Breakfast with the Investigators:
Systemic Management of Melanoma

CME Information

TARGET AUDIENCE

This program is intended for medical oncologists, hematology-oncology fellows and other allied healthcare professionals involved in the treatment of melanoma.

OVERVIEW OF ACTIVITY

Despite increased awareness and extensive attempts to publicize risk factors and screening, current estimates suggest that 76,380 men and women will be diagnosed with melanoma and 10,130 individuals will die from the disease in 2016 within the United States alone. Because of its cutaneous location and its high metastatic potential, management of melanoma remains a major challenge. Clinicians are routinely faced with the task of identifying which patients are appropriate candidates for adjuvant therapy and with what specific intervention, and until recently treatments for advanced disease had been relatively limited in their overall effectiveness. However, unprecedented new strides have been made in defining molecular mechanisms of critical importance to melanoma development, progression and metastasis. Similarly, increased understanding of the pathophysiology behind melanoma's traditional chemoresistance has resurrected a keen research focus on therapeutic immune system modulation. In this regard, pivotal presentations over the past several years have reflected the success of these efforts, paving the way for the first new FDA-endorsed treatment options for patients with metastatic melanoma in more than a decade and the expanded role of novel targeted agents in the treatment of advanced disease. All of these new therapeutic options have been heralded as major breakthroughs by the melanoma community but have challenged practicing clinicians to quickly understand how best to safely integrate them into current management algorithms.

These video proceedings from a CME symposium held during the 2016 ASCO Annual Meeting feature discussions with leading researchers with an expertise in melanoma regarding actual cases from their practices and the published data that drive clinical decision-making for patients in those and diverse other situations. By providing information on the latest research developments and their potential application to routine practice, this activity is designed to assist medical oncologists, hematology-oncology fellows and other healthcare providers with the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

- Appreciate the recent FDA indication for ipilimumab as adjuvant therapy, and identify patients for whom this therapeutic approach should be considered after surgical removal of primary melanoma.
- Consider age, performance status and other disease-related factors to guide the selection of first- and later-line therapy for patients with metastatic BRAF wild-type melanoma.
- Appraise clinical trial evidence to identify the role of available immunotherapeutic approaches in the management of metastatic BRAF mutation-positive melanoma.
- Recall existing and emerging research demonstrating the effect of combining BRAF and MEK inhibitors for patients with BRAF mutation-positive metastatic melanoma, and use this information to guide treatment planning.
- Recognize immune-related adverse events associated with immune checkpoint inhibitors, and offer supportive management strategies to minimize and/or ameliorate these side effects.
- Recall new data with investigational agents and strategies demonstrating promising activity in melanoma, and discuss ongoing trial opportunities with eligible patients.

ACCREDITATION STATEMENT

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CREDIT DESIGNATION STATEMENT

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Successful completion of this CME activity enables the participant to earn up to 1.25 MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the

CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Please note, this program has been specifically designed for the following ABIM specialty: **medical oncology**.

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HOW TO USE THIS CME ACTIVITY

This CME activity consists of a video component. To receive credit, the participant should watch the video, complete the Post-test with a score of 80% or better and fill out the Educational Assessment and Credit Form located at **ResearchToPractice.com/ASCOMelanoma16/CME**.

CONTENT VALIDATION AND DISCLOSURES

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FACULTY — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

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Hardware/Software Requirements:
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 7 or later, Firefox 3.0 or later, Chrome, Safari 3.0 or later
Adobe Flash Player 10.2 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

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Select Publications

A phase III, randomized, double-blind, placebo-controlled study of vemurafenib (RO5185426) adjuvant therapy in patients with surgically resected, cutaneous BRAF mutant melanoma at high risk for recurrence. NCT01667419

A randomized phase III trial of dabrafenib + trametinib followed by ipilimumab + nivolumab at progression versus ipilimumab + nivolumab followed by dabrafenib + trametinib at progression in patients with advanced BRAFV600 mutant melanoma. NCT02224781

COMBI-AD: A phase III randomized double blind study of dabrafenib (GSK2118436) in combination with trametinib (GSK1120212) versus two placebos in the adjuvant treatment of high-risk BRAF v600 mutation-positive melanoma after surgical resection. NCT01682083

Dummer R et al. **LOGIC2: Phase 2, multi-center, open-label study of sequential encorafenib/binimetinib combination followed by a rational combination with targeted agents after progression, to overcome resistance in adult patients with locally-advanced or metastatic BRAF V600 melanoma.** *Proc ESMO* 2015;**Abstract 3310**.

Flaherty K et al. **NEMO: A phase 3 trial of binimetinib (MEK162) versus dacarbazine in patients with untreated or progressed after first-line immunotherapy unresectable or metastatic *NRAS*-mutant cutaneous melanoma.** *Proc ASCO* 2014;**Abstract TPS9102**.

Goldberg SB et al. **Activity and safety of pembrolizumab in patients with metastatic non-small cell lung cancer with untreated brain metastases.** *Proc ASCO* 2015;**Abstract 8035**.

González-Cao M et al. **Other targeted drugs in melanoma.** *Ann Transl Med* 2015;3(18):266.

Hodi FS et al. **Imatinib for melanomas harboring mutationally activated or amplified KIT arising on mucosal, acral, and chronically sun-damaged skin.** *J Clin Oncol* 2013;31(26):3182-90.

Inman S. **Binimetinib improves PFS in NRAS-mutant melanoma.** Available at: **http://www.onclive.com/web-exclusives/binimetinib-improves-pfs-in-nras-mutant-melanoma**.

Johnson DB et al. **Ipilimumab therapy in patients with advanced melanoma and preexisting autoimmune disorders.** *JAMA Oncol* 2016;2(2):234-40.

Johnson DB et al. **Impact of NRAS mutations for patients with advanced melanoma treated with immune therapies.** *Cancer Immunol Res* 2015;3(3):288-95.

Johnson GL et al. **Molecular pathways: Adaptive kinome reprogramming in response to targeted inhibition of the BRAF-MEK-ERK pathway in cancer.** *Clin Cancer Res* 2014;20(10):2516-22.

Kluger HM et al. **Safety and activity of pembrolizumab in melanoma patients with untreated brain metastases.** *Proc ASCO* 2015;**Abstract 9009**.

Larkin J et al. **Combined nivolumab and ipilimumab or monotherapy in untreated melanoma.** *N Engl J Med* 2015;373(1):23-34.

Long GV et al. **Pembrolizumab (pembro) plus ipilimumab (ipi) for advanced melanoma: Results of the KEYNOTE-029 expansion cohort.** *Proc ASCO* 2016;**Abstract 9506**.

Long GV et al. **Baseline and postbaseline characteristics associated with treatment benefit across dabrafenib and trametinib registration pooled data.** *Proc Society for Melanoma Research Congress* 2015.

Long GV et al. **Combined BRAF and MEK inhibition versus BRAF inhibition alone in melanoma.** *N Engl J Med* 2014;371(20):1877-88.

Long G et al. **NEMO: A phase 3 trial of binimetinib (MEK162) versus dacarbazine in patients with advanced NRAS-mutant melanoma who are untreated or have progressed on or after immunotherapy.** *Cancer Res* 2015;75(14);**Abstract B16**.

Ma Q et al. **Prevalence of autoimmune comorbidities in patients with metastatic melanoma in the US.** *Proc ASCO* 2016;**Abstract 9529**.

Menzies AM et al. **Anti-PD-1 therapy in patients with advanced melanoma and preexisting autoimmune disorders (AD) or major toxicity with ipilimumab (IPI).** *Proc ASCO* 2016;**Abstract 9515**.

Robert C et al. **Improved overall survival in melanoma with combined dabrafenib and trametinib.** *N Engl J Med* 2015;372(1):30-9.

Select Publications

Van Herpen C et al. **A phase 1b/2 study of ribociclib (LEE011; CDK4/6 inhibitor) in combination with binimetinib (MEK162; MEK inhibitor) in patients with NRAS-mutant melanoma.** *Proc European Cancer Conference* 2015;**Abstract 3300**.

Van Herpen C et al. **Overall survival and biomarker results from a phase 2 study of MEK1/2 inhibitor binimetinib (MEK162) in patients with advanced NRAS-mutant melanoma.** *Proc ESMO* 2014;**Abstract LBA35**.