

Why test PD-L1 in non-small cell lung cancer?

Fact Sheet



Unmet need in NSCLC

- Lung cancer is one of the most common malignancies and is a leading cause of cancer-related death worldwide^{1,2}
- Non-small cell lung cancer (NSCLC) accounts for the majority (80–85%) of all cases of lung cancer¹

At **diagnosis**, ~70% of patients with NSCLC have inoperable, locally **advanced tumours** or metastatic disease^{3,4}

- Although treatment advances have led to improvements in survival, the overall prognosis for NSCLC remains poor^{4,5}



Anti-PD-1/PD-L1 immunotherapy is an important treatment choice in NSCLC

The programmed cell death-1 (**PD-1**)/programmed cell death ligand-1 (**PD-L1**) pathway is an important **checkpoint** used by tumour cells (TCs) to **inhibit antitumour immune responses**^{6,7}

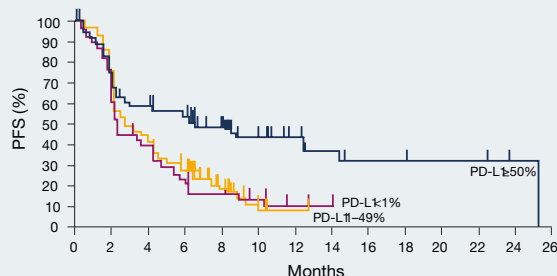
- Anti-PD-1/PD-L1 antibodies, alone or in combination with chemotherapy, have shown antitumour activity across multiple tumour types, including non-small cell lung cancer (NSCLC)^{6–8}
- Studies have shown greater efficacy with anti-PD-1/PD-L1 immunotherapy in patients with tumours expressing higher levels of PD-L1^{6,8–13}



Evidence for PD-L1 testing NSCLC

- The predictive nature of PD-L1 expression levels in patients with NSCLC has been reported in a number of key trials evaluating anti-PD-1/PD-L1 immunotherapy, including KEYNOTE 001 (NCT01295827), CheckMate 057 (NCT01673867) and Study 1108 (NCT01693562; NSCLC cohort)^{9–13}
- In addition, the KEYNOTE 024 trial showed clinical benefit in terms of overall survival (OS) and progression-free survival (PFS) for first-line pembrolizumab versus chemotherapy in patients with NSCLC with ≥50% PD-L1 expression on TCs (PD-L1 TC ≥50%)¹³
- In KEYNOTE 001, patients with high PD-L1 expression (PD-L1 TC ≥50%) had a significantly greater objective response rate (ORR), median PFS (Figure 1), and OS compared with patients with low PD-L1 expression (PD-L1 TC <50%)⁹
- In the exploratory post-hoc analysis of POSEIDON, patients with PD-L1-positive mNSCLC achieved better survival with durvalumab + chemotherapy ± tremelimumab versus chemotherapy alone. For patients with PD-L1-negative mNSCLC, the addition of tremelimumab to durvalumab and chemotherapy improved survival⁸

Figure 1: PFS according to the percentage of TCs with membranous PD-L1 staining (KEYNOTE 001)⁹



- In CheckMate 057, there was a strong predictive association between PD-L1 expression in the tumour and clinical outcome at all expression levels, for all efficacy endpoints¹⁰

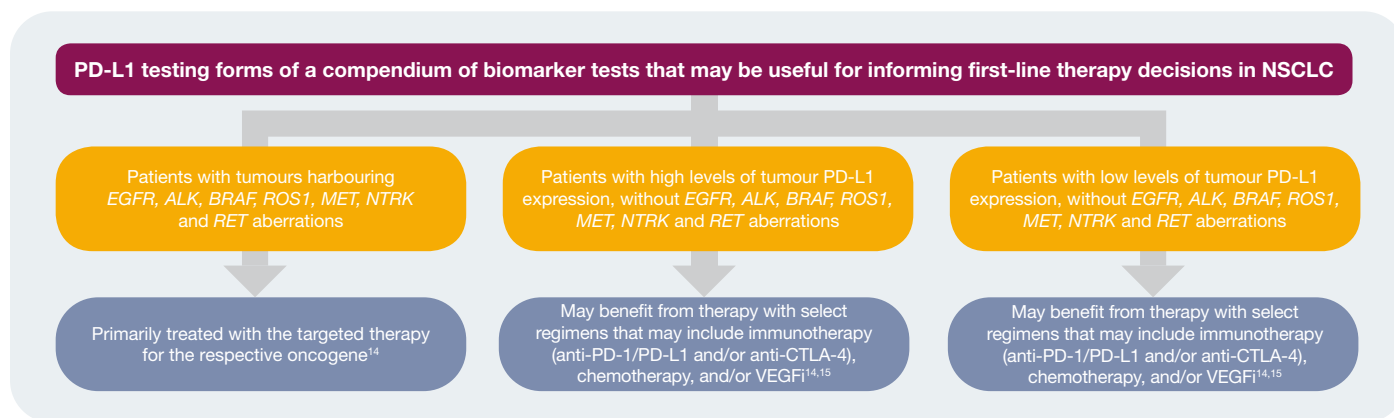
Study 1108 (Phase 1/2 study, NSCLC cohort)
ORR: **25% PD-L1 high** tumours* versus
6% PD-L1 low/negative tumours¹²

*≥25% of TCs staining for PD-L1 at any intensity

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- Testing for PD-L1 can therefore help inform treatment decisions, so that the most appropriate therapeutic choices can be made for each patient (Figure 2)

Figure 2: Measuring tumour PD-L1 expression can help inform treatment decisions in NSCLC^{14,15}



Implications in the clinic

- Determining tumour PD-L1 expression level can help to identify patients with NSCLC who are more likely to benefit from anti-PD-1/PD-L1 antibody therapy^{7,9-13}



Context

- There remains significant unmet need for improving outcomes in patients with NSCLC
- Immunotherapy with anti-PD-1/PD-L1 antibodies has shown efficacy in the treatment of NSCLC
- Tumours expressing high levels of PD-L1 are more likely to respond to anti-PD-1/PD-L1 immunotherapy than those expressing low levels of PD-L1
- Evidence supports the clinical efficacy of anti-PD-1/PD-L1 immunotherapy as first-line treatment for patients expressing high levels of PD-L1
- Testing tumour PD-L1 expression levels can help a physician determine the most appropriate therapeutic strategy for patients with NSCLC

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