

Liver transplantation for HCC. The Barcelona Intention-to-treat experience

Jordi Bruix.
BCLC Group. Liver unit.
Hospital Clínic.
University of Barcelona

Miami 2003.

Treatment of Hepatocellular Carcinoma

Barcelona-Clínica Liver Cancer (BCLC) Group.
Liver Unit. Hospital Clínic. 2002.

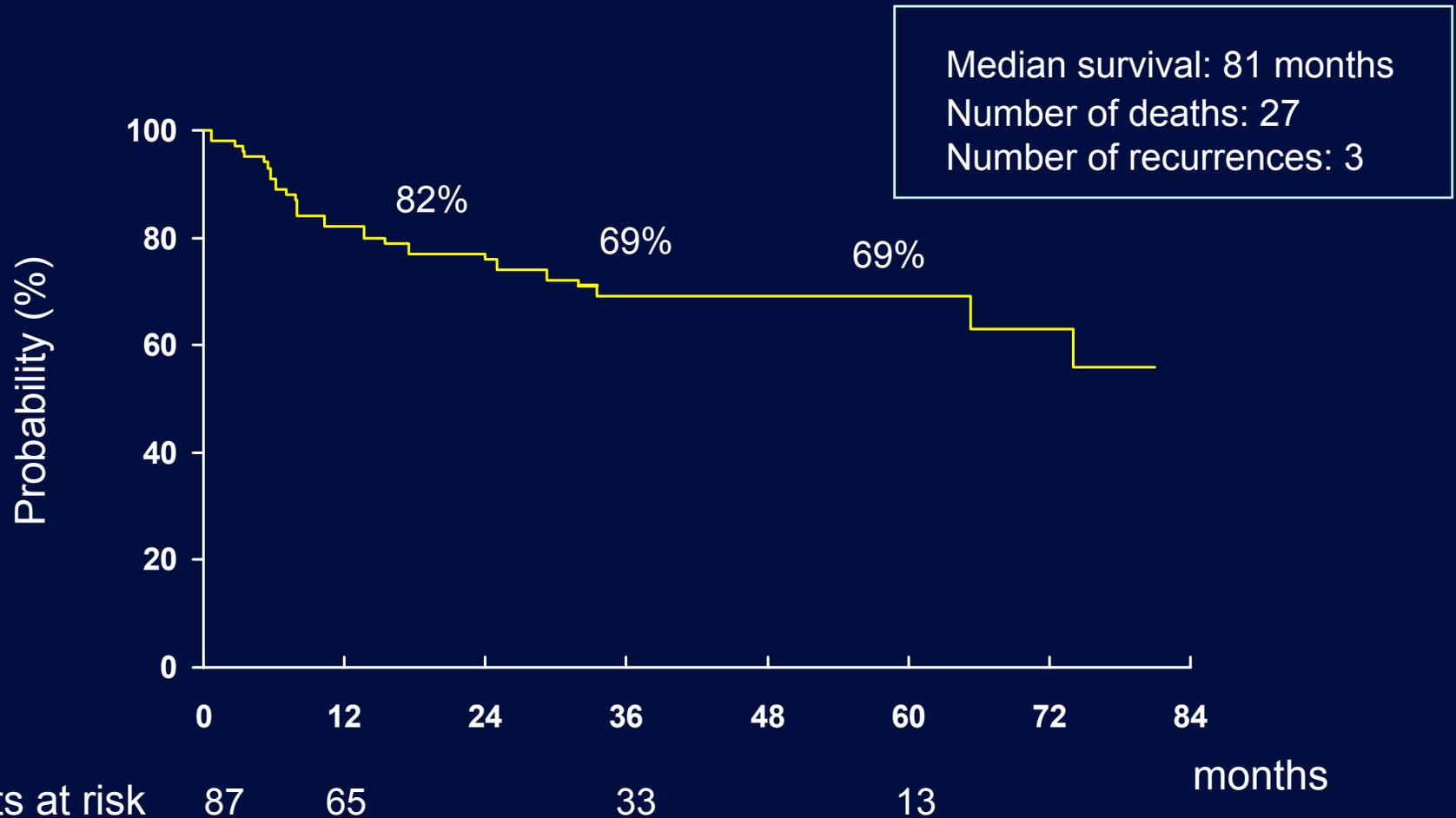
- Radical therapies (30%)
 - Surgical resection
 - Liver Transplantation (CLT/LDLT)
 - Percutaneous ethanol injection/Radiofrequency
- Palliative therapies (40-50%)
 - Transarterial embolization/ Chemoembolization
 - Transarterial embolization-percutaneous treatments
 - Hormonal treatments/ Immunotherapy
 - Antiproliferative agents
- Symptomatic treatment (20-30%)

Liver transplantation for HCC

Characteristics of patients (n=87)

• Mean age (yr)	55± 6.6
• Sex (M/F)	65/22
• Etiology (VHC/VHB/alcohol/ others)	77/3/9/2
• Indication for OLT (HCC/Cirrhosis)	59/28
• Child-Pugh (A/B/C)	37/38/12
• Okuda Stage(1/2/3)	35/47/5
• Ascites	39
• Analitical Data	
Bilirubin (mg/dL)	2.2±1.7
Serum albumin (g/L)	32.9 ± 5
Prothrombin activity (%)	62 ± 16
AFP(<10/ 10-100/>100 ng/mL)	51/28/8
• Pathological tumor stage	
< 5cm/>5cm/multinodular	44/2/33
Mean tumor size (mm)	24.1±13
• Mean waiting time (days)	105 ± 111

Overall survival of HCC patients treated by OLT



Llovet et al. Hepatology, 1999

Liver transplantation for HCC

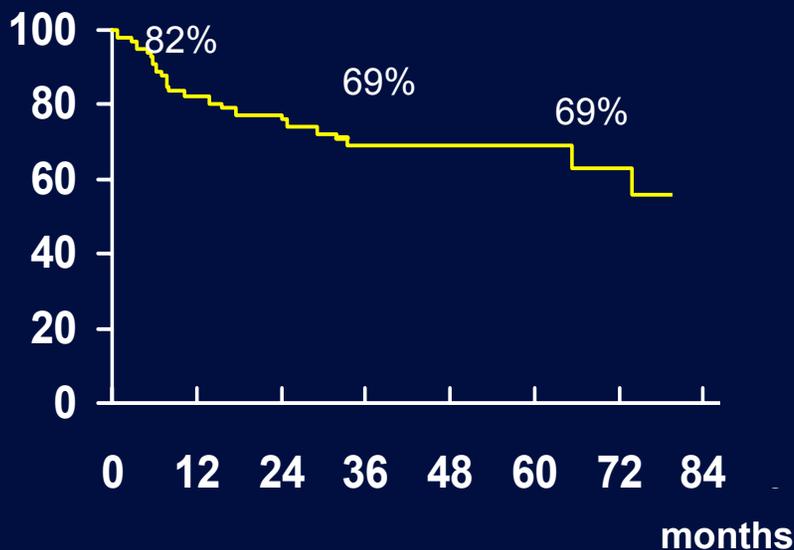
Characteristics of patients according to period of time

Variables	1989-1995 (n=50)	1996-97 (n=37)	p
• Drop -outs during waiting list	0	8 (23%)	0.001
• Mean waiting time (days)	62± 46	162± 143	0.0001
• Mean age (yr)	53± 7	56± 5	NS
• Sex (M/F)	38/12	27/10	NS
• Etiology (VHC/VHB/alcohol/ others)	42/2/4/2	31/1/5/0	NS
• Indication for OLT (HCC/Cirrhosis)	33/17	29/8	NS
• Child-Pugh (A/B/C)	21/21/8	16/17/4	NS
• Blood group (O/A/B/AB)	23/19/7/1	14/16/5/2	NS
• Bilirubin (mg/dL)	2.1±1.6	2.3±1.8	NS
• AFP(<10/ 10-100/>100 ng/mL)	28/18/3	22/10/5	NS
• Histological tumor stage			
Single/ Multinodular	29/21	12/17	NS
Mean tumor size (mm)	26.4 ± 12.3	27 ± 11	NS
Microvascular invasion	14	8	NS

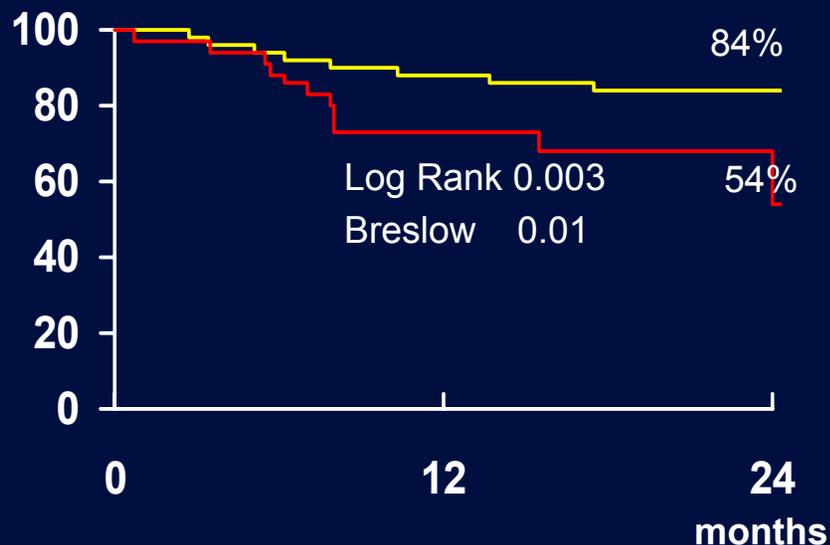
Intention-to-treat assessment of OLT for HCC

Impact of exclusions while waiting

Overall survival



Survival according to time period

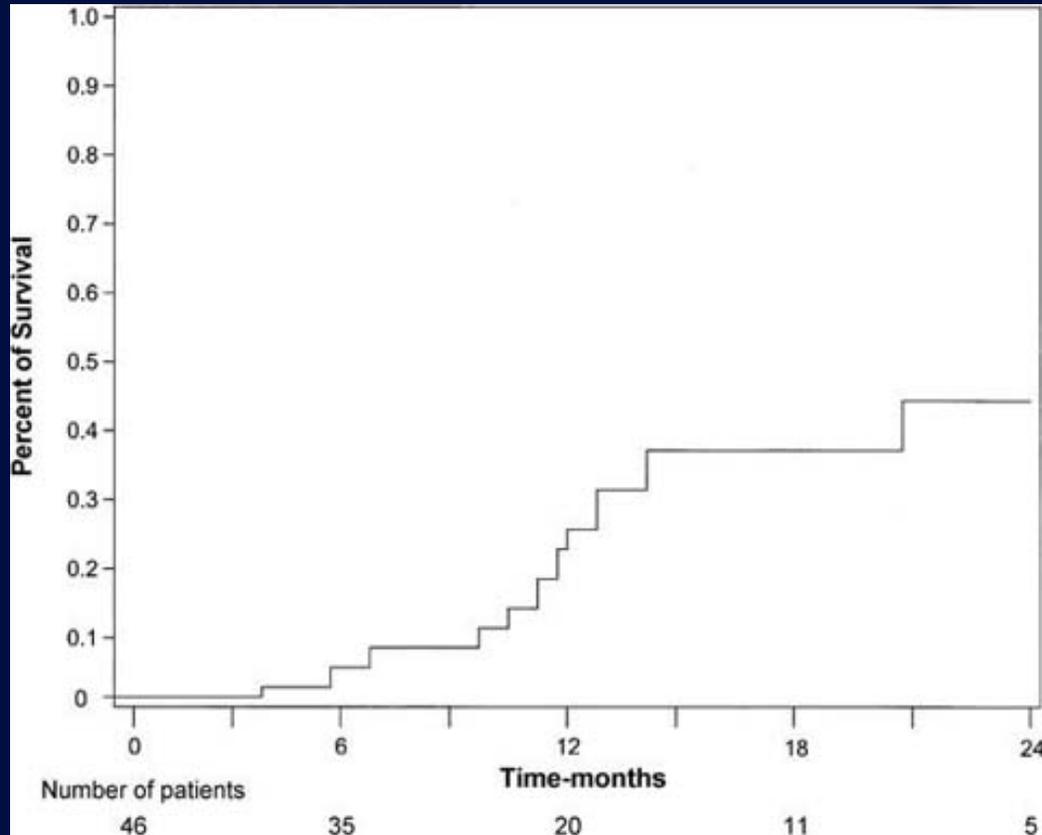


- 1989-95 (Drop-out = 0; n = 50)
- 1996-97 (Drop-out = 23%; n = 37)
 - 6 m: 11%
 - 12 m: 38%

Predictors of survival: exclusion while waiting.

Predictors for exclusion: length of waiting time, increased AFP.

Drop out while waiting for OLT due to tumor progression

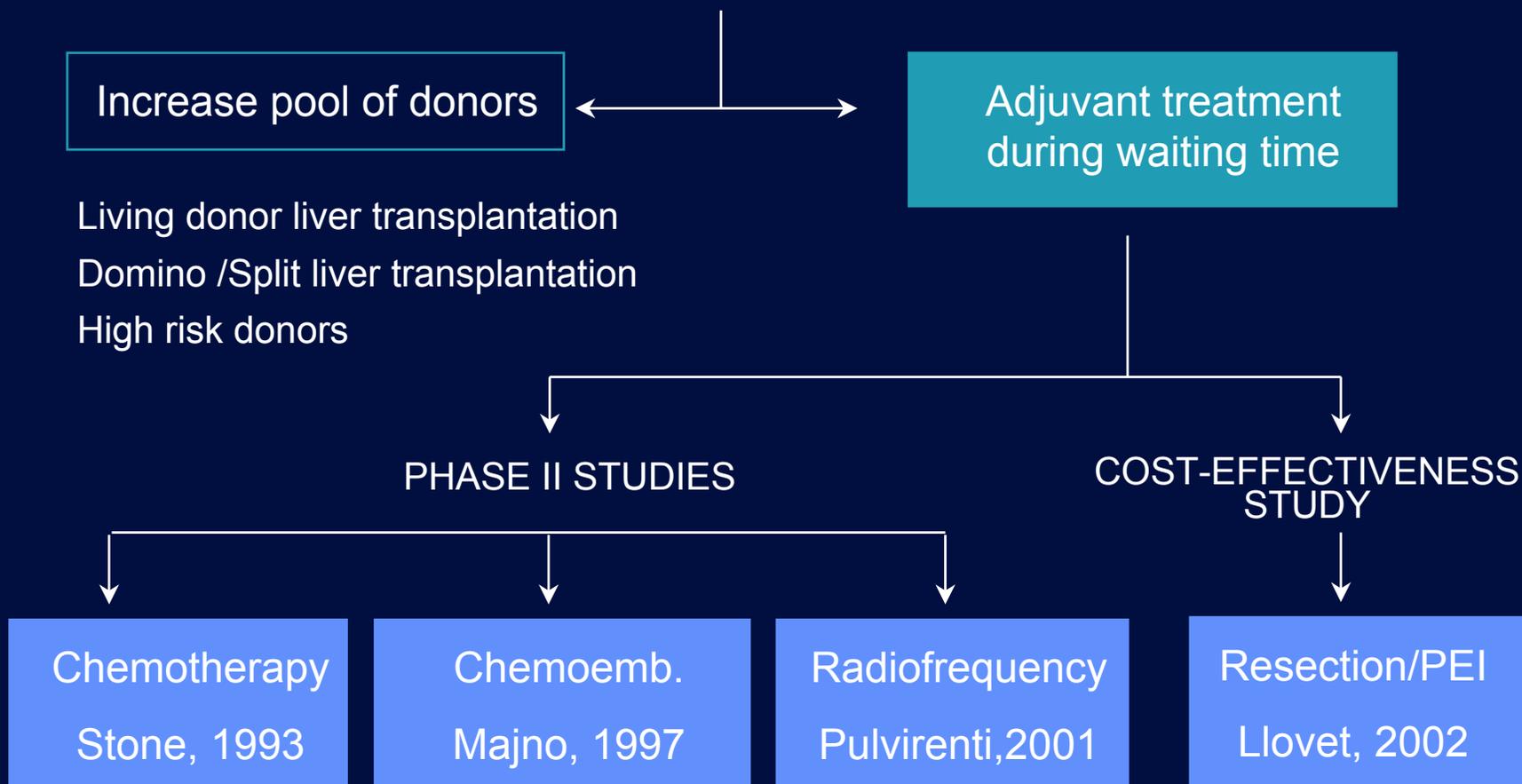


Yao et al Liver Transplantation 2002.

Liver Transplantation for HCC

Strategies to decrease drop-out rate

Cirrhotic patients with early HCC waiting for cadaveric liver transplantation



Controversial issues in LT for HCC

- Should the criteria be expanded?
- How should diagnosis/staging be done?
- Should HCC receive priority?
- Who should be excluded from the waiting list?
- How will this affect the non-HCC population?
- Which non-HCC candidates should be excluded?
- Will critically ill patients achieve optimal results?

Liver Transplantation for HCC

Outcomes applying restrictive selection criteria

Authors	n	Selection criteria	Rec	Survival
Mazzaferro, NEJM 1996	48	Single < 5cm 3 nodules < 3cm	8%	74%*
Bismuth, Semin Liver Dis 1999	45	Single < 3cm 3 nodules < 3cm	11%	74%
Llovet, Hepatology 1999	79	Single < 5cm	4%	75%
Jonas, Hepatology 2001	120	Single < 5cm 3 nodules < 3cm	16%	71%

* 4-yr survival

LT for Hepatocellular carcinoma

Rationale for extended indications

Tumor progression after enlisting with optimal criteria

Mazzaferro et al NEJM 1996

Llovet et al Hepatology 1997, Hepatology 1999

Trasplantation with known advanced tumor stage

Ringe et al World J Surg 1991

McPeake et al J Hepatol 1993

Bismuth et al Ann Surg 1993

Majno et al Ann Surg 1997

Marsh et al Hepatology 1997

Jonas et al Hepatology 2001

Yao et al Hepatology 2001

How long will patients wait?

LDLT for HCC: BCLC Extended indications

Expected survival at 5 years: 50%

Inclusion criteria

- Solitary HCC ≤ 7 cm
- Multifocal HCC: < 3 nodules ≤ 5 cm or 5 nodules ≤ 3 cm
- “Downstaging” to conventional criteria lasting ≥ 6 months

Exclusion criteria

- Age > 70 years
- Tumor size > 7 cm with/without satellites
- Diffuse HCC
- Vascular invasion or extrahepatic spread

Bruix and Llovet, Hepatology 2002

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EASL Conference on HCC. Barcelona, 2000.

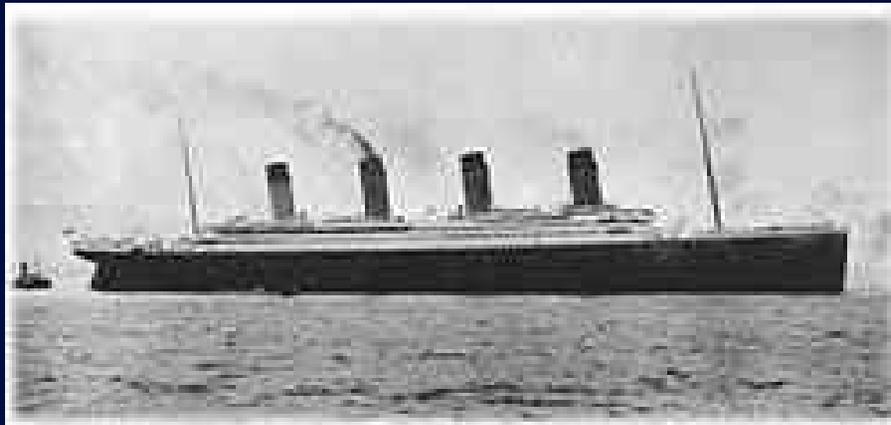
Diagnostic criteria for HCC

- Cyto-histological criteria.
- Non-invasive criteria (cirrhotic patients)
 1. Radiological criteria: Two coincidental imaging techniques*
 - Focal lesion > 2cm with arterial hypervascularization
 2. Combined criteria: One imaging technique associated to AFP
 - Focal lesion > 2cm with arterial hypervascularization
 - AFP levels > 400 ng/mL.

* Four techniques considered : US, Spiral CT, MRI and angiography.

The Titanic Consideration

- # Limited resource, excessive demand
- # More passengers on board !!



Pruett, Hepatology 2002