Study title:

Single-arm Study With Bimiralisib in Patients With HNSCC Harboring NOTCH1 Loss of Function Mutations

ClinicalTrials.gov record number:

NCT03740100

MD Anderson protocol number:

2018-1003

PIQUR number:

PQR309-009

Document:

Statistical Plan

Date:

September 24, 2018

1.1 Statistical hypotheses

This is an open-label, single arm, two-stage study evaluating clinical efficacy, safety and pharmacokinetics of bimiralisib in patients with recurrent or metastatic HNSCC harboring *NOTCH1* LOF mutations. The primary goal of the clinical trial is to determine the objective response rate (ORR, including confirmed complete and partial responses) in patients with r/m HNSCC harboring *NOTCH1* to oral bimiralisib. An ORR of 10% or less is considered to be uninteresting and therefore this study has been designed with a reasonable power to detect a response rate of 30%.

1.2 Sample size determination

To minimize accrual if bimiralisib is ineffective, a Simon's optimal two-stage design is used. In order to have 80% power to detect a response rate of 30%, (one-sided α=0.05 and β=0.20) up to 10 patients will be enrolled in the first stage. If 1 or 0 patient respond to the treatment, the trial will be closed due to futility and the treatment is considered ineffective. If two or more patients have an objective response, the study will enroll an additional 19 patients in the second stage. The null hypothesis (H0: ORR $\leq$ 10%) will be rejected if the number of responses is $\geq$ 6 in 29 patients.

If patients withdraw consent or drop out for other reasons unrelated to safety or disease progression, they may be replaced (see section **Error! Reference source not found.**). We anticipate up to 20% of patients to drop out, resulting in enrollment of up to 35 patients in total.

This sample size is also reasonable to evaluate the pharmacokinetic and other correlative science endpoints; yet, no explicit sample size justification is made for these exploratory endpoints.