

Liver Transplantation for HCC

Which Criteria ?

Jacques Belghiti - François Durand

Claire Francoz

Hepato-Biliary-Pancreatic Liver Surgery and Liver Transplantation Unit

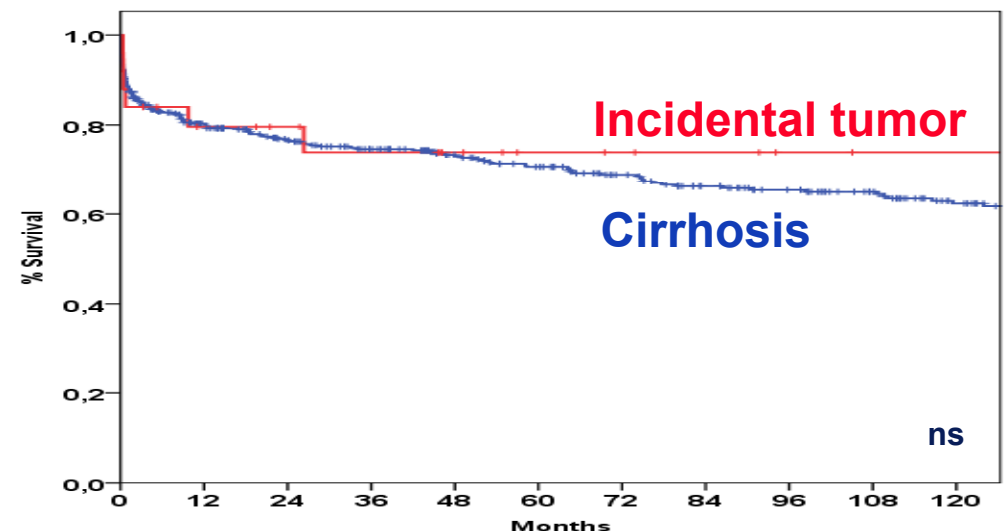
Hôpital Beaujon (AP-HP), Clichy - University Paris 7

Liver Transplantation Unique Transplantation for Malignancy

- Transplantation for Unresectable HCC

Table 2. LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA

Center	Year	Patients	30-Day Mortality (%)	Recurrence (%)	1-Year Survival (%)	2-Year Survival (%)	3-Year Survival (%)	5-Year Survival (%)
University of Pittsburgh, Pittsburgh, PA ³⁷	1988	80	13*	37	64	—	45	45
King's College Hospital, London, UK ³⁸	1987	50	23–32*	65	42–48	37–38	—	—
Queen Elizabeth Hospital, Birmingham, UK ³⁹	1989	21	38	29	45	21	21	21
Medizinische Hochschule, Hannover, Germany ⁴⁰	1990	87	13–24	—	55	40	30	20
Massachusetts General Hospital, Boston, MA ⁴¹	1990	24	17	25	71	56	42	—
UCLA, Los Angeles, CA ⁴² †	1992	44						



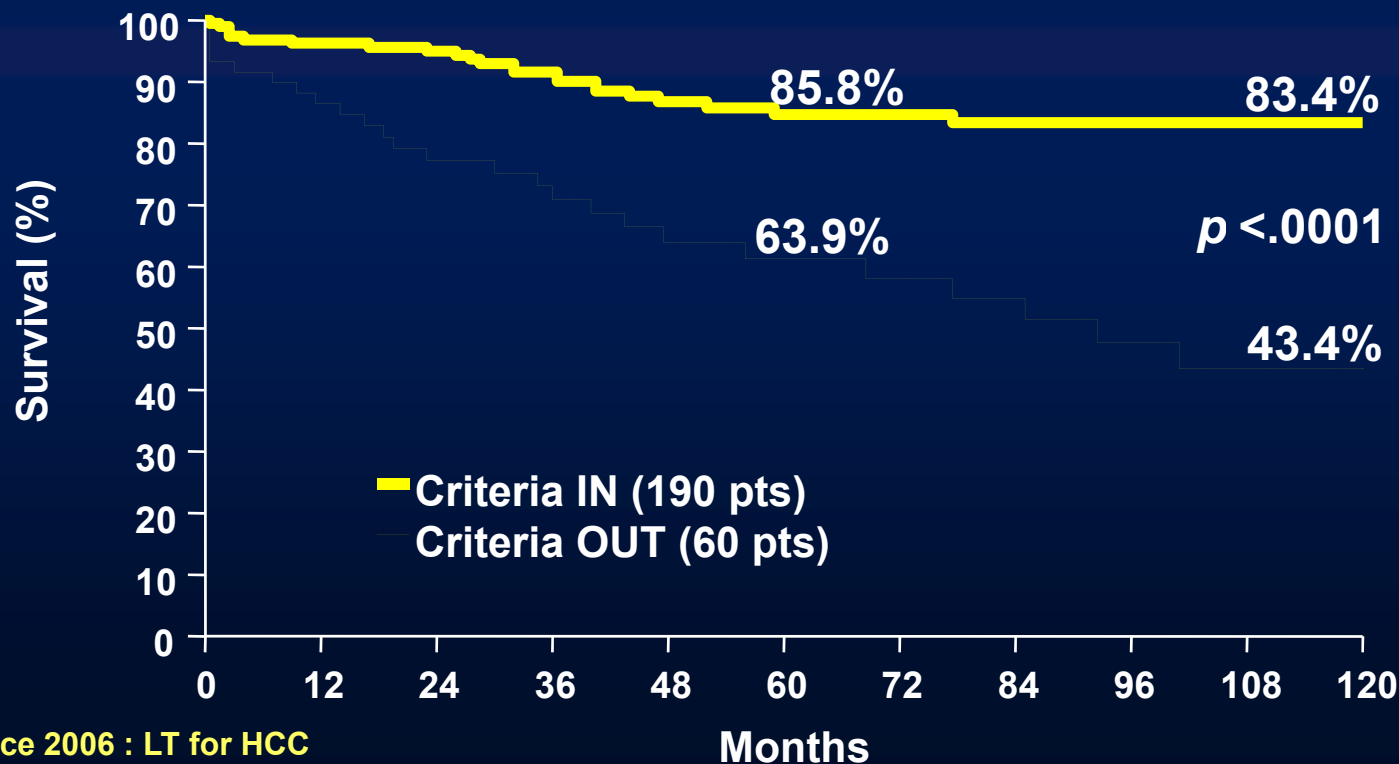
Efficiency of Liver Transplantation for HCC

- From Undetectable to Morphological HCC.

- Milan Criteria: Mazzaferro et al. N Eng J Med 1996

- Single tumor < 5 cm or 2 to 3 none > 3 cm*

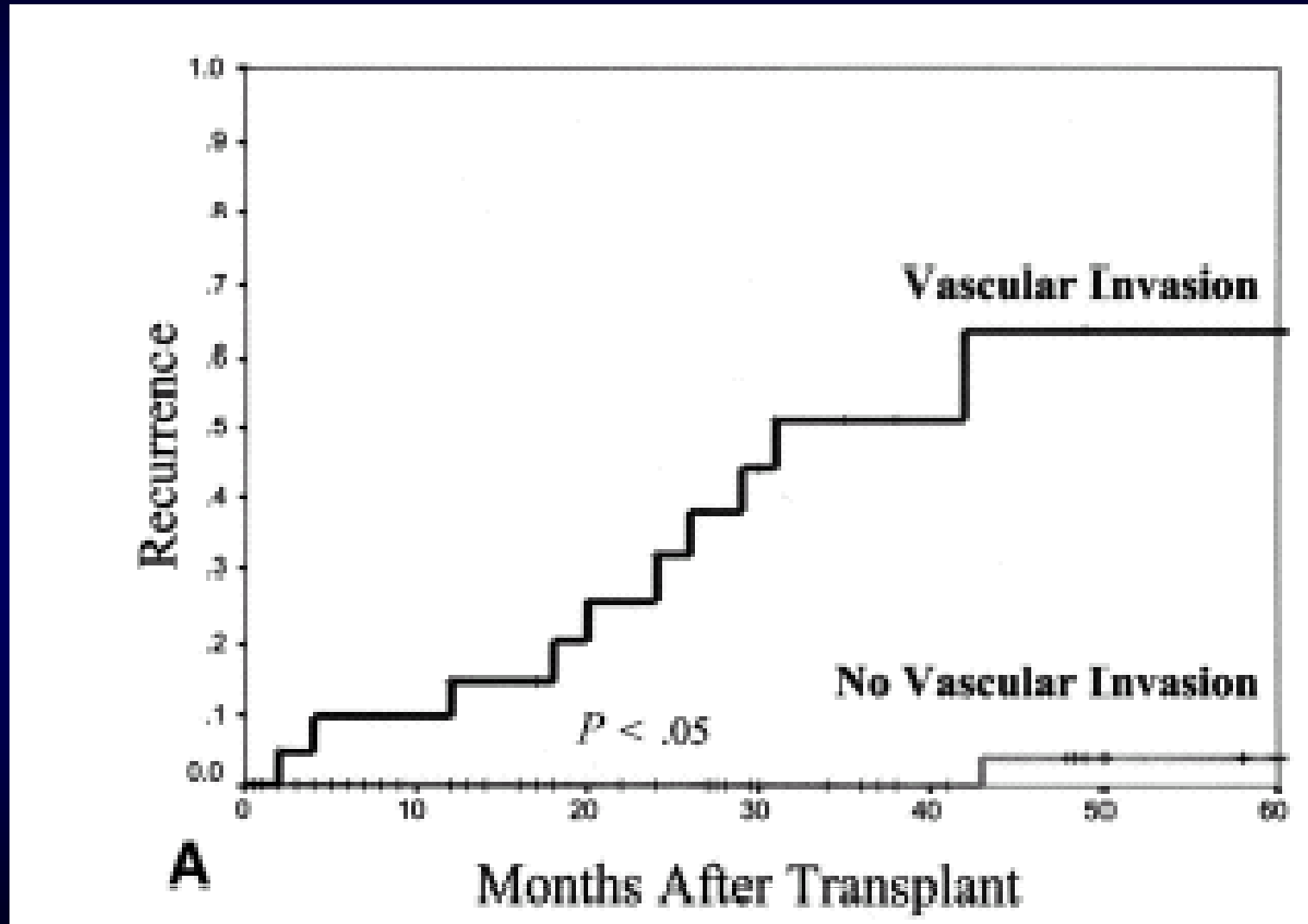
- Absence of vascular invasion*



LT for HCC – Milan Criteria

- Excellent results: Recommended by nearly all institution conferences on Liver Allocation in Patients with HCC.
- Rational for selective criteria:
 - Recurrence of HCC after LT : disastrous prognosis !
 - » Rapid progression due to immunosuppression
 - » Short life expectancy
 - Graft should be use in oncologic patients with the same prognosis than in non HCC patient.

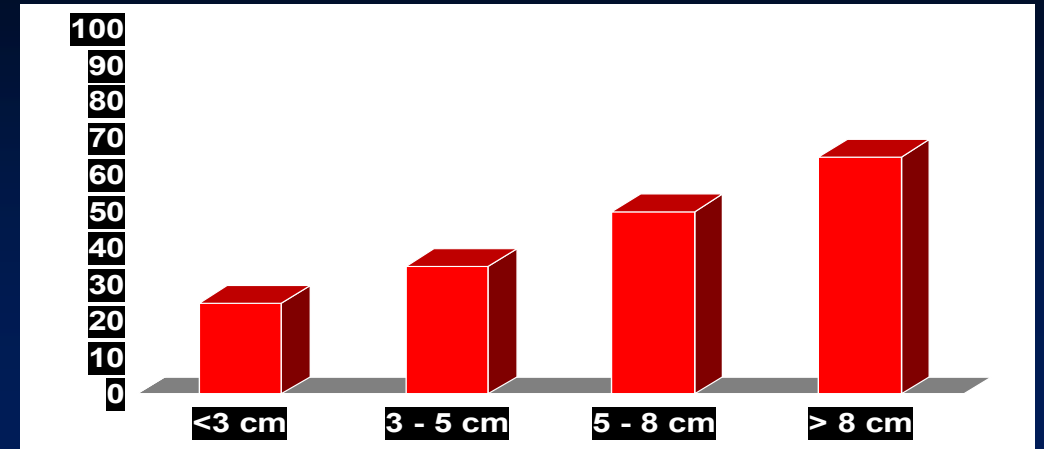
Vascular invasion is the most important predictive factor of recurrence of HCC after LT



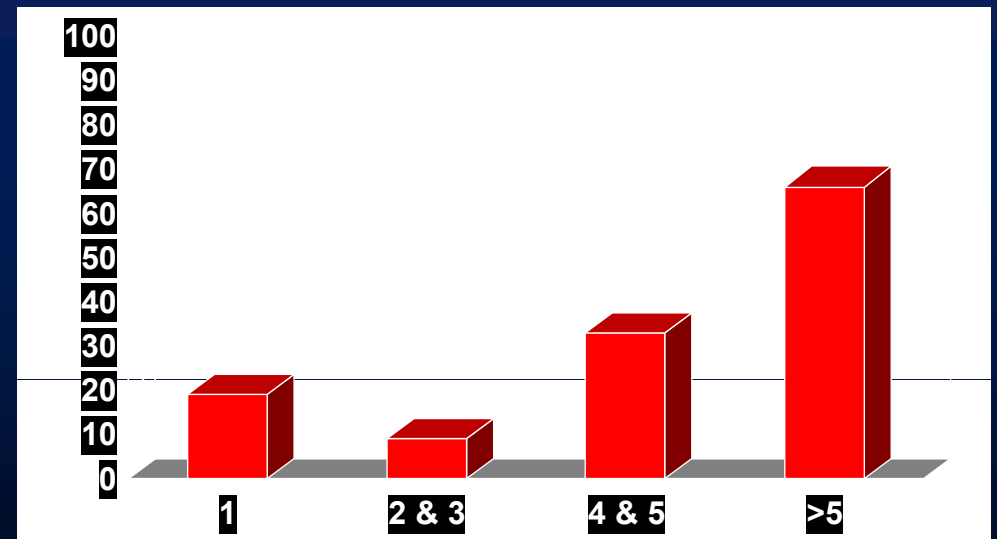
Hemming et al. Ann Surg, 2002.

The risk of vascular invasion increases with

1. size of tumors



2. number of tumors



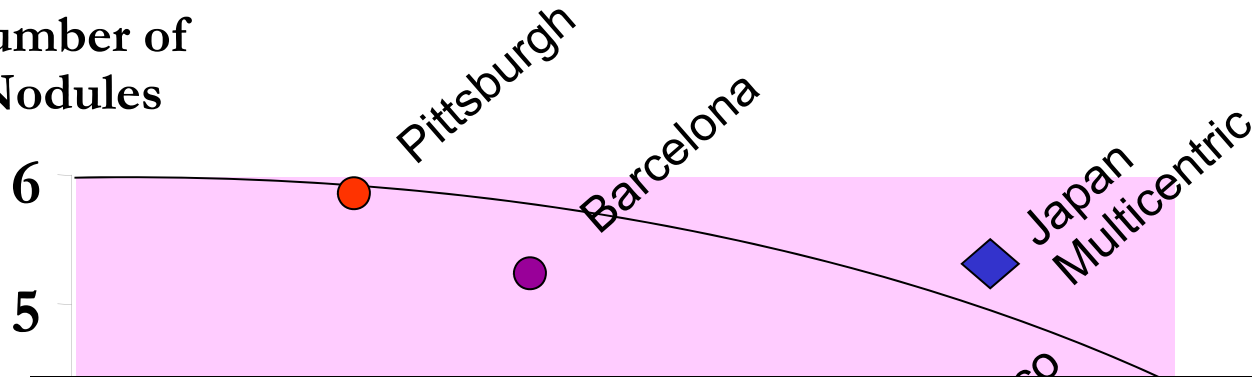
Some Patients beyond MC (size and number of nodules) without vascular invasion could be good candidates

Expanded Criteria for HCC LT

2004 - 2010 Author (Institution)	Proposed criteria			5-yr survival
	main	total \emptyset	nodules	
Yao (UCSF)	6.5 cm	< 8cm	2 – 3	80%
Herrero (Pamplona)	6 cm		2-3 < 5cm	73%
Kneteman (Edmonton)	7.5 cm		any < 5cm	55%
Silva (Valencia)		< 10 cm	3 < 5 cm	69%
Guiteau (Dallas)	< 6cm	< 9 cm	2-3 < 5cm	77%
Lee (ASAN)	< 6.5 cm		< 6	76%
Ito (Kyoto)		< 10	nodules < 5 cm	78%
Suguwara (Tokyo)	< 5 cm		< 5	73%
Zheng (Hangzhou)		< 8 cm		72%

The metroticket paradigm

Number of Nodules

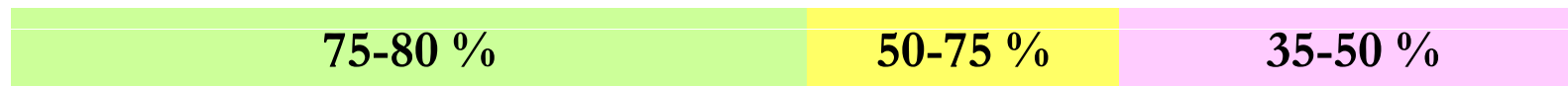


the longer the trip
the higher the price

Dual charges for extending criteria:

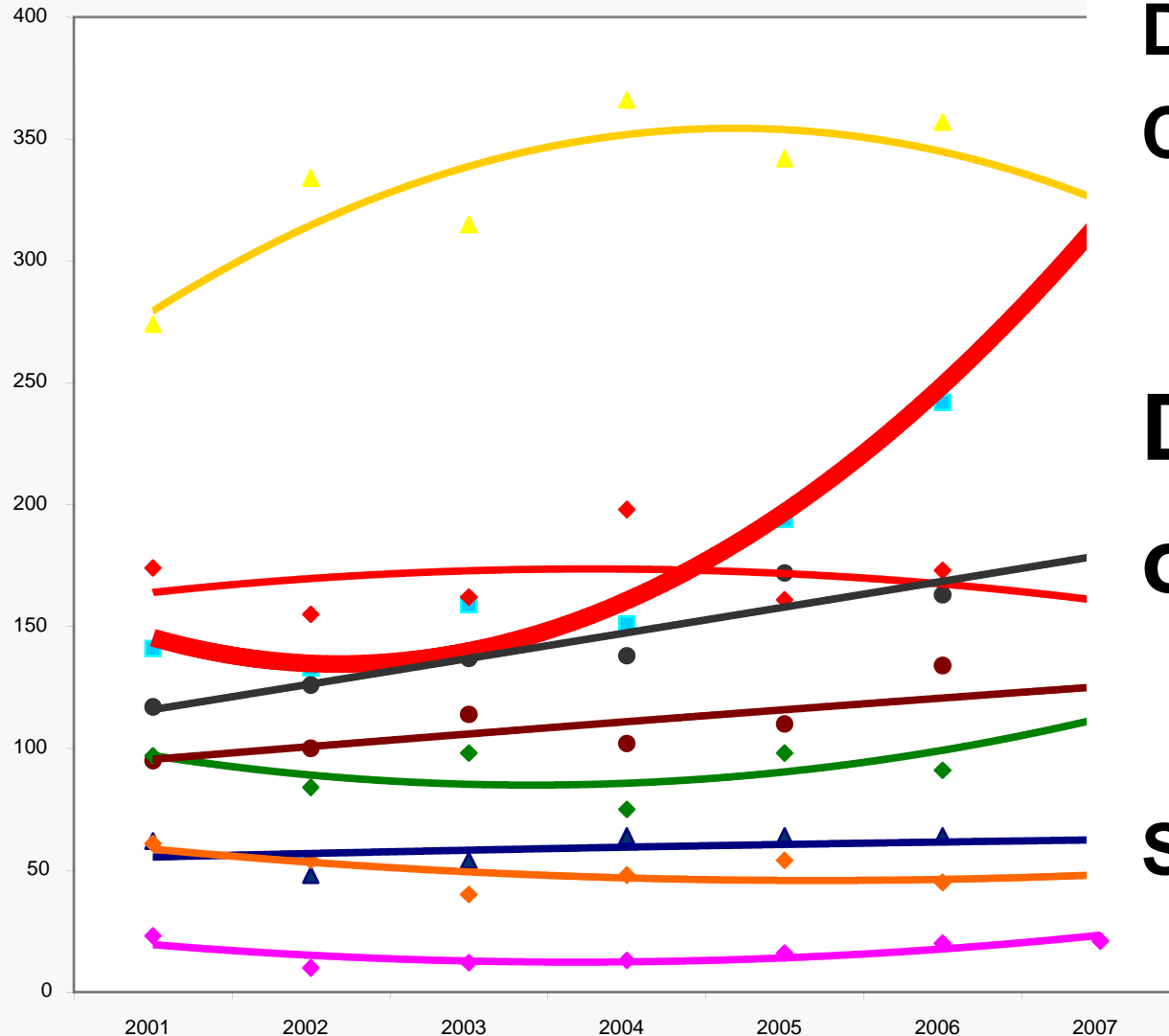
- Inferior outcome after transplantation
- Negative impact on the waiting time and wait list mortality

Tumor Size (cm)



Expected 5-year survival

Patients Listed for LT: 2001 - 2007



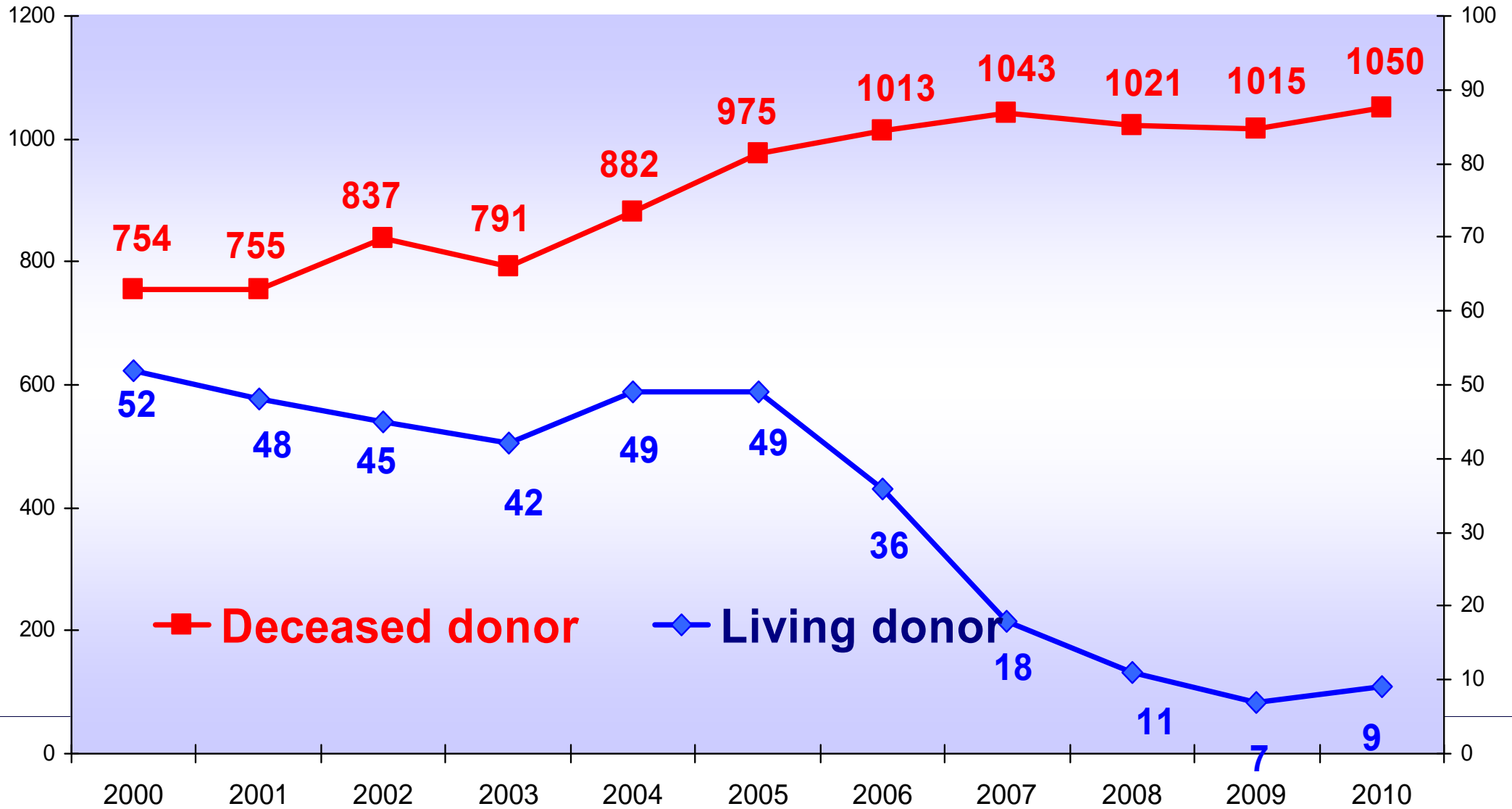
Decrease of Alcohol Cirrhosis

Dramatic increase of HCC

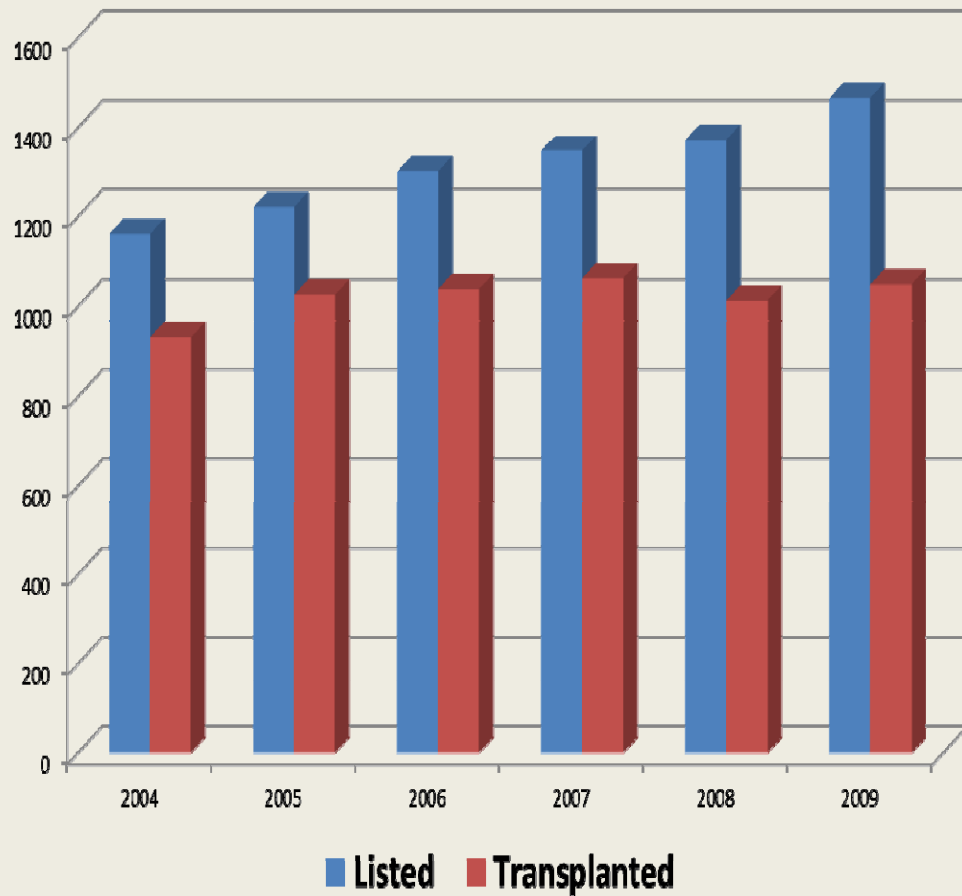
Stability other etiologies



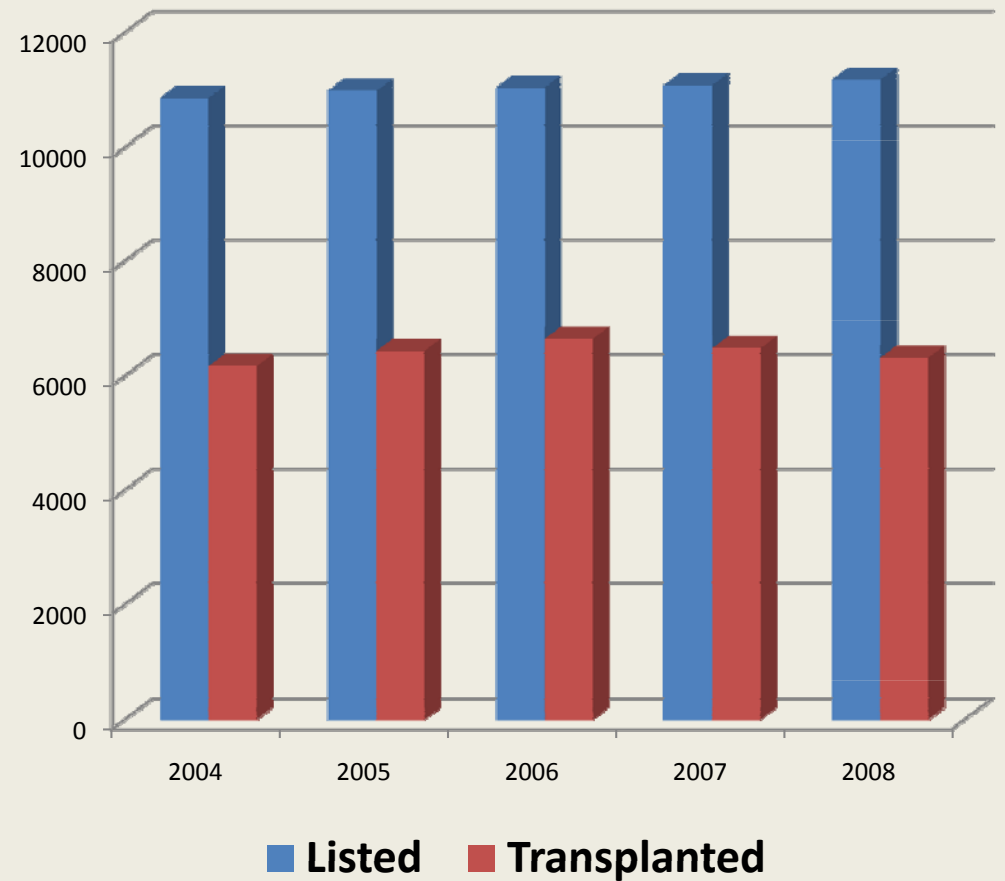
Adult-to-adult LDLT in France



Organ shortage



Data Agence de la Biomédecine



Data UNOS

Increase time on the waiting list

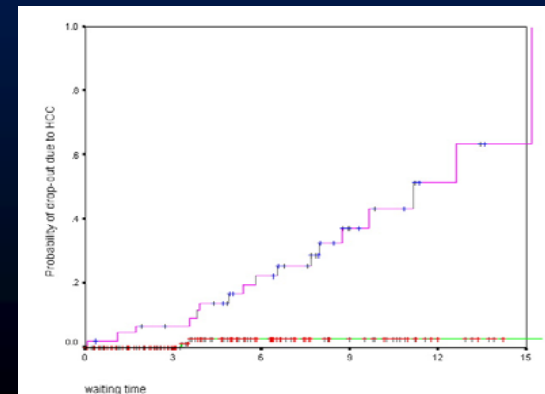
Transplantation
decision

Transplantation

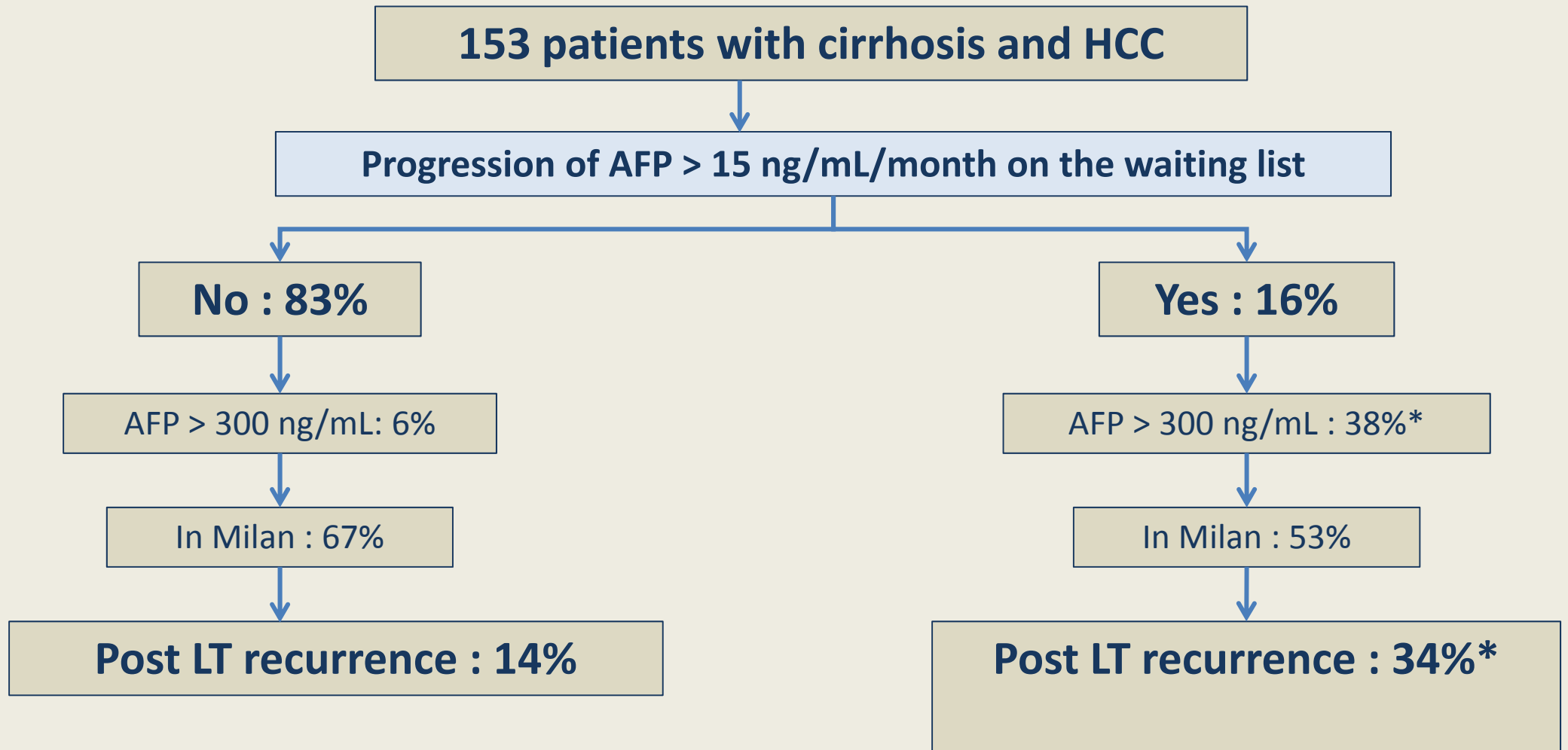


- **Tumor progression** ⇒ Risk of Drop-out (2 - 4% / months)
- Increased with elevated AFP

Llovet et al. Hepatology, 2003A



Impact of AFP on recurrence



Factors with an impact on recurrence

- Tumor size
- Number of nodules
- Microvascular invasion
- Tumor differentiation
- Serum alpha fetoprotein
- CK19
- PET scan

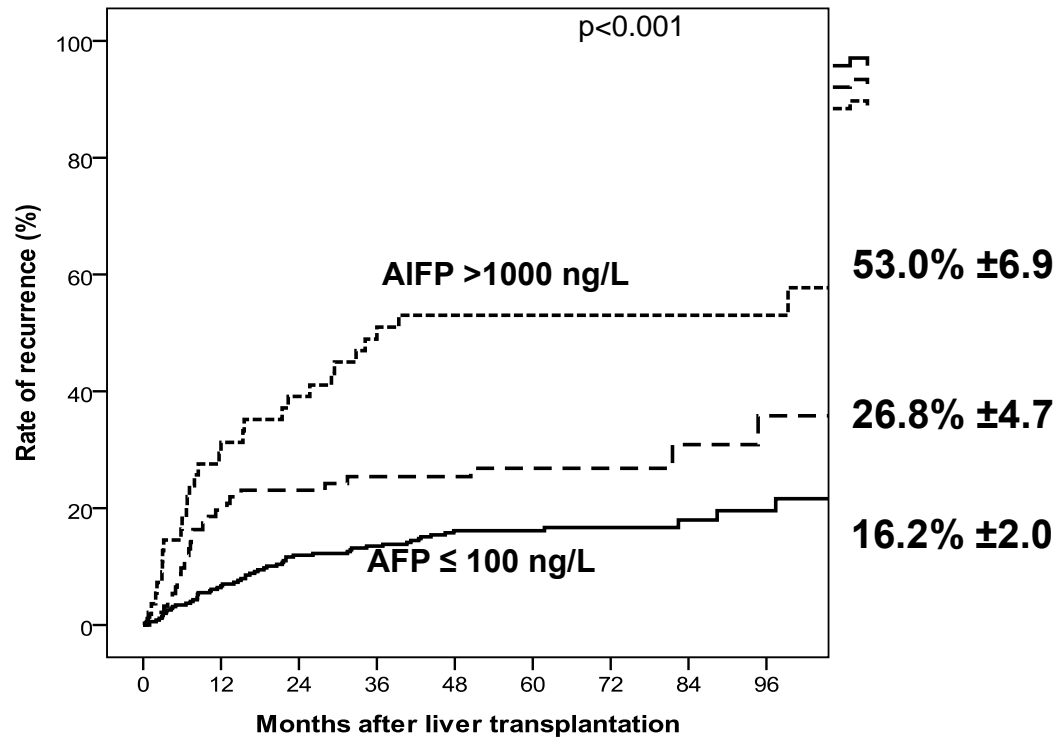
Morphological

After LT

Under investigation



Rate of recurrence according to alpha fetoprotein level in the training cohort (n = 557 patients)



Variables	Hazard ratio
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Largest diameter	
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≤ 3	1
3 - 6	1.31
> 6	3.84

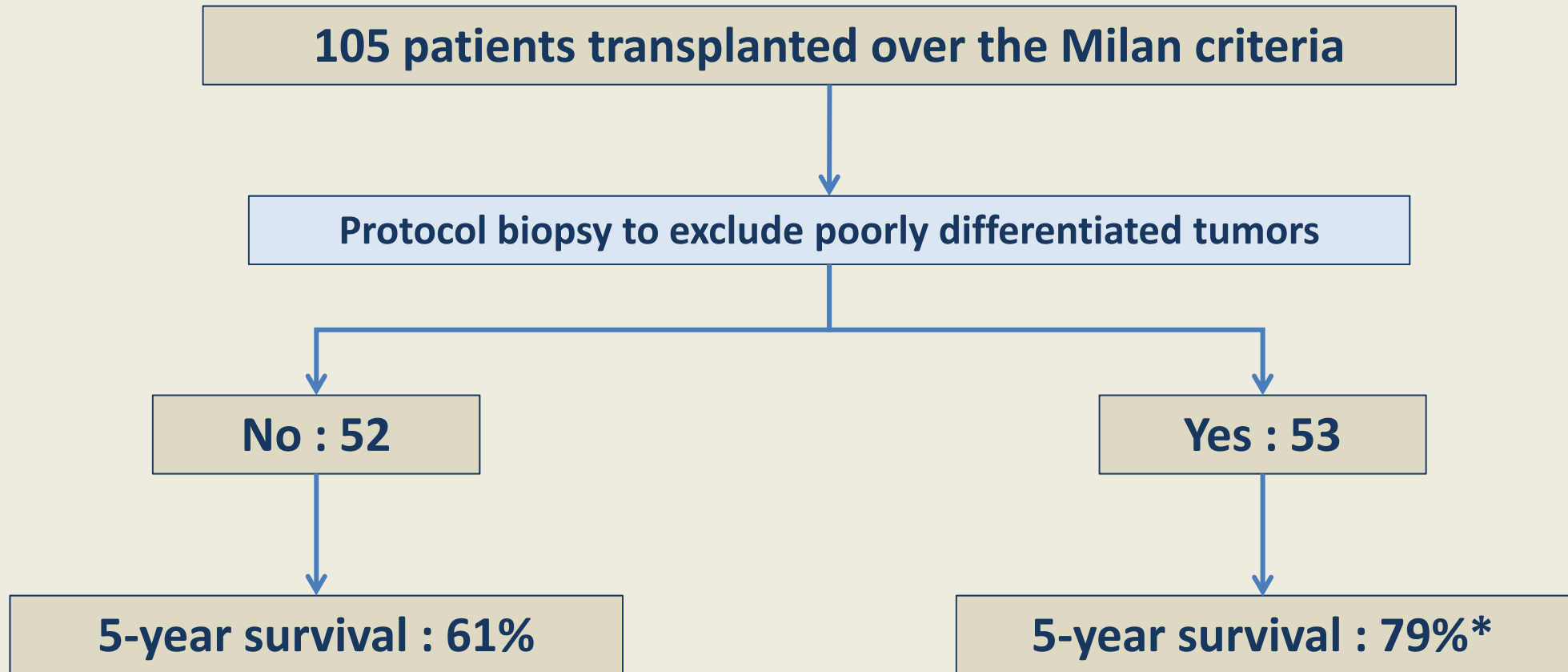
Number of nodules	
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1-3	1
4 and more	2.01

AFP level (ng/mL)	
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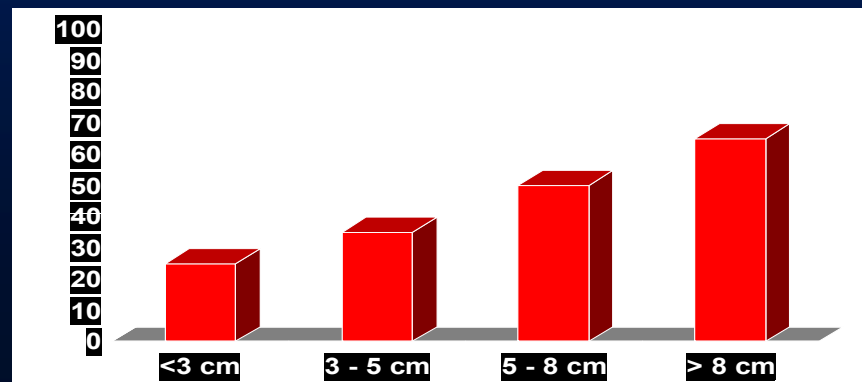
≤ 100	1
]100-1000]	1.95
> 1000	2.57

Impact of differentiation on recurrence



LT for HCC including AFP and Differentiation

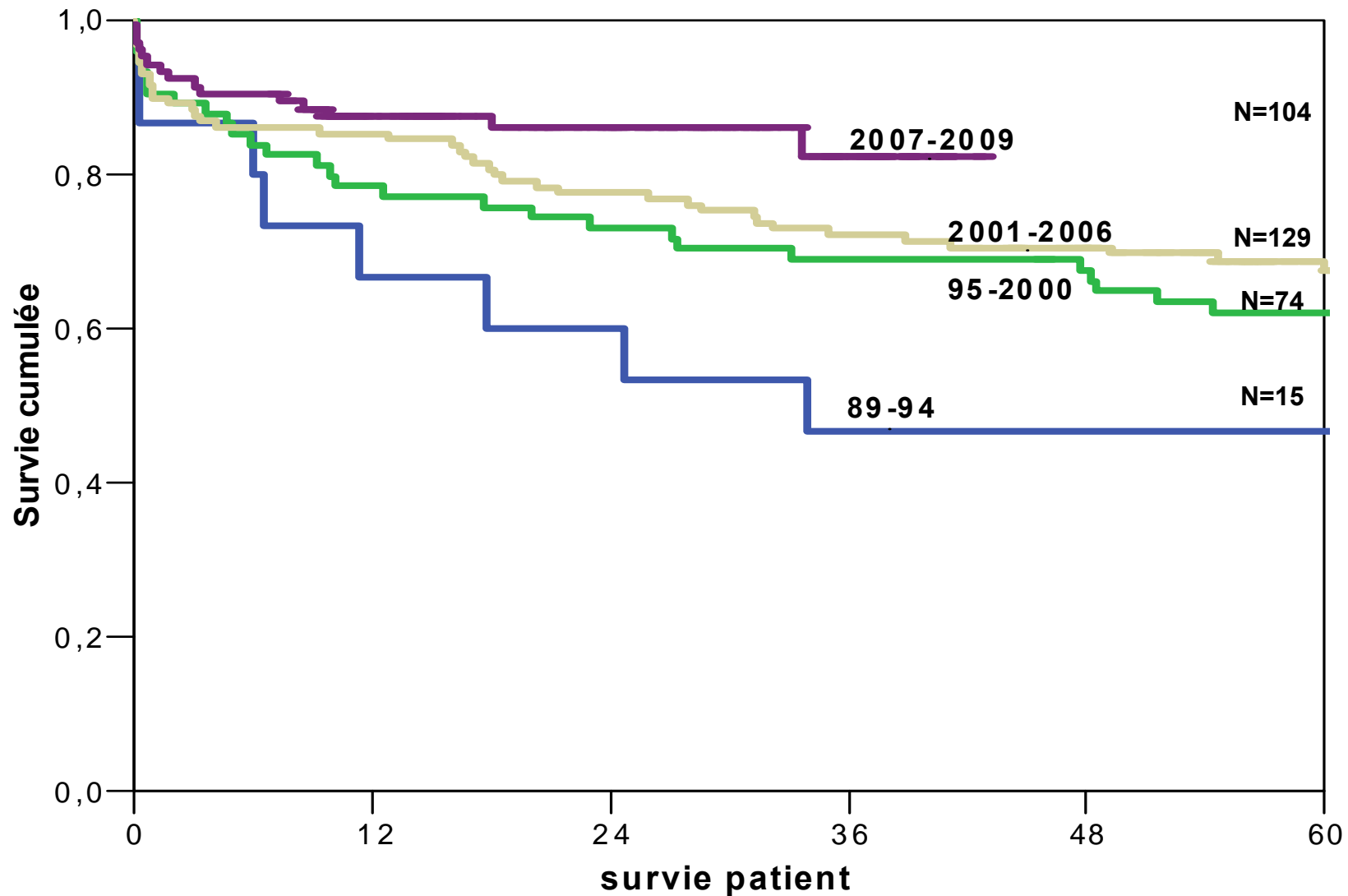
- Extension of morphological criteria of Milan with Low AFP and/or Good Differentiation → Results of LT similar to LT within MC.
- Hyper-selection of patients within MC



More selective criteria of LT for HCC:

- **Towards “zero recurrence”**
 - **Stay in Radiologic Milan Criteria**
 - **Exclude patients with α foeto > 400**
 - **Preoperative biopsy (or resection) to exclude poor differentiate T and/or CCK component**
- **Combine LT with partial Liver Resection.**

Long Term survival after LT for HCC Beaujon (n = 322)



Conclusion

- **Survival rate after LT for HCC should be similar to LT for other indications.**
- **In a period of drastic organ shortage, a zero recurrence rate is a desirable goal**
- **Using tools such as serum AFP and tumor differentiation help further reduce the risk of recurrence**
 - **Allowing some expansion of Milan criteria**
 - **Restricting some patients within the Milan criteria who are not good candidates**

