

**Abstract N°: 1024****Metastatic Basal Cell Carcinoma: Treatment with a potentially best in class Hedgehog Inhibitor, Taladegib**

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**Introduction & Objectives:** Basal cell carcinoma (BCC) is considered the most common malignancy in Caucasians. It accounts for about 80% of all non-melanoma skin tumors, characteristically arising in areas of the body exposed to the sun, its most common location is the head and neck, and it is characterized by slow, locally aggressive growth. Fewer than 1% of basal cell carcinomas metastasize beyond the primary cancer site. For patients with advanced BCCs not amenable to local therapies such as surgery or radiation therapy, options for systemic therapy include, Hedgehog pathway inhibitors, Checkpoint inhibitor immunotherapy and Chemotherapy. We have identified a specific patient population in our ongoing Phase 2a clinical trial where metastatic BCC patients with PTCH1 Loss of Function mutations, who were refractory to vismodegib and immunotherapy responded to Taladegib, a potentially best in class hedgehog pathway inhibitor with a more manageable safety profile. We report here for the first time, a metastatic BCC patient treated with Taladegib who is currently on the study for about 12 months.

**Materials & Methods:** This clinical trial with a 2-stage design aims to evaluate the efficacy and safety of ENV- 101 (Taladegib), a potent Hedgehog (Hh) pathway inhibitor, in patients with refractory advanced solid tumors characterized by loss of function (LOF) mutations in the Patched-1 (PTCH1) gene. Stage 1 of this study will enroll approximately 44 patients randomized between two dose levels. As appropriate, Stage 2 of the study will expand enrollment based on the results of Stage 1. Taladegib is administered once daily at either 200 mg or 300 mg with an option to lower the dose to manage adverse events. Patient is a 76 year old male with unspecified malignant neoplasm of skin of left upper limb including shoulder BCC. Patient underwent surgery and radiation therapy. Patient was further treated by vismodegib for 12 months followed by Cemiplimab.

**Results:** Patient enrolled in June 2022 with mBCC was assessed at C3 with Stable disease (29.8% reduction). Patient's dose was modified to 200 mg at C3 due to fatigue. At C5, the investigator assessed the patient a partial response (PR=50.8%). The radiographs and CT scans showed PR subsequently at C7, C9 and C11. Patient reported fatigue, alopecia, muscle spasms and dyspnea during the study. Patient is currently on the study with durable response ongoing at 11 months. The study is currently enrolling mBCC patients along with other multiple histologies.

**Conclusion:** For the first time we report here that mBCC patients who were refractory to current standard of care treatments responded to taladegib with a duration of response of around one year with fewer and manageable adverse effects.