NEO GENOMICS

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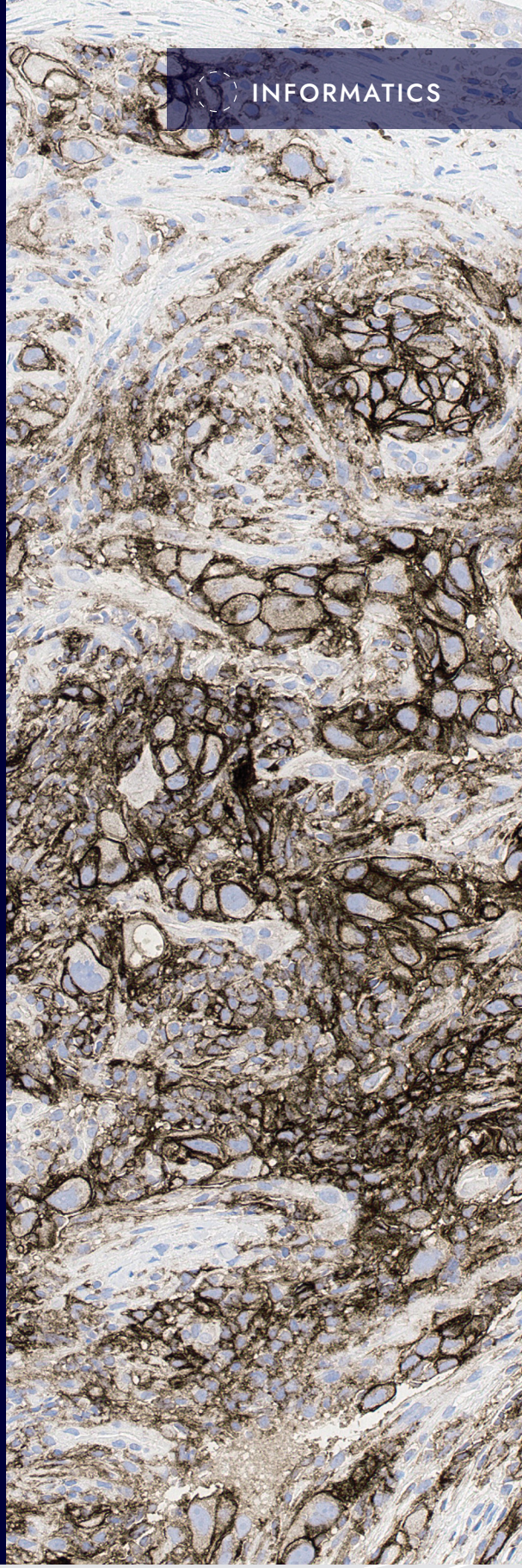

LITE PAPER

Real-World PD-L1 Testing Data Provides Insight into the Evolving Immuno-oncology Landscape

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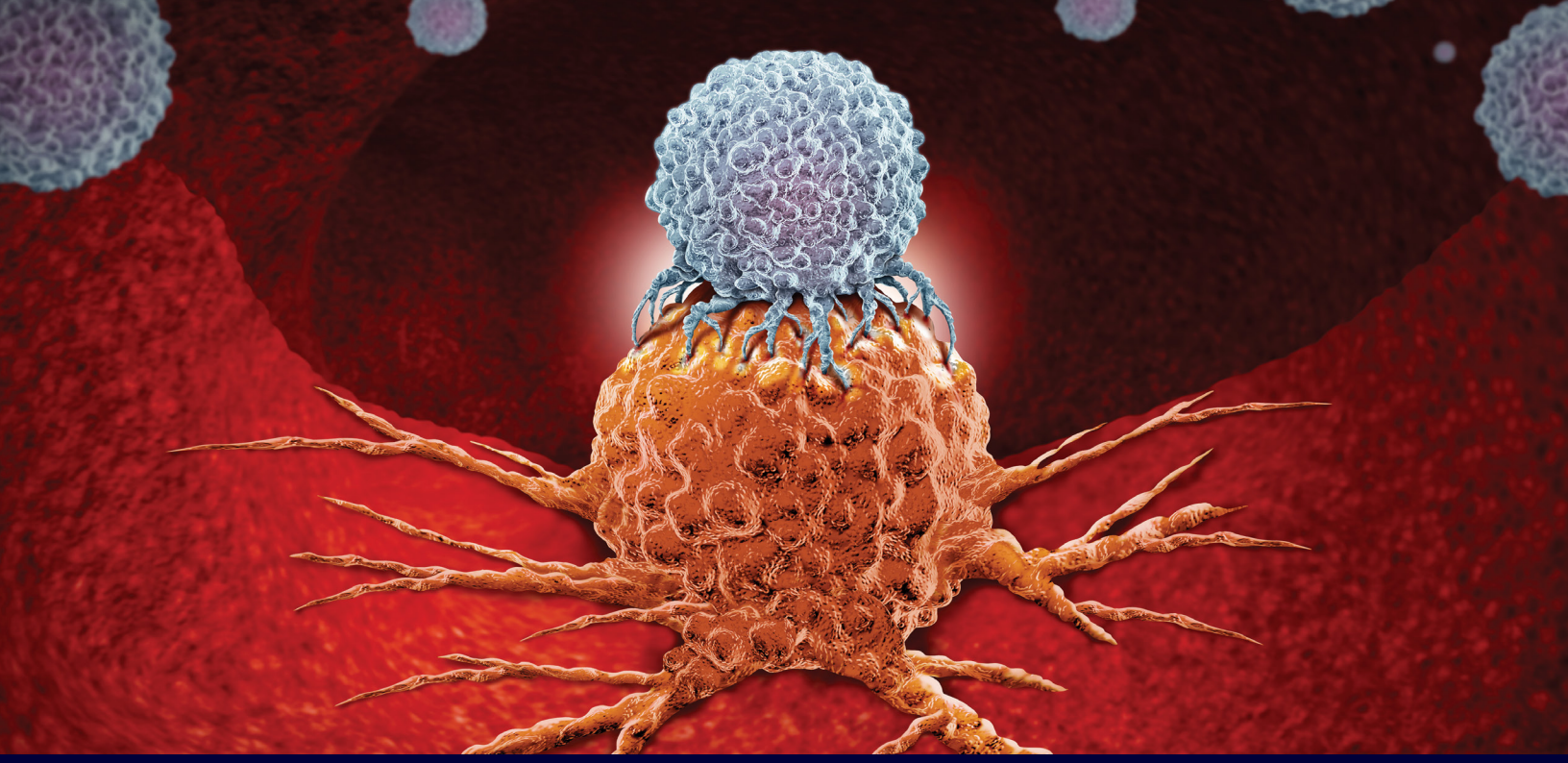
As the leading laboratory for PD-L1 testing in the US, NeoGenomics takes a critical look at PD-L1 trends in the community setting to understand how testing has evolved along with the expanding treatment landscape.



Introduction

In the 1940's, a *Boston Children's Hospital* pathologist by the name of Sidney Farber began experimenting with a class of drugs known as anti-folates in pediatric leukemia patients. Sidney Farber's work was groundbreaking, not just because he was the first to form the concept of treating cancer with a "drug," but also because he was one of the first in history to show that cancer, a disease which was originally thought to be "uncurable," could in fact be cured. Since then, cancer therapies and patient quality of life has improved exponentially. However, these improvements aren't just due to the development of newer chemotherapeutic drugs and their revised treatment protocols, but also due to the development of targeted precision medicines. For example, in the case of non-small cell lung cancer (NSCLC), the 5-year survival of EGFR-mutated patients treated with a kinase inhibitor is approximately 24% vs. 9% with conventional chemotherapy.[1,2] In the rare instances of a NSCLC patient harboring an ALK or ROS1 fusion, 5-year survival when undergoing targeted therapy can exceed 50%.[1,3] However, if there has been one therapeutic category that strikes awe in the oncology community, it's immunotherapy.

Checkpoint inhibitors revolutionized the oncology treatment landscape

Originally inspired by the research of 19th century clinician-scientist William Coley, the development of immunotherapy has led to unparalleled breakthroughs in the treatment of advanced cancers and is now a staple in standard of care. Of these therapies, immune checkpoint blockade, including PD-L1 inhibitors, are at the forefront of treatment algorithms across indications. Three years after the approval of the first checkpoint inhibitor (ipilimumab) which targeted CTLA-4, the first PD-L1 inhibitors (pembrolizumab and nivolumab) were approved in 2014 for the treatment of melanoma. With clinical trials demonstrating startling overall survivals of up to 26 months in patients with metastatic disease,[4,5] these two therapies rapidly disseminated across indications, with NSCLC being the first in 2015, followed by renal cell carcinoma, Hodgkin lymphoma, head and neck cancer, and urothelial carcinoma. Today, there are five additional therapies on market which target PD-L1 (atezolizumab, durvalumab, avelumab, cemiplimab, and dostarlimab), (Fig. 1), and over 5,600 clinical trials.[6] In the only eight years since the first checkpoint inhibitor launched, oncologists have routinely begun incorporating immunotherapy as standard of care across tumor types.

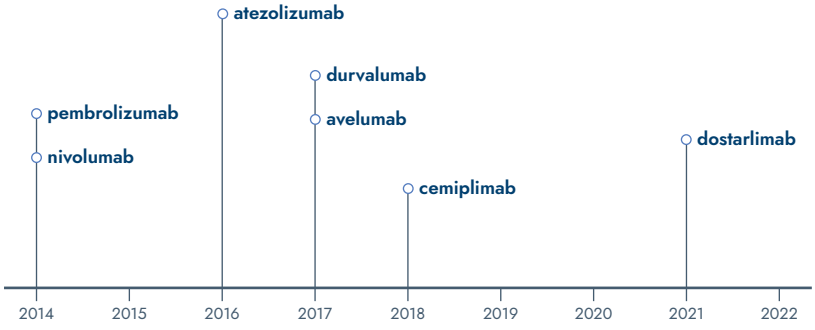
The diagnostic landscape for immuno-oncology is complex

Patients are deemed eligible for PD-L1 inhibitors based on whether or not their tumors express the PD-L1 protein using a particular scoring criteria and cut-off value. Each on-market PD-L1 immunohistochemistry companion diagnostic test uses a specific scoring criteria — tumor proportion score (TPS), combined positive score (CPS), PD-L1 tumor cell staining (TC), or PD-L1 immune cell staining (IC). (Fig. 2) A patient is eligible for a PD-1 inhibitor based on the score for the specific approved CDx clone. That is to say, a patient who is PD-L1 positive with the 22C3 clone, a companion diagnostic test for the drug pembrolizumab, will be unable to undergo treatment with atezolizumab unless they receive a positive result with the SP142 clone and vice versa. Scoring criteria are not only unique among different clones, but also across indications for the same clone. For example, the NSCLC scoring criteria for 22C3 is based off of TPS, while all other 22C3 indications are based on CPS; in the case of SP142, IC or TC is used instead of CPS or TPS. Naturally, with different assays and scoring methods, PD-L1 status can differ not only by indication, but also by clone, indicating that PD-L1 scoring and treatment selection are both heterogeneous and complex.

OVER
5.6K
CLINICAL TRIALS TARGET PD-L1

FIG.1

TIMELINE OF PD-L1 INHIBITOR DRUG APPROVALS



In just 8 years, there are now 7 therapies that target PD-L1.

FIG.2

COMPARISON OF PD-L1 CLONES & SCORING METHODS BY TUMOR TYPE

CLONE	SCORING	
	Lung	Other tumor types
22C3	TPS	CPS
28-8	TPS	TPS
LDT	TC/IC	IC
SP142	TC/IC	IC
SP263	TC/IC	IC

Real-world lab data is critical for understanding testing and treatment trends and patient outcomes

As the complexity of the immuno-oncology (IO) space expands, we sought to understand PD-L1 testing trends and prevalence in the community setting to determine whether these trends have kept pace with the evolving treatment landscape. Our data shows that PD-L1 is the most frequently ordered biomarker in NSCLC ordering algorithms, followed by EGFR, ALK, and ROS1. When looking at the population of >50,000 patients who have undergone PD-L1 testing at NeoGenomics across 5 different assays over the past year, we found >90% of PD-L1 testing was done using a companion diagnostic (CDx) clone as opposed to a laboratory developed test (LDT). (Fig. 3) Of all PD-L1 orders, 22C3 was overwhelmingly the most frequently ordered clone, constituting over 82% of all total PD-L1 orders, as well as over 95% of orders on lung cancer patients. Second was the NeoGenomics LDT (ZR3 clone), which was ordered in 8% of patients. SP142 constituted 6% of ordering volume, followed by 28-8 (5% of patients) and SP263 (<1% of patients)

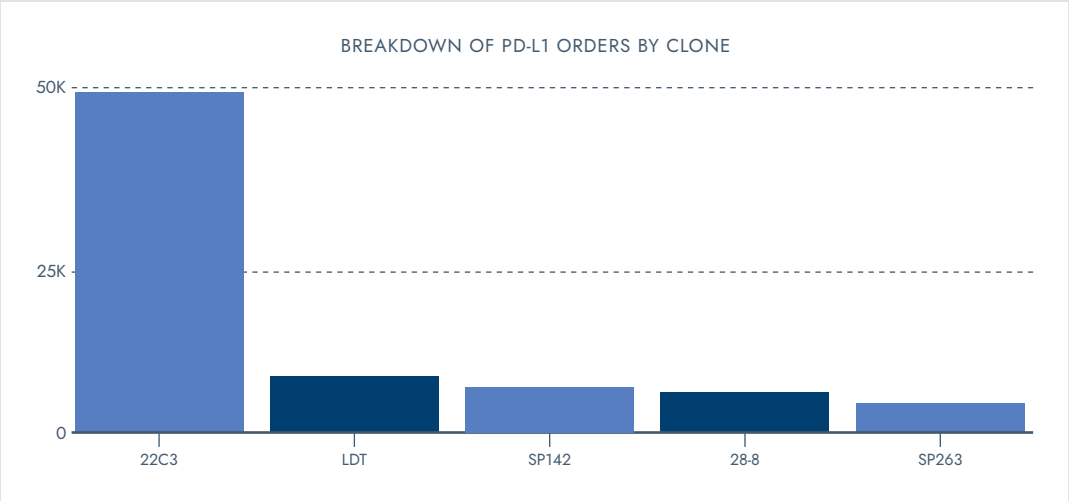
Given the large disparity of 22C3 testing when compared to other clones, we sought to better understand PD-L1 ordering and serial testing trends across indications. Patients tested for 22C3, 28-8, and SP263 predominately had a lung tumor, while patients tested for SP142 were predominantly breast cancer patients. Nearly half of patients tested with the LDT consisted of other tumor types outside of the indications approved for the current PD-L1 CDx tests, indicating that oncologists have an intense interest in using PD-L1 inhibitors outside of approved indications. We also found that not only was 22C3 the most predominantly used clone in practice, but it was also the clone most likely to be repeated. While this may indicate a preference of providers for treating with pembrolizumab, it's important to mention that quite frequently patients will also undergo testing with multiple clones along with 22C3.

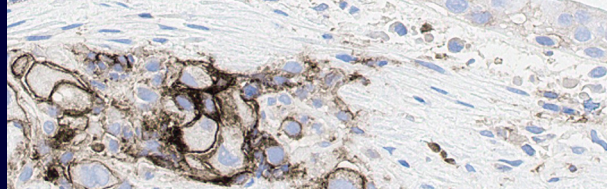
In the case of serial testing with different clones, the mean duration between PD-L1 tests is 14 days, indicating that providers are interested in identifying multiple therapeutic options for their patients. But, does this mean that patients who undergo PD-L1 testing with 22C3 or another assay will have similar results across clones? Not necessarily. In fact, when looking at the concordance of results across assays, the data shows that at least in the case of 22C3, results were only highly concordant with 28-8. Consistent with the literature, SP142 was least concordant overall.[7] This is to say that a PD-L1 positive result in 22C3 may not necessarily correlate to a PD-L1 positive result in another clone, or a result that is expressed as highly.

>90%

OF PD-L1 TESTING WAS DONE USING A COMPANION DIAGNOSTIC (CDX) CLONE

FIG.3





With over 92% of PD-L1 orders consisting of CDx and the majority of PD-L1 LDT orders consisting of tumor types outside of approved CDx indications, the message is quite clear: clinicians want their patients on these therapies. Unfortunately, the reality is that not all patients who undergo PD-L1 testing will respond to immune checkpoint blockade even if they have a positive result. Our data shows that across all indications, nearly 75% of patients who undergo PD-L1 testing will have a positive result (when controlling for invalid results). When looking at 22C3 specifically, 15–30% of patients will have a highly expressed PD-L1 result which would intuitively suggest an improved response to treatment. In the case of NSCLC, when we control for patients harboring mutations/fusions in EGFR, ALK, and ROS1, which are associated with resistance to PD-L1 inhibitors regardless of expression level, we find that 75% of PD-L1-positive patients will be eligible for IO. (Fig. 4) However, only approximately 20% of patients across indications will receive an objective response to immunotherapy while only 13% will have a durable remission.[6] Selecting the wrong treatment can at times be even worse than no treatment.[8,9] As such, comprehensive genomic and cancer testing are paramount in not only improving the risk stratification and response of patients eligible for this class of therapies, but also for identifying additional targetable alterations.

Through linkage of laboratory data with clinical data from electronic health records and medical and pharmacy claims, patient outcomes can be tracked over time to further demonstrate the importance of appropriate testing and therapy selection.

Leverage the leading PD-L1 testing laboratory to develop strategic insights

As the IO treatment landscape continues to evolve, a deep understanding of IO-eligible patients and scoring paradigms is critical for further refinement of this class of therapy. However, equally as important is understanding how these scoring paradigms, in conjunction with IO-eligibility, risk stratification, and drug resistance and sensitivity biomarkers influence real-world treatment selection and therapeutic outcomes. Where clinical guidelines provide a framework for treatment with IO, examination of testing and treating patterns in clinical practice provides crucial insight into patient outcomes to inform optimal therapeutic selection.

NEARLY

75%

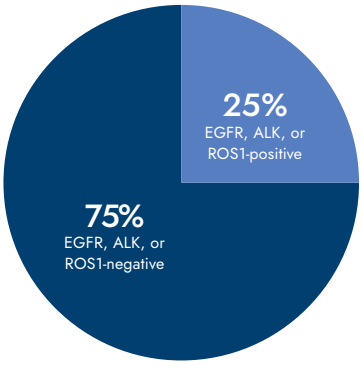
OF PATIENTS WHO UNDERGO PD-L1 TESTING WILL HAVE A POSITIVE RESULT

LEARN MORE

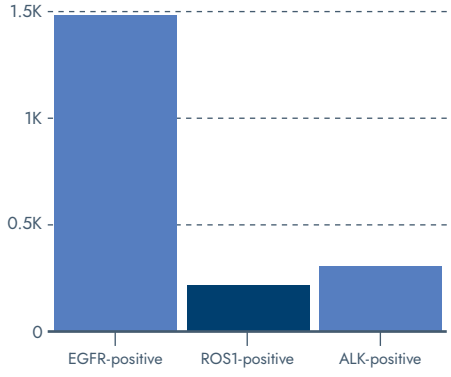
Contact us to learn how we can utilize our NeoNucleus™ database to answer your strategic questions across the entire drug development lifecycle through commercialization. See how we pair claims and third-party data to help you holistically understand the patient journey from initial diagnosis to treatment selection and beyond.

FIG. 4

EGFR, ALK, AND ROS1 STATUS AMONG PD-L1+ LUNG CANCER PATIENTS



BREAKDOWN BY EGFR, ALK, AND ROS1 POSITIVE LUNG CANCER PATIENTS



FOOTNOTES / REFERENCES

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