Evidence Profile 6.2. Radiotherapy vs. Placebo

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Radiotherapy**	**Placebo**	**Relative (95% CI)**	**Absolute (95% CI)**		
Bone pain relief (categorical) (complete response, follow up: 1-3 months; assessed with: VAS<15 or "pain free")												
2 [1,2]	RCT	serious [A]	not serious	serious [B]	none	none	51/134 (38%)	17/85 (20%)	**RR 1.92** (1.18, 3.12)	**351 more per 1000** (from 69 to 807 more)	Low	CRITICAL
Bone pain relief (categorical) (improvement [complete or partial response], follow up: 2-3 months or nd; assessed with: VAS≥2/10 reduction in bone pain ["very good"])												
4 [1,3,4,5]	RCT	very serious [D]	not serious	not serious	serious [C]	none	71/107 (66%)	45/104 (43%)	**RR 1.35** (0.89, 2.07)	**235 more per 1000** (from 75 fewer to 707 more)	Very Low	CRITICAL
Pain relief (continuous) (follow up: range 1 to 2 months; assessed with: VAS, NRS; Scale: 0 to 100 [worst] [E])												
5 [2,4,5,6,8]	RCT	serious [F]	not serious [G]	not serious	not serious	none	241	145	**Diff -41** (-64, -18)		Moderate	CRITICAL
Pain reduction maintenance												
0									not estimable			CRITICAL
Skeletal-related events, any (follow up: range 1.8 to 3 years)												
2 [8,9]	RCT	not serious	not serious	not serious	not serious	none	427/978 (43%)	345/680 (50%)	**RR 0.86** (0.77, 0.95) HR 0.73 (0.62, 0.86) [H]	**34 fewer per 1000** (from 20 to 83 fewer)	High	IMPORTANT
Skeletal-related events, fracture (follow up: range 1.8 to 3 years)												
2 [8,9]	RCT	not serious	serious [I]	not serious	serious [J]	none	47/978 (4.8%)	32/680 (5.1%)	RR 1.05 (0.53, 2.08)	**3 fewer per 1000** (from 55 fewer to 24 more)	Low	
Skeletal-related events, spinal cord compression (follow up: range 1.8 to 3 years)												
2 [8,9]	RCT	not serious	serious [I]	not serious	serious [J]	none	76/978 (8.3%)	67/680 (9.7%)	RR 0.82 (0.39, 1.71)	**18 fewer per 1000** (from 59 fewer to 69 more)	Low	
Skeletal-related events, bone surgery (follow up: 1.8 years)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Placebo	Relative (95% CI)	Absolute (95% CI)		
1 [8]	RCT	not serious	N/A	not serious	serious [J]	single study	16/378 (4.2%)	11/379 (2.9%)	RR 1.46 (0.69, 3.10)	**13 more per 1000** (from 13 fewer to 40 more)	Low	
Skeletal-related events, hypercalcemia (follow up: 1.8 years)												
1 [8]	RCT	not serious	N/A	not serious	very serious [J]	single study	2/378 (0.5%)	0/379 (0%)	RR 5.01 (0.24, 104)	**5 more per 1000** (from 2 fewer to 13 more)	Very Low	
Quality of life (categorical) (follow up: 3 years; assessed with: FACT-P; improvement ≥10 increase on a scale of 0 to 156 [best])												
1 [9]	RCT	not serious	not serious	serious [K]	not serious	single study	150/600 (25%)	48/301 (16%)	**RR 1.57** (1.17, 2.10)	90 more per 1000 (from 27 to 176 more)	Low	IMPORTANT
Quality of life (follow up: range 1.8 to 3 years; assessed with: FACT-P; Scale: 0 to 100 [best] [E])												
2 [8,9]	RCT	not serious	not serious	serious [K]	not serious	none	3427	3047	Diff 1.5 (-0.4, 3.3)		Moderate	IMPORTANT
Functional outcomes, Social (follow up: 1.8 years; assessed with: FACT-P-social; Scale: 0 to 100 [best] [E])												
1 [8]	RCT	not serious	not serious	serious [K]	serious [J]	single study	2993	2921	Diff -1.1 (-1.9, -0.3) [L]		Very Low	IMPORTANT
Functional outcomes, Physical (follow up: 1.8 years; assessed with: FACT-P-physical; Scale: 0 to 100 [best] [E])												
1 [8]	RCT	not serious	not serious	serious [H]	serious [I]	single study	2993	2921	Diff 1.4 (0.5, 2.3) [L]		Very Low	IMPORTANT
Adverse events: bone flare (follow up: soon after treatment)												
3 [2,5,7]	RCT	not serious	not serious	not serious	very serious [C, J]	none	13/192 (6.8%)	5/102 (4.9%)	**RR 1.30** (0.50, 3.42)	20 more per 1000 (from 34 fewer to 164 more)	Low	IMPORTANT

***Abbreviations: CI**: confidence interval; **Diff**: difference (between groups); **FACT**: Functional Assessment of Cancer Therapy; **HR**: hazard ratio; **nd**: no data (not reported); **NS:** not statistically significant**; RCT**: randomized controlled trial(s); **RR**: relative risk (log scale); **VAS**: Visual Analog Scale.*

Explanations

A. High attrition rate.
B. One trial's outcome was not true complete response (VAS <15); other trial did not define pain free.
C. Fewer than 300 participants.
D. High attrition rate, lack of blinding, possible selective outcome reporting, no data on follow up time.
E. Scales transformed to 0 to 100, as necessary.
F. High attrition rate, lack of blinding, possible selective outcome reporting.
G. Inconsistent in magnitude but not in direction. See figure.
H. Reported in Radiotherapy 13.6 and 15.6 months until first skeletal-related event. Placebo 11.2 and 9.8 months, respectively.
I. The two study estimates were in opposite directions.
J. Wide confidence interval.
K. FACT (total score) is a measure of quality of life that mix concepts of both quality of life and functional outcomes. We treated the total score as a quality of life measure and the relevant subscores as functional outcomes, but these do not cleanly measure function.
L. Not statistically significant per study (therefore the calculated estimate here from the single study is inaccurately precise).

References

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