Head & Neck

Phase IIb, Randomised, Double-Blind Trial of GC4419 Versus Placebo to Reduce Severe Oral Mucositis Due to Concurrent Radiotherapy and Cisplatin For Head and Neck Cancer.

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PURPOSE

Oral mucositis (OM) remains a common, debilitating toxicity of radiation therapy (RT) for head and neck cancer. The goal of this phase IIb, multi-institutional, randomised, double-blind trial was to compare the efficacy and safety of GC4419, a superoxide dismutase mimetic, with placebo to reduce the duration, incidence, and severity of severe OM (SOM).

PATIENTS AND METHODS

A total of 223 patients (from 44 institutions) with locally advanced oral cavity or oropharynx cancer planned to be treated with definitive or post-operative intensity-modulated radiotherapy (IMRT; 60 to 72 Gy [≥ 50 Gy to two or more oral sites]) plus cisplatin (weekly or every three weeks) were randomly assigned to receive 30 mg (n = 73) or 90 mg (n = 76) of GC4419 or to receive placebo (n = 74) by 60-minute intravenous administration before each IMRT fraction. The World Health Organization (WHO) grade of OM was assessed biweekly during IMRT and then weekly for up to eight weeks after IMRT. The primary endpoint was duration of SOM tested for each active dose level versus placebo (intent-to-treat population, two-sided α of 0.05). The National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03, was used for adverse event grading.

RESULTS

Baseline patient and tumour characteristics as well as treatment delivery were balanced. With 90 mg GC4419 versus placebo, SOM duration was significantly reduced (P = 0.024; median, 1.5 v 19 days). SOM incidence (43% v 65%; P = .009) and severity (grade 4 incidence, 16% v 30%; P = .045) also were improved. Intermediate improvements were seen with the 30-mg dose. Safety was comparable across arms, with no significant GC4419-specific toxicity or increase of known toxicities of IMRT plus cisplatin. The two-year follow-up for tumour outcomes is ongoing.

CONCLUSION

GC4419 at a dose of 90 mg produced a significant, clinically meaningful reduction of SOM duration, incidence, and severity with acceptable safety. A phase III trial (ROMAN; ClinicalTrials.gov identifier: NCT03689712) has begun.