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Prognostic value of tumour infiltrating lymphocytes in young triple negative breast cancer patients who did not receive adjuvant systemic treatment; by the PARADIGM study group

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Background

Uncertainty exists whether all young (< 40 years) patients with triple negative breast cancer (TNBC) require (neo)adjuvant chemotherapy. Increasing stromal tumour infiltrating lymphocytes (TIL) have been associated with improved outcome. However, limited data are available for young patients. We investigated whether TIL could aid in identifying a subgroup of young TNBC patients for whom de-escalating (neo)adjuvant chemotherapy could be considered.

Methods

All women <40 years, diagnosed with TanyNOMO breast cancer between 1989 and 2000 were selected from the Netherlands Cancer Registry. We excluded women who received adjuvant systemic treatment. ER, PgR, and HER2 status were reassessed and TIL were scored for the triple negative (ER/PgR < 10% and HER2 negative) subset according to an established standard. Multivariable Cox regression was performed for overall (OS) and distant recurrence-free survival (DRFS). We used continuous TIL score, T-stage, tumour grade, histological subtype, and local treatment as covariates. For DRFS we censored patients at the time of a second primary tumour.

Results

We identified 481 TNBC patients, with a median age of 35 years (range 22 – 39). Most tumours were grade 3 (86%), pT1C (49%), median TIL score was 25% (IQR 5 – 70). In total, 122 DRFS events (25%) (89 metastases, 33 deaths), and 170 deaths (35%) occurred during a median of 16.2 and 21.2 years follow-up, respectively. In total, 110 (23%) patients developed a second primary tumour. OS at 10 and 15 years for patients with TIL ≥ 30% and <75% (n=127) was 80% (95% CI 73 - 87) and 76% (95% CI 69 – 84), DRFS was 84% (95% CI 78 – 91) and 83% (95% CI 76 – 90), respectively. For patients with ≥ 75% TIL (n=107) OS and DRFS at 10 and 15 year were 95% (95% CI 91 – 99), 93% (95% CI 89 – 99), 98% (95% CI 95 – 100) and 98% (95% CI 95 – 100), respectively. Risk of death or DRFS event reduced significantly for each 10% TIL increment (aHRs 0.83; 95% CI 0.79-0.88 and 0.74; 95% CI 0.68-0.80, respectively).

Conclusions

In young (<40 year), systemically untreated, N0, TNBC patients TIL provide important prognostic information. Subsequent investigations to de-escalate systemic therapy in a subgroup of young TNBC patients may be warranted.

Legal entity responsible for the study

The PARADIGM study group.

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Disclosure

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