Supplementary File

Treatment discontinuation, patient-reported toxicities and quality-of-life by age following trastuzumab emtansine or paclitaxel/trastuzumab (ATEMPT)

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**Supplementary Table 1: Baseline characteristics for patients included and excluded from analysis**

| Characteristics                              | In analysis (n=366) | Excluded (n=131) | Overall ATEMPT population (N=497) |
|----------------------------------------------|---------------------|------------------|-----------------------------------|
| **Age, years**                              |                     |                  |                                   |
| Mean (SD)                                   | 56.11 (10.48)       | 56.16 (10.29)    | 56.13 (10.42)                    |
| Median (range)                              | 56.69 (23.24, 85.90)| 56.19 (34.05, 78.56)| 56.52 (23.24, 85.90)          |
| ≤50 years                                   | 124 (34%)           | 45 (34%)         | 169 (34%)                        |
| >50 years                                   | 242 (66%)           | 86 (66%)         | 328 (66%)                        |
| **Sex (n, %)**                              |                     |                  |                                   |
| Female                                      | 366 (100%)          | 125 (95%)        | 491 (99%)                        |
| Male                                        | 0 (0%)              | 6 (5%)           | 6 (1%)                           |
| **Race (n, %)**                             |                     |                  |                                   |
| Asian                                       | 18 (5%)             | 8 (6%)           | 26 (5%)                          |
| Black                                       | 22 (6%)             | 6 (5%)           | 28 (6%)                          |
| White                                       | 307 (84%)           | 113 (86%)        | 420 (85%)                        |
| More than one/Other/Unknown                 | 19 (5%)             | 4 (3%)           | 23 (5%)                          |
| **Ethnicity (n, %)**                        |                     |                  |                                   |
| Hispanic                                    | 7 (2%)              | 5 (4%)           | 12 (2%)                          |
| Non-Hispanic                                | 332 (91%)           | 117 (89%)        | 449 (90%)                        |
| Unknown                                     | 27 (7%)             | 9 (7%)           | 36 (7%)                          |
| **Baseline menopausal status (n, %)**       |                     |                  |                                   |
| Premenopausal                               | 133 (36%)           | 34 (26%)         | 167 (34%)                        |
| Postmenopausal                              | 233 (64%)           | 69 (53%)         | 302 (61%)                        |
| Missing                                     | 0 (0%)              | 28 (21%)         | 28 (6%)                          |
| **Tumor Size (n, %)**                       |                     |                  |                                   |
| ≤0.1 cm                                     | 6 (2%)              | 5 (4%)           | 11 (2%)                          |
| >0.1-0.5 cm                                 | 52 (14%)            | 18 (14%)         | 70 (14%)                         |
| >0.5-1.0 cm                                 | 121 (33%)           | 46 (35%)         | 167 (34%)                        |
| >1.0-1.5 cm                                 | 117 (32%)           | 36 (27%)         | 153 (31%)                        |
| >1.5-2.0 cm                                 | 70 (19%)            | 26 (20%)         | 96 (19%)                         |
| **Treatment arm (n, %)**                    |                     |                  |                                   |
| TH                                          | 82 (22%)            | 32 (24%)         | 114 (23%)                        |
| T-DM1                                       | 284 (78%)           | 99 (76%)         | 383 (77%)                        |
| **ER/PR expression (n, %)**                 |                     |                  |                                   |
| Negative (<1%)                              | 90 (25%)            | 34 (26%)         | 124 (25%)                        |
| Low Positive (1-9%)                         | 24 (7%)             | 4 (3%)           | 28 (6%)                          |
| Positive (>=10%)                            | 252 (69%)           | 93 (71%)         | 345 (69%)                        |
| **Surgery type (n, %)**                     |                     |                  |                                   |
| Lumpectomy                                  | 231 (63%)           | 76 (58%)         | 307 (62%)                        |
| Mastectomy                                  | 134 (37%)           | 55 (42%)         | 189 (38%)                        |
| Unilateral                                  | 74 (20%)            | 27 (21%)         | 101 (20%)                        |
| Bilateral                                   | 57 (16%)            | 27 (21%)         | 84 (17%)                         |
| Unknown type*                               | 3 (1%)              | 1 (0%)           | 4 (1%)                           |
| Missing                                     | 1 (0%)              | 0 (0%)           | 1 (0%)                           |
| **Radiotherapy (n, %)**                     |                     |                  |                                   |
| Yes                                         | 238 (65%)           | 70 (53%)         | 308 (62%)                        |
| No                                          | 126 (34%)           | 56 (43%)         | 182 (37%)                        |
| Missing                                     | 2 (1%)              | 5 (4%)           | 7 (1%)                           |
| **Endocrine therapy at 18 months (n, %)**   |                     |                  |                                   |
| Yes                                         | 235 (64%)           | 85 (65%)         | 320 (64%)                        |
| No                                          | 131 (36%)           | 46 (35%)         | 177 (36%)                        |

SD, standard deviation; ER, estrogen receptor; PR, progesterone receptor; T-DM1, trastuzumab emtansine; TH, paclitaxel plus trastuzumab
Table shows interactions terms for arm*age-group taken from linear (RSCL, WPAI, FACT-B) and logistic (APA, PNQ) multivariable regression models. Values are mean differences/odds ratios measured between age-groups (within each arm) or between arms (within each age group) and respective interaction p-values. Variables tested include age-group, arm, arm*age-group, race, early discontinuation, surgery type, receipt of radiotherapy, receipt of endocrine therapy at 18 months and the respective PRO score at baseline. Unless otherwise noted, for FACT-B and WPAI:SHP a positive score indicates superior outcome for the first comparator group, for RSCL a positive score indicates inferior outcome for the first comparator group.

T-DM1, trastuzumab emtansine; TH, paclitaxel plus trastuzumab; FACT-B, Functional Assessment of Cancer Therapy-Breast Cancer; RSCL, Rotterdam Symptom Checklist; WPAI:SHP, Work Productivity and Activity Impairment Questionnaire: Specific Health Problem; APA, Alopecia Patient Assessment; PNQ, Patient Neurotoxicity Questionnaire
Patient-reported outcome measure | Mean difference (95% CI)
--- | ---
**FACT-B total score**
≤ 50 | 6.48 (6.01, 12.46)
> 50 | -1.51 (-6.31, 3.29)
**Physical well-being**
≤ 50 | 1.35 (0.15, 2.56)
> 50 | 1.43 (0.26, 2.60)
**Social/family well-being**
≤ 50 | 2.81 (0.64, 4.98)
> 50 | -0.11 (-1.04, 1.43)
**Emotional well-being**
≤ 50 | 0.54 (-0.74, 1.82)
> 50 | 0.20 (-0.82, 1.21)
**Functional well-being**
≤ 50 | 1.82 (-0.24, 3.88)
> 50 | -0.49 (-2.13, 1.16)
**Breast cancer subscale**
≤ 50 | 1.92 (0.05, 3.79)
> 50 | -0.41 (-1.95, 1.12)
**Physical symptom distress***
≤ 50 | -0.14 (-2.64, 2.36)
> 50 | -0.54 (-2.32, 1.44)
**Psychological distress***
≤ 50 | 0.65 (-0.69, 2.00)
> 50 | -0.19 (-1.29, 0.91)
**Activity level**
≤ 50 | 0.44 (-0.89, 1.77)
> 50 | 0.40 (-0.62, 1.41)
**Overall valuation of life***
≤ 50 | 0.32 (-0.12, 0.77)
> 50 | 0.02 (-0.32, 0.35)
**% time work missed due to breast cancer***
≤ 50 | -2.39 (-9.94, 5.17)
> 50 | -0.18 (-9.14, 8.77)
**% impairment at work due to breast cancer***
≤ 50 | 4.95 (-1.84, 11.75)
> 50 | 2.63 (-4.57, 9.83)
**% overall work impairment due to breast cancer***
≤ 50 | 3.59 (-4.20, 11.39)
> 50 | 2.60 (-6.85, 11.21)
**% activity impairment due to breast cancer***
≤ 50 | 5.68 (-1.96, 13.32)
> 50 | 6.53 (0.28, 12.79)

Patient-reported outcome measure | Odds Ratio (95% CI)
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**APA - any hair loss***
≤ 50 | 0.51 (0.10, 2.54)
> 50 | 1.62 (0.63, 4.15)
**PNQ - Any moderate, moderate-severe or severe neuropathy***
≤ 50 | 3.13 (0.98, 10.06)
> 50 | 3.00 (1.46, 6.17)

*Reference group reversed so that positive score indicates superior outcome for patients treated with T-DM1*
Supplementary Note: List of Participating Institutional Review Boards (IRBs)

The following sites approved this study:

1. Dana Farber/ Harvard Cancer Center
2. Sarah Cannon Research Institute
3. University of North Carolina
4. Eastern Maine Medical Center (Northern Light)
5. Indiana University Washington University (St. Louis)
6. The Ohio State University
7. University of California, San Francisco
8. Johns Hopkins University
9. MD Anderson Cancer Center
10. St Luke Mountain State Tumor Institute
11. Loyola University
12. Memorial Sloan Kettering Cancer Center
13. Duke University Medical Center
14. North Shore-Long Island Jewish Health System
15. Baylor College of Medicine
16. Georgetown University
17. University of Chicago
18. The Mayo Clinic Cancer Center
19. University of Michigan
20. University of Pittsburgh Medical Center
21. University of Washington
22. University of Alabama
23. Georgetown University
24. Vanderbilt University