Fall 2022 NIH/NCI Workshop: Shaping the Landscape of Brain Metastases Research
(All times are in Eastern Time Zone.)

Thursday September 29, 2022

8-8:10 AM Welcome: Mansoor Ahmed and Norman Coleman

8:10-9:45 AM Session 1

What matters most to patients?

Moderators: Michelle Kim (Michigan) and Minesh Mehta (Miami Baptist)

8:10-8:15 AM Minesh Mehta (5 min): Overview

8:15-8:30 AM Patient Speaker #1 (15 min): Laura Crandon, patient representative (Grasp Cancer)

8:30-8:45 AM Patient Speaker #2 (15 min): Niki Kozak, patient representative

8:45-9:40 AM Panel discussion with audience participation

Topics: Are our research, assessments and clinical trials aligning with what matters most to patients? If not, what are the barriers? What additional priorities should we be focusing on, in the spectrum of prevention, diagnosis, surveillance, treatment, and survivorship?

Moderators: Michelle Kim and Minesh Mehta

Panelists:
- Laura Crandon (patient representative)
- Niki Kozak (patient representative)
- Terri Armstrong (NIH)
- Shawn Hervey-Jumper (UCSF)
- Aki Morikawa (University of Michigan)
- Nicole Willmarth (American Brain Tumor Association)
- David Arons (National Brain Tumor Society)

9:40-9:45 AM Chair Summary (5 min) Minesh Mehta

9:45-10:00 Break

10:00-11:40 Session 2

What are the key challenges to overcoming the neurocognitive and functional sequelae of therapy?

Moderators: DeeDee Smart (NIH) and Jona Hattangadi-Gluth (UCSD)

Speaker 1: (10 min) – DeeDee Smart – Overview of key challenges in characterizing and overcoming cognitive and functional treatment sequelae

Speaker 2: (10 min) – Charles Limoli (UC Irvine) – Understanding normal tissue stress-response to radiation and systemic therapy, FLASH, GRID

Speaker 3: (10 min) - Susanna Rosi (UCSF) - Normal tissue effects, gender differences in neurocognitive effects of therapy
10:40-11:35 AM  Panel Discussion with audience participation

Topic: Can distant intracranial control be achieved without compromising neurocognitive or functional outcomes? What tools or studies are needed to understand the cognitive or functional impact of repeated radiosurgery or CNS-active drug therapies, and the mechanisms (e.g. inflammation) whereby normal tissue is affected?

**Moderators:** DeeDee Smart (NIH) and Jona Hattangadi-Gluth (UCSD)

**Panelists:**
- Susanna Rosi (UCSF)
- Charles Limoli (UC Irvine)
- Shawn Hervey-Jumper (UCSF)
- Jorg Dietrich (MGH)
- Michelle Monje (Stanford)
- Christina Weyer Jamora (UCSF)

11:35-11:40 AM  Chair Summary (5 min) DeeDee Smart

11:40 AM–12:30 PM  Lunch

12:30-3:20 PM  **Session 3**

How do we translate promising science to patient benefit?

12:30-1:20 PM  Translating preclinical breakthroughs: Challenges by Disease Site

**Moderators:** Pat Steeg (NIH) and Brunilde Gril (NIH)

Speaker 1 (10 min) – Michael Davies (MD Anderson) Overview of key barriers to understanding the pathophysiology of brain metastases and improving disease outcome [pre-recorded if unavailable]

Speaker 2 (10 min) – Pat Steeg (NIH), breast cancer

Speaker 3 (10 min) – Jacob Kaufman (OSU), non-small cell lung cancer

Speaker 4 (10 min) - Michael Pacold (NYU), melanoma

Speaker 5 (10 min) - Adrienne Boire (MSKCC), leptomeningeal disease

1:20-2:20 PM  Panel Discussion with audience participation

Topics: What are the primary challenges and barriers to translating promising scientific concepts into impactful clinical trials that influence practice and benefit patients (in particular, in lung, breast, melanoma and leptomeningeal disease)? How close are we to implementing strategies in preventing brain metastases in patients? Do these mechanisms vary by histology or tumor type? Are there common biomarkers for metastatic development that are shared across the most common tumor types that metastasize to brain?

**Moderators:** Pat Steeg and Brunilde Gril

**Panelists:**
- Michael Davies (MD Anderson)
Jacob Kaufman (OSU)
Michael Pacold (NYU)
Adrienne Boire (MSKCC)
Calvin Han (FDA)
Michael Espey (NIH)

2:20-2:25 PM  Chair Summary (5 min) Pat Steeg
2:25-2:40 PM  Break
2:40-3:20 PM  Promising Translational Concepts: Onset, progression, and treatment response

Moderators: Brunilde Gril (NIH) and Pat Steeg (NIH)
Speaker 1 (10 min) Shizhen Emily Wang (UCSD) Cancer cell-secreted extracellular vesicles regulate glial-metastasis metabolic crosstalk
Speaker 2 (10 min) Melanie Hayden Gephart – (Stanford and MetNet) – Mechanisms of brain metastases onset and progression, preclinical models of radiotherapy resistance
Speaker 3 (10 min) Manuel Valiente (CNIO, Madrid) - Stratification of radiosensitive brain metastases based on an actionable S100A9/RAGE resistance mechanism
Speaker 4 (10 min) Eva Hernando – (NYU) – Melanoma, neuroinflammation and promotion of brain metastases

3:20-5:15 PM  Session 4: Break-out and group discussions

Identifying candidate solutions to the most pressing scientific questions

Primary question for discussion by each Break-Out: What are the most promising strategies “ready-for-prime-time” to predict response to standard therapies and to prevent local and in particular, distant intracranial failure?

Sub question 1: How do we best address the prevention of brain metastases?
Sub question 2: How do we implement these strategies while maximizing functional outcomes?

3:20-4:05  Break-out Group 1 (45 min)
Moderators: Pat Steeg and Kim Margolin

Break-out Group 2 (45 min)
Moderators: Brunilde Gril and Minesh Mehta

Break-out Group 3 (45 min)
Moderators: DeeDee Smart and Jona Hattangadi-Gluth

4:05-4:25 PM  Summary Discussion
Moderators: Hussein Tawbi (MD Anderson) and Dan Trifiletti (Mayo)

Summary Group 1 (5 min) Kim Margolin
Summary Group 2 (5 min) Minesh Mehta
Summary Group 3 (5 min) Jona Hattangadi-Gluth

4:25-5:10 PM  Panel Summary Discussion (45 min)
**Moderators:** Hussein Tawbi (MD Anderson) and Dan Trifiletti (Mayo)
**Panelists:**
- Caroline Chung (MD Anderson)
- Upal Basu-Roy (LUNGevity)
- Christine Hodgdon (Grasp Cancer and LBBC)
- Eva Galanis (Mayo)
- Vik Vikram (NIH)
- Nyun Calvin Han (FDA)
- Gelareh Zadeh (Toronto)
- Robyn Burnes (Melanoma Research Foundation)

5:10 – 5:15 PM  Chair Summary (5 min) Hussein Tawbi (MD Anderson)

5:15 – 5:20 PM  Summary & Wrap up (5 min) Michelle Kim (Michigan)

Friday September 30, 2022

8:00-9:55 AM  Session 5

**How do we define a common purpose and break the silos?**

8:00-9:00 AM  **Moderators:** Minesh Mehta (Miami Baptist) and Isabella C. Glitza Oliva (MD Anderson)

Speaker 1 (10 min) Minesh Mehta - History of brain metastases trials, what are the cooperative groups doing, what is the “next generation” of brain metastases clinical trials
Speaker 2 (10 min) Ayal Aizer (Brigham) Professional society efforts (SNO)
Speaker 3 (10 min) Carey Anders (Duke) – Multi-institutional consortia efforts (CIMARa)
Speaker 4 (10 min) Nicole Willmarth (ABTA) – metastatic brain tumor collaborative
Speaker 5 (10 min) Kirk Tanner (NBTS) – metastatic brain tumor research priorities and industry partnership
Speaker 6 (10 min) Michelle Kim (NIH/NCI Brain Mets Interest Group)

9:00-9:50 AM  Discussion with audience participation

*What are the research priorities of the various stakeholders with respect to brain metastases research? How do we break the silos and begin to unify efforts and define common priorities to collaborate to advance the science, clinical trials, and our clinical care? How might existing and emerging initiatives be combined to advance the field? Are some “high risk” research endeavors better undertaken by individual institutions, or in partnership with industry? How do we take the cutting edge science discussed in Day 1 into the multi-institutional NCTN setting?*
Moderators: Minesh Mehta and Isabella C. Glitza Oliva (MD Anderson)
Panelists:
Jerry Jaboin (University of Oklahoma)
Joanne Davis (Radiosurgery Society)
John Buatti (Iowa)
Michael Lim (Stanford)
Manmeet Ahluwalia (Miami Baptist)
Jonathan Knisely (Cornell)
Veronica Chiang (Yale)

9:50-9:55 AM Chair Summary: Minesh Mehta (5 min)

9:55-10:05 Break

10:05-12:15 Session 6

How do we take promising science into clinical trials to address the most critical unmet needs?

How do we tackle the most difficult questions in brain metastases research? Is the metastatic biology of brain metastases altered in the setting of radiotherapy (high dose or conventional)? How might this influence the chief clinical problem of distant intracranial failure after local therapy? Based on preclinical evidence, what might the most promising combinations or sequencing of radiotherapy + drug therapy be?

10:05-10:35 Are we asking the right questions?
Moderator: Jing Li (MDACC)
Speaker 1 (10 min) John de Groot (USCF) – Overview – How do we bridge the gap between science and our clinical trials to address the most significant unanswered questions in brain metastasis research?
Speaker 2 (10 min) Ranjit Bindra (Yale) – How can we optimize targeted therapies?
Speaker 3 (10 min) Sylvia Formenti (Cornell) – How do we optimally combine radiation and systemic therapies to improve outcomes?

10:35-11:15 Are we addressing the right endpoints?
Moderator: Rupesh Kotecha (Miami Baptist)
Speaker 1 (10 min) Nancy Lin (Dana Farber) – Endpoints for drug therapy trials – beyond RECIST and RANO, should we hold the bar higher?
Speaker 2 (10 min) Ben Ellingson (UCLA) The potential of advanced imaging and AI for assessing and predicting response and toxicity
Speaker 3 (10 min) Vinai Gondi (Northwestern) - Beyond overall survival – functional, neurocognitive and other novel endpoints for NCI-sponsored trials
Speaker 4 (10 min) Christine Hodgdon (Grasp Cancer and LBBC) – Patient perspectives: Addressing the unmet needs in CNS metastases

11:15-12:10 Discussion with audience participation

Topic: What novel strategies (or combinations of therapies) can address the most insurmountable challenges of brain metastasis research? What are the steps we need to take to systematically address these challenges?
What are the key mechanisms and research questions we should focus on to advance the landscape of brain metastasis research and to improve the therapeutic ratio? How do we optimally implement advanced technologies, and combine them with novel systemic agents to improve outcomes? Besides overall survival, what other endpoints (e.g. freedom from neurologic death?) should be considered meaningful in brain metastases trials moving forward? For drug therapy trials, should more robust endpoints (rather than response rate) and comparative study designs with effective standard therapy (i.e. radiation) as control be utilized?

**Moderators:** Jing Li and Rupesh Kotecha

**Panelists:**
- John de Groot (UCSF)
- Ben Ellingson (UCLA)
- Nancy Lin (Dana Farber)
- Hussein Tawbi (MD Anderson)
- Vinai Gondi (Northwestern)
- Paul Sperduto (Duke)
- Christine Hodgdon (Grasp Cancer and LBBC)
- Nyun Calvin Han (FDA)

**12:10-12:15 PM**  
Chair Summary (Jing Li, MD Anderson) 5 min

**12:15 – 1:00 PM**  
Lunch

**1:00-4:00 PM**  
**Session 7**

**How should we optimize shared data collection to minimize disparities and accelerate discovery and well-designed clinical trials?**

**1:00-1:30 PM**  
**Moderators:** Jill Barnholtz-Sloan (NIH) and Ben Ellingson (UCLA)

Speaker 1 (10 min) Priscilla Brastianos –Biomarker discovery (tissue and imaging) to inform novel clinical research

Speaker 2 (10 min) Katherine Peters (Duke) Patient-reported outcomes, provider assessments, and novel data collection devices as complements to conventional measures

Speaker 3 (10 min) Eudocia Lee (Dana Farber) Disparities in access, outcomes and clinical trial enrollment in the brain metastases population

**1:30-2:30 PM**  
Break-out and group discussions (60 min)

Primary question for each Break-Out Group: How should a shared resource be developed to collect multi-dimensional datasets to accelerate discovery and meaningfully inform high-yield clinical trials?

Sub question 1: What specific barriers (e.g. in the NCTN, in industry partnerships) must be addressed to achieve this?

Sub question 2: How do we ensure adequate inclusion and representation of all patients in our discovery and clinical research processes?

**Break-out Group 1 (60 min)**  
**Moderators:** Jill Barnholtz-Sloan (NIH) and Ben Ellingson (UCLA)
Break-out Group 2 (60 min)
**Moderators:** Carey Anders (Duke) and Jordi Rodon Ahnert (MD Anderson)

Break-out Group 3 (60 min)
**Moderators:** Melanie Hayden Gephart (Stanford and MetNet) and Eudocia Lee (DFCI)

2:30-2:45 PM  Break

2:45-3:05 PM  Summary Discussion
**Moderators:** Adrienne Boire and Mustafa Khasraw
Summary Group 1 (5 min): Jill Barnholtz-Sloan
Summary Group 2 (5 min): Jordi Rodon Ahnert
Summary Group 3 (5 min): Eudocia Lee

3:05-4:00 PM  Panel Summary Discussion
**Moderators:** Adrienne Boire (MSKCC) and Mustafa Khasraw (Duke)
**Panelists:**
- Jona Hattangadi-Gluth (UCSD)
- Daniel Trifiletti (Mayo)
- Debra Yeboa (MD Anderson)
- Richard Pazdur (FDA)
- Elshad Hasanov (MD Anderson)
- Rohan Ramakrishna (Cornell)
- Vik Vikram (NIH)
- Michael Espey (NIH)

4:00-4:15 PM  Summary of workshop findings and recommended research priorities
Minesh Mehta

4:15-4:30 PM  Closing: Mansoor Ahmed and Norman Coleman
**White Paper**
Follow-up collaborative in-person meeting
Future directions

(Updated: Sept 19, 2022)