LBA21 InterAACT: A multicentre open label randomised phase II advanced anal cancer trial of cisplatin (CDDP) plus 5-fluorouracil (5-FU) vs carboplatin (C) plus weekly paclitaxel (P) in patients (pts) with inoperable locally recurrent (ILR) or metastatic treatment naïve disease - An International Rare Cancers Initiative (IRCI) trial

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Background: Whilst advanced squamous cell carcinoma of the anal canal (SCCA) is a rare disease incidence has risen by 2%/year for the past decade. There is no consensus on management of these pts who generally have a poor overall survival (OS) and to date no randomised trial has been completed. The combination of fluoropyrimidine / platinum agents is often considered standard 1st line therapy whilst taxanes have shown activity. We conducted a randomised phase II study to establish a standard of care.

Methods: Eligible pts randomised in 1:1 ratio to CDDP (60 mg/m^2, D1q21)/5-FU (1000 mg/m^2/24h, D1-4q21) or C (AUC 5, D1q28)/P (80 mg/m^2, D1,8,15q28). Stratification factors were performance status (PS), extent of disease, HIV status & country. Primary endpoint was response rate (RR). Based on a RR estimate of 40% in the CDDP/5-FU arm, 80 pts were required to detect 10% difference in RR between the 2 arms with 80% power (phase II selection trial pick the winner design). Secondary endpoints include progression-free survival (PFS), OS, toxicity, quality of life & feasibility.

Results: Between 2014-2017, 91 pts were randomised (46 CDDP/5-FU, 45 CP) from 31/60 centres; Median age 61 yrs; Female 67%;12% locally advanced, 88% metastatic. RR :57.1% in CDDP/5-FU and 59.0 % in CP. Median PFS: 5.7 mths for CDDP/FU versus 8.1mths for CP, $p = 0.375$. Median OS 12.3 mths for CDDP/FU versus 20 mths for CP, HR 2.0 $p = 0.014$. Grade $\geq$3 toxicity occurred in 32 pts (76%) in CDDP/5-FU and 30 pts (71%) in CP. Reported Serious Adverse Events: 62% in CDDP/5-FU and 36% in CP, $p = 0.016$.

Conclusions: InterAACT is the first prospective randomised trial in this setting. In this pick the winner design CP demonstrated similar response rate but less toxicity thus is declared the winner. We have successfully demonstrated the feasibility of international collaboration in a rare cancer. These data establish CP as a standard of care for 1st line treatment of advanced SCCA & serve as a future backbone for the addition of novel agents in phase II/III trials.

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