IMpassion130: final OS analysis from the pivotal Phase III study of atezolizumab + nab-paclitaxel vs placebo + nab-paclitaxel in previously untreated locally advanced or metastatic triple-negative breast cancer

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Disclosure information

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The global Phase III IMpassion130 study

- The primary PFS analysis from IMpassion130 demonstrated statistically significant benefit with A + nP vs P + nP in the ITT and PD-L1 IC+ populations\(^1\).
- At two interim OS analyses, although not formally tested per the pre-specified statistical analysis plan, clinically meaningful OS improvement was seen in PD-L1 IC+ patients\(^1,2\).
- A + nP was tolerable, with a safety profile consistent with that of each agent\(^1,2\).
- Here, we present the final mature OS analysis from IMpassion130, including updated safety.

**IMpassion130 study design**

- Previously untreated mTNBC
- ECOG PS 0-1
- Tumour tissue for PD-L1 testing

*Randomization stratified by: liver metastases, prior taxanes, PD-L1 IC status*

- Co-primary endpoints
  - PFS (ITT and PD-L1 IC+)\(^a\)
  - OS (tested in ITT, then if significant in PD-L1 IC+ patients)

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OS in the ITT population

Median OS (95% CI): 18.7 mo (16.9, 20.8)
21.0 mo (19.0, 23.4)

3-year OS: 28%
3-year OS: 25%

Stratified HR (95% CI): 0.87 (0.75, 1.02); P = 0.077

Data cutoff, 14 April 2020. Median survival follow-up, 18.8 months (all patients). OS events (ITT population): 322 (71%) in the A + nP arm; 344 (76%) in the P + nP arm. Percent of ITT patients alive on treatment (or in survival follow-up): 6% (15%) in A + nP arm and 2% (17%) in P + nP arm.

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OS in the PD-L1 IC+ population

Stratified HR (95% CI): 0.67 (0.53, 0.86)

Data cutoff, 14 April 2020. OS events (PD-L1 IC+ population): 120 (65%) in the A + nP arm; 139 (76%) in the P + nP arm. NE, not estimable. *P value not displayed because OS in the PD-L1 IC+ population not formally tested due to the hierarchical study design.

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OS by PD-L1 IC status (PD-L1 IC+ vs PD-L1 IC–)

Stratified HR (95% CI):
- PD-L1 IC+: 0.67 (0.53, 0.86)
- PD-L1 IC–: 1.02 (0.84, 1.24)

Median OS (95% CI):
- PD-L1 IC+: 17.9 mo
- PD-L1 IC–: 19.7 mo

Time (months)

Overall survival

No. at risk:
- A +nP (PD-L1 IC–): 266 249 229 197 177 149 132 116 98 86 75 63 43 26 16 9 7 2 1
- P +nP (PD-L1 IC+): 184 170 150 132 113 95 85 72 66 62 54 47 28 14 7 6 3 1 NE
- P +nP (PD-L1 IC–): 267 250 229 200 181 160 140 122 106 91 84 74 61 38 26 14 4 3 1

Data cutoff, 14 April 2020.
## Safety summary

<table>
<thead>
<tr>
<th>Exposure</th>
<th>A + nP (n = 460)</th>
<th>P + nP (n = 430)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median treatment duration</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Up to 24 months</td>
<td>60 (13%)</td>
<td>19 (4%)</td>
</tr>
<tr>
<td>≥ 24 months</td>
<td>38 (8%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td><strong>Mean dose intensity</strong></td>
<td>96%</td>
<td>NE</td>
</tr>
<tr>
<td><strong>AE(^a)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3/4</td>
<td>233 (51%)</td>
<td>183 (43%)</td>
</tr>
<tr>
<td>Grade 5(^b)</td>
<td>6 (1%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>AE leading to withdrawal of any treatment</td>
<td>88 (19%)</td>
<td>36 (8%)</td>
</tr>
<tr>
<td>AE leading to withdrawal of indicated treatment</td>
<td>37 (8%)</td>
<td>4 (1%)</td>
</tr>
<tr>
<td><strong>Most common AESIs (medical concept)(^c)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>270 (59%)</td>
<td>179 (42%)</td>
</tr>
<tr>
<td>Rash</td>
<td>165 (36%)</td>
<td>112 (26%)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>84 (18%)</td>
<td>19 (4%)</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>22 (5%)</td>
<td>5 (1%)</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>18 (4%)</td>
<td>1 (&lt; 1%)</td>
</tr>
<tr>
<td>Hepatitis (diagnosis)</td>
<td>11 (2%)</td>
<td>7 (2%)</td>
</tr>
</tbody>
</table>

**Based on safety-evaluable population. AESI, AE of special interest. \(^a\) Most common AEs of any cause (all grade AEs ≥ 25% in either arm; A + nP vs P + nP): alopecia (57% vs 57%), fatigue (47% vs 45%), nausea (47% vs 38%), diarrhoea (33% vs 35%), anaemia (28% vs 27%), cough (27% vs 19%), constipation (25% vs 25%) and headache (25% vs 22%). \(^b\) Treatment-related Grade 5 AEs: autoimmune hepatitis (A), septic shock, (A + nP), hepatic failure (P + nP). \(^c\) Grouped MedDRA preferred terms for sponsor-defined AESIs based on immune-mediated risks of atezolizumab and other in-class agents.**

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IMpassion130 final analysis: summary

- Here we report mature OS data from the pre-specified final OS analysis
  - The OS boundary for statistical significance was not crossed in the ITT population, precluding further formal testing
  - Clinical meaningful OS benefit was observed in the PD-L1 IC+ population
    - Final OS HR, 0.67 (95% CI: 0.53, 0.86) and a +7.5-mo median OS improvement with A + nP vs P + nP
  - OS results in the PD-L1 IC+ population were consistent with the first and second interim analyses
    - OS HR, 0.62 (95% CI: 0.45, 0.86) in the first interim analysis and 0.71 (95% CI: 0.54, 0.93) in the second interim analysis

- With additional follow-up, A + nP remained tolerable
  - The safety profile was consistent with those of the individual treatment components
  - No new safety signals were identified

- These results support a positive benefit-risk profile for A + nP as first-line therapy in patients with PD-L1 IC+ mTNBC
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