Wits University Donald Gordon Medical Centre

Patient-centred. Independent. Academic.

MEDICLINIC

ABOi in Liver transplantation

Dr L Brannigan

WITS TRANSPLANT

Progressive medicine, exceptional care.

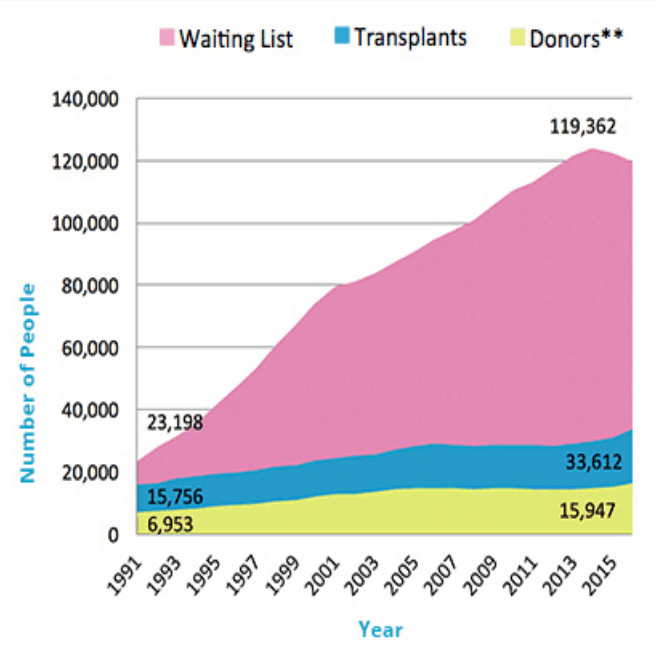
DECLARATIONS

Nil relevant to this talk

The state of play

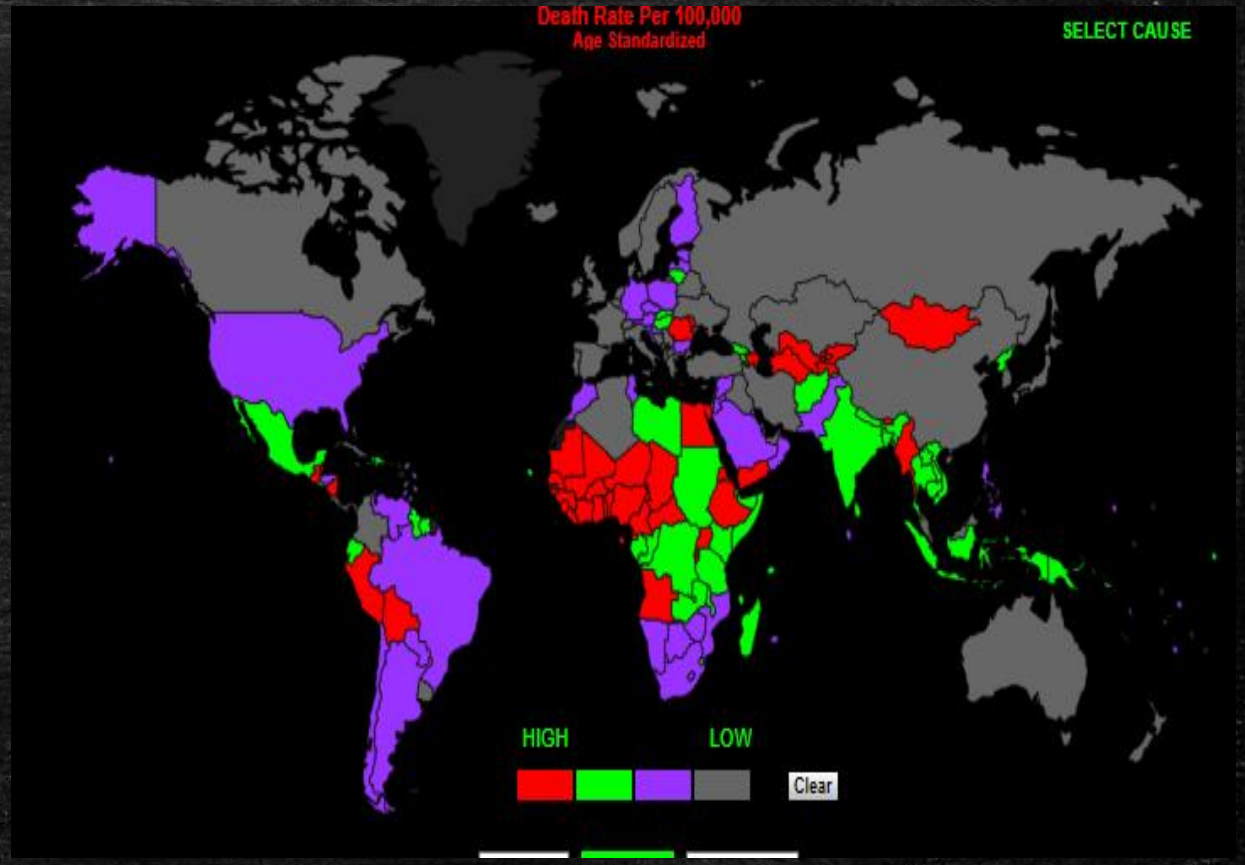
the organ shortage continues

Each year, the number of people on the waiting list continues to be much larger than both the number of donors and transplants, which grow slowly.



Data from optn.transplant.hrsa.gov and OPTN/SRTR Annual Report. OPTN has current, in-depth statistics. Click to view.

Description of The Organ Shortage Continues Graph



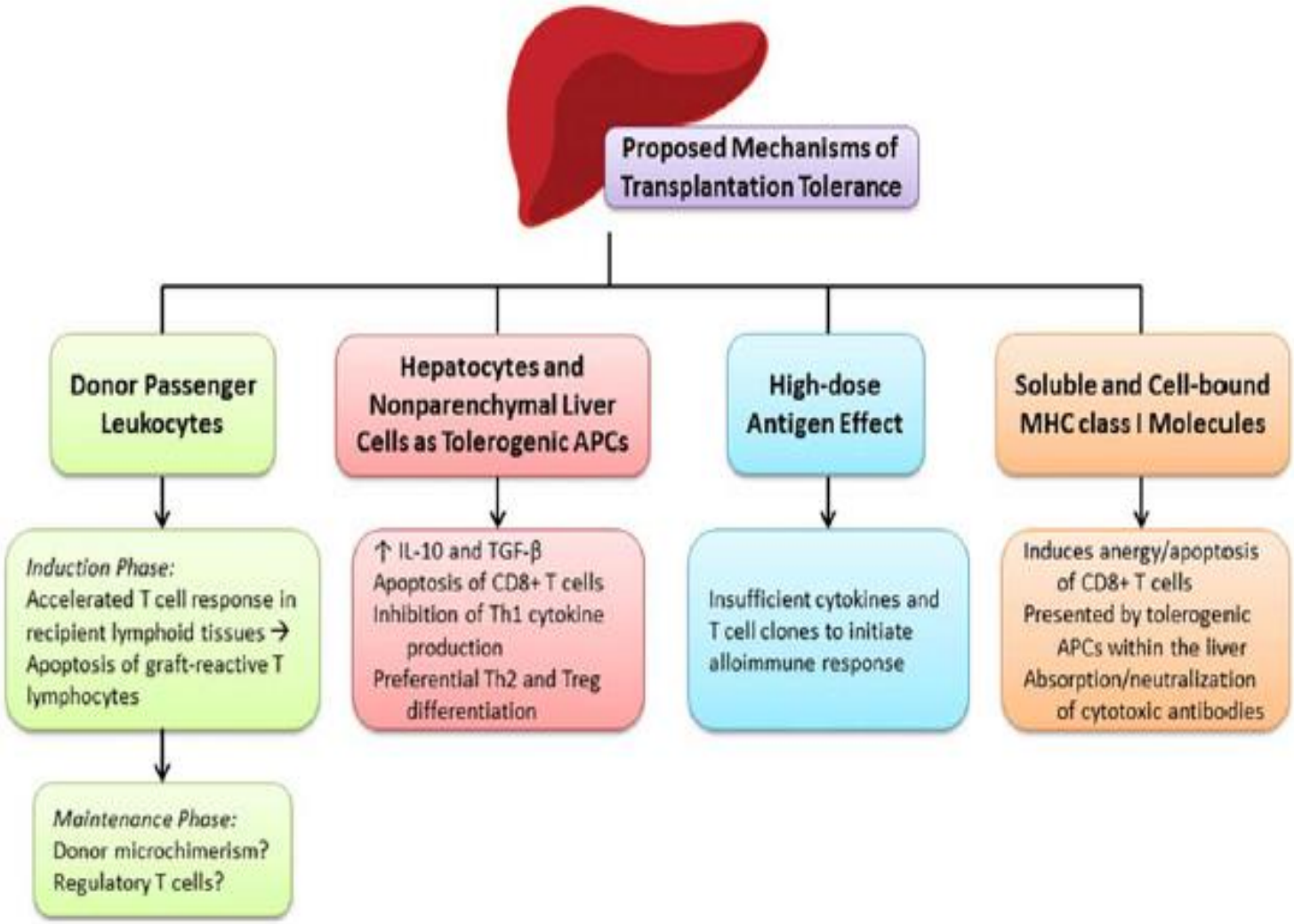


FIG 1 Proposed mechanisms for the immunomodulatory properties of the transplanted liver. Abbreviations: APC, antigen-presenting cell; IL-10, interleukin-10; TGF-β, transforming growth factor β. Adapted with permission from *SOJ Immunology*.[2] Copyright 2017, Shuo Wang et al.

Early results

- 1. Worsened patient and graft survival
- More ABMR
- Higher rates of vascular complications
- Higher rates of CMV complications
- Higher rates of biliary complications

World Journal of Gastroenterology

Submit a Manuscript: http://www.f6publishing.com

World J Gastroenterol 2017 September 21; 23(35): 6516-6533

DOI: 10.3748/wjg.v23.i35.6516

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

META-ANALYSIS

Outcomes after liver transplantation in accordance with ABO compatibility: A systematic review and meta-analysis

TRANSPLANT INTERNATIONAL

Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

Liver transplantation with deceased ABO-incompatible donors is life-saving but associated with increased risk of rejection and post-transplant complications

Trygve Thorsen,[1] Ulrika S. Dahlgren,[2] Einar Martin Aandahl,[1,3,4] Krzysztof Grzyb,[5] Tom H. Karlsen,[6,7,8] Kirsten M. Boberg,[7] Lennart Rydberg,[9] Christian Naper,[10] Aksel Foss[1,8] and William Bennet[2]

1 Section for Transplant Surgery, Department of Transplantation Medicine, Oslo University Hospital, Oslo, Norway
2 Transplant Institute, Sahlgrenska University Hospital, Sahlgrenska Academy, Gothenburg, Sweden
3 Biotechnology Centre of Oslo, University of Oslo, Oslo, Norway
4 Centre for Molecular Medicine Norway, Nordic EMBL Partnership, University of Oslo, Oslo, Norway
5 Department of Pathology, Oslo University Hospital, Oslo, Norway
6 Section for Gastroenterology, Department of Transplantation Medicine, Norwegian PSC Research Centre, Oslo University Hospital, Oslo, Norway
7 Section for Gastroenterology, Department of Transplantation Medicine, Oslo University Hospital, Oslo, Norway
8 Institute of Clinical Medicine, University of Oslo, Oslo, Norway
9 Department of Clinical Chemistry and Transfusion Medicine, Sahlgrenska Academy, Sahlgrenska University Hospital, Gothenburg, Sweden
10 Oslo University Hospital, Institute of Immunology, Oslo, Norway

Pathogenesis

ABO Recipient-Donor Compatibility

Recipient Blood Type	Compatible Donor Blood Types	Incompatible Donor Blood Types
A	A, O	B, AB
B	B, O	A, AB
AB	A, B, AB, O	none
O	O	A, B, AB

Besides RBC's, blood type antigens also exist on lymphocytes, platelets, epithelial and endothelial cells.

Game changer KNIGHT

- Better understanding of immunogenic processes such as immunogenic accommodation
- Splenectomy
- 2003 Anti-CD20 monoclonal AB introduced
- Plasma exchange therapies
- De-sensitization
- Antigen specific immunoadsorption

Hindawi
Gastroenterology Research and Practice
Volume 2019, Article ID 8589402, 16 pages
https://doi.org/10.1155/2019/8589402

Review Article

ABO-Incompatible Adult Living Donor Liver Transplantation in the Era of Rituximab: A Systematic Review and Meta-Analysis

Dipesh Kumar Yadav,[1] **Yong Fei Hua**,[1,2] **Xueli Bai**,[1] **Jianying Lou**,[3] **Risheng Que**,[1] **Shunling Gao**,[1] **Yun Zhang**,[3] **Ji Wang**,[1] **Qinfen Xie**,[4] **Muhammad Ibrahim Alhadi Edoo**,[1] **Vikram Kumar Chutturghoon**,[1] **and Tingbo Liang**[1]

[1]*Department of Hepatobiliary and Pancreatic Surgery, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, 310003 Zhejiang, China*
[2]*Department of Hepatobiliary and Pancreatic Surgery, Ningbo Medical Center Lihuili Eastern Hospital, Medical School of Ningbo University, Ningbo, 315041 Zhejiang, China*
[3]*Department of Hepatobiliary and Pancreatic Surgery, The Second Affiliated Hospital, Zhejiang University School of Medicine, 88 Jiefang Road, Hangzhou, 310009 Zhejiang, China*
[4]*Department of Hepatobiliary Surgery, Shulan (Hangzhou) Hospital, Hangzhou, 310000 Zhejiang, China*

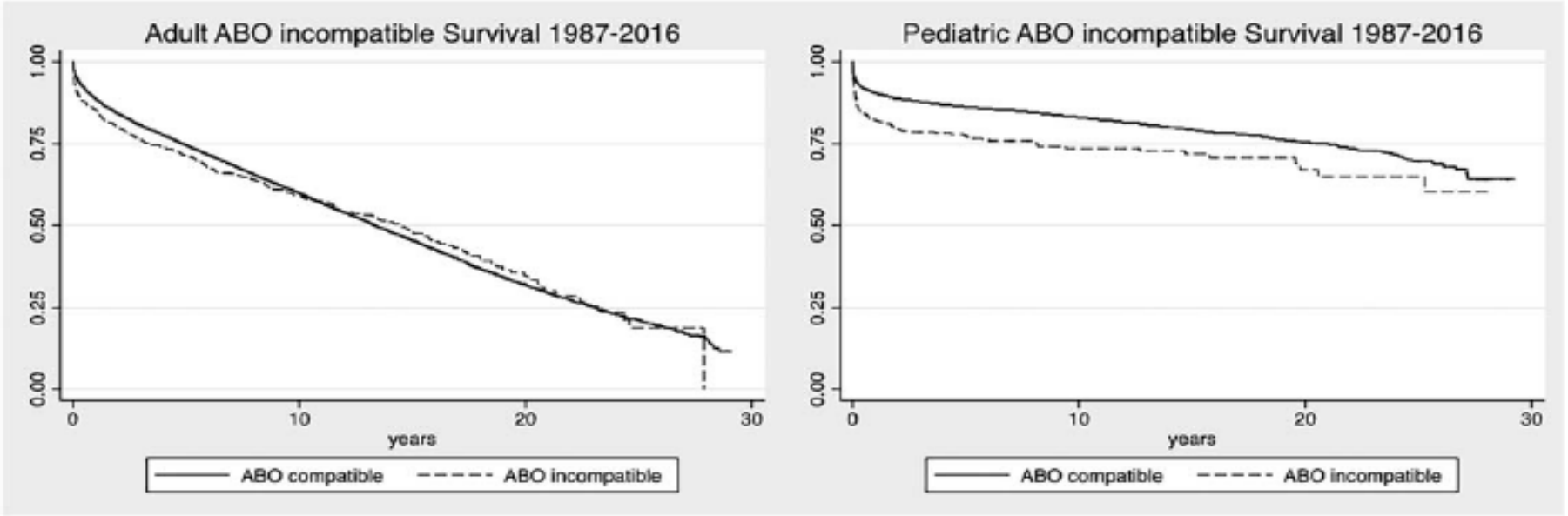


FIG 3 UNOS 1987-2016 deidentified patient-level data. (A) Overall adult survival stratified by donor/recipient blood type relationship in LT (ABO-ILT versus ABO-CLT). (B) Overall pediatric survival stratified by donor/recipient blood type relationship in LT (ABO-ILT versus ABO-CLT). *y* axis: percentage recipient survival of total recipients. *x* axis: years after LT.

TABLE 2.

Clinical outcomes between ABOi and non-ABOi group

	ABOi (n = 29)	Non-ABOi (n = 131)	*P*
Bacterial infection	10 (34.5%)	33 (25.2%)	0.356
CMV infection	14 (48.3%)	42 (32.1%)	0.131
Fungal infection	1 (3.4%)	9 (6.9%)	0.691
PVS/PVT	3 (10.3%)	7 (5.3%)	0.390
HVS	1 (3.4%)	7 (5.3%)	0.999
HAT	1 (3.4%)	3 (2.3%)	0.554
Biliary complication	3 (10.3%)	24 (18.3%)	0.415
ACR	13 (44.8%)	46 (35.1%)	0.396
AMR	2 (6.9%)	0 (0%)	0.036

CMV, cytomegalovirus; PVS, portal vein stenosis; PVT, portal vein thrombosis; HVS, hepatic vein stenosis; HAT, hepatic artery thrombosis.

TABLE 3.

Clinical outcomes between rituximab-treated and non–rituximab-treated ABOi group

	Rituximab-treated ABOi (until 2010, n = 3)	Rituximab-treated ABOi (from 2010, n = 7)	Non–rituximab-treated ABOi (n = 19)	*P*
Bacterial infection	3 (100.0%)	1 (14.3%)	6 (31.6%)	0.030
CMV infection	2 (66.7%)	3 (42.9%)	9 (47.4%)	0.781
Fungal infection	1 (33.3%)	0 (0%)	0 (0%)	0.011
PVS/PVT	1 (33.3%)	1 (14.3%)	1 (5.3%)	0.308
HVS	0 (0%)	0 (0%)	1 (5.3%)	0.761
HAT	0 (0%)	1 (14.3%)	0 (0%)	0.196
Biliary complication	1 (33.3%)	0 (0%)	2 (10.5%)	0.284
ACR	2 (66.7%)	0 (0%)	11 (57.9%)	0.023
AMR	1 (33.3%)	1 (14.3%)	0 (0%)	0.072

A summary of the results

- Safe in paediatrics with comparable results especially with wait list mortality taken into account
- 1, 3 and 5 year patient and graft survival in adult living donor ABOi comparable
- DFS in the HCC group was comparable
- Rates of cmv infection, biliary complications and ABMR higher in ABOi
- Data on acute liver failure/urgent indications is still lacking

The Johannesburg WDGMC experience

- 25 cases: 7 pediatric and 18 adult
- Indications: Acute, HCC, Metatstatic colorectal cancer, NASH, Biliary atresia, polycystic and others
- Protocolised treatment constantly evolving

Criteria

- 1. Must fulfil general transplant candidate selection criteria
- 2. No ABOc graft available
- 3. Initial ABO isoagglutinin titer of less than 512
- 4. Must be willing to accept an ABOi transplant and undergoe extended consenting process

Our protocol

- Pre-transplant exchange
- Thymoglobulin induction
- Post-operative exchange targeting ISOAGGLUTININ levels of <1:32 but as low as possible
- Rituximab targeted against CD 19/ CD 20 levels
- Routine immunosuppression with steroid/CIN/MMF
- Immunoglobulin
- Attention to CMV and other infectious complications

What we have learnt so far…

- 1. The process can be and is life saving even in ALF without de-sensitization
- 2. Plasma exchange is associated with significant morbidity (immunoadsorption columns)
- 3. The infection risk appears comparable as the studies suggest
- 4. More dangerous issue appears to be the "RUNAWAY IMMUNITY TRAIN"
- 5. We have to constantly evolve the protocol: thymoglobulin use, IVIg, Plex and others

TAKE HOME