#19 SAFETY AND EFFICACY OF AN LED-BASED INTRAORAL DEVICE FOR DAILY PHOTOBIOMODULATION THERAPY PRIOR TO CANCER TREATMENT FOR REDUCING SEVERITY OF ORAL MUCOSITIS IN HEAD AND NECK CANCER PATIENTS

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ABSTRACT

Purpose/Objective(s): Oral mucositis (OM) is one of the most prevalent and debilitating toxicities of head and neck cancer (HNC) treatment. Pharmacological interventions are limited; however, supportive care treatment guidelines from the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) recommend photobiomodulation (PBM) therapy for the prevention and treatment of OM. PBM therapy utilizes non-ionizing light in the visible and near-infrared light spectra to modulate biological systems, including wound healing. The aim of this study was to evaluate the safety and efficacy of an intraoral device designed to deliver PBM therapy (660 nm, 6 J/cm^2) to all oral soft tissues during a 10-minute daily treatment procedure.

Methods: This was a prospective, randomized (1:1), double-blind, sham-controlled trial (NCT03972527) across 12 US cancer centers. Eligible HNC patients received a continuous course of intensity-modulated radiation therapy (IMRT) over 6-8 weeks with or without concurrent chemotherapy. Eligibility required that at least two oral cavity sites received >50 Gray, with a maximum cumulative dose of 70 Gray administered. Pain medications and oral mouthwashes were permitted. Participants received daily 10-minute PBM therapy immediately prior to scheduled radiation therapy (RT), as well as daily and weekly assessments, and a follow up visit two weeks post-treatment.

Results: Eighty-five subjects completed the trial. Treatment was found to be safe with no device-related adverse events and was well tolerated with 98.3% of device sessions (2,574 of 2,619) completed in full. Key findings included a statistically significant reduction in the incidence of severe oral mucositis (SOM) across 6 weeks of RT [WHO Oral Toxicity Scale Grade 3 or 4: 36.8% active vs. 57.1% sham, a 36% relative reduction; p = 0.046] and at two weeks post-treatment [10.8% active vs. 36.4% sham, a 70% relative reduction; p = 0.042]. Furthermore, active arm subjects reported statistically significant lower increases in both mouth and throat soreness [1.5 active vs. 2.2 sham (5 pt scale); p = 0.029] and throat pain [3.8 active vs. 5.3 sham (10 pt scale); p = 0.028] over 6 weeks of RT using a validated patient-reported outcome tool (Oral Mucositis Weekly Questionnaire). Among subjects starting cancer treatment without prior placement of a percutaneous endoscopic gastrostomy (PEG) feeding tube, there was a 59% reduction in PEG placements [15.2% active vs. 37% sham; p = 0.073].

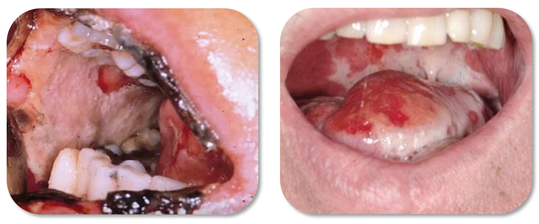
Conclusion: Clinical, patient-reported, and functional outcomes consistently favored the active arm. The LED-based intraoral medical device was effective in reducing SOM in subjects undergoing radiation therapy with or without concurrent chemotherapy. The device's safety, tolerability, and positive clinical outcomes suggest its potential as a promising intraoral PBM intervention for managing OM in patients undergoing HNC treatment, addressing a significant challenge in oncological supportive care.

PURPOSE AND BACKGROUND

Study Aim: To evaluate the safety and efficacy of an intraoral PBM Device (The MuReva OM^{TM}) designed to deliver PBM therapy (660 nm, 6 J/cm^2) to all oral mucositis susceptible soft tissues during a 10-minute daily treatment procedure immediately prior to scheduled radiation therapy (RT).

Oral Mucositis (OM)

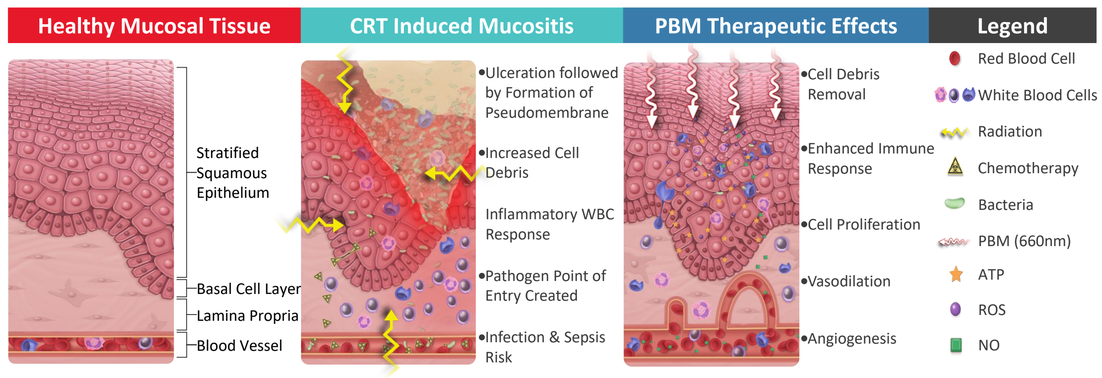
- Common[1,2], debilitating[3,4], and painful side effect of cancer therapy
- Characterized by inflammation and ulceration
- Severe toxicity threatening quality/quantity of life[5]



Severe Oral Mucositis

PBM

- Low-Energy
- Non-Thermal
- Non-Ionizing
- Recommended[6]
- 50+ Publications



MATERIALS AND METHODS

Design	• Prospective, Double-Blind, Randomized (1:1), Sham Controlled [NCT0397527] • Subjects completed daily 10-minute study treatments immediately prior to RT • Comprehensive daily/weekly evaluations (6-8-wk IMRT + 2-week follow-up)
Key Eligibility	• Adult patients with SCC of the oral cavity, oropharynx, or base of tongue • Continuous IMRT over an estimated 6-8 weeks (50-70 Gy); ≥2 oral sites >50Gy • With/without chemotherapy [Cisplatin (qwk/q3wk) or Carboplatin (qwk)]
Metrics	• Physician evaluations (Oral Mucositis Grading) • Patient reported outcomes (OMWQ-HN, UW-QoL) • Functional changes (swallowing, PEG tube placements)
Permitted/ Restricted	• Pain medications, magic mouthwashes permitted • Smoking, alcohol, medications to treat/prevent OM prohibited
Regulatory	• Breakthrough Device Designation granted by FDA in 2021 • Non-Significant Risk Status

WHO Grading Scale

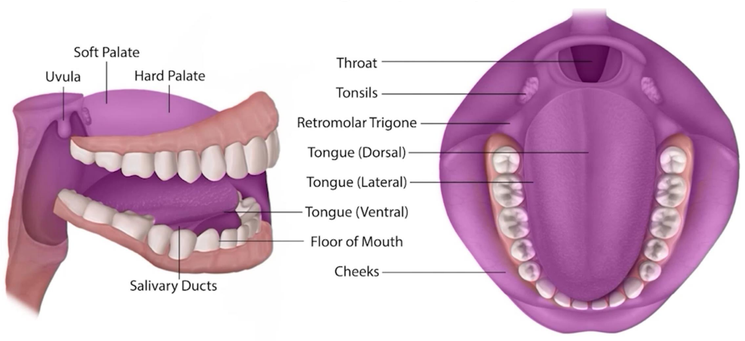
- Evaluates mixed variables
  - Objective – Ulceration/erythema
  - Functional – Dietary changes
- Severe OM – Grade 3 or 4
- Add'l assessments ensure consistent scoring
  - Oral – Confirm ulcer/erythema location
  - Dietary – Confirm limitation reason

Grade 0: No Changes
Grade 1: Soreness / Erythema
Grade 2: Erythema, Ulcers; can eat solid foods
Grade 3: Ulcers; requires liquid diet only
Grade 4: Alimentation not possible
Grade 5: Death

The MuReva OM^{TM} (Intra-Oral PBM Device)

The MuReva OM^{TM} with Accessories

Tissue Targets (In Purple)



Over-Tongue Emitter

Targeted Delivery to Cheeks, Tongue and Soft Palate/Tongue

Under-Tongue Emitter

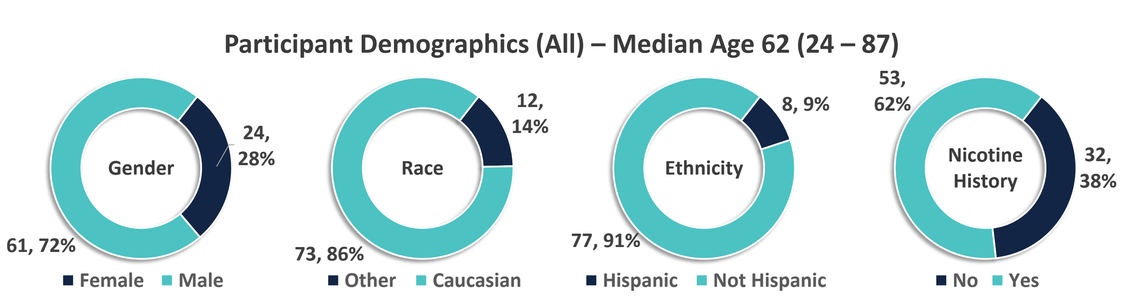
Targeted Delivery to Ventral/Lateral Tongue, Floor of Mouth, Salivary Glands

Nominal dosage of 6 J/cm^2 (660nm) delivered in 10min. therapy

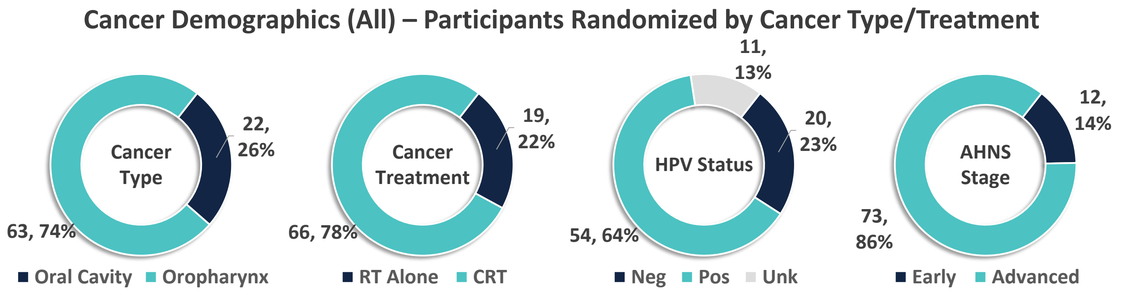
RESULTS

- 85 participants enrolled at 12-US cancer centers (42 MuReva; 43 Sham); Median Age
- 10 participants withdrew (no consistent/concerning trends for withdrawn participants)
- Demographic distributions similar between study arms

Participant Demographics (All) – Median Age 62 (24 – 87)



Cancer Demographics (All) – Participants Randomized by Cancer Type/Treatment

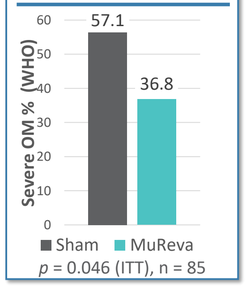


Daily MuReva Treatment was Well Tolerated with Strong Compliance and No Device-AEs

98.2% Treatment Compliance	99.5% Treatment Tolerability	0 Device-Related Adverse Events
• Study treatment was easily integrated into RT workflow • 2574 treatments started	• Results confirm patient-friendly mouthpiece design • 2561 10-min treatments	• Results consistent with prior PBM research • 2574 total treatments

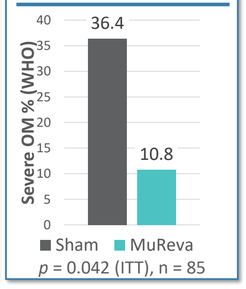
Clinical, patient-reported, and functional outcomes consistently favored the active arm

Incidence of Severe OM — 36% Relative Reduction Over 6 Weeks



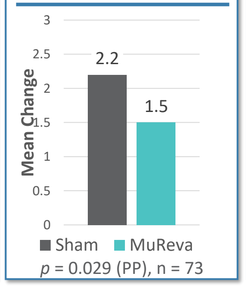
p = 0.046 (ITT), n = 85

Post RT Recovery — 70% Relative Reduction 2 Week Post RT



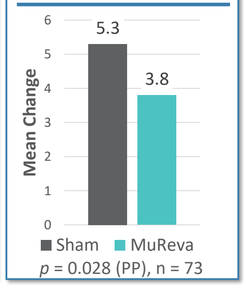
p = 0.042 (ITT), n = 85

Mouth/Throat Soreness — 32% Relative Reduction Over 6 Weeks



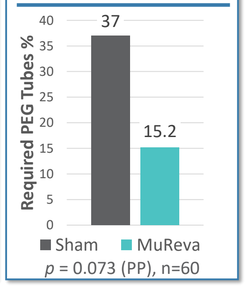
p = 0.029 (PP), n = 73

Throat Pain Change — 28% Relative Reduction Over 6 Weeks



p = 0.028 (PP), n = 73

Surgical Feeding Tube — 59% Relative Reduction All Weeks



p = 0.073 (PP), n=60

CONCLUSION and DISCUSSION

- Clinical, patient-reported, and functional outcomes consistently favored the active arm.
- The LED-based intraoral medical device was effective in reducing severe OM in subjects undergoing` radiation therapy with or without concurrent chemotherapy.
- The safety, tolerability, and positive clinical outcomes suggest potential as a promising intraoral PBM intervention for managing OM in patients undergoing HNC treatment, addressing a significant challenge in oncological supportive care.

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