Clinical Outcomes with Pembrolizumab and Nivolumab in Resected Advanced Melanoma: Real-World Evidence

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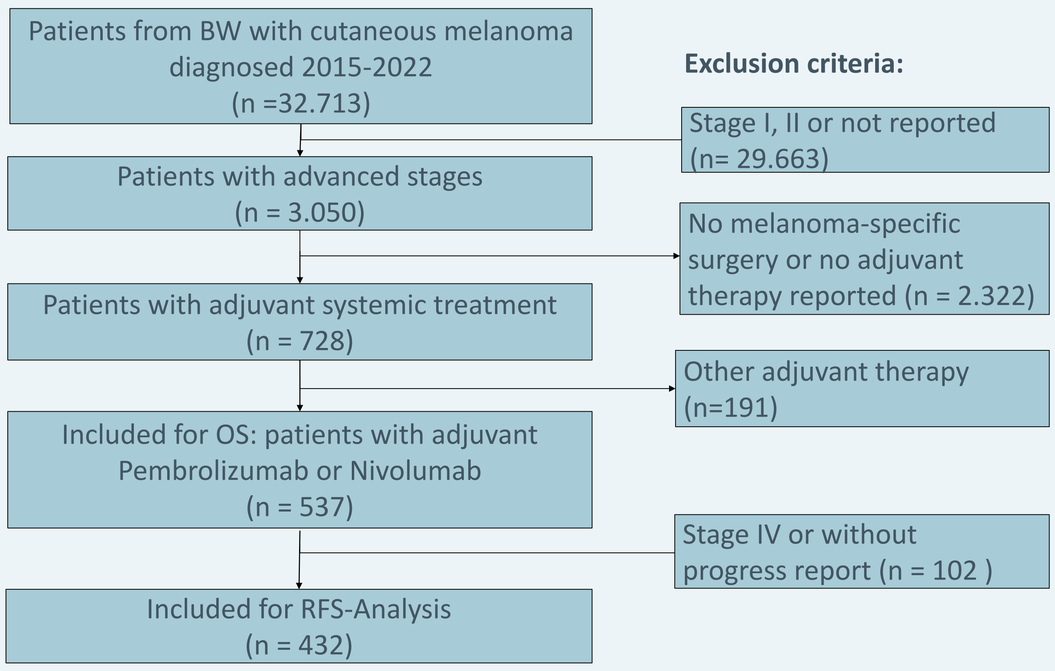
Background

- KEYNOTE 054 and CheckMate 238 are pivotal RCTs evaluating the efficacy of Pembrolizumab and Nivolumab in improving recurrence-free survival (RFS) in resected stage III/IV melanoma. The corresponding overall survival (OS) data for both studies are not yet mature.
- This study aims to evaluate the real-world clinical outcomes of Pembrolizumab and Nivolumab in patients with resected advanced cutaneous melanoma, comparing these results with those from clinical trials using data from the Baden-Württemberg State Cancer Registry (BWCR) in Germany.

Methods

- Records of patients residing in Baden-Württemberg (Germany) with cutaneous melanoma diagnosed in 2015-2022, aged 18 years or older, were selected from the BWCR database.
- Inclusion criteria were resected Stage III or IV melanoma, melanoma-specific surgery and systemic therapy with Pembrolizumab or Nivolumab.
- RFS and OS were analyzed using Kaplan-Meier methods and multivariable Cox models, adjusted for age, sex, histology, stage, lactate dehydrogenase (LDH) levels, and ulceration.

Fig. 1: Consort Diagram



Results: Baseline characteristics

A total of 537 patients were identified based on the inclusion criteria.

- 61.3% were male.
- The median age was 62,4 years, which is 6-8 years older than in both RCTs.
- The ulceration rate of 52% was higher compared to 42% reported in the RCTs.
- 12% of patients had metastatic disease, with 80% of metastases involving the lungs.

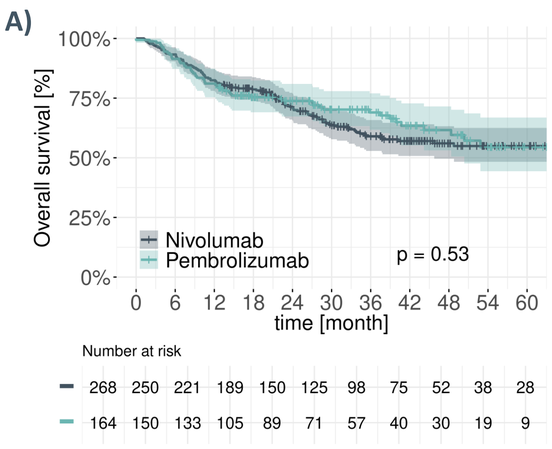
	Overall	Nivolumab	Pembrolizumab	P - value
Total – no. (%)	537	324 (60.3)	213 (39.7)	
Age – mean (SD)	62.36 (15.3)	61.35 (15.6)	63.88 (14.7)	0.060
Sex – no. (%)				0.587
▪ M	329 (61.3)	202 (62.3)	127 (59.6)	
▪ W	208 (38.7)	122 (37.7)	86 (40.4)	
Stage – no. (%)				0.414
▪ IIIA-IIIB	184 (34.2)	105 (22.4)	79 (37.1)	
▪ IIIC-IIID	243 (45.2)	156 (48.2)	87 (40.9)	
▪ III	25 (4.7)	17 (5.2)	8 (3.8)	
▪ IV	85 (15.8)	46 (14.2)	39 (18.3)	
LDH – no. (%)				0.618
▪ < 251	92 (53.5)	54 (55.7)	38 (50.7)	
▪ > 250	80 (46.5)	43 (44.3)	37 (49.3)	
Ulceration – no. (%)				0.027
▪ yes	247 (52.2)	157 (56.7)	90 (45.9)	
▪ no	226 (47.8)	120 (43.3)	106 (54.1)	

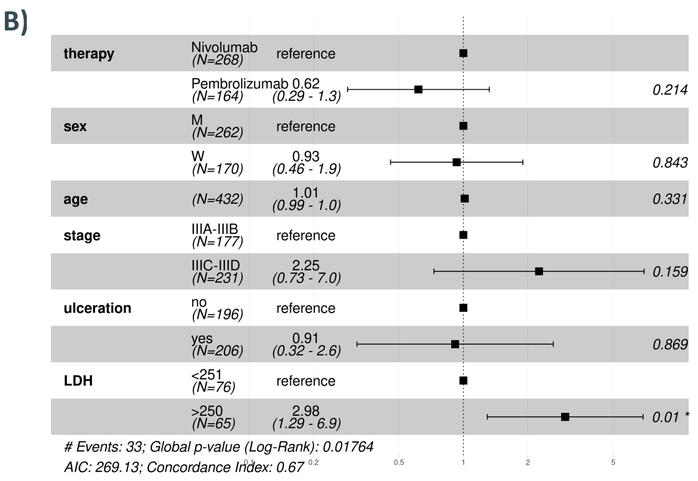
Tab 1: Baseline clinical and patient characteristics

Results: Survival

- Clinical outcomes for Pembrolizumab and Nivolumab were comparable (Fig.2A, 3A).
- After a median follow-up of 34 months, the 3-year RFS was 62.4%, with an estimated 5-year RFS of 54.9% (Fig. 2C).
- The primary prognostic factor for RFS was elevated LDH level (HR 3.3, 95% CI 1.7–6.6). (Fig.2B)

Stage III: Recurrence-free survival





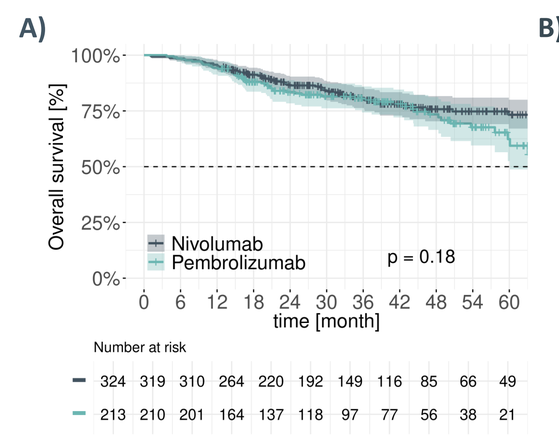
C)

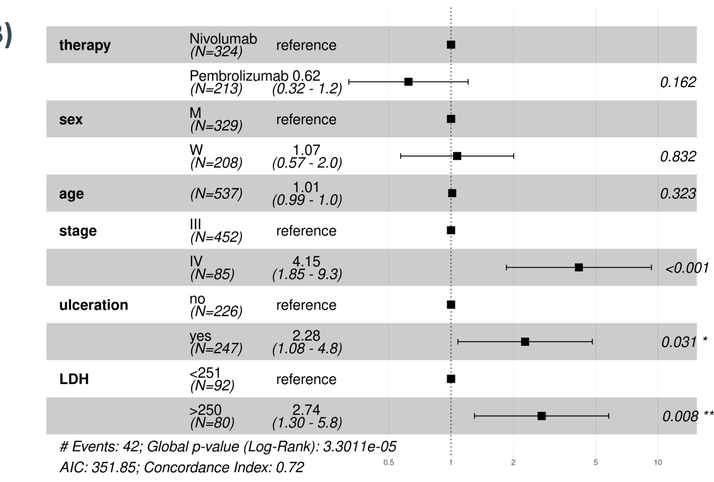
Source	Therapy	3y RFS	5y RFS
BWCR	Pembrolizumab and Nivolumab	62.4%	54.9%
BWCR	Pembrolizumab	68.6%	54.1%
BWCR	Nivolumab	59.0%	54.9%
Keynote 054	Pembrolizumab	63.7%	55.4%
CheckMate 238	Nivolumab	-	50%

Fig. 2: Patients with stage III resected melanoma.
A) RFS B) Multivariable Cox Analysis C) Comparison of RFS rates between BWCR and RCT data

- The 3-year OS rate was 80.5%, with an estimated 5-year OS of 73.3%, closely aligning with the 5-year OS observed in CheckMate 238 (Fig.3C).
- The primary prognostic factor for OS was elevated LDH level (HR 2.7, 95% CI 1.3–5.8).
- Additionally, ulceration was associated with worse OS outcomes (HR 2.28, 95% CI 1.08–4.8).
- The presence of metastasis increased the risk for OS, with an HR of 4.15 (95% CI 1.85–9.3).

Stage III or IV: Overall survival





C)

Source	Therapy	3y OS	5y OS
BWCR	Pembrolizumab and Nivolumab	80.5%	69.1%
BWCR	Pembrolizumab	80.0%	62.4%
BWCR	Nivolumab	80.9%	73.3%
Keynote 054	Pembrolizumab	-	-
CheckMate 238	Nivolumab	-	76%

Fig. 2: Patients with advanced melanoma (stage III or IV).
A) OS B) Multivariable Cox Analysis C) Comparison of OS rates between BWCR and RCT data

Conclusion

- The 3- and 5-year RFS rates from our data closely mirror the results reported in both RCTs.
- Furthermore, our overall survival data complement the findings from these trials.
- Overall, our study underscores the potential of leveraging real-world data from modern state-run cancer registries to bridge the gap between clinical trials and everyday oncology practice, providing valuable insights for clinicians when making real-world treatment decisions.

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