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Tolerance profile of patients treated with Everolimus: approximately 20 patients followed at the National Institute of Oncology, Rabat (INO)

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ABSTRACT

Introduction:
Everolimus, an mTOR pathway inhibitor, is a recognized therapeutic option for several advanced solid cancers. Although its safety profile has been documented in clinical trials, it remains poorly studied in real- world settings, particularly in Morocco.
Objective:
Evaluate the clinical and biological tolerability of Everolimus in patients with metastatic cancer treated at the National Institute of Oncology (INO) in Rabat.
Methods:
This is a retrospective descriptive and analytical study conducted between January 2020 and October 2022. Twenty patients, mostly with hormone receptor-positive breast cancer, were treated with Everolimus as monotherapy or in combination with hormone therapy. Tolerance was assessed according to version 5.0 of the CTC-NCI criteria.
Results:
The average age of the patients was 53 years, with a predominance of women 16 patients (80%). Breast cancer accounted for 70% of indications (14 patients). The adverse effects reported were moderate, with hyperglycemia in 20% of cases (4 patients), requiring oral antidiabetic treatment, and grade 1 mucositis in 10% of cases (2 patients) . No serious infectious events were observed.
Conclusion:
Everolimus showed a good tolerance profile in our cohort, with manageable toxicities under close monitoring. These results confirm the feasibility of its use in real-world practice, while highlighting the importance of personalized follow-up. Larger studies, including pharmacogenetic evaluation, are needed to refine the therapeutic strategy in the Moroccan population.

KEYWORDS

mucositis, metastatic cancer, targeted therapy, tolerance, everolimus

MAIN ARTICLE

Introduction

Everolimus is an inhibitor of the mammalian target of rapamycin (mTOR) signaling pathway, a key therapeutic target involved in the regulation of cell growth, proliferation, and angiogenesis [1]. Through this mechanism of action, Everolimus has been established as a treatment option for several oncological indications, including advanced hormone receptor-positive breast cancer, anti-VEGF-resistant clear cell renal cell carcinoma, and non-functional neuroendocrine tumors of pancreatic, pulmonary, or gastrointestinal origin [2,3].

Despite its demonstrated efficacy in multiple clinical trials, Everolimus is frequently associated with adverse events-some of which may be severe-potentially affecting patients' quality of life and leading to dose modifications or treatment discontinuation [4]. The most commonly reported toxicities include stomatitis, skin rash, metabolic disturbances (e.g., hyperglycemia, hyperlipidemia), and non-infectious interstitial pneumonitis [5,6]. A thorough understanding of its safety profile is therefore essential for optimal patient management, particularly as real-world data-outside of controlled clinical trials-remain scarce, especially in low- and middle-income countries.

In this context, we conducted a retrospective study at the National Institute of Oncology (INO) in Rabat, Morocco, aimed at characterizing the safety profile of Everolimus in a cohort of 20 patients with various oncological malignancies treated between January 2020 and October 2022. This analysis intends to compare local clinical experience with data from international studies, and to identify areas for improving the monitoring and management of Everolimus-related adverse events in real-world settings.

Methods

This retrospective, descriptive, and analytical study was conducted at the National Institute of Oncology (INO) in Rabat, Morocco. It included a cohort of 20 patients treated with Everolimus between January 2020 and October 2022. Clinical and therapeutic data were systematically retrieved from the hospital information system (HIS), ensuring data traceability and completeness.

The study population consisted of patients with metastatic cancers, primarily hormone receptor-positive breast cancer-who received Everolimus either as monotherapy or in combination with endocrine therapy (Fulvestrant or Exemestane).

For each patient included in the study, a set of clinical and therapeutic variables was systematically collected. This included anonymized patient identification using coded initials, as well as the age at the time of treatment initiation. The patients' medical history was reviewed, with particular attention to the presence of metabolic comorbidities such as diabetes. Information on the histopathological diagnosis and the specific tumor type was documented. The line of therapy at which Everolimus was introduced was recorded, along with any prior treatments received, including the use of CDK4/6 inhibitors. The mode of Everolimus administration was noted, distinguishing between monotherapy and combination therapy. Additionally, the number of treatment cycles administered was documented. Finally, any adverse events experienced during therapy were reported and graded according to the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.

Inclusion criteria were: age ≥18 years, histologically confirmed malignancy, approved clinical indication for Everolimus, and adequate documentation of longitudinal medical follow-up. Patients enrolled in experimental protocols or with incomplete clinical data were excluded.

All patients underwent comprehensive biological evaluations before each treatment cycle, including complete blood counts, serum glucose levels, renal and hepatic function tests, and electrolytes, in order to enable early detection of potential toxicities.

To prevent stomatitis, all patients received prophylactic treatment with a dexamethasone-based mouthwash following the SWISH (Steroid Wash for Inhibition of Stomatitis in HDAC

Inhibitor Therapy) protocol. This mouthwash was prepared either in a hospital or community pharmacy by diluting injectable dexamethasone (e.g., 4 mg/mL) in 0.9% sodium chloride or sterile water to achieve a final concentration of 0.5 mg/mL. Patients were instructed to rinse with 10 mL of this solution for two minutes without swallowing, then spit it out, avoiding food or drink intake for 30 minutes. This procedure was repeated four times daily.

Adverse events were documented through clinical follow-up visits and electronic health records. Particular attention was paid to toxicities typically associated with mTOR inhibitors, including mucositis, metabolic disturbances (hyperglycemia, hyperlipidemia), hematologic toxicity, and infectious complications. Adverse events were classified by type, frequency, severity (grade 1 to 5), and time to onset from treatment initiation.

Results

Patient Characteristics and Therapeutic Modalities

The study included a total of 20 patients treated with Everolimus at the National Institute of Oncology (INO) in Rabat. Of these, 80% were female (n = 16) and 20% male (n = 4). The mean age at the start of treatment was 53 years. Only one patient had notable medical history, namely well-controlled type 2 diabetes managed with oral antidiabetic therapy (table1).

Characteristics	**Values**
female sexe	16 patients (80%)
male sexe	4 patients (20%)
Mean age	53 years
Medical history	1 patient with controlled type 2 diabetes

Table 1 : Demographic characteristics of patients treated with Everolimus (N=20)

Tumor Location and Treatment Indications

Hormone receptor-positive metastatic breast cancer was the most common indication for Everolimus, accounting for 70% of cases (n = 14). Renal cell carcinomas and neuroendocrine tumors were equally represented, each in 15% of patients (n = 3 respectively) (table2). Notably, 10% of patients (n = 2) had previously received treatment with CDK4/6 inhibitors before starting Everolimus due to disease progression.

Indications	Values
Metastatic breast cancer	14 patients (70%)
Renal cell carcinoma	3 patients (15%)
Neuroendocrine tumors	3 patients (15%)

Table 2 : Tumor location (N=20)

Treatment Modalities and Monitoring

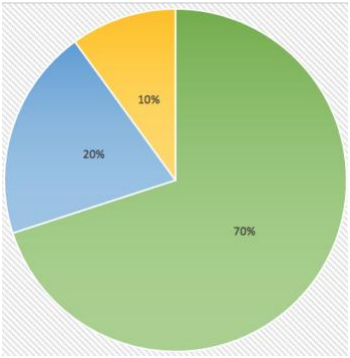
In terms of treatment regimens, 70% of patients (n = 14) received Everolimus in combination with endocrine therapy (Fulvestrant or Exemestane), while 30% (n = 6) received Everolimus as monotherapy. The average duration of treatment was eight months.

Before each treatment cycle, a comprehensive biological assessment was systematically performed, with particular attention to detecting metabolic disorders. To prevent stomatitis, all patients received a dexamethasone-based mouthwash, in accordance with the SWISH protocol, which is recommended in the literature to reduce the incidence of Everolimus-induced oral mucositis [7].

All patients were administered a fixed daily dose of 10 mg Everolimus, with no need for dose adjustment throughout the treatment period (table3). Adverse events were assessed according to CTCAE version 5.0 criteria [8]. Overall, toxicities were mild: grade 1 mucositis was reported in 10% of patients (n = 2), which resolved rapidly with enhanced symptomatic management. Hyperglycemia was observed in 20% of patients (n = 4), necessitating the initiation of oral antidiabetic treatment with metformin (figure *1*). No cases of interstitial pneumonitis, opportunistic infections, or severe systemic infections were observed in this cohort.

Parameters	Values
Everolimus + Hormone therapy	14 patients (70%)
Everolimus monotherapy	6 patients (30%)
Average treatment duration	8 months
Dosage	10 mg/day (100%)
Dose adjustment	0 (0%)
Stomatitis prevention protocol	20 (100%)

Table 3: *Treatment modalities (N=20)*



70% (N=14): No side effects

20% (N=4): Hyperglycémia

10% (N=2): Stomatits

Figure 1: *Sides effects under Everolimus (N=20)*

Discussion

The analysis of this cohort of 20 patients treated with Everolimus at the National Institute of Oncology (INO) in Rabat provides an overall tolerance profile that is generally satisfactory and consistent with data from the international literature.

Demographic Profile and Therapeutic Indications

The predominance of female patients (80%) reflects the high prevalence of hormone receptor-positive metastatic breast cancer, which was the primary indication for treatment in 70% of cases. This demographic and clinical profile is in line with findings from the BOLERO-2 trial, in which Everolimus combined with Exemestane significantly improved progression-free survival in this patient population [2]. Other indications such as renal cell carcinoma (15%) and neuroendocrine tumors (15%) are also supported by the RECORD-1 and RADIANT-3 studies, respectively [3].

Metabolic Tolerance and Toxicities

The toxicities observed in our cohort were generally mild to moderate. Hyperglycemia occurred in 20% of patients, an expected adverse event resulting from mTOR pathway inhibition and its metabolic consequences [7]. This incidence is slightly higher than those

reported in the BOLERO-2 (12%) and RECORD-1 (13%) trials, but was effectively managed with the introduction of metformin [2,9].

Stomatitis was observed in one patient (10%, grade 1) and was effectively prevented using a dexamethasone-based mouthwash according to the SWISH protocol, confirming the preventive efficacy of this approach as demonstrated in the SWISH trial (grade ≥2 stomatitis: 2%) [10]. No cases of pneumonitis or opportunistic infections were reported, likely due to close monitoring and rigorous patient selection.

Study Limitations

Several limitations of our study must be acknowledged. Firstly, the small sample size (n=20) limits the statistical power and generalizability of the findings. Moreover, although data collection was conducted retrospectively, the primarily descriptive nature of the analysis restricts the ability to make comparative assessments. Finally, the absence of pharmacokinetic monitoring of Everolimus precludes the correlation between plasma concentrations and observed adverse events-an important aspect given the interindividual variability in drug metabolism [11].

Clinical Implications

Despite these limitations, our findings yield several practical insights. Close clinical and laboratory follow- up is essential to detect and manage adverse events promptly. The favorable safety profile observed in our cohort also suggests that individualized dose adjustments-though not implemented in this study-could be beneficial in cases of more pronounced toxicity. Furthermore, patient education regarding the prevention of stomatitis, treatment adherence, and early recognition of warning signs should be systematized to improve treatment adherence and quality of life [12].

Future Perspectives

These results highlight the need to develop a national oncology pharmacovigilance registry to better characterize the safety profile of targeted therapies such as Everolimus in real-world settings. Larger-scale studies integrating pharmacokinetic and pharmacogenetic parameters would also be valuable to evaluate the impact of local genetic variability (notably CYP3A4/5,

ABCB1) on treatment efficacy and toxicity [13]. Such data would support a more personalized therapeutic approach tailored to the Moroccan context.

Conclusions

Despite being conducted on a limited sample, this study highlights the overall favorable tolerability profile of Everolimus in patients treated at the National Institute of Oncology, particularly in hormone receptor- positive metastatic breast cancer. The observed metabolic and mucosal adverse events were mostly of low grade and were effectively managed through close clinical monitoring and appropriate preventive measures, such as dexamethasone-based mouthwash.

These findings emphasize the importance of a multidisciplinary approach, including regular biological monitoring, continuous clinical vigilance, and proactive patient education to enhance treatment adherence and reduce complications. They also demonstrate that, even in resource-limited settings, targeted therapies like Everolimus can be administered safely and effectively, provided that a rigorous medical framework is in place.

However, the methodological limitations of the study-such as the small sample size, absence of pharmacokinetic data, and non-randomized design-warrant caution in generalizing the results. These constraints underscore the need for national registries and prospective multicenter studies, incorporating pharmacogenetic assessments tailored to the Moroccan population. Such approaches will contribute to more individualized therapeutic strategies, improved treatment tolerance, and ultimately better quality of life and clinical outcomes for patients receiving Everolimus.

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