Avelumab as second-line or later treatment in patients with metastatic Merkel cell carcinoma: real-world treatment patterns in France

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SCOPE

- **This retrospective study reports real-world outcomes and treatment patterns with second-line or later (2L+) avelumab monotherapy in patients with metastatic Merkel cell carcinoma (mMCC) in France using national data from 2 linked databases**

CONCLUSIONS

- **This study provides insight into treatment patterns and outcomes in patients with mMCC receiving 2L+ avelumab in routine clinical practice in France**
  - **Median overall survival (OS) was 14.6 months (95% CI, 9.9-21.3 months)**
  - **Median time to treatment failure (TTF; defined as discontinuation for any reason) was 8.5 months (95% CI, 6.2-10.5 months)**
  - **A majority of evaluable patients received subsequent treatment following avelumab (69.7%), most commonly with chemotherapy alone (50.6%)**
- **These real-world data confirm the findings of the JAVELIN Merkel 200 trial and support the recommendation of avelumab as standard of care in patients with mMCC**

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BACKGROUND

- MCC is a rare and aggressive skin cancer; prior to the approval of immune checkpoint inhibitors, patients with mMCC had a poor prognosis, with a 5-year survival rate of 17%-20%[1,2]
- Although MCC is considered chemosensitive, responses are not often durable[3]
- Avelumab (anti–PD-L1 antibody) has been approved in multiple countries for the treatment of mMCC based on results from the phase 2 JAVELIN Merkel 200 trial (NCT02155647)[4-8]
  - In JAVELIN Merkel 200, avelumab treatment resulted in meaningful long-term OS in patients with mMCC and disease that progressed after prior chemotherapy (part A) and patients without prior treatment (part B)[4,5]
  - In patients with prior chemotherapy treated with avelumab (part A), median OS was 12.6 months, and median progression-free survival (PFS) was 2.7 months[4,9]
- The French Health Technology Assessment Agency requested the collection of real-world data from patients with mMCC from a comprehensive registry
  - Initial real-world data from patients who received 2L+ avelumab in France were reported at a previous congress[10]
  - Here, we report further analyses from this population, including OS and previously unreported analyses of treatment patterns and TTF

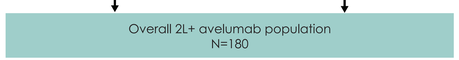
METHODS

- This retrospective, noninterventional, real-world study evaluated patients with mMCC in France using 2 databases
  - CARADERM is a French national database of rare dermatologic cancers
  - The Système National des Données de Santé (SNDS) is a national healthcare database that contains data on health insurance, prescriptions, and hospital records
- Probabilistic linkage was performed to identify patients registered in both databases; data on patients receiving care either at CARADERM reference sites or at sites outside the CARADERM network were captured
  - Data linkage was primarily based on the use of the following indirect identification variables: sex, birth date, National Directory of Health and Social Establishments number, treatment initiation date, and death
- For this analysis, eligible patients were aged ≥18 years, had been diagnosed with mMCC, and had initiated 2L+ avelumab outside a clinical trial between August 2016 and December 2019
- Patients were followed up for 24 months after initiation of avelumab
- The primary endpoint was OS at 24 months, which was analyzed using Kaplan-Meier methodology
- Safety data were not collected
- TTF (secondary endpoint) was defined as time from avelumab initiation to discontinuation for any reason, including progression, toxicity, or death
- Details of first-line (1L) and subsequent treatment and PFS data were only available for patients in the CARADERM database

RESULTS

- Overall, 180 patients who received 2L+ avelumab were identified (**Figure 1**)
  - Data were available for 112 patients in the CARADERM database and for 68 additional patients after SNDS linkage

Figure 1. Patient population



2L+, second line or later; **mMCC**, metastatic Merkel cell carcinoma.

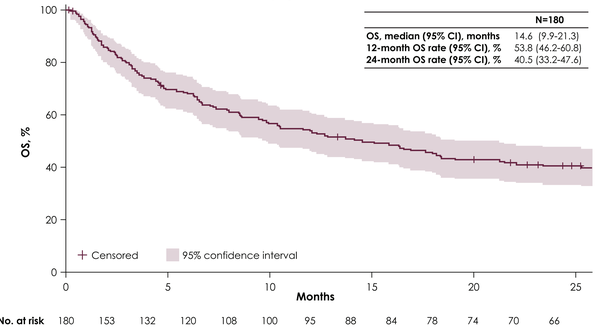
- Baseline characteristics are presented in **Table 1**
  - Median age at diagnosis was 74.0 years, 66.7% of patients were male, and 98.3% had received 1L chemotherapy alone
  - The most common 1L chemotherapy regimens in evaluable patients (CARADERM database) were cisplatin or carboplatin + etoposide (59.1%) and etoposide alone (12.7%)
- Median follow-up from start of avelumab treatment was 13.1 months
- Of patients who had data available on treatment status at last follow-up (n=175), 16 (9.1%) were receiving avelumab, 55 (31.4%) had discontinued treatment, 100 (57.1%) had died, and 4 (2.3%) were lost to follow-up
- In the CARADERM database, 89 patients (79.5%) had discontinued avelumab
  - The most common reasons for discontinuation of avelumab where reported (n=88) were progressive disease (36.4%), complete response (17.0%), death (13.6%), and intolerable toxicity (11.4%)
  - Reasons for discontinuation of avelumab were not evaluable in non–CARADERM database patients

Table 1. Baseline demographics

	CARADERM database (n=112)	Non–CARADERM database (n=68)	Total (N=180)
Age at diagnosis, median (IQR), years	74 (67-80)	73 (67-82)	74 (67-81)
Sex, n (%)			
Male	68 (60.7)	52 (76.5)	120 (66.7)
Female	44 (39.3)	16 (23.5)	60 (33.3)
First-line treatment, n (%)			
Chemotherapy alone	110 (98.2)	67 (98.5)	177 (98.3)
Immunotherapy alone	2 (1.8)	0	2 (1.1)
Chemotherapy + immunotherapy	0	1 (1.5)	1 (0.6)
First-line chemotherapy regimen, n (%)	**n=110**		
Cisplatin/carboplatin + etoposide	65 (59.1)		
Etoposide	14 (12.7)		
Cisplatin/carboplatin + paclitaxel	5 (4.5)		
Doxorubicin	5 (4.5)		
Cisplatin/carboplatin	4 (3.6)		
Paclitaxel	3 (2.7)		
Cisplatin/carboplatin + cyclophosphamide	2 (1.8)	Not reported	Not applicable
Cisplatin/carboplatin + other	1 (0.9)		
Cyclophosphamide	1 (0.9)		
Doxorubicin + cyclophosphamide	1 (0.9)		
Etoposide + cyclophosphamide	1 (0.9)		
Temozolomide	1 (0.9)		
Other	7 (6.4)		

- In the overall 2L+ population, median OS from the start of 2L+ avelumab was 14.6 months (95% CI, 9.9-21.3 months; **Figure 2**)
  - OS rates at 12 and 24 months were 53.8% (95% CI, 46.2%-60.8%) and 40.5% (95% CI, 33.2%-47.6%), respectively
- In CARADERM database patients:
  - Median PFS was 3.6 months (95% CI, 2.7-7.5 months)
  - The objective response rate was 55.3% (95% CI, 45.3%-65.4%), including complete response in 31.9% of patients
- PFS and response were not evaluable in non–CARADERM database patients

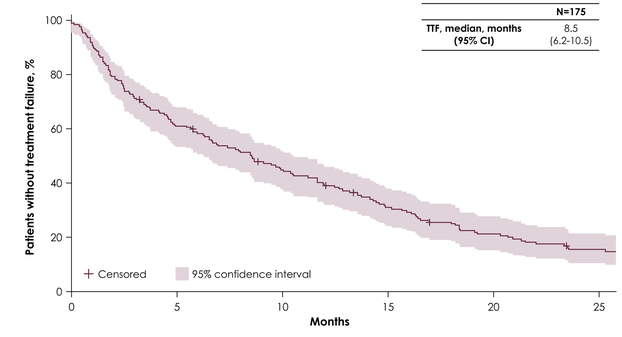
Figure 2. OS with 2L+ avelumab in the overall population



2L+, second line or later; **OS**, overall survival.

- In the overall 2L+ population, median TTF was 8.5 months (95% CI, 6.2-10.5 months; **Figure 3**)
- Rates of patients without treatment failure at 12 and 24 months were 38.9% (95% CI, 31.6%-46.1%) and 15.5% (95% CI, 10.4%-21.4%), respectively
- In CARADERM vs non–CARADERM database patients, median TTF was 9.9 months (95% CI, 6.5-14.3 months) and 6.5 months (95% CI, 4.4-9.5 months), respectively
- Among patients who had data available on subsequent treatment after discontinuing avelumab (CARADERM database only; n=89), 62 patients (69.7%) received subsequent treatment, including chemotherapy alone in 45 (50.6%) and other treatments in 17 (19.1%) (**Table 2**)

Figure 3. Time to treatment failure with 2L+ avelumab in the overall population



2L+, second line or later; **TTF**, time to treatment failure.

Table 2. Subsequent treatment after avelumab in the CARADERM population

n (%)	n=89
Subsequent treatment	62 (69.7)
Chemotherapy	45 (50.6)
Radiotherapy + chemotherapy	6 (6.7)
Chemotherapy + immunotherapy	2 (2.2)
Palliative care	5 (5.6)
Surgery + chemotherapy	2 (2.2)
Chemotherapy + targeted therapy	2 (2.2)
No subsequent treatment	27 (30.3)

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