**Supplementary table 1.** Findings of multivariable linear regressions analyzing genetic associations between candidate gene SNPs and lipid profiles in exemestane-treated participants complementary to statistically significant findings in letrozole-treated participants.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Cohort | Number | Lipid Parameter | Model | Gene (SNP) | MAF | HWE P-value | Number of HOM | Minor Allele | Mean Change, mg/dL (SE) | P-value |
| All Patients on Exemestane  | 143 | TG | Recessive | *CYP19A1* (rs10046) | 0.48 | 0.62 | 34 | A | -1.2 (10.6) | 0.91 |
| 143 | TG | Recessive | *CYP19A1*(rs2289105) | 0.48 | 0.62 | 34 | C | -0.8 (10.6) | 0.94 |
| 143 | TG | Recessive | *CYP19A1*(rs3759811) | 0.45 | 0.72 | 25 | C | -1.56 (12.0) | 0.9 |
| 143 | TG | Recessive | *CYP19A1*(rs700518) | 0.47 | 0.87 | 30 | C | -2.7 (11.0) | 0.81 |
| 143 | TG | Recessive | *CYP19A1*(rs4775936) | 0.43 | 1.0 | 27 | T | 5.32 (10.7) | 0.62 |
| 143 | HDL | Additive | *CYP19A1*(rs4646) | 0.31 | 0.69 | 12 | A | 2.48 (1.9) | 0.2 |
| 143 | TG | Recessive | *CYP19A1*(rs749292) | 0.45 | 0.87 | 28 | A | 5.72 (10.5) | 0.6 |
| 143 | TG | Additive | *CYP19A1*(rs749292) | 0.45 | 0.87 | 28 | A | 1.33 (6.0) | 0.83 |
| Patients on Exemestane taking LAM  | 49 | HDL | Additive | *CYP19A1*(rs749292) | 0.4 | 0.23 | 5 | A | -8.1 (5.7) | 0.17 |
| 49 | HDL | Dominant | *CYP19A1*(rs749292) | 0.4 | 0.23 | 5 | A | -10.9 (7.2) | 0.14 |
| 49 | HDL | Dominant | *CYP19A1*(rs1008805) | 0.44 | 1.0 | 9 | G | 7.1 (5.2) | 0.19 |
| 49 | HDL | Additive | *CYP19A1*(rs10046) | 0.46 | 0.57 | 9 | A | -9.3 (5.5) | 0.1 |
|  | 49 | HDL | Additive | *CYP19A1*(rs2289105) | 0.46 | 0.77 | 9 | C | -9.6 (5.7) | 0.1 |

**Supplementary table 2.** Findings of multivariable linear regressions analyzing genetic associations between candidate gene SNPs and lipid profiles in only Caucasian women taking both letrozole and exemestane complementary to statistically significant findings in letrozole-treated participants. \*new significant finding (in letrozole only), and corresponding data for exemestane (additive rs1062033 and dominant rs1062033 models were not included due to number of homozygotes <5)

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| AI (number) | Lipid Parameter | Model | Gene (SNP) | MAF | HWEP-value | Number of HOM | Minor Allele | Mean Change, mg/dL (SE) | P-value |
| All Patients Irrespective of LAM Use |
| Letrozole (137) | TG | Recessive | *CYP19A1* (rs10046) | 0.49 | 0.38 | 29 | A | -30.92 (8.2) | 0.00023 |
| Exemestane (127) | TG | Recessive | *CYP19A1* (rs10046) | 0.48 | 0.72 | 27 | G | 2.51 (3.2) | 0.43 |
| Letrozole(137) | TG | Recessive | *CYP19A1* (rs2289105) | 0.49 | 0.39 | 29 | C | -30.98 (8.2) | 0.00024 |
| Exemestane (127) | TG | Recessive | *CYP19A1* (rs2289105) | 0.48 | 1.0 | 28 | T | 8.78 (11.8) | 0.46 |
| Letrozole (137) | TG | Recessive | *CYP19A1* (rs3759811) | 0.46 | 0.28 | 22 | C | -33 (9.4) | 0.00065 |
| Exemestane (127) | TG | Recessive | *CYP19A1* (rs3759811) | 0.49 | 0.45 | 25 | C | -3 (12.4) | 0.81 |
| Letrozole (137) | TG | Recessive | *CYP19A1* (rs749292) | 0.41 | 0.47 | 20 | A | -37.47 (9.3) | 0.000095 |
| Exemestane (127) | TG | Recessive | *CYP19A1* (rs749292) | 0.33 | 0.69 | 15 | G | 4.92 (15.6) | 0.75 |
| Letrozole (137) | TG | Additive | *CYP19A1* (rs749292) | 0.41 | 0.47 | 20 | A | -19.51 (5.0) | 0.00017 |
| Exemestane (127) | TG | Additive | *CYP19A1* (rs749292) | 0.46 | 0.86 | 25 | A | 1.98 (6.5) | 0.76 |
| Patients on LAM |
| Letrozole (44) | HDL | Additive | *CYP19A1* (rs749292) | 0.47 | 0.54 | 8 | A | 6 (1.3) | 0.000065 |
| Exemestane (43) | HDL | Additive | *CYP19A1* (rs749292) | 0.41 | 0.34 | 5 | A | -7.85 (6.0) | 0.2 |
| \* Letrozole (44) | HDL | Dominant | *CYP19A1* (rs749292) | 0.47 | 0.54 | 8 | A | 8.26 (2.1) | 0.00035 |
| Exemestane (43) | HDL | Dominant | *CYP19A1* (rs749292) | 0.41 | 0.34 | 5 | A | -10.63 (7.8) | 0.18 |
| Letrozole (44) | HDL | Additive | *CYP19A1* (rs1062033) | 0.47 | 0.54 | 8 | G | 6.2 (1.3) | 0.000023 |
| \* Letrozole (44) | HDL | Dominant | *CYP19A1* (rs1062033) | 0.47 | 0.54 | 8 | G | 8.26 | 0.00035 |
| Letrozole (44) | HDL | Dominant | *CYP19A1* (rs1008805) | 0.42 | 0.21 | 5 | G | -6.96 (2.2) | 0.003 |
| Exemestane (43) | HDL | Dominant | *CYP19A1* (rs1008805) | 0.46 | 0.76 | 8 | G | 5.54 (9.5) | 0.56 |
| Letrozole (44) | HDL | Additive | *CYP19A1* (rs1008805) | 0.42 | 0.21 | 5 | G | -5.01 (1.6) | 0.003 |
| Exemestane (43) | HDL | Additive | *CYP19A1* (rs1008805) | 0.46 | 0.76 | 8 | G | 9.46 (6.0) | 0.13 |
| Letrozole (44) | HDL | Dominant | *CYP19A1* (rs752760) | 0.45 | 0.75 | 8 | T | -8.28 (2.0) | 0.00018 |
| Exemestane (43) | HDL | Dominant | *CYP19A1* (rs752760) | 0.48 | 0.54 | 10 | T | 1.66 (9.1) | 0.86 |

**Supplementary table 3.** Significant findings of multivariable linear regressions analyzing genetic associations between candidate gene SNPs and lipid profiles without adjusting for changes in plasma estradiol concentrations.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Cohort | AI | Lipid Parameter | Model | Gene (SNP) | MAF | HWE P-value | Number of HOM | Minor Allele | Mean Change, mg/dL (SE) | P-value |
| All Patients on Letrozole (n=160) | Letrozole | TG | Recessive | *CYP19A1* (rs10046\*) | 0.48 | 0.63 | 34 | A | -29.8 (7.3) | 0.000082 |
| Letrozole | TG | Recessive | *CYP19A1*(rs2289105\*) | 0.48 | 0.87 | 34 | C | -29.8 (7.4) | 0.000085 |
| Letrozole | TG | Recessive | *CYP19A1*(rs3759811\*) | 0.43 | 0.61 | 25 | C | -30.8 (8.5) | 0.00043 |
| Letrozole | TG | Recessive | *CYP19A1*(rs749292\*) | 0.41 | 0.51 | 24 | A | -32.8 (8.3) | 0.00012 |
| Letrozole | TG | Additive | *CYP19A1*(rs749292\*) | 0.41 | 0.51 | 24 | A | -17.1 (4.5) | 0.00021 |
| Patients on LAM (n=52) | Letrozole | HDL | Additive | *CYP19A1*(rs749292\*) | 0.47 | 0.58 | 10 | A | 5.8 (1.4) | 0.00011 |
| Letrozole | HDL | Additive | *CYP19A1*(rs1062033\*) | 0.42 | 0.58 | 8 | C | 5.8 (1.4) | 0.00019 |
| Letrozole | HDL | Dominant | *CYP19A1*(rs1008805\*) | 0.38 | 0.24 | 5 | G | -8.0 (2.0) | 0.0002 |
| Letrozole | HDL | Additive | *CYP19A1*(rs1008805\*) | 0.38 | 0.24 | 5 | G | -5.8 (1.6) | 0.00054 |