ESOTLJ2.0
TRANSPLANTATION LEARNING JOURNEY
•onlineexperience• 15-17 November 2020

Scientific Highlights

Transplantation Learning Journey
15-17 November 2020

About TLJ 2.0

TLJ is a comprehensive 360 experience, enabling participants to grow their knowledge and develop collaborations on a range of topics in transplantation.

Designed to promote discussion and interaction before and after the meeting, the programme is developed by ESOT's Sections and Committees with the aim of providing value to all audiences.

This Report summarises the scientific highlights from TLJ 2.0, which was held from 15-17 November 2020.

To find out more about TLJ 2.0, please visit: **tlj-esot.org**

To find out more about ESOT, please visit: **esot.org**

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WS01

New surrogate endpoints in transplantation

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WS01

NEW SURROGATE ENDPOINTS IN TRANSPLANTATION

Futuristic transplants moving closer

The promise of xenotransplantation to overcome the scarcity of human organs has progressed so far that consensus on clinical trial design for animal to human transplants is now needed, WS01 reported.

Maarten Naesens, Clinical Director at the Nephrology and Renal Transplantation unit of the University Hospitals Leuven and Professor at the Department of Microbiology, Immunology and Transplantation at KU Leuven, Belgium, told the first session of TLJ 2.0 that progress has been 'really tremendous' with genetically-engineered animal organs 'almost ready' for clinical trial in humans.

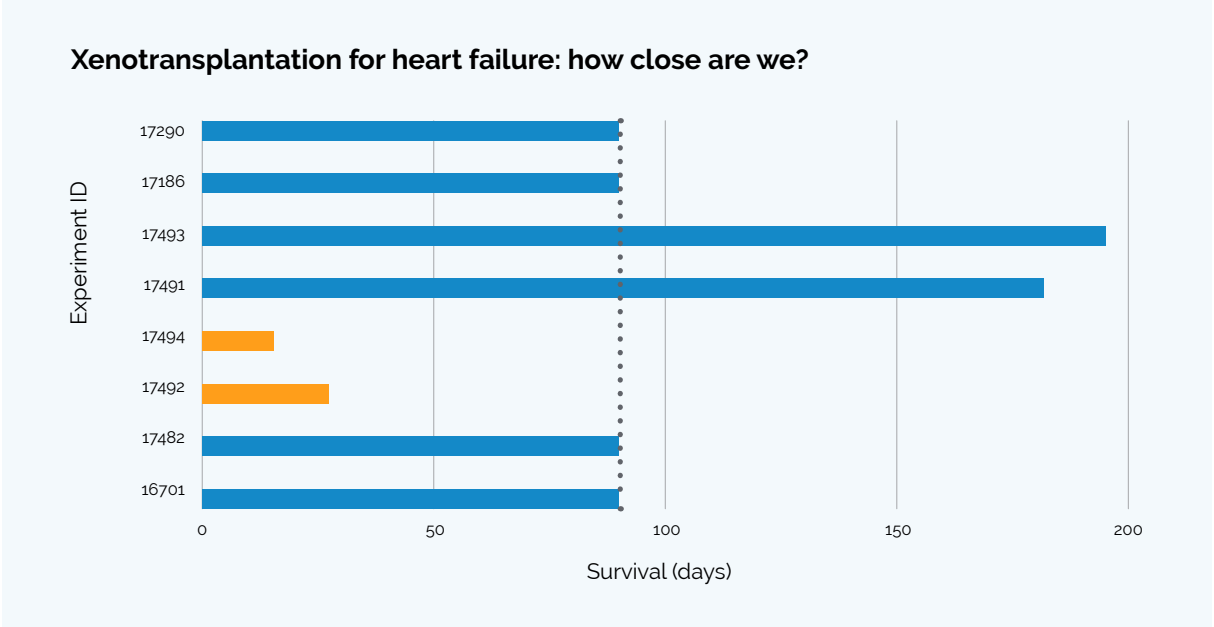
Pig to primate transplants using hearts and kidneys has been successful, functioning for many months without any sign of problems, the 19-member workstream had reported.

His colleague Emmanule Cozzi, a clinical immunologist at the Padua Medical Centre who is Past President of the International Xenotransplantation Association (IXA), had remarked they 'seem to survive forever.'

> Naesens highlighted the work of the Center for Innovative Medical Models in Munich, a Specified Pathogen Free (SPF) breeding facility where research[1] by workstream member Bruno Reichart on heart transplants in primates with heart failure was carried out. Reichart, a former cardiothoracic surgeon who carried out the first heart transplant in Germany in 1981, found only two primates died because of porcine CMV infection but all the others survived for at least 80 days, two of them far longer.

A review of the regulatory landscape by workstream member Prof Linda Scobie from the Department of Biological and Biomedical Sciences at Glasgow Caledonian University, indicated no major hurdles for the concept of xenotransplantation, but the need for alignment with a vast amount of guidelines and directives about safety, quality, processing, traceability etc.

1 B.Reichart et al, JHLTx, 2020



Eligibility the big issue

The next question to be answered was inclusion criteria — which patients should be considered suitable for Phase 1 & 2 clinical trials. The workstream is proposing those who are at high risk of human-to-human transplants, such as HLA incompatible highly sensitized patients in end stage kidney failure who otherwise would have to remain on dialysis long-term.

Richard N Pierson, the Scientific Director of the Center for Transplantation Sciences at Massachusetts General Hospital, Boston, who gave an overview on the ethics of xenotransplantation in the Focus session, agreed that the patient population should be those with 'no good options' such as sensitized patients with dialysis access problems. But he added it was important not to include people who are 'desperate.'

TLJ attendees heard that xenotransplantation is not the only way to overcome the scarcity of organs. Other futuristic innovations included organ resuscitation by machine perfusion, which recovers and treats organs not able to function well; recellularised organs and also pluripotent stem cell-derived organs. These are all becoming a reality, Martin Hoogduijn, an associated professor at the section Nephrology and Transplantation of the Department of Internal Medicine, Erasmus Medical Center in Rotterdam, told an earlier webinar.

Prof Naesens said:

> "At this early stage it's extremely important to think about the end goal of all these very basic research endeavaours; at the moment the end goal is how could these innovative technologies be implemented in clinical trials, how should we seek authorities' approval of study designs before we could ever use that in clinical practice."

Patient involvement 'crucial'

Workstream member Kevin Fowler, a US patient advocate and kidney recipient, had told the team that to recruit patients for complex and potentially risky trials, trust must be built through systematic engagement. 'Patient involvement is crucial to success,' Naesens said.

The European Union has indicated that it is interested in moving the field forward, with Anna-Pia Papageorgiou, a policy officer at the Commission, reporting the feedback that "we are not too scared of bold and futuristic types of research."

Prof Pierson, a cardiac surgeon and Chair of the Ethics Committee for the International Xenotransplantation Association, discussed the 'unknown unknowns' of xenotransplantation in his live Focus.

These included risks to recipients but also potentially to caregivers and society at large if infection occurs which may be transmittable. He said we might never be able to completely exclude these risks before clinical trials. He also raised the question of whether we can ever get truly informed consent in such trials.

For a lively discussion he was joined by Emanuele Cozzi, Stefan Schneeberger, Deputy Director of the Department of Visceral, Transplant and Thoracic Surgery and Head of the Transplant and Hepatobiliary Surgery Program at the Innsbruck Medical University, Austria, Professor James Neuberger, Consultant Physician in the Liver Unit in Queen Elizabeth Hospital, Birmingham, UK and Colin White, the National Projects Manager with the Irish Kidney Association.

> Prof Pierson said it was 'entirely acceptable' to allow people to take that risk as long as all the available information was fully shared.

The workstream is drafting a consensus document/white paper and Prof Naesens asked for contributions to take this forward, including identification of the remaining hurdles to tackle before clinical use, current legislation and examples from other fields such as Advanced Therapy Medicinal Products (ATMPs), clinical trial design and endpoints.

Prof Naesens said it may seem early to initiate these discussions on the clinical trial design, inclusion criteria and endpoints but the workstream's discussions quickly illustrated some knowledge gaps in the current preclinical research.

He said involvement of ethicists, clinical trialists, the health authorities, the patients and the society at large is necessary, as some very sensitive issues will need to be addressed before embarking on such clinical trials. "A very wide and open interaction about these topics is therefore very timely," he concluded.

WS02

Cytomegalovirus (CMV) Infection and disease

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WS02

CMV INFECTION AND DISEASE

Harmonising CMV strategies

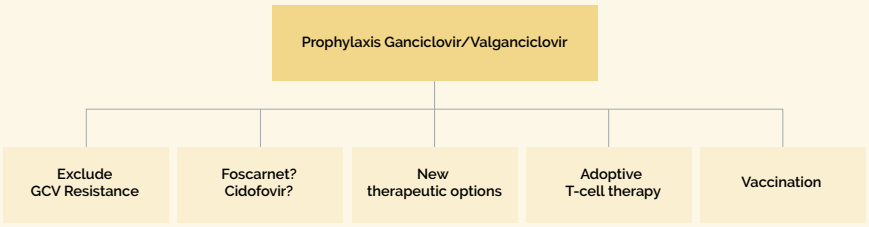
A study on prevention, diagnosis and treatment of CMV infection by ESOT's Workstream 2 has shed further light on variation across Europe and a divergence from international management guidelines, Prof Paolo Grossi said.

This variation includes differences in the use of universal prophylaxis with an anti-viral drug and/or preemptive therapy (PET), which is recommended in the literature.[1] Valganciclovir is currently the most commonly used drug for universal prophylaxis.

	D+R-	D+R+	D-R+	D-R-
Prophylaxis	173	99	87	32
PET	21	71	64	47
PET after Prophylaxis	28	12	14	5
none	2	42	59	140

While there is no perfect treatment, especially for 'never do well' patients, an 'increased armamentarium' of new anti-viral drugs such as letermovir are on the horizon, which may facilitate a safer and more effective strategy to prevent CMV infection in this population, the TLJ 2.0 heard.

'Never do well' patients



Cytomegalovirus (CMV) infection is the single most important pathogen affecting solid organ transplant recipients (SOT), with significant impact on patient and graft survival. It can cause pneumonia and GI tract infections, and indirect effects such as immunosuppression, super-infections and damage to the donated organ.

Workstream 2, led by Prof Grossi, Professor of Infectious Diseases at the University of Insubria, Varese, Italy, with eight other members, carried out a multi-centre study on current knowledge gaps with the aim of proposing prospective studies to improve patient survival in the future.

They received 224 responses, 85% from European transplant centres, with 50% answered by transplant physicians.

1 Kotton C, et al. Transplantation 2018;102: 900–931

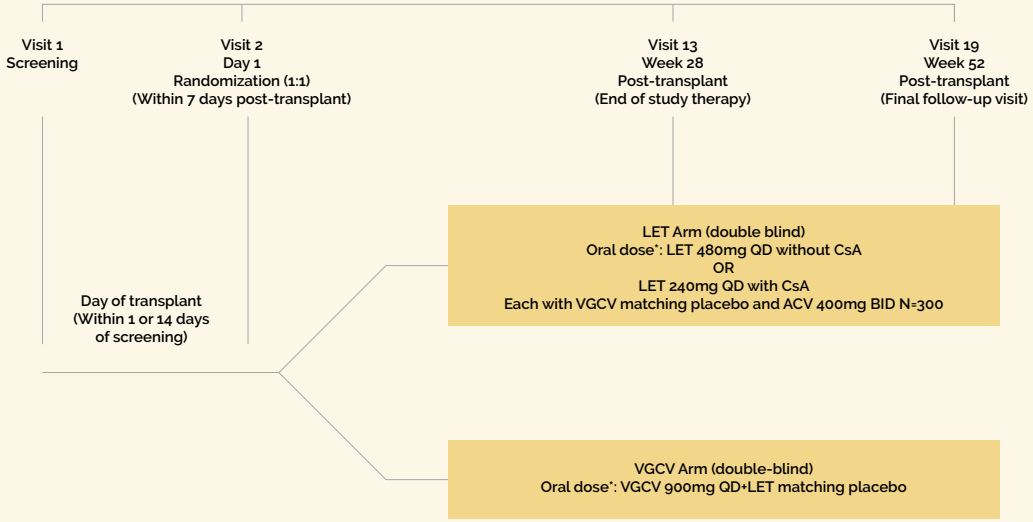
The results, which have been submitted to Transplant International for publication, found that following D-R- transplants, 32 centres were using prophylaxis and 47 PET despite very low risk, which Prof Grossi said was 'surprising.'

And a number of centres used no preventive therapy at all in patients with certain serostatus – for example in D+ R+, 42 used none (18%); in D-R+ 59 used none (26%).

Most centres started prophylaxis within the first week, with 124 starting 1-3 days after transplant.

For D+R- cases, most continued for 6 months, but in lung transplants, 61% continued for 12 months.

Letermovir prophylaxis in KT



Toxicity and the need for alternative therapies

> Almost all (95%) centres reported using valganciclovir for D+R- patients. However, 64% of reported myelotoxicity, notably leukopenia and neutropenia, which prompted discontinuation of prophylaxis in at least 10% of patients. Dose reduction or discontinuation of the treatment increase the risk of more bacterial infections and CMV infection for the patient.

In terms of tools used to diagnose/monitor CMV infections, 124 (55%) were using Quantitative whole blood DNA PCR, followed by 91 (41%) using Quantitative plasma DNA PCR. While 162 use the WHO standard units for reporting quantitative DNA PCR, 7 did not and 55 did not know.

Prof Grossi said the results of this survey may help in designing future studies aimed at evaluating the safety and efficacy of new strategies to prevent CMV infection and disease in SOT recipients in Europe.

He added: "We will continue this project to try to harmonise management of CMV infection in this challenging population."

Anti-virals on horizon

The later Focus session highlighted promising developments in preventative therapies.

Professor Nissam Kamar, from the Department of Nephrology and Organ Transplantation at Toulouse University Hospital, said Letermovir, a CMV-specific terminase enzyme inhibitor, has been approved for use in stem cell transplants and was being tested on kidney transplants patients. He was 'hopeful' for the results, he said.

He also raised the prospect of mTOR inhibitors in the prevention of CMV for D+R- cases, telling the live Q&A that when used in combination with prophylaxis they may reduce late onset disease.

Jose Maria Aguado, Head of the Infectious Diseases Unit at the University hospital 12 de Octubre, Madrid, agreed that there was an 'increased armamentarium' against CMV, with Letermovir for prophylaxis and Maribavir for therapy of refractory-resistant CMV.

However he said there is a particular need for a drug against CMV in 'never do well patients.' Those cases are "very frustrating… where the clinician is not sure what to do," he said.

Autologous adoptive T-cell therapy, which has some trial data from Australia is a 'fantastic' approach but is probably too complicated, he concluded, while a vaccine is some way off.

> Prof Grossi told the live Q&A that Letermovir could be an 'excellent alternative' to Valganciclovir for kidney recipients. "We will have to see the final results but if it's similar to what we have seen in stem cell transplants it could be a great opportunity for prophylaxis in this population."

In the panel commentary, Dr Raj Thuraisingham, consultant nephrologist at Barts Health in London, UK, and chair of ESOT's Education Committee, said that because of the need for dose adjustment related to kidney function and the issues with myelotoxicity with Valganciclovir, it was 'exciting' to hear about these developments. He also welcomed the potential use of Maribavir as a 'rescue drug' in cases of resistance.

WS03

Cancer in pre and post transplant patients

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WS03

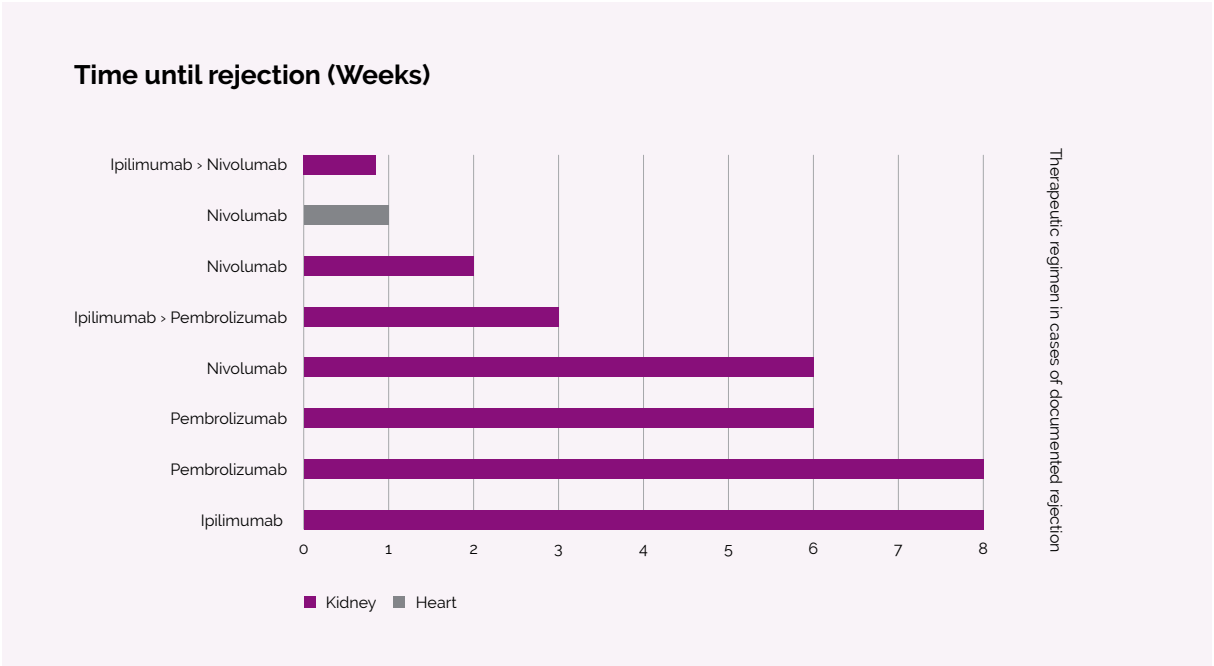
CANCER IN PRE AND POST TRANSPLANT PATIENTS

Withdraw suppression before immunotherapy

A radical solution is needed to combat the risk of acute organ rejection when reducing immuno-suppressant drugs in kidney transplant patients being treated for cancer, day 1 of the TLJ 2.0 conference heard.

Immunotherapy — using checkpoint inhibitors (CPI) — has revolutionised cancer treatment in the general population by utilising the body's immune system to fight malignancy with its own T cells.

Umberto Maggiore, Associate Professor of Nephrology at the University of Parma, and Chief of the Transplant Program at the University Hospital of Parma, told the virtual conference that CPIs may now be the way forward to treat cancer in transplant patients.



However, in order for them to work, immunosuppression needs to be reduced which risks the 'catastrophe' of acute organ rejection which may cause death in recipients of life-saving organs, he said.

> If immunosupression reduction can be managed, potentially, CPIs may be more efficacious in SOT recipients compared to non-SOT recipients with cancer — and consensus is now required on how best to achieve this.

In the Focus section for WS03 he showed data[1] in kidney transplant patients who had cancer treated with CPIs. A quarter had a response against the cancer and no rejection, while a quarter had a response and a rejection. The remaining 50% had no response, half with rejection, half without.

The key question is how maintenance anti-rejection treatment can be safely reduced to let checkpoint inhibitors fully unleash T cells against cancer but at the same time minimize the risk of graft loss due to rejection.

It has been suggested that the use of mTOR-inhibitors may offer an opportunity to uncouple CPI toxicity (rejection) and efficacy (anti-tumoral action). However, the pooled case series report so far do not seem to support the universal use of mTOR-inhbitors in solid organ transplant recipients with cancer undergoing CPI treatment.

He proposed that, in kidney transplant recipients, who can resort to dialysis in case of rejection-induced graft failure, the option of completely withdrawing immunosuppressants before immunotherapy — and in case of severe rejection, of performing graft nephrectomy to avoid having to stop CPI, should be included among the possible therapeutic strategies.

Discussing this option with patients before cancer treatment should be considered, he said. There should be a tailored approach as one size does not fit all — not all cancers are equal in terms of their effect on the immune system. "We have to have a different approach,' he said.

Cancer management for transplant patients

Transplant recipients are at an increased risk of cancer, particularly virus-induced cancer such as post-transplant lymphoproliferative disorders and Kaposi sarcoma, but also many other cancer types which occur more frequently because of reduced immunosurveillance.

Earlier in the Report session, Dr Rachel Hellemans, from the Department of Nephrology, Antwerp University Hospital, said there was 'little known' about the optimal management of maintenance anti-rejection therapy of solid organ transplant recipients who have previously been treated with curative intent for solid organ cancer (excluding non-melanoma skin cancer) or post-transplant lymphoma (PTLD).

The limited guidelines and consensus statements suggest an overall reduction of immunosuppression, balanced to acute rejection risk, but there is little direct evidence on safety and efficacy, she continued.

Oncologists use calculations to decide on the best treatment strategy but these are based on non-transplant patients. Transplant recipients may have a worse prognosis, with more aggressive disease, and even with local stage cancers, have an up to 2 or 3 times higher risk of dying, possibly due to being more susceptible to micro metastases because of reduced immunosurveillance.

So, she said there was a balancing act — to reduce or switch immunosuppressants but also avoid rejection or other adverse events.

The team explored 2 questions — should anti-rejection therapy be reduced in potentially cured transplant non-skin cancer in solid organ transplant recipients? Or should they be switched to an mTOR inhibitor such as everolimus?

In answer to these questions, they found no strong direct evidence. In the latter there was some expert guidance from the KDIGO 2009 on kidney transplantation and consensus reports on heart[2] and kidney[3] recipients.

Which drug to counter a decrease in immunosuppression?

Switching from calcineurin inhibitor (CNI) to an mTORi, which is already approved (though at higher dosage compared to those used for maintenance anti-rejection treatment) as a treatment for certain breast cancers, neuroendocrine tumors and renal cell carcinoma, seems an attractive option. A meta-analysis of RCT on mTORi-based CNI-free regimens in kidney transplant recipients showed that it reduces the risk of de novo non-melanoma skin cancer in kidney transplant recipients but this is less clear in non-skin cancers.[4]

Moreover, US registry data for kidney transplants[5] shows no significant reduction in cancer (excluding non-melanoma skin cancer) with sirolimus, and an increase in prostate cancer. Meta-analyses have shown that in kidney transplants switching to mTORi-based CNI-free regimens increased the risk of acute rejection[6] and frequently led to discontinuation due to adverse events (22 % vs 10 %) compared with remaining on a standard CNI-based regime.[7] Finally, Knoll et al have shown that CNI-free mTORI-inhibitor based immunusspressive regimens may be associated with an increased mortality.[3]

Rather than switching to CNI-free mTOR-inhibitors based regmens, one may consider the option of using mTOR-inhibitors associated with low or very-low dose CNI, as used in the TRANSFORM study. In de novo kidney transplant recipients this strategy is not associated with increased risk of acute rejection. However, a recent meta-analysis[8] showed the evidence that combining mTORi with low dose CNI prevents the occurrence of cancer is still very limited.

Finally, all the evidence that we have mentioned so far, comes from RCT on the general kidney transplant population. We do not have any direct evidence on the effect of mTORi based regimens in solid organ transplant recipients treated for cancer with curative intent.

In conclusion, there is currently not enough evidence for universally switching to mTOR-inhibitors in solid organ transplant recipients who have been treated for cancer with curatve intent. Benefit and risk should be discussed with the patient.

Notable recent advances with checkpoint inhibtors in 2018-2020:

Skin
Melanoma nivolumab
nivolumab + ipilimumab
Merkel cell avelumab
Squamous cell cemiplimab

Lung
nivolumab+ipililumab
durvalumab after standard
chemotherapy and radiation

Breast
pembrolizumab
+ standard neoadjuvant therapy
(high-risk, HER2-neg)

Bladder
multitreatment
chemotherapy +
of checkpoint inhibition

Kidney
nivolumab prembolizumab
avelumab

Head and neck
nivolumab

Liver
nivolumab

Stomach
pembrolizumab

Q&A session

Dr Hellemans told the Live Q&A that the safety of the use of CPI in kidney transplant recipients returning to dialysis is unclear.

Dr Raj Thuraisingham, consultant nephrologist, agreed with Prof Maggiore that an individualised approach is best, equipping patients to make an informed decision, and added that the data on 25% of KTR gaining a response against cancer without rejection was very useful when advising them.

He told the live panel discussion, "You are asking [the patient] to swap one quality of life for another quality of life. What is the real gain from that, if it's a matter of weeks or months it gives them? If it's longer than that or even a cure, then you could have a completely different view. It's a big decision to make."

1 D'Izarny-Gargas Am J Transplant 2020;20:2457
2 Epailly E et al. Clin Transplant 2011; 25(5): E475-86
3 Campistol JM et al. Nephrol Dial Transplant 2007; 22(S1): i36-41
4 Knoll et al, BMJ 2014.
5 Yanik EL et al. Am J Transplant 2015; 15(1): 129-36
6 Lim et al, AJT 2014
7 Lim WH et al. Am J Transplant 2014; 14(9): 2106-19
8 Montero Transplantaton 2019

WS04

Normothermic regional perfusion (NRP) in donation after circulatory death

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WS04

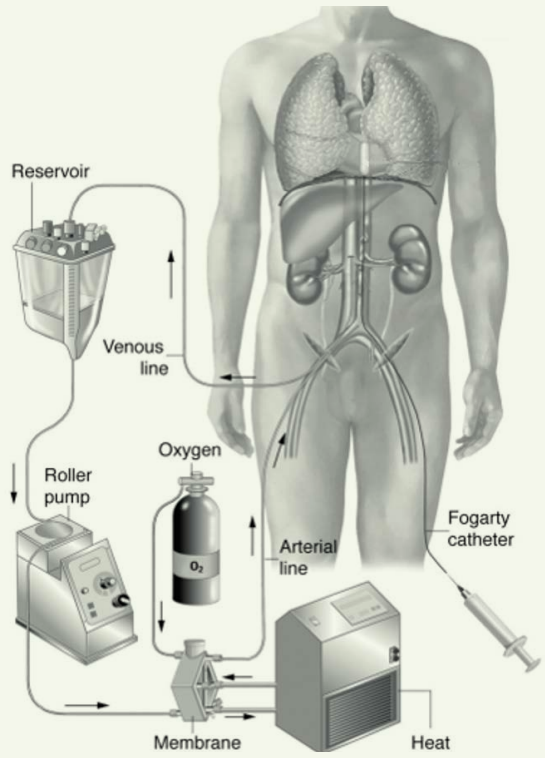
NRP IN DONATION AFTER CIRCULATORY DEATH

Boost NRP to boost organs

Normothermic Regional Perfusion (NRP) is a complex technique, but transplant teams should be encouraged to use it in Donation after Circulatory Death (DCD) to increase the number of organs available and reduce post-transplant complications associated with DCD donation. The Workstream has focused on centralising and reviewing all the evidence behind the technique and has set up a network of European experts to compile best practice recommendations on how to run NRP in clinical practice.

"NRP is an important technique to understand as it tackles the two main issues of DCD donation, namely lower organ utilisation rates compared to donation after brain death and specific post-transplant complications", workstream leader Professor Ina Jochmans, Abdominal Transplant Surgeon at the University Hospitals Leuven in Belgium, said. "In some countries, such as Spain and France, it has already become the standard technique of DCD organ procurement. And, as figures from 2007 and 2017 show, with a continued increase in DCD donation in Europe, we expect NRP to be more widely implemented in the coming years".

Regional perfusion restores circulation *in situ* in DCD donors (1)



1 Fondevila AJT 2007

NRP restores the blood circulation in the abdomen or both abdomen and chest after the donor has died. By returning blood flow to the organs, their energy levels can be improved before the organs are removed and stored so that the organ is in better shape at time of transplantation. Furthermore, NRP allows organ function to resume which allows assessing for viability.

Trained NRP teams are key

In the focus session Dr David Paredes, a specialist in transplant coordination and Dr Amelia Hessheimer, Attending Surgeon in the Hepatopancreatobiliary Surgery & Liver Transplantation Unit both at the Hospital Clínic in Barcelona, Spain, reviewed the NRP technique in detail.

The technique requires more coordination, planning, infrastructure, personnel, and expertise than rapid recovery in DCD, with at least two surgeons, a scrub nurse, a circulating nurse, and a perfusionist. It also takes more time than direct procurement. Typically NRP takes 2 hours, and can range between 1-4 hours.

Dr Paredes told the Focus session that the increased complexity should not dissuade from implementation. "It can be done in many settings; this is a good technique to learn." The basic principles of the technique are straightforward. They involve aortic cannulation, venous drainage, and occlusion of head and neck arteries and can be carried out in an emergency room, ICU, or operating theatre. The kit includes a pump, heat exchanger, membrane oxygenator and crystalloid priming solution to fill the circuit tubing. Dr Paredes explained that it is vital to analyse results and consult colleagues regarding any problems that are encountered. He concluded, "Communication is the key to success of NRP."

The workstream includes a subgroup to discuss ethical aspects related to NRP to provide a framework to guide discussions and debates in centres with active programmes and those wishing to start. "Indeed, care needs to be taken to not inadvertently re-establish blood perfusion to the brain, as concern has been expressed that this threatens the 'permanence principle' on which death in DCD donation is declared,[2]" Prof. Jochmans said. Technical modifications have been proposed to avoid reperfusion of the brain. In the Focus session, Dr Hessheimer explained thoraco-abdominal NRP is more complex than abdominal NRP, due to the special efforts needed to ensure permanent loss of circulation to the brain is maintained. "It's not something to be done by inexperienced or unprepared groups," she said, adding that further experience in this technique is necessary before any statements regarding practice and utility can be made.

Recharging the battery

Giving an overview, Professor Jochmans said there are fewer liver, pancreas, heart, and lung transplants donated after circulatory death compared with brainstem death (DBD). For example, in the UK there were 79 liver transplants DBD vs 29 DCD in the reference year 2018-2019[3] which she said was a 'substantial and important decrease in organ utilisation.'

A second issue is that DCD organs have an increased risk of complications — they are not normally used in heart transplants, and in kidney and liver donations there are commonly complications such as primary non function of the organ or damage to the intrahepatic bile ducts. This happens because warm ischaemia — restriction in blood supply — during a DCD procedure depletes energy stores before the organ goes onto cold storage, where metabolic changes still happen further depleting energy. When the organ comes out of storage and is reperfused, 'the battery is drained,' she explained. NRP builds in a period during which the battery can be recharged, effectively restoring adenosine triphosphate (ATP) stores.

Increasing organ utilisation in DCD

Prof Jochmans discussed whether NRP solves the two issues for DCD donations of low utilisation and increased complications.

Preliminary research from the UK shows that more abdominal organs are transplanted after NRP in comparison to after direct procurement — for example with NRP, 64 % of DCD livers are transplanted compared with 25% without.[4] A 2020 review of abdominal NRP in DCD says it is feasible and safe with good function after transplantation.[5]

The workstream is carrying out a systematic review of the evidence throughout the temperature settings, and in all 5 organs. A preliminary summary of this systematic review, she said, was 'encouraging' with the outcomes 'similar to better' compared with direct procurement and transplant in DCD or even DBD. Now good quality evidence from prospective studies, ideally randomised, is needed, with outcome definitions aligned, she said.

The workstream is working towards a consensus document and continuing the systematic review of literature of all types of regional perfusion and reported outcomes for kidney, liver, pancreas, heart, and lung; reported techniques; and reported viability testing criteria.

Prof Vassilios Papalois, President of ESOT, said it is crucial that the NRP teams are integrated with the procurement teams with the right structure to support them as they are serving the same cause from different perspectives.

Consultant nephrologist and chair of ESOT's Education Committee, Dr Raj Thuraisingham, said the technique should be embraced. "What's striking is how complex it is and yet it's something we should be thinking about as we need to maximise the number of organs we can use. We have rather crude ways of assessing how well an organ will do. This gives us the opportunity to not only restore the organ but to assess its function."

2 Dalle Ave et al, J Med Ethics 2016
3 NHSBT Annual Activity Report for 2018-2019, courtesy C Watson
4 Oniscu et al, ESOT 2019 meeting, Transplant Int 32(Suppl 2), 125
5 FEM van de Leemkolk et al. Transplantation September 2020

WS05

It's not only extended donor criteria, it's extending the donor pool

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WS05
IT'S NOT ONLY EXTENDED DONOR CRITERIA, IT'S EXTENDING THE DONOR POOL

Shift focus to EOL

The focus for organ procurement must be shifted from death to End of Life (EOL), allowing doctors to take account of the patients' values as well as increasing the number of available organs, Giuseppe Feltrin told the TLJ on Day 2.

Dr Feltrin, a cardiac surgeon from Padua in Italy and member of the Scientific Board of European Donation and Transplant Coordination Organisation (EDTCO), proposed a call to action for colleagues to introduce the Intensive Care to facilitate Organ Donation (ICOD) protocols into their hospitals to extend the donor pool.

Rather than being an inappropriate use of Intensive Care facilities, each donation can lead to six transplanted organs, providing 55.8 years of life.[1]

He said: "It was quite clear to us, if it is intuitive that talking about organ donation means talking about a dead patient…we agreed we need to move forward, focus organ donation on the dying patient, shifting from death to the end of life."

Dr Feltrin began by re-stating the huge variation in donation rates in Europe — with lots of different reasons including resource but also of attitudes by clinicians to organ donation.

He said: "We as donor coordinators are under pressure to get people off the waiting lists and we are struggling to fill the gap between demand and supply."

The 'ideal' donor refers to a Donor after Brain Death (DBD), who is less than age 40 and died of cranial trauma without cardiovascular risk factors. However, the lack of ideal donors means that transplant teams are now grafting organs that would previously have been considered unacceptable.

But he said the reason behind promoting the ICOD principles was not simply to increase the number of available organs.

Civic Right to Donate

Prof Feltrin said donation is a social responsibility and a civic right, so the health care system and the responsible doctor should activate all necessary mechanisms to make the will to donate become a reality — allowing autonomy for the patient.

And he said that end-of life care should be a holistic concept, not limited to medical aspects, where donation should be routinely considered as an option.

Promoting the inclusion of donation in EOL care is good medical practice,
preserves the donor's rights within an institutional frame and can be easily achieved in all hospitals.

In the second Report presentation, Dr Nuria Masnou, In-Hospital transplant coordinator and Head of teaching studies at University Hosital Josep Tueta in Girona, Spain said a new aspect to this discussion was the importance of the values of the potential donor.

She said the best interests of the patient extend beyond their physical care to their values, wishes, and beliefs. The desire to donate gives clinicians the authority to take reasonable steps to ensure

donation occurs.

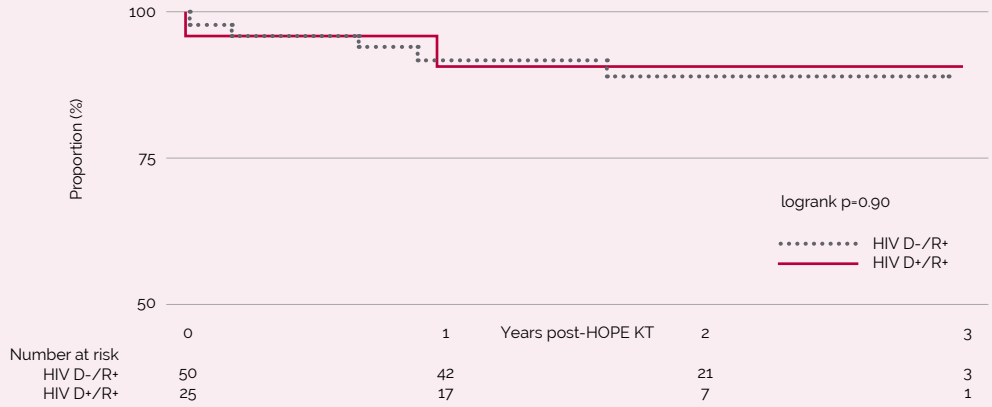
This will maximise the chance of fulfilling the donor's wishes about what happens to them after death; enhance the donor's chances of performing an altruistic act; and promote the prospects of positive memories of the donor after death.

When someone has an acute devastating brain injury there should be a continuum of care involving palliation and discussion of donation. She said: "We all agreed organ donation has to be a part of end-of-life care."

In the live Q&A, Peter Veitch, consultant in general surgery and renal transplantation in the UK, said potentially this approach could increase donations by 30%. When asked if there is a capacity issue, he said most NHS transplant centres could cope and in fact he added 'we would be absolutely delighted' with such a rise.

The workstream's remit is to explore new options to increase the supply of organs beyond Expanded-criteria donors (ECDs). That means balancing the acceptable limit when assessing the risk of transmission of infectious disease or for cancer, considering donors with a history of cancer, or previous Hepatitis C or B infection.

Graft survival by donor HIV status



HIV+ donors a reality

In the later Focus session Prof Paolo Grossi, Professor of Infectious Diseases at the University Of Insubria, Varese, Italy, presented fascinating research on the possibilities for HIV+ people to become effective donors, another way of extending the donor pool.

He said a pilot study showed graft survival outcomes for HIV+ patients given kidneys from HIV+ donors were similar to HIV- donors.[2]

He explained there was the growing possibility of living HIV + organ donations, and eventually HIV+ donations to HIV- patients. Going further, Hepatitis C patients may also be able to donate given advances in therapy in this area, but further data is needed.

While experimental at this stage, Prof Grossi said if he was in the position of urgently needing a transplant: "I would prefer to live with HIV taking a pill every day than dying HIV negative."

Dr Aurora Navarro, Medical biovigilance officer Catalan Transplant Organization (OCATT) and

medical coordinator for Notify Project (World Health Organization) in Barcelona demonstrated how in Spain 2-3% of donors have past cancer.

Since 2013 a registry has documented these cases with two year follow up. Of the 432 cases from 2013-2016, there has been no transmission. Cancer of the Central Nervous System was by far the most common malignancy.[3]

But when the cancer is not previously known about, there is the risk of transmission — there were 49 donors and 97 recipients where any malignancy was not known. Twelve recipients were diagnosed with cancer and five died.[4]

Dr Navarro said we have to be clear that zero risk does not exist, but use the knowledge and data available to indivualise risk. She advocated the establishment of biovigilance registries and said better tools are needed to test for infections and malignancies in donor organs.

Making EOL meaningful

In the live panel discussion, commentators Pisana Ferrari, patient advocate, and Gabriel Oniscu, Secretary of ESOT, welcomed the 'really interesting' and positive developments. Ms Ferrari said donation may make the EOL process more 'meaningful' for families, though acknowledged it was culturally sensitive.

Mr Oniscu, Director of the Transplant Centre at the Royal Infirmary of Edinburgh, a surgeon with a special interest in liver, pancreas and kidney transplantation said incorporating donation discussion as part of end of life care would enable doctors to honour people's wishes.

"We are moving to a collaborative approach where there is not an absolute divide between donation and everything else, it's a continuum and a part of EOL care," he said.

"Realities across Europe are different and each pathway of EOL care has to be adapted to the local realities, and through an educational approach, increase donation."

1 Cabré L, et al. Med Intesniva 2002; 26.
2 Durand C, et al. Am J Transplant. 2020 Jul 23. doi: 10.1111/ajt.16205. Epub ahead of print
3 http://www.ont.es/mailings/MEMORIA%20ANUAL%20DRNE%202013%202014.pdf
4 Non Standard Risk Donation. ONT report 2018. http://www.ont.es/mailings/MEMORIA%20ANUAL%20DRNE%202013%202014.pdf

WS06

HLA desensitization

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WS06

HLA DESENSITIZATION

Action on Sensitization

UP to 30% of people needing a transplant are 'highly sensitized' with HLA antibodies, leaving them with long or indefinite waits for a transplant — and the numbers appear to be increasing, UK data suggests.

Even if sensitized patients are fortunate enough to find an appropriate donor, the transplant is at higher risk of complications, Nizam Mamode, Professor of Transplant Surgery at Guy's and Great Ormond Street Hospitals in London, UK, told attendees at the second day of the TLJ 2.0.

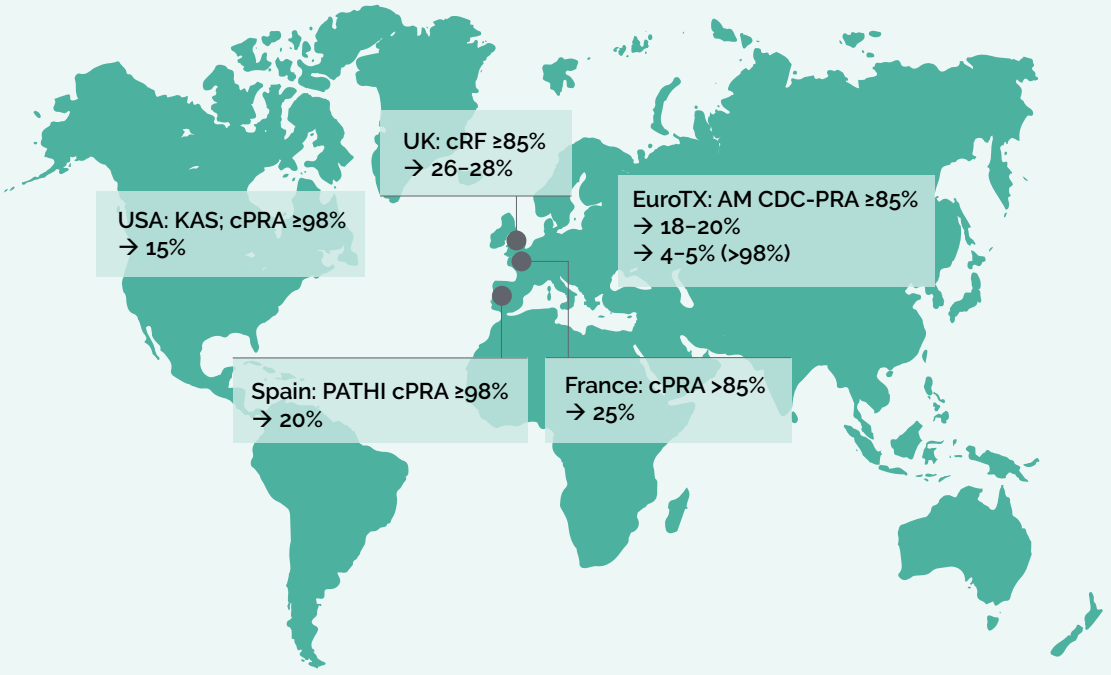
When sensitization is not adequately suppressed, the presence of such antibodies in the recipient's blood is likely to result in antibody-mediated rejection (AMR) and early graft loss.

New approaches are therefore needed to enhance the chances of transplantation in the highly sensitized — especially as deaths from chronic kidney disease are expected to double to 2.2 million by 2040, with a 'surprising' global prevalence of 9.1%.[1]

Prof Mamode said the fact that this is a pressing issue was demonstrated by the high number of views the group's October webinar had received — 454 — the most of any of the workstreams.

In the Report session for WS06, he presented the results of a European wide survey of transplant professionals and patient groups conducted by WS06 on approaches to sensitized patients.

Landscape of Highly Sensitized patients worldwide according to different immune assays



Survival worse than cancer

Prof Mamode began by outlining how kidney transplants have very good outcomes — with a 5 year survival of 94%.[2] However renal registry data shows that for those 65 or over who remain on dialysis, the 5 year survival is poor — 30%, which is worse than major cancers.

And although the waiting list has come down from over 7000 to under 5000 in the UK, it is starting to level off because the 'harder to transplant 'cases accumulate on the waiting list.

He gave example of Lucy who was transplanted at a very young age with her father's kidney. As donor organs only last 25-30 years, she is likely to need a second transplant. It is at that stage where sensitization issues may arise — causes include a previous transplant, pregnancy, or a blood transfusion.

Kidney disease patients will not be offered a deceased donor organ to which they have HLA Antibodies in most allocation systems. Living donations can't go ahead if the recipient has HLA Ab which cause a positive cross match.

The workstream is attempting to find answers to important questions: what is the best way to remove/inactivate antibodies; which patients are at higher risk; and what should we offer them — a direct transplant, a kidney sharing scheme or no transplant at all?

The aim is to produce a guideline on the management of patients with HLA antibodies. Prof Mamode said: "Work is underway but we need your input to form a useful guideline. We will not have all the answers, but might be able to provide helpful information."

In the Focus session, Frans Claas, director of the Eurotransplant Reference Laboratory and Professor of Immunogenetics of Transplantation at the Leiden University Medical Center in the Netherlands, explained that there are two different strategies to enhance transplantation of highly sensitized patients.

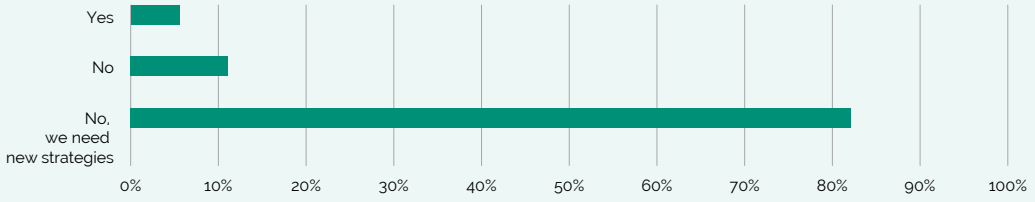
Prioritization schemes and desensitization

One is finding HLA compatible transplants through a mismatch program or paired kidney donation. The second is carrying out HLA incompatible transplants where doctors try to remove the antibodies, a process called desensitization.

Before that can happen, clinicians have to define HLA sensitization and a highly sensitized patient.

A questionnaire was distributed by ESOT and answered by 45 centers all over Europe and further afield which found 'enormous variation.'

Do you think current desensitization immuosuppressive strategies are sufficiently effective to carry out HLA incompatible kidney transplantations?



There was 'no consensus at all' on threshold for a highly sensitized patient and their eligibility for a special program. The definition of highly sensitized varied from under 5% to 98%. The eligibility for a special programme ranged from under 35% to 100%.

He said there is a need for clear guidelines for defining what is a clinically relevant antibody and when doctors should consider a patient for inclusion in a special programme.

As it is very difficult to transplant a highly sensitized patient, attention should also be given to strategies to prevent sensitization.

Next, Dr Sian Griffin, Consultant Nephrologist at University Hospital of Wales, Cardiff, UK, and the General Secretary of the British Transplant Society, presented on a comparison of approaches to HLA incompatibility in Europe.

She said there were increasing opportunities for sensitized patients, with Eurotransplant and Scandiatransplant offering acceptable mismatch programmes.

But a survey of 47 centres in 25 countries again showed large variability in definitions of HLA incompatible transplants. A third said their country/region did not have a prioritization programme to increase the likelihood of receiving a compatible donor.

Most did have a paired kidney exchange scheme in varying stages of development but none said it was successful for most patients. Half said it was successful for a few, and half successful for many.

Only 40% said the different strategies to find a HLA compatible kidney transplant donor in their country was sufficient to transplant the majority of highly sensitized patients waitlisted.

More than 80% said the current desensitization immunosuppressive strategies are not sufficiently effective to carry out HLA incompatible kidney transplantations.

Dr Griffin said: "This emphasises the importance of exploiting existing strategies with avoidance of sensitization where possible, the use of deceased prioritisation schemes and Kidney Sharing Schemes, and the development of therapeutics to enable this group of patients to receive successful transplantation."

In the live Q&A, Prof Mamode said a trans-national kidney donor and recipient list similar to the European bone marrow donation scheme could be the way forward to enhance options.

In the panel discussion, Gabriel Oniscu, Secretary of ESOT and Director of the Transplant Centre at the Royal Infirmary of Edinburgh, said the issue is not a concept easily grasped by many people. He said: "It was quite telling that it had so many hits on YouTube for this workstream highlighting the interest in these patients."

He also commented on the 'staggering statistics' that 20-30% on the waiting list fit this category, indicating that treating these patients will require a lot of resource. "It will be draining the resources of many transplant centres if we don't act."

At present he said there is no 'magic bullet' to solve the problem, and this is why promise of xenotransplantation for these patients was raised in the Live Q&A.

1 GBD Chronic Kidney Disease Collaboration Lancet 2020
2 NHS Blood and Transplant figures, UK

WS07

COVID-19

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WS07
COVID-19

Rethink care due to COVID-19

Interim results of a major study by ESOT led by Dr Alexandre Loupy have revealed just how much COVID-19 has impacted transplantation — and how patients in some countries have been hit far more than others.

The 22-country prospective observational study is evaluating how many solid organ transplants (SOTs) were performed relative to the number of COVID-19 cases, and compared with activity in 2019.

The first tranche of data covers from the time the WHO reported 100 cases globally to the end of May 2020.

It shows a dramatic decrease of activity in France across the whole of the country. The US, while initially affected with a 30% reduction, restarted after April, and returned to normal after a few months, with New York maintaining a degree of activity consistently.

But in Germany there was no significant modification of organ transplants compared with 2019.

Going forward, the study will be not just another registry, but a global picture over time, running until 2022, workstream leader Prof Vassilios Papalois, President of ESOT, a transplant and general surgeon, said.

While the pandemic has reduced capacity and caused concern for patients on the waiting list and those who are post-transplant, important lessons have been learned for the future, he said. WS07 was established to critically analyse and learn from the vast and varied experiences of different countries throughout the pandemic.

Papalois, Professor of Transplantation Surgery at Imperial College Healthcare NHS Trust in London, added that the way transplant professionals and patients came together to face this 'major crisis' was an 'absolute triumph of humanity.' Once COVID-19 hit, ESOT worked closely with the EU's DG SANTE, ECDC, National and International Transplant Societies, Professional Organisations and patient groups.

COVID-19 and Immunosuppression

The workstream wanted to learn about SARS-COV-2 in the context of the immune-suppressed patient. In the initial phase of COVID-19 infection when the immune system is stressed, immunosuppression can have a detrimental effect. However, in the second phase of COVID-19 infection when the immune system can go on overdrive, immunosuppression can be potentially beneficial. This is something that the group plan to explore further along with conducting a critical appraisal of the upcoming vaccinations and their effectiveness and risk for transplant patients.

> *One of the main topics focussed on by the workstream is clinical pathways, including the patient perspective. Here clinicians need to 'rethink everything,' he said, and ask: who should be transplanted in this environment and are we serving their best interests?*

Centres may have to think about sharing resources with others and potentially consolidating. Non-transplant professionals may be called in to support services due to redeployment.

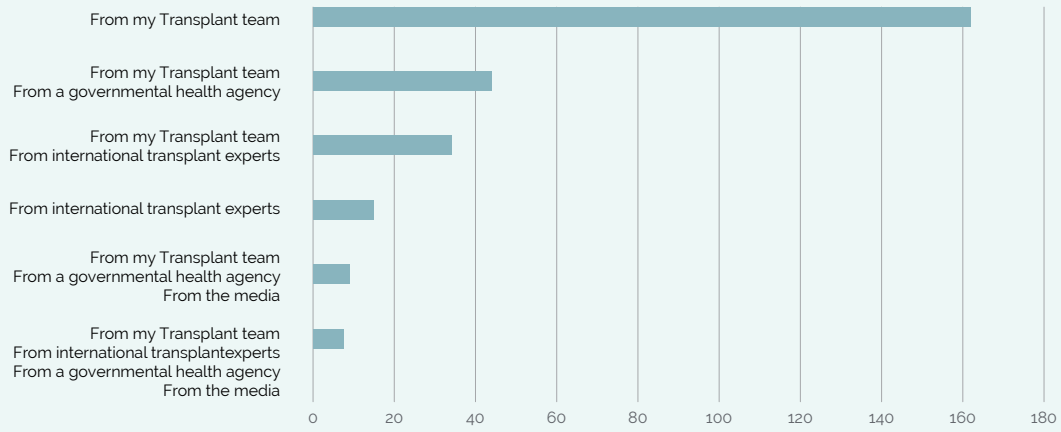
He advised clinicians to start from scratch and re-write the "books" gradually; do what is actually needed not what you are used to doing or like to do; and keep the patients away from the hospital as much as possible. He added: "It is crucial to minimise or mitigate risk."

With follow up, he warned clinicians not to be possessive as patients will wish to be far from hospital. He said: "Telemedicine can be a great investment. Technology will improve dramatically in the years to come."

Giving patients information directly

Patient participation is extremely important and ESOT is fully involved in this engagement. He said the tip of the iceberg is a COVID-19 information for patients survey in October which had 350 responses.

Who would you like to receive information from in situations like this in the future?



It found that patients received information on COVID-19 from all sorts of sources and some that were not credible. Many (n=64) heard from the news, and 31 from social media reports.
A minority said it was confusing, hard to understand and made them worried.

Most (162) say they would prefer to gain the information from the transplant team. Prof Papalois said this was 'crucial to understand."

He added: "Our patients put their faith in us when it comes to information, this is something we need to take very seriously into consideration for our future practice."

In the later Focus session, Alexandre Loupy, Head of the Paris Transplant Group, went into greater detail about the activity survey, which looked at kidney, heart, lung and liver transplants, using multi national data sources, including the US CDC-John Hopkins University dashboard.

He said: "This report illustrates how high-value medical procedures can be impacted by an epidemic with immediate consequences for vulnerable patient groups." He said it would be useful to public health officials, professional societies and patient advocacy groups in their planning and risk mitigation.

A future update measuring the dynamics of transplant recovery up to 2022 will include more countries.

In the live Q&A, workstream member Maria Irene Bellini, an Italian transplant surgeon, said living kidney donation took a 'massive hit' as it was not ethical to expose living donors to the risk of hospital treatment and possible COVID-19. 'That's not something we can defend easily," she said.

Challenges

Who will be transplanted?
Preferred modality DD vs. LD
Where?
By whom? Workforce planning
How? Clinical pathways
Follow up
Ethical Challenges
Patient Perspective

Risk and shared decision-making

Prof Papalois said that when Imperial restarted transplants, they only carried out low-risk activity to minimise the chance of complications and extended hospital stays.

The experts said it was a fine balance as patients on the kidney waiting list with end stage disease on dialysis have a higher risk of comorbidities and therefore more risk if they become infected with COVID-19.

Natalie Vallant, a surgeon at Guys Hospital London, said the patients on the waiting list should be informed of the risks and benefits of transplant over staying on dialysis. She advocated "a very honest discussion with them and the family so everyone is on board with the decision made."

In the live panel discussion, patient advocate and lung recipient Pisana Ferrari said shared decision making is the way forward. "This is a very good example. We are increasingly moving towards this from what I have heard in the TLJ."

She added COVID-19 was very stressful for those on waiting lists and those who had received transplants, with cancelled appointments. "For people waiting for a transplant these delays are a terrible thing to go through psychologically with no end in sight — and after a transplant you want to get on with your life."

Fellow panellist surgeon Gabriel Oniscu, Director of the Transplant Centre at the Royal Infirmary of Edinburgh and Secretary of ESOT, agreed that this element must not be forgotten by clinicians.

> *"The paramount point is that we should not underestimate the effect of COVID-19 on patients, not just physical management but on a psychological level."*

Learning Workstream

Combatting patients' uncertainty and fear

In collaboration with

ESOT EDTCO European Donation and Transplant Coordination Organisation

ESOT ELPAT Ethical Legal and Psychosocial Aspects of organ Transplantation

ESOT ETAHP European Transplant Allied Healthcare Professionals

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LEARNING WORKSTREAM

Combatting patients' uncertainty and fear

A major survey with the aim of grasping the lived experience and main concerns of 330 transplant recipients from more than 27 countries presented in the Learning Workstream Report showed they faced a life of uncertainty, with fear of graft rejection being the highest concern.

Anna Forsberg-R.N., Professor in Transplant Nursing at Lund University and Skane University Hospital, Sweden, presented the survey results which found infection risk — a live issue with COVID-19 — and striving to live a healthy life were key concerns, as well as worries about the donor's family and how the donor died.

While many seek support for these issues, some patients are not prepared to talk about them, the ESOT survey, carried out in collaboration with the European Transplant Patient Organization, found.

> Prof Forsberg said the results demonstrated that health professionals should pay attention to the psychological aspects of the recipient, take the patient seriously and offer person-centred care.
>
> Adopting well-known principles used in rehab medicine to develop and implement post-operative plans by transplant professionals would facilitate adaptation and help organ recipients regain a new, but different life, she said.

In the Focus session, two transplant recipients shared their inspirational and emotional stories about how they cope with these concerns on film and also in person in the Q&A session, moderated by Emma Massey who is a clinical psychologist from the Erasmus Medical Center in the Netherlands.

Emma Dalman, 34, from Sweden, received a heart in 2013 aged 27. She appeared live from hospital where she is being treated for an infection — one of the fears noted by the survey respondents.

She worries about rejection — sometimes more, sometimes less — made worse by the fact that two close friends Sophia and Martha died within months of each other following transplants.

This has made the former dietician at times scared to go to sleep at night for fear of dying like her friend, and worried about her future and therefore reluctant to save for her retirement.

She said: "I have time periods when I don't worry so much and everything is happy and golden, then there are times I'm convinced I will not live to see retirement . When I am more down, stressed, a lot is happening at once, or if someone I know passed away, it's tough."

Taking control

However in the last year she has taken control and started to save for her retirement and other plans, including become a student in environmental issues and sustainability . She said: "I realised I have to live life to the full and appreciate the second chance I have been given. My parents and friends mean the world to me, I have to live on for them as they have to live on for me."

I realised I have to live life to the full and appreciate the second chance I have been given. My parents and friends mean the world to me, I have to live on for them as they have to live on for me.

Emma Dalman, aged 34

Austrian airline pilot Klaus Granegger, aged 65, received a kidney in 2012 after being on dialysis for five years which had halted his career.

But within a year of receiving his 'perfect kidney,' keeping fit and active with Nordic walking, he was well enough to resume his job in the sky and worked as a pilot for an airline in Greece for a further six years.

He doesn't fear graft rejection. He prepared for his transplant with pyschological support, seminars and meditation and keeps mentally positive now. He told the TLJ "For me, the kidney lasts as long as I will live. I'm sure about it. I feel perfect, I feel full of power, even more healthy than ever.

If I have to die now for any reason, I can say I had the best life. I think I will live for the next 20 years healthy and wealthy for the rest of my lifetime.

Klaus Granegger, aged 65

Both Emma and Klaus have daily rituals where they give thanks to the donor who saved their life. For Klaus, this happens early. "Every morning I do a short prayer, thank you for being healthy, thank you the body, for the soul, thank you for my life, for this donor." He has even given his kidney a name, Lullaby.

For Emma, she has a notebook where, every evening, she writes down three things she is grateful for — and every day she includes that fact that her heart is still beating. "I don't take that for granted any more. It helps me see things more clearly, appreciate life and everything I have been given, it's a really awesome life."

Seeking support in difficult times

Emma Massey said their stories confirmed the importance for patients of taking control, making plans, being positive, staying fit and seeking support in more difficult times.

In the Live Q&A, Pisana Ferrari, patient advocate, founding member of the Italian Pulmonary Hypertension Association and a double lung transplant recipient of 18 years, said it was a great presentation which resonated with her everyday life.

She is always concerned at having all her pills never running out, as they are not available over the counter, and she schedules check-ups months in advance.

After her transplant she feared she would never see her daughter grow up, but now she has watched her graduate and get married.

> Pisana Ferrari said: "I commend ESOT for doing this initiative….There's a need for patients to have more information and guidance, things we can do and not do, there's a big gap there…. patients are often quite lost and lacking vital information.'

Dealing with uncertainty

In the final session Matilda Almgren R.N., PhD presented a framework of uncertainty after organ transplantation involving the complex process of adaptation and how the organ recipients try to balance expectations and disappointments while adapting to a life with a transplant. Professor Forsberg then finally presented a different perception of graft rejection from the transplanted persons' perspective, an understanding quite different from the professionals' view. A platform was made for future discussions at the ESOT congress in Milan, 2021.

Specialty Sessions

EKITA
Challenges in paediatric combined organ transplantation

ECCTA
Functional drivers in outcomes of CT transplantation

BSC
Metabolic Profiling in Transplantation

Learning Working Stream
Uncertainty in illness: impact on patient self-efficacy and self-management

SPECIALTY SESSIONS

EKITA

CHALLENGES IN PAEDIATRIC COMBINED ORGAN TRANSPLANTATION

World first para-kidney transplant

Three leading surgeons described their pioneering intricate work transplanting combined organs in children including the world's first simultaneous parathyroid and kidney transplantation in a child.

The European Kidney Transplant Association (EKITA) Specialty Session, heard how Nicos Kessaris, a transplant surgeon at Guy's Hospital, Evelina London Children's Hospital and Great Ormond Street Hospital, London carried out the operation on Patient M who had a kidney donated by her father.

As well as being the first combined transplant of its kind globally given the age of the recipient, it was the UK's first living donor parathyroid transplant.

Patient M had been diagnosed with Bartter syndrome, a group of very similar kidney disorders leading to an imbalance of potassium, sodium chloride and related molecules.

There is only one other simultaneous living related donor double transplant in the literature, involving a 23 year old recipient in 2016.

Mr Kessaris said in the short term she had a 'very satisfactory' outcome, demonstrating its feasibility.

Long-term care needed

In the same session, Nigel Heaton, Professor of Liver Transplantation Kings College, London and Head of the liver transplant programme at King's College Hospital for the past 25 years, gave an overview of combined kidney and liver transplantation in children .

He said living donation gives best results regarding survival, with children aged 1-5 having the best outcomes. The liver is transplanted first and has to be 2% of the recipient's bodyweight.

There have been just under 300 operations since 1983-2016, mostly teenagers[1], with 79% survival over 10 years which compares with 77% when the liver alone is transplanted.[2]
Data from Poland and Birmingham confirms this pattern.

He concluded by saying this is an uncommon procedure involving complex team work, with the patients requiring long term care. "We need a new group of specialists to manage these children as they go into adult life," he said.

Finally, Dr Zdenka Reinhardt, Consultant Paediatric Cardiologist and Transplant Physician at Freeman Hospital, Newcastle upon Tyne, UK, talked about combined heart and kidney transplantation. Two were carried out in the UK between 2016-20 and she said it was increasingly recognised for those with heart and renal failure. There may be lower rates of rejection than HTx alone.

Moderators Robert Langer, a professor of surgery and a previous Chairman of EKITA, and Dr Jelena Stojanovic, a paediatric nephrologist and EKITA Board Member, said the presentations were 'wonderful examples' of how transplant teams can achieve long term quality of life for children with complex medical conditions requiring multi solid organ transplant.

1 Cha et al, Clinics in Surgery 2017
2 Calinescu et al, Am J Transplant 2014; 14: 2861-8

SPECIALTY SESSIONS

ECTTA

FUNCTIONAL DRIVERS IN OUTCOMES OF CT TRANSPLANTATION

Pre-hab for frailty

Frailty is the 'Achille's heel' of cardiothoracic transplantation but it can be reduced before surgery, and a common language is needed to discuss it amongst clinicians, the ECCTA session heard.

Professor Robin Vos, from the Leuven Lung Transplant Group in Belgium, reviewed various frailty assessment tools but said they do a 'poor job' of differentiating between organ failure and age-related frailty.

He demonstrated that pre-transplant frailty is associated with decreased survival after a lung transplant and increased length of stay.[3]

He said there was a need for prehab as well as rehab after surgery, as frailty can improve, leading to better surgical outcomes. He said the transplant patients who did not improve or got worse had a higher risk of dying from surgery.

A pilot study in mobile technology to treat patients at home suggests it is helpful, depending on which frailty measure is used.[4]

Some patients become frail after a transplant but the majority no longer showed frailty six months after the operation, indicating it was disease-related.[5]

Consensus on tools

In the Q&A, Dr Vos said clinicians should all be aware of best practice when it comes to which frailty test to use. "We should open a forum to come to consensus," he said.

In the next session, Francesco Cacciatore, Professor of Internal Medicine and Geriatrics at the Department of Medical Translational Science University of Naples "Federico II", Italy presented results of his study that even low levels of physical exercise protects against mortality in heart failure patients.[6] Pharmacological intervention could also help patients on the waiting list get into a better condition.[7]

He concluded that two assessments — of sarcopenia and physical frailty, and multidimensional frailty — are indicated in heart transplant candidates.

Then Dr Erik Verschuuren, from the Lung Transplant Program, University of Groningen, in The Netherlands, gave a presentation about functional outcomes after lung transplant, highlighting a group of transplant recipients climbing Mount Kilimanjaro to raise awareness.

He conducted a pilot study on the effectiveness of rehab in 57 lung recipients. Six months after transplant, the participants had a 5 day comprehensive assessment and intervention program on exercise and lifestyle with physiotherapist, dietician and psychologist input and supervised training, followed by a six month maintenance program in primary care. All had clinical improvement. An RCT of 106 people is now ongoing.

3 Wilson ME, et al. J Heart Lung Transplant 2016
4 Singer JP Clin Transplant 2018
5 Vedano A, et al. J Heart Lung Transplant 2019
6 European Journal of Preventive Cardiology
7 ESC Heart Failure

SPECIALTY SESSIONS

BSC

METABOLIC PROFILING IN TRANSPLANTATION

Diet restrictions to improve outcomes

Short term calorie restrictions can improve transplantation outcomes and may also increase chemotherapy tolerability, Dutch research indicates.

Ron de Bruin, Senior Scientist, Department of Surgery, Erasmus Medical Center in Rotterdam, presented his research which asks whether short term calorie restriction can increase stress resistance — important as it may protect against acute oxidative damage induced by ischaemia reperfusion injury.

In animal studies a three day protein free diet did protect against this damage. In the clinic, living kidney donors and bariatric patients were put on the same restriction.

He found that the with the restricted diet, the kidneys improved function after the transplant and there was a decrease in slow graft function and acute rejection. The average weight loss was 2kg.[8]

He concluded that a five day Protein Carb Restriction diet before transplantation surgery does improve outcomes. A second study showed it may also increase chemotherapy tolerability.[9]

Fasting and monocytes

In the same session, Stefan Jordan, from the Charité — Universitätsmedizin in Berlin and principle investigator for Microbiology, Metabolism & Inflammation, discussed how calories regulate the immune system, specifically the Inflammatory Monocyte Pool.

He showed how animal, tissue and clinical studies showed an association with fasting and reduction of monocytes.[10]

Immunologist Dr Kylie James, from Addenbrookes hospital in Cambridge, UK, said understanding how the microbiome and immune system exist together spatially in health is important for them to understand what goes wrong during disease.

In her research she took swabs from five donors to look at bacteria in three regions of the gut. She found there was consistency in the regions of gut but subtle differences, with a richer microbiome driving plasma cell responses in the sigmoid colon.[11]

Dr James said this was the first time we have seen in healthy tissue that this organ is not a homogenous ball of cells but is more distinct.

8 Jongbloed et al., Aging 2020
9 Van Eerden et al, Clin Pharm & Therapeutics, in press
10 Jordan et al., Cell 2019
11 James KR, et al., Nature Immunology, 2020

SPECIALTY SESSIONS

EDTCO | ELPAT | ETAHP

LEARNING WORKSTREAM

UNCERTAINTY IN ILLNESS: IMPACT ON PATIENT SELF-EFFICACY AND SELF-MANAGEMENT

In collaboration with the transplanted patient group

Controlling the uncontrollable

Transplant patients view their body and its functioning in a very different way to the medical perspective so clinicians should ask questions to fully understand their mindset, and help them navigate their future around fear of graft rejection, the Learning Workstream session heard.

Anna Forsberg, Professor in Transplant Nursing Lund University and Skane University Hospital, Lund, Sweden, said clinicians talk about immune graft rejection on a cellular level but the patients view it in terms of the consequences for daily life.

Previous research has shown they experience a 'constant ever present perpetual threat.'[12]

Prof Forsberg interviewed 16 people aged 19-65 in a new study. She found they are constantly striving to control this 'invisible threat' with a variety of mechanisms, including relying on fate or luck, adhering to medicines and immunosuppressants and being healthy and avoiding alcohol.

Prof Forsberg suggested a new approach for clinicians. She said: "Ask the patient: 'when I say graft rejection, how do you perceive it?' Listen to the patient narrative, instead of giving all this medical info which does not make sense."

Matilda Almgren, a registered nurse specialising in intensive care, from the thoracic intensive care unit at Skane, said that patient follow up concentrates on survival and graft rejection, when the person receiving the follow up simply wants to return to normal healthy life.

Expand follow-up

Her research showed there is uncertainty over survival and recovery — that it is not as much as expected and not as quickly as hoped — as well as struggles with performance and relationships, and expectations from family and friends.

She said some patients felt abandoned, missed healthcare support and that they are not taken seriously when they reveal uncertainty about the future, such as questions about 'will I be able to see my kids grow up.' She concluded that follow-up should be broadened and not focussed on medical issues only.

In the live Q&A, Ms Forsberg continued her theme. She advised clinicians to 'align with the patient' and admit their own lack of control. She added: "Patients have taught me almost everything I know about what it means to be a human and a recipient."

Angelika Widhalm, founder and president of the patient organization Hepatitis Aid Austria — Platform Healthy Liver (HAA), and a liver recipient, said she agreed a different approach was needed to give patients the right support.

She said: "Patients say, 'can you prepare me for what is coming up, what does this mean for my family?' These are coming to Patients' Associations — so we need to find a way to implement Patients Associations more into the whole system."

12 Nilsson M, Persson L-O, Forsberg A. Perceptions of experiences of graft rejection among organ transplant recipients— striving to control the uncontrollable. J Clin Nurs 2008; 17: 2408—17.

Join us at ESOT Congress 2021

This year, the ESOT Congress is being held in Milan from 29 August - 1 September 2021 and will be taking place online and in person.

Through a multidisciplinary approach, the congress will feature the latest research and innovation from the most prominent scientists and physicians in the field of organ transplantation.

Guaranteed to motivate and inspire, this landmark meeting will provide a unique opportunity to connect science and medicine.

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The ESOT Congress serves as a premier platform for researchers from across the globe to present their organ transplantation research.

We invite clinicians, scientists, researchers, nurses and allied health professionals to submit abstracts and present their latest transplant research.

Programme

The scientific programme has been developed based on five key domains that encompass the most relevant topics in organ transplantation.

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About ESOT

Objectives

The European Society for Organ Transplantation (ESOT) was founded over 30 years ago and is dedicated to the pursuit of excellence in organ transplantation. Facilitating a wealth of international clinical trials and research collaborations over the years, ESOT remains committed to its primary aim of improving patient outcomes in transplantation. With a community of over 8,000 members from around the world, ESOT is an influential international organisation and the facilitator of the biennial congress which hosts approximately 3,500 experts who come to meet to explore and discuss the latest scientific research. ESOT attracts the foremost transplantation experts to work in its committees and sections, and has an impressive track record in supporting research, supporting extensive education, and promoting changes in European policy.

Mission, Vision and Values

ESOT is committed to advancing research and clinical practice in the field of organ transplantation to improve the lives of everyone affected. The combined efforts of all stakeholders in the public and private sectors, and civil society are essential to halting and reversing the need for organ transplantation. As such, ESOT acknowledges that every voice is valued.

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