Clinical Confirmation of Higher Exposure to Niraparib in Tumor vs Plasma in Patients with Breast Cancer

Laura Spring,1 Ming Shan,2 Minetta C. Liu,3 Erika Hamilton,1 Cesar A. Santa-Maria,1 Hanna Ira,4 Steven Iakobt,1 James Reeves,5 Laff W. Ellsion,6 Andre Liem,7 Adriana Miliana Nairame,8 Julie Nangila,9 David Page,10 Peng Pan,11 Kaiming Sun,12 Julie R. Graham,13 Sebastian Hazard,12 Hyo Han12

Background
- Niraparib is a selective oral (poly)ADP-ribose polymerase 1/2 inhibitor approved as maintenance treatment for patients with recurrent ovarian cancer who are in complete or partial response to platinum-based chemotherapy.
- Animal models revealed unique pharmacokinetic properties of niraparib, including higher concentrations in tumors than in plasma (Figure 2).12
- Higher niraparib tumor concentrations were associated with improved tumor control.
- Another (poly)ADP-ribose polymerase 1/2 inhibitor, rucaparib, demonstrated lower tumor concentration compared with patients in preclinical and clinical studies.2

Objective
- To analyze intra-tumoral niraparib concentration and compare niraparib tumor and plasma concentrations in patients with breast cancer.

Methods
- Sample were collected from patients enrolled in an ongoing pilot study evaluating the antitumor activity and safety of niraparib as neoadjuvant treatment for HER2-negative, BRCA-1/2-mutated localized breast cancer (NCT03329937).
- Tumor biopsies and plasma samples were obtained at the end of the second treatment cycle (day 14–17).
- Niraparib concentration in plasma and tumor samples for each patient were determined using qualified liquid chromatography–tandem mass spectrometry methods to determine steady-state maximum concentration ($C_{\text{max}}$) and trough concentration ($C_{\text{trough}}$).

Table 1. Patient Demographics and Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total (n=14)</th>
<th>Age group, n (%), years</th>
<th>BRCA mutation status, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>Median</td>
<td>50.2</td>
<td>3 (21.4)</td>
</tr>
<tr>
<td>Age group (n)</td>
<td>21 (15.7)</td>
<td>1 (0.7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>&gt;65 years</td>
<td>10 (71.4)</td>
<td>10 (71.4)</td>
<td>8 (57.1)</td>
</tr>
</tbody>
</table>

Table 2. Niraparib Concentrations in Plasma and Tumor

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Highest plasma niraparib concentration (nM)</th>
<th>Niraparib concentrations in plasma and tumor (nM)</th>
<th>Tumor vs Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10360</td>
<td>$C_{\text{max}}$=1753 ± 1787 nM, $C_{\text{trough}}$=173 ± 2761 nM</td>
<td>&gt;26.7</td>
</tr>
<tr>
<td>2</td>
<td>10380</td>
<td>$C_{\text{max}}$=1764 ± 1796 nM, $C_{\text{trough}}$=174 ± 2762 nM</td>
<td>&gt;26.7</td>
</tr>
</tbody>
</table>

Figure 1. Steady-State Pharmacokinetics (PK) of Niraparib and Olaparib

Figure 2. Conclusions
- These results provide the first data of the intra-tumor concentration of niraparib in the clinical setting.
- The concentration of niraparib was on average 35-fold greater in tumor tissue than in plasma.
- Confirm that niraparib concentration is higher in tissue compared with baseline concentration.
- Efficacy results will be reported at a future meeting.

References