A reversible increase in bilirubin was observed in nearly all subjects, with the RAL exposures in this trial being comparable with other published data. Bilirubin elevations were not accompanied by changes in markers of liver toxicity. Co-administration of FDV 240 mg QD (the highest dose in clinical development) with RAL was associated with a modest but statistically significant increase in the area under the plasma concentration–time curve at steady state over the uniform dosing interval (AUC) for RAL-glucuronide, when RAL was administered alone or with FDV (Figures 1–2). Collectively, these results suggest that RAL and FDV can be safely co-administered.

**METHODS**

**Trial design**

- **Phase I**: open-label, two-period, fixed-sequence study in healthy volunteers.
- **Phase II**: open-label, two-period, fixed-sequence study in healthy volunteers.
- **FDV dosing and RAL dosing** were administered during two treatment sequences (Figure 1).
- **Treatment A**: RAL 400 mg BID on Days 1–3, RAL 400 mg QD on Day 4
- **Treatment B**: RAL 400 mg BID on Days 1–3, RAL 400 mg QD on Day 4, and FDV 240 mg BID during Days 2–5

**Study day**

- Day 1
- Day 2
- Day 3
- Day 4
- Day 5
- Days 6–17
- Days 18–22
- Days 23–27
- Days 28–32

**Randomisation and Concomitant Medication**

- 25 subjects entered the study, of whom 24 were treated.
- One subject was unable to swallow the RAL tablet and was therefore not treated.
- This study was carried out by Boehringer Ingelheim.

**Safety**

- AEs were noted with the known safety profiles of FDV and RAL.
- There were no serious AEs, and no clinically relevant events were reported.
- No other relevant changes in laboratory parameters, vital signs, or ECGs were observed.

**ACKNOWLEDGEMENTS**

- Medical writing assistance, supported by Boehringer Ingelheim, was provided by Esther Race and Katrin Gudmundsdottir at Choice Healthcare Solutions during preparation of this poster.

**CONCLUSION**

- Collectively, these results suggest that RAL and FDV can be safely co-administered without any dose adjustment.

**REFERENCES**

- Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; Boehringer Ingelheim Pharma GmbH & Co. KG, Biebrzych, Germany; CRS Clinical Research Services, Mannheim, Germany; Boehringer Ingelheim Ltd, Burlington, ON, Canada.

**TABLE 1. Demographics and baseline characteristics**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Fasting</th>
<th>Fasting</th>
<th>Gender</th>
<th>Gender</th>
<th>Ethnicity</th>
<th>Ethnicity</th>
<th>BMI, kg/m²</th>
<th>BMI, kg/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>5 (20.8)</td>
<td>13 (54.2)</td>
<td>5 (20.8)</td>
<td>11 (46.1)</td>
<td>5 (20.8)</td>
<td>15 (62.5)</td>
<td>23.8 ± 3.5</td>
<td>23.5 ± 3.8</td>
</tr>
<tr>
<td>B</td>
<td>5 (20.8)</td>
<td>10 (41.7)</td>
<td>5 (20.8)</td>
<td>13 (54.2)</td>
<td>5 (20.8)</td>
<td>10 (41.7)</td>
<td>23.8 ± 3.6</td>
<td>23.5 ± 3.6</td>
</tr>
</tbody>
</table>

**TABLE 2. Steady-state PK of RAL and RAL-glucuronide after administration of RAL alone**

<table>
<thead>
<tr>
<th>PK parameter</th>
<th>Treatment A</th>
<th>Treatment B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax,ss (ng/mL)</td>
<td>5,772</td>
<td>7,733</td>
</tr>
<tr>
<td>AUC,ss (ng·h/mL)</td>
<td>16,135</td>
<td>22,042</td>
</tr>
</tbody>
</table>

**TABLE 3. Summary of AEs**

<table>
<thead>
<tr>
<th>System organ class</th>
<th>Treatment A</th>
<th>Treatment B</th>
</tr>
</thead>
<tbody>
<tr>
<td>General disorders and administration site conditions: fatigue, feeling of relaxation.</td>
<td>7 (30.4)</td>
<td>0</td>
</tr>
<tr>
<td>Gastrointestinal disorders: nausea, diarrhea, vomiting, flatulence, abdominal discomfort, constipation</td>
<td>18 (75.0)</td>
<td>7 (30.4)</td>
</tr>
<tr>
<td>Respiratory tract disorders: upper respiratory tract infections, nasal congestion, pharyngitis</td>
<td>1 (4.2)</td>
<td>0</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**SUPPORT**

- AEs were consistent with the known safety profiles of FDV and RAL.

**SUMMARY**

- Co-administration of FDV 240 mg QD at the highest dose in clinical development was found to be safe and well-tolerated in a 2-period fixed-sequence study in healthy volunteers.

**DISCLOSURES**


**ACKNOWLEDGEMENTS**

- Medical writing assistance, supported by Boehringer Ingelheim, was provided by Esther Race and Katrin Gudmundsdottir at Choice Healthcare Solutions during preparation of this poster.

**CONCLUSION**

- Collectively, these results suggest that RAL and FDV can be safely co-administered without any dose adjustment.