Clinical Management of Hepatitis C in Iran: A Consensus-Based National Guideline: Update

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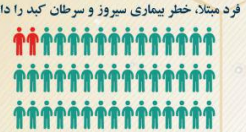
آنچه درباره هپاتیت سی باید بدانید ...

شبکه هپاتیت ایران

تعداد مبتلایان به هپاتیت سی در ایران: ۱۸۶۰۰۰ نفر



- تعداد بیماران درمان نشده
- تعدادبیماران تشخیص داده نشده
- تعداد بیماران در ایران

راه های اصلی انتقال

- تزریق ناسالم در معتادین (راه اصلی انتقال در ایران)
- رفتارهای جنسی پر خطر
- سابقه انتقال خون قبل از سال ۱۳۷۵

تشخیص

- بیماری با یک آزمایش خون ساده قابل تشخیص اولیه می باشد.

درمان

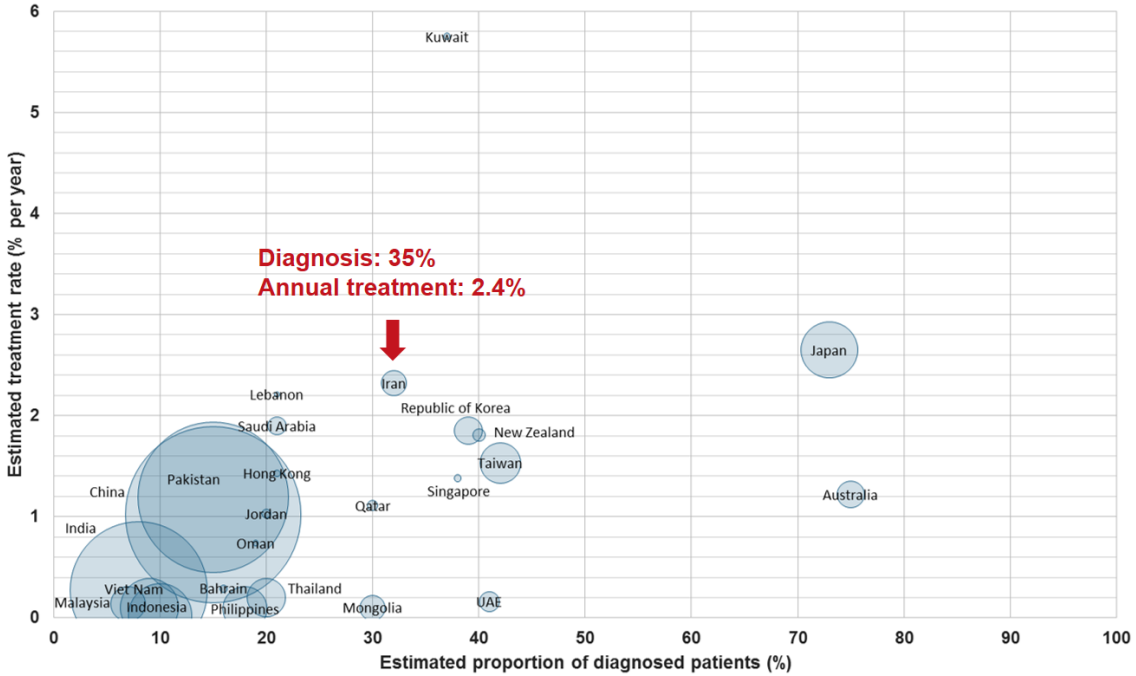
- درمان بیماری با اثربخشی بالا (٪۹۵<) و عوارض کم در ایران با هزینه مناسب در دسترس می باشد.

Infographic:mnima+98-9128059726

Hepatitis C Virus Infection and Its Prevalence

- Less than 0.5% of General population are HCV infected in Iran and the main risk factors are history of blood transfusion before 1996 and history of IDUs
- The special group such as Hemophilia and Thalassemia and Hemodialysis patients selected for screening and treatment during recent 10 years and now..
- IDUs cases are the main high risk group now and harm reduction and other strategies should attenuated now.
- Treatment is a part of prevention for decrease the chance of transmission

Diagnosis rate



Hajarizadeh B, et al. Hepat Mon 2016; Razavi H, et al. JVH 2014; Hatzakis A, et al. JVH 2015; Sibley A, et al. JVH 2015

Is it enough?

Public awareness is important and effective in Iran

We should focus on high risk groups

Public awareness is important and effective in Australia
It can be more effective if it would be targeted to the right population

Hepatitis C Therapy Introduction

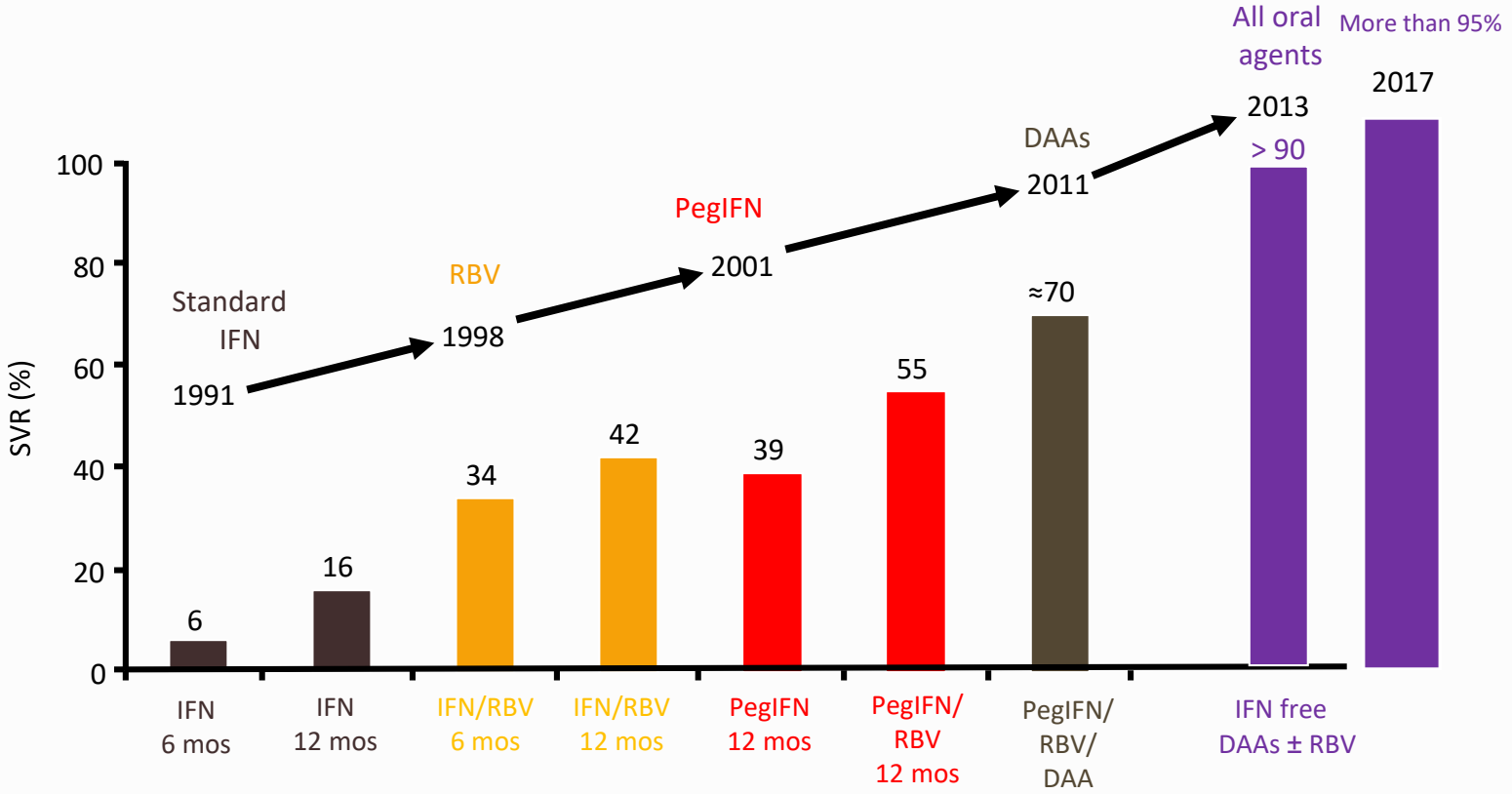
Treatment (Goal, When, Whom)

- ✓ **The goal of treatment is to reduce all-cause mortality and liver related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by a sustained virologic response.**

- ✓ **Treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy.**

- ✓ **Patients with short life expectancies owing to liver disease should be managed in consultation with an expert**

AASLD Guideline. March 2016



Adapted from the US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27-28, 2011, Silver Spring, MD., actualized

Side Effects of PegIFN/Ribavirin

"Interferon Man"

- Depression ranging from mild to suicidality
- Irritability, aggressive behavior
- Worsening of mania
- Fatigue
- Insomnia
- Myalgias, fever, flu-like symptoms
- Hair loss
- Cytopenias


RBV
Interferon
Peg-Interferon

Before 2014

IFN based Regimens

- **Long duration: 24- 48 weeks**
- **Poor compliance:**
- **35-45% dose reduction**
- **14-19% treatment discontinuation**

- **SVR rate clinical trial : <50%**
- **SVR real world : 16-59%**

After 2014

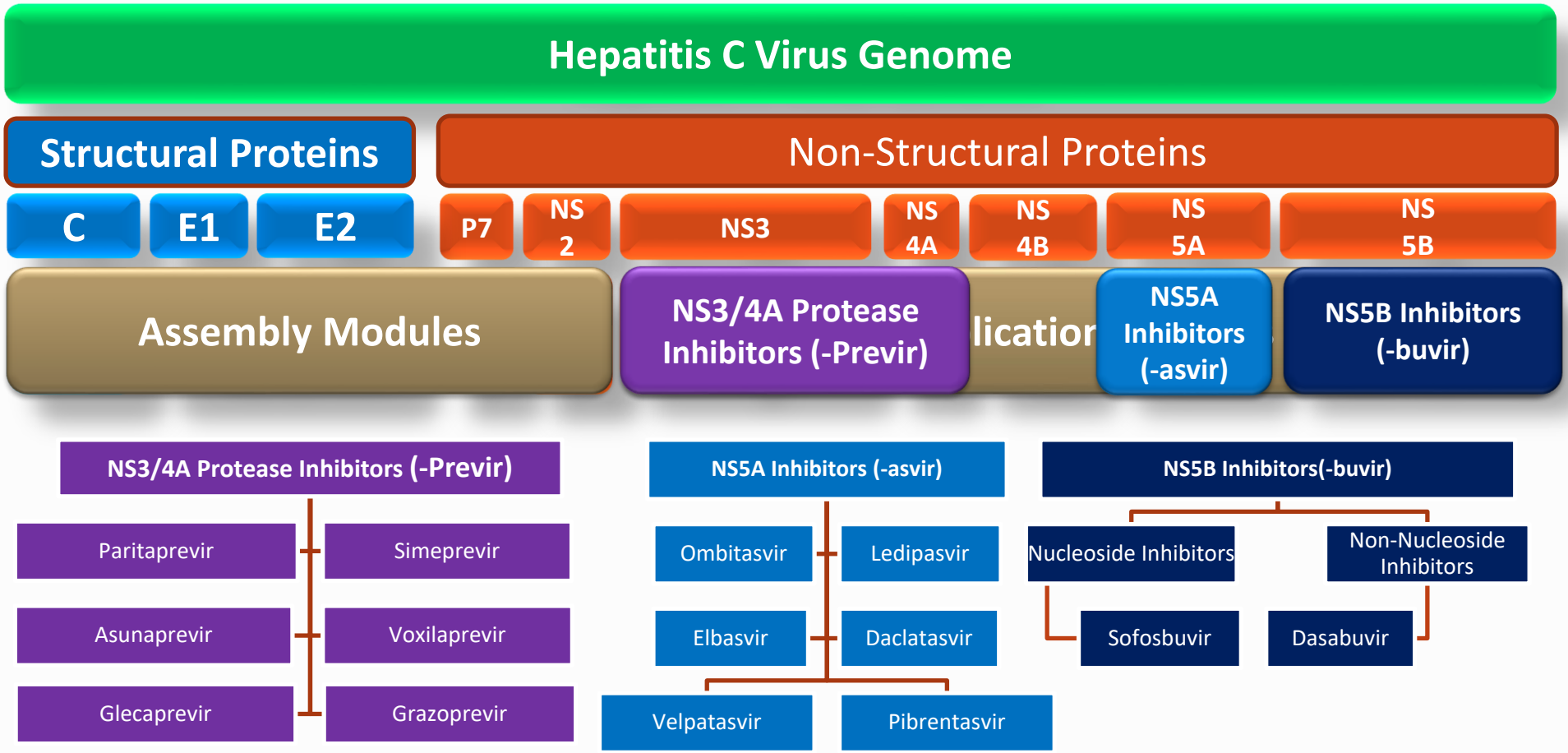
IFN free All Oral Regimens

- **Short duration: 8 – 12 weeks , 24 weeks in special population**
- **Minimal adverse effects**
- **Improved compliance: >95%**

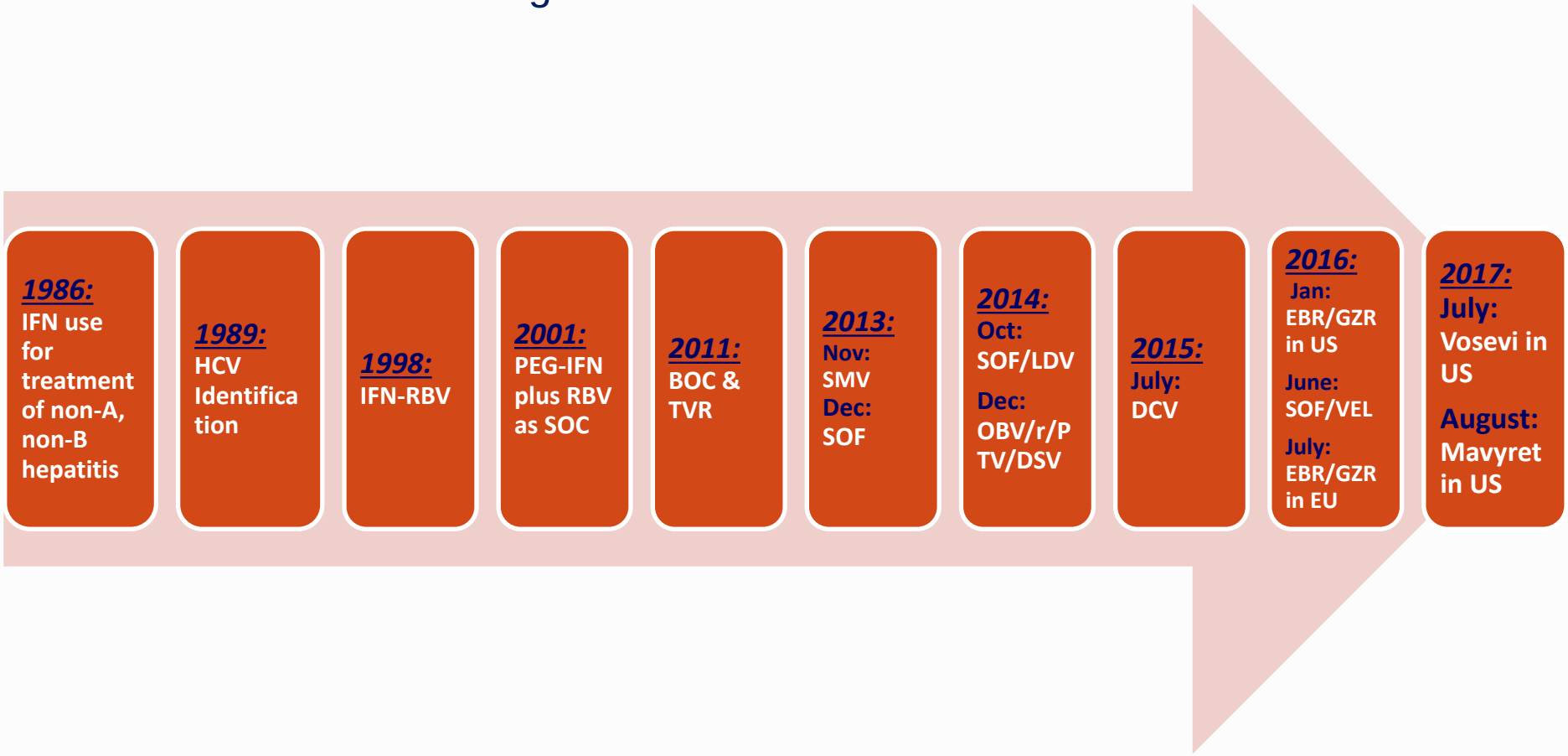
- **SVR Rate clinical trial : >95%**
- **SVR rate real world: ?**

Di Bisceglie A et al. AASLD 2013, McHuchisen JG et al. N Eng J Med 1998, Manns MP et al. Lancet 2001 , Mchutchison JG et al. N Eng J Med 2009, McComb JS et al. EASL 2015; S191, Morisco F et al. Rev Recent Clin Trials 2015

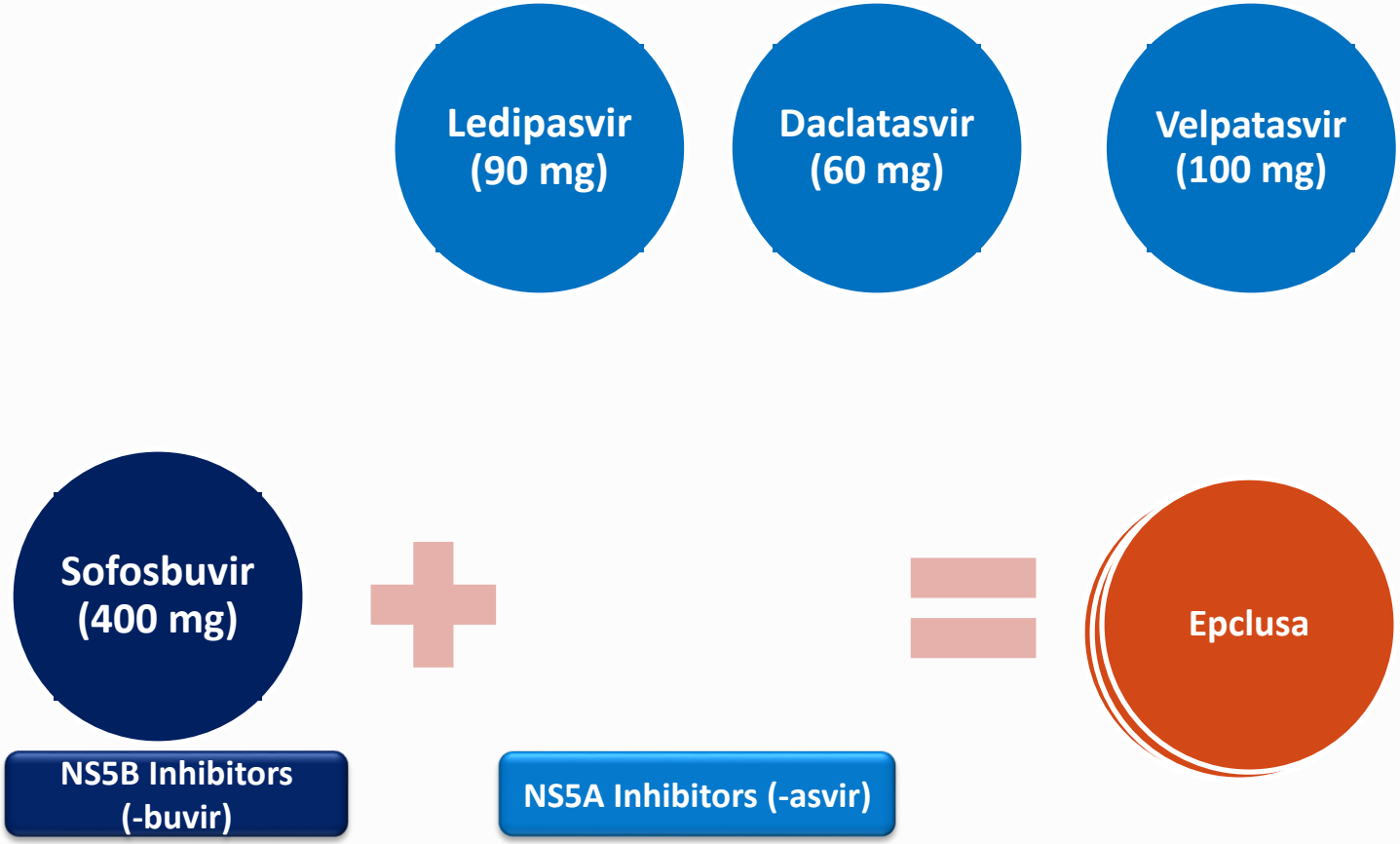
HCV Genome and Available Approved Direct Acting Antivirals



Milestones in HCV Management



Combination of NS5B and NS5A Inhibitors



Combination of NS5B and NS5A Inhibitors

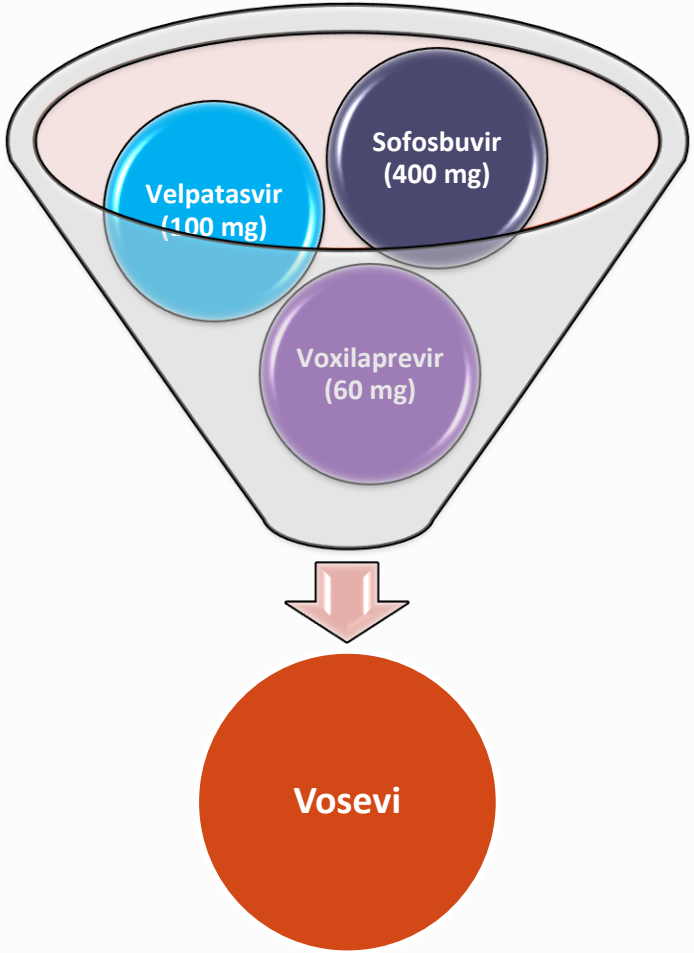
NS5B Inhibitors (-buvir)

+

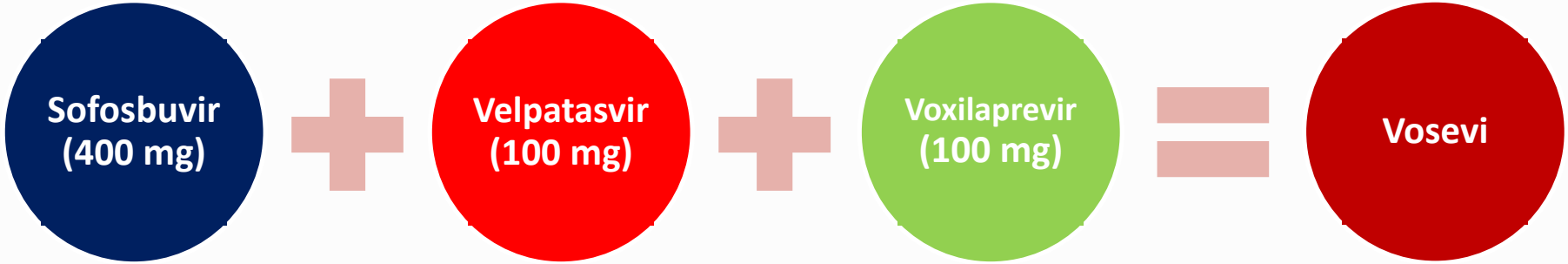
NS5A Inhibitors (-asvir)

+

NS3/4A Protease Inhibitors (-Previr)

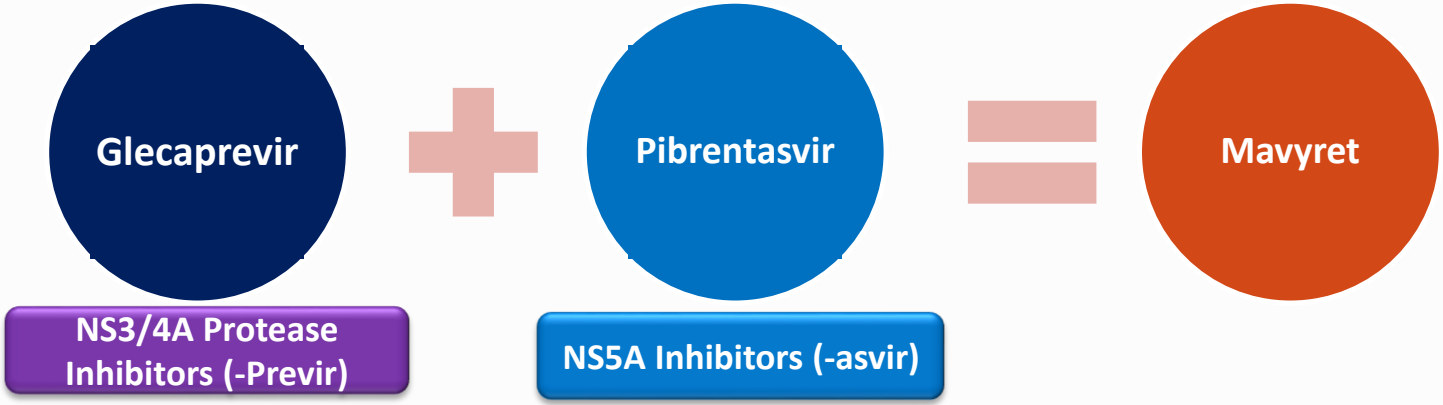


Combination of NS5B and NS5A and NS3/4A Protease Inhibitors



- For treatment of HCV genotypes 1-6 without cirrhosis (liver disease) or with mild cirrhosis
- The first treatment approved for patients who have been previously treated with the DAA sofosbuvir or NS5A Inhibitors
- The most common adverse reactions : headache, fatigue, diarrhea and nausea
- It is contraindicated in patients taking the drug rifampin.

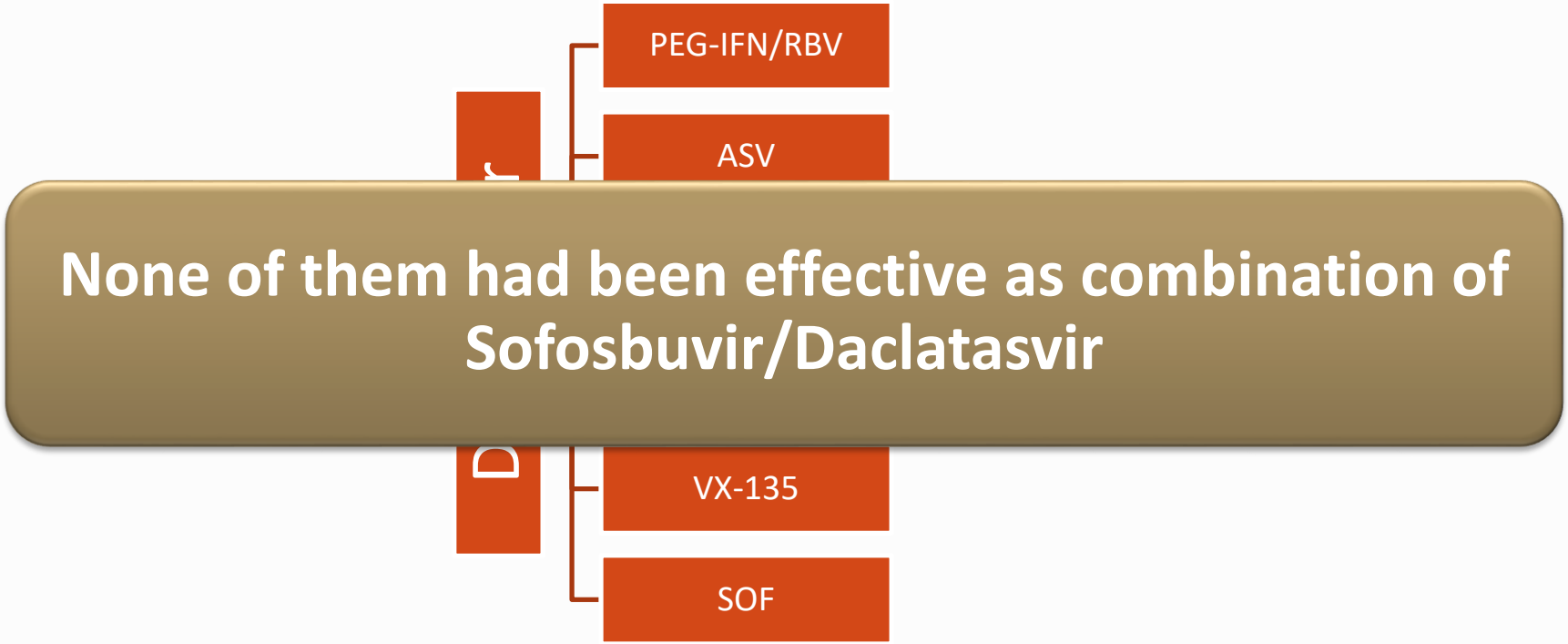
Combination of NS3/4A Protease and NS5A Inhibitors



Combination of NS5A and NS3/4A Protease Inhibitors

- **To treat HCV genotypes 1-6 without cirrhosis (liver disease) or with mild cirrhosis, including patients with moderate to severe kidney disease**
- **To treat HCV genotype 1 infection, previously treated with a regimen containing an NS5A inhibitor or an NS3/4A protease inhibitor but not both.**
-
- **It is the first treatment of eight weeks duration approved for non-cirrhotic and naïve HCV-Infected Patients with all genotypes**
- **The most common adverse : headache, fatigue and nausea.**
- **It is not recommended in patients with moderate cirrhosis and contraindicated in patients with severe cirrhosis of those taking the drugs Atazanavir and rifampin.**

Daclatasvir Has Been Used in Different Regimens



Alavian SM, Rezaee-Zavareh MS. Daclatasvir-based Treatment Regimens for Hepatitis C Virus Infection: A Systematic Review and Meta-Analysis. Hepatitis Monthly. 2016;16(9):e41077. doi:10.5812/hepatmon.41077

Grouping the HCV Patients

Non-Cirrhotics

Genotypes
1a/1b/2/3/4/5/6

Compensated Cirrhosis
Child A

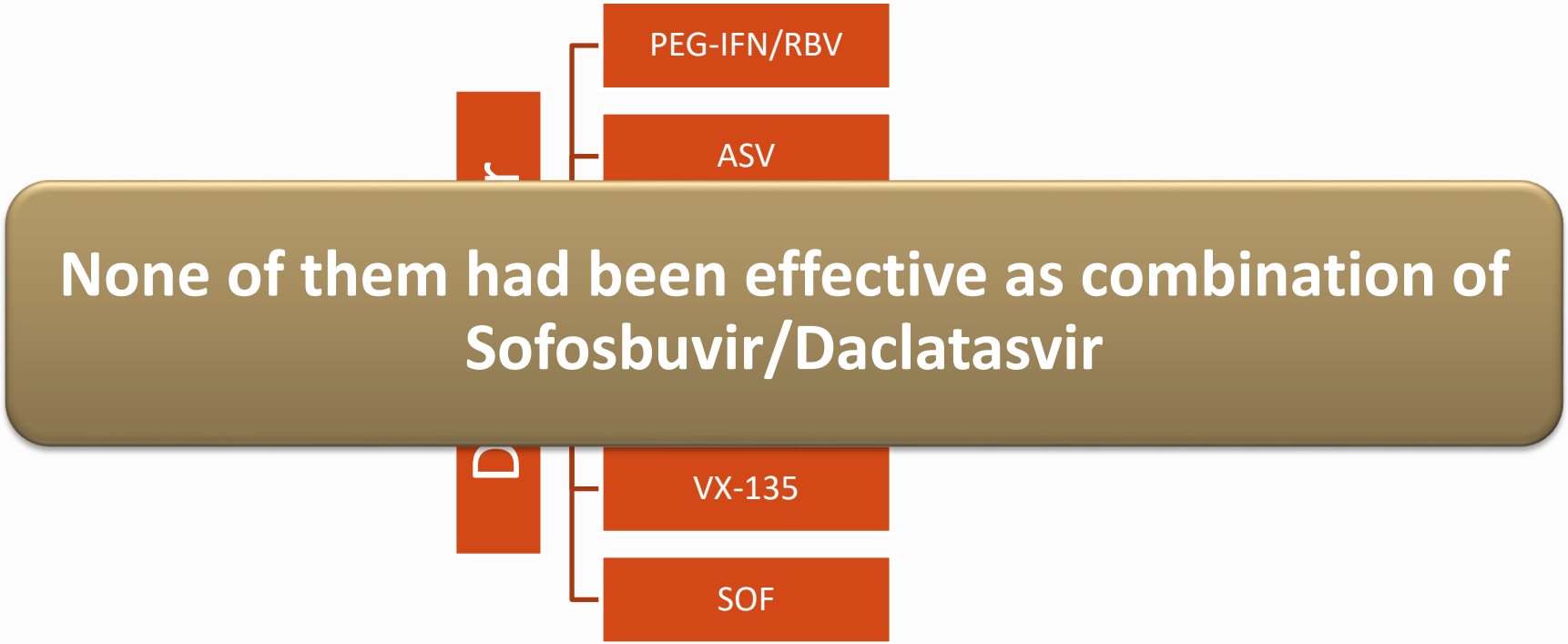
Previous treatment failure with DDAs

Decompensated Cirrhosis
Child B and C up to 12, MELD up to 20

Status of GFR and renal failure

Very decompensated Cirrhosis
Child > 12, MELD>20

Daclatasvir Has Been Used in Different Regimens



Alavian SM, Rezaee-Zavareh MS. Daclatasvir-based Treatment Regimens for Hepatitis C Virus Infection: A Systematic Review and Meta-Analysis. Hepatitis Monthly. 2016;16(9):e41077. doi:10.5812/hepatmon.41077

Sofosbuvir/Ledipasvir for Treatment of genotype-1 HCV Infection

Only in treatment regimen of 12 weeks of SOF/LDV, cirrhosis had a significant effect on the SVR12

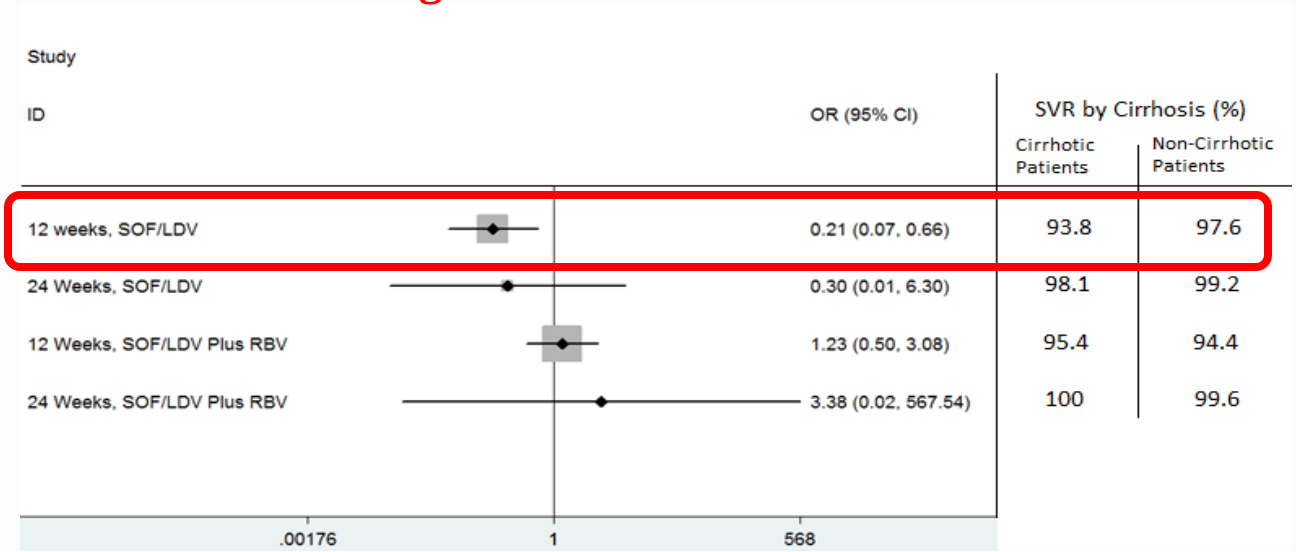
Treatment-experience with PEG-IFN had no significant effect on these regimens

NS5A resistance-associated variants at baseline were associated with decrease in the rate of SVR

Rezaee-Zavareh MS, Sharafi H, Hesamizadeh KH, Behnava B, Gholami-Fesharaki, Alavian SM. Combination of Ledipasvir and Sofosbuvir for Treatment of Hepatitis C Virus Genotype 1 Infection: Systematic Review and Meta-analysis.Annals of Hepatology. In press

Sofosbuvir/Ledipasvir (HARVONI) Effect of cirrhosis

Only in treatment regimen SOF/LDV, cirrhosis had a significant effect on SVR12



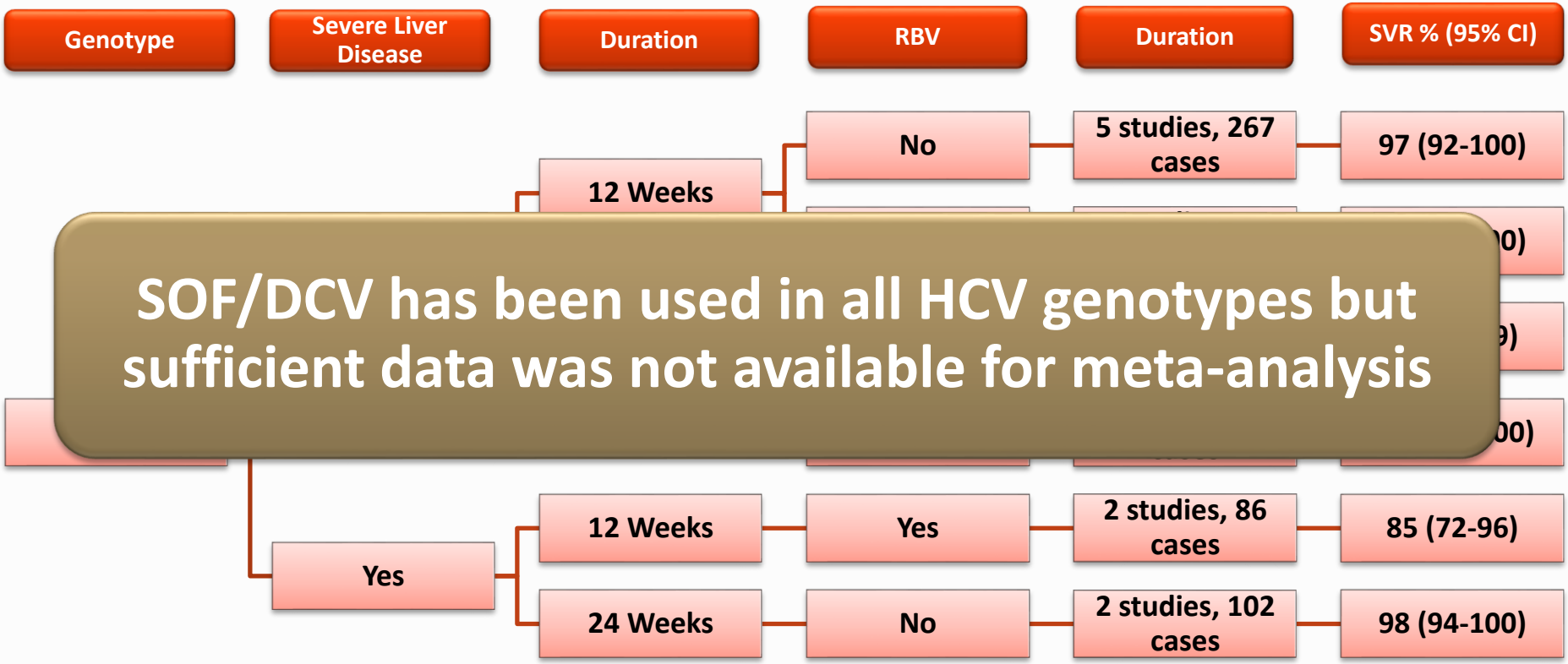
Effect of Cirrhosis on the Sustained Virologic Response for Regimen Sofosbuvir Plus Ledipasvir With or Without Ribavirin for 12 or 24 Weeks
Our Unpublished Meta-Analysis

Rezaee-Zavareh MS, Sharafi H, Hesamizadeh KH, Behnava B, Gholami-Fesharaki, Alavian SM. Combination of Ledipasvir and Sofosbuvir for Treatment of Hepatitis C Virus Genotype 1 Infection: Systematic Review and Meta-analysis.Annals of Hepatology. In press

DAAs Contraindications

Drug	Contraindication/Warning
Daclatasvir	Drug Influencing CYP3A, Co-administration with Amiodarone
Sofosbuvir	Co-administration with Amiodarone, patients with estimated GFR of less than 30 mL/min/1.73 m^2. Caution is needed for co-administration with beta blockers
Ledipasvir/Sofosbuvir	Co-administration with Amiodarone, inducers of p-glycoprotein, patients with estimated GFR of less than 30 mL/min/1.73 m^2
Velpatasvir/Sofosbuvir	Inducers of p-glycoprotein, patients with estimated GFR of less than 30 mL/min/1.73 m^2, Co-administration with Amiodarone
Simeprevir	Cirrhotic patients with Child Pugh class B and C

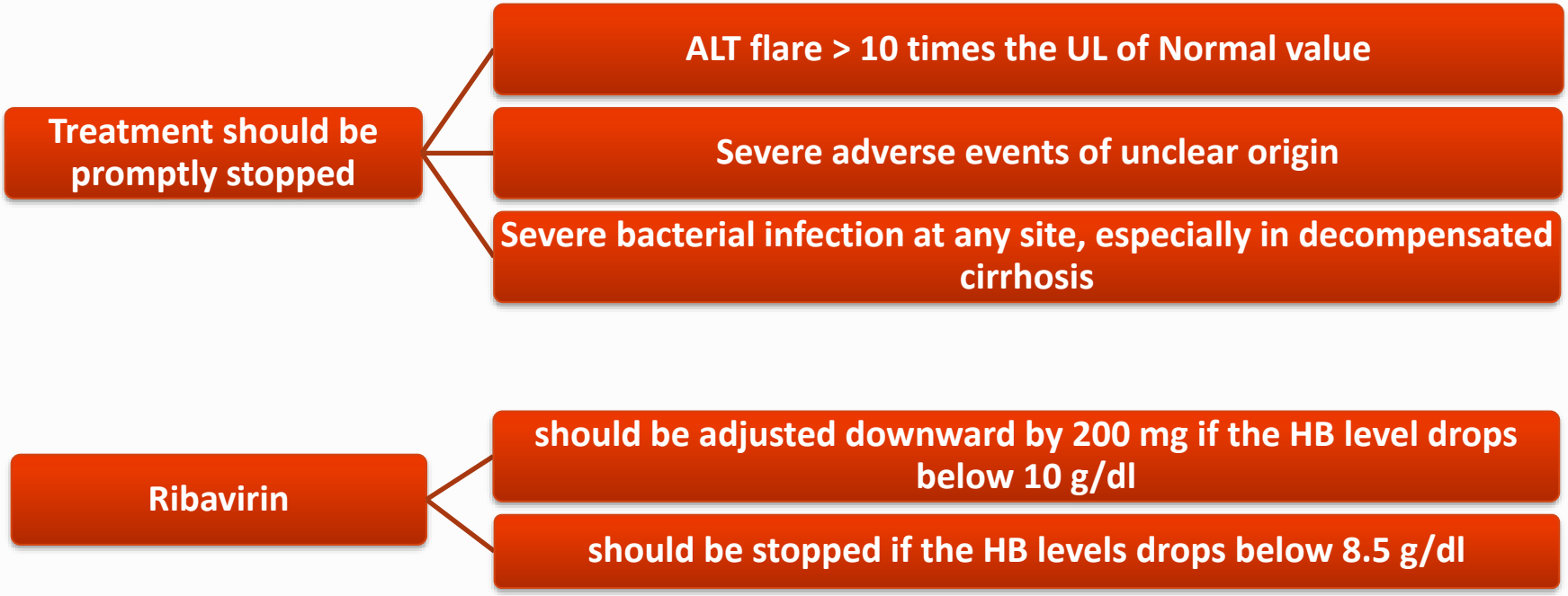
Sofosbuvir/Daclatasvir for Treatment of genotype-1 HCV Infection



SOF/DCV has been used in all HCV genotypes but sufficient data was not available for meta-analysis

Alavian SM, Rezaee-Zavareh MS. Daclatasvir-based Treatment Regimens for Hepatitis C Virus Infection: A Systematic Review and Meta-Analysis. Hepatitis Monthly. 2016;16(9):e41077. doi:10.5812/hepatmon.41077

Treatment Dose Reduction and Discontinuation



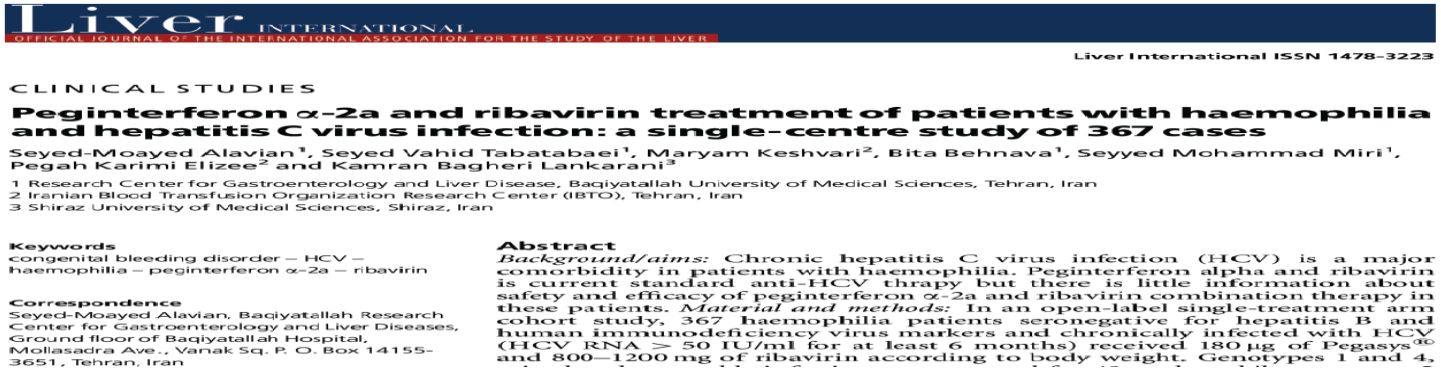
Post Treatment Follow-up

Post-treatment follow-up of patients who achieve an SVR

Non-cirrhotic patients	• **Check the ALT and HCV RNA (or HCV core antigen) at 48 weeks post-treatment and Discharge the patients if ALT is normal and HCV RNA is negative**
Advanced fibrosis (F3) or Cirrhotic patients	• **Surveillance for HCC every 6 months by means of ultrasound**
PWID or men who have sex with men	• **Annual HCV RNA assessment**

Iranian Experiences

Treatment (A Brief History)



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CLINICAL STUDIES

Peginterferon α-2a and ribavirin treatment of patients with haemophilia and hepatitis C virus infection: a single-centre study of 367 cases

Seyed-Moayed Alavian[1], Seyed Vahid Tabatabaei[1], Maryam Keshvari[2], Bita Behnava[1], Seyyed Mohammad Miri[1], Pegah Karimi Elizee[2] and Kamran Bagheri Lankarani[3]

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2 Iranian Blood Transfusion Organization Research Center (IBTO), Tehran, Iran
3 Shiraz University of Medical Sciences, Shiraz, Iran

Keywords
congenital bleeding disorder – HCV – haemophilia – peginterferon α-2a – ribavirin

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Abstract
Background/aims: Chronic hepatitis C virus infection (HCV) is a major comorbidity in patients with haemophilia. Peginterferon alpha and ribavirin is current standard anti-HCV therapy but there is little information about safety and efficacy of peginterferon α-2a and ribavirin combination therapy in these patients. *Material and methods:* In an open-label single-treatment arm cohort study, 367 haemophilia patients seronegative for hepatitis B and human immunodeficiency virus markers and chronically infected with HCV (HCV RNA > 50 IU/ml for at least 6 months) received 180 μg of Pegasys® and 800–1200 mg of ribavirin according to body weight. Genotypes 1 and 4,

Two hundred and twenty-five subjects **61%** achieved SVR, 66 patients relapsed and 30 subjects did not respond and nine patients developed breakthrough during treatment. Peg interferon alpha-2a in combination with weight-based ribavirin has SVR rate of **51%** for genotype 1 and **71%** for genotype non-1 infections in hemophilia patients.

Alavian SM, et al. Peginterferon alpha-2a and ribavirin treatment of patients with haemophilia and hepatitis C virus infection: a single-centre study of 367 cases. Liver Int. 2010

Treatment (A Brief History)

Table 2. Multivariate analysis of sustained virological response after antiviral therapy including the entire study population

Determinant	OR (95% CI)
Age <24 (median)	1.9 (1.1–3.1)
BMI <25	2.1 (1.3–3.4)
Viral load < 600 000 IU/ml	1.8 (1.1–2.9)
Genotype non-1	1.9 (1.1–3.2)

CI, confidence interval; OR, odds ratio.

Alavian SM, et al. Peginterferon alpha-2a and ribavirin treatment of patients with haemophilia and hepatitis C virus infection: a single-centre study of 367 cases. Liver Int. 2010

Generic DAA is available in Iran

The preliminary data showed the **SVR** more than **95%** in Iranian HCV-G1 with all Iranian generic drugs

The Efficacy of 12 Weeks of Sofosbuvir-Daclatasvir (Sovodak), and Ribavirin in Treating Hepatitis C Patients with Cirrhosis, Genotypes 1 and 3

- The combination of Sofosbuvir-daclatasvir **(Sovodak)** can be used to treat **all genotypes** of hepatitis C.

- Current guidelines for treating hepatitis C cirrhosis do not clarify weather **12** weeks or **24** weeks of treatment is appropriate.

Merat S, Sharifi AH, Haj-Sheykholeslami A, Poustchi H, Fattahi B, Nateghi-Baygi A, Alavian, SM, Malekzadeh R. The Efficacy of 12 Weeks of Sofosbuvir, Daclatasvir, and Ribavirin in Treating Hepatitis C Patients with Cirrhosis, Genotypes 1 and 3. Hepat Mon. 2016

The Efficacy of 12 Weeks of Sofosbuvir-Daclatasvir (Sovodak), and Ribavirin in Treating Hepatitis C Patients with Cirrhosis, Genotypes 1 and 3, Continue

- One hundred patients with hepatitis C and cirrhosis infected with Genotypes 1 and 3 were included in the present study. They were treated with 1 tablet of a combination pill of 400 mg sofosbuvir and 60 mg daclatasvir daily **(Sovodak)** and weight-based **ribavirin** for 12 weeks
- Response to treatment was assessed 12 weeks after the end of the treatment with a sensitive assay (SVR12).
- Among the 94 patients who finished the study, 92 achieved SVR12 (**98%**, per-protocol, **92%** intention-to-treat). None of the patients reported any side effects.

- **Conclusions:** The fixed-dose combination drug of **Sovodak** with weight-base ribavirin for 12 weeks is **extremely effective** and **safe** in treating HCV patients with **Genotypes 1 and 3 and cirrhosis.**

Merat S, Sharifi AH, Haj-Sheykholeslami A, Poustchi H, Fattahi B, Nateghi-Baygi A, Alavian, SM, Malekzadeh R. The Efficacy of 12 Weeks of Sofosbuvir, Daclatasvir, and Ribavirin in Treating Hepatitis C Patients with Cirrhosis, Genotypes 1 and 3. Hepat Mon. 2016

Efficacy and Safety of Generic Sofosbuvir/Ledipasvir (Sobopasvir) Fixed-dose Combination in Iranian Patients with Chronic Hepatitis C Virus Infection

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Iran Hepatitis Network,
Co-authored by: Heidar Sharafi, Mehri Nikbin, Seyed Hoda Alavian, Bita Behnava,

Introduction: Hepatitis C virus (HCV) infection as a global health concern has infected around 2% of world population. Introduction of direct-acting antiviral regimens such as Sofosbuvir/Ledipasvir (SOF/LDV) made the treatment of HCV infection superior to previous HCV antiviral therapies in term of efficacy and feasibility. This study aimed to assess the efficacy and safety of generic SOF/LDV in Iranian patients with HCV infection.

Method and Materials: This prospective cohort study was conducted on HCV-infected patients referred Middle East Liver Diseases Center in 2016. Non-cirrhotic patients were treated with daily fixed-dose combination of SOF/LDV (Sobopasvir) for 12 weeks. In cases with compensated cirrhosis, patients were treated with SOF/LDV plus daily weight adjusted RBV for 12 weeks. If the patient with cirrhosis was RBV intolerant, he/she was treated with daily fixed-dose combination of SOF/LDV for 24 weeks.

Results: In this study, 30 patients with mean age 52.9

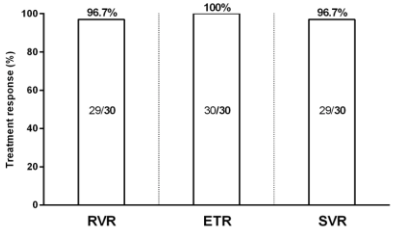


Figure 1. Responses to Treatment with Sofosbuvir/Ledipasvir Fixed-dose Combination

30 patients were enrolled and most of them were cirrhotic (53.3%), infected with HCV-1a (46.7%) and had previous history of HCV antiviral therapy (62.1%). RVR was observed in 29 (96.7%, 95%CI=83.3%-99.4%) and SVR in 29 (96.7%, 95%CI=83.3%-99.4%). The only case of treatment failure was a relapse. No serious treatment adverse-event was observed during the treatment course.

Conclusions: The generic SOF/LDV was efficacious and safe for treatment of Iranian patients with chronic HCV infection.

Sharafi H, Nikbin M, Alavian SH, Behnava B, Alavian SM. Efficacy and Safety of Generic Sofosbuvir/Ledipasvir Fixed-Dose Combination in Iranian Patients with Chronic Hepatitis C Virus Infection. Hepatitis monthly. 2017;17(6):e12216.

Recommendations for the Clinical Management of Hepatitis C in Iran:
A Consensus-Based National Guideline.
By **Iran Hepatitis Network**

Alavian SM, et al. Recommendations for the Clinical Management of Hepatitis C in Iran: A Consensus-Based National Guideline. Hepat Mon. 2016

- Assessment of liver disease severity is recommended prior to therapy.
- Identifying patients with cirrhosis or advanced (bridging) fibrosis is of particular importance, as the choice of the treatment regimen and the post-treatment prognosis depend on the stage of fibrosis.

Treatment of HCV-Genotype 1 Infection

SOF/VEL

Non-Cirrhotic and Naive to SOF-Based Regimens	Non-Cirrhotic with History of SOF-Based Therapy	Compensated Cirrhosis[a] (Child A) and Naive to SOF-Based Regimens	Compensated Cirrhosis[a] (Child A) with History of SOF-Based Therapy	Decompensated Cirrhosis (Child B or C)
A. Daily DCV (60 mg) + Daily SOF (400 mg) for 12 weeks[b]	A. Daily DCV (60 mg) + Daily SOF (mg) with RBV (ks[b]	A. Daily DCV (60 mg) + Daily SOF (400 mg) for 24 weeks or plus Daily weight adjusted RBV (1000 - 1200 mg) for 12 weeks[b]	A. Daily DCV (60 mg) + Daily SOF g) plu 1200	A. Daily DCV (60 mg) + Daily SOF (400 mg) with Daily RBV (1000 - 1200 mg) for 24 weeks or without RBV[b,c]
B. Daily LDV (90 mg)+ Daily SOF (400mg) for 12 weeks[b]	B. D ly S w V (1000 00 mg) fo weeks[b]	B. Daily LDV (90 mg)+ Daily SOF (400mg) for 24 weeks or plus Daily weight adjusted RBV (1000 - 1200 mg) for 12 weeks[b]	B SO g) plu weight adjusted RBV (1000 - 1200 mg) for 24 weeks[b]	B. Daily LDV (90 mg)+ Daily SOF (400mg) with Daily RBV (1000 - 1200 mg) for 24 weeks or without RBV[b,c]
C. As al tive: D SOF (400 N α-2a (18 1.5 μg/Kg adju mg) for 12 we ks				

Abbreviations: DCV, Daclatasvir; LDV, Ledipasvir; SOF, Sofosbuvir; RBV, Ribavirin.
[a] Including patients with pre-cirrhosis (F3-F4).
[b] There is not any priority between suggested regimens above. Both regimens are available now.
[c] 24 weeks without RBV in cases with RBV intolerance or contraindication.

Alavian SM, et al. Recommendations for the Clinical Management of Hepatitis C in Iran: A Consensus-Based National Guideline. Hepat Mon. 2016

Update on Treatment of HCV-Genotype 1 Infection

Treatment Naïve Patients without Cirrhosis	DAA-naïve Patients with Compensated Cirrhosis[b] (Child A) and/or History of PegIFN/RBV Therapy	DAA-naïve Patients with Decompensated Cirrhosis (Child B or C)	DAA-experienced Patients
A. Daily DCV (60 mg) + Daily SOF (400 mg) for 12 weeks	A. Daily DCV (60 mg) + Daily SOF (400 mg) with Daily RBV (1000-1200 mg) for 12 weeks[c]	A. Daily DCV (60 mg) + Daily SOF (400 mg) with Daily RBV (1000-1200 mg) for 24 weeks[c]	A. Daily VEL (100 mg) + Daily SOF (400mg) with Daily RBV (1000-1200 mg) for 24 weeks[c]
A. Daily LDV (90 mg) + Daily SOF (400mg) for 12 weeks	A. Daily LDV (90 mg) + Daily SOF (400mg) with Daily RBV (1000-1200 mg) for 12 weeks[c]	A. Daily LDV (90 mg) + Daily SOF (400mg) with Daily RBV (1000-1200 mg) for 24 weeks[c]	
A. Daily VEL (100 mg) + Daily SOF (400 mg) for 12 weeks	A. Daily VEL (100 mg) + Daily SOF (400 mg) for 12 weeks	A. Daily VEL (100 mg) + Daily SOF (400mg) with Daily RBV (1000-1200 mg) for 24 weeks[c]	

[a]Abbreviation: DCV, Daclatasvir; SOF, Sofosbuvir; LDV, Ledipasvir; VEL, Velpatasvir; RBV, Ribavirin.

[b]Including patients with pre-cirrhosis (F3-F4)

[c]24 weeks without RBV in cases with RBV intolerance or contraindication

Alavian SM, Sharafi H. Update on Recommendations for the Clinical Management of Hepatitis C in Iran 2017. Hepat Mon 2017. In press

Treatment of Hepatitis C Virus Genotype 3 Infection

SOF/VEL

Non-cirrhotic and Naive to SOF-Based Regimens	Non-Cirrhotic with History of SOF-Based Therapy	Compensated Cirrhosis[a] (Child A) and Naive to SOF-Based Regimens	Compensated Cirrhosis[a] (Child A) with History of SOF-Based Therapy	Decompensated Cirrhosis (Child B or C)
A. Daily DCV (60 mg) + Daily SOF (400 mg) for 12 weeks	A. Dail[illegible] Daily SOF (40[illegible] [illegible]y RBV (1000 - 120[illegible] [illegible]2 weeks	A. Daily DCV (60 mg) + Daily SOF (400 mg) with Daily RBV (1000 - 1200 mg) for 24 weeks	A. Dai[illegible] (6[illegible] Daily SOF (4[illegible] [illegible]ily RBV (1000 - 12[illegible] [illegible]r 24 weeks	A. Daily DCV (60 mg) + Daily SOF (400 mg) with Daily RBV (1000 - 1200 mg) for 24 weeks or without RBV[b]
B. As alternative: Daily SOF (400 [illegible] Weekly P[illegible] α[illegible] Or [illegible] μg[illegible] adjust[illegible] [illegible] mg) for 12 w[illegible]				
C [illegible] (40[illegible] [illegible]aily w[illegible] adjus[illegible]RBV (1000 - [illegible] mg) for 24 weeks				

Abbreviation: DCV, Daclatasvir; RBV, Ribavirin; SOF, Sofosbuvir.
[a] Including patients with pre-cirrhosis (F3-F4).
[b] 24 weeks without RBV in cases with RBV intolerance or contraindication.

Alavian SM, et al. Recommendations for the Clinical Management of Hepatitis C in Iran: A Consensus-Based National Guideline. Hepat Mon. 2016

Update on Treatment of HCV-Genotype 3 Infection

Treatment Naïve Patients without Cirrhosis	DAA-naïve, PegIFN/RBV-experienced Patients without Cirrhosis	DAA-naïve Patients with Cirrhosis (Child A) ± History of PegIFN/RBV Therapy	DAA-naïve Patients with Decompensated Cirrhosis (Child B or C)	DAA-experienced Patients
A. Daily DCV (60 mg) + Daily SOF (400 mg) for 12 weeks	A. Daily DCV (60 mg) + Daily SOF (400 mg) with Daily RBV (1000-1200 mg) for 12 weeks[c]	A. Daily DCV (60 mg) + Daily SOF (400 mg) with Daily RBV (1000-1200 mg) for 24 weeks[c]	A. Daily DCV (60 mg) + Daily SOF (400 mg) with Daily RBV (1000-1200 mg) for 24 weeks[c]	A. Daily VEL (100 mg) + Daily SOF (400mg) with Daily RBV (1000-1200 mg) for 24 weeks[c]
A. Daily VEL (100 mg) + Daily SOF (400 mg) for 12 weeks	A. Daily VEL (100 mg) + Daily SOF (400 mg) with Daily RBV (1000-1200 mg) for 12 weeks[c]	B. Daily VEL (100 mg) + Daily SOF (400 mg) with Daily RBV (1000-1200 mg) for 12 weeks[c]	B. Daily VEL (100 mg) + Daily SOF (400 mg) with Daily RBV (1000-1200 mg) for 24 weeks[c]	

[a]Abbreviation: DCV, Daclatasvir; SOF, Sofosbuvir; LDV, Ledipasvir; VEL, Velpatasvir; RBV, Ribavirin.

[b]Including patients with pre-cirrhosis (F3-F4)

[c]24 weeks without RBV in cases with RBV intolerance or contraindication

Alavian SM, Sharafi H. Update on Recommendations for the Clinical Management of Hepatitis C in Iran 2017. Hepat Mon 2017. In press

HCV Treatment Flowchart
for PHC Providers

MELDcenters

HCV Ab → + → HCV RNA (RT-PCR)

HCV Ab → − → No HCV Infection

HCV RNA (RT-PCR) → − → HCV Spontaneous Clearance

HCV RNA (RT-PCR) → +

Diagnosis

Assessment of Liver Diseases & Other Parameters

- Non-Cirrhotic, No Previous History of Treatment
  - HCV Genotype 1,4 → LDV/SOF, 12 W or DCV+SOF, 12 W
  - HCV Genotype 2,3 → DCV+SOF, 12 W
- Decompensated Cirrhosis, CKD, HCV/HIV, Thalassemia Liver Transplanted Patient → Specialized Health Care Providers
- Cirrhotic and/or Previous History of Treatment
  - HCV Genotype 1,4 → LDV/SOF + RBV, 12 W or DCV+SOF + RBV, 12 W
  - HCV Genotype 2 → DCV+SOF, 12 W
  - HCV Genotype 3 → DCV+SOF + RBV, 24 W

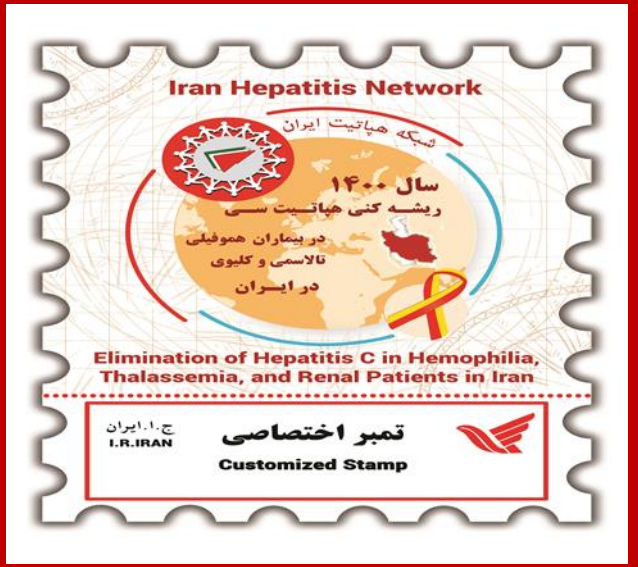
Treatment Regimen

Abbreviation: LDV, Ledipasvir; DCV, Daclatasvir; SOF, Sofosbuvir; CKD, Chronic Kidney Disease; W, Week

Alavian SM, et al. Recommendations for the Clinical Management of Hepatitis C in Iran: A Consensus Based National Guideline. Hepatitis Monthly. 2016;16(8):e40959
Sharafi H, et al. Efficacy and Safety of Generic Sofosbuvir/Ledipasvir Fixed-Dose Combination in Iranian Patients with Chronic Hepatitis C Virus Infection. Hepatitis Monthly. 2017;17(6):e12216.

Elimination of HCV infection in Iran will be in 2030 but in thalassemia and hemophilia is possible in 2020!

Solution



Wo
More support for therapy
More attention to blood safety
More education the nurses in thalassemia centers Increase the thalassemia patients awareness regarding the issue.

Treatment with Sofosbuvir/Daclatasvir and Sofosbuvir/Ledipasvir, EASL 2016

SOF/DCV for 12 weeks can be used in all HCV genotypes and SOF/LDV for 12 weeks can be used in genotypes 1, 4, 5 or 6 HCV infection. Rules for adding RBV to treatment protocol or increasing its duration are as follow:

12 weeks with RBV	• All treatment experienced patients infected with genotypes 1a, 3, 4, 5 or 6 HCV. • All decompensated cirrhotic or Post liver transplanted cases except for genotype 3 infected patients.
24 weeks with RBV	• Cirrhotic or Post liver transplanted cases infected with genotype 3 HCV.
24 weeks without RBV	• When we need RBV for therapy and there is a contraindication for or intolerance to it

Abbreviation: SOF, sofosbuvir; LDV, ledipasvir; DCV, daclatasvir; RBV, ribavirin; HCV, hepatitis C virus

Non-HCC cases, awaiting LT with MELD score < 18-20 should be treated for HCV and then transplanted. These cases with MELD ≥ 18-20 should be first transplanted and then treated. HCC cases, Non-cirrhotic or compensated cirrhotic awaiting LT should receive therapy and LT simultaneously

Co administration with amiodarone or inducers of p-glycoprotein and eGFR <30 ml/min/1.73, are contraindications for using SOF/DCV and SOF/LDV.

For drug-drug interaction visit http://www.hep-druginteractions.org/.