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NCCN Guidelines Panel: Melanama

On behalf of Genentech, I respectfully request the NCCN Melanoma Guideline Panel to review the enclosed data for Zelboraf™ (vemurafenib) for the treatment of patients with unresectable or metastatic melanoma.

Specific Changes: Consider the available data on the use of Zelboraf for the treatment of patients with unresectable or metastatic melanoma for your updating purposes.

FDA Clearance: On August 17, 2011, Genentech, a member of the Roche Group, received FDA approval for Zelboraf for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation, as detected by an FDA approved test.[1] In addition, the companion diagnostic test, cobas® 4800 BRAF V600 Mutation Test, was also approved on August 17, 2011. Please refer to the enclosed Zelboraf prescribing information for the full FDA-approved indication and safety information.

Rationale: The FDA approval of Zelboraf is based on results from two clinical studies (BRIM3 and BRIM2) in people with BRAF V600E mutation-positive, unresectable or metastatic melanoma, as detected by the cobas 4800 BRAF V600 Mutation Test.[2] BRIM3 is a randomized, open-label, controlled, multicenter, Phase III study that compared Zelboraf to dacarbazine chemotherapy in 675 patients with previously untreated BRAF V600E mutation-positive, unresectable or metastatic melanoma.[1,3] Compared with dacarbazine, Zelboraf significantly improved both overall survival and progression-free survival, the co-primary endpoints of the study; the respective hazard ratios were 0.44 (95% CI: 0.33-0.59; p<0.0001) and 0.26 (95% CI: 0.20-0.33; p<0.0001).[1] BRIM2 is a single-arm, multicenter, open-label Phase II study that enrolled 132 patients with previously treated BRAF V600E mutation-positive unresectable or metastatic melanoma.[1,4,5] In BRIM2, Zelboraf was associated with an overall response rate of 52% (95% CI: 43-61%).[1]

The following enclosures are included for your review (copyright-paid where applicable):

- Chapman PB, Hauschild A, Robert C, et al. Improved survival with vemurafenib in melanoma with BRAF V600E mutation. N Engl J Med. 2011;364(26):2507-2516.
- Ribas A, Kim K, Schuchter L, et al. BRIM 2: An open-label, multicenter phase II study of vemurafenib (PLX4032, RG7204) in previously treated patients with BRAF V600E mutation-positive metastatic melanoma. J Clin Oncol 2011;29. ASCO Abstract #8509.
- Ribas A, Kim K, Schuchter L, et al. BRIM 2: An open-label, multicenter phase II study of vemurafenib (PLX4032, RG7204) in previously treated patients with BRAF V600E mutation-positive metastatic melanoma. ASCO Oral Presentation #8509. Presented at: ASCO Annual Meeting; June 3-7, 2011; Chicago, IL.

- Zelboraf™ Prescribing Information

Cited References

1. Zelboraf™ [prescribing information]. Genentech, a Member of Roche. South San Francisco, CA. July 2011.
2. FDA approves Zelboraf (vemurafenib) and companion diagnostic for BRAF mutation-positive metastatic melanoma, a deadly form of skin cancer. [press release]. South San Francisco: Genentech, A Member of the Roche Group; July 17, 2011. Accessed July 17, 2011, from http://www.gene.com/gene/news/press-releases/display.do?method=detail&id=13567.
3. Chapman PB, Hauschild A, Robert C, et al. Improved survival with vemurafenib in melanoma with BRAF V600E mutation. N Engl J Med. 2011;364(26):2507-2516.
4. Ribas A, Kim K, Schuchter L, et al. BRIM 2: An open-label, multicenter phase II study of vemurafenib (PLX4032, RG7204) in previously treated patients with BRAF V600E mutation-positive metastatic melanoma. J Clin Oncol 2011;29. ASCO Abstract #8509.
5. Ribas A, Kim K, Schuchter L, et al. BRIM 2: An open-label, multicenter phase II study of vemurafenib (PLX4032, RG7204) in previously treated patients with BRAF V600E mutation-positive metastatic melanoma. ASCO Oral Presentation #8509. Presented at: ASCO Annual Meeting; June 3-7, 2011; Chicago, IL.