Ombitasvir/paritaprevir/ritonavir with or without dasabuvir for treating chronic hepatitis C

Addendum to ERG commentary on company additional analyses

Produced by	Southampton Health Technology Assessments Centre (SHTAC)
Correspondence to	Jeremy Jones Principal Research Fellow Southampton Health Technology Assessments Centre (SHTAC) University of Southampton First Floor, Epsilon House Enterprise Road, Southampton Science Park Southampton SO16 7NS

Date completed 17th June 2015

Table of Contents

4. Subgroup analyses to explore the effect on the incremental cost-effectiveness ratios (ICERs) of the treatment duration of 3D plus ribavirin for people with genotype 1a CHC with compensated cirrhosis 3

Table of tables

Table 1 SVRs for 3D plus ribavirin used in the base case and in sub-group analyses..... 3
Table 2 Cost effectiveness of anti-viral therapy for people with treatment-naive genotype 1a CHC with compensated cirrhosis 6
Table 3 Cost effectiveness of anti-viral therapy for treatment-experienced people with genotype 1a CHC with compensated cirrhosis, who have relapsed after achieving SVR with previous therapy 7
Table 4 Cost effectiveness of anti-viral therapy for treatment-experienced people with genotype 1a CHC patients with compensated cirrhosis, who have achieved a partial response to previous therapy 8
Table 5 Cost effectiveness of anti-viral therapy for treatment-experienced people with genotype 1a CHC with compensated cirrhosis, who were null responders to previous therapy 9
Table 6 Cost effectiveness of anti-viral therapy for treatment-experienced people (overall) with genotype 1a CHC with compensated cirrhosis..... 10

4. Subgroup analyses to explore the effect on the incremental cost-effectiveness ratios (ICERs) of the treatment duration of 3D plus ribavirin for people with genotype 1a CHC with compensated cirrhosis

The company response reports sub-group analyses for treatment-naïve and treatment-experienced GT1a HCV patients (and for GT1 overall) showing the effect of varying duration of treatment with 3D plus ribavirin. The company response only reports analyses for the overall group of treatment-experienced patients, and not for the separate sub-groups (prior relapse, partial response and null response). The NICE request for additional analysis is not explicit regarding the presentation of these results, although the specification of each population as separate items in the request (labelled 4a to 4d) might indicate these sub-groups should also be presented separately. The ERG re-ran the sub-group analyses, to confirm the results reported in the company response - results for each sub-group of treatment-experienced patients are presented in this document (see Table 3 to Table 5).

The company provides very limited detail on the methods adopted for the analysis and a very brief summary of the results. The SVRs used to model costs and outcomes with 12 weeks of 3D plus ribavirin are not reported in the response document. The ERG extracted the SVRs from the electronic model submitted as part of the company response and these are reported in Table 1.

Table 1 SVRs for 3D plus ribavirin used in the base case and in sub-group analyses

Patient population	Treatment duration (weeks)	SVR
Genotype 1a, treatment-naive, with compensated cirrhosis	24	94.6% (53/56)
	12	92.2% (59/64)
Genotype 1a, patients who relapsed following response to previous anti-viral treatment, with compensated cirrhosis	24	100.0% (13/13)
	12	93.3% (14/15)
Genotype 1a, partial responders to previous anti-viral treatment, with compensated cirrhosis	24	100.0% (10/10)
	12	100.0% (11/11)
Genotype 1a, null responders to previous anti-viral treatment, with compensated cirrhosis	24	92.9% (39/42)
	12	80.0% (40/50)

Source: Table 2 Poordad F et al. ABT-450/r-Ombitasvir and Dasabuvir with Ribavirin for Hepatitis C with Cirrhosis. New England Journal of Medicine 2014:370(21):1973-1982.

Cost effectiveness results for the sub-group analyses are presented in a series of tables in the company response (Tables 73 to 84), which include columns reporting ICERs for each treatment relative to peginterferon and ribavirin (labelled “ICER vs baseline”) and the difference in the ICER for 3D plus ribavirin compared with the base case analysis (Tables 1 to 18 in the response document). This presentation is not fully incremental, since it does not account for exclusion of some comparators due to dominance/ extended dominance.

This commentary includes tables reporting fully incremental base case analyses (24 weeks of 3D plus ribavirin for patients with compensated cirrhosis) and cost effectiveness estimates for 12 weeks of 3D plus ribavirin in the same patient population. The tables also include a plot of the cost effectiveness results for the base case (in black text, also indicating the non-dominated/ non-extendedly dominated interventions included in the fully incremental analysis) and for the shorter duration of treatment (in red, also indicating the non-dominated/ non-extendedly dominated comparator(s) used in calculating the fully incremental ICER for 12 weeks of 3D plus ribavirin).

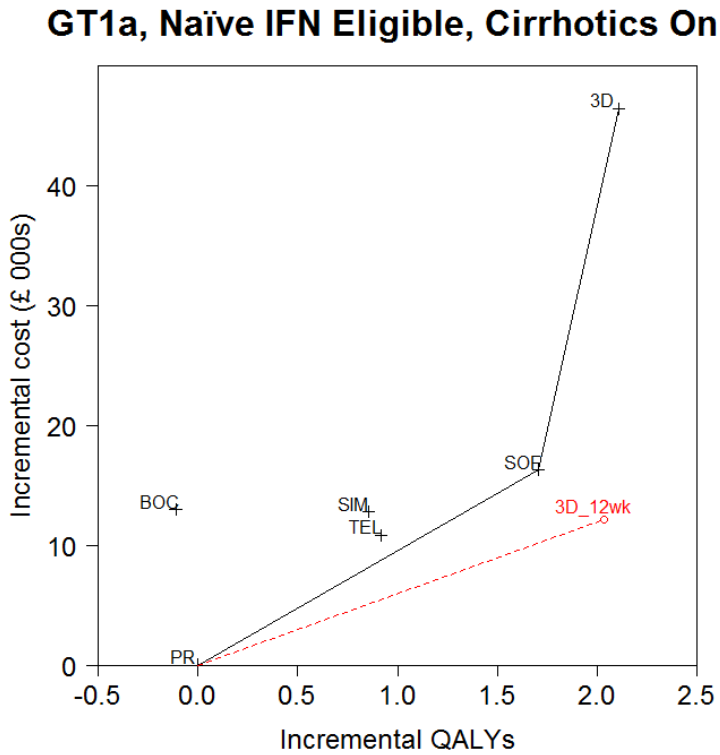
Table 2 presents results for people with treatment-naive genotype 1a CHC with compensated cirrhosis. In the base case, the ICER for 24 weeks of 3D plus ribavirin is £75,360 (incremental to Sofosbuvir+PegIFN+RBV). In the sub-group analysis, where treatment duration is reduced to 12 weeks, but with a relatively small decrease in SVR, all comparators (other than peginterferon and ribavirin) are excluded by dominance/ extended dominance and the ICER for 3D plus ribavirin reduces substantially, to £5,985.

Table 3 to Table 5 present results for sub-groups of treatment-experienced people with genotype 1a CHC patients with compensated cirrhosis. Note that there is no row for 12 weeks of 3D plus ribavirin for the group of null responders to previous treatment as their treatment duration remains at 24 weeks, as indicated in the NICE specification of additional analyses. The impact of shorter duration of treatment with 3D plus ribavirin for treatment experienced patients who might be offered this option is similar to that for treatment-naïve patients (more favourable ICERs associated with shorter treatment duration [reducing from £51,305 to £8,529 for prior relapsers and from £24,431 to £4,583 for partial responders], due to a sizable reduction in treatment cost, but comparatively small reduction in SVR). It should be noted that these sub-group analyses are based on very small numbers of patients (between 10 and 15 patients studied for the sub-groups of prior relapsers and partial responders).

Table 6 presents cost effectiveness results for treatment-experienced people (overall) which, again, suggests a more favourable ICER for shorter duration of treatment (reducing from £26,516 to £9,301)

Table 2 Cost effectiveness of anti-viral therapy for people with treatment-naive genotype 1a CHC with compensated cirrhosis

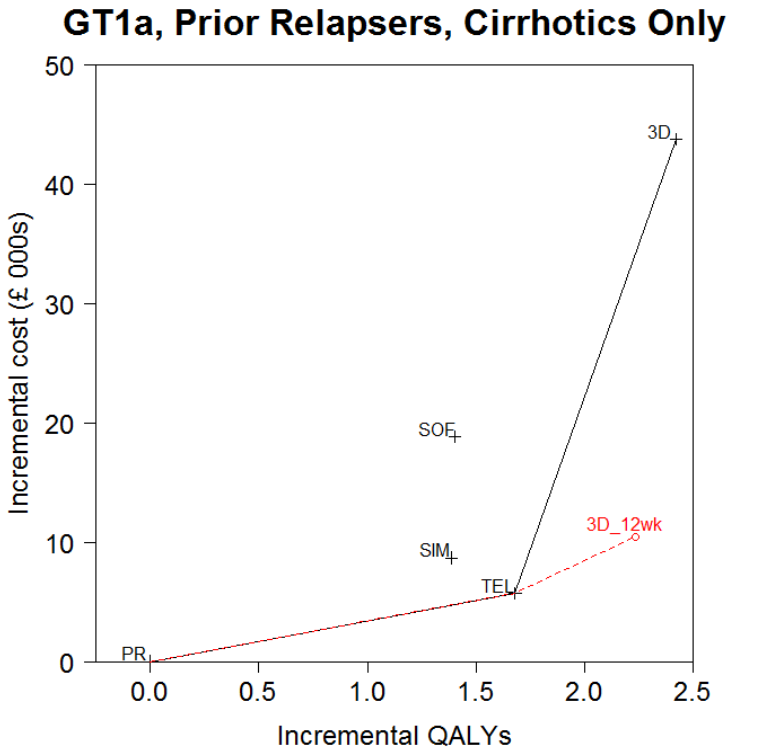
Genotype 1a, treatment-naive, interferon-eligible, with compensated cirrhosis					
	Total		Incremental		ICER (£ per QALY gained)
	Cost (£)	QALY	Cost (£)	QALY	
Boceprevir+ PegIFN+RBV	58,024	7.97	12,967	-0.11	Dominated
PegIFN+RBV	45,057	8.08	NA		
Simeprevir+ PegIFN+RBV	57,832	8.94	12,775	0.85	Extended dominance
Telaprevir+ PegIFN+RBV	55,907	9.00	10,850	0.92	
Sofosbuvir+ PegIFN+RBV	61,347	9.79	16,290	1.70	9,555
3D+RBV (24 weeks)	91,507	10.19	46,450 (30,161)	2.11 (0.40)	75,360
3D+RBV (12 weeks)	57,225	10.12	12,169	2.03	5,985 [a]



Notes: incremental costs/ QALYs in parentheses are calculated against non-dominated/ non-extendedly dominated alternative
[a] incremental costs, QALYs and ICER calculated by comparison with PegIFN+RBV

Table 3 Cost effectiveness of anti-viral therapy for treatment-experienced people with genotype 1a CHC with compensated cirrhosis, who have relapsed after achieving SVR with previous therapy

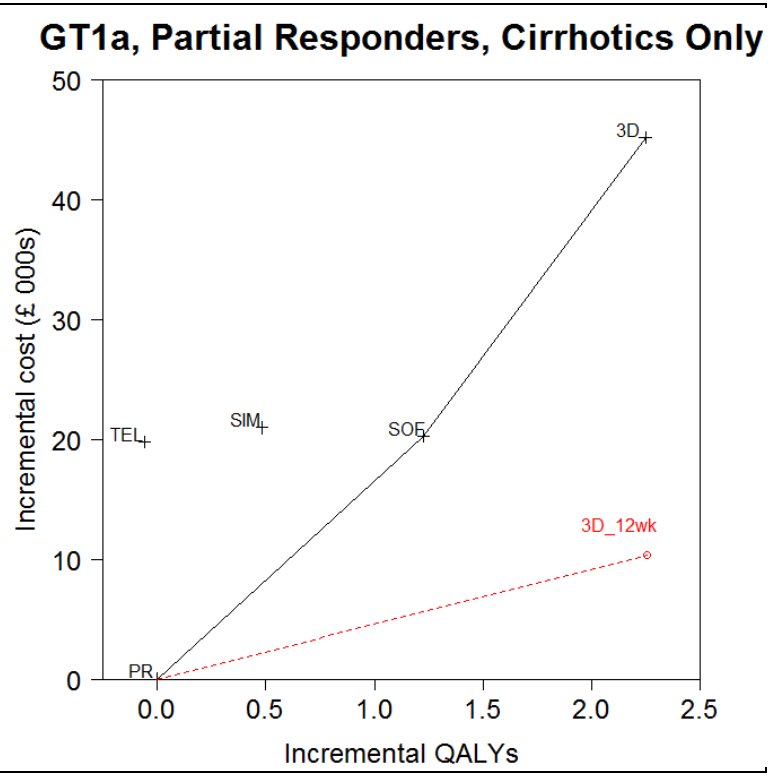
Genotype 1a, treatment-experienced (prior relapsers), interferon-eligible, with compensated cirrhosis					
	Total		Incremental		ICER (£ per QALY gained)
	Cost (£)	QALY	Cost (£)	QALY	
PegIFN+RBV	45,349	7.47	NA		
Simeprevir+ PegIFN+RBV	54,038	8.86	8,689	1.39	Extended dominance
Sofosbuvir+ PegIFN+RBV	64,197	8.87	18,848	1.40	
Telaprevir+ PegIFN+RBV	51,060	9.15	5,711	1.68	3,400
3D+RBV (24 weeks)	89,113	9.89	43,764 (38,053)	2.42 (0.74)	51,305
3D+RBV (12 weeks)	55,801	9.70	10,452 (4,741)	2.24 (0.56)	8,529 [a]



Notes: incremental costs/ QALYs in parentheses are calculated against non-dominated/ non-extendedly dominated alternative
[a] incremental costs, QALYs and ICER calculated by comparison with Telaprevir+PegIFN+RBV

Table 4 Cost effectiveness of anti-viral therapy for treatment-experienced people with genotype 1a CHC patients with compensated cirrhosis, who have achieved a partial response to previous therapy

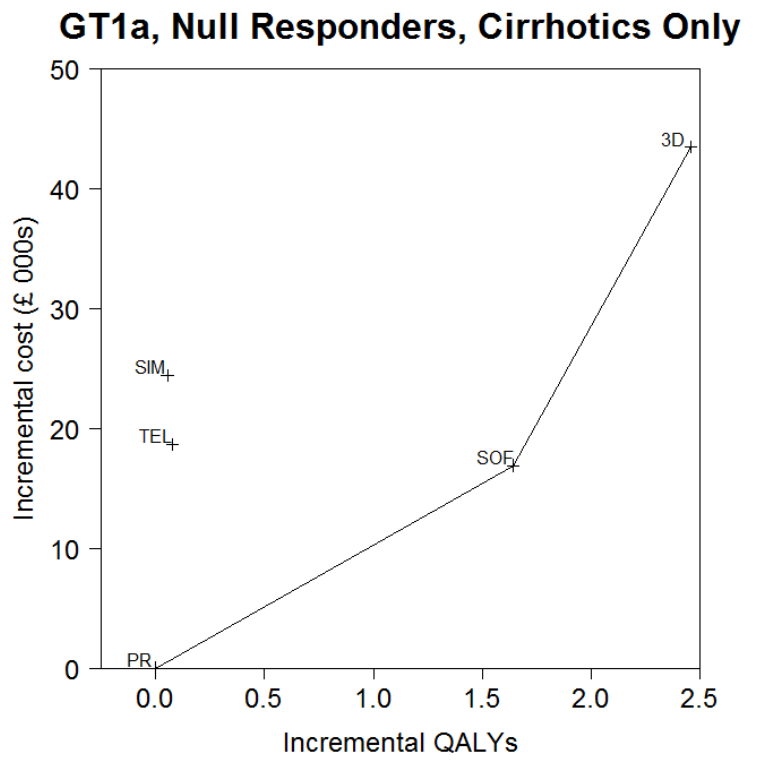
Genotype 1a, treatment-experienced (partial responders), interferon-eligible, with compensated cirrhosis					
	Total		Incremental		ICER (£ per QALY gained)
	Cost (£)	QALY	Cost (£)	QALY	
Telaprevir+ PegIFN+RBV	63,721	7.58	19,787	-0.06	Dominated
PegIFN+RBV	43,934	7.64	NA		
Simeprevir+ PegIFN+RBV	64,918	8.13	20,984	0.48	Extended dominance
Sofosbuvir+ PegIFN+RBV	64,197	8.87	20,263	1.23	16,520
3D+RBV (24 weeks)	89,113	9.89	45,179 (24,916)	2.25 (1.02)	24,431
3D+RBV (12 weeks)	54,254	9.90	10,320	2.25	4,583 [a]



Notes: incremental costs/ QALYs in parentheses are calculated against non-dominated/ non-extendedly dominated alternative
[a] incremental costs, QALYs and ICER calculated by comparison with PegIFN+RBV

Table 5 Cost effectiveness of anti-viral therapy for treatment-experienced people with genotype 1a CHC with compensated cirrhosis, who were null responders to previous therapy

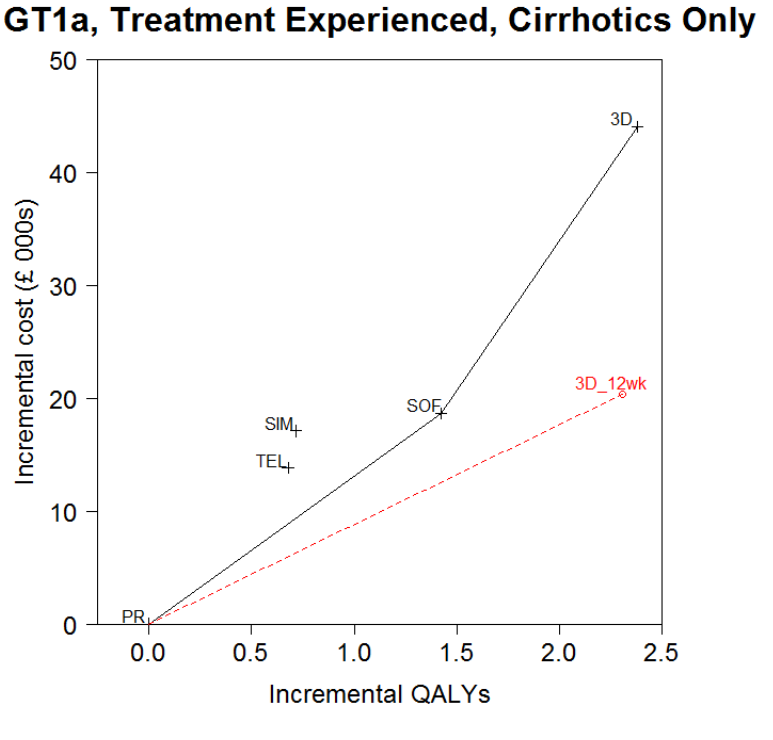
Genotype 1a, treatment-experienced (null responders), interferon-eligible, with compensated cirrhosis					
	Total		Incremental		ICER (£ per QALY gained)
	Cost (£)	QALY	Cost (£)	QALY	
PegIFN+RBV	47,283	7.23	NA		
Simeprevir+ PegIFN+RBV	71,743	7.28	24,460	0.05	Extended dominance
Telaprevir+ PegIFN+RBV	65,959	7.31	18,675	0.08	
Sofosbuvir+ PegIFN+RBV	64,197	8.87	16,913	1.64	10,311
3D+RBV (24 weeks)	90,771	9.69	43,488 (26,574)	2.46 (0.82)	32,604 [a]



Notes: incremental costs/ QALYs in parentheses are calculated against non-dominated/ non-extendedly dominated alternative
[a] incremental costs, QALYs and ICER calculated by comparison with Sofosbuvir+PegIFN+RBV

Table 6 Cost effectiveness of anti-viral therapy for treatment-experienced people (overall) with genotype 1a CHC with compensated cirrhosis

Genotype 1a, treatment-experienced (overall), interferon-eligible, with compensated cirrhosis					
	Total		Incremental		ICER (£ per QALY gained)
	Cost (£)	QALY	Cost (£)	QALY	
PegIFN+RBV	45,505	7.45	NA		
Telaprevir+ PegIFN+RBV	59,328	8.13	13,823	0.68	Extended dominance
Simeprevir+ PegIFN+RBV	62,614	8.17	17,109	0.72	
Sofosbuvir+ PegIFN+RBV	64,197	8.87	18,692	1.42	13,157
3D+RBV (24 weeks)	89,610	9.83	44,105 (25,414)	2.38 (0.96)	26,516
3D+RBV (12 weeks)	65,828	9.76	20,323	2.31	8,812 [a]



Notes: incremental costs/ QALYs in parentheses are calculated against non-dominated/ non-extendedly dominated alternative
[a] incremental costs, QALYs and ICER calculated by comparison with PegIFN+RBV