

Supplementary Material

Tumor-infiltrating lymphocytes predict improved overall survival after post-mastectomy radiotherapy: a study of the randomized DBCG82bc cohort

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Supplementary Figure 4

Predictive impact of TILs on overall survival in ER negative patients according to HER2 status 5

Supplementary Table 1

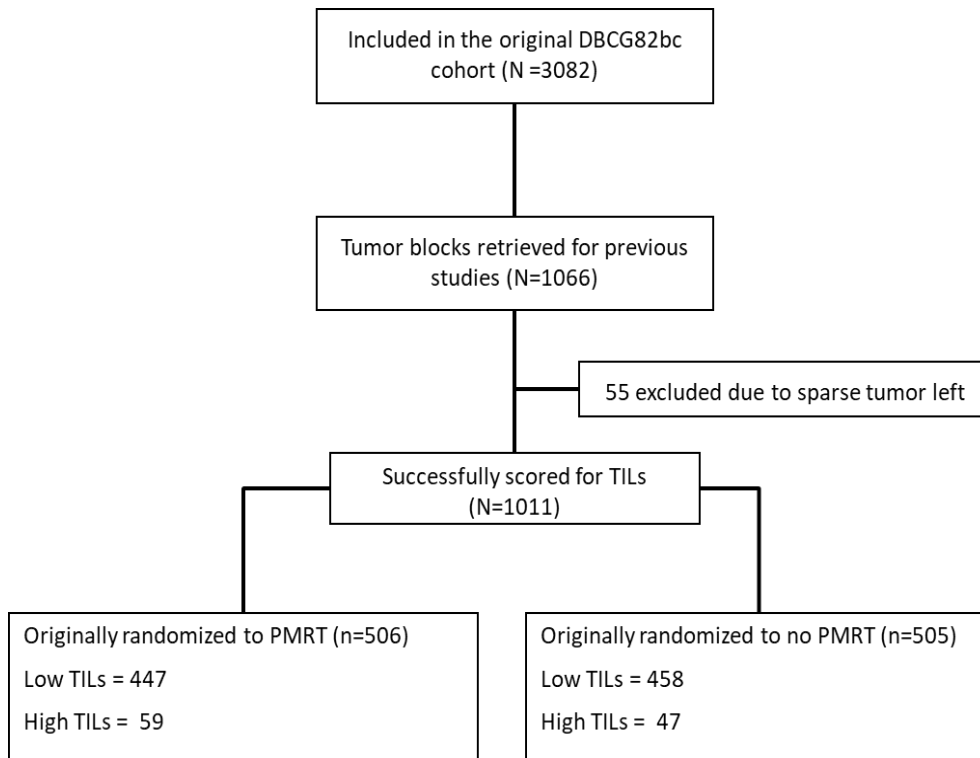
Interobserver agreement in assessment of tumor-infiltrating lymphocytes, TILs (with 95% CI).

The cut off value for distinguishing between low and high TILs was chosen as the cut off (30%) with the best combination of high Fleiss' kappa value and an optimal concordance rate.

Intraclass correlation coefficient (ICC)	0.74 (0.72-0.77)
Fleiss' kappa values	
TILs 0–10%, 11–39%, ≥40%	0.57 (0.51-0.62)
TILs 0–20%, 21–49%, ≥50%	0.52 (0.45-0.59)
TILs <10% vs ≥10%	0.58 (0.53-0.63)
TILs <20% vs ≥20%	0.65 (0.59-0.72)
TILs <30% vs ≥30%	0.63 (0.54-0.72)
TILs <40% vs ≥40%	0.54 (0.43-0.65)
TILs <50% vs ≥50%	0.47 (0.34-0.61)
TILs <60% vs ≥60%	0.38 (0.22-0.55)
Concordance rates	
TILs 0–10%, 11–39%, ≥40%	0.84 (0.81-0.86)
TILs 0–20%, 21–49%, ≥50%	0.90 (0.88-0.92)
TILs <10% vs ≥10%	0.80 (0.77-0.82)
TILs <20% vs ≥20%	0.91 (0.89-0.93)
TILs <30% vs ≥30%	0.94 (0.92-0.96)
TILs <40% vs ≥40%	0.95 (0.93-0.96)
TILs <50% vs ≥50%	0.96 (0.94-0.97)
TILs <60% vs ≥60%	0.97 (0.95-0.98)

Supplementary Figure 1

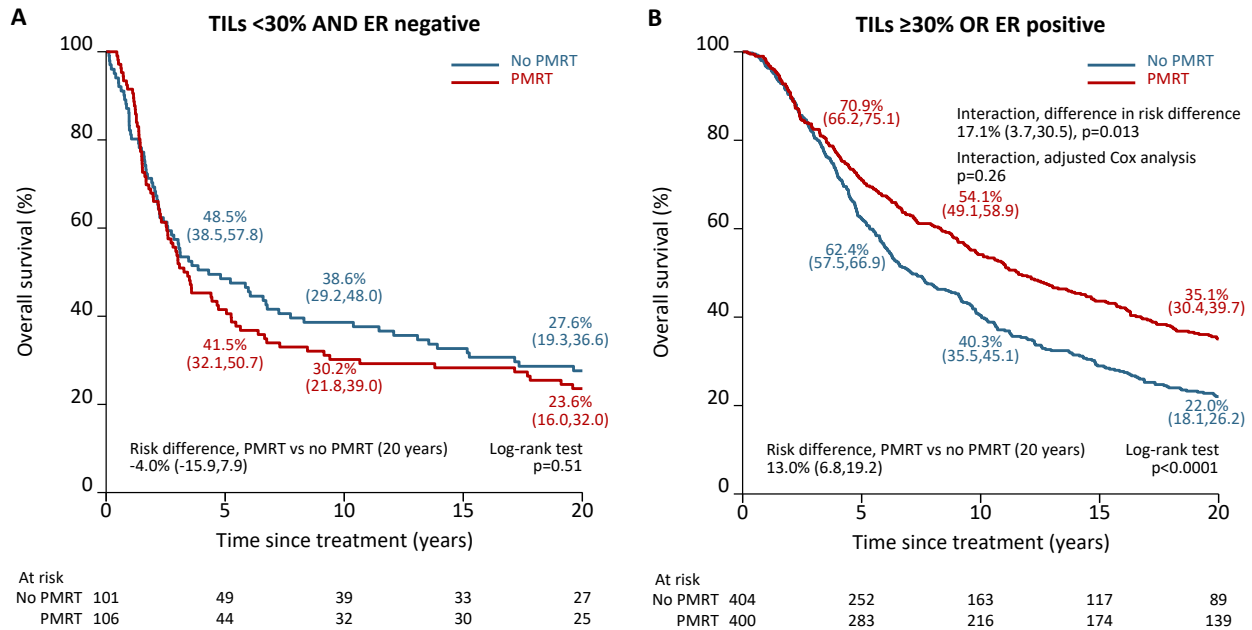
CONSORT diagram of patients from the DBCG82bc cohort (Danish Breast Cancer Group) included in the present study.



PMRT, post-mastectomy radiotherapy; TILs, tumor infiltrating lymphocytes

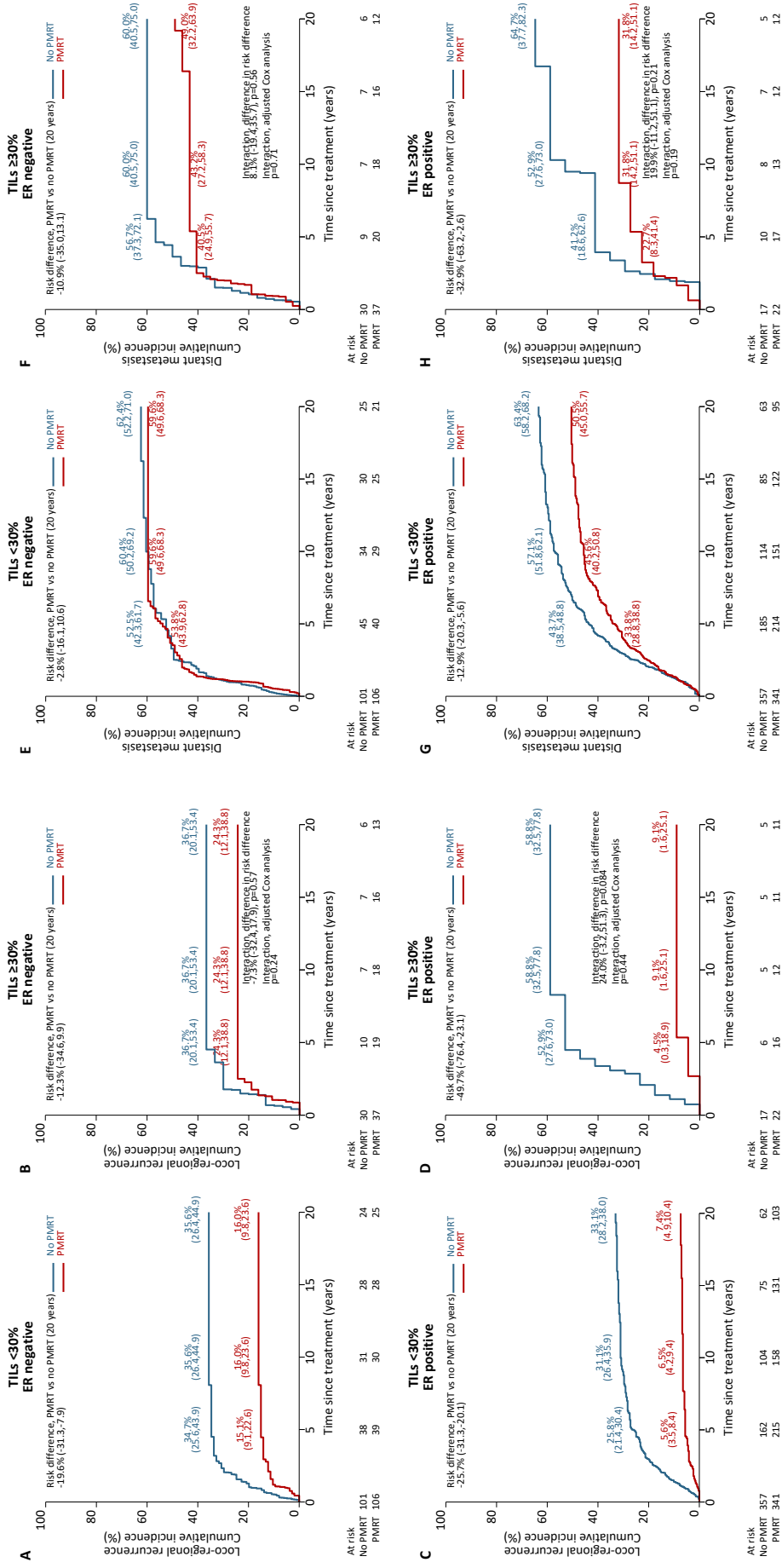
Supplementary Figure 2

Kaplan-Meier plots for overall survival (OS) for (A) patients with estrogen receptor (ER) negative tumors with low TILs level and (B) the remaining patients with either ER positive tumors or tumors with high level of TILs stratified according to randomization to post-mastectomy radiotherapy (PMRT) or not (red – PMRT, blue – no PMRT). Actuarial risks at 5, 10 and 20 years are provided as well as difference in actuarial risks with 95% confidence intervals at 20 years. P-values for Log Rank tests on Kaplan-Meier estimates are stated as well as interaction tests between TILs and PMRT for adjusted Cox analysis and for risk differences.



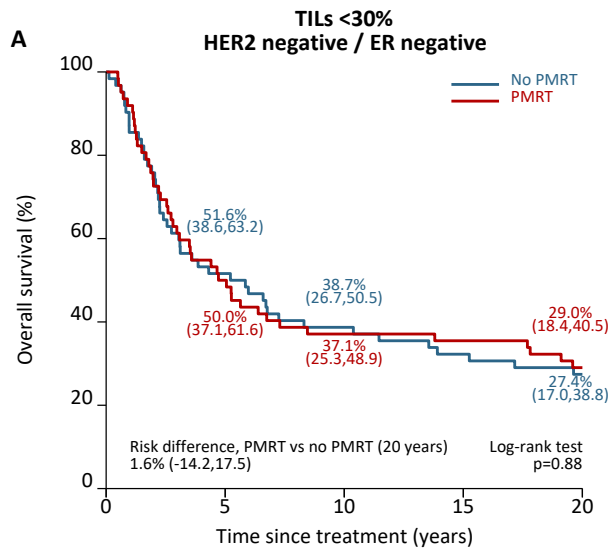
Supplementary Figure 3

Cumulative incidence plots for loco-regional recurrence (LRR) and risk of distant metastasis (DM) for (A, B and E, F) for estrogen receptor (ER) negative and (C, D and G, H) ER-positive tumors divided according to level of tumor infiltrating lymphocytes (TILs) and stratified according to randomization to post-mastectomy radiotherapy (PMRT) or not (red – PMRT, blue – no PMRT). Actuarial risks at 5, 10 and 20 years and difference in actuarial risks (risk difference) at 20 years with 95% confidence intervals are provided. Interaction tests between TILs and PMRT is stated for adjusted Cox analysis and for risk differences.

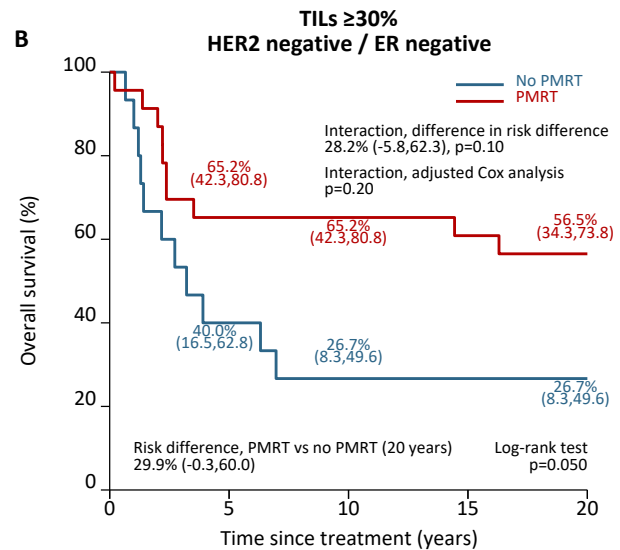


Supplementary Figure 4

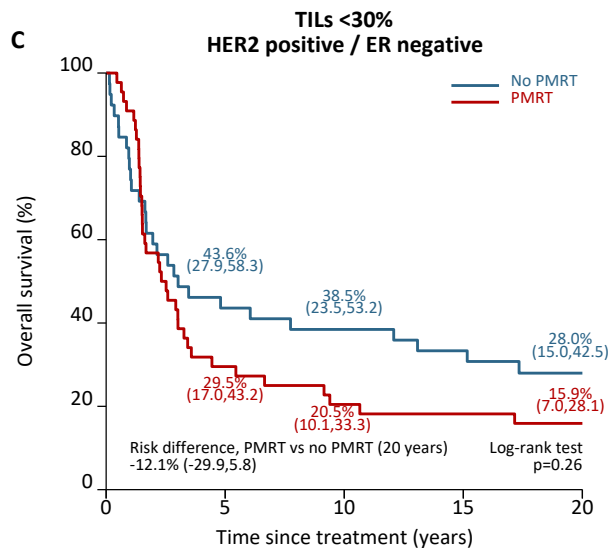
Kaplan-Meier plots for overall survival (OS) for (A, B) estrogen receptor (ER) negative/HER2 negative and (C, D) ER negative/HER2-positive tumors divided according to level of tumor infiltrating lymphocytes (TILs) and stratified according to randomization to post-mastectomy radiotherapy (PMRT) or not (red – PMRT, blue – no PMRT). Actuarial risks at 5, 10 and 20 years and difference in actuarial risks (risk difference) at 20 years with 95% confidence intervals are provided. Interaction tests between TILs and PMRT is stated for adjusted Cox analysis and for risk differences.



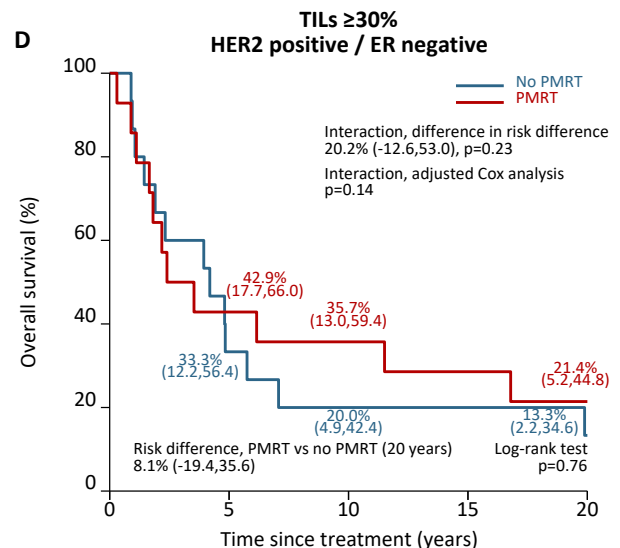
At risk	0	5	10	15	20
No PMRT	62	32	24	20	17
PMRT	62	31	23	22	18



At risk	0	5	10	15	20
No PMRT	15	6	4	4	4
PMRT	23	15	15	14	13



At risk	0	5	10	15	20
No PMRT	39	17	15	13	10
PMRT	44	13	9	8	7



At risk	0	5	10	15	20
No PMRT	15	5	3	3	2
PMRT	14	6	5	4	3