SUPPLEMENTAL ON-LINE MATERIAL

Saab S, et al. Cost-effectiveness of currently recommended direct-acting antiviral treatments in patients infected with genotypes 1 or 4 hepatitis C virus in the US

Supplemental Figure A1. Cost-effectiveness acceptability curves for the analysis of GT1 treatment-naïve patients. Curves shown represent results from 500 Monte Carlo simulations in probabilistic sensitivity analysis of treatment options compared in the GT1 treatment-naïve patients. Each line (representing a different treatment option) shows the percentage of simulations where that option was the most cost-effective at each willingness-to-pay threshold. Note that only options that were estimated to be most cost-effective in at least one simulation appear in figure.

Supplemental Figure A2. Cost-effectiveness acceptability curves for the analysis of GT1 treatment-experienced patients. Curves shown represent results from Monte Carlo simulations in probabilistic sensitivity analysis of treatment options compared in the GT1 treatment-experienced patients. Each line (representing a different treatment option) shows the percentage of simulations where that option was the most cost-effective at each willingness-to-pay threshold. Note that only options that were estimated to be most cost-effective in at least one simulation appear in figure.

Supplemental Figure A3. Cost-effectiveness acceptability curves for the analysis of non-cirrhotic GT4 treatment-naïve patients. Curves shown represent results from Monte Carlo simulations in probabilistic sensitivity analysis of treatment options compared in the GT4 non-cirrhotic treatment-naïve patients. Each line (representing a different treatment option) shows the percentage of simulations where that option was the most cost-effective at each willingness-to-pay threshold. Note that only options that were estimated to be most cost-effective in at least one simulation appear in figure.

Supplemental Figure A4. Cost-effectiveness acceptability curves for the analysis of non-cirrhotic GT4 treatment-experienced patients. Curves shown represent results from Monte Carlo simulations in probabilistic sensitivity analysis of treatment options compared in the GT4 non-cirrhotic treatment-experienced patients. Each line (representing a different treatment option) shows the percentage of simulations where that option was the most cost-effective at each willingness-to-pay threshold. Note that only options that were estimated to be most cost-effective in at least one simulation appear in figure.

Supplemental Figure A5. Tornado diagram comparing 3D±R (Intervention) to SOF/LDV (Comparator) in GT1 treatment-naïve patients. The diagram shows the impact of individually varying parameters in the base case expressed in incremental net monetary benefit (INMB) assuming a payer willingness-to-pay of \$100,000. Positive INMB values indicate that 3D±R is cost-effective and negative INMB values indicate that SOF/LDV is cost-effective. The diagram shows the impact of the 20 most influential parameters. The tornado diagram is centered on the base case INMB value for the comparison of 3D±R to SOF/LDV in GT1 treatment-naïve patients, which is \$4,343.

Supplemental Figure A6. Tornado diagram comparing 3D±R (Intervention) to SOF/LDV (Comparator) in GT1 treatment-experienced patients. The diagram shows the impact of individually varying parameters in the base case expressed in incremental net monetary benefit (INMB) assuming a payer willingness-to-pay of \$100,000. Positive INMB values indicate that 3D±R is cost-effective and negative INMB values indicate that SOF/LDV is cost-effective. The diagram shows the impact of the 20 most influential parameters. The tornado diagram is centered on the base case INMB value for the comparison of 3D±R to SOF/LDV in GT1 treatment-experienced patients, which is \$23,287.

Supplemental Figure A7. Tornado diagram comparing 2D+R (Intervention) to SOF/LDV (Comparator) in non-cirrhotic GT4 treatment-naïve patients. The diagram shows the impact of individually varying parameters in the base case expressed in incremental net monetary benefit (INMB) assuming a payer willingness-to-pay of \$100,000. Positive INMB values indicate that 2D+R is cost-effective and negative INMB values indicate that SOF/LDV is cost-effective. The diagram shows the impact of the 20 most influential parameters. The tornado diagram is centered on the base case INMB value for the comparison of 2D+R to SOF/LDV in non-cirrhotic GT4 treatment-naïve patients, which is \$31,175.

Supplemental Figure A8. Tornado diagram comparing 2D+R (Intervention) to SOF/LDV (Comparator) in non-cirrhotic GT4 treatment-experienced patients. The diagram shows the impact of individually varying parameters in the base case expressed in incremental net monetary benefit (INMB) assuming a payer willingness-to-pay of \$100,000. Positive INMB values indicate that 2D+R is cost-effective and negative INMB values indicate that SOF/LDV is cost-effective. The diagram shows the impact of the 20 most influential parameters. The tornado diagram is centered on the base case INMB value for the comparison of 2D+R to SOF/LDV in non-cirrhotic GT4 treatment-experienced patients, which is \$64,070.

Supplemental Table A1. Patient characteristics, transition-state probabilities, costs, and health-utilities

Variable	Base Case Value	Sensitivity, Low	Sensitivity, High	PSA, Second Statistical Moment ^a	Distribution in PSA	Source
Patient Characteristics^b						
<i>Base case (Treatment-naïve GT1)</i>						
Age (years)	52.8	47.8	57.8	5	Gamma	AbbVie trials
Male	61.1%	56.1%	66.1%	713	Beta	AbbVie trials
Stage of fibrosis at model entry						
No fibrosis (F0)	26.7%	100%	0%	N=713	Dirichelt	AbbVie trials
Portal fibrosis (F1)	35.6%	0%	0%		Dirichelt	AbbVie trials
Periportal fibrosis (F2)	17.0%	0%	0%		Dirichelt	AbbVie trials
Bridging fibrosis (F3)	9.3%	0%	0%		Dirichelt	AbbVie trials
Compensated fibrosis (F4)	11.5%	0%	100%		Dirichelt	AbbVie trials
% of non-cirrhotic patients who have pre-treatment HCV RNA < 6 million IU/mL	26.0%	0.0%	71.0%	0.05	Beta	AbbVie trials
<i>Base case (Treatment-experienced GT1)</i>						
Age (years)	55.1	50.1	60.1	5	Gamma	AbbVie trials
Male	65.1%	60.1%	70.1%	381	Beta	AbbVie trials
Stage of fibrosis at model entry						
No fibrosis (F0)	20.0%	100%	0%	N=381	Dirichelt	AbbVie trials
Portal fibrosis (F1)	26.6%	0%	0%		Dirichelt	AbbVie trials
Periportal fibrosis (F2)	13.1%	0%	0%		Dirichelt	AbbVie trials
Bridging fibrosis (F3)	9.9%	0%	0%		Dirichelt	AbbVie trials
Compensated fibrosis (F4)	30.5%	0%	100%		Dirichelt	AbbVie trials
<i>Base case (Treatment-naïve GT4 non-cirrhotic)</i>						
Age (years)	52.8	47.8	57.8	5	Gamma	AbbVie trials
Male	61.1%	56.1%	66.1%	713	Beta	AbbVie trials
Stage of fibrosis at model entry						
No fibrosis (F0)	30.2%	100%	0%	N=713	Dirichelt	AbbVie trials
Portal fibrosis (F1)	40.2%	0%	0%		Dirichelt	AbbVie trials
Periportal fibrosis (F2)	19.2%	0%	0%		Dirichelt	AbbVie trials

Bridging fibrosis (F3)	10.5%	0%	100%		Dirichelt	AbbVie trials
Compensated fibrosis (F4)	0.0%	0%	0%	NA	NA	
<i>Subgroup (Treatment-experienced GT4 non-cirrhotic)</i>						
Age (years)	55.1	50.1	60.1	5	Gamma	AbbVie trials
Male	65.1%	60.1%	70.1%	381	Beta	AbbVie trials
Stage of fibrosis at model entry						
No fibrosis (F0)	28.7%	100%	0%	N=381	Dirichelt	AbbVie trials
Portal fibrosis (F1)	38.3%	0%	0%		Dirichelt	AbbVie trials
Periportal fibrosis (F2)	18.8%	0%	0%		Dirichelt	AbbVie trials
Bridging fibrosis (F3)	14.2%	0%	100%		Dirichelt	AbbVie trials
Compensated fibrosis (F4)	0.0%	0%	0%	NA	NA	
Transition State Probabilities						
<i>Fibrosis progression</i>						
Males						
<40	0.050	0.030	0.090	0.015	Beta	Assumed equal 40-49
40-49	0.050	0.030	0.090	0.015	Beta	Liu 2012 ¹
50-59	0.120	0.070	0.140	0.018	Beta	Liu 2012 ¹
60-69	0.200	0.120	0.300	0.045	Beta	Liu 2012 ¹
70-79	0.260	0.140	0.380	0.060	Beta	Liu 2012 ¹
>=80	0.371	0.140	0.475	0.084	Beta	Interpolated from 70-79
Females						
<40	0.030	0.010	0.060	0.013	Beta	Assumed equal 40-49
40-49	0.030	0.010	0.060	0.013	Beta	Liu 2012 ¹
50-59	0.060	0.030	0.110	0.020	Beta	Liu 2012 ¹
60-69	0.110	0.040	0.210	0.043	Beta	Liu 2012 ¹
70-79	0.140	0.080	0.240	0.040	Beta	Liu 2012 ¹
>=80	0.200	0.080	0.300	0.055	Beta	Liu 2012 ¹
<i>Non-fibrosis progression</i>						
Recovered (SVR), no HCV, history of severe fibrosis (CC) to HCC	0.012	0.003	0.022	0.005	Beta	Cardoso 2010 ²
CC to DCC	0.040	0.030	0.050	0.005	Beta	Liu 2012 ¹
CC to HCC (first year)	0.020	0.017	0.030	0.003	Beta	Liu 2012 ¹
DCC to HCC (first year)	0.020	0.017	0.030	0.003	Beta	Liu 2012 ¹
LT						

DCC to LT (first year)	0.050	0.000	0.400	0.100	Beta	Liu 2012 ¹
HCC to LT (first year)	0.150	0.050	0.400	0.088	Beta	Liu 2012 ¹
Liver-related mortality						
DCC to liver death	0.260	0.120	0.330	0.053	Beta	Liu 2012 ¹
HCC first year to liver death	0.720	0.580	0.800	0.055	Beta	Liu 2012 ¹
HCC subsequent year to liver death	0.250	0.160	0.300	0.035	Beta	Liu 2012 ¹
LT to liver death	0.140	0.134	0.150	0.004	Beta	Liu 2012 ¹
After LT to liver death	0.050	0.049	0.051	0.000	Beta	Liu 2012 ¹
Viral reinfection	0.010	0.000	0.020	NA	NA	Assumed
Spontaneous remission from F0	0.012	0.007	0.017	0.003	Beta	Liu 2012 ¹
Treatment SVR^c						
<i>Overall GT1</i>						
3D±R	97.0%	94.7%	99.1%	See note ^c	Beta	SAPPHIRE I ³ and II ⁴ ; PEARL II ⁵ , III ⁶ and IV ⁶ ; and TURQUOISE II ⁷
SOF/LDV	96.0%	91.0%	99.7%	See note ^c	Beta	ION-1 ⁸ , ION-2 ⁹ , ION-3 ¹⁰
<i>Treatment-naïve GT1</i>						
3D±R	97.0%	95.4%	98.6%	See note ^c	Beta	SAPPHIRE I ³ ; PEARL III ⁶ and IV ⁶ ; and TURQUOISE II ⁷
SOF/LDV	96.4%	92.1%	99.6%	See note ^c	Beta	ION-1 ⁸ and ION-3 ¹⁰
<i>Treatment-experienced GT1</i>						
3D±R	97.1%	93.8%	100.0%	See note ^c	Beta	SAPPHIRE II ⁴ ; PEARL II ⁵ ; and TURQUOISE II ⁷
SOF/LDV	96.1%	90.9%	100.0%	See note ^c	Beta	ION-2 ⁹
<i>Overall GT4 non-cirrhotic</i>						
2D+R	100.0%	100.0%	100.0%	See note ^c	Beta	PEARL I ^{7,11}
SOF/LDV	91.5%	78.8%	100.0%	See note ^c	Beta	Abergel et al. ¹²
<i>Treatment-naïve GT4 non-cirrhotic</i>						
2D+R	100.0%	100.0%	100.0%	See note ^c	Beta	PEARL I ¹¹
SOF/LDV	95.2%	86.1%	100.0%	See note ^c	Beta	Abergel et al. ¹²
<i>GT4 non-cirrhotic treatment-experienced</i>						
2D+R	100.0%	100.0%	100.0%	See note ^c	Beta	PEARL I ¹¹
SOF/LDV	84.6%	65.0%	100.0%	See note ^c	Beta	Abergel et al. ¹²

Costs						
<i>Direct medical annual costs by health state</i>						
No fibrosis (F0)	\$165	\$165	\$3,842	\$165	Gamma	Younossi 2014 ¹³
Portal fibrosis (F1)	\$165	\$165	\$3,842	\$165	Gamma	Younossi 2014 ¹³
Periportal fibrosis (F2)	\$165	\$165	\$3,842	\$165	Gamma	Younossi 2014 ¹³
Bridging fibrosis (F3)	\$165	\$165	\$3,842	\$165	Gamma	Younossi 2014 ¹³
Compensated fibrosis (F4)	\$760	\$315	\$2,665	\$760	Gamma	Younossi 2014 ¹³
No HCV	\$0	\$0	\$165	NA	NA	Assumed
Recovered (SVR), no HCV, history of mild fibrosis	\$83	\$0	\$165	\$83	Gamma	Younossi 2014 ¹³
Recovered (SVR), no HCV, history of moderate fibrosis	\$83	\$0	\$165	\$83	Gamma	Younossi 2014 ¹³
Recovered, no HCV, history of severe fibrosis (CC)	\$381	\$0	\$760	\$381	Gamma	Younossi 2014 ¹³
DCC	\$33,314	\$31,005	\$35,622	\$1,154	Normal	McAdam-Marx 2011 ¹⁴
HCC (first year)	\$52,248	\$46,055	\$58,440	\$3,096	Normal	McAdam-Marx 2011 ¹⁴
HCC (subsequent years)	\$52,248	\$46,055	\$58,440	\$3,096	Normal	McAdam-Marx 2011 ¹⁴
LT (first year)	\$201,765	\$183,850	\$219,680	\$8,958	Normal	McAdam-Marx 2011 ¹⁴
LT (subsequent years)	\$45,481	\$36,394	\$54,567	\$4,543	Normal	McAdam-Marx 2011 ¹⁴
<i>Treatment-related adverse events</i>						
Anemia	\$1,259	\$0	\$5,609	\$1,259	Gamma	Gao 2012 ¹⁵
Rash	\$328	\$0	\$459	\$328	Gamma	Gao 2012 ¹⁵
Depression	\$849	\$0	\$849	\$849	Gamma	Gao 2012 ¹⁵
Neutropenia	\$523	\$0	\$785	\$523	Gamma	Brogan 2014 ¹⁶
Thrombocytopenia	\$3,616	\$0	\$3,616	\$3,616	Gamma	Poordad 2011 ¹⁷
Health utilities^d						
No fibrosis (F0)	0.980	0.700	1.000	NA	Beta	Liu 2012 ¹
Portal fibrosis (F1)	0.980	0.700	1.000	NA	Beta	Liu 2012 ¹
Periportal fibrosis (F2)	0.850	0.660	1.000	NA	Beta	Liu 2012 ¹
Bridging fibrosis (F3)	0.850	0.660	1.000	NA	Beta	Liu 2012 ¹
Compensated fibrosis (F4)	0.790	0.460	1.000	NA	Beta	Liu 2012 ¹
No HCV	1.000	0.740	1.000	NA	Beta	Assumed
Recovered (SVR), no HCV, history of	1.000	0.740	1.000	NA	Beta	Liu 2012 ¹

mild fibrosis						
Recovered (SVR), no HCV, history of moderate fibrosis	0.933	0.710	1.000	NA	Beta	Liu 2012 ¹
Recovered (SVR), no HCV, history of severe fibrosis (CC)	0.933	0.600	1.000	NA	Beta	Liu 2012 ¹
DCC	0.720	0.257	0.913	NA	Beta	Liu 2012 ¹
HCC (first year)	0.720	0.150	0.950	NA	Beta	Liu 2012 ¹
HCC (subsequent years)	0.720	0.150	0.950	NA	Beta	Liu 2012 ¹
LT (first year)	0.825	0.636	1.000	NA	Beta	Liu 2012 ¹
LT (second year)	0.825	0.636	1.000		Beta	Liu 2012 ¹
Discount rate						
Costs	3.0%	0.0%	7.0%	NA	NA	Gold 1996 ¹⁸ ; Weinstein 1996 ¹⁹
Health-Utilities	3.0%	0.0%	7.0%	NA	NA	Gold 1996 ¹⁸ ; Weinstein 1996 ¹⁹
Time horizon (in years)	70	10	70	NA	NA	Assumed

Footnotes

- ^a Second statistical moment is standard error where available. If standard error was not available, standard deviation was used. If neither were available for a beta distribution, the N was used and a binomial distribution was assumed.
- ^b The patients baseline characteristic parameter inputs are only presented for treatment-naïve and treatment experienced. The overall GT1 and GT4 values are the weighted average from the share of treatment-naïve and -experienced patients in the AbbVie trials (i.e., 65.2% of treatment-naïve patients).
- ^c The table presents weighted average SVR rates for the base case, the low, and the high values. These SVR rates are weighted using the fibrosis distribution and the share of treatment-naïve and -experienced patients for overall GT1 and GT4 non-cirrhotic, where applicable. The second moments are calculated using the sample size and the SVR rate for each patient segment by fibrosis severity: mild [F0-F1], moderate [F2-F3], and severe [F4].
- ^d The health-utilities values for the probabilistic sensitivity analyses are calculated using the alpha and beta parameters provided in Liu 2012¹.

References for Supplemental Material

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