

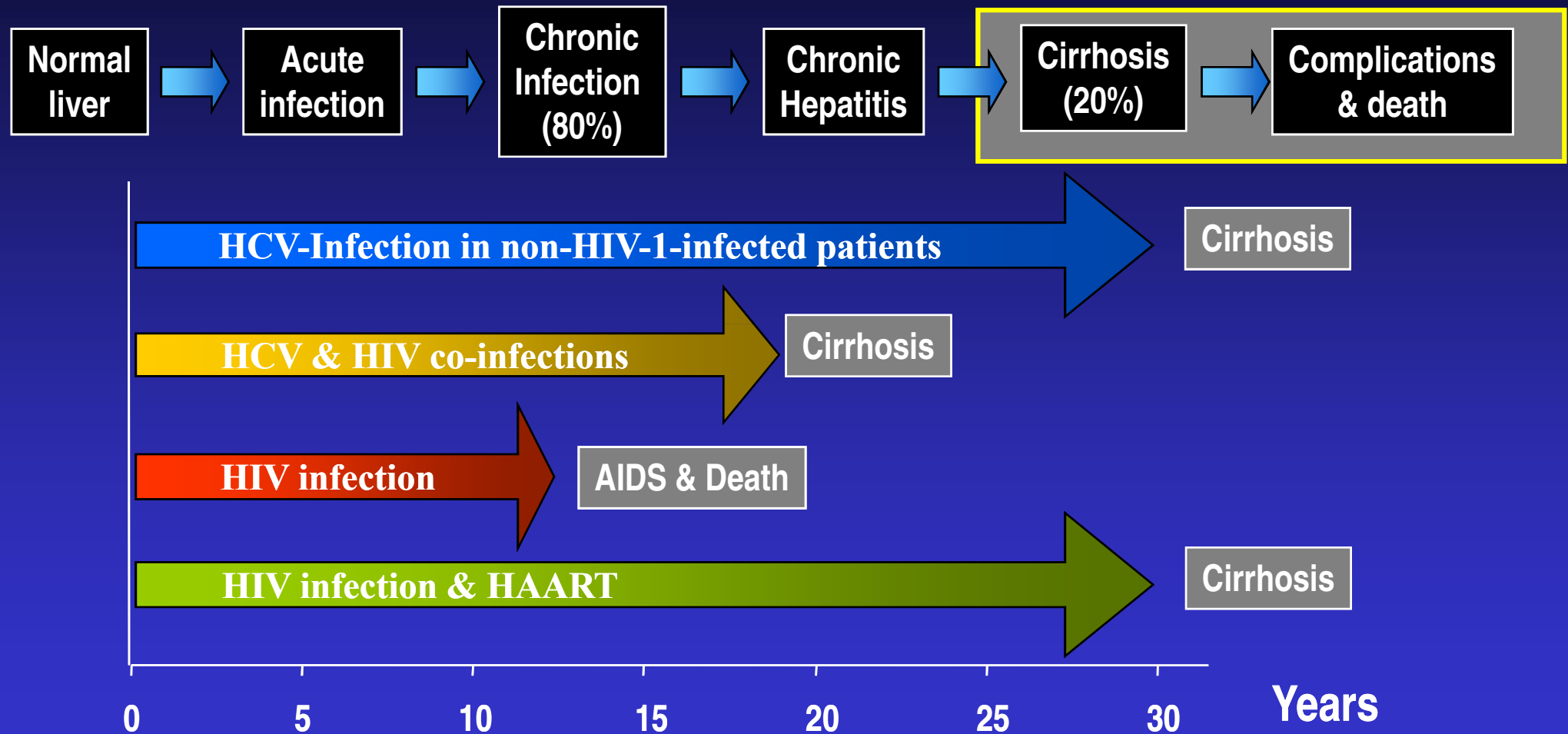
Trasplante Hepático en Pacientes Infectados por el VIH

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La Historia Natural de la Infección por VHC se acelera en los pacientes coinfectados por VIH



*Lauer GM. N Engl J Med. 2001 & Soriano V. AIDS. 2002.

Experiencia en Trasplante hepático en pacientes coinfectados VIH-VHC

- **HIV inclusion criteria**
- **Liver transplantation**
- **Conclusiones & Future Research**

<http://www.gesida.seimc.org>

CONSENSUS DOCUMENT

GESIDA/GESITRA-SEIMC, PNS and ONT Consensus Document on solid organ transplant (SOT) in HIV infected

VIH no es contraindicación para TOS
Estudio Prospectivo
Aproximación multidisciplinar

^aAIDS Study Group (GESIDA) of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC). ^bInfection in Transplant Study Group (GESITRA). ^cHepatology Service. Hospital Clínic. Barcelona. ^dDigestive Surgery Service. Hospital de Bellvitge. Hospitalet de Llobregat Barcelona. ^eCommittee of the *Action Guidelines for Viral Diseases in Haemodialysis* of the Spanish Nephrology Society. ^fTransplant and Cardiac Insufficiency Study Group of the Spanish Heart Society. ^gProgramme for the Prevention and Care of AIDS in Catalonia. ^hCatalonian Transplant Organization (OCATT). ⁱGovernment Delegation for the National Drugs Plan, Ministry of Health (MSC). ^jNational AIDS Plan Secretariat (PNS) of the MSC. ^kNational Transplant Organization of the MSC.

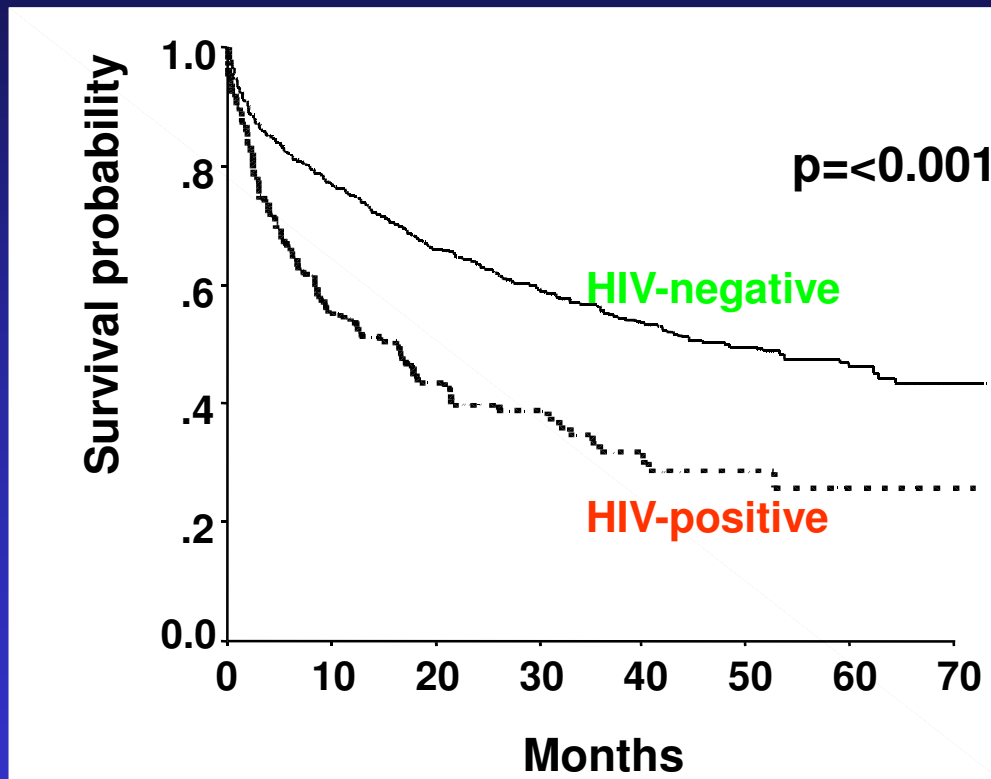
Recomendaciones Actuales: Criterios de inclusion para TOS en pacientes infectados por VIH en España.

Miró JM et al. Enferm Infecc Microbiol Clin. 2005; 23:353-61.

- **Organ criteria:** the same as for the non-HIV-infected population.
- **HIV criteria:**
 - 1) **Clinical:** no previous C events (CDC, 1993) except some OIs (TB, Can, PCP); and,
 - 2) **Immunological:** pre-SOT CD4 cell count >100 cells/mm³ for OLT and > 200 cells/mm³ for other SOT; **and,**
 - 3) **Virological:** RNA HIV-1 viral load BDL on cART or, if detectable, post-SOT suppression predicted.
- **Drug use:** A) No heroin or cocaine use for >2 years;
B) No alcohol use for >6 months.

Coinfección VIH acorta la supervivencia de pacientes con Cirrosis descompensada por VHC

Pineda JA et al. Hepatology. 2005, 41:779-89.



Survival among HCV-infected individuals with and without HIV coinfection

	1-year	2-years	5-years
HCV	74%	61%	44%
HCV/HIV	54%	40%	25%

No. at risk

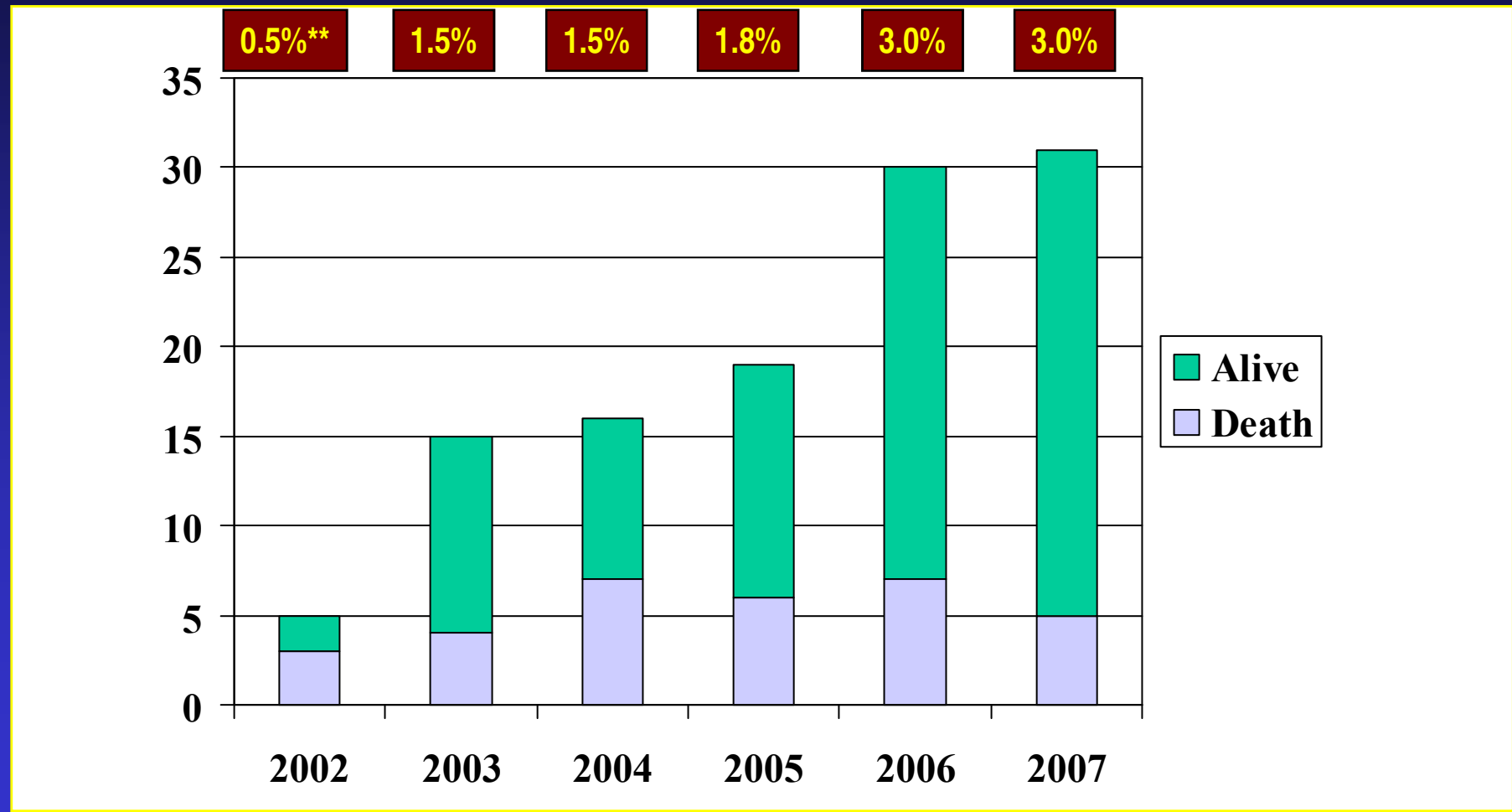
HIV-negative 1037 619 429 313 208 133 62 9

HIV-positive 180 75 46 30 19 11 5 3

Cohorte española de TOH en pacientes infectados VIH (FIPSE TOH-VIH-05 / GESIDA 45-05)(2002-08)

PROVINCIA	CENTRO	TOTALES TH	RE - TH	EXITUS TH	TOTALES LE	ACTIVOS LE	EXITUS LE
Barcelona	H. Clínico i Provincial	12	1	2	12	4	1
Barcelona	H Bellvitge	14		4	7	1	
Valencia	H. La Fé de Valencia	13		2	11	2	1
Barcelona	H. General Vall d'Hebrón	18	1	3	9	0	1
Málaga	H. Carlos Haya	1		1	5	3	1
Granada	H Univ. Virgen Nieves	0		0	0	0	
Vizcaya	H. de Cruces	21	1	5	12	2	1
Zaragoza	H Clínico Lozano Blesa	7	1	0	7	0	1
La Coruña	H Santiago Compostela	3		2	5	0	1
Cantabria	H. Marqués Valdecilla	1		1	1	1	
La Coruña	H. Juan Canalejo	4		2	4	1	
Asturias	H Central de Asturias	5		1	5	0	
Madrid	H Ramón y Cajal	10		3	10	3	3
Córdoba	H. Reina Sofía	8		4	8	2	
Madrid	H. Gregorio Marañón	10	1	4	8	0	1
Madrid	H. 12 de Octubre	18	1	4	25	7	2
Murcia	H Virgen de la Arrixaca	2		2	1	0	
Sevilla	H. Univ. Virgen del Rocío	3		1	3	0	
	TOTAL	150	6	41	133	26	13

TOH en España en pacientes infectados VIH en la era TARGA -- (2002-07) (N=116*)



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

TOH en España en pacientes infectados VIH en la era TARGA -- (2002-07)

Datos Demográficos (N=112)

Male gender	84 (75%)
Age (years)	43 (39;46)**
HIV risk factor	
- Former i.v. drug use	82 (73%)
- Sexual	19 (17%)
- Hemophilia	5 (4%)
- Other	6 (5%)
Race: Caucasian	110 (98%)

* Median (IQR)

TOH en España en pacientes infectados VIH en la era TARGA -- (2002-07)

Características de la enfermedad hepática(N=112)

Liver cirrhosis etiology*

- HCV	92 (82%)
- HBV**	1 (1%)
- HCV+HBV**	19 (17%)

Child-Pugh stage (WL)

- A	15 (13%)
- B	45 (40%)
- C	46 (41%)

MELD (WL) (median [IQR]) 14 [11;18]

*25 patients (22%) had a hepatocellular carcinoma (HCC); HCV genotypes 1/4 in 73 (65%); genotypes 2/3 in 25 (22%); 4 other genotypes; 5 cases had a non-typable genotype and no data in 5 cases ** Delta co-infection in nine cases.

TOH en España en pacientes infectados VIH en la era TARGA -- (2002-07)

Características TAR pre-TOH (N=112)

ART regimens

- Efavirenz-based ART	43 (39%)
- PI-based ART	36 (32%)
- 3/4 NRTI*	11 (10%)
- Other combinations	21 (19%)

CD4 count (cel./mm ³)	276 (182;402)**
CV < 200 copies/mL	106 (95%)

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

TOH en España en pacientes infectados VIH en la era TARGA -- (2002-07)

Donante :Características (N=108)

Age (yr.)	52 (40;68)*
Male Gender	68 (61%)
Etiology of death	
- Craneal traumatism	33 (29%)
- Stroke	49 (44%)
- Other	22 (20%)
Marginal donors	15 (13%)
Cold isquemia (min)	334 (250; 480)*

* Median (IQR).

TOH en España en pacientes infectados VIH en la era TARGA -- (2002-07)

Características TOH (N=112)

Time on waiting list (mo.)	4 (2-7)*
Type of liver	
- Cadaveric	99%
- Living-donor	1%
Blood transfusion (Units)	4 (1;7)
Follow-up (mo.)	18 (8-29)

* Median (IQR).

TOH en España en pacientes infectados VIH en la era TARGA -- (2002-07)

Evolución Postoperatoria (N=112)

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

Surgical complications 48 (43%)

- Biliary fistula 13

- Hepatic artery 9

- Surgical wound infection 3

- Other complications 36

Re-transplantation 4 (4%)

- PGF 2

- Arterial thrombosis 1

- HCV recurrence 1

* Median (IQR).

TOH en España en pacientes infectados VIH en la era TARGA -- (2002-07)

Mortalidad (N=32; 29%)

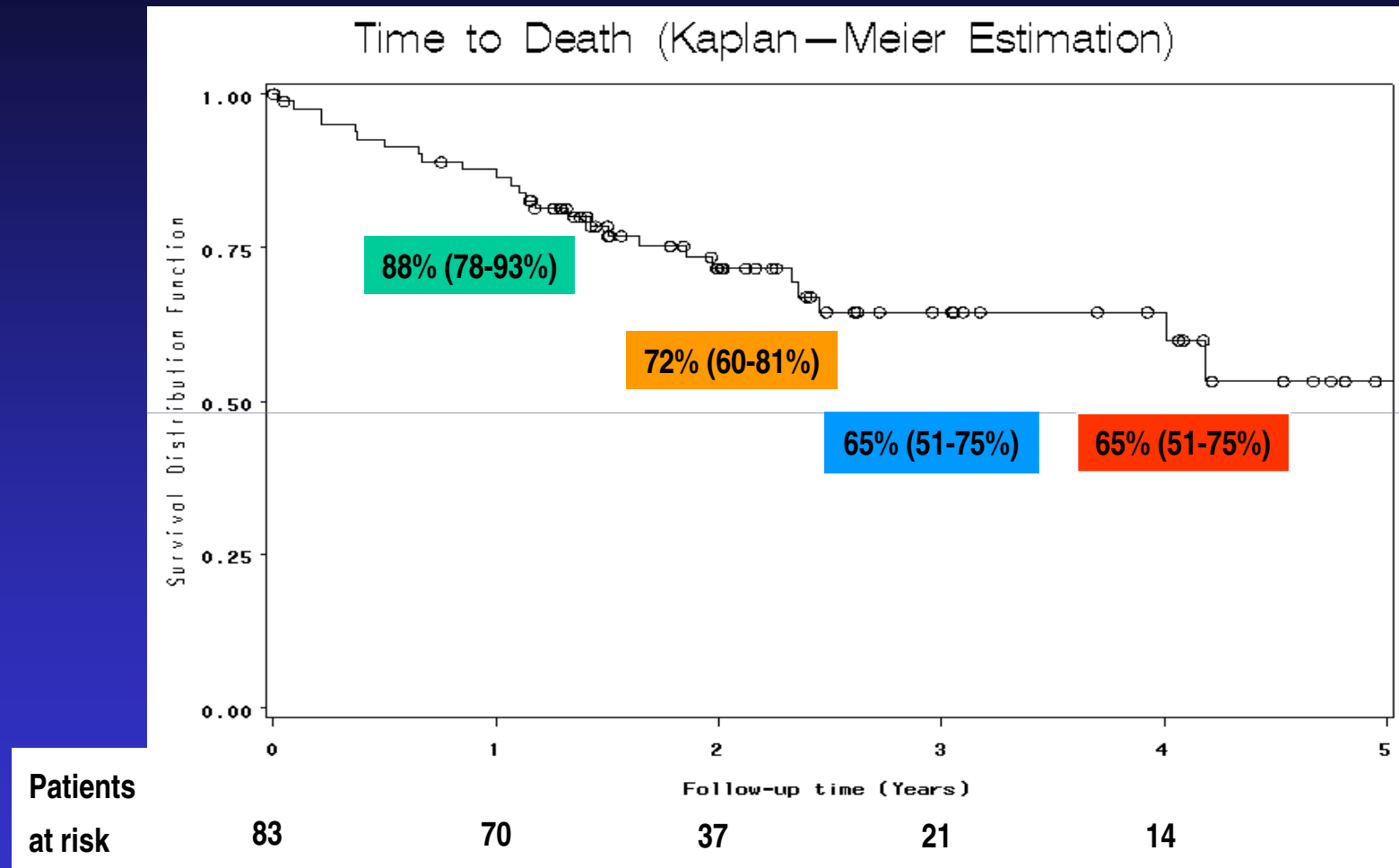
Early mortality (<6 mo.)	9 (28%)
- Post-op. complications	4
- Severe cholestatic HCV hepatitis	2
- Other*	3
Late mortality (>6 mo.)	23 (72%)
- Graft ELSD – HCV reinfection	11
- Chronic rejection	4
- Other**	8

* Massive variceal bleeding, lactic acidosis – mitochondrial toxicity and CMV disease 1 case each.

** MOF (2), OI (2), Cancer (2), mucormycosis (1) and lactic acidosis – mitochondrial toxicity (1).

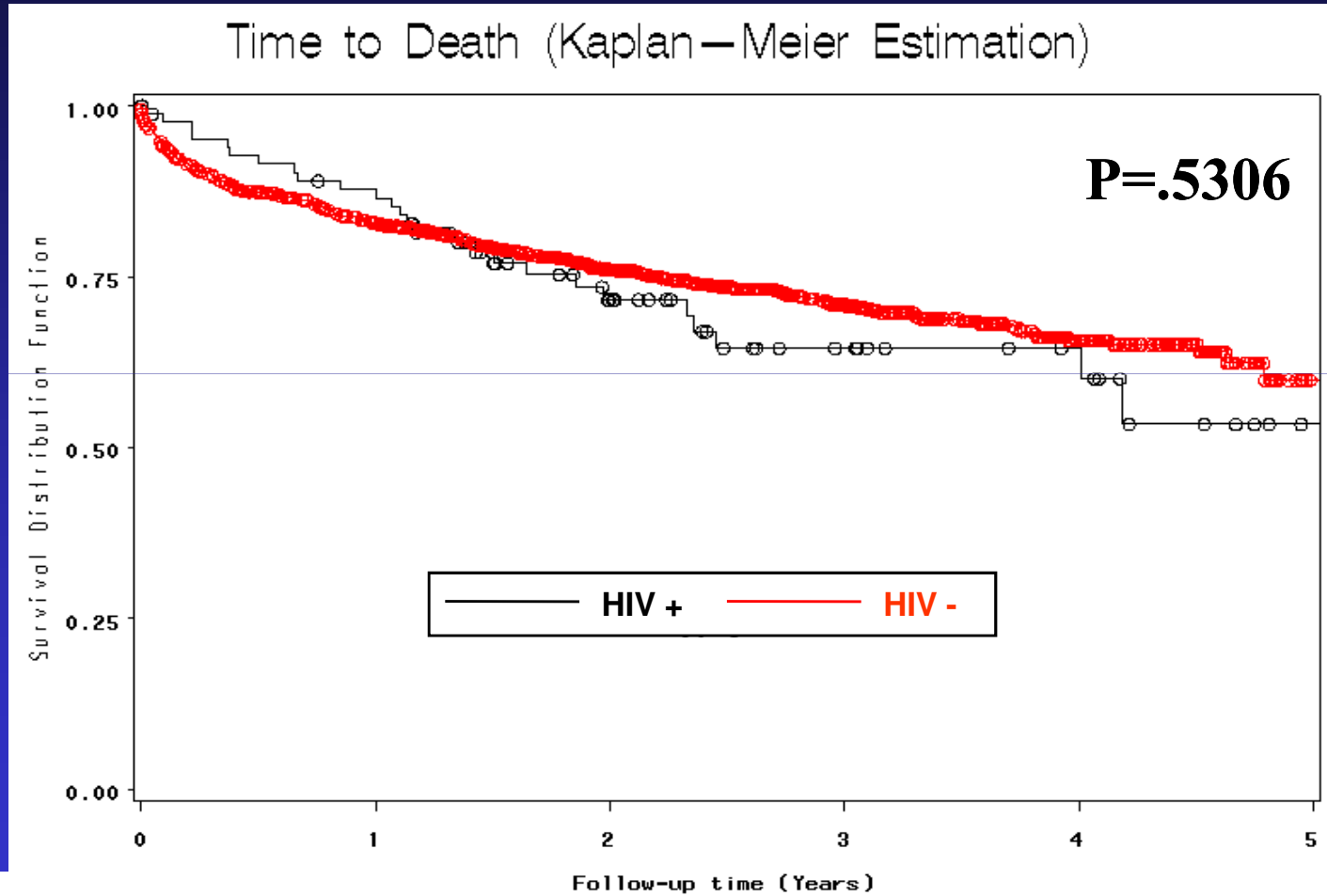
TOH en España en pacientes infectados VIH en la era TARGA -- (2002-07)

Supervivencia (N=83)*



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

Supervivencia a los 4 años tras TOH: 82 pacientes VIH+ vs 1.489 pacientes VIH- (2002-06)



Patients at risk	HIV -	1489	1085	763	492	298	120
	HIV +	83	70	37	20	14	2

TOH en España en pacientes infectados VIH en la era TARGA -- (2002-07)

Infecciones post TOH (N=112)

Type of infections

0-30

31-180

>180 days

Viral

16

9

5

PCP

1

-

-

Bacterial

24

7

3

Mycobacterial (TB)

-

-

2

Fungal

1

6

5

Other

4

-

2

Total

48

22

17

TOH en España en pacientes infectados VIH en la era TARGA -- (2002-07)

Características TAR post TOH(N=112)

Antiretroviral therapy was started 9 (5;19)* days after liver transplantation.

ART regimens

- Efavirenz-based ART	50 (50%)
- PI-based ART	29 (29%)
- 3/4 NRTI*	4 (4%)
- Other combinations	17 (17%)

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

TOH en España en pacientes infectados VIH en la era TARGA -- (2002-07)

VIH & cART post TOH (N=112)

CD4+ cells/μL	Plasma HIV-1 RNA
Median (IQR)	VL<200 copies/mL

Before OLT	276 (182;402)	95%
+ 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%

TOH en España en pacientes infectados VIH en la era TARGA -- (2002-07)

Eventos B y C post TOH (N=112)

B events 3 (2.5%)

- Oral candidiasis 3

C events 7 (6%)

- Disseminated *M. tuberculosis* 2

- CMV disease 2

- Esophageal candidiasis 1

- Disseminated Herpes simplex 1

- *Pneumocystis jiroveci* pneumonia 1

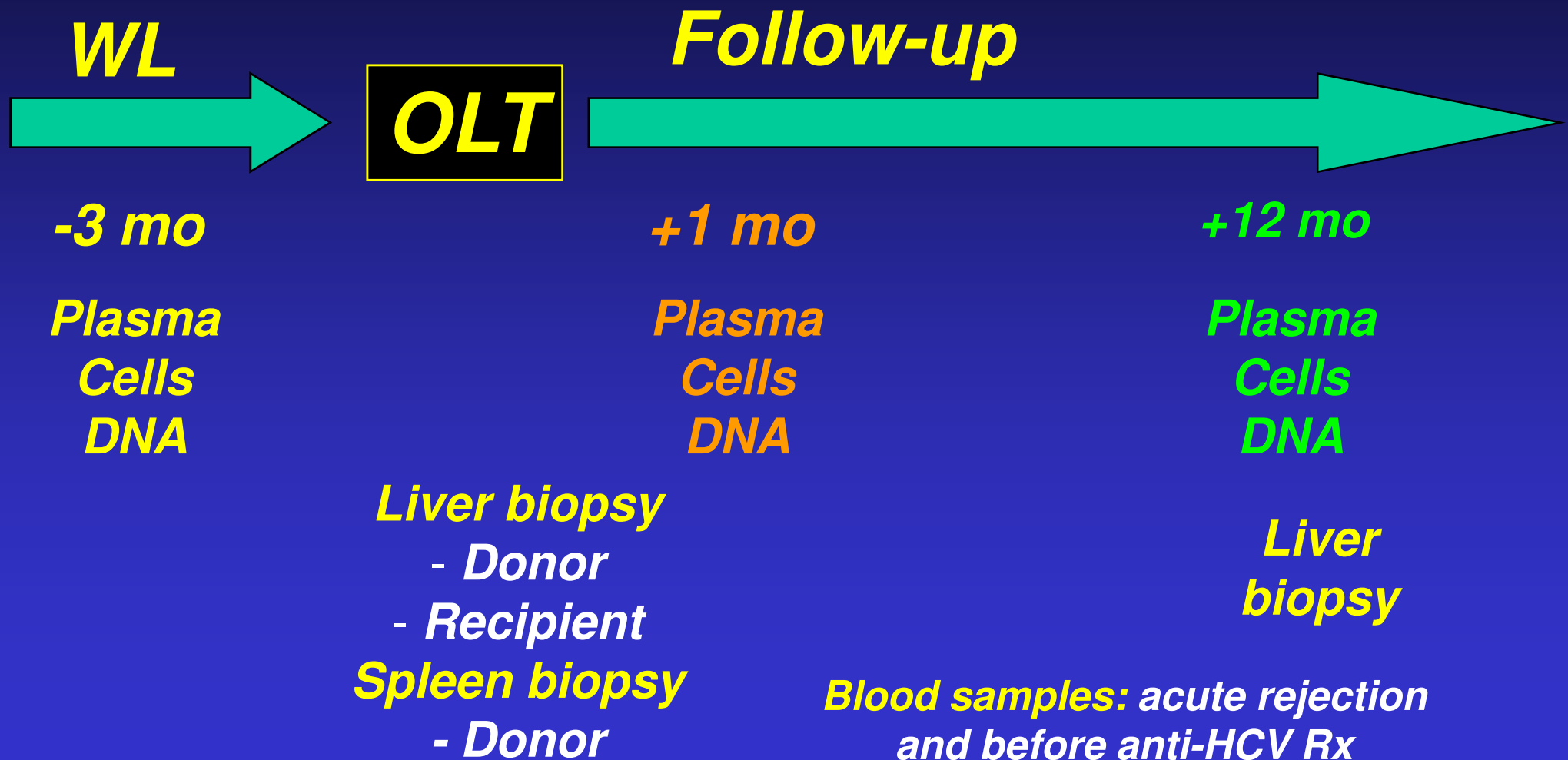
Futuras Areas de Investigación

- To create an International/European project of SOT in HIV-infected patients.
- **To know long-term survival (5-10 years).**
- To improve the management of PK/PD interactions between immunosuppressive, antiretroviral and anti-HCV drugs.
- **To reduce the rates of acute rejection.**
- To improve the management of HCV re-infection and the effectiveness of the Rx.

TOH en España en pacientes VIH (cohorte FIPSE): LINEAS DE INVESTIGACIÓN

- *5-year prognosis (HIV+/-): Drs. Miro/Rimola/Mahillo*
 - *Acute rejection. Drs. Rafecas/Rimola/Fortún*
- *Natural history HCV(HIV+/-): Drs. Valdivieso /Castells/de la Torre*
- *Rx of HCV reinfection: Drs. Castells/Valdivieso/delaTorre*
 - +
 - *Infections: Drs. Moreno/Fortun/Blanes*
 - *HIV & cART (PK interactions; toxicity):Drs. Gonzalez/Miro/Miralles*
- *Waiting list prognosis (HIV+/-): Drs. Rimola/Rafecas/de la*

TOH en España en pacientes VIH (cohorte FIPSE): BIOBANCO



CONCLUSIONES

- **Survival of HCV/HBV HIV-coinfected patients with ESLD is shorter than non-HIV-infected population and their mortality in OLT waiting list is also higher.**
- **Liver transplantation in HIV-infected patients have a mid term (3 years) survival similar to HIV-negative patients.**
- **Mortality in OLT HIV-HCV co-infected patients was mainly related to HCV re-infection.**
- **LT in HBV-HIV co-infection has a very good prognosis.**

AGRADECIMIENTOS

- **To our patients**
- To all “**HIV colleagues**” (GESIDA/SEIMC, RIS)
- To all “**SOT teams**”, who have made this reality possible (SETH/SEN-GESITRA/SEIMC)
- To all **SOT & HIV GO & NGO**, for their constant support (ONT, SPNS/MSC, OCATT, FIPSE, FEAT, gTt, CESIDA)

- **OLT experts**

Grossi PA, Carosi G (Italy); Samuel D (France); Brook G (UK); Roland M, Stock P (USA).

