TPS3633 **Poster Session**

A biomarker enrichment trial of anti-EGFR agents in right primary tumor location (rPTL), *RAS* wild-type (*RAS*-wt) advanced colorectal cancer (aCRC): ARIEL (ISRCTN11061442).

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Background: Meta-analysis of 6 RCTs indicates that anti-EGFR agents are ineffective in rPTL *RAS*-wt aCRC (Arnold D, et al. *Ann Oncol*. 2017;28:1713-1729). However, data from the phase III PICCOLO and COIN trials suggest high tumor expression of the EGFR ligands, EREG and AREG, confers sensitivity to anti-EGFR agents in a subset of this population (Adams RA, et al. *J Clin Oncol*. 2012;30(30_suppl):32-32; Seligmann JF, et al. *Ann Oncol*. 2020;31:1021-1029). More data is needed before ligand assessment can be integrated into routine care: to date, *EREG/AREG* mRNA has only been assessed retrospectively, and feasibility of timely delivery of results must be demonstrated. The ARIEL trial aims to determine whether first-line chemotherapy plus cetuximab or panitumumab is more effective than chemotherapy alone in achieving early tumor shrinkage (ETS) after 8 weeks of treatment in patients (pts) with *EREG/AREG*-high rPTL *RAS*-wt aCRC. **Methods:** ARIEL is a multicentre, phase IV, open label, biomarker enrichment RCT. Pts with previously untreated rPTL *RAS*-wt (or *RAS*-unknown) aCRC are eligible for registration and *EREG/AREG* assessment using archival FFPE tumor tissue. Those confirmed as *RAS*-wt *EREG/AREG*-high (expression above 30th centile based on PICCOLO)[3] are eligible for randomization to chemotherapy alone (fluoropyrimidine backbone plus irinotecan or oxaliplatin) *vs* chemotherapy (FOLFOX or FOLFIRI) plus anti-EGFR therapy (panitumumab or cetuximab) (options at physician's discretion). Pts with *EREG/AREG*-low tumors are not eligible for randomization but may consent to translational research and follow-up. The primary endpoint is ETS at 8 weeks (≥30%, yes *vs* no). Secondary endpoints are depth of response at 16 weeks, overall survival, overall treatment utility, pt-reported quality of life, cost per QALY, pt acceptability of trial procedures, and safety. Pre-trial work-up included cross-validation of the *EREG/AREG* RT-qPCR assay at trial laboratories in Leeds and Birmingham, UK demonstrating reproducibility of biomarker results. Recruitment to an internal pilot phase is currently ongoing to demonstrate feasibility of timely delivery of biomarker results to sites (lower limit of 90% CI of mean result delivery time for first 20 pts must include 3 weeks). Mean monthly recruitment rate will be assessed at 18 months to determine likelihood of completion of the trial within the 3 year recruitment period. ARIEL is funded by the UK National Institute for Health Research (NIHR) and opened the first of 40 sites in February 2022. 440 pts will be registered for biomarker assessment in order to randomize 162 pts. All pts will be followed-up to 1 year post-randomisation, with a final assessment in all pts when the last pt has completed a year of follow-up (median 3.5 years). ARIEL is participating in the NIHR Associate PI scheme. Clinical trial information: 11061442. Research Sponsor: National Institute for Health Research, United Kingdom.