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

SwissNET

Präsident: Prof. Emanuel Christ
Registerleiter: Dr. Attila Kollàr

Introduction to the 2017-2018 annual SwissNET report of the past president

During the last months, SwissNET has confirmed its leading role in the medical management of NET patients in Switzerland and at an international level. The SwissNET registry includes now about 1500 patients. Updates of the data set include systemic therapies and the new NEC G3 classification.

Developments of ENETS Centers of Excellence (CoE) in Switzerland is an ongoing process: Zurich already and applications were accepted for Lausanne and Basel with a possible opening in 2019. The concept that the SwissNET database would be used as the CoE database per centre was largely accepted. This will save time and costs and facilitate our collaboration with ENETS.

Thanks to the hard work undertaken by Attila Kollar and our fruitful collaboration with ENETS and the Registry meetings, Switzerland belongs to the core of the multinational ENETS registry (www.enets.org/the_registry.html) who was launched in 2015. In 2018, data from seven countries (Belgium, Czech Republic, Germany, Greece, Poland, Spain and Switzerland) were presented at ASCO and will be published soon (1). SwissNET contributed for 1338 patients out of the 10'102. This is to date the largest multinational dataset of NEN patients. Follow-up data highlighted the crucial role of the WHO grading.

NET patients' quality of life is an important priority and our collaboration with the VictoryNET Foundation is crucial. They will continue to sponsor the training for dedicated clinical NET nurses (next one in 2019) and contribute to patients' information through their website (2).

Finally yet importantly, we must highlight and thank the sponsoring who supports our activities and enables the future and the success of the database: Novartis, Pfizer Oncology and Ipsen. Our now well established annual sponsor meeting improved transparency and promotion of our achievements and upcoming projects.

Prof. Maurice Matter, Médecin chef

Service de Chirurgie Viscérale, CHUV Lausanne.

Fellow of the European Society of Endocrine Surgery

Past president SwissNET

ENETS member

1. Borbath I, et al. Assessing prognosis of neuroendocrine neoplasms: Results of a collaborative multinational effort including over 10.000 European patients - The ENETS registry. 2018 ASCO Annual Meeting. http://abstracts.asco.org/214/AbstView_214_216103.html or J Clin Oncol 36, 2018 (suppl; abstr 4095).
2. www.victorynet.org

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Database Report 2017

In total, 1428 patients are included in the SwissNET registry. Since the last statistical analysis of the SwissNET data 183 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 2.4 years. There was no change in the mean age at diagnosis in comparison to data from 2013. (Table 1)

Table 1: Patient characteristics

Measurement	2014	2015	2016	2017
Number of patients	**835**	**1050**	**1245**	**1428**
Females	46%	46%	47%	47
Males	54%	54%	53%	53
Age at diagnosis (y)				
Mean	59.3	59.9	59.6	60.1
Follow-up				
Median (years)	2	2.1	2.23	2.38

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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 1/2)

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

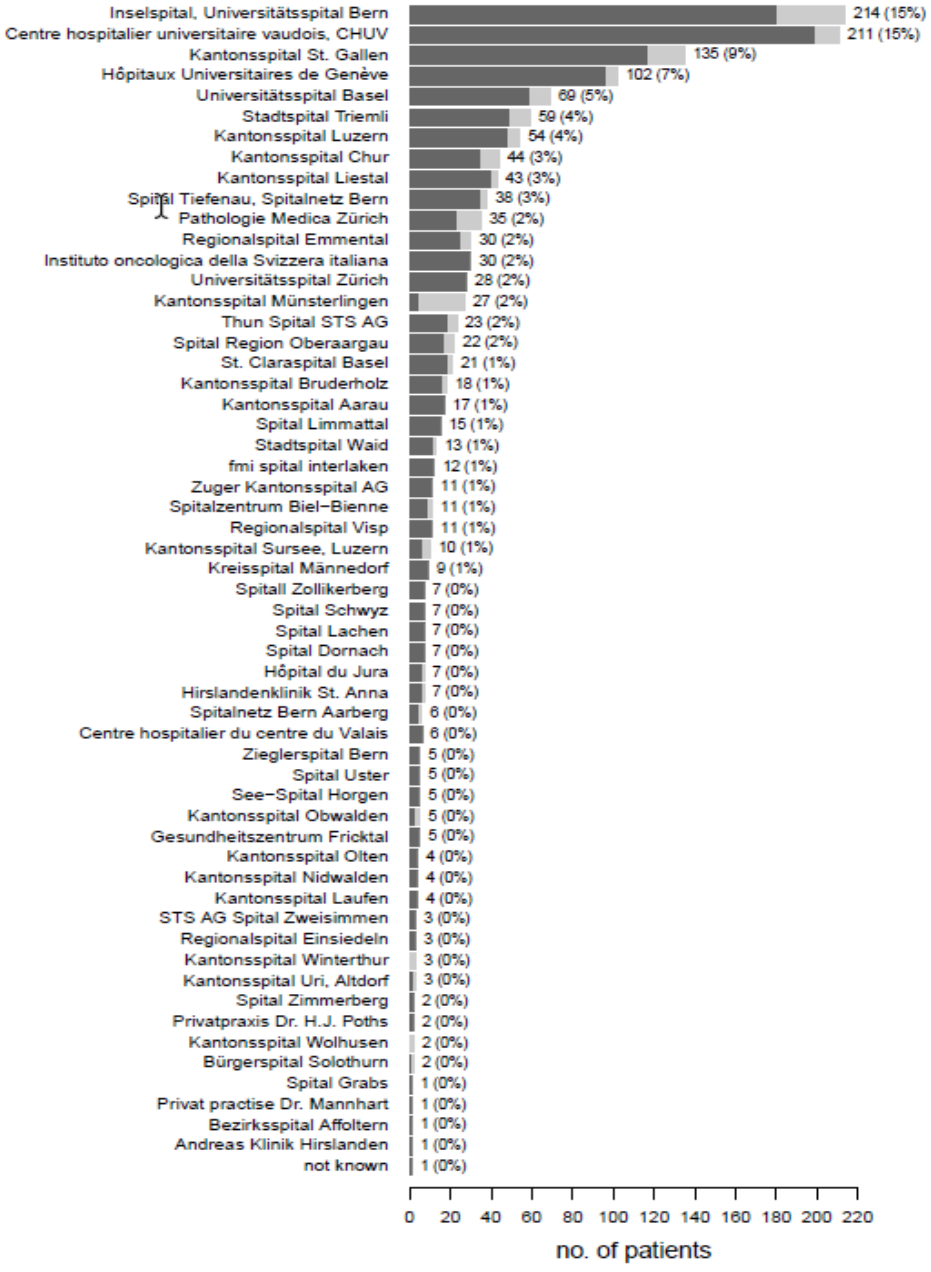
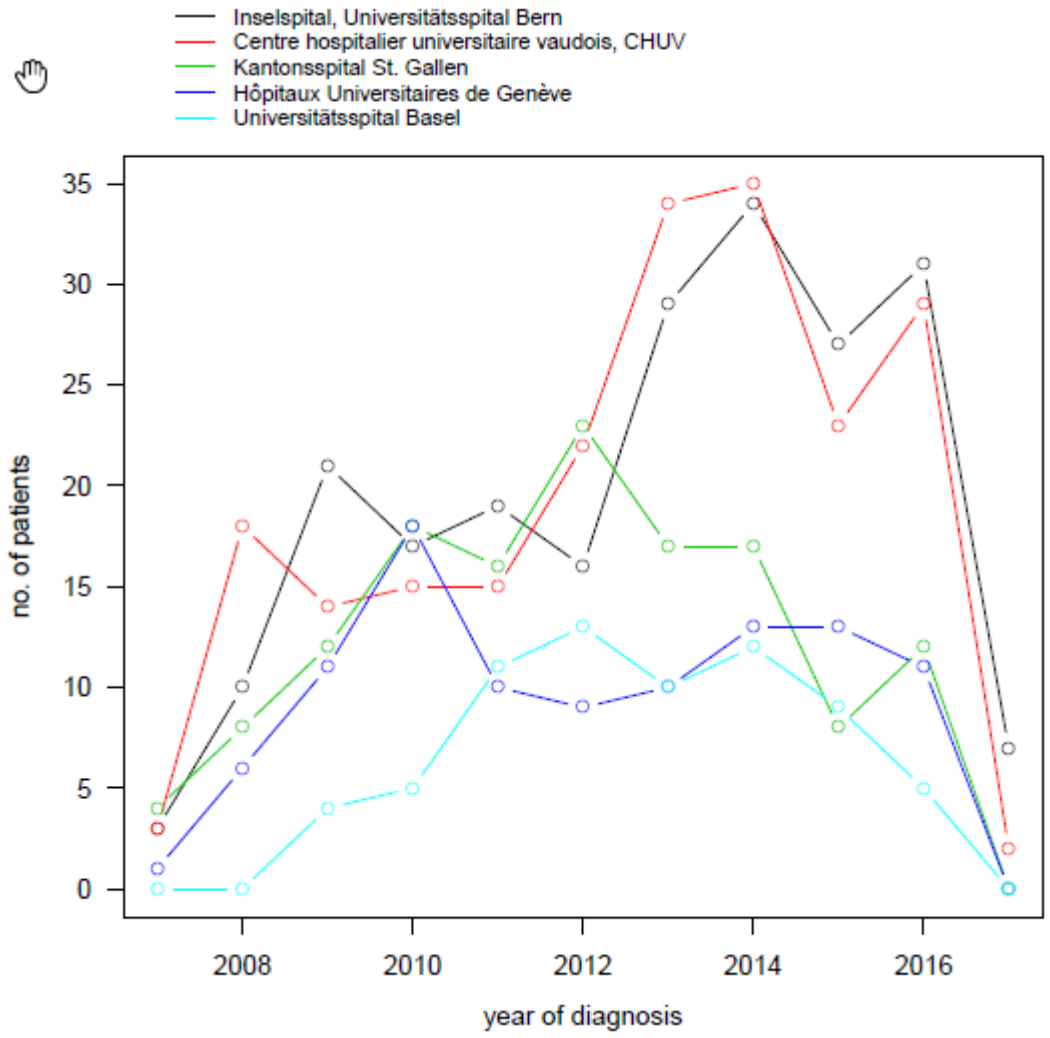


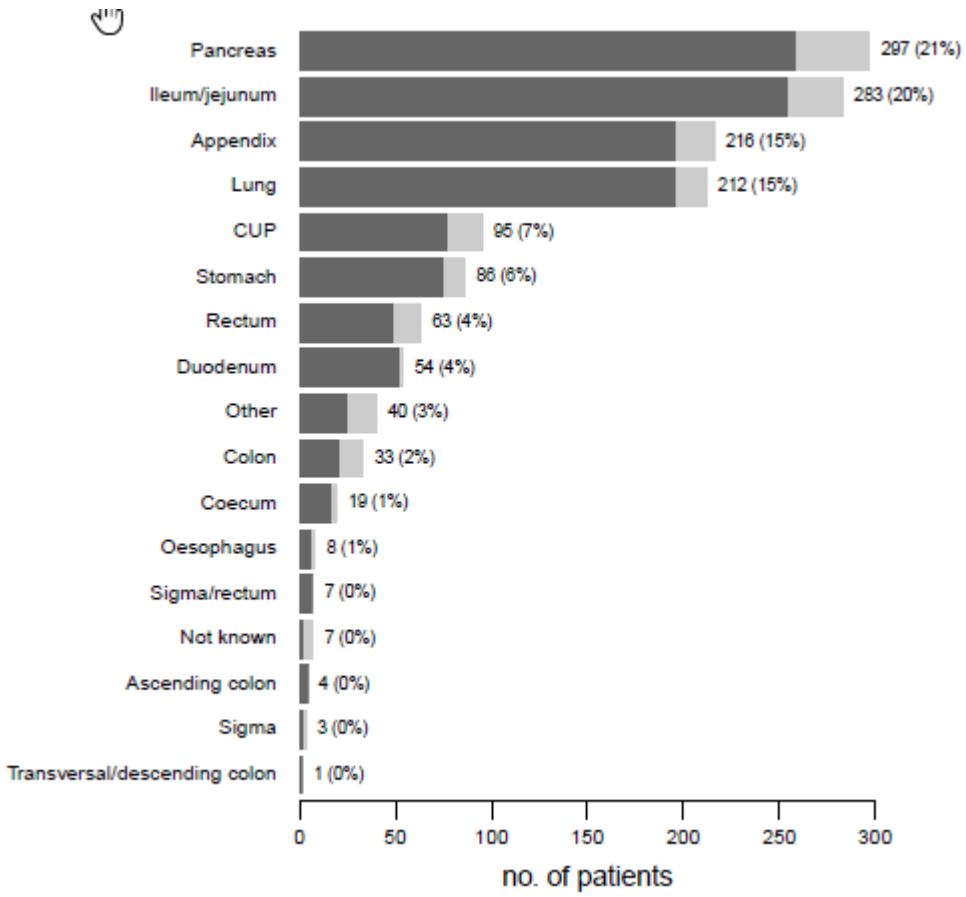
Figure 2: Number of patients recruited each year for the main centers



Distribution of primary sites and tumor grade

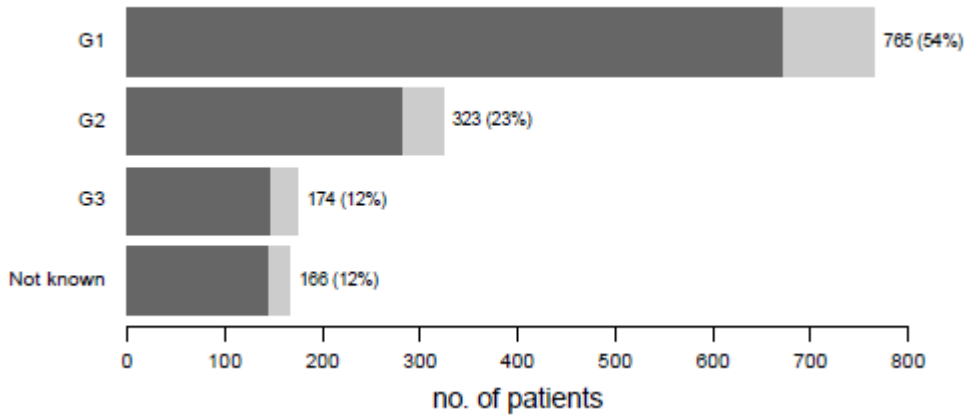
Most of the NET registered in the database are of pancreatic and ileal/jejunal origin. NET of the appendix, lung and of unknown origin are quite common, too. There's a slight, but steady increase in the incidence of NET at rarer primary sites. (Figure 3)

Figure 3: 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 4)

Figure 4: Tumor grading



Treatment

Surgery

Surgery represents the most common treatment modality used (74% of patients). Tumor resection was performed in 44% and 55% in university hospitals and general hospitals, respectively (Table 2).

Table 2: Surgery

	no. of surgeries	n (%)	no. of patients	n (%)*
Total	1426 (1.3 per patient)		1060	
Center	1424		1059	
University hospital		610 (43%)		462 (44%)
General hospital		774 (54%)		584 (55%)
Private practise		25 (2%)		23 (2%)
Not known		15 (1%)		11 (1%)

Systemic treatment

The number of patients treated with different kinds of systemic therapies are limited, but steadily increasing (table 3)

Table 3: overview of systemic treatments

modality	drug	Patient number
biotherapy	Octreotid LAR	120
	Lanreotid	47
PRRT	Y-90-DOTATOC	81
	Lu- 77-DOTATATE	35
	Lu-177-DOTATOC	54
Molecular Tx	Sunitinib	20
	Everolimus	41
Chemotherapy	-	154

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 4).

Table 4: somatostatin analogues

drug	year	Patient no.
Octreotid LAR	2014	65/87 (75%)
	2015	91/121 (75%)
	2016	108/149 (72%)
	2017	120/170 (71%)
Lanreotid	2014	11/87 (13%)
	2015	22/121 (18%)
	2016	34/149 (23%)
	2017	47/170 (28%)
Pasireotid	2014	2/87 (2%)
	2015	2/121 (2%)
	2016	3/149 (2%)
	2017	4/170 (2%)

Table 5: somatostatin analogues treatment according to primary NET site

	Octreotide LAR (N = 120)	Octreotide s.c. (N = 46)	Lanreotide (N = 47)
Lung	6 (5%)	0 (0%)	0 (0%)
Pancreas	33 (28%)	21 (46%)	20 (43%)
Duodenum	1 (1%)	1 (2%)	1 (2%)
Ileum/jejunum	44 (37%)	13 (28%)	15 (32%)
Coecum	1 (1%)	0 (0%)	1 (2%)
Colon	1 (1%)	1 (2%)	0 (0%)
Rectum	1 (1%)	0 (0%)	1 (2%)
CUP	28 (23%)	9 (20%)	8 (17%)
Other	4 (3%)	0 (0%)	0 (0%)
Not known	1 (1%)	1 (2%)	1 (2%)

Table 6: somatostatin analogues treatment according to NET differentiation

	Octreotide LAR (N = 120)	Octreotide s.c. (N = 46)	Lanreotide (N = 47)
G1	39 (33%)	18 (39%)	19 (40%)
G2	53 (44%)	19 (41%)	21 (45%)
G3	12 (10%)	4 (9%)	2 (4%)
Not known	10 (8%)	1 (2%)	2 (4%)

Chemotherapy

In total, 188 patients were treated with classical chemotherapeutical agents. Carboplatin, cisplatin and etoposide were the drugs most commonly used in the metastatic setting. This is in contrast to the reported NET grading in our cohort. Based on the results of the NORDIC trial the efficacy of the agents mentioned above is mainly limited to poorly differentiated NET/NEC with a high (55% proliferation index) (Table 7).

Table 7: chemotherapy agents

	no. of chemotherapies	n (%)	no. of patients	n (%)*
Total	1175 (6.3 per patient)		188	
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 41 and 20 patients, respectively (Table 8).

Table 8: molecular therapies

	no. of molecular therapies	n (%)	no. of patients	n (%)*
Total	91 (1.6 per patient)		58	
Drug	91		58	
Bevacizumab		1 (1%)		1 (2%)
RAD001/Everolimus		51 (56%)		41 (71%)
Sunitinib		27 (30%)		20 (34%)
Other Drug		12 (13%)		10 (17%)

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

Sunitinib is commonly used in pancreatic NET which mirrors its approval. The use of molecular therapies according to primary NET site and NET differentiation is illustrated in table 9 and 10.

Table 9: molecular treatment according to primary NET site

	Bevacizumab (N = 1)	RAD001/Everolimus (N = 41)	Sunitinib (N = 20)	Other Drug (N = 10)
Lung	0 (0%)	3 (7%)	1 (5%)	4 (40%)
Stomach	0 (0%)	0 (0%)	1 (5%)	0 (0%)
Pancreas	1 (100%)	18 (44%)	12 (60%)	4 (40%)
Ileum/jejunum	0 (0%)	12 (29%)	2 (10%)	2 (20%)
CUP	0 (0%)	5 (12%)	3 (15%)	0 (0%)
Other	0 (0%)	3 (7%)	1 (5%)	0 (0%)

Table 10: 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

81 and 89 patients underwent a PRRT 90-Y-Dotatoc and 177-lutetium containing treatment, respectively. External radiation therapy seems to be an attractive treatment option in individual cases, as well (Table 12).

Table 12: radiotherapy and targeted nuclear therapy

	no. of irradiations	n (%)	no. of patients	n (%)*
Total	495 (2.6 per patient)		190	
Mode	494		189	
External		112 (23%)		57 (30%)
PRRT Y-90-Dotatoc		146 (30%)		81 (43%)
PRRT 177-lutetium Dotatate		84 (17%)		35 (19%)
PRRT Lutetium Dotatoc		118 (24%)		54 (29%)
SIRT		22 (4%)		17 (9%)
Other		10 (2%)		10 (5%)
Not known		2 (0%)		1 (1%)
Center	492		189	
University hospital		456 (93%)		170 (90%)
General hospital		29 (6%)		20 (11%)
Private practise		5 (1%)		3 (2%)
Not known		2 (0%)		2 (1%)

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

Table 13: radiotherapy and targeted nuclear therapy according to primary NET site

	External (N = 57)	PRRT Y-90-Dotatoc (N = 81)	PRRT 177-lutetium Dotatate (N = 35)	PRRT Lutetium Dotatoc (N = 54)	SIRT (N = 17)	Other (N = 10)	Not known (N = 1)
Lung	29 (51%)	5 (6%)	2 (6%)	4 (7%)	0 (0%)	1 (10%)	1 (100%)
Oesophagus	3 (5%)	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 (12%)	37 (46%)	14 (40%)	17 (31%)	9 (53%)	1 (10%)	0 (0%)
Duodenum	0 (0%)	2 (2%)	2 (6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ileum/jejunum	3 (5%)	19 (23%)	11 (31%)	17 (31%)	4 (24%)	0 (0%)	0 (0%)
Coecum	0 (0%)	0 (0%)	0 (0%)	1 (2%)	1 (6%)	1 (10%)	0 (0%)
Appendix	0 (0%)	1 (1%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)
Colon	1 (2%)	1 (1%)	2 (6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ascending colon	1 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Rectum	1 (2%)	1 (1%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)
CUP	3 (5%)	11 (14%)	4 (11%)	10 (19%)	2 (12%)	2 (20%)	0 (0%)
Other	9 (16%)	2 (2%)	0 (0%)	2 (4%)	1 (6%)	5 (50%)	0 (0%)
Not known	0 (0%)	1 (1%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)

Table 14: radiotherapy and targeted nuclear therapy according to NET differentiation

	External (N = 57)	PRRT Y-90-Dotatoc (N = 81)	PRRT 177-lutetium Dotatate (N = 35)	PRRT Lutetium Dotatoc (N = 54)	SIRT (N = 17)	Other (N = 10)	Not known (N = 1)
G1	3 (5%)	23 (28%)	10 (29%)	17 (31%)	2 (12%)	2 (20%)	0 (0%)
G2	11 (19%)	32 (40%)	16 (46%)	22 (41%)	9 (53%)	3 (30%)	1 (100%)
G3	25 (44%)	13 (16%)	6 (17%)	5 (9%)	5 (29%)	2 (20%)	0 (0%)
Not known	16 (28%)	7 (9%)	2 (6%)	7 (13%)	1 (6%)	2 (20%)	0 (0%)

Outcome

In total, the remission status at last visit is recorded in 1243 patients. No survival analysis has been performed in 2017.

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
- **Sadowski SM**, Christ E, Bédat B et al. Nationwide multicenter study on the management of pulmonary neuroendocrine (carcinoid) tumors. Endocr Connect. 2018 Jan;7(1):8-15.

b) Ongoing

Title	Collaboration	Author(s)
"Value of octreoscan and 18F-FDG PET for clinical prognosis of patients with neuroendocrine neoplasms"	national	Pralong F. et al
eviNET - A network meta-analysis of therapeutic options for the treatment of neuroendocrine tumors	national	Kaderli R, Walter M et al.
Treatment pattern in neuroendocrine tumors: Analysis of the SwissNET Database	national	Kollár A, Trepp R et al.
The ENETS Registry: First Results of a Collaborative Effort Including Over 12.000 Patients with Neuroendocrine Neoplasms (NENs) from 7 European Countries	international	Borbath Y, Kollár A. et al
Surgery is there an indication for G3 neuroendocrine neoplasms	international	Merola E, Christ E, Perren A, Kollár A

Financing

With regard to the finances, we received sFr.40'000 from two sponsors and the membership fees added up to 1'950.-. The total income in 2016 was sFr. 41'950. - , roughly 25'000.- less than in 2015. This is because 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%). Because the income was lower than anticipated (Ipsen), the account closed with a negative balance sheet of 29'216.-. With the exception of the expenses for the CTU (<5000.- instead of the budget of 1'100.-), all the other expenses were +/- within budget or lower.

The fortune of SWISSNet per 31. December 2016 add up to sFr. 141'020.-. It can, therefore, 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 around sFr 75'000/year. With the available finances and without our sponsors we can cover maximally two-three further years, which is required for a non-profit organisation. Furthermore, it is likely that we shall have to increase the activity level of our research nurses since there are more and follow-up data to 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. This will be a priority task of the next committee members.