Quizz 1

Nouveau patient, transaminases normales et sérologie Hep C +

1. Il n'y a rien à faire vu l'absence d'hépatite biologique.
2. Je vais régulièrement vérifier les TGP et si +, je referai la sérologie.
3. Je l'interroge sur les facteurs de risque d'avoir pu contracter l'Hep C.
4. Je demande une virémie quantitative.

Quizz 2

Un patient avec sérologie Hep C + et transaminases normales n'est pas contagieux

– vrai ou faux ?

Quizz 3

Si un patient aux transaminases normales est séro+ HCV...

1. … après un traitement anti-HCV, il n'est pas guéri de cette infection.
2. … (hors contexte d'un traitement) il n'a que 15% de risque d'avoir développé une fibrose hépatique significative.
3. … (hors contexte d'un traitement), c'est qu'il s'est spontanément guéri de son hépatite virale C au stade précoce.

Quizz 4

Elle avait des Ac anti-VHC en 2010 et était en bonne santé ; rien ne fut donc fait. Elle devient fatiguée. Ses TGO sont à 1.1 x Nle, ses TGP à 1.4 x Nle. Que faire ?

1. Redoser les Ac anti-HCV.
2. Virémie qualitative (PCR ⊕ ou ⊗).
3. Adresser à l'hépatologue.
4. Interdire de voir ses petits-enfants avant la mise au point du dit hépatologue.

Quizz 5

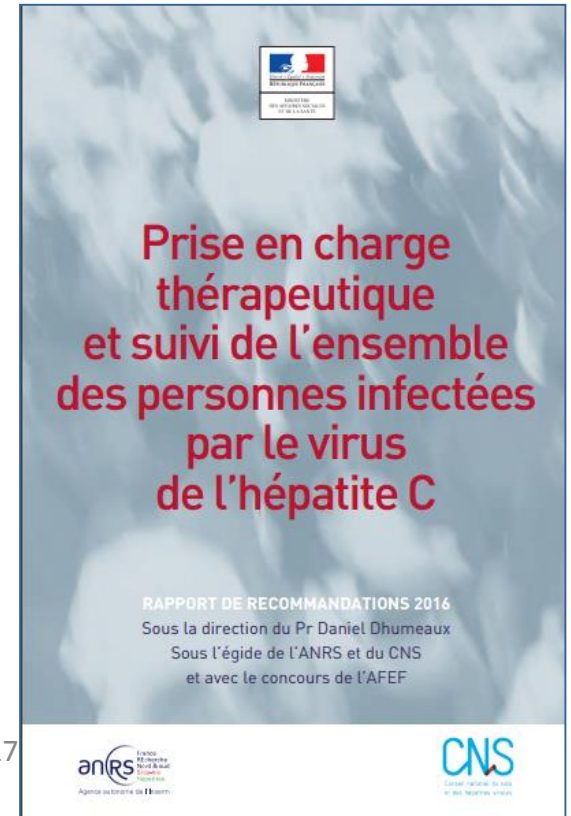
Mon patient, 78 ans, a une bonne santé, des TGP élevées et des Ac anti-HCV :

1. Il a certainement aujourd'hui une hépatite C.
2. Vu son âge, il ne tirera aucun bénéfice d'un traitement par antiviraux oraux modernes.
3. Il ne tirerait de bénéfice d'un traitement par antiviraux oraux modernes que s'il n'est pas arrivé au stade de cirrhose.

Une référence

→

http://www.afef.asso.fr/ckfinder/userfiles/files/recommandations-textes-officiels/recommandations/rapportDhurmeaux2.pdf



Hepatitis C in Belgium - 2017
An ever changing paradigm

Docteur Jean-Paul Martinet

jean-paul.martinet@uclouvain.be

CHU UCL Namur

Mont-Godinne

Equipes - réseau

Dr O. Borgniet Dr M. Gehenot Dr Z. Hassoun
Dr JP Martinet

CHU
UCL
NAMUR

Dinant • Godinne • Sainte-Elisabeth

Généralistes – Hépatologues - Chirurgiens

HCV transmission

Hepatitis C is transmitted by exposure to **infected blood**, primarily through:

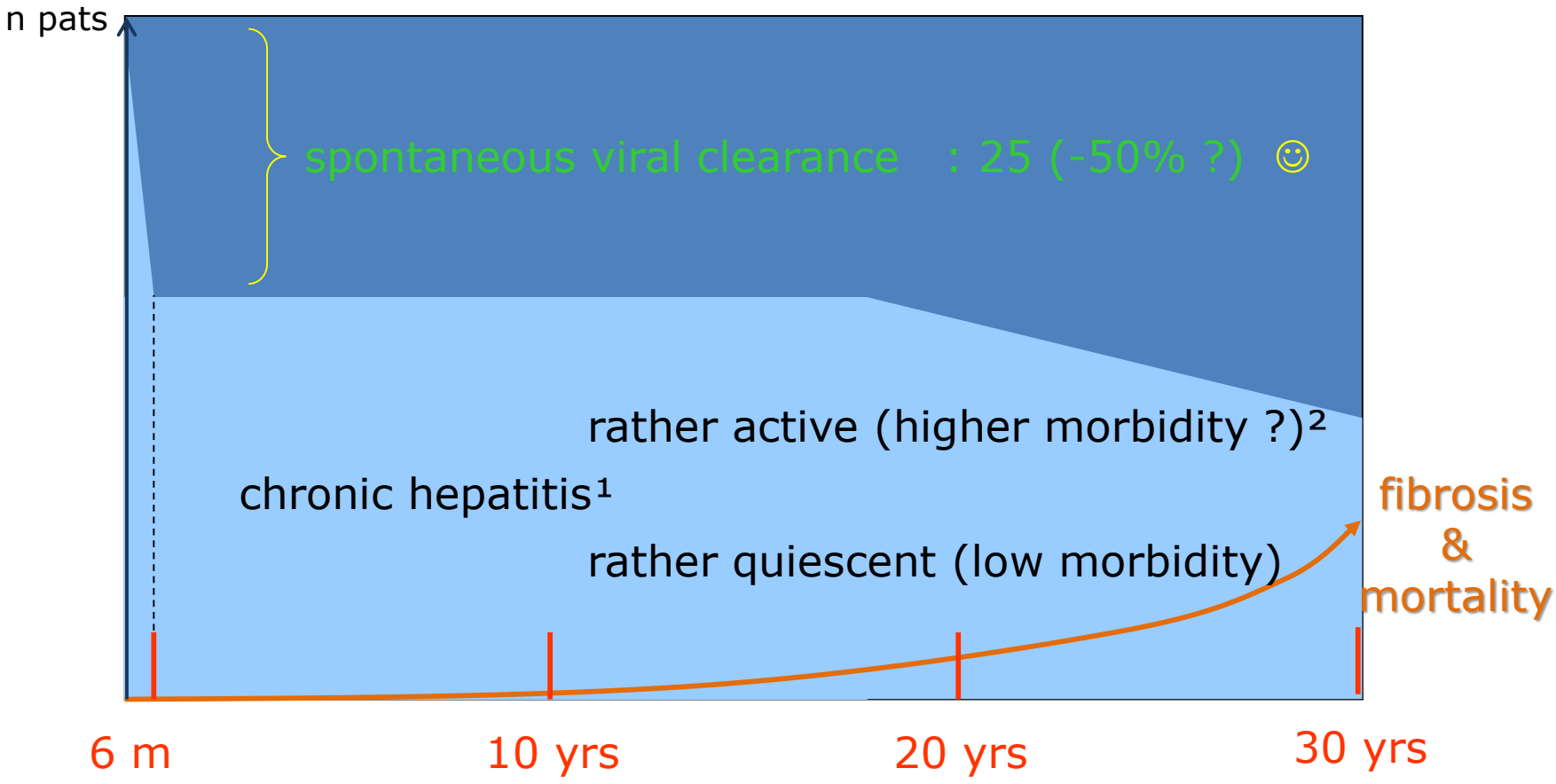
- Shared drug-use paraphernalia
- Transfusion with infected blood products (rare after 1992)
- Hemodialysis

Hepatitis C is transmitted **infrequently through**:

- Occupational exposure
- Sexual activity with acutely and chronically infected persons
- Mother-to-child transmission

Transmission route*	Common	Infrequent	Never
Foodborne			X
Waterborne			X
Occupational exposure		X	
IV drug use	X		
Transfusion (before 1992)	X		
Hemodialysis	X		
Sexual		X	
Household		X	
Mother to newborn		X	

Natural history of hepatitis C



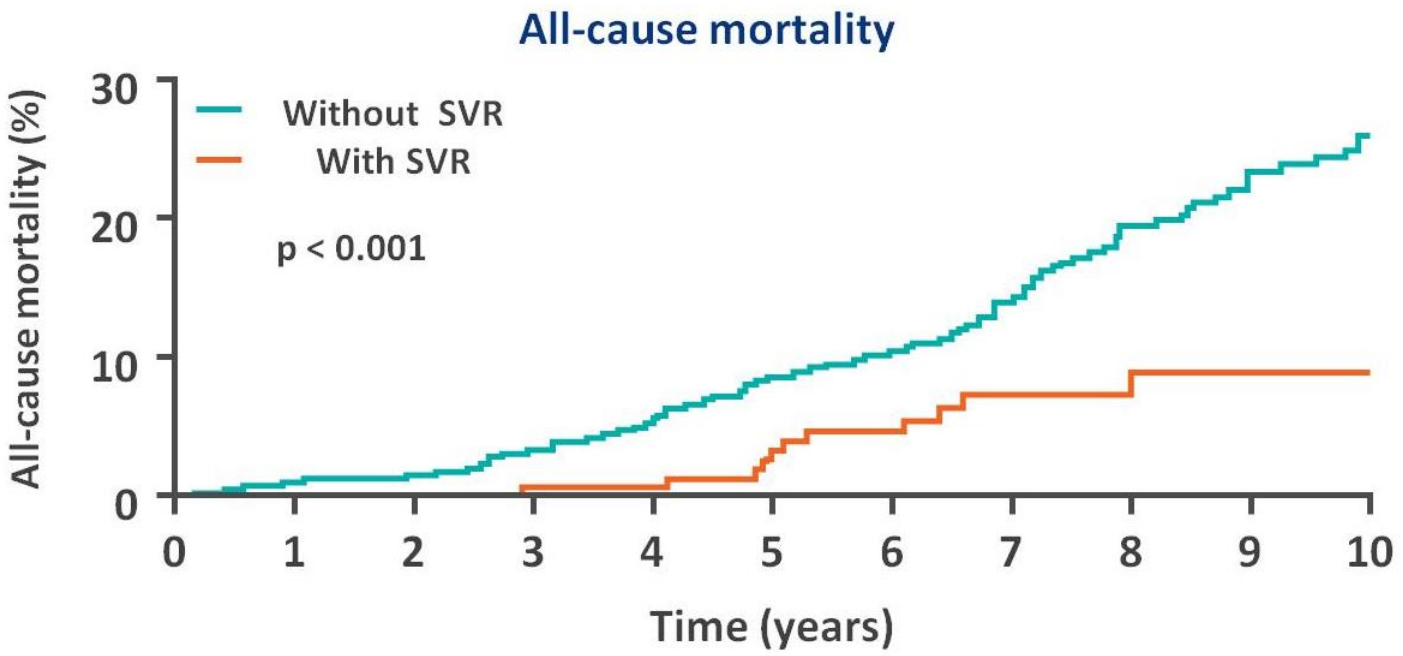
¹ most cases of HCV seropositive patients
² including HCV-related lymphoma, cryoglobulinemia, extreme fatigue

Extra-hepatic manifestations

MEH de l'hépatite C → dépistage intelligent !

- fatigue, psychasthénie, dépressions
- cryoglobulinémies mixtes
  - purpura
  - arthralgies (cryo = FR-like)
  - polynévrites
  - glomérulonéphrites
  - pseudo-Sjögren
- thrombocytopénies
- affections cutanées
  - sécheresses (cut.-muqueuses) lichen plan
  - phénomène de Raynaud
  - livedo
- lymphome B grandes cellules

Mortality rate w/wo SVR

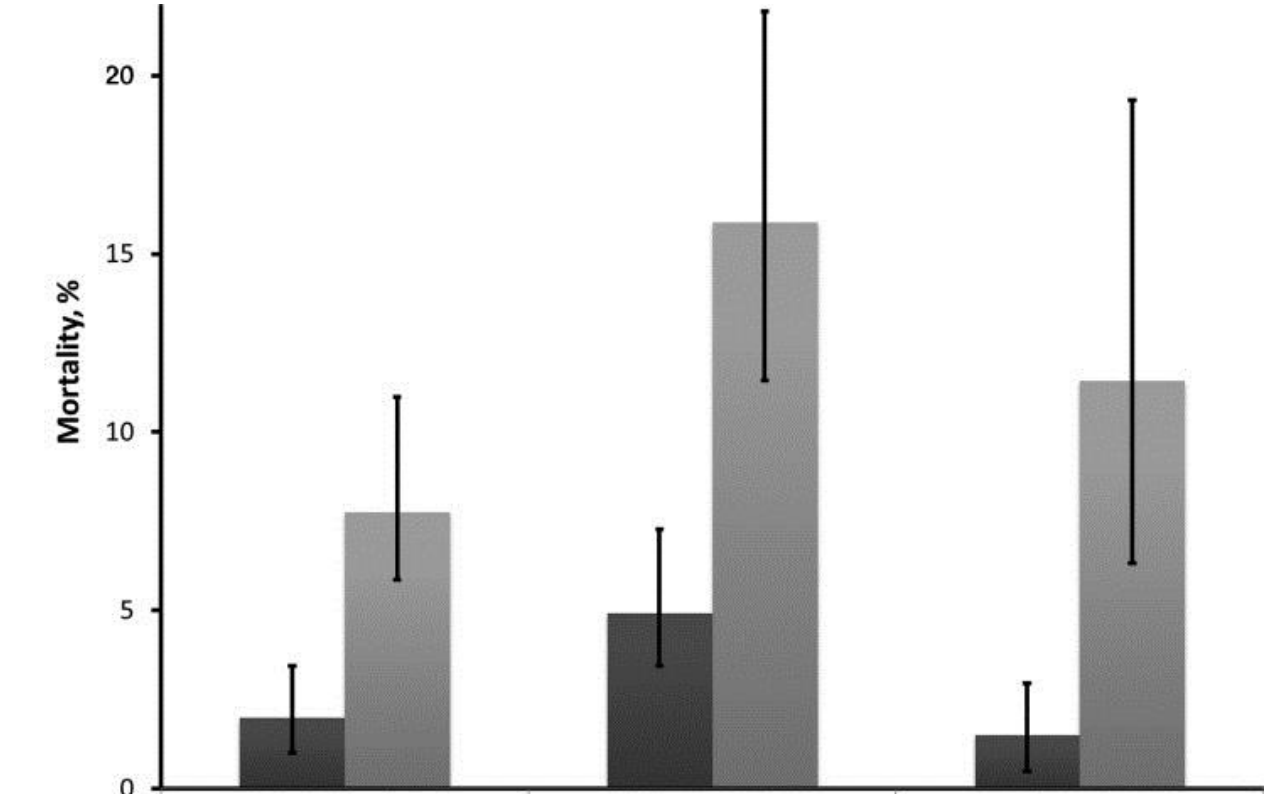


No. at risk

Without SVR	405	393	382	363	344	317	295	250	207	164	135
With SVR	192	181	168	162	155	144	125	88	56	40	28

SVR decreases mortality rates in patients with advanced fibrosis (Ishak score 4–6)

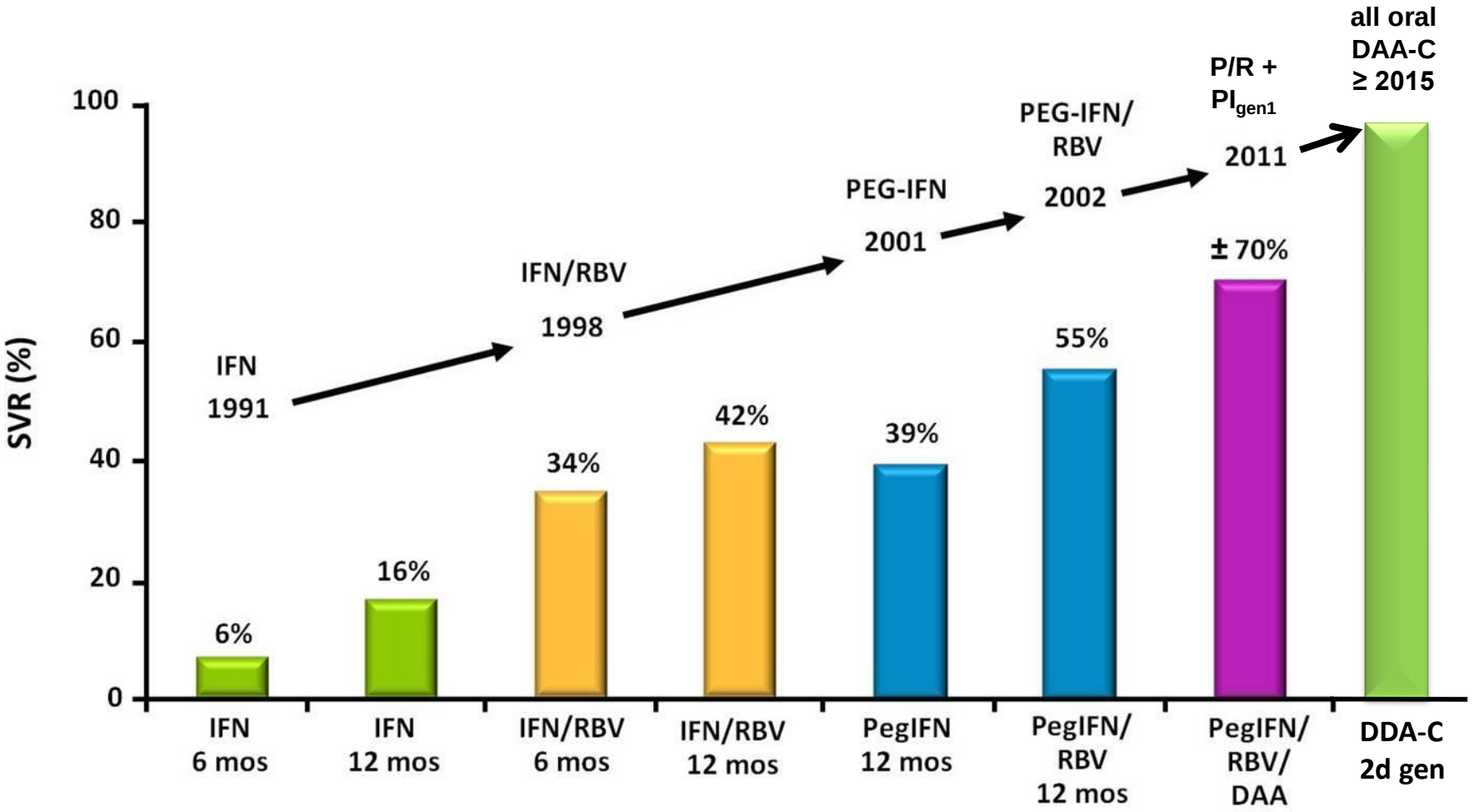
Mortality rate w/wo SVR



	General cohort	Cirrhotic cohort	Co-infected cohort
SVR	1.98 (1.00, 3.45)	4.90 (3.45, 7.28)	1.49 (0.50, 2.96)
non-SVR	7.75 (5.86, 10.98)	15.88 (11.44, 21.80)	11.44 (6.33, 19.31)

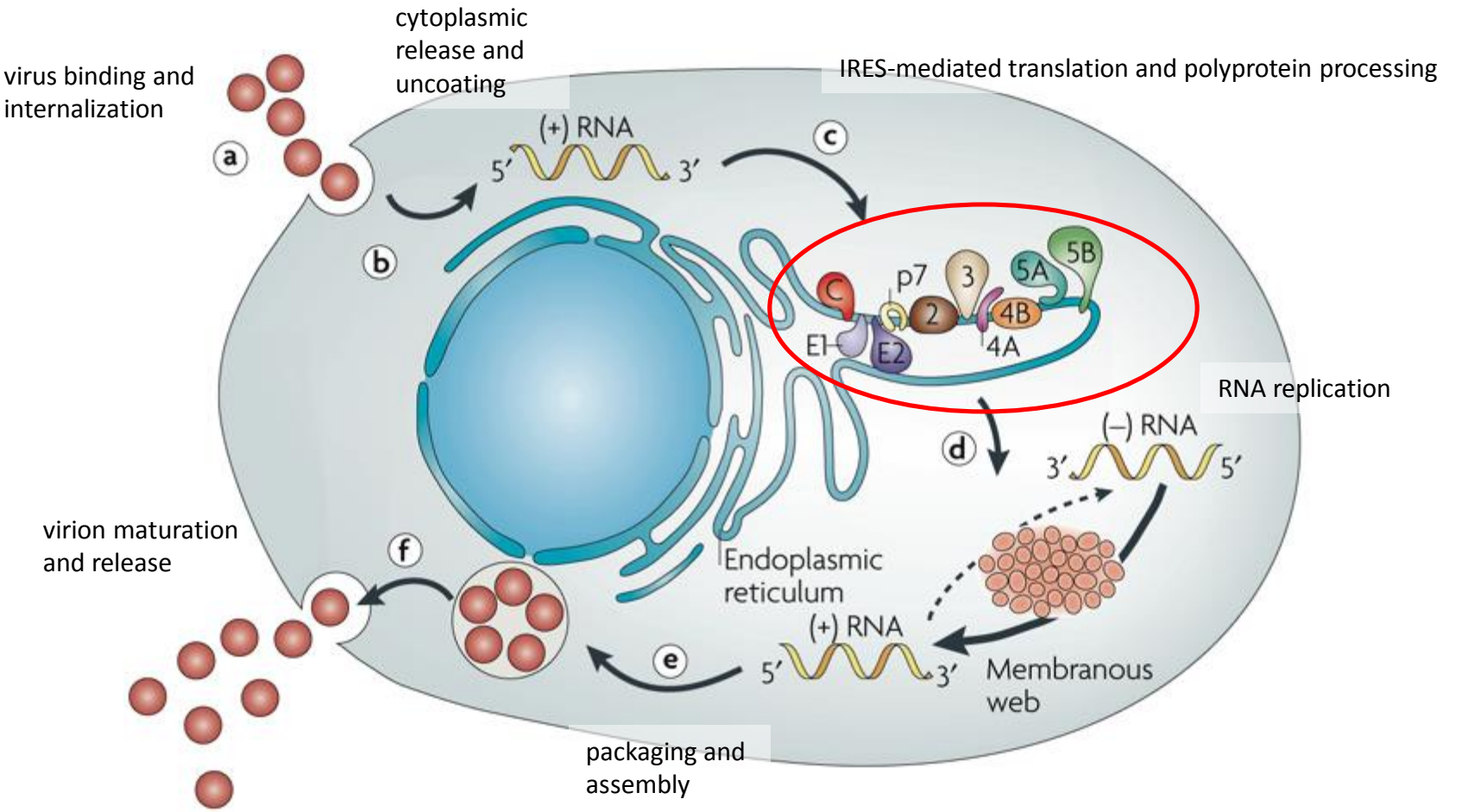
Simmons,- CID 2015

Response rates from IFNα-based to all oral therapies



Adapted from the US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27-28, 2011, Silver Spring, MD. Available at: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AntiviralDrugsAdvisoryCommittee/UCM254076.pdf. Accessed July 18, 2013.

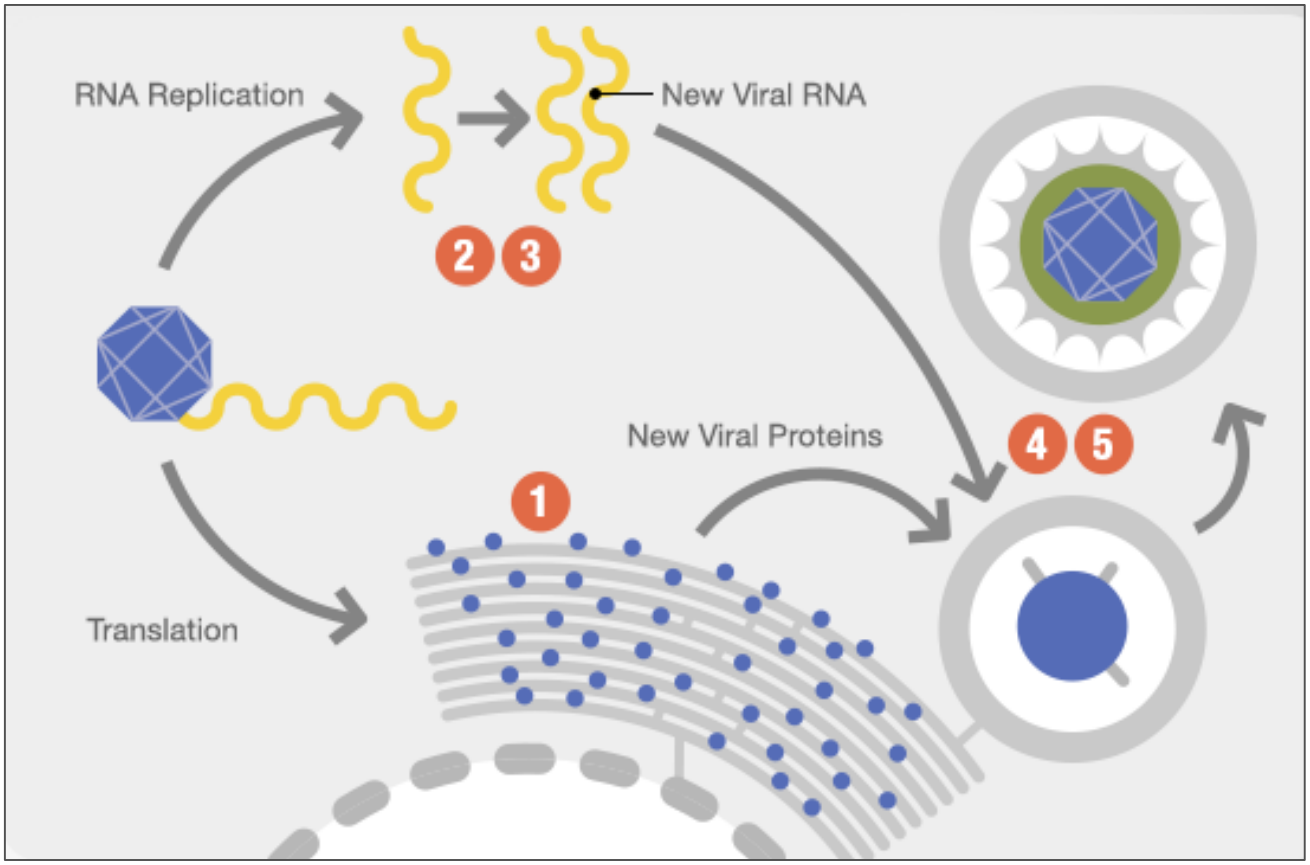
The hepatitis C virus life cycle



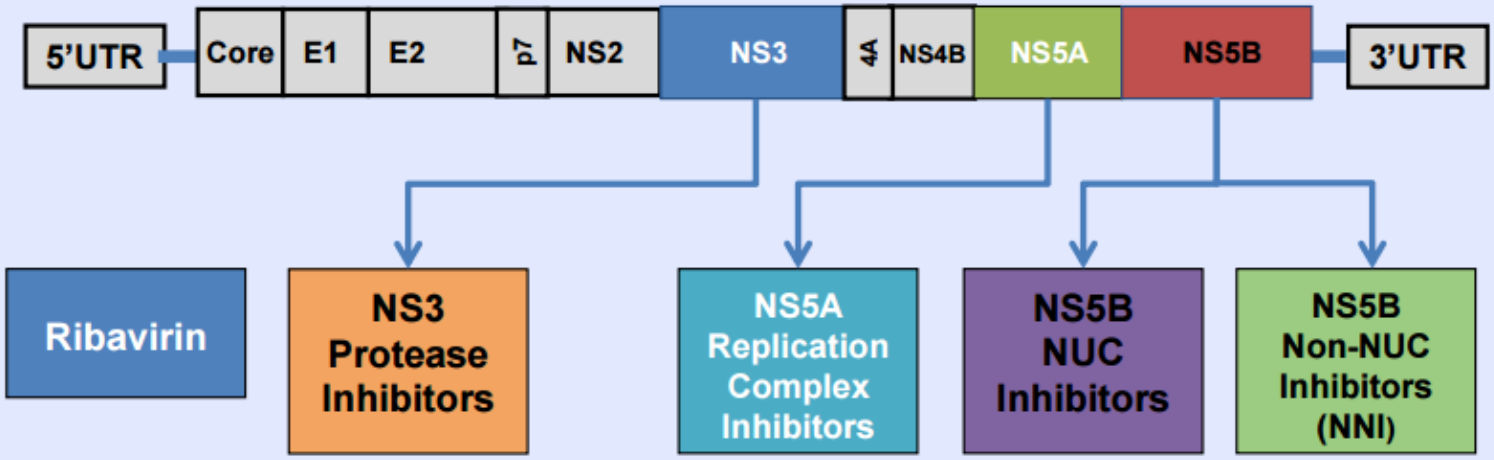
Moradpour,- Nature Reviews-Microbiology 2007

Where to hit

1. **Protease inhibitor** (cyclic and linear)
2. **NS5B nucleoside polymerase inhibitor**
3. **NS5B non-nucleoside polymerase inhibitor**
4. **NS5A inhibitor**
5. **Cyclophiline inhibitor**



Anti-HCV DAA's



NB : common root name for each drug class

Who should be treated ?

- All patients (…)
  - who are willing to be treated
  - treatment-naïve & -experienced
  - and who have no contra-indication to treatment.

- Costs induce prioritization

« Prioritization$_{2015}$ » → « w/o delay$_{2016}$ » (1)

- F4 + F3 → **F2** (jan. 2017)
- significant extra-hepatic disease
  - cryoglobulinemia and vasculitis
  - immune complex-related nephropathy
  - non-Hodgkin B cell lymphoma
  - debilitating fatigue
- HIV and/or HBV co-infection
- transplantations :
  - pats awaiting liver transplantation if MELD score 18-20, i.e. waiting time > 6 months
  - non-liver solid organ transplanted pats
  - recurrence after liver transplantation
  - stem cells transplant pats

EASL 2016 guidelines statement

« Prioritization$_{2015}$ » → « w/o delay$_{2016}$ » (2)

- diabetic pats
- higher risk for HCV transmission
  - IVDU
  - prisoners
  - haemodialysis
  - child-bearing potential
  - very active homosexual men

EASL 2016 guidelines statement

Remboursements B 2017

- **F2** (jan. 2017)
- facteurs de risque reconnus permettant le remboursement quelque soit le niveau de fibrose :
  - transplantations (organes pleins – moëlle, listé ou Tx faite)
  - co-infections : HCV + HIV et HCV + HBV
  - dialysé chronique
  - patients avec coagulopathie (dont hémophilie)
  - patients avec hémoglobinopathie
  - maladie extra-hépatique liée au VHC :
    - lymphome B diffus à grandes cellules
    - vasculite immuno-médiée
    - cryoglobulinémie avec atteinte rénale

New from mid 2016

- **IFN-containing options**
  - Not more recommended
    - heterogeneity of per capita outcomes and health insurance coverages
    - efficacy, ease to use and tolerability of DAAs overcome these historical constraint
  - remain acceptable if IFN-free solutions unavailable

EASL 2016 guidelines statement

New in 2016

- **SOF + SIM**
  - Real world data show relatively low SVR_{12} SOF-SIM comparing combinations even containing SOF
  - SIM not recommended if other DAAs available
  - SOF remains the backb of many combinations

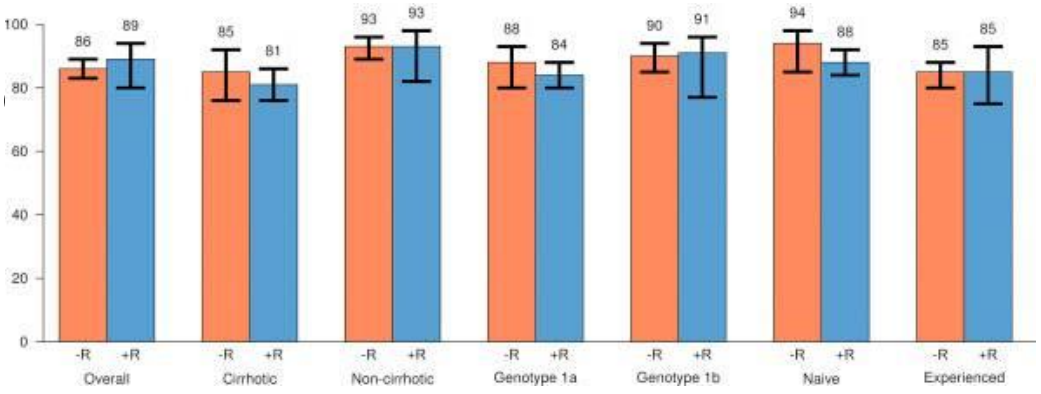
- SOF-SIM $\rightarrow$ SVR_{12} : 84 %

  German Hepatitis-C Registry[a]

Table 1: Treatment regimens and SVR12 data of patients with HCV GT1*

Regimen	Patients n	SVR12 ITT n/total (%)	NR/relapse n/total# (%)	lost n/total (%)
IFN+RBV+SOF	303	238/303 (79%)	52/303 (17%)	13/303 (4%)
SIM+SOF ± RBV	256	215/256 (84%)	31/256 (12%)	10/256 (4%)
SOF+DCV ± RBV	432	398/432 (92%)	24/432 (6%)	10/432 (2%)
SOF/LDV ± RBV	833	750/833 (90%)	53/833 (6%)	30/833 (4%)
OBV/PTV/r + DSV ± RBV	95	83/95 (87%)	9/95 (9%)	3/95 (3%)

HCV-TARGET study[b] in GT1 pats



[a] Mauss,- Jhepatol 2016; 64, S828

[b] MSulkowski,- Gastroenterology 2016

New in 2016, 2017

- **GT-2**
  - exit SOF + RBV
  - welcome to
    - SOF + velpatasvir (VEL)
    - SOF + daclatasvir (DCV)

New in 2016, 2017

- **GT-3**
  - exit SOF + PegIFN + RBV
  - welcome to
    - SOF + velpatasvir (VEL)
    - SOF + daclatasvir (DCV)
  - Coming soon :
    - glecaprevir + pibrentasvir
    - SOF + VEL + voxilaprevir

New in 2016

- **HIV-HCV co-infection**
  - no more considered as « special group »[a]
  - Recommended combos
    - SOF + DCV
    - SOF + LDV
    - SOF + VEL
    - …
  - drug to drug interactions lead the choice of presumably well tolerated DAAs

All-oral anti-HCV DAAs

Inhibited enzymes				Brand Names	Pharma		
NS-3 PI	NS-5A RCI	NS-5B Nuc I	NS-5B NonNuc I		mg/pil	dose	€ / 28 pils
SIM				Olysio®	150	qd	*8833*
		SOF		Sovaldi®	400	qd	*14487*
	DCV			Daklinza®	60 (30)*	qd	*9760*
PTV(riton)	OMV			Viekirax®	75/12,5	2 pils qd	*12678*
			DSV	Exviera®	250	bid	*1102*
	LDV	SOF		Harvoni®	90/400	qd	*18285*
	VEL	SOF		Epclusa®	100/400	qd	***18285***
GZR	EVR			Zepatier®	100/50	qd	***15953***

SIM = simeprevir ; SOF = sofosbuvir ; DCV = daclatasvir ; PTV(riton) = ritonavir-boosted paritaprevir ; OMV = ombitasvir ; DSV = dasabuvir ; LDV = ledipasvir ; VEL = velpatasvir ; GZR = grazoprevir ; EVR = elbasvir

All-oral anti-HCV DAAs

Brand Names	Caveats						
	Renal impairm (CrCl < 30 ml/min)	Child-PT B / C	CYP3A inducers[1]	P-gp inducers[1]	CYP3A4 inhibitors[2]	OATP inhibitors[3]	others
Olysio®	allowed	not indicated	avoid		avoid	avoid	photoSe
Sovaldi®	not indicated	allowed	allowed	avoid	allowed	allowed	
Daklinza®	allowed	allowed	avoid	avoid	avoid	avoid	30 or 90 mg dpding on anti-HIV
Viekirax®	allowed	not indicated	avoid	avoid	avoid	avoid	anti-HIV caution
Exviera®	allowed	not indicated	avoid	avoid	avoid	avoid	
Harvoni®	not indicated	allowed	caution	avoid	caution	allowed	anti-HIV caution
Epclusa®	not indicated[4]	allowed	avoid	avoid	avoid	avoid	PPI spacing
Zepatier®	allowed	not indicated	avoid		avoid	avoid	anti-HIV caution

[1] Reduce DAA concentrations. Ex : phenytoïn, carbamazepin, RMP, rifabutin, hypericum, efavirenz…

[2] Increase DAA concentrations. Ex : amiodarone, macrolides, CyA, fluconazole, grapefruit, metronidazole, omeprazole, sertraline, valproate…

[3] Increase DAA concentrations. Ex : "HIV"-navirs, cyclosporin...

[4] VEL is not influenced itself by renal function

A key Internet resource is www.hep-druginteractions.org where recommendations are regularly updated.

All-oral anti-HCV DAAs

5 caractéristiques

- combinaisons indispensables.
- chers. Mais… merci Maggy.
- efficaces (>95% SVR en itt)
- peu d'E2
- 12 semaines (rares prolongations)

GT-1b non cirrhotic

NON CIRRHOTICS				duration (wks)	RBV need		Severe renal impairment
*Experienced**							
SIM		SOF		12	no		not indicated
	LDV	SOF		12	no	* PR ± PI-1	not indicated
	VELPA	SOF		12	no		not indicated
GZR	EBR			12	no	* PR	allowed
GZR	EBR			12	RBV	* PR + PI-1	allowed
PTV	OMV		DSV	12	no		allowed
	DCV	SOF		12			not indicated
Naïve							
SIM		SOF		12	no		not indicated
	LDV	SOF		8° - 12	no	° RNA < 6 Miu	not indicated
	VELPA	SOF		12	no		not indicated
GZR	EBR			12	no		allowed
PTV	OMV		DSV	12	no		allowed
	DCV	SOF		12			not indicated

** Experienced : former IFN therapy with or w/o PI.*

GT-1b cirrhotic

CIRRHOTICS					duration (wks)	RBV need		Severe renal impairment
Decompensated								
Experienced or naïve								
	VELPA	SOF			12	RBV		not indicated
	DCV	SOF			12	RBV		not indicated
	LDV	SOF			12	RBV		not indicated
Compensated								
*Experienced**								
SIM		SOF			24	no		not indicated
	LDV	SOF			12	no		not indicated
	VELPA	SOF			12	no		not indicated
GZR	EBR				12	no	* PR	allowed
GZR	EBR				12	RBV	* PR + PI-1	allowed
PTV	OMV			DSV	12	no		allowed
	DCV	SOF			12	RBV		not indicated
Naïve								
SIM		SOF			24	no		not indicated
	LDV	SOF			12	no		not indicated
	VELPA	SOF			12	no		not indicated
GZR	EBR				12	no		allowed
PTV	OMV			DSV	12	no		allowed
	DCV	SOF			12	RBV		not indicated

GT1a non cirrhotic

NON CIRRHOTICS				duration (wks)	RBV need	
*Experienced**						
SIM °		SOF		12	no	
	LDV	SOF		12	RBV	* DAA-naïve °
	VELPA	SOF		12	no	
GZR	EBR			12	no	* PR w/o NS5a RNPs
GZR	EBR			12	RBV	* PR + PI-1
GZR	EBR			16	RBV	* PR with NS5a RNPs
PTV	OMV		DSV	12	RBV	
	DCV	SOF		12		
Naïve						
SIM °		SOF		12	no	
	LDV	SOF		12	no	
	VELPA	SOF		12	no	
GZR	EBR			12	no	w/o NS5a RNPs
GZR	EBR			16	RBV	with NS5a RNPs
PTV	OMV		DSV	12	RBV	
	DCV	SOF		12		

** Experienced : former IFN therapy with or w/o PI.*

: no more recommended (SVR 12 : 84 - 90 %)

° even with NS5a RAVs ; if proven absence of Ravs, RBV not needed ; 24 wks if RBV not tolerated

GT1a cirrhotic

CIRRHOTICS				duration (wks)	RBV need	
Decompensated						
Experienced or naïve						
	VELPA	SOF		12	RBV	
	DCV	SOF		12	RBV	
	LDV	SOF		12	RBV	
Compensated						
*Experienced**						
SIM		SOF		24	no	
	LDV	SOF		12	RBV	* DAA-naïve °
	VELPA	SOF		12	no	
GZR	EBR			12	no	* PR w/o NS5a RNPs
GZR	EBR			12	RBV	* PR + PI-1
GZR	EBR			16	RBV	* PR with NS5a RNPs
PTV	OMV		DSV	24	RBV	
	DCV	SOF		12	RBV	
Naïve						
SIM		SOF		24	no	
	LDV	SOF		12	no	
	VELPA	SOF		12	no	
GZR	EBR			12	no	w/o NS5a RNPs
GZR	EBR			16	RBV	with NS5a RNPs
PTV	OMV		DSV	24	RBV	
	DCV	SOF		12	RBV	

° even with NS5a RAVs ; if proven absence of Ravs, RBV not needed ; 24 wks if RBV not tolerated

: no more recommended (SVR 12 : 84 - 90 %)

GT-2 non cirrhotic

NON CIRRHOTICS			duration (wks)	RBV need	Severe renal impairment
*Experienced**					
		SOF	12	RBV	not indicated
	VELPA	SOF	12	no	not indicated
	DCV	SOF	12	no	not indicated
Naïve					
		SOF	12	RBV	not indicated
	VELPA	SOF	12	no	not indicated
	DCV	SOF	12	no	not indicated

** Experienced : former IFN therapy with or w/o PI.*

: no more recommended (SVR 12 : 80 - 90 %)

GT-2 cirrhotic

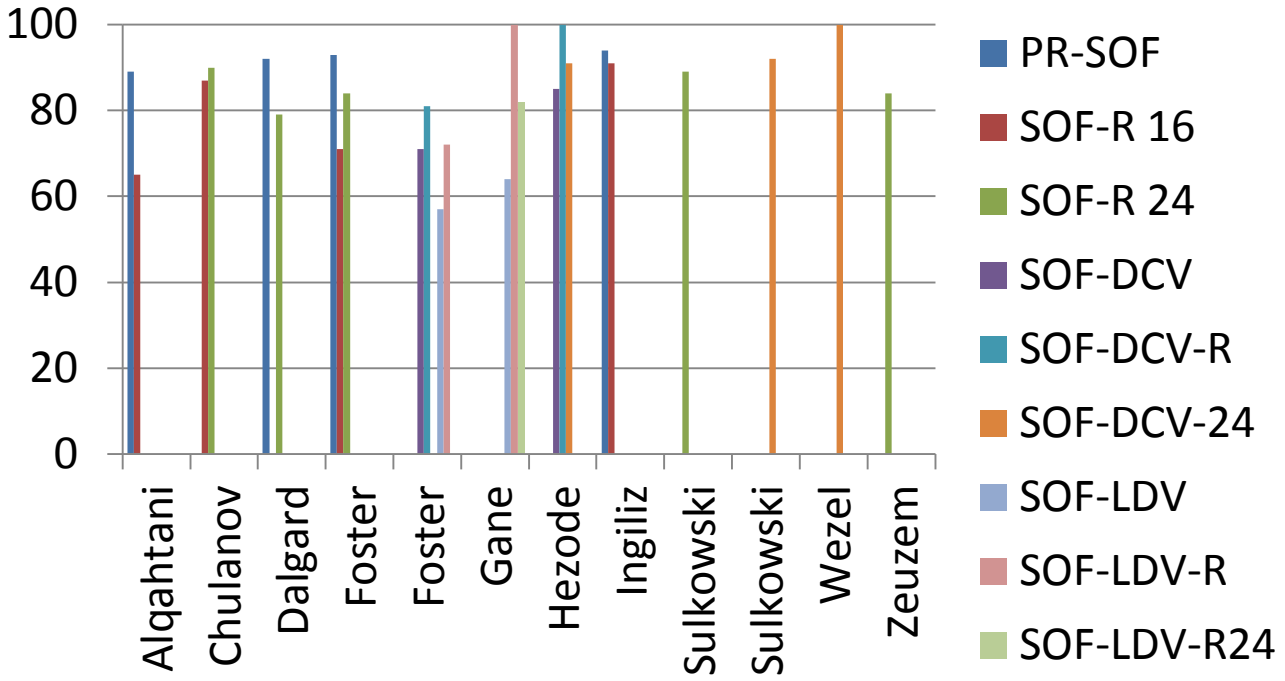
CIRRHOTICS			duration (wks)	RBV need	Severe renal impairment
Decompensated					
Experienced or naïve					
	VELPA	SOF	12	RBV	not indicated
Compensated					
*Experienced**					
		SOF	12	RBV	not indicated
	VELPA	SOF	12	no	not indicated
	DCV	SOF	12	no	not indicated
Naïve					
		SOF	12	RBV	not indicated
	VELPA	SOF	12	no	not indicated
	DCV	SOF	12	no	not indicated

** Experienced : former IFN therapy with or w/o PI.*

: no more recommended (SVR 12 : 60 - 80 %)

GT3

- GT3 becomes *the* difficult-to-treat HCV genotype



- *Peginterferon reported still valuable in 2015 recommendations*

[1] Ampuero J,- WJG 2016

GT-3 non cirrhotic

NON CIRRHOTICS			duration (wks)	RBV need	Severe renal impairment
*Experienced**					
		SOF	24	RBV	not indicated
	VELPA	SOF	12	RBV	not indicated
	DCV	SOF	12	no	not indicated
Naïve					
		SOF	24	RBV	not indicated
	VELPA	SOF	12	no	not indicated
	DCV	SOF	12	no	not indicated

* Experienced : former IFN therapy with or w/o PI.

GT-3 cirrhotic

CIRRHOTICS			duration (wks)	RBV need	Severe renal impairment
Decompensated					
Experienced or naïve					
	VELPA	SOF	12 °	RBV	not indicated
	DCV	SOF	12[1]	RBV	not indicated
Compensated					
*Experienced**					
	VELPA	SOF	12	RBV	not indicated
	DCV	SOF	24[2]	RBV	not indicated
Naïve					
	VELPA	SOF	12	no	not indicated
	DCV	SOF	24[2]	RBV	not indicated

° Only 85% SVR12 with SOF-VEL-RBV 12 wks ;

[1] Only 71% SVR12 with SOF-DCV-RBV 12 wks ;

[2] In ALLY-3+ study 16 weeks of SOF-DCV-RBV increased the SVR12 to 92% (n=26)

GT-4 non cirrhotic

NON CIRRHOTICS			duration (wks)	RBV need	Severe renal impairment
*Experienced**					
PTV	OMV		12	RBV	allowed
	LDV	SOF	12	no	not indicated
	VELPA	SOF	12	no	not indicated
	DCV	SOF	12	no	not indicated
SIM		SOF	12	no	not indicated
GZR	EBR		16	RBV	allowed
Naïve					
PTV	OMV		12	RBV	allowed
	LDV	SOF	12	no	not indicated
	VELPA	SOF	12	no	not indicated
	DCV	SOF	12	no	not indicated
SIM		SOF	12	no	not indicated
GZR	EBR		12	no	allowed

* Experienced : former IFN therapy with or w/o PI.

GT-4 cirrhotic

CIRRHOTICS				duration (wks)	RBV need	Severe renal impairment
Decompensated						
Experienced or naïve						
	VELPA	SOF		12	RBV	not indicated
Compensated						
*Experienced**						
PTV	OMV			12	RBV	allowed
	LDV	SOF		12	no	not indicated
	VELPA	SOF		12	no	not indicated
	DCV	SOF		12	RBV°	not indicated
SIM		SOF		24	no	not indicated
GZR	EBR			16	RBV	allowed
Naïve						
PTV	OMV			12	RBV	allowed
	LDV	SOF		12	no	not indicated
	VELPA	SOF		12	no	not indicated
	DCV	SOF		12	RBV°	not indicated
SIM		SOF		24	no	not indicated
GZR	EBR			12	no	allowed

GT-5 & GT-6

			duration (wks)	RBV need
CIRRHOTICS				
Decompensated				
Experienced or naïve				
	VELPA	SOF	12	RBV
Compensated				
*Experienced**				
	LDV	SOF	12	no
	VELPA	SOF	12	no
	DCV	SOF	12	no
Naïve				
	LDV	SOF	12	no
	VELPA	SOF	12	no
	DCV	SOF	12	no
NON CIRRHOTICS	Same as compensated cirrotics			

* Experienced : former IFN therapy with or w/o PI.

Nota : none of these combination is allowed in case of severe renal disease (CrCl < 30 ml/min/1.73m²)

DAA among genotypes - summary

Brand Names	Combination regimen				GT1a	GT1b	GT2	GT3	GT4	GT5 & 6
Sovaldi®	SOF	RBV								
Sovaldi® + Olysio®	SOF	SIM							12 naive	
	SOF	SIM	RBV						12 TE	
Harvoni®	SOF	LDV			12 naive°	8[1]-12 naive			12 naive°	12 naive°
	SOF	LDV	RBV		12 PR-exp				12 PR-exp	12 PR-exp
Sovaldi + Daklinza®	SOF	DCV			12 naïve[hiv]	12 DAAnaïve	12	12 ? F3	12 naive	12 naive°
	SOF	DCV	RBV		12 TE/RAV[d]			12[6] 24[7]	12 TE	12 PR-exp
Epclusa®	SOF	VEL			12	12	12 naive,? F3	12 naive,? F3	12	12
	SOF	VEL	RBV		RBV not needed ?			12[5]		
Exviera® + Viekirax®	DSV	PTV®	OMV			8[2]-12				
	DSV	PTV®	OMV	RBV	12 ? F3	24 in F4				
Viekirax®	RBV	PTV®	OMV						12	
Zepatier®	GZR	EVR			12 low vir[3]	12			12 naive	
	GZR	EVR	RBV		16 ?RAV?[4]				12 high vir[8]	

See notae next page !

Conditions still remain

Notae :

° 24 wks if PR-experienced pats not candidate for RBV

[1] Only in non-cirrhotics, low viraemic

[hiv] DCV 30mg if ritonavir/cobicistat atazanavir or elvitegravir / 90 mg if efavirenz

[d] TE = previous PR, no DAA (grade C2) ; OR proven RAV. If RBV intolerance, treat 24 wks

[2] caution in F3 pats

[3] low viremia (>800.000 ui/ml) OR proven absence of NS5A RAV

[4] viremia > 800.000 ui/ml AND unknown NSA5 RAV status

[5] unknown NS5A RAV status AND either cirrhosis or TE ; OR proven NS5A RAV

[6] unknown NS5A RAV status or presence of NS5A RAV, and NO cirrhosis.

[7] 24 wks if cirrhosis (grade C2 ; 16 wks probably sufficient).

[8] viremia > 800.000 ui/ml (by analogy with GT 1a)

however

« One Size Fits All Pills » to come soon !

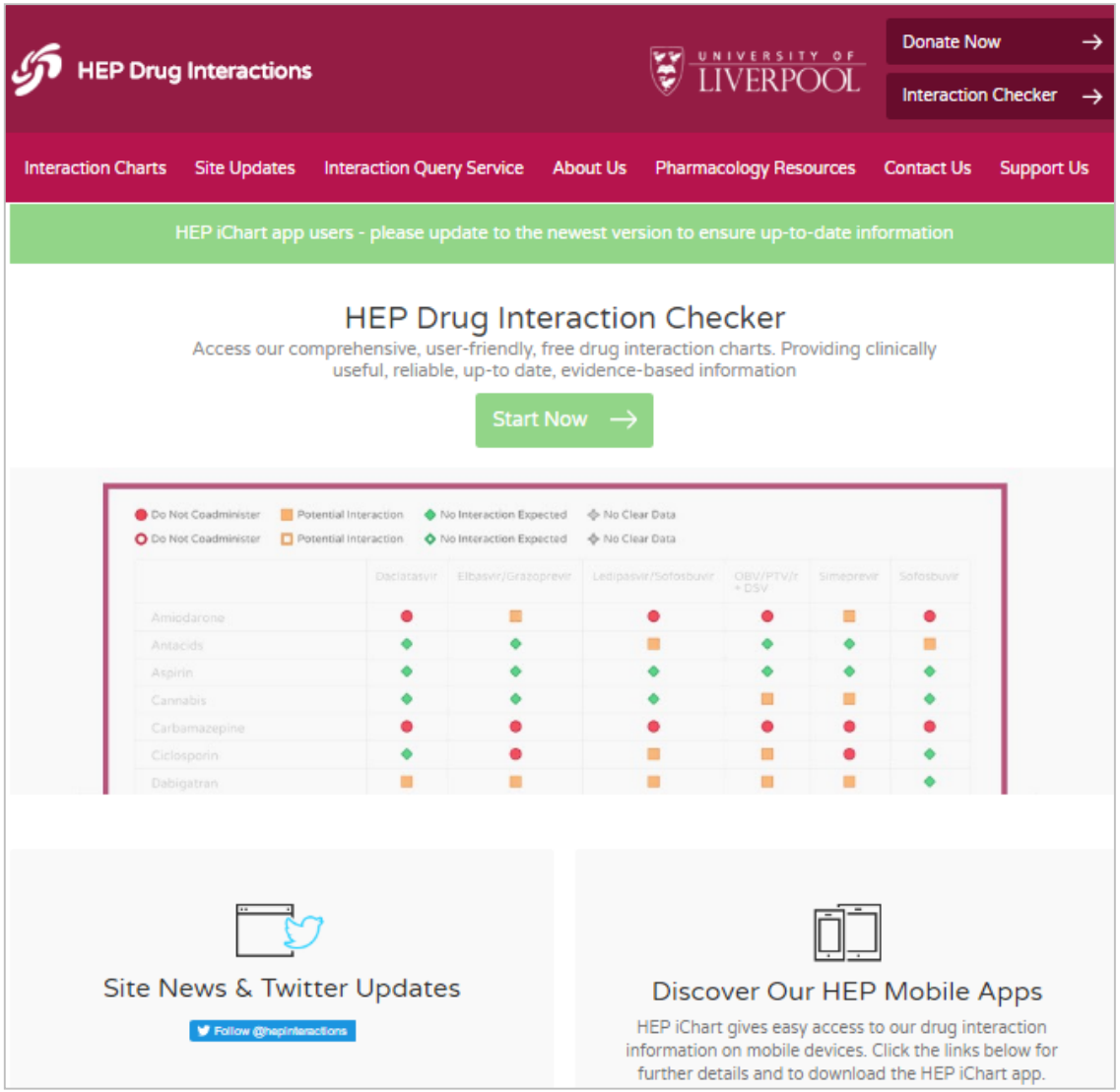
Treament monitoring

- Efficacy
- Special groups
  - decompensated cirrhosis (CPT class B)
  - severe kidney disease
- Tolerance
  - adverse effects
  - drug-drug interactions
- Liver disease remains… or appear
  - cirrhotic
  - development of NASH

Tolerance

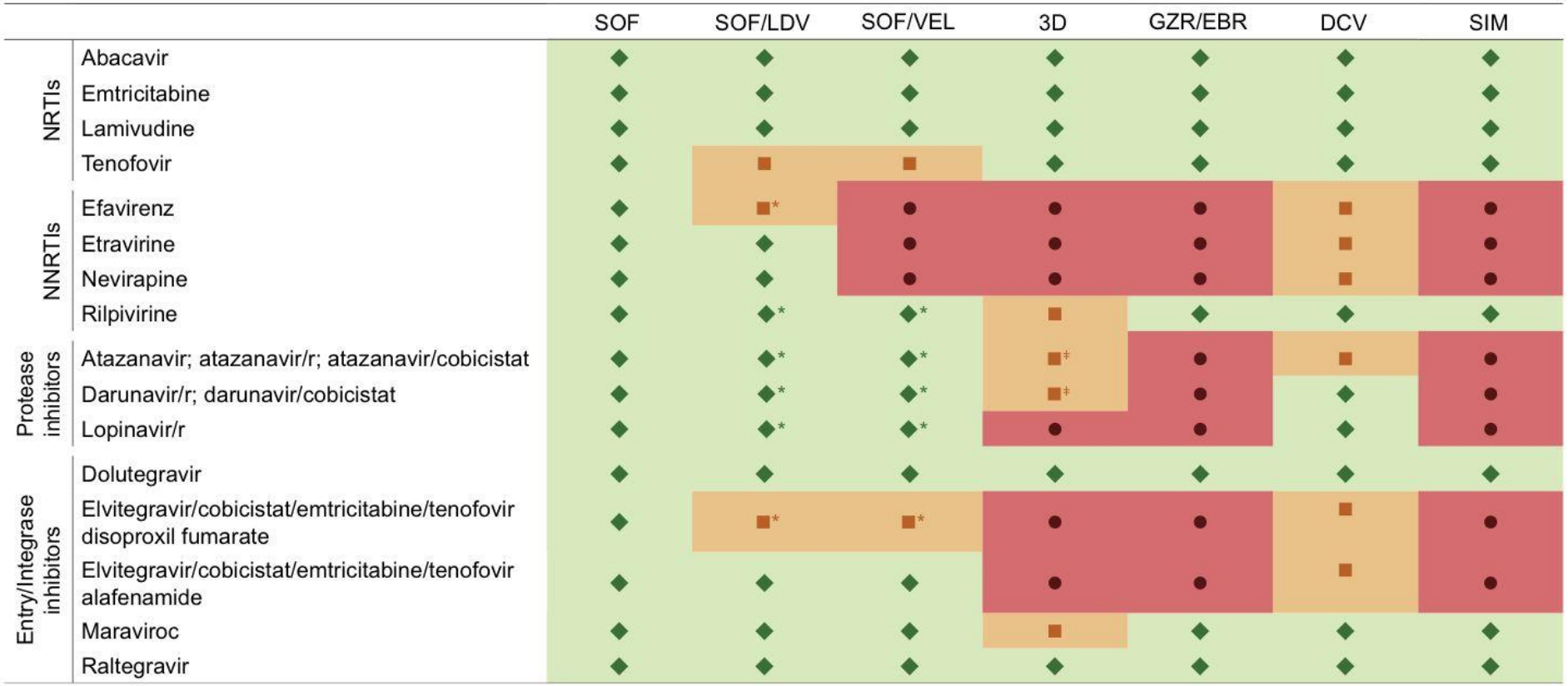
- DAAs vs placebo : same prevalence of AE
- common AE :
  - 20-25% : fatigue & headaches
  - insomnia, nausea, pruritus, ↑arterial pressure, transient hyperbilirubinemia or ALAT increase
- Post-marketing reports
  - avoid amiodarone
  - SIM : photosensitivity (even in Blacks)
  - 2D : pruritus
  - RBV : better tolerance with DAAs (≠ IFN)

http://www.hep-druginteractions.org/



DDI Recommendations

Drug-drug interactions between HCV DAAs and HIV antiretrovirals.

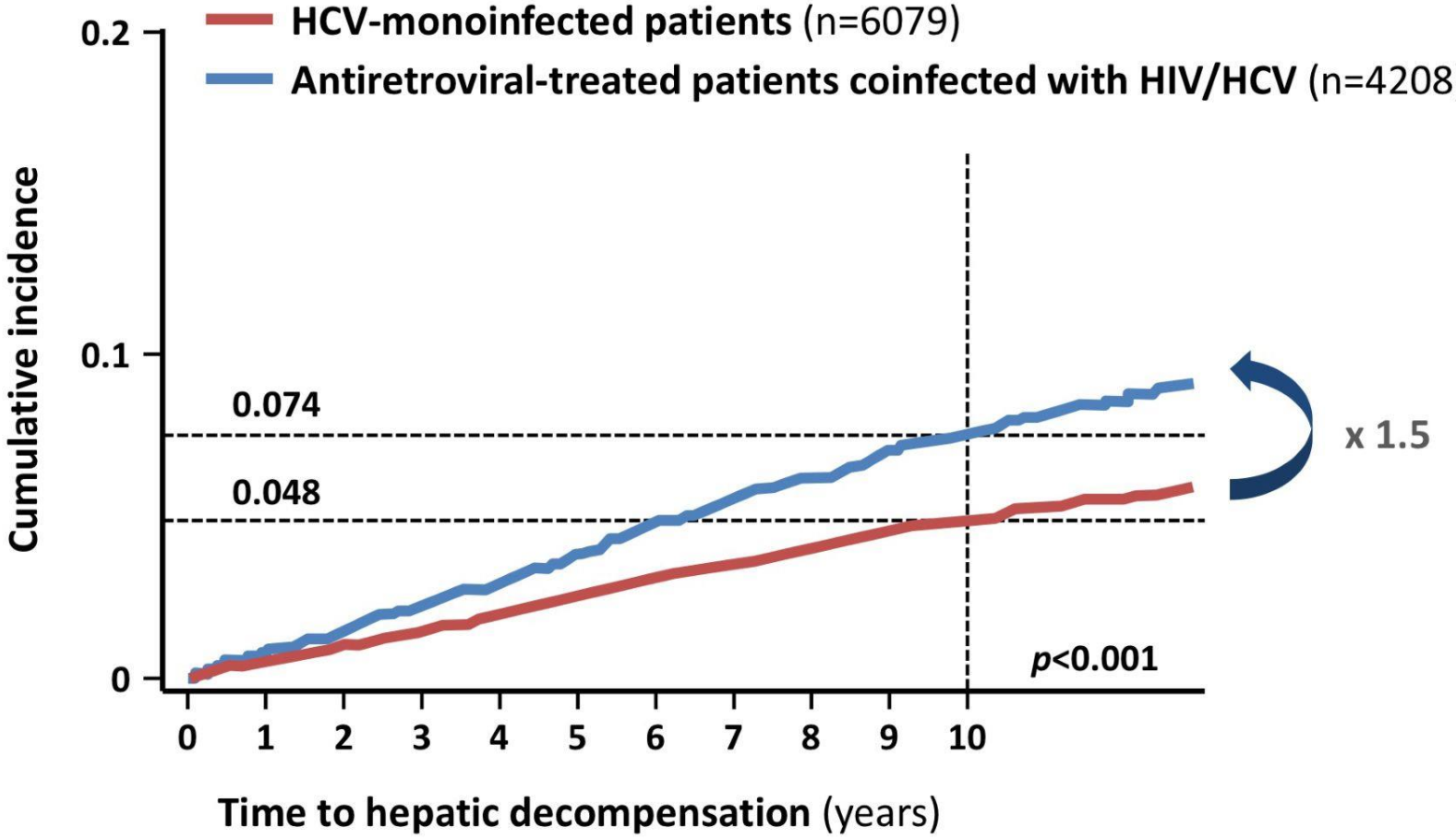


SOF, sofosbuvir; SOF/LDV, sofosbuvir plus ledipasvir; SOF/VEL, sofosbuvir plus velpatasvir; 3D, ritonavir-boosted paritaprevir, plus ombitasvir and dasabuvir; GZR/EBR, grazoprevir plus elbasvir; DCV, daclatasvir; SIM, simeprevir; r, ritonavir.

Colour legend

- ◆ No clinically significant interaction expected.
- ■ Potential interaction which may require a dosage adjustment, altered timing of administration or additional monitoring.
- ● These drugs should not be co-administered.

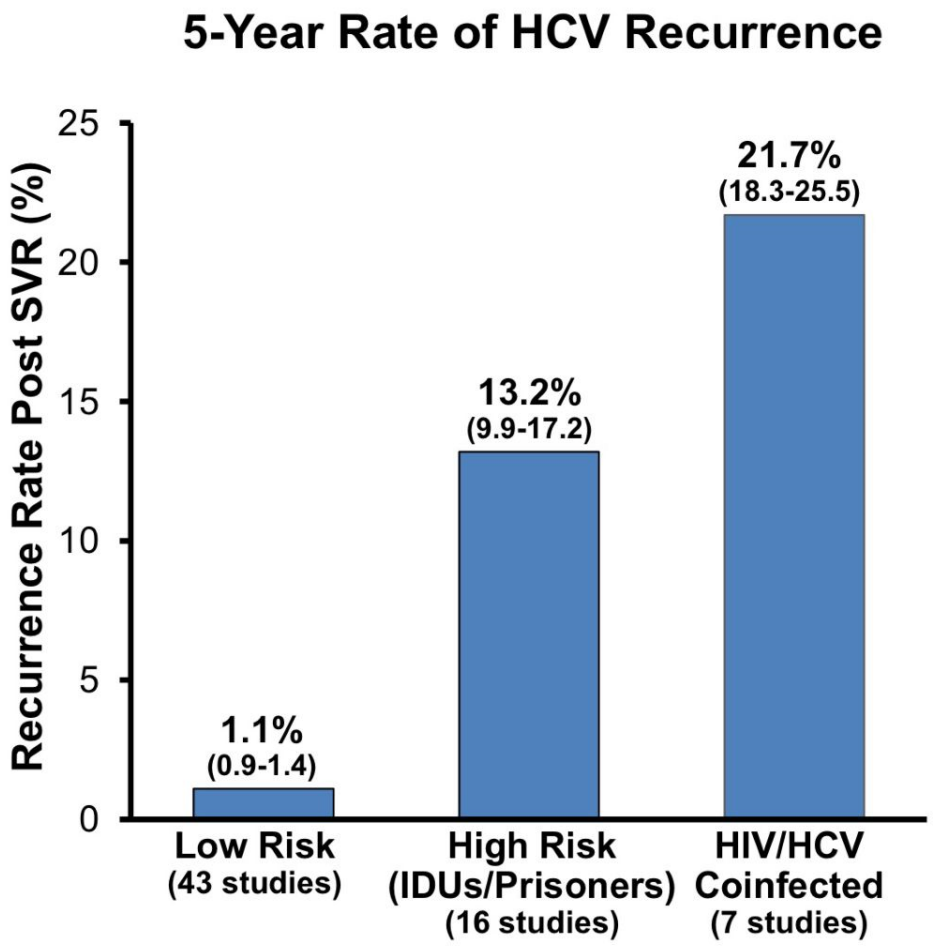
HCV Disease Progression Remains Faster in Coinfected Patients, Despite Effective ART



Adapted from: Lo Re 3rd V, et al. Ann Intern Med 2014;160:369–79.[286]

Risk of Late Relapse or HCV Reinfection After SVR

- Meta-analysis of all studies with >6 months post-SVR follow-up (66 studies, 11,071 HCV patients)
  - Monoinfected, low risk (n=9419; 4.1 years follow-up)
  - Monoinfected, high risk (n=819; 2.9 years follow-up)
  - HIV coinfected (n=833; 3.1 years follow-up)
- HCV recurrence (late relapse or reinfection)
- 5-year rate of HCV recurrence post SVR
  - 20 times more frequent among HIV/HCV coinfected versus low-risk, HCV infected
  - Large difference in event rates by risk group suggest reinfection is significantly more common than relapse



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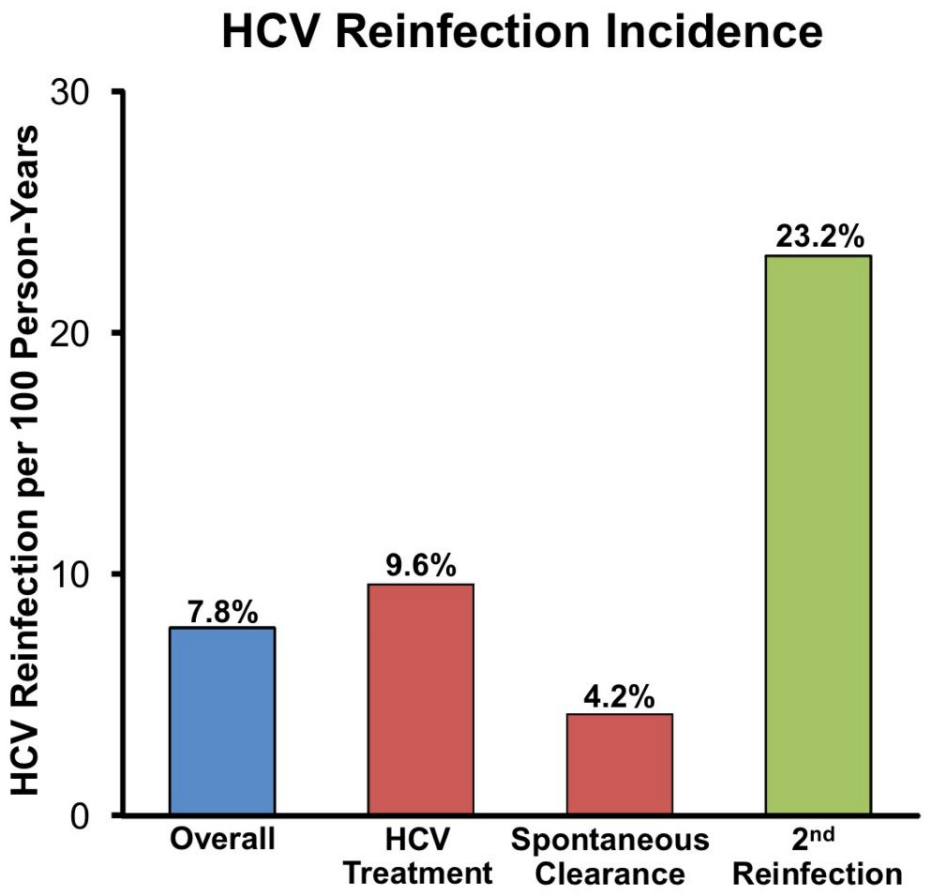
Hill AM, et al. 22nd CROI. Seattle, 2015. Abstract 654.

London Cohort: HCV Reinfection Rates Among HIV-Infected MSMs (2004-2012)

- Retrospective analysis (n=191 incident HCV infections)
  - HIV-infected MSMs with no history of IDU
  - Achieved spontaneous clearance of HCV (n=31) or SVR following HCV treatment
- Follow-up (562 patient-years)
  - ART during follow-up: 89%
- High HCV reinfection rates among MSMs and very high 2nd HCV reinfection rates
  - Trend towards higher reinfection rate among those receiving HCV treatment versus spontaneous HCV clearance



HCV reinfection: new, positive HCV-RNA PCR results ≥24 weeks after end of treatment or viral clearance (or <24 weeks if different HCV genotype).

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Martin T, et al. *AIDS*. 2013;27:2551-2557.

Dépistage 1

- Eradication ⇒ traitements ⇒ dépistage
- Recommandations classiques :
  - Dans la population générale
    - transfusion, grosse intervention < 1991
    - ictère non expliqué formellement dans le passé
    - tout utilisateur de stupéfiants (snif, iv)
    - « sous le même toit » (no panic : risque faible)
    - nouveau-né d'une maman séropositive pour le VHC
    - partenaire séropositif pour VHC (stt si homosexuel masculin)
    - détenus

Dépistage 2

- Recommandations classiques :
  - anomalie de santé (patients):
    - élévation chronique des transaminases TGP (même inconstamment)
    - tout patient dialysé
    - tout patient avec une coagulopathie clinique
    - tout cirrhotique
    - tout patient HBV ⊕ ou HIV ⊕
- Manifestations Extra-Hépatiques
- Tests « minute »
    - Ora Quick, …

Dépistage 3

- Accompagner le dépistage positif :
  - stade de l'hépatopathie
  - conseil quant aux options thérapeutiques
    - selon EG, co-morbidités, espérance de vie, contre-indications
  - conseil quant à la surveillance de la santé hépatique
    - dépistage carcinome hépatocellulaire si cirrhose
  - protéger le foie
    - Alcool
    - Vaccins vs HAV et HBV
    - Rationaliser la pharmacopée individuelle
    - Check VIH
    - Faire maigrir les forts BMI (> 25)

Envoi à l'hépatologue

- Préparer :
  - atcds médicaux et facteur(s) de risque identifié(s)
  - liste actualisée des traitements médicamenteux
  - la ou les biologies indicatives
    - TGP & Ac anti-VHC
    - autres étiologies éventuellement réfutées
- Mieux vaut l'avis du spécialiste puis de nombreuses années sans y retourner, que beaucoup d'années sans son avis et une hépatopathie qui aurait dû être arrêtée

Quand traiter ?

Pourquoi

ne pas

traiter ?

viral eradication >< disease cure

- infectious disease
  - viral
  - RNA
  - 6 genotypic groups
  - reinfection rates
  - outbreaks
  - individual eradication
- liver disease
  - severity d< on fibrosis
  - ≤ F3 : reversibility
  - F4 : irreversibility
  - multiple aetiologies
  - increasing NASH
  - risk for HCC remains

Hepatocellular carcinoma after SVR

- 33005 pats HCV oct ‘99 – déc 2010
- 10817 SVR

  (follow up de 30562 patients/années)
- 100 HCC

  0,33 % par an

  1,39 % par an si cirrhotique

  risque supérieur si : diabète sucré

  > 64 ans

  génotype 3

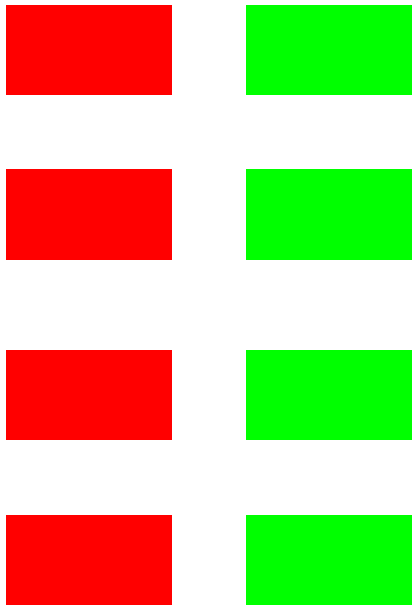
El Serag,- Hepatology 2016

Nous, après l'éradication virale

- ARN du VHC 48 semaines après la SVR
- Suivi au moins tous les six mois si :
  - fibrose sévère (F3 – F4) : avec échographie
  - consommation d'alcool (3 VS 🚹 - 2 VS 🚺)
  - surpoids (BMI > 25)
  - diabète sucré
  - risque élevé de réinfection
    - détenus
    - homosexuels stt 🚹

Quizz 1

- Nouveau patient, sérologie Hep C + et transaminases normales
  1. Il n'y a rien à faire vu l'absence d'hépatite biologique.
  2. Je vais régulièrement vérifier les TGP et si +, je referai la sérologie.
  3. Je l'interroge sur les facteurs de risque d'avoir pu contracter l'Hep C.
  4. Je demande une virémie quantitative.

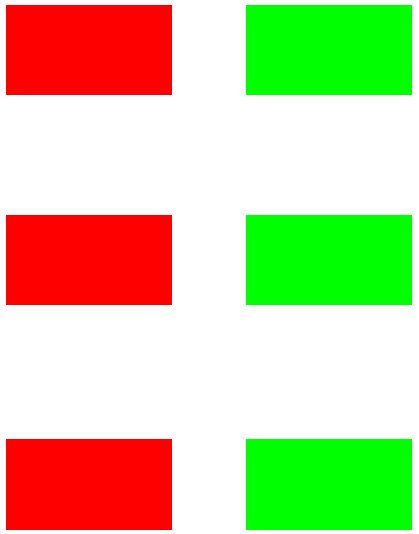


Quizz 2

- Un patient avec sérologie Hep C + et transaminases normales n'est pas contagieux

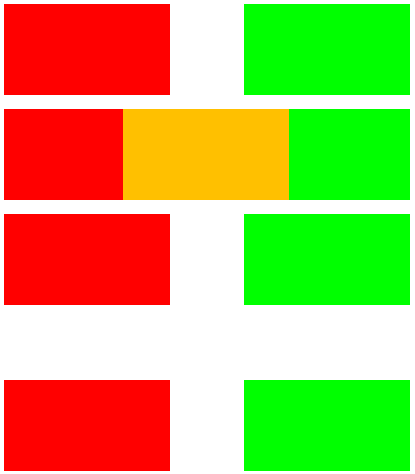
Quizz 3

- Si un patient aux transaminases normales est séro+ HCV...
  1. … après un traitement anti-HCV, il n’est pas guéri de cette infection.
  2. … (hors contexte d’un traitement) il n'a que 15% de risque d'avoir développé une fibrose hépatique significative.
  3. … (hors contexte d’un traitement), c’est qu’il s'est spontanément guéri de son hépatite virale C au stade précoce.



Quizz 4

- Elle avait des Ac anti-VHC en 2010 et était en bonne santé ; rien ne fut fait. Elle devient fatiguée. Ses TGO sont à 1.1 x vn, ses TGP à 1.4 x vn. Que faire ?
  1. Redoser les Ac anti-HCV.
  2. Virémie qualitative (PCR ⊕ ou ⊗).
  3. Adresser à l'hépatologue.
  4. Interdire de voir ses petits-enfants avant d'avoir été mise au point par le-dit hépatologue.



Quizz 5

- Mon patient, 78 ans, a une bonne santé, des TGP élevées et des Ac anti-HCV :
  1. Il a certainement aujourd'hui une hépatite C.
  2. Vu son âge, il ne tirera aucun bénéfice d'un traitement par antiviraux oraux modernes.
  3. Il ne tirerait de bénéfice d'un traitement par antiviraux oraux modernes que s'il n’est pas arrivé au stade de cirrhose.