The Current and Future Role of Immunotherapies in the Management of Genitourinary Cancers

CME Information

TARGET AUDIENCE

This activity has been designed to meet the educational needs of medical and radiation oncologists, urologists and other allied healthcare professionals.

OVERVIEW OF ACTIVITY

The past several years have seen an explosion in the emergence of new potential therapies that leverage the natural ability of the human body to attack and treat cancer. Known as immune-mediated therapies or cancer immunotherapies, these promising treatments are taking center stage at medical conferences and generating excitement all over the world. Although they may be diverse in terms of their biology and current clinical management, genitourinary (GU) cancers — prostate cancer, renal cell carcinoma (RCC), bladder cancer, et cetera — are unified in their potential as fertile ground for immunologic therapy and research and have been at the forefront of both past and current efforts in this regard. Not surprisingly, with the many exciting advances rapidly occurring both within the field of GU tumors and elsewhere, a number of vexing questions and clinical challenges are emerging simultaneously.

These video proceedings from a CME symposium held during the 2016 Genitourinary Cancers Symposium feature discussions with leading investigators in the management of prostate, renal and bladder cancer regarding actual patient cases and related clinical research findings. By providing information on important immunotherapeutic developments, this activity will assist medical and radiation oncologists, urologists and other healthcare professionals to address existing management uncertainties and determine the current and future roles of immunotherapeutic interventions for patients with common GU cancers.

LEARNING OBJECTIVES

- Develop a basic understanding of the human immune response, and identify the underlying mechanisms by which various tumor types evade this process to proliferate and grow.
- Analyze the biologic basis for various immunotherapeutic strategies designed to boost an individual's immune response to combat cancer.
- Effectively apply evidence-based research findings in the determination of best-practice sequencing of available systemic therapies for patients with advanced prostate cancer, bladder cancer and RCC.
- Compare and contrast the mechanisms of action, efficacy and safety/toxicity of approved and investigational immunotherapies for the treatment of prostate cancer, RCC, bladder cancer and other GU tumors to determine the current and/or potential utility of these agents in clinical practice.
- Appraise the rationale for and clinical data with investigational anti-PD-1 and anti-PD-L1 antibodies for metastatic RCC and bladder cancer.
- Recognize immune-related adverse events and other common side effects associated with approved and developmental immunotherapeutic agents in order to offer supportive management strategies.
- Recall the design of ongoing clinical trials evaluating novel immunotherapeutic approaches, and counsel appropriately selected patients with GU cancers about trial availability and participation.

ACCREDITATION STATEMENT

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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/GUCancers16/Immunotherapy/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

Charles G Drake, MD, PhD

A phase 1b, open-label, multicenter, multidose, dose-escalation study of MDX-1106 in subjects with selected advanced or recurrent malignancies. NCT00730639

Drake CG et al. **Survival, safety, and response duration results of nivolumab (anti-PD-1; BMS-936558; ONO-4538) in a phase I trial in patients with previously treated metastatic renal cell carcinoma (mRCC): Long-term patient follow-up.** *Proc ASCO* 2013;**Abstract 4514**.

IMvigor210: A Phase II, multicenter, single-arm study of atezolizumab (MPDL3280A) in patients with locally advanced or metastatic urothelial bladder cancer. NCT02108652

Thomas Powles, MBBS, MRCP, MD

Herbst RS et al. **Predictive correlates of response to the anti-PD-L1 antibody MPDL3280A in cancer patients.** *Nature* 2014;515(7528):563-7.

Hoffman-Censits JH et al. **IMvigor 210, a phase II trial of atezolizumab (MPDL3280A) in platinum-treated locally advanced or metastatic urothelial carcinoma (mUC).** Genitourinary Cancers Symposium 2016;**Abstract 355**.

Kohrt H et al. **Intratumoral characteristics of tumor and immune cells at baseline and on-treatment correlated with clinical responses to MPDL3280A, an engineered antibody against PD-L1.** *Proc SITC* 2013;**Abstract O12**.

Powles T et al. **Immune biomarkers associated with clinical benefit from atezolizumab (MPDL3280a; anti-PD-L1) in advanced urothelial bladder cancer (UBC).** *Proc SITC* 2015;**Abstract P83**.

Powles T et al. **MPDL3280A (anti-PD-L1) treatment leads to clinical activity in metastatic bladder cancer.** *Nature* 2014;515(7528):558-62.

Rosenberg JE et al. **Atezolizumab in patients (pts) with locally-advanced or metastatic urothelial carcinoma (mUC): Results from a pivotal multicenter phase II study (IMvigor 210).** *Proc ECC* 2015;**Abstract 21LBA**.

Tumeh PC et al. **PD-1 blockade induces responses by inhibiting adaptive immune resistance.** *Nature* 2014;515(7528):568-71.

Susan F Slovin, MD, PhD

Antonarakis ES et al. **Sipuleucel-T (sip-T)–induced proliferative CD8+ T-cell responses to immunizing and secondary antigens.** Genitourinary Cancers Symposium 2016;**Abstract 165**.

Antonarakis ES et al. **Immune responses and clinical outcomes in STAND, a randomized phase 2 study evaluating optimal sequencing of sipuleucel-T (sip-T) and androgen deprivation therapy (ADT) in biochemically-recurrent prostate cancer (BRPC) after local therapy failure.** *Proc ASCO* 2015;**Abstract 5030**.

Kantoff PW et al; IMPACT Study Investigators. **Sipuleucel-T immunotherapy for castration-resistant prostate cancer.** *N Engl J Med* 2010;363(5):411-22.

Petrylak DP et al. **STRIDE, a randomized, phase 2, open-label study of sipuleucel-T with concurrent vs sequential enzalutamide in metastatic castration-resistant prostate cancer (mCRPC).** *Proc ESMO* 2014;**Abstract 774P**.

Vanderlugt CL, Miller SD. **Epitope spreading in immune-mediated diseases: Implications for immunotherapy.** *Nat Rev Immunol* 2002;2(2):85-95.

Elizabeth R Plimack, MD, MS

A phase III, open-label, randomized study of atezolizumab (anti-PD-L1 antibody) in combination with bevacizumab versus sunitinib in patients with untreated advanced renal cell carcinoma. NCT02420821

A randomized, controlled phase III study investigating IMA901 multipeptide cancer vaccine in patients receiving sunitinib as first-line therapy for advanced/metastatic renal cell carcinoma. NCT01265901

ADAPT: An international phase 3 randomized trial of autologous dendritic cell immunotherapy (AGS-003) plus standard treatment of advanced renal cell carcinoma. NCT01582672

CheckMate 214: A phase 3, randomized, open-label study of nivolumab combined with ipilimumab versus sunitinib monotherapy in subjects with previously untreated, advanced or metastatic renal cell carcinoma. NCT02231749

Hammers HJ et al. **Expanded cohort results from CheckMate 016: A phase I study of nivolumab in combination with ipilimumab in metastatic renal cell carcinoma (mRCC).** *Proc ASCO* 2015;**Abstract 4516**.

Select Publications

Motzer RJ et al. **Nivolumab for metastatic renal cell carcinoma (mRCC): Results of a randomized, dose-ranging phase II trial.** *Proc ASCO* 2014;**Abstract 5009**.

Sharma P et al. **CheckMate 025: A randomised, open-label, phase III study of nivolumab (NIVO) versus everolimus (EVE) in advanced renal cell carcinoma (RCC).** *Proc ECC* 2015;**Abstract LBA3**.

David F McDermott, MD

Amos SM et al. **Autoimmunity associated with immunotherapy of cancer.** *Blood* 2011;118(3):499-509.

Hammers HJ et al. **Expanded cohort results from CheckMate 016: A phase I study of nivolumab in combination with ipilimumab in metastatic renal cell carcinoma (mRCC).** *Proc ASCO* 2015;**Abstract 4516**.

Johnson DB et al. **Therapeutic advances and treatment options in metastatic melanoma.** *JAMA Oncol* 2015;1(3):380-6.

Motzer RJ et al. **Nivolumab versus everolimus in advanced renal-cell carcinoma.** *N Engl J Med* 2015;373(19):1803-13.

Ribas A. **Tumor immunotherapy directed at PD-1.** *N Engl J Med* 2012;366(26):2517-9.

Weber JS et al. **Management of immune-related adverse events and kinetics of response with ipilimumab.** *J Clin Oncol* 2012;30(21):2691-7.