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

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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
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**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Reserved for guidelines that are based on level I or level II evidence.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suggestion</td>
<td>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.</td>
</tr>
<tr>
<td>No guideline possible</td>
<td>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.</td>
</tr>
</tbody>
</table>

Limitations of practice guidelines

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


Figure Legend:
Barriers to Physician Adherence to Practice Guidelines in Relation to Behavior ChangeReprinted from JAMA.
Can we learn from Palifermin?

Preclinical data, Positive Phase II results

2004: Amgen sponsored Phase III
- Auto/TBI
- Positive results
- NEJM

2005: FDA approved
- Auto/Allo HSCT not specified

2008: NCCN guidelines
- Auto/TBI

Today
- Cost effectiveness?
- Indications?
- Institutional preferences
- Utilization

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

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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).”

“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

**Extraoral LLLT daily beginning 1st day of conditioning**

- Conditioning (length varies depending on regimen)

  - THOR Model LX2M
    - LED array (660nm/850nm)
    - 50mW/cm²

- Six sites treated
  - 60 seconds = 3.0 J/cm²
  - 6 minutes treatment time

**Oral assessments (QD) through day +20 or discharge**
Our Vision

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