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UTAH SOCIETY OF HEALTH-SYSTEM PHARMACISTS

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Now We Got Bad Blood: Desensitization in Solid Organ Transplant

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Disclosure

- Relevant Financial Conflicts of Interest
  - **CE Presenter, Bridget Bucher, PharmD:**
    - None
  - **CE Mentor, Todd Larson, PharmD, BCTXP:**
    - None
  - **CE Mentor, Kelsea Zukauckas, PharmD, BCPS:**
    - None
- Off-Label Uses of Medications
  - **Bortezomib, Carfilzomib, Intravenous Immune Globulin (IVIG), Rituximab, Tocilizumab**
- Investigational Agents
  - **Clazakizumab, Imlifidase**

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Learning Objectives – Pharmacists

- Describe the clinical significance of HLA sensitization in the solid organ transplant population
- Identify the mechanism of agents and modalities currently used in desensitization regimens
- Evaluate existing literature and protocols supporting the role of desensitization therapy
- Formulate an appropriate treatment plan for a highly sensitized transplant recipient

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Learning Objectives – Technicians

- Recognize various agents used for desensitization in solid organ transplant
- Apply knowledge on the preparation of agents used for desensitization
- Discuss potential cost barriers associated with desensitization therapies

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Abbreviations

ACR – Acute Cellular Rejection	**IdeS** – IgG-Degrading Enzyme Derived from *Streptococcus pyogenes*	**PML** – Progressive Multifocal Leukoencephalopathy
ADR – Adverse Drug Reactions	**IgG** – Immunoglobulin G	**POD** – Post-Op Day
AKI – Acute Kidney Injury	**IL-6** – Interleukin-6	**PRA** – Panel Reactive Antibody
AMR – Antibody Mediated Rejection	**IL-6R** – Interleukin-6 Receptor	**SAE** – Serious Adverse Events
AWP – Average Wholesale Price	**IV** – Intravenous	**SC** – Subcutaneous
D5W – 5% Dextrose	**IVIG** – Intravenous Immune Globulin	**SWFI** – Sterile Water for Injection
DDKT – Deceased Donor Kidney Transplantation	**LRKT** – Living Related Kidney Transplantation	**TCR** – T cell Receptor
DSA – Donor Specific Antibody	**MHC** – Major Histocompatibility Complex	**TPE** – Therapeutic Plasma Exchange
FDA – Food and Drug Administration	**PLEX** – Plasma Exchange	**TXP** – Transplant
HLA – Human Leukocyte Antigen	**PMH** – Past Medical History	**UTI** – Urinary Tract Infection

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Background

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Immunology Refresher

INNATE IMMUNE SYSTEM

- *Nonspecific* immune response to a foreign pathogen
- Serves as the first-line of defense:
  - Physical barriers
  - Chemical barriers
  - Phagocytic cells (macrophages, neutrophils, etc.)

ADAPTIVE IMMUNE SYSTEM

- Memory response to a *specific* foreign pathogen
  - Cell-mediated immunity:
    - Cytotoxic (CD8+) and helper (CD4+) T cells
  - Humoral immunity:
    - Antibody production by B cells and plasma cells

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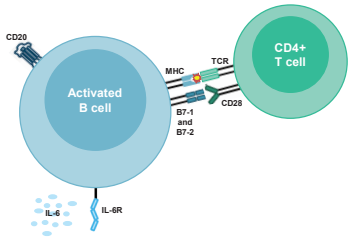
Adaptive Immune System

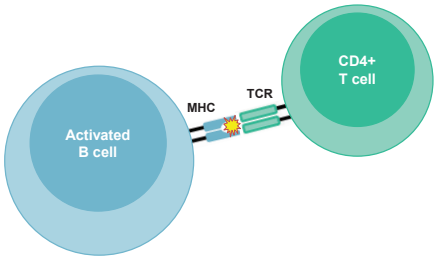


Step 1: Antigen presenting cell (ex: B cell) presents foreign antigen to T cell

Loupy, et al. *N Engl J Med* 2018; 379(12):1150-1160.

Transplant Immunology

- Major histocompatibility complex (MHC) molecules present antigens to T cells
  - MHC = human leukocyte antigen (HLA)
- In transplant, rejection can occur from foreign antigens (i.e., transplanted allograft)
  - MHC molecules are major antigen targets of rejection
  - Direct vs. indirect recognition



Human Leukocyte Antigen

HLA genes follow Mendelian inheritance and are co-dominantly expressed

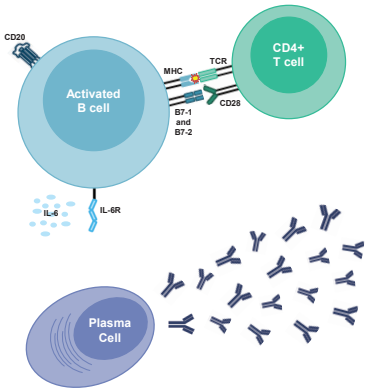
HLA Class I

- HLA-A, HLA-B, and HLA-C
- Found on all nucleated cells
- Present antigens to cytotoxic (CD8+) T cells → destruction

HLA Class II

- HLA-DR, HLA-DQ, and HLA-DP
- Found on antigen presenting cells
- Present antigens to helper (CD4+) T cells → antibody production

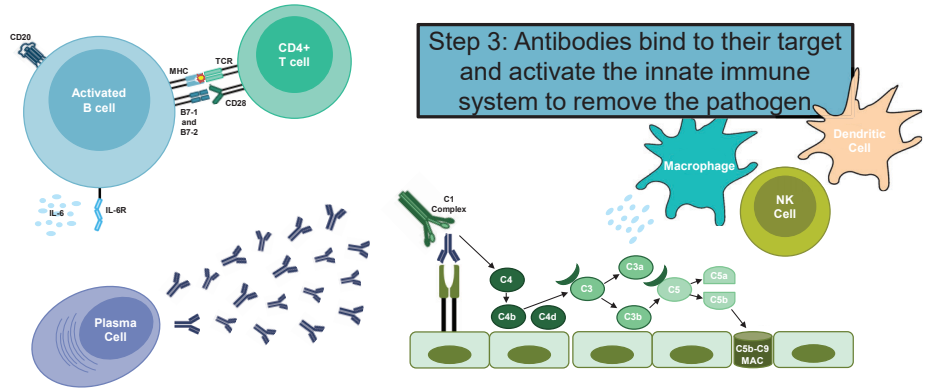
Adaptive Immune System



Step 2: Activated B cell matures into memory B cells or plasma cells, which produce antibodies

Loupy, et al. *N Engl J Med* 2018; 379(12):1150-1160.

Adaptive Immune System



Loupy, et al. *N Engl J Med* 2018; 379(12):1150-1160.

Measuring Antibodies

Exposure to foreign HLA can result in development of anti-HLA antibodies

Panel Reactive Antibody (PRA)

Cross-Matching ⟷ Donor-Specific Antibodies (DSA)

Measuring Antibodies

Panel Reactive Antibody (PRA)

- *Performed pre-transplant*
- Measurement of recipient's antibodies to a panel of human antigens
- Represents the percentage of the population the recipient has pre-formed antibodies against
- Example: recipient with PRA of 80% is incompatible with 80% of donors

Prospective Cross-Matching

- *Performed at the time of transplant*
- Recipient serum potentially containing DSA is mixed with donor T or B lymphocytes
- Positive crossmatch indicates DSA, increasing the risk of rejection

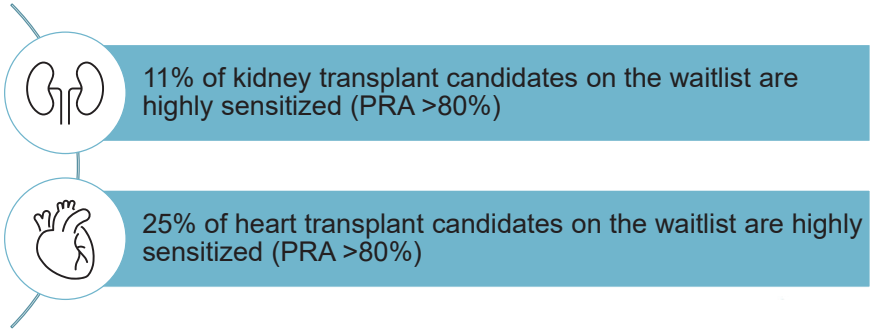
Donor-Specific Antibodies (DSA)

- *Performed pre- or post-transplant*
- Detects specific antibodies against a particular donor's HLA antigens
- DSA may be pre-formed (developed before transplant) or de-novo (developed after transplant)

Sensitization Events

Transplantation	Pregnancy	Transfusions
Mechanical circulatory devices	Graft tissue (cardiac valves)	Vaccinations

Sensitization in Transplant



11% of kidney transplant candidates on the waitlist are highly sensitized (PRA >80%)

25% of heart transplant candidates on the waitlist are highly sensitized (PRA >80%)

Based on OPTN data as of February 2023.

Impact of Sensitization in Transplant

- Increased waitlist time
- Increased morbidity and mortality on the waitlist
- Risk of hyperacute rejection
- Increased rates of antibody mediated rejection (AMR)
- Early graft loss

Desensitization Overview

Patient Case

- CV is a 33-year-old female
- PMH:
  - Hypoplastic left heart syndrome
  - Cirrhosis secondary to congenital heart disease
- Listed for dual heart-liver transplant in 9/2022
- 100% PRA at the time of listing
  - Sensitization events: multiple congenital heart surgeries and transfusions for menorrhagia

What is Desensitization?

Designed to reduce and remove pre-formed antibodies prior to transplant

Goals:
- Increase access to transplant by expanding the donor organ pool
- Prevent AMR

Therapies first utilized in the oncology population

Primarily studied in kidney transplant candidates

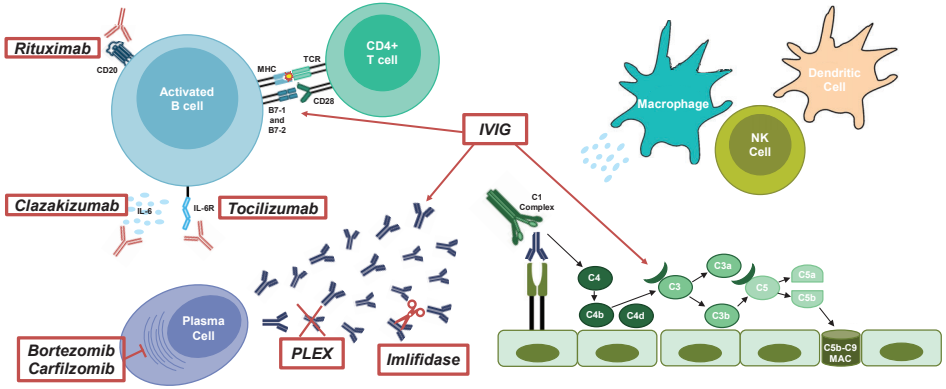
Desensitization Therapy*

Backbone Agents	Alternative Agents	Refractory Agents

• IVIG
• Plasmapheresis
• Rituximab
	• Proteosome Inhibitors:
	  • Bortezomib
	  • Carfilzomib
		• Tocilizumab
		• Clazakizumab
		• Imlifidase

*No drug therapies are currently FDA approved for desensitization in solid organ transplant

Desensitization Therapy Targets



Loupy, et al. *N Engl J Med* 2018; 379(12):1150-1160.

Backbone Agents

IVIG Mechanism of Action

- Several proposed mechanisms of action:
  - Neutralization of circulating anti-HLA antibodies
  - Inhibition of complement activation
  - Binding to Fc receptors on immune cells
  - Prevents rebound of pre-formed antibodies by providing circulating IgG

IVIG Dosing and Administration

Dose

- 0.1 g/kg/dose to 2 g/kg/dose IV
  - *Low-Dose*
  - *High-Dose*

Preparation

- Not compounded
- Spike and hang IVIG product from vial

Administration

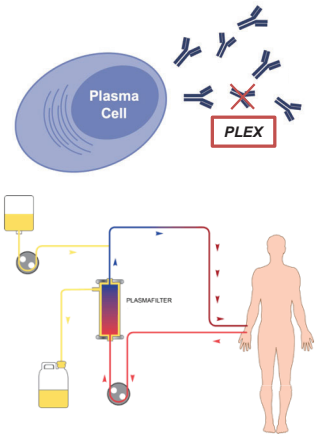
- Premedication recommended with acetaminophen and diphenhydramine prior to infusion
- Infusion rate dependent on IVIG product

Adverse Reactions

- Infusion reactions
- Boxed warnings:
  - Renal dysfunction and acute renal failure (sucrose containing products)
  - Thromboembolic events

Plasmapheresis

- Plasmapheresis = Plasma Exchange (PLEX) = Therapeutic Plasma Exchange (TPE)
- Approved for desensitization in ABO incompatible kidney transplant
- Mechanism of action:
  - Direct removal of anti-HLA antibodies



IVIG and Plasmapheresis Literature

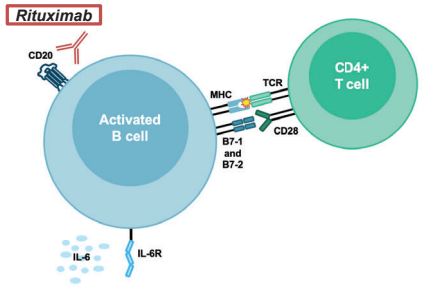
	Trial	Intervention	Outcomes
High-Dose IVIG	Glotz, et al. 2002. • Pilot trial • N=15	Pre-txp: IVIG 2 g/kg monthly x 3 months Post-txp: IVIG 2 g/kg on POD 0, 1, 20, 21, 40, 41	• 87% (13/15) transplanted • 11 DDKT – mean PRA 64% before vs. 14% after • 2 LRKT – positive crossmatch before vs. negative after • 77% (10/13) developed rebound DSA • 2 episodes of graft loss (1 thrombosis, 1 rejection)
	Jordan, et al. 2004. • Randomized, double-blind, placebo-controlled trial • N=101	Pre-txp: IVIG 2 g/kg monthly x 4 months (additional doses at 12 and 24 months if not transplanted) Post-txp: IVIG 2 g/kg monthly x 4 months	• IVIG improved transplant rates compared with placebo (35% vs 17%, P=0.048) • IVIG significantly reduced PRA levels (P=0.033), but mean PRA remained >40% • IVIG decreased waitlist times compared with placebo (4.8 years vs. 10.3 years, P=0.034)

Low-Dose IVIG + PLEX	Montgomery, et al. 2011.
	• Matched control trial
	• N=215
		Pre-txp: mean of 4±4 PLEX sessions with 0.1 g/kg Cytogam after each session
		Post-txp: mean of 5±4 PLEX sessions with 0.1 g/kg Cytogam after each session
			• 98% (211/215) transplanted
			• Improved survival rates with treatment vs. dialysis-only vs. dialysis-only or HLA compatible transplant; P <0.001
			  • 1 year: 90.6%, 91.1%, 93.1%
			  • 3 years: 85.7%, 67.2%, 77%
			  • 5 years: 80.6%, 51.5%, 65.6%
			  • 8 years: 80.6 %, 30.5 %, 49.1%

Glotz, et al. *Am J Transplant* 2002; 2:758–760.
Jordan, et al. *JASN* 2004; 15(12):3256-3262.
Montgomery, et al. *N Engl J Med* 2011; 365:318-326.

Rituximab Mechanism of Action

- Chimeric monoclonal antibody directed against CD20 on the surface of B cells
- Induces apoptosis of B cells via antibody-dependent cytotoxicity and complement-dependent cytotoxicity



Rituximab. Lexicomp, 2023.

Rituximab Dosing and Administration

Dose

- 375 mg/m^2/dose or 1000 mg IV
- Dosing regimen is institution specific

Preparation

- Compounded in normal saline or D5W
- Dilute to concentration of 1-4 mg/mL

Administration

- Pre-medicate with acetaminophen and diphenhydramine prior to infusion
- Infusion rates:
  - Initial: 50 mg/hr (titrate to max of 400 mg/hr)
  - Subsequent: 100 mg/hr (titrate to max of 400 mg/hr)

Adverse Reactions

- Infusion reactions (decreases with subsequent infusions)
- Risk for bacterial/viral infections, progressive multifocal leukoencephalopathy (PML), and hepatitis B virus reactivation
- Vaccines may be ineffective

Rituximab. Lexicomp, 2023.

Rituximab Literature

	Trial	Intervention	Outcomes
IVIG + rituximab	Vo, et al. 2008. • Exploratory, open-label, phase 1-2, single center study • N=20	Pre-txp: IVIG 2 g/kg (day 0 and 30) + rituximab 1 g (day 7 and 22)	• 80% (16/20) transplanted • Mean PRA 77% before vs. 44% after (P<0.001) • 50% experienced acute rejection (31% were AMR) • 12-month patient and graft survival were 100% and 94%, respectively
IVIG + rituximab	Vo, et al. 2014. • Double-blind, placebo-controlled trial • N=15	Pre-txp: IVIG 2 g/kg (day 1 and 20) + rituximab 1 g or placebo (day 15) Post-txp: IVIG 2 g/kg (within 10 days of txp) + rituximab 1 g or placebo (at 6 months)	• 87% (13/15) transplanted (7 placebo vs. 6 rituximab) • All AMR occurred in placebo group (N=3, P=0.06) • All graft loss occurred in placebo group (N=2) • Rituximab had benefit on renal function at 6- and 12-months post-txp (P=0.046)

IVIG + PLEX + rituximab	Stegall, et al. 2006.
	• Single center, retrospective study
	• N=61
		Protocol 1 (N=13)
		• IVIG 2.1-3 g/kg pre-txp
		Protocol 2 (N=32)
		• PLEX, IVIG 0.1 g/kg, and rituximab 375 mg/m^2 4-7 days pre-txp
		Protocol 3 (N=16)
		• Protocol 2 + thymoglobulin 1.5 mg/kg x 5 doses pre-txp
			• Negative crossmatch achieved in:
			  • 36% (5/13) receiving protocol 1
			  • 84% (27/32) receiving protocol 2
			  • 88% (14/16) receiving protocol 3
			• AMR rates were 80% vs. 37% vs. 29%, respectively (P<0.05)

Vo, et al. *N Engl J Med* 2008; 359:242-251.
Vo, et al. *Transplantation* 2014; 98:312-319.
Stegall, et al. *Am J Transplant* 2006; 6:346–351.

Desensitization Protocols

Transplant Center	Antibody-Removal Technique	Rituximab
Cedars-Sinai	High-dose IVIG	Yes
Johns Hopkins	Low-dose IVIG and plasmapheresis	Yes
Mayo Clinic	Low-dose IVIG and plasmapheresis	No
University of Illinois	Low-dose IVIG and plasmapheresis	No

UofU Desensitization Protocol #1

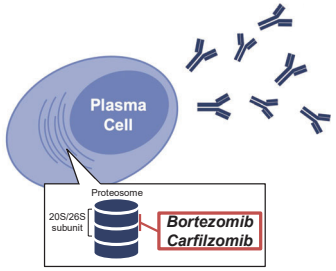
First-line therapy for outpatient candidates

Day 0	IVIG 1 g/kg x 2 days
↓	
Day 7	Rituximab 1 g
↓	
Day 21	Check PRA
↓	
Day 30	IVIG 1 g/kg x 2 days
↓	
Day 44	Check PRA
	↓
	Transplant or if PRA >50%, consider protocol #2

Alternative Agents

Proteosome Inhibitor Mechanism of Action

- Bortezomib:
  - 1st generation, reversible inhibitor of the 26S proteasomal subunit
- Carfilzomib:
  - 2nd generation, irreversible inhibitor of the 20S proteasomal subunit
- Induce apoptosis of plasma cells by disrupting protein processing



Bortezomib. Lexicomp, 2023.
Carfilzomib. Lexicomp, 2023.

Proteosome Inhibitor Dosing and Administration

Dose

- Bortezomib: 1.3-1.5 mg/m²/dose
- Carfilzomib: 20-36 mg/m²/dose
- Dosing regimen is institution specific

Preparation

- Prepare in negative pressure chemotherapy hood
- Bortezomib: reconstitute with normal saline (1 mg/mL IV or 2.5 mg/mL SC)
- Carfilzomib: reconstitute with SWFI (2 mg/mL) and add to 50 mL of D5W

Administration

- Bortezomib: rapid IV push or SC
  - Pre-medicate with ondansetron
- Carfilzomib: IV infusion over 10-30 minutes
  - Hydrate with fluids prior to administration and pre-medicate with dexamethasone

Adverse Reactions

Class Effects
Bone marrow suppression
Gastrointestinal side effects

Bortezomib	Carfilzomib
Hepatotoxicity	Infusion reactions
Peripheral neuropathy	Cardiovascular events
	Nephrotoxicity

Bortezomib. Lexicomp, 2023.
Carfilzomib. Lexicomp, 2023.

Bortezomib Literature

Trial	Intervention	Outcomes
Woodle, et al. 2015. • Prospective, multiphase trial • N=44	Pre-txp: bortezomib (1.3 mg/m^2) x 6-8 doses w/ or w/o PLEX + rituximab (375 mg/m^2) x 1 dose (max 500 mg)	• 43.2% (19/44) transplanted • 13.5% (6/44) had ≥50% PRA reduction • Rebound DSA at ≥90 days was observed depending upon the protocol used • ACR and AMR rates were 18.8% and 12.5% at 6 months
Patel, et al. 2011. • Single center, pilot study • N=7 • PRA ≥50% despite IVIG and rituximab	Pre-txp: bortezomib (1.3 mg/m^2) on days 1, 4, 7, and 10 with 2 PLEX sessions before each dose	• 85.7% (6/7) transplanted • Mean PRA reduced from 62% to 35% (P=0.01) • ADR: anemia (N=1), leukopenia (N=3), neuropathy (N=1), sepsis related death (N=2)

Woodle, et al. *Am J Transplant* 2015; 15:101-118.
Patel, et al. *J Heart Lung Transplant* 2011; 30:1320-1326.

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Carfilzomib Literature

Trial	Intervention	Outcomes
Tremblay, et al. 2019. • Prospective, non-randomized trial • N=16	Group A (N=6) • 12 doses of carfilzomib (escalating from 20-36 mg/m^2), followed by 3 PLEX sessions pre-txp Group B (N=10) • Group A + additional weekly PLEX sessions prior to carfilzomib	• Significant reduction in HLA antibodies (69.8% for group A, P=0.031; 80.1% for group B, P=0.938) • Rebound antibodies occurred between 81 and 141 days • ADR: nausea (N=8), anemia (N=3), fatigue (N=3), headache (N=3), paresthesias (N=3), thrombocytopenia (N=3), vomiting (N=3)
Sriwattanakomen, et al. 2021. • Retrospective, single center study • N=9	Pre-txp: PLEX + carfilzomib (20 mg/m^2) on days 1, 2, 8, 9, 15, and 16, followed by IVIG 2 g/kg after carfilzomib on day 16 Total of 20 cycles administered across 9 candidates	• 66.7% (6/9) transplanted • Mean PRA reduced from 76% to 40% (P=0.001) • Rebound PRA of 22% • 1 patient treated for AMR • ADR: AKI (N=6), thrombocytopenia (N=3)

Tremblay, et al. *Am J Transplant* 2020; 20(2):411-421.
Sriwattanakomen, et al. *J Heart Lung Transplant* 2021; 40(7):595-603.

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UofU Desensitization Protocol #2

Day 0	PLEX
Day 1	PLEX + Bortezomib 1.3 mg/m^2
↓	
Day 3	PLEX
Day 4	PLEX + Bortezomib 1.3 mg/m^2
↓	
Day 7	PLEX
Day 8	PLEX + Bortezomib 1.3 mg/m^2
↓	
Day 10	PLEX
Day 11	PLEX + Bortezomib 1.3 mg/m^2
↓	
Day 25	Check PRA

First-line therapy for inpatient candidates or those w/ PRA >50% after protocol #1

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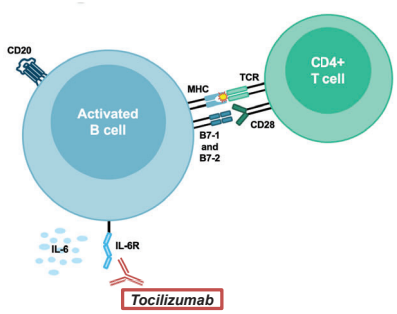
Refractory Agents

Tocilizumab Mechanism of Action

- Humanized monoclonal antibody which antagonizes the interleukin-6 (IL-6) receptor
- Endogenous IL-6 mediates a variety of immune responses:
  - Activation and proliferation of T cells
  - Differentiation of B cells
  - Antibody production



Tocilizumab. Lexicomp, 2023.

Tocilizumab Dosing and Administration

Dose
- 8 mg/kg/dose IV monthly
- Dosing regimen is institution specific

Preparation
- Dilute solution in normal saline or half-normal saline
- Final volume is 100 mL in patients >30 kg

Administration
- Obtain QuantiFERON-TB Gold prior to administration
- IV infusion over ≥60 minutes
- Pre-medicate with acetaminophen, diphenhydramine, and steroids

Adverse Reactions
- Infusion reactions
- Neutropenia and thrombocytopenia
- Hepatotoxicity

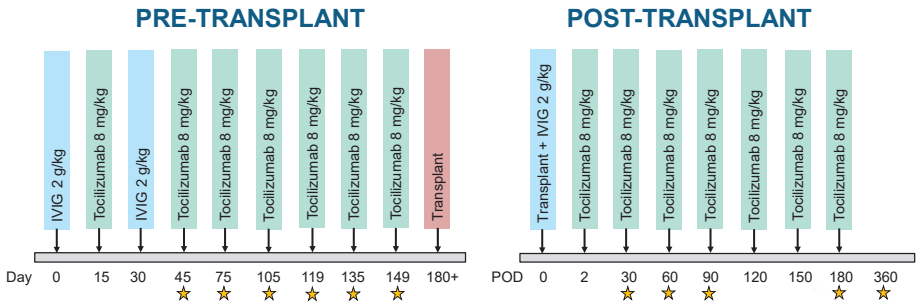
Tocilizumab. Lexicomp, 2023.

Tocilizumab Literature

Trial	Intervention	Outcomes
Vo, et al. 2015. • Phase I/II, single center, open label, pilot, exploratory study • N=10 • Patients non-responsive to IVIG + rituximab	Pre-txp: IVIG 2 g/kg (day 1 and 30) + tocilizumab 8 mg/kg on day 15, then monthly x 6 months Post-txp: IVIG 2 g/kg on POD 0 + tocilizumab 8 mg/kg on POD 2, then monthly x 6 months	• 50% (5/10) transplanted • Mean DSA significantly reduced (P=0.03) • Time to transplant was 8.1 months vs. 25 months prior to tocilizumab • No rejection at 6 months, 1 episode of mild AMR at 12 months • SAE: pneumonia (N=1), Bell's Palsy (N=1), infective colitis (N=1)

Vo, et al. *Transplantation* 2015; 99(11):2356-2363.

Example Tocilizumab Protocol

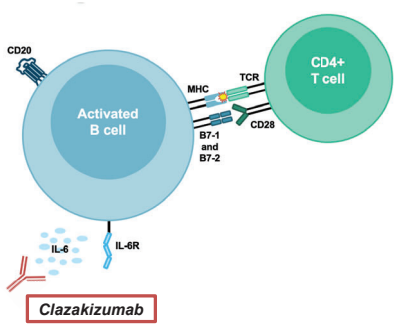


★: Protocol DSA

Vo, et al. *Transplantation* 2015; 99(11):2356-2363.

Clazakizumab Mechanism of Action

- Investigational drug
- Humanized monoclonal antibody targeted against IL-6
- Blocks activation and proliferation of T cells, differentiation of B cells, and antibody production

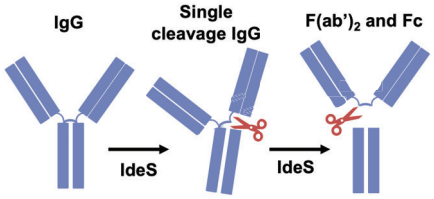


Clazakizumab Literature

Trial	Intervention	Outcomes
Vo, et al. 2022. • Phase II, open label, single-arm exploratory study • N=20	Pre-txp: • 5 PLEX sessions (day -15 to 0) • IVIG 2 g/kg x 1 (day 0) • Clazakizumab 25 mg SC monthly x 6 doses starting day 7 Post-txp: • IVIG 1 g/kg (POD 0 and 1) • Clazakizumab 25 mg SC monthly x 6 doses starting POD 5	• 90% (18/20) transplanted • Significant reduction in class I (P=0.001) and class II (P=0.006) antibodies • Patient and graft survival at 12 months were 100% and 94%, respectively • 4 patients experienced rejection: chronic active T cell mediated rejection (N=1), chronic active AMR (N=2), mixed rejection (N=1) • Most common ADR was thrombocytopenia (N=8)

Imlifidase (IdeS) Mechanism of Action

- Investigational agent
- Imlifidase = **I**gG-**d**egrading **e**nzyme derived from ***S****treptococcus pyogenes* (IdeS)
- Recombinant cysteine protease derived from *S. pyogenes* that cleaves IgG in 2 steps:
  1) Single cleavage of IgG (1 heavy chain remains intact)
  2) Full cleavage of IgG (results in a $F(ab')_2$ fragment and Fc fragment)
- Fc region unable to interact with Fc receptors, preventing antibody response



Imlifidase (IdeS) Literature

Trial	Intervention	Outcomes

Jordan, et al. 2017.
• 2 separate open-label, single-group, phase I/II trials
• N=25
	• United States (N=14):
	  • IdeS 0.24 mg/kg IV 4-6 hours pre-txp
	  • IVIG 2 g/kg (POD 7-14)
	  • Rituximab 375 mg/m^2 (POD 14-21)
	• Sweden (N=11):
	  • IdeS 0.25 or 0.5 mg/kg IV 4-6 hours pre-txp
		• 96% (24/25) transplanted
		  • 1 episode hyperacute rejection (non-HLA antibodies)
		• Near complete or complete reduction of HLA antibodies at 6 and 24 hours after treatment
		• AMR occurred in 10 patients (7 United States, 3 Swedish)
		• SAE: bacteremia (N=1), abdominal infection (N=1), catheter infection (N=1), parvovirus (N=1), myalgia (N=1)

Jordan, et al. 2021. • Open-label, single-arm, phase 2 (Highdes) trial • N=19	• IdeS 0.25 mg/kg IV on POD 0 (additional dose within 2 days if negative crossmatch not achieved) • IVIG 2 g/kg on POD 7 • Rituximab 1 g on POD 9	• 94.7% (18/19) transplanted • 2 patients with primary graft dysfunction • 89.5% (17/19) achieved negative crossmatch within 24 hours • Antibody rebound occurred in all but 2 patients • AMR occurred in 7 patients (38.9% with onset between POD 2 and 19) • ADR: infusion related reactions (N=2) and UTI (N=1)

Additional Considerations

Additional Considerations

- Currently, no drug therapies are FDA approved for desensitization
- Desensitization agents often require prior authorizations due to high drug costs
- Desensitization requires extensive coordination amongst the transplant multidisciplinary team

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Don't Blame Me… for the Cost

Drug	Average Wholesale Price (AWP)	Cost per Cycle (70 kg patient)
IVIG (Gammagard)	$19.37 per mL	$54,236
Rituximab (Rituxan)	$112.74 per mL	$11,274
Bortezomib (Velcade)	$1923.58 per 3.5 mg	$5,144
Carfilzomib (Kyprolis)	$595.84 per 10 mg	$12,870
Tocilizumab (Actemra)	$151.76 per mL	$30,048

Lexicomp, 2023.

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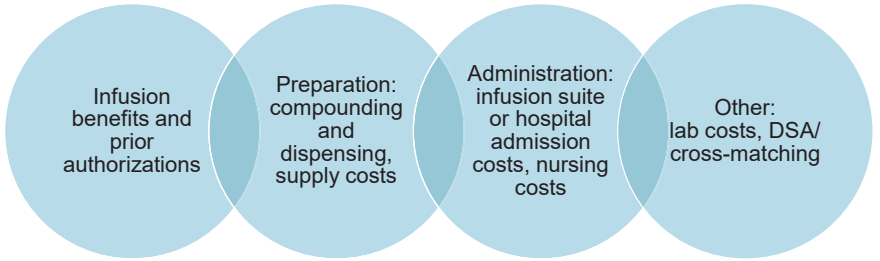
Additional Cost Considerations



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Summary of Desensitization

Pros	Cons
• Reduce/remove antibodies • Expansion of donor pool • Less AMR and death compared to historical controls	• Antibody rebound • Cost • Infection (prolonged immunosuppression) • Variable effectiveness • Unpredictable timing

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Putting it Together

USHP

Patient Refresher

- CV is a 33-year-old female
- Listed for dual heart-liver transplant in 9/2022 secondary to hypoplastic left heart syndrome and cirrhosis
- 100% PRA at the time of listing

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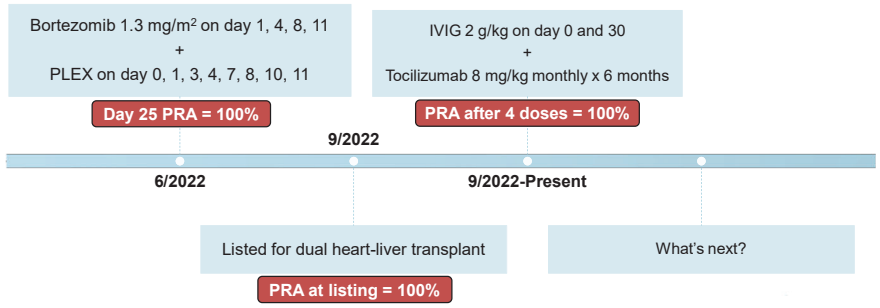
Patient Case



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Key Takeaways

- Development of anti-HLA antibodies results from exposure to foreign HLA
- Desensitization therapies target various steps affecting antibody production with the goal to reduce and remove pre-formed antibodies
- Protocols are transplant center-specific, and there are no prospective trials comparing various agents
- IVIG ± PLEX ± rituximab remain first-line therapies for stable patients on the waitlist
- Proteosome inhibitors, tocilizumab, and investigational agents are reserved for high-risk patients and those refractory to first-line therapies

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