Seeing the Full Picture: Structured Model Conceptualisation to Incorporate the Dual Burden of Tumour Progression and Visual Morbidity in Choroidal Melanoma

Poster: EE714

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KEY TAKEAWAYS

Structured model conceptualisation with early clinical and patient expert involvement is essential to capture all dimensions of complex diseases

In choroidal melanoma, this iterative approach resulted in a novel model structure incorporating both tumour progression and vision-related morbidity

INTRODUCTION

- Choroidal melanoma (CM) is a rare primary eye cancer[1]
- Existing therapies provide good local tumour control, but lead to progressive vision-related morbidity (VRM) due to radiation-associated complications (plaque brachytherapy, proton beam therapy) or removal of the eye (enucleation)[1]
- If the cancer metastasises, patients will also experience cancer-related morbidity and mortality[1]
- Existing cost-effectiveness models (CEMs) in CM were developed for the metastatic setting and therefore may not capture VRM relevant to treatment of localised disease

OBJECTIVE

Develop a CEM structure that incorporates both oncological and VRM aspects of CM through structured model conceptualisation

METHODS

Population: early-stage disease/early CM (defined by either clinical features, actual or predicted growth, or cytological/genetic drivers)

Targeted review of:

- Clinical guidelines for CM
- Previous HTAs (NICE, SMC, NCPE, PBAC, CDA, IQWiG/G-BA, HAS, AETS, AIFA) and published economic models in CM
- NICE single technology appraisals (STA) and highly specialised technology (HST) appraisals in other eye conditions

Developed initial influence diagram to represent the interactions between the main components of the disease, treatments, and outcomes

Initial model conceptualisation

Tested the influence diagram and model concept with clinical and patient experts

Revised the model based on feedback

LIMITATIONS

- Model complexity requires higher level programming
- Tracking patients across VRM categories results in reduced power as patient numbers in each category can be low
- Due to a lack of data, the model assumes VRM varies by initial treatment and time since treatment, but not by time spent with the primary tumour controlled or progressing.

RESULTS

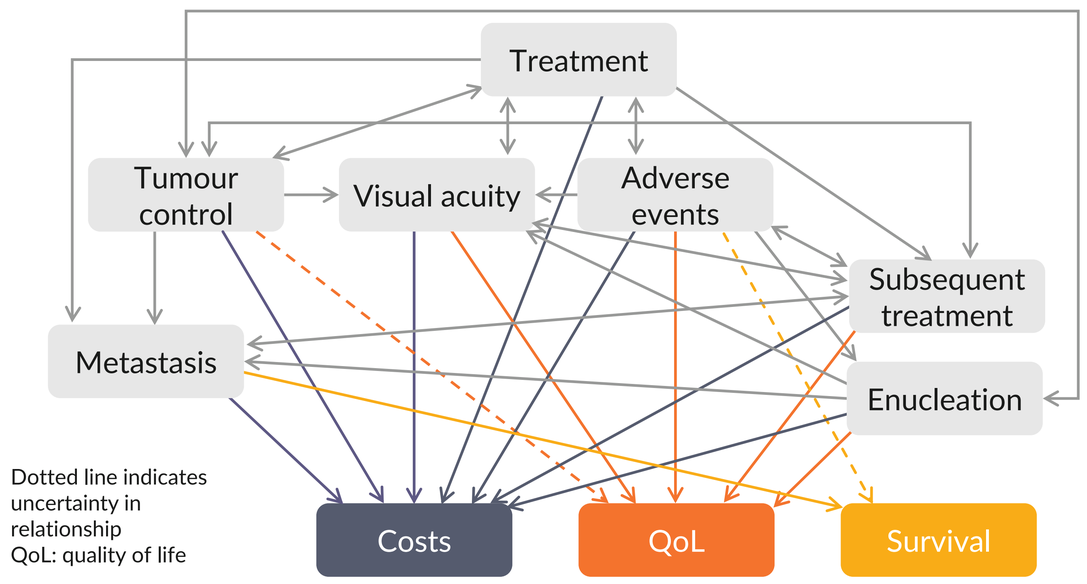
5 HTA appraisals for tebentafusp for the treatment of advanced uveal melanoma
NICE, SMC, IQWiG, CDA, PBAC

24 NICE appraisals in other eye conditions
23 STA, 1 HST

- no existing model has structurally incorporated both vision-related morbidity and oncological outcomes
- existing models in eye conditions are primarily based on visual acuity (VA) health states

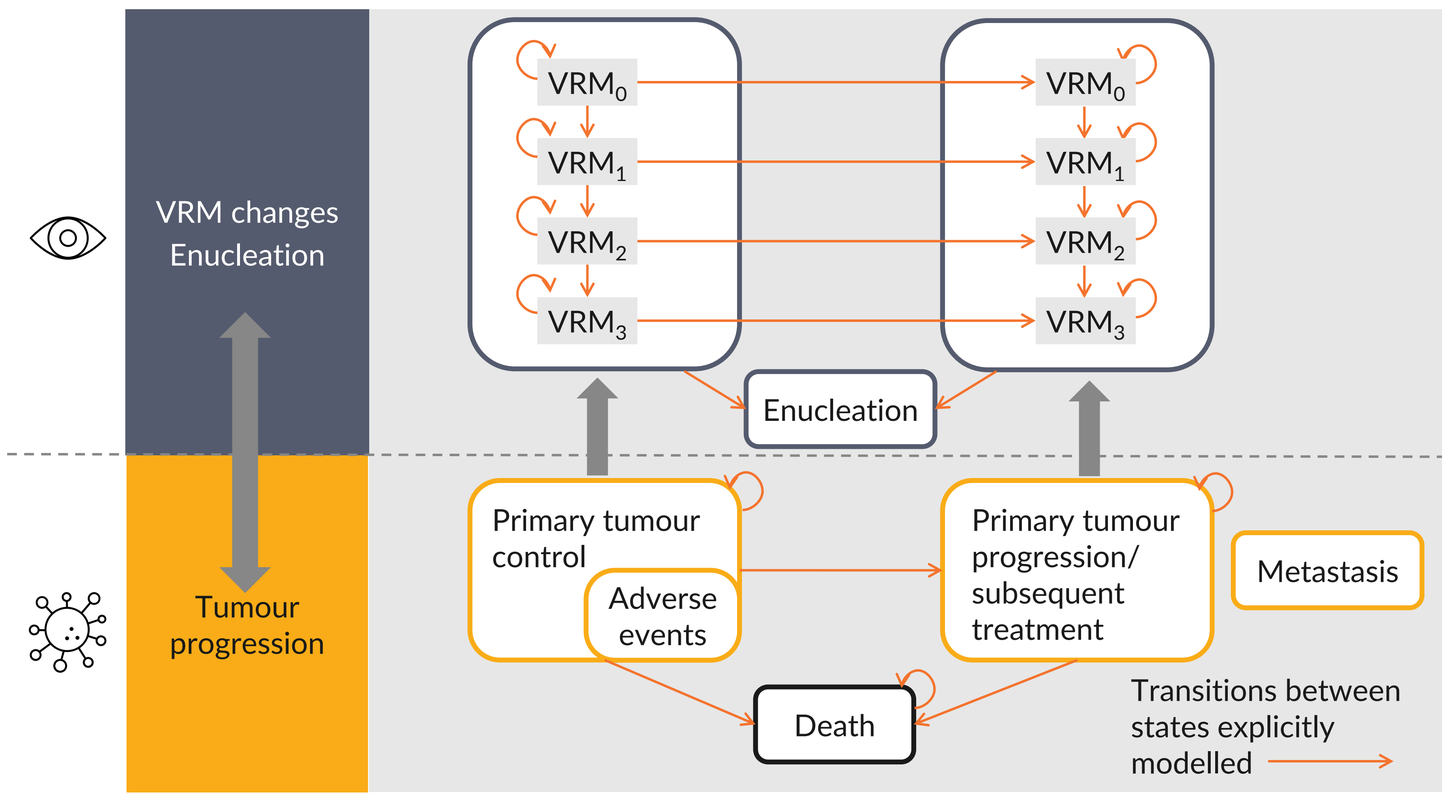
- A conceptual model was developed (**Figure 1**), which is a simplified representation of the impact of CM and treatment options on quality of life, all-cause mortality and costs

Figure 1. Influence diagram of choroidal melanoma



- Guided by the conceptual framework and existing modelling precedent, a novel cohort state-transition model was developed that tracked and linked oncology and VA outcomes over time
- Clinical/patient experience highlighted the burden of **treatment-induced VRM other than decreased VA** e.g., poor depth perception, double vision, flashing lights
- The model was revised to include VRM categories that combine changes in VA with or without additional visual impairments (**Figure 2**)

Figure 2. Final model structure



- VRM transitions depend on initial treatment and time since treatment, not time in tumour states.
- Time-dependent transition probabilities reflect the natural trajectory of vision loss following treatment
- Whilst modelled independently, the two dimensions interact; progression triggers subsequent treatment, shaping the VRM trajectory
- Enucleation is captured separately, reflecting quality of life impacts beyond VRM category alone

CONCLUSIONS

- Existing modelling approaches in choroidal melanoma focused on oncology outcomes and did not capture vision-related morbidity relevant for patients who are being treated for localised disease
- Existing models in other eye conditions mainly use visual acuity to measure disease progression; however, patient representatives stated that this does not fully capture the impact of treatment-related complications in choroidal melanoma
- Therefore, a novel cohort model capturing multiple aspects of vision-related morbidity while incorporating long-term oncology outcomes was developed
- Future developments could include incorporation of indirect effects of tumour control on mortality through metastasis risk; additional vision-related morbidity categories; incorporation of the effects of visual impairment on mortality[2]

Visible Analytics
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ISPOR Europe 2026
8–11 November
Vienna, Austria

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1. Kaliki and Shields. Eye (Lond). 2017;31(2):241
2. Christ et al. Invest Ophthalmol Vis Sci. 2008. 49(8):3318.