Idefirix®▼(imlifidase) Clinical Trials Program

Idefirix®▼(imlifidase) is licensed throughout the European Union for desensitization treatment of highly sensitized adult kidney transplant patients with a positive crossmatch against an available deceased donor.[1] The use of imlifidase should be reserved for patients unlikely to be transplanted under the available kidney allocation system including prioritization programs for highly sensitized patients.[1]

The clinical trials program for imlifidase consists of:

- 1x Phase 1 double-blind, randomized, dose-finding study in healthy subjects
- 4x Phase 2 open-label, single-arm studies evaluating the dosing, efficacy, and safety of imlifidase in sensitized patients with end-stage renal disease (ESRD) awaiting transplantation

IMLIFIDASE CLINICAL EFFICACY AND SAFETY

Efficacy

Data from the Phase 2 studies have demonstrated the ability of imlifidase to inactivate immunoglobulin G (IgG) antibodies to enable kidney transplantation in sensitized patients. During these studies, treatment with imlifidase permitted transplantation in all patients who were crossmatch positive before treatment.[1-6] All patients had near-complete or complete reductions of levels of IgG antibodies at 6 hours and 24 hours after treatment.[5]

Safety

As imlifidase temporarily reduces the level of IgG, there is a potential increased risk of infections, but this can be mitigated through the provision of antibiotics. In addition to the standard of care infection prophylaxis in kidney transplantation in general (against Pneumocystis carinii, cytomegalovirus and oral candida), it is recommended that imlifidase patients receive prophylactic oral antibiotics covering respiratory tract pathogens for 4 weeks.[2]

Antibody mediated rejection (AMR) may occur as a consequence of rebound of anti-HLA antibodies otherwise known as donor-specific anitbodies (DSA). Patients with very high levels of DSA before transplantation are more likely to experience early AMR that requires intervention. Most patients in the clinical studies had rebound of DSA that peaked between 7 and 21 days after imlifidase treatment, and AMR occurred in approximately 30% of the patients. All patients with AMR in clinical studies were successfully managed with standard of care treatment.[2]

OVERVIEW OF IMLIFIDASE CLINICAL TRIAL PROGRAM

Trial	Design	Key Efficacy Findings	Key Safety Findings
Phase I NCT01802697 – Study 01 (Sweden) Completed 2014	Single-center, double-blind, randomized, 29 healthy subjects	Ascending doses (0.01mg/kg, 0.04mg/kg, 0.12mg/kg, or 0.24mg/kg) of imlifidase rapidly and efficiently inactivated IgG in humans and the effect remained for several days.[3]	The most common adverse events (AEs) were nasopharyngitis, headache and fatigue. Nasopharyngitis was reported for 10 out of 20 subjects on imlifidase and for six out of nine subjects on placebo. None of the AEs were reported as serious, met any dose limiting toxicity criteria, or led to withdrawal of the study drug.[3]
Phase 2 NCT02224820 - Study 02 (Sweden) Completed 2015	Single-center, open-label, 8 ESRD patients	Imlifidase treatment at either 0.12mg/kg x 2, 0.25mg/kg x 2, or 0.25mg/kg x 2 doses resulted in rapid and efficient degradation of plasma IgG within 24 hours of administration of the final dose, remaining low for up to a week.[4]	A total of 76 AEs were reported of which 27 were product-related. There were 5 serious AEs (SAEs) reported, four of which were product-related: two cases of pneumonia, one suspected upper respiratory infection and one case of myalgia.[4]
Phase 2 NCT02475551 - Study 03 (Sweden) Completed 2016	Single-center, open-label, 10 ESRD patients	Imlifidase treatment resulted in complete elimination of total IgG and HLA antibodies within 6 hours. All IgG molecules remained inactivated for approximately 1 to 2 weeks. Transplantation was successful in all patients with 100% graft survival at 6 months.[4]	A total of 37 SAEs were observed in 15 patients, 5 of which were considered as related to imlifidase. There were 13 infectious complications that generally responded to treatment and resolved in time.[5]
Phase 2 NCT02426684 – Study 04 (US) Completed 2018	Single-center, open-label, 17 ESRD patients	Imlifidase treatment resulted in complete elimination of total IgG and HLA antibodies within 6 hours. All IgG molecules remained inactivated for approximately 1 to 2 weeks. Transplantation was successful in all patients with 94% graft survival and one graft loss at 6 months.[4]	A total of 37 SAEs were reported observed in 15 patients, 5 of which were considered as related to imlifidase. There were no significant infectious complications in this patient cohort.[4]
Highdes Phase 2 NCT02790437 – Study 06 (US, France, Sweden) Completed 2018	Multi-center, open-label, 19 ESRD patients	Achieved primary endpoint of imlifidase converting positive crossmatch to negative in 17 out of 18 patients. One patient's crossmatch remained borderline positive, but was not determined to be prohibitive to proceed to transplant. Treatment with imlifidase efficiently reduced donor-specific antibodies (DSA) within 6 hours. Imlifidase permitted transplantation in all patients. At 6-months, graft survival was 89%. Patient survival was 100%.[6,7]	All patients reported at least one treatment-emergent adverse event (TEAE) within 30 days of imlifidase dosing, but only 7 events in 6 patients were classified as possibly or probably related to treatment. Most TEAEs, regardless of relationship to imlifidase, were mild to moderate in severity. There were 18 serious TEAEs reported, of which 2 were classified as product-related.[6,7]
Long-Term Observational Prospective Study - NCT03611621 expected to last 5 years (US, France & Sweden) Ongoing	Follow up of imlifidase-permitted transplants that took place in the Phase II trials	Interim data at 2 years showed graft survival of 90% (n=31). At 2 years, 1 case of antibody-mediated rejection (AMR) occurred later than 6 months post-transplantation. 93% of patients had satisfactory or good kidney function (n=46).[8]	This is an efficacy study investigating patient and graft survival and no safety parameters are being collected.

For full efficacy and safety information please view the product's initial Summary of Characteristics or for further information on the clinical trials, please visit **www.clinicaltrials.gov**

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6. Lonze BE, et al. *Ann Surg* 2018;268(3):488-496.
7. Jordan SC, et al. *Transplantation* October 21 2020 – volume online first issue.
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