**BACKGROUND**

- Dapagliflozin, a sodium-glucose cotransporter 2 (SGLT2) inhibitor, lowers plasma glucose by inhibiting renal reabsorption of glucose and by promoting urinary glucose excretion.

- During phases 2 and 3, the proportion of patients with increased liver function laboratory values was not significant. However, one case of "fatality" drug-related liver injury was observed in the dapagliflozin arm. After additional follow-up, the case was later reclassified as autonomic neuropathy.

- This post-authorisation safety study was required by the European Medicines Agency at the time of dapagliflozin's approval in Europe.

**OBJECTIVE**

- To evaluate the risk of acute liver injury (ALI) in patients with type 2 diabetes mellitus, the incidence of hospitalization for acute liver injury (hALI) in new users of dapagliflozin with new users of comparator glucose-lowering drugs (GLD).

**METHODOLOGY**

- **Data Sources**
  - This was a non-interventional, post-authorisation safety study conducted using data from three longitudinal, population-based data sources (Table 1).

- **Study Population**
  - Patients were identified at the first recorded prescription or dispensing of dapagliflozin or comparator GLD.

- **Study Period**
  - Patients were followed from the day after the date of the index episode.

- **Data Sources**
  - This post-authorization safety study was required by the European Medicines Agency at the time of dapagliflozin's approval in Europe.

<table>
<thead>
<tr>
<th>Data Sources</th>
<th>Country</th>
<th>Study Population</th>
<th>Start Date</th>
<th>End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPRD</td>
<td>UK</td>
<td>GP records linked to hospital electronic health records</td>
<td>13 Nov 2012</td>
<td>31 Dec 2016</td>
</tr>
<tr>
<td>HIRD</td>
<td>US</td>
<td>Commercial claims data; ages ≥ 65 years,</td>
<td>09 Jan 2014</td>
<td>26 Feb 2019</td>
</tr>
<tr>
<td>Medicare</td>
<td>US</td>
<td>Government-sponsored programs; ages ≥ 65 years</td>
<td>09 Jan 2014</td>
<td>31 Dec 2015</td>
</tr>
</tbody>
</table>

**RESULTS**

- The mean number of months of dapagliflozin exposure for the index episode was 14.7 months in CPRD, 8.2 months in the HIRD, and 7.2 months in Medicare.

- The person-years of dapagliflozin and comparator exposure, respectively, were:
  - CPRD: 50,066 (9,027) vs. 61,176 (11,332)
  - HIRD: 9,765 (391) vs. 18,774 (1,714)
  - Medicare: 19,340 (196) vs. 44,053 (2,583)

- The adjusted pooled Incidence Rate Ratio (IRR) estimate was below the null value though with wide CIs in all data sources. The incidence rate ratio for hALI was 0.92 (95% CI, 0.68-1.25).

**DISCUSSION**

- The adjusted pooled IRR estimate was below the null value though with wide CIs in all data sources due to a small number of hALI events.

- The results were consistent with those from a post-hoc analysis of the data from this study compared with placebo in the DECLARE-TIMI 58 trial that reported a similarly null effect estimate for hepatic adverse events (hazard ratio, 0.92 [95% CI, 0.68-1.25]).

**CONCLUSIONS**

- The risk of acute liver injury in real-world use of dapagliflozin, as measured by hospitalization for acute liver injury, did not show evidence of an increased risk compared with other GLDs.

**REFERENCES**