The Value of Real-World Evidence (RWE) in Melanoma in Health Technology Assessment (HTA) Appraisals

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Introduction

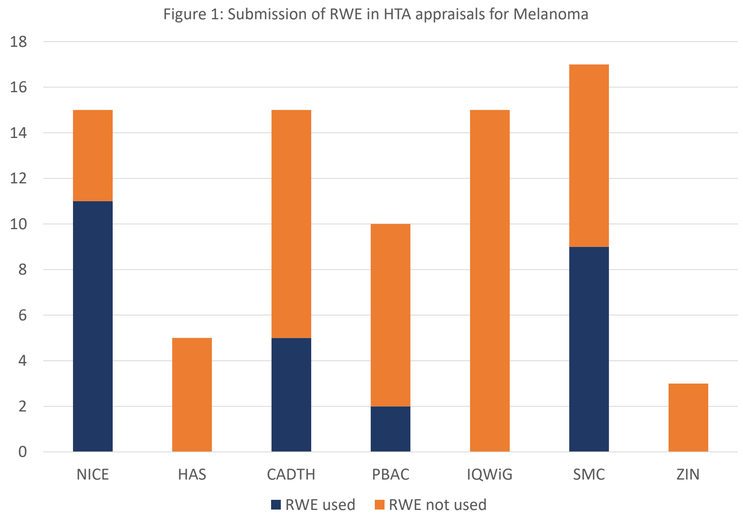
Increasingly real-world evidence (RWE) is also appraised to support the value of new health technologies that ensures timely patient access.[1] RWE is considered as evidence gathered outside of RCTs and derived from data obtained from non-randomized trials, observational studies, or databases amongst others. Decisions to reimburse are typically based on randomized controlled trials (RCTs) which often have high internal validity but low external validity.[2] Real-world data (RWD) may provide complimentary evidence that support data from RCTs. This analysis aims to assess the value of RWE in recent HTA appraisals for melanoma drugs in England, France, Canada, Australia, Germany, Scotland, and the Netherlands.

Methods

All publicly available appraisal reports from the NICE,UK; HAS, France; CADTH/pCODR(Canada), PBAC,Australia; IQWiG, Germany; SMC, Scotland; ZIN, Netherlands; between 1st January, 2011 and 30th September, 2022 for melanoma drugs were identified, from which RWE and reimbursement outcomes were extracted. From the analysed appraisals, matched product was identified, i.e. product which had been appraised in each of the target countries for the same indication to further explore similarities and differences in the use of RWE.

Results – RWE reports assessed

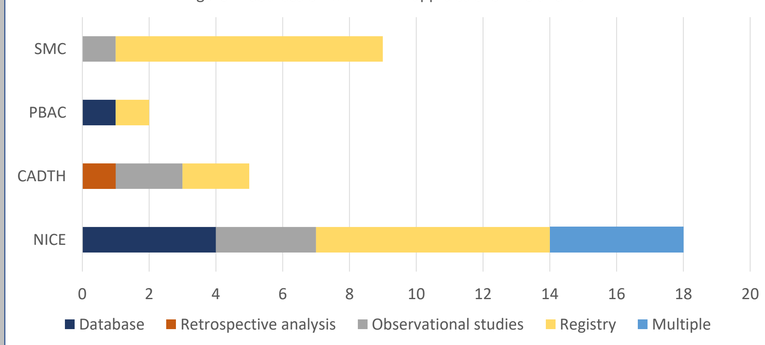
Figure 1: Submission of RWE in HTA appraisals for Melanoma



Eighty melanoma health technologies appraisal reports were assessed, of which RWE was submitted in 27 reports (33.75%); specifically, 11/15 of NICE appraisals, 2/10 of PBAC, 5/15 of pCODR, 0/5 of HAS, 0/15 of IQWIG, 9/17 of SMC, and 0/3 of ZIN.

Results – Sources of RWE in appraisals

Figure 2: Sources of RWE in HTA appraisals for Melanoma



NICE, CADTH, PBAC AND SMC have used various sources of RWE. NICE has utilized RWE from most of the sources in the study. NICE utilized RWE data from registries and chart audits to verify treatment patterns in target subgroup population. For CADTH retrospective analysis was often submitted to estimate the number of patients eligible for treatment in the target population.

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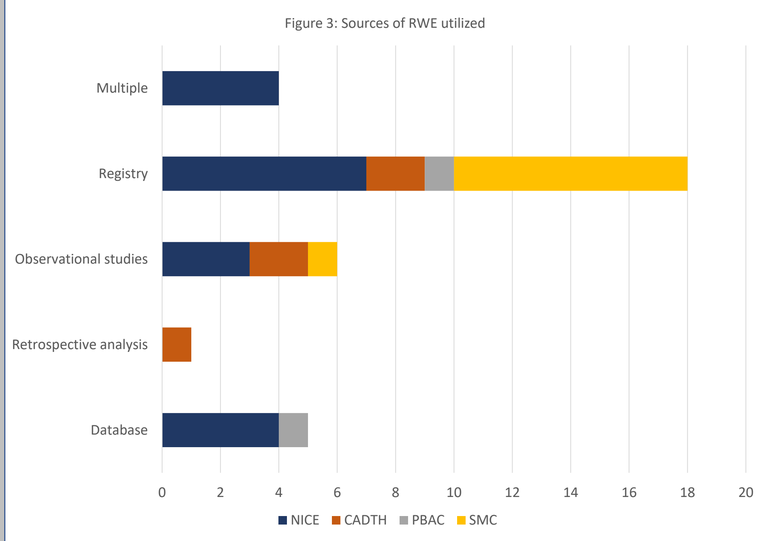
Results – Sources of RWE utilized

Figure 3: Sources of RWE utilized



RWE from registry data (19 studies), observational studies (6 studies), retrospective analyses (1 study) , or databases (4 studies), was submitted to identify treatment patterns and patient characteristics, and as supportive evidence for the economic evaluation, such as long-term survival data extrapolation and validation of economic model inputs. Where clinical efficacy data was submitted on single-arm study, RWE was submitted to reduce uncertainty. NICE, PBAC, SMC, and PBAC has cited RWE use for drug effectiveness while the ZIN and IQWiG have cited RWE for evidence on prevalence. The melanoma technologies assessed were nivolumab, dabrafenib/trametinib, encorafenib /binimetinib, pembrolizumab, talimogene laherparepvec, ipilimumab, dabrafenib, cobimetinib/vemurafenib, vemurafenib, amongst others.

Results – RWE used of Nivolumab submission

A matched product was identified named nivolumab which was appraised in each of the target countries for the same indication to further explore the use of RWE in melanoma appraisals.

Year	HTA	Indication	How RWE was used
2021	NICE	Nivolumab for adjuvant treatment of completely resected melanoma with lymph node involvement or metastatic disease	It extrapolated the overall survival data from the indirect comparison for 10 years and used the American Joint Committee on Cancer data for long-term survival (the same as the extrapolation of recurrence fee survival).
2016	CADTH	Nivoluman for Metastatic Melanoma	The OS data presented in this review are from the pre-specified interim analysis of OS of a database.
2017	PBAC	Nivolumab (Melanoma): Injection concentrate for I.V. infusion 40 mg in 4 mL, Injection concentrate for I.V. infusion 100 mg in 10 mL; Opdivo® for metastaic melanoma	Clinicopathologic data collected from the Melanoma Institute Australia (MIA) research database, including 4,540 patients with locoregional metastasis and no concurrent or prior diagnosis of distant metastasis
2016	SMC	As monotherapy for the treatment of advanced (unresectable or metastatic) melanoma in adults.	The sources of the clinical data used in the analysis included a covariate adjusted indirect comparison which compared nivolumab with ipilimumab and the BRAF inhibitors using parametric survival modelling of patient level data. Long-term melanoma registry data were used to capture overall survival (OS) from year 2 onwards for dacarbazine and the BRAF inhibitors.

Conclusion

RWE adds value to HTA appraisals particularly by supporting economic evaluation such as long-term survival extrapolation assumptions, to identify treatment patterns and patient characteristics. This allows expedited access of technologies in areas of high unmet clinical need through managed access schemes.

References

1. Khosla S, White R, Medina J, Ouwens M, Emmas C, Koder T, Male G, Leonard S. Real world evidence (RWE) - a disruptive innovation or the quiet evolution of medical evidence generation? F1000Res. 2018 Jan 25;7:111. doi: 10.12688/f1000research.13585.2. PMID: 30026923; PMCID: PMC6039945.

2. Spieth PM, Kubasch AS, Penzlin AI, Illigens BM, Barlinn K, Siepmann T. Randomized controlled trials - a matter of design. Neuropsychiatr Dis Treat. 2016 Jun 10;12:1341-9. doi: 10.2147/NDT.S101938. PMID: 27354804; PMCID: PMC4910682.

Conflict of Interest

Ritu Shah, Mahendra Rai, Raju Gautam, Ram Prasanna are employees of EVERSANA at the time of conduct of the study