Optimal management of ascites

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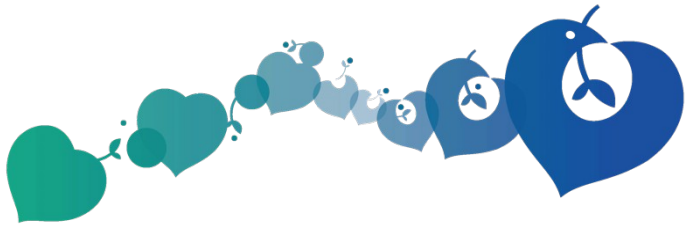
Disclosure



- Gore, Abbvie, Gilead

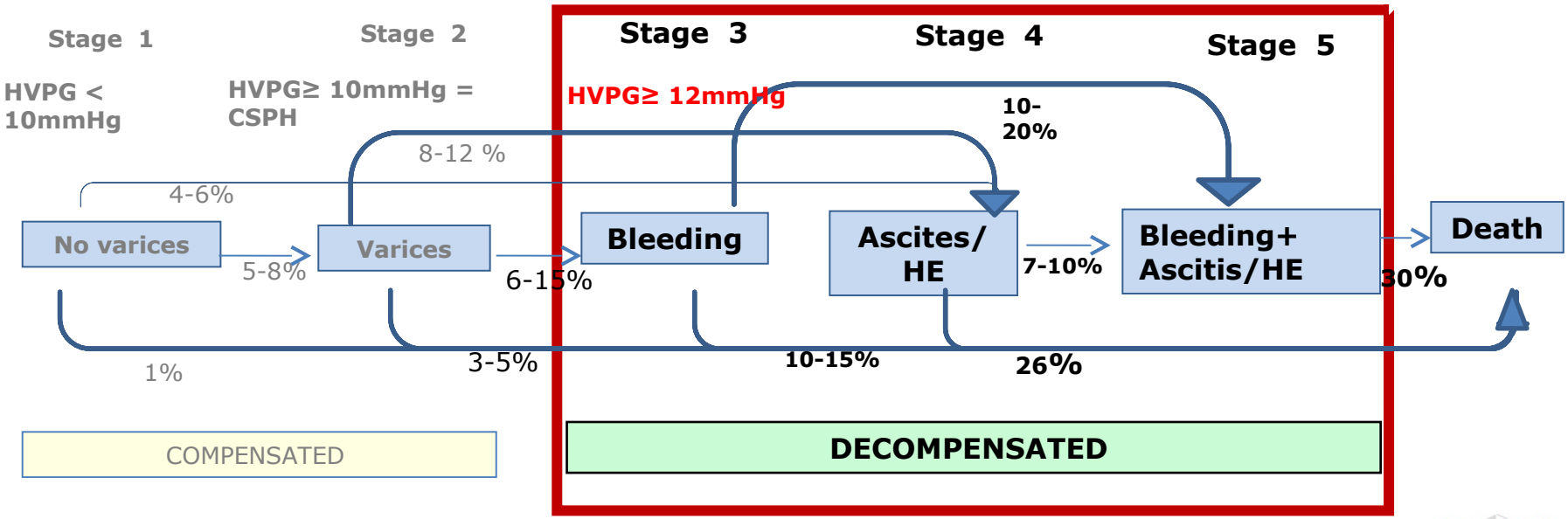
Ascites: definition

- More than 25 ml fluid in the peritoneal cavity
- 50% of pts within 10 years of the diagnosis of cirrhosis
- Classic complication of advanced cirrhosis and it often marks the first sign of hepatic decompensation
- Not only a cosmetic problem …associated with a 50% mortality rate within the 3 years

Prognostic value of different stages of cirrhosis

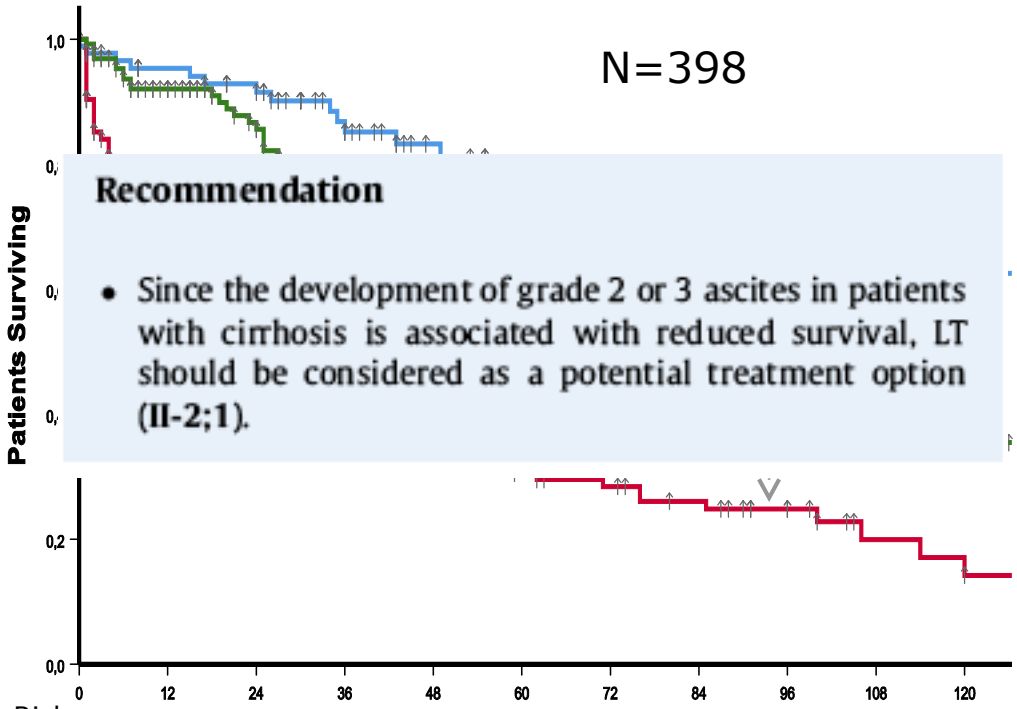
Different stages of decompensated cirrhosis:

- Bleeding without any other decompensation
- Ascites without bleeding
- Bleeding and any other decompensation



Adapted from D'Amico , AP&T 2014; De Franchis R, J Hepatology 2015

Prognostic value of different stages of cirrhosis



N=398

Recommendation

- Since the development of grade 2 or 3 ascites in patients with cirrhosis is associated with reduced survival, LT should be considered as a potential treatment option **(II-2;1)**.

Bleeding alone

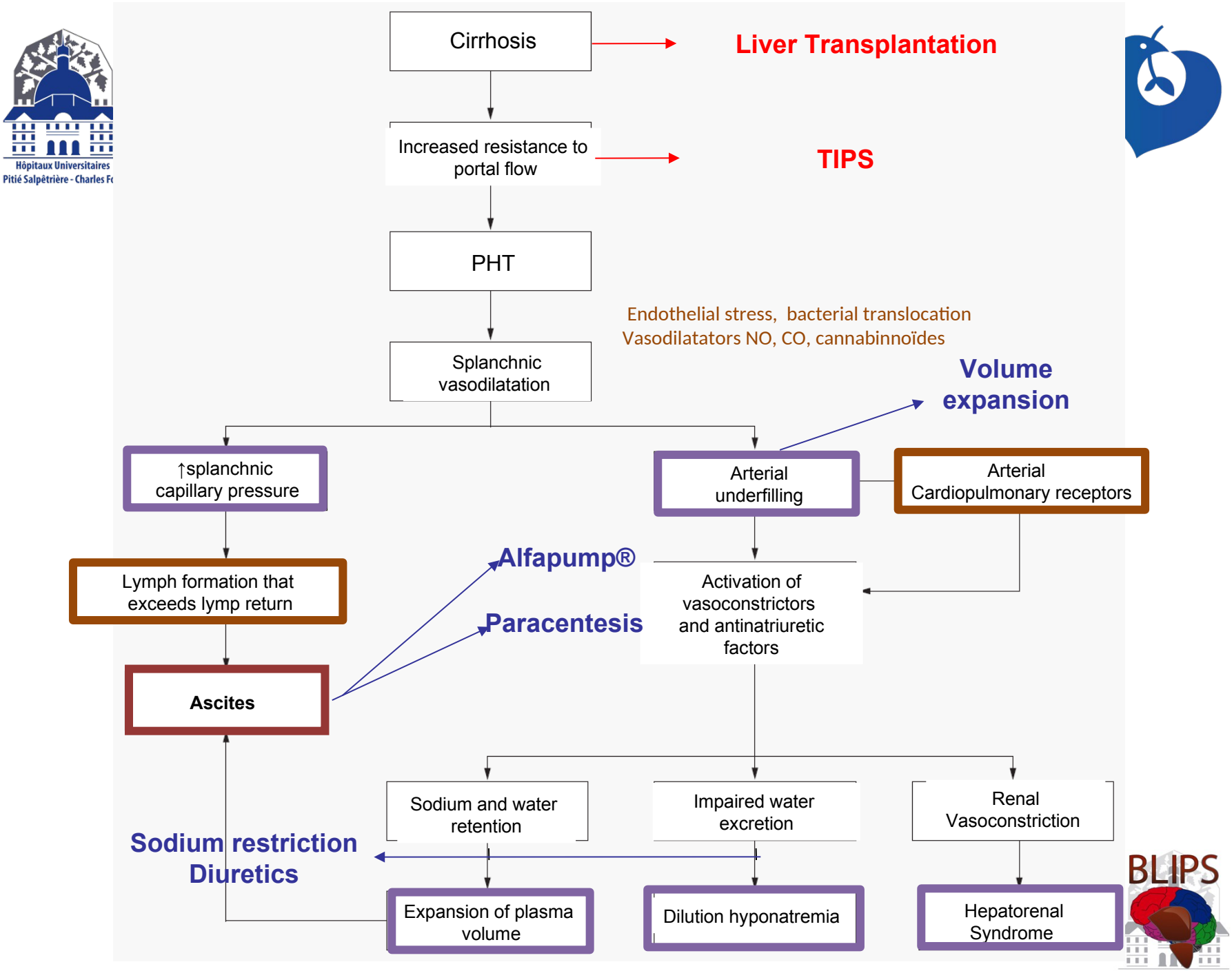
Ascites(±HE)

Bleeding & Ascites(±HE)

Patients at Risk

Bleeding	90	79	66	55	43	31	19	7	7	4	2
Ascites	131	120	108	96	84	71	60	48	36	24	12
Bleeding+Ascites	177	166	153	142	130	118	106	93	82	70	58

Garcia-Guix M et al., CO 155
C Villanueva


Cirrhosis
Liver Transplantation
Increased resistance to portal flow
TIPS
PHT
Endothelial stress, bacterial translocation
Vasodilatators NO, CO, cannabinnoïdes
Splanchnic vasodilatation
Volume expansion
↑splanchnic capillary pressure
Arterial underfilling
Arterial Cardiopulmonary receptors
Lymph formation that exceeds lymp return
Alfapump®
Paracentesis
Activation of vasoconstrictors and antinatriuretic factors
Ascites
Sodium and water retention
Impaired water excretion
Renal Vasoconstriction
Sodium restriction
Diuretics
Expansion of plasma volume
Dilution hyponatremia
Hepatorenal Syndrome
BLIPS

Recurrent/recidivant ascites: a single definition ?

Special Article

Definition and Diagnostic Criteria of Refractory Ascites and Hepatorenal Syndrome in Cirrhosis

VICENTE ARROYO,[1] PERE GINÈS,[1] ALEXANDER L. GERBES,[2] FRANCIS J. DUDLEY,[3] PAOLO GENTILINI,[4] GIACOMO LAFFI,[4] TELFER B. REYNOLDS,[5] HELMER RING-LARSEN,[6] AND JÜRGEN SCHÖLMERICH[7]

Recidivant Ascites. The ascites that recurs at least on three occasions within a 12-month period despite prescription of dietary sodium restriction and adequate diuretic dosage.

Recidivant ascites: ascites that recurs at least on 3 occasions within a 12-month period despite adequate treatment
Early recurrent ascites: recurrence within 4 weeks after initial control

Arroyo et al., Hepatology 1996

EASL 2018

Non refractory ascites: Therapeutic options

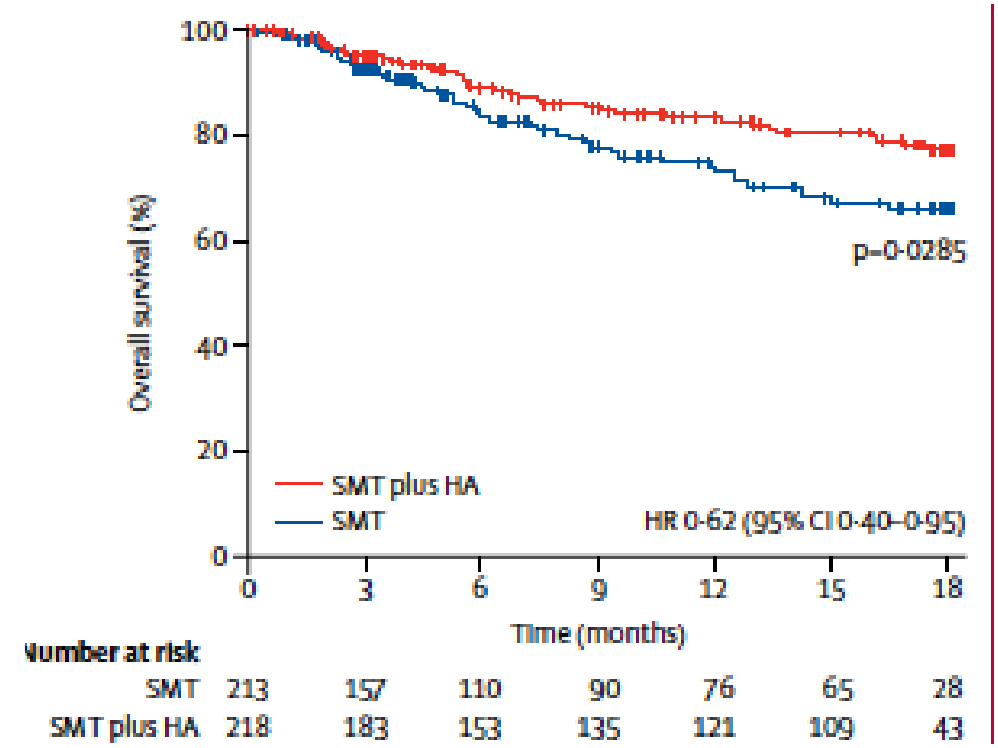
- Sodium restriction and diuretics
- Paracentesis
- Repeated albumin infusion
- TIPS
- Treatment of the underlying disease may improve ascites (alcohol abstinence or viral suppression)

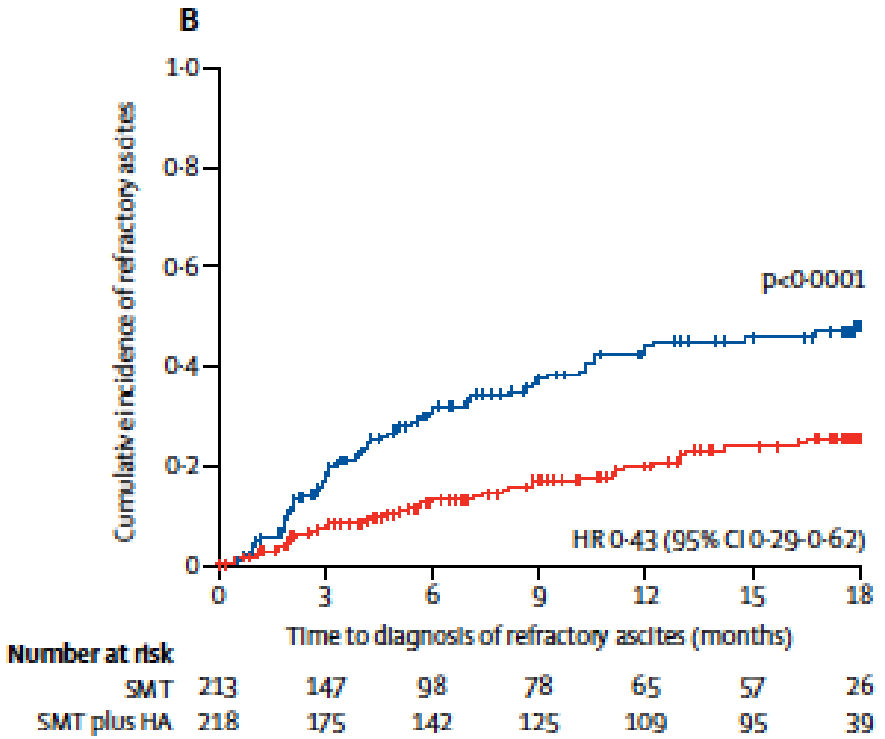
Non refractory ascites: Therapeutic options

- Sodium restriction and diuretics
- Paracentesis
- **Repeated albumin infusion**
- **TIPS**
- Treatment of the underlying disease may improve ascites (alcohol abstinence or viral suppression)

Non refractory ascites: Albumin: the ANSWER study

40g twice a week for two weeks and then 40g weekly in patients treated with diuretics

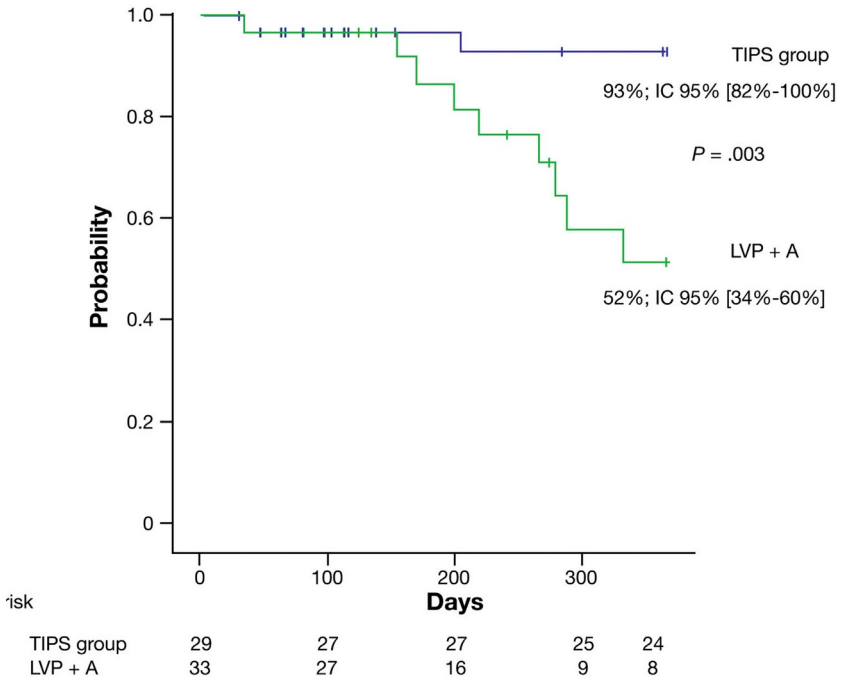




Caraceni et al.
The Lancet 2018

Covered TIPS in recurrent ascites: Transplant-free survival

- 62 patients with recurrent ascites:
  - 2 LVP with a minimal interval of 3 weeks
  - less than 6 within 3 months
  - 30% with a history of variceal bleeding
  - 20% with a history of renal failure
- 10 mm TIPS dilated to 8 or 10 (PPG<12 mmHg)



Bureau et al., Gastroenterology 2017

Parameters associated with survival

	Alive n = 51	Dead or transplanted n = 11	Univariate	Multivariate
INR	1,4 ± 0,3	1,5± 0,2	p=0,009	0,8 [0,3-2,3] NS
Serum sodium (mmo/l)	134 ± 4	129 ± 3	p=0,001	0,9 [0,9-1,0] NS
Bilirubin (mmol/l)	15 ± 12	27 ± 21	p=0,05	1,0 [1,0-1,0] NS
TIPS / LVP+A	93 % / 73 %	7 % / 27 %	p=0,048	2,0 [1,1-4,0] p=0,03

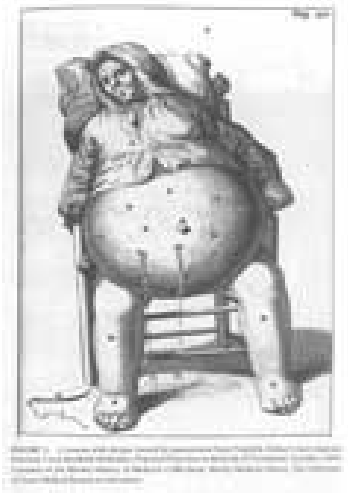
Bureau et al., Gastroenterology 2017

Refractory ascites:
Therapeutic options

- **Liver transplantation**
- **TIPS**
- **LVP + albumin**
- **Peritoneo-vesical shunt = AlfaPump®**

EASL 2018

Refractory ascites:
LVP or TIPS ?



?

6 Randomized controlled trials

Lebrec D et al., J Hepatol 1996
Rössle M et al., NEJM 2000*
Gines P et al., gastroenterology 2002
Sanyal A et al., Gatsroenterology 2003
Salerno F et al., Hepatology 2004*
Narahara Y et al., J Gastroenterol 2011

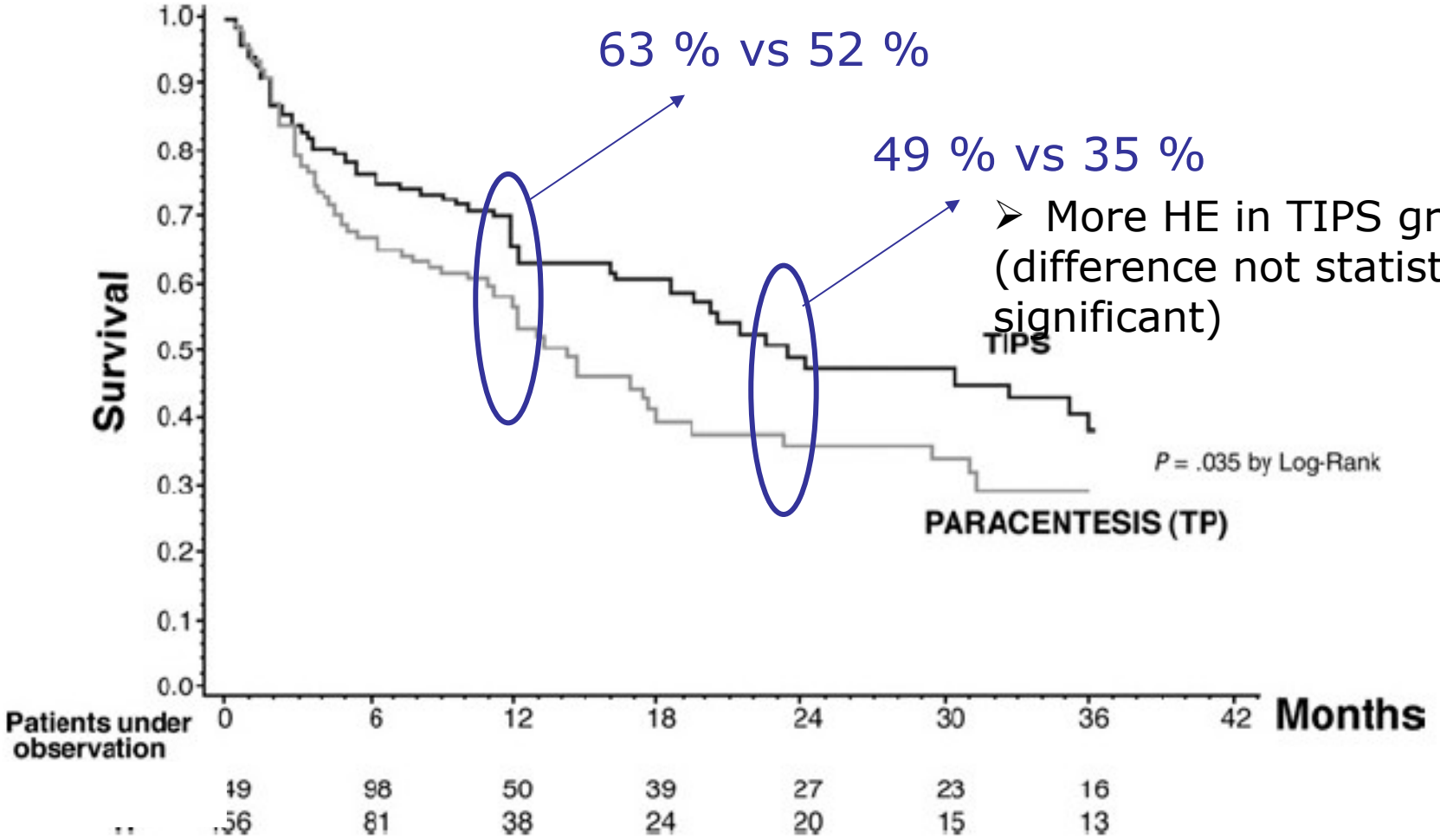
7 meta-analyses

Deltenre P et al., Liv Int 2005
Albillos A et al., J Hepatol 2005
D'Amico G et al., Gastroenterology 2005
Saab S et al., Cochrane 2006
Salerno F et al., Gastroenterology 2007
Chen RP et al., J Clin Gastroenterol 2014
Bai M et al., WJG 2014

- *including recurrent ascites
- Bare-metal stents
- Some rather severe patients (Bili 5-10 mg/dl)

TIPS and refractory ascites: meta-analyse of 4 RCT, individual data

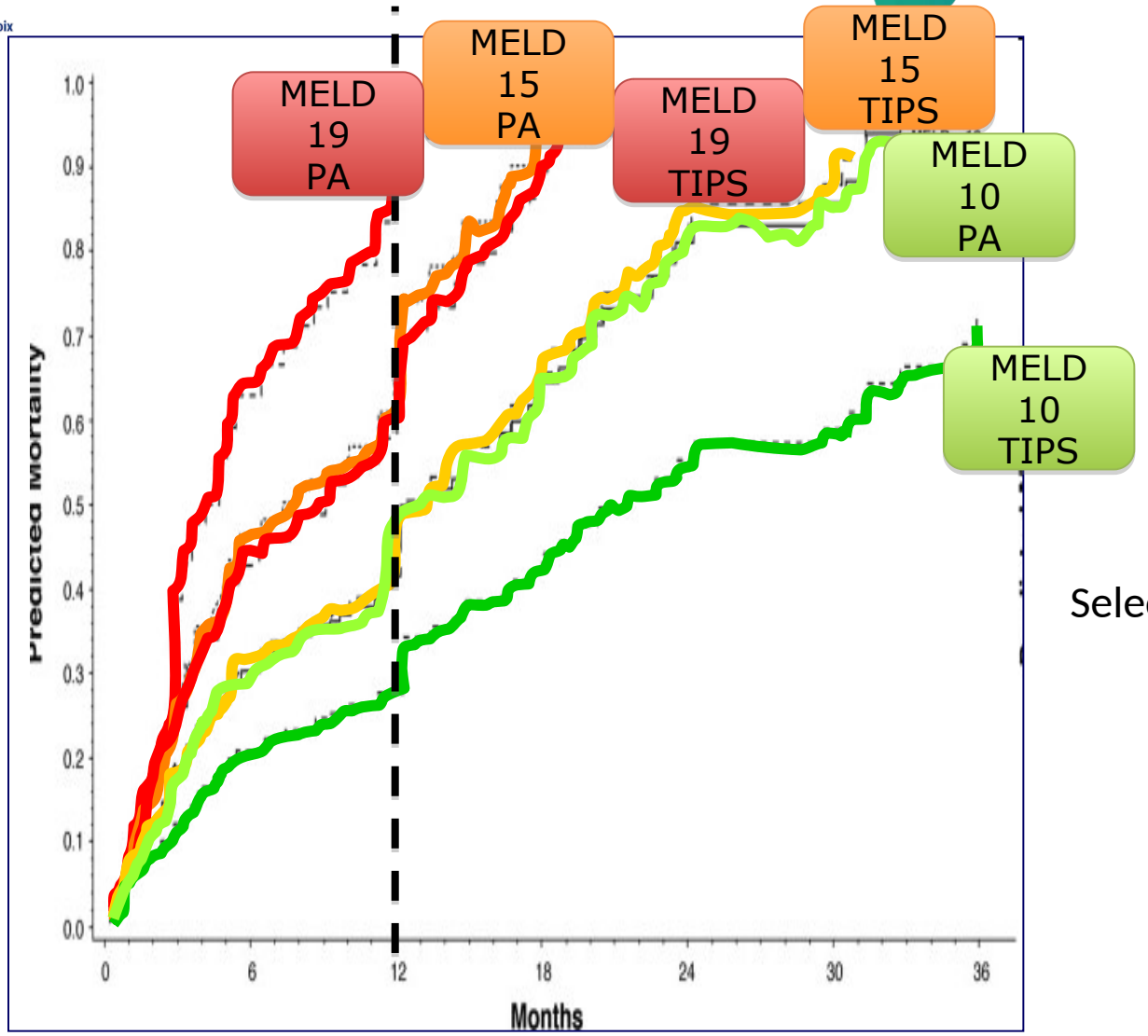
(non covered TIPS, n=305)



- More HE in TIPS group (difference not statistically significant)

Salerno F et al., Gastroenterology 2007

TIPS and refractory ascites: meta-analyse



Selection of patients+++

Salerno F et al., Gastroenterology 2007

TIPS & ascites: how to select the patients ?

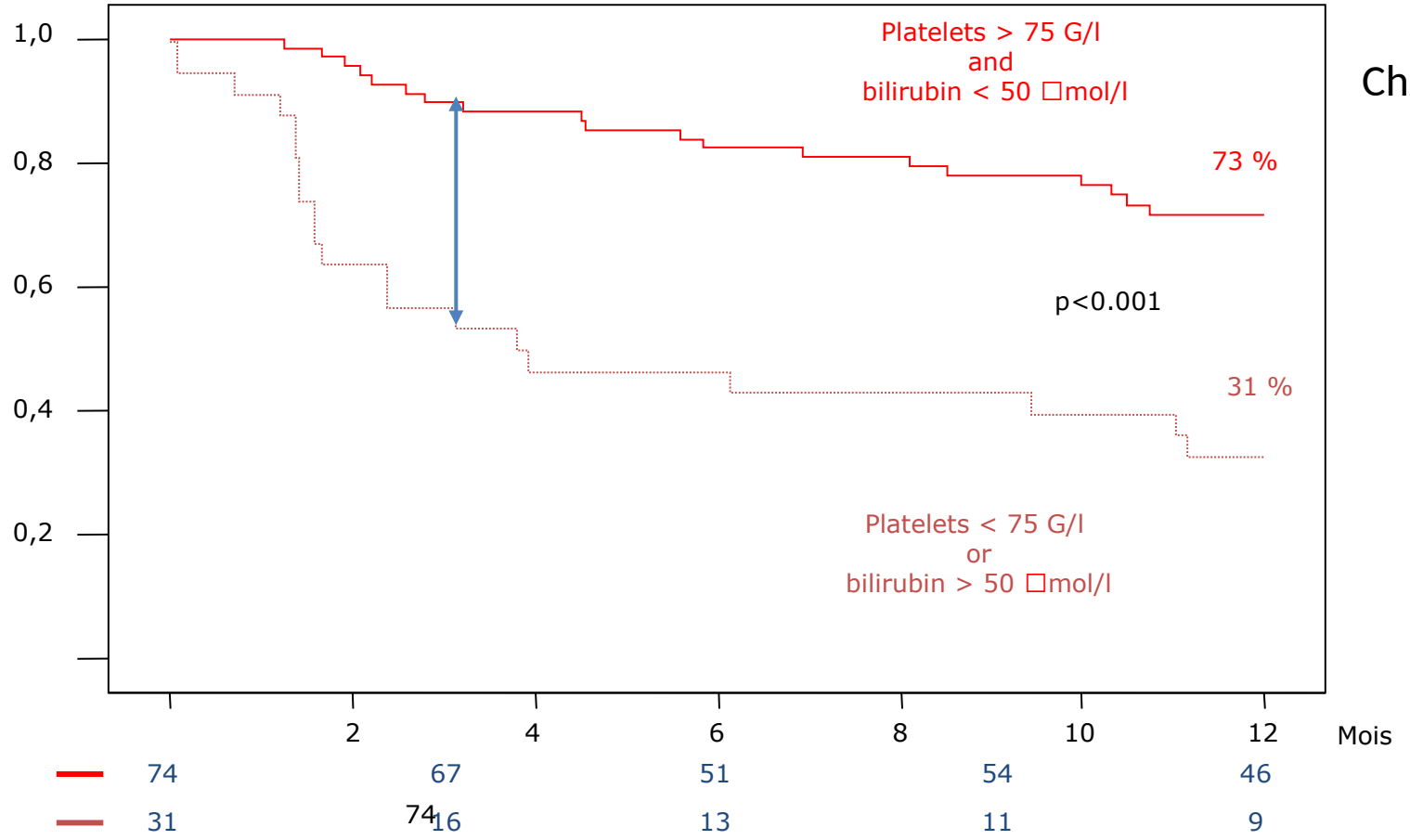
3 main issues after TIPS placement:

- Liver failure and death
- Cardiac decompensation≈20%
- HE≈35% (refractory HE ≈5%)

→ Discuss TIPS placement AND liver transplantation **at the same time**

(no TIPS/ TIPS failure/ complication after TIPS)

Covered TIPS in refractory ascites:
It's all about patients selection



Child Pugh<13

Bureau et al. J Hepatol 2011

Covered TIPS in refractory ascites:
It's all about patients selection

- ✓ Risk of HE after TIPS
  - ✓ Age >65 (or 70?)
  - ✓ High MELD score
  - ✓ High Child-Pugh score
  - ✓ MHE
  - ✓ Previous episode of HE
  - ✓ Sarcopenia

- ✓ Selection of patients
  - ✓ Age <65
  - ✓ MELD score<19
  - ✓ Child-Pugh score<13
  - ✓ <2 previous episodes of HE

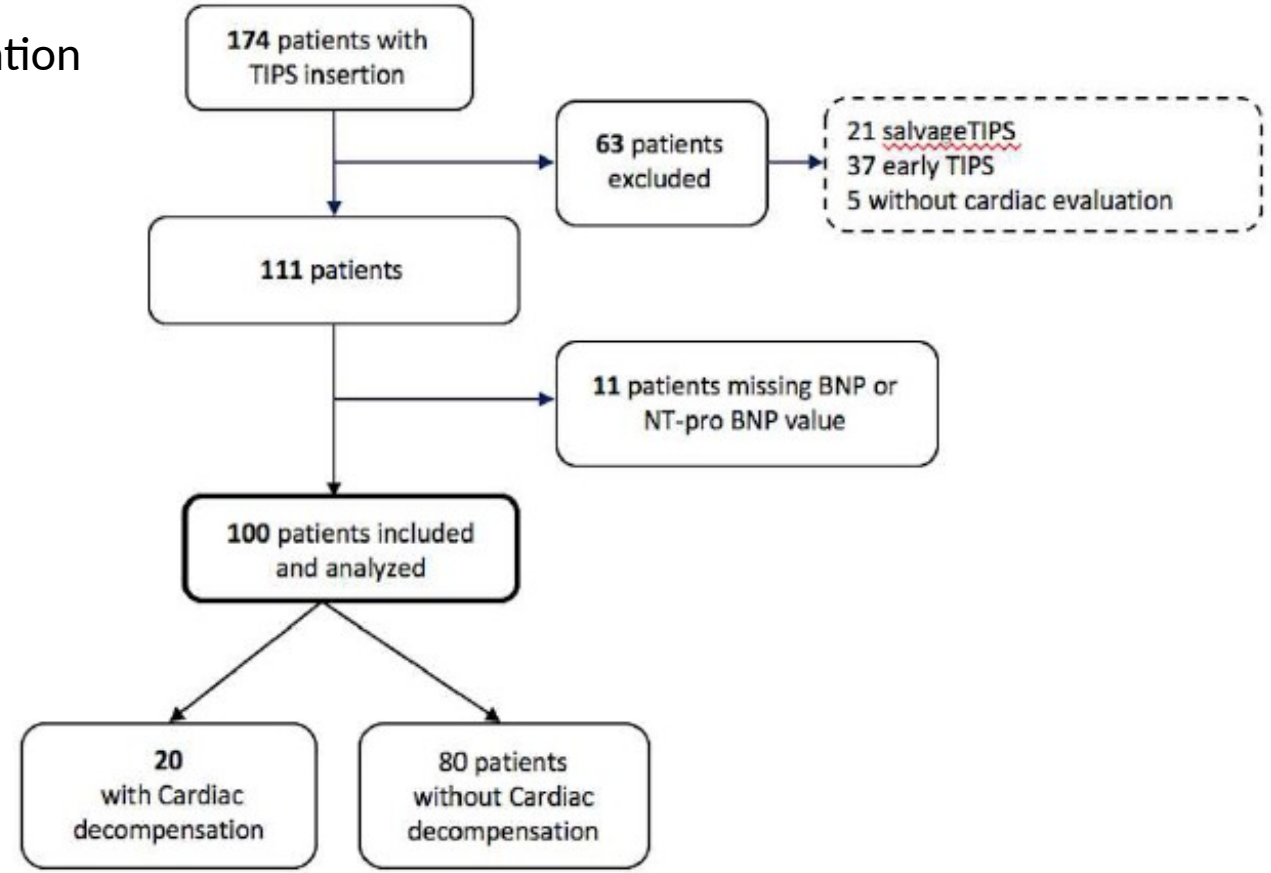
Nardelli et al.,Clinical Gastro 2017

Saad et al., Annals of Hepatology 2016

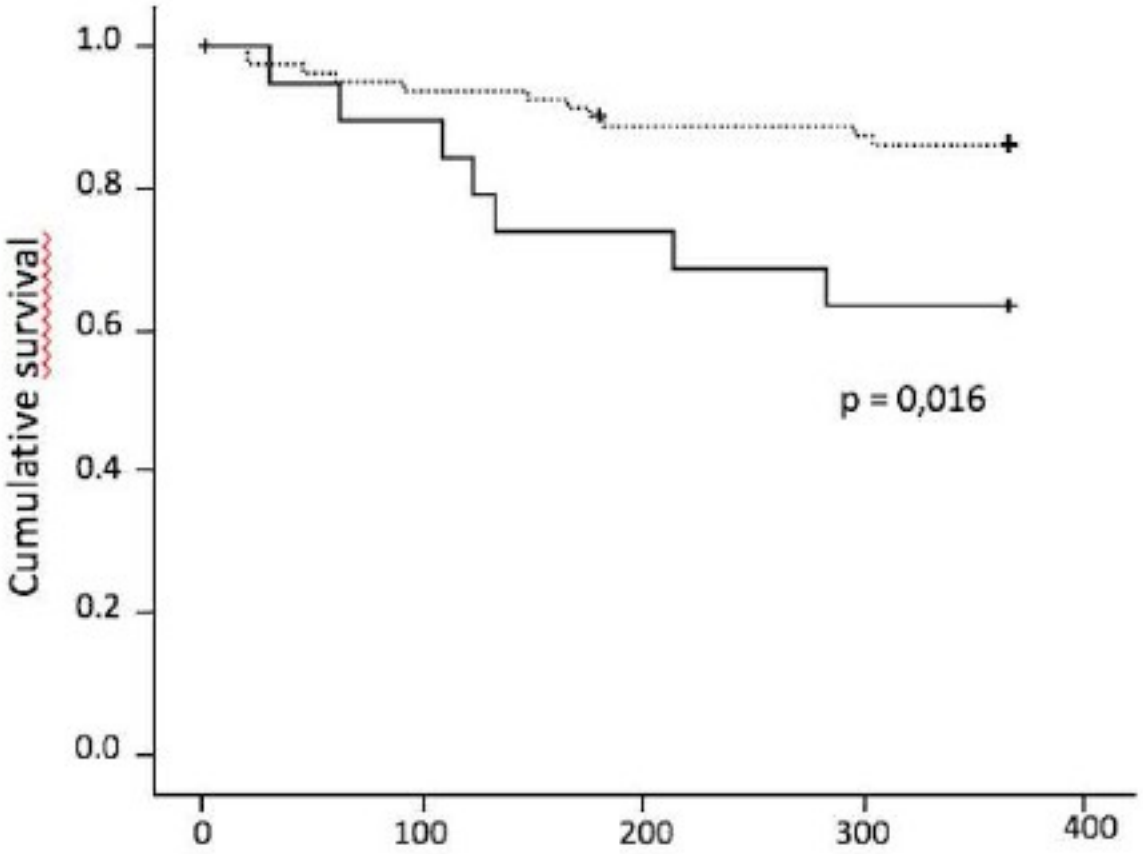
AFEF 2019CPG for the diagnosis and management of HE in patients with cirrhosis

Covered TIPS in refractory ascites:
It's all about patients selection

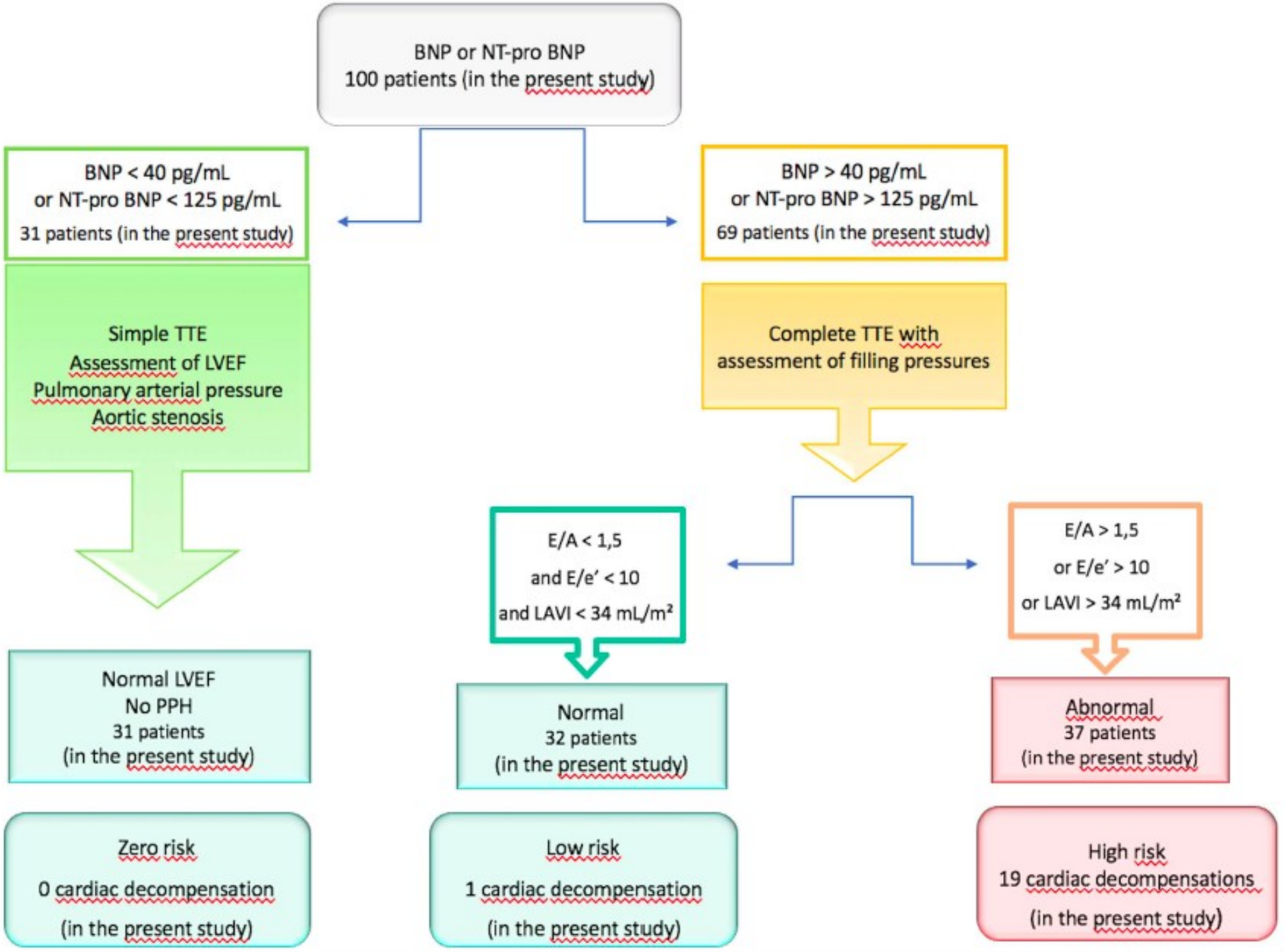
Careful cardiac evaluation
Biological
TTE



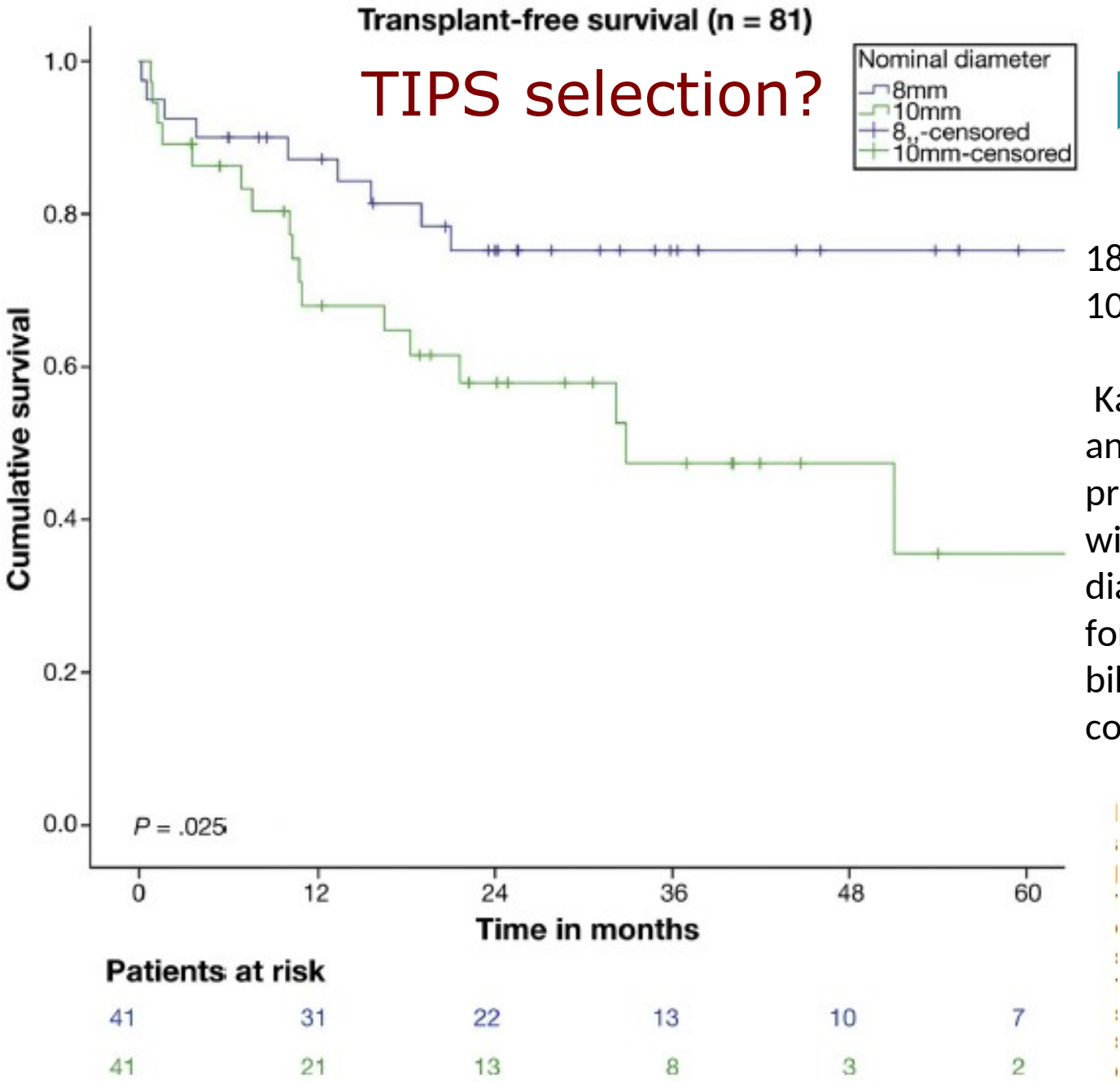
Billey et al. Hepatology 2019



·····	No cardiac decompensation	80	75	69	67	66
——	Cardiac decompensation	20	17	14	12	11


BNP or NT-pro BNP
100 patients (in the present study)
BNP < 40 pg/mL
or NT-pro BNP < 125 pg/mL
31 patients (in the present study)
BNP > 40 pg/mL
or NT-pro BNP > 125 pg/mL
69 patients (in the present study)
Simple TTE
Assessment of LVEF
Pulmonary arterial pressure
Aortic stenosis
Complete TTE with
assessment of filling pressures
E/A < 1,5
and E/e' < 10
and LAVI < 34 mL/m²
E/A > 1,5
or E/e' > 10
or LAVI > 34 mL/m²
Normal LVEF
No PPH
31 patients
(in the present study)
Normal
32 patients
(in the present study)
Abnormal
37 patients
(in the present study)
Zero risk
0 cardiac decompensation
(in the present study)
Low risk
1 cardiac decompensation
(in the present study)
High risk
19 cardiac decompensations
(in the present study)

TIPS selection?

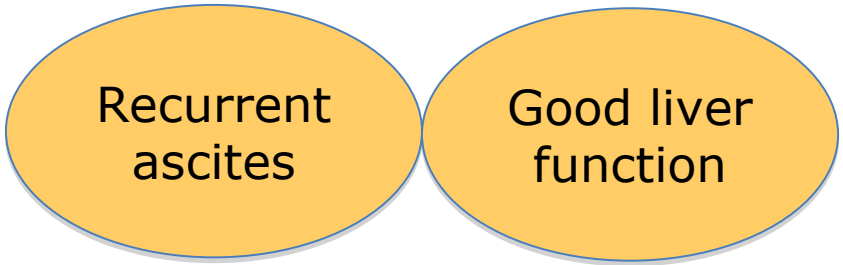


185 pts included
107 for refractory ascites

Kaplan–Meier analysis comparing 1:1 propensity-matched patients with 8-mm or 10-mm stent diameters adjusted for age, MELD, and bilirubin concentration.

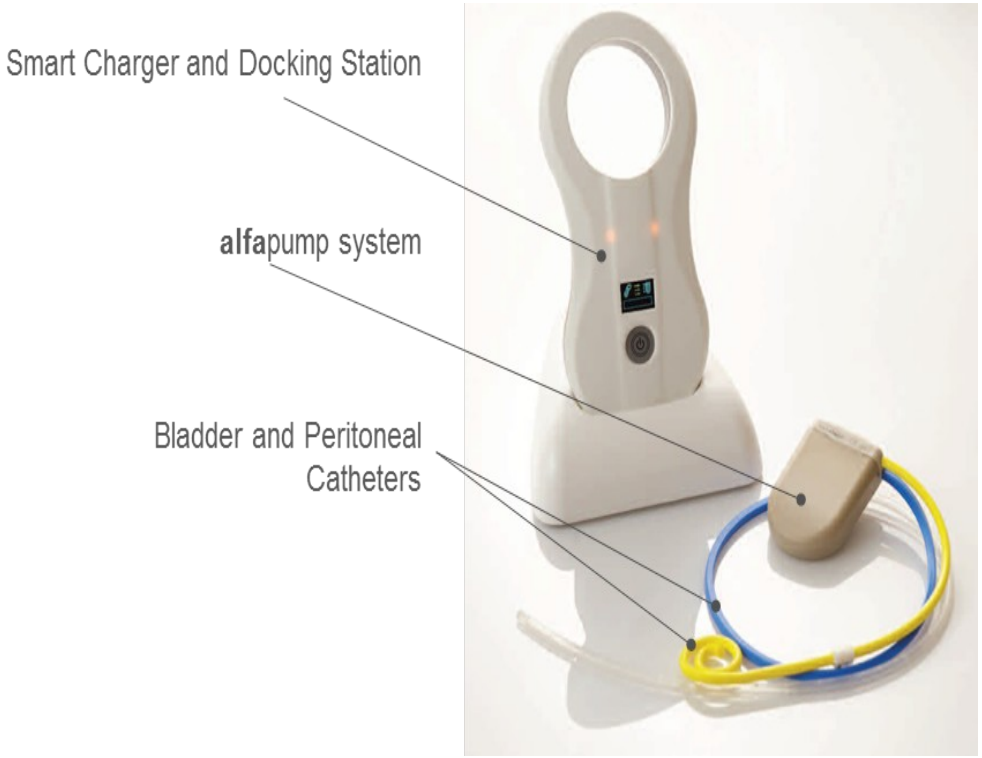
Trebicka et al. Clinical Gastro 2019

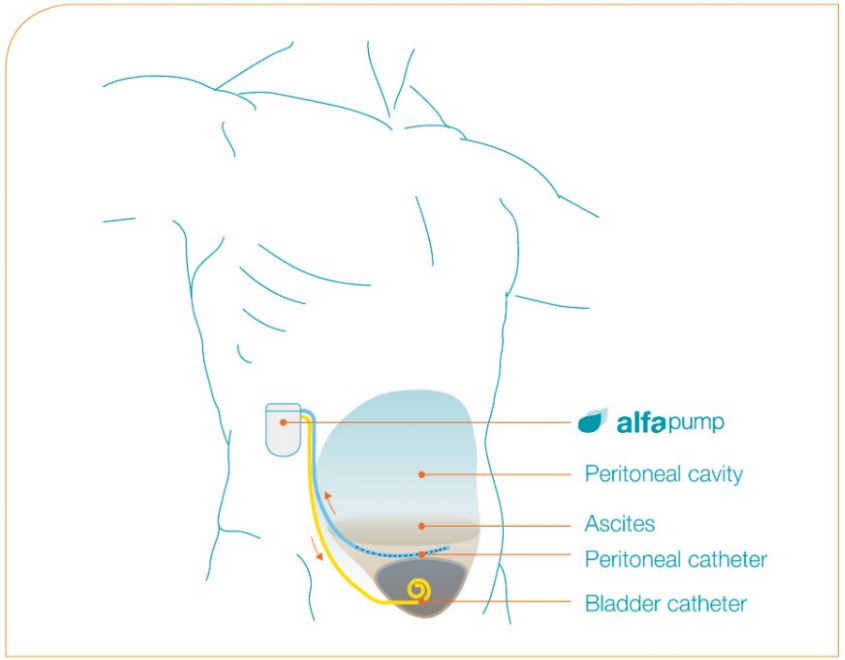
TIPS & ascites: how to select the patients ?



- Careful selection
  - NOT too late
  - BiliT < 50 µmol/L
  - Plt > 75G/L
  - Child-Pugh score <13, MELD score<19
  - No chronic HE, < 2 previous episodes of HE
  - No infection (delay)
  - BNP< 40 Nt-pro BNP<125 and normal echocardiography
  - No pulmonary hypertension

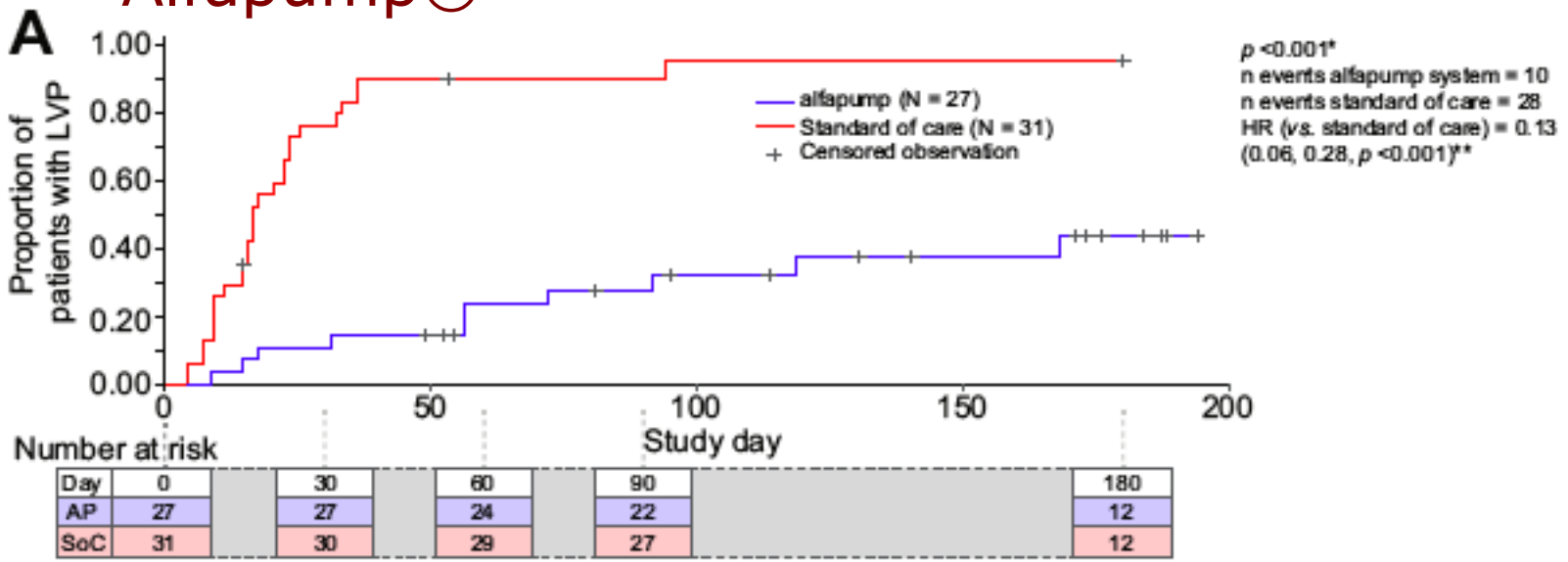
Refractory ascites: Alfapump®

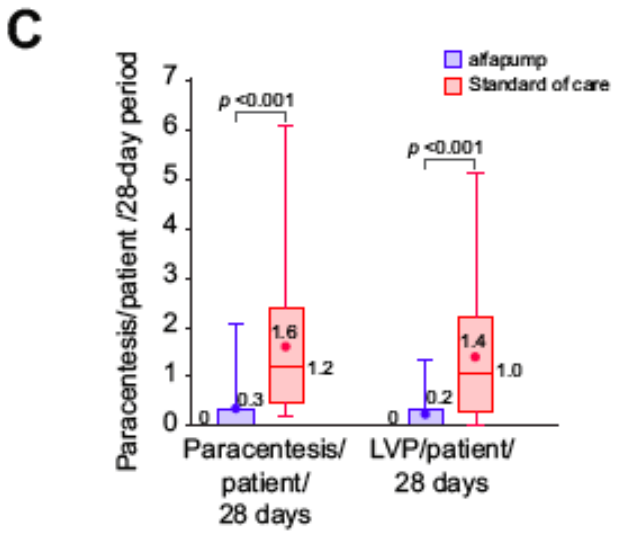




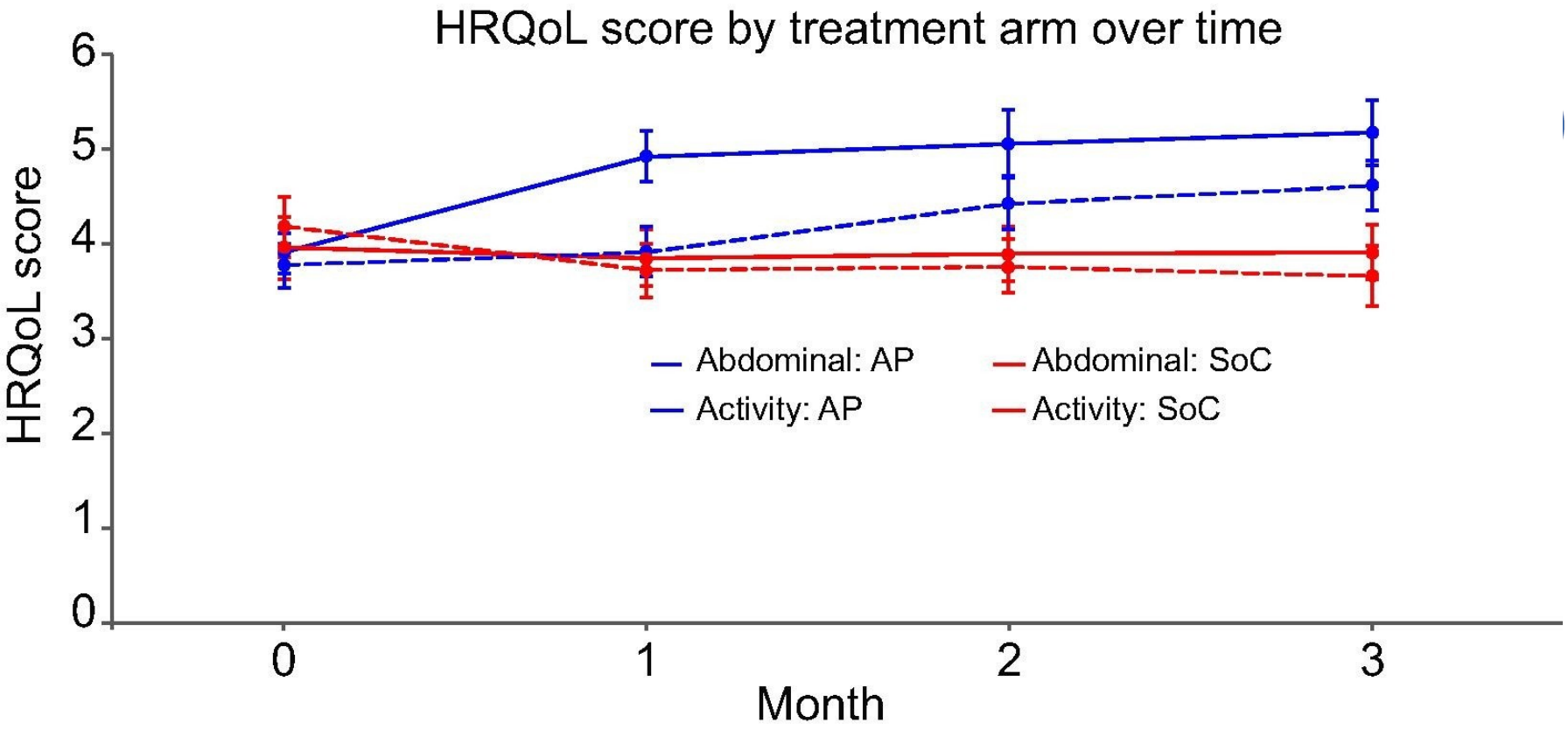
- Fully implantable, programmable and rechargeable pump system that diverts ascitic fluid from the peritoneal cavity to the urinary bladder
- Antibioprophylaxis
- No recommendation regarding albumin infusion

Refractory ascites:
Alfapump®





Bureau C et al., J Hepatol 2017



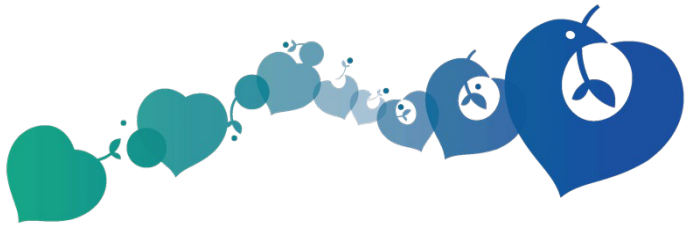
Number of patients completing survey for abdominal and activity

Month	0	1	2	3
AP	27	26	22	22
SoC	31	29	29	27

- Improvement of quality of life and nutritional status
- Learning curve+++

Bureau C et al., J Hepatol 2017

Ascites
Conclusions



- Ascites: poor prognosis; diuretics, sodium restriction and treatment of underlying disease
- TIPS should be discussed « early » in the course of ascites
- Discussion TIPS/LT at the same time
- Alfapump® may improve quality of life
  - Renal function
  - HE?
  - Costs

Hôpitaux Universitaires
Pitié Salpêtrière - Charles Foix

Merci

BLIPS