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The AIM-HN Study: A registrational-directed study evaluating the efficacy of tipifarnib in patients with recurrent or metastatic head and neck squamous cell carcinoma with *HRAS* mutations

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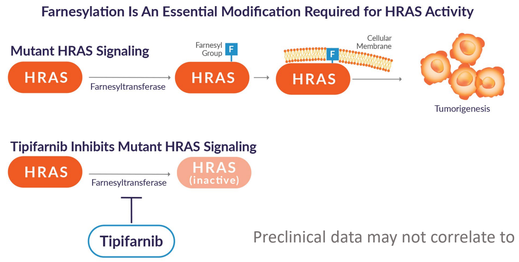
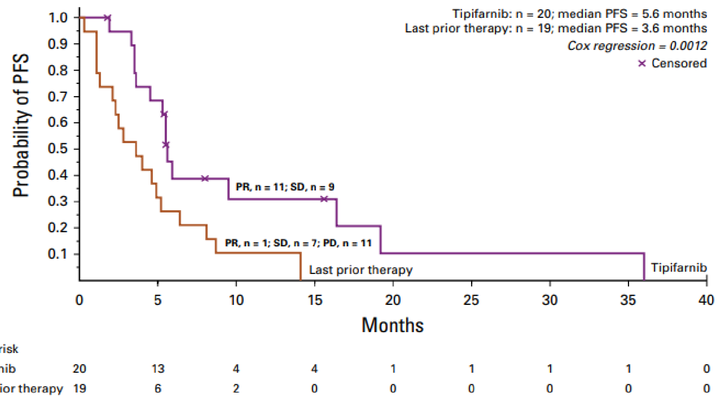
BACKGROUND

- *HRAS* mutations define a unique molecular subset of ~ 4-8% of head and neck squamous cell carcinoma (HNSCC)[1]. Evidence suggests that these tumors respond poorly to standard systemic therapy, and the impact of *HRAS* missense mutations on clinical outcomes is currently being evaluated.
- Tipifarnib is a potent, selective inhibitor of farnesyltransferase, a critical enzyme required for HRAS activity[2].



Preclinical data may not correlate to clinical outcomes

- Data from a Phase 2 proof of concept study for tipifarnib in *HRAS* mutant HNSCC demonstrated an overall response rate of 55% (95% CI, 31.5 to 76.9), a median progress-free survival of 5.6 months, and a median overall survival of 15.4 months in in patients with high variant allele (VAF) frequency (≥20%). These patients had received a median of two prior lines of systemic therapy. The safety profile of tipifarnib was tolerable and manageable in this study[3].



METHODS

An open-label registrational-directed study evaluating the efficacy and safety of tipifarnib in patients with *HRAS*-mutant HNSCC

AIM-HN
KURA KO-TIP-007

Tipifarnib Treatment Cohort

Low VAF (<20%) | **High VAF (≥20%)**

Enrollment based on Key Eligibility Criteria → **Tipifarnib Treatment (N=80)**
600 mg orally, BID on days 1-7 and 15-21 of 28-day treatment cycles

Key Inclusion Criteria

- Histologically confirmed HNSCC not amenable to local therapy with curative intent
- Documented treatment failure from most recent prior therapy, and from at least one prior platinum-containing regimen, in any treatment setting
- Known tumor missense *HRAS* mutation and VAF value
- Measurable disease by RECIST v1.1
- ECOG performance status of 0-1

Key Exclusion Criteria

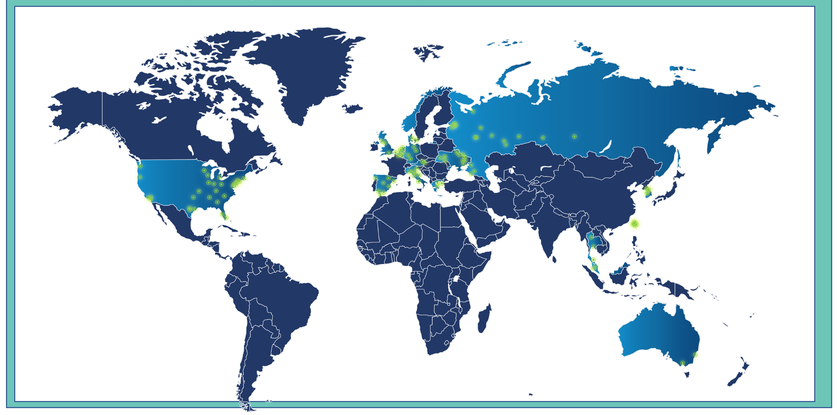
- Salivary gland, thyroid, (primary) cutaneous squamous or non-squamous histologies
- Intolerable Grade 2 or ≥ Grade 3 neuropathy or unstable neurological symptoms within 4 weeks of Cycle 1 Day 1
- Active, uncontrolled infections requiring systemic therapy

Primary Objective:
Objective response rate (ORR) in high VAF population, using RECIST v1.1 by Independent Review Facility

Secondary Objectives:
ORR in all VAF population
Duration of response in high and all VAF populations
PFS
OS
Quality of Life
Safety and tolerability
Pharmacokinetics

Participating Sites: 132 sites globally

North America, Europe, Asia Pacific, Russia and Ukraine



Status: Currently enrolling
The Independent Data Monitoring Board last reviewed data in March 2021 and recommended the trial continue as planned.

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ClinicalTrials.gov identifier: NCT03719690

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2. Gilardi M, Wang Z, Proietto M, et al. Tipifarnib as a Precision Therapy for HRAS-Mutant Head and Neck Squamous Cell Carcinomas. Mol Cancer Ther. 2020
3. Ho AL, Brana I, Haddad R, et al. Tipifarnib in Head and Neck Squamous Cell Carcinoma With HRAS Mutations [published online ahead of print, 2021 Mar 22]. J Clin Oncol. 2021