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EPICS Lung Cancer in 2022 and Beyond

November 4–5, 2022

Report Contents

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Meeting Snapshot

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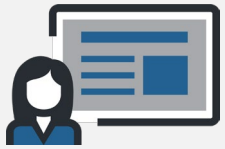
VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
November 4–5, 2022



DISEASE STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in lung cancer
- > 10 from US
- > 1 from Canada

LUNG CANCER-SPECIFIC DISCUSSIONS on therapeutic advances and their application in clinical decision-making

Panel Consisting of 11 North American Lung Cancer Experts

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Natasha Leighl, MD, FRCP, FASCO
University of Toronto

Paul Paik, MD
Memorial Sloan Kettering Cancer Center

Shirish Gadgeel, MD
Henry Ford Cancer Institute

Jamie Chaft, MD
Memorial Sloan Kettering Cancer Center

Fred Hirsch, MD, PhD
The Tisch Cancer Institute

Paul Bunn, MD, FASCO
University of Colorado School of Medicine

Roy Herbst, MD, PhD
Yale Cancer Center

Antoinette J. Wozniak, MD, FRCPC, FASCO
University of Pittsburgh

Martin Edelman, MD
Fox Chase Cancer Center

CHAIR:
Corey Langer, MD, FACP
University of Pennsylvania

Ignacio I. Wistuba, MD
MD Anderson Cancer Center

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Meeting Agenda – Day 1

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Time	Topic	Speaker/Moderator
2.30 PM – 2.35 PM	Welcome and Introductions	Corey Langer, MD, FACP
2.35 PM – 2.55 PM	Prognostic and Predictive Biomarkers in Non-small Cell Lung Cancer (NSCLC): Pathologic Implications, Clinical and Research Relevance	Ignacio Wistuba, MD
2.55 PM – 3.25 PM	Discussion: Prognostic and Predictive Biomarkers in Non-small Cell Lung Cancer (NSCLC) – Pathologic Implications, Clinical and Research Relevance	All
3.25 PM – 3.40 PM	Immunotherapy in Unresectable Stage III NSCLC	Fred Hirsch, MD, PhD
3.40 PM – 4.00 PM	Discussion: Immunotherapy in Unresectable Stage III NSCLC	All
4.00 PM – 4.10 PM	*EGFR* (Less Common Mutations, Including Exon 20 Insertions)	Natasha Leighl, MD
4.10 PM – 4.20 PM	Discussion: *EGFR* (Less Common Mutations, Including Exon 20 Insertions)	All
4.20 PM – 4.30 PM	Break	All
4.30 PM – 4.45 PM	Therapeutic Landscape for Fusion-Positive NSCLC (*ALK, ROS1, NTRK, RET*)	Shirish Gadgeel, MD
4.45 PM – 5.15 PM	Discussion: Therapeutic Landscape for Fusion-Positive NSCLC (*ALK, ROS1, NTRK, RET*)	All
5.15 PM – 5.30 PM	Inhibiting Oncogenic Mutations: Overcoming Mutant *KRAS, HER2, MET,* and *BRAF*	Paul Paik, MD
5.30 PM – 6.00 PM	Discussion: Inhibiting Oncogenic Mutations – Overcoming Mutant *KRAS, HER2, MET,* and *BRAF*	All
6.00 PM – 6.10 PM	Promising New Targets/Agents in Lung Cancer: ADCs and Beyond	Martin Edelman, MD
6.10 PM – 6.30 PM	Discussion: Promising New Targets/Agents in Lung Cancer – ADCs and Beyond	All
6.30 PM	Adjourn	Corey Langer, MD, FACP

Meeting Agenda – Day 2

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Time	Topic	Speaker/Moderator
8.00 AM – 8.05 AM	Review Agenda and Framework for Day 2	Corey Langer, MD, FACP
8.05 AM – 8.20 AM	Perioperative Immunotherapy in Early NSCLC	Jamie Chaft, MD
8.20 AM – 9.00 AM	Discussion: Perioperative Immunotherapy in Early NSCLC	All
9.00 AM – 9.10 AM	New Directions for *EGFR*-Mutated NSCLC	Antoinette Wozniak, MD
9.10 AM – 9.30 AM	Discussion: New Directions for *EGFR*-Mutated NSCLC	All
9.30 AM – 9.45 AM	First-Line Immunotherapy in Metastatic NSCLC: Single Agent or Combination?	Roy Herbst, MD, PhD
9.45 AM – 10.20 AM	Discussion: First-Line Immunotherapy in Metastatic NSCLC – Single Agent or Combination?	All
10.20 AM – 10.30 AM	Break	All
10.30 AM – 10.40 AM	New Directions for Second-Line Therapy	Natasha Leighl, MD
10.40 AM – 11.00 AM	Discussion: New Directions for Second-Line Therapy	All
11.00 AM – 11.20 AM	Emergence of Immunotherapy and New Agents in SCLC	Paul Bunn, MD, FASCO
11.20 AM – 12.00 PM	Discussion: Emergence of Immunotherapy and New Agents in SCLC	All
12.00 PM	Conclusions and Adjourn	Corey Langer, MD, FACP

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Summaries of Faculty Presentations

Prognostic and Predictive Biomarkers in Non-small Cell Lung Cancer

Presented by Ignacio Wistuba, MD

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> The expanding application of new therapies

New Directions for *EGFR*-Mutated NSCLC (1/2)

Presented by Antoinette Wozniak, MD, FACP, FASCO

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- For patients with resectable, *EGFR*

Resistance Mechanisms to Osimertinib

New Directions for *EGFR*-Mutated NSCLC (2/2)

Presented by Antoinette Wozniak, MD, FACP, FASCO

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> For patients with metastatic, *EGFR* mutation-positive disease, a major focus

EGFR (Less Common Mutations, Including Exon 20 Insertions)

Presented by Natasha Leighl, MD, FRCPC, FASCO

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> For patients with *EGFR* exon 20 insertion

Therapeutic Landscape for Fusion-Positive NSCLC (*ALK*, *ROS1*, *NTRK*, *RET*) (1/2)

Presented by Shirish Gadgeel, MD

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> For the detection of oncogenic fusions, RNA-based testing remains an important

Therapeutic Landscape for Fusion-Positive NSCLC (*ALK*, *ROS1*, *NTRK*, *RET*) (2/2)

Presented by Shirish Gadgeel, MD

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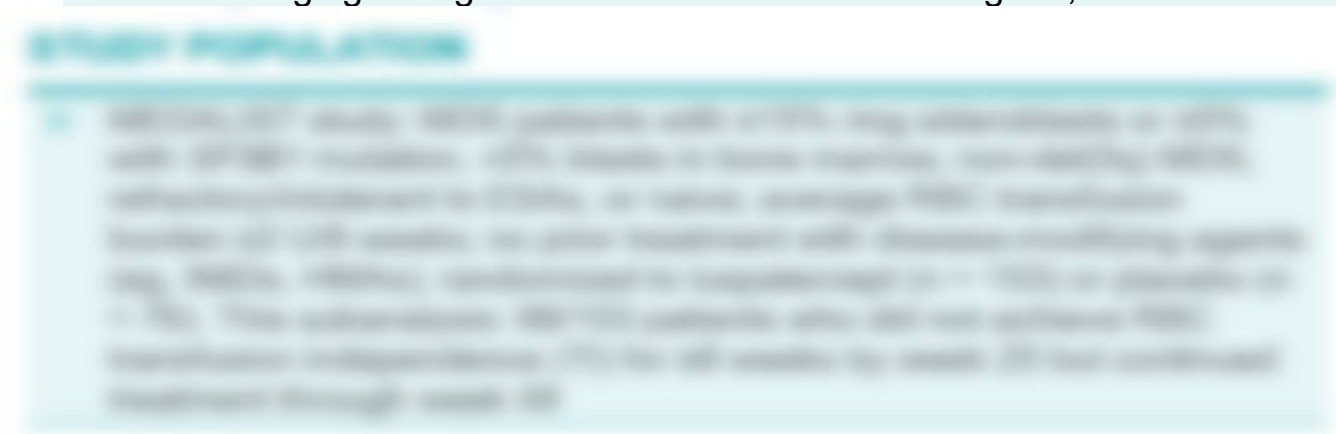
- An emerging oncogenic fusion involves the *NRG1* gene, which codes for a



Inhibiting Oncogenic Mutations: Overcoming Mutant *KRAS*, *HER2*, *MET*, and *BRAF* (1/2)

Presented by Paul Paik, MD

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> Over the past year, phase III data on

Inhibiting Oncogenic Mutations: Overcoming Mutant *KRAS*, *HER2*, *MET*, and *BRAF* (2/2)

Presented by Paul Paik, MD

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- Approved therapy is available for the following oncogenic mutations
  - *KRAS* G12C (approved: sotorasib)
  - Accelerated approval was granted to sotorasib in 2021 on the basis of the

Promising New Targets/Agents in Lung Cancer: ADCs and Beyond

Presented by Martin Edelman, MD

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> Several ADCs are in development in lung

Perioperative Immunotherapy in Early NSCLC (1/2)

Presented by Jamie Chaft, MD

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> A major recent advance in the treatment of

Perioperative IO Summary (Opinion)

Perioperative Immunotherapy in Early NSCLC (2/2)

Presented by Jamie Chaft, MD

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> The CheckMate 816 study yielded FDA approval in March 2022 for neoadjuvant nivolumab

Immunotherapy in Unresectable Stage III NSCLC

Presented by Fred Hirsch, MD, PhD

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> The PACIFIC trial defined the current standard of care

First-Line Immunotherapy in Metastatic NSCLC: Single Agent or Combination? (1/2)

Presented by Roy Herbst, MD, PhD

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> Multiple immunotherapy-based regimens

First-Line Immunotherapy in Metastatic NSCLC: Single Agent or Combination? (2/2)

Presented by Roy Herbst, MD, PhD

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- Single-agent immunotherapy
  - Pembrolizumab (PD-L1 ≥1%) (KEYNOTE-024/042)

New Directions for Second-Line Therapy

Presented by Natasha Leighl, MD, FRCPC, FASCO

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- The management of patients whose disease has

Emergence of Immunotherapy and New Agents in SCLC (1/2)

Presented by Paul Bunn, MD

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> For patients with newly diagnosed,

Emergence of Immunotherapy and New Agents in SCLC (2/2)

Presented by Paul Bunn, MD

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> For subsequent lines of therapy, lurbinectedin and topotecan are FDA-approved options;

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Key Insights

Prognostic and Predictive Biomarkers in Non-small Cell Lung Cancer (1/2)

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> Regarding collection of tissue and liquid biopsies, a wide range of practices are carried out at the experts' institutions; while tissue is generally collected by default, approaches to simultaneous collection of a liquid biopsy vary due to a lack of standard procedures

Prognostic and Predictive Biomarkers in Non-small Cell Lung Cancer (2/2)

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- The experts also mentioned issues with accessing their patients' molecular testing results, as these are not

New Directions for *EGFR*-Mutated NSCLC

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> With regard to testing of patients with early-stage disease, the experts' institutions generally carry out broad NGS testing

EGFR (Less Common Mutations, Including Exon 20 Insertions)

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Therapeutic Landscape for Fusion-Positive NSCLC (*ALK, ROS1, NTRK, RET*) (1/2)

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> The experts clarified that actionable molecular alterations in NSCLC refer to the alterations with approved agents, generally divided into

Therapeutic Landscape for Fusion-Positive NSCLC (*ALK, ROS1, NTRK, RET*) (2/2)

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- In patients with a *ROS1* fusion, the experts generally use entrectinib as initial therapy, particularly if the patient has CNS metastases; however, entrectinib is associated with toxicity (eg, CNS effects, cardiac toxicity, Achilles tendinitis)

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Inhibiting Oncogenic Mutations: Overcoming Mutant *KRAS*, *HER2*, *MET*, and *BRAF* (1/2)

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> The experts cited a study that showed a continuing lack of molecular testing in community practice; while 80% of the patients were tested for

Inhibiting Oncogenic Mutations: Overcoming Mutant *KRAS*, *HER2*, *MET*, and *BRAF* (2/2)

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- *HER2*
  - Expert opinion is that trastuzumab deruxtecan has potential as first-line therapy in patients with NSCLC

Promising New Targets/Agents in Lung Cancer: ADCs and Beyond

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> Expert opinion is that ADCs have potential in lung cancer; however, an important first step is to beat docetaxel in phase III trials of previously treated patients

Perioperative Immunotherapy in Early NSCLC (1/2)

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> Regarding the decision between neoadjuvant and adjuvant immunotherapy, varying approaches were described by the experts; at some

Perioperative Immunotherapy in Early NSCLC (2/2)

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> In terms of a histology-based difference in outcome after neoadjuvant immunotherapy, one of the experts stated

Immunotherapy in Unresectable Stage III NSCLC

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> The experts mentioned the need to determine which patients with unresectable stage III NSCLC truly require a year of consolidation

First-Line Immunotherapy in Metastatic NSCLC: Single Agent or Combination?

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> For patients with newly diagnosed, stage IV NSCLC and PD-L1 expression of 50% or higher, without bulky or aggressive disease, the experts

New Directions for Second-Line Therapy (1/2)

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> The experts remarked on the number of phase III trials without biomarker selection

New Directions for Second-Line Therapy (2/2)

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> The experts mentioned unmet needs in the current inventory of clinical trials

Emergence of Immunotherapy and New Agents in SCLC

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> One of the pathology experts stated that many institutions use cytology-based samples for diagnosis, which works for molecular analysis of