Health-related Quality of Life (HRQoL) in Patients with Advanced Neuroendocrine Tumors (NET) by Tumor Origin in the Phase 3 RADIANT-4 Trial

Marianne E. Pavel[1]; Jonathan R. Strosberg[2]; Lida Pacaud[3]; Evgeny Degtyarev[3]; Maureen P. Neary[4]; Matthias Hunger[5]; Jennifer Eriksson[5]; Jean-François Ricci[6]; Nicola Fazio[7]; Matthew Kulke[8]; Simron Singh[9]; James C. Yao[10]

[1]Charité Berlin Campus Virchow-Klinikum; [2]Moffitt Cancer Centre; [3]Novartis Pharma AG; [4]Novartis Pharmaceuticals Corporation; [5]Mapi; [6]Wellmera AG; [7]Istituto Europeo di Oncologia, IRCCS; [8]Dana Farber Cancer Institute; [9]Sunnybrook Health Sciences Centre; [10]University of Texas MD Anderson Cancer Center

Background: In the RADIANT-4 trial, everolimus plus best supportive care (BSC) improved progression-free survival (PFS) compared to placebo plus BSC in 302 patients with advanced progressive nonfunctional NET of gastrointestinal (GI) or lung origin (Yao, Lancet 2015). In addition, HRQoL was maintained with no statistically or clinically relevant differences in patients receiving everolimus compared to placebo (Pavel, ASCO 2016). Further post-hoc analyses are presented to assess treatment effect on HRQoL by tumor origin.

Methods: HRQoL was measured with the FACT-G questionnaire (total score range: 0-108 points). FACT-G was completed at baseline and every 8 weeks until month 12, then every 12 weeks until study drug discontinuation. Time to definite deterioration (TDD) of ≥7 points (minimal important difference, MID) in FACT-G total score was a pre-specified secondary endpoint for the overall trial population.

Results: Of 302 patients, 90 had lung NET (n=63 everolimus and n=27 placebo) and 211 had GI NET (n=141 everolimus and n=70 placebo). GI subgroup included patients with NET of ileum, rectum, jejunum, stomach, duodenum, colon, caecum, appendix, or cancer of unknown primary (CUP; N=36; generally known as GI origin).

No differences were observed between the treatment arms in TDD of the FACT-G total score in the GI and the Lung subgroup scores, with numerically longer median TTD favoring treatment with everolimus (see Table). There are some limitations in analyses in Lung subgroup due to small sample sizes.

Presented at NANETS 2016

Conclusion: In addition to PFS benefits, HRQoL is maintained in the overall population and GI and Lung sub-groups, with no relevant differences, despite usual toxicities of active cancer treatment. These analyses will support clinical management of NET patients relevant to benefit-risk decision making and may be used in payer evaluations in regions where benefit of everolimus will be assessed separately in patients with NET of GI or Lung origin.

Table 1: TTD on FACT-G Total Score by Treatment and Tumor Origin

	Everolimus + BSC Median in months (95% CI)	Placebo + BSC Median in months (95% CI)	Hazard Ratio from stratified Cox Model (95% CI)
GI sub-group	14.52 (9.63; NR)	9.23 (4.30; NR)	0.72 (0.45; 1.16)
Lung sub-group	9.13 (5.55; 13.01)	7.29 (2.79; NR)	1.12 (0.49; 2.54)
Overall population	11.27 (9.27;19.35)	9.23 (5.52; NR)	0.81 (0.55, 1.21)