**Additional file 5: Association between tamoxifen treatment and risk of CBC stratified by CYP2D6 Activity Score in the WECARE Study Population—Non-Hispanic Whites.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Activity Scorea** | **No Tamoxifen Treatment** | | | **Tamoxifen Treatment** | | | |
|  | **Cases**  **N (%)** | **Controls**  **N (%)** | **RR**  **(95% CI)** | **Cases**  **N (%)** | **Controls**  **N (%)** | **RRc**  **(95% CI)c** | **p-het** |
| 2 | 330 (35) | 487 (37) | Ref | 162 (41) | 242 (36) | 0.88 (0.66, 1.19) | 0.02 |
| 1.5 | 169 (18) | 185 (14) | Ref | 53 (13) | 117 (17) | 0.46 (0.29, 0.71) |
| 1 | 295 (32) | 411 (32) | Ref | 118 (30) | 215 (32) | 0.56 (0.41, 0.78) |
| 0.75 | 24 (3) | 26 (2) | Ref | 12 (3) | 16 (2) | 0.56 (0.19, 1.59) |
| 0.5 | 57 (6) | 97 (7) | Ref | 35 (9) | 50 (7) | 1.10 (0.60, 2.04) |
| 0 | 56 (6) | 94 (7) | Ref | 19 (5) | 31 (5) | 1.10 (0.54, 2.24) |
| **Activity Score Phenotypeb** |  |  |  |  |  |  |  |
| EM | 794 (85) | 1083 (83) | Ref | 333 (83) | 574 (86) | 0.66 (0.53, 0.83) | 0.19 |
| IM | 81 (9) | 123 (9) | Ref | 47 (12) | 66 (10) | 0.96 (0.56, 1.63) |
| PM | 56 (6) | 94 (7) | Ref | 19 (5) | 31 (5) | 1.11 (0.54, 2.26) |

Abbreviations: RR: Rate Ratio, CI: confidence interval, EM: extensive metabolizer, IM: intermediate metabolizer, PM: poor metabolizer, AS: Activity Score

aActivity Score is derived from diploid phenotypes: PM/PM (0), PM/IM (0.5), IM/IM (0.75), PM/EM (1), IM/EM (1.5), EM/EM (2)

bActivity Score Phenotype defined as: EM: having at least one EM allele (ie., AS≥1), IM: having no EM alleles and at least one IM allele (i.e., AS = 0.5-0.75), PM: having two PM alleles (i.e., AS = 0)

cAdjusted for age at first primary, age at menopause two years prior to first primary, histology of first primary, stage of first primary, family history of breast cancer, chemotherapy at first primary, radiation at first primary, other hormonal therapy for a first primary, number of full term pregnancies at first primary, age at menarche, ER status of first breast cancer diagnosis.