KD025 for Patients with Chronic Graft Versus Host Disease (cGVHD)  
Long-term Follow-up of a Phase 2a Study (KD025-208)

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INTRODUCTION

KD025 is an orally available Pha-associated coiled-coil kinase 2 (ROCK2) selective inhibitor in clinical development for interstitial and fibrotic disease indications. KD025 has been shown to dramatically reduce fibrosis and collagen production in preclinical models of interstitial and nontubular helper cells while upregulating Treg cells, as well as decrease collagen deposition and matrix metalloproteinase formation and proliferation. Therefore, KD025 may potentially impact the immunologic and fibrotic components of cGVHD.

METHODS

Key Eligibility Criteria:  
- Adults with advanced or refractory cGVHD  
- ≥2 prior lines of steroid treatment (≥30 days)  
- Not refractory to prior line (n=13)  
- ≤3 Organs involved (n=27)  
- Nonsevere cGVHD (n=12)  
- Relapse underlying disease (n=2)  
- On study deaths (n=1)

RESULTS

Baseline Characteristics

<table>
<thead>
<tr>
<th>Cohort 1</th>
<th>Cohort 2</th>
<th>Cohort 3</th>
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<tbody>
<tr>
<td>Median (range) yrs, age</td>
<td>53 (20-62)</td>
<td>55 (30-75)</td>
</tr>
<tr>
<td>Male/Female (%)</td>
<td>70/24</td>
<td>54/44</td>
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<tr>
<td>Median time cGVHD diagnosis to enrollment, mos</td>
<td>26.4</td>
<td>18.0</td>
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<tr>
<td>Median time transplant to enrollment, mos</td>
<td>39.0</td>
<td>29.0</td>
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<tr>
<td>No. involved organs (%)</td>
<td>8 (47)</td>
<td>10 (63)</td>
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<tr>
<td>Median predose dose at BL (mg/kg/day)</td>
<td>0.22</td>
<td>0.19</td>
</tr>
<tr>
<td>Median prior lines of therapy</td>
<td>3</td>
<td>2</td>
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Overall Response Rate

ORR of 65% across all three cohorts: Responsiveness Across Key Patient Subgroups

- Kaplan-Meier median DOR of 35 weeks in mITT responder population
- 51% of responders maintained a response for >2 weeks

Time to Response

- Responses were rapid: ~75% of responders achieved a response by Week 8 assessment
- 4/35 responses occurred after 24 weeks of treatment with KD025

Duration of Response (DOR)

- ORR determined from time of first clinical improvement
- Number of responders: 9 (33) Cohort 1, 9 (33) Cohort 2, 14 (47) Cohort 3
- Median DOR observed in responders across ≤3+ event (per investigator)

Patient Disposition

Median Duration of Follow-Up: 24 months

- Complete responses (CRs) observed in lower GI, upper GI, esophagus, joints/fascia, mouth, liver, eyes, and skin
- Partial responses (PRs) observed in lungs

Responses Across Organ Systems in Responders

- Complete responses (CRs) observed in lower GI, upper GI, esophagus, joints/fascia, mouth, liver, eyes, and skin

Failure Free Survival (FFS) and Overall Survival (OS)

- Overall Survival: 100% in responders who achieved CR for ≥7 point reduction in LSS Score

Safety

- No significant differences in safety across all cohorts
- Commonly reported AEs

CONCLUSIONS

- KD025 was well tolerated:
  - AE consistent with those expected in cGVHD patients receiving corticosteroids
- ORR of 65% across all three cohorts:  
  - Responses observed across all key subgroups
  - Responses observed in all affected organ systems, including in organs with extrinsic disease
- Durable and clinically meaningful outcomes:
  - Median DOR of 35 weeks amongst responders
  - 1 year FFS: 47%; 2 year FFS: 32%; 6 month FFS with PR/CR: 37%