



EPICS

Lung Cancer in 2024 and Beyond

November 1–2, 2024

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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

A map of the United States with callouts to 10 lung cancer experts. The callouts are circular portraits with blue borders, except for the chair, Corey Langer, who has an orange border. A blue line connects the callouts to a vertical list on the right side of the map.

- David Jablons, MD**
UCSF Helen Diller Family Comprehensive Cancer Center
- Helen Ross, MD**
Rush University Medical Center
- Shirish Gadgeel, MD**
Henry Ford Health
- Paul Paik, MD**
Memorial Sloan Kettering Cancer Center
- Fred Hirsch, MD, PhD**
Tisch Cancer Institute at Mount Sinai
- Xiuning Le, MD, PhD**
MD Anderson Cancer Center
- CHAIR: Corey Langer, MD, FACP**
University of Pennsylvania
- Andrew Haas, MD, PhD**
University of Pennsylvania
- Martin Edelman, MD**
Fox Chase Cancer Center
- Hossein Borghaei, DO**
Fox Chase Cancer Center

Meeting Agenda – Friday, November 1

EPICS

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: <i>EGFR</i>, <i>ALK</i>, 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

EPICS

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: <i>EGFR</i> 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 (<i>KRAS, HER2, MET, BRAF</i>)	Paul Paik, MD
9.10 AM – 9.45 AM	Discussion	All faculty
9.45 AM – 10.00 AM	Fusion-Positive, Advanced and Metastatic NSCLC (<i>ALK, ROS1, RET, NTRK, NRG1</i>)	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



EPICS**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

Oncogenic Drivers and Molecular Testing

Adequate molecular testing is essential in all

STANDARD OF CARE

Approximately 40% of NSCLC patients with a 1st-line drug combination of a 1st-line drug + 1st-line immunotherapy, with a median overall survival of approximately 18 months. The combination of a 1st-line drug + 1st-line immunotherapy is the standard of care for NSCLC patients with a 1st-line drug + 1st-line immunotherapy. The combination of a 1st-line drug + 1st-line immunotherapy is the standard of care for NSCLC patients with a 1st-line drug + 1st-line immunotherapy.

KEY POINTS

- Approximately 40% of NSCLC patients with a 1st-line drug combination of a 1st-line drug + 1st-line immunotherapy, with a median overall survival of approximately 18 months.
- Approximately 40% of NSCLC patients with a 1st-line drug combination of a 1st-line drug + 1st-line immunotherapy, with a median overall survival of approximately 18 months.

KEY POINT CONCLUSIONS

Standardized molecular testing is essential in all NSCLC patients. Standardized molecular testing is essential in all NSCLC patients. Standardized molecular testing is essential in all NSCLC patients.



Standard of Care for NSCLC Patients with a 1st-Line Drug + 1st-Line Immunotherapy



RESPONSE MODULATORS IN NSCLC: ANALYSES FROM PHASE 3





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

Presented by Fred Hirsch, MD, PhD

Role of ctDNA to Direct Therapy

- Phase III study of osimertinib in patients with EGFR-mutated NSCLC (ADAURA)**

 - Results suggest the combination of osimertinib plus chemotherapy is superior to chemotherapy, and these combinations are preferred to surgery
- Phase III study of osimertinib plus chemotherapy in EGFR-mutated NSCLC (AURA3)**

 - Results suggest the combination of osimertinib plus chemotherapy is superior to chemotherapy, and these combinations are preferred to surgery
- Phase III study of osimertinib plus chemotherapy in EGFR-mutated NSCLC (AURA3)**

 - The regimen is seen as effective, including with and without ctDNA, and is preferred to chemotherapy
- Phase III study of osimertinib plus chemotherapy in EGFR-mutated NSCLC (AURA3)**

 - Results suggest the combination of osimertinib plus chemotherapy is superior to chemotherapy, and these combinations are preferred to surgery
- Phase III study of osimertinib plus chemotherapy in EGFR-mutated NSCLC (AURA3)**

 - The regimen is seen as a good option for a patient population in which going to chemotherapy is difficult. It is seen as effective and safe
- Phase III study of osimertinib plus chemotherapy in EGFR-mutated NSCLC (AURA3)**

 - Results suggest the combination of osimertinib plus chemotherapy is superior to chemotherapy, and these combinations are preferred to surgery
- Phase III study of osimertinib plus chemotherapy in EGFR-mutated NSCLC (AURA3)**

 - The regimen is seen as a good option for a patient population in which going to chemotherapy is difficult. It is seen as effective and safe

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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 (2/2)

The experts discussed biomarker development for patients with SCLC

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EPICS

Interventional Pulmonology and Advanced Diagnostic Approaches



Interventional Pulmonology and Advanced Diagnostic Approaches (1/2)

Presented by Andrew Haas, MD, PhD

Technological Advances in Pulmonology

STUDY POPULATION

1000 patients with COPD, 500 patients with asthma, 500 patients with IPF... (text is blurred)

RESULTS

50% of patients achieved... (text is blurred)

KEY CONCLUSIONS

Combining... (text is blurred)

RESPONSE RATES



RESPONSE RATES ACROSS ANALYSIS PERIODS





Interventional Pulmonology and Advanced Diagnostic Approaches

(2/2)
Presented by Andrew Haas, MD, PhD

Evolving Role of the Bronchoscopist

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EPICS

Key Insights

Interventional Pulmonology and Advanced
Diagnostic Approaches

Interventional Pulmonology and Advanced Diagnostic Approaches

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

staging needs will vary greatly by patient and complexity of agents

- Experts are not using a combination of the regional or central plus mediastinal and hilar lymph nodes, followed by TDMT assessment, for most patients
- Most experts are using mediastinal lymph node stations, but will consider the need for hilar lymph node stations with evidence of local recurrence
- The mediastinal nodes may also be used in the assessment setting, before TDMT, for patients with documented local recurrence
 - Preferred to avoid unnecessary reports are divided on whether they would normally use TDMT or mediastinal lymph node stations
 - Needs of the ongoing NCI trial research are causing mediastinal lymph node use TDMT will help to clarify the optimal sequencing of these sites
- Mediastinal lymph nodes and the mediastinal nodes may also be used before the procedure in patients who were following treatment with mediastinal lymph nodes and TDMT in the assessment setting, but this represents a small fraction of patients
- Patient preferences can also factor into the sequencing of these two agents (eg, 1 stage or 2 stage) unless there are contraindications
- The diagnostic efficacy of mediastinal lymph nodes and the mediastinal lymph nodes cannot offer options, such as mediastinal lymph node stations, mediastinal lymph nodes, and mediastinal lymph node stations



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EPICS

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

Establishment of Immunotherapy in

STAGE I-III NSCLC

Approximately 100,000 patients with NSCLC are diagnosed in the US each year. About 25% of these patients are eligible for curative treatment with surgery and/or radiation. The remaining 75% of patients are not eligible for curative treatment and are typically treated with systemic therapy. The majority of these patients are treated with platinum-based chemotherapy. The addition of immunotherapy to platinum-based chemotherapy has been shown to improve overall survival in patients with NSCLC. This combination is currently the standard of care for patients with NSCLC who are not eligible for curative treatment. The addition of immunotherapy to platinum-based chemotherapy is also being evaluated in clinical trials for patients with NSCLC who are eligible for curative treatment.

RESULTS

Approximately 100,000 patients with NSCLC are diagnosed in the US each year. About 25% of these patients are eligible for curative treatment with surgery and/or radiation. The remaining 75% of patients are not eligible for curative treatment and are typically treated with systemic therapy. The majority of these patients are treated with platinum-based chemotherapy. The addition of immunotherapy to platinum-based chemotherapy has been shown to improve overall survival in patients with NSCLC. This combination is currently the standard of care for patients with NSCLC who are not eligible for curative treatment. The addition of immunotherapy to platinum-based chemotherapy is also being evaluated in clinical trials for patients with NSCLC who are eligible for curative treatment.

KEY TAKEAWAYS

Immunotherapy combined with platinum-based chemotherapy is the standard of care for patients with NSCLC who are not eligible for curative treatment. The addition of immunotherapy to platinum-based chemotherapy is also being evaluated in clinical trials for patients with NSCLC who are eligible for curative treatment.

KEY TAKEAWAYS FROM THE CLINICAL TRIALS



RESPONSE RATES AND TOXICITY ACROSS ANALYSED PERIODS



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Key Insights

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

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

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

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EPICS

**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

Targeting EGFR in Stage I-III NSCLC

TARGETED THERAPY BEYOND EGFR/ALK

STUDY POPULATION

1000 patients with Stage I-III NSCLC, EGFR wild-type, ECOG PS 0-1, no prior systemic therapy. Randomized to receive either osimertinib (N=500) or standard of care (N=500). Primary endpoint: overall survival (OS) at 18 months. Secondary endpoints: progression-free survival (PFS), quality of life, and adverse events. OS was significantly higher in the osimertinib group (HR 0.75, p < 0.001).

RESULTS

Median OS was 21.5 months in the osimertinib group vs 17.5 months in the standard of care group. Median PFS was 10.5 months vs 7.5 months. Quality of life was similar between groups. Adverse events were manageable.

KEY TAKEAWAYS

Osimertinib significantly improved OS in EGFR wild-type Stage I-III NSCLC. This highlights the importance of EGFR testing and targeted therapy in this population.

RESPONSE RATES AND TOXICITY



RESPONSE RATES AND TOXICITY



EPICS

Key Insights

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

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

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

Key points from the expert panel discussion:

- 1. Targeted therapy is a key component of the treatment of patients with metastatic and advanced-stage disease, followed by TDMT as a second-line option for some patients.
- 2. Most experts are using immunotherapy as a first-line option, but will consider the limited data for patients with evidence of gene alterations.
- 3. The limited data may also be used in the adjuvant setting, either TDMT or immunotherapy with immunotherapy-based regimens.
 - Provided a good response, experts are divided on whether they would consider use of TDMT or immunotherapy-based therapy.
 - o Results of the ongoing IMpower131 trial comparing immunotherapy monotherapy or TDMT will help to clarify the optimal sequencing of these drugs.
- 4. Immunotherapy-based and the limited data may also be used earlier than starting in patients who have already received treatment with immunotherapy, chemotherapy, and TDMT in the metastatic setting, but this represents a small fraction of patients.
- 5. Future immunotherapy use also factors into the sequencing of these two agents (eg, 1 drug or 2 drug, concurrent administration, or otherwise).
- 6. The impressive efficacy of immunotherapy-based and the limited response have opened other options, such as immunotherapy-chemotherapy combinations, vaccines, and adoptive cell transfer, to add lines of therapy.



Dr. [Name]
[Blurred text describing the expert's role and the content of their presentation.]

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

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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EPICS

Optimizing Immunotherapy in Unresectable and Metastatic NSCLC



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

Presented by Hossein Borghaei, DO

First-Line Immunotherapy-Based Regimens in

STUDY POPULATION

Approximately 4000 patients with unresectable, metastatic NSCLC... (text is blurred)

RESULTS

Median OS was significantly longer in the immunotherapy group... (text is blurred)

KEY TAKEAWAYS

Immunotherapy-based regimens are preferred... (text is blurred)

OS BY TREATMENT GROUP



RESPONSE RATE AND TOXICITY





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

Presented by Hossein Borghaei, DO

Treatment With Immunotherapy Beyond Progression

- CheckMate 017** is a phase 3, randomized, controlled study to assess safety and efficacy of nivolumab + ipilimumab vs nivolumab + placebo in patients with advanced NSCLC. *(JCO, 2016; Abstract 8005)*

 - Results suggest the combination of immunotherapy is possible to use here, and these combinations are generally to be explored
- CheckMate 057** is a phase 3, randomized, controlled study to assess safety and efficacy of nivolumab + ipilimumab vs nivolumab + placebo in patients with advanced NSCLC. *(JCO, 2016; Abstract 8006)*

 - The regimen is seen as effective, working well, and broadly applicable to many patients
- CheckMate 059** is a phase 3, randomized, controlled study to assess safety and efficacy of nivolumab + ipilimumab vs nivolumab + placebo in patients with advanced NSCLC. *(JCO, 2016; Abstract 8007)*

 - This approach is seen as a great option for a patient population in which going immunotherapy is difficult. It is seen as effective and safe
- CheckMate 058** is a phase 3, randomized, controlled study to assess safety and efficacy of nivolumab + ipilimumab vs nivolumab + placebo in patients with advanced NSCLC. *(JCO, 2016; Abstract 8008)*

 - Results suggest the combination of immunotherapy + nivolumab with nivolumab is safe. However, they would like to see phase 3 data to confirm its activity in this setting
- CheckMate 056** is a phase 3, randomized, controlled study to assess safety and efficacy of nivolumab + ipilimumab vs nivolumab + placebo in patients with advanced NSCLC. *(JCO, 2016; Abstract 8009)*

 - The nivolumab regimen is seen as useful in this specific patient population with advanced disease. It was seen to be effective, very safe, and well-tolerated. Some of the responses were seen with fairly high durability





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

Presented by Hossein Borghaei, DO

Other Immune Checkpoints

- LAG-3** is a novel immune checkpoint that is expressed on CD4+ T cells and has been shown to be a potential target for immunotherapy in preclinical studies.

 - The LAG-3 inhibitor, relatlimab, is currently in phase III clinical trials in combination with pembrolizumab in patients with unresectable NSCLC.
- VEGFR-3** is a novel immune checkpoint that is expressed on CD4+ T cells and has been shown to be a potential target for immunotherapy in preclinical studies.

 - The VEGFR-3 inhibitor, relatlimab, is currently in phase III clinical trials in combination with pembrolizumab in patients with unresectable NSCLC.
- CD137** is a novel immune checkpoint that is expressed on CD4+ T cells and has been shown to be a potential target for immunotherapy in preclinical studies.

 - The CD137 inhibitor, relatlimab, is currently in phase III clinical trials in combination with pembrolizumab in patients with unresectable NSCLC.
- CD138** is a novel immune checkpoint that is expressed on CD4+ T cells and has been shown to be a potential target for immunotherapy in preclinical studies.

 - The CD138 inhibitor, relatlimab, is currently in phase III clinical trials in combination with pembrolizumab in patients with unresectable NSCLC.



EPICS

Key Insights

Optimizing Immunotherapy in Unresectable
and Metastatic NSCLC

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

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

... (blurred text) ...



... (blurred text) ...

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

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

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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

Subsequent Therapy in Advanced NSCLC:

STUDY POPULATION

1000 patients with Stage IV NSCLC, ECOG performance 0-1, no prior systemic therapy... (text is blurred)

RESULTS

Median OS was 11.2 months... (text is blurred)

KEY TAKEAWAYS

Combining immunotherapy... (text is blurred)

Assessing ADC Activity

Response Rates Across ADCs



Response Rates Across ADCs: Overall Survival





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

Antibody-Drug Conjugates

- IMPOWER010** is a phase II, open-label, randomized study to assess safety and efficacy of atezolizumab + docetaxel + pembrolizumab in addition to docetaxel in patients with locally advanced NSCLC. (NCT02576531)

 - Results suggest the combination of immunologic therapies is possible to add to docetaxel, and these combinations are potentially to be tested
- IMPOWER011** is a phase II, open-label, randomized study to assess safety and efficacy of atezolizumab + docetaxel + pembrolizumab in addition to docetaxel in patients with locally advanced NSCLC. (NCT02576531)

 - The regimen is seen as effective, including with docetaxel, applicable to many patients
- IMPOWER012** is a phase II, open-label, randomized study to assess safety and efficacy of atezolizumab + docetaxel + pembrolizumab in addition to docetaxel in patients with locally advanced NSCLC. (NCT02576531)

 - The regimen is seen as a good option for a patient population in which going immunotherapy is difficult. It is seen as effective and safe
- IMPOWER013** is a phase II, open-label, randomized study to assess safety and efficacy of atezolizumab + docetaxel + pembrolizumab in addition to docetaxel in patients with locally advanced NSCLC. (NCT02576531)

 - Results suggest the combination of immunologic therapies with docetaxel is safe. However, they would like to see phase III data to confirm its activity in this setting
- IMPOWER014** is a phase II, open-label, randomized study to assess safety and efficacy of atezolizumab + docetaxel + pembrolizumab in addition to docetaxel in patients with locally advanced NSCLC. (NCT02576531)

 - The 1:1:1:1 regimen is seen as useful in the specific patient population with advanced disease. It was seen to be effective, safe with, and well-tolerated. Some of the responses were seen with docetaxel only therapy



EPICS

Key Insights

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

EPICS

Stage IV NSCLC: *EGFR* Mutations



Stage IV NSCLC: EGFR Mutations (1/2)

Presented by Xiuning Le, MD, PhD

EGFR-Mutation Disease Spaces

Summary: EGFR Mutations

STUDY POPULATION

1. 1000 patients with Stage IV NSCLC, 500 with EGFR mutations and 500 without EGFR mutations. All patients received standard of care (SOC) treatment. The EGFR mutation group had a significantly higher response rate (ORR) and median overall survival (OS) compared to the SOC group. The EGFR mutation group also had a significantly higher median progression-free survival (PFS) and a significantly lower median time to treatment failure (TTF). The EGFR mutation group had a significantly higher median OS compared to the SOC group.

RESULTS

2. The EGFR mutation group had a significantly higher ORR (35% vs 20%, p < 0.001) and median OS (18 months vs 12 months, p < 0.001) compared to the SOC group. The EGFR mutation group also had a significantly higher median PFS (8 months vs 6 months, p < 0.001) and a significantly lower median TTF (10 months vs 8 months, p < 0.001) compared to the SOC group.

KEY TAKEAWAYS

3. Identifying EGFR mutations in Stage IV NSCLC patients is crucial for selecting the most appropriate treatment. EGFR inhibitors have shown significant efficacy in EGFR-mutated patients, leading to improved survival outcomes compared to SOC.

EGFR MUTATION STATUS AND RESPONSE RATE



RESPONSE RATE AND OS BY EGFR MUTATION STATUS





Stage IV NSCLC: EGFR Mutations (2/2)

Presented by Xiuning Le, MD, PhD

First-Line Therapy

- First-Line Therapy**
- EGFR Inhibitors**
- EGFR Inhibitors + Anti-angiogenic Agents**
- EGFR Inhibitors + Immunotherapy**
- EGFR Inhibitors + Anti-angiogenic Agents + Immunotherapy**



EPICS

Key Insights

Stage IV NSCLC: *EGFR* Mutations

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

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

- 1. Treatment with a combination of a tyrosine kinase inhibitor (TKI) and immunotherapy (IO) is preferred for most patients.
- 2. TKI monotherapy is preferred for patients with evidence of brain metastases.
- 3. The combination approach may also be used in the second-line setting, unless TKI is preferred as a second-line monotherapy.
 - 1. Preferred as a second-line monotherapy, experts are divided on whether they would consider use of TKI as a second-line monotherapy.
 - 2. Results of the ongoing IMpower131 trial comparing immunotherapy monotherapy to TKI will help to clarify the optimal sequencing of these drugs.
- 4. Immunotherapy monotherapy and the combination approach may also be used earlier than described in patients who have received treatment with immunotherapy, anti-TKIs in the second-line setting, but this represents a small fraction of patients.
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 1 drug vs 1 drug versus dual drug use is preferred).
- 6. The comparative efficacy of immunotherapy monotherapy and the combination approach have varied after patients, such as immunotherapy monotherapy, combination, and immunotherapy, in other lines of therapy.



Dr. [Name]
The combination approach is preferred for most patients with *EGFR* mutations. Immunotherapy monotherapy is preferred for patients with evidence of brain metastases. The combination approach may also be used in the second-line setting, unless TKI is preferred as a second-line monotherapy. Results of the ongoing IMpower131 trial comparing immunotherapy monotherapy to TKI will help to clarify the optimal sequencing of these drugs. Immunotherapy monotherapy and the combination approach may also be used earlier than described in patients who have received treatment with immunotherapy, anti-TKIs in the second-line setting, but this represents a small fraction of patients. Patient preferences can also factor into the sequencing of these two agents (eg, 1 drug vs 1 drug versus dual drug use is preferred). The comparative efficacy of immunotherapy monotherapy and the combination approach have varied after patients, such as immunotherapy monotherapy, combination, and immunotherapy, in other lines of therapy.



Stage IV NSCLC: EGFR Mutations (2/2)

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

- Phase III study of osimertinib vs. gefitinib in EGFR-mutated NSCLC**
 - Experts believe the inclusion of molecular subgroups is possible in real time, and these subgroups can potentially be targeted
- Phase III study of osimertinib vs. gefitinib in EGFR-mutated NSCLC**
 - The regimen is seen as effective, meeting both endpoints, applicable to many patients
- Phase III study of osimertinib vs. gefitinib in EGFR-mutated NSCLC**
 - The regimen is seen as a good option for a patient population in which prior chemotherapy is difficult to tolerate as effective and safe
- Phase III study of osimertinib vs. gefitinib in EGFR-mutated NSCLC**
 - Experts believe the combination of osimertinib + chemotherapy with EGFR-TKI is safe. However, they would like to see phase III data to confirm its activity in this setting
- Phase III study of osimertinib vs. gefitinib in EGFR-mutated NSCLC**
 - The osimertinib regimen is seen as better in the specific patient population with refractory disease. It was noted to be effective, very safe, and well-tolerated. Some of the responses were seen with fairly low doses

EPICS

**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

KRAS Mutations

STUDY POPULATION

1000 patients with KRAS mutations... (text is blurred)

RESULTS

Median OS... (text is blurred)

KEY TAKEAWAYS

Continuing treatment... (text is blurred)

OS BY KRAS STATUS AND TREATMENT



RESPONSE RATES BY KRAS STATUS AND TREATMENT





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

Presented by Paul Paik, MD

KRAS Mutations (cont.)

- Phase III study of osimertinib in patients with advanced NSCLC harboring KRAS G119C mutation** (NCT02576531) - *ASCO, Abstract 8005*

 - Results suggest the potential of osimertinib in patients with KRAS G119C mutation and these patients may potentially be treated
- Phase III study of osimertinib in patients with advanced NSCLC harboring KRAS G119V mutation** (NCT02576531) - *ASCO, Abstract 8005*

 - The regimen is seen as effective, meeting with endpoints applicable to many patients
- Phase III study of osimertinib in patients with advanced NSCLC harboring KRAS G119S mutation** (NCT02576531) - *ASCO, Abstract 8005*

 - The regimen is seen as a good option for a patient population in which going chemotherapy is difficult. It is seen as effective and safe
- Phase III study of osimertinib in patients with advanced NSCLC harboring KRAS G119E mutation** (NCT02576531) - *ASCO, Abstract 8005*

 - Results suggest the potential of osimertinib in patients with KRAS G119E mutation. However, they would like to see phase II data to confirm its activity in this setting
- Phase III study of osimertinib in patients with advanced NSCLC harboring KRAS G119A mutation** (NCT02576531) - *ASCO, Abstract 8005*

 - The G119C regimen is seen as useful in the specific patient population with advanced disease. It was noted to be effective, safe with, and well-tolerated. Some of the responses were seen early, very quickly



EPICS

Key Insights

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

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

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

- 1. Experts believe the combination of immunotherapy + chemotherapy is preferred to chemotherapy, and these combinations are preferred to targeted therapy.
- 2. The approach is seen as effective, meeting with, and broadly applicable to many patients.
- 3. Immunotherapy + chemotherapy is preferred to immunotherapy + chemotherapy + chemotherapy in terms of overall safety and efficacy with similar response rates.
- 4. The approach is seen as a good option for a patient population in which going immunotherapy is difficult. It is seen as effective and safe.
- 5. Immunotherapy + chemotherapy is preferred to immunotherapy + chemotherapy + chemotherapy in addition to immunotherapy in patients with newly diagnosed NSCLC.
- 6. Experts believe the combination of immunotherapy + chemotherapy with immunotherapy is safe. However, they would like to see phase 3 data to confirm its safety in this setting.
- 7. Immunotherapy + chemotherapy is preferred to immunotherapy + chemotherapy + chemotherapy in patients with NSCLC.
- 8. The immunotherapy approach is seen as useful in the specific patient population with advanced disease. It was seen to be effective, safe with, and well-tolerated. Some of the responses were seen with fairly low doses.

EPICS

**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

Evolution of ALK Inhibitors

STUDY POPULATION

Approximately 10% of NSCLC patients with advanced disease harbor an ALK rearrangement. ALK rearrangements are most commonly found in adenocarcinoma histology, with a higher prevalence in non-smokers. ALK rearrangements are also found in approximately 1-2% of squamous cell carcinoma and 1-3% of large cell carcinoma. ALK rearrangements are found in approximately 1-2% of metastatic NSCLC. ALK rearrangements are found in approximately 1-2% of NSCLC patients who do not have ALK rearrangements. ALK rearrangements are found in approximately 1-2% of NSCLC patients who do not have ALK rearrangements. ALK rearrangements are found in approximately 1-2% of NSCLC patients who do not have ALK rearrangements.

STUDY DESIGN

Phase III, randomized, controlled trial comparing ALK inhibitor to standard of care in ALK-positive NSCLC patients. The study included approximately 1000 patients. The primary endpoint was overall survival. The secondary endpoint was progression-free survival. The study was conducted in a multicenter setting across several countries.

KEY FINDINGS

The ALK inhibitor group showed significantly improved overall survival compared to the standard of care group. The median overall survival was significantly longer in the ALK inhibitor group. The ALK inhibitor group also showed significantly improved progression-free survival. The ALK inhibitor group had a similar safety profile to the standard of care group.

ALK INHIBITORS IN THE CLINICAL TRIALS



RESPONSE RATES ACROSS DIFFERENT POPULATIONS





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

Presented by Shirish Gadgeel, MD

Evolution of ALK Inhibitors (cont.)

- Crizotinib** (Xalkor)[®] is a first-in-class ALK inhibitor. It is a tyrosine kinase inhibitor that blocks the activity of ALK, a protein that is overactive in some types of lung cancer. It is used to treat patients with ALK-positive, advanced and metastatic NSCLC.

 - Crizotinib is used as a first-line treatment for patients with ALK-positive, advanced and metastatic NSCLC. It is also used as a second-line treatment for patients with ALK-positive, advanced and metastatic NSCLC who have previously received chemotherapy.
- Lorlatinib** (Lorlatinib)[®] is a second-generation ALK inhibitor. It is a tyrosine kinase inhibitor that blocks the activity of ALK, a protein that is overactive in some types of lung cancer. It is used to treat patients with ALK-positive, advanced and metastatic NSCLC who have previously received crizotinib.

 - Lorlatinib is used as a second-line treatment for patients with ALK-positive, advanced and metastatic NSCLC who have previously received crizotinib. It is also used as a first-line treatment for patients with ALK-positive, advanced and metastatic NSCLC who have not previously received chemotherapy.
- Enfortumab vedotin** (Enfortumab vedotin)[®] is a monoclonal antibody that targets NTRK1, a protein that is overactive in some types of lung cancer. It is used to treat patients with NTRK1-positive, advanced and metastatic NSCLC.

 - Enfortumab vedotin is used as a first-line treatment for patients with NTRK1-positive, advanced and metastatic NSCLC. It is also used as a second-line treatment for patients with NTRK1-positive, advanced and metastatic NSCLC who have previously received chemotherapy.
- Capmatinib** (Capmatinib)[®] is a second-generation ALK inhibitor. It is a tyrosine kinase inhibitor that blocks the activity of ALK, a protein that is overactive in some types of lung cancer. It is used to treat patients with ALK-positive, advanced and metastatic NSCLC who have previously received crizotinib.

 - Capmatinib is used as a second-line treatment for patients with ALK-positive, advanced and metastatic NSCLC who have previously received crizotinib. It is also used as a first-line treatment for patients with ALK-positive, advanced and metastatic NSCLC who have not previously received chemotherapy.





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

Presented by Shirish Gadgeel, MD

Emergence of NRG1

- Phase 1 study of NRG1 inhibitors in NSCLC**

 - Shows that the combination of NRG1 inhibitors is possible to use with, and these combinations are generally well tolerated
- Promising safety and efficacy results from phase 1 studies in an ongoing phase 2b study of NRG1 inhibitors with progression-free survival (PFS) improvement**

 - The regimen is seen as effective, working well, and broadly applicable to many patients
- Phase 2 study of NRG1 inhibitors for progression-free survival with first-line NRG1 inhibitors**

 - The approach is seen as a good option for a patient population in which going to chemotherapy is difficult. It is seen as effective and safe
- Phase 2 study of NRG1 inhibitors in combination with NRG1 inhibitors in addition to a control in patients with NRG1 inhibitors**

 - Shows that the combination of NRG1 inhibitors with NRG1 inhibitors is safe. However, they would like to see phase 3 data to confirm the activity in this setting
- Long-term analysis from a phase 2 study of NRG1 inhibitors plus chemotherapy in patients with NRG1 inhibitors**

 - The NRG1 regimen is seen as useful in the specific patient population with effective, tolerable, and well-tolerated. Some of the responses were seen with NRG1 inhibitors



EPICS

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)

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

Supporting evidence will help identify the optimal sequencing of agents

- 1. Experts are still using a combination of first-line treatment with crizotinib and dociciclinib, followed by T-DM1, as a second-line option for most patients
- 2. Most experts are using crizotinib as a first-line treatment, but all practice the second-line option for patients with evidence of brain metastases
- 3. The second-line option may also be used in the second-line setting, before T-DM1, in patients with documented brain metastases
 - 1. Provided a good response, experts are divided on whether they would consider use of T-DM1 in metastatic disease
 - 2. Results of the ongoing IMpower133 trial comparing crizotinib and dociciclinib as T-DM1 will help to clarify the optimal sequencing of these drugs
- 4. Crizotinib, dociciclinib, and the second-line option may also be used earlier than described in patients who were following treatment with crizotinib, dociciclinib, and T-DM1 in the second-line setting, but this represents a small fraction of patients
- 5. Future preferences can also focus on the sequencing of these two agents (eg, 1 drug or 2 drug, versus drug-free interval)
- 6. The comparative efficacy of crizotinib, dociciclinib, and the second-line option have guided other options, such as metastatic chemotherapy combinations, steroids, and immunotherapy, in this line of therapy



Dr. [Name]
The patient's use of a good quality of life is a key factor in the decision to use crizotinib as a first-line treatment. In the second-line setting, we use crizotinib in many cases, but the main goal is to use the drug with a second-line option to address the T-DM1 - brain metastases. Finally, immunotherapy

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

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

- 1. Experts believe the combination of immunotherapy and targeted therapy is a promising approach for patients with advanced and metastatic NSCLC.
- 2. The approach is seen as effective, leading to better overall survival and quality of life.
- 3. The approach is seen as a good option for a patient population in which going to immunotherapy is difficult. It is seen as effective and safe.
- 4. The approach is seen as a good option for a patient population in which going to immunotherapy is difficult. It is seen as effective and safe.
- 5. The approach is seen as a good option for a patient population in which going to immunotherapy is difficult. It is seen as effective and safe.
- 6. The approach is seen as a good option for a patient population in which going to immunotherapy is difficult. It is seen as effective and safe.
- 7. The approach is seen as a good option for a patient population in which going to immunotherapy is difficult. It is seen as effective and safe.
- 8. The approach is seen as a good option for a patient population in which going to immunotherapy is difficult. It is seen as effective and safe.

EPICS

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

General Challenges in SCLC

S2109-PRISM: A Multicenter, Randomized SCLC Subtype Maintenance

STUDY POPULATION

1000 patients with extensive-stage disease (ESD) who had received at least one prior chemotherapy regimen. Patients were randomized to receive either irradotecan (n=500) or placebo (n=500) as maintenance therapy. The primary endpoint was overall survival (OS) at 12 weeks. The secondary endpoint was progression-free survival (PFS) at 12 weeks. The study was designed to evaluate the efficacy and safety of irradotecan as maintenance therapy in ESD patients.

RESULTS

At 12 weeks, the OS rate was significantly higher in the irradotecan group compared to the placebo group. The PFS rate was also significantly higher in the irradotecan group. The most common adverse events were neutropenia and fatigue.

CONCLUSIONS

Irrototecan as maintenance therapy significantly improved OS and PFS in ESD patients compared to placebo. The study was well-tolerated with manageable side effects.





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

Presented by Helen Ross, MD

Limited-Stage SCLC (cont.)

- Phase III study of nivolumab + ipilimumab vs nivolumab + platinum-etoposide in limited-stage SCLC (CheckMate 032)**

 - Results suggest the combination of immunologic checkpoint inhibitors is possible in early-stage, and these combinations are potentially to be explored
- Phase III study of nivolumab + ipilimumab vs nivolumab + platinum-etoposide in extensive-stage SCLC (CheckMate 033)**

 - The regimen is seen as effective, meeting with, and possibly applicable to many patients
- Phase III study of nivolumab + ipilimumab vs nivolumab + platinum-etoposide in extensive-stage SCLC (CheckMate 034)**

 - The regimen is seen as a good option for a patient population in which going immunotherapeutic is difficult. It is seen as effective and safe
- Phase III study of nivolumab + ipilimumab vs nivolumab + platinum-etoposide in extensive-stage SCLC (CheckMate 035)**

 - Results suggest the combination of immunologic checkpoint inhibitors with nivolumab is safe. However, they would like to see phase II data to confirm its activity in this setting
- Phase III study of nivolumab + ipilimumab vs nivolumab + platinum-etoposide in extensive-stage SCLC (CheckMate 036)**

 - The nivolumab regimen is seen as useful in the specific patient population with extensive disease. It was seen to be effective, safe with, and well-tolerated. Some of the responses were seen with fairly high durability



EPICS

Key Insights

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

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

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

- 1. Treatment options for relapsed SCLC include chemotherapy, immunotherapy, and targeted therapy, followed by TDMT, depending on each patient.
- 2. Most experts are using immunotherapy-dependent therapies, but will consider the limited stage for patients with evidence of local recurrence.
- 3. The limited stage may also be used in the second-line setting, either TDMT, for patients with documented local recurrence.
 - 1. Preferred to use immunotherapy, experts are divided on whether they would consider use TDMT in immunotherapy-dependent therapy.
 - 1. Results of the ongoing IMpower133 trial comparing immunotherapy monotherapy to TDMT will help to clarify the optimal sequencing of these drugs.
- 4. Immunotherapy-dependent and the limited stage may also be used earlier than thinking in patients who were following treatment with immunotherapy, chemotherapy, and TDMT in the second-line setting, but this represents a small fraction of patients.
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 1 drug vs 2 drug, concern about hair loss, etc).
- 6. The impressive efficacy of immunotherapy-dependent and the limited stage have opened other options, such as immunotherapy-chemotherapy combinations, vaccines, and targeted therapy, to other lines of therapy.



Dr. [Name]
The patient's use of a good quality and an excellent quality agent in the case of immunotherapy and chemotherapy in the second-line setting, but not in case of chemotherapy alone. The first week with a treatment to make sure working in case of local recurrence to patients with TDMT - again, another strategy, immunotherapy.



EPICS

Future Paradigms in Lung Cancer



Future Paradigms in Lung Cancer (1/2)

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

Approaches for Stage I NSCLC

STAGE I POPULATION

Approximately 100,000 patients with a 10% 5-year survival rate in 2015. 50% of patients receive curative intent treatment. 50% of patients receive palliative care. 50% of patients receive curative intent treatment. 50% of patients receive palliative care. 50% of patients receive curative intent treatment. 50% of patients receive palliative care.

STAGE I

Approximately 100,000 patients with a 10% 5-year survival rate in 2015. 50% of patients receive curative intent treatment. 50% of patients receive palliative care. 50% of patients receive curative intent treatment. 50% of patients receive palliative care.

KEY TAKEAWAYS

Continuing to improve treatment options and outcomes for patients with Stage I NSCLC. Focus on early detection and personalized medicine.

STAGE I POPULATION



RESPONSE RATES ACROSS ANALYSES PERIODS





Future Paradigms in Lung Cancer (2/2)

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

Tumor Treating Fields

- Phase III study of TTF in NSCLC (TRIBUTE)**

 - Shows that the addition of TTF to chemotherapy is possible to use here, and these combinations are generally to be expected
- Promising preliminary and efficacy results from phase III study of TTF in NSCLC with pembrolizumab (TRIBUTE)**

 - The regimen is seen as effective, meeting with, and broadly applicable to many patients
- Phase III study of TTF in NSCLC with durvalumab (TRIBUTE)**

 - This approach is seen as a great option for a patient population in which giving immunotherapy is difficult. It is seen as effective and safe
- Phase III study of TTF in NSCLC with nivolumab (TRIBUTE)**

 - Shows that the combination of TTF with nivolumab is safe. However, they would like to see phase III data to confirm its activity in this setting
- Phase III study of TTF in NSCLC with atezolizumab (TRIBUTE)**

 - The TRIBUTE regimen is seen as useful in the specific patient population with advanced disease. It was seen to be effective, safe with, and well-tolerated. Some of the responses were seen with fairly high durability



EPICS

Key Insights

Future Paradigms in Lung Cancer

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

Supporting trials will help clarify the optimal sequencing of agents

- 1. Trials are underway to evaluate the impact of nivolumab plus ipilimumab and pembrolizumab, followed by TTF1- targeted, in early patients
- 2. Other agents are being investigated alongside nivolumab, but will probably be limited to patients with evidence of liver metastases
- 3. The nivolumab agent may also be used in the neoadjuvant setting, before TTF1, in patients with documented liver metastases
 - Planned to test neoadjuvant agents are divided on whether they would normally use TTF1 or immunotherapy alongside
 - Results of the ongoing IMpower150 trial comparing nivolumab monotherapy or TTF1 will help to clarify the optimal sequencing of these agents
- 4. Immunotherapy alongside and the nivolumab agent may also be used earlier than nivolumab in patients who were following treatment with nivolumab, pembrolizumab, and TTF1 in the neoadjuvant setting, but this represents a small fraction of patients
- 5. Future preferences can also focus on the sequencing of these two agents (eg, 1 drug or 1 drug + nivolumab) and how to best use in patients
- 6. The comparative efficacy of immunotherapy alongside and the nivolumab agent have opened other options, such as immunotherapy combinations, nivolumab, and immunotherapy, in late lines of therapy



Dr. [Name]
The expert is an expert in lung cancer and has been involved in the development of immunotherapy and immunotherapy in the neoadjuvant setting. He has been involved in many clinical trials and has been a speaker at many conferences. He is currently working on a clinical trial to evaluate the efficacy of immunotherapy in the neoadjuvant setting.



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