INTERVIEW

Claudine Isaacs, MD

Dr Isaacs is Professor of Medicine and Oncology and Co-Director of the Breast Cancer Program at Georgetown University's Lombardi Comprehensive Cancer Center in Washington, DC.

Tracks 1-12

Track 1 **Case discussion:** A 47-year-old woman with a 3.4-cm, poorly differentiated, triple-negative IDC

Track 2 Surgical clip placement for patients undergoing neoadjuvant chemotherapy for BC

Track 3 Adjuvant and neoadjuvant options for newly diagnosed TNBC

Track 4 NSABP-B-51: A Phase III trial evaluating radiation therapy in patients with positive axillary nodes prior to neoadjuvant chemotherapy that convert to pathologically negative axillary nodes after neoadjuvant chemotherapy

Track 5 Alliance A011202: An ongoing Phase III trial evaluating the role of axillary lymph node dissection for patients who have positive sentinel lymph node disease after neoadjuvant chemotherapy

Track 6 Approach to administering neoadjuvant therapy for patients with HER2-positive BC

Track 7 NSABP-B-50-I (KATHERINE): A Phase III trial of T-DM1 versus trastuzumab as adjuvant therapy for patients with HER2-positive BC who have residual tumor in the breast or axillary nodes after neoadjuvant treatment

Track 8 Viewpoint on the results of a joint analysis of the IBCSG TEXT and SOFT trials evaluating adjuvant exemestane with ovarian suppression in premenopausal BC

Track 9 **Case discussion:** A 40-year-old woman with a 2-cm, ER/PR-positive, HER2-negative, node-negative IDC and a 21-gene Recurrence Score of 12

Track 10 Use of the 21-gene Recurrence Score to guide adjuvant chemotherapy decision-making for patients with limited nodal involvement

Track 11 **Case discussion:** A 58-year-old woman with de novo metastatic ER/PR-positive, HER2-negative IDC

Track 12 Perspective on the results of 2 randomized Phase III trials evaluating primary tumor resection for patients with mBC

Select Excerpts from the Interview

Track 7

DR LOVE: Can you talk about the ongoing NSABP-B-50-I trial of T-DM1 versus trastuzumab for patients with residual disease at surgery after receiving preoperative systemic treatment (4.1)?

DR ISAACS: That is an interesting and important trial. I view residual disease after neoadjuvant chemotherapy differently in patients with hormone receptor-positive and hormone receptor-negative breast cancer. For patients with hormone receptor-positive disease, it is important to inform them that whether or not they achieve a pCR is not as clinically significant. The trial will determine whether T-DM1 is better than

trastuzumab and will be worthwhile for patients with HER2-positive disease with significant residual tumors.

4.1

NSABP-B-50-I (KATHERINE): Ongoing Phase III Trial Evaluating T-DM1 versus Trastuzumab as Adjuvant Therapy for Patients with HER2-Positive Primary Breast Cancer with Pathologic Residual Tumor in the Breast or Axillary Lymph Node After Preoperative Therapy

Protocol ID: NCT01772472

Target Accrual: 1,484

Eligibility

- HER2-positive invasive breast cancer
- Clinical Stage T1-4/N0-3/M0 at presentation
- No Stage T1a/bN0 or Stage IV breast cancer allowed

R

T-DM1 (IV)
3.6 mg/kg every 3 weeks for 14 cycles

Trastuzumab (IV)
6 mg/kg every 3 weeks for 14 cycles

www.clinicaltrials.gov. Accessed September 2014.

Track 12

DR LOVE: Would you discuss the results of the 2 randomized Phase III trials presented at the 2013 San Antonio Breast Cancer Symposium evaluating the role of locoregional therapy for women presenting with de novo Stage IV disease?

DR ISAACS: One of the trials was conducted in India, and it evaluated women with complete or partial responses to first-line chemotherapy (Badwe 2013; [4.2]). These patients were randomly assigned to locoregional therapy or no locoregional therapy, and the trial produced no difference in overall survival. The issue with this study is that none of the women with HER2-positive disease received HER2-targeted therapy. We know what a profound effect that has on treatment outcome. Also, it was not a

4.2

Results of 2 Phase III Trials Evaluating Primary Tumor Resection for Patients with Stage IV Breast Cancer

Study design	Tata Memorial (India)[1] (n = 350)	MF 07-01 (Turkey)[2] (n = 293)
Initial systemic therapy before randomization	CEF with or without a taxane	None
Primary endpoint	Overall survival	Overall survival
Efficacy		
Overall survival	LRT vs no LRT HR 1.04, $p = 0.79$	Surgery vs systemic therapy HR 0.76, $p = 0.20$
Bone-only metastases	HR 1.43, p = NR	HR 0.60, $p = 0.15$
Solitary bone metastasis	NR	HR 0.23, $p = 0.02$

CEF = cyclophosphamide/epirubicin/fluorouracil; LRT = locoregional therapy; HR = hazard ratio; NR = not reported

[1] Badwe R et al. San Antonio Breast Cancer Symposium 2013;**Abstract S2-02**; [2] Soran A et al. San Antonio Breast Cancer Symposium 2013;**Abstract S2-03**.

big trial, with only 350 enrolled patients. One of the questions regarding the trial is whether the approach applies to our current standard, especially for patients with HER2-positive disease.

The other Phase III trial was from Turkey (Soran 2013; [4.2]). It randomly assigned women who were diagnosed at presentation with metastatic disease to up-front systemic therapy with or without locoregional therapy. Thereafter, patients who received systemic therapy only were allowed to undergo locoregional therapy if the treating physician or healthcare team decided that it was needed for palliation. A 4-month improvement in overall survival was found for women who received up-front locoregional therapy, although the difference was not statistically significant.

The results suggested a benefit for those with a solitary bone metastasis. I believe that an issue with the Turkish trial is that not all the women from whom biopsies were obtained had bone metastases. Perhaps some had bone islands or benign masses.

It is clear from these 2 trials that we need to temper our enthusiasm for locoregional therapy. There is no question about that. In the United States I believe we had a tendency to favor surgery for these women before the results of the Indian and Turkish trials were presented.

Although the 2 trials produced negative results and did not definitely answer the question about the benefits of up-front locoregional therapy for Stage IV disease, the results should encourage us to enroll patients in the ongoing clinical trials that will more definitively answer the question. The ongoing ECOG-E2108 trial will address the question of whether early surgery is more effective than palliative therapy for patients with metastatic breast cancer (4.3). ■

4.3

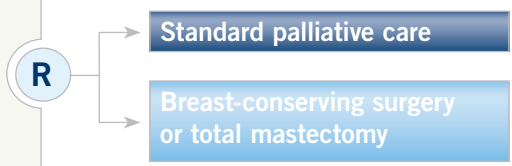
ECOG-E2108: Ongoing Phase III Trial of the Value of Early Local Therapy for the Intact Primary Tumor in Patients with Metastatic Breast Cancer

Protocol ID: NCT01242800

Target Accrual: 880

Eligibility

- Intact, invasive breast cancer (Stage IV disease)
- Involvement of at least 1 organ system with distant metastatic disease
- No recurrent disease
- No synchronous contralateral breast cancer



Khan SA. San Antonio Breast Cancer Symposium 2013. No abstract available; **www.clinicaltrials.gov**. Accessed September 2014.

SELECT PUBLICATIONS

Badwe R et al. **Surgical removal of primary tumor and axillary lymph nodes in women with metastatic breast cancer at first presentation: A randomized controlled trial.** San Antonio Breast Cancer Symposium 2013;**Abstract S2-02**.

Khan SA. **Does primary tumor resection improve survival for patients with Stage IV breast cancer?** San Antonio Breast Cancer Symposium 2013. No abstract available

Soran A et al. **Early follow up of a randomized trial evaluating resection of the primary breast tumor in women presenting with de novo stage IV breast cancer; Turkish study (protocol MF07-01).** San Antonio Breast Cancer Symposium 2013;**Abstract S2-03**.