Supplementary Materials for Floris *et al.* "Body mass index and tumor infiltrating lymphocytes in triple-negative breast cancer"

Supplementary Table 1. Patient and tumor characteristics according to the three BMI categories.

	All patients (n=445)	Lean (n=236)	Overweight (n=132)	Obese (n=77)	p-value
Age, categorical					
≤40 years	110 (24.7)	73 (30.9)	25 (18.9)	12 (15.6)	.006
41-50 years	128 (28.8)	70 (29.7)	40 (30.3)	18 (23.4)	
≥50 years	207 (46.5)	93 (39.4)	67 (50.8)	47 (61.0)	
Age, continuous					
Mean (SD)	49.4 (11.4)	47.3 (11.2)	51.6 (11.8)	52.2 (10)	<.001
Median (IQR)	49 (41-57)	46.5 (39-54)	51 (43-59.2)	53 (46-59)	
Range	25-84	25-84	27-79	32-76	
Menopausal status					
Pre	255 (58.2)	153 (66.2)	67 (51.1)	35 (46.1)	.001
Post	183 (41.8)	78 (33.8)	64 (48.9)	41 (53.9)	
Missing	7	5	1	1	
Tumor size (cT)					
cT1	46 (10.3)	34 (14.4)	7 (5.3)	5 (6.5)	.001
cT2	246 (55.3)	135 (57.2)	71 (53.8)	40 (51.9)	
cT3	108 (24.3)	55 (23.3)	38 (28.8)	15 (19.5)	
cT4a-c	13 (2.9)	4 (1.7)	4 (3.0)	5 (6.5)	
cT4d	32 (7.2)	8 (3.4)	12 (9.1)	12 (15.6)	
Nodal status (cN)					
cN0	182 (40.9)	97 (41.1)	47 (35.6)	38 (49.4)	.051
cN1	193 (43.4)	110 (46.6)	60 (45.5)	23 (29.9)	
cN2	23 (5.2)	12 (5.1)	6 (4.5)	5 (6.5)	
cN3	47 (10.6)	17 (7.2)	19 (14.4)	11 (14.3)	
Stage					
Stage I	19 (4.3)	15 (6.4)	2 (1.5)	2 (2.6)	.044
Stage II	268 (60.2)	149 (63.1)	73 (55.3)	46 (59.7)	
Stage III	158 (35.5)	72 (30.5)	57 (43.2)	29 (37.7)	
Histological grade					
Grade 1	2 (0.5)	2 (0.9)	0 (0.0)	0 (0.0)	.290
Grade 2	48 (10.9)	31 (13.4)	12 (9.2)	5 (6.5)	
Grade 3	390 (88.6)	199 (85.8)	119 (90.8)	72 (93.5)	
Missing	5	4	1	0	
sTIL, categorical					
<30%	346 (77.8)	184 (78.0)	97 (73.5)	65 (84.4)	.189
≥30%	99 (22.2)	52 (22.0)	35 (26.5)	12 (15.6)	
sTIL, continuous					
Mean (SD)	18.9 (20.5)	18.7 (20.7)	21 (20.3)	16.1 (20.5)	.018
Median (IQR)	11 (5-24)	11 (4.8-24.2)	13.3 (6.6-30)	8.3 (4-15)	
Range	0-90	0-88	0-90	0-83.3	
Neoadjuvant					

treatment					
Anthra	57 (12.8)	32 (13.6)	20 (15.2)	5 (6.5)	.361
Anthra-Tax	296 (66.5)	159 (67.4)	82 (62.1)	55 (71.4)	
Anthra-Tax-Carbo	52 (11.7)	27 (11.4)	14 (10.6)	11 (14.3)	
Other	40 (9)	18 (7.6)	16 (12.1)	6 (7.8)	
pCR (ypT0ypN0)					
No	264 (59.3)	131 (55.5)	84 (63.6)	49 (63.6)	.237
Yes	181 (40.7)	105 (44.5)	48 (36.4)	28 (36.4)	

The "n" denotes the number of patients. Percentages are expressed between brackets. P-values are from the Fisher exact test and Kruskal-Wallis test when comparing categorical and continuous variables against three categories BMI, respectively. IQR: interquartile range, SD: standard deviation.

Supplementary Figure 1. Study flow chart. BMI: body mass index, CP: clinic-pathological variables, EFS: event-free survival, H&E: hematoxylin and eosin, NACT: neoadjuvant chemotherapy, OS: overall survival, pCR: pathological complete response, sTIL: stromal tumor-infiltrating lymphocytes, TNBC: triple-negative breast cancer.
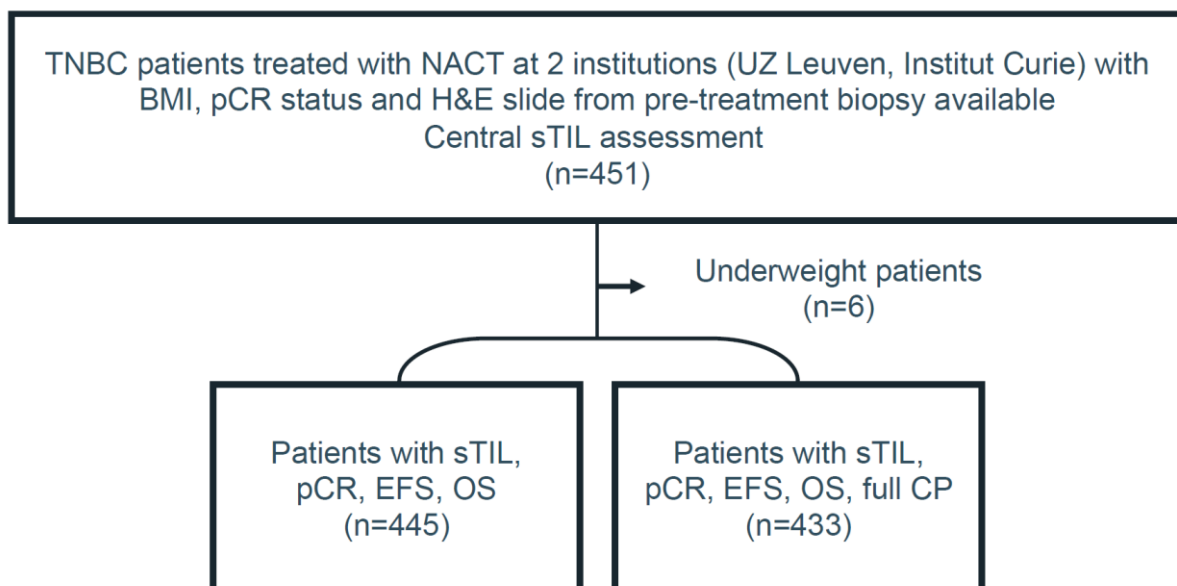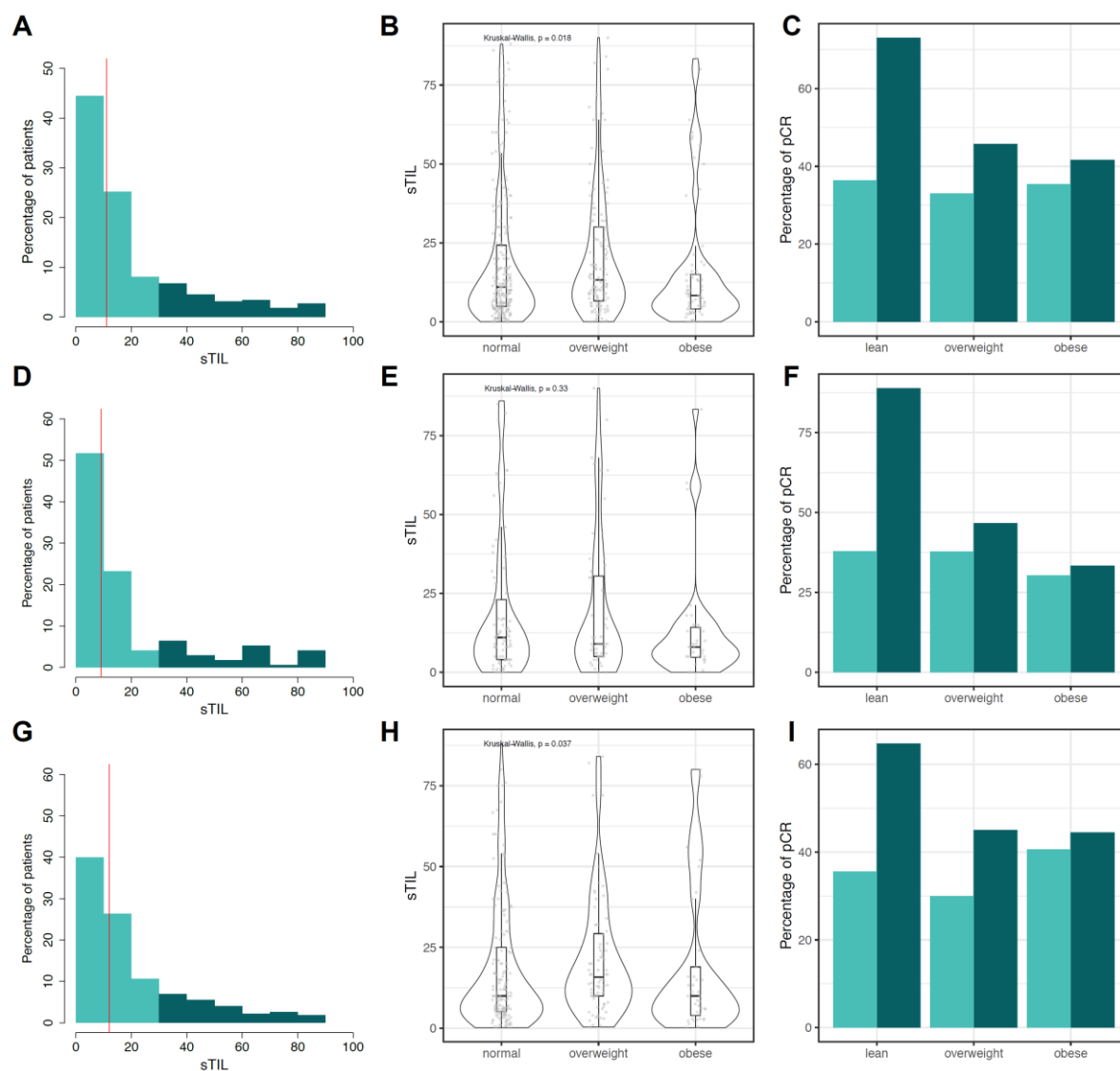
From top to bottom each row of three panels refer to the global (A, B, C), UZ leuven (D, E, F) and Institut Curie (G, H, I) cohorts respectively. These cohorts represent 445, 172, 273 patients respectively. Each column of three panels refers to: (A, D, G) distribution of sTIL across the cohort in percentage. Light and dark green indicate low and high sTIL respectively, according to recent literature in TNBC. The red line indicates the median. (B, E, H) Distribution of sTIL according to the 3 categories of BMI. Violin plots indicate the probability density of the data, boxplots represent the median (bold line) and interquantile range (rectangle). Dots report the actual distribution of the values. P-values from a Kruskal-Wallis test are reported on top. (C, F, I) pCR rate according to the 3

categories of BMI and the level of sTIL. Low and high sTIL are depicted in light and dark green respectively.

Supplementary Figure 3. Association between sTIL and survival according to BMI, with pCR as covariate.
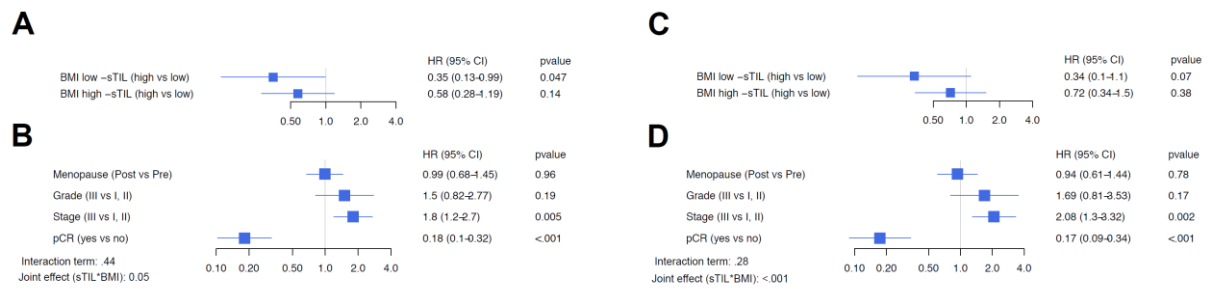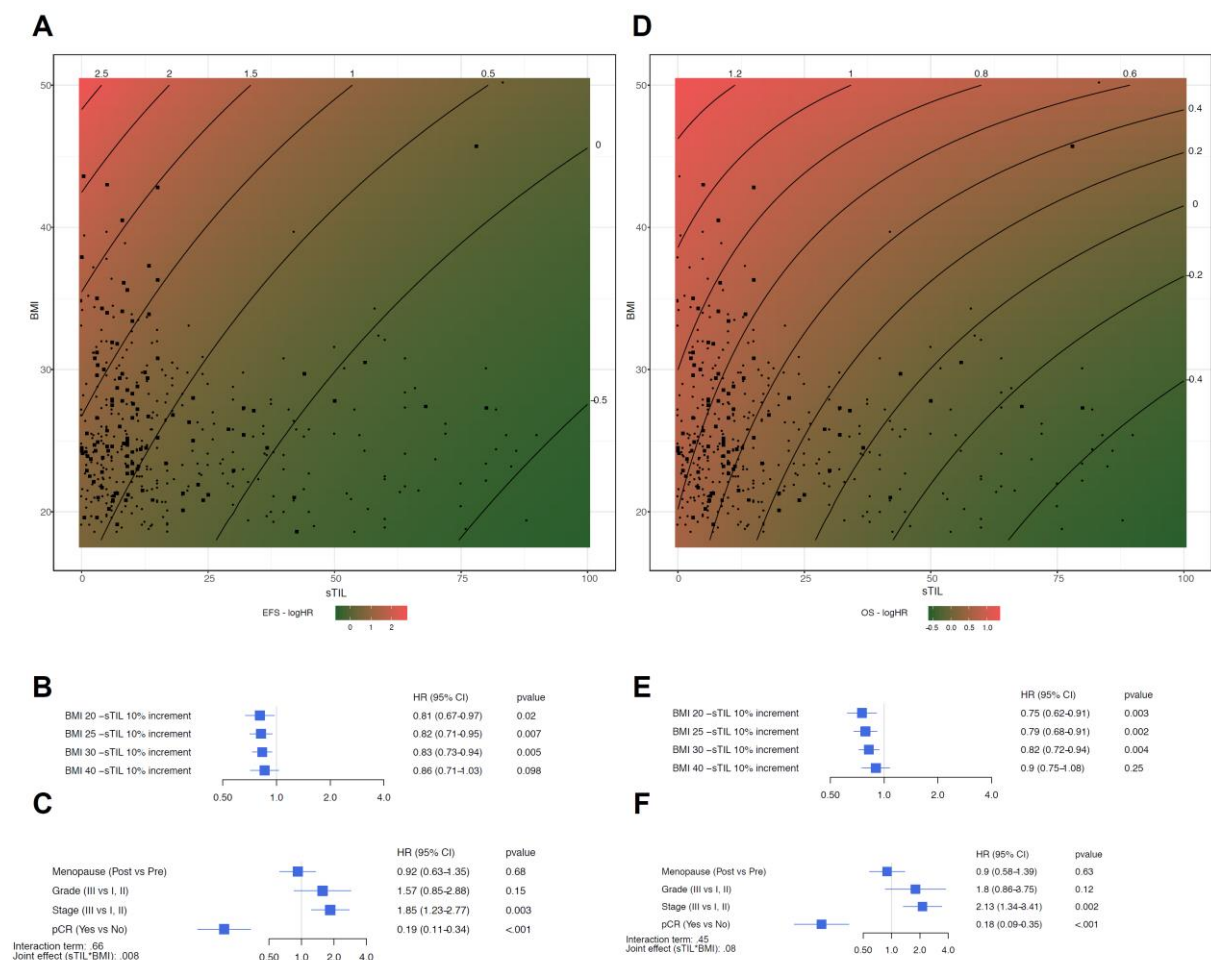

(A, B) association between sTIL and EFS according to BMI. (C, D) association between sTIL and OS according to BMI. sTIL and BMI are considered as categorical variables, center as a stratification factor. Panels A, C represent the interaction between BMI and sTIL and panels B, D the adjustment variables of the models. All reported p-values are from Wald tests, except for the joint effect that reports a p-value from a likelihood ratio test considering the two main terms sTIL and BMI as well as their interaction.

Supplementary Figure 4. Association between sTIL and survival according to BMI (continuous analysis).
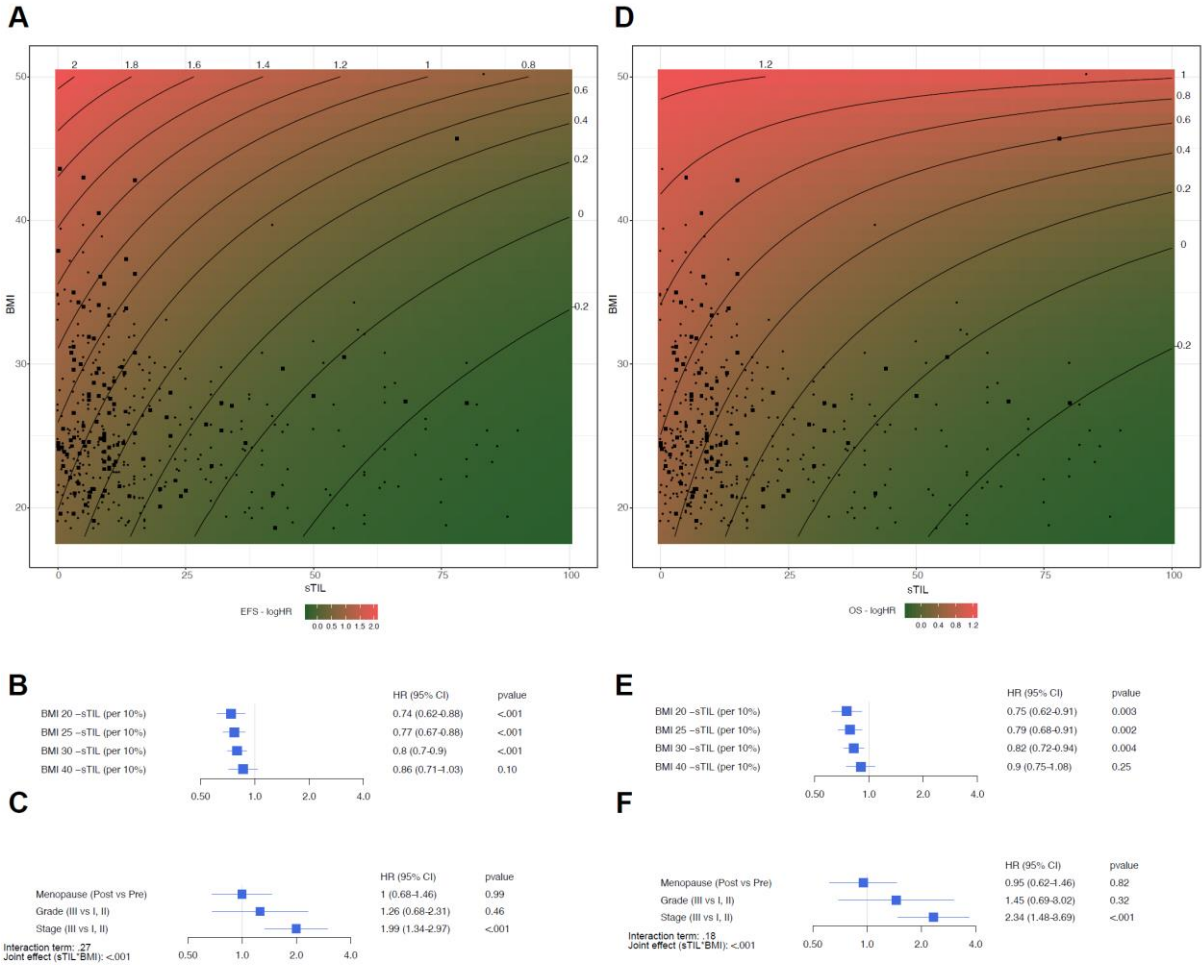
(A, B, C) Association between sTIL and EFS according to BMI. (D, E, F) Association of sTIL and OS according to BMI. sTIL and BMI are considered as continuous variables. In panels A and D EFS and OS logHR are computed from Cox proportional hazard models adjusted for menopausal status, grade, and stage, stratified for centers. The reference is taken for 30% sTIL and 20 kg/m^2 BMI. Panels B, E represent the interaction between BMI and sTIL and panels C, F the adjustment variables of the models. All reported p-values are from Wald tests, except for the joint effect that reports a p-value from a likelihood ratio test considering the two main terms sTIL and BMI as well as their interaction.

Supplementary Figure 5. Association between sTIL and survival according to BMI, with pCR as covariate (continuous analysis).

(A, B, C) Association between sTIL and EFS according to BMI. (D, E, F) Association of sTIL and OS according to BMI. sTIL and BMI are considered as continuous variables. In panels A and D EFS and OS logHR are computed from Cox proportional hazard models adjusted for menopausal status, grade, stage and pCR, stratified for centers. The reference is taken for 30% sTIL and 20 kg/m^2 BMI. Panels B,E represent the interaction between BMI and sTIL and panels C,F the adjustment variables of the models. All reported p-values are from Wald tests, except for the joint effect that report a p-value of an ANOVA with a Chi-squared test considering the two main terms sTIL and BMI as well as their interaction.