CALIFORNIA TECHNOLOGY ASSESSMENT FORUM℠

New Treatments for Patients with Hepatitis C

Public Meeting

March 10, 2014

Agenda

- **Meeting Convened** | 10:00 – 10:15 am
- **Presentation of the Evidence and Voting Questions, Q&A** | 10:15 – 11:15 am
- **Discussion and Public Comments** | 11:15 – 11:45 am
- **Roundtable: Q&A with Experts** | 11:45 am – 12:30 pm
- **Working Lunch** | 12:30 – 1:15 pm
- **CTAF Deliberation and Votes** | 1:15 – 2:15 pm
- **Roundtable Discussion and Best Practice/Policy Recommendations** | 2:15 – 3:50 pm
- **Summary and Closing Remarks** | 3:50 – 4:00 pm
- **Meeting Adjourned** | 4:00 pm

➢ **Download meeting materials: www.tinyurl.com/ctafhepc**

CALIFORNIA TECHNOLOGY ASSESSMENT FORUM℠

Simeprevir and Sofosbuvir for the Treatment of Chronic Hepatitis C Infections

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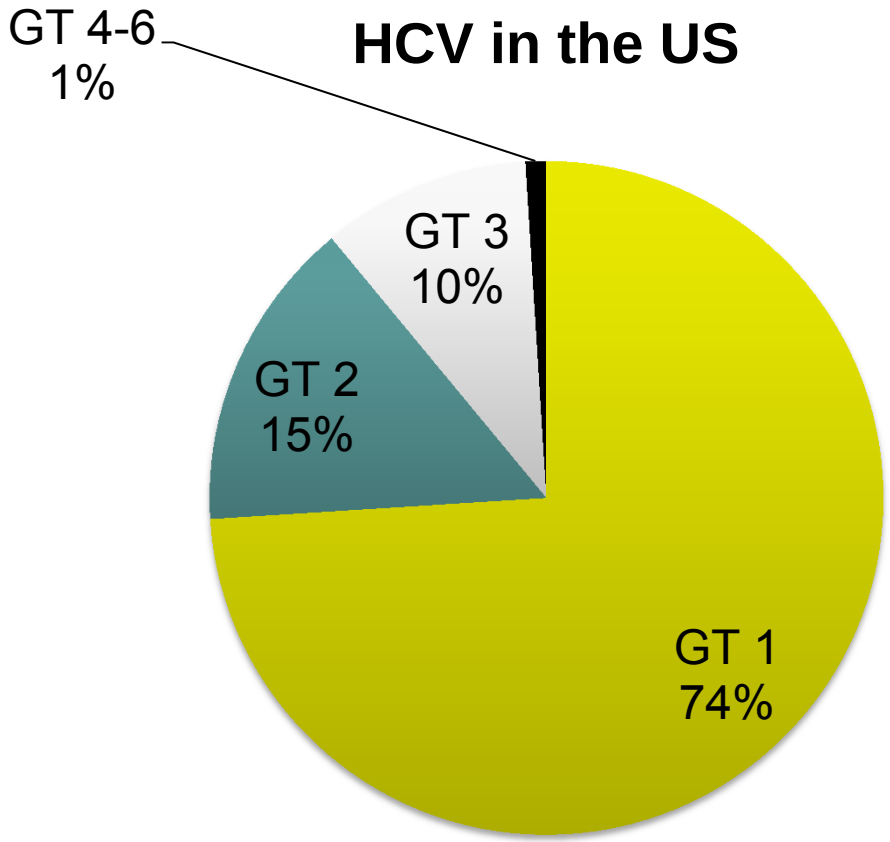
March 10, 2014

I have no conflicts of interest.

Acknowledgment: Rena Fox, MD and Clinical Care Options for slides incorporated into this presentation

Six HCV Genotypes

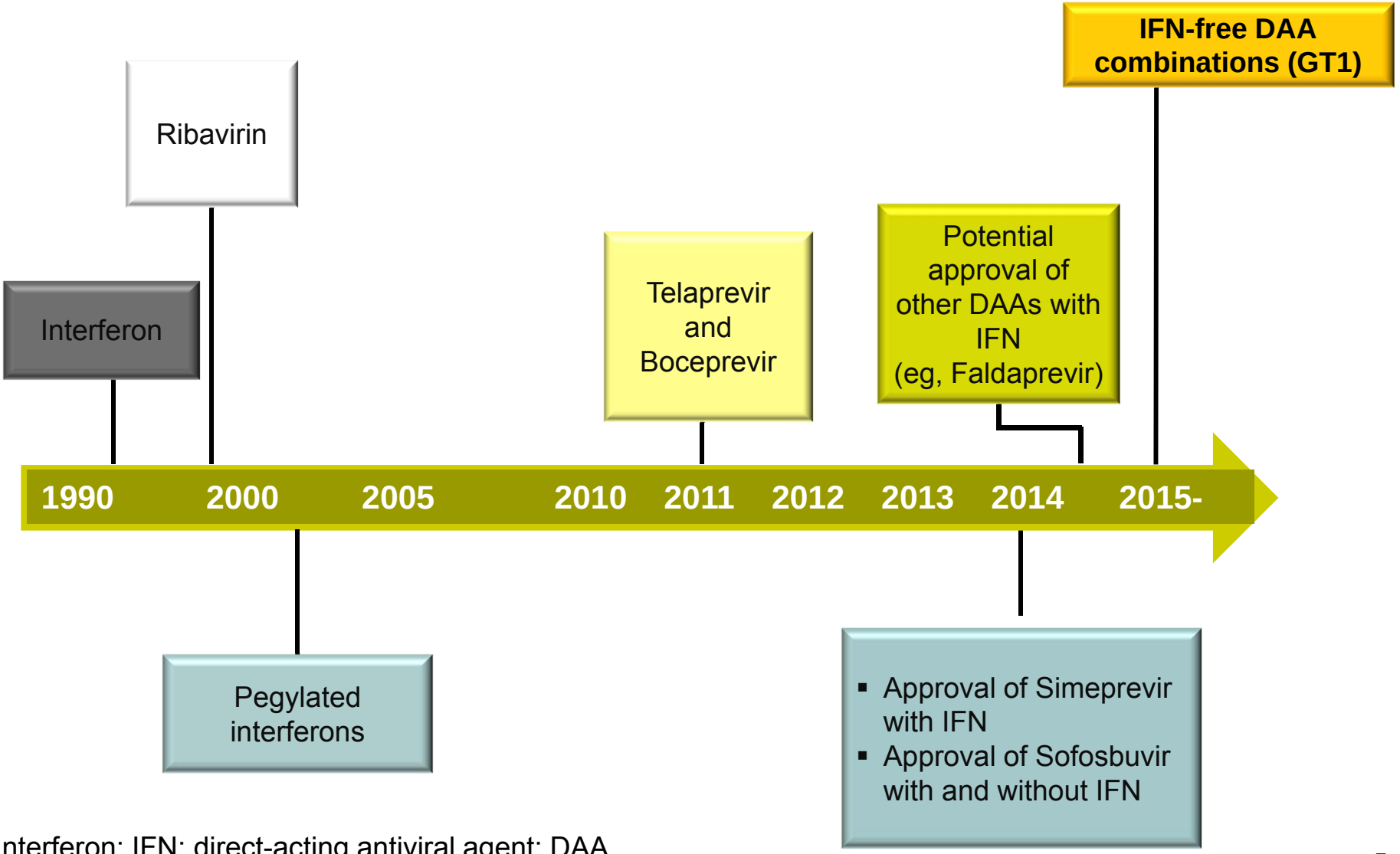


This CTAF assessment will focus on genotypes 1, 2 and 3.

Natural History of HCV Infection

Condition	Number of individuals
Infection with hepatitis C	100
Develop symptoms	20-30
Remain asymptomatic	70-80
Develop chronic infection	75-85
Develop chronic liver disease	60-70
Develop cirrhosis over 20-30 years	5-20
Die from cirrhosis or liver cancer	1-5

HCV Therapy: Past, Present and Future



Interferon: IFN; direct-acting antiviral agent: DAA

Treatment of Chronic HCV Infection

- Goal: prevent cirrhosis and hepatocellular carcinoma (HCC)
- Interferon + ribavirin has been the backbone of therapy
- Surrogate outcome in clinical trials
  - Sustained virologic response (SVR)

SVR12 versus SVR24 and Cure

Weeks after treatment	Undetectable RNA (N)	Percentage
0	336	100
12	303	90
24	**300**	**89**
72	293	87

PILLAR Study: Fried MW. Hepatology. Dec 2013;58(6):1918-1929.

Meta-analysis: SVR24 represents long-term cure in 98-100%.

Ng V, Saab S. *Clinical gastroenterology and hepatology.* Nov 2011;9(11):923-930.

SVR Is Associated with Reduced Mortality among HCV-Infected Persons

- 530 patients followed for 8.4 years after treatment
- 192 (36%) achieved SVR
- SVR: 74% reduction in all cause mortality
- SVR: 94% reduction in liver-related mortality or transplant

van der Meer AJ, et al. *JAMA.* 2012:308(24):2584-2593.

Current Treatment for GT 1: PR

- Pegylated interferon plus ribavirin for 48 weeks
  - Modest SVR24: 40 to 50%
    - Lower SVR24 in observational studies
  - Many contraindications
    - Psychiatric illness, autoimmune disease, advanced liver disease
  - Many side effects
    - Fatigue, fever, anemia, depression, anxiety

Current Treatment for GT 1: B&T

- 2011: the first DAAs approved for GT 1
  - PR + boceprevir or telaprevir
- Benefits
  - Improved SVR24: 70 to 75% in treatment naïve
  - Shorter duration in some patients – response guided therapy: 24 to 48 weeks
- Burdens
  - More pills: 6-12 a day on a q 8 hour schedule
  - Increase in anemia from 30% to 50%
  - Dysguesia, rash, drug interactions

Current Treatment for GT 2/3: PR

- Pegylated interferon plus ribavirin for 24 weeks
  - Better SVR24: 75 to 80%
  - Shorter therapy: 24 weeks rather than 48
  - The same contraindications and side effects, but for half the time

NEW DIRECT ACTING ANTI-VIRAL THERAPY

Classes of DAAs: Existing Drugs and Drugs in Development

NS3/4 Protease Inhibitors	Nucleos(t)ide NS5B Polymerase Inhibitors	Non-nucleos(t)ide NS5B Polymerase Inhibitors	NS5A Inhibitors
Telaprevir	**Sofosbuvir**	BI-207127	Daclatasvir
Boceprevir	Mericitabine	VX-222	Ledipasvir
Simeprevir		ABT-333	ABT-267
Danoprevir		BMS-791325	
ABT- 450		Tegobuvir	
Faldaprevir		GS-9669	
Asunaprevir			
GS-9451			

Simeprevir

- Protease inhibitor
  - Similar to telaprevir, boceprevir
- FDA approved November 2013
  - For use in Genotype 1 only
  - Requires IFN and Ribavirin
  - Total 24-48 week course (response guided therapy)
- Once per day, oral, easier to tolerate

Sofosbuvir

- Polymerase inhibitor
- FDA approved December 2013
  - Breakthrough designation: SVR12, uncontrolled studies
  - For use in all genotypes
  - Approved with IFN and without IFN
  - Approved in HIV-HCV co-infection
- Initially focused on genotypes 2 & 3

EVIDENCE REVIEW

Genotype 1

- No head to head trials of regimens incorporating simeprevir or sofosbuvir with the standard of care PR plus either boceprevir or telaprevir
- No head to head trials of regimens incorporating simeprevir or sofosbuvir with each other
- Network meta-analysis (NMA) performed using comparisons with PR to allow for indirect comparisons
- No trials with patient-oriented outcomes (decompensated cirrhosis, HCC, transplant, death)

Genotypes 2 & 3

- Simpler: no boceprevir, telaprevir, simeprevir
- Sofosbuvir regimens all interferon-free

Clinical Outcomes

- Benefits
  - SVR12 or SVR24
- Harms
  - Adverse events during treatment
  - Treatment burden (injections, pills)

Simeprevir

- 7 randomized trials with PR as a control
  - Three are phase 3 trials with FDA approved dose (QUEST-1, QUEST-2, PROMISE)
  - All genotype 1
  - All interferon eligible
- 5 additional trials

Sofosbuvir

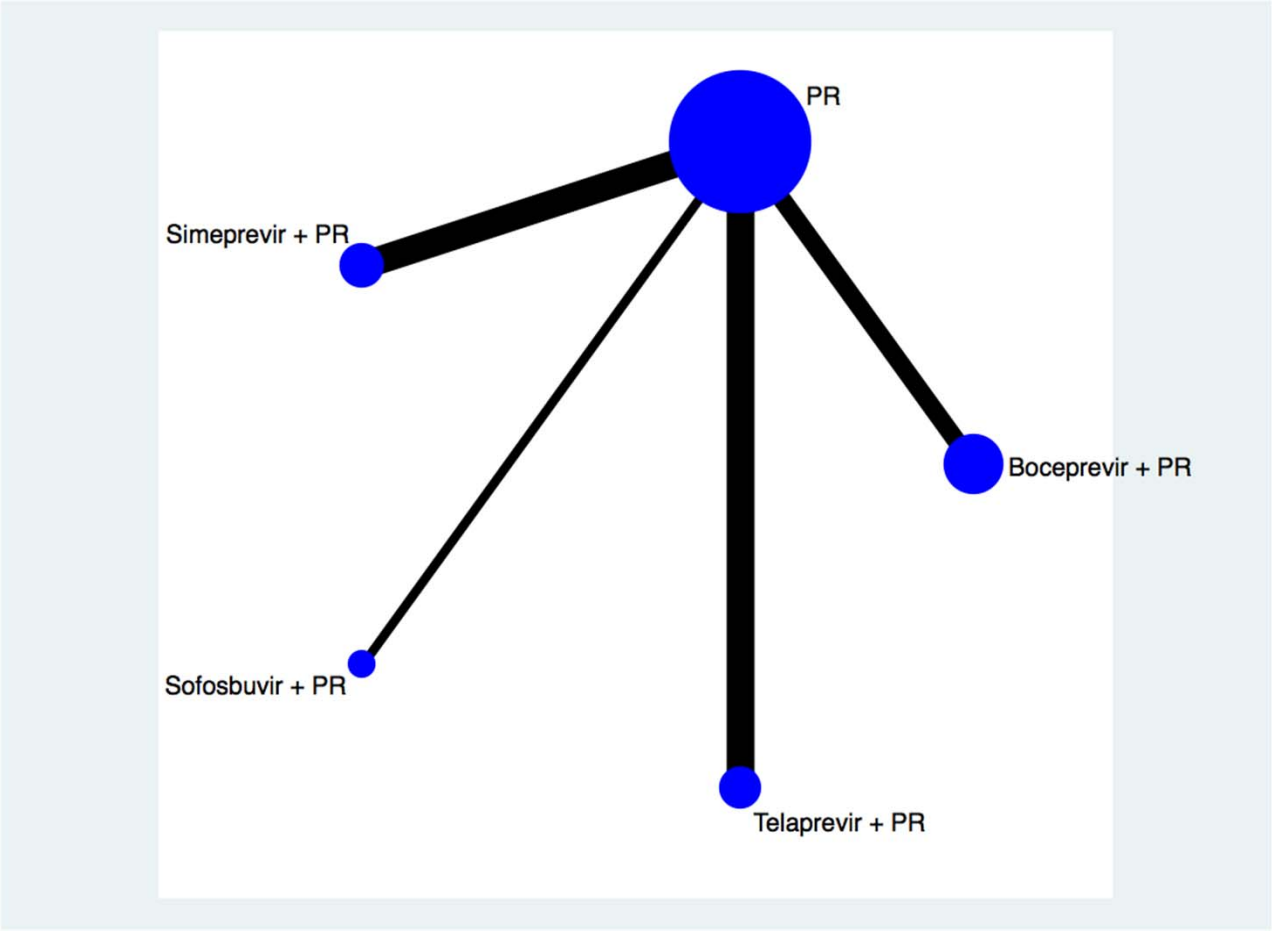
- 3 randomized trials with PR as a control
  - One phase 3 trial for genotype 2&3 with FDA approved dose (FISSION)
  - Mix of genotypes 1 – 3
  - All interferon eligible
- 10 additional trials
  - One placebo controlled phase 3 trial for genotype 2&3 among interferon intolerant, unwilling, or ineligible patients (POSITRON)

GENOTYPE 1

TREATMENT-NAÏVE

INTERFERON ELIGIBLE

Network Plot
GT 1, Treatment-naïve



Summary Estimates from the NMA Genotype 1, Treatment-naïve SVR

Treatment	SVR12	95% CI	P versus PR
PR	47%	41% to 52%	-
Boceprevir + PR	73%	68% to 77%	<0.001
Telaprevir + PR	74%	69% to 79%	<0.001
Simeprevir + PR*	84%	78% to 88%	<0.001
Sofosbuvir + PR	83%	79% to 87%	<0.001

* Excludes patients with the Q80K mutation

HARMS

- Simeprevir + PR versus PR 12 weeks
  - Fewer adverse events (AEs) stopping treatment (2.6% versus 4.5%*)
  - Comparable common AEs
  - More photosensitivity (3.3%) and elevated bilirubin (2.0%)
- Sofosbuvir + PR versus PR 24 weeks
  - Fewer AEs stopping treatment (2% versus 11%)
  - Comparable common AEs
- Simeprevir or sofosbuvir versus telaprevir
  - No direct data, but fewer pills and likely less anemia

GENOTYPE 1

TREATMENT NAÏVE

INTERFERON INELIGIBLE

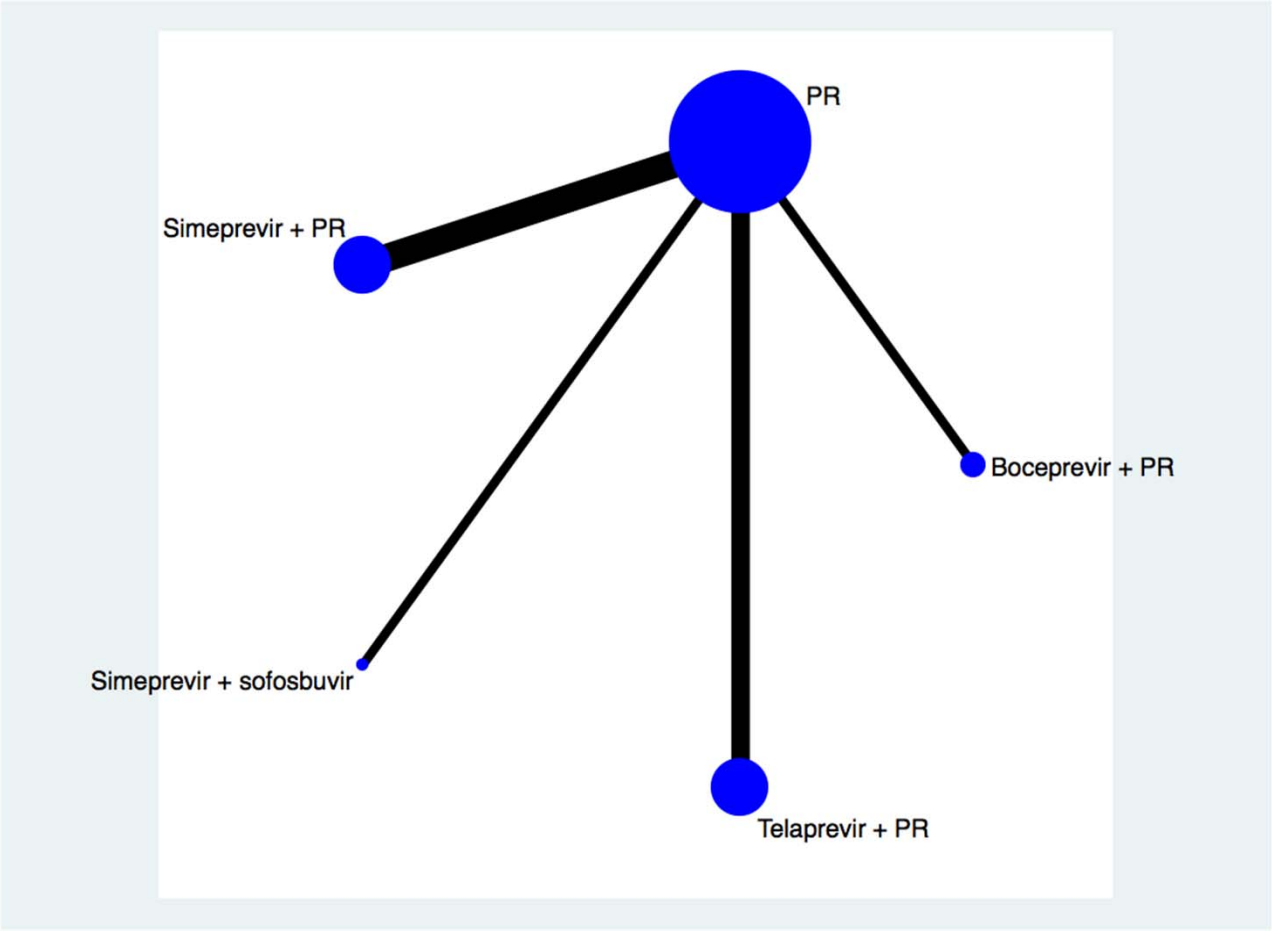
GT 1, Naïve, IFN ineligible

- No controlled studies
- No studies of simeprevir without interferon
- 3 studies of sofosbuvir + R for 12 or 24 weeks
  - Largest n = 25
  - SVR from 47% to 84%
  - Likely fewer AEs and no injections because IFN-free

GENOTYPE 1

TREATMENT-EXPERIENCED
INTERFERON ELIGIBLE

Network Plot
GT 1, Treatment-experienced



Summary Estimates from the NMA Genotype 1, Treatment-experienced

Treatment	SVR12	95% CI	P versus PR
PR	22%	15% to 29%	-
Boceprevir + PR	64%	49% to 76%	<0.001
Telaprevir + PR	70%	61% to 77%	<0.001
Simeprevir + PR*	70%	58% to 79%	<0.001
Sofosbuvir + PR	?	?	?
Simeprevir + sofosbuvir (+ R)	90%	78% to 96%	<0.001

* Excludes patients with the Q80K mutation

- FDA model for sofosbuvir: Treatment naïve with poor prognosis
  - **71%** based on 52 patients in NEUTRINO study

HARMS

- Same as treatment naïve: less burdensome than PR or PR + boceprevir or telaprevir

GENOTYPE 1

TREATMENT-EXPERIENCED
INTERFERON INELIGIBLE

GT 1, Experienced, IFN ineligible

- No controlled studies
- No studies of simeprevir or sofosbuvir except in combination in this population
- SMV + SOF (+ R) in treatment experienced: COSMOS
  - **SVR12 = 90%**
- Likely fewer AEs and no injections with IFN-free treatment

GENOTYPE 2

TREATMENT-NAIVE

GT 2, Treatment-naïve

	SOF + R 12 W	PR 24 W
Benefits: SVR12	97%	78%
Harms		
Stopped due to AE	1.4%	11%
Flu-like illness	2.8%	18%

FISSION trial: N = 137, open label.
AEs across all trials of sofosbuvir in GT 2 and 3

Summary: higher SVR12, fewer side effects, shorter treatment, no injections.

GENOTYPE 2

TREATMENT-EXPERIENCED

GT 2, Treatment-experienced

	SOF + R 12 W	PR 24 W
Benefits: SVR12	86%, 90%	-
Harms		
Stopped due to AE	1.4%	11%
Flu-like illness	2.8%	18%

Two uncontrolled trials
FUSION: N = 36
VALENCE: N = 42
AEs across all trials of sofosbuvir in GT 2 and 3

Summary: higher SVR12, fewer side effects, shorter treatment, no injections.

GENOTYPE 3

TREATMENT-NAIVE

GT 3, Treatment-naïve

	SOF + R 24 W	PR 24 W
Benefits: SVR12	93%	No control
Harms		
Stopped due to AE	1.4%	11%
Flu-like illness	2.8%	18%

FISSION trial: N = 359, open label, randomized trial of SOF + R for 12 weeks.
- SVR12 56% versus 62% for PR

AEs across all trials of sofosbuvir in GT 2 and 3

Summary: likely higher SVR12 for 24 week course (VALENCE), fewer side effects, no injections. Same treatment length.

GENOTYPE 3

TREATMENT-EXPERIENCED

GT 3, Treatment-experienced

	SOF + R 24 W	PR 24 W
Benefits: SVR12	77%	No control
Harms		
Stopped due to AE	1.4%	11%
Flu-like illness	2.8%	18%

VALENCE: N = 42 SVR12 = 77% SOF + R 24W
AEs across all trials of sofosbuvir in GT 2 and 3

Summary: Modest SVR12, few side effects, no injections.
Same treatment length.

Limitations

- Genotype 1: No completed trials compare the new drug regimens to the recent standard of care: PR plus boceprevir or telaprevir
- Many of the trials of sofosbuvir were small and uncontrolled
- All results are based on surrogate outcomes: SVR24 or SVR12

Key Comments Received

- The data for simeprevir in patients without the Q80K mutation should be presented.
- The SVR of 57% from the PR control group in the POSITRON study (*actually PROTON*) is likely to be spuriously high given historical data and biases the analysis against sofosbuvir.

Model of Clinical and Economic Outcomes of Treatment Options for Hepatitis C

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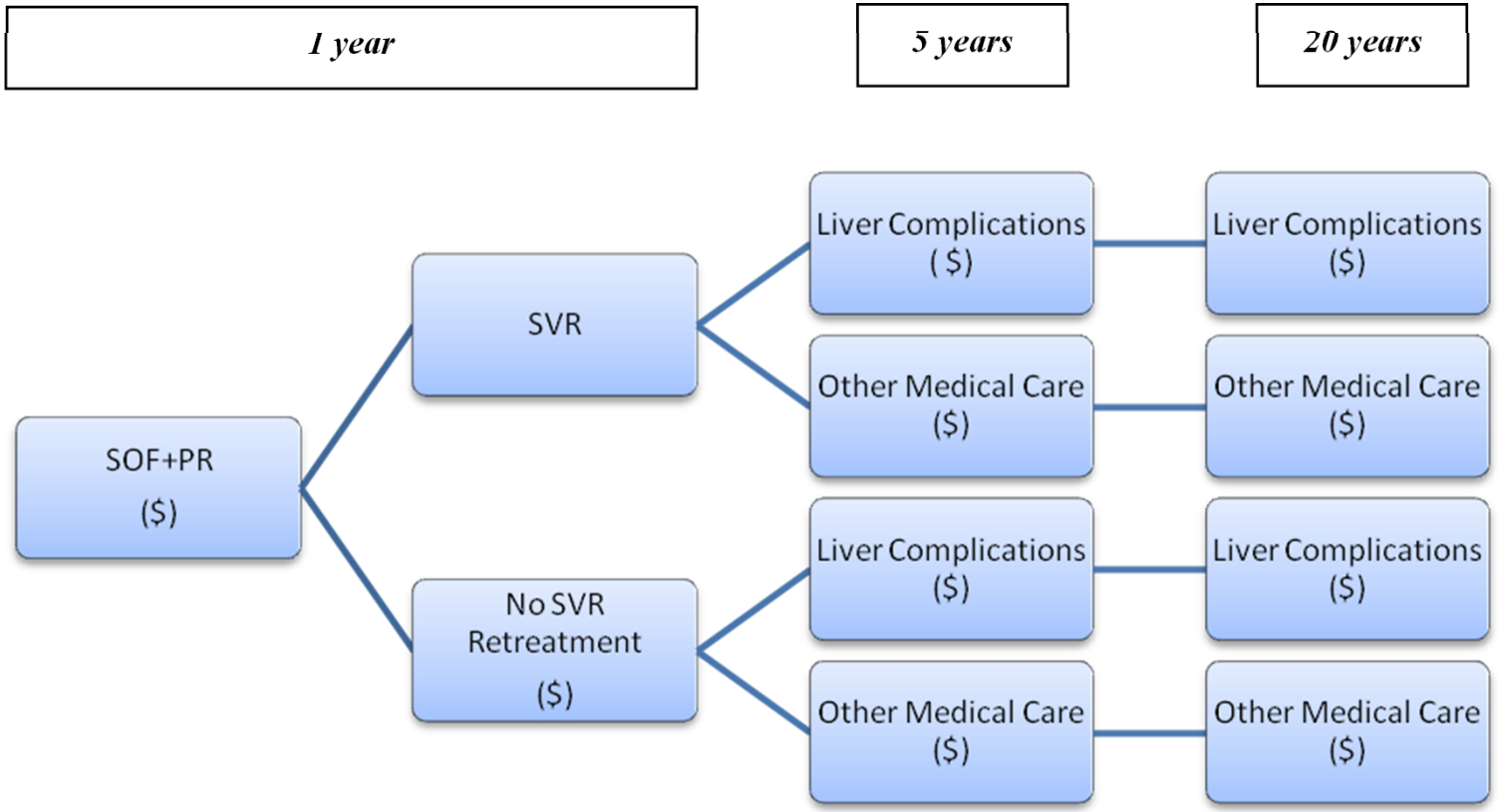
March 10, 2014

Model Overview

- Model of clinical and economic effects of sofosbuvir and simeprevir in hypothetical cohorts of 1,000 60-year-old newly-diagnosed patients:
  - Cohorts defined by genotype, interferon eligibility, and prior treatment status (i.e., treatment-naïve vs. treatment-experienced)
  - Perspective of 3rd party payer taken
  - Outcomes and costs measured at one, 5, and 20 years following treatment
  - Regimens selected in concordance with AASLD/IDSA/IAS guideline recommendations for each population of interest
- Findings also extrapolated to California Hepatitis C population

Depiction of Model Flow



NOTE: "$" indicates model elements with calculated cost

TEL: Telaprevir; PR: Pegylated interferon + ribavirin; SVR: Sustained virologic response

Model Overview

- Effectiveness based on SVR from network meta-analysis or individual studies:
  - SVR from *initial* course of therapy determines outcome
  - SVR reduces rate of downstream liver complications and lowers cost of annual medical care
- Costs:
  - Initial course of therapy
  - Retreatment for those not achieving SVR
  - Management of liver complications and other annual medical care (SVR and non-SVR)

Key Assumptions

- Full compliance with and completion of therapeutic regimen
- Cost per SVR and downstream cost offsets based on effectiveness of *initial* course of therapy only
- Clinical benefits limited to SVR and its effects on downstream liver-related complications
- Costs limited to drug therapy and downstream management of liver disease and other medical care
- No differential costs assumed for identification/management of side effects and other drug-related harms
- Costs measured for assumed *re*treatment regimens, but effectiveness was not

RESULTS: GENOTYPE 1

Genotype 1, Treatment-naïve, Interferon Eligible

Table 23 Page 5

Regimen	SVR (per 1,000)	D/C due to any AE (per 1,000)	Cost per Add'l SVR ($)	Add'l 1-year Rx Costs ($, millions) *	Total Cost Offsets† vs. Usual Care ($, millions)	
					5-year	20-year
TEL+PR (12/24)	740	140	---	---	---	---
SMV+PR (12/24)	840	64	$73,200	($1.8)	($2.4)	($7.7)
SOF+PR (12/12)	830	55	$138,800	$4.3	($2.2)	($7.0)

SVRs obtained from ICER network meta-analysis

*Includes cost of initial therapy + retreatment with most effective regimen available
†Based on reduced rates of liver-related complications and greater % of patients achieving SVR
SVR: Sustained virologic response; D/C: Discontinuation; AE: Adverse event

Genotype 1, Treatment-naïve, Interferon Ineligible

Table 23 Page 5

Regimen	SVR (per 1,000)	D/C due to any AE (per 1,000)	Cost per Add'l SVR ($)	Add'l 1-year Rx Costs ($, millions) *	Total Cost Offsets† vs. Usual Care ($, millions)	
					5-year	20-year
No Rx	0	0	---	---	---	---
SOF+R (24)	720	13	$244,933	$219.6	($17.2)	($55.6)
SOF+SMV+R (12)	900	50	$171,707 vs. No Rx ↑SVR, ↓$ vs. SOF+R	$170.0	($21.5)	($69.6)

SVRs obtained from PHOTON-1/QUANTUM (SOF+R) and COSMOS (SOF+SMV+R)

*Includes cost of initial therapy + retreatment with most effective regimen available
†Based on reduced rates of liver-related complications and greater % of patients achieving SVR
SVR: Sustained virologic response; D/C: Discontinuation; AE: Adverse event

Genotype 1, Treatment-experienced, Interferon Eligible

Table 24 Page 8

Regimen	SVR (per 1,000)	D/C due to any AE (per 1,000)	Cost per Add'l SVR ($)	Add'l 1-year Rx Costs ($, millions)*	Total Cost Offsets† vs. Usual Care ($, millions)	
					5-year	20-year
TEL+PR (12/24)	700	140	---	---	---	---
SMV+PR (12/24)	700	64	N/C	$7.3	$0	$0
SOF+PR (12/12)	710	55	$1.2 m	$10.9	($0.2)	($0.8)
SOF+SMV+R (12)	900	50	$352,800	$39.7	($4.8)	($15.5)

SVRs obtained from ICER network meta-analysis (TEL+PR and SMV+PR), FDA estimate based on NEUTRINO (SOF+PR), and COSMOS (SOF+SMV+R)

*Includes cost of initial therapy + retreatment with most effective regimen available
†Based on reduced rates of liver-related complications and greater % of patients achieving SVR
SVR: Sustained virologic response; D/C: Discontinuation; AE: Adverse event; N/C: Not calculable

Genotype 1, Treatment-experienced, Interferon Ineligible

Table 24 Page 8

Regimen	SVR (per 1,000)	D/C due to any AE (per 1,000)	Cost per Add'l SVR ($)	Add'l 1-year Rx Costs ($, millions)*	Total Cost Offsets† vs. Usual Care ($, millions)	
					5-year	20-year
No Rx	0	0	---	---	---	---
SOF+R (24)	610	13	$289,102	$236.6	($14.6)	($47.2)
SOF+SMV +R (12)	900	50	$171,707 vs. No Rx ↑SVR, ↓$ vs. SOF+R	$170.0	($21.5)	($69.6)

SVRs obtained from PHOTON-1/QUANTUM adjusted downward for Rx-experienced (SOF+R) and COSMOS (SOF+SMV+R)

*Includes cost of initial therapy + retreatment with most effective regimen available
†Based on reduced rates of liver-related complications and greater % of patients achieving SVR
SVR: Sustained virologic response; D/C: Discontinuation; AE: Adverse event

RESULTS: GENOTYPE 2

Genotype 2, Treatment-naïve, Interferon Eligible

Table 25
Page 10

Regimen	SVR (per 1,000)	D/C due to any AE (per 1,000)	Cost per Add'l SVR ($)	Add'l 1-year Rx Costs ($, millions)*	Total Cost Offsets† vs. Usual Care ($, millions)	
					5-year	20-year
PR (24)	780	84	---	---	---	---
SOF+R (12)	970	13	$332,842	$46.5	($4.5)	($14.7)

SVRs obtained from VALENCE and FISSION

*Includes cost of initial therapy + retreatment with most effective regimen available
†Based on reduced rates of liver-related complications and greater % of patients achieving SVR
SVR: Sustained virologic response; D/C: Discontinuation; AE: Adverse event

Genotype 2, Treatment-naïve, Interferon Ineligible

Table 25
Page 10

Regimen	SVR (per 1,000)	D/C due to any AE (per 1,000)	Cost per Add'l SVR ($)	Add'l 1-year Rx Costs ($, millions)*	Total Cost Offsets† vs. Usual Care ($, millions)	
					5-year	20-year
No Rx	0	0	---	---	---	---
SOF+R (12)	930	13	$94,813	$94.3	($22.3)	($71.8)

SVR obtained from POSITRON

*Includes cost of initial therapy + retreatment with most effective regimen available
†Based on reduced rates of liver-related complications and greater % of patients achieving SVR
SVR: Sustained virologic response; D/C: Discontinuation; AE: Adverse event

Genotype 2, Treatment-experienced, Interferon Eligible

Table 26
Page 12

Regimen	SVR (per 1,000)	D/C due to any AE (per 1,000)	Cost per Add'l SVR ($)	Add'l 1-year Rx Costs ($, millions)*	Total Cost Offsets† vs. Usual Care ($, millions)	
					5-year	20-year
PR (24)	710	84	---	---	---	---
SOF+R (12)	880	13	$372,000	$48.3	($4.1)	($13.1)

SVRs obtained from VALENCE/FISSION adjusted downward for Rx-experienced (PR), and from VALENCE and FUSION (SOF+R)

*Includes cost of initial therapy + retreatment with most effective regimen available
†Based on reduced rates of liver-related complications and greater % of patients achieving SVR
SVR: Sustained virologic response; D/C: Discontinuation; AE: Adverse event

Genotype 2, Treatment-experienced, Interferon Ineligible

Table 26
Page 12

Regimen	SVR (per 1,000)	D/C due to any AE (per 1,000)	Cost per Add'l SVR ($)	Add'l 1-year Rx Costs ($, millions)*	Total Cost Offsets† vs. Usual Care ($, millions)	
					5-year	20-year
No Rx	0	0	---	---	---	---
SOF+R (12)	880	13	$100,200	$98.8	($21.1)	($68.0)

SVR for SOF+R assumed to be equivalent to interferon-eligible population (from VALENCE and FUSION) in absence of data in this population

*Includes cost of initial therapy + retreatment with most effective regimen available
†Based on reduced rates of liver-related complications and greater % of patients achieving SVR
SVR: Sustained virologic response; D/C: Discontinuation; AE: Adverse event

RESULTS: GENOTYPE 3

Genotype 3, Treatment-naïve, Interferon Eligible

Table 27
Page 14

Regimen	SVR (per 1,000)	D/C due to any AE (per 1,000)	Cost per Add'l SVR ($)	Add'l 1-year Rx Costs ($, millions)*	Total Cost Offsets† vs. Usual Care ($, millions)	
					5-year	20-year
PR (24)	620	84	---	---	---	---
SOF+R (24)	930	13	$488,439	$96.7	($7.4)	($24.0)

SVRs obtained from FISSION (PR) and VALENCE (SOF+R)

*Includes cost of initial therapy + retreatment with most effective regimen available
†Based on reduced rates of liver-related complications and greater % of patients achieving SVR
SVR: Sustained virologic response; D/C: Discontinuation; AE: Adverse event

Genotype 3, Treatment-naïve, Interferon Ineligible

Table 27
Page 14

Regimen	SVR (per 1,000)	D/C due to any AE (per 1,000)	Cost per Add'l SVR ($)	Add'l 1-year Rx Costs ($, millions)*	Total Cost Offsets† vs. Usual Care ($, millions)	
					5-year	20-year
No Rx	0	0	---	---	---	---
SOF+R (24)	630	13	$279,924	$241.6	($15.1)	($48.7)

SVR obtained based on overall data from POSITRON (treatment-naïve and treatment-experienced)

*Includes cost of initial therapy + retreatment with most effective regimen available
†Based on reduced rates of liver-related complications and greater % of patients achieving SVR
SVR: Sustained virologic response; D/C: Discontinuation; AE: Adverse event

Genotype 3, Treatment-experienced, Interferon Eligible

Table 28
Page 16

Regimen	SVR (per 1,000)	D/C due to any AE (per 1,000)	Cost per Add'l SVR ($)	Add'l 1-year Rx Costs ($, millions)*	Total Cost Offsets† vs. Usual Care ($, millions)	
					5-year	20-year
PR (24)	510	84	---	---	---	---
SOF+R (24)	770	13	$582,369	$105.6	($6.2)	($20.1)

SVRs obtained from FISSION adjusted downward for treatment-experienced (PR), and from VALENCE (SOF+R)

*Includes cost of initial therapy + retreatment with most effective regimen available
†Based on reduced rates of liver-related complications and greater % of patients achieving SVR
SVR: Sustained virologic response; D/C: Discontinuation; AE: Adverse event

Genotype 3, Treatment-experienced, Interferon Ineligible

Table 28
Page 16

Regimen	SVR (per 1,000)	D/C due to any AE (per 1,000)	Cost per Add'l SVR ($)	Add'l 1-year Rx Costs ($, millions)*	Total Cost Offsets† vs. Usual Care ($, millions)	
					5-year	20-year
No Rx	0	0	---	---	---	---
SOF+R (24)	630	13	$279,924	$241.6	($15.1)	($48.7)

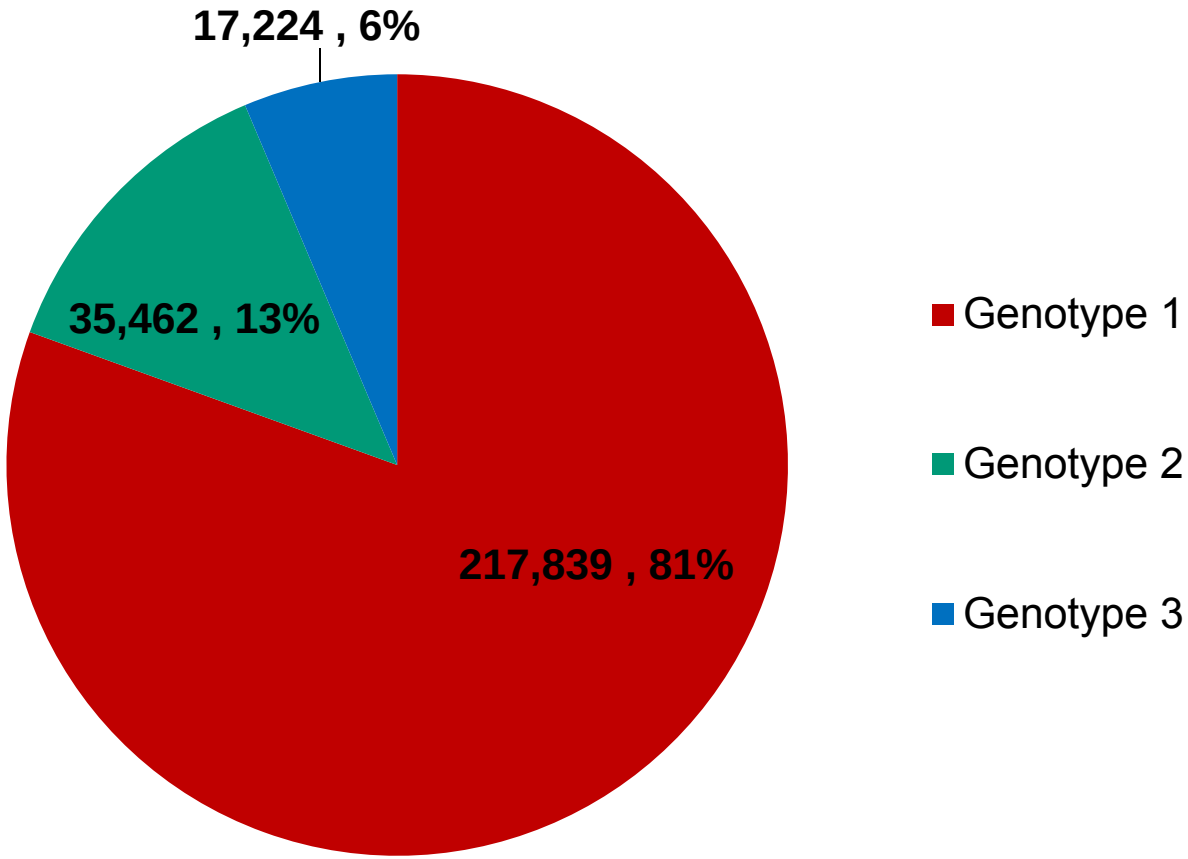
SVR obtained based on overall data from POSITRON (treatment-naïve and treatment-experienced)

*Includes cost of initial therapy + retreatment with most effective regimen available
†Based on reduced rates of liver-related complications and greater % of patients achieving SVR
SVR: Sustained virologic response; D/C: Discontinuation; AE: Adverse event

Analyses of Budget Impact in California

- Size of infected population estimated using published estimates from NHANES and other sources
- Impact assessed within genotype/prior treatment status/IFN eligibility stratum
  - Based on change from prior standard of care to most effective regimen
  - Assessed alternatively for all patients and only those who have advanced liver disease
- Additional assumptions:
  - % of patients know they are infected (50% vs. 75%)
  - Treatment-naïve %: 75%
  - Interferon-ineligible %: 30%
  - % with advanced liver disease: 33%

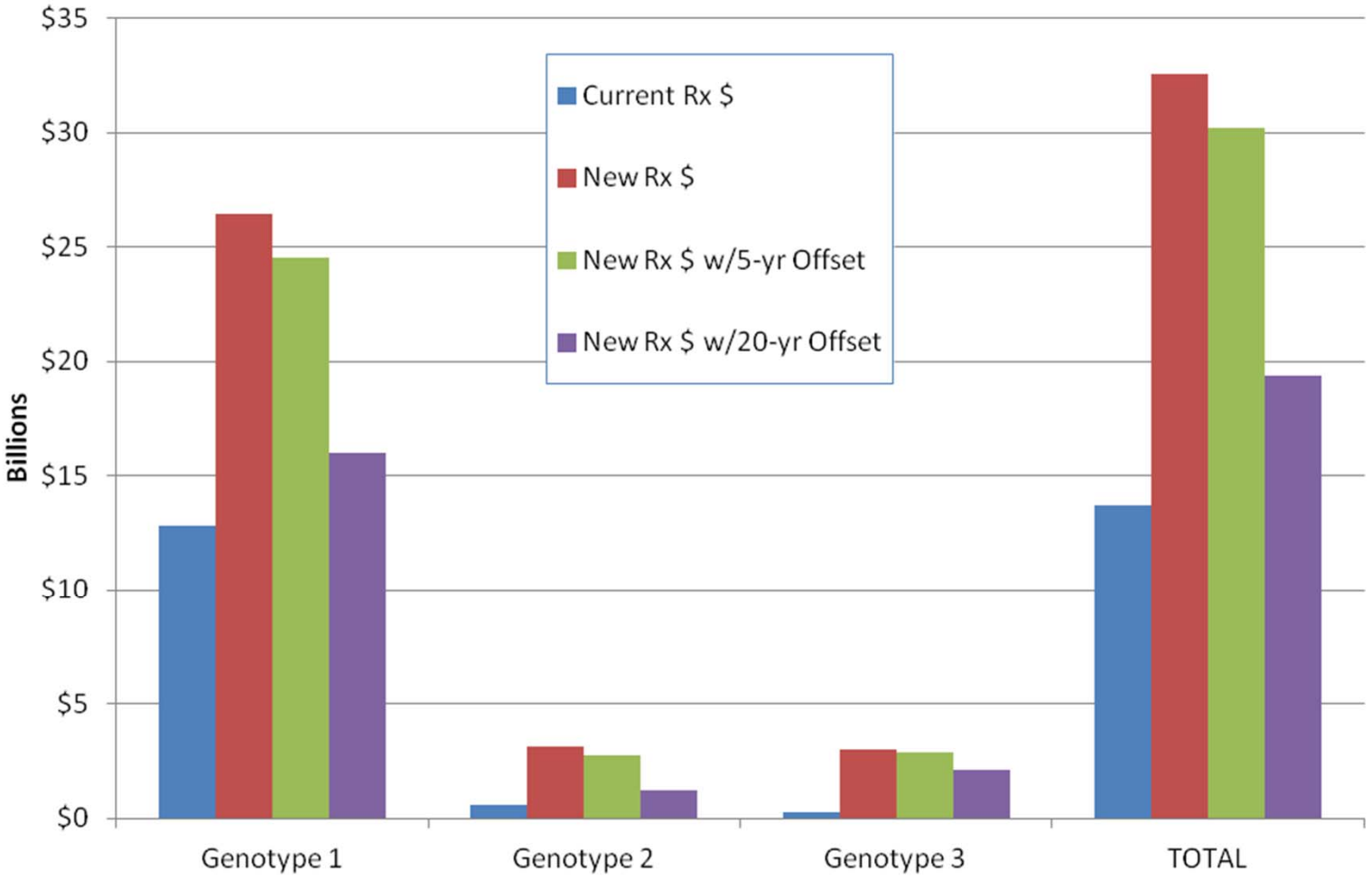
Distribution of CA Hepatitis C Population by Genotype*



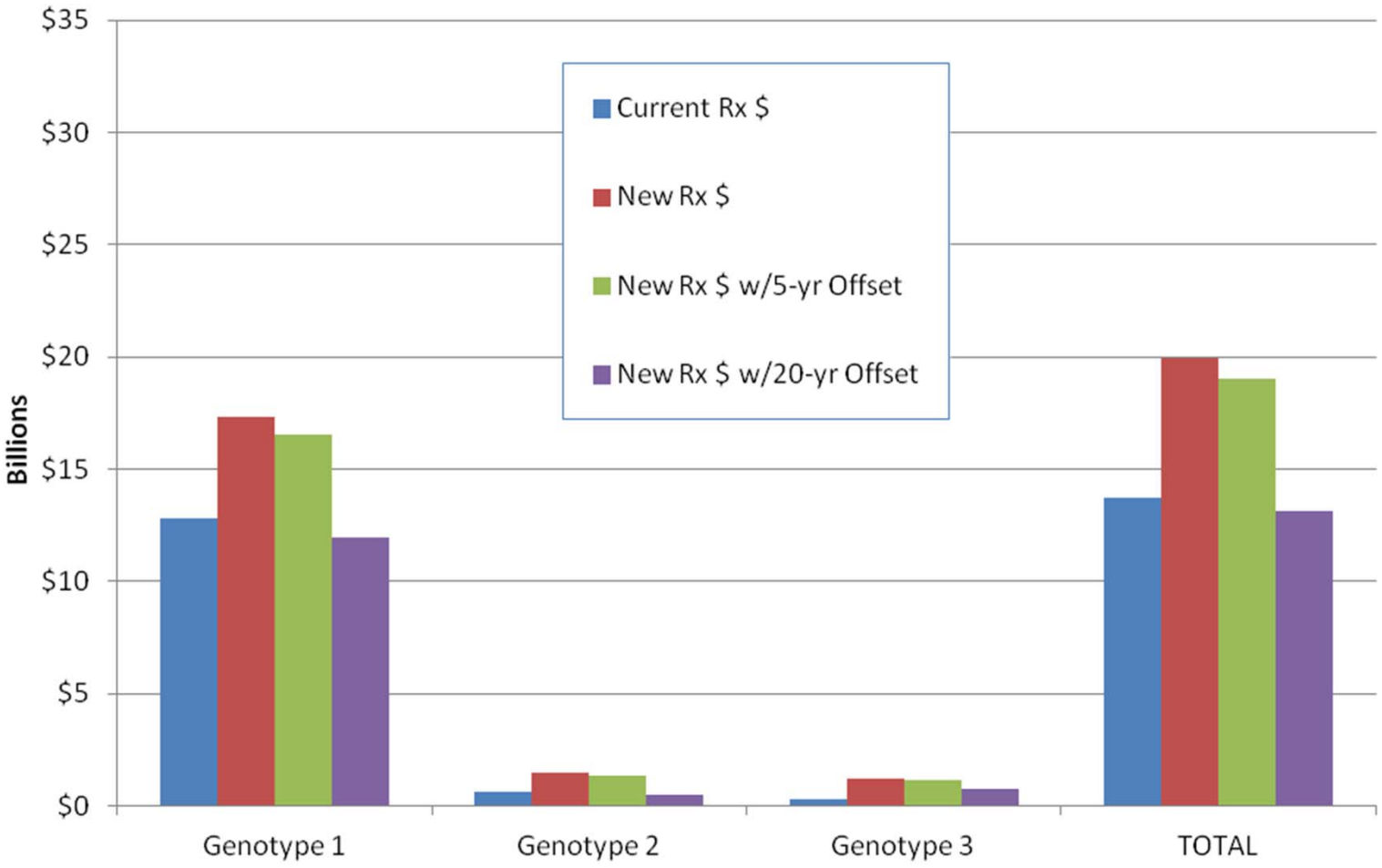
*Among assumed 50% who are aware of infection

RESULTS: AWARENESS OF INFECTION BY 50%

Budget Impact: All Patients Who are Aware of Infection Get New Drugs (n=270,525)



Budget Impact: Only Patients with Advanced Liver Disease Get New Drugs (n=89,544)



PMPM Calculation

- Avg. PMPM premium, CA large group DMHC-regulated health plan: $350*
- Prevalence of chronic HCV in typical 1 million member plan: 17,000
  - Number aware of infection and presenting for treatment (50%): 8,500
- Avg. cost increase per patient (based on ICER analysis) from switching to newer regimens: ~$70,000
  - On a PMPM basis: $49
  - % increase: 14.1%
  - % increase if only patients with advanced liver disease treated: 4.7%

*California Health Benefits Review Program. CHBRP Health Plan Actuarial Model, 2010.

Model Limitations

- Insufficient data for quantitative synthesis in many cases, reliance on individual study estimates
- Assumed perfect compliance with and completion of drug regimens
- Clinical effects and costs of drug-related adverse effects not considered
- Other benefits of treatment (e.g., improved quality of life, work/school productivity) not measured

Key Comments Received

- Consider additional benefits of reducing pool of prevalent infection
- Increasing age at diagnosis will place burden on Medicare
- Model results most sensitive to assumptions regarding costs (of drugs and disease-related complications) and SVR rates
- Key subpopulations (e.g., HIV co-infection, relapsers vs. non-responders, genotype 1 subtypes) not explicitly modeled
- Consideration of other benefits (e.g., quality of life)
- Benefits of SVR more fully realized in simulation models that mimic progression of disease

BACKUP SLIDES

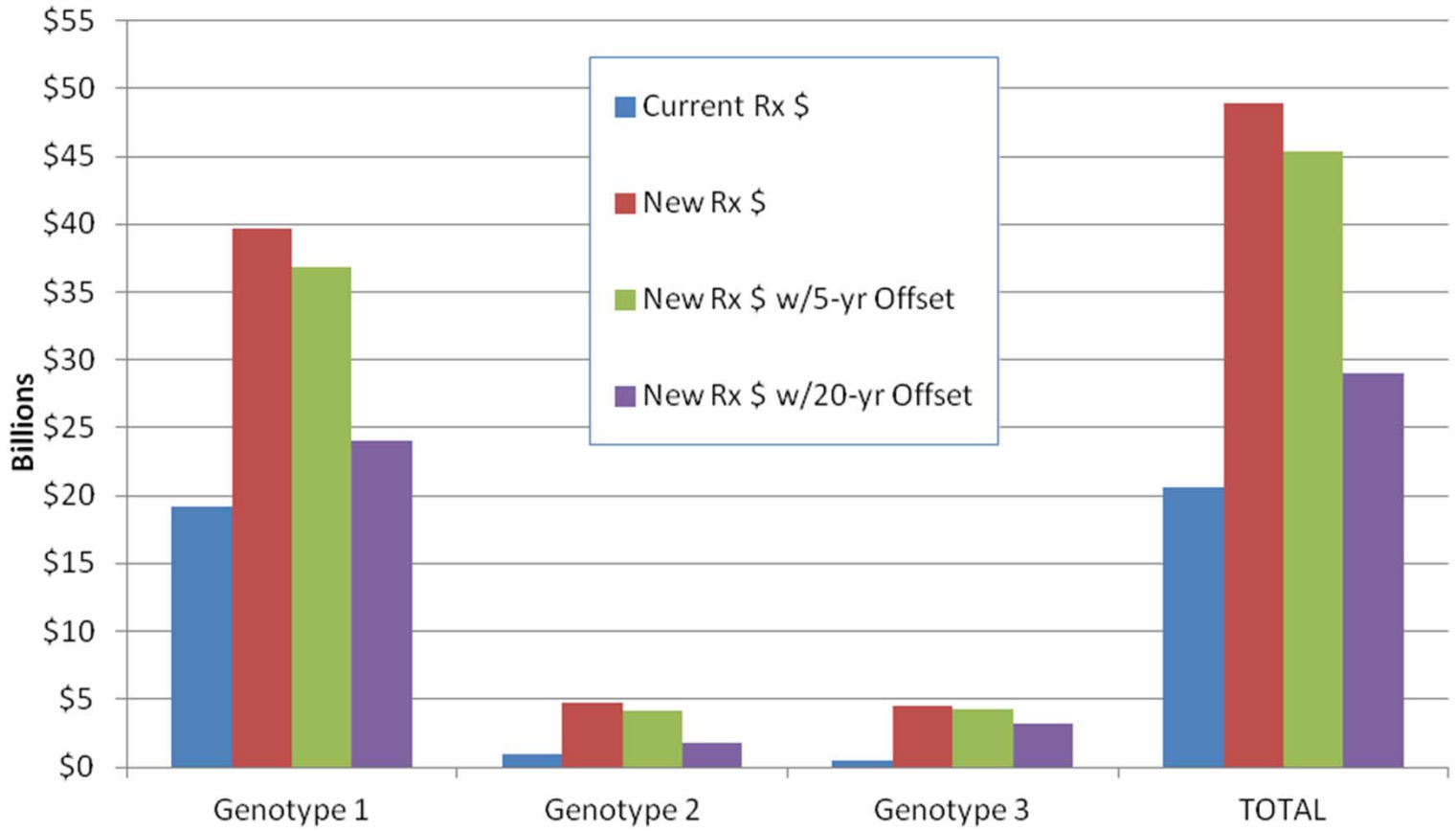
Cost per SVR: New Regimens vs. PR Alone (Genotype 1, IFN-eligible)

Treatment Status/ Regimen	SVR	Cost ($)	Cost per Add'l SVR ($)
Treatment-Naive			
PR (48)	470	$49,872	---
SMV+PR (12/24)	840	$91,296	$111,957
SOF+PR (12/12)	830	$96,468	$129,433
Treatment-Experienced			
PR (48)	220	$49,872	---
SMV+PR (12/24)	700	$91,296	$86,300
SOF+PR (12/12)	710	$96,468	$95,094

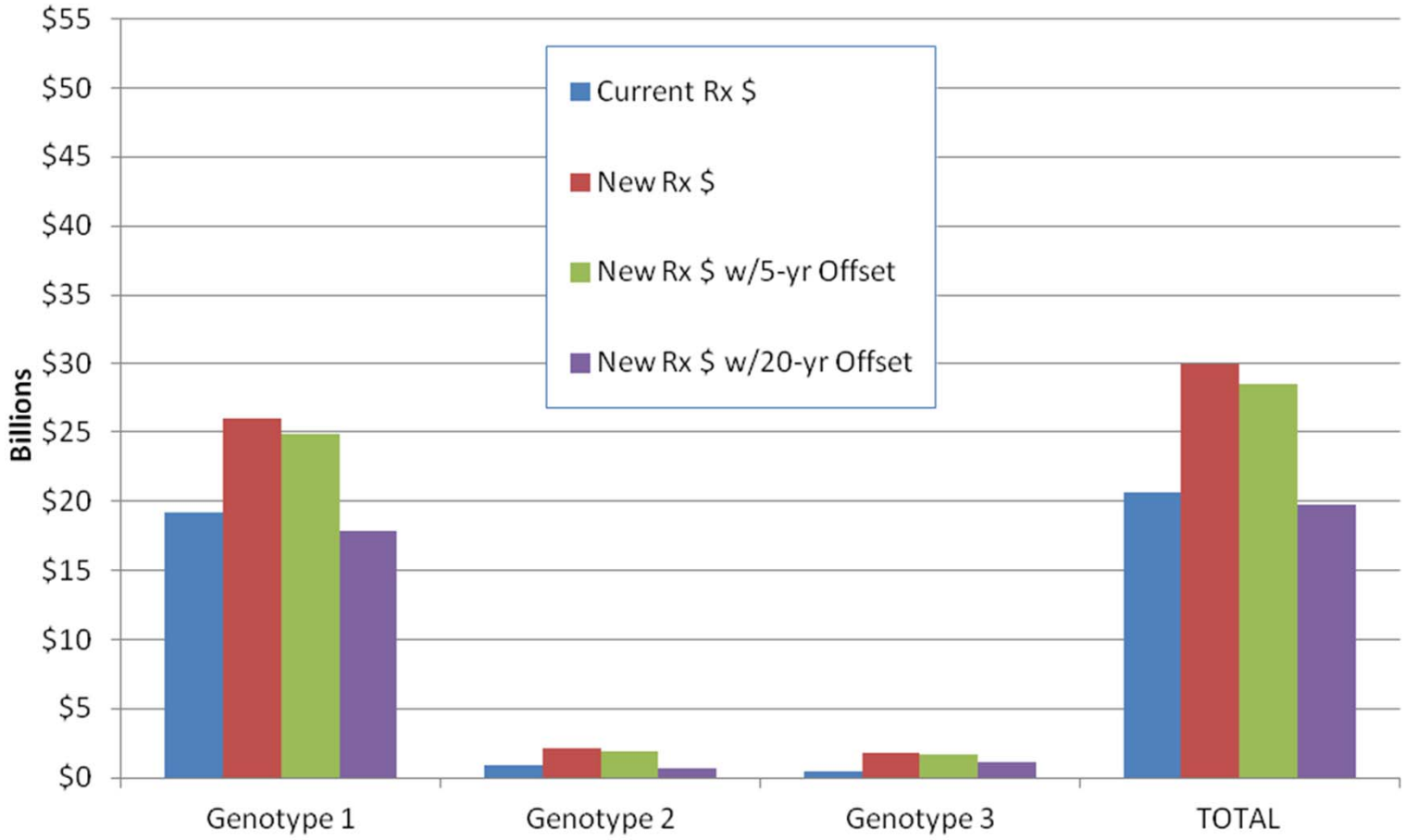
Cost-Effectiveness Benchmarks

Modality	Population	Result	Reference
Telaprevir+PR vs. PR alone	Hepatitis C patients at NYC medical center (Genotype 1)	$189,000 per additional SVR	Bichoupan et al., AASLD proceedings November 2013
Response-guided PR vs. PR alone	Decision analysis (Genotypes 1/2/3)	$17,000-$24,000 per additional SVR	Buti et al., Alimentary Pharmacology & Therapeutics, 2007
Darunavir-based HAART vs. Control PI-based HAART	Analysis of POWER clinical trial	$1,000-$79,000 per “success” (undetectable viral load)	Hill et al., Pharmacoeconomics, 2010

Budget Impact, All Patients Who are Aware of Infection (n=405,788)



Budget Impact, Patients w/Advanced Liver Disease Only (n=134,316)



Results: Genotype 1, Treatment-Experienced, Interferon Eligible

- Cost per additional SVR for SOF+PR:
  - vs. SMV+PR: $129,300
- Cost per additional SVR for SOF+SIM+R:
  - vs. SMV+PR: $274,957
  - vs. SOF+PR: $305,621

Thank you!

Policy Roundtable Panelists

- Sylvia Carlisle, MD, MBA, Managing Medical Director, Anthem Blue Cross
- Ryan Clary, Executive Director, National Viral Hepatitis Roundtable
- Rena K. Fox, MD, Professor of Clinical Medicine, Division of General Internal Medicine, UCSF
- R. Todd Frederick, MD, Transplant Hepatologist and Fellowship Director of Transplant Hepatology, Department of Transplantation, Division of Hepatology, California Pacific Medical Center
- Amandeep Sahota, MD, MS, Transplant Hepatologist and Southern California Permanente Medical Group Regional Hepatitis C Champion, Kaiser Permanente, Los Angeles
- Robert Snediker, Principal Liaison, HECOR, Janssen Pharmaceuticals
- John Yao, MD, MBA, MPH, Senior Medical Director, Blue Shield of California

Closing

- Further public comments accepted until: March 17, 2014, 5 pm PT
- Report dissemination plans
- Next meeting: July 11, 2014, Los Angeles
- Next topic: Treatment of Migraine Headaches