Association between BMI, vitamin D, and estrogen levels in postmenopausal women using adjuvant letrozole: A prospective study

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**Supplementary Figure 1.** (A) Box and whisker plot representing median, first and third quartiles and minimum and maximum values of estradiol or (B) estrone in 112 women at day 1 (typical use of letrozole) and day 29 (2.5 mg/day of monitored letrozole use) (C) CRP, insulin, and leptin are markers of inflammation, insulin resistance, and adiposity, respectively. Correlation between these markers and estradiol or estrone.
### Supplementary Table 1. Additional baseline characteristics of patients.
Data obtained from standardized entrance questionnaire and baseline bloodwork at study enrollment.

| Characteristic                        | Observation (Day 1-28; n=112) | Intervention (Day 29-58; n=31) |
|---------------------------------------|-------------------------------|-------------------------------|
| Untanned skin colour                  |                               |                               |
| Very Fair/Fair                        | 76 (67.9%)                    | 18 (58.1%)                    |
| Medium/Olive                          | 30 (26.8%)                    | 9 (29%)                       |
| Brown/Very Dark                       | 6 (5.4%)                      | 4 (12.9%)                     |
| Baseline glucose (mmol/L)             |                               |                               |
| Mean (SD)                             | 5.6 (1.2)                     | 5.9 (1.9)                     |
| Median (Range)                        | 5.3 (4.5 - 14.5)              | 5.4 (4.6 - 14.5)              |
| Previous or ongoing smoking           |                               |                               |
| Yes                                   | 42 (37.5%)                    | 12 (38.7%)                    |
| No                                    | 70 (62.5%)                    | 19 (61.3%)                    |
| Previous or ongoing alcohol consumption |                               |                               |
| Yes                                   | 56 (50%)                      | 14 (45.2%)                    |
| No                                    | 56 (50%)                      | 17 (54.8%)                    |
| Characteristic | Observation (Day 1-28; n=112) | Intervention (Day 29-58; n=31) |
|---------------|-------------------------------|--------------------------------|
| T-stage       |                               |                                |
| T1            | 46 (41.1%)                    | 11 (35.5%)                     |
| T2            | 46 (41.1%)                    | 16 (51.6%)                     |
| T3            | 15 (13.4%)                    | 3 (9.7%)                       |
| T4            | 3 (2.7%)                      | 1 (3.2%)                       |
| TX            | 2 (1.8%)                      | 0 (0%)                         |
| N-stage       |                               |                                |
| N0            | 59 (52.7%)                    | 14 (45.2%)                     |
| N1            | 34 (30.4%)                    | 10 (32.3%)                     |
| N2            | 11 (9.8%)                     | 4 (12.9%)                      |
| N3            | 8 (7.1%)                      | 3 (9.7%)                       |
| Histological diagnosis |               |                                |
| Ductal        | 83 (74.1%)                    | 27 (87.1%)                     |
| Lobular       | 13 (11.6%)                    | 2 (6.5%)                       |
| Mixed         | 13 (11.6%)                    | 2 (6.5%)                       |
| Other         | 3 (2.7%)                      | 0 (0%)                         |
| Tumour Grade  |                               |                                |
| Grade I       | 10 (8.9%)                     | 1 (3.2%)                       |
| Grade II      | 71 (63.4%)                    | 20 (64.5%)                     |
| Grade III     | 29 (25.9%)                    | 10 (32.3%)                     |
| Unknown       | 2 (1.8%)                      | 0 (0%)                         |
| Lymphovascular invasion |             |                                |
| Positive      | 56 (50%)                      | 19 (61.3%)                     |
| Negative      | 53 (47.3%)                    | 12 (38.7%)                     |
| Unknown       | 3 (2.7%)                      | 0 (0%)                         |
| Estrogen Receptor |                             |                                |
| Negative      | 0 (0%)                        | 0 (0%)                         |
| Positive      | 112 (100%)                    | 31 (100%)                      |
| Progesterone Receptor |             |                                |
| Negative      | 20 (17.9%)                    | 3 (9.7%)                       |
| Positive      | 92 (82.1%)                    | 28 (90.3%)                     |
| HER2 Receptor |                               |                                |
| Negative      | 100 (89.3%)                   | 27 (87.1%)                     |
| Positive      | 12 (10.7%)                    | 4 (12.9%)                      |

**Supplementary Table 2. Patient tumor characteristics.** Data obtained from clinical and pathological staging as reported by central confirmation of pathology specimen acquired via the patient electronic medical record.
| Characteristic | Observation (Day 1-28; n=112) | Intervention (Day 29-58; n=31) |
|---------------|-------------------------------|-------------------------------|
| Surgery       |                               |                               |
| Lumpectomy    | 65 (58%)                      | 21 (67.7%)                    |
| Mastectomy    | 47 (42%)                      | 10 (32.3%)                    |
| Radiation     |                               |                               |
| No            | 15 (13.4%)                    | 2 (6.5%)                      |
| Yes           | 97 (86.6%)                    | 29 (93.5%)                    |
| Chemotherapy  |                               |                               |
| None          | 37 (33%)                      | 9 (29%)                       |
| FEC-Docetaxel | 46 (41.1%)                    | 16 (51.6%)                    |
| TC            | 17 (15.2%)                    | 4 (12.9%)                     |
| AC-Taxol      | 8 (7.1%)                      | 2 (6.5%)                      |
| Other         | 4 (3.6%)                      | 0 (0%)                        |
| Herceptin     |                               |                               |
| No            | 100 (89.3%)                   | 27 (87.1%)                    |
| Yes           | 12 (10.7%)                    | 4 (12.9%)                     |
| Tamoxifen     |                               |                               |
| No            | 44 (39.3%)                    | 15 (48.4%)                    |
| Yes           | 68 (60.7%)                    | 16 (51.6%)                    |

**Supplementary Table 3. Patient treatment characteristics.** Data was obtained from patient treatment history extracted from patient electronic medical record.
| Adverse Events                  | Observation (Day 1-28; n=121) | Intervention (Day 29-58; n=31) |
|--------------------------------|--------------------------------|--------------------------------|
|                                | Grade 1 or 2 | Grade 3 | Grade 1 or 2 | Grade 3 |
| Abdominal Pain                 | 1            | -       | -            | -       |
| Amnesia                        | -            | -       | 1            | -       |
| Anemia                         | -            | -       | 1            | -       |
| Arthralgia                     | 1            | -       | 6            | 1       |
| Bloating                       | -            | -       | 1            | -       |
| Breast Infection               | -            | -       | -            | 1       |
| Cardiac Disorder               | -            | -       | 1            | -       |
| Conjunctivitis                 | 1            | -       | -            | -       |
| Constipation                   | -            | 1       | 1            | -       |
| Cough                          | 4            | -       | -            | -       |
| Diarrhea                       | 1            | -       | 2            | -       |
| Dyspnea                        | 1            | -       | -            | -       |
| Epistaxis                      | -            | -       | 1            | -       |
| Fatigue                        | 1            | -       | 2            | -       |
| Flu-like Symptoms              | 2            | -       | -            | -       |
| Headache                       | 1            | -       | -            | 1       |
| Infection (other)              | -            | -       | 1            | -       |
| Insomnia                       | -            | -       | 1            | -       |
| Myalgia                        | -            | -       | 2            | -       |
| Nausea                         | 1            | -       | 1            | -       |
| Premature Menopause            | -            | -       | 2            | -       |
| Renal Colic                    | -            | 1       | -            | -       |
| Shingles                       | -            | -       | 1            | -       |
| Sinusitis                      | 1            | -       | -            | -       |
| Stroke                         | 1            | -       | -            | -       |
| Tooth Infection                | 1            | -       | -            | -       |
| Upper Respiratory Infection    | 1            | -       | 1            | -       |
| Urinary Tract Infection        | 1            | -       | 1            | -       |
| Uterine Hemorrhage             | 1            | -       | 1            | -       |

**Supplementary Table 4. Adverse Events Type.** List of adverse events observed during the trial. Events are separated by event type and grade.
|                         | Observational Cohort Completers (n=112) | Interventional Cohort Completers (n=34) |
|-------------------------|----------------------------------------|-----------------------------------------|
|                         | Day 1 | Day 1 | Day 29 | Mean | Mean | Day 29 | Mean | Day 58 | Mean | stES | Day 29 | Mean | Mean | Mean | Mean | stES |
| BPI-SF Pain             | 1.66  | 1.5   | 1.64   | 0.08  |      | 2.24  | 2.13 | 2.03   |      | -0.05|      |      |      |      |      |      |
| BPI-SF Interference     | 1.48  | 0.99  | 1.26   | 0.18  |      | 2.54  | 1.92 | 1.63   |      | -0.11|      |      |      |      |      |      |
| FACT-ES                 | 9.55  | 62.41 | 62.86  | 0.05  |      | 12.91 | 59.52| 59.39  |      | -0.01|      |      |      |      |      |      |

**Supplementary Table 5.** Change in quality of life indices during day 1 to 28 and during day 29 to 58. The standardized effect size (stES) for change is the difference in mean scores divided by the standard deviation (SD) at the start day. The indices are the pain and interference scores of the BPI-SF (Brief Pain Inventory, Short Form) and the FACT-ES (Functional Assessment of Cancer Therapy – Endocrine Score) score.