Cisplatin plus gemcitabine versus paclitaxel plus gemcitabine as first-line therapy for metastatic triple-negative breast cancer (CBCSG006): a randomised, open-label, multicentre, phase 3 trial

Xi-Chun Hu et al, Lancet Oncology, doi: http://dx.doi.org/10.1016/S1470-2045(15)70064-1
Platinum-based chemotherapy in TNBC significantly increases pathologic complete response rates. The CBCSG006 trial compared the efficacy of cisplatin with gemcitabine vs. paclitaxel with gemcitabine as first line treatment in metastatic TNBC.

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Xi-Chun Hu et al, Lancet Oncology, doi: http://dx.doi.org/10.1016/S1470-2045(15)70064-1
Chinese patients with metastatic TNBC and no prior chemotherapy for metastatic disease. Patients who received taxanes in the adjuvant or neoadjuvant setting were included if relapse occurred at least 6 months after treatment was completed.

**Endpoints:**
- Primary: PFS
- Secondary: OS, ORR, safety

**Trial design:** phase III, open-label, non-inferiority, superiority RCT

**Experimental:** Cisplatin (75 mg/m² D1) + Gemcitabine (1,250 mg/m² D1&8) q3w

**Control:** Paclitaxel (175 mg/m² D1) + Gemcitabine (1,250 mg/m² D1&8) q3w

Xi-Chun Hu et al, Lancet Oncology, doi: http://dx.doi.org/10.1016/S1470-2045(15)70064-1
### RESULTS - EFFICACY

N=240 enrolled, 236 analyzed by modified ITT

<table>
<thead>
<tr>
<th></th>
<th>Cisplatin/Gemcitabine</th>
<th>Paclitaxel/Gemcitabine</th>
<th>Hazard Ratio</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS</td>
<td>7.73 months</td>
<td>6.7 months</td>
<td>0.692 (0.523–0.915)</td>
<td>&lt;0.0001 (non-inferiority) 0.009 (superiority)</td>
</tr>
<tr>
<td>OS</td>
<td>No difference</td>
<td></td>
<td>0.902 (0.605-1.344)</td>
<td>0.611</td>
</tr>
<tr>
<td>ORR</td>
<td>64%</td>
<td>49%</td>
<td>-</td>
<td>0.018</td>
</tr>
</tbody>
</table>

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RESULTS – Adverse Events

• Toxicities were consistent with known adverse events for Cisplatin, Paclitaxel and Gemcitabine.

• More patients in the Cisplatin/Gemcitabine arm required dose reductions (40% vs. 30%).

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Discussion

- First line treatment with Cisplatin and Gemcitabine improved PFS in Chinese patients with metastatic TNBC compared to Paclitaxel with Gemcitabine.
- Study data was immature for OS analysis and further follow-up is needed. Crossover was observed after disease progression and may confound OS result.
- A retrospective study by Villeareal.Garza et al (Breast Cancer Res Treat 2014 Aug 8;146 (3):567-72) found that metastatic TNBC patients treated with platinum-based chemotherapy had better OS (14.5 vs. 10 months, p = 0.041) compared to those who received non-platinum based treatment.

Xi-Chun Hu et al, Lancet Oncology, doi: http://dx.doi.org/10.1016/S1470-2045(15)70064-1
Recent data presented at SABCS 2014 meeting from the TNT trial, confirms the benefit of Platinums over Docetaxel for patients with BRCA +ve breast cancer.

Overall this study confirms that platinums are active agents in treatment of TNBC, we still need more data to confirm if the benefit is restricted only to BRCA +ve patients, or if we can identify another subgroup of TNBC that will derive a greater benefit from platinums.

First line Cisplatin and Gemcitabine is a treatment option for patients with metastatic TNBC.

Study results should be interpreted with caution since the trial was limited to Chinese population, central assessment for outcomes was not conducted and OS efficacy is pending.

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