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Expression of human leukocyte antigen G (HLA-G) in basal cell carcinoma

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Background: Basal cell carcinoma (BCC) is the most frequent nonmelanoma skin cancer. Human leukocyte antigen G (HLA-G) is an important molecule to imune tolerance as well as for suppressive functions. It has direct inhibitory effects on natural killer cells, dendritic cells, T cells and has tolerogenic indirect effects by inducing regulator T cells (Treg). The ectopic HLA-G expression in cancer appears to be a strategy used by tumor cells to evade immune surveillance promoting the progression of the malignancy.

Objective: Evaluate the expression and distribution of HLA-G in BCC subtypes, by immunohistochemestry.

Materials and methods: 26 BCC specimens (16 nodular and 10 superficial) from patients followed-up in the Dermatology Outpatient Clinic of the University Hospital of the School of Medicine of Ribeirão Preto, University of São Paulo, Brazil, were analyzed by immunohistochemestry.

Results: The sample (n = 26) aged between 35-89 years (mean age: 72.96 y) had a slight predominance of men (54%); 84.62% of the BCC were located in sun-exposed area, 46.15% were cephalic. Nodular BCC showed a more evident and concentrated inflammatory infiltrate around the tumor blocks; while superficial BCC showed a diffuse inflammatory infiltrate throughout the dermis. HLA-G presented striking expression at intratumoral and peritumoral sites for all samples. The nodular BCC tumor cells had a higher expression of HLA-G moderated-intensity marked cells ($P = .04$) when compared to superficial BCC. Often, marking the dermal peritumoral inflammatory infiltrate extended into areas of absence of tumor. Rarely was noted marking dermal inflammatory infiltrate below normal epidermis, however, the normal epidermis showed no expression for the marker. All samples had HLA-G immunostaining in intra- and peritumoral (PT) sites, being more intense and evident in PT infiltration in relation to intratumoral. The expression mainly occurred in the infiltrate around tumor cells. The most striking PT immunostaining than intratumoral suggests that the involvement of HLA-G molecule—possible actions in suppressing tumor interface with normal tissues—allow tumor invasion.

Conclusion: The rare presence of HLA-G expression in dermal inflammatory infiltrate below the normal epidermis suggests a closer relationship between tumors cells and HLA-G. Our findings corroborate the presence of HLA-G expression on the BCC, and its possible immunomodulary action, contributing to the escape of tumor cells.

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First-in-human phase 1 safety study of BLZ-100 in subjects with skin cancer

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BLZ-100 is an intraoperative, fluorescent imaging agent designed to specifically label malignant tissue and enable more complete surgical resection of tumor tissue. BLZ-100 achieves tumor targeting through the peptide portion of the molecule, a modified chlorotoxin (CTX) peptide, and its imaging properties from the coupled near-infrared fluorescent dye, indocyanine green. In order to characterize the safety of BLZ-100, a first-in-human, phase 1 dose escalation and expansion study in subjects with suspected, nonmelanotic skin cancer is being conducted. BLZ-100 is administered via a 15-minute IV infusion to subjects approximately 2 days before planned excision of their skin tumor. Dose escalation is being conducted according to a traditional "3 + 3" design. Dose-limiting toxicity is defined as any related adverse event of = grade 3 severity occurring within 7 days of BLZ-100 administration. Measures of safety include patient or physician reported adverse events (AE), laboratory measures of hematology, liver and kidney function, and coagulation parameters and changes in vital signs and electrocardiograms (ECG). Blood samples were collected to measure BLZ-100 serum concentrations. Fluorescence imaging of suspected skin tumors in situ was conducted using a Fluobeam 800 device. Portions of the excised skin specimens were also subjected to fluorescent image analysis using an Odyssey scanner and immunohistochemistry analysis for the presence of annexin A2 expression (presumed target for BLZ-100). Safety data from the first 3 cohorts of subjects are available. No dose limiting toxicities, infusion reactions or serious adverse events have been observed in the first 9 subjects treated with BLZ-100 doses of 1, 3, or 6 mg. Four subjects have reported a total of 7 possibly related AEs, all of which were grade 1 in severity. No unique AE occurred in more than one subject. Gastrointestinal disorders was the most commonly affected system organ class. No clinically significant changes in laboratory assessments, vital signs or ECGs have been noted. Fluorescent signal from the region of the suspected tumor was detected as soon as 2 hours post dose at doses of 3 mg and above. Overall, single IV administration of BLZ-100 at doses up to 6 mg to subjects with nonmelanotic skin cancer has been well tolerated. No significant or clear pattern of toxicities has been observed. Updated safety and imaging information will be provided in the presentation.

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Giant Merkel cell carcinoma

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A 60-year-old woman with history of type II diabetes, Chagas disease, obesity and NHL, diagnosed and treated in 2011 until the disease went into remission. In August 2013, tumors lesions appeared on the patient's right shoulder and on the distal part of her right arm. A biopsy was performed and inmunohistochemical techniques reported neoplasia of neuroendocrine origin (Merkel). Radiotherapy was started in September 2013. In January 2014 she was admitted in the Department of Internal Medicine of our clinic and the Dermatology Department was consulted. The patient's overall condition was poor. The physical examination showed a tumor of considerable size on her right arm. It was an erythematous infiltrated plaque, with cobblestone aspect, covered with multiple hemorrhagic blisters, some of which were necrotic. The lesion was associated with lymphedema. A new biopsy confirmed the diagnosis of neuroendocrine neoplasia. It was considered a sign of the disease progression, which finally caused the death of the patient. This is a very infrequent and aggressive type of cutaneous neuroendocrine cancer, with a short-term poor prognosis.

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Higher recurrence rates of head and neck nodular basal cell carcinoma treated with topical photodynamic therapy (MAL-PDT) compared to surgical excision: A randomized controlled study

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Background: According to the European guideline for topical photodynamic therapy (PDT) in 2012, this therapy shows efficacy for treating of thin basal cell (BCC). However, there is a lack of comparative studies between PDT and surgical excision for the treatment of nodular BCCs.

Objectives: To compare immediate and late therapeutic response to topical methyl-aminolaevulinate photodynamic therapy (MAL-PDT) and surgical excision of primary nodular BCC of head and neck.

Methods: Randomized clinical and controlled trial. The Research Ethics Committee of Botucatu Medical School approved this study, and consent was obtained from each patient. Inclusion criteria: primary nodular BCC in the head and neck with a diameter up to two inches; exclusion criteria: no histologic confirmation of nodular BCC, Gorlin syndrome or contraindication to surgical resection or PDT. The treatment was decided by random drawing. Surgical excision was performed with 4-mm lateral margins protocol. MAL-PDT was performed according to standard protocol in two sessions with an interval of 1 week. Previously the lesions were shaved. The occlusion time was 3 hours and after the area was illuminated with a 630-nm LED lamp. The response to the treatment was evaluated at 3 months and relapse at 6, 12, 18 months or more.

Results: We selected 81 patients with 92 lesions but 24 of them were excluded. Sixty-eight lesions were followed up, 33 in the MAL-PDT group and 35 in the surgical excision group. There was no statistically significant difference between groups concerning the above variables ($P > .05$). In the group treated with PDT, three lesions (9.0%) showed no response after 3 months of therapy, they underwent surgical excision that confirmed the presence of residual tumor by histopathologic analysis. In the surgery group, no patient had clinical suspicious lesions of residual tumor after three months. In the MAL-PDT group, there were 12 recurrences (36.4%): 5 lesions in 6 months, 2 in 12 months, 3 in 18 month and 2 had later recurrences (more than three years) of follow-up. All these patients were submitted to surgical excision and confirmed nodular BCC by histopathology. There was no recurrence in the group treated with surgery ($P < .01$).

Conclusion: MAL-PDT for head and neck nodular BCCs presents high clearance of lesions after three months but the relapse rate is significantly higher than after surgical excision, requiring attention to indications of this therapy.

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