# Case presentation: West Coast transplant ID conference

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# Case presentation

- [redacted] year old patient with T2DM, known NASH cirrhosis since 2017 c/b esophageal varices, portal HTN, splenomegaly, pancytopenia (WBC 1.5-2, Hgb 8-9, MCV 70's-80's, plt 100-150K) attributed to sequestration
- Presented in 2019 with thrush→ referred to ID→ HIV+ with VL 60,337, CD4=38 (8%)
  - no resistance mutations on genotyping
  - IGRA, Toxo, Hep C, Hep B, RPR all negative
- Bone marrow bx: hypercellular marrow with trilineage hematopoiesis, CD4:CD8 ratio 1:20, AFB and GMS stains negative. Routine culture held x 21 days negative

- Social hx: from [redacted], lived in [redacted] before moving to US in mid-1990's. Steadily employed in service industries and construction. No hx of substance use. Mode of HIV infection unclear.
- Started bictegravir-emtricitabine-tenofovir (Biktarvy) + dapsone (sulfa allergic) + weekly azithromycin

| date | viral load | WBC | CD4 abs | CD4% |
|---|---|---|---|---|
| 10/9/19 | 60,337 | 2.11 | 38 | 8 |
| 11/27/19 | UD | 1.14 | 26 | 11 |
| 12/31/19 | UD | 2.54 | 30 | 16 |
| 3/23/20 | UD | 1.17 | 44 | 11 |
| 6/29/20 | D, < LLQ | 1.75 | 32 | 10 |
| 11/16/20 | D, < LLQ | 1.4 | 37 | 12 |
| 4/21/21 | UD | 1.3 | 38 | 11 |
| 10/25/21 | UD | 1.35 | 52 | 7 |
| 11/8/21 | UD | 2.25 | 44 | 10 |
| 5/3/22 | UD | 1.71 | 44 | 12 |

[redacted] is referred to ID for assessment as a candidate for OLT. Hepatology feels [redacted] is a very good candidate from their standpoint. MELD = 16. What is your recommendation?

A. [redacted] is not a candidate due to continued CD4 lymphopenia, with guideline-based threshold being ≥ 100
B. Proceed with transplant listing with clear understanding of risks, both to the patient and programmatic

# Criteria for SOT in PLWH

| | Spain [5] | Italy [19] | UK [21] | USA [20] | France [6,22] |
|---|---|---|---|---|---|
| **Previous C events [92]** | | | | | |
| Opportunistic infections | None except PCP, TB, OC | None except PCP, TB, OC | None after HAART-induced immune reconstitution | All except untreatable diseases[a] | None except PCP, TB, OC |
| Malignant neoplasms | No | No | | No | Not defined |
| **$CD4^+$ T-cells/$mm^3$** | | | | | |
| Liver transplantation | >100[b] | >100[b] | >200 or >100 if portal hypertension | >100[b] | >100[c] |
| Other SOT | >200 | >200 | >200 | >200 | Not defined |
| **Plasma HIV RNA viral load** | | | | | |
| BDL on HAART[d] | Yes | Yes | Yes | Yes | Yes |

SOT, solid organ transplantation; BDL, below detection limit (<50 copies/mL); TB, tuberculosis; PCP, *Pneumocystis jiroveci* pneumonia; OC, esophageal candidiasis.
[a]Only untreatable diseases are exclusion criteria for SOT (e.g. progressive multifocal leukoencephalopathy, chronic cryptosporidiosis, multidrug-resistant systemic fungal infections, primary CNS lymphoma and visceral Kaposi sarcoma).
[b]Patients with previous opportunistic infections should have >200 CD4 cells/$mm^3$.
[c]No exclusion criteria are available for patients with <100 CD4/$mm^3$; cases should be evaluated on an individual basis.
[d]If plasma HIV RNA viral load is detectable, post-transplant suppression with HAART should be provided for all liver recipients.

*Clin Microbiol Infect* 2014; **20** (Suppl. 7): 119–130

# Solid organ transplantation in the HIV-infected patient: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice

**TABLE 1** Suggested criteria for transplantation in HIV-infected Individuals[a,24]

| | Kidney transplant | Liver transplant | Heart transplant |
|---|---|---|---|
| Meet center-specific inclusion criteria | X | X | X |
| CD4 count >100 cells/μL (without history of OI) | NR[b] | X[c] | NR |
| CD4 count >200 cells/μL during 3 mo prior to transplantation | X | X | X |
| Undetectable HIV viral load while receiving antiretroviral therapy | X | X | X |
| Detectable HIV viral load due to intolerance of HAART, HIV can be suppressed post-tx | NR | X | NR |
| Documented compliance with a stable antiretroviral regimen | X | X | X |
| Absence of active opportunistic infection and malignancy[d] | X | X | X |
| Absence of chronic wasting or severe malnutrition | X | X[e] | X |

- The large outcomes studies we are familiar with that inform our approach to SOT in PLWH in the era of modern ARV have excluded those with CD4 < 100 for OLT
- Studies examining outcomes prior to modern ARV are not directly applicable now

# Survival of Human Immunodeficiency Virus–Infected Liver Transplant Recipients

Retrospective review of 24 persons transplanted at 5 centers (Pitt, Miami, UCSF, King's College, Minnesota) between 1997-2001

No CD4 or viral load- based inclusion/exclusion criteria

**Table 1. Baseline demographic and clinical characteristics of 24 human immunodeficiency virus (HIV)–positive subjects at liver transplantation.**

| Characteristic | Value |
|---|---|
| Age, median (range), years | 46 (15–66) |
| Race | |
| White | 21 (87.5) |
| Black | 2 (8.3) |
| Asian | 1 (4.2) |
| Sex | |
| Male | 20 (83.3) |
| Female | 4 (16.7) |
| Cause of end-stage liver disease | |
| Hepatitis C virus infection | 15[a] (62.5) |
| Hepatitis B virus infection[b] | 7 (29.2) |
| Fulminant hepatic failure[c] | 3 (13.0) |
| HIV risk group | |
| Homosexual | 7 (29.2) |
| Heterosexual | 5 (20.8) |
| Hemophiliac | 5 (20.8) |
| Bisexual | 3 (12.5) |
| Injection drug user | 3[d] (12.5) |
| Transfusion recipient | 2 (8.3) |
| Unknown | 1 (4.2) |
| Preoperative laboratory value,[e] median (range) | |
| Alanine aminotransferase,[f] U/mL | 82 (25–648) |
| Total bilirubin, mg/dL | 3.2 (0.7–27.0) |
| Creatinine, mg/dL | 0.9 (0.5–2.2) |
| International normalized ratio | 1.5 (0.6–3.6) |
| MELD score[g] | 15 (7–33) |
| Platelet count, no. x $10^3$ platelets/$\mu$L | 73 (28–185) |
| $CD4^+$ cell count,[h] cells/$\mu$L | 188 (76–973) |
| HIV RNA PCR load,[i] copies/mL | <400 (<400–179,000) |
| Preoperative antiretroviral therapy | |
| Ever received | |
| Protease inhibitor | 13[j] (54.2) |
| NNRTI | 8 (34.8) |
| NRTI only | 3 (12.5) |
| None | 2 (8.3) |
| Intolerance | 4 (16.7) |

The Journal of Infectious Diseases 2003; 188:1412–20

# Survival of Human Immunodeficiency Virus–Infected Liver Transplant Recipients

**Table 4. Demographic and clinical characteristics of and survival among human immunodeficiency virus (HIV)–positive liver transplant recipients.**

| Characteristic | Survivors ($n$ = 18) | Nonsurvivors ($n$ = 6) | RR[a] | $P$[b] |
|---|---|---|---|---|
| Age, median (range), years | 48 (33–66) | 39 (15–43) | 0.42[c] | .026[c] |
| Cause of end-stage liver disease | | | | |
| Hepatitis C virus infection | 9 (50.0) | 6 (100.0) | ...[d] | .023 |
| Hepatitis B virus infection | 9 (50.0) | 1 (16.7) | 0.21 | .090 |
| Fulminant hepatic failure | 3 (16.7) | 0 (0) | 0.00[e] | .414 |
| Antiretroviral therapy intolerance | | | | |
| Before OLTX | 2 (11.1) | 2 (33.3) | 3.58 | .239 |
| After OLTX | 2 (11.1) | 4 (66.7) | 7.27 | .044 |
| Pre-OLTX CD4+ cell count | | | | |
| Median cells/μL | 209 | 170 | 1.02[f] | .338 |
| <200 Cells/μL | 8 (44.4) | 4 (66.7) | 1.69 | .602 |
| Post-OLTX CD4+ cell count | | | | |
| Median cells/μL | 311 | 135 | 0.81[f] | .003 |
| <200 Cells/μL | 1 (5.9)[g] | 3 (60.0) | 21.53 | .005 |
| Pre-OLTX HIV RNA PCR load | | | | |
| Median copies/mL | ≤50 | ≥400 | 1.00 | .589 |
| >400 Copies/mL | 4 (22.2) | 2 (33.3) | 2.15 | .494 |
| Post-OLTX HIV RNA PCR load | | | | |
| Median copies/mL | ≤50 | ≤50 | 1.02 | .139 |
| >400 Copies/mL | 0 (0) | 2 (33.3) | 27.75 | .016 |

# HIV-Infected Liver and Kidney Transplant Recipients: 1- and 3-Year Outcomes

Prospective outcomes study between 03/2000-09/2003 at 4 centers (UCSF, Maryland, Penn, Mt Sinai)

HIV-related transplant criteria:

CD4> 200 (kidney) or > 100 (liver) for 6 months prior to transplant

Undetectable HIV VL on stable ARV regimen for 3 months prior to transplant

*For liver recipients who were unable to tolerate HAART, HIV study specialists predicted complete suppression of HIV viremia following transplantation, based on medication and HIV RNA history and antiretroviral resistance test results.*

History of OI was exclusion criteria 03/2000-04/2002, thereafter allowed except for PML, lymphoma, visceral KS, chronic cryptosporidiosis

*American Journal of Transplantation 2008; 8: 355–365*

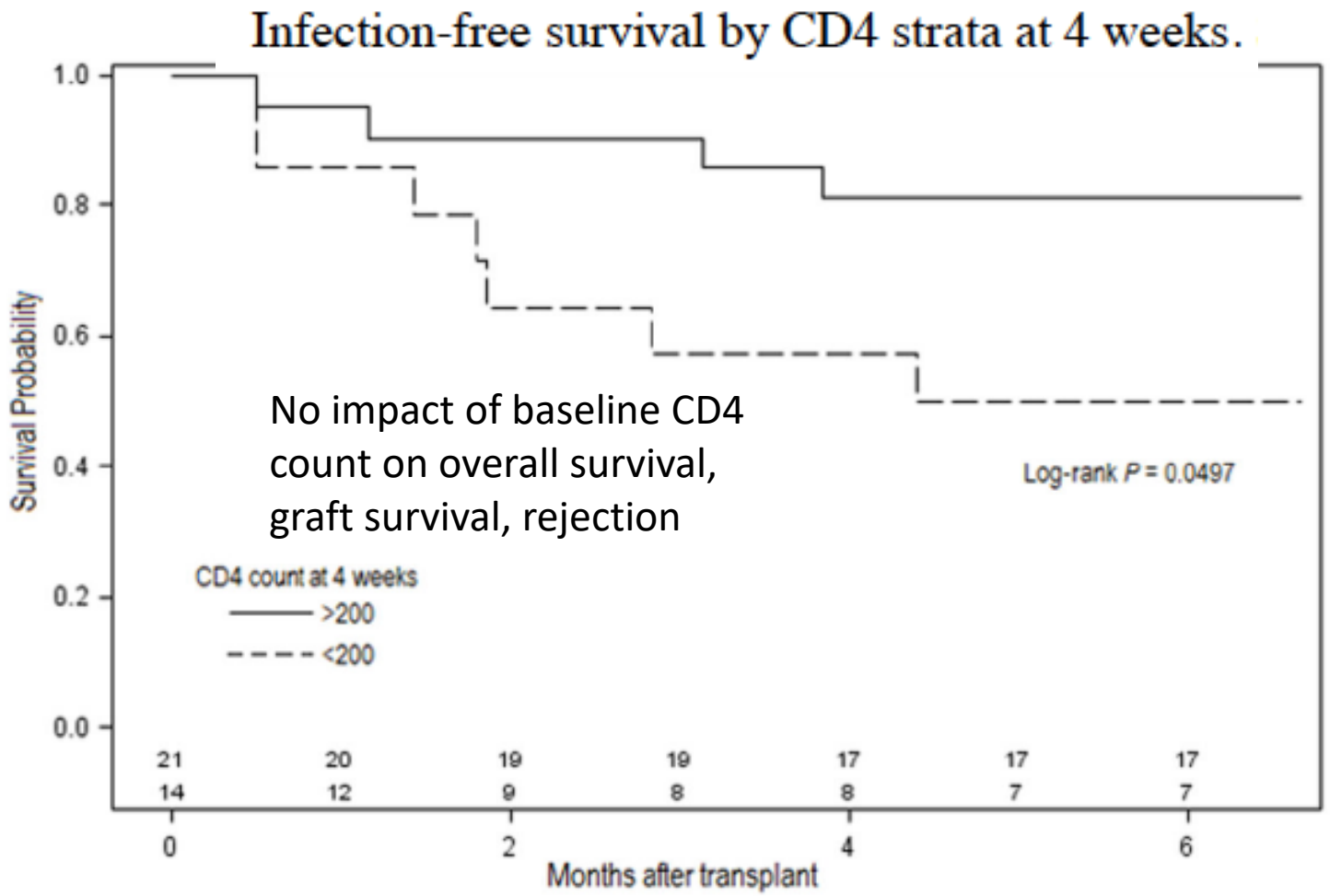
# Pre-transplant CD4 count influences immune reconstitution and risk of infectious complications in HIV+ kidney allograft recipients

Association between pre-transplant CD4 count and risk of CD4 lymphopenia <200 cells/mm$^3$ following kidney transplant

| Variable | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | RR (CI) | *P* value | Adjusted RR (CI) | *P* value |
| ***CD4<200 at 4 weeks*** | | | | |
| Age (<40 years) | 1.8 (0.5–6.3) | 0.37 | 1.8 (0.5–6.1) | 0.32 |
| Male gender | 1.3 (0.4–3.5) | 0.64 | | |
| African-American | 0.9 (0.4–2.1) | 0.75 | | |
| Baseline CD4 <350 | 2.5 (1.2–5.1) | **0.01** | 2.6 (1.3–5.1) | **0.01** |
| HCV co-infection | 1.3 (0.4–3.8) | 0.64 | | |
| ***CD4<200 at 52 weeks*** | | | | |
| Age (<40 years) | 0.8 (0.2–3.7) | 0.82 | 0.8 (0.2–3) | 0.75 |
| Male gender | 4.9 (0.3–78.1) | 0.26 | | |
| African-American | 1.7 (0.2– 12.5) | 0.58 | | |
| Baseline CD4 <350 | 14.3 (2–102.1) | **0.01** | 14.3 (2–100.4) | **0.01** |
| HCV co-infection | 0.5 (0.03–7) | 0.59 | | |

*Am J Transplant*. 2016 August ; 16(8): 2463–2472. doi:10.1111/ajt.13782.

# Pre-transplant CD4 count influences immune reconstitution and risk of infectious complications in HIV+ kidney allograft recipients



# What about the hypersplenism? Should we expect a bump in WBC and CD4 count after OLT?

- Unclear how much hypersplenism is contributing to CD4 lymphopenia as CD4 % remains quite low.
- How much reversal of hypersplenism is expected after OLT and what could be effect on WBC?

# Pretransplantation splenomegaly frequently persists after liver transplantation and can manifest as hypersplenism and graft fibrosis - a retrospective study

*Transplant International* 2020; 33: 1807–1820

- Among 119 patients with pre-transplant SM, 33 patients (27.4%) had a decrease in splenic volume after OLT that did not meet the definition of SM

**Table 3.** Impact of splenomegaly three years after liver transplantation on laboratory data

| Variables | Post-transplantation SM ($n$ = 90) (60.4%) | Post-transplantation non-SM ($n$ = 59) (39.6%) | $P$ value |
|---|---|---|---|
| BSA ($m^2$) | 1.4 (0.9–1.6) | 1.5 (1.1–1.7) | 0.346 |
| SV/BSA ($ml/m^2$) | 251.3 (199.1–377.3) | 114.9 (87–131.4) | **<0.001** |
| Percent reduction of SV/BSA after LT | 36% (−17%–51%) | 41% (28%–64%) | **0.031** |
| Liver volume (ml) | 917 (559–1172) | 894 (591–1130) | 0.992 |
| WBC count ($\times 10^3/\mu l$) | 5.2 (4–6.7) | 6.3 (5.1–7.7) | **0.003** |
| Hemoglobin (g/dl) | 12.7 (10.6–13.9) | 12.5 (11.6–13.6) | 0.707 |
| PLT count ($\times 10^3/\mu l$) | 143 (89–189) | 203 (170–256) | **<0.001** |
| PLT count < 150.000/µl (%) | 51 (56.7%) | 9 (15.3%) | **<0.001** |
| PLT count < 100.000/µl (%) | 26 (28.9%) | 0 (0%) | **<0.001** |
| PLT count < 50.000/µl (%) | 4 (4.4%) | 0 (0%) | 0.152 |
| INR | 1.1 (1–1.2) | 1 (1–1.1) | **0.007** |
| AST (U/l) | 31 (22–44) | 24 (16–35) | **0.001** |
| ALT (U/l) | 23 (14–45) | 14(11–23) | **<0.001** |
| Total bilirubin (mg/dl) | 0.7 (0.5–1.1) | 0.7 (0.5–0.9) | 0.797 |
| Albumin (g/dl) | 4 (3.7–4.3) | 4 (3.7–4.3) | 0.902 |
| METAVIR score: ≥F2 | 15/70 (21.4%) | 1/36 (2.8%) | **0.010** |

# What about splenectomy, either pre- or post-transplant?

**Table 2.** Indications for treatment of hypersplenism

| Indication | Frequency |
|---|---|
| Increase counts to | |
| Allow use of interferon and/or ribavirin to treat hepatitis B/C | Common |
| Allow use of chemotherapy | Common |
| Preceding elective surgery to reduce bleeding risk | Uncommon |
| Severe abdominal pain secondary splenic enlargement or infarction | Rare |
| Severe bleeding in tissues and gums thought to be secondary to thrombocytopenia | Uncommon |
| Treatment of splenic artery steal syndrome or hypersplenism post-transplant | Uncommon |

Liver Int. 2015; 35: 1492–1498

# Interventions for hypersplenism

**Table 3.** Treatments for hypersplenism

| | | Splenectomy | | | | |
|---|---|---|---|---|---|---|
| | TIPS | Open | Laparoscopic | PSE | RFA | Eltrombopag platelets only |
| Efficacy | 0 | ++++ | ++++ | +++ | ++ | +++ |
| Safety | ++++ | +++ | +++ | +++ | +++ | ++++ |
| Complications | | | | | | |
| PVT | + | ++++ | ++++ | ++ | ++ | ++ |
| Pain | + | +++ | ++ | +++ | ++ | 0 |
| Splenic abscess | 0 | 0 | 0 | ++ | + | 0 |
| Bleeding | + | ++ | + | + | ++ | 0 |

+ to ++++ increasing benefit or likelihood of a complication.

RFA, radiofrequency ablation; PSE, partial splenic embolization; PVT, portal vein thrombosis; TIPS, transjugular intrahepatic portosystemic shunt.

Risk of PVT reduced with use of anti-thrombin III concentrate

# Laparoscopic splenectomy is an effective and safe intervention for hypersplenism secondary to liver cirrhosis

**Table 4** Changes in blood counts and liver function before and after the operations

| Variables | Preoperation | Postoperation | *p* value |
|---|---|---|---|
| Platelet count ($\times 10^9$/L) | | | |
| Group 1 | 41.6 [19] | 232.6 [135.8] | 0 |
| Group 2 | 36.8 [19.3] | 202.0 [142.1] | 0 |
| WBC ($\times 10^9$/L) | | | |
| Group 1 | 2.69 [1.71] | 9.47 [2.85] | 0 |
| Group 2 | 3.53 [2.99] | 10.24 [2.49] | 0 |
| Hemoglobin (g/dl) | | | |
| Group 1 | 112.6 [17.8] | 93.3 [12.4] | 0.015 |
| Group 2 | 107.9 [18.6] | 86.7 [14.1] | 0 |
| ALT (IU/L) | | | |
| Group 1 | 29.3 [18.3] | 25.2 [11.1] | NS |
| Group 2 | 35.1 [18.5] | 28.2 [16.5] | NS |
| AST (IU/L) | | | |
| Group 1 | 43.2 [22.6] | 36.5 [19.3] | NS |
| Group 2 | 39.2 [17.1] | 33.2 [15.2] | NS |
| TBIL (μmol/L) | | | |
| Group 1 | 20.1 [8.5] | 18.4 [8] | NS |
| Group 2 | 29.3 [13.1] | 24.7 [15.5] | NS |

Group 1 = LS
Group 2 = OS

Data are means with standard deviations in brackets unless otherwise indicated

*WBC* white blood cell, *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *TBIL* total bilirubin, *NS* not significant

Surg Endosc (2011) 25:3791–3797

# What about splenectomy at the time of transplant?

- Splenectomized patients had significantly increased OR time (842 minutes vs. 786 minutes, P = 0.024)
- Trend towards increase blood loss (7465 gram vs. 6195 gram, P = 0.082) but not bleeding-related reoperation (6.9% vs. 4.3%, P = 0.414), post-transplantation bacteremia (38.8% vs. 48.3%, P = 0.185) (all patients vaccinated appropriately)

**Table 5.** Three years post-transplantation outcomes of splenectomized and spleen-preserved patients matched using pr

| | | | |
|---|---|---|---|
| ALT (U/l) | 16 (11–27) | 18 (13–38) | 0.132 |
| Total bilirubin (mg/dl) | 0.7 (0.6–0.9) | 0.8 (0.6–1.1) | 0.055 |
| Albumin (g/dl) | 4.1 (3.8–4.2) | 4.1 (3.8–4.3) | 0.247 |
| PLT count < 150.000/µl (%) | 2 (2.63%) | 33 (42.3%) | **<0.001** |
| PLT count < 100.000/µl (%) | 1 (1.32%) | 13 (16.7%) | **<0.001** |
| PLT count < 50.000/µl (%) | 1 (1.32%) | 1 (1.28%) | 0.985 |
| WBC count < 5.000/µl (%) | 9 (11.8%) | 39 (50%) | **<0.001** |
| METAVIR score: ≥F2 | 3/42 (7.1%) | 12/45 (26.7%) | **0.022** |

*Transplant International* 2020; 33: 1807–1820

# So what happened?

- Transplant Surgery was to reach out to colleagues at other institutions with more experience in this area than OHSU
- Ultimately, programmatic decision made by Transplant Surgery and Hepatology to list for OLT