Phase 1 Study of Cemiplimab, a Human Monoclonal Antibody to Programmed Death-1, in Japanese Advanced Malignancies: Results from the Dose Exploration Study

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Background

- Cemiplimab is a high-affinity, highly potent, human monoclonal antibody directed against programmed death-1 (PD-1) which blocks the interaction between PD-1 and its ligand.
- The two-part Phase 1 study (NCT03233139) evaluates safety, tolerability, and pharmacokinetics (PK) of cemiplimab in Japanese patients with advanced malignancies.
- In Part 1, two dosing regimens of cemiplimab were evaluated: patients in Part 1A were enrolled in 3 cohorts types.
- In Part 2, cemiplimab was in combination with pembrolizumab in patients with NSCLC.

Objectives

- The primary objectives of the study were to assess the safety, tolerability, and PK of cemiplimab in Japanese patients with advanced malignancies.
- The secondary objective was to assess the immunogenicity of cemiplimab in these patients.
- The exploratory objective of Part 1 was to evaluate tumor response to cemiplimab monotherapy in Japanese patients with advanced malignancies.

Methods

- In Part 1 of the study, patients with advanced malignancies were enrolled to receive cemiplimab 250 mg or 350 mg every 3 weeks (Q3W) intravenously (IV) for up to 156 weeks.
- Key inclusion criteria for Part 1 included Eastern Cooperative Oncology Group (ECOG) performance status of 0–1, adequate hematologic and hepatic function. Patients were excluded if they had received prior treatment for their malignancy.
- Patients were excluded from Part 1 of the study if they received prior treatment with agents targeting anti-PD-1/PD-L1 (1–2) pathways, had ongoing or recent autoimmune disease that required systemic immunosuppressive therapy, had an HIV infection, were pregnant, or had a history of significant hypersensitivity reactions.
- Tumor response was assessed using Response Evaluation Criteria In Solid Tumors version 1.1 (RECIST 1.1) by investigators in Part 1 after every 8 weeks, and by independent radiologic review of scans performed at least 8 weeks after the first dose in Part 2.

Results

Table 1. Baseline characteristics, disposition, and treatment exposure

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- Thirteen patients with advanced malignancies were enrolled. Patient baseline characteristics are presented in Table 1.
- The median number of administrations of cemiplimab was 4 (range 1–26) and the median duration of exposure was 13.1 weeks (range 3.0–80.9). The median duration of follow-up was 8.11 months (range: 2.0–18.8). The treatment-naive Japenese patients with advanced malignancies were enrolled.
- Prior cancer-related surgery, n (%): 6 (46.2%
- Prior cancer-related radiotherapy, n (%): 4 (30.8%
- The most common reason for treatment discontinuation was fatigue, hyperthyroidism, and increased aspartate aminotransferase (ALT).
- Each of the four grade 3–4 adverse events occurred once: autonomic crisis, death, hypothyroidism, and hypophysitis.

Clinical efficacy

- Recurrence per investigators assessment is summarized in Table 3.
- At the time of data cut-off, Part 1 of the study was fully enrolled. Eleven patients (84.6%) had confirmed response: 1 complete response and 10 partial responses.
- The median duration of follow-up at the time of data cut-off was 8.11 months (range: 2.0–18.8).
- No dose-limiting toxicities were observed.

Pharmacokinetics

- Cemiplimab serum exposure and PK parameters are comparable between Japanese and non-Japanese patients.

Conclusions

- Cemiplimab monotherapy showed an acceptable safety profile and antitumor activity in Japanese patients with advanced malignancies.
- The safety profile was comparable with those previously reported for cemiplimab and other anti-PD-1 agents.
- Cemiplimab 350 mg Q3W dosing regimen was selected for the expansion cohorts, Part 2 is open and enrolling patients with NSCLC in Japan.

References


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