had partial response and 9 patients (28%) had stable disease. Progressive disease was observed in 11 (34.5%) patients. There was no difference in terms of objective response rate between anthracycline-containing regimen and nonanthracycline-containing regimen (42% versus 31%, \( P = 0.5 \)) or between single agent and combination chemotherapy (42% versus 35%, \( P = 0.7 \)).

The median follow-up among surviving patients was 62 months (range 20–103). Median PFS was 4.3 months (95% CI 2.1–6.4) (Figure 1). The 3-month, 6-month and 1-year PFS rates were 63% (95% CI 48–78), 43% (95% CI 18–58) and 21% (95% CI 8–34), respectively. On univariate analysis, PS > 1 was the sole factor significantly associated with PFS: 0.8 months (95% CI 0–1.8) versus 7.1 months (95% CI 4.9–9.3), \( P < 0.0001 \).

At the time of analysis, 27 patients (69%) had died. The median OS for the entire cohort of patients was 14 months (95% CI 0–28) (Figure 1). The 6-month, 1-year and 2-year OS rates were 66% (95% CI 51–81), 56% (95% CI 40–72) and 36% (95% CI 21–51), respectively. On univariate analysis, PS > 1 was the sole factor significantly associated with OS: 1.8 months (95% CI 0–3.8) versus 19 months (95% CI 5–33), \( P < 0.0001 \). Twelve patients had surgical resection of metastatic disease. Their survival ranged between 2.2 and 60.8 months.

After completion of first-line chemotherapy, 19 patients received at least one new line of chemotherapy. Three patients had partial response in the second-line setting lasting from 3 to 13 months. All of them were treated with gemcitabine–docetaxel (Taxotere) after disease progression on the first-line anthracycline-containing regimen. One objective response was also observed in the third-line setting with trabectedin.

The overall objective response rate of 37% in our study was significantly higher than in WDLPS/DDLPS, which was 12% in the largest series reported to date [2]. The median OS of patients with advanced PLPS (14 months) was comparable to that of other sarcoma subtypes. Recent studies have shown that a subset of PLPS is characterized by mutations or deletions affecting the tumor suppressor \( NF1 \) gene and up to 60% of PLPS exhibit TP53 mutation [1–3]. The \( NF1 \)-encoded protein, neurofibromin, plays a crucial role in the regulation of the mTOR and of the MAPK pathways [4, 5]. This report provides the data that could be used as a reference for future studies investigating drugs targeting these pathways and other relevant molecular aberrations.

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Pregnancy unbosoms the heart of breast cancer survivors

We read with interest the proposed guideline of the Late Effects of Childhood Cancer task force of the Dutch Childhood Oncology Group for risk-based screening for asymptomatic cardiac dysfunction in childhood cancer survivors in the February issue of this journal [1]. The concern about subclinical asymptomatic cardiotoxicity that is put forward is...
not only relevant for childhood cancer survivors but also for the increasing number of successfully treated primary breast cancer survivors.

Data from large adjuvant breast cancer trials show a 0%–3.2% incidence of clinical heart failure (CHF). Moreover, subclinical treatment-related cardiac dysfunction may progress to CHF when additional stressors challenge the cardiovascular system. Potential stressors include ‘classical’ risk factors for cardiovascular disease and challenges to the hemodynamic system like a pregnancy. We would like to illustrate this with a 36-year-old pT1N0Mx breast cancer survivor, who received, after mastectomy and sentinel lymph node procedure, a standard adjuvant regimen consisting of five cycles 5-fluorouracil (500 mg/m²), epirubicin (90 mg/m²) and cyclophosphamide (500 mg/m²), followed by 3-weekly trastuzumab (first dose 8 mg/kg, thereafter 6 mg/kg) at our hospital. Trastuzumab was prematurely discontinued due to persistent asymptomatic decline in left ventricular ejection fraction (LVEF). One year after this treatment she got pregnant; during the third trimester, she developed CHF. The cardiologist initiated conservative treatment with activity limitation. Her complaints resolved after delivery but recurred 1.5 years later. Echocardiography revealed hypokinetic septal wall motion, diastolic dysfunction and a decreased LVEF of 44%. Since then she is on anticongestive medication [angiotensin converting enzyme (ACE) inhibition], which resulted in an improved and ongoing stable cardiac situation currently for 3 years.

Each year, breast cancer is diagnosed in > 400 000 women in Europe, with ∼13% < 44 years of age [2]. As 5% of breast
cancer survivors get pregnant after treatment [3], together with the increasing maternal age at birth of the first child, it is expected that the percentage of breast cancer survivors who become pregnant will rise. Cohort studies indicate that pregnancy-related cardiac morbidity risk is modest for adult childhood cancer survivors treated with anthracyclines; however, the extent and impact of this issue for breast cancer survivors are as yet not clear.

Intensified cardiac function monitoring during pregnancy is recommended in patients with congenital heart disease or cardiac dysfunction of various origins [4] and for childhood cancer survivors treated with potentially cardiotoxic regimens [5]. We advocate a similar approach for adult breast cancer survivors, for which a scheme as presented in Figure 1 might be feasible. In this scheme, women at increased risk for (subclinical) treatment-related cardiotoxicity should undergo screening for potential symptoms and signs of HF before or in the early stage of pregnancy, during, as well as at least 72 h post-partum. Importantly, close collaboration with cardiologists, oncologists, gynecologists and general practitioners is essential to implement such a strategy. Whether prophylactic treatment with medication to avoid CHF is effective is unknown. Diuretics and β-blockade may be effective, but ACE inhibitors and angiotensin II receptor antagonists are contraindicated because of teratogenicity.

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