Schweizer Register für Neuroendokrine Tumore
Le Registre Suisse des tumeurs neuroendocrines
Registro Svizzero per i Tumori Neuroendocrini

SwissNET

Präsident: PD Dr. Maurice Matter
Registerleiter: Dr. Attila Kollàr

Introduction to the 2016 annual SwissNET , report of the president

2016-2017 is an interesting transition period. While SwissNET data base is regularly growing thanks to the efforts of all partners, ENETS contacts are improving as well. A future collaboration with the ENETS database is in the pipeline with discussions among the "ENETS register group". The tasks in many Swiss Centers is to get an accreditation as "ENETS Center of Excellence". Zürich is the first but not the last. This will improve overall the quality of care of NET patients regarding treatments but also knowledge of the disease among medical and general populations. In this setting the plan to cooperate with VictoryNET Foundation did materialize with a training course for clinical nurses dedicated to NET patients, with the help of Mrs. Catherine Bouvier, who is an English clinical nurse pioneer in the patients'information and support (1). The course took place in Bern in February 2017 and it is planned to go forward. The SwissNET website will be the ideal place for more useful information to patients but also health care professionals.

Foreign collaboration include our contacts with the Groupe Français des Tumeurs Endocrines (GTE), who invited us again in the 2016 conference. Our scientific activity based on our data is growing and is translated in many publications.

All these activities need sponsoring and these partners must be thanked for their support: Novartis, Pfizer Oncology and Ipsen. They are enabling the work of our association. In this setting it was decided to meet annually in order to present our activities, results and upcoming projects.

SwissNET is going on as the only available source for NETs data in Switzerland. The future will include NET training and facilities as well as ongoing collaboration with ENETS.

Dr. Maurice Matter, PD & MER
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Fellow of the European Society of Endocrine Surgery
President SwissNET
ENETS member

1. https://www.netpatientfoundation.org/

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Database Report 2016

Based on discussions within the SwissNET committee and at a meeting with our sponsors the following changes with regards to data documentation and data reporting has been made:

- Modification of the data set for biotherapy, molecular therapy and chemotherapy in order to improve completeness and interpretation of data
- Report expansion on specific treatments and their assignment to primary site and differentiation of NET

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Data analysis 2016

In total, 1245 patients are included in the SwissNET registry. Since the last statistical analysis of the SwissNET data 195 additional patients were registered and documented which represents a significant increase in patient number.

Patient and tumor characteristics

Patient characteristics and Follow up

The distribution of male and female patients (male: 53%, female: 47%) is relatively equal. The median follow up time increased to 2.2 years. There was no change in the mean age at diagnosis in comparison to data from 2013. (Table 1)

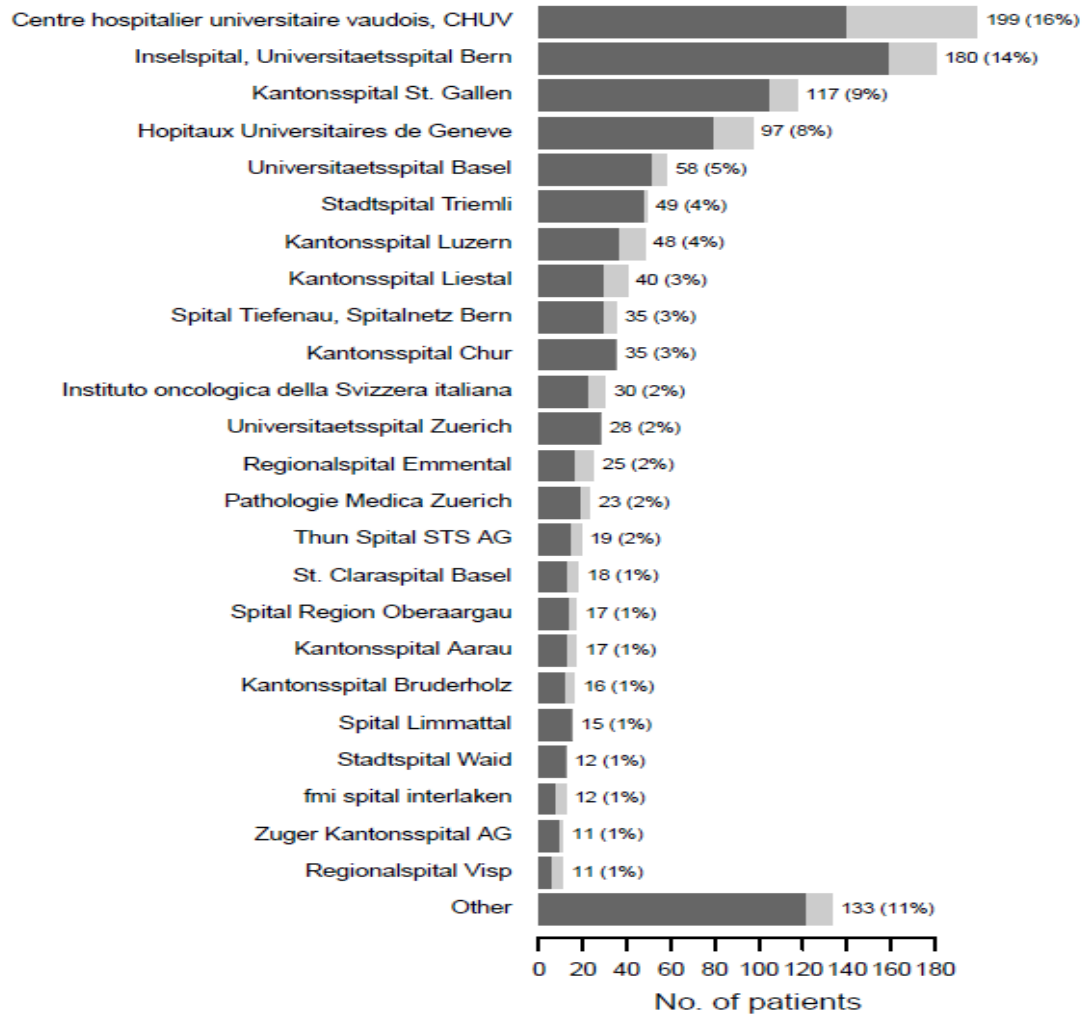
Table 1: Patient characteristics

Measurement	2013	2014	2015	2016
Number of patients	**671**	**835**	**1050**	**1245**
Females	47%	46%	46%	47%
Males	53%	54%	54%	53%
Age at diagnosis (y)				
Mean	59	59.3	59.9	59.6
Follow-up				
Median (years)	1.25	2	2.1	2.23

Recruitment

Virtually all institutions, hospitals and cantons are recruiting NET patients. Most of the patients are still recruited by the established major centers in Lausanne, Berne, , St. Gallen, Geneve and Basel. However, half of the included patients are from other hospitals or private practices. (Figure 1)

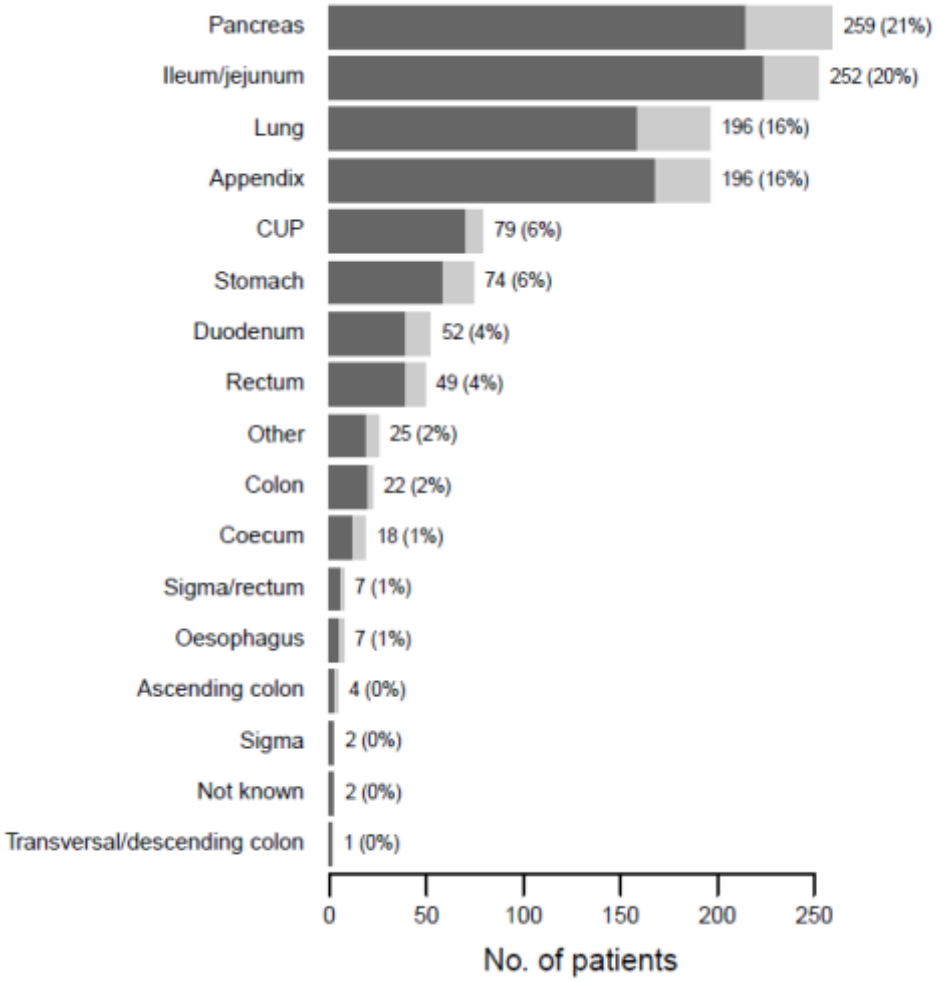
Figure 1: Recruitment of patients: dark grey: 2008-2015, grey: 2016



Distribution of primary sites and tumor grade

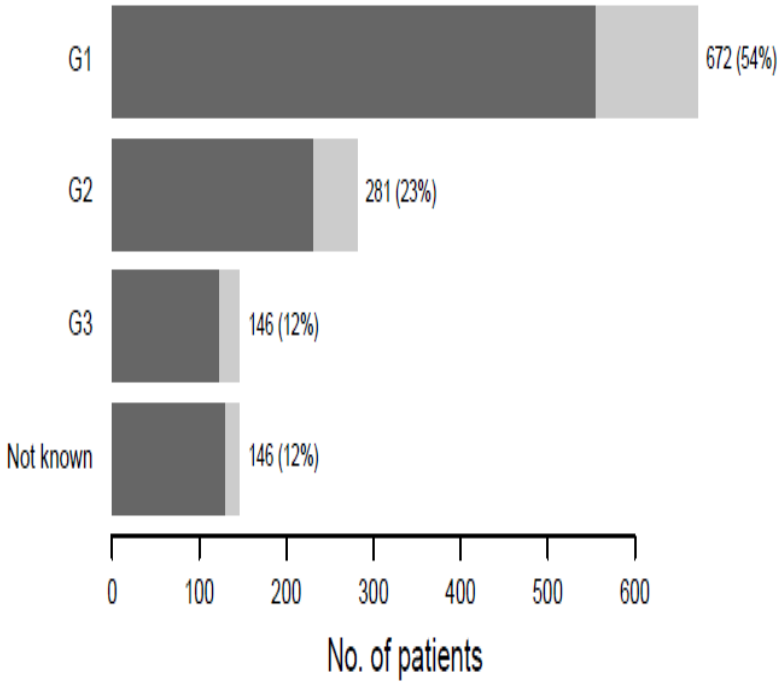
Most of the NET registered in the database are of pancreatic and ileal/jejunal origin. NET of the appendix, lung and of unknown origin are quite common, too. There's a slight, but steady increase in the incidence of NET at rarer primary sites. (Figure 2)

Figure 2: Distribution of primary sites of NET



The following differentiation is based on the WHO 2010 classification. Well differentiated neuroendocrine tumors are still the largest group of tumors. Neuroendocrine neoplasms G3 are much rarer. (Figure 3)

Figure 3: Tumor grading



Treatment

Surgery

Surgery represents the most common treatment modality used (74% of patients). Tumor resection was performed in 45% and 54% in university hospitals and general hospitals, respectively (Table 2).

Table 2: Surgery

	no. of surgeries	n (%)	no. of patients	n (%)*
Total	1264 (1.4 per patient)		926	
Center	1258		923	
University hospital		550 (44%)		415 (45%)
General hospital		681 (54%)		503 (54%)
Private practise		14 (1%)		12 (1%)
Not known		13 (1%)		9 (1%)

somatostatin analogues

Octreotide and lanreotide were the most commonly prescribed somatostatin analogues. Whereas the use of octreotid was slightly below the percentage of last year, the use of lanreotide has increased. The promising results of the Clarinet-trial might explain this observation (Table 3).

Table 3: somatostatin analogues

drug	year	Patient no.
Octreotid LAR	2014	65/87 (75%)
	2015	91/121 (75%)
	2016	108/149 (72%)
Lanreotid	2014	11/87 (13%)
	2015	22/121 (18%)
	2016	34/149 (23%)
Pasireotid	2014	2/87 (2%)
	2015	2/121 (2%)
	2016	3/149 (2%)

Table 4: somatostatin analogues treatment according to primary NET site

	Octreotide LAR (N = 108)	Octreotide s.c. (N = 43)	Lanreotide (N = 34)	Pasireotide (N = 3)	Other Drug (N = 4)
Lung	6 (6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pancreas	30 (28%)	21 (49%)	14 (41%)	0 (0%)	2 (50%)
Duodenum	1 (1%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)
Ileum/jejunum	40 (37%)	12 (28%)	10 (29%)	2 (67%)	1 (25%)
Coecum	1 (1%)	0 (0%)	1 (3%)	0 (0%)	0 (0%)
Colon	2 (2%)	2 (5%)	0 (0%)	1 (33%)	0 (0%)
Rectum	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CUP	24 (22%)	7 (16%)	8 (24%)	0 (0%)	1 (25%)
Other	3 (3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 5: somatostatin analogues treatment according to NET differentiation

	Octreotide LAR (N = 108)	Octreotide s.c. (N = 43)	Lanreotide (N = 34)	Pasireotide (N = 3)	Other Drug (N = 4)
G1	39 (36%)	18 (42%)	13 (38%)	3 (100%)	1 (25%)
G2	43 (40%)	17 (40%)	15 (44%)	0 (0%)	2 (50%)
G3	11 (10%)	4 (9%)	2 (6%)	0 (0%)	0 (0%)
Not known	10 (9%)	1 (2%)	1 (3%)	0 (0%)	0 (0%)

Chemotherapy

In total, 158 patients were treated with classical chemotherapeutical agents. Carboplatin, cisplatin and etoposide were the drugs most commonly used in the metatstatic setting. This is in contrast to the reported NET grading in our cohort. Based on the results of the NORDIC trial the efficacy of these agents is mainly limited to G1 and G2 differentiated neoplasms (Table 6).

Table 6: chemotherapy agents

	no. of chemotherapies	n (%)	no. of patients	n (%)*
Total	1122 (7.1 per patient)		158	
Drug	1111		154	
Carboplatin		199 (18%)		80 (52%)
Cisplatin		144 (13%)		54 (35%)
Cyclophosphamide		18 (2%)		12 (8%)
Dacarbazin		2 (0%)		1 (1%)
Doxorubicin		33 (3%)		16 (10%)
Etoposide		294 (26%)		104 (68%)
5-FU		70 (6%)		20 (13%)
Streptozotocin		42 (4%)		15 (10%)
Temozolomide		58 (5%)		24 (16%)
Capecitabine		32 (3%)		19 (12%)
Other Drug		219 (20%)		60 (39%)

*Patients do not sum up as they can have several chemotherapies

Molecular therapies

As expected, everolimus and sunitinib were the most common used melocular therapy agent, in 36 and 18 patients, respectively (Table 7).

Table 7: molecular therapies

	no. of molecular therapies	n (%)	no. of patients	n (%)*
Total	77 (1.5 per patient)		50	
Drug	77		50	
Bevacizumab		1 (1%)		1 (2%)
RAD001/Everolimus		44 (57%)		36 (72%)
Sunitinib		24 (31%)		18 (36%)
Other Drug		8 (10%)		7 (14%)

*Patients do not sum up as they can have several molecular therapies

Table 8: molecular treatment according to primary NET site

	Bevacizumab (N = 1)	RAD001/Everolimus (N = 36)	Sunitinib (N = 18)	Other Drug (N = 7)
Lung	0 (0%)	2 (6%)	0 (0%)	3 (43%)
Stomach	0 (0%)	0 (0%)	1 (6%)	0 (0%)
Pancreas	1 (100%)	15 (42%)	11 (61%)	3 (43%)
Ileum/jejunum	0 (0%)	10 (28%)	2 (11%)	1 (14%)
CUP	0 (0%)	6 (17%)	3 (17%)	0 (0%)
Other	0 (0%)	3 (8%)	1 (6%)	0 (0%)

Table 9: molecular treatment according to NET differentiation

	Bevacizumab (N = 1)	RAD001/Everolimus (N = 36)	Sunitinib (N = 18)	Other Drug (N = 7)
G1	0 (0%)	6 (17%)	1 (6%)	0 (0%)
G2	0 (0%)	17 (47%)	11 (61%)	4 (57%)
G3	0 (0%)	5 (14%)	4 (22%)	2 (29%)
Not known	1 (100%)	6 (17%)	2 (11%)	1 (14%)

radiotherapy and targeted nuclear therapy

77 and 73% patients underwent a PRRT 90-Y-Dotatoc and 177-lutetium Dotatate treatment. External radiation therapy seems to be an attractive treatment option in individual cases, as well (Table 10).

Table 10: radiotherapy and targeted nuclear therapy

	no. of irradiations	n (%)	no. of patients	n (%)*
Total	420 (2.5 per patient)		165	
Mode	420		165	
External		99 (24%)		46 (28%)
PRRT Y-90-Dotatoc		140 (33%)		77 (47%)
PRRT 177-lutetium Dotatate		61 (15%)		28 (17%)
PRRT Lutetium Dotatoc		91 (22%)		43 (26%)
SIRT		20 (5%)		15 (9%)
Other		7 (2%)		7 (4%)
Not known		2 (0%)		1 (1%)
Center	419		164	
University hospital		393 (94%)		150 (91%)
General hospital		23 (5%)		15 (9%)
Private practise		1 (0%)		1 (1%)
Not known		2 (0%)		2 (1%)

*Patients do not sum up as they can have several irradiations

Table 11: radiotherapy and targeted nuclear therapy according to primary NET site

	External (N = 46)	PRRT Y-90-Dotatoc (N = 77)	PRRT 177-lutetium Dotatate (N = 28)	PRRT Lutetium Dotatoc (N = 43)	SIRT (N = 15)	Other (N = 7)	Not known (N = 1)
Lung	28 (61%)	5 (6%)	2 (7%)	3 (7%)	0 (0%)	0 (0%)	1 (100%)
Oesophagus	2 (4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Stomach	0 (0%)	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pancreas	7 (15%)	35 (45%)	10 (36%)	17 (40%)	9 (60%)	1 (14%)	0 (0%)
Duodenum	0 (0%)	1 (1%)	1 (4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ileum/jejunum	3 (7%)	19 (25%)	8 (29%)	11 (26%)	3 (20%)	0 (0%)	0 (0%)
Coecum	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (7%)	1 (14%)	0 (0%)
Appendix	0 (0%)	1 (1%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)
Colon	0 (0%)	1 (1%)	2 (7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ascending colon	1 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CUP	2 (4%)	11 (14%)	5 (18%)	8 (19%)	2 (13%)	2 (29%)	0 (0%)
Other	3 (7%)	2 (3%)	0 (0%)	2 (5%)	0 (0%)	3 (43%)	0 (0%)
Not known	0 (0%)	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 12: radiotherapy and targeted nuclear therapy according to NET differentiation

	External (N = 46)	PRRT Y-90-Dotatoc (N = 77)	PRRT 177-lutetium Dotatate (N = 28)	PRRT Lutetium Dotatoc (N = 43)	SIRT (N = 15)	Other (N = 7)	Not known (N = 1)
G1	2 (4%)	22 (29%)	9 (32%)	14 (33%)	2 (13%)	1 (14%)	0 (0%)
G2	10 (22%)	30 (39%)	12 (43%)	15 (35%)	8 (53%)	3 (43%)	1 (100%)
G3	19 (41%)	12 (16%)	4 (14%)	5 (12%)	4 (27%)	1 (14%)	0 (0%)
Not known	13 (28%)	7 (9%)	2 (7%)	6 (14%)	1 (7%)	1 (14%)	0 (0%)

Outcome

In total, the remission status at last visit is recorded in 1103 patients, 53% of patients are documented to be in complete remission. Partial remission, stable and progressive disease are recorded in 1%, 13%, and 8%, respectively. In 18% the remission status is not known (Table 13). No survival analysis has been performed in 2016.

Table 13: Remission status

Result, last visit	1103	
Complete remission		582 (53%)
Partial remission		16 (1%)
Stable disease		141 (13%)
Progressive disease		83 (8%)
Relapse		5 (0%)
Dead		75 (7%)
Not known		201 (18%)

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Research projects

a) published

- **Gouffon M**, Iff S, Ziegler K et al. Diagnosis and workup of 522 consecutive patients with neuroendocrine neoplasms in Switzerland. Swiss Med Wkly. 2014 Feb 19;144:w13924

- **Kollár A,** Blank A, Perren A et al. Additional malignancies in patients with neuroendocrine tumours: analysis of the SwissNET registry. Swiss Med Wkly. 2016 Nov 12;146:w14362

b) Ongoing

- Value of octreoscan and 18F-FDG PET for clinical prognosis of patients with neuroendocrine neoplasms (**Prof. F. Pralong**, Lausanne)

- Evidence-based medicine in neuroendocrine tumors: impact on long-term survival (eviNET study) (**Prof. M. Walter and Dr. R. Kaderli**, Bern)

- Management of pulmonary carcinoids (typical and atypical): the Swiss experience (**Dr. S. Sadowski**, Geneva)

- Surgery: is there an indication for G3 Neuroendocrine Neoplasms? (**Prof. M. Pavel, Prof. E. Christ, Prof. A. Perren, Dr. A Kollàr**, Bern)

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Financing

With regard to the finances we received sFr.90'000 from our three sponsors and the membership fees added up to 1'100.-. The total income in 2016 was sFr. 91'100.- , roughly 25'000.- more than in 2015. This is due to the fact that Ipsen paid up for 2016 and 2017 at the beginning of December 2016. The main expenses include the salary for the research nurses working at the two sites (sFr. Inselspital Bern; 40% and CHUV; 20%). The database was successfully moved to a web-based platform. The coordinator for this task (Dr. A. Blank, Institute of Pathology) moved in a clinical position resulting in decrease in spending of sFr. 15'000.-. Due to the fact that the income was higher as anticipated (Ipsen), the account closed with a positive balance sheet of +17'682. All the other expenses were within +/- within budget or lower.

The fortune of SWISSNet per 31. December 2016 add up to sFr. 171'237.-. It, therefore, can be stated that SWISSNet is financially still in a healthy situation. However, we have to consider the fact that to cover the current budget we need about sFr 75'000/year. With the available finances and without our sponsors we can cover maximally two further years, which is required for non-profit societies. Furthermore, it is likely that we shall have to increase the activity level of our research nurses since there are more and more follow-up data to be put into the database. I, therefore, think that we have to aim for a budget of close to sFr. 100'000/year in order to fulfil all the tasks of SWISSNet in the future. Consequently, we should aim to recruit additional sponsors for SWISSNet. Unfortunately, so far we did not find additional sponsors during 2016. We have to expand the activity in this direction.