Ingenol Mebutate for Recalcitrant Chronic Actinic Cheilitis

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Key Words
Ingenol mebutate · Chronic actinic cheilitis · Imiquimod · Photodynamic therapy

Abstract
We present the case of a healthy 76-year-old man with a whitish, hyperkeratotic lesion of the lower lip diagnosed as actinic cheilitis (AC) previously treated with classic red light photodynamic therapy 5 years ago. Initial treatment with 5% imiquimod cream – also with intensified application – failed. After 2 cycles thrice daily, consecutive applications of 150 μg/g ingenol mebutate gel at 3 weeks’ interval, the lesions cleared completely. Surprisingly, no pustular or crusting reaction or other side effect occurred contrary to expectation. Remission was stable for 10 months, when recurrence occurred. Ingenol mebutate proved to be a feasible and safe treatment in this otherwise refractory case of AC.

Introduction
Actinic cheilitis (AC) is an intraepithelial squamous cell carcinoma of the vermilion of the lower lip, caused by chronic continuous damage by ultraviolet light. It is characterized by scaling and crusting of the vermilion of the lip and by a loss of the usually accurate delineation between the vermilion border and the cornified epidermis of the lip. We report a case of AC resistant to treatment with 5% imiquimod cream, successfully treated with 150 μg/g ingenol mebutate gel.
Ingenol mebutate is a macrocyclic diterpene ester, registered for the treatment of actinic keratosis [1]. In order to achieve its therapeutic effect, this molecule usually provokes a transitory intense inflammatory reaction including redness and oozing, pustules and crusts on the site of the application. It has been described as a possible therapeutic option in several case reports [2, 3]. In our case of recalcitrant AC, 3 once-daily applications of 150 μg/g ingenol mebutate gel on 3 consecutive days were able to clear the disease without any local skin reaction. This remission lasted for about 10 months, after which a mild cheilitis recurred. We treated this with another cycle of 3 once-daily applications of 150 μg/g ingenol mebutate gel, leading to clinical remission once more.

**Discussion**

AC is a common condition with the potential to progress to invasive squamous cell carcinoma. Treatment modalities comprise classic dermatosurgery (vermilionectomy), cryosurgery, topical 5-fluorouracil, topical imiquimod, conventional and pulsed carbon dioxide lasers, chemical peel, photodynamic therapy and electrodessication with varying cure rates and distinct side effects. Ingenol mebutate is a macrocyclic diterpene ester, registered for the treatment of actinic keratosis [1]. In order to achieve its therapeutic effect, this molecule usually provokes a transitory intense inflammatory reaction including redness and oozing, pustules and crusts on the site of the application. It has been described as a possible therapeutic option in several case reports [2, 3]. In our case of recalcitrant AC, 3 once-daily applications of 150 μg/g ingenol mebutate gel on 3 consecutive days were able to clear the disease without any local skin reaction. This remission lasted for about 10 months, after which a mild cheilitis recurred. The recurrence was again successfully treated with a cycle of ingenol mebutate.

Treatment of AC with 150 μg/g ingenol mebutate gel proved to be a feasible and safe method of treatment in this otherwise refractory case.
Statement of Ethics
Subject has given his informed consent.

Disclosure Statement
Emmanuel Laffitte and Michael Mühlstädt served as speaker and/or advisor for LEO Pharma.

References
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