IMscin001 (Part 2: Randomized Phase III): Pharmacokinetics (PK), efficacy and safety of atezolizumab subcutaneous (SC) vs intravenous (IV) in previously treated locally advanced or metastatic non-small cell lung cancer (NSCLC)

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Declaration of interests

Dr Mauricio Burotto reports the following disclosures:

- Advisory boards, speaking at industry symposiums or consulting roles for AstraZeneca, Bristol Myers Squibb, F. Hoffmann-La Roche Ltd, MSD and Novartis
Background & Methods

- The PD-L1 inhibitor atezolizumab is approved for IV use in several solid tumour types\(^1,2\)
- To reduce treatment burden and improve convenience and efficiencies in healthcare, a fixed dose of atezolizumab SC\(^a\) was developed, which is based on the recombinant human hyaluronidase technology
- IMscin001 is a Phase Ib\(^3/\)III study. Here we report the Phase III (Part 2) portion of the open-label, randomized, multicentre IMscin001 study (NCT03735121) aimed to investigate non-inferiority of drug exposure at Cycle 1 after second-line single-agent atezolizumab SC vs IV administration in patients with locally advanced/metastatic NSCLC following progression under platinum-containing therapy

**Co-primary endpoints:**
- Cycle 1 observed trough serum concentration (\(C_{\text{trough}}\))
- MP AUC\(0-21\) days

**Secondary endpoints:**
- MP steady state \(C_{\text{trough}}\) and AUC
- Safety
- Efficacy: objective response rate, duration of response, overall survival, progression-free survival
- Immunogenicity

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Exposure of atezolizumab SC was non-inferior to IV

- For both Cycle 1 C\textsubscript{t\text{rough}} and AUC\textsubscript{0-21 days}, the lower bounds of the 90% CI of the GMR were above the pre-defined non-inferiority margin of 0.8, and therefore the study was positive.

<table>
<thead>
<tr>
<th>Geometric Mean (% Coefficient of Variation)</th>
<th>Atezolizumab</th>
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<tr>
<td></td>
<td>SC</td>
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<tr>
<td>Co-primary endpoints</td>
<td></td>
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<tr>
<td>Cycle 1 Observed\textsuperscript{a} C\textsubscript{t\text{rough}}</td>
<td>µg/mL</td>
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<tr>
<td>MP\textsuperscript{b} Cycle 1 AUC\textsubscript{(0-21d)}</td>
<td>µg•d/mL</td>
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<tr>
<td>Secondary endpoints</td>
<td></td>
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<tr>
<td>MP\textsuperscript{b} C\textsubscript{t\text{rough}} at steady state</td>
<td>µg/mL</td>
</tr>
<tr>
<td>MP\textsuperscript{b} AUC at steady state</td>
<td>µg•d/mL</td>
</tr>
</tbody>
</table>

Median follow-up: 4.7 mo. Data cut-off: 26 Apr 2022. GMR, geometric mean ratio; MP, model-predicted. \textsuperscript{a} Sample sizes for Cycle 1 observed C\textsubscript{t\text{rough}} were n=205 (SC) and n=97 (IV). \textsuperscript{b} Sample sizes for all MP data were n=246 (SC) and n=122 (IV).
Exposure of atezolizumab SC was consistent with those observed with atezolizumab IV across approved indications

- Similar systemic exposure following atezolizumab SC and IV administration supports the use of SC for other approved indications

Median follow-up: 4.7 mo. Data cut-off: 26 Apr 2022. a y-axis is capped at 300 µg/mL; actual data extends to ~600 µg/mL. b Cycle 1 represents single dose PK and single dose PK was not collected in IMpassion130. c Observed Day 14 or 21 Ctrough (µg/mL). Clinical trial identifiers are as follows: IMscin001: NCT03735121, IMpower130: NCT02367781, IMpower133: NCT02763579, IMpower150: NCT02366143, IMpower010: NCT02486718, IMpower110: NCT02409342, OAK: NCT02080827, IMspire150: NCT02900672, IMvigor210: NCT02108652, IMvigor211: NCT02302807, IMbrave150: NCT03434379, IMpassion130: NCT02425891.

https://bit.ly/3U1WZ1Y Burotto et al. IMscin001 Part 2. Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.
Efficacy was similar between arms

- PFS was considered mature, with 68% of events observed in both arms
- PFS and objective response rate were similar between arms

Median follow-up: 4.7 mo. Data cut-off: 26 Apr 2022. NE, non-estimable. *Objective response rate was defined as the proportion of patients with a complete response or partial response, as determined by the investigator according to Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST 1.1); no complete responses were recorded for either group. Overall survival and duration of response were immature at primary analysis.
Safety was similar between arms

- Imbalances in either direction were investigated and no safety signals were identified
- Infusion-related reactions occurred in 3.2% of patients in the IV arm and no patients in the SC arm
- Number of injection site reactions was low and mild in nature (mostly Grade 1)

Median follow-up: 4.7 mo. Data cut-off: 26 Apr 2022.
Immunogenicity was similar between arms

<table>
<thead>
<tr>
<th>Atezolizumab</th>
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<tbody>
<tr>
<td></td>
<td>SC</td>
<td>IV</td>
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<tr>
<td>Baseline prevalence of ADAs to atezolizumab</td>
<td></td>
<td></td>
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<tr>
<td>Baseline evaluable patients, n</td>
<td>241</td>
<td>115</td>
</tr>
<tr>
<td>Patients with a positive sample at baseline, n (%)</td>
<td>7 (2.9%)</td>
<td>3 (2.6%)</td>
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<tr>
<td>Incidence of treatment-emergent ADAs to atezolizumab</td>
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<td></td>
</tr>
<tr>
<td>Post-baseline evaluable patients</td>
<td>221</td>
<td>108</td>
</tr>
<tr>
<td>Patients positive for treatment-emergent ADAs, n (%)</td>
<td>43 (19.5%)</td>
<td>15 (13.9%)</td>
</tr>
<tr>
<td>Treatment-induced ADAs, n</td>
<td>42</td>
<td>15</td>
</tr>
<tr>
<td>Treatment-enhanced ADAs, n</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

- Treatment-emergent atezolizumab anti-drug antibodies for both arms were within the historical range across atezolizumab IV indications\(^a\)
- Prevalence and incidence of anti-rHuPH20 antibodies were within the historical range of other anti-cancer SC products (not shown)

Median follow-up: 4.7 mo. Data cut-off: 26 Apr 2022. ADAs, anti-drug antibodies; rHuPH20, recombinant human hyaluronidase.

Summary

- The study was positive, with both co-primary endpoints showing non-inferiority of exposure following atezolizumab SC vs atezolizumab IV
- Drug exposure following atezolizumab SC was similar to the exposure seen in other approved clinical studies for atezolizumab IV
- Efficacy, safety and immunogenicity were similar between arms and consistent with the known atezolizumab IV profile across indications
- These data support the use of atezolizumab SC as an alternative to atezolizumab IV, which has the potential to improve efficiencies in healthcare and increase convenience for both patients and healthcare professionals
Acknowledgements

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