A Phase 1/2 trial to evaluate the safety and antitumor activity of tipifarnib and alpelisib for patients with HRAS-overexpressing and/or PIK3CA-mutated/amplified recurrent/metastatic head and neck squamous cell carcinoma (The KURRENT Trial)

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**Key Inclusion Criteria**
- Age ≥18 years
- Histologically confirmed HNSCC not amenable to local therapy with curative intent
- Documented treatment failure from at least one prior therapy in the R/M setting
- Tumors with HRAS overexpression and/or PIK3CA mutation and/or amplification
- Measurable disease by RECIST v1.1

**Key Exclusion Criteria**
- Salivary gland, thyroid, (primary) cutaneous squamous or non-squamous histologies
- Prior treatment (at least 1 full treatment cycle) with a F11, PI3K, mTOR, or AKT inhibitor
- Last dose of any prior checkpoint inhibitor therapy must have been administered at least 2 weeks prior to Cycle 1 Day 1
- Intolerable Grade 2, or ≥ Grade 3 neuropathy or evidence of unstable neurological symptoms within 4 weeks of Cycle 1 Day 1

**Primary Objective:**
- Determine the recommended dose and regimen
- Evaluate the safety and tolerability of tipifarnib and alpelisib in combination

**Secondary Objectives:**
- Overall response rate (ORR) and disease control rate (DCR)
- Pharmacokinetics of tipifarnib and alpelisib in combination
- Anti-tumor activity in terms of PFS and rate of PFS at 6-months
- Estimate the OS and rate of OS at 12-months

**Participating Sites:**

**Status:** The trial opened for enrollment in October 2021 and is currently enrolling.

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**REFERENCES**

1TCGA Data
3-68.