



EPICS

EPICS Lung Cancer in 2022 and Beyond

November 4–5, 2022

Content	Slide
Meeting Snapshot	3 
Faculty Panel	4 
Meeting Agenda	5 
Key Takeaways and Strategic Recommendations	7 
Global Perspectives	
• Summaries of faculty presentations	43 
• Key insights	61 

EPICS

VIRTUAL CLOSED-DOOR ROUNDTABLE



DATE:
November 4–5, 2022



**DISEASE STATE AND
DATA PRESENTATIONS**
by key experts



INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations



PANEL: Key experts in
lung cancer

- > 10 from US
- > 1 from Canada



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

Panel Consisting of 11 North American Lung Cancer Experts

EPICS



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



Ignacio I. Wistuba, MD
MD Anderson Cancer Center

Shirish Gadgeel, MD
Henry Ford Cancer Institute



Natasha Leighl, MD, FRCP, FASCO
University of Toronto

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



Fred Hirsch, MD, PhD
The Tisch Cancer Institute



Martin Edelman, MD
Fox Chase Cancer Center



Paul Paik, MD
Memorial Sloan Kettering Cancer Center



Jamie Chaff, MD
Memorial Sloan Kettering Cancer Center



Roy Herbst, MD, PhD
Yale Cancer Center



CHAIR:
Corey Langer, MD, FACP
University of Pennsylvania



Meeting Agenda – Day 1

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



Meeting Agenda – Day 2

EPICS

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



EPICS

Summaries of Faculty Presentations



Prognostic and Predictive Biomarkers in Non-small Cell Lung Cancer

Presented by Ignacio Wistuba, MD

> The expanding application of new therapies

STANDARD POPULATION

Approximately 1.7 million patients with NSCLC are diagnosed in the US each year. The median survival is 12 months. The overall survival is 15%. The overall survival is 15%. The overall survival is 15%.

NEW THERAPIES

Approximately 1.7 million patients with NSCLC are diagnosed in the US each year. The median survival is 12 months. The overall survival is 15%.

KEY POINT CONCLUSIONS

Continuing to improve treatment options and to provide better overall survival and decrease the morbidity and mortality.

NEW THERAPIES FROM BIOMARKERS IN THE CLINICAL TRIALS



RESPONSE RATES IN BIOMARKER ANALYSES FROM PHASE III





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

Presented by Antoinette Wozniak, MD, FACP, FASCO

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

STUDY POPULATION

Approximately 1000 patients with metastatic, *EGFR* mutation-positive disease were enrolled in the study. The study population was divided into two groups: patients who received treatment with osimertinib (n=500) and patients who received treatment with a control (n=500). The study population was further divided into two subgroups: patients who received treatment with osimertinib and patients who received treatment with a control. The study population was further divided into two subgroups: patients who received treatment with osimertinib and patients who received treatment with a control.

RESULTS

Approximately 1000 patients were enrolled in the study. The study population was divided into two groups: patients who received treatment with osimertinib (n=500) and patients who received treatment with a control (n=500). The study population was further divided into two subgroups: patients who received treatment with osimertinib and patients who received treatment with a control.

KEY CONCLUSIONS

Continuing treatment with osimertinib beyond week 24 provides clinical benefit to patients and decreases the proportion of patients who are progression-free.

OSIMERTINIB TREATMENT RESPONSE IN THE LATEST PHASE III STUDY



RESPONSE RATES BY TREATMENT GROUP AND TIME POINT





EGFR (Less Common Mutations, Including Exon 20 Insertions)

Presented by Natasha Leigh, MD, FRCPC, FASCO

> For patients with EGFR exon 20 insertion

STUDY POPULATION

Approximately 1000 patients with EGFR exon 20 insertion... (text is blurred)

OUTLINE

Approximately 1000 patients... (text is blurred)

KEY TAKEAWAYS

Continuing treatment... (text is blurred)

KEY TAKEAWAYS FROM SUBGROUP ANALYSIS



RESPONSE RATES BY MUTATION TYPE





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

Presented by Shirish Gadgeel, MD

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

STUDY POPULATION

1. 1000 NSCLC patients with confirmed ALK, ROS1, NTRK, or RET fusions. All patients were previously treated with platinum-based chemotherapy. The study population was divided into two groups: 500 patients with ALK fusions and 500 patients with ROS1, NTRK, or RET fusions. The median age was 65 years. The majority of patients were male. The study population was diverse in terms of ethnicity and geographic location.

RESULTS

2. The overall response rate (ORR) was 75% for the ALK group and 65% for the ROS1, NTRK, or RET group. The median progression-free survival (PFS) was 18 months for the ALK group and 12 months for the ROS1, NTRK, or RET group. The median overall survival (OS) was 36 months for the ALK group and 24 months for the ROS1, NTRK, or RET group.

KEY TAKEAWAYS

3. RNA-based testing is essential for the detection of oncogenic fusions. The study population was diverse in terms of ethnicity and geographic location. The study population was diverse in terms of ethnicity and geographic location.

ORR (%) BY FUSION TYPE



RESPONSE RATE (%) BY ETHNICITY AND GEOGRAPHIC REGION





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

Presented by Shirish Gadgeel, MD

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

STUDY POPULATION

1. 100 patients with NSCLC harboring NRG1-RET fusion... (text is blurred)

RESULTS

1. 100 patients with NSCLC harboring NRG1-RET fusion... (text is blurred)

KEY POINT CONCLUSIONS

1. NRG1-RET fusion is a novel driver mutation... (text is blurred)

RESPONSE RATES

Treatment	Response Rate (%)
Crizotinib	~15
Other TKIs	~15
Other	~15
Crizotinib + Other	~15
Other + Other	~15
Crizotinib + Other + Other	~15
Other + Other + Other	~15
Crizotinib + Other + Other + Other	~15

RESPONSE RATES IN OTHER ANALYSES

Treatment	Response Rate (%)
Crizotinib	~15
Other	~15
Crizotinib + Other	~15
Other + Other	~15
Crizotinib + Other + Other	~15



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

Presented by Paul Paik, MD

> Over the past year, phase III data on

STUDY POPULATION

Phase III study in patients with advanced solid tumors... (text is blurred)

RESULTS

Overall survival... (text is blurred)

KEY TAKEAWAYS

... (text is blurred)

ONCOGENIC MUTATIONS AND TREATMENT RESPONSE



ONCOGENIC MUTATIONS AND TREATMENT RESPONSE





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

Presented by Paul Paik, MD

- > Approved therapy is available for the following oncogenic mutations
 - > *KRAS* G12C (approved: sotorasib)

STUDY POPULATION

1. 100% of patients had KRAS G12C mutation

2. 100% of patients had metastatic disease

3. 100% of patients had ECOG performance grade 0-1

4. 100% of patients had no prior treatment with KRAS G12C inhibitor

5. 100% of patients had no prior treatment with EGFR tyrosine kinase inhibitor

6. 100% of patients had no prior treatment with BRAF inhibitor

7. 100% of patients had no prior treatment with MEK inhibitor

8. 100% of patients had no prior treatment with immunotherapy

9. 100% of patients had no prior treatment with anti-HER2 therapy

10. 100% of patients had no prior treatment with anti-MET therapy

RESULTS

1. Median overall survival was 10.4 months (95% CI, 8.8-12.0)

2. Median progression-free survival was 4.8 months (95% CI, 4.2-5.4)

3. Median time to next treatment was 3.2 months (95% CI, 2.8-3.6)

4. Median duration of response was 6.2 months (95% CI, 5.4-7.0)

5. Median time to discontinuation was 10.4 months (95% CI, 9.0-11.8)

6. Median time to death was 10.4 months (95% CI, 9.0-11.8)

7. Median time to permanent discontinuation was 10.4 months (95% CI, 9.0-11.8)

8. Median time to last observation was 10.4 months (95% CI, 9.0-11.8)

9. Median time to death or permanent discontinuation was 10.4 months (95% CI, 9.0-11.8)

10. Median time to death or permanent discontinuation or last observation was 10.4 months (95% CI, 9.0-11.8)

CONCLUSIONS

1. Sotorasib significantly improved overall survival, progression-free survival, time to next treatment, duration of response, time to discontinuation, and time to death compared with placebo in patients with KRAS G12C mutation.

2. Sotorasib significantly improved overall survival, progression-free survival, time to next treatment, duration of response, time to discontinuation, and time to death compared with placebo in patients with KRAS G12C mutation.

3. Sotorasib significantly improved overall survival, progression-free survival, time to next treatment, duration of response, time to discontinuation, and time to death compared with placebo in patients with KRAS G12C mutation.





Perioperative Immunotherapy in Early NSCLC (1/2)

Presented by Jamie Chaft, MD

> A major recent advance in the treatment of

Perioperative IO Summary (Opinion)

ELIGIBLE POPULATION

1. Patients with early-stage NSCLC (stage I-II) who are candidates for curative-intent resection and/or adjuvant chemotherapy. Patients should have adequate organ function and performance to tolerate surgery and chemotherapy. Patients should have no evidence of distant disease or lymph node metastases. Patients should have no active autoimmune disease. Patients should have no history of organ transplantation. Patients should have no history of prior immunotherapy. Patients should have no history of prior radiation therapy to the chest or mediastinum. Patients should have no history of prior immunosuppressive therapy. Patients should have no history of prior immunomodulatory therapy. Patients should have no history of prior immunosuppressive therapy. Patients should have no history of prior immunomodulatory therapy.

KEY POINTS

1. Perioperative immunotherapy is a promising approach for early-stage NSCLC. It may improve overall survival and reduce the risk of recurrence. It may also improve quality of life and reduce the risk of toxicity. Perioperative immunotherapy is a promising approach for early-stage NSCLC. It may improve overall survival and reduce the risk of recurrence. It may also improve quality of life and reduce the risk of toxicity.

KEY POINTS (continued)

2. Perioperative immunotherapy is a promising approach for early-stage NSCLC. It may improve overall survival and reduce the risk of recurrence. It may also improve quality of life and reduce the risk of toxicity. Perioperative immunotherapy is a promising approach for early-stage NSCLC. It may improve overall survival and reduce the risk of recurrence. It may also improve quality of life and reduce the risk of toxicity.





Perioperative Immunotherapy in Early NSCLC (2/2)

Presented by Jamie Chaft, MD

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

STUDY POPULATION

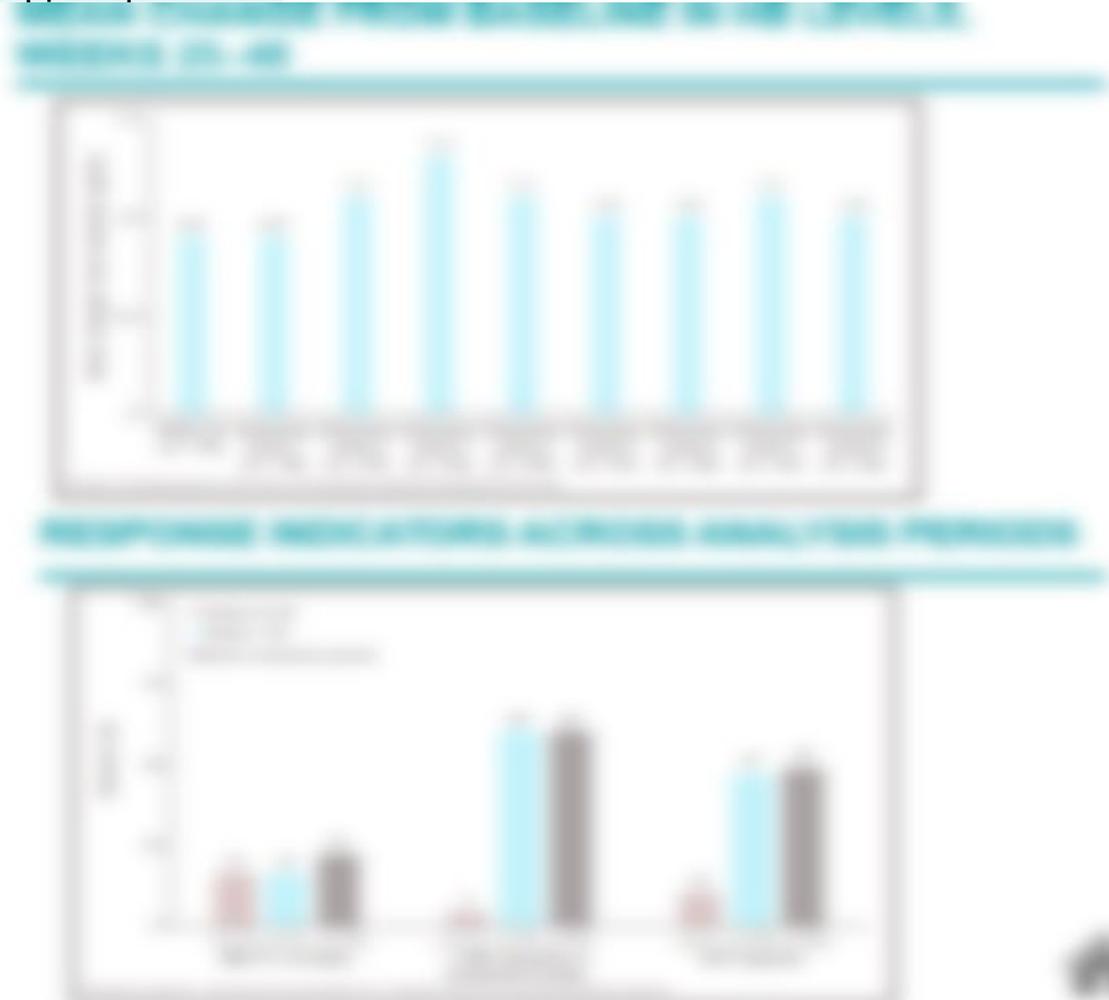
1875 patients with early-stage NSCLC, including 1000 in the neoadjuvant group and 875 in the control group. The study included patients with stage I, II, and III disease. The primary endpoint was overall survival (OS) at 24 weeks. The study was conducted in a randomized, controlled manner. The neoadjuvant group received nivolumab (480 mg IV q2w) for 8 weeks, followed by surgery. The control group received surgery alone. The study was conducted in a randomized, controlled manner. The neoadjuvant group received nivolumab (480 mg IV q2w) for 8 weeks, followed by surgery. The control group received surgery alone.

RESULTS

1875 patients were included in the study. 1000 patients were in the neoadjuvant group and 875 patients were in the control group. The primary endpoint was overall survival (OS) at 24 weeks. The study was conducted in a randomized, controlled manner. The neoadjuvant group received nivolumab (480 mg IV q2w) for 8 weeks, followed by surgery. The control group received surgery alone.

KEY CONCLUSIONS

Neoadjuvant nivolumab significantly improved OS compared to surgery alone. The study was conducted in a randomized, controlled manner. The neoadjuvant group received nivolumab (480 mg IV q2w) for 8 weeks, followed by surgery. The control group received surgery alone.

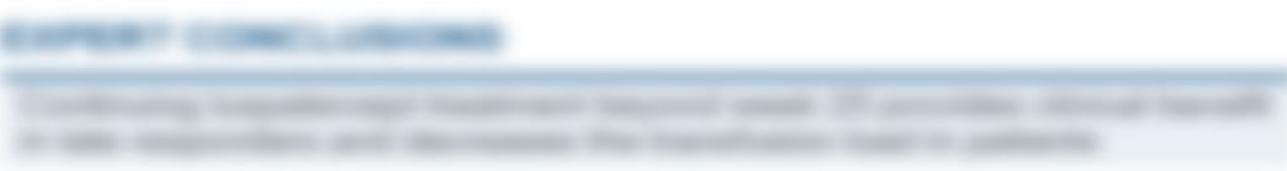




First-Line Immunotherapy in Metastatic NSCLC: Single Agent or Combination? (2/2)

Presented by Roy Herbst, MD, PhD

- > Single-agent immunotherapy
 - > Pembrolizumab (PD-L1 $\geq 1\%$) (KEYNOTE-024/042)
 - > Atezolizumab (PD-L1 $\geq 50\%$) (IMpower110)





New Directions for Second-Line Therapy

Presented by Natasha Leigh, MD, FRCPC, FASCO

> The management of patients whose disease has

STUDY POPULATION

Phase III, randomized, controlled trial comparing docetaxel + erlotinib (n=200) with docetaxel + placebo (n=200) in patients with previously treated metastatic NSCLC. Primary endpoint: overall survival (OS). Secondary endpoints: progression-free survival (PFS), quality of life (QoL), and adverse events. The trial was conducted in 15 countries. The median OS was 10.1 months in the docetaxel + erlotinib group and 9.1 months in the docetaxel + placebo group. The median PFS was 4.1 months in the docetaxel + erlotinib group and 3.8 months in the docetaxel + placebo group. The QoL was significantly better in the docetaxel + erlotinib group. The adverse events were similar in both groups.

RESULTS

OS: 10.1 months (95% CI, 9.1-11.1) vs 9.1 months (95% CI, 8.1-10.1), p=0.001. PFS: 4.1 months (95% CI, 3.6-4.6) vs 3.8 months (95% CI, 3.3-4.3), p=0.001. QoL: significantly better in the docetaxel + erlotinib group. Adverse events: similar in both groups.

KEY TAKEAWAYS

Docetaxel + erlotinib significantly improved OS and PFS compared with docetaxel + placebo in patients with previously treated metastatic NSCLC. The QoL was also significantly better in the docetaxel + erlotinib group.

OS: TIME TO NEXT TREATMENT IN THE LATEST 100 PATIENTS



RESPONSE: METASTASIS AT FIRST ANALYSIS PERIOD





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

Presented by Paul Bunn, MD

> For patients with newly diagnosed,



STANDARD OF CARE

1. 2009 NCCN guideline: 4 cycles of platinum-based doublet chemotherapy (PD-L1 negative) or 2-4 cycles of PD-L1 inhibitor + platinum-based doublet chemotherapy (PD-L1 positive) followed by maintenance immunotherapy (atezolizumab or durvalumab) if PD-L1 positive. The combination of PD-L1 inhibitor + platinum-based doublet chemotherapy is preferred for patients with PD-L1 positive tumors. The combination of PD-L1 inhibitor + platinum-based doublet chemotherapy is preferred for patients with PD-L1 negative tumors.

KEY POINTS

1. 2017 NCCN guideline: 4 cycles of platinum-based doublet chemotherapy (PD-L1 negative) or 2-4 cycles of PD-L1 inhibitor + platinum-based doublet chemotherapy (PD-L1 positive) followed by maintenance immunotherapy (atezolizumab or durvalumab) if PD-L1 positive. The combination of PD-L1 inhibitor + platinum-based doublet chemotherapy is preferred for patients with PD-L1 positive tumors. The combination of PD-L1 inhibitor + platinum-based doublet chemotherapy is preferred for patients with PD-L1 negative tumors.

KEY POINT CONCLUSIONS

1. Immunotherapy is now a standard of care for SCLC. 2. Immunotherapy is preferred for patients with PD-L1 positive tumors. 3. Immunotherapy is preferred for patients with PD-L1 negative tumors.

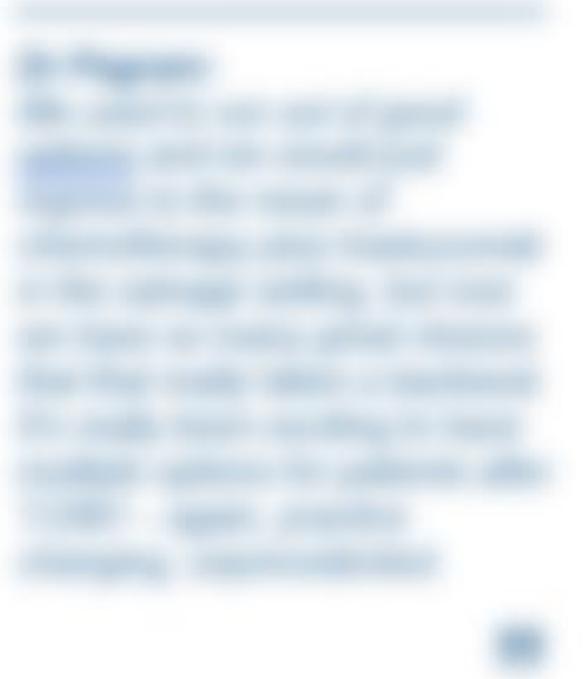


EPICS

Key Insights

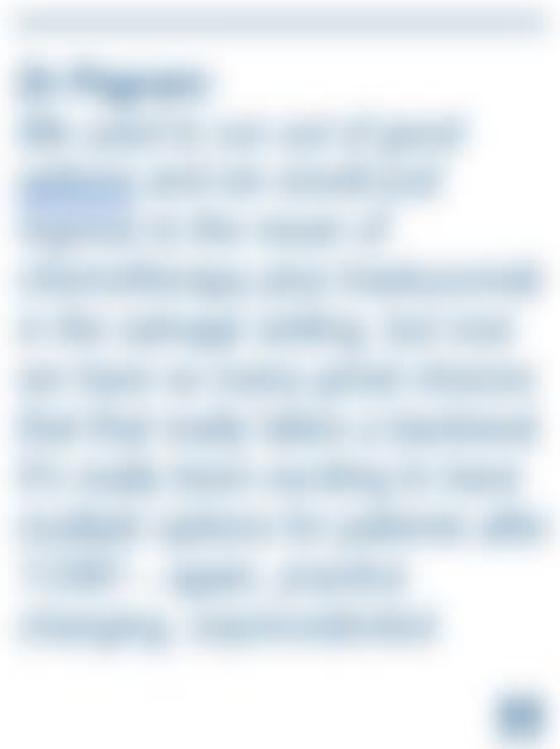
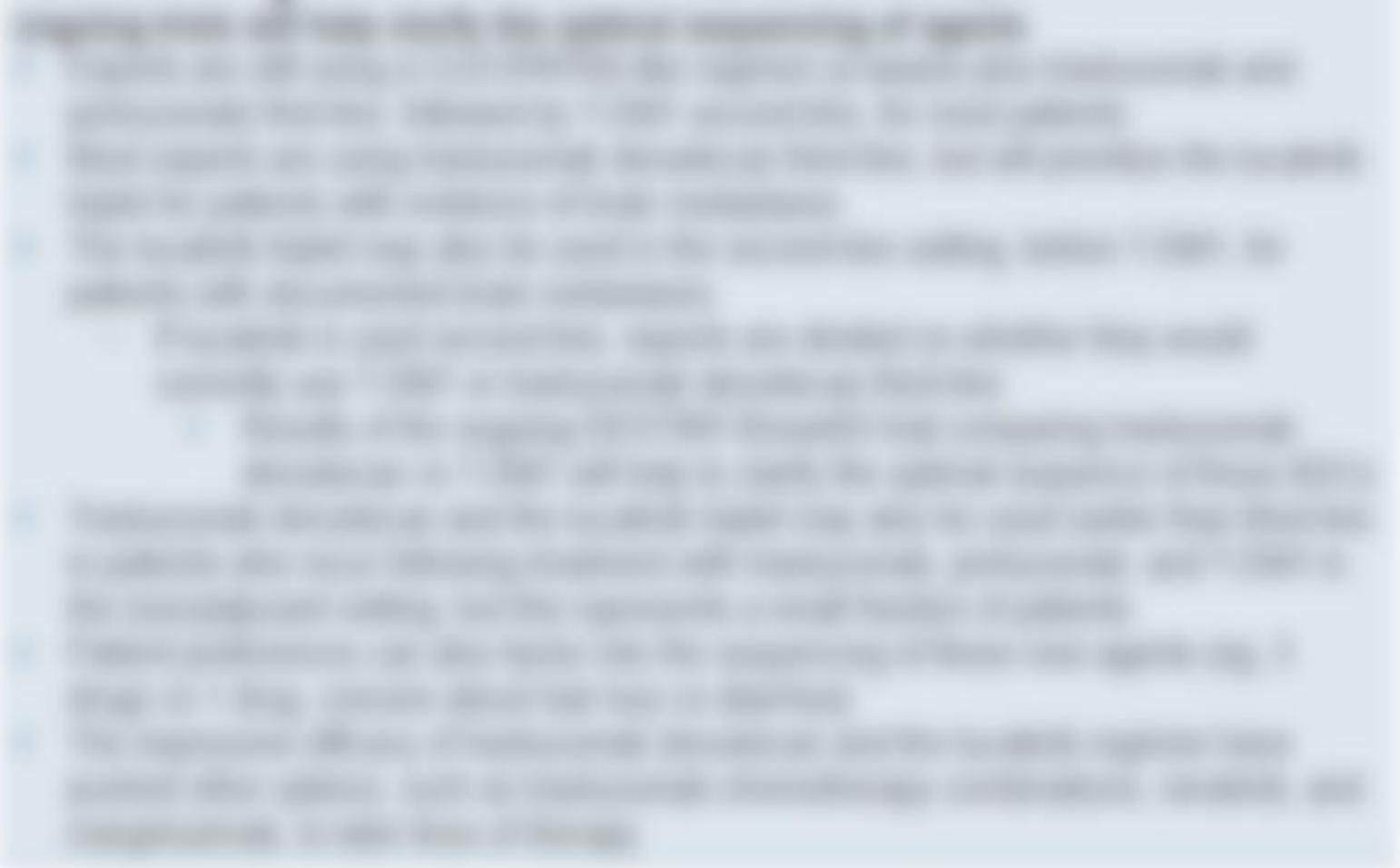
Prognostic and Predictive Biomarkers in Non-small Cell Lung Cancer (1/2)

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



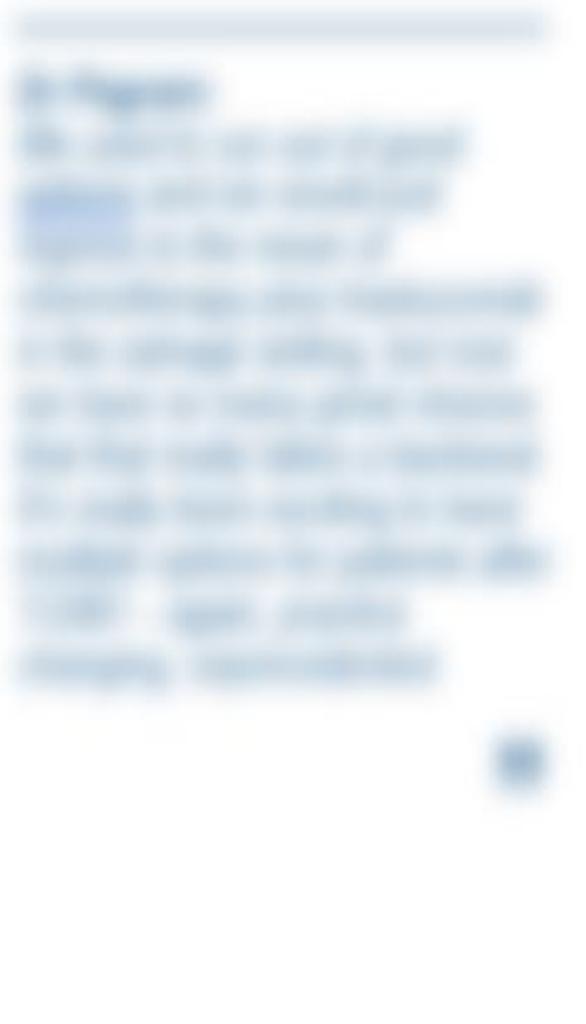
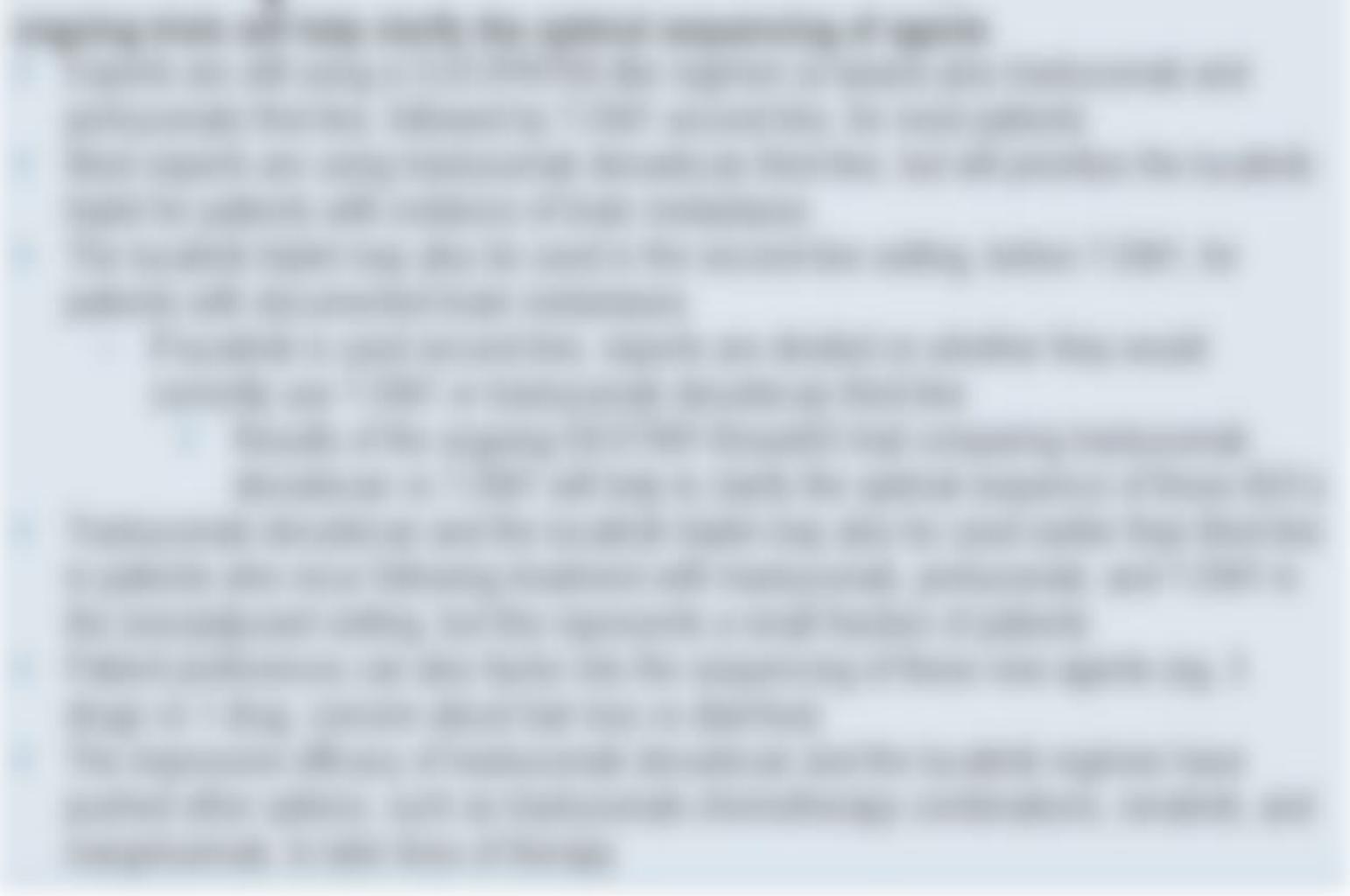
Prognostic and Predictive Biomarkers in Non-small Cell Lung Cancer (2/2)

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



New Directions for *EGFR*-Mutated NSCLC

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



EGFR (Less Common Mutations, Including Exon 20 Insertions)

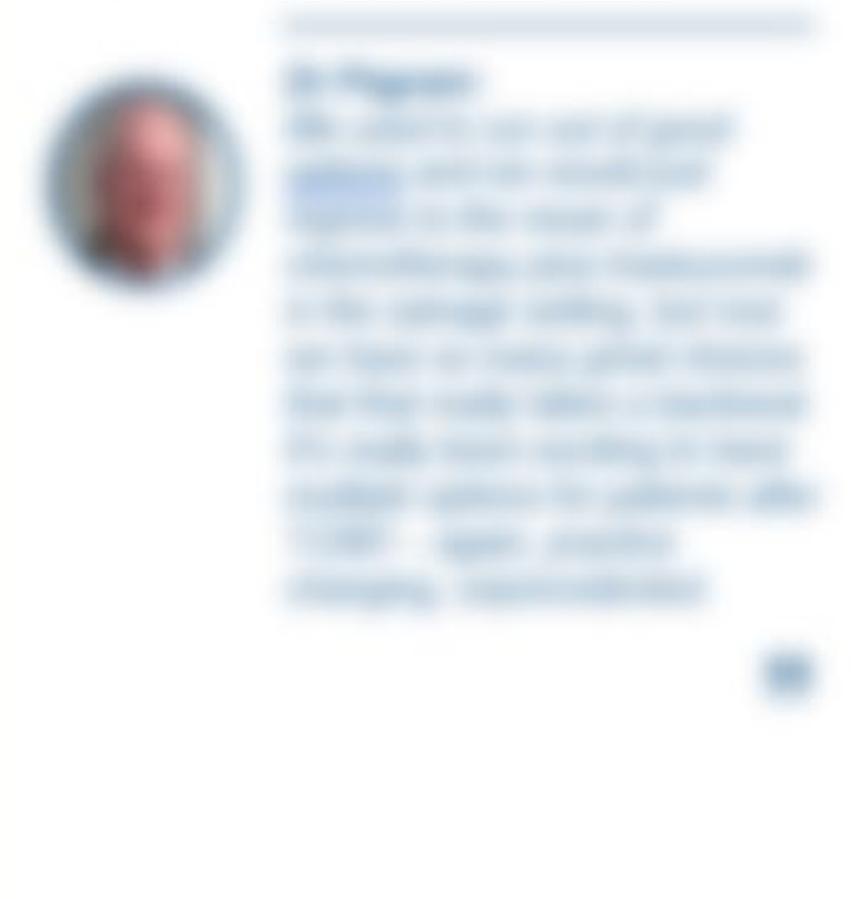
[Blurred text area containing illegible content]



[Blurred text area containing illegible content]

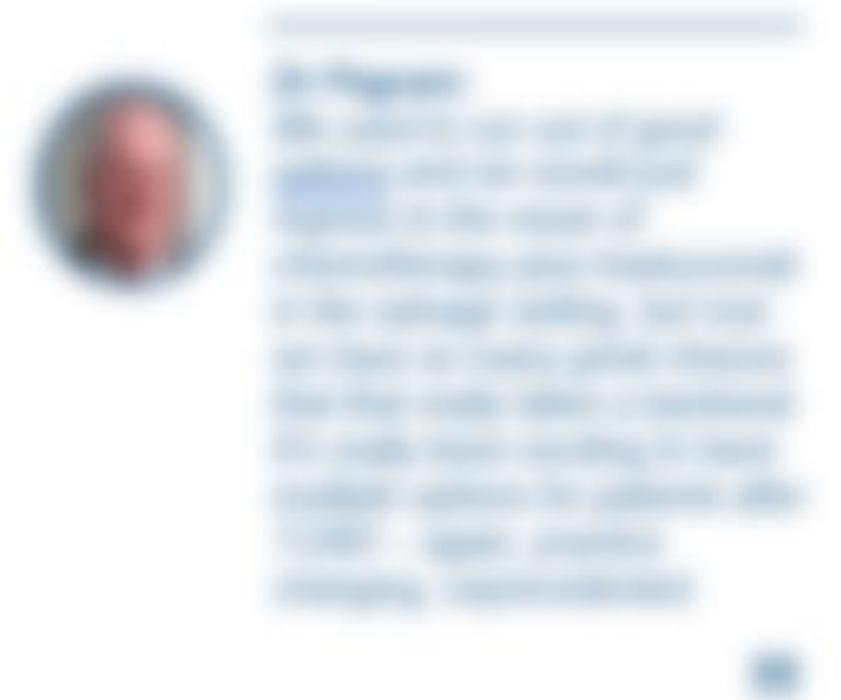
Therapeutic Landscape for Fusion-Positive NSCLC (*ALK*, *ROS1*, *NTRK*, *RET*) (1/2)

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

A blurred screenshot of a presentation slide. The slide contains several paragraphs of text and a diagram. The diagram appears to be a circular flow or a network of nodes, but the details are obscured by the blur. The text is also illegible due to the low resolution.Another blurred screenshot of a presentation slide, similar to the one on the left. It contains text and a diagram, but the content is not discernible due to the blurring effect.

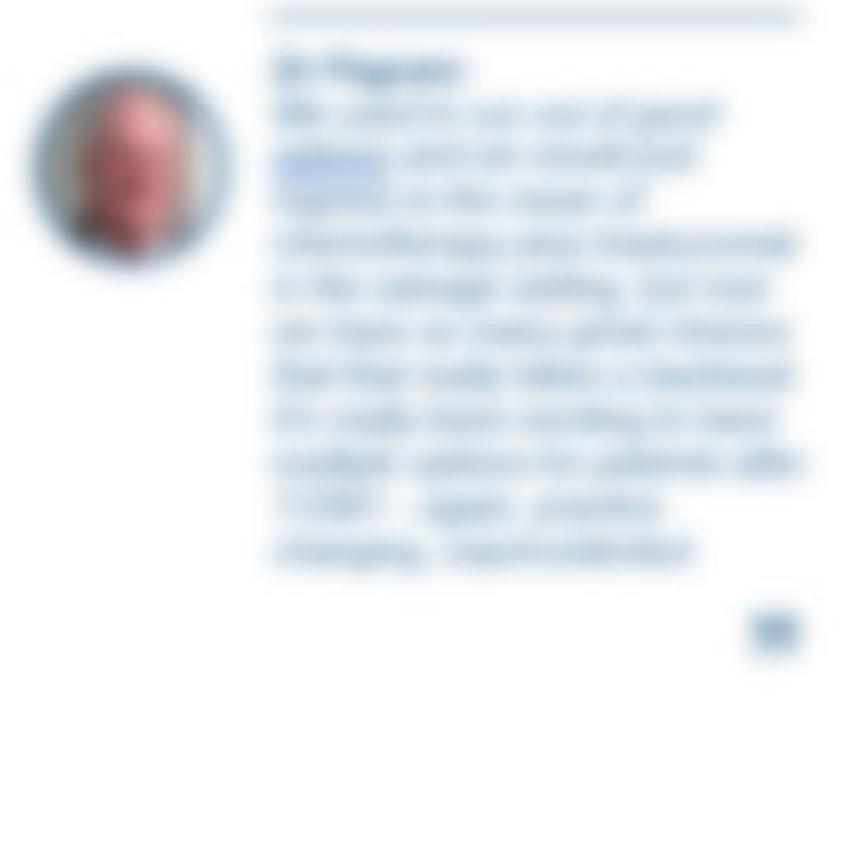
Therapeutic Landscape for Fusion-Positive NSCLC (*ALK*, *ROS1*, *NTRK*, *RET*) (2/2)

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



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

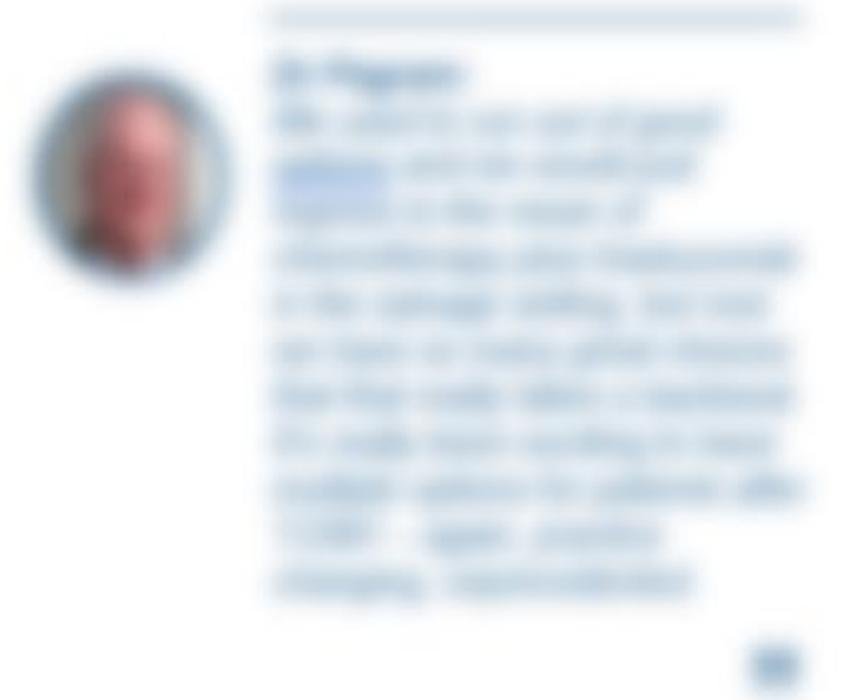
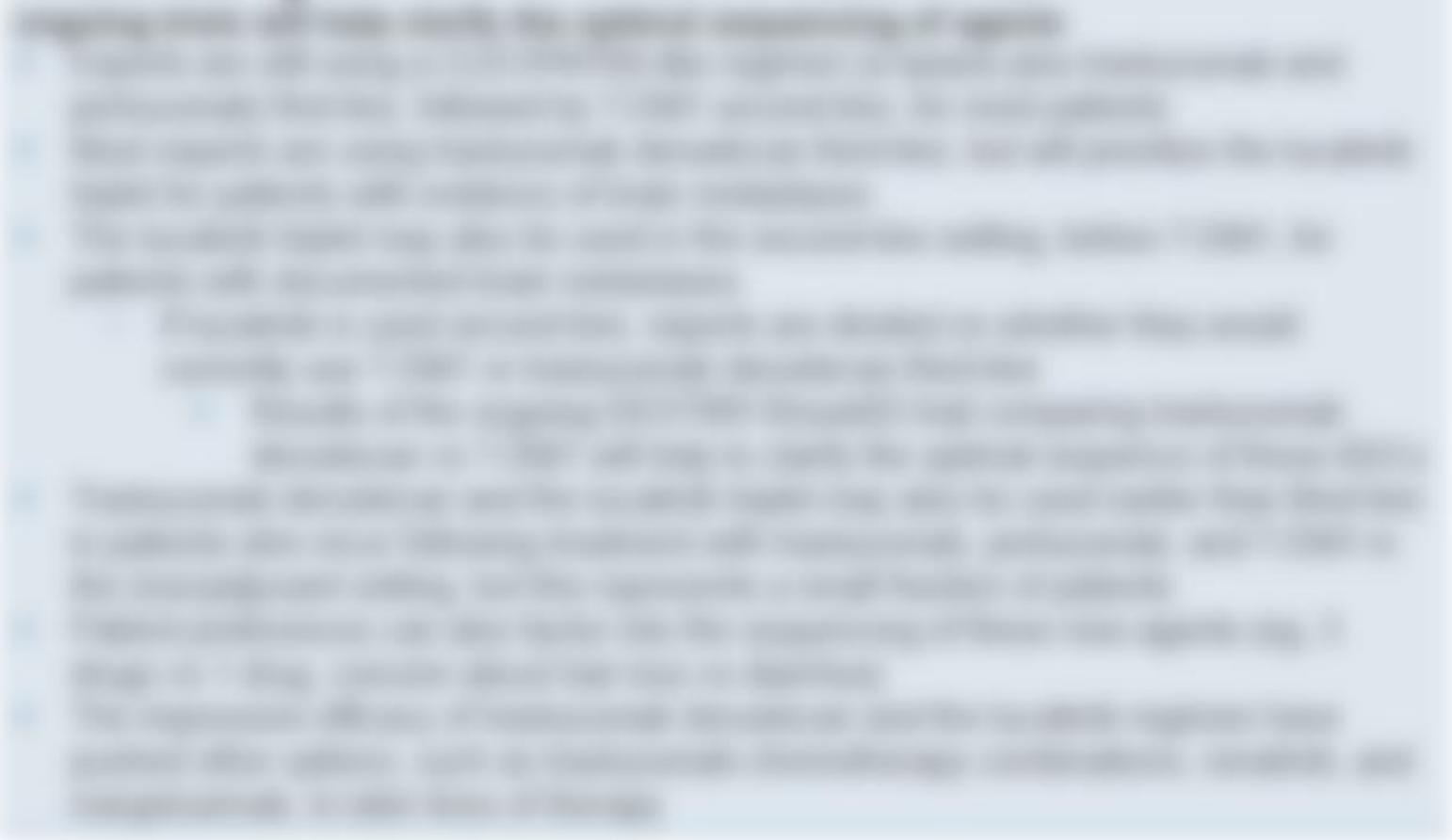
> The experts cited a study that showed a continuing lack of molecular testing in community practice; while 80% of the patients were tested for



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

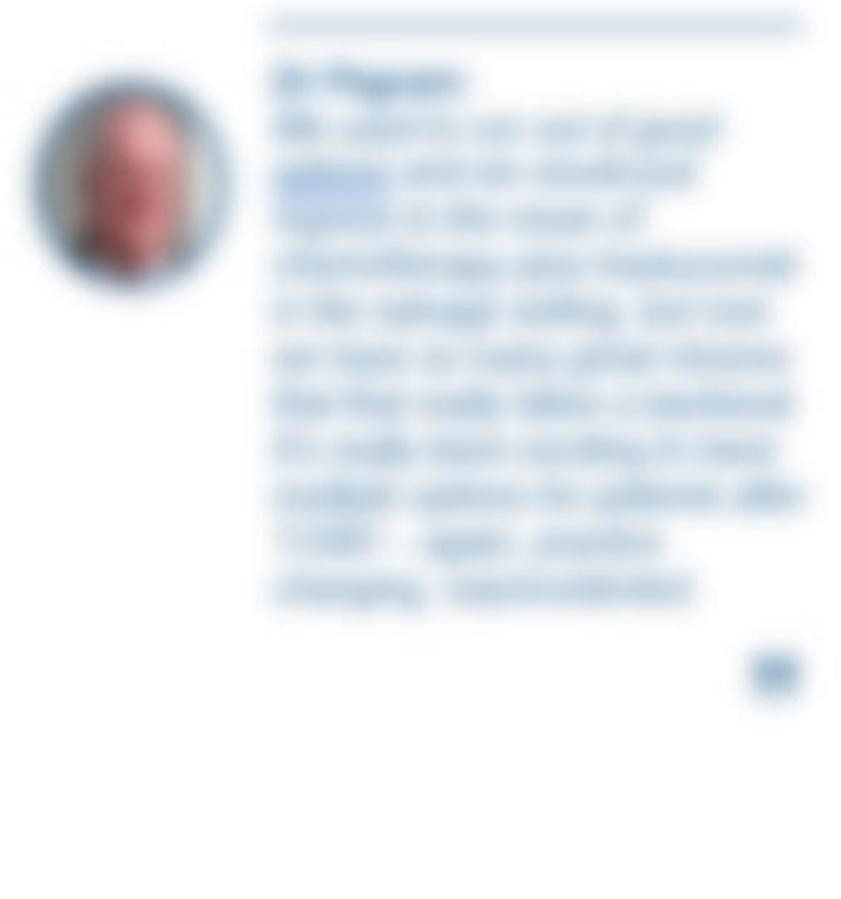
> *HER2*

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



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

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



Perioperative Immunotherapy in Early NSCLC (1/2)

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

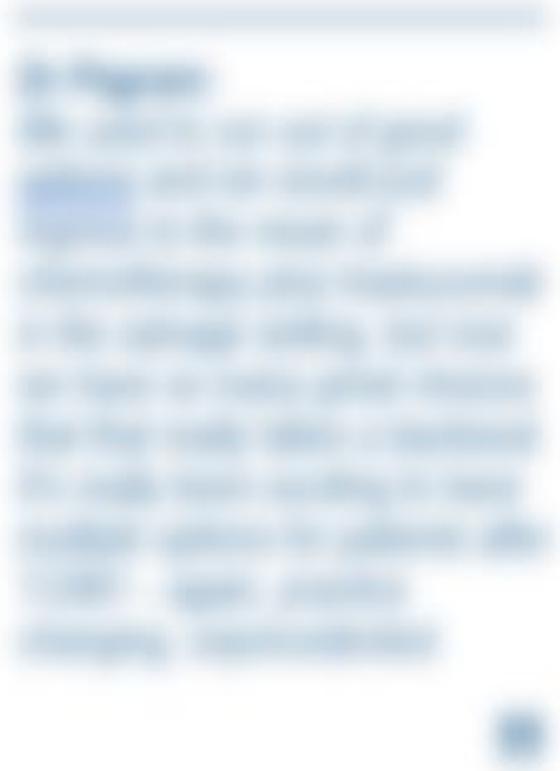
[Blurred content area]



[Blurred content area]

Perioperative Immunotherapy in Early NSCLC (2/2)

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



Immunotherapy in Unresectable Stage III NSCLC

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

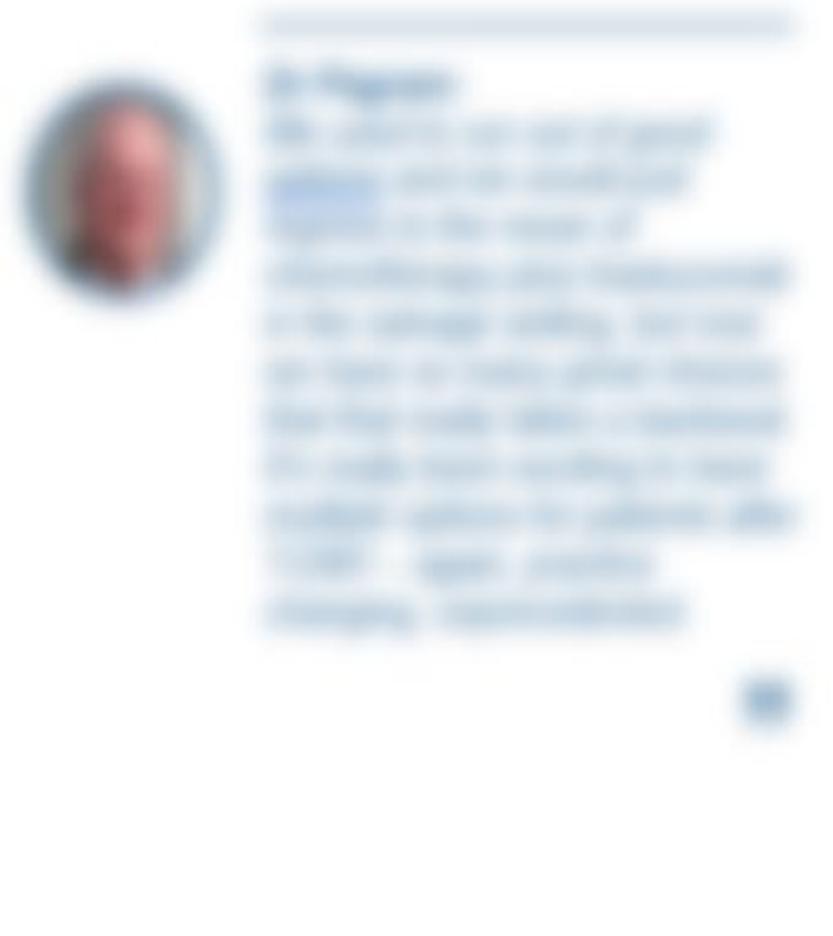
[Blurred content area containing text and possibly a list of points]



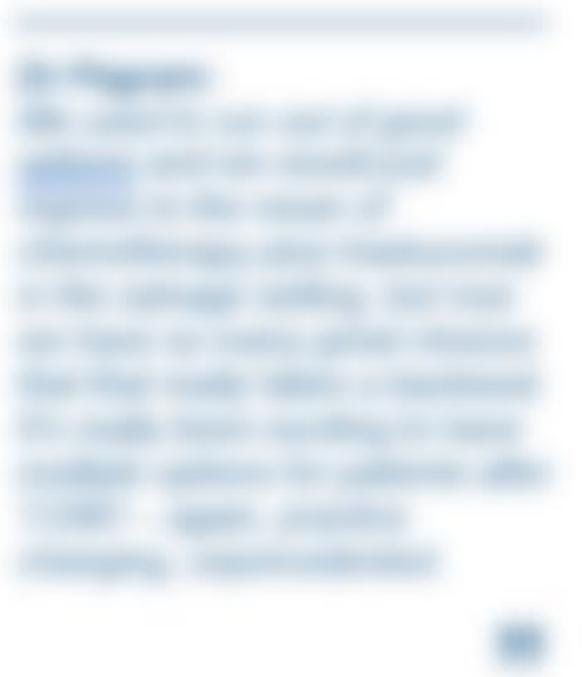
[Blurred content area containing text and possibly a list of points]

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

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

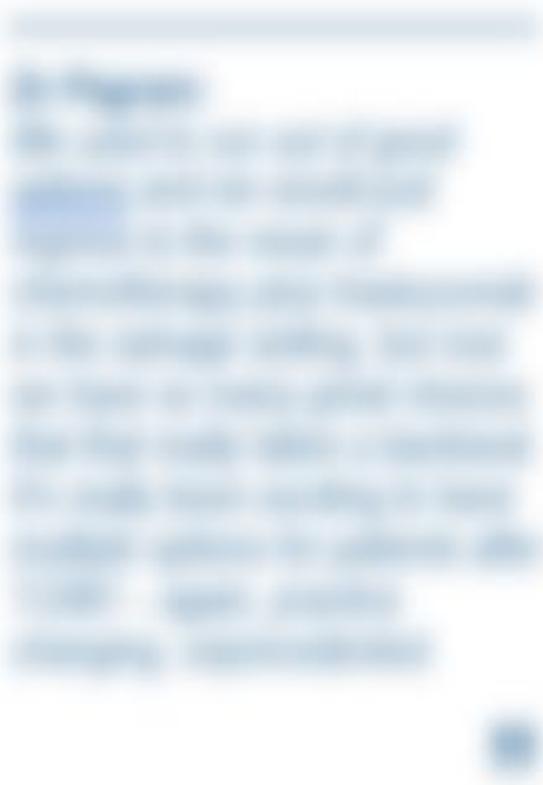
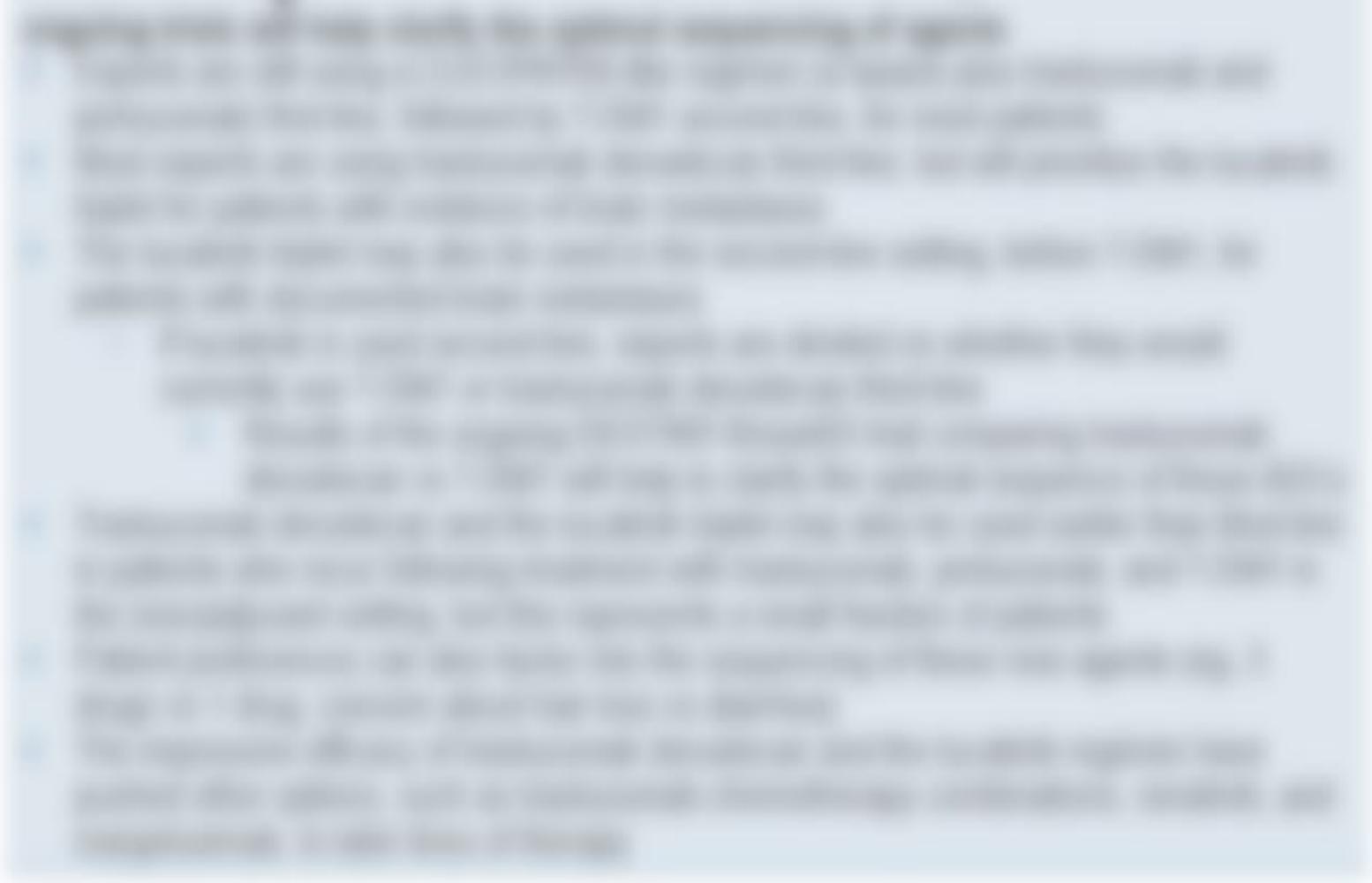


> The experts remarked on the number of phase III trials without biomarker selection



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

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



Emergence of Immunotherapy and New Agents in SCLC

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

[Blurred text area containing a list of bullet points and paragraphs, likely representing a transcript of a discussion or a list of key points related to the topic of immunotherapy and new agents in SCLC.]



[Blurred text area containing a list of bullet points and paragraphs, likely representing a transcript of a discussion or a list of key points related to the topic of immunotherapy and new agents in SCLC.]