# HBV, HCV, HIV and Kidney Transplantation

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# Objectives

- Review the prevalence of hepatitis B (HBV), hepatitis C (HCV) and human immunodeficiency virus (HIV) in ESRD population
- Transplant evaluation of patients with these viral infections
- Kidney transplantation in patients with HBV, HCV or HIV; immunosuppression, outcomes and new developments

# HBV, HCV, HIV Infections

- Chronic HBV, HCV or HIV infections-were relative contraindications to kidney transplant in the past
- Concerns:
  - Effects of immunosuppressive drugs on viral replication-acceleration of liver injury and progression to hepatocellular failure/death
  - Development of *de novo* glomerulonephritis in the graft
  - Serious opportunistic infections/malignancy

# Hepatitis B (HBV)

- The prevalence of chronic HBV infection-differs between regions
  - Low rates (≤2%) in Western Europe and the U.S
  - Intermediate rates (2–8%) in Mediterranean countries and Japan
  - High rates (8–20%) in Western Pacific, Southeast Asia and Sub-Saharan Africa
- According to WHO, in 2022, approximately 254 million people-chronic hepatitis B virus carriers in the world
  - About 2 billion people with evidence of past or present infection
  - Annual mortality of 800,000 people (cirrhosis and HCC)
- Successful vaccination in CKD/ESRD patients, improved infection control in dialysis units, and widespread use of EPO rather than blood transfusions for anemia

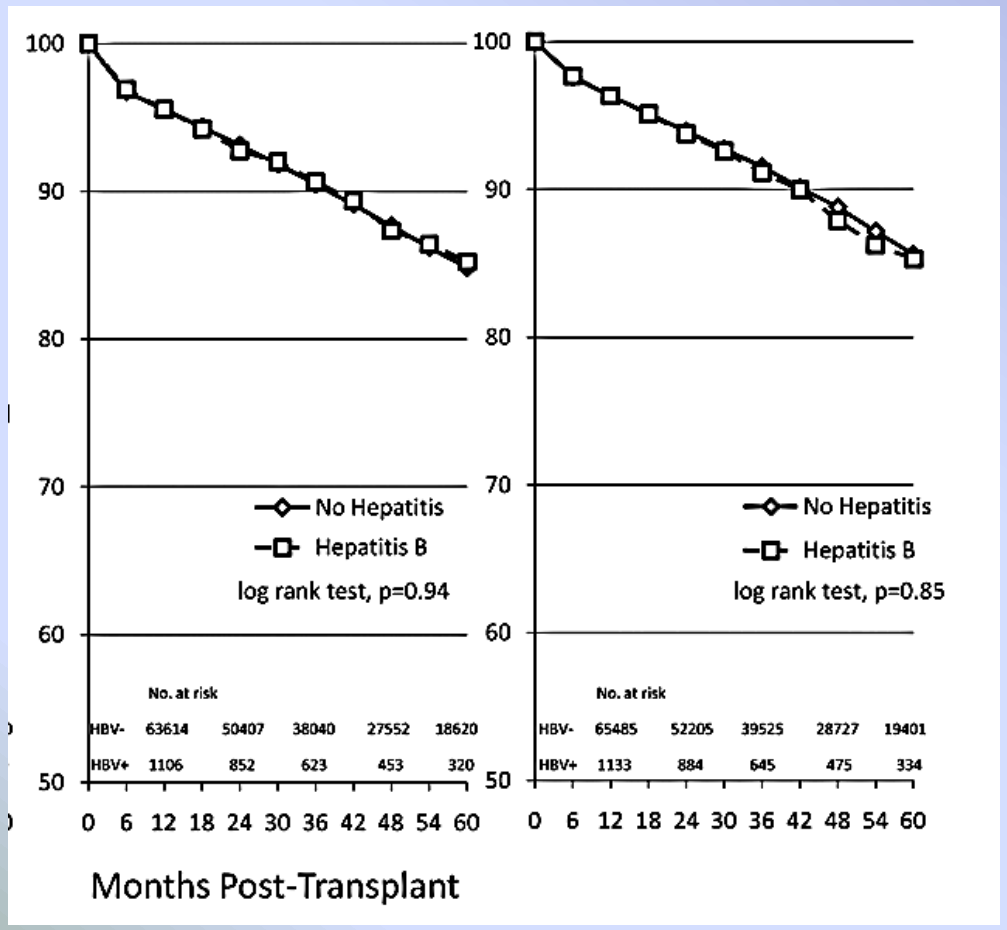
# Potential Complications after Transplantation

- HBV reactivation/chronic hepatitis and cirrhosis
- Massive liver necrosis due to fulminant hepatitis
- Severe cholestatic hepatitis
- HBV-related membranous nephropathy
- Hepatocellular carcinoma

# Transplant Evaluation of Patients with HBV

- All candidates should be screened-serologies and HBV viral load
- All candidates should be vaccinated if they are HBsAb negative
  - HBsAb levels ≥10 IU/L does not eliminate the risk of HBV reactivation (no ideal titer)
- Chronic HBV is NOT a contraindication
- All candidates who are HBsAg positive must be referred to Hepatology
  - Most patients require a liver biopsy-to make sure that they do not have cirrhosis or portal hypertension, and assess the need for treatment

# Impact of Pre-existing HBV Infection on Outcomes




- 1346 HBsAg+ recipients from UNOS database 2001-2007
- 5 yr death-censored **graft survival** 85.2% and **patient survival** 85.3% in HbsAg+; **no significant difference from HBV- patients**
- 5-yr cumulative incidence of **hepatic failure higher in HBV+ recipients** (1.3% *vs* 0.2%; $P < 0.001$)-still low, 5x risk of severe liver disease in HBV+ recipients-lamivudine was used

*Reddy P, et al. CJASN 2011*

# Impact of HBV Infection on Outcomes

- Retrospective cohort on OPTN data from 2000 to 2019; results at 15 years posttransplant
- **No statistically significant differences in PS and GS** among D–R-(178,374 KTs), D–R+(3,577 KTs), and D+R–(144 KTs) groups, nor was the patient or GS different between donor and recipient HBsAg+ status
- Most of the studies reporting adverse outcomes after KT following HBV infection were prior to the widespread use of antiviral therapy

*Yuan Q, et al. Clin Transplant 2021*

# Impact of HBV Infection on Outcomes

- UNOS database (from 1999 to o 2021): 448 HBV-positive donors-353 kidneys and 56 hearts were transplanted; 312 kidneys and 45 hearts were transplanted in HBsAg negative recipients; **similar 10-year PS and GS for both kidney** and heart transplant recipients (*Singal AK, et al. Transplantation 2024)*
- SRTR data base (2006-2021): HBV prevalence 1.7% in kidney recipients; posttransplant PS of patients with vs without HBV+ similar in all solid organ transplants *(Alqahtani SA, et al. J Viral Hepat 2024)*

# HBV Reactivation after Transplantation

- Retrospective study from Mayo Clinic; 180 nonliver solid organ transplants
- Past HBV infection: HBcAb+ and HBsAg negative
- Chronic HBV infection: HBcAb+ and HBsAg positive
- HBV reactivation: HBV DNA became detectable or reappearance of HBsAg

*Chiu C, et al Clin Transplant 2024*

# HBV Reactivation after Transplantation

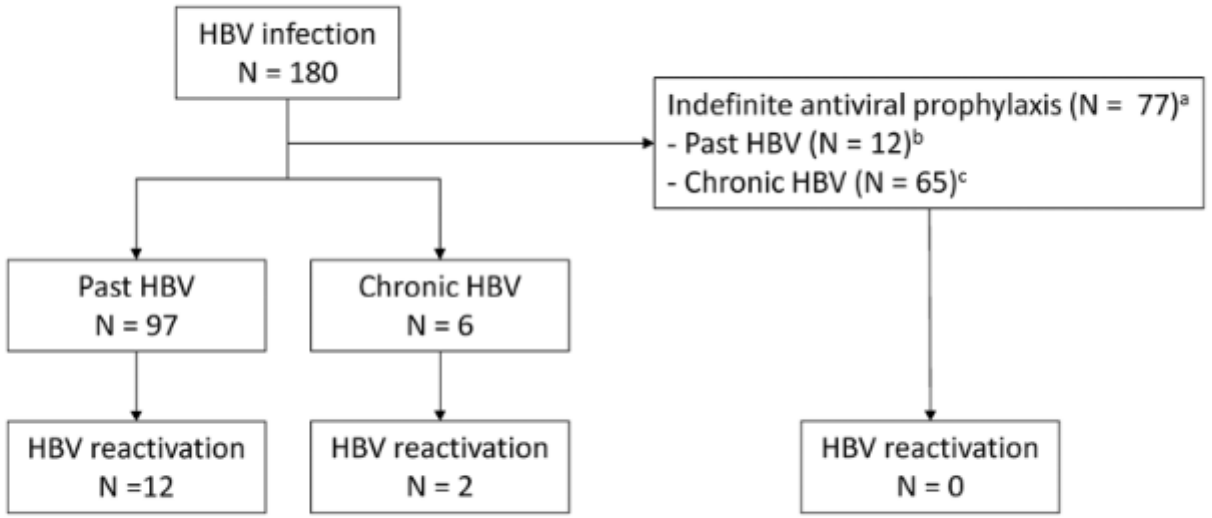



**FIGURE 1** | Patient selection for the current study. HBV, hepatitis B virus. (a) 44 entecavir, 27 tenofovir alafenamide, and six tenofovir disoproxil fumarateb. (b) 12 kidney transplantc. (c) 58 kidney transplant, four heart transplant, and three lung transplant.

-12% HBV reactivation in nonliver SOT recipients with past HBV (16% in kidney transplant recipients)

-**No HBV reactivation in 77 recipients on antiviral prophylaxis** (*Chiu C, et al Clin Transplant 2024)*

-Risk factors: **absence of HBsAb, use of high-dose steroids** *(Tsai HJ, et al. Transpl Int 2023)*

# HBV Therapies
## Consensus Guidelines

- Effective antivirals with HBV DNA suppression have improved outcomes significantly
  - **Lamivudine** was the primary antiviral agent used for the treatment of chronic HBV both before and after transplantation
  - **New agents**: potent oral nucleoside analogs with a high genetic barrier to resistance such as **entecavir (ETV) and tenofovir** (very low resistance rates (<1%) in treatment naive patients)
  - Once therapy is started, should continue indefinitely

*Te H, Doucette K. Clin Transplan 2019 (AST ID Community of Practice Guidelines)*

# Antiviral Treatments for HBV Infection

| Drug | Anti-viral potency | Barrier to resistance | Side effects |
|---|---|---|---|
| **Adefovir** | + | ++ | Nephrotoxicity, diabetes insipidus, Fanconi syndrome |
| **Lamivudine** | ++ | + | Lactic acidosis, pancreatitis |
| **Emtricitabine** | ++ | + | Lactic acidosis, anemia, leukopenia |
| **Telbivudine** | +++ | + | Neuropathy, myopathy, elevated creatinine kinase |
| **Entecavir** | +++ | +++ | Lactic acidosis, transaminitis |
| **Tenofovir** | +++ | +++ | Nephrotoxicity, Fanconi syndrome, lactic acidosis, osteomalacia |

# HBV-positive Donors

- **The risk of HBV transmission from HBsAg negative but HBcAb-positive kidney donors is extremely low** *(Huprikar S, et al AJT 2015; Terrault NA, et al Hepatology 2018)*
- Anti-HBs positive recipient getting anti-HBc positive kidney: no prophylaxis needed
- Anti-HBs negative recipient getting anti-HBc positive kidney: antiviral prophylaxis should be considered for up to 1-year posttransplant
  - Liver enzymes, HBsAg and HBV DNA should be monitored
- Organs from HBsAg+ donors-not routinely transplanted in the U.S
  - Could be considered in endemic regions-potential donors are frequently HBsAg+; indefinite prophylaxis with ETV or tenofovir is recommended for all recipients

# Hep B Viremic donors (NAT+)

- 16 DD kidney transplants from HBV nucleic acid testing positive (NAT+) kidneys, used in older recipients (68±5 years)-to reduce the wait times
- NAT window periods: average of 11-13 days for HIV, 20-22 days for HBV and 3-5 days for HCV
- 5 had natural immunity and 11 had vaccine immunity
- Treated with entecavir-started pre-operatively, for 52 weeks
- 3/15 had detectable HBV PCR 1-week posttransplant, but negative at 12 months
- No outcome differences; long-term follow-up still needed

*Lopez-Soler R, et al. Transpl Infect Dis 2024*

# Recommendations

- Initial screening for HBV should be done at the time of transplant candidate assessment; non-immune candidate should be vaccinated (ESRD patients' response rate 55-67%)
- HBsAg-positive non-hepatic SOT candidates should undergo additional testing-HBeAg, anti-HBe, HBV viral load, liver enzymes, and abdominal ultrasound
- If treatment is indicated, tenofovir disoproxil fumarate (TDF), tenofovir alafenamide (TAF), or ETV is preferred due to their potency and high barriers to resistance, replacing lamivudine (if renal dysfunction, ETV or TAF is preferred)
- HBsAg-negative, anti-HBc positive subjects should be monitored for HBV infection posttransplant
- All patients should be monitored for risk of disease progression and hepatocellular carcinoma (HCC)

*Te H, Doucette K. Clin Transplant 2019 (AST ID Community of Practice Guidelines)*

# HBV Infection Protocol for Kidney Transplant Candidates at Mayo Clinic Study Sites

| | |
|---|---|
| (i) | HBsAg + OR detectable HBV DNA candidates should undergo evaluation by hepatology or infectious disease consultants pre-transplantation. HBV DNA must be less than 50 IU/mL before listing for transplantation. HBV DNA is monitored after transplantation at 1, 4, 8, and 12 months, and then annually. |
| (ii) | HBcAb + / HBsAb – candidates undergo routine monitoring for HBV DNA after transplantation at 1, 4, 8, and 12 months, then annually. |
| (iii) | HBcAb + candidates (regardless of HBsAb status) who were receiving rituximab or alemtuzumab were recommended antiviral prophylaxis for 1 year and had HBV DNA monitored every three months for 1 year after completing prophylaxis. |
| (iv) | HBsAg and HBV DNA should be checked in cases where increases in liver function test results are observed. |

a. This protocol was created on March 04, 2021. The latest update was on November 15, 2023.

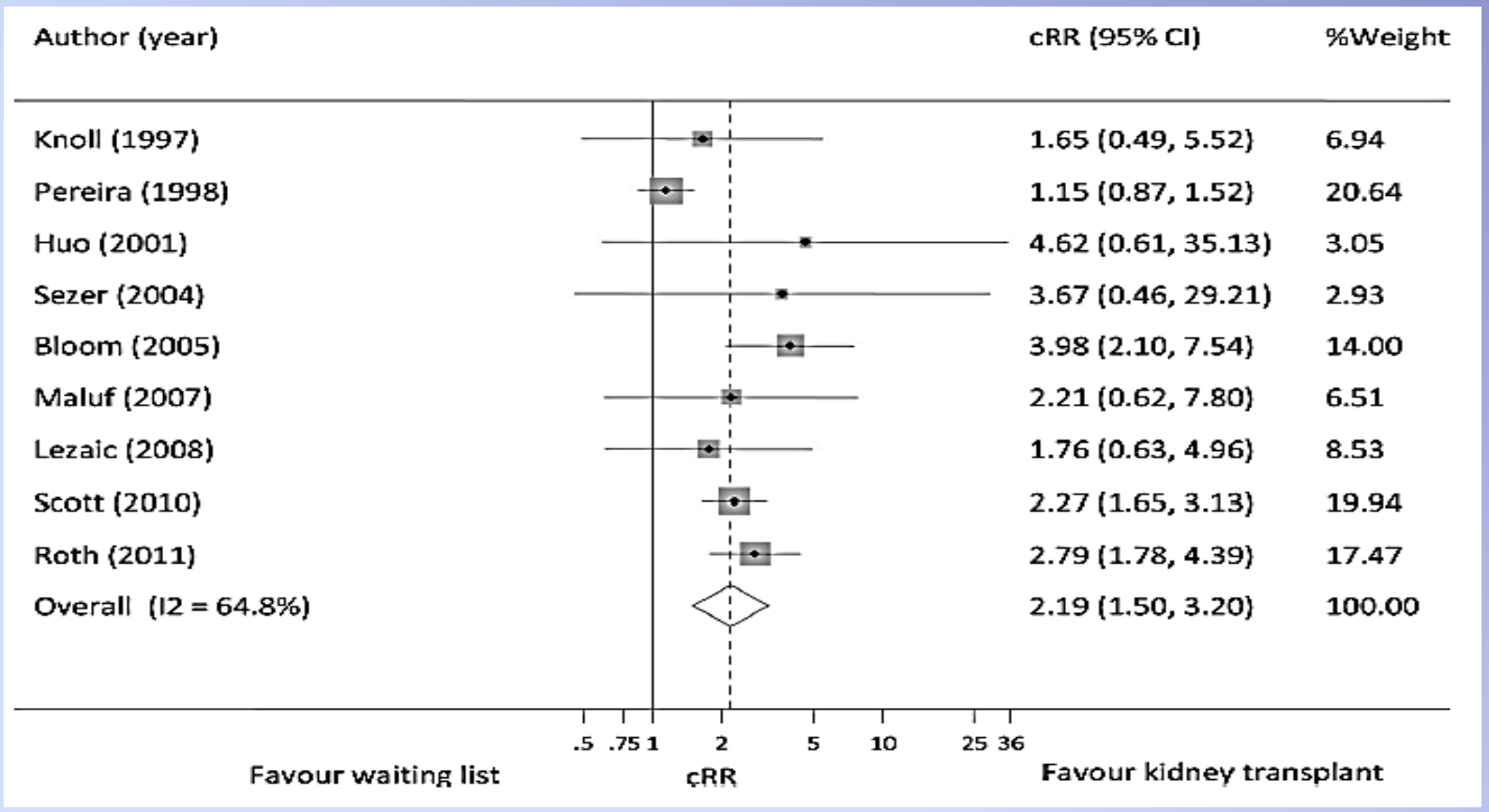
*Chiu C, et al Clin Transplant 2024*

# Hepatitis C (HCV)

- Estimated to affect about 115 million worldwide (80 million chronically infected); ECDC estimation in Europe 2.4 million with chronic HCV
- Prevalence in patients with ESRD (worldwide 5-60%) far exceeds that of the general population (5-10% in the US)
- HCV-infected patients with CKD: **increased mortality** and **accelerated rate of progression** to ESRD
- Liver failure and HCC-major long-term complications
- **HCV infection in the recipient is NOT a contraindication for kidney transplant**
- **Patients co-infected with HIV (prevalence about 6%)**- have an **increased mortality** and **overall worse prognosis**

*Ladino M, et al. JASN 2016, Belga S, et al. World J Gastroenterol 2016*

*Awan A, et al. Ann Intern Med 2023*




- Meta-analysis (overall mortality): **Patients with HCV infection on waiting list** had **2.19 times higher** risk for death than patients who had kidney transplantation
- **Transplant provides a survival benefit for HCV+ patients**
- Benefit of kidney transplantation-approx **55% lower risk of death at 5 years**
- Waiting list group had **higher risk of cardiovascular diseases**
- Survival advantage particularly in HCV patients **aged 45 years or older**

*Ingsathit A, et al. Transplantation 2013*

# Kidney Transplantation in HCV-Positive Patients

- SRTR database, from 2006 to 2021; **higher post-transplant mortality in kidney transplant recipients with HCV+** (antibody testing, not PCR) (13,994 vs HCV- 265,003) (1-year: 6% vs. 3%; 5-year: 21%vs. 13%; 10-year: 47% vs. 31%; all p < .0001); **no association of HCV+ with the rate of graft loss** *(Alqahtani SA, et al J Viral Hepat 2024)*
- OPTN database from 1994-2019; **pre-DAA, for HCV+ recipients, receiving an HCV+ kidney-associated with 1.28-fold higher mortality and 1.22 fold higher death-censored graft failure compared to receiving an HCV- kidney**
- HCV dual infection group (both donor and recipient HCV+) had worse outcomes
- **In the DAA era, the risk associated with HCV+ in donor and/or recipients was no longer significant** except for impaired patient survival in the dual-infected *(Yuan Q, et al. World J Transplant 2023)*

# HCV and Kidney Transplant

- Kidney transplantation is the best therapeutic option for patients with CKD G5 irrespective of presence of HCV infection
- Screening all patients for HCV infection at the time of evaluation for (using an immunoassay followed by nucleic acid testing (NAT) if immunoassay is positive)
- All kidney transplant candidates with HCV to be evaluated for severity of liver disease and presence of portal hypertension prior to acceptance for kidney transplantation (might need liver biopsy) *KDIGO 2022 Practice Guideline. Kidney Int 2022*

# HCV and Kidney Transplant

- Patients with HCV, compensated cirrhosis, and no portal hypertension undergo isolated kidney transplantation
- Patients with decompensated cirrhosis or clinically significant portal hypertension (i.e., hepatic venous pressure gradient ≥10 mm Hg or evidence of portal hypertension on imaging/exam) undergo a simultaneous liver/kidney transplantation

*KDIGO 2022 Practice Guideline. Kidney Int 2022*

# HCV and Kidney Transplant

- All kidney transplant candidates with HCV be considered for direct-acting antiviral (DAA) therapy, either before or after transplantation
- Timing of HCV treatment in relation to kidney transplantation (before vs. after) should be based on: **donor type** (living vs. deceased donor), **wait-list times** by donor type, **center-specific policies** governing the use of kidneys from HCV-infected deceased donors, and **severity of liver fibrosis**

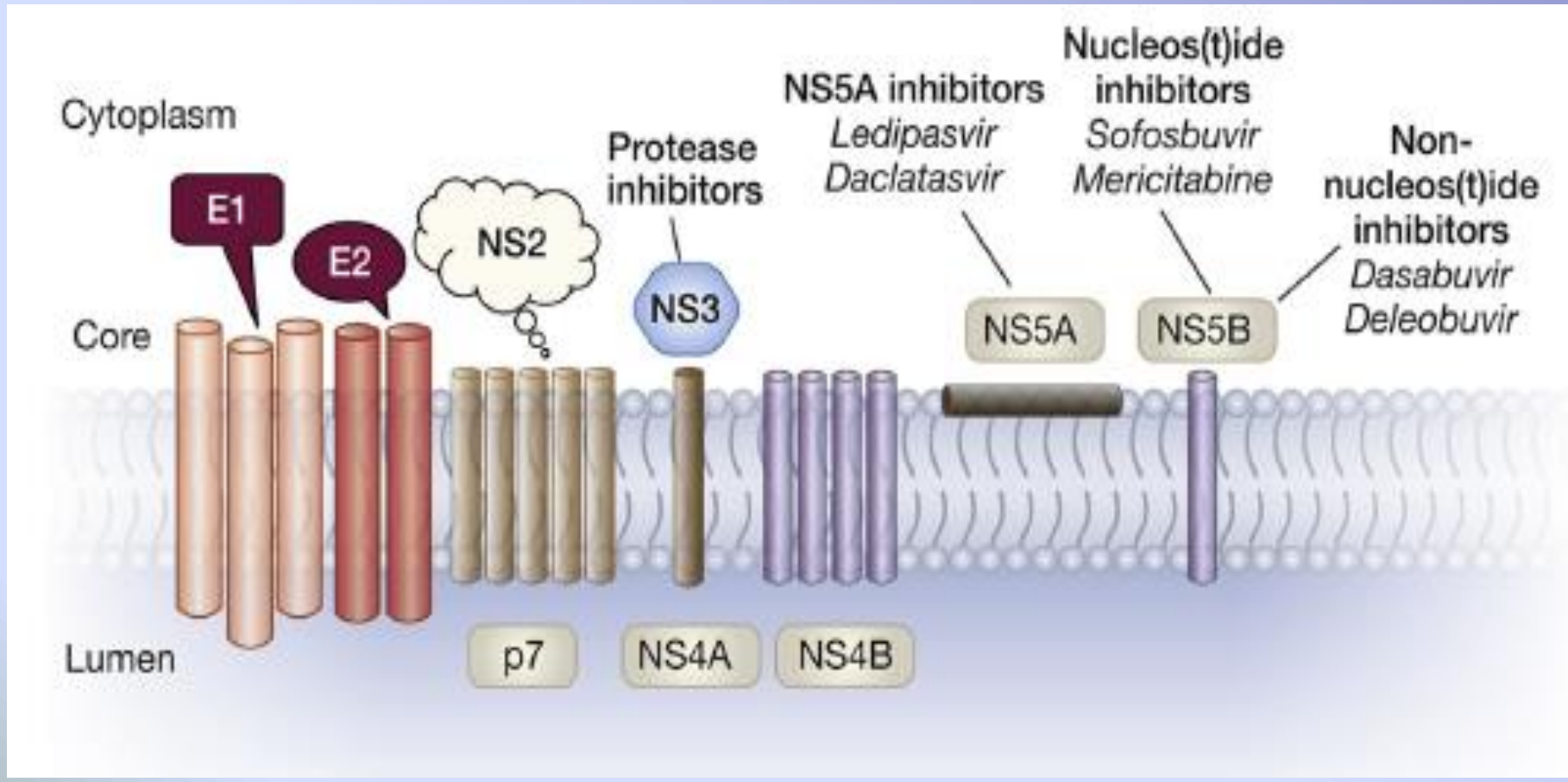
*KDIGO 2022 Practice Guideline. Kidney Int 2022*

# Treatment of HCV-KDIGO Guidelines

- Interferon based-low response rate and poor tolerability
- Treatment with interferon after transplant is not recommended-increased rejection risk
- Interferon-free direct acting antiviral (DAA) regimens-sustained virologic response rates 92-100%; efficacious posttransplant and well tolerated
- FDA Approval in 8/2017-Glecaprevir and Pibrentasvir
- The choice of specific regimen should be based on prior treatment history, drug-drug interactions, GFR, stage of liver fibrosis, kidney and liver transplant candidacy, and comorbidities

*KDIGO guidelines. Kidney Int 2022*

# DAA Agents for Treatment of HCV-Targeting the Essential Proteins for HCV Replication



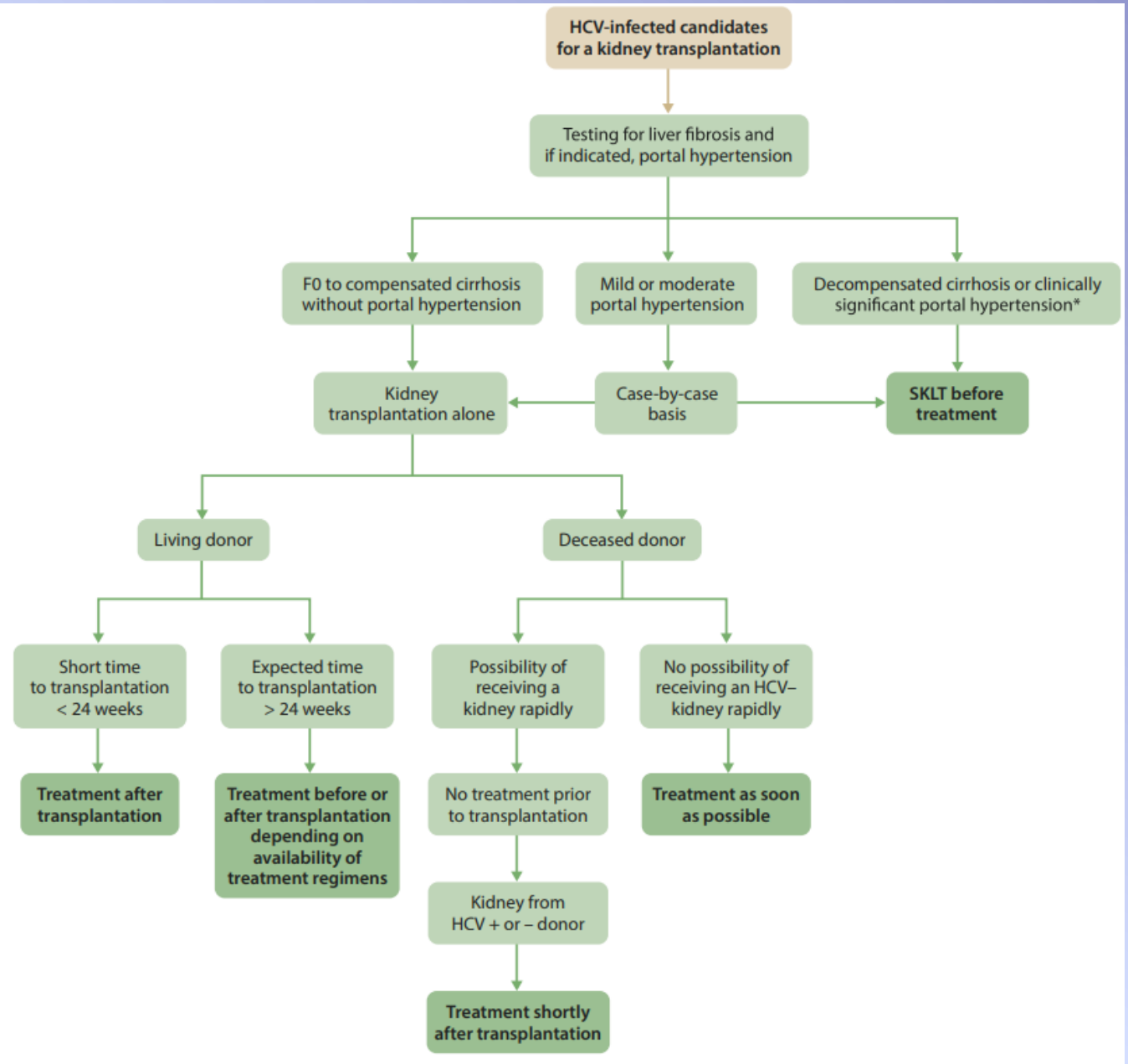

•The HCV genome and target sites of action

*Fabrizi F, et al. Kidney Int 2016*

# HCV Treatment

| CKD populations | Direct acting antiviral (DAA) regimens[a] | HCV genotypes | Quality of evidence (total N)[b] |
|---|---|---|---|
| G1–G3b,[c] not KTR | Any licensed DAA regimen | All | Not evaluated |
| G4–G5ND,[d] including KTR[e,f] | Sofosbuvir / Daclatasvir, 12 or 24 wk<br>Glecaprevir / Pibrentasvir, 8 wk<br>Grazoprevir / Elbasvir, 12 wk<br>Sofosbuvir / Velpatasvir, 12 wk<br>Sofosbuvir / Ledipasvir, 12 wk | All<br>All<br>1a, 1b, 4<br>All<br>All | High (571)<br>High (132)<br>High (857)<br>Low (99)<br>Very low (43) |
| G5D[g] | Sofosbuvir / Velpatasvir, 12 wk<br>Glecaprevir / Pibrentasvir, 8 wk<br>Sofosbuvir / Daclatasvir, 12 or 24 wk<br>Sofosbuvir / Ledipasvir, 12 wk<br>Grazoprevir / Elbasvir, 12 wk<br>PrO ± D, 12 wk<br>Daclatasvir / Asunaprevir, 24 wk | All<br>All<br>All<br>All<br>1a, 1b, 4<br>1a, 1b, 4<br>1b | High (405)<br>Moderate (529)<br>Moderate (278)<br>Moderate (220)<br>Moderate (962)<br>Moderate (582)<br>Low (341) |
| KTR,[e] G1–G3b[c] | Sofosbuvir / Ledipasvir, 12 or 24 wk<br>Sofosbuvir / Daclatasvir, 12 or 24 wk<br>PrO ± D, 12 wk<br>Grazoprevir / Elbasvir, 12 wk | All<br>All<br>1a, 1b, 4<br>1a, 1b, 4 | High (300)<br>High (290)<br>Very low (33)<br>Very low (21) |

*KDIGO 2022 Practice Guideline. Kidney Int 2022*




Proposed management strategy in HCV-infected transplant candidate. *KDIGO 2022 Practice Guideline. Kidney Int 2022*

# Treatment of HCV

- **Warning:** reactivation of **hepatitis B** infection following successful **therapy of HCV infection** with DAA-based therapy
- In patients with HCV and CKD, serum markers of HBV infection (HBsAg, HBV DNA) should be obtained prior to antiviral therapy

# Use of HCV-positive Kidneys

- HCV+ organs to HCV+ recipients or HCV- recipients
- Overall shortage of suitable donor kidneys/long waiting times; not every center accepts these kidneys
- Risk of superinfection with other HCV genotypes
- With new direct-acting antivirals to cure HCV, no need to limit to genotype 1 recipients
- Significant increase in HCV+ kidney utilization after DAA availability

# Transplanting Hepatitis C Kidneys into Negative Kidney Recipients (THINKER)

- Open-label, single-group, pilot trial at the University of Pennsylvania; (ClinicalTrials.gov number, NCT02743897)
- 10 patients received HCV-infected kidneys (median age: 59 years; half were men and 2 were black; median time from eligibility to transplantation was 58 days)
- Patients had detectable HCV RNA on day 3 posttransplant

*Goldberg DS, et al. NEJM 2017*

# THINKER STUDY

- Nine had HCV genotype 1a infection; none had identifiable NS5A resistance
- Patients were treated with elbasvir–grazoprevir posttransplant
- All recipients were cured of HCV (sustained virologic response 12 weeks after the end of treatment)
- Proteinuria (at an estimated level of 2 g per day of urinary protein excretion) in one patient (FSGS on biopsy)

*Goldberg DS, et al. NEJM 2017*

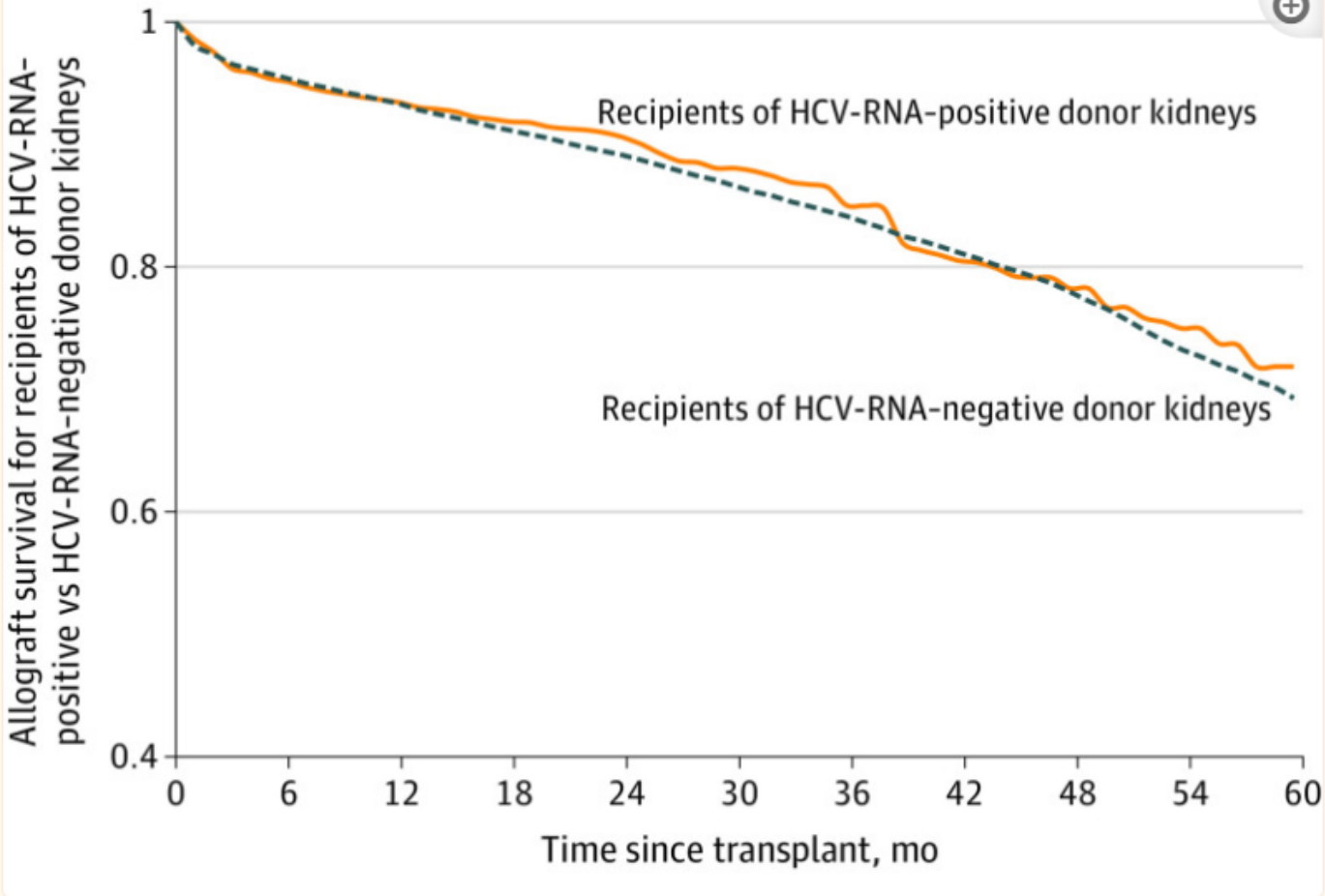



Figure.

**Five-Year Allograft Survival Comparing Recipients of Kidney Transplants From HCV-RNA–Positive vs HCV-RNA–Negative Deceased Donors**

OPTN data 2016-2021; no significant difference in 5-year allograft survival in DAA era. *Schaubel DE, et al. JAMA 2022*

# HCV-positive Donors and HCV-negative Recipients-Meta-analysis

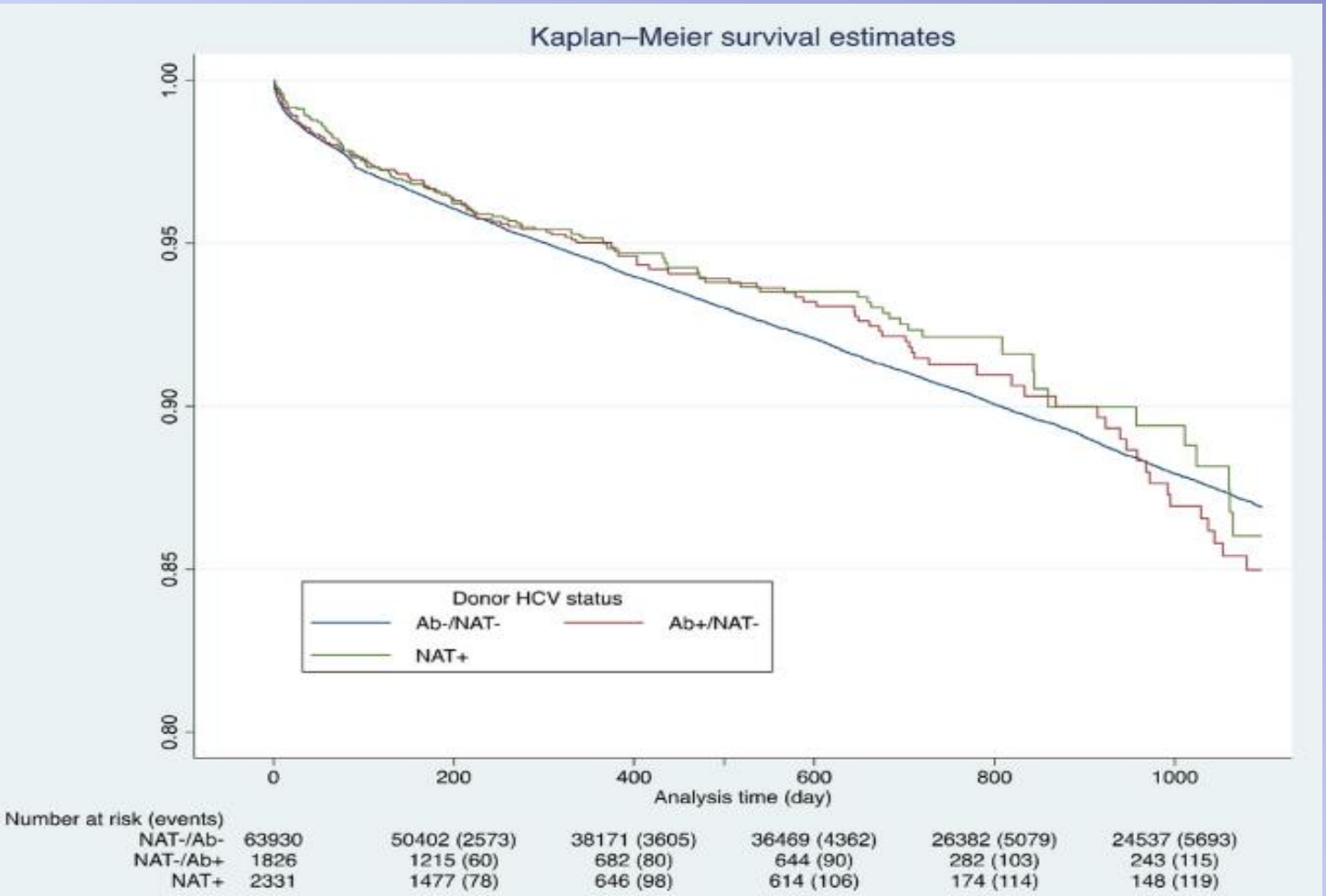
- 16 studies, 557 patients, received DAA therapy (from 2008-2021)
- Most studies used 12-week DAA treatment (highly efficient)
- High rates of sustained viral response, low rates of adverse events, and excellent patient and allograft survival 1 years after transplantation
- DAA-associated side effects across studies 0.4%
- Willingness to accept HCV+ kidney might still decrease the wait-list time

*Gordon CE, et al. Am J Kidney Dis 2023*

# HCV-positive Donors and HCV-negative Recipient

- OPTN database, from 3/2015 to 5/2021 (since 12/2014 the OPTN has required that all solid organ donor be screened for HCV using both HCV NAT and serology)
- 68,087 HCV-negative recipients; 3 years of follow-up
- 63,930 (93.9%) received a KT from HCV negative donor, 1826 (2.7%) from HCV Ab+/NAT negative donor, and 2331 (3.4%) from HCV NAT+ donor

*Sutcliffe S, et al. Am J Transplant 2023*




-No association was observed between donor HCV status and KT failure over 3 years follow-up; longer-term studies needed

-HCV-positive donors tend to have lower KDRI scores, to be younger, fewer comorbidities, and less glomerulosclerosis on biopsy

*Sutcliffe S, et al. Am J Transplant 2023*

# Use of DAAs Posttransplant

| DAA | CYP3A4 Inhibition | Adjust Dose for eGFR < 30 mL/min |
|---|---|---|
| **NS3 Protease Inhibitors** | | |
| Boceprevir | ++ | – |
| Telaprevir | +++ | – |
| Simeprevir | + | – |
| Paritaprevir (ritonavir boosted) | +++ | – |
| **NS5A** | | |
| Ledipasvir | – | – |
| Ombitasvir | – | – |
| **NS5B Nucleoside Inhibitor** | | |
| Sofosbuvir | – | ++ |
| **NS5B N006Fn-Nucleoside Inhibitor** | | |
| Dasabuvir | + | – |

- DAA-immunosuppressive drug-drug interactions are very important
- CNI levels have been shown to fluctuate during and even after DAA treatment is completed
- **Need for careful monitoring of kidney function and CNI drug levels both during and after therapy**
- Combined efforts by hepatologists and transplant nephrologists

*Sawinski D, et al. Transplantation 2015*

# Use of HCV-positive Kidneys

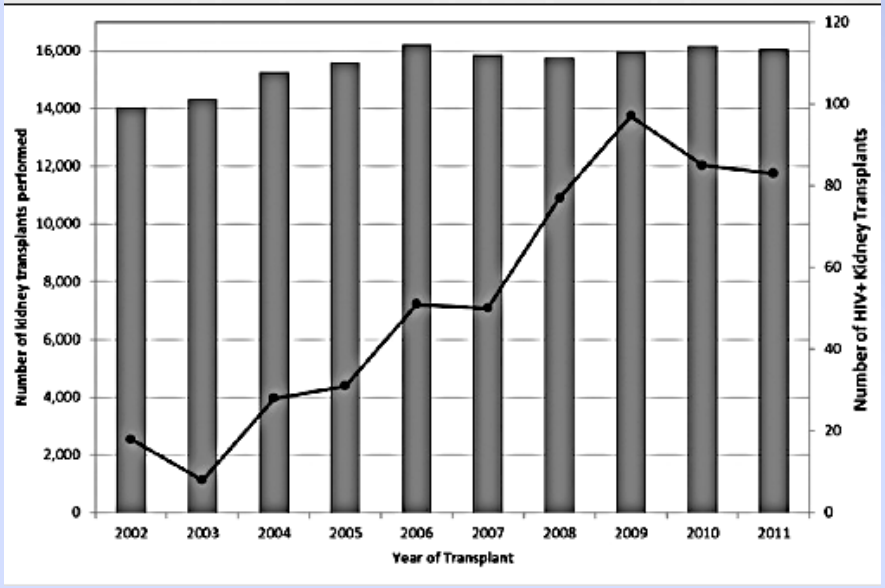
- Kidneys from HCV-infected donors be considered regardless of HCV status of potential recipients
- When transplanting kidneys from HCV-infected donors into HCV-uninfected recipients, transplant centers must ensure that patients receive education and are engaged in discussion to provide informed consent
  - Patients should be informed of the risks/benefits of transplantation with an HCV-infected kidney, including the need for DAA treatment
  - Transplant centers should confirm availability of DAAs for initiation in the early post-transplant period
- Pangenotypic DAA regimens, including sofosbuvir-based regimens, and genotype-specific regimens-safe and effective for advanced CKD and for kidney transplant recipients

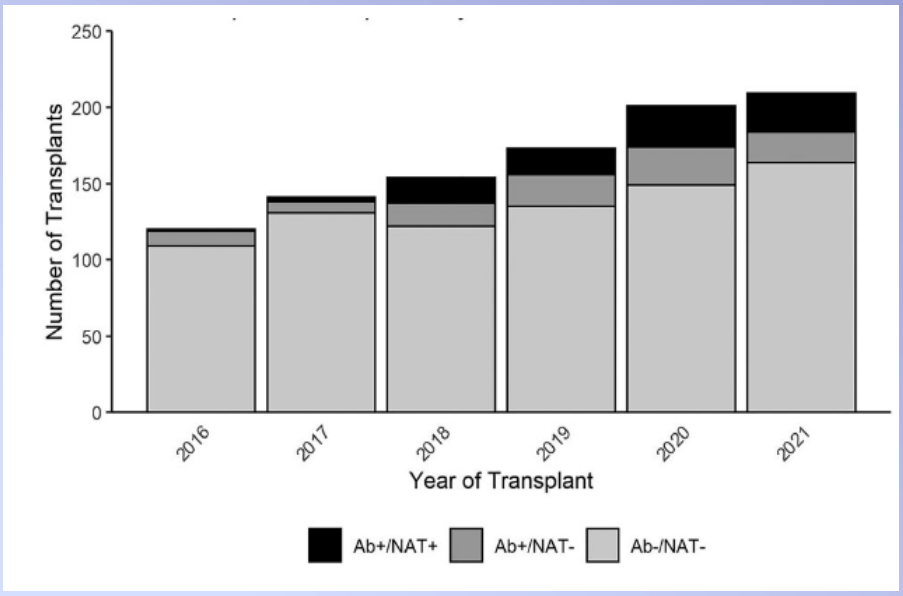
*KDIGO 2022 Practice Guideline. Kidney Int 2022*

# HIV and Kidney Transplantation

- With highly active antiretroviral (HAART) use-decline in HIV-associated morbidity and mortality; number of patients living with HIV increased-manageable chronic condition
- **Kidney transplantation in HIV-infected ESRD patients offers significant survival benefit compared with remaining on dialysis**
- Kidney transplantation is now offered and recommended as an acceptable treatment option for HIV+ ESRD patients
- People with HIV significantly less likely to be waitlisted (positive HIV-status was associated with 57% lower likelihood of waitlisting) *Shelton B, et al. AIDS 2024*

# HIV and Kidney Transplantation
# Kidney Transplant Volume




*Locke J, et al. JASN 2015*

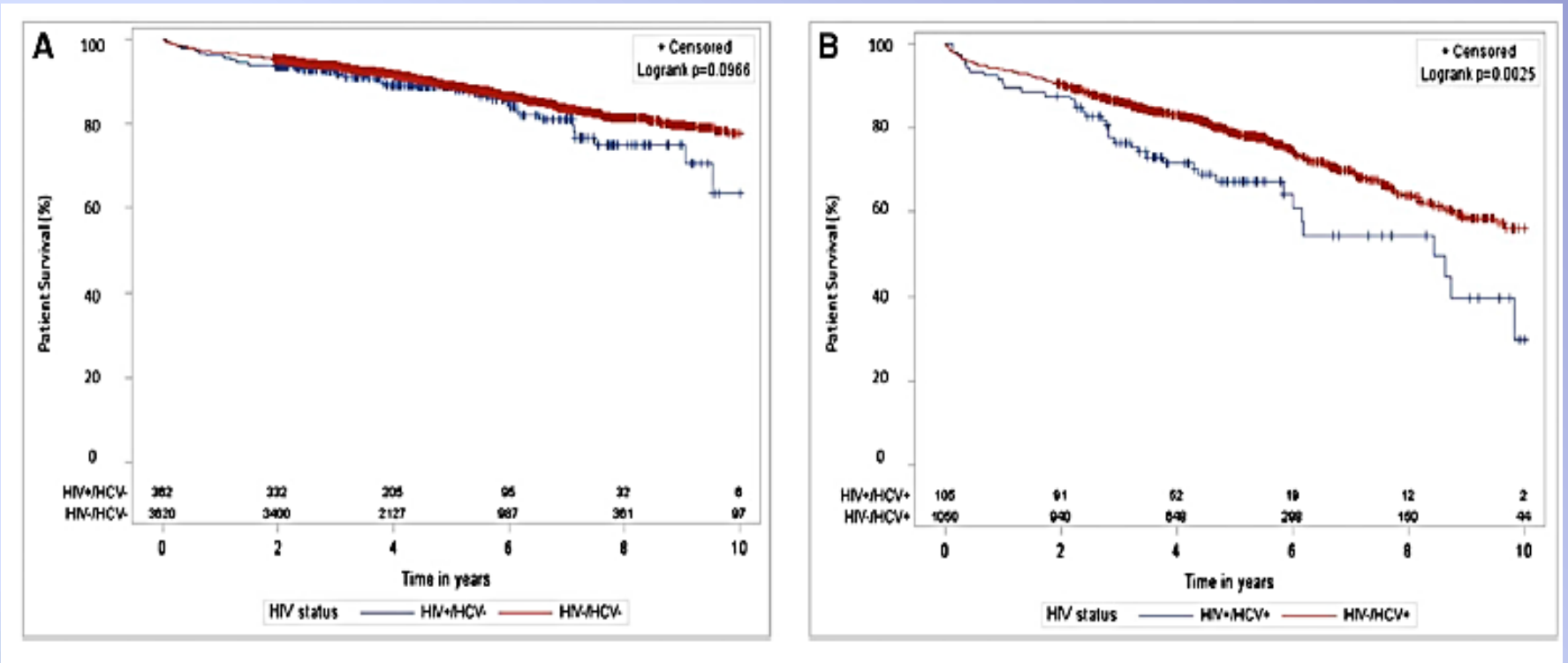
*Fontana L, et al. Transplant Infect Dis 2023*

-The number of kidney transplants performed among HIV+ ESRD patients between 2002 and 2011 (left)-

-The number of kidney recipients from donors with HIV (HIV ab/NAT+) has increased over time

# Patient Survival-HIV+ Patients

## (SRTR; 2002–2011; 510 adults, median follow-up:3.8 years)

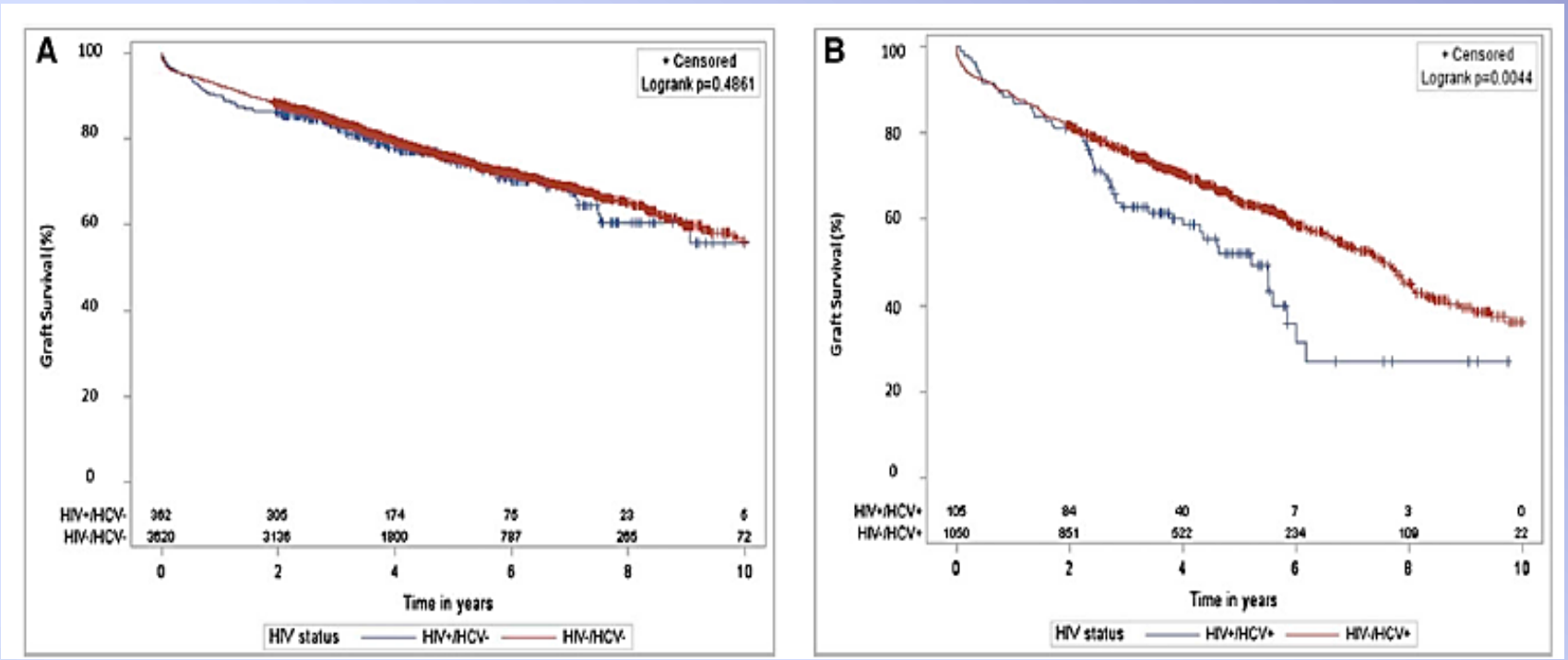



- **PS: similar for HIV-monoinfected recipients** and HIV negative/HCV negative controls both at 5 years and 10 years
- **HIV/HCV coinfected recipients had worse PS** compared with HIV-negative/HCV positive controls

*Locke J, et al. JASN 2015*

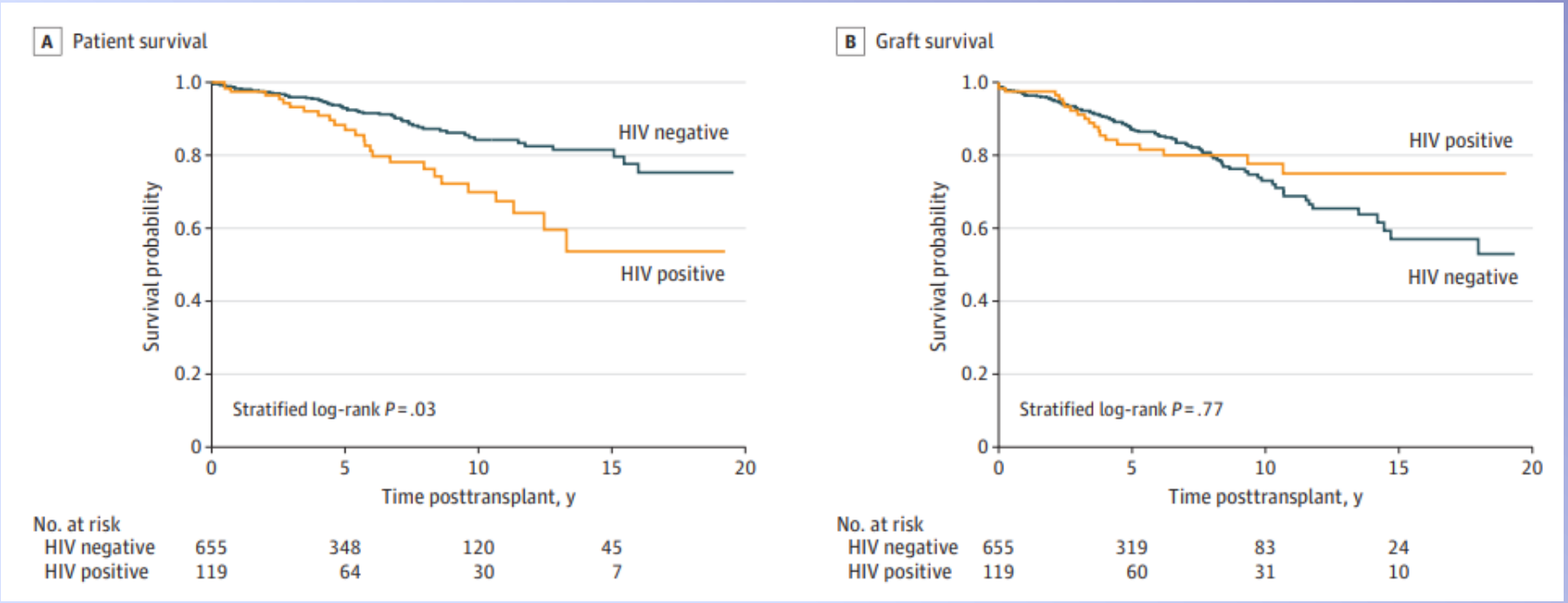
# Graft Survival-HIV+ Patients

## (SRTR; 2002–2011; 510 adults, median follow-up:3.8 years)




- **GS: similar for HIV-monoinfected recipients** and HIV negative/HCV negative controls both at 5 years and 10 years
- **HIV/HCV coinfected recipients had worse GS** compared with HIV-negative/HCV positive controls

*Locke J, et al. JASN 2015*




-Retrospective data from UCSF, 2000-2019

-655 HIV-negative recipients, 119 HIV-positive recipients

-**Patient survival at 15 years posttransplant 79.6% vs 53.6% (lower in HIV positive patients)**

-**Graft survival at 15 years posttransplant 57% vs 75%-comparable-**GS was better in patients without acute rejection

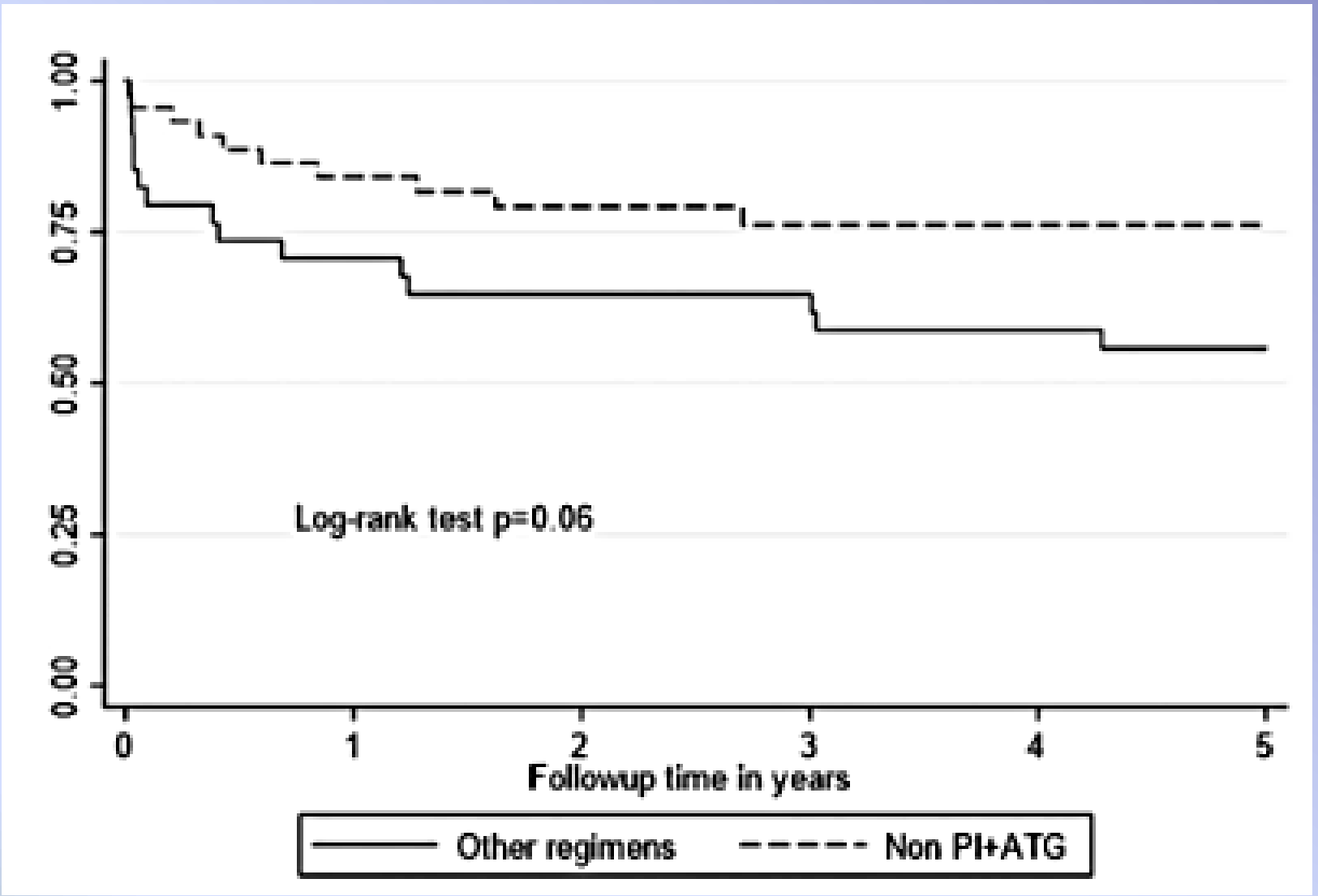
*Zarinsefat A, et al. Jama Surg 2022*

# HIV-Choice of Immunosuppression

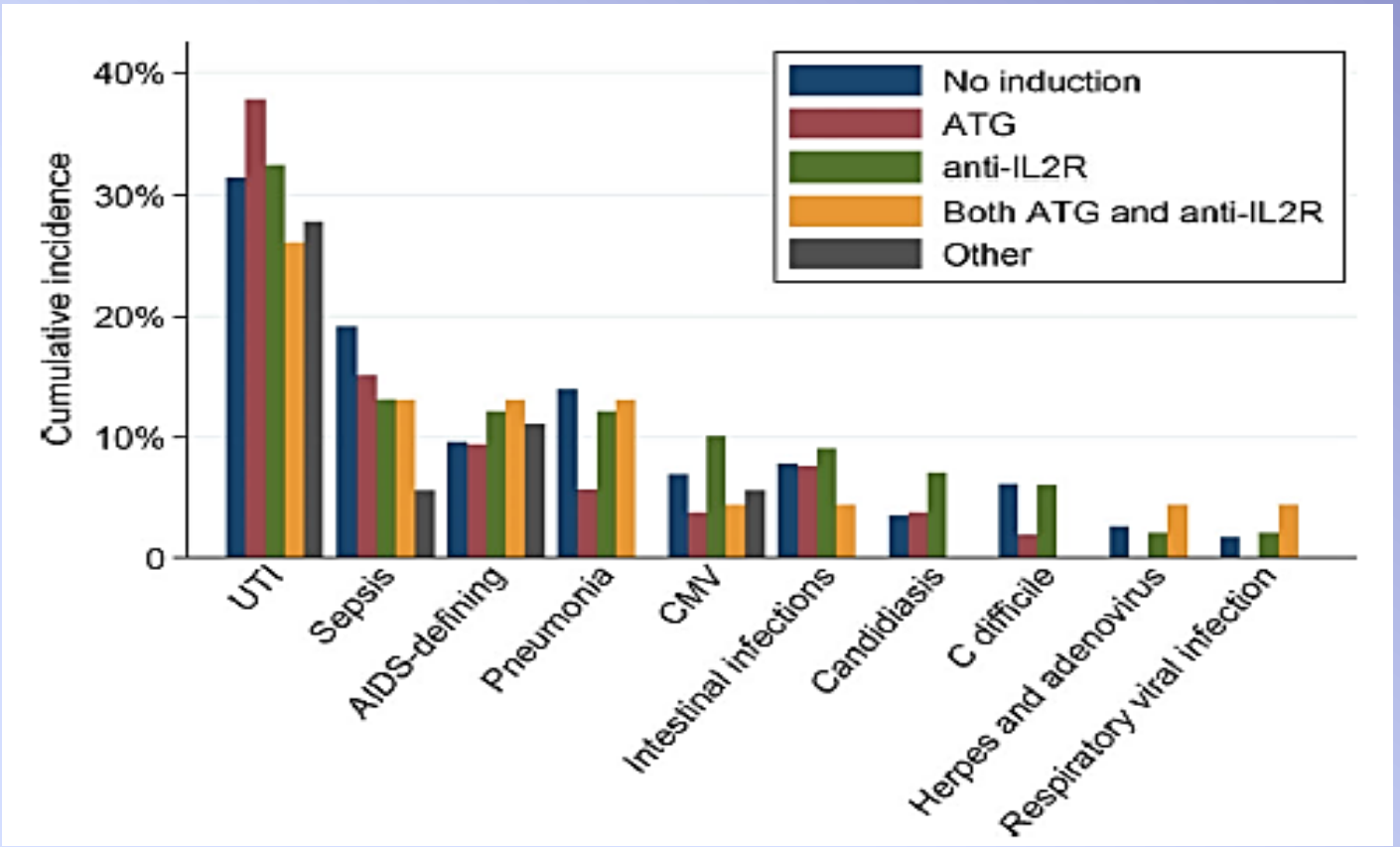
| | HIV-negative (n=93,027) | HIV-positive (n=516) | *P* |
|---|---|---|---|
| Induction therapy | | | <0.001 |
| None | 21.4 | 35.1 | |
| ATG | 43.5 | 25.8 | |
| IL-2 inhibitor | 23.1 | 33.5 | |
| Alemtuzumab | 12.0 | 5.6 | |
| Maintenance therapy | | | <0.001 |
| Neither | 5.0 | 9.3 | |
| CNI-based | 89.0 | 83.7 | |
| Sirolimus-based | 6.1 | 7.0 | |

| | Rejection (1 year, RR) | 95% CI | *P* |
|---|---|---|---|
| Induction therapy | | | |
| None | Reference | | |
| ATG | 0.39 | 0.18–0.87 | 0.02 |
| IL-2 inhibitor | 1.11 | 0.66–1.86 | 0.7 |
| Alemtuzumab | 1.6 | 0.8–3.2 | 0.2 |
| Maintenance therapy | | | |
| CNI-based | Reference | | |
| Sirolimus-based | 2.15 | 1.2–3.87 | 0.01 |
| Neither CNI or sirolimus-based | 1.21 | 0.58–2.54 | 0.6 |

- SRTR data: 2003-2011, 516 adults: HIV-positive patients had a **1.77-fold higher risk of AR** at 1 year (15% vs 8%); patients that received **ATG induction had a 2.6-fold or 61% lower risk of AR at 1 year** compared with no induction therapy
- Sirolimus-based therapy had a 2.2-fold higher risk of AR at 1 year (*Locke J, et al. Transplantation 2014)*
- 78 recipients with median f/u 7.1 years; AR 37%; **patients who had rATG induction without protease inhibitors had less rejection** *(Marks CR, et al. Transpl Infect Dis 2024)*




-PS 83% and GS 67%; 5-year rejection free survival in patients receiving Non-PI-based antiretrovirals with rATG induction vs others *(Marks CR, et al. Transpl Infect Dis 2024)*




- 830 HIV+ kidney transplant recipients (from 2000-2014, SRTR)
- HIV+ recipients who received induction spent fewer days in the hospital, had lower rates of DGF, less graft loss, lower rates of AR (with ATG induction), and a trend toward lower mortality
- **Induction therapy was not associated with increased infections**

*Kucirka LM, et al. AJT 2016*

# Impact of Antiretroviral Therapies on Outcomes

- 332 HIV+ kidney transplant recipients
- Protease inhibitor (PI)-based regimens; **associated with 1.8-fold increased risk of allograft loss** (greatest risk observed in the first post-transplant year); 1.9-fold increased risk of death as compared to non-PI regimens
- Suggests-whenever possible recipients **should be converted to a non-PI regimen prior to transplant**

*Sawinski D, et al. AJT 2017*

# HIV Medications and Immunosuppression

- Profound/complex **drug-drug interactions**, especially with protease inhibitors (potent inhibitors of cytochrome P450 3A4, the main metabolic pathway for CNIs)
- Frequent drug level monitoring of CNIs
- New integrase inhibitors, CCR5-antagonists and fusion inhibitors cause significantly less pharmacokinetic interactions
- Must work closely with a Transplant Infectious Diseases expert

# HIV and Kidney Transplantation

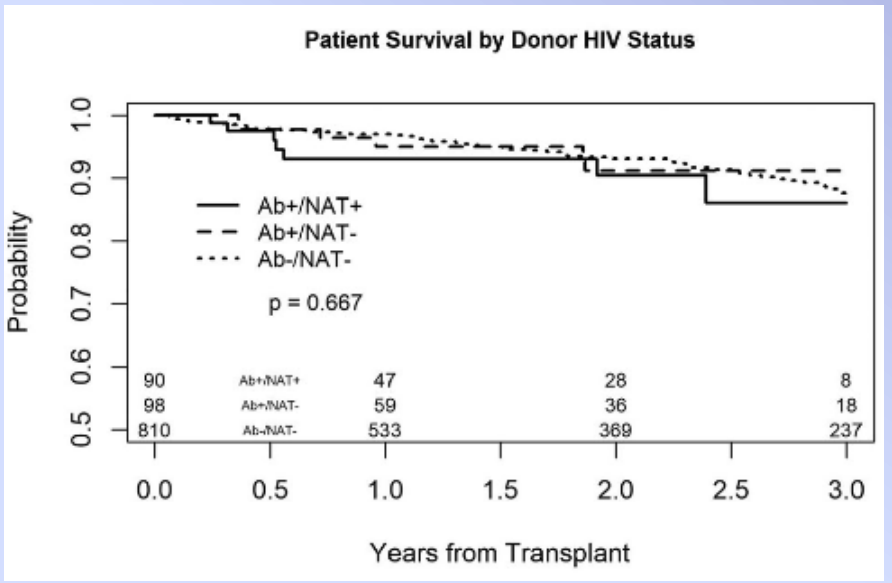
- Prospective, nonrandomized study of kidney transplantation in **27 HIV-infected patients** (CD4 count>200 and undetectable HIV RNA level)-all on antivirals; **received HIV positive kidneys**-results at 5 years
- Patient survival: 84% at 1 year, 84% at 3 years, and 74% at 5 years; graft survival:  93%, 84%, and 84%
- Rejection rates were 8% at 1 year and 22% at 3 years
- HIV infection remained well controlled, with undetectable virus in blood after the transplantation
- Follow-up study of 51 recipients; 5-year PS and GS 83.3% and 78.7%, respectively

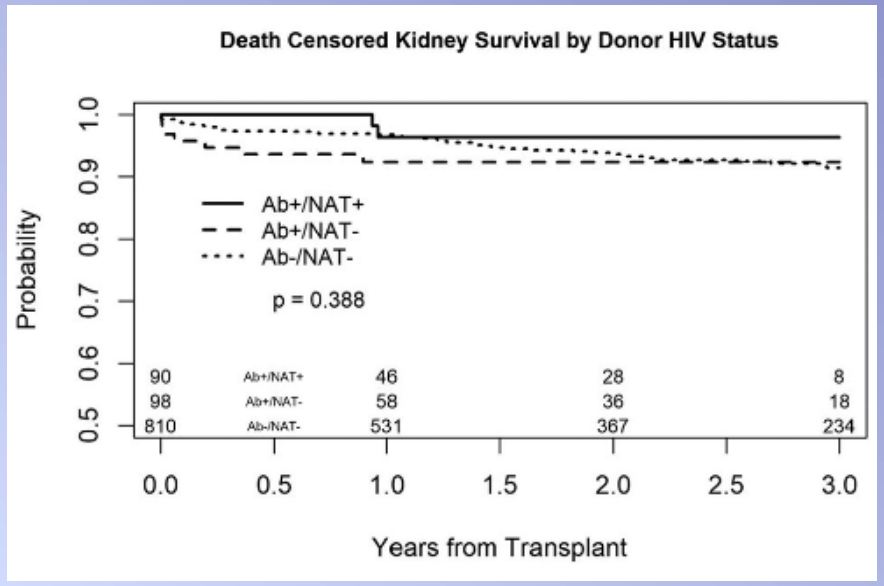
*Muller E, et al. NEJM 2015*

*Selhorst P, et al. NEJM 2019*

# HIV Organ Policy Equity Act (HOPE Act)

- Enacted on November 21, 2013; reversed the federal ban on HIV-to-HIV transplantation, implemented in 2015
- Allows for the development and publication of criteria for research relating to transplantation of organs from donors with HIV into individuals who are HIV positive
- The first HIV-to-HIV kidney and liver transplants were performed at Johns Hopkins in March of 2016
- 24 transplant centers approved to perform HIV-to-HIV transplants; 324 patients, 70% of those enrolled in HOPE received a KT during the 4.5 y study period (vs 43% non-HOPE candidates) *Motter JD, et al. Transplantation 2024*
- Organ transplantation from suspected HIV false-positive donors is an unexpected benefit of the HOPE Act; higher rate of transplantation and shorter wait time (the median wait time 10.3 mo)




-SRTR database in the US; 1/2016-12/2021
-HIV positive recipients; at 3 years, PS and DCGS were similar by donor HIV status
-PS at 1 and 3 years for recipients (n=90) who received a kidney Ab+/NAT+ was 93% and 86%, respectively
-Acute rejection, re-hospitalization and scr at 12 months were similar

*Fontana L, et al. Transpl Infect Dis 2023*

# Evaluation of HIV Positive Candidates

- All patients are required to have standard evaluation in addition to HIV-specific criteria:
  - CD4 count >200/$mm^3$
  - An undetectable HIV viral load on stable antiviral therapy for at least 6 months prior to transplant
  - To be evaluated for potential drug interactions
  - No significant opportunistic infections or malignancy
  - Careful assessment of social support and substance abuse history
  - Evaluation by Transplant Infectious Diseases team and most of the time Hepatology (due to HCV or HBV coinfection)

# Summary

- HBV positive recipient outcomes have improved significantly with vaccination and antiviral therapy
- HbcAb positive organs can be used safely
- Treatment of HCV with interferon-free regimens is now possible; HCV positive kidneys are now transplanted
- HIV+ kidney transplant recipients have excellent patient and allograft survival, but high incidence of acute rejection