PD-L1 TESTING AS A MODEL FOR THE IMPACT OF BIOMARKER ADOPTION ON DRUG LAUNCH SUCCESS

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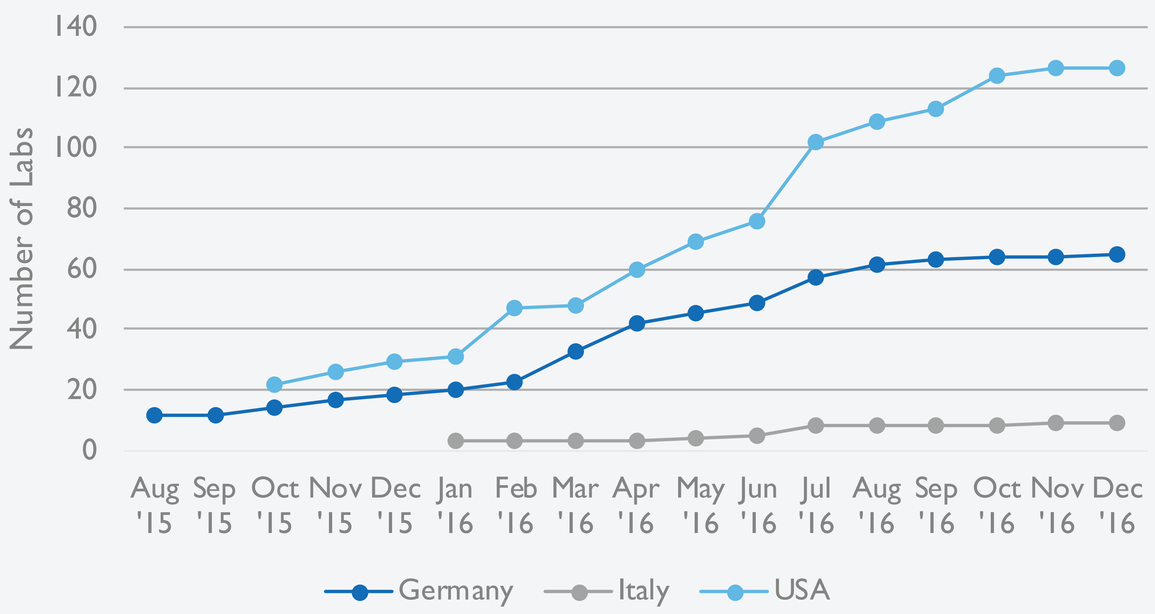
Introduction

Key to the success of precision medicine is implementation of biomarker testing. Immuno-oncology (IO)-based therapies have achieved over six indications in recent years, and serve as an example highlighting the challenges of integrating drug launch with implementation of biomarker testing. Four unique antibody clones have been used to test PD-L1 expression in therapeutic clinical trials and several additional commercially available antibody clones are used in clinical laboratories. Laboratory developed tests (LDTs) have been developed using combinations of antibody clones, reagents and varying instrumentation. Due to this variety of antibodies and testing methodologies, as well as differing cut-off points for staining positivity, testing for PD-L1 expression has become a challenge for pathologists and for clinicians intending to treat patients with IO therapies.

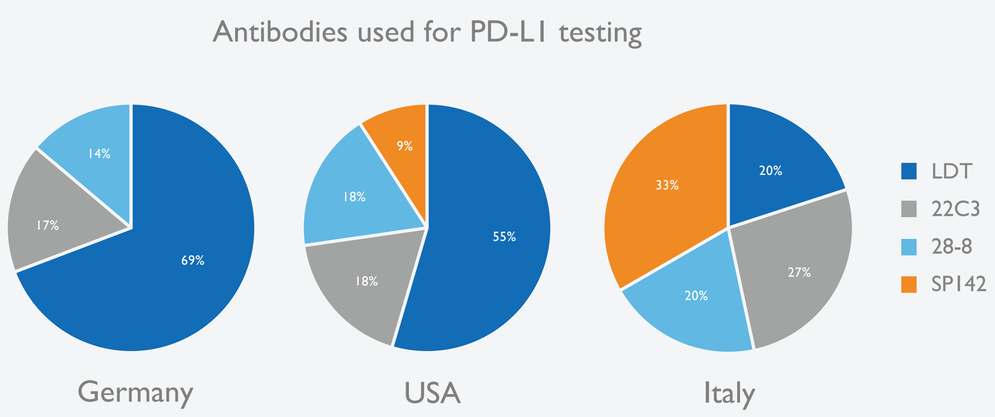
In order to better understand adoption and PD-L1 testing dynamics, Diaceutics conducted a longitudinal analysis of PD-L1 test adoption in non-small cell lung cancer (NSCLC) in three key countries (Italy, Germany and the USA) using data from the Diaceutics' laboratory database. In addition, we mapped the factors that influence laboratory adoption of PD-L1 testing including training, reimbursement, platform and kit/antibody availability.

PD-L1 lab adoption



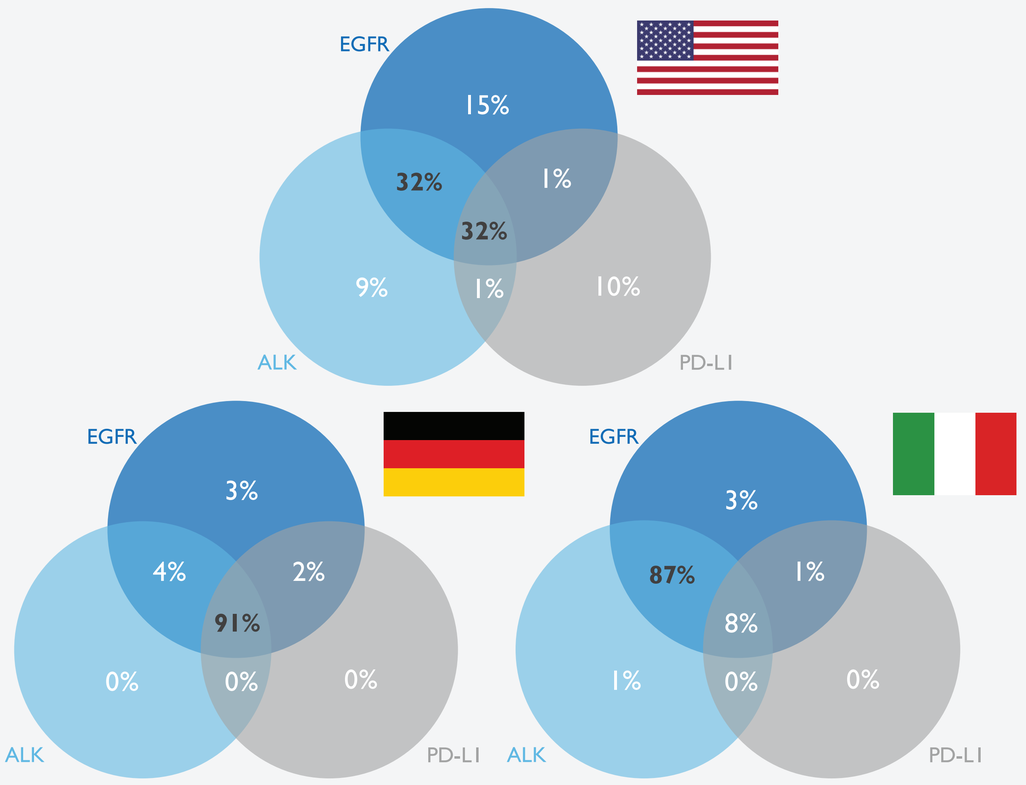
IO therapy and PD-L1 testing were introduced in the US and EU markets at approximately the same time. However, adoption of PD-L1 testing in the US has been more rapid than in most countries. In Germany, 93% of major centres testing for NSCLC offer the PD-L1 test. A similar landscape is observed in the US, whereas in Italy, only 9% of the major NSCLC centres have adopted PD-L1 testing.

PD-L1 test adoption by country



In the United States, the therapeutic label specifically calls for use of the FDA-approved test, whereas in the EU, therapeutic labels only require the use of a validated test. Despite the FDA regulation, 55% of labs in the US have adopted an LDT for PD-L1 testing.
Similarly, in Germany, 69% of the tests are performed using an LDT. In Italy, there is lower LDT adoption. In general, the use of LDTs has been associated with fast test adoption.

PD-L1 and other NSCLC biomarkers



With approval of IO therapy in first line setting in NSCLC, the integration of PD-L1 as a standard biomarker in NSCLC testing will enable treatment decisions. The demand for testing PD-L1 status in parallel with established markers such as Epidermal Growth Factor Receptor (EGFR) mutation detection and anaplastic lymphoma kinase (ALK) rearrangement will increase. In the US, the shift to include PD-L1 together with EGFR and ALK at primary diagnosis is becoming more evident. Due to the low adoption of PD-L1 testing in Italy, few labs have adopted a parallel testing model for all three biomarkers. Nearly all labs in Germany (91%) are currently testing all three biomarkers.

Education and harmonization studies

Educational programs and training play a pivotal role in adoption. In the US, there are different initiatives for pathology education, including a long-term educational program sponsored by Dako (https://pdl122c3-learning.dako.com/) and numerous webinar training sessions sponsored by both diagnostic manufacturers and professional societies. The German Pathology Society (DGP) and quality assurance organization QuIP have promoted over 35 training sessions for German pathologists, which has led to significantly faster adoption and validation of PD-L1 testing. In addition, the German harmonization study enabled an easier choice of methodology among all the currently available tests (www.ncbi.nlm.nih.gov/pubmed/27389313). In Italy, only 5 training sessions have been performed and a harmonization study has yet to be completed, contributing to the lower adoption of PD-L1 testing in Italy.

Conclusion

PD-L1 expression correlates to the success of anti-PD1 treatment in NSCLC and other tissue types. Educational programs, society guidelines and early harmonization studies conducted and supported by a local pathology society (as seen in Germany), and various forums for training, can have a major impact on test adoption.
Promoting a test via education of clinicians on the treatment possibilities depending on the status of different markers will have a major impact on the therapeutic landscape. In markets with rapid test adoption there is a correlation with LDT use - embracing LDTs can have a major impact for rapid market penetration, especially outside the US.
Testing biomarkers in parallel enables not only a better decision for patient treatment, but also reduces the time necessary for therapeutic decision-making.
A better understanding of the specific factors that influence biomarker testing adoption for each country, and implementation of programs to overcome these barriers, would improve access to novel biomarker testing and improve therapeutic adoption rates.