

Liver transplantation with extended Milan criteria

Pr Olivier Detry

Dpt of Abdominal Surgery & Transplantation
CHU Liege, University of Liege

**20th BASL Wintermeeting &
11th Interuniversity Liver Course**
Friday 4th and Saturday 5th of December 2015



Liver transplantation for HCC: do size & number really matter??

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LIVER TRANSPLANTATION FOR THE TREATMENT OF SMALL HEPATOCELLULAR CARCINOMAS IN PATIENTS WITH CIRRHOSIS

VINCENZO MAZZAFERRO, M.D., ENRICO REGALIA, M.D., ROBERTO DOCI, M.D., SALVATORE ANDREOLA, M.D., ANDREA PULVIRENTI, M.D., FEDERICO BOZZETTI, M.D., FABRIZIO MONTALTO, M.D., MARIO AMMATUNA, M.D., ALBERTO MORABITO, PH.D., AND LEANDRO GENNARI, M.D., PH.D.

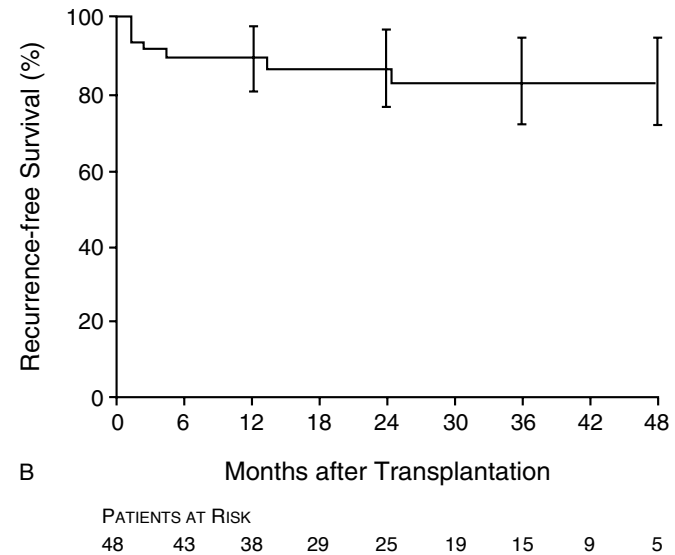
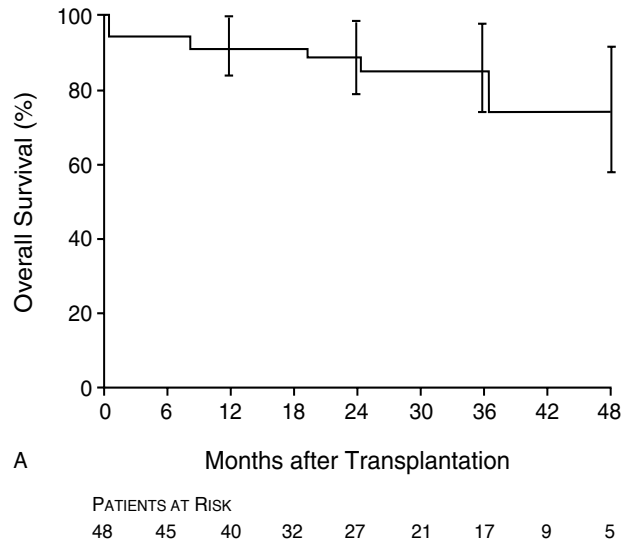
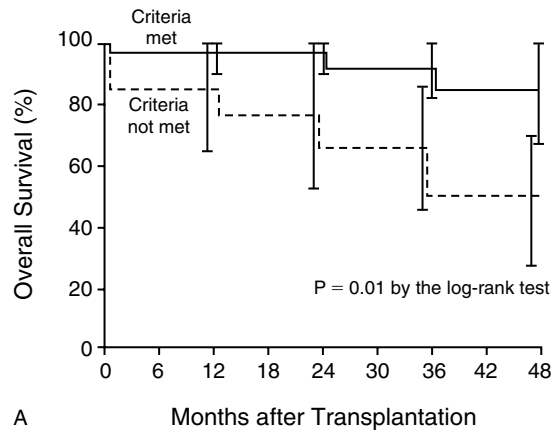


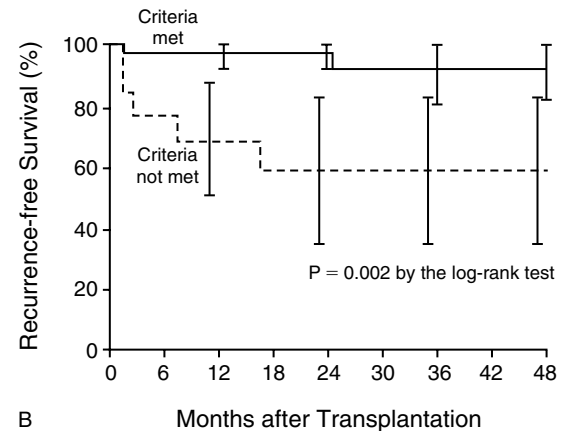
Figure 1. Overall Survival (Panel A) and Recurrence-free Survival (Panel B) after Liver Transplantation in 48 Patients with Small Hepatocellular Carcinomas and Cirrhosis.

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PATIENTS AT RISK		0	6	12	18	24	30	36	42	48
Criteria met	35	34	31	24	21	16	13	6	3	
Criteria not met	13	13	11	8	6	6	4	4	3	



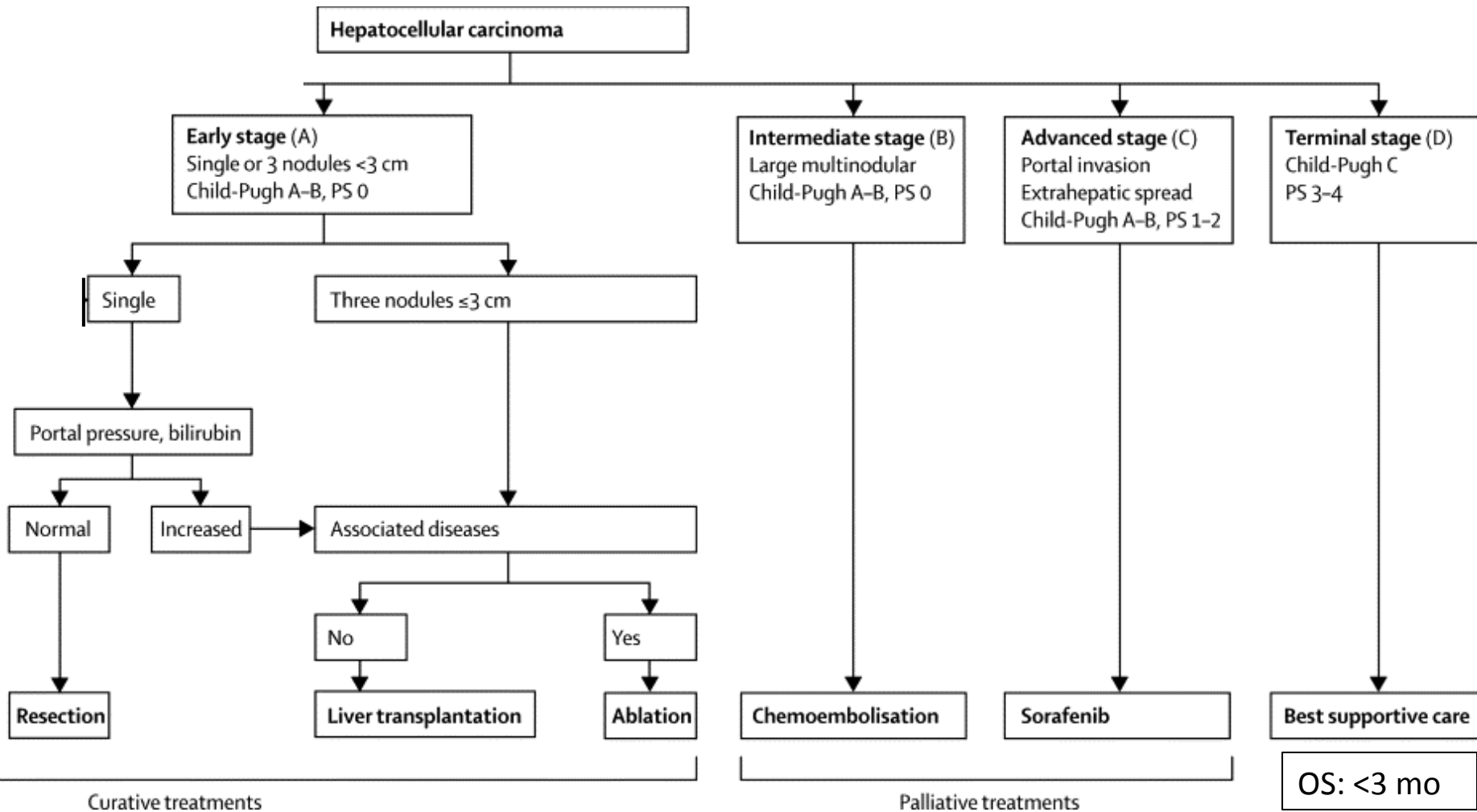
PATIENTS AT RISK		0	6	12	18	24	30	36	42	48
Criteria met	35	34	31	24	21	15	12	6	3	
Criteria not met	13	10	9	5	5	5	4	3	3	

Figure 3. Correlation of Post-Transplantation Pathological Confirmation of Early-Stage Hepatocellular Carcinoma with Overall Survival (Panel A) and Recurrence-free Survival (Panel B) among 48 Patients with Cirrhosis.

LTx & HCC recurrence

- No HCC: no recurrence
- Incidental HCC: very rare recurrence
- Very large HCC and/or neoplastic macroscopic thrombosis: recurrence

- In between?
 - MILAN criteria
 - other criteria?!
 - where to put the limit ?
- Major ethical issue !



Without treatment: median survival < 3 yrs
Median OS > 60 mo; 5-yr survival: 40-70%

Without Treat: OS: 16 mo
OS: 20 mo

Without Treat: OS: 8 mo
OS: 11 mo (6-14)

HCC Milan

- Eurotransplant liver graft allocation:
 - HCC within Milan: SE (Exceptional MELD)
 - HCC outside Milan: MELD allocation
MELD
center offer
DCD LT
 - Downstaged HCC: NSE

Milan out HCC criteria

- UCSF: 1 nodule ≤ 6.5 cm, ≤ 3 nodules (largest 4.5 cm & total $\leq \textcircled{8}$ cm)
- up-to-7: ≤ 7 nodules, largest ≤ 7 cm
- Tokyo: 5-5 rule: ≤ 5 nodules, largest ≤ 5 cm
- Hangzhou: total $\leq \textcircled{8}$ cm or $> \textcircled{8}$ cm with AFP < 400 ng/ml
- Asan (South Korea): ≤ 5 cm, ≤ 6 nodules
- Shanghai: 1 nodule ≤ 9 cm, ≤ 3 nodules (largest 5 cm & total $\leq \textcircled{9}$ cm)

AFP model

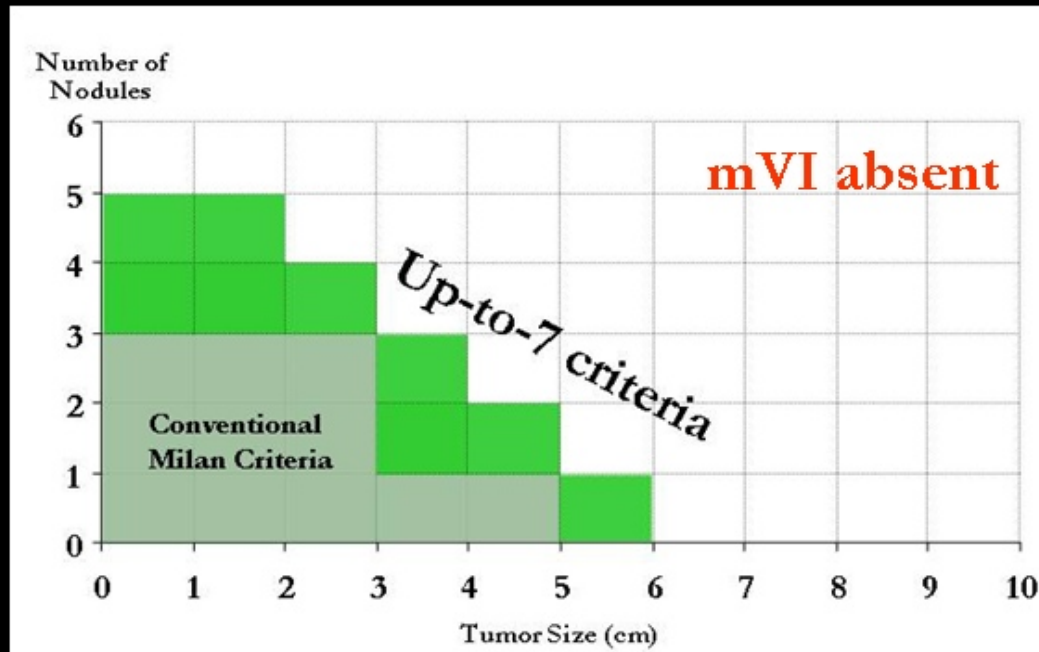
Table 2. Simplified, User-Friendly Version of the AFP Model

Variables	β coefficient	Hazard ratio	Points
Largest diameter, <i>cm</i>			
≤3	0	1	0
3–6	0.272	1.31	1
>6	1.347	3.84	4
Number of nodules			
1–3	0	1	0
≥4	0.696	2.01	2
AFP level, <i>ng/mL</i>			
≤100	0	1	0
100–1000	0.668	1.95	2
>1000	0.945	2.57	3

Low risk: ≤ 2
High risk: > 2

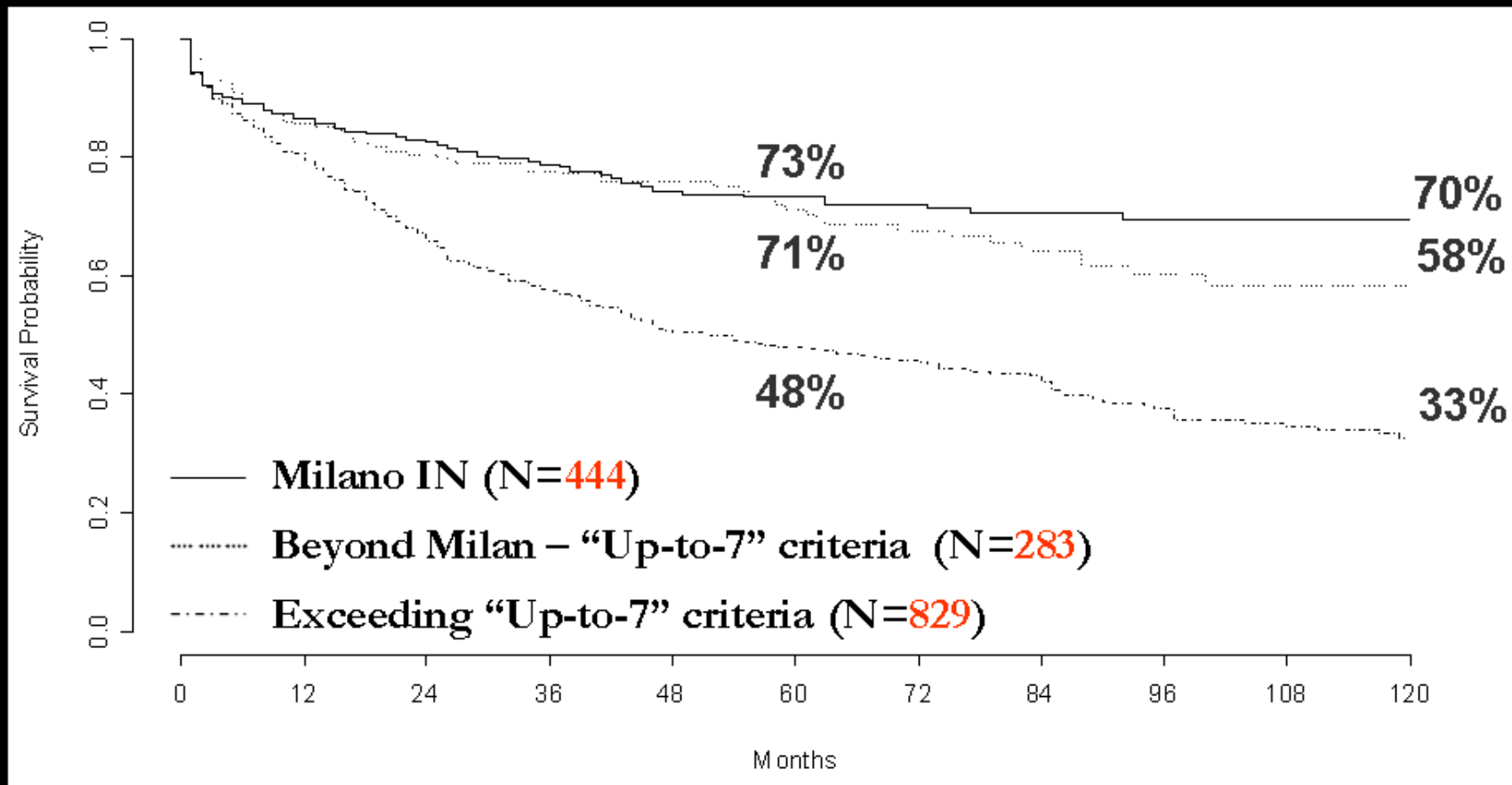
NOTE. The score is calculated by adding the individual points for each obtained variable. A cut-off value of 2 separates between patients at high and low risk of recurrence. In this simplified version, a cut-off value of 2 selected exactly the same patients as the original Cox score cut-off value of 0.7.

The “up-to-7 Criteria”



The “up-to-7” criteria could be a good starting point for prospective clinical trials on expansion of Milan Criteria

Proving the existence of a good outcome group (“up-to-7”) outside the Conventional Milan Criteria



Median follow-up: 53 months

Which HCC patients are ideal candidates for OLT?

Jeroen Dekervel, MD

On behalf of the Belgium Liver Intestinal Advisory Committee (BeLIAC) and the Belgian Transplantation Society (BTS)

2015 Eurotransplant Annual Meeting



Models tested on Be-LIAC cohort

Milan Criteria



< 5 cm (> 2 cm)



< 3 cm

Mazzaferro et al. NEJM 2006

aFP model

Point system

Number of lesions
Size of lesions
aFP level

≤ 2 points
=
low risk

Duvoux et al. Gastroenterology 2012

Asan Criteria

Largest lesion
≤ 5 cm

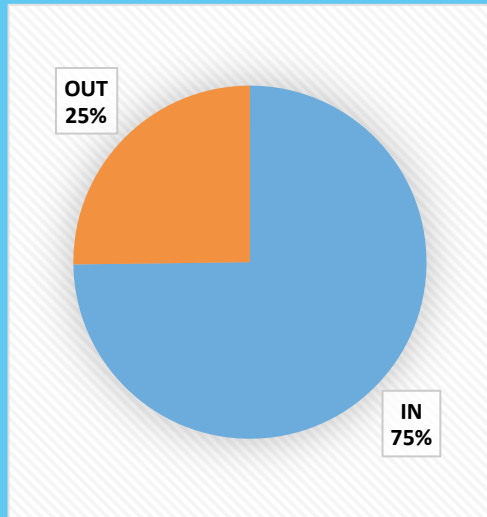
AND

Number of lesions
≤ 6

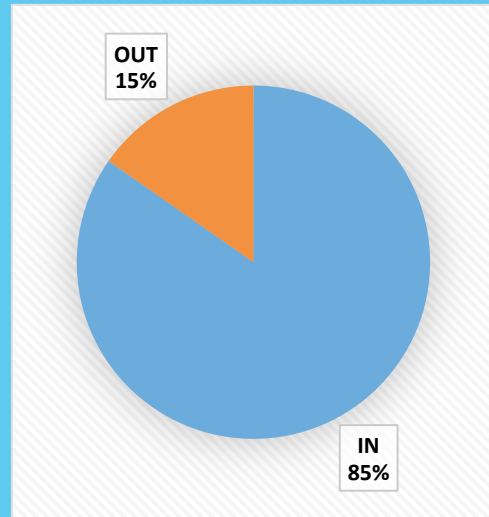
Lee et al. Liver Transpl 2008

Be-LIAC cohort

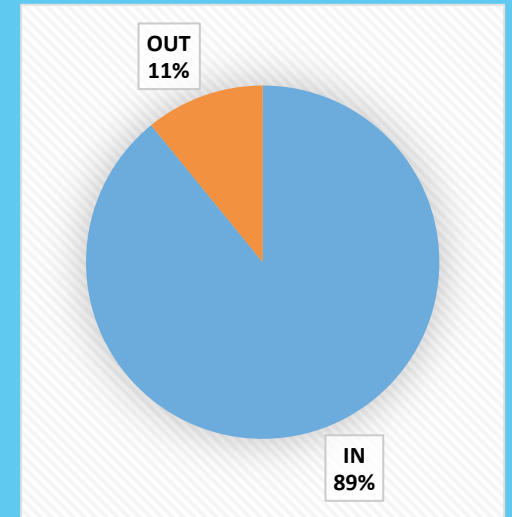
Milan Criteria



aFP model



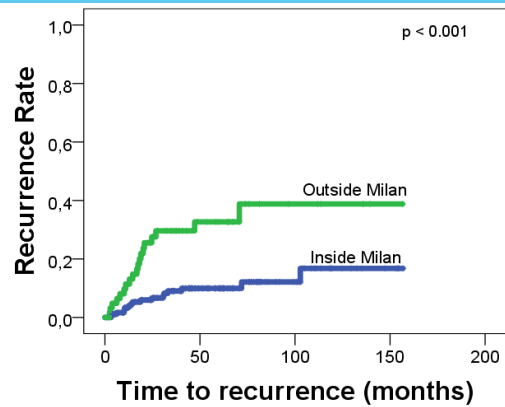
Asan Criteria



* At time of listing

Be-LIAC cohort

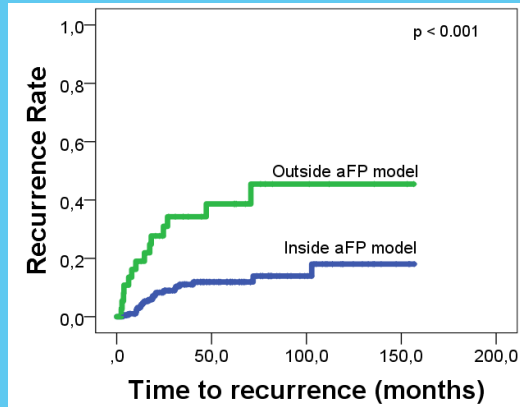
Milan Criteria



5 yr Recurrence rate

IN 10 % ± 2.5
OUT 33 % ± 7

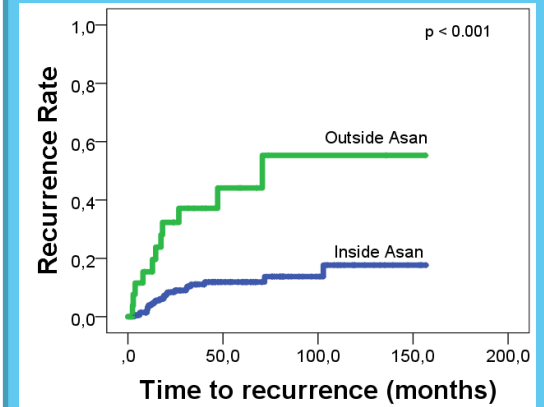
aFP model



5 yr Recurrence rate

IN 12% ± 2.5
OUT 39 % ± 9

Asan Criteria



5 yr Recurrence rate

IN 12% ± 2.5
OUT 44 % ± 11

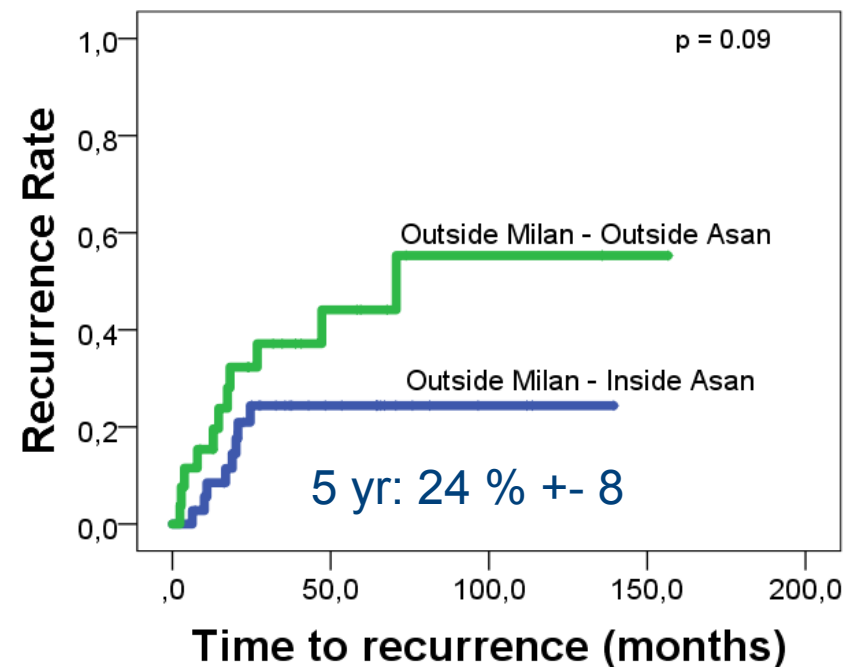
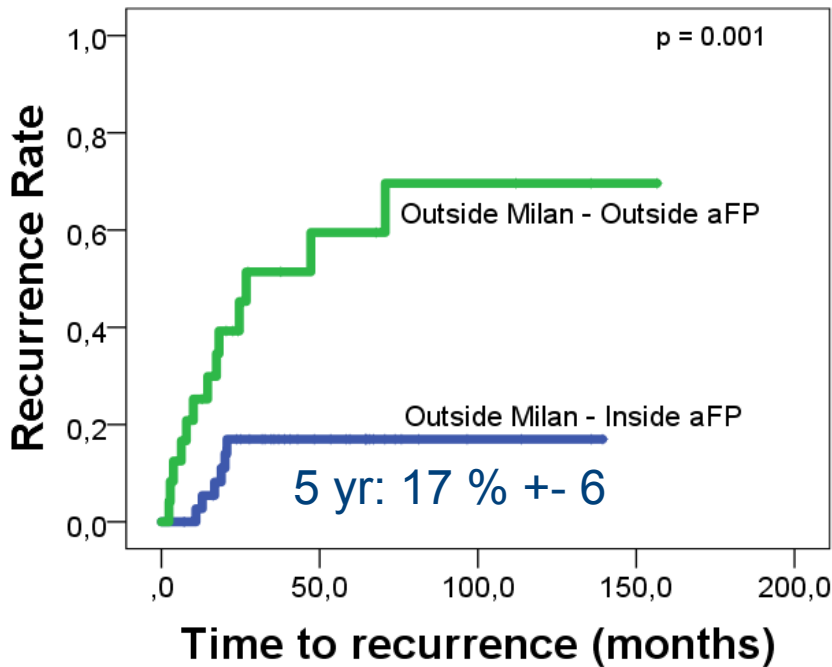
Be-LIAC cohort

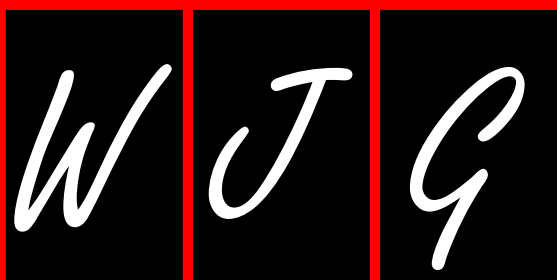
aFP model

		IN	OUT
Milan	IN	167 (69 %)	13 (5%)
	OUT	38 (16%)	24 (10%)

Asan criteria

		IN	OUT
Milan	IN	177 (74 %)	0 (0 %)
	OUT	36 (15 %)	26 (11 %)





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EVIDENCE-BASED MEDICINE

Prognostic value of ^{18}F -FDG PET/CT in liver transplantation for hepatocarcinoma

Olivier Detry, Laurence Govaerts, Arnaud Deroover, Morgan Vandermeulen, Nicolas Meurisse, Serge Malenga, Noella Bletard, Charles Mbendi, Anne Lamproye, Pierre Honoré, Paul Meunier, Jean Delwaide, Roland Hustinx

Patients

- 52 LT for HCC during the study period
- 27 fulfilled the inclusion criteria
 - 13 Milan in (SE)
 - 14 Milan out (rescue allocation & DCD)
- Mean follow-up: 26 months
- Mean interval between PET & LT: 4 months

Original article

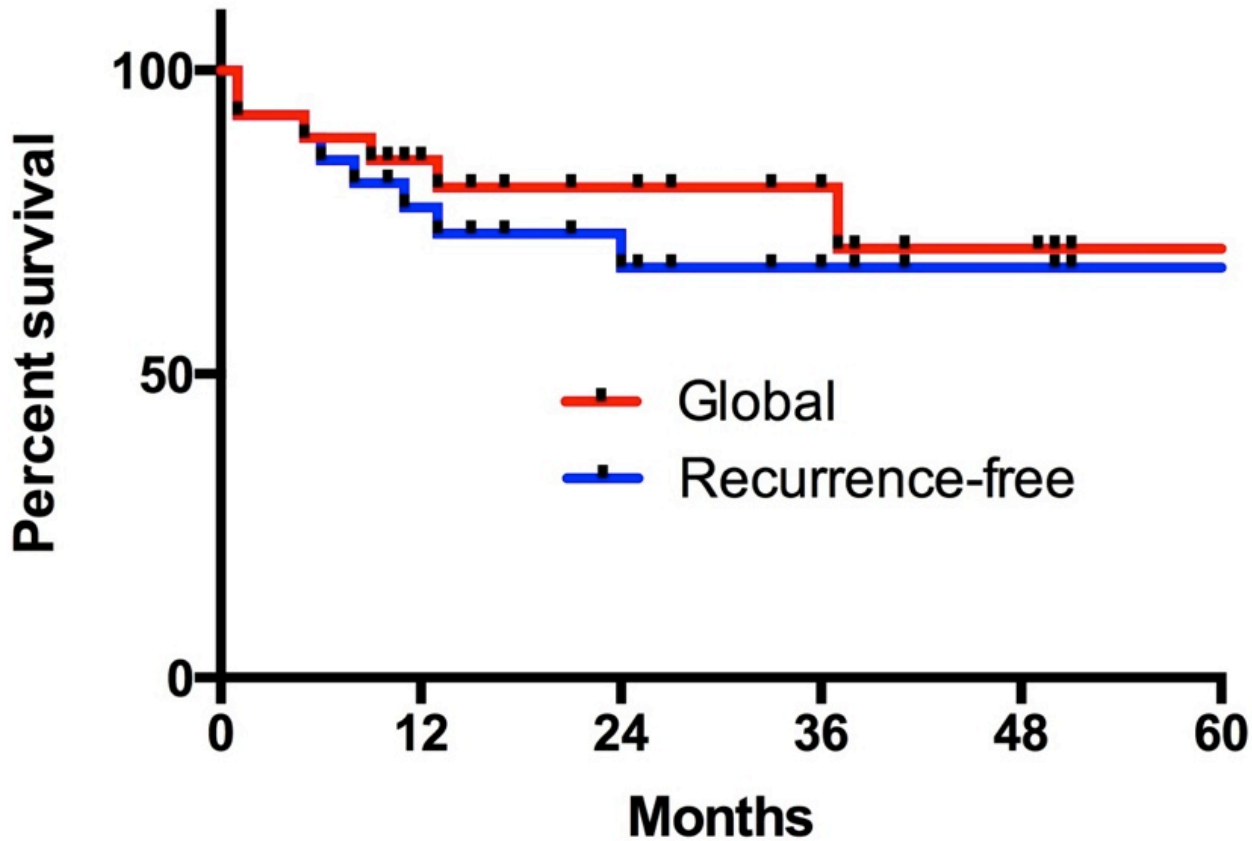
Donor age as a risk factor in donation after circulatory death liver transplantation in a controlled withdrawal protocol programme

O. Detry¹, A. Deroover¹, N. Meurisse¹, M. F. Hans¹, J. Delwaide², S. Lauwick³, A. Kaba³, J. Joris³, M. Meurisse¹ and P. Honoré¹

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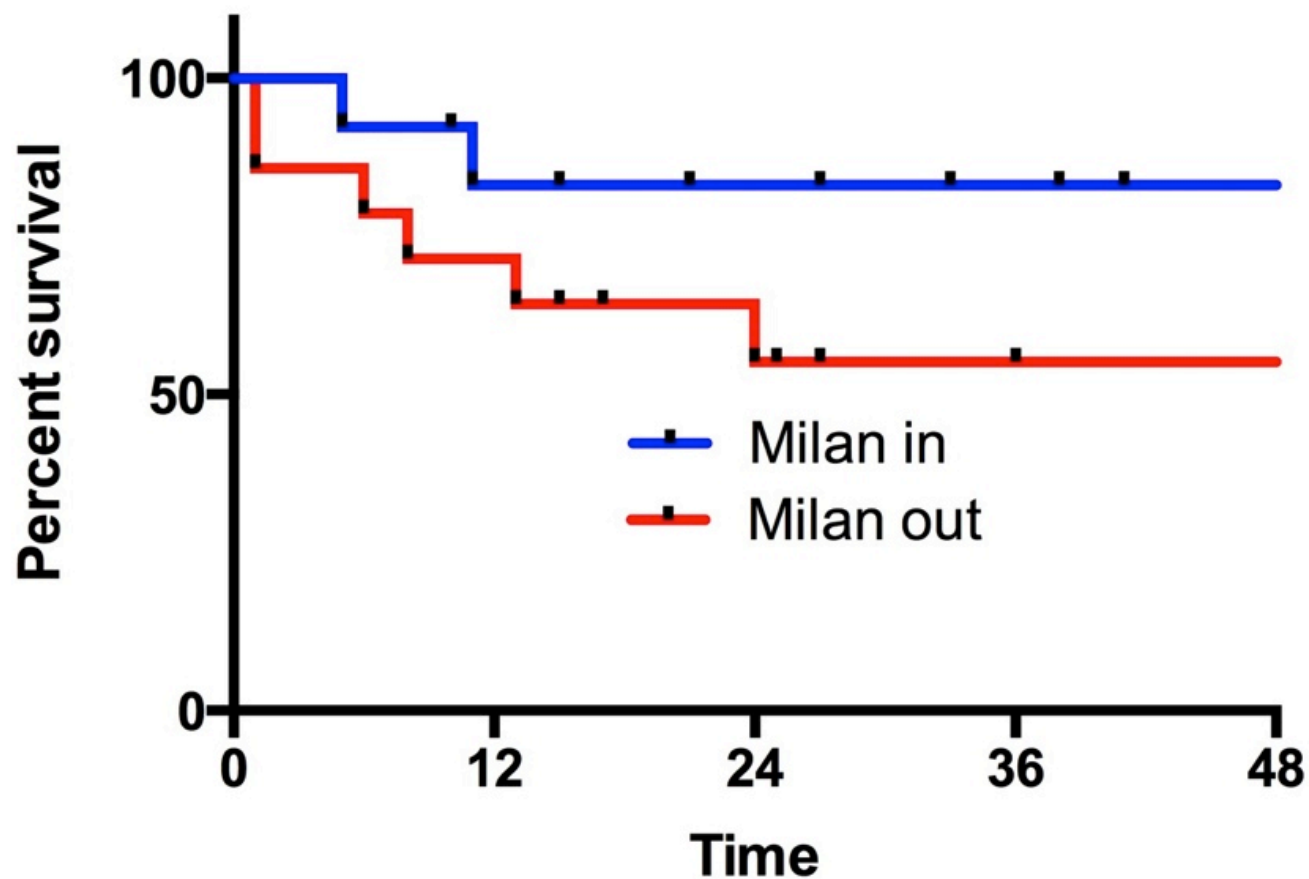
Correspondence to: Professor O. Detry, Department of Abdominal Surgery and Transplantation, CHU Liège, Sart Tilman B35, B4000 Liège, Belgium (e-mail: olivier.detry@transplantation.be)

Patient survival

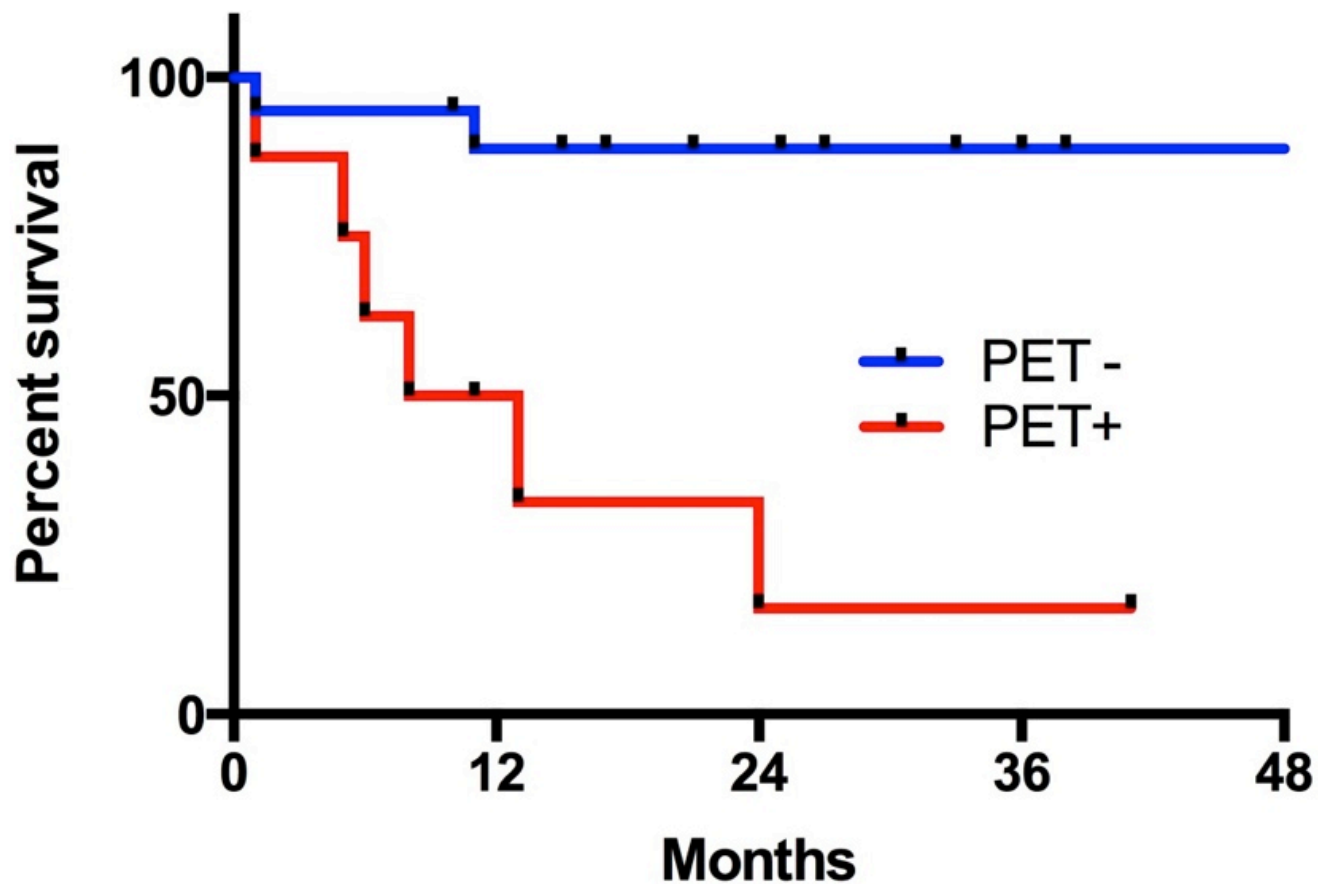


- One year survival: 85%
- Five-year survival: 70.6%

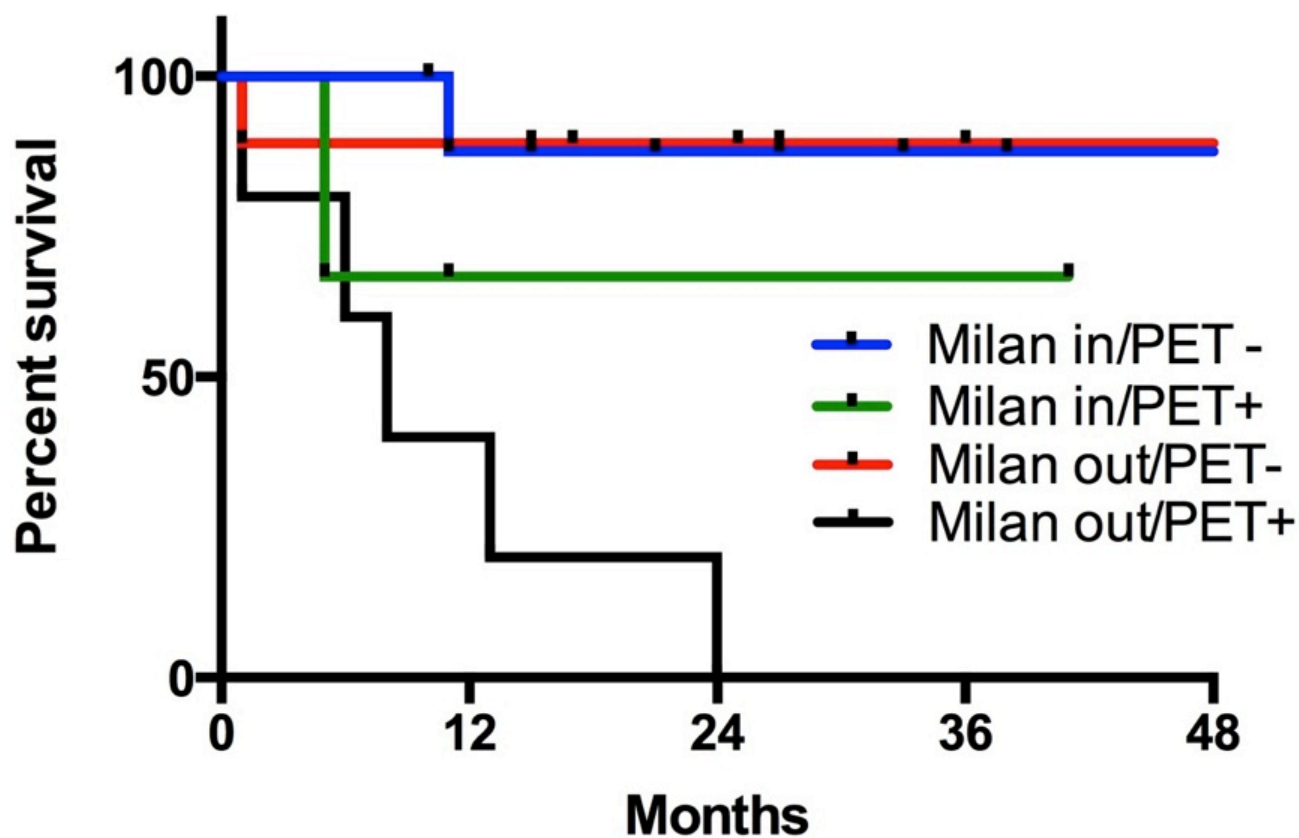
Recurrence-free survival



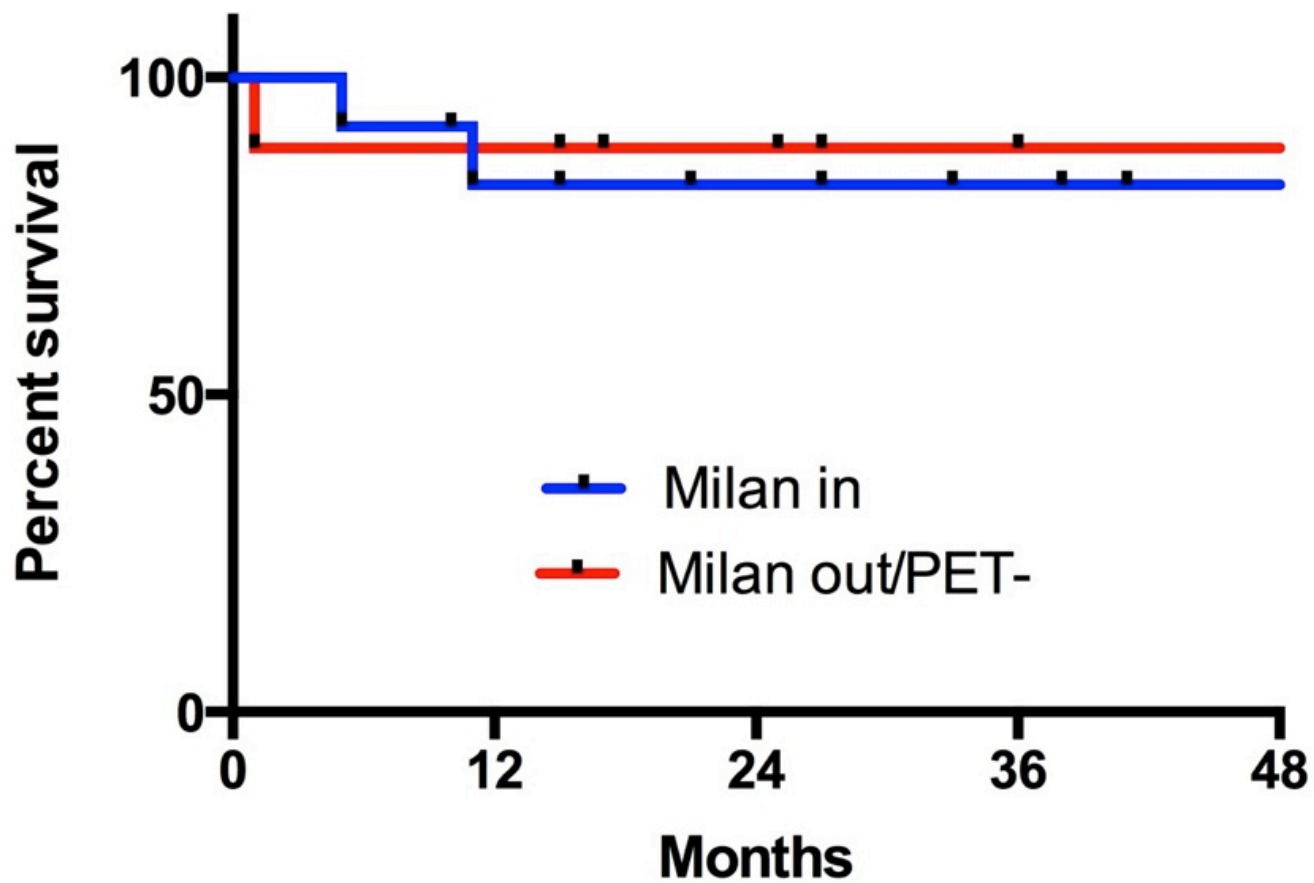
Recurrence-free survival



Recurrence-free survival



Recurrence-free survival



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YES!

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HCC

- Number of nodules & size is not the magic bullet
- MILAN criteria are too restrictive and should be enlarged
- **Tumor biology & differentiation**
 - AFP
 - Response to adjuvant therapy
 - PET scan ?
- Post transplant chemotherapy ?