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Phase III randomised trial comparing intense dose-dense chemotherapy to tailored dose-dense chemotherapy in high-risk early breast cancer (GAIN-2)

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BACKGROUND
The GAIN-2 trial was designed to identify a superior intense dose-dense (idd) strategy for high-risk patients with early breast cancer. Here, we report an interim analysis, at which the predefined futility boundary was crossed.

PATIENTS AND METHODS
GAIN-2 was an open-label, randomised, multicentre phase III trial. Two thousand eight hundred and eighty seven patients were randomised 1:1 between three courses each of idd epirubicin (E) 150 mg/m, nab-paclitaxel (nP) 330 mg/m and cyclophosphamide (C) 2000 mg/m (iddEnPC) versus four cycles of leucocyte nadir-based tailored and dose-dense EC (dtEC) followed by four cycles of tailored and dose-dense docetaxel (dtD) (dtEC-dtD).

RESULTS
The duration of median follow-up was 45.8 (range 0.0-88.3) months. Trial objectives included invasive disease-free survival (iDFS) as the primary end-point. A total of 593 patients received the treatment as neoadjuvant chemotherapy. At the time of futility interim analysis, 414 events for iDFS were reported. Overall, there was no difference in iDFS between iddEnPC and dtEC-dtD with 4-year iDFS rates of 84.3% (95% confidence interval (CI) 82.0-86.4%). Among all predefined subgroups, hormone receptor-positive and human epidermal growth factor receptor 2-negative (HR+/HER2-), lobular cancer and ≤50 years subgroups predicted for better iDFS in the dtEC-dtD arm. Overall, 88.1% of patients completed all treatment in both arms. Haematological toxicity grade 3/4 and grade 3/4 non-haematological adverse events were significantly higher with iddEnPC (iddEnPC 50.8% vs dtEC-dtD 45.1%, P = 0.002), especially arthralgia and peripheral sensory neuropathy. Two treatment-related deaths occurred during dtEC-dtD, corresponding to a

low mortality rate of 0.07%.

CONCLUSIONS
iDFS is equal in both regimens, but tailoring dose-dense chemotherapy improved outcomes in HR+/HER2-, lobular cancer and patients ≤50 years.

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