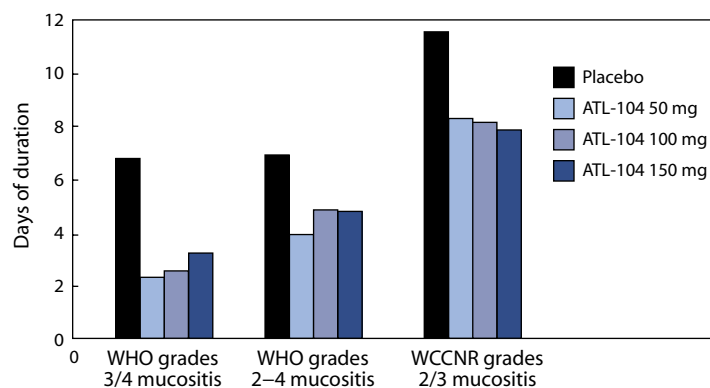


A randomized, double-blind, placebo-controlled, multicenter trial of ATL-104, a swallowable mouthwash, in patients with oral mucositis following peripheral blood stem cell transplantation

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Origin of Study	United Kingdom
Type of Study	RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER TRIAL
Objectives	Assess the effect of ATL-104, a swallowable mouthwash, on mucositis in patients receiving high-dose melphalan (Alkeran) or carmustine (BiCNU), etoposide, cytarabine, and melphalan (BEAM) before an autologous peripheral blood stem cell transplant (PBSCT).
Study Design	<p>Each dose consisted of 15 mL of solution containing 50 mg, 100 mg, or 150 mg of ATL-104 or placebo. For 3 days before chemotherapy and 3 days following transplantation, patients swished the solution in their mouths for 15–30 seconds and then swallowed it.</p> <p>For 28 days following dosing or until discharge, assessments were made for pain, ulceration, and other factors contributing to the World Health Organization (WHO) or Western Consortium Cancer for Nursing Research (WCCNR) mucositis scale.</p> <p>The first portion of the study used a dose-ascending design, beginning with 50 mg of ATL-104; patients were randomized to receive the drug or placebo at a ratio of 3:1.</p> <p>A safety review was performed after dosing of 8 patients at each dose.</p> <p>After the 150-mg cohort was treated, a randomized parallel-arm design with all doses and placebo was used.</p>
Patients	In all, 63 patients (46 males) were treated, and 54 patients received all six doses and were assessed fully.
Observations	At all doses, ATL-104 produced a consistent reduction in duration of all grades of oral mucositis when compared with placebo (no testing for statistical significance was planned; Figure).

Duration of Mucositis



Randomized, double-blind, placebo-controlled, multicenter trial of ATL-104

ATL-104 had no clear effect on the incidence of mucositis or patients' pain perception. It was well tolerated at all doses.

Conclusions

ATL-104 reduced the duration of mucositis in patients following conditioning for and completion of PBSCT.

ATL-104 did not alter appreciably the adverse event profile attributed to chemotherapy.

Discussion

Patients undergoing PBSCT frequently develop oral mucositis, a serious complication characterized by often debilitating ulcers. Despite the availability of a number of topical and systemic agents, management of oral mucositis remains challenging.

Phytohemagglutinin is a protein that stimulates mitosis of gastrointestinal epithelial cells. This trial assessed the safety and efficacy of ATL-104, a recombinant version of the L-form of phytohemagglutinin. ATL-104 is resistant to degradation by acid and proteases and is formulated as a swallowable mouthwash.

Study participants were patients receiving high-dose melphalan or BEAM in preparation for autologous PBSCT. In equal numbers, they were treated with differing doses of the drug—50, 100, or 150 mg—or a placebo for 3 days before chemotherapy and 3 days after transplantation.

The duration of WHO grade 3/4 mucositis was 3.4 to 4.4 days (51% to 64%) shorter in the ATL-104 groups than in the placebo group. Similarly, the duration of WCCNR grade 2/3 mucositis was 3.4 to 3.8 days (29% to 33%) shorter with the active treatment. Finally, the duration of mouth ulcers scored between 1 and 4 was 0.8 to 2.7 days (15% to 43%) shorter with ATL-104.

The incidences of WHO grade 3/4 mucositis and of WCCNR grade 2/3 mucositis did not differ by group. In addition, treatment did not influence the proportion of patients reporting oral pain or soreness.

“ATL-104 at all doses produced a consistent reduction in duration of all grades of oral mucositis, compared with placebo” the investigators assert, adding that the treatment was also well tolerated regardless of dose.

Key Points

- ATL-104 reduced the duration of mucositis in patients following conditioning for and accomplishment of PBSCT.
- Larger, randomized clinical trials of ATL-104 should be done.

Reference

Hunter A, Mahendra P, Wilson K, et al. A randomised, double-blind, placebo-controlled, multicentre trial of ATL-104, a swallowable mouthwash, in patients with oral mucositis following peripheral blood stem cell transplantation. Presented at the 48th Annual Meeting of the American Society of Hematology; December 9–12, 2006; Orlando, Florida. Abstract 45.