RWD156

Validation of Real-World Recurrence-Free Survival (rwRFS) and Distant Metastasis-Free Survival Endpoints (rwDMFS) in Early-Stage Melanoma.

Carole R. Berini, PhD[1], Jessica K Paulus, ScD[1], Malcolm Charles, MS[1], Zhaohui Su, PhD[1], Paul Conkling, MD[1], Nina Balanchivadze, MD[2], **Shan Jiang, PhD[3]**, Kaushal Desai, PhD[3].

[1] Ontada, Boston, MA; [2] The US Oncology Network, Norfolk, VA; [3] Merck & Co., Inc., Rahway, NJ, USA

Background

- Real-world (RW) evidence has been used to evaluate the real-world effectiveness of various advanced stage cancer treatments.[1]
- Compared to measures such as progression-free survival and overall survival, little is known regarding the validity of real-world early-stage clinical outcomes in melanoma.[2,3]

Objective

To examine the concordance between rwRFS and rwDMFS estimates from the KEYNOTE-716 trial as a measure of real-world endpoint validity, specifically in a community oncology setting using data from The US Oncology Network.

Methods

- Retrospective observational study using electronic health records from The US Oncology Network to identify patients diagnosed with stage IIB-IIC cutaneous melanoma between 01/01/2018 and 05/31/2023 who had not initiated adjuvant therapy 12 weeks post resection with clear margins.
- Patients were followed through 07/31/2023.
- Real-world proxies for trial eligibility criteria were developed and applied to define a RW-cohort closely matching KEYNOTE-716.
- Matching-Adjusted Indirect Comparison (MAIC) analysis was performed to adjust for available baseline demographic and clinical characteristics.
- Hazard ratios (HR) were used to compare rwRFS and rwDMFS with estimates from the placebo arm of KEYNOTE-716 before (crude) and after MAIC was applied (adjusted).

Figure 1: Patient population attrition

Patients newly diagnosed with Stage IIB-IIC cutaneous melanoma prior to 31 March 2022 (n=1653) in pre-curated data

Not started adjuvant treatment within 12 weeks post surgery with complete resection with clear margins from 01 January 2020 to 31 March 2023 (n=248)Dec

Random subsample (n=171) underwent custom chart abstraction to apply clinical trial eligibility

Patient excluded based on confirmed:
- Behavioral health issues/substance use (25%)
- ECOG >1 (4%)
- Autoimmune disease (2%)
- Active infection (1%)

Resulting in the study RW cohort (n=75)

Contact information

Contact Dr. Desai at kaushal.desai@merck.com for questions and comments

Disclosures

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Results

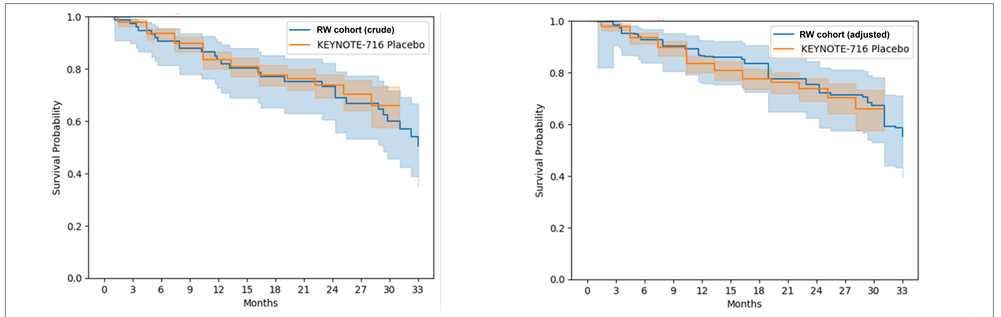
- Patients in the RW cohort (n=248) were older (71 vs. 61 median years) and more had ECOG performance status 1 (37% vs 7%).
- There were no statistically significant differences between the KEYNOTE-716 placebo arm RFS and rwRFS in crude (HR: 1.04, 95% CI: 0.65 - 1.65, p=0.873) nor adjusted (HR: 0.85, 95% CI: 0.52, 1.40, p=0.527) analyses.
- Similarly, there were no statistically significant differences in KEYNOTE-716 placebo arm DMFS and rwDMFS in either crude (HR: 1.36, 95% CI: 0.84 - 2.19, p=0.206) nor adjusted analyses (HR: 1.20, 95% CI: 0.76, 1.97, p=0.462).

Table 1: Demographic and Clinical characteristics for Trial and RW patients

Variable	KEYNOTE 716 placebo group	RW cohort (crude)	RW cohort (adjusted)
Number of Patients	489	75	75
Age group at index (years), N (%)			
< 65	295 (6(	%)	42 (56%)
>= 65	194 (4(	%)	33 (44%)
Sex, N (%)			
Female	200 (4	%)	32 (43%)
Male	289 (5	%)	43 (57%)
Race, N (%)			
White/Caucasian	439 (90%)	65 (87%)	67 (89%)
Other	5 (1%)	4 (5%)	2 (3%)
Not documented	45 (9%)	6 (8%)	6 (8%)
Ethnicity, N (%)			
Hispanic, Latino/a, Spanish origin	30 (6%)	2 (3%)	1 (1%)
Not Hispanic, Latino/a, Spanish origin	409 (84%)	61 (81%)	66 (88%)
Not documented	50 (10%)	12 (16%)	8 (11%)
ECOG, N (%)			
0	452 (92%)	47 (63%)	65 (87%)
1+*	36 (7%)	28 (37%)	10 (13%)
Not documented	1 (0%)	0 (0%)	0 (0%)

* - one trial patient was reported to have ECOG score = 2, all rw patients had an ECOG score < 2

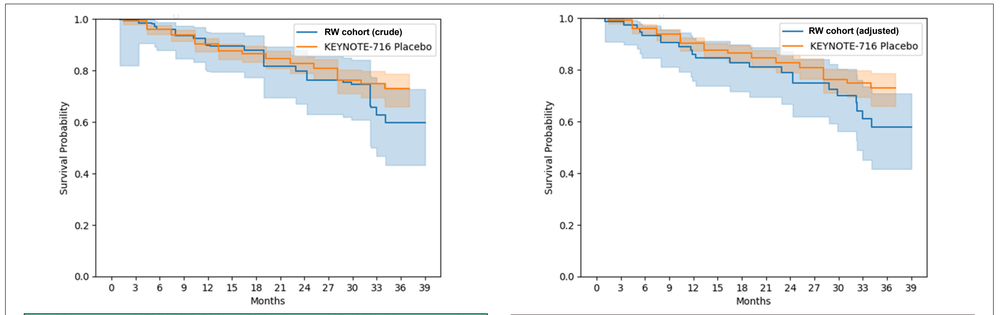
Figure1: Kaplan Meier Curves and Wald test for RFS in real-world vs. KEYNOTE-716 patients with melanoma



Variable	KEYNOTE-716 Placebo group	RW cohort (crude)	HR (95% CI)	p-value
N	489	75		
Events (%)	115 (24%)	27 (36%)	1.04 (0.65, 1.65)	0.8730
Median (95% CI)	NR	NR		
Q1, Q3	7.43, 25.17	10.25, 29.24		

Variable	KEYNOTE-716 placebo group	RW cohort (adjusted)	HR (95% CI)	p-value
N	489	75		
Events (%)	115 (24%)	27 (36%)	0.85 (0.52, 1.40)	0.5271
Median (95% CI)	NR	NR		
Q1, Q3	7.43, 25.17	10.25, 29.24		

Figure 2: Kaplan Meier Curves and Wald test for DMFS in real-world vs. KEYNOTE-716 patients with melanoma



Variable	KEYNOTE-716 placebo group	RW cohort (crude)	HR (95% CI)	p-value
N	489	75		
Events (%)	95 (19%)	22 (29%)	1.36 (0.84, 2.19)	0.2056
Median (95% CI)	NR	NR		
Q1, Q3	7.43, 28.12	10.61, 29.93		

Variable	KEYNOTE-716 placebo groups	RW cohort (adjusted)	HR (95% CI)	p-value
N	489	75		
Events (%)	95 (19%)	22 (29%)	1.20 (0.74, 1.97)	0.4619
Median (95% CI)	NR	NR		
Q1, Q3	7.43, 28.12	10.61, 29.93		

Conclusions

By applying real-world definitions to align key study design elements with the KEYNOTE-716 trial and leveraging curated real-world data from The US Oncology Network, endpoints rwRFS and rwDMFS are concordant with clinical trial control arm estimates in early-stage melanoma. These results increase confidence in the validity of real-world outcomes for early-stage melanoma.

Limitations

- Though confounding was addressed through careful design and MAIC analyses, this study may be limited by unmeasured confounding between real-world cohorts and KEYNOTE trial groups. Differences between real-world and trial-based RFS and DMFS endpoints may also impact results.
- Requiring 12 weeks with no treatment post surgery was done to align the real-world population with the placebo-treated trial group. However, this likely introduced selection bias, which will be addressed in follow-up analyses.
- Real-world data are subject to misclassification of treatments, patient factors and outcomes.
- The US Oncology Network and non-network practices serve diverse patients, nonetheless, results from this study are most generalizable to other community oncology practices that adhere to evidence-based treatment guidelines.
- As the study objectives were limited to evaluation of concordance with trial estimates, the real-world cohort excluded patients that would be ineligible for trial KN-716. The resulting real-world population may not be representative of the entire real-world population.

References

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