Oncologic Drugs Advisory Committee (ODAC) Meeting

[April 29, 2021]

NDA/BLA# 125514 S-042
Drug name: pembrolizumab
Applicant: Merck Sharp & Dohme Corp.

ERRATA

To the Combined FDA and Applicant ODAC Briefing Document

Errata to the Briefing Document:

Background from the Applicant:

The Applicant would like to provide the following clarification to the text in the briefing document. KEYNOTE-240 more strictly categorized viral hepatitis than KEYNOTE-224, based on input from investigators and our Scientific Advisory Committee. In KEYNOTE-240, those defined as HBV positive had positive hepatitis B surface antigen and/or detectable viral DNA, while those who were hepatitis C (HCV) positive were defined as having detectable HCV RNA and positive anti-HCV antibody. This is described in the primary KEYNOTE-240 publication (Finn et al, JCO 2020). In contrast, KEYNOTE-224 included seropositivity consistent with a prior or active infection with HBV or HCV. So, in addition to those included in KEYNOTE-240, KEYNOTE-224 included those who were anti-HBc positive, HBsAg negative and with undetectable viral load as HBV positive, and those who were HCV antibody positive but had undetectable viral load as HCV positive. Overall, viral hepatitis as a possible etiology for HCC was seen in a higher proportion of patients in KEYNOTE-240 than in KEYNOTE-224, if the KEYNOTE-224 definition is applied to KEYNOTE-240.

1. On Page 20 section 3.3.2.2.2 Demographics and Baseline Characteristics

   The etiology of underlying liver disease was non-viral for most participants, with 25.9% and 21.5% of participants in the pembrolizumab and placebo groups positive for HBV, respectively, and 15.5% and 15.6% positive for HCV, respectively.

Applicant would like to add the following clarification regarding HBV and HCV infection definition consistent with previously published data (Finn et al, JCO 2020) to the text. Therefore, replace the text above with:

> "The etiology of underlying liver disease was non-viral for most participants, with 25.9% and 21.5% of participants in the pembrolizumab and placebo groups positive for HBV, respectively, and 15.5% and 15.6% positive for HCV, respectively. **HBV infection in KEYNOTE-240 is defined as hepatitis B surface antigen positive and/ or detectable HBV DNA, and HCV infection defined as anti–hepatitis C antibody positive and detectable HCV RNA.**" Revision to add, '. HBV infection in KEYNOTE-240 is defined as hepatitis B surface antigen positive and/ or detectable HBV DNA, and HCV infection defined as anti– hepatitis C antibody positive and detectable HCV RNA'.

2. On Page 31, Section 3 Pembrolizumab Clinical Studies in HCC (The FDA's Position)

   Overall, both KEYNOTE-224 and KEYNOTE-240 enrolled patients with HCC with a variety of risk factors although a higher proportion of patients in KEYNOTE-240 had cirrhosis of non-viral etiology.

Based on the applicant's clarification above in #1, FDA agrees to replace the text above in #2 with the following:

> "Overall, both KEYNOTE-224 and KEYNOTE-240 enrolled patients with HCC with a variety of risk factors ~~although a higher proportion of patients in KEYNOTE-240 had cirrhosis of non-viral etiology~~."