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Enfortumab vedotin plus pembrolizumab in collecting duct and renal medullary carcinoma (REPRINT – MeetURO 4/25 trial): Preliminary results from Simon's first stage (NCT06302569)

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Background

Collecting Duct Carcinoma (CDC) and SMARCB1-deficient renal medullary carcinoma (RMC) are rare, aggressive renal cancers with poor prognosis and no standard of care.

Methods

REPRINT is a prospective, single-center, phase II trial (Simon's two-stage design) of pembrolizumab (P) 200 mg q3w + enfortumab vedotin (EV) 1.25 mg/kg on days 1 and 8 of each 21-day cycle for 3 cycles, then P maintenance (EV reintroduction allowed at progression) in CDC and RMC patients (pts). Primary endpoint: was objective response rate (ORR) per RECIST v.1.1. Secondary endpoints included progression-free survival (PFS). Central pathological review was mandatory. Here, we report first stage results.

Results

Of 13 pts enrolled (May 2025–April 2026), 9 were evaluable after central pathology review (7 CDC, 2 RCCU-MP, a subtype of RMC not associated with sickle hemoglobinopathies). Metastatic sites included lung (77%), lymph node (88%) and bone (33%). All pts received 3 cycles of P + EV. The ORR was 22% (2/9), with both responses occurring in the 2 RCCU-MP pts: 1 achieved complete response in lung disease with stable disease (SD) in nodal sites, and 1 patient achieved a partial response (PR) in lung disease; no objective responses were observed in the 7 CDC pts. Disease control rate (DCR) was 55% (2/9 PR + 3/9 SD). Median PFS was 5.2 months (95% CI, 3.4–NR), with a median follow-up of 3.9 months. No G3-4 adverse events were observed. Both responders had negative membranous NECTIN-4 expression, SMARCB1 deficiency, PD-L1 CPS of 10% and 20% and tumor mutational burden (TMB) of 1,6 and 3.8 mut/Mbp, respectively. Longitudinal peripheral blood flow cytometry monitoring revealed that PR/SD pts showed higher baseline frequencies of PD-1$^+$ CD8$^+$ T cells together with consistently lower levels of CD14$^+$HLA-DR$^-$ (MDSC-like) monocytes over time, whereas PD (n=2) pts were characterized by lower baseline PD-1$^+$ CD8$^+$ cells and a sustained expansion of CD14$^+$HLA-DR$^-$ suppressive monocytes.

Conclusions

P + EV demonstrated preliminary antitumor activity in RMC and CDC, meeting the criteria to proceed beyond the first stage of Simon's two-stage design in the REPRINT trial.

Clinical trial identification

NCT06302569.

Legal entity responsible for the study

The authors.

Funding

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Disclosure

G. Procopio: Financial Interests, Personal, Advisory Board: Astellas, AstraZeneca, Amgen, Bayer, BMS; Financial Interests, Advisory Board: MSD, Pfizer; Financial Interests, Research Grant: MSD, Gilead Science, JnJ; Non-Financial Interests, Member of Board of Directors: ASCO guidelines; Financial Interests, Member of Board of Directors: AIOM. M. Stellato: Financial Interests, Advisory Board: MSD, Eisai, Ipsen. E. Verzoni: Financial Interests, Advisory Board: MSD, Novartis, Ipsen. All other authors have declared no conflicts of interest.

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