

Universal HCV treatment: Strategies for simplification

**PARIS
HEPATOLOGY
CONFERENCE**

30 January 2017

Tarik Asselah (MD, PhD)

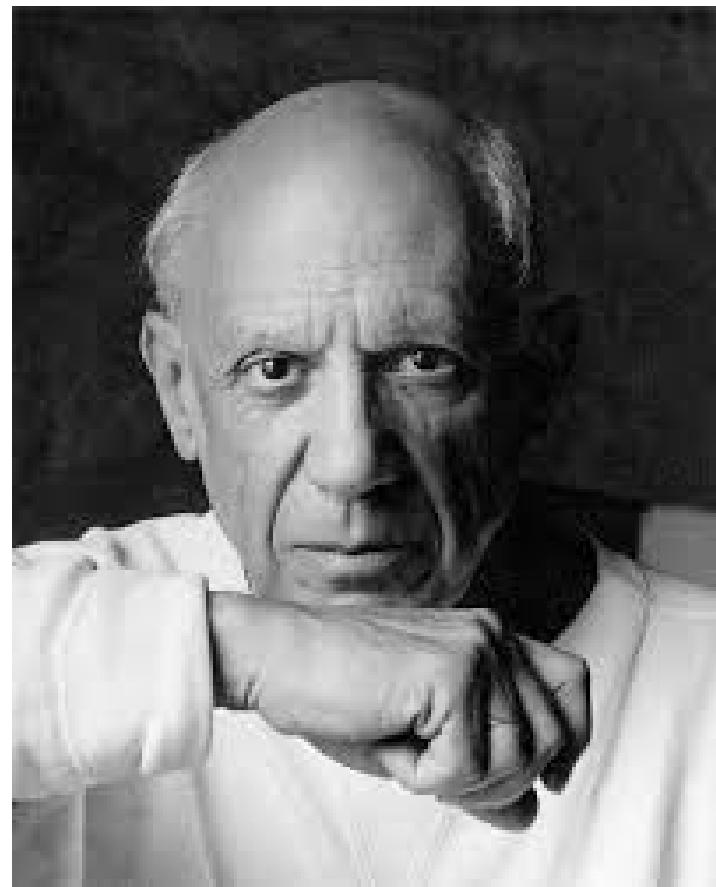
Hepatology & Chief INSERM UMR 1149,
Hôpital Beaujon, Clichy, France.

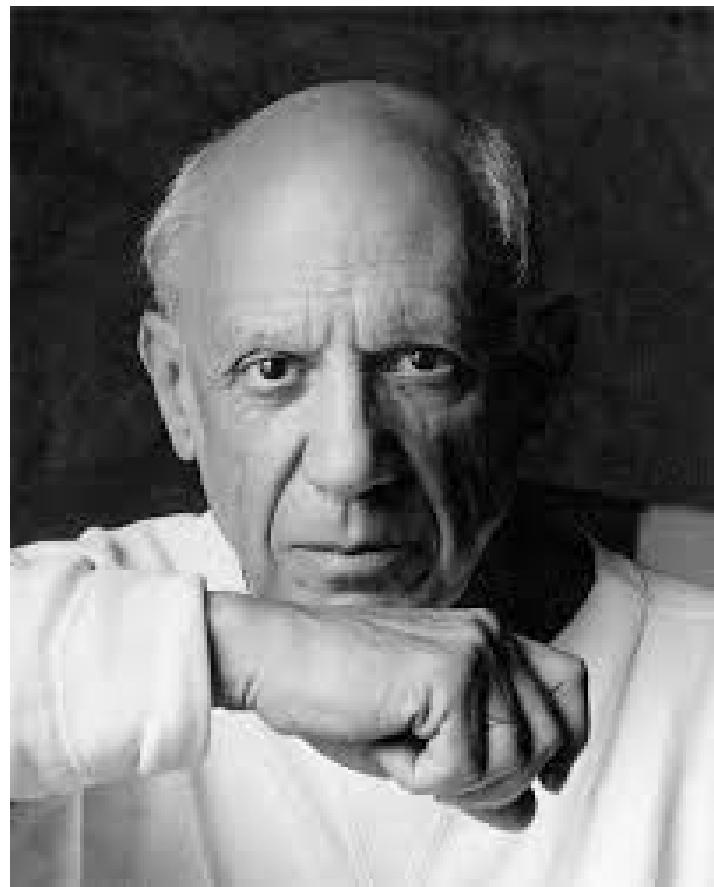


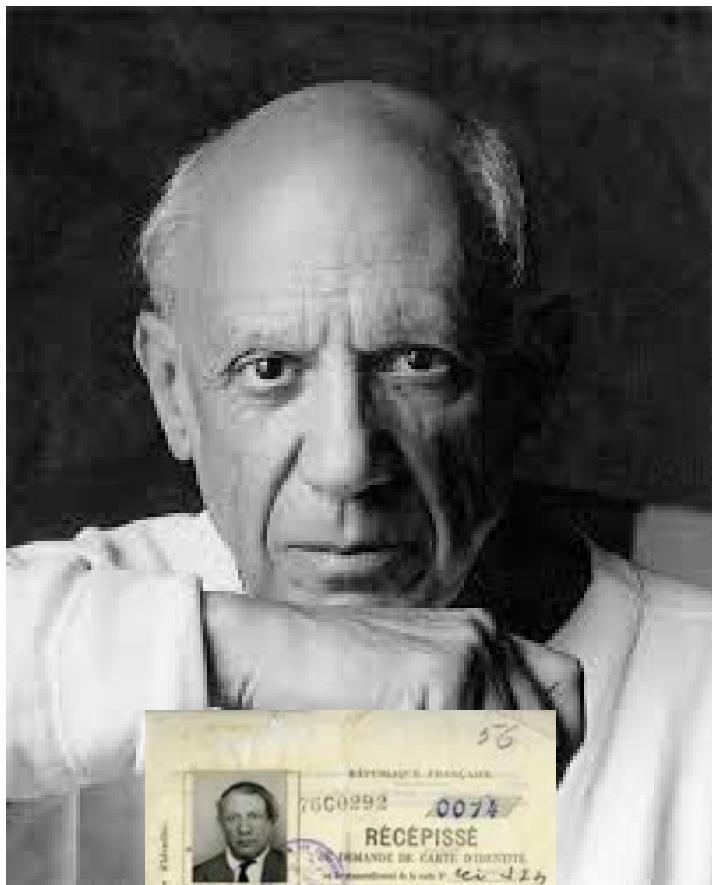
Disclosures

- Employee of Paris Public University Hospitals (AP-HP, Beaujon's Hospital) and University of Paris
- Principal investigator for research grants : Funds paid to Hospital (AP-HP)
 - Consultant, expert and speaker for: Abbvie, Bristol-Myers Squibb, Gilead, Janssen, Merck Sharp Dohme, Roche.
 - Grants from : ANR, CNRS , INSERM , University of Paris, ANRS









56

RÉPUBLIQUE FRANÇAISE

76C0292 0074

RÉCÉPISSE

Demande de CARTE D'IDENTITÉ

La demande de la carte d'identité

est déposée à la date du 26.6.1951

à Paris

Le demandeur est un homme de 43 ans

nom : Luis Pello y Pascos

prix : 25.000 francs

lieu : Espagne

profession : artiste peintre

Date de naissance : 26.6.1907

Lieu de naissance : Paris

Numéro de la carte : 76C0292

Date de validité : 26.6.1951

Signature : J. P. P.

Conditions d'émission : La carte d'identité sera émise par l'autorité compétente dans le territoire où l'émissaire a été nommé par le ministre des Affaires étrangères ou son représentant pour ce service. La carte d'identité sera émise par l'autorité compétente dans le territoire où l'émissaire a été nommé par le ministre des Affaires étrangères ou son représentant pour ce service.

Conditions de renouvellement : La carte d'identité sera renouvelée par l'autorité compétente dans le territoire où l'émissaire a été nommé par le ministre des Affaires étrangères ou son représentant pour ce service.

Conditions de perte : Si la carte d'identité est perdue, il faut la déclarer à l'autorité compétente dans le territoire où l'émissaire a été nommé par le ministre des Affaires étrangères ou son représentant pour ce service.

Conditions de vol : Si la carte d'identité est volée, il faut la déclarer à l'autorité compétente dans le territoire où l'émissaire a été nommé par le ministre des Affaires étrangères ou son représentant pour ce service.

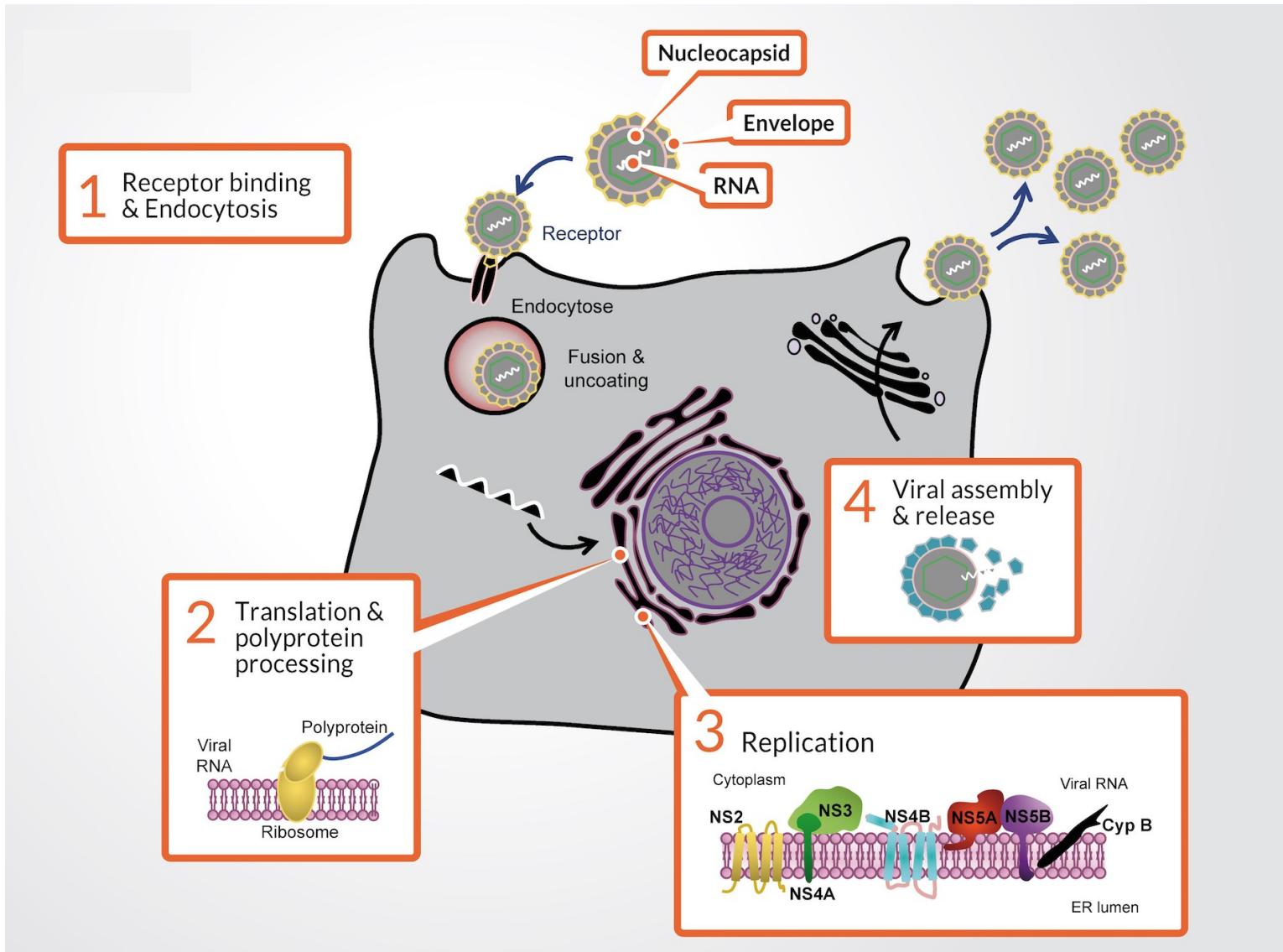
Universal HCV treatment: Strategies for simplification

The goal of this lecture will be to understand direct-acting antivirals (DAAs) revolution and to propose a rational approach to simplify therapy, to achieve HCV elimination.

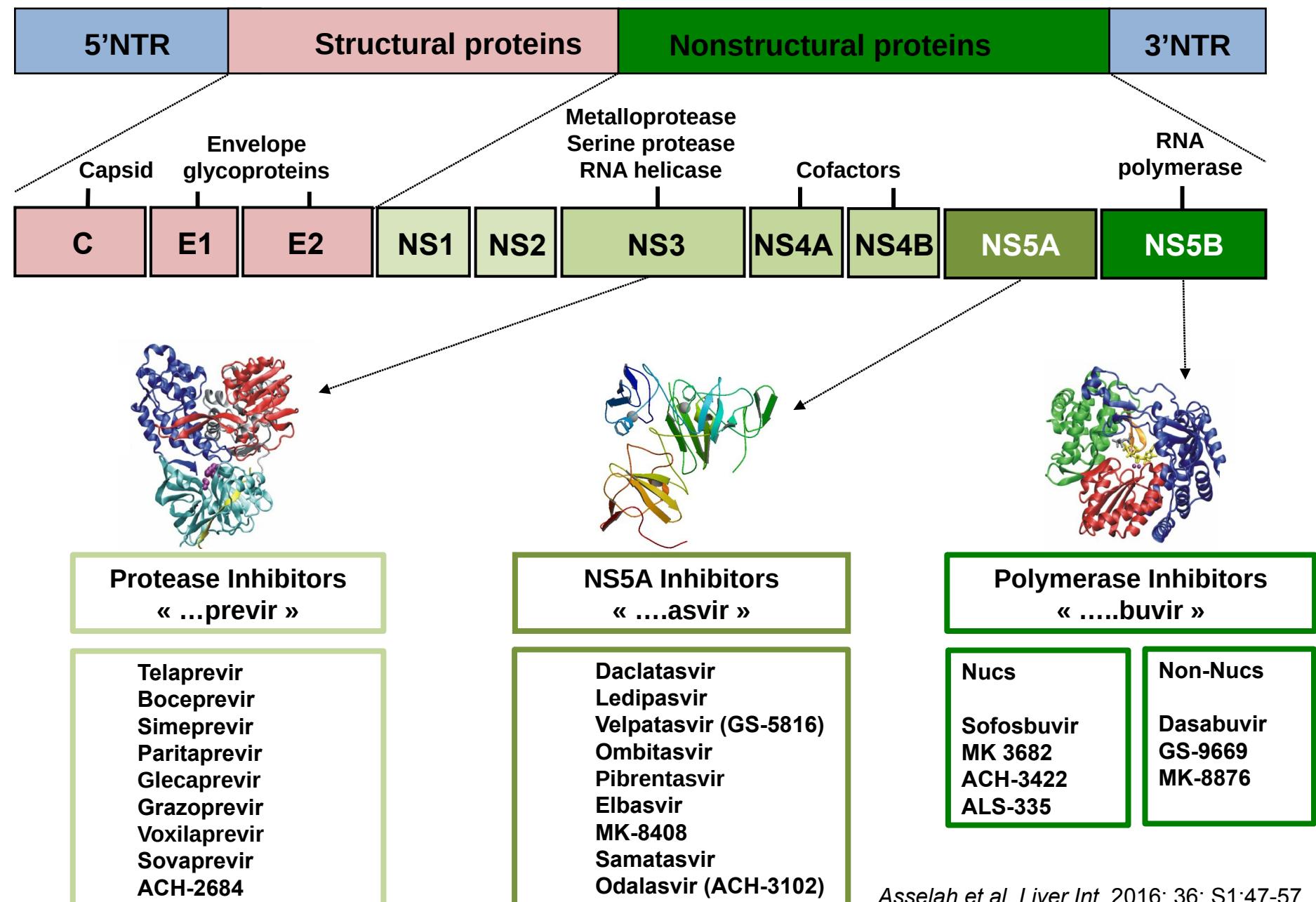
Universal HCV treatment: Strategies for simplification

- ✓ Direct-acting antivirals (DAAs)
- ✓ Treatment simplification
- ✓ Universal treatment
- ✓ Take home messages

HCV viral cycle



Direct-acting antivirals : a Revolution



Goals obtained by achieving **Sustained Virological Response (SVR) ≈ cure**

- Eradicate the virus (HCV clearance)
- Reduce necroinflammation
- Stop fibrosis progression

Goals obtained by achieving Sustained Virological Response (SVR) ≈ cure

- Eradicate the virus (HCV clearance)
- Reduce necroinflammation
- Stop fibrosis progression
- Prevent cirrhosis & complications
- Prevent hepatocellular carcinoma
- Reduce extra-hepatic manifestations
- Increase survival

ANRS CO22 HEPATHER: Outcomes in patients treated with DAAs

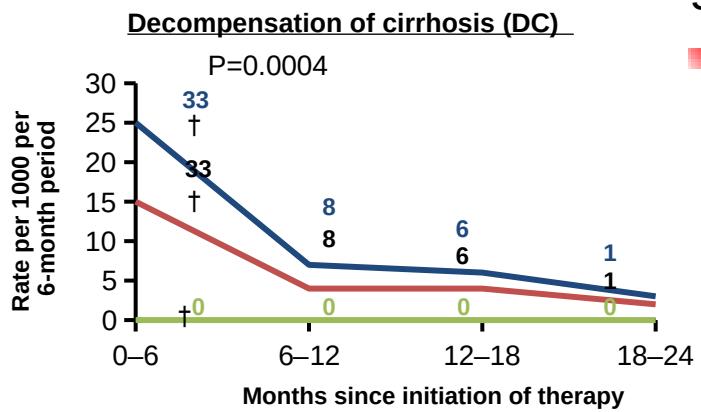
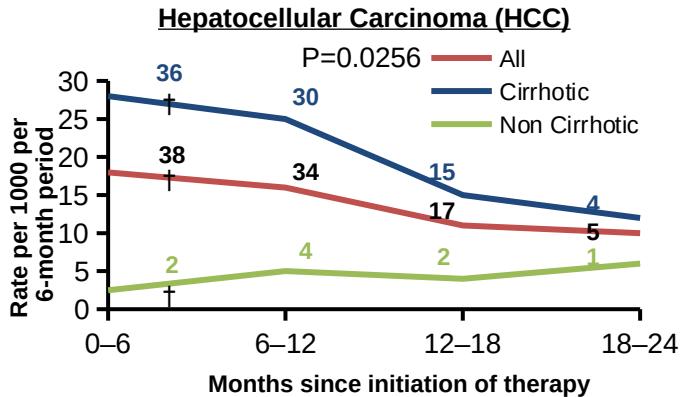
2156 patients (63% with cirrhosis at baseline) were followed-up for a median of 18 months

Outcome incidence rates over the first 24 months after initiating DAA therapy*

ANRS CO22 HEPATHER: Outcomes in patients treated with DAAs

2156 patients (63% with cirrhosis at baseline) were followed-up for a median of 18 months

Outcome incidence rates over the first 24 months after initiating DAA therapy*



HCC incidence rates decreased by 43% after 12 months from initiation of therapy ($P=0.0256$)

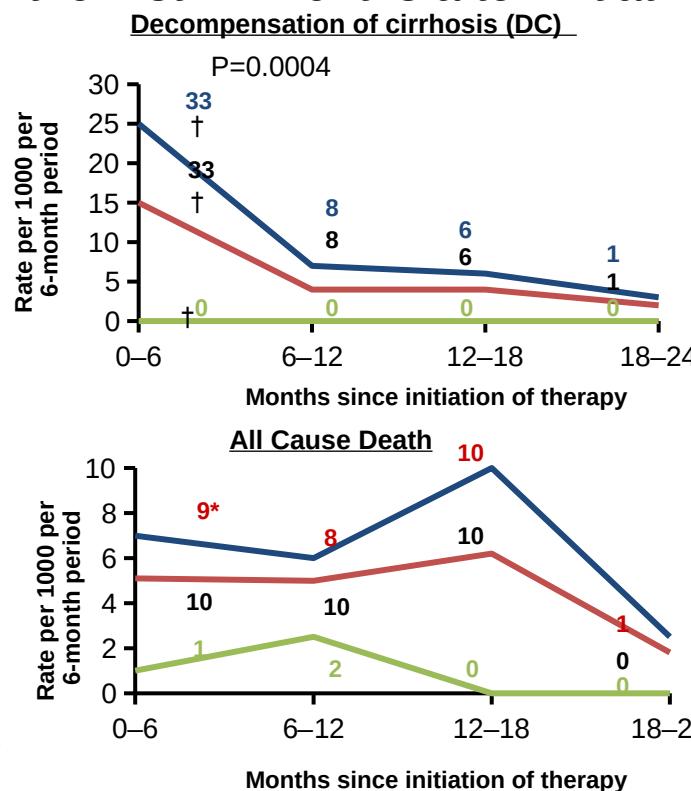
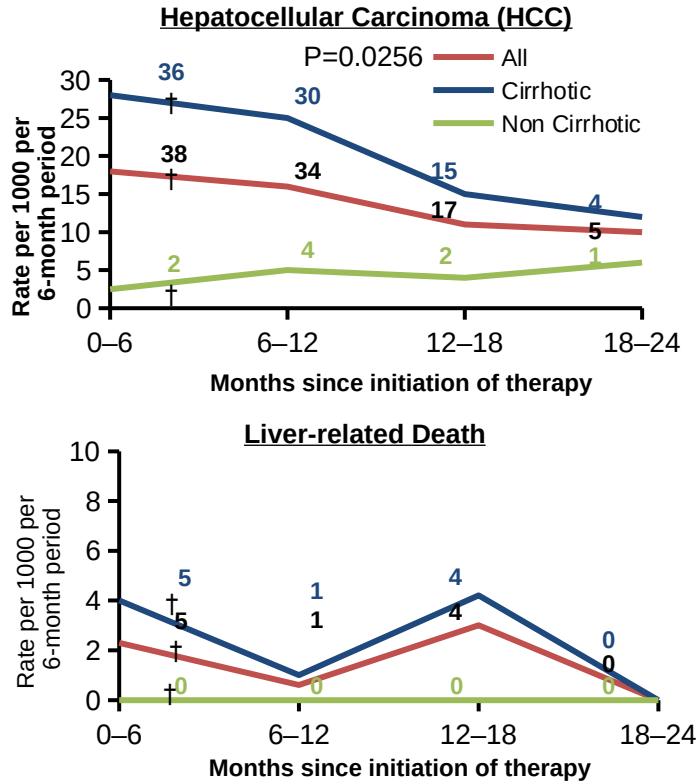
DC incidence rates decreased by 77% after 6 months from initiation of therapy ($P=0.0004$)

*SOF + RBV (n=283); SOF + PEG-IFN + RBV (n=228); SOF + DCV ± RBV (n=1048) or SOF + SMV ± RBV (n=597); †Number of events per period

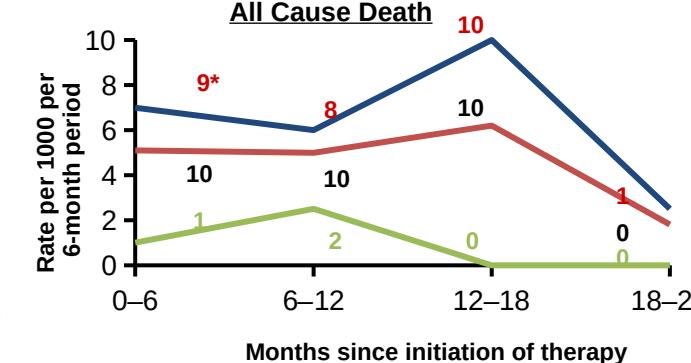
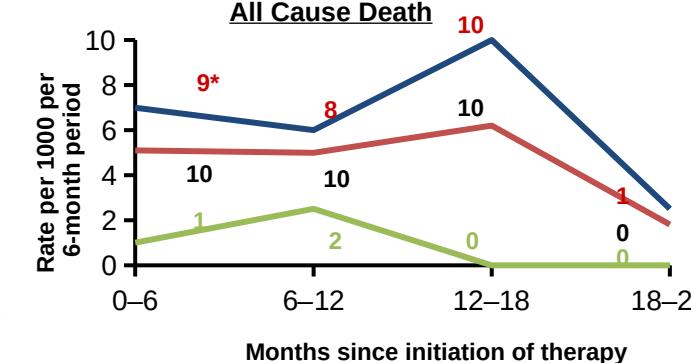
ANRS CO22 HEPATHER: Outcomes in patients treated with DAAs

2156 patients (63% with cirrhosis at baseline) were followed-up for a median of 18 months

Outcome incidence rates over the first 24 months after initiating DAA therapy*



- HCC incidence rates decreased by 43% after 12 months from initiation of therapy ($P=0.0256$)
- DC incidence rates decreased by 77% after 6 months from initiation of therapy ($P=0.0004$)
- Major HCV-related outcomes decreased after DAA-based therapy



*SOF + RBV (n=283); SOF + PEG-IFN + RBV (n=228); SOF + DCV ± RBV (n=1048) or SOF + SMV ± RBV (n=597); †Number of events per period

Top Priorities for Direct-Acting Antiviral Agents

Potency (SVR)

Genotype Coverage

Resistance Barrier

Safety/Tolerability

Top Priorities for Direct-Acting Antiviral Agents

Potency (SVR)

Genotype Coverage

Resistance Barrier

Safety/Tolerability

Treatment Duration

Half life & Pills burden

Drug-drug Interaction

Access/Cost

Universal HCV treatment: Strategies for simplification

- ✓ Direct-acting antivirals (DAAs)
- ✓ **Treatment simplification**
- ✓ Universal treatment
- ✓ Take home messages

Treatment simplification

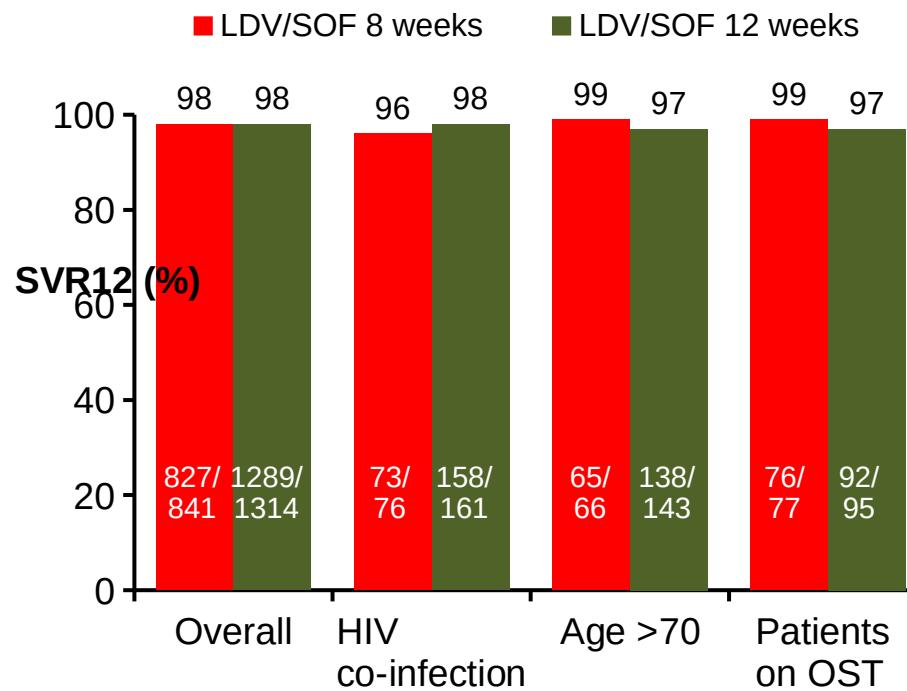
- ✓ No ribavirin
- ✓ Shorten treatment duration
- ✓ Pan-genotypic efficacy
- ✓ Reduce pill burden

LDV/SOF for 8 or 12 weeks in HCV mono- and HIV/HCV co-infected patients

(German Hepatitis C-Registry)

Analysis of 2485 HCV GT 1 patients treated with LDV/SOF for 8 weeks or 12 weeks under real-world conditions

Virological response (per protocol)



Garnet : 8 weeks 3D in GT1b non cirrhotic patients



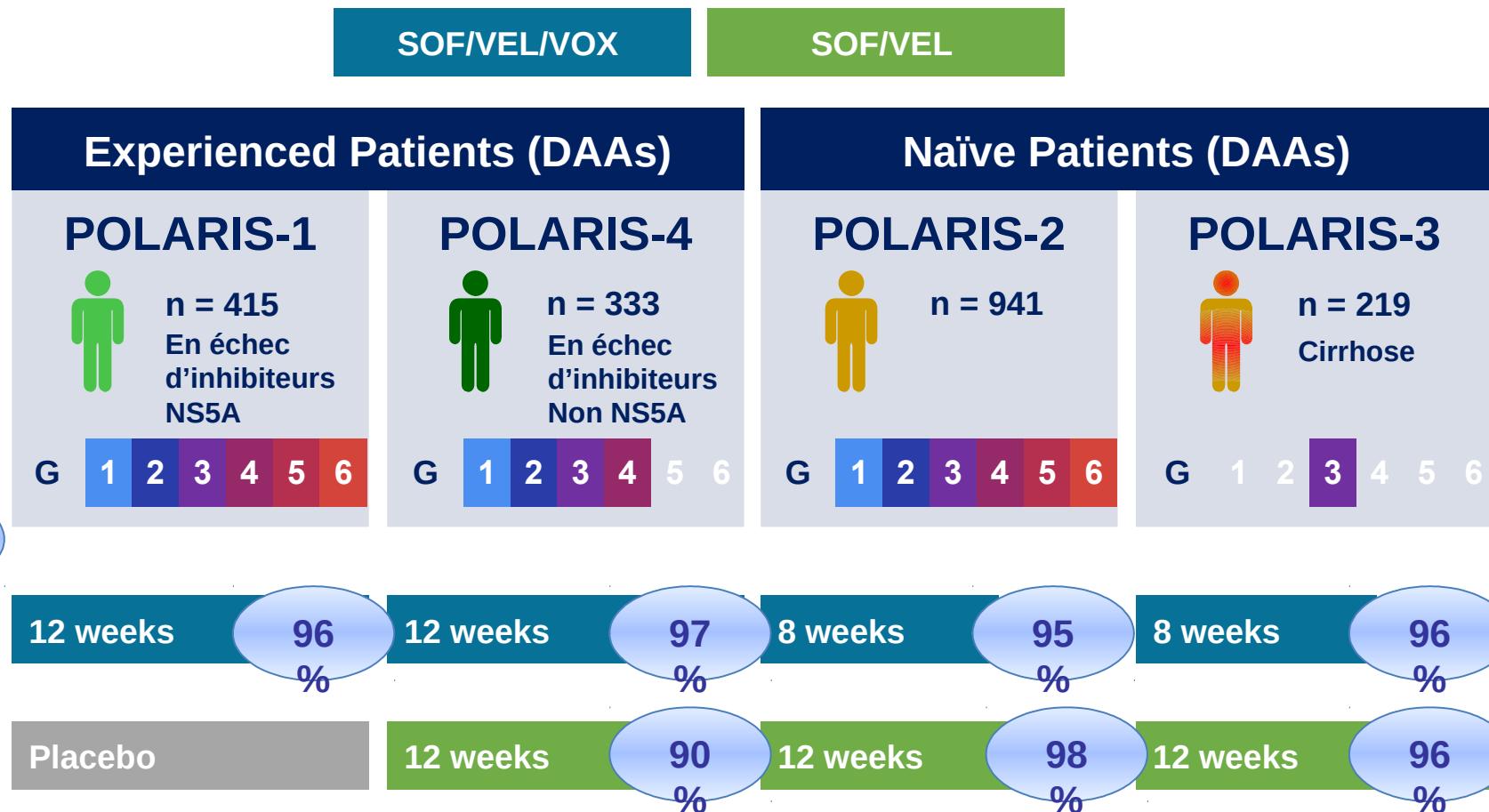
ITT: tous les patients ayant reçu au moins une dose de traitement

mITT-GT: ITT modifiée: exclusion des 3 patients non G1b

mITT-GT-VF: mITT-GT exclusion des échecs non virologiques

Available and future DAAs (high efficacy and good tolerance) provide a unique opportunity to establish a program for HCV elimination

POLARIS : sofosbuvir/velpastasvir/voxilaprevir



Bourlière et al, AASLD 2016, A194
Zeuzem et al, AASLD 2016, A109

Jacobson et als, AASLD 2016, LB-12
Foster et al, AASLD 2016, A258

Glecaprevir/Pibrentasvir: Program

ENDURANCE Trials

GT1 non-cirrhotic including
HIV co-infection: 8 vs 12 weeks

GT2 placebo-controlled: 12 weeks
GT3 active comparator: 12 weeks
GT4-6: 12 weeks

MAGELLAN Trials

GT1,4-6 prior DAA failures:
12 vs 16 weeks

EXPEDITION Trials

GT1, 2, 4-6 cirrhotic
GT1-6 all stages of renal impairment

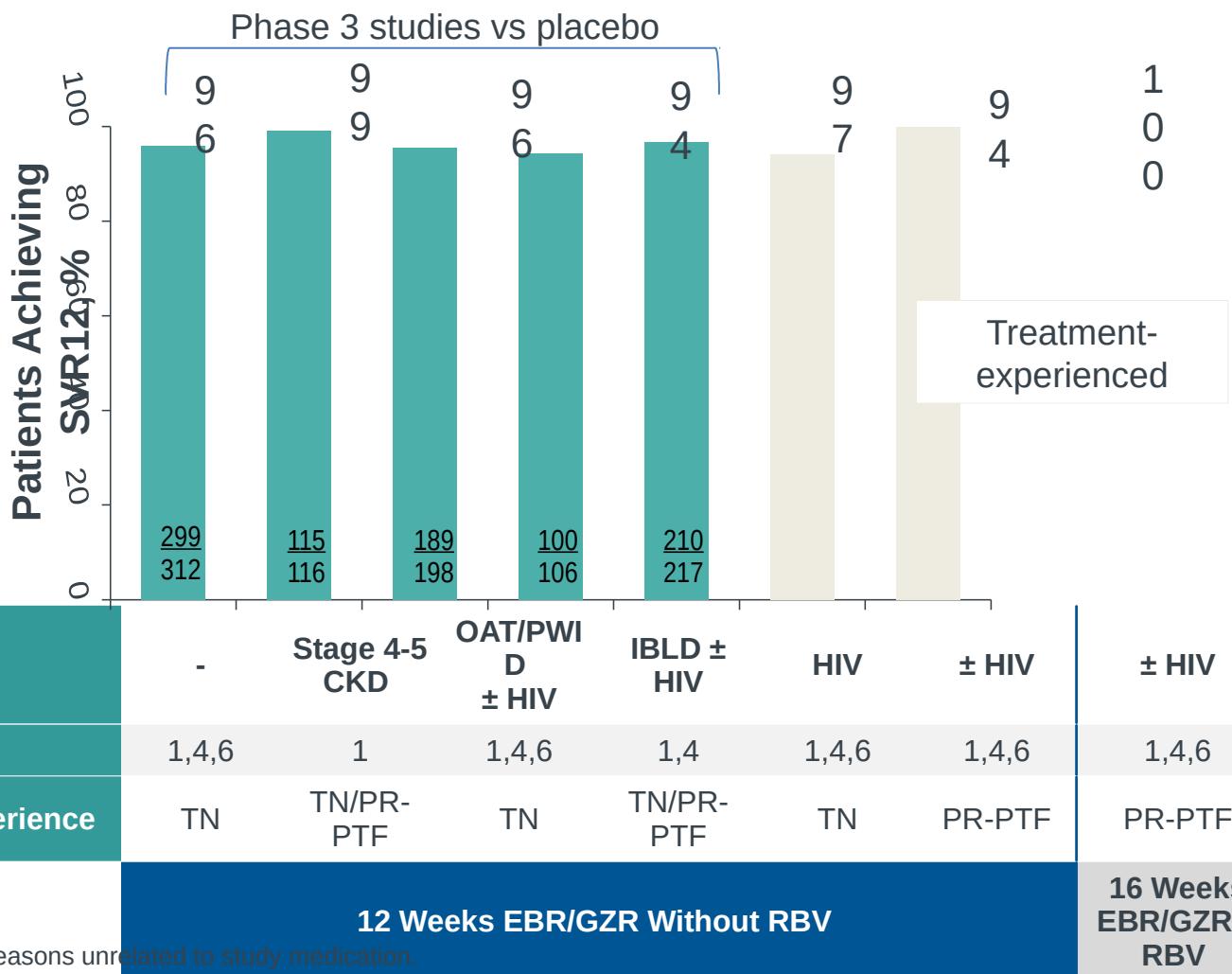
SURVEYOR Trials

GT2, 4-6 non-cirrhotic: 8 weeks
GT3 cirrhotic: 12 vs 16 weeks

EBR/GZR: Efficacy in Different Patient Populations 1-

6

Overall mFASa
SVR12 rates from
the Phase 3
clinical trial
program



amFAS excludes patients who failed for reasons unrelated to study medication.

EBR/GZR = elbasvir/grazoprevir; SVR12 = sustained virologic response 12 weeks after the cessation of treatment; CKD = chronic kidney disease; OAT = opioid agonist therapy; PWID = people who inject drugs; IBLD = inherited blood disorders; TN = treatment naive; HIV = human immunodeficiency virus;

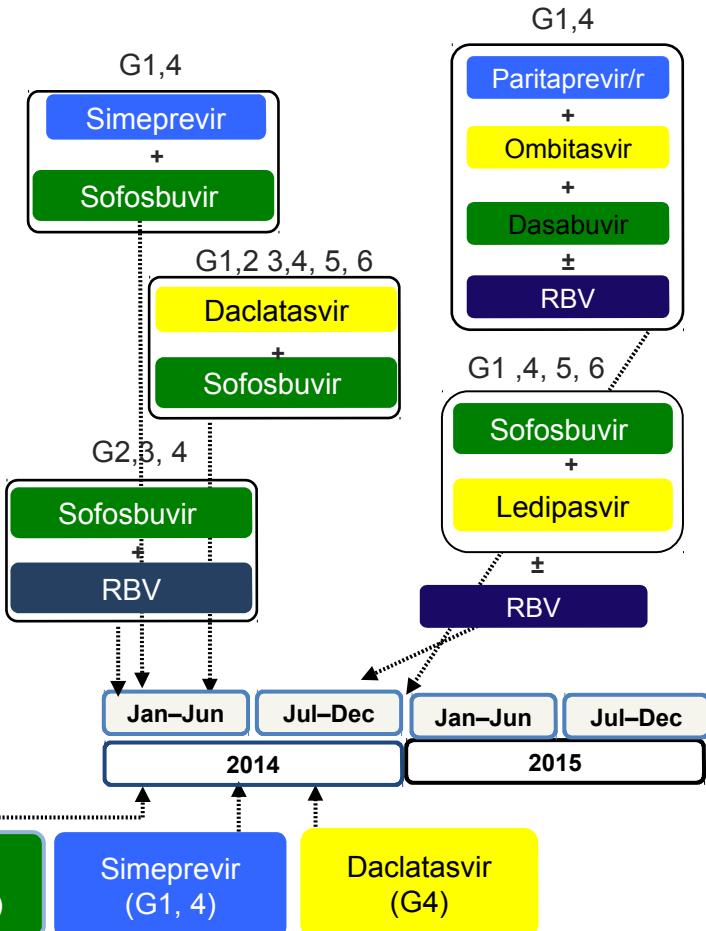
TE = treatment experienced; RBV = ribavirin; PR = peginterferon + ribavirin; PTF = prior-treatment failure; mFAS= modified full analysis set.

1. Roth D et al. Lancet. 2015;386:1537–1545. 2. Dore GJ et al. EASL 2016, SAT-163. 3. Hezode C et al. EASL 2016, SAT-128. 4. Zeuzem S et al. Ann intern Med. 2015;163:1–13. 5. Rockstroh JK et al. Lancet HIV. 2015;2:e319–e327. 6. Kwo P et al. Gastroenterology. 2017;152:164–175.

Current Therapies

IFN-free

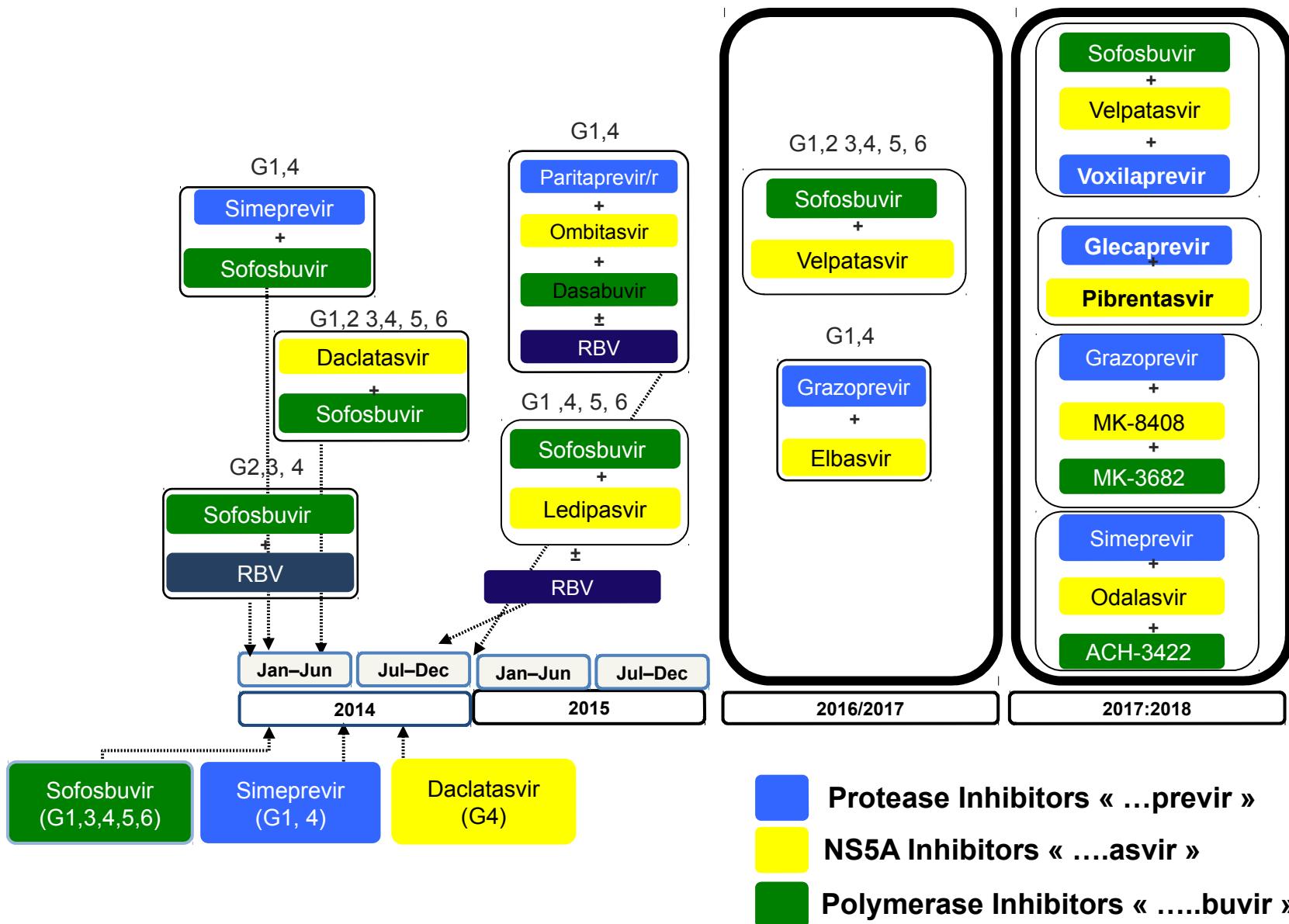
With IFN



- Protease Inhibitors « ...previr »
- NS5A Inhibitors «asvir »
- Polymerase Inhibitors «buvir »

Current and Future Therapies

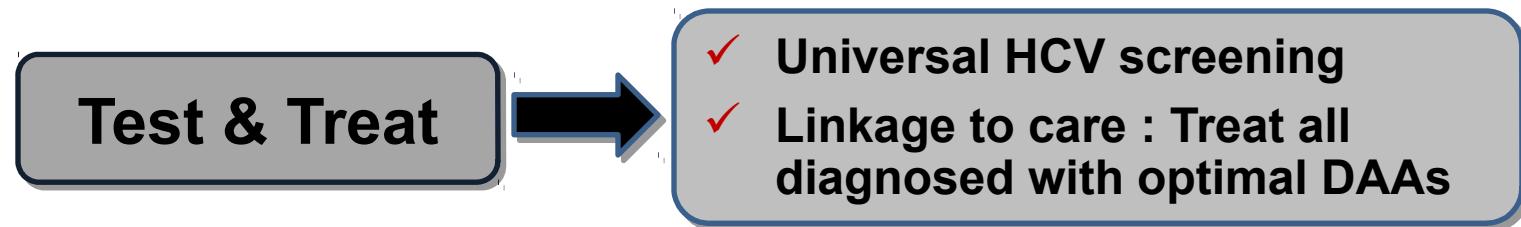
IFN-free



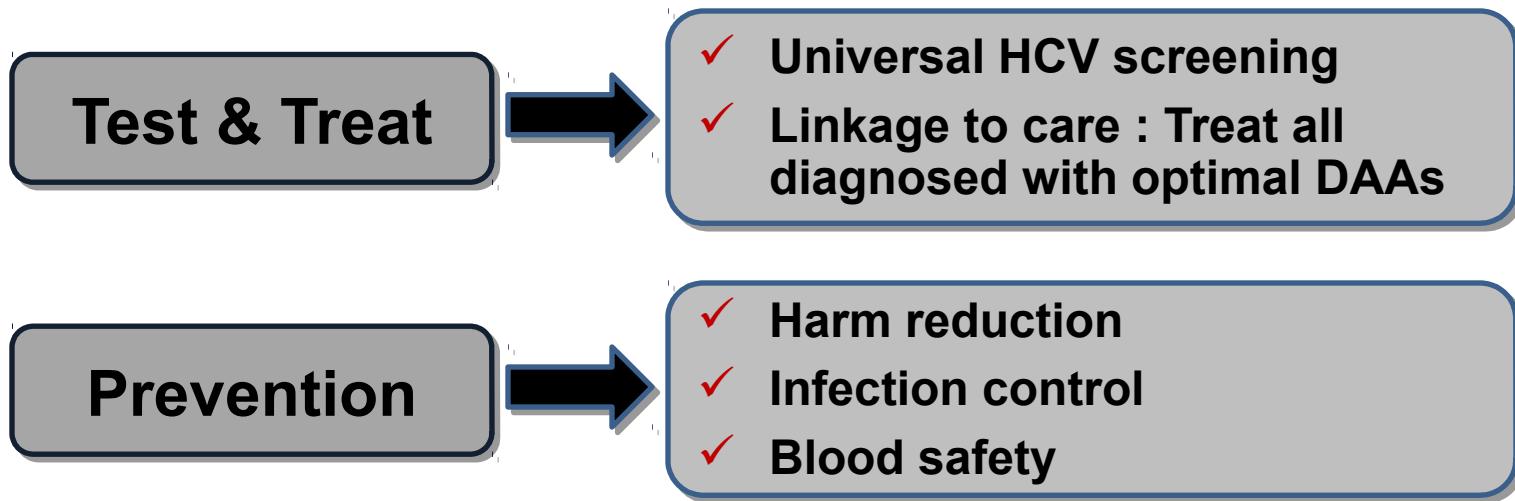
Universal HCV treatment: Strategies for simplification

- ✓ Direct-acting antivirals (DAAs)
- ✓ Treatment simplification
- ✓ **Universal treatment**
- ✓ Take home messages

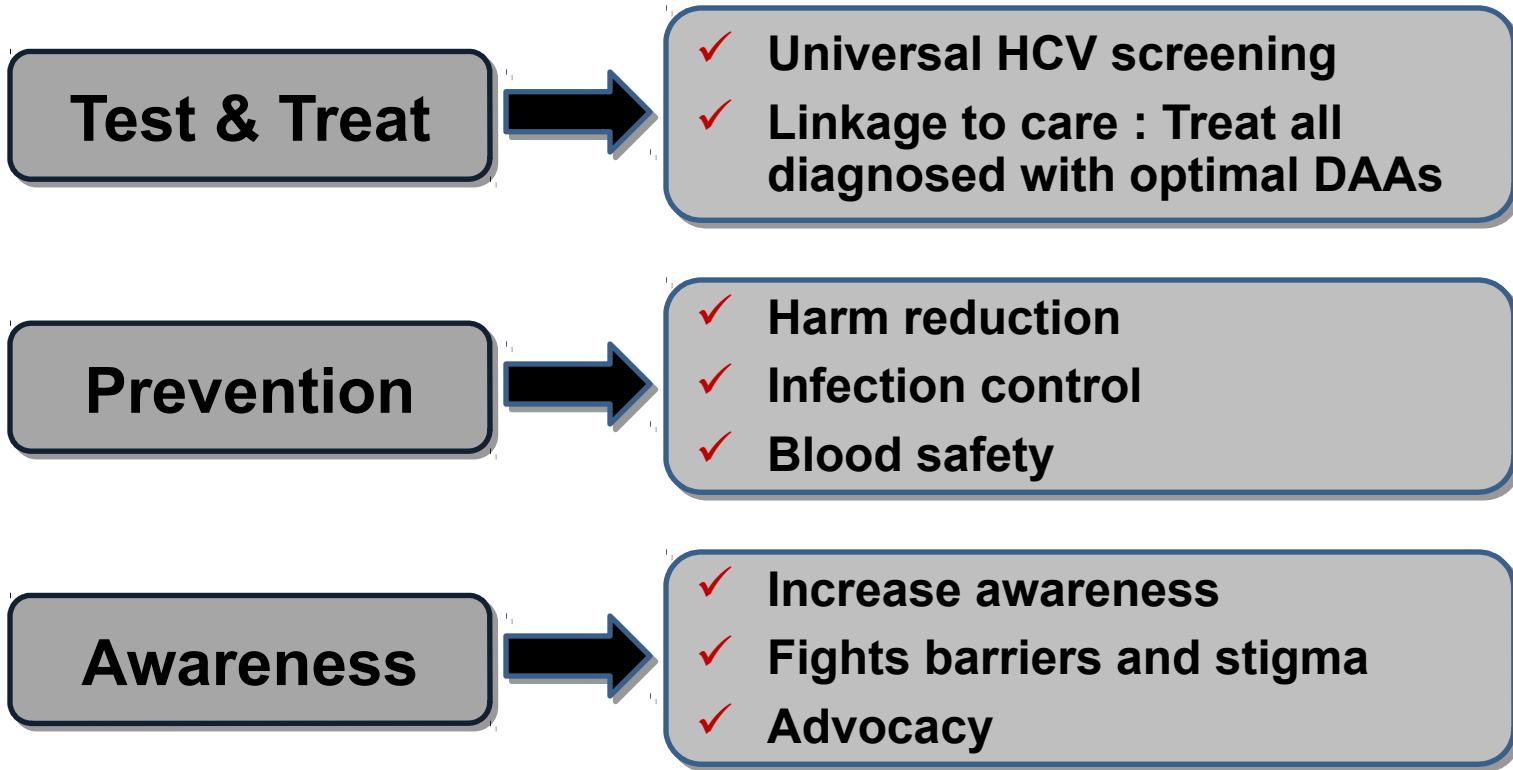
Strategies for HCV elimination



Strategies for HCV elimination

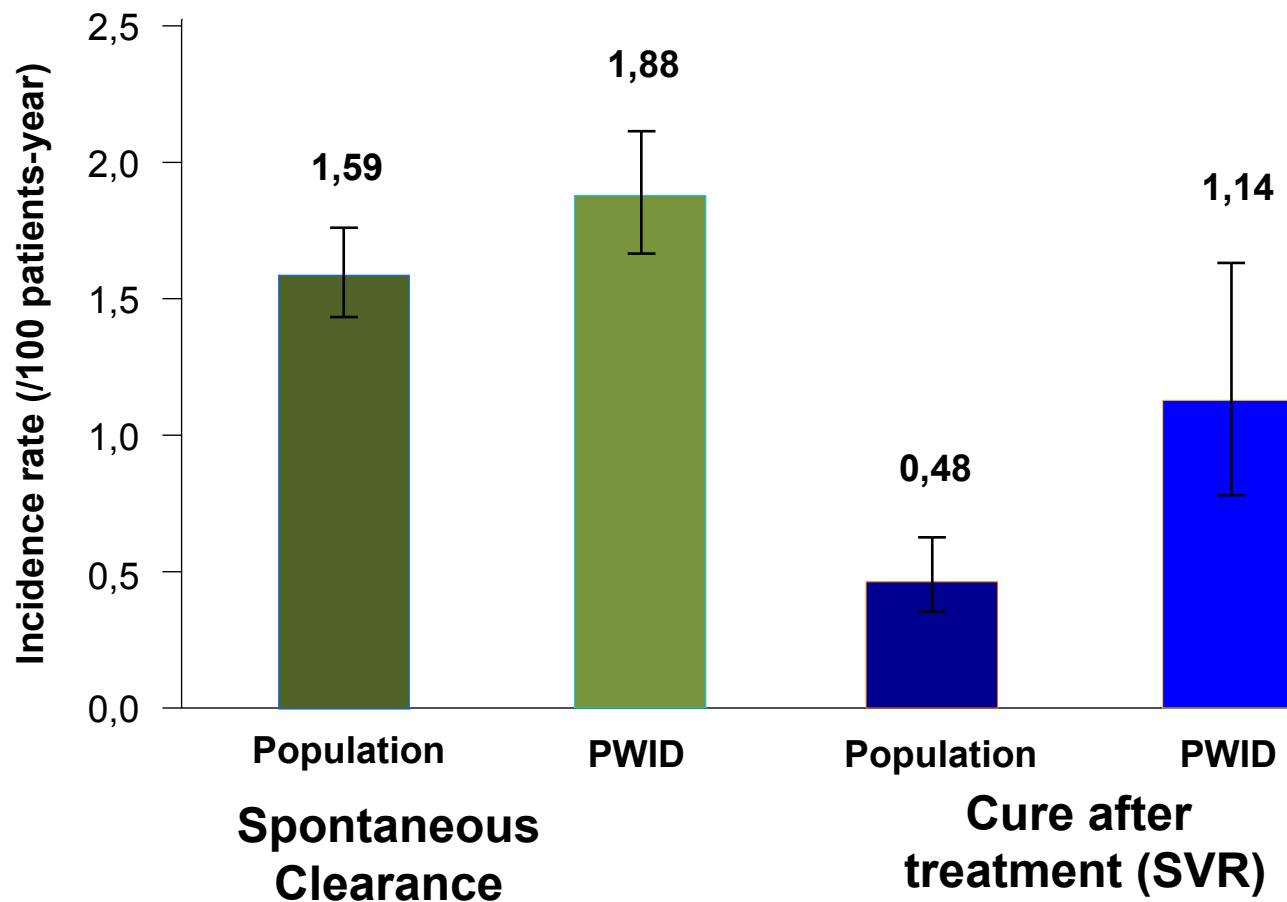


Strategies for HCV elimination



HCV re-infection

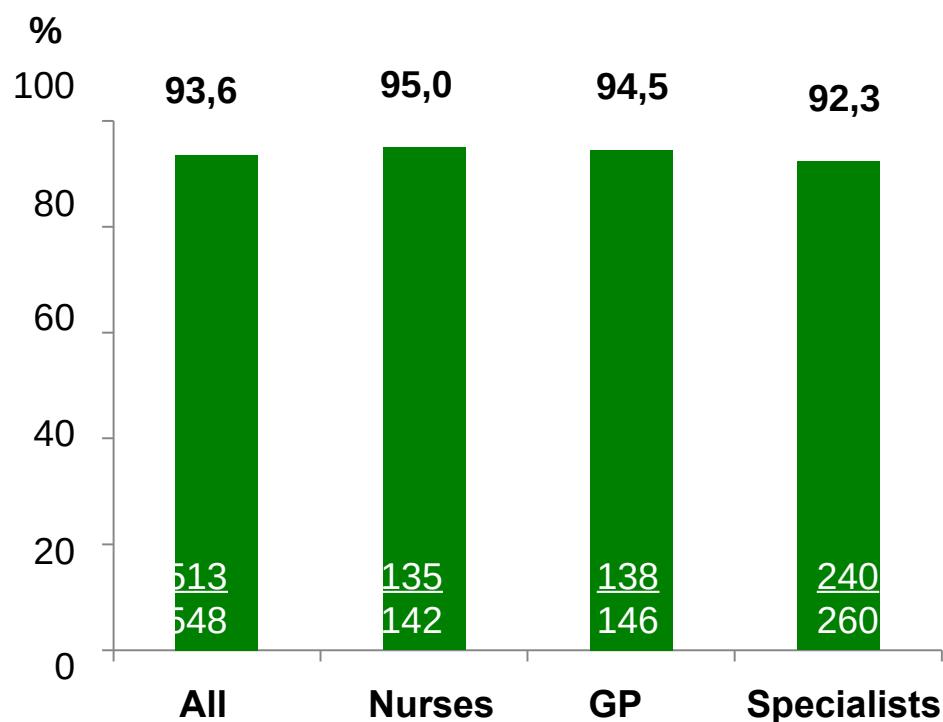
Re-infection rate in total population and among PWID (Canada)



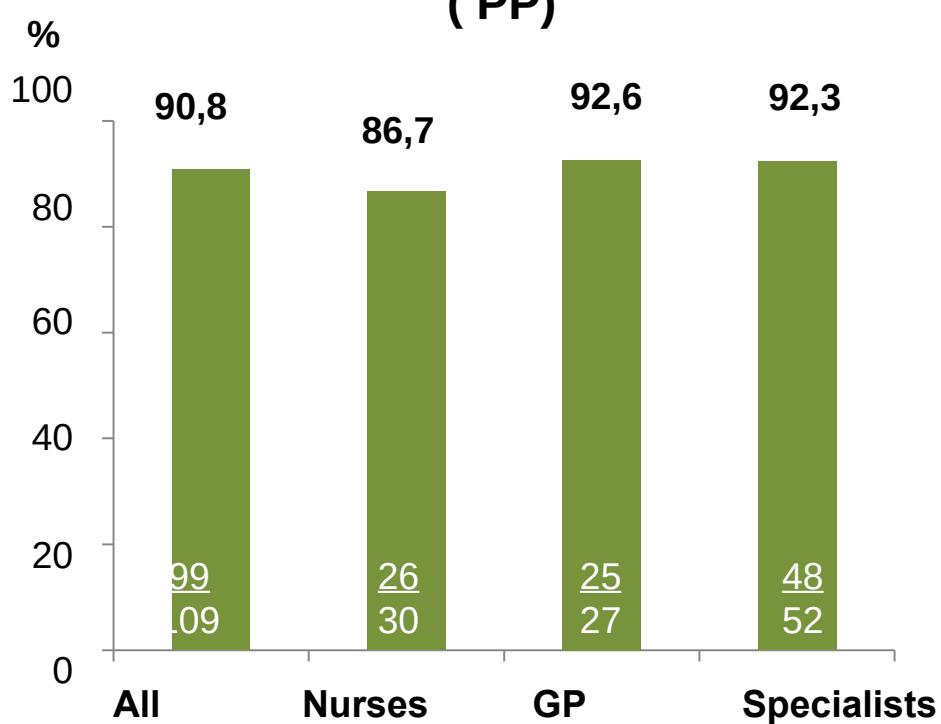
DAAs therapies: Increase Prescribers

Prospective study ASCEND (USA) : 600 patients treated with SOF/LDV by
6 Hepato-Gastroenterologists, 5 GP, 5 nurses after a **SPECIFIC EDUCATION**

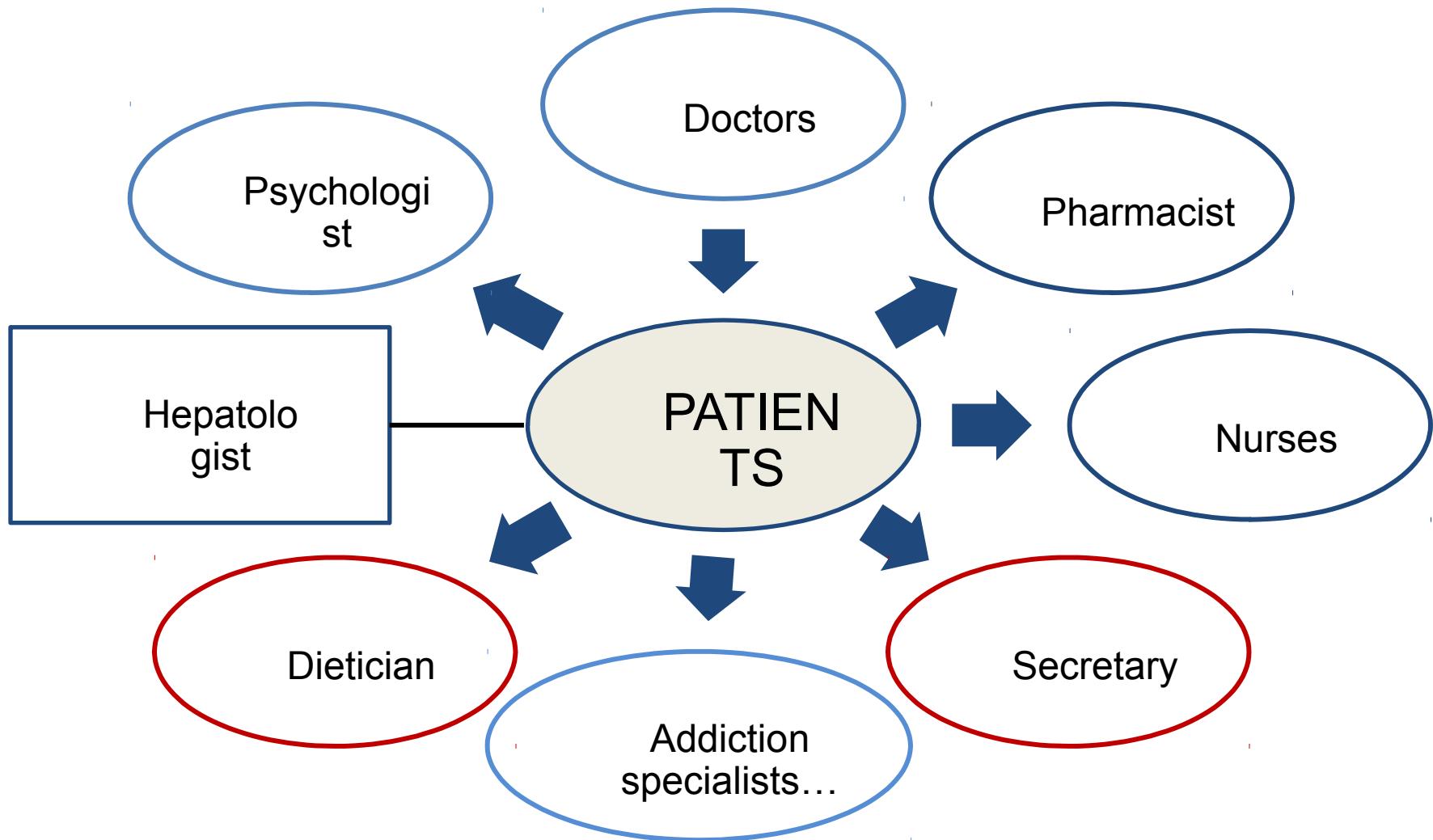
SVR 12 (PP)



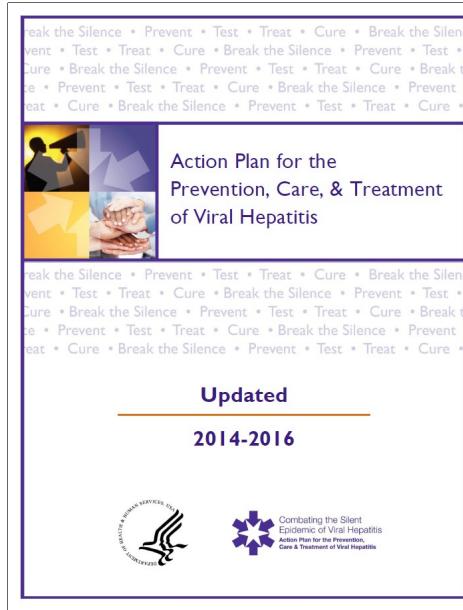
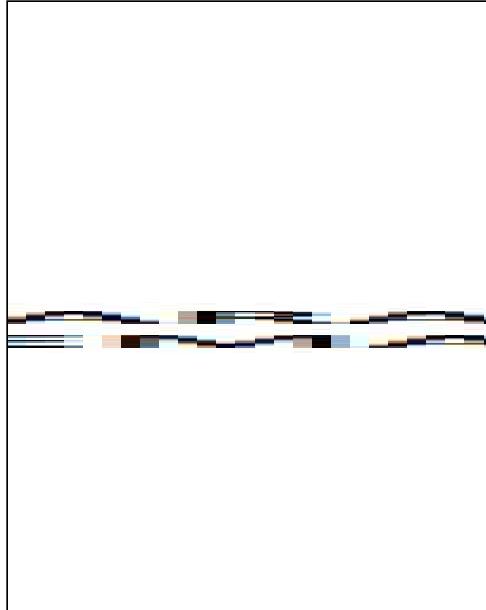
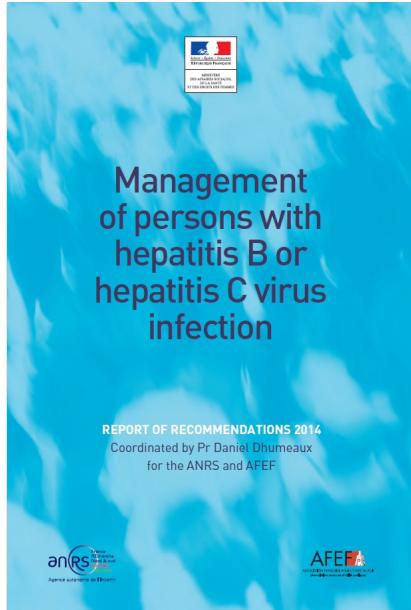
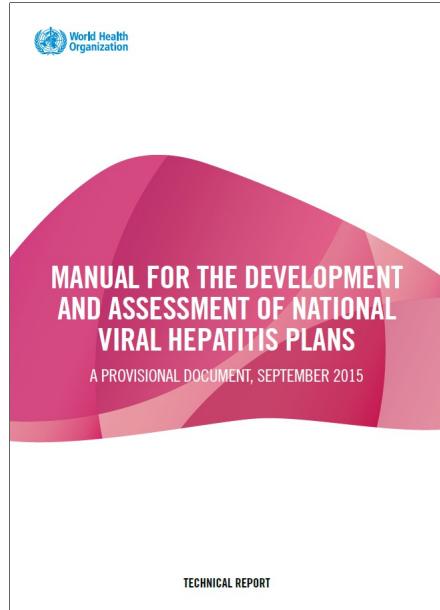
SVR 12 patients with cirrhosis (PP)



Therapeutic Patient Education: a multidisciplinary team



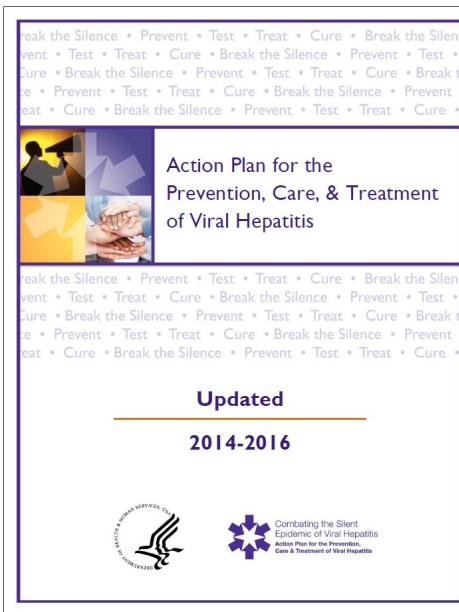
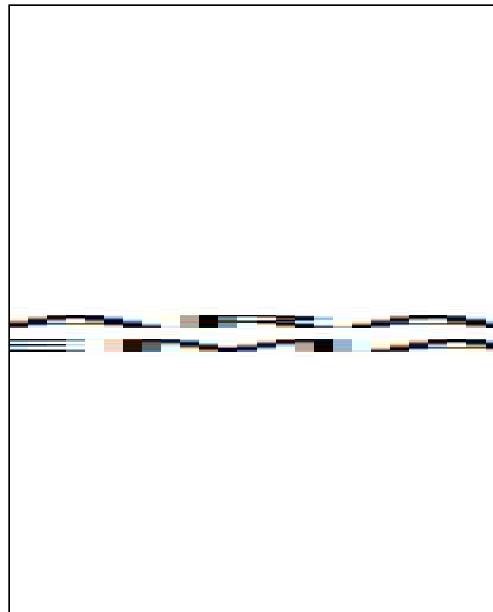
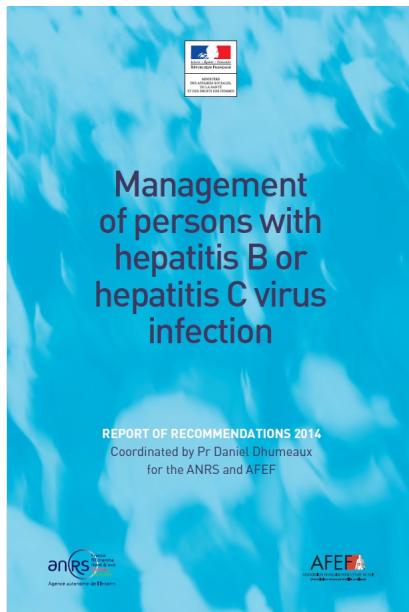
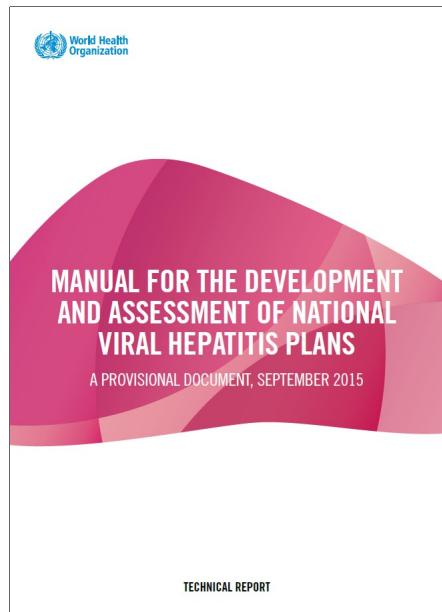
Hepatitis plans for HCV elimination



National action plans and strategies:

http://www.msssi.gob.es/ciudadanos/enfLesiones/enfTransmisibles/docs/plan_estrategico_hepatitis_C.pdf;
[http://www.health.gov.au/internet/main/publishing.nsf/Content/A68444CDED77B3A9CA257BF0001CFD80/\\$File/Hep-C-Strategy2014-v3.pdf](http://www.health.gov.au/internet/main/publishing.nsf/Content/A68444CDED77B3A9CA257BF0001CFD80/$File/Hep-C-Strategy2014-v3.pdf); <http://www.afef.asso.fr/ckfinder/userfiles/files/actualites/veille/French-report-Dhumeaux.pdf>;
<https://www.aids.gov/pdf/viral-hepatitis-action-plan.pdf>; <http://iris.wpro.who.int/handle/10665.1/13141>;
http://apps.who.int/iris/bitstream/10665/183726/1/9789241509350_eng.pdf (all accessed January 2017)

Hepatitis plans for HCV elimination



France : universal access to HCV treatment

National action plans and strategies:

http://www.msssi.gob.es/ciudadanos/enfLesiones/enfTransmisibles/docs/plan_estrategico_hepatitis_C.pdf;
[http://www.health.gov.au/internet/main/publishing.nsf/Content/A68444CDED77B3A9CA257BF0001CFD80/\\$File/Hep-C-Strategy2014-v3.pdf](http://www.health.gov.au/internet/main/publishing.nsf/Content/A68444CDED77B3A9CA257BF0001CFD80/$File/Hep-C-Strategy2014-v3.pdf); <http://www.afef.asso.fr/ckfinder/userfiles/files/actualites/veille/French-report-Dhumeaux.pdf>;
<https://www.aids.gov/pdf/viral-hepatitis-action-plan.pdf>; <http://iris.wpro.who.int/handle/10665.1/13141>;
http://apps.who.int/iris/bitstream/10665/183726/1/9789241509350_eng.pdf (all accessed January 2017)

Universal HCV treatment: Strategies for simplification

- ✓ Direct-acting antivirals (DAAs)
- ✓ Treatment simplification
- ✓ Universal treatment
- ✓ Take home messages**

Universal HCV treatment: Strategies for simplification

Take Home Messages

HCV cure

- Combining DAAs results in high SVR (> 95%) and short duration (8-12weeks).

HCV elimination requires improvement in:

- Screening (linkage to care)
- Prevention
- Access to treatment