LBA27
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>
<thead>
<tr>
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<th>ERDA 8 mg with UpT (n = 18)</th>
<th>ERDA 8 mg + CET (n = 19)</th>
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</thead>
<tbody>
<tr>
<td>ORR, % (95% CI)</td>
<td>33 (13-59)</td>
<td>68 (43-87)</td>
</tr>
<tr>
<td>Confirmed CR, n</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>DCR, % (95% CI)</td>
<td>100 (82-100)</td>
<td>90 (67-99)</td>
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<tr>
<td>Median DOR (95% CI), mo</td>
<td>NE (4.4-NE)</td>
<td>6.9 (1.6-NE)</td>
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<tr>
<td>Confirmed response ongoing, n/N/N/5/6</td>
<td>10/13</td>
<td></td>
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<tr>
<td>Median TTR, mo</td>
<td>2.3</td>
<td>1.8</td>
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</tbody>
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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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Disclosure

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