APPENDIX 13: RANDOMIZED CONTROLLED TRIALS OF ANY INTERVENTION FOR THE PREVENTION OF ORAL MUCOSITIS IN PEDIATRIC PATIENTS RECEIVING TREATMENT FOR CANCER OR UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION – OUTCOMES

First Author (Year)	COMPARISONS	OUTCOMES				
		Number Received Intervention Group 1	Number Received Intervention Group 2	Description of Main Mucositis Findings	Description of Main Pain Findings	Description of Adverse Events
Patte (2002) [1]	Lenograstim versus no lenograstim	75	73	Incidence grade 3 and 4 mucositis similar between arms	Not reported	Not reported
Michel (2000) [2]	Lenograstim versus no lenograstim	34	33	GCSF reduced incidence mucositis (6% vs 19%; P=0.04) after R3 but not after COPADM (65% vs 75%; P=NS)	Not reported	Not reported
Lehrnbecher (2007) [3]	GCSF versus no GCSF	161	156	GCSF no impact on incidence grades 3 and 4 mucositis (26.6% with GCSF vs 23.6% without GCSF; P=0.59)	Not reported	Not reported
Ladenstein (2010) [4]	Filgrastim versus no filgrastim	110	114	Grade 2 to 4 mucositis significantly less with GCSF (2%) compared with no GCSF (6%; P=0.002)	Not reported	Tolerance to GCSF good, only expected adverse effects reported
Cesaro (2013) [5]	Pegfilgrastim versus filgrastim	32	29	No significant difference in Grade 2 to 4 mucositis with GCSF (76%) vs pegfilgrastim (59%). No significant difference in severity or duration between groups	Not reported	Both pegfilgrastim and filgrastim well tolerated, no significant adverse effects
Fox (2009) [6]	Pegfilgrastim versus filgrastim	17	17	Grade 2 to 4 mucositis occurred in 4 patients with pegfilgrastim and 7 patients with GCSF, respectively, during cycles 1 to 4	Not reported	Pegfilgrastim and GCSF well tolerated, adverse events similar between arms
Wexler (1996) [7]	GMCSF versus no GMCSF	19	18	No significant differences in mucositis grade in cycles 1-2 and 3-18 between GMCSF and control groups	Not reported	Not reported
Uderzo (2011) [8]	Glutamine enriched versus standard nutrition	60	58	Mucositis in the first 3 to 4 weeks from HSCT in 94.8% and 96.7% in standard and glutamine enriched groups (P=0.68)	Not reported	Not reported
Aquino (2005) [9]	Glutamine versus glycine	57	63	Mean mucositis score 3.0±0.3 vs 3.9±0.4 (P=0.07) in glutamine and glycine groups. No difference in maximum mucositis score (P=0.7)	Not reported	No statistically significant difference in toxicity between groups
Ward (2009) [10]	Enteral glutamine versus no glutamine	50	50	No significant difference in severe mucositis (P=0.942) or duration of severe mucositis	Not reported	No adverse effects attributed to glutamine
Sencer (2012) [11]	Traumeel S versus placebo	98	92	Mean Walsh area under curves similar in two groups: 71.7 (SE 7.2) with Traumeel S and 69.8 (SE 8.2) with placebo. No difference in WHO scores.	Not reported	No significant difference in adverse events between group
Oberbaum (2001) [12] (companion paper: [13])	Traumeel S versus placebo	15	15	33% with Traumeel S did not develop mucositis vs 7% with placebo. Mean area under curve mucositis scores 10.4 with Traumeel S vs 24.3 with placebo (P<0.01).	5 in Traumeel S group had any oral pain vs 14 in placebo group	High incidence of serious complications but no significant difference between the groups

First Author (Year)	COMPARISONS	OUTCOMES				
		Number Received Intervention Group 1	Number Received Intervention Group 2	Description of Main Mucositis Findings	Description of Main Pain Findings	Description of Adverse Events
Abramoff (2008) [14]	Low level light therapy versus placebo	11	11	At the third evaluation, 73% prophylactic laser group did not have mucositis vs 27% placebo (P=0.03)	Not reported	Not reported
Cruz (2007) [15]	Low level light therapy versus no low level light therapy	29	31	No significant difference in mucositis grade on day 8 (P=0.234) or day 15 (P=0.208)	Not reported	Not reported
Raether (1989) [16]	Chlorhexidine versus placebo	23	24	No significant difference in severity of oral ulceration between chlorhexidine and placebo groups (P=0.18)	Not reported	Not reported
Cheng (2004) [17] (companion papers:[18] , [19])	Benzydamine versus chlorhexidine	40	40	Ulcerative lesions in 27% (chlorhexidine) and 59% (benzydamine) (P<0.05). 26% and 48% using chlorhexidine and benzydamine had WHO grade 2 mucositis (P<0.05)	Significant difference in mean area under the curve of mouth pain (chlorhexidine 1.35±2.26 vs benzydamine 3.09±3.21; P=0.05)	Not reported
Shenep (1988) [20]	Sucralfate versus placebo	24	24	Objective observers noted more moderate and severe oral ulceration in placebo vs sucralfate groups (38% vs 12%; P=0.12)	58% patients sucralfate reported no oral pain vs 25% placebo (P=0.06)	8 in placebo and 4 in sucralfate experienced rashes (P=0.18). One placebo patient had unexplained papilledema
Sung (2007) [21]	Topical vitamin E versus placebo	22	23	No difference in objective mucositis scores with mean score 0.2 with vitamin E vs 0.3 with placebo .	Vitamin E did not reduce pain VAS scores, mean scores of 0.9 (on a scale of 0–10) in each group	No unexpected toxicity with topical vitamin E. Many children complained study solution difficult to use because of oily texture
de Koning (2007) [22]	TGF-b2-enriched feeding versus placebo	25	25	Grade 3 or 4 mucositis occurred in 40% with TGF-b2-treatment vs 32% with placebo	Not reported	No significant difference between the TGFb2 and placebo arms for any of toxicity parameters
Gandemer (2007) [23]	Chewing gums versus no chewing gum	73	72	No overall reduction in severe oral mucositis in gum (51%) vs control arms (44%; P=0.67)	Unable to assess pain because too few evaluations	Proportion of patients experiencing adverse events did not differ between arms
Rojas de Morales (2001) [24]	Oral disease preventive protocol versus oral physiotherapy	5	7	No significant difference in mucositis (P>0.05)	Not reported	Not reported

Abbreviations: GCSF – granulocyte colony stimulating factor; GMCSF – granulocyte-macrophage colony stimulating factor; NS – not significant; HSCT – hematopoietic stem cell transplantation; SE – standard error; VAS – visual analogue scale

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