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Results of two open label Multicentre phase II pilot studies with Herceptin in combination with docetaxel and platinum salts (Cis or Carboplatin) (TCH) as Therapy for Advanced Breast Cancer (ABC) in women with tumors over-expressing the HER2-neu proto-oncogene

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Preclinical data indicate that docetaxel (T) and/or platinum salts (C) are highly synergistic with Herceptin (H). This synergy, taken together with the activity of these drugs in ABC, and the need to develop non-anthracycline containing regimens with H, led to our performing two pilot studies to evaluate the safety and efficacy of T and H in combination with cisplatin (TCisH) or carboplatin (TCarboH). Both studies enrolled ABC patients whose tumors were positive for the HER2 alteration by immunohistochemistry (IHC) or fluorescent in-situ hybridization (FISH), with retrospective analysis by FISH planned on all primary tumors. T (75 mg/m²) and C (cis 75mg/m², Carbo, AUC of 6) were given on day 1, and then q3wks up to 8 cycles, H was given on day 1 cycle 1 (4mg/kg) then continued weekly at 2mg/kg for 1 year or until progression.

Results: Enrollment is complete with 61 TCisH pts and 60 TCarboH pts. Interim results are on 34 TCisH pts (162 cycles) and 27 TCarboH pts (159 cycles). Pt characteristics for TCisH and TCarboH respectively were: prior adj chemo 56% and 67%, visceral mets 76% and 78%, liver mets 38% and 26%, lung mets 35% and 56%, bone mets 44% and 41%, and 3 or more organs involved 32% and 26%. Febrile neutropenia was 9% on TCisH and 11% on TCarboH, there was one grade 3 infection on TCarboH. G3-4 non-hematological toxicities for TCisH and TCarboH respectively were: nausea 12% and 7%, vomiting 6% and 4%, diarrhea 9% and 4%, stomatitis 3% and 11%, and neurosensory 3% and 0%. There were no G3-4 renal or ototoxicities. Grade 1-2 ototoxicities were seen in 18% of TCisH pts. One pt in each study developed CHF (1 prior cardiac history). Responses were seen in 26/34 (3 CRs, 23 PRs, ORR 76%) of TCisH pts HER2 positive by IHC, and in 10/14 (3 CRs, 7 PRs, ORR 71%) TCarboH patients HER2 positive by FISH.

Conclusion: These pilot studies show that the TCH combinations are feasible and are active in ABC, and justify their study in random assignment trials. BCIRG is conducting such studies in both the metastatic and adjuvant settings. Final results for all patients will be presented.