What being highly sensitised means for people with end-stage kidney disease: transplantation can be an option

Educational booklet developed with the support of Hansa Biopharma

Why HLAs are important

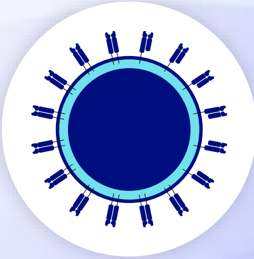
People who are waiting for a kidney transplant need a donor kidney that is compatible with their body. A number of factors, including blood type, organ size and human leukocyte antigen (HLA) antibody profile determine compatibility.

HLAs are molecules that sit on the surface of all cells within the body. They help the immune system distinguish the body's own cells (i.e. 'authorised personnel') from other cells (i.e. 'unknown personnel').

A donor kidney's HLA profile must closely align with the recipient's HLA profile for it to be a suitable match and for the transplant to stand a good chance of success.[1]

Why HLAs are important

Everyone has a unique combination of HLAs that are found on the surface of most cells within their body



How a person's immune system responds to different HLAs can be compared to an authorised personnel list for a restricted facility (i.e. their body)

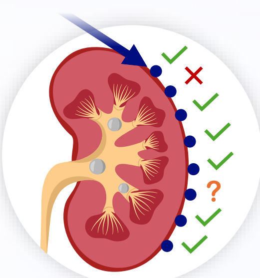
Their own HLAs are considered known and friendly: 'authorised personnel'

HLAs that are different to their own, and that their body has previously been exposed to are considered known and unfriendly: 'no entry'

HLAs that they have never been exposed to are considered unknown and unfriendly: 'unknown personnel'

More compatible kidney

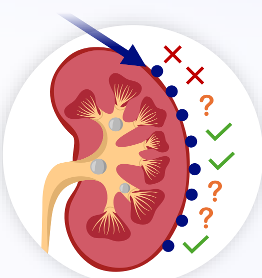
HLAs



Donor kidney

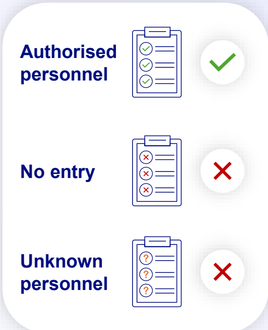
Less compatible kidney

HLAs



Donor kidney

Recipient's HLA lists



For a donor kidney to have the best chance of acceptance, most of the donor kidney's HLAs must be on the recipient's 'authorised personnel' list, with as few as possible on the 'no entry' list. The more HLAs on the 'no entry' and 'unknown personnel' lists, the more likely it is that the recipient's immune system will recognise the donor kidney as foreign and attack it, which may lead to organ damage and rejection

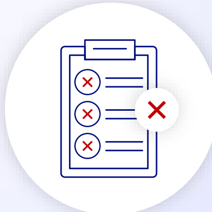
What being highly sensitised means

A person may become highly sensitised if they are exposed to the cells of another person, for example via receiving a blood transfusion.[1,2] When the body's immune system is exposed to the cells of another person, it identifies those cells as 'unknown personnel' as they have a different unique combination of HLAs on their surface. The immune system wants to remove any cells that are unknown as it sees them as a threat to the body. To do this, the immune system produces anti-HLA antibodies, which bind to the HLAs on the unknown cell's surface and kill the cell.[2,3] The immune system remembers any unknown cells it comes across and adds them to its 'no entry' list to be able to quickly and easily identify and kill them if they enter the body again in the future. People who are highly sensitised have a long 'no entry' list for HLAs and a high number of anti-HLA antibodies.[2]

People who are highly sensitised to HLAs make up approximately 30% of people waiting for a kidney transplant.[4] Finding a donor kidney that is a suitable match is difficult for people who are highly sensitised, as they have a very long list of 'no entry' HLAs, and so they can face long waiting times on transplant lists.[1,2,4]

What being highly sensitised means

Blood transfusion **Pregnancy** **Organ transplant**



A person's immune system may encounter HLAs that are different to their own, i.e. 'unauthorised personnel', through exposure to other people's cells via blood transfusion, pregnancy or organ transplant

Any HLAs that were previously unknown are added to the 'no entry' list for the immune system to better recognise them next time. The immune system treats the body as a highly restricted facility – no new HLAs can join the 'authorised personnel' list

The immune system will protect the person by developing anti-HLA antibodies to attack and remove the newly listed 'no entry' HLAs

---

Highly sensitised person

=

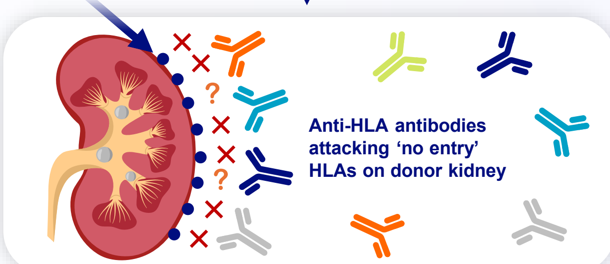
Very long HLA 'no entry' list

+

High levels of anti-HLA antibodies

HLAs

Donor kidney



People who are highly sensitised have, over time, developed a very long HLA 'no entry' list and a lot of anti-HLA antibodies. This usually happens when their body has been exposed to numerous foreign HLA antigens via blood transfusion, pregnancy or a previous organ transplant. Having such a long 'no entry' list and high levels of anti-HLA antibodies makes it hard to find a suitable donor kidney

Why desensitisation could be your solution

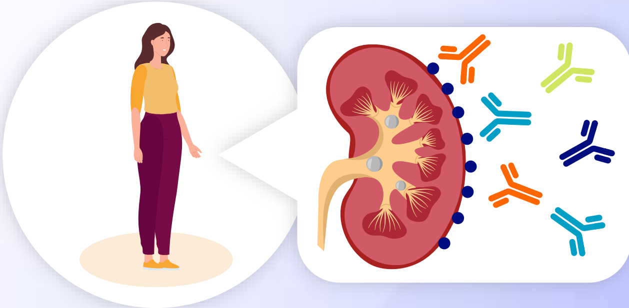
Kidney transplantation is often the most effective treatment for people with end-stage kidney disease.[2] However, for a highly sensitised person, pursuing a kidney transplant may present a challenge, as a suitable donor kidney may be difficult to find.

Desensitisation is a type of treatment that temporarily reduces the number of anti-HLA antibodies a person has.[2] This means a donor kidney can be transplanted without the anti-HLA antibodies reacting and attacking the donor kidney, leading to a higher chance of success. Desensitisation treatment must be timed perfectly to coincide with the availability of a suitable donor kidney for transplantation. Various desensitisation treatments are available, with differing methods of administration (e.g. via injection) and delivery timescales varying from 24 hours to 4 months.[5,6] After the transplant, anti-rejection medicine is given to keep the recipient's levels of anti-HLA antibodies low enough to prevent their body from recognising the donor kidney's HLAs as 'unknown' or 'no entry'.

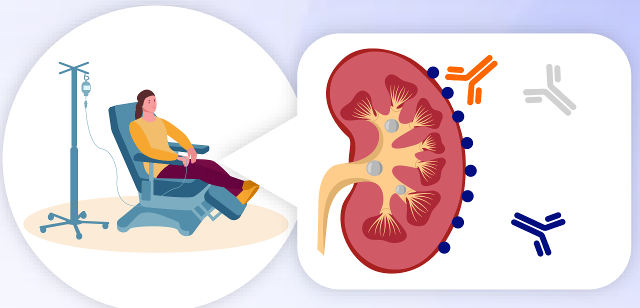
Desensitisation treatment may increase a highly sensitised recipient's chance of finding a suitable match.[7]

Why desensitisation could be your solution

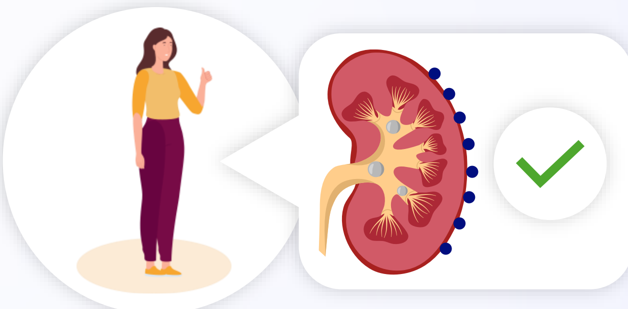
High level of anti-HLA antibodies = a barrier to finding a suitable donor



Desensitisation treatment in progress = lowering levels of anti-HLA antibodies, and therefore lowering the sensitisation barrier to finding a suitable donor



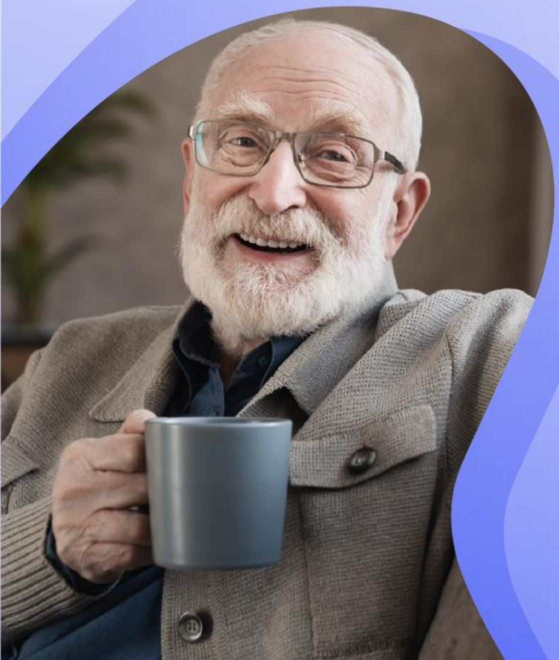
Successful completion of desensitisation treatment = low level of residual anti-HLA antibodies and an increased chance of finding a suitable donor



Treatment must perfectly coincide with the availability of a suitable 'mismatched' donor kidney

Delisting is another option that may increase your chances of finding a suitable donor kidney

Delisting of anti-HLA antibodies is another way of increasing the chances of a highly sensitised person finding a donor kidney that is a suitable match.[7] The highly sensitised person's doctor reviews their HLA 'no entry' list to decide if part of the list could be ignored. The doctor may decide part of the list can be ignored if the specific anti-HLA antibody response is not viewed as dangerous or if it can be appropriately managed. The doctor would then remove the parts of the list that they think can be ignored from the recipient's profile in the donor allocation system. This increases the chance of the system allocating the patient a suitable donor match.



Questions

Please speak to your doctor or healthcare provider to find out more information on the potential of receiving a kidney transplant as a person with highly sensitised end-stage kidney disease.

Suggested questions to discuss with your doctor:

What does being highly sensitised mean for my chances of finding a kidney donor, and how is this measured?

Are there any special programmes or matching schemes I can join to increase my chances of finding a suitable donor organ?

Questions

What steps can I take, medically or lifestyle-wise, to stay eligible and ready for a kidney transplant while I wait?

References

1. Rees L, Kim JJ. HLA sensitisation: can it be prevented? Paediatric Nephrology 2015;30:577–587.
2. May FNJ, Rees MT, Griffin S, Fildes JE. Understanding immunological response to desensitisation strategies in highly sensitised potential kidney transplant patients. Transplantation Reviews 2021;35:100596.
3. Carey BS, Poulton KV, Poles A. Factors affecting HLA expression: a review. International Journal of Immunogenetics 2019;46:307–320.
4. Dudreuilh C, Basu S, Shaw O, et al. Highly sensitised individuals present a distinct Treg signature compared to unsensitised individuals on haemodialysis. Frontiers in Transplantation 2023;2:1165320.
5. electronic Medicines Compendium (eMC). 2024. Idefirix 11mg powder for concentrate for solution for infusion: summary of product characteristics (SmPC). Available from: https://www.medicines.org.uk/emc/product/13155/smpc/print (Accessed 27 May 2025).
6. Kakuta Y, Satoh S, Watarai Y, et al. Successful desensitization of T cell flow cytometry crossmatch positive renal transplant recipients using plasmapheresis and super high-dose intravenous immunoglobulin. Transplantation Direct 2017;4:e336.
7. Dudreuilh C, Jarvis P, Beadle D, et al. Can regulatory T cells improve outcomes of sensitised patients after HLA-Ab incompatible renal transplantation: study protocol for the Phase IIa GAMECHANgER-1 trial. BMC Nephrology 2023;24:117.

Additional Resources

EKPF website

This booklet has been developed by EKPF with the aim of providing clear, accessible information to support patients and caregivers. The production and distribution of this resource have been made possible through an educational grant and logistical support from Hansa Biopharma, Lund Sweden.

EKPF
EUROPEAN KIDNEY PATIENTS' FEDERATION
CEAPIR