Current status and perspective of ABO-incompatible liver transplantation

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Why incompatible?
Annual Liver Transplantations in Korea

- **DDLT**
- **LDLT**

2000: 34 DDLT, 179 LDLT
2001: 37 DDLT, 274 LDLT
2002: 28 DDLT, 307 LDLT
2003: 50 DDLT, 319 LDLT
2004: 64 DDLT, 480 LDLT
2005: 66 DDLT, 529 LDLT
2006: 118 DDLT, 563 LDLT
2007: 128 DDLT, 605 LDLT
2008: 233 DDLT, 694 LDLT
2009: 236 DDLT, 718 LDLT
2010: 242 DDLT, 801 LDLT
2011: 313 DDLT, 897 LDLT
2012: 363 DDLT, 921 LDLT
2013: 367 DDLT, 821 LDLT
2014: 404 DDLT, 861 LDLT
2015: 456 DDLT, 939 LDLT

2015 KONOS online data

- 83.4% DDLT
- 77.5% LDLT
- 67.2% Total
Waiting List on KONOSOS Registry

- Cummulative No. on Waiting List
- Annual Increased No. on Waiting List
- No of DDLT

From KONOS Annual Report 2013
Donor Shortage
To expand donor pool...

Volume
- Dual graft
- Rt post
- LL+S1

Function
- Marginal graft
- Steatosis
- Old age

Immune
- ABOi LDLT
Liver may be less susceptible than other organs to an antibody reaction.

1974, Starzl TE et al, Transplant Proc
1984, Iwatsuki S et al, Transplant Proc
1990, Gugenheim J et al, Lancet
Antibody mediated rejection

Hepatic necrosis
Intrahepatic biliary complication
ABO incompatible Transfusion

Donor (Ag)

Recipient (Ab)

hemagglutinin

Humoral Rejection

Endothelial Damage
Living related liver transplantation across ABO blood groups with FK506 and OKT3.

Second Department of Surgery, Faculty of Medicine, Kyoto University, Japan.

Living related liver transplantation across ABO blood groups.
Second Department of Surgery, Faculty of Medicine, Kyoto University, Japan.

Successful use of an enhanced immunosuppressive protocol with plasmapheresis for ABO-incompatible mismatched grafts in liver transplant recipients.
Mor E, Skerrett D, Manzarbeitia C, Sheiner PA, Schwartz ME, Emre S, Thung SN, Miller CM.
Department of Surgery, Mount Sinai Medical Center, New York, New York 10029, USA.

Hemagglutinin levels < 1:16
Desensitization!
Rituximab: Anti-CD20 Monoclonal antibody
Pre-transplant Desensitization

Plasmapheresis / Exchange transfusion

Splenectomy

Rituximab

PV infusion

HA infusion

Both or Select one

Both or Select one

New Protocol of Immunosuppression for Liver Transplantation Across ABO Barrier: The Use of Rituximab, Hepatic Arterial Infusion, and Preservation of Spleen


Transplantation Proceedings, 37, 1718–1719 (2005)
ABO incompatible LDLT In KOREA
Trend of Number of Korean Centers with the Experience of ABO-i ALDLT
(From Mar 2007 to Dec 2013)

Song GW et al. Korean Experience of ABOi LDLT. Presented in IHPBA2014 Korea Seoul
Annually Increased Number of ABOi LDLT in Korea (From Mar 2007 to Dec 2013)

Almost 20% of total adult LDLT

Song GW et al. Korean Experience of ABOi LDLT. Presented in IHPBA2014 Korea Seoul
Changes of DSZ Protocol for ABOi-ALDLT in Korea

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Plasma exchange</th>
<th>Rituximab</th>
<th>Local infusion therapy</th>
<th>Splenectomy</th>
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<td>2011</td>
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</tbody>
</table>

Wang et al. LDLT across ABO blood-type barrier in Korea. Presented in CAST 2011 Korea Seoul
387 cases ABOi ALDLT from 10 Korean Centers

Underlying Disease

- HBV (N=280, 72.2%)
- ALC (N=44, 11.3%)
- HCV (N=39, 10.1%)
- Others (N=24, 6.3%)

HCC (+) N=184 (47.6%)

Song GW et al. Korean Experience of ABOi LDLT. Presented in IHPBA2014 Korea Seoul
387 cases **ABOi ALDLT from 10 Korean Centers**

Recipient-Donor ABO Blood Group Mismatch

- **O** and **A**
  - N=102 (26.4%)

- **O** and **B**
  - N=74 (19.1%)

- **O** and **AB**
  - N=17 (4.4%)

- **A** and **B**
  - N=52 (13.4%)

- **A** and **AB**
  - N=49 (12.7%)

- **B** and **A**
  - N=51 (13.2%)

- **B** and **AB**
  - N=42 (10.9%)

**A-Barrier 50.5%**

**B-Barrier 45.2%**

Song GW et al. Korean Experience of ABOi LDLT. Presented in IHPBA2014 Korea Seoul
Survival Outcome of ABOi ALDLT
(From Mar 2007 to Dec 2013)

387 cases ABOi ALDLT from 10 Korean Centers

• Mean Follow-Up Period: $20.8 \pm 15.1 \ (0.5\sim84.3) \ mos.$
Risk Factor Analysis for Survival Outcome

307 cases ABOi ALDLT from 8 Korean Centers

MELD ≥20

MELD <20

MELD ≥20

Infectious Cx

Post-LT Inf (-)

Post-LT Inf (+)

1/2/3 Yr-PSR

97.0/93.9/93.9%

81.5/78.3/78.3%

1/2/3 5Yr-PSR

80.1/73.1/73.1%

AMR (HN or DIHBS)

AMR (-)

AMR (+)

1/2/3 Yr-PSR

95.1/92.1/92.1%

87.6/73.6/73.6%

P=0.000

P=0.002

P=0.010

Song GW et al. Korean Experience of ABOi LDLT. Presented in IHPBA2014 Korea Seoul
How about HCC patients?
Immune suppression

Cancer prevention
YUHS experience of ABOi LDLT for HCC recipient

2010~2015
237 HCC patients who underwent LT
Demographics of LT for HCC

M:F = 197:40
Mean age of recipients: 54.4 ± 7.3 years
Mean age of donors: 35.4 ± 13.1 years
Mean f/u duration: 29.3 ± 18.8 months
ABO incompatible: 23 cases (9.7%)
LDLT:DDLT = 153:84 (64.6% LDLT)
Above MC
Within MC
13.1% (n=31)

n=206

Milan criteria

ABOi LT

9.7% (n=23)

ABO-i
ABO-com

Within MC
Above MC

9.7%
Post-transplant HCC recurrence

- Recurrence: 13.9% (n=33)
- No recurrence: 14.0% (N=214)

ABO-c (N=214):
- Recurrence: 13.0%
- No recurrence: 14.0%

ABO-i (N=23):
- Recurrence: 13.0%
- No recurrence: 14.0%
Recurrence Free Survival Rate

81.6%

83.9%

Recurrence free survival rate (%)

Post-transplant years

ABO-c

ABO-i
Recurrence Free Survival Rate

Within Milan Criteria

Above Milan Criteria

Recurrence free survival rate (%)

Post-transplant years

ABO-c

ABO-i

ABO-c

ABO-i
Case Presentation

고OO (F/49)

Pre-transplant diagnosis: HCC (B-viral)
AFP: 356.21, PIVKA-II: 16 (9.2cm size)

Pre-transplant treatment
2009.10 TACI & HA port insertion
2009.11~12 CCRT (5FU + Tomotherapy)
2010.01 FP chemotherapy
2010.03 Extended Lt. hemihepatectomy
2011.05 TACI d/t Recurred HCC in Rt. Lobe
2011.05~10 Sorafenib (Jaundice + Ascites)
2011.11 ERBD d/t biliary stricture
Extended Lt. hemihepatectomy

Pathologic report
Mixed type (HCC + CCC)
TACI d/t Recurred HCC in Rt. lobe

Post-TACI CT (Peribiliary necrosis)
Peribiliary necrosis
No visible hilar PV and HA
Donor evaluation

Patient’s son (M/20)

ABO blood type: $\text{B}^+ \rightarrow \text{O}^+$ (recipient)

GRWR: 1.29
YUHS Protocol for ABO incompatible LDLT

**Plasma Exchange**

- **Rituximab**
  - Day: -14 to -10
- **Basiliximab**
  - Day: 4, 7

**Spleen preservation**

- No local injection

**TAC**

- Dose: 0.1 mg/day
- Trough level: 8-12 ng/mL

**MMF**

- Dose: 1000 mg/day

**PL**

- Dose: 20 mg/day

**LT (day)**

(21-28)
Post-transplant 49 months

No recurrence

AFP: 2.21
PIVKA-II: 12
In conclusion,

ABO incompatibility $\rightarrow$ No more hurdle

Pre-transplant MELD
Post-transplant infection
Antibody mediated rejection

$\rightarrow$ independent risk factors for survival
In conclusion,

Desensitization protocol
⇒ More simplified

Applying for the HCC patients?
⇒ No difference of recurrence rates.
⇒ Further study will be needed.
In conclusion,

- Large cohort data

  Patient selection guideline
  Standard desensitization protocol
Thank you for your attention

Hope to be free from HCC