FDA Approves Pembrolizumab as First-Line Combination Therapy with Pemetrexed and Carboplatin for Metastatic Non-squamous NSCLC Irrespective of PD-L1 Expression

First approval for an anti-PD-1 therapy as a combination in metastatic non-squamous NSCLC

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- **Topic**: **Lung and other thoracic tumours** / **Cancer Immunology and Immunotherapy**

On 10 May 2017, Merck, known as MSD outside the US and Canada, announced that the US Food and Drug Administration (FDA) has approved pembrolizumab (KEYTRUDA®), the anti-PD-1 therapy, in combination with **pemetrexed** and **carboplatin** (pem/carbo), a commonly used chemotherapy regimen, for the first-line treatment of metastatic non-squamous non-small cell lung cancer (NSCLC), irrespective of PD-L1 expression. Under the FDA's accelerated approval regulations, this indication is approved based on tumour response rate and progression-free survival (PFS). Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

The approval was based on data from KEYNOTE-021, Cohort G1, in 123 previously untreated patients with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumour aberrations and irrespective of PD-L1 expression. In this trial, pembrolizumab plus pem/carbo demonstrated an objective response rate (ORR) that was nearly double the ORR of pem/carbo alone (55% [95% CI: 42, 68] compared to 29% [95% CI: 18, 41], respectively; all responses were partial responses). Among patients who received pembrolizumab plus pem/carbo, 93% had a duration of response of six months or more (range 1.4+ to 13.0+ months) compared to 81% who received pem/carbo alone (range 1.4+ to 15.2+ months). In addition, findings demonstrated an improvement in PFS (HR 0.53 [95% CI, 0.31-0.91; p=0.0205]), with a median PFS of 13.0 months (95% CI, 8.3-not estimable) for patients treated with pembrolizumab plus pem/carbo compared to 8.9 months (95% CI, 4.4-10.3) with pem/carbo alone.

Immune-mediated adverse reactions occurred with pembrolizumab including pneumonitis, colitis, hepatitis, endocrinopathies, and nephritis. Based on the

severity of the adverse reaction, pembrolizumab should be withheld or discontinued and corticosteroids administered when appropriate. Pembrolizumab can also cause severe or life-threatening infusion-related reactions. Monitor patients for signs and symptoms of infusion-related reactions; for grade 3 or 4 reactions, stop infusion and permanently discontinue pembrolizumab. Based on its mechanism of action, pembrolizumab can cause foetal harm when administered to a pregnant woman. Female patients of reproductive potential should be advised of the potential hazard to a foetus.

The combination therapy indication makes pembrolizumab an option for more patients. Pembrolizumab is the only anti-PD-1 antibody approved in the first-line setting as both monotherapy and combination therapy for appropriate patients with metastatic NSCLC. Pembrolizumab is approved as monotherapy in the first-line setting for patients with metastatic NSCLC whose tumours have high PD-L1 expression (tumour proportion score [TPS] ≥50%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumour aberrations. Pembrolizumab as monotherapy is also indicated for the second-line or greater treatment of patients with metastatic NSCLC whose tumours express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumour aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving pembrolizumab.

When administering pembrolizumab in combination with pem/carbo, pembrolizumab should be administered first prior to chemotherapy when given on the same day. In metastatic NSCLC, pembrolizumab is approved at a fixed dose of 200 mg administered as an intravenous infusion over 30 minutes every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression; pemetrexed and carboplatin should be administered according to their FDA-approved labels.

The news release of Merck & Co., Inc., Kenilworth, NJ, US includes “forward-looking statements”. These statements are based upon the current beliefs and expectations of the company’s management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful.