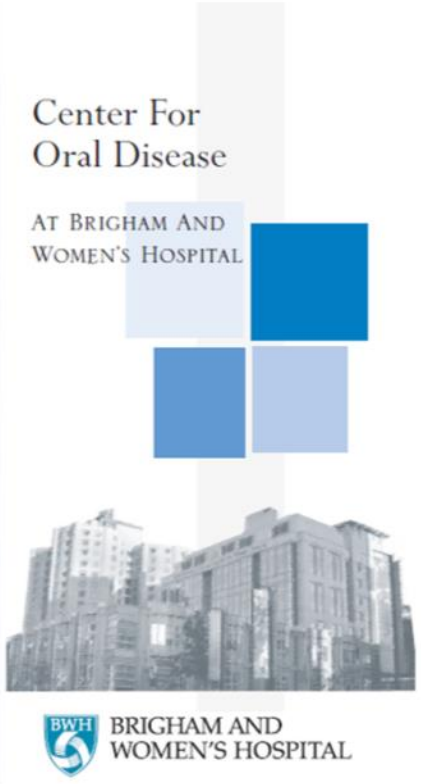
LLLT for Prevention of Oral Mucositis
what is the path forward?



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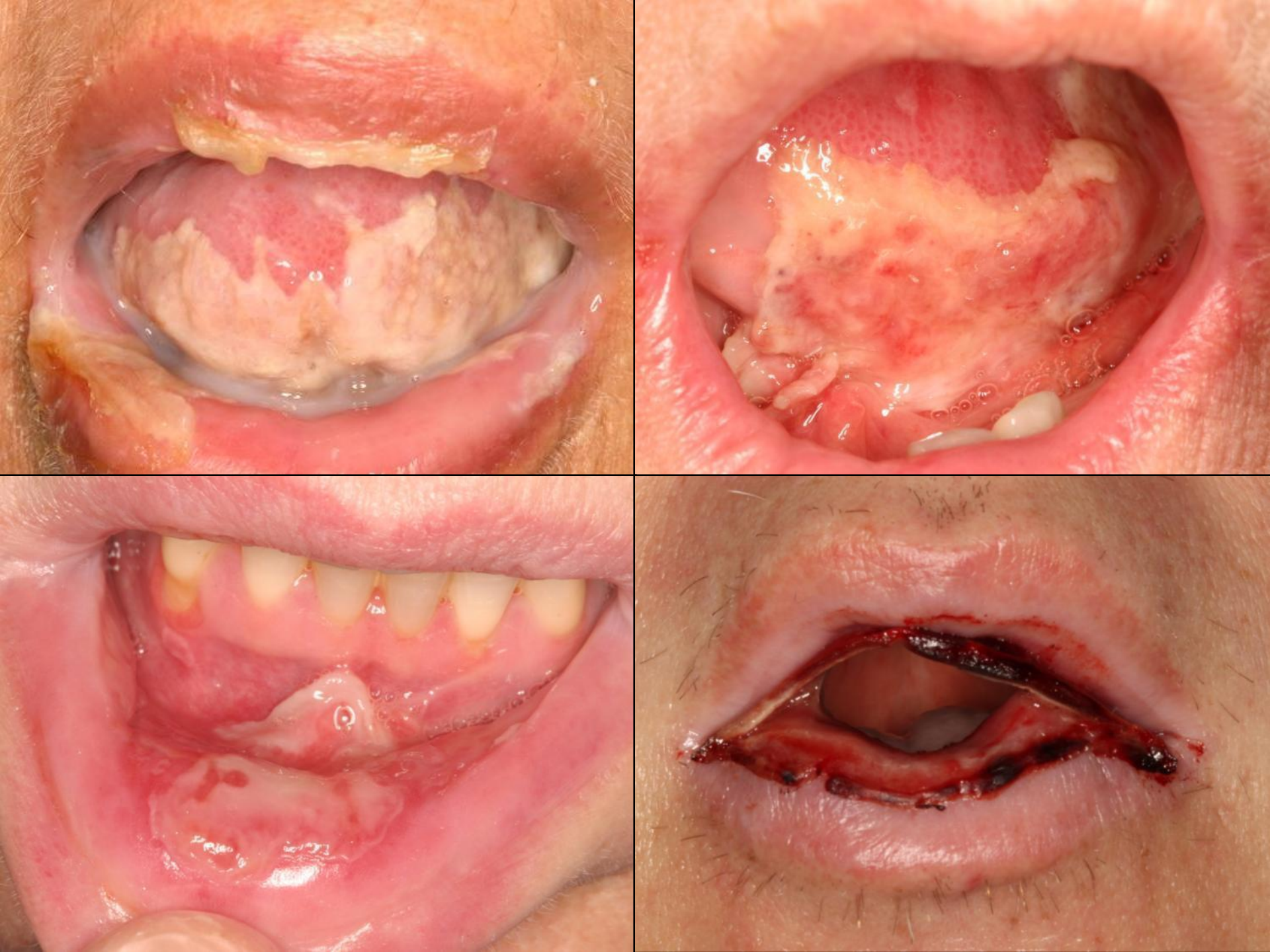
CANCER CENTER

Acknowledgments

- Joseph Antin, MD
  - Dana-Farber/Brigham and Women's Cancer Center, Co-Director, Adult Hematopoietic Stem Cell Transplantation Program
- Leslie Lehmann, MD
  - Medical Director, Pediatric Stem Cell Transplant Unit, Boston Children's Hospital
- Stephen Sonis, DMD, DMSc
  - Chief, Division of Oral Medicine and Dentistry, Brigham and Women's Hospital and Dana-Farber Cancer Institute
- Lillian Sung, MD, PhD
  - Department of Haematology/Oncology, The Hospital for Sick Children

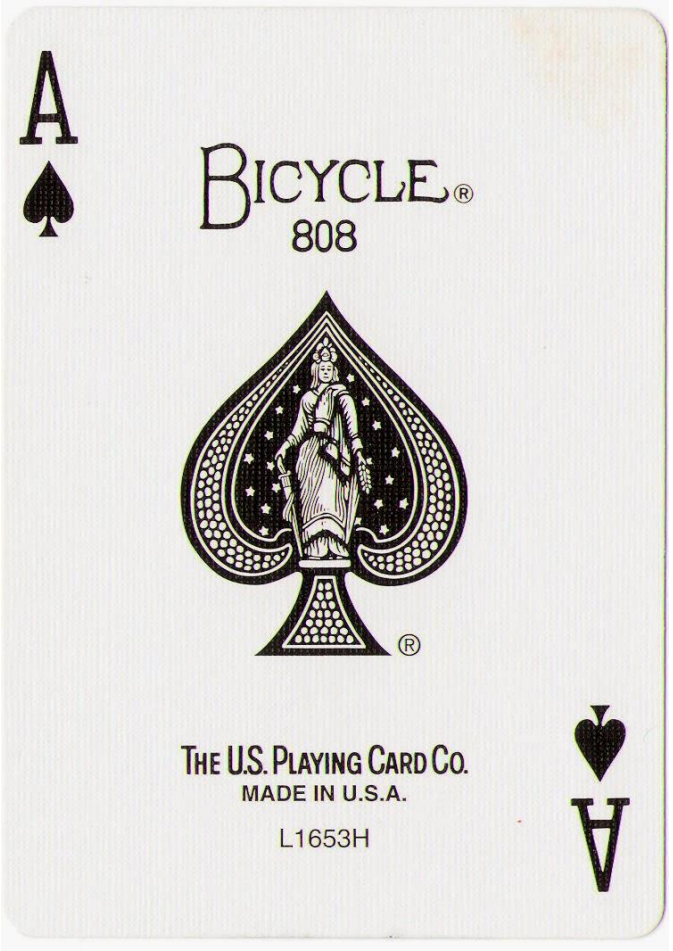
Research support by THOR Photomedicine, Ltd




Clinical reports, Randomized controlled trials, Definitive published data
Relevant clinical practice guidelines, Policy statements, Reimbursement mechanism
Clinical leadership, Adoption into standard of care

What about all of the RCTs???

- Preclinical data/model?
  - drug development model….
- Lack of large, multi-institutional studies
- Study design, quality, details provided, variable parameters
- Publication impact
- Overall credibility



MASCC/ISOO Guidelines

- The panel **recommends** that low-level laser therapy (wavelength at 650 nm, power of 40 mW, and each square centimeter treated with the required time to a tissue energy dose of 2 J/cm2), be used to *prevent* oral mucositis in patients receiving HSCT conditioned with high-dose chemotherapy, with or without total body irradiation (II)
- The panel **suggests** that low-level laser therapy (wavelength around 632.8 nm) be used to *prevent* oral mucositis in patients undergoing radiotherapy, without concomitant chemotherapy, for head and neck cancer (III)

TABLE 2. Criteria for Each Guideline Category

Recommendation	Reserved for guidelines that are based on level I or level II evidence.
Suggestion	Used for guidelines that are based on level III, level IV, and level V evidence; this implies panel consensus regarding the interpretation of this evidence.
No guideline possible	Used when there is insufficient evidence on which to base a guideline; this implies 1) that there is little or no evidence regarding the practice in question, or 2) that the panel lacks consensus on the interpretation of existing evidence.

Adapted from Somerfield MR, Padberg JR, Pfister DG, et al. ASCO clinical practice guidelines: process, progress, pitfalls, and prospects. *Class Pap Curr Comments*. 2000;4:881-886.[21]

Lalla R, et al. Cancer 2014;000:000–000

Limitations of practice guidelines

- Competing guidelines
  - which to follow, why?
- Source of guidelines
- Frequency of updates
- Cost effectiveness of interventions?
- Institutional preferences

From: **Why Don't Physicians (and Patients) Consistently Follow Clinical Practice Guidelines? Comment on "Worsening Trends in the Management and Treatment of Back Pain"**

JAMA Intern Med. 2013;173(17):1581-1583. doi:10.1001/jamainternmed.2013.7672

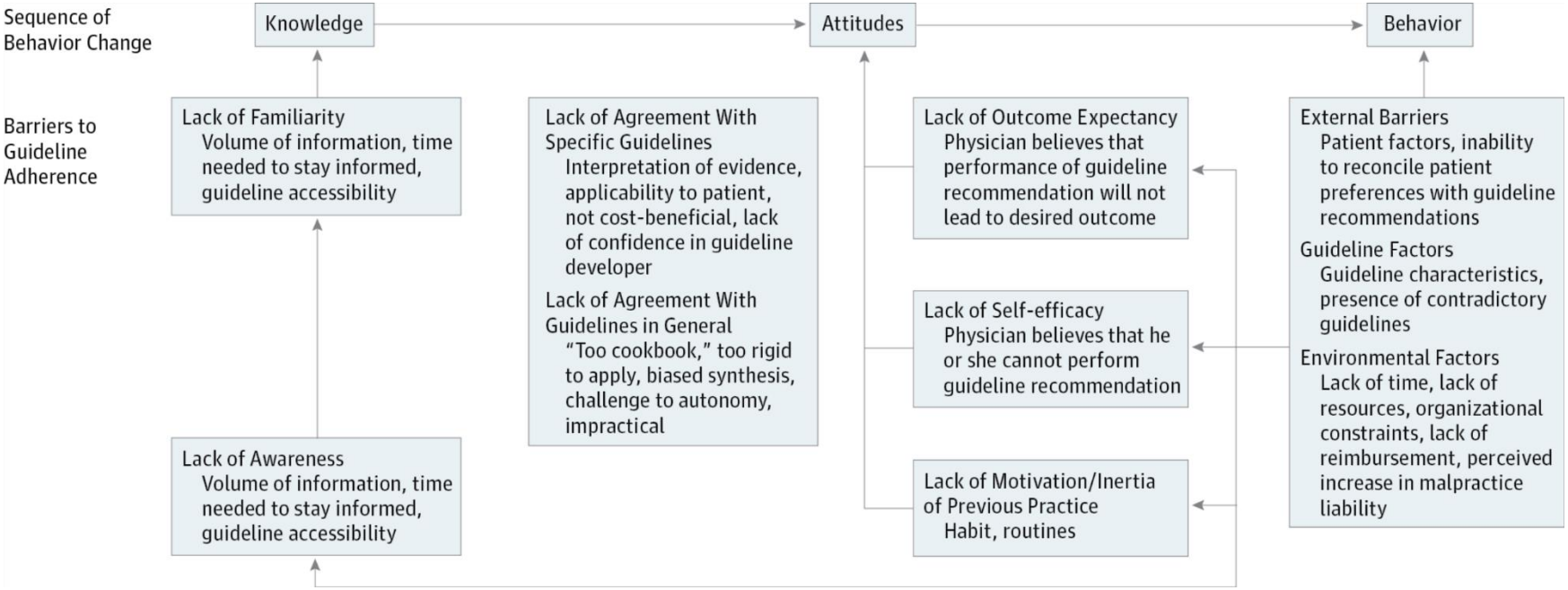
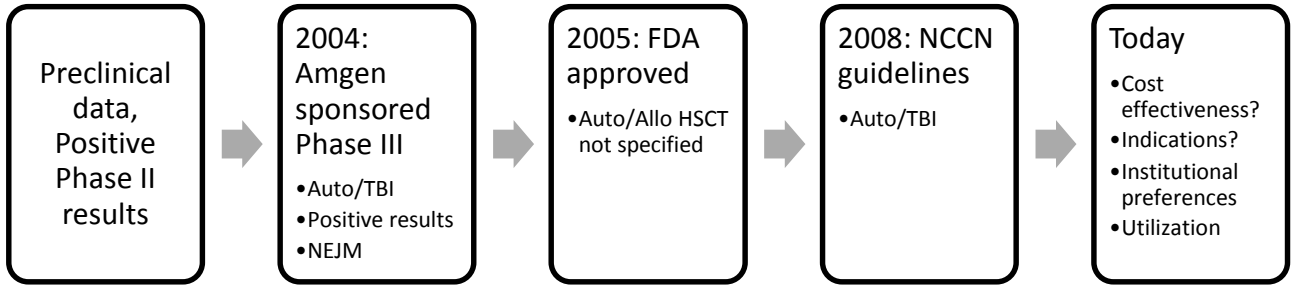


Figure Legend:

Barriers to Physician Adherence to Practice Guidelines in Relation to Behavior ChangeReprinted from JAMA.

Can we learn from Palifermin?



Biol Blood Marrow Transplant 20 (2014) 852–857

Pharmacoeconomic Analysis of Palifermin to Prevent Mucositis among Patients Undergoing Autologous Hematopoietic Stem Cell Transplantation

Ajay K. Nooka [1,*], Heather R. Johnson [1], Jonathan L. Kaufman [1], Christopher R. Flowers [1], Amelia Langston [1], Conor Steuer [1], Michael Graiser [1], Zahir Ali [1], Nishi N. Shah [1], Sravanti Rangaraju [1], Dana Nickleach [2], Jingjing Gao [2], Sagar Lonial [1], Edmund K. Waller [1]

[1] *Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, Georgia*
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"Median total transplant charges were significantly higher in the palifermin-treated group, after controlling for inflation (myeloma: $167,820 versus $143,200, P < .001; lymphoma: $168,570 versus $148,590, P < .001)."

ORIGINAL ARTICLE

Palifermin is efficacious in recipients of TBI-based but not chemotherapy-based allogeneic hematopoietic stem cell transplants

JD Goldberg[1,2], J Zheng[3], H Castro-Malaspina[1,2], AA Jakubowski[1,2], G Heller[3], MRM van den Brink[1,2] and M-A Perales[1,2]

Palifermin, a recombinant human keratinocyte growth factor, is commonly given to prevent mucositis following autologous transplantation. In the allogeneic hematopoietic stem cell transplant (allo-HSCT) setting, safety and efficacy data are limited. We conducted a retrospective study in 251 patients undergoing allo-HSCT, 154 of whom received peritransplant palifermin. In all patients, palifermin significantly decreased the mean number of days of total parenteral nutrition (TPN, 13 vs 16 days, $P = 0.006$) and patient-controlled analgesia (PCA, 6 vs 10 days, $P = 0.023$), as well as the length of initial hospital stay (LOS, 32 vs 37 days, $P = 0.014$). However, the effect of palifermin was only significant in patients who received a TBI- but not BU-based chemotherapy conditioning regimen. In TBI recipients, palifermin decreased the mean number of days of TPN (13 vs 17 days, $P < 0.001$) and PCA (7 vs 12 days, $P = 0.033$), and the length of stay (32 vs 38 days, $P = 0.001$). Palifermin did not affect GVHD, graft failure or relapse. Therefore, in the largest analysis with this patient population to date, we demonstrate that palifermin is safe in allo-HSCT patients, decreases TPN and PCA use and decreases LOS following TBI-based but not chemotherapy-based allo-HSCT.

Bone Marrow Transplantation (2013) **48,** 99–104; doi:10.1038/bmt.2012.115; published online 2 July 2012

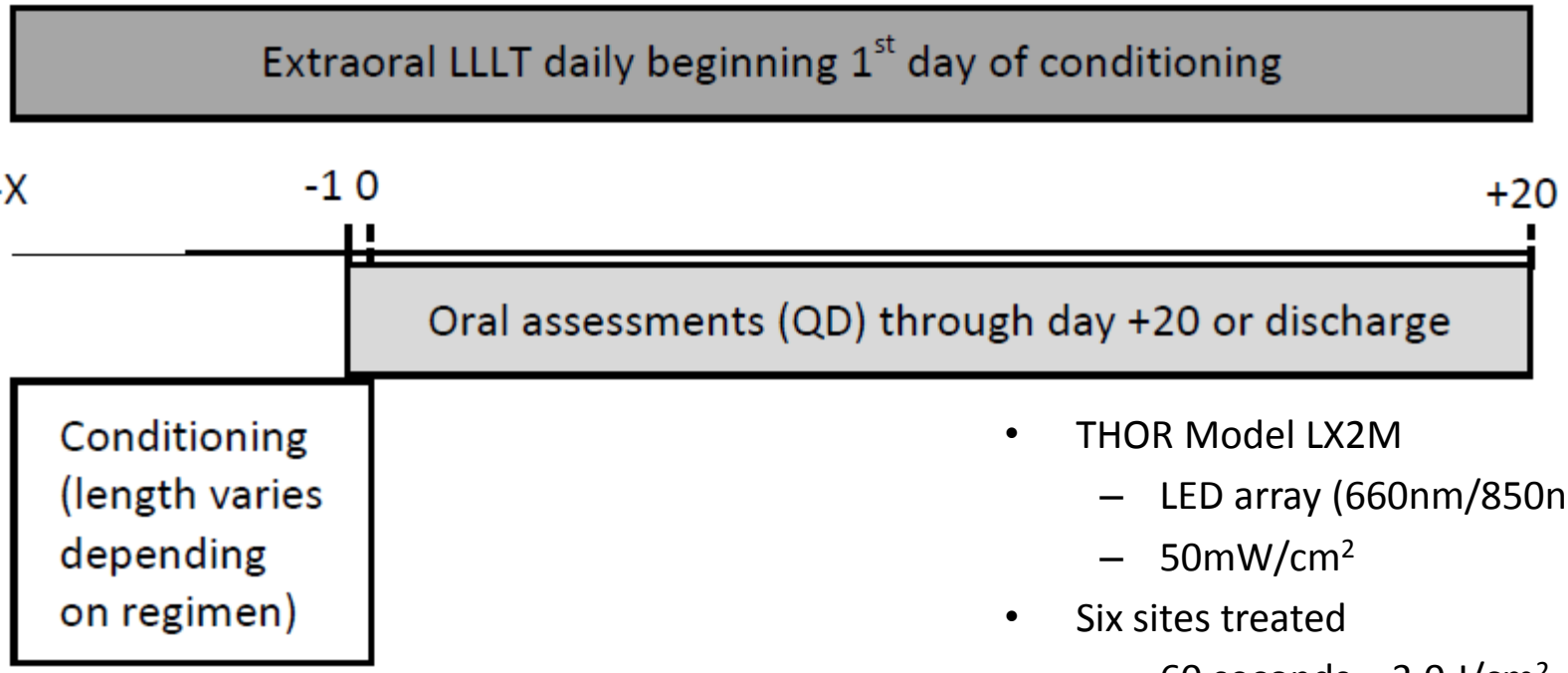
Keywords: allogeneic transplant; mucositis; palifermin

"Therefore, in the largest analysis with this patient population to date, we demonstrate that palifermin is safe in allo-HSCT patients, decreases TPN and PCA use and decreases LOS following TBI-based but not chemotherapy-based allo-HSCT."

Barriers, and the Pathway Forward

- Data from multi-center RCT is essential
  - must be high quality design
  - best if conducted in the US/Canada
- Publication relevance, impact
  - BMT, BBMT, NEJM
  - anything less carries no weight
- Invasiveness (risk/benefit)
  - lower threshold compared with drug
  - unlikely to be harmful
  - more likely to be incorporated into SOC
- Role of clinical guidelines
  - ASBMT guideline/statement or nothing
  - MASCC/ISOO carries no weight
- Cost
  - bundled care
  - third party reimbursement
  - demonstrate cost effectiveness, value
- Preclinical model
  - efficacy
  - MOA
  - non-tumor effect (H/N)
- Definitive “no harm” studies (H/N)
  - requires long-term follow-up
- Marketing
  - which device, parameters, why? training

Feasibility pilot study evaluating extraorally delivered low level light therapy (LLLT) for the prevention of oropharyngeal mucositis in pediatric patients undergoing myeloablative hematopoietic cell transplantation



- THOR Model LX2M
  - LED array (660nm/850nm)
  - 50mW/cm^2
- Six sites treated
  - 60 seconds = 3.0 J/cm^2
  - 6 minutes treatment time

Our Vision

- Complete feasibility protocol
- Model for optimal dosimetry
- Finalize clinical protocol
- Secure funding for definitive multicenter RCT
- Publish in top tier journal
- Implementation