Clinical Benefits of Liposomal Amikacin for Inhalation as Assessed by the Cystic Fibrosis Questionnaire-Revised

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Introduction
- Liposomal amikacin for inhalation (LAI) is a novel lipid formulation of amikacin (Figure 1) that is being developed for lung infections due to Pseudomonas aeruginosa (PA) and non-tuberculous mycobacteria (NTM).

Key features of LAI:
- Delivers highly bioavailable amikacin (~0.3 mm) eradicating endobronchial PA colonies
- Penetration of drug into biofilm
- High lung concentrations
- Low systemic exposure

The Cystic Fibrosis Questionnaire-Revised (CFQ-R) is an objective HRQoL measure for cystic fibrosis (CF) that meets US Food and Drug Administration (FDA) requirements for PROs containing both generic and disease-specific domains.

Clea R-108 study design
- 12 weeks of treatment
- 2 cycles on-treatment
- 1 cycle off-treatment
- Primary endpoint: Relative Change in FEV1 at Week 24

Table 3. Summary of AEs (Safety Population a)

<table>
<thead>
<tr>
<th>Variable (n=148)</th>
<th>LAI (n=135)</th>
<th>TIS (n=134)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment emergent AEs</td>
<td>122 (90.8)</td>
<td>110 (82.6)</td>
<td>0.025</td>
</tr>
<tr>
<td>Patient with TEAEs, n (%)</td>
<td>125 (92.6)</td>
<td>115 (85.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Grade 3: severe</td>
<td>52 (41.9)</td>
<td>57 (42.7)</td>
<td>0.777</td>
</tr>
<tr>
<td>Grade 4: life-threatening</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1.000</td>
</tr>
<tr>
<td>Grade 5: death</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Results

LAI administered once daily was generally safe and well tolerated up to and including chronic bronchopulmonary exacerbations due to PA.

The majority of patients in the LAI (34.5%) and TIS (34.2%) groups experienced at least one exacerbation event. Cycles 1 and 2 were on-treatment while cycle 3 was off-treatment. There were no unexpected adverse events (AEs), and the study was maintained over the course of 3 cycles (Figure 4).

Conclusions
- LAI was well tolerated, and no unexpected AEs were observed.
- LAI administered once daily was comparable with TIS administered twice daily, the standard of care for patients with CF chronically infected with PA, in improving lung function.
- Random effects model analysis of the CFQ-R provides additional evidence of the benefit of LAI.

Lower CFQ-R Treatment Burden was associated with treatment with LAI. Lower perceptions of Treatment Burden may promote adherence and may have positive effects on outcomes in the long-term.

References
- 3.

Disclosures
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