Advanced small intestine well-differentiated neuroendocrine tumours (Wd-SiNET): A Survey of Practice on 3rd line treatment

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Background

Selection of third-line treatment after somatostatin analogues (SSA) and Peptide Receptor Radionuclide Therapy (PRRT) for Wd-SiNETs remains challenging.

This study aimed to understand current practice and rationale for decision-making in the 3rd-line setting after SSA and PRRT.

Methods

An online survey (replies collected between 5/8/2020 and 21/9/2020) was built. Weighted average (WA) of likelihood of usage between responders (1 very unlikely; 4 very likely) was used to reflect the relevance of factors explored.

Results

A total of 28 replies; medical oncologist (53.6%), gastroenterologist (17.9%); United Kingdom (21.4%), Spain (17.9%), Italy (14.3%). Majority from ENETS CoE (57.1%), who followed ENETS guidelines (82.1%) (Table 1 for full details).

		Number of responses	Percentage (%)
Specialty	Medical Oncology	15	53.6%
	Clinical Oncology	3	10.7%
	Gastroenterology	5	17.7%
	Endocrinology	3	10.7%
	Surgery	2	7.1%
Country of practice	Belgium	2	7.1%
	Germany	1	3.6%
	France	2	7.1%
	Italy	4	14.3%
	Netherlands	2	7.1%
	Spain	5	17.9%
	Sweden	2	7.1%
	Switzerland	2	7.1%
	United Kingdom	6	21.4%
	Other	2	7.1%
Practice at ENETS Centre of Excellence	Yes	16	57.1%
	No	12	42.9%
Use of guidelines to inform management of SBNETs	Yes	28	100.0%
Guidelines used	ENETS guidelines	23	82.1%
	ESMO guidelines	0	0.0%
	NCCN guidelines	0	0.0%
	NANETS guidelines	0	0.0%
	Other	5	17.7%

Table 1: Baseline characteristics of responders. ENETS: European Society of Neuroendocrine Tumours; SBNETs: well-differentiated small bowel neuroendocrine tumours; NANETS: North American Neuroendocrine Tumor Society; ESMO: European Society for Medical Oncology; NCCN: National Comprehensive Cancer Network.

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Results (continuation)

Predominant treatment algorithm

Overall (Figure 1), 3rd-line treatment for Wd-SiNETs was: everolimus (EVE) (66.7%), PRRT (18.5%), liver embolization (LE) (7.4%) and interferon (IFN) (3.7%); chemotherapy (0%); decision was based on clinical trial data (59.3%), or personal experience (22.2%).

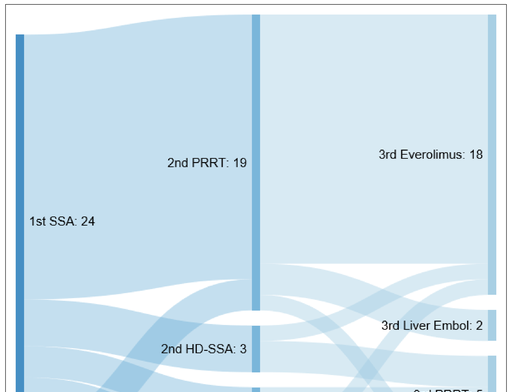

Figure 1: Summary of treatment predominant flow by line of therapy. SSA: somatostatin analogues; PRRT: peptide receptor radionuclide therapy; Liver Embol: liver embolization; HD-SSA: high-dose of SSA

Remaining uncertainties (PRRT)

Regarding the use of PRRT, most considered this only after clinical or radiological progression on SSA (76.9%); however, there was no consensus regarding the use of concomitant SSA during/after PRRT (Figure 2).

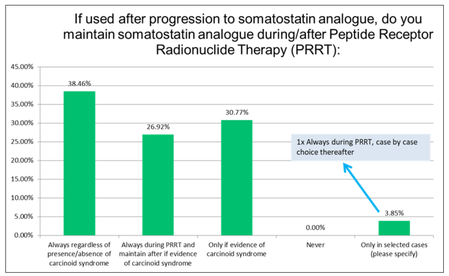

Figure 2: Ongoing controversies around use of PRRT in current practice

Factors associated with treatment decision making process

- The likelihood of using SSAs for all SBNET patients (regardless of baseline characteristics) in the first-line setting had a weighted average of 3.48 (out of a maximum on 4) (Figure 3.A).
- In terms of the use of PRRT in the second-line setting, the patients who were most likely to receive PRRT (Figure 3.B) were those with positive SSTR imaging (weighted average 3.81/4) and slow progression (>1 year) (weighted average 3.62/4), among others.
- EVE was likely used if Ki-67 <10% (WA 3.27/4) or age <70 years (WA 3.23/4), in the 3rd-line setting (WA 3.23/4); irrespective of presence/absence of carcinoid syndrome (CS), rate of progression or extent of disease (Figure 3.C).
- Chemotherapy was chosen if rapid progression (within 6 months) (WA 3.35/4), Ki-67 10-20% (WA 2.77/4), negative SSTR2 imaging (WA 2.65/4) or high tumour burden (WA 2.77/4); temozolomide or streptozocin was used with capecitabine or 5-FU (57.7%), FOLFOX (23.1%) (Figure 3.D).
- LE was selected if presence of CS (WA 3.24/4) or Ki-67 <10% (WA 2.8/4), after progression to other treatments (WA 2.8/4) (Figure 3.D).
- IFN was rarely used (WA 1.3/4) (Figure 3.F).

Figure 3: Factors associated with use specific treatments. SSTR2 –ve: somatostatin receptor positive disease (imaging based); SSTR2 +ve: somatostatin receptor negative disease (imaging based); heter: heterogeneous; mts: metastases; m: months; TOTAL: represents the average of all factors

Conclusions

Selection of 3rd line therapy is based on multiple factors mainly Ki-67, rate of progression, CS and tumour burden; decisions should be made within a multidisciplinary setting.