An Exploratory Cost-Effectiveness Analysis of Cancer Vaccines in Combination with Current Immune Checkpoint Inhibitors Vs Immune Checkpoint Inhibitor Monotherapy: A Case Study for V940 in High-Risk Stage 3 Melanoma in the US

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Objective

To explore the cost-effectiveness of V940 in combination with pembrolizumab contingent on patent expiration (and subsequent 90–99% approximate discount on list price) of immune checkpoint inhibitor (ICI) therapies within the US market.

Background

- Therapeutic cancer vaccines have been in development over the past decade as a promising type of immunotherapy (IO). They are expected to soon enter the market and may provide a step-change in the care for patients with solid tumours. Cancer vaccine market entry is expected to coincide with patent expiration, and therefore price reduction, of some ICI therapies, which represent current standard of care.
- V940 is one such example of a cancer vaccine currently in development. V940 generates specific T cell responses based on the unique mutational signature of a patient's tumour. V940 is being investigated in the clinical trial V940-001 in combination with pembrolizumab (V940 + pembrolizumab) for the adjuvant treatment of patients with resected high-risk stage three melanoma.[1]

Methods

- A lifetime four-state (recurrence-free [RF], locoregional recurrence [LR], distant metastases [DM] and death) partitioned survival model was developed leveraging a published model.[2]
  - Pembrolizumab monotherapy was modelled in line with its licence and pivotal trial, KEYNOTE-054,[3,4] and at the current list price of $22,674 per dose.[5] V940 + pembrolizumab was modelled in line with the phase three trial, V940-001.[1]
  - Pembrolizumab monotherapy survival curves were derived from Bensimon (2019).[2] The efficacy of V940 in combination with pembrolizumab was derived from hazard ratios (HRs) from indicative data from KEYNOTE-942 which were applied to the pembrolizumab survival curves.[6] The RF survival (RFS) HR was 0.51, DM-free survival (DMFS) HR was 0.384 and the overall survival (OS) HR was derived as an average of the RFS and DMFS HR in the absence of indicative data for this outcome.[†]
  - Subsequent treatment costs, disease management costs and terminal care costs were modelled in line with Bensimon (2019).[2] A willingness to pay (WTP) threshold of $100,000 per QALY gained, a lifetime time horizon and 3.5% discounting (for both costs and benefits) were assumed.
- A threshold analysis was conducted to observe the incremental cost-effectiveness ratio (ICER) of V940 + pembrolizumab vs pembrolizumab monotherapy, whilst V940 unit price was varied and V940 + pembrolizumab efficacy was set by the indicative data from KEYNOTE-942.[6]
- A second threshold analysis was conducted to test the efficacy at which V940 + pembrolizumab would be cost-effective vs pembrolizumab monotherapy. For the purpose of this exploratory analysis the HRs for OS, RFS and DMFS were set to the same value and all three varied simultaneously while the cost-effectiveness price was observed.

Results

- A reduction in pembrolizumab price improves cost-effectiveness estimates for V940 despite both treatment arms experiencing an equal reduction in treatment acquisition cost per dose. This result is driven by V940 + pembrolizumab's higher survival within year one of the RF state which results in more doses of pembrolizumab being received in that arm.
  - If V940 enters the market whilst pembrolizumab is not yet generic (at current list price), V940 is expected to be cost-effective up to an approximately 14% higher cost per dose compared to pembrolizumab's current list price. If V940 enters the market when pembrolizumab is generic (assumed 99% discount on current list price), V940 would be cost-effective up to an approximately 20% higher cost per dose compared to pembrolizumab's current list price. This is presented in **Figure 1** and assumes HRs are aligned with indicative data from the KEYNOTE-942 trial.[6]
- As expected, an increase in vaccine efficacy allows for a higher cost-effective vaccine price, as seen in **Figure 2**. Assuming V940 enters the market at the same list price (cost per dose) as pembrolizumab, a HR (equivalent for OS, RFS and DMFS) of approximately 0.752 would be needed for V940 + pembrolizumab to be cost-effective versus pembrolizumab monotherapy at a 0% discount from list price and a HR of approximately 0.758 would be needed compared to pembrolizumab monotherapy at a generic price (assumed 99% discount).

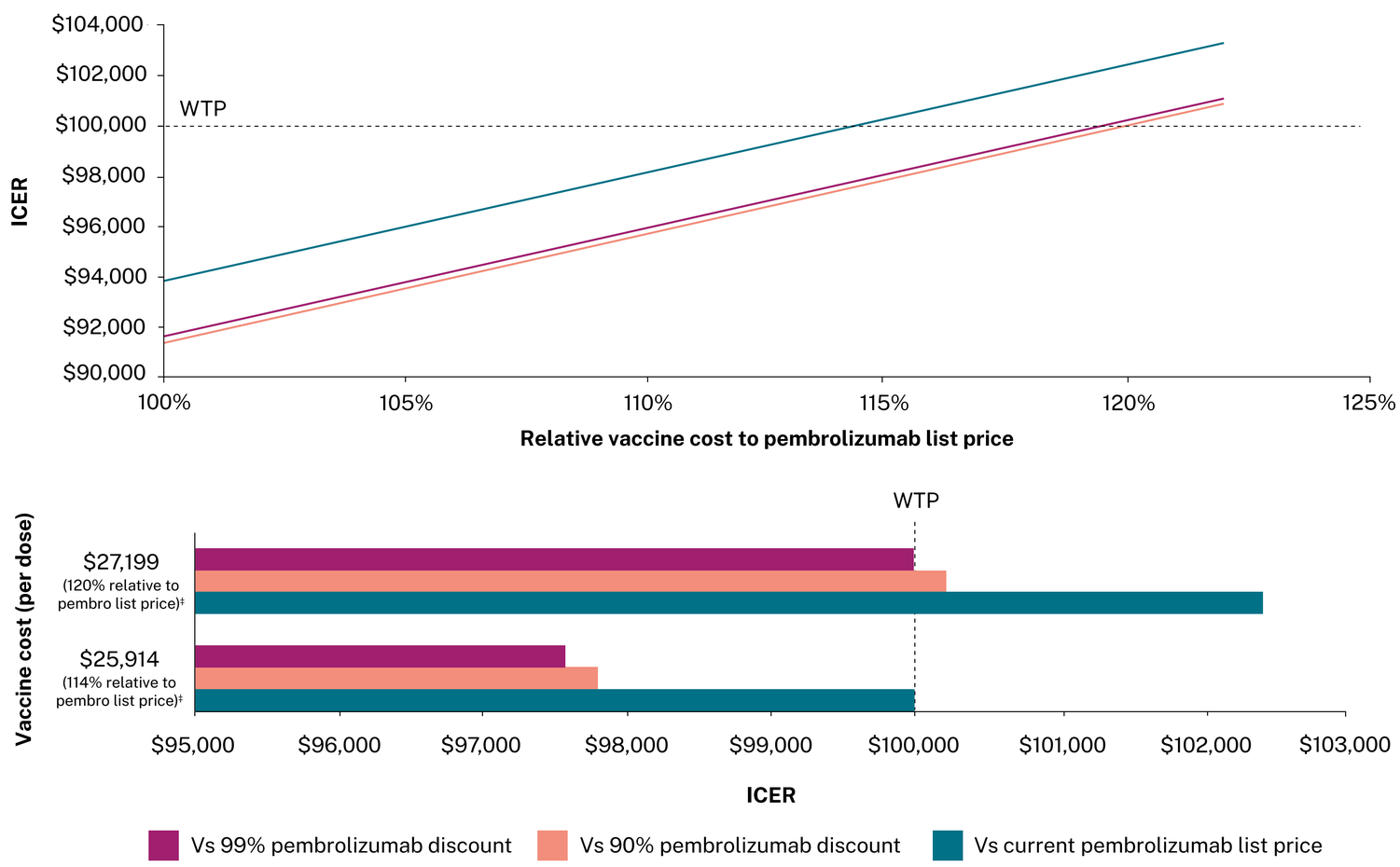
Conclusion

The cost-effectiveness of cancer vaccines such as V940 will be dependent on pricing strategy, however preliminary trial results suggest it will likely be cost-effective at a higher price point (cost per dose) than the current list price of pembrolizumab at a WTP threshold of $100,000 per QALY gained. Exploratory analyses also indicate that the large discounts (expected to be 90–99%) seen due to patent expiry will lead to a higher cost-effective vaccine price.

[†]Within the corresponding abstract of this poster, OS HR was derived as an average of RFS and DMFS HRs but was incorrectly calculated as 0.46, this has been updated to the correct value of 0.45 for this poster.

FIGURE 1

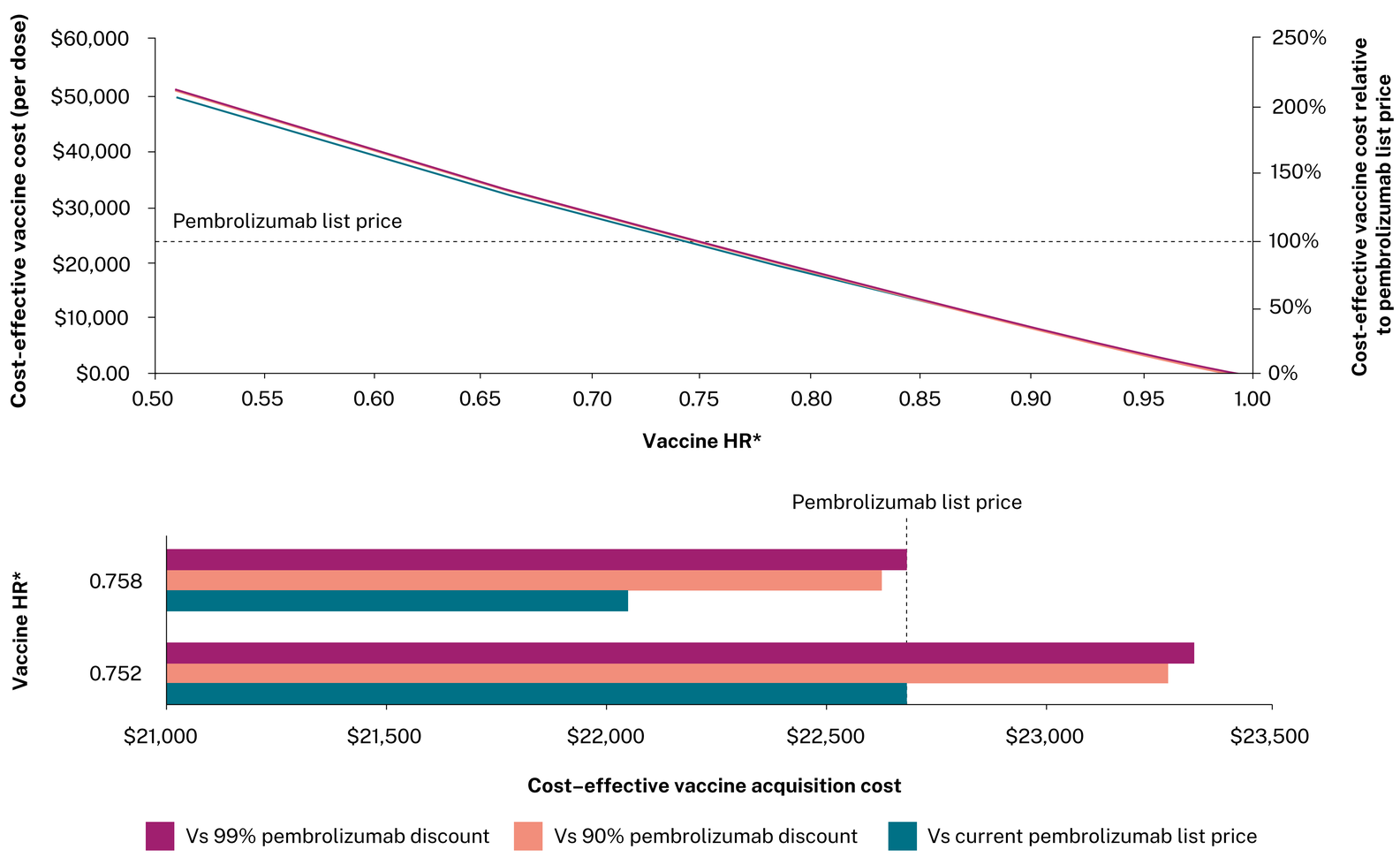
Relationship between vaccine cost and expected ICER (V940 + pembrolizumab vs pembrolizumab monotherapy)



‡Given to the closest 1%.

FIGURE 2

Impact of vaccine efficacy on cost-effective acquisition cost



*HR are applied to OS, RFS and DMFS and are rounded for presentation purposes. 90% pembrolizumab discount is obscured by the 99% list price trend lines.

Abbreviations: DMFS: distant metastases-free survival; **HR:** hazard ratio **ICER:** incremental cost-effectiveness ratio; **OS:** overall survival; **Pembro:** pembrolizumab; **RFS:** recurrence-free survival; **WTP:** willingness to pay.

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