Melanoma and Nonmelanoma Skin Cancers

TARGET AUDIENCE

This activity is intended for medical oncologists, hematology-oncology fellows and other healthcare providers involved in the treatment of melanoma and nonmelanoma skin cancers.

OVERVIEW OF ACTIVITY

Melanoma and nonmelanoma skin cancers (basal cell carcinoma [BCC] and cutaneous squamous cell cancer [SCC]), taken together, likely represent the most prevalent form of human cancer. Fortunately, the vast majority of skin cancers present as minimally invasive BCC and SCC and, as such, are highly curable with local treatment alone. However, in rare instances, these characteristically indolent lesions do progress and necessitate systemic intervention with the support of limited randomized clinical evidence. In contrast, malignant melanoma is the most aggressive form of skin cancer with a predilection toward distant metastases even when identified in the clinically early stages of disease. Thus, melanoma and nonmelanoma skin cancers are quite distinct entities, each posing unique challenges to the oncology community. This program uses a review of recent publications and presentations, faculty cases and Q&A to assist medical oncologists, hematology-oncology fellows and other healthcare providers with the formulation of up-to-date clinical management strategies for skin cancer.

LEARNING OBJECTIVES

- Provide a summary of the scientific rationale and research results that support the activity of novel chemotherapeutic and targeted agents and immunotherapeutic strategies in patients with melanoma, and appraise their clinical applicability.
- Consider the oncogenic mutations that play an important role in the etiology and pathogenesis of melanoma when formulating treatment strategies using biologic therapies.
- Recognize the cutaneous and other commonly observed adverse events associated with BRAF-targeted therapy for patients with advanced-stage melanoma, and employ management strategies to minimize and/or manage these side effects.
- Recognize immune-related adverse events associated with anti-CTLA-4 antibody therapy, and offer supportive management strategies to minimize and/or manage these side effects.
- Assess recent Phase III data evaluating *nab* paclitaxel versus dacarbazine in patients with treatment-naïve metastatic melanoma, and revisit the role of cytotoxic chemotherapy in the management of the disease.
- Explain the fundamental role of hedgehog signaling in BCC pathogenesis and treatment.
- Recall the design of ongoing clinical trials in advanced melanoma and nonmelanoma skin cancer, and consent or refer eligible patients for study participation.

ACCREDITATION STATEMENT

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Research To Practice designates this enduring material for a maximum of 1.5 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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 75% or better and fill out the Educational Assessment and Credit Form located at ResearchToPractice.com/RTPTV2013/Archive/CME.

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reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

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

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Advisory Committee: Boehringer Ingelheim Pharmaceuticals Inc, Eisai Inc, Millennium: The Takeda Oncology Company, Novartis Pharmaceuticals Corporation, Sanofi; **Consulting Agreements:** Genentech BioOncology, GlaxoSmithKline, Momenta Pharmaceuticals Inc, Otsuka Pharmaceutical Co Ltd, Roche Laboratories Inc; **Contracted Research:** Novartis Pharmaceuticals Corporation, Sanofi.

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MODERATOR — Dr Love is president and CEO of Research To Practice, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Algeta US, Allos Therapeutics, Amgen Inc, ArQule Inc, Astellas, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, Biodesix Inc, Biogen Idec, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Daiichi Sankyo Inc, Dendreon Corporation, Eisai Inc, EMD Serono Inc, Foundation Medicine Inc, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, Incyte Corporation, Lilly USA LLC, Medivation Inc, Merck, Millennium: The Takeda Oncology Company, Mundipharma International Limited, Novartis Pharmaceuticals Corporation, Onyx Pharmaceuticals Inc, Prometheus Laboratories Inc, Regeneron Pharmaceuticals, Sanofi, Seattle Genetics, Spectrum Pharmaceuticals Inc and Teva Oncology.

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This activity is supported by educational grants from Bristol-Myers Squibb Company, Celgene Corporation, Genentech BioOncology and Prometheus Laboratories Inc.

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

Last review date: April 2013

Expiration date: April 2014

Select Publications

A phase II, multicenter, open-label, three-cohort trial evaluating the efficacy and safety of vismodegib (GDC-0449) in operable basal cell carcinoma (BCC). NCT01201915

A pilot study to investigate the off label use of vismodegib as an adjuvant to surgery for basal cell carcinoma tumors (BCC). NCT01631331

A single arm, open-label, phase II, multicentre study, to assess the safety of vismodegib (GDC-0449) in patient with locally advanced or metastatic basal cell carcinoma (BCC). NCT01367665

Ally M et al. **Vismodegib as an adjuvant to surgery for basal cell carcinomas.** *Proc American Academy of Dermatology* 2012. **No Abstract Available**

Atkins MB et al. **High-dose recombinant interleukin 2 therapy for patients with metastatic melanoma: Analysis of 270 patients treated between 1985 and 1993.** *J Clin Oncol* 1999;17(7):2105-16.

Chapman PB et al. **Updated overall survival (OS) results for BRIM-3, a phase III randomized, open-label, multicenter trial comparing BRAF inhibitor vemurafenib (vem) with dacarbazine (DTIC) in previously untreated patients with BRAFV600E-mutated melanoma.** *Proc ASCO* 2012;**Abstract 8502**.

Chapman PB et al. **Improved survival with vemurafenib in melanoma with BRAF V600E mutation.** *N Engl J Med* 2011;364(26):2507-16.

Chapman PB et al. **Phase III randomized, open-label, multicenter trial (BRIM3) comparing BRAF inhibitor vemurafenib with dacarbazine (DTIC) in patients with ^{V600E}BRAF-mutated melanoma.** *Proc ASCO* 2011;**Abstract LBA4**.

Hersh E et al. **Phase 3, randomized, open-label, multicenter trial of *nab*-paclitaxel (*nab*-P) vs dacarbazine (DTIC) in previously untreated patients with metastatic malignant melanoma (MMM).** *Proc Society for Melanoma Research* 2012. **No Abstract Available**

Hodi FS et al. **Clinical activity and safety of anti-PD-1 (BMS-936558, MDX-1106) in patients with advanced melanoma (MEL).** *Proc ASCO* 2012;**Abstract 8507**.

Hodi FS et al. **Improved survival with ipilimumab in patients with metastatic melanoma.** *N Engl J Med* 2010;363(8):711-23.

Joseph RW et al. **Correlation of NRAS mutations with clinical response to high-dose IL-2 in patients with advanced melanoma.** *J Immunother* 2012;35(1):66-72.

Karia PS et al. **Cutaneous squamous cell carcinoma: Estimated incidence of disease, nodal metastasis, and deaths from disease in the United States, 2012.** *J Am Acad Dermatol* 2013;pii:S0190-9622(12)02329-8;[Epub ahead of print].

McArthur GA et al. **Efficacy of vemurafenib in BRAFV600K mutation-positive melanoma disease: Results from the Phase 3 clinical study BRIM3.** *Proc Society for Melanoma Research* 2012. **No Abstract Available**

ML28485: Phase 2B single-site, open-label, nonrandomized study evaluating efficacy of oral vismodegib in various histologic subtypes (infiltrative/morpheaform, nodular and superficial) of high risk and/or locally advanced basal cell carcinoma. NCT01700049

Placebo-controlled, double blind study to assess efficacy and safety of oral vismodegib for the treatment of basal cell carcinoma preceding excision by Mohs micrographic surgery (MMS). NCT01543581

Robert C et al. **Ipilimumab plus dacarbazine for previously untreated metastatic melanoma.** *N Engl J Med* 2011;364(26):2517-26.

Sekulic A et al. **Efficacy and safety of vismodegib in advanced basal-cell carcinoma.** *N Engl J Med* 2012;366(23):2171-9.

Topalian SL et al. **Safety, activity, and immune correlates of anti-PD-1 antibody in cancer.** *N Engl J Med* 2012;366(26):2443-54.