Feasibility and Efficacy of Split-Dose Cisplatin with Atezolizumab for Cisplatin-Ineligible Urothelial Carcinoma (SOGUG-AUREA): Final Results

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BACKGROUND

- Recent research suggests cisplatin offers immunomodulatory benefits with atezolizumab (ATZ) compared to carboplatin (1).
- Nivolumab + gemcitabine/cisplatin is emerging as the new frontline standard for urothelial carcinoma (UC) (2).
- In this phase 2 trial (NCT04602078), we investigated the feasibility and efficacy of combining ATZ with a split-dose cisplatin regimen in UC patients ineligible for full cisplatin doses. Here, we present the final results of this study.

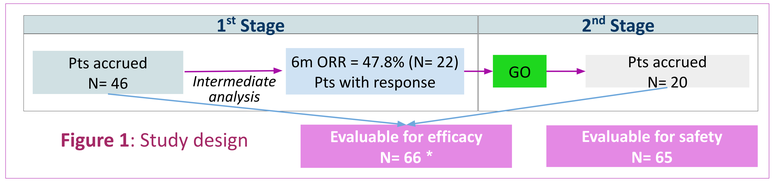


Figure 1: Study design

METHODS

- The phase II SOGUG-AUREA clinical trial recruited treatment-naive patients in advanced or metastatic settings considered unfit for full dose of cisplatinum-based chemotherapy (CT) (**Fig.1**). Patients received a split dose of cisplatin (35 mg/m^2) and gemcitabine (1000 mg/m^2) days 1 and 8 (up to 6 cycles) in combination with 3-weekly ATZ 1200 mg in D1 intravenously until progression, unacceptable toxicity, or absence of clinical benefit. Here we present the final results for confirmed objective response rate (ORR) according to RECIST 1.1 (primary endpoint).

Table 1. Baseline characteristics

Age, years	Median (range)	71 (49-85)
Gender, n (%)	Male	57 (86.4)
ECOG; n (%)	0	17 (25.8)
	1	34 (51.5)
	2	15 (22.7)
Stage at initial Dx; n (%)	Locally advanced	44 (66.7)
	Metastatic	28 (42.4)
Metastatic locations; n (%)	Lymph nodes	49 (74.2)
	Lung	36 (54.5)
	Liver	12 (18.2)
Reason unfit for full dose CT; n (%)	ECOG 2	15 (22.7)
	Age > 70 years	36 (54.5)
	CrCl 30-60 ml/min	33 (50.0)

RESULTS

- 66 patients were included between Jan 2021 and Mar 2022. Baseline characteristics are outlined in **Table 1**.
- The confirmed ORR was 48.5% (95% CI: 36-61), with 7 (10.61%) patients having CR (**Fig.2a**). The median duration of the response was 9.2 m (95%CI: 5.5-16.8) (**Fig.2b**).
- After a median follow-up of 11.6 m (range: 0.6-35.3), median PFS was 6.9 m (95%CI: 6.7-9.4), 12-m PFS rate of 31.0% (95% CI: 21.4-44.8) (**Fig.3**).
- The median OS was 12.9 m (95% CI: 10.2-20.2), with a 24-m OS rate of 30.1% (95%CI: 20.6-44.0) (**Fig.4**).
- Most frequent grade 3-4 toxicities were neutropenia (31.8%), anemia (25.8%) and thrombocytopenia (19.7%) (**Fig.5**).

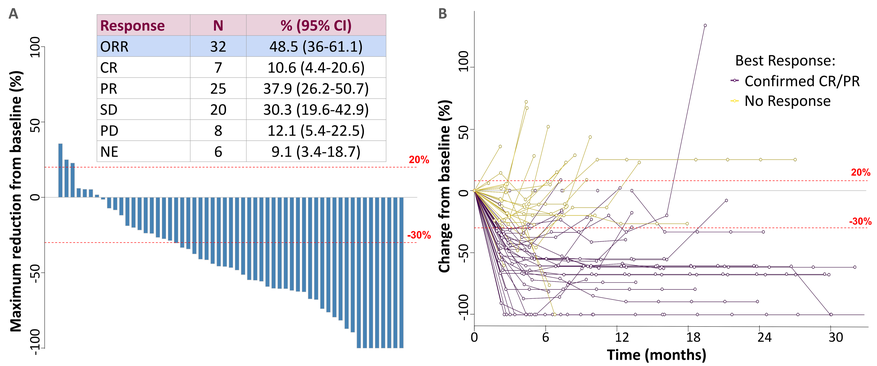


Figure 2: Tumor Response rates. a) Waterfall plot showing the maximum reduction of the target lesions from baseline. b) Spider plot showing the changes from baseline tumor burden.

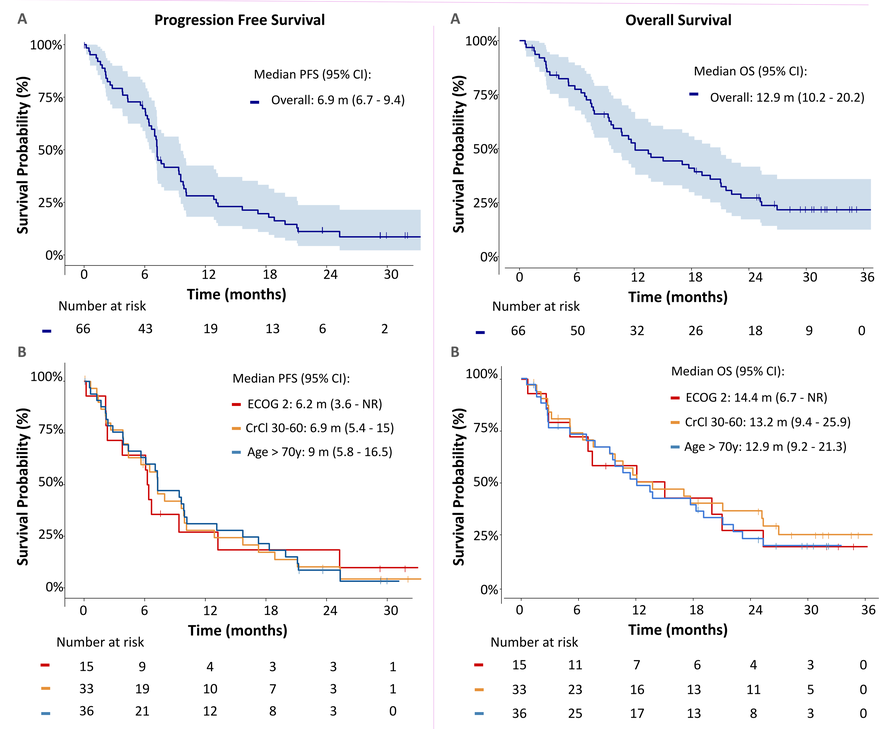
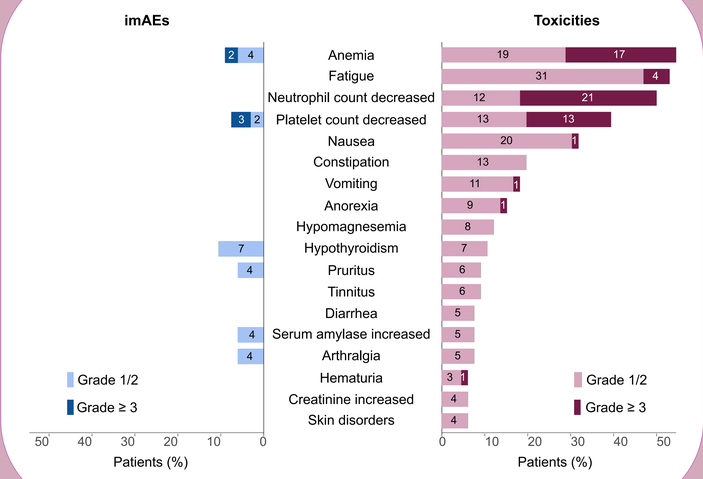


Figure 3: PFS in full dataset (a) and according to cisplatin unfit criteria (b).

Figure 4: OS in full dataset (a) and according to cisplatin unfit criteria (b).

CONCLUSIONS

- ATZ plus split doses of CT showed signs of activity in line with other chemo-ICI combinations surpassing the futility threshold in terms of ORR, in frail patients with UC.
- The combination was administered safely and raised no new safety concerns.
- Six patients (9.1%) had durable responses maintained for more than 2 years.
- A third of patients were still alive after 2 years. Safety profile was consistent with previous experience.



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