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abstracts

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Neoadjuvant chemotherapy for resectable oesophageal and junctional adenocarcinoma: results from the UK Medical Research Council randomised OEO5 trial (ISRCTN 01852072)

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Introduction: Chemotherapy in addition to surgery improves outcomes in gastro-oesophageal cancer. Both the OEO2 (neoadjuvant) and MAGIC (peri-operative) trials showed statistically significant improvements in overall survival though only 55% of patients in the MAGIC trial received post-operative treatment. We investigated whether more neoadjuvant chemotherapy (4 cycles epirubicin/cisplatin /capecitabine (ECX)) compared to a standard approach (2 cycles of cisplatin/ 5-fluorouracil) would improve outcomes.

Methods: A multi-centre, randomised, phase III trial comparing 2 cycles of CF with 4 cycles of ECX followed by oesophagectomy with 2-field lymphadenectomy for lower oesophageal and junctional (Types I and II) adenocarcinoma. Primary outcome was overall survival (OS); 842 patients (677 deaths) would detect an increase in 3-year survival from 30% to 38% (or 37%) with 82% (or 70%) power with $2\alpha = 5\%$. Deaths accrued more slowly than anticipated but the Independent Data Monitoring Committee considered the data sufficiently robust for release. Secondary outcomes include disease-free (DFS) and progression-free survival (PFS), pathological R0 resection rate, Mandard grade and quality of life (QoL).

Results: From 2005-2011, 897 patients (451 CF, 446 ECX) from 72 UK centres were randomly allocated (1:1). Baseline characteristics were similar between the groups (overall, male 90%, median age 62 (IQR 56-67), staging included PET 60%, T3 N0 22%, T3 N1 65%). 96% CF received 2 cycles, 89% ECX > 3 cycles. Grade 3/4 toxicity was lower with CF (30% v 47% $p < 0.001$). Of those patients having a resection R0 rates were CF 60%, ECX 66% with a Mandard grade $\leq$3 achieved in CF 15% v ECX 32% with 3% and 11% achieving complete response. Post-operative complications were similar (CF 57%, ECX 62%) as were deaths at 30 (CF 2%, ECX 2%) and 90 days post-surgery (CF 4%, ECX 5%). PFS and DFS favoured ECX, hazard ratio (HR, 95% CI) PFS 0.86 (0.74-1.01), DFS 0.88 (0.75-1.03). HR for OS was 0.92 (0.79-1.08, $p = 0.3017$) based on 315 CF and 298 ECX deaths, with similar 3 year survival rates CF 39% (35-44%) vs ECX 42% (37-46%). Exploratory subgroup analyses suggested that N0 patients may benefit from ECX, HR for OS was 0.68 (0.47-0.97). There were no clinically important differences in QoL (global QoL and oesophageal cancer specific domains from the EORTC QLQ-C30 and QLQ-OES18 questionnaires), either pre-operatively or 3-months post-operatively.

Conclusion: There is some evidence of a benefit from the prolonged ECX regimen, in terms of PFS, DFS and tumour regression at resection, but this does not translate into a survival benefit. Ongoing translational work is aimed at identifying subsets of patients that might benefit from the triplet anthracycline containing regimen.