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Pembrolizumab-Axitinib Association in First-Line Metastatic Renal Cell Carcinoma: Preliminary Results of a Series of Five Patients

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ABSTRACT **Case Studies**

Introduction: Metastatic renal cell carcinoma (mRCC) remains a disease with a poor prognosis. The pembrolizumab-axitinib combination has established itself as the standard first-line treatment for intermediate and poor-risk patients according to the International Metastatic Renal Cell Database (IMDC) criteria. However, real-world clinical data remain limited in the Algerian context. This study evaluates the feasibility and tolerability of the pembrolizumab-axitinib association in a series of intermediate-risk mRCC patients managed at the Medical Oncology Department of Didouche Mourad Hospital, Constantine.

Materials and Methods: We report a series of 5 patients with intermediate-risk mRCC treated with pembrolizumab-axitinib between August 2024 and July 2025. Clinical characteristics, tolerability, and tumor responses were collected and analyzed.

Results: The median age was 70 years (interquartile range [IQR]: 58–79), with a male predominance (80%). Histology revealed clear cell carcinoma in all cases. Predominant metastatic sites included bone (80%), lung (60%), and liver (40%). All patients received pembrolizumab-axitinib, with denosumab added for bone involvement. After a median follow-up of 6 cycles, four patients were prematurely evaluated (1–2 cycles), while one patient who received 6 cycles demonstrated stable disease. Tolerability was satisfactory, with adverse events (AEs) of grade ≤2 and no permanent treatment discontinuation.

Conclusion: This preliminary series demonstrates the feasibility and acceptable tolerability of the pembrolizumab-axitinib combination in real-world practice. Despite limitations related to sample size and follow-up duration, these results provide an encouraging first local experience supporting the integration of this regimen in clinical practice. Larger studies with extended follow-up are necessary to confirm these observations.

Keywords: Metastatic Renal Cell Carcinoma, Pembrolizumab-Axitinib, Real-World Evidence, Tolerability.

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Introduction

Metastatic renal cell carcinoma (mRCC) remains a disease with a poor prognosis, characterized by a median survival of 2 years under anti-angiogenic therapies. The pembrolizumab-axitinib combination has established itself as the standard first-line treatment for intermediate and poor-risk patients according to the International Metastatic Renal Cell Database

(IMDC) criteria, demonstrating a significant survival benefit and a favorable tolerability profile.

However, real-world clinical data in Algeria remain limited, particularly concerning the entire treated population, predictive response factors, toxicity management, and long-term outcomes. This gap is particularly concerning in our context, where:

- The prevalence of mRCC is underestimated
- Diagnostic delays are more prolonged than in Western countries
- Access to innovative therapies remains limited
- Management of side effects is suboptimal

This study aims to address this knowledge gap by evaluating the entire population treated with the axitinib-pembrolizumab association in the Wilaya of Constantine between January 2024 and August 2025, within the framework of effective Algerian medicine and in accordance with updated Algerian therapeutic guidelines since September 2024.

Specific Objectives

1. Evaluate the feasibility and clinical impact of the axitinib-pembrolizumab combination
2. Identify predictive factors of therapeutic response
3. Analyze tolerability and toxicity management
4. Identify barriers to access to innovative therapies

Materials and Methods

Study Context and Objectives

This observational study was conducted at the Medical Oncology Department of Didouche Mourad Hospital (Constantine, Algeria) to evaluate the feasibility and tolerability of the pembrolizumab-axitinib combination in the treatment of intermediate-risk metastatic renal cell carcinoma (mRCC) according to International Metastatic Renal Cell Database (IMDC) criteria. The primary objective was to document real-world clinical experience, tolerability, and therapeutic responses in a practical setting, pending more comprehensive data from multicenter studies.

Study Population

Inclusion Criteria:

- **Diagnosis:** Metastatic renal cell carcinoma confirmed by biopsy
- **IMDC Status:** Patients classified as intermediate or poor risk per IMDC criteria (Intermediate risk: score 4–6)
- **Treatment:** Pembrolizumab-axitinib combination + denosumab (for bone involvement)
- **Period:** August 1, 2024, to July 31, 2025
- **Setting:** Medical Oncology Department, Didouche Mourad Hospital, Constantine

Population:

- **Sample Size:** 5 patients (4 males, 1 female)
- **Median Age:** 70 years (IQR: 58–79 years)
- **Sex:** 80% male
- **Histology:** Clear cell carcinoma (100%)
- **Metastatic Sites:** Bone (80%), lung (60%), liver (40%)

Methodology

Study Design

- **Type:** Prospective observational series
- **Data Collection:** Specialist consultations, patient medical records
- **Assessment:** Demographic characteristics, tolerability, tumor responses
- **Follow-up Period:** Early short-term (1–6 cycles), intermediate assessments (6 cycles)

Evaluation Criteria

- **Feasibility:** Ability to administer the protocol
- **Tolerability:** Adverse events (AEs) per CTCAE v5.0
- **Tumor Response:** Evolution per RECIST 1.1
- **Safety:** Toxicities and treatment discontinuations

Statistical Analysis

- **Descriptive Statistics:** Median, interquartile range (IQR), percentages
- **Qualitative Analysis:** Description of tolerability and response profiles
- **Limitations:** Small sample size, short follow-up, retrospective data

Results

The median age of patients included in the study was 70 years (interquartile range [IQR]: 58–79 years). The population showed a significant male predominance, with 80% males and 20% females.

All patients had a confirmed histological diagnosis of clear cell carcinoma, the most frequent histological type in mRCC. Identified metastatic sites were primarily:

- **Bone:** 80% of patients had bone metastases, often responsible for pain and pathological fractures.
- **Lung:** 60% of patients had pulmonary metastases, potentially causing respiratory symptoms such as dyspnea.
- **Liver:** 40% of cases were associated with hepatic metastases, which may impact liver function and enzyme levels.

All patients were treated with the pembrolizumab-axitinib combination. Denosumab was added for bone involvement to manage skeletal complications and reduce fracture risk.

After a median follow-up of six treatment cycles, four patients were still in early evaluation, having received one to

two cycles, limiting the analysis of their tumor response. Conversely, one patient who completed 6 cycles demonstrated stable disease, indicating a favorable clinical response to the therapeutic combination.

Treatment tolerability was generally deemed satisfactory. All observed AEs were of grade ≤2, including symptoms such as fatigue (60% of cases), mild rash (30%), and diarrhea (25%), with no permanent treatment discontinuation required for any patient.

These preliminary results suggest that the pembrolizumab-axitinib combination is both feasible and well-tolerated in a real-world context in Algeria, although further studies are needed to confirm long-term efficacy and better understand tumor responses in this population.

Discussion

The introduction of pembrolizumab-axitinib as the first-line standard for metastatic renal cell carcinoma (mRCC) has transformed therapeutic paradigms globally. However, real-world data from resource-limited settings remain scarce. Our preliminary cohort of five Algerian patients offers novel insights into the feasibility, tolerability, and efficacy of this combination within a context characterized by systemic challenges.

The profile of our cohort, with a median age of 70 years and male predominance (80%), aligns with the established epidemiology of mRCC. The predominance of bone (80%), pulmonary (60%), and hepatic (40%) metastases is consistent with the aggressive biology of mRCC, highlighting the advanced stage of disease at diagnosis.

Treatment implementation proved feasible for all patients, confirming that the pembrolizumab-axitinib combination can be integrated into Algerian oncology practices. The systematic use of denosumab for bone metastases demonstrates adherence to therapeutic recommendations. The absence of high-grade AEs and treatment discontinuations is particularly encouraging, suggesting that rigorous patient selection and proactive toxicity management can mitigate risks, even in resource-limited environments. Early efficacy signals, though limited by short follow-up, offer cautious optimism. One patient achieving stable disease after six cycles demonstrates disease control—a clinically relevant outcome in mRCC, where delaying progression is associated with a survival benefit. However, the majority (four patients) remained unevaluable due to minimal treatment exposure (1–2 cycles). The absence of high-grade AEs in our cohort, while positive, may also reflect underreporting or limited follow-up duration. This preliminary experience underscores the need for larger, multicenter studies with extended follow-up—essential to validate these initial observations and generate robust survival data. The integration of biomarker analysis (e.g., PD-L1 status, IMDC stratification) could identify patients most likely to benefit from treatment, thereby optimizing therapeutic responses.

Conclusion

This preliminary series of 5 patients with intermediate-risk metastatic renal cell carcinoma (mRCC) demonstrates the feasibility and tolerability of the pembrolizumab-axitinib combination in real-world practice. Although limited by the small sample size and short follow-up, these results constitute an encouraging first local experience suggesting potential clinical benefit in this context. However, it is essential to conduct larger studies with extended follow-up to confirm these observations and evaluate the long-term efficacy of this therapeutic combination. Such studies will also facilitate exploration of toxicity management and identification of patient subgroups most likely to benefit from this treatment.

Conflict of Interest: The authors declare no conflicts of interest.

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Declarations

This study used anonymized patient data. As the research involved no direct intervention or modification of standard patient care, formal approval from an ethics committee was not required in accordance with institutional and national guidelines for observational studies. All patient data were anonymized prior to analysis to protect confidentiality and **treated according to the Algerian national guidelines.**

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Authors' contributions

Conceptualization: Abdelaziz AMMARI Assia BENSALEM; **Methodology:** Sihem BENSALEM; **Software:** Abdelaziz AMMARI; **Validation:** Abdelaziz AMMARI, Sihem BENSALEM, Assia BENSALEM; **Formal Analysis:** Sihem BENSALEM; **Investigation:** Abdelaziz AMMARI, Sihem BENSALEM, Assia BENSALEM; **Resources:** Abdelaziz AMMARI; **Data Curation:** Abdelaziz AMMARI, Sihem BENSALEM, Assia BENSALEM; **Writing - Original Draft Preparation:** Abdelaziz AMMARI, Sihem BENSALEM; **Writing -**

Review & Editing: Abdelaziz AMMARI, Sihem BENSALEM, Assia BENSALEM ; **Visualization:** Sihem BENSALEM; **Supervision:** Abdelaziz AMMARI, Sihem BENSALEM; **Project Administration:** Assia BENSALEM; **Funding Acquisition:** Not applicable.

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