Title:	A MULTI-CENTER, DOUBLE-BLIND, RANDOMIZED, PLACEBO CONTROLLED, PARALLEL-GROUP STUDY, COMPARING TEST TOPICAL PRODUCT TO BRAND TOPICAL PRODUCT AND BOTH ACTIVE TREATMENTS TO A PLACEBO CONTROL IN THE TREATMENT OF ACTINIV KERATOSIS
Study Period:	6 weeks (42 Days)
Study Medication:	1. Test Topical Product 2. Reference Topical Product 3. Vehicle of the Test Topical Product
Study Objectives:	To evaluate Equivalence of Test Topical Product to Reference Topical Product and the statistical superiority of Test and Reference over the vehicle and to compare the severity of irritation and incidence of adverse events in treated patients in all treatment groups.
Study Design:	Subjects with actinic keratosis on the face or bald scalp with at least 5 lesions and no more than 10 lesions, will be admitted into this multi-center, double-blind, randomized, vehicle-controlled, parallel-group study
Dosing:	Subjects will be randomized in a 2:2:1 ratio to the test product (200 subjects), reference product (200 subjects) or vehicle treatment group (100 subjects), respectively (study medications). Subjects will apply the study medications to the affected areas on the face or bald scalp twice daily for 2 weeks. Subjects will use an amount of cream sufficient to cover the affected area. Study medication will be spread as a thin layer, avoiding the eyes, lips, inside the nose, mouth and all mucous membranes.
Methodology:	Clinical and Safety Evaluations will be performed at: 1. Visit 1/Baseline, Day 1 2. Visit 2/Week 1, Day 8 (+/- 2 Days) 3. Visit 4/Week 2, Day 15 (+/- 2 Days) 4. Visit 5/Week 6, Day 43 (+/- 4 Days) Subjects will be admitted into the study after all inclusion/exclusion criteria have been met, including a clinical diagnosis of actinic keratosis and after written informed consent has been obtained. Efficacy assessments will include face, forehead or bald scalp lesions counts and investigator's assessment ranging from 0 (Clear) to 3 (Grade III). Investigators will be provided with instructions for lesion counts to ensure consistency of procedure. Safety will be assessed at all visits and will include monitoring local and systemic adverse experiences; the

	Investigator Cutaneous Safety Assessment rating of erythema (erythema, redness and dermatitis) and dryness on a scale ranging from 0 (None) to 3 (Severe); and the subject assessment of Local Tolerability rating itching, burning, and stinging on a scale ranging from 0 (None) to 3 (Severe). Subjects will return to centers for cutaneous safety, efficacy and local tolerability assessments at Weeks 1, 2 and 6. Adverse events and concomitant medications will be assessed throughout the treatment period. A urine pregnancy test is required at baseline, week 2 and week 6 for all females of childbearing potential.
Clinical trial duration	Duration of study period: 42 days Duration of treatment period: 14 days Subjects that exhibited a serious adverse event (SAE) will be followed up until the SAE stabilizes or resolves, based on the investigator's medical judgment.
Investigational product dosage	Products will be applied twice daily for 14 days. The Product will be supplied in 20-gram tubes.
Subject inclusion criteria	Subjects may participate in the study if they meet all of the following criteria: 1. Male and female subjects 18 years of age or older. 2. Subject is willing and able to give written informed consent and capacity for protocol compliance. 3. In good general health Based on medical records 4. At least five (5) and no more than ten (10) clinically typical, visible or palpable, discrete, AK lesions, each at least 4 mm in diameter on the face (excluding ears) or balding scalp. 5. Females must be post-menopausal, surgically sterile, or use an effective method of birth control with a negative urine pregnancy test (UPT) at the Baseline Visit.
Subject exclusion criteria	The presence of any of the following will exclude the potential study participant from entry into the study: 1. Subject is pregnant, lactating, or is planning to become pregnant during the study. 2. Presence of atopic dermatitis, basal cell carcinoma, eczema, psoriasis, rosacea, squamous cell carcinoma or other possible confounding skin conditions on the face or bald scalp. 3. Subject is currently enrolled in an investigational drug or device study. 4. Subject has used an investigational drug or investigational device treatment within 30 days prior to the Baseline Visit.

	5. Subject has hyperkeratotic, hypertrophic, or large mat-like AKs (e.g., AK >1 cm^2 in size) within the Treatment Area. 6. Subject has the need or plans to be exposed to artificial tanning devices or excessive sunlight during the trial. 7. Subject is immunosuppressed (e.g., human immunodeficiency virus (HIV), systemic malignancy, graft host disease, etc.) 8. Subject has experienced an unsuccessful outcome from previous topical fluorouracil therapy (an unsuccessful outcome is defined as after a reasonable therapeutic trial with no compliance issues and the topical drug did not work). 9. Subject has a history of sensitivity to any of the ingredients in the test articles. 10. Subject has known dihydropyrimidine dehydrogenase (DPD) enzyme deficiency. 11. Subject used topical creams, lotions, or gels of any kind within the selected Treatment Area within one day prior to entry into the study. 12. Subject has used topical medications; corticosteroids, alpha hydroxy acids (e.g., glycolic acid, lactic acid, etc. >5%), beta hydroxy acid (salicylic acid >2%), urea >5%, 5-fluorouracil, diclofenac, imiquimod, ingenol mebutate, or prescription retinoids (e.g., tazarotene, adapalene, tretinoin) within the selected Treatment Area (face or balding scalp) within one (1) month prior to the Baseline Visit. 13. Subject has had cryodestruction, curettage, photodynamic therapy, surgical excision, or other treatments for AK within the selected Treatment Area (face or balding scalp) within one (1) month prior to the Baseline Visit. 14. Subject has used oral corticosteroid therapy, interferon, cytotoxic drugs, immunomodulators, immunosuppressive therapies, or retinoids within one month prior to the Baseline Visit. 15. Subject has had dermatologic procedures or surgeries such as: laser resurfacing, Psoralen + ultraviolet A (PUVA) therapy, ultraviolet B therapy, chemical peels, or dermabrasion within the selected Treatment area (face or balding scalp) within six months prior to the Baseline Visit. 16. Subject has lesions suspicious for skin cancer (skin cancer not ruled

	out by biopsy) or untreated skin cancers within the selected Treatment Area (face or balding scalp). 17. Subject has any skin pathology or condition on the face or balding scalp that, in the investigator's opinion, could interfere with the evaluation of the test article or requires the use of interfering topical, systemic, or surgical therapy. 18. Subject has any condition which, in the investigator's opinion, would make it unsafe or preclude the subject's ability to fully participate in this research study. 19. Subject is unable to communicate or cooperate with the investigator due to language problems, poor mental development, impaired cerebral function, or physical limitations. 20. Subject is known to be noncompliant or is unlikely to comply with the requirements of the study protocol (e.g., due to alcoholism, drug dependency, mental incapacity) in the opinion of the investigator. 21. Subject has been previously enrolled in the same study.
Criteria for discontinuation of study	Patients will be considered discontinued from the study after randomization for any of the following reasons: 1. Adverse reaction, including drug-induced irritation of such severity that the patient will stop use of the study drug before completing 2 weeks of treatment 2. Non-compliant with study requirements 3. Decision by the patient not to continue 4. Judgment by the investigator that it is not in the patient's best interest to continue
Treatment Compliance	Patients will apply at least 75% to 125% of the expected 28 applications (21 to 35 applications) of study medication to be considered compliant with the treatment regimen. Treatment compliance will be verified by using patient diaries. The study tubes will be weighed and recorded in a dispensing log by study staff. At the conclusion of the study, patients will be asked to return their unused study medication to be returned to the sponsor.

Primary efficacy endpoints	To assess the proportion of patients in the PP population with treatment success defines as complete clearing (100% of all AK lesions within the treatment area) at week 6 Visit 4, 4 weeks follow-up) after completion of 2 weeks of treatment. The sponsor will perform descriptive statistics for the proportion of patients with complete clearing of all lesions or only residual smooth flat redness present without elevation above the skin for each treatment group at week 6 in both the ITT and PP population
Secondary efficacy endpoints	To assess the statistical superiority of Test Topical Product and Reference Topical Product over Vehicle.
Safety endpoints	To compare the severity of irritation (as evidenced by erythema, redness and dermatitis) and, subject assessment of itching, burning, and stinging.
Dosing Safety:	Adverse events will be evaluated by monitoring local and systemic adverse reactions: subjects will be asked about AEs at each visit; descriptions of AEs will include: date of onset, date ended, severity, seriousness, relationship to study drug, action taken with study drug, corrective treatment and outcome. In addition, subjects with serious adverse events (SAE) will be followed up until the SAE stabilizes or resolves, based on the investigator's judgment.

Study Flow Chart

PROCEDURES	VISIT 1 BASELINE Day1	VISIT 2 WEEK 1 Day 8 +/-2 days	VISIT 3 WEEK 2 Day 15 (End of Tretatment) +/-2 days	VISIT 4 WEEK 6 Day 43 (End of study) +/-3 days
Medical History and Inclusion/Exclusion Criteria	X			
Informed Consent	X			
Demographics	X			
Urine Pregnancy (If applicable)	X[2]		X	X
Assessment of Eligibility	X		X	X
Dispense Product	X			
Collect Product and weighing			X	
Cutaneous Safety Assessment	X	X	X	X
Photo-documentation	X			X
Subject compliance reviewed (Diary)	X	X	X	
Concomitant Medications	X[2]	X	X	X
Assessment of AEs/ con med	X	X	X	X