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SINGLE CENTER EXPERIENCE OF EVEROLIMUS COMBINED WITH LONG-ACTING OCTREOTIDE IN PATIENTS (PTS) WITH PRETREATED ADVANCED WELL DIFFERENTIATED NEUROENDOCRINE TUMOURS (NETS) OF DIFFERENT ORIGIN

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Aim: To evaluate efficacy and safety of everolimus combined with long-acting octreotide in heavily pretreated patients with NETs. To determine predictive factors for everolimus efficacy.

Methods: 33 pts with progressive well differentiated NETs (G1,G2) were treated with everolimus 10 mg q.d. combined with octreotide LAR 30-40 mg till progression or intolerability. All pts were evaluable for efficacy and toxicity. The mean age was 54 years (25-72), 11 male, 22 female. The most of pts had pancreatic NETs–13 (39%) pts. There were 19 (57.6%) NETs of foregut origin, 8 (24.2%) NETs of midgut origin, 1 (3%) hindgut NET and 5 (15.2%) of unknown origin. 21 pts had 0-1-2 prior lines of chemotherapy and 12 pts were heavily pretreated with more than 3 lines of chemotherapy. Primary tumor was resected in 16 (48.5%) pts. Previous treatment included interferon α, octreotide LAR, XeDox, EP and various combinations of temozolomide, paclitaxel and fluoropyrimidines.

Results: There was 1 partial response (3%), 25 pts had stable disease (76%) and 7 pts (21%) had progressive disease. The median progression-free survival (PFS) reached 8.6 months (95% CI: 4.2-13). In a subgroup of heavily pretreated pts with more than 3 lines of chemotherapy median PFS was 3.2 months (95% CI: 1.3-5.1), in a subgroup of pts with 0-2 lines of chemotherapy median PFS was 11.1 months (95% CI: 4.8-16.6) (p = 0.002). PFS in pts with clinically significant toxicity that led to everolimus dose reduction reached 17 months and in pts without dose reduction - 4 months (95% CI: 2.1-5.9) (p = 0.029). Univariate analysis showed that pts with less than three lines of chemotherapy, pts with everolimus dose reduction and with normal baseline chromogranin A level were predictive of PFS benefit. Multivariable analysis showed only less than 3 prior treatment lines significantly correlating with longer PFS. Main toxicity events included stomatitis, fatigue and rash. Three pts stopped treatment due to toxicity. Dose of everolimus was reduced in 19 (57.6%) pts.

Conclusions: Preliminary data suggests that everolimus should be used preferably in the early stages of NET treatment, the observed adverse events correlated with the known toxicity profile. Clinically significant toxicity and baseline chromogranin A level may be predictive of everolimus efficacy in well differentiated NETs.

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