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# Durable Complete Response to First Line Treatment with Avelumab in an Elderly, Multimorbid Patient with Advanced Merkel Cell Carcinoma: A Case Report

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## Abstract

**Introduction:** Metastatic Merkel Cell Carcinoma (MCC) is characterized by poor prognosis and poor response to cytotoxic chemotherapy. Immune Checkpoint Inhibitors (ICIs) were evaluated in several clinical trials, providing interesting results in terms of activity and efficacy, with a generally manageable safety profile. Limited data are available for use of ICIs in patients affected by multiple chronic diseases. We present the case of a patient with several comorbidities treated with Avelumab for advanced MCC, who developed a durable complete response.

**Case description:** A 78-year-old woman with several chronic diseases was treated with Avelumab for MCC with lung and subcutaneous metastases, developing radiological complete response after 5 cycles. Treatment was well tolerated and no severe adverse events were observed.

**Conclusion:** Our case shows that Avelumab is an active and safe treatment in multimorbid patients with advanced MCC. More consistent data from randomized clinical trials are needed to confirm these results in a large patient population presenting these special features.

**Keywords:** Merkel cell carcinoma • Overall survival • Cancer • Ultraviolet radiation • Computed tomography

## Introduction

Merkel Cell Carcinoma (MCC) is a highly aggressive and relatively rare cutaneous neuroendocrine cancer, with a noticeable increase in incidence during the last decade. Pathogenesis is associated with chronic exposure to ultraviolet radiation (similarly to other skin cancers), Merkel Cell Polyomavirus infection and immunosuppressive conditions. Histological diagnosis is essential to distinguish MCC from other skin cancers and it is based on immunohistochemistry: tumor cells show neuroendocrine markers, such as chromogranin, synaptophysin and neuron-specific enolase [1].

For patients with non metastatic disease, 5 year Overall Survival (OS) rate varies between 27% and 55%, depending on clinical and pathological stage. Treatment options mainly include surgery, radiation therapy and integrated approaches, such as concurrent chemoradiotherapy (especially for locally advanced, unrespectable disease).

Patients with distant metastases have a really poor prognosis (only 13% are alive 5 years after diagnosis of metastatic disease). For several years, the only available treatment in metastatic MCC was chemotherapy (including mainly platinum and etoposide, similarly to small cell lung cancer, which shares neuroendocrine features), that provides a median OS of only 9 months in this setting [2].

Over the past 5 years, several studies have evaluated efficacy, activity and safety of Immune Checkpoint Inhibitors (ICIs) in metastatic MCC. Avelumab, an anti-PDL1 fully-human monoclonal antibody, was associated with a durable and sustained response (confirmed objective response rate, ORR, was 31.8%) and a manageable safety profile in patients with advanced MCC progressed after cytotoxic chemotherapy [3]. In a multicenter phase 2 pivotal trial,

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first line Avelumab monotherapy was associated with durable and consistent response (ORR was 39.7%, median duration of response 18.2 months); after a median follow up of 21.2 months median OS was 20 months, while safety profile was comparable to other ICI and was generally manageable, just 18.1% of patients experienced grade >3 treatment related adverse events [4]. Avelumab became the first ICI to receive approval in USA European Union in patients with advanced MCC.

We present the case of an elderly, multimorbid patient, with metastatic MCC, treated with Avelumab and experiencing complete metabolic remission after 5 cycles. Additionally, she was previously treated with Vismodegib for Basal Cell Carcinoma (BCC) and reported clinical complete response.

## Case Presentation

We report the case of a 78-year-old woman, with a medical history including Parkinson disease, arterial hypertension, bipolar disorder and hyperuricemia; concomitant medications were Pramipexole, Telmisartan, Lithium salt, Citalopram, Allopurinol. Because of these several comorbid illnesses, woman presented an Eastern Oncology Cooperative Group-Performance Status (ECOG PS).

After the diagnosis of relapsing BCC of the right temple (progressing after local excision and radiotherapy), patient was directed to our center to evaluate the feasibility of medical therapy. She has been treated with Vismodegib for 2 years and experienced complete remission; she took the last dose in early 2018.

In May 2018, during periodic follow up, dermatological examination noticed an indurated, violaceus nodule on the back; patient underwent wide local excision and histopathological examination was positive for neuroendocrine, Merkel cell carcinoma of the skin, without involvement of lateral surgical margins.

Positron Emission Tomography using 18F-fluorodeoxyglucose ($^{18}$F-FDG and PET), performed in June 2018 to exclude distant metastases, highlighted involvement of locoregional, left axillary lymph nodes (Standardized Uptake Value, SUV, of 5). Consequently, in July-August 2018, the patient underwent left axillary node dissection (2 out of 26 resected nodes were positive for MCC), followed by axillary-supraclavicular radiotherapy; then, she underwent a follow up program, which consisted of periodic dermatologic visits and imaging exams (such as FDG PET).

In July 2019, patient experienced disease progression: FDG PET highlighted several lung (maximum SUV of 8 in left lower lobe) and subcutaneous metastases (maximum SUV of 8 on the back and on the chest wall). Subcutaneous tissue ultrasound confirmed pathological nodules on the chest wall.

Although patients with ECOG PS greater than 1 were usually excluded from clinical trials concerning ICI in MCC, after adequate discussion with patient and her relatives about risk-benefit ratio, considering data about high activity and efficacy and good safety profile, we decided to start the treatment with Avelumab.

On July 23, 2019, she began first line treatment with Avelumab at standard dose (10 mg/kg intravenously every 2 weeks); she was premedicated with antihistamine and acetaminophen before the first four infusions. She experienced low grade fever for two days after first drug infusion, resolved with common antipyretic medications; there were not any other adverse events reported. Clinical laboratory values were tested before each drug administration: Patient did not experience any significant modification in blood cell count, renal and liver function. We did not report any change in patient's quality of life that was investigated every 2 weeks. Physical examination showed a clear reduction in subcutaneous nodules since the initial administrations.

On October 2, 2019, after 5 cycles of Avelumab, FDG PET showed complete metabolic remission of lung and subcutaneous lesions. In consideration of early and excellent response and good tolerance, in accordance with the patient, we decided to continue the treatment.

After 6 further cycles of Avelumab, we performed another imaging evaluation of disease: On January 5, 2020, Computed Tomography (CT) chest and abdomen scans confirmed durable complete remission of disease. Treatment was generally well tolerated: patient experienced localized pruritus, responsive to topical steroids. After 16th Avelumab administration, on May 14, 2020, at 10-months follow up, FDG PET showed the preservation of metabolic complete remission of disease.

In consideration of good tolerance and excellent response, patient continued Avelumab administration for up to 52 total cycles; at 30-months follow up, FDG PET and CT chest and abdomen scans confirmed persistence of complete response.

Treatment is currently ongoing and was well tolerated; patient's general clinical condition remained stationary during immunotherapy. No signs of relapse of basal cell carcinoma disease were observed during periodic examinations (Figure 1).

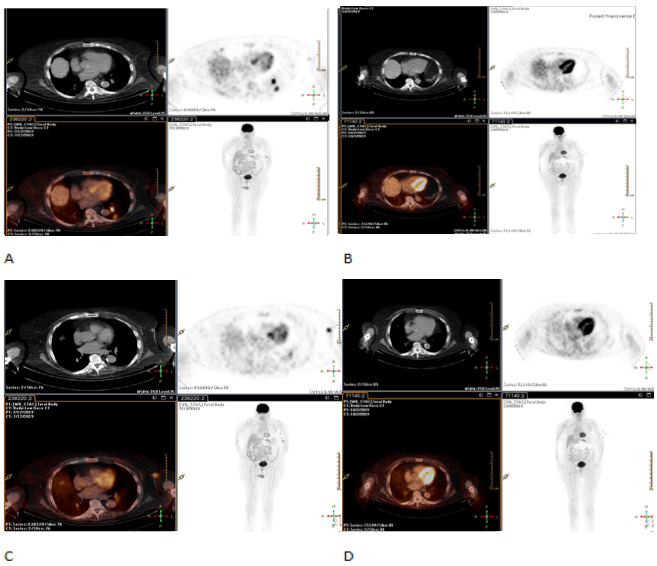


**Figure 1.** Baseline (A,C) and first evaluation (B,D; after 5 doses of Avelumab) of lung and subcutaneous metastases with FDG PET.

## Results and Discussion

Although patients with ECOG PS greater than 1 and multiple comorbidities were generally excluded from clinical trials concerning ICI in MCC and other diseases, this clinical case confirms manageable toxicity profile of immunotherapy in this subgroup of patients. Patients with ECOG PS greater than 1 were included in a global expanded access program, but they were only 9.2% [5,6].

We confirmed positive data about activity and efficacy of Avelumab in mMCC: In Javelin Merkel 200 part B, complete response is observed in 16.4% of patients.

## Conclusion

Our case confirmed two main features of responses to Avelumab in this pivotal trial: they are typically early (93.5%of responders had a response by 3 months) and durable (Kaplan-Meier estimated proportion of responses with duration of at least 24 months was 45%).

Analyses of clinical data from Javelin Merkel 200 part A (which evaluates Avelumab in patients with mMCC progressed on chemotherapy) highlighted strong association between early objective response and improved overall survival.

However, there are few data regarding the optimal duration of treatment with ICIs, and when to stop immunotherapy in patients achieving a response remains currently an unanswered question.

Despite the encouraging outcome reported in our clinical case, we need more data, derived from randomized clinical trials, to corroborate the potential role of ICIs in this special population.

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## Conflicts of Interest

The authors declare that there is no conflict of interest.

## References

1. Amaral, Teresa, Ulrike Leiter and Claus Garbe. “Merkel Cell Carcinoma: Epidemiology, Pathogenesis, Diagnosis and Therapy.” *Rev Endocr Metab Disord* 18(2017): 517-532.
2. Lebbe, Celeste, Jürgen C Becker, Jean-Jacques Grob and Josep Malvehy, et al. “Diagnosis and Treatment of Merkel Cell Carcinoma. European Consensus-Based Interdisciplinary Guideline.” *Eur J Cancer* 51(2015): 2396-403.
3. Kaufman, Howard, Jeffery Russell, Omid Hamid and Shailender Bhatia, et al. “Avelumab in Patients with Chemotherapy-Refractory Metastatic Merkel Cell Carcinoma: A Multicentre, Single-Group, Open-Label, and Phase 2 Trial.” *Lancet Oncol* 17(2016): 1374-1385.
4. D'Angelo, Sandra P, Celeste Lebbé, Laurent Mortier and Andrew S Brohl, et al. “First-Line Avelumab In A Cohort Of 116 Patients With Metastatic Merkel Cell Carcinoma (JAVELIN Merkel 200): Primary and Biomarker Analyses of a Phase II Study.” *J Immunother Cancer* 9(2021): e002646.
5. Walker, John, Celeste Lebbé, Giovanni Grignani and Paul Nathan, et al. “Efficacy and Safety of Avelumab Treatment in Patients with Metastatic Merkel Cell Carcinoma: Experience from a Global Expanded Access Program.” *J Immunother Cancer* 8(2020): e000313.
6. Zhu, Na, Dingyu Zhang, Wang Wenling and Li Xingwang, et al. “A Novel Coronavirus from Patients with Pneumonia in China, 2019”. *N Engl J Med* 382(2020): 727-733.

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