BACKGROUND

- Agomelatine is a melatonergic agent and 5-HT2C antagonist indicated for major depressive episodes in adults.
- Hepatotoxicity, including acute liver injury (ALI), is an identified risk in the risk management plan for agomelatine, and hepatotoxic reactions have been observed with other antidepressants; however, population-based studies quantifying this risk are scarce.

OBJECTIVE

- To evaluate the risk of ALI associated with the use of agomelatine and other selected antidepressant drugs.

METHODS

Study Design and Data Sources

- Multinational, multiple-data source, nested case-control study of new users of agomelatine and other selected antidepressants.
- Population-based data sources: Epichron (Aragon, Spain), SIDIAP (Catalonia, Spain), GepHRD (Germany), and Danish and Swedish national registers.

Study Population

- The selection of cases and controls is described in Figure 1.

RESULTS

Study Population

- There were 3,238,495 new users of study antidepressants (74,440 new users of agomelatine).
- The cohort attrition process in each data source is presented in Figure 3.

Main Results

- The main results for agomelatine and the other antidepressants for the primary endpoint are presented in Figure 4 (11 of 472 cases for the primary endpoint was identified. PPs for the primary endpoint ranged from 60% to 84%.
- A total of 178 cases (confirmed by validation) for the secondary endpoint and 1,078 cases for the tertiary endpoint were identified. Results for the secondary OR (0.45; CI 0.30-0.67) and tertiary endpoints (OR: 0.79; CI 0.50-1.25) were similar to the results of the primary endpoint. PPs for the tertiary endpoint ranged from 6% to 47%.
- For the other study antidepressants that were compared with citalopram, most OR point estimates were also below 1.00 except for the tertiary endpoint, for which paroxetine and venlafaxine showed an increased risk of ALI.
- Results of the planned SAs for agomelatine and the other antidepressants were, in general, consistent with the main analysis and produced combined OR point estimates for agomelatine below 1.00 for current use.

DISCUSSION

Main Results—Cont’d

- The results of this study do not suggest that the risk of ALI with the use of agomelatine constitutes a public health problem, at least among the most frequently prescribed antidepressants in Denmark and Sweden, and risk-minimisation measures similar to those in this study.
- Despite the pharmacoeconomic methods used to minimize its presence, bias as a result of potential misclassification of exposures or endpoints, and of residual confounding, is still possible.

CONCLUSIONS

- The results of the study did not suggest that the risk of ALI with the use of agomelatine constitutes a public health problem, at least among the most frequently prescribed antidepressants in Denmark and Sweden, and risk-minimisation measures similar to those in this study.
- When compared with citalopram, most antidepressants evaluated had OR point estimates for ALI below 1.00. However, specific studies to investigate this potential association of citalopram with ALI would be needed.