Report on the Evaluation Results

Investigator Initiated Clinical Trials programme (IICT) 2015

FNSNF
Swiss National Science Foundation

1. IICT programme

In 2015, the Swiss National Science Foundation (SNSF) issued its first call for proposals aimed at supporting independent investigator initiated clinical trials (IICT). The call concerned prospective, randomised, interventional, multicentre studies of new or existing treatments. Studies had to be outside the industry focus and their topics under-researched (e.g. rare diseases, paediatric diseases, therapy combinations, dosage reduction studies and rehabilitation measures).

2. Funded proposals

The first IICT call resulted in the supporting of nine proposals with a total funding of CHF 12.6 million.

Project number **Principal Investigator, institution** **Further applicants, institution**	**Title**	**Total duration (months)**	**Number of Patients**	**Number of Recruiting sites**	**Funding (CHF)**
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	48	200	3	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.	48	220	6	1,355,350
33IC30_166819 Calmy Alexandra, University Hospital Geneva Vernazza Pietro, Cantonal Hospital St. Gallen Fehr Jan, University Hospital Zurich	Evaluation of a simplified strategy for the long-term management of HIV infection: a non-inferiority, randomized, controlled, open-label clinical trial (The SIMPL-HIV Trial)	60	212	7	1,311,630
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	36	170	10	903,305

Project number **Principal Investigator, institution** **Further applicants, institution**	**Title**	**Total duration (months)**	**Number of Patients**	**Number of Recruiting sites**	**Funding (CHF)**
33IC30_166785 Daniel Guido Fuster, 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	60	412	8	2,438,923
33IC30_166872 Thomas Lüscher, University Hospital Zurich	Controlled Level EVERolimus in Acute Coronary Syndromes (CLEVER-ACS)	48	150	6	948,996
33IC30_166844 Gerhard Rogler, University Hospital Zurich Stephan Vavricka, 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	42	112	11	1,021,317
33IC30_166855 Markus Schwerzmann, Inselspital Bern Matthias Greutmann, University Hospital Zurich Daniel Tobler, 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	60	98	6	1,982,082
33IC30_166811 Rudolf Wüthrich, University Hospital Zurich Carsten Wagner, University Hospital Zurich	Preservation of kidney function in kidney transplant recipients by alkali therapy (Preserve Transplant Study)	60	180	3	1,517,467
Total			1754	60*	**12,622,780**

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

Table 1. Clinical studies funded by the first IICT call in alphabetic order.

Funded projects are based at the University Hospitals and/or Universities of Basel, Bern, Geneva, Lausanne and Zurich, as well as of researchers at the Cantonal Hospital St. Gallen and the Triemli Hospital Zurich.

1754 patients are planned to be enrolled in the SNSF-supported studies. All five Swiss university hospitals, four cantonal hospitals and five other institutions in Switzerland are involved in their recruitment. 14 foreign hospitals in Germany, France, Belgium, Spain and Romania are participating in the studies in order to achieve the required number of patients.

3. Overview of all applications

The first IICT call has attracted considerable attention from the clinical research community. 112 research groups expressed their intention to submit a proposal and 75 of them actually submitted one. The total funding requested was CHF 116 million.

The SNSF received applications from a broad field of medical disciplines. Researchers in cardiology, paediatrics, neurology and oncology submitted over 50% of the applications.

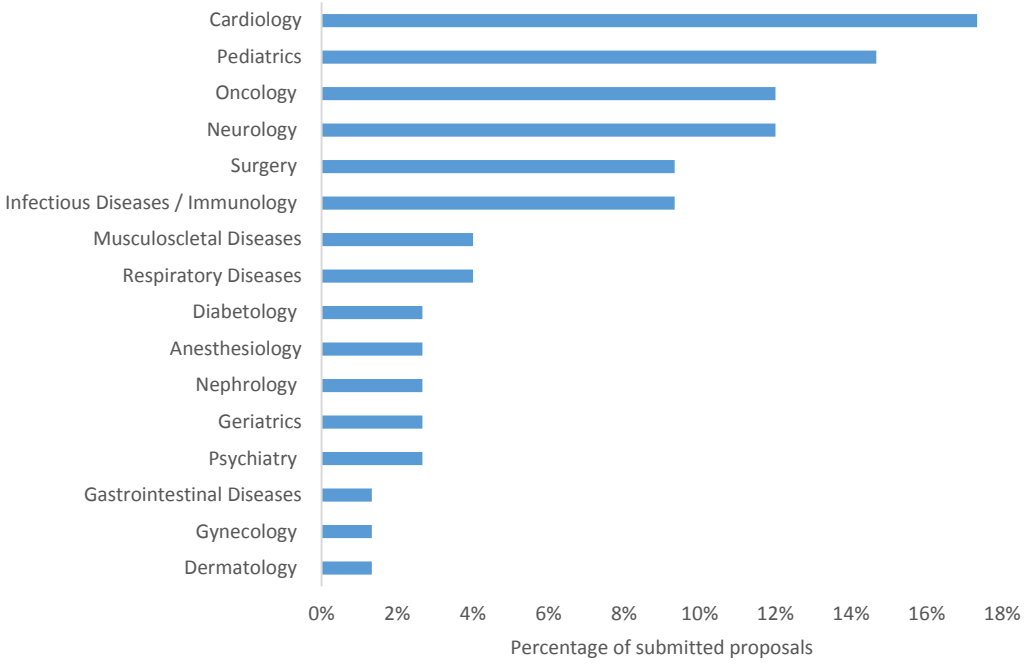

Figure 1. Percentage of submitted proposals by medical field.

25% of the submitted applications did not satisfy the formal call specifications. The SNSF did not consider them for evaluation. One application was found to be clearly insufficient in at least one evaluation criterion and was rejected without an external review procedure. Lack of randomisation was the main reason for a non-consideration decision, followed by study designs that were explicitly excluded from the call.

Reason for non-consideration decision	Number of proposals
Trial is not randomised	9%
Requested study duration is too long	3%
Application for an observational study	5%
Application for an exploratory study	4%
Origin of study is outside Switzerland	3%
Application for technology development of a novel treatment	3%
No intervention in patients	3%
Unjustified single-centre study	1%
Late resubmission of required documents	1%

Table 2. Reasons for non-consideration decisions.

The SNSF evaluated the remaining 55 proposals. Most of these proposals were conceived by groups based at University Hospital Zurich, followed by University Hospital Geneva, University Hospital Bern, University Hospital Basel, University Hospital Lausanne and the Cantonal Hospital St. Gallen.

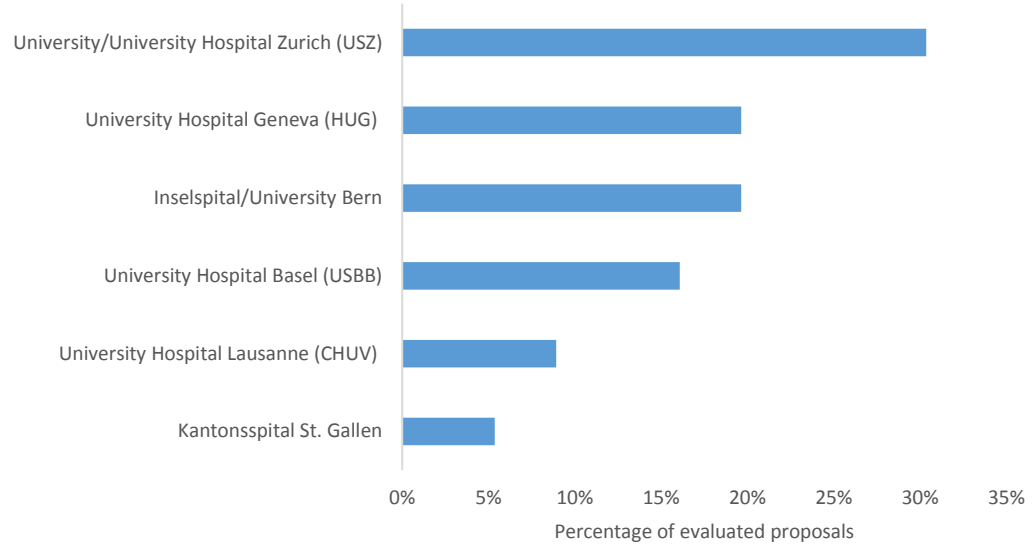

Figure 2: Main institutions of the evaluated proposals.

Applicants requested an average funding of CHF 1,685,634 (median CHF 1,604,564) per clinical study, with a minimum of CHF 506,504 and a maximum of CHF 3,725,413.

More than 50% 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 212 (median), ranging from 18 to 6624 patients. In 12% of the evaluated applications the planned patient number was more than 1000, and in 14% less than 100.

The study teams consisted of five applicants on average. They planned to collaborate with seven project partners (mean) and eight recruiting sites (mean).

	Mean	Median	Minimum	Maximum
Number of applicants	5	4	1	12
Number of project partners	7	5	0	32
Number of recruiting sites	8	6	1	32

Table 3. Number of applicants, project partners and recruiting sites of the evaluated applications.

4. Evaluation and funding decision

4.1 Evaluation of the proposals

Out of 55 proposals, two were rated A and seven AB. The SNSF funded them all. 46 proposals were assessed with a lower rating.

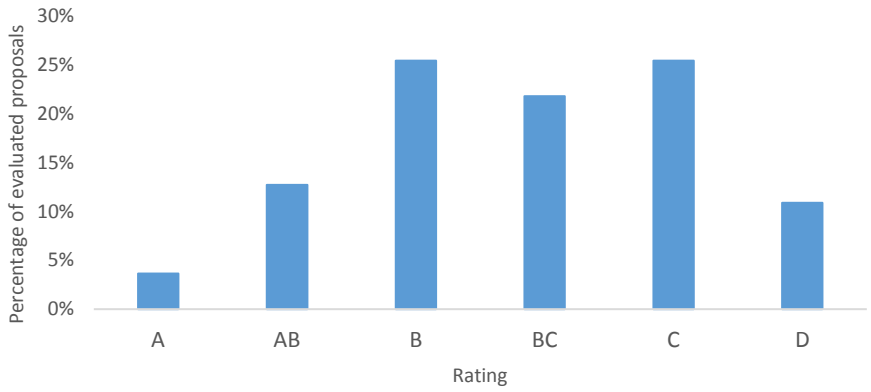

Figure 3. Ratings of the evaluated proposals.

In almost one third of the applications, the international evaluation panel and the external reviewers criticised the fact that the planned study was of limited clinical relevance or would lack a significant impact on clinical practice. Additionally, in 15% of the proposals, limitations in respect of originality or innovation, a limited public interest or an expected low knowledge gain led to a lowering of the rating.

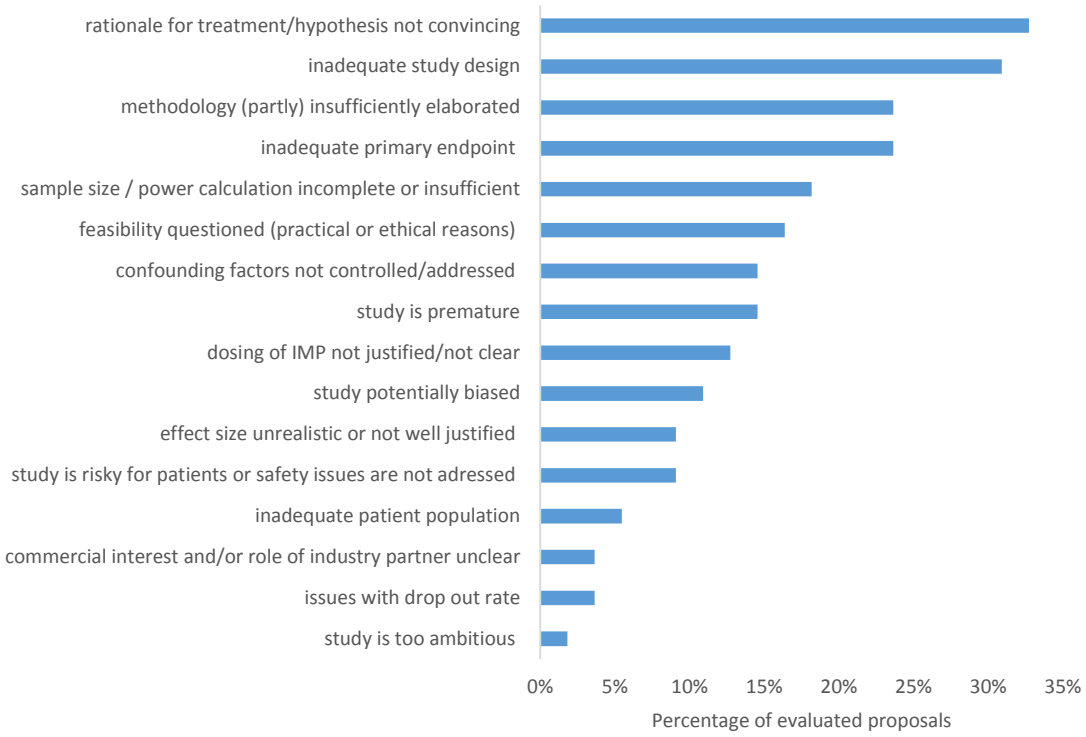

Figure 4. Criticisms raised in regard to the evaluation criteria of feasibility and methodology of the proposed studies.

Regarding the suitability of the methodological approach and the feasibility of the project, the most common criticism was the unconvincing justification for the treatment or rationale for the proposed hypothesis. An inadequate study design, an insufficiently elaborated methodology and an inadequate primary endpoint were further reasons for the reduced ratings.

Concerning the scientific track record and the applicants' expertise in relation to the project, in almost one third of the applications it was revealed that the applicants have limited experience in the conduct of multicentre randomised controlled trials. In 15% of the applications the lack of a specialist on the research team with expert knowledge required to cover a specific aspect of the study was criticised.

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