Local therapy for the primary site in De Novo Stage IV breast cancer

Seema A. Khan
Professor of Surgery, Bluhm Family Professor of Cancer Research,
Breast Surgery,
Northwestern University,
Chicago, Illinois, U.S.A.

Background. Until 2001, the paradigm guiding management of women with de novo metastatic breast cancer (dnMBC) stipulated that primary site locoregional therapy (PSLT) did not alter the course of metastatic disease and was necessary only for palliation of symptoms. Since 2002, retrospective data began questioning this paradigm. However, selection biases driving an observed survival advantage associated with PSLT in dnMBC were quickly recognized and led to several randomized clinical trials (RCTs) addressing this question.

Methods and Results. Four published RCTs have since tested the value of PSLT added to systemic therapy (ST) or not, with overall survival (OS) as the primary endpoint. The results of three published trials show no OS benefit for the addition of PSLT: Indian Tata Memorial, U.S./Canada E2108, and Austrian POSYTIVE (although POSYTIVE did not reach full accrual). The fourth RCT (Turkey, MF07-01) shows an OS benefit for PSLT at 5 years (42% versus 24% in the ST arm, HR 0.66, 95% CI 0.49 – 0.88). However, the 5-year survival in the PSLT arm of MF07-01 is similar to both arms of E2108, suggesting that the worse survival in the ST arm of MF07-01 is a result of biologically worse disease (from imbalanced randomization). Locoregional control was improved by PSLT in all trials but without improvement in quality of life.

Discussion of possible benefit of PSLT in patients with oligometastatic disease continues, but is not supported by recent results of BR002 presented at ASCO in 2022, where 70% of patients had only one metastatic lesion, and 20% of patients had dnMBC with a controlled primary site.

Conclusions. Present evidence fails to refute the 20th century paradigm guiding management of de novo metastatic breast cancer. Discussion continues regarding the survival value of PSLT in patients with bone-only or oligometastases, but unbiased evidence is lacking.