

July 24, 2014

**The impact of re-irradiation of painful osseous metastases on quality of life and function: A secondary analysis of the NCIC SC.20 randomized trial**

**Chow, et al**

**Appendix 1: Baseline data of patients included in the BPI analysis**

N= 471

<b>Treatment Arm</b>	
Single (8Gy)	233 (49.5)
Multiple(20Gy)	238 (50.5)
<b>Age (years)</b>	
Mean	65.2
Std	11.49
Median	65.6
<b>Gender</b>	
Female	200 (42.5)
Male	271 (57.5)
<b>Primary Malignancy</b>	
Prostate	141 (29.9)
Breast	140 (29.7)
Lung	89 (18.9)
Kidney	19 (4.0)
Colon	18 (3.8)
Esophageal	7 (1.5)
Other	34 (7.2)
Unknown	14 (3.0)
<b>Karnofsky Performance status</b>	
Unknown	4 (0.8)
50-60	83 (17.6)
70-80	260 (55.2)
90-100	124 (26.3)
<b>Worst Pain at Baseline</b>	
2-4	67 (14.3)
5-6	131 (27.8)
7-10	269 (57.2)
<b>Site of Painful Lesion</b>	
Head and Neck	1 (0.2)
Lower limbs	26 (5.5)
Upper limbs	39 (8.3)
Pelvis/Hips	169 (35.9)
Cervical spine	5 (1.1)
Cervicothoracic spine	8 (1.7)
Lumbosacral spine	86 (18.3)
Thoracic spine	47 (10.0)
Thoracolumbar spine	34 (7.2)
Superficial bones	56 (11.9)
<b>Reason for re-irradiation</b>	
Further pain relief desired	50 (10.6)
No Response	74 (15.7)
Pain returned	347 (73.7)
<b>Baseline OME (daily mg)</b>	
n	470
Mean	110
Std	272.3
Median	30

**Appendix 2: Baseline data of patients included in the QoL analysis**

N = 338

**Treatment Arm**

Single(8Gy)	170 (50.3)
Multiple(20Gy)	168 (49.7)

**Age (years)**

Mean	64.43
Std	11.63
Median	64.35

**Gender**

Female	151 (44.7)
Male	187 (55.3)

**Primary Malignancy**

Breast	107 (31.7)
Prostate	90 (26.6)
Lung	69 (20.4)
Kidney	11 (3.3)
Colon	14 (4.1)
Esophageal	7 (2.1)
Rectum	4 (1.2)
Other	16 (4.8)
Unknown	10 (3.0)

**Karnofsky performance status**

Unknown	4 (1.2)
50-60	53 (15.6)
70-80	186 (55.1)
90-100	95 (28.1)

**Worst Pain at Baseline**

2-4	48 (14.2)
5-6	98 (29.0)
7-10	189 (55.9)

**Site of Painful Bone Lesion**

Pelvis/Hips	125 (37.0)
Lumbosacral spine	60 (17.8)
Superficial bones	43 (12.7)
Thoracic spine	33 (9.8)
Upper limbs	27 (8.0)
Lower limbs	21 (6.2)
Thoracolumbar spine	21 (6.2)
Cervical spine	4 (1.2)
Cervicothoracic spine	4 (1.2)

**Reason for re-irradiation**

Further pain relief desired	33 (9.8)
No Response	68 (20.1)
Pain returned	237 (70.1)

**Baseline OME (daily mg)**

n	338
Mean	119.1
Std	305.1
Median	34.5

**Appendix 3: BPI-PS Pain score only as criteria for response****Table 1: Baseline BPI (scale 0-10) in responders and non-responders**

Domain/Item	Responders			Non-Responders			P value
	N	Mean	SD	N	Mean	SD	
General Activity	336	5.7	2.8	183	5.7	2.7	0.85
Mood	335	4.3	3.0	183	4.3	2.7	0.93
Walking Ability	335	5.5	3.2	181	5.4	3.3	0.94
Normal Work	337	6.0	3.0	178	6.2	2.9	0.65
Relations with Other People	337	3.2	3.0	182	3.1	3.0	0.60
Sleep	337	4.2	3.1	182	4.1	3.0	0.68
Enjoyment of Life	335	4.9	3.2	182	5.3	3.1	0.15

**Table 2: Change of BPI (scale 0-10) in responders and non-responders at 2 months**

Domain/Item	Responders				Non-Responders				p-value
	N	Mean	SD	95% CI	N	Mean	SD	95% CI	
General Activity	325	-2.6	3.3	(-2.91, -2.19)	182	0.4	2.7	(0.04, 0.82)	P < 0.0001
Mood	324	-2.0	3.3	(-2.39, -1.68)	181	0.2	3.2	(-0.3, 0.64)	P < 0.0001
Walking Ability	327	-2.0	3.5	(-2.37, -1.62)	179	0.4	3.0	(0, 0.88)	P < 0.0001
Normal Work	325	-2.1	3.6	(-2.46, -1.67)	176	0.2	2.9	(-0.2, 0.66)	P < 0.0001
Relations With Other People	327	-1.4	3.0	(-1.74, -1.09)	180	0.7	3.2	(0.24, 1.19)	P < 0.0001
Sleep	328	-2.1	3.3	(-2.44, -1.73)	182	-0.2	3.2	(-0.69, 0.25)	P < 0.0001
Enjoyment of Life	323	-1.8	3.3	(-2.18, -1.46)	178	0.2	3.5	(-0.29, 0.74)	P < 0.0001

**Table 3: BPI/Response proportion in responders and non-responders at 2 months**

Domain/Item	Responder		Non-Responder		Chisq-p
	BPI change $\leq$ -2		BPI change $\leq$ -2		
	Yes N (%)	No N (%)	Yes N (%)	No N (%)	
General Activity	189 (58)	136 (42)	38 (21)	144 (79)	<0.0001
Mood	166 (51)	158 (49)	58 (32)	123 (68)	<0.0001
Walking Ability	180 (55)	147 (45)	46 (26)	133 (74)	<0.0001
Normal Work	173 (53)	152 (47)	39 (22)	137 (78)	<0.0001
Relations with other people	140 (43)	187 (57)	35 (19)	145 (81)	<0.0001
Sleep	165 (50)	163 (50)	63 (35)	119 (65)	0.0006
Enjoyment of Life	164 (51)	159 (49)	52 (29)	126 (71)	<0.0001

**Table 4: Baseline EORTC QLQ-C30 in responders and non-responders**

Domain/Item	N	Responders		Non-Responders			P value
		Mean	SD	N	Mean	SD	
Physical Functioning	238	53.1	22.2	130	51.1	23.6	0.27
Role Functioning	238	44.0	31.0	130	41.7	31.1	0.50
Emotional Functioning	234	66.9	22.4	127	63.1	25.0	0.22
Cognitive Functioning	237	74.5	23.7	130	70.9	24.7	0.16
Social Functioning	235	62.1	30.4	129	58.3	31.9	0.31
Fatigue	235	50.7	25.6	129	50.9	26.0	0.84
Nausea and Vomiting	235	13.9	21.6	129	11.8	19.4	0.65
Pain	233	65.9	23.7	129	67.1	23.1	0.59
Dyspnea	238	26.6	30.3	130	29.2	30.5	0.37
Sleep	235	41.7	33.6	129	42.4	31.4	0.71
Appetite	235	29.4	33.5	129	28.2	30.5	0.99
Constipation	234	28.1	32.6	129	34.1	35.0	0.11
Diarrhea	235	7.2	17.7	129	7.8	19.8	0.98
Financial	235	18.2	30.4	129	22.0	32.7	0.26
Global QOL	235	49.7	21.1	128	48.0	19.4	0.42

**Table 5: Change of EORTC QLQ-C30 in responders and non-responders at 2 months**

Domain/Item	Responders				Non-Responders				p-value
	N	Mean	SD	95% CI	N	Mean	SD	95% CI	
Physical Functioning	237	3.7	19.6	(1.16, 6.16)	130	-4.7	20.5	(-8.19, -1.14)	P < 0.0001
Role Functioning	237	5.9	31.0	(1.96, 9.86)	130	-5.3	31.7	(-10.71, 0.2)	P = 0.0008
Emotional Functioning	232	6.2	22.9	(3.28, 9.17)	126	-0.3	24.3	(-4.58, 3.91)	P = 0.03
Cognitive Functioning	235	3.8	22.6	(0.94, 6.72)	130	-2.3	23.6	(-6.37, 1.76)	P = 0.03
Social Functioning	233	4.6	29.8	(0.75, 8.4)	127	-3.7	28.7	(-8.67, 1.32)	P = 0.02
Fatigue	234	-4.2	26.8	(-7.61, -0.75)	128	4.1	22.1	(0.25, 7.91)	P = 0.004
Nausea and Vomiting	233	-1.1	25.8	(-4.45, 2.17)	128	1.3	23.5	(-2.51, 5.64)	P = 0.3
Pain	230	-24.1	29.3	(-27.85, -20.27)	124	-2.3	25.4	(-6.76, 2.19)	P < 0.0001
Dyspnea	236	1.3	30.2	(-2.58, 5.12)	129	2.3	29.1	(-2.43, 7.6)	P = 0.6
Sleep	233	-15.0	37.2	(-19.8, -10.24)	129	-4.4	28.7	(-9.34, 0.56)	P = 0.004
Appetite	234	-2.7	37.9	(-7.56, 2.15)	128	4.2	32.4	(-1.45, 9.78)	P = 0.1
Constipation	232	-6.2	32.6	(-10.37, -1.98)	126	-4.2	26.8	(-10.65, 2.18)	P = 0.7
Diarrhea	233	3.9	26.1	(0.52, 7.21)	128	6.5	25.1	(2.16, 10.86)	P = 0.5
Financial	233	-1.6	24.0	(-4.66, 1.51)	128	3.9	21.2	(0.24, 7.57)	P = 0.08
Global QOL	229	4.9	24.2	(1.81, 8.09)	125	-3.7	22.4	(-7.59, 0.26)	P = 0.0006

**Table 6: QOL/Response proportion in responders and non-responders at 2 months**

Domain/Item	Responders		Non-Responders		Chisq-p
	QOL change $\geq$ 10		QOL change $\geq$ 10		
	Yes N (%)	No N (%)	Yes N (%)	No N (%)	
Physical Functioning	83 (35)	154 (65)	26 (20)	104 (80)	0.0026
Role Functioning	105 (44)	132 (56)	36 (28)	94 (72)	0.0018
Emotional Functioning	88 (38)	144 (62)	35 (28)	91(72)	0.0534
Cognitive Functioning	89 (38)	146 (62)	41 (32)	89 (68)	0.2262
Social Functioning	88 (38)	145 (62)	44 (35)	83 (65)	0.5569
Global QOL	83 (36)	146 (64)	27 (22)	98 (78)	0.0044

  

Domain/Item	QOL change $\geq$ 10		QOL change $\geq$ 10		Chisq-p
	QOL change $\geq$ 10		QOL change $\geq$ 10		
	Yes N (%)	No N (%)	Yes N (%)	No N (%)	
Fatigue	102 (44)	132 (56)	37 (29)	91 (71)	0.0060
Nausea	61 (26)	172 (74)	31 (24)	97 (76)	0.6824
Pain	166 (72)	64 (28)	47 (38)	77 (62)	<0.0001
Dyspnea	47 (20)	189 (80)	25 (19)	104 (81)	0.9022
Sleep	102 (44)	131 (56)	40 (31)	89 (69)	0.0172
Appetite	67 (29)	167 (71)	26 (20)	102 (80)	0.0833
Constipation	71 (31)	161 (69)	38 (30)	88 (70)	0.9304
Diarrhea	22 (9)	211 (91)	10 (8)	118 (92)	0.6023
Financial	33 (14)	200 (86)	12 (9)	116 (91)	0.1877

**Table 7: Left panel: difference in BPI scores between ICE responders and pain score only responders. Right panel: difference in scores between ICE non-responders and pain score only non-responders.**

Domain/Item	Responders*			Non-Responders		
	Mean	95% CI	p-value	Mean	95% CI	p-value
General Activity	-0.2	(-0.47, 0.07)	0.14	-0.7	(-1.05, -0.38)	p<0.0001
Mood	-0.3	(-0.57, -0.001)	0.05	-0.5	(-0.87, -0.16)	0.004
Walking Ability	-0.2	(-0.46, 0.11)	0.24	-0.6	(-0.95, -0.23)	0.001
Normal Work	-0.3	(-0.56, 0.03)	0.08	-0.5	(-0.92, -0.17)	0.005
Relations with Other People	-0.2	(-0.42, 0.12)	0.28	-0.5	(-0.86, -0.17)	0.003
Sleep	-0.02	(-0.31, 0.27)	0.89	-0.6	(-0.95, -0.23)	0.001
Enjoyment of Life	-0.2	(-0.54, 0.05)	0.11	-0.4	(-0.79, -0.05)	0.03

\* Note: Difference of BPI/QoL between ICE and pain score only was calculated using a weighted average of the 6 patient groups: A: pain score responders and ICE responders, B: pain score responders and ICE non-responders, C: pain score non-responders and ICE responders, D: pain score non-responders and ICE non-responders, E: pain score responders and ICE missing, F: pain score non-responders and ICE missing. The corresponding 95% C.I and p-value were based on the generalized linear models.

**Table 8: Left panel: difference in QoL scores between ICE responders and pain score only responders. Right panel: difference in scores between ICE non-responders and pain only non-responders.**

Domain/Item	Responders			Non-Responders		
	Mean	95% CI	p-value	Mean	95% CI	p-value
Physical Functioning	3.1	(1.17, 5.11)	0.002	-1.2	(-3.76, 1.32)	0.3
Role Functioning	4.2	(1.04, 7.30)	0.009	0.004	(-4.03, 4.03)	0.998
Emotional Functioning	2.9	(0.54, 5.35)	0.02	-0.48	(-3.56, 2.61)	0.7
Cognitive Functioning	1.4	(-0.99, 3.72)	0.26	0.3	(-2.71, 3.29)	0.9
Social Functioning	2.5	(-0.45, 5.50)	0.1	0.4	(-3.48, 4.24)	0.8
Fatigue	-2.9	(-5.47, -0.33)	0.03	0.5	(-2.76, 3.81)	0.8
Nausea and Vomiting	-1.3	(-3.90, 1.23)	0.3	0.6	(-2.71, 3.85)	0.7
Pain	-4.0	(-6.85, -1.20)	0.005	-2.3	(-5.92, 1.32)	0.2
Dyspnea	0.7	(-2.37, 3.73)	0.7	-0.8	(-4.69, 3.18)	0.7
Sleep	-0.5	(-4.11, 3.02)	0.8	-2.1	(-6.57, 2.42)	0.4
Appetite	-3.0	(-6.73, 0.64)	0.1	2.3	(-2.36, 7.04)	0.3
Constipation	-2.7	(-6.19, 0.88)	0.14	2.2	(-2.30, 6.68)	0.3
Diarrhea	2.5	(-0.12, 5.17)	0.06	-1.8	(-5.20, 1.53)	0.3
Financial	1.4	(-0.97, 3.72)	0.25	-1.0	(-4.04, 1.99)	0.5
Global QOL	3.2	(0.79, 5.58)	0.01	-1.0	(-4.13, 2.13)	0.5