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ATA Hotel, Varese (Italy), May 19th 2017

European Experience in Liver Transplantation in HIV-infected patients

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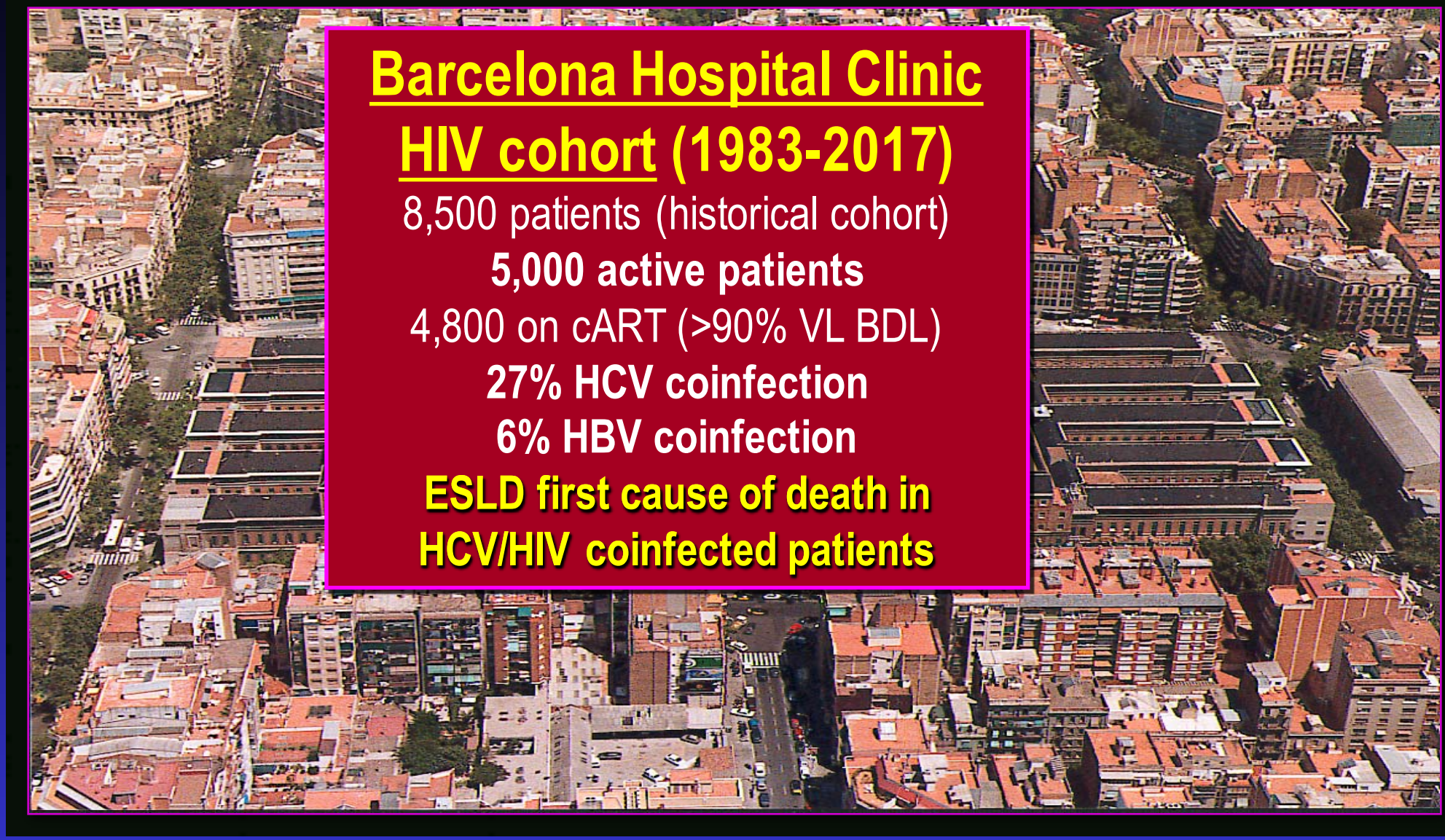


Members of the Hospital Clinic Solid Organ Transplantation in HIV-infected Patients Working Group (Barcelona, Spain)

Infectious Diseases

Liver Transplant

Renal Transplant

Cardiac Transplant

HIV-infected patients with ESOD are routinely evaluated for SOT

Multidisciplinary approach

Prospective evaluation

Social Worker

C. Lanaspa

M. Monrás

M. Tuset

P. Grossi

D. Samuel

CLÍNIC BARCELONA Hospital Universitari

IDIBAPS Institut D'Investigacions Biomèdiques August Pi i Sunyer

UNIVERSITAT DE BARCELONA

fipse fundación para la investigación y la prevención del SIDA en España

RIS Red Española de Investigación en SIDA G03/173 Spanish AIDS Research Network

Evaluation for Liver, Kidney, and Heart Transplantation of Spanish HIV-1–Infected Patients With ESOD

Hosp. Clinic, Barcelona (Spain) between 2000-2017

- **Liver transplantation**
  - No. patients / No. admitted WL: 290 / 75
  - No. transplanted: 32 (11%)
- **Kidney (Pancreas) transplantation**
  - No. patients / No. admitted WL: 30 (3) / 24 (3)
  - No. who underwent transplant: 15 (1) (50%)
- **Heart transplantation**
  - No. patients / No. admitted WL: 4 / 3
  - No. who underwent transplant: 3

European Experience in LT in HIV-infected Patients

Outline

- HIV inclusion criteria for LT
- Natural history of liver transplantation
- Anti-HCV Therapy. Role DAA
- Antiretroviral therapy
- Concluding remarks

HIV Criteria for SOT: European and U.S. Recom

	Spain[1]	A.[4]
C events		
- OIs	Some*	t*
- Neoplasms	No	*
CD4 count		
- OLT	>100	0
- Other SOT	>200	0
VL BDL**	Yes	s

* Spain: TB, PCP or candidasis; USA: Only PML, cryptos iteria.
** If VL was detectable, post-OLT suppression predicted nsion.

[1]Miró, EIMC, 2005; [2]Centro Naz
2005/2006; [4]CCTAT, Am

EACS European AIDS Clinical Society

2018 Guidelines will include a section of SOT in HIV-infection as part of routine clinical care

English

European Experience in LT in HIV-infected Patients

Outline

- HIV inclusion criteria for LT
- Natural history of liver transplantation
- Anti-HCV Therapy. Role DAA
- Antiretroviral therapy
- Concluding remarks

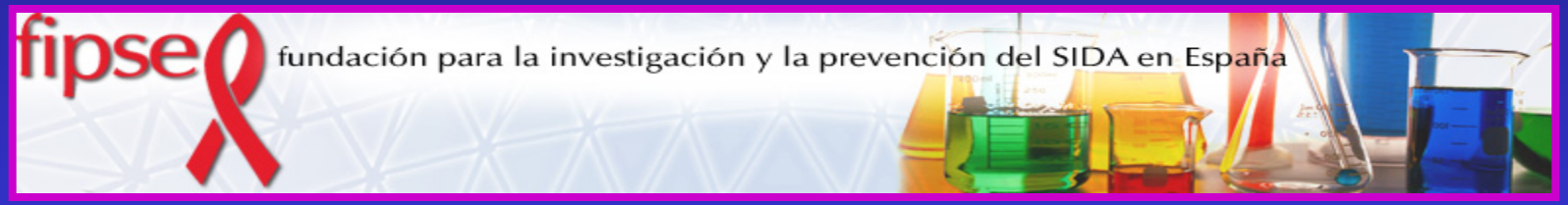
FIPSE-Funded Clinical Trial:
Liver Transplantation (N=250)
in Spanish HIV-Infected Patients
at 23 Spanish Transplant Centers (2002-12)

PI: José M. Miró (H. Clinic, Barcelona, Spain)

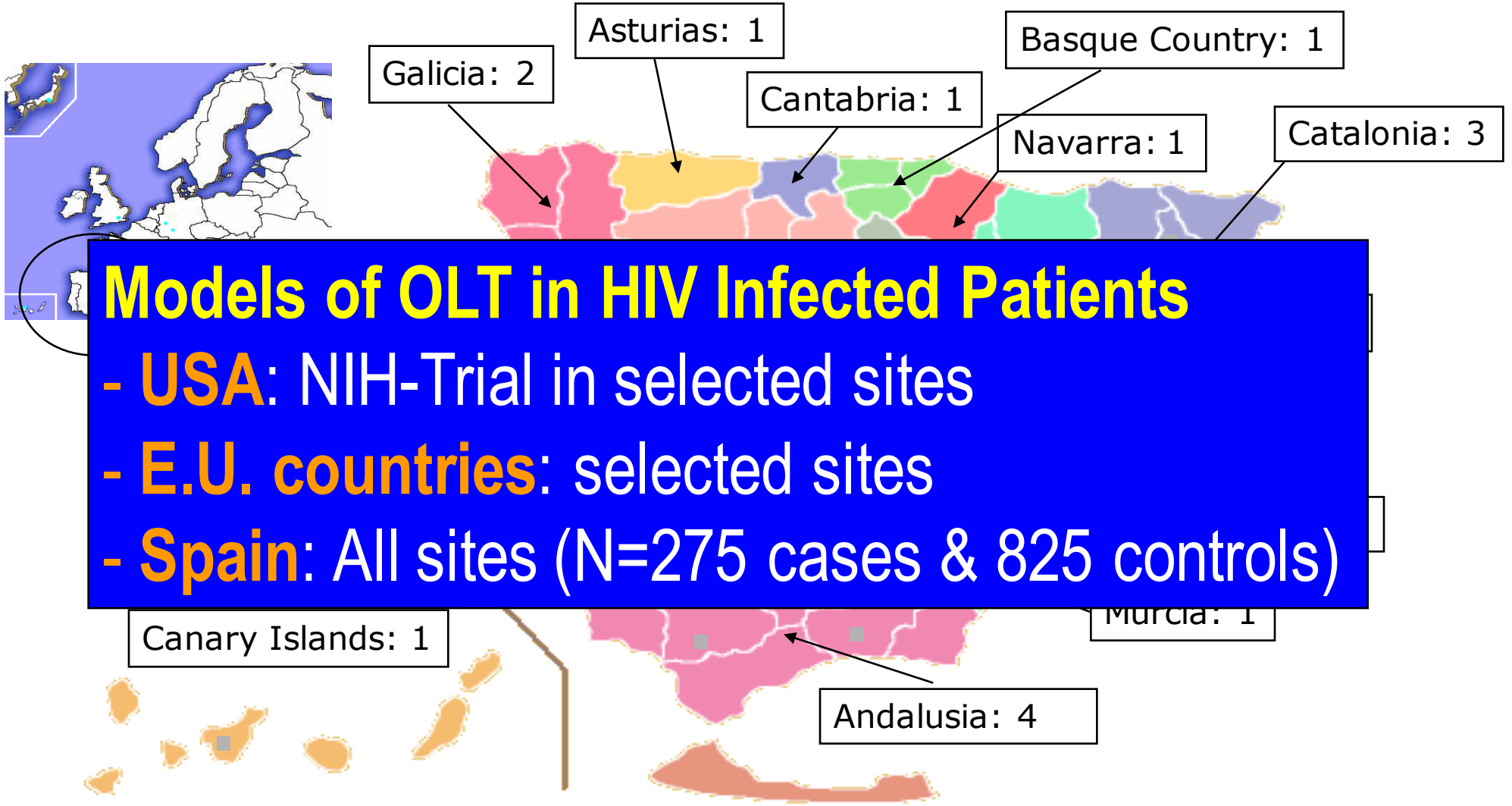
Co-PI: Spanish Transplant Centers

AEC-GESIDA / GESITRA (SEIMC)

SETH / ONT / SPNS (MSC)



Geographic Distribution of the 23 Hospitals Participating in the LT-HIV FIPSE/GESIDA Cohort Study (2002-12)



Models of OLT in HIV Infected Patients

- **USA**: NIH-Trial in selected sites
- **E.U. countries**: selected sites
- **Spain**: All sites (N=275 cases & 825 controls)

American Journal of Transplantation 2012; 12: 1866–1876
Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2012.04028.x

Outcome of HCV/HIV-Coinfected Liver Transplant Recipients: A Prospective and Multicenter Cohort Study

J. M. Miro[a,*], M. Montejo[b], L. Castells[c,d], A. Rafecas[e], S. Moreno[f], F. Agüero[a], M. Abradelo[g], P. Miralles[h], J. Torre-Cisneros[i], J. D. Pedreira[j], E. Cordero[k], G. de la Rosa[l], B. Moyano[m], A. Moreno[a], I. Perez[a], A. Rimola[a,d] and the Spanish OLT in HIV-Infected Patients Working Group investigators†

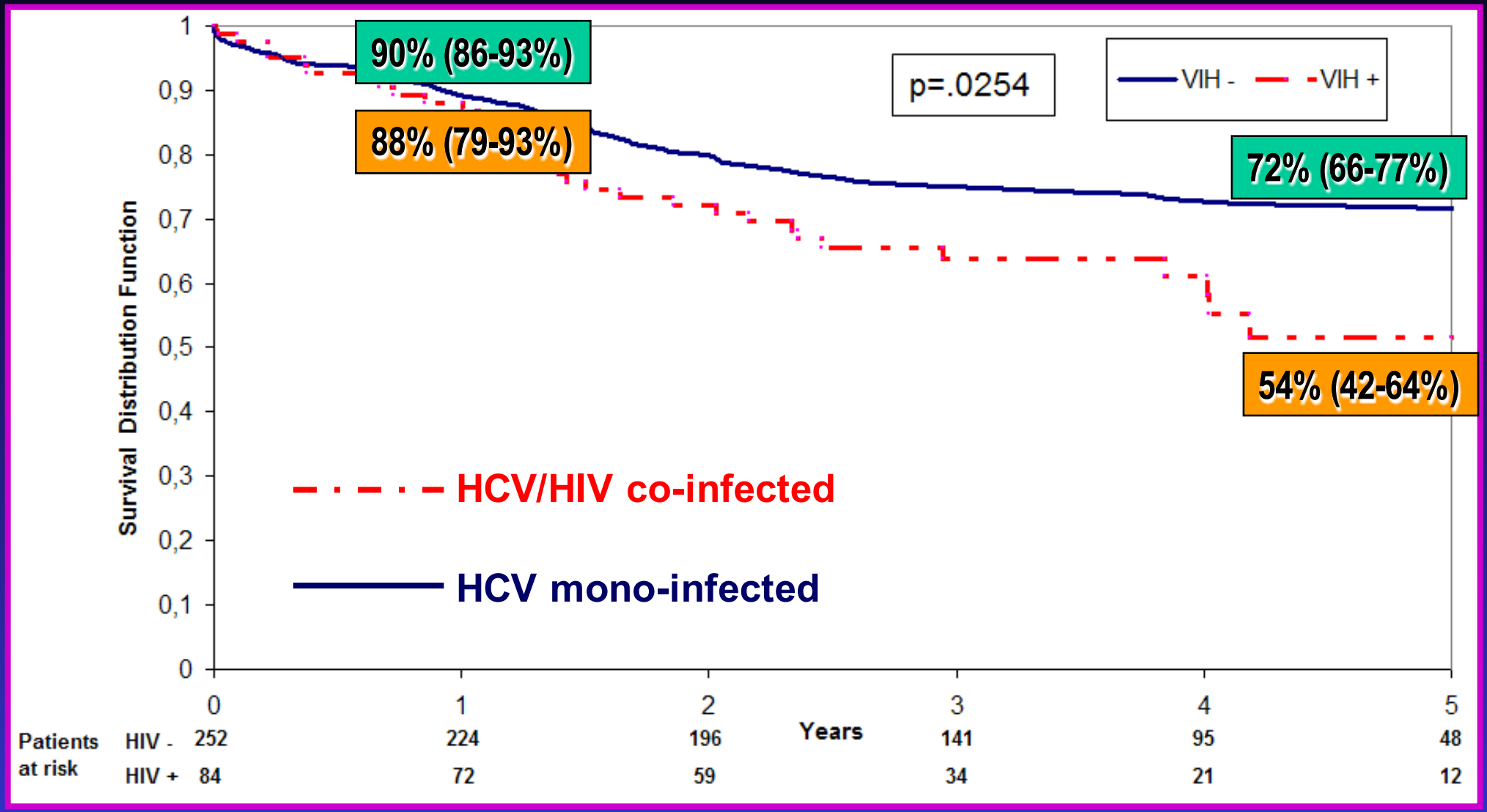
[a] *Hospital Clinic—IDIBAPS, University of Barcelona, Barcelona, Spain*
[b] *Hospital Universitario de Cruces, Bilbao, Spain*
[c] *Hospital Universitari Vall d'Hebrón, Barcelona, Spain*

with <1 liver transplantation/year in HIV-infected patients) that allowed us to identify a subset of 60 (71%) patients with a similar 5-year prognosis (69% [95% CI, 54–80]) to that of HCV-monoinfected recipients. In conclusion, 5-year survival in HCV/HIV-coinfected liver recipients was lower than in HCV-monoinfected recipients, although an important subset with a favorable prognosis was identified in the former.

Key words: HCV infection, HIV infection, Liver Transplantation, Spain, Survival

Abbreviations: AIDS, acquired immunodeficiency

Case (N=84) - Control (N=252) Study: Survival After OLT in HCV-Infected Patients According to HIV Status



Cause of Death in HCV-infected LT Recipients

Spanish prospective, multicenter, cohort study (FIPSE Study)

Preliminary results (2002-2006; end of follow-up: 2010)

Cause of death	HCV/HIV (n = 84)	HCV (n = 252)	p value
HCV recurrence	**18 (21%)**	**31 (12%)**	**0.049**
Infection	7 (8%)	15 (6%)	NS
Tumors	3 (4%)	4 (2%)	NS
Technical problems	0	6 (2%)	NS
Other	8 (10%)	19 (8%)	NS

Miro JM on behalf FIPSE. Am J Transpl; 2012; 12:1866-76

RESULTS

Predictors of post-OLT mortality in HCV/HIV co-infected patients

All variables: pre-, peri-, and post-OLT

	p value	Hazard ratio (95% CI)
HCV genotype 1	0.008	2.98 (1.32-6.76)
Donor risk index	<0.001	9.48 (2.75-32.73)
Negative plasma HCV RNA viral load at any time (before or after OLT)	0.009	0.14 (0.03-0.62)

Recipient age, gender, BMI, CD4, MELD & Child scores, HBV coinfection, Center with <1 OLT in HIV-infected patients/year, donor age, non-craneal trauma as cause of donor brain death, acute and chronic rejection, SVR to anti-HCV Rx , Pre-OLT and post-OLT peak HCV viral load, severe infection, invasive fungal infection and HCC were not associated with death.

Miro JM on behalf the FIPSE cohort. Am J Transplant. 2012.

RESULTS

Predictors of post-OLT mortality in HCV/HIV co-infected patients

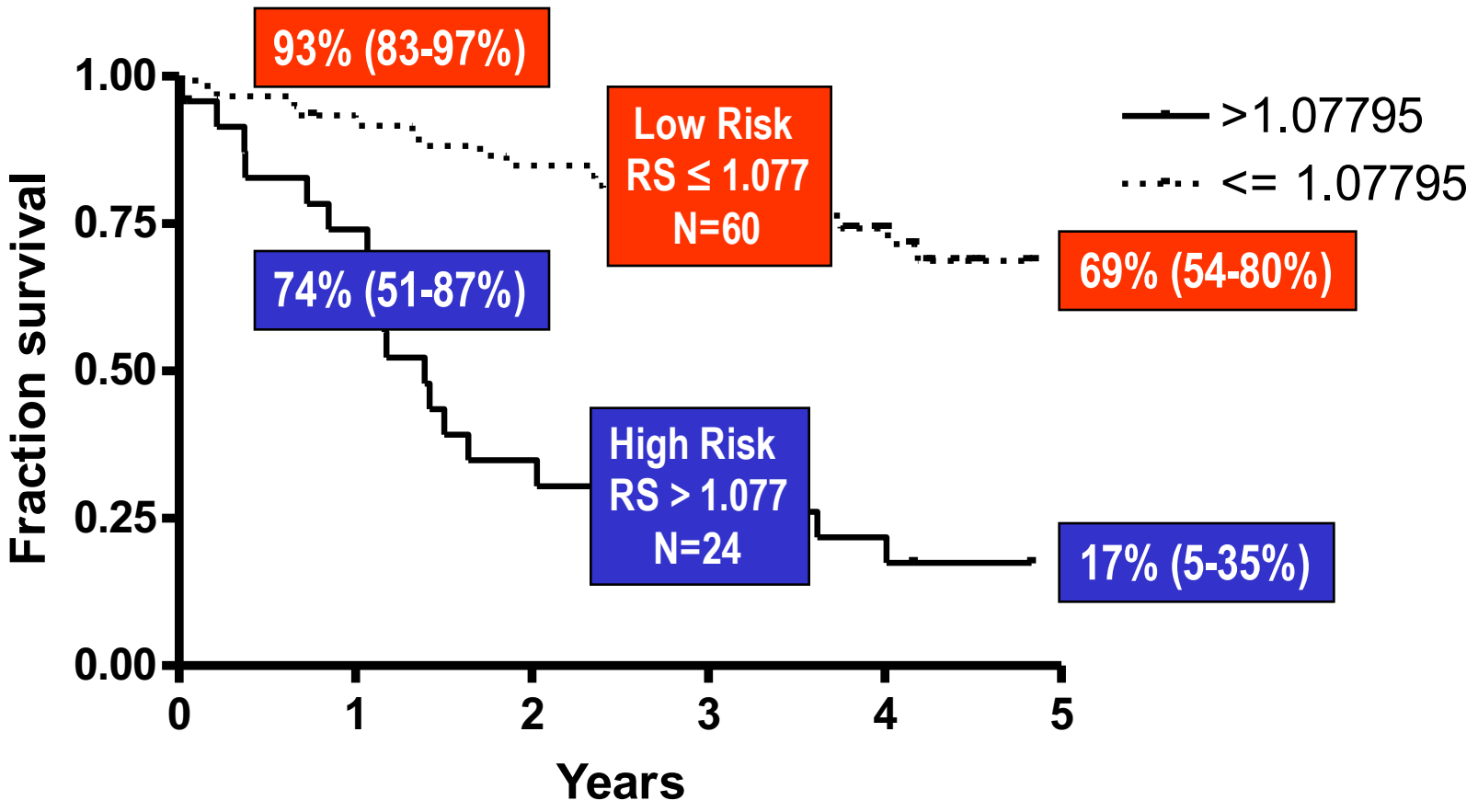
Only Pre-OLT variables

	p value	Hazard ratio (95% CI)
Pre-OLT MELD score	0.023	1.06 (1.02-1.11)
Center with <1 OLTs in HIV+/year	0.009	2.82 (1.30-6.94)
HCV genotype 1	0.029	2.27 (1.09-4.76)

Risk score for mortality = exp [0.81966* if HCV Genotype 1 + 0.05748 * Pre-OLT MELD + 1.03540 if Center < 1 OLT in HIV+/year]

Miro JM on behalf the FIPSE cohort. Am J Transplant. 2012.

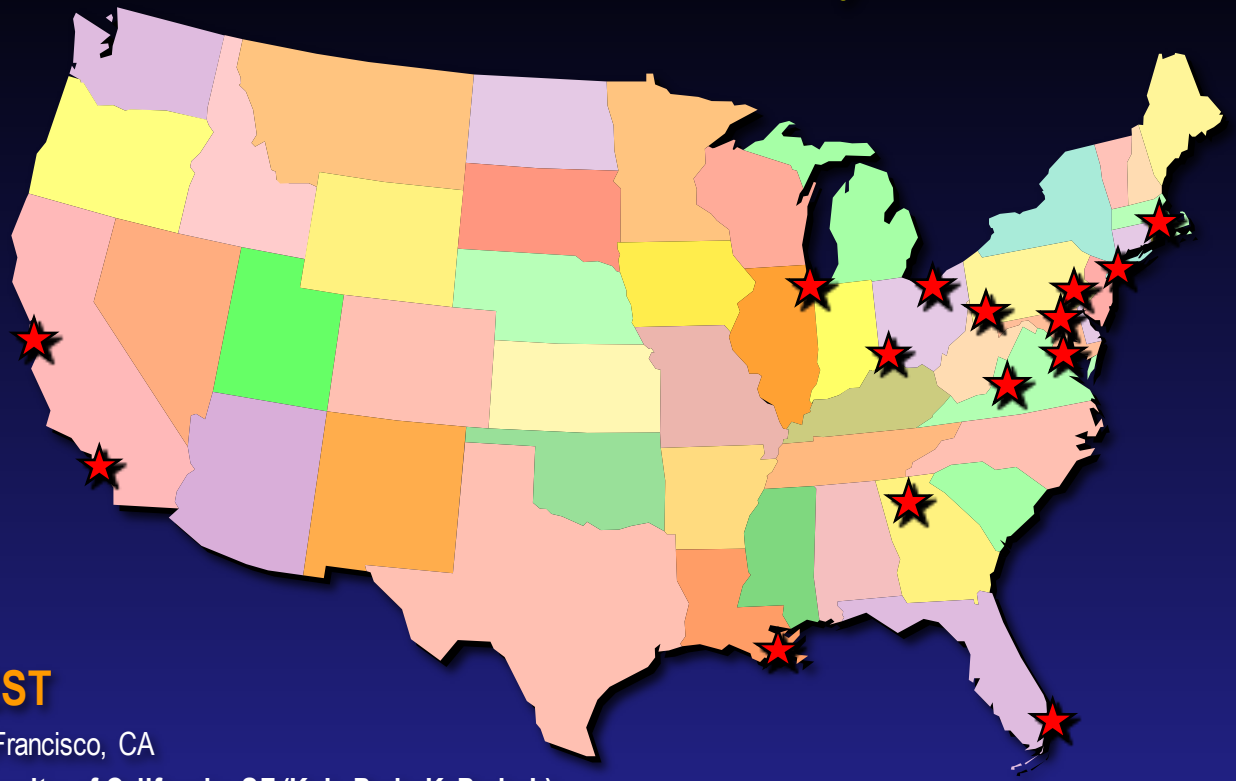
Post-OLT Survival in HCV/HIV Co-infected Patients According to their Risk Score (RS) for Mortality



>1.07795	24	17	8	6	5	2
<= 1.07795	60	55	50	45	29	16

Miro JM on behalf the FIPSE cohort. Am J Transplant. 2012.

NIH TRIAL 150 Kidney and 125 Liver Transplants



NORTHEAST

Baltimore, MD

Johns Hopkins (K,L)

University of Maryland (K)

Boston, MA

Beth Israel Deaconess Medical Center (K, L)

New York, NY

Mt. Sinai School of Medicine (K, L, Peds K)

Columbia University (L, Peds L)

Philadelphia, PA

Drexel University (L)

University of Pennsylvania (K, L)

Pittsburgh, PA

University of Pittsburgh (K, L)

Washington, D.C.

Washington Hospital Center (K)

Georgetown Medical Center (K, L)

WEST

San Francisco, CA

University of California, SF (K, L, Peds K, Peds L)

Los Angeles, CA

Cedars-Sinai (L)

MID-WEST

Chicago, IL

University of Chicago (K, L, Peds K, Peds L)

Rush University (K, L)

Northwestern (K, L)

Cincinnati, OH

University of Cincinnati (K, L)

Cleveland, OH

Cleveland Clinic (K, L)

SOUTHEAST

Atlanta. GA

Emory University (K)

Charlottesville, VA

University of Virginia (K,L)

Miami, FL

University of Miami (K)

New Orleans, LA

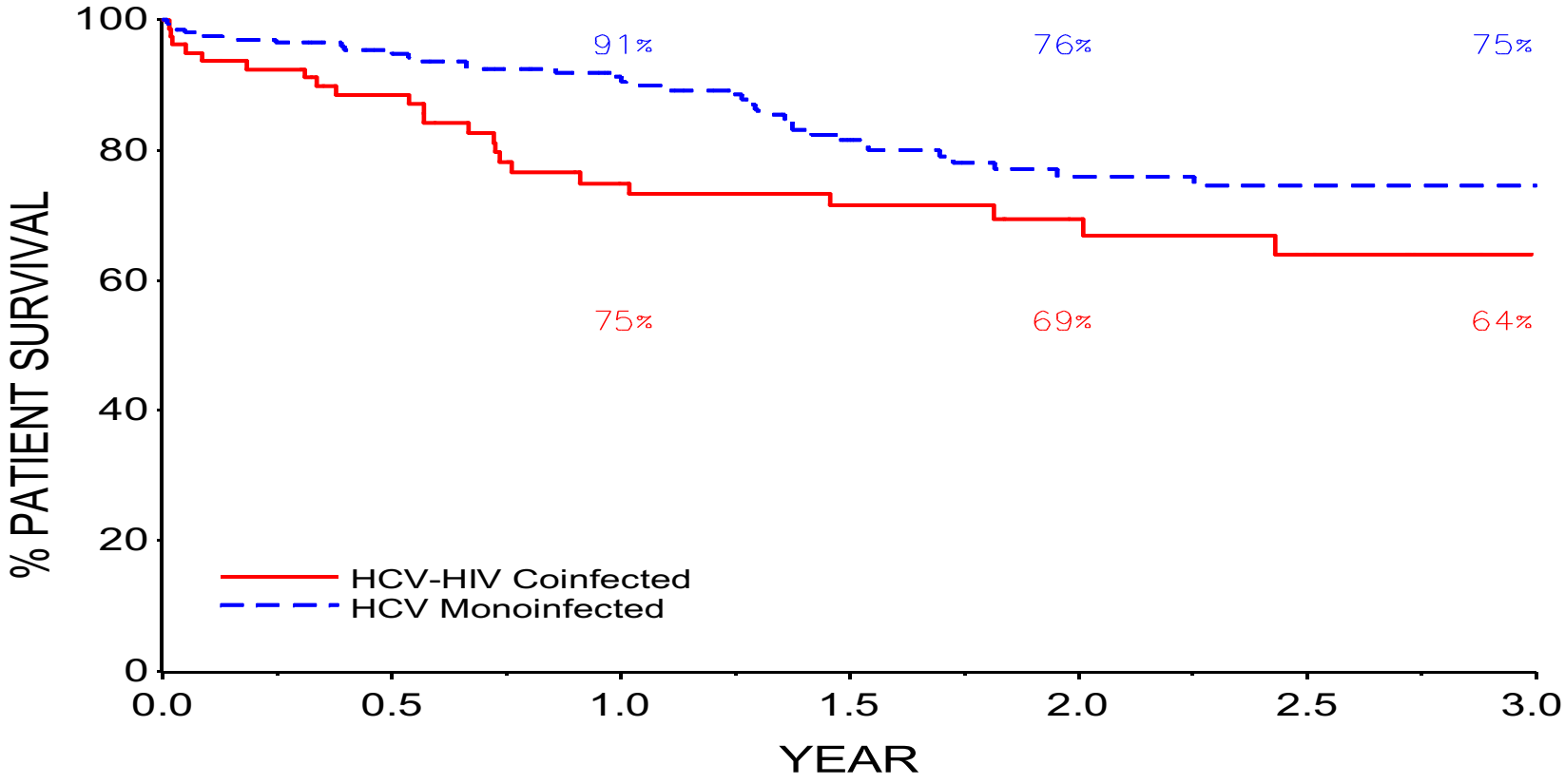
Tulane (K, L, Peds K, Peds L)

Preliminary HCV-HIV Analysis

- HCV-HIV co-infected (n=81) vs HCV mono-infected (n=213)
  - Controls: HCV mono-infected recipients matched on study site; single vs dual organ transplant; HCC
- Predictors of patient and graft survival

Terrault et al, Liver Transplantation. 2012

Patient Survival: HCV



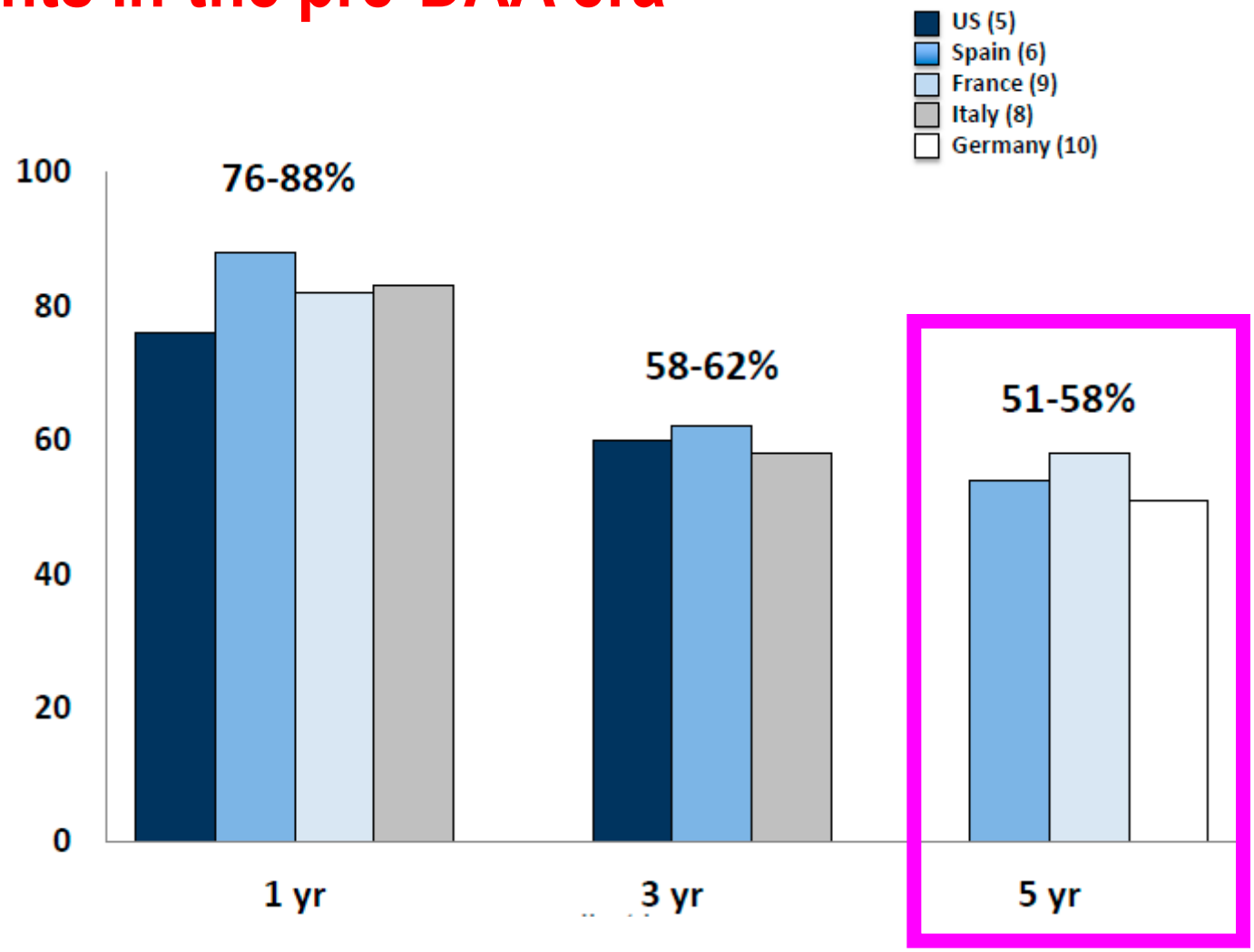
HCV mono-infected	N=135	N=67	N=22
HCV-HIV co-infected	N=46	N=28	N=14

Mortality Predictors in HCV/HIV co-infected Recipients in USA

Predictor Multivariate Analysis	Hazard Ratio (95% CI)	P value
Dual Kidney-Liver	5.5 (1.8, 16.9)	0.003
HCV+ Donor	4.5 (1.8,11.2)	0.001
BMI at Listing <21	2.7 (1.0, 7.3)	0.05
Treated Acute Rejection	2.9 (1.2, 7.0)	0.02

Terrault et al, Liver Transplantation. 2012

Cumulative Patient Survival at 5 yr. in HIV-HCV Infected LT Recipients in the pre-DAA era



Stock P & Terrault N. Hepatology, 2015.

Survival of OLT in HCV/HIV-Coinfected Recipients in the pre-DAA era

Lower than HIV-negative recipients but still acceptable

Is liver transplantation (LT) feasible in HIV-infected patients with hepatocellular carcinoma (HCC)?

Limited data

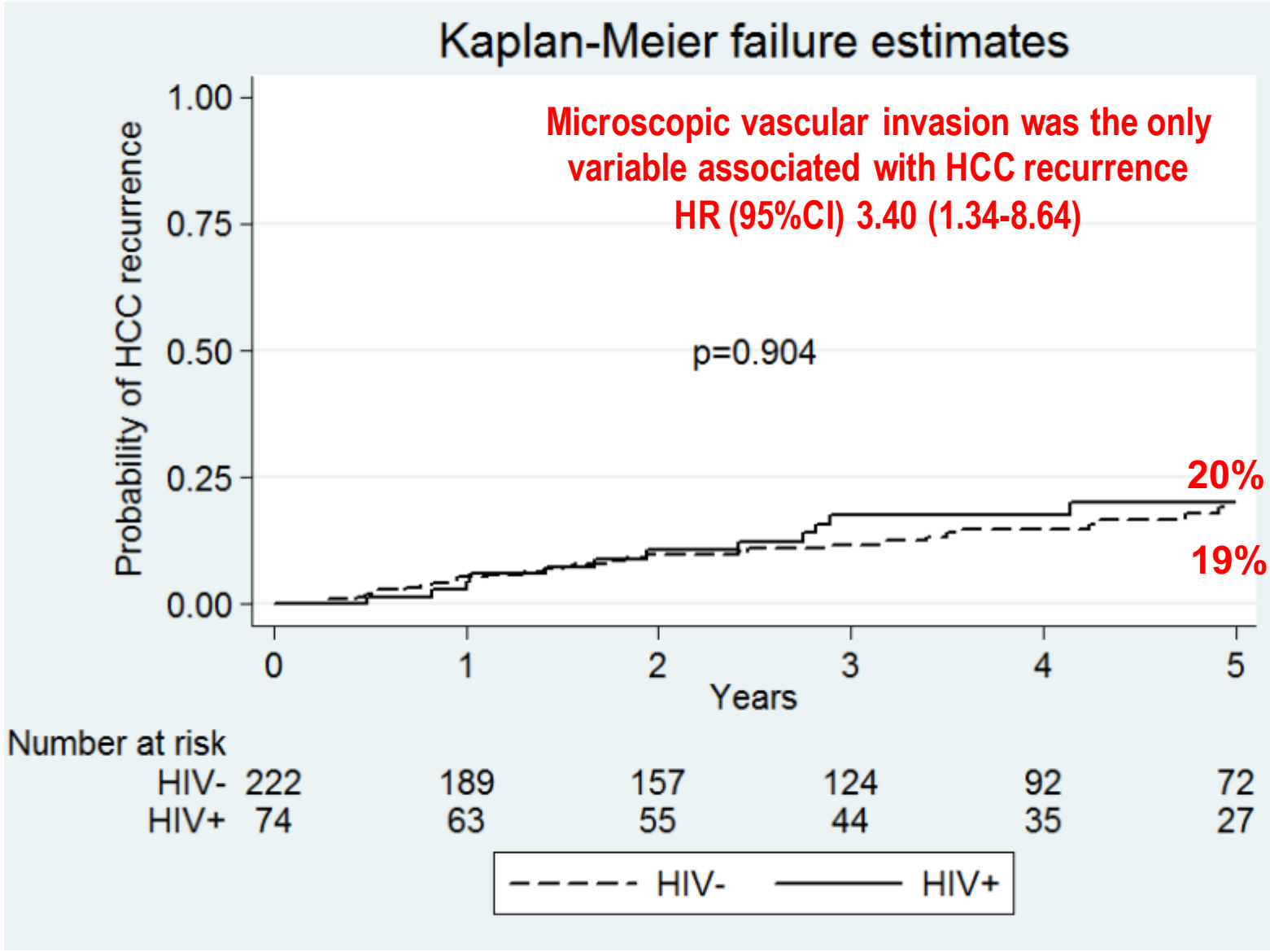
HEPATOLOGY
Official Journal of the American Association for the Study of Liver Diseases

Human Immunodeficiency Virus Infection Does Not Worsen Prognosis of Liver Transplantation for Hepatocellular Carcinoma

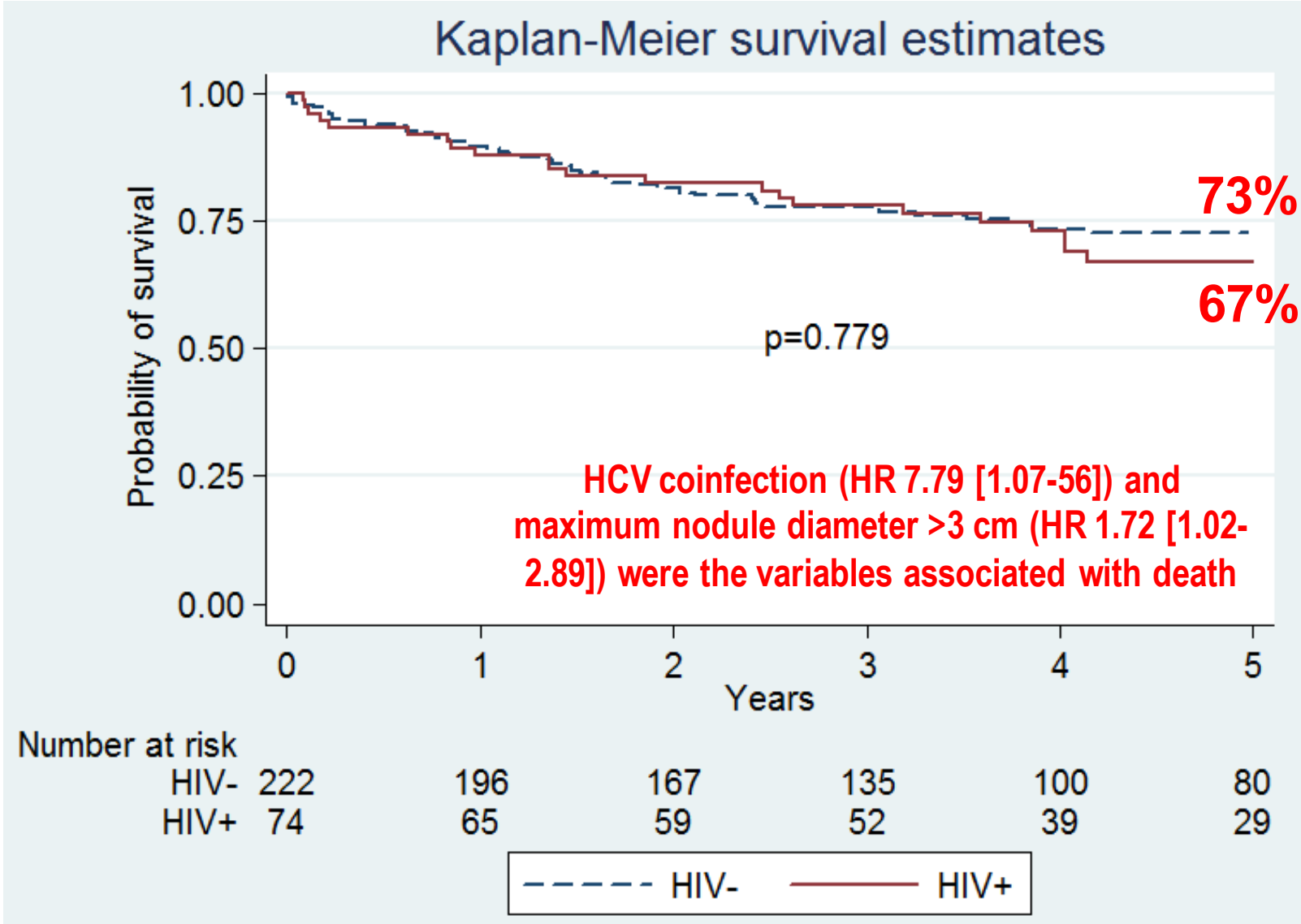
Fernando Agüero,[1] Alejandro Forner,[2,3] Christian Manzardo,[1] Andres Valdivieso,[4,5] Marino Blanes,[6] Rafael Barcena,[7] Antoni Rafecas,[8] Lluis Castells,[3,9] Manuel Abradelo,[10] Julian Torre-Cisneros,[11] Luisa Gonzalez-Dieguez,[12] Magdalena Salcedo,[13] Trinidad Serrano,[14] Miguel Jimenez-Perez,[15] Jose Ignacio Herrero,[3,16,17] Mikel Gastaca,[4,5] Victoria Aguilera,[3,6] Juan Fabregat,[8] Santos del Campo,[7] Itxarone Bilbao,[9] Carlos Jimenez Romero,[10] Asuncion Moreno,[1] Antoni Rimola,[3,18] Jose M. Miro[1] and the FIPSE Investigators

Hepatology. 2016;63:488-498

Similar HCC recurrence in LT recipients with and without HIV infection



Similar survival after LT in patients with and without HIV infection



Is liver retransplantation (reLT) feasible in HIV-infected recipients?

Limited data

American Journal of Transplantation 2012; 12: 2465–2476
Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2012.04142.x

Liver Retransplantation in HIV-Infected Patients: A Prospective Cohort Study

M. Gastaca[a,†], F. Aguero[b,†], A. Rimola[c,d], M. Montejo[a], P. Miralles[e], R. Lozano[f], L. Castells[d,g], M. Abradelo[h], M. de la Mata[d,i], F. San Juan Rodríguez[j], E. Cordero[k], S. del Campo[l], C. Manzardo[c], J. O. de Urbina[a], I. Pérez[c], G. de la Rosa[m], J. M. Miro[c,*] and the FIPSE OLT-HIV investigators[n]

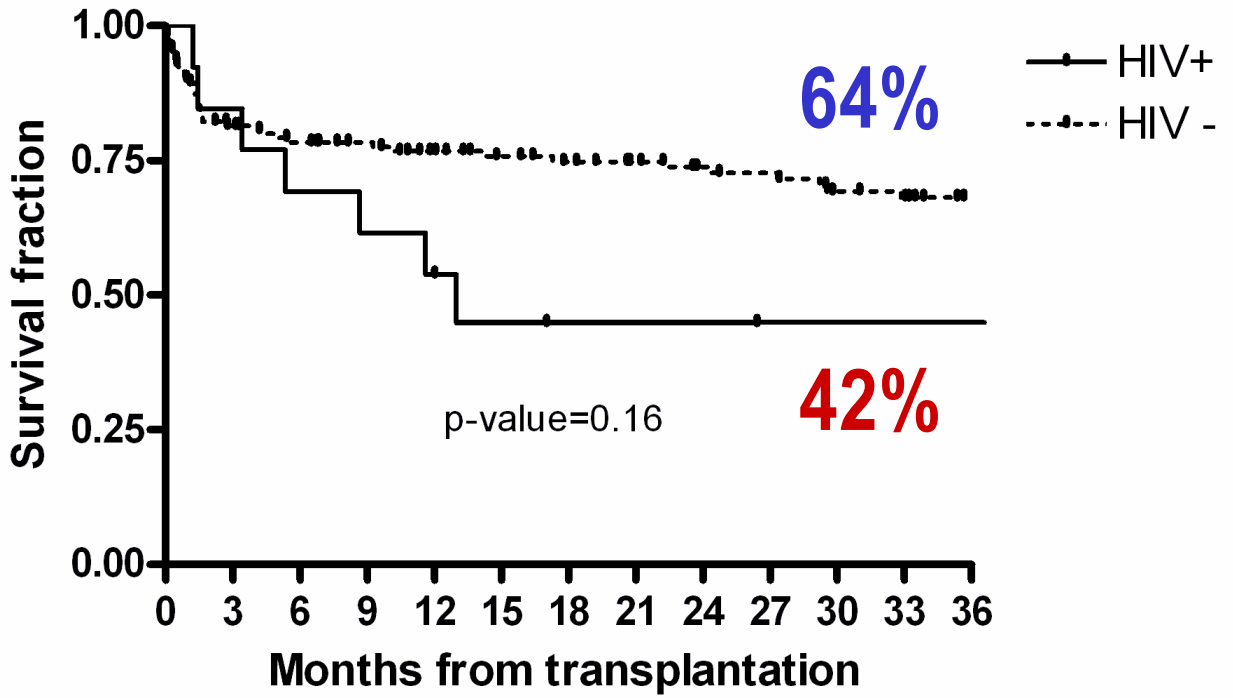
[a] *Hospital Universitario de Cruces, University of the Basque Country, Bilbao, Spain*
[b] *Training Unit in Preventive Medicine and Public Health, Parc de Salut Mar-UPF-ASPB, Barcelona, Spain*
[c] *Hospital Clinic-IDIBAPS, University of Barcelona, Barcelona, Spain*
[d] *CIBEREHD, Spain*
[e] *Hospital General Universitario Gregorio Marañón, Madrid, Spain*
[f] *Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain*

retransplantation showed better 3-year survival probability (80% and 67%, respectively), similar to that in their respective HIV-negative counterparts (72% and 70%). In HIV-infected and HIV-negative patients, 3-year survival probability in those with positive HCV RNA at retransplantation was 22% versus 65% (p = 0.008); in those with early retransplantation, 3-year survival probability was 25% versus 56% (p = 0.282). HIV infection was controlled with antiretroviral therapy after retransplantation. In conclusion, HIV-infected patients taken as a whole have unsatisfactory survival after liver retransplantation, although patients with undetectable HCV RNA at retransplantation or undergoing late retransplantation show a more favorable outcome.

Key words: Chronic rejection, HBV infection, HCV infection, HCV recurrence, HIV infection, liver retransplantation, primary-graft nonfunction, Spain, survival, vascular thrombosis.

Probability of survival after reLT in HIV-infected Recipients

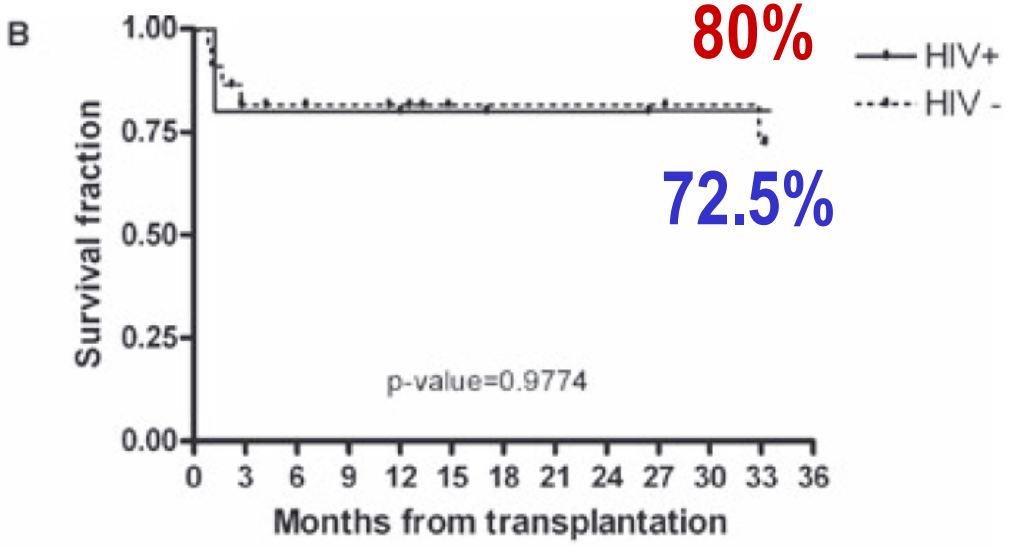
Gastaka M on behalf the FIPSE cohort. Am J Transplant. 2012; 2465-78.



Months	0	1	3	12	24	36
HIV -	157	126	108	87	68	52
HIV+	14	13	11	6	4	3

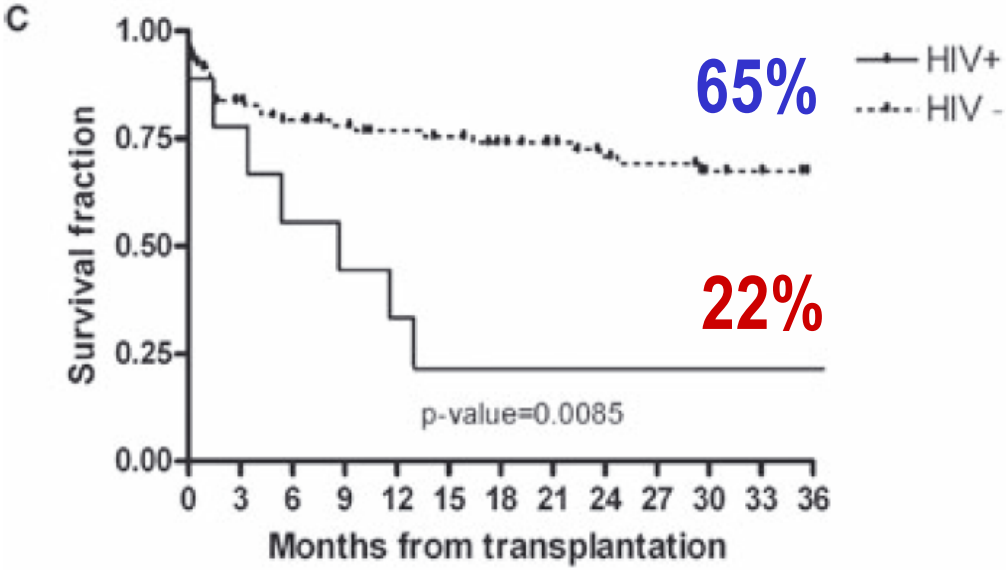
Probability of survival in patients with negative HCV RNA (B) and in positive HCV RNA (C) at reLT

HCV RNA -



Months	0	1	3	12	24	36
HIV -	23	21	16	13	10	7
HIV+	5	5	4	4	2	1

HCV RNA +



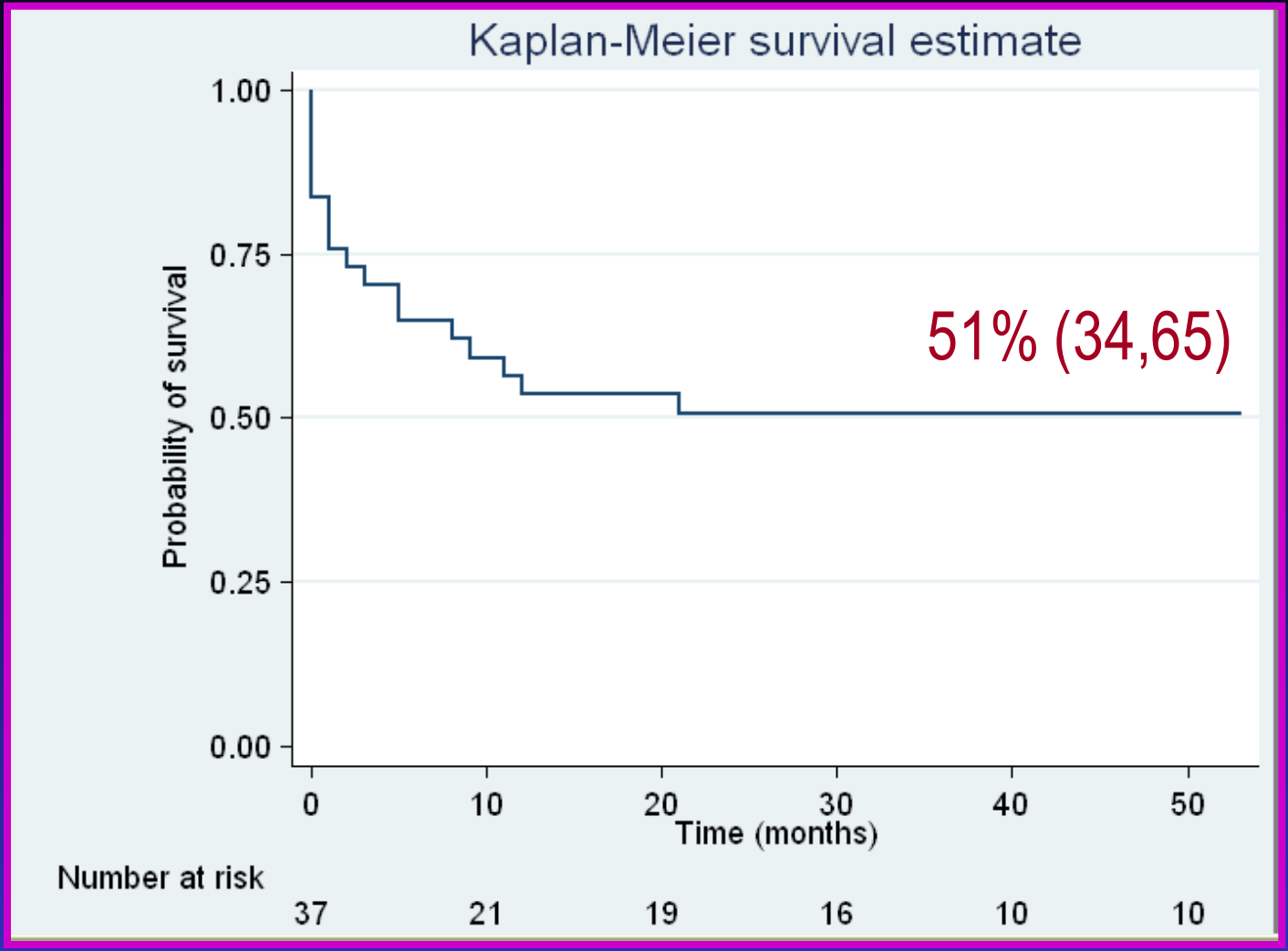
Months	0	1	3	12	24	36
HIV -	100	84	74	59	44	34
HIV+	9	8	7	3	2	2

Gastaka M on behalf the FIPSE cohort. Am J Transplant. 2012; 2465-78.

NEAT 023: Patients with Liver Retransplantation (reLT) According to the Participant Country (1997-2012)

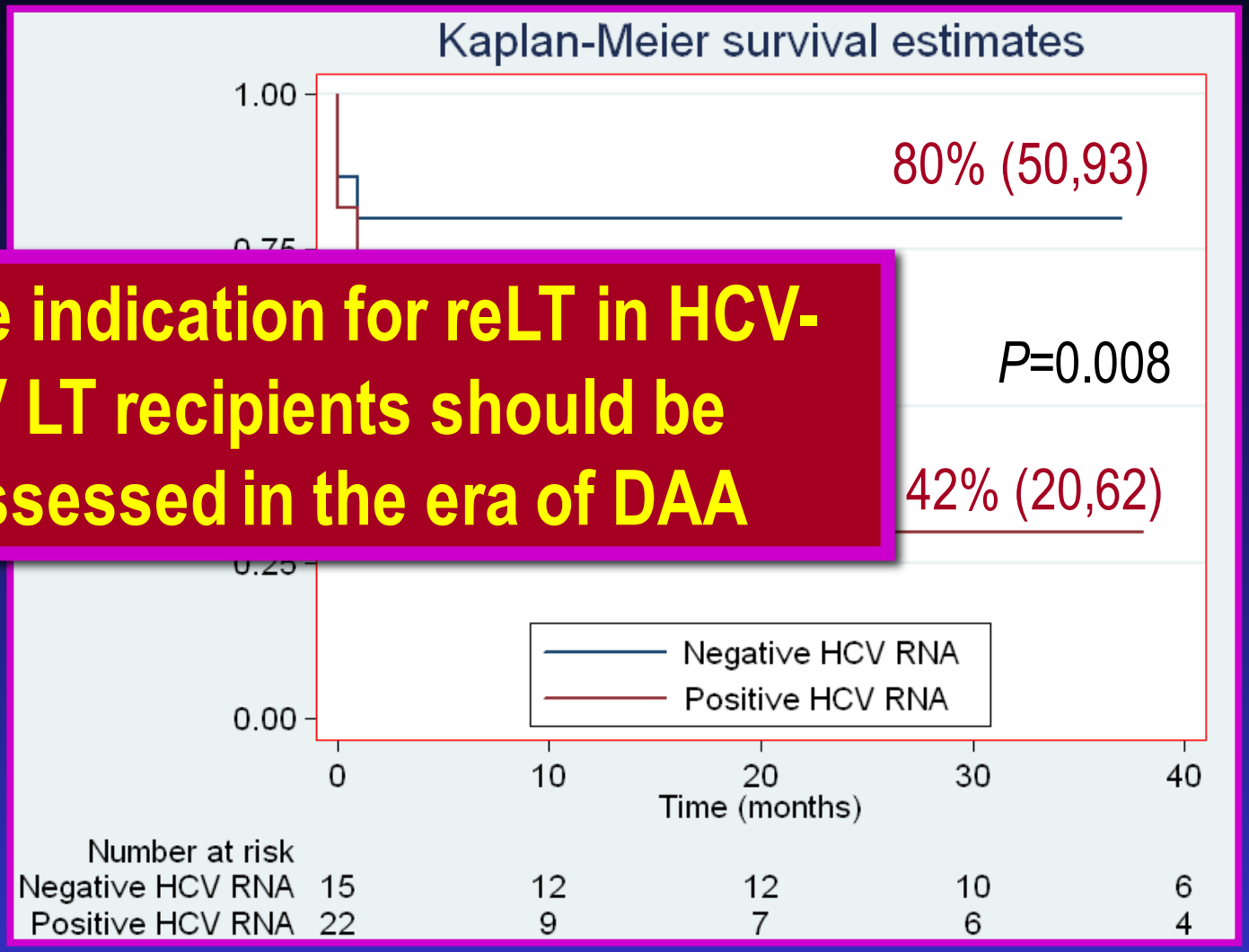
	Number Primary LT	Number reLT (%)
Spain	270	14 (5)
USA	125	9 (7)
Italy	118	5 (4)
Germany	30	4 (13)
UK	24	2 (8)
Argentina	10	1 (11)
Portugal	13	1 (8)
Switzerland	10	1 (10)
Total	600	37 (6)

Overall patient survival rate after reLT



Agüero F, et al. Am J Transplant, 2016.

Patient survival rates according to HCV RNA status at reLT



→ The indication for reLT in HCV-HIV LT recipients should be reassessed in the era of DAA

Agüero F, et al. Am J Transplant, 2016

European Experience in LT in HIV-infected Patients

Outline

- HIV inclusion criteria for LT
- Natural history of liver transplantation
- Anti-HCV Therapy. Role DAA
- Antiretroviral therapy
- Concluding remarks

What is the efficacy of Peg-INF plus RBV for treating recurrent HCV after OLT in HIV/HCV-coinfected recipients?

Very low for HCV GT 1/4

Limited data with DAAs

Efficacy of anti-HCV Rx in HCV/HIV Coinfected Recipients: The NIH Cohort (N=39)

- Peg-INF+RBV was started in 39 of 89 HCV-HIV OLT recipients (44%).
- Rates of SVR according to HCV genotypes:

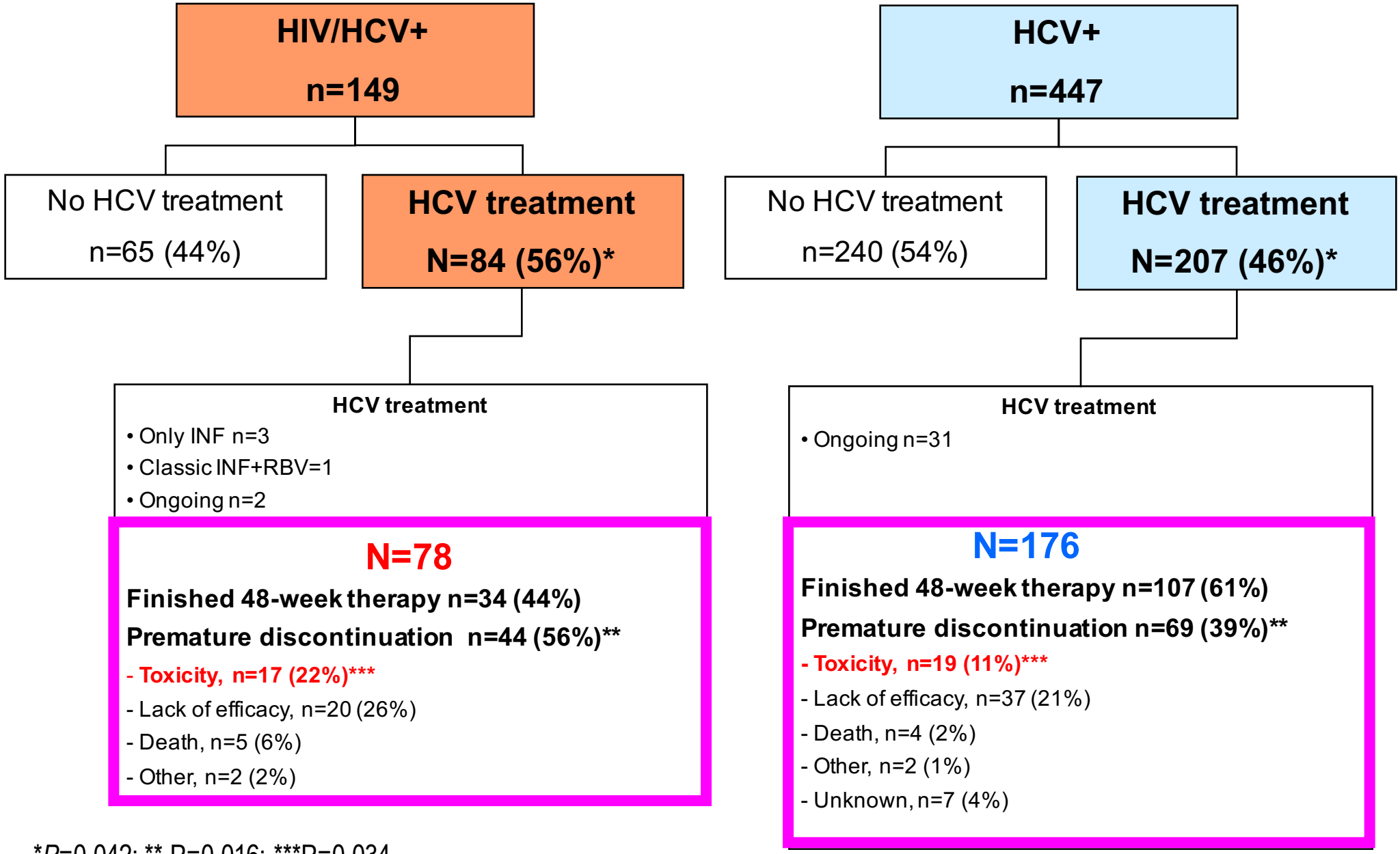
Modified ITT analysis

Overall	Genotype 1	Genotype Non-1
N=37	N=31	N=6
5 (14%)	3 (10%)	2 (33%)

SVR = Sustained response.

Terrault N et al. Am J Transplant. 2014 Mar 17. doi: 10.1111/ajt.12668. [Epub ahead of print]

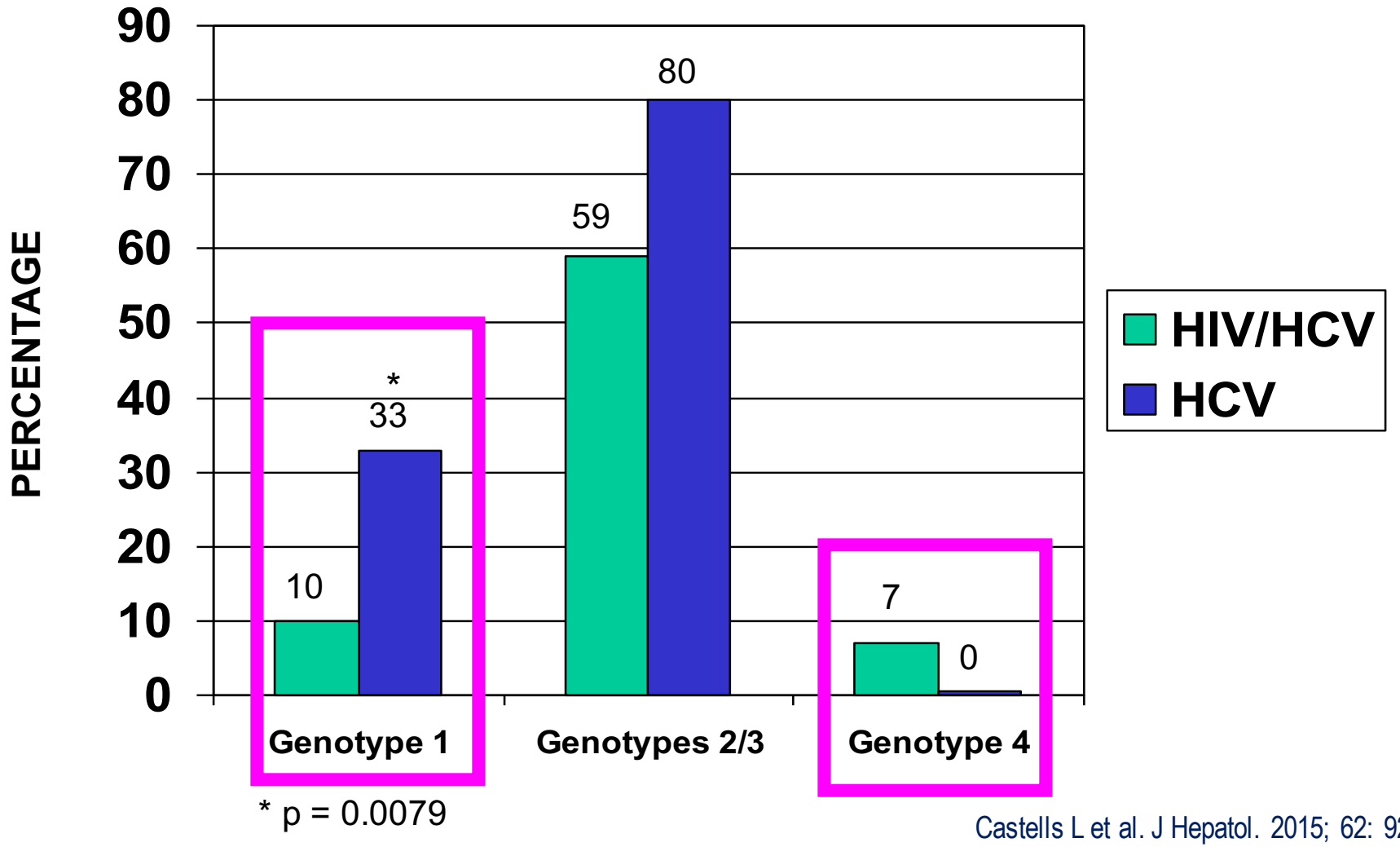
Spanish Cohort (Castells L, J Hepatol, 2015)



*P=0.042; ** P=0.016; ***P=0.034

Virological Response (II)

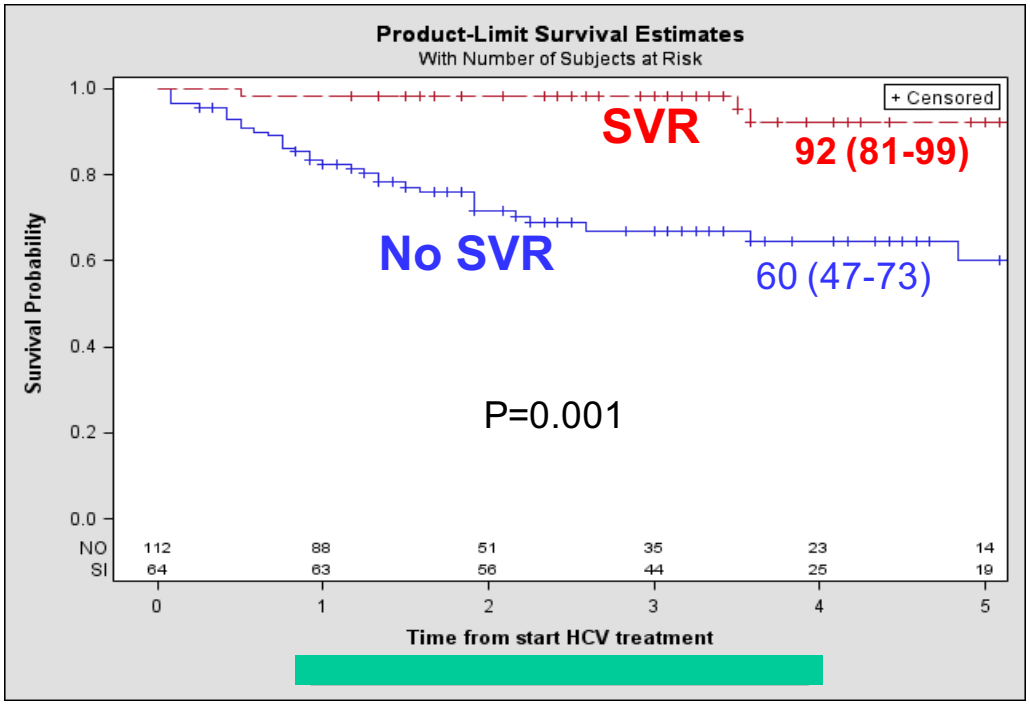
SVR according to genotype



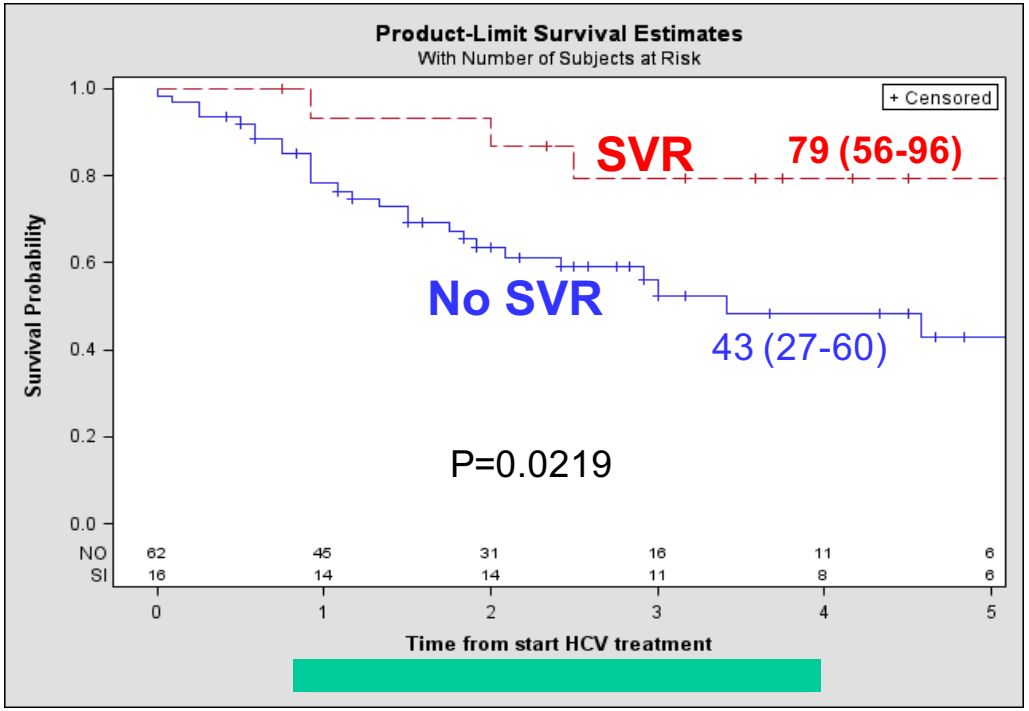
Castells L et al. J Hepatol. 2015; 62: 92–100

Survival After Anti-HCV Therapy

HCV-monoinfected patients



HCV/HIV-coinfected patients



Castells L et al. J Hepatol. 2015; 62: 92–100

What is the efficacy of therapy with new DAAs for treating recurrent HCV infection after OLT in HCV-monoinfected recipients?

It seems similar to that seen in HIV-negative recipients

Studies with Sofosbuvir-based anti-HCV Therapy to Treat HCV Recurrence in HCV/HIV LT Recipients

	N. cases	Fibrosis stage	SVR12 rates
US, single center[1]	9	≤F2	87.5%
Europe, multicenter[2]	20	F3/F4	89%
Spain, single center[3]	11	F3/F4	100%

1. Grant JL et al. AIDS 2016, 30:93–98; 2. Campos-Varela I et al Aliment Pharmacol Ther. 2016, on line;
3. Londoño M et al. JAC 2016 submitted.

Treatment of severe recurrent HCV after LT in HIV-infected patients using Sofosbuvir-based therapy*

Campos-Varela I et al. Aliment Pharmacol Ther. 2016 Apr 21. doi: 10.1111/apt.13629. [Epub ahead of print]

Table 2 | Response (HCV RNA <25 IU/mL) during and after treatment

	Overall (n = 20)	Early severe recurrence (n = 9)	Compensated and decompensated cirrhosis (N = 11)	P-value
During treatment, n (%)*				
At week 4	14/20 (70)	5/9 (56)	9/11 (82)	0.20
At week 12	18/18 (100)	9/9 (100)	9/9 (100)	NA
At week 24	12/12 (100)	6/6 (100)	6/6 (100)	NA
In post-treatment follow-up, n (%)†				
At week 12 (SVR12)	16/18 (89)	7/9 (78)	9/9 (100)	0.13

* HCV RNA <25 IU/mL response during treatment is in patients for whom HCV-RNA results are available.

HCV LLOQ: <25 UI/mL.

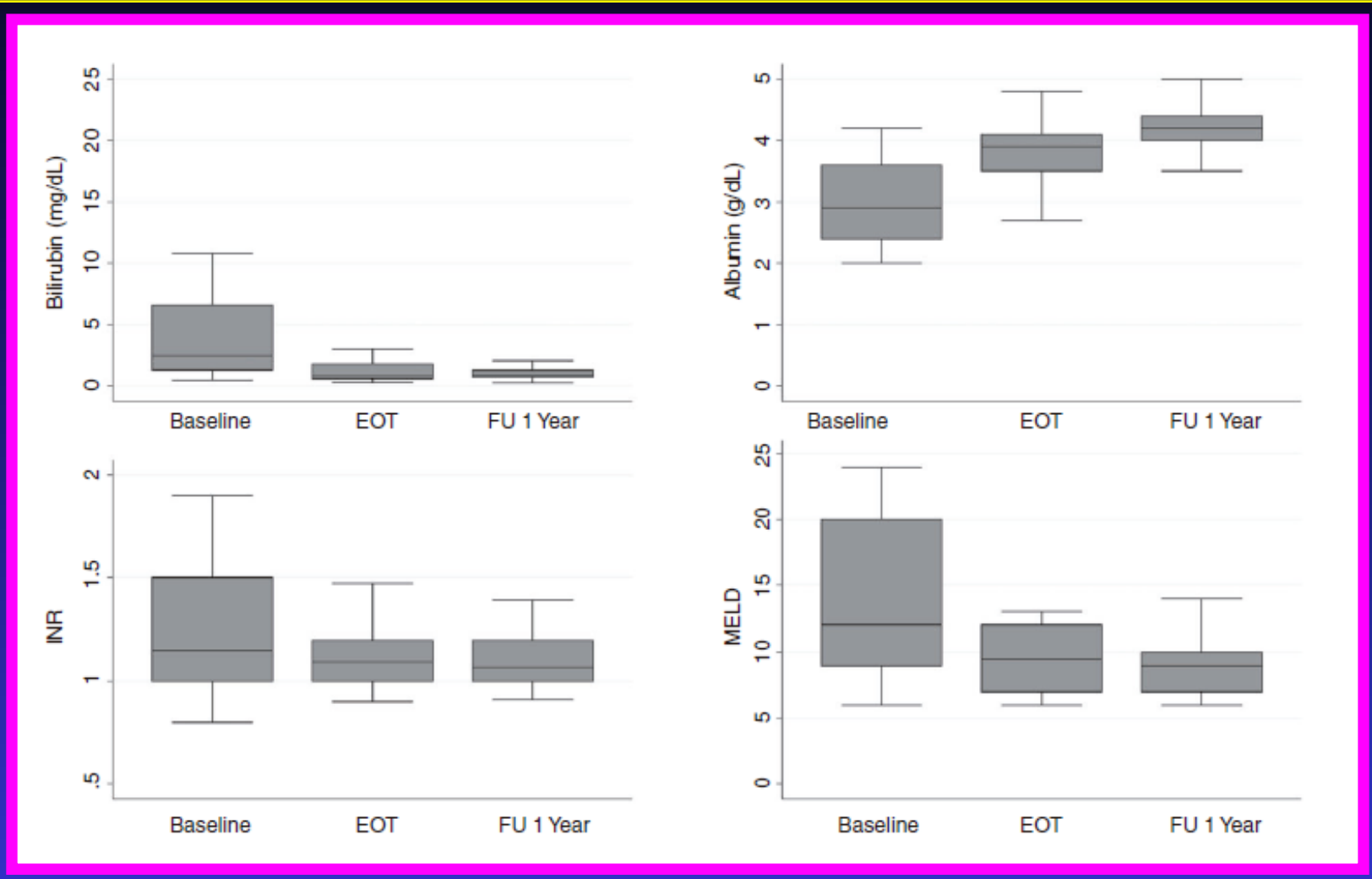
SVR≈90%

† One patient died and one underwent LT during the study and were not included in the efficacy analysis, both with decompensated cirrhosis.

*SOF+RBV, 11; SOF+DCV+RBV, 5; SOF+SIM+RBV, 3 and SOF+RBV+Peg-INF 1 case.
Sofosbuvir was given a median time of 24 weeks

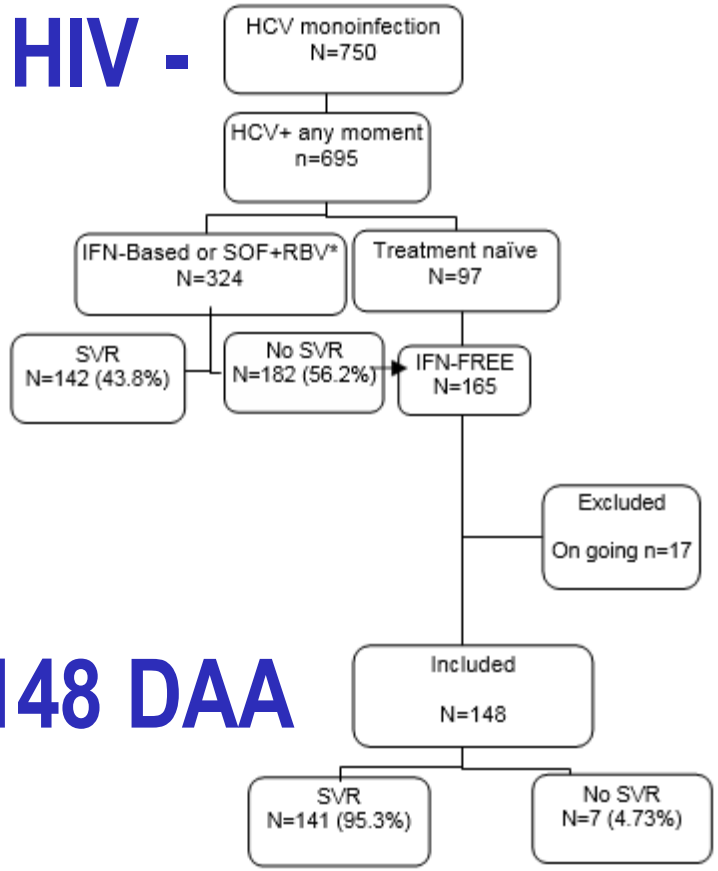
SVR was associated with an improvement of laboratory test scores over time in LT HIV-infected recipients

Campos-Varela I et al. Aliment Pharmacol Ther. 2016 Apr 21. doi: 10.1111/apt.13629. [Epub ahead of print]



Interferon-free therapy is effective and safe for HCV recurrence in HCV/HIV LT recipients: the FIPSE cohort

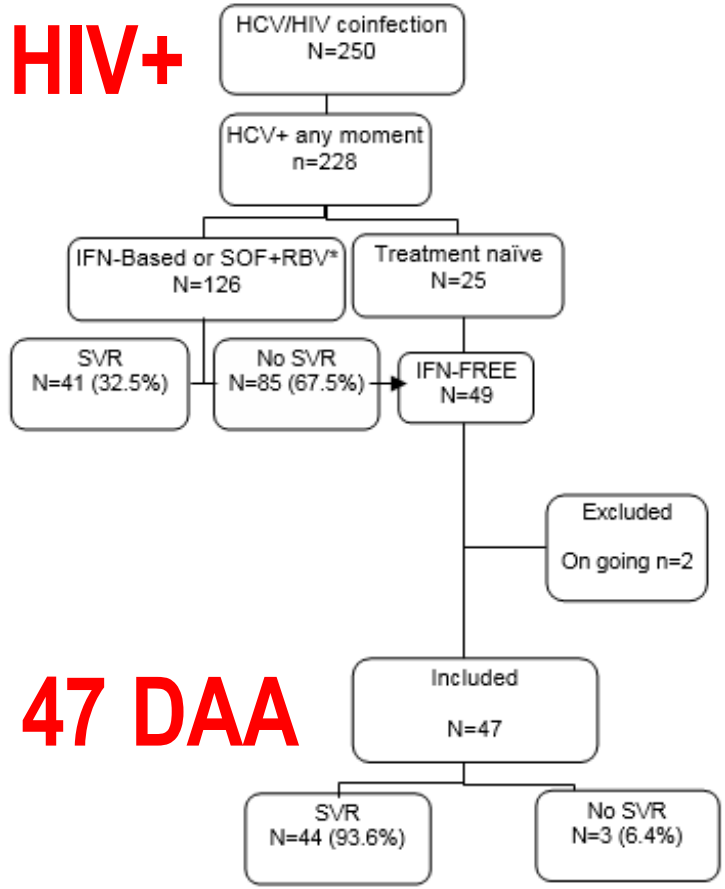
750 HIV -



N = 148 DAA

SVR in HIV- = 95%

250 HIV+



N = 47 DAA

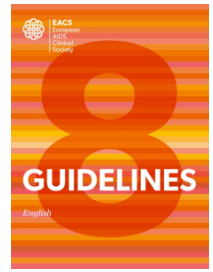
SVR in HIV+ = 94%

Manzardo C et al. CROI 2017 Abstract P#540

European Experience in LT in HIV-infected Patients

Outline

- HIV inclusion criteria for LT
- Natural history of liver transplantation
- Anti-HCV Therapy: Role DAA
- Antiretroviral therapy
- Concluding remarks



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ART Panel Chair: José M. Gatell Barcelona
ART Panel Vice-Chair: Anton Pozniak London
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Initial Combination Regimen for ART-naïve Adult HIV-positive Persons

A) Recommended regimens (one of the following to be selected)[*,**]

Regimen	Dosing	Food requirement	Caution
2 NRTIs + INSTI			
ABC/3TC/DTG[(i, ii)]	ABC/3TC/DTG 600/300/50 mg, 1 tablet qd	None **STR**	Al/Ca/Mg-containing antacids should be taken well separated in time (minimum 2h after or 6h before).
TDF/FTC[(iii, iv)] + DTG **Dolutegravir**	TDF/FTC 300[(viii)]/200 mg, 1 tablet qd + DTG 50 mg, 1 tablet qd	None	
TDF/FTC/EVG/c[(iii, iv, v)] **Elvitegravir**	TDF/FTC/EVG/c 300[(viii)]/200/150/150 mg, 1 tablet qd	With food **STR**	Al/Ca/Mg-containing antacids should be taken well separated in time (minimum 2h after or 6h before).
TDF/FTC[(iii, iv)] + RAL **Raltegravir**	TDF/FTC 300[(viii)]/200 mg, 1 tablet qd + RAL 400 mg, 1 tablet bid	None	Al/Ca/Mg-containing antacids should be taken well separated in time (minimum 2h after or 6h before).
2 NRTIs + NNRTI			
TDF/FTC/RPV[(iii)] **Rilpivirine**	TDF/FTC/RPV 300[(viii)]/200/25 mg, 1 tablet qd	With food (min 390 Kcal required) **STR**	Only if CD4 count >200 cells/µL and HIV VL <100,000 copies/mL. PPI contraindicated; H2 antagonists to be taken 12h before or 4h after RPV.
2 NRTIs + PI/r			
TDF/FTC[(iii, iv)] + DRV/r **Darunavir/r**	TDF/FTC 300[(viii)]/200 mg, 1 tablet qd + DRV 800 mg, 1 tablet qd + RTV 100 mg, 1 tablet qd	With food	Monitor in persons with a known sulfonamide allergy.

Raltegravir-based ART Avoids PK Interactions Between Immunosuppressants and ARTs

- **Raltegravir*-based cART (2 NUCs)**

  (Tricot L et al. Am J Transplant. 2009; 9:1-7)

  - Preliminary experience in 13 patients (OLT, 8; RT, 5)
  - No DDIs between RAL and CsA, FK and Sirolimus
  - No episodes of acute rejection

- **Maraviroc**-based cART (2 NUCs)**
- **Enfuvirtide-based cART (3 NUCs)**

*and probably Dolutegravir; **Maraviroc has anti-rejection properties.

Drug–Drug Interactions (DDI) of IS with ARVs

	Immunosuppressants	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	VGI	RAL	ABC	FTC	3TC	TAF	TDF	ZDV
CS	prednisone	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
AM	azathioprine	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
AM	mycophenolate	↔	↓	↔	↓	↓	↓	↔	↓E13%	↔	↔	↔	↓	↓?	↔	↔	↔	↔	E[b]	↓?
CNI	cyclosporine	↑[a]	↑[a]	↑[a]	↑[a]	↑[a]	↓[a]	↓[a]	↓[a]	E	E	↔	↑[a]	↔	↔	↔	↔	E	E[b]	↔
CNI	tacrolimus*	↑[a]	↑[a]	↑[a]	↑[a]	↑[a]	↓[a]	↓[a]	↓[a]	↔	↔	↔	↑[a]	↔	↔	↔	↔	↔	↔[b]	↔
mTOR	everolimus	↑[a]	↑[a]	↑[a]	↑[a]	↑[a]	↓[a]	↓[a]	↓[a]	↔	↔	↔	↑[a]	↔	↔	↔	↔	↔	↔	↔
mTOR	sirolimus	↑[a]	↑[a]	↑[a]	↑[a]	↑[a]	↓[a]	↓[a]	↓[a]	↔	↔	↔	↑[a]	↔	↔	↔	↔	↔	↔[b]	↔
Other	anti-thymocyte glo	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Other	basiliximab	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
Other	belatacept	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔

Legend:

↑ = potential elevated exposure of the immunosuppressant; ↓ = potential decreased exposure of the immunosuppressant;
↔ = no significant effect
D = potential decreased exposure of ARV drug; E = potential elevated exposure of ARV drug.
ATV/c = atazanavir coformulated with cobicistat (300/150 mg QD); DRV/c = darunavir coformulated with cobicistat (800/150 mg QD)
* available as prolonged release formulation
Numbers refer to decreased/increased AUC of the immunosuppressant as observed in drug-drug interaction studies
a = TDM of immunosuppressant is recommended; b = monitor renal function
AM = antimetabolite; CNI = calcineurin inhibitors; CS = corticosteroids; mTOR = mTOR inhibitors

Colors legend:

- no clinically significant interaction expected
- these drugs should not be coadministered
- potential clinically significant interaction that is likely to require additional monitoring, alteration of drug dosage or timing of administration
- potential interaction likely to be of weak intensity. Additional action/monitoring or dosage adjustment is unlikely to be required

Drug–Drug Interactions (DDI) of DAAs with ARVs

Hepatitis C Directly Acting Antivirals (DAAs)	Daclatasvir	Ledipasvir/Sofosbuvir	OBV/PTV/r + DSV	Simeprevir	Sofosbuvir
Daclatasvir	n/a	◇	●	◇	◇
Ledipasvir/Sofosbuvir	◇	n/a	●	●	●
OBV/PTV/r + DSV	●	●	n/a	●	●
Simeprevir	◇	●	●	n/a	◇
Sofosbuvir	◇	●	●	◇	n/a
HIV Entry/Integrase Inhibitors	**Daclatasvir**	**Ledipasvir/Sofosbuvir**	**OBV/PTV/r + DSV**	**Simeprevir**	**Sofosbuvir**
Dolutegravir	◇	◇	◇	◇	◇
Maraviroc	◇	□	□	◇	◇
Raltegravir	◇	◇	◇	◇	◇
HIV NNRTIs	**Daclatasvir**	**Ledipasvir/Sofosbuvir**	**OBV/PTV/r + DSV**	**Simeprevir**	**Sofosbuvir**
Etravirine	□	◇	●	●	◇
Rilpivirine	◇	◇	□	◇	◇
HIV NRTIs	**Daclatasvir**	**Ledipasvir/Sofosbuvir**	**OBV/PTV/r + DSV**	**Simeprevir**	**Sofosbuvir**
Abacavir	◇	◇	◇	◇	◇
Lamividine	◇	◇	◇	◇	◇
Tenofovir	◇	□	◇	◇	◇
HIV Protease Inhibitors	**Daclatasvir**	**Ledipasvir/Sofosbuvir**	**OBV/PTV/r + DSV**	**Simeprevir**	**Sofosbuvir**
Atazanavir	□	◇	□	●	◇
Darunavir	◇	◇	□	●	◇
Lopinavir	◇	◇	□	●	◇

Potential for ledipasvir (LDV)-mediated increase in tenofovir levels, especially if tenofovir used with RTV. Avoid LDV if CrCl < 60 mL/min or if receiving tenofovir with RTV-boosted PI

www.hep-druginteractions.org (March'16)

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Conclusions

- LT evaluation in HIV-infected patients with ESLD is currently part of routine clinical care.
- Survival of LT in HIV/HCV-coinfected recipients with SVR treated with Peg-INF plus RBV is 80% at 5-yr and similar to that seen in HCV monoinfected recipients.
- SVR rates in HCV/HIV LT recipients with INF-free regimens are >90% and similar to that seen in HCV monoinfected patients.
- LT is effective for HIV-infected patients with HCC.
- But … there are new challenges in this field …

New Challenges in Liver Transplantation in HIV-infected Patients

- Long-term (10 yr.) outcomes in SVR
- Cancer *de novo* risk
- Predictors of acute rejection
- Best ART regimen (DTG*, MVC**, TAF)
- HIV D+ / R+ Transplantation

*3TC+Dolutegravir; **Maraviroc has anti-rejection properties.

PADDLE Study: DTG+3TC

EACS 2015 # LBPS4/1

Viral Suppression at Week 24

#	SCR	BSL	Day 2	Day 4	Day 7	Day 10	W.2	W.3	W.4	W.6	W.8	W.12	W.24
1	5.584	10.909	3.701	383	101	71	<50	<50	<50	<50	<50	<50	<50
2	8.887	10.233	5.671	318	<50	<50	<50	<50	<50	<50	<50	<50	<50
3	67.335	**151.569**	37.604	1.565	1.178	266	97	53	<50	<50	<50	<50	<50
4	99.291	**148.370**	11.797	3.303	432	179	178	55	<50	<50	<50	<50	<50
5	34.362	20.544	4.680	1.292	570	168	107	<50	<50	<50	<50	<50	<50
6	16.024	14.499	3.754	1.634	162	<50	<50	<50	<50	<50	<50	<50	<50
7	37.604	18.597	2.948	819	61	<50	<50	<50	<50	<50	<50	<50	<50
8	25.071	24.368	6.264	1.377	Not done	268	105	<50	<50	<50	<50	<50	<50
9	14.707	10.832	Not done	516	202	<50	<50	<50	<50	<50	<50	<50	<50
10	10.679	7.978	5.671	318	<50	<50	<50	<50	<50	<50	<50	<50	<50
11	50.089	**273.676**	160.974	68.129	3.880	2.247	784	290	288	147	<50	<50	<50
12	13.508	64.103	3.496	3.296	135	351	351	84	67	<50	<50	<50	<50
13	28.093	33.829	37.350	26.343	539	268	61	<50	<50	<50	<50	<50	<50
14	15.348	15.151	3.994	791	198	98	<50	61	64	<50	<50	<50	<50
15	23.185	23.500	15.830	4.217	192	69	<50	<50	<50	Not done	<50	<50	<50
16	11.377	3.910	370	97	143	<50	<50	<50	<50	<50	<50	<50	<50
17	39.100	25.828	11.879	1.970	460	147	52	<50	<50	<50	<50	<50	<50
18	60.771	73.069	31.170	2.174	692	358	156	<50	<50	<50	<50	<50	<50
19	82.803	**106.320**	35.517	2.902	897	352	168	76	<50	<50	<50	<50	<50
20	5.190	7.368	3.433	147	56	<50	<50	<50	<50	<50	<50	<50	<50

Cahn et al. EACS 2015; Barcelona, Spain. Abstract LBPS4/1.

From Week 8 onwards all patients had pVL < 50 copies/mL

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