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Erdafitinib (ERDA) or ERDA plus cetrelimab (CET) for patients with metastatic or locally advanced urothelial carcinoma (mUC) and Fibroblast Growth Factor Receptor alterations (FGFRa): First phase (Ph) II results from the NORSE study

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Background

First-line (1L) therapy for cisplatin (cis)-ineligible patients (pts) with mUC includes alternative chemotherapy or anti-PD-(L)1 monotherapy for PD-L1 positive tumors. The pan-FGFR inhibitor ERDA has established clinical benefit in 2L mUC for pts with targetable *FGFRa*. ERDA combined with the anti-PD-1 CET could expand 1L options for pts with *FGFRa*. The Ph 1b part of NORSE (NCT03473743) determined a tolerable dose of ERDA + CET in pts with 2L mUC. We report early results from the Ph 2 part of NORSE evaluating ERDA or ERDA + CET in cis-ineligible pts with 1L mUC and *FGFRa*.

Methods

NORSE Ph 2 is enrolling pts ≥ 18 y with mUC, select *FGFRa* (mutation/fusion), and measurable disease (no prior systemic therapy for mUC, cis ineligible). Pts are randomized 1:1 to receive once-daily ERDA 8 mg (with pharmacodynamically guided uptitration [UpT] to 9 mg) or ERDA 8 mg (no UpT) + IV CET 240 mg every 2 wks at cycles 1-4 and 480 mg every 4 wks thereafter. Primary end points are investigator-assessed overall response rate (ORR) per RECIST 1.1 and safety; secondary include disease control rate (DCR), time to response (TTR), and duration of response (DOR).

Results

As of July 19, 2021, 53 pts were randomized; 26 to ERDA and 27 to ERDA + CET. For ERDA vs ERDA + CET: median age was 75 vs 69 y; visceral metastases were present in 54% vs 52%; ECOG was 0-1 in 77% vs 63%. Efficacy data in response-evaluable pts are shown in the table. The safety set comprised 24 pts who received ERDA and 24 who received ERDA + CET. The most frequent treatment-emergent adverse events were hyperphosphatemia (ERDA vs ERDA + CET, 58% vs 58%), stomatitis (63% vs 54%), and diarrhea (50% vs 42%).Table: LBA27

Efficacy in response evaluable pts

	ERDA 8 mg with UpT (n = 18)	ERDA 8 mg + CET (n = 19)
ORR, % (95% CI)	33 (13-59)	68 (43-87)
Confirmed CR, n	1	4
DCR, % (95% CI)	100 (82-100)	90 (67-99)
Median DOR (95% CI), mo	NE (4.4-NE)	6.9 (1.6-NE)
Confirmed response ongoing, n/N	5/6	10/13
Median TTR, mo	2.3	1.8

Conclusions

ERDA + CET showed clinically meaningful responses in cis-ineligible patients with 1L mUC and *FGFRa*. Safety was generally consistent with ERDA alone. Enrollment is ongoing.

Clinical trial identification

NCT03473743.

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