Supplemental material

Inclusion criteria:

1. Signed and dated informed consent
2. ≥ 18 years of age
3. Fluent in Danish
4. Clinical actinic keratosis (AK) diagnosis confirmed by principal investigator (PI)
5. Can present a skin area of 25 cm² with 4 to 8 AK lesions located in face, neck or chest
6. AK lesions in target area severity grade 1 or 2 as defined by the Olsen clinical criteria for AK
7. Able to and willing to follow trial procedures including application of AVX001 and using the Study App
8. Have a suitable smartphone to complete the trial tasks (Android operating system: Android 8.1 or higher; iPhone with iOS 12.4 or higher)
9. Females must either be of non-childbearing potential (either be surgically sterile [hysterectomy or tubal ligation] or post-menopausal) or must be using a highly effective method of contraception approved by the Danish Ethics Committee. Contraception must be maintained for the duration of the study.
   a) A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. A high follicle stimulating hormone (FSH) level in the postmenopausal range may be used to confirm a post-menopausal state in women not using hormonal contraception or hormonal replacement therapy. However in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient (CTFG 2020)
      • For women not taking hormonal contraception with amenorrhea for less than 12 months and just a single FSH measurement in postmenopausal range, a decision can be made by the PI whether it is appropriate for them to undergo a confirmatory FSH measurement or commence a highly effective method of birth control
   b) Highly effective methods of birth control are defined as those, alone or in combination, that result in a low failure rate (less than 1% per year) when used consistently and correctly (ICH 2009)
      Such methods include:
      • Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation: oral, intravaginal, transdermal
      • Progestogen-only hormonal contraception associated with inhibition of ovulation: oral, injectable, implantable
      • Intrauterine device (IUD)
      • Intrauterine hormone-releasing system (IUS)
      • Bilateral tubal occlusion
      • Vasectomised partner
      • Sexual abstinence

Exclusion criteria:

1. AK lesions classified as Olsen grade 3 in target area
2. Atypical AK lesions in the target area, including suspected squamous cell carcinoma or basal cell carcinoma

3. Under suspicion of, or current skin cancer diagnosis in the target area. Subjects who have had squamous cell carcinoma, basal cell carcinoma or melanoma and have completed curative therapy at least 12 months prior to screening and are in remission can be considered to participate in the trial at the investigator’s discretion.

4. Any dermatological condition in the target area that can be exacerbated by treatment or affect trial assessments, including but not limited to psoriasis vulgaris, atopic dermatitis, rosacea, urticaria, scabies, or herpes simplex.

5. Received drugs with immunosuppressive, immunomodulating, or cell-differentiation inducing drugs including but not limited to methotrexate, cyclosporine, azathioprine, oral retinoids, 6 months prior to baseline visit.

6. Received systemic corticosteroids including but not limited to betamethasone, dexamethasone, metilprednisolone (except if via inhale or intranasal delivery) 6 months prior to baseline visit.

7. Received lesion- or field-directed therapy within 2 cm of the target area for trial treatment one month prior to baseline visit, including:
   a. topical drugs, including but not limited to topical fluorouracil, imiquimod, ingenol mebutate and diclofenac
   b. destructive therapies, including but not limited to surgery, cryotherapy, dermabrasion, and photodynamic therapy
   c. field ablation treatments, including but not limited to chemical peels, laser resurfacing.

8. Recipient of organ transplant including but not limited to bone marrow, kidney, liver, heart.

9. Any unstable neurological or psychiatric disorder as judged by the investigator which has the potential to affect the safety of the participant, influence on trial objectives or impede the participant’s ability to complete the trial.

10. History of chronic alcohol- or drug abuse within 12 months prior to screening or any condition associated with poor compliance at the investigator’s discretion.

11. Received treatment with any non-approved drug substance within the last 4 weeks prior to baseline visit.

12. Known allergy or intolerance to fish, shellfish or fish oil.

13. Concurrent participation in any other clinical trial or participation in any clinical trial treatments 4 weeks prior to enrollment.

14. Pregnant or lactating.