

## Effects of trilaciclib prior to chemotherapy ± atezolizumab on T-cell activation in patients with newly diagnosed extensive-stage small cell lung cancer

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### Introduction

Chemotherapy ± immunotherapy has demonstrated meaningful clinical benefit to patients (pts) with extensive-stage small cell lung cancer (ES-SCLC); however, chemotherapy-induced damage to the immune system can potentially diminish treatment efficacy. Trilaciclib (T) is an intravenous cyclin-dependent kinase 4/6 inhibitor that protects hematopoietic stem and progenitor cells from chemotherapy-induced damage (myeloprotection) and may directly enhance antitumor immunity. Here, we evaluated the immune effects of T in pts with ES-SCLC receiving T or placebo (P) prior to first-line etoposide plus carboplatin (E/C) or E/C plus atezolizumab (E/C/A) in two phase 2 clinical trials.

### Methods

Genomic DNA, extracted from peripheral blood mononuclear cells (baseline and on treatment) and archival tumor tissue (baseline), was analyzed using the immunoSEQ<sup>®</sup> Assay (Adaptive Biotechnologies). T-cell receptor (TCR) β CDR3 regions were amplified and sequenced to identify and quantitate the abundance of each unique TCRβ CDR3. Clonal frequencies were compared at baseline and on treatment, and statistical differences between T and P were determined by Wilcoxon rank sum test. Antitumor response was defined as complete/partial response.

### Results

In both studies, peripheral T-cell clonal expansion was greater among pts receiving T versus P. Among pts receiving E/C, those in the T/E/C group with an antitumor response had significantly more peripheral clonal expansion than P responders (median 23 vs 12 clones;  $P=0.04$ ) and a greater number of tumor-associated expanded clones ( $P=0.03$ ). T responders had more newly detected expanded peripheral clones compared with P responders (6 vs 1.5 clones;  $P=0.06$ ) and T nonresponders ( $P=0.02$ ). Increased clonal expansion in T responders was more evident after two cycles of E/C versus four, suggesting that T results in a rapid T-cell response.

Similarly, among pts receiving E/C/A, those in the T/E/C/A group with an antitumor response had significantly more peripheral clonal expansion than P responders (median 90 vs 43 clones;  $P=0.002$ ) and T nonresponders ( $P=0.016$ ). T responders also had more newly expanded peripheral clones compared with P responders (68 vs 11 clones;  $P=0.003$ ) and T nonresponders ( $P=0.02$ ). There was no increase in tumor-associated expanded clones among T responders compared to P responders, possibly due to the time point at which clonal expansion was assessed (after four cycles) or the addition of atezolizumab. Associations between peripheral and tumor-associated clonal expansion and survival will be presented.

**Conclusions**

The data suggest that, among pts treated with T/E/C or T/E/C/A, increased clonal expansion is associated with clinical response, indicating that T may enhance antitumor immunity in pts with ES-SCLC treated with chemotherapy.

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