Lack of pharmacokinetic drug–drug interaction between benvomofovir and razasvir in healthy participants

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BACKGROUND

• Bemifosovir (BEM) and razasvir (RZR) are potent, pan-genotypic inhibitors of the HCV NS5B polymerase and NS5A protein, respectively.
• Combinations of BEM with daclatasvir, an NS5A inhibitor, and RZR with uprifosibuvir, an experimental nucleotide NS5B inhibitor, were safe and well tolerated, and independently achieved high rates of sustained virologic response at 12 weeks in HCV-infected participants1,2
• In vitro studies demonstrate that BEM is approximately 10-fold more active vs sofosbuvir against laboratory strains and clinical isolates of HCV genotypes 1–5, and retains full activity against S282T, an amino acid substitution associated with sofosbuvir resistance
• BEM and RZR exhibited synergistic anti-HCV activity in vitro.

RESULTS

Study population

• All 32 participants completed the study and were included in the PK and safety analysis populations
• Participants were generally matched across cohorts (Table 1)

Table 1. Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cohort 1</th>
<th>Cohort 2</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, n (%)</td>
<td>Male 21 (65.6)</td>
<td>Male 21 (65.6)</td>
<td>Male 22 (65.6)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td>White 16 (47.1)</td>
<td>White 16 (47.1)</td>
<td>White 16 (47.1)</td>
</tr>
<tr>
<td>Mean age (SD, min–max)</td>
<td>41.4 (16.0, 23–55)</td>
<td>41.4 (16.0, 23–55)</td>
<td>41.4 (16.0, 23–55)</td>
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</tbody>
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PK analysis: DDI

• Coadministered RZR did not significantly alter the plasma PK of BEM (Figure 2; Figure 4)
• Coadministered BEM decreased the total and peak exposures of RZR by approximately 20–25%, while the trough exposure of RZR was minimally affected (Figure 3; Figure 5)

CONCLUSIONS

• Here we report the first clinical data for the coadministration of BEM and RZR
• The study drugs were well tolerated and plasma PK profiles were not substantially affected by food nor concomitant dosing, the latter indicating lack of DDI between BEM and RZR
• These data support the evaluation of BEM and RZR administered once daily for 8 weeks in HCV-infected patients is ongoing

Safety

• All treatment-emergent AEs (TEAEs) were non-serious. Nearly all TEAEs were mild (1/69 TEAEs was of moderate severity)
• No deaths or serious TEAEs were reported and no participants were withdrawn due to a TEAE
• No clinically significant laboratory abnormalities, physical examination, ECG, or vital sign measurements were observed

Acknowledgements

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Disclosures

Xiao-Jian Zhou, Maureen Montordon, Shannan Lynch, Keith Pietropaolo, Bruce Belanger, Arantxa Horga, and Janet Hammond are employees of Atea Pharmaceuticals and may own stock in Atea Pharmaceuticals, Boston, MA, USA.

SmartKa, principal investigator of the study, is an employee of Alliances Company Inc, Montreal, Canada, which was contracted to perform this research.

References

3. Lawitz E, et al. AASLD International Liver Congress; poster Th4A36;
7. NCT07531843, ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT07531843
9. NCT05904470, ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT05904470

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