

APPENDIX 5: RANDOMIZED CONTROLLED TRIALS OF CRYOTHERAPY FOR THE PREVENTION OF ORAL MUCOSITIS IN ADULT AND PEDIATRIC PATIENTS RECEIVING TREATMENT FOR CANCER OR UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION - METHODOLOGY

METHODOLOGY					RISK OF BIAS FOR RANDOMIZED CONTROL TRIALS					
First Author (Year)	RCT or quasi-RCT	Study design: (Parallel group, Cross-over, N-of-1)	Scales Used to Measure Mucositis	Frequency and Timing of Mucositis Assessment	Adequate sequence generation?	Adequate allocation concealment?	Participants and personnel blinded?	Outcome assessors blinded?	Loss to follow-up is less than 20% and/or equally distributed between both interventions?	Study free of selective reporting?
Katransci (2012) [1]	RCT	Parallel group	WHO	Days 7, 14 and 21 after chemotherapy	Yes	Unclear	No	No	Yes	Yes
Salvador (2012) [2]	RCT	Parallel group	WHO	Days 3, 6, 9, and 12 after stem cell infusion	Yes	Unclear	No	Yes	Yes	Yes
Sorensen (2008) [3]	RCT	Parallel group	CTCAE v2.0	Day 14 and 28	Unclear	Unclear	No	No	Yes	Yes
Svanberg (2007) [4] (companion papers: [5], [6])	RCT	Parallel group	OMAS, WHO	Start of chemotherapy daily until day 21	Unclear	Unclear	No	No	Yes	Yes
Gori (2007) [7]	RCT	Parallel group	WHO	Day stem cell infusion until day 20	Unclear	Unclear	No	No	Yes	Yes
Papadeas (2007) [8]	Quasi-RCT	Parallel group	4 point grading scale	Once, one month after treatment	No	No	No	Yes	No	Yes
Lilleby (2006) [9]	RCT	Parallel group	CTCAE v2.0	Daily from day 2 to day 28 post stem cell infusion	Unclear	Unclear	No	No	Yes	Yes
Baydar (2005) [10]	Quasi-RCT	Extended cross-over	WHO	Days 5, 10, 15 and 21 from chemotherapy start	No	Unclear	No	No	Yes	Yes
Karagozoglou (2005) [11]	Quasi-RCT	Parallel group	Patient-judged mucositis grading and physician-judged mucositis grading	Patient report: Daily from day 1 of chemotherapy until day 21; Physician report - days 1 and 21, and days 2 and 3 if patient in clinic	No	Unclear	No	No	Yes	Yes
Nikoletti (2005) [12]	RCT	Cross-over	Oral Assessment Guide and Western Consortium Cancer Nursing Research Scale	Baseline and day 15 of each chemotherapy course	Unclear	Unclear	No	No	No	Yes

METHODOLOGY					RISK OF BIAS FOR RANDOMIZED CONTROL TRIALS					
First Author (Year)	RCT or quasi-RCT	Study design: (Parallel group, Cross-over, N-of-1)	Scales Used to Measure Mucositis	Frequency and Timing of Mucositis Assessment	Adequate sequence generation?	Adequate allocation concealment?	Participants and personnel blinded?	Outcome assessors blinded?	Loss to follow-up is less than 20% and/or equally distributed between both interventions?	Study free of selective reporting?
Cascinu (1994) [13]	RCT	Parallel group	Global assessment of the physicians' judgment and patients' description of mucositis severity graded 0-4	Once weekly until start of next course	Unclear	Unclear	No	No	Yes	Yes
Rocke (1993) [14]	RCT	Parallel group	Physician and patient judged mucositis graded 0 to 4	Physician: Approximately 1 month after treatment initiation; Patient: 2 to 3 weeks after treatment initiation	Unclear	Unclear	No	No	Yes	Yes
Mahood (1991) [15]	RCT	Parallel group	Physician and patient judged mucositis graded 0 to 4	Physician: Approximately 1 month after treatment initiation; Patient: 2 to 3 weeks after treatment initiation	Unclear	Unclear	No	No	Yes	Yes
Kakoei (2013) [16]	RCT	Parallel group	Physician and patient judged mucositis graded 0 to 4	Days 1, 7 and 14	Unclear	Unclear	No	No	Yes	No

Abbreviations: RCT – randomized controlled trial; WHO – World Health Organization; OMAS – Oral Mucositis Assessment Scale; CTCAE – Common Terminology Criteria for Adverse Events

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