












EPICS

Conference Coverage: ASCO 2023 – Focus on Lung Cancer

Full Report

June 16, 2023

Content	Slide
Meeting Snapshot	3 
Faculty Panel	4 
Meeting Agenda	5 
Key Insights and Strategic Recommendations	6 
Immunotherapy in Resectable NSCLC	13 
Updates in Stage IV NSCLC	20 
<i>EGFR</i> Mutations	29 
Other Oncogenic Drivers	39 
Small Cell Lung Cancer	50 

EPICS

VIRTUAL CLOSED-DOOR ROUNDTABLE



DATE:
June 16, 2023



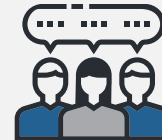
**DISEASE STATE AND
DATA PRESENTATIONS**
by key experts



INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations



PANEL: Key experts in
lung cancer
> 5 from US
> 3 from Europe



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

Panel Consisting of 5 US and 3 European Lung Cancer Experts

Marina Chiara Garassino, MD
University of Chicago



Lynette Sholl, MD
Harvard Medical School



CHAIR:

Corey J. Langer, MD, FACP
University of Pennsylvania



Roy Herbst, MD, PhD
Yale Cancer Center



Benjamin Besse, MD, PhD
Institute Gustave Roussy



Solange Peters, MD, PhD
University Hospital of Lausanne



Mark Socinski, MD
AdventHealth Cancer Institute



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



Meeting Agenda

Time (EDT)	Topic	Speaker/Moderator
12.00 PM – 12.05 PM	Welcome and Introductions	Corey J. Langer, MD, FACP
12.05 PM – 12.20 PM	Immunotherapy in Resectable NSCLC	Marina Chiara Garassino, MD
12.20 PM – 12.50 PM	Discussion	All faculty
12.50 PM – 1.00 PM	Updates in Stage IV NSCLC	Solange Peters, MD, PhD
1.00 PM – 1.20 PM	Discussion	All faculty
1.20 PM – 1.30 PM	EGFR Mutations	Roy Herbst, MD, PhD
1.30 PM – 1.45 PM	Discussion	All faculty
1.45 PM – 1.55 PM	Break	
1.55 PM – 2.10 PM	Other Oncogenic Drivers	Enriqueta Felip, MD, PhD; Mark Socinski, MD
2.10 PM – 2.30 PM	Discussion	All faculty
2.30 PM – 2.40 PM	Small Cell Lung Cancer	Benjamin Besse, MD, PhD
2.40 PM – 2.55 PM	Discussion	All faculty
2.55 PM – 3.00 PM	Wrap-up Comments and Adjourn	Corey J. Langer, MD, FACP

EPICS

Congress Highlights

Immunotherapy in Resectable NSCLC

AEGEAN: A phase 3 trial of neoadjuvant durvalumab + chemotherapy followed by adjuvant durvalumab in patients with resectable NSCLC

Heymach JV, et al. AACR 2023, Abstract CT005

STUDY POPULATION

- > Resectable, stage IIA–IIIB (N2) NSCLC by AJCC 8th edition

EVENT-FREE SURVIVAL

Figure 1: Event-Free Survival (EFS) in the Overall Population (N=200)



Figure 2: Response Rate (RR) in the Overall Population (N=200)



KEYNOTE-671: Randomized, double-blind, phase 3 study of pembrolizumab or placebo plus platinum-based chemotherapy followed by resection and pembrolizumab or placebo for early stage NSCLC

Wakelee HA, et al. ASCO 2023, Abstract LBA100

STUDY POPULATION

> Resectable, stage II–IIIB (N2) NSCLC by AJCC 8th edition

EVENT-FREE SURVIVAL

STUDY POPULATION

177 patients were enrolled in the study, with 100 patients in the pembrolizumab group and 77 patients in the placebo group. All patients had stage II–IIIB (N2) NSCLC by AJCC 8th edition. The median age was 65 years (range, 45–85 years). The majority of patients (80%) were male. The median time from diagnosis to enrollment was 1.1 years (range, 0–3.5 years). All patients had undergone resection of the primary tumor and had no evidence of disease at the time of randomization. The median time from randomization to resection was 1.1 months (range, 0–3.5 months). All patients received platinum-based chemotherapy (paclitaxel, carboplatin, or cisplatin) as part of their study treatment.

RESULTS

177 patients were enrolled in the study, with 100 patients in the pembrolizumab group and 77 patients in the placebo group. All patients had stage II–IIIB (N2) NSCLC by AJCC 8th edition. The median age was 65 years (range, 45–85 years). The majority of patients (80%) were male. The median time from diagnosis to enrollment was 1.1 years (range, 0–3.5 years). All patients had undergone resection of the primary tumor and had no evidence of disease at the time of randomization. The median time from randomization to resection was 1.1 months (range, 0–3.5 months). All patients received platinum-based chemotherapy (paclitaxel, carboplatin, or cisplatin) as part of their study treatment.

CONCLUSIONS

Combining pembrolizumab with platinum-based chemotherapy followed by resection and pembrolizumab or placebo significantly improved event-free survival in patients with resectable, stage II–IIIB (N2) NSCLC.



Perioperative toripalimab + platinum-doublet chemotherapy vs chemotherapy in resectable stage II/III non-small cell lung cancer (NSCLC): Interim event-free survival (EFS) analysis of the phase III NEOTORCH study

Lu S et al. ASCO 2023, Abstract 8501

STUDY POPULATION

> Resectable, stage II–III NSCLC

EVENT-FREE SURVIVAL

STUDY POPULATION

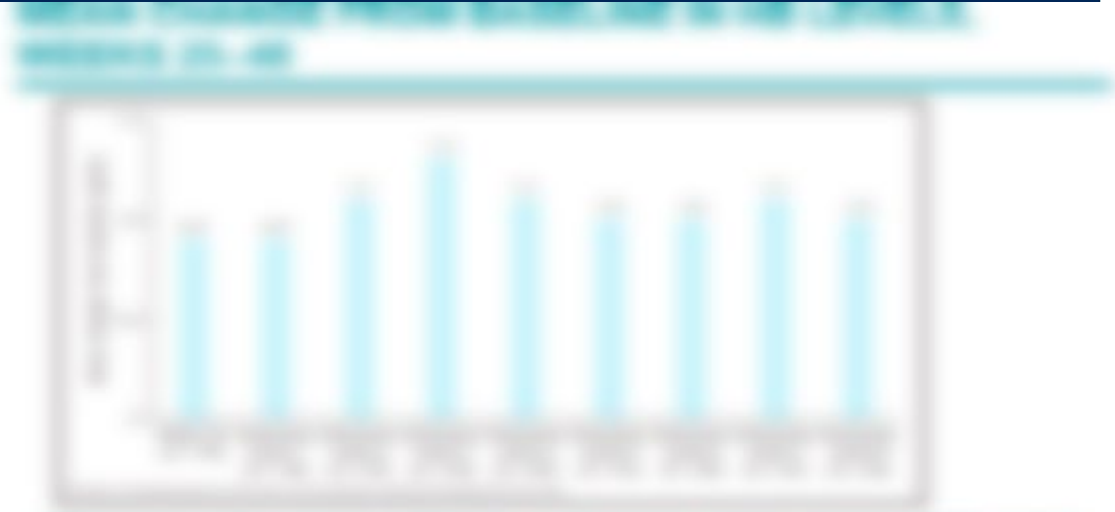
1700 patients with resectable stage II–III NSCLC were randomized to receive either toripalimab + platinum-doublet chemotherapy (n = 850) or platinum-doublet chemotherapy (n = 850). The primary endpoint was event-free survival (EFS), defined as the time from random assignment to death due to any cause, relapse, or progression. Secondary endpoints included overall survival (OS), progression-free survival (PFS), and quality of life. The study is ongoing, and patients are being followed up.

RESULTS

At the interim analysis, 1700 patients were included in the primary endpoint analysis. The median follow-up was 12.1 months. The EFS rate was significantly higher in the toripalimab + platinum-doublet chemotherapy group compared with the platinum-doublet chemotherapy group (P < .001).

CONCLUSIONS

Perioperative toripalimab + platinum-doublet chemotherapy significantly improved EFS compared with platinum-doublet chemotherapy in resectable stage II–III NSCLC.



EPICS

Key Insights

Immunotherapy in Resectable NSCLC

Immunotherapy in Resectable NSCLC (1/2)

The experts view perioperative immunotherapy (ie, immunotherapy both pre- and postsurgery) positively, although they recognize that

Supporting trials will help clarify the optimal sequencing of agents

- 1. Trials are underway to evaluate the sequence of immune checkpoint inhibitors and conventional therapy, followed by TDMT, compared to conventional therapy.
- 2. These studies are using conventional chemotherapy regimens, but will evaluate the overall impact on patients with evidence of local recurrence.
- 3. The overall impact may also be used in the adjuvant setting, before TDMT, in patients with microvascular invasion.
- 4. Considered a local recurrence, experts are divided on whether they would currently use TDMT in microvascular invasion.
 - 5. Results of the ongoing IMpower010 trial comparing conventional chemotherapy to TDMT will help to clarify the optimal sequencing of these agents.
- 6. Conventional chemotherapy and the overall impact may also be used before first recurrence in patients who were following treatment with conventional chemotherapy and TDMT in the adjuvant setting, but this represents a small fraction of patients.
- 7. Future publications can also focus on the sequencing of these two agents (eg, 1 drug or 1 drug, versus what has been in clinical).
- 8. The comparative efficacy of conventional chemotherapy and the overall impact have proven other options, such as conventional chemotherapy combinations, steroids, and immunotherapy, is still under review.



Dr. [Name]
The overall impact of immunotherapy is still unclear, but we are seeing positive results in the adjuvant setting. We are also seeing positive results in the overall impact on patients with evidence of local recurrence. We are also seeing positive results in the overall impact on patients with evidence of local recurrence. We are also seeing positive results in the overall impact on patients with evidence of local recurrence.



Immunotherapy in Resectable NSCLC (2/2)

For patients who achieve a pCR after the neoadjuvant component in a perioperative approach, expert opinion is that there are

[Blurred text block]

[Blurred text block]

[Blurred text block]

EPICS

Congress Highlights

Updates in Stage IV NSCLC

Updates on Abstract 397600: ARC-7: Randomized phase 2 study of domvanalimab + zimberelimab ± etrumadenant versus zimberelimab in first-line, metastatic, PD-L1-high non-small cell lung cancer (NSCLC)

Johnson ML, et al. ASCO 2023, Abstract 397600

STUDY POPULATION

> Treatment-naive, metastatic NSCLC; PD-L1 ≥50%

PROGRESSION-FREE SURVIVAL

PROGRESSION-FREE SURVIVAL (PFS) AT 12 MONTHS



RESPONSE RATES AT 12 MONTHS



Safety, pharmacokinetics (PK), pharmacodynamics (PD) and preliminary efficacy of AZD2936, a bispecific antibody targeting PD-1 and TIGIT, in checkpoint inhibitor (CPI)-experienced advanced/metastatic non-small-cell lung cancer (NSCLC): First report of ARTEMIDE-01

Rohrberg KS et al. ASCO 2023, Abstract 9050

STUDY POPULATION

> Stage III unresectable/IV NSCLC; PD-L1 $\geq 1\%$

BEST PERCENTAGE CHANGE IN LESION SIZE



Safety and clinical activity of target-preserving anti-CTLA-4 antibody ONC-392 as monotherapy in NSCLC patients who progressed on PD(L)1-targeted immunotherapy

He K, et al. ASCO 2023, Abstract 9024

STUDY POPULATION

> Pts with metastatic NSCLC, no targetable mutations; progressed

BEST PERCENTAGE CHANGE IN LESION SIZE



TROPION-Lung02: Datopotamab deruxtecan (Dato-DXd) plus pembrolizumab (pembro) with or without platinum chemotherapy (Pt-CT) in advanced non-small cell lung cancer (aNSCLC)

Goto Y et al. ASCO 2023, Abstract 9004

STUDY POPULATION

> Pts with advanced/metastatic NSCLC and ≤2 prior therapies

BEST PERCENTAGE TUMOR CHANGE FROM BASELINE



Tumor Treating Field (TTFields) therapy with standard of care (SOC) in metastatic non-small cell lung cancer (mNSCLC) following platinum failure: Randomized, phase 3 LUNAR study

Leal T, et al. ASCO 2023, Abstract LBA9005

STUDY POPULATION

> Pts with metastatic NSCLC progressing on or after platinum-

OS IN PATIENTS RECEIVING IMMUNOTHERAPY + TTF

OS IN PATIENTS RECEIVING IMMUNOTHERAPY + TTF



RESPONSE RATES IN PATIENTS RECEIVING IMMUNOTHERAPY + TTF



EPICS

Key Insights

Updates in Stage IV NSCLC

Updates in Stage IV NSCLC (1/2)

The experts believe the phase III LUNAR trial evaluating Tumor Treating Fields (TTF) therapy showed a positive OS signal in

Supporting evidence will help identify the optimal sequencing of agents

- 1. Tumor Treating Fields (TTF) and chemotherapy (CT) are being evaluated in the treatment of advanced-stage non-small cell lung cancer (NSCLC). TTF is a non-invasive, non-systemic therapy that uses electric fields to disrupt cancer cell growth. TTF is being evaluated in combination with CT in the LUNAR trial.
- 2. The LUNAR trial is a phase III, randomized, controlled trial that will evaluate the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.
- 3. The LUNAR trial is a phase III, randomized, controlled trial that will evaluate the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.
- 4. The LUNAR trial is a phase III, randomized, controlled trial that will evaluate the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.
- 5. The LUNAR trial is a phase III, randomized, controlled trial that will evaluate the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.
- 6. The LUNAR trial is a phase III, randomized, controlled trial that will evaluate the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.
- 7. The LUNAR trial is a phase III, randomized, controlled trial that will evaluate the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.
- 8. The LUNAR trial is a phase III, randomized, controlled trial that will evaluate the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.



...the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.

...the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.

...the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.

...the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.

...the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.

...the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.

...the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.

...the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.

...the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.

...the overall survival (OS) of patients with advanced-stage NSCLC who receive TTF in combination with CT compared to CT alone.

Updates in Stage IV NSCLC (2/2)

Expert opinion is that TIGIT is a valid therapeutic target in NSCLC, but clinical trials with different anti-TIGIT agents so far have yielded

[Blurred content]

[Blurred content]

EPICS

Congress Highlights

EGFR Mutations

Overall survival analysis from the ADAURA trial of adjuvant osimertinib in patients with resected EGFR-mutated (EGFRm) stage IB–IIIA non-small cell lung cancer (NSCLC)

Herbst RS, et al. ASCO 2023, Abstract LBA3

STUDY POPULATION

- > Pts with completely resected, stage IB–IIIA NSCLC and an *EGFR* exon 19 deletion or L858R mutation

OVERALL SURVIVAL (STAGE II/IIIA)

- Adjuvant osimertinib demonstrated a statistically and clinically significant improvement in OS vs placebo in the



BLU-945 monotherapy and in combination with osimertinib (OSI) in previously treated patients with advanced *EGFR*-mutant (*EGFRm*) NSCLC in the phase 1/2 SYMPHONY study

Elamin YY, et al. ASCO 2023, Abstract 9011

STUDY POPULATION

- > Pts with metastatic, *EGFR*-mutated NSCLC and at least 1 T790M-targeting *EGFR* TKI; PD on osimertinib as last therapy

TUMOR RESPONSE: BLU-945 + OSIMERTINIB



Randomized phase 3 study of first-line AZD3759 (zorifertinib) versus gefitinib or erlotinib in EGFR-mutant (*EGFRm*⁺) non-small-cell lung cancer (NSCLC) with central nervous system (CNS) metastasis

Wu YL, et al. ASCO 2023, Abstract 9001

STUDY POPULATION

> Pts with advanced *EGFR*-mutated NSCLC (exon 19 del or L858R)

PROGRESSION-FREE SURVIVAL

STUDY POPULATION

1. 1000 pts with advanced *EGFR*-mutated NSCLC (exon 19 del or L858R) were randomized to AZD3759 (n=500) or gefitinib/erlotinib (n=500). The study was stratified by CNS metastasis status (CNS+ vs CNS-). The primary endpoint is progression-free survival (PFS) in the CNS+ population. Secondary endpoints include overall survival (OS), quality of life (QoL), and adverse events (AE). The study is ongoing and will continue to enroll patients through 2024.

RESULTS

1. In the CNS+ population, AZD3759 significantly improved PFS compared to gefitinib/erlotinib (HR: 0.75, 95% CI: 0.60-0.95, p=0.02). OS was not significantly different between groups (HR: 1.05, 95% CI: 0.85-1.30, p=0.65). QoL was similar between groups. AE were similar between groups.

CONCLUSIONS

1. AZD3759 significantly improved PFS compared to gefitinib/erlotinib in the CNS+ population. OS was not significantly different between groups. QoL was similar between groups. AE were similar between groups.



BL-B01D1, a first-in-class EGFRxHER3 bispecific antibody-drug conjugate (ADC), in patients with locally advanced or metastatic solid tumor: Results from a first-in-human phase 1 study

Zhang L, et al. ASCO 2023, Abstract 3001

STUDY POPULATION

> Pts with advanced solid tumors; experienced failure of standard

TUMOR RESPONSE IN EGFR-MUTATED NSCLC



SKB264 (TROP2-ADC) for the treatment of patients with advanced NSCLC: Efficacy and safety data from a phase 2 study

Fang W, et al. ASCO 2023, Abstract 9114

STUDY POPULATION

> Pts with advanced solid tumors

TUMOR RESPONSE



STUDY POPULATION

100 patients with advanced solid tumors, including NSCLC, were enrolled in the study. The majority of patients had NSCLC, with a median age of 65 years. The study population was diverse in terms of ethnicity and gender. All patients had previously received systemic therapy for their advanced disease. The study was conducted in a multicenter setting across several countries. The primary endpoint of the study was overall survival. Secondary endpoints included objective response rate, progression-free survival, and quality of life. The study was designed as a phase 2, open-label, multicenter trial. Patients were randomized to receive SKB264 or a placebo. The study was conducted in accordance with the principles of the Declaration of Helsinki. The study was approved by the local ethics committees at all participating sites. The study was registered at ClinicalTrials.gov.

RESULTS

The study population was well-tolerated. The most common adverse events were fatigue, nausea, and diarrhea. The overall survival was significantly higher in the SKB264 group compared to the placebo group. The objective response rate was also significantly higher in the SKB264 group. The progression-free survival was also significantly higher in the SKB264 group. The quality of life was significantly better in the SKB264 group compared to the placebo group.

CONCLUSIONS

SKB264 (TROP2-ADC) is a promising treatment for patients with advanced NSCLC. The study demonstrated that SKB264 is well-tolerated and significantly improves overall survival, objective response rate, progression-free survival, and quality of life compared to placebo. Further studies are needed to confirm these findings in a larger, randomized, phase 3 trial.

Sunvozertinib for the treatment of NSCLC with EGFR Exon20 insertion mutations: The first pivotal study results

Wang M, et al. ASCO 2023, Abstract 9002

STUDY POPULATION

- > Advanced NSCLC with an *EGFR* exon 20 insertion mutation and 1–3 prior lines of therapy, including platinum-based chemotherapy

ANTITUMOR ACTIVITY BY MUTATION SUBTYPE



EPICS

Key Insights

EGFR Mutations

Regarding molecular testing of patients who progress on osimertinib, the pathology expert mentioned that their institution uses a

- 1. Testing for EGFR mutations in the region of exon 20 (T790M) and exon 21 (L858R) is recommended for all patients.
- 2. The results of the testing for EGFR mutations in the region of exon 20 (T790M) and exon 21 (L858R) can be used to guide treatment decisions for patients with EGFR mutations.
- 3. The results of the testing for EGFR mutations in the region of exon 20 (T790M) and exon 21 (L858R) can also be used to guide treatment decisions for patients with EGFR mutations.
- 4. The results of the testing for EGFR mutations in the region of exon 20 (T790M) and exon 21 (L858R) can also be used to guide treatment decisions for patients with EGFR mutations.
- 5. The results of the testing for EGFR mutations in the region of exon 20 (T790M) and exon 21 (L858R) can also be used to guide treatment decisions for patients with EGFR mutations.
- 6. The results of the testing for EGFR mutations in the region of exon 20 (T790M) and exon 21 (L858R) can also be used to guide treatment decisions for patients with EGFR mutations.
- 7. The results of the testing for EGFR mutations in the region of exon 20 (T790M) and exon 21 (L858R) can also be used to guide treatment decisions for patients with EGFR mutations.
- 8. The results of the testing for EGFR mutations in the region of exon 20 (T790M) and exon 21 (L858R) can also be used to guide treatment decisions for patients with EGFR mutations.



pathology expert mentioned that their institution uses a

Testing for EGFR mutations in the region of exon 20 (T790M) and exon 21 (L858R) is recommended for all patients.

The results of the testing for EGFR mutations in the region of exon 20 (T790M) and exon 21 (L858R) can be used to guide treatment decisions for patients with EGFR mutations.

The results of the testing for EGFR mutations in the region of exon 20 (T790M) and exon 21 (L858R) can also be used to guide treatment decisions for patients with EGFR mutations.

The results of the testing for EGFR mutations in the region of exon 20 (T790M) and exon 21 (L858R) can also be used to guide treatment decisions for patients with EGFR mutations.

The results of the testing for EGFR mutations in the region of exon 20 (T790M) and exon 21 (L858R) can also be used to guide treatment decisions for patients with EGFR mutations.

The results of the testing for EGFR mutations in the region of exon 20 (T790M) and exon 21 (L858R) can also be used to guide treatment decisions for patients with EGFR mutations.

The results of the testing for EGFR mutations in the region of exon 20 (T790M) and exon 21 (L858R) can also be used to guide treatment decisions for patients with EGFR mutations.

Regarding efforts to improve on first-line osimertinib monotherapy in metastatic disease, such as combination regimens or new

[Blurred content]

[Blurred content]

EPICS

Congress Highlights

Other Oncogenic Drivers

Adagrasib (MRTX849) in patients with advanced/metastatic KRASG12C-mutated non-small cell lung cancer (NSCLC): Preliminary analysis of mutation allele frequency

Janne PA, et al. ELCC 2023, Abstract 8MO

STUDY POPULATION

- > Pts with advanced NSCLC and a *KRAS* G12C mutation
- > Prior immunotherapy and chemotherapy

PROGRESSION-FREE SURVIVAL BY MAFC

Progression-Free Survival (n=36)^b



The primary endpoint analysis of SCARLET study: A single-arm, phase II study of sotorasib plus carboplatin-pemetrexed in patients with advanced non-squamous, non-small cell lung cancer with KRAS G12C mutation (WJOG14821L)

Sakata S, et al. ASCO 2023, Abstract 9006

STUDY POPULATION

> Pts with advanced NSCLC and a KRAS G12C mutation

TUMOR RESPONSE

ORR 39.0% (95% CI 30.0-47.0%)



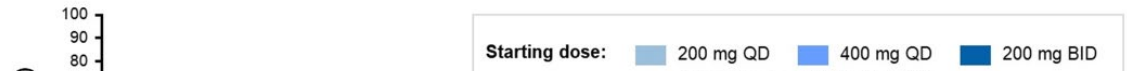
KonTRAsT-01 update: Safety and efficacy of JDQ443 in *KRAS* G12C-mutated solid tumors including non-small cell lung cancer (NSCLC)

Cassier PA, et al. ASCO 2023, Abstract 9007

STUDY POPULATION

> Pts with solid tumors and a *KRAS* G12C mutation

TUMOR RESPONSE



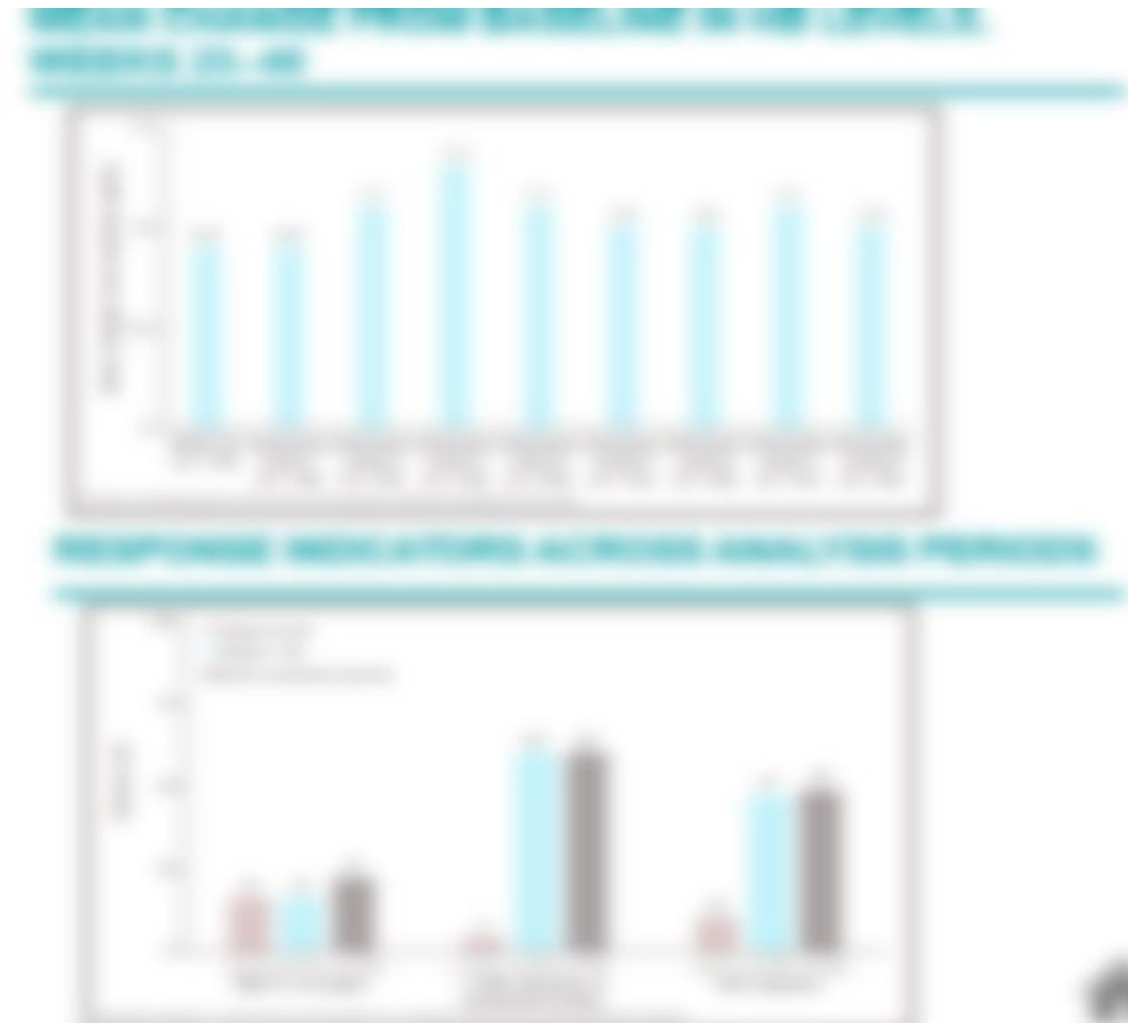
Biomarker subgroup analyses of CodeBreakK 200, a phase 3 trial of sotorasib versus (vs) docetaxel in patients (pts) with pretreated *KRAS* G12C-mutated advanced non-small cell lung cancer (NSCLC)

Skoulidis F, et al. ASCO 2023, Abstract 9008

STUDY POPULATION

> Pts with advanced NSCLC and a *KRAS* G12C mutation

PROGRESSION-FREE SURVIVAL BY COALTERATION



Intracranial efficacy of sotorasib versus docetaxel in pretreated *KRAS* G12C-mutated advanced non-small cell lung cancer (NSCLC): Practice-informing data from a global, phase 3, randomized, controlled trial (RCT)

Dingemans AMC, et al. ASCO 2023, Abstract LBA9016

STUDY POPULATION

> Pts with advanced NSCLC and a *KRAS* G12C mutation

CNS PROGRESSION-FREE SURVIVAL



Efficacy and safety of encorafenib (enco) plus binimetinib (bini) in patients with *BRAF*^{V600E} metastatic non-small cell lung cancer (NSCLC) from the phase 2 PHAROS study

Riely GJ, et al. ASCO 2023, Abstract 9018

STUDY POPULATION

> Pts with advanced NSCLC and a *BRAF* V600E mutation

TUMOR RESPONSE

STUDY POPULATION

1. 100 patients with advanced NSCLC and a *BRAF* V600E mutation were enrolled in the PHAROS study. The study was a phase 2, open-label, randomized controlled trial comparing the combination of encorafenib plus binimetinib (encorafenib/bini) to the combination of encorafenib plus trametinib (encorafenib/trametinib). The primary endpoint was overall survival (OS) at 12 weeks. The secondary endpoints were progression-free survival (PFS), objective response rate (ORR), and adverse events (AE). The study was conducted in a multicenter setting across several countries. The median age of the patients was 68 years, and the majority were male. The most common histology was adenocarcinoma. The median time from diagnosis to enrollment was 12 months. The study was terminated early due to a significant difference in OS between the two groups.

RESULTS

1. The median OS at 12 weeks was significantly longer in the encorafenib/bini group compared to the encorafenib/trametinib group. The median OS was 12.5 weeks in the encorafenib/bini group versus 8.5 weeks in the encorafenib/trametinib group. The difference was statistically significant (p < 0.001). The ORR was also significantly higher in the encorafenib/bini group (35%) compared to the encorafenib/trametinib group (25%). The most common AEs were diarrhea, rash, and fatigue, which were generally mild to moderate in severity.

CONCLUSIONS

1. The combination of encorafenib plus binimetinib significantly improved OS and ORR compared to encorafenib plus trametinib in patients with advanced NSCLC and a *BRAF* V600E mutation. This combination represents a promising treatment option for this patient population.



FAK inhibition with novel FAK/ALK inhibitor APG-2449 could overcome resistance in NSCLC patients who are resistant to second-generation ALK inhibitors

Ma Y, et al. ASCO 2023, Abstract 9015

STUDY POPULATION

> Pts with solid tumors and an *ALK* or *ROS1* fusion

TUMOR RESPONSE, SECOND-GEN ALK TKI RESISTANT

75% PR



RESPONSE, METASTASIS, AND TOXICITY ANALYSIS PER GROUP



EPICS

Key Insights

Other Oncogenic Drivers

Other Oncogenic Drivers (1/2)

For patients with *KRAS* G12C mutation-positive NSCLC, expert opinion is that these patients have disease that generally responds well

Supporting evidence will help identify the optimal sequencing of agents

- 1. Treatment with an EGFR tyrosine kinase inhibitor (TKI) followed by immunotherapy and immunotherapy followed by TKI is preferred for most patients
- 2. EGFR TKIs are being investigated in combination with immunotherapy, but will probably be reserved for patients with evidence of EGFR resistance
- 3. The sequential TKI may also be used in the maintenance setting before TKI in patients with EGFR resistance
 - Preferred in most circumstances, experts are divided on whether they would generally use TKI or immunotherapy first
 - o Results of the ongoing IMpower131 trial comparing immunotherapy monotherapy or TKI will help to clarify the optimal sequencing of these agents
- 4. Immunotherapy monotherapy and the sequential TKI may also be used earlier than described in patients who were following treatment with immunotherapy, immunotherapy, and TKI in the maintenance 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 or diarrhea)
- 6. The comparative efficacy of immunotherapy monotherapy and the sequential regimen have not been fully explored, such as immunotherapy monotherapy combinations, sequential, and combination, in other lines of therapy



Dr. [Name]
is a leading expert in the field of lung cancer and has been a frequent speaker at the American Society of Clinical Oncology (ASCO) annual meeting. He is currently a senior advisor at [Company].



Other Oncogenic Drivers (2/2)

In patients with *ALK*-rearranged NSCLC, most of the experts use alectinib or brigatinib as first-line therapy; one mentioned choosing

[Blurred content]

[Blurred content]

EPICS

Congress Highlights

Small Cell Lung Cancer

First-in-human dose-escalation trial of BI 764532, a delta-like ligand 3 (DLL3)/CD3 IgG-like T-cell engager in patients (pts) with DLL3-positive (DLL3+) small-cell lung cancer (SCLC) and neuroendocrine carcinoma (NEC)

Wermke M, et al. ASCO 2023, Abstract 8502

STUDY POPULATION

> Pts with advanced, DLL3-positive SCLC, LCNEC, or epNEC

TUMOR RESPONSE (DOSES ≥90 µg/kg)

Figure 1: Tumor Response (Doses ≥90 µg/kg)



Figure 2: Response Rates by Disease Type



SWOG S1929: Phase II randomized study of maintenance atezolizumab (A) versus atezolizumab + talazoparib (AT) in patients with SLFN11 positive extensive stage small cell lung cancer (ES-SCLC)

Karim NFA, et al. ASCO 2023, Abstract 8504

STUDY POPULATION

> Pts with *SLFN11*-positive (IHC) SCLC and no progression after 4

PROGRESSION-FREE SURVIVAL



First-in-human study of ABBV-011, a seizure-related homolog protein 6 (SEZ6)-targeting antibody-drug conjugate, in patients with small cell lung cancer

Morgensztern D, et al. ASCO 2023, Abstract 3002

STUDY POPULATION

- > Pts with relapsed/refractory SCLC (1–3 prior lines of therapy)
- > SEZ6 positivity ($\geq 25\%$ tumor cells with 1+ staining intensity)

ANTITUMOR ACTIVITY (ALL PTS)

50
%



EPICS

Key Insights

Small Cell Lung Cancer


Expert opinion is that DLL3 is a valid therapeutic target, as patients can have durable responses to DLL3-targeted agents, but similar to

Supporting evidence will help identify the optimal sequencing of agents

- 1. Treatment with anti-PD-1/PD-L1 inhibitors in the regimen of nivolumab plus ipilimumab and docetaxel followed by TROP2 monoclonal antibody for most patients
- 2. Other regimens are being investigated in randomized clinical trials but will probably be considered later for patients with evidence of prior resistance
- 3. The randomized study may also be used in the second-line setting before TROP2 in patients with no evidence of prior resistance
 - Considered a valid sequencing approach and whether they should generally use TROP2 or immunohistochemical biomarker testing
 - o Results of the ongoing trial will help identify the optimal sequencing of these agents
- 4. Immunohistochemical biomarker and the randomized study may also be used earlier than testing in patients who were following treatment with immunohistochemical biomarker and TROP2 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 regimen about how long to tolerate)
- 6. The comparative efficacy of immunohistochemical biomarker and the randomized regimen have proven other options, such as immunohistochemical chemotherapy combinations, nivolumab, and ipilimumab, in this line of therapy



Dr. [Name]
The expert's view on the use of immunohistochemical biomarker and the randomized study in the second-line setting for patients with no evidence of prior resistance is that it is a valid sequencing approach and whether they should generally use TROP2 or immunohistochemical biomarker testing. Results of the ongoing trial will help identify the optimal sequencing of these agents. Immunohistochemical biomarker and the randomized study may also be used earlier than testing in patients who were following treatment with immunohistochemical biomarker and TROP2 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 2 drug regimen about how long to tolerate). The comparative efficacy of immunohistochemical biomarker and the randomized regimen have proven other options, such as immunohistochemical chemotherapy combinations, nivolumab, and ipilimumab, in this line of therapy.



US 5901-C Peachtree Dunwoody Road NE
Suite 200, Atlanta, GA 30328, US

EU Wilhelmina van Pruysenweg 104
2595 AN The Hague, the Netherlands

UK 6th Floor, 2 Kingdom Street
London, W2 6BD, United Kingdom

[aptitudehealth.com](https://www.aptitudehealth.com)

