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A phase II study of foretinib in triple-negative, recurrent/metastatic breast cancer: NCIC CTG trial IND.197 (NCT01147484).

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Background: Met, a receptor tyrosine kinase, is preferentially expressed in basal-like compared to luminal breast cancer. In murine models, overexpression of the oncogenic Met receptor transgene induces tumors with human basal gene expression characteristics supporting Met

inhibition as a treatment strategy for triple negative (TN) breast cancer. Foretinib is an oral multi-kinase inhibitor of Met, RON, AXL, TIE-2 and VEGF receptors with anti-tumor activity in advanced HCC and papillary renal cell cancer. **Methods:** Patients (pts) with TN breast cancer and 0-1 prior regimens for metastatic disease received daily foretinib 60 mg po in a 2-stage single arm trial. Primary endpoints were objective response and early progression rates per RECIST 1.1. Tumor samples were centrally reviewed to confirm ER/PR/HER2 status and for correlative studies including Met, PTEN and EGFR expression. Stage 1 accrual required 23 response-evaluable Met unselected patients with accrual continuing if >/= 1 response or < 17 early progressions (PD <= 8 weeks on study) were observed. **Results:** Accrual is 29 pts to date; 24 are eligible, 22 evaluable for toxicity and 15 for response. Median age is 56 y (43-81), ECOG PS 0-1 in 23/24. Grade 3 laboratory adverse events were: lymphopenia (9%), elevations in ALT (5%), GGT (5%) and INR (5%). Treatment-related non-hematologic toxicities included (all/grade 3-4) fatigue (64%/5%), nausea (55%/5%), diarrhea (41%/5%), hypertension (32%/14%), vomiting (27%/0%), anorexia (23%/5%) and rash (14%/0%). Three SAEs possibly related to foretinib included; asymptomatic pulmonary embolism, reversible CHF and pleural effusion with QTc prolongation. One PR (7%), 8 early PD (53%) and 6 SD (40%) have been observed to date with median SD duration of 5.4 months (range 2.7-5.5). Preliminary correlative results (IHC): 5/8 (62.5%) evaluable Met positive cases had SD and 4/5 (80%) Met negative cases had PD as best response. Met IHC was negative in the pt with PR. **Conclusions:** Foretinib shows preliminary evidence of activity and tolerability in metastatic, TN breast cancer. Stage 2 of accrual will include 15 pts with pre-treatment biopsies of metastases and circulating tumor cell collection.