# Efficacy of single fraction conventional radiation therapy for painful uncomplicated bone metastases: a systematic review

Ronald Chow<sup>1</sup>, Peter Hoskin<sup>2</sup>, Drew Hollenberg<sup>1</sup>, Michael Lam<sup>1</sup>, Kristopher Dennis<sup>3</sup>, Stephen Lutz<sup>4</sup>, Henry Lam<sup>1</sup>, Aruz Mesci<sup>1</sup>, Carlo DeAngelis<sup>1</sup>, Stephanie Chan<sup>1</sup>, Edward Chow<sup>1</sup>

<sup>1</sup>Sunnybrook Odette Cancer Centre, Toronto, Canada <sup>2</sup>Mount Vernon Hospital, Imperial College, London, United Kingdom <sup>3</sup>The Ottawa Hospital, University of Ottawa, Ottawa, Canada & Sunnybrook Radiation Oncology OF Offawa Hospital, Oniversity of Offama, Offama, Offama, Offama, Offama, Offama, USA UNIVERSITY OF TORONTO <sup>4</sup>Blanchard Valley Regional Cancer Center, Findlay, USA

## Objective

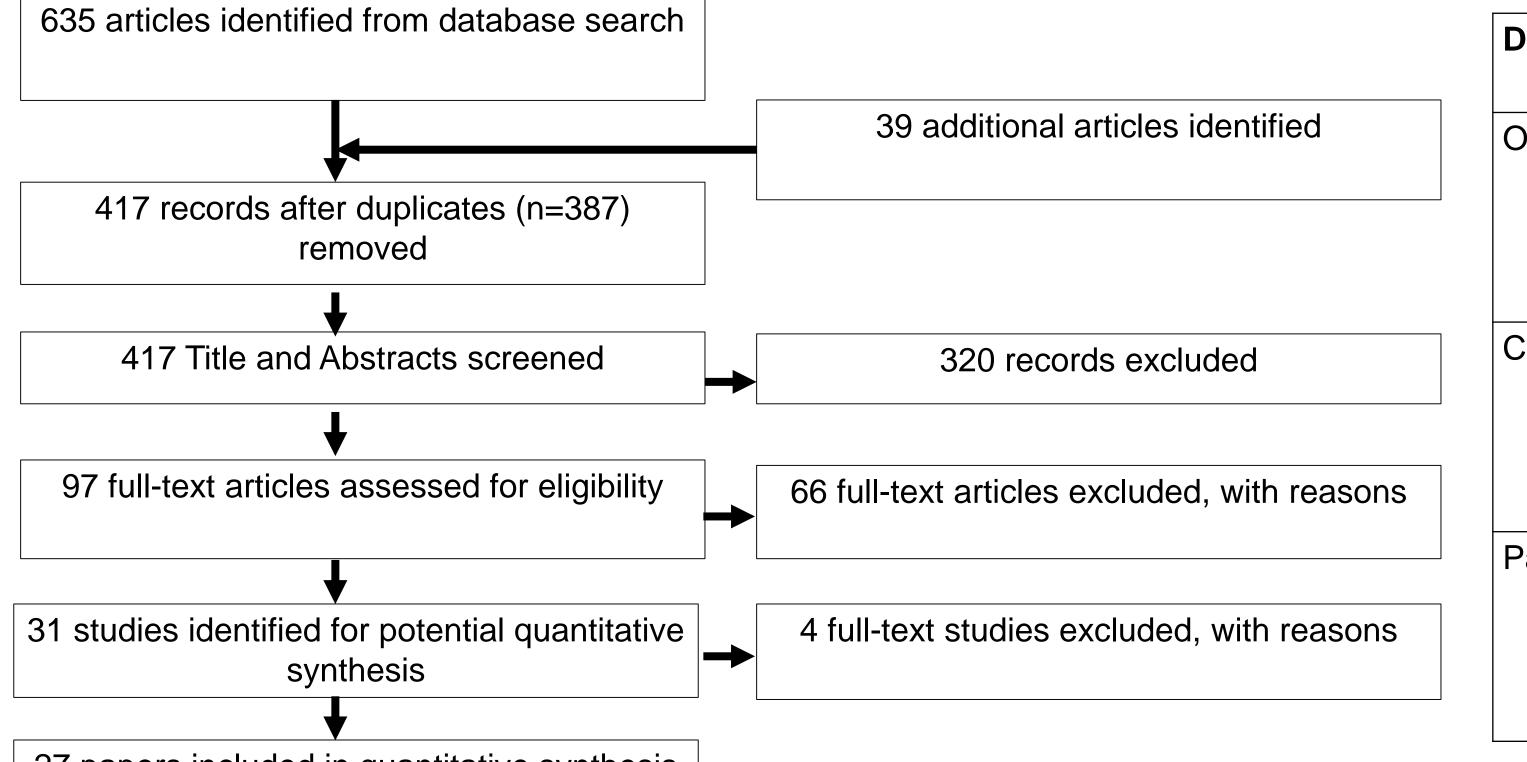
### Methods

- Portray pain response rates for single fraction radiation
  - therapy (SFRT)
- A literature search was conducted in Ovid MEDLINE(R) <1946 to June 2015 Week 3>, Embase Classic & Embase <1947 to 2016 Week 26> and Cochrane Central Register of Controlled Trials <May 2016>
- References were included if they reported outcomes of SFRT administered for the first time
- When possible, partial response (PR), complete response (CR) and overall response (OR) rates were noted under the analysis of both Intention-To-Treat (ITT) and Evaluable Patients (EP)



### Results

#### **PRISMA Flow Diagram**



#### Pain Response by Dose

Dose	Response Rate				
	ITT	EP			
Overall Response					
4Gy	322/598 (54%)	322/488 (66%)			
6Gy	274/369 (74%)	274/340 (81%)			
8Gy	1807/3006 (60%)	1807/2500 (72%)			
10Gy	108/134 (81%)	108/129 (84%)			
Complete Response					
4Gy	128/598 (21%)	129/488 (26%)			
6Gy	112/369 (30%)	112/340 (33%)			
8Gy	659/2970 (22%)	649/2433 (27%)			
10Gy	50/134 (37%)	50/129 (39%)			
Partial Response					
4Gy	193/598 (32%)	193/488 (40%)			
6Gy	162/369 (44%)	162/340 (48%)			
8Gy	1120/2970 (38%)	1120/2466 (45%)			
10Ġy	58/134 (43%)	58/129 (45%)			

27 papers included in quantitative synthesis (meta-analysis)

Study	Dose	Pain Assessment					Pain Response Rates			
		ΤοοΙ	Response		OR		CR		PR	
					ITT	EP	ITT	EP	ITT	EP
Amouzegar-	8Gy	4-point numerical	1 month	CR: pain reduction of 2 grades or more	21/36	21/27	6/36	6/27	15/36	15/27
Hashemia et al		scale		PR: pain reduction of 1 grade or more but less than 2 grades	(58%)	(78%)	(17%)	(22%)	(42%)	(56%)
2008										
Anter 2015	8Gy	Numeric Rating	3 months	CR: no pain 3 months after RT	33/51	33/44	8/51	8/44	25/51	25/44
		Scale		PR: at least 2 points lower than baseline	(65%)	(75%)	(16%)	(18%)	(49%)	(57%)
Badzio et al	8Gy	4-point pain	4 weeks	CR: complete disappearance of pain and withdrawal of analgesic drugs	53/72	53/64	23/72	23/64	30/72	30/64
2003		intensity scale		PR: decrease in pain score or decrease in dose of analgesic drug	(74%)	(83%)	(32%)	(36%)	(42%)	(47%)
Bayard et al	8Gy	Visual Analog	1 month	CR: no pain	35/45	35/45	7/45	7/45	28/45	28/45
2014		Score		PR: decrease in pain score	(78%)	(78%)	(16%)	(16%)	(62%)	(62%)
Berwouts et al	8Gy	Visual Analog	1 month	CR: no pain with no increase in daily oral morphine equivalent	8/15	8/14	2/15	2/14	6/15 (40%)	6/14
2015	Score		PR: score reduction of 2 or more, and no increase in daily oral morphine	(53%)	(57%)	(13%)	(14%)		(43%)	
				equivalent						
Bone Pain Trial	8Gy	Pain	1 month	CR: no pain	282/383	282/351	92/383	92/351	190/383	190/351
Working Party		Questionnaire		PR: lesser degree of pain	(74%)	(80%)	(24%)	(26%)	(50%)	(54%)
1999										
Cole 1989	8Gy	Physician consult	6 months	N/A	13/16	13/14	N/A	N/A	N/A	N/A
		and patient diary			(81%)	(93%)				
Foro Arnalot et 8Gy	8Gy	Ordinal pain scale	3 weeks	CR: absence of pain without need for increasing analgesia	59/78	59/76	12/78	12/76	47/78	47/76
al 2008 Gaze et al 1997 10Gy	-			PR: improvement of equal or greater than 2 on scale with no need for	(76%)	(78%)	(15%)	(16%)	(60%)	(62%)
				increasing analgesia						· · · ·
	Five-point	1 month	CR: complete pain relief	108/134	108/129	50/134	50/129	58/134	58/129	
	1009	categorical scale		PR: decrease in pain score	(81%)	(84%)	(37%)	(39%)	(43%)	(45%)
Guden et al	66.	11-point scale	4 weeks	CR: no pain	55/62	55/62	23/62	23/62	32/62	32/62
2002	UCy			PR: decrease in pain by at least 4 points	(89%)	(89%)	(37%)	(37%)	(52%)	(52%)
Hartsell et al	8Gy	Brief Pain	3 months	CR: no pain	187/455	187/288	44/455	44/288	143/455	143/288
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2005	<u> </u>	Inventory	1 month	PR: at least 2 points lower than initial response	(41%)	(65%)	(10%)	(15%)	(31%)	(50%)
Hayashi et al	8Gy	11-point scale	1 month	CR: absence of pain without need for increasing analgesics	9/12	9/12	2/12	2/12	7/12	7/12
2014				PR: improvement of equal or greater than 2 on pain scale without need for	(75%)	(75%)	(17%)	(17%)	(58%)	(58%)
				increasing analgesia, or decrease in analgesia		/= _	/			
Hoskin et al	4Gy	4-point	4 weeks	CR: no pain	75/137	75/98	25/137	25/98	50/137	50/98
1992		categorical pain		PR: improvement in pain score by at least one category	(55%)	(77%)	(18%)	(26%)	(37%)	(51%)
	8Gy	scale			94/133	94/96	22/133	22/96	72/133	72/96
					(71%)	(98%)	(17%)	(23%)	(54%)	(75%)
Hoskin et al	4Gy	4-point	4 weeks	CR: no pain	186/326	186/260	87/326	87/260	99/326	99/260
2015 8Gy		categorical pain		PR: improvement in pain score by at least one category	(57%)	(72%)	(27%)	(33%)	(30%)	(38%)
	scale			227/325	227/274	95/325	95/274	132/325	132/274	
					(70%)	(83%)	(29%)	(35%)	(41%)	(48%)
Jeremic et al	4Gy	4-point	4 weeks	CR: complete disappearance of pain	51/109	51/109	16/109	16/109	35/109	35/109
1998		categorical pain		PR: improvement in pain score by at least one category	(47%)	(47%)	(15%)	(15%)	(32%)	(32%)
	6Gy	scale			70/108	70/108	23/108	23/108	47/108	47/108
8					(65%)	(65%)	(21%)	(21%)	(44%)	(44%)
	8Gy				81/110	81/110	28/110	28/110	53/110	53/110
	-				(74%)	(74%)	(25%)	(25%)	(48%)	(48%)
Majumder et al	8Gy	Visual Analog	1 month	CR: no pain	24/31	24/27	3/31	3/27	21/31	21/27
2012		Scale		PR: reduction of 2 or more points without analgesic increase	(77%)	(89%)	(10%)	(11%)	(68%)	(78%)
Nielson et al	8Gy	Visual Analog	4 weeks	CR: absence of pain	60/120	60/106	11/120	11/106	49/120	49/106
	- 1	e e		PR: improvement of at least one-category	(50%)	(57%)	(9%)	(10%)	(41%)	(46%)
1998		Scale					\~``\		51/248	• •
1998 Nuzzo et al	8Gv	Scale Visual Analog	3 weeks				58/248	<u>אאר אאר</u>		J1//48
Nuzzo et al	8Gy	Visual Analog	3 weeks	CR: no pain with no associated increase in daily oral morphine equivalent	109/248	109/248	58/248 (23%)	58/248		51/248 (21%)
	8Gy		3 weeks	CR: no pain with no associated increase in daily oral morphine equivalent PR: reduction of 2 or more on pain score without change in daily oral			58/248 (23%)	(23%)	(21%)	(21%)
Nuzzo et al	8Gy	Visual Analog	3 weeks	CR: no pain with no associated increase in daily oral morphine equivalent PR: reduction of 2 or more on pain score without change in daily oral morphine, or no change in score and increase in daily oral morphine of at	109/248	109/248	-	-		-
Nuzzo et al 2015	,	Visual Analog Scale		CR: no pain with no associated increase in daily oral morphine equivalent PR: reduction of 2 or more on pain score without change in daily oral morphine, or no change in score and increase in daily oral morphine of at least 25%	109/248 (44%)	109/248 (44%)	(23%)	(23%)	(21%)	(21%)
Nuzzo et al	8Gy 8Gy	Visual Analog		CR: no pain with no associated increase in daily oral morphine equivalent PR: reduction of 2 or more on pain score without change in daily oral morphine, or no change in score and increase in daily oral morphine of at least 25% CR: complete loss of pain	109/248 (44%) 33/140	109/248 (44%) 33/49	(23%) 13/140	(23%) 13/49	(21%) 20/140	(21%) 20/49
Nuzzo et al 2015 Price et al 1986	, 8Gy	Visual Analog Scale 4-point pain scale	28 days	CR: no pain with no associated increase in daily oral morphine equivalent PR: reduction of 2 or more on pain score without change in daily oral morphine, or no change in score and increase in daily oral morphine of at least 25% CR: complete loss of pain PR: reduced pain	109/248 (44%) 33/140 (24%)	109/248 (44%) 33/49 (67%)	(23%) 13/140 (9%)	(23%) 13/49 (27%)	(21%) 20/140 (14%)	(21%) 20/49 (41%)
Nuzzo et al 2015	,	Visual Analog Scale	28 days	CR: no pain with no associated increase in daily oral morphine equivalent PR: reduction of 2 or more on pain score without change in daily oral morphine, or no change in score and increase in daily oral morphine of at least 25% CR: complete loss of pain PR: reduced pain CR: no pain	109/248 (44%) 33/140 (24%) 10/26	109/248 (44%) 33/49 (67%) 10/21	(23%) 13/140 (9%) 1/26	(23%) 13/49 (27%) 1/21	(21%) 20/140 (14%) 9/26	(21%) 20/49 (41%) 9/21
Nuzzo et al 2015 Price et al 1986 Price et al 1988	, 8Gy 4Gy	Visual Analog Scale 4-point pain scale 4-point pain scale	28 days 2 months	CR: no pain with no associated increase in daily oral morphine equivalent PR: reduction of 2 or more on pain score without change in daily oral morphine, or no change in score and increase in daily oral morphine of at least 25% CR: complete loss of pain PR: reduced pain CR: no pain PR: improvement in pain score by at least one category	109/248 (44%) 33/140 (24%) 10/26 (38%)	109/248 (44%) 33/49 (67%) 10/21 (48%)	(23%) 13/140 (9%) 1/26 (4%)	(23%) 13/49 (27%) 1/21 (5%)	(21%) 20/140 (14%) 9/26 (35%)	(21%) 20/49 (41%) 9/21 (43%)
Nuzzo et al 2015 Price et al 1986	, 8Gy	Visual Analog Scale 4-point pain scale 4-point pain scale 4-point	28 days	CR: no pain with no associated increase in daily oral morphine equivalent PR: reduction of 2 or more on pain score without change in daily oral morphine, or no change in score and increase in daily oral morphine of at least 25% CR: complete loss of pain PR: reduced pain CR: no pain PR: improvement in pain score by at least one category CR: no pain with no analgesia or adjuvant analgesia	109/248 (44%) 33/140 (24%) 10/26 (38%) 73/137	109/248 (44%) 33/49 (67%) 10/21 (48%) 73/119	(23%) 13/140 (9%) 1/26 (4%) 35/137	(23%) 13/49 (27%) 1/21 (5%) 35/119	(21%) 20/140 (14%) 9/26 (35%) 38/137	(21%) 20/49 (41%) 9/21 (43%) 38/119
Nuzzo et al 2015 Price et al 1986 Price et al 1988	, 8Gy 4Gy	Visual Analog Scale 4-point pain scale 4-point pain scale 4-point categorical pain	28 days 2 months	CR: no pain with no associated increase in daily oral morphine equivalent PR: reduction of 2 or more on pain score without change in daily oral morphine, or no change in score and increase in daily oral morphine of at least 25% CR: complete loss of pain PR: reduced pain CR: no pain PR: improvement in pain score by at least one category CR: no pain with no analgesia or adjuvant analgesia PR: improvement in pain score by at least one grade with no increase in	109/248 (44%) 33/140 (24%) 10/26 (38%)	109/248 (44%) 33/49 (67%) 10/21 (48%)	(23%) 13/140 (9%) 1/26 (4%)	(23%) 13/49 (27%) 1/21 (5%)	(21%) 20/140 (14%) 9/26 (35%)	(21%) 20/49 (41%) 9/21 (43%)
Nuzzo et al 2015 Price et al 1986 Price et al 1988 Roos et al 2005	, 8Gy 4Gy 8Gy	Visual Analog Scale 4-point pain scale 4-point pain scale 4-point categorical pain scale	28 days 2 months 4 weeks	CR: no pain with no associated increase in daily oral morphine equivalent PR: reduction of 2 or more on pain score without change in daily oral morphine, or no change in score and increase in daily oral morphine of at least 25% CR: complete loss of pain PR: reduced pain CR: no pain PR: improvement in pain score by at least one category CR: no pain with no analgesia or adjuvant analgesia PR: improvement in pain score by at least one grade with no increase in analgesia	109/248 (44%) 33/140 (24%) 10/26 (38%) 73/137 (53%)	109/248 (44%) 33/49 (67%) 10/21 (48%) 73/119 (61%)	(23%) 13/140 (9%) 1/26 (4%) 35/137 (26%)	(23%) 13/49 (27%) 1/21 (5%) 35/119 (29%)	(21%) 20/140 (14%) 9/26 (35%) 38/137 (28%)	(21%) 20/49 (41%) 9/21 (43%) 38/119 (32%)
Nuzzo et al 2015 Price et al 1986 Price et al 1988	, 8Gy 4Gy 8Gy	Visual Analog Scale 4-point pain scale 4-point pain scale 4-point categorical pain	28 days 2 months 4 weeks	CR: no pain with no associated increase in daily oral morphine equivalent PR: reduction of 2 or more on pain score without change in daily oral morphine, or no change in score and increase in daily oral morphine of at least 25% CR: complete loss of pain PR: reduced pain CR: no pain PR: improvement in pain score by at least one category CR: no pain with no analgesia or adjuvant analgesia PR: improvement in pain score by at least one grade with no increase in	109/248 (44%) 33/140 (24%) 10/26 (38%) 73/137	109/248 (44%) 33/49 (67%) 10/21 (48%) 73/119	(23%) 13/140 (9%) 1/26 (4%) 35/137	(23%) 13/49 (27%) 1/21 (5%) 35/119	(21%) 20/140 (14%) 9/26 (35%) 38/137	(21%) 20/49 (41%) 9/21 (43%) 38/119
Nuzzo et al 2015 Price et al 1986 Price et al 1988 Roos et al 2005	, 8Gy 4Gy 8Gy	Visual Analog Scale 4-point pain scale 4-point pain scale 4-point categorical pain scale	28 days 2 months 4 weeks	CR: no pain with no associated increase in daily oral morphine equivalent PR: reduction of 2 or more on pain score without change in daily oral morphine, or no change in score and increase in daily oral morphine of at least 25% CR: complete loss of pain PR: reduced pain CR: no pain PR: improvement in pain score by at least one category CR: no pain with no analgesia or adjuvant analgesia PR: improvement in pain score by at least one grade with no increase in analgesia	109/248 (44%) 33/140 (24%) 10/26 (38%) 73/137 (53%)	109/248 (44%) 33/49 (67%) 10/21 (48%) 73/119 (61%)	(23%) 13/140 (9%) 1/26 (4%) 35/137 (26%)	(23%) 13/49 (27%) 1/21 (5%) 35/119 (29%)	(21%) 20/140 (14%) 9/26 (35%) 38/137 (28%)	(21%) 20/49 (41%) 9/21 (43%) 38/119 (32%)
Nuzzo et al 2015 Price et al 1986 Price et al 1988 Roos et al 2005 Safwat et al	, 8Gy 4Gy 8Gy 8Gy	Visual Analog Scale 4-point pain scale 4-point pain scale 4-point categorical pain scale 5-point	28 days 2 months 4 weeks	CR: no pain with no associated increase in daily oral morphine equivalent PR: reduction of 2 or more on pain score without change in daily oral morphine, or no change in score and increase in daily oral morphine of at least 25% CR: complete loss of pain PR: reduced pain CR: no pain PR: improvement in pain score by at least one category CR: no pain with no analgesia or adjuvant analgesia PR: improvement in pain score by at least one grade with no increase in analgesia	109/248 (44%) 33/140 (24%) 10/26 (38%) 73/137 (53%) 14/20	109/248 (44%) 33/49 (67%) 10/21 (48%) 73/119 (61%) 14/20	(23%) 13/140 (9%) 1/26 (4%) 35/137 (26%)	(23%) 13/49 (27%) 1/21 (5%) 35/119 (29%)	(21%) 20/140 (14%) 9/26 (35%) 38/137 (28%)	(21%) 20/49 (41%) 9/21 (43%) 38/119 (32%)
Nuzzo et al 2015 Price et al 1986 Price et al 1988 Roos et al 2005 Safwat et al 2007	, 8Gy 4Gy 8Gy 8Gy	Visual Analog Scale 4-point pain scale 4-point pain scale 4-point categorical pain scale 5-point categorical scale	28 days 2 months 4 weeks 6 weeks	CR: no pain with no associated increase in daily oral morphine equivalent PR: reduction of 2 or more on pain score without change in daily oral morphine, or no change in score and increase in daily oral morphine of at least 25% CR: complete loss of pain PR: reduced pain CR: no pain PR: improvement in pain score by at least one category CR: no pain with no analgesia or adjuvant analgesia PR: improvement in pain score by at least one grade with no increase in analgesia N/A	109/248 (44%) 33/140 (24%) 10/26 (38%) 73/137 (53%) 14/20 (70%)	109/248 (44%) 33/49 (67%) 10/21 (48%) 73/119 (61%) 14/20 (70%)	(23%) 13/140 (9%) 1/26 (4%) 35/137 (26%) N/A	(23%) 13/49 (27%) 1/21 (5%) 35/119 (29%) N/A	(21%) 20/140 (14%) 9/26 (35%) 38/137 (28%) N/A	(21%) 20/49 (41%) 9/21 (43%) 38/119 (32%) N/A
Nuzzo et al 2015 Price et al 1986 Price et al 1988 Roos et al 2005 Safwat et al 2007 Steenland et al	, 8Gy 4Gy 8Gy 8Gy	Visual Analog Scale 4-point pain scale 4-point pain scale 4-point categorical pain scale 5-point categorical scale	28 days 2 months 4 weeks 6 weeks N/A	CR: no pain with no associated increase in daily oral morphine equivalent PR: reduction of 2 or more on pain score without change in daily oral morphine, or no change in score and increase in daily oral morphine of at least 25% CR: complete loss of pain PR: reduced pain CR: no pain PR: improvement in pain score by at least one category CR: no pain with no analgesia or adjuvant analgesia PR: improvement in pain score by at least one grade with no increase in analgesia N/A CR: 0 to 1 pain score, independent of analgesics consumption	109/248 (44%) 33/140 (24%) 10/26 (38%) 73/137 (53%) 14/20 (70%) 392/579	109/248 (44%) 33/49 (67%) 10/21 (48%) 73/119 (61%) 14/20 (70%) 392/545	(23%) 13/140 (9%) 1/26 (4%) 35/137 (26%) N/A 199/579	(23%) 13/49 (27%) 1/21 (5%) 35/119 (29%) N/A 199/545	(21%) 20/140 (14%) 9/26 (35%) 38/137 (28%) N/A 193/579	(21%) 20/49 (41%) 9/21 (43%) 38/119 (32%) N/A 193/545

#### Conclusions

• The most commonly administered 8Gy cannot decisively be determined as the optimal dose for pain relief, but the few head-to-head studies that compared 8Gy to 4Gy and 6Gy proved that it was more efficacious

We thank the generous support of Bratty Family Fund, Michael and Karyn Goldstein Cancer Research Fund, Joey and Mary Furfari Cancer Research Fund, Pulenzas Cancer Research Fund, Joseph and Silvana Melara Cancer Research Fund, and Ofelia Cancer Research Fund.