IMpower010: exploratory analysis of tumour mutational burden and disease-free survival with adjuvant atezolizumab in NSCLC

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IMpower010 DFS by TMB status https://ter.li/yub395
Introduction and methods

• IMpower010 met its primary DFS endpoint, leading to approval of atezolizumab after complete resection and adjuvant chemotherapy for patients with stage II-IIIA PD-L1 TC ≥1% NSCLC (US, Japan and other countries), stage II-IIIA PD-L1 TC ≥50% NSCLC (Canada, UK, and other countries) and stage II-IIIA PD-L1 TC ≥50% NSCLC excluding those with EGFR/ALK+ disease (EU)

• Clinical response to PD-(L)1 inhibitors has been associated with high TMB

• We present an exploratory analysis of DFS by TMB status, including in PD-L1 expression subgroups

IMpower010 study design

• Completely resected stage IB-IIIA NSCLC per UICC/AJCC v7
  • Stage IB tumors ≥4 cm
  • ECOG PS of 0-1
  • Lobectomy/pneumonectomy
  • Tumor tissue for PD-L1 analysis

• 1-4 cycles cisplatin + pemetrexed, gemcitabine, docetaxel or vinorelbine

• No crossover

• Survival follow-up

R 1:1

Atezolizumab
1200 mg Q3W;
16 cycles (n=507)

BSC (n=498)

N=1005

Stratification factors
• Sex
• Histology
• Stage
• PD-L1 status per SP142

Primary endpoints
• Investigator-assessed DFS tested hierarchically

Key secondary endpoints
• OS in ITT (stage IB-IIIA)
• DFS in PD-L1 TC ≥50% (SP263) stage II-IIIA

• Whole exome sequencing data from patients with stage II-IIIA NSCLC was used to calculate TMB

• DFS was analysed using the primary analysis data (clinical cutoff date: 21 January 2021)

IMpower010: NCT02486718. AJCC, American Joint Committee on Cancer; BSC, best supportive care; DFS, disease-free survival; ITT, intent to treat; OS, overall survival; TC, tumour cell; TMB, tumour mutation burden; UICC, Union for International Cancer Control. 1. Felip, E et al Lancet 2021; 938; 1344-1357; 2. Niu, M et al Exp Hematol Oncol 2021; 10:18.
DFS by TMB status in the stage II-IIIA TMB-evaluable population

- Baseline characteristics of the stage II-IIIA TMB-evaluable population (n=549) were similar between treatment arms and consistent with those of the stage II-IIIA population\(^1\) (not shown)

<table>
<thead>
<tr>
<th>No. at risk</th>
<th>Months</th>
<th>DFS (%)</th>
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<tbody>
<tr>
<td>TMB-H: atezo</td>
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<tr>
<td>TMB-L: atezo</td>
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<tr>
<td>TMB-H: BSC</td>
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<tr>
<td>TMB-L: BSC</td>
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- In both treatment arms, improved DFS was observed in the TMB-H vs TMB-L populations
- DFS improvement with atezolizumab vs BSC was similar for the TMB-H and TMB-L populations

HR, hazard ratio; mDFS, median disease-free survival; NR, not reached; TMB-H, high tumour mutation burden; TMB-L, low tumour mutation burden. TMB-H (n=273) and TMB-L (n=276) were defined as TMB levels above or below the median (6.23 mutations/Mb), respectively. 1. Felip, E et al Lancet 2021; 938:1344-57.
DFS by PD-L1 status\(^a\) in the stage II-IIIA TMB-H subgroup

- 53% of patients in the PD-L1–positive subgroup and 45% of patients in the PD-L1–negative subgroup were TMB-H
- DFS improvement with atezolizumab was greater in the PD-L1–positive than in the PD-L1–negative subgroup

\(^a\) by the VENTANA SP263 PD-L1 assay
DFS by PD-L1 status\(^a\) in the stage II-IIIA TMB-L subgroup

- DFS improvement with atezolizumab was greater in the PD-L1–positive than in the PD-L1–negative subgroup

\(^a\) by the VENTANA SP263 PD-L1 assay
Conclusions

- This exploratory analysis of DFS by TMB status in patients with stage II-IIIA NSCLC from IMpower010 showed improved mDFS for the TMB-H vs TMB-L subgroups in both the atezolizumab and BSC arms.

- DFS improvement with atezolizumab vs BSC was similar for both the TMB-H and TMB-L stage II-IIIA populations, suggesting that TMB may not be predictive of a DFS treatment effect.

- Although subgroup analyses were limited by small sample sizes, DFS improvement with adjuvant atezolizumab was greater for PD-L1–positive than for PD-L1–negative subgroups, regardless of TMB status.
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