Avelumab in metastatic Merkel cell carcinoma: conditional survival and long-term safety in patients treated for ≥1 or ≥2 years in JAVELIN Merkel 200

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JAVELIN Merkel 200

CONCLUSIONS

- **This post hoc analysis from the JAVELIN Merkel 200 phase 2 trial examined the probability of additional overall survival (OS) and safety in patients with metastatic Merkel cell carcinoma (mMCC) who received ≥1 or ≥2 years of avelumab as first-line (1L) or second-line or later (2L+) treatment**
- **Among patients in the 1L cohort who had received 1 year of treatment (40/116 [34.5%]), the probability of an additional 1, 2, or 3 years of OS was 97.4%, 89.5%, and 75.2%, respectively**
  - **In patients in the 1L cohort who had received 2 years of treatment (22/116 [19.0%]), the probability of an additional 1 or 2 years of OS was 100% and 81.0%, respectively**
- **Among patients in the 2L+ cohort who had received 1 year of treatment (23/88 [26.1%]), the probability of an additional 1, 2, or 3 years of OS was 87.0%, 78.3%, and 69.6%, respectively**
  - **In patients in the 2L+ cohort who had received 2 years of treatment (13/88 [14.8%]), the probability of an additional 1 or 2 years of OS was 92.3% and 84.6%, respectively**
- **Among patients from both cohorts combined who were still receiving treatment, rates of grade ≥3 treatment-related adverse events (TRAEs) occurring after 1 or 2 years were low (19.0% and 5.7%, respectively)**
- **Overall, these results inform prognosis and show that patients with mMCC who survive for ≥1 or ≥2 years while receiving avelumab treatment have a high probability of additional years of OS, with low rates of grade ≥3 TRAEs**

PLAIN LANGUAGE SUMMARY

- **The JAVELIN Merkel 200 clinical trial showed that avelumab treatment helps people with metastatic Merkel cell cancer live longer**
- **In this new analysis from the trial, researchers looked at people who had lived for at least 1 or 2 years while receiving avelumab to see how likely they were to stay alive**
  - **In people who had received 1 year of avelumab as their first treatment for metastatic Merkel cell cancer, the likelihood of surviving for an additional 1, 2, or 3 years was 97%, 90%, and 75%**
  - **In people who had chemotherapy before receiving avelumab for 1 year, the likelihood of living for an additional 1, 2, or 3 years was 87%, 78%, and 70%, respectively**
  - **People who had received 2 years of avelumab treatment also had a high likelihood of living for an additional 1 year (more than 90%) or 2 years (more than 80%)**
  - **In people who received avelumab treatment for at least 1 or 2 years, severe side effects occurred after 1 year in 19% and after 2 years in 6%, respectively**
- **Overall, these results suggest that people with metastatic Merkel cell cancer who live for at least 1 year while receiving avelumab treatment have a high likelihood of surviving for another 1, 2, or 3 years, or longer, with a low frequency of severe side effects**

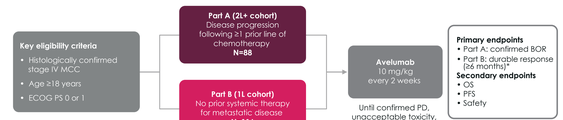
BACKGROUND

- In the JAVELIN Merkel 200 trial, avelumab given as 1L or 2L+ treatment for patients with mMCC was associated with clinically meaningful long-term OS, which compared favorably with historical studies of chemotherapy[1,2]
  - After ≥4 years of follow-up in patients treated with 1L avelumab (N=116), 1-, 2-, and 4-year OS rates were 60%, 49%, and 38%, respectively[1,3]
  - After ≥5 years of follow-up in patients treated with 2L+ avelumab (N=88), 1-, 2-, and 5-year OS rates were 50%, 36%, and 26%, respectively[2,4]
  - In both cohorts, avelumab treatment resulted in low rates of grade 3/4 TRAEs and TRAEs leading to treatment discontinuation[3,4]
- Results from the trial supported the regulatory approval of avelumab for the treatment of mMCC in multiple countries worldwide and the inclusion of avelumab in international treatment guidelines as a preferred or recommended treatment[5,6]
- Here, we report post hoc analyses from the JAVELIN Merkel 200 trial that assessed the probability of additional OS and safety in patients treated with avelumab for ≥1 or ≥2 years

METHODS

- JAVELIN Merkel 200 (NCT02155647) is an international, open-label, phase 2 trial that enrolled patients with histologically confirmed stage IV MCC
  - Cohorts of patients who had disease progression following ≥1 prior line of chemotherapy (2L+ cohort; part A) or no prior systemic therapy for metastatic disease (1L cohort; part B) were enrolled separately (**Figure 1**)
  - Patients were unselected for tumor PD-L1 expression and Merkel cell polyomavirus status
- Patients received avelumab monotherapy every 2 weeks until confirmed disease progression, unacceptable toxicity, or patient withdrawal
- In this post hoc analysis, subgroups of patients who had been treated with avelumab for ≥1 or ≥2 years were analyzed

Figure 1. JAVELIN Merkel 200 study design[3,4]



1L, first line; **2L+**, second line or later; **BOR**, best overall response; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **MCC**, Merkel cell carcinoma; **OS**, overall survival; **PD**, progressive disease; **PFS**, progression-free survival.
*Objective response (complete or partial response), determined by independent review committee per RECIST 1.1, with a duration ≥6 months.

RESULTS

- In total, 116 patients received 1L avelumab and 88 patients received 2L+ avelumab
  - Median follow-up was 54.3 months in the 1L cohort (data cutoff: 2 February 2022) and 65.1 months in the 2L+ cohort (data cutoff: 25 September 2020)
- In patients who received 1L or 2L+ avelumab, treatment duration was ≥1 year in 40 (34.5%) and 23 (26.1%) and ≥2 years in 22 (19.0%) and 13 (14.8%), respectively
- Compared with the overall 1L and 2L+ cohorts, subgroups with ≥1 or ≥2 years of avelumab treatment included higher proportions of patients with ECOG PS 0 (1L cohort, 72.5%-72.7% vs 62.1%; 2L+ cohort, 69.2%-78.3% vs 55.7%) and PD-L1+ tumors (1L cohort, 27.3%-27.5% vs 18.1%; 2L+ cohort, 73.9%-76.9% vs 64.8%) (**Table 1**)

Table 1. Baseline characteristics in the overall 1L and 2L+ cohorts and in subgroups with ≥1 or ≥2 years of avelumab treatment

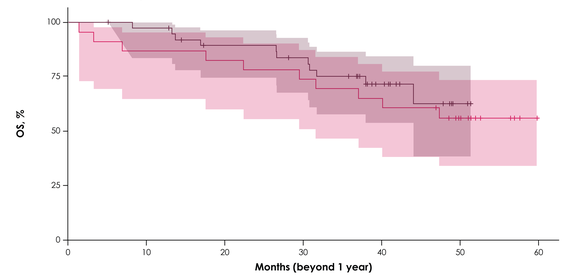
	1L cohort			2L+ cohort		
	Overall (N=116)	≥1 year (n=40)	≥2 years (n=22)	Overall (N=88)	≥1 year (n=23)	≥2 years (n=13)
Age, median (range), years	74.0 (41-93)	72.5 (41-88)	70.0 (52-87)	72.5 (33-88)	74.0 (55-86)	71.0 (55-86)
Sex, n (%)						
Male	81 (69.8)	32 (80.0)	17 (77.3)	65 (73.9)	18 (78.3)	11 (84.6)
Female	35 (30.2)	8 (20.0)	5 (22.7)	23 (26.1)	5 (21.7)	2 (15.4)
Geographic region, n (%)						
North America	29 (25.0)	12 (30.0)	6 (27.3)	51 (58.0)	11 (47.8)	8 (61.5)
Western Europe	75 (64.7)	24 (60.0)	13 (59.1)	29 (33.0)	9 (39.1)	5 (38.5)
Australia	9 (7.8)	3 (7.5)	2 (9.1)	5 (5.7)	2 (8.7)	0
Asia	3 (2.6)	1 (2.5)	1 (4.5)	3 (3.4)	1 (4.3)	0
ECOG PS, n (%)						
0	72 (62.1)	29 (72.5)	16 (72.7)	49 (55.7)	18 (78.3)	9 (69.2)
1	44 (37.9)	11 (27.5)	6 (27.3)	39 (44.3)	5 (21.7)	4 (30.8)
Visceral metastases, n (%)						
Present	79 (68.1)	24 (60.0)	15 (68.2)	47 (53.4)	11 (47.8)	8 (61.5)
Absent	35 (30.2)	15 (37.5)	6 (27.3)	41 (46.6)	12 (52.2)	5 (38.5)
Unknown	2 (1.7)	1 (2.5)	1 (4.5)	0	0	0
PD-L1 status, n (%)*						
Positive	21 (18.1)	11 (27.5)	6 (27.3)	57 (64.8)	17 (73.9)	10 (76.9)
Negative	87 (75.0)	26 (65.0)	15 (68.2)	16 (18.2)	4 (17.4)	2 (15.4)
Unknown	8 (6.9)	3 (7.5)	1 (4.5)	15 (17.0)	2 (8.7)	1 (7.7)
MCPyV status, n (%)†						
Positive	70 (60.3)	25 (62.5)	15 (68.2)	46 (52.3)	11 (47.8)	6 (46.2)
Negative	37 (31.9)	12 (30.0)	6 (27.3)	31 (35.2)	11 (47.8)	6 (46.2)
Unknown	9 (7.8)	3 (7.5)	1 (4.5)	11 (12.5)	1 (4.3)	1 (7.7)

1L, first line; **2L+**, second line or later; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **IHC**, immunohistochemistry; **MCPyV**, Merkel cell polyomavirus.
*PD-L1+ status was defined as expression in ≥1% of tumor cells (Dako PD-L1 73-10 IHC assay). †Assessed by IHC.

- In patients who had received 1 year of avelumab treatment (**Figure 2A**), the probability of an additional 1, 2, or 3 years of OS, respectively, was:
  - 1L cohort: 97.4%, 89.5%, and 75.2%
  - 2L+ cohort: 87.0%, 78.3%, and 69.6%
- In patients who had received 2 years of avelumab treatment (**Figure 2B**), the probability of an additional 1 or 2 years of OS, respectively, was:
  - 1L cohort: 100% and 81.0%
  - 2L+ cohort: 92.3% and 84.6%

Figure 2. Additional OS in patients who had received 1 or 2 years of avelumab treatment in the 1L and 2L+ cohorts

A. Patients with ≥1 year of avelumab treatment

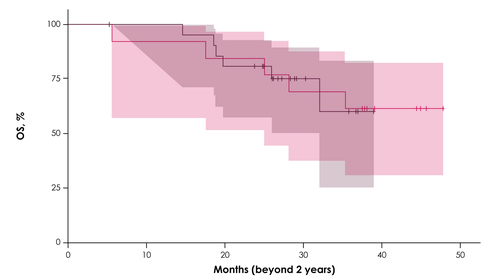


No. at risk

1L	40	38	32	29	17	2	0
2L+	23	20	19	17	15	9	0

	1L cohort (n=40)	2L+ cohort (n=23)
Probability of additional OS beyond 1 year (95% CI), %		
1 year	97.4 (83.2-99.6)	87.0 (64.8-95.6)
2 years	89.5 (74.3-95.9)	78.3 (55.4-90.3)
3 years	75.2 (57.7-86.3)	69.6 (46.6-84.2)

B. Patients with ≥2 years of avelumab treatment



No. at risk

1L	22	21	17	6	0	0
2L+	13	12	11	9	4	0

	1L cohort (n=22)	2L+ cohort (n=13)
Probability of additional OS beyond 2 years (95% CI), %		
1 year	100 (NE)	92.3 (56.6-98.9)
2 years	81.0 (56.9-92.4)	84.6 (51.2-95.9)

1L, first line; **2L+**, second line or later; **NE**, not evaluable; **OS**, overall survival.

- Among patients who were still receiving avelumab treatment at specified time points, rates of AEs and TRAEs decreased over time (**Table 2**)
  - Any-grade TRAEs occurred after 1 year in 74.6% of patients and after 2 years in 45.7%, including grade ≥3 TRAEs in 19.0% and 5.7%, respectively

Table 2. Summary of AEs occurring at any time and after ≥1 or ≥2 years of avelumab treatment in the pooled 1L and 2L+ cohorts

Patients, n (%)	Occurred at any time (all treated patients; n=204)	Occurred after ≥1 year (patients with ≥1 year of treatment; n=63)	Occurred after ≥2 years (patients with ≥2 years of treatment; n=35)
AE of any grade	202 (99.0)	59 (93.7)	30 (85.7)
Grade ≥3 AE	140 (68.6)	34 (54.0)	13 (37.1)
TRAE of any grade	164 (80.4)	47 (74.6)	16 (45.7)
Grade ≥3 TRAE	34 (16.7)	12 (19.0)	2 (5.7)
Serious AE	112 (54.9)	30 (47.6)	15 (42.9)
Serious TRAE	29 (14.2)	9 (14.3)	4 (11.4)
AE leading to discontinuation of avelumab	31 (15.2)	10 (15.9)	3 (8.6)
TRAE leading to discontinuation of avelumab	13 (6.4)	6 (9.5)	2 (5.7)
AE leading to death	29 (14.2)	4 (6.3)	2 (5.7)
TRAE leading to death	0	0	0
irAE of any grade	54 (26.5)	9 (14.3)	1 (2.9)
Grade ≥3 irAE	11 (5.4)	1 (1.6)	0

1L, first line; **2L+**, second line or later; **AE**, adverse event; **irAE**, immune-related AE; **TRAE**, treatment-related AE.

- In general, types of TRAEs that occurred after 1 or 2 years of treatment were consistent with those observed in the overall population (**Table 3**)

Table 3. Most common TRAEs occurring at any time and after ≥1 or ≥2 years of avelumab treatment in the pooled 1L and 2L+ cohorts

	Occurred at any time (all treated patients; n=204)		Occurred after ≥1 year (patients with ≥1 year of treatment; n=63)		Occurred after ≥2 years (patients with ≥2 years of treatment; n=35)	
Patients, n (%)	**Any grade**	**Grade ≥3**	**Any grade**	**Grade ≥3**	**Any grade**	**Grade ≥3**
Any TRAE	164 (80.4)	34 (16.7)	47 (74.6)	12 (19.0)	16 (45.7)	2 (5.7)
Pruritus	26 (12.7)	1 (0.5)	10 (15.9)	0	2 (5.7)	0
Fatigue	47 (23.0)	1 (0.5)	6 (9.5)	0	2 (5.7)	0
Asthenia	26 (12.7)	0	5 (7.9)	0	1 (2.9)	0
Rash	15 (7.4)	0	5 (7.9)	0	1 (2.9)	0
Hypothyroidism	14 (6.9)	1 (0.5)	4 (6.3)	0	0	0
Lipase increased	8 (3.9)	4 (2.0)	4 (6.3)	2 (3.2)	2 (5.7)	0
Platelet count decreased	7 (3.4)	0	4 (6.3)	0	2 (5.7)	0
Alanine aminotransferase increased	9 (4.4)	2 (1.0)	3 (4.8)	0	0	0
Arthralgia	10 (4.9)	0	3 (4.8)	0	1 (2.9)	0
Aspartate aminotransferase increased	8 (3.9)	1 (0.5)	3 (4.8)	0	0	0
Thrombocytopenia	3 (1.5)	1 (0.5)	3 (4.8)	1 (1.6)	1 (2.9)	1 (2.9)

TRAEs of any grade that occurred in ≥4% of patients who were treated for ≥1 or ≥2 years are shown.
1L, first line; **2L+**, second line or later; **TRAE**, treatment-related adverse event.

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