

**TRAINING MANUAL FOR  
TREATMENT ADVOCATES**

**HEPATITIS C VIRUS  
& COINFECTION  
WITH HIV**

**TAG**  
Treatment Action Group

**TAG**

# HCV TREATMENT OPTIONS

- Treating HCV is never an emergency, but early treatment prevents further liver damage.
- **DAAs are easier to take, and better tolerated than PEG-IFN and RBV.**
- Treatment is recommended for all people with HCV, even those without liver damage.
  - Treating HCV is important for HIV-coinfected people because they may get liver damage more quickly than people with HCV alone.
- Despite treatment guidelines recommending treatment for all, many national health systems, private and public payers currently limit treatment to only those people with advanced fibrosis.
- People with very **advanced liver damage** can be treated for HCV, but they may require treatment **for up to 24 weeks and/or ribavirin**, and treatment is less effective.
- Patients with advanced liver disease or liver cancer (***hepatocellular carcinoma***, or HCC) should discuss treatment options with their doctors, including liver transplant.
  - People will need close monitoring to check whether cancer develops or returns.

## Direct-acting antivirals are:

- Easier to take. DAAs are oral medications, taken either once or twice a day. Some medications are combined in single-tablet formulations (called ***fixed-dose combinations***, or FDCs). Some need to be taken with food;
- Highly effective. Cure rates have reached over 95% with some DAA combinations;
- Effective against many or all HCV genotypes; and
- Safe and tolerable. Unlike PEG-IFN and RBV, DAAs have fewer side effects—and they are usually mild.

Duration of treatment depends on whether or not a person has cirrhosis.

# HCV treatments (1/4)

- **Pegylated interferon (PEG-IFN)** - no longer recommended by WHO and AASLD/IDSA, and is only recommended EASL when there are no other options.
  - It may still be used in countries without access to DAAs or in prisons.
- **Ribavirin (RBV)** - same family as some of the treatments used to treat HIV, called *nucleoside analogues*, but it does not work as an HIV treatment.
  - RBV is taken as pills or capsules twice a day.
  - Dose depends on a person's weight.
  - RBV can increase cure rates in people with cirrhosis and is sometimes added to DAAs
  - Causes several unpleasant side effects:
    - Anemia, insomnia, fatigue, irritability, and depression
  - Not recommended for men and women who are planning a pregnancy, since it **causes birth defects**. Male partners of women who become pregnant or who breastfeed should **use condoms for six months after completing HCV treatment**.

# HCV treatments (2/4)

- **Sofosbuvir (Sovaldi<sup>®</sup>, or SOF)** - must be used with other DAAs.
  - In US, used to treat genotypes 1, 2, 3, and 4 for people over the age of 12.
  - SOF is taken once daily, with or without food, for 12 to 24 weeks.
- **Daclatasvir (Daklinza<sup>™</sup>, or DCV)** - taken with SOF, once daily with or without food for 12 or 24 weeks.
  - In US, DCV is approved for people over 18 years old who have HCV genotype 1 or genotype 3 (although it has been used in other genotypes).
- **Sofosbuvir/daclatasvir (Darvoni, or SOF/DCV)** - treats all genotypes and must be taken once daily for 12 weeks.
  - It can be used to treat people before or after liver transplant, with cirrhosis and/or HIV.
- **Simeprevir (Olysio<sup>®</sup>, or SMP)** - approved for genotype 1
  - Must be taken with once daily, with food, for 12 or 24 weeks. It is rarely used in high-income countries.

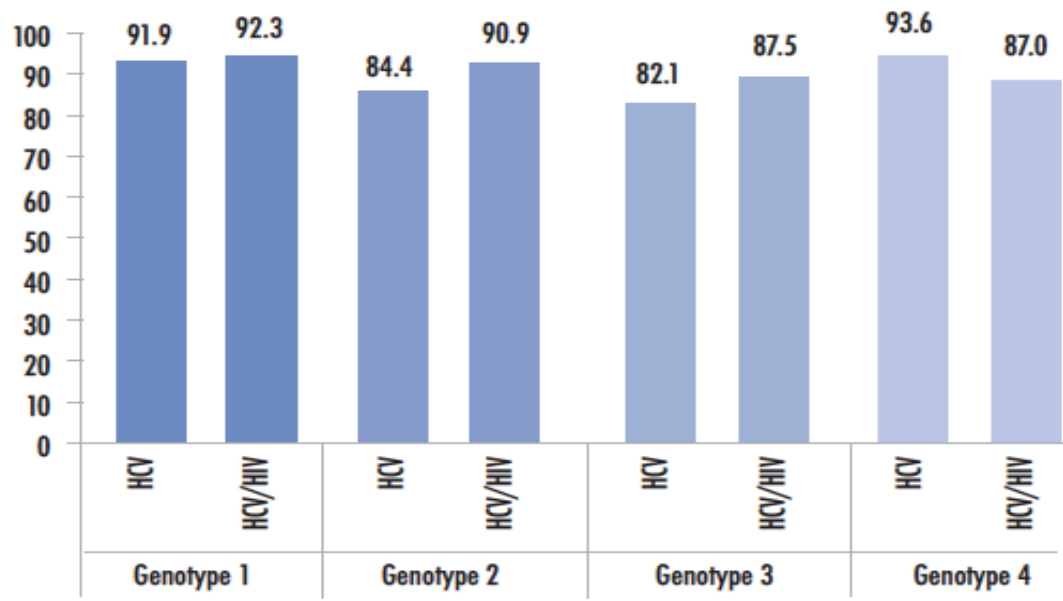
# HCV treatments (3/4)

- **Sofosbuvir/ledipasvir (Harvoni<sup>®</sup>, or SOF/LED)** - two medications in one pill, taken daily, with or without food, for 8 to 24 weeks.
  - In US, it is used to treat hepatitis C genotypes 1, 4, 5, and 6 in people who are over 12 years old.
  - Harvoni approved for people with HCV genotype 1 who have advanced (decompensated) cirrhosis, and for liver transplant recipients who have HCV genotype 1 or 4.
  - Used to treat people with HIV.
  - Studies have shown it to be effective at 8 weeks in people with genotype 1 and without cirrhosis who have not previously been treated with DAAs.
- **Paritaprevir/ritonavir/ombitasvir and dasabuvir (Viekira XR<sup>™</sup>)** - combination of HCV medications.
  - In US, Viekira XR<sup>™</sup> is approved for people with hepatitis C genotype 1 who are over 18 years old.
  - Viekira XR<sup>™</sup> previously approved and prescribed as a twice-daily formula known as Viekira Pak.
  - Latest XR regimen contains the same medicines, in the same amounts, as Viekira Pak, now in a once-daily package.

# HCV treatments (4/4)

- **Sofosbuvir/velpatasvir/voxilaprevir (Vosevi<sup>®</sup>, or SOF/VEL/VOX)** - fixed-dose combination taken once daily for 12 weeks.
  - Does not require RBV.
  - Can effectively treat all genotypes, including difficult-to-treat genotype 3, people with or without cirrhosis, and people with chronic kidney disease.
  - In US, marketed as a salvage treatment regimen for people who previously failed DAA treatment, but it is approved as a first-line treatment, taken for 12 weeks, in the European Union.
- **Glecaprevir/pibrentasvir (Mavyret<sup>™</sup>, or G/P)** - fixed-dose combination, taken once daily with food for 8, 12, or 16 weeks.
  - Can effectively treat all genotypes, including difficult-to-treat genotype 3, people with or without cirrhosis, and people with chronic kidney disease.
  - Shows a high SVR of 95 percent with eight weeks of treatment in people without cirrhosis who have never been treated with DAAs before, making it the **shortest treatment course** currently available.
- **Sofosbuvir/ravidasvir (SOF/RVD)** - generic regimen currently under study in clinical trials, which may be used to treat all genotypes.
  - Taken once daily for 12 weeks, or 24 weeks for people with compensated cirrhosis.

# SVR12 Rates by HCV Genotype and Treatment Group

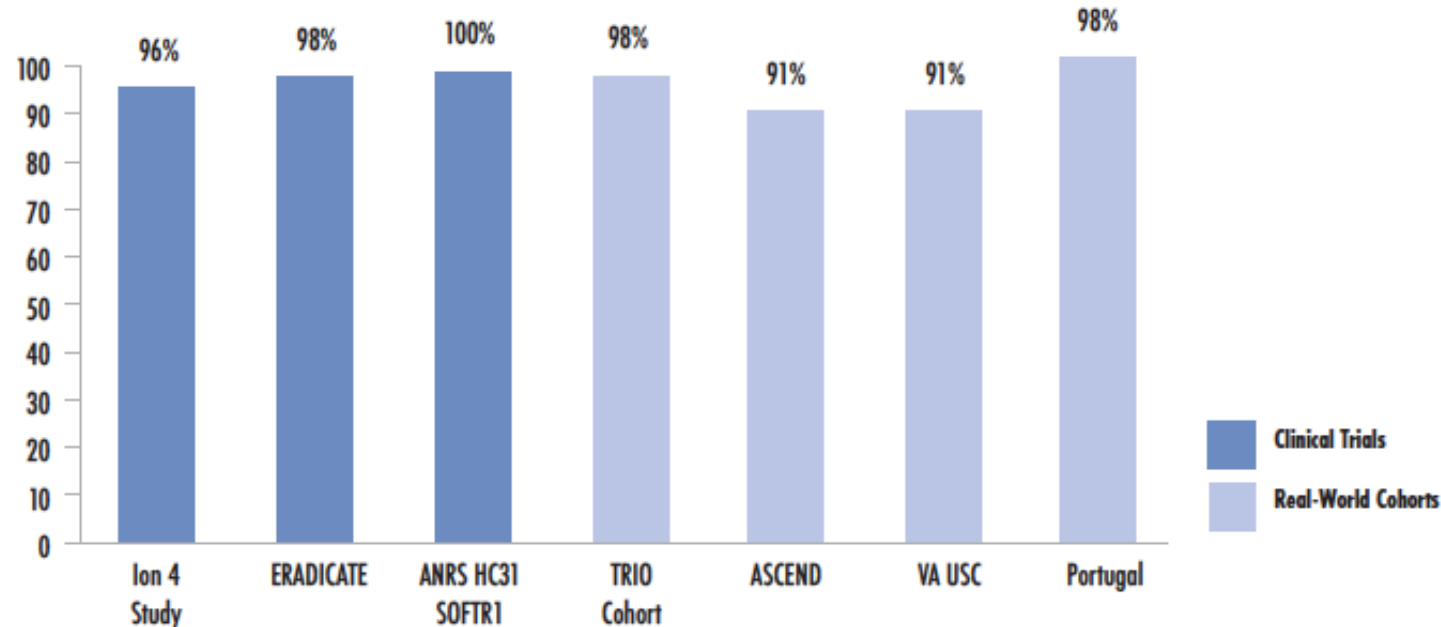


Source: Jurgen R. "Summary for AASLD 2016 for Hepatitis C: New HCV two and three drug regimens on their way: What do they promise? And what do clinicians need to look out for under DAA combination therapy and beyond SVR?" Reported from 67th Annual Meeting of the American Association for the Study of Liver Diseases; 2016 November 11-15; Boston, MA.

- Using SOF/LED, SOF/DCV with and without RBV, according to genotypes, DAAs are effective among HCV mono-infected and HIV/HCV coinfecting people.
- Most mono-infected people achieved **over 90% SVR rates for 12 weeks** of treatment, including people with cirrhosis.
- HIV/HCV cure rates at week 12 actually have higher results than in mono-infected people, except for genotype 4.



# Clinical Trials Compared to Real-World Cohorts



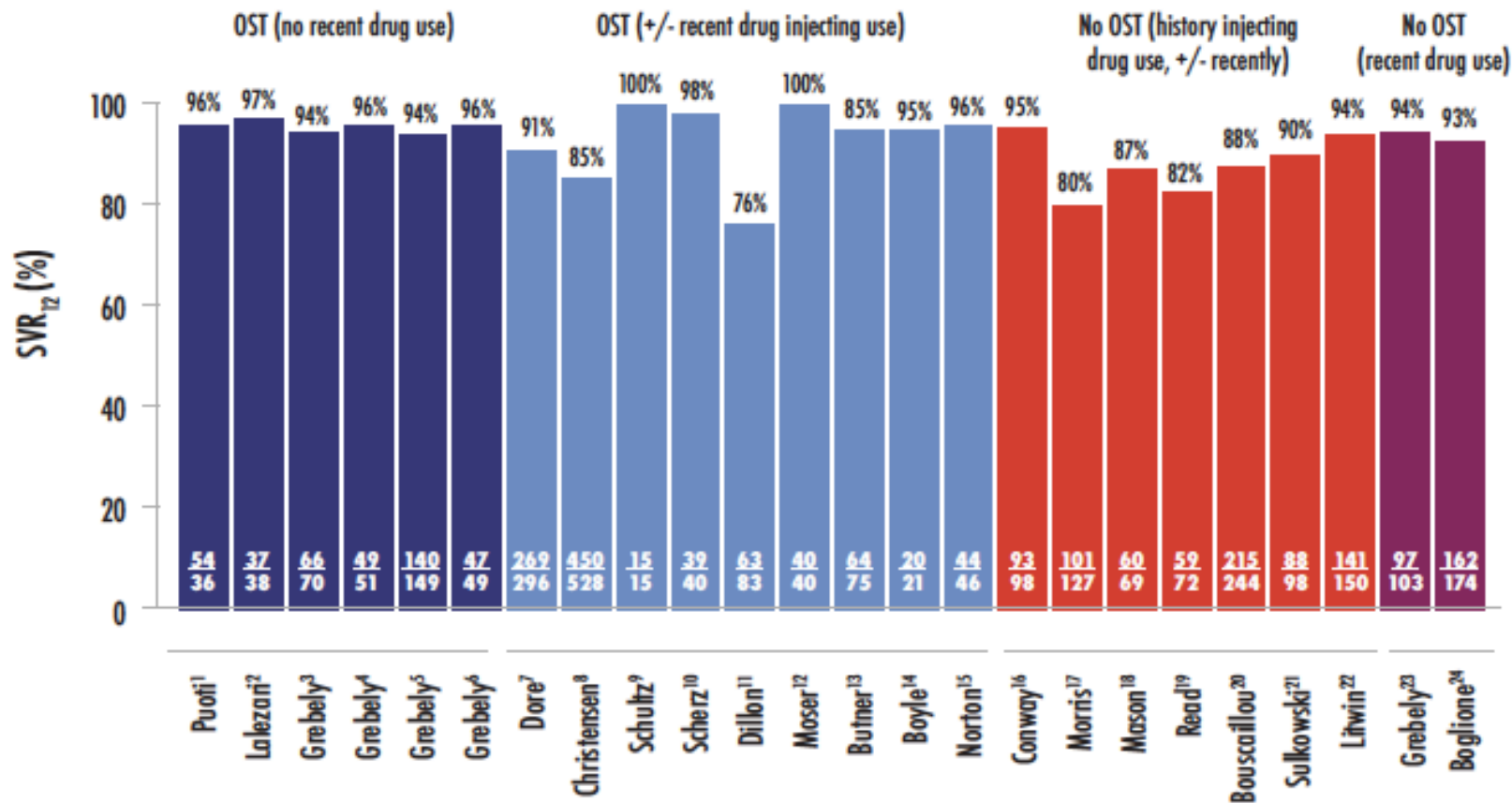
Source: Naggie S et al. Real World Effectiveness of Ledipasvir/Sofosbuvir (LDV/SOF) in Patients Coinfected With HCV and HIV-1: A Comparative Analysis of Clinical Trials with Four Real World Cohorts. Poster presented at: 67th Annual Meeting of the American Association for the Study of Liver Diseases; 2016 November; Boston, MA; Abstract 898.

- DAAs show **comparative rates** for HIV/HCV coinfected people in clinical trials as in real-world studies.
- As with HIV treatments, the newer HCV medicines need to be taken regularly—missing doses can lead to **drug resistance**.

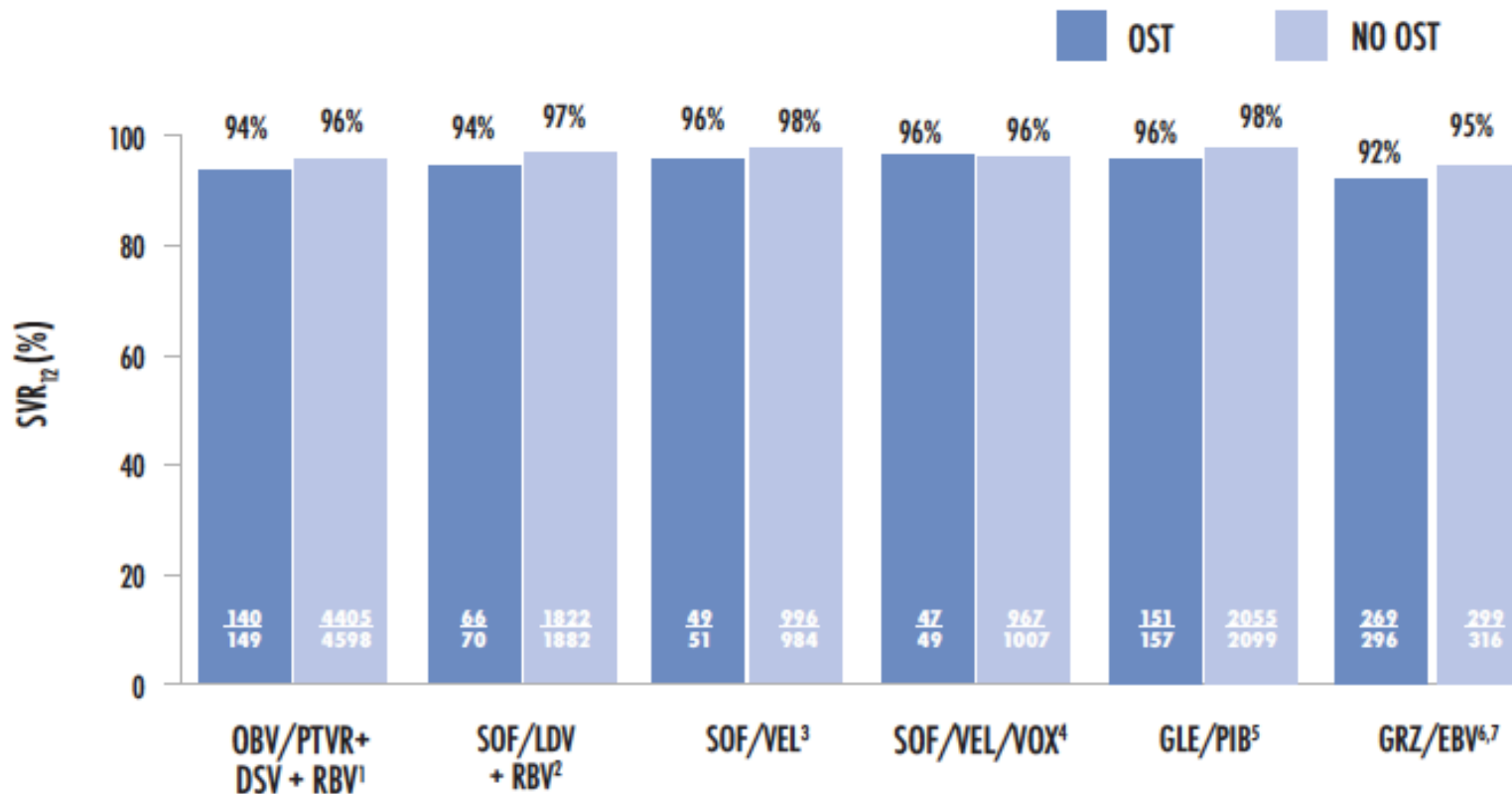
# Real-World Data in People Who Use Drugs

- HCV transmission among people who inject drugs continues to be the main driver of the global epidemic.
- Stigmatization, discrimination, and myths that active drug users cannot adhere to daily treatment regimens have resulted in treatment restrictions and other policies that further marginalize those we need to engage the most.
- **Trials of DAA treatment in active drug users and people receiving opioid substitution therapy show HCV cure rates comparable to those in clinical trials** can be achieved among people who continue to use and/or inject drugs during treatment.
- DAA treatment among people on OST and who are active or former people who inject drugs **achieves similar outcomes as in non-drug using groups.**
- **There is no scientific evidence for denying treatment to people who use drugs.**

# SVR12 among people on OST and former/recent people who inject drugs



# People Receiving OST: Phase II/III Trials



- Adherence to HCV treatment regimens is shown to be good among people who use drugs or other substances.
- **PREVAIL study** compared no treatment intervention vs. direct observed therapy using blister packs to give treatment to people.
- Results showed that **drug use did not associate with poor adherence.**

# Is a Vaccine for HCV Still Necessary?

- Vaccines for HAV and HBV exist, but a ***prophylactic*** (preventative) HCV vaccine has eluded researchers.
- HCV is considered to be a master virus, with the ability to mutate rapidly and to adapt quickly so as to stay ahead of detection and response by the human immune system.
- A vaccine would be beneficial to prevent transmission among networks of people who inject drugs, sexual networks, or other groups such as prisoners, who may be repeatedly exposed to the virus.
- With this rationale, preventative vaccine trials are underway to prove efficacy and safety
- Results in the coming years will determine the role of vaccines in ending the HCV epidemic.

## ADVOCACY EXERCISE

### Discussion Questions:

1. Do you know which HCV treatments are available in your country?
2. If available, do you know how much they cost?

### Action Steps:

1. What can you do to make more information about these treatments available for people who need them?
2. What can we do to make HCV treatment more accessible?
3. What efforts can be made to ensure people who inject or use drugs can access DAAs?