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448P Progression-free survival (PFS) as a surrogate end point for overall survival (OS) in the first line (1L) setting among patients with metastatic triple-negative breast cancer (mTNBC)

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Background: OS is often considered the gold standard in oncology trials for evaluating treatment efficacy. However, treatment crossovers (as part of study design or standard of care [SOC]) can confound OS interpretation. Predicting OS from a surrogate end point not affected by crossovers (eg, PFS) is of interest. We evaluated if PFS can be a surrogate for OS in 1L treatment of mTNBC (overall and by programmed death ligand 1 [PD-L1] status).

Methods: A systematic literature review was conducted using Embase®, MEDLINE® (database inception—Nov 5, 2024) for randomized controlled trial (RCT) and non-RCT, and Cochrane CENTRAL via OvidSP (1948—Nov 5, 2024) for RCT. Trial-level (HR_{OS} vs HR_{PFS} via Bayesian trivariate random effects meta-analysis) and individual-level (OS vs PFS distributions generated via simulation) surrogacy were evaluated with PD-L1+% as a covariate. Sensitivity analyses excluded studies with treatment crossovers (1 study design, 6 SOC). The impact of each study in predicting HR_{OS} using HR_{PFS} was determined by leave-one-out cross-validation (LOOCV). Surrogate threshold effect (STE), the HR_{PFS} value at the upper bound of 95% Credible Interval with predicted HR_{OS}=1, was calculated.

Results: 56 comparisons from 52 studies were included. Overall, estimated STE was 0.81. Trial-level surrogacy showed strong correlation between HR_{PFS} and HR_{OS}, but PD-L1+% was not correlated with HR_{PFS} or HR_{OS} **(Table)**. Individual-level surrogacy showed stronger correlations in PD-L1+ vs PD-L1− subgroups **(Table)**. Sensitivity analyses results were consistent but with slightly lower STE (0.76). LOOCV analysis showed 100% predictive accuracy.

Table: 448P

Trial-Level Surrogacy Correlation*

	HR_{OS}	HR_{PFS}	PD-L1+ %
HR_{OS}	1.00	0.87 (95% CrI, 0.71 to 0.94)	−0.05 (95% CrI, −0.45 to 0.09)
HR_{PFS}	-	1.00	−0.02 (95% CrI, −0.49 to 0.13)

Individual-Level Surrogacy Correlation

	All Comers	PD-L1+	PD-L1−
Pearson's Correlation (Simulation) (95% CI)	0.63 (0.61-0.66)	0.94 (0.93-0.95)	0.51 (0.47-0.54)

*All analyses were conducted using log-scale CI, confidence interval; CrI, credible interval; HR, hazard ratio; PD-L1, programmed death-ligand 1; PFS, progression-free survival; OS, overall survival.

Conclusions: PFS remained a valid surrogate for OS, even after excluding studies with treatment crossovers in the 1L setting of mTNBC. A stronger association was observed in the PD-L1+ population. These findings support the use of PFS to predict OS benefit in future mTNBC trials.

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449P Impact of a previous malignancy on the presentation and outcomes of metastatic breast cancer: A nationwide ESME study

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Background: As the population of cancer survivors increases, the incidence of second primary malignancies is rising. Although breast cancer is frequent in this context, large-scale data assessing the impact of a previous non-breast malignancy on the clinical presentation and outcomes of metastatic breast cancer (mBC) remain limited.

Methods: We conducted a retrospective study of the ESME database (NCT03275311), a French nationwide cohort of patients treated for mBC. Patients with prior non-breast malignancy (*Prev*) were compared with those with no cancer history (*NoPrev*). Primary endpoint was clinicopathological presentation at mBC diagnosis; secondary endpoints included OS and PFS. Sensitivity analyses used multivariate and propensity score-adjusted models.