

## Supplementary Online Content

Salgado R, Denkert C, Campbell C, et al. Tumor-infiltrating lymphocytes and associations with pathological complete response and event-free survival in HER2-positive early-stage breast cancer treated with lapatinib and trastuzumab: a secondary analysis of the NeoALTTO Trial. *JAMA Oncol*. Published online April 30, 2015. doi:10.1001/jamaoncol.2015.0830

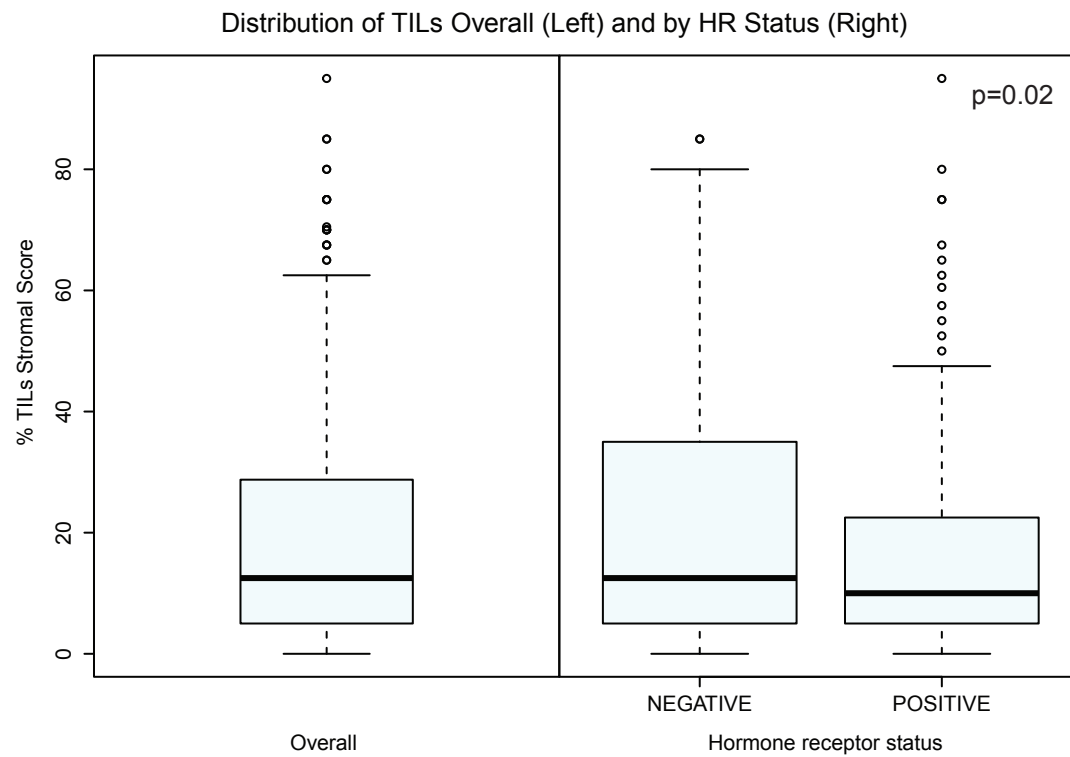
**eFigure 1.** Distribution of stromal TILs in whole cohort of HER2-positive primary breast cancer as well as according to HR status. P value represents a Mann-Whitney test.

**eFigure 2.** Cubic splines to explore the relationship between TILs and pCR and EFS. As seen, the relationship between TILs and pCR is not linear: rates of pCR increase sharply at TILs levels of 5% (A); however, is linear between TILs and EFS (B)

**eTable.** Multivariate analyses with lapatinib-only treatment arm

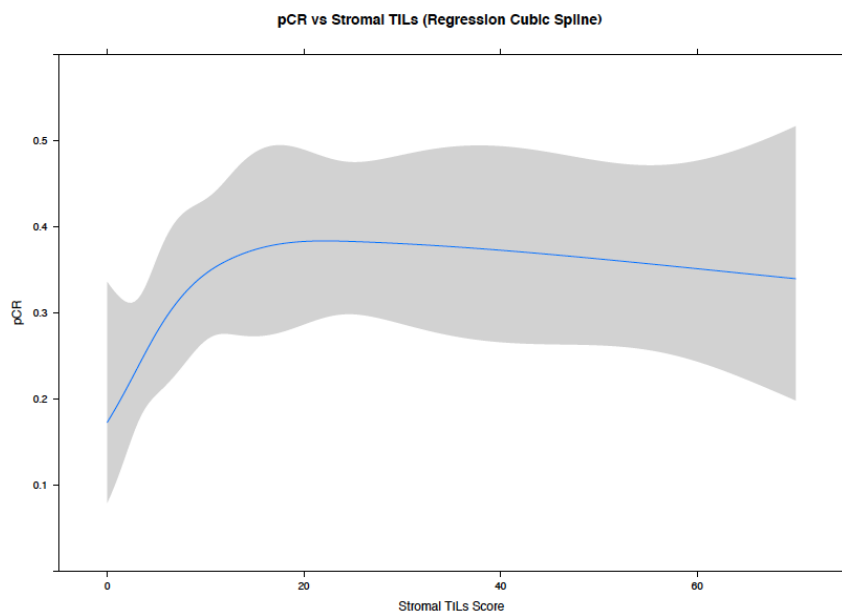
This supplementary material has been provided by the authors to give readers additional information about their work.

**eFigure 1.** Distribution of stromal TILs in whole cohort of HER2-positive primary breast cancer as well as according to HR status. P value represents a Mann-Whitney test.

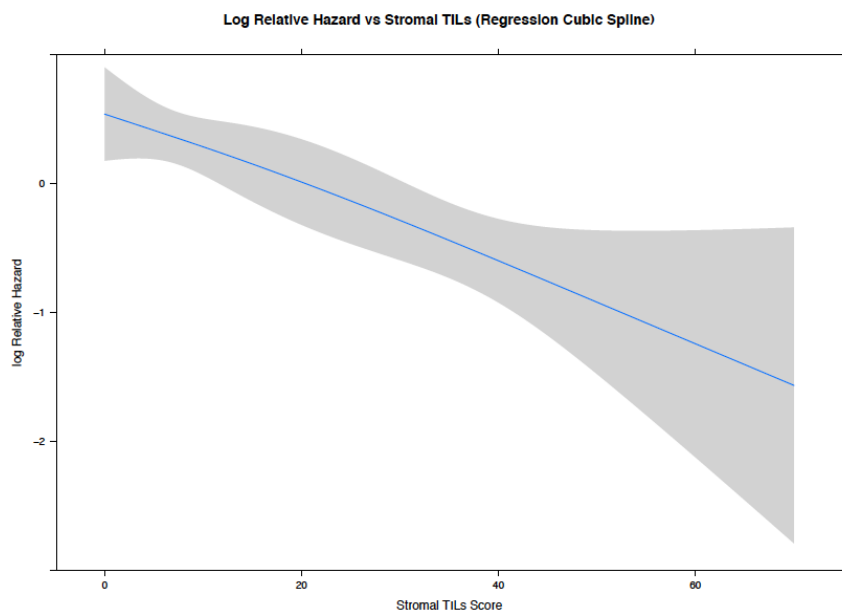


**eFigure 2.** Cubic splines to explore the relationship between TILs and pCR and EFS. As seen, the relationship between TILs and pCR is not linear: rates of pCR increase sharply at TILs levels of 5% (A); however, is linear between TILs and EFS (B)

**A**



**B**



**eTable. Multivariate analyses with lapatinib-only treatment arm****(A) Analysis without pCR (baseline characteristics) (n=387)**

<b>Multivariate Effect</b>	<b>Pvalue</b>	<b>Hazard Ratio</b>
Stromal TILs %	0.0001	HR: 0.97 (Per unit increase, 95% CI: 0.95-0.98)
Hormone Receptor Status	0.0679	HR: 0.68 (Ref = Negative, 95% CI: 0.44-1.03)
Nodal Status	0.2622	HR: 1.35 (Ref = N0/1, 95% CI: 0.77-2.25)
Tumour Size	0.587	HR: 1.13 (Ref = T2, 95% CI: 0.73-1.72)
Planned Conservative Surgery	0.0284	HR: 0.56 (Ref = Not a candidate, 95% CI: 0.32-0.92)
Treatment Lapatinib alone	0.1786	HR: 1.40 (Ref = Trastuzumab alone, 95% CI: 0.86-2.30)
Treatment combination	0.3643	HR: 0.78 (Ref = Trastuzumab alone, 95% CI: 0.45-1.33)

**(B) Landmark analyses including pCR (n=387)**

<b>Multivariate Effect</b>	<b>Pvalue</b>	<b>Hazard Ratio</b>
Stromal TILs %	0.0002	HR: 0.97 (Per unit increase, 95% CI: 0.96-0.99)
Hormone Receptor Status	0.0246	HR: 0.61 (Ref = Negative, 95% CI: 0.40-0.94)
Nodal Status	0.2229	HR: 1.39 (Ref = N0/1, 95% CI: 0.80-2.31)
Tumour Size	0.8521	HR: 1.04 (Ref = T2, 95% CI: 0.67-1.60)
Planned Conservative Surgery	0.0239	HR: 0.54 (Ref = Not a candidate, 95% CI: 0.31-0.90)
Treatment Lapatinib alone	0.1712	HR: 1.41 (Ref = Trastuzumab alone, 95% CI: 0.86-2.33)
Treatment combination	0.7122	HR: 0.90 (Ref = Trastuzumab alone, 95% CI: 0.51-1.55)
pCR	0.0018	HR: 0.42 (Ref = No pCR, 95% CI: 0.23-0.71)