

SEVERE ORAL MUCOSITIS (SOM) MITIGATION BY GENETICALLY MODIFIED *LACTOCOCCUS LACTIS* BACTERIA (LLB) PRODUCING HUMAN TREFOIL FACTOR 1 (hTFF1; AG013) IN PATIENTS BEING TREATED WITH CONCOMITANT CHEMORADIATION (CRT) FOR ORAL AND OROPHARYNGEAL CANCERS (OCOPC)

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BACKGROUND

SOM is a devastating consequence of CRT. hTFF1 is a naturally occurring protein that can protect the mucosa. LLB were genetically modified (GM) to produce hTFF1, formulated as an oral rinse and attenuated SOM in patients receiving chemotherapy. The GM LLB lack all necessary components for survival and multiplication. The objective of this ongoing Phase 2 trial is to assess the safety and efficacy of AG013 as a SOM intervention.

METHODS

This is a double-blind, randomized, placebo-controlled trial recruiting ~200 patients with OCOPC at 48 sites (US and Europe). Patients (PTS) receive cumulative RT (cumRT) between 50 Gy – 72 Gy, 2.0-2.2 Gy QD + QW/Q3W cisplatin. At least two mucosal sites at risk of SOM receive minimal cumRT of 50 Gy. PTS are randomized 1:1 to receive placebo or AG013 [LLB strain sAGX0085 engineered to secrete hTFF1 (2x10¹¹ CFU/15 mL tid)] starting on CRT day 1 and continuing 2 weeks post-CRT. Beginning on CRT day 1 and continuing Q2W until resolution, OM is assessed by trained assessors and scores assigned centrally. The primary and secondary efficacy endpoints are SOM duration and incidence (WHO criteria). AEs are

described by NCI-CTCv4. A DSMB performed a safety analysis following accrual of the first 24 PTS. Tumor response to CRT is evaluated for 1-year post CRT.

RESULTS

71 PTS have been randomized across 48 study sites. Complete OM data are available for 42 PTS for whom blinded evaluation (active and placebo) demonstrated an overall SOM incidence of 52%. SOM was noted at 81 of 547 visits (14.8%). 25 PTS have stopped active treatment; 2 for non-compliance, 5 for AEs, and 18 lost to follow-up or unwilling or unable to conform to the protocol. Unexpected SAEs were noted in 9 PTS. No study drug-associated cases of bacteremia or sepsis were seen. DSMB review after the first 24 PTS concluded that there were no contraindications to study continuance

CONCLUSIONS

Observations based on blinded data suggest that AG013 offers a safe, well-tolerated, and potentially efficacious platform to deliver an effective protein intervention for SOM mitigation.