



## NORTHWEST AIDS EDUCATION AND TRAINING CENTER

# New Directly Acting Antivirals for Hep C

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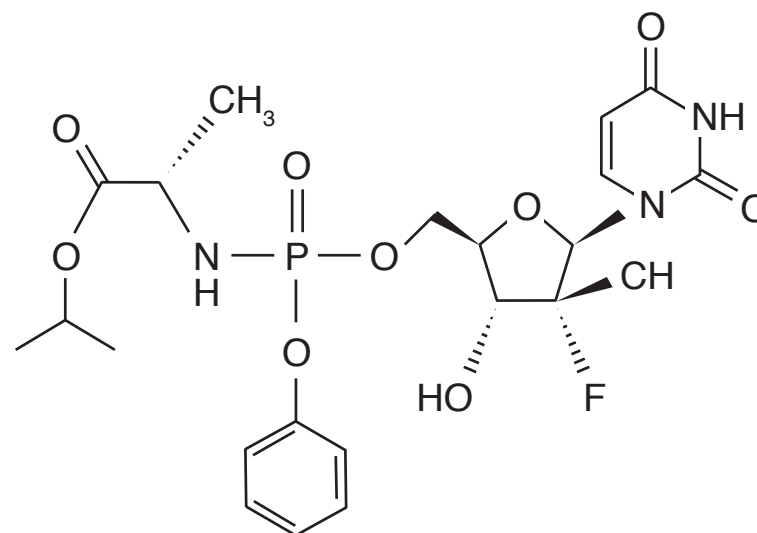
# Objectives

- To understand the proper dose and duration of sofosbuvir
- To know the common side effects and drug-drug interactions with sofosbuvir
- To understand the coming pipeline for Hep C antivirals and how to weigh the decision to treat now or to wait

# Sofosbuvir

# Sofosbuvir (SOF, GS 7977)

- Potent HCV-specific nucleotide analog (chain terminator)
- Safe and well tolerated
  - Once daily, no food effect
  - No significant drug interactions
  - No safety signals in preclinical/clinical studies
- High barrier to resistance
  - No virologic breakthrough to date
- Pangenotypic antiviral effect
- Safe and well tolerated in ~3000 patients in Phase 2 and Phase 3 studies



# FDA label for Sofosbuvir (Sovaldi)

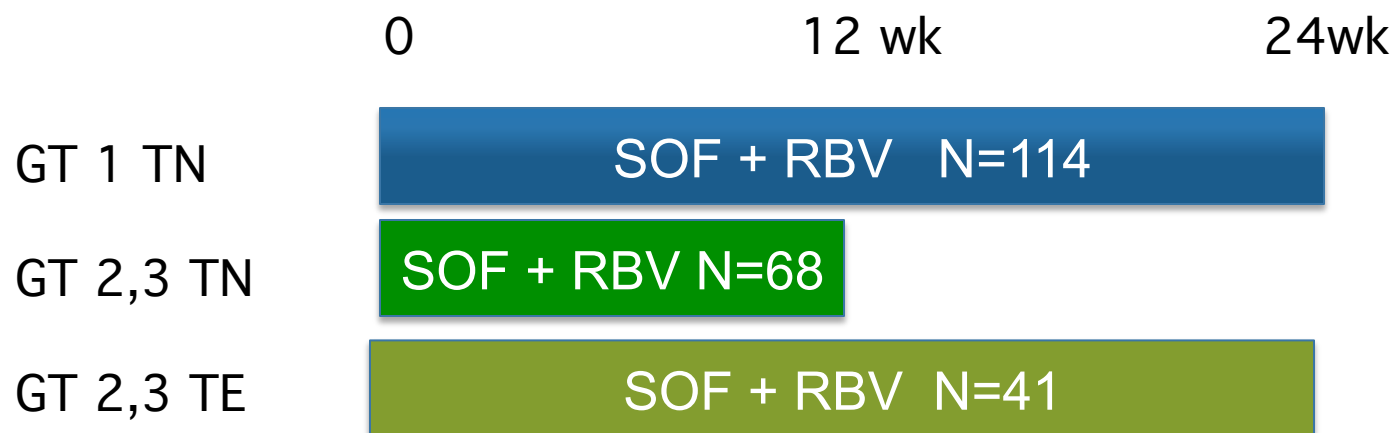
- GT 2 and 3 naives
- GT 2 and 3 intolerant or non-responders
- GT 1,4 naives and P/R failures (non-decompensated cirrhotics and non-cirrhotics)
- Patients with HCC and awaiting liver txp
- **Both HIV+ and HIV-**

# Dosage and Duration

- 400 mg tablet once daily
- No food effect
- “SOVALDI in combination with ribavirin for 24 weeks can be considered for CHC patients with genotype 1 infection who are interferon ineligible.”

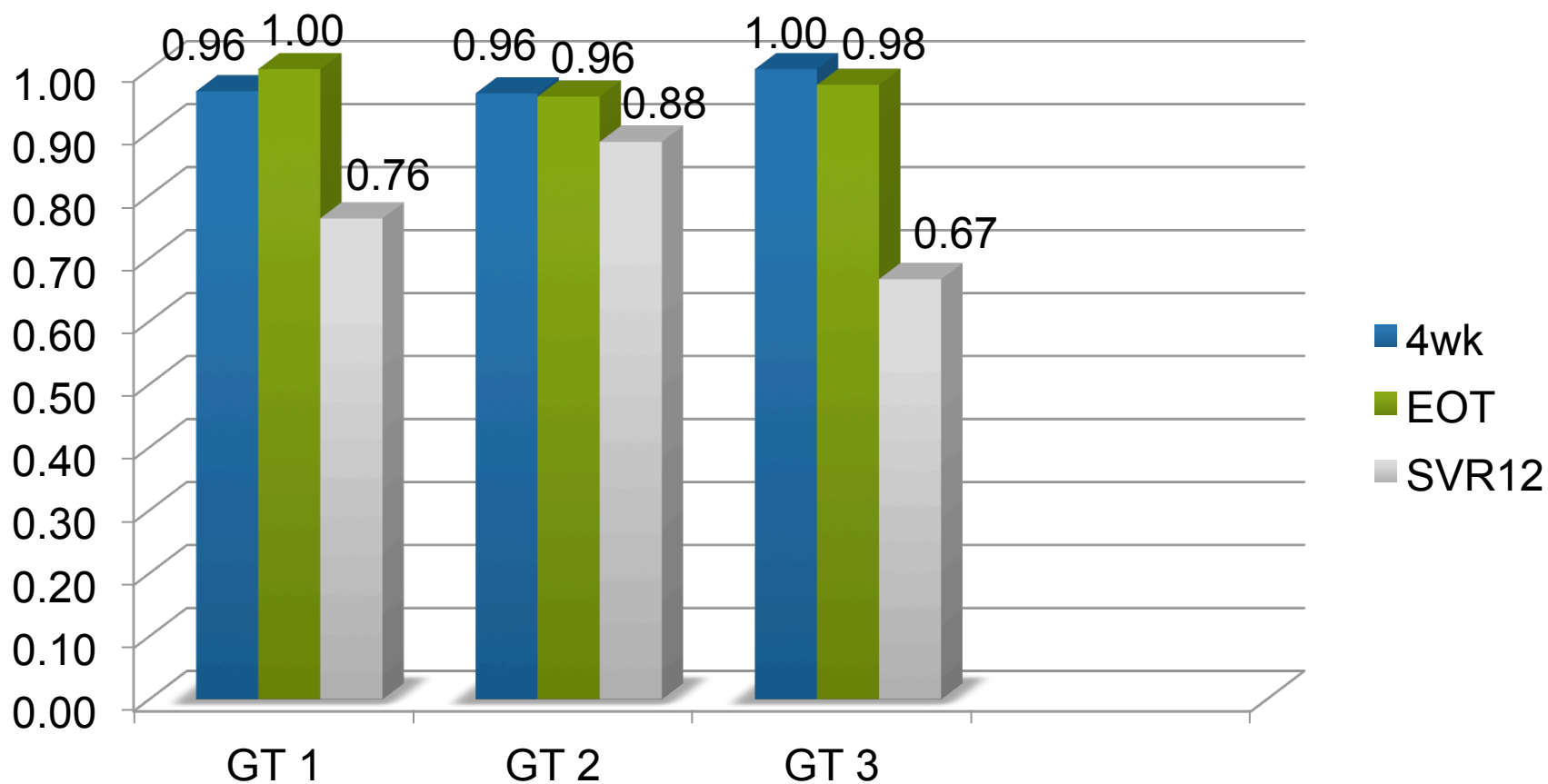
	SOF, PegIFN, & RVN	SOF/RBV
GT1: naïve, P/R failures, HIV+/-	12 weeks	-
GT 2: naïve or P/R failures	-	12 wks
GT 3: naïve or P/R failures	-	24 wks
HCC, awaiting OLT		48 wks

# HIV/HCV Coinfected Patients: PHOTON-1



- Wide range of ARVs permitted
- Compensated cirrhotics permitted
- HIV RNA had to be undetectable for at least 8 wks
- CD4 >200 cells/ml if on ARVs or >500 cells/ml if untreated

# Similar SVR12 Results as HIV- Patients





# Adverse Events

- No difference c/w HIV-
- 2 pts had detectable HIV RNA but was due to poor adherence
- No change in CD4 count

# Side Effects of Sofosbuvir

Side Effect	SOF/RBV	IFN/RBV
Fatigue	36%	55%
Headache	25	44
Nausea	18	29
Insomnia	12	29
Anemia	8	12
Flu syn	3	18
Chills	3	18
Rash	9	18
Diarrhea	9	17
Myalgia	8	16
Neutropenia	0	12

- Prior nucleotide analogs had cardiac (long QT), hepatic (ALT flares) and GI toxicity (nausea)
- Fewer side effects w/ SOF/RBV vs. IFN/RBV
- No diff b/t triple tx and IFN/RBV
- Low dropout rate w/ SOF: 1-2%

# Laboratory Monitoring

Patient	Baseline	2 wks	4 wks	8 wks	12 wks	24 wks	36 wks
GT 1,4	HIV RNA, CD4, HCV RNA, TSH, CBC, LFTs	CBC w/ diff	CBC w/ diff, LFTs	CBC w/ diff	CBC, LFTs, TSH, HCV RNA, CD4, HIV	HCV RNA	
GT 2	HCV RNA, CBC, LFTs	CBC	CBC	CBC	CBC, LFTs, HCV RNA	HCV RNA	
GT 3	HCV RNA, CBC, LFTs	CBC	CBC	CBC	CBC	CBC, LFTs, HCV RNA	HCV RNA

Consider more frequent LFTs in cirrhosis

If patient develops anemia, will need more frequent CBC

# How to Manage Anemia

Laboratory Values	Reduce RBV to 600 mg/d if:	Discontinue RBV if:
Hgb in pts with no cardiac disease	<10 g/dL	<8.5 g/dL
Hgb in pts w/ hx of stable cardiac dz	>2 g/dL in Hgb during any 4 wk period	<12 g/dL despite 4 wks at reduced dose

# Drug-Drug Interactions

- Sofosbuvir is metabolized by human cathepsin A (CatA), carboxylesterase 1 (CES1) and histidine triad nucleotide-binding protein 1 (Hint1)
- SOF is not inducer or inhibitor of CYP450, UGT1A1 or drug transporters!
- Sofosbuvir is a substrate of P-gp and BCRP.
- Do NOT use St. John's Wort, rifamycins, phenytoin (*Dilantin*) or carbamazepine (*Tegretol*), **tipranavir/ritonavir** with sofosbuvir.
- Methadone, many HIV ARVs (TDF, RAL, RPV, DAR, EFZ), many immunosuppressants are ok

# Cost and Patient Assistance

- Avg wholesale price = \$1000 per pill
- \$84,000 for 12 wks
- \$168,000 for 24 wks
- [www.MySupportPath.com](http://www.MySupportPath.com), 1-855-7MyPath  
(1-855-769-7284)
- Sovaldi Co-pay Coupon Program (\$5 co-pay)
- Patient assistance program for uninsured
- Patient Access Network (PAN) Foundation for high deductibles

# The Coming Pipeline for HIV/HCV

- Protease Inhibitors:
  - 1<sup>st</sup> Generation: Telaprevir, Boceprevir, Simeprevir, Faldaprevir, Asunaprevir
  - 2<sup>nd</sup> Generation: MK 5172 (2015-6)
- NS5a Inhibitors
  - Daclatasvir (2014-5), Ledipasvir (2014-5), ABT 267
- Non-nucleoside inhibitors
  - GS9669, ABT 333/r

# Treat Now or Wait?

- GT 2 or 3: treat now
- GT 1 or 4: strongly consider treating now
- Prioritize those with more advanced fibrosis or w/ hx of IRIS in liver