NCSCG Liver Symposium 2019

HCC and Transplant Debate #2:
YES for transplant for large tumors

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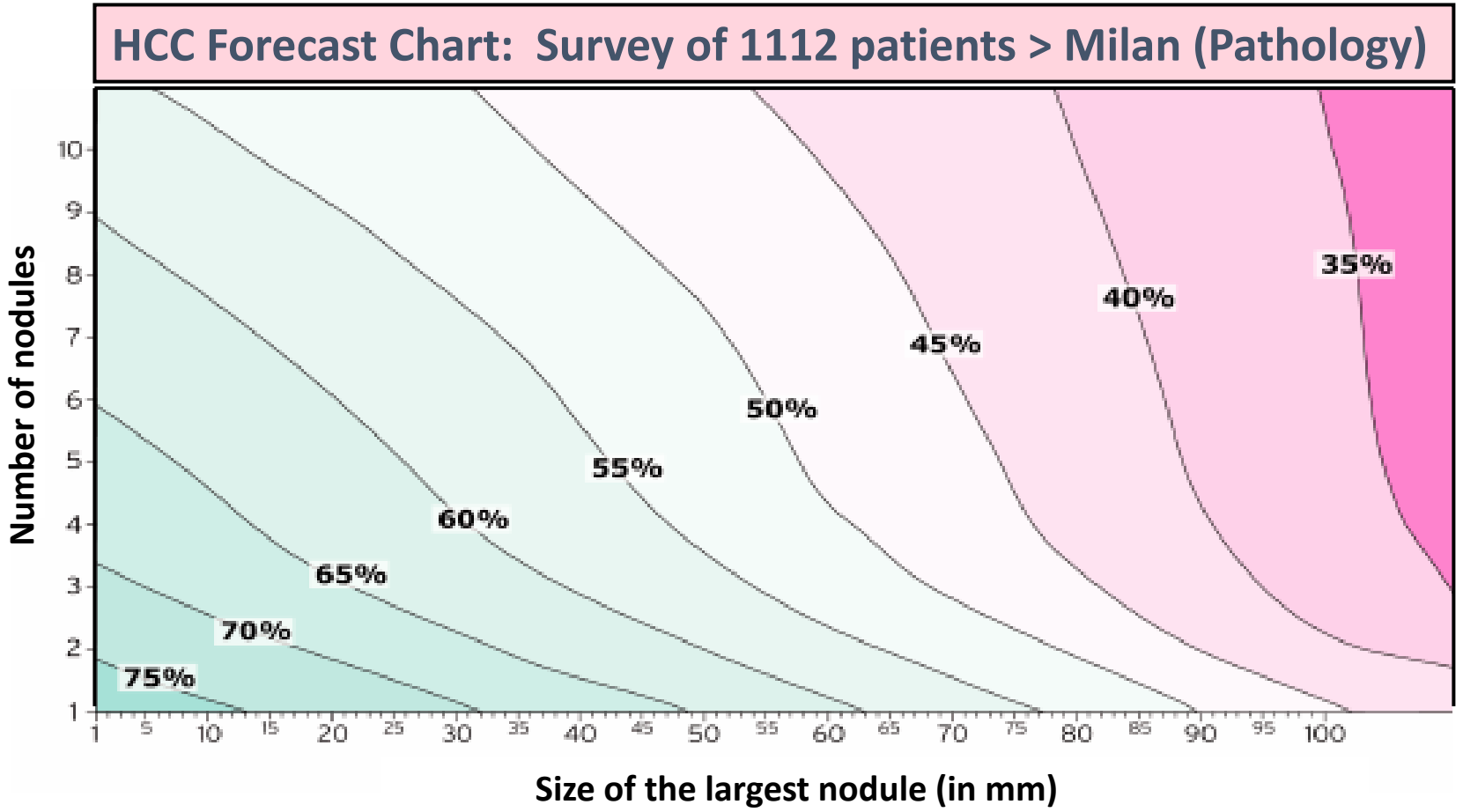
Case 2

- 55 year-old man with HCV-cirrhosis, history of sustained virologic response after anti-viral therapy, now with two hypervascular lesions with washout measuring 6.0 cm and 3.0 cm in the right lobe on MRI of the abdomen (LI-RADS 5).
- He has normal liver function (total bilirubin 1.0, INR 1.1) and no ascites or encephalopathy (Child's A cirrhosis); platelet count of 75, splenomegaly, no varices on EGD. His alpha-fetoprotein was 15. His BMI was 25.
- Debate: Transplant or no transplant

  Renu: No transplant

  Francis: Transplant (down-stage)

The HCC "Metro-ticket" – Tumor Size and Number



Courtesy of Dr. Vincenco Mazzaferro, with permission

Mazzaferro et al. Lancet Oncology 2009;10:35-43

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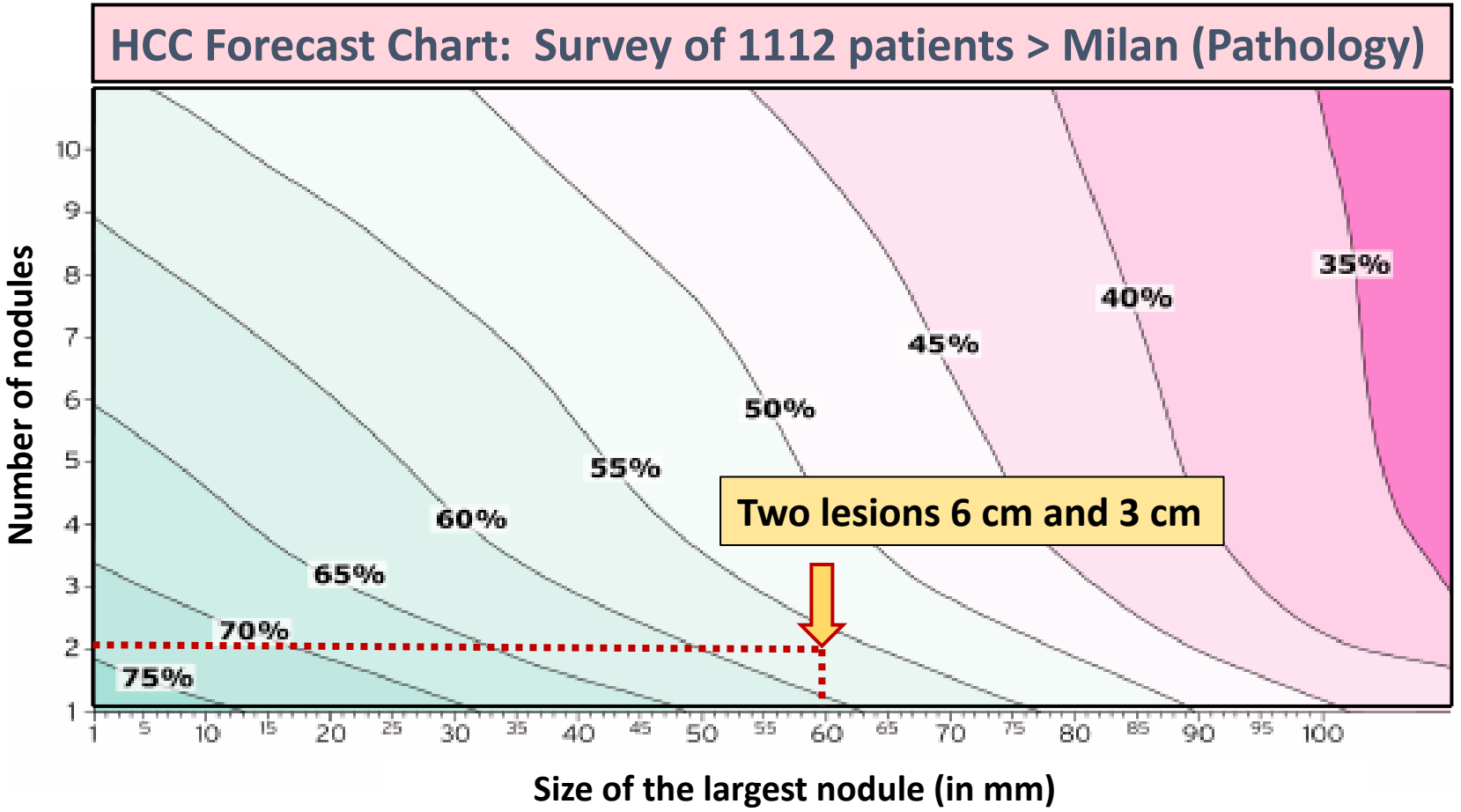

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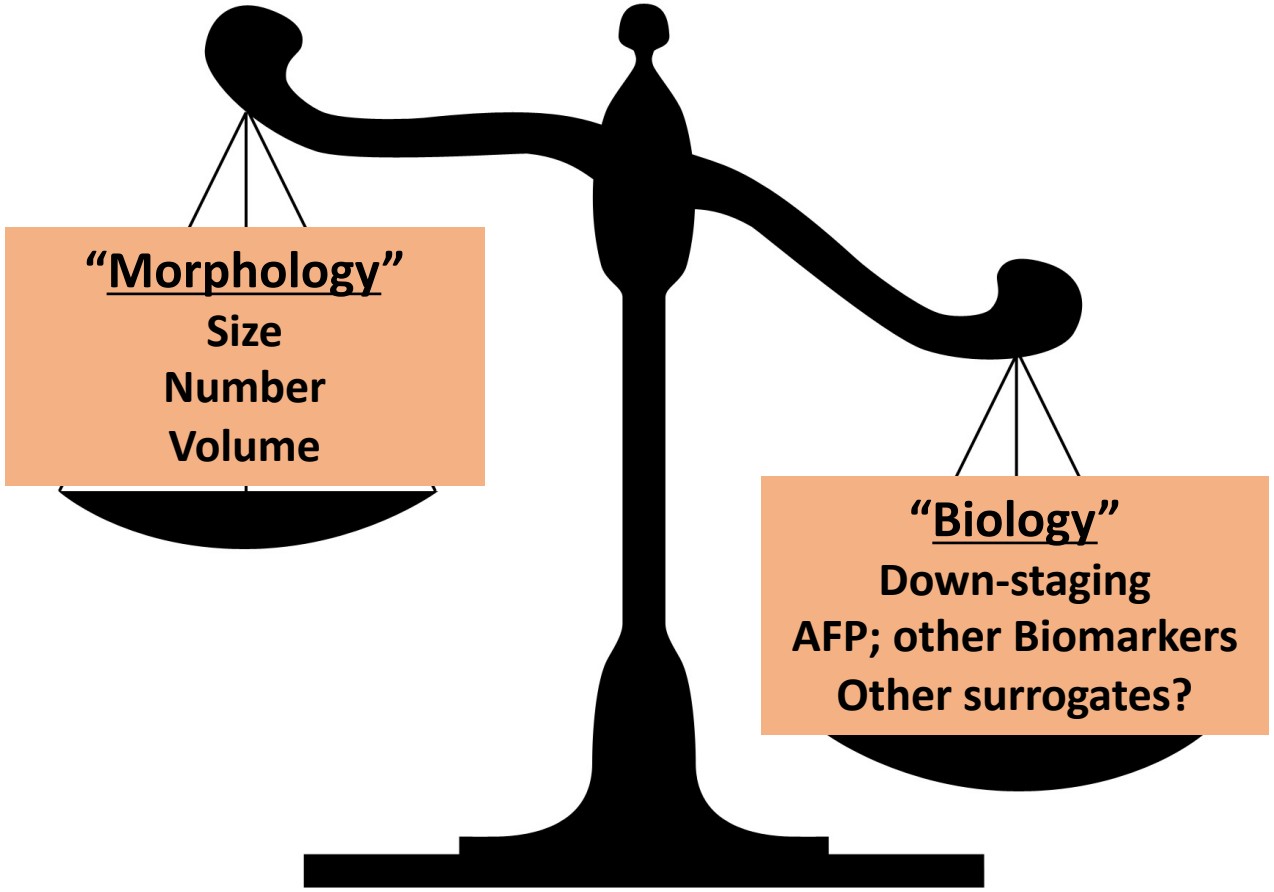
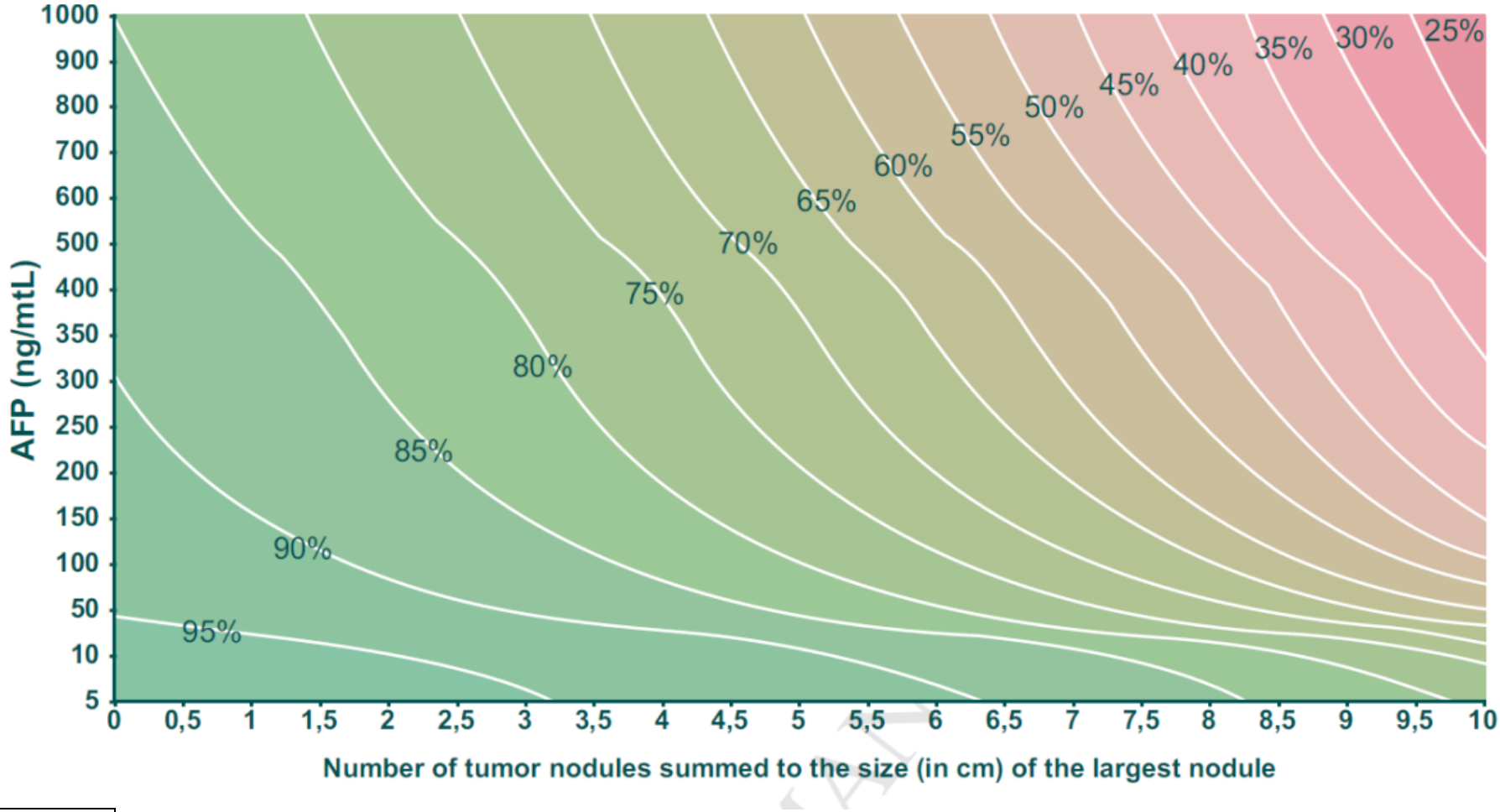
Liver Transplant for HCC

Changing views on Selection Criteria



Metro-ticket 2.0: AFP + Tumor Burden



Mazzaferro et al. Gastroenterology 2018;154:128-139

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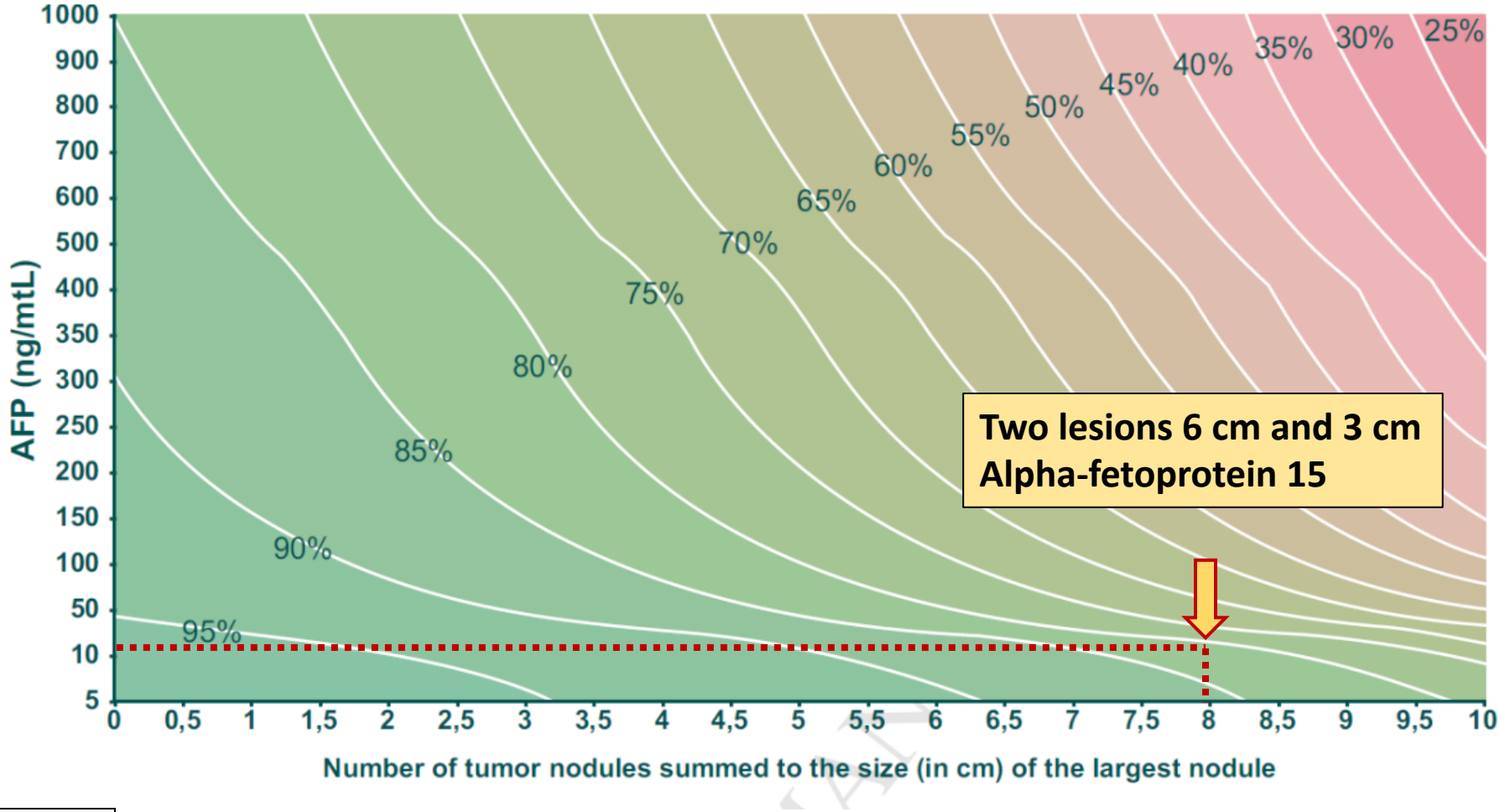

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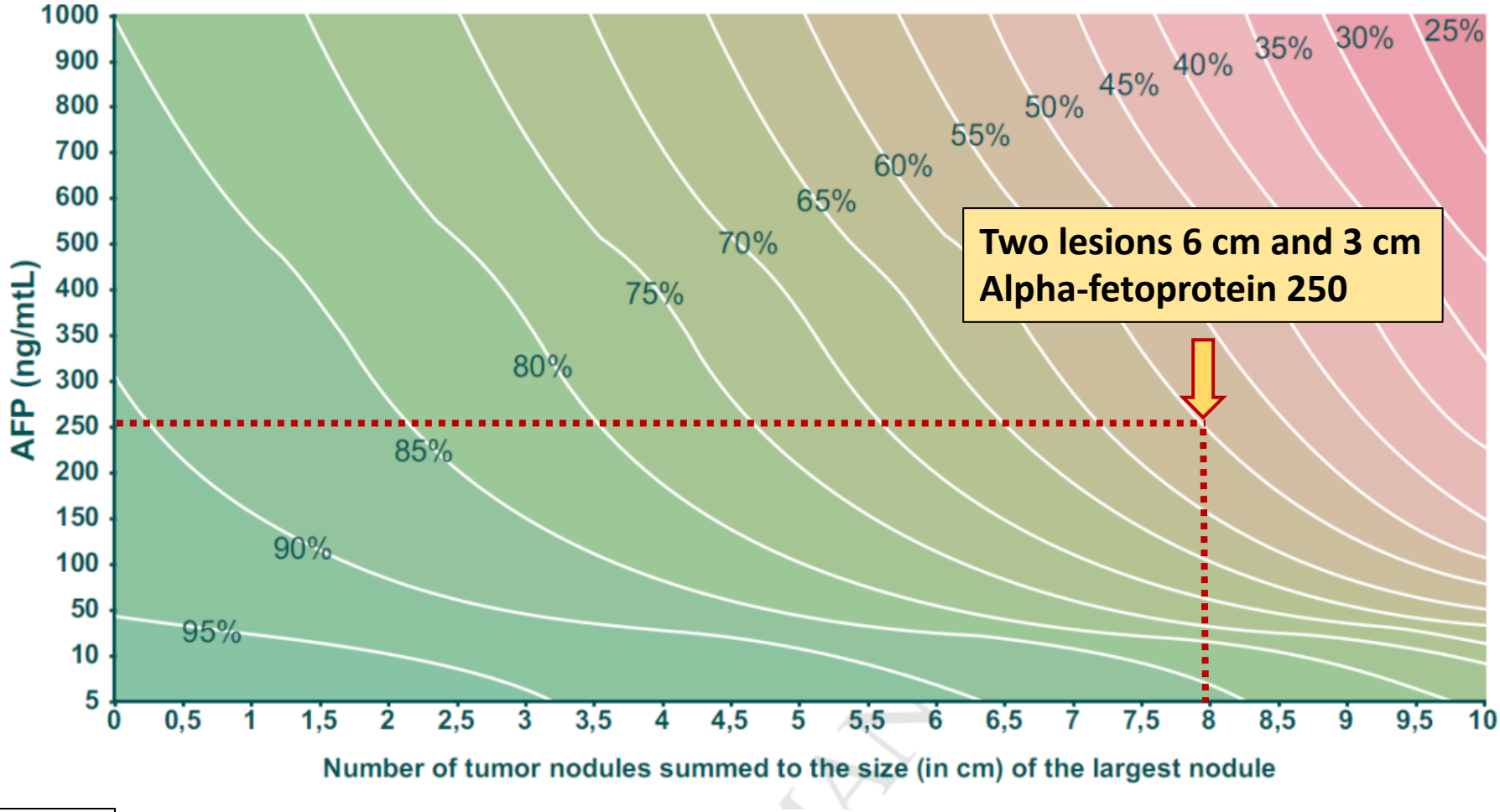

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Pre-transplant Prognostic Models (selected)

Pre-Transplant Selection	Tumor Burden	Biomarkers	AUROC
US National Policy [1,2]	Milan or Down-staged to Milan	No AFP ≥ 1000 (reduced to < 500)	
French AFP Model [3]	Largest tumor Size and total number	AFP	0.7
Metro-ticket 2 [4]	Largest tumor Size and total number	AFP	0.72
HCC-HALT* [5]	Tumor burden score (size and number)	AFP	0.61
TTV + AFP [6]	TTV ≤ 115 cm^3	AFP ≤ 400 ng/ml	
Pre-MORAL [7]	Largest tumor size	AFP, NLR	0.82

**Include MELD-Na*

1. Yao FY, et al. Hepatology 2015;61:1968-1977
2. Hameed B. et al. Liver Transpl 2014;20:945-951
3. Duvoux et al. Gastroenterology 2012;143:986-94
4. Mazzaferro et al. Gastroenterology 2018;154:128-139
5. Sasaki et al. Lancet Gastroenterol Hepatol 2017; 2:595-603
6. Toso et al. Hepatology 2015;62:158-165
7. Halazun KJ, et al. Ann Surg 2017;265:557-564

Down-staging of HCC for Transplant

- Definition: Reduction in the size of tumor using local regional therapy to meet acceptable criteria for liver transplant [1]
- Tumor response: Based on radiographic measurement of the size of all viable tumors, not including the area of necrosis from local regional therapy [2]
- A selection tool for tumors with more favorable biology that respond to down-staging treatment and also do well after liver transplant [1]

1. Yao & Fidelman. Hepatology 2016;63:1014-1025

2. EASL Guidelines - Briux J. et al. J Hepatol 2001;35: 421–430

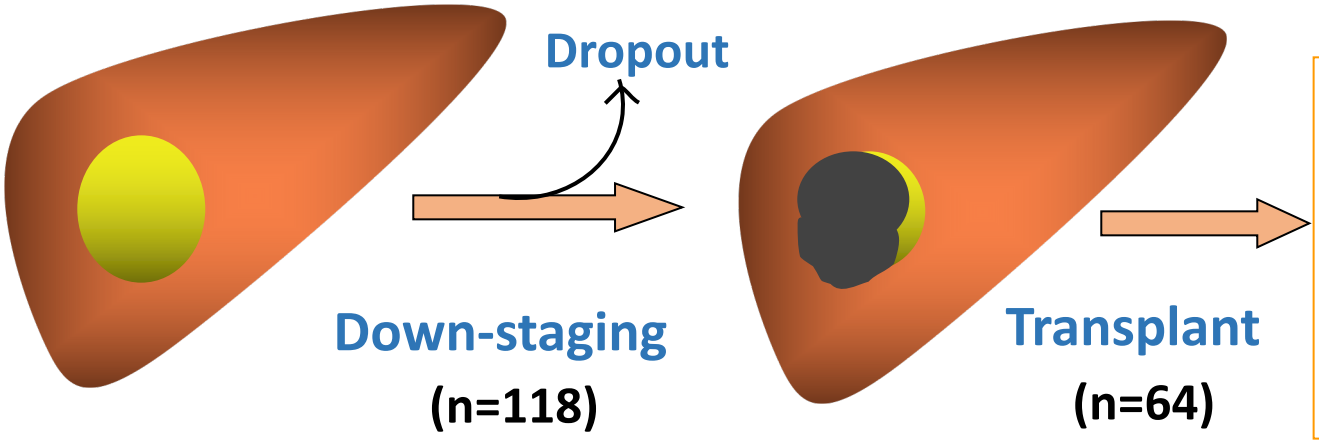
UCSF Down-Staging Protocol for Transplant

Minimum observation 3 months

Meeting Milan criteria

(n=41)

Dropout



Down-staging

(n=118)

Transplant

(n=64)

Median f/u 3.8 years

- 5 HCC recurrence (8%)
- 78% 5-yr survival post-transplant
- 91% 5-yr recurrence free probability
- 56% 5-yr intention-to-treat survival

Inclusion Criteria for Down-staging

1 tumor ≤ 8 cm

2-3 tumor ≤ 5 cm + total diameter ≤ 8 cm

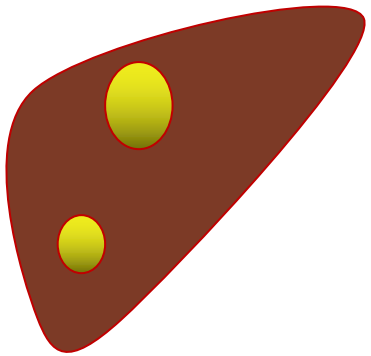
4-5 tumor ≤ 3 cm + total diameter ≤ 8 cm

→ US national policy

Yao FY et al. Hepatology 2015;61:1968-1977

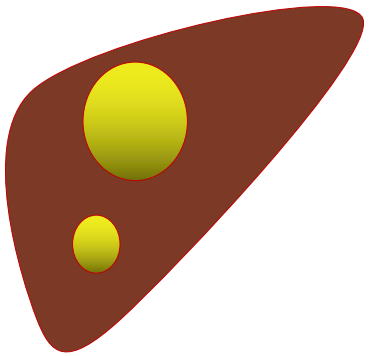
HCC Transplant Criteria at UCSF

Two lesions 6 cm & 3 cm
Outside these criteria



UCSF Down-staging Criteria

- 1 lesion 5.1-8 cm
- 2-3 lesions ≤ 5 cm
- 4-5 lesions ≤ 3 cm
- Total Tumor Diameter ≤ 8 cm
- No extra-hepatic disease

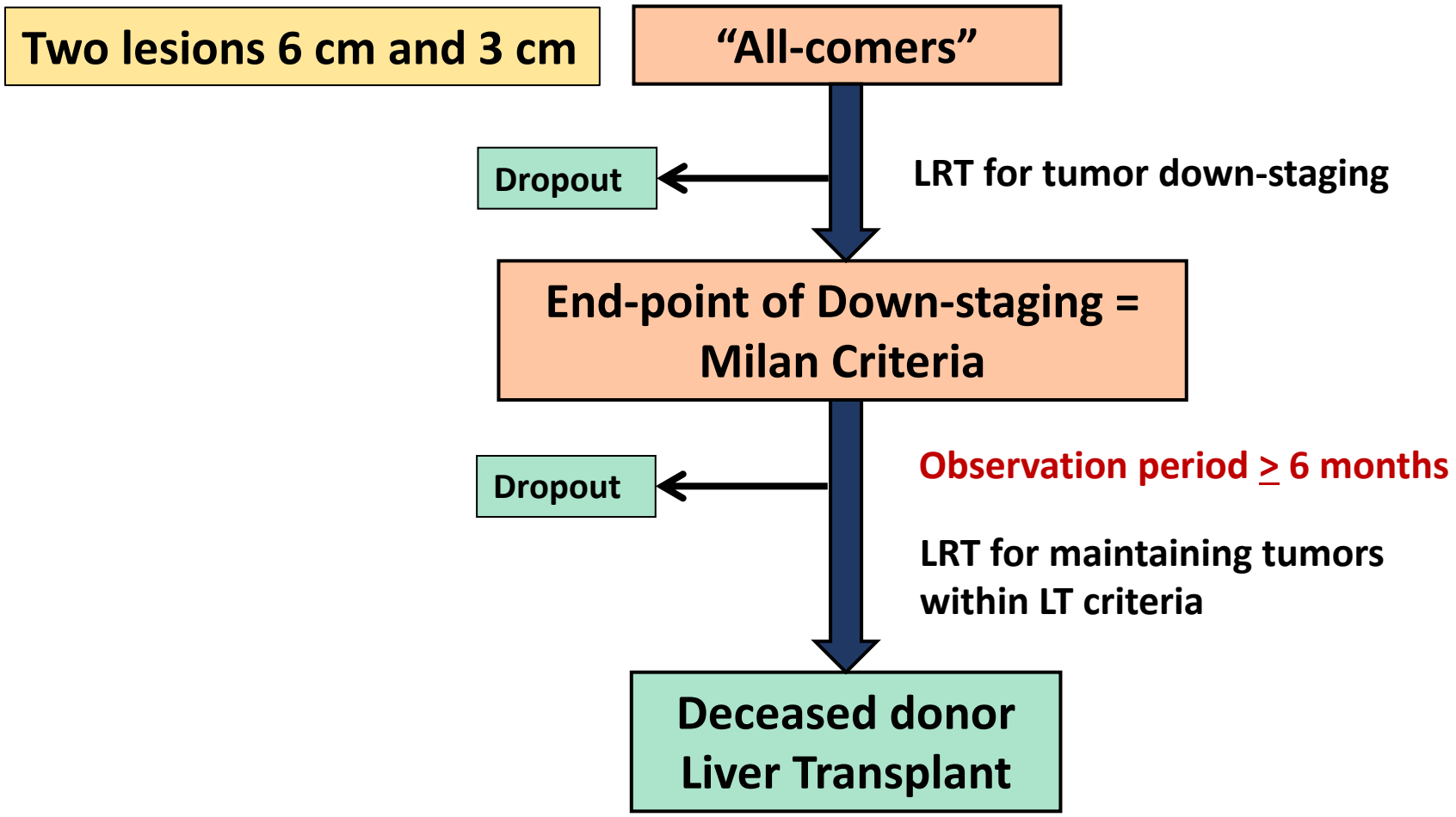


UCSF "All-Comers" Criteria

- Any number of tumors
- Total Tumor Diameter > 8 cm
- No extra-hepatic disease

Require longer period of observation after down-staging (6 months)

“All-comers” Down-staging Protocol



Sinha J et al. Hepatology 2019;70:1185-1196

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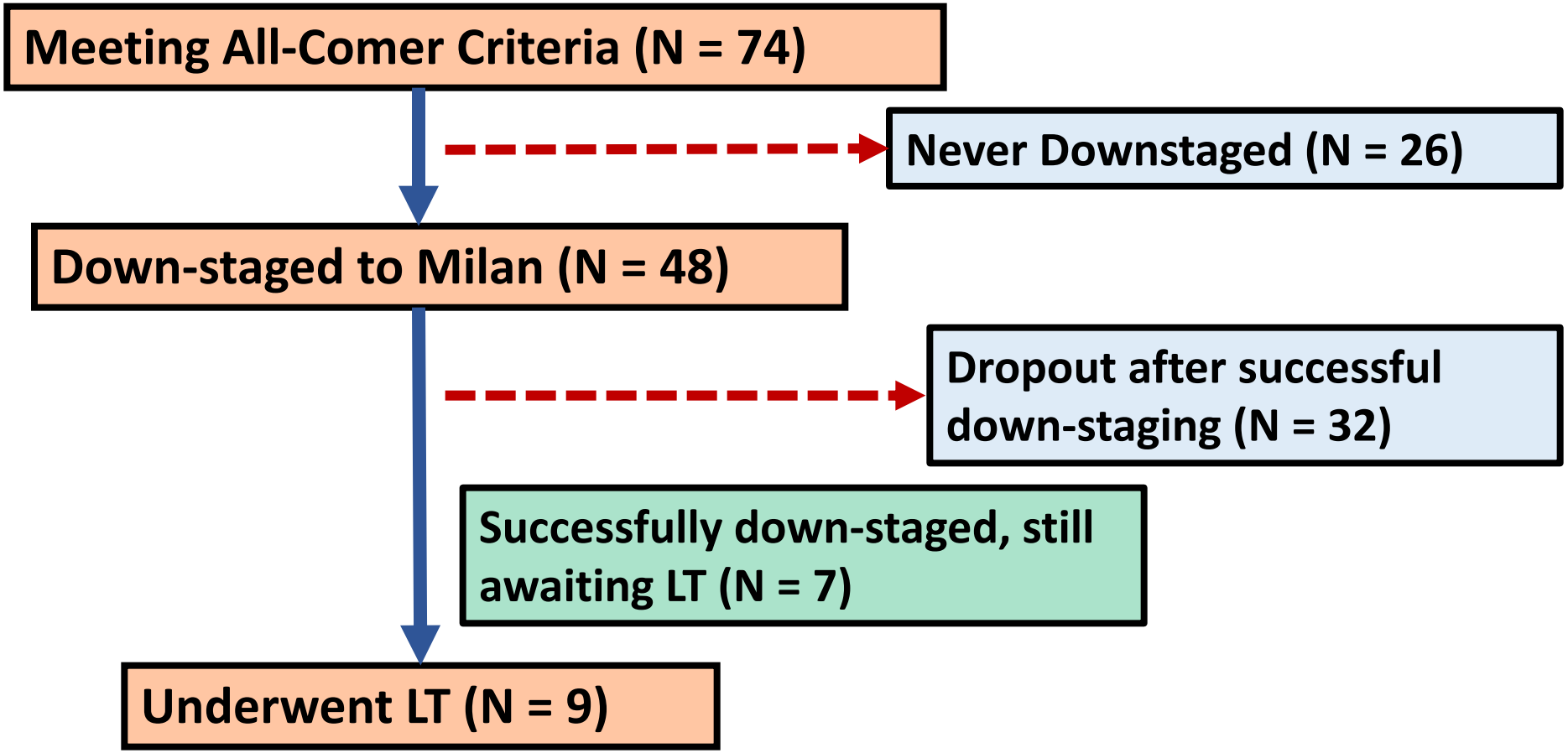

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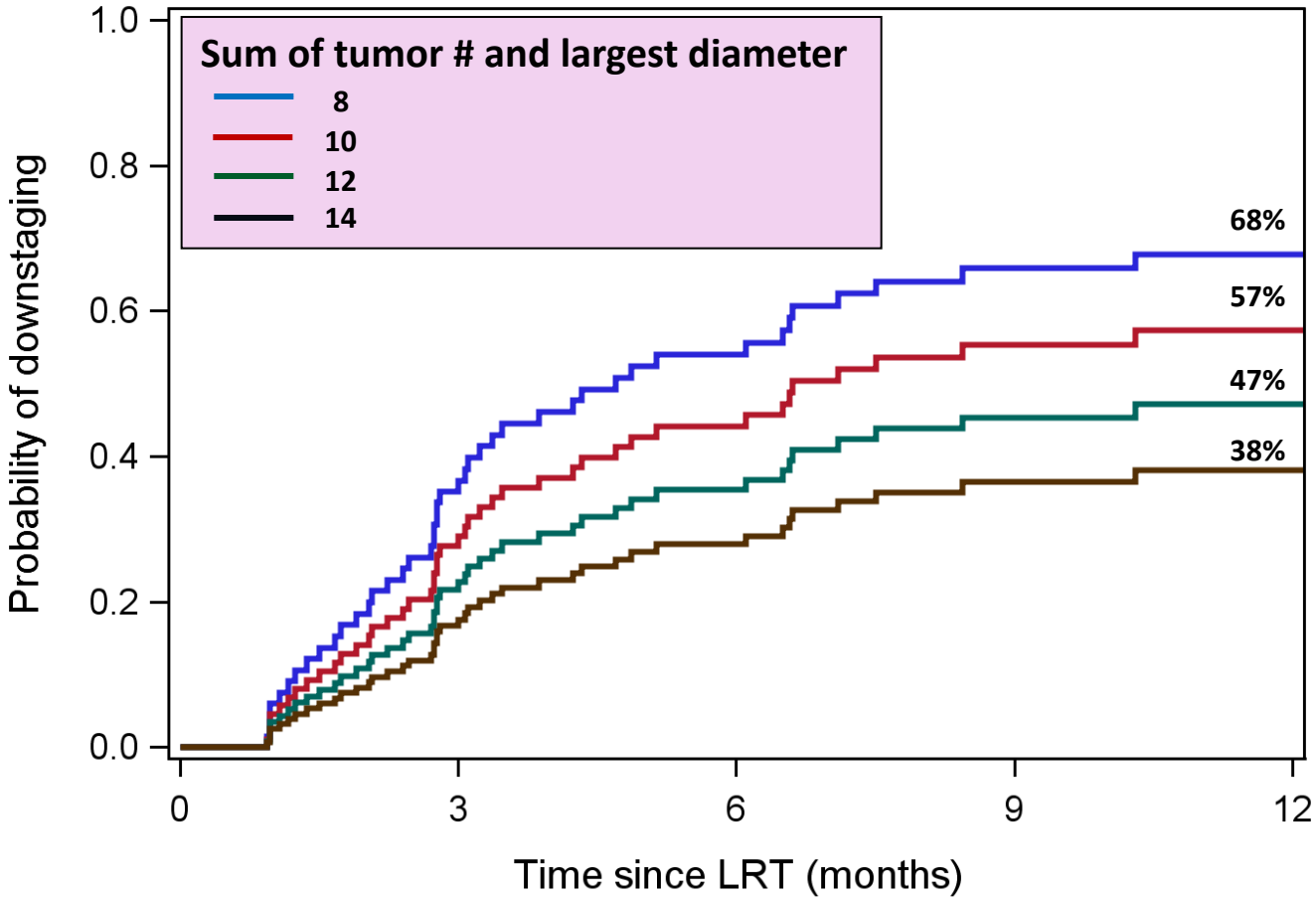
Probability of Down-staging (all-comers)



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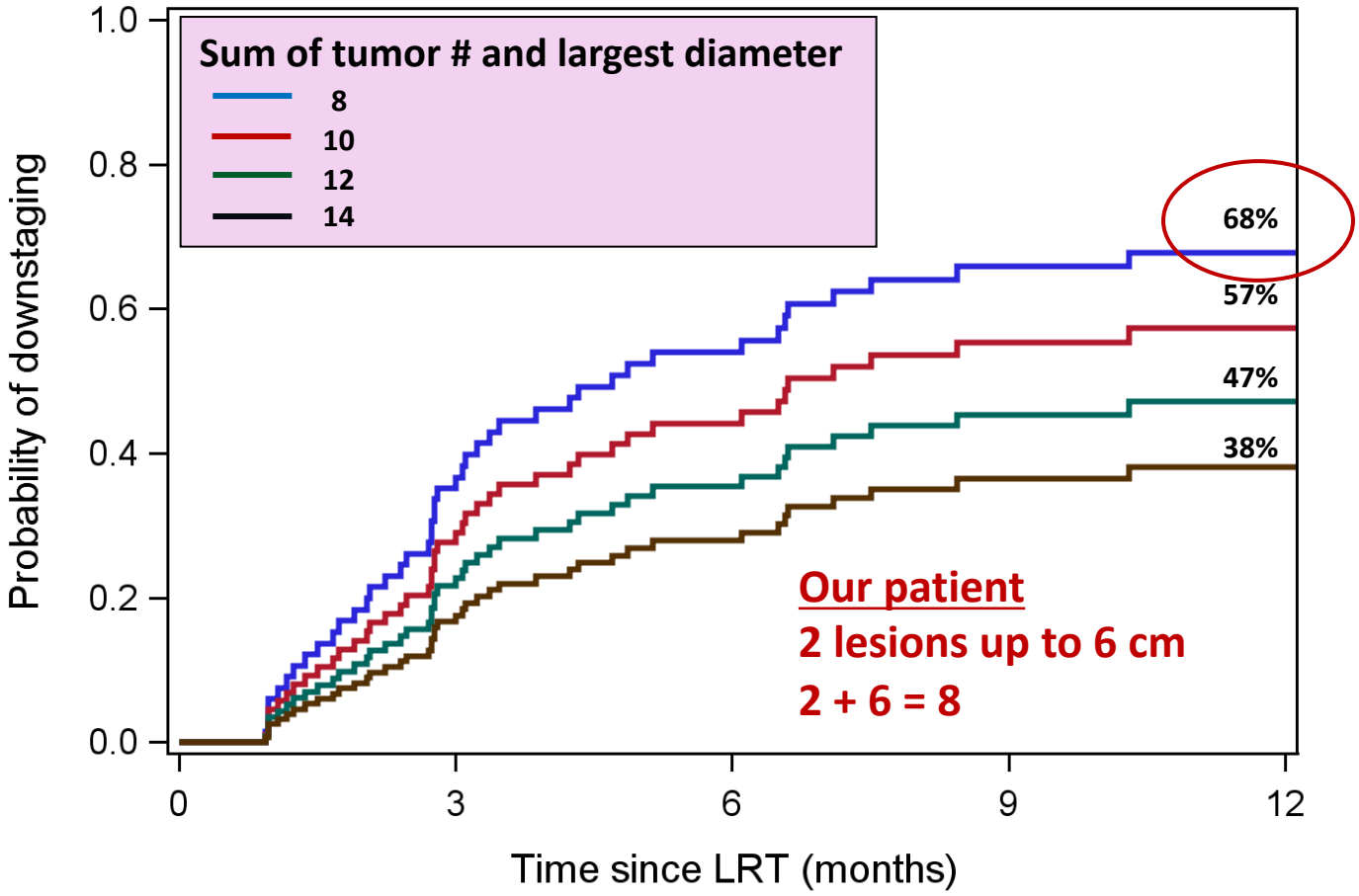

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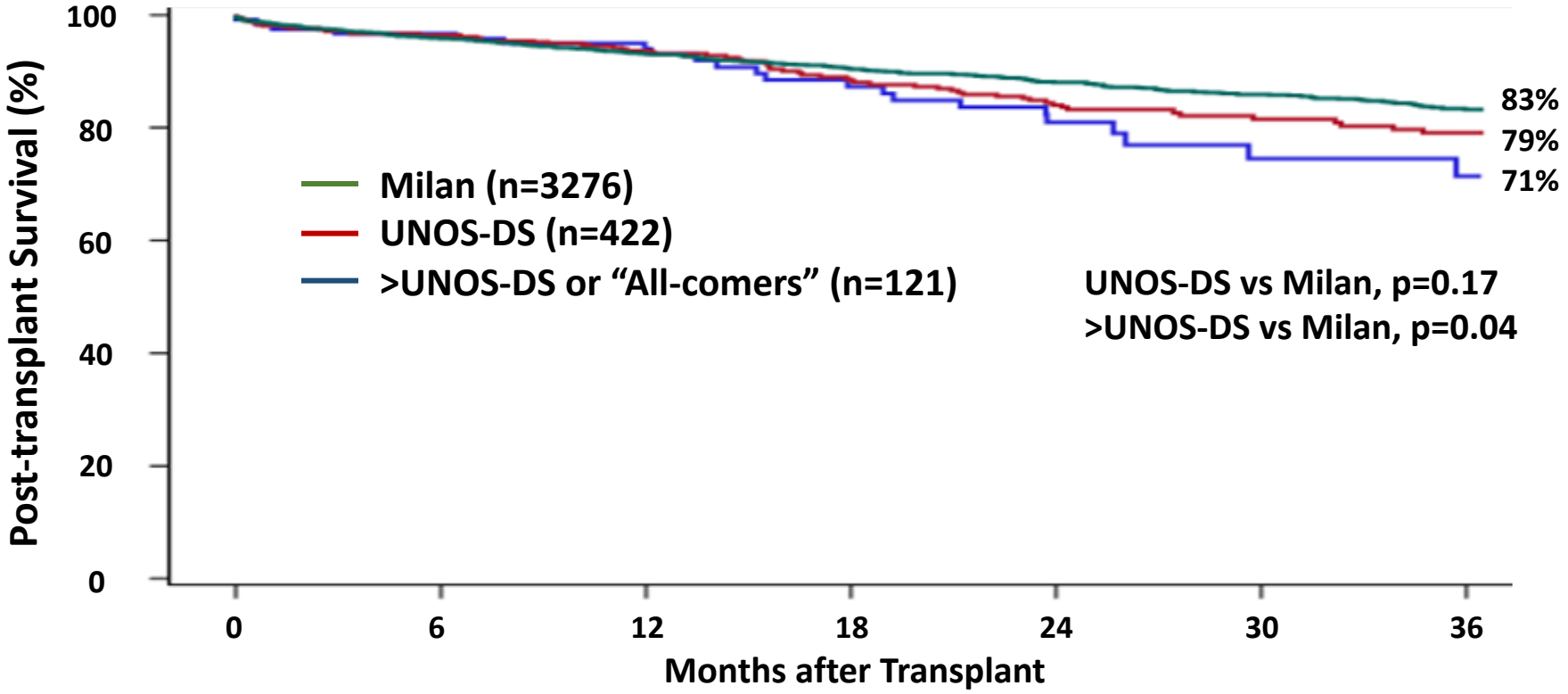
“All comers” Down-Staging Protocol

- A subset of patients in the “all-comers” group may benefit from liver transplant
- There are upper limits in tumor burden beyond which successful liver transplant after down-staging becomes an unrealistic goal
- Strategies to shorten waiting time (high-risk donors) or living donor liver transplant

Post-transplant survival after down-staging

The effects of initial tumor burden



UCSF/ UNOS-down-staging Inclusion Criteria

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Mehta N, et al. Hepatology [Epub]

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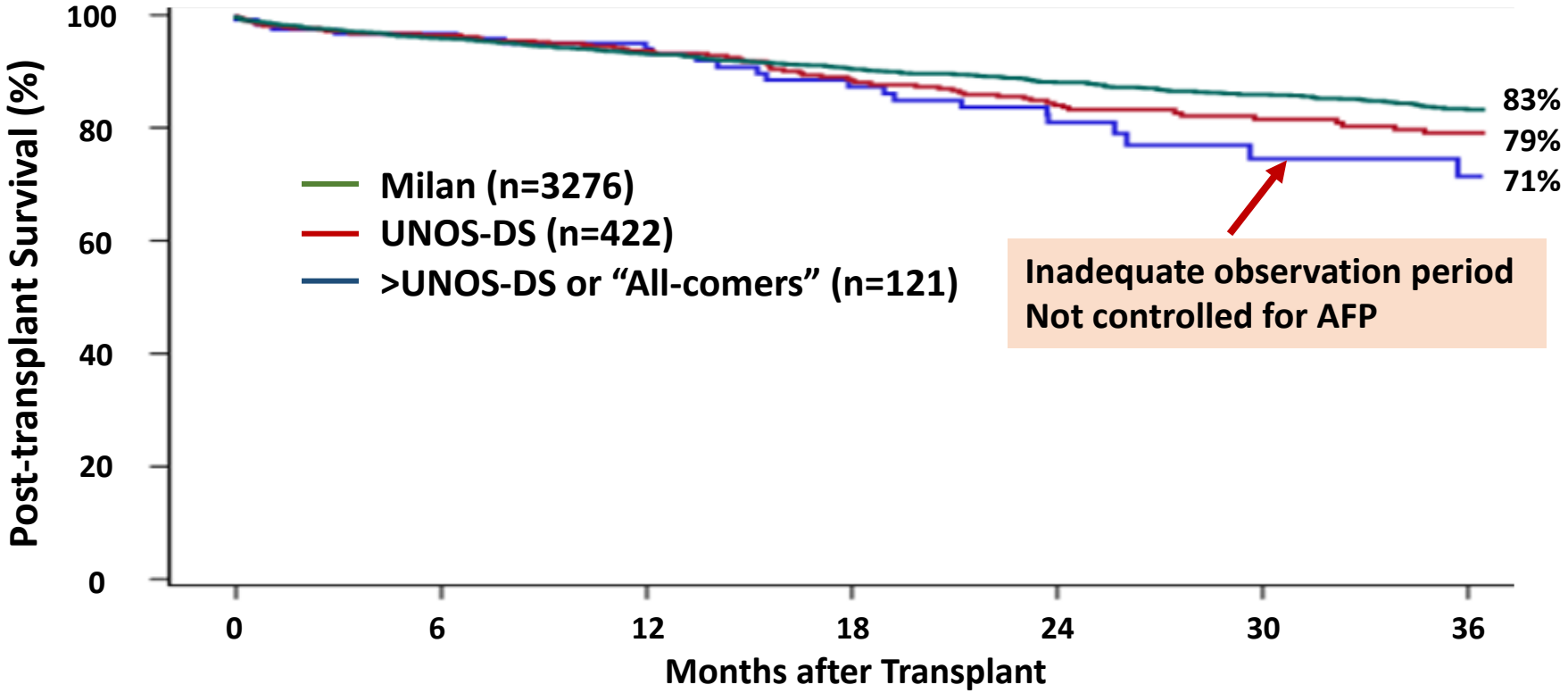

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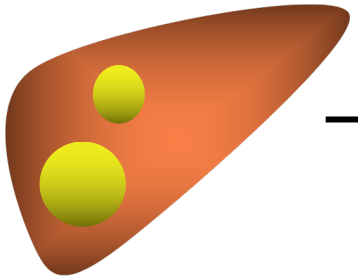
Large tumors: Transplant or no transplant?

2 lesion 6 cm & 3 cm, AFP 15

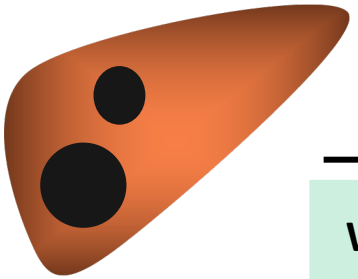


No transplant; TACE or Y-90 for "palliation"

5-yr survival 20-30%

☐

Down-staging



List for LT if successful down-staging to Milan

Wait for LT

☑

Liver transplant

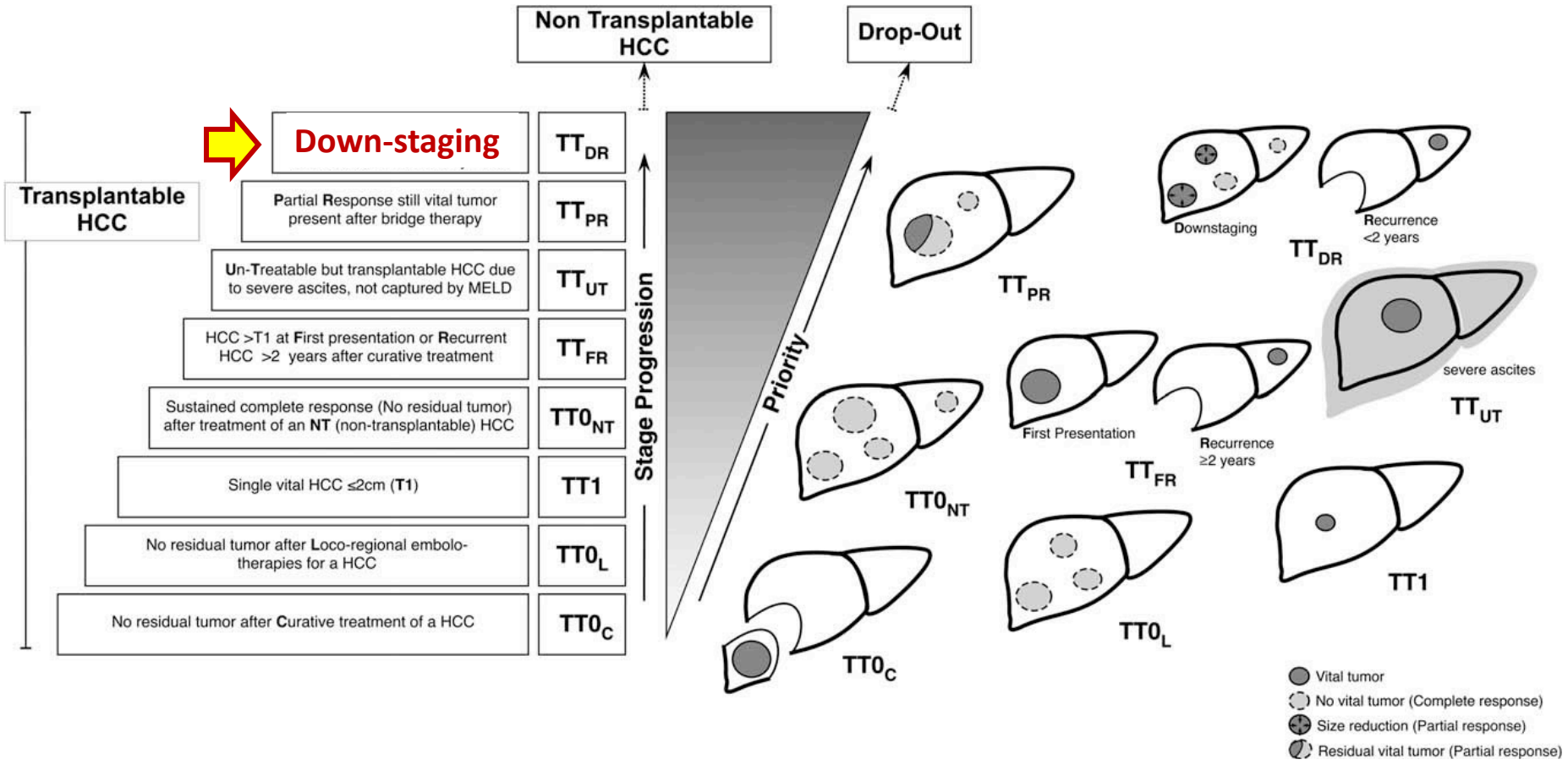
5-yr post-LT survival 70%

Tumor progression & dropout (selection)

Dropout due To long wait-time

Transplant benefit high (compared to alternatives)

Transplant benefit and priority for organ allocation



Mazzaferro V, et al. Hepatology 2016;63:1707-1717

Summary

- Paradigm shift in patient selection for liver transplant, incorporating response to local regional therapy/ down-staging and tumor markers (AFP) and not relying solely on tumor burden.
- Based on initial tumor burden in this case, at least 2/3 probability of successful down-staging to Milan.
- “Transplant benefit” high after successful down-staging for large tumors vs palliative TACE or Y-90 radioembolization.

Thank You!