Dose-finding Phase 2 study to evaluate the efficacy and safety of the novel BTK inhibitor LOU064 in patients with CSU inadequately controlled by H1-antihistamines

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Introduction

• LOU064 is a novel highly selective and potent covalent oral Bruton’s Tyrosine Kinase (BTK) inhibitor that showed a favourable safety profile in a first-in-human study with healthy volunteers and asymptomatic atopic subjects (clinicaltrial.gov number: NCT03591880).

• The covalent binding of LOU064 to BTK resulted in potent and lasting inhibition of BTK-dependent pharmacodynamic biomarkers even with very low and transient systemic drug exposures.

• LOU064 has good pharmacodynamic efficacy, including reduction of wheal size in skin prick tests with a fast onset of action. This makes it a strong candidate for oral treatment of basophil- and mast-cell driven skin diseases like chronic spontaneous urticaria (CSU).

• The primary objective of this study is to characterize the dose-response relationship of LOU064 administered once or twice daily in subjects with CSU with respect to change from baseline in the Urticaria Activity Score (UAS7) at Week 4.

• The aim of this poster is to describe the design of the ongoing Phase 2b study that is based on the findings of the first-in-human study.

Materials and methods

Study design

• A multicentre, randomized, double-blind, placebo-controlled Phase 2b dose-finding study to investigate the efficacy, safety and tolerability of LOU064 in adults with CSU inadequately controlled by H1-antihistamines, is being conducted (NCT03926611).

• Participants are randomized to receive once- or twice-daily treatment with high-, medium- or low-dose LOU064, or placebo for 12 weeks followed by a 4-week treatment-free follow-up period (Figure 1).

• Patients are required to be on a stable treatment regimen with a second generation H1-antihistamine at locally approved doses throughout the entire study.

• For treatment of intolerable CSU symptoms during the study, a second generation H1-antihistamine (that differed from the background H1-antihistamine) is available on an as needed basis as rescue medication.

• Concomitant medications that might affect CSU (including but not limited to 1st generation H1-antihistamines, leucotriene receptor antagonists and anti-IgE biologics such as omalizumab) are prohibited throughout the study.

Study objectives and endpoints

• The primary and secondary objectives and endpoints are displayed in Table 2.

• Efficacy, safety and tolerability will be assessed over the entire period of the study.

Table 1. Key inclusion and exclusion criteria

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<th>Inclusion</th>
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<tr>
<td>≥18 years of age</td>
<td>A clearly defined predominant or sole trigger of their chronic urticaria (i.e. chronic inducible urticaria)</td>
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<tr>
<td>CSU for ≥6 months</td>
<td>Other diseases with symptoms of urticaria or angioedema</td>
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<tr>
<td>A 7-day Urticaria Activity Score (UAS7) ≥16 and HSST7≥8 at randomization</td>
<td>Other skin disease associated with chronic itching that might influence in the investigators opinion, the study evaluations, and results</td>
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Table 2. Study objectives and endpoints

<table>
<thead>
<tr>
<th>Primary objective</th>
<th>Primary endpoint</th>
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<td>To characterize the dose-response relationship of LOU064 administered once or twice daily in subjects with CSU</td>
<td>Change from baseline in UAS7 at week 4</td>
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Secondary objectives

Secondary endpoints

• To evaluate the efficacy of LOU064 compared to placebo | The number of responders with UAS7=0 (clinical response) and UAS7≤6 (disease control) over time |

• To evaluate the effect of LOU064 on disease- and CSU-related QoL | Dermatology Life Quality Index score of 0 or 1 (disease-related), and change from baseline in DLQI (CSU-related) at Week 4 and 12 |

• To evaluate the effect of LOU064 on angioedema | The cumulative number of weeks free from angioedema with a 7-day angioedema activity score of 0 between baseline and Week 12 |

• To evaluate the safety and tolerability of LOU064 in subjects with CSU | Concentrations in blood and calculation of PK at Week 4 and 12 |

• To evaluate the safety and tolerability of LOU064 in subjects with CSU | Occurrence of emergent adverse events and serious adverse events during the study |

Conclusion

• This poster describes the design of the Phase 2b study from which the results are expected to characterize the dose- and exposure-response relationships for once and twice daily dosing, and enable the determination of the optimal dosing regimen for LOU064 in Phase 3 studies.

Reference


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Conflict of Interest