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Impact of Drug-Gene-Interaction, Drug-Drug-Interaction, and Drug-Drug-Gene-Interaction on (es)Citalopram Therapy: The PharmLines Initiative

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ABSTRACT

We explored the association between CYP2C19/3A4 mediated drug-gene-interaction (DGI), drug-drug-interaction (DDI) and drug-drug-gene-interaction (DDGI) and (es)citalopram dispensing course. A cohort study was conducted among adult Caucasians from the Lifelines cohort (167,729 participants) and linked dispensing data from the IADB.nl database as part of the PharmLines Initiative. Exposure groups were categorized into (es)citalopram starters with DGI, DDI and DDGI. The primary outcome was drug switching and/or dose adjustment, and the secondary was early discontinuation after the start of (es)citalopram. Logistic regression modeling was applied to estimate adjusted odd ratios with their

confidence interval. We identified 316 (es)citalopram starters with complete CYP2C19/3A4 genetic information. The CYP2C19 IM/PM and CYP3A4 NM combination increased risks of switching and/or dose reduction (OR: 2.75, 95% CI: 1.03–7.29). The higher effect size was achieved by the CYP2C19 IM/PM and CYP3A4 IM combination (OR: 4.38, 95% CI: 1.22–15.69). CYP2C19/3A4 mediated DDIs and DDGIs showed trends towards increased risks of switching and/or dose reduction. In conclusion, a DGI involving predicted decreased CYP2C19 function increases the need for (es)citalopram switching and/or dose reduction which might be enhanced by co-presence of predicted decreased CYP3A4 function. For DDI and DDGI, no conclusions can be drawn from the results.

Keywords: (es)citalopram; drug-gene-interaction; drug-drug-interaction; drug-drug-gene-interaction; the