

## Transplantation complete but viruses lurking

2-Hour Oral Session

Hall L, RAI Amsterdam - April 14<sup>th</sup>, 2019

# HIV-positive Donor to Positive Recipient Liver Transplantation: A Nationwide Survey

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# Transparency Declaration

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Dr. José M Miró has received honoraria for speaking or participating in Advisory Boards and/or research grants from the following Pharmaceutical Companies:

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# Background

- Liver transplantation (LT) using HIV- organs in HIV+ recipients has good outcomes<sup>1</sup>.
- HIV+ donor organs (mostly kidney) can now be transplanted into HIV+ recipients (HIV D+/R+) with end-stage organ disease in several countries<sup>1</sup>.

<sup>1</sup>Miro JM et al. Intensive Care Med. 2019;45:398-400.

# HIV D+/R+ renal transplantation in South Africa

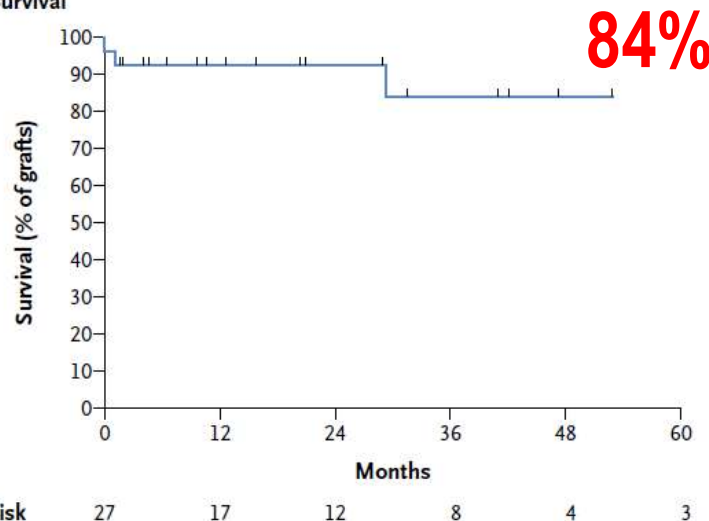
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## ORIGINAL ARTICLE

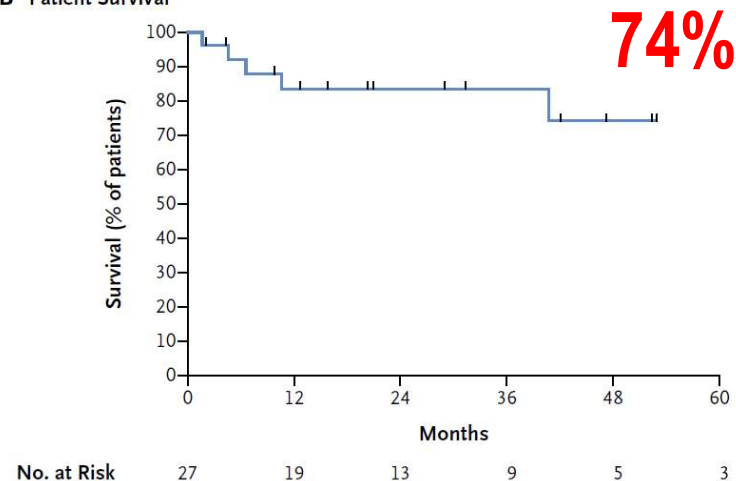
### HIV-Positive-to-HIV-Positive Kidney Transplantation — Results at 3 to 5 Years

Elmi Muller, M.B., Ch.B., M.Med., Zunaid Barday, M.B., Ch.B.,  
Marc Mendelson, M.D., Ph.D., and Delawir Kahn, M.B., Ch.B., Ch.M.

A Graft Survival



B Patient Survival



Muller E et al. NEJM. 2015;372:613-20.

# HIV D+/R+ liver transplantation in Europe

American Journal of Transplantation 2016; 16: 2473–2478  
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## Case Report

## HIV-Positive-to-HIV-Positive Liver Transplantation

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## Introduction

Concerns about donor-derived human immunodeficiency virus (HIV) transmission have excluded HIV-positive patients from organ donation lists in most countries. This leads to the loss of an estimated 356 potential organ donors per year in the United States (1). HIV-positive solid organ transplant candidates remain disadvantaged on waiting lists with an increased risk of death, particularly in HIV-hepatitis C virus (HCV)-coinfected individuals with liver disease (2–4). Despite a higher relative risk of experiencing graft failure compared to HIV-negative controls, HIV status was not associated with an increased risk of death in a cohort of solid organ transplant recipients in the United States (5). The concern that transplantation of organs from HIV-positive donors might harm transplant recipients remains. Indeed, transmission of a new HIV strain to an immunosuppressed HIV-positive recipient could potentially lead to uncontrolled viral replication, immune dysregulation, and opportunistic infections (4,6). So far, reports on the transplant of HIV-positive organs have been limited to kidney transplantation in South Africa from treatment-naïve or first-line antiretroviral therapy (ART)-treated HIV-positive donors to HIV-positive recipients (7). The Swiss

## HIV-Positive-to-HIV-Positive Liver Transplantation

**TO THE EDITOR:** The use of liver grafts from deceased human immunodeficiency virus (HIV)-positive persons has historically been avoided, in part owing to concerns about HIV superinfection and transmitted drug resistance. However, the number of patients on the active liver-only transplant waiting list is rising in the United Kingdom and has not been matched by a similar increase in organ donations. Transplantation from

an HIV-positive person to an HIV-positive person offers one solution to this shortfall. We present a case of liver transplantation from a donor positive for HIV type 1 (HIV-1) to a recipient co-infected with hepatitis C virus (HCV) and HIV-1 who required transplantation for primary liver cancer complicating cirrhosis.

A 47-year-old man was referred to the Birmingham Liver Unit for assessment of a single hepato-

N ENGL J MED 375:18 NEJM.ORG NOVEMBER 3, 2016



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SWISS  
TRANSPLANT  
COHORT  
STUDY

Calmy Al et al. Am J Transplant. 2016; 16:2473-8.  
Hathorn E et al. N Engl J Med. 2016; 375:1807-9.

# HIV D+/R+ liver transplantation in USA (HOPE)

| Outcomes                        | HIV D-/R+<br>(N=17) | HIV D+/R+<br>(N=16) | P value    |
|---------------------------------|---------------------|---------------------|------------|
| Rejection, n (%)                | 3 (17%)             | 2 (13%)             | 0.9        |
| Opportunistic Infections; n (%) | 2 (12%)             | 5 (31%)             | 0.3        |
| Breakthrough HIV; n (%)         | 0 (0%)              | 1 (6%)              | 0.9        |
| Malignancy; n (%)               | 0 (0%)              | 1 (6%)              | 0.9        |
| Graft failure; n (%)            | 0 (0%)              | 1 (6%)              | 0.9        |
| <b>Death; n (%)</b>             | <b>0 (0%)</b>       | <b>2 (13%)</b>      | <b>0.4</b> |

Graft failure in HIV D+/R+ patients occurred 30 days post-transplant; liver-only recipient; One of the three HIV D-/R+ recipient was an SLK recipient; rejection observed in the liver; HIV RNA of 2380 copies/mL week 1 post-transplant. Kaposi sarcoma in HIV D+/R+ recipient, diagnosed 160 days post-transplant; liver-only recipient.

**Death (n=2):** Day 9 post transplant, respiratory failure (D+); Day 140 post-transplant, pulmonary hypertension (D+), not deemed related to donor HIV status

Courtesy Dr. C.M. Durand, April 2019

# Background

- Liver transplantation (LT) using HIV- organs in HIV+ recipients has good outcomes<sup>1</sup>.
- HIV+ donor organs (mostly kidney) can now be transplanted into HIV+ recipients (HIV D+/R+) with end-stage organ disease in several countries<sup>1</sup>.
- Spain has one of the biggest cohort of LT in HIV-infected patients and the world's highest donor rate, but using organs from HIV-infected donors is forbidden by law since 1987.

## Objectives

- To know the opinion of liver transplant (LT) teams on this new strategy and their attitude toward HIV D+/R+ LT throughout a nationwide survey.

<sup>1</sup>Miro JM et al. Intensive Care Med. 2019;45:398-400.

# Methods (I)

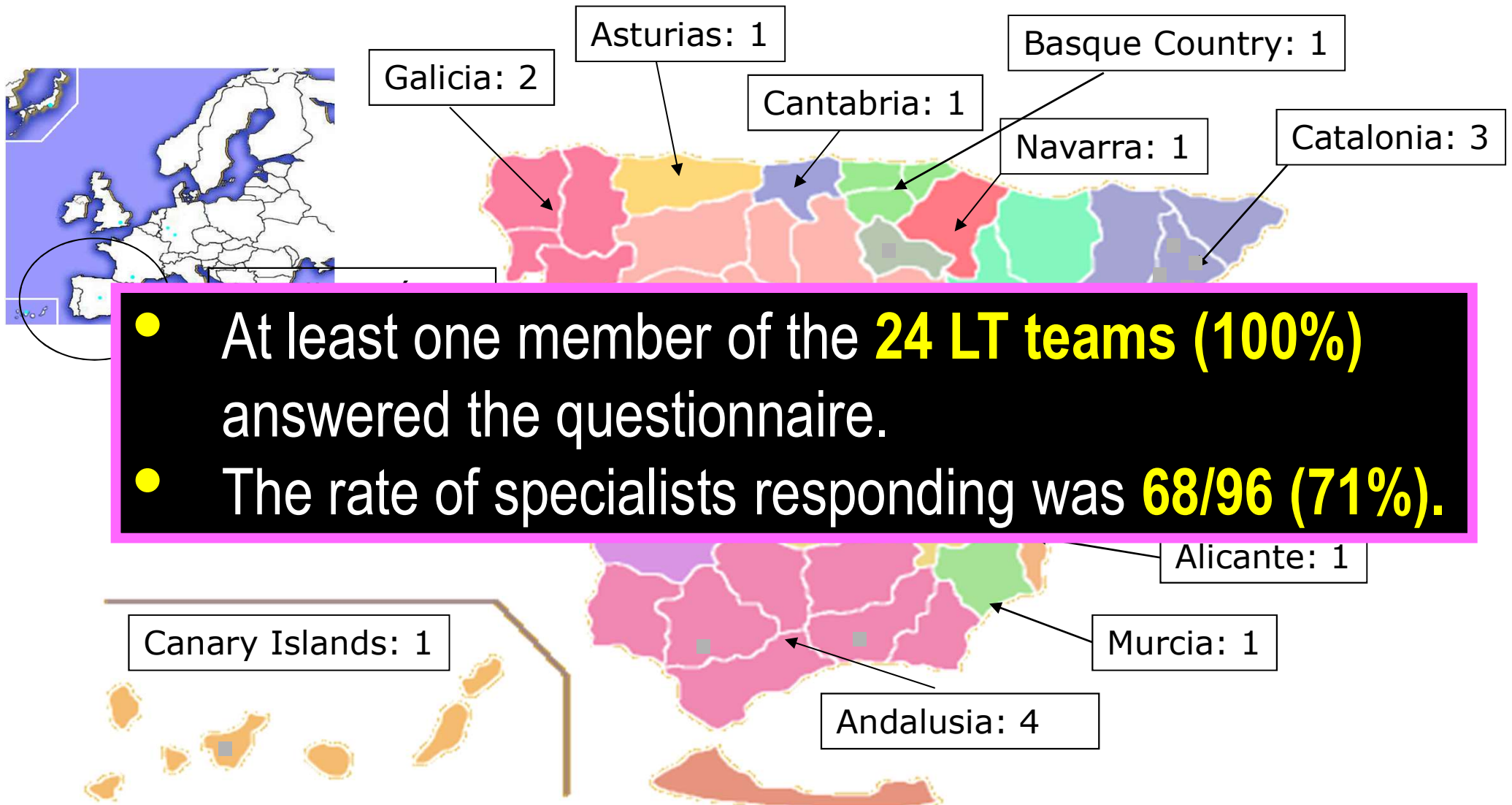
- The survey was conducted in 2018 and was sent to the four members of de LT teams (specialists in HIV/infectious diseases [**HIV/ID**], hepatology [**HEP**], liver surgery [**SURG**] and transplant coordination [**TC**]) from the 24 Spanish adult LT centers participating in the FIPSE LT in HIV-infected recipients.
- The standardized questions were answered through a personalized questionnaire (***REDCap software***), with responses given using an analog scale from 0 (fully disagree) to 10 (fully agree).
- The responses were correlated according to the specialty of the LT team from each center.



# Methods (and II)

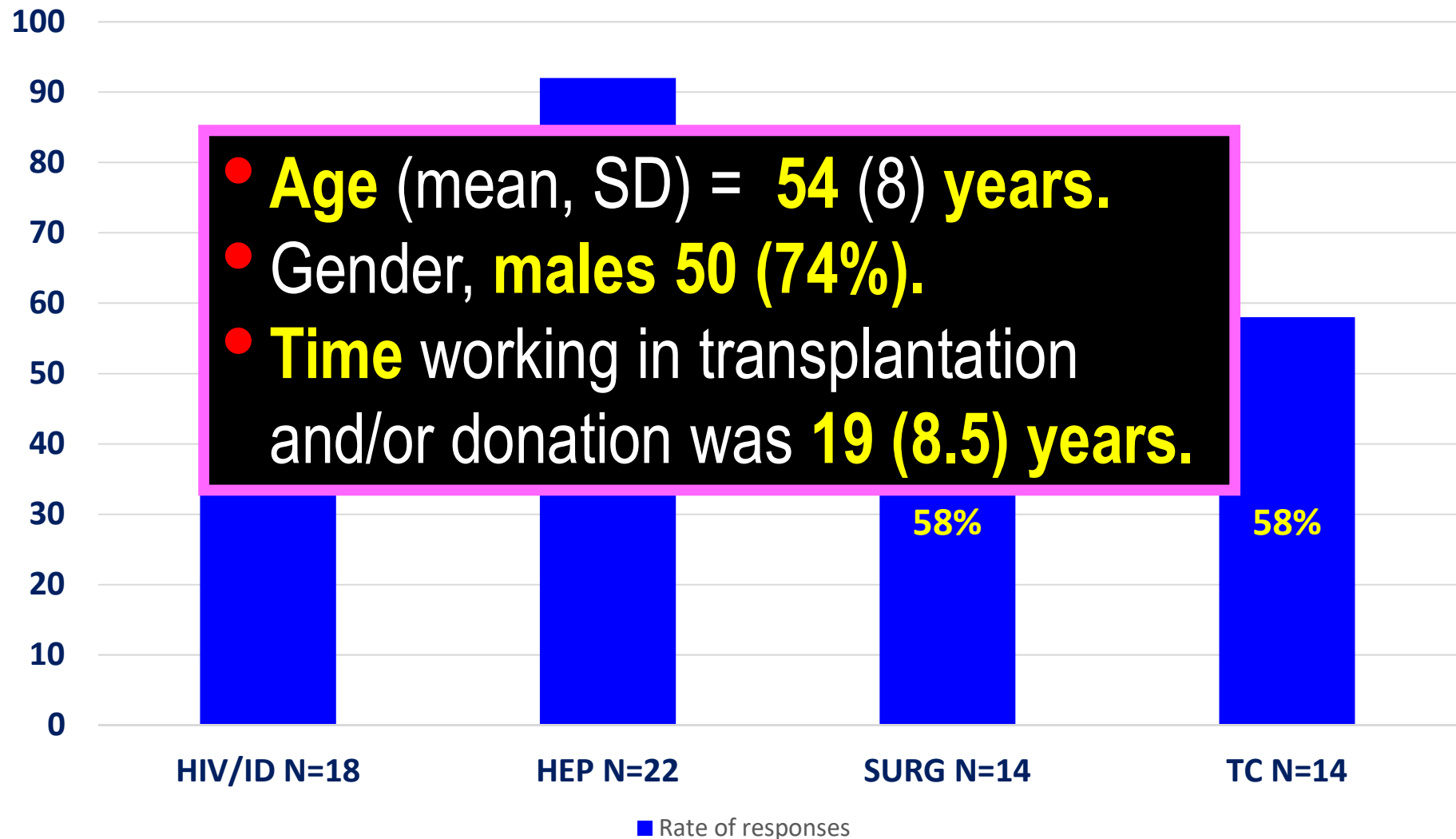
- Variables were described with median and interquartile range (IQR) and with frequency and percent, as appropriate.
- In order to compare characteristics between groups the Chi-squared or Fisher's exact test and Kruskal-Wallis test were performed for categorical and continuous variables, respectively.

# Results: Geographic Distribution of the 24 Spanish Centers Participating in HIV D+/R+ Liver Transplantation Survey



# Results: Demographic data

## Rate of Responses by Specialty



HIV/ID: HIV/infectious diseases; HEP: hepatology; SURG: liver surgery; TC: transplant coordination teams.

# Results: According to the Specialty (I)

|  | HIV/ID<br>N=18 | HEP<br>N=22 | SURG<br>N=14 | TC<br>N=14 |
|--|----------------|-------------|--------------|------------|
| <b>Deceased donor*</b>                         |                |             |              |            |
| - VS on ART**                                  | 9.5 (8,10)     | 7.5 (6,8)   | 10 (5,10)    | 9.5 (3,10) |
| - No VS off ART                                | 2.5 (0,7)      | 2 (0,5)     | 1 (0,2)      | 3 (0,5)    |
| - HIV diagnosis at<br>transplant evaluation    | 3 (0,5)        | 1.5 (0,4)   | 0 (0,2)      | 3.5 (0,4)  |
| - High risk donor, HIV-                        | 9 (7,10)       | 8 (6,9)     | 8 (5,8,10)   | 9 (8,10)   |
| - Serodiscordant HIV-<br>donor but HIV+ couple | 9 (7,10)       | 9 (8,9)     | 8 (6,10)     | 8.5 (1,10) |

VS = HIV virologically suppression; ART = Antiretroviral therapy; HIV/ID: HIV/infectious diseases; HEP: hepatology; SURG: liver surgery; TC: transplant coordination teams. 0 = Fully disagree; 10 = Fully agree. \* Median (IQR) \*\* P value: 0.044.

# Results: According to the Specialty (II)

Living donor\*

- VS on ART\*\*

| HIV/ID<br>N=18 | HEP<br>N=22 | SURG<br>N=14 | TC<br>N=14 |
|----------------|-------------|--------------|------------|
| 8 (6,10)       | 7 (5,8)     | 7 (0,10)     | 8 (0,10)   |

VS = HIV virologically suppression; ART = Antiretroviral therapy; HIV/ID: HIV/infectious diseases; HEP: hepatology; SURG: liver surgery; TC: transplant coordination teams. 0 = Fully disagree; 10 = Fully agree. \* Median (IQR) \*\* P value: 0.628.

# Results: According to the Specialty (III)

| HIV/ID<br>N=18 | HEP<br>N=22 | SURG<br>N=14 | TC<br>N=14 |
|----------------|-------------|--------------|------------|
|----------------|-------------|--------------|------------|

- Use of specific  
Consent Form for HIV-  
infected receptors\*

**10 (9,10)**

9 (8,10)

10 (9,10)

9 (5,10)

- Willingness to  
participate in a HIV  
D+/R+ trial, (%)

**100%**

86%

86%

71%

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**83%,  $p = 0.172$**

HIV/ID: HIV/infectious diseases; HEP: hepatology; SURG: liver surgery; TC: transplant coordination teams.

0 = Fully disagree; 10 = Fully agree. \* Median (IQR) P values: >.05.

# Results

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**There were no differences by age, gender or transplant activity** (global and HIV) except in these two issues:

- **Women** were more in agreement to use organs from HIV negative donors, high risk or with serodiscordant couples.
- **Younger specialists** were more in agreement to participate in a potential HIV D +/-R+ trial.

**The reasons for not participating in a potential HIV D +/-R+ trial were:** No need (fewer HIV recipients and high donor rate in Spain), 55%; lack of evidence, 22%; and; no reasons, 22%.

# Conclusions

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- HIV D+/R+ LT is feasible and currently is under research studies.
- Most Spanish LT team specialists would use livers from virologically suppressed HIV-infected deceased or living donors for HIV-infected recipients with indications for LT.
- Conversely, they would not use organs from donors that were not HIV suppressed or in which HIV-infection was diagnosed at the time of transplant evaluation.
- The results of this survey could initiate a change of the donor law in Spain.



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