MAL-PDT OR PLACEBO CREAM IN NODULAR BASAL CELL CARCINOMA : RESULTS OF AN AUSTRALIAN DOUBLE BLIND RANDOMIZED MULTICENTER STUDY

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INTRODUCTION

Basal Cell Carcinoma (BCC) is a highly frequent skin malignancy, and accounts for approximately 75% of all non-melanoma skin cancers, affecting mostly the head and neck in fair-skinned individuals.

Simple surgical excision is currently regarded as the treatment of choice; however cosmetic outcome is often less than optimal. Photodynamic therapy (PDT) is a treatment modality, involving the activation of a photosensitizing agent by light, leading to the formation of reactive oxygen species. This process results in local tissue destruction and may therefore offer an attractive alternative to surgery. Application of methylaminolevulinate (MAL) leads to the selective formation of photoactive porphyrins in tumor cells. Previous clinical experience has been promising and patients with nodular Basal Cell Carcinoma (nBCC) were recruited for participation in this multicenter, randomized trial to assess the efficacy, safety and cosmetic outcome of MAL-PDT [1-5].

OBJECTIVE

To assess the histological lesion complete response (CR) rates, clinical lesion complete response, cosmetic outcome and adverse events (AE) following treatment with MAL-PDT.

METHODS

Study design

- Randomised, parallel group, placebo-controlled, double blind multicentre study.

Patient Selection

Male or female patients aged 18 years or older with nodular BCC lesion(s). Lesions that were morpheic, pigmented, larger than 20 mm in diameter or located in the facial H-zone were excluded.

Treatment

- PDT was performed using 160 mg/g MAL cream or placebo cream (Fig. 1). The total light (570-670nm) dose (fluence) was 75 J/cm^2, and the light intensity on the skin was not to exceed 200 mW/cm^2. The average time needed for a light dose of 75 J/cm^2 was about 10 minutes, depending on the size of the field of illumination;
- Prior to illumination, lesions were prepared with a small dermal curette to facilitate access of cream and light to all parts of the lesion. PDT was repeated 7 days later;
- At the 3-month follow-up, partial responder lesions (> 50% decrease in lesion diameter) were given two additional PDT sessions one week apart before the final response evaluation 6 months later (9 months after the initial trial treatment);
- Lesions showing no response (NR) (< 50% improvement) or progression (P) at the 3-month follow-up were excised immediately;
- Lesions showing CR were left for 3 more months, and then excised six months after their last treatment;
- The specimen obtained was sliced into sections not more than 3 mm thick. The centre of each specimen was sequentially sectioned in 1 mm increments for the first 3 mm in either direction from the centre. The remainder of the specimen was sectioned every 3 mm.

Efficacy Assessment

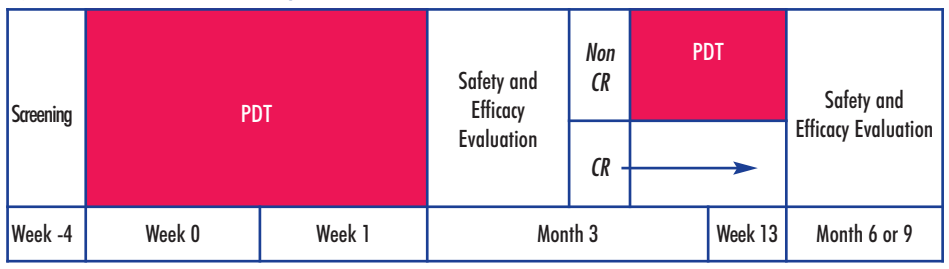
- The histological lesion CR rate;
- The clinical lesion CR rate;
- The cosmetic outcome 3 and 6 months after last PDT.

Safety

- Tolerability up to 6 months after the last treatment

Fig. 1

SEQUENCE AND DURATION OF STUDY PERIODS



RESULTS

Patient disposition

- A total of 66 patients were included in the study; 33 in the MAL-PDT group and 33 in the placebo-PDT group. Demographic data was similar in both groups (Table 1);
- The 66 patients included in the study had in total 74 lesions (Fig.2). The 33 patients treated with MAL-PDT had 36 lesions (49%) and the 33 patients treated with placebo-PDT had 38 lesions (51%). Lesion characteristics were similar in both groups, but lesion locations differed: twice as many lesions on the trunk and extremities were treated with MAL-PDT (Table 2). All patients were included in the ITT analysis; the PP analysis included 61 patients with 63 lesions;
- Of the initial 74 lesions, 70 (95%) were treated: 34 lesions with MAL-PDT and 36 lesions with placebo PDT. The remaining 4 lesions, two in the MAL-PDT group and two in the placebo group, were not treated, as they were not nodular BCC lesions.

Efficacy

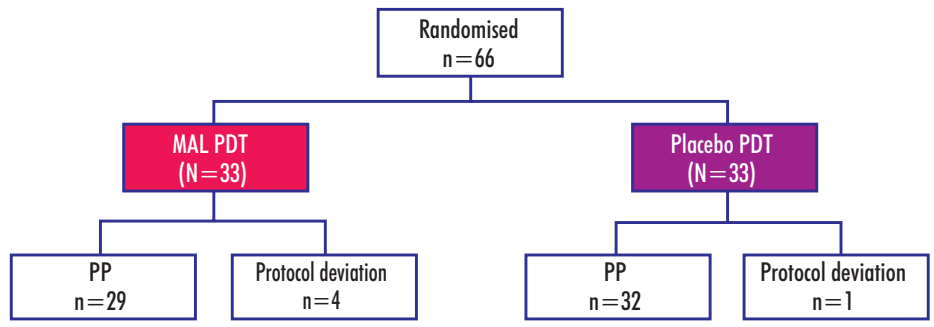
- MAL-PDT was shown to be superior to placebo-PDT ($p<0.001$);
- In the PP analysis in the MAL-PDT group, the overall histological lesion response was 73% versus 21% in the placebo-PDT group (Table 3);
- The clinically evaluated complete lesion response was 83% in the MAL-PDT group and 27% in the placebo-PDT group;
- In the MAL-PDT group, among 26 lesions assessed as clinically cured, 22 (85%) had no signs of malignancy at histological evaluation, suggesting that approximately 15% could potentially show up as clinical recurrences later, if they had not been excised;
- The cosmetic outcome of the lesions that responded completely to MAL-PDT was rated by the investigators as excellent or good for 95% of the lesions and by the patients for all lesions (Fig. 3);
- In the patient satisfaction assessment (all patients included), 67% of patients rated MAL-PDT as better and 11% as worse than previously received treatments.

Safety

MAL-PDT was associated with expected local phototoxic reactions such as stinging, pain and burning sensation. Most of these adverse events were transient, and graded as mild or moderate (in the MAL group, 50% were mild and 50% were moderate and in the placebo group 83% were mild and 17% were moderate). No severe local adverse events were reported. There were no treatment-related serious or systemic adverse events.

Fig. 2

DISPOSITION OF PATIENTS



Deviations/discontinuations:
2 withdrawn consent before excision, 1 death, 1 time window deviation, 1 lesion not prepared before treatment

Table 1

PATIENT DEMOGRAPHICS AT BASELINE

	Age			GENDER			
				Male		Female	
Treatment	n	Mean	Std	n	%	n	%
MAL-PDT	33	70	10	22	67	11	33
Placebo-PDT	33	66	11	27	82	6	18

Table 2

LESION DESCRIPTION AT BASELINE AND LOCATION

Treatment	Mean largest lesion diameter (range)(mm)	Mean lesion depth (range) (mm)	Number of lesions	Lesion location			
				Face n (%)	Neck n (%)	Trunk n (%)	Extremities n (%)
Total	8.6 (6-22)	1.1 (0.4-2.9)	70	17 (24)	3 (4)	31 (44)	19 (27)
MAL-PDT	8.6 (6-18)	1.2 (0.4-2.9)	34	9 (26)	3 (9)	11 (32)	11 (32)
Placebo-PDT	8.6 (6-22)	1.1 (0.5-2.8)	36	8 (22)	0 (0)	20 (56)	8 (22)

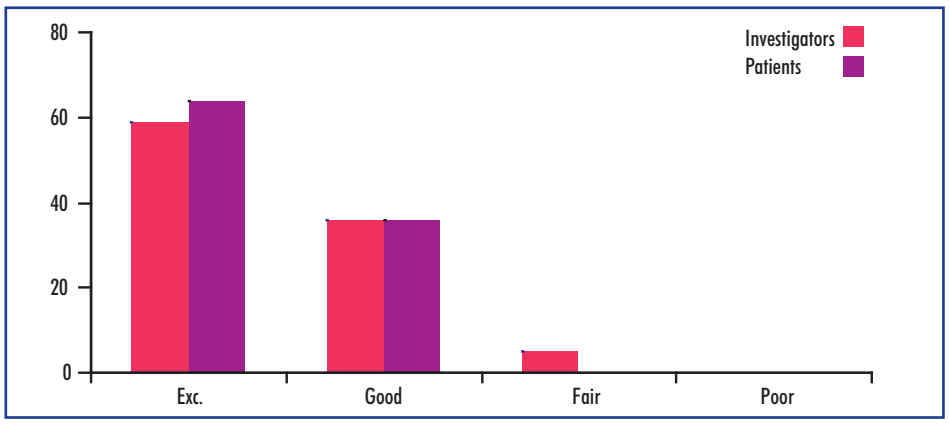
Table 3

HISTOLOGICAL CONFIRMED LESION RESPONSE

	MAL-PDT		Placebo-PDT	
	Lesions complete response	Lesions in non-complete response	Lesions in complete response	Lesions in non-complete response
	n (%)	n (%)	n (%)	n (%)
N=63	22 (73)	8 (27)	7 (21)	26 (79)

Fig. 3

INVESTIGATOR AND PATIENT ASSESSMENT OF GLOBAL COSMETIC OUTCOME



COSMETIC OUTCOME

at baseline | *3 months after MAL-PDT* | *6 months after MAL-PDT*

CONCLUSIONS

- MAL-PDT is a good treatment alternative to existing therapies, in particular in areas where an excellent cosmetic outcome is crucial.
- MAL-PDT is effective.
- MAL-PDT is well-tolerated.

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