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Faculty of Health, Medicine and Life Sciences

Early Health Technology Assessment of the Lymphocyte Antigen 75 Biomarker for Cutaneous Melanoma

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Abbreviations. SLNB: Sentinel lymph node biopsy; LY75: Lymphocyte antigen 75; CAU: Care as usual; TP: True positive; FP: False positive; TN: True negative, FN: False negative; NMB: Net Monetary benefit

Introduction

Adjuvant treatment selection and prognosis options for patients with advanced melanoma continue to be **suboptimal**. Sentinel lymph node biopsy (SLNB), the standard practice to classify patients' melanoma stage and guide treatment decisions, can fail to accurately identify a significant proportion of patients that require adjuvant treatment with immunotherapy (1,2).

However, a new **biomarker**, the lymphocyte antigen 75 (**LY75**), could be used in the diagnostic pathway to improve adjuvant treatment decisions, patient outcomes and cost-effectiveness(3).

Aim: This study provided an **early health technology assessment** of the added value of LY75 compared with care as usual (CAU) in patients suspected of having cutaneous melanoma in all stages of the disease (i.e., stage I/II/III/IV) through model-based cost-effectiveness analyses.

Methods

Model type: Decision tree to classify patients as TP/FP/TN/FN combined with a probabilistic state-transition with three health states (Progression free, progressed disease and death).

Software: Microsoft Excel ©

Perspective: Societal with lifetime horizon.

Intervention: Six strategies that included LY75 testing in different positions in the diagnostic pathway (Figure 1).

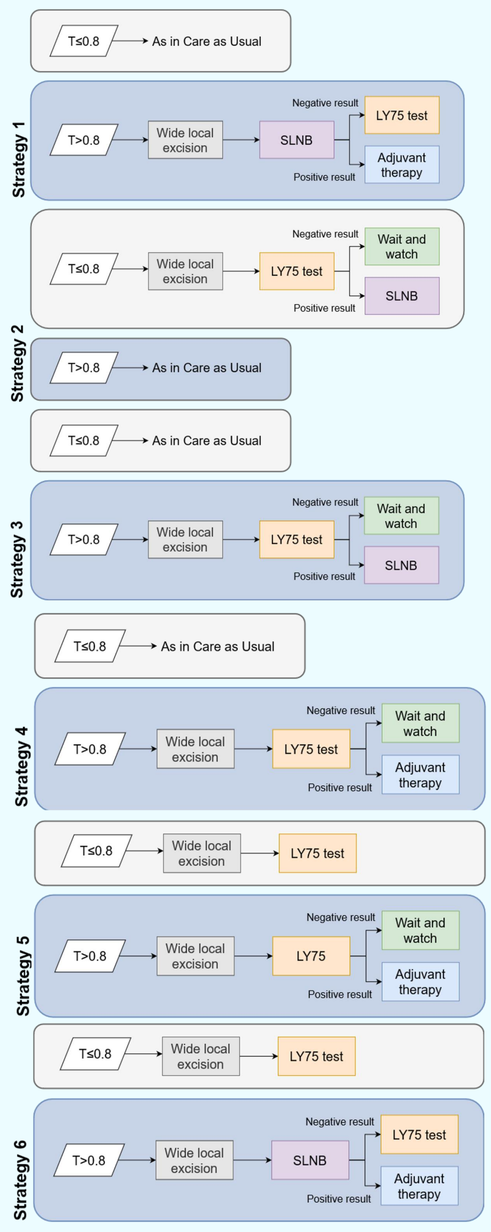
Comparator: CAU (Figure 1).

Inputs: Derived from relevant and up-to-date literature.

- Test accuracy and survival data calculated based on prospective studies (3,4).
- Prevalence of patients requiring treatment (4,5)
- Utility values (6,7)
- Costs: tests costs, health state costs, and event costs (8,9).

Outcomes: Sensitivity and specificity, expected costs and QALYs, sensitivity and scenario analyses.

Figure 1: CAU (Left). LY75 testing strategies (Right). T: Tumor size in mm



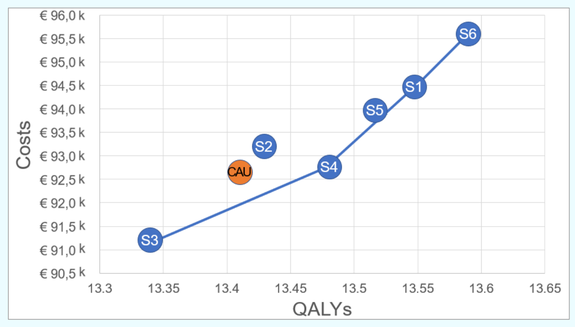
Results

Strategies 6 and 3 lead to the highest sensitivity and specificity, respectively (Table 1). As per **Figure 2**, strategy 2 and CAU brought less benefit and higher costs than the other strategies.

Table 1: Base case results. iNMB; incremental net monetary benefit with WTP at €80,000 per QALY compared to CAU

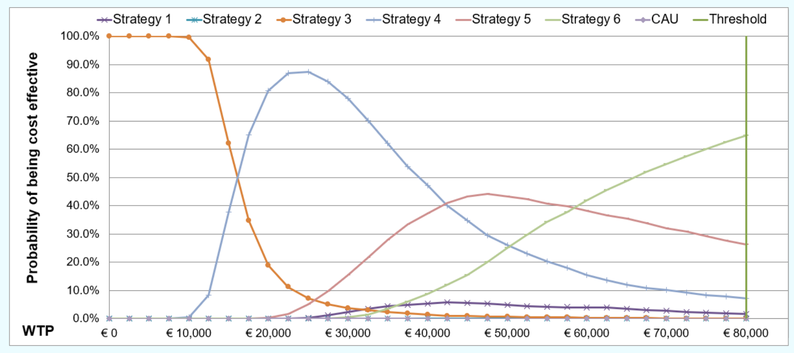
	Sensitivity	Specificity	ICER	iNMB (80)
Strategy 1	0.70	0.86	€13,435	€ 9,112
Strategy 2	0.48	0.88	€26,900	€ 1,176
Strategy 3	0.30	0.98	€21,484	-€ 3,989
Strategy 4	0.57	0.95	€1,608	€ 5,387
Strategy 5	0.65	0.90	€11,040	€ 7,743
Strategy 6	0.79	0.81	€16,449	€ 11,468
CAU	0.44	0.89	-	-

Deterministic and probabilistic (5,000 simulations) analyses showed similar robust results, with strategies 6 and 1 being the most cost-effective in almost all cases. Test sensitivity and number of false negative patients were the most influential parameters for NMB.



As per **Figure 2**, at higher WTP thresholds, CAU is less likely to be cost-effective.

Figure 2: (Above) Cost-effectiveness frontier. (Below) Cost-effectiveness acceptability curves.



Discussion

Five of the six proposed strategies resulted in QALY gains and higher costs compared to CAU. Strategies focused on adding LY75 after a negative SLNB result led to better health outcomes while remaining **cost-effective**.

Multiple **assumptions** were deemed necessary in this study, such as the independence of accuracy results of test sequence or clinicians acting upon the results of LY75 in the same way as they would do for SLNB. Given the reduced evidence on LY75, **incremental strategies** should be explored for **LY75 evidence collection** and **positioning** in the current care pathway.

Conclusion

LY75 can potentially be a **cost-effective add-on** or even **replacement** of CAU to guide adjuvant treatment decisions, given Dutch WTP thresholds. Our analyses showed that strategies focused on **preventing under-treatment** with adjuvant therapy led to higher NMB. These strategies should be prioritised in **further research** on LY75 accuracy. Nonetheless, value of information analyses are still necessary for the **incremental** development of the LY75.

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