A Phase IIa trial of Subcutaneously Administered PD-L1 Antibody ASC22 (Envafolimab) in Patients with Chronic Hepatitis B

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Disclosure

Conflict of Interest Disclosure Statement
I, Guiqiang Wang, received research fund from Ascletis and serve as a consultant or advisory board member for Abbott, AbbVie, Bristol-Myers Squibb, Gilead Sciences, Janssen, and Roche.

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Background of Chronic Hepatitis B (CHB)

An insufficient T-cell response to HBV antigen is characteristic of CHB and limits durable viral control and clearance.

T-cell exhaustion is a major pathway mediating impaired in situ response.

Dysfunctional T-cells have more PD-1 expression.

Blockade of PD-1/PD-L1 pathway might be a cure for CHB

- Blockade of PD-1/PD-L1 pathway can restore T Cell immune function.

- Combining anti-PD1/anti-PD-L1 drug with nucleos(t)ide analogue or other anti-viral treatment may be a solution to cure CHB.

Envafolimab (ASC22), an anti-PD-L1 antibody

- A humanized single-domain PD-L1 antibody fused with human IgG1 Fc.
- A BLA submitted for oncology indication with large safety data.
- Compared to conventional PD-L1 antibodies, ASC22’s unique competitive profile includes:
  - half-size of conventional PD-L1 Ab
  - Subcutaneously injectable
  - High affinity and room temp stability
  - Low immunogenicity

ASC22 Phase IIa Study Design (NCT04465890)

Aim: Efficacy and safety assessment of ASC22 in single dose.

Enrollment

NAs experienced patients (n = 9)
- HBV DNA < 20 IU/mL
- HBeAg negative
- HBsAg < 10000 IU/mL
- Non cirrhosis
- AST, ALT ≤ 2 × ULN

Cohort 1:
ASC22 0.3mg/kg (n=3)

Cohort 2:
ASC22 1.0mg/kg (n=3)

Cohort 3:
ASC22 2.5mg/kg (n=3)

Continue NAs treatment
Continue NAs treatment
Continue NAs treatment

Efficacy: HBsAg change from the baseline
Safety: Adverse events reported
Baseline HBsAg levels were comparable.
HBsAg Reduction is ASC22 Dose Dependent

Among 3 patients receiving 2.5 mg/kg dose, 1 patient achieved a maximum HBsAg reduction of $1.2 \log_{10} \text{IU/mL}$. 
Monitoring of IFN-γ Responses during Follow-up

IFN-γ was increasing after ASC22 treatment and peaked around Day 15.
An ALT flare was observed on Day 57 when HBsAg reached maximum reduction.

HBsAg reduction was accompanied by elevation of IFN-γ.
# Safety Profile of ASC22 During Follow-up

<table>
<thead>
<tr>
<th></th>
<th>ASC22 0.3mg/kg (n=3)</th>
<th>ASC22 1.0mg/kg (n=3)</th>
<th>ASC22 2.5mg/kg (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>3 (100)</td>
<td>3 (100)</td>
<td>3 (100)</td>
</tr>
<tr>
<td>Overall Safety</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any AE</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Any Grade 3/4</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<tr>
<td>ASC22 related AE</td>
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<td>0 (0)</td>
</tr>
<tr>
<td>SAE</td>
<td>0 (0)</td>
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<td>0 (0)</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>ALT/AST</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

- All AEs were grade 1.
- No Grade ≥ 2 AE occurred.
- No premature withdrawal or death.
Summary of ASC22 Phase IIa Study

- Single subcutaneous dose ASC22 (Envafolimab) induced a dose-dependent reduction of HBsAg.
- Single subcutaneous dose ASC22 up to 2.5 mg/kg is safe and well-tolerated.
- IFN-γ was increasing after single subcutaneous dose ASC22 treatment.
- ASC22 has potential to cure CHB patients in combination with other therapies.
- Based on the positive results from this Phase IIa trial, ASC22 Phase IIb trial (24-week treatment of ASC22, Q2W plus NAs) has been initiated.
Thank You

On behalf of all ASC22 investigators and their teams, thank you to our patients and their families.

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