European Commission Approves Pembrolizumab for First-Line Treatment of Patients with Metastatic NSCLC Whose Tumours Have High PD-L1 Expression with No EGFR or ALK Positive Tumour Mutations

Approval is based on data showing improved OS and PFS with pembrolizumab compared to chemotherapy

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On 31 January 2017, Merck, known as MSD outside the United States and Canada, announced that the European Commission has approved pembrolizumab (KEYTRUDA®), the anti-PD-1 therapy, for the first-line treatment of metastatic non-small cell lung cancer (NSCLC) in adults whose tumours have high PD-L1 expression (tumour proportion score [TPS] of 50% or more) with no EGFR or ALK positive tumour mutations. It is first anti-PD-1 therapy approved in Europe for previously untreated patients with metastatic NSCLC.

The approval is based on phase III data which demonstrated superior overall survival (OS) and progression-free survival (PFS) with pembrolizumab compared to chemotherapy, the current standard of care for this advanced NSCLC setting. The approval allows marketing of pembrolizumab in all 28 EU member states plus Iceland, Lichtenstein and Norway, at the approved dose of every three weeks until disease progression or unacceptable toxicity.

In August 2016, pembrolizumab was approved in Europe for previously-treated patients with locally advanced or metastatic NSCLC whose tumours express PD-L1 (TPS of 1% or more) and who have received at least one prior chemotherapy regimen.

The European Commission's approval is based on data from KEYNOTE-024, a randomised, open-label, phase III study evaluating pembrolizumab monotherapy at a fixed dose of 200 mg compared to standard of care platinum-containing chemotherapy (pemetrexed plus carboplatin, pemetrexed plus cisplatin,

gemcitabine plus cisplatin, gemcitabine plus carboplatin, or paclitaxel plus carboplatin) for the treatment of patients with both squamous and non-squamous metastatic NSCLC.

The study enrolled 305 patients who had not received prior systemic chemotherapy treatment for their metastatic disease and whose tumours had high PD-L1 expression with no EGFR or ALK aberrations. The primary endpoint was PFS; additional efficacy outcome measures were OS and objective response rate (ORR).

In the study, pembrolizumab reduced the risk of disease progression or death by 50% compared to chemotherapy (HR, 0.50 [95% CI, 0.37, 0.68]; p<0.001). The median PFS for pembrolizumab was 10.3 months (95% CI, 6.7-not reached) compared to 6.0 months for chemotherapy (95% CI, 4.2-6.2). At six months and 12 months, respectively, 62% and 48% of patients treated with pembrolizumab were alive and had no disease progression compared to 50% and 15% of those receiving chemotherapy.

Additionally, pembrolizumab resulted in a 40% reduction in the risk of death compared to chemotherapy (HR, 0.60 [95% CI, 0.41, 0.89]; p=0.005); this finding includes the 66 patients (43.7%) on the chemotherapy arm who crossed over in-study to receive pembrolizumab once their cancer had progressed; median OS was not reached in either group. The OS rate at 6 months and 12 months, respectively, was 80% and 70% in patients treated with pembrolizumab compared to 72% and 54% in those receiving chemotherapy.

Further, ORR was 45% for patients receiving pembrolizumab (95% CI, 37-53), including six complete responses, compared to 28% with chemotherapy (95% CI, 21-36), including one complete response.

The safety analysis supporting the European approval of pembrolizumab was based on 2,953 patients with advanced melanoma or NSCLC across four doses in studies KEYNOTE-001, KEYNOTE-002, KEYNOTE-010 and KEYNOTE-024 combined. The most common adverse reactions (≥10%) with pembrolizumab were fatigue (24%), rash (19%), pruritus (17%), diarrhoea (12%), nausea (11%) and arthralgia (10%). The majority of adverse reactions reported were of grade 1 or 2 severity. The most serious adverse reactions were immune-related adverse reactions and severe infusion-related reactions.

The news release of Merck & Co., includes “forward-looking statements”.