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INNOVATIONS

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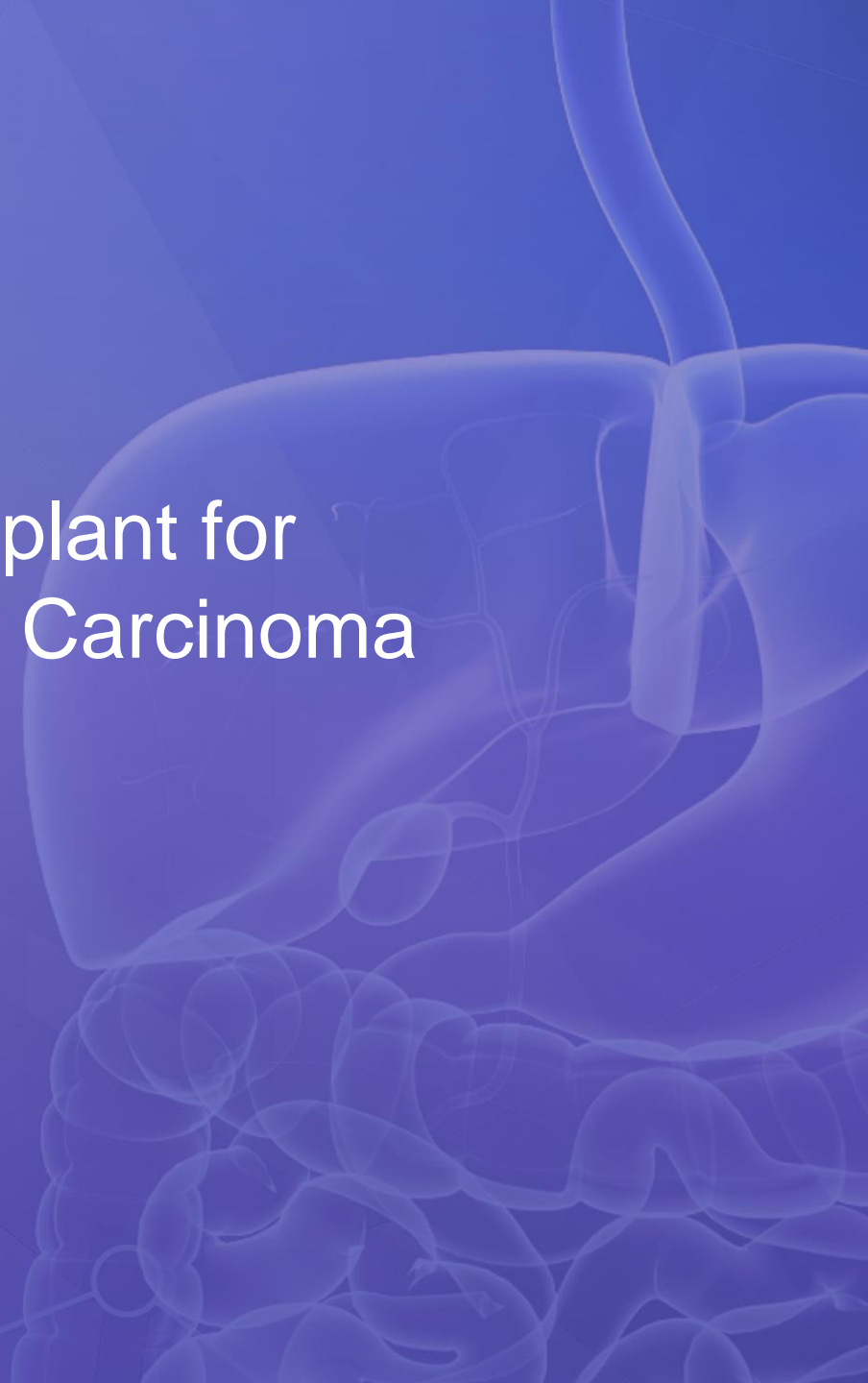


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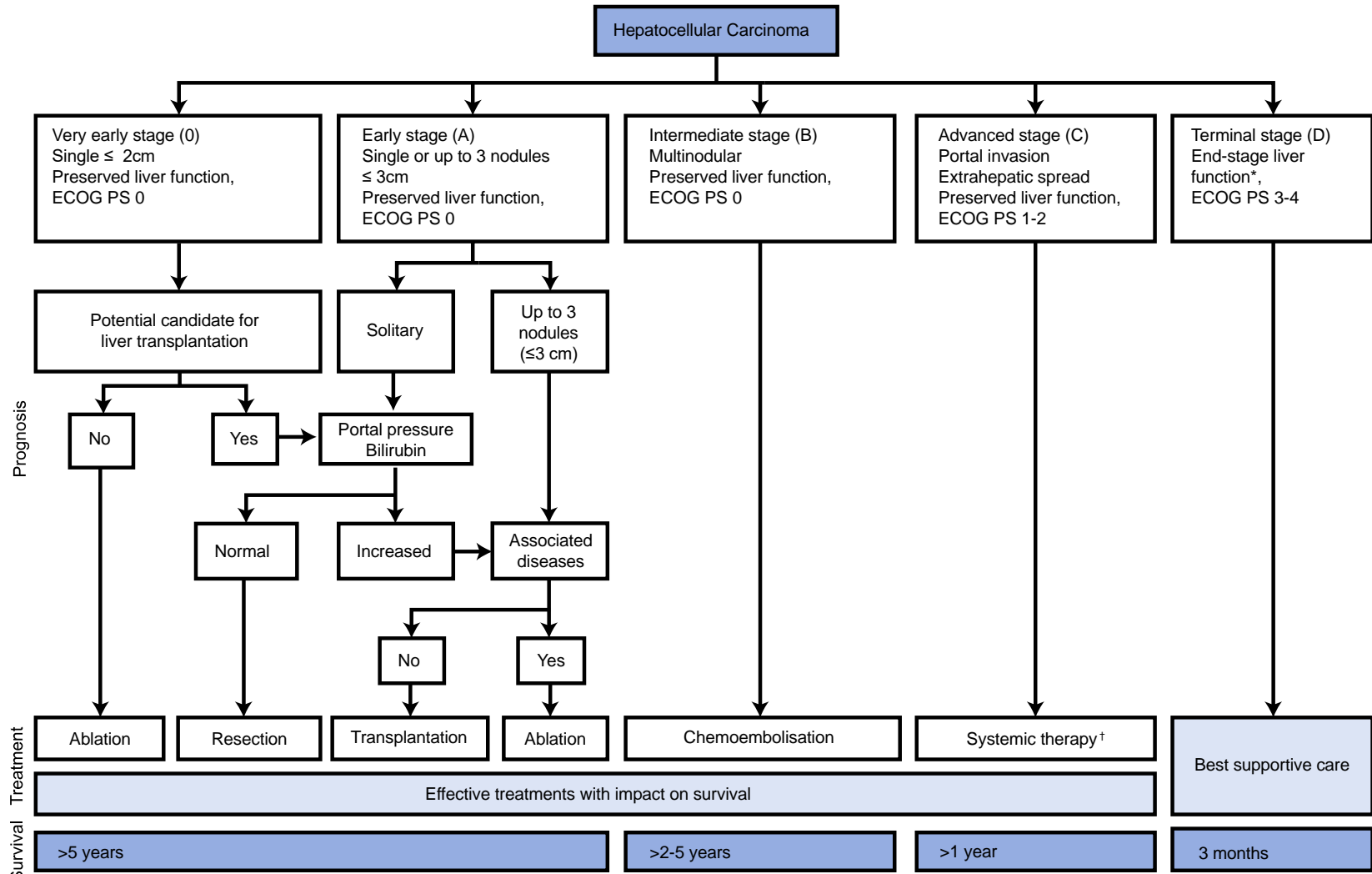
Provided by



# Liver Transplant for Hepatocellular Carcinoma



# Transplant for HCC: BCLC Staging System



# Surgical Management of HCC

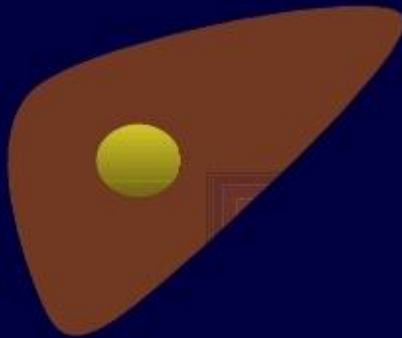
## Milestones in Liver Surgery

Langenbuch	1887	1st successful resection
Keen	1892	1st liver resection series
Lortat-Jacob	1952	1st anatomic resection
Quattlebaum	1952	1st US anatomic resection
Longmire	1961	Technical advances
Starzl	1963	First human OLT

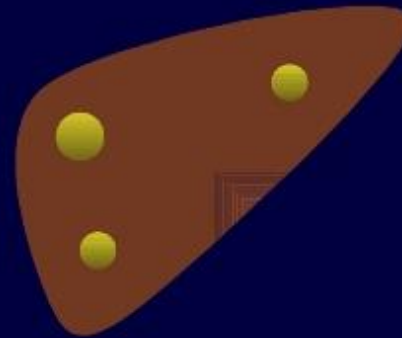
# Liver Transplant for HCC

## Liver Transplant for HCC in cirrhosis Milan Criteria (Stage I+II)

Single, not > 5cm



Up to 3, none > 3cm



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**Absence of Macroscopic Vascular Invasion**  
**Absence of Extrahepatic Spread**

# UNOS MELD Exception for HCC

## Key Points

- LI-RADS-5 (definite HCC) and OPTN 5 lesions must meet nearly identical combinations of imaging criteria: arterial phase hyperenhancement, capsule appearance, washout appearance, and threshold growth.
- The use of liver directed therapy as a bridge to transplant and in downstaging patients is common practice.
- HCC patients must wait 6 months from listing before being granted a MELD exception score of 28, and the MELD score then increases via extension every 3 months to a maximum score of 34.
- Liver transplantation to treat HCC within the Milan criteria has good outcomes with a 5-year disease-free survival rate comparable to patients transplanted without malignancy.

# HCC Treatment

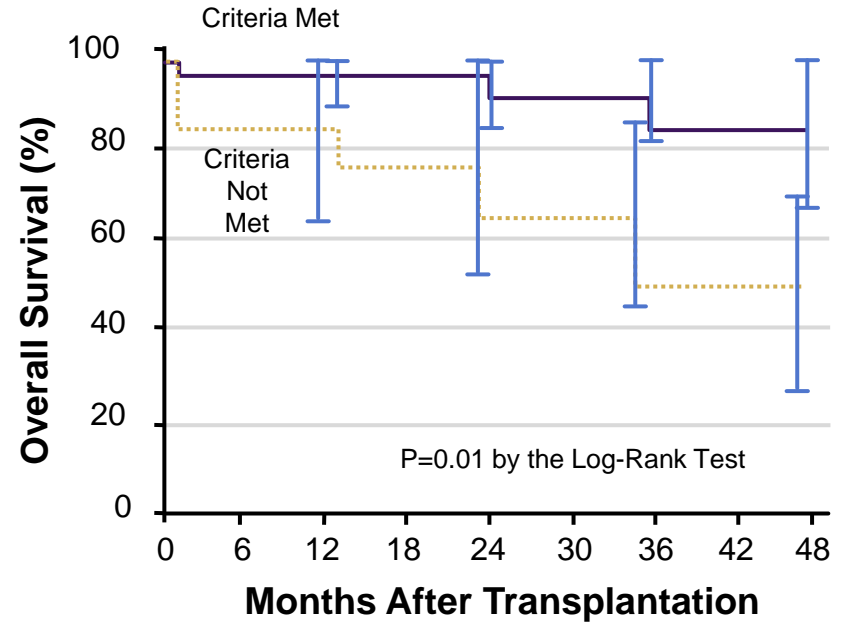
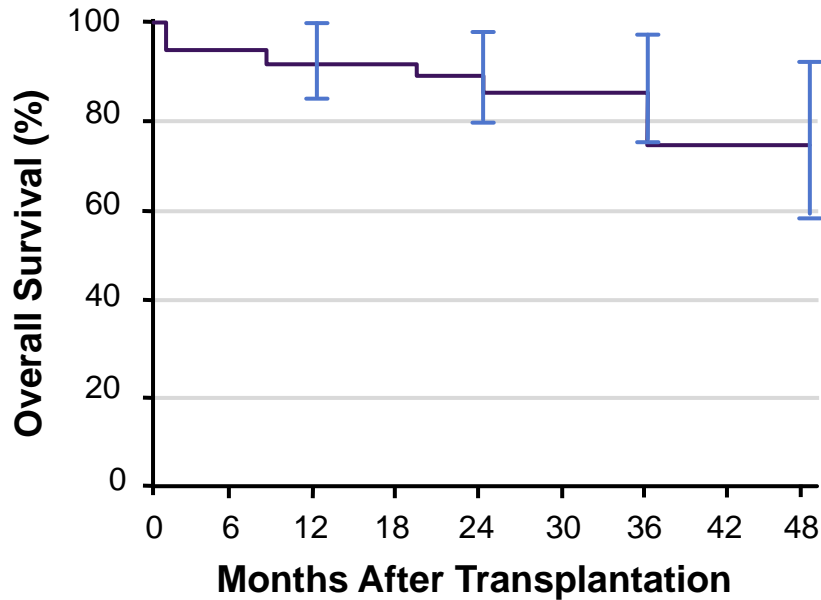
## Liver Transplantation for Small HCC: Milan Criteria

- 48 patients with cirrhosis and HCC
  - Single tumors  $\leq 5$  cm or no more than 3 nodules,  $\leq 3$  cm
  - No vascular invasion
  - No distant metastases
- 75% 4-year survival, 83% recurrence-free
- 27% exceeded criteria on path review
- 50% 4-year survival, 59% recurrence-free



# HCC Treatment

## Liver Transplantation for Small HCC: Milan Criteria



Patients at Risk									Patients at Risk																	
48	45	40	32	27	21	17	9	5	<b>Criteria Met</b>																	
									35	34	31	24	21	16	13	6	3	<b>Criteria Not Met</b>								
									13	13	11	8	6	6	4	4	3									



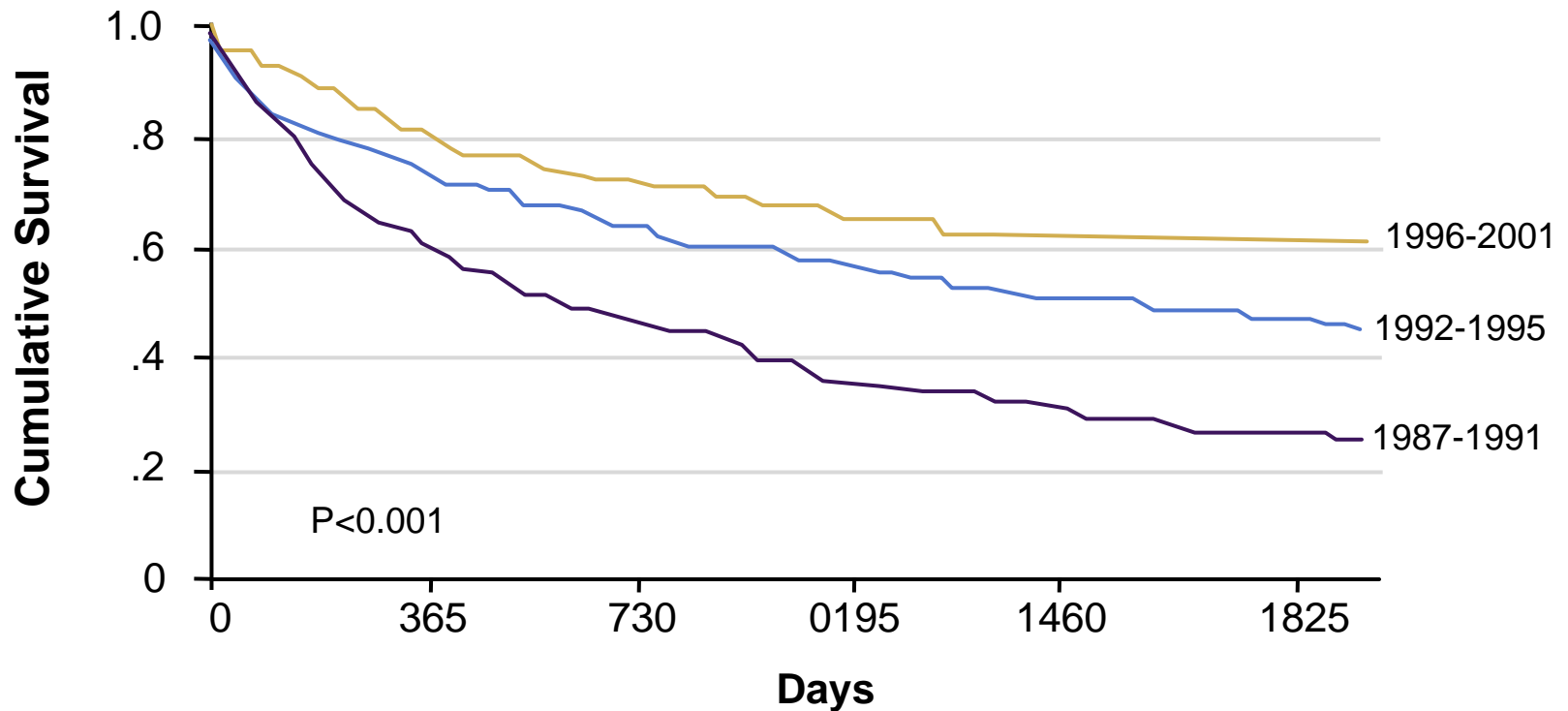
# HCC Treatment

## UNOS Criteria for Liver Transplantation for HCC

- Liver ultrasound
- CT or MRI of abdomen showing tumor(s)
  - One 2-5 cm or two or three nodules all < 3 cm
- CT of chest that rules out metastatic disease
- One of the following:
  - a vascular blush in the lesion
  - an alpha-fetoprotein level of >200 ng/ml,
  - an arteriogram confirming a tumor
  - biopsy confirming HCC
  - chemoembolization, RFA, cryo, or chemical ablation
- Rising AFP  $\geq$  500 ng/ml if no evidence of a mass

# HCC Treatment

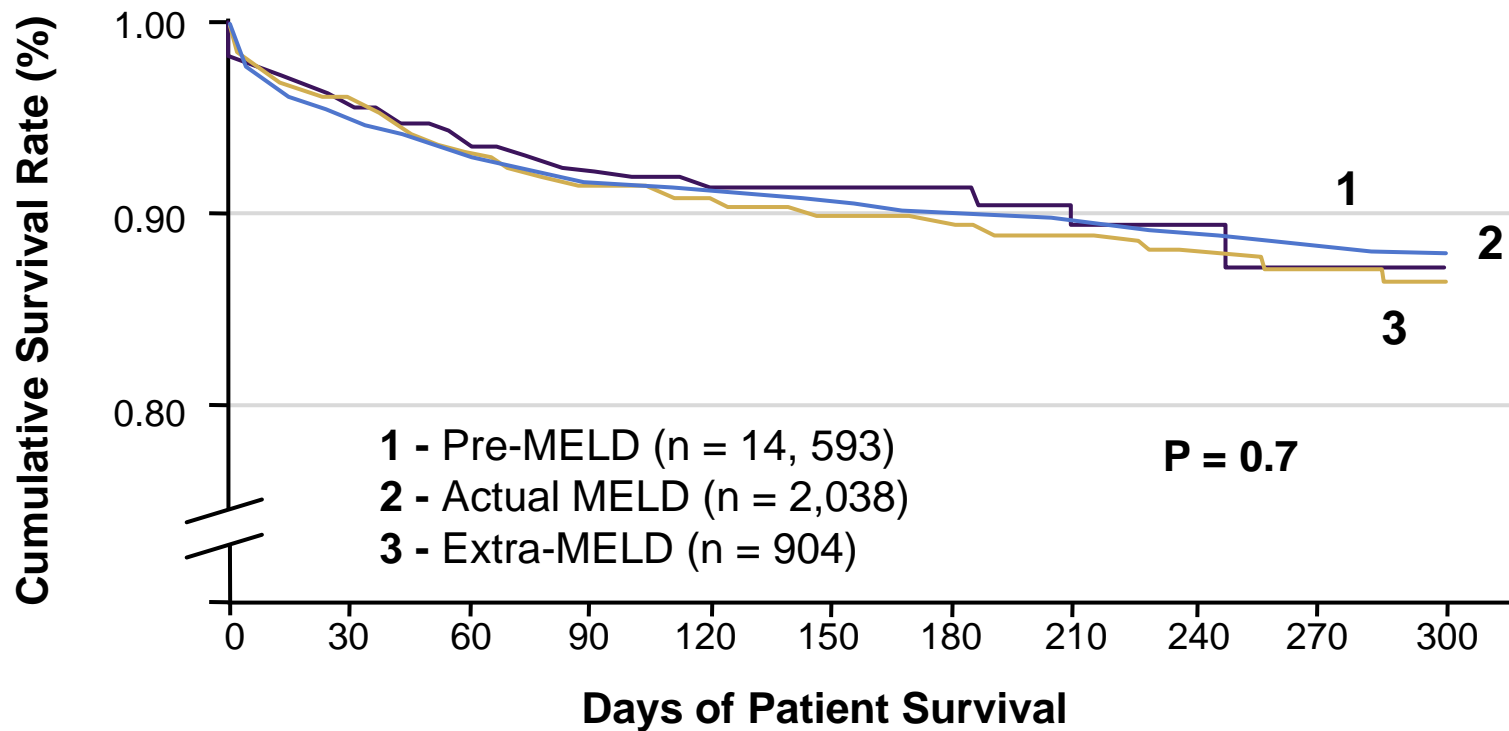
## Survival After Transplant for HCC: UNOS Experience



Patients at Risk						
	0	1 Year	2 Year	3 Year	4 Year	5 Year
1987-1992	433	141	105	80	62	51
1992-1995	282	183	148	119	103	79
1996-2001	270	227	141	70	29	9

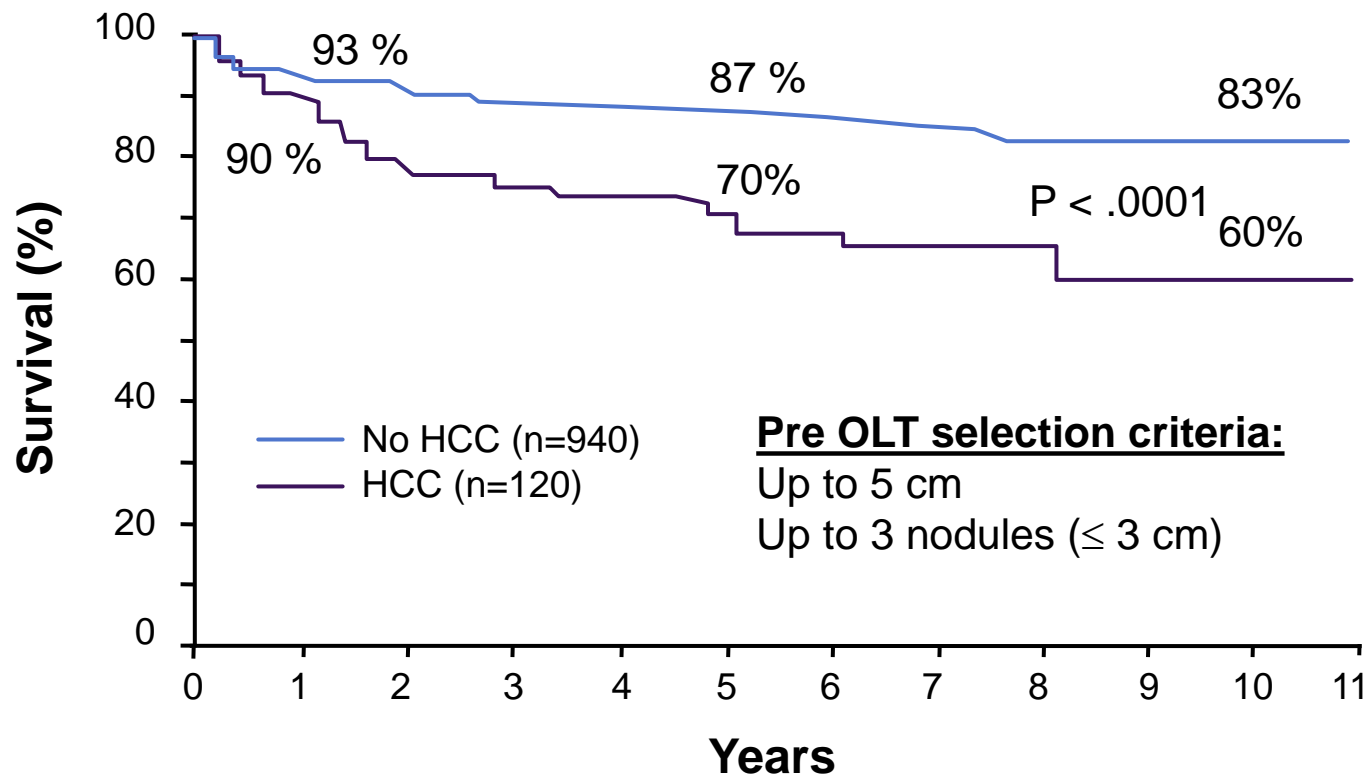
# HCC Treatment

## Survival of UNOS Patients Given Extra MELD Points (710 of 904 had HCC)



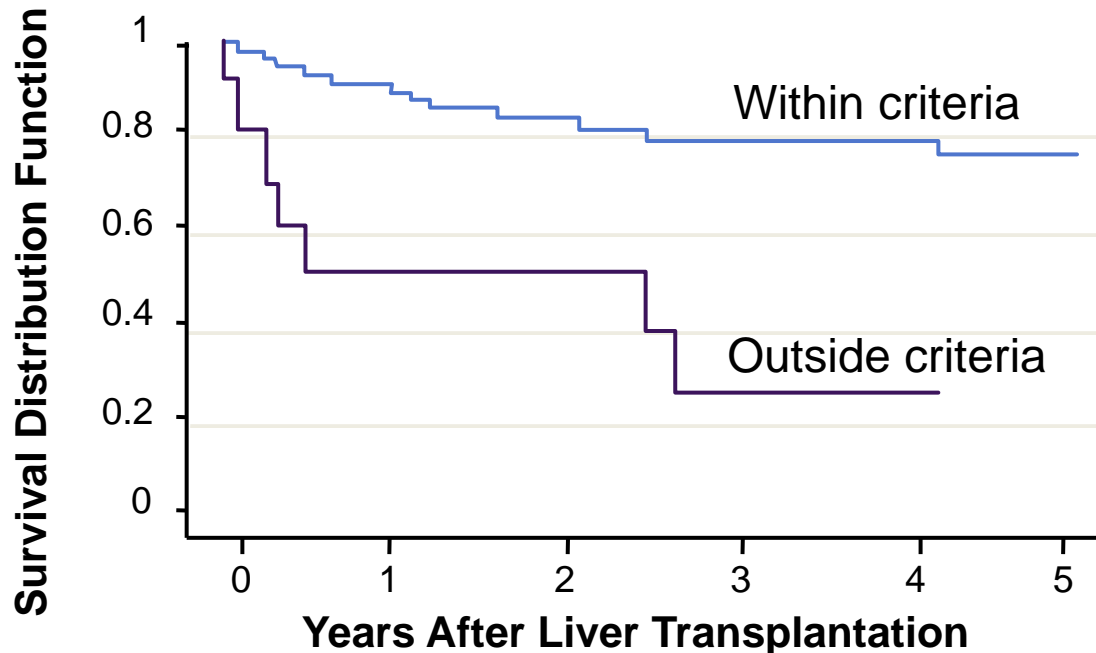
# HCC Treatment

## Long-Term Survival After OLT for HCC: Humboldt University, Berlin



# HCC Treatment

## Expanding the Criteria for Liver Transplantation: UCSF Criteria 2001



- Solitary lesion
  - $\leq 6.5$  cm
- Multiple
  - $\leq 3$  nodules
  - Largest  $\leq 4.5$  cm
  - Total tumor diameter  $\leq 8$  cm

Meet New Staging Criteria			
Yes	6049	3725	2016
No	105	42	10

Predictors for poor survival:

AFP >1000, total tumor > 8 cm, age > 55, poorly differentiated histology

Study drawbacks: Retrospective; size based on explant pathology, not on pre-listing or pre-transplant radiology

# HCC Treatment

## Resection vs Transplantation for HCC: Intention-to-Treat Analysis

By “Intention-to-Treat analysis”, survival is comparable between OLT and Resection

Drop-out rate and waiting time are key

- 77 surgical resection
  - 1-, 3- and 5-year survival: 85%, 62%, 51%
- 87 listed for OLT with known HCC
- 8 patients dropped-out due to tumor progression (6) and liver failure (2)
  - 1-, 3- and 5-year “Intention-to-Treat” survival: 84%, 69%, 69%

# HCC Treatment

## Resection versus Transplantation

### **RESECTION**

- Potentially curative
- Readily available
- Non-cirrhotic or...
- Compensated cirrhosis without significant portal hypertension
- Higher rate of recurrence of HCC
- Better survival within 3 years
- No immunosuppression
- Lifetime surveillance

### **TRANSPLANTATION**

- Potentially curative
- Advanced cirrhosis
- Shortage of donor livers
- Drop-out while awaiting transplantation
- Higher post-operative mortality; significant morbidity from recurrent hepatitis C no longer an issue
- Lifetime immunosuppression



# HCC Treatment Resection vs. Transplant for HCC Three Year Recurrence Rates

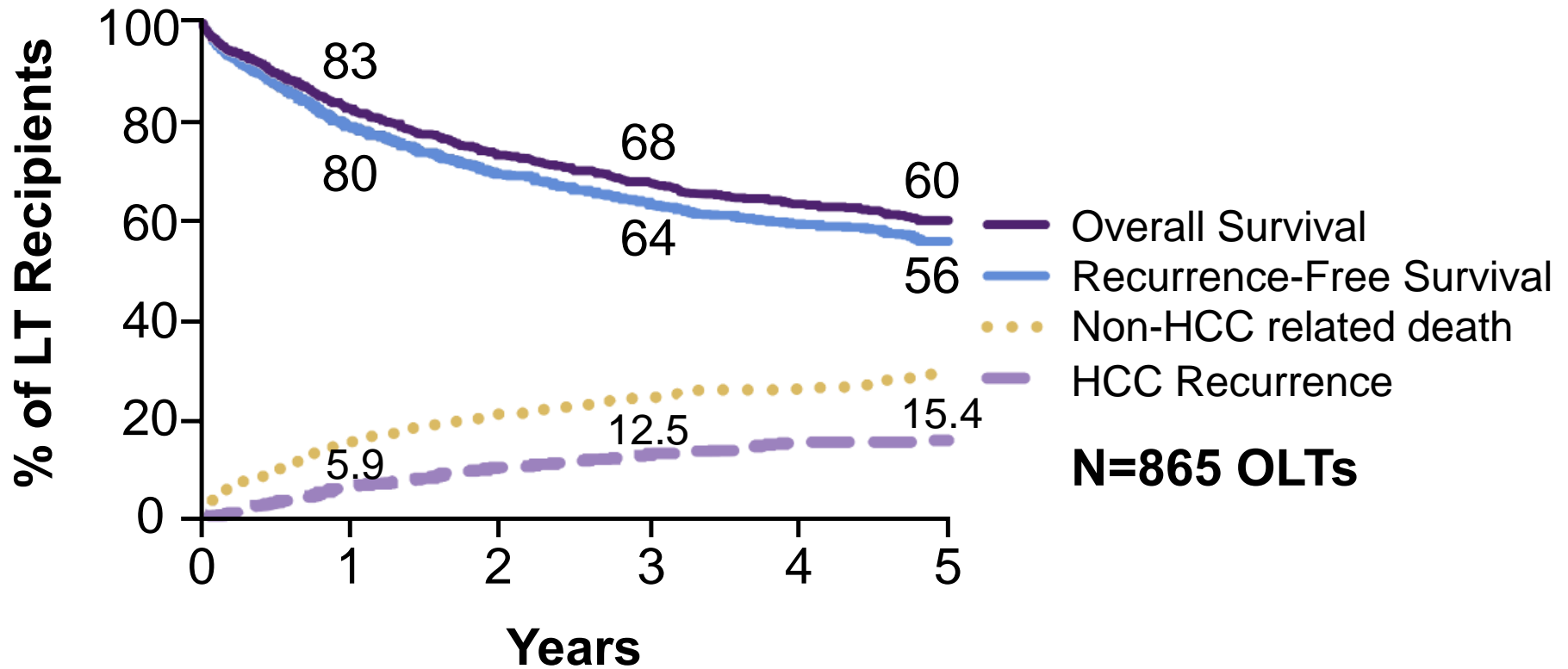
Author/Year	Number		Recurrence	
	Resection	Transplant	Resection	Transplant
Iwatsuki 1991	76	105	50.0%	42.9%
Michel 1995	20	21	70.0%	14.3%
Vargas 1995	35	11	40.0%	0%
Tan 1995	12	15	25.0%	20.0%
Otto 1998	52	50	53.8%	36.0%
Llovet 1999	77	87	33.8%	2.3%
Weimann 1999	32	31	18.8%	0%
Figueras 2000	35	85	65.0%	0%
DeCarlis 2001	154	121	47.4%	9.0%
<b>Overall</b>			<b>20.0-70.0%</b>	<b>0-43.0%</b>

# HCC Treatment Survival After Resection vs. Transplant

Author/Year	Number		3-Year Survival		5-Year Survival	
	Resection	Transplant	Resection (%)	Transplant (%)	Resection (%)	Transplant (%)
Ringe 1991	131	61	42.3	15.2	35.8	15.2
Iwatsuki 1991	76	105	47.2	39.2	32.9	35.6
Bismuth 1993	60	61	49.0	49.0		
Michel 1995	20	21	77.0	72.0	41.0	72.0
Vargas 1995	35	11				
Tan 1995	12	15	33.0	63.0		
Otto 1998	52	50	40.0	47.0		
Llovet 1999	77	87	62.0	69.0	51.0	69.0
Weimann 1999	32	31	41.3	71.7	34.5	62.8
Figueras 2000	35	85	57.0	74.0	51.0	60.0
DeCarlis 2001	154	121			46.1	63.6
<b>Overall</b>					<b>33.0-51.0%</b>	<b>15.0-72.0%</b>

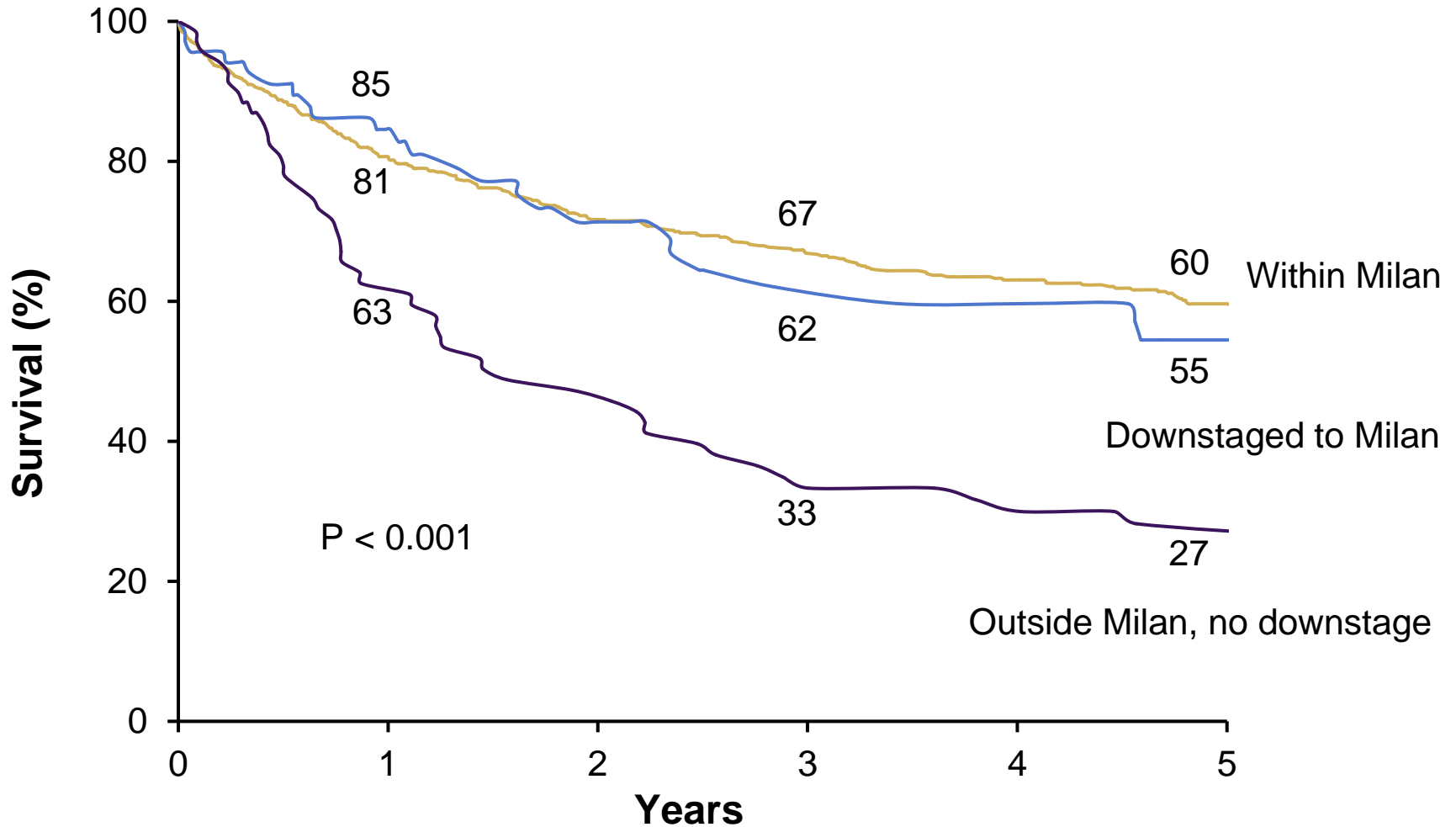
# Surgical Management of HCC

## Liver Transplant for HCC- UCLA



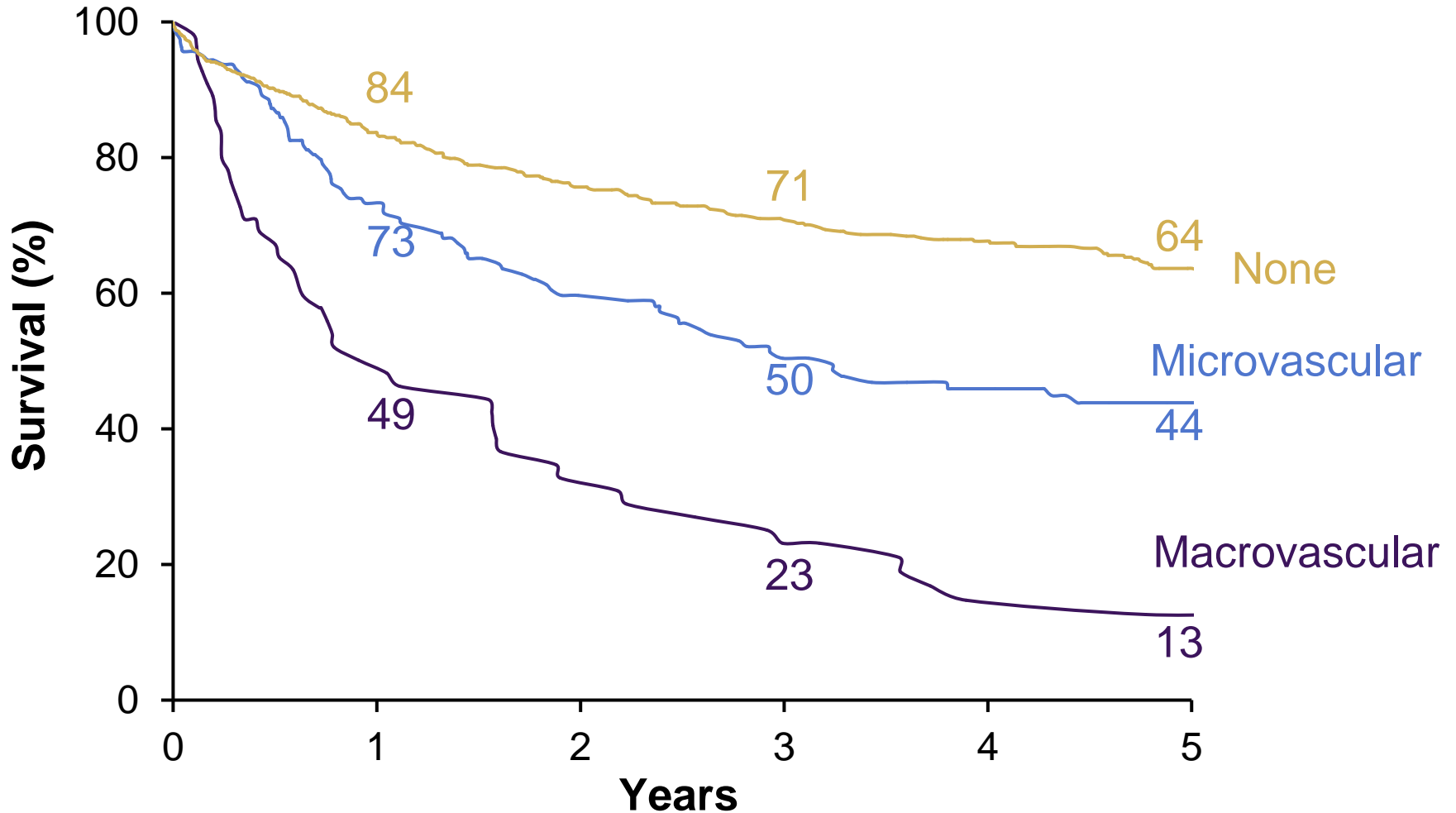
# Surgical Management of HCC

## Recurrence-Free Survival by Radiographic Size Criteria



# Surgical Management of HCC

## Recurrence-Free Survival by Vascular Invasion



# Conclusions: Transplant for HCC

- Best option for selected patients with early HCC and little or no fibrosis
- Most HCC in USA is not resectable
- Evaluation and listing for transplant is complex and burdensome, but potentially lifesaving
- All members of the multi-disciplinary team play a role and have a say in the outcome

Thank you!

