Dana-Farber Cancer Institute

PS3-11-04, Abstract #1079

The ATOP TRIAL: Adjuvant Ado-Trastuzumab Emtansine (T-DM1) for Older Patients with Human Epidermal Growth Factor Receptor 2 (HER2)-Positive Breast Cancer

HARVARD MEDICAL SCHOOL

NCT03587740 and formerly Academic and Community Research United (ACCRU) RU011301I

Rachel A Freedman[1], Hillary Heiling[1], Kathryn J Ruddy[2], Lauren Rogak[2], Mina Sedrak[3], Amylou Dueck[2], Heshan Liu[2], Ashton Fraettarelli[1], Stefan Atanasov[1], Michelle DeMeo[1], Paulina Lange[1], Adriana Perilla Glen[1], Sarah Sinclair[4], Deborah Dillon[5], Joanne Mortimer[6], Mary Anne Fenton[7], Jeanna Walsh[1], Laura Spring[8], Hyman Muss[9], Natalie Sinclair[1], Erika Hamilton[10], Chau Dang[11], Sara Giordano[1], Meredith Faggen[1], Steven Lo[12], Charles Kuzma[13], Sheila Lemke[14], Philip Stella[15], Rex Mowat[16], Mary Wilkinson[17], Julia Rauch[18], Nabihah Tayob[2], Eric Winer[19]

[1]Dana-Farber Cancer Institute (Boston, MA); [2]Mayo Clinic (Rochester, MN [KJR], and Phoenix, AZ [LR, AD]); [3]UCLA (LA, CA); [4]Northern Light (Bangor, ME), [5]Brigham and Women's Hospital (Boston, MA),[6]City of Hope (Duarte, CA), [7]Brown University (Providence, RI), [8]Massachusetts General Hospital (Boston, MA), [9]University of North Carolina [UNC] (Chapel Hill, NC), [10]Sarah Cannon Research Institute (Nashville, TN); [11]Memorial Sloan Kettering Cancer Center (New York, NY), [12] Stamford Health (Stamford, CT); [13]First Health of the Carolinas (Pinehurst, NC) [14]SUNY Upstate (Syracuse, NY); [15]Trinity Health (Ann Arbor, MI), [16]Toledo Community Oncology Program (Toledo, OH); [17]Medical Oncology and Hematology Associates of N. Virginia (Fairfax, VA), [18]UNC Rex (Garner, NC); [19] Yale Cancer Center (New Haven, CT)

BACKGROUND

- 10-15% of cancers in older women are HER2+ (Laird-Fick, JGO, 2013)
- Despite expected benefits of trastuzumab-based regimens, many older women do not receive standard adjuvant therapy, in large part because of toxicity and comorbidity concerns (Freedman et al, BCRT 2014, Reeder-Hayes et al JCO 2016)
- T-DM1 is tolerable and highly efficacious in the metastatic, post neoadjuvant, and lower-risk/stage I HER2+ settings

→ Appealing (potential) alternative adjuvant treatment option for older patients

Study Hypothesis: T-DM1 will show promising efficacy and will be tolerable for older patients

STUDY OBJECTIVES

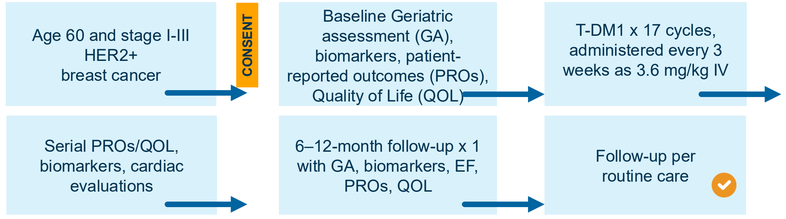
Primary Objective: Invasive disease-free survival (iDFS) (STEEP) - occurrence of any of the following:

- Ipsilateral invasive breast cancer/regional recurrence
- Distant recurrence
- Death attributable to any cause
- Contralateral invasive breast cancer
- Second non-breast invasive cancer, excluding in-situ events

Secondary Objectives: Overall survival (OS), iBCFS (invasive breast cancer-related events or any-cause deaths), toxicity

Correlative Objectives: {results all forthcoming}: associations of toxicity & outcomes with Geriatric assessment (GA) measures, patient-reported outcomes, quality of life, biomarkers of aging

Figure 1. STUDY SCHEMA



METHODS – TRIAL DESIGN

- Single-arm, open-label, multicenter, phase 2 study
- Summarized iDFS for evaluable patients with Kaplan-Meier (K-M) curve
- 5-year iDFS landmark was estimated from K-M curve, and a 2-sided 90% CI will be provided
- Characterized toxicity

KEY ELIGIBILITY

Key Inclusions

- Age ≥60, stage I-III breast cancer
- HER2+ disease by central review
- ECOG PS 0-2
- Cardiac ejection fraction ≥ 50%
- Surgical excision with negative margins; Treatment of axilla per clinician discretion
- Patient declined standard treatment *OR* patient was not a candidate for standard therapy

Key Exclusions

- T4 tumors
- Acute cardiac disease
- Concurrent 2nd malignancy or past malignancy with >30% estimated 5-year risk of relapse
- Prior T-DM1 or trastuzumab
- Any neoadjuvant chemotherapy
- Synchronous HER2-negative breast cancer requiring chemotherapy

111 evaluable patients started protocol T-DM1 during 12/2015 - 9/2020; Median follow-up 4.9 years (IQR 4.2, 5.5 years)

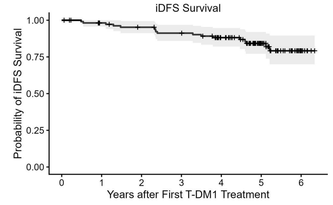
RESULTS – SELECTED BASELINE CHARACTERISTICS [N=111]

Age (yrs) (Median 71, range 60-88)	n (%)	Selected Comorbidity (patient report)	n (%)
60-65	33 (29.7%)	Hypertension	49 (44.1%)
66-70	22 (19.8%)	Cardiac disease	22 (19.8%)
71-75	25 (22.5%)	Diabetes	14 (12.6%)
76-80	18 (16.2%)	Stroke	5 (4.5%)
>80	13 (11.7%)	**Cancer Stage**	
Race		I	77 (69.4%)
White	79 (71.2%)	IIA	27 (24.3%)
Black	5 (4.5%)	IIB	2 (1.8%)
Other/missing	27 (24.3%)	IIIA	4 (3.6%)
ECOG PS		IIIC	1 (0.9%)
0	88 (79.3%)	**Tumor Size (pathologic T stage)**	
1	21 (18.9%)	<1 cm	22 (19.8%)
2	2 (1.8%)	1-2 cm	56 (50.5%)
Reason for Enrollment		2.1-5 cm	29 (26.1%)
Patient declined std treatment	77 (69.4%)	>5 cm	4 (3.6%)
Comorbidity concerns	4 (3.6%)	**Node Positive**	16 (14.4%)
Concerned std treatment too toxic	18 (16.2%)	**Hormone Receptor Positive**	78 (70.3%)
Other/unknown	12 (10.8%)	**Breast Preservation**	66 (59.5%)

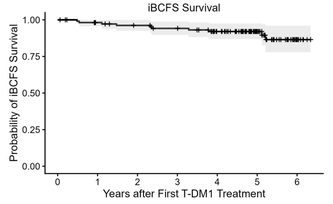
RESULTS – iDFS AND iBCFS EVENTS

iDFS Events	n (%)
Ipsilateral invasive breast cancer	1 (0.9%)
Contralateral invasive breast cancer	3 (2.7%)
Distant recurrence (n=2 for chest wall, n=1 for liver)	3 (2.7%)
Non-breast cancer primary (n=1 for colon, biliary, mesothelioma, rectal; n=3 for skin)	7 (6.3%)
Death due to breast cancer	2 (1.8%)
Death due to other reason (pulmonary infection, deemed not related to tx)	1 (0.9%)
Alive at last follow-up	94 (84.7%)
iBCFS Events	**n (%)**
Ipsilateral invasive breast cancer	1 (0.9%)
Contralateral invasive breast cancer	3 (2.7%)
Distant recurrence	3 (2.7%)
Death due to breast cancer	2 (1.8%)
Death due to other reason	1 (0.9%)
Alive at last follow-up	94 (84.7%)
Censored at new primary non-breast invasive cancer	7 (6.3%)

RESULTS – Figure 2. iDFS and iBCFS



N	Events	3-year iDFS (90% CI)	5-year iDFS (90% CI)
111	17	91% (86%, 97%)	84% (77%, 92%)



N	Events	3-year iBCFS (90% CI)	5-year iBCFS (90% CI)
111	10	94% (90%, 99%)	92% (87%, 97%)

Toxicity: Possibly/probably/definitely related to treatment (grade 2+) reported in n=5+

TOXICITY	GRADE 2+	GRADE 2	GRADE 3	GRADE 4
All Toxicities	**91 (82%)**	**59 (53.2%)**	**31 (27.9%)**	**1 (0.9%)**
Fatigue	34 (30.6%)	32 (28.8%)	2 (1.8%)	0 (0%)
Peripheral Sensory Neuropathy	22 (19.8%)	18 (16.2%)	4 (3.6%)	0 (0%)
Anemia	15 (13.5%)	10 (9%)	5 (4.5%)	0 (0%)
Anorexia	13 (11.7%)	13 (11.7%)	0 (0%)	0 (0%)
Aspartate Aminotransferase Increased	13 (11.7%)	11 (9.9%)	2 (1.8%)	0 (0%)
Nausea	13 (11.7%)	13 (11.7%)	0 (0%)	0 (0%)
Alanine Aminotransferase Increased	11 (9.9%)	6 (5.4%)	5 (4.5%)	0 (0%)
Dry Mouth	10 (9.0%)	9 (8.1%)	1 (0.9%)	0 (0%)
Urinary Tract Infection	10 (9%)	10 (9%)	0 (0%)	0 (0%)
Neutrophil Count Decreased	9 (8.1%)	6 (5.4%)	3 (2.7%)	0 (0%)
Bilirubin Increased	9 (8.1%)	8 (7.2%)	1 (0.9%)	0 (0%)
Headache	8 (7.2%)	6 (5.4%)	2 (1.8%)	0 (0%)
Platelet Count Decreased	8 (7.2%)	6 (5.4%)	1 (0.9%)	1 (0.9%)
Myalgia	7 (6.3%)	7 (6.3%)	0 (0%)	0 (0%)
Hypertension	7 (6.3%)	5 (4.5%)	2 (1.8%)	0 (0%)
Watering Eyes	6 (5.4%)	6 (5.4%)	0 (0%)	0 (0%)
Weight Loss	6 (5.4%)	5 (4.5%)	1 (0.9%)	0 (0%)
Alkaline Phosphatase Increased	5 (4.5%)	5 (4.5%)	0 (0%)	0 (0%)
Dysgeusia	5 (4.5%)	5 (4.5%)	0 (0%)	0 (0%)
Lymphocytes Decreased	5 (4.5%)	3 (2.7%)	2 (1.8%)	0 (0%)
Constipation	5 (4.5%)	5 (4.5%)	0 (0%)	0 (0%)
Dyspnea	5 (4.5%)	4 (3.6%)	1 (0.9%)	0 (0%)
Epistaxis	5 (4.5%)	5 (4.5%)	0 (0%)	0 (0%)
Mucositis Oral	5 (4.5%)	4 (3.6%)	1 (0.9%)	0 (0%)

T-DM1 Total Cycles Received	n (%)
1-9 cycles	19 (17.1%)
10-16 cycles	27 (24.3%)
17 cycles	65 (58.6%)

Off Treatment Reason	n (%)
Treatment Completed Per Protocol	65 (58.6%)
Relapse During Active Treatment	1 (0.9%)
Adverse Event / Side Effect / Complication	32 (28.8%)
Other Complicating Disease	1 (0.9%)
Patient Withdrew	7 (6.3%)
Death on study	1 (0.9%)
Other	4 (3.6%)

STUDY LIMITATIONS

- Treatment paradigms have shifted to neoadjuvant treatment for stage II-III patients
- Some subgroups small, limiting detailed analysis by tumor features and age

CONCLUSIONS

- ATOP demonstrated encouraging 5-year iDFS and manageable toxicity, with only 3 distant recurrences and 2 breast cancer-related deaths among 111 pts
- Despite higher-risk disease and more competing non-breast cancer events, breast cancer outcomes were similar to historical controls (e.g., 97% in 'ATEMPT')
- Future endpoints include analyses of patient-reported outcomes, biomarkers of aging, longitudinal functional status.

Study funded by Gateway for Cancer Research, Susan G Komen, the Gloria Spivak Faculty Advancement Fund, and Genentech. We thank all of the patients who participated in this study.

This presentation is the intellectual property of the author/presenter. Contact them at for permission to reprint and/or distribute.