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Clinical Meeting & Exhibition

Updates in Transplantation 2016

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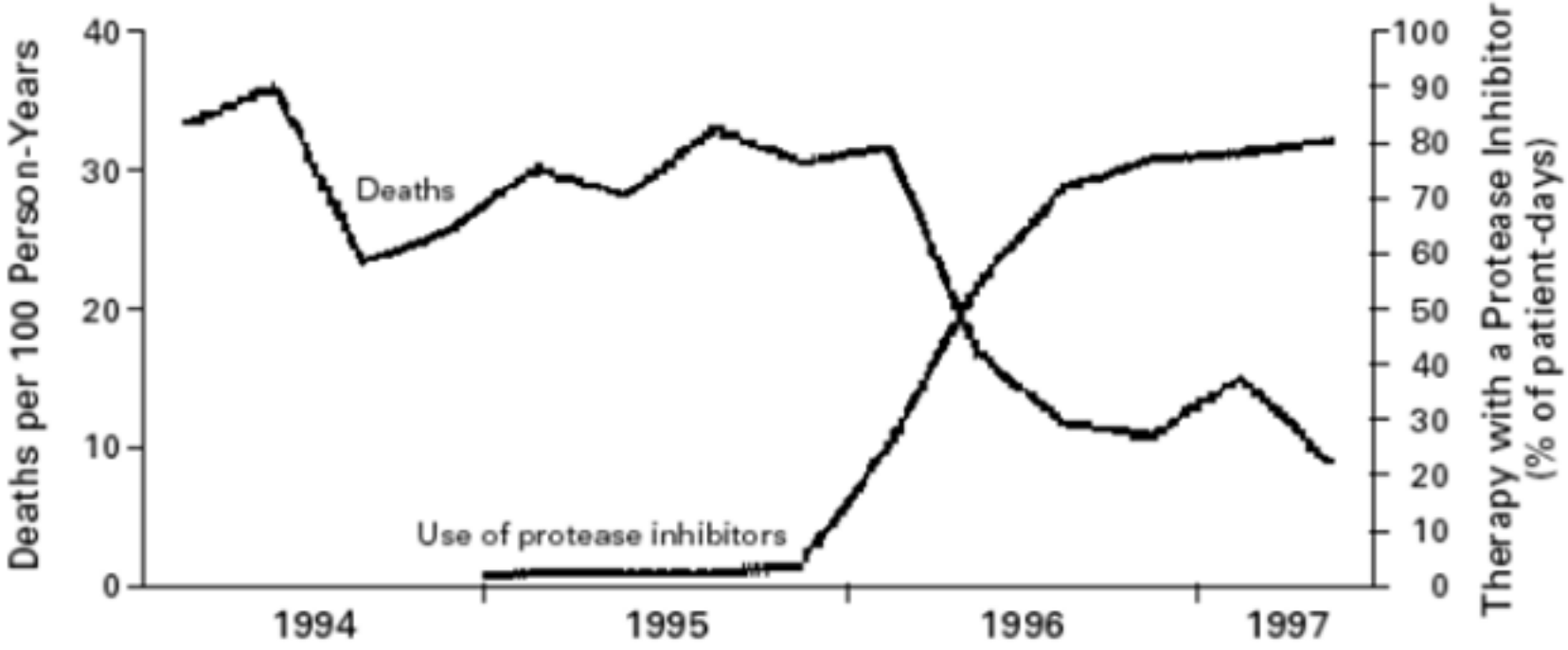
Disclosure

- The program chair and presenters for this continuing education activity have reported no relevant financial relationships.

Objectives

- Summarize the major updates in transplantation in the past year, including the rising prevalence of transplantation in HIV+ recipients
- Assess the advantages and limitations of HIV pharmacotherapy in the pre-, peri-, and post-transplant settings
- Evaluate immunosuppression and opportunistic infection prophylaxis regimens specific to the HIV+ transplant recipient
- Create an effective post-transplant immunosuppressive regimen for an HIV+ transplant recipient

Introduction of HAART in 1996



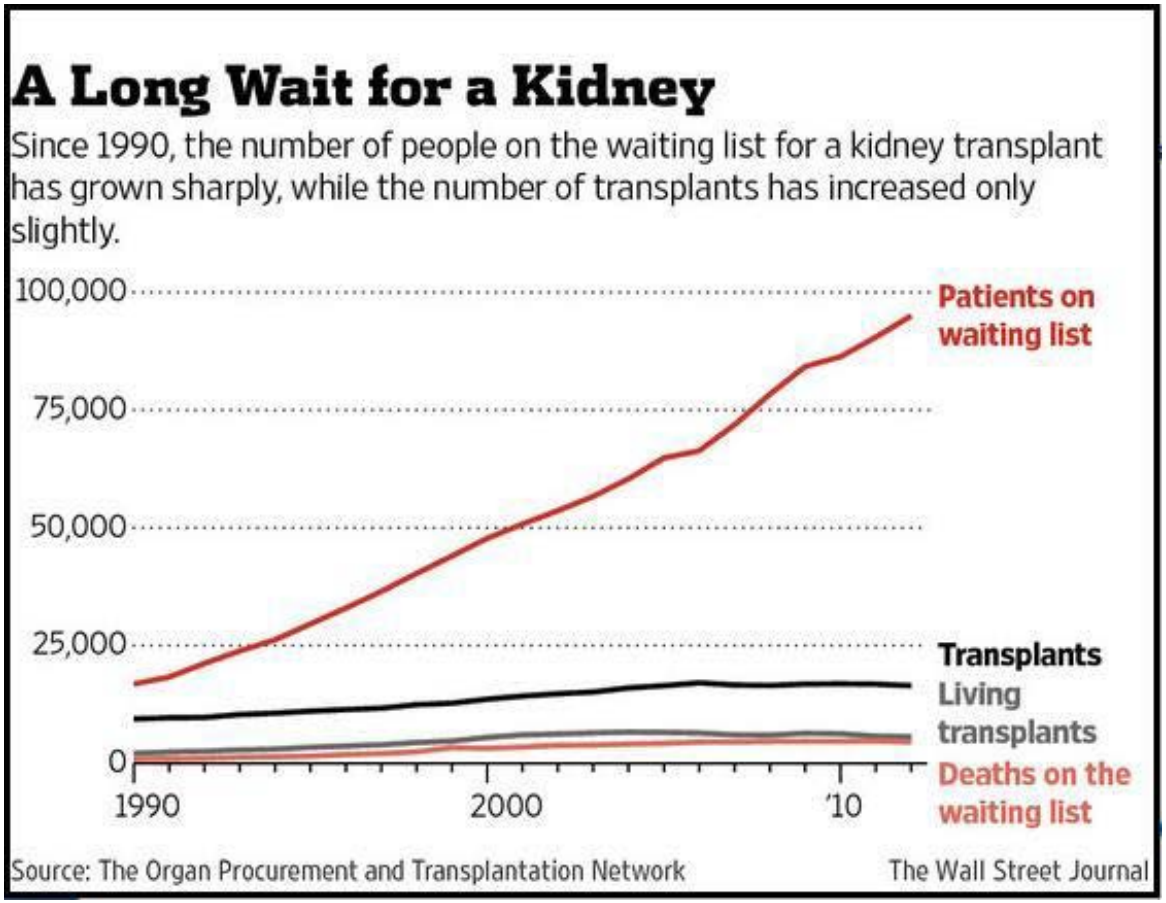
Palella et al. N Engl J Med. 1998.

Development of ESRD & ESLD in HIV Patients

- Increased life expectancy of patients with HIV
- Development of long-term complications
  - Risk of end stage renal disease (ESRD)
    - HIV associated nephropathy
    - ART related kidney damage
  - Risk of end stage liver disease (ESLD)
    - Co-infection with HCV or HBV

Roland et al. Transplantation. 2003.

Organ Supply & Demand



Becker et al. Wall Street Journal. 2014.

HIV Organ Policy Equity (HOPE) Act

- Will allow for research into transplanting organs from HIV-positive donors into HIV-positive recipients
- Enacted on November 21, 2013
- In 2016, first HIV-to-HIV kidney and liver transplant in US was performed

Image courtesy of www.livingbank.com

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Updates in Transplantation 2016

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Objectives

- Assess advantages and limitations of HIV pharmacotherapy in the pre-, peri-, and post-transplant setting

Who Should Get Antiretroviral Therapy?

- DHHS Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents recommend initiating antiretroviral therapy (ART) in **ALL** HIV-infected patients, regardless of CD4 cell count (AI)

- Initiation at any CD4 cell count may delay or prevent HIV-associated morbidity (e.g., HIV-associated nephropathy (HIVAN), liver disease, cardiovascular disease, neurologic complications and malignancies), mortality and transmission

Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/ContentFiles/Adultand AdolescentGL.pdf. Updated: 7/14/16.; NEJM. 2015;373:795-807;NEJM. 2015:373:808=22.

What to Start

- Three drugs from at least 2 classes (i.e., two mechanisms of action)
  - NRTI – nucleos(t)ide reverse transcriptase inhibitor
  - NNRTI – non-nucleoside reverse transcriptase inhibitor
  - PI – protease inhibitor
  - INSTI – integrase strand transfer inhibitor
  - EI – entry inhibitor
- Usually 2 from the NRTI class and a 3rd agent from NNRTI, PI, INSTI or EI class

What to Start

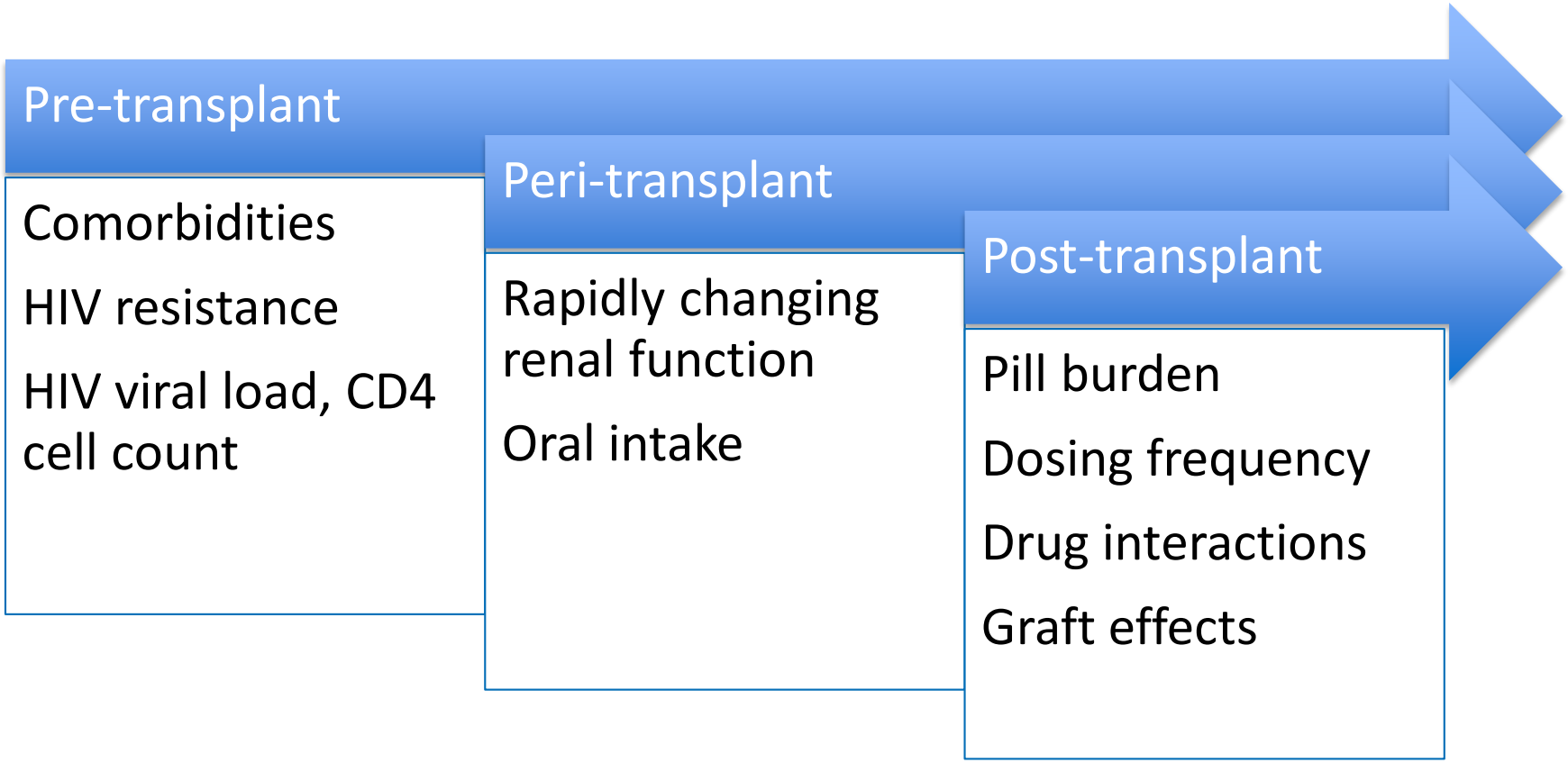
NRTI	NNRTI	PI	INSTI	EI
Abacavir Didanosine Emtricitabine Lamivudine Stavudine Tenofovir Zidovudine	Efavirenz Etravirine Nevirapine Rilpivirine	Atazanavir Darunavir Fosamprenavir Indinavir Lopinavir Nelfinavir Saquinavir Tipranavir	Dolutegravir Elvitegravir Raltegravir	Enfuviritide Maraviroc

DHHS Recommended Regimens

- INSTI-based Regimen
  - Dolutegravir/Abacavir/Lamivudine
  - Dolutegravir PLUS Tenofovir/Emtricitabine
  - Elvitegravir/cobicistat/Tenofovir/Emtricitabine
  - Raltegravir PLUS Tenofovir/Emtricitabine
- PI-based Regimen
  - Darunavir PLUS ritonavir PLUS Tenofovir/Emtricitabine

Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf.
Updated: 7/14/2016

Considerations When Selecting ART for Transplant Patients



Comorbidity Considerations

- Cardiovascular disease
  - Abacavir associated increased risk of myocardial infarction
  - PI-based therapy associated with dyslipidemia
- Co-infection with hepatitis B
  - Lamivudine and tenofovir can be used to treat HIV and HBV co-infected patients
- Co-infection with hepatitis C
  - Drug interactions
- Chronic kidney disease
  - Avoid tenofovir disoproxil fumarate (CrCl <70 mL/min)
  - Avoid tenofovir alafenamide (CrCl <30 mL/min)
- Severe liver disease
  - Avoid abacavir
  - Use PI with caution (dose adjustments, some contraindicated)

Immediate Peri-transplant Considerations

- Kidney transplant
  - NRTIs (except abacavir) require renal dose adjustment and dose should be modified during peri-transplant period as renal function improves
  - Avoid single tablet regimens and NRTI fixed-dose combination products until renal function improves/stabilizes
- Liver transplant
  - Avoid ART that requires high calorie intake (e.g., rilpivirine) or acid environment for absorption (e.g., atazanavir, rilpivirine)

Pill Burden

- Pill burden
  - Single-tablet regimens preferred
  - Associated with increased adherence (OR 1.98, p <0.001), virologic suppression (OR 1.21, p <0.001) and reduced hospitalizations (HR 0.69, p <0.001) as compared to multiple-tablet regimens (based on prescription data)

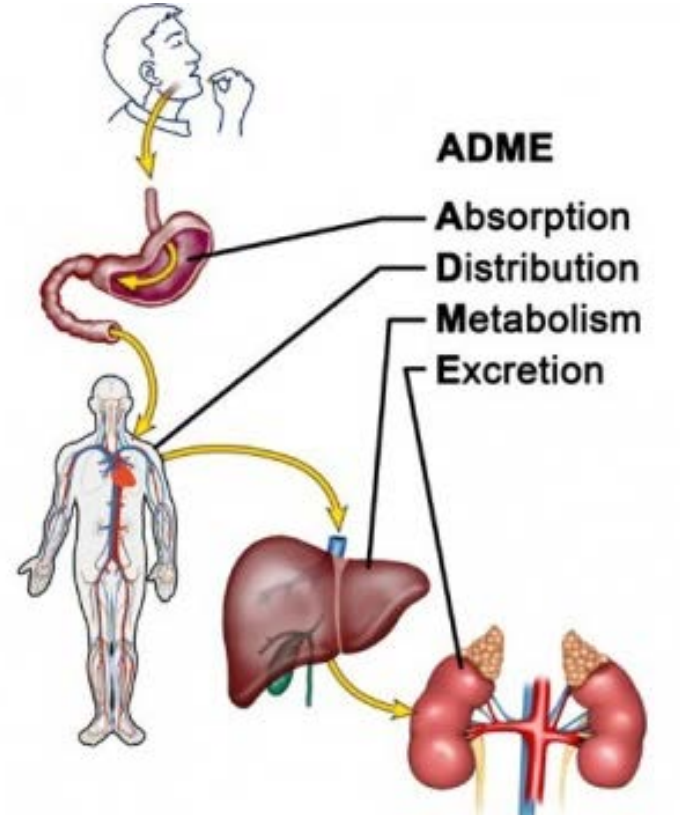
- Dosing frequency
  - Once-daily dosing preferred
  - Associated with increased adherence compared with twice-daily dosing in randomized controlled trials

Nachega JB. Clin Infect Dis. 2014. 58:1297-1307.; Sutton SS. Pharmacotherapy. 2016; 36:385-401.; Sutton SS. Am J Manag Care. 2016;22:242-8.

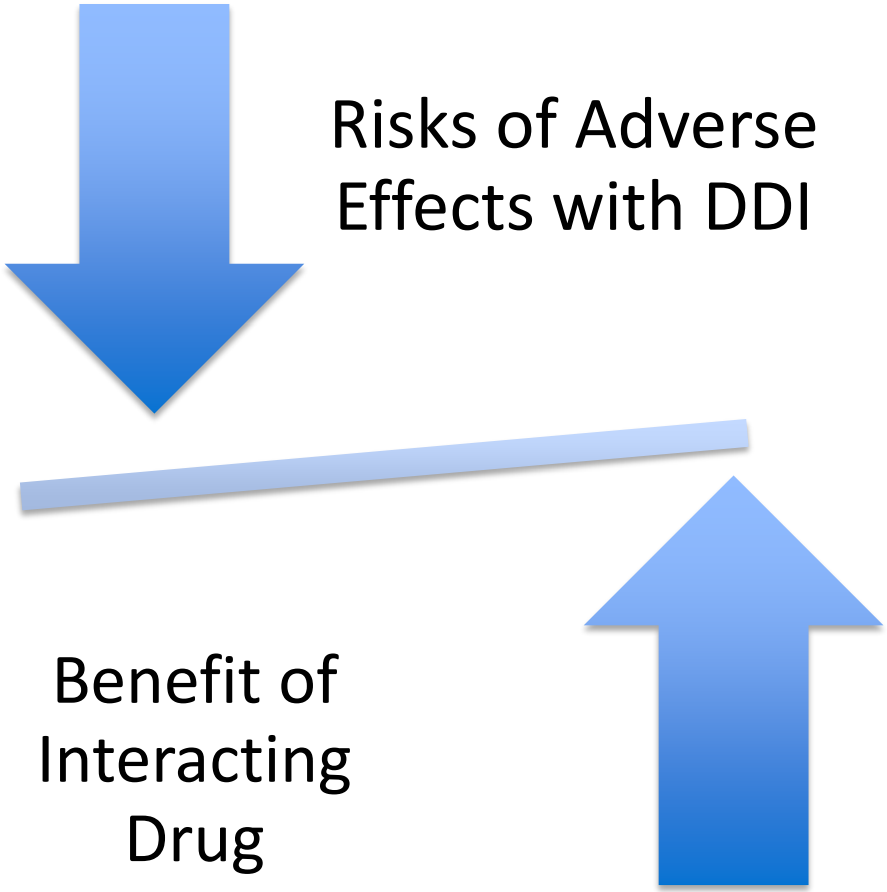
Combination Products	
NRTI Combinations	
Combivir®	Lamivudine/zidovudine
Descovy®	Emtricitabine/tenofovir alafenamide
Epzicom®	Abacavir/lamivudine
Trizivir®	Abacavir/lamivudine/zidovudine
Truvada®	Emtricitabine/tenofovir disoproxil fumarate
PI/Booster Combinations	
Evotaz®	Atazanavir/cobicistat
Kaletra®	Lopinavir/ritonavir
Prezcobix®	Darunavir/cobicistat
Single Tablet Regimens	
Atripla®	Efavirenz/emtricitabine/tenofovir disoproxil fumarate
Complera®	Rilpivirine/emtricitabine/tenofovir disoproxil fumarate
Genvoya®	Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide
Odefsey®	Rilpivirine/emtricitabine/tenofovir alafenamide
Stribild®	Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate
Triumeq®	Dolutegravir/abacavir/lamivudine

Drug Interactions with ART

- **Absorption**
  - E.g. chelation, gastric acid, P-gp
- Distribution
  - E.g. competition for protein binding
- **Metabolism**
  - E.g. CYP450 enzymes
- Elimination
  - E.g. inhibition of renal clearance



Managing Drug Interactions



1. Review available pharmacokinetic and clinical data
2. Assess clinical significance
3. Identify potential alternatives
4. If no alternatives, consider monitoring parameters

Overview Drug Interaction Concerns

- Calcineurin inhibitors (CNI) and mTOR inhibitors with PI, ritonavir, cobicistat and NNRTI
- INSTI with oral electrolyte repletion
- Acid suppression with atazanavir and rilpivirine

CNI and ART

- Cyclosporine and tacrolimus are major substrates of CYP3A4 and P-gp
- Interactions with PI, ritonavir, or cobicistat (inhibitors of CYP3A4) can result in increased exposure of CNI and increased toxicity
- Interactions with NNRTIs (inducers of CYP3A4) may result in decreased exposure of CNI and loss of efficacy
  - Note: rilpivirine is not an inducer of 3A4

Management of CNI with ART

- Tacrolimus
  - Ritonavir-boosted therapy can result in a 5- to 10-fold increase in AUC and >10-fold increase in half-life
  - Cobicistat is expected to have the same effect a ritonavir
  - Variability amongst PI and interpatient variability exists
  - Consider initial dose of 0.5-1 mg once weekly with close monitoring and adjustments based on tacrolimus levels
- Cyclosporine
  - PI, ritonavir, cobicistat can result in 5-fold increase in trough concentrations and prolong elimination half-life by 2-fold
  - Consider reducing initial daily dose by 80% with close monitoring of cyclosporine A levels

Frassetto L. Biopharm Drug Dispos. 2013;34:442-51.; Mertz D. Am J Kidney Dis. 2009;54:e1-4.; Schonder KS. Ann Pharmacother. 2003;37:1793-6.; Vogel M. Liver Transplantation. 2004;10:939-44.

Management of CNI with NNRTI Therapy

- Efavirenz, etravirine and nevirapine are moderate inducers of 3A4 and may result in significant reductions of CNI concentrations
- Interaction not well studied – if co-administration required close monitoring of trough concentrations should guide dose adjustments
  - Muller *et al*. reported a median tacrolimus dose was 8.5 mg Q12H in patients on efavirenz or nevirapine
  - Frassetto *et al.* reported similar doses of cyclosporine with efavirenz and nevirapine as non-HIV-infected patients
- Full induction (or de-induction) of CYP3A4 enzymes may take up to 2-4 weeks when starting (or stopping) NNRTI therapy

Frassetto L. Biopharm Drug Dispos. 2013;34:442-51.; Mertz D. Am J Kidney Dis. 2009;54:e1-4.; Muller E. NEJM. 2015;372:613-620; Frassetto L. Transplantation. 2005;80:13-7.

m-TOR Inhibitors with ART

- Sirolimus and everolimus are major substrates of CYP3A4 and P-gp
- Interactions with PI, ritonavir and cobicistat may lead to significant increases in AUC
  - Jain *et al.* reported 60% increase in AUC and 9-fold increase in trough levels with nelfinavir co-administration
  - Barau *et al.* reported once weekly sirolimus dosing (1.5 mg) to maintain sirolimus troughs of 8-10 ng/mL
- Interaction with NNRTI not well studied – if co-administration required close monitoring of trough concentrations should guide dose adjustments
  - Full induction/de-induction of CYP3A4 enzymes may take up to 2-4 weeks when starting or stopping NNRTI therapy

Jain AK. Liver Transplant. 2002;8:838.; Barau C. Fundam Clin Pharmacol. 2009;23:423-5.

INSTI and Oral Electrolyte Replacement

- INSTI form a metal-drug complex with polyvalent cations resulting in impaired oral absorption
  - Al, Mg, Ca-containing antacids (e.g., Maalox, Tums), supplements (MVI, PhosLo) or Fe products
  - Only applies to oral products – IV electrolytes are not an issue
- Degree of interaction and management varies with INSTI

Roberts JL. Pharmacotherapy. 2011;31(10):298e-302e.

Raltegravir and Oral Electrolyte Replacement

- **Avoid** Mg-containing products with twice daily raltegravir
- $CaCO_3$: **Use with CAUTION**
  - Manufacturer states that the interaction did not lead to clinically meaningful changes to raltegravir concentrations
  - Case report of virologic failure with reduced raltegravir serum levels in a patient on $CaCO_3$ and raltegravir

	Simultaneous	2 hr before	2 hr after	6 hr before	6 hr after
RAL + Mg-Al	Cmax: ↓46% AUC: ↓49% Cmin: ↓63%	Cmax: ↓51% AUC: ↓51% Cmin: ↓56%	Cmax: ↓22% AUC: ↓30% Cmin: ↓57%	Cmax: ↓10% AUC: ↓13% Cmin: ↓50%	Cmax: ↓10% AUC: ↓11% Cmin: ↓49%
RAL + $CaCO_3$ (3 g)	Cmax: ↓52% AUC: ↓55% Cmin: ↓32%	-	-	-	-

Roberts JL. Pharmacotherapy. 2011;31(10):298e-302e.
Isentress. [Package Insert]. Merck & Co. Updated 2/2015.

Dolutegravir and Oral Electrolyte Replacement

- **Space** Mg-Al-containing products
- $CaCO_3$: **Use with CAUTION**
  - Give simultaneously with food OR space administration
- Space administration: 2 hr before or 6 hr after dolutegravir

	Simultaneous	2 hr after/Fed*		Simultaneous	2 hr after/Fed
DTG + Mg-Al	Cmax: ↓72% AUC: ↓74% Cmin: ↓74%	Cmax: ↓18% AUC: ↓26% Cmin: ↓30%	**DTG + $FeSO_4$ (324 mg)**	Cmax: ↓57% AUC: ↓54% Cmin: ↓56%	Cmax: no effect AUC: no effect Cmin: no effect
DTG + $CaCO_3$ (1.2 g)	Cmax: ↓37% AUC: ↓39% Cmin: ↓39%	Cmax: no effect AUC: no effect Cmin: no effect	**DTG + MVI**	Cmax: ↓35% AUC: ↓37% Cmin: ↓32%	-

*Mg-Al not studied under fed conditions

Tivicay. [Package Insert]. ViiV Healthcare. Updated 8/2015.

Elvitegravir and Oral Electrolyte Replacement

- Data on the effect of polyvalent cations on elvitegravir concentrations is limited
  - No data on simultaneous administration
  - Spacing by 2 and 4 hours did not affect elvitegravir

- Manufacturer recommends to space antacids (Mg-Al or $CaCO_3$) by 2 hours

Viteka. [Package Insert]. Gilead Sciences, Inc. Updated 9/2014.

Acid Suppression

- Not limited to transplant patients
- Atazanavir and rilpivirine are more soluble and best absorbed at lower gastric pH
- Management
  - Atazanavir: Space administration of all acid-suppressing medications (e.g., PPI, H2RA, antacids)
  - Rilpivirine: **avoid** PPI, space administration of other acid-suppressing medications (e.g., H2RA, antacids)

Optimal ART Regimens

NRTI	NNRTI	PI	INSTI	EI
Abacavir Didanosine Emtricitabine Lamivudine Stavudine Tenofovir Zidovudine	Efavirenz Etravirine Nevirapine Rilpivirine	Atazanavir Darunavir Fosamprenavir Indinavir Lopinavir Nelfinavir Saquinavir Tipranavir	Dolutegravir Elvitegravir Raltegravir	Enfuviritide Maraviroc

Optimal ART Regimens

NRTI	
Abacavir Didanosine **Emtricitabine** **Lamivudine** Stavudine **Tenofovir** Zidovudine	• Lamivudine or emtricitabine preferred • Abacavir if HLA-B5701 negative and low cardiac risk • Tenofovir alafenamide preferred over tenofovir disoproxil fumarate given less renal and bone toxicity • Tenofovir/emtricitabine NRTI backbone preferred in patients co-infected with hepatitis B virus

Optimal ART Regimens

NNRTI	
Efavirenz Etravirine Nevirapine Rilpivirine	• Avoid efavirenz, nevirapine, etravirine given significant and complicated drug interactions with CNI • Avoid rilpivirine in patients that require acid suppression or unable to intake at least 500 calories with each dose

Optimal ART Regimens

PI	
Atazanavir Darunavir Fosamprenavir Indinavir Lopinavir Nelfinavir Saquinavir Tipranavir	• Avoid PI-based therapy given significant and complicated drug interactions with CNI, m-TOR inhibitors

Optimal ART Regimens

INSTI	
Dolutegravir Elvitegravir Raltegravir	• Dolutegravir preferred • Avoid raltegravir in patients that require oral magnesium for repletion • Avoid elvitegravir since requires cobicistat or ritonavir for PK enhancement

Optimal ART Regimens

EI	
Enfuviritide **Maraviroc**	• Maraviroc if R5 trophic virus – potential additive benefit of graft protection

Key Takeaways

- Optimal management strategy is to avoid PI-, EVG-, and NNRTI-based therapy when possible
  - If co-administration is required, closely monitor CNI and m-TOR serum levels initially and when changing ART
- Many other drug interactions with ART to consider outside immunesuppressants
- Dolutegravir with an NRTI-backbone is preferred

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Hospital of the University of Pennsylvania

Rejection is more common in HIV+ kidney transplant recipients than HIV- recipients

A TRUE

B FALSE

KTX Key Trial

Methods	Prospective, multi-center KTX performed 2003 – 2009 (n=150)		
Findings	Patient survival 1 year 94.6±2% 3 years 88.2±3.8%	Graft survival 90.4% 73.7%	Rejection 31% 41%
	Only half of rejection episodes responded to steroids		

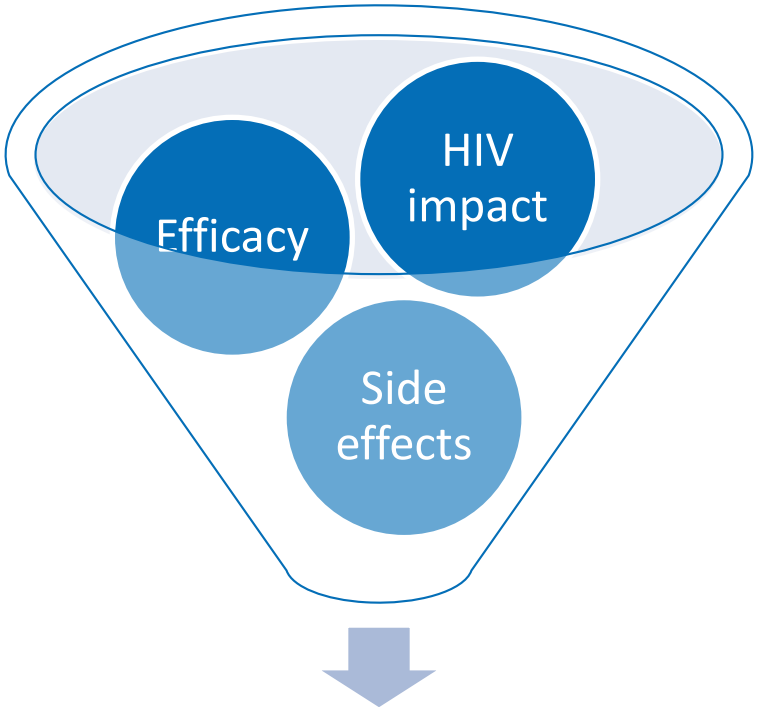
Stock PG et al. NEJM 2010;363:2004-14

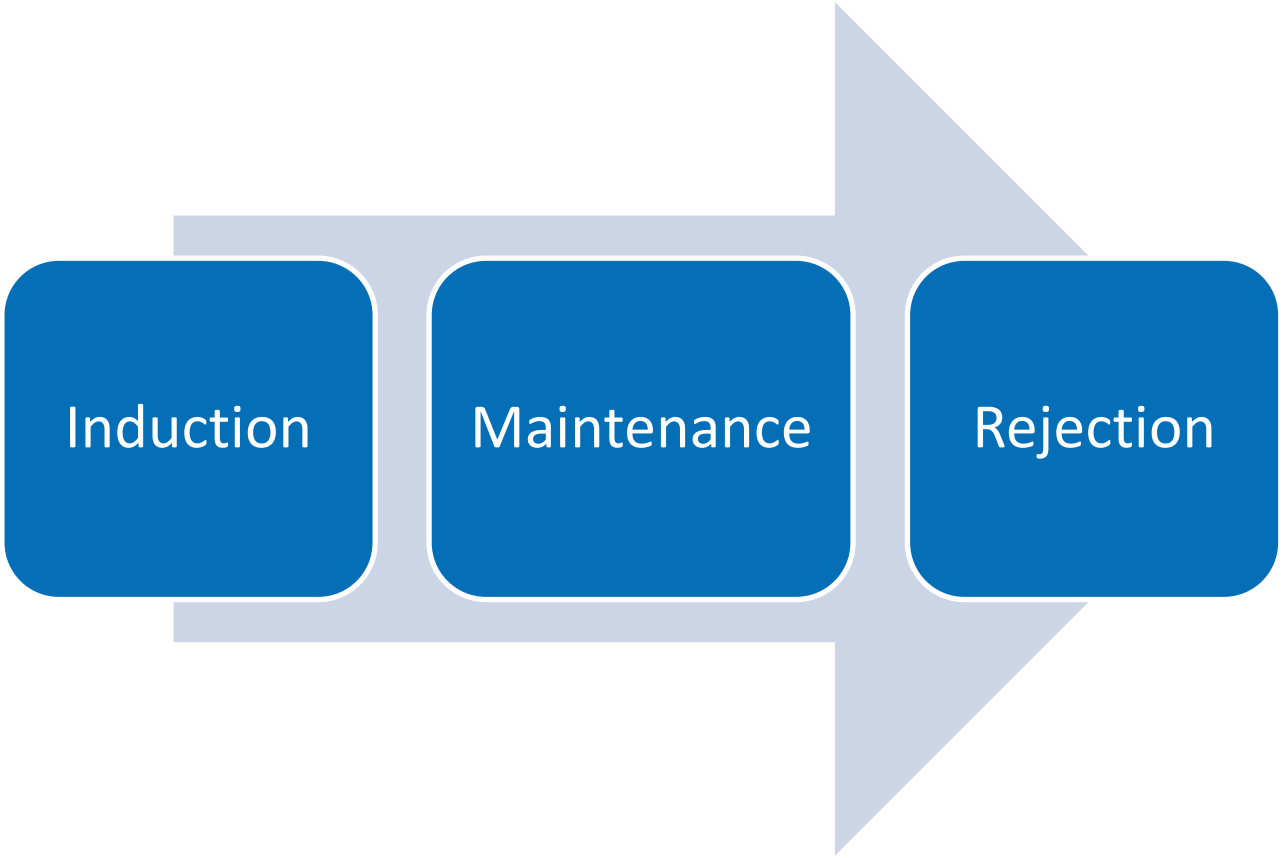
Objectives

- Evaluate immunosuppression and opportunistic infection prophylaxis regimens specific to the HIV+ transplant recipient

- Create an effective post-transplant immunosuppressive regimen for an HIV+ transplant recipient

Immunosuppression Considerations




Induction
Maintenance
Rejection

KTX Induction

Methods	Scientific Registry of Transplant Recipients KTX performed 2000 – 2014 (n=830)
Findings	Induction reduced hospital stay and lowered rates of delayed graft function as well as graft loss
	Anti-thymocyte globulin associated with lowered rates of acute rejection (wRR 0.59, 95% CI 0.35-0.99) compared to other strategies
	Induction did not increase infection rate

Kurcirka LM et al. Am J Trans 2016;16:2368-76

KTX Anti-Thymocyte Globulin Induction

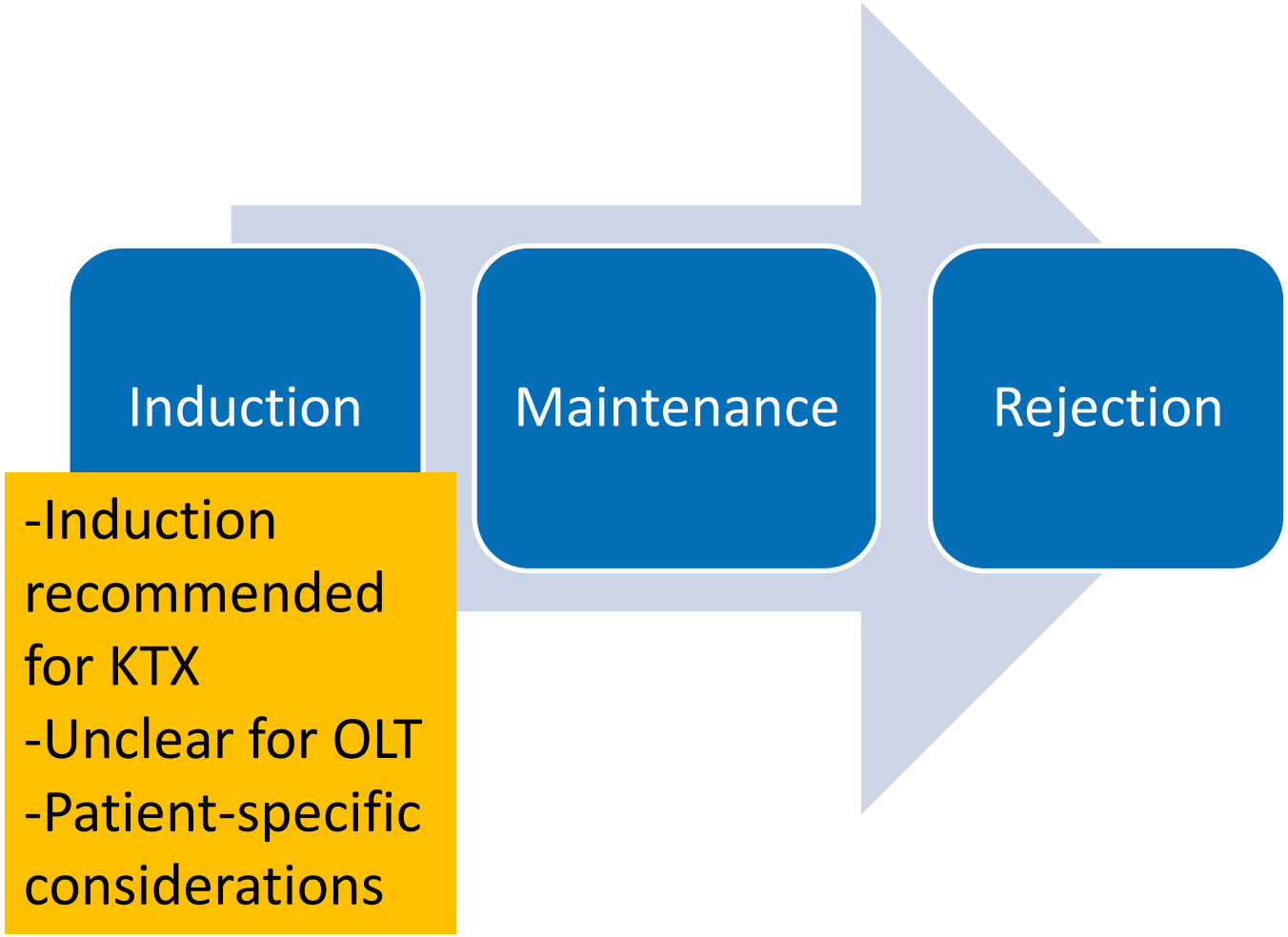
Methods	Single center KTX performed 2006 – 2013 and received anti-thymocyte globulin (n=38)
	Baseline CD4+ count > 350 versus < 350 cells/mm^3
Findings	Median follow-up 2.6 years
	Increased rate of severe CD4+ lymphopenia & higher serious infection rate in patients with pre-transplant CD4+ count < 350 cells/mm^3

Suarez JF et al. Am J Trans 2016;16:2463-72

KTX Basiliximab Induction

Methods	Multi-center KTX performed 2005 – 2009 (n=27)	
	Basiliximab Cyclosporine or tacrolimus Mycophenolate mofetil Methylprednisolone/prednisone taper	
Findings	Patient survival 1 year 100% 2 years 98%	Graft survival 1 year 98% 2 years 96%
	15% had acute cellular rejection	

Touzot M et al. Am J Trans 2010;10:2263-9


Induction
Maintenance
Rejection
-Induction recommended for KTX
-Unclear for OLT
-Patient-specific considerations

Calcineurin Inhibitors

- Cyclosporine has theoretical anti-HIV and anti-HCV activity
- Tacrolimus preferred over cyclosporine due to lower rejection rates
- C_0 correlates well with AUC for tacrolimus but not for cyclosporine

Blumberg EA, Rogers CC. Am J Trans 2013;13(S4):169-78
Stock PG et al. N Engl J Med 2010;363:2004-14
Frassetto LA et al. Transplantation 2014;97:702-7

KTX Calcineurin Inhibitors

Methods	National observational study (UK) KTX performed 2005 – 2013 without primary graft failure (n=78)
Findings	Acute rejection rate at 1 year (p=0.003): Cyclosporine 58% Tacrolimus 21%

Gathogo E et al. Transplantation 2016;100(4):871-8

Antiproliferatives

- Mycophenolate products may suppress HIV replication particularly in a NRTI regimen
- Mycophenolate products are more potent and preferred over azathioprine

Margolis DM et al. J Acquir Immune Defic Syndr 2002;31:45-9

Belatacept

- Belatacept potential advantages
  - Fewer drug-drug interactions
  - Side effect profile

KTX De Novo Belatacept

- Case report of de novo belatacept, mycophenolate mofetil and prednisone with basiliximab induction
- No rejection or graft loss withIN 18 months of follow-up

Cohen EA et al. Am J Trans 2016;16:2753-7

KTX Belatacept Conversion

- Case report
- Initial immunos were basiliximab, mycophenolate, tacrolimus and prednisone taper
- Conversation from tacrolimus at week 14 due to delayed graft function
- Dialysis was no longer indicated at 21 weeks
- One borderline rejection episode treated with prednisone boluses

Ebcioglu Z et al. Am J Trans 2016;16:3278-81

Sirolimus

- Sirolimus inhibits HIV-1 progression via
  - Reducing CCR5-gene transcription
  - Blocking interleukin-2 intracellular secondary messenger (mTOR)
  - Up-regulating the β-chemokine macrophage inflammatory protein
- Possibly reservoir-modifying activity
- Associated with lower post-transplant HIV DNA levels
- May have anti-HHV8 activity so possible role with Kaposi's sarcoma

Stock PG et al. Am J Trans 2014;14:1136-41
Blumberg EA, Rogers CC. Am J Trans 2013;13:169-78
Di Benedetto FD et al. Transplantation 2010;89(6):733-8

OLT Sirolimus Conversion

Methods	Single-center OLT performed 2003 - 2009 (n=14)
	Initial immunos were tacrolimus (n=2) or cyclosporine (n=12) plus steroids
	Cyclosporine was changed to sirolimus for 6 patients due to renal dysfunction or Kaposi's sarcoma
Findings	Reduced HIV & HCV viral load with sirolimus

Di Benedetto FD et al. Transplantation 2010;89(6):733-8

KTX Early Steroid Withdrawal

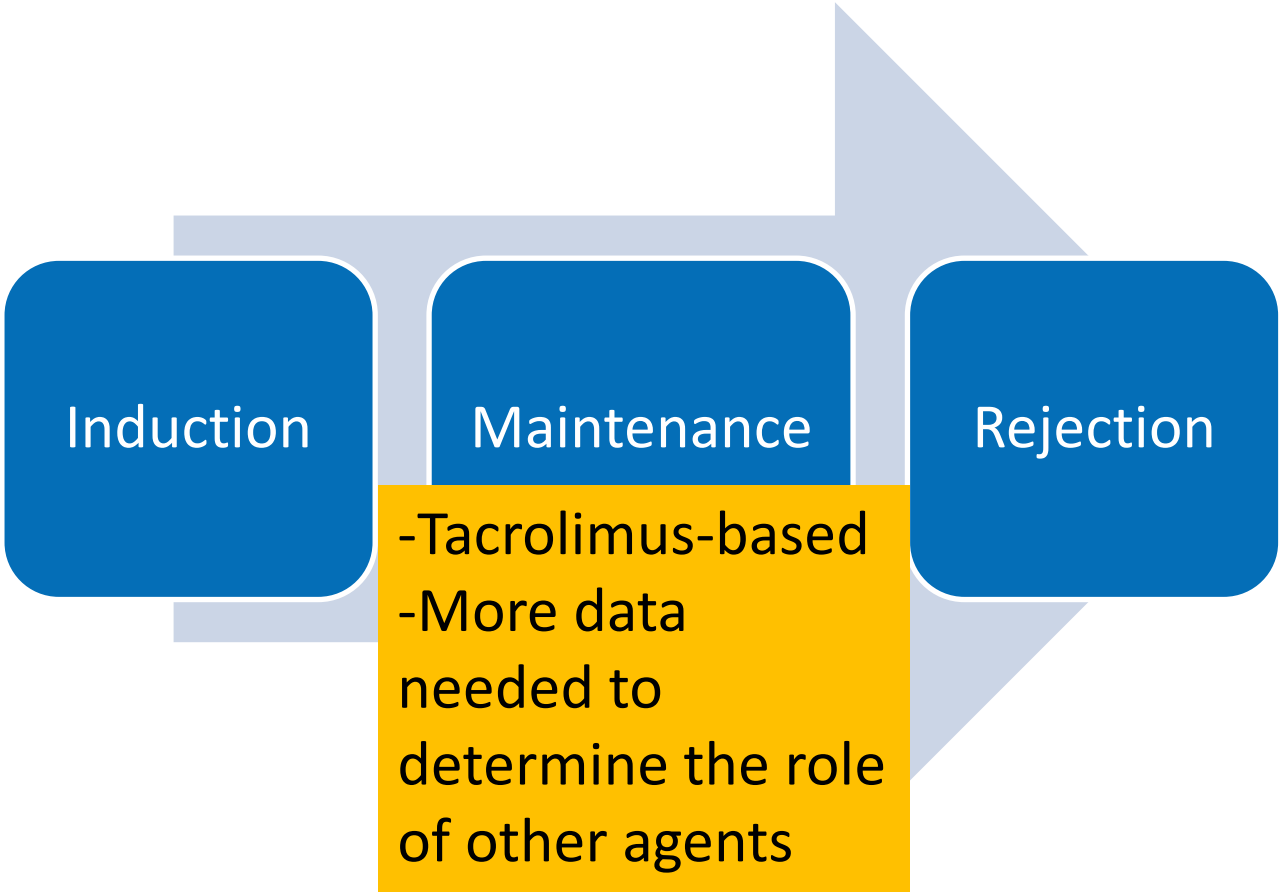
Methods	Single-center KTX performed 2006 – 2010 (n=11)
	9 anti-thymocyte globulin, 2 basiliximab Methylprednisolone days 0-4 Tacrolimus Mycophenolate mofetil
Findings	1 year outcomes: Acute rejection 9% Patient survival 100% Graft survival 91% (primary non-function)

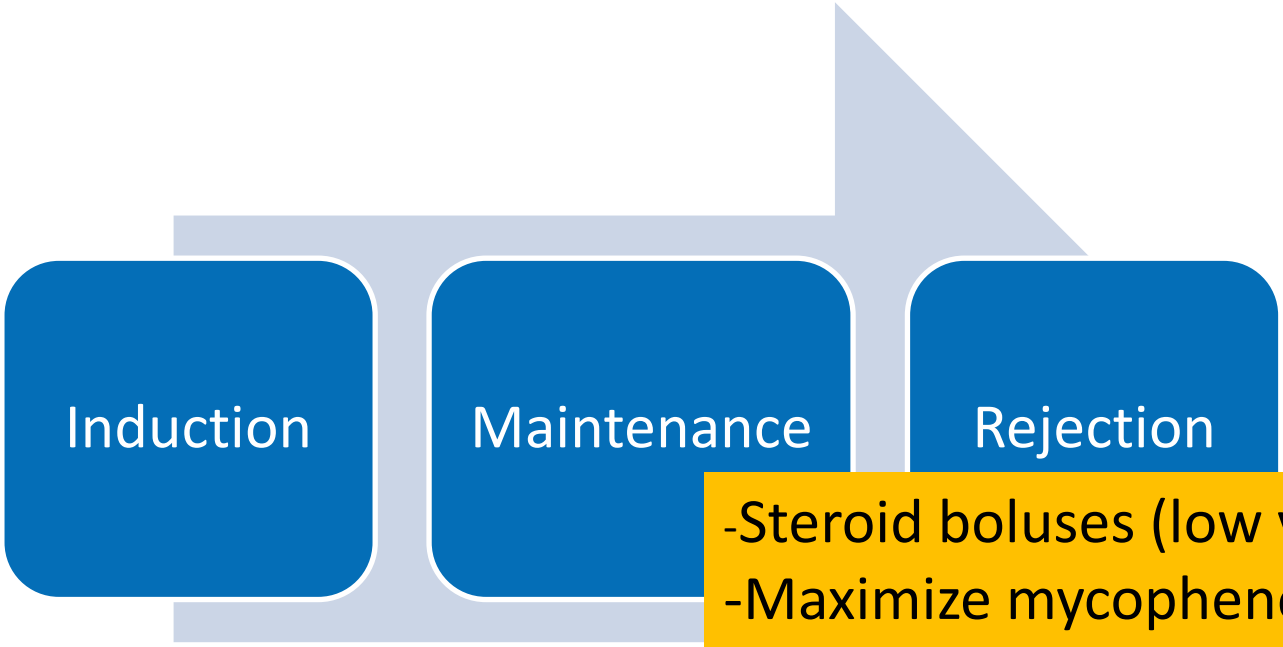
Muthukumar T et al. Transplantation 2013;95(5):711-20

KTX Early Steroid Withdrawal

Methods	Single-center KTX performed 2007 – 2012 (n=13)
	Basiliximab, methylprednisone taper x 5 days, calcineurin inhibitor, & mycophenolic acid
Findings	61.5% patients had acute rejection with half resuming steroids
	4 year outcomes: Patient survival 100% Graft survival 89%
	eGFR 58±40 ml/min if patient had acute rejection versus 76±6 ml/min if no rejection

Bossini N et al. Transplant Int 2014;27:1050-9





-Steroid boluses (low vs high)
-Maximize mycophenolate and calcineurin inhibitor
-Sirolimus
-Avoid anti-thymocyte globulin unless refractory

Fox AM, Vagefi PA, Stock PG. J Semin Liver Dis 2012;32:177-85
Carter JT et al. Am J Trans 2006;6:753-60

Opportunistic infections are more common in HIV+ kidney transplant recipients than in HIV- recipients

A TRUE

B FALSE

OI Primary Prophylaxis Recommendations

Infection	Agent of Choice	Criteria & Duration for Primary Prophylaxis
Pneumocystis pneumonia	Sulfamethoxazole/ trimethoprim	Lifelong
Cytomegalovirus	Valganciclovir	CMV IgG+ donor or recipient. Continue x ≥ 3 months

Chin-Hong P et al. Infect Dis Clin North Am 2013;27(2):459-71
Blumberg EA, Rogers CC. Am J Trans 2013;13:169-78
Harbell J et al. Curr HIV/AIDS Rep 2013;10:217-25

OI Primary Prophylaxis Recommendations (cont'd)

Infection	Agent of Choice	Criteria & Duration for Primary Prophylaxis
Toxoplasma gondii	Sulfamethoxazole/ trimethoprim	Toxoplasmosis IgG+ donor or IgG+ recipient with CD4+ count ≤ 200 cells/mm^3
Mycobacterium avium complex	Azithromycin	CD4+ count ≤ 50-75 cells/mm^3. Continue until > 100 cells/mm^3 x 6 months

Chin-Hong P et al. Infect Dis Clin North Am 2013;27(2):459-71
Blumberg EA, Rogers CC. Am J Trans 2013;13:169-78
Harbell J et al. Curr HIV/AIDS Rep 2013;10:217-25

OI Primary Prophylaxis Recommendations (cont'd)

Infection	Agent(s) of Choice	Criteria & Duration for Primary Prophylaxis
Histoplasma capsulatum	Itraconazole	CD4+ count < 150 cells/mm^3 plus occupational or residential risk factors
Coccidioido-mycosis	Fluconazole or itraconazole	IgG or IgM+ if from an endemic area when CD4+ count < 250 cells/mm^3. Lifelong if donor history of coccidioides

Chin-Hong P et al. Infect Dis Clin North Am 2013;27(2):459-71
Blumberg EA, Rogers CC. Am J Trans 2013;13:169-78
Harbell J et al. Curr HIV/AIDS Rep 2013;10:217-25

Key Takeaways

- More experience is needed to determine patient-specific optimal immunosuppression

- Opportunistic infection prophylaxis strategies differ from standard organ transplant protocols so close attention needs to be paid

Patient Case

JR is a 43 yo male with past medical history significant for HIV, hypertension and ESRD secondary to HIV-associated nephropathy on hemodialysis three times a week. He is being considered for a kidney transplant and presents to clinic today for antiretroviral therapy modification in preparation for transplant.

His HIV has been well controlled for the past 3 months on darunavir 800 mg once daily, ritonavir 100 mg once daily, raltegravir 400 mg twice daily and tenofovir disoproxil fumarate 300 mg once weekly. He reports missing 1-2 doses per month. His most recent CD4 436 cells/mm^3 and HIV RNA <20 copies/mL. He has no HIV resistance detected.

Patient Case

Current medications:
Nifedipine XL 90 mg once daily
Atorvastatin 20 mg daily
Aspirin 81 mg daily
Cinacalcet 90 mg daily
Sevelamer 800 mg three times daily with meals
Darunavir 800 mg daily
Ritonavir 100 mg daily
Raltegravir 400 mg twice daily
Tenofovir DF 300 mg once weekly

Labs:
Na: 135 mEq/L
K: 4.7 mEq/L
Cl: 100 mEq/L
Ca: 9.7 mg/dL

Scr: 7.8 mg/dL
BUN: 45 mg/dL

Gluc: 147 mg/dL

AST: 20 U/L
ALT: 18 U/L
Alk phos: 60 U/L
T. bilirubin: 0.5 mg/dL

HLA-B5701: negative

How would you modify his ART today?

- A Discontinue raltegravir and change to dolutegravir 50 mg once daily. Continue tenofovir DF 300 mg once weekly, darunavir 800 mg once daily, ritonavir 100 mg once daily
- B Discontinue all current antiretrovirals and start dolutegravir 50 mg once daily and Descovy® (tenofovir AF/emtricitabine 25/200 mg) once daily
- C Discontinue all current antiretrovirals and start dolutegravir 50 mg once daily, lamivudine 50 mg x 1 dose then 25 mg daily after HD, and abacavir 600 once daily
- D Discontinue all current antiretrovirals and start Triumeq® (dolutegravir/abacavir/lamivudine 50/600/300 mg) once daily

What information about your recommended ART should you relay to his inpatient team for peri-transplant management ?

- A Dolutegravir inhibits metabolism of tacrolimus, empirically reduce tacrolimus dose to 0.5 mg once weekly and monitor levels
- B Lamivudine dose should be adjusted as the patient's renal function improves post-kidney transplant
- C Abacavir dose should be adjusted as the patient's renal function improves post-kidney transplant
- D Can start single-tablet regimen of Triumeq® (dolutegravir/abacavir/lamivudine 50/600/300 mg) once daily on post-op day 1

Patient Case

Current medications:
Nifedipine XL 90 mg once daily
Atorvastatin 20 mg daily
Aspirin 81 mg daily
Cinacalcet 90 mg daily
Sevelamer 800 mg three times daily with meals

- Consider other medications that may need dose adjustments when changing ART
- Consider increasing atorvastatin to 40-80 mg with discontinuation of darunavir/ritonavir

JR has a KTX offer. Current PRA is 80% and CD4+ count is 450 cells/mm^3. What is your recommendation for induction?

A No induction

B Anti-thymocyte globulin

C Basiliximab

What maintenance immunosuppression regimen do you recommend?

- A Tacrolimus, prednisone
- B Tacrolimus, mycophenolate mofetil, prednisone
- C Cyclosporine, mycophenolate mofetil, prednisone
- D None of the above

Acknowledgements

- Emily Blumberg, MD
- Christine Durand, MD
- ASHP Section of Clinical Specialists & Scientists

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