BAYOU: Phase II study of efficacy and safety of durvalumab plus olaparib as first-line therapy in cisplatin-eligible patients (pts) with stage IV urothelial cancer (UC)

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Background: UC is platinum-responsive and hypothesized to be sensitive to targeted DNA-damaging agents such as PARP inhibitors (PARPi). Cisplatin (cis)-ineligible pts with metastatic/unresectable primary UC have limited effective treatment options. Immune checkpoint blockade may increase the proportion of pts that respond to PARPi. Durvalumab is a selective, high-affinity, engineered, human IgG1 monoclonal Ab that blocks PD-L1 binding to PD-1 and CD80. In UC, the combination of olaparib (a PARPi) + durvalumab may broaden the therapeutic effect of monotherapy given their different mechanisms of action, with potentially enhanced benefit for pts with metastatic/unresectable UC and DNA repair deficiencies (mutations in homologous recombination repair genes [HRRm]).

Trial design: BAYOU is a double-blind, randomized, placebo-controlled, multicenter phase 2 study designed to assess the efficacy and safety of durvalumab + olaparib vs durvalumab + placebo in cis-ineligible pts with stage IV UC. Adult pts (≥18 years) who are cis-ineligible with histologically/cytologically confirmed unresectable stage IV UC, WHO performance status 0-2, and with known HRRm status will be enrolled. Pts with active/prior autoimmune disorders, brain metastases, prior PARPi/immune therapy, current/prior immunosuppressive agents, non-UC invasive malignancies, and concomitant use of strong CYP3A inhibitors/inducers are excluded. All pts will be randomized (1:1) to durvalumab (1500 mg intravenous, every 4 weeks) + placebo or durvalumab + olaparib (tablet) until disease progression. Olaparib dose will be 300 mg twice daily in pts with CrCl >50 mL/min and 200 mg twice daily in pts with CrCl 31 to ≤ 50 mL/min. The primary endpoint is progression-free survival in HRRm patients (investigator assessed, RECIST v1.1). Secondary endpoints are overall survival (OS), duration of response, objective response rate, proportion of pts alive and progression-free at 6 months, and OS at 18 months. Safety, pharmacokinetics, and immunogenicity will also be assessed. The trial is currently enrolling pts.

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