gastrointestinal tumours, colorectal

FINAL RESULTS OF A RANDOMIZED PHASE II STUDY WITH NEO-ADJUVANT TRIPLET OR DOUBLET THERAPY, RADIATION AND TOTAL MESORECTAL EXCISION FOR LOCALLY ADVANCED RECTAL CANCER: AXE BEAM


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Aim: To assess the activity and safety of bevacizumab (A) with capecitabine (X) and radiotherapy (RT) with or without oxaliplatin (E) in the preoperative treatment (thx) of locally advanced rectal cancer (LARC). To identify biomarkers for early response prediction.

Methods: Patients (pts) with LARC were randomized to RT (1.8Gy/day) with the triplet A (5mg/kg), X (1650mg/m2/day) and E (50mg/m2) in Arm A or the doublet A + X without E in Arm B. Chemoradiotherapy (CRT) started at 2 weeks after 1st infusion of A and continued for 5 weeks. Total mesorectal excision (TME) was planned at 6-8 weeks post CRT. Pathological complete response (pCR) rate in Arm A was the primary endpoint. Safety profile and identification of biomarkers for early response prediction were secondary endpoints. Immunohistochemical staining for the functionality of blood vessels, proliferation and hypoxia as well as Luminex analyses to assess changes in circulating VEGF ligands are performed on tissues and blood samples from consenting pts.

Results: Eighty-four pts with median age 61 completed thx, 81 including surgery, with a relative dose intensity of 98% for A and X and 93% for E. During CRT, serious adverse events (SAEs) were more frequent in Arm A vs Arm B: fever (4 vs 0), diarrhea (3 vs 0), infection (4 vs 1). Postoperative SAEs (wound infections, leaks) occurred in 17 pts, 10 in Arm A and 7 in Arm B. Five pts deceased post-study, 3 due to distant disease progression, 2 to postoperative complications. Total post-surgery data are available for 81 pts. pCR was seen in 18 pts, 33% (14/43) in Arm A and 10% (4/41) in Arm B in an intent-to-treat analysis (ITT). The rate of good responders (Dworak TRG 3, 4) was higher in Arm A 29/43 vs Arm B 16/41 in ITT. Changes of the pericyte coverage of the blood vessels were observed. The decrease of plasma concentration of PDGF-AA and PDGF-BB correlated with pCR (p = 0.04 and 0.03 respectively).

Conclusions: Both triplet and doublet combination showed acceptable safety profiles. The addition of E to X and A with RT seemed beneficial in terms of pCR rates in this patient population, with a slight increase of toxicity. The main endpoint has been reached with 14/43 pCRs in Arm A. PDGF may be a predictor of response in this setting. Final data after a blind central review of the main endpoint and translational research data will be available at the conference. Support from Roche and Sanofi Aventis.

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