When Does a Treatment Effect Really Stop? Exploration of Different Methods for Modelling Treatment Waning

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OBJECTIVES
• We aimed to investigate the implications of different waning methods used in past NICE appraisals for predicted survival, using published CheckMate-057 (NCT01673867) data on nivolumab-versus-docetaxel in metastatic NSCLC, as a case study.

BACKGROUND
• Novel treatments, such as immune-oncology therapies (IOs), have emerged in recent years as potential treatments for a variety of cancers. Due to their mechanism of action, these treatments may offer a long-term treatment effect following treatment discontinuation.1
• Treatment effect duration is a common uncertainty in health technology assessment (HTA) and treatment waning is frequently considered in cost-effectiveness analyses.

METHODS
• Nivolumab and docetaxel were modelled using independent extrapolations of Kaplan-Meier (KM) data from the CheckMate-057 trial in a metastatic non-small cell lung cancer (NSCLC).1 We also modelled modelling docetaxel by applying a cox-regression model hazard ratio (HR) to the nivolumab extrapolation.

RESULTS
• There is limited guidance on treatment waning and there is inconsistency in HTA about how it is implemented. Treatment waning methodology is an area of uncertainty in cost-effectiveness analyses in HTA submissions.

CONCLUSIONS
• In our research, the choice of waning method is most influential when both the intervention and comparator are modelled independently in this situation. The choice between applying a HR versus equalisation of hazards, and between immediate versus gradual waning, can both have substantial impact on the results.

• When the comparator is modelled by applying a HR to the intervention, the choice of waning method has a minimal impact on the results, and only the choice between immediate or gradual waning results in any non-negligible variation.

• The absence of more data commonly results in uncertainty regarding long-term extrapolation, particularly for novel therapies such as IOs. Consequently, the results of this case study indicate that gradual waning methods based on the equalisation of hazards may represent the most appropriate approach for reducing variation in projected survival outcomes in instances where there is uncertainty associated with the choice of the most appropriate curve for the intervention.

• The variation between treatment waning methods, further methodological guidance and transparency in the implementation of waning methods would be valuable for future HTA and cost-effectiveness assessments.

REFERENCES