

# Use of Recombinant Human Keratinocyte Growth Factor (Palifermin) Can Reduce Severe Oral Mucositis in Patients With Hematologic Malignancies Undergoing Autologous Peripheral Blood Progenitor Cell Transplantation After Radiation-Based Conditioning

## Authors

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## Origin of Study

USA

## Type of Study

PHASE III, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

## Objectives

Determine the efficacy of intravenous recombinant human keratinocyte growth factor (palifermin) in reducing severe (World Health Organization [WHO] grades 3-4) oral mucositis and related clinical sequelae in patients with hematologic malignancies undergoing total body irradiation (TBI) and high-dose chemotherapy combined with autologous peripheral blood progenitor cell transplantation (PBPC)

## Study Design

Patients were randomized (1:1) to receive placebo or palifermin 60 µg/kg daily for 3 consecutive days before TBI and 3 consecutive days after PBPC.

Oral mucositis and patient-reported outcomes, including mouth and throat soreness, were assessed daily until oral mucositis grades returned to WHO grade ≤ 2.

## Patients

In all, 212 patients received 12 Gy of TBI with 60 mg/kg etoposide and 100 mg/kg cyclophosphamide as conditioning treatment before autologous PBPC.

## Observations

Patient-reported outcomes were consistent with clinical findings.

Palifermin-treated patients had less need for intravenous or transdermal opioid analgesics (median morphine equivalent dose for palifermin was 212 mg vs 552 mg for placebo) and total parenteral nutrition (11% for palifermin vs 40% for placebo).

Palifermin significantly reduced the incidence and duration of severe oral mucositis in patients with hematologic malignancies undergoing PBPC after TBI and chemotherapy conditioning:

### Incidence and Duration of Severe Oral Mucositis

	PLACEBO	PALIFERMIN	P VALUE
Incidence of WHO grade 3 oral mucositis	98%	63%	< 0.001
Incidence of WHO grade 4 oral mucositis	62%	20%	< 0.001
Days of WHO grades 3-4 oral mucositis (mean ± SD)	10.4 ± 6.2	3.7 ± 4.1	< 0.001

Palifermin was well tolerated. Adverse events included mild skin and oral erythema, with or without edema, and asymptomatic, transient increases in serum amylase and lipase levels, which occurred marginally more frequently in palifermin-treated patients than in placebo-treated patients.

## Palifermin Reduces Severe Oral Mucositis in Patients With Hematologic Malignancies Undergoing Autologous PBPC

### Conclusions

Palifermin improved patients' mouth and throat soreness and significantly reduced mucositis-related clinical sequelae.

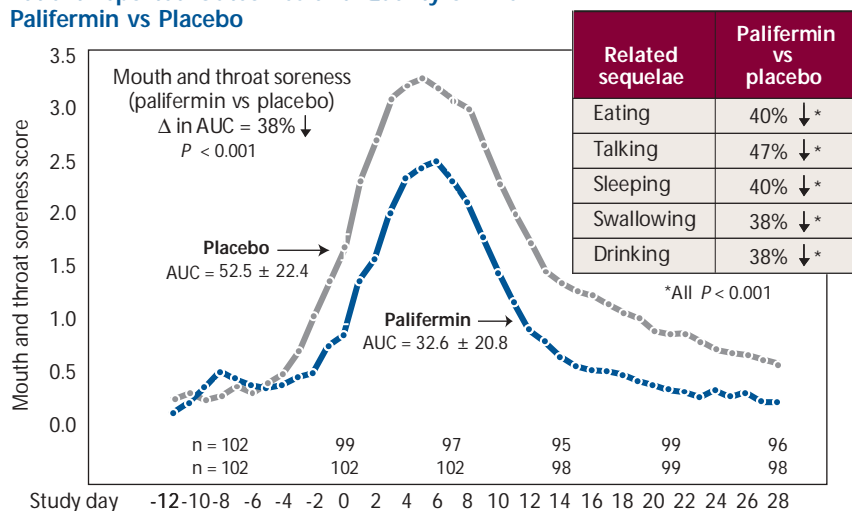
### Discussion

For patients with hematologic malignancies, the established conditioning regimen is TBI combined with high-dose chemotherapy (etoposide and cyclophosphamide) and autologous PBPC. However, the incidence of severe oral mucositis with this treatment is usually > 80%.

Spielberger and colleagues attempted to determine whether intravenous palifermin was effective in reducing severe oral mucositis and related clinical sequelae in patients with hematologic malignancies undergoing TBI and high-dose chemotherapy/autologous PBPC. On the WHO oral mucositis scale, severe symptoms consist of ulcers, extensive erythema, and the inability to swallow a solid diet (grade 3) and mucositis to the extent that alimentation is not possible (grade 4).

Currently, there is no standard therapy available to prevent or reduce the effects of oral mucositis. The use of palifermin as a treatment option in this patient population was studied in this phase III, randomized, double-blind, placebo-controlled trial.

### Patient-Reported Outcomes and Quality of Life: Palifermin vs Placebo



In this study, 212 patients received 12 Gy of TBI with 60 mg/kg of etoposide and 100 mg/kg of cyclophosphamide as conditioning treatment before autologous PBPC. Patients were randomized to receive placebo or palifermin (60 µg/kg per day) for 3 consecutive days before TBI and 3 consecutive days after PBPC. Outcomes, including patient-reported soreness of the mouth and throat, were assessed daily until the grades of oral mucositis returned to at least WHO grade 2.

Patient-reported outcomes were consistent with the clinical findings. The use of palifermin reduced both the duration and incidence of severe oral mucositis. In addition, patients who received palifermin

required less use of intravenous and/or transdermal opioid analgesics and total parenteral nutrition. Adverse events included mild skin and oral erythema, with and without edema. Overall, palifermin was well tolerated at the dose and schedule used, according to Dr. Ricardo Spielberger, who presented his group's findings in June at the 39th Annual Meeting of the American Society of Clinical Oncology.

### Key Points

- At the study dose of 60 µg/kg per day, palifermin significantly reduced the duration and incidence of severe oral mucositis, as well as the use of parenteral and transdermal opioid analgesics.
- Patient-reported outcomes, such as soreness of the mouth and throat, were improved with the use of palifermin.

### References

Spielberger R, Emmanouilides C, Stiff P, et al. Use of recombinant human keratinocyte growth factor (rHuKGF) can reduce severe oral mucositis in patients (pts) with hematologic malignancies undergoing autologous peripheral blood progenitor cell transplantation (auto-PBPC) after radiation-based conditioning—results of a phase 3 trial. Paper presented at the 39th Annual Meeting of the American Society of Clinical Oncology; May 31–June 3, 2003; Chicago, Ill. Abstract 3642.

Stiff P, Bensinger W, Emmanouilides C, et al. Treatment of mucositis with palifermin improves patient function and results in a clinically meaningful reduction in mouth and throat soreness (MTS): phase 3 results. Paper presented at the 45th Annual Meeting of the American Society of Hematology; December 6–9, 2003; San Diego, Calif. Abstract 676. See page 75.