

**Neratinib + capecitabine sustains health-related quality of life while improving progression-free survival in patients with HER2-positive metastatic breast cancer and  $\geq 2$  prior HER2-directed regimens**

Breast Cancer Research and Treatment

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**Online Resource 1** Proportion of patients completing the EORTC QLQ-C30 summary score and QLQ-BR23 systemic therapy side effects scale at scheduled assessments

EORTC assessment	Patients completing, % (n/N)	
	N+C	L+C
<b>QLQ-C30 summary score</b>		
Baseline	100.0 (275/275)	100.0 (281/281)
Cycle 3	96.4 (265/275)	96.1 (270/281)
Cycle 5	84.0 (210/250)	84.6 (215/254)
Cycle 7	87.9 (181/206)	87.3 (178/204)
Cycle 9	83.1 (147/177)	81.0 (132/163)
Cycle 11	75.7 (112/148)	75.6 (90/119)
Cycle 13	83.2 (99/119)	76.2 (64/84)
Cycle 15	83.3 (80/96)	71.0 (44/62)
Cycle 17	88.6 (70/79)	78.0 (32/41)
Cycle 19	83.3 (55/66)	84.4 (27/32)
<b>QLQ-BR23 systemic therapy side effects</b>		
Baseline	100.0 (276/276)	100.0 (283/283)
Cycle 3	94.9 (262/276)	96.5 (273/283)
Cycle 5	83.7 (210/251)	85.2 (218/256)
Cycle 7	87.9 (182/207)	87.3 (179/205)
Cycle 9	84.3 (150/178)	81.1 (133/164)
Cycle 11	77.2 (115/149)	76.7 (92/120)
Cycle 13	83.3 (100/120)	75.0 (63/84)
Cycle 15	83.5 (81/97)	72.1 (44/61)
Cycle 17	88.8 (71/80)	77.5 (31/40)
Cycle 19	82.1 (55/67)	83.9 (26/31)

*EORTC* European Organization for Research and Treatment of Cancer, *L+C* lapatinib plus capecitabine, *N+C* neratinib plus capecitabine, *QLQ-BR23* Quality of Life Questionnaire Breast Cancer-Specific Module, *QLQ-C30* Quality of Life Questionnaire core module

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**Online Resource 2** Mixed-model analysis results (change from baseline)

	Overall Treatment Difference Estimate	p-value <sup>a</sup>
<b>QLQ-C30 Summary Score<sup>b</sup></b>		
Treatment (N+C vs. L+C)	0.59	0.5147
Visit <sup>c</sup>		0.0067
<b>Global health status scale</b>		
Treatment (N+C vs. L+C)	2.20	0.0923
Visit <sup>c</sup>		0.0360
<b>Physical functioning scale</b>		
Treatment (N+C vs. L+C)	0.77	0.5219
Visit <sup>c</sup>		0.1644
<b>Fatigue scale</b>		
Treatment (N+C vs. L+C) <sup>b</sup>		0.0144
Visit <sup>c</sup>		0.0893
Treatment Interaction with Visit <sup>c</sup>		0.0111
<b>Constipation scale</b>		
Treatment (N+C vs. L+C)	2.89	0.0291
Visit <sup>c</sup>		0.2208
<b>Diarrhea scale</b>		
Treatment (N+C vs. L+C)	9.30	<0.0001
Visit <sup>c</sup>		<0.0001
<b>BR23 systemic therapy side effects scale</b>		
Treatment (N+C vs. L+C)	-0.77	0.3805
Visit <sup>c</sup>		0.0021

<sup>a</sup> p-value is from type 3 test of fixed effect.

<sup>b</sup> Treatment effect is not meaningful in the presence of a significant interaction and is not shown.

<sup>c</sup> Visit or visit by treatment interaction effect is not the effect estimate of interest and is not shown.

*QLQ-BR23* Quality of Life Questionnaire Breast Cancer-Specific Module, *EORTC* European Organisation for Research and Treatment of Cancer, *L+C* lapatinib plus capecitabine, *N+C* neratinib plus capecitabine, *QLQ-C30* Quality of Life Questionnaire core module