Trial title	A study to assess the efficacy of an emollient cream in reducing skin reactions of patients treated for their Actinic Keratosis with 5-fluorouracil 4% treatment
Disease 	Actinic Keratosis (AK)
Treatment 	Drug: 5-fluorouracil 4% topical formulation (Tolak®) Device : Glycerol/Vaseline/Paraffin cream (emollient cream Dexeryl®)
Participants 	Adult participants with 5 or more actinic keratosis lesions on the face, and/or ears and/or scalp
Trial dates 	From 16 February 2021 (first patient first visit) to 31 January 2022 (last patient visit)
Trial Locations 	France, Germany, Italy, Spain
We do research to improve patient care. This trial will help us to answer important questions about treatment of Actinic Keratosis	

This document is a summary of trial results and conclusions written for public and people who took part in the trial.

This summary was finalized on November 2022. The information in this summary does not include additional information available after this date.

For people who took part in the trial, Pierre Fabre Pharmaceutical group would like to say

THANK YOU

We hope this document helps you understand and feel proud of your key role in medical research. If you have questions about the results, please speak with the doctor or staff at your study site.

To learn about the trial and its conduct

- What was the purpose of the trial?
- What were the objectives and how were they evaluated?
- How was the trial carried out?

To get a summary of trial results:

- What were the results of the trial?

THE TRIAL	
What was the purpose of the trial?	Actinic Keratosis (AK) treatments such as topical 5-fluorouracil formulations induce frequent local skin reactions. These reactions are temporary and are a normal response to treatment but can lead some patients to discontinue the therapy. The purpose of this study was to evaluate if the use of an emollient cream (glycerol/paraffin/petroleum) may reduce skin reactions of patients treated with Tolak® for their Actinic Keratosis.
What were the objectives and how were they evaluated?	The primary objective was to compare the Local Skin Reaction score (LSR score) on the area treated at the end of a 4-week therapy between the group of patients having received 5-fluorouracil 4% associated with an emollient cream (called the intervention group) and the group of patients having received 5-fluorouracil 4% only (called the control group). The LSR score includes the evaluation of 6 usual types of skin reactions: - erythema (the redness of the skin), - erosion and ulceration (losses of superficial parts of the skin that can lead to a sore), - swelling (skin oedema), - crusting, - flaking and scaling (related to an excessive dryness of the skin), - vesiculation and pustulation (appearance of small blisters filled with fluid). The score was assessed by the doctor and ranges from 0 (absence of skin reaction) to a maximum of 24 (maximal severity for all types of reactions). In addition, secondary objectives of the trial included: • A comparison of the local skin reaction during 5-fluorouracil 4% treatment course between patients with and without emollient cream based on the patients' self-evaluations (subjective symptoms). • A comparison of the tolerability to 5-fluorouracil 4% therapy between patients with and without emollient cream. The tolerability was assessed regarding proportion of patients who stopped their treatment prematurely due to local skin reactions.

	• A comparison of the clinical response to 5-fluorouracil 4% therapy between patients with and without emollient cream. The clinical response was assessed by the evolution of number of AK lesions from trial entry to 4 weeks after the end of the therapy
How was the trial carried out?	This trial was conducted at 22 centres that recruited 145 participants, including 7 centres in Germany (67 participants), 5 in France (24 participants), 5 in Italy (24 participants) and 5 in Spain (30 participants). The total duration of the study was one year from February 2021 (first visit of the first patient) to January 2022 (last visit of the last patient). Participants were patients with at least 5 lesions of actinic keratosis (AK) on the face, and/or ears and/or scalp. The total duration of the study for each participant was 8 weeks including 4 visits (inclusion visit, Week 2, Week 4 and Week 8). Participants were assigned to one of the two treatment groups (intervention or control) by randomisation . 5 fluorouracil 4% cream was to be applied once daily in the evening for 4 weeks. Emollient cream was to be applied once daily in the morning for 8 weeks.

TThis is a summary of the main results and conclusions of this trial. Please note that:

- These are the results from all the participants combined. The individual results of each participant might be different and are not in this summary.
- This summary reflects the outcome of one single trial and that other trials may show other results or other outcomes.

❖ Daily application of the emollient cream does not improve local skin reactions induced by Tolak® therapy.

LSR score at the end of the Tolak® therapy, was similar in both treatment groups:

- For participants receiving Tolak® and the emollient cream (intervention group), mean LSR total score increased from 1.6 to 7.1.
- For participants receiving Tolak® only (control group), mean LSR total score increased from 1.6 to 7.7.

The small difference observed in favour of intervention group is not sufficient to be considered as a real benefit for the participants.

Number of participants having reported a severe side effect related to skin reaction during the trial was similar with 5 participants (7.1%) from intervention group and 6 (8.6%) from control group. Assessment of skin reaction based on subjective symptoms was also comparable between groups.

❖ Tolerability to Tolak® is not improved by application of the emollient cream.

During the trial, 7 participants (9.9%) in the control group and 9 participants (12.3%) in the intervention group discontinued therapy due to a side effect related to skin reaction.

❖ Daily application of the emollient cream does not change efficacy of Tolak® therapy.

Eight weeks after the start of treatments (4 weeks after the end of Tolak® therapy), mean reduction of AK lesions was 72% in both groups. The number of participants for whom all AK lesions had disappeared was slightly higher in intervention group (38.6%) than in control group (33.3%).

- The side effects reported during the trial are well known and correspond to those usually experienced during Tolak® therapy.

Around 20% (15 out of 73) of participants in the intervention group and around 18% (13 out of 71) of patients in the control group had side effects. At least all the side effects were related to local skin reactions such as erythema and swelling. Some of these reactions were associated with burning sensation, itching, or pain. Side effects were localised and temporary. Half of them required additional medications, mainly topical corticosteroids, and emollients.

None of the side effects were serious (a side effect is considered 'serious' if it is life-threatening, needs hospital care, or causes lasting problems).

Glossary	
Side effects	Side effects are unwanted medical events (such as headache) that happen during the trial and that are related or possibly related to trial treatment.
Randomisation	Randomisation is the assignment to one of the treatment groups using an element of chance Neither the researcher nor the participant chooses which treatment the participant will receive. Using chance to assign people to groups means that the effects of the treatment can be compared more fairly.
Tolak®	5-fluorouracil 4% (Tolak®) is a cream indicated in adults for the topical treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis lesions on the face and/or ears and/or scalp.
Emmolient cream	The emollient cream containing glycerol, vaseline and paraffin is marketed as a non-medicinal treatment (Dexeryl®) for signs and symptoms of skin dryness in various skin diseases.
Tolerability	Tolerability to a treatment is the degree to which a patient can accept side effects. Tolerability can be assessed regarding the proportion of patients with treatment dose reductions, interruptions or discontinuations due to side effects. Requirement of additional therapies is also a key parameter of tolerability assessment.

Cinical Trial identification	
Protocol Number	W00118CR401
Protocol Version	3.0 dated 22 March 2021
Full trial title	Frequency and Intensity of local reactions in patients treated with 4% 5-FU vs 4% 5-FU associated with an emollient cream: a randomised, controlled clinical trial
Registry ID	EudraCT Number: 2020-000851-11 ClinicalTrials.gov : NCT04875026

Who sponsors this trial?	
Name and contact details of the sponsor	Pierre Fabre Dermatologie Les Cauquillous 81500 Lavaur-France .