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I have no financial relationships to disclose within the past 12 months relevant to my presentation

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Spanish Cohort of HIV-Infected Patients with Orthotopic Liver Transplantation (OLT): Evaluation of 112 Cases in the Highly Active Antiretroviral (HAART) Era (2002-07).

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OLT in Spanish HIV-1-infected patients in the HAART era (2002-07)

OBJECTIVE

To describe the baseline clinical characteristics and the evolution of 112 Spanish HIV-1-infected patients who underwent liver transplantation (OLT) in the highly active antiretroviral (HAART) era (2002-2007).

OLT in Spanish HIV-1-infected patients in the HAART era (2002-07)

PATIENTS & METHODS

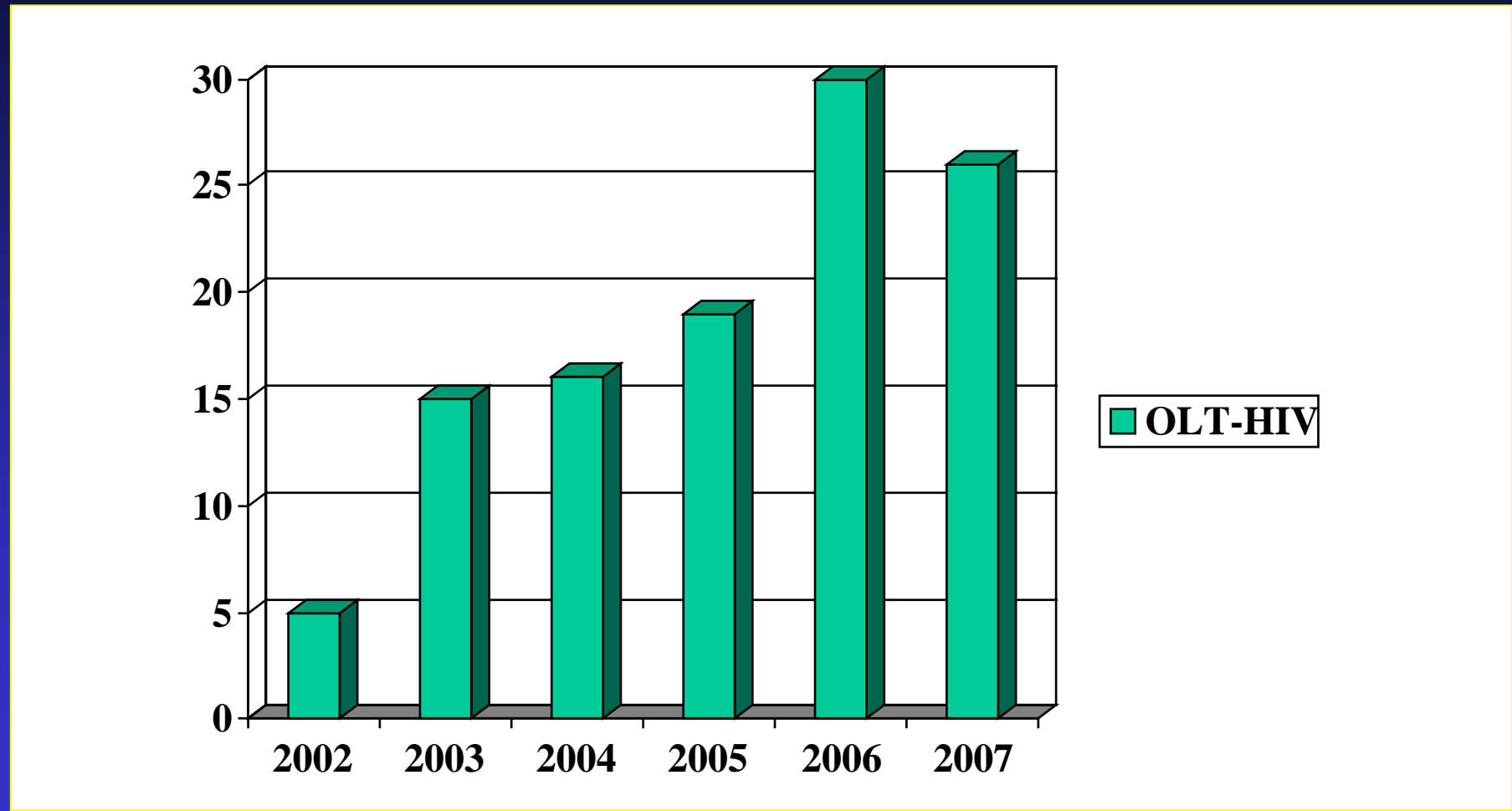
- **Prospective study of all HIV-1-infected patients who underwent OLT in Spain.**
- **HIV (stage, CD4 cell count, plasma HIV-1 RNA viral load, ART), liver disease (etiology, stage) and OLT characteristics at baseline and after OLT were collected using an standardized CRF.**
- **Each site used the same immunosuppressive regimens & prophylaxis protocols as for their HIV-negative patients.**
- **Cohort study. Descriptive analysis.**

OLT in Spanish HIV-1-infected patients in the HAART era (2002-07)

OLT INCLUSION CRITERIA

- **Liver criteria:** the same as for the non-HIV-1 infected population.
- **HIV criteria:** No previous C events (CDC, 1993) except some OIs (TB, PCP, Can), pre-OLT CD4 cell count greater than 100 cells/mm³ and undetectable plasma RNA HIV-1 viral load on HAART or detectable plasma viral load off HAART with post-transplant suppression predicted.
- **Drug abuse:** A) No heroin or cocaine abuse for >2 years; B) No alcohol abuse for >6 months.

OLT in Spanish HIV-infected patients in the HAART era (2002-07) (N=112*)



* 5 patients had retransplantation.

Spanish Cohort of OLT in HIV-infected patients (FIPSE OLT-HIV-05 / GESIDA 45-05)(N=112)

	OLT	Waiting List	Death
H Clínico Lozano Blesa Zaragoza	4*	0	0
C Hosp Univ Santiago de Compostela	2	1	0
H Univ Marqués de Valdecilla Santander	1	0	1
C Hosp Juan Canalejo La Coruña	2	2	0
H Central de Asturias Oviedo	3	2	0
H Ramón y Cajal Madrid	8	2	3
H Univ Virgen del Rocío Sevilla	2	0	1
H Reina Sofía Córdoba	6	1	3
H 12 de Octubre Madrid	11	7	2
H Gregorio Marañón Madrid	9*	0	4
H Virgen de la Arrixaca Murcia	2	1	2
H Clínic I Provincial Barcelona	9*	4	2
H General Vall D'Hebrón Barcelona	12*	2	2
H Bellvitge Hospitalet Llobregat	13	1	2
H La Fé Valencia	10	2	2
H Carlos Haya Málaga	1	4	1
H Cruces Bilbao	19*	1	5

*5 patients had retransplantation.

OLT in Spanish HIV-1-infected patients in the HAART era (2002-07)

Demographics (N=107*)

Male gender	79 (74%)
Age (years)	42 (39;46)**
HIV risk factor	
- Former i.v. drug abuse	79 (74%)
- Sexual	17 (16%)
- Hemophilia	3 (3%)
- Other	4 (4%)
Race: Caucasian	103 (96%)

*** 5 did not meet the HIV inclusion criteria**

**** Median (IQR).**

OLT in Spanish HIV-1-infected patients in the HAART era (2002-07)

Liver disease characteristics (N=107)

Liver cirrhosis etiology*

- HCV	84 (75%)
- HBV**	5 (5%)
- HCV+HBV**	13 (12%)

Child-Pugh stage

- A	13 (12%)
- B	45 (42%)
- C	44 (41%)

MELD (median [IQR]) 14 [10;19]

***16 patients (18%) had a hepatocellular carcinoma (HCC).**

HCV genotypes 1/4 in 57 (67%); genotypes 2/3 in 18 (21%).

10 cases had a non-typable genotype.

**** Delta co-infection in six cases.**

OLT in Spanish HIV-1-infected patients in the HAART era (2002-07)
ART characteristics before OLT (N=107)

ART regimens

- Efavirenz-based ART	41 (38%)
- PI-based ART	30 (28%)
- 3/4 NRTI*	11 (10%)
- Other combinations	25 (23%)

CD4 count (cel./mm³) **276 (170;408)****

CV < 200 copies/mL **101 (94%)**

* Abacavir-based ART; ** Median (IQR).

OLT in Spanish HIV-1-infected patients in the HAART era (2002-07)

OLT Characteristics (N=107)

Time on waiting list (mo.) 4 (2-7)*

Type of liver

- Cadaveric	92%
- Living-donor	1%

Follow-up (mo.) 13 (6-29)**

* Median (IQR); ** Four patients required re-transplantation.

OLT in Spanish HIV-1-infected patients in the HAART era (2002-07)

Post-Operative Outcome (N=107)

Hospitalization stay (days) 21 (16-37)*

Surgical complications 59 (55%)
- Biliary fistula 12

Acute Rejection 47 (44%)
Chronic Rejection 2 (2%)

Re-transplantation 5 (5%)
- PNF 2
- Art. thrombosis 1
- HCV recurrence 2

*** Median (IQR).**

OLT in Spanish HIV-1-infected patients in the HAART era (2002-07)

HIV & ART after OLT (N=107)

ANTIRETROVIRAL THERAPY (ART)

- Re-started in all cases a median (IQR) time of 10 (4; 19) days after OLT.

HIV DISEASE PROGRESSION

- Six C events: CMV (2), VZV (2), PCP and TB one case each.

	CD4+ cells/ μ L Median (IQR)	Plasma HIV-1 RNA VL<200 copies/mL
Before OLT	276 (170;408)	94%
+ 3 mo (N=92)	288 (193;420)	93%
+ 12 mo (N=70)	309 (197;424)	94%
+ 24 mo (N=39)	260 (197;470)	92%
+ 36 mo (N=23)	262 (156;500)	95%
+ 48 mo (N=14)	258 (156;372)	93%

OLT in Spanish HIV-1-infected patients in the HAART era (2002-07)

Mortality (N=28; 26%)

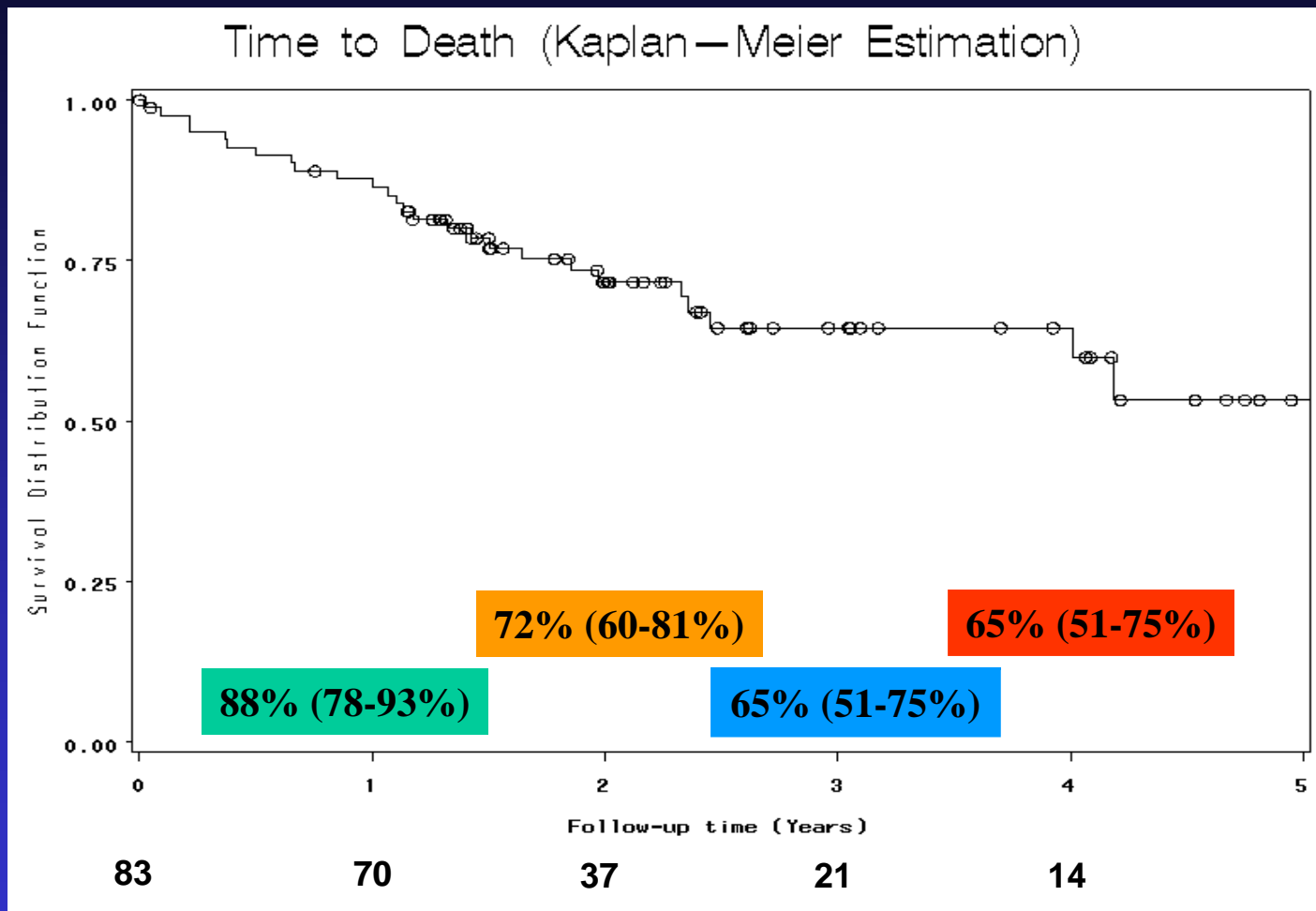
Early mortality (<6 mo.)	8 (29%)
- Post-op. complications	4
- Severe cholestatic HCV hepatitis	2
- Other*	2
Late mortality (>6 mo.)	20 (71%)
- Graft ELSD – HCV reinfection	9
- Chronic rejection	4
- Other**	7

* Massive variceal bleeding and lactic acidosis – mitochondrial toxicity;

** MOF (2), OI (2), Cancer, mucormycosis and lactic acidosis – mitochondrial toxicity.

OLT in Spanish HIV-1-infected patients in the HAART era (2002-07)

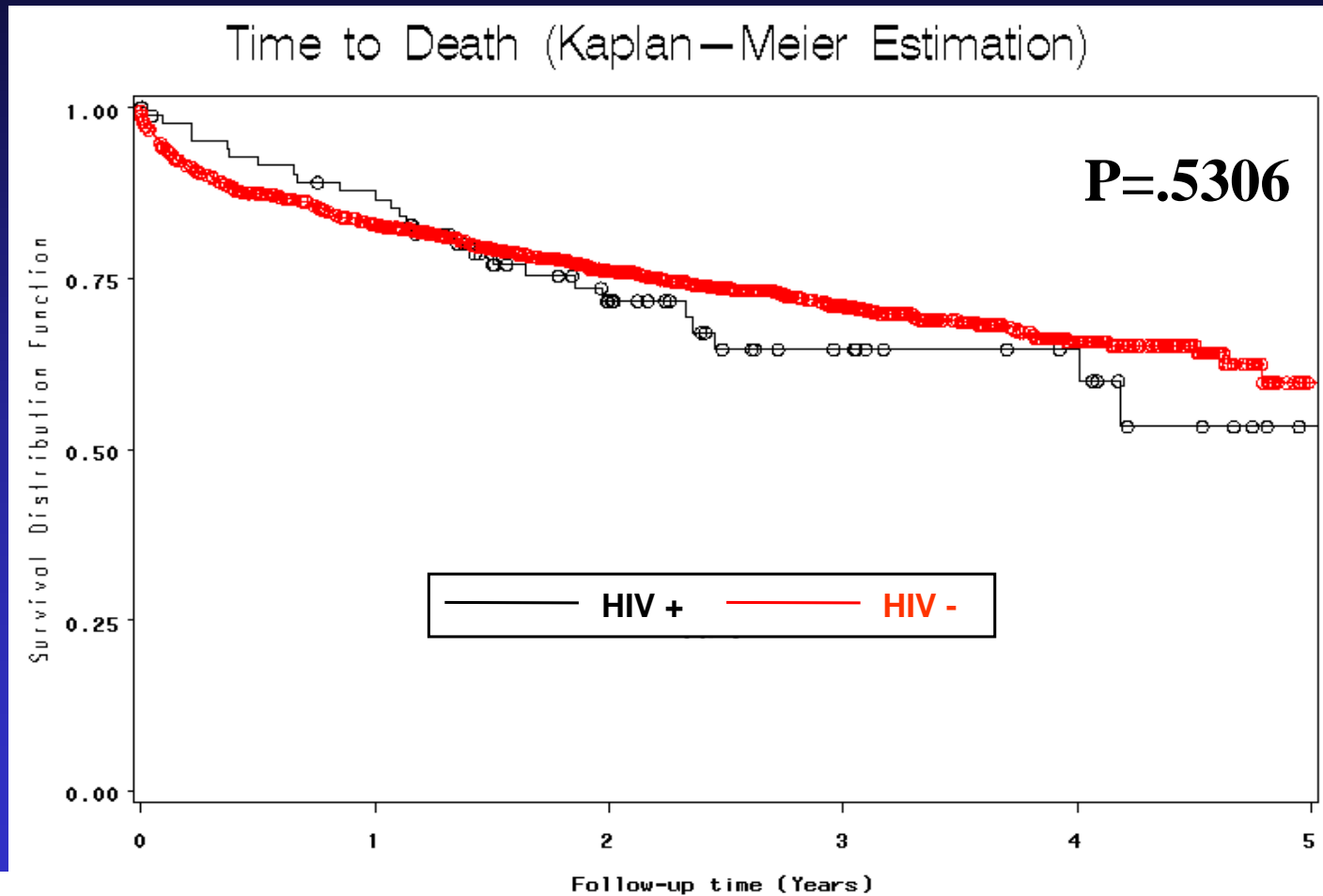
Patient Survival (N=83)*



Patients
at risk

* Survival analysis was performed including only patients underwent OLT between 2002 and 2006 and followed until December 31st, 2007.

Cumulative survival after OLT, comparing 83 HIV-positive and 1,499 HIV-negative HBV- or HCV-positive OLT recipients (2002-07).



Patients at risk	HIV -	1499	1093	766	495	300	120
	HIV +	83	70	37	21	14	2

OLT in Spanish HIV-1-infected patients in the HAART era (2002-07)

CONCLUSIONS

- **The first case of OLT in Spain was performed in January 2002. Since then, 107 patients have been transplanted within the Spanish criteria at 17 (90%) sites.**
- **Most cases of OLT in Spain were due to HCV-infection in former i.v. drug users.**
- **HCV re-infection is the major cause of mortality after OLT (39,3%).**

OLT in Spanish HIV-1-infected patients in the HAART era (2002-07)

CONCLUSIONS

- **HIV disease can be adequately controlled after OLT.**
- **At present, OLT for selected HIV-1-infected patients is a safe and effective procedure with a short and mid-term survival that is comparable to the HIV-negative population.**

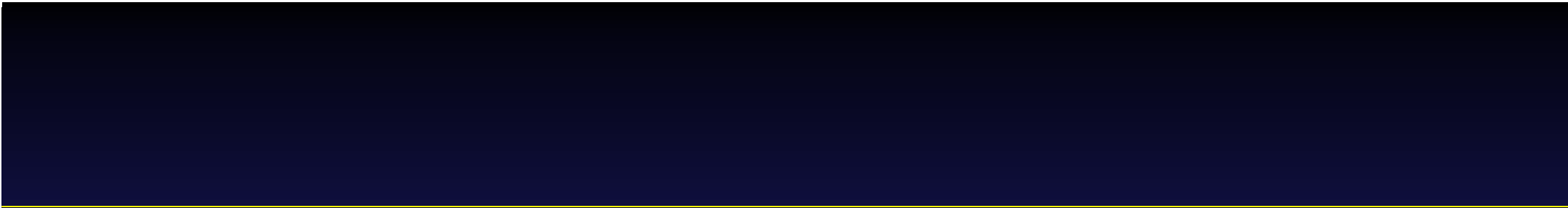
OLT in Spanish HIV-1-infected patients in the HAART era (2002-07)

ACKNOWLEDGEMENTS

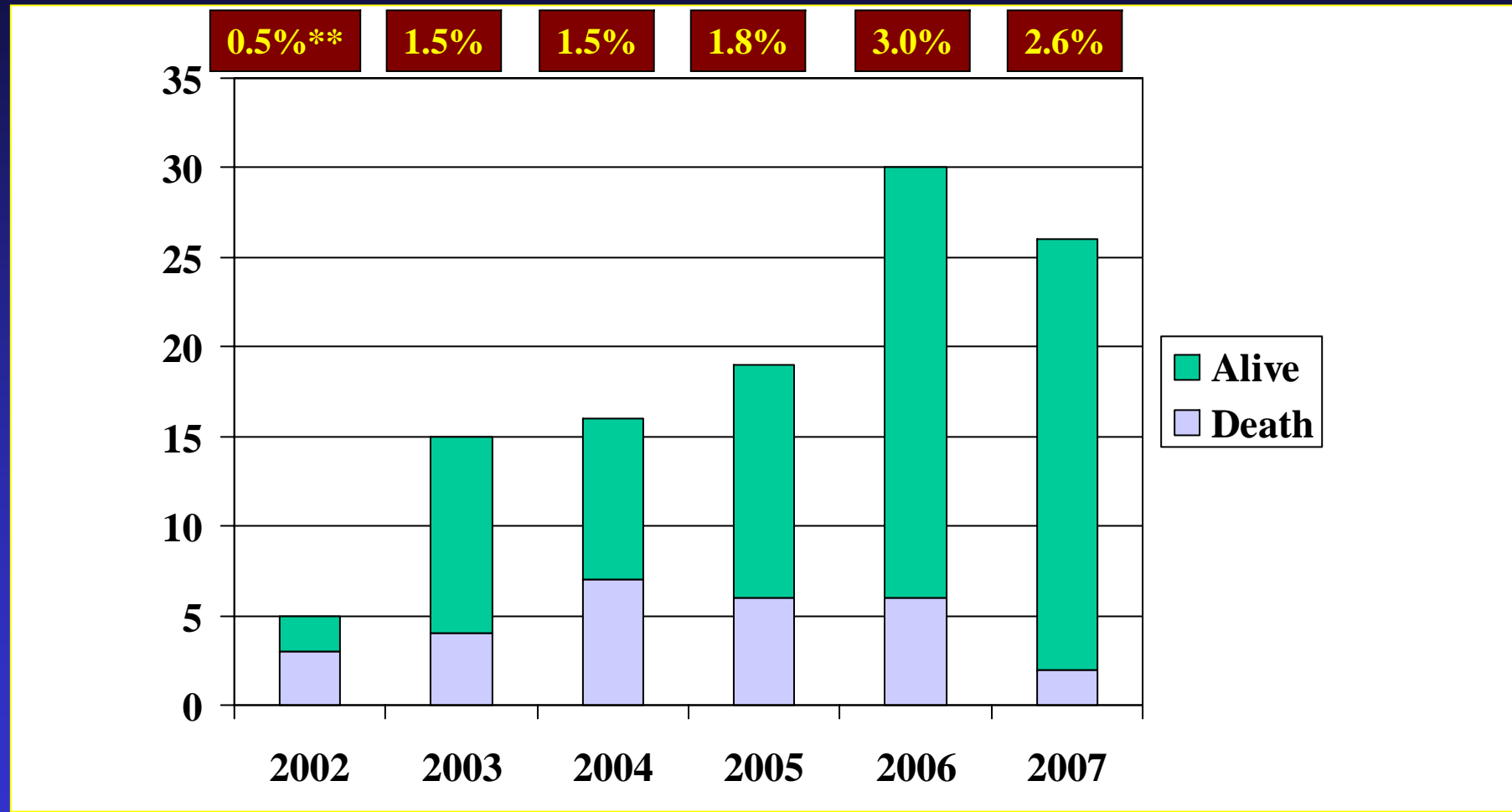
- **Fundación para la Investigación y Prevención del SIDA en España (FIPSE).**
- **Grupo de Estudio de Sida (GESIDA/SEIMC).**
- **Sociedad Española de Trasplante Hepático (SETH).**
- **Grupo de Estudio de Infecciones en Trasplantados. (GESITRA/SEIMC).**

- **Secretaría del Plan Nacional del Sida (SPNS) del Ministerio de Sanidad y Consumo (MSC).**
- **Organización Nacional de Trasplante (ONT).**

Our patients.



OLT in Spanish HIV-infected patients in the HAART era (2002-07) (N=112*)



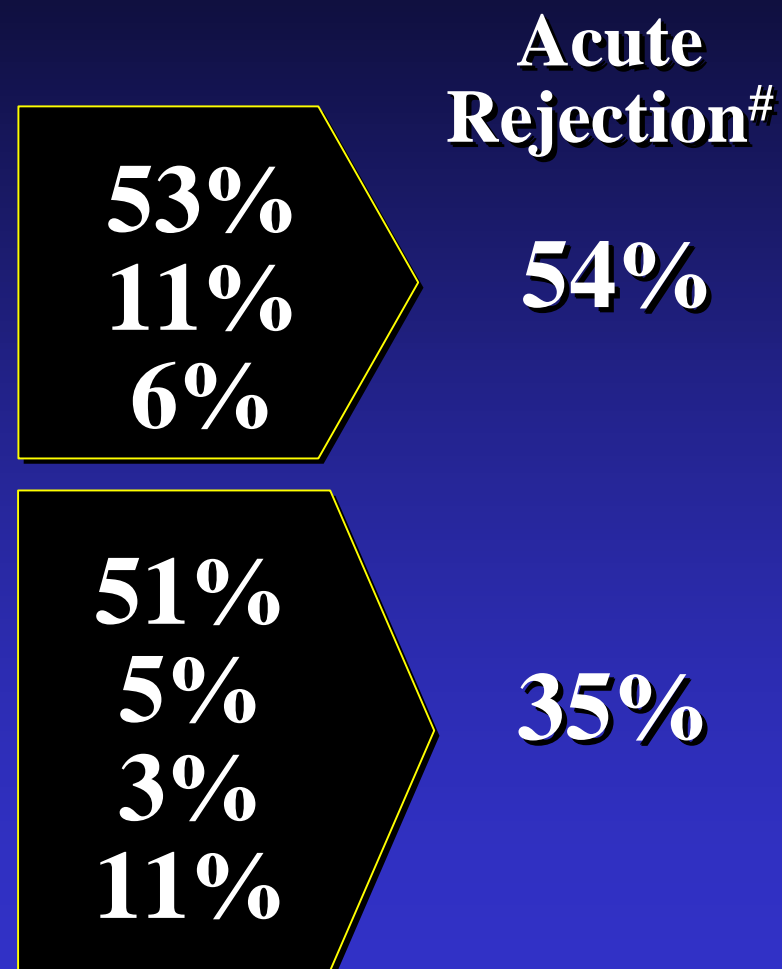
*5 patients had retransplantation; ** OLT in HIV-infected recipients/OLT in general population ratio.

OLT in Spanish HIV-1-infected patients in the HAART era (2002-07)

Immunosuppressive regimens (N=107)

- Cyclosporine A (CsA)
 - + Prednisone, or
 - + IL-2 Ra*, or
 - + Prednisone plus MMF

- Tacrolimus
 - + Prednisone, or
 - + Prednisone + MMF**
 - + Prednisone + IL-2 Ra*
 - + MMF or IL-2 Ra*



*Basiliximab (Simulect®); ** MMF = Mycophenolate mophetil; # p=0.21; RR=1.55 [0.88-2.71]