182P Efficacy and tolerability of neratinib in advanced HER-2 positive breast cancer: A single institution experience

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Background: Neratinib is an oral small-molecule irreversible pan-HER tyrosine kinase inhibitor in late stage clinical development for advanced HER-2 positive breast cancer. Prophylactic loperamide (4mg qds Day 1, tds days 2-14, bd days 15-28 then prn) and budesonide (9mg od for 28 days) are required to reduce the incidence and severity of diarrhoea.

Methods: Patients enrolled within the Puma Biotechnology Neratinib Managed Access Program between 01/01/2016 and 01/06/2018 with advanced HER2 positive breast cancer were identified for this retrospective analysis. Data were collected from electronic patient records. The primary endpoint was progression free survival (PFS). Secondary objectives were overall survival (OS), response rate (RR, RECIST v1.1), clinical benefit rate (CBR) and toxicity graded by CTCAE v4.0.

Results: We identified 29 patients, median age 54 years (IQR: 50-61) who received a median of 4 (range 1-6) prior lines of therapy for advanced breast cancer. 15 patients (51.7%) received neratinib 240mg/day as monotherapy (one with sc trastuzumab), 14 (48.2%) in combination with capecitabine 1500mg/m^2/day for 2 weeks of a 3 week cycle. Median follow-up was 8.5 months (IQR: 5.1 – 11.6). Median PFS was 7.4 months (95%CI 3.5 – 17.9) and was significantly longer with combination therapy than monotherapy (17.9 (3.5-NR) vs 5.8 months (2.0-10.2), P = 0.043). Median OS was not reached but was not significantly different in the two treatment cohorts. The RR in monotherapy patients was 33% compared to 57% in combination patients. Two combination patients had complete responses which remain ongoing at 17 and 25 months. The CBR was 47% and 79% respectively. Grade 3-4 toxicities were reported in 4 patients (13.8%). Dose delays were required in 19 patients (65.5%), dose reductions in 4 (13.8%) and discontinuation in 4 due to pneumonitis (n = 1); nausea and vomiting (n = 2) and diarrhoea (n = 1). Any grade diarrhoea was reported by 15 patients (51.7%) despite prophylaxis, as above. There was no grade 3-4 diarrhoea.

Conclusions: In this cohort of heavily pre-treated HER2 positive advanced breast cancer patients, neratinib demonstrated durable anti-cancer activity with a manageable toxicity profile both as monotherapy and in combination with capecitabine.

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