# C-14

## Efficacy of 177Lu-edotreotide vs everolimus in patients with grade 1 or grade 2 GEP-NETs: Phase 3 COMPETE trial (post hoc subgroup analyses)

*Jaume Capdevila[1], Henning Jann[2], Catherine Ansquer[3], Emmanuel Deshayes[4], Rocio Garcia-Carbonero[5], Alexandre Teulé Vega[6], Richard Paul Baum[7], Hein Jan Verberne[8], Jaroslaw Bogdan Cwikla[9], Rajaventhan Srirajaskanthan[10], Louis De Mestier[11], Chiara Maria Grana[12], Andreas Buck[13], Dieter Hörsch[14], Marianne Pavel[15], Lawrence Oliver Dierickx[16], Michael Michael[17], Jonathan Strosberg[18], Attila Kollàr[19], Paula Jimenez-Fonseca[20], Andreas Kluge[21], Veronika Smutna[22], Richardus Vonk[22], Konstantin Zhernosekov[23], Thomas Walter[24].*

*[1]Vall d'Hebron Hospital Universitari and Neuroendocrine and Endocrine Tumor Translational Research Program (NET-VHIO), Vall d'Hebron Institute of Oncology (VHIO); [2]Charité – Universitätsmedizin Berlin; [3]Centre Hospitalier Universitaire de Nantes; [4]Institut du Cancer de Montpellier Val d'Aurelle and Montpellier University; [5]Hospital Universitario 12 de Octubre, Imas[12], UCM; [6]Institut Català d'Oncologia; [7]Curanosticum Wiesbaden-Frankfurt; [8]Amsterdam UMC; [9]Diagnostic and Therapeutic Center – Gammed and School of Medicine University of Warmia and Mazury Olsztyn; [10]King's College Hospital; [11]Beaujon Hospital; [12]IRCCS European Institute of Oncology; [13]Universitätsklinikum Würzburg; [14]Zentralklinik Bad Berka GmbH; [15]Universitätsklinikum Erlangen; [16]Institut Universitaire du Cancer Toulouse Oncopole; [17]Peter MacCallum Cancer Centre and University of Melbourne; [18]Moffitt Cancer Center; [19]Bern University Hospital; [20]Universitario Central de Asturias; [21]ABX-CRO advanced pharmaceutical services Forschungsgesellschaft mbH; [22]ITM Oncologics GmbH; [23]ITM Medical Isotopes GmbH; [24]Edouard Herriot Hospital.*

### BACKGROUND

$^{177}$Lu-edotreotide is an innovative radiopharmaceutical therapy agent, assessed in COMPETE, a Phase III, multicenter, randomized, controlled and open-label trial comparing $^{177}$Lu-edotreotide with a targeted molecular therapy (everolimus) in patients with WHO grade 1 or grade 2 gastroenteropancreatic-neuroendocrine tumors (GEP-NETs). Here, we focus on post hoc efficacy analyses of $^{177}$Lu-edotreotide in clinically important subgroups.

### METHODS

Eligible patients (aged ≥18 years) with inoperable, progressive, somatostatin receptor positive GEP-NETs (Ki-67 ≤20%) were randomized (2:1) to receive $^{177}$Lu-edotreotide (4 cycles of 7.5 GBq/cycle every 12 weeks, or until disease progression) or everolimus (10 mg daily up to 30 months, or until disease progression). The primary endpoint was progression free survival (PFS) per RECIST v1.1 assessed by Blinded Independent Central Review (BICR). Key secondary endpoints were objective response rate (ORR) and overall survival (OS).

### RESULTS

309 patients were randomized to $^{177}$Lu-edotreotide (n=207) or everolimus (n=102). Median PFS was significantly prolonged by $^{177}$Lu-edotreotide vs. everolimus (23.9 months vs. 14.1 months; p=0.0223; HR=0.673, 95% CI [0.477, 0.948]). Centrally assessed ORR was significantly higher with $^{177}$Lu-edotreotide vs. everolimus (21.9% vs. 4.2%; p<0.0001). Preliminary median OS was numerically prolonged for $^{177}$Lu-edotreotide vs. everolimus (63.4 months vs. 58.7 months; p=0.3230; HR=0.826,

95% CI [0.565, 1.208]). The subgroup analyses showed consistent improvements in PFS, ORR, and OS across subgroups, except for OS (immature data) reported in the treatment-naïve subgroup (Table).

**Table:** Subgroup analyses based on central (BICR) assessment

| Subgroups | Median PFS<br>$^{177}$Lu-edotreotide vs. everolimus (months) | ORR<br>$^{177}$Lu-edotreotide vs. everolimus (%) | Median OS<br>$^{177}$Lu-edotreotide vs. everolimus (months) |
|---|---|---|---|
| **Grade 1** | 24.5 (n=104) vs. 17.4 (n=63) | 15.8 (n=101) vs. 3.3 (n=61) | NR (n=104) vs. NR (n=63) |
| **Grade 2** | 21.6 (n=102) vs. 10.6 (n=37) | 28.3 (n=99) vs. 3.1 (n=32) | 56.7 (n=102) vs. 41.4 (n=37) |
| **GE-NET** | 23.9 (n=88) vs. 12.0 (n=43) | 6.0 (n=84) vs. 5.0 (n=40) | 63.4 (n=88) vs. 58.7 (n=43) |
| **P-NET** | 24.5 (n=119) vs. 14.7 (n=59) | 33.3 (n=117) vs. 3.6 (n=55) | 65.7 (n=119) vs. 49.3 (n=59) |
| **Treatment-naïve (1st line)** | NR (n=30) vs. 18.1 (n=17) | 17.9 (n=28) vs. 5.9 (n=17) | 57.4 (n=30) vs. NR (n=17) |
| **Prior therapy (2nd line)** | 23.9 (n=177) vs. 14.1 (n=85) | 22.5 (n=173) vs. 3.8 (n=78) | 63.4 (n=177) vs. 43.3 (n=85) |

n=total number of patients; NR=not reached

## CONCLUSIONS

$^{177}$Lu-edotreotide demonstrated statistically significant improvements in PFS and ORR vs. everolimus. Despite the immature data, potential OS benefit was observed with $^{177}$Lu-edotreotide vs. everolimus. The efficacy of $^{177}$Lu-edotreotide was largely maintained across the subgroups (origin, grade, and prior treatment). These findings confirm the meaningful clinical benefit of $^{177}$Lu-edotreotide vs. everolimus in GEP-NETs patients with high unmet needs.

## ABSTRACT ID 33388