**BACKGROUND**

- Bronchiolitis obliterans syndrome (BOS) is a fatal, rapidly progressive lung disease caused by T-cell-mediated inflammation that leads to blockage of the bronchioles, resulting in respiratory failure and death.\(^1,^2\)
- Approximately 4% to 10% of patients who undergo allogeneic hematopoietic stem cell transplantation (allo-HSCT) will develop BOS.\(^3,^4\) (Fig 1)
- 72% to 100% develop BOS as a respiratory form of chronic graft-versus-host disease (cGVHD).
- Median time to BOS diagnosis ranges from 273 to 547 days post-transplant in literature.
- A diagnosis of BOS confers a significant increase in the risk of transplant-related mortality.\(^4,^5\) (Fig 2)

**RESULTS**

- 1068 patient-months of L-CsA-i use were collected from 85 patients with LTx.
- L-CsA-i was well tolerated and no patients discontinued due to intolerability.
- Most common reported symptoms were: cough 22%; dyspnoea 7%; pharyngeal soreness 1%; and wheezing 1%.
- L-CsA-i administered 5 mg or 10 mg bid by inhalation results in nominal serum levels and does not accumulate over time. (Fig 5)
  - Maximum serum CsA concentration was 57.42 ± 34.26 ng/mL.
  - Trough levels for up to 2 years of daily administration were 4-5 ng/mL (compared to systemic CsA target levels of 200-300 ng/mL).\(^6\)
- Lung function (FEV1) did not continue to decline in patients with LTx who received L-CsA-i. (Fig 6)
- A safety study of L-CsA-i for the treatment of BOS following allo-HSCT is planned.
- L-CsA-i is an investigational drug that to date has been demonstrated to be safe and well tolerated in >1000 patient-months of exposure.
- Ongoing and planned trials for the development of L-CsA-i to treat patients with BOS are planned.

**CONCLUSIONS**

- The pathophysiology of BOS is the same regardless of aetiology.
- L-CsA-i is an investigational drug that to date has been demonstrated to be safe and well tolerated in >1000 patient-months of exposure.
- BOSTON-1 and BOSTON-2, paired Phase 3 efficacy and safety studies of L-CsA-i for the treatment of BOS following LTx, are ongoing (Fig 7).
- A safety study of L-CsA-i for the treatment of BOS following allo-HSCT is planned.

**METHODS**

- Retrospective review of two clinical studies of L-CsA-i (isotonic, 4 mg/mL) for BOS associated with LTx.
- Patients were randomized to receive L-CsA-i plus SOC versus SOC alone.\(^6\)
- Patients in the L-CsA-i arms received either 5 mg (single transplant) or 10 mg (double transplant) bid via inhalation.\(^6\)
- Blood samples for PK analysis were collected before inhalation and after inhalation, at 15, 30, and 60 mins post dosing and 2, 4, 8, and 12 hrs post dosing.
- Local and general tolerability of L-CsA-i were investigated.

**REFERENCES**


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