Review: Long-term ursodeoxycholic acid does not prevent mortality or morbidity in primary biliary cirrhosis


**Question**
In patients with primary biliary cirrhosis, does long-term ursodeoxycholic acid (UDCA) decrease mortality and disease progression?

**Data sources**
English-language studies were identified by searching MEDLINE and EMBASE/Excerpta Medica (1987 to July 1998) using the terms primary biliary cirrhosis, ursodeoxycholic acid, and treatment. Lists of conference abstracts and bibliographies of relevant review articles and studies were also scanned.

**Study selection**
Randomized controlled trials were selected if UDCA was compared with placebo, patients had confirmed primary biliary cirrhosis with no biliary obstruction, and follow-up was > 6 months.

**Data extraction**
Data were extracted on patient numbers and characteristics, laboratory values, study quality, and outcomes (death, death related to liver disease, transplantation, death or transplantation, complications of liver disease, side effects, and study-specific predefined end points). Missing data were also sought from trial investigators.

**Main results**
164 articles were assessed; 11 met the inclusion criteria. 1272 patients were studied: Mean age range was 49 to 57 years, mean follow-up was 9 to 64 months, and mean daily dose of UDCA was 7.7 to 15.0 mg/kg of body weight. No differences were found in any of the outcomes for any trial or meta-analysis of the trials (Table), except for 1 study of 190 patients that found a decreased rate of treatment failure with UDCA. No effect or very little effect was shown for fatigue, pruritus, hepatic fibrosis, progression of histologic stage, or most other histologic features. UDCA treatment decreased laboratory levels of alkaline phosphatase, γ-glutamyl transpeptidase, alanine transaminase, and aspartate transaminase. Bilirubin levels were reduced in some studies, but serum albumin levels and prothrombin times did not change in most studies.

**Conclusion**
Long-term ursodeoxycholic acid does not improve outcomes (death, death related to liver disease, liver transplantation, liver transplantation or death, ascites or bleeding, side effects, or rate of treatment failure).

**Data**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Number of studies</th>
<th>Combined odds ratio (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>8</td>
<td>1.18 (0.70 to 1.99)</td>
</tr>
<tr>
<td>Liver-related death</td>
<td>4</td>
<td>0.74 (0.24 to 2.40)</td>
</tr>
<tr>
<td>Liver transplantation</td>
<td>8</td>
<td>1.21 (0.75 to 1.95)</td>
</tr>
<tr>
<td>Death or liver transplantation</td>
<td>8</td>
<td>1.20 (0.83 to 1.74)</td>
</tr>
<tr>
<td>Ascites or hemorrhage</td>
<td>5</td>
<td>1.19 (0.56 to 2.53)</td>
</tr>
<tr>
<td>Author-defined primary end point</td>
<td>11</td>
<td>1.53 (0.97 to 2.42)</td>
</tr>
</tbody>
</table>

*Der Simonian and Laird methods.

Thus, is UDCA nothing but a glorified and expensive placebo? The verdict is not in yet. The ultimate study—a placebo-controlled trial with sufficient numbers of events—has yet to be done. There is a hint that UDCA could be active: 1 of the most relevant prognostic indicators, serum bilirubin levels, was decreased in 7 of 11 studies. Goulis and colleagues assume that this is simply a washout effect; however, serum bilirubin level has recently been shown to be a valid prognostic factor even in UDCA-treated patients (1) and may be the sole predictor of death or need for liver transplantation. Thus, further placebo-controlled trials of adequate duration are needed.

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**Reference**