

Age difference in pain and patient reported outcomes: a secondary analysis of the NCIC CTG SC.20 randomized trial

Ronald Chow¹, Keyue Ding², Ralph M Meyer³, Yvette M van der Linden⁴, Daniel Roos⁵, William Hartsell⁶, Peter Hoskin⁷, Jackson SY Wu⁸, Abdenour Nabid⁹, Manouk van Acht¹⁰, Gijs Wanders¹¹, Scott Babington¹², William F Demas¹³, Carolyn F Wilson², Rebecca KS Wong¹⁴, Michael Brundage¹⁵, Liting Zhu², Edward Chow¹

¹Sunnybrook Odette Cancer Centre, University of Toronto, Toronto, Canada

²Canadian Cancer Trials Group, Cancer Research Institute, Queen's University, Kingston, Canada

³Juravinski Hospital and Cancer Centre and McMaster University, Hamilton, Canada

⁴Leiden University Medical Centre, Leiden and Radiotherapy Institute Friesland, Leeuwarden, Netherlands

⁵Royal Adelaide Hospital, University of Adelaide, Adelaide, Australia

⁶Northwestern Medicine Central DuPage Hospital, Warrenville, USA

⁷Mount Vernon Hospital Cancer Centre, Middlesex, United Kingdom

⁸Tom Baker Cancer Centre, University of Calgary, Calgary, Canada

⁹Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, Canada

¹⁰ErasmusMC, Rotterdam, Netherlands

¹¹MAASTRO Clinic, Maastricht, Netherlands

¹²Christchurch Hospital, Christchurch, New Zealand

¹³Akron City Hospital, Northeast Ohio Medical University, Akron, USA

¹⁴Princess Margaret Cancer Centre, Radiation Medicine Program, Ontario Canada Institute, Toronto, Canada

¹⁵Queen's University, Kingston, Canada



Objective

- Explore age difference in response and patient reported outcomes in cancer patients with bone metastases undergoing re-irradiation

Methods

- Secondary analysis of the NCIC Clinical Trials Group Symptom Control Trial SC.20 (NCIC CTG SC.20), which was a non-blinded, randomized, controlled trial that investigated the efficacy and safety of single versus multiple fraction e-irradiation
- Patients were accrued between January 2004 and May 2012 from nine countries
- Adults diagnosed with cancer reporting pain corresponding to sites of previously irradiated, radiologically confirmed bone metastases were eligible
- Scores of patients under/over 70 years of age from the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30) and Brief Pain Inventory (BPI) at baseline and 2 months post-radiotherapy were analysed
- Subgroup analyses were carried out amongst responders and non-responders
- Due to multiple comparisons, p-values less than 0.01 were considered statistically significant

Conclusions

- Palliative re-irradiation provides equivalent rates of pain relief irrespective of the patient's age
- This study supports consideration of repeat palliative radiotherapy for younger and older cancer patients alike

Results

- 847 patients were analysed, with more than half of the cohort (59%) being male
- Younger and older patients had similar survival and response to radiation
- No significant difference in change in worst pain score or oral morphine equivalents (OME) intake from baseline to month 2
- Younger responders demonstrated slightly better improvement in BPI items of normal work and enjoyment of life compared to older responders; there was no difference in terms of C30 scores

Patient demographics and baseline characteristics

	<70 years, N (%)	≥70 years, N (%)
Gender		
Female	286 (52.5)	62 (20.5)
Male	259 (47.5)	240 (79.5)
Primary Cancer Site		
Breast	187 (34.3)	36 (11.9)
Lung	139 (25.5)	51 (16.9)
Prostate	78 (14.3)	151 (50.0)
Others	141(25.9)	64 (21.2)
Karnofsky performance status (KPS)		
50-60	106 (19.4)	75 (24.8)
70-80	306 (56.1)	160 (53.0)
90-100	128 (23.5)	61 (20.2)
Unknown	5 (0.9)	6 (2.0)
Worst pain score at baseline		
1 to 4	58 (10.6)	44 (14.6)
5 to 8	360 (66.1)	189 (62.6)
9 to 10	110 (20.2)	60 (19.9)
Unknown	17 (3.2)	9 (2.9)
Site of painful bone metastases		
Spine or Head and Neck	202 (37.1)	105 (34.8)
Pelvis/Hips	187 (34.3)	120 (39.7)
Upper or lower limbs	90 (16.5)	39 (12.9)
Superficial bones	65 (11.9)	38 (12.6)
Unknown	1 (0.2)	0 (0.0)
Baseline total daily oral morphine equivalent (OME) (mg)		
N	524	292
Mean (SD)	157.4 (328.5)	93.94 (273.1)
Range	0-4130	0-4050

Baseline BPI and C30 scores

Domain	<70 years			≥70 years			P value
	N	Mean	SD	N	Mean	SD	
BPI							
General activity	502	6.1	2.8	278	2.8	2.8	0.01
Mood	504	4.7	2.9	277	2.9	2.9	0.03
Walking ability	502	5.6	3.2	276	3.2	3.2	0.84
Normal work	501	6.6	2.9	274	2.9	2.9	<0.01
Relationships with others	504	3.6	3.0	278	3.0	3.0	<0.01
Sleeping	505	4.7	3.2	278	3.2	3.2	<0.01
Enjoyment of life	504	5.6	3.1	277	3.1	3.1	<0.01
EORTC QLQ-C30							
Physical functioning	387	50.0	23.6	186	50.4	23.6	0.82
Role functioning	388	38.5	30.9	186	44.0	30.9	0.05
Emotional functioning	381	62.2	24.5	185	69.8	24.5	<0.01
Cognitive functioning	387	70.9	25.8	186	74.3	25.8	0.13
Social functioning	383	55.5	30.6	185	62.6	30.6	0.01
Fatigue	384	56.4	25.9	186	51.6	25.9	0.04
Nausea and vomiting	383	16.7	24.0	186	12.5	24.0	0.05
Pain	382	71.5	22.7	185	65.9	22.7	0.01
Dyspnea	388	29.4	31.5	186	28.0	31.5	0.61
Sleep	384	45.1	34.4	186	37.3	34.4	0.01
Appetite	383	35.2	34.6	185	30.8	34.6	0.16
Constipation	383	30.5	33.8	185	30.5	33.8	0.97
Diarrhea	383	9.2	20.7	186	7.7	20.7	0.41
Financial	383	26.5	34.9	185	10.5	34.9	<0.01
Global QOL	382	45.5	21.8	183	46.9	21.8	0.49

Changes in BPI scores for responders and non-responders

Domain	Responders			Non-responders			P value
	N	Mean	SD	N	Mean	SD	
<70 years							
General activity	137	-3.0	3.3	197	-0.7	3.3	<0.01
Mood	136	-2.6	3.1	195	-0.4	3.1	<0.01
Walking ability	136	-2.4	3.6	194	-0.5	3.6	<0.01
Normal work	138	-2.7	3.6	193	-0.6	3.6	<0.01
Relations with others	139	-1.8	2.9	195	-0.0	2.9	<0.01
Sleeping	139	-2.4	3.2	196	-1.0	3.2	<0.01
Enjoyment of life	138	-2.4	3.3	192	-0.6	3.3	<0.01
≥70 years							
General activity	87	-2.4	3.1	94	-0.1	3.1	<0.01
Mood	88	-1.9	3.1	94	-0.3	3.1	<0.01
Walking ability	86	-1.7	3.6	97	0.1	3.6	<0.01
Normal work	86	-1.7	3.3	92	-0.2	3.3	<0.01
Relations with others	85	-1.1	2.6	96	0.3	2.6	<0.01
Sleeping	86	-1.7	2.9	97	-0.7	2.9	0.04
Enjoyment of life	84	-1.5	2.9	95	0.3	2.9	<0.01

*Bolted figures indicates statistically significant values, p≤0.01

Changes in worst pain score and daily oral morphine equivalent at month 2

	<70 years, n (%)	≥70 years, n (%)	Total, n (%)
Change in worst pain score			
N	359	200	559
Mean (std)	-2.93 (3.00)	-2.66 (3.10)	-2.84(3.03)
Min, max	-10, 4	-10, 4	-10, 4
Change in daily oral morphine equivalent (mg)			
N	384	209	593
Mean (std)	32.02 (184)	13.54 (84.19)	25.51 (156.4)
Min, max	-827, 1797	-360, 623	-827, 1797

Std, standard deviation

Changes in BPI and C30 Scores at month 2

Domain	<70 years			≥70 years			P value
	N	Mean	SD	N	Mean	SD	
BPI							
General activity	334	-1.6	3.4	181	-1.2	3.4	0.20
Mood	331	-1.3	3.5	182	-1.1	3.5	0.40
Walking ability	330	-1.3	3.5	183	-0.7	3.5	0.07
Normal work	331	-1.5	3.7	178	-0.9	3.7	0.10
Relationships with others	334	-0.8	3.4	181	-0.4	3.4	0.20
Sleeping	335	-1.6	3.5	183	-1.1	3.5	0.17
Enjoyment of life	330	-1.4	3.5	179	-0.5	3.5	0.01
EORTC QLQ-C30							
Physical functioning	253	1.0	20.5	121	0.1	20.5	0.70
Role functioning	253	3.2	31.3	121	-0.6	31.3	0.29
Emotional functioning	245	4.5	23.6	120	3.0	23.6	0.56
Cognitive functioning	251	1.9	24.2	121	2.2	24.2	0.89
Social functioning	248	2.2	30.3	119	1.0	30.3	0.72
Fatigue	248	-2.6	25.5	121	1.6	25.5	0.14
Nausea and vomiting	247	-1.7	24.7	121	2.6	24.7	0.12
Pain	244	-17.2	29.8	117	-15.0	29.8	0.50
Dyspnea	252	2.4	31.0	119	1.1	31.0	0.70
Sleep	248	-13.0	35.9	120	-6.7	35.9	0.10
Appetite	248	-1.2	36.4	121	1.7	36.4	0.47
Constipation	247	-5.1	36.7	118	-5.4	36.7	0.95
Diarrhea	247	3.4	25.2	121	7.2	25.2	0.18
Financial	248	0.7	25.9	120	0.6	25.9	0.96
Global QOL	244	2.0	23.3	116	1.9	23.3	0.97

*Bolted figures indicates statistically significant values, p≤0.01

Changes in BPI and C30 scores for responders

Domain	<70 years			≥70 years			P value
	N	Mean	SD	N	Mean	SD	
BPI							
General activity	137	-3.0	3.3	87	-2.4	3.3	0.24
Mood	136	-2.6	3.1	88	-1.9	3.1	0.07
Walking ability	136	-2.4	3.6	86	-1.7	3.6	0.15
Normal work	138	-2.7	3.6	86	-1.7	3.6	0.04
Relations with others	139	-1.8	2.9	85	-1.1	2.9	0.07
Sleeping	139	-2.4	3.2	86	-1.7	3.2	0.09
Enjoyment of life	138	-2.4	3.3	84	-1.5	3.3	0.03
EORTC QLQ-C30							
Physical functioning	107	6.5	19.1	65	7.2	19.1	0.81
Role functioning	107	12.8	28.7	65	5.6	28.7	0.14
Emotional functioning	101	9.5	20.8	65	8.6	20.8	0.78
Cognitive functioning	105	4.8	19.7	65	5.9	19.7	0.71
Social functioning	105	7.6	26.3	64	6.3	26.3	0.76
Fatigue	103	-7.8	26.6	65	-6.0	26.6	0.66
Nausea and vomiting	103	-2.9	20.1	65	-1.8	20.1	0.76
Pain	102	-28.8	26.1	63	-27.0	26.1	0.68
Dyspnea	107	1.9	30.7	64	2.1	30.7	0.96
Sleep	102	-19.3	34.3	65	-9.7	34.3	0.07
Appetite	103	-6.5	31.7	65	-4.6	31.7	0.72
Constipation	103	-7.8	32.1	63	-10.6	32.1	0.57
Diarrhea	102	5.6	23.0	65	7.7	23.0	0.57
Financial	104	-1.6	24.3	65	2.1	24.3	0.31
Global QOL	103	7.6	23.5	64	9.0	23.5	0.71

We thank all investigators, clinical research assistants and patients for participation in this study coordinated by the NCIC Clinical Trials Group. This study was supported by the NCIC CTG's programmatic grants from the Canadian Cancer Society Research Institute; the RTOG grant U10 CA21661 and CCOP grant U10 CA37422 from the National Cancer Institute in the US. Funding for Australia & New Zealand was from Cancer Council Australia (Grant for International Infrastructure Support) and Royal Adelaide Hospital (Special Purposes Fund Research Grant). The Dutch Cancer Society funded the national data management for Dutch patients (Dutch Cancer Society; CKTO 2004-06). Funding from the French investigators was from Assistance Publique-Hopitaux de Paris.