BF-200 ALA for the photodynamic treatment of non-aggressive basal cell carcinoma: Results of a phase III comparator trial

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Introduction

Basal cell carcinoma (BCC) represents the most common type of non-melanoma skin cancer (NMSC) worldwide, showing dramatically increasing incidence rates. Surgical excision is the most appropriate treatment of BCC. Nevertheless, alternative therapeutic concepts must be considered to overcome drawbacks associated with physical treatments, particularly cosmetic outcome, incomplete tumor excision, the need for reconstructive surgery after treatment of multiple or larger lesions or treatment related morbidity.

Photodynamic therapy (PDT) is characterized by short treatment and down time, excellent patient compliance, high efficacy rates and remarkable cosmetic results. PDT using registered BF-200 ALA (a nanoemulsion formulation containing 7.8% 5-aminolevulinic acid, FDA approved under the brand name Ameluz®) is highly effective in the treatment of mild to moderate actinic keratosis on the face and scalp and of field cancerization in adults[1,2,3,4].

This study (ALA-BCC-CT008) was conducted to demonstrate the non-inferiority of BF-200 ALA compared to MAL (a cream containing 16% methyl-aminolevulinate) in the treatment of thin non-aggressive basal cell carcinoma (BCC) using PDT[5]. Based on this trial, BF-200 ALA gel was recently approved in the EU for the treatment of superficial and/or nodular BCC, unsuitable for surgical treatment.

Trial protocol - ALA-BCC-CT008

Medication

- BF-200 ALA contains 7.8% 5-aminolevulinic free acid (ALA) equivalent to 10% ALA hydrochloride
- MAL contains 16.8% methyl-aminolevulinate (MAL) equivalent to 21.3% MAL hydrochloride

Patients

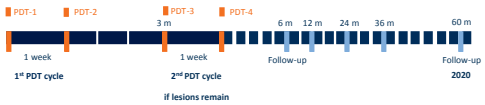
- This randomized, observer-blind, multinational phase III trial with an ongoing 5-year follow-up was conducted in 24 centers in Germany and the UK
- Male and female subjects (> 18 years of age) diagnosed with 1-3 non-aggressive BCC on the face/scalp, neck/trunk, and/or extremities were enrolled
- A total of 281 BCC-patients were included and randomized in two study arms, 138 treated with BF-200 ALA and 143 with MAL
- All patients were Caucasian and the mean age was 66.9 (± 11.54) years (PPP, per protocol population)
- 87% of the patients (PPP) belonged to Fitzpatrick Skin Type I and II

Treatment procedure

- Histologic confirmation of non-aggressiveness and a thickness ≤ 2 mm was performed according to WHO guidelines
- All lesions surfaces were scraped gently using a curette or scalpel blade to gently remove exposed tumor material
- Two PDT-sessions one week apart (PDT-cycle) were performed using a LED red light source (635 nm; light dose of 37 J/cm²) 3 h after drug application
- In case of remaining lesions twelve weeks after the 1st PDT-cycle, patients were retreated with another cycle (2nd PDT-cycle)

Endpoints and follow-up

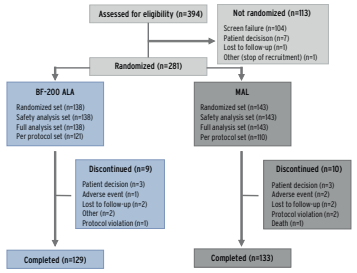
- The main endpoints comprised patient and lesion complete clearance 12 weeks after the last PDT
- Follow-up analyses were performed at 6, 12, 24, 36 and 60 months



- Primary endpoint: patient complete clearance 12 weeks after last PDT
- Secondary endpoint: lesion complete clearance 12 weeks after last PDT

Patient disposition and lesion characteristics - ALA-BCC-CT008

A. Patient disposition



B. BCC lesion characteristics before treatment

Variable	BF-200 ALA	MAL	Total
BCC lesions at baseline	148	127	275
BCC lesions at baseline per patient, Mean (SD)	1.2 (0.49)	1.2 (0.39)	1.2 (0.45)
BCC subtype*, n (%)			
nBCC only	21 (17.4)	21 (19.1)	42 (18.2)
sBCC only	95 (78.5)	83 (75.5)	178 (77.1)
Others	5 (4.1)	6 (5.5)	11 (4.8)
Location, n (%)			
Face/scalp	17 (11.5)	17 (13.6)	34 (12.4)
Neck/trunk	97 (65.5)	87 (68.5)	184 (66.9)
Extremities	34 (23.0)	23 (18.1)	57 (20.7)
Thickness of BCC lesions (mm) overall, Mean (SD)	0.41 (0.32)	0.46 (0.36)	0.44 (0.34)

*patient-based (data presented per-protocol population)

Results - ALA-BCC-CT008

A. Patient complete clearance rates

12 weeks after last PDT (PPP)	BF-200 ALA	MAL
patient complete clearance rate* [%]	93.4	91.8
only superficial (sBCC) [%]	94.7	96.4
only nodular (nBCC) [%]	85.7	76.2
BCC face & scalp [%]	76.9	71.4
BCC trunk [%]	97.4	95.9

*primary clinical endpoint

Morton et al., Br. J. Dermatol. 2017; in revision

- BF-200 ALA shows a trend towards higher efficacy than MAL in the treatment of non-aggressive BCC
- High statistical significance for non-inferiority of BF-200 ALA (major statistical endpoint)
- Thicker and nodular BCCs respond better to BF-200 ALA than MAL
- Treatment emergent adverse events were comparable between the two treatment groups

B. Lesion complete clearance rates

Lesion complete clearance rates (PPP)	BF-200 ALA	MAL
12 weeks after the last treatment		
lesion complete clearance rate [%]	94.6	92.9
only superficial (sBCC) [%]	95.8	96.9
only nodular (nBCC) [%]	89.3	78.6
0-1 mm [%]	96.4	95.7
1-2 mm [%]	72.7	66.7
cleared lesions remaining cleared 12 months after the last treatment		
only superficial (sBCC) [%]	94.6	92.1
only nodular (nBCC) [%]	90.9	90.0

Morton et al., Br. J. Dermatol. 2017; in revision

- High lesion complete clearance rates were achieved in lesions with a baseline thickness of up to 1.0 mm
- More than 90% of initially cleared lesions were still cleared 12 months after the last treatment
- All subgroup analyses revealed non-inferiority of BF-200 ALA

C. Improvement of sun-damaged skin

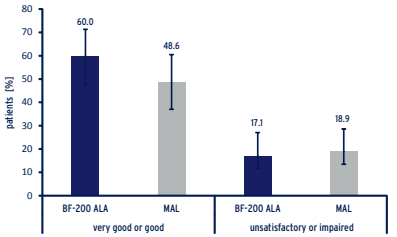


Figure 1: Skin impairment improvement 12 weeks after the last PDT. Several parameters of skin damage were rated on a 4-point scale before the first PDT and at the end of study visit 12 weeks after the last PDT. Improvement of sun damage was calculated on the base of these assessments. Patients with baseline impairment >0: BF-200 ALA, n=70, MAL, n=74. Morton et al., BJD, 2017; in revision.

- PDT with BF-200 ALA results in a predominantly very good or good overall cosmetic outcome 12 weeks after the last PDT

CONCLUSION

In the present phase III study, PDT of non-aggressive BCC was performed using BF-200 ALA gel compared to MAL cream.

- BF-200 ALA-PDT is confirmed significantly non-inferior to MAL-PDT for the treatment of non-aggressive BCC
- BF-200 ALA-PDT is a highly effective treatment with a trend towards higher clearance rates for thicker and nodular lesions
- Lesion recurrence rates were similar or slightly lower for BF-200 ALA gel compared to MAL after 12 months
- The very good and good cosmetic outcome of BCC treatment supports the favourable cosmetic results generally achieved by PDT

This study reinforces the high ranking of PDT in the treatment of thin non-aggressive BCC.

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