

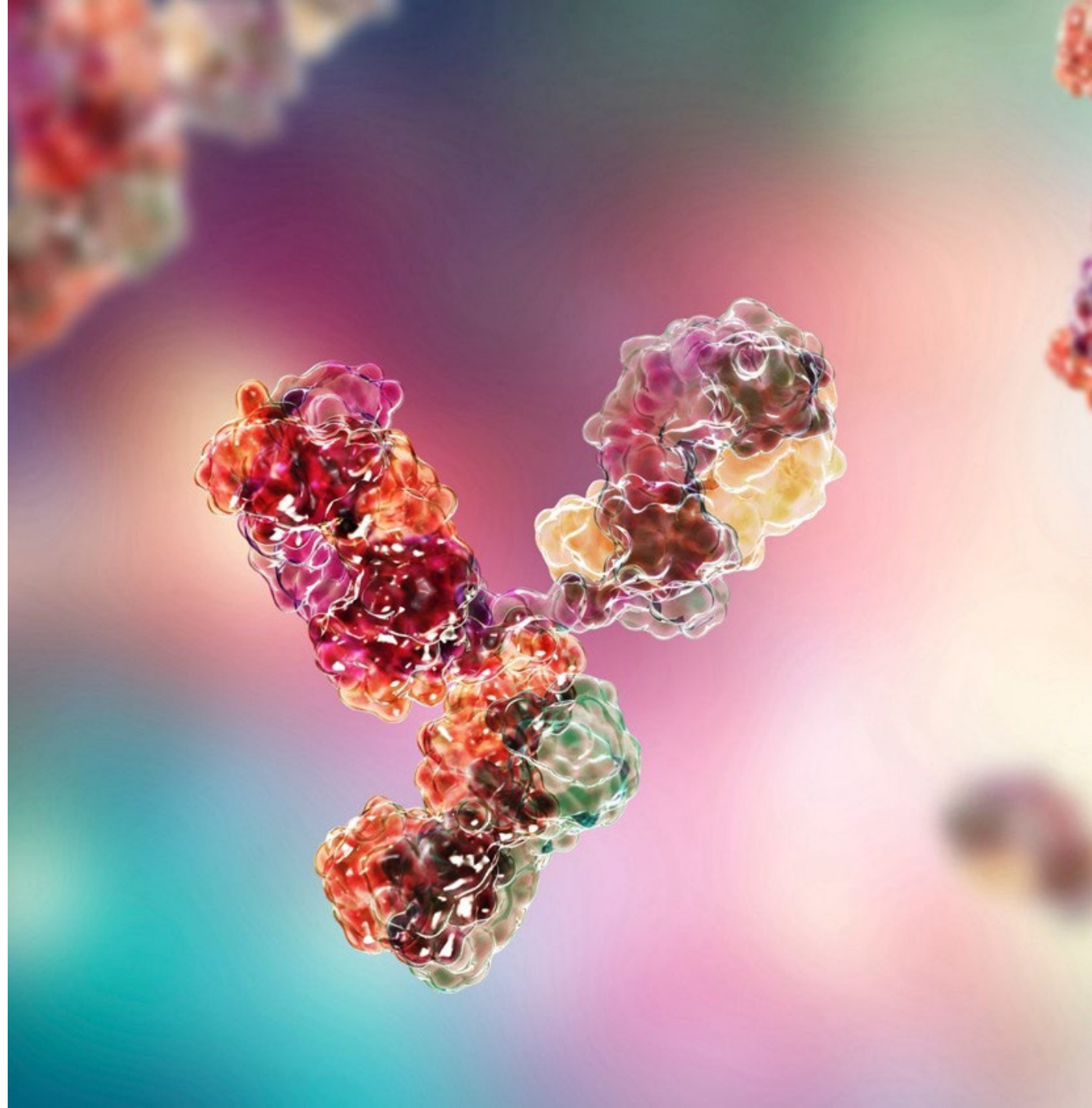
Administration of imlifidase

ICD-10 Coordination and Maintenance
Committee Update

Fall 2026

Disclaimer:

Imlifidase is an investigational compound being studied for the reduction of donor-specific antibodies to a level consistent with crossmatch conversion enabling human leukocyte antigen incompatible transplantation. It has not been approved for use by the FDA.



Current State of Kidney Transplant

The latest USRDS report indicates that the number of Americans living with ESRD reached an all-time high of 831,192 at the end 2023.¹

- ESRD patients on dialysis had a mortality rate 3.4 times higher than those who received a kidney transplant.

A significant portion of ESRD patients on transplant waiting list have preformed anti-HLA antibodies against potential donor tissues due to prior exposure to foreign antigens (e.g., pregnancy, blood transfusion, or previous transplants).^{2,3,4}

For patients with a wide range of anti-HLA antibodies, it is extremely difficult to find a compatible donor, even after revisions to the kidney allocation system.

- Patients with cPRA $\geq 99.9\%$ (reflecting the proportion of deceased donors whose organs would be immunologically incompatible) have the longest waiting time and the lowest rate of deceased donor transplantation; in this group, more patients die or are removed from the waiting list than are transplanted.^{5,6,7}

Current transplant center specific experimental desensitization protocols aimed at removing DSA show variable efficacy and are inefficient, taking days to weeks to reduce DSA levels and rarely achieve a level consistent with crossmatch conversion to proceed with transplantation.

Consequently, patients with cPRA $\geq 99.9\%$ represent a population with significant unmet medical need for efficient therapies that reduce DSA and enable access to deceased donor kidney transplantation.

USRDS, United States Renal Data System; **ESRD**, end-stage renal disease; **HLA**, human leukocyte antigen; **cPRA**, calculated panel reactive antibody; **DSA**, donor-specific antibodies;

Imlifidase for Desensitization in Kidney Transplantation

Pharmacology

- Cysteine protease derived from immunoglobulin G (IgG)-degrading enzyme of *Streptococcus pyogenes*.^{7,8}
- Transient IgG inactivation within 2-6 hours of dosing.^{7,8}
- Endogenous IgG returns after 1-2 weeks of administration.^{7,8}

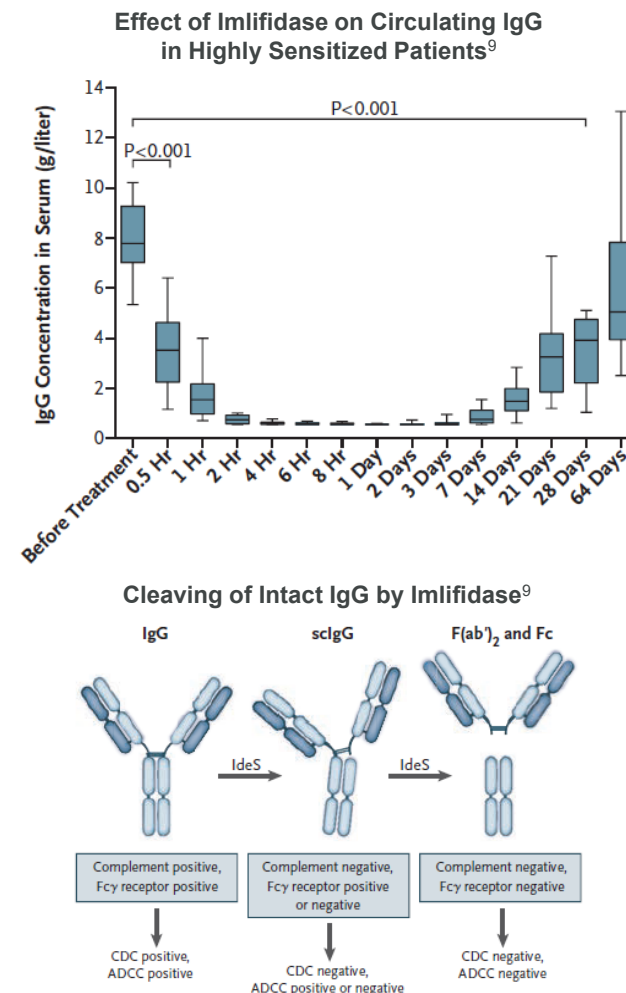
Mechanism of Action

- Cleaves the heavy chains of all human IgG subclasses that leads to elimination of Fc dependent effector function, including CDC, ADCC, and ADCP. IgG of the B-cell receptor complex is also cleaved resulting in a subset of B cells temporarily incapable of responding to their antigen.¹⁰
- Reduces DSA to a level consistent with crossmatch conversion thus enabling HLA incompatible transplantation.⁸

Dosing and Administration

- Single dose of 0.25mg/kg of total body weight
- Administered as a 15-minute IV infusion
- Within 24 hours of kidney transplantation

ADCC, antibody dependent cell-mediated cytotoxicity; **ADCP**, antibody dependent cellular phagocytosis; **BLA**, biologic license application; **CDC**, complement dependent cytotoxicity; **DSA**, donor-specific antibody; **IV**, intravenous;



Anticipated Imlifidase Treatment Journey



Pre-transplantation	Imlifidase Infusion	Transplantation	Post-transplant Management
Active and waiting in UNet SM	Up to 24 hours prior to transplantation	Induction therapy POD 0-6	Maintenance immunosuppression POD 1-onward
• Transplant evaluation and waitlisting • Obtain necessary prior authorizations for transplant	• Organ offer accepted, patient admitted to observation unit • 1 dose of corticosteroid and antihistamine premedication • Imlifidase infused over 15 minutes, repeat if needed	• DSA reduction deemed acceptable to move forward to surgery • Corticosteroid POD 0-onward; • rATG 1.5mg/kg POD 4-6	• TAC/MMF/Prednisone POD 0-onward • Rituximab up to 1gm POD 7 • IVIg up to 140gm POD 8-9
The infusion of imlifidase will be recorded in the medical record, physician's orders, progress notes and the medication administration record (MAR) similar to how other infused substances are documented.			

Select elements of the anticipated treatment journey are provided. The anticipated treatment journey is subject to change based on the final prescribing information if imlifidase is approved. The transplantation process provided above is based on the clinical trial protocol of the ConfideS study as well as real-world commercial use and country-specific treatment guidelines in Europe.
POD, post operative day; rATG, rabbit Anti-Thymocyte Globulin; TAC: tacrolimus; MMF: mycophenolate mofetil; IVIg, intravenous immunoglobulin

Imlifidase Phase 2 Programs in Kidney Transplant

Study	Patient	Primary Endpoint	Other Endpoints	Prior Desensitization	Publications
Study -02 (Sweden)	8 HS	Safety	HLA antibody reduction (MFI <1100 in SAB assay)	None	Lorant et al. 2018 ¹¹
Study -03 (Sweden)	10 HS	Safety and DSA reduction	HLA antibody reduction (MFI <1100 in SAB assay)	None	Jordan et al. 2017 ⁹
Study -04 (USA)	17 HS	Safety and DSA reduction	Renal function (creatinine; proteinuria; DSA 0-180)	Mixed	Jordan et al. 2017 ⁹
Study -06/HIGHDES (USA, France, Sweden)	18 HS	XM conversion	DSA reduction (2-48 h) time to XM- (CDC and FC)	Mixed	Jordan et al. 2021 ¹² Lonze et al. 2018 ¹³
Long-term follow-up of Transplanted Patients (USA, France, Sweden)	46 TP	5-year clinical follow up (pooled analysis including 3-year interim data)		Mixed	Kjellman et al. 2021 ¹⁴ Lorant et al. 2025 ¹⁵

CDC, complement-dependent cytotoxicity; **DSA**, donor-specific antibody; **FC**, flow cytometry; **HLA**, human leukocyte antigen; **HS**, highly sensitized; **MFI**, mean fluorescence intensity; **SAB**, single-antigen bead; **TP**, transplanted; **XM**, crossmatch

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Long Term Follow-Up of Positive Crossmatch Kidney Transplant Recipients from Phase 2 Programs

39 crossmatch positive transplants at 6 transplant programs¹⁴

- Imlifidase 0.25 mg/kg IV prior to kidney transplant
- 32 DDKT and 7 LDKT, median cPRA 99.62% (IQR 94.92-99.96%)

Outcomes

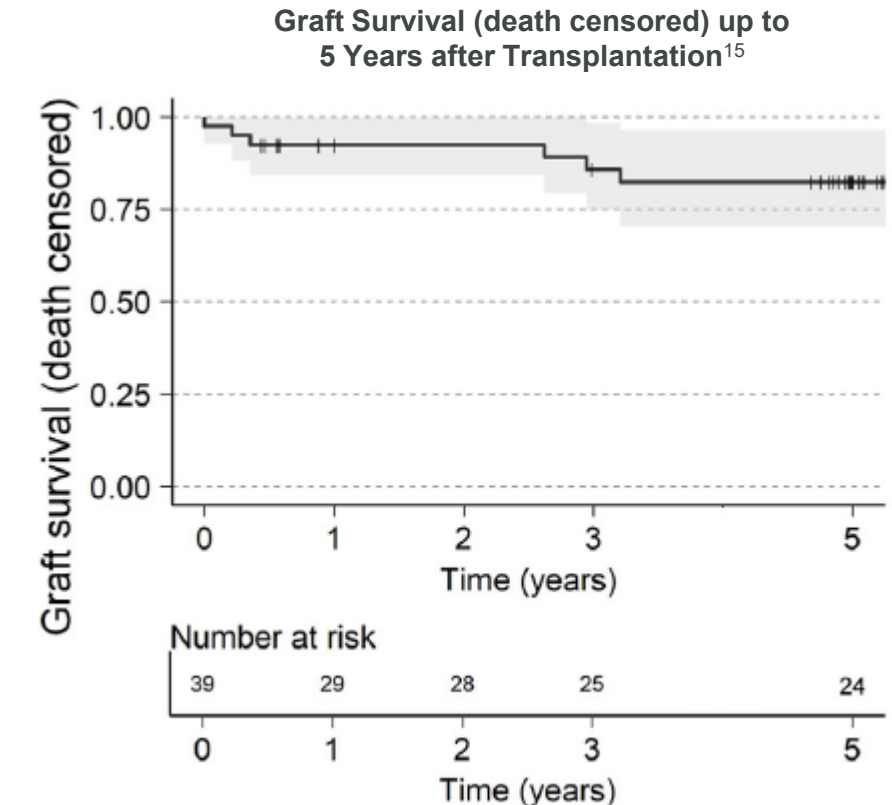
- Patient survival: 100% at 6 months, 90% at 3 and 5 years^{14,15}
- Graft survival: 84% at 3 years, 82% at 5 years^{14,15}
 - 3 graft losses within 6 months: non-IgG mediated hyperacute rejection, 2 primary non-function¹⁴
 - 2 graft losses between 2-3 years: immunosuppression reduction¹⁴
 - 1 graft loss between 3-5 years: decline in graft function over time¹⁵

Rejection¹⁴

- Highest risk in the first few weeks
- 28% within the first month; 38% at 6 months (4 additional patients)
- No patient with late clinical AMR

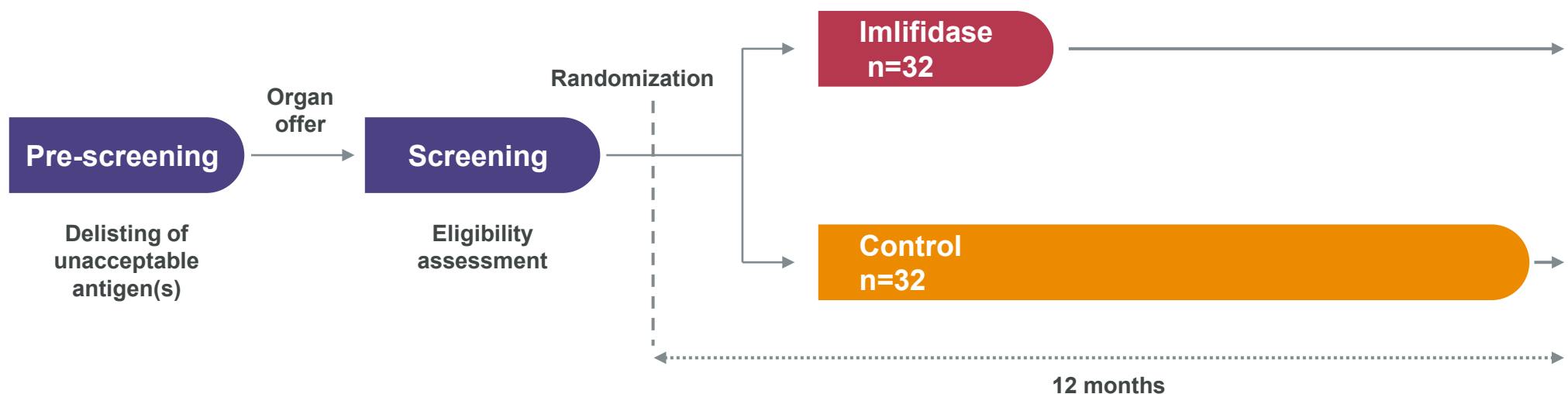
eGFR: 55 mL/min/1.73m² at 3 years and 50 mL/min/1.73m² at 5 years^{14,15}

AMR, antibody mediated rejection; **cPRA**, calculated panel reactive antibody; **DDKT**, deceased donor kidney transplant; **LDKT**, living donor kidney transplant; **eGFR**, estimated glomerular filtration rate; **IQR**, interquartile range; **IV**, intravenous;



Imlifidase Phase 3 Pivotal Trial (ConfldeS)

Open-label, controlled randomized controlled trial in highly sensitized patient population with a cPRA value $\geq 99.90\%$



After Randomization:

Imlifidase arm: accept organ offer; if treatment results in crossmatch conversion from positive to negative, then proceed to transplant (n=28/32 patients transplanted at randomization)

Control arm: EITHER accept organ offer, use non-approved local desensitization and proceed to transplant, OR reject organ offer and wait for more compatible organ offer(s) later during the 12-month period (n=15/32 patients transplanted during the 12 months post-randomization)

ConfldeS Demographics & Baseline Characteristics

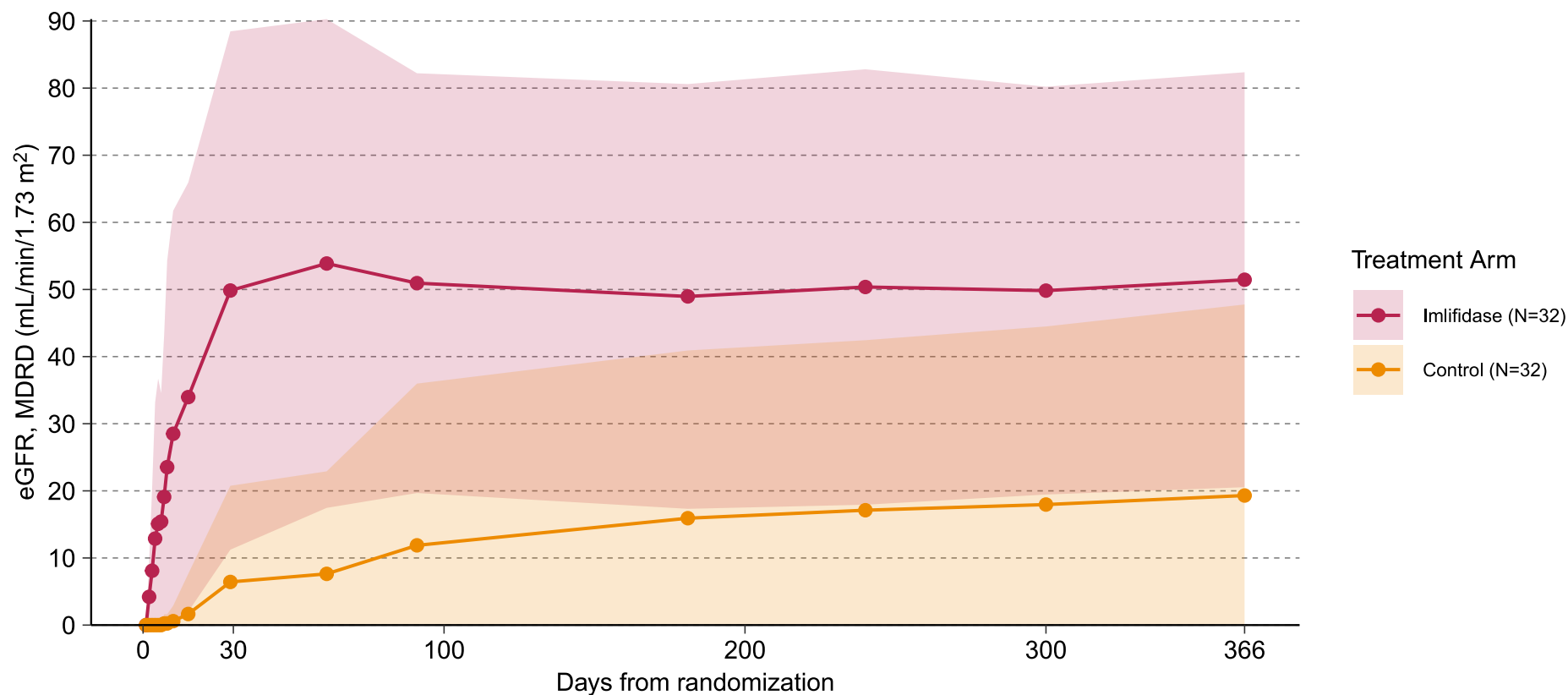
Characteristics	Imlifidase (n=32)	Control (n=32)	p-values
Mean patient age (SD) — yr	45.8 (12.3)	44.7 (12.5)	ns
Female — no. (%)	18 (56.3)	15 (46.9)	ns
Race — no. (%)			
Asian	1 (3.1)	2 (6.3)	ns
Black	16 (50.0)	14 (43.8)	
White	14 (43.8)	13 (40.6)	
Other	0 (0)	2 (6.3)	
Mixed	1 (3.1)	1 (3.1)	
Mean time on waitlist (SD) — yr	7.3 (6.8)	5.2 (3.7)	ns
Previous transplant — no. (%)	30 (94)	23 (72)	ns
Median baseline sum DSA (range) — MFI	33,452 (2190–157,217)	21,860 (4465–86,154)	ns
Mean cold ischemia time (SD) — h	25.2 (9.5)	19.6 (7.4)	ns
Delayed graft function — no. (%)	10 (36)	6 (47)	ns

DSA, donor-specific antibody; h, hours; MFI, mean fluorescence intensity; ns, not significant; SD, standard of deviation; yr, years.

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ConfldeS Primary Endpoint – eGFR at 12 Months

- At 12 months, eGFR in imlifidase patients were 51.5 compared with 19.3 mL/min/1.73 m² in the control arm
- Resulting in a clinical and significant difference of 32.2 mL/min/1.73 m² in favor of imlifidase (p<0.0001)



eGFR, estimated glomerular filtration rate; MDRD, modification of diet in renal disease.

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Dialysis Dependency

- At 12 months, fewer imlifidase patients were dependent on dialysis compared with control arm patients
- Imlifidase arm: 5 patients; control arm: 17 patients (p=0.0007)

CKD stage at 12 months for transplanted patients		
eGFR (mL/min/1.73 m ²)	Imlifidase (n=28) no. (%)	Control (n=15) no. (%)
>90	4 (14)	0
≥60	8 (28)	4 (27)
30–59	14 (50)	5 (33)
15–29	1 (4)	1 (7)
<15	1 (4) deceased	5 (33)

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

ConfideS Patient Survival & AEs

- Patient survival was 97% in the imlifidase arm compared with 100% in the control arm
- The profile of AEs and SAEs reflects typical post-transplant complications associated with current post-operative immunosuppressive practice and is in line with previous clinical trial experience
- No imlifidase infusion was discontinued due to an AE
- No new safety signals were detected in the trial

AE, adverse event; **SAE**, serious adverse event.

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