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What impacts the cost-effectiveness of PD-L1 testing in non-small cell lung cancer?

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ABSTRACT

Programmed Death Ligand 1(PD-L1) testing is recommended for patients with Non-Small Cell Lung Cancer (NSCLC) at stage IIIB and IV, adenocarcinoma and squamous cell carcinoma. Up to now, no clinical-pathological parameters are perfectly able to select a positive PD-L1-patient. For this reason PD-L1 testing is mandatory for patients with advanced NSCLC for whom an immune checkpoint inhibitor treatment is appropriate. Several studies on the cost-effectiveness of immune checkpoint inhibitors in this subset of patients have been published.

Chouaid et al. (*Lung Cancer* 127, 2019, 44–52) assessed the cost-effectiveness of pembrolizumab versus standard of care platinum-based chemotherapy from the French health care system perspective.

The authors did not, however, mention that the type of PD-L1 testing used can impact the cost of therapy, which varies according to methods used and to the country where PD-L1 testing is performed. The lack of specific guidelines can lead to discrepancies in technical and/or clinical validation procedures of PD-L1 testing, and that this also impacts the cost of therapy. In conclusion, the effect of PD-L1 testing on cost-effectiveness of immune checkpoint inhibitors depends on the antibody and platform used for patient selection. The barriers to overcome are the limited quantity of biological material available and lack of standardization of the PD-L1 IHC test methods.

Programmed Death Ligand 1(PD-L1) testing is recommended for patients with Non-Small Cell Lung Cancer (NSCLC) at stage IIIB and IV, adenocarcinoma and squamous cell carcinoma. Up to now, no clinical-pathological parameters are perfectly able to select a positive PD-L1-patient. For this reason PD-L1 testing is mandatory for patients with advanced NSCLC for whom an immune checkpoint inhibitor treatment is appropriate. Several studies on the cost-effectiveness of immune checkpoint inhibitors in this subset of patients have been published [1–3]. Chouaid et al. assessed the cost-effectiveness of pembrolizumab versus Standard of Care (SoC) platinum-based chemotherapy from the French health care system perspective. A three-state partitioned survival model was adapted to project outcomes and costs of squamous and non-squamous NSCLC patients respectively, over a 10- year time horizon [1]. They did not, however, mention that the type of PD-L1 testing used can impact the cost of therapy, which varies according to methods adopted and to the country where PD-L1 testing is performed. When selecting patients for treatment with the anti-programmed death 1(PD1)/PD-L1 drug, in the U.S., the FDA requires the use of a specific antibody and platform. Conversely, the European Medicines Agency does not limit the use of specific PD-L1 antibodies and platforms and so European laboratories can decide how to perform PD-L1 testing and whether to carry out the technical/ clinical test validation, or both, leading to potential discrepancies in technical and/or clinical validation procedures and impacting treatment costs. The type of antibodies and platforms for immunohistochemistry (IHC) influence PD-L1 results and patient selection.

The most frequently used anti PD-L1 antibody clones are Dako (22C3,

28-8, Agilent Technologies, Santa Clara, CA) and Roche Ventana (SP263, SP142, Tucson, AZ). In the Blueprint study [4], both Dako antibodies and the SP263 Roche Ventana antibody showed similar immunoreactivity in tumor cells, whereas SP142 displayed greater positivity in inflammatory cells than the other antibodies. We also observed different results for the two Roche Ventana antibody clones in terms of PD-L1 expression in inflammatory and epithelial cells (Fig. 1A-B).

A specific diagnostic test may be chosen on the basis of reagent costs or platform used in an institute. This can be a limit for countries with poor economic resources and few dedicated personnel. In fact, the lack of technology and of a Pathology Unit in a centre can delay the start of treatment because specimens are usually processed elsewhere and also because PD-L1 evaluation is not concomitant with that of other biological markers. Another important issue concerns the reimbursement of reagent costs given that the cost of PD-L1 evaluation using IHC may not be covered by the National Health Service. The choice of platform and PD-L1 IHC test may be company-sponsored, influencing the type of test used and thus also patient selection.

In fact, PD-L1 expression may vary on the basis of the cut-off scoring system

used to evaluate antibody positivity.

The authors concluded that Pembrolizumab appears cost-effective versus SoC chemotherapy for first-line treatment of PD-L1- positive (50%) metastatic NSCLC patients in France, assuming willingness-to-pay under 100,000€

Quality –Adjusted Life Year [1].

Although PD-L1 biomarker assessment has a much lower cost than that of PD-L1 therapy (PD-L1 reagents cost from €50-150 according to the PD-L1 IHC test used), its potential impact on the cost of treatment is very high.

This highlights the importance of choosing the most suitable PD-L1 test.

In conclusion, the effect of PD-L1 testing on cost-effectiveness of immune checkpoint inhibitors depends on the antibody and platform used for patient selection. The barriers to overcome are the limited

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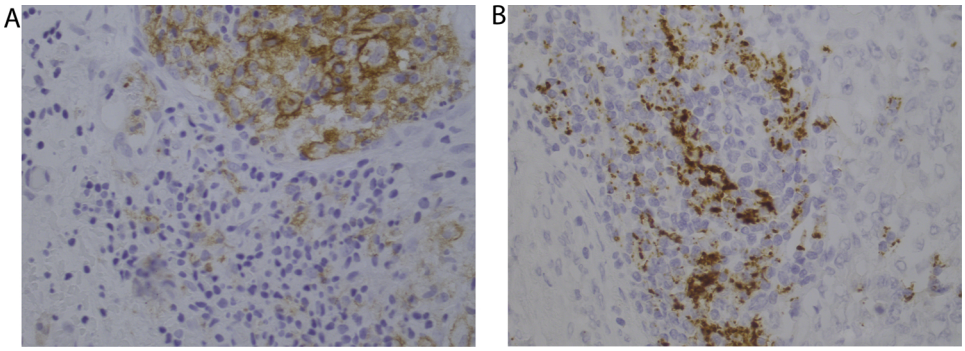

Fig. 1. Paraffin-embedded stained section of tissue samples from patients with non-small cell lung cancer stained on the Ventana BenchMark XT platform using A) SP263 Roche-Ventana antibody: strongly PD-L1-positive epithelial cells and a few weakly-positive lymphocytes and macrophages are present (magnification ×40) and B) SP142 Roche-Ventana antibody: strongly PD-L1-positive lymphocytes and macrophages and negative epithelial cells are present (magnification ×40).

quantity of biological material available and lack of standardization of the PD-L1 IHC test methods.

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Disclosure

The author has no conflicts of interest to declare.

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