neuroendocrine & endocrine tumours and cup

CLINICAL OUTCOMES FROM THE UK CUP-ONE STUDY: A MULTI-CENTRE TRIAL TO ASSESS THE EFFICACY OF EPIRUBICIN, CISPLATIN AND CAPECITABINE (ECX) IN CARCINOMAS OF UNKNOWN PRIMARY (CUP) WITH PROSPECTIVE VALIDATION OF MOLECULAR CLASSIFIERS


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Aim: A multi-centre single-arm phase II trial of epirubicin, cisplatin and capecitabine (ECX) to establish the efficacy of the ECX regimen, and an associated translational study incorporating the prospective validation of molecular classifiers and exploratory metabolomics.

Methods: CUP-ONE combines a multicentre phase II trial of epirubicin, cisplatin and capecitabine (ECX) [Part 2] and a concurrent translational study [Part 1] incorporating blinded prospective validation of 3 diagnostic molecular classifiers. ‘Good’ CUP subsets are specifically excluded (i.e. mid-line tumours, germ-cell origin, isolated axillary or neck lymphadenopathy and neuroendocrine). Part 2 assessed treatment outcomes to evaluate, after exclusion of the ‘best’ CUP subsets, ECX was a valuable treatment. This was formally assessed by overall RECIST response rate (ORR) using a Simon’s two-stage minimax design to test the null hypothesis that the true ORR is <20% versus the alternative that it is >= 40% (95% power, 5% 1-sided). This required 57 patients. Secondary endpoints were progression-free survival (PFS), overall survival (OS) and quality of life (QoL).

Results: Since February 2010, CUP-ONE has recruited 531 patients to Part 1 (still open) and 59 to Part 2 (54 in both). Part 2 closed to recruitment in February 2013. Results are presented for 58 eligible patients. Demographics: Male 47%, female 53%. ECOG PS 0: 38%, 1: 62%. Median age: 63 (range 29-78). 91% Stage IV, 5% Stage III. 81% adenocarcinoma, 5% squamous carcinoma, 50% poorly or undifferentiated pathology. Study therapy: 30% completed 8 cycles of ECX (median 5 cycles). Efficacy: The null hypothesis was rejected with an estimated ORR of 35% (90% CI 25%-47%; CR 7%; PR 28%; SD 26%, PD 30%). Median PFS 6.9 months (80% CI 4.8, 7.8), median OS 10.2 months (80% CI 8.3, 11.1). Treatment toxicities were acceptable with 54% recording worst AE grade <3.

Conclusions: CUP-ONE is the largest prospective CUP trial incorporating detailed diagnostic biomarkers including gene expression profiling. After excluding ‘best’ prognosis CUP patients, ECX proved an active and well-tolerated regimen. Correlation with translational outputs and QoL analysis is ongoing.

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