2014 Chabner Colloquium
Collaboration in Cancer Trials

Featuring a thoughtful look at the potential for collaboration between academia and industry

Monday–Tuesday, November 10–11, 2014

The Liberty Hotel
215 Charles Street
Boston, Massachusetts
# 2014 Chabner Colloquium: Collaboration in Cancer Drug Trials

**Meeting Agenda**

**Monday, November 10, 2014**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker(s)</th>
<th>Institution(s)</th>
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<tbody>
<tr>
<td>8:00-8:15AM</td>
<td>Welcome and Introduction</td>
<td>Martin J. Murphy, DMedSc, PhD</td>
<td>Convener, Society for Translational Oncology</td>
</tr>
<tr>
<td>8:15-9:00AM</td>
<td>New Insights into Metabolic Regulation of Cancer Growth</td>
<td>Nabeel Bardeesy, MD</td>
<td>Massachusetts General Hospital Cancer Center, Harvard Medical School</td>
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<td>9:00-9:45AM</td>
<td>The Histone Deacetylase SIRT6: Linking Epigenetics to Cancer Metabolism</td>
<td>Raul Mostoslavsky, MD, PhD</td>
<td>Massachusetts General Hospital Cancer Center, Harvard Medical School</td>
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<tr>
<td>9:45-10:30AM</td>
<td>Improving the Treatment of Prostate Cancer</td>
<td>Johann S. de Bono, MB ChB, FRCP, MSc, PhD</td>
<td>The Institute of Cancer Research, The Royal Marsden</td>
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<tr>
<td>10:30-10:45AM</td>
<td>Beverage Break</td>
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<tr>
<td>10:45-11:45AM</td>
<td>Immunotherapy</td>
<td>Steven A. Rosenberg, MD, PhD</td>
<td>National Cancer Institute</td>
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<tr>
<td>11:45AM-12:30PM</td>
<td>Buffet Lunch: 5th Floor Rotunda</td>
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<tr>
<td>1:30-2:15PM</td>
<td>Hematological Malignancies</td>
<td>Timothy A. Graubert, MD</td>
<td>Massachusetts General Hospital Cancer Center, Harvard Medical School</td>
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<td>2:15-3:00PM</td>
<td>Understanding Myelodysplastic Syndromes (MDS)</td>
<td>Benjamin L. Ebert, MD</td>
<td>Brigham and Women’s Hospital, Harvard Medical School</td>
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<td>3:00-3:45PM</td>
<td>Pathogenesis and Therapy of IDH/TET-Mutant Myeloid Malignancies</td>
<td>Ross L. Levine, MD</td>
<td>Memorial Sloan Kettering Cancer Center</td>
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<td>3:45-4:00PM</td>
<td>Beverage Break</td>
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<tr>
<td>4:00-4:15PM</td>
<td>Junior Faculty Forum</td>
<td>Aditya Bardia, MD, MPH</td>
<td>Massachusetts General Hospital Cancer Center, Harvard Medical School</td>
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<td>4:15-4:30PM</td>
<td>Molecular Interrogation of Circulating Tumor Cells for Drug Development</td>
<td>Aaron N. Hata, MD, PhD</td>
<td>Massachusetts General Hospital Cancer Center, Harvard Medical School</td>
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<td></td>
<td>in Breast Cancer</td>
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<tr>
<td>4:30-4:45PM</td>
<td>Evolution of Acquired Resistance to Targeted Therapies in Lung Cancer</td>
<td>Supriya Saha, MD, PhD</td>
<td>Massachusetts General Hospital Cancer Center, Harvard Medical School</td>
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<td>4:45-5:00PM</td>
<td>From Model Systems to Drug Discovery: Understanding IDH Mutant</td>
<td>Gregory M. Cote, MD, PhD</td>
<td>Massachusetts General Hospital Cancer Center, Harvard Medical School</td>
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<td>Intrahepatic Cholangiocarcinoma</td>
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<td>5:00-5:20PM</td>
<td>Targeting EZH2 in SWI/SNF Altered Sarcomas</td>
<td>Marios Giannakis, MD, PhD</td>
<td>Dana-Farber Cancer Institute, Harvard Medical School</td>
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<td>5:20PM</td>
<td>Adjourn Day 1</td>
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## Tuesday, November 11, 2014

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Presenter</th>
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<tr>
<td>7:50-8:00AM</td>
<td>Welcome and Introduction</td>
<td>Martin J. Murphy, DMSc, PhD, Convener, Society for Translational Oncology</td>
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<tr>
<td>8:00-8:45AM</td>
<td><strong>Metabolic Lesions in Cancer</strong></td>
<td>Matthew Vander Heiden, MD, PhD, Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology</td>
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<tr>
<td>8:45-9:30AM</td>
<td>Exploiting Methylthioadenosine Phosphorylase Deficiency in Cancer</td>
<td>Joseph R. Bertino, MD, Rutgers Cancer Institute of New Jersey and Robert Wood Johnson Medical School</td>
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<tr>
<td>9:30-10:15AM</td>
<td>Systematic Analysis of the Cellular Response to Mitochondrial Dysfunction</td>
<td>Robert Bao, PhD, Massachusetts General Hospital, Harvard Medical School</td>
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<td>10:15-10:30AM</td>
<td>Beverage Break</td>
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<tr>
<td>10:30-11:15AM</td>
<td><strong>Genetic Profiling for Treatable Mutations</strong></td>
<td>John Iafrate, MD, PhD, Massachusetts General Hospital Cancer Center, Harvard Medical School</td>
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<td>11:15AM-12:00PM</td>
<td>Lessons From the Study of Extraordinary Responders</td>
<td>David B. Solit, MD, Memorial Sloan Kettering Cancer Center</td>
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<tr>
<td>12:00-12:15PM</td>
<td>Closing Remarks</td>
<td>Bruce A. Chabner, MD, Massachusetts General Hospital Cancer Center, Harvard Medical School</td>
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<tr>
<td>12:15PM</td>
<td>Adjourn Day 2</td>
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<td>Buffet Lunch: 5th Floor Rotunda</td>
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The content of each presentation does not necessarily reflect the views of the Society for Translational Oncology, *The Oncologist*, or the Massachusetts General Hospital or any of its affiliates.

Slides will not be printed for the meeting in an effort to protect the environment. Any requests for slides should be directed to the specific presenter as STO does not have permission to distribute slides on their behalf.
Overview

In the field of oncology, the rapid pace of discovery and a better understanding of prevention, detection, the microenvironment, and treatment of cancer will lead to improved patient outcomes. Accurately tailored cancer treatment and individualized therapy will focus on tumor biology and host factors. The healthcare provider will need to be well informed in order to provide the most effective therapy for a particular patient with the fewest associated risks and toxicities. In oncology, our understanding of the complexity of the disease is expanding at an exponential rate.

Target Audience

This activity is designed to meet the educational needs of physicians and scientists in academic and practice settings who wish to advance their knowledge of the research into new treatments and improve their competence in the care of patients with cancer.

Accreditation

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Society for Translational Oncology and The Massachusetts General Hospital. The Society for Translational Oncology is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation

The Society for Translational oncology designates this live activity for a maximum of 10 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

CME Credit

In order to receive CME credit, learners must sign in, review the CME information (accreditation, learning objectives, faculty disclosures, etc.) and attend the CME activity. Learners will be asked to complete an electronic activity evaluation following the meeting to indicate the number of credit hours claimed. Certificates will be provided upon completion of the evaluation.

To obtain CME credit, please visit: http://bit.ly/2014ChabnerCMECredit.

ACKNOWLEDGEMENTS

STO gratefully acknowledges educational grants in partial support of this activity from:

- Chugai Academy for Advanced Oncology (CHAAO)
- Incyte Corporation
- Merrimack Pharmaceuticals, Inc
- Pfizer, Inc
- sanofi-aventis US
- Epizyme
- Lilly USA, LLC
- Novartis
- Prometheus Laboratories, Inc
- Sigma-Tau Pharmaceuticals, Inc

THE PHYSICIAN PAYMENTS SUNSHINE ACT (SUNSHINE ACT) COMPLIANCE

Effective August 1, 2013, The Centers for Medicare & Medicaid Services (CMS) required reporting of any direct or indirect payments made to any US Healthcare Professional by pharmaceutical and device manufacturers and applicable group purchasing organizations (GPOs) under its Open Payments program.

In order to comply with the requirements of the pharmaceutical and device manufacturers who have provided support for this CME activity, no food and beverage costs associated with this activity have been covered by their funding. Therefore, there has been no indirect payment or transfer of value for your attendance at this meeting.

NO data regarding your participation at this meeting will be reported to CMS.
In accordance with ACCME Standards for Commercial Support and the policies of the Society for Translational Oncology (STO), persons participating in this activity who are in a position to control the content have disclosed all relevant relationships with any commercial interest. On the basis of disclosed information, STO identifies and resolves all conflicts of interest before delivery of content.

STO staff involved in the development of this activity have nothing to disclose.

The following faculty have indicated that they have had relevant financial relationship(s) with a commercial interest within the past 12 months or that they have nothing to disclose.

Robert Bao, PhD
Nothing to disclose

Nabeel Bardeesy, MD
Nothing to disclose

Aditya Bardia, MD, MPH
Nothing to disclose

Joseph R. Bertino, MD
Nothing to disclose

Bruce A. Chabner, MD
Consultant/advisory role: Merrimack Pharmaceuticals, Sanofi, Epizyme
Employment: PharmaMar (Board of Directors)
Expert testimony: Eli Lilly
Ownership interests: PharmaMar (Zeltia), Pharmaclycics, Gilead, Exelixis, Celgene, Seattle Genetics

Gregory M. Cote, MD, PhD
Consultant/advisory role: Advance Medical
Research funding: Chordoma Foundation

Johann S. de Bono, MB ChB, FRCP, MSc, PhD
Consultant/advisory role: Johnson & Johnson, Astellas, Medivation, AstraZeneca, Sanofi
Research funding: AstraZeneca, Sanofi, Genentech

Soldano Ferrone, MD, PhD
Nothing to disclose

Benjamin L. Ebert, MD
Consultant/advisory role: Genoptix, Inc, Celgene
Research funding: Celgene

Keith Flaherty, MD
Employment: Clovis Oncology (Board of Directors), Loxo Oncology (Board of Directors)
Consultant/advisory role: Glaxo SmithKline, Roche, Sanofi, Momenta, Astex, Ziopharm, Viralytics

Marios Giannakis, MD, PhD
Nothing to disclose

Timothy A. Graubert, MD
Consultant/advisory role: Genoptix Inc

Aaron N. Hata, MD, PhD
Honoraria: Amgen, Inc

F. Stephen Hodi, Jr, MD
Consultant/advisory role: (Uncompensated) Bristol-Myers Squibb, Merck, Genentech, Novartis
Research funding: (Funds to institution) Bristol-Myers Squibb, Merck, Genentech, Novartis

James Iafrate, MD
Intellectual property right/inventor/patent: Bioreference Labs, Enzymatics
Consultant/advisory role: Enzymatics, Constellation, Chugai, Debiopharm
Ownership interest: Enzymatics

Ross L. Levine, MD
Consultant/advisory role: Agios Pharmaceuticals

Raul Mostoslavsky, MD, PhD
Nothing to disclose

Steven A. Rosenberg, MD, PhD
Nothing to disclose

David Ryan, MD
Consultant/advisory role: MedImmune, LLC

Supriya Saha, MD, PhD
Nothing to disclose

David Solit, MD
Consultant/advisory role: Pfizer, Inc

Matthew Vander Heiden, MD, PhD
Consultant/advisory role: Agios Pharmaceuticals
Ownership interest: Agios Pharmaceuticals
LEARNING OBJECTIVES

After successful completion of this educational activity, participants should be able to:

• Explain the use of testing for EGFR mutations at diagnosis of NSCLC.
• Explain the role of stress response pathways in the metabolic homeostasis of pancreatic cancer cells.
• Discuss the molecular mechanisms regulating metabolism of cancer cells.
• Describe the function of the mammalian sirtuin SIRT6, a histone deacetylase, in controlling expression of key metabolic and ribosomal genes during oncogenic transformation.
• Discuss interpatient heterogeneity of advanced prostate cancer, clonal evolution with treatment, mechanisms of treatment resistance, and the use of novel therapeutic strategies.
• Describe the role of immunotherapy in the treatment of cancer.
• Explain the mechanisms of action for immune checkpoint antibodies.
• Cite the side effects and management strategies for immune checkpoint antibodies.
• Describe the landscape of recurrently mutated genes in AML.
• Discuss the implications of intra-patient clonal heterogeneity in AML.
• Review the somatic mutations that predict prognosis in MDS independent of existing clinical parameters.
• Describe the key biological processes that are altered by genetic mutations in MDS, including RNA splicing, cohesin ring function, epigenetic regulation, kinase signaling, and transcription factors.
• Discuss the molecular basis of lenalidomide activity in MDS.
• Explain the biologic and prognostic role of TET2/IDH mutations in leukemia.
• Explain the role of epigenetic therapies in TET2/IDH-mutant leukemias.
• Describe the potential use of molecular analysis of circulating tumor cells for drug development in breast cancer.
• Discuss the mechanisms of resistance to targeted therapies in lung cancer.
• Explain the pathogenesis of IDH mutant cholangiocarcinoma.
• Discuss EZH2 inhibition as a therapeutic target in SWI/SNF altered malignancies.
• Describe the role of serine metabolism in cancer.
• Discuss the use of antifolates and related targets for cancer therapy.
• Explain the prevalence of consequences of methylthioadenosine phosphorylase (MTAP) deficiency in cancer.
• Describe the role of inhibitors of de novo purine synthesis (e.g., thioguanine) and their potential as effective treatment for patients with cancers lacking MTAP.
• Explain the role of mitochondria in the proper functioning of cellular one-carbon metabolism.
• Describe the relationship between one-carbon defects and mitochondrial disease manifestation.
• Cite current genomic methods for profiling human tumors.
• Describe the benefits and limitations of genomically focused clinical trial designs.
Recently Published Results

A Phase I/II Study of XELIRI Plus Bevacizumab as Second-Line Chemotherapy for Japanese Patients With Metastatic Colorectal Cancer (BIX Study)

A Phase II Study of Ifosfamide, Methotrexate, Etoposide, and Prednisolone for Previously Untreated Stage I/II Extranodal Natural Killer/T-Cell Lymphoma, Nasal Type: A Multicenter Trial of the Korean Cancer Study Group

S-1 as Monotherapy or in Combination With Leucovorin as Second-Line Treatment in Gemcitabine-Refractory Advanced Pancreatic Cancer: A Randomized, Open-Label, Multicenter, Phase II Study

A Pilot Study of Estradiol Followed by Exemestane for Reversing Endocrine Resistance in Postmenopausal Women With Hormone Receptor-Positive Metastatic Breast Cancer

A Phase I/II Study Combining Erlotinib and Dasatinib for Non-Small Cell Lung Cancer

Ventriculolumbar Perfusion Chemotherapy With Methotrexate for Treating Leptomeningeal Carcinomatosis: A Phase II Study
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