multicentre randomized controlled trial	2016	48	874	3	1,897,332
33IC30_166827 Bassetti Claudio, Inselspital Bern Ott Sebastian, Inselspital Bern Wiest Roland, Inselspital Bern	Early Sleep Apnea Treatment in Stroke: A Randomized, Rater-Blinded, Clinical Trial of Adaptive Servo-Ventilation	2015	48	200	6	1,143,710
33IC30_166826 Berger Gregor, PUK, University of Zurich Schmeck Klaus, UPK, University of Basel Walitza Susanne, PUK, University of Zurich	Omega-3 fatty acids as first-line treatment in paediatric depression. A 36-week, multi-centre, double-blind, placebo-controlled randomized superiority study.	2015	48	220	7	1,355,350
33IC30_173508 Bischoff-Ferrari Heike, University Hospital Zurich Guggensberger Roman, University Hospital Zurich Kressig Reto, Felix Platter – Hospital Basel	Sarcopenia Prevention with a Targeted Exercise and Protein Supplementation Program	2016	54	810	7	2,448,688
33IC30_173539 Buclin Thierry, University Hospital Lausanne Decosterd Isabelle, University Hospital Lausanne Piguet Valérie, University Hospital Geneva	N-of-1 within-patient trials to improve the rational use of therapeutic drugs: Evaluation of their contribution in personalizing the treatment of chronic pain	2016	45	240	4	499,400

SNF number Principal investigator, institution Further applicants, institution	Title	IICT call	Total duration (months)	Number of patients	Number of recruiting sites	Funding (CHF)
33IC30_166909 Dutkowski Philipp, University Hospital Zurich Clavien Pierre-Alain, University Hospital Zurich	Hypothermic oxygenated perfusion (HOPE) for human livers - a prospective randomized European Liver Transplant Trial	2015	36	170	13	903,305
33IC30_166785 Fuster Daniel Guido, Inselspital Bern Beat Roth, Inselspital Bern Olivier Bonny, University Hospital Lausanne	Randomized double-blind placebo-controlled trial assessing the efficacy of Standard and low-dose hydrochlorothiazide treatment in the prevention of recurrent calcium nephrolithiasis	2015	60	412	12	2,438,923
33IC30_166872 Lüscher Thomas, University Hospital Zurich	Controlled Level EVERolimus in Acute Coronary Syndromes (CLEVER-ACS)	2015	48	150	8	948,996
33IC30_173545 Manuel Oriol, University Hospital Lausanne Berger Christoph, University Children's Hospital Zurich Dickenmann Michael, University Hospital Basel Müller Nicolas, University Hospital Zurich Van Delden, Christian, University Hospital Geneva	Reducing the Burden of Influenza after Solid-Organ Transplantation: the STOP-FLU trial [Swiss Trial in Solid Organ Transplantation on Prevention of influenza]	2016	36	780	9	1,651,666
33IC30_166844 Rogler Gerhard, University Hospital Zurich Vavricka Stephan, City Hospital Triemli Zurich	Multi-centre, multi-national, double-blind, placebo-controlled study to evaluate the efficacy and safety of an anthocyanin-rich extract (ACRE) in moderately active ulcerative colitis	2015	42	112	11	1,021,317
33IC30_166855 Schwerzmann Markus, Inselspital Bern Greutmann Matthias, University Hospital Zurich Tobler Daniel, University Hospital Basel	Effect of phosphodiesterase-5 inhibition with tadalafil on systemic right ventricular function – a multi-centre, double-blind, randomised, placebo-controlled clinical trial	2015	60	98	7	1,982,082

SNF number **Principal investigator, institution** **Further applicants, institution**	**Title**	**IICT call**	**Total duration (months)**	**Number of patients**	**Number of recruiting sites**	**Funding (CHF)**
33IC30_173532 Van den Anker Johannes, University Children's Hospital Basel Bielicki Julia, University Children's Hospital Basel Christ-Crain Mirjam, University Hospital Basel Heiniger Ulrich, University Hospital Basel	A randomised controlled trial of adjunct corticosteroid therapy in hospitalised children with community acquired pneumonia (CAP): THE KIDS-STEP STUDY	2016	60	700	8	1,671,327
33IC30_173534 Widmer Andreas, University Hospital Basel Kuster Stefan, University Hospital Zurich Marschall Jonas, Inselspital Bern	Chlorhexidine vs PVP iodine in alcohol for disinfection of the surgical site: a cluster-randomized multicenter trial	2016	48	2000	3	1,015,986
33IC30_166811 Wüthrich Rudolf, University Hospital Zurich Wagner Carsten, University Hospital Zurich	Preservation of kidney function in kidney transplant recipients by alkali therapy (Preserve Transplant Study)	2015	60	180	3	1,517,467
Total				7300	116*	22,327,179

*This number includes institutes within hospitals (e.g. university hospitals are counted multiple times)

Table 3. Clinical studies funded by IICT programme in alphabetic order of the principal investigators.

Publishing information

Published by

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05.03.2018