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EPICS Global Perspectives in Lung Cancer – WCLC and ESMO 2021

24 September 2021

Report Contents

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Meeting Snapshot

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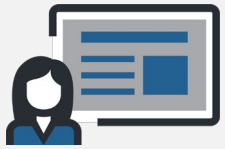
VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
24 September 2021



DISEASE STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in lung cancer

- > 6 from the US
- > 3 from Europe

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

Panel Consisting of 6 North American and 3 European Lung Cancer Experts

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David Jablons, MD
University of California
San Francisco

Marina Chiara Garassino, MD
University of Chicago

Natasha Leighl, BSc, MMSc, MD
University of Toronto

Lynette Sholl, MD
Brigham and Women's
Hospital

Nasser Hanna, MD
Indiana University
School of Medicine

CHAIR:
Corey Langer, MD, FACP
University of Pennsylvania

Benjamin Besse, MD, PhD
Institute Gustave Roussy

Solange Peters, MD, PhD
University Hospital of Lausanne

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

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Meeting Agenda

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Time (EST)	Topic	Speaker/Moderator
11.00 AM – 11.05 AM	Welcome, Introduction, and Meeting Objectives	Corey Langer, MD, FACP
11.05 AM – 11.15 AM	Perioperative Immunotherapy in Early Stage NSCLC	David Jablons, MD
11.15 AM – 11.30 AM	Discussion and Key Takeaways	
11.30 AM – 11.40 AM	Immunotherapy in Unresectable Stage III NSCLC	Nasser Hanna, MD
11.40 AM – 11.55 AM	Discussion and Key Takeaways	
11.55 AM – 12.10 PM	Immunotherapy in Metastatic NSCLC and Subsequent Therapy	Solange Peters, MD, PhD
12.10 PM – 12.35 PM	Discussion and Key Takeaways	
12.35 PM – 12.50 PM	*EGFR* (Common Mutations): Resectable and Metastatic	Enriqueta Felip, MD, PhD
12.50 PM – 1.10 PM	Discussion and Key Takeaways	
1.10 PM – 1.15 PM	BREAK	
1.15 PM – 1.20 PM	*EGFR* (Less Common Mutations, Including Exon 20 Insertions)	Natasha Leighl, BSc, MMSc, MD
1.20 PM – 1.35 PM	Discussion and Key Takeaways	
1.35 PM – 1.50 PM	Oncogenic Drivers: Mutations	Corey Langer, MD, FACP
1.50 PM – 2.05 PM	Discussion and Key Takeaways	
2.05 PM – 2.15 PM	Oncogenic Drivers: Fusions	Marina Garassino, MD
2.15 PM – 2.30 PM	Discussion and Key Takeaways	
2.30 PM – 2.40 PM	SCLC and Second-Line NSCLC: Old and New Data	Benjamin Besse, MD, PhD
2.40 PM – 3.00 PM	Discussion and Key Takeaways	
3.00 PM	Closing Remarks and Adjourn	Corey Langer, MD, FACP

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Congress Highlights

IMpower010: Adjuvant atezolizumab versus BSC: Outcomes by prior Therapy and PD-L1; Sites of Relapse

Altorki N, et al. 2021, WCLC PL02.05
Felip E, et al. 2021, ESMO LBA9

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STUDY POPULATION

- Completely resected, stage IB–IIIA NSCLC per UICC/AJCC v7.

Forest Plot: DFS by Surgery/PD-L1 Expression Level

Long Term Survival in Operable Stage IIIA NSCLC Patients Treated With Neoadjuvant Nivolumab Plus Chemotherapy - NADIM Study

Provencio M, et al. 2021, WCLC OA20.01

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STUDY POPULATION

> Patients with resectable stage IIIA NSCLC treated with

3-Year OS

SAKK 16/14 - T-Cell Receptor Repertoire Metrics Predict Response to Neoadjuvant Durvalumab in Patients With Stage IIIA(N2) NSCLC

Rothschild S, et al. 2021, WCLC MA09.02

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STUDY POPULATION

- Patients with stage IIIA-N2 NSCLC receiving neoadjuvant

Correlation Between Baseline TCR Evenness and EFS

COAST: an open-label, randomized, phase II platform study of durvalumab alone or in combination with novel agents in patients with locally advanced, unresectable, Stage III NSCLC

Martinez-Marti A, et al. 2021, ESMO LBA42

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STUDY POPULATION

> Patients with unresectable stage III NSCLC

COAST: Progression-Free Survival

PFS by investigator assessment

PACIFIC-R Real-World Study: Treatment Duration and Interim Analysis of Progression-Free Survival in Unresectable Stage III NSCLC Patients Treated with Durvalumab After Chemoradiotherapy

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Girard N, et al. 2021, ESMO 1171MO

STUDY POPULATION

> Patients with unresectable stage III NSCLC

PFS by Subgroup

Real-world PFS by Subgroup

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Durvalumab ± Tremelimumab + Chemotherapy as First-line Treatment for mNSCLC: Results from the Phase III POSEIDON Study

Johnson M, et al. 2021, WCLC PL02.01

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STUDY POPULATION

> Patients with treatment-naive, metastatic NSCLC

Survival With Durvalumab-Tremelimumab + Chemotherapy vs Chemotherapy

EMPOWER-Lung 3: Cemiplimab in combination with platinum doublet chemotherapy for first-line (1L) treatment of advanced non-small-cell lung cancer (NSCLC)

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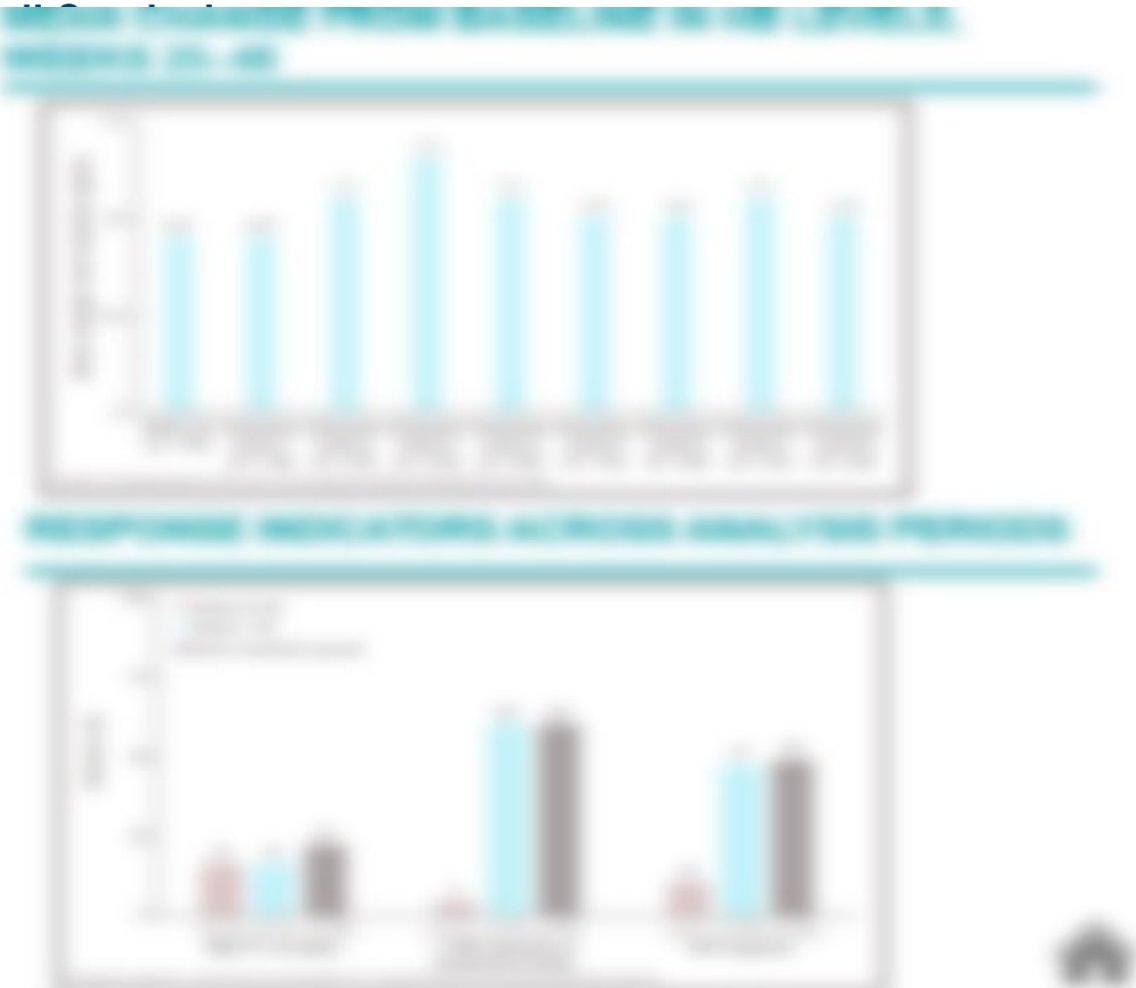
Gogishvili M, et al. 2021, ESMO LBA51

STUDY POPULATION

> Patients with treatment-naive, metastatic NSCLC

Primary Endpoint: OS



First-line Nivolumab + Ipilimumab + Chemo in Patients With Advanced NSCLC and Brain Metastases: Results From CheckMate 9LA

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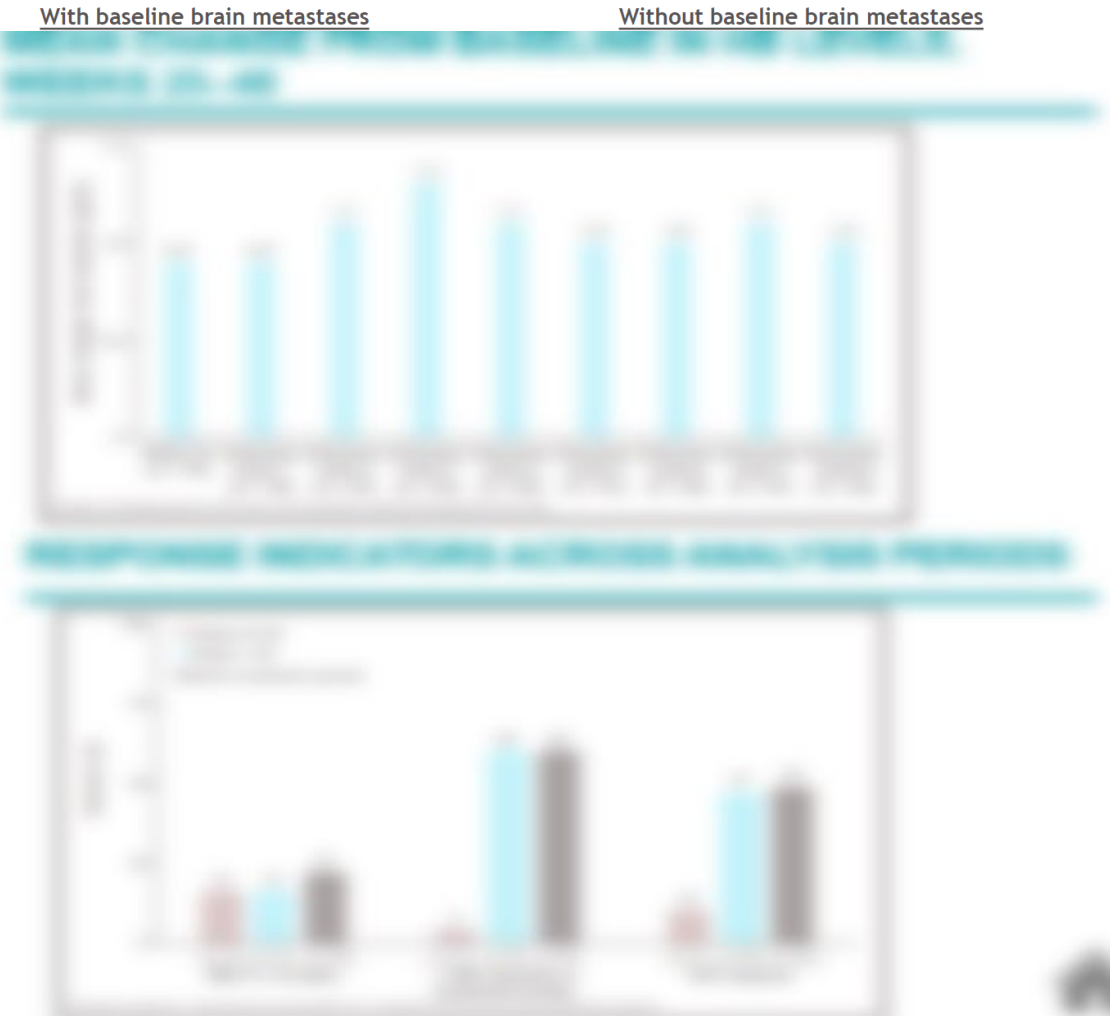
Carbone DP, et al. 2021, WCLC OA09.01

STUDY POPULATION

> Patients with treatment-naive, metastatic NSCLC

OS by Baseline Brain Metastases



ATEZO-BRAIN: Single Arm Phase II Study of Atezolizumab Plus Chemotherapy in Stage IV NSCLC With Untreated Brain Metastases

Nadal E, et al. 2021, WCLC OA09.02

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STUDY POPULATION

> Treatment-naive patients with untreated brain metastases

Progression-Free Survival

Systemic PFS by RECIST v1.1 Intracranial PFS by RANO-BM

Primary results of a randomized phase II study of osimertinib plus bevacizumab versus osimertinib monotherapy for untreated patients with non-squamous non-small-cell lung cancer harboring EGFR mutations; WJOG9717L study

Kenmotsu H, et al. 2021, ESMO LBA44

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STUDY POPULATION

> Patients with newly diagnosed, *EGFR* mutation-positive NSCLC

PFS by Independent Review

ORCHARD osimertinib + savolitinib interim analysis: A biomarker-directed phase II platform study in patients (pts) with advanced non-small cell lung cancer (NSCLC) whose disease has progressed on first line (1L)

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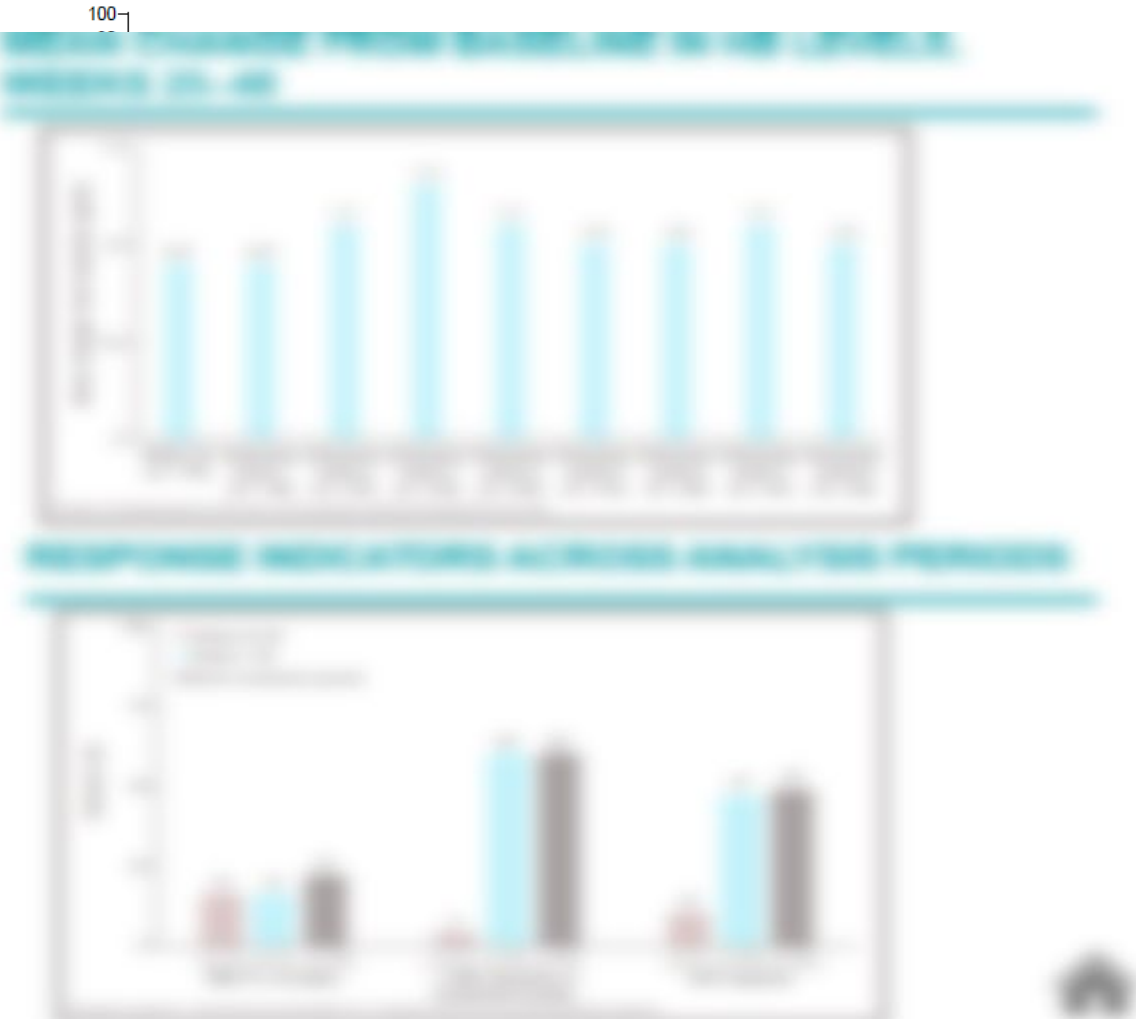
Yu HA, et al. 2021, ESMO 1239P

STUDY POPULATION

> Patients with *EGFR* mutation-positive NSCLC and *MET*

Antitumor Activity of Osimertinib + Savolitinib in Patients With *MET* Alterations



Tepotinib Plus an EGFR TKI in Patients with *EGFR*-mutant NSCLC and Resistance to EGFR TKIs Due to MET Amplification (METamp)

Liam CK, et al. 2021, WCLC P51.01

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STUDY POPULATION

> Patients with resistance to 1G/2G EGFR TKI and with *MET*

PFS: Tepotinib-Gefitinib vs Chemotherapy in *MET*amp

Amivantamab Monotherapy and in Combination with Lazertinib in Post-Osimertinib EGFR-mutant NSCLC: Analysis from the CHRYSALIS Study

Leighl NB, et al. 2021, ESMO 1192MO

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STUDY POPULATION

> Patients with osimertinib-pretreated, *EGFR* mutation-positive

Overall Response Rate

Amivantamab plus lazertinib in post-osimertinib, post-platinum chemotherapy *EGFR*-mutant non-small cell lung cancer (NSCLC): Preliminary results from CHRYSALIS-2

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Shu CA, et al. 2021, ESMO 1193MO

STUDY POPULATION

Activity of Amivantamab + Lazertinib by Cohort

Pembrolizumab in Combination With Platinum-Based Chemotherapy in Recurrent EGFR/ALK-Positive Non-Small Cell Lung Cancer (NSCLC)

Gadgeel SM, et al. 2021, WCLC OA09.03

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STUDY POPULATION

> Patients with *EGFR* or *ALK* molecular rearrangements

Overall Survival

Mobocertinib in *EGFR* Exon 20 Insertion–Positive Metastatic NSCLC Patients With Disease Control on Prior EGFR TKI Therapy

Spira AI, et al. 2021, WCLC OA15.01

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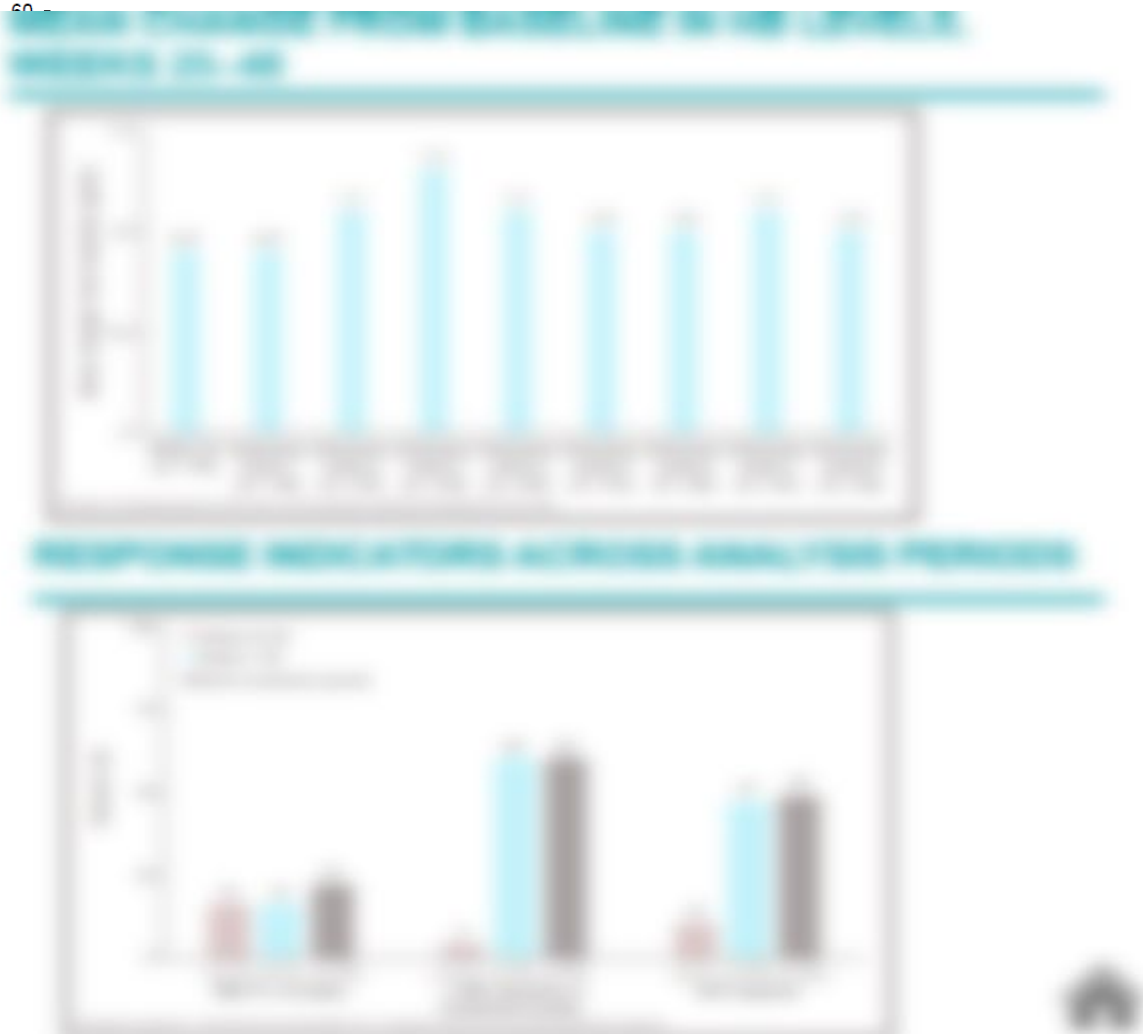
STUDY POPULATION

- Patients with an *EGFR* exon 20 insertion and progressive disease

Antitumor Activity in Patients With Prior TKI



Mobocertinib in Platinum-Pretreated *EGFR* Exon 20 Insertion+ Metastatic NSCLC Patients With/Without Prior Anti-PD(L)-1 Therapy

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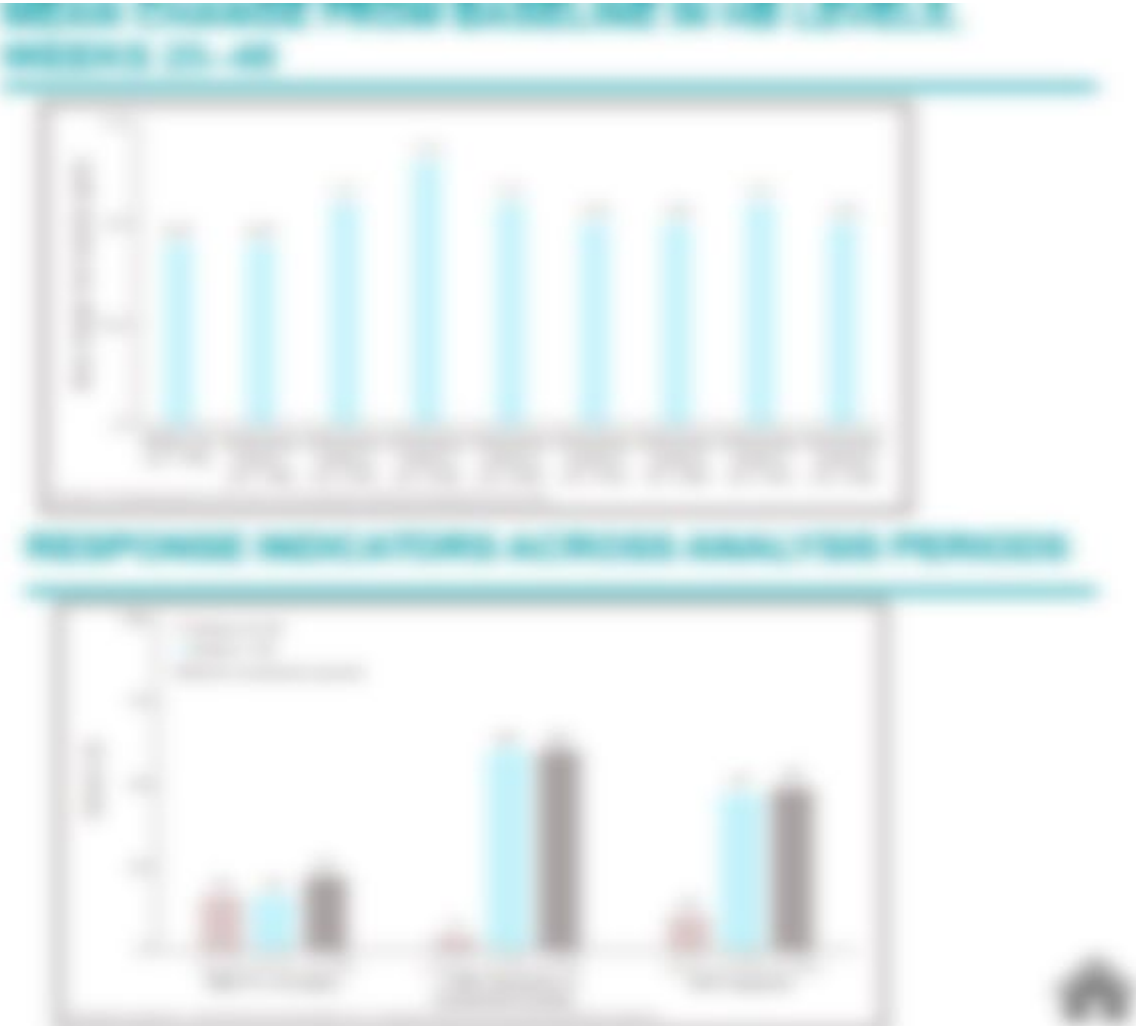
Janne PA, et al. 2021, WCLC FP09.01

STUDY POPULATION

> Patients with platinum-pretreated NSCLC and an *EGFR* exon 20

Antitumor Activity in Patients With Prior Platinum ± Prior Immunotherapy



Phase I Studies of DZD9008, an Oral Selective EGFR/HER2 Inhibitor in Advanced NSCLC with *EGFR* Exon20 Insertion Mutations

Janne P, et al. 2021, WCLC OA15.02

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STUDY POPULATION

> Patients with previously treated NSCLC and an *EGFR* exon 20

Antitumor Activity of DZD9008 in Different *EGFR* Exon 20 Insertions

High dose osimertinib in patients with advanced stage *EGFR* exon 20 mutation-positive NSCLC: Results from a phase II multicenter study, POSITION20

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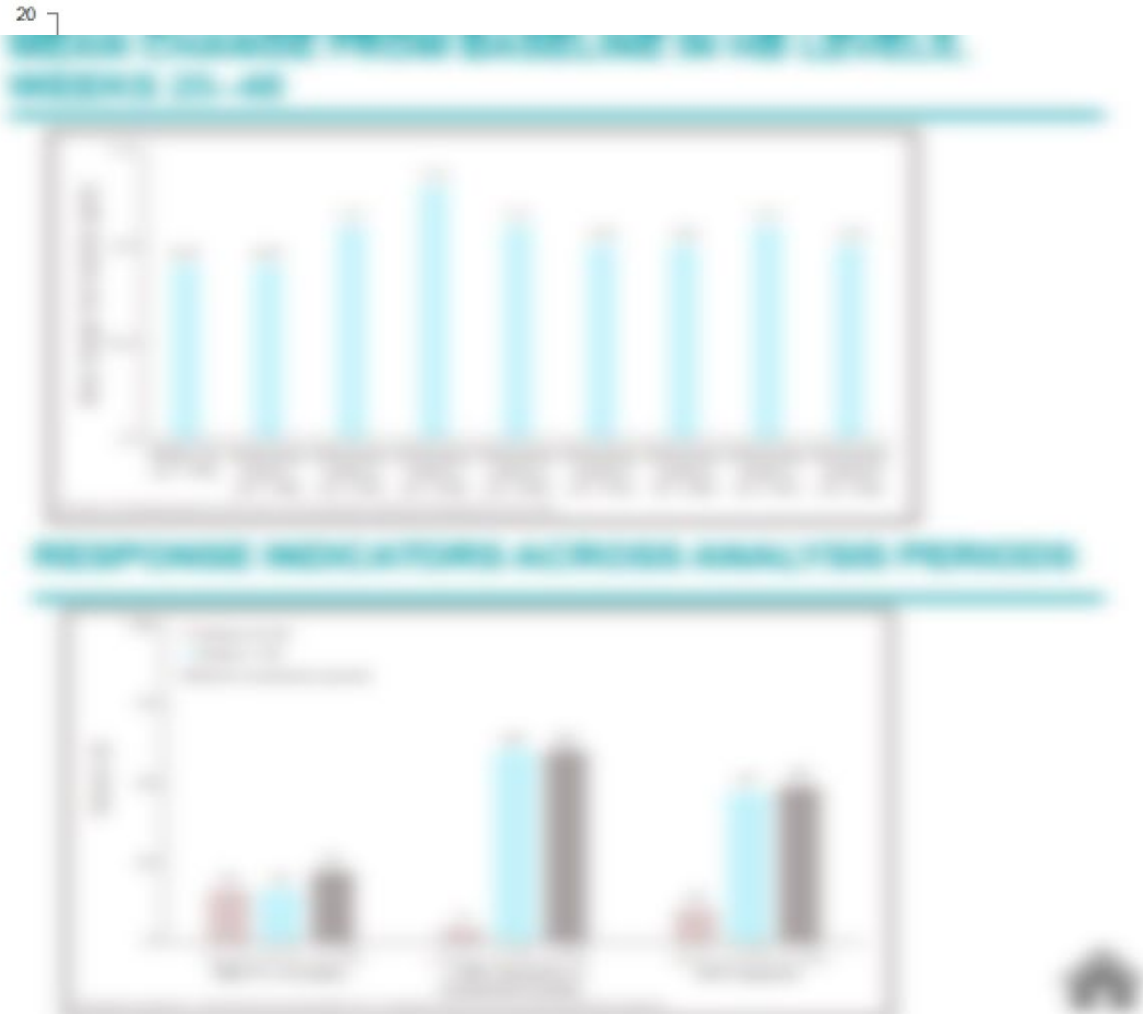
Zwierenga F, et al. 2021, ESMO 1214P

STUDY POPULATION

- Patients with NSCLC and an *EGFR* exon 20 alteration (mutation,

Antitumor Activity of Osimertinib 160 mg/Day in NSCLC With *EGFR* Exon 20 Insertions



Genomic Profiles and Potential Determinants of Response and Resistance in *KRAS* p.G12C-mutated NSCLC Treated With Sotorasib

Skoulidis F, et al. 2021, WCLC MA14.03

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STUDY POPULATION

> Patients with a *KRAS* G12C mutation treated with sotorasib

Grouping of Patients by Response Pattern and Co-mutation

Tepotinib in Patients with *MET* exon 14 (METex14) Skipping NSCLC as Identified by Liquid (LBx) or Tissue (TBx) biopsy

Felip E, et al. 2021, WCLC P45.03

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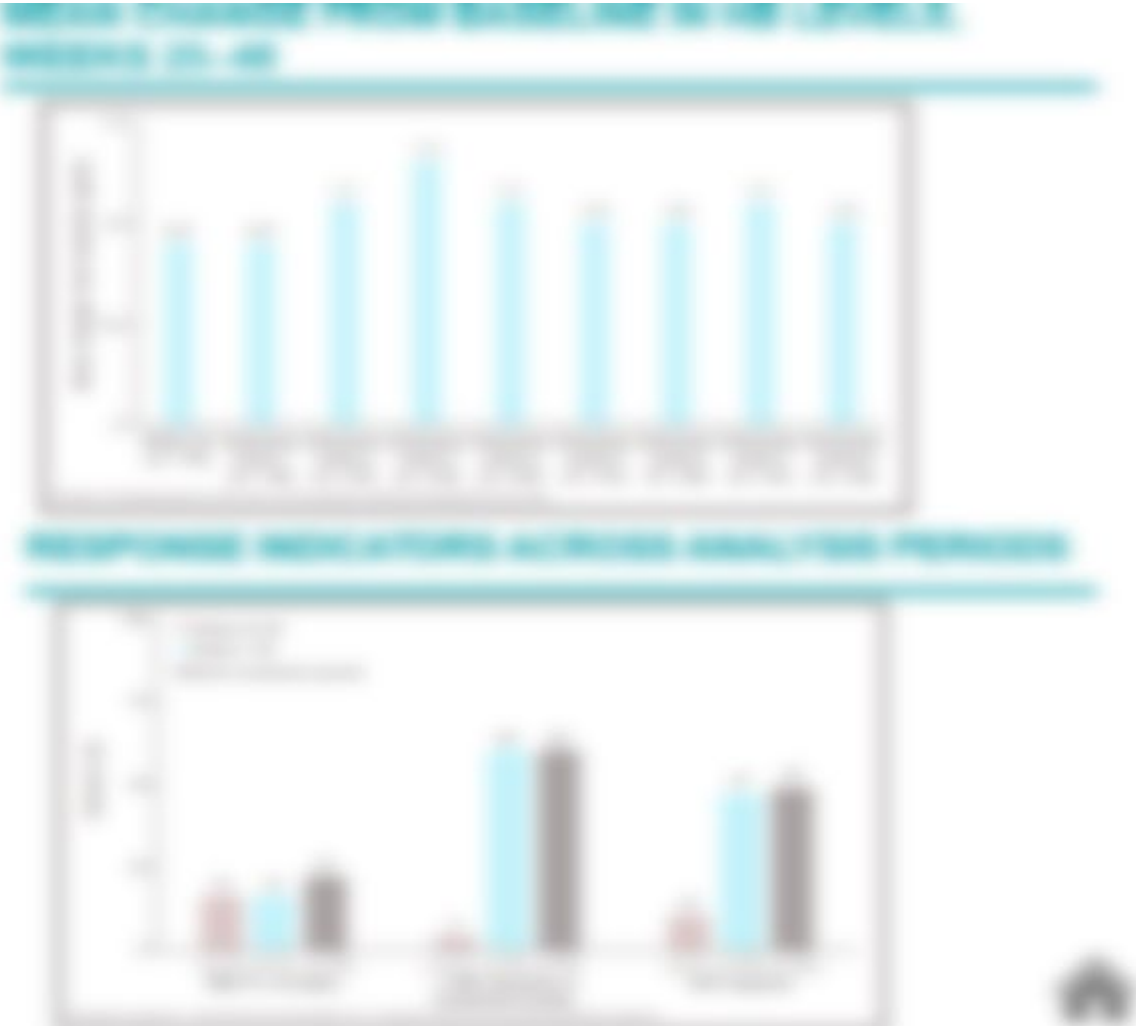
STUDY POPULATION

> Patients with a *MET* exon 14 mutation detected by tissue- or liquid-

Outcome by Biopsy Type Across Treatment Lines



Efficacy and safety of tepotinib in patients (pts) with advanced age: VISION subgroup analysis of pts with *MET* exon 14 (METex14) skipping NSCLC

Garassino M, et al. 2021, ESMO 1254P

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STUDY POPULATION

> Patients with NSCLC and a *MET* exon 14 mutation

PFS by Age Group

Amivantamab in Non-small Cell Lung Cancer (NSCLC) with *MET* Exon 14 Skipping (METex14) Mutation: Initial Results from CHRYSALIS

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Spira AI, et al. 2021, WCLC OA15.03

STUDY POPULATION

> Patients with NSCLC and a *MET* exon 14 mutation

Antitumor Activity by Prior Therapies

Telisotuzumab Vedotin (teliso-v) Monotherapy in Patients With Previously Treated c-Met+ Advanced Non-Small Cell Lung Cancer

Camidge DR, et al. 2021, WCLC OA15.04

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STUDY POPULATION

- Patients with NSCLC, *MET* expression, and ≤2 prior lines of

Antitumor Activity in Nonsquamous, *EGFR* Wild-Type

Primary Data from DESTINY-Lung01: A Phase II Trial of Trastuzumab Deruxtecan (T-DXd) in Patients (Pts) With *HER2*-Mutated (HER2m) Metastatic Non–Small Cell Lung Cancer (NSCLC)

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Li BT, et al. 2021, ESMO LBA45

STUDY POPULATION

> Patients with NSCLC and a *HER2* mutation

T-DXd: Updated Antitumor Activity in *HER2*-Mutated NSCLC

Efficacy and Safety of Poziotinib in treatment-naïve NSCLC harboring *HER2* exon 20 mutations: A multinational Phase II study (ZENITH20-4)

Cornelissen R, et al. 2021, ESMO LBA46

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STUDY POPULATION

> Treatment-naive patients with NSCLC and a *HER2* exon 20

Antitumor Activity of Poziotinib in *HER2*-Mutated NSCLC

MET-Driven Acquired Resistance (AR) in Fusion-Positive Non-Small Cell Lung Cancer (NSCLC)

Lee JK, et al. 2021, WCLC MA02.03

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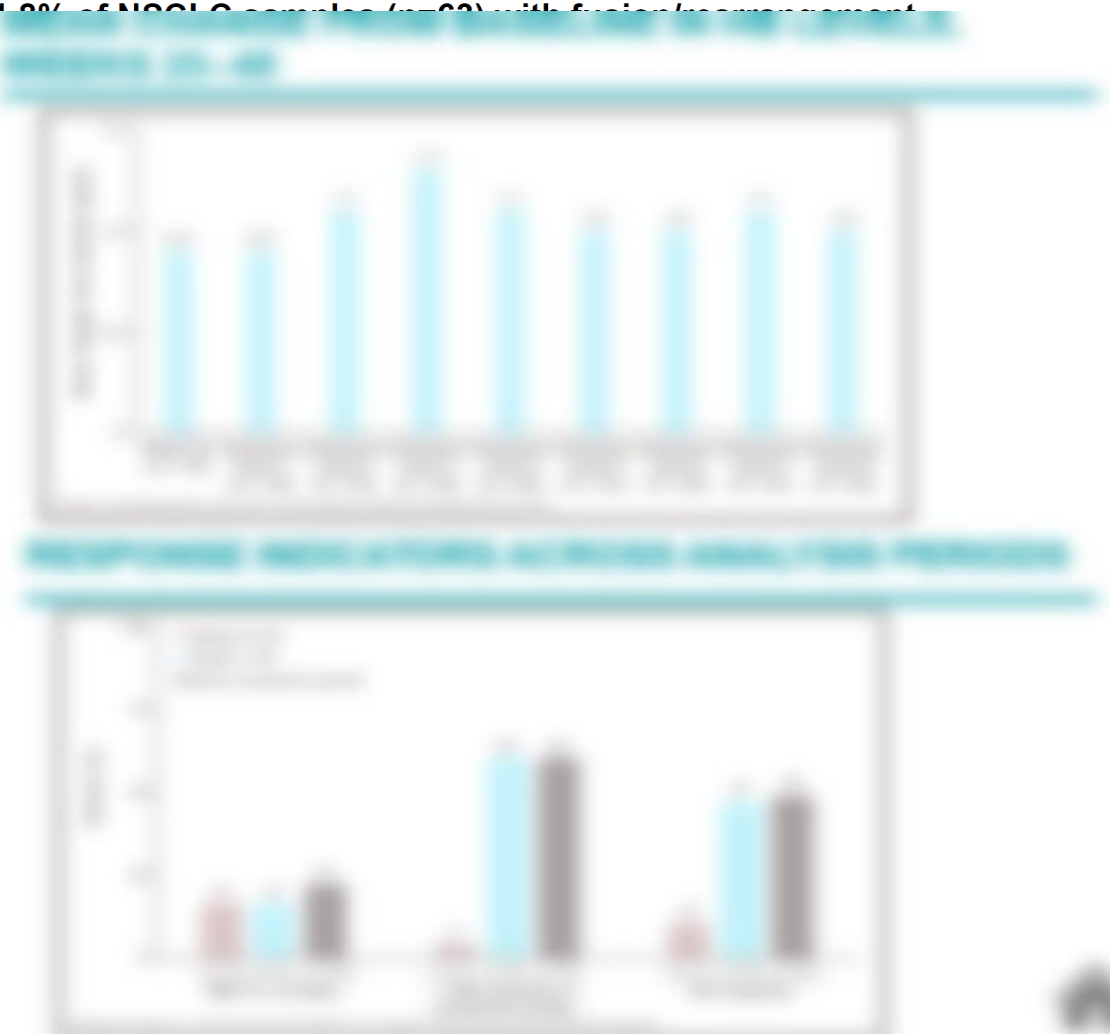
STUDY POPULATION

> Patients with advanced NSCLC and oncogenic fusions

Rate of *MET* Alterations in Patients With an Oncogenic Fusion



Durvalumab ± tremelimumab + platinum-etoposide in first-line extensive-stage SCLC (ES-SCLC): 3-year overall survival update from the Phase III CASPIAN study

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Paz-Ares L, et al. 2021, ESMO LBA61

STUDY POPULATION

- Patients with newly diagnosed ES-SCLC

CASPIAN: 3-Year OS

Lurbinectedin/doxorubicin versus CAV or Topotecan in Relapsed SCLC Patients: Phase III Randomized ATLANTIS Trial

Paz-Ares L, et al. 2021, WCLC PL02.03

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STUDY POPULATION

> Patients with SCLC and 1 prior line of chemotherapy

ATLANTIS: Overall Survival

DUBLIN-3 (BPI-2358-103): A Global Phase (Ph) III Trial with the Plinabulin/ Docetaxel (Plin/Doc) combination vs. Doc in Second/Third-Line NSCLC Patients (pts) with *EGFR*-wild type (wt) Progressing on a Prior Platinum-Based Regimen

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Feinstein T, et al. 2021, ESMO LBA48

STUDY POPULATION

> Patients with metastatic NSCLC and 1–2 prior lines of therapy

DUBLIN-3: Overall Survival

MRTX-500: Phase II Trial of Sitravatinib (Sitra) + Nivolumab (Nivo) in Patients (Pts) With Nonsquamous (NSQ) Non–Small-Cell Lung Cancer (NSCLC) Progressing on or After Prior Checkpoint Inhibitor (CPI) Therapy

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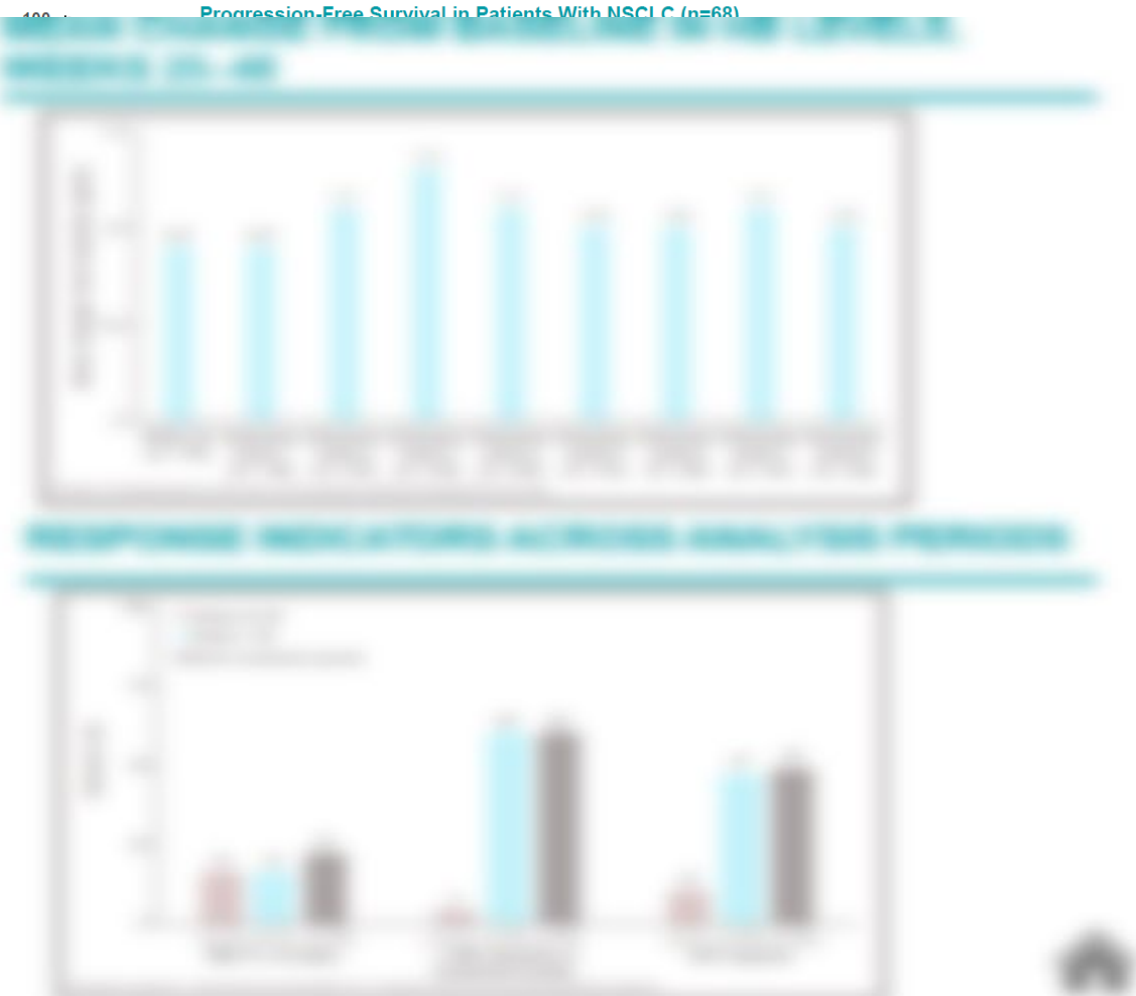
Leal TA, et al. 2021, ESMO 1191O

STUDY POPULATION

> Patients with advanced NSCLC and response or stable disease to

PFS With Sitravatinib-Nivolumab in IO-Pretreated Patients



TROPION-PanTumor01: Updated Results From the NSCLC Cohort of the Phase I Study of Datopotamab Deruxtecan in Solid Tumors

Garon EB, et al. 2021, WCLC MA03.02

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STUDY POPULATION

> Patients with solid tumors

Datopotamab Deruxtecan: Antitumor Activity

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Key Insights

Key Insights: Perioperative Immunotherapy in Early Stage NSCLC (1/2)

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The experts discussed the DFS results from the IMpower010 trial of adjuvant atezolizumab, broken down by PD-L1 expression levels

Key Insights: Perioperative Immunotherapy in Early Stage NSCLC (2/2)

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In terms of endpoints for neoadjuvant immunotherapy, expert

Key Insights: Immunotherapy in Unresectable Stage III NSCLC

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For patients with unresectable stage III NSCLC that is *EGFR* mutation positive, the experts think there are insufficient data on which

Key Insights: Immunotherapy in Metastatic NSCLC and Subsequent Therapy (1/2)

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The experts discussed which patients with PD-L1 expression ≥50% would receive chemotherapy in addition to immunotherapy

- Never-smoking patients and patients with a high tumor burden were mentioned by experts as those whom they would treat with

Key Insights: Immunotherapy in Metastatic NSCLC and Subsequent Therapy (2/2)

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The pathology expert mentioned approaches to improve the

Expert opinion is that the adenosine pathway has viable

Key Insights: *EGFR* (Common Mutations) – Resectable and Metastatic

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In general, there is wide variation in testing practices at the various institutions of the expert panel

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Key Insights: *EGFR* (Less Common Mutations, Including Exon 20 Insertions)

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For first-line treatment of patients with an *EGFR* exon 20 insertion, the majority of the experts would use chemotherapy + bevacizumab, with one of the experts choosing chemotherapy + immunotherapy

Key Insights: Oncogenic Drivers – Mutations (1/2)

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KRAS

The experts generally consider sotorasib and adagrasib to be similar agents, although more data are still needed, including results in subgroups and data with combinations

Key Insights: Oncogenic Drivers – Mutations (2/2)

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MET

The experts discussed agents for patients with *MET* exon 14 mutations

HER2

Trastuzumab deruxtecan (T-DXd) is considered a promising drug for patients with *HER2* mutations

Key Insights: Oncogenic Drivers – Fusions (1/2)

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ALK

Most of the experts use alectinib in the first-line setting for patients with *ALK* rearrangements; however, approximately half occasionally use brigatinib in this setting

Key Insights: Oncogenic Drivers – Fusions (2/2)

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Post-TKI Therapy

For patients with oncogenic fusions who progress on available TKIs, the experts use chemotherapy as the standard subsequent treatment

Testing for Fusions

The pathology expert described the importance of RNA-based testing to detect certain fusions

Key Insights: SCLC and Second-Line NSCLC – Old and New Data (1/2)

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SCLC

Expert opinion is that selecting the best second-line option in patients with SCLC is difficult

Key Insights: SCLC and Second-Line NSCLC – Old and New Data (2/2)

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NSCLC

> Data with sitravatinib + nivolumab generated mixed reactions from the experts