Dermatology Practical & Conceptual

Impact of Xerosis in Patients with Cancer Receiving Epidermal Growth Factor Receptor or Mitogen-Activated Protein Kinase Inhibitors: ATIXI, A Non-Interventional Prospective Pilot Study

Pietro Quaglino[1], Giuseppe Argenziano[2], Emi Dika[3,4], Michela Starace[4,5], Simone Amabile[1], Paolo Fava[1], Elvira Moscarella[2], Bianca Maria Piraccini[4,5], Alain Delarue[6], Olivia Dialla[7], Fabienne Zumaglini[6], Giampiero Girolomoni[8]

1 Dermatologic Clinic, Department of Medical Sciences, University of Turin, Turin, Italy
2 Dermatology Unit, Department of Mental and Physical Health and Preventive Medicine, University of Campania Luigi Vanvitelli Naples, Italy
3 Oncologic Dermatology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy
4 Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Italy
5 Dermatology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Policlinico S. Orsola-Malpighi, Bologna, Italy
6 Pierre Fabre, Lavaur, France
7 Pierre Fabre, Boulogne-Billancourt, France
8 Department of Medicine, Section of Dermatology, University of Verona, Italy

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Corresponding Author: Fabienne Zumaglini, Pierre Fabre Dermatologie, Les Cauquillous, 81500 Lavaur, France. Phone: +33 642 44 41 15 E-mail: fabienne.zumaglini@pierre-fabre.com

Introduction

Dermatological adverse events are commonly experienced by patients during anticancer treatment [1, 2]. Xerosis is frequently associated with epidermal growth factor receptor inhibitor (EGFRi) or mitogen-activated protein kinase inhibitor (MEKi) treatment [3]. While xerosis is typically mild-to-moderate in intensity, it can significantly impact quality of life [4], especially in patients receiving long-term anticancer therapy.

Case Presentation

We conducted a non-interventional prospective pilot study at three oncology centers in Italy to identify the proportion of patients with emerging or worsening xerosis among those receiving targeted anticancer therapies associated with the highest risk of xerosis: EGFRis and MEKis. Eligible patients were ≥18 years old with cancer initiating treatment with an EGFRi or MEKi. Patients were assessed at three study visits (Visit 1 was considered baseline). Study assessments included xerosis severity (using Overall Dry Skin [ODS] scores and Common Terminology Criteria for Adverse Events [CTCAE] classifications), skin dryness (using Hydration Index [HI] scores), and treatments.

Between 2019 and 2022, 22 patients (mean age 57.3 years) completed all three study visits. The majority (90.9%) received a MEKi (trametinib: n=18, binimetinib: n=2) and two (9.1%) patients received an EGFRi (osimertinib). MEKis were administered with a BRAF inhibitor in all but one patient. Of these 22 patients, five (22.7%) either developed xerosis (n=3; 13.6%, 95% CI: 2.9–34.9) or had a worsening of their preexisting xerosis (n=2; 9.1%, 95% CI: 1.1–29.2) during treatment (Figure 1). Xerosis severity (CTCAE criteria) was considered Grade 1 in 5 (22.7%) patients and Grade 2 in 3 (13.6%) patients at Visit 3 (Table 1). Approximately one-third of patients received emollient treatments during the study (Table 1). HI scores decreased, with a mean ± SD change from baseline of –5.10 ± 17.22 and –6.30 ± 20.68 at Visits 2 and 3 (Table 1).

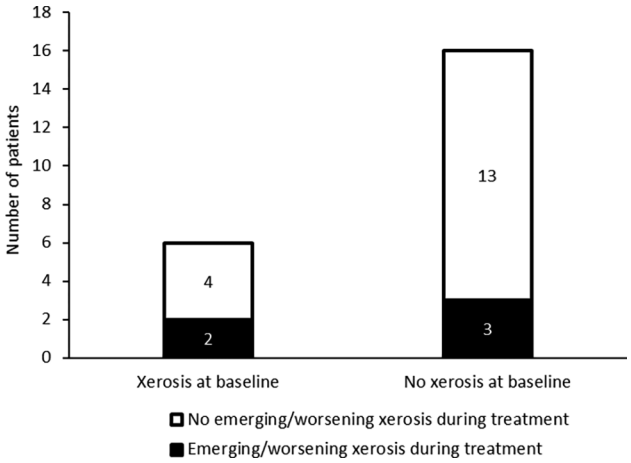

Figure 1. Number of patients who attended all three study visits with emerging or worsening xerosis while receiving epidermal growth factor receptor or mitogen-activated protein kinase inhibitors (n=22).

Table 1. Outcomes in the Patients Who Attended All 3 Study Visits (n=22).

	Visit 1 (BL)	Visit 2	Visit 3
Xerosis, *n* (%)	6 (27.3)	5[a] (22.7)	8[b] (36.4)
Xerosis location, n (%)			
Lower limbs	4 (18.2)	4 (18.2)	7 (31.8)
Upper limbs	3 (13.6)	4 (18.2)	6 (27.3)
Hands	2 (9.1)	2 (9.1)	3 (13.6)
Emollients, n (%)	7 (31.8)	7 (31.8)	8 (36.4)
Emollients and topical barrier products	5 (22.7)	6 (27.3)	8 (36.4)
ODS score, mean ± SD	0.32 ± 0.6	0.32 ± 0.6	0.64 ± 1.0
ODS score, n (%)			
0	16 (72.7)	17 (77.3)	14 (63.6)
1	5 (22.7)	3 (13.6)	3 (13.6)
2	1 (4.5)	2 (9.1)	4 (18.2)
3	0	0	1 (4.5)
Xerosis severity, CTCAE classification, n (%)			
Grade 1	6 (27.3)	4 (18.2)	5 (22.7)
Grade 2	0	1 (4.5)	3 (13.6)
HI score, mean ± SD	38.59 ± 13.36	33.48 ± 11.17	31.66 ± 14.10[c]
HI score, n (%)			
<30 (very dry)	6 (27.3)	8 (36.4)	10 (47.6)[c]
30–45 (dry)	8 (36.4)	11 (50.0)	6 (28.6)[c]
>45 (sufficiently hydrated)	8 (36.4)	3 (13.6)	5 (23.8)[c]

[a]Xerosis resolved in one patient between baseline and Visit 2, then reappeared at Visit 3; [b]Xerosis resolved in one patient after the baseline visit; [c]n=21. Abbreviations: BL: baseline; CTCAE: Common Terminology Criteria for Adverse Events; HI: Hydration Index; ODS: overall dry skin; SD: standard deviation.

Conclusions

Although small and without a control group, this pilot study showed that less than one-quarter of patients (22.7%) initiating EGFRis or MEKis developed xerosis (n=3; 13.6%) or experienced worsening of their pre-existing xerosis (n=2; 9.1%). The incidence of xerosis in the current study was broadly similar than that previously reported with other targeted anticancer therapies (20.1%–46.5%) [3]. Future research on the frequency and impact of xerosis is warranted in a larger cohort of patients receiving EGFRis or MEKis over a prolonged treatment period in real-world clinical practice.

The pathogenesis of xerosis is related mostly to the mechanism of action of EGFRis and MEKis, since inhibition of EGFR signaling pathway disrupts epidermal differentiation and homeostasis, causing inflammation, ultraviolet sensitivity, dry skin, and alterations to skin barrier function [5,6]. Currently, there are no guidelines on how to manage xerosis in patients receiving anticancer treatments, but an algorithm based on CTCAE grading is recommended for early identification and prevention of xerosis and others skin complications [3]. Use of moisturizers and barrier replacement creams is essential.

While the patients in the current study had xerosis of Grade 1 or 2 severity, its associated burden should not be underestimated. Prevention, early detection, and treatment of xerosis should be appropriately considered.

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