Immune cell activation and DOM and Zimberelimab (ZIM) in Combination With Chemotherapy vs Pembrolizumab (PEMBRO) and Chemotherapy in Patients With Untreated Metastatic Non-Small Lung Cancer (mNSCLC) With No Actionable Gene Alterations

Delvys Rodriguez-Abreu, 1 Joaquim Bosch-Barrera, 2 Janelle E. Gray, 3 Myung Ju Ahn, 4 Melissa Johnson, 5 Xinwei Yu, 4 Saad Mohamed, 2 Xueying Chen, 4 Patrick Phuong, 4 Jongseok Kim, 4 Martin Reck 6

Hospital Universitaria IDIAR de Gran Canaria, Gran Canaria, Spain; 2Department of Medical Oncology, Catalan Institute of Oncology, Hospital Universitari Dr Josephina Girona, Girona, Spain; 3Moffitt Cancer Center, Tampa, FL, USA; 4Samsung Medical Center, Seoul, South Korea; 5Saint Cannon Research Institute, Nashville, TN, USA; 6Gilead Sciences, Inc., Foster City, CA, USA

References:
5. Immunity

The primary objective is to compare the effect of domvanalimab and zimberelimab in combination with chemotherapy relative to pembrolizumab (Group A vs Group B) on objective response rate and duration of response by BICR, safety, and quality of life.

Key Eligibility Criteria

Inclusion

- Patients aged ≥ 18 years with pathologically confirmed mNSCLC at the time of enrollment
- Measurable disease per RECIST v1.1 criteria by investigator assessment
- Documented negative test results for EGFR and ALK gene alterations in patients with non–NSCLC
- Adequate tumor tissue from locations not treated prior to biopsy to evaluate PD-L1 staining for randomization
- No prior systemic treatment for NSCLC
- ECCOG PS 0 or 1
- Adequate organ function

Exclusion

- Mixed SCLC and NSCLC histology; active second malignancy within 3 years prior to enrollment
- Prior treatment with any anti–PD-1, anti–PD-L1, or any other antibody targeting an immune checkpoint
- Known genetic alterations in ROS1, RET, TRK, BRAF, RET, or other actionable driver oncogenes with approved therapies
- Active autoimmune disease that required systemic treatment in past 2 years
- Uncontrolled CNS metastases and/or carcinomatous meningitis
- History of neocarcinogenesis after treatment with pembrolizumab
- Patients with brain metastases are excluded (except those with no active CNS disease at the time of enrollment or an interval of 4 weeks from the last treatment of brain metastases and brain MRI as clinically indicated)

Study Objectives

- The primary objective is to compare the effect of domvanalimab and zimberelimab in combination with chemotherapy relative to pembrolizumab in combination with chemotherapy (Group A vs Group B) on objective response rate and duration of response by BICR, safety, and quality of life.

Study Design

- STAR-121 is a phase 3, global, open-label randomized study evaluating the safety and efficacy of domvanalimab and zimberelimab plus chemotherapy versus pembrolizumab plus chemotherapy as first-line therapy for patients with mNSCLC with no EGFR or ALK aberrations or other known actionable gene alterations
- Approximately 120 patients will be randomized into 3 groups (A, B, or C) in a 4:4:1 ratio and stratified by baseline PD-L1 tumor proportion score (< 50% vs ≥ 50%), histology (squamous vs nonsquamous), and geographic region (Asia vs East Asia vs non-East Asia)

Study Endpoints

- The primary analysis of primary endpoints will be conducted using log-rank test stratified by randomization stratification factors between Group A and B
- A Cox regression model stratified by randomization stratification factors will be used to estimate hazard ratio and 95% CI

Table 1. Primary, secondary, and exploratory endpoints

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<th>Primary endpoints</th>
<th>Secondary endpoints</th>
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<td>Progression-free survival by BICR</td>
<td>Objective response rate by BICR</td>
<td>Safety</td>
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<td>Duration of response by BICR</td>
<td>Correlation of response with tumor and biomarkers</td>
<td>Patient-reported outcomes</td>
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Figure 2. STAR-121 study design

Figure 1. Checkpoint inhibition and the TIGIT pathway

Figure 3. STAR-121 study sites

As of Aug 8, 2023, the STAR-121 phase 3 study (NCT05502237) is currently enrolling patients globally in North America, South America, Europe, and Asia

For more information, please visit https://clinicaltrials.gov/ct2/show/NCT05502237