14th Residential Course on Clinical Pharmacology of Antiretrovirals

Turin, 16-18 January 2019

Case-based discussion on extra-hepatic morbidities in HCV+ patients

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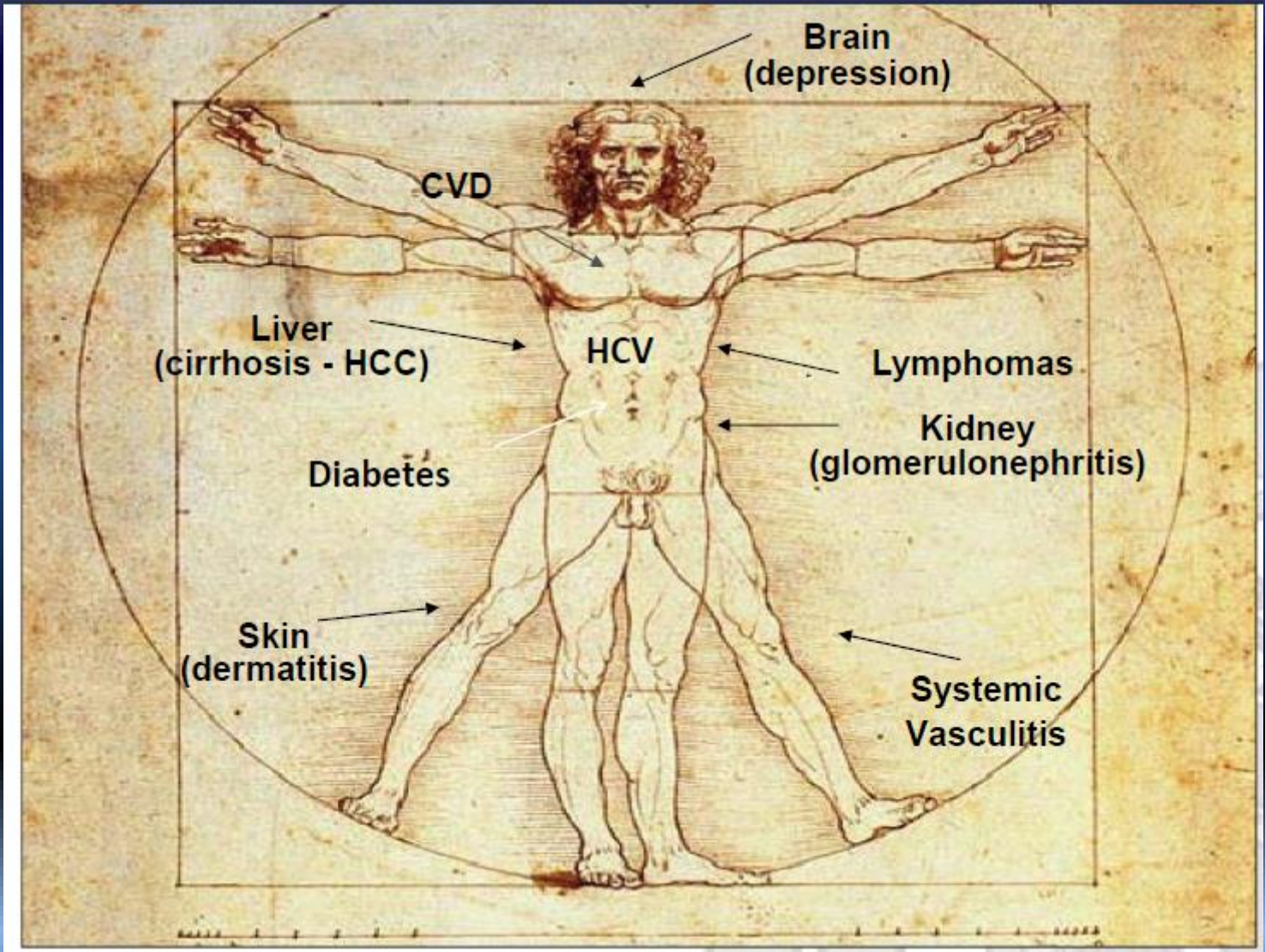
Amedeo di Savoia Hospital

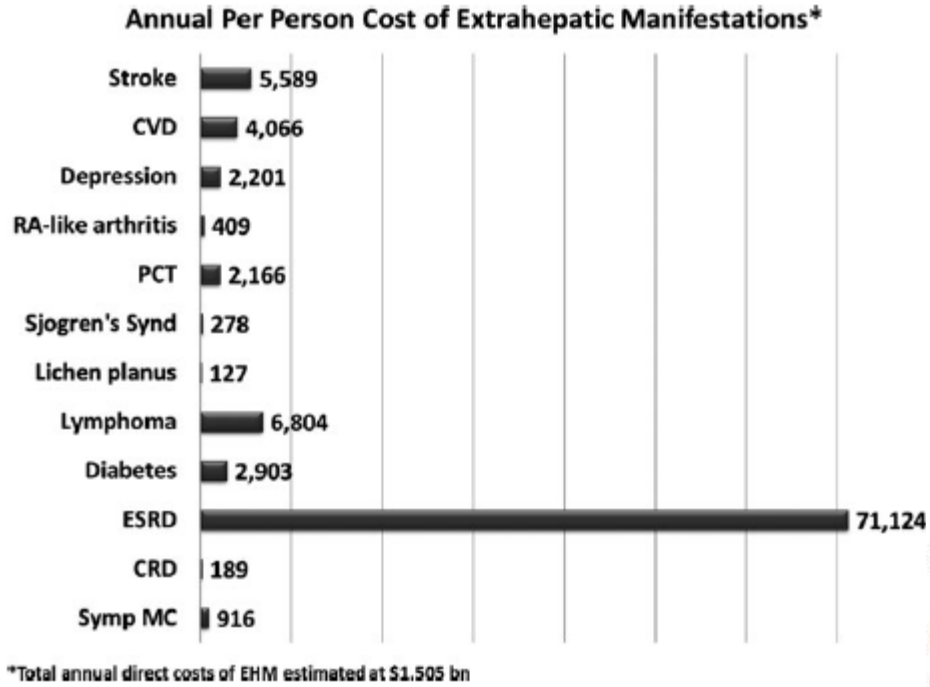
Extra-hepatic manifestations of HCV



Direct medical costs	Direct non-medical costs	Indirect costs
• Hospitalization • Tests • Outpatient consultations • Pharmacological therapy • Managing adverse events • Rehabilitation	• Nursing home care • Paid home caregiving • Patient transport to/from hospital	• Productivity losses (absenteeism, presenteeism, early retirement, early mortality etc.) • Productivity losses for unpaid caregivers (family, friends)

YOUNOSSI ET AL.

J Viral Hepat. 2018;25(Suppl. 3):6–14.



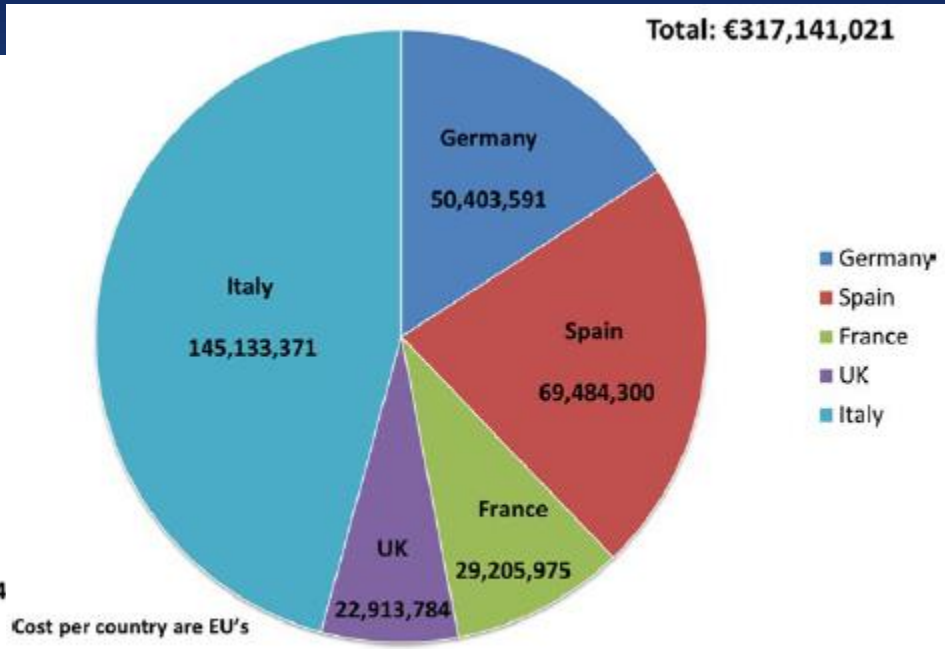
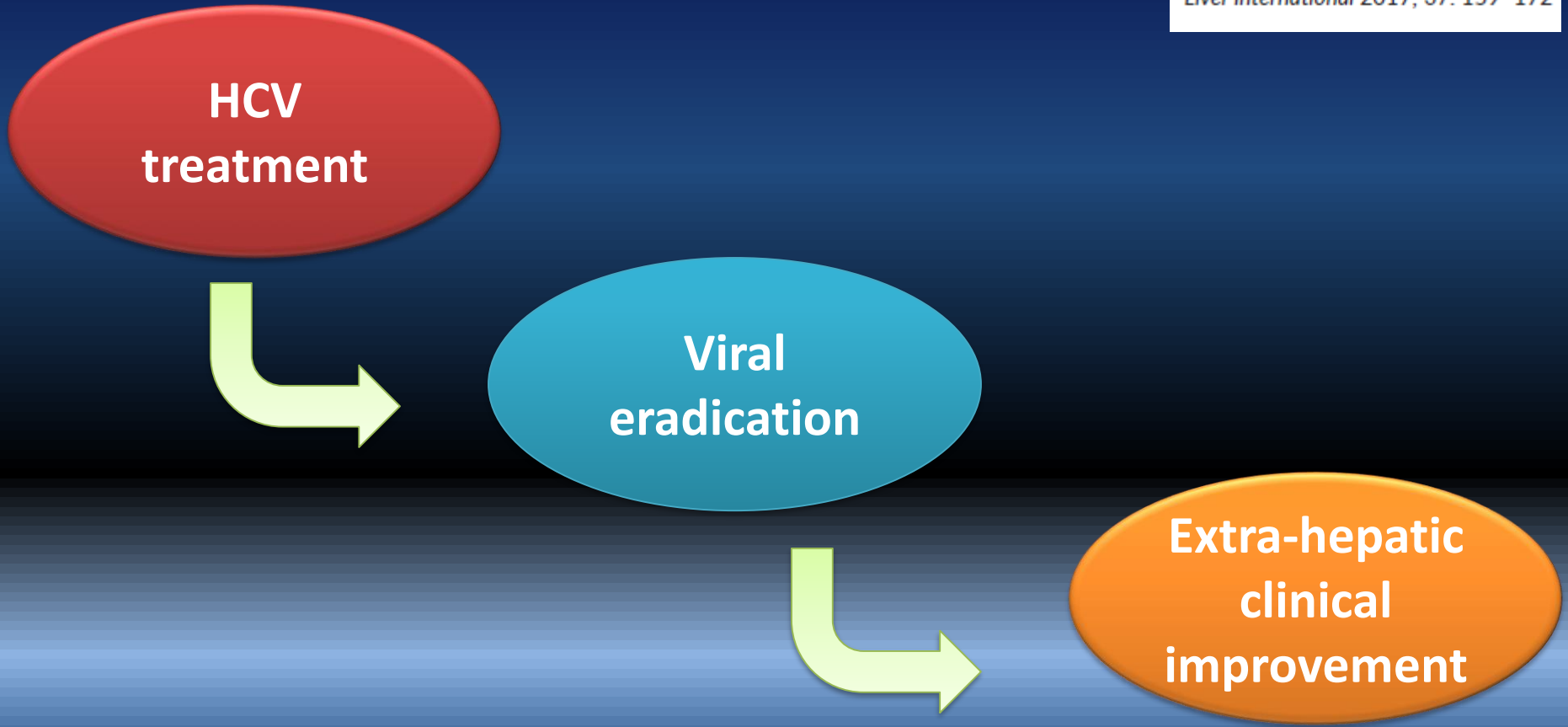


FIGURE 4 Costs of selected hepatitis C virus-related extrahepatic manifestation by European country

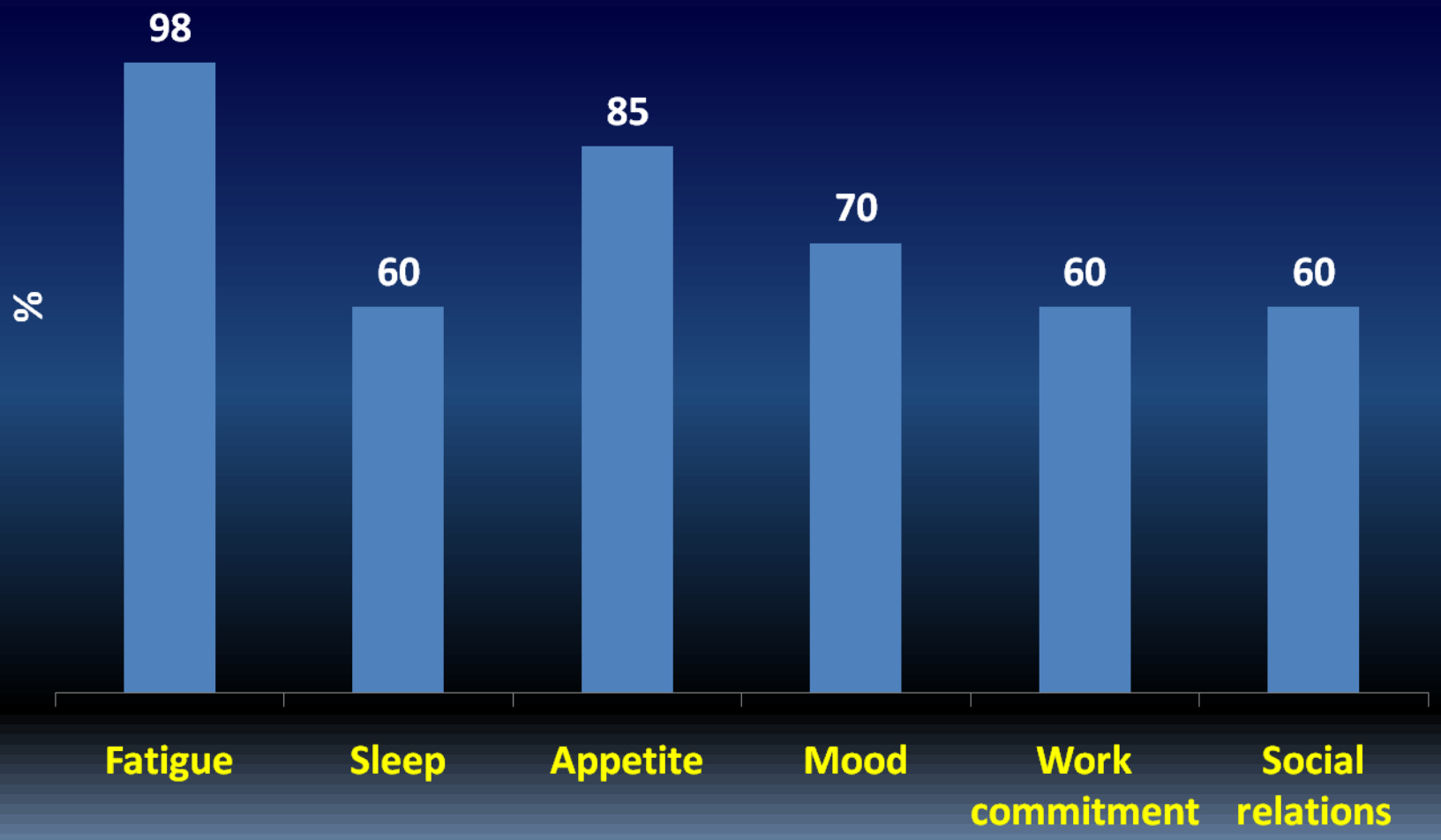
TABLE 1 Risk of selected EHMs in HCV infected patients compared to those without HCV[3]

EHM	Pooled prevalence in HCV patients (95% CI)	Pooled prevalence in non-HCV populations (95% CI)	Risk of condition in HCV patients compared to non-HCV patients (95% CI)
Mixed cryoglobulinemia	30.1% (21.4%-8.9%)	1.9% (0.4%-3.4%)	OR: 11.50 (4.56-29.00)
Depression	24.5% (14.1%-34.9%)	17.2% (13.4%-21.0%)	OR: 2.30 (1.31-4.01)
Type 2 diabetes mellitus	15% (13%-18%)	10% (6%-15%)	OR: 1.58 (1.30-1.86)

Liver International 2017; 37: 159–172



Main subjective improvements after SVR



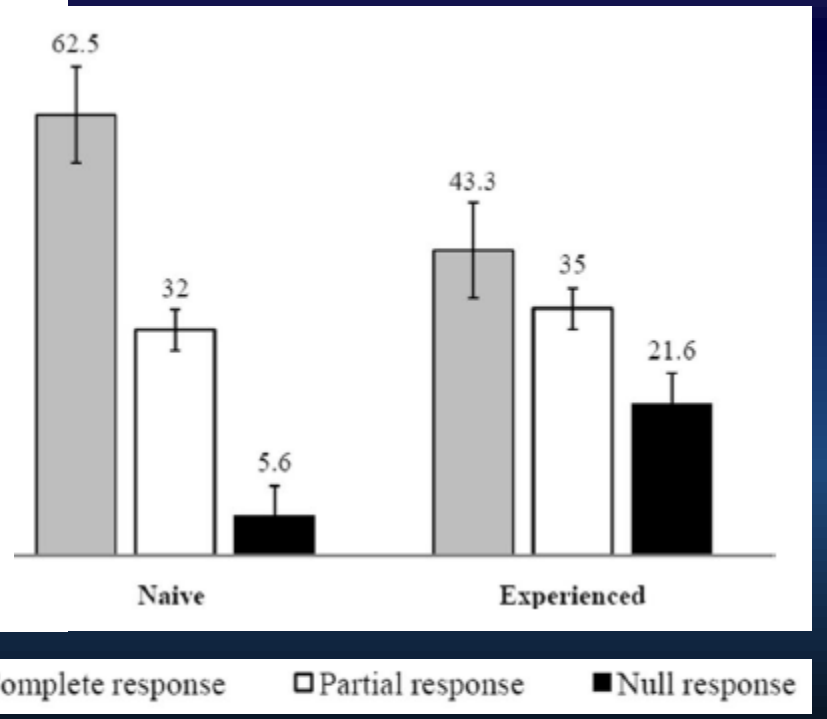
Data from treated patients Amedeo di Savoia 2015-2018

Treatment with DAA in HCV and MC+

L. Boglione et al.

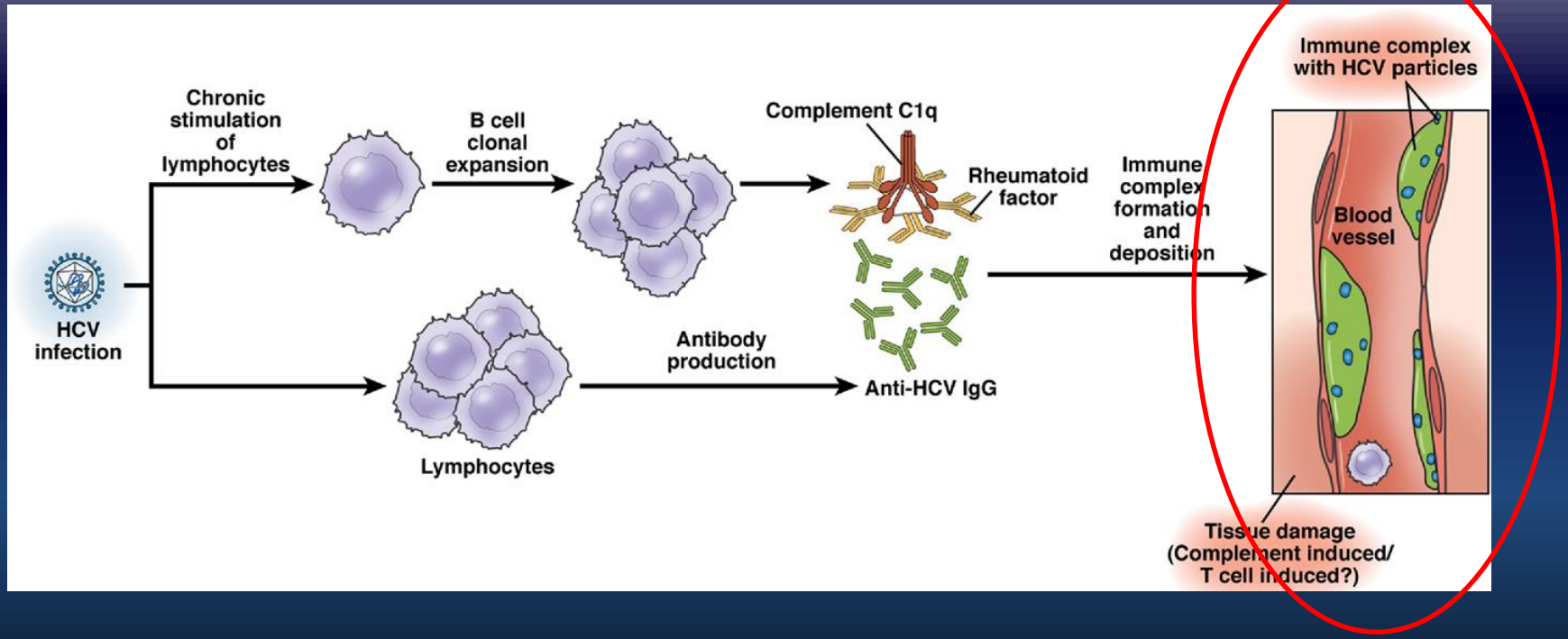
Archives of Virology (2018) 163:961–967

	N, %
Virological response	
SVR12	132 (100)
Immunological response	
Complete response	71 (53.8)
Partial response	44 (33.3)
Null response	17 (12.8)
Clinical response	
Persistence of symptoms	15 (11.4)
Improvement of symptoms	31 (23.5)
Worsening of symptoms	1 (0.8)
Resolution of symptoms	10 (7.6)



Clinical response (symptoms improvement or resolution) 31%

Multivariate analysis	
Years of HCV infection < 20	2.448 (1.335–6.202) $p = 0.019$
Treatment naive	2.885 (1.404–9.660) $p = 0.025$



Persistence of cellular clone

Irreversibility of tissue damage

Improvement of glicemic control in DM-II HCV+

RESEARCH ARTICLE

WILEY JOURNAL OF MEDICAL VIROLOGY

Significant improvement of glycemic control in diabetic patients with HCV infection responding to direct-acting antiviral agents

J Med Virol. 2018;90:320–327.

CIANCIO ET AL.

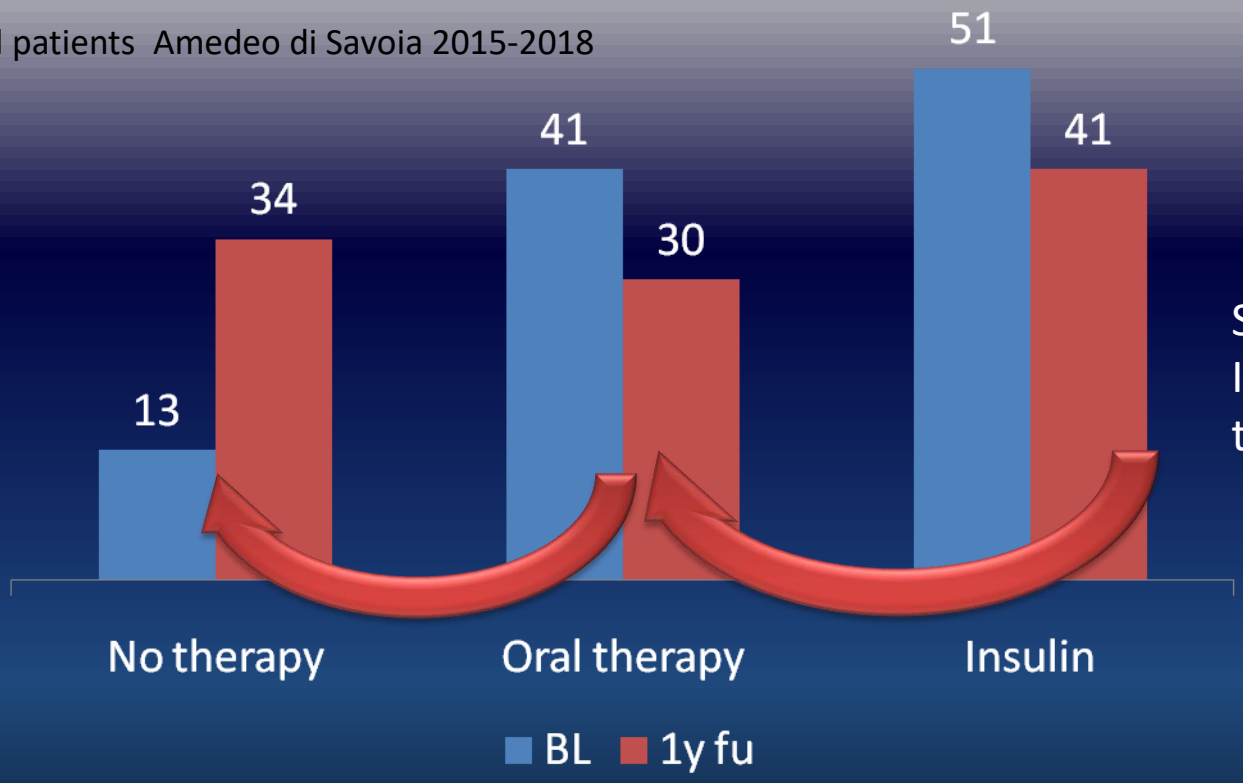
TABLE 4 Anthropometric, biochemical, and metabolic variations in sustained responders and relapsing/untreated patients

	Group 1 (101 patients)			Group 2 (21 patients)		
	Baseline	End of study	P	Baseline	End of study	P
AST (IU/mL)[a]	42.3 ± 37.6	28.2 ± 11.0	0.02	40.3 ± 38.4	42.2 ± 39.8	0.85
ALT (IU/mL)[a]	81.2 ± 77.2	36.0 ± 12.0	<0.001	78.7 ± 67.3	82.2 ± 71.6	0.74
GGT (IU/mL)[a]	87.8 ± 81.0	62.5 ± 73.2	0.02	65.2 ± 64.0	67.0 ± 68.1	0.43
Bilirubin (mg/dL)[b]	1.0 (0.6-1.8)	0.8 (0.7-1.1)	0.12	0.9 (0.6-1.3)	1.0 (0.7-1.4)	0.52
Albumin (g/L)[b]	42 (31-48)	44 (33-49)	0.09	43 (34-47)	42 (33-48)	0.78
INR[b]	1.3 (1.0-1.8)	1.0 (1.0-1.5)	0.08	1.2 (1.0-1.7)	1.3 (1.0-2.1)	0.33
Leukocytes ($x10^3$/μL cells)[b]	4.2 (2.2-7.8)	5.4 (3.3-8.2)	0.07	4.4(2.8-6.2)	4.1 (2.3-7.3)	0.64
Platelets ($x10^3$/μL cells)[b]	155 (62-287)	173 (52-274)	0.08	164 (73-245)	162 (68-274)	0.35
Glucose (mg/dL)[a]	152.4 ± 56.4	134.3 ± 41.3	0.002	145.3 ± 30.2	140.0 ± 47.9	0.71
HbA1c (mmoL/moL)[a]	52.2 ± 15.4	46.5 ± 16.2	<0.001	53.4 ± 9.5	55.3 ± 20.6	0.78
HOMA-IR[a]	5.2 ± 2.5	3.1 ± 1.6	<0.001	4.9 ± 2.6	4.6 ± 2.3	0.29
Body weight (kg)[a]	75.3 ± 13.7	77.9 ± 19.8	0.02	76.6 ± 19.3	76.9 ± 20.7	0.56

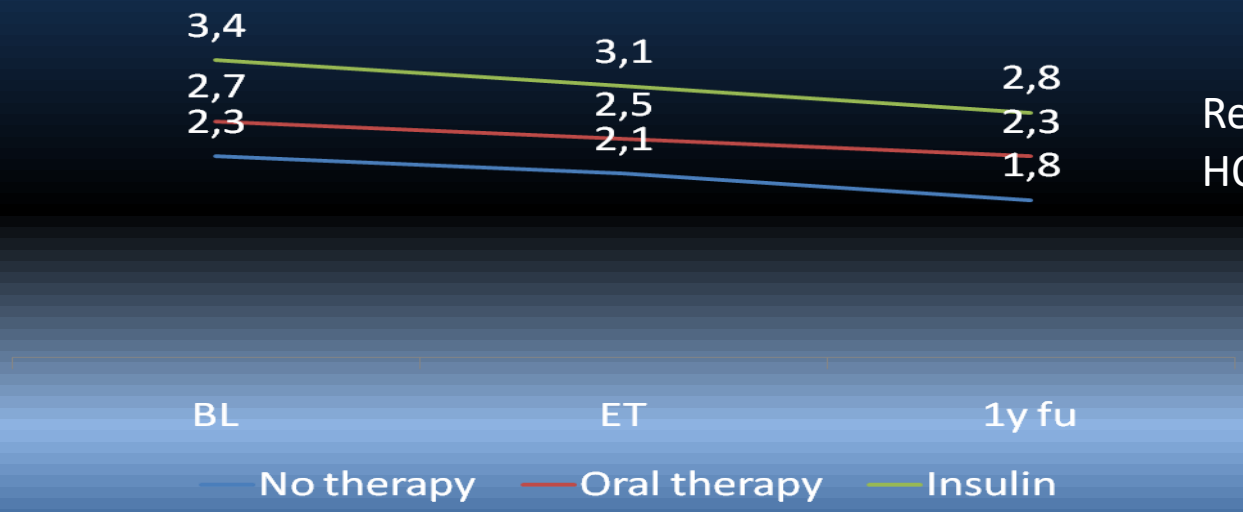
SVR

No SVR

Data from treated patients Amedeo di Savoia 2015-2018



Swithc from Insulin to oral therapy



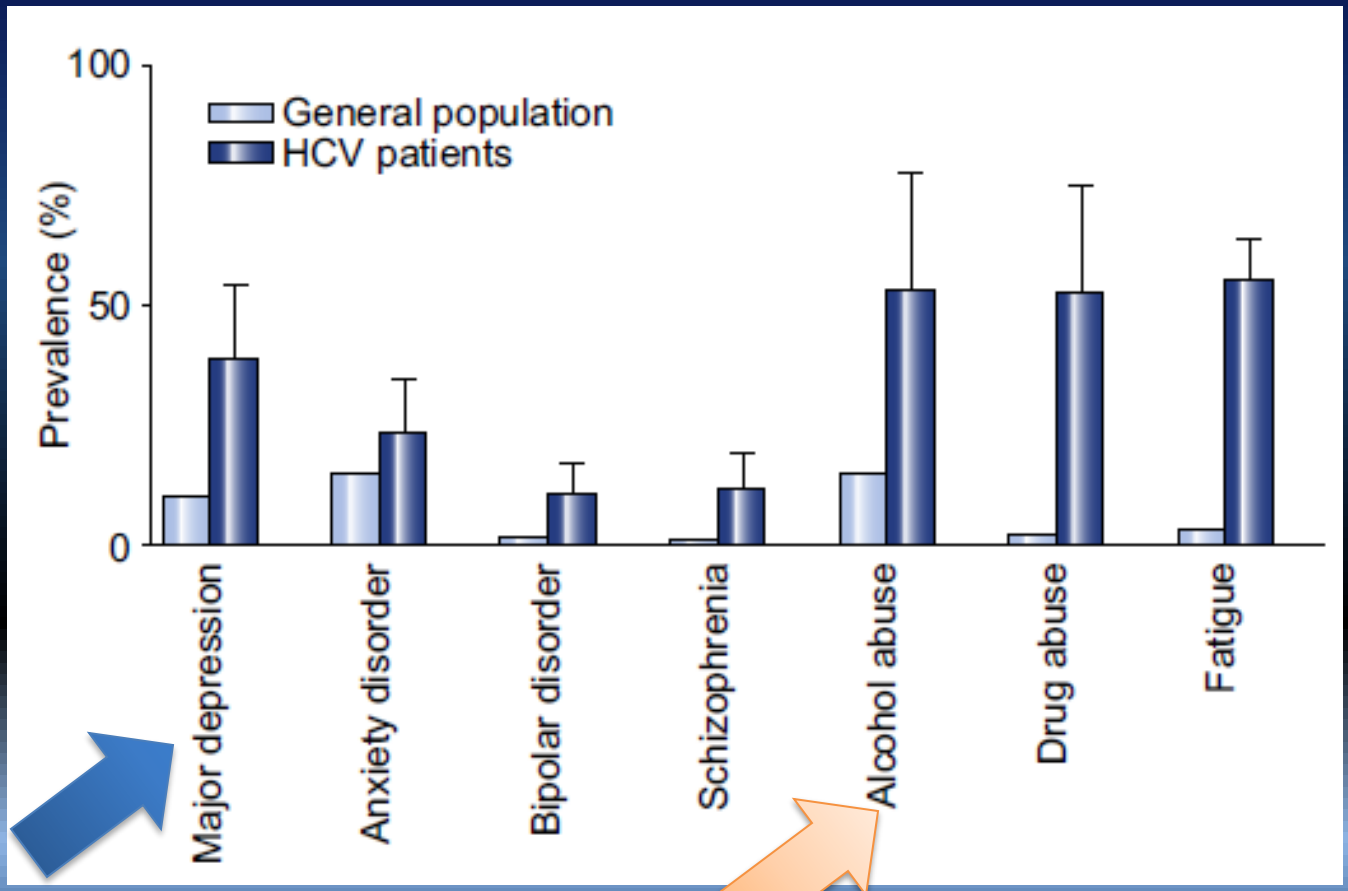
Reduction of HOMA-index

Meeting Report

EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

Hepatitis C infection, antiviral treatment and mental health: A European expert consensus statement

Martin Schaefer[1,2,*], Lucile Capuron[3], Astrid Friebe[4], Crisanto Diez-Quevedo[5], Geert Robaeys[6], Sergio Neri[7], Graham R. Foster[8], Achim Kautz[9], Daniel Forton[10], Carmine M. Pariante[11]



REVIEW

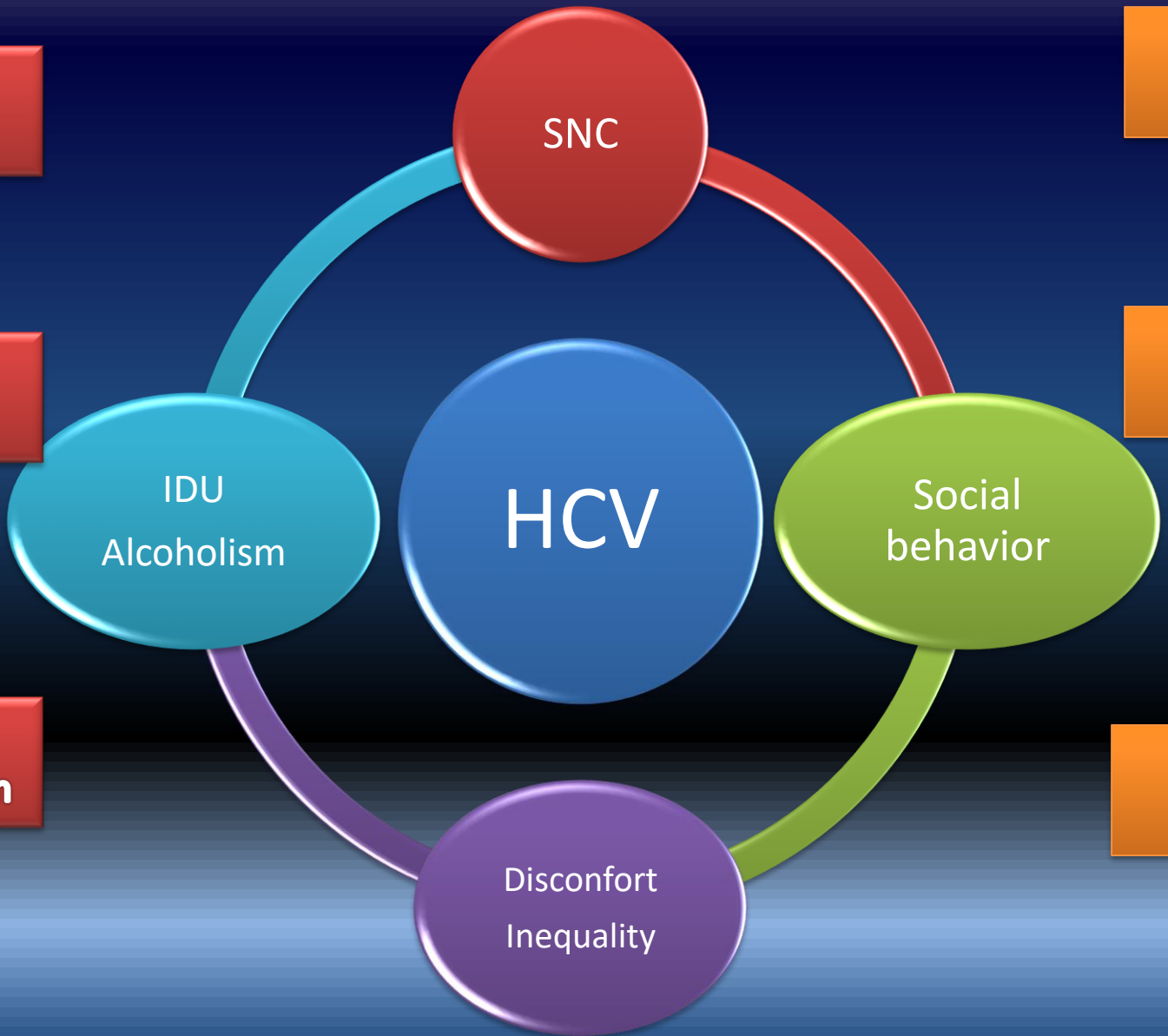
Hepatitis C virus and neurological damage

World J Hepatol 2016 April 28; 8(12): 545-556

HCV

SNC

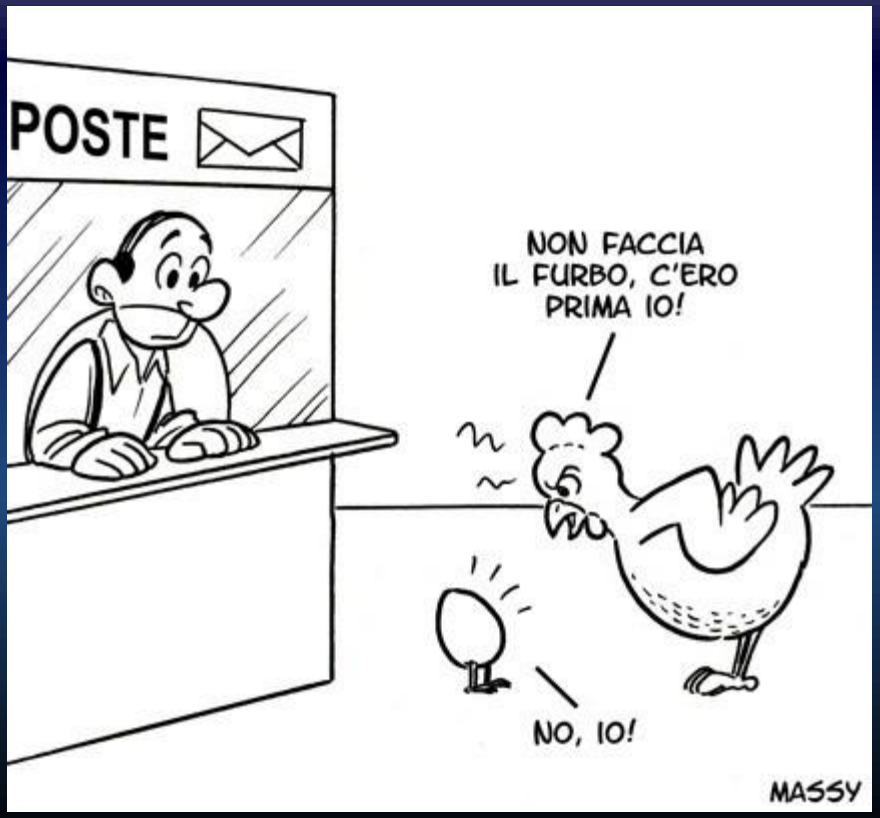
IDU
Alcoholism



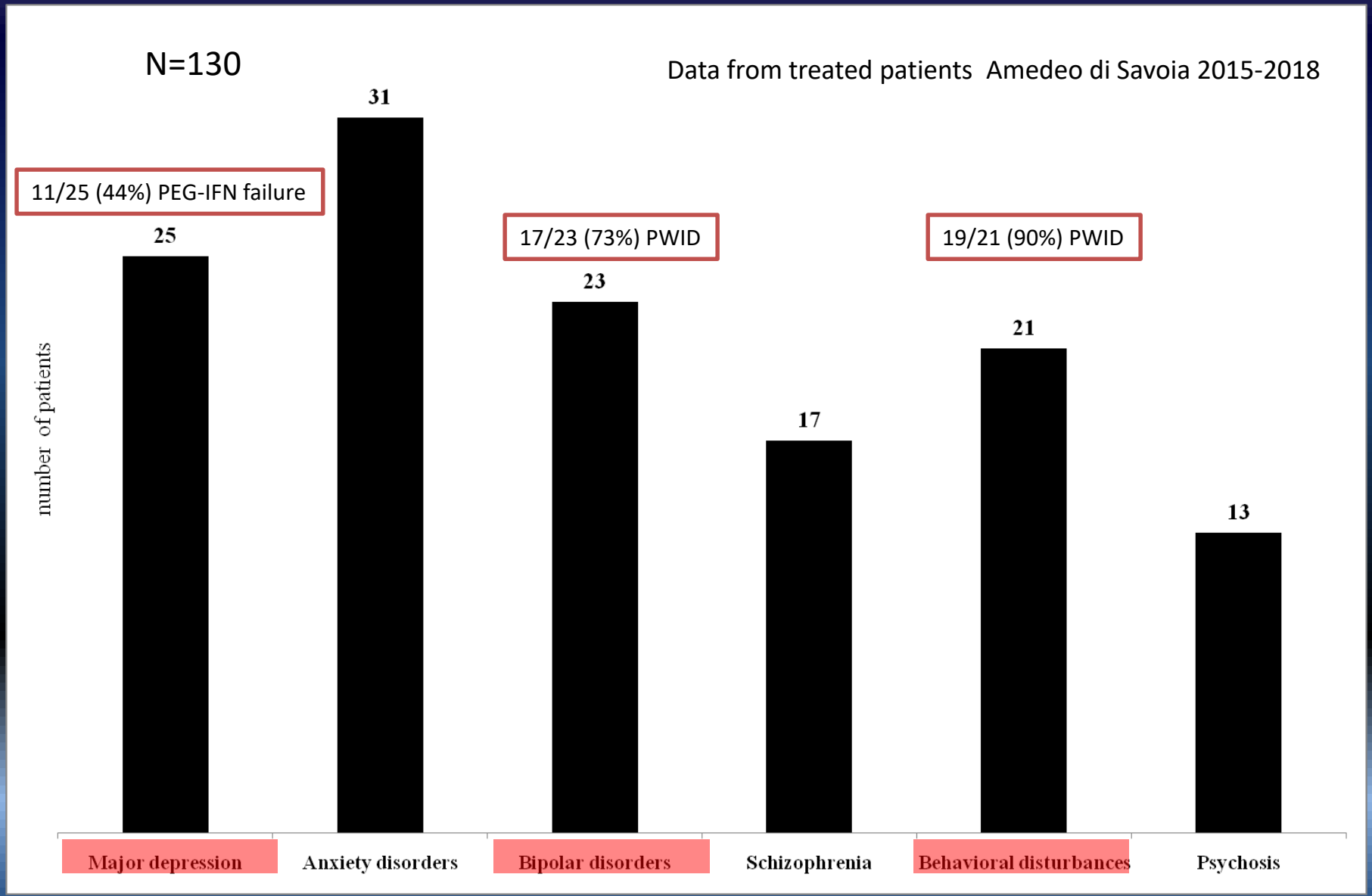
HCV

IDU

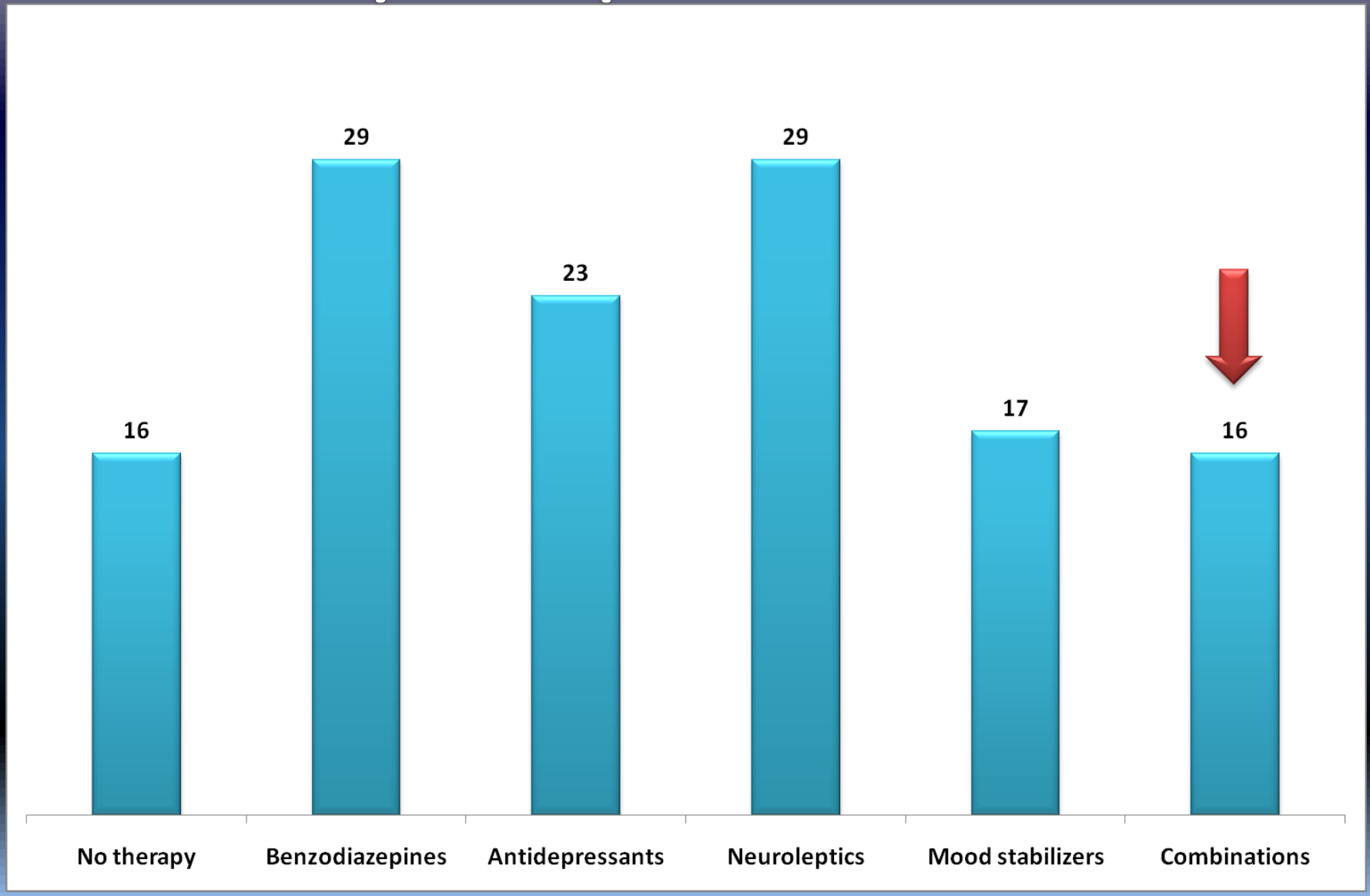
SNC


POSTE
NON FACCIA IL FURBO, C'ERO PRIMA IO!
NO, IO!
MASSY

HCV+ treated patients with psychiatric disease



Psychotropic medications



Data from treated patients Amedeo di Savoia 2015-2018

Flunitrazepam

Aripiprazole

Risperidone

Mirtazapine

Escitalopram

Brotizolam

Quetiapine

Carbamazepine

Sertraline

Buspirone

Psychosis
Paranoid schizophrenia

Bipolar disorder

Maniacal psychosis

Hepat Mon. 2016 December; 16(12):e41564. doi: 10.5812/hepatmon.41564.

Published online 2016 December 3. **Review Article**

Liver Illness and Psychiatric Patients

Paul Carrier,[1,2,*] Marilyne Debette-Gratien,[1,2] Murielle Girard,[3] Jérémie Jacques,[1] Philippe Nubukpo,[4]

Medications and drugs	Potential Toxicity	Type of Injury	In Hepatic Insufficiency
Benzodiazepines	Rare	Cytolytic or cholestatic	Induce or aggravate encephalopathy
Mood stabilizers			
Valprate	+	Steatosis, mitochondrial toxicity	Contra-indicated Careful prescription
Carbamazepine	Rare	Idiosyncratic	
Lithium	Rare	Hyperbilirubinemia	Can aggravate liver function
Anti-depressants			
Tricyclics	+	Idiosyncratic, more rarely hypersensitivity	Change of dose or interruption in the majority of treatments
SSRI	+	Generally cytolytic injury	
SNRI	+		
Buproprion	Rare	Essentially risk of steatosis (clozapine, olanzapine ++)	
Neuroleptics			Generally contra- indicated in patients with decompensated cirrhosis
Phenothiazines	++	More rarely, idiosyncratic or hypersensitivity	
Butyrophenones	+		
Clozapine	+		
Olanzapine	+		
Quetiapine	Rare		
Risperidone	Rare		

Table 4D. Drug-drug interactions between HCV DAAs and central nervous system drugs.

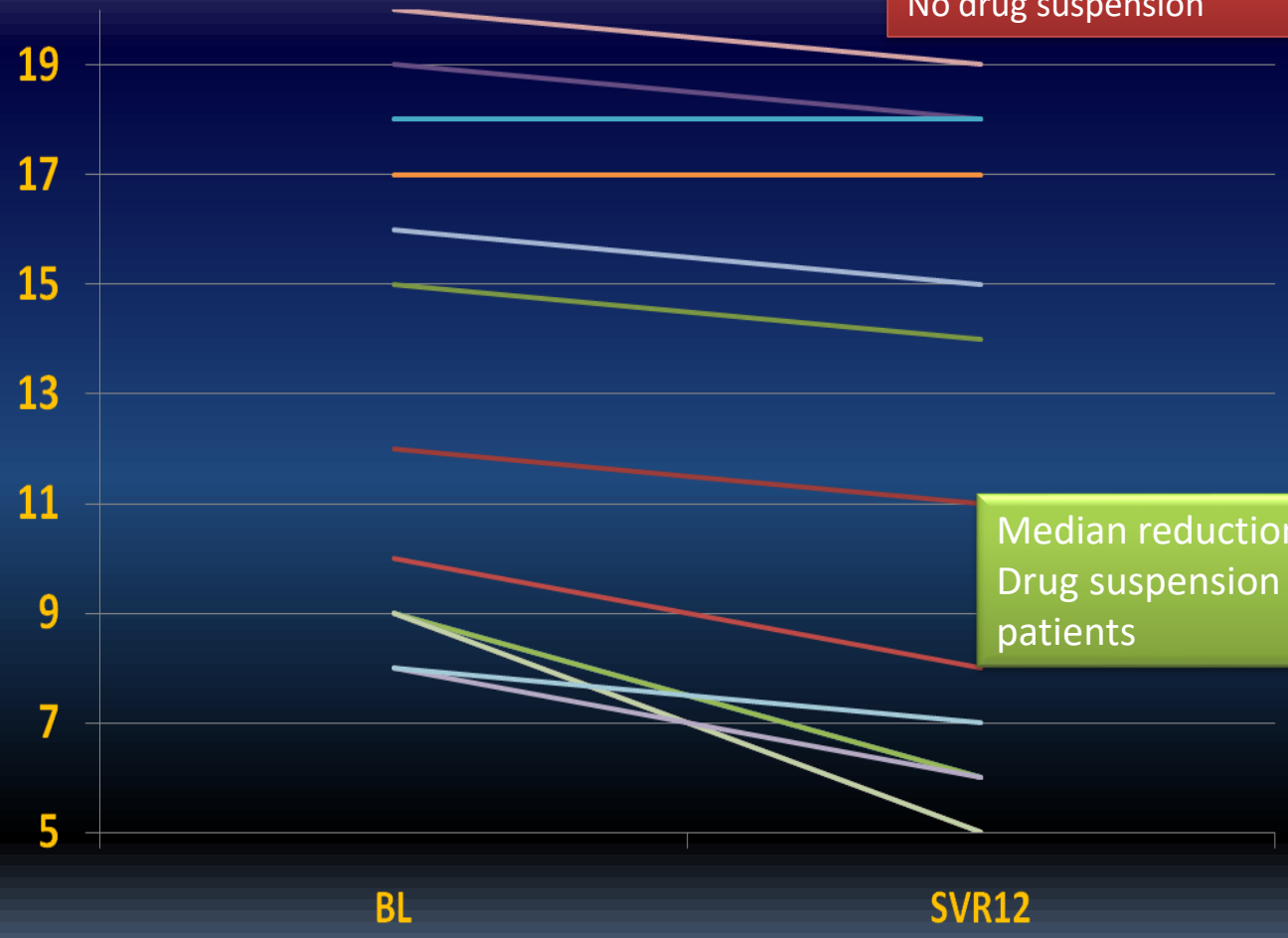
		SOF	SOF/ LDV	SOF/ VEL	OBV/ PTV/r + DSV	GZR/ EBR	SOF/ VEL/ VOX	GLE/ PIB
Anti-depressants	Amitriptyline	◆	◆	◆	■	◆	◆	◆
	Citalopram	◆	◆	◆	◆	◆	◆	◆
	Duloxetine	◆	◆	◆	◆	◆	◆	◆
	Escitalopram	◆	◆	◆	◆	◆	◆	◆
	Fluoxetine	◆	◆	◆	◆	◆	◆	◆
	Paroxetime	◆	◆	◆	◆	◆	◆	◆
	Sertraline	◆	◆	◆	■	◆	◆	◆
	Trazodone	◆	◆	◆	■	◆	◆	◆
	Venlafaxine	◆	◆	◆	■	◆	◆	◆
Anti-psychotics	Amisulpiride	◆	◆	◆	◆	◆	◆	◆
	Aripiprazole	◆	◆	◆	■	■	◆	■
	Chlorpromazine	◆	◆	◆	■	◆	◆	◆
	Clozapine	◆	◆	◆	■	◆	◆	■
	Flupentixol	◆	◆	◆	■	◆	◆	◆
	Haloperidol	◆	◆	◆	■	◆	◆	◆
	Olanzapine	◆	◆	◆	■	◆	◆	◆
	Paliperidone	◆	■	◆	◆	◆	■	■
	Quetiapine	◆	◆	◆	●	■	◆	■
	Risperidone	◆	◆	◆	■	◆	◆	◆
	Zuclopentixol	◆	◆	◆	■	◆	◆	◆

The effect of SVR on psychiatric disorders

- Theoretically, the HCV resolution could improve the psychiatric diseases
- This effect could be probably observed only in mild-moderate diseases such as anxiety or sleep disorders (with chance of drug suspension).
- In severe psychiatric diseases remains difficult the treatment suspension/reduction and the effect of HCV eradication is not easily demonstrable

Effect of SVR on the sleep disorders

Insomnia score
ISI index
0-7 normal
8-14 mild
15-21 moderate
>21 severe



SUMMARY

- Extra-hepatic manifestations have a great impact on the quality of life and costs in HCV+
- Viral eradication generally leads to improvement of symptoms related to extra-hepatic morbidities
- Major benefit were observed in glicemic control and mixed cryoglobulinemia
- Not fully demonstrable this effect on more severe psychiatric disorders


Thanks for your Time