CATIE

Canada's source for HIV and hepatitis C information

La source canadienne de renseignements sur le VIH et l'hépatite C

Hep C: New Therapies and Implications

Presented by: Curtis Cooper, MD, FRCPC

January 8, 2015

Hep C: New Therapies and Implications

Dr. Curtis Cooper trained at the University of Saskatchewan (MD 1994). He received certification in Internal Medicine in 1997 and in Infectious Diseases in 1999 while at the University of Manitoba. He completed an HIV Research Fellowship and Masters of Epidemiology in 2002 at the University of Ottawa. He is currently an Associate Professor with the University of Ottawa, Scientist with the Ottawa Hospital Research Institute, Infectious Diseases Consultant with the Ottawa Hospital Division of Infectious Diseases and Director of The Ottawa Hospital Viral Hepatitis Program. He holds an Applied HIV Research Chair with the Ontario HIV Treatment Network. As a clinical researcher, his research activities encompass viral hepatitis, HIV, and vaccine development. His work is focused on the development of new therapeutic agents and the delivery of treatment that maximizes safety, adherence and safety. Is an active researcher with several cohort studies (CANOC, OHTN Cohort Study). He is co-chair of the CIHR Canadian HIV Trials Network Co-Infection Core research group, member of the Canadian Association of HIV Researchers executive and mentor with the National CIHR Research Training Program-Hep C.

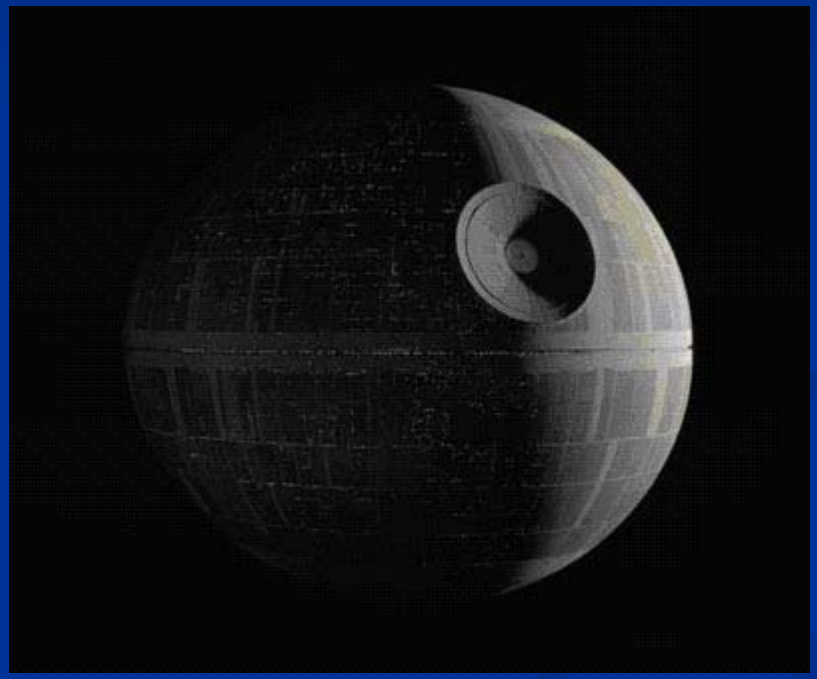
CATIE

Hep C: New Therapies and Implications

Curtis Cooper, MD, FRCPC
Associate Professor-University of Ottawa
The Ottawa Hospital- Infections Diseases
Director- Ottawa Hospital and Regional Hepatitis Program

Disclosures

- Industry
  - Investigator: Merck, Vertex, Roche, BI, Janssen, GS, BMS, ABV
  - Consultant /Advisor: Merck, Vertex, Roche, BI, GS, ABV
  - Speaker: Merck, Roche, BI, BMS, Janssen
- Government
  - CADTH
  - OHTN
  - CIHR
  - PCIRN
  - Health Canada
  - Ontario MOH



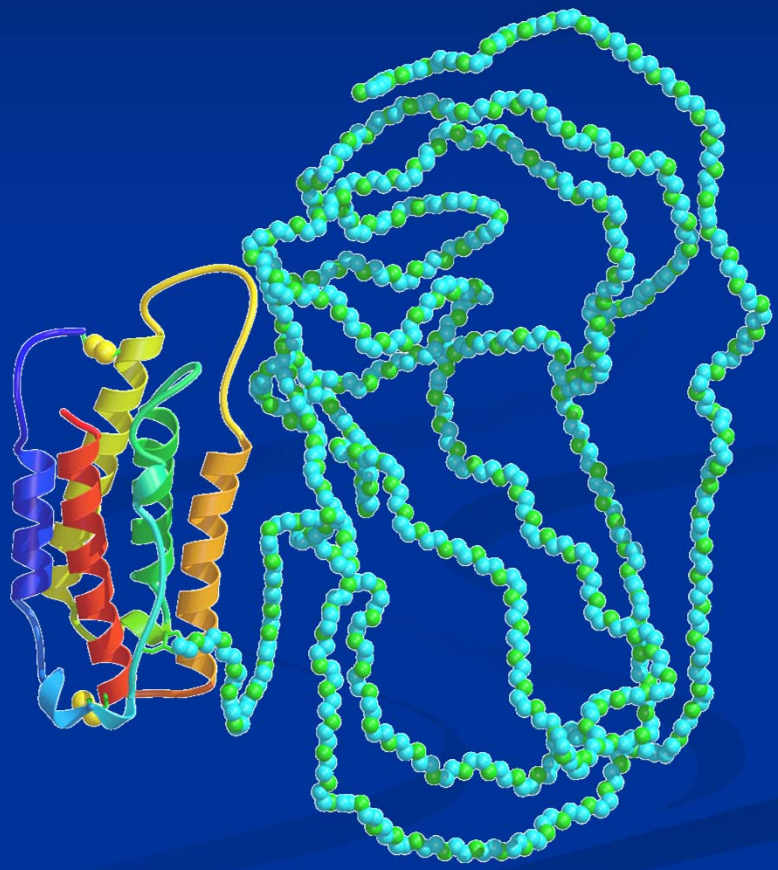
Overview

- Current standard of care
- Newer agents just approved by Health Canada
- Implications

Funded HCV Therapies

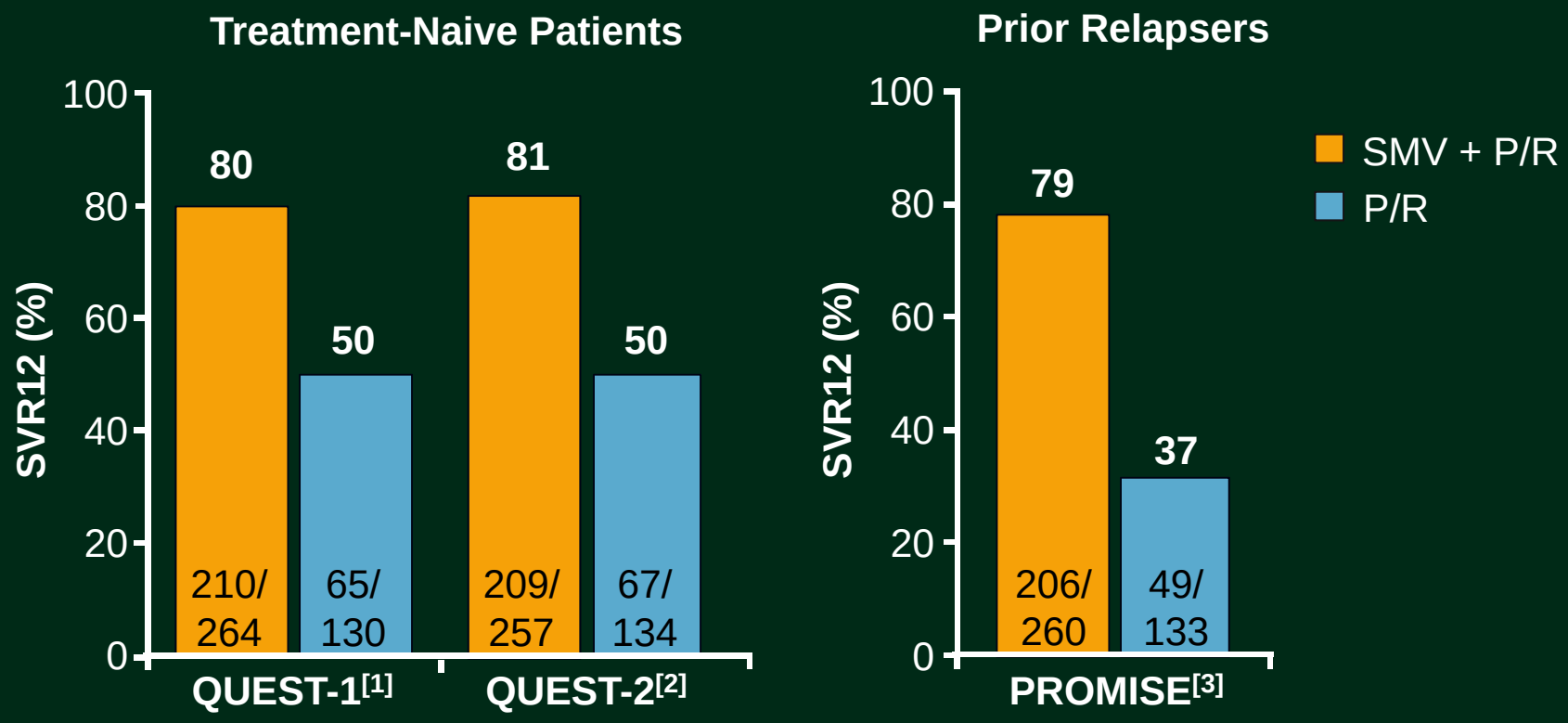
- PEG-Interferon α / Ribavirin
- +/- Protease Inhibitor (Boceprevir, Telaprevir, Simeprevir)
- Duration of Tx

- Definition of Success
  - HCV RNA negative 3 months post therapy (Sustained Virologic Response=Cure)



New Advances

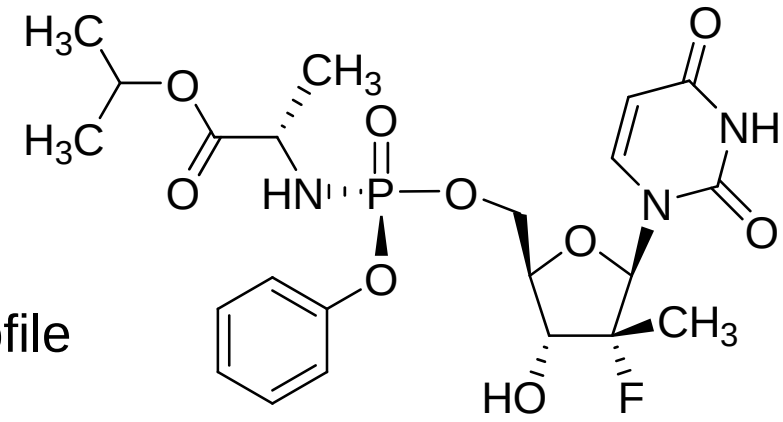
QUEST-1, QUEST-2, PROMISE: Simeprevir + P/R in GT1 Tx-Naive Patients/Relapsers



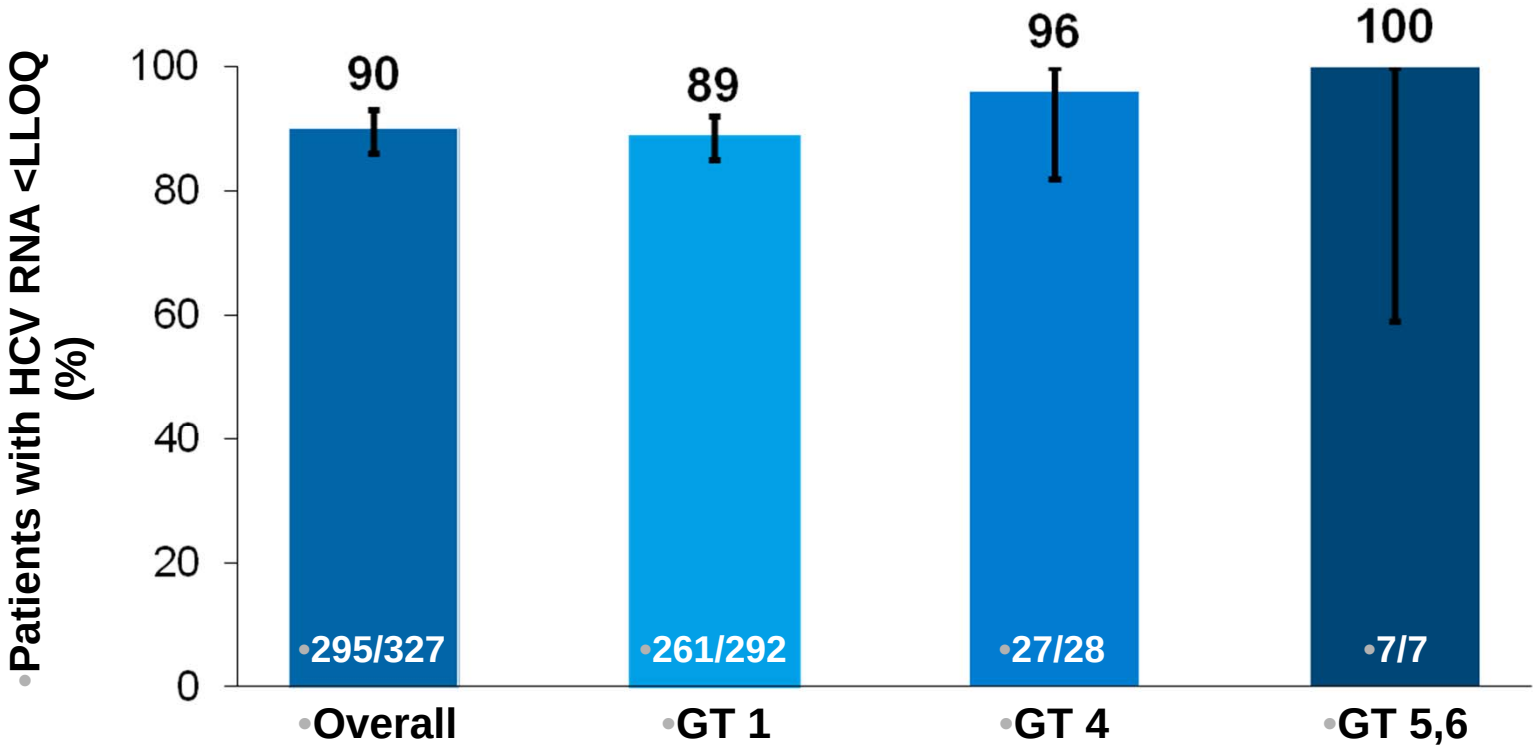
1. Jacobson I, et al. EASL 2013. Abstract 1425. 2. Manns M, et al. EASL 2013. Abstract 1413.
3. Lawitz E, et al. DDW 2013. Abstract 869b.

Sofosbuvir (SOF, GS-7977)

- HCV-specific nucleotide polymerase inhibitor (chain terminator)
- Potent pan-genotypic antiviral activity against HCV GT1–6
- High barrier to resistance
- Once-daily, oral, 400-mg tablet
- Favorable clinical pharmacology profile
  - No food effect
  - No significant drug interactions
- Generally safe and well-tolerated in clinical studies to date (> 2,000 patients)
  - No safety signal in preclinical/clinical studies



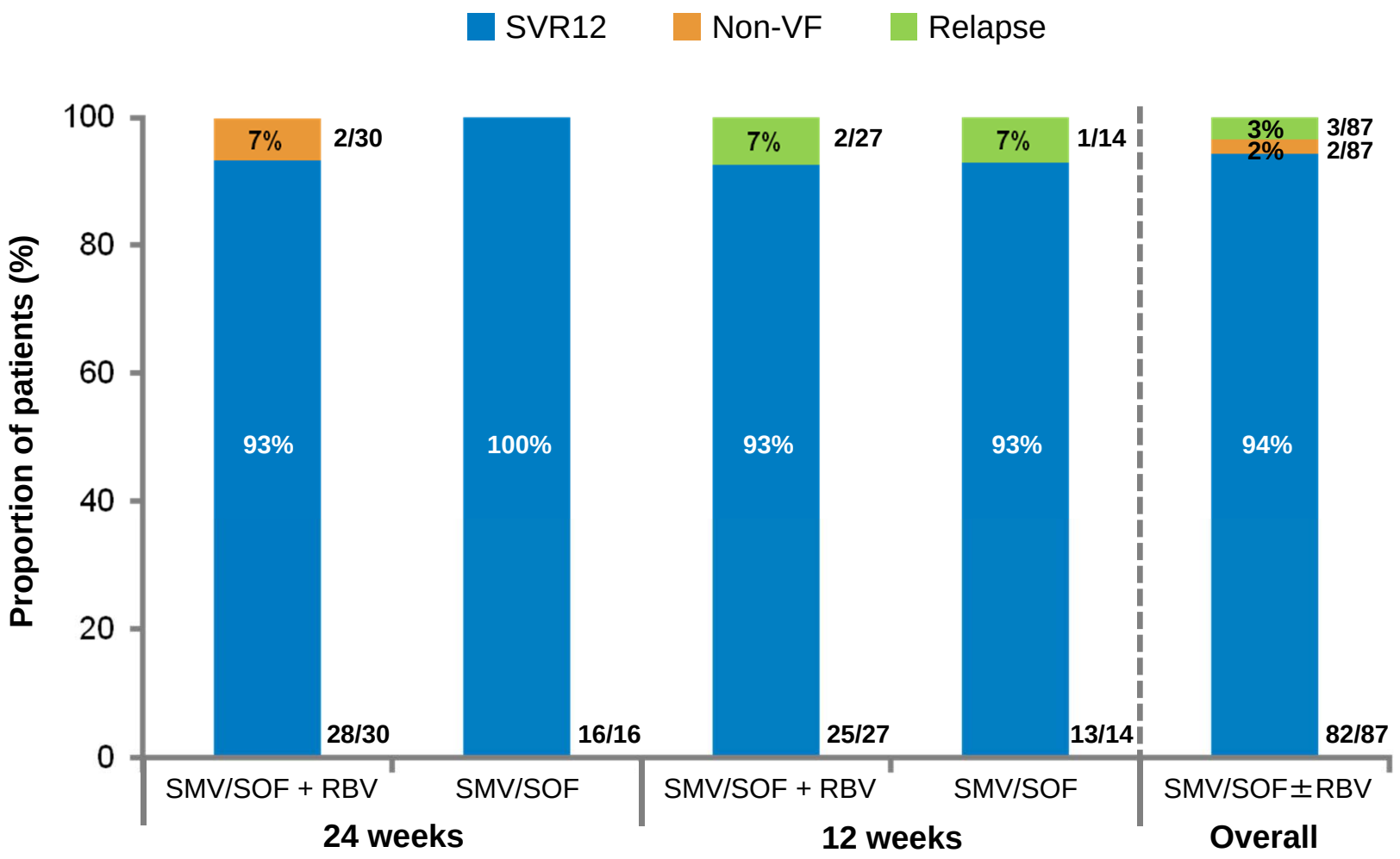
Phase 3: NEUTRINO GT 1, 4, 5, 6 Treatment-Naïve
SVR12 by HCV Genotype



- Open label, single arm study of PegIFN-Ribavirin-SOF x 12/52
- Error bars represent 95% confidence intervals
- Lawitz E, et al. EASL 2013. Amsterdam, The Netherlands. Oral #1411

COSMOS: SOF-SMV

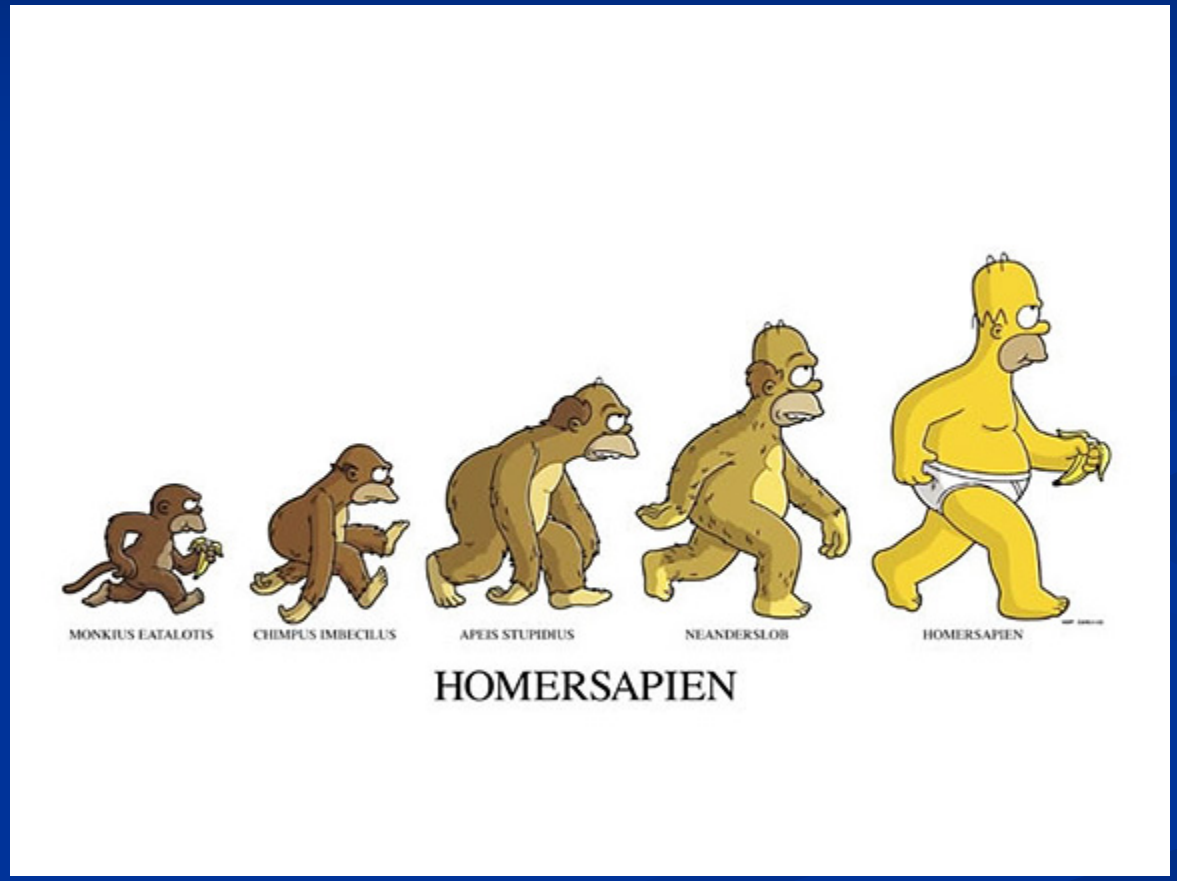
COSMOS (Cohort 2): SVR12



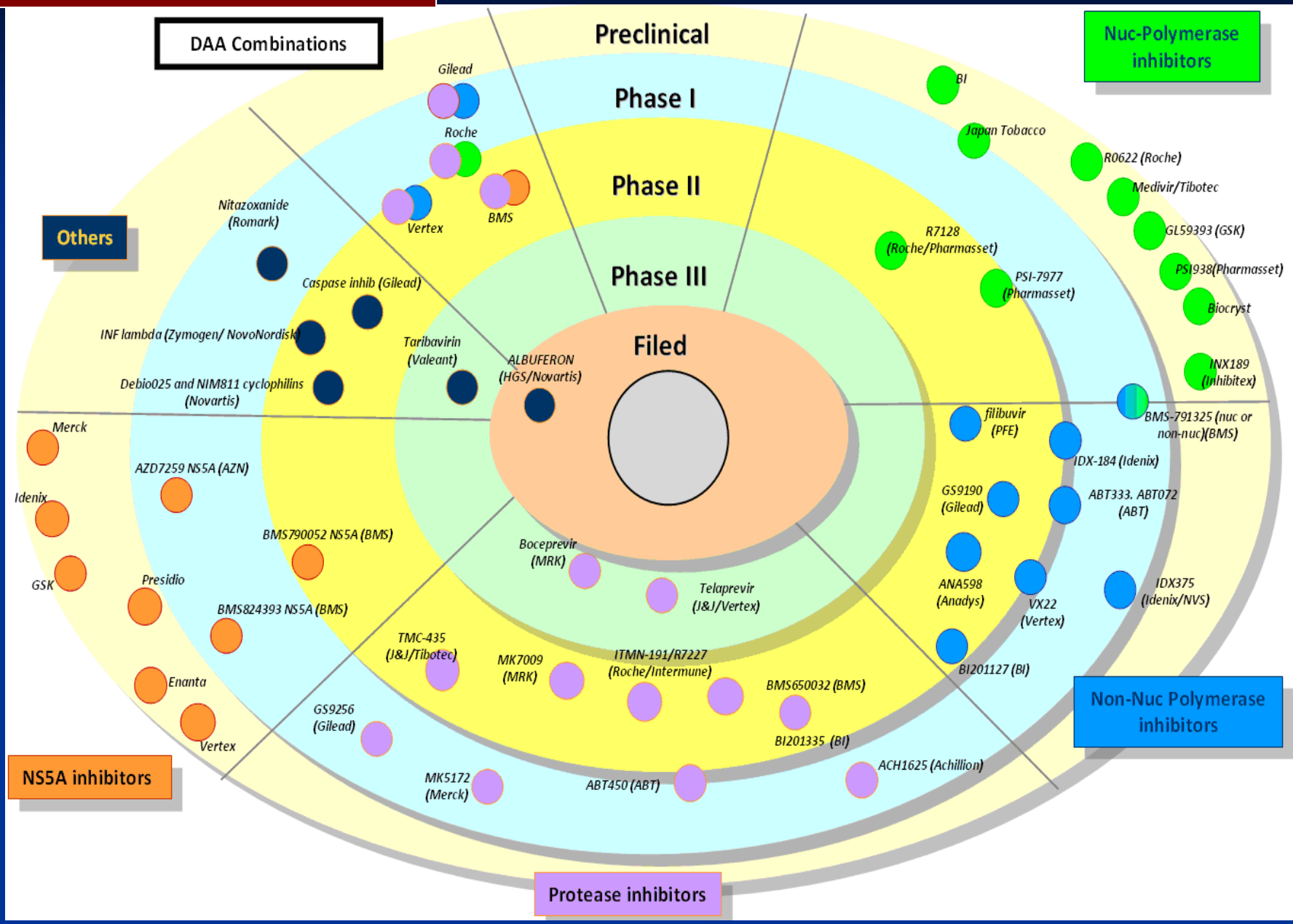
Non-VF, patients who did not achieve SVR12 for reasons other than virologic failure

ITT, intent-to-treat; Non-VF, Non-virologic failure; RBV, ribavirin; SMV, simeprevir; SOF, sofosbuvir; SVR12, sustained virologic response 12 weeks after planned treatment end

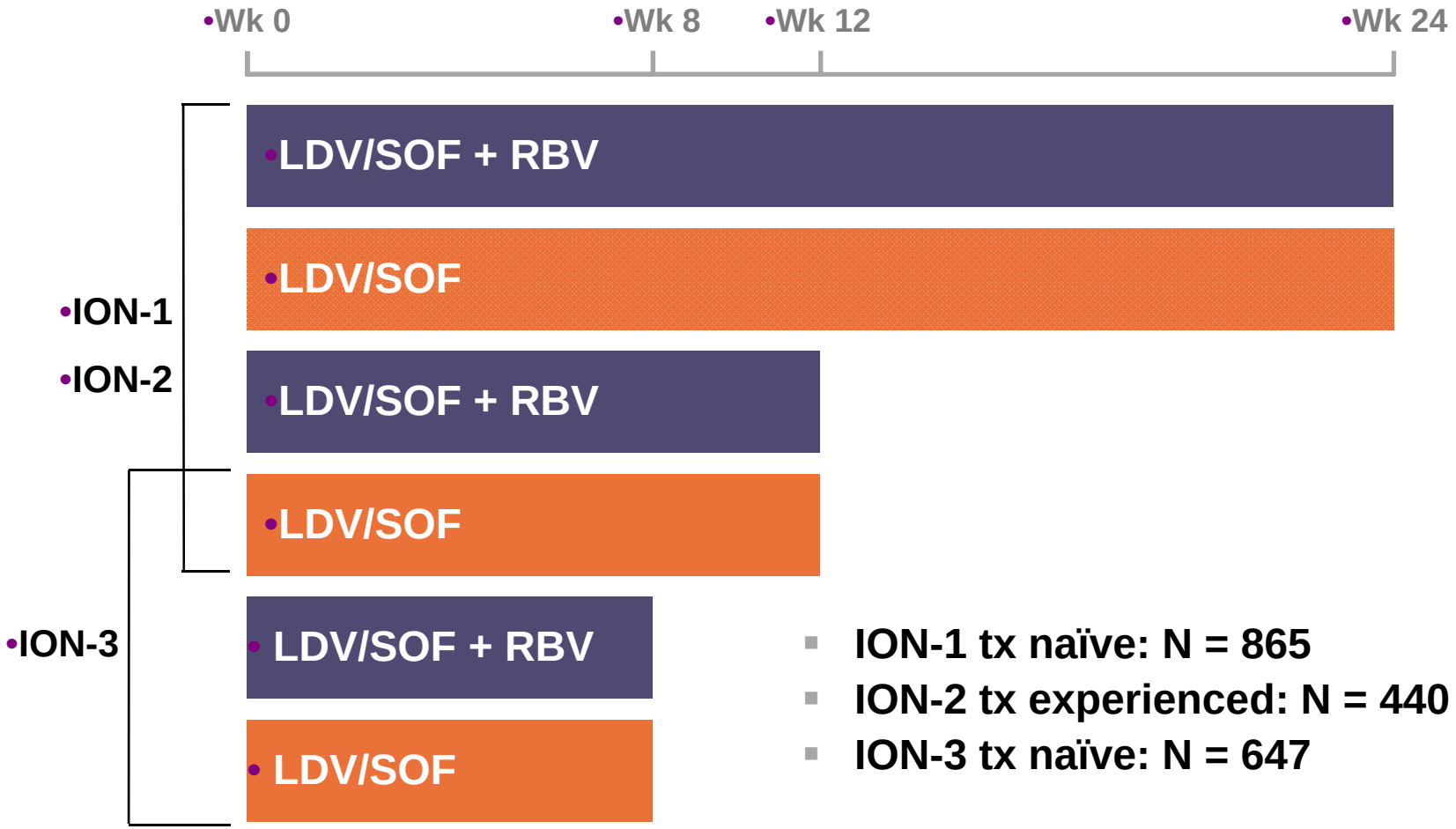
New Therapies



Direct Acting Antiviral Drug (DAA) Combinations



•LDV/SOF Phase 3 Program (ION-1, ION-2, ION-3)

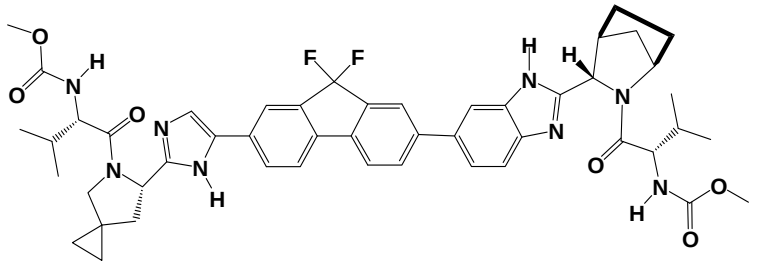


- ION-1 tx naïve: N = 865
- ION-2 tx experienced: N = 440
- ION-3 tx naïve: N = 647

•N=1952 total patients

Ledipasvir (LDV, GS-5885)

- NS5A is essential for RNA replication and post-replication assembly and secretion
- LDV has picomolar potency against genotype 1a and 1b HCV

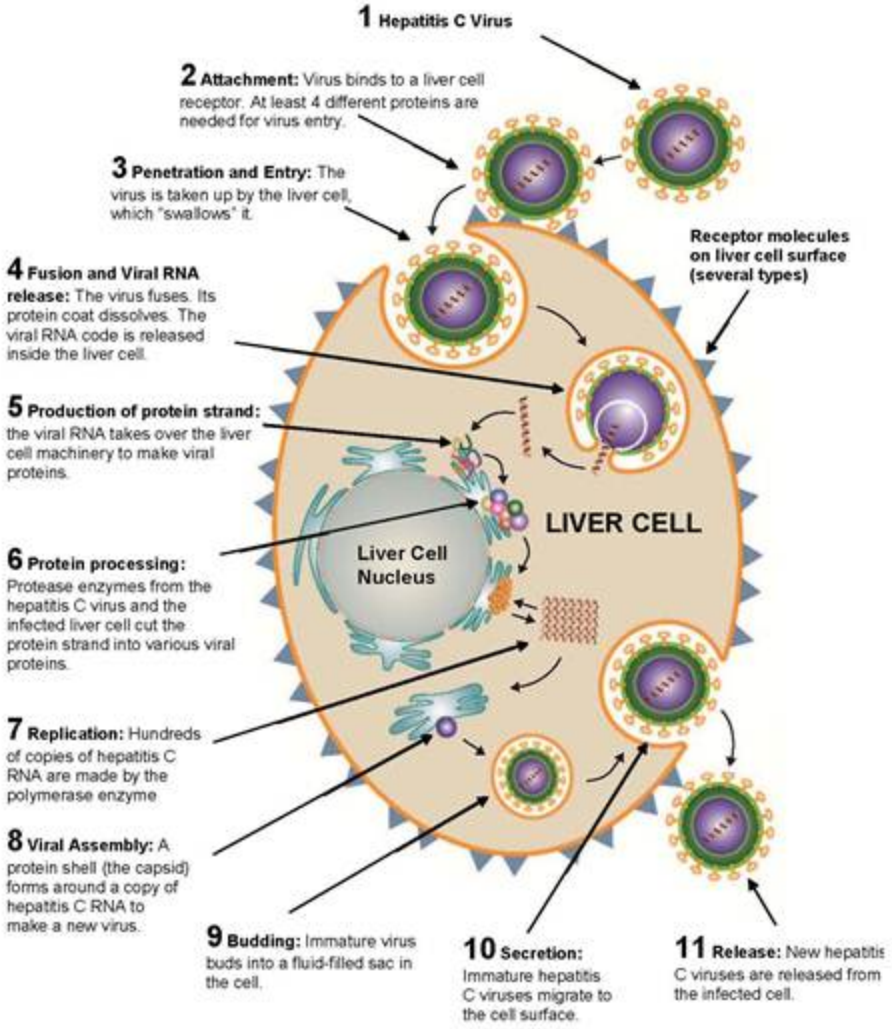


- Effective against signature NS5B-resistant mutant S282T
- Once-daily oral dosing
- Dosed in >3000 patients
- No clinically significant drug-drug interactions with sofosbuvir

•**Lawitz EJ et al, *J Hepatol* 2012; 57: 24–31; Gane EJ, et al. CROI 2013; Atlanta, GA. Oral #41LB**

AbbVie Direct-Acting Antivirals Evaluated in Phase 3 Trials: Mechanism of Action

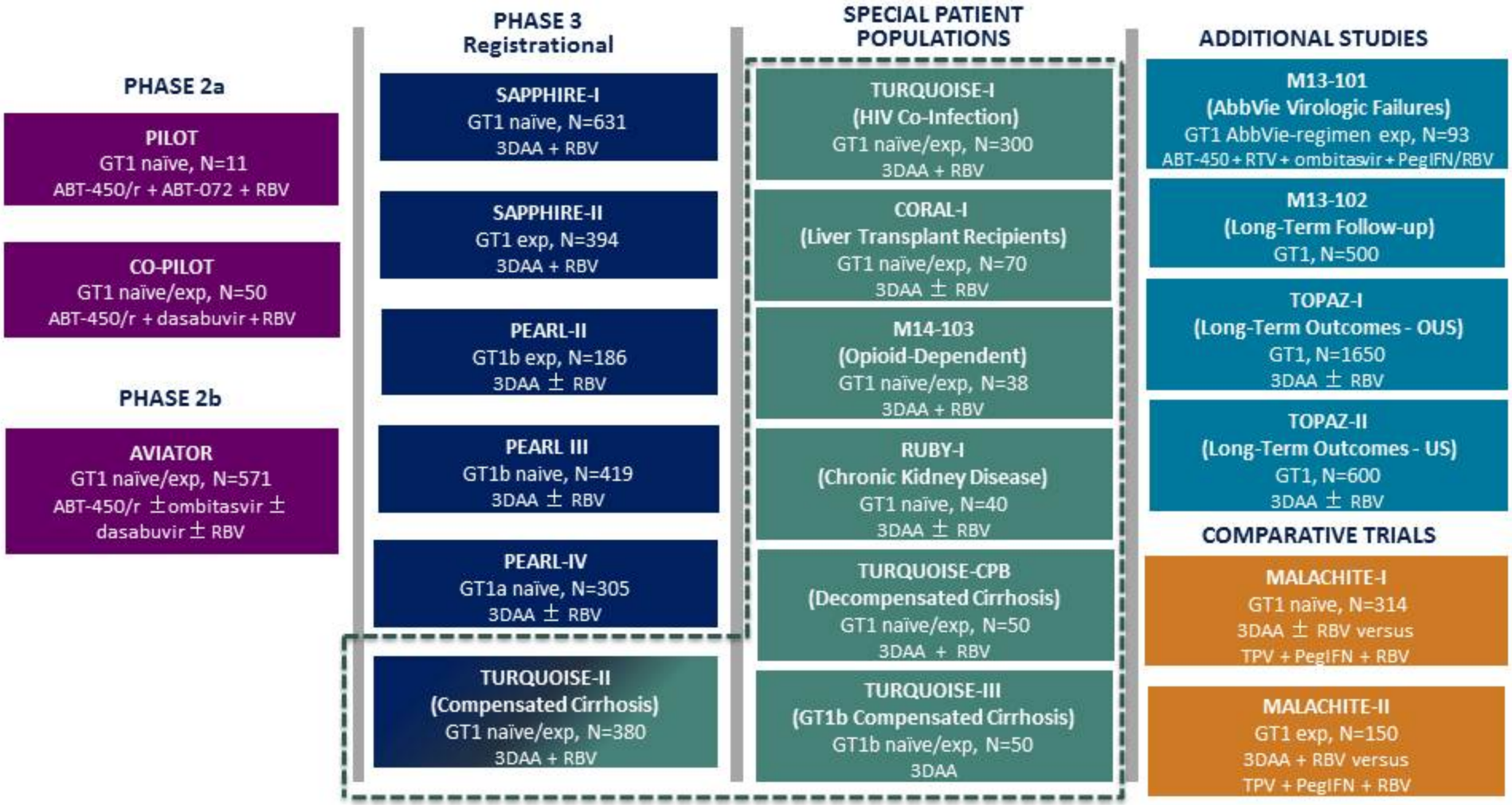
- ABT-450
  - Inhibitor of HCV NS3/4A protease and is co-administered with ritonavir (ABT-450/r) which acts as a pharmacokinetic enhancer[1,2]
- Ombitasvir (ABT-267)
  - Inhibitor of HCV NS5A
- Dasabuvir (ABT-333)
  - Non-nucleoside inhibitor of HCV NS5B polymerase



Source: Fact Sheet 670. Hepatitis C Virus Life Cycle. The AIDS InfoNet Web site. http://www.aidsinfonet.org/fact_sheets/view/670. Updated August 10, 2014. Accessed October 17,2014.

1. Feld JJ, et al. *N Eng J Med*. 2014;370(17):1594-1603.
2. Menon RM, et al. Poster #57. HepDART 2009.

AbbVie's 3DAA HCV Clinical Development Program



Abbreviations: 3DAA, ABT-450/r, ombitasvir and dasabuvir; ABT-450/r, ABT-450 with ritonavir; CPB, Child Pugh B; DAA, Direct Acting Antivirals; Exp, PegIFN/RBV experienced; GT, genotype; HCV, hepatitis C virus; OUS, Outside the United States; PegIFN, pegylated interferon; RBV, ribavirin; TPV, telaprevir; US, United States

Reference: www.clinicaltrials.gov

Implications

Who Benefits Now?
Who Benefits Later?
Funding

- Privately Insured
- Province of Residence

Who Benefits Now?
Who Benefits Later?
Fibrosis Stage

- Cirrhosis
  - CP-A
  - CP-B
  - CP-C
- F3
- F2
- F0-1
- Post Transplant

Who Benefits Later? The Marginalized

- Rural
- HIV
- Substance Users
- Mental Health
- Aboriginals
- Incarcerated

Discussion