

Subset of People With Head and Neck Cancer Respond Well to Tipifarnib

A small study looked at response rates among those with HRAS-mutant head and neck carcinoma.

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People with recurrent and metastatic head and neck squamous cell carcinoma (HNSCC) harboring what are known as HRAS gene mutations responded well to the investigational farnesyl transferase inhibitor tipifarnib in a small trial.

Alan L. Ho, MD, PhD, a medical oncologist at Memorial Sloan Kettering Cancer Center, presented findings from a Phase II clinical trial of tipifarnib in this population at the recent International Conference on Molecular Targets and Cancer Therapeutics, jointly sponsored by the American Association for Cancer Research (AACR), the National Cancer Institute and the European Organization for Research and Treatment of Cancer.

“Recurrent and/or metastatic HNSCC is an incurable and devastating disease for which new treatments are needed,” Ho said in a [press release](#). “If this trial is successful, tipifarnib could represent a targeted drug treatment personalized to the genomics of HNSCC patients’ tumors.”

The HRAS gene encodes instructions for making proteins that play a critical role in cell division. HRAS mutations lead to the production of abnormal proteins that allow cancer cells to grow out of control. Mutations in HRAS and the related genes KRAS and NRAS are thought to drive nearly a third of all malignancies. Data on [one of the first KRAS inhibitors](#) was also presented at the conference.

Tipifarnib targets the enzyme farnesyl transferase, which is a key player in the HRAS gene’s ability to drive cancer growth. Although it was initially developed to target tumors that harbor mutations in any of the three RAS genes, it works best against HRAS mutations. Some 5% to 8% of people with advanced head and neck cancer have tumors with HRAS mutations.

The RUN-HN study, sponsored by Kura Oncology, recruited individuals with squamous cell

carcinoma of the head and neck or elsewhere in the body. Everyone in the study cohort had cancer that had relapsed or was resistant to treatment. They had received a median of two previous treatments and had experienced progression of their cancer. These included platinum chemotherapy, immunotherapy or the targeted therapy Erbitux (cetuximab) with or without chemotherapy.

The primary objective of the study was overall response, meaning complete or partial tumor shrinkage. After this objective was met, the study design was amended to include more of the participants most likely to respond to tipifarnib—specifically, those with head and neck cancer with HRAS mutations at a frequency of at least 20% or 35%, depending on their lab values.

Participants were treated with 600 to 900 milligrams of tipifarnib given orally twice daily in 28-day cycles. They received treatment each day of the first and third weeks of each cycle, with the second and fourth weeks off.

At the time of the conference presentation, there were data on 21 study participants with head and neck cancer and 10 with other squamous cell carcinomas. Among the 18 individuals with head and neck cancer and a mutation frequency of at least 20%, the overall response rate was 56%. An additional eight people had stable disease without further progression; most of these experienced tumor shrinkage that did not reach the threshold for partial response.

The median length of progression-free survival in this group was 6.1 months, including 8.3 months for those who had a partial response and 4.5 months for those with stable disease. None of these individuals had had durable responses to their most recent treatment, with only a median of 2.8 months between starting that therapy and cancer progression.

Tipifarnib was generally safe and well tolerated. Overall, the side effects proved manageable and in line with the safety findings of previous clinical trials. The most common severe adverse health events (Grade 3 or higher) were blood and lymphatic system disorders (45%) and gastrointestinal problems (15%). The 600 mg twice-daily dose was better tolerated than higher doses and was selected for future studies.

“Tipifarnib may represent a promising new therapy for HRAS-mutant HNSCC patients. The success of the trial also speaks to the promise of utilizing genomic sequencing of diseases to identify highly effective therapies that are personalized to the specific biology of each individual patient’s tumor,” Ho said.

The study is limited by its small size. As Ho told conferencegoers, more research is needed to more firmly establish tipifarnib’s effectiveness.

Kura Oncology has initiated a larger study called AIM-HN that is evaluating tipifarnib in previously treated people with HRAS-mutant head and neck cancer (ClinicalTrials.gov number [NCT03719690](#)).

In September, Kura [announced promising findings](#) from a Phase II study of tipifarnib for people with bladder cancer that had relapsed or was nonresponsive to prior treatment. Five out of 13 participants (38%) had objective responses. The company said further details would be presented at a future meeting.

Kura Oncology provided funding, including for travel and conference fees, for Ho and his team.

To read a press release about the study, [click here](#).

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<http://beta.docker.cancerhealth.com/article/subset-people-head-neck-cancer-respond-tipifarnib>