

CLINICAL FLASHCARDS

How Immunotherapy Unmasks Invisible Lung Cancer

The Life Science Feed

QUESTION

Which biomarker is considered the current clinical standard for guiding immune checkpoint inhibitor therapy in NSCLC?

ANSWER

PD-L1 expression by immunohistochemistry (specifically tumour proportion score).

QUESTION

In the KEYNOTE-024 trial, what was the required PD-L1 TPS threshold for pembrolizumab monotherapy to outperform chemotherapy?

ANSWER

A TPS of $\geq 50\%$.

QUESTION

What was the five-year Overall Survival (OS) rate for patients receiving pembrolizumab in the KEYNOTE-024 trial?

ANSWER

31.9%.

QUESTION

What was the five-year Overall Survival (OS) rate for the chemotherapy arm in the KEYNOTE-024 trial?

ANSWER

16.3%.

QUESTION

In the KEYNOTE-042 trial, which specific PD-L1 subgroup was the primary driver of the overall survival benefit?

ANSWER

The TPS $\geq$ 50% subgroup.

QUESTION

What is the standard first-line treatment preference for patients with a PD-L1 TPS in the 1–49% range?



ANSWER

Chemotherapy plus immunotherapy combinations.

QUESTION

Why is PD-L1 TPS considered a limited biomarker regarding its measurement scale?

ANSWER

It is a continuous variable that is treated as a categorical one by regulatory cutoffs.

QUESTION

List two factors that contribute to the high variability of PD-L1 expression within the same patient.

ANSWER

Variability between different biopsies of the same tumour and differences between primary and metastatic sites.

QUESTION

What is the biological rationale behind using Tumour Mutational Burden (TMB) as a biomarker for immunotherapy?

ANSWER

Highly mutated tumours generate more neoantigens, making them more immunogenic.

QUESTION

Which trial investigated the use of atezolizumab specifically in TMB-high patients?



ANSWER

IMpower110.

QUESTION

What clinical finding should immediately prompt comprehensive NGS testing rather than starting immunotherapy in a high PD-L1 patient?

ANSWER

The patient being a never-smoker or being young (suggesting a potential driver mutation).

QUESTION

Why must driver mutation status (like EGFR or ALK) take precedence over PD-L1 status in treatment selection?

ANSWER

Patients with these alterations have worse outcomes on pembrolizumab monotherapy compared to targeted inhibitors like osimertinib.

QUESTION

What is the proposed mechanism by which chemotherapy enhances the response to PD-1 blockade?

ANSWER

Chemotherapy-induced immunogenic cell death increases tumour antigen presentation.

QUESTION

Which trial established pembrolizumab plus platinum-pemetrexed as the first-line standard for non-squamous NSCLC?



ANSWER

KEYNOTE-189.

QUESTION

What was the median OS for the pembrolizumab plus chemotherapy arm in KEYNOTE-189?

ANSWER

22 months.

QUESTION

Which trial established pembrolizumab plus carboplatin-paclitaxel (or nab-paclitaxel) as the standard for squamous NSCLC?

ANSWER

KEYNOTE-407.

QUESTION

Describe the treatment regimen used in the CheckMate 9LA trial.

ANSWER

Nivolumab plus ipilimumab combined with two cycles of chemotherapy.

QUESTION

What was the purpose of the limited two-cycle chemotherapy 'primer' in the CheckMate 9LA regimen?

ANSWER

To provide rapid disease control while reducing the cumulative toxicity of long-term chemotherapy.

QUESTION

Which trial established the chemotherapy-free combination of nivolumab and ipilimumab for patients with PD-L1 $\geq$ 1%?

ANSWER

CheckMate 227.

QUESTION

What are the two most common immune-related adverse events associated with dual checkpoint blockade (PD-1 plus CTLA-4)?



ANSWER

Colitis and hepatitis.

QUESTION

Which trial established a four-drug regimen including atezolizumab and bevacizumab for NSCLC?

ANSWER

IMpower150.

QUESTION

Which specific patient subgroup progressed on targeted therapy showed benefit in the IMpower150 trial?

ANSWER

Patients with EGFR mutations.

QUESTION

What was the outcome of the Phase 3 SKYSCRAPER-01 trial investigating tiragolumab (anti-TIGIT)?

ANSWER

It failed to meet its primary endpoint of Progression-Free Survival (PFS).

QUESTION

What is the target of the drug relatlimab?

ANSWER

LAG-3 (Lymphocyte-activation gene 3).

QUESTION

According to the source, why might immune checkpoint combinations that work in melanoma fail in NSCLC?

ANSWER

The NSCLC immune microenvironment is often more immunosuppressive and influenced by smoking history and heterogeneity.

QUESTION

What does 'perioperative' therapy entail in the context of recent NSCLC clinical trials?

ANSWER

Administering treatment (like immunotherapy) both before (neoadjuvant) and after (adjuvant) surgery.

QUESTION

Which trial was the first Phase 3 to show benefit for a neoadjuvant plus adjuvant pembrolizumab design?

ANSWER

KEYNOTE-671.

QUESTION

What was the Event-Free Survival (EFS) Hazard Ratio reported for pembrolizumab in KEYNOTE-671?

ANSWER

0.59.

QUESTION

What was the Pathological Complete Response (pCR) rate for pembrolizumab plus chemotherapy in KEYNOTE-671?

ANSWER

18.1%.

QUESTION

In the CheckMate 77T trial, what was the Pathological Complete Response (pCR) rate for the nivolumab arm?

ANSWER

25.3%.

QUESTION

Define Pathological Complete Response (pCR) in the context of surgical resection.

ANSWER

The absence of any viable tumour cells remaining in the resected tissue specimen.

QUESTION

Which trial investigated osimertinib after chemoradiation in unresectable stage III EGFR-mutant NSCLC?

ANSWER

LAURA.

QUESTION

What was the Progression-Free Survival (PFS) for the osimertinib arm in the LAURA trial compared to placebo?

ANSWER

39.1 months versus 5.6 months.

QUESTION

What is the Hazard Ratio (HR) for PFS reported in the LAURA trial?

ANSWER

0.16.

QUESTION

Which trial evaluated adjuvant atezolizumab following surgery and chemotherapy in stage II–IIIA NSCLC?

ANSWER

IMpower010.

QUESTION

In IMpower010, which PD-L1 subgroup showed the most pronounced disease-free survival benefit?

ANSWER

The PD-L1 $\geq 50\%$ group.

QUESTION

Why is molecular testing now essential before initiating treatment for resectable NSCLC?

ANSWER

Because driver mutations (like EGFR) fundamentally change the perioperative approach, such as using targeted therapy instead of immunotherapy.

QUESTION

According to the LAURA trial results, what is the new standard of care for unresectable stage III EGFR-mutant NSCLC?

ANSWER

Osimertinib following concurrent chemoradiation.

QUESTION

List three specialties that should be included in a multidisciplinary team (MDT) for resectable NSCLC.

ANSWER

Medical oncology, thoracic surgery, and radiation oncology.

QUESTION

Which future biomarker focuses on assessing the composition of the tumour microenvironment using multiple stains?



ANSWER

Multiplex immunohistochemistry (IHC).

QUESTION

What role might ctDNA dynamics play as an emerging biomarker in NSCLC?

ANSWER

Acting as a refined predictor of treatment response and disease monitoring.

QUESTION

What is the primary clinical risk of giving pembrolizumab monotherapy to a patient with an EGFR mutation?

ANSWER

Worse clinical outcomes compared to standard targeted therapy (osimertinib).

QUESTION

Under what condition is immunotherapy-chemotherapy combination considered PD-L1 agnostic?

ANSWER

When it is approved for use regardless of the patient's PD-L1 expression level (e.g., KEYNOTE-189).

QUESTION

Which two drugs are combined in the dual checkpoint blockade strategy used in CheckMate 227?

ANSWER

Nivolumab and ipilimumab.

QUESTION

Identify two rare but serious immune-related adverse events mentioned as a focus for oncology teams.

ANSWER

Myocarditis and pneumonitis.

QUESTION

How did the 24-month OS rate in KEYNOTE-671 compare between the pembrolizumab and placebo arms?

ANSWER

79.9% for pembrolizumab versus 77.6% for placebo.

QUESTION

In the context of the CheckMate 77T trial, what was the EFS Hazard Ratio?

ANSWER

0.58.

QUESTION

What is the clinical standard regarding the timing of MDT input for potentially resectable NSCLC?

ANSWER

MDT input should be obtained before any treatment is initiated.

QUESTION

Which anti-LAG-3 antibody showed benefit in melanoma but has limited data in NSCLC?



ANSWER

Relatlimab.

QUESTION

What is the main advantage of the CheckMate 9LA regimen for patients sensitive to chemotherapy side effects?

ANSWER

It involves only two cycles of chemotherapy, reducing cumulative toxicity.

QUESTION

The standard of care for most advanced NSCLC patients without driver mutations is _____.

ANSWER

Immunotherapy (checkpoint inhibitors).

QUESTION

Concept: Tumour Proportion Score (TPS)

ANSWER

Definition: A measure of PD-L1 expression on tumour cells used to guide immunotherapy selection.

QUESTION

Concept: Neoantigens

ANSWER

Definition: New antigens formed by tumour mutations that can be recognised by the immune system.

QUESTION

Concept: Immunogenic Cell Death

ANSWER

Definition: A form of cell death induced by certain chemotherapies that triggers an immune response against the tumour.

QUESTION

Which trial focused on squamous histology using pembrolizumab, carboplatin, and paclitaxel?



ANSWER

KEYNOTE-407.

QUESTION

What is the target of the checkpoint inhibitor atezolizumab?

ANSWER

PD-L1.

QUESTION

What is the target of the checkpoint inhibitor nivolumab?

ANSWER

PD-1.

QUESTION

What was the OS benefit for pembrolizumab plus platinum-pemetrexed in KEYNOTE-189 compared to chemotherapy alone?



ANSWER

22 months versus 10.7 months.

QUESTION

For which histology is the platinum-pemetrexed plus pembrolizumab combination typically used?

ANSWER

Non-squamous NSCLC.

QUESTION

What was the Pathological Complete Response rate in the chemotherapy-only arm of KEYNOTE-671?

ANSWER

4.0%.

QUESTION

What was the Pathological Complete Response rate in the chemotherapy-only arm of CheckMate 77T?

ANSWER

4.7%.

QUESTION

Which trial established adjuvant atezolizumab for resected stage II-III A disease?

ANSWER

IMpower010.

QUESTION

The _____ trial showed that stage III EGFR-mutant patients have almost no progression events on osimertinib post-chemoradiation.

ANSWER

LAURA

QUESTION

Which checkpoint combination drug targets CTLA-4?

ANSWER

Ipilimumab.

QUESTION

In CheckMate 227, what was the required PD-L1 level for the OS benefit shown at five years?

ANSWER

TPS $\geq$ 1%.