Oncology Investigators Provide Perspectives on the Prevention and Management of Tumor Lysis Syndrome (Video Program)

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists, hematology-oncology fellows, physician assistants and other allied healthcare professionals involved in the treatment of hematologic cancers.

OVERVIEW OF ACTIVITY

Tumor lysis syndrome (TLS) is an oncologic emergency characterized by the rapid onset of hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia and/or acute renal failure. Despite the relatively rare incidence of TLS, the clinical landscape of this syndrome changed dramatically with the April 11, 2016 FDA approval of the Bcl-2 inhibitor venetoclax for relapsed/refractory chronic lymphocytic leukemia (CLL) harboring the del(17p) chromosomal abnormality. Given the availability of venetoclax and emerging evidence of its antitumor activity in non-del(17p) CLL and other cancer types, it is likely that concern over TLS will greatly increase in general oncology practice. To bridge the gap between research and patient care, this program uses one-on-one discussions with leading oncology and nephrology investigators to help overcome clinician uncertainties and alleviate current practice gaps surrounding the prevention and management of this potentially devastating complication of effective cancer treatment.

LEARNING OBJECTIVES

- Understand the pathophysiology of TLS, recognize its disease- and treatment-related risk factors and establish an evidence-based approach for the prevention and management of this oncologic emergency.
- Identify patients at increased risk for TLS or its complications (eg, those with increased baseline uric acid, the elderly, those with renal or cardiac dysfunction), and institute appropriate treatment modifications, including early intervention with rasburicase.
- Formulate an approach to manage TLS-associated metabolic abnormalities — hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia and concomitant renal insufficiency — including recognition of when nephrology consultation is warranted.
- Appraise the risk-benefit profiles of chemoimmunotherapy treatments and targeted agents and regimens for CLL, and develop management strategies for the unique toxicities associated with recently approved therapeutics.
- Recognize the increased risk of TLS in patients with CLL treated with venetoclax, and implement approaches to ensure that appropriate administration protocols are followed to mitigate the risk of this potentially fatal toxicity.

ACCREDITATION INFORMATION FOR PHYSICIANS

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Research To Practice designates this enduring material for a maximum of 2 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

ACCREDITATION INFORMATION FOR PHYSICIAN ASSISTANTS

AAPA accepts certificates of participation for educational activities certified for *AMA PRA Category 1 Credit* from organizations accredited by ACCME or a recognized state medical society. PAs may receive a maximum of 2 Category 1 Credits for completing this activity.

AMERICAN BOARD OF INTERNAL MEDICINE (ABIM) — MAINTENANCE OF CERTIFICATION (MOC)

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 2 Medical Knowledge 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**.

Personal information and data sharing: Research To Practice aggregates deidentified user data for program-use analysis,

program development, activity planning and site improvement. We may provide aggregate and deidentified data to third parties, including commercial supporters. We do not share or sell personally identifiable information to any unaffiliated third parties or commercial supporters. Please see our privacy policy at **ResearchToPractice.com/Privacy-Policy** for more information.

HOW TO USE THIS CME ACTIVITY

This CME activity consists of a video component. To receive credit, the participant should review the CME information, 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/TumorLysis17/Video/CME**. The corresponding audio program is available as an alternative at **ResearchToPractice.com/TumorLysis17**.

CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess conflicts of interest with faculty, planners and managers of CME activities. Conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the RTP scientific staff and an external, independent physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

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

William G Wierda, MD, PhD
DB Lane Cancer Research Distinguished Professor
Department of Leukemia
Division of Cancer Medicine
The University of Texas MD Anderson Cancer Center
Houston, Texas

Consulting Agreement: Sanofi Genzyme; **Contracted Research:** AbbVie Inc, Acerta Pharma, Genentech BioOncology, Gilead Sciences Inc, GlaxoSmithKline, Juno Therapeutics, Karyopharm Therapeutics, Kite Pharma Inc, miRagen Therapeutics Inc, Novartis, Pharmacyclics LLC, an AbbVie Company, Sunesis Pharmaceuticals Inc.

Amit Lahoti, MD
Associate Professor
Department of Nephrology
Division of Internal Medicine
The University of Texas MD Anderson Cancer Center
Assistant Professor
Department of Internal Medicine
Baylor College of Medicine
Instructor, Division of Internal Medicine
The University of Texas Medical School at Houston
Houston, Texas

No relevant conflicts of interests to disclose.

EDITOR — **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, 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, administered by Janssen Scientific Affairs LLC, 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, Pfizer Inc, 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.

RESEARCH TO PRACTICE STAFF AND EXTERNAL REVIEWERS — The scientific staff and reviewers for Research To Practice have no relevant conflicts of interest to disclose.

This educational activity contains discussion of published and/or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantor.

This activity is supported by an educational grant from AbbVie Inc.

Hardware/Software Requirements:
A high-speed Internet connection

A monitor set to 1280 x 1024 pixels or more

Internet Explorer 11 or later, Firefox 56 or later, Chrome 61 or later, Safari 11 or later, Opera 48 or later

Adobe Flash Player 27 plug-in or later

Adobe Acrobat Reader

(Optional) Sound card and speakers for audio

Last review date: November 2017

Expiration date: November 2018

Select Publications

A phase II study of venetoclax and ibrutinib in patients with chronic lymphocytic leukemia (CLL). NCT02756897

Alakel N et al. **Prevention and treatment of tumor lysis syndrome, and the efficacy and role of rasburicase.** *Onco Targets Ther* 2017;10:597-605.

Caravaca-Fontán F et al. **Tumor lysis syndrome in solid tumors: Clinical characteristics and prognosis.** *Med Clin (Barc)* 2017;148(3):121-4.

Cheson BD et al. **Tumor lysis syndrome in chronic lymphocytic leukemia with novel targeted agents.** *Oncologist* 2017;[Epub ahead of print].

Criscuolo M et al. **Tumor lysis syndrome: Review of pathogenesis, risk factors and management of a medical emergency.** *Expert Rev Hematol* 2016;9(2):197-208.

Davids MS et al. **Phase I first-in-human study of venetoclax in patients with relapsed or refractory non-Hodgkin lymphoma.** *J Clin Oncol* 2017;35(8):826-33.

Durani U et al. **In-hospital outcomes of tumor lysis syndrome: A population-based study using the National Inpatient Sample.** *Oncologist* 2017;[Epub ahead of print].

Feng X et al. **Efficacy and cost of single-dose rasburicase in prevention and treatment of adult tumour lysis syndrome: A meta-analysis.** *J Clin Pharm Ther* 2013;38(4):301-8.

Garimella PS et al. **Impact of dialysis requirement on outcomes in tumor lysis syndrome.** *Nephrology (Carlton)* 2017; 22(1):85-8.

Howard SC et al. **Tumor lysis syndrome in the era of novel and targeted agents in patients with hematologic malignancies: A systematic review.** *Ann Hematol* 2016;95(4):563-73.

Jeon YW et al. **Effectiveness of single-dose rasburicase in patients with lymphoid malignancies at a high risk for tumor lysis syndrome.** *Clin Lymphoma Myeloma Leuk* 2017;17(9):595-603.

Jones GL et al; British Committee for Standards in Haematology. **Guidelines for the management of tumour lysis syndrome in adults and children with haematological malignancies on behalf of the British Committee for Standards in Haematology.** *Br J Haematol* 2015;169(5):661-71.

Lacava V et al. **Nephro-oncology: A link in evolution.** *Ren Fail* 2015;37(8):1260-6.

Lameire N et al. **Acute kidney injury in critically ill cancer patients: An update.** *Crit Care* 2016;20(1):209.

Ñamendys-Silva SA et al. **Tumor lysis syndrome in the emergency department: Challenges and solutions.** *Open Access Emerg Med* 2015;7:39-44.

Roberts AW et al. **Targeting BCL2 with venetoclax in relapsed chronic lymphocytic leukemia.** *N Engl J Med* 2016;374(4): 311-22.

Seymour JF et al. **Venetoclax plus rituximab in relapsed or refractory chronic lymphocytic leukaemia: A phase 1b study.** *Lancet* Oncol 2017;18(2):230-40.

Seymour JF. **Effective mitigation of tumor lysis syndrome with gradual venetoclax dose ramp, prophylaxis, and monitoring in patients with chronic lymphocytic leukemia.** *Ann Hematol* 2016;95(8):1361-2.

Standard chemoimmunotherapy (FCR/BR) versus rituximab + venetoclax (RVe) versus obinutuzumab (GA101) + venetoclax (GVe) versus obinutuzumab + ibrutinib + venetoclax (GIVe) in fit patients with previously untreated chronic lymphocytic leukemia (CLL) without del(17p) or TP53 mutation (GAIA). NCT02950051

Stilgenbauer S et al. **Venetoclax in relapsed or refractory chronic lymphocytic leukaemia with 17p deletion: A multicentre, open-label, phase 2 study.** *Lancet Oncol* 2016;17(6):768-78.

Study of ibrutinib combined with venetoclax in subjects with mantle cell lymphoma (SYMPATICO). NCT03112174

Titus-Rains KS et al. **Ibrutinib-associated tumor lysis syndrome in chronic lymphocytic leukemia/small lymphocytic lymphoma and mantle cell lymphoma: A case series and review of the literature.** *J Oncol Pharm Pract* 2017;[Epub ahead of print].

Turtle CJ et al. **Durable molecular remissions in chronic lymphocytic leukemia treated with CD19-specific chimeric antigen receptor-modified T cells after failure of ibrutinib.** *J Clin Oncol* 2017;35(26):3010-20.

Usami E et al. **Analysis of the incidence of tumor lysis syndrome in patients with hematological malignancies treated with rasburicase.** *Mol Clin Oncol* 2017;6(6):955-9.

Wilson FP, Berns JS. **Onco-nephrology: Tumor lysis syndrome.** *Clin J Am Soc Nephrol* 2012;7(10):1730-9.