FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Oncologic Drugs Advisory Committee (ODAC) Meeting
April 27-29, 2021

QUESTIONS

BLA 761034/S-018

TECENTRIQ (atezolizumab)

Applicant: Genentech, Inc.

INDICATION: In combination with paclitaxel protein-bound for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells (IC) of any intensity covering ≥ 1% of the tumor area), as determined by an FDA-approved test.

Given the following:

- Accelerated approval based on small progression free survival (PFS) with non-significant overall survival (OS)
- Benefit not verified in confirmatory trial in same disease setting
- Possible detriment in OS in confirmatory trial
- Alternative/ongoing trials are not in combination with nab-paclitaxel or in same disease setting

1. **VOTE:** Should the indication for the atezolizumab in combination with nab-paclitaxel for the treatment of adult patients with unresectable locally advanced or metastatic TNBC whose tumors are PDL-1+ be maintained on the market while additional trial(s) are conducted or completed?

    a. If your answer is "yes", please discuss after the vote, what ongoing or alternative trials may serve to confirm clinical benefit.

QUESTIONS (cont.)

BLA 125514/S-017

KEYTRUDA (pembrolizumab)

Applicant: Merck Sharp & Dohme Corp.

INDICATION: Treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy.

Given the following:

- Benefit not verified in confirmatory trial in same disease setting
- OS benefit and regular approval in 2nd line setting for pembrolizumab (KN-045)
- Treatment landscape is changed with OS benefit from alternative checkpoint inhibitor in maintenance setting (avelumab)
- Alternative/ongoing trials in different disease setting or population, or design does isolate the effect

1. **VOTE:** Should the indication for pembrolizumab for the first-line treatment of cisplatin-ineligible and carboplatin-ineligible patients with advanced/metastatic urothelial carcinoma be maintained pending conduct or completion of additional trial(s)?

    a. If your answer is “yes”, please discuss after the vote, what trials may serve to confirm clinical benefit including KN-045.

QUESTIONS (cont.)

BLA 761034/S-001

TECENTRIQ (atezolizumab)

Applicant: Genentech, Inc.

INDICATION: Treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy.

Given the following:

- Benefit not yet verified in confirmatory trial in same disease setting
- Benefit not verified in 2nd line metastatic setting and indication withdrawn
- Adjuvant trial did not meet primary endpoint
- Treatment landscape has changed with demonstrated OS benefit from alternative checkpoint inhibitor in maintenance setting

1. **VOTE:** Should the indication for atezolizumab for the first-line treatment of cisplatin-ineligible patients with advanced/metastatic urothelial carcinoma be maintained pending final OS results from IMvigor130?

QUESTIONS (cont.)

BLA 125514/S-024

KEYTRUDA (pembrolizumab)

Applicant: Merck Sharp & Dohme Corp.

INDICATION: Treatment of patients with recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test, with disease progression on or after two or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy.

Given the following:

- Low response rate in third-line setting [13% (11% in known microsatellite stable (MSS)]
- Treatment landscape has changed with nivolumab approval in the first-line setting based on improvement in OS
- Two trials with monotherapy comparisons in the first- and second-line settings did not confirm benefit
- Ongoing trials will not assess the monotherapy effect

1. **VOTE:** Should the indication for the monotherapy use of pembrolizumab in PD-L1 CPS ≥ 1 gastric/GEJ adenocarcinoma (third-line or greater) be maintained pending conduct or completion of additional trials?

    a. If your answer is "yes", please discuss after the vote what ongoing or alternative trials may serve to confirm clinical benefit.

QUESTIONS (cont.)

BLA 125514/S-042

KEYTRUDA (pembrolizumab)

Applicant: Merck Sharp & Dohme Corp.

INDICATION: Treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

Given the following:

- Low response rate of monotherapy in post-sorafenib setting
- Treatment landscape changed with OS benefit of alternative checkpoint inhibitor (atezolizumab) in combination with bevacizumab in the first-line setting
- Benefit not confirmed in the same (post-sorafenib) setting in KEYNOTE-240

1. **VOTE**: Should the indication for the monotherapy use of pembrolizumab in patients previously treated with sorafenib be maintained pending conduct or completion of additional trials?

    a. If your answer is "yes", please discuss after the vote what ongoing or alternative trials, including whether KEYNOTE-394 in the same setting, may serve to confirm clinical benefit.

QUESTIONS (cont.)

BLA 125554/S-041

OPDIVO (nivolumab)

Applicant: Bristol-Myers Squibb Company

INDICATION: As a single agent for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

Given the following:

- Low response rate of monotherapy in post-sorafenib setting.
- Treatment landscape changed with OS benefit of alternative checkpoint inhibitor (atezolizumab) in combination with bevacizumab in the first-line setting.
- Negative monotherapy trial versus sorafenib in the first-line setting.
- The combination indication for nivolumab and ipilimumab will be maintained. The response rate of combination therapy is higher than monotherapy.

1. **VOTE:** Should the indication for the monotherapy use of nivolumab in patients previously treated with sorafenib be maintained pending conduct or completion of additional trial(s)?

    a. If your answer is “yes”, please discuss after the vote what ongoing or alternative trials may serve to confirm clinical benefit.