Long term follow-up after treatment with Ombitasvir/Paritaprevir/ritonavir±Dasabuvir±Ribavirin in the AMBER – real world experience study

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HEP DART
Kona, Hawaii, 3-7 December 2017

Disclosures

Advisor and/or speaker for:

AbbVie, Bristol-MyersSquibb, Gilead, Janssen, Merck, Novartis, Roche

16 centers participating in the AMBER study (2014-2015)

Predictors of rapid virologic response during Ombitasvir/Paritaprevir/Ritonavir ±Dasabuvir ±Ribavirin treatment of genotype 1 and 4 real life AM

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HEP DART
Maui, 6-10 December 2015

Predictors of rapid virologic response during Ombitasvir/Paritaprevir/Ritonavir ±Dasabuvir ±Ribavirin treatment of genotype 1 and 4 HCV infected patients in the real life AMBER study.

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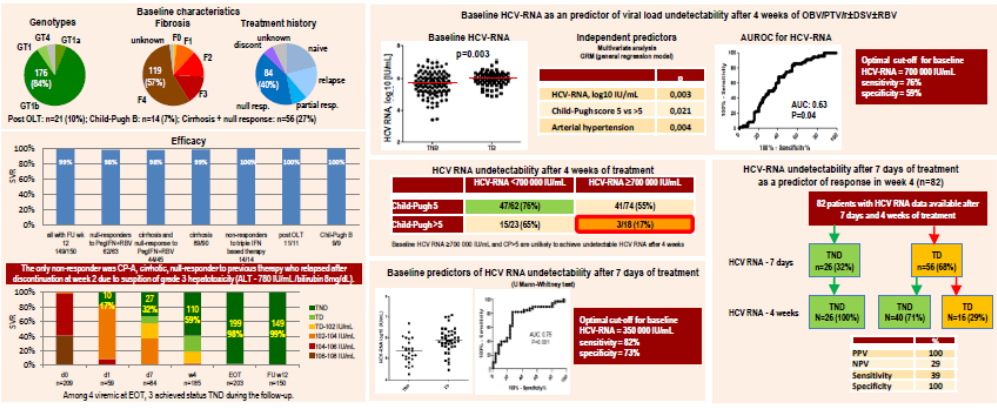
N=209

BACKGROUND:
Ombitasvir/Paritaprevir/Ritonavir±Dasabuvir±Ribavirin (OBV/PTV/r±DSV ±RBV) was demonstrated highly effective in clinical trials. Maintained 4 weeks of HCV RNA undetectability seems to be sufficient to clear the virus. The aim of this multicenter, real-life, investigator initiated study was to confirm efficacy of this regimen in real-life settings and demonstrate possible baseline predictors of rapid virologic response (RVR) which could provide rationale for possible shortening of treatment to 8 weeks.

METHODS:
OBV/PTV/r ±DSV ±RBV was administered to 209 patients infected in 96% with genotype 1 (mostly 1b) or 4, including 119 cirrhotics, mostly treatment experienced (72%); 40% were null-responders to IFN containing regimens and 16 failed previous triple therapy. Treatment was scheduled for 12 weeks (84%) or 24 weeks and in 75% RBV was added. Week 4 data were available in 185 patients, which were included into this analysis.

CONCLUSIONS
1. In this real-life study carried-out mostly in treatment experienced patients infected with genotype 1b we demonstrated almost 100% efficacy even in cirrhotics, OLT and Child-Pugh patients, null-responders to PegIFN+RBV and non-responders to triple therapy.
2. Shortening of treatment with OBV/PTV/r ±DSV ±RBV to 8 weeks can be considered in patients with Child-Pugh score of 5 and baseline viral load below 700 000 IU/mL, with undetectable HCV RNA after 4 weeks of treatment.
3. This hypothesis need to be confirmed in prospective study.

RESULTS
HCV RNA was undetectable in 9 (15%) and 26 (32%) patients after 1 and 7 treatment days respectively. HCV RNA was undetectable in 102 (60%) at week 4 and in 144 (98%) at EOT. Among 65 patients with available data, SVR12 was achieved in 63 (97%). The first non-responder was GT1b infected, cirrhotic, null-responder to IFN-based dual therapy, discontinued after 2 weeks of treatment. The second was GT1b infected, non-cirrhotic, relapser to IFN-based therapy, with detectable but unquantifiable viral load at 12 weeks follow-up. Univariate analysis demonstrated that RVR was significantly associated with baseline HCV RNA (p<0.001), cirrhosis (p=0.036), Child-Pugh score (p=0.014) and platelet count (p=0.03). In multivariate analysis low baseline HCV RNA, Child-Pugh score and MELD were independently associated with HCV RNA undetectability at week 4 of treatment. Day 7 undetectable HCV RNA demonstrated 100% positive predictive value for RVR.



AP&T Alimentary Pharmacology and Therapeutics

Aliment Pharmacol Ther 2016; 44: 946–956

Real-world effectiveness and safety of ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin in hepatitis C: AMBER study

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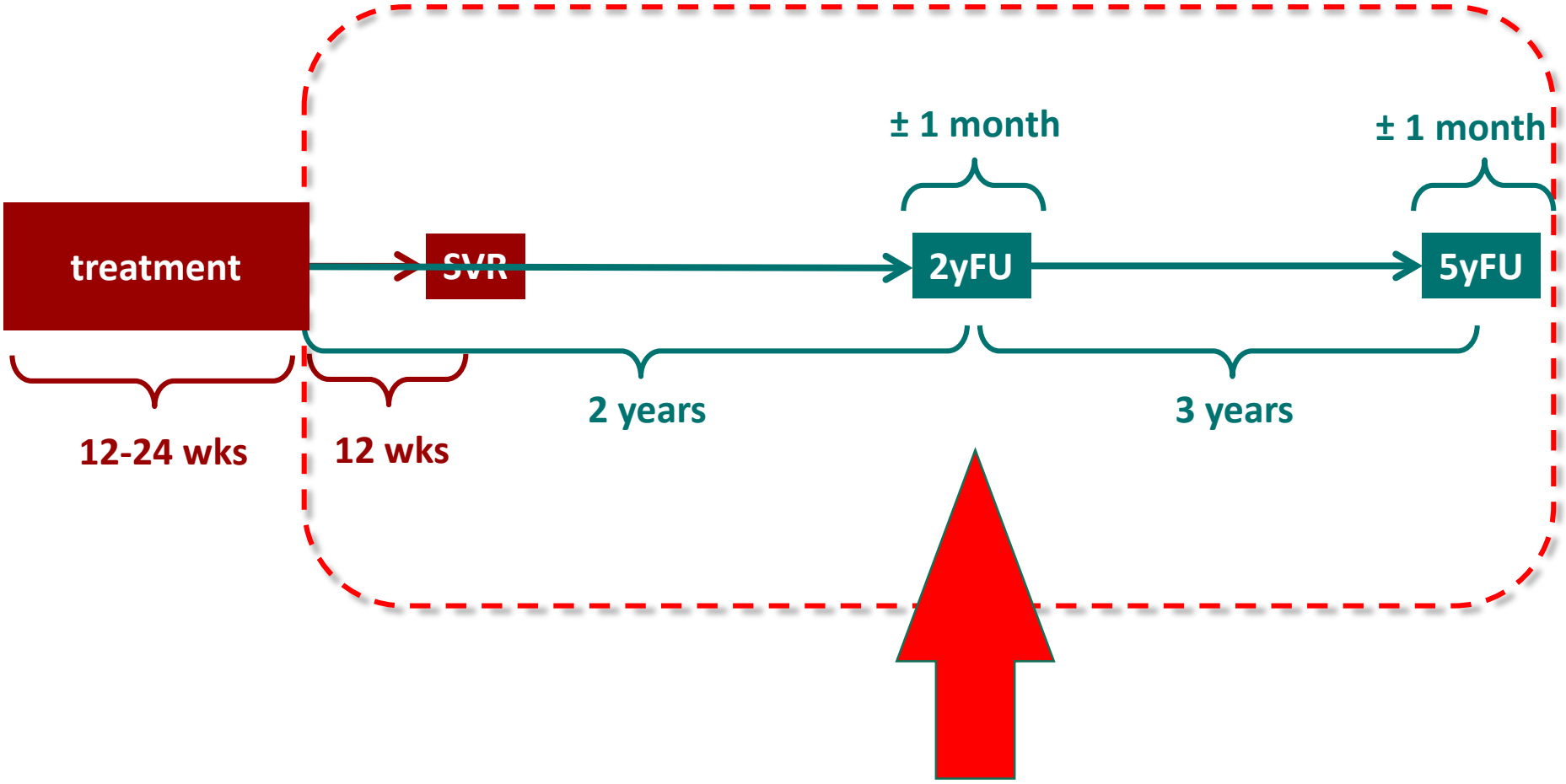
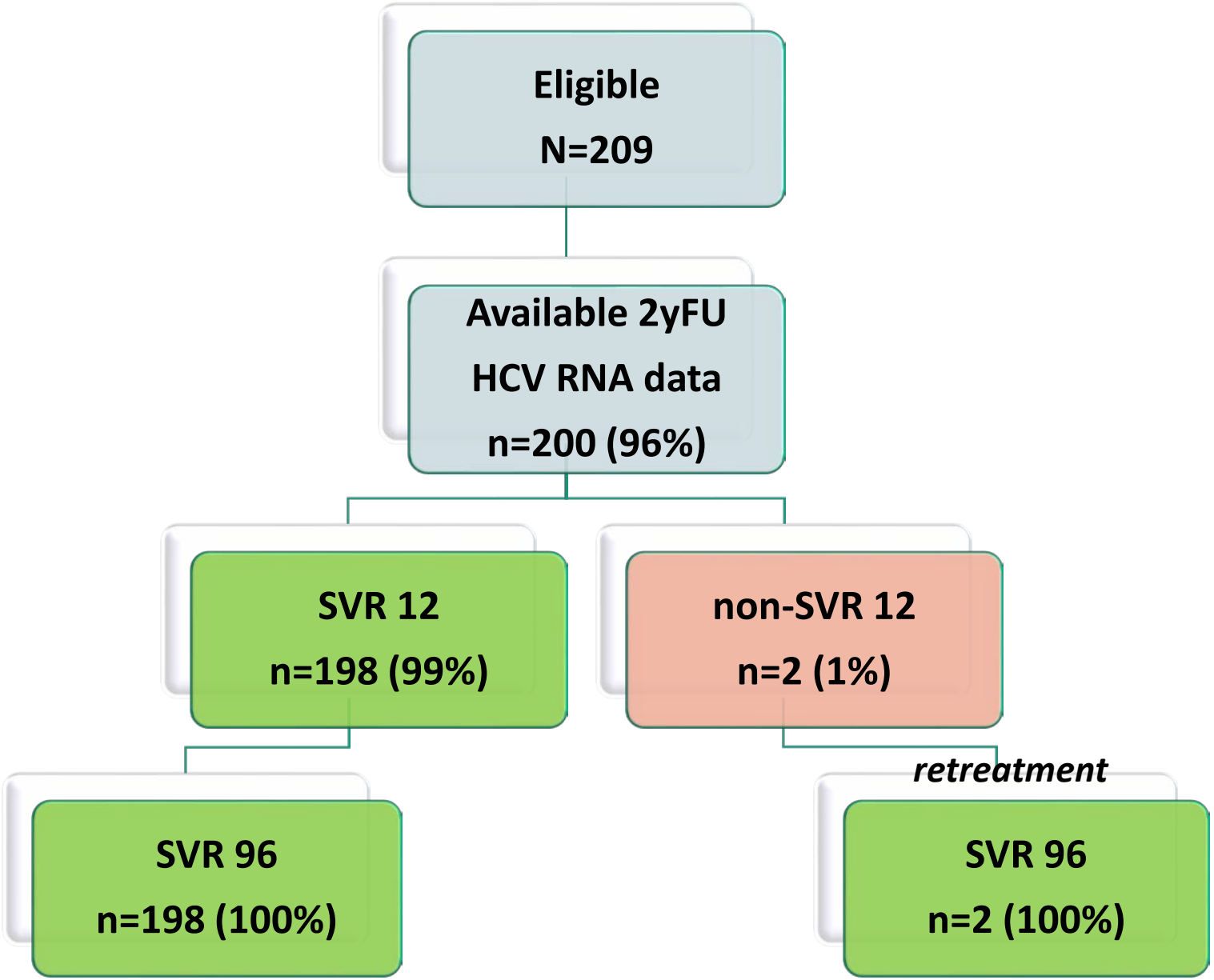
Design of the study

treatment and regular follow-up
AMBER study, 2014-2015

long-term follow-up



2-years virologic response follow-up



Baseline characteristics of patients included in long term follow-up

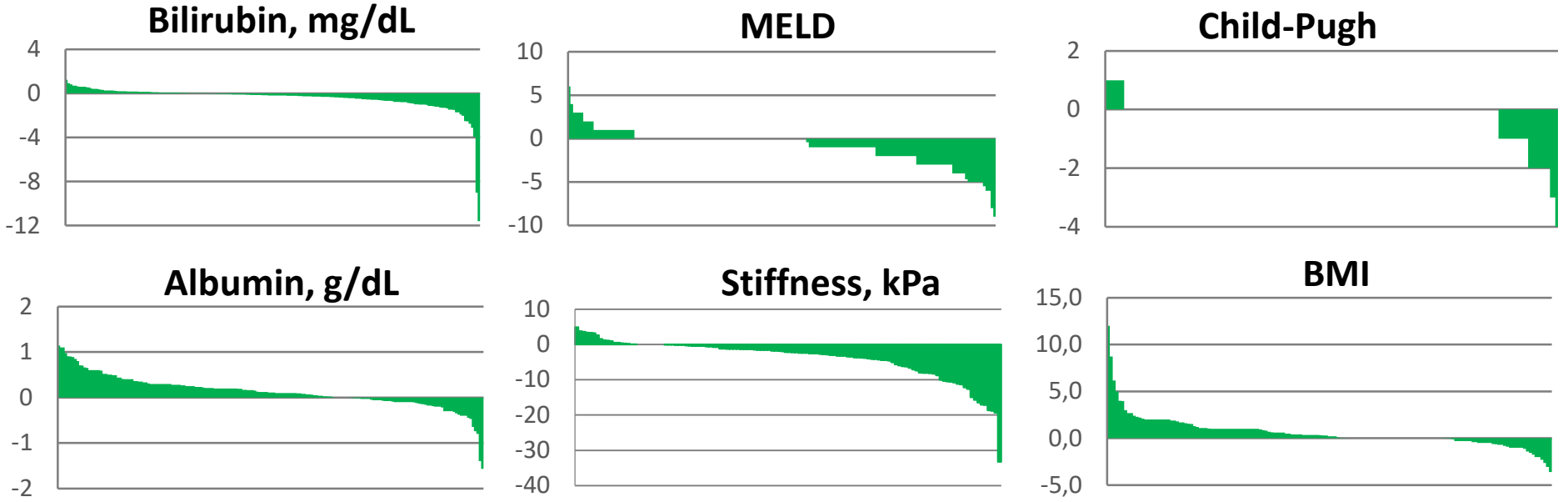
	n = 202
Age at baseline (yrs), mean ±SD	54 ±12
Males, n (%)	112 (55)
BMI (kg/m2), mean ± SD	26 ±4
HCV genotype, n (%)	
1	6 (3)
1a	11 (5)
1b	178 (89)
4	7 (3)
History of previous therapy, n(%)	
treatment naive	49 (24)
relapsers	37 (18)
partial and null responders	101 (50)
unknown or discontinued	15 (8)
Fibrosis, n (%)	
F0-1	21 (12)
F2-3	49 (27)
F4	110 (61)

Events observed during 2 years follow-up

Event	n = 202
Deaths (HCC, CCC, colorectal cancer, post-OLTx complications)	4 (2%)
Ascites	10 (6%)
Encephalopathy	4 (2%)
Variceal bleadinng	1 (0.5%)
Hepatocellular carcinoma	7 (3%)
Liver transplantation	3 (2%)
Severe bacterial infection (sepsis, SBP)	5 (3%)
Patients needed admission to hospitals	33 (18%)
Renal insufficiency (including hepato-renal syndr.)	2 (1%)

Liver function measures at EOT and 2yFU

In patients with available paired data



Mean values

	n	EOT mean	EOT SD	2yFU mean	2yFU SD	p
stiffness, kPa	120	16.6	11.8	12.7	9.1	0.005
bilirubin, mg/dL	124	1.38	1.41	0.93	0.56	0.000
albumin, g/dL	180	4.20	0.52	4.32	0.42	0.014
Child-Pugh	167	5.36	0.86	5.18	0.48	0.013
MELD	167	8.70	2.74	7.82	2.05	0.001
BMI	155	26.3	4.3	26.9	4.6	0.206

Mean changes between EOT and 2yFU values in cirrhotics and non-cirrhotics

	cirrhotics		non-cirrhotics		p
	mean	SD	mean	SD	
stiffness, kPa	-5.8	6.5	-0.9	1.8	0.000
bilirubin, mg/dL	-0.63	1.55	-0.15	0.50	0.012
albumin, g/dL	0.18	0.38	0.06	0.34	0.030
INR	-0.06	0.13	-0.02	0.08	0.031
Child-Pugh	-0.26	0.81	-0.03	0.31	0.039
MELD	-0.93	2.25	-0.75	1.68	0.591
BMI	0.57	1.83	0.59	1.55	0.953

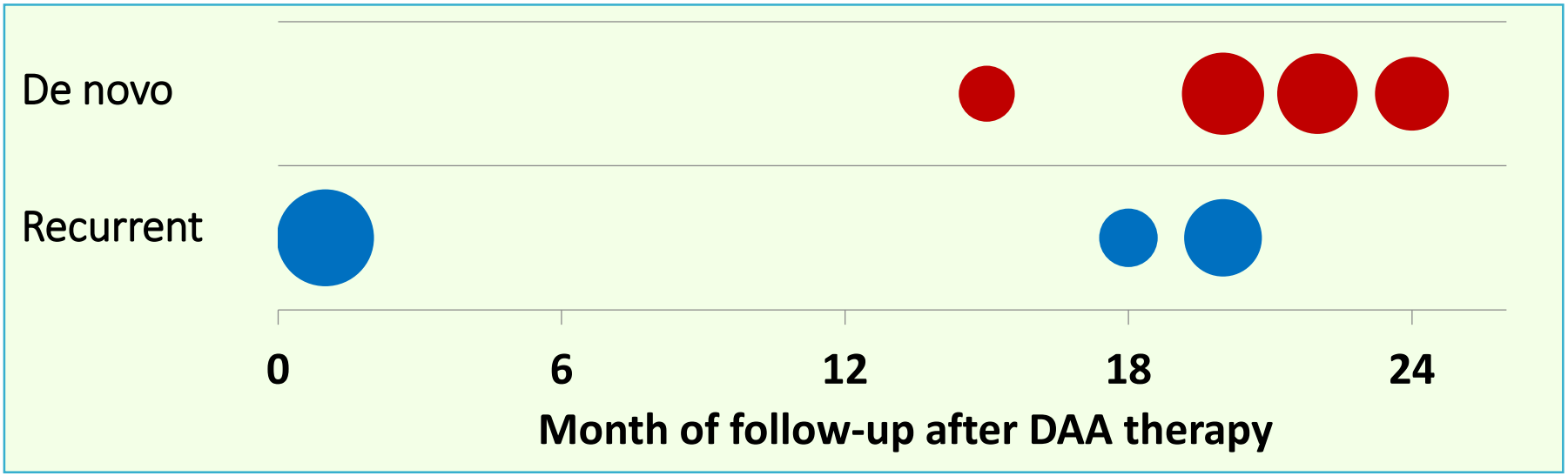
negative mean value - decrease, positive mean value - increase

HCC cases within 2 years follow-up

#	Gender	age	Fibrosis	GT	Tx history	No of lesions	De novo / Recurrence	Month of dgn after DAA	max size mm	treatment	Died in 2yFU?
1	F	68	4	1b	REL	2	de novo	20	47	RFA	NO
2	M	60	4	1b	NUL	2	recurrence	18	24	RFA	NO
3	M	53	4	1b	PAR	3	de novo	22	45	OLTx	NO
4	M	59	4	1b	NAI	1	de novo	24	38	Resection	NO
5	F	61	4	1b	NAI	2	recurrence	20	42	RFA	NO
6	M	59	3	1b	NUL	1	de novo	15	22	Sorafenib	NO
7	M	69	1	1b	NUL	1	recurrence	1	66	Sorafenib	YES

Recurrent and de novo HCC cases

size and time of development



Conclusions

1. **Two years follow-up confirmed durability of virologic response after treatment with Ombitasvir/Paritaprevir/ritonavir ±Dasabuvir ±Ribavirin.**

2. **Significant improvement of major measures of hepatic function and reduction of hepatic stiffness was observed during 2yFU, particularly in cirrhotics.**

3. **Unfortunately in 11% patients even successful therapy did not prevent hepatic decompensation, HCC development or death.**

4. **De novo HCC developed at least 15 months after therapy.**