Bristol Myers Squibb™

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NCCN Guidelines® Panel: Melanoma Panel

On behalf of Bristol Myers Squibb, we respectfully request the NCCN Melanoma Panel to review the data recently presented at American Society of Clinical Oncology (ASCO) 2021 Meeting on the use of OPDIVO® (nivolumab) plus YERVOY® (ipilimumab) for the treatment of patients with Melanoma.

Specific Changes:
We respectfully request the panel's consideration of the enclosed data and inclusion of an alternative regimen for nivolumab + ipilimumab (nivolumab 3 mg/kg Q3W + ipilimumab 1 mg/kg Q3W for 4 doses followed by nivolumab 480 mg Q4W) as a category 2A recommendation (ME-I, pg-1 of 8)

- We also request the panel to consider updating systemic therapy considerations for anti-PD-1/ipilimumab dosing and anti-PD-1 monotherapy dosing on pg. ME-J 1 of 4 to reflect this longer term data from this alternate regimen.

FDA Clearance:
OPDIVO® is indicated as an adjuvant treatment option for patients with melanoma with lymph node involvement or metastatic disease who have undergone complete resection.[1]

OPDIVO® is indicated as monotherapy or in combination with YERVOY® for the treatment of patients with unresectable or metastatic melanoma.[1,2]

YERVOY® is indicated as monotherapy for the treatment of patients with unresectable or metastatic melanoma in adults and pediatric patients (12 years and older).[2]

Rationale:

This data is being submitted in response to a standing request from the NCCN® for new data.

Previous Study Submission to NCCN ®:

- Please note clinical data from the CheckMate 511 trial was published in the Journal of Clinical Oncology on February 27th, 2019 and previously submitted to the NCCN® panel on March 08, 2019.

Study Summary:

CheckMate 511, is a phase 3b/4, randomized, double-blinded safety study, which evaluated two dosing regimens for previously untreated, unresectable or metastatic melanoma (nivolumab 3 mg/kg in combination with ipilimumab 1 mg/kg [NIVO3 + IPI1] and nivolumab 1 mg/kg in combination with ipilimumab 3 mg/kg [NIVO1 + IPI3].

The FDA-approved dosing regimen for the treatment of patients with unresectable or metastatic melanoma is nivolumab 1 mg/kg administered as an intravenous infusion over 30 minutes, followed by ipilimumab 3 mg/kg administered as an intravenous infusion over 90 minutes, every 3 weeks for a maximum of 4 doses or until unacceptable toxicity, whichever occurs earlier. After completing 4 doses of the combination therapy, administer nivolumab as a single agent, either as 240 mg every 2 weeks or 480 mg every 4 weeks, as an intravenous infusion over 30 minutes until disease progression or unacceptable toxicity[1]

Here we are submitting 3 year results from the CheckMate 511 study recently presented at the ASCO 2021 meeting. In the CheckMate 511 study, patients with previously untreated, unresectable stage III or stage IV melanoma were randomized 1:1 to NIVO3 + IPI1 or to NIVO1 + IPI3 and received 4 doses of the combination during the induction phase of the study. In the maintenance phase following combination therapy, patients in both groups received open-label NIVO 480 mg every 4 weeks for a maximum of 24 months or until unacceptable toxicity or disease progression, whichever came first. The primary endpoint compared the incidence of grade 3–5 treatment-related adverse events (TRAEs) between treatment groups. Secondary efficacy endpoints included objective response rate (ORR), progression-free survival (PFS), and overall survival (OS), though the study was not designed or powered to demonstrate non-inferiority for these outcomes. With 3-years minimum follow-up, the median follow-up was 44.4 months with NIVO3 + IPI1 and 43.9 months with NIVO1 + IPI3.[3]

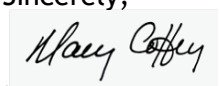
In the primary analysis of the study, the incidence of grade 3–5 TRAEs (primary endpoint) was lower in the NIVO3 + IPI1 group than in the NIVO1 + IPI3 group, occurring in 34% and 48% of patients, respectively. The difference in grade 3–5 TRAE rates between the groups was −14.4% (95% CI, −24.5 to −4.3). TRAEs leading to treatment discontinuation occurred in 43 patients (24%) in the NIVO3 + IPI1 group and 60 patients (34%) in the NIVO1 + IPI3 group. The most common TRAEs in both groups were diarrhea, fatigue, and pruritus. Although not designed or powered to demonstrate non-inferiority for secondary efficacy endpoints, ORR was 47.2% and 52.8% for NIVO3 + IPI1 and NIVO1 + IPI3, respectively. 3-year PFS rates for NIVO3 + IPI1 and NIVO1 + IPI3 were 38% and 43%, respectively. 3-year OS rates for NIVO3 + IPI1 and NIVO1 + IPI3 were 59% and 61%, respectively. With 3 years follow-up, this study provides important information regarding the benefit–risk profile of both dosing regimens of NIVO + IPI in patients with advanced melanoma.[3]

As part of this submission, the following resources are enclosed for your review:

1. Product Information, OPDIVO® (nivolumab) injection for intravenous infusion. Bristol Myers Squibb, Princeton, NJ. May 2021.
2. Product Information, YERVOY® (ipilimumab) injection for intravenous infusion. Bristol Myers Squibb, Princeton, NJ. May 2021.
3. Lebbé C, Meyer N, Mortier L, et al. Two dosing regimens of nivolumab plus ipilimumab for advanced melanoma: 3-year results of CheckMate 511 trial. Presented at the American Society of Clinical Oncology (ASCO); Annual Meeting; June 4-8, 2021.

Thank you for your consideration of this request.

Sincerely,



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