NEOPOWER: A PHASE II STUDY OF NEOADJUVANT PD-1 BLOCKADE WITH CEMIPLIMAB IN HIGH RISK LOCALIZED, LOCALLY RECURRENT AND REGIONALLY ADVANCED CUTANEOUS SQUAMOUS CELL CARCINOMA

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Background PD-1 blockade achieves response rates of ~50% in patients with unresectable or metastatic cutaneous squamous cell carcinoma (CSCC); furthermore, responses are durable lasting greater than 6 months in 60% of patients. Given the efficacy of PD-1 therapy in treating CSCC, we hypothesize that the use of 3 cycles of neoadjuvant cemiplimab therapy may help not only achieve improved surgical cure but also induce long-term control for this patient population, and with a reasonable toxicity profile. This study seeks to evaluate PD-1 therapy in the neoadjuvant setting for patients with resectable CSCC, including those with high-risk localized disease, locally recurrent, and regionally advanced disease.

Methods NeoPOWER (NCT04315701) is a phase 2, multicenter, open-label study of neoadjuvant cemiplimab in patients with resectable CSCC. A total of 34 patients will be enrolled. Eligible patients must have measurable and resectable CSCC, according to one of the following categories: 1) high-risk localized CSCC, defined by clinical risk factors including tumor diameter >2.0 cm, tumors >1.0 cm in high risk locations, and/or pathological risk factors including depth>6mm, poorly differentiated histology, or perineural invasion, 2) locally recurrent CSCC that has failed prior surgery or radiation, or 3) regionally advanced CSCC, including in-transit, subcutaneous or lymph node metastases. Patients with unresectable or distant metastatic disease are not eligible. Patients will be treated with cemiplimab 350 mg IV every 3 weeks for 3 cycles, then will undergo surgery with curative intent; one additional cycle of cemiplimab may be administered prior to surgery, per investigator discretion. All patients will require baseline imaging prior to therapy, and again prior to surgical resection. The primary efficacy endpoint will be pathological partial response (PRR), defined as less than 50% viable tumor cells on pathologic evaluation of resected surgical specimens. Secondary endpoints include pathologic complete response (PCR), RECIST 1.1 objective response rate (ORR) at 9 weeks, progression-free survival (PFS) at 12 months, and toxicity. This study will employ a Simon two-stage design with an accrual goal of 34 patients, to provide 80% power to detect a targeted PRR of 40% for neoadjuvant cemiplimab; the first stage will include 13 patients, and if 4 or more PPR are observed, then the second stage may allow for an additional 21 patients. Correlative biomarkers will include analyze CD8+ T-cell infiltration, PD-L1 expression and tumor mutational burden (TMB), among others. As of June 2023, 12 of 34 planned subjects have been enrolled.

Ethics Approval The study was approved by the institutional review board at each site and was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines of the International Conference on Harmonization. All patients provided written informed consent.

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