Avelumab in patients with previously treated Merkel cell carcinoma (JAVELIN Merkel 200): updated overall survival data after >5 years of follow-up

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JAVELIN Merkel 200

SCOPE

- **We report long-term overall survival (OS) data, after >5 years of follow-up, from part A of the JAVELIN Merkel 200 study that evaluated avelumab monotherapy in a cohort of patients with metastatic Merkel cell carcinoma (mMCC) whose disease had progressed following ≥1 prior line of chemotherapy**

CONCLUSIONS

- **To our knowledge, this is the longest follow-up for a cohort of patients with mMCC treated with an immune checkpoint inhibitor reported to date**
- **Avelumab monotherapy led to meaningful long-term OS in patients with mMCC whose disease had progressed following chemotherapy**
- **Longer OS was reported in patients with PD-L1+ vs PD-L1– tumors, but, as previously reported, responses to avelumab occurred in patients regardless of PD-L1 status[1]**
  - **The OS benefit observed in both subgroups greatly exceeds that seen in retrospective analyses of second-line or later chemotherapy in patients with mMCC[2,3]**
- **These results further support the role of avelumab as a standard of care for patients with mMCC**

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BACKGROUND

- Patients with mMCC have a poor prognosis, with a historical 5-year OS rate from diagnosis of approximately 14%[4]
- Although mMCC is considered sensitive to chemotherapy, duration of response tends to be limited[2,3,5]
  - Historically, in patients with chemotherapy-refractory mMCC, the 1-year OS rate following further chemotherapy treatment was 0%[2,3]
- Avelumab (anti–PD-L1) became the first approved treatment for patients with mMCC based on results from the phase 2 JAVELIN Merkel 200 trial[6]
  - The trial investigated avelumab monotherapy in 2 cohorts of patients with mMCC: as second-line or later treatment in patients with disease progression after ≥1 line of chemotherapy (part A) and as first-line treatment (part B)
- A summary of previously reported efficacy outcomes from part A, after ≥3 years of follow-up, are shown in **Table 1**
- Here we report 5-year OS data from part A of JAVELIN Merkel 200

Table 1. Efficacy outcomes after ≥3 years of follow-up[1]

	Overall population (N=88)	PD-L1+ (n=57)	PD-L1– (n=16)
ORR (95% CI), %	33.0 (23.3-43.8)	36.8 (24.4-50.7)	18.8 (4.0-45.6)
PFS rate (95% CI), %			
2 years	26 (17-36)	NA	NA
3 years	21 (12-32)	NA	NA
OS, median (95% CI), months	12.6 (7.5-17.1)	12.9 (8.7-29.6)	7.3 (3.4-14.0)
OS rate (95% CI), %			
3 years	32 (23-42)	NA	NA
3.5 years	31 (22-41)	NA	NA

NA, not available; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival.

METHODS

- The design of the phase 2, single-arm, open-label JAVELIN Merkel 200 trial (NCT02155647) has been reported previously[1,7]
- In part A, eligible patients had measurable (per RECIST 1.1) and histologically confirmed stage IV MCC that had progressed following ≥1 prior line of chemotherapy
  - Eligible patients also had an ECOG PS of 0-1 and were unselected for tumor PD-L1 expression
  - Patients were excluded if they had received previous therapy with immune checkpoint inhibitors
- Patients received avelumab 10 mg/kg by 1-hour intravenous infusion every 2 weeks until confirmed disease progression, unacceptable toxicity, or withdrawal
- OS was analyzed using the Kaplan-Meier method; 95% CIs for the median were calculated using the Brookmeyer-Crowley method
- PD-L1 expression was measured using the PD-L1 73-10 immunohistochemistry assay
  - PD-L1+ status was defined as ≥1% expression in tumor cells

RESULTS

Patient disposition

- A total of 88 patients were enrolled and treated with avelumab (**Table 2**)
  - Patient disposition is shown in **Table 3**
- As of September 25, 2020 (data cutoff), median follow-up was 65.1 months (range, 60.8-74.1 months)

Table 2. Baseline characteristics[1]

	N=88
Median age (range), years	72.5 (33-88)
Sex, n (%)	
Male	65 (73.9)
Female	23 (26.1)
ECOG PS, n (%)	
0	49 (55.7)
1	39 (44.3)
Site of primary tumor, n (%)	
Skin	67 (76.1)
Nonskin*	14 (15.9)
Missing	7 (8.0)
Visceral disease at study entry, n (%)	
Present	47 (53.4)
Absent	41 (46.6)
No. of prior systemic anticancer treatments, n (%)	
1	52 (59.1)
2	25 (28.4)
≥3	11 (12.5)
Tumor PD-L1 status, n (%)†	
Positive	57 (64.8)
Negative	16 (18.2)
Not evaluable	15 (17.0)
Tumor MCPyV status, n (%)	
Positive	46 (52.3)
Negative	31 (35.2)
Not evaluable	11 (12.5)

MCPyV, Merkel cell polyomavirus.
*Nonskin sites include lymph node (n=12 [13.6%]) and other sites (cheek mucosa and rectosigmoid junction; n=2 [2.3%]).
†PD-L1+ status was defined as expression on ≥1% of tumor cells, assessed using a Dako PD-L1 73-10 IHC assay.
From D'Angelo SP, et al. Avelumab in patients with previously treated metastatic Merkel cell carcinoma: long-term data and biomarker analyses from the single-arm phase 2 JAVELIN Merkel 200 trial. J Immunother Cancer. 2020;8:e000674. Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/).

Table 3. Patient disposition

n (%)	N=88
Received ≥1 dose of study treatment	88 (100.0)
Treatment ongoing	1 (1.1)
Off treatment	87 (98.9)
Reason for discontinuation of treatment	87 (98.9)
AE	11 (12.5)
Lost to follow-up	1 (1.1)
Protocol noncompliance	1 (1.1)
Death	10 (11.4)
Disease progression	45 (51.1)
Withdrew consent	9 (10.2)
Other*	10 (11.4)
Discontinued treatment but still in follow-up	19 (21.6)
Reinitiated treatment with avelumab	1 (1.1)
Discontinued from the trial	68 (77.3)
Lost to follow-up	3 (3.4)
Death	58 (65.9)
Withdrew consent	7 (8.0)

AE, adverse event.
*Including complete response for ≥6 months on treatment (per protocol; n=5 [5.7%]) and switch to commercial avelumab for patient convenience (n=2 [2.3%]).

Overall survival

- Median OS was 12.6 months (95% CI, 7.5-17.1 months) in the overall population
  - OS rates at 4 and 5 years were 30% (95% CI, 20%-40%) and 26% (95% CI, 17%-36%), respectively
  - **Figure 1** shows OS for avelumab in comparison with retrospective analyses of second-line or later chemotherapy in patients with mMCC
- Longer median OS was observed in patients with PD-L1+ vs PD-L1– tumors (12.9 months [95% CI, 8.7-29.6 months] vs 7.3 months [95% CI, 3.4-14.0 months], respectively) and a higher 5-year OS rate (28% [95% CI, 17%-40%] vs 19% [95% CI, 5%-40%]) (**Figure 2**)

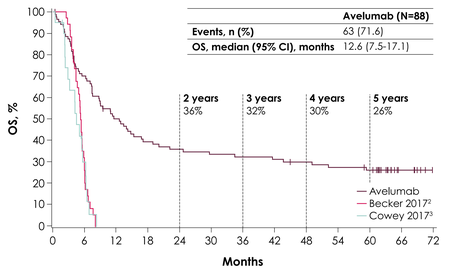
Deaths

- At data cutoff, 63 patients (71.6%) had died
  - The most common cause of death was disease progression (n=49 [55.7%])
  - Other causes were unknown reason (n=9 [10.2%]), adverse event (AE) not related to study treatment (n=3 [3.4%]), and other reason (n=2 [2.3%])
- No deaths due to treatment-related AEs were reported

Subsequent treatment

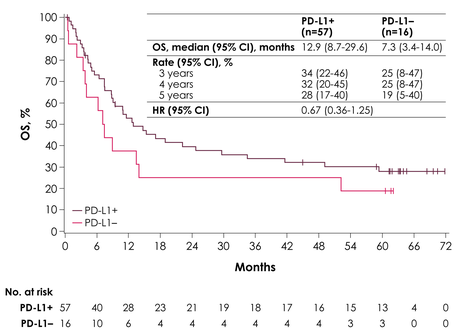
- In total, 26 patients (29.5%) received subsequent anticancer therapy (**Table 4**)
- The most common subsequent therapies were avelumab (n=4 [4.5%]), carboplatin + etoposide (n=4 [4.5%]), and pembrolizumab (n=4 [4.5%])

Figure 1. Overall survival in all patients compared with historical chemotherapy data



OS, overall survival.
This figure is for illustrative purposes only and is not a head-to-head comparison.

Figure 2. Overall survival in subgroups defined by PD-L1 status



HR, hazard ratio; **OS**, overall survival.

Table 4. Subsequent anticancer drug treatment

	N=88
Received subsequent therapy, n (%)	26 (29.5)
Avelumab	4 (4.5)
Carboplatin + etoposide	4 (4.5)
Pembrolizumab	4 (4.5)
Everolimus	3 (3.4)
Nivolumab	3 (3.4)
Pazopanib	3 (3.4)
Capecitabine	2 (2.3)
Cyclophosphamide + doxorubicin + vincristine	2 (2.3)
Paclitaxel	2 (2.3)
Pegylated liposomal doxorubicin hydrochloride	2 (2.3)
Temozolomide	2 (2.3)
Topotecan	2 (2.3)
Amrubicin	1 (1.1)
Carboplatin	1 (1.1)
Carboplatin + paclitaxel	1 (1.1)
Cisplatin	1 (1.1)
Combinations of antineoplastic agents	1 (1.1)
Cyclophosphamide	1 (1.1)
Ipilimumab + nivolumab	1 (1.1)
Octreotide	1 (1.1)
Sunitinib	1 (1.1)
Somatostatin	1 (1.1)
Other therapeutic product	1 (1.1)

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