What Urologists Want to Know:
Addressing Current Questions and Controversies Regarding the Role of Immune Checkpoint Inhibitors in the Management of Bladder Cancer

CME Information

TARGET AUDIENCE

This activity has been designed to meet the educational needs of urologists and other allied healthcare professionals involved in the treatment of bladder cancer.

OVERVIEW OF ACTIVITY

The American Cancer Society estimates that 79,030 new cases of bladder cancer will be diagnosed in 2017 and 16,870 deaths will be attributable to this disease. Bladder cancer incidence and death rates in women have actually seen a slight decline, whereas for men, while incidence rates are also falling, mortality rates have remained relatively stable. The disease remains the fourth most common cancer in the United States and is 3 times as likely to be found in men as in women. Although bladder cancer is a heterogeneous collection of diseases, more than 90% of patients are diagnosed with its most common form, urothelial carcinoma, and the remaining 10% present with less prevalent phenotypes, including squamous, small cell and adenocarcinomas. For those patients with metastatic lesions beyond the bladder, cure is not attainable, and therapeutic options for these individuals have historically been limited to cytotoxic approaches, which confer marginal benefits. However, this trend appears to have shifted due to the success of various immune checkpoint inhibitors in the treatment of advanced or metastatic disease. This success will likely create an environment in which expert perspectives and ongoing discussion are needed to help tease out whether these agents are more similar than they are different or if, in fact, one may be more appropriate for use over the others.

These video proceedings from a live CME symposium feature discussions with leading investigators in the management of bladder cancer regarding actual patient cases and related clinical research findings. By providing information on important therapeutic developments, this activity will assist medical and radiation oncologists, urologists and other healthcare professionals to address existing management uncertainties for patients with bladder cancer.

LEARNING OBJECTIVES

- Develop a basic understanding of the human immune response, and identify the underlying mechanisms by which various tumors evade this process to proliferate and grow.
- Analyze the biologic basis for the development of immune checkpoint inhibitors designed to boost an individual's immune response for the treatment of urothelial bladder carcinoma (UBC).
- Compare and contrast the mechanisms of action, efficacy and safety of approved and investigational immune checkpoint inhibitors for the treatment of advanced UBC to determine the current and/or potential utility of each in clinical practice.
- Recognize immune-related adverse events and other common side effects associated with approved and developmental checkpoint inhibitors used in the management of UBC, and offer supportive management strategies to minimize and/or manage these side effects.
- Review ongoing research to assist in the identification of biomarkers, tumor characteristics and other clinical features that are indicative of response to immune checkpoint inhibitors in patients with UBC.
- Describe ongoing clinical trials evaluating novel applications of immune checkpoint inhibitors alone or in combination with other systemic approaches, and counsel appropriately selected patients with UBC about trial availability and potential 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 80% or better and fill out the Educational Assessment and Credit Form located at **ResearchToPractice.com/AUABladder17/CME**.

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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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MODERATOR — **Dr Love** 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, Acerta Pharma, Adaptive Biotechnologies, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Ariad Pharmaceuticals Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Baxalta Inc, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, CTI BioPharma Corp, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, Halozyme Inc, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Kite Pharma Inc, Lexicon Pharmaceuticals Inc, Lilly, Medivation Inc, a Pfizer Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Natera Inc, Novartis, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro Inc, Teva Oncology and Tokai Pharmaceuticals Inc.

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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

Sia Daneshmand, MD

Grossman HB et al. **Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer.** *N Engl J Med* 2003;349(9):859-66.

Meeks JJ et al. **A systematic review of neoadjuvant and adjuvant chemotherapy for muscle-invasive bladder cancer.** *Eur Urol* 2012;62(3):523-33.

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von der Maase H et al. **Long-term survival results of a randomized trial comparing gemcitabine plus cisplatin, with methotrexate, vinblastine, doxorubicin, plus cisplatin in patients with bladder cancer.** *J Clin Oncol* 2005;23(21):4602-8.

von der Maase H et al. **Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin, and cisplatin in advanced or metastatic bladder cancer: Results of a large, randomized, multinational, multicenter, phase III study.** *J Clin Oncol* 2000;18(17):3068-77.

Zargar-Shoshtari K et al. **A multi-institutional analysis of outcomes of patients with clinically node positive urothelial bladder cancer treated with induction chemotherapy and radical cystectomy.** *J Urol* 2016;195(1):53-9.

Charles G Drake, MD

Dunn GP et al. **Cancer immunoediting: From immunosurveillance to tumor escape.** *Nat Immunol* 2002;3(11):991-8.

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

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Zhang L et al. **Intratumoral T cells, recurrence, and survival in epithelial ovarian cancer.** *N Engl J Med* 2003;348(3):203-13.

Jonathan E Rosenberg, MD

Balar AV et al. **Atezolizumab as first-line treatment in cisplatin-ineligible patients with locally advanced and metastatic urothelial carcinoma: A single-arm, multicentre, phase 2 trial.** *Lancet* 2017;389(10064):67-76.

Bellmunt J et al. **Pembrolizumab as second-line therapy for advanced urothelial carcinoma.** *N Engl J Med* 2017;376(11): 1015-26.

Powles T et al. **A phase 3 study of first-line durvalumab (MEDI4736) ± tremelimumab versus standard of care (SoC) chemotherapy (CT) in patients (pts) with unresectable stage IV urothelial bladder cancer (UBC): DANUBE.** *Proc ASCO* 2016; **Abstract TPS4574**.

Rosenberg JE et al. **Atezolizumab in patients with locally advanced and metastatic urothelial carcinoma who have progressed following treatment with platinum-based chemotherapy: A single-arm, multicentre, phase 2 trial.** *Lancet* 2016; 387(10031):1909-20.

Sharma P et al. **Nivolumab in metastatic urothelial carcinoma after platinum therapy (CheckMate 275): A multicentre, single-arm, phase 2 trial.** *Lancet Oncol* 2017;18(3):312-22.

Sharma P et al. **Efficacy and safety of nivolumab monotherapy in metastatic urothelial cancer: Results from the phase I/II CheckMate 032 study.** *Proc ASCO* 2016;**Abstract 4501**.

Elizabeth R Plimack, MD, MS

Eigentler TK et al. **Diagnosis, monitoring and management of immune-related adverse drug reactions of anti-PD-1 antibody therapy.** *Cancer Treat Rev* 2016;45:7-18.

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

Khan SA et al. **Prevalence of autoimmune conditions among patients with lung cancer: Implications for immunotherapy treatment options.** *Proc ASCO* 2016;**Abstract 9039**.

Kyi C et al. **Ipilimumab in patients with melanoma and autoimmune disease.** *J Immunother Cancer* 2014;2(1):35.

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Michot JM et al. **Immune-related adverse events with immune checkpoint blockade: A comprehensive review.** *Eur J Cancer* 2016;54:139-48.

Weber JS, Drakeman DL. **Safety profile of nivolumab monotherapy: A pooled analysis of patients with advanced melanoma.** *J Clin Oncol* 2016;34(24):2937-8.

Robert S Svatek, MD

An open label, single-arm, phase 2 study of neoadjuvant pembrolizumab (MK-3475) before cystectomy for patients with muscle-invasive urothelial bladder cancer. NCT02736266

Phase II trial of atezolizumab in BCG-unresponsive non-muscle invasive bladder cancer. NCT02844816