



## Effective Health Care Treatment of Malignant Melanoma

### Results of Topic Selection Process & Next Steps

The nomination, Treatment of Malignant Melanoma with Immunotherapy, is a topic with many interventions. Current guidance related to checkpoint inhibitors, including Ipilimumab, is extensive, and includes five sets of NICE technology appraisal guidelines (2012, 2014, two in 2015, and 2016), two systematic reviews (2012 and 2015), and one in-progress systematic review examining the efficacy and safety of PD-1 and PD-L1 inhibition agents for advanced melanoma (anticipated completion date: August 2015). Related to cytokines, a 2006 cancer care guideline on single agent interleukin-2 for malignant melanoma was reaffirmed in 2010, a 2013 Cochrane systematic review examined the disease-free survival and overall survival effects of interferon alpha as adjuvant treatment for people with high-risk cutaneous melanoma, and a 2010 systematic review evaluated the development, pharmacologic properties, safety profile and current clinical efficacy of recombinant IL-21. In addition, an in-process Cochrane review will compare all systemic therapies for the treatment of metastatic cutaneous melanoma, including immunotherapy that includes cytokines, checkpoint inhibitors, and immunochemotherapy. Due to the existing evidence reviews, no further activity will be taken on checkpoint inhibitors and cytokines.

Research examining cancer vaccines, oncolytic virus therapy, adoptive T-cell therapy, and monoclonal antibodies is too limited at this time for consideration for a systematic review. No further activity will be taken for this topic.

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- National Institute for Health and Care Excellence (NICE). Ipilimumab for previously untreated advanced (unresectable or metastatic) melanoma. London (UK): National Institute for Health and Care Excellence (NICE) 2014:Jul. 52 p. (Technology appraisal guidance; no. 319).
- National Institute for Health and Clinical Excellence (NICE). Ipilimumab for previously treated advanced (unresectable or metastatic) melanoma. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Dec. 45 p. (Technology appraisal guidance; no. 268).
- National Institute for Health and Clinical Excellence (NICE). Nivolumab for treating advanced (unresectable or metastatic) melanoma. London (UK): National Institute for Health and Clinical Excellence (NICE); 2016 Feb. 35p. (Technology appraisal guidance; no. 384).

- National Institute for Health and Care Excellence (NICE). Pembrolizumab for advanced melanoma not previously treated with ipilimumab. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Nov 25. 33 p. (Technology appraisal guidance; no. 366).
- National Institute for Health and Care Excellence (NICE). Pembrolizumab for treating advanced melanoma after disease progression with ipilimumab. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Oct 7. 33 p. (Technology appraisal guidance; no. 357).

## Topic Description

**Nominator(s):** Patient with melanoma

**Nomination Summary:** The nominator was treated with ipilimumab and unfortunately suffered significant side effects with no delay in the progression of the disease. The nominator states that he/she now has two significant conditions. The nominator feels that had he/she known about the statistics on the incidence of a person getting the side effects from this drug, he/she may have chosen not to take the drug. The nominator asserts that research on this topic would assist him/her and similar patients in making an informed decision on the harms and benefits of immunotherapy on malignant melanoma and whether he/she should take the prescribed drugs.

**Key Questions from Nominator:**

1. What are the harms and benefits of treatment of malignant melanoma with immunotherapy such as ipilimumab?
2. Although the nominator refers to ipilimumab in the nomination, we also considered other immunotherapies in addition to ipilimumab after consulting with our clinical reviewer.

## Considerations

- The topic meets EHC Program selection criteria. (For more information, see <http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/>.)
- Melanoma is a type of cancer with a poor prognosis. The 5-year survival rate is around 97% for stage IA melanoma and about 15%-20% for stage IV melanoma.<sup>1</sup> Advances in medical treatment options for metastatic melanoma now include immunotherapy in addition to surgery and conventional cytotoxic chemotherapies. The nominator has specifically focused on ipilimumab, which is an immunotherapy drug used to treat advanced melanoma. However, challenges still remain concerning optimization of dosing and avoidance of toxicities associated with the use of immunotherapy drugs. Future research is also needed to establish how combination treatments of immunotherapy drugs with conventional agents can be effective for the treatment of melanoma. Evidence-based knowledge of the evolving immunological treatments for melanoma will help clinicians and patients to understand the risks and benefits of these treatments and assist clinicians and their patients in making an informed decision about the most appropriate treatment options to consider.
- Five NICE Technology Appraisal Guidelines were published between 2012-2016 examined various treatments for melanoma and made recommendations such as ipilimumab for previously untreated advanced melanoma,<sup>2</sup> ipilimumab for previously treated advanced melanoma,<sup>3</sup> nivolumab as monotherapy,<sup>4</sup> pembrolizumab for treating advanced melanoma that had not been previously treated with ipilimumab,<sup>5</sup> and pembrolizumab for treating advanced malignant melanoma that had been previously treated with ipilimumab but had progressed.<sup>6</sup>
- A new AHRQ systematic review would have only a limited impact at this time, given the recent systematic reviews and guidelines on this topic. Additionally, there are several ongoing systematic reviews related to this topic.

## References

1. American Cancer Society. What are the survival rates for melanoma skin cancer, by stage? American Cancer Society, 2016. Accessed on February 3, 2016. <http://www.cancer.org/cancer/skincancer-melanoma/detailedguide/melanoma-skin-cancer-survival-rates>.
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6. National Institute for Health and Care Excellence (NICE). Pembrolizumab for treating advanced melanoma after disease progression with ipilimumab. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Oct 7. 33 p. (Technology appraisal guidance; no. 357).