Estimating scenarios for survival time in patients with metastatic melanoma receiving immunotherapy or targeted therapy.

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Introduction

- An accurate understanding of survival time helps patients make decisions approaching end of life.[1-4]
- Unfortunately, many patients do not understand their prognosis.[2,3,5-8]
- Estimating survival in metastatic melanoma is difficult, as immunotherapy and targeted therapies revolutionize care.
- We have previously proposed that three scenarios of survival – worst-case, typical, and best-case – may be a useful tool for communicating life expectancy.[6,9-12]
- The worst-case scenario (the 5-10% of patients with the shortest survival time) is calculated by multiplying 0.25x the median overall survival (OS) and corresponds to the 90th percentile; most-likely (middle 50%) is 0.5x – 2x and 25th; and best-case (top 5-10%) is 3x and 10th (**Figure 1**).

Objectives

- We aimed to determine whether three survival scenarios (worst-case, typical, best-case), calculated using multiples of median OS, 0.25x, 0.5-2x, 3x), accurately estimate prognosis for metastatic melanoma patients receiving immunotherapy and/or targeted therapy.

Subjects and Methods

- We searched Medline, EMBASE, Cochrane Central Register of Controlled Trials for phase II/III randomized controlled trials (treatment arms n ≥90) of patients with unresectable stage IIIC/IV cutaneous melanoma receiving immunotherapy and/or targeted therapy from 01/2001 to 08/2022.
- We extracted survival data and compared our multiples of median OS to the extracted survival times.
- We hypothesized that multiplying the median of each OS curve by four simple multiples would allow us to estimate its percentiles, which can be regarded as representative scenarios, as follows: 0.25x for the 90th, 0.5x for the 75th, 2x for the 25th and 3x for the 10th.
- Based on our previous work, we deemed each estimate to be accurate if it was 0.75 – 1.33 x the actual value as found through digitizing the OS curve.

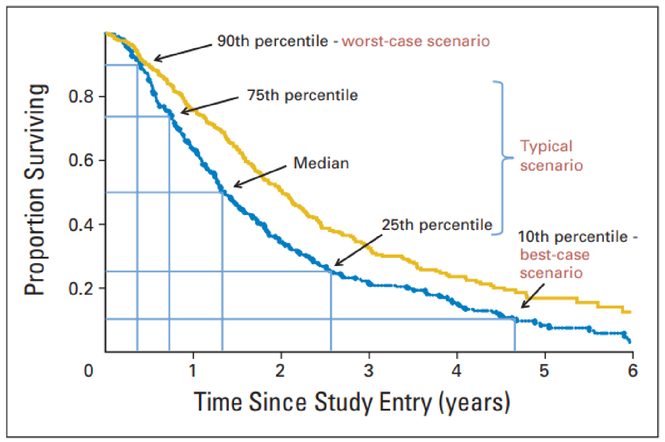

Figure 1. Survival curve percentiles and their corresponding scenarios.

Results

- 27 trials (13,059 patients) were included. Our estimates of worst-case scenarios ranged from 3.29 to 18.25 months; most-likely (lower-typical) from 6.57 to 36.5 and (upper-typical) from 26.28 to 146.01 months; and best-case from 39.43 to 219.02 months, among patients receiving first-line targeted and immunotherapy, respectively.
- Our multiples of the median OS accurately estimated survival from anywhere between 14.3% to 100% of estimates (**Table 1**).
- Our scenarios tended to be more accurate for those receiving targeted (most between 70% to 100% accuracy) than immunotherapy (some as low as 14.3%); and second- (all between 50 to 100%) than first-line (some as low as 14.3%).
- The median OS was reached in one arm of combination first-line immunotherapy, limiting our ability to analyze scenarios. When we were inaccurate, we tended to overestimate.

Table 1. Proportions of scenarios that accurately estimate survival (n=arms that met the percentile).

	1L mono-immuno	1L combo-immuno	1L mono-targeted	1L combo-targeted	2L all immuno	2L all targeted
0.25 x median est. 90th percentile (worst-case)	14.3% (n=7)	0% (n=1)	100.0% (n=3)	100.0% (n=2)	50.0% (n=14)	70.0% (n=10)
0.5 x median est. 75% percentile (lower-typical)	42.9% (n=6)	0% (n=1)	100.0% (n=3)	100.0% (n=2)	71.4% (n=14)	70.0% (n=10)
2 x median est. 25% percentile (upper-typical)	50.0% (n=2)	NR (n=0)	67.0% (n=3)	100.0% (n=2)	83.3% (n=6)	50.0% (n=6)
3x median est. 10th percentile (best-case)	NR (n=0)	NR (n=0)	NR (n=0)	NR (n=0)	100.0% (n=1)	100.0% (n=2)

Conclusions

- We found that survival scenarios generated from simple multiples of median OS were variably accurate at estimating survival in metastatic melanoma patients treated with immunotherapy and targeted therapy, with improved accuracy for those receiving targeted therapy and second line therapy.
- This study was limited by small sample sizes and immature data. The accuracy of our scenarios was more variable than previous work done by our team.

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The authors have no conflicts to disclose.

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