IMpassion130: updated OS from a global, randomized, double-blind, placebo-controlled, Phase III study of atezolizumab + nab-paclitaxel in previously untreated locally advanced or metastatic TNBC

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Disclosures

• Dr Peter Schmid has the following financial relationships to disclose:
  • Grants, support of parent study and funding of editorial support from F. Hoffmann-La Roche during the conduct of the study
  • Grants and research support to institution from AstraZeneca, Roche/Genentech, Oncogenex, Novartis, Astellas outside this study
  • Honoraria from Pfizer, AstraZeneca, Novartis, Roche, Merck, Boehringer Ingelheim, Bayer, Eisai, Celgene and Puma outside this study
  • Uncompensated steering committee member for the IMpassion130 trial
  • Spouse is an employee of Roche
Background

• Patients with mTNBC have a poor prognosis with SOC chemotherapy alone; the median OS is approximately 18 months\textsuperscript{1-5}

• IMpassion130 is the first Phase III study of cancer immunotherapy in mTNBC to demonstrate clinical benefit in PD-L1+ patients\textsuperscript{6}

• Clinically meaningful improvement in OS was observed in the PD-L1+ population at the first interim OS analysis (43% deaths in the ITT population)\textsuperscript{6}

• We present the second interim OS analysis from IMpassion130 after 59% deaths in the ITT population

PD-L1+: PD-L1 on ≥ 1% of IC as percentage of tumor area assessed by VENTANA SP142 IHC assay.

IC, tumor-infiltrating immune cells.

IMpassion130 Study Design

Patients with metastatic or inoperable, locally advanced TNBC without prior therapy for advanced TNBC

Stratification factors:
- Prior (curative setting) taxane use (yes vs no)
- Liver metastases (yes vs no)
- PD-L1 IC status (positive [≥ 1%] vs negative [< 1%])

• Co-primary endpoints in ITT and PD-L1 IC+: PFS and OS
• Pre-specified hierarchical testing of OS in ITT and, if significant, in PD-L1 IC+ patients
• In both treatment arms, 41% of patients were PD-L1 IC+

Atezolizumab
840 mg IV q2w
+ nab-paclitaxel
100 mg/m² IV on d1, d8, d15

Placebo
q2w IV
+ nab-paclitaxel
100 mg/m² IV on d1, d8, d15

Treatment until PD or intolerable toxicity

Survival follow-up

* Prior chemotherapy in the curative setting allowed if treatment-free interval ≥ 12 months. † 28-day cycle. ‡ Centrally evaluated per VENTANA SP142 IHC assay.
§ Efficacy endpoints assessed by investigators per RECIST 1.1. NCT02425891.
Primary PFS Analysis in the ITT and PD-L1 IC+ Subgroup

• PFS benefit driven by PD-L1 IC+ patients, as a treatment effect was not observed in PD-L1 IC− patients\(^1\)

• Based on these data,\(^2\) atezolizumab + nab-paclitaxel received accelerated approval by the FDA\(^3\) and is recommended for patients with PD-L1 IC+ mTNBC in the NCCN\(^4\) and AGO\(^5\) guidelines


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Patient Disposition at Second Interim OS Analysis

**Second Interim OS Analysis**

<table>
<thead>
<tr>
<th>Patient Disposition</th>
<th>Atezolizumab + nab-paclitaxel (n = 451)</th>
<th>Placebo + nab-paclitaxel (n = 451)</th>
</tr>
</thead>
</table>

**Patients on study, n (%)**

<table>
<thead>
<tr>
<th>Alive on treatment</th>
<th>39 (9%)</th>
<th>13 (3%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive in survival follow-up</td>
<td>133 (30%)</td>
<td>135 (30%)</td>
</tr>
</tbody>
</table>

**Patients who discontinued study, n (%)**

<table>
<thead>
<tr>
<th>Dead</th>
<th>255 (57%)</th>
<th>279 (62%)</th>
</tr>
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<tbody>
<tr>
<td>Lost to follow-up</td>
<td>24 (5%)</td>
<td>24 (5%)</td>
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</table>

**First Interim Analysis (59% IF)**

- 12.9 months mFU
- 43% deaths in ITT population

**Second Interim Analysis (80% IF)**

- 18.0 months mFU
- 59% deaths in ITT population

IF, information fraction; mFU, median follow-up.
Clinical cutoff date: January 2, 2019.
OS in ITT Population

Stratified HR, 0.86
(95% CI: 0.72, 1.02)
Log-rank $P = 0.0777$

<table>
<thead>
<tr>
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<th>24-Month OS Rate (95% CI)</th>
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<tbody>
<tr>
<td>A + nab-P (n = 451)</td>
<td>42% (37, 47)</td>
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<tr>
<td>P + nab-P (n = 451)</td>
<td>39% (34, 44)</td>
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NE, not estimable. Clinical cutoff date: January 2, 2019. Median PFS (95% CI) is indicated on the plot. Median FU (ITT): 18.0 mo.
OS in PD-L1+ Population

Stratified HR, 0.71\(^a\)
(95% CI: 0.54, 0.93)

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<thead>
<tr>
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<th>24-Month OS Rate (95% CI)</th>
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<tbody>
<tr>
<td>A + nab-P (n = 185)</td>
<td>51% (43, 59)</td>
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<tr>
<td>P + nab-P (n = 184)</td>
<td>37% (29, 45)</td>
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Patients at risk

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<thead>
<tr>
<th></th>
<th>A + nab-P</th>
<th>P + nab-P</th>
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\(^a\) Not formally tested due to pre-specified hierarchical analysis plan.

Clinical cutoff date: January 2, 2019. Median PFS (95% CI) is indicated on the plot. Median FU (ITT): 18.0 months.
Comparison of OS in PD-L1+ and PD-L1− Populations

Clinical cutoff date: January 2, 2019.

<table>
<thead>
<tr>
<th>Population</th>
<th>Median OS, mo</th>
<th>HR (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>A + nab-P</td>
<td>25.0</td>
<td>0.71 (0.54, 0.93)</td>
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<tr>
<td>P + nab-P</td>
<td>18.0</td>
<td></td>
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<tr>
<td>PD-L1 IC+</td>
<td>19.7</td>
<td>0.97 (0.78, 1.20)</td>
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<tr>
<td>PD-L1 IC−</td>
<td>19.6</td>
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OS (%)

Time (months)

A + nab-P (PD-L1+ n = 185)
P + nab-P (PD-L1+ n = 184)
A + nab-P (PD-L1− n = 266)
P + nab-P (PD-L1− n = 267)
## Subsequent Therapies

### Atezolizumab + nab-paclitaxel (n = 451)

- Anti-metabolite: 42% (Atezolizumab) vs 45% (Placebo)
- Platinum compound: 27% (Atezolizumab) vs 27% (Placebo)
- Anti-neoplastic agent NEC: 18% (Atezolizumab) vs 22% (Placebo)
- Cytotoxic antibiotic (i.e., anthracycline): 15% (Atezolizumab) vs 21% (Placebo)
- Alkylating agent: 11% (Atezolizumab) vs 16% (Placebo)
- Taxane: 8% (Atezolizumab) vs 12% (Placebo)
- Vinca alkaloid: 6% (Atezolizumab) vs 8% (Placebo)
- Immune checkpoint inhibitor: 4% (Atezolizumab) vs 6% (Placebo)
- Angiogenesis inhibitor: 4% (Atezolizumab) vs 5% (Placebo)

### Placebo + nab-paclitaxel (n = 451)

- Anti-metabolite: 45% (Placebo) vs 45% (Placebo)
- Platinum compound: 27% (Placebo) vs 27% (Placebo)
- Anti-neoplastic agent NEC: 22% (Placebo) vs 22% (Placebo)
- Cytotoxic antibiotic (i.e., anthracycline): 21% (Placebo) vs 21% (Placebo)
- Alkylating agent: 16% (Placebo) vs 16% (Placebo)
- Taxane: 12% (Placebo) vs 12% (Placebo)
- Vinca alkaloid: 8% (Placebo) vs 8% (Placebo)
- Immune checkpoint inhibitor: 6% (Placebo) vs 6% (Placebo)
- Angiogenesis inhibitor: 5% (Placebo) vs 5% (Placebo)

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**NEC, not elsewhere classified.**

Data cutoff: January 2, 2019. Presented data limited to therapies received by ≥ 5% of patients in any treatment arm. 

- **Anti-metabolite:** Includes capecitabine, gemcitabine, gemcitabine hydrochloride, fluorouracil, methotrexate, cytarabine, decitabine, flouxuridine, methotrexate sodium, pemetrexed, tegafur.
- **Immune checkpoint inhibitor:** Includes monoclonal antibodies targeting PD-L1, PD-1 and CTLA-4.

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**Dr Peter Schmid**

**IMpassion130: Updated OS**

Updated Safety Analysis

- Safety data remain consistent with those previously published
- See poster #149 for further safety analysis details (Schneeweiss et al.) and poster #148 for patient-reported outcomes (Adams et al.)


* Median follow-up 15.6 mo (4.5 months after primary PFS analysis).

\[\text{AESI} \] requiring systemic corticosteroids

Conclusions

• IMpassion130 is the first and only Phase III study to show the clinically meaningful benefit of first-line immunotherapy in mTNBC

• PD-L1 IC status predicts clinical benefit with atezolizumab + nab-paclitaxel

• Although not formally testable due to the pre-specified statistical analysis plan, a median OS improvement from 18 to 25 months was observed in the PD-L1+ population (HR, 0.71)

• Atezolizumab + nab-paclitaxel was well tolerated, with no cumulative toxicities and no new- or late-onset safety signals

• Atezolizumab + nab-paclitaxel sets a new benchmark as the first therapy to cross the 2-year landmark OS benefit in first-line therapy for PD-L1+ mTNBC

• Atezolizumab + nab-paclitaxel is approved by the FDA\textsuperscript{1} and recommended for the treatment of patients with PD-L1 IC+ mTNBC in the NCCN\textsuperscript{2} and AGO\textsuperscript{3} guidelines

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