# Palifermin, administered for 3 days only, is effective in minimising mucositis in patients undergoing HSCT and receiving chemoradiotherapy conditioning

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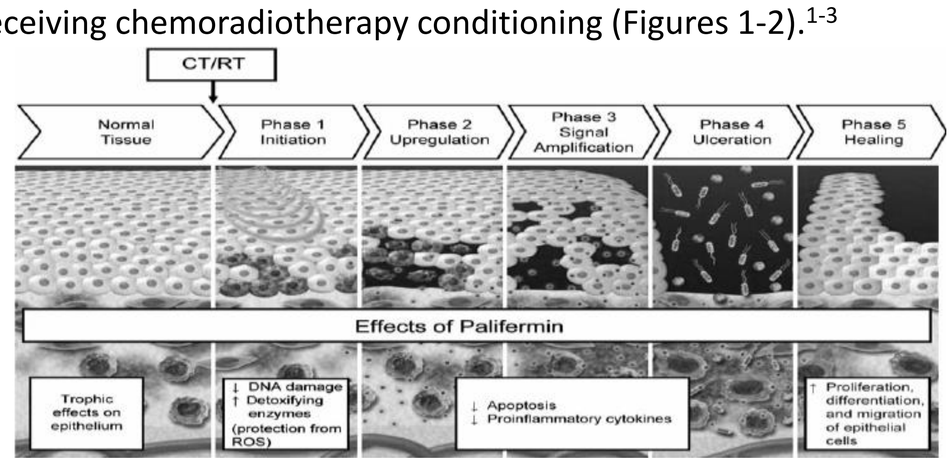
## Background

Myeloablative allogeneic haemopoietic stem cell transplantation (HSCT) is an established treatment for haematologic malignancies. Mucositis, resulting from injury to epithelial cells lining the oral cavity and gastrointestinal tract, is a complication of both high-dose chemotherapy and radiation-based conditioning.[1-3] Palifermin is a recombinant human keratinocyte growth factor with proven clinical efficacy in mitigating mucositis in patients undergoing HSCT and receiving chemoradiotherapy conditioning (Figures 1-2).[1-3]




**Figures 1: Mechanisms by which palifermin ameliorates mucositis**

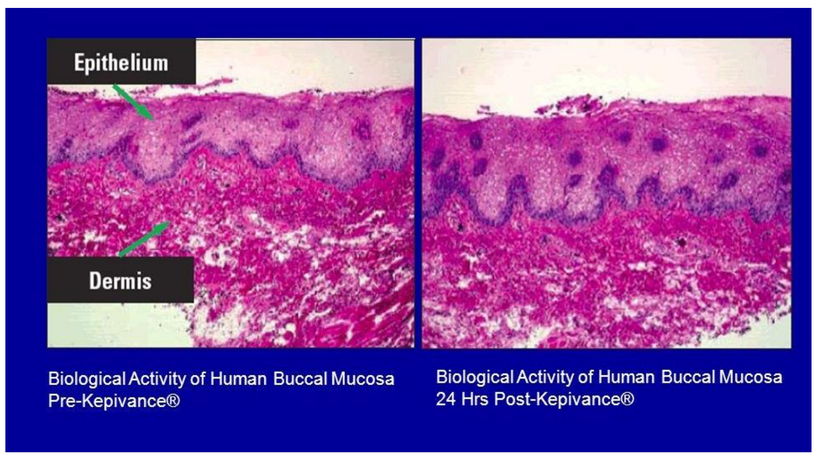



**Figure 2: Biological effects of palifermin on human buccal mucosa**

Palifermin, administered as per the product information[4], for 6 doses of 60mcg/kg/day, as IV bolus injection for 3 consecutive days before and 3 consecutive days after chemoradiotherapy costs $AUS10,000. A review of the literature, including pre-clinical studies and those investigating modified dosing regimens in various settings indicated efficacy of palifermin, even with attenuated dosing.[5-7] A shorter course of palifermin would provide clinical benefit at a cost that was not prohibitive for routine use in selected patients. A 3 day regimen was approved by the institution's Drug and Therapeutics Committee.

## Aim

To evaluate the effectiveness of a modified palifermin dosing schedule administered for 3 doses before chemoradiotherapy in patients undergoing stem cell transplantation (SCT).

## Methods

For this single centre study, consecutive patients receiving total body irradiation (TBI) and chemotherapy conditioning for allogeneic HSCT were eligible to receive 3 doses of palifermin. Medical records and dispensing histories were retrospectively reviewed.

Primary outcome was duration of parenteral nutrition (PN) and parenteral analgesia (PA), defined as regular intermittent PA or patient controlled analgesia (PCA). The incidence and duration of grade 3 and 4 mucositis, as per the World Health Organisation (WHO) oral mucositis scale, was also measured.

Results were compared to those from published studies which reported on similar patient cohorts who received 6 doses of palifermin and TBI-based conditioning.[1,3]

## Results

Over a two year period, palifermin was administered as 3 daily doses to 31 patients with a median age of 39 years (Table 1).

**Table 1: Demographics of patients receiving 3 days palifermin**

| Characteristic | n=31 |
|---|---|
| **Male, n (%)** | 14 (45.2) |
| **Median age (range), years** | 39 (20-55) |
| **Median weight at initiation of conditioning (range), kg** | 76 (38-172) |
| **Primary diagnosis, n (%)** | |
| Acute Myeloid Leukaemia | 18 (58.1) |
| B Cell Acute Lymphoblastic Leukaemia | 8 (25.8) |
| T Cell Acute Lymphoblastic Leukaemia | 2 (6.5) |
| Acute Leukaemia Mixed Phenotype | 1 (3.2) |
| Mantle Cell Lymphoma | 1 (3.2) |
| Myelodysplastic Syndrome | 1 (3.2) |
| **Conditioning regimen, n (%)** | |
| Cyclophosphamide & Total Body Irradiation | 28 (90.3) |
| Cyclophosphamide, Fludarabine & Total Body Irradiation | 3 (9.7) |

PN was required by 23 patients and PA by 15 patients in the study cohort. The duration of PN and PA use was similar to that of the literature cohort with no statistically significant difference (Table 2).

**Table 2: Parenteral nutrition and parenteral analgesia use of literature[1] and study**

| | Literature n=121 | Study n=31 | P value |
|---|---|---|---|
| Parenteral nutrition use mean (SD), days | 13.0 (6.3) | 13.2 (6.5) | ns |
| Parenteral analgesia use, mean (SD), days | 7.0 (9) | 8.4 (4.1) | ns |

The incidence and duration of Grade 3 and 4 mucositis was also comparable to that reported in published studies (Table 3).

**Table 3: Grade 3/4 mucositis in the literature[3] and study cohorts**

| | Literature n=106 | Study n=31 | P value |
|---|---|---|---|
| Grade 3/4 mucositis incidence (n) | 63% (67) | 61% (19) | ns |
| Grade 3/4 mucositis duration, median (range), days | 6.0 (1-22) | 7 (2-18) | ns |

## Discussion

Acknowledging the limitations of the retrospective nature of this study, and the comparison to published data, these results indicate the efficacy of a shorter course of palifermin.

The study cohort included patients who had undergone allogeneic HSCT with similar conditioning to those in the published study used to compare the use of PA and PN.[1] The study used for comparison of grade 3 and 4 mucositis, also included patients who underwent autologous HSCT.[3]

Palifermin 60mcg/kg/day, intravenously administered for 3 days before chemoradiotherapy for allogeneic HSCT, is effective in minimising mucositis, duration of PN and PA and is an effective alternative for the 6 day schedule with significant cost savings.

## References

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