NUC-1031 in combination with cisplatin for first-line treatment of advanced biliary tract cancer

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Background

• No approved agents exist for the treatment of locally advanced/metastatic biliary tract cancer (BTC)
• Current standard of care remains gemcitabine + cisplatin: OS 11.7 months (ABC-02)1
• Resistance to chemotherapy associated with poor survival prognosis
• Effective new agents and combinations are required

NUC-1031: The First Anti-Cancer ProTide

• A new class of anti-cancer agents
• ProTide transformation of gemcitabine
• Overcomes key gemcitabine resistance mechanisms2
• Cellular uptake independent of nucleoside transporters (hENT1)
• Activation independent of deoxycytidine kinase (dCK)
• Protected from breakdown by cytidine deaminase (CDA)
• In comparison to gemcitabine, NUC-1031 has3
  • Greater plasma stability (t1/2 8.3 hours vs 1.5 hours)
• Activation independent of deoxycytidine kinase (dCK)
  transporters  (hENT1)

NuTide:121 Study Design

Inclusion

• ≥18 years of age
• Histologically or cytologically-confirmed adenocarcinoma of the biliary tract (intra and extra-hepatic cholangiocarcinoma, gallbladder, or ampullary cancers) that is locally advanced, unrespectable or metastatic
• Life expectancy ≥16 weeks
• ECOG performance status 0 or 1
• Adequate biliary drainage with no evidence of ongoing infection

Enrollment

Treatment

Endpoints

ABC-08 Study (Phase Ib Study NUC-1031 + cisplatin)

Safety Profile

• NUC-1031 + cisplatin was well tolerated
• No unexpected adverse events (AEs)
• Multiple cycles administered (median 8; range 3.5-14)
• No dose-limiting toxicities (DLTs)
• Grade 3 AEs included: fatigue (21%), neutropenia (14%), pyrexia (14%), nausea (7%), and increased liver function enzymes (ALT; 14%, AST; 7%)
• No Grade 4 treatment-related AEs
• No patients discontinued due to NUC-1031 related events

Treatment duration and best overall response by BTC anatomic site of origin

Efficacy - Objective Response Rates in ABC-08 and ABC-02

<table>
<thead>
<tr>
<th></th>
<th>ABC-08</th>
<th>ABC-02</th>
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<tbody>
<tr>
<td>NUC-1031 + cisplatin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ITT</td>
<td>7%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Evaluate</td>
<td>11%</td>
<td>11%</td>
</tr>
<tr>
<td>Complete Response</td>
<td>43%</td>
<td>25.5%</td>
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<tr>
<td>Partial Response</td>
<td>5%</td>
<td>26.1%</td>
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Objective Response Rate (Efficacy Evaluable Population, n=11)

Summary

• NUC-1031 + cisplatin shows encouraging efficacy compared to standard of care
• All BTC subtypes sensitive to NUC-1031 + cisplatin
• Durable responses
• NUC-1031 + cisplatin is well-tolerated over multiple cycles in patients with BTC
• NuTide:121 is a global phase III study that will be conducted at ~100 sites across North America, Europe and Asia-Pacific
• NUC-1031 + cisplatin has the potential to improve survival outcomes in patients with BTC
• For further study information contact: NuTide121@nucana.com

References: