Efficacy of red-light photodynamic therapy with 10% ALA gel in relation to the epidermal extent of atypical keratinocytes in actinic keratosis - Retrospective exploratory analysis of three pivotal phase III trials

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Deep in dermatology

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Synopsis

Actinic keratosis (AK)
- Precancerous epidermal lesions
- Predominantly found in chronically sun exposed skin areas

Assessment
- Clinically (common): thickness and hyperkeratotic status, mild, moderate, or severe (acc. to Olsen [1])
  ! BUT: clinical classification is not a conclusive indicator of extent of atypical keratinocytes [1-3]
- Histologically: e.g. keratinocyte intraepithelial neoplasia (KIN) grading (acc. to Cockerell [4]), see Figure 1A

Treatment
- e.g. red-light photodynamic therapy (PDT) with 10% 5-aminolevulinic acid (ALA) gel or methyl aminolevulinate (MAL) cream (not available in US)

Objective

The aim was to evaluate if the effectiveness of red-light photodynamic therapy (PDT) for treating AK was influenced by the epidermal extent of keratinocyte atypia.

Methods

- Retrospective analysis
- Three pivotal phase III studies (ALA-AK-CT002, -003 and -007 [5-7])
- Histological and clinical data from a total of 762 lesions
- Punch biopsy at the screening visit
- Treatment scheme:
  - 3 h incubation of either 10% ALA gel, MAL or vehicle
  - Illumination with broad- or narrow-spectrum red-light lamp
  - Clinical clearance assessed 12 weeks after the last PDT

For this exploratory analysis, lesion clearance was evaluated in relation to the KIN grade of each respective lesion at the screening visit.

Results

Lesion clearance rates (PDT with narrow-spectrum red-light LED lamp)
- 10% ALA gel: KIN I: 100%, KIN II: 98.1%, KIN III: 94.7%
- MAL: KIN I: 92.9%, KIN II: 90.2%, KIN III: 87.5%

Data for PDT with 10% ALA gel suggest higher clearance rates for all KIN grades compared to PDT with MAL (see Figure 1B). One limitation of the study is the small number of lesions in some subgroups.

What is the 10% ALA gel?

The nanoemulsion-based 5-aminolevulinic acid gel (Ameluz®; 10% ALA gel) in combination with a specific narrow-spectrum red-light LED lamp (BF-RhodoLED® and RhodoLED® XL) is FDA-approved for lesion- and field-directed treatment of mild-to-moderate AKs on the face/scalp [8].

One key advantage of the 10% ALA gel formulation (compared to e.g. MAL): deeper epidermal penetration [9].

Figure 1A: Histological classification according to Cockerell [4]

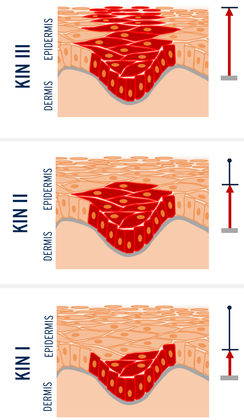

Figure 1B: AK lesion clearance rates by treatment and KIN grade
Each bar represents the percentage of AK lesions cleared/not cleared with the respective photosensitizing prodrug (10% ALA gel, MAL) or vehicle and red-light illumination, with color code indicating lamp type:

- Total
- Broad-spectrum red-light lamp
- Narrow-spectrum red-light LED lamp

The numbers adjacent to the bars correspond to the number of AK lesions considered for the respective subgroup (n).
* The three lesions were located on the face/forehead and were illuminated with the Omnilux lamp; one was of mild and two were of moderate severity.

CONCLUSION

Red-light PDT appears to be an effective treatment option for AK regardless of the extend of epidermal keratinocyte atypia.
AK lesion clearance rates when using red-light PDT with 10% ALA gel or MAL does not seem to depend on KIN grades (I-III). This exploratory analysis also suggests a higher efficacy of 10% ALA gel compared to MAL for all KIN grades, which is consistent with the better penetration of 10% ALA gel.

References
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ALA-AK-CT002 ALA-AK-CT003 ALA-AK-CT007