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Correlation of SUV on Early Interim PET with Recurrence-Free Survival and Overall Survival in Primary Operable HER2-Positive Breast Cancer (the TBCRC026 Trial)

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Predictive biomarkers of response to human epidermal growth factor receptor 2 (HER2)–directed therapy are essential to inform treatment decisions. The TBCRC026 trial reported that early declines in tumor SUVs corrected for lean body mass (SUL_{max}) on ^{18}F-FDG PET/CT predicted a pathologic complete response (pCR) to HER2 therapy with neoadjuvant trastuzumab and pertuzumab (HP) without chemotherapy in estrogen receptor (ER)–negative, HER2-positive breast cancer. We hypothesized that ^{18}F-FDG PET/CT SUL_{max} parameters would predict recurrence-free survival (RFS) and overall survival (OS). **Methods:** Patients with stage II/III ER-negative, HER2-positive breast cancer received neoadjuvant HP (n = 88). pCR after HP alone was 22% (18/83), additional nonstudy neoadjuvant therapy was administered in 28% (25/88), and the majority received adjuvant therapy per physician discretion. ^{18}F-FDG PET/CT was performed at baseline and at cycle 1, day 15 (C1D15). RFS and OS were summarized using the Kaplan–Meier method and compared between subgroups using logrank tests. Associations between ^{18}F-FDG PET/CT (≥40% decline in SUL_{max} between baseline and C1D15, or C1D15 $SUL_{max} \leq 3$) and pCR were evaluated using Cox regressions, where likelihood ratio CIs were reported because of the small numbers of events. **Results:** Median follow-up was 53.7 mo (83/88 evaluable), with 6 deaths and 14 RFS events. Estimated RFS and OS at 3 y was 84% (95% CI, 76%–92%) and 92% (95% CI, 87%–98%), respectively. A C1D15 SUL_{max} of 3 or less was associated with improved RFS (hazard ratio [HR], 0.36; 95% CI, 0.11–1.05; P = 0.06) and OS (HR, 0.14; 95% CI, 0.01–0.85; P = 0.03), the latter statistically significant. The association of an SUL_{max} decline of at least 40% (achieved in 59%) with RFS and OS did not reach statistical significance. pCR was associated with improved RFS (HR, 0.25; 95% CI, 0.01–1.24; P = 0.10) but did not reach statistical significance. **Conclusion:** For the first time, we report a potential association between a C1D15 SUL_{max} of 3 or less on ^{18}F-FDG PET/CT and RFS and OS outcomes in patients with ER-negative, HER2-positive breast cancer receiving neoadjuvant HP alone. If confirmed in future studies, this imaging-based biomarker may facilitate early individualization of therapy.

Key Words: FDG PET/CT; HER2-positive; breast cancer; biomarkers; neoadjuvant

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The current standard of care for patients with stage II–III human epidermal growth factor receptor 2 (HER2)–positive breast cancer is neoadjuvant chemotherapy in combination with HER2-directed therapy. This approach has resulted in improved surgical outcomes and high rates of pathologic complete response (pCR), an accepted surrogate endpoint for survival outcomes (*1–4*). Additionally, this strategy offers the opportunity to adapt postoperative treatment based on the response to the therapy (*5–7*). Excellent progress has undoubtedly been made in the treatment of this disease; however, the neoadjuvant approach is not without potential adverse effects. It is recognized that there may be subgroups of patients who need this aggressive standard approach and others who may be cured with less intensive regimens with fewer short- and long-term toxicities. Thus, predictive biomarkers of response to therapy are urgently needed to help tailor treatment recommendations.

Ongoing efforts are investigating a more individualized approach to care. The use of early ^{18}F-FDG PET/CT to predict breast cancer treatment response has been of increasing interest (*8,9*). The TBCRC026 study examined dual HER2 therapy with neoadjuvant trastuzumab and pertuzumab (HP) without chemotherapy in primary operable estrogen receptor (ER)–negative, HER2-positive breast cancer and reported pCR rates of 22%. Early changes in tumor SUVs corrected for lean body mass (SUL_{max}) on ^{18}F-FDG PET/CT predicted pCR to neoadjuvant HP alone, suggesting that this may serve as a potential imaging biomarker of response to therapy (*10*). Indeed, the preoperative period has been recognized as an ideal setting for evaluating surrogate biomarkers for the

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prediction of treatment response, and there is a growing body of evidence to support imaging biomarkers in HER2-positive disease (*11–13*). Few studies, however, have examined the relationship between metabolic response on ^{18}F-FDG PET/CT after neoadjuvant dual HER2 therapy and long-term patient outcomes.

We thus hypothesized that predefined ^{18}F-FDG PET/CT SUL_{max} parameters would be associated with improved recurrence-free survival (RFS) and overall survival (OS) in patients with primary operable ER-negative, HER2-positive breast cancer receiving neoadjuvant HER2-directed therapy. To test this hypothesis, we performed a secondary planned biomarker analysis of the TBCRC026 clinical trial dataset.

MATERIALS AND METHODS

Study Design

TBCRC026 was a single-arm multicenter trial investigating biomarkers of response to preoperative HER2-directed therapy without chemotherapy (Supplemental Fig. 1; supplemental materials are available at http://jnm.snmjournals.org) (*10*). The primary objective was to correlate baseline and early percentage change (by cycle 1, day 15 [C1D15]) in SUL_{max} on ^{18}F-FDG PET/CT of the primary breast cancer with pCR after 4 cycles of neoadjuvant HP, without chemotherapy. The institutional review board approved this study, and all patients gave written informed consent.

Pertuzumab (840-mg loading dose, then 420 mg) and trastuzumab (8 mg/kg loading dose, then 6 mg/kg) were administered intravenously every 3 wk. ^{18}F-FDG PET/CT was performed at baseline and at 15 d after commencement of HP (C1D15). Further neoadjuvant nonstudy therapy (chemotherapy or HER2-directed therapy) was administered as per physician discretion, if there was an incomplete response or disease progression on initial therapy (*10*). Tumor biopsy was undertaken to histologically confirm residual disease, before additional treatment. Any patient who received additional systemic therapy by definition was classified as not achieving pCR after HP alone, per the study protocol. Postoperative systemic therapy and radiation per the standard of care were recommended. All patients regardless of pCR status were recommended to undergo adjuvant chemotherapy if this was not received preoperatively, as per the standard of care.

Eligibility criteria included women 18 y or older with untreated, histologically confirmed infiltrating carcinoma of the breast, clinical stage T2–4(a–c), any N, M0, and tumors expressing ER of no more than 10% and being HER2-positive, by local pathology review (*14,15*). The participants agreed to study-specific procedures including 2 serial ^{18}F-FDG PET/CT scans.

^{18}F-FDG PET/CT Procedures

^{18}F-FDG PET/CT was performed at baseline and at C1D15, with a 3-d window permitted, according to a detailed imaging manual published previously (*10*). Administration of intravenous ^{18}F-FDG was followed by a 60-min uptake phase, with subsequent ^{18}F-FDG PET/CT imaging from the mid skull to the mid femur. All procedures were conducted in conformance with the ^{18}F-FDG PET/CT uniform protocol for imaging in clinical trials and the profile of the Radiologic Society of North America Quantitative Imaging Biomarkers Alliance (*16,17*). Images were assessed centrally, with reviewers masked to clinical information.

SUL_{max} rather than SUV was recorded, as the former is less weight-dependent than the latter and has been shown to be more consistent in normal tissues among individuals. The primary breast cancer lesions were measured by placing a spheric volume over the target area, with avoidance of surrounding normal tissue, and recording the SUL_{max}.

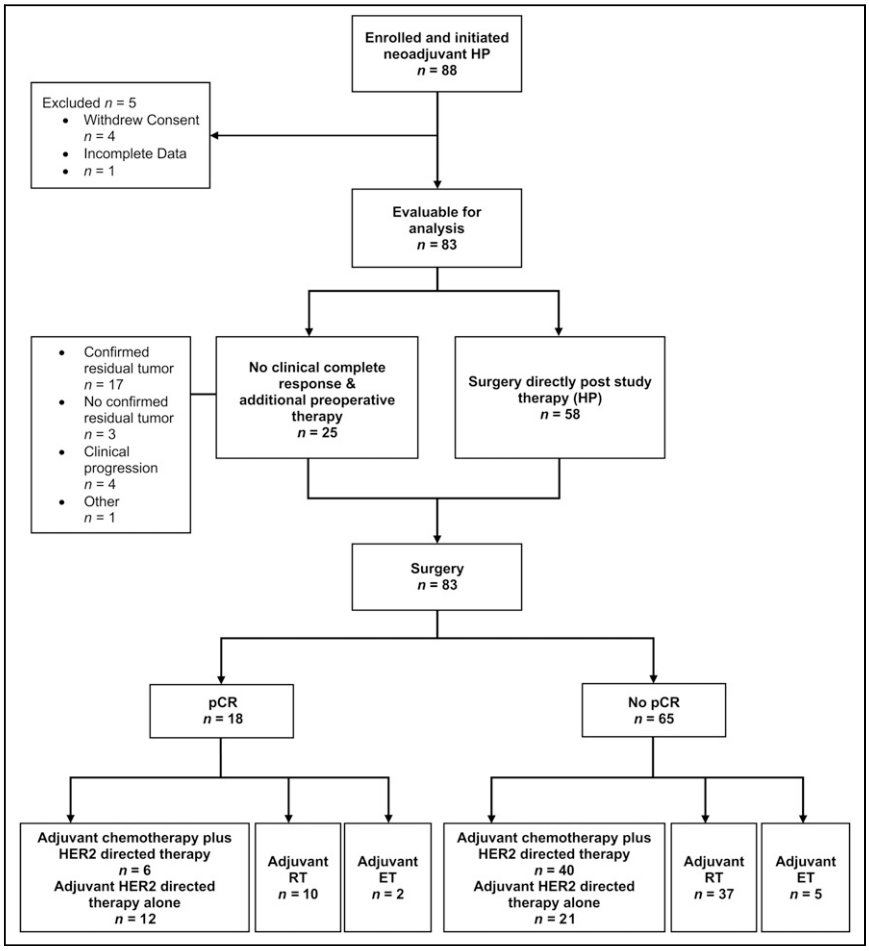

FIGURE 1. Study flowchart indicating therapies received. RT = radiotherapy; ET = endocrine therapy.

Statistical Analysis

The secondary preplanned endpoints reported here include the correlation of, first, at least a 40% decline in SUL_{max} between baseline and C1D15 and, second, a C1D15 SUL_{max} of 3 or less on ^{18}F-FDG PET/CT with RFS and OS. RFS was defined as the interval from the date of the first cycle of treatment to ipsilateral invasive breast tumor recurrence, locoregional recurrence, distant recurrence, or death of any cause, whichever occurred first. OS was defined as the interval from the date of the first cycle of treatment to death (*18*). Both RFS and OS were censored at the last study contact if no events were observed.

To be evaluable for this analysis, participants had to have both baseline and C1D15 ^{18}F-FDG PET/CT performed; SUL_{max}, RFS, and OS data collected; and pCR status after HP (without chemotherapy) evaluated. pCR was determined in the surgical specimen and defined as no viable invasive cancer in the breast and axilla (local pathology review)

TABLE 1
Patient Characteristics (Evaluable Population, $n = 83$)

Characteristic	Data
Age (y)	
Median	58
Range	29–82
Race	
White	70 (84)
Black	7 (8)
Other	6 (7)
Menopausal status	
Premenopausal	27 (33)
Postmenopausal	56 (67)
ECOG performance status	
0	72 (87)
1	11 (13)
Tumor size (cm)	
Median	3.9
Range	2–15
Baseline clinical stage	
II	71 (86)
III	12 (14)
Tumor grade	
2	20 (24)
3	63 (76)
Baseline ER status	
<1%	72 (87)
1%–10%	11 (13)
Additional neoadjuvant therapy	25 (30)
Taxane-based	7 (28)
Carboplatin/taxane	15 (60)
Anthracycline-based	2 (8)
HER2-directed	1 (4)
Surgery	
Mastectomy	46 (55)
Breast-conserving therapy	29 (35)
Not applicable	8 (10)
pCR	
Yes	18 (22)
No	65 (78)
Adjuvant chemotherapy	46 (55)
Taxane-based	21 (46)
Carboplatin/taxane	17 (40)
Anthracycline-based	8 (17)
Adjuvant HER2-targeted therapy	79 (95)
Trastuzumab	56 (67)
HP	22 (27)
Trastuzumab emtansine	1 (1)
Adjuvant radiotherapy	
Yes	47 (57)
No	36 (43)
Adjuvant endocrine therapy	
Yes	7 (8)
No	76 (92)

ECOG = Eastern Cooperative Oncology Group.
Data are number and percentage, except for age and tumor size.

after HP without chemotherapy. Participants with residual disease after 12 wk of HP or clinical progression on HP were classified as non-pCR.

RFS and OS were summarized using the Kaplan–Meier methods and were compared between subgroups using logrank tests. Their associations with ^{18}F-FDG PET/CT (≥40% decline in SUL_{max} between baseline and C1D15, or C1D15 $SUL_{max} \leq 3$) and pCR were evaluated using Cox regressions, with likelihood ratio CIs being reported because of small event numbers.

RESULTS

Patient and Treatment Characteristics

Patient clinicopathologic characteristics were previously described and are available in Supplemental Table 1 (*10*). In summary, 88 women were enrolled from January 2014 to August 2017; 83 were evaluable for the survival analysis. Eighty-five percent of participants completed all 4 cycles of neoadjuvant HP. Twenty-five patients (28%) received additional nonstudy therapy neoadjuvantly and were classified as not obtaining pCR (Table 1). In 22% (18/83) of patients, pCR was observed after 4 cycles of HP alone.

Adjuvant therapy was advised as per the standard of care, and a summary of treatments received is available in Figure 1 and Table 1. There were 22 patients who received no adjuvant or neoadjuvant chemotherapy because of patient or physician preference. Most participants received adjuvant HER2-directed therapy (79/83; 95%), including trastuzumab ($n = 56$; 67%), HP ($n = 22$; 27%), and, in 1 patient with residual disease, adjuvant trastuzumab emtansine, which was not available for this indication in the earlier years of the study. Adjuvant radiation was completed by 57% (47/83), and adjuvant endocrine therapy by 8% (7/83) (Table 1). This was in keeping with the study eligibility criteria, which permitted enrollment of patients with tumors expressing ER of no more than 10%.

RFS and OS Analyses

The median follow-up was 53.7 mo, with 6 deaths and 14 RFS events occurring. The estimated RFS at 3 y was 84% (95% CI, 76%–92%), and the estimated OS at 3 y was 92% (95% CI, 87%–98%).

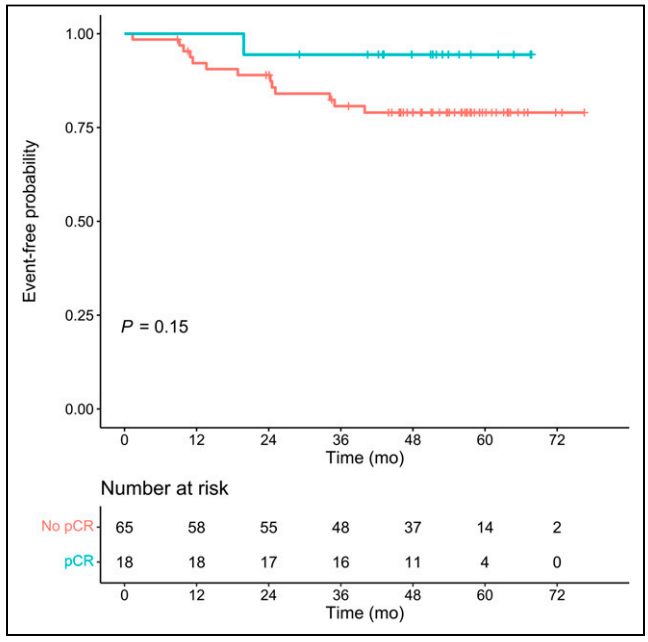

FIGURE 2. RFS by pCR.

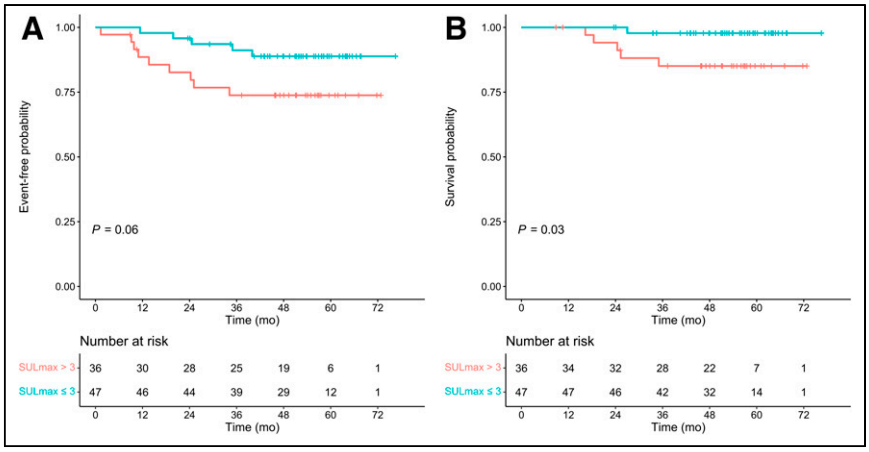

FIGURE 3. (A) RFS by C1D15 SUL_{max} (≤3 vs. >3). (B) OS by C1D15 SUL_{max} (≤3 vs. >3).

RFS events included 1 locoregional recurrence and 13 distant recurrences. The most common sites of distant relapse were lung (n = 4) and liver (n = 2). One patient relapsed with intracranial disease and with liver and bone involvement, and 1 patient developed bone-only disease. Of patients experiencing an RFS event, most (8/14, 57%) were lymph node–positive at baseline and all had at least T2 tumors with a median size of 3.5 cm—tumor characteristics indicating a higher-risk disease. Most events were in patients who did not achieve pCR (13/14, 93%) and occurred despite the majority's (10/14, 71%) receiving a complete course of adjuvant or neoadjuvant chemotherapy in addition to study therapy (HP). In terms of HER2-targeted therapy, most patients with RFS events received trastuzumab monotherapy in the adjuvant setting (8/14, 57%), with the addition of pertuzumab to trastuzumab in 3 patients and trastuzumab emtansine in 1 patient. Only one of these recurrence events, and subsequent death, occurred in a patient who had achieved a pCR after HP alone.

In keeping with the prognostic value of obtaining a pCR in published neoadjuvant breast cancer studies, pCR was associated with improved RFS (hazard ratio [HR], 0.25; 95% CI, 0.01–1.24; P = 0.10) and OS (HR, 0.65; 95% CI, 0.03–4.06; P = 0.69), although the observed trends did not reach statistical significance at this early point in the study (Fig. 2).

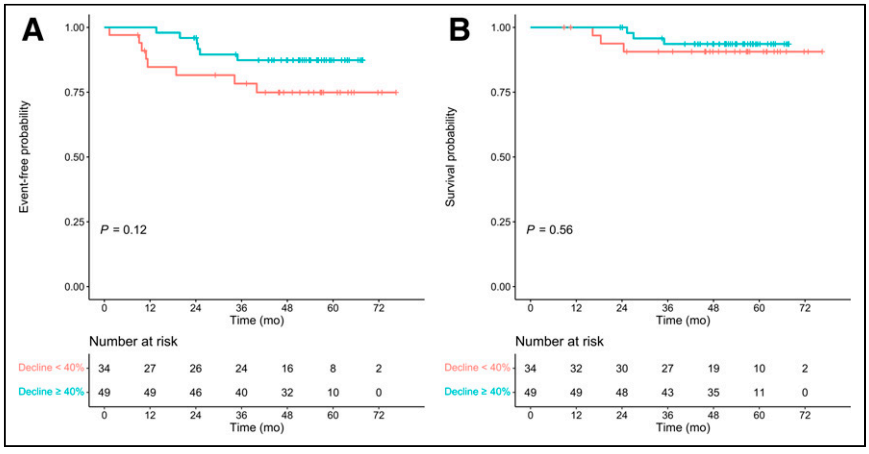

FIGURE 4. (A) RFS by SUL_{max} decline (≥40% vs. <40%). (B) OS by SUL_{max} decline (≥40% vs. <40%).

Correlation of SUL_{max} with OS and RFS

A summary of baseline and C1D15 SUL_{max} has been previously reported and is available for reference in Supplemental Table 1. Regarding the association of SUL_{max} on ^{18}F-FDG PET/CT and survival outcomes, achieving an SUL_{max} of 3 or less by C1D15 was associated with an improved RFS, although not statistically significant (HR, 0.36; 95% CI, 0.11–1.05; P = 0.06). The 3-y RFS probability was 91% (95% CI, 83%–100%) in those with a C1D15 SUL_{max} of 3 or less, versus 74% (95% CI, 60%–90%) in those who did not achieve an SUL_{max} of 3 or less. Interestingly, this biomarker parameter, achieved in 57% of patients, was associated with a statistically significant improvement in OS (HR, 0.14; 95% CI, 0.01–0.85; P = 0.03). The 3-y OS was 98% (95% CI, 94%–100%), versus 85% (95% CI, 74%–98%) in those who failed to achieve an SUL_{max} of 3 or less (Figs. 3A and 3B).

A similar proportion of patients (59%) achieved an SUL_{max} decline of at least 40% between baseline and C1D15 after starting therapy. The association between an SUL_{max} decline of at least 40% and RFS (HR, 0.45; 95% CI, 0.15–1.28; P = 0.13) and OS (HR, 0.62; 95% CI, 0.12–3.37; P = 0.56) did not reach statistical significance (Figs. 4A and 4B). Finally, the adjusted effect of a C1D15 SUL_{max} of more than 3 on RFS did not reach statistical significance in the multivariable Cox regression that included the clinical variables of age, tumor grade, and tumor size (Table 2).

DISCUSSION

In this updated analysis of the TBCRC026 trial, we have demonstrated an association between a C1D15 SUL_{max} of 3 or less on ^{18}F-FDG PET/CT and improved survival outcomes in patients with ER-negative, HER2-positive breast cancer receiving neoadjuvant HER2-directed therapy. Patients receiving HP alone who achieved an SUL_{max} of 3 or less on their C1D15 ^{18}F-FDG PET/CT experienced improved RFS (HR, 0.36; 95% CI, 0.11–1.05; P = 0.06) and statistically significantly improved OS (HR, 0.14; 95% CI, 0.01–0.85; P = 0.03), when compared with those who did not achieve this SUL_{max}. This C1D15 SUL_{max} was achieved in almost 60% of patients, suggesting that it may be a clinically useful biomarker.

One of the earliest reports suggesting that ^{18}F-FDG PET/CT may be a promising biomarker in HER2-positive early breast cancer was from the NeoALTTO PET substudy, which prospectively evaluated whether changes in SUV could predict response to neoadjuvant anti-HER2 therapy comprising trastuzumab and lapatinib (*13*). Metabolic responders (>15% reduction in SUV as determined by the study protocol) had higher pCR rates than nonresponders (42% vs. 21% at week 2; 44% vs. 19% at week 6) (*13*). More recently, studies have focused on neoadjuvant regimens incorporating more modern HER2-directed regimens including

TABLE 2
Univariable and Multivariable Analysis of Association of C1D15 SUL_{max} of 3 or Less with RFS

	Univariable analysis		Multivariable analysis	
Variable	HR	*P*	HR	*P*
C1D15 15 SUL_{max} ≤3	0.36 (0.11–1.05)	0.06	0.41 (0.12–1.22)	0.1
Age	1.02 (0.98–1.07)	0.3	1.04 (0.99–1.1)	0.16
Grade III	0.81 (0.27–2.94)	0.7	0.68 (0.22–2.58)	0.55
Baseline tumor size (cm)	1.21 (0.97–1.45)	0.09	1.23 (0.96–1.5)	0.09

Data in parentheses are 95% CIs.

HP and the antibody–drug conjugate trastuzumab emtansine. The PHERGain phase II trial (n = 356) randomized patients to neoadjuvant docetaxel, carboplatin, and HP (n = 71, group A) or HP alone (n = 285, group B). ^{18}F-FDG PET/CT was performed at baseline and after 2 cycles of treatment (*11*). The investigators defined metabolic response after 2 cycles as an SUV decline of at least 40% from baseline. Approximately 40% of patients who were designated as metabolic responders and continued dual anti-HER2 therapy achieved a pCR without the addition of chemotherapy, whereas nonresponders in group B switched to neoadjuvant chemotherapy combined with HP. The study met its first coprimary endpoint (*11*). The phase II PREDIX HER2 trial found that neoadjuvant therapy with docetaxel and HP had pCR rates similar to those of the single agent trastuzumab emtansine. ^{18}F-FDG PET/CT was performed initially and after cycles 2 and 6 of neoadjuvant treatment. In a secondary analysis, a decrease in the SUV_{max} by at least 68.7% (the median SUV_{max} decline from baseline to cycle 2) was used as a cutoff and was associated with pCR in 57% of patients, versus 17% for patients with an SUV_{max} less than the median (*12*).

The aforementioned studies differed from TBCRC026 in their design, with heterogeneous treatment regimens administered, varying eligibility criteria with regard to ER status, and SUV thresholds generally ranging from 40% to 60% assessed at varying times after initiation of therapy. Only the TBCRC026 trial was designed prospectively to determine the optimum ^{18}F-FDG PET/CT threshold for response as its primary objective (*10*). It is thus clear that further prospective studies are required to validate ^{18}F-FDG PET/CT as a biomarker across several standard treatment regimens. If confirmed, this noninvasive biomarker may be incorporated in future clinical trials aiming to determine the clinical utility of this approach in treatment decision making. This paradigm of biomarker development has led to the successful clinical implementation of interim ^{18}F-FDG PET/CT scanning in lymphoma, with an escalated treatment approach being recommended for patients not achieving the desired ^{18}F-FDG PET/CT response (*19,20*). The EA1211/DIRECT trial (NCT05710328), led by the ECOG-ACRIN research group, will aim to prospectively validate the 40% SUL_{max} decline threshold at 15 d after initiation of therapy as the optimum cut point across standard-of-care HER2-directed neoadjuvant regimens. If this threshold is validated, future trials may consider a response-guided treatment strategy, with the goal of changing practice.

Ultimately, for those with early-stage, curable HER2-positive breast cancer, long-term survival outcomes are the most important endpoint. We found that pCR after HP alone was associated with numerically improved RFS; however, this difference did not reach statistical significance. Whether the prognostic value of pCR in HER2-positive breast cancer is equivalent if obtained with or without chemotherapy has been debated (*21*). In addition to our single-arm study results, others have observed acceptable long-term outcomes with HER2-directed therapy alone, suggesting that achieving a pCR translates into improved outcomes irrespective of the type of neoadjuvant treatment received (*21,22*). That a subset of patients can achieve a pCR and have excellent long-term outcomes without conventional chemotherapy highlights the need for identification of robust biomarkers and a careful study design to select this cohort. This approach is indeed appealing but will require further validation and clinical utility studies before it can be incorporated into routine clinical practice.

We acknowledge the limitations of this study, which include the heterogeneity in the postoperative therapy received and the possible effect of this heterogeneity on evaluating long-term outcomes. The C1D15 SUL_{max} of 3 or less was associated with significantly improved OS in the univariable analysis but did not reach statistical significance in the multivariable analysis. Because this was a secondary analysis, the study was not adequately powered for the endpoints of RFS and OS, and we therefore await confirmatory studies with larger patient numbers. We used the absolute SUL_{max} and its change as our markers of PET metabolic activity, rather than PERCIST 1.0. This study was designed before PERCIST was widely deployed and has identified a larger percentage change for response evaluation (specific to a breast cancer population) than PERCIST 1.0. In addition, some tumors that were small and not ^{18}F-FDG–avid in TBCRC026 might not have been metabolically assessable by PERCIST 1.0 at baseline. Additional studies using PERCIST 1.0 or a modified PERCIST threshold are warranted, as the PERCIST 1.0 responders across a wide range of tumor types appear to have outcomes superior to nonresponders. The change in SUV or SUL_{max} appears to be a more reliable technical metric than absolute SUL_{max}, which can vary by manufacturer and reconstruction method. Thus, the absolute SUL_{max} threshold would be more difficult to apply routinely than the relative change metric. Further studies and technical standardization could help address this concern.

CONCLUSION

To our knowledge, this is the first report of a potential association between a C1D15 SUL_{max} of 3 or less on ^{18}F-FDG PET/CT after 2 wk of neoadjuvant HP alone and RFS and OS outcomes. If confirmed in larger studies, early neoadjuvant interim PET/CT may become a key tool used to adapt therapy for patients with breast cancer in the coming years. Patients demonstrating an early metabolic

response could potentially be spared additional chemotherapy, whereas nonresponders could go on to receive intensification of treatment. The ultimate goal will be to facilitate PET biomarker–informed early individualization of therapy to maximize efficacy and minimize toxicity for patients with early-stage HER2-positive breast cancer. We believe such an approach would be SMART in that it would allow us to "Scan More And Reduce Therapies."

DISCLOSURE

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Mothaffar Rimawi received support for the present article from Genentech; grants from Pfizer; and consulting fees from Macrogenics, SeaGen, Novartis, and AstraZeneca and is coinventor on patent PCT/US21/70543 (Methods for Breast Cancer Treatment and Prediction of Therapeutic Response), filed and owned by the Baylor College of Medicine. Jennifer Specht received support for the present article from the Breast Cancer Foundation, TBCRC026, and Genentech (institutional grant) and has a leadership role with TBCRC (institutional principal investigator). Anna Maria Storniolo received funding from TBCRC (to the institution) for the present article. Vicente Valero received honoraria from Roche and Genentech; received support for meetings and travel from Roche; and is on the advisory board for AstraZeneca. 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Antonio Wolff is on the Data and Safety Monitoring Board for ALEXANDRA/IMpassion030 (a Roche trial led by the Breast International Group) and honoraria from the Breast International Group. Ashley Ciminio-Mathews received payments (to the institution) from BMS. Richard Wahl is on the advisory board for Clarity Pharmaceuticals, Voximetry, and Seno Medical; owns stock in Clarity Pharmaceuticals; has stock options in Voximetry; receives honoraria from BMS, Actinium Pharmaceuticals, Jubilant Draximage, Siemens, Abderra, Radiopharm Therapeutics, and ITM; and receives research support from Actinium Pharmaceuticals, BMS, Bayer, ITM, Siemens, and White Rabbit AI. Vered Stearns received research grants (to the institution) from Abbvie, Biocept, Novartis, Pfizer, Puma Biotechnology, and QUE Oncology; became a member of the advisory board for Novartis on October 25, 2021; is chair of the Data and Safety Monitoring Board for AstraZeneca; and received nonfinancial support from Foundation Medicine. 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KEY POINTS

QUESTION: We hypothesized that ^{18}F-FDG PET/CT SUL_{max} parameters would predict RFS and OS in patients with early-stage ER-negative, HER2-positive breast cancer receiving HP without chemotherapy.

PERTINENT FINDINGS: Patients underwent ^{18}F-FDG PET/CT at baseline and at C1D15. The metabolic endpoint of a C1D15 SUL_{max} of 3 or less was associated with a statistically significant improvement in OS (HR, 0.14; $P = 0.03$).

IMPLICATIONS FOR PATIENT CARE: If validated in future studies, this noninvasive imaging biomarker may facilitate early adoption of therapy for patients with early-stage HER2-positive breast cancer, resulting in improved efficacy and reduced toxicity.

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