MANAGEMENT OF CUTANEOUS TOXICITY INDUCED BY EPIDERMAL GROWTH FACTOR RECEPTOR INHIBITORS (EGFR-I) IN SQUAMOUS CELL CARCINOMAS OF THE HEAD AND NECK, COLORECTAL OR LUNG CANCER

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BACKGROUND

Epidermal Growth Factor Receptor-Inhibitors (EGFR-I) frequently induce skin or appendage toxicities. These toxicities may impact patient's quality of life and lead to a reduction in the dose or even the discontinuation of the anti-tumor treatment, inducing a possible decrease of the treatment response. Pre-emptive use of doxycyclin and emollients have already been reported in the litterature [1].
Wound healing products can also be used to manage cutaneous toxicities in association of pharmacological measures.

DESIGN

CICAFIX is a prospective interventional, monocentric, randomized (1:1 ratio), controlled, open-labeled study.

Sample size - A minimum of 80 evaluable patients (40 per group) was required to show a 2-point increase of satisfaction in favour of repairing balm (non-parametric test, estimated standard deviation of 2.5 points, 90% power, two-sided alpha of 5%).

Treatments - To be applied since the beginning of EGFR-I treatment of the face then on the skin lesions:

- Group A: **Repairing balm** (with glycerin, shea butter, panthenol, madecassoside, copper-zinc gluconate)
- Group B: **Standard emollient** (with glycerin, petrolatum)

All patients were planned to receive a body care emollient (with shea butter, niacinamide, aqua posae, and thermal spring water), a cleansing syndet (with glycerin, niacinamide and thermal spring water) and doxycyclin 100mg per day from the start of the study as a pre-emptive therapy.

OBJECTIVES

Primary objective: To compare the overall satisfaction of patients using a standard emollient or a repairing balm for the management of EGFR-I induced skin toxicities. Primary endpoint: patient overall satisfaction at 1 month (on a scale from 0 to 10).
Secondary objectives:

- Satisfaction at 2 months,
- Quality of life, using Dermatology Life Quality Index (DLQI),
- Epidermal repair score (SCOREPI - range 1-41: 5 items to evaluate the severity of skin damage (skin lesions surface, erythema, desquamation, superficial and deep fissures/cracks) [2],
- Safety, assessed through adverse events (AE) grading according to the Common Terminology.

STUDY POPULATION

- Adult men and women ≥ 18 years at the day of inform consent signature,
- Patients with relapsing or metastatic head and neck squamous cell carcinoma, colorectal or lang cancers,
- No prior treatment with EGFR-I,
- No unresolved prior treatment related skin toxicity,
- No concomitant radiotherapy.

RESULTS

From February 2018 to March 2021, 102 pts were randomized (50 in the repairing balm group and 52 in the standard emollient group) with a mean age of 63.6 years. 74.5% of the patients were male, 83.3% were treated for a head and neck squamous cell carcinoma.

PATIENTS CHARACTERISTICS

		Group A N=50		Group B N=52	
Age	Mean (std)	64.0 (11.1)		63.2 (7.9)	
	Median (min; max)	64.0 (39; 96)		63.5 (49; 82)	
Sexe	F	12	(24.0%)	14	(26.9%)
	M	38	(76.0%)	38	(73.1%)
PS ECOG	0-1	33	(68.8%)	35	(67.3%)
	2-3	15	(31.3%)	17	(32.7%)
	Missing data	2		0	
Cancer type					
Head and neck squamous cell carcinoma		42	(84.0%)	43	(82.7%)
Colorectal cancer		4	(8.0%)	5	(9.6%)
Pulmonary cancer		4	(8.0%)	4	(7.7%)
Metastatic disease*		24	(48.0%)	25	(48.1%)
Doxycycline exposure*		41	(82.0%)	42	(80.8%)

* No misssing data

SATISFACTION, QUALITY OF LIFE (DLQI) AND SCOREPI

Overall satisfaction in both groups was high with a median value of 8.

SATISFACTION

	Group A N=50	Group B N=52	All N=102	Test
Overall satisfaction – Day 30 (primary endpoint)				
N (missing)	37 (13)	40 (12)	77 (25)	Wilcoxon
Mean (std)	7.3 (2.2)	7.8 (2.3)	7.6 (2.3)	P = 0.245
Median (Q1; Q3)	**8.0** (6.0; 9.0)	**8.0** (7.0; 10.0)	**8.0** (6.0; 10.0)	
Overall satisfaction – Day 60				
N (missing)	30 (20)	33 (19)	63 (39)	Wilcoxon
Mean (std)	7.6 (2.3)	7.6 (2.4)	7.6 (2.3)	P = 0.877
Median (Q1; Q3)	**8.0** (7.0; 9.0)	**8.0** (7.0; 9.0)	**8.0** (7.0; 9.0)	

SAFETY

87% of patients had at least one cutaneous AE during study topical steroids, but only 3 patients required the use of dermocorticoides during the study (1 in group A, 2 in group B).

Only 1 patient in group B stopped the EGFR-I treatment due to skin toxicity (fissures).

The median delay to observe the first skin toxicity was 18 days in group A and 22 days in group B.

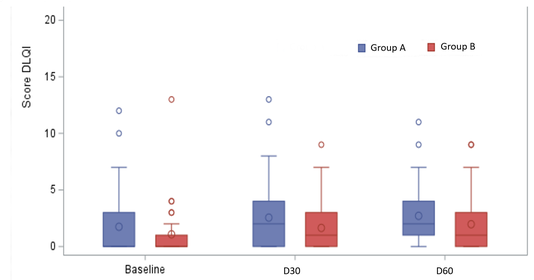
TREATMENTS

Delivered: **Study treatments**

	Group A N=50	Group B N=52
Number of patients (%)	44 (88%)	44 (85%)
Mean quantity of product per patient (min-max)	156 ml (80-440).	330 mg (250-750)

86% of all patients received the body care emollient and the cleansing syndet.

Observance (followed with a patient diary):
More than 70% did not report application of the products either on the face, lesions either on face or fissures with a same proportion in the 2 groups (35 patients in both groups).



Patients' quality of life was mildly altered during the study. DLQI score evolution could be linked with both the underlying cancer and skin toxicities.

SCOREPI mean score at day 30 was respectively 4.1 (± 3.9) in Group A and 3.4 (± 3.3) in Group B (NS). At day 60, mean score was 6.0 (± 4.9) and 3.3 (± 4.0) for A and B, respectively.

PT	Group A (N=49)				Group B (N=47)			
	1	2	3	Any grade	1	2	3	Any grade
FOLLICULITIS	4 (8.2%)	3 (6.1%)	0 (0.0%)	7 (14.3%)	4 (8.5%)	0 (0.0%)	0 (0.0%)	4 (8.5%)
DERMATITIS ACNEIFORM	9 (18.4%)	4 (8.2%)	0 (0.0%)	13 (26.5%)	10 (21.3%)	0 (0.0%)	1 (2.1%)	11 (23.4%)
DRY SKIN	4 (8.2%)	0 (0.0%)	0 (0.0%)	4 (8.2%)	6 (12.8%)	2 (4.3%)	0 (0.0%)	8 (17.0%)
RASH	21 (42.9%)	1 (2.0%)	2 (4.1%)	24 (49.0%)	20 (42.6%)	4 (8.5%)	0 (0.0%)	24 (51.1%)
SKIN EXFOLIATION	9 (18.4%)	0 (0.0%)	2 (4.1%)	11 (22.4%)	4 (8.5%)	2 (4.3%)	0 (0.0%)	6 (12.8%)
SKIN FISSURES	12 (24.5%)	1 (2.0%)	0 (0.0%)	13 (26.5%)	13 (27.7%)	0 (0.0%)	0 (0.0%)	13 (27.7%)
SKIN LESION	15 (30.6%)	3 (6.1%)	0 (0.0%)	18 (36.7%)	17 (36.2%)	1 (2.1%)	0 (0.0%)	18 (38.3%)

CONCLUSION

Although efficacy hypothesis was not reached, possibly due to the pre-emptive treatment both groups received including doxycyclin, body emollient and cleansing syndet, and the low compliance to study treatments, the management of cutaneous toxicities with a repairing balm containing panthenol and madecassoside has a positive impact on patient satisfaction and SCOREPI and is a well-tolerated therapeutic option.

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