Table S1: Odds ratio table comparing CD169^{+}/TLLS^{+} co-infiltration and TLLS^{+} infiltration with tumor and metastasis clinicopathological features and other immune cell infiltration.

Clinicopathological features		CD169^{+}/TLLS^{+} PT				CD169^{+}/TLLS^{+} LNM				TLLS^{+} PT				TLLS^{+} LNM			
		OR	95% CI	P-value[a]	N	OR	95% CI	P-value[a]	N	OR	95% CI	P-value[a]	N	OR	95% CI	P-value[a]	N
Age	>50 y	1			180	1			74	1			85	1			48
	<50 y	0.65	0.192 – 2.214	0.54	11	0.64	0.295 – 1.383	0.25[b]	41	1.97	0.81 – 4.78	0.14[b]	106	0.84	0.39 – 1.79	0.70[b]	67
Overall Survival	>5 y	1			180	1			74	1			67	1			42
	<5 y	**0.29**	0.080 – 1.014	**0.053**	11	**3.51**	1.429 – 8.603	**0.005**[b]	41	**0.41**	0.18 - 0.94	**0.045**[b]	124	**2.63**	1.20 – 5.76	**0.018**[b]	73
Relapse free interval	>5 y	1			170	1			71	1			108	1			77
	<5 y	0.31	0.065 – 1.478	0.20	11	1.75	0.773 – 3.971	0.18[b]	41	**0.31**	0.11 - 0.85	**0.018**[b]	73	1.64	0.70 – 3.81	0.30[b]	35
Tumor Size	T1	1			179	1			74	1			80	1			34
	>T1	1.29	0.365 – 4.569	0.76	11	0.48	0.211 – 1.101	0.081[b]	40	1.19	0.51 – 2.78	0.83[b]	110	0.62	0.27 – 1.43	0.30[b]	80
Ki67 PT	Low	1			167	1			66	1			115	1			75
	High	**5.43**	1.386 – 21.276	**0.018**	11	1.09	0.448-2.635	0.85[b]	38	2.04	0.881-4.725	0.092[b]	63	0.94	0.395-2.258	0.90[b]	29
Ki67 LNM	Low	1			87	1			64	1			62	1			69
	High	3.33	0.526 – 21.114	0.33	5	0.57	0.210-1.530	0.26[b]	29	2.90	0.718-11.712	0.122[b]	30	1.30	0.530-3.169	0.57[b]	30
ER PT	Neg	1			172	1			68	1			36	1			21
	Pos	**0.26**	0.076-0.920	**0.042**	11	1.51	0.532-4.285	0.44[b]	38	0.49	0.19 - 1.24	0.18[b]	147	0.92	0.35 – 2.46	0.87	85
ER LNM	Neg	1			89	1			67	1			24	1			28
	Pos	**0.10**	0.010-1.043	**0.051**	4	0.50	0.119-1.241	0.13[b]	31	**0.17**	0.04 - 0.79	**0.025**[b]	69	0.48	0.19 – 1.22	0.12[b]	70
PR PT	Neg	1			171	1			65	1			79	1			42
	Pos	0.92	0.269-3.116	1	11	0.92	0.407-2.067	0.83[b]	38	0.51	0.22 - 1.18	0.14[b]	103	0.66	0.30 – 1.47	0.32[b]	61
PR LNM	Neg	1			89	1			66	1			57	1			60
	Pos	0.37	0.040-3.429	0.65	5	0.56	0.222-1.388	0.21[b]	31	0.63	0.15 - 2.61	0.74[b]	37	**0.43**	0.18 – 0.99	**0.044**[b]	37
HER2 PT	Neg	1			171	1			171	1			166	1			95
	Pos	2.49	0.490 – 12.68	0.25	11	2.49	0.490 – 12.678	0.25	11	2.18	0.65 – 7.37	0.25	16	0.92	0.24 – 3.47	1.0	10
HER2 LNM	Neg	1			79	1			79	1			69	1			77
	Pos	2.79	0.234 – 33.264	0.41	3	2.79	0.234 – 33.264	0.41	3	2.96	0.48 - 18.12	0.24	12	0.71	0.21 – 2.41	0.76	12
Cell infiltration association																	
FoxP3 PT	Neg	1			164	1			60	1			68	1			40
	Pos	**0.59**	0.515- 0.666	**0.007**	11	1.45	0.619-3.384	0.39[b]	36	**8.54**	1.94 - 37.63	**0.001**[b]	107	1.91	0.83 – 4.41	0.13[b]	56
FoxP3 LNM	Neg	1			70	1			61	1			24	1			26
	Pos	0.66	0.555- 0.778	0.55	3	1.47	0.466-4.641	0.59	19	2.61	0.29 - 23.71	0.66	49	1.83	0.71 – 4.72	0.21[b]	54
CD169 PT	Neg	1			180	1			65	1			138	1			79
	Pos	---	---	---	11	2.43	0.514 – 11.505	0.25[b]	38	**3.77**	1.61 - 8.82	**0.004**[b]	53	1.02	0.40 – 2.62	0.97[b]	24
CD169 LNM	Neg	1			96	1			74	1			50	1			57
	Pos	2.5	0.462 – 13.521	0.44	7	---	---	---	41	2.04	0.58 – 7.27	0.36[b]	53	**4.76**	2.12 – 10.71	**0.0001**[b]	58

Abbreviations: PT = Primary Tumor. LNM = Lymph node metastases. OR = Odds ratio. 95% CI = 95% confidence interval. N = Number of patients. ER = Estrogen Receptor. PR = progesterone Receptor. HER2 = Human epidermal growth factor receptor 2.

a= Fisher exact test unless otherwise stated. two tailed

b= Pearson's chi square test. two-tailed

Supplementary Figure legends

Figure S1:

Kaplan Meier survival showing the differences in 25 year breast cancer specific survival (BCSS) and recurrence free interval (RFI) for specific immune cell populations infiltrating lymph node metastases (LNM). *P* values by the log rank test are highlighted in bold when significant. On the left, the impact of immune cell infiltration for CD169+ TAMs, TLLS and CD169+ TAMS/TLLS was investigated as prognostic markers for BCSS. On the right, the impact of CD169+ TAMs, TLLS and CD169+ TAMS/TLLS was investigated as a prognostic marker for RFI. Green lines indicate LNMs with CD169+ TAMs, TLLS or CD169+ TAMS/TLLS infiltration and black lines indicate the absence of CD169+ TAMs, TLLS or CD169+ TAMS/TLLS.

Figure S1

Lymph Node Metastases
Long term prognosis

BCSS | *RFI*

CD169 + TLLS
■ Negative ■ Positive

p = 0.194

Survival proportion

Time to death due to Breast Cancer (Years)

| No. at | - | 74 | 40 | 13 | 6 | 1 | 0 |
| Risk | + | 41 | 33 | 10 | 2 | 1 | 0 |

CD169 + TLLS
■ Negative ■ Positive

p = 0.287

Disease free survival proportion

Time to cancer recurrence (Years)

| No. at | - | 63 | 19 | 5 | 2 | 0 |
| Risk | + | 39 | 16 | 4 | 0 | 0 |

CD169
■ Negative ■ Positive

p = 0.240

Survival proportion

Time to death due to Breast Cancer (Years)

| No. at | - | 57 | 31 | 11 | 5 | 1 | 0 |
| Risk | + | 58 | 42 | 16 | 3 | 1 | 0 |

CD169
■ Negative ■ Positive

p = 0.973

Disease free survival proportion

Time to cancer recurrence (Years)

| No. at | - | 47 | 15 | 5 | 2 | 0 |
| Risk | + | 55 | 20 | 4 | 0 | 0 |

TLLS
■ Negative ■ Positive

p = 0.494

Survival proportion

Time to death due to Breast Cancer (Years)

| No. at | - | 46 | 23 | 8 | 3 | 1 | 0 |
| Risk | + | 69 | 50 | 19 | 5 | 1 | 0 |

TLLS
■ Negative ■ Positive

p = 0.273

Disease free survival proportion

Time to cancer recurrence (Years)

| No. at | - | 39 | 11 | 3 | 0 | 0 |
| Risk | + | 63 | 24 | 6 | 0 | 0 |

Figure S2:

Kaplan Meier analyses performed on matched donors. Four types of associations were compared: patients lacking immune cells infiltration in both PT and LNM, patients having immune cells infiltrating in both PT and LNM and patients having cell infiltration in either PT or LNM. In the left panel, BCSS was investigated for all three types of cell infiltration. In the right panel, the same analysis was performed for RFI. *P* value by the log rank test.

Figure S2

BCSS | RFI

CD169 + TLLS (left, BCSS)
PT⁻/LNM⁻ · PT⁺/LNM⁻ · PT⁻/LNM⁺ · PT⁺/LNM⁺
p = 0.105

CD169 + TLLS (right, RFI)
p = 0.103

CD169 (left)
p = 0.038

CD169 (right)
p = 0.096

TLLS (left)
p = 0.034

TLLS (right)
p = 0.029
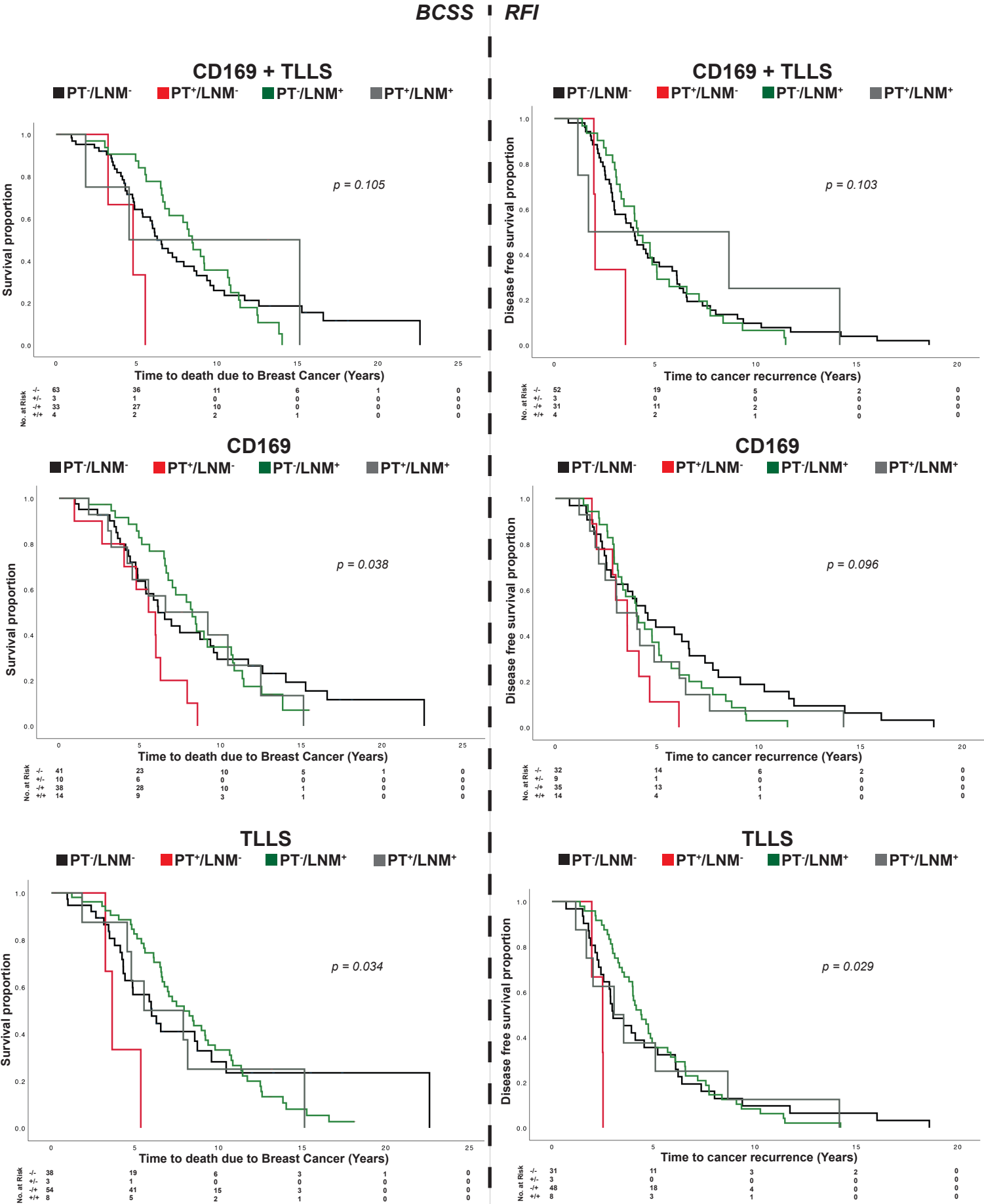
Figure S3:

Forest plots with Cox regression analyses (BCSS). Forest plots showing Cox regression analysis on 25 year BCSS (PT) and 10 year BCSS (LNM) in breast cancer patients with CD169^{+} TAMs, TLLS or CD169^{+} TAMS/TLLS presence, adjusted individually and all together for confounders such as receptor expression status (ER, PR, HER2), T_{regs} presence, Ki67 levels, tumor size and age at diagnosis. Hazard ratios are indicated with dots together with horizontal lines representing the 95% confidence interval.

Figure S3

Multiple Cox regression analysis
Forest Plots - Breast cancer specific survival

PT | *LNM*

A. CD169 + TLLS

Unadjusted (n=190)	p=0.063
+ FoxP3 (n=174)	p=0.168
+ ER (n=182)	p=0.096
+ PR (n=181)	p=0.019
+ HER2 (n=181)	p=0.092
+ Ki67 (n=177)	p=0.171
+ Tumor size (n=189)	p=0.016
+ Nodal status (186)	p=0.015
+ Age (n=190)	p=0.003
Adjusted (n=154)	p=0.007

Hazard ratio with 95%CI

B. CD169 + TLLS

Unadjusted (n=114)	p=0.017
+ FoxP3 (n=80)	p=0.036
+ ER (n=97)	p=0.002
+ PR (n=96)	p=0.077
+ HER2 (n=88)	p=0.037
+ Ki67 (n=93)	p=0.163
+ Tumor size (n=113)	p=0.067
+ Age (n=114)	p=0.066
Adjusted (n=73)	p=0.057

Hazard ratio with 95%CI

C. CD169

Unadjusted (n=190)	p=0.049
+ TLS (n=190)	p=0.171
+ FoxP3 (n=174)	p=0.208
+ ER (n=182)	p=0.227
+ PR (n=181)	p=0.072
+ HER2 (n=181)	p=0.034
+ Ki67 (n=177)	p=0.174
+ Tumor size (n=189)	p=0.012
+ Nodal status (186)	p=0.017
+ Age (190)	p=0.289
Adjusted (n=154)	p=0.774

Hazard ratio with 95%CI

D. CD169

Unadjusted (n=114)	p=0.025
+ TLLS (n=114)	p=0.083
+ FoxP3 (n=80)	p=0.040
+ ER (n=97)	p=0.001
+ PR (n=96)	p=0.063
+ HER2 (n=88)	p=0.038
+ Ki67 (n=93)	p=0.119
+ Tumor size (n=113)	p=0.127
+ Age (n=114)	p=0.048
Adjusted (n=80)	p=0.046

Hazard ratio with 95%CI

E. TLLS

Unadjusted (n=190)	p=0.001
+ CD169 (n=190)	p=0.003
+ FoxP3 (n=174)	p=0.013
+ ER (n=182)	p=0.004
+ PR (n=181)	p=0.007
+ HER2 (n=181)	p=0.001
+ Ki67 (n=177)	p=0.003
+ Tumor size (n=189)	p=0.0002
+ Nodal status (186)	p=0.001
+ Age (n=190)	p=0.001
Adjusted (n=154)	p=0.040

Hazard ratio with 95%CI

F. TLLS

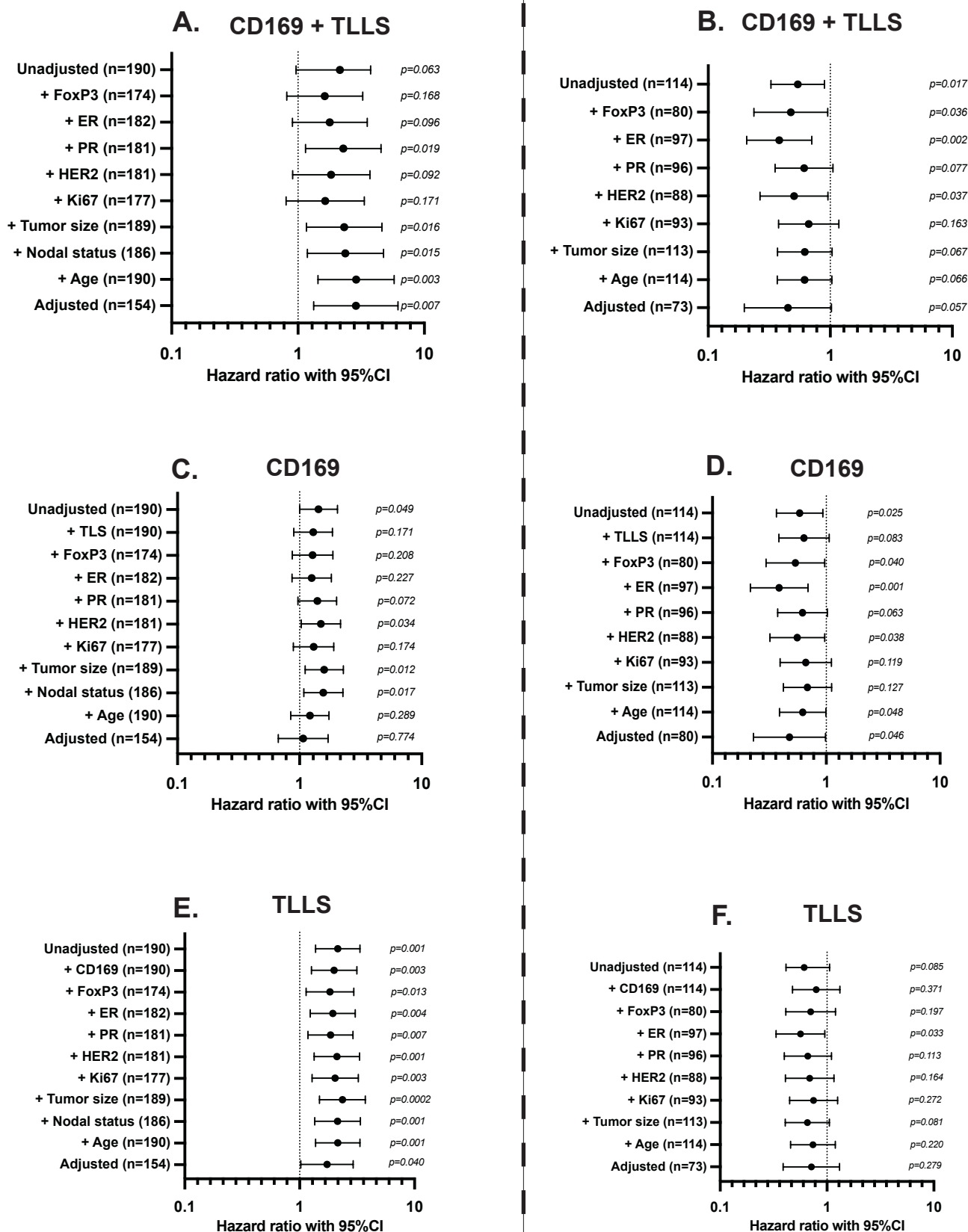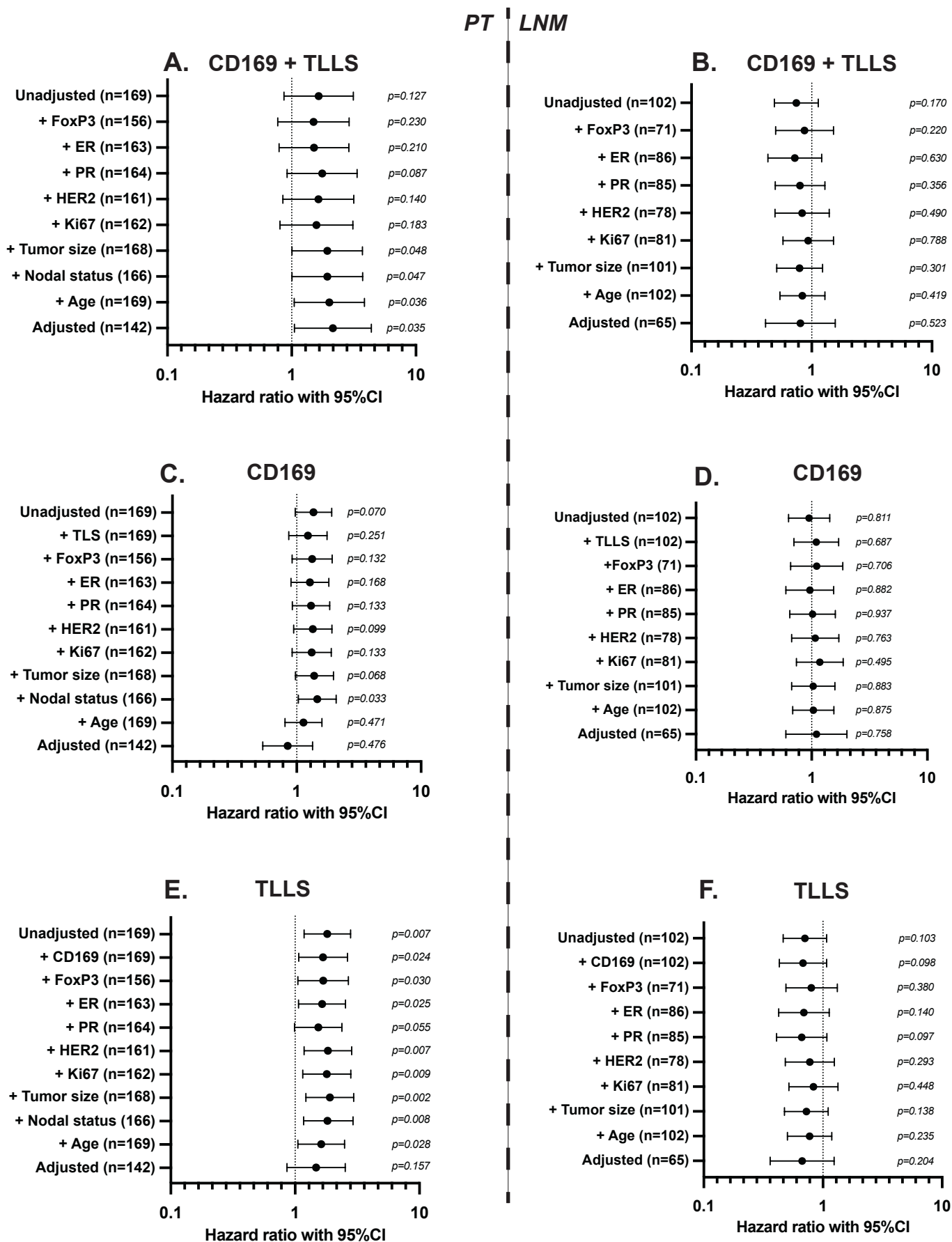|	
Unadjusted (n=114)	p=0.085
+ CD169 (n=114)	p=0.371
+ FoxP3 (n=80)	p=0.197
+ ER (n=97)	p=0.033
+ PR (n=96)	p=0.113
+ HER2 (n=88)	p=0.164
+ Ki67 (n=93)	p=0.272
+ Tumor size (n=113)	p=0.081
+ Age (n=114)	p=0.220
Adjusted (n=73)	p=0.279

Hazard ratio with 95%CI

Figure S4:

Forest plots with Cox regression analyses (RFI). Forest plots showing Cox regression analysis on 25 year RFI (PT) and 10 year RFI (LNM) in breast cancer patients with CD169^{+} TAMs, TLLS or CD169^{+} TAMS/TLLS presence, adjusted individually and all together for confounders such as receptor expression status (ER, PR, HER2), T_{regs} presence, Ki67 levels, tumor size and age at diagnosis. Hazard ratios are indicated with dots together with horizontal lines representing the 95% confidence interval.

Multiple Cox regression analysis
Forest Plots - Recurrence free interval

PT | *LNM*

A. CD169 + TLLS

Unadjusted (n=169)	p=0.127
+ FoxP3 (n=156)	p=0.230
+ ER (n=163)	p=0.210
+ PR (n=164)	p=0.087
+ HER2 (n=161)	p=0.140
+ Ki67 (n=162)	p=0.183
+ Tumor size (n=168)	p=0.048
+ Nodal status (166)	p=0.047
+ Age (n=169)	p=0.036
Adjusted (n=142)	p=0.035

Hazard ratio with 95%CI

B. CD169 + TLLS

Unadjusted (n=102)	p=0.170
+ FoxP3 (n=71)	p=0.220
+ ER (n=86)	p=0.630
+ PR (n=85)	p=0.356
+ HER2 (n=78)	p=0.490
+ Ki67 (n=81)	p=0.788
+ Tumor size (n=101)	p=0.301
+ Age (n=102)	p=0.419
Adjusted (n=65)	p=0.523

Hazard ratio with 95%CI

C. CD169

Unadjusted (n=169)	p=0.070
+ TLS (n=169)	p=0.251
+ FoxP3 (n=156)	p=0.132
+ ER (n=163)	p=0.168
+ PR (n=164)	p=0.133
+ HER2 (n=161)	p=0.099
+ Ki67 (n=162)	p=0.133
+ Tumor size (n=168)	p=0.068
+ Nodal status (166)	p=0.033
+ Age (169)	p=0.471
Adjusted (n=142)	p=0.476

Hazard ratio with 95%CI

D. CD169

Unadjusted (n=102)	p=0.811
+ TLLS (n=102)	p=0.687
+FoxP3 (71)	p=0.706
+ ER (n=86)	p=0.882
+ PR (n=85)	p=0.937
+ HER2 (n=78)	p=0.763
+ Ki67 (n=81)	p=0.495
+ Tumor size (n=101)	p=0.883
+ Age (n=102)	p=0.875
Adjusted (n=65)	p=0.758

Hazard ratio with 95%CI

E. TLLS

Unadjusted (n=169)	p=0.007
+ CD169 (n=169)	p=0.024
+ FoxP3 (n=156)	p=0.030
+ ER (n=163)	p=0.025
+ PR (n=164)	p=0.055
+ HER2 (n=161)	p=0.007
+ Ki67 (n=162)	p=0.009
+ Tumor size (n=168)	p=0.002
+ Nodal status (166)	p=0.008
+ Age (n=169)	p=0.028
Adjusted (n=142)	p=0.157

Hazard ratio with 95%CI

F. TLLS

Unadjusted (n=102)	p=0.103
+ CD169 (n=102)	p=0.098
+ FoxP3 (n=71)	p=0.380
+ ER (n=86)	p=0.140
+ PR (n=85)	p=0.097
+ HER2 (n=78)	p=0.293
+ Ki67 (n=81)	p=0.448
+ Tumor size (n=101)	p=0.138
+ Age (n=102)	p=0.235
Adjusted (n=65)	p=0.204

Hazard ratio with 95%CI

Figure S5:

Complete heat maps, containing sample hierarchical clusters with Pearson correlations
between *SIGLEC1* (CD169) and gene signatures for tertiary lymphoid structures (TLS), B_{regs}
or T_{regs}. Patients are characterized based on their molecular subtype of breast cancer,
aggressive subtypes in red (Basal-like, HER2$^+$ and Luminal B) and luminal A or normal-like
subtypes in green. Upregulated genes are shown in yellow while downregulated genes are
shown in blue. The threshold for upregulation/downregulation was set at 1/-1 based on
median centered gene relations. The highlighted areas represent clusters with positive cell
infiltration correlations shown in Figure 4.

Figure S5

Complete sample Hierarchical clustering with pearson correlations

Downregulated genes   *Upregulated genes*

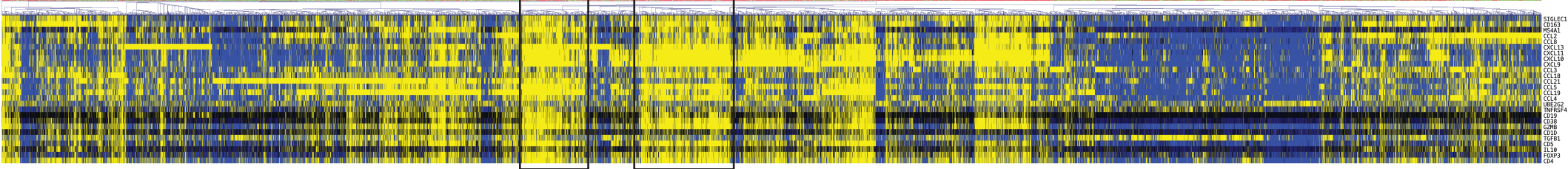Basal   Normal-like
Her2   Luminal A
Luminal B

CD169 gene signature in relation to TLS gene signature, Median centered genes relations
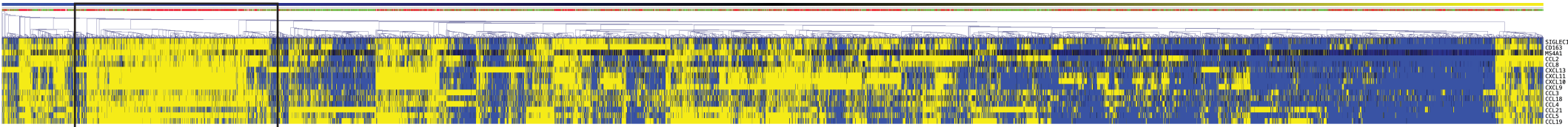
CD169 compared to Breg gene signature, Median centered genes relations
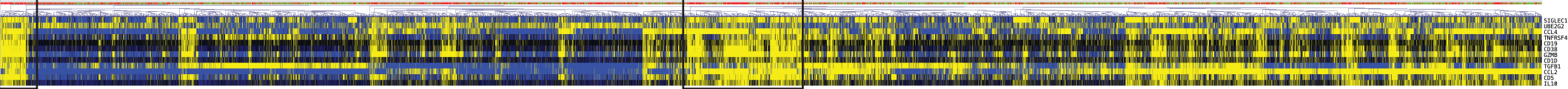
CD169 compared to TLS, Breg and Treg gene signatures, Median centered genes relations

CD169 differential gene signature, Median centered genes relations