Uveal Melanoma : Am I Cured Yet ?

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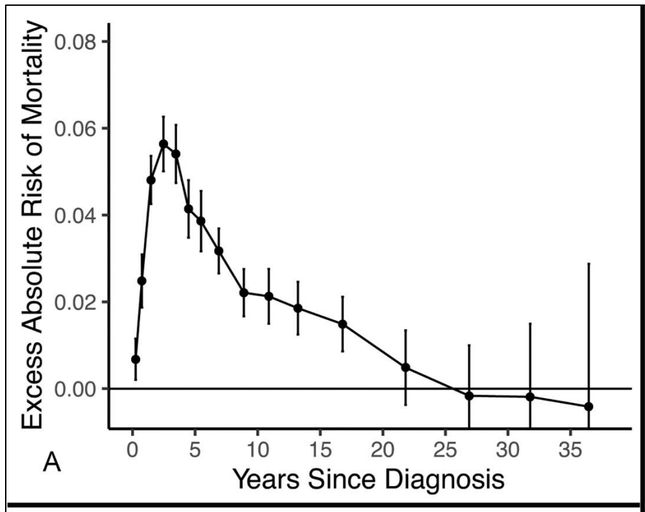
Aim: To investigate time to cure and cured fraction in patients with uveal melanoma.

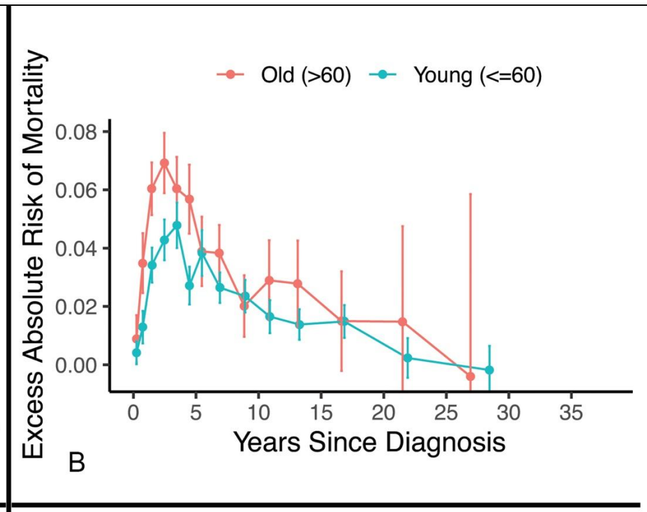
Introduction: When does the long-term survivorship translate into cure from uveal melanoma? The goal of this study was to integrate uveal melanoma SEER data and molecularly prognosticated patient data to assess, the fraction of patients that survive through times of excess mortality. Conditional on parametric models of EAR, we estimate subtype and total times to cure (TTC) and fraction of patients alive at TTC, i.e. cured fractions (CF).

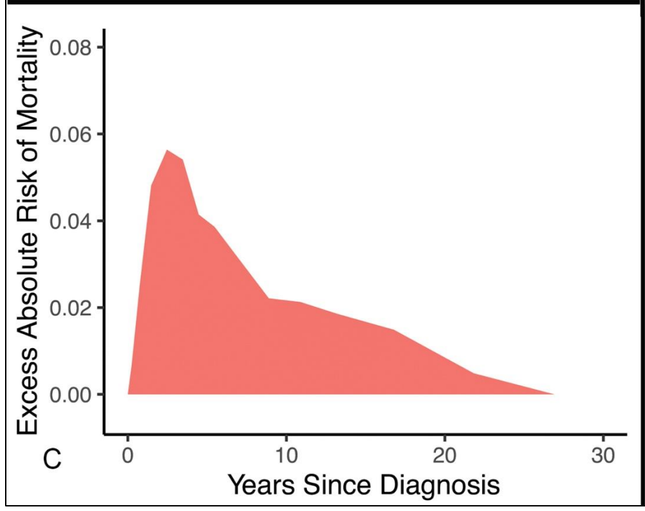
Methods: Integrative analysis of SEER data (1975-2016; 10678 cases) was subjected to survival analysis wherein a statistical cure (i.e. population level) was defined as the time when excess absolute risks of death (EAR) returned to a normal zero value (**Figure 1**). Complementary institutional data (788 cases) that characterized the mutational status of uveal melanoma was used for biological interpretation of waveforms underlying SEER EAR time course (**Figure 2**). Conditional metastasis free survival (cMFS) and conditional overall survival (cOS) were calculated based on the observed MFS and OS.

Results: SEER EAR can be modelled as a sum of two waves. The first wave peaks at ~3 years and is negligible by 15 years, at which time the second wave peaks. Institutional data suggest that the first wave is due to BAP1 mutant cases (204/355 = 57.5% (52-63%, 95% CI) and that the second wave is due to *BAP1* wild type *SF3B1* mutant cases (60/355 = 17% (13-21%)). The overall statistical cured fraction of 60% is reached by ~25 years (time to cure).

Conclusions: Benefits of ocular therapy for curing uveal melanoma may be questionable because statistical cures reflect deaths of poor prognosis cases and survival of good prognosis cases. Mutational subtyping of uveal melanoma might be the preferred method for prognostication Changes in uveal melanoma patient management is needed to improve survival.







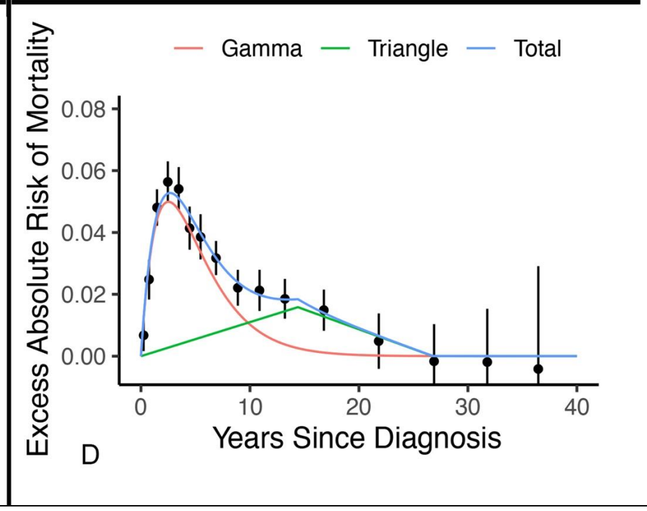
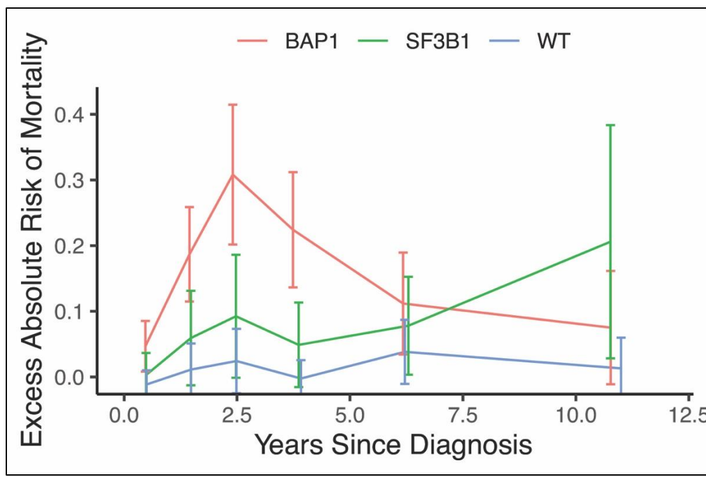


Figure 1. SEER Data. With all groups pooled (**A**), EAR peaks to 0.056 in (2,3] (times >2 years and ≤3), rapidly falls to 0.022 in (8,10], and slowly tapers thereafter to ~0 by year ~25 (time to cure). EAR amplitude depends on age (**B**; P<0.0001). The area under the curve (AUC) is 0.512 (**C**), so CF = $e^{-.512}$ = 0.60. The sum of the gamma function wave and triangle wave yield a reasonable fit to pooled EAR values (**D**).

Figure 2. Excess absolute risks of death time courses of *BAP1* and *SF3B1* mutant cases are similar to the gamma and triangle waveforms in Figure 1D.



Singh AD, Zabor EC, Radivoyevitch T. Estimating Cured Fractions of Uveal Melanoma. *JAMA Ophthalmol.* 2021;139(2):174–181.