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Global Perspectives in Lung Cancer in 2023

September 25 and 29, 2023

Full Report

Report Contents

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Meeting Snapshot

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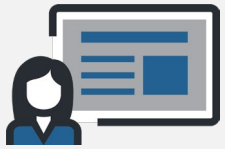
VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
September 25 and 29, 2023



DISEASE STATE AND DATA PRESENTATIONS by key experts

INSIGHT REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in lung cancer

- 5 from North America
- 2 from Europe

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

Panel Consisting of 5 North American and 2 European Lung Cancer Experts

Natasha B. Leighl, MD, FRCPC, FASCO
University of Toronto

Nasser Hanna, MD
Indiana University School of Medicine

CHAIR:
Corey J. Langer, MD, FACP
University of Pennsylvania

Solange Peters, MD, PhD
University Hospital of Lausanne

Ignacio I. Wistuba, MD
MD Anderson Cancer Center

Enriqueta Felip, MD, PhD
Vall d'Hebron University Hospital

Mark A. Socinski, MD
AdventHealth Cancer Institute

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Meeting Agenda – Day 1

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Time	Topic	Speaker/Moderator
10.30 AM – 10.35 AM	**Welcome and Introductions**	Corey Langer, MD, FACP
10.35 AM – 10.55 AM	**Prognostic and Predictive Biomarkers in Non-Small Cell Lung Cancer (NSCLC): The Pathologist's Perspective**	Ignacio Wistuba, MD
10.55 AM – 11.25 AM	Key Questions and Topics for Discussion	All
11.25 AM – 11.40 AM	**New Directions for *EGFR*-Mutated NSCLC**	Natasha Leighl, MD, FRCPC, FASCO
11.40 AM – 12.00 PM	Key Questions and Topics for Discussion	All
12.00 PM – 12.10 PM	***EGFR* (Less Common Mutations, Including Exon 20 Insertions)**	Mark Socinski, MD
12.10 PM – 12.20 PM	Key Questions and Topics for Discussion	All
12.20 PM – 12.30 PM	Break	All
12.30 PM – 12.45 PM	**Therapeutic Landscape for Fusion-Positive NSCLC (*ALK, ROS1, NTRK, RET*)**	Nasser Hanna, MD
12.45 PM – 1.15 PM	Key Questions and Topics for Discussion	All
1.15 PM – 1.30 PM	**Inhibiting Oncogenic Mutations: Overcoming Mutant *KRAS, HER2, MET,* and *BRAF***	Solange Peters, MD, PhD
1.30 PM – 2.00 PM	Key Questions and Topics for Discussion	All
2.00 PM – 2.10 PM	**Promising New Targets/Agents in Lung Cancer: ADCs and Beyond**	Solange Peters, MD, PhD
2.10 PM – 2.30 PM	Key Questions and Topics for Discussion	All
2.30 PM	**Adjourn**	Corey Langer, MD, FACP

Meeting Agenda – Day 2

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Time	Topic	Speaker/Moderator
10.30 AM – 10.35 AM	**Review Agenda and Framework for Day 2**	Corey Langer, MD, FACP
10.35 AM – 10.50 AM	**Immunotherapy in Early NSCLC**	Enriqueta Felip, MD, PhD
10.50 AM – 11.40 AM	Key Questions and Topics for Discussion	All
11.40 AM – 11.50 AM	**Immunotherapy in Unresectable Stage III NSCLC**	Mark Socinski, MD
11.50 AM – 12.10 PM	Key Questions and Topics for Discussion	All
12.10 PM – 12.25 PM	**First-Line Immunotherapy in Metastatic NSCLC: Single Agent or Combination?**	Solange Peters, MD, PhD
12.25 PM – 1.05 PM	Key Questions and Topics for Discussion	All
1.05 PM – 1.15 PM	Break	All
1.15 PM – 1.30 PM	**Emergence of Immunotherapy and New Agents in SCLC**	Nasser Hanna, MD
1.30 PM – 1.55 PM	Key Questions and Topics for Discussion	All
1.55 PM – 2.05 PM	**New Directions for Second-Line Therapy**	Natasha Leighl, MD, FRCPC, FASCO
2.05 PM – 2.30 PM	Key Questions and Topics for Discussion	All
2.30 PM	**Conclusions and Adjourn**	Corey Langer, MD, FACP

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Congress Highlights

Osimertinib With/Without Platinum-Based Chemotherapy as First-line Treatment in Patients with EGFRm Advanced NSCLC (FLAURA2)

Janne P, et al. WCLC 2023. Abstract PL03.13

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STUDY POPULATION

> Previously untreated, advanced *EGFR*-mutated NSCLC

PROGRESSION-FREE SURVIVAL (PER INVESTIGATORS)

Patritumab Deruxtecan (HER3-DXd) in EGFR-Mutated NSCLC Following EGFRTKI and Platinum-Based Chemotherapy: HERTHENA-Lung01

Yu HA, et al. WCLC 2023. Abstract OA05.03

EPICS

STUDY POPULATION

> Advanced, *EGFR*-mutated NSCLC progressing on prior EGFR

BEST PERCENTAGE CHANGE IN LESION SIZE

IMpower151: Phase III Study of Atezolizumab + Bevacizumab + Chemotherapy in 1L Metastatic Nonsquamous NSCLC

Zhou C, et al. WCLC 2023. Abstract OA09.06

EPICS

STUDY POPULATION

> Stage IV, nonsquamous NSCLC; no prior chemotherapy

PROGRESSION-FREE SURVIVAL (*EGFR/ALK* POSITIVE)

Tepotinib + Osimertinib in EGFR-mutant NSCLC with MET Amplification Following 1L Osimertinib: INSIGHT 2 Primary Analysis

Kim TM, et al. WCLC 2023. Abstract OA21.05

EPICS

STUDY POPULATION

> Advanced, *EGFR*-mutated NSCLC with resistance to osimertinib

BEST PERCENTAGE CHANGE IN LESION SIZE

Amivantamab, Lazertinib Plus Platinum-based Chemotherapy in EGFR-mutated Advanced NSCLC: Updated Results from CHRYSALIS-2

Lee SH, et al. WCLC 2023. Abstract MA13.06

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STUDY POPULATION

> Advanced, *EGFR*-mutated NSCLC with prior TKI (≤3 prior lines)

BEST PERCENTAGE CHANGE IN LESION SIZE

FAVOUR: A Phase 1b Study of Furmonertinib, an Oral, Brain Penetrant, Selective EGFR Inhibitor, in Patients with Advanced NSCLC with *EGFR* Exon 20 Insertions

Han B, et al. WCLC 2023. Abstract OA03.04

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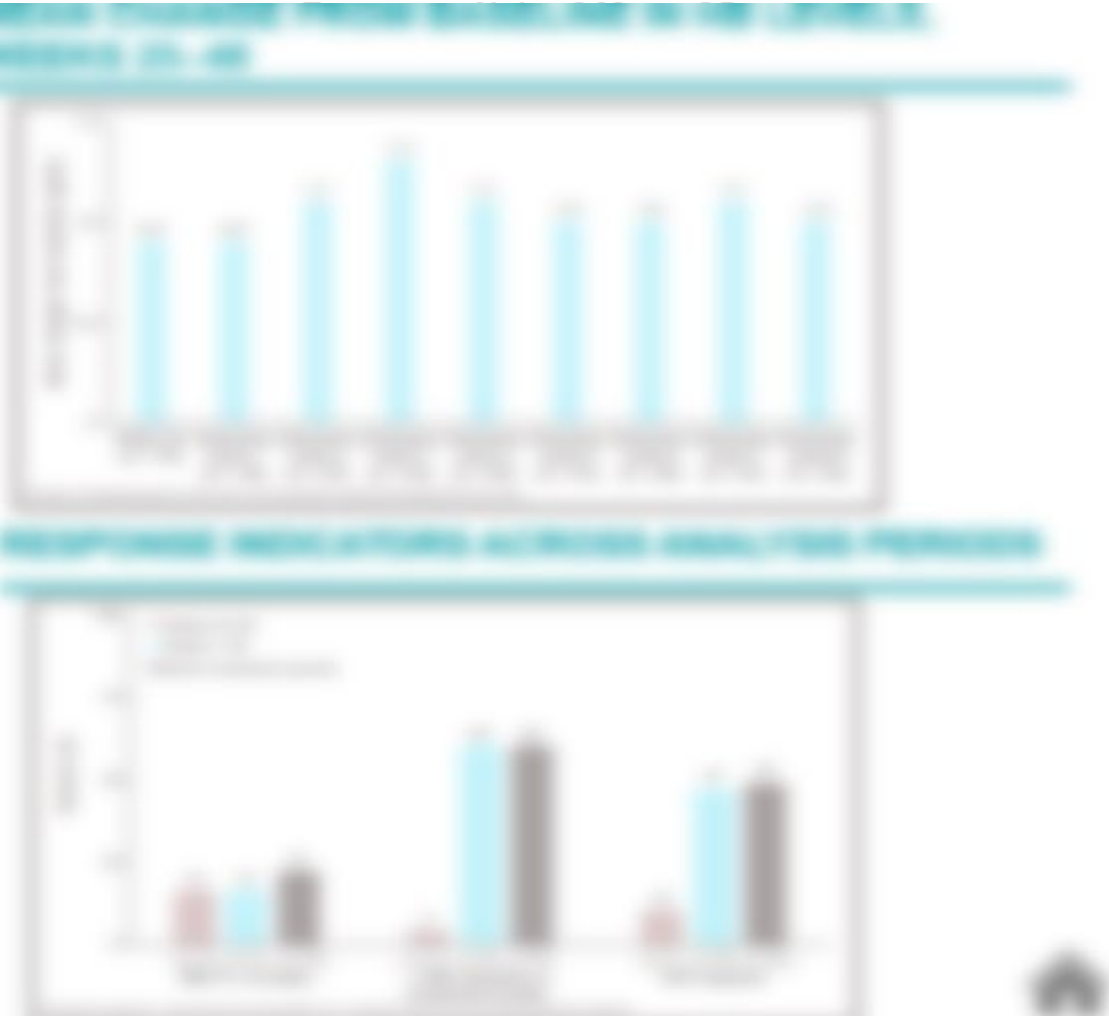
STUDY POPULATION

- Advanced NSCLC with an *EGFR* exon 20 insertion

BEST PERCENTAGE CHANGE IN LESION SIZE



KRYSTAL-1: Two-Year Follow-Up of Adagrasib (MRTX849) Monotherapy in Patients with Advanced/Metastatic KRASG12C-Mutated NSCLC

Gadgeel S, et al. WCLC 2023. Abstract MA06.04

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STUDY POPULATION

> Unresectable/metastatic NSCLC with a *KRAS* G12C mutation

OVERALL AND PROGRESSION-FREE SURVIVAL

CodeBreaK 101: Safety and Efficacy of Sotorasib with Carboplatin and Pemetrexed in KRAS G12C-Mutated Advanced NSCLC

Clarke JM, et al. WCLC 2023. Abstract MA06.05

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STUDY POPULATION

> Advanced, *KRAS* G12C-mutated NSCLC

PERCENTAGE CHANGE IN TUMOR FROM BASELINE

Trastuzumab Deruxtecan in Patients with HER2-Mutant Metastatic Non-Small Cell Lung Cancer: Primary Results of DESTINY-Lung02

Janne P, et al. WCLC 2023. Abstract MA13.10

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STUDY POPULATION

> Metastatic, *HER2*-mutated NSCLC

PROGRESSION-FREE AND OVERALL SURVIVAL

PFS

Beamion Lung 1, a Phase Ia/Ib Trial of the HER2 TKI, BI 1810631 in Patients with Advanced Solid Tumors with HER2 Aberrations

Yamamoto N, et al. WCLC 2023. Abstract MA13.08

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STUDY POPULATION

> Advanced solid tumors with *HER2* aberrations

PERCENTAGE CHANGE IN TUMOR FROM BASELINE

A Phase 3b Study of 1L Savolitinib in Patients with Locally Advanced or Metastatic NSCLC Harboring MET Exon 14 Mutation

Lu S, et al. WCLC 2023. Abstract OA21.03

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STUDY POPULATION

> Locally advanced/metastatic NSCLC, treatment naive

PERCENTAGE CHANGE IN TUMOR FROM BASELINE

Amivantamab in Patients with Advanced NSCLC and MET Exon 14 Skipping Mutation: Results from the CHRYSALIS Study

Leighl N, et al. WCLC 2023. Abstract OA21.04

EPICS

STUDY POPULATION

> Advanced NSCLC with a *MET* exon 14 mutation

PERCENTAGE CHANGE IN TUMOR FROM BASELINE

Neoadjuvant Durvalumab + Chemotherapy Followed by Adjuvant Durvalumab in Resectable *EGFR*-Mutated NSCLC (AEGEAN)

He J, et al. WCLC 2023. Abstract OA12.06

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STUDY POPULATION

> Resectable, stage IIA–IIIB (N2) NSCLC by AJCC 8th edition

EVENT FREE SURVIVAL (*EGFR* MUTATED)

Real-World Outcomes with Durvalumab After Chemoradiotherapy in Unresectable Stage III EGFR-Mutated NSCLC (PACIFIC-R)

Peters S, et al. WCLC 2023. Abstract OA17.03

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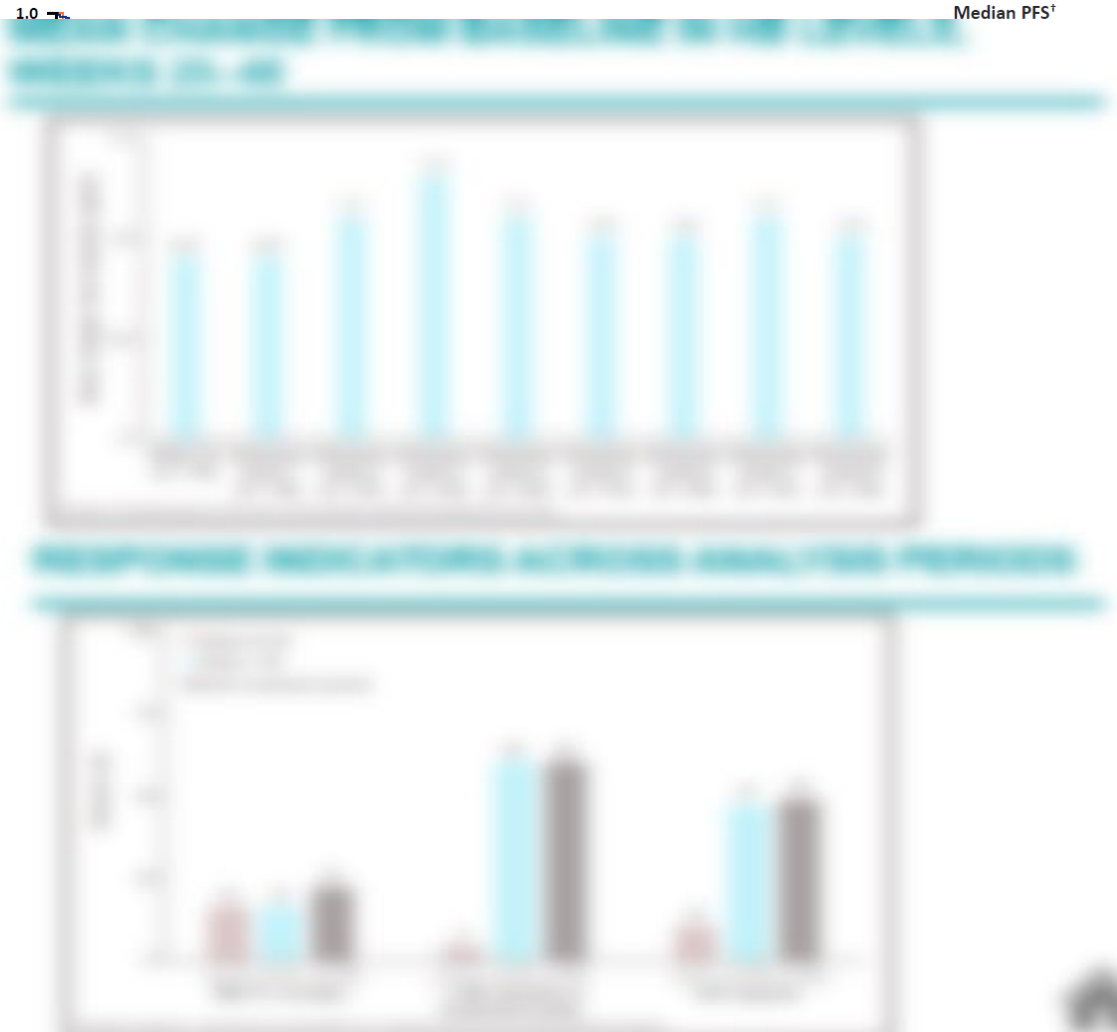
STUDY POPULATION

> Unresectable stage III NSCLC; no PD after CRT

PFS BY *EGFR* MUTATION STATUS



Consolidation EGFR-Tyrosine Kinase Inhibitor (TKI) vs Durvalumab vs Observation in Unresectable *EGFR*-Mutant Stage III NSCLC

Nassar AH, et al. WCLC 2023. Abstract MA16.11

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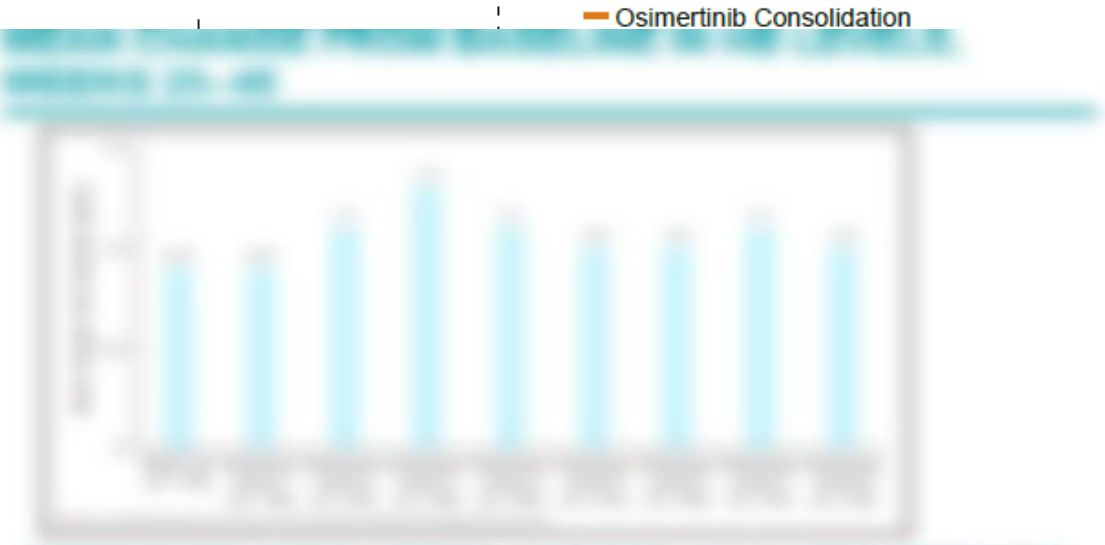
STUDY POPULATION

> Unresectable, *EGFR* mutated, stage III NSCLC

DISEASE-FREE SURVIVAL



Six-year Survival and HRQoL Outcomes with 1L Nivolumab + Ipilimumab in Patients with Metastatic NSCLC from CheckMate227

Ramalingam SS, et al. WCLC 2023. Abstract OA14.03

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STUDY POPULATION

> Stage IV NSCLC, no prior systemic therapy, no *EGFR/ALK*

OVERALL SURVIVAL

OS in patients with tumor PD-L1 ≥ 1%

5-Year Survival of Pembrolizumab Plus Chemotherapy for Metastatic NSCLC With PD-L1 Tumor Proportion Score <1%

Gadgeel S, et al. WCLC 2023. Abstract OA14.05

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STUDY POPULATION

> Pts from KEYNOTE-189/-407 and extension studies (stage IV

OVERALL SURVIVAL

Sacituzumab Govitecan + Pembrolizumab in 1L Metastatic Non-Small Cell Lung Cancer: Preliminary Results of the EVOKE-02 Study

Cho BC, et al. WCLC 2023. Abstract OA05.04

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STUDY POPULATION

> Stage IV NSCLC, no known actionable genomic alterations, no

PERCENTAGE CHANGE IN TUMOR FROM BASELINE

Datopotamab Deruxtecan (Dato-DXd) + Durvalumab ± Carboplatin in Advanced/mNSCLC: Initial Results from Phase 1b TROPION-Lung04

Papadopoulos KP, et al. WCLC 2023. Abstract OA05.06

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STUDY POPULATION

> Stage IV NSCLC without actionable genomic alterations

PERCENTAGE CHANGE IN TUMOR FROM BASELINE

Five-Year Survival in Patients with ES-SCLC Treated with Atezolizumab in IMpower133: IMbrella A Extension Study Results

Liu SV, et al. WCLC 2023. Abstract OA01.04

EPICS

STUDY POPULATION

> Previously untreated ES-SCLC, including 18 pts from the IMbrella

OVERALL SURVIVAL

Phase I Dose Escalation Trial Of The DLL3/CD3 Igg-Like T Cell Engager BI 764532 In Patients with DLL3+ Tumors: Focus on SCLC

Wermke M, et al. WCLC 2023. Abstract OA01.05

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STUDY POPULATION

> Advanced SCLC, LCNEC, or epNEC failing or ineligible for

PERCENTAGE CHANGE IN TUMOR FROM BASELINE (SCLC)

Ifinatamab Deruxtecan (I-DXd; DS-7300) in Patients with Refractory SCLC: A Subgroup Analysis of a Phase 1/2 Study

Johnson M, et al. WCLC 2023. Abstract OA05.05

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STUDY POPULATION

> Advanced/unresectable solid tumors

PERCENTAGE CHANGE IN TUMOR FROM BASELINE

Benmelstobart with Anlotinib plus Chemotherapy as First-line Therapy for ES-SCLC: A Randomized, Double-blind, Phase III Trial

Cheng Y, et al. WCLC 2023. Abstract OA01.03

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STUDY POPULATION

> ES-SCLC with no prior systemic therapy

OVERALL SURVIVAL

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Key Takeaways

Prognostic and Predictive Biomarkers in NSCLC: The Pathologist's Perspective (1/2)

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> There is a wide range of approaches to molecular testing in NSCLC among the experts, ranging from testing all patients with NSCLC to only

Prognostic and Predictive Biomarkers in NSCLC: The Pathologist's Perspective (2/2)

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> There are varying approaches among the panelists' institutions for storing molecular test results; proactive approaches at one institution

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

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> Regarding the FLAURA2 trial evaluating the addition of platinum-based chemotherapy to osimertinib, expert opinion is that the combination

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

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> The experts would like to see phase III data with HER3-DXd before deciding where this agent belongs in the treatment continuum for *EGFR*-

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EGFR (Less Common Mutations, Including Exon 20 Insertions)

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> Postmeeting update: On October 2, 2023, it was announced that the indication for mobocertinib in *EGFR* exon 20-mutated NSCLC was

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

EPICS

> Regarding molecular testing for oncogenic fusions, the pathology expert confirmed that RNA-based testing (vs DNA-based) is the best

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

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> In terms of frequency of brain imaging, the experts request this follow-up every 6 months

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

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> *KRAS*

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

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> *BRAF* V600E

Promising New Targets/Agents in Lung Cancer: ADCs and Beyond (1/2)

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> While ADCs can demonstrate activity even in unselected patients, the experts expressed a desire to identify selection criteria, given that

Promising New Targets/Agents in Lung Cancer: ADCs and Beyond (2/2)

EPICS

> Regarding other investigational approaches, expert opinion is that bispecific agents will play an increasingly important role in lung cancer; on

Immunotherapy in Early NSCLC (1/2)

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- Postmeeting update: On October 16, 2023, the US FDA approved neoadjuvant pembrolizumab + chemotherapy and adjuvant pembrolizumab for patients with resectable (tumors that are ≥4 cm or node-positive) NSCLC on the basis of the KEYNOTE-671 trial
- Regarding testing of patients with resectable NSCLC, PD-L1 and *EGFR* testing carried out at the experts' institutions

Immunotherapy in Early NSCLC (2/2)

EPICS

> Expert opinion is that it is still too early to consider de-escalation approaches, even for patients who achieve a pCR after neoadjuvant

Immunotherapy in Unresectable Stage III NSCLC

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> For patients with *EGFR*-mutated, unresectable stage III NSCLC, the experts would not offer consolidation immunotherapy; if available,

Durm GA, et al. *Cancer.* 2023;129(2):264-271.

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

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> For patients with PD-L1–negative NSCLC, most experts would offer a regimen with combination immunotherapy including a CTLA-4 inhibitor,

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

EPICS

> Currently, most of the experts do not use investigational biomarkers, such as *STK11* mutation status, to select patients for immunotherapy;

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

EPICS

> Expert opinion is that bispecific agents such as tarlatamab have demonstrated impressive results in SCLC. In terms of incorporating into first-

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

EPICS

> The experts agreed that the ETER701 trial from China evaluating the addition of benmelstobart and anlotinib to first-line chemotherapy in ES-

New Directions for Second-Line Therapy

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> Regarding the phase III TROPION-Lung01 comparing Dato-DXd with docetaxel in patients with previously treated NSCLC, the experts stated

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