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**Abstract Title**

**#640 Outcomes of CUPem: A prospective Phase II multicentre clinical Trial of Pembrolizumab in patients with pre-treated Cancer of Unknown Primary**

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| Type: Abstract |
| Topic:  Clinical practice |

**Background**

Cancer of unknown primary (CUP) remains a common major challenge, diagnosed by serially excluding known sites of origin. Median survival, excluding rarer favourable subsets, with first-line combination cytotoxics (platinum based) remain poor under 10 months. Less than 10% are amenable to therapies linked to actionable mutations and less than 20% suitable for 2nd line therapies, with few studies beyond first line therapy and no standard of care. CUP may have unique biology in relation to immune system evasion leading to early metastatic spread. We investigated the feasibility of treatment with Pembrolizumab after failure of at least one line of therapy in a prospective phase 2 trial

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**Methods**

The study was initiated in 2019 to recruit a minimum of 57 CUP patients treated with and progressing after at least one line of chemotherapy with RECIST measurable disease, across 3 UK centres with Pembrolizumab 200 mg IV Q21d until disease progression or intolerance. Significant Covid trial recruitment disruption in this rare population, revised the study design down to a minimum of 31 patients, (after an interim pre-planned futility analysis at 24 patients) which gave a power 0.80 to detect a 2 months PFS improvement

**Results**

35 patients consented with 30 patients assessable (Database lock Aug 2023). Median age 60 (range 33–77), 67% female, ECOG 0-1 vs 2: 83/17%. 63% had 1 line of prior chemotherapy, 27% 2 lines, 10% 3 or more lines & 10% prior radiotherapy. Median PFS (first RECIST PD) was 4.0 months (95% CI 3.2-7.5) and Median OS 11.5 months (95% CI 6.5-NR). At 6/12/18/24 & 36 months, the percentage of patients not progressing on trial treatment were 33/23/17/13/13% respectively. 2 patients who had not progressed, stopped treatment due to related AEs, one of whom has maintained stable disease for >36 mths including 9 months after discontinuation. Pembrolizumab was very well tolerated and there were no unexpected adverse events.

**Conclusions**

Pembrolizumab should be further investigated in CUP with promising activity and sustained disease control in a significant minority of patients beyond 2nd line with overall survival similar to first line CUP studies. Ongoing Clinico-translational research may identify predictive biomarkers.

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**Clinical Trial Identification**

Eudract Ref: 2018-001327-39

**ClinicalTrials.gov ID NCT03752333**

**Sponsors of study: Imperial College London**

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