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Intralesional administration of L19IL2/L19TNF in difficult-to-treat non-melanoma skin cancer shows a favorable safety profile and preliminary clinical activity

L. Flatz[1], U. Leiter-Stoppke[1], F. Meraz-Torres[2], F. Wolfsperger[2], A. Meiwes[2], N. Wagner[3], L. Nadal[4], E. Puca[4], G. Elia[5], A. Covelli[5], D. Neri[6], C. Antonio[7], T.M.S. Amaral[2]

[1] Department of Dermatology, University Hospital Tuebingen, Tuebingen, Germany, [2] Dermato-Oncology Department, Skin Cancer Clinical Trials Center, University of Tuebingen, Tuebingen, Germany, [3] Dermatology, Kantonsspital St. Gallen, St. Gallen, Switzerland, [4] Philogen, Sovicille, Italy, [5] Clinical Dept., Philochem AG, Otelfingen, Switzerland, [6] Chemistry and Applied Biosciences Department, Philogen S.p.A. - Administrative Office, Sovicille, Italy[7] Dermatology, Cantonal Hospital, St. Gallen, Switzerland

Background

Non-melanoma skin cancers (NMSC), including squamous cell carcinoma (SCC) and basal cell carcinoma (BCC), are the most common forms of skin cancer, with a rising incidence due to deficient sun protection and growing life expectancy. Treatment options include surgery, radiotherapy, immunotherapy, targeted therapy, or chemotherapy. Surgery typically offers high cure rates; however, surgery's suitability and/or effectiveness in certain patients (pts) may be limited by disease factors (location, functional and cosmetic impairment) or pts factors (age, comorbidities, personal preferences). Initial intralesional treatment with immunostimulatory drugs may be another therapeutic approach, potentially curing NMSC or making surgery less invasive. Here we investigate a combination of 2 immune cytokines (Bifikafusp alfa (L19IL2) and Onfekafusp alfa (L19TNF) targeting the extra domain B of fibronectin (EDB) for selective delivery of immunostimulatory payloads to the tumor site. EDB is virtually absent in healthy adult tissues but highly expressed in tumors, including NMSC.

Methods

In a single-arm, ongoing, phase II study (NCT04362722), pts with locally advanced, non-metastatic, node-negative, single or multifocal NMSC, not eligible for surgery or radiotherapy or who refuse it, are treated with 4 weekly intratumoral administrations of L19IL2/IL19TNF. 14 pts (11 BCC and 3 cSCC) have been treated and are evaluable for safety and efficacy.

Results

Administration of L19IL2/L19TNF was well tolerated with no grade 4-5 adverse events (AE). The most common treatment-related AEs were flu-like symptoms (36.4%), pyrexia (27.3%), face edema, chills, and injection site reaction (13.6%), all transient, managed with symptomatic therapy. In BCC cohort, ORR was assessed on day 36 with a 27.3% RR. In the follow-up, 5/11pts achieved pathological complete response (pCR) with an average time to pCR of 66 days from the first administration. In the 3 SCC pts, ORR was 33.3 % with 1 pCR.

Conclusions

The tolerable safety profile of L19IL2/L19TNF and the results obtained in pts with NMSC justify further exploring the potential of intralesional administration of immunostimulatory drugs in this setting.

Clinical trial identification

EudraCT 2020-003299-42, NCT 04362722.

Legal entity responsible for the study

Philogen SpA.

Funding

Philogen SpA.

Disclosure

L. Flatz: Financial Interests, Personal, Stocks or ownership: Hookipa Pharma; Financial Interests, Personal, Invited Speaker: BMS, Novartis, Sanofi; Financial Interests, Personal, Advisory Board: BMS, Novartis, Sanofi, Philogen; Financial Interests, Institutional, Research Funding:

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