Submitted by:
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NCCN Guidelines® Panel: Melanoma

Dear Panel Members,

On behalf of Bristol-Myers Squibb Company, I respectfully request the Melanoma Panel to consider including YERVOY® (ipilimumab) in Section ME-4 of the NCCN Guidelines in the adjuvant treatment of fully resected Stage III melanoma.

FDA Clearance: The FDA-approved YERVOY® (ipilimumab) on October 28, 2015 for the adjuvant treatment of patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy.[1] Ipilimumab was also approved on March 25, 2011 for the treatment of unresectable or metastatic melanoma.

Rationale for Proposed Change: In support of the requested change, FDA approval was based on a Phase 3 registrational randomized trial (CA184-029) in patients with resected Stage IIIA (lymph node >1mm) or Stage IIIB/C (no in-transit metastases) melanoma metastatic to lymph nodes only. Enrollment required complete and adequate resection of melanoma with full lymphadenectomy within 12 weeks prior to randomization.[2]
BMS Study Number CA184-029: In this Phase 3 study, patients were randomized 1:1 to receive 4 doses of either ipilimumab 10 mg/kg (n=475) or placebo (n=476) Q3W, followed by treatment Q12W at the same dose up to 3 years until documented disease recurrence or unacceptable toxicity.[2]

- Primary endpoint, independent review committee assessed median recurrence-free survival (RFS) was 26.1 months (95% CI: 19.3, 39.3) vs 17.1 months (95% CI: 13.4, 21.6) in ipilimumab vs placebo groups at median follow-up of 2.74 years (HR=0.75; 95% CI:0.64,0.90; *P*=0.0013); 3-year RFS rates were 46.5% (95% CI: 41.5, 51.3) vs 34.8% (95% CI: 30.1, 39.5) in ipilimumab vs placebo groups, respectively. Analysis of overall survival will occur at the time of 491 deaths.
- Grade 3 and 4 immune-related AEs (irAEs) due to study drug were reported by 37% and 6% of ipilimumab patients vs 2% and <1% of placebo patients, respectively; 82-95% of Grade 2-4 irAEs, excluding endocrine irAEs, in the ipilimumab group resolved to baseline or Grade 1 in median time of 4 to 8 weeks following protocol-specified treatment algorithms. Five deaths were attributable to study treatment in the ipilimumab group.

The following resources are included for your review in support of this proposed inclusion/change:

[1] YERVOY Prescribing Information
[2] Eggermont AM, Chiarion-Sileni V, Grob JJ, et al. Adjuvant ipilimumab versus placebo after complete resection of high-risk stage III melanoma (EORTC 18071): a randomised, double-blind, phase 3 trial. *Lancet Oncol*. 2015 May;16(5):522-30.

We acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of this/these publications. Thank you for your consideration of this request.

Sincerely,

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