How immunotherapies have altered the future of cancer treatment: Patients living longer, healthier lives

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Background and objective

Immunotherapies have led to a paradigm shift in mortality rates for patients with melanoma resulting in an overall improvement in their survival and quality of life. This review maps this shift by comparing changes in patient outcomes, alongside the frequency of positive HTA decisions for immunotherapy treatments in the UK and Australia between 2019 and 2023.

Methods

A TLR was conducted using Embase, ClinicalTrials.gov, and PubMed, for pivotal clinical trials, and the UK's NICE and Australia's PBAC databases for TAs for immunotherapies in melanoma.
RCTs conducted between 2019 and 2023, in patients with treatment-naive melanoma, were included to capture the most recently reported trials and associated outcomes with the longest follow-up. The search in HTA databases did not include a time limit to ensure that all key immunotherapies available for the treatment of melanoma across both HTA markets were represented in the results.

Results

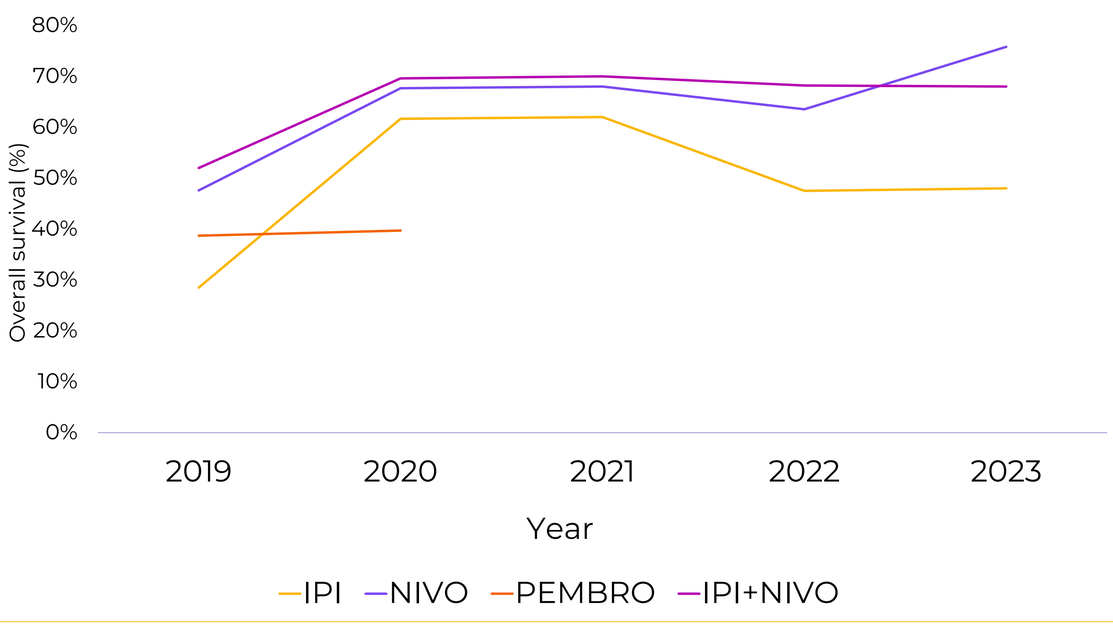
Pivotal clinical trials

Overall, 19 RCTs reported updated results for ipilimumab, nivolumab, and pembrolizumab (1-19). Of these, 5 RCTs reported results for ipilimumab (1,8,14-16), 12 for nivolumab (2,4,6,8,10-11,13-19), and 2 for pembrolizumab (7,12) as monotherapy regimens. Results for ipilimumab used in combination with nivolumab were reported across 8 trials (3,5,6,9,11,17,18,19). Where reported, baseline patient characteristics were largely comparable across these trials and included mostly male patients over the age of 55 years, with ECOG scores between 0 and 1.

Increasing OS rates

Average long-term (>1-year follow-up) OS rates followed an upward trend for nivolumab and pembrolizumab (monotherapy) and ipilimumab when used with nivolumab, as shown in Figure 1. The average OS rate, which was 48% in 2019, increased to 76% in 2023 for patients treated with nivolumab (2,4,6,8,10-11,13-19). Similarly, the OS rate, which was 52% in 2019, increased to 72% in 2023 for patients treated with combined ipilimumab and nivolumab (3,5-6,9,11,17-19). Likewise, the OS rate, which was 29% in 2019, increased to 62% in 2022 and then decreased to 48% in 2023 for patients treated with ipilimumab (1,8,4-16). The average OS rate for patients treated with pembrolizumab (7,12) was 39% in 2019, which increased to 40% in 2020.

Figure 1. Trend in overall survival of melanoma patients treated with immunotherapy between 2019 and 2023

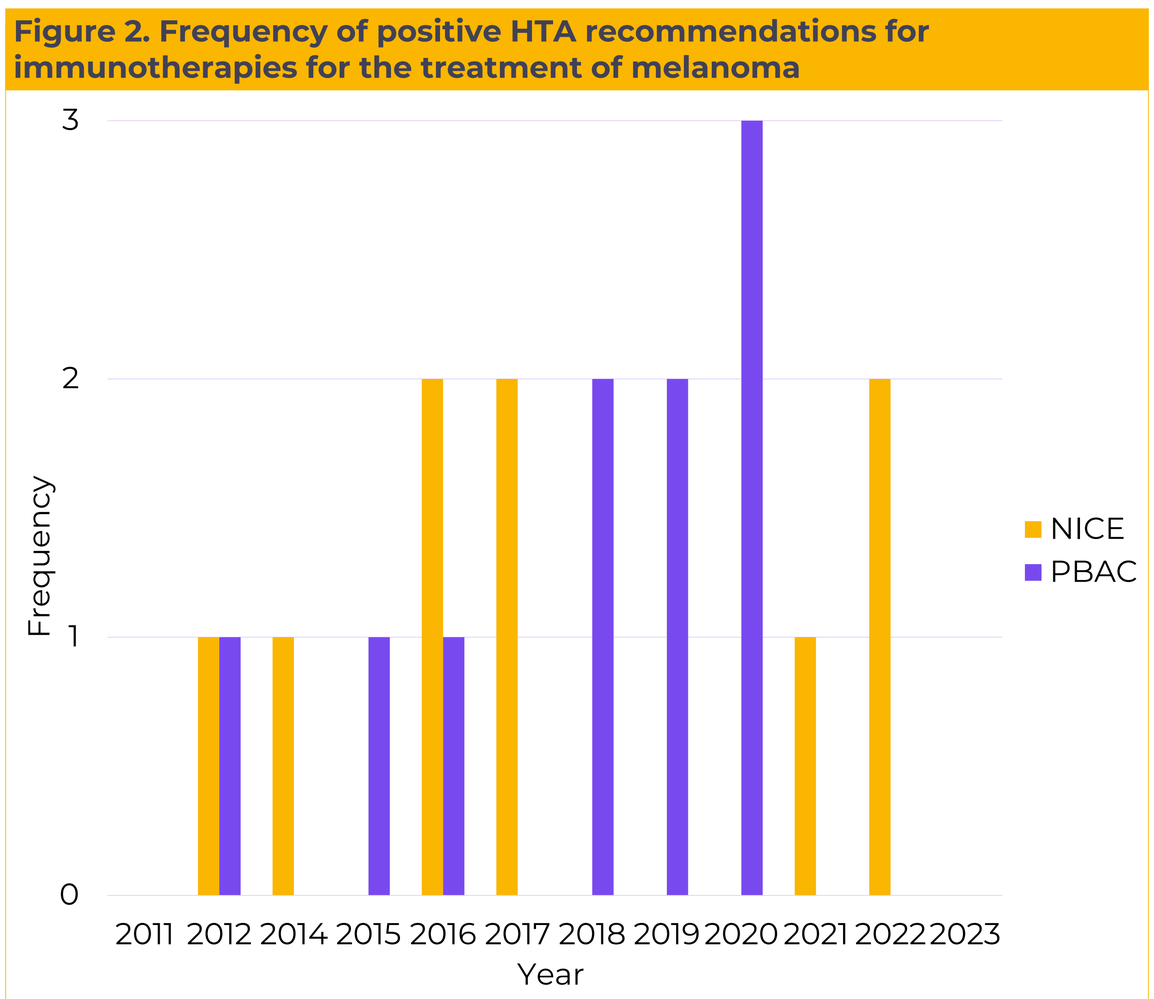


HTA database search results (UK and Australia)

A search of NICE's TA database returned 9 TA guidance documents for immunotherapies in melanoma, all of which received a positive recommendation (20-28).
Ipilimumab was the first immunotherapy to have received a positive recommendation in 2012 for patients with melanoma (27-28), followed by nivolumab (25-26) and combined nivolumab and ipilimumab therapy (24) in 2016, and pembrolizumab (20-23) in 2017.

Between 2012 and 2020, a review of PBAC's HTA database returned 21 guidance documents for immunotherapy in melanoma, of which 57.1% (n=12) achieved a positive recommendation (29-48). Ipilimumab was the first immunotherapy to be recommended for the treatment of melanoma (29) in 2012, followed by nivolumab (34) in 2015, combined nivolumab and ipilimumab therapy (31) in 2018, and pembrolizumab (40) in 2015.

Figure 2. Frequency of positive HTA recommendations for immunotherapies for the treatment of melanoma



Discussion

Comparing the OS reported in clinical trials since 2019 and the frequency of positive recommendations for immunotherapy-based treatment regimens for patients with melanoma, it can be observed that as average survival rates improved, so did the number of positive recommendations.
The main limitations of this TLR can be attributed to the efficacy outcomes being limited to OS, variability in the definition of OS which has not been accounted for, and the varying sample sizes across the clinical trials included in the results.
There is an opportunity for further research into changes in PFS, RFS, and PROs for patients with melanoma being treated with immunotherapy-based regimens. Analysis of outcomes by subgroups, irrespective of whether the tumour is resected or unresected and of the stage of disease progression, will provide further insight into how immunotherapies have led to an overall improvement in the long-term survival and quality of life in patients with melanoma.

Conclusions

Overall, it is evident that an **increased availability** of safe and effective immunotherapies has led to a **positive shift in mortality** rates for patients with melanoma when assessed for key outcomes.
A growing trend in positive recommendations for immunotherapies for melanoma in the last 5 years is suggestive of an increased confidence in the clinical trial data and a clear upward trajectory in the benefit being demonstrated with the use of pembrolizumab, nivolumab, and ipilimumab.

Abbreviations: ECOG, Eastern Cooperative Oncology Group; HTA, health technology assessment; IPI, ipilimumab; NICE, National Institute for Health and Care Excellence; NIVO, nivolumab; OS, overall survival; PBAC, Pharmaceutical Benefits Advisory Committee; PEMBRO, pembrolizumab; PFS, progression-free survival; PRO, patient-reported outcome; RCT, randomised controlled trial; RFS, relapse-free survival; TA, technology appraisal; TLR, targeted literature review; UK, United Kingdom

References

1. ASCIERTO et al., 2020
2.ASCIERTO et al., 2019
3.ATKINS et al., 2023
4.HODI et al., 2023
5.LARKIN et al., 2019
6. LIVINGSTONE et al., 2022
7.LONG et al., 2020
8.MANDALA et al., 2021
9.NAMIKAWA et al., 2020
10.aROBERT et al., 2020

For the full reference list, please refer to the Supplementary Appendix

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