

Terapia ed Eliminazione di HCV

Milano 25 Settembre 2023

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Financial Disclosures

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AbbVie, Gilead Sciences

Advisory committees:

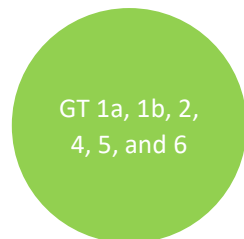
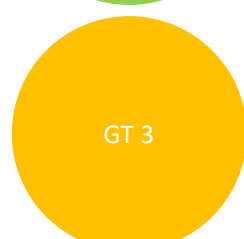
Merck, Gilead Sciences, AbbVie, Intercept,
Mylan, Sobi and Alfasigma

Speaking and teaching:

Gilead Sciences, Abbvie, Alfasigma, Sobi
and Takeda

EASL HCV Treatment Algorithm for TN/TE Patients Without Cirrhosis or With Compensated Cirrhosis

Treatment recommendations for HCV-mono-infected or HCV/HIV coinfecting adult (aged ≥18 years) and adolescent (aged 12–17 years) patients with chronic HCV without cirrhosis or with CC* including TN and TE†

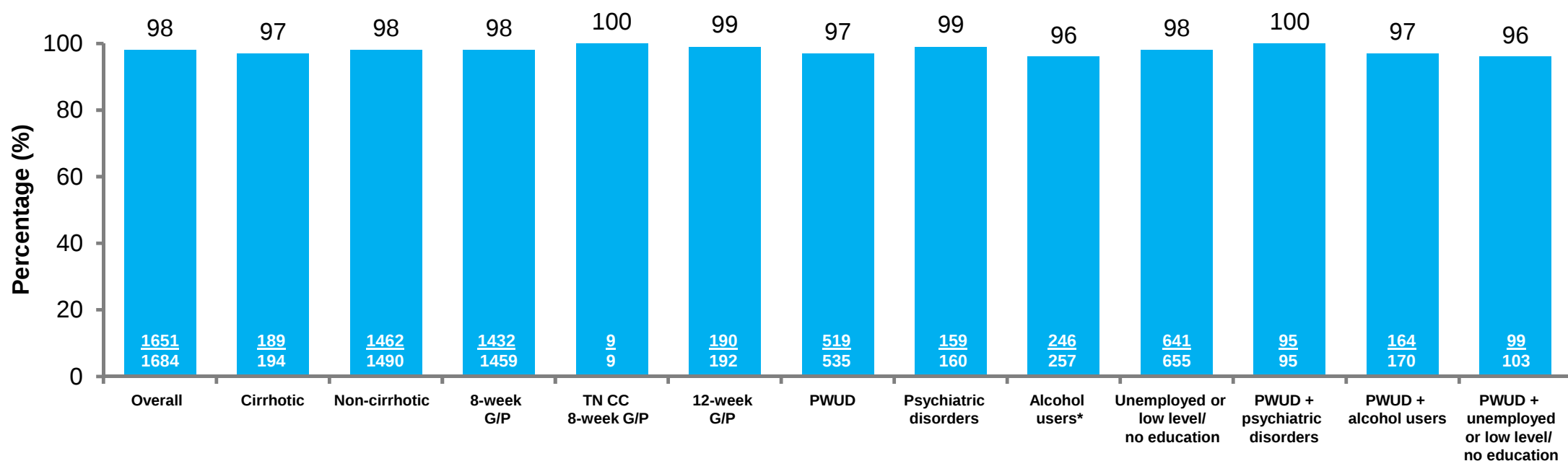
		Treatment-naïve		Treatment experienced	
		G/P	SOF/VEL	G/P	SOF/VEL
 GT 1a, 1b, 2, 4, 5, and 6	Without cirrhosis	8 weeks	12 weeks	8 weeks	12 weeks
	With compensated cirrhotic	8 weeks	12 weeks	12 weeks	12 weeks
 GT 3	Without cirrhosis	8 weeks	12 weeks	12 weeks	12 weeks
	With compensated cirrhotic	8–12 weeks‡	12 weeks with weight-based RBV§	16 weeks	12 weeks with weight-based RBV§

*Child-Pugh A; †TE to pegIFN + RBV, pegIFN-α + RBV + SOF or SOF + RBV; ‡In TN patients infected with GT3 with CC, treatment with G/P can be shortened to 8 weeks, but more data are needed to consolidate this recommendation; § If resistance testing is formed, only patients with the NS5A Y93H RAS at baseline should be treated with SOF/VEL + RBV or with SOF/VEL/VOX, whereas patients without the Y93H RAS should be treated with SOF/VEL alone. CC, compensated cirrhosis; EASL, European Association for the Study of the Liver; G/P, glecaprevir/pibrentasvir; GT, genotype; pegIFN, pegylated interferon; RAS, resistance-associated substitution; RBV, ribavirin; SOF, sofosbuvir; TE, treatment experienced; TN, treatment-naïve; VEL, velpatasvir.

1. EASL. *J Hepatol* 2020 Nov;73(5):1170-1218. doi: 10.1016/j.jhep.2020.08.018. Epub 2020 Sep 15. 2. Maviret (GLE/PIB) US Prescribing Information.

Optimal Efficacy of DAAs in Real-World Historically Underserved Patients

Pooled analysis of the effectiveness of G/P in patients with HCV GT1–6 without cirrhosis or with compensated cirrhosis from underserved patient populations in a PMOS across 9 countries between Nov 2017 and Jan 2020 (N = 2036)

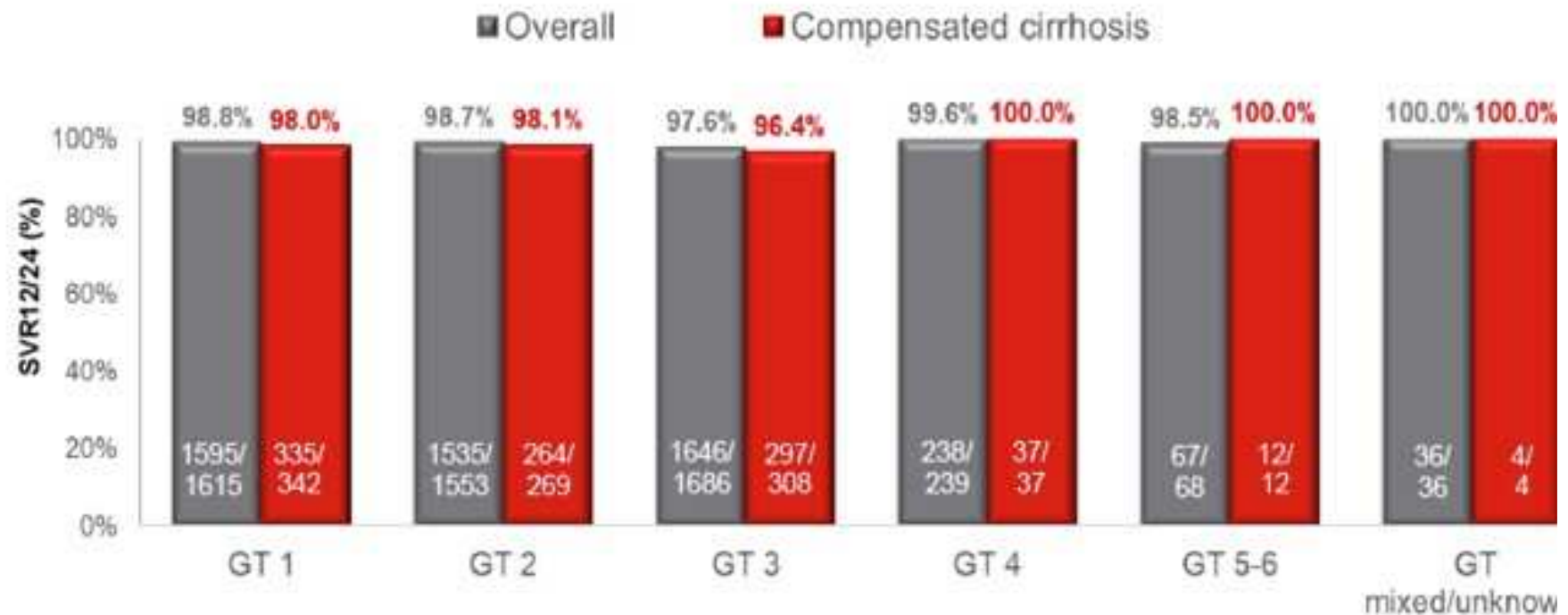


* Patients who consumed more than 2 drinks/day.

CC, compensated cirrhosis; PMOS, post-marketing observational study; PWUD, people who use drugs; TN, treatment naive.

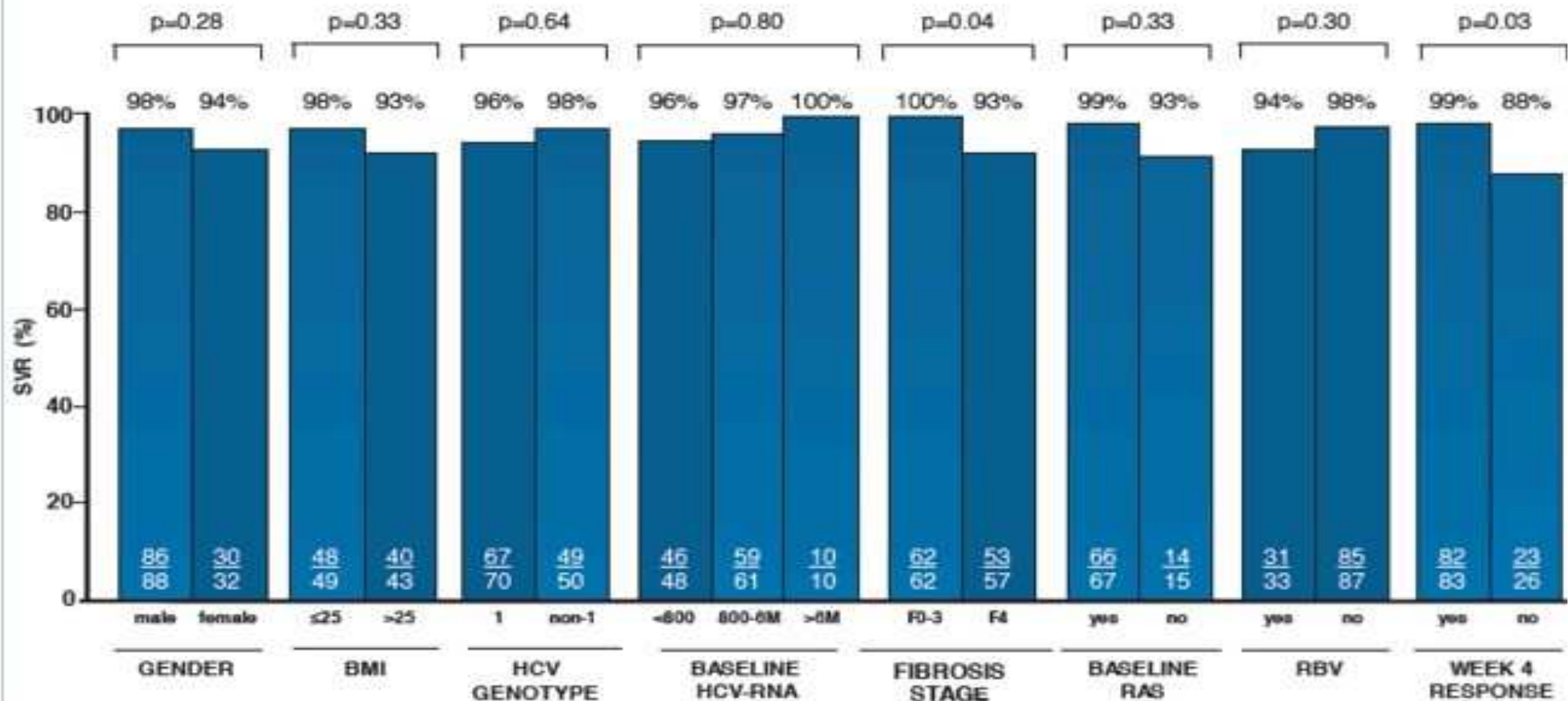
Real World Studies Confirm the Efficacy of Sofosbuvir/Velpatasvir

SVR12/24 results by **genotype and presence of cirrhosis**
(per protocol)

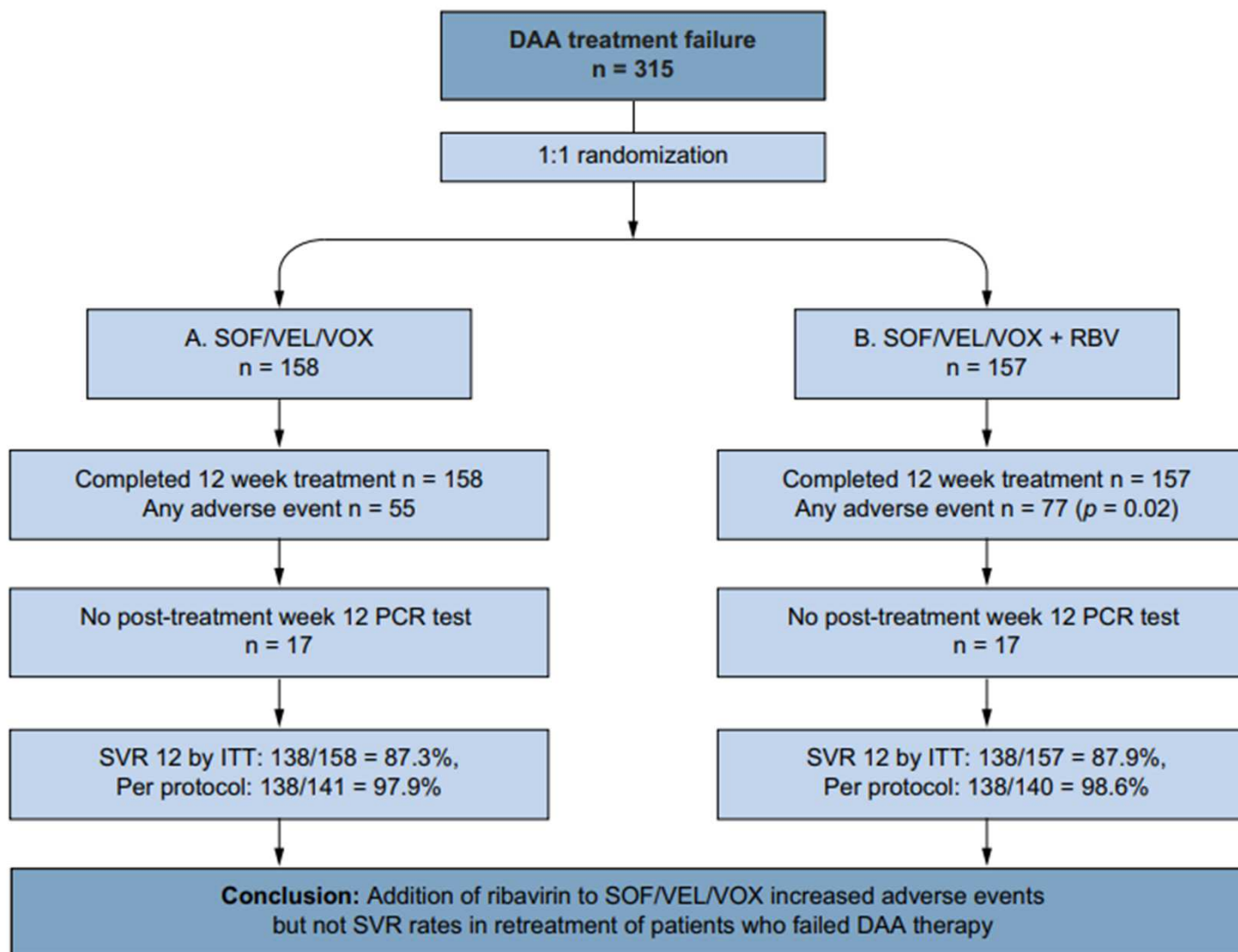


Real World Studies Confirm the Efficacy of Sofosbuvir/Velpatasvir/Voxilaprevir

Cirrhosis ($p=0.03$) and detectable HCV-RNA at treatment week 4 ($p=0.03$) were associated with treatment failure.



Sofosbuvir/Velpatasvir/Voxilaprevir is Highly Effective Without Rbv In DAA Failures

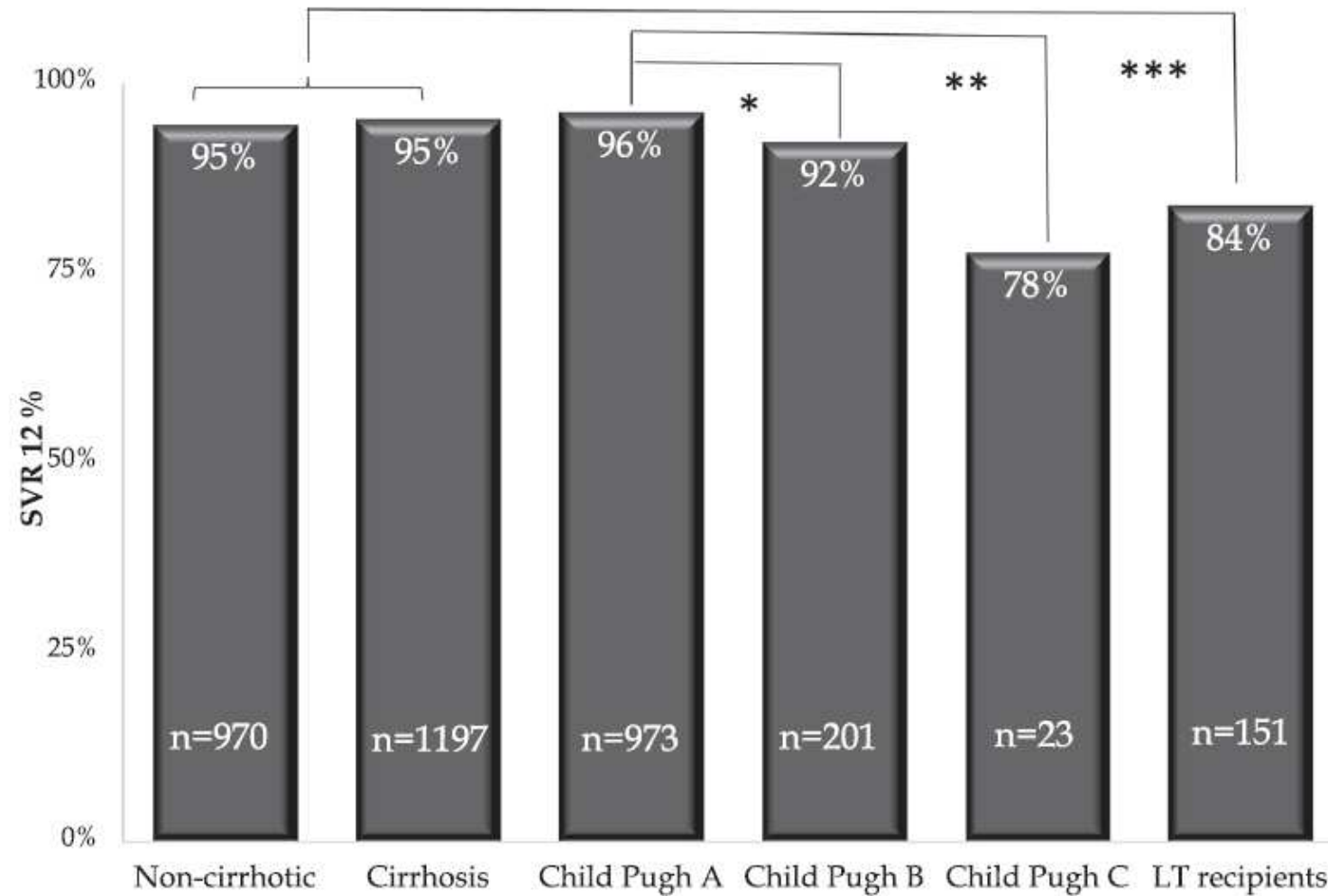


Do We Still Have Any Open Question?

Are there any cases when treatment efficacy is impaired?

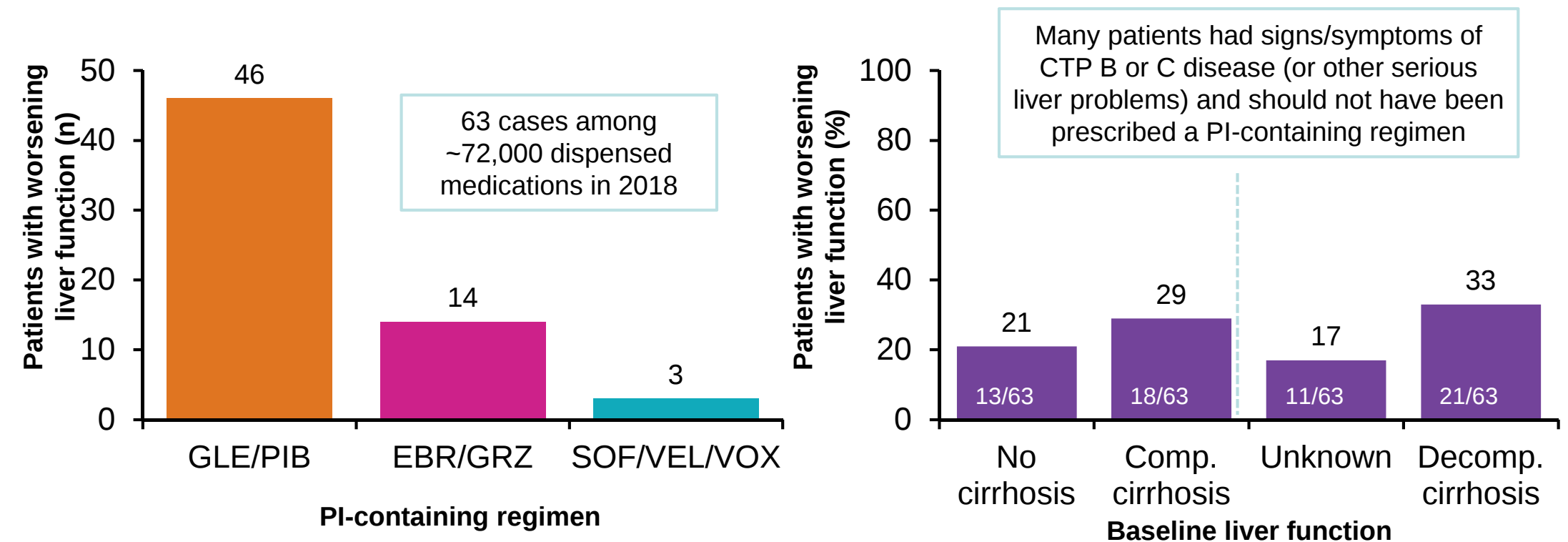
Are there any cases when treatment is unsafe or harmful?

Decompensated Cirrhosis is Associated with Reduced SVR Rates



Protease inhibitors are contraindicated in CTP B & C

Liver decompensation associated with DAA use in FAERS database or literature to 8 January 2019



Disease Severity Impacts the PK of PIs

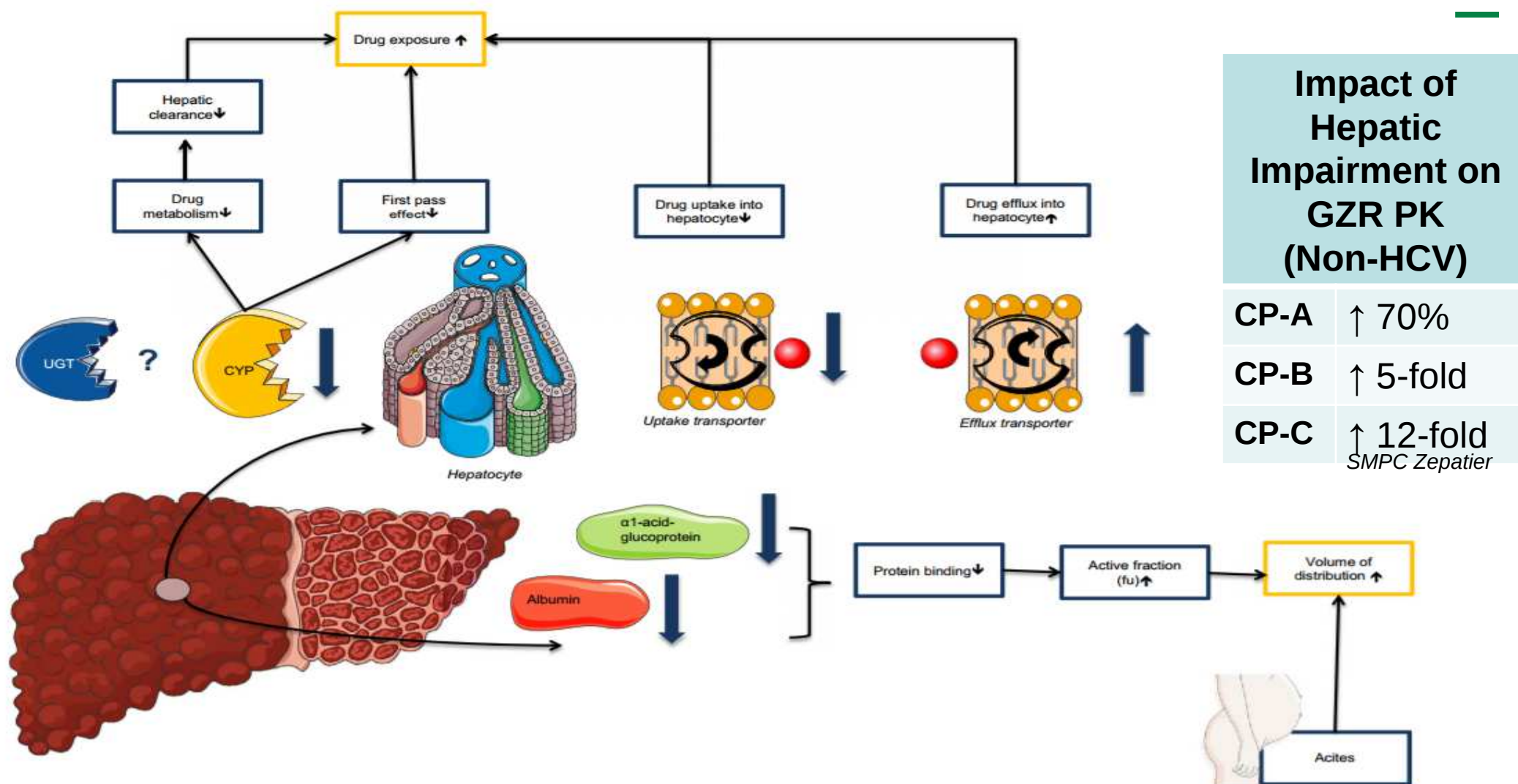


Fig. 2 Overview of the pathophysiological changes in patients with liver cirrhosis that influence drug metabolism and therefore the pharmacokinetics of drugs. *CYP* cytochrome P450, *UGT* uridine diphosphate-glucuronosyltransferase, ↓ indicates decrease, ↑ indicates increase

ORIGINAL ARTICLE

Real-world effectiveness and safety of direct-acting antivirals in patients with cirrhosis and history of hepatic decompensation: Epi-Ter2 Study

Aleksandra Berkan-Kawir

[Zdunek](#) Krzysztof Tomas

Iwona Buczyńska, Monika

Jakub Klapaczynski, Włod

Aleksander Garlicki, Marek

Białkowska-Warzecha, Ol

... See fewer authors ^

First published: 02 March

Liver
INTERNATIONAL

RESEARCH LETTER

Sofosbuvir/velpatasvir/voxilaprevir for hepatitis C virus retreatment in decompensated cirrhosis

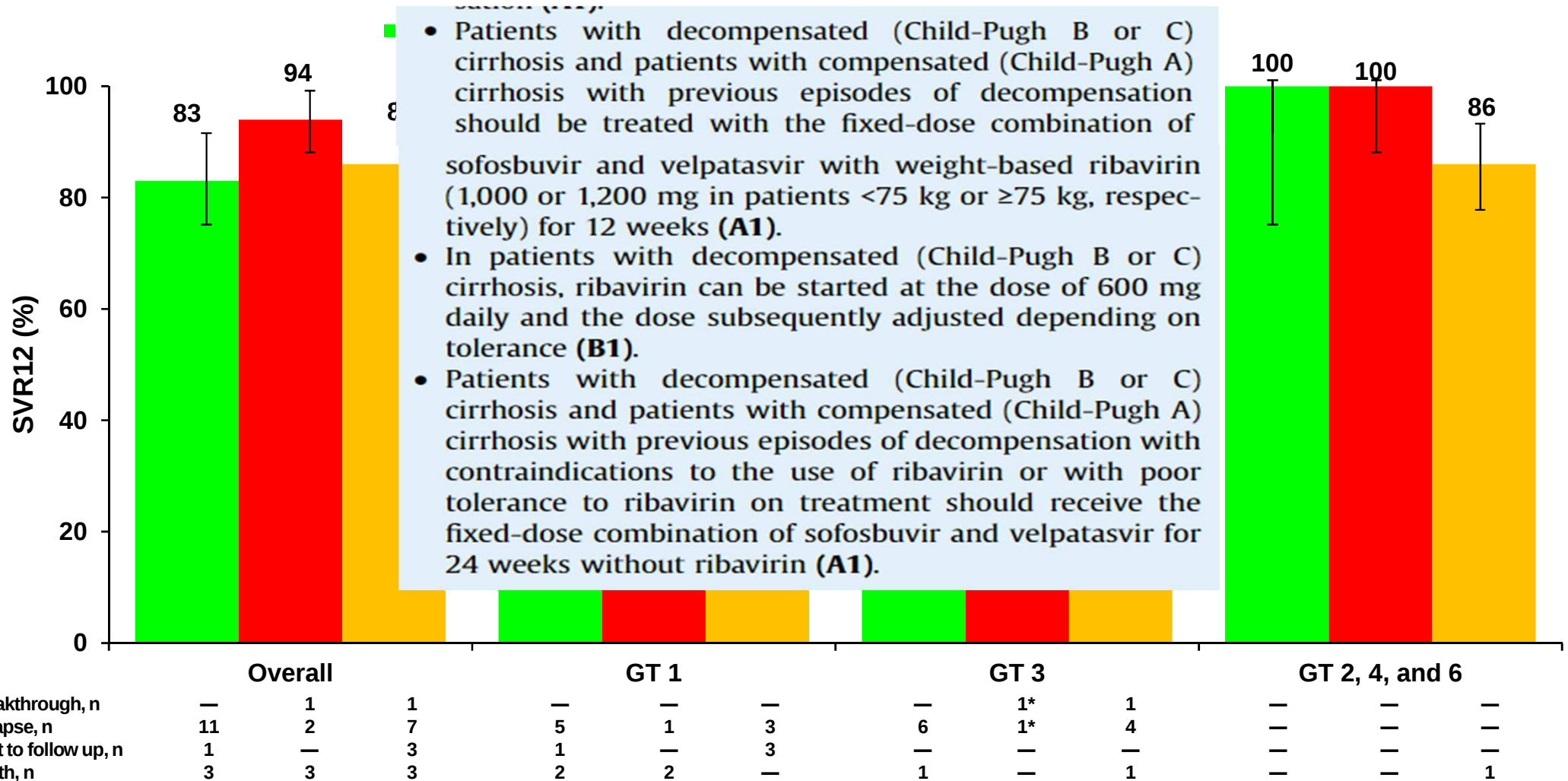
Sonalie Patel [X](#), Michelle T. Martin, Steven L. Flamm

First published: 30 September 2021 | <https://doi.org/10.1111/liv.15075>

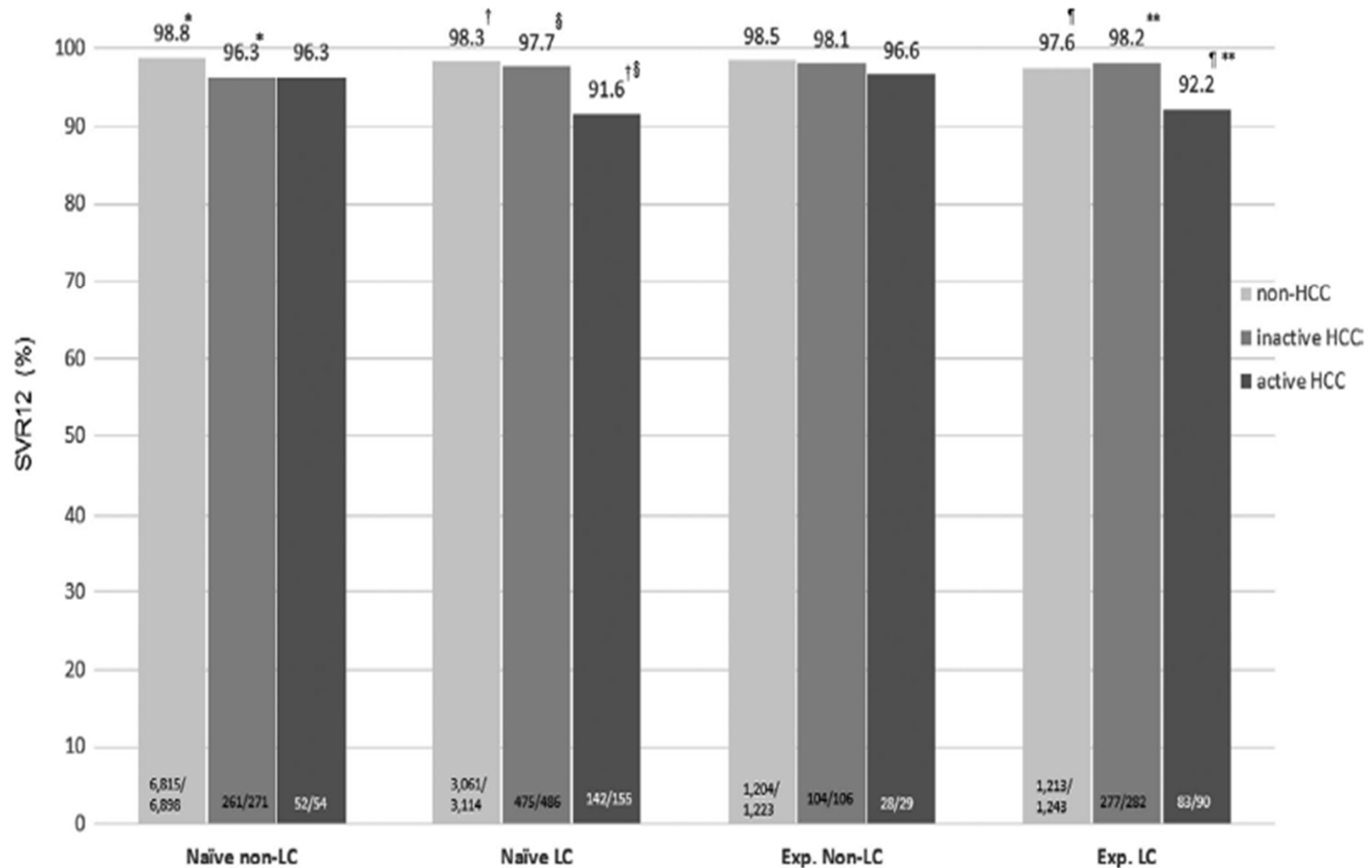
TABLE 1 Patient characteristics

Patient	1	2	3	4	5	6
Age (years)	82	63	57	56	62	52
Gender	Male	Male	Female	Male	Female	Male
BMI (kg/m ²)	30.6	22.5	29.2	37.6	29.3	34.3
Genotype/subtype	1b	3a	1a	1a	1a	3a
CTP Class (points)	B (8)	B (8)	B (7)	B (8)	B (9)	C (10)
Week 4						
HCV RNA (IU/ml)	Not detected	Not detected	126	Not detected	Not detected	Not detected
CTP Class (points)	B (8)	B (7)	A (6)	B (7)	B (8)	B (7)
MELD-Na	15	14	11	10	15	16
Week 8						
HCV RNA (IU/ml)	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected
CTP class (points)	B (8)	B (7)	A (6)	B (7)	B (7)	B (7)
MELD-Na	16	17	11	13	15	13
Week 12 (end of treatment)						
HCV RNA (IU/ml)	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected
CTP class (points)	B (8)	B (7)	A (6)	B (7)	B (7)	B (7)
MELD-Na	17	13	12	12	14	17
Week 16 (end of treatment)						
HCV RNA (IU/ml)	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected
CTP class (points)	B (7)	B (7)	A (5)	B (7)	B (7)	B (9)
MELD-Na	12	11	9	11	14	14

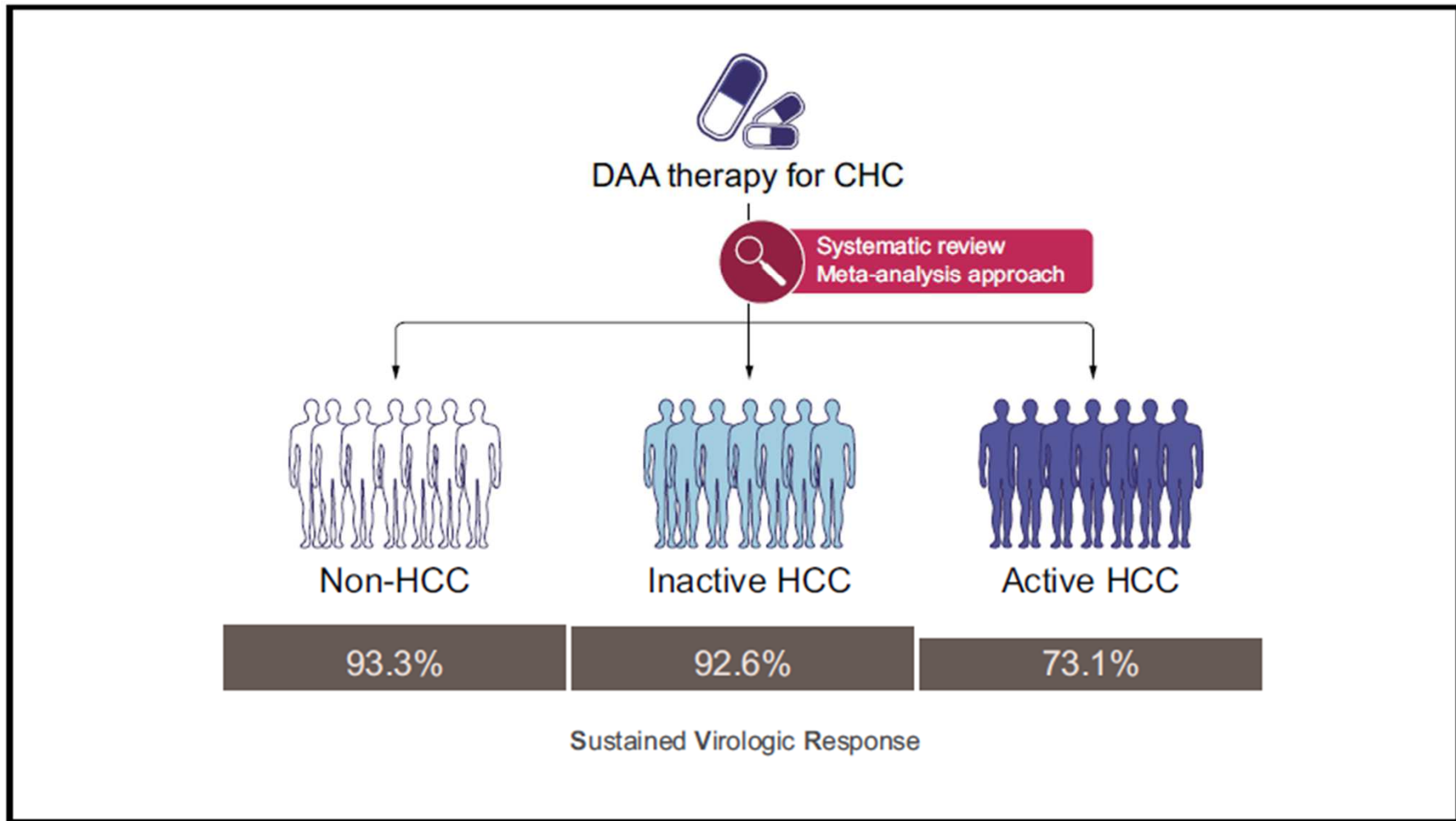
ASTRAL-4: SOF/VEL ± RBV in HCV Patients with Decompensated Liver Disease



HCC is Associated with Reduced SVR Rates



HCC is Associated with Reduced SVR Rates



High Rates of HCC Recurrence post DAA Therapy

Research Article

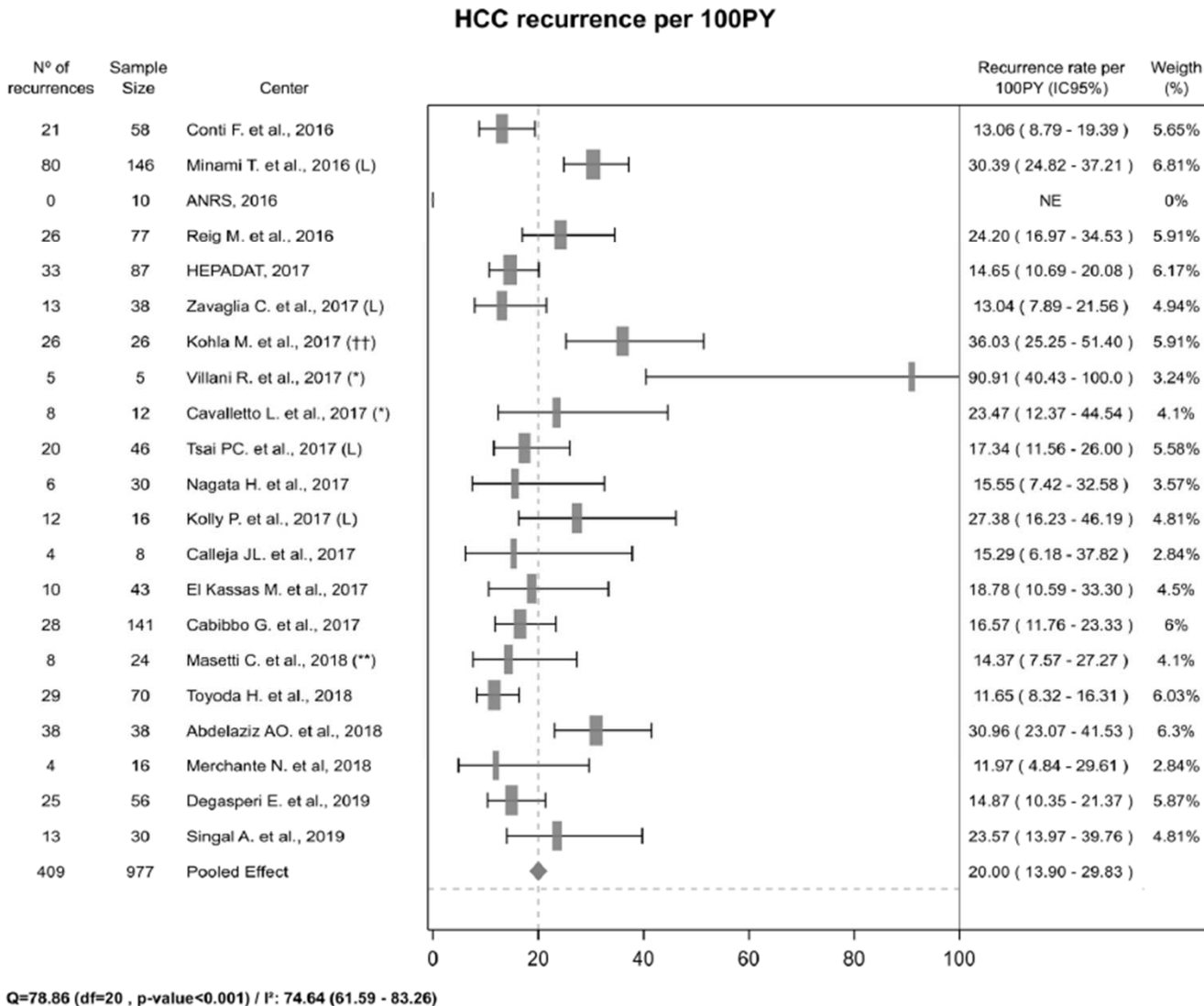


Unexpected high rate of early tumor recurrence in patients with HCV-related HCC undergoing interferon-free therapy[☆]

María Reig^{1,†}, Zoe Mariño^{2,†}, Christie Perelló³, Mercedes Iñarrairaegui⁴, Andrea Ribeiro¹, Sabela Lens², Alba Díaz⁵, Ramón Vilana⁶, Anna Darnell⁶, María Varela⁷, Bruno Sangro⁴, José Luis Calleja³, Xavier Forns^{2,†}, Jordi Bruix^{1,*,‡}

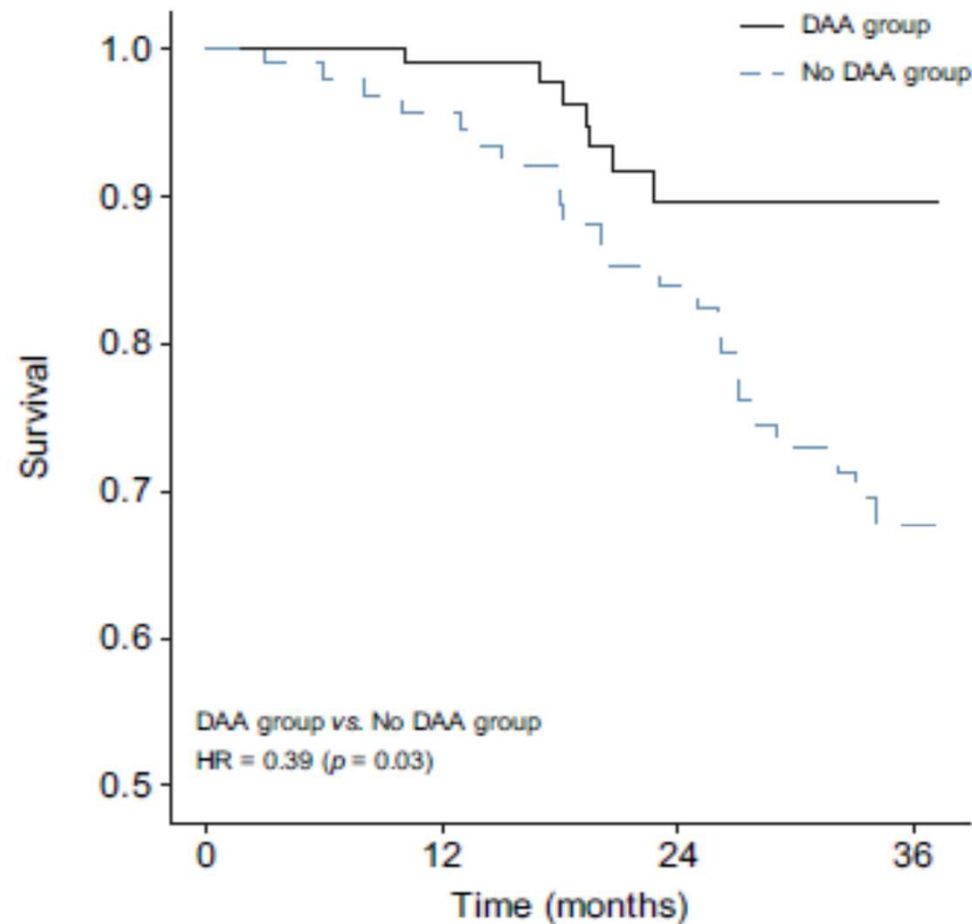
¹Barcelona Clinic Liver Cancer (BCLC) Group, Liver Unit, Hospital Clinic Barcelona, IDIBAPS, University of Barcelona, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Barcelona, Spain; ²Liver Unit, Hospital Clinic, IDIBAPS, University of Barcelona, CIBERehd, Barcelona, Spain; ³Liver Unit, Hospital Universitario Puerta de Hierro, CIBERehd, IDIPHIM, Madrid, Spain; ⁴Unidad de Hepatología, Clínica Universidad de Navarra, IDISNA, CIBERehd, Pamplona, Spain; ⁵Department of Pathology, BCLC Group, Hospital Clínic Barcelona, IDIBAPS, University of Barcelona, Spain; ⁶Department of Radiology, BCLC Group, Hospital Clinic Barcelona, University of Barcelona, Spain; ⁷Liver Unit, Hospital Universitario Central de Asturias, Oviedo, Spain

DAAs do not Increase the Risk of HCC Recurrence



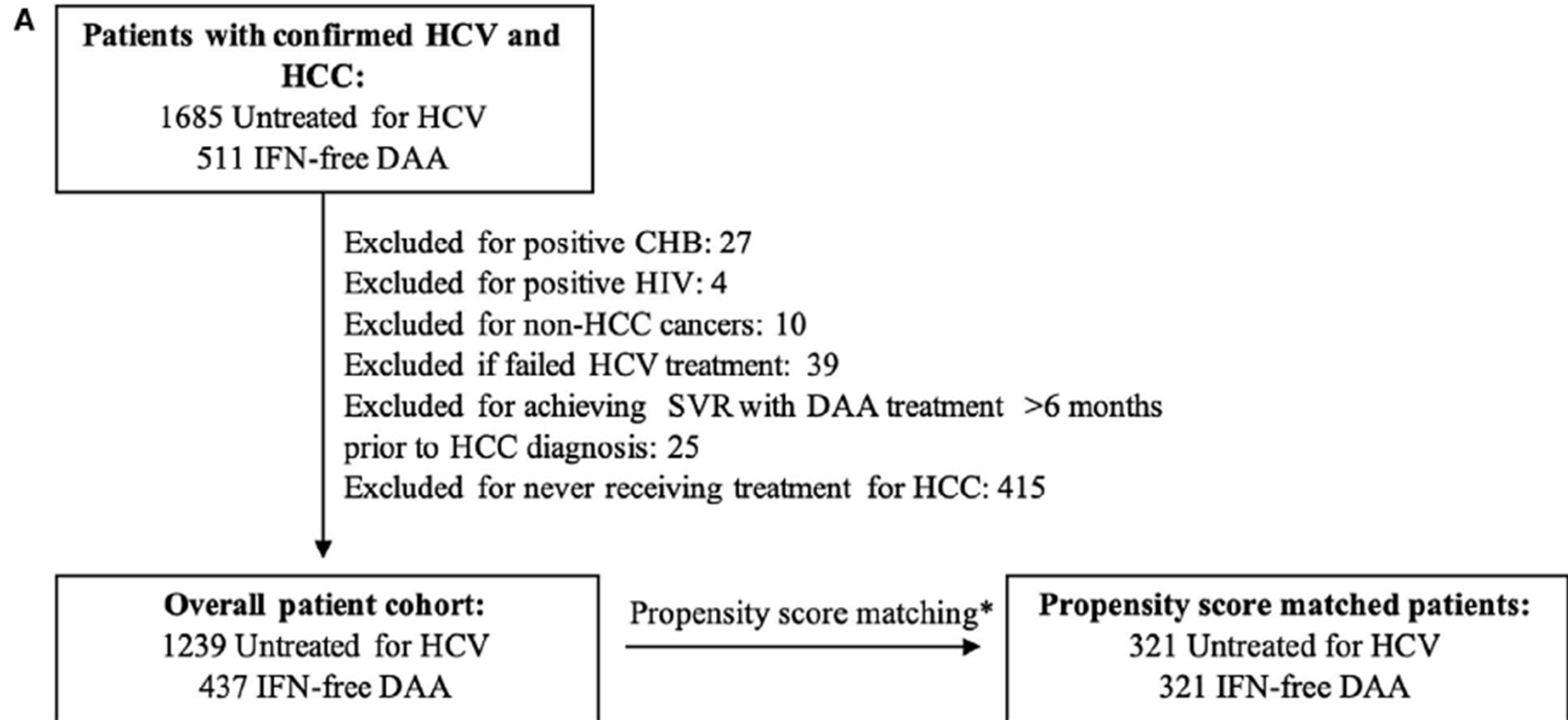
The limited results of the MIPD prompted us to develop an additional assessment using the ITA.LI.CA. database.¹⁷ We compared the rate of HCC recurrence between our multicentre cohort of 977 DAA-exposed patients after successful treatment of HCC and a cohort of 328 DAA-unexposed patients that were matched through a PS, yielding 167 pairs. Our analysis revealed that the recurrence rate after DAA treatment in patients with early HCC stages was high and did not significantly differ to that of DAA-unexposed patients. Although the risk was hetero-

Improved Survival of HCV Patients Who Received DAAs After HCC Treatment

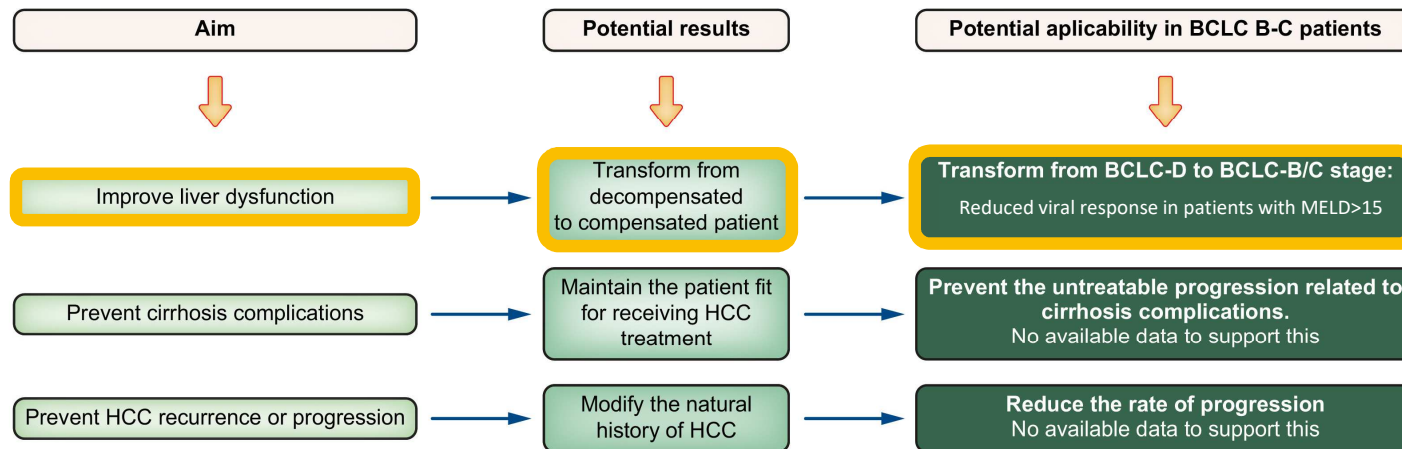


N° at risk				
DAA group	102	88	39	1
No DAA group	102	81	59	34

Improved Survival of HCV Patients with HCC Who Received DAAs



Antiviral Therapy in The Setting of HCC

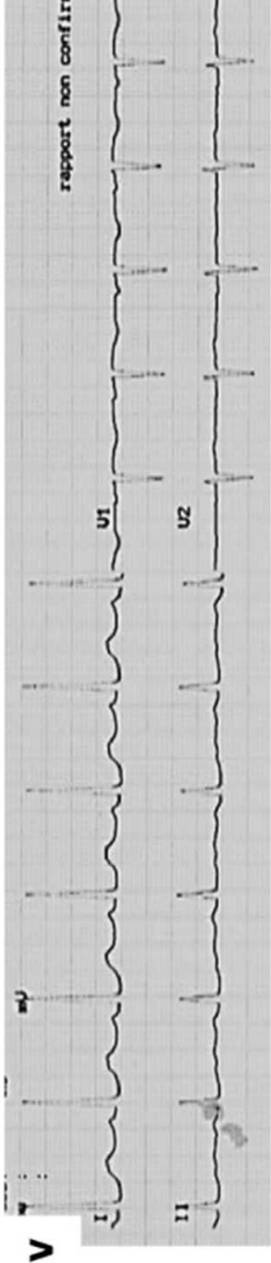
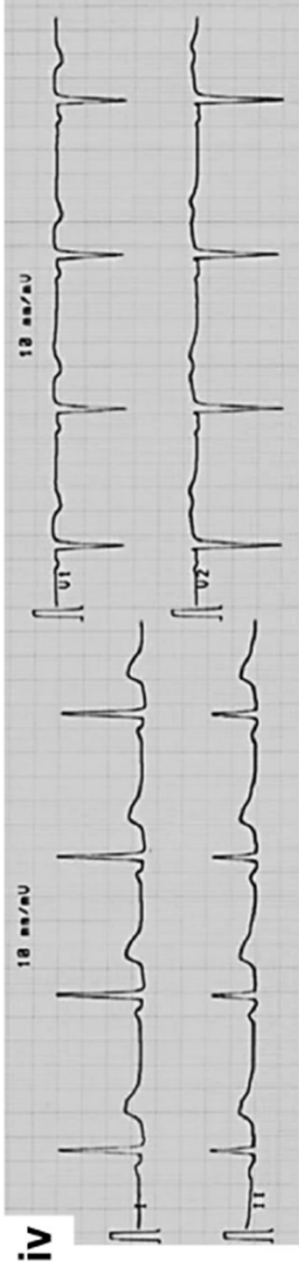
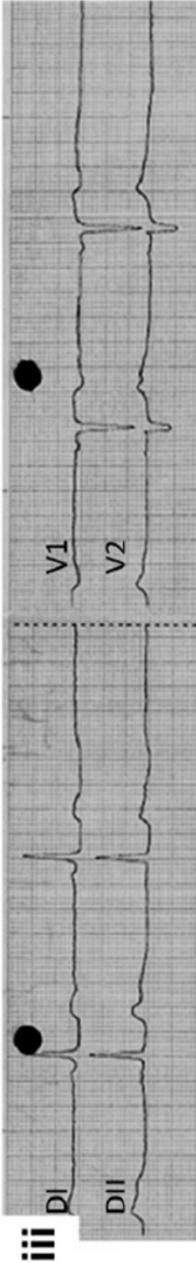
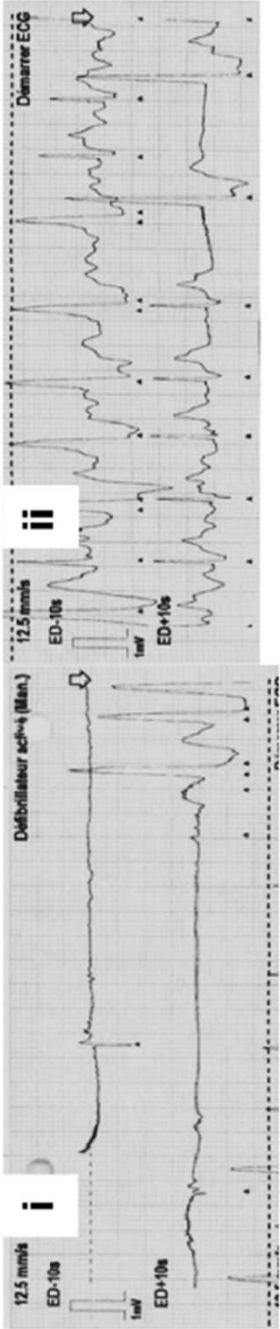


- ✓ Identify the determinants for BCLC-D stage (i.e. liver dysfunction vs ECOG-PS/tumor burden)
- ✓ Reduced viral response in decompensated cirrhosis (DAA)
- ✓ Reduced response in active HCC (DAA)

BRIEF REPORT

ED
Dr
S
L
V

Patient 1



Delay after sofosbuvir and daclatasvir intake	Heart rate (bpm)
30 min	0 / 55
2 hours	38
1 day	50
5 days	75

INTERNAL MEDICINE

CASE REPORT

Ventricular Tachycardia as a Complication of Ledipasvir and Sofosbuvir Treatment for HCV Infection

Kazushige Nirei¹, Hitomi Nakamura¹, Shunichi Matsuoka¹, Yoichiro Yamana¹,
Shunichi Yoda², Atsushi Hirayama² and Mitsuhiro Moriyama¹

Abstract

We experienced two patients with serious arrhythmias associated with the administration of ledipasvir (LDV) and sofosbuvir (SOF). Neither patient took amiodarone, an agent for which concomitant use is prohibited. One patient was 82 years old and hypertensive; the other was 72 years old and had no cardiovascular

Christopher Brynczka, Jose Lebron, Joseph DeGeorge & Frederick Sanna Just

DAA Therapy During HCC Treatment is Possible

● Do Not Coadminister ■ Potential Interaction ▲ Potential Weak Interaction ◆ No Interaction Expected

Results Key

	ELB/GZR	G/P	SOF/VEL	SOF/VEL/VOX
Amiodarone	■	■	●	●

Single Case

Elbasvir/Grazoprevir, an Alternative in Antiviral Hepatitis C Therapy in Patients under Amiodarone Treatment

Lina Weiss^{a, b} Kerstin Wustmann^c Mariam Semmo^d
Markus Schwerzmann^c Nasser Semmo^a

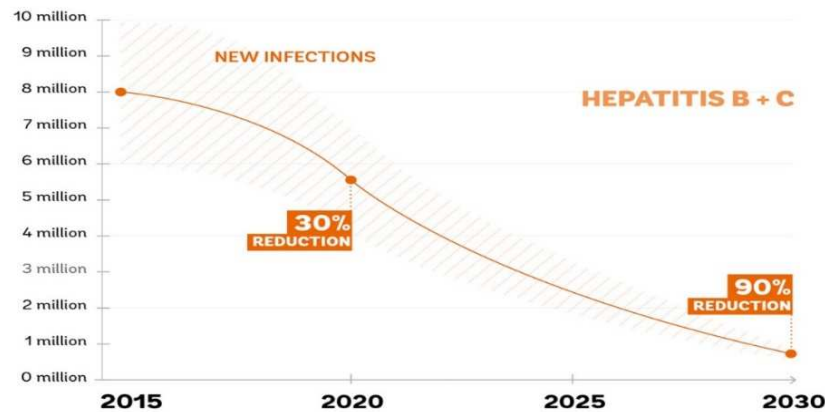
DAAs As The Key To HCV Elimination



No Age Limit
Safe in Organ Trasplant
Safe in decompensated cirrhosis
Safe in the Liver Transplant waiting list
No formal contraindications to treatment

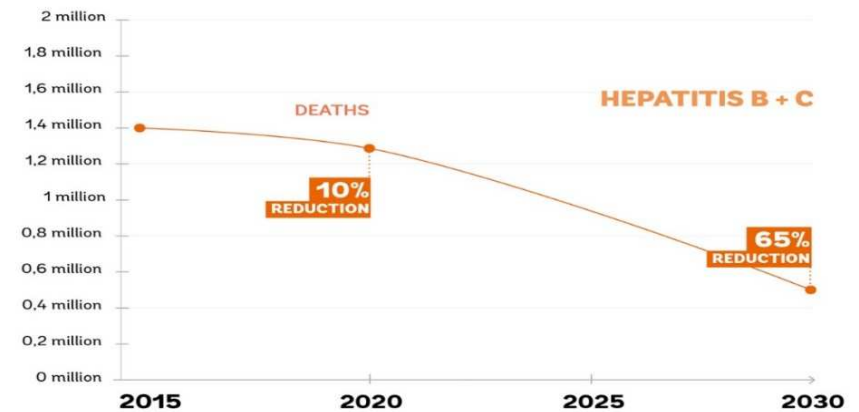
What does elimination mean? Impact targets

90% reduction in new cases of
of chronic HBV and HCV infection



From 6-10 million infections to 900,000 infections

65% reduction in deaths from
chronic HBV and HCV



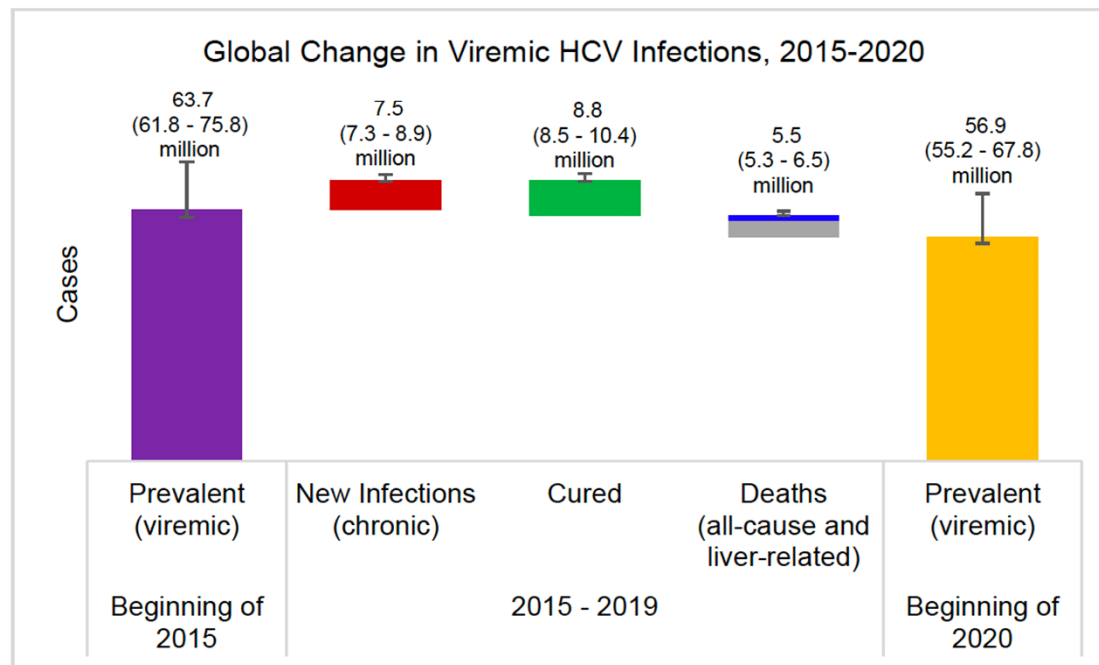
From 1.4 million deaths to under 500,000 deaths

HEPATITIS STRATEGY, 2016: ELIMINATION BY 2030

	Interventions	2030 targets
1. Service coverage	1. Three dose hepatitis B vaccine	90%
	2. HBV PMTCT	90%
	3. Blood and injection safety	100 % screened donations
		90% reuse-prevention devices
	4. Harm reduction	300 injection sets/PWID/yr
	5. Treatment	90% diagnosed
		80% eligible treated
2. Impact	A. Incidence reduction	90%
	B. Mortality reduction	65%

Updated HCV Epidemiology in 2020

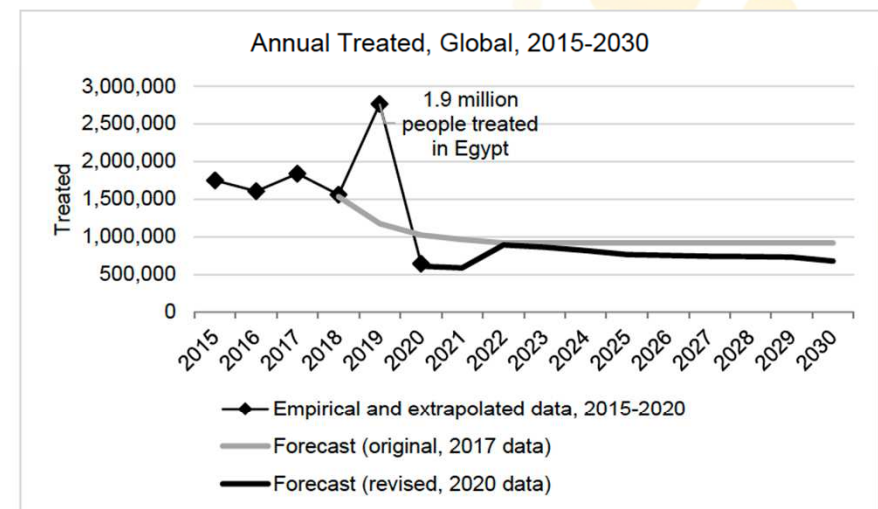
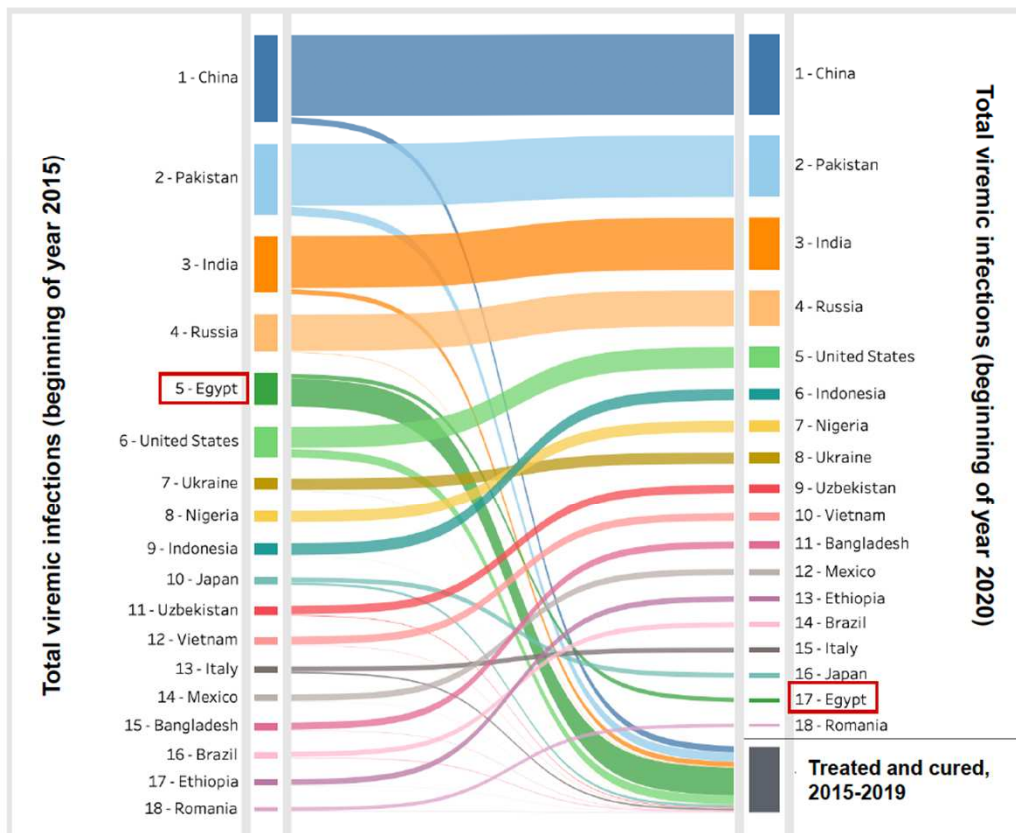
Viremic infections have declined since 2015, due to new/improved data, as well as mortality and cure



Updated estimates for Egypt, Brazil and Nigeria, as well as a new estimate for Democratic Republic of the Congo have contributed to a lower baseline prevalence in 2015

DAA and HCV Elimination Worldwide

Of the >10 million persons initiated on DAAs between 2015 and the end of 2020, more than a third were in Egypt.





Volume 228, Issue
Supplement_3
15 September 2023

[< Previous](#)

[Next >](#)

JOURNAL ARTICLE

From Prioritization to Universal Treatment: Successes and Challenges of Hepatitis C Virus Elimination in Italy

[Get access >](#)

Loreta A Kondili ✉, Lucia Craxì, Felice Nava, Sergio Babudieri,
Roberta D'Ambrosio, Andrea Marcellusi, Francesco Saverio Mennini,
Sabrina Valle, Pierluigi Russo, Pier Paolo Olimpieri, Massimo Andreoni,
Alessio Aghemo

The Journal of Infectious Diseases, Volume 228, Issue Supplement_3, 15
September 2023, Pages S211–S220, <https://doi.org/10.1093/infdis/jiad038>

Published: 13 September 2023

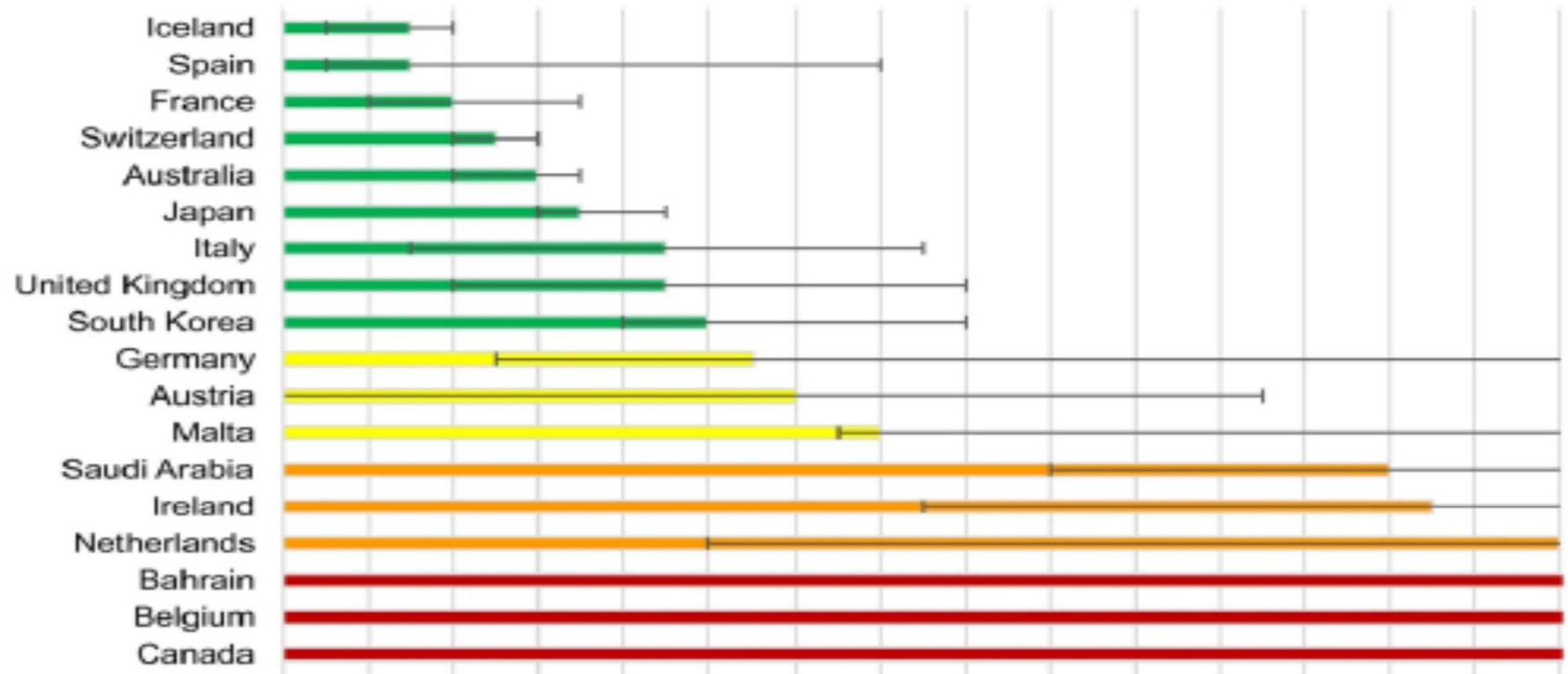
N° TRATTAMENTI CUMULATI

Trend cumulativo dei trattamenti avviati



**250.779 «avviati» sono i trattamenti (solo pazienti eleggibili)
con almeno una scheda di dispensazione farmaco**

HCV Elimination: Data From 2019



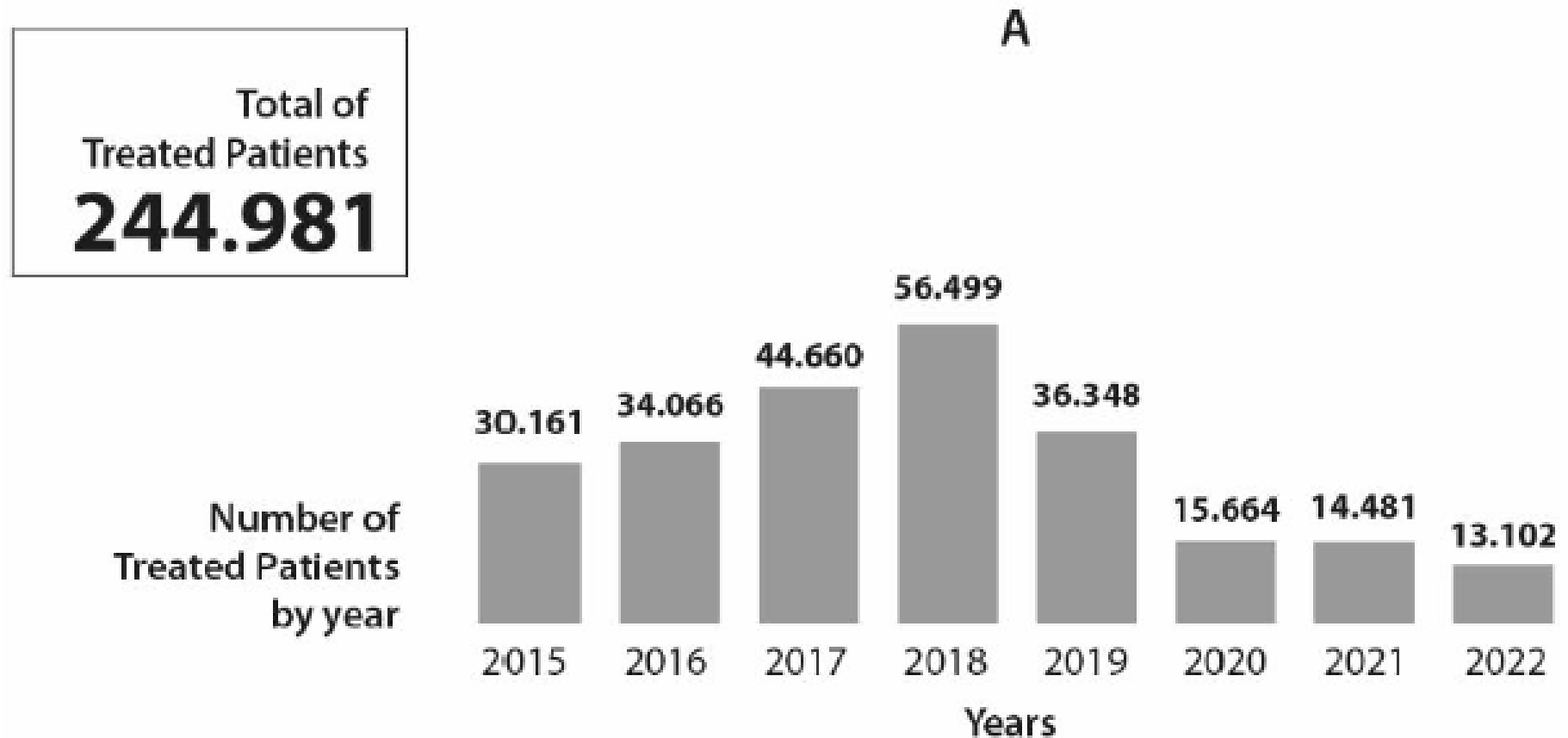
Country or territory

HCV Elimination in Italy: Lessons to be Learnt

	Political will	Financed national program	Harm reduction program	Expanded treatment capacity	Removed restrictions	Monitoring & evaluation	Awareness & active screening	Linkage to care programs
Australia	Yes ^{1,13}	Yes ¹³	Yes ^{13,14}	Yes ¹³⁻¹⁵	Yes ¹⁴	Yes [†]	Yes ^{13,14}	Yes [†]
France	Yes ¹	Yes ¹⁴	Yes ¹⁴	Yes [†]	Yes ¹⁴	Yes [†]	Yes ¹⁴	Yes [†]
Iceland	Yes ¹⁶	Yes ¹⁶	Yes [†]	N/r ^a	Yes ¹⁶	Yes ¹⁶	N/r ^b	Yes [†]
Italy	Yes [†]	Yes ¹⁴	No [†]	No [†]	Yes ¹⁴	Yes ¹⁴	No [†]	No [†]
Japan	Yes [†]	Yes ¹³	Yes ¹³	N/r ^c	Yes [†]	Yes [†]	Yes [†]	Yes [†]
South Korea	Yes [†]	Yes [†]	Yes [†]	No [†]	Yes [†]	Yes [†]	Yes [†]	Yes [†]
Spain	Yes [†]	Yes ¹⁴	N/r ^d	Yes [†]	Yes [†]	Yes ¹⁴	Yes [†]	No [†]
Switzerland	Yes [†]	No ¹⁴	Yes ¹⁴	No [†]	Yes [†]	Yes [†]	N/r ^e	No [†]
United Kingdom	Yes ^{†1,17}	Yes ^{†14,17}	Yes ^{†14}	Yes [†]	Yes ⁵¹⁴	Yes ⁵¹⁴	Yes [†]	Yes [†]

To Achieve HCV elimination Italy must treat 41300 Pts per year

Decreasing Number of HCV Treatments in Italy



Decreto attuativo, ex-post DL Milleproroghe

- Con il DL «**Milleproroghe**» **2020** è stato approvato l'emendamento che stanziava **71,5 milioni di euro per il biennio 2020-2021**, per attuare l'avvio di una **campagna di screening gratuito per l'HCV**, per le seguenti fasce di popolazione:
 - tutta la popolazione iscritta all'anagrafe sanitaria e nata dal 1969 al 1989;
 - i soggetti seguiti dai servizi pubblici per le Dipendenze (SerD), indipendentemente dalla coorte di nascita e dalla nazionalità;
 - i **soggetti detenuti in carcere**, indipendentemente dalla coorte di nascita e dalla nazionalità
- Il **17 dicembre 2020** la Conferenza Stato-Regioni ha deliberato la ripartizione delle somme destinate al finanziamento dello screening nazionale gratuito per l'epatite C, sancendo l'Intesa sul decreto attuativo del Ministro della Salute ex-post DL "Milleproroghe" e chiedendo che l'utilizzo dei fondi venisse prorogato al 31 dicembre **2022**.

CHI
 Cittadini molisani
 nati tra il 1969 e il 1989

QUANDO
 Ogni sabato
 a partire dal 2 aprile fino
 al 31 dicembre 2022
 dalle ore 9.00 alle ore
 12.00

DOVE
 Campobasso Punto
 prelievi
 Distretto via U. Petrella,
 Ternoletti Punto prelievi
 Distretto via del Molinello,
 Isernia area ambulatorio
 Ospedale Venziale

COME
 prenotando
 dal lunedì al venerdì dalle
 8.00 alle 17.00
 da telefonare fisso al numero
 800639595
 o da cellulare al numero
 0875752626

**IL TEST È GRATUITO
 NON È NECESSARIA
 L'IMPAGINATIVA DEL
 MEDICO CURANTE**

Programma per l'attuazione
del Piano di Eliminazione
del Virus C dell'epatite
in Regione Lombardia

**SCREENING
GRATUITO
PER HCV**

**nei soggetti nati
tra il 1969 e 1989**

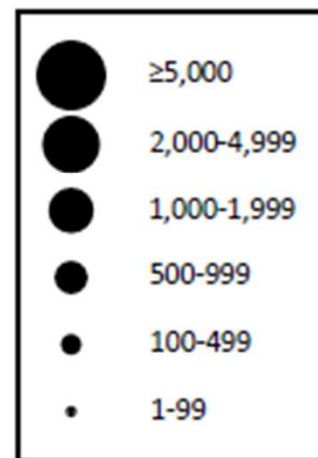
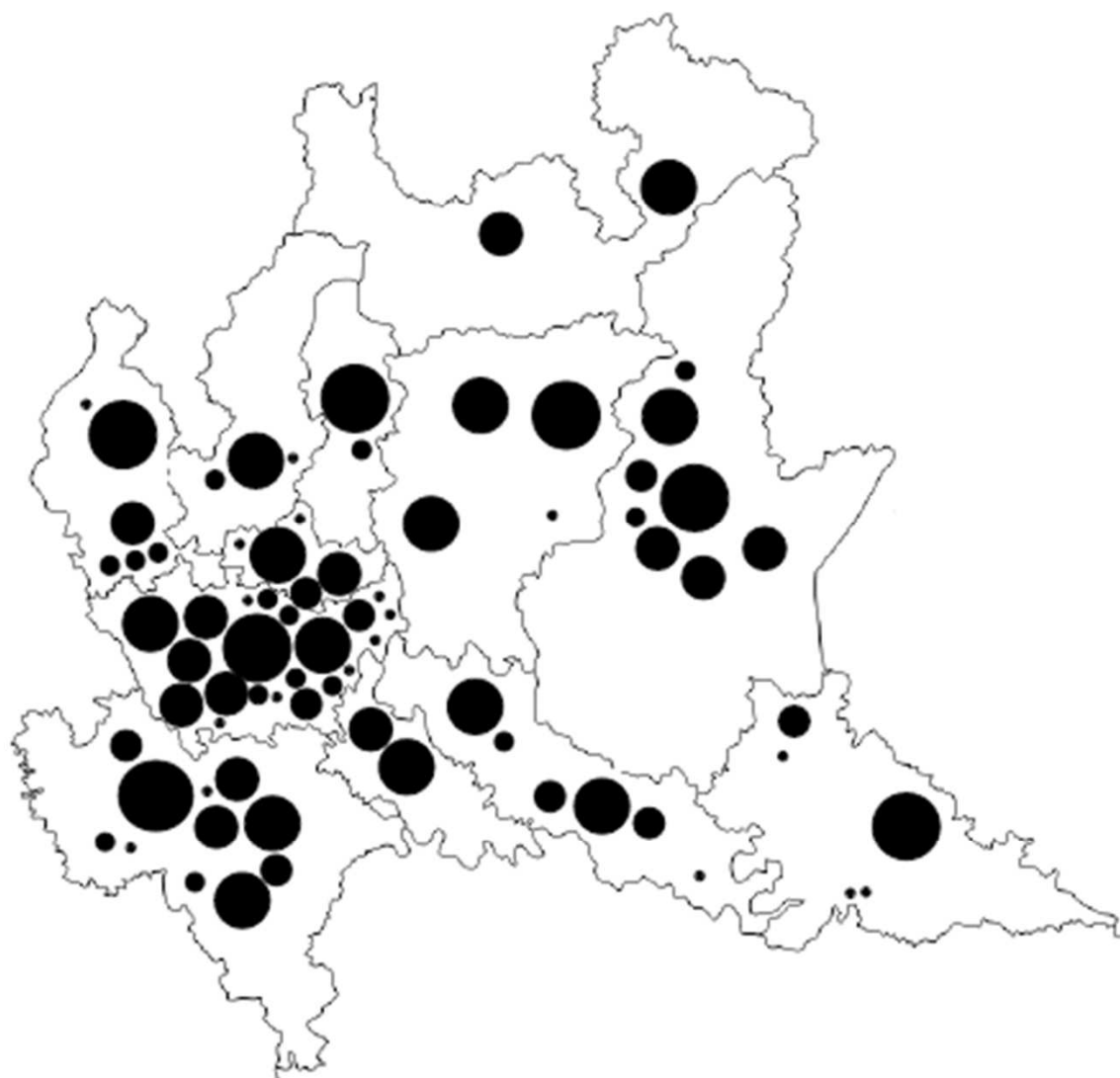
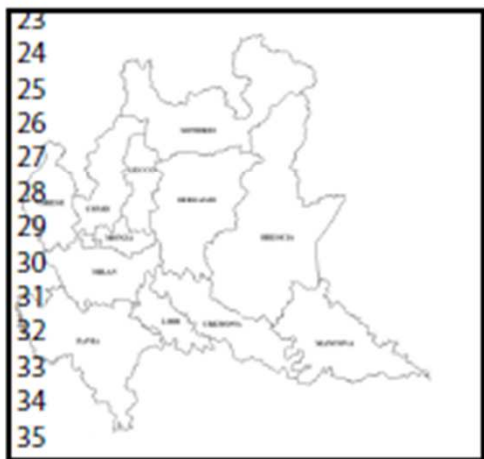
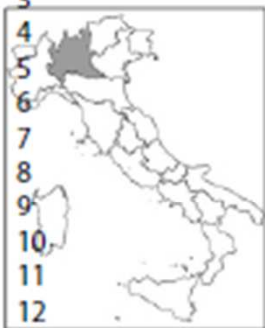
Regione
Lombardia

 **REGIONE DEL VENETO**

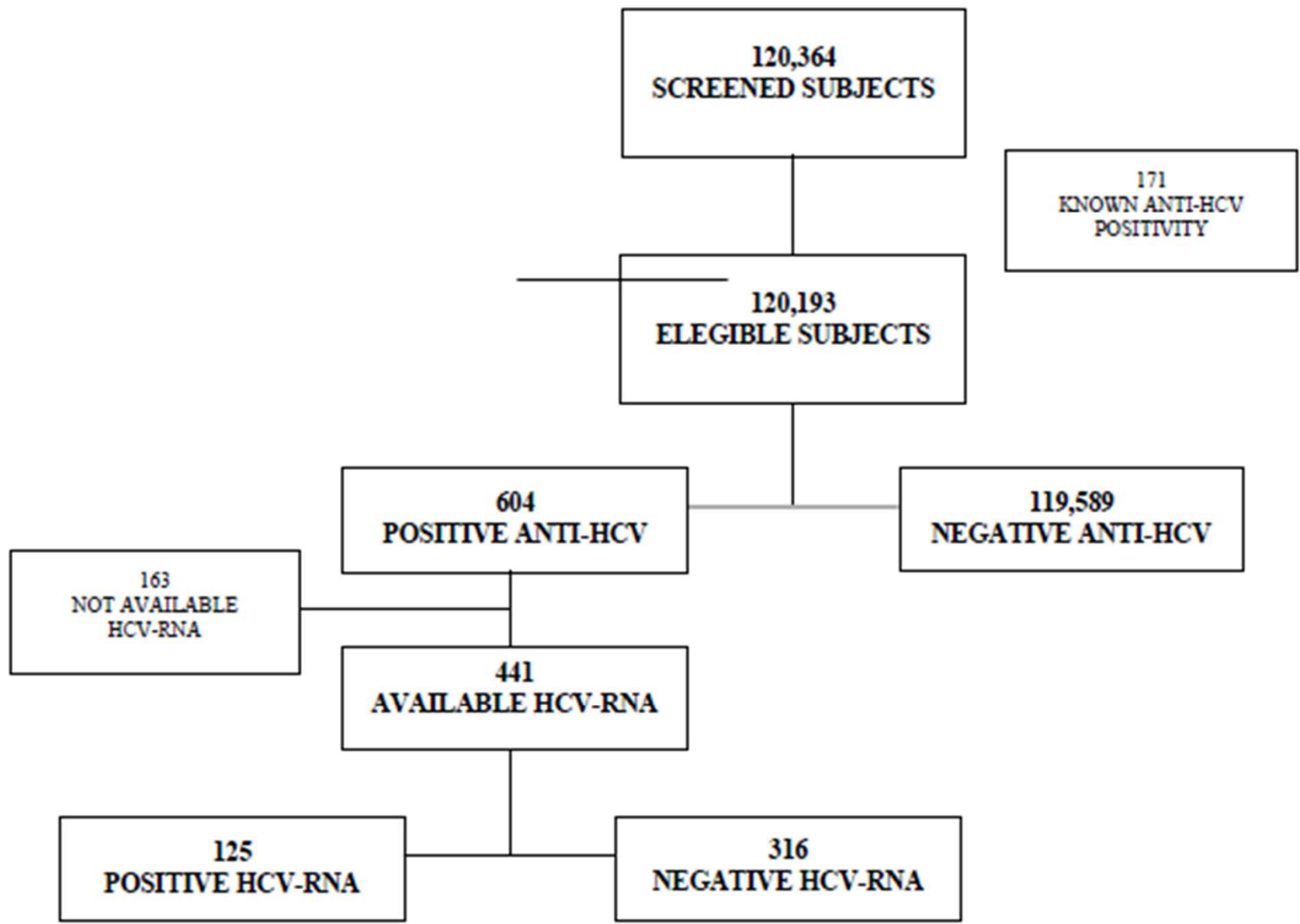
 **AZIENDA
ZERO**

 **EPATITE C**
SE C'È, SI CURA!

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Lo screening nazionale gratuito per l'HCV

Dati preliminari – Rendicontazione al 31/12/2022

Popolazione generale '69-89

Totale soggetti screenati:

N. 488.571

Test di screening:

- Ricerca Ab su prelievo venoso (94,5%)
- Ricerca Ab su sangue capillare (5,5%)
- Ricerca Ab su saliva (0,05%)

Modelli organizzativi:

- **Screening con chiamata attiva:** Servizio di prevenzione territoriale/ASL/MMG (lettera, messaggio SMS, fascicolo sanitario elettronico FSE, contattati dal MMG)
- **Screening opportunistico:** in occasione di accesso alle strutture sanitarie (PS, ospedale, ambulatori, centri prelievi, ecc.); in occasione di somministrazione dose vaccino COVID-19/tamponi
- **Accesso libero, autoprenotazione online, open day dedicati**

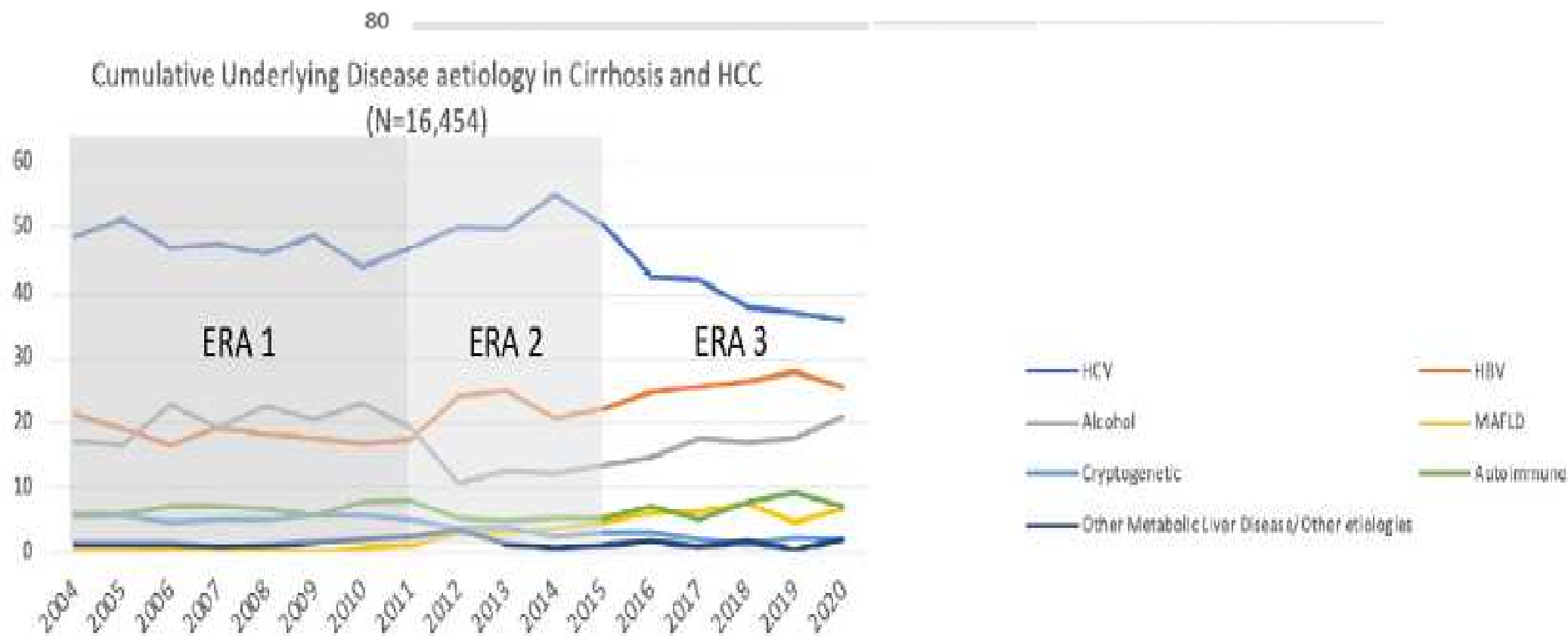
Lo screening nazionale gratuito per l'HCV
Risultati preliminari – Rendicontazione al 31/12/2022

Popolazione generale '69-89

ESTENSIONE = INVITATI/ TARGET	COPERTURA = TESTATI/ TARGET	ADESIONE = TESTATI/ INVITATI	POSITIVI test ricerca Ab (%)	ADESIONE AL TEST DI CONFERMA (%)	POSITIVI test di conferma (%)	DETECTION RATE (%) = INF. ATTIVA/ TESTATI*1000	SOGG. CON INF. ATTIVA AVVIATI AL TRATTAMENTO (%)
18,0	4,1	22,9	0,7	86,2	29,1	1,8	32,7

Identificati n. 892 soggetti con infezione attiva da HCV

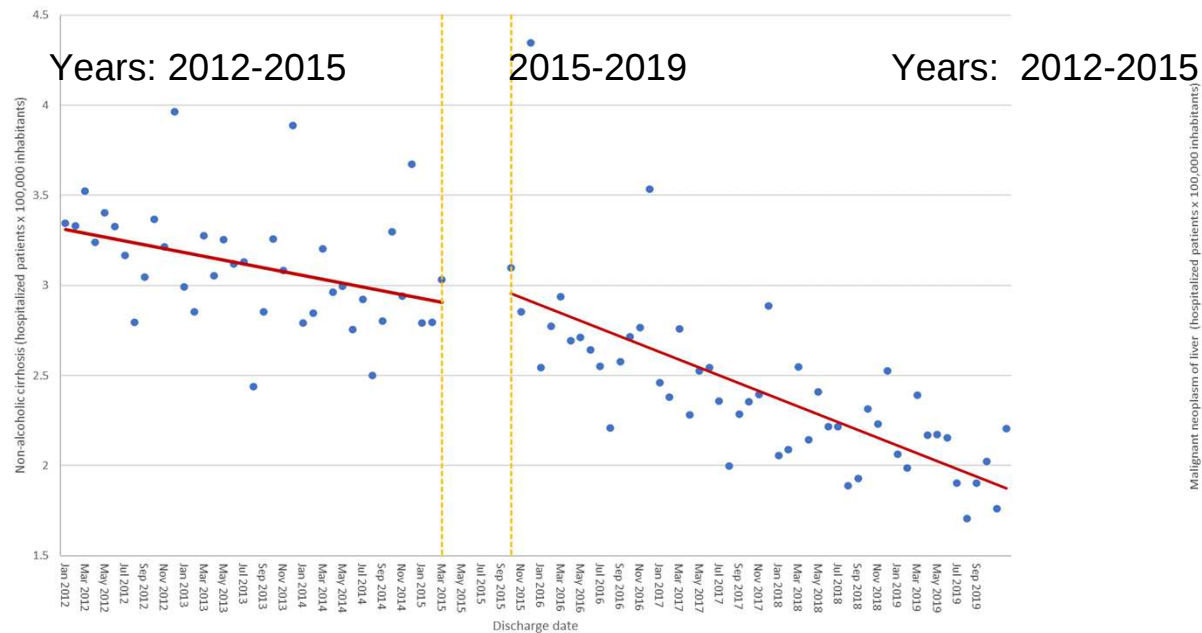
Temporal Trends of Waitlisting for LT in Italy



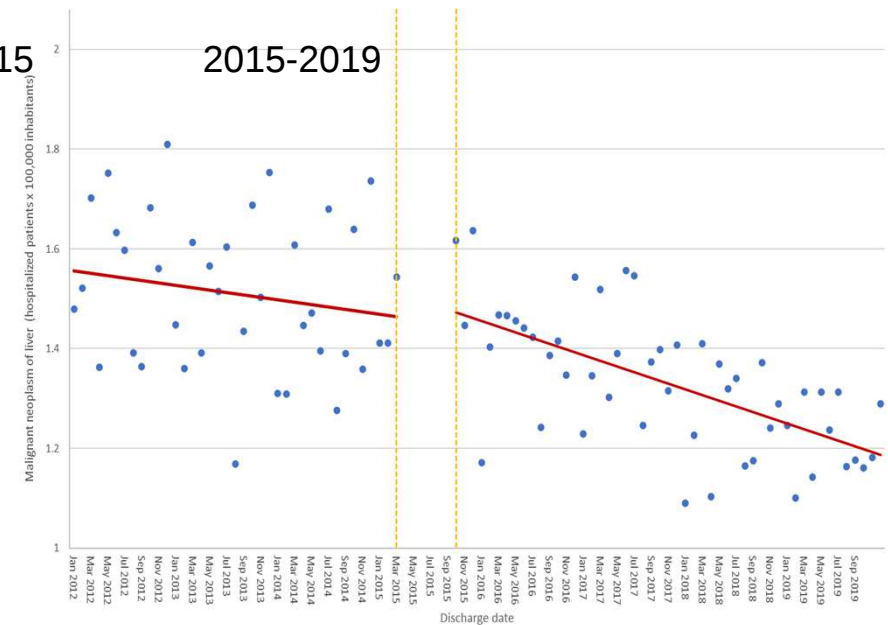
	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
—●— Cirrhosis	74,6	68,5	64,2	64,2	64,5	63,1	64,5	63,7	57,3	53,3	51,3	52,4	46,3	43,6	41,7	46,9	46,2
—●— HCC	20,1	27,7	31,7	31,8	31,1	30,6	28,5	28,5	38,5	43,2	45,5	44,2	50,3	52,2	53,5	44,8	46,7
-●- Other	3,7	2,1	2,3	3	2,2	4,3	6	6,1	2,9	1,4	1,8	1,6	1,7	2,2	2,5	3,6	3,7
—●— • MELD Exceptions	0,6	0,7	0,7	0,7	1,4	1,8	0,9	1,2	0,8	1,8	0,8	1,4	1	1,3	1,3	3,1	1,65
..... Other Malignancies	1	1	1,1	0,3	0,8	0,2	0,1	0,5	0,5	0,3	0,6	0,4	0,7	0,7	1	1,6	1,7

Decreasing Hospitalization Rate of patients with HCV-induced liver disease

Trend of Hospitalizations for HCV Liver Cirrhosis



Trend of Hospitalizations for HCV Liver Cancer



Hospitalizations for HCV and HCV-related diseases in the last decade: data analysis of records of hospital discharge (SDO) at national level

Mennini FS, Sciatella P, Simonelli C, Marcellusi A, Kondili LA. EASL 2022 presentation (submitted manuscript)