

# **Nivolumab cost-effectiveness improves by selecting non-squamous NSCLC PD-L1+ patients**

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Nivolumab (NIV), a checkpoint inhibitor approved for all squamous and non-squamous non-small cell lung cancer (NSCLC) patients in 2015, is not cost-effective when compared to treatment with docetaxel (DOC), chemotherapy medication. However, a Swiss analysis showed the cost-effectiveness of NIV is improved when patients are treated with NIV based on PD-L1 positivity (PD-L1+), or if there is a reduction in dose or drug price.

NIV, an antibody that targets programmed cell death protein 1 (PD1) by blocking a signal that would have otherwise prevented T cells from attacking cancer cells, was recently approved for use in several countries as second-line treatment for patients with advanced squamous or non-squamous NSCLC. There is a growing global concern over the cost and value of cancer care and treatment especially as it relates to recently approved cancer drugs like NIV. In December 2015, the United Kingdom National Institute for Health and Care Excellence (NICE) reported that for squamous NSCLC, NIV was not cost-effective per quality-adjusted life year (QALY) gained. Further, in February 2016 a Canadian study comparing NIV to DOC and erlotinib in NSCLC found that NIV had the highest expected per-patient cost, but also improved per-patient life years (LYs) and QALYs. While there are reports of NIV not being cost-effective in squamous NSCLC, it's a worthwhile endeavor to explore the cost-effectiveness of NIV on non-squamous NSCLC.

A group of Swiss investigators used a literature-based Markov modelling approach to calculate the incremental cost effectiveness ratio (ICER) for NIV compared to DOC in patients with non-squamous NSCLC from Switzerland's healthcare system perspective. The model was constructed based on the clinical data from the CheckMate-057 study and compared: 1) all patients treated with DOC; 2) all patients treated with NIV; and 3) patients treated according to their PD-L1 status ( $\geq 1\%$  or  $\geq 10\%$  tumor positivity by immunohistochemistry testing). The primary measurement endpoint was the ICER expressed as cost per QALY gained using NIV compared to DOC in patients with NSCLC. The secondary endpoint was the ICER comparing PD-L1 testing with DOC or NIV. The ICERs were compared to a possible willingness-to-pay (WTP) threshold of CHF100,000 per QALY gained. The effect of reduction of dose and price of NIV on ICERs were also assessed. Effectiveness data were inferred from the progression-free survival (PFS) and overall survival (OS) outcomes reported in the original CheckMate-057 trial publication and supplementary materials. Cost was established using Swiss public healthcare prices when available.

The results of the study published in the *Journal of Thoracic Oncology*, the official journal of the International Association for the Study of Lung Cancer (IASLC), demonstrated that giving NIV only to patients with positive PD-L1 tests compared to treating all patients with DOC or all patients with NIV was more cost effective in both scenarios. Treating all patients with NIV compared to all with DOC resulted in a ICER of CHF177,478/QALY gained, whereas, treating only patients with  $\geq 1\%$  or  $\geq 10\%$  PD-L1+ with NIV compared to DOC resulted in ICERs of CHF133,267/QALY and CHF124,891/QALY, respectively, both ICERs above the WTP CHF100,000 threshold. Although NIV for all patients was weakly dominated by the test-based strategies (and a comparison not justified from a health economic perspective), treating only patients with PD-L1+ with NIV versus all patients with NIV is more cost-effective. Treating patients with  $\geq 1\%$  or  $\geq 10\%$  PD-L1+ resulted in ICERs of

CHF65,774/QALY and CHF37,860/QALY, respectively, resulting in ICERs below the WTP threshold of CHF100,000/QALY. Further, reduction of dose to 1mg/kg and reducing NIV price by at least 45% reduced ICERs to below the WTP threshold.

The authors comment that, "The easiest way to improve cost-effectiveness is to lower drug prices. Depending on the setting, a cost reduction of NIV by at least 33% (NIV given to patients with PD-L1+ tumors versus DOC) or 45% (NIV given to all patients versus DOC) resulted in ICERs below or near the WTP threshold. It will be interesting to see if NICE reaches similar conclusions for non-squamous NSCLC and if they can negotiate a lower price for NIV in the UK. Although our results are not directly generalizable to other countries, the Swiss system is comparable to the US system and to many European countries in terms of patient care and cost. However, in our analysis, both PD-L1 test strategies (NIV only for those patients reaching the  $\geq 1\%$  or  $\geq 10\%$  positive thresholds) resulted in higher mean costs but also better effectiveness than treating all patients with NIV. PD-L1 testing should be considered in [patients](#) with non-squamous NSCLC who are candidates for PD-L1 checkpoint inhibitor therapy."

**More information:** Klazien Matter-Walstra et al. A cost-effectiveness analysis of nivolumab versus docetaxel for advanced non-squamous non-small cell lung cancer including PD-L1 testing, *Journal of Thoracic Oncology* (2016). [DOI: 10.1016/j.jtho.2016.05.032](https://doi.org/10.1016/j.jtho.2016.05.032)

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