Rucaparib + sunitinib goveican (SG): Initial data from the phase Ib/II SEASTAR study [NCT03992131]

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Background: Precisely, PARP inhibitors (PARPi) + TOP1 inhibitors have shown highly synergistic antitumour effects, but clinical development has been hampered by overlapping toxicities. Tumour-targeted delivery of a TOP1 inhibitor may reduce systemic toxicity of the combination; thus, we evaluated the PARPi rucaparib + SG, an antibody-drug conjugate composed of an anti-Trop2 antibody covalently attached to the metabolic active of irinotecan (SN-38) via a unique hydrolyzable linker.

Methods: For phase Ib, eligible patients (pts) who had metastatic triple-negative breast cancer (TNBC), urothelial cancer (UC); platinum-resistant ovarian cancer (OC); or solid tumour with deleterious with HRR gene mutations. All 6 pts continued treatment (range, 12–27+ weeks), with side effects effectively managed with dose modification and/or GF support. Three pts had a confirmed PR, including 2 pts previously treated with niraparib until PD, 2 responders did not have HRR gene mutations.

Results: In cohort 1, grade (G) 4 neutropenia during C1 was dose limiting (n/N 1/300 mg PO BID + SG 6 mg/kg (TNBC); urothelial cancer (UC); platinum-resistant ovarian cancer (OC); or solid tumour with deleterious with HRR gene mutations. All 6 pts continued treatment (range, 12–27+ weeks), with side effects effectively managed with dose modification and/or GF support. Three pts had a confirmed PR, including 2 pts previously treated with niraparib until PD, 2 responders did not have HRR gene mutations.

Conclusions: Initial encouraging signs of antitumour activity were seen with rucaparib + SG in pts with advanced solid tumours, including pts with prior PARPi exposure.


https://doi.org/10.1016/j.annonc.2020.08.660

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