

## Introduction to the 2014 annual SwissNET, report of the president

Since the foundation of SwissNET in 2007 many developments have been achieved. The interest in neuroendocrine tumours (NETs) is reflected by the growing number of SwissNET members and by a growing attendance at the ENETS annual meeting. Thanks to our sponsors; in 2015 again a SwissNET premeeting at ENETS was organized with a high attendance. It is an important event, because meeting motivated Swiss Colleagues and friends, and Swiss expertise reinforces collaborations and multidisciplinary use of the SwissNET database. The latter, conducted by Dr. Attila Kollar and Dr. Annika Blank is now an ongoing powerful tool for the analysis of Swiss patients with neuroendocrine neoplasms. Tasks for 2015 include adaptation to the Swiss Human Research Act in order to improve access and use of data.

Medical literature confirms the increasing incidence rates of gastro-entero-pancreatic NETs (1). However NETs are still rare diseases and as such need expertise. Centers of excellence (as defined by ENETS guidelines) are created all around Europe and will be developed in Switzerland as well (like in Zürich already). Concentration of expertise and network management aimed by the Highly Specialized Medicine organization is mandatory. SwissNET organisation will fulfill this need and contribute to medical information in Switzerland. In this setting SwissNET coordinates have been included in the Orpha.net organization (2).

We have again to acknowledge that SwissNET works are achieved, thanks to the continuous support of our sponsoring: Novartis, Pfizer Oncology and Ipsen. Their ongoing collaboration will enable the future of our association.

Dr. Maurice Matter, PD & MER

Médecin adjoint. President SwissNET 2015-2016

1) Fraenkel M, Kim M, Faggiano A, de Herder WW, Valk GD. Incidence of gastroenteropancreatic neuroendocrine tumours: a systematic review of the literature. *Endocr Rel Cancer* 2014, 21: R153–R163.

2) <https://www.orpha.net/>

## Database Report 2014

The year 2014 was an eventful year for SwissNET.

The first milestone, which was planned and organized months before, was the transfer of patient data from an access-based database on a stand-alone computer to a web-based version. The data transfer was prepared in close cooperation with the clinical trial unit Bern (CTU) and aimed to structural changes with updates in classification and a more intuitive way of data entry. The tumor classification was standardized and updated to the current WHO classification. Therapeutic options were included, whereas others were deleted due to changes in therapeutic guidelines. The new database also offers more options to record hereditary disease such as von Hippel-Lindau syndrome or tuberous sclerosis.

After several steps of data validation, the SwissNET registry is now accessible online since January 2015. This up-to-date database version has the advantage of an easy analysis of the included data at any time, e.g. for research projects or the annual report.

Since neuroendocrine neoplasms are rare tumors, research was one of the major reasons to establish the Swiss registry for neuroendocrine tumors. As a result of an increasing interest in research projects based on the SwissNET database, regulations were urgently needed to define a standardized application procedure. For this purpose SwissNET implemented an application form and defined the process of decision finding by the scientific committee. Since the establishment, SwissNET received 3 applications for research projects.

The most recent achievement is the renewal of the ethical approval of the registry, which was confirmed in April 2015. The new "Humanforschungsgesetz" made it necessary to replace the already existing ethical approval from 2009.

## Analysis of data 2014

Since the last statistical analysis of the SwissNET data, 164 additional patients were included leading to an increase of 24% (in total 835 patients).

### a) Patient characteristics and Follow up

The distribution of male and female patients (male: 54%, female: 46%) is relatively equal. The median follow up time increased by 3.5 months. There was no change in the mean age at diagnosis in comparison to data from 2013.

Measurement	2013	2014
<b>Number of patients</b>	<b>671</b>	<b>835</b>
Females	317 (47%)	387 (46%)
Males	354 (53%)	448 (54%)
<b>Follow-up</b>		
Median (years)	1.25	1.6
<b>Age at diagnosis in years</b>		
Mean	59	59.3
Standard deviation	15.9	15.6

Table 1: Patient characteristics

### b) Recruitment

Most of the patients are still recruited by the established major centers Berne, Lausanne, St. Gallen, Geneva and Basel. Nonetheless, half of the included patients are from other hospitals or private practices.

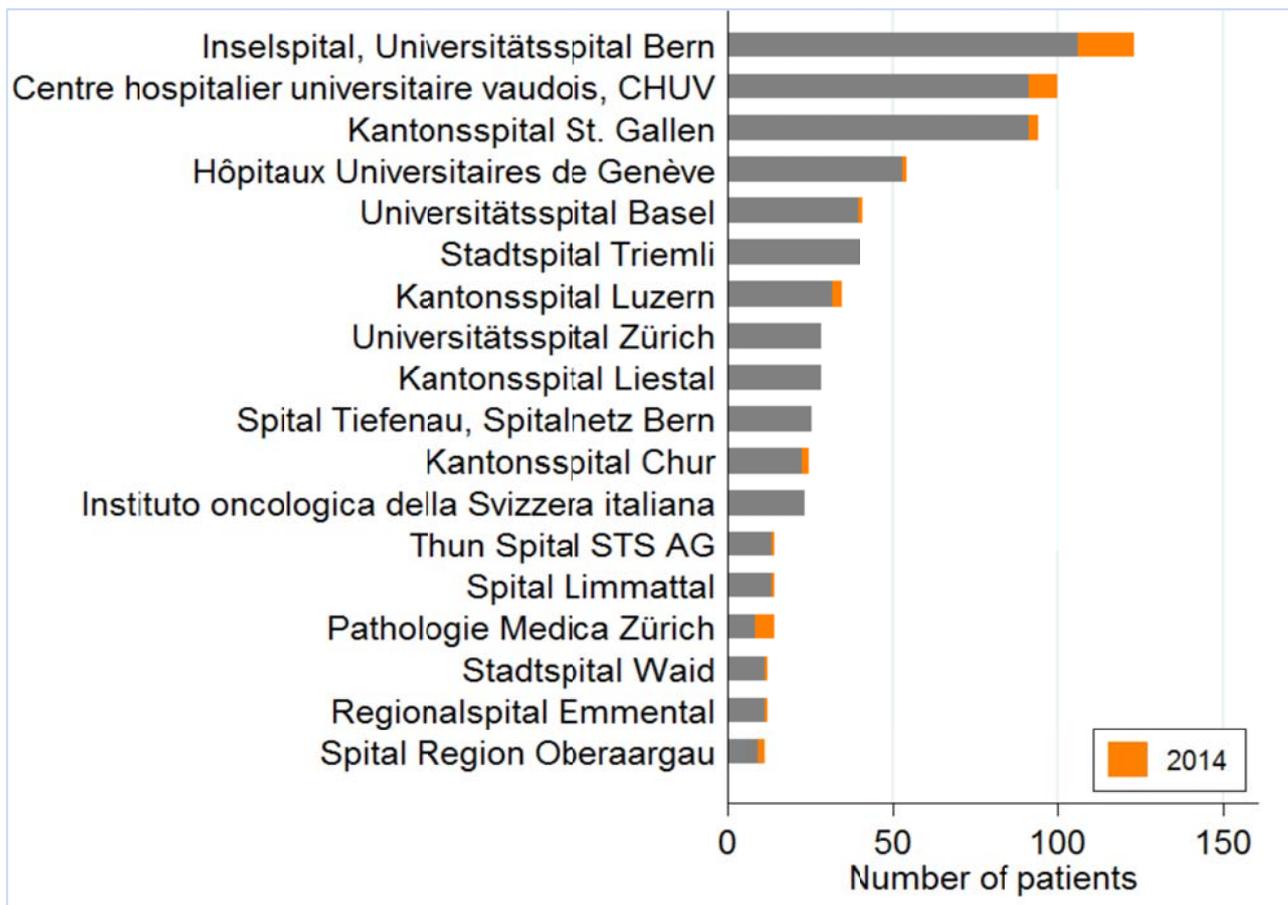
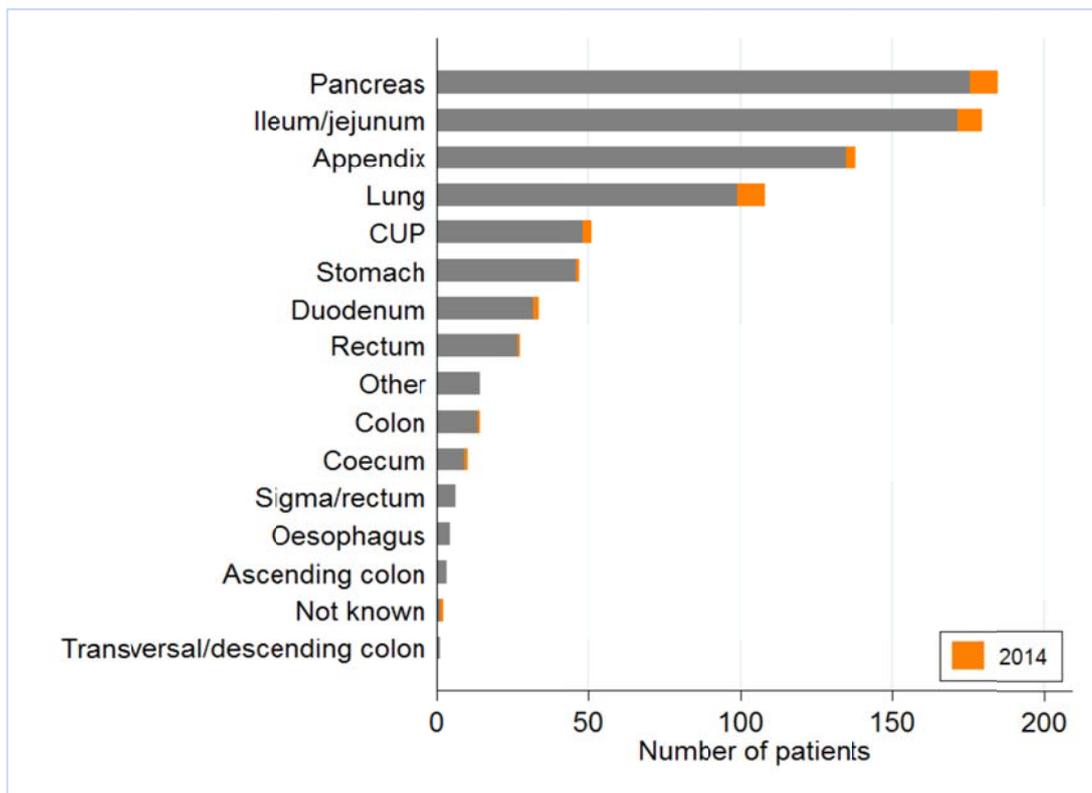


Figure 1: Recruitment of patients: grey: 2008-2013, orange: 2014

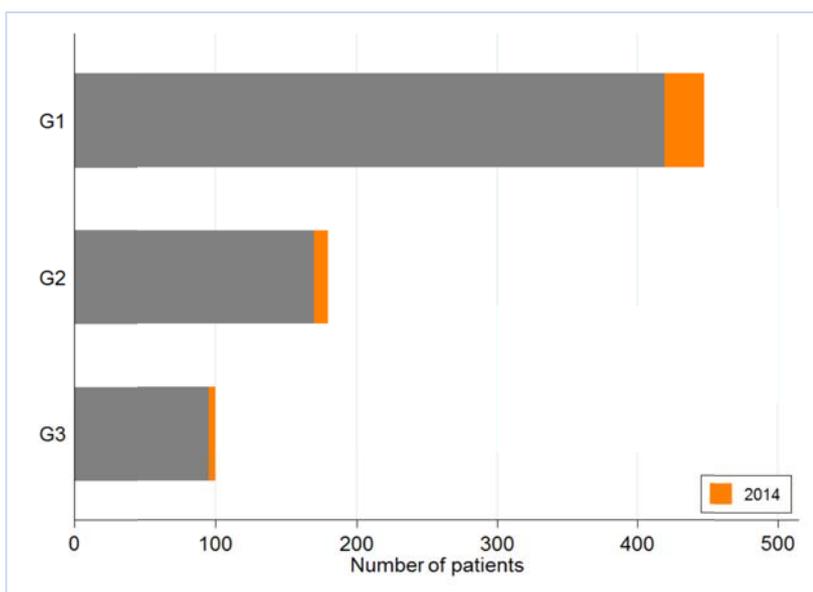
### c) Distribution of primary sites and tumor grade

Due to the high percentage of patients from the major centers, the most common primary site in the SwissNET registry is the pancreas, which also had the highest percentage of increase in patients numbers, followed by the ileum and the lung.



**Figure 2: Distribution of primary sites of NET**

Well differentiated neuroendocrine tumors are still the largest group of tumors. Neuroendocrine carcinomas are much rarer.



**Figure 3: Tumor grading**

#### d) Treatment

Surgery is, as expected, the most common first line therapy, which was performed for 85% of patients. Medical therapy as first therapeutic option is only rarely performed, although it plays an important role in case locally advanced or metastatic stage. Ablative therapy, as first line therapy, only accounts for 1% of patients.

Measurement	2014
<b>First therapy (number of patients)</b>	<b>719</b>
Surgery	619 (85%)
Medical therapy	81 (11%)
Irradiation	22 (3%)
Ablative therapy	6 (1%)

**Table 2: Distribution of performed first therapy**

In total, 221 patients were treated with systemic treatment options, either as first line intervention or at some point after primary surgery. 46% of those patients received chemotherapy, 40% biotherapy, 14% molecular therapy.

Octreotide was the most common used biotherapeutic agent (95 patients; 69%), RAD001/Everolimus was the most common used molecular therapy agent (21 patients; 15%).

Measurement	2014
<b>Medical therapy (number of patients)</b>	
Biotherapy	87 (40%)
Chemotherapy	102 (46%)
Molecular Therapy	32 (14%)

**Table 3: Distribution of performed medical procedures**

Measurement	2014
<b>Biotherapy (number of therapies)</b>	<b>147</b>
Interferon alfa-2b: Intron A	0
Interferon alfa-2a: Roferon	0
Lanreotide autogel	6 (4%)
Lanreotide LAR	4 (3%)
Lanreotide s.c.	1 (<1%)
Octreotide LAR	92 (63%)
Octreotide s.c.	36 (24%)
SOM 230 LAR	4 (3%)
Other	4 (3%)
<b>Chemotherapy (number of therapies)</b>	<b>795</b>
Carboplatin	142 (18%)
Cisplatin	111 (14%)
Cyclophosphamide	13 (2%)
Dacarbazin	2 (<1%)
Doxorubicin	21 (3%)
Etoposide	215 (27%)
5-FU	45 (6%)
Streptozotocin	33 (4%)
Temozolomide	43 (5%)
Capecitabine	11 (1%)
Other drugs	159 (20%)
<b>Molecular Therapy (number of therapies)</b>	<b>53</b>
Bevacizumab	1 (2%)
RAD001/Everolimus	33 (62%)
Sunitinib	14 (26%)
Other drugs	5 (9%)

**Table 4: Distribution of performed medical procedures**

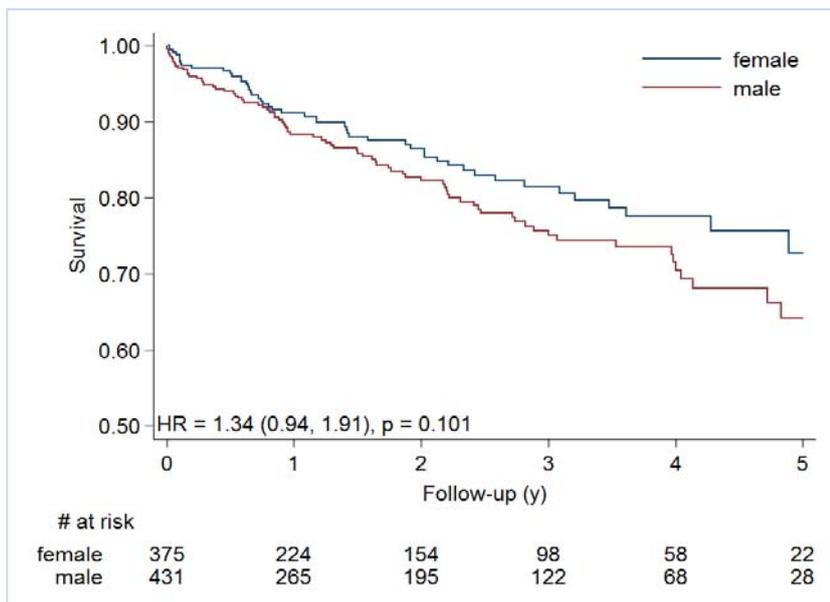
### e) outcome

41% of patients had a complete remission; stable disease was recorded for 7%, progressive disease for 2% and partial remission for less than 1% of patients. The remission status was recorded as unknown in 33%. This relatively high number is due to the adjustments to the new database structure. Our study nurses are requested to fill in those missing data. Out of the recorded patients in the SwissNET database, 17% died. Tumor-related death was recorded in 62%. 30% of patients died from a different reason.

Measurement	2014
<b>Remission status (last visit)</b>	<b>812</b>
Complete remission	328 (41%)
Partial remission	3 (<1%)
Progressive disease	17 (2%)
Stable disease	57 (7%)
Not known	265 (33%)
Relapse	1 (<1%)
Dead	141 (17%)
Tumor-related death	88 (62%)
No tumor-related death	42 (30%)
Not known	11 (8%)

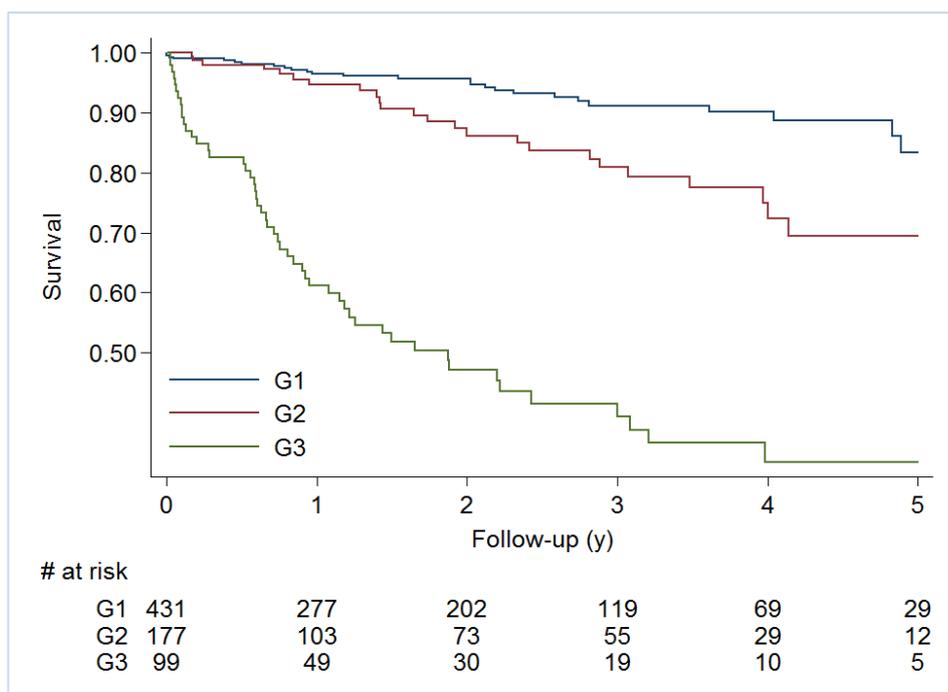
**Table 5: Remission status**

Female had a marginal, statistical not significant, better outcome in comparison to male patients.



**Figure 4: Cumulative mortality of NET patients after major diagnosis by gender. HR: hazard ratio from a Cox proportional hazard models with corresponding 95% confidence intervals.**

The survival analysis demonstrated a significant worse outcome for patients with poorly differentiated (G3) neuroendocrine neoplasms. Patients with well differentiated tumors, G1, had the best prognosis.



**Figure 5: Cumulative mortality of NET patients after major diagnosis by maximal histological grading.**

## Financing

With regard to the finances we received sFr. 65'000 from our three sponsors and the membership fees added up to 1'125.-. Together with the interest of the bank account the total income in 2014 was sFr. 66'203.- The main expenses include the salary for the research nurses working at the two sites (sFr. Inselspital Bern; 20-30% and CHUV; 20%). Furthermore Dr. Annika Blank started to work 20% as a coordinator of SWISSNET in Bern (Institute of Pathology). Her main task was to give the necessary medical support to the research nurses and prepare and accomplish the move of the database to a web-based tool (in close collaboration with the CTU). The move of the database resulted in some extra costs that were lower than anticipated in the budget. Due to the fact that all the other expenses (overheads for the research nurses, homepage, costs for the general assembly) were considerably lower, the balance closed with only a small negative balance sheet of sFr. -2'887.-

The fortune of SwissNET per 31. December 2014 add up to sFr. 162'352.-. 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 70'000 – 75'000/year. With the available finances and without our sponsors we can cover maximally two further years. 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 the task of SwissNET in the near future.