APTITUDE HEALTH

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GLOBAL PERSPECTIVE ON LUNG CANCER IN 2019 AND BEYOND: EXPERT PERSPECTIVE AND STRATEGIC INSIGHTS: *FINAL REPORT*

BACKGROUND

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- On September 10, adjacent to the 2019 World Conference on Lung Cancer (WCLC), Aptitude Health brought together an international group of experts in lung cancer to attend a small expert roundtable

- The goal of the expert roundtable was to discuss the latest therapeutic developments and translational research in lung cancer treatment, apply these advances to dynamic and oftentimes individualized clinical decision making, and explore how emerging data will affect ongoing research, development of new compounds, and future treatment paradigms

AGENDA

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Time	Topic	Speaker/Moderator
17.00 – 17.10	Welcome, Introductions, and Meeting Objectives	Corey Langer, MD
17.10 – 17.20	Immunotherapy in Metastatic NSCLC	Solange Peters, MD, PhD
17.20 – 17.55	Discussion	
17.55 – 18.05	Immunotherapy in Potentially Curable (Stage I–III) NSCLC	Jamie Chaft, MD
18.05 – 18.30	Discussion	
18.30 – 18.40	Evolving Standards in Small Cell Lung Cancer	Antoinette Wozniak, MD
18.40 – 19.00	Discussion	
19.00 – 19.15	BREAK	
19.15 – 19.25	Extending Outcomes in *EGFR*-Mutated NSCLC	Roy Herbst, MD, PhD
19.25 – 19.55	Discussion	
19.55 – 20.05	Targeting *ALK* and Other Oncogenic Drivers	Enriqueta Felip, MD, PhD
20.05 – 20.30	Discussion	
20.30	Closing Remarks and Adjourn	Corey Langer, MD

FACULTY

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- Chair: Corey Langer, MD, FACP
  - University of Pennsylvania
- Benjamin Besse, MD, PhD
  - Gustave Roussy
- Jamie Chaft, MD
  - Memorial Sloan Kettering Cancer Center
- Enriqueta Felip, MD, PhD
  - Vall d'Hebron University Hospital
- Roy Herbst, MD, PhD
  - Yale Cancer Center
- Keith M. Kerr, FRCPath
  - Aberdeen University Medical School
- Solange Peters, MD, PhD
  - Lausanne University Hospital
- Ignacio I. Wistuba, MD
  - MD Anderson Cancer Center
- Antoinette Wozniak, MD
  - University of Pittsburgh Medical Center

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Key Takeaways

KEY TAKEAWAYS (1/4)

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> Immunotherapy in Metastatic Non-Small Cell Lung Cancer (NSCLC)

KEY TAKEAWAYS (2/4)

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- **Immunotherapy in Potentially Curable Stage I-III NSCLC**
  - The experts disagreed with the PACIFIC requirement in the European approval of durvalumab in stage II-IIIA NSCLC
  - Expert opinions is that a full year of consolidation durvalumab is difficult for patients to complete, which may not be anticipated from the advance event rate in the PACIFIC study
  - For patient with unresectable, stage III NSCLC that is not an ESCPR candidate, the experts would still generally offer consolidation durvalumab after chemoradiation therapy (CRT)
  - The experts thought that endpoints (e.g., major pathologic response (MPR), pathologic complete response (pCR)) needed to be validated for surrogacy and durable of immunotherapy in patients with resectable NSCLC
- **Evolving Standards in Small Cell Lung Cancer (SCLC)**
  - The experts did not support the CASPIAN trial to change first-line practice in early stage SCLC although the use of a regimen beyond chemotherapy could be welcomed
  - There was enthusiasm from the experts regarding lurbinectedin in patients with previously treated SCLC
  - Expert opinions on final biomarker research should be prioritized in SCLC

KEY TAKEAWAYS (3/4)

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> Extending Outcomes in *EGFR*-Mutated NSCLC

KEY TAKEAWAYS (4/4)

EPICS

> Targeting *ALK* and Other Oncogenic Drivers

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Immunotherapy in Metastatic NSCLC

IMMUNOTHERAPY IN METASTATIC NSCLC – OVERVIEW (1/2)

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- Dr Peters discussed ongoing developments in the application of immunotherapy-based
  - Expert opinion is that tumor mutational burden (TMB) is still not ready for routine clinical application as a selection biomarker for immunotherapy.
  - The experts were concerned that emerging immunotherapy biomarkers, such as CTRT, are tumor suppressors, and inactivation may not always be detected by next-generation sequencing (NGS) panels, which are focused on mutations.
  - It was thought by experts that combinations of markers may be the future of patient selection for immunotherapy.
  - The use of immunotherapy before receiving molecular tests was mentioned by experts as an issue, because if a patient is subsequently revealed to have an EGFR mutation, they may not derive benefit from the immunotherapy, and an EGFR tyrosine kinase inhibitor (TKI) cannot be started immediately due to potential toxic interactions with the immune checkpoint inhibitor.

IMMUNOTHERAPY IN METASTATIC NSCLC – OVERVIEW (2/2)

EPICS

- Other biomarkers appear to correlate with benefit from immunotherapy

IMMUNOTHERAPY IN METASTATIC NSCLC – DISCUSSION HIGHLIGHTS (1/6)

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- Expert opinion is that TMB is not ready for routine clinical use, although efforts are

IMMUNOTHERAPY IN METASTATIC NSCLC – DISCUSSION HIGHLIGHTS (2/6)

EPICS

- The experts thought that tissue-based testing was currently preferable to blood-based testing for
  - Expert opinion in that tumor mutational burden (TMB) is still not ready for routine clinical application as a selection biomarker for immunotherapy
  - The experts were concerned that emerging immunotherapy biomarkers, such as STK11, are tumor suppressors, and inactivation may not always be detected by next-generation sequencing (NGS) panels, which are focused on mutations
  - It was thought by experts that combinations of markers may be the future of patient selection for immunotherapy
  - The use of immunotherapy before receiving molecular tests was mentioned by experts as an issue, because if a patient is subsequently revealed to have an EGFR mutation, they may not derive benefit from the immunotherapy, and an EGFR tyrosine kinase inhibitor (TKI) cannot be started immediately, due to potential toxic interactions with the immune checkpoint inhibitor

IMMUNOTHERAPY IN METASTATIC NSCLC – DISCUSSION HIGHLIGHTS (3/6)

EPICS

- Regarding the role of *STK11* testing, none of the experts uses this in the clinic to make
  - Expert opinion is that tumor mutational burden (TMB) is still not ready for routine clinical application as a selection biomarker for immunotherapy
  - The experts were concerned that emerging immunotherapy biomarkers, such as STK11 and tumor suppressors, and mechanism may not always be detected by next-generation sequencing (NGS) panels, which are focused on mutations
  - It was thought by experts that combinations of markers may be the future of patient selection for immunotherapy
  - The use of immunotherapy before receiving molecular tests was mentioned by experts as an issue, because if a patient is subsequently revealed to have an EGFR mutation, they may not derive benefit from the immunotherapy, and an EGFR tyrosine kinase inhibitor (TKI) cannot be started immediately due to potential toxic interactions with the immune checkpoint inhibitor

IMMUNOTHERAPY IN METASTATIC NSCLC – DISCUSSION HIGHLIGHTS (4/6)

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- The experts discussed the press release regarding the NEPTUNE trial of

IMMUNOTHERAPY IN METASTATIC NSCLC – DISCUSSION HIGHLIGHTS (5/6)

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- Regarding the use of immunotherapy in patients with oncogene-driven, stage IV NSCLC,
  - [illegible]
  - [illegible]
  - [illegible]
  - [illegible]

IMMUNOTHERAPY IN METASTATIC NSCLC – DISCUSSION HIGHLIGHTS (6/6)

EPICS

- For patients with a high PD-L1 expression, the treatment decision is driven mainly by
  - [illegible]
  - [illegible]
  - [illegible]
  - [illegible]

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Immunotherapy in Potentially Curable (Stage I–III) NSCLC

IMMUNOTHERAPY IN POTENTIALLY CURABLE (STAGE I–III) NSCLC – OVERVIEW (1/2)

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- Dr Chaft discussed clinical research on immunotherapy in patients with stage I–III NSCLC

IMMUNOTHERAPY IN POTENTIALLY CURABLE (STAGE I–III) NSCLC – OVERVIEW (2/2)

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- Immunotherapy-based approaches have been investigated in patients with resectable disease

IMMUNOTHERAPY IN POTENTIALLY CURABLE (STAGE I–III) NSCLC – DISCUSSION HIGHLIGHTS (1/4)

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- Regarding the European approval of durvalumab in patients with stage III NSCLC, the

IMMUNOTHERAPY IN POTENTIALLY CURABLE (STAGE I–III) NSCLC – DISCUSSION HIGHLIGHTS (2/4)

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- A potential obstacle to PD-L1 testing mentioned by one of the pathology experts is that
  - Expert opinion is that tumor mutational burden (TMB) is still not ready for routine clinical application as a selection biomarker for immunotherapy
  - The experts were concerned that emerging immunotherapy biomarkers, such as CTRT, are tumor suppressors, and inactivation may not always be detected by next-generation sequencing (NGS) panels, which are focused on mutations
  - It was thought by experts that combinations of markers may be the future of patient selection for immunotherapy
  - The use of immunotherapy before receiving molecular tests was mentioned by experts as an issue, because if a patient is subsequently revealed to have an EGFR mutation, they may not derive benefit from the immunotherapy, and an EGFR tyrosine kinase inhibitor (TKI) cannot be started immediately, due to potential toxic interactions with the immune checkpoint inhibitor

IMMUNOTHERAPY IN POTENTIALLY CURABLE (STAGE I–III) NSCLC – DISCUSSION HIGHLIGHTS (3/4)

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- In patients with *EGFR* mutations, the experts would generally offer consolidation

IMMUNOTHERAPY IN POTENTIALLY CURABLE (STAGE I–III) NSCLC – DISCUSSION HIGHLIGHTS (4/4)

EPICS

- In terms of adding immunotherapy to CRT, expert opinion is that this can be carried out,
  - [illegible]
  - [illegible]
  - [illegible]
  - [illegible]

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Evolving Standards in Small Cell Lung Cancer

EVOLVING STANDARDS IN SMALL CELL LUNG CANCER – OVERVIEW (1/2)

- Dr Wozniak presented an overview of the developing therapeutic landscape in SCLC
  - [illegible]
  - [illegible]
  - [illegible]
  - [illegible]

EVOLVING STANDARDS IN SMALL CELL LUNG CANCER – OVERVIEW (2/2)

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- With the establishment of immunotherapy in the first-line setting, new mechanisms of

EVOLVING STANDARDS IN SMALL CELL LUNG CANCER – DISCUSSION HIGHLIGHTS (1/3)

- The experts generally did not expect the results of the CASPIAN trial to change practice in

EVOLVING STANDARDS IN SMALL CELL LUNG CANCER – DISCUSSION HIGHLIGHTS (2/3)

- For patients with previously treated SCLC, expert opinion is that lurbinectedin is a

EVOLVING STANDARDS IN SMALL CELL LUNG CANCER – DISCUSSION HIGHLIGHTS (3/3)

- One of the pathology experts stressed the need for establishing biomarkers in SCLC;
  - Expert opinion is that tumor mutational burden (TMB) is still not ready for routine clinical application as a predictive biomarker for immunotherapy.
  - The experts were concerned that emerging immunotherapy biomarkers, such as CTRT, are tumor suppressors, and inactivation may not always be detected by next-generation sequencing (NGS) panels, which are focused on mutations.
  - It was thought by experts that combinations of markers may be the future of patient selection for immunotherapy.
  - The use of immunotherapy before receiving molecular tests was mentioned by experts as an issue, because if a patient is subsequently revealed to have an EGFR mutation, they may not derive benefit from the immunotherapy, and an EGFR tyrosine kinase inhibitor (TKI) cannot be started immediately, due to potential toxic interactions with the immune checkpoint inhibitor.

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Extending Outcomes in *EGFR*-Mutated NSCLC

EXTENDING OUTCOMES IN *EGFR*-MUTATED NSCLC – OVERVIEW (1/2)

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- Dr Herbst reviewed developments in the management of patients with *EGFR* mutation-
  - [illegible]
  - [illegible]
  - [illegible]
  - [illegible]

EXTENDING OUTCOMES IN *EGFR*-MUTATED NSCLC – OVERVIEW (2/2)

EPICS

- Mechanisms of resistance to EGFR TKIs include upregulation of *MET*, thus MET inhibitors

EXTENDING OUTCOMES IN *EGFR*-MUTATED NSCLC – DISCUSSION HIGHLIGHTS (1/3)

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- The experts generally agreed that single-agent osimertinib is the first-line therapy of

EXTENDING OUTCOMES IN *EGFR*-MUTATED NSCLC – DISCUSSION HIGHLIGHTS (2/3)

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- Upon progression on osimertinib, chemotherapy is a common approach used by the

EXTENDING OUTCOMES IN *EGFR*-MUTATED NSCLC – DISCUSSION HIGHLIGHTS (3/3)

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- For patients with an *EGFR* exon 20 mutation, chemotherapy/immunotherapy is the

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Targeting *ALK* and Other Oncogenic Drivers

TARGETING *ALK* AND OTHER ONCOGENIC DRIVERS – OVERVIEW (1/2)

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- Dr Felip addressed efforts to target oncogenic drivers beyond *EGFR* in NSCLC
  - Expert opinion is that tumor mutational burden (TMB) is still not ready for routine clinical application as a selection biomarker for immunotherapy
  - The experts were concerned that emerging immunotherapy biomarkers, such as CPS/TC, and tumor suppressors, and mechanism may not always be detected by next-generation sequencing (NGS) panels, which are focused on mutations
  - It was thought by experts that combinations of markers may be the future of patient selection for immunotherapy
  - The use of immunotherapy before receiving molecular tests was mentioned by experts as an issue, because if a patient is subsequently revealed to have an *EGFR* mutation, they may not derive benefit from the immunotherapy, and an *EGFR* tyrosine kinase inhibitor (TKI) cannot be started immediately, due to potential toxic interactions with the immune checkpoint inhibitor

TARGETING *ALK* AND OTHER ONCOGENIC DRIVERS – OVERVIEW (2/2)

EPICS

- Dr Felip addressed efforts to target oncogenic drivers beyond *EGFR* in NSCLC (cont'd)

TARGETING *ALK* AND OTHER ONCOGENIC DRIVERS – DISCUSSION HIGHLIGHTS (1/3)

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- The experts agreed that the *KRAS* G12C inhibitor AMC 510 was active, with few primary

TARGETING *ALK* AND OTHER ONCOGENIC DRIVERS – DISCUSSION HIGHLIGHTS (2/3)

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- The experts thought that the activity of the RET inhibitors selpercatinib (formerly LOXO-

TARGETING *ALK* AND OTHER ONCOGENIC DRIVERS – DISCUSSION HIGHLIGHTS (3/3)

- According to the pathology experts, there still remain several barriers to obtaining rapid testing

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Key Takeaways and Strategic Recommendations

KEY TAKEAWAYS AND STRATEGIC RECOMMENDATIONS (1/8)

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KEY TAKEAWAYS AND STRATEGIC RECOMMENDATIONS (2/8)

EPICS

KEY TAKEAWAYS AND STRATEGIC RECOMMENDATIONS (3/8)

EPICS

KEY TAKEAWAYS AND STRATEGIC RECOMMENDATIONS (4/8)

EPICS

KEY TAKEAWAYS AND STRATEGIC RECOMMENDATIONS (5/8)

EPICS

KEY TAKEAWAYS AND STRATEGIC RECOMMENDATIONS (6/8)

EPICS

KEY TAKEAWAYS AND STRATEGIC RECOMMENDATIONS (7/8)

EPICS

KEY TAKEAWAYS AND STRATEGIC RECOMMENDATIONS (8/8)

EPICS