Background
• Pembrolizumab plus platinum-based chemotherapy has shown improved overall survival (OS), progression-free survival (PFS), and ORR versus chemotherapy alone regardless of tumor proportion score (TPS) in patients with advanced non-small-cell lung cancer (NSCLC).1

In an analysis of data pooled from 3 randomized studies, KEYNOTE-021 cohort G5, KEYNOTE-189, and KEYNOTE-407, pembrolizumab plus chemotherapy improved OS (hazard ratio [HR] 0.63; 95% CI, 0.56–0.70), PFS (HR, 0.57; 95% CI, 0.48–0.67), and ORR (20.1% vs 9.5% versus chemotherapy alone in patients with PD-L1–negative disease [TPS ≤1%]).2

Objectives
• Conduct an exploratory pooled analysis of pembrolizumab plus chemotherapy in East Asian patients with advanced or metastatic PD-L1–negative NSCLC.

Methods
Study Design, Patients, and Treatment
Table 1. Study Designs for the Studies Included in the Pooled Data Set

<table>
<thead>
<tr>
<th>Clinical Study</th>
<th>Study Design</th>
<th>Endpoints</th>
</tr>
</thead>
</table>
| KEYNOTE-021 cohort G5 | Randomized phase 2 | Pembrolizumab 200 mg Q3W plus paclitaxel/nab-paclitaxel Q3W plus carboplatin
| KEYNOTE-021 cohort G5 | Randomized phase 2 | Pembrolizumab 200 mg Q3W plus paclitaxel/nab-paclitaxel Q3W plus carboplatin
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| KEYNOTE-189 | Phase 3 | Pembrolizumab 200 mg Q3W plus pemetrexed Q3W
| KEYNOTE-189 | Phase 3 | Pembrolizumab 200 mg Q3W plus pemetrexed Q3W
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Assessments
PDL-1 expression was assessed centrally using the PD-L1 IHC pharmDex™ assay (Agilent Technologies, Carpinteria, CA).

• Tumor response was assessed per RECIST version 1.1 by blinded independent central review.

• Adverse events (AEs) were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.0 (version 4.03 for KEYNOTE-407).

• Safety was assessed in the pooled population of patients who received ≥1 dose of trial treatment.

The Kaplan-Meier method was used to estimate OS, PFS, ORR, and PFS2.

• H0% and 95% CI for OS, ORR, and PFS2 were assessed using a stratified Cox regression model with the stratum of the timing of treatment assignment.

• All analyses were descriptive only and not adjusted for multiplicity.

• The database cut-off dates were August 18, 2016 for KEYNOTE-021, August 26, 2020 for KEYNOTE-189 and KEYNOTE-189 Japan extension, and September 30, 2020 for KEYNOTE-407 and KEYNOTE-407 China extension.

Results
Patients
• Median time from randomization to data cutoff for the pooled analysis was 33.4 (range, 25.3–49.2) months.

Of 1630 total patients enrolled in the 5 randomized studies, 107 (7%) were enrolled in East Asia, had PD-L1–negative NSCLC, and were included in this pooled analysis.

• At data cutoff, 9 patients in the pembrolizumab plus chemotherapy group and 1 patient in the chemotherapy group alone had completed treatment.

• 1 patient from each treatment group had ongoing treatment at data cutoff.

Efficacy
Table 2. Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pembrolizumab + Chemotherapy</th>
<th>Chemotherapy Alone</th>
<th>ORR (95% CI), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), y</td>
<td>63 (21–91)</td>
<td>63 (21–90)</td>
<td>71.4 (57.8–82.7)</td>
</tr>
<tr>
<td>ECOG PS</td>
<td>2 (0–2)</td>
<td>2 (0–2)</td>
<td>43.1 (29.3–57.8)</td>
</tr>
</tbody>
</table>

Figure 1. Overall Survival

Figure 2. Progression-Free Survival

Figure 3. Progression-Free Survival 2 (PFS2)

Table 3. Tumor Response

<table>
<thead>
<tr>
<th>ORR (95% CI), %</th>
<th>Pembrolizumab + Chemotherapy</th>
<th>Chemotherapy Alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>71.4 (57.8–82.7)</td>
<td>43.1 (29.3–57.8)</td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Adverse Events

<table>
<thead>
<tr>
<th>AE, n (%)</th>
<th>Pembrolizumab + Chemotherapy</th>
<th>Chemotherapy Alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1–2</td>
<td>109 (92.9)</td>
<td>51 (94.2)</td>
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<tr>
<td>Grade 3–5</td>
<td>6 (5.2)</td>
<td>2 (3.9)</td>
</tr>
</tbody>
</table>

Figure 3. Progression-Free Survival 2 (PFS2)

Table 5. Immune-Mediated Adverse Events and Influenza Reactions

<table>
<thead>
<tr>
<th>AE, n (%)</th>
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Conclusions
Pembrolizumab plus chemotherapy provided clinically meaningful benefit versus chemotherapy alone in this pooled analysis of East Asian patients with PD-L1–negative advanced or metastatic NSCLC.

• Pembrolizumab plus chemotherapy prolonged OS, PFS, and PFS2 versus chemotherapy alone.

• ORR was higher with pembrolizumab plus chemotherapy versus chemotherapy alone.

• Pembrolizumab plus chemotherapy had manageable safety in these East Asian patients with PD-L1–negative NSCLC.

These results are consistent with the global phase 3 studies and support continued use of pembrolizumab plus chemotherapy as a standard of care therapy in patients with NSCLC without EGFR/ALK alterations, regardless of PD-L1 expression.

Acknowledgments
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References

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