IMpower131: Primary PFS and Safety Analysis of a Randomized Phase III Study of Atezolizumab + Carboplatin + Paclitaxel or Nab-Paclitaxel vs Carboplatin + Nab-Paclitaxel as 1L Therapy in Advanced Squamous NSCLC

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IMpower131: Study Design

**Stage IV squamous NSCLC**
- Chemotherapy naive
- ECOG PS 0 or 1
- Any PD-L1 IHC status

Stratification factors:
- Sex
- PD-L1 IHC expression
- Liver metastases

N = 1021

**Co-primary endpoints**
- Investigator-assessed PFS per RECIST v1.1 (ITT)
- OS (ITT)

**Secondary endpoints**
- PFS and OS in PD-L1 subgroups
- ORR, DOR; safety

**Arm A**
Atezolizumab + Carboplatin + Paclitaxel
4 or 6 cycles

**Arm B**
Atezolizumab + Carboplatin + Nab-Paclitaxel
4 or 6 cycles

**Arm C (control)**
Carboplatin + Nab-Paclitaxel
4 or 6 cycles

**Maintenance therapy**
(no crossover permitted)

**Until PD per RECIST v1.1 or loss of clinical benefit**

**Best Supportive Care**

**Until PD per RECIST v1.1**

**R 1:1:1**

Atezolizumab 1200 mg IV q3w; carboplatin AUC 6 IV q3w; nab-paclitaxel 100 mg/m² IV qw; paclitaxel 200 mg/m² IV q3w.

*Patients with a sensitising EGFR mutation or ALK translocation must have disease progression or intolerance to treatment with ≥ 1 approved targeted therapies. Testing for EGFR mutation or ALK translocation was not mandatory.

*PD-L1 expression was evaluated using the VENTANA SP142 IHC assay.
INV-Assessed PFS in the ITT Population (Arm B vs Arm C)

- Data cutoff: January 22, 2018.
- INV, investigator, * Stratified HR.

**Progression-Free Survival (%)**

| Time (months) | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 |
|---------------|---|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| **12-month PFS** | 100 | 90 | 80 | 70 | 60 | 50 | 40 | 30 | 20 | 10 | 0 |

**No. at risk**

- Arm B: Atezo + CnP
  - 343 318 294 268 257 212 172 151 134 111 86 61 42 33 32 24 21 18 16 12 11 5 5 4 3 2 1
- Arm C: CnP
  - 340 322 279 244 227 183 128 95 79 57 48 40 28 21 19 12 12 11 10 6 6 4 3 3 2 2 1

**Median PFS (95% CI), mo**
- Arm B: Atezo + CnP 6.3 (5.7, 7.1)
- Arm C: CnP 5.6 (5.5, 5.7)

**HR* (95% CI), P value**
- 0.71 (0.60, 0.85), 0.0001

**Minimum follow-up, 9.8 mo**
**Median follow-up, 17.1 mo**
INV-Assessed PFS in PD-L1 Subgroups

- PFS benefit was observed with atezolizumab + CnP (Arm B) vs CnP (Arm C) across all PD-L1 subgroups

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>n (%)</th>
<th>PFS HR (95%CI)</th>
<th>Median PFS, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-L1 positive (TC1/2/3 or IC1/2/3)</td>
<td>351 (52)</td>
<td>0.61 (0.48, 0.77)</td>
<td>7.0 5.6</td>
</tr>
<tr>
<td>PD-L1 high (TC3 or IC3)</td>
<td>101 (15)</td>
<td>0.44 (0.27, 0.71)</td>
<td>10.1 5.5</td>
</tr>
<tr>
<td>PD-L1 low (TC1/2 or IC1/2)</td>
<td>250 (37)</td>
<td>0.70 (0.53, 0.92)</td>
<td>6.0 5.6</td>
</tr>
<tr>
<td>PD-L1 negative (TC0 and IC0)</td>
<td>331 (48)</td>
<td>0.81 (0.64, 1.03)</td>
<td>5.7 5.6</td>
</tr>
<tr>
<td>ITT population</td>
<td>683 (100)</td>
<td>0.71 (0.60, 0.85)</td>
<td>6.3 5.6</td>
</tr>
</tbody>
</table>

Data cutoff: January 22, 2018.
*Stratified HR for ITT; unstratified HRs for all PD-L1 subgroups.
INV-Assessed PFS in PD-L1 Subgroups (Arm B vs Arm C)

Data cutoff: January 22, 2018.

* Unstratified HR.
First Interim OS in the ITT Population (Arm B vs Arm C)

Data cutoff: January 22, 2018.

*a* Stratified HR.
First Interim OS in PD-L1 Subgroups (Arm B vs Arm C)

**PD-L1 High TC3 or IC3**

- Atezo + CnP (n = 53)
- CnP (n = 48)

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<thead>
<tr>
<th></th>
<th>Atezo + CnP</th>
<th>CnP</th>
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</thead>
<tbody>
<tr>
<td>12-month OS</td>
<td>67%</td>
<td>52%</td>
</tr>
<tr>
<td>24-month OS</td>
<td>47%</td>
<td>30%</td>
</tr>
<tr>
<td>Median OS, mo</td>
<td>23.6</td>
<td>14.1</td>
</tr>
<tr>
<td>HR* (95% CI)</td>
<td>0.56 (0.32, 0.99)</td>
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**PD-L1 Low TC1/2 or IC1/2**

- Atezo + CnP (n = 129)
- CnP (n = 121)

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<thead>
<tr>
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<th>Atezo + CnP</th>
<th>CnP</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-month OS</td>
<td>54%</td>
<td>64%</td>
</tr>
<tr>
<td>24-month OS</td>
<td>28%</td>
<td>37%</td>
</tr>
<tr>
<td>Median OS, mo</td>
<td>12.4</td>
<td>16.6</td>
</tr>
<tr>
<td>HR* (95% CI)</td>
<td>1.34 (0.95, 1.90)</td>
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**PD-L1 Negative TC0 and ICO**

- Atezo + CnP (n = 160)
- CnP (n = 171)

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<th>Atezo + CnP</th>
<th>CnP</th>
</tr>
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<tbody>
<tr>
<td>12-month OS</td>
<td>53%</td>
<td>53%</td>
</tr>
<tr>
<td>24-month OS</td>
<td>30%</td>
<td>16%</td>
</tr>
<tr>
<td>Median OS, mo</td>
<td>13.8</td>
<td>12.5</td>
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<tr>
<td>HR* (95% CI)</td>
<td>0.86 (0.65, 1.15)</td>
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Data cutoff: January 22, 2018.

* Unstratified HR.
Summary

- IMpower131 met the co-primary endpoint of investigator-assessed PFS with atezolizumab + CnP (Arm B) vs CnP (Arm C) in the ITT population.

- PFS benefit in Arm B vs Arm C was observed across all PD-L1-expressing subgroups and was enriched in subgroups with higher PD-L1 expression.

- Atezolizumab + CnP has a manageable safety profile consistent with known safety risks of the individual therapies; no new safety signals were identified.

- OS continues to be followed, with the next interim OS analysis anticipated later in 2018.