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FINAL RESULTS FROM QUASAR2, A MULTICENTRE, INTERNATIONAL RANDOMISED PHASE III TRIAL OF CAPECITABINE (CAP) +/- BEVACIZUMAB (BEV) IN THE ADJUVANT SETTING OF STAGE II/III COLORECTAL CANCER (CRC)

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Aim: The aims of Q2 were to assess whether the addition of BEV 7.5mg/kg q3/52 (12/12) to single agent CAP 1250mg/m2, 14 of every 21/7 (6/12), increases disease-free (DFS) and overall survival (OS) in CRC patients after resection of the primary; and to validate suggested, or discover new, biomarkers of BEV efficacy and toxicity.

Methods: A phase III international randomised controlled trial, coordinated by the UK and recruiting in 6 countries. In addition to the collection of data on toxicity, DFS and OS, a biobank comprising 1500 FFPE blocks and 1000 germline DNA samples was established. Hypothesis-driven biomarkers (MSI status and epithelial/stromal ratio) and hypothesis-driven biomarkers (chromosomal instability, ras, raf, POLE and an 80-gene ion torrent panel) were analysed to assess their prognostic and predictive (BEV) utility.

Results: 1941 patients were randomised in a 1:1 ratio and demographics and disease characteristics were well balanced between the two arms. DFS in the whole trial population demonstrates that BEV does not improve outcome in this setting (3 year DFS 75.2% for CAPBEV vs 78.2% for CAP; HR = 1.06; p = 0.54). Similarly OS was not improved (3 year OS 85.5% for CAPBEV vs 87.2% for CAP; p = 0.38; HR = 1.12). There may be a temporal trend in HRs (HRs: 1 year 0.83 [0.61-1.13], 2 year 0.87 [0.65-1.17], 3 year 1.32 [0.9-1.98]). Biomarker analyses confirm that high tumour stromal content confers a worse prognosis (3 year DFS HR 1.58 [1.22-2.05]; p = 0.001). MSS positivity was associated with a worse DFS in patients treated with CAP/BEV compared to those treated with CAP alone (n = 840; HR 1.43; p = 0.005) suggesting a negative predictive effect for BEV: For MSI positive patients, there was no significant difference in DFS between the two arms (n = 135; HR 0.74; p = 0.42).

Conclusions: Q2 supports data from two other trials suggesting no role for BEV in the adjuvant setting of CRC. The Q2 biobank and linked database allows further collaborative biomarker hypotheses to be tested. There is a rationale for meta-analysis of all BEV adjuvant CRC studies to more fully explore the putative temporal effect of BEV administration on DFS.

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