

**Neoadjuvant metformin added to systemic therapy  
reduces the proliferative activity of breast cancer residual disease**

**SUPPLEMENTARY INFORMATION**

**Table S1. Association of the interaction between baseline Ki67 score and pCR by treatment arm**

	Non-pCR (N, %)	pCR (%)	OR (95% CI)	p-value	OR (95% CI)	p-value
<b>Ki67 VA</b>						
<20%	6 (66.67%)	3 (33.33%)	1		1	
≥20%	23 (37.30%)	38 (62.30%)	2.73 (0.39-18.88)	0.309	3.36 (0.76-14.82)	0.110
<b>Arm</b>						
B	14 (38.89%)	22 (61.12%)	1		1	
A	15 (44.12%)	19 (55.88%)	0.50 (0.03-8.95)	0.638	0.78 (0.29-2.06)	0.613
<b>Ki67*Arm</b>			1.65 (0.08-35.39)	0.749		
<b>Ki67 ADIA</b>						
<20%	8 (72.73%)	3 (27.27%)	1		1	
≥20%	21 (35.39%)	38 (64.41%)	5.73 (0.53-61.75)	0.150	4.76 (1.13-20.09)	0.034
<b>Arm</b>						
B	14 (38.89%)	22 (61.12%)	1		1	
A	15 (44.12%)	19 (55.88%)	1.20 (0.07-19.63)	0.898	0.93 (0.34-2.51)	0.879
<b>Ki67*Arm</b>			0.74 (0.04-14.79)	0.845		

**Table S2. Association of the interaction between baseline Ki67 score and pCR in the metformin-containing arm A**

	Non-pCR (N, %)	pCR (%)	OR (95% CI)	p-value
<b>Ki67 VA</b>				
<20%	3 (75.00%)	1 (25.00%)	1	
≥20%	12 (40.00%)	18 (60.00%)	4.50 (0.42-48.53)	0.215
<b>Ki67 ADIA</b>				
<20%	5 (71.43%)	2 (28.57%)	1	
≥20%	10 (37.04%)	17 (62.96%)	4.25 (0.69-26.13)	0.118

**Table S3. Association of the interaction between baseline Ki67 score and pCR in the control arm B**

	Non-pCR (N, %)	pCR (%)	OR (95% CI)	p-value
<b>Ki67 VA</b>				
<20%	3 (60.00%)	2 (40.00%)	1	
≥20%	11 (35.48%)	20 (64.52%)	2.73 (0.39-18.88)	0.309
<b>Ki67 ADIA</b>				
<20%	3 (75.00%)	1 (25.00%)	1	
≥20%	11 (34.38%)	21 (65.63%)	5.73 (0.53-61.75)	0.150

**Table S4. Association of the interaction between baseline Ki67 score and pCR by treatment arm adjusted by HR status**

	Non-pCR (N, %)	pCR (%)	OR (95% CI)	p-value	OR (95% CI)	p-value
<b>Ki67 VA</b>						
<20%	6 (66.67%)	3 (33.33%)	1		1	
≥20%	23 (37.30%)	38 (62.30%)	2.86 (0.40-20.25)	0.293	3.25 (0.72-14.60)	0.125
<b>Arm</b>						
B	14 (38.89%)	22 (61.12%)	1		1	
A	15 (44.12%)	19 (55.88%)	0.54 (0.03-9.97)	0.680	0.71 (0.26-1.93)	0.503
<b>Ki67*Arm</b>						
			1.36 (0.06-30.51)	0.845		
<i>HR</i>						
<i>ER and/or PR+</i>	19 (47.50%)	21 (52.50%)	1		1	
<i>ER and PR-</i>	10 (27.78%)	20 (66.67%)	1.81 (0.65-5.02)	0.253	1.83 (0.67-5.05)	0.242
<b>Ki67 ADIA</b>						
<20%	8 (72.73%)	3 (27.27%)	1		1	
≥20%	21 (35.39%)	38 (64.41%)	6.98 (0.61-80.01)	0.119	5.57 (1.26-24.74)	0.024
<b>Arm</b>						
B	14 (38.89%)	22 (61.12%)	1		1	
A	15 (44.12%)	19 (55.88%)	1.14 (0.07-19.96)	0.929	0.83 (0.30-2.11)	0.723
<b>Ki67*Arm</b>						
			0.70 (0.03-14.56)	0.815		
<i>HR</i>						
<i>ER and/or PR+</i>	19 (47.50%)	21 (52.50%)	1		1	
<i>ER and PR-</i>	10 (33.33%)	20 (66.67%)	2.28 (0.78-6.63)	0.131	2.21 (0.77-6.35)	0.140

**Table S5. Association of the interaction between baseline Ki67 score and pCR in the metformin-containing arm a adjusted by HR status**

	Non-pCR (N, %)	pCR (%)	OR (95% CI)	p-value
<b>Ki67 VA</b>				
<20%	3 (75.00%)	1 (25.00%)	1	
≥20%	12 (40.00%)	18 (60.00%)	3.90 (0.35-43.51)	0.269
<i>HR</i>				
<i>ER and/or PR+</i>	9 (52.94%)	8 (47.06%)	1	
<i>ER and PR-</i>	6 (35.29%)	11 (64.71%)	1.81 (0.03-7.46)	0.410
<b>Ki67 ADIA</b>				
<20%	5 (71.43%)	2 (28.57%)	1	
≥20%	10 (37.04%)	17 (62.96%)	4.94 (0.75-32.62)	0.097
<i>HR</i>				
<i>ER and/or PR+</i>	11 (57.89%)	8 (42.11%)	1	
<i>ER and PR-</i>	6 (31.58%)	13 (68.42%)	2.45 (0.56-10.69)	0.233

**Table S6. Association of the interaction between baseline Ki67 score and pCR in the control arm B adjusted by HR status**

	Non-pCR (N, %)	pCR (%)	OR (95% CI)	p-value
<b>Ki67 VA</b>				
<20%	3 (60.00%)	2 (40.00%)	1	
≥20%	11 (35.48%)	20 (64.52%)	2.86 (0.40-20.33)	0.294
<i>HR</i>				
<i>ER and/or PR+</i>	10 (43.48%)	13 (56.52%)	1	
<i>ER and PR-</i>	4 (30.77%)	9 (69.237%)	1.81 (0.42-7.87)	0.428
<b>Ki67 ADIA</b>				
<20%	3 (75.00%)	1 (25.00%)	1	
≥20%	11 (34.38%)	21 (65.63%)	6.80 (0.58-79.14)	0.126
<i>HR</i>				
<i>ER and/or PR+</i>	10 (41.67%)	14 (58.33%)	1	
<i>ER and PR-</i>	4 (23.53%)	13 (76.47%)	2.10 (0.45-9.84)	0.347