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Lung Cancer in 2024 and Beyond

November 1–2, 2024

Report Contents

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Meeting Snapshot

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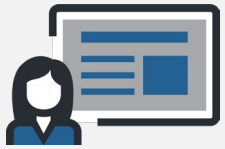
LIVE CLOSED-DOOR ROUNDTABLE

DATE:
November 1–2, 2024



DISEASE STATE AND DATA PRESENTATIONS by key experts

INSIGHT REPORT including postmeeting analyses and actionable recommendations

PANEL: 10 key US experts in lung cancer

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

Panel Consisting of 10 Lung Cancer Experts

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Meeting Agenda – Friday, November 1

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Time (ET)	Topic	Speaker/Moderator
2.00 PM – 2.05 PM	**Welcome and Introductions**	Corey J. Langer, MD, FACP
2.05 PM – 2.20 PM	**Prognostic and Predictive Biomarkers in Lung Cancer (NSCLC): Pathologic Implications, Clinical and Research Relevance**	Fred Hirsch, MD, PhD
2.20 PM – 2.40 PM	Discussion	All faculty
2.40 PM – 2.55 PM	**Interventional Pulmonology and Advanced Diagnostic Approaches**	Andrew Haas, MD, PhD
2.55 PM – 3.10 PM	Discussion	All faculty
3.10 PM – 3.25 PM	**Stage I–III NSCLC: How Best to Apply Immunotherapy?**	David Jablons, MD
3.25 PM – 3.50 PM	Discussion	All faculty
3.50 PM – 4.00 PM	**Stage I–III Oncogene-Driven NSCLC: *EGFR, ALK,* and Beyond**	Shirish Gadgeel, MD
4.00 PM – 4.20 PM	Discussion	All faculty
4.20 PM – 4.30 PM	***Break***	
4.30 PM – 4.50 PM	**Optimizing Immunotherapy in Unresectable and Metastatic NSCLC**	Hossein Borghaei, DO
4.50 PM – 5.20 PM	Discussion	All faculty
5.20 PM – 5.35 PM	**Subsequent Therapy in Stage IV NSCLC: Have We Moved Beyond Docetaxel? Will ADCs Enable Us to Do So?**	Martin Edelman, MD
5.35 PM – 6.00 PM	Discussion	All faculty
6.00 PM	**Wrap-Up and Adjourn**	Corey J. Langer, MD, FACP

Meeting Agenda – Saturday, November 2

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Time (ET)	Topic	Speaker/Moderator
8.00 AM – 8.05 AM	**Review Agenda and Framework for Day 2**	Corey J. Langer, MD, FACP
8.05 AM – 8.20 AM	**Stage IV NSCLC: *EGFR* Mutations**	Xiuning Le, MD, PhD
8.20 AM – 8.50 AM	Discussion	All faculty
8.50 AM – 9.10 AM	**Other Mutations in Advanced and Metastatic NSCLC *(KRAS, HER2, MET, BRAF)***	Paul Paik, MD
9.10 AM – 9.45 AM	Discussion	All faculty
9.45 AM – 10.00 AM	**Fusion-Positive, Advanced and Metastatic NSCLC *(ALK, ROS1, RET, NTRK, NRG1)***	Shirish Gadgeel, MD
10.00 AM – 10.30 AM	Discussion	All faculty
10.30 AM – 10.40 AM	***Break***	
10.40 AM – 10.55 AM	**Small Cell Lung Cancer: Limited- to Extensive-Stage Disease**	Helen Ross, MD
10.55 AM – 11.20 AM	Discussion	All faculty
11.20 AM – 11.35 AM	**Future Paradigms in Lung Cancer**	Martin Edelman, MD, and David Jablons, MD
11.35 PM – 12.00 PM	Discussion	All faculty
12.00 PM	**Conclusions and Adjourn**	Corey J. Langer, MD, FACP

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Prognostic and Predictive Biomarkers in Lung Cancer (NSCLC): Pathologic Implications, Clinical and Research Relevance

Prognostic and Predictive Biomarkers in Lung Cancer (NSCLC): Pathologic Implications, Clinical and Research Relevance (1/2)

Presented by Fred Hirsch, MD, PhD

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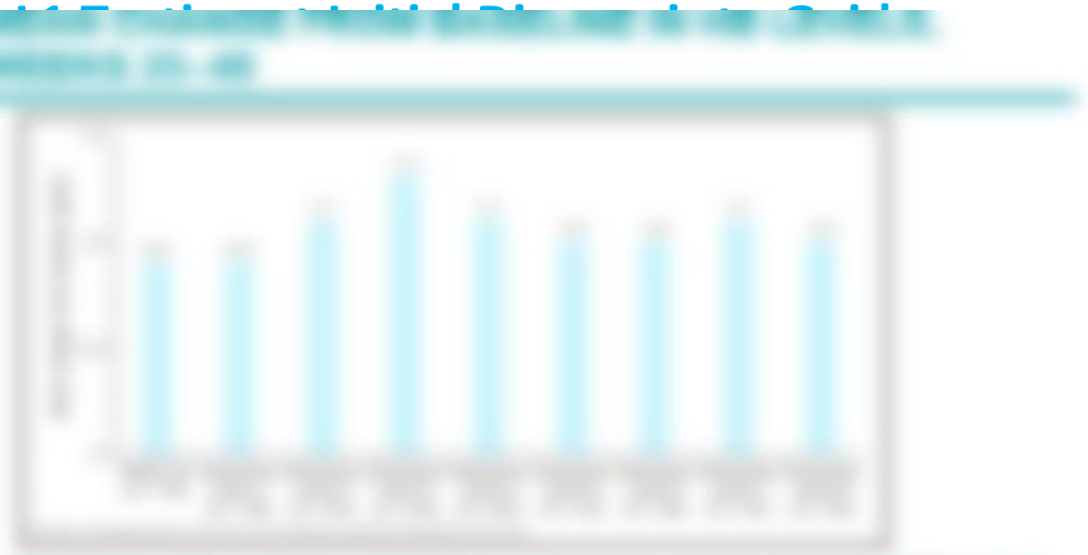
Oncogenic Drivers and Molecular Testing

Adequate molecular testing is essential in all



Prognostic and Predictive Biomarkers in Lung Cancer (NSCLC): Pathologic Implications, Clinical and Research Relevance (2/2)

Presented by Fred Hirsch, MD, PhD

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Role of ctDNA to Direct Therapy

randomized phase 2 study – (ICML) Zhang #26

- Experts believe the resolution of molecular phenotype is possible in real time, and these vulnerabilities can potentially be targeted

Promising tolerability and efficacy results from dose-escalation in an ongoing phase I/II study of mosunetuzumab with polatuzumab vedotin for relapsed/refractory B-cell NHL – (ENA) Ghosh #6222

- The regimen is seen as effective, exciting, safe, and broadly applicable to many patients

Mosunetuzumab (monoun) monotherapy for elderly/unfit patients with first-line DLBCL continues to show promising safety and efficacy with durable complete responses – (ENA) Olszewski #EP101

- This approach is seen as a great solution for a patient population in whom giving immunochemotherapy is difficult. It is viewed as effective and safe

FIRST-MIND: a phase Ib, open-label, randomized study to assess safety of tafasitamab or tafasitamab + lenalidomide in addition to R-CHOP in patients with newly diagnosed DLBCL – (ENA) Bonada #EP104

- Experts believe the combination of tafasitamab + lenalidomide with R-CHOP is safe. However, they would like to see phase III data to confirm its activity in this setting

Long-term analyses from L-MIND, a phase II study of tafasitamab plus lenalidomide (len) in patients with R/R DLBCL – (ICML) Duell #29

- The L-MIND regimen is seen as useful in the specific patient population with refractory disease. It was noted to be effective, very safe, and well tolerated. Some of the responses seen were clearly very durable

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Key Insights

Prognostic and Predictive Biomarkers in Lung Cancer (NSCLC): Pathologic Implications, Clinical and Research Relevance

Prognostic and Predictive Biomarkers in Lung Cancer (NSCLC): Pathologic Implications, Clinical and Research Relevance (1/2)

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For patients with newly diagnosed, stage IV NSCLC, most of the experts request liquid biopsy, with approximately one-third

Prognostic and Predictive Biomarkers in Lung Cancer (NSCLC): Pathologic Implications, Clinical and Research Relevance (2/2)

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The experts discussed biomarker development for patients with SCLC

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Interventional Pulmonology and Advanced Diagnostic Approaches

Interventional Pulmonology and Advanced Diagnostic Approaches (1/2)

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Presented by Andrew Haas, MD, PhD

Technological Advances in Pulmonology

Interventional Pulmonology and Advanced Diagnostic Approaches (2/2)

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Presented by Andrew Haas, MD, PhD

Evolving Role of the Bronchoscopist

[redacted]

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Key Insights

Interventional Pulmonology and Advanced Diagnostic Approaches

Interventional Pulmonology and Advanced Diagnostic Approaches

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The pulmonology expert emphasized the need to conduct a complete staging assessment during the bronchoscopy procedure; tissue

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Stage I–III NSCLC: How Best to Apply Immunotherapy?

Stage I–III NSCLC: How Best to Apply Immunotherapy? (1/2)

Presented by David Jablons, MD

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Establishment of Immunotherapy in

Stage I–III NSCLC: How Best to Apply Immunotherapy? (2/2)

Presented by David Jablons, MD

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Outstanding Questions to Optimize Immunotherapy in Resectable NSCLC

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Key Insights

Stage I–III NSCLC: How Best to Apply Immunotherapy?

Stage I–III NSCLC: How Best to Apply Immunotherapy? (1/2)

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In patients who have a pCR with neoadjuvant immunotherapy plus chemotherapy, the experts were divided regarding the use of

Stage I–III NSCLC: How Best to Apply Immunotherapy? (2/2)

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Expert opinion is that the exploratory data showing benefit with perioperative immunotherapy in patients with multi-station N2 nodal

[redacted]

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Stage I–III Oncogene-Driven NSCLC: *EGFR*, *ALK*, and Beyond

Stage I–III Oncogene-Driven NSCLC: *EGFR*, *ALK*, and Beyond (1/2)

Presented by Shirish Gadgeel, MD

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Targeting EGFR in Stage I–III NSCLC

Stage I–III Oncogene-Driven NSCLC: *EGFR*, *ALK*, and Beyond (2/2)

Presented by Shirish Gadgeel, MD

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Targeting ALK in Stage I–III NSCLC

randomized phase 2 study – (ICML; Zhang #28

- Experts believe the resolution of molecular phenotype is possible in real time, and these vulnerabilities can potentially be targeted

Promising tolerability and efficacy results from dose-escalation in an ongoing phase I/II study of mosunetuzumab with polatuzumab vedotin for relapsed/refractory B-cell NHL – (ENA; Ghosh #6222

- The regimen is seen as effective, exciting, safe, and broadly applicable to many patients

Mosunetuzumab (mosun) monotherapy for elderly/unfit patients with first-line DLBCL continues to show promising safety and efficacy with durable complete responses – (ENA; Chunwelo #EP102

- This approach is seen as a great solution for a patient population in whom giving immunochemotherapy is difficult. It is viewed as effective and safe

FIRST-MIND: a phase Ib, open-label, randomized study to assess safety of ibrutinib/lenalidomide or ibrutinib/lenalidomide in addition to R-CHOP in patients with newly diagnosed DLBCL – (ENA; Beraldo #EP104

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Long-term analyses from L-MIND, a phase II study of tafasitamab plus lenalidomide (len) in patients with R/R DLBCL – (ICML; Duell #28

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Key Insights

Stage I–III Oncogene-Driven NSCLC: *EGFR*, *ALK*, and Beyond

Stage I–III Oncogene-Driven NSCLC: *EGFR*, *ALK*, and Beyond (1/2)

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The experts think that adjuvant targeted therapy would be appropriate for patients with an *EGFR* mutation or an oncogenic fusion:

Stage I–III Oncogene-Driven NSCLC: *EGFR*, *ALK*, and Beyond (2/2)

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The experts agreed that AEs are a major issue with targeted therapy in patients with stage I–III NSCLC compared with patients who

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Optimizing Immunotherapy in Unresectable and Metastatic NSCLC

Optimizing Immunotherapy in Unresectable and Metastatic NSCLC (1/3)

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Presented by Hossein Borghaei, DO

First-Line Immunotherapy-Based Regimens in

Optimizing Immunotherapy in Unresectable and Metastatic NSCLC (2/3)

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Presented by Hossein Borghaei, DO

Treatment With Immunotherapy Beyond Progression

[redacted]

Optimizing Immunotherapy in Unresectable and Metastatic NSCLC (3/3)

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Presented by Hossein Borghaei, DO

Other Immune Checkpoints

[redacted]

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Key Insights

Optimizing Immunotherapy in Unresectable and Metastatic NSCLC

Optimizing Immunotherapy in Unresectable and Metastatic NSCLC (1/2)

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Expert opinion is that PD-L1 cutoffs in stage IV NSCLC need to be further refined, as illustrated by the PD-L1–expression tertiles with

Optimizing Immunotherapy in Unresectable and Metastatic NSCLC (2/2)

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While favorable outcomes were observed in patients with squamous histology in the EMPOWER-Lung 1 study of cemiplimab vs

[redacted]

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Subsequent Therapy in Stage IV NSCLC: Have We Moved Beyond Docetaxel? Will ADCs Enable Us to Do so?

Subsequent Therapy in Stage IV NSCLC: Have We Moved Beyond Docetaxel? Will ADCs Enable Us to Do so? (1/2)

Presented by Martin Edelman, MD

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Subsequent Therapy in Advanced NSCLC:

Subsequent Therapy in Stage IV NSCLC: Have We Moved Beyond Docetaxel? Will ADCs Enable Us to Do so? (2/2)

Presented by Martin Edelman, MD

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Antibody-Drug Conjugates

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Key Insights

Subsequent Therapy in Stage IV NSCLC: Have We Moved Beyond Docetaxel? Will ADCs Enable Us to Do so?

Subsequent Therapy in Stage IV NSCLC: Have We Moved Beyond Docetaxel? Will ADCs Enable Us to Do so?

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For patients with progression on single-agent immunotherapy, the experts would add chemotherapy and continue immunotherapy

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Stage IV NSCLC: *EGFR* Mutations

Stage IV NSCLC: *EGFR* Mutations (1/2)

Presented by Xiuning Le, MD, PhD

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EGFR-Mutation Disease Spaces

Summary: EGFR Mutations

Stage IV NSCLC: *EGFR* Mutations (2/2)

Presented by Xiuning Le, MD, PhD

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First-Line Therapy

[redacted]

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Key Insights

Stage IV NSCLC: *EGFR* Mutations

Stage IV NSCLC: *EGFR* Mutations (1/2)

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For patients with newly diagnosed, stage IV NSCLC and an *EGFR* mutation, the experts would use a combination approach for

Stage IV NSCLC: *EGFR* Mutations (2/2)

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For patients with *EGFR*-mutated NSCLC whose disease progresses on a TKI, the experts generally request both liquid and tissue

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Other Mutations in Advanced and Metastatic NSCLC (*KRAS*, *HER2*, *MET*, *BRAF*)

Other Mutations in Advanced and Metastatic NSCLC (*KRAS*, *HER2*, *MET*, *BRAF*) (1/2)

Presented by Paul Paik, MD

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KRAS Mutations

Other Mutations in Advanced and Metastatic NSCLC (*KRAS*, *HER2*, *MET*, *BRAF*) (2/2)

Presented by Paul Paik, MD

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KRAS Mutations (cont.)

[redacted]

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Key Insights

Other Mutations in Advanced and Metastatic NSCLC (*KRAS*, *HER2*, *MET*, *BRAF*)

Other Mutations in Advanced and Metastatic NSCLC (*KRAS*, *HER2*, *MET*, *BRAF*) (1/2)

EPICS

Regarding first-line phase III trials of KRAS G12C inhibitors vs immunotherapy plus chemotherapy, the experts think that OS data are

Other Mutations in Advanced and Metastatic NSCLC (*KRAS*, *HER2*, *MET*, *BRAF*) (2/2)

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For patients with newly diagnosed NSCLC and a *MET* exon 14 skipping mutation, the experts were split in terms of using targeted

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Fusion-Positive, Advanced and Metastatic NSCLC (*ALK*, *ROS1*, *RET*, *NTRK*, *NRG1*)

Fusion-Positive, Advanced and Metastatic NSCLC (*ALK*, *ROS1*, *RET*, *NTRK*, *NRG1*) (1/3)

Presented by Shirish Gadgeel, MD

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Evolution of ALK Inhibitors

Fusion-Positive, Advanced and Metastatic NSCLC (*ALK*, *ROS1*, *RET*, *NTRK*, *NRG1*) (2/3)

Presented by Shirish Gadgeel, MD

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Evolution of ALK Inhibitors (cont.)

[redacted]

Fusion-Positive, Advanced and Metastatic NSCLC (*ALK*, *ROS1*, *RET*, *NTRK*, *NRG1*) (3/3)

Presented by Shirish Gadgeel, MD

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Emergence of NRG1

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Key Insights

Fusion-Positive, Advanced and Metastatic NSCLC (*ALK*, *ROS1*, *RET*, *NTRK*, *NRG1*)

Fusion-Positive, Advanced and Metastatic NSCLC (*ALK*, *ROS1*, *RET*, *NTRK*, *NRG1*) (1/2)

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For patients with newly diagnosed NSCLC and an *ALK* fusion, approximately two-thirds of the experts have switched to lorlatinib due

Fusion-Positive, Advanced and Metastatic NSCLC (*ALK*, *ROS1*, *RET*, *NTRK*, *NRG1*) (2/2)

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Given the longer survival in lung cancer made possible by immunotherapy and targeted therapy, the experts think that cancer

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Small Cell Lung Cancer: Limited- to Extensive-Stage Disease

Small Cell Lung Cancer: Limited- to Extensive-Stage Disease (1/2)

Presented by Helen Ross, MD

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General Challenges in SCLC

S2409-PRISM A Multicohort PRecision SCLC Subtype Maintenance

STUDY POPULATION

OUTCOMES

EXPERT CONCLUSIONS

Small Cell Lung Cancer: Limited- to Extensive-Stage Disease (2/2)

Presented by Helen Ross, MD

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Limited-Stage SCLC (cont.)

[redacted]

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Key Insights

Small Cell Lung Cancer: Limited- to Extensive-Stage Disease

Small Cell Lung Cancer: Limited- to Extensive-Stage Disease

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For patients with relapsed SCLC, the experts generally view re-challenge possible if at least 6 months have passed since treatment. They

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Future Paradigms in Lung Cancer

Future Paradigms in Lung Cancer (1/2)

Presented by Martin Edelman, MD, and David Jablons, MD

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Approaches for Stage I NSCLC

Future Paradigms in Lung Cancer (2/2)

Presented by Martin Edelman, MD, and David Jablons, MD

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Tumor Treating Fields

[redacted]

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Key Insights

Future Paradigms in Lung Cancer

Future Paradigms in Lung Cancer

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Expert opinion is that TTFs should be explored in the neoadjuvant setting; this could involve assessing the pCR rate in 50 to 60

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