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SOGUG-Vexillum: Phase II non randomized clinical trial of nivolumab / ipilimumab maintenance following first-line chemotherapy in unresectable locally advanced or metastatic urothelial cancer

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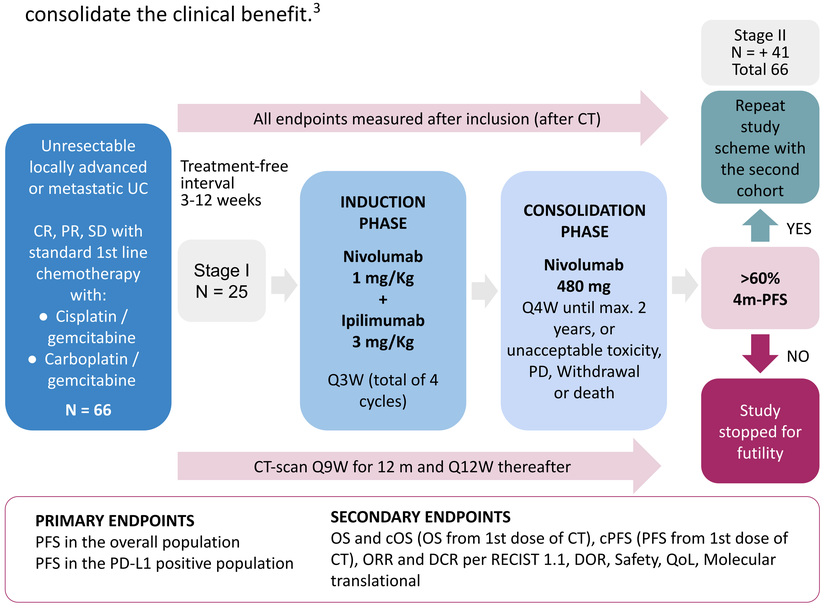
BACKGROUND

- Nivolumab (nivo) 1mg/kg plus ipilimumab (ipi) 3mg/kg achieved an ORR of 42.4% in refractory metastatic urothelial carcinoma (mUC) with a manageable safety profile [1,2].
- The addition of nivo and ipi subsequently to first-line chemotherapy (CT) could consolidate the clinical benefit.[3]



Abbreviations: CR: complete response; PR: partial response; SD: stable disease; PD: progressive disease; EOT: End of Treatment; PFS: Progression-free Survival; OS: Overall Survival; ORR: Objective Response Rate; RECIST 1.1: Response Evaluation Criteria In Solid Tumors; DOR: Duration of the response; m: months; QoL: Quality of Life; CT: chemotherapy.

Figure 1: Study design

METHODS

- VEXILLUM is a single arm, open-label,multicenter study evaluates the effectiveness of ipi 3 mg/kg in combination with nivo 1 mg/kg (Q3W) for 4 cycles followed by nivo maintenance therapy (Q4W) in delaying disease progression in patients with mUC that did not progress after first-line platinum-based CT (at least 4-6 cycles of CT) (Fig.1)
- Autoimmune disease, immune deficiency, and symptomatic brain metastasis were excluded.
- Sample size was estimated using a simon II stage design for 4-months PFS rate (H_0= 40%; H_1= 60; α= 0.05; β= 80%; attrition 10%)requiring 25 patients in the 1st stage and up to 66 in total. Here we report the interim analysis for 1st stage. **(Fig. 1)**

RESULTS

- As of January 2024, the 1st accrual stage was completed with 25 evaluable patients. Baseline characteristics are outlined in the **table 1**.
- Median follow-up of 6.8 months (95% CI: 6.2-10.5), the survival outcomes are shown below **(Fig.2)**

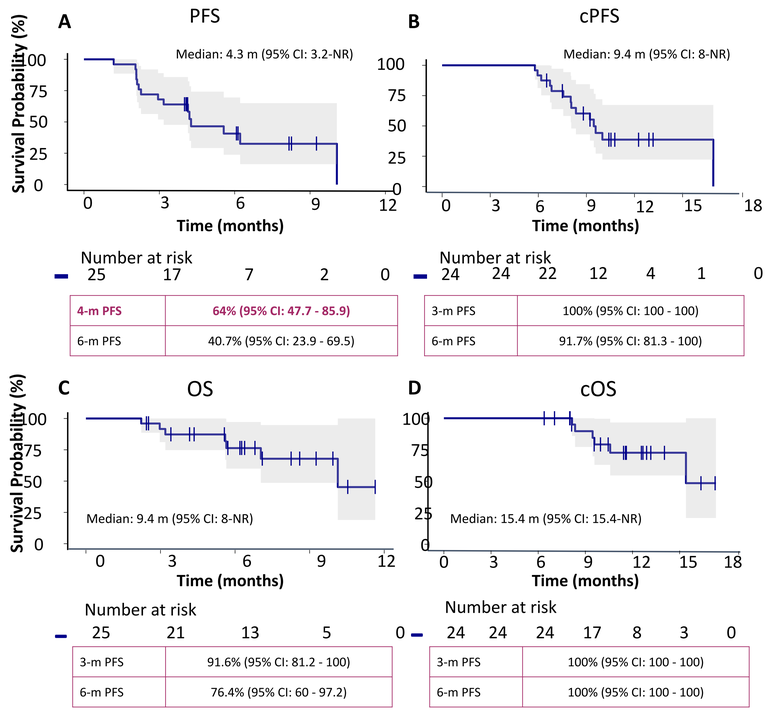


Figure 2: Survival outcomes

- The median duration of treatment was 2.6 months (95% CI: 2.1, 5.7). Nivo and ipi were permanently discontinued due to toxicity in 3 (12%) and 1 (4.2%) patients, respectively. Nivo doses were delayed in 8 (32%) patients and ipi in 3 (12%) for management of toxicity.
- Grade ≥3 toxicities were reported in 8 (32%) patients, being the most common: Immune-mediated hepatitis (8%), ALT/AST increased (8%) and diarrhea (8%). **(Fig.3)**

CONCLUSIONS

Maintenance treatment with nivo and ipi showed preliminary efficacy consolidating clinical benefit to CT with a manageable safety profile. The 4-m PFS rate surpassed the futility threshold in the interim analysis. Final survival results are awaited.

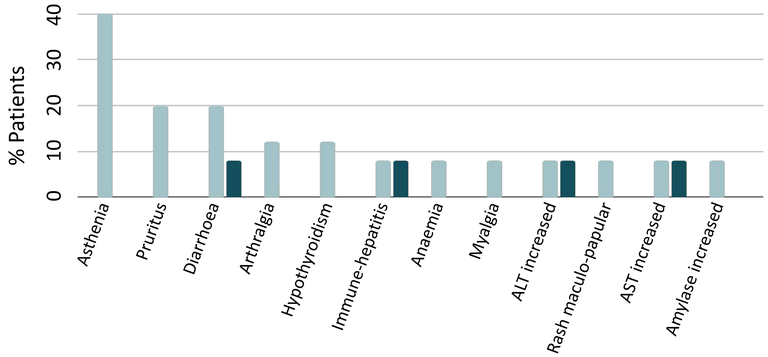


Figure 3: Most frequent toxicities

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Table 1. Baseline characteristics

Age, years	Median (range)	64 (53-79)
Gender, n (%)	Male	20 (80)
ECOG	1	13 (52)
	2	12 (48)
Chemotherapy n (%)	Gemcitabine/Carboplatin	11 (44)
	Gemcitabine/Cisplatin	14 (56)
Best response Chemotherapy, n (%)	CR	4 (16)
	PR	12 (48)
	SD	9 (36)

REFERENCES
1. de Velasco G, et al. JCO 2023
2. Sharma P et al. J Clin Oncol. 2019
3. Motzer RJ, et al Cancer 2022

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