A COST-EFFECTIVENESS ANALYSIS OF LDV/SOF+RBV FOR 12 WEEKS VS. LDV/SOF 24 WEEK VS. SOF+SMV 24 WEEKS IN CHC GT1 TE CIRRHOTIC PATIENTS

Reported by Jules Levin
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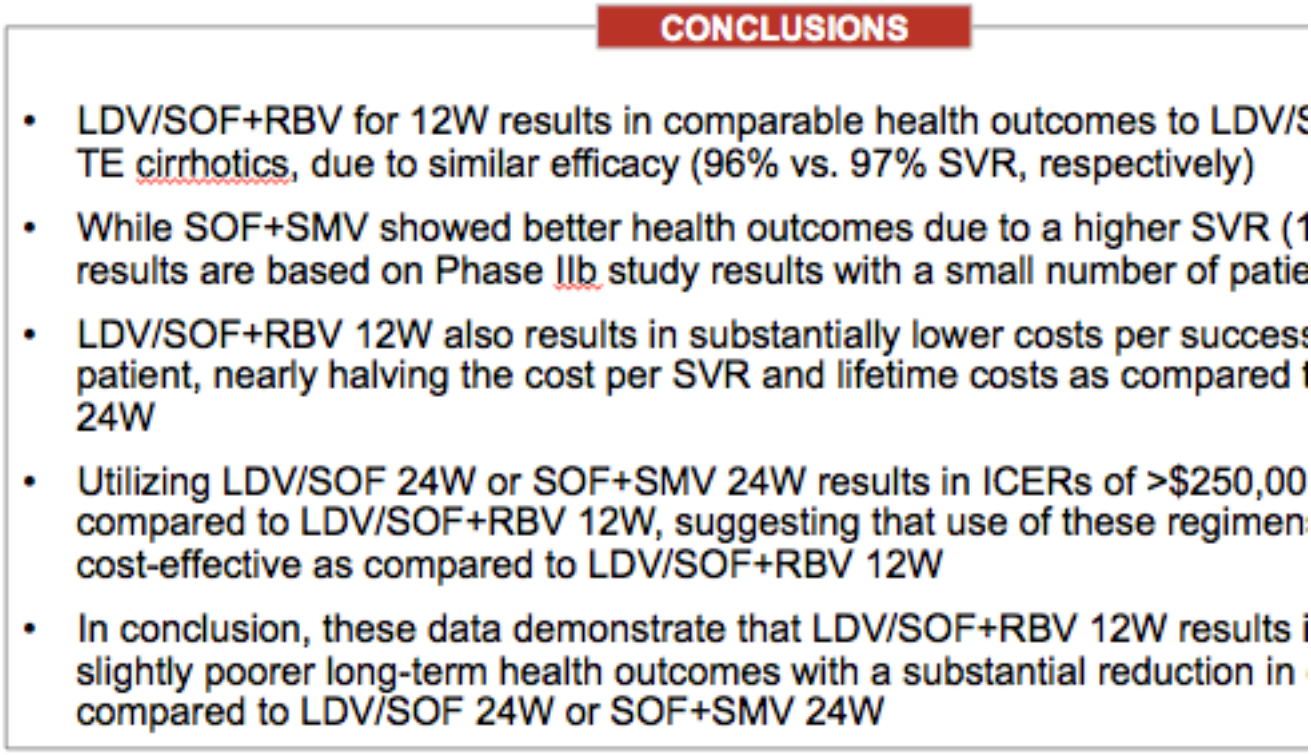
Ahmed, A[1]; Dieterich, DT[2]; Park, H[3]; Saab, S[4]; Gordon, SC[5]; Younossi, ZM[6]

CONCLUSIONS



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ORAL PRESENTATION

Digestive Disease Week 2015

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WASHINGTON, DC

BACKGROUND AND AIMS

BACKGROUND

- Ledipasvir / sofosbuvir (LDV/SOF) is the first all-oral, PR-free regim
  high efficacy in HCV patients, including difficult-to-treat TE, cirrhotic
- LDV/SOF+RBV 12W has demonstrated similar efficacy to LDV/SO
  clinical trials (SVR 12 of 96% and 97%, respectively)[2]
- Sofosbuvir in combination with simeprevir (SOF+SMV), has been s
  have similar efficacy to LDV/SOF as measured in a phase 2b clinic

OVERALL STUDY AIM

To **evaluate the lifetime health and economic outcomes** fro
decision-analytic model for **LDV/SOF+RBV versus SOF+SMV** in
treatment-experienced patients with **compensated cirrhos**

LDV/SOF = ledipasvir / sofosbuvir; RBV = ribavirin; TE = treatment-experienced; CC = compensated cirrhosis;
1. Afdhal et al., 2014; 2. Bourliere et al., 2014; 3. Lawitz et al., 2014

BASELINE PATIENT CHARACTERISTICS

CHARACTERISTIC	VALUE
OVERALL	
Mean Age	52 years
Mean Weight	72 kg
FIBROSIS DISTRIBUTION	
F4	100%
SUBGENOTYPE[1]	
1a	68%
1b	32%

- The analysis modeled GT1 TE, CC HCV patients from a US third-payer perspective for a lifetime horizon
  - All costs and outcomes were discounted at 3.0%
- All sources were derived from the literature and validated by a na panel of 5 hepatologists as being reflective of the USA patient po

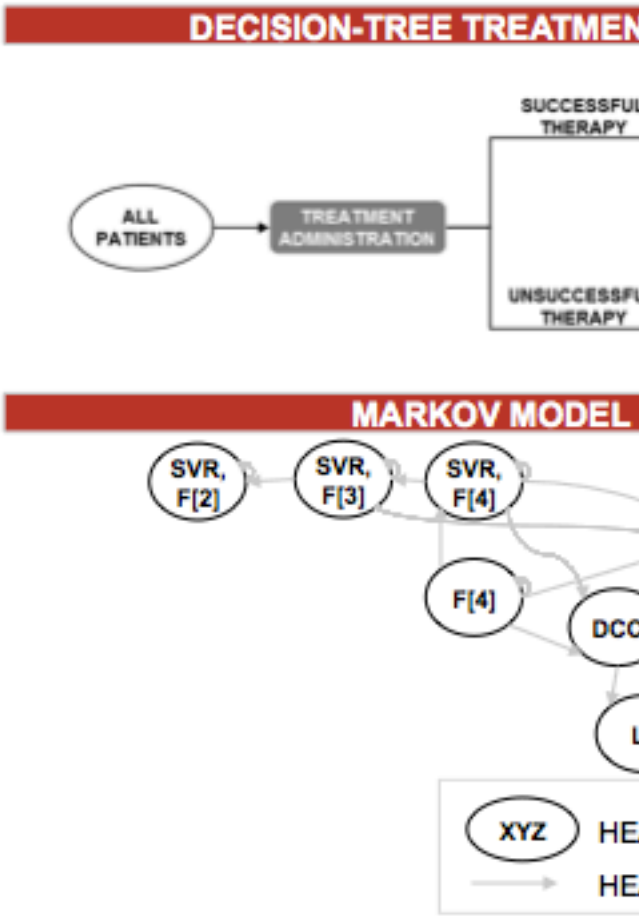
TE = treatment-experienced; CC = compensated cirrhosis
1. Ditah et al., 2014

References

1.Ditah I, Ditah F, Devaki P, Ewelukwa O, Ditah C, Njei B, Luma HN, et al. The changing epidemiology of hepatitis C virus infection in the United States: National Health and Nutrition Examination Survey 2001 through 2010. J Hepatol 2014;60:691-698.

MODEL STRUCTURE

- The model included an initial decision-tree treatment phase followed by a Markov state-transition model
- The model cycle length was 1 year
- At any point, patients can die due to natural mortality; after transitioning to advanced liver disease, patients can also die from end-stage liver disease complications (i.e., extra mortality – EM)



SVR = sustained virologic response; F = METAVIR fibrosis stage; DCC = decompensated cirrhosis; HCC = hepatocellular carc
LT = liver transplant; PLT = post-liver transplant; EM = extra mortality

TRANSITION PROBABILITIES

- Transition probabilities were based on a literature review, public sources, and consensus by a panel of 5 hepatologists

FROM	TO	ANNUAL TRANSITION PROBABILITY	
F3 SVR	F2 SVR	0.267	
	HCC	0.003	Die
	DCC	0	E
F4	DCC	0.039	
	HCC	0.024	
F4 SVR	F3 SVR	0.076	[
	DCC	0.003	Die
	HCC	0.006	Die
DCC	HCC	0.014	
	Liver transplant	0.031	
	Death	0.129	S
HCC	Death	0.485	
Liver transplant	Death, year 1	0.107	
Post–liver transplant	Death, year 2	0.049	

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2.Morgan RL, Baack B, Smith BD, Yartel A, Pitasi M, Falck-Ytter Y. Eradication of hepatitis C virus infection and the development of hepatocellular carcinoma: a meta-analysis of observational studies. Ann Intern Med 2013;158:329-337.

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EFFICACY AND UTILITY INPUTS

- SVR rates, adverse events, and treatment duration values we from relevant clinical trials
  - Data not reported for granular fibrotic stages was inferre relative risk approach and validated by a national panel c hepatologists
- Utility scores for each health state were sourced from clinical published literature
  - Utility decrements were assigned to each specific treatm based on clinical trial data and published literature

SVR RATE		
REGIMEN	SVR: F4 1a	SVR: F4 1b
LDV/SOF+RBV 12W[1,2]	96%	97%
LDV/SOF 24W[1,2]	100%	100%
SOF + SMV 24W[3]	100%	100%

HEALTH STATE
F4[4]
F4 SVR[5]
DECOMPENSATED CIRRHOSIS[4]
HCC[5]
LIVER TRANSPLANT[6]
POST-LIVER TRANSPLANT[4]
UTILITY CHANGE ON TREATME
LDV/SOF+RBV 12W[7]
LDV/SOF 24W[7]
SOF + SMV 24W[8]
NO TREATMENT[3]

1. Bourliere et al., 2014; 2. Afdhal et al., 2014; 3. Lawitz et al., 2014; 4. McLernon et al., 2008; 5. Wright and Tompkins, 2006; 6. Hsu et al., 2012; 7. Younossi et al., 2015; 8. Assumption

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Assumption validated by national panel of hepatologists.

COST INPUTS

- Costs include drug acquisition costs, monitoring costs, adverse event costs, and health state costs
  - The cost of each regimen incorporates WAC costs[1] scaled by treatment duration along with adverse event costs (drug and management costs)
  - In each health state, the baseline cost of disease has been sourced from publications that evaluated the direct medical costs of HCV
  - Patients who achieve SVR are assumed to only require long-term costs related to monitoring of DCC and HCC

MOLECULE	
TOTAL COSTS	
LDV/SOF+RBV 12W	
SOF+SMV 24W	
LDV/SOF 24W	
HEALTH STATE	
F4[2,3]	
F4 SVR Year 1[4]	
F4 SVR Years 2-3[4]	
F4 SVR Year 4 Onwards[4]	
DCC[2,3]	
HCC[5]	
LT[2,3]	
PLT[2,3]	

F = METAVIR fibrosis stage; DCC = decompensated cirrhosis; HCC = hepatocellular carcinoma; LT = liver transplant; PLT = pc
EM = extra mortality; SOF = sofosbuvir; SMV = simeprevir; RBV = ribavirin; LDV/SOF = ledipasvir / sofosbuvir
1. Redbook, 2014; 2. Gordon, 2012; 3. McAdam-Marx, 2011; 4. Assumption validated by a national panel of hepatologists; 5. C

References

1.RedBook. Red Book Online. Micromedex 2.0; 2014.
2.Gordon SC, Hamzeh FM, Pockros PJ, Hoop RS, Buikema AR, Korner EJ, Terrault NA. Hepatitis C virus therapy is associated with lower health care costs not only in

noncirrhotic patients but also in patients with end-stage liver disease. Aliment Pharmacol Ther 2013a;38:784-793.
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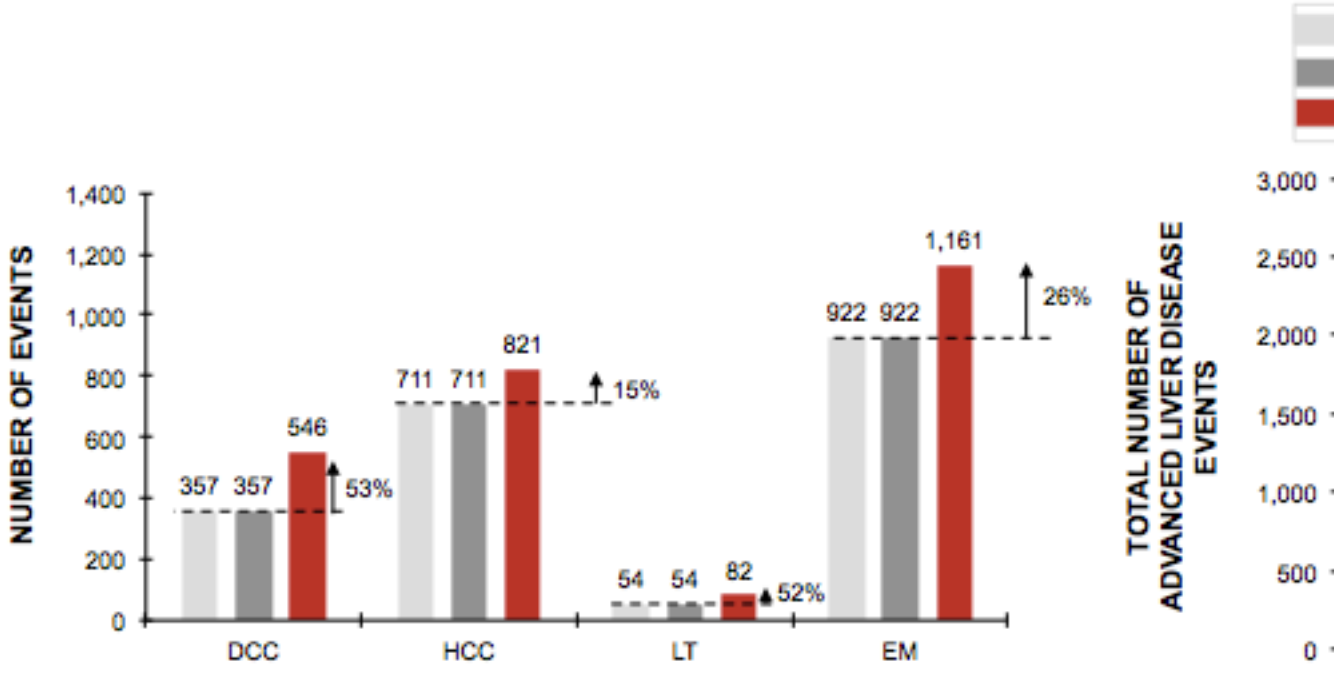
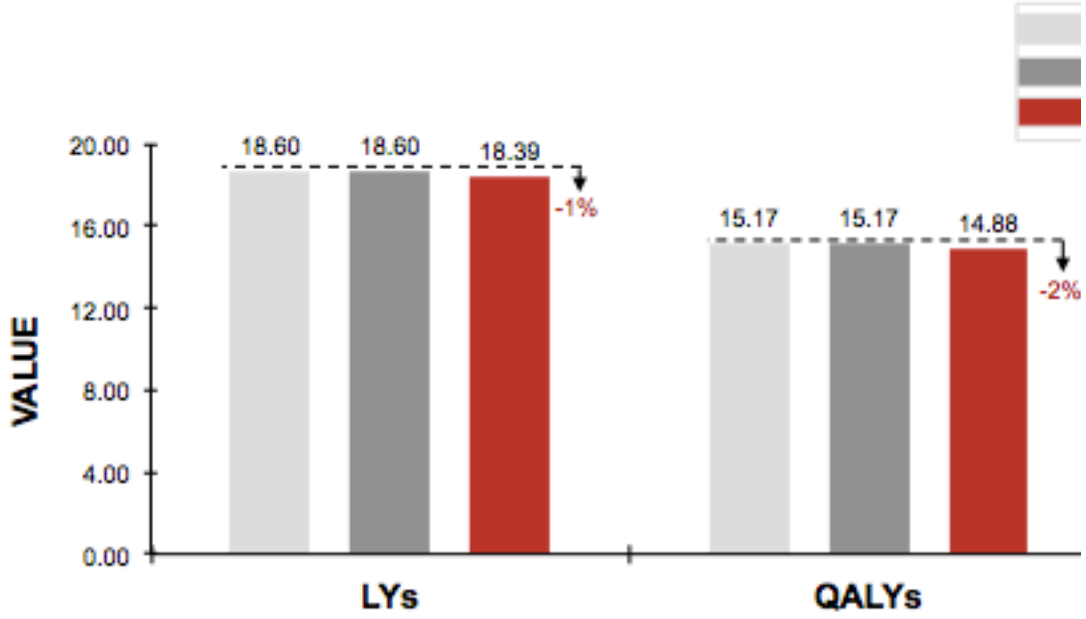
HEALTH OUTCOMES: ADVANCED LIVER DISEASE EVENTS



- LDV/SOF 24W and SOF+SMV 24W show equal efficacy in terms of life outcomes, with similar numbers of patients experiencing DCC, HCC, LT
- Utilizing LDV/SOF+RBV 12W results in an increase of all ESLD events increase in advanced liver disease events of 26% (ranging from a 14% vs. LT, respectively)

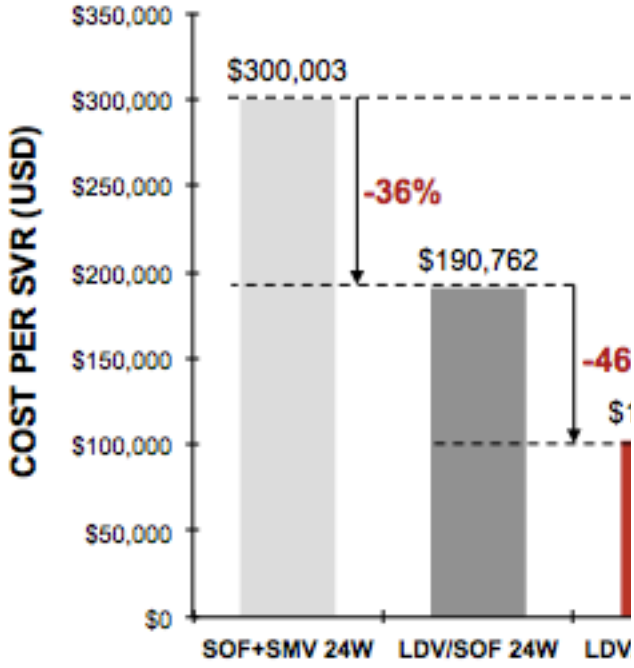
HEALTH OUTCOMES: LIFE YEARS AND QALYs



- Utilizing LDV/SOF+RBV 12W results in an decrease of in LYs by 1.1 QALYs by 1.9%
  - These decreases are driven by slightly lower efficacy and the a RBV, which results in a decrement in utility on treatment

COST PER SVR RESULTS

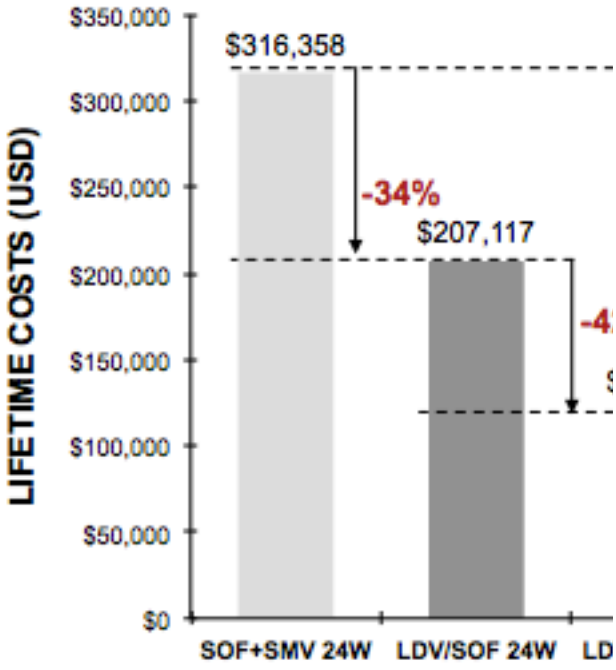
- Utilizing LDV/SOF+RBV 12W shows a significant decrease in costs compared to SOF+SMV 24W and LDV/SOF 24W due to its similar efficacy given at a substantially lower cost
- LDV/SOF+RBV shows a 66% decrease in cost per SVR versus SOF+SMV 24W and a 46% decrease in cost per SVR versus LDV/SOF 24W



LIFETIME COSTS

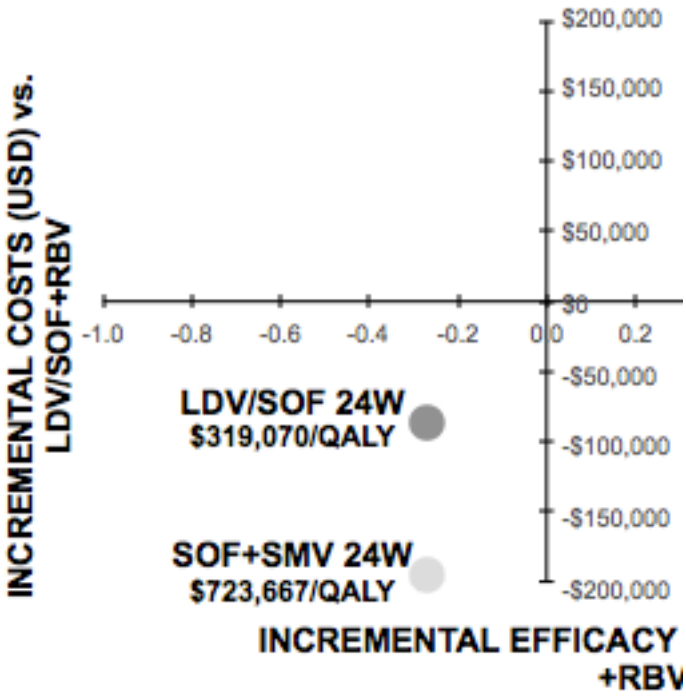
- Utilizing LDV/SOF+RBV 12W shows a significant decrease in lifetime costs compared to SOF+SMV 24W and LDV/SOF 24W due to its similar efficacy given at a substantially lower cost

- LDV/SOF+RBV shows a 62% decrease in lifetime costs versus SOF+SMV 24W and a 42% decrease in cost per SVR versus LDV/SOF 24W



ICERs

- LDV/SOF 24W and SOF +SMV 24W both result in more QALYs as well as higher cost as compared to LDV/ SOF+RBV 12W
- LDV/SOF 24W and SOF +SMV 24W have ICERs of $319,070/QALY and $723,667/QALY, respectively, vs. LDV/SOF+RBV 12W, well above the $50,000/QALY willingness-to-pay threshold in the USA
- Therefore, LDV/SOF 24W and SOF+SMV 24W are not cost-effective as compared to LDV/ SOF+RBV 12W



STUDY LIMITATIONS

LIMITATIONS

- In order to estimate the long-term (lifetime) impact from a clinical trial settir projected the course of liver disease for a cohort of patients based on estir natural disease progression data derived from the literature rather than clir however, these estimates apply equally to all therapies
- To estimate the efficacy and safety of the regimens within this model, data sourced across studies from the published clinical trials, due to a lack of re as well as no direct head-to-head comparisons for LDV/SOF to SOF+SMV
- As real-world data was not used for efficacy or safety inputs, model results reflective of outcomes observed in the real-world