**Title:** Impact of chemotherapy relative dose intensity on cause-specific and overall survival for stage I-III breast cancer: ER+/PR+, HER2- vs. triple-negative

**Running head:** Chemotherapy relative dose intensity by breast cancer subtype

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**Online Resource 1**. Formula used for calculation of chemotherapy relative dose intensity.

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| $$RDI=\frac{ADI}{SDI}$$ |
| $$ADI=\frac{Dose\_{Actual}}{Time\_{Actual}×BSA}$$ |
| $$SDI=\frac{Dose\_{Standard}}{Time\_{Standard}×BSA}$$ |
| $$BSA=\sqrt{\frac{Height \left(cm\right)×Weight (kg)}{3600}}$$ |

Abbreviations: RDI: relative dose intensity; ADI: actually received dose intensity; SDI: standard dose intensity; BSA: body surface area.

Notes: Doseactual represents the total dosage patients actually received and Dosestandard represents the total dosage required by standard regimens. Timeactual is the total time in week patients used to receive the therapy and Timestandard is the total time including all planned cycles recommended by standard regimens. If a patient received fewer cycles than recommended standard cycles, for the missed cycles, the dose was counted as zero and time was counted as time required by standard regimen. RDI was calculated for each drug and then averaged across all the chemotherapeutic agents in the regimen. If the RDI is higher than 100% for certain drug, the RDI for this agent was counted as 100%.

**Online Resource 2**. Sensitivity analysis - Inverse probability treatment weighted (IPTW) adjusteda hazard ratios (HR) for time to cause-specific and overall survival for different cutoff points of relative dose intensity (RDI) among stage I-III estrogen receptor or progesterone receptor positive and human epidermal growth factor 2 receptor negative (ER+/PR+, HER2-) and triple-negative breast cancer patients whose breast cancer was diagnosed as the only or the first primary tumor.

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| --- | --- | --- | --- | --- |
| RDI | nb | % of reduced RDI | **Cause-specific survival** | **Overall survival** |
| Adjusted HR | P | Adjusted HR | P |
| **ER+/PR+, HER2- (N=453)** |
| RDI<95% vs. ≥95% | 427 | 56.67 | 0.75 (0.37, 1.54) | 0.43 | 0.99 (0.53, 1.85) | 0.98 |
| RDI<90% vs. ≥90% | 444 | 42.12 | 1.34 (0.64, 2.79) | 0.44 | 1.49 (0.80, 2.79) | 0.21 |
| RDI<85% vs. ≥85% | 424 | 32.08 | 1.93 (0.93, 4.00) | 0.08 | **2.36 (1.28, 4.38)** | **0.006** |
| RDI<80% vs. ≥80% | 338 | 26.33 | 1.37 (0.59, 3.16) | 0.46 | 1.92 (0.97, 3.79) | 0.06 |
| RDI<75% vs. ≥75% | 244 | 25.00 | 1.13 (0.45, 2.85) | 0.80 | 1.63 (0.83, 3.19) | 0.15 |
| **Triple-negative (N=161)** |
| RDI<95% vs. ≥95% | 151 | 57.62 | 0.85 (0.40, 1.79) | 0.66 | 0.93 (0.46, 1.89) | 0.84 |
| RDI<90% vs. ≥90% | 154 | 41.56 | 0.95 (0.43, 2.09) | 0.90 | 1.25 (0.61, 2.53) | 0.54 |
| RDI<85% vs. ≥85% | 130 | 32.31 | 1.10 (0.49, 2.45) | 0.82 | 1.32 (0.64, 2.72) | 0.46 |
| RDI<80% vs. ≥80% | 95 | 30.53 | 1.45 (0.58, 3.62) | 0.43 | 1.48 (0.66, 3.30) | 0.34 |
| RDI<75% vs. ≥75% | 81 | 24.69 | 2.34 (0.89, 6.18) | 0.09 | 1.80 (0.73, 4.46) | 0.20 |

aFor ER+/PR+, HER2- breast cancers and triple-negative breast cancers, covariates adjusted including age at diagnosis, race, insurance status, marital status, census tract poverty level, AJCC stage, Bloom-Richardson grade, tumor size, lymph node involvement, Charlson Comorbidity Index, use of granulocyte-Growth Factors/Cytokines, delayed chemotherapy, regimen. For ER+/PR+ and HER2- breast cancers, use of hormone therapy was additionally adjusted.

bN shows the total number of patients in the analytic dataset (after excluding the patients whose propensity score is <0.1 or >0.9).