A randomized, double blind, vehicle-controlled multicenter phase III study to evaluate the safety and efficacy of BF-200 ALA and narrowband red light in the treatment of superficial basal cell carcinoma (sBCC) with photodynamic therapy (PDT)

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Synopsis

Basal cell carcinoma (BCC) represents the most frequent nonmelanoma skin cancer (NMSC) affecting mainly adult, fair-skinned individuals. BCCs develop predominately in sun-damaged skin with an incidence rate of 1,406/100,000 in the United States (US) (1998/99), 3,252/100,000 in Queensland/Australia (1997) and 143/100,000 in Germany (2004)[1]. Incidence rates in the US dramatically increased by 50% in males and by 20% in females from 1977/78 to 1998/99[1].
Other authors describe an annual increase by 3 to 10%[2]. The average probability to develop a BCC throughout a lifetime is ~30%, whereas the risk of developing additional BCCs after the first one is with 44% considerably higher[3].
Based on their histology, BCCs are classified as non-aggressive, low risk BCCs with good to intermediate prognosis and aggressive, high-risk forms with fundamentally different biological characteristics[3]. Superficial BCC (sBCC) account for 10-38% of BCCs and are generally classified non-aggressive or at least less aggressive subtypes[4].

Trial protocol - Actinic Keratosis

Objectives

- The current pivotal Phase III study (NCT03573401; recruiting), aims to demonstrate the efficacy and safety of PDT with BF-200 ALA (Ameluz®) performed with the narrowband, red light PDT illumination source BF-RhodoLED® (~635 nm; 37J/cm²) in comparison to the respective vehicle treatment for sBBC.

Medication

- BF-200 ALA gel (contains 10% ALA hydrochlorid equivalent to 7.8% 5-aminolevulinic free acid (ALA))
- Vehicle to BF-200 ALA gel

Patients & treatment procedure

The study foresees randomization of 186 subjects at a ratio of 4:1 (drug vs. vehicle) at approximately 15 clinical sites in the US. All subjects will receive one obligatory PDT cycle with 2 PDT sessions per cycle, 1-2 weeks apart. In case of partial or no response, a second PDT cycle will be administered 3 months later. All subjects will receive surgical excision treatment of at least one lesion at the end of the last PDT cycle for histological assessment. This lesion is selected during the randomization visit and is referred to as Main Target Lesion (MTL).
After completing the dosing phase, all subjects will be followed up for 5 years. All subjects will receive excision of their Main Target Lesion at latest at the end of the clinical observation period (Visit 8) for histopathological evaluation of lesion status irrespective of the outcome of the clinical assessment.

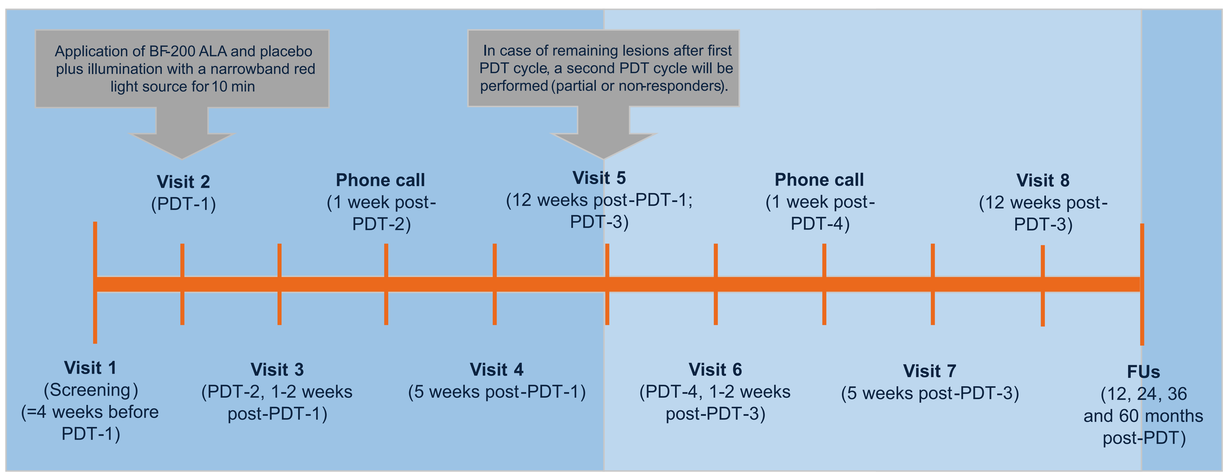
Endpoints

Primary endpoint:

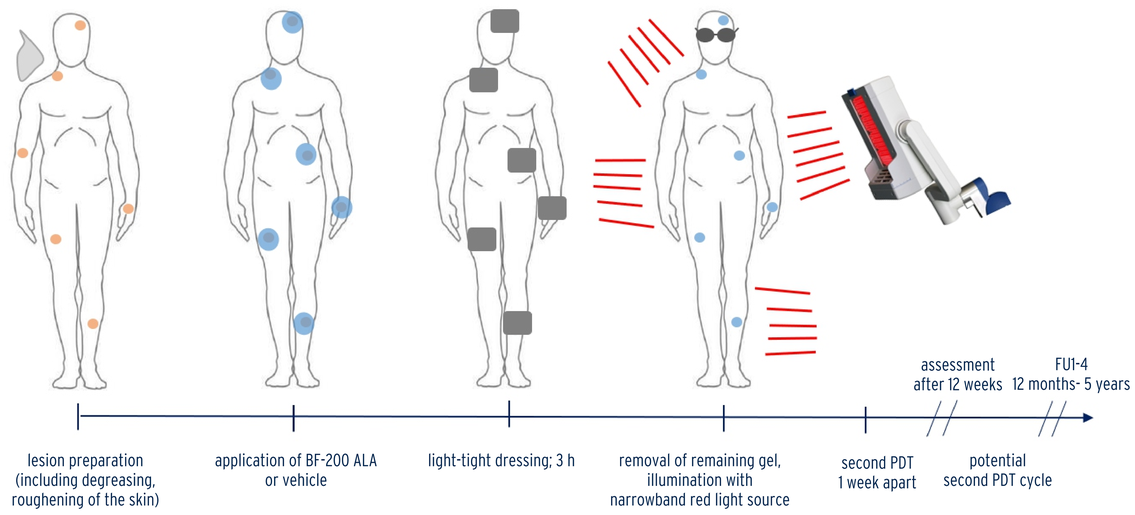
- Composite clinical & histological response of subject's Main Target Lesion (MTL) as assessed 12 weeks after start of last PDT cycle

Selected secondary endpoints (after last PDT cycle):

- Clinical response rate of MTL
- Histological response rate of MTL
- Subject complete clearance of all treated lesions
- Investigator-related aesthetic appearance (before biopsy)



Schematic overview: PDT for sBCC treatment



Medical need for alternative BCC treatment options

According to recent guidelines, the **goal of primary BCC treatment is the clearance of lesions while maintaining function as well as cosmesis[5].**
Currently, surgical treatment is the standard of care as it provides excellent efficacy for treating sBCCs. However, it can result in scarring, often causing a high burden for patients. In addition, there are also cases where surgery is contraindicated or impractical due to e.g. a large size of the tumor or morbidity of the subject.
Consequently, there is a need for alternative treatments for BCCs that circumvent the surgical drawbacks by providing robust clinical efficacy and favorable cosmetic outcomes, which is an important factor for treatment preference, especially if BCCs are located on the head or trunk[6].
In recent years, red light photodynamic therapy (PDT) utilizing photosensitizer precursors such as aminolevulinic acid (ALA), a precursor of protoporphyrin IX (PpIX) has become increasingly important in treating sBCCs, as PDT provides high efficacy along with low recurrence rates and an excellent cosmetic outcome[7].

PDT with BF-200 ALA for BCC treatment in the EU

BF-200 ALA, which matches these requirements, was granted marketing approval for the treatment of superficial and nodular BCC in the European Union (EU) in January 2017. This approval was primarily based on a single pivotal study that demonstrated the efficacy and safety of BF-200 ALA PDT in conjunction with a narrowband red light source (~635 nm; 37 J/cm²) for the treatment of non-aggressive superficial and/or nodular BCC with a thickness of <2 mm. The control group received PDT with methylaminolevulinic acid (MAL) and 281 subjects were randomized at 24 sites in Germany and the UK. Each subject had up to 3 BCCs, which were treated with 1 or 2 cycles of PDT that consisted of 2 PDTs 1 week apart. All subjects entered a 5-year follow-up phase 12 weeks after their last PDT, which is still ongoing.
When assessed 12 weeks after the last PDT cycle, patients that received BF-200 ALA showed complete remission of 93.4% vs. 91.8% of non-aggressive BCCs in patients that received MAL (per protocol population). Even higher clearance rates from 94.7% vs 96.4% were observed when looking exclusively at sBCCs. A recurrence was observed for 6.8% of lesions treated with BF-200 ALA and for 8.2% of lesions treated with MAL at the 1-year follow-up[7].

NCT03573401

This study is sponsored by Biofrontera Bioscience GmbH (Germany).

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