CLINICAL FLASHCARDS

Outsmarting Shape-Shifting Lung Cancer Resistance

The Life Science Feed

QUESTION

What is the median Progression-Free Survival (PFS) for first-line osimertinib monotherapy in EGFR-mutant NSCLC?

ANSWER

Nearly 19 months.

QUESTION

What is the median Progression-Free Survival (PFS) for first-line osimertinib plus chemotherapy in the FLAURA2 trial?

ANSWER

25 months.

QUESTION

According to the source, what is the most common on-target EGFR resistance mutation following osimertinib treatment?

ANSWER

C797S.

QUESTION

What percentage of patients develop the C797S resistance mutation after osimertinib therapy?

ANSWER

15-20%.

QUESTION

What percentage of patients develop MET amplification as a resistance mechanism post-osimertinib?

ANSWER

15-20%.

QUESTION

What is the recommended re-biopsy protocol at the point of progression after osimertinib?

ANSWER

Simultaneous tissue and liquid biopsy.

QUESTION

The SAVO-Lung trial provided phase 3 data for which drug combination in MET-amplified, post-osimertinib patients?

ANSWER

Savolitinib and osimertinib.

QUESTION

Under what molecular configuration might C797S respond to a combination of 1^{st} and 3^{rd} generation TKIs?

ANSWER

When C797S is in trans with T790M.

QUESTION

What is the name of the novel EGFR inhibitor in development that targets the C797S mutation?

ANSWER

BLU-701.

QUESTION

Which trial established amivantamab plus carboplatin-pemetrexed as an active regimen after osimertinib progression?

ANSWER

MARIPOSA-2.

QUESTION

In the MARIPOSA-2 trial, what was the response rate for the amivantamab plus chemotherapy arm compared to 13% for chemotherapy alone?

ANSWER

33%.

QUESTION

What was the Progression-Free Survival (PFS) for the amivantamab-chemotherapy combination in MARIPOSA-2?

ANSWER

6.3 months.

QUESTION

Which antibody-drug conjugate (ADC) showed a response rate of nearly 30% in the HERTHENA-Lung01 trial?

ANSWER

Patritumab deruxtecan (HER3-DXd).

QUESTION

What percentage of EGFR-mutant patients transform to small cell lung cancer (SCLC) at the point of progression on osimertinib?

ANSWER

5-14%.

QUESTION

What is the standard treatment regimen for patients whose EGFR-mutant NSCLC transforms into small cell lung cancer?

ANSWER

Platinum-etoposide (often with atezolizumab).

QUESTION

In the driver-negative second-line setting, the REVEL trial established docetaxel plus _____ as a standard.

ANSWER

Ramucirumab.

QUESTION

What targets are inhibited by nintedanib in the LUME-Lung 1 trial context?

ANSWER

VEGFR, PDGFR, and FGFR.

QUESTION

The REVEL trial showed an Overall Survival (OS) improvement of 10.5 months versus _____ months for docetaxel alone.

ANSWER

9.1 months.

QUESTION

Which TROP2-directed ADC was shown to be superior to docetaxel in the TROPION-Lung01 trial?

ANSWER

Datopotamab deruxtecan (dato-DXd).

QUESTION

Approximately what percentage of lung adenocarcinoma patients possess the KRAS G12C mutation?

ANSWER

13%.

QUESTION

Which trial established sotorasib as superior to docetaxel for KRAS G12C-mutant NSCLC?

ANSWER

CodeBreaK 200.

QUESTION

Co-mutations in which two genes are known to blunt the efficacy of both Immunotherapy and KRAS inhibitors?

ANSWER

STK11 and KEAP1.

QUESTION

What are the two targets of the bispecific antibody ivonescimab?

ANSWER

PD-1 and VEGF.

QUESTION

In the HARMONi-2 trial, what was the median PFS for ivonescimab compared to 5.8 months for pembrolizumab?

ANSWER

11.1 months.

QUESTION

What was the Hazard Ratio (HR) for PFS in the HARMONi-2 trial comparing ivonescimab to pembrolizumab?

ANSWER

0.51.

QUESTION

Which KRAS mutation is noted to be more common than G12C in lung cancer and is a target for the emerging drug MRTX1133?

ANSWER

G12D.

QUESTION

Concept: RAS-ON inhibitors

ANSWER

Definition: Agents that lock KRAS in its active state regardless of the specific mutation type.

QUESTION

Which RAS-ON inhibitor from Revolution Medicines has shown early activity in KRAS-mutant solid tumours?

ANSWER

RMC-6236.

QUESTION

Which LAG-3 inhibitor is currently being evaluated in NSCLC combination studies?

ANSWER

Favezelimab.

QUESTION

What is the proposed mechanism of the second-generation CTLA-4 antibody botensilimab?

ANSWER

Specific depletion of regulatory T-cells within the tumour.

QUESTION

What two trials are mentioned regarding the adjuvant or unresectable stage III setting for EGFR-mutant patients?

ANSWER

LAURA and ADAURA.

QUESTION

Why is comprehensive ctDNA analysis considered essential at disease progression in EGFR-mutant NSCLC?

ANSWER

To identify resistance mechanisms and monitor emerging alterations in real time.

QUESTION

In the LUME-Lung 1 trial, which histological subgroup showed an OS benefit with docetaxel plus nintedanib?

ANSWER

Adenocarcinoma.

QUESTION

According to the podcast, what is the 'central challenge' in oncology?

ANSWER

Resistance.

QUESTION

Term: Ivonescimab

ANSWER

Definition: A bispecific antibody targeting both PD-1 and VEGF in a single molecule.

QUESTION

Why is VEGF inhibition combined with PD-1 blockade in agents like ivonescimab?

ANSWER

To address two distinct immunosuppressive mechanisms in the tumour microenvironment simultaneously.

QUESTION

The historical second-line standard for driver-negative NSCLC included docetaxel alone or docetaxel plus which two types of inhibitors?

ANSWER

Ramucirumab or nintedanib.

QUESTION

What biological event causes C797S to prevent osimertinib from working?

ANSWER

The mutation prevents osimertinib binding to the EGFR protein.

QUESTION

Other than MET and C797S, name two other less common resistance mechanisms seen post-osimertinib.

ANSWER

RET fusions and KRAS mutations.

QUESTION

Which trial platform was mentioned for comparing amivantamab-based regimens and HER3-DXd at ASCO 2026?

ANSWER

ASCO 2026 abstracts (specifically comparing HERTHENA-Lung01 and MARIPOSA-2 data).

QUESTION

What is the primary clinical utility of liquid biopsy platforms during NSCLC treatment?

ANSWER

Molecular tracking of resistance to guide subsequent treatment decisions.

QUESTION

True or False: Routine Immunotherapy (IO) re-challenge is strongly supported by current data after progression on first-line IO-chemotherapy.

ANSWER

False.

QUESTION

What rationale exists for combining bevacizumab with atezolizumab in the second line?

ANSWER

VEGF inhibition may restore immune infiltration blunted by the tumour microenvironment.

QUESTION

In the CodeBreaK 200 trial, in which patient subgroup were sotorasib responses found to be more durable?

ANSWER

Patients without STK11 or KEAP1 co-mutations.

QUESTION

What phase is the KRAS G12D inhibitor MRTX1133 currently in as of the podcast date?

ANSWER

Phase 1 dose-escalation.

QUESTION

Which trial established the benefit of VEGF plus PD-L1 inhibition in first-line patients, including those with partial IO pretreatment?

ANSWER

IMpower150.

QUESTION

Name one category of ADC development meant to overcome payload-related resistance.

ANSWER

ADCs with novel payloads less prone to resistance.

QUESTION

What are the 'three pillars' of best-practice NSCLC management for 2026 according to the podcast?

ANSWER

Molecular profiling at every decision point, multidisciplinary review, and clinical trial enrolment.

QUESTION

The HARMONi-2 trial comparing ivonescimab to pembrolizumab was initially conducted in which country?

ANSWER

China.

QUESTION

In the post-osimertinib setting, what therapy should be used if no clearly actionable resistance mechanism is found?

ANSWER

Platinum-based chemotherapy, amivantamab-based combinations, or ADCs.

QUESTION

How does the C797S mutation 'in cis' with T790M affect treatment response compared to 'in trans'?

ANSWER

The combination of 1^{st} and 3^{rd} generation TKIs does not work if the mutations are in cis.

QUESTION

Which drug is mentioned as a MET inhibitor that has shown improved outcomes in MET-amplified patients post-osimertinib?

ANSWER

Savolitinib.

QUESTION

What is the significance of HER3 in the context of post-osimertinib NSCLC?

ANSWER

It is the target for the ADC patritumab deruxtecan (HER3-DXd) in heavily pre-treated patients.

QUESTION

Which VEGFR2 antibody was used in the REVEL trial?

ANSWER

Ramucirumab.

QUESTION

According to the transcript, why is missing a small cell transformation diagnosis considered a 'consequential error'?

ANSWER

Because transformed tumours have poor outcomes on NSCLC-directed therapy and require SCLC-specific regimens.

QUESTION

What is the main advantage of dato-DXd over docetaxel mentioned in TROPION-Lung01?

ANSWER

A more favourable tolerability profile.

QUESTION

What emerging class of ADCs targets two different antigens simultaneously?

ANSWER

Bispecific ADCs.

QUESTION

At ASCO 2026, data on managing relapse after which adjuvant trial is highly anticipated?

ANSWER

The LAURA trial.

QUESTION

How does VEGF suppression in the tumour microenvironment affect T-cell function?

ANSWER

It suppresses T-cell activity.

QUESTION

What is the status of molecular profiling throughout the patient journey according to the 2026 outlook?

ANSWER

It has moved from best practice to essential practice at diagnosis, progression, and serially during treatment.

QUESTION

Identify the trial: Ivonescimab plus chemotherapy versus pembrolizumab plus chemotherapy in PD-L1-positive non-squamous NSCLC.

ANSWER

HARMONi-A.

QUESTION

Which gene alteration is specifically addressed by the drug capmatinib?

ANSWER

MET (amplification).

QUESTION

In the LUME-Lung 1 trial, what was the OS for the docetaxel plus nintedanib arm?

ANSWER

12.6 months.

QUESTION

How many episodes are in the NSCLC Deep Dive series mentioned in the transcript?

ANSWER

4.

QUESTION

What is the name of the pharmaceutical company developing the RAS-ON inhibitor RMC-6236?

ANSWER

Revolution Medicines.

QUESTION

In EGFR-mutant disease, what informs treatment more than any imaging endpoint during progression?

ANSWER

Molecular tracking (via liquid biopsy/ctDNA).

QUESTION

What is the primary focus of Segment 2 in the podcast transcript?

ANSWER

Managing driver-negative patients after IO-chemotherapy progression (second line).

QUESTION

What type of therapy is typically used after a treatment break in IO-experienced patients despite lack of robust trial support?

ANSWER

Immune checkpoint inhibitor (IO) retreatment/re-challenge.

QUESTION

The MARIPOSA-2 trial compared chemotherapy alone to amivantamab-chemotherapy with and without which other drug?

ANSWER

Lazertinib.

QUESTION

What is the specific target of the ADC in the HERTHENA-Lung01 trial?

ANSWER

HER3.

QUESTION

The transcript mentions that STK11 and KEAP1 status should be part of which diagnostic profile?

ANSWER

The molecular portrait guiding treatment beyond first-line.

QUESTION

What is the median PFS difference between pembrolizumab and ivonescimab in the HARMONi-2 trial?

ANSWER

5.3 months (11.1 vs 5.8).

QUESTION

What global confirmatory trial will determine if ivonescimab reshapes first-line standard of care?

ANSWER

The global HARMONi trial.

QUESTION

What specific patient population was enrolled in the HARMONi-2 trial?

ANSWER

PD-L1-high NSCLC patients.

QUESTION

Besides savolitinib, name two other MET inhibitors mentioned for MET-amplified resistance.

ANSWER

Tepotinib and capmatinib.

QUESTION

What does the term 'IO-refractory' refer to in the context of NSCLC?

ANSWER

Disease that has progressed during or after treatment with immune checkpoint inhibitors.

QUESTION

Which trial focused on HER3-DXd in metastatic EGFR-mutated NSCLC?

ANSWER

HERTHENA-Lung01.

QUESTION

In the context of the pipeline, what is 'favezelimab'?

ANSWER

A LAG-3 inhibitor.

QUESTION

According to Segment 3, what is the most anticipated emerging targeted class at ASCO 2026?

ANSWER

KRAS G12D inhibitors.

QUESTION

What was the response rate for chemotherapy alone in the MARIPOSA-2 trial?

ANSWER

13%.