535P Pre-specified pilot analysis of a randomised pilot/phase II/III trial comparing standard dose vs dose-escalated concurrent chemoradiotherapy (CRT) in anal cancer (PLATO-ACT5)

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Background: The PLATO platform consists of 3 anal cancer trials (ACT) across the loco-regional disease spectrum (ACT3, 4 and 5). ACT5 tests the benefit of RT dose escalation using intensity modulated RT (IMRT) in locally advanced disease. We planned to analyse treatment compliance, acute toxicity and patient reported outcomes (PROs) on the first 60 patients (pts) prior to the phase II/III trial (final target n = 640) to evaluate the need for protocol modifications.

Methods: Pts with T2 N1-3, T3-4 N any M0 squamous cancer of the anus entered a prospective, multi-centre, open-labelled randomised 3-arm trial, and received 28 fractions (F) of IMRT at total standard dose of 53.2Gy or escalated to 58.8Gy or 61.6Gy to the gross tumour (40Gy in 28F elective nodal irradiation in all arms). All pts received

concurrent mitomycin 12mg/m2 day 1 and capecitabine (CAP) 825mg/m2 twice daily (week days) or 5-fluorouracil 1000mg/m2 days 1-4 and 29-32. Compliance to RT (no delay >3 days due to toxicity) and chemotherapy, worst acute toxicity during treatment (CTCAEv4) and PROs up to 6 months (EORTC-QLQ C30 and ANL27) were analysed.

Results: 60 pts were enrolled from 12 UK sites (53.2Gy n = 19; 58.8Gy n = 21; 61.6Gy n = 20). 78% female, median age 61 years (36 -77), 67% T2/3 and 28% ECOG PS1. All pts received planned RT dose with no delays >3days. Chemotherapy (5FU n = 18; CAP n = 42) modifications were: 8.3% (n = 5) overall dose reductions and 35% (n = 15) temporary CAP omissions (range 1-5 days). Pts had acceptable acute toxicity/PROs for both experimental arms not requiring protocol modification. Worst reported CTCAE toxicity grade (G) per pt: G2 51.7% (n = 31), G3 47.6% (n = 28, 19 radiation dermatitis, 7 diarrhoea), G4 1.7% (n = 1; thrombocytopenia). PRO compliance was 86.7% at 6 months. Pre-specified PRO items on quality of life, pain, and bowel toxicity were worst in final treatment week, improving by 6 weeks and returned to baseline or better by 6 months.

Conclusions: RT dose intensification appears safe with acceptable compliance, acute toxicity and PROs at 6 months. Data Monitoring Committee approved phase II with no treatment schedule changes but included a 6 month clinician toxicity assessment. Phase II will open in June 2019.

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