Introduction

In January, the 24th Eurotransplant winter meeting in Fügen, Austria, took place. During this meeting Eurotransplant was honored with the presence of two representatives of the Health & Consumer Protection Directorate-General of the European Commission. A summary of the highlights of the Board meeting is published in this Newsletter. But I would specifically like to mention several important topics.

On May 26, the Republic of Croatia intends to become a full member of Eurotransplant. Furthermore, it is expected that a preliminary cooperation agreement with Hungary will be signed before this summer. Finally, during the Eurotransplant annual meeting in September, the Foundation will celebrate its 40th anniversary. We hope to welcome you all at this event, which will take place on September 20 and 21, 2007, in Noordwijk.

During the winter meeting, the winner of the Henk Schippers Award 2006, Dr. Peter Horn, gave a lecture on future trends in transplantation. It was a fascinating presentation and a report of this lecture is also published in this Newsletter.

If you are a young investigator, then take the opportunity to visit page 6 of the Newsletter. We are looking forward to your application for the Henk Schippers Young Investigator Award 2007!
## NUMBER OF POST-MORTEM ORGANS USED FOR TRANSPLANTATION

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He-Heart  Ki-Kidney  Pa-Pancreas  Li-Liver  SLu-Lung  BKi-both Kidneys  BLu-Both Lungs  SLi-Split Liver
## Calendar of Events

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<td>4th Leiden International Medical Student Conference (LIMSC)</td>
<td>March 15 – 17, 2007</td>
<td>Leiden, the Netherlands</td>
<td>For information: Medische Faculteit der Leidse Studenten (M.F.L.S.) Attn: LIMSC K1-R P.O. Box 9600 2300 RC Leiden the Netherlands Tel: +31 71 526 4484 Fax: +31 71 526 4371 E-mail: <a href="mailto:limsc@lumc.nl">limsc@lumc.nl</a> Website: <a href="http://www.limsc.nl">www.limsc.nl</a></td>
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<td>British Transplant Society 10th Annual Congress</td>
<td>March 28 – 30, 2007</td>
<td>Manchester, United Kingdom</td>
<td>For information: British Transplantation Society, Mrs. Sally Ros Association House South Park Road Macclesfield, Cheshire, SK11 6SH United Kingdom Tel: +44 1625 504060 E-mail: <a href="mailto:sally@resourcesforassociations.co.uk">sally@resourcesforassociations.co.uk</a> Website: <a href="http://www.bts2007.org.uk">www.bts2007.org.uk</a></td>
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<td>3rd International Meeting on the Small-For-Size in Liver Surgery</td>
<td>March 23, 2007</td>
<td>Ghent, Belgium</td>
<td>For information: Organization Secretariat Mrs Inge Baek Hepatobiliary and Liver Transplantation Service Ghent University Hospital Medical School 2 K 12 IC De Pintelaan 185 B – 9000 Ghent Tel: +32 9 240 5519 Fax: +32 9 240 3891 E-mail: <a href="mailto:inge.baek@uzgent.be">inge.baek@uzgent.be</a> Website: <a href="http://www.smallforsize.be">www.smallforsize.be</a></td>
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<td>3rd ELITA-ELTR Wintermeeting</td>
<td>March 24 – 27, 2007</td>
<td>Obergurgl, Tirol, Austria</td>
<td>For information: Universitätsklinik Innsbruck Linda Partl Anichstr. 35 A-6020 Innsbruck Fax: +43 512 504 22602 E-mail: <a href="mailto:linda.partl@uklibk.ac.at">linda.partl@uklibk.ac.at</a> Website: <a href="http://www.congress-innsbruck.at/events/wintermeeting">www.congress-innsbruck.at/events/wintermeeting</a></td>
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<tr>
<td>27th ISHLT Annual Meeting and Scientific Sessions</td>
<td>April 25 – 26, 2007</td>
<td>San Francisco, USA</td>
<td>For information: ISHLT Lisa Edwards, Director of Meetings 14673 Midway Road, Suite 200 Addison, TX 75001 - U.S.A. Telephone: +1 972 490 9495 Telefax: +1 972 490 9499 E-mail: <a href="mailto:lisa.edwards@ishlt.org">lisa.edwards@ishlt.org</a> Website: <a href="http://www.ishlt.org">www.ishlt.org</a></td>
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<td>3rd Annual Meeting of the Deutsche Stiftung OrganTransplantation</td>
<td>May 31 – June 1, 2007</td>
<td>Berlin, Germany</td>
<td>For information: Deutsche Stiftung Organtransplantation Emil von Behring-Passage 63263 Neu Isenburg Germany E-mail: <a href="mailto:kongress@dso.de">kongress@dso.de</a></td>
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<td>EuroTransplant Annual Meeting</td>
<td>September 20 – 21, 2007</td>
<td>Noordwijk, the Netherlands</td>
<td>For information: Eurotransplant International Foundation Mrs Marianne Franzen P.O. Box 2301 2304 CH Leiden the Netherlands Tel: +31 71 5795795 Fax: +31 71 5790057 E-mail: <a href="mailto:m.franzen@eurotransplant.nl">m.franzen@eurotransplant.nl</a> Website: <a href="http://www.eurotransplant.nl">www.eurotransplant.nl</a></td>
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Future Trends in Transplantation: Gene Transfer Meets Organ Transfer

Traditionally, gene therapy has mainly been viewed as a replacement of defective or deficient genes. However, this ‘gene replacement therapy’ as a treatment of congenital genetic defects and acquired disorders has more lately been supplemented by gene therapy approaches relying rather on the enhancement/improvement of cell features. Genetic modification of both allogeneic and autologous cells can also be used to achieve tolerance to transplanted cells, tissues or organs.

One of the clinically most critical factors for the recipient is organ rejection triggered by the recipient’s immune system. Development of effective multidrug immunosuppressive regimens and improvements in the management of chronically immunosuppressed patients have led to a substantial improvement of patient and allograft survival in clinical organ transplantation. Unfortunately, significant problems of morbidity and mortality related to chronic immunosuppression remain. These side effects are inherent to any approach aiming at reducing the immune response by treating the recipient. Thus, there is a need for inducing specific unresponsiveness (tolerance) to clinical solid organ or stem cell derived allografts. Most desirable would be a stable, normal graft function in the total absence of a requirement for maintenance of immunosuppression. Alternatively, the concept of employing tolerogenic strategies to permit graft acceptance with dramatically reduced immunosuppression requirements would already be a significant improvement.

In addition, the emergence of cell-based regenerative medicine as potential therapy for substitution of tissues (Horn et al., 2006b) is intimately correlated with the necessity to inhibit the host immune response to the modified autologous or transdifferentiated allogeneic cells. One of the most sought after goals in cell as well as organ transplantation is therefore the ability to induce specific immunologic tolerance to transplantation antigens since this would allow the replacement of host organs or tissues without the need for immunosuppression. In principle, this may be achieved by either altering properties of the host’s immune system, by achieving a state of specific tolerance (or ignorance), or alternatively by altering the properties of the transplanted cells and tissues, by making these less immunogenic.

Organ transplantation after establishing hematopoietic (micro) chimerism

A promising way of establishing specific tolerance to transplantation antigens is to induce lymphohematopoietic chimerism through allogeneic stem cell transplantation. The establishment of mixed cellular chimerism by stem cell transplantation in adult animals can lead to specific tolerance in an otherwise fully immunocompetent host (reviewed in (Sykes, 1996)). However, stem cell transplantation across major histocompatibility complex (MHC) barriers has drawbacks as a means of inducing tolerance to allogeneic organs because of the difficulty in obtaining suitable matched bone marrow (BM) donors, the severity of the preparative regimen required, the high rates of engraftment failure, and the potential for inducing severe graft-versus-host disease. Different strategies of improving stem cell transplantation protocols based on the genetic modification of the allogeneic cells have been developed (Horn et al., 2004). One of those is the in vivo selection of stem cells.

In vivo selection

In vivo selection increases the proportion of circulating gene-modified cells by conferring a selective growth or survival advantage and in an allogeneic transplantation setting thus allows the selective outgrowth of transduced allogeneic HSCs in their natural environment after transplantation. The preferential expansion of transduced cells following transplantation can be achieved by either modifying the HSCs with genes that provide a proliferative advantage (Neff et al., 2002); or by modifying HSCs with drug resistance genes that will allow the elimination of nontransduced cells (Neff et al., 2003). HSCs are transplanted into the recipient and the appropriate selection agent is administered after allowing sufficient time for the engraftment of the transplant.

Engraftment of allogeneic stem cells relies in part on eliminating the recipient’s HSCs by treatment of the recipient with myeloablative or myelosuppressive doses of total body irradiation or chemotherapeutic agents prior to transplantation of stem cells. The toxicity associated with
this conditioning of the host is one of the most limiting factors in hematopoietic stem cell transplantation, limiting its application to otherwise healthy, relatively young patients.

One strategy to reduce the upfront toxicity has been the use of nonmyeloablative or reduced-intensity conditioning regimens which has been used to condition elderly or ill patients with hematological malignancies for allogeneic hematopoietic cell transplantation. Initial mixed donor/host chimerism (i.e. the coexistence of hematopoietic cells of host and donor origin) has been observed in most patients after such transplants.

It has been demonstrated that shifting such a mixed chimerism in favor of donor hematopoeisis by in vivo selection using the chemotherapy resistance methylguanine methyltransferase (MGMT) is feasible and not associated with any significant toxicity (Neff et al., 2003). By equipping the transplanted allogeneic stem cells with a chemo-resistance gene, it may thus be possible to extend part of the myelosuppressive treatment to after the transplantation procedure and to further reduce the pretransplant conditioning. In vivo selection also could obviate the need to include lymphocytes in the graft, thus reducing morbidity and mortality related to graft-versus-host disease (Neff et al., 2003).

Decreasing the immunogenicity of organs and cellular therapeutics

It is very well established that the main histocompatibility complex (MHC), in humans the human leukocyte antigens (HLA) are the main targets for organ or cell rejection (Horn et al., 2006a). Thus, reducing HLA expression can prevent the immune system from recognizing immunogenic peptides in the genetically modified autologous transplant. Reducing the expression of only one or two mismatched HLA alleles in an otherwise matched graft may allow to optimize the degree of matching of recipient and donor cells. The principle of this approaches is that not the recipient’s immune system but the transplanted donor cells are modified to induce immunologic tolerance in the recipient (Figueiredo et al., 2007). Silencing the expression of HLA class I antigens on transplanted cells or tissues might thus prevent rejection without the risk of the hazardous side effects associated with a general impairment of the immune system. This strategy would allow for minimizing post-transplant long-term immunosuppressive therapy.

A significant reduction in MHC expression can be achieved by targeting HLA mRNA transcripts by RNA interference (RNAi) (Figueiredo et al., 2007). RNAi has recently emerged as a powerful genetic tool for silencing gene expression (Elbashir et al., 2001).

A variety of strategies to express interfering RNAs with the use of virus vector-based cassettes have been explored, including retroviral and lentiviral vectors (Scherr et al., 2003). Recently, it was shown that silencing HLA antigens in class- or gene-specific manner by lentiviral-mediated delivery of RNAi expression cassettes can inhibit T cell mediated immune recognition as well as complement-mediated cytotoxicity (Figueiredo et al., 2007).

The principle of MHC manipulation in general can be used both to individualize allogeneic cells by eliminating single MHC mismatches or, even more attractive, by devising cells with a MHC “knockout” phenotype, to establish off-the-shelf products of allogeneic cell based therapeutics in regenerative medicine. This approach may also allow for the development of a “stealth organ”, less prone to HLA-mediated rejection (Saito, 2007).

References
Henk Schippers became the first Eurotransplant Director in 1970. After 5 years, he was appointed as Secretary Treasurer of the Board until his death in 2003. Henk laid the foundations for the administration of Eurotransplant. He successfully completed negotiations with the insurance companies and began the international network, which is the hallmark of Eurotransplant.

Purpose
The purpose of this award is to encourage young clinical and/or scientific investigators to pursue a career in the field of organ and tissue transplantation. It is our hope that this research will be invigorated by the work of young, talented individuals supported by stable multi-year funding. The Henk Schippers Young Investigator Award is especially meant to enable the investigator to present his/her results of clinical and/or scientific organ transplantation related investigations at well recognized and respected (inter)national transplantation congresses or symposia, e.g. European Society for Organ Transplantation (ESOT).

Eligibility
Candidates (< 35 years) must have attained a masters or PhD degree, and at least have an appointment as a junior faculty member. Individuals at the Associate Professor level are not eligible. Clinicians must have finished their residency no more than five years prior to applying and investigators must have completed their post-doctoral training no more than five years prior to applying. Applications coming from the entire European region will be accepted.

Terms
The recipient will receive 2,000 Euro. This award will be made available to the individual applicant and must be used for direct expenses. A progress report will be required. Applicants can provide a paper, also after presentation at a specific meeting and the candidate chosen can use the money in the next year. The Eurotransplant International Foundation will retain the right to unilaterally cancel any awards for non-compliance or non-performance.

Application procedure
Candidates must submit:
- A completed curriculum vitae;
- An application letter for which purpose he/she will use the award;
- Applications must also contain a letter of nomination from a faculty sponsor who will accept responsibility for monitoring the awardee.
- Applications must be entirely in the English language.

One original and five collated copies of all parts of the application must be received on or before the due date at the Eurotransplant International Foundation in Leiden, Central Office.

Original signatures must be contained on one copy of the application. Non-complying applications will be returned without review.

Deadline
The application deadline is May 12, 2007.

Selection
The selection committee, Board members of the Eurotransplant International Foundation, will consider all proposals. Decisions of the selection committee will be announced by July 31, 2007.

The award will be presented at the annual Assembly / Presidential Symposium. The winner of the award will be invited to present his/her data (15 minutes talk including discussion) either at the annual Presidential Symposium on September 20, 2007 or at the ET Winter Meeting in Fügen, January 2008. Travel costs will be reimbursed.

Award management
Award payments will be made following written acceptance by awardee.

Change in status of awarded
Awards are to remain solely with the designated awardee and may not be transferred to any other person. If a recipient decides not to attend the anticipated congress, the award will be terminated as described above.

Inquiries
Direct all inquiries to:
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Eurotransplant International Foundation
P.O. Box 2304
2301 CH Leiden
The Netherlands
Tel: +31 71 5795795
Fax: +31 71 5790057
E-mail: secretariat@eurotransplant.nl
Website: www.eurotransplant.nl
Summary of the meetings of the Eurotransplant International Board on January 24 and 25, 2007 in Fügen Austria

Verena Diepeveen-Huijsman, secretary of the Board

Due to late arrivals of Board members as a result of bad weather conditions at Munich airport, the Board meeting was divided into two sessions: One was held on January 24, the second one on January 25, 2007.

The Board had a successful meeting with two representatives of the Health & Consumer Protection Directorate-General of the European Commission. These representatives gave a report on an open consultation: Regulatory options for organ donation and transplantation at EU level. This meeting was also attended by representatives of national authorities of the ET countries.

The preliminary cooperation agreement with the Republic of Croatia will be replaced by a full membership cooperation agreement. It is planned to sign this agreement in the city of Split on May 26, 2007.

A festivity committee was established which will work on a scientific program for the annual ET meeting which will be related to ET’s 40th anniversary. The committee consists of Board members and is chaired by Vanrenterghem.

The Board was informed that negotiations with the health insurers were concluded successfully, resulting in an agreement on the ET budget for the year 2007.

It was decided to organize annual bilateral meetings with legal institutions or national authorities ET is dealing with. These institutions are e.g. the German Bundesärztekammer (BÄK), Dutch Transplant Foundation (NTS), Belgian Transplant Council (BTR), Slovenija-Transplant, Österreichisches Bundesinstitut für Gesundheitswesen (ÖBIG). Although Bio Implant Services (BIS) is not a national representative to ET and ET is not involved in tissue allocation, ET directors will meet with BIS on an operational level since ET and BIS share personnel, IT infrastructure and other facilities.

The Board was informed on the progress regarding the planned cooperation with Hungary. It is expected that a preliminary cooperation agreement can be ready to be signed before the Summer of 2007.

Reports of the ET Kidney Advisory Committee (ETKAC), Liver Intestine Advisory Committee (ELIAC), Pancreas Advisory Committee (EPAC), Thoracic Advisory Committee (EthAC), Organ Procurement Committee (OPC), Tissue Typing Advisory Committee (TTAC) and were discussed. Since all reports will be published in this issue of the ET Newsletter, there is no need to further elaborate on these reports in this summary.

The ETKAC, EThAC and TTAC submitted recommendations to the Board. The approved recommendations are also published in this Newsletter.

The Board discussed the results of a successful meeting that took place in presence of CSWG and OPC representatives as well as with representatives of three ET countries that have their own electronic data exchange models. The purpose of this meeting was to present all three models and to gain a detailed insight into the individual model’s functionalities.

The conclusions of the meeting were:
1. The three countries had to develop their own systems due to legal requirements.
2. All participants agreed that a common donor data set, defined by the OPC, will have to be provided in a standard format to ET (standard interface).
3. Countries are allowed to perform changes provided that they inform ET beforehand. Changes are to be paid by the country itself.
4. Possibilities of transfer of large files, like X-rays, will be explored by the CSWG.

ET’s medical liability was another issue of discussion. The liability insurance of ET as well as possibilities to limit ET’s liability and its liabilities towards participating ET countries is currently investigated. A final report including suggestions for improvement (if needed) will be discussed at the next Board meeting.

The Board extensively discussed the speeding up of its internal decision making process. Two steps to achieve this are currently considered:
1. Advisory Committee (AC) meetings should take place immediately prior to Board meetings. This change will lead to a time saving of approximately four months since recommendations can be decided upon by the Board immediately after an AC meeting.
2. Most recommendations are usually approved without major discussion; a minority of recommendations are only rejected for very clear, e.g. political, reasons. For this reason it was suggested that e.g. the directors, and the presidents screen recommendations and assess whether or not they should be regarded as ‘critical’ or ‘non-critical’. ‘Non-critical’ recommendations can be sent around by e-mail to the Board whereas ‘critical’ recommendations should be discussed during Board meetings. The Board members support this proposal, however, they prefer that all recommendations are sent to all Board members rather than to the presidents only and that they will be given the opportunity to ‘flag’ recommendations. ‘Flagged’ recommendations will be discussed at a next Board meeting whereas ‘non-flagged’ recommendations can be considered to be
accepted by the Board. In case a recommendation is flagged by only one or a few members, then these members will be approached personally in order to explain the contents of the recommendation involved once again, possibly resulting in an approval.

These options will be further discussed during the next Board meetings after which a final decision will be taken.

The continuation of the ET winter meeting in Fügen has also been discussed. The current attendance rate to the meeting has made clear that the current structure needs to be changed. Next year it will be the 25th anniversary of the winter meeting; it was decided to celebrate this event in any case in Fügen. Ideas for restructuring of the meeting will be investigated.

The Board was informed about the progress and financial implications of two European Community (EC) projects, Eurocet and DOPKI, in which ET is currently involved. ET was assigned money for participation in the projects. With regard to Eurocet, it was stated that due to overestimation a part of the money was not used. This amount will not be claimed by ET and has been given back to the project coordinator for redistribution to other project participants or responsibilities.

### KIDNEY ADVISORY COMMITTEE

**RKAC03.06**

If one or more consecutive kidney transplants fail within 3 months after transplantation, and the patient is re-entered on the waiting list, waiting time will be returned starting from the dialysis time before the first failed transplant.

**RKAC05.06**

Children either on dialysis or registered on the Eurotransplant waiting list before the age of 16, should keep their pediatric status until their first successful graft, irrespective of their age at the time of an offer. In case of a preemptive registration on the kidney waiting list, the pediatric status will end on the 17th birthday, if dialysis is not initiated before this date.

### THORACIC ADVISORY COMMITTEE

**RThAC04.06**

For HU patients older than 50 years, the donor age profile will not be taken into account in the matching and offering process of donor organs.

### TISSUE TYPING ADVISORY COMMITTEE

**RTTAC03.06 (rephrased) [combined ETKAC / TTAC recommendation]**

In case of a fully homozygous donor, zero HLA mismatch recipients will be ranked according to their extent of homozygosity (descending from fully homozygous to heterozygous recipients). After two years the effect of this rule will be analyzed. An extension to not fully homozygous donors might then be needed.

**RTTAC01.07**

Introduce in ENIS a possibility to indicate if a cross match must be done at the donor center (indication to be done by tissue typing laboratory only). This will prevent shipment of sera without complement fixing antibodies, which will always lead to negative cross matches in the donor center.

### ETHICS COMMITTEE

**REC05.06 (rephrased)**

‘The Eurotransplant International Foundation condemns unreservedly any activity that transgresses an individual’s human rights or involves the coercion of an individual to become an organ donor. The commercial exploitation of organs from executed prisoners is considered a breach of human rights and is an unacceptable practice. Aware of the burden of human suffering that flows from the world-wide shortage of ethically acceptable organs, any act that risks calling the practice of transplantation into disrepute is to be regretted.’
The following reports from the Advisory Committees were discussed by the Eurotransplant International Board on January 25, 2007 in Fügen, Austria.

A scientific steering committee consisting of national ETKAC representatives has been established.

D. Study related biopsies in donor kidneys

The ETKAC is of the opinion that biopsies in donor kidneys are only allowed on specific conditions.

E. Information regarding statistics on immunized and retransplant ESP recipients

Prof. Frei, who had been asked to provide raw data on ESP recipients, seems to be reluctant to provide these data due to the fact the article concerned has not yet been published. The ETKAC chairman and the ET medical director in the meantime sent a letter to Frei in which they gave guarantees with respect to the usage of his data. The ETKAC hopes that Frei will provide the data under these conditions.

F. Statement on the intention of RKAC03.96 and RKAC02.01 (return of waiting time)

During the previous ETKAC meeting the rationale of recommendation RKAC03.96, intended for transplants that developed a primary non function, has been discussed and resulted in the decision to formulate a statement on the intention of recommendations dealing with return of waiting time. To this end the ETKAC combined RKAC03.96 and RKAC02.01 which resulted in RKAC03.06.

G. Time point of determination of the pediatric status

The current recommendation RKAC02.01 gives the benefit of the pediatric status only to recipients who are registered on the Eurotransplant waiting list before their 16th birthday. This, on the one hand means a disadvantage to recipients on dialysis before their 16th birthday, but registered on the waiting list thereafter. On the other hand it might stimulate centers to register their recipients preemptive only in order to get the pediatric status.

In order not to disadvantage any pediatric recipient and to avoid abuse of the pediatric status, the ETKAC decided to abolish RKAC02.02 and formulates RKAC05.06 instead.

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Report of the 29th meeting of the Eurotransplant Kidney Advisory Committee (ETKAC)

Chairman: Prof. Dr. J. de Fijter
Secretary: Dr. J. de Boer

The ETKAC met on Wednesday, November 29, 2006

Members present: 11 + 1 observer + 1 external advisor + 1 director

Members absent: 5

A. Double matching points for homozygous donors and recipients

Following a discussion that homozygous recipients are disadvantaged in the current allocation scheme, the TTAC formulated RTTAC03.06 which was also discussed by the ETKAC. The TTAC proposal is based on the following considerations:

– If either a donor or recipient is homozygous on one or more loci, the homozygous antigen is entered twice into the system. This would be permissible because with DNA techniques, full homozygosity can be proven in 99% of the cases.

– On calculating the HLA mismatches each donor/recipient pair of antigens is compared separately. Using this scheme heterozygous recipients no longer will have zero mismatches in case of a homozygous donor and consequently will have less allocation points for the mismatch factor.

B. Progress report on implementation of recommendations

RKAC02.06 on pediatric allocation was discussed by the German Bundesärztekammer where no objections against implementation seem to exist. Implementation is expected by mid 2007.

C. Progress on study protocol Eurotransplant Senior DR-compatible Program (ESDP)

This study protocol was again discussed and accepted by the ETKAC with some minor adaptations.

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C. Progress on study protocol Eurotransplant Senior DR-compatible Program (ESDP)

This study protocol was again discussed and accepted by the ETKAC with some minor adaptations.
H. Discussion on extended matching criteria

Following an overview of allocation and transplant outcome of kidneys of donors aged >74 years, the ETKAC decided that in case offers from this category of donors are declined 5 times for medical reasons, both kidneys can be offered for one recipient as a rescue offer. The outcome of transplants allocated according to this scheme, will be presented at the next ETKAC meeting.

I. ETKAC representation in the OPC

The ETKAC appointed the new member, Prof. P. Fornara from Halle, as the new representative in the OPC.

J. Miscellaneous

- The Slovenian ETKAC representative will temporarily be replaced by another representative.
- Living donor list exchange is still under discussion in the Dutch government.
- The Belgian Transplant Society will seek ET’s assistance in establishing a living donor registry.

Report of the meeting of the Eurotransplant Liver Intestine Advisory Committee (ELIAC)

Chairman: Prof. Dr. J. Lerut
Secretary: Dr. T. Gerling

The ELIAC met on Wednesday, December 6, 2006
Members present: 9 + 1 observer + 1 director
Members absent: 2

A. Announcements

Two new members of the ELIAC are introduced. The first, Dr. Kocman from Zagreb, Croatia, has officially been an observer since July 2006, but this is the first occasion that he is present at a meeting. The ELIAC hopes to have him as a permanent member in 2007 if negotiations will be successfully completed. The second is Prof. Hauss from Leipzig, Germany, who replaces Rogiers as the third German representative. Rogiers has left Hamburg to take up a position in Ghent as of December 1, 2006.

Van Zwet reports on behalf of the directors that on December 5, 2006 budget negotiations were held with the German health care insurers that resulted in an acceptance of the proposal for financing of MELD.

B. Progress report on the implementation of MELD

B.1 Implementation plan for MELD in ET

The secretary reports on the activities that took place since the last ELIAC meeting. The most important ones are the four workshops held in November (see below). Also, information has been spread widely, also involving patient groups in Belgium and Germany. Dutch patients will be approached separately by the Dutch Transplantation Foundation (NTS).

The member site’s Library now contains a separate MELD section. Here members find the most recent information, i.e. a MELD presentation and the new ET manual.

B.2 Presentation working group MELD

The ELIAC is presented the MELD working group that is still busy with the finalization of MELD in order to enable the implementation on December 16, 2006.

The four workshops, that were organized at the central office in Leiden in November 2006, were very successful as 27 of the 37 centers participated. Two centers, Leiden and Leuven, did not participate as they were involved as advisors in the remote user group in the design of the web application. The other centers could not arrange to come on one of the dates but committed themselves to contact neighboring centers for information. The feedback from all users was positive and some of their suggestions could even be incorporated in the design.

The general project leader gives a demonstration of the web application specifically built for MELD. The application will not replace ENIS as the initial registration still has to be performed through ENIS. Nonetheless, once the recipient is registered all waiting list management for a recipient can be performed through the web application. Parts of the application include the extensive overview of a center’s waiting list (center wordlist), downgrades, functionality of email notifications for recertification/ reconfirmation/ downgrades, updates of MELD scores, initial request of (non-)standard exceptions and their reconfirmation.

Another change to be implemented, though independent of MELD, concerns the donor-specific patient profile with regard to the acceptance of split livers. Centers will now
have to indicate one of the four types (LLS, ERL, LL, RL) and option 'either' has been removed. This should help to further improve allocation and makes better analyses possible as the split types are also used in the database.

B.3 NSE operational guidelines

The ELIAC decided to lay down operational guidelines for the future ELIAC audits that will only concern high urgent (HU) and approved combined organs (ACO) cases.

It is also decided not to allow for substitutes in an ELIAC member’s center. The ELIAC wants to ensure that only ELIAC members perform audits as such substitutes would not be familiar with the level of information present in the ELIAC in all cases. This could jeopardize the position of the ELIAC.

The ELIAC will in the future have all ELIAC audits discussed during meetings as a standard agenda point to increase uniformity in future decisions on these exceptional cases.

B.4 Transition from current ELAS to MELD-based ELAS

The secretary presents a document regarding the strategy for implementation of MELD, based on all decisions made in previous ELIAC meetings or by national authorities.

The strategy includes the transition of all patients (lab MELD, pediatric MELD, NT, HU, ACO), calculation of waiting time (MELD-specific vs. total), exceptions (T2 and (non-) standard exception status, Dutch regulation), donor profiles (split liver) and expected short-term course after implementation.

Gerling demonstrates that out of the total number of T2 recipients (N=176) some 22% will receive an exceptional status on the date of implementation as they are now T2 with either HCC, oxalosis, FAP or polycystic liver disease. All other recipients will be stratified by their lab MELD. The distribution of MELD scores among patients in current urgencies T2-T4 show that about 40% of the T2 recipients already have a lab MELD 19 or higher. As a result about 50-60% of the T2 recipients, regular and standard exceptions, will have rank fairly high. Nonetheless, a considerable number of T3 and T4 recipients also have high scores, giving them the chance to receive an organ according to the new ELAS. This confirms the strategy chosen to not give all T2 recipients priority. Only the Dutch group decided to do this, but this in view of only 5% of the waiting list in T2.

Furthermore, centers are very active in reviewing their waiting list and adding missing lab MELDs in their patients (completeness on December 5, 2006 is 85% vs. 58% on October 26, 2006). As an effect of the cessation of the current ELAS, centers seem to register less T2 patients as expressed in a weekly overview of the ET waiting list.

The waiting list on November 20, 2006 contained 210 adult T2 patients, as opposed to 174 on December 4, 2006. This could also help to try and transplant as many T2 patients as possible reducing the group to be transferred even further.

Van Zwet proposes to inform all centers after the successful implementation on December 16, 2006 by fax. As of that moment all functionality is available and centers can e.g. apply for standard exceptions with all rules applicable as defined for each country.

C. Eurotransplant’s 40th anniversary

On the occasion of ET’s 40th anniversary in 2007 the agenda for the liver users meeting was already discussed. The ELIAC agreed to focus on the aspect of ‘how to enlarge the (available) liver organ pool’ such as extended criteria donors, liver splitting between adults, NHBD liver transplantation and domino liver transplantation. High profile speakers will already be contacted. One presentation will address ET’s contributions to the development of liver transplantation; Prof. Margeirter will be asked to give this talk as he was active in the field during the last four decades.

Report of the meeting of the Eurotransplant Pancreas Advisory Committee (EPAC)

Chairman: Prof. Dr. W. Schareck
Secretary: Dr. M. Slot

The EPAC met on Thursday, October 5, 2006 at the Holiday Inn in Leiden
Members present: 8
Members absent: 2

A. Progress report on implementation of recommendations

The EPAC was informed that the BÄK had installed a special pancreas committee to deal with the approval of recommendations. After this committee had approved the recommendations, the priority pancreas/kidney recipients over kidney recipients in type II diabetes or other kidney diseases had to be discussed once again within the Ständige Kommission Organtransplantation. In the meantime, this discussion has been ended in favour of the combined kidney pancreas transplantations. The recommendations still have to be implemented, but they are allowed for now. For the future, it is proposed to phrase recommendations in such general way that daily practice changes do not have to be approved every time by national authorities. Furthermore, they will be prepared very thoroughly avoiding the need to add more recommendations on the same topic within a short period of time.
B. Presentation of the trial on the comparison of UW vs. HTK by Prof. W. Steurer from Tübingen

Prof. Steurer presents the results he has obtained so far with the UW vs. HTK trial. The analyses until now show that there are no major differences between the two groups.

C. Comparison of double layer method vs. single layer method

The publications so far on this subject are conflicting. The EPAC discussed whether a study on the subject should be started. In general, all EPAC members agree that an experienced procurement team may have much more influence on islet transplant results than using SLM or DLM. Starting a study on DLM however may stimulate the procurement in general. The conclusion of the EPAC is that a study on DLM is not feasible, mainly because it is too expensive.

D. Progress report on the retrospective study on the PASS score

The PANcreas Suitability Score (PASS) system which was developed by Prof. Schareck is now retrospectively studied. Preliminary results are promising, but more analyses have to be done.

Also, a prospective study should be performed as now only part of the PASS could be studied. A proposal for financing a prospective study by a Dutch foundation will be written.

E. Miscellaneous

The following topics were briefly discussed:
1. Criteria for procurement surgeons; the EPAC feels that it is unacceptable that good pancreata are lost due to procurement damage. Several problems are recognized. Prof. Schareck is asked to bring these forward in the Board.
2. Pancreas follow-up registry; building of this registry is planned for 2007. The EPAC would like to be involved in building this registry.

The EThAC decided to submit the previously rejected RThAC02.06 again to the Board. An additional argument is that allocation will become more efficient since it is expected that RThAC02.06 will result in using more strict donor profiles by the centers.

The EThAC has asked the ET office to take care that implementation of RThAC02.04 (gender specific donor profiles) will be sped up.

B. Thoracic Allocation System

The general opinion in the EThAC is that the thoracic allocation is not functioning well with regard to the HU patients and that this mainly is a German problem, due to the large amount of German patients on the HU lists. Several suggestions for improvement were discussed and will be further investigated, e.g. limitation of duration on HU, introduction of modulation of donor age profiles.

C. Guidelines for thoracic auditors

In order to achieve a more reasonable rate of HU request refusals, the EThAC discussed the possibility that auditors can contact each other for discussion on a given request. Since the majority of the EThAC supported this proposal, the proposal was accepted.

The EThAC members are of the opinion that the audit reimbursement fee should be increased in order to achieve a better quality of the audit task which is very crucial for the allocation process.

D. Lung Transplant Registry

The EThAC agreed with the ET proposal of restricting the items for the new lung follow-up web pages to the items that were already in the old system adding only the items needed for the BQS.

E. Difficult-to-allocate organs and rescue allocation

An analysis of the first year experience after the introduction of patient and center specific donor profiles showed that for so-called difficult-to-allocate organs ET could follow now even regular allocation procedures. This is due to the fact that centers can exclude difficult-to-allocate organs in the donor specific profiles as a consequence of which their patients will not appear in the match list resulting in a speeding up of the allocation process.
F. Study proposals

The EThAC discussed and agreed upon the following study proposals:
A. Switching maintenance immunosuppressive regimen after heart transplantations – a review of the Eurotransplant database
B. Life-Year benefits of limiting cold ischaemic time in donor hearts.

E. Discussion about direct feedback of procurement

It was stated that the organ procurement surgeons should receive feedback. For this purpose, quality forms should be received in an electronic form. In order to achieve this:
1. ET has to implement electronic quality reports;
2. Electronic data exchange on quality with other organizations that also collect data (like NTS and DSO) should be established;
3. These electronically collected quality forms should then be used to give feedback to the procuring surgeon and to inform the recipient surgeon.

Report of the meeting of the Eurotransplant Organ Procurement Committee (OPC)

Chairman: Prof.Dr. D. Ysebaert
Secretary: Dr. A. Rahmel / Ms. V. Niehe, MD

The OPC met on Monday, December 18, 2006
Members present: 10
Members absent: 3

A. Reasons for not reporting organs for donation

ET will look at the differences in percentages of transplanted organs in the different regions of ET. Based on these results a decision should be made how to go ahead with the evaluation whether it was justified not to report certain organs to ET.

B. Definitions of malignancy, sepsis, meningitis in relation to donor reporting

The OPC agreed with the definitions currently used by ET:
- Malignancy known in the previous history: enter Yes
- Sepsis and meningitis but adequately treated: enter No.
  If a culture is available the result should be provided.
- In case of doubt the medical doctor on duty should be consulted

C. Election of a vice-chairman of the OPC

Bösebeck was unanimously elected as vice-chairman.

D. Tissue procurement in framework of study protocol

The OPC discussed if it is allowed for a center to explant aorta tissue at time of a heart transplantation for experimental use. It was decided to check whether the law in the different ET countries and the ET manual contain information about vessels to be explanted with an organ.

Report of the meeting of the Eurotransplant Tissue Typing Advisory Committee (TTAC)

Chairman: Prof.Dr. F. Claas
Secretary: Prof.Dr. I. Doxiadis

The TTAC met on Wednesday, December 13, 2006
Members present: 8 + 1 observer + 1 director
Members absent: 1

A. Reports of the various ET Advisory Committees, ET Board and national societies

Reports of the Committees and the Board have been presented in the ET Newsletter for which reason there is no need to elaborate on them in this TTAC report.

The following relevant information was reported by Germany and the Netherlands:

Germany
- Introduction of ISYS: there is an ongoing discussion on the financial support of the TTC performing cross matches for organ donors. The information flow at present goes from ET to DSO and then to the relevant TTC. A maximum of 10 patients are listed for cross matching. This national problem will be discussed elsewhere and reported back to the TTAC.
- Match comment: many TTC in Germany use the field match comment to report additional information such as B cell cross match results. This field is not reported to the recipient center. The problem was discussed and well understood. A possible solution should be searched in the mutual discussion group between ET and DSO (Kontaktgruppe).
- It seems that reporting screening data to ET is very slow in Germany. (In the Netherlands there is a direct connection between the labs and ET which enables fast transfer of data).
- Information on other than kidney transplantations: the information of previous non-renal transplants does not appear on the screen or on the waiting lists. In order to be able to take correct decisions, such information should be available for the TTC.
The Netherlands
The Dutch TTC and the transplantation centers will perform a kidney transplantation without prospective cross matches when a patient is unsensitized. Outcome of such transplantation will be monitored and reported elsewhere.

B. Status on ongoing points

Status of RTTAC02.06 regarding virtual PRA
The TTAC has proposed that for a period of two years that both PRA and virtual PRA should be used in ENIS. The PRA value is not reliable and is based solely on complement dependent antibodies. Using the virtual PRA also patients with no complement fixing antibodies can profit from the points of a higher PRA value. The specificities reported for the virtual PRA will be treated as unacceptable for the patients. For the cross match at the donor center the TTAC proposes that a column is introduced in ENIS showing that the respective patient must be cross matched at the donor center. Patients with non-complement fixing antibodies will be marked and no cross match will be performed at the recipient center. This introduction will reduce costs since sera of such patients will not be sent around. The decisive cross match will be done at the recipient center, where the relevant sera and methods are available. (RTTAC01.07).

New labels for cross match serum tubes
The labels were tested at the ETRL and found acceptable. For the future the following information must be on the label:
Name (4 first digits)
Full ET-number
Center
Bleeding date
The information will be retrieved from ET.

HLA-C and DQ specific antibodies and allocation of organs
The Dutch TTC decided to type and report HLA-C and HLA-DQ to ENIS.

C. New points

Report of cross matches to ET
The TTC must report the results of the cross match for patients outside their region as positive or negative and if applicable with and without DTT. It is the responsibility of the recipient center to accept or deny an offer after receiving this information.

Sorting of serum specificities and unacceptable antigens
The TTAC proposes to ask the IT department to offer this possibility and sort the specificities in a numeric order from HLA-A (1-n) to HLA-DQ (1-n).

External Proficiency Testing (EPT) on DNA typing
The ETRL proposes to stop with the EPT on DNA typing. However, before doing so the TTAC proposes to inform EFI and especially the relevant Committees (EPT and Accreditation) in order for them to anticipate on the eventual consequences of this change.

Discard of sera from non-renal patients
Sera of non-renal patients are accumulating in the different TTC. The TTAC proposes to discard these outdated sera after one year post bleeding date. However, the ETHAC will be informed and asked to take measurements prior to the introduction of this step.

Study on non-complement fixing antibodies
The TTAC proposes a study on the clinical relevance of such antibodies. A protocol will be sent to the members of the TTAC and then to the centers.

EFI accreditation
The TTAC proposes after long discussion to introduce a maximum time period of 6 months for a TTC to apply for a renewal of the accreditation. The total procedure i.e. application and accreditation should not exceed one year. TTC extending this period will not be allowed anymore to enter data in ENIS. Permission will be asked from the TTC to obtain the information on their accreditation status from the EFI accreditation office.

Manual
The ET manual chapter on Histocompatibility will be rephrased and the members of the TTAC will be asked to approve the changes.

Bw4/Bw6 in ENIS
The TTAC discussed a proposal to use these public antigens in the screening field and unacceptable field in ENIS.

AM study
A study conducted by the ETRL showed that still many highly sensitized patients do not profit from the AM program. Transplant centers will be informed accordingly. It is the responsibility of the recipient center to work on the definition of AM and the request for entering the patient in the program.
PROGRAM

Wednesday, January 24, 2007

Welcome and Dinner

Thursday, January 25, 2007

Introduction and welcome

NEWS FROM TISSUE TYPING LABORATORIES
Chairman: F. Claas (Leiden – NL)

New aspects in screening and crossmatching

Update on relevance of HLA, non-HLA and sCD30 in kidney transplantation

Discussion

EXTENDING LIVING DONATION FRONTIERS
Chairman: U. Heemann (Munich – G)

Dutch living donor kidney exchange program, 3 years results

AB0-incompatible living donor liver transplantation with antigen specific immuno-adsorption and without splenectomy

Donor selection and donor complications in living donor liver transplantation

Discussion

Coffee break

ORGAN TRANSPLANTATION AND CONCOMITANT DISEASES
Chairman: R. Margreiter (Innsbruck – A)

Organ transplantation and HIV infection

Organ transplantation and HIV infection
Outcome of patients with hepatocellular carcinoma listed for liver transplantation with the Eurotransplant allocation system: a study of the Belgian Liver Intestine Committee

Discussion

HENK SCHIPPERS AWARD LECTURE
Chairman: B. Meiser (Munich – G)

Future trends in transplantation: gene transfer meets organ transfer

Discussion

ORGAN TRANSPLANTATION IN EUROPE
Chairman: Y. Vanrenterghem (Leuven – B)

Lung transplantation across Europe

Report on the open consultation: policy options for organ donation and transplantation at EU level

Discussion

Friday, January 26, 2007

CURRENT DEVELOPMENTS IN ORGAN PROCUREMENT
Chairman: D. Ysebaert (Antwerp – B)

Clinical results of heart transplantation after warm beating organ transportation using the Organ Care System (OCS)

Pancreas procurement – the achilles tendon of pancreas transplantation

Kidney transplantation with non-heart-beating donors – are the results comparable to the heart beating donors?

Discussion

INDUCTION THERAPY – ESTABLISHED AND NEW WAYS
Chairman: R. Ploeg (Groningen – NL)

The role of induction therapy in heart transplantation; insights after >1000 heart transplants in Vienna

Alemtuzumab (Campath-1H) induction followed by tacrolimus monotherapy vs tacrolimus based triple therapy drug immunosuppression in renal transplantation – one year results of a multicenter study

Discussion
Discussion

Coffee break

DIFFERENT ASPECTS OF LIVER ALLOCATION AND TRANSPLANTATION
Chairman: K-W. Jauch (Munich – G)

- Transition to a new liver allocation system (MELD) in Eurotransplant – the early experience
  T. Gerling (Leiden – NL)
- Liver cell transplantation for inborn errors of metabolism
  E. Sokal (Brussels – B)
- Combined lung and liver transplantation
  M. Strüber (Hannover – G)

Discussion

BASIC SCIENCE – BENCH TO BEDSIDE
Chairman: G. Laufer (Innsbruck – A)

- The prognostic relevance of mRNA expression of Epithelial to Mesenchymal Transition related molecules in Renal Allograft Protocol Biopsies
  M. Roos-van Groningen (Leiden – NL)

Discussion

SPECIAL LECTURE

- Transplant Adventure Camps for Kids: spreading our wings
  L. Schick (Anzère – CH)

Discussion

Closing remarks
B. Meiser (Munich – G)

This meeting was generously supported by:

ASTELLAS PHARMA GmbH
ROCHE
NOVARTIS PHARMA
FRESENIUS BIOTECH GmbH
BIOTEST PHARMAZEUTIKA GmbH
DR. FRANZ KÖHLER CHEMIE GmbH
MERCK SHARP & DOHME GmbH
WYETH PHARMACEUTICALS
BRISTOL MEYERS SQUIBB
GENZYME GmbH
## Results Eurotransplant Slalom 2007

### Ladies

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Senior

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Companies – Ladies

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Snowboard

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The Eurotransplant Duty Office can be reached 24 hours per day at 0031 71 5795795. Please note that all phone calls to the Duty Office and the Medical Staff are logged and recorded. Recording of these conversations is in accordance with Dutch Law.
Announcement

The 2007 Eurotransplant annual Meeting

will take place on September 20 – 21, 2007 in Noordwijk, the Netherlands