## 1387P Differences in multikinase inhibitors (MKI) toxicity profile according to gender. A pooled analysis of three phase II trials with lenvatinib, pazopanib and sorafenib in patients (pts) with advanced gastroenteropancreatic (GEP) neuroendocrine tumours (NETs)

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**Background:** There is a dearth of understanding of gender influence in targeted therapies toxicity. Increasing evidence suggests a possible different toxicity profile according to gender, but mostly retrospective studies in common tumors. Currently, data from prospective studies are minimal. In the present study, we will review MKI toxicity profiles according to gender in pts with NETs in three clinical trials.

**Methods:** Multicenter open-label phase II studies TALENT, PAZONET and GETNE0801 included pts with advanced GEP NETs treated with lenvatinib, pazopanib, and sorafenib-bevacizumab respectively. All studies were performed by the Spanish Task Force Group for Neuroendocrine Tumors (GETNE). All pts were included in the review, considering all toxicity grades with an incidence higher than 5% for the univariate analysis. Bevacizumab specific toxicities were excluded in patients from GETNE0801 trial. Additionally, all grade 3-4 toxicities were analyzed separately.

**Results:** 199 pts (46.23% female) with 1349 adverse events (AEs) (12.23% G3-4) divided into 125 categories were included. In female patients, nausea/vomiting, skin disorders (excluding palmar-plantar erythrodysesthesia), liver alterations (including transaminase and bilirubin), headache, pyrexia, hair disorders and dizziness were significantly more common (Table). The only toxicity with a higher incidence in men was dysphonia (OR 0.42, 95% CI 0.2-0.9, p0.02). The only G3-4 toxicity significantly more frequent in women was liver toxicity (20.65% vs. 7.55%, OR 3.18, p0.009).

**Table: 1387P**

| Toxicity (all grades) | Women (%) | Men (%) | Difference (%) | Odds Ratio (95% CI) | p |
|---|---|---|---|---|---|
| Nausea/Vomiting | 63.04 | 44.86 | 18 | 2.09 | 0.01 |
| Skin disorders | 60.87 | 45.79 | 15 | 1.84 | 0.03 |
| Liver toxicity | 57.61 | 30.84 | 26 | 3.04 | 0.0002 |
| Headache | 28.26 | 12.15 | 16 | 2.84 | 0.005 |
| Pyrexia | 17.39 | 5.61 | 11 | 3.44 | 0.01 |
| Hair disorders | 20.65 | 8.41 | 12 | 2.83 | 0.01 |
| Dizziness | 17.39 | 6.54 | 10 | 3.00 | 0.02 |
| Dysphonia | 16.30 | 37.38 | 21 | 0.32 | 0.001 |

**Conclusions:** In our study, we observed significant differences in toxicity AEs by gender, especially in women with seven increased toxicities. A different approach in toxicity management should be adopted based on gender in pts with GEP NETs treated with MKI.

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