



EPICS

EPICS – Lung Cancer in 2021 and Beyond

December 3–4, 2021

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EPICS

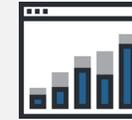
VIRTUAL CLOSED-DOOR ROUNDTABLE



DATE:
December 3–4, 2021



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



INSIGHT REPORT
including postmeeting
analyses and actionable
recommendations



PANEL: Key experts in
lung cancer

- > 8 from US
- > 1 from Canada



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

Panel Consisting of 8 US and 1 Canadian Lung Cancer Experts

A map of the United States with circular callouts for 8 US and 1 Canadian lung cancer experts. The callouts are placed over various geographic locations: California, Texas, Indiana, Michigan, Pennsylvania, New York, and Ontario, Canada. Each callout contains a portrait of the expert and their name, credentials, and affiliation.

- Edward Garon, MD, MS**
University of California
Los Angeles
- Karen L. Reckamp, MD**
Cedars-Sinai Medical Center
- Antoinette J. Wozniak, MD, FACP, FASCO**
University of Pittsburgh
- Nasser Hanna, MD**
Indiana University
School of Medicine
- Ignacio I. Wistuba, MD**
MD Anderson Cancer Center
- David Spigel, MD**
Sarah Cannon Research
Institute
- Corey Langer, MD, FACP**
CHAIR:
University of Pennsylvania
- Roy S. Herbst, MD, PhD**
Yale Cancer Center
- Natasha Leigh, MMSc, MD, FRCPC, FASCO**
University of Toronto

Meeting Agenda – Day 1 (1/2)

EPICS

Time – Eastern Time (US)	Topic	Speaker/Moderator
5.00 PM – 5.05 PM (5 min)	Welcome and Introductions	Corey J. Langer, MD, FACP
5.05 PM – 5.25 PM (20 min)	Prognostic and Predictive Biomarkers in NSCLC – Clinical vs Research Relevance (excluding <i>EGFR/ALK</i>)	Ignacio Wistuba, MD
5.25 PM – 5.55 PM (30 min)	Discussion – Prognostic and Predictive Biomarkers in NSCLC – Clinical vs Research Relevance (excluding <i>EGFR/ALK</i>)	Moderator: Corey J. Langer, MD, FACP
5.55 PM – 6.10 PM (15 min)	New Directions for <i>EGFR</i> -Mutant NSCLC	Antoinette Wozniak, MD, FACP, FASCO
6.10 PM – 6.30 PM (20 min)	Discussion – New Directions for <i>EGFR</i> -Mutant NSCLC	Moderator: Corey J. Langer, MD, FACP
6.30 PM – 6.40 PM (10 min)	Emergence of Immunotherapy and Bispecifics in SCLC	Antoinette Wozniak, MD, FACP, FASCO
6.40 PM – 6.50 PM (10 min)	Discussion – Emergence of Immunotherapy and Bispecifics in SCLC	Moderator: Corey J. Langer, MD, FACP
6.50 AM – 7.00 PM (10 min)	BREAK	



Meeting Agenda – Day 1 (2/2)

EPICS

Time – Eastern Time (US)	Topic	Speaker/Moderator
7.00 PM – 7.15 PM (15 min)	Therapeutic Landscape for Fusion-Positive NSCLC (<i>ALK, ROS1, NTRK, RET</i>)	Karen Reckamp, MD, MS
7.15 PM – 7.45 PM (30 min)	Discussion – Therapeutic Landscape for Fusion-Positive NSCLC (<i>ALK, ROS1, NTRK, RET</i>)	Moderator: Corey J. Langer, MD, FACP
7.45 PM – 8.00 PM (15 min)	Inhibiting Oncogenic Mutations: Overcoming Mutant <i>KRAS, HER2, MET, and BRAF</i>	David Spigel, MD
8.00 PM – 8.30 PM (30 min)	Discussion – Inhibiting Oncogenic Mutations: Overcoming Mutant <i>KRAS, HER2, MET, and BRAF</i>	Moderator: Corey J. Langer, MD, FACP
8.30 PM – 8.40 PM (10 min)	New Directions for Second-Line Therapy	Edward Garon, MD
8.40 PM – 9.00 PM (20 min)	Discussion – New Directions for Second-Line Therapy	Moderator: Corey J. Langer, MD, FACP
	Adjourn	Corey J. Langer, MD, FACP



Meeting Agenda – Day 2 (1/2)

EPICS

Time – Eastern Time (US)	Topic	Speaker/Moderator
9.00 AM – 9.05 AM (5 min)	Welcome and Introductions	Corey J. Langer, MD, FACP
9.05 AM – 9.20 AM (15 min)	Perioperative Immunotherapy in Early NSCLC	Karen Reckamp, MD, MS
9.20 AM – 9.50 AM (30 min)	Discussion – Perioperative Immunotherapy in Early NSCLC	Moderator: Corey J. Langer, MD, FACP
9.50 AM – 10.00 AM (10 min)	Immunotherapy in Unresectable Stage III NSCLC	Nasser Hanna, MD
10.00 AM – 10.20 AM (20 min)	Discussion – Immunotherapy in Unresectable Stage III NSCLC	Moderator: Corey J. Langer, MD, FACP
10.20 AM – 10.35 AM (15 min)	First-Line Immunotherapy in Metastatic NSCLC – Single Agent or Combination?	Roy Herbst, MD, PhD
10.35 AM – 11.05 AM (30 min)	Discussion – First-Line Immunotherapy in Metastatic NSCLC: Single Agent or Combination?	Moderator: Corey J. Langer, MD, FACP
11.05 AM – 11.15 AM (10 min)	BREAK	



Meeting Agenda – Day 2 (2/2)

EPICS

Time – Eastern Time (US)	Topic	Speaker/Moderator
11.15 AM – 11.30 AM (15 min)	Biomarkers for Immunotherapy – Making Sense of the Chaos	Roy Herbst, MD, PhD
11.30 AM – 11.50 AM (20 min)	Discussion – Biomarkers for Immunotherapy – Making Sense of the Chaos	Moderator: Corey J. Langer, MD, FACP
11.50 AM – 12.00 PM (10 min)	<i>EGFR</i> (Less Common Mutations, Including Exon 20 Insertions)	Natasha Leighl, MD, MMSc, FRCPC, FASCO
12.00 PM – 12.10 PM (25 min)	Discussion – <i>EGFR</i> (Less Common Mutations, Including Exon 20 Insertions)	Moderator: Corey J. Langer, MD, FACP
12.10 PM – 12.20 PM (10 min)	Promising New Targets/Agents in Lung Cancer	David Spigel, MD
12.20 PM – 12.40 PM (20 min)	Discussion – Promising New Targets/Agents in Lung Cancer	Moderator: Corey J. Langer, MD, FACP
	Conclusions and Adjourn	Corey J. Langer, MD, FACP



EPICS

Summaries of Faculty Presentations



Prognostic and Predictive Biomarkers in NSCLC (2/2)

Presented by Ignacio Wistuba, MD

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

Presented by Antoinette Wozniak, MD, FACP, FASCO

> The most significant advance in the

A Patients with Stage II to IIIA Disease

ADAURA: Adjuvant

STUDY POPULATION

10,111 patients with EGFR-mutant NSCLC, including 5,055 with Stage II to IIIA disease, were randomized to receive either adjuvant osimertinib or placebo. The median time to progression was significantly longer in the osimertinib group (17.5 months) compared with the placebo group (13.8 months). The median overall survival was also significantly longer in the osimertinib group (30.3 months) compared with the placebo group (27.2 months). The median time to death or discontinuation of treatment was significantly longer in the osimertinib group (27.5 months) compared with the placebo group (23.8 months).

RESULTS

10,111 patients with EGFR-mutant NSCLC, including 5,055 with Stage II to IIIA disease, were randomized to receive either adjuvant osimertinib or placebo. The median time to progression was significantly longer in the osimertinib group (17.5 months) compared with the placebo group (13.8 months). The median overall survival was also significantly longer in the osimertinib group (30.3 months) compared with the placebo group (27.2 months). The median time to death or discontinuation of treatment was significantly longer in the osimertinib group (27.5 months) compared with the placebo group (23.8 months).

KEY TAKEAWAYS

Continuing osimertinib treatment beyond week 24 provides clinical benefit in EGFR-mutant NSCLC and decreases the proportion of patients with

ADJUVANT TREATMENT REGIMENS



RESPONSE RATES BY EGFR MUTATION STATUS





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

Presented by Antoinette Wozniak, MD, FACP, FASCO

> Key areas of investigation include improving the efficacy of first-line

STUDY POPULATION

Approximately 1000 patients with EGFR-mutant NSCLC... (text is blurred)

OUTLINE

Approximately 1000 patients... (text is blurred)

KEY TAKEAWAYS

Continuing investigation... (text is blurred)

KEY TAKEAWAYS FROM SUBGROUPS IN THE CLINICAL TRIALS



RESPONSE MEASUREMENTS IN OTHER ANALYSES PERFORMED





EGFR (Less Common Mutations, Including Exon 20 Insertions) (1/2)

Presented by Natasha Leighl, MD, MMSc, FRCPC, FASCO

> EGFR exon 20 insertions represent 4% to

- Patients with EGFR exon20ins are a population with significant unmet needs

STUDY POPULATION

1. 1000 patients with EGFR exon 20 insertions were enrolled in a phase II study. The study included patients with various EGFR exon 20 insertion mutations. The study population was diverse in terms of age, gender, and ethnicity. The study was conducted in multiple countries. The study results showed that patients with EGFR exon 20 insertions have a significant unmet need for treatment. The study also showed that patients with EGFR exon 20 insertions have a higher rate of resistance to EGFR inhibitors compared to patients with other EGFR mutations.

RESULTS

2. The study results showed that patients with EGFR exon 20 insertions have a higher rate of resistance to EGFR inhibitors compared to patients with other EGFR mutations. The study also showed that patients with EGFR exon 20 insertions have a higher rate of progression-free survival compared to patients with other EGFR mutations.

KEY TAKEAWAYS

3. EGFR exon 20 insertions represent a significant unmet need for treatment. Patients with EGFR exon 20 insertions have a higher rate of resistance to EGFR inhibitors compared to patients with other EGFR mutations. The study also showed that patients with EGFR exon 20 insertions have a higher rate of progression-free survival compared to patients with other EGFR mutations.

EGFR EXON 20 INSERTIONS REPRESENT A SIGNIFICANT UNMET NEED FOR TREATMENT



RESPONSE RATES AND PROGRESSION-FREE SURVIVAL IN EGFR EXON 20 INSERTION PATIENTS





EGFR (Less Common Mutations, Including Exon 20 Insertions) (2/2)

Presented by Natasha Leigh, MD, MMSc, FRCPC, FASCO

> In 2021, 2 agents were approved as subsequent therapy specifically

STUDY POPULATION

Approximately 1000 patients with EGFR mutations, including Exon 20 insertions, were included in the study. The study population was divided into two groups: one receiving the investigational agent and the other receiving standard of care. The primary endpoint was overall survival, and the secondary endpoint was progression-free survival. The study was a phase III, randomized, controlled trial.

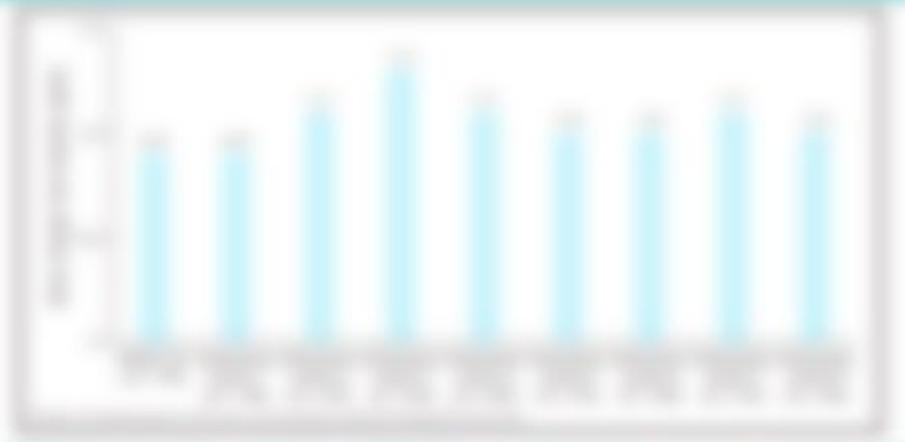
RESULTS

The study demonstrated that the investigational agent significantly improved overall survival compared to standard of care in patients with EGFR mutations, including Exon 20 insertions. The hazard ratio for overall survival was 0.75 (95% CI 0.60-0.95), p < 0.001.

KEY TAKEAWAYS

The study highlights the importance of EGFR testing in patients with NSCLC and the potential for improved outcomes with targeted therapy in patients with EGFR mutations, including Exon 20 insertions.

KEY TAKEAWAYS FROM STUDY ON THE EFFICACY OF EGFR INHIBITORS IN NSCLC



RESPONSE RATES IN EGFR MUTATED NSCLC PATIENTS





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

Presented by Karen Reckamp, MD, MS

> A key consideration for oncogenic fusions is

Methods for Fusion Detection:



STUDY POPULATION

1. 1000 NSCLC patients with ALK, ROS1, NTRK, or RET fusions... (text is blurred)

RESULTS

2. 100% of patients with ALK, ROS1, NTRK, or RET fusions... (text is blurred)

KEY TAKEAWAYS

3. Identifying oncogenic fusions... (text is blurred)

Methods for Fusion Detection



RESPONSE RATES WITH ALK, ROS1, NTRK, AND RET INHIBITORS





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

Presented by Karen Reckamp, MD, MS

> *NRG1* represents an emerging class of oncogenic fusions, with a

STUDY POPULATION

1. 100 patients with NSCLC harboring *NRG1* gene rearrangements... (text is blurred)

RESULTS

1. 100 patients with NSCLC harboring *NRG1* gene rearrangements... (text is blurred)

KEY POINT CONCLUSIONS

1. Identifying *NRG1* rearrangements... (text is blurred)

ONCOLOGIC PROFILES OF *NRG1* FUSIONS



RESPONSE RATES OF *NRG1* FUSIONS





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

Presented by David Spigel, MD

> The most recent development in actionable

Sotorasib

Figure 1: Overall Survival in the LIBERTY-001 Study



Figure 2: Response Rate in the LIBERTY-001 Study



STUDY POPULATION

1. 1000 patients with KRAS G12C mutation, ECOG performance grade 0-1, no prior systemic anticancer therapy, and no prior KRAS-targeted therapy. Randomized to Sotorasib (n=500) or Placebo (n=500). Primary endpoint: Overall survival (OS). Secondary endpoints: Response rate (RR), progression-free survival (PFS), and quality of life.

RESULTS

2. OS significantly improved in the Sotorasib group compared to the Placebo group (p < 0.001). RR was significantly higher in the Sotorasib group (p < 0.001).

CONCLUSIONS

3. Sotorasib significantly improved OS and RR in patients with KRAS G12C mutation compared to placebo.



Perioperative Immunotherapy in Early NSCLC

Presented by Karen Reckamp, MD, MS

> The use of immunotherapy in patients with resectable

STUDY POPULATION

1000 patients with early-stage NSCLC, including 500 in the control group and 500 in the immunotherapy group. The study population was stratified by stage (I, II, III) and histology (adenocarcinoma, squamous cell carcinoma). The immunotherapy group received a combination of pembrolizumab and nivolumab. The control group received a combination of platinum-based chemotherapy and surgery. The study was conducted in a randomized, controlled manner.

RESULTS

The immunotherapy group showed significantly better overall survival compared to the control group. The median overall survival was 36 months in the immunotherapy group versus 28 months in the control group. The difference was statistically significant (p < 0.05).

KEY TAKEAWAYS

Combining immunotherapy with surgery significantly improved overall survival in early-stage NSCLC patients. This approach may be a promising treatment strategy for these patients.

PERIOPERATIVE TREATMENT STRATEGIES IN EARLY NSCLC



RESPONSE RATES AND SURVIVAL ANALYSIS PERIODS





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

Presented by Roy Herbst, MD, PhD

> There are currently multiple options for first-

A Current First Line Treatment Algorithm

STUDY POPULATION

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

RESULTS

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

KEY TAKEAWAYS

Combining immunotherapy with chemotherapy... (text is blurred)

RESPONSE RATES BY TREATMENT GROUP



RESPONSE RATES BY TREATMENT GROUP





Biomarkers for Immunotherapy – Making Sense of the Chaos

Presented by Roy Herbst, MD, PhD

> PD-L1 is still the main biomarker for

STUDY POPULATION

1000 patients with advanced melanoma... randomized to nivolumab or ipilimumab... overall survival... median OS... 15.7 months vs 12.3 months... p < 0.001... 10% of patients with PD-L1 expression... 10% of patients with PD-L1 expression... 10% of patients with PD-L1 expression...

RESULTS

1000 patients with advanced melanoma... randomized to nivolumab or ipilimumab... overall survival... median OS... 15.7 months vs 12.3 months... p < 0.001... 10% of patients with PD-L1 expression... 10% of patients with PD-L1 expression... 10% of patients with PD-L1 expression...

KEY TAKEAWAYS

Continuing immunotherapy treatment beyond week 24 provides clinical benefit in all subgroups and decreases the proportion of patients...

PD-L1 Expression and Clinical Outcomes



RESPONSE RATES BY PD-L1 EXPRESSION STATUS





New Directions for Second-Line Therapy

Presented by Edward Garon, MD

> Treatment of patients with advanced

STUDY POPULATION

1. 1000 patients with advanced NSCLC, ECOG performance 0-1, no prior systemic therapy, no EGFR/ALK alterations, randomized to docetaxel or docetaxel + ramipril. Primary endpoint: overall survival. Secondary endpoints: progression-free survival, quality of life, adverse events. Docetaxel + ramipril group showed significantly improved overall survival compared to docetaxel alone (HR 0.85, 95% CI 0.75-0.96, p=0.004). Median OS was 10.1 months vs 8.5 months. Docetaxel + ramipril group also showed significantly improved progression-free survival (HR 0.75, 95% CI 0.65-0.86, p<0.001). Quality of life and adverse events were similar between groups.

RESULTS

2. 1000 patients with advanced NSCLC, ECOG performance 0-1, no prior systemic therapy, no EGFR/ALK alterations, randomized to docetaxel or docetaxel + ramipril. Primary endpoint: overall survival. Secondary endpoints: progression-free survival, quality of life, adverse events. Docetaxel + ramipril group showed significantly improved overall survival compared to docetaxel alone (HR 0.85, 95% CI 0.75-0.96, p=0.004). Median OS was 10.1 months vs 8.5 months.

KEY TAKEAWAYS

Combining ramipril with docetaxel improved overall survival compared to docetaxel alone and decreased the number of patients with adverse events.

KEY TAKEAWAYS FROM SUBANALYSIS OF THE CLINICAL TRIAL



RESPONSE RATES AND TOXICITY ANALYSIS PERIOD





Emergence of Immunotherapy and Bispecifics in SCLC

Presented by Antoinette Wozniak, MD, FACP, FASCO

> After several decades with little progress, a new first-

STUDY POPULATION

Approximately 400 patients with SCLC, including 200 with a PSOR treatment, 200 with a best supportive care (BSC) treatment, or 100 with a combination of PSOR and BSC. The combination group received PSOR until progression, followed by BSC. The combination group had a significantly higher median overall survival (OS) compared to the PSOR group (11.1 months vs 8.4 months, p < 0.001).

RESULTS

Median OS was 11.1 months for patients receiving PSOR, 8.4 months for patients receiving BSC, and 11.1 months for patients receiving PSOR followed by BSC. The OS benefit was consistent across all subgroups.

KEY TAKEAWAYS

Combining immunotherapy treatment beyond week 20 provides clinical benefit in SCLC patients and decreases the proportion of patients with progression-free survival (PFS) at 6 months.

Median Overall Survival (OS) by Treatment Group



Response Rate (RR) by Treatment Group



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Key Insights

Prognostic and Predictive Biomarkers in NSCLC (1/2)

The experts would use liquid-based testing primarily for patients who were diagnosed outside their institution and/or if there is concern about

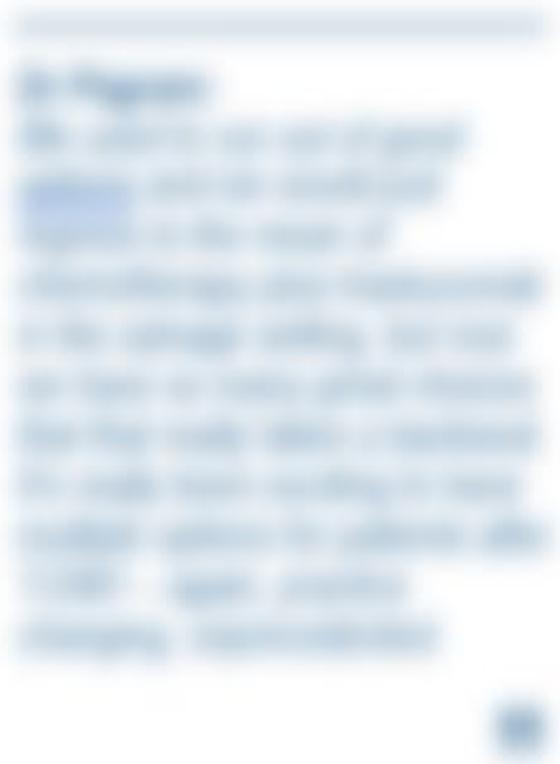
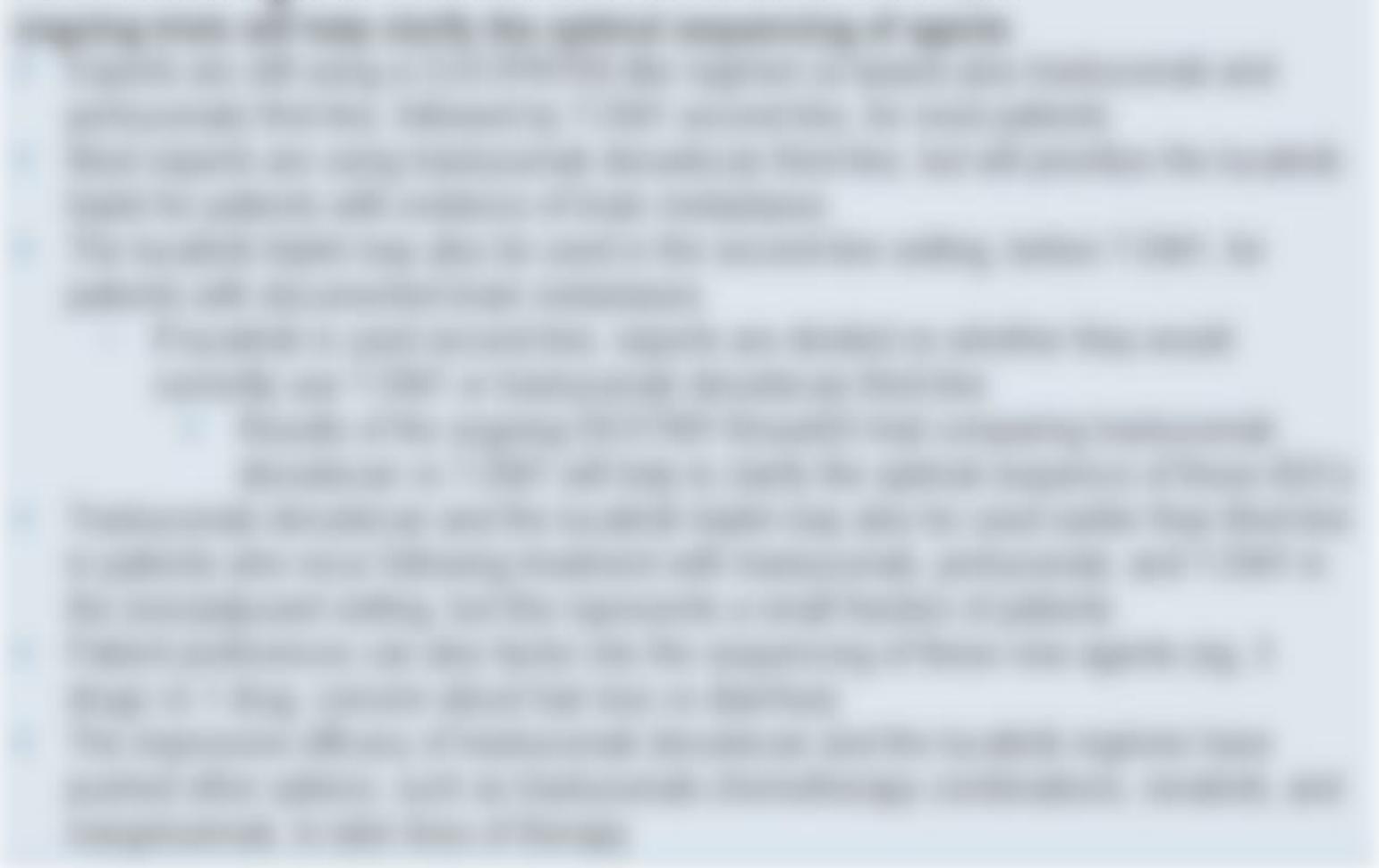
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Prognostic and Predictive Biomarkers in NSCLC (2/2)

Expert opinion is that *MET* amplification is an actionable marker, and



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

Molecular testing of patients with early stage NSCLC varied, ranging from *EGFR* only (n = 1), to *EGFR* and *ALK* (n = 1) and NGS-based testing

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

In the metastatic setting, the experts generally administer carboplatin-

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EGFR (Less Common Mutations, Including Exon 20 Insertions)

For patients with an EGFR exon 20 insertion, the experts would recommend chemotherapy without immunotherapy in the frontline setting

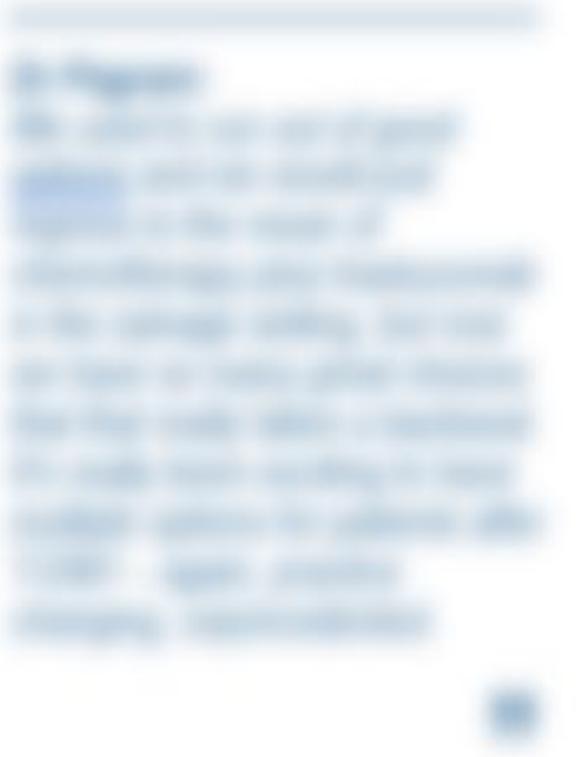
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Therapeutic Landscape for Fusion-Positive NSCLC (*ALK*, *ROS1*, *NTRK*, *RET*)

Expert opinion is that more education is needed to ensure that all appropriate patients have access to molecular testing for oncogenic fusions;

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

Testing results for *KRAS* are seen as an area of educational need for community oncologists

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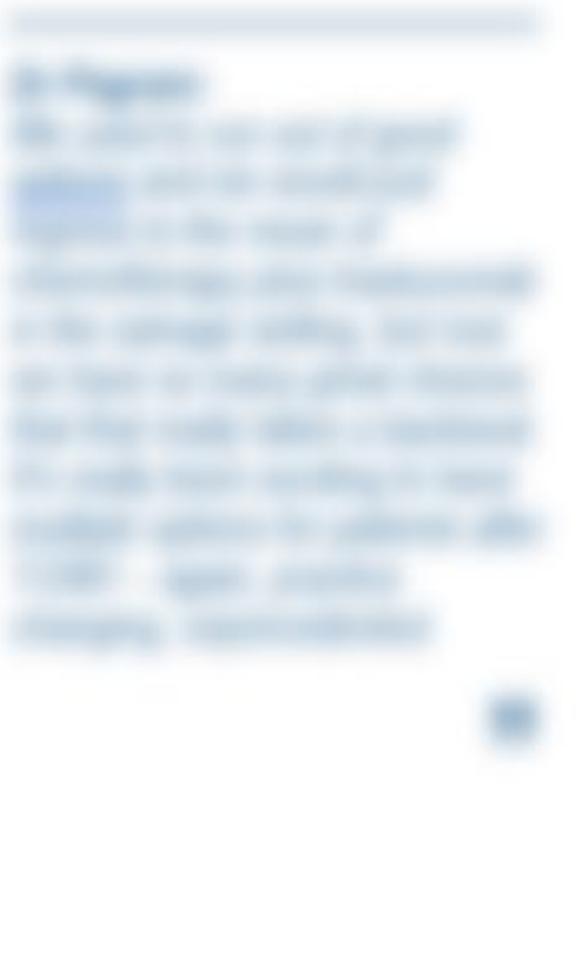
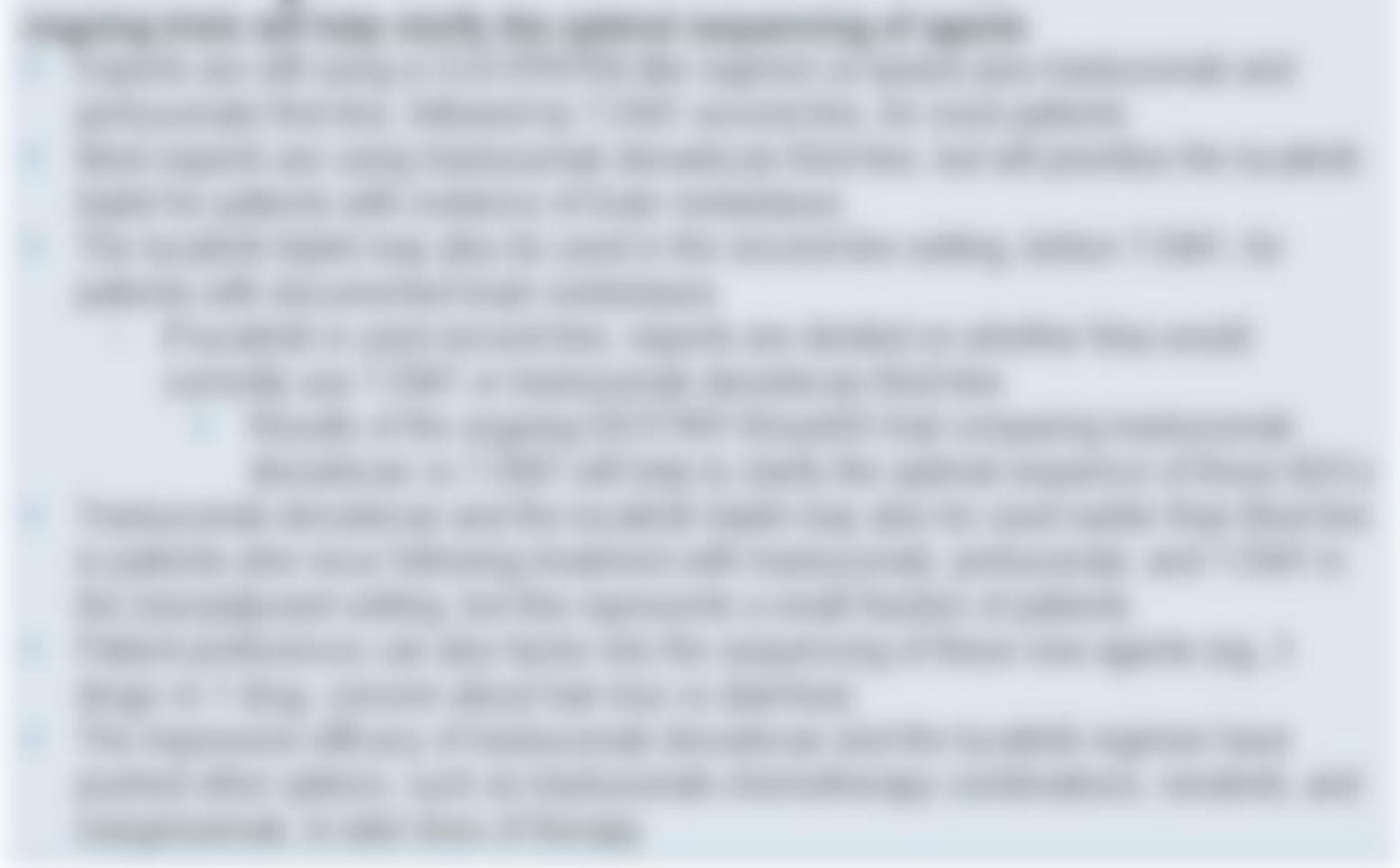


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Inhibiting Oncogenic Mutations: Overcoming Mutant *KRAS*, *HER2*, *MET*, and *BRAF* (2/2)

In patients with *HER2* mutations, the experts currently would use

Regarding amivantamab, one of the experts with extensive



Antibody-drug conjugates are of interest to the experts

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Perioperative Immunotherapy in Early NSCLC (1/2)

The experts discussed the assessment of pathologic complete response (pCR) and major pathologic response (MPR) in patients with NSCLC who

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Perioperative Immunotherapy in Early NSCLC (2/2)

Expert opinion is that it will be important to develop a management strategy for patients who

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Immunotherapy in Unresectable Stage II NSCLC

The experts generally do not use PD-L1 in deciding whether to offer a patient consolidation immunotherapy after CRT

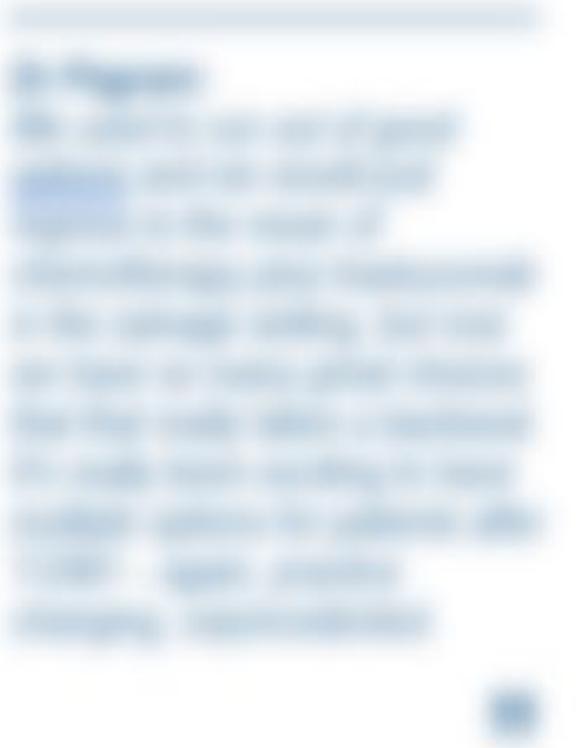
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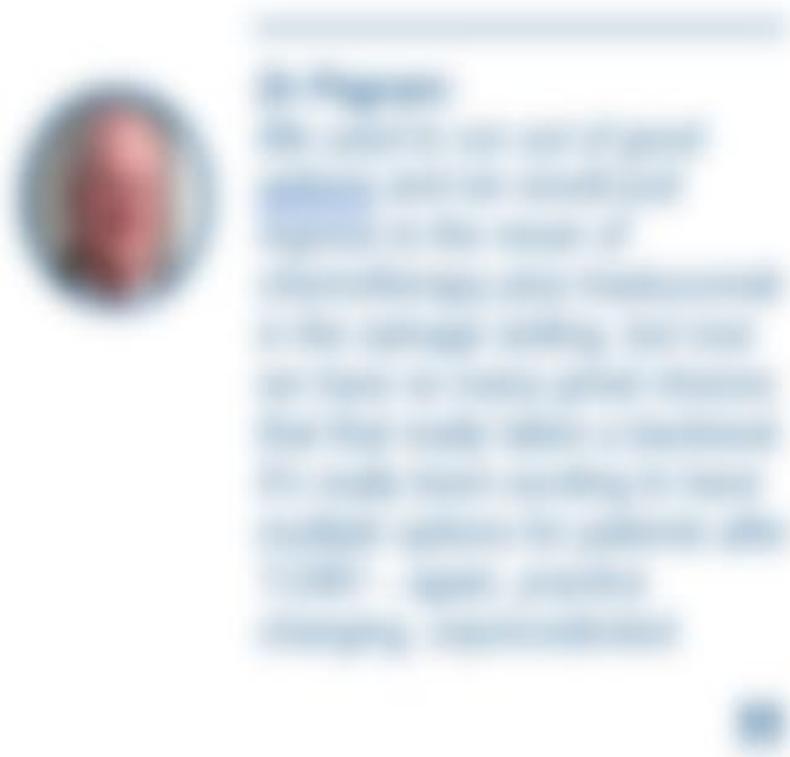
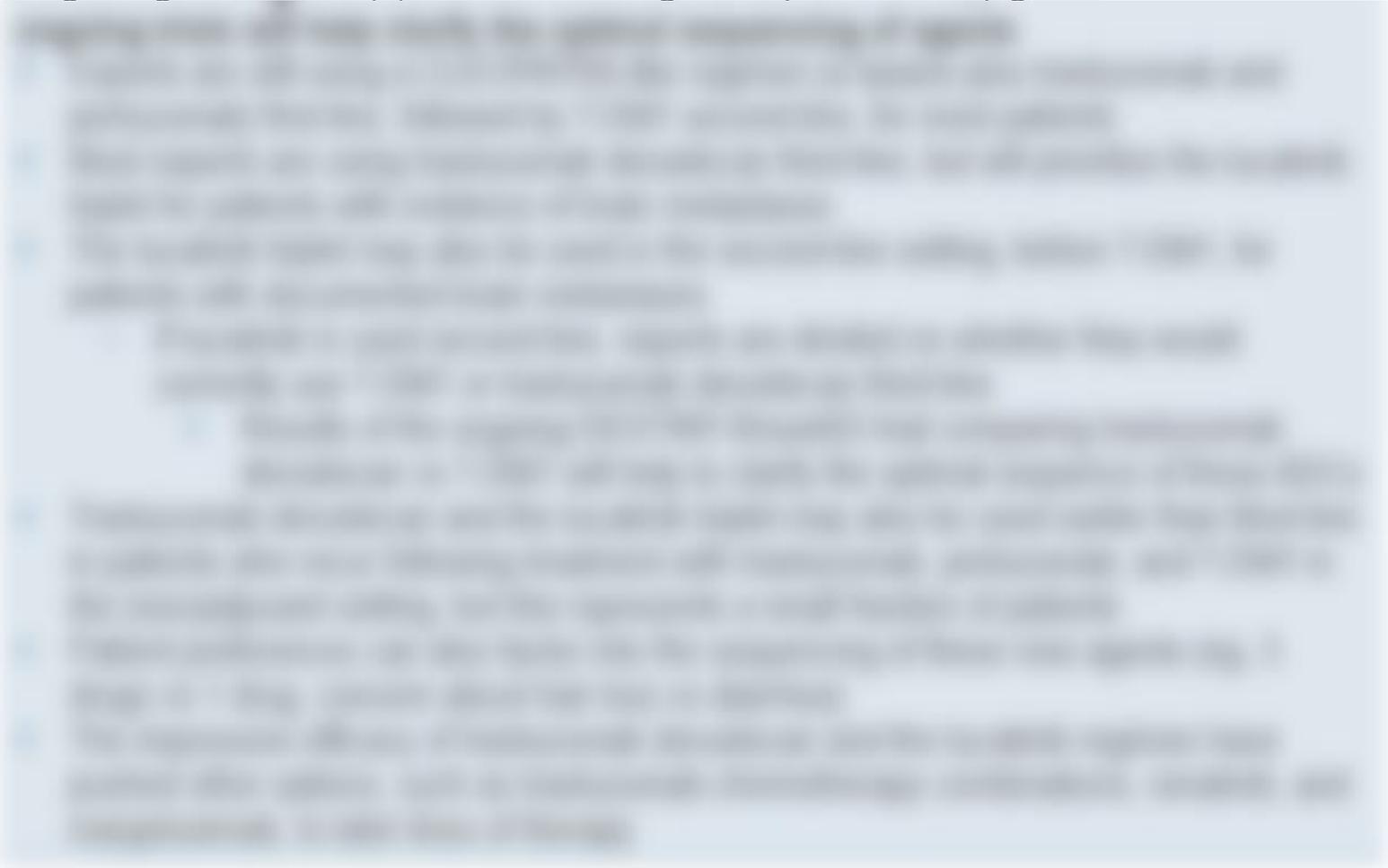
First-Line Immunotherapy in Metastatic NSCLC – Single Agent or Combination? (1/2)

The experts were asked about turnaround time for PD-L1 testing; most are able to obtain results within 1 to 2 days

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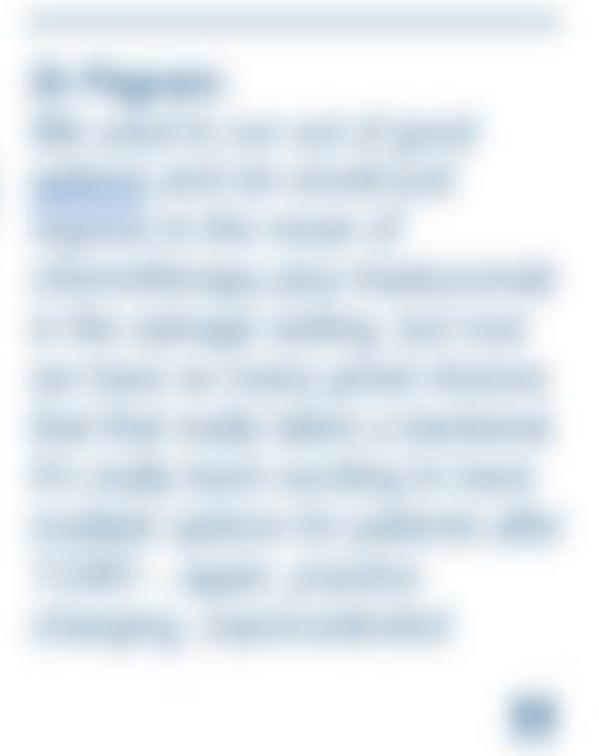
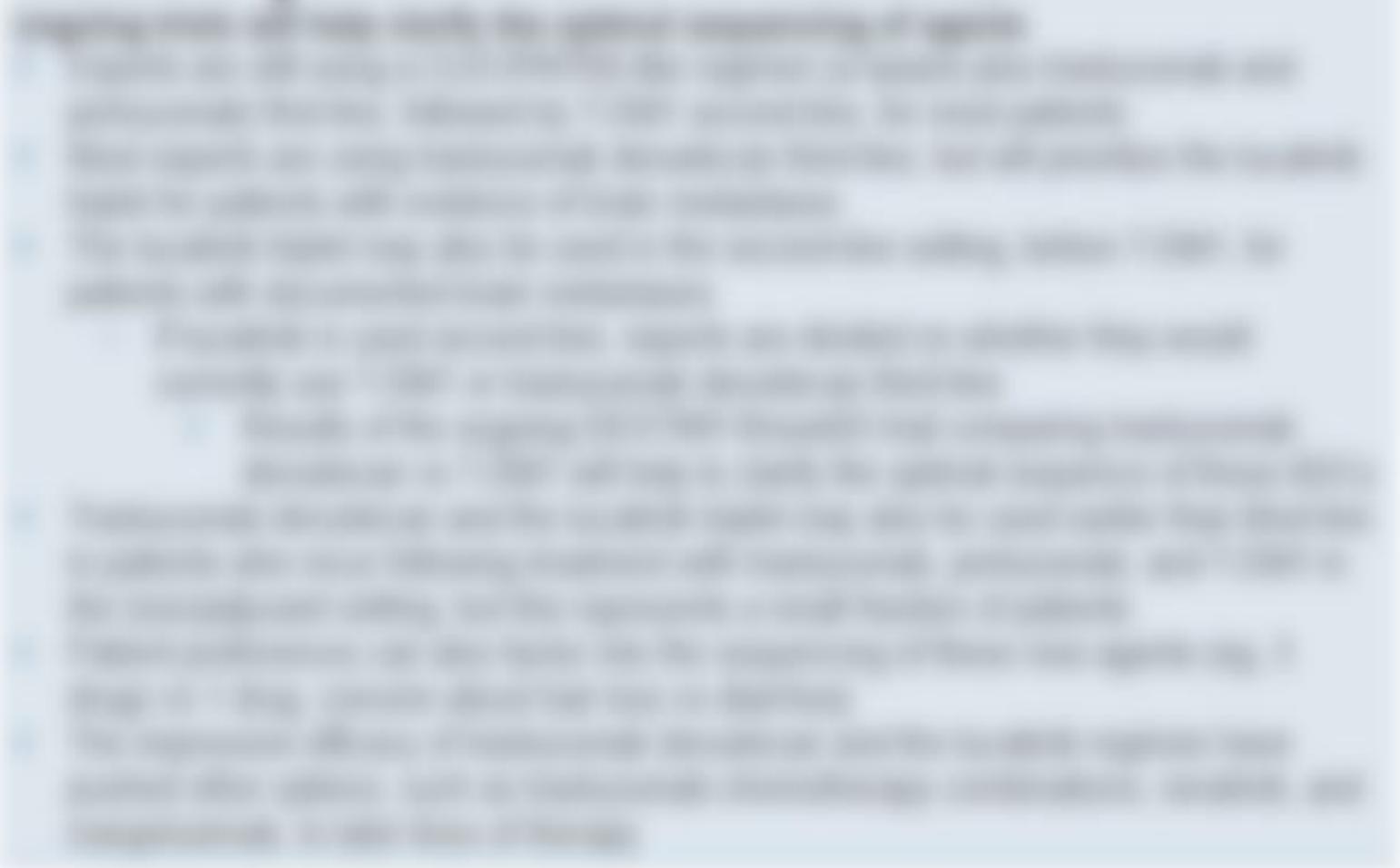
First-Line Immunotherapy in Metastatic NSCLC – Single Agent or Combination? (2/2)

Regarding the anti-PD-(L)1 antibodies being developed in China (eg,



Biomarkers for Immunotherapy – Making Sense of the Chaos

The experts do not think it is necessary to subdivide the PD-L1 $\geq 50\%$ population to isolate “very high expressors” (eg, $\geq 90\%$)



New Directions for Second-Line Therapy

Therapy post-chemotherapy/immunotherapy remains the biggest challenge in NSCLC

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Emergence of Immunotherapy and Bispecifics in SCLC

Regarding biomarkers in SCLC, the pathology expert mentioned that a major challenge is obtaining high-quality tissue; crush artifacts are common,

