



Transplantation in Highly-Sensitized Patients: The Unmet Need



Hansa Biopharma

- Hansa Biopharma is a Swedish biopharmaceutical clinical-stage based in Lund
- Approx. 60 employees world wide
- Company was founded in 2007
- We focus on rare patients, not rare diseases
- Our pipeline is based on an immunomodulatory enzyme platform that has the potential to reduce specific immune responses.



AAKP 50 Years: Congratulations



Addressing a significant unmet need

Human leukocyte antigen (HLA) sensitization is a major immunological barrier to kidney transplantation and desensitization may be warranted

HLA sensitization occurs in patients with anti-HLA antibodies to potential donors (DSAs), resulting in significantly lower likelihood of donor matching and face prolonged waiting times

Highly sensitized patients are more likely to remain on long-term dialysis

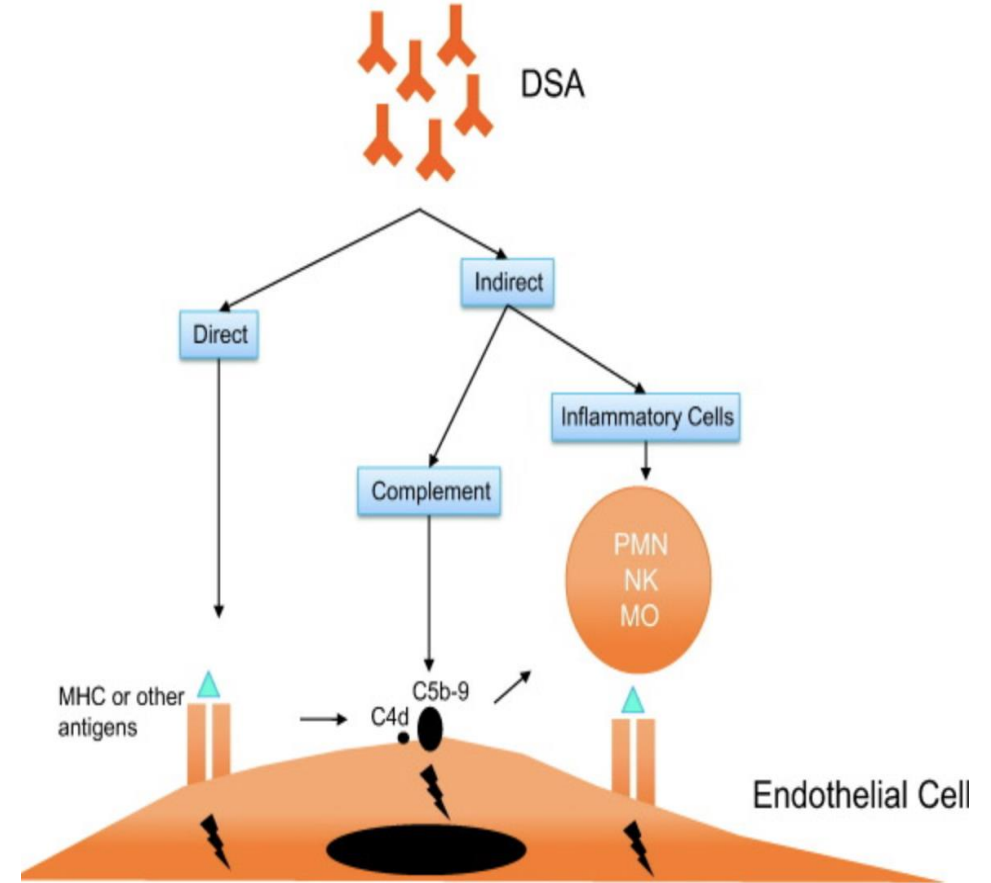
~ 9,000 patients die every year on kidney transplant waitlists in the U.S. and Europe¹

¹ Organ Procurement and Transplantation Network (OPTN); EDQM Council of Europe

Antibodies and Sensitization

An antibody is a protein molecule produced by the immune system in response to a foreign body, such as virus or a transplanted organ. In the case of transplantation these are called Donor Specific Antibodies (DSA)

- Previous exposure to foreign tissue, such as a prior transplant, blood transfusion or pregnancy
- High antibody levels that react to foreign tissue, make it harder to match for donor kidneys
- Sensitized candidates wait three to four times longer than unsensitized patients for a compatible deceased donor



Garg, 2017-Transplantation, 31(4), 257-267
OPTN/UNOS CPRA and Its Importance in Organ Transplantation

Measuring the level of sensitization when waitlisted

With the Panel Reactive Antibody (PRA) test the antihuman antibodies in the blood are measured

The PRA score is expressed as a percentage, which can range from 0 to 99 percent, that represents the likelihood of your blood having an antibody against a particular donor

A PRA of 20 percent means you have antibodies to approximately 20 percent of the population. Having antibodies against foreign tissues makes it difficult to find a compatible living or deceased donor kidney

cPRA calculates the likelihood that the recipient and donor would be incompatible and translates to waiting time

The probability of transplantation for a sensitized patient

- Highly sensitized patients are highly unlikely to receive a transplant
 - Low probability to find a matching organ
 - A waiting time that is anticipated to be much longer than for the average patient
 - How long can a patient wait?

Probability of finding a match decreases by:

- Grade of sensitization (PRA) and HLA-antibody profile
- Blood-group
- Geographic location and size of donor pool
- Time

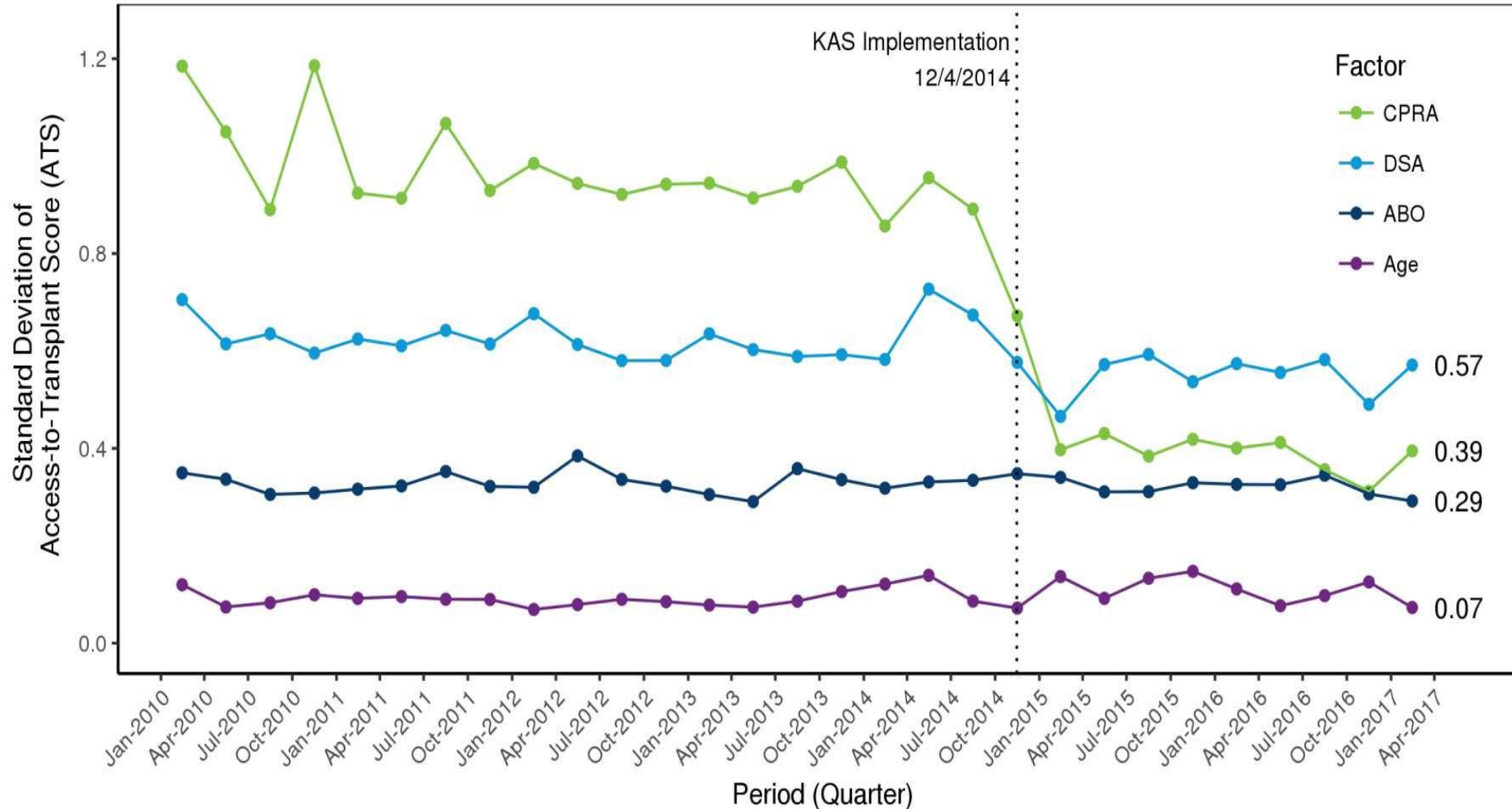
Probability of finding a match increases by:

- Access to living donor and desensitization programs
- Access to living donor paired-donation programs
- Access to priority programs

cPRA (%)	Theoretical match runs 95% acceptable donor
10	2
50	5
80	14
85	19
90	29
95	59
99	300
99.5	600
99.9	3,000
99.99	30,000
99.999	300,000

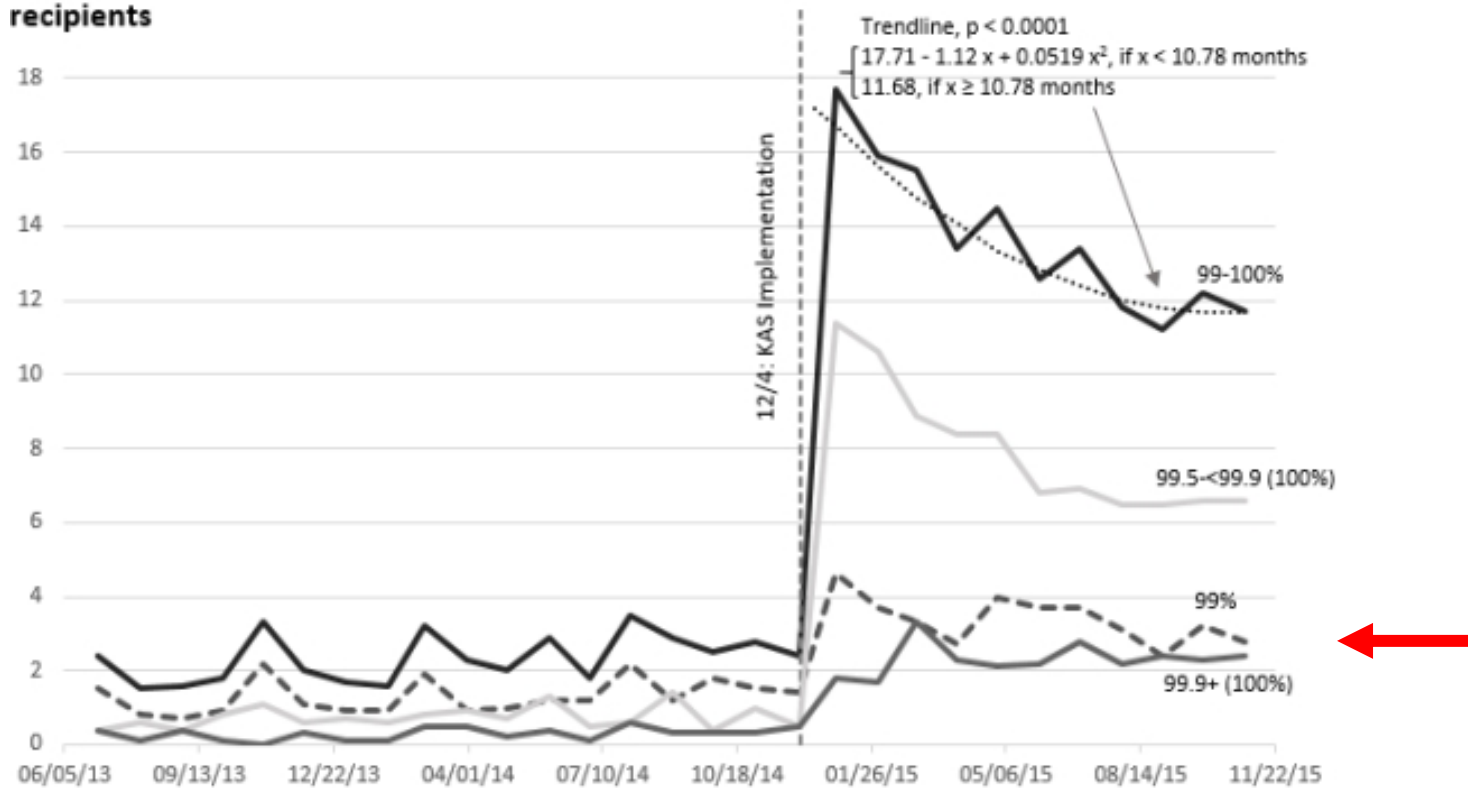
Keith DS and Vranic GM, Approach to the Highly Sensitized Kidney Transplant Candidate, Clin J Am Soc Nephrol. 2016 Apr 7; 11(4): 684–693.

Kidney Allocation System (KAS) has given priority to those in need



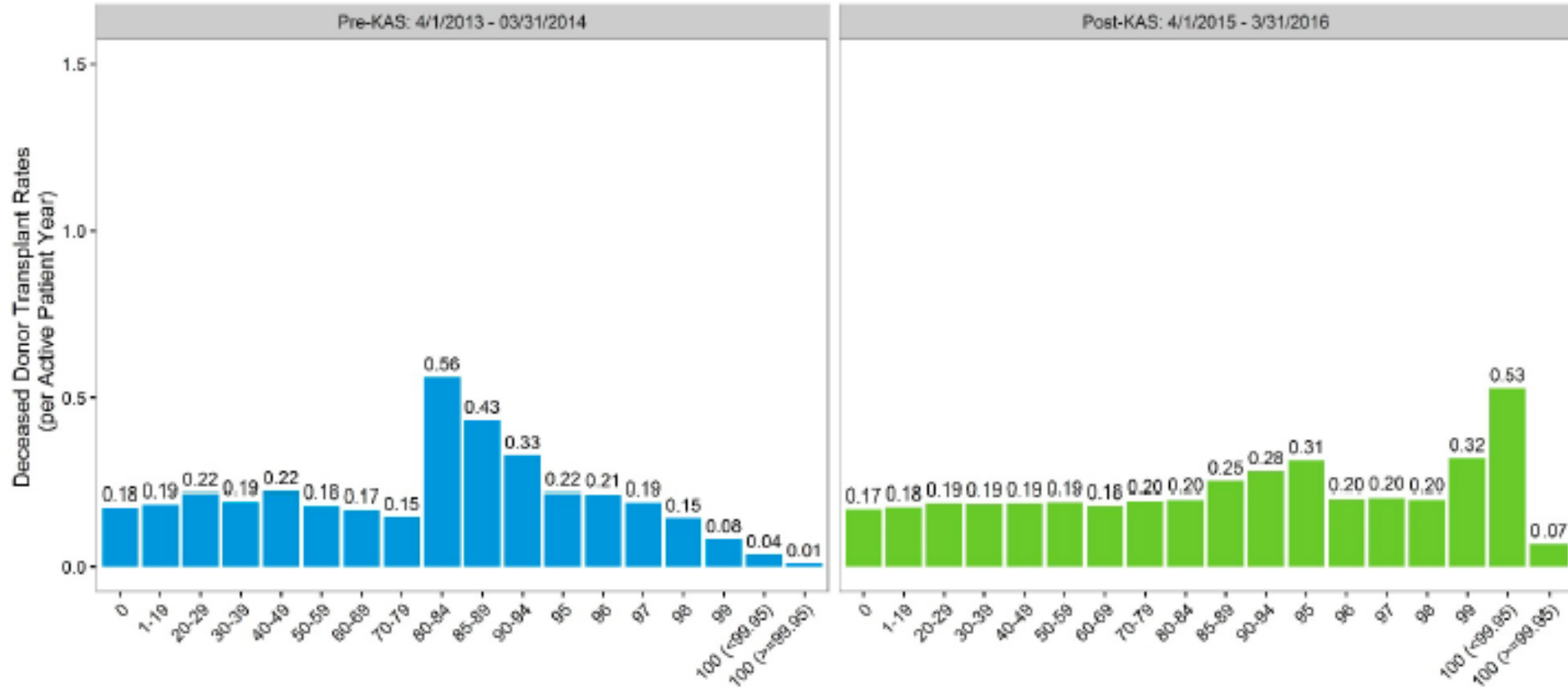
KAS has positively impacted the 99-100% cPRA Group

Figure 1. Percent of solitary deceased donor kidney transplants into 99-100% CPRA recipients



Kucheryavaya A, Aeder M, Turgeon N, Klassen D, Stewart D. 99% and 100% CPRA Patients Since KAS: A Substantial Increase in Transplants with Strong Evidence of a Bolus Effect. [abstract]. *Am J Transplant*. 2016; 16 (suppl 3). <https://atcmeetingabstracts.com/abstract/99-and-100-cpra-patients-since-kas-a-substantial-increase-in-transplants-with-strong-evidence-of-a-bolus-effect/>. Accessed May 14, 2019.

US Transplants by cPRA Score



Source: Organ Procurement and Transplantation Network Report on Equity in Access 2016

DSAs and Immunological Barrier to Transplant

- KAS has given priority to people with 99-100% cPRA
- However the percentage of transplanted people in the 99.9%+ has not increased to the extent of the overall 99-100% group
- People in this group face an IgG immunological barrier that delays access to transplant significantly
- Currently, there are no approved options to remove donor specific antibodies for these patients
- A small number of centers have developed institutional protocols to remove donor specific antibodies, that provide an option for some patients, mostly in living donor situations

Investigational IgG degrading enzyme: Imlifidase

- Imlifidase is currently in development in kidney transplant:
 - IgG-specific degrading enzyme of *S. pyogenes* (not IgM, IgA, IgD or IgE)
 - Cleaves all forms of IgG *in vitro*: free, bound to antigen and B-cell receptor (IgG-type)
 - A two-step cleavage reaction
 - Inhibits Fc-mediated activities
 - In Phase 2 studies it has been observed that imlifidase cleaves all IgG and all 35 highly-sensitized patients were transplanted

