AbbVie's response to the specification for further work following the Appraisal Committee meeting on 1 April 2015 for ombitasvir/paritaprevir/ritonavir with or without dasabvuvir for treating chronic hepatitis C [ID731]

Following a teleconference on the 8th of April 2015, NICE has made a request of AbbVie to conduct further analyses for ombitasvir/paritaprevir/ritonavir with or without dasabuvir for treating adults with genotypes 1a, 1b and 4 to be made available for the next Appraisal Committee meeting on the 6th of May 2015. AbbVie welcomes the opportunity to re-engage NICE and is pleased to be able to provide results for the additional work requested by the NICE technical team (see below in this document). We also appreciate the opportunity to discuss these results during the Committee Meeting on the 6th of May. In addition to this report, we submit a revised, fully executable version of the excel model. In summary, all the new analyses requested by NICE have been included on separate sheets within the model to ease the navigation and review (please see purple tabs in the model):

- Sheet "Basecase - Incremental Analysis": This sheet details the base case results in a similar fashion as before (i.e., incremental analysis). The only difference is that we now display the results for a) Any Fibrosis Stage, b) Non-Cirrhotics Only, and c) Cirrhotics only. In addition, we now include the additional requested comparators (e.g., SOF+PR in treatment-experienced, SMV+PR in null and partial responders).

- Sheet "SA - AbbVie UK Crosswalk": This sheet details the results of our old scenario 20 on the trial-based utilities but with the format of the base case tables (i.e, incremental analysis – dominance/extended dominance) and with the new data included (see 1st bullet).

- Sheet "SA - Pooled Increment on SVR": This sheet details the results of the newly requested utility scenario using the base case utilities, except for the recovered health states where we apply a pooled increment of +[redacted] (see cells O157-O167 on the InputsOutputs sheet for the health utilities under this scenario). Similar to above, the results are displayed with the format of the base case tables (i.e, incremental analysis – dominance/extended dominance) and with the new data (see 1st bullet).

- Sheet "SA - AbbVie Duration in GT1a CC": This sheet details the results of the newly requested scenario where only GT1a compensated cirrhotic patients Null Responders are to be treated with 24 weeks (see cells F65 and L64-L66 on the InputsOutputs sheet for the parameters that allow a change of the duration between 12 and 24 weeks in GT1a compensated cirrhotic patients). The format of these tables is in the original format of our scenario analyses (no mention of dominance/extended dominance but we compare the pairwise ICERs vs. PR against the ICERs in the base case and report the difference).

- A new sheet has also been added ("SA - SVR from Janssen MTC") which details the results of a scenario where we use alternative SVR data for telaprevir + pegIFN-RBV, boceprevir+pegIFN-RBV and simeprevir+pegIFN-RBV coming from the ERG's adaptation of Janssen's MTC.

Further analyses requested by NICE technical team:

1) *Provide revised incremental cost-effectiveness analyses for the different regimens of ombitasvir/paritaprevir/ritonavir with or without dasabuvir (3D or 2D) presented separately for people with and without cirrhosis, and by treatment history. The analyses should incorporate the following:*
   - *The patient populations, treatment regimens and treatment durations specified in the summary of product characteristics table 1.*
   - *Comparison with all NICE recommended comparators (including simeprevir in combination with peginterferon plus ribavirin) using appropriate treatment durations based on the respective summaries of product characteristics specifications.*

As already highlighted in our submission, no trials were conducted with sofosbuvir + PR in treatment-experienced, genotype 1 patients. Therefore our original submission did not include sofosbuvir + PR as the comparator for 3D in treatment-experienced patients. However, given this regimen has recently been recommended by NICE for this group of patients, and in response to the request from NICE above, AbbVie developed a way to model it. Below we outline a bullet pointed summary of assumptions we have had to make to allow this regimen to be modelled for the GT1 treatment-experienced patients as well as GT4 treatment-naïve patients with cirrhosis.

At the time of our submission, AbbVie would have also liked to include simeprevir + PegIFN + RBV as a comparator for GT1 patients, given that the preliminary recommendations from NICE recommended simeprevir + PegIFN + RBV for HCV GT1. However, the license for simeprevir states that GT1a HCV patients with Q80K positive polymorphism should consider alternative therapy. Having analysed the manufacturer's submission (MS) and the ERG report for simeprevir, AbbVie could only find data stratified by fibrosis status for the ITT population (Table 17, page 51 of MS), and not for patients who are Q80K negative. AbbVie's economic model requires that data are stratified by fibrosis status. This is because it is well documented that fibrosis status, especially cirrhosis, effects the probability of achieving an SVR for the PegIFN containing regimens, and therefore an overall SVR estimate may over- or underestimate a regimen depending on the percentage of cirrhotic patients included at baseline – particularly in analyses where there has been no adjustment for the presence of cirrhosis or other known prognostic factors affecting response.

However, given NICE requested the inclusion of simeprevir + pegIFN + RBV as a comparator for GT1 patient populations, simeprevir has been incorporated into AbbVie's economic model treatment library based on data for the GT1 ITT patient population, as this was deemed to be the most appropriate available data. In a summary, pooled ITT data from QUEST-1 and QUEST-2 trials were used as the basis for the clinical effectiveness presented for GT1, GT1a and GT1b treatment-naïve patients (all fibrosis stages). It must be noted that the manufacturer of simeprevir used different definitions of mild and moderate fibrosis to AbbVie, namely, mild fibrosis was defined as no or minimal and portal fibrosis (F0-F2), whereas moderate fibrosis corresponds to the bridging fibrosis group only (F3). QUEST-1 and QUEST-2 trials did not report patients with Metavir F2 score in a way that permitted consolidation of this group within the moderate health state (consistent with AbbVie's model structure). Therefore, we use simeprevir's SVR rates for mild and moderate patients as defined by Janssen. Alongside the inclusion of the ITT population, this is a further the limitation of the analysis.

A detailed description of the data and all the sources used to model GT1 treatment-experienced patients and GT4 naïve and experienced patients respectively is available within the cost-effectiveness model (please see SMV + PR Inputs tab).

As mentioned in the introduction, AbbVie also conducted a scenario analysis using alternative SVR rates for simeprevir + pegIFN + RBV, telaprevir + pegIFN + RBV and boceprevir + pegIFN + RBV in GT1, treatment-naïve patients based on the mixed treatment comparison (MTC) reported in the CS for simeprevir and further exploratory work undertaken by the ERG using the output of this MTC to derive adjusted estimates of relative effectiveness for the said regimens (see table 35 of the ERG report for ombitasvir/paritaprevir/ritonavir with or without dasabuvir for treating chronic hepatitis C). The ERG has estimated fibrosis-stage specific SVRs for simeprevir + PegIFN + RBV, telaprevir + PegIFN + RBV and boceprevir + pegIFN + RBV using the stratified PegIFN + RBV SVRs from the ADVANCE trial (as reported in the AbbVie's model) and the odds ratio for each regimen relative to PegIFN+RBV (reported in Table 85 of simeprevir MS). Given that the SVRs were reported only for GT1 patients overall, rather than for subgenotypes (GT1a and GT1b), AbbVie limited this scenario analysis to GT1 patients only – all fibrosis stages, non-cirrhotic and cirrhotic patients.

However, as explained within AbbVie's original submission and response to the clarification questions (and acknowledged by the ERG), the results of this exploratory MTC should be regarded with caution because: 1) they are based on limited trial evidence, 2) the SVRs generated through this analyses have used odds ratios derived using the overall SVR rates reported for the trials which have not been adjusted for different proportions of patients with GT1a or GT1b subgenotypes or different fibrosis stage. As a consequence, the SVR rates for the comparators, particularly for the cirrhotic patient population, have been significantly over-estimated.

Summary of inclusion of new data for SOF+PR in UK model

The following data for SOF+PR was added to the model:

- Naïve GT4 cirrhotics
- Null Responders GT1, GT1a, GT1b, GT4 in non- cirrhotics and cirrhotics
- Partial Responders GT1, GT1a, GT1b, GT4 in non- cirrhotics and cirrhotics
- Prior Relapsers GT1, GT1a, GT1b, GT4 in non- cirrhotics and cirrhotics

<u>Assumptions for SVRs</u>

- **Naïve GT4 cirrhotics**

Because of the very low sample size of naïve GT4 cirrhotic patients in Neutrino trial (only one GT4 patient with cirrhosis participated in the trial and did not achieve an SVR), we extrapolate the data from naïve GT1 cirrhotic patients instead (note: assumed SVR for GT4 patients with cirrhosis is 80.8%).

- **Null Responders, Partial Responders, and Prior Relapsers - GT1 – Non Cirrhotics**

No trial has been conducted in treatment experienced GT1 patients, so no trial data are available. Based on the data presented in the manufacturer's submission for sofosbuvir/ledipasvir, and using the same assumptions made by the manufacturer of

sofosbuvir/ledipasvir for GT1, treatment-experienced patients, we assume an SVR rate of 74% for null and partial responders as well as prior relapsers. Because the model requires the 'n' (number achieving SVR) and 'N' (total number of subjects) to be established, we will assume the N to be the same as in GT1 naïve non-cirrhotics and thus, n will be equal to N * SVR.

- **Null Responders, Partial Responders, and Prior Relapsers - GT1a, GT1b, and GT4 – Non Cirrhotics**

Because of the lack of available data, GT1a, GT1b, and GT4 will all be assumed to be equal to GT1.

- **Null Responders, Partial Responders, and Prior Relapsers - GT1 – Cirrhotics**

No trial data available. The manufacturer's submission for sofosbuvir/ledipasvir assumes an SVR rate of 74% for treatment-experienced GT1 cirrhotic patients (the same SVR as for the non-cirrhotic patients). However, AbbVie disagrees with applying the same SVR rate for non-cirrhotic and cirrhotic patients given a significant drop in SVR rate observed between non-cirrhotic and cirrhotic GT1 patients in the Neutrino trial. Thus, following the same logic, the 74% SVR will be adjusted based on the decrement observed between non-cirrhotic and cirrhotic naïve GT1 patients (i.e., 74% * 80.8%/91.7% = 65.2%). Again, because the model requires the n and N numbers, we will assume the N to be the same as in GT1 naïve cirrhotic patients and thus, n will be equal to N * SVR.

- **Null Responders, Partial Responders, and Prior Relapsers - GT1a, GT1b, and GT4 – Cirrhotics**

Same assumption, i.e., GT1a, GT1b, and GT4 will all be assumed to be equal to GT1.

Assumptions for Duration of therapy

For each of the subgroups above, we will assume duration to be the same as the Neutrino trial which recruited patients not previously treated with HCV genotype 1, 4, 5, and 6.

Because 1) the Neutrino trial did not present the duration stratified by genotype/sub-genotype and by cirrhosis status and 2) there is no trial data in treatment-experienced patients, AbbVie believes this is a reasonable assumption.

Assumptions for Disutility and Rate of Adverse Events

For each of the subgroup above, we will assume disutility and rate of AEs to be the same as the Neutrino trial.

Justification is the same as for duration.

Revised base case results for GT1, GT1a, GT1b, GT4 treatment naïve and experienced, interferon-eligible patients, **any fibrosis stage, non-cirrhotic and cirrhotic patients** are summarised below across Table 1- Table 24.

Table 1: Genotype 1 treatment-naïve interferon eligible patients – Any fibrosis stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£22,872	19.68	13.72	NA	NA	NA	NA	NA
PR + Boceprevir	£32,147	19.94	14.22	£9,275	0.26	0.50	£18,366	Extended dominance
PR + Telaprevir	£35,887	20.16	14.55	£13,014	0.48	0.83	£15,602	Extended dominance
Simeprevir + PR	£36,934	20.17	14.62	£14,062	0.49	0.90	£15,595	Extended dominance
AbbVie regimen	£43,624	20.59	15.21	£20,752	0.91	1.50	£13,864	£13,864
Sofosbuvir + PR	£44,337	20.46	15.01	£21,465	0.78	1.29	£16,618	Dominated

Table 2: Genotype 1 treatment-naïve interferon eligible patients – Non-cirrhotic only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£20,483	20.22	14.33	NA	NA	NA	NA	NA
PR + Boceprevir	£29,404	20.51	14.90	£8,921	0.30	0.57	£15,766	Extended dominance
PR + Telaprevir	£33,748	20.62	15.16	£13,265	0.40	0.82	£16,110	Extended dominance
Simeprevir + PR	£34,736	20.64	15.23	£14,253	0.42	0.90	£15,826	Extended dominance
AbbVie regimen	£39,556	20.94	15.77	£19,073	0.72	1.43	£13,306	£13,306
Sofosbuvir + PR	£42,400	20.86	15.59	£21,916	0.65	1.26	£17,363	Dominated

Table 3: Genotype 1 treatment-naïve interferon eligible patients – Cirrhotic only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£44,374	14.87	8.18	NA	NA	NA	NA	NA
PR + Telaprevir	£55,132	16.03	9.11	£10,757	1.16	0.93	£11,560	Extended dominance
Simeprevir + PR	£56,721	15.97	9.09	£12,346	1.10	0.91	£13,537	Extended dominance
PR + Boceprevir	£56,827	14.79	8.13	£12,453	-0.08	-0.04	-£289,717	Dominated
Sofosbuvir + PR	£61,777	16.80	9.73	£17,402	1.92	1.56	£11,182	£11,182

AbbVie regimen	£80,238	17.43	10.24	£35,864	2.55	2.07	£17,350	£36,139

Table 4: Genotype 1a treatment-naïve interferon eligible patients – Any fibrosis stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£23,305	19.63	13.64	NA	NA	NA	NA	NA
PR + Boceprevir	£32,905	19.86	14.09	£9,601	0.22	0.45	£21,411	Extended dominance
PR + Telaprevir	£36,378	20.10	14.47	£13,073	0.47	0.82	£15,865	Extended dominance
Simeprevir + PR	£37,639	20.10	14.50	£14,334	0.46	0.85	£16,773	Extended dominance
Sofosbuvir + PR	£44,064	20.49	15.06	£20,760	0.85	1.41	£14,680	Extended dominance
AbbVie regimen	£45,110	20.57	15.18	£21,805	0.93	1.54	£14,199	£14,199

Table 5: Genotype 1a treatment-naïve interferon eligible patients - Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£20,888	20.18	14.26	NA	NA	NA	NA	NA
PR + Boceprevir	£30,114	20.44	14.77	£9,226	0.27	0.51	£18,069	Extended dominance
PR + Telaprevir	£34,208	20.57	15.07	£13,320	0.40	0.81	£16,373	Extended dominance
Simeprevir + PR	£35,395	20.58	15.11	£14,507	0.40	0.85	£16,976	Extended dominance
AbbVie regimen	£39,955	20.92	15.73	£19,067	0.75	1.47	£12,949	£12,949
Sofosbuvir + PR	£42,144	20.89	15.64	£21,256	0.71	1.38	£15,383	Dominated

Table 6: Genotype 1a treatment-naïve interferon eligible patients - Cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£45,057	14.76	8.08	NA	NA	NA	NA	NA
PR + Telaprevir	£55,907	15.90	9.00	£10,850	1.14	0.92	£11,815	Extended dominance
Simeprevir + PR	£57,832	15.78	8.94	£12,775	1.02	0.85	£14,944	Extended dominance
PR + Boceprevir	£58,024	14.58	7.97	£12,967	-0.17	-0.11	-£116,181	Dominated

Sofosbuvir + PR	£61,347	16.87	9.79	£16,290	2.11	1.70	£9,555	£9,555
AbbVie regimen	£91,507	17.36	10.19	£46,450	2.60	2.11	£22,066	£75,360

Table 7: Genotype 1b treatment-naïve interferon eligible patients - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£23,305	19.63	13.64	NA	NA	NA	NA	NA
PR + Boceprevir	£32,905	19.86	14.09	£9,601	0.22	0.45	£21,411	Extended dominance
PR + Telaprevir	£36,378	20.10	14.47	£13,073	0.47	0.82	£15,865	Extended dominance
Simeprevir + PR	£37,639	20.10	14.50	£14,334	0.46	0.85	£16,773	Extended dominance
Sofosbuvir + PR	£44,064	20.49	15.06	£20,760	0.85	1.41	£14,680	Extended dominance
AbbVie regimen	£45,110	20.57	15.18	£21,805	0.93	1.54	£14,199	£14,199

Table 8: Genotype 1b treatment-naïve interferon eligible patients - Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£19,844	20.28	14.45	NA	NA	NA	NA	NA
PR + Boceprevir	£29,110	20.54	14.95	£9,265	0.26	0.50	£18,399	Extended dominance
PR + Telaprevir	£33,115	20.68	15.27	£13,271	0.40	0.82	£16,135	Extended dominance
Simeprevir + PR	£33,972	20.71	15.37	£14,128	0.44	0.92	£15,303	Extended dominance
AbbVie regimen	£38,677	20.98	15.84	£18,833	0.70	1.39	£13,515	£13,515
Sofosbuvir + PR	£43,503	20.76	15.39	£23,659	0.48	0.95	£24,988	Dominated

Table 9: Genotype 1b treatment-naïve interferon eligible patients - Cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£43,298	15.06	8.32	NA	NA	NA	NA	NA
PR + Telaprevir	£54,065	16.22	9.25	£10,766	1.16	0.93	£11,584	Extended dominance

AbbVie regimen	£55,388	17.58	10.36	£12,090	2.52	2.04	£5,924	£5,924
Simeprevir + PR	£55,434	16.19	9.26	£12,136	1.13	0.94	£12,909	Dominated
PR + Boceprevir	£56,331	14.87	8.20	£13,033	-0.18	-0.12	-£108,273	Dominated
Sofosbuvir + PR	£63,636	16.48	9.48	£20,338	1.42	1.16	£17,468	Dominated

Table 10: Genotype 1 treatment-experienced (overall) interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£30,128	17.13	11.07	NA	NA	NA	NA	NA
PR + Telaprevir	£42,646	17.92	12.10	£12,518	0.78	1.04	£12,095	Extended dominance
Simeprevir + PR	£45,312	17.98	12.25	£15,184	0.84	1.18	£12,816	Extended dominance
Sofosbuvir + PR	£50,691	18.17	12.51	£20,564	1.03	1.44	£14,256	Extended dominance
AbbVie regimen	£51,882	18.72	13.19	£21,754	1.58	2.12	£10,258	£10,258

Table 11: Genotype 1 treatment-experienced (overall) interferon eligible - Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£22,432	18.76	12.82	NA	NA	NA	NA	NA
PR + Telaprevir	£35,402	19.33	13.90	£12,970	0.57	1.07	£12,105	Extended dominance
Simeprevir + PR	£38,408	19.33	14.02	£15,977	0.57	1.20	£13,361	Extended dominance
AbbVie regimen	£39,173	19.68	14.78	£16,741	0.92	1.95	£8,581	£8,581
Sofosbuvir + PR	£44,336	19.41	14.22	£21,904	0.65	1.40	£15,692	Dominated

Table 12: Genotype 1 treatment-experienced (overall) interferon eligible - Cirrhotics Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£46,482	13.68	7.33	NA	NA	NA	NA	NA
PR + Telaprevir	£58,040	14.92	8.29	£11,557	1.24	0.96	£12,071	Extended dominance

Simeprevir + PR	£59,982	15.10	8.49	£13,500	1.43	1.16	£11,623	Extended dominance
Sofosbuvir + PR	£64,197	15.52	8.87	£17,714	1.84	1.54	£11,492	£11,492
AbbVie regimen	£78,890	16.67	9.81	£32,407	3.00	2.48	£13,060	£15,631

Table 13: Genotype 1a treatment-experienced (overall) interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£29,458	17.22	11.16	NA	NA	NA	NA	NA
PR + Telaprevir	£43,559	17.81	11.96	£14,101	0.59	0.80	£17,543	Extended dominance
Simeprevir + PR	£47,176	17.76	11.97	£17,718	0.54	0.81	£21,839	Extended dominance
Sofosbuvir + PR	£50,691	18.17	12.51	£21,233	0.95	1.35	£15,756	Extended dominance
AbbVie regimen	£55,552	18.71	13.17	£26,093	1.50	2.01	£12,978	£12,978

Table 14: Genotype 1a treatment-experienced (overall) interferon eligible - Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£21,907	18.81	12.91	NA	NA	NA	NA	NA
PR + Telaprevir	£36,138	19.27	13.77	£14,231	0.46	0.86	£16,487	Extended dominance
AbbVie regimen	£39,524	19.66	14.74	£17,617	0.86	1.84	£9,589	£9,589
Simeprevir + PR	£39,911	19.20	13.76	£18,005	0.39	0.86	£21,026	Dominated
Sofosbuvir + PR	£44,336	19.41	14.22	£22,429	0.60	1.31	£17,079	Dominated

Table 15: Genotype 1a treatment-experienced (overall) interferon eligible - Cirrhotics Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£45,505	13.83	7.45	NA	NA	NA	NA	NA
PR + Telaprevir	£59,328	14.72	8.13	£13,823	0.89	0.68	£20,403	Extended dominance
Simeprevir + PR	£62,614	14.69	8.17	£17,109	0.86	0.72	£23,905	Extended dominance

Sofosbuvir + PR	£64,197	15.52	8.87	£18,692	1.69	1.42	£13,157	£13,157
AbbVie regimen	£89,610	16.70	9.83	£44,105	2.87	2.38	£18,539	£26,516

Table 16: Genotype 1b treatment-experienced (overall) interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£30,738	17.06	10.98	NA	NA	NA	NA	NA
PR + Telaprevir	£41,579	18.04	12.26	£10,841	0.98	1.28	£8,474	Extended dominance
AbbVie regimen	£43,790	18.72	13.22	£13,052	1.66	2.24	£5,828	£5,828
Simeprevir + PR	£43,918	18.14	12.46	£13,180	1.08	1.48	£8,917	Dominated
Sofosbuvir + PR	£50,691	18.17	12.51	£19,953	1.10	1.53	£13,064	Dominated

Table 17: Genotype 1b treatment-experienced (overall) interferon eligible - Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£22,909	18.72	12.75	NA	NA	NA	NA	NA
PR + Telaprevir	£34,542	19.40	14.04	£11,633	0.68	1.29	£9,008	Extended dominance
Simeprevir + PR	£37,285	19.42	14.21	£14,376	0.71	1.46	£9,841	Extended dominance
AbbVie regimen	£38,398	19.71	14.84	£15,489	0.99	2.09	£7,401	£7,401
Sofosbuvir + PR	£44,336	19.41	14.22	£21,427	0.69	1.47	£14,587	Dominated

Table 18: Genotype 1b treatment-experienced (overall) interferon eligible - Cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£47,375	13.54	7.22	NA	NA	NA	NA	NA
AbbVie regimen	£55,249	16.62	9.77	£7,874	3.08	2.55	£3,087	£3,087
PR + Telaprevir	£56,534	15.15	8.47	£9,159	1.61	1.25	£7,306	Dominated
Simeprevir + PR	£58,015	15.41	8.73	£10,640	1.87	1.51	£7,024	Dominated

Sofosbuvir + PR	£64,197	15.52	8.87	£16,822	1.98	1.65	£10,185	Dominated

Table 19: Genotype 4 treatment-naïve interferon eligible patients - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£21,940	20.03	14.33	NA	NA	NA	NA	NA
Simeprevir + PR	£35,869	20.31	14.79	£13,929	0.28	0.46	£30,076	Extended dominance
AbbVie regimen	£41,401	20.63	15.29	£19,462	0.60	0.96	£20,234	£20,234
Sofosbuvir + PR	£43,291	20.56	15.20	£21,351	0.53	0.87	£24,556	Dominated

Table 20: Genotype 4 treatment-naïve interferon eligible patients - Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£19,286	20.58	15.00	NA	NA	NA	NA	NA
Simeprevir + PR	£33,701	20.76	15.40	£14,415	0.19	0.41	£35,386	Extended dominance
AbbVie regimen	£36,490	20.98	15.84	£17,204	0.40	0.85	£20,351	£20,351
Sofosbuvir + PR	£41,237	20.98	15.81	£21,951	0.40	0.81	£27,135	Dominated

Table 21: Genotype 4 treatment-naïve interferon eligible patients - Cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£45,822	15.06	8.32	NA	NA	NA	NA	NA
Simeprevir + PR	£55,377	16.22	9.28	£9,555	1.17	0.96	£9,902	£9,902
Sofosbuvir + PR	£61,777	16.80	9.73	£15,955	1.74	1.41	£11,280	£14,238
AbbVie regimen	£85,602	17.49	10.33	£39,781	2.43	2.01	£19,794	£40,025

Table 22: Genotype 4 treatment-experienced (overall) interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental	Incremental	Incremental	ICER vs.	ICER incremental

				costs, £	LYGs	QALYs	baseline	
No treatment	£24,245	16.84	10.80	NA	NA	NA	NA	NA
Simeprevir + PR	£45,366	18.00	12.38	£21,122	1.17	1.58	£13,393	Extended dominance
Sofosbuvir + PR	£50,691	18.17	12.51	£26,447	1.33	1.70	£15,512	Extended dominance
AbbVie regimen	£52,199	18.73	13.24	£27,954	1.89	2.43	£11,485	£11,485

Table 23: Genotype 4 treatment-experienced (overall) interferon eligible - Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
No treatment	£16,186	18.57	12.58	NA	NA	NA	NA	NA
AbbVie regimen	£36,536	19.71	14.84	£20,350	1.14	2.27	£8,977	£8,977
Simeprevir + PR	£37,421	19.48	14.30	£21,236	0.91	1.72	£12,320	Dominated
Sofosbuvir + PR	£44,336	19.41	14.22	£28,150	0.84	1.64	£17,132	Dominated

Table 24: Genotype 4 treatment-experienced (overall) interferon eligible - Cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
No treatment	£41,370	13.16	7.03	NA	NA	NA	NA	NA
Simeprevir + PR	£62,249	14.87	8.30	£20,879	1.71	1.27	£16,500	Extended dominance
Sofosbuvir + PR	£64,197	15.52	8.87	£22,827	2.36	1.84	£12,432	£12,432
AbbVie regimen	£85,482	16.66	9.82	£44,112	3.50	2.79	£15,815	£22,331

Table 1 to Table 23 present a summary of the revised base case results requested by NICE, reflecting populations, treatment-regimen and treatment-durations specified in the summary of product characteristics for Viekirax and Exviera, table 1 (see tab 'Basecase - Incremental Analysis'). In no cases is the AbbVie Regimen dominated; in all cases it is the QALY maximising treatment. In the GT1 treatment naïve overall, GT1 treatment experienced overall, GT4 treatment naïve overall, and GT4 treatment experienced overall, the AbbVie Regimen is the most-cost-effective option. The AbbVie Regimen is the most-cost-effective option in all comparisons involving non-cirrhotic patients. In 3 out of 23 base case comparisons, the AbbVie Regimen was not the most-cost-effective option, including the list of comparisons below:

- Genotype 1 treatment-naïve interferon eligible - Cirrhotic Only: £36,139/QALY
- Genotype 1a treatment-naïve interferon eligible - Cirrhotic Only: £75,360/QALY
- Genotype 4 treatment-naïve interferon eligible - Cirrhotic Only: £40,025/QALY

In all cases this was in part driven by GT1a and GT4 cirrhotic patients who were assumed to universally (100%) receive 24 weeks of the AbbVie Regimen. In addition, in the absence of SVR data for SOF+PR regimen in GT4 treatment-naïve cirrhotic patients, AbbVie extrapolated SVR from GT1 cirrhotic patients and thus applied 80.8% SVR for this group of patients. As discussed previously in the document, a large uncertainty is associated with this assumed efficacy estimate given that given that only one treatment-naïve GT4 patient with cirrhosis participated in the Neutrino trial and that patients did not achieve an SVR.

2) *Provide two scenario analyses around utility values, with results presented in a fully incremental manner for all AbbVie's treatment regimens (as specified in the summary of product characteristics table 1) in comparison with all relevant comparators:*
   - *a scenario analysis, using a utility increment for sustained virological response (SVR) over the baseline utility values (based on Shepherd et al. 2007), estimated from the difference between pooled EQ-5D values collected at base-line and at 12 week post treatment time point (PTW12) in people who achieved SVR from the trials;*

A pooled 'utility gain' associated with the achievement of virologic cure has been estimated from the EQ-5D-5L responses of patients who achieved SVR across AbbVie's registration trials and the updated cost-effectiveness results presented in Table 25– Table 48. [redacted] and was applied to the Shepherd et al. base case utilities for mild, moderate and cirrhosis health states to derive utilities for the recovered health states. The trial-based utility gain is noticeably lower than the one reported by Shepherd et al. (0.05), which AbbVie used in its base-case analysis. It must be noted that the utility gain reported by Shepherd et al. was used in the comparators' cost-effectiveness analyses that have recently been appraised and recommended by NICE (e.g., sofosbuvir+pegIFN-RBV and simeprevir+PegIFN-RBV). It is worthwhile also pointing out that the protocols for all of AbbVie's registration trials demanded that all PRO Instruments were completed prior to any discussion of adverse events or any review of laboratory findings, including HCV RNA levels. Therefore, patients completing EQ-5D-5L questionnaire wouldn't have been aware of their SVR status at the time patient reported outcome data were collected. As a result, the psychological and emotional benefits of achieving cure have not been captured and have therefore resulted in a likely underestimation of the utility gain associated with SVR12.

Table 25: Genotype 1 treatment-naïve interferon eligible patients – Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£22,872	19.68	13.40	NA	NA	NA	NA	NA
PR + Boceprevir	£32,147	19.94	13.76	£9,275	0.26	0.36	£25,486	Extended dominance
PR + Telaprevir	£35,887	20.16	14.00	£13,014	0.48	0.60	£21,609	Extended dominance
Simeprevir + PR	£36,934	20.17	14.06	£14,062	0.49	0.66	£21,399	Extended dominance
AbbVie regimen	£43,624	20.59	14.50	£20,752	0.91	1.11	£18,772	£18,772
Sofosbuvir + PR	£44,337	20.46	14.35	£21,465	0.78	0.95	£22,660	Dominated

Table 26: Genotype 1 treatment-naïve interferon eligible patients – Non-Cirrhotic only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£20,483	20.22	14.00	NA	NA	NA	NA	NA
PR + Boceprevir	£29,404	20.51	14.41	£8,921	0.30	0.41	£21,884	Extended dominance
PR + Telaprevir	£33,748	20.62	14.59	£13,265	0.40	0.59	£22,651	Extended dominance
Simeprevir + PR	£34,736	20.64	14.65	£14,253	0.42	0.65	£22,007	Extended dominance
AbbVie regimen	£39,556	20.94	15.04	£19,073	0.72	1.04	£18,297	£18,297
Sofosbuvir + PR	£42,400	20.86	14.91	£21,916	0.65	0.91	£24,017	Dominated

Table 27: **Genotype 1 treatment-naïve interferon eligible patients - Cirrhotic Only**

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£20,483	20.22	14.00	NA	NA	NA	NA	NA
PR + Boceprevir	£29,404	20.51	14.41	£8,921	0.30	0.41	£21,884	Extended dominance
PR + Telaprevir	£33,748	20.62	14.59	£13,265	0.40	0.59	£22,651	Extended dominance
Simeprevir + PR	£34,736	20.64	14.65	£14,253	0.42	0.65	£22,007	Extended dominance
AbbVie regimen	£39,556	20.94	15.04	£19,073	0.72	1.04	£18,297	£18,297
Sofosbuvir + PR	£42,400	20.86	14.91	£21,916	0.65	0.91	£24,017	Dominated

Table 28: Genotype 1a treatment-naïve interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£23,305	19.63	13.34	NA	NA	NA	NA	NA
PR + Boceprevir	£32,905	19.86	13.67	£9,601	0.22	0.32	£29,694	Extended dominance
PR + Telaprevir	£36,378	20.10	13.94	£13,073	0.47	0.59	£21,972	Extended dominance
Simeprevir + PR	£37,639	20.10	13.97	£14,334	0.46	0.62	£22,996	Extended dominance
Sofosbuvir + PR	£44,064	20.49	14.38	£20,760	0.85	1.04	£20,055	Extended dominance
AbbVie regimen	£45,110	20.57	14.48	£21,805	0.93	1.13	£19,252	£19,252

Table 29: Genotype 1a treatment-naïve interferon eligible - Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£20,888	20.18	13.95	NA	NA	NA	NA	NA
PR + Boceprevir	£30,114	20.44	14.32	£9,226	0.27	0.37	£25,026	Extended dominance
PR + Telaprevir	£34,208	20.57	14.53	£13,320	0.40	0.58	£23,020	Extended dominance
Simeprevir + PR	£35,395	20.58	14.56	£14,507	0.40	0.62	£23,584	Extended dominance
AbbVie regimen	£39,955	20.92	15.02	£19,067	0.75	1.07	£17,833	£17,833
Sofosbuvir + PR	£42,144	20.89	14.95	£21,256	0.71	1.00	£21,321	Dominated

Table 30: Genotype 1a treatment-naïve interferon eligible - Cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£45,057	14.76	7.89	NA	NA	NA	NA	NA
PR + Telaprevir	£55,907	15.90	8.64	£10,850	1.14	0.74	£14,620	Extended dominance
Simeprevir + PR	£57,832	15.78	8.59	£12,775	1.02	0.70	£18,332	Extended dominance
PR + Boceprevir	£58,024	14.58	7.81	£12,967	-0.17	-0.08	-£152,710	Dominated

Sofosbuvir + PR	£61,347	16.87	9.27	£16,290	2.11	1.38	£11,816	£11,816
AbbVie regimen	£91,507	17.36	9.60	£46,450	2.60	1.70	£27,268	£92,828

Table 31: Genotype 1b treatment-naïve interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£22,190	19.76	13.48	NA	NA	NA	NA	NA
PR + Boceprevir	£31,832	19.98	13.80	£9,642	0.22	0.32	£30,309	Extended dominance
PR + Telaprevir	£35,210	20.23	14.08	£13,020	0.48	0.60	£21,644	Extended dominance
Simeprevir + PR	£36,119	20.26	14.16	£13,929	0.51	0.67	£20,673	Extended dominance
AbbVie regimen	£40,348	20.64	14.56	£18,159	0.88	1.08	£16,820	£16,820
Sofosbuvir + PR	£45,516	20.33	14.20	£23,327	0.57	0.72	£32,606	Dominated

Table 32: Genotype 1b treatment-naïve interferon eligible - Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£19,844	20.28	14.08	NA	NA	NA	NA	NA
PR + Boceprevir	£29,110	20.54	14.45	£9,265	0.26	0.36	£25,476	Extended dominance
PR + Telaprevir	£33,115	20.68	14.67	£13,271	0.40	0.58	£22,687	Extended dominance
Simeprevir + PR	£33,972	20.71	14.75	£14,128	0.44	0.66	£21,289	Extended dominance
AbbVie regimen	£38,677	20.98	15.10	£18,833	0.70	1.02	£18,538	£18,538
Sofosbuvir + PR	£43,503	20.76	14.77	£23,659	0.48	0.69	£34,297	Dominated

Table 33: Genotype 1b treatment-naïve interferon eligible - Cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£43,298	15.06	8.08	NA	NA	NA	NA	NA
PR + Telaprevir	£54,065	16.22	8.83	£10,766	1.16	0.75	£14,336	Extended dominance

AbbVie regimen	£55,388	17.58	9.73	£12,090	2.52	1.65	£7,316	£7,316
Simeprevir + PR	£55,434	16.19	8.85	£12,136	1.13	0.77	£15,860	Dominated
PR + Boceprevir	£56,331	14.87	7.99	£13,033	-0.18	-0.09	-£141,774	Dominated
Sofosbuvir + PR	£63,636	16.48	9.03	£20,338	1.42	0.95	£21,504	Dominated

Table 34: Genotype 1 treatment-experienced (overall) interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£30,128	17.13	10.96	NA	NA	NA	NA	NA
PR + Telaprevir	£42,646	17.92	11.70	£12,518	0.78	0.74	£16,916	Extended dominance
Simeprevir + PR	£45,312	17.98	11.82	£15,184	0.84	0.86	£17,672	Extended dominance
Sofosbuvir + PR	£50,691	18.17	12.03	£20,564	1.03	1.07	£19,300	Extended dominance
AbbVie regimen	£51,882	18.72	12.53	£21,754	1.58	1.57	£13,854	£13,854

Table 35: Genotype 1 treatment-experienced (overall) interferon eligible - Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£22,432	18.76	12.71	NA	NA	NA	NA	NA
PR + Telaprevir	£35,402	19.33	13.45	£12,970	0.57	0.73	£17,658	Extended dominance
Simeprevir + PR	£38,408	19.33	13.54	£15,977	0.57	0.83	£19,286	Extended dominance
AbbVie regimen	£39,173	19.68	14.09	£16,741	0.92	1.38	£12,172	£12,172
Sofosbuvir + PR	£44,336	19.41	13.70	£21,904	0.65	0.99	£22,234	Dominated

Table 36: Genotype 1 treatment-experienced (overall) interferon eligible - Cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£46,482	13.68	7.24	NA	NA	NA	NA	NA
PR + Telaprevir	£58,040	14.92	7.99	£11,557	1.24	0.75	£15,376	Extended dominance

Simeprevir + PR	£59,982	15.10	8.17	£13,500	1.43	0.92	£14,599	Extended dominance
Sofosbuvir + PR	£64,197	15.52	8.48	£17,714	1.84	1.24	£14,331	£14,331
AbbVie regimen	£78,890	16.67	9.23	£32,407	3.00	1.98	£16,333	£19,642

Table 37: Genotype 1a treatment-experienced (overall) interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£29,458	17.22	11.03	NA	NA	NA	NA	NA
PR + Telaprevir	£43,559	17.81	11.60	£14,101	0.59	0.57	£24,712	Extended dominance
Simeprevir + PR	£47,176	17.76	11.62	£17,718	0.54	0.59	£30,213	Extended dominance
Sofosbuvir + PR	£50,691	18.17	12.03	£21,233	0.95	1.00	£21,334	Extended dominance
AbbVie regimen	£55,552	18.71	12.52	£26,093	1.50	1.49	£17,524	£17,524

Table 38: Genotype 1a treatment-experienced (overall) interferon eligible - Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£21,907	18.81	12.77	NA	NA	NA	NA	NA
PR + Telaprevir	£36,138	19.27	13.36	£14,231	0.46	0.59	£24,139	Extended dominance
AbbVie regimen	£39,524	19.66	14.07	£17,617	0.86	1.29	£13,613	£13,613
Simeprevir + PR	£39,911	19.20	13.36	£18,005	0.39	0.59	£30,356	Dominated
Sofosbuvir + PR	£44,336	19.41	13.70	£22,429	0.60	0.93	£24,200	Dominated

Table 39: Genotype 1a treatment-experienced (overall) interferon eligible - Cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£45,505	13.83	7.34	NA	NA	NA	NA	NA
PR + Telaprevir	£59,328	14.72	7.87	£13,823	0.89	0.53	£26,067	Extended dominance
Simeprevir + PR	£62,614	14.69	7.91	£17,109	0.86	0.57	£29,899	Extended dominance

Sofosbuvir + PR	£64,197	15.52	8.48	£18,692	1.69	1.14	£16,387	£16,387
AbbVie regimen	£89,610	16.70	9.24	£44,105	2.87	1.90	£23,176	£33,332

Table 40: Genotype 1b treatment-experienced (overall) interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£30,738	17.06	10.90	NA	NA	NA	NA	NA
PR + Telaprevir	£41,579	18.04	11.82	£10,841	0.98	0.92	£11,795	Extended dominance
AbbVie regimen	£43,790	18.72	12.56	£13,052	1.66	1.66	£7,874	£7,874
Simeprevir + PR	£43,918	18.14	11.97	£13,180	1.08	1.07	£12,272	Dominated
Sofosbuvir + PR	£50,691	18.17	12.03	£19,953	1.10	1.13	£17,677	Dominated

Table 41: Genotype 1b treatment-experienced (overall) interferon eligible - Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£22,909	18.72	12.66	NA	NA	NA	NA	NA
PR + Telaprevir	£34,542	19.40	13.55	£11,633	0.68	0.89	£13,103	Extended dominance
Simeprevir + PR	£37,285	19.42	13.67	£14,376	0.71	1.01	£14,195	Extended dominance
AbbVie regimen	£38,398	19.71	14.14	£15,489	0.99	1.48	£10,480	£10,480
Sofosbuvir + PR	£44,336	19.41	13.70	£21,427	0.69	1.04	£20,658	Dominated

Table 42: Genotype 1b treatment-experienced (overall) interferon eligible - Cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£47,375	13.54	7.16	NA	NA	NA	NA	NA
AbbVie regimen	£55,249	16.62	9.20	£7,874	3.08	2.04	£3,861	£3,861
PR + Telaprevir	£56,534	15.15	8.14	£9,159	1.61	0.99	£9,291	Dominated
Simeprevir + PR	£58,015	15.41	8.36	£10,640	1.87	1.20	£8,837	Dominated

Sofosbuvir + PR	£64,197	15.52	8.48	£16,822	1.98	1.32	£12,712	Dominated

Table 43: Genotype 4 treatment-naïve interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£21,940	20.03	13.83	NA	NA	NA	NA	NA
Simeprevir + PR	£35,869	20.31	14.19	£13,929	0.28	0.35	£39,423	Extended dominance
AbbVie regimen	£41,401	20.63	14.56	£19,462	0.60	0.73	£26,730	£26,730
Sofosbuvir + PR	£43,291	20.56	14.48	£21,351	0.53	0.65	£33,029	Dominated

Table 44: Genotype 4 treatment-naïve interferon eligible - Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£19,286	20.58	14.47	NA	NA	NA	NA	NA
Simeprevir + PR	£33,701	20.76	14.78	£14,415	0.19	0.31	£47,202	Extended dominance
AbbVie regimen	£36,490	20.98	15.10	£17,204	0.40	0.63	£27,422	£27,422
Sofosbuvir + PR	£41,237	20.98	15.06	£21,951	0.40	0.59	£37,146	Dominated

Table 45: Genotype 4 treatment-naïve interferon eligible - Cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£45,822	15.06	8.08	NA	NA	NA	NA	NA
Simeprevir + PR	£55,377	16.22	8.86	£9,555	1.17	0.78	£12,176	£12,176
Sofosbuvir + PR	£61,777	16.80	9.23	£15,955	1.74	1.15	£13,922	£17,713
AbbVie regimen	£85,602	17.49	9.71	£39,781	2.43	1.63	£24,340	£48,791

Table 46: Genotype 4 treatment-experienced (overall) interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
No treatment	£24,245	16.84	10.80	NA	NA	NA	NA	NA
Simeprevir + PR	£45,366	18.00	11.91	£21,122	1.17	1.10	£19,149	Extended dominance
Sofosbuvir + PR	£50,691	18.17	12.03	£26,447	1.33	1.23	£21,588	Extended dominance
AbbVie regimen	£52,199	18.73	12.57	£27,954	1.89	1.77	£15,803	£15,803

Table 47: Genotype 4 treatment-experienced (overall) interferon eligible - Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
No treatment	£16,186	18.57	12.58	NA	NA	NA	NA	NA
AbbVie regimen	£36,536	19.71	14.14	£20,350	1.14	1.56	£13,027	£13,027
Simeprevir + PR	£37,421	19.48	13.74	£21,236	0.91	1.16	£18,307	Dominated
Sofosbuvir + PR	£44,336	19.41	13.70	£28,150	0.84	1.12	£25,097	Dominated

Table 48: Genotype 4 treatment-experienced (overall) interferon eligible - Cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
No treatment	£41,370	13.16	7.03	NA	NA	NA	NA	NA
Simeprevir + PR	£62,249	14.87	8.02	£20,879	1.71	0.98	£21,262	Extended dominance
Sofosbuvir + PR	£64,197	15.52	8.48	£22,827	2.36	1.44	£15,800	£15,800
AbbVie regimen	£85,482	16.66	9.24	£44,112	3.50	2.21	£19,975	£27,877

The use of the Pooled Increment on SVR approach modestly increased the ICERs relative to the base case (See tab 'SA - Pooled Increment on SVR'). For example, the ICER in the "Genotype 1 treatment-naïve interferon eligible patients - Any Fibrosis Stage" increased from £13,864/QALY in the base case to £18,772/QALY in the AbbVie UK Crosswalk sensitivity analysis. This sensitivity essentially assumes an almost 0 increase in health utility conditional on getting an SVR. Inspection of the 'Vera-Llonch' utility gain associated with SVR and requested by NICE to be applied across all chronic HCV technologies recently appraised indicates that the increase in HRQoL occurs after 12 weeks post treatment; those authors observed an increase at week 72 post baseline. AbbVie has provided this sensitivity analysis within its original submission.

- *a scenario analysis using alternative health state utility values based on the EQ-5D data from the trials (the health state values used in the company's scenario 20 [table 127, HSU scenario 2, page 393]).*

  The use of the AbbVie UK Crosswalk slightly increased the ICERs relative to the base case (See tab 'SA - AbbVie UK Crosswalk'). For example, the ICER in the "Genotype 1 treatment-naïve interferon eligible patients - Any Fibrosis Stage" this scenario analysis increased the ICER from £13,864/QALY in the base case to £16,875/QALY in the AbbVie UK Crosswalk sensitivity analysis. The results of this scenario analysis are summarised in Table 49– Table 72.

Table 49: Genotype 1 treatment-naïve interferon eligible patients – Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£22,872	19.68	16.29	NA	NA	NA	NA	NA
PR + Boceprevir	£32,147	19.94	16.67	£9,275	0.26	0.38	£24,148	Extended dominance
PR + Telaprevir	£35,887	20.16	16.93	£13,014	0.48	0.65	£20,136	Extended dominance
Simeprevir + PR	£36,934	20.17	16.99	£14,062	0.49	0.70	£20,119	Extended dominance
AbbVie regimen	£43,624	20.59	17.52	£20,752	0.91	1.23	£16,875	£16,875
Sofosbuvir + PR	£44,337	20.46	17.34	£21,465	0.78	1.05	£20,476	Dominated

Table 50: Genotype 1 treatment-naïve interferon eligible patients – Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£20,483	20.22	16.86	NA	NA	NA	NA	NA
PR + Boceprevir	£29,404	20.51	17.29	£8,921	0.30	0.43	£20,612	Extended dominance
PR + Telaprevir	£33,748	20.62	17.46	£13,265	0.40	0.60	£22,230	Extended dominance
Simeprevir + PR	£34,736	20.64	17.52	£14,253	0.42	0.66	£21,653	Extended dominance
AbbVie regimen	£39,556	20.94	17.96	£19,073	0.72	1.10	£17,385	£17,385
Sofosbuvir + PR	£42,400	20.86	17.82	£21,916	0.65	0.96	£22,783	Dominated

Table 51: Genotype 1 treatment-naïve interferon eligible patients – Cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£44,374	14.87	11.13	NA	NA	NA	NA	NA
PR + Telaprevir	£55,132	16.03	12.22	£10,757	1.16	1.09	£9,846	Extended dominance
Simeprevir + PR	£56,721	15.97	12.19	£12,346	1.10	1.07	£11,587	Extended dominance
PR + Boceprevir	£56,827	14.79	11.07	£12,453	-0.08	-0.05	-£227,286	Dominated
Sofosbuvir + PR	£61,777	16.80	12.95	£17,402	1.92	1.83	£9,535	£9,535
AbbVie regimen	£80,238	17.43	13.55	£35,864	2.55	2.42	£14,795	£30,823

Table 52: Genotype 1a treatment-naïve interferon eligible patients – Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£23,305	19.63	16.05	NA	NA	NA	NA	NA
PR + Boceprevir	£32,905	19.86	16.39	£9,601	0.22	0.34	£28,395	Extended dominance
PR + Telaprevir	£36,378	20.10	16.68	£13,073	0.47	0.63	£20,772	Extended dominance
Simeprevir + PR	£37,639	20.10	16.70	£14,334	0.46	0.65	£21,976	Extended dominance
Sofosbuvir + PR	£44,064	20.49	17.19	£20,760	0.85	1.14	£18,260	Extended dominance
AbbVie regimen	£45,110	20.57	17.30	£21,805	0.93	1.25	£17,449	£17,449

Table 53: Genotype 1a treatment-naïve interferon eligible patients – Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£20,888	20.18	16.63	NA	NA	NA	NA	NA
PR + Boceprevir	£30,114	20.44	17.02	£9,226	0.27	0.39	£23,634	Extended dominance
PR + Telaprevir	£34,208	20.57	17.22	£13,320	0.40	0.58	£22,889	Extended dominance
Simeprevir + PR	£35,395	20.58	17.25	£14,507	0.40	0.62	£23,549	Extended dominance
AbbVie regimen	£39,955	20.92	17.75	£19,067	0.75	1.12	£17,028	£17,028
Sofosbuvir + PR	£42,144	20.89	17.68	£21,256	0.71	1.05	£20,332	Dominated

Table 54: Genotype 1a treatment-naïve interferon eligible patients – Cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£45,057	14.76	10.80	NA	NA	NA	NA	NA
PR + Telaprevir	£55,907	15.90	11.86	£10,850	1.14	1.06	£10,274	Extended dominance
Simeprevir + PR	£57,832	15.78	11.78	£12,775	1.02	0.98	£13,058	Extended dominance
PR + Boceprevir	£58,024	14.58	10.67	£12,967	-0.17	-0.13	-£97,879	Dominated

Sofosbuvir + PR	£61,347	16.87	12.76	£16,290	2.11	1.96	£8,312	£8,312
AbbVie regimen	£91,507	17.36	13.22	£46,450	2.60	2.42	£19,203	£65,696

Table 55: Genotype 1b treatment-naïve interferon eligible patients – Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£22,190	19.76	16.78	NA	NA	NA	NA	NA
PR + Boceprevir	£31,832	19.98	17.11	£9,642	0.22	0.34	£28,770	Extended dominance
PR + Telaprevir	£35,210	20.23	17.44	£13,020	0.48	0.67	£19,571	Extended dominance
Simeprevir + PR	£36,119	20.26	17.52	£13,929	0.51	0.74	£18,856	Extended dominance
AbbVie regimen	£40,348	20.64	18.00	£18,159	0.88	1.22	£14,856	£14,856
Sofosbuvir + PR	£45,516	20.33	17.58	£23,327	0.57	0.80	£29,032	Dominated

Table 56: Genotype 1b treatment-naïve interferon eligible patients – Non-cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£19,844	20.28	17.33	NA	NA	NA	NA	NA
PR + Boceprevir	£29,110	20.54	17.72	£9,265	0.26	0.39	£23,789	Extended dominance
PR + Telaprevir	£33,115	20.68	17.94	£13,271	0.40	0.61	£21,666	Extended dominance
Simeprevir + PR	£33,972	20.71	18.03	£14,128	0.44	0.69	£20,377	Extended dominance
AbbVie regimen	£38,677	20.98	18.41	£18,833	0.70	1.08	£17,431	£17,431
Sofosbuvir + PR	£43,503	20.76	18.07	£23,659	0.48	0.73	£32,202	Dominated

Table 57: Genotype 1b treatment-naïve interferon eligible patients – Cirrhotic Only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£43,298	15.06	11.79	NA	NA	NA	NA	NA
PR + Telaprevir	£54,065	16.22	12.93	£10,766	1.16	1.14	£9,443	Extended dominance

AbbVie regimen	£55,388	17.58	14.29	£12,090	2.52	2.50	£4,837	£4,837
Simeprevir + PR	£55,434	16.19	12.94	£12,136	1.13	1.15	£10,583	Dominated
PR + Boceprevir	£56,331	14.87	11.64	£13,033	-0.18	-0.15	-£84,649	Dominated
Sofosbuvir + PR	£63,636	16.48	13.21	£20,338	1.42	1.42	£14,298	Dominated

Table 58: Genotype 1 treatment-experienced (overall) interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£30,128	17.13	13.44	NA	NA	NA	NA	NA
PR + Telaprevir	£42,646	17.92	14.18	£12,518	0.78	0.74	£16,863	Extended dominance
Simeprevir + PR	£45,312	17.98	14.31	£15,184	0.84	0.87	£17,405	Extended dominance
Sofosbuvir + PR	£50,691	18.17	14.54	£20,564	1.03	1.10	£18,641	Extended dominance
AbbVie regimen	£51,882	18.72	15.11	£21,754	1.58	1.66	£13,076	£13,076

Table 59: Genotype 1 treatment-experienced (overall) interferon eligible – Non-cirrhotic only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£22,432	18.76	15.03	NA	NA	NA	NA	NA
PR + Telaprevir	£35,402	19.33	15.59	£12,970	0.57	0.56	£23,203	Extended dominance
Simeprevir + PR	£38,408	19.33	15.67	£15,977	0.57	0.64	£24,892	Extended dominance
AbbVie regimen	£39,173	19.68	16.11	£16,741	0.92	1.08	£15,495	£15,495
Sofosbuvir + PR	£44,336	19.41	15.81	£21,904	0.65	0.78	£28,262	Dominated

Table 60: Genotype 1 treatment-experienced (overall) interferon eligible – Non-cirrhotic only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£46,482	13.68	10.06	NA	NA	NA	NA	NA
PR + Telaprevir	£58,040	14.92	11.19	£11,557	1.24	1.13	£10,210	Extended dominance

Simeprevir + PR	£59,982	15.10	11.42	£13,500	1.43	1.36	£9,910	Extended dominance
Sofosbuvir + PR	£64,197	15.52	11.86	£17,714	1.84	1.80	£9,840	£9,840
AbbVie regimen	£78,890	16.67	12.96	£32,407	3.00	2.90	£11,163	£13,324

Table 61: Genotype 1a treatment-experienced (overall) interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£29,458	17.22	13.41	NA	NA	NA	NA	NA
PR + Telaprevir	£43,559	17.81	13.96	£14,101	0.59	0.56	£25,242	Extended dominance
Simeprevir + PR	£47,176	17.76	13.98	£17,718	0.54	0.58	£30,602	Extended dominance
Sofosbuvir + PR	£50,691	18.17	14.42	£21,233	0.95	1.02	£20,824	Extended dominance
AbbVie regimen	£55,552	18.71	14.97	£26,093	1.50	1.57	£16,651	£16,651

Table 62: Genotype 1a treatment-experienced (overall) interferon eligible – Non-cirrhotic only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£21,907	18.81	14.99	NA	NA	NA	NA	NA
PR + Telaprevir	£36,138	19.27	15.45	£14,231	0.46	0.46	£31,221	Extended dominance
AbbVie regimen	£39,524	19.66	16.02	£17,617	0.86	1.03	£17,047	£17,047
Simeprevir + PR	£39,911	19.20	15.46	£18,005	0.39	0.47	£38,390	Dominated
Sofosbuvir + PR	£44,336	19.41	15.73	£22,429	0.60	0.74	£30,233	Dominated

Table 63: Genotype 1a treatment-experienced (overall) interferon eligible – Cirrhotic only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£45,505	13.83	10.04	NA	NA	NA	NA	NA
PR + Telaprevir	£59,328	14.72	10.82	£13,823	0.89	0.78	£17,790	Extended dominance
Simeprevir + PR	£62,614	14.69	10.85	£17,109	0.86	0.81	£21,052	Extended dominance

Sofosbuvir + PR	£64,197	15.52	11.65	£18,692	1.69	1.61	£11,610	£11,610
AbbVie regimen	£89,610	16.70	12.74	£44,105	2.87	2.70	£16,330	£23,296

Table 64: Genotype 1b treatment-experienced (overall) interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£30,738	17.06	13.62	NA	NA	NA	NA	NA
PR + Telaprevir	£41,579	18.04	14.56	£10,841	0.98	0.95	£11,437	Extended dominance
AbbVie regimen	£43,790	18.72	15.40	£13,052	1.66	1.78	£7,338	£7,338
Simeprevir + PR	£43,918	18.14	14.74	£13,180	1.08	1.12	£11,780	Dominated
Sofosbuvir + PR	£50,691	18.17	14.81	£19,953	1.10	1.19	£16,741	Dominated

Table 65: Genotype 1b treatment-experienced (overall) interferon eligible – Non-cirrhotic only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£22,909	18.72	15.19	NA	NA	NA	NA	NA
PR + Telaprevir	£34,542	19.40	15.84	£11,633	0.68	0.65	£17,912	Extended dominance
Simeprevir + PR	£37,285	19.42	15.94	£14,376	0.71	0.75	£19,087	Extended dominance
AbbVie regimen	£38,398	19.71	16.31	£15,489	0.99	1.12	£13,831	£13,831
Sofosbuvir + PR	£44,336	19.41	15.98	£21,427	0.69	0.79	£27,265	Dominated

Table 66: Genotype 1b treatment-experienced (overall) interferon eligible – Cirrhotic only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£47,375	13.54	10.27	NA	NA	NA	NA	NA
AbbVie regimen	£55,249	16.62	13.45	£7,874	3.08	3.18	£2,477	£2,477
PR + Telaprevir	£56,534	15.15	11.86	£9,159	1.61	1.58	£5,789	Dominated
Simeprevir + PR	£58,015	15.41	12.17	£10,640	1.87	1.90	£5,612	Dominated
Sofosbuvir + PR	£64,197	15.52	12.33	£16,822	1.98	2.05	£8,188	Dominated

Table 67: Genotype 4 treatment-naïve interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£21,940	20.03	16.85	NA	NA	NA	NA	NA
Simeprevir + PR	£35,869	20.31	17.35	£13,929	0.28	0.50	£27,972	Extended dominance
AbbVie regimen	£41,401	20.63	17.89	£19,462	0.60	1.04	£18,783	£18,783
Sofosbuvir + PR	£43,291	20.56	17.79	£21,351	0.53	0.94	£22,663	Dominated

Table 68: Genotype 4 treatment-naïve interferon eligible – Non-cirrhotic only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£19,286	20.58	17.54	NA	NA	NA	NA	NA
Simeprevir + PR	£33,701	20.76	17.99	£14,415	0.19	0.44	£32,548	Extended dominance
AbbVie regimen	£36,490	20.98	18.47	£17,204	0.40	0.92	£18,673	£18,673
Sofosbuvir + PR	£41,237	20.98	18.43	£21,951	0.40	0.88	£24,806	Dominated

Table 69: Genotype 4 treatment-naïve interferon eligible –Cirrhotic only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
Peg + Riba (PR)	£45,822	15.06	10.59	NA	NA	NA	NA	NA
Simeprevir + PR	£55,377	16.22	11.59	£9,555	1.17	0.99	£9,616	£9,616
Sofosbuvir + PR	£61,777	16.80	12.05	£15,955	1.74	1.46	£10,949	£13,806
AbbVie regimen	£85,602	17.49	12.66	£39,781	2.43	2.07	£19,222	£38,911

Table 70: Genotype 4 treatment-experienced (overall) interferon eligible - Any Fibrosis Stage

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
No treatment	£24,245	16.84	13.50	NA	NA	NA	NA	NA
Simeprevir + PR	£45,366	18.00	15.30	£21,122	1.17	1.80	£11,752	Extended dominance

Sofosbuvir + PR	£50,691	18.17	15.47	£26,447	1.33	1.97	£13,438	Extended dominance
AbbVie regimen	£52,199	18.73	16.32	£27,954	1.89	2.81	£9,935	£9,935

Table 71: Genotype 4 treatment-experienced (overall) interferon eligible – Non-cirrhotic only

Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
No treatment	£16,186	18.57	15.26	NA	NA	NA	NA	NA
AbbVie regimen	£36,536	19.71	17.69	£20,350	1.14	2.43	£8,370	£8,370
Simeprevir + PR	£37,421	19.48	17.11	£21,236	0.91	1.86	£11,446	Dominated
Sofosbuvir + PR	£44,336	19.41	17.02	£28,150	0.84	1.76	£15,951	Dominated

Table 72: Genotype 4 treatment-experienced (overall) interferon eligible – Cirrhotic only

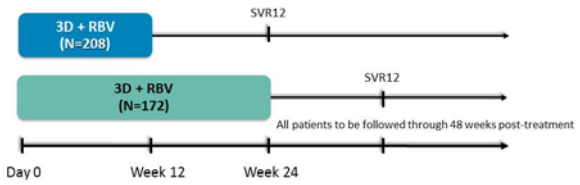
Regimen	Total costs, £	Total LYG	Total QALYs	Incremental costs, £	Incremental LYGs	Incremental QALYs	ICER vs. baseline	ICER incremental
No treatment	£41,370	13.16	9.77	NA	NA	NA	NA	NA
Simeprevir + PR	£62,249	14.87	11.45	£20,879	1.71	1.67	£12,473	Extended dominance
Sofosbuvir + PR	£64,197	15.52	12.17	£22,827	2.36	2.40	£9,511	£9,511
AbbVie regimen	£85,482	16.66	13.40	£44,112	3.50	3.63	£12,164	£17,355

3) *Confirm the marketing position of AbbVie relating to 12 weeks' treatment in people with genotype 1a chronic hepatitis C with cirrhosis with justification for a 12 week treatment regimen in this population, and with reference to the marketing authorisation/summary of product characteristics. Comment whether a 12 week treatment with 2D plus ribavirin would be an option for some patients with genotype 4 chronic hepatitis C with cirrhosis as well. Please also provide the relevant details from the clinical guideline (published in March/April 2015) referred to in the Committee discussion that has made recommendations relating to the use/duration of 3D plus ribavirin and 2D plus ribavirin for these populations.*

Abbvie can confirm that the marketing position for 3D allows for the recommendation of 12 weeks of therapy in GT1a cirrhotic patients with all three favourable baseline laboratory values (AFP < 20 ng/mL, platelets ≥ 90 x 109/L and albumin ≥ 35 g/L). This is consistent with the summary of product characteristics' (SmPC) for both ombitasvir/paritaprevir/ritonavir and dasabuvir which form the basis of the EMA's regulatory approval and licensed indication. Background information related to this positioning is provided below.

The safety and efficacy of ombitasvir/paritaprevir/ritonavir and dasabuvir (3D) administered with ribavirin (RBV) in compensated cirrhotic patients was established in the TURQUOISE 2 study which was an open label study conducted in 380 patients across 78 sites in Europe and North America and dedicated to cirrhotic patients. Patients were randomised to receive 3D with RBV for either 12 weeks or 24 weeks. This study included patients with GT1a and GT1b viral sub-genotype. It also included patients that were both treatment naïve as well as patients with prior experience of non-curative pegylated-interferon (pegIFN) + RBV therapy.

TURQUOISE-II Study Design: Phase 3 Trial Conducted Exclusively in GT1-Infected Cirrhotic Patients (N=380)



3D: co-formulated ABT-450/r/ombitasvir, 150 mg/100 mg/25 mg QD; dasabuvir, 250 mg BID

RBV: 1000-1200 mg daily according to body weight (<75 kg and ≥75kg, respectively)

Adapted from the Fred Poordad presentation at ILC/EASL on April 12, 2014

The primary study objectives were to assess the rate of sustained virologic response (SVR) in the 12-week and 24-week groups for non-inferiority and superiority to a historical control using the SVR of telaprevir plus pegINF and RBV in patients with HCV genotype 1 infection and compensated cirrhosis. The key secondary efficacy end point was the percentage of patients with an SVR in the 24-week group as compared with the 12-week group. Other secondary efficacy end points were the percentage of patients in each group with virologic failure during treatment or relapse after treatment. The rate of SVR at post-treatment week 12 was also determined for patient subgroups defined according to pre-specified baseline demographic or clinical characteristics. SVR results are presented below.

SVR12 for GT1-infected subjects with compensated cirrhosis who were treatment naïve or previously treated with pegIFN/RBV

	12 weeks			24 weeks		
	n/N	**%**	**CI**	**n/N**	**%**	**CI**
Overall SVR12	191/208	91.8%	87.6, 96.1	166/172	96.5	93.4, 99.6
HCV GT1a	124/140	88.6	83.3, 93.8	115/121	95.0	91.2, 98.9
Treatment Naive	59/64	92.2		53/56	94.6	
Prior pegIFN/RBV null responders	40/50	80.0		39/42	92.9	
Prior pegIFN/RBV partial responders	11/11	100		10/10	100	
Prior pegIFN/RBV prior relapsers	14/15	93.3		13/13	100	
HCV GT1b	67/68	98.5	95.7, 100	51/51	100	93.0, 100
Treatment Naive	22/22	100		18/18	100	
Prior pegIFN/RBV null responders	25/25	100		20/20	100	
Prior pegIFN/RBV partial responders	6/7	85.7		3/3	100	
Prior pegIFN/RBV prior relapsers	14/14	100		10/10	100	
Outcome for subjects without SVR						
On-treatment Virologic Failure	1/208	0.5		3/172	1.7	
Relapse	12/203	5.9		1/164	0.6	
Other	4/208	1.9		2/172	1.21	

In the 12-week treatment arm SVR rates were above 90% in all but two of the subgroups presented above. These two subgroups were the GT1b prior pegIFN/RBV prior partial responders and the GT1a prior null responders. The SVR rate in the GT1b pegIFN/RBV prior partial responders was 85.7% due to one of the seven patients in this small group experiencing a post treatment relapse. In the GT1a prior null responders seven of fifty patients in this group experienced post treatment relapse and three did not achieve an SVR for reasons other than on-treatment virologic failure or relapse. Review of the 24 week data for the GT1a prior null responders shows that an SVR rate of 92.9% was achieved (n = 39/42).

Based on these data AbbVie's submission for a marketing authorisation for 3D to the EMA proposed 12 weeks of treatment for all GT1a cirrhotic patients other than prior null responders for whom 24 weeks was proposed. Discussions with EMA in this regard led to AbbVie conducting a post-hoc analysis specifically looking at predictors of relapse in GT1a cirrhotic patients treated with 12 weeks of 3D. This resulted in the inclusion of a statement in the Summary of Product Characteristics' for 3D stating that, in subjects with all three favourable baseline laboratory values (AFP < 20 ng/mL, platelets ≥ 90 x 109/L and albumin ≥ 35 g/L), relapse rates were similar in subjects treated for 12 or 24 weeks. The additional information contained in the SmPCs for Viekirax® (ombitasvir/paritaprevir/ritonavir) and Exviera® (dasabuvir) in relation to this statement is detailed below.

	Viekirax and Exviera with RBV 12-week arm	***Viekirax and Exviera with RBV 24-week arm***
Number of Responders at the End of Treatment	*135*	*113*
AFP <20 ng/ml, platelets ≥ 90 x 10^9/L, AND albumin ≥ 35 g/L prior to treatment*		
Yes (for all three parameters listed above)	*1/87 (1%)*	*0/68 (0%)*
No (for all three parameters listed above)	*10/48 (21%)*	*1/45 (2%)*
**AFP = serum alpha fetoprotein*		

In subjects with all three favourable baseline laboratory values (AFP < 20 ng/mL, platelets ≥ 90 x 109/L, and albumin ≥ 35 g/L), relapse rates were similar in subjects treated for 12 or 24 weeks.

Based on this information within the SmPCs for ombitasvir/paritaprevir/ritonavir and dasabuvir AbbVie can confirm that the marketing position for 3D allows for the recommendation of 12 weeks of therapy in GT1a cirrhotic patients with all three favourable baseline laboratory values (AFP < 20 ng/mL, platelets ≥ 90 x 109/L and albumin ≥ 35 g/L).

As discussed in AbbVie's first appraisal committee meeting, in early March 2015 the national societies (BASL, BHIVA, BIA, BSG & BVHG), which represent clinicians with an interest in hepatitis C, convened a meeting of approximately 80 individuals at which a consensus was reached on evidence based treatment and management recommendations to guide clinicians and commissioners (please find the recommendations from this meeting enclosed in our response). In respect of GT1 patients with compensated cirrhosis the following recommendations are made:

Genotype 1 Patients with compensated cirrhosis/severe fibrosis/major extra-hepatic manifestations

Preferred treatment is with all oral direct acting antiviral regimens. The following options are all acceptable on efficacy and safety criteria:

*Ombitasvir/Paritaprevir (r)/Dasabuvir +/- ribavirin**	*12 weeks (Child Pugh A only)*
*Sofosbuvir/Ledipasvir +/- ribavirin**	*12 weeks*
Sofosbuvir/Simeprevir +/- ribavirin	*12 weeks*
Sofosbuvir/Daclatasvir +/- ribavirin	*12 weeks*

For patients with genotype 1a virus, and previous null response to PEG-interferon/Ribavirin, treatment should be 24 weeks of Ombitasvir/Paritaprevir (r)/Dasabuvir/Ribavirin.

These recommendations are made based on the strong evidence base provided by the TURQUOISE 2 study showing that GT1a cirrhotic prior null responders benefit from an extension in treatment duration from 12 to 24 weeks of therapy with 3D plus ribavirin as per the original submission for marketing authorisation to EMA by AbbVie.

Review of the post-hoc analysis by AbbVie referred to above shows significant overlap between GT1a prior null responders and those with one or more unfavourable baseline characteristics detailed in section 5.1 of the ombitasvir/paritaprevir/ritonavir and dasabuvir SmPCs. Over 50% of GT1a cirrhotic prior null-responders treated with 12 weeks of 3D plus RBV in the TURQUOISE 2 study had one or more unfavourable baseline characteristics and would therefore be recommended for 24 weeks of therapy with 3D. Included in this group of patients with unfavourable baseline characteristics are all seven of the GT1a cirrhotic prior null responders who experienced a post treatment relapse following 12 weeks of therapy with 3D in the TURQUOISE 2 study.

AbbVie estimates that if all GT1a cirrhotic prior null responders were to be treated with 24 weeks of 3D this would constitute 9.9% of all GT1a cirrhotics. This figure is based on an assumption that, of all GT1a cirrhotics, 67% will be treatment naïve, 33% will be treatment experienced and that of those treatment experienced patients, 30% will be prior null responders. The post-hoc analysis referred to earlier demonstrated that, of those GT1a treatment naïve or treatment experienced cirrhotic patients treated with 12 weeks of 3D plus RBV in the TURQUOISE 2 study, 36% had one or more unfavourable baseline

characteristics and would be recommended for 24 weeks of therapy as per the SmPCs for ombitasvir/paritaprevir/ritonavir and dasabuvir.

In relation to the question on the use of 12 weeks of therapy with 2D plus ribavirin as an option for some patients with genotype 4 chronic hepatitis C with cirrhosis, AbbVie can confirm that this is not currently a position we could support, there is currently no supporting data in this regard and this is not included within the licensed indication or SmPC for ombitasvir/paritaprevir/ritonavir.

4) *Using appropriate SVR rates (for the 12 week regimen or 24 week regimen) from the TURQUOISE II trial, provide subgroup analyses to explore the effect on the incremental cost-effectiveness ratios (ICERs) of the following:*

    a. *12 week treatment duration of 3D plus ribavirin for people with treatment naïve genotype 1a CHC with compensated cirrhosis.*

    b. *12 week treatment duration of 3D plus ribavirin for treatment experienced genotype 1a CHC with compensated cirrhosis who have relapsed after achieving SVR with previous therapy.*

    c. *12 week treatment duration of 3D plus ribavirin for treatment experienced genotype 1a CHC with compensated cirrhosis who have achieved a partial response to previous therapy.*

    d. *24 week treatment duration of 3D plus ribavirin for treatment experienced genotype 1a CHC with compensated cirrhosis who had not responded to previous therapy (null responders).*

A modification was made to the model (See tab 'SA - AbbVie Duration in GT1a CC) to accommodate this scenario. Below we present results of those comparisons mostly impacted by this scenario. Given that the cost related to 24 weeks of therapy for all GT1a patients with compensated cirrhosis drove all GT1 cases where the AbbVie Regimen's ICER exceeded 30,000 £/QALY threshold, this sensitivity was impactful. In fact, both cases where the AbbVie 3D regimen was not the most cost-effective regimen, it is now the most cost-effective regimen in this sensitivity.

- Genotype 1 treatment-naïve interferon eligible – Cirrhotic patients Only: (ICER changed from £36,139/QALY to dominant or extended dominant)
- Genotype 1a treatment-naïve interferon eligible - Cirrhotic Only: (ICER changed from £75,360/QALY to dominant or extended dominant)

Note that this sensitivity did not apply to the GT1b and GT4 cases.

Table 73: Genotype 1 treatment-naïve interferon eligible patients – Any Fibrosis Stage

Regimen	Total costs, £	Total QALYs	Incremental costs, £	Incremental QALYs	ICER vs. baseline (Scenario)	Change from Basecase
Peg + Riba (PR)	£22,872	13.72	NA	NA	NA	NA
PR + Boceprevir	£32,147	14.22	£9,275	0.50	£18,366	£0
PR + Telaprevir	£35,887	14.55	£13,014	0.83	£15,602	£0
Simeprevir + PR	£36,934	14.62	£14,062	0.90	£15,595	£0
AbbVie regimen	£41,266	15.21	£18,394	1.49	£12,329	-£1,535
Sofosbuvir + PR	£44,337	15.01	£21,465	1.29	£16,618	£0

Table 74: Genotype 1 treatment-naïve interferon eligible patients – Non cirrhotic Only

Regimen	Total costs, £	Total QALYs	Incremental costs, £	Incremental QALYs	ICER vs. baseline (Scenario)	Change from Basecase
Peg + Riba (PR)	£20,483	14.33	NA	NA	NA	NA
PR + Boceprevir	£29,404	14.90	£8,921	0.57	£15,766	£0
PR + Telaprevir	£33,748	15.16	£13,265	0.82	£16,110	£0
Simeprevir + PR	£34,736	15.23	£14,253	0.90	£15,826	£0
AbbVie regimen	£39,556	15.77	£19,073	1.43	£13,306	£0
Sofosbuvir + PR	£42,400	15.59	£21,916	1.26	£17,363	£0

Table 75: Genotype 1 treatment-naïve interferon eligible patients – Cirrhotic Only

Regimen	Total costs, £	Total QALYs	Incremental costs, £	Incremental QALYs	ICER vs. baseline (Scenario)	Change from Basecase
Peg + Riba (PR)	£44,374	8.18	NA	NA	NA	NA
PR + Telaprevir	£55,132	9.11	£10,757	0.93	£11,560	£0
AbbVie regimen	£56,652	10.19	£12,278	2.02	£6,085	-£11,265
Simeprevir + PR	£56,721	9.09	£12,346	0.91	£13,537	£0
PR + Boceprevir	£56,827	8.13	£12,453	-0.04	-£289,717	£0
Sofosbuvir + PR	£61,777	9.73	£17,402	1.56	£11,182	£0

Table 76: Genotype 1a treatment-naïve interferon eligible patients – Any Fibrosis Stage

Regimen	Total costs, £	Total QALYs	Incremental costs, £	Incremental QALYs	ICER vs. baseline (Scenario)	Change from Basecase
Peg + Riba (PR)	£23,305	13.64	NA	NA	NA	NA
PR + Boceprevir	£32,905	14.09	£9,601	0.45	£21,411	£0
PR + Telaprevir	£36,378	14.47	£13,073	0.82	£15,865	£0
Simeprevir + PR	£37,639	14.50	£14,334	0.85	£16,773	£0
AbbVie regimen	£41,682	15.17	£18,377	1.53	£12,023	-£2,176
Sofosbuvir + PR	£44,064	15.06	£20,760	1.41	£14,680	£0

Table 77: Genotype 1a treatment-naïve interferon eligible patients – Non cirrhotic Only

Regimen	Total costs, £	Total QALYs	Incremental costs, £	Incremental QALYs	ICER vs. baseline (Scenario)	Change from Basecase
Peg + Riba (PR)	£20,888	14.26	NA	NA	NA	NA
PR + Boceprevir	£30,114	14.77	£9,226	0.51	£18,069	£0
PR + Telaprevir	£34,208	15.07	£13,320	0.81	£16,373	£0
Simeprevir + PR	£35,395	15.11	£14,507	0.85	£16,976	£0
AbbVie regimen	£39,955	15.73	£19,067	1.47	£12,949	£0
Sofosbuvir + PR	£42,144	15.64	£21,256	1.38	£15,383	£0

Table 78: Genotype 1a treatment-naïve interferon eligible patients – Cirrhotic Only

Regimen	Total costs, £	Total QALYs	Incremental costs, £	Incremental QALYs	ICER vs. baseline (Scenario)	Change from Basecase
Peg + Riba (PR)	£45,057	8.08	NA	NA	NA	NA
PR + Telaprevir	£55,907	9.00	£10,850	0.92	£11,815	£0
AbbVie regimen	£57,225	10.12	£12,169	2.03	£5,985	-£16,082
Simeprevir + PR	£57,832	8.94	£12,775	0.85	£14,944	£0
PR + Boceprevir	£58,024	7.97	£12,967	-0.11	-£116,181	£0
Sofosbuvir + PR	£61,347	9.79	£16,290	1.70	£9,555	£0

Table 79: Genotype 1 treatment-experienced (overall) interferon eligible – Any Fibrosis Stage

Regimen	Total costs, £	Total QALYs	Incremental costs, £	Incremental QALYs	ICER vs. baseline (Scenario)	Change from Basecase
Peg + Riba (PR)	£30,128	11.07	NA	NA	NA	NA
PR + Telaprevir	£42,646	12.10	£12,518	1.04	£12,095	£0
Simeprevir + PR	£45,312	12.25	£15,184	1.18	£12,816	£0
AbbVie regimen	£46,646	13.17	£16,518	2.10	£7,848	-£2,410
Sofosbuvir + PR	£50,691	12.51	£20,564	1.44	£14,256	£0

Table 80: Genotype 1 treatment-experienced (overall) interferon eligible – Non-cirrhotic Only

Regimen	Total costs, £	Total QALYs	Incremental costs, £	Incremental QALYs	ICER vs. baseline (Scenario)	Change from Basecase
Peg + Riba (PR)	£22,432	12.82	NA	NA	NA	NA
PR + Telaprevir	£35,402	13.90	£12,970	1.07	£12,105	£0
Simeprevir + PR	£38,408	14.02	£15,977	1.20	£13,361	£0
AbbVie regimen	£39,173	14.78	£16,741	1.95	£8,581	£0
Sofosbuvir + PR	£44,336	14.22	£21,904	1.40	£15,692	£0

Table 81: Genotype 1 treatment-experienced (overall) interferon eligible – Cirrhotic Only

Regimen	Total costs, £	Total QALYs	Incremental costs, £	Incremental QALYs	ICER vs. baseline (Scenario)	Change from Basecase
Peg + Riba (PR)	£46,482	7.33	NA	NA	NA	NA
PR + Telaprevir	£58,040	8.29	£11,557	0.96	£12,071	£0
Simeprevir + PR	£59,982	8.49	£13,500	1.16	£11,623	£0
AbbVie regimen	£62,527	9.76	£16,045	2.43	£6,599	-£6,461
Sofosbuvir + PR	£64,197	8.87	£17,714	1.54	£11,492	£0

Table 82: Genotype 1a treatment-experienced (overall) interferon eligible – Any Fibrosis Stage

Regimen	Total costs, £	Total QALYs	Incremental costs, £	Incremental QALYs	ICER vs. baseline (Scenario)	Change from Basecase
Peg + Riba (PR)	£29,458	11.16	NA	NA	NA	NA
PR + Telaprevir	£43,559	11.96	£14,101	0.80	£17,543	£0
Simeprevir + PR	£47,176	11.97	£17,718	0.81	£21,839	£0
AbbVie regimen	£47,941	13.15	£18,483	1.99	£9,301	-£3,677
Sofosbuvir + PR	£50,691	12.51	£21,233	1.35	£15,756	£0

Table 83: Genotype 1a treatment-experienced (overall) interferon eligible – Non-cirrhotic only

Regimen	Total costs, £	Total QALYs	Incremental costs, £	Incremental QALYs	ICER vs. baseline (Scenario)	Change from Basecase
Peg + Riba (PR)	£21,907	12.91	NA	NA	NA	NA
PR + Telaprevir	£36,138	13.77	£14,231	0.86	£16,487	£0
AbbVie regimen	£39,524	14.74	£17,617	1.84	£9,589	£0
Simeprevir + PR	£39,911	13.76	£18,005	0.86	£21,026	£0
Sofosbuvir + PR	£44,336	14.22	£22,429	1.31	£17,079	£0

Table 84: Genotype 1a treatment-experienced (overall) interferon eligible –Cirrhotic only

Regimen	Total costs, £	Total QALYs	Incremental costs, £	Incremental QALYs	ICER vs. baseline (Scenario)	Change from Basecase
Peg + Riba (PR)	£45,505	7.45	NA	NA	NA	NA
PR + Telaprevir	£59,328	8.13	£13,823	0.68	£20,403	£0
Simeprevir + PR	£62,614	8.17	£17,109	0.72	£23,905	£0
Sofosbuvir + PR	£64,197	8.87	£18,692	1.42	£13,157	£0
AbbVie regimen	£65,828	9.76	£20,323	2.31	£8,812	-£9,727

5) *Provide probabilistic sensitivity analyses for each base-case analyses varying parameters to a meaningful degree around the value used in the base-case, with the source and rationale for each variation.*

32 probabilistic sensitivity analyses have been provided for the below outlined patient segments, following closely the revised base case analyses:

Segment	Any Fibrosis Stage	Non-Cirrhotic Patients	Cirrhotic Patients
GT1, treatment-naive, IFN-eligible patients	+	+	+
GT1a, treatment-naive, IFN-eligible patients	+	+	+
GT1b, treatment-naive, IFN-eligible patients	+	+	+
GT1, treatment-experienced, IFN-eligible patients	+	+	+
GT1a, treatment-experienced, IFN-eligible patients	+	+	+
GT1b, treatment-experienced, IFN-eligible patients	+	+	+
GT4, treatment-naïve, IFN-eligible patients	+	+	+
GT4, treatment-experienced, IFN-eligible patients	+	+	+
GT1, treatment naïve, IFN-unsuitable*	-	+	+
GT1, treatment experienced, IFN-unsuitable*	-	+	+
GT4, treatment naïve, IFN-unsuitable*	-	+	+
GT4, treatment experienced, IFN-unsuitable*	-	+	+

*In the interest of time, PSA analyses all IFN-unsuitable groups were limited to non-cirrhotic and cirrhotic patients only

All distributions around the SVRs were calculated using beta distributions applying the method of moments based on the numbers of responders and non-responders recorded in the trials. We fit the beta distribution using the method of moments (as opposed to counts of the events of interest, and the complements of those counts). The method of moments requires the standard error be calculated (the standard deviation was not used in these calculations). The standard error was calculated as (SQRT(p*(1-p)/N), consistent with the binomial distribution.

Our approach can be verified by visual inspection of the model on the tab called '3D Inputs', for example. Cells G7, H7, and I7 contain the parameters: n(SVR), N, and prob(SVR) respectively (the numeric values for these parameters are 405, 423, and 95.7% in the arm in row 7 (arm for Naïve IFN Eligible, GT1a, for the AbbVie regimen). Cell AX7 contains the standard error, or SQRT(I7*(1-I7)/H7)=0.010. Cells AY7 and AZ7 contain the alpha and beta parameter of the Beta distribution, calculated based on the method of moments Beta (404.043, 17.957); the alpha was calculated as I7*(((I7*(1-I7))/AX7^2)-1)=403.043. The beta was calculated as ((((I7*(1-I7))/AX7^2)-1)-AY7)= 17.957. For an overview of this approach, please refer to pages 88-89 in Briggs, Andrew, Mark Sculpher, and Karl Claxton. *Decision modelling for health economic evaluation.* Oxford university press, 2006.

The method of moments Beta (403.043, 17.957) has nearly identical parameters to the Beta using counts and complements of counts, which would be Beta (n(SVR), N-n(SVR)), or (405, 18) using the same data. AbbVie believes our approach is appropriate because some subgroups did not have counts and complements of counts (i.e., integers), namely GT1a and GT1b fibrosis subgroups for competitor regimens (data not reported or in the public domain), which therefore had to be imputed. Accordingly, our use of the method of moments Beta, which does not require counts as integers, seems appropriate. Of note, our methodological approach was identically extended to all arms and comparisons, including intervention and all comparators.

Probabilistic sensitivity analysis: multiple CEACs

The 32 PSAs were generally aligned with the base case results. In 29 out of 32 PSAs, the AbbVie Regimen was the most optimal regimen at the willingness to pay threshold of £30,000/QALY. In the other 3 comparisons, the AbbVie Regimen was not the most-cost-effective option, including the list of comparisons below. In each case, sofosbuvir+PR was the preferred therapy. As highlighted previously no trial was conducted that contained a robust sample of GT4, treatment-naïve sofosbuvir+PR patients; only one patient was included in NEUTRINO trial. Our analysis used hypothetical numbers for sofosbuvir+PR in this case. In each of the cases below, the assumption was made that GT1a and GT4 cirrhotic patients universally (100%) received 24 weeks (and not 12 weeks) of the AbbVie Regimen.

1. Figure 3. CEAC, GT1, treatment-naïve (IFN-eligible) patients, cirrhotic only
2. Figure 6. CEAC, GT1a, treatment-naïve (IFN-eligible) patients, cirrhotic only
3. Figure 21. CEAC, GT4, treatment-naïve (IFN-eligible) patients, cirrhotic only

Figure 1. GT1, treatment-naïve (IFN-eligible) patients, any fibrosis stage

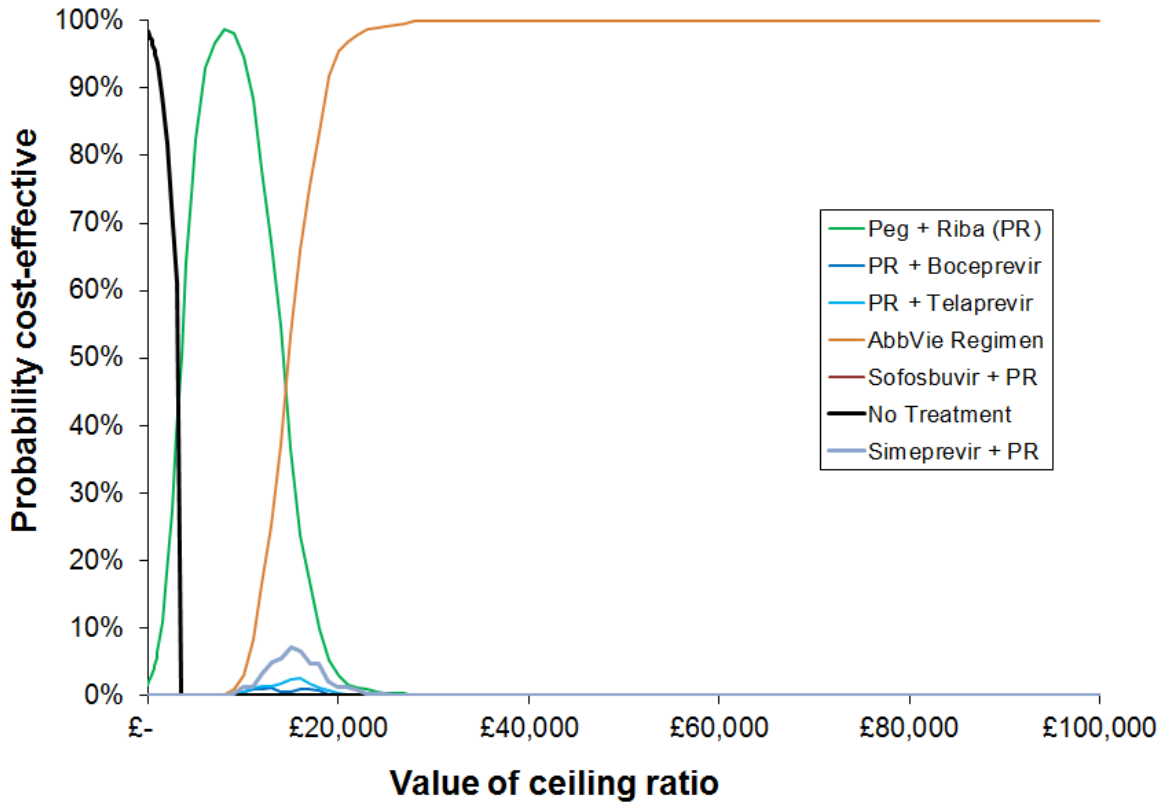


Figure 2. GT1, treatment-naïve (IFN-eligible) patients, non-cirrhotic only

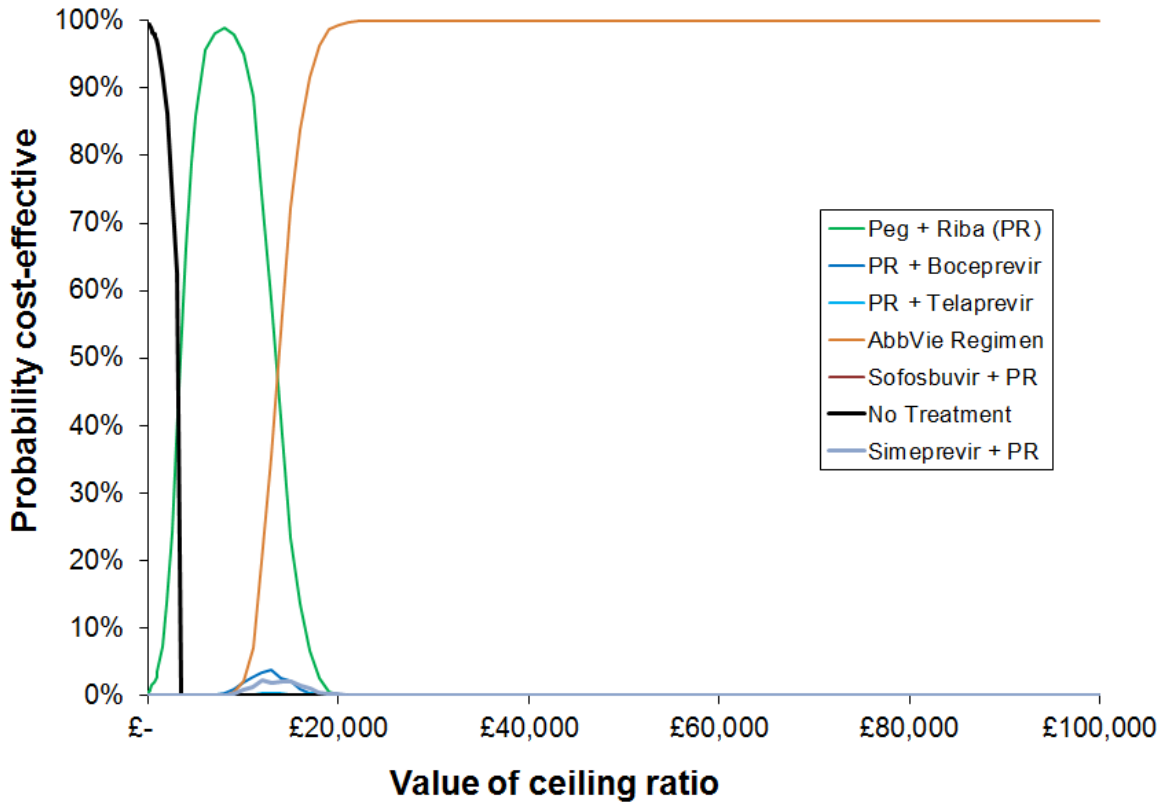


Figure 3. GT1, treatment-naïve (IFN-eligible) patients, cirrhotic only

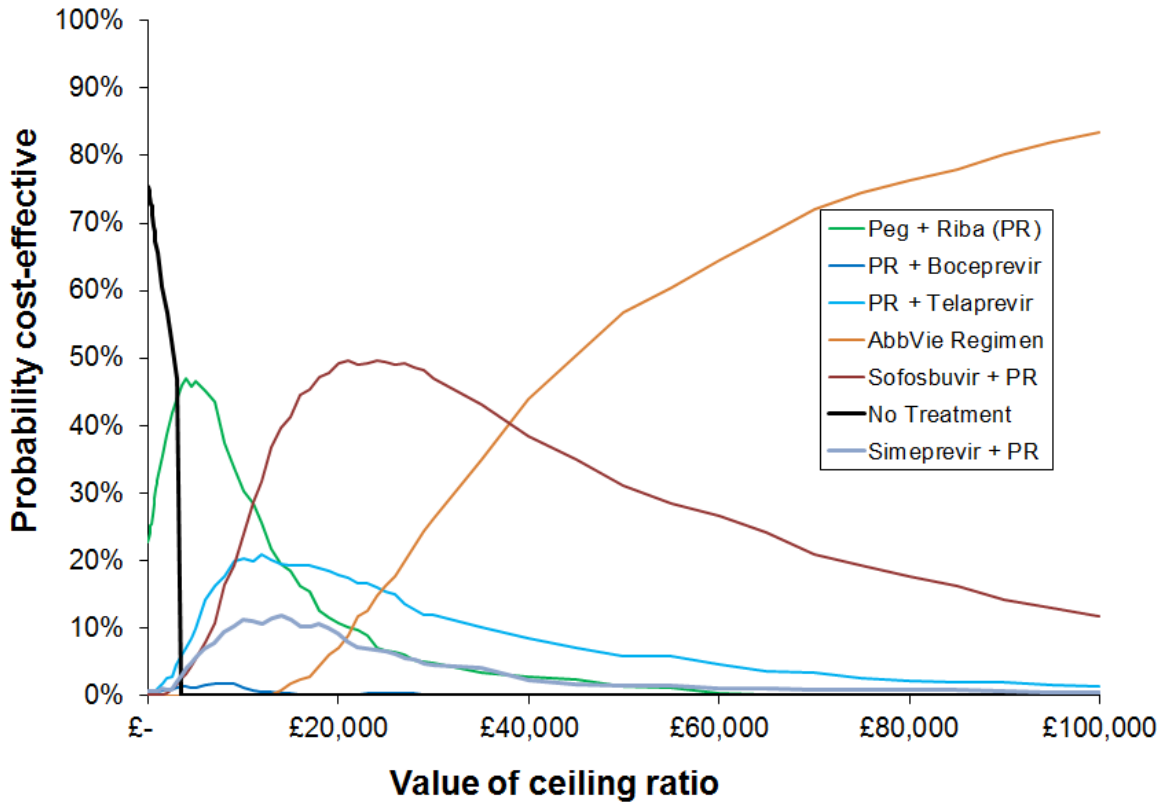


Figure 4. GT1a, treatment-naïve (IFN-eligible) patients, any fibrosis stage

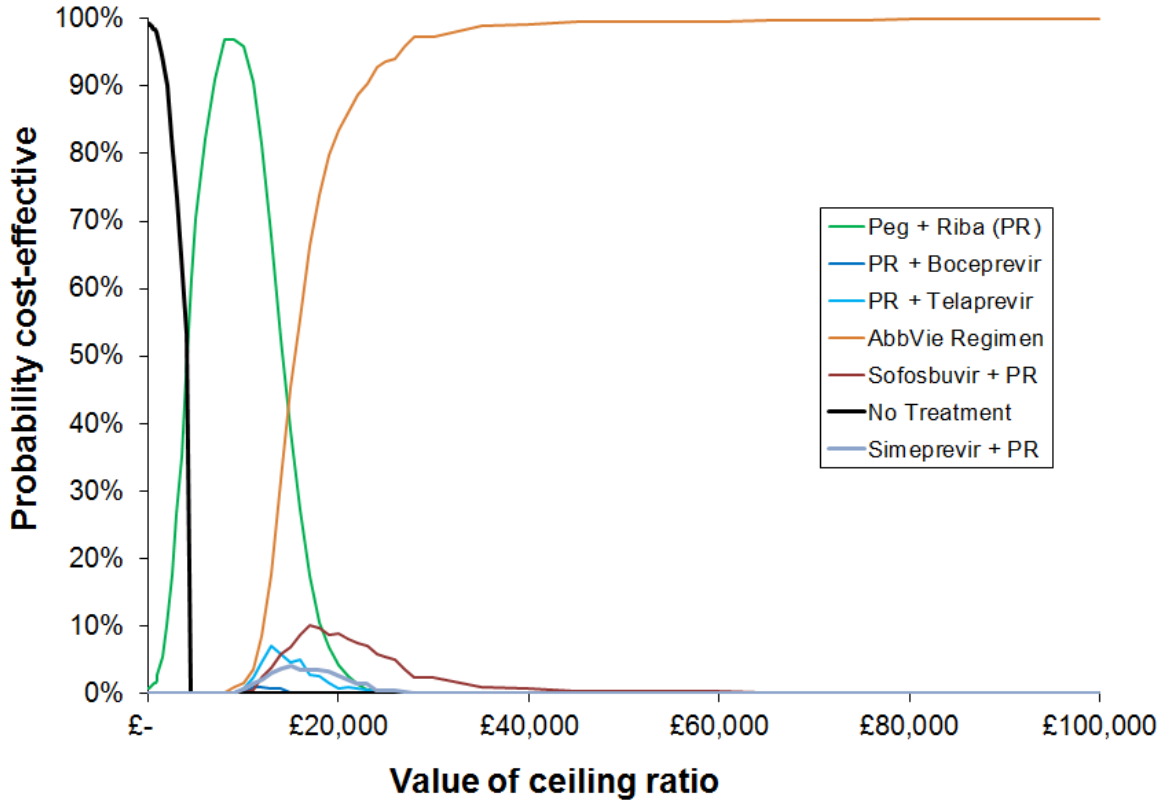


Figure 5. GT1a, treatment-naïve (IFN-eligible) patients, non-cirrhotic only

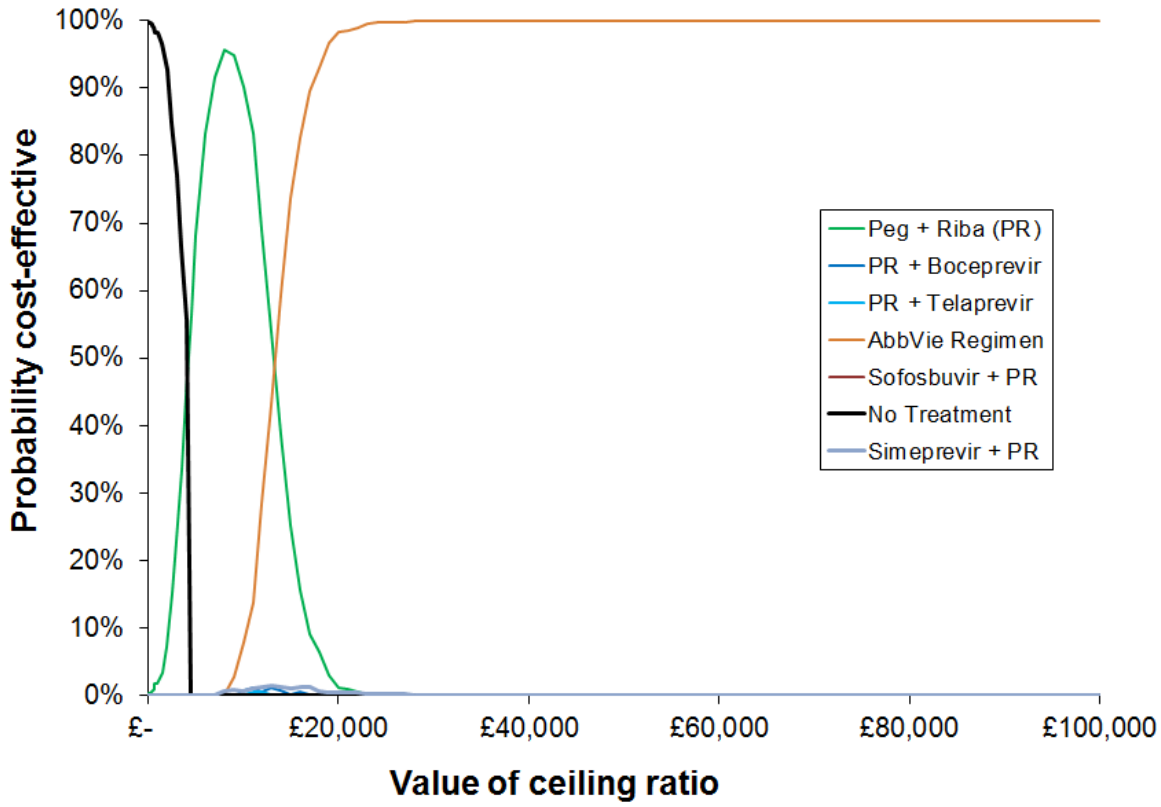


Figure 6. GT1a, treatment-naïve (IFN-eligible) patients, cirrhotic only

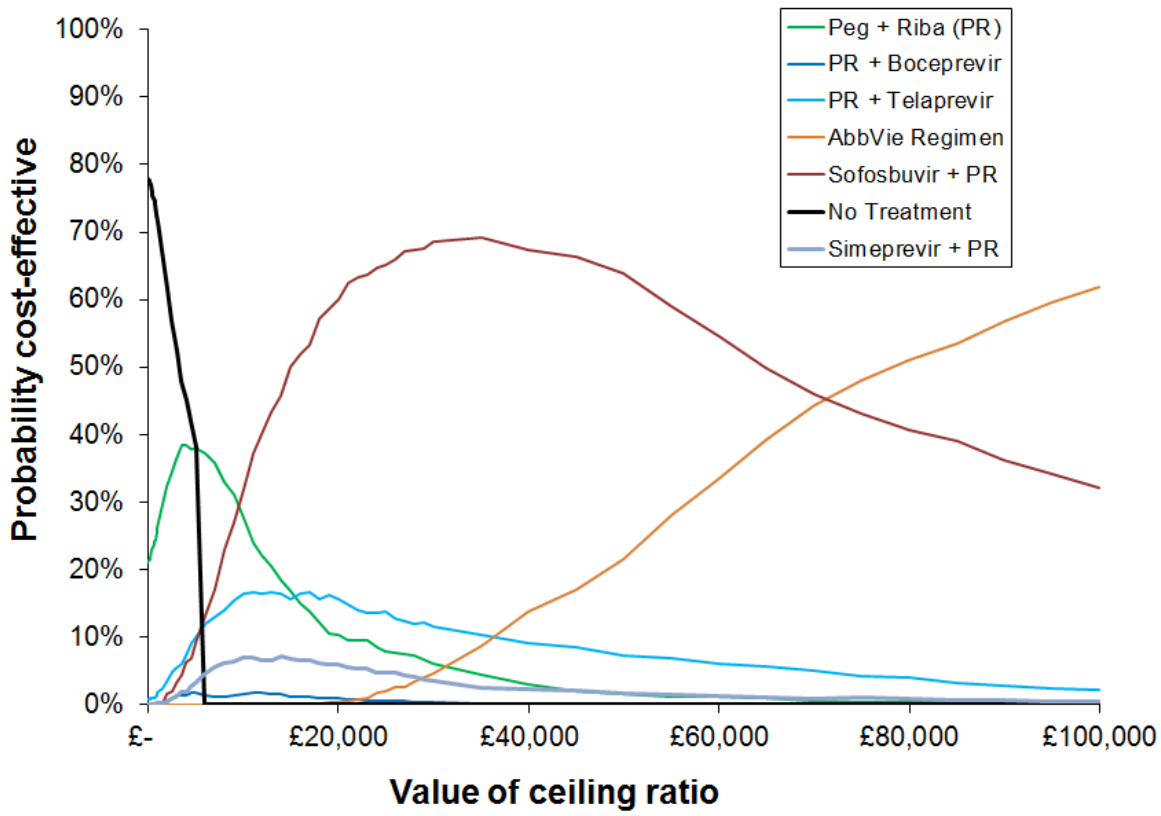


Figure 7. GT1b, treatment-naïve (IFN-eligible) patients, any fibrosis stage

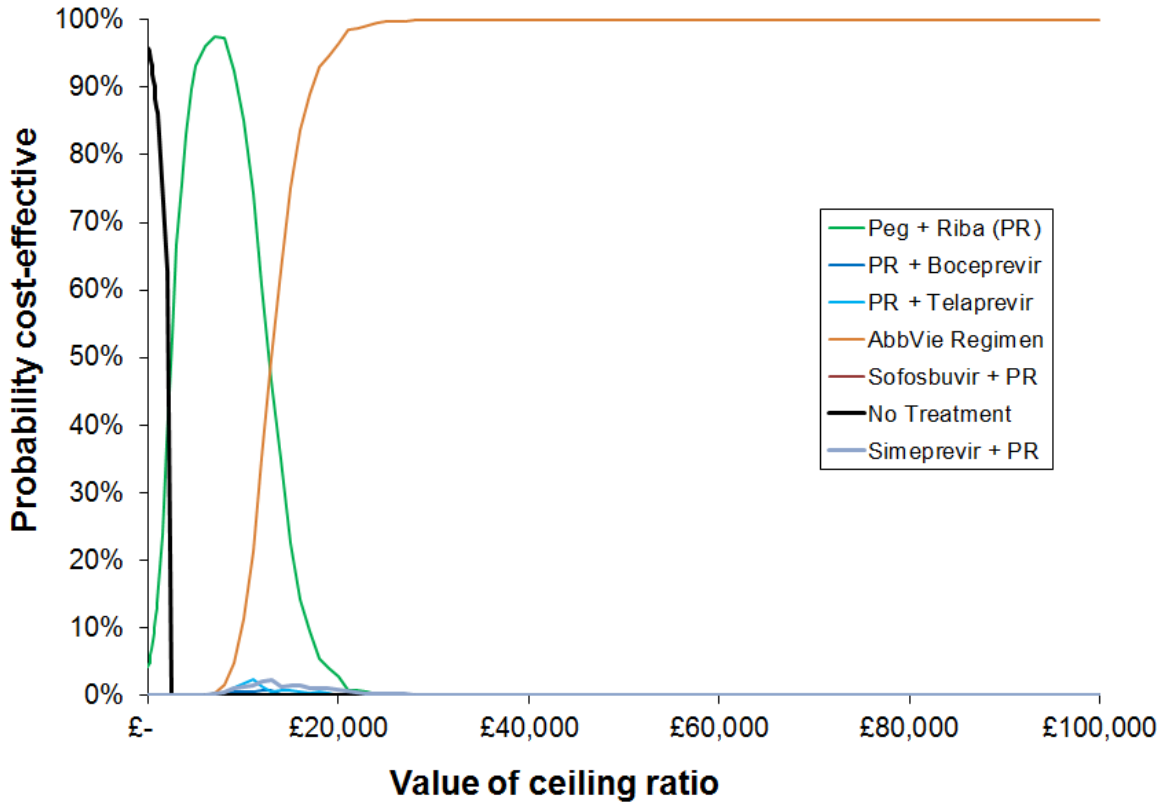


Figure 8. GT1b, treatment-naïve (IFN-eligible) patients, non-cirrhotic only

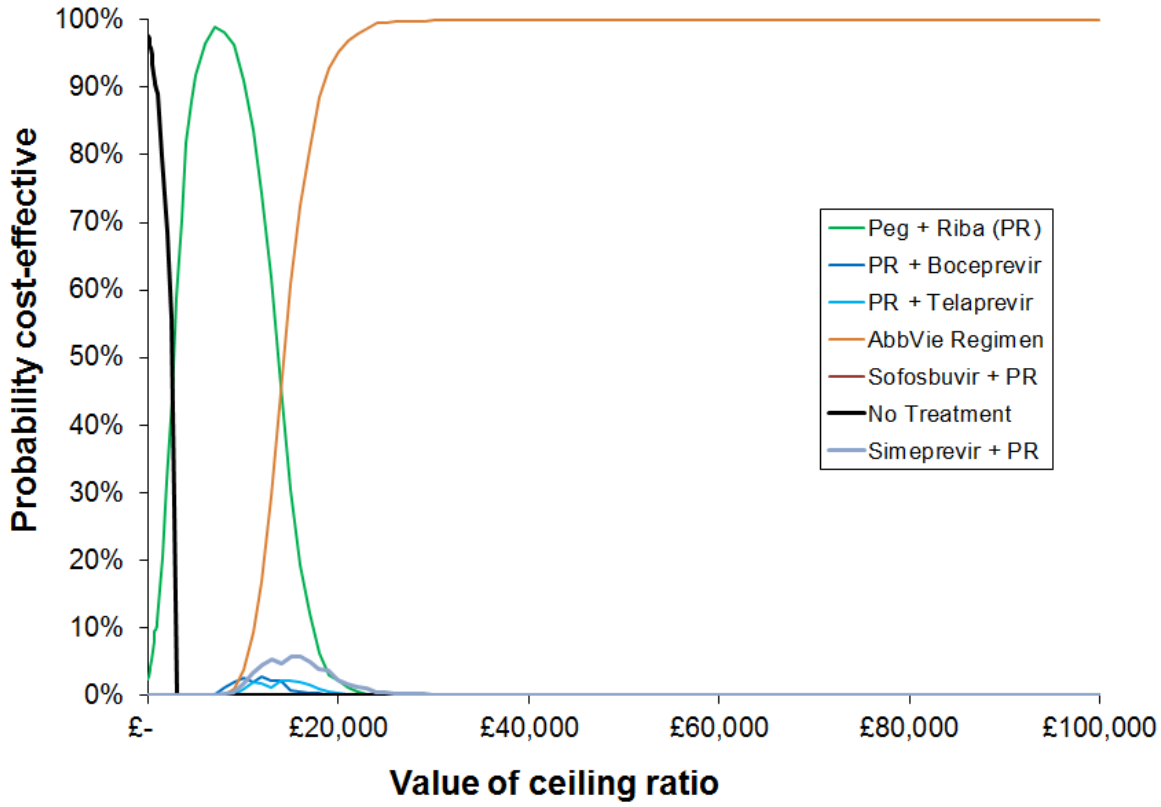


Figure 9. GT1b, treatment-naïve (IFN-eligible) patients, cirrhotic only

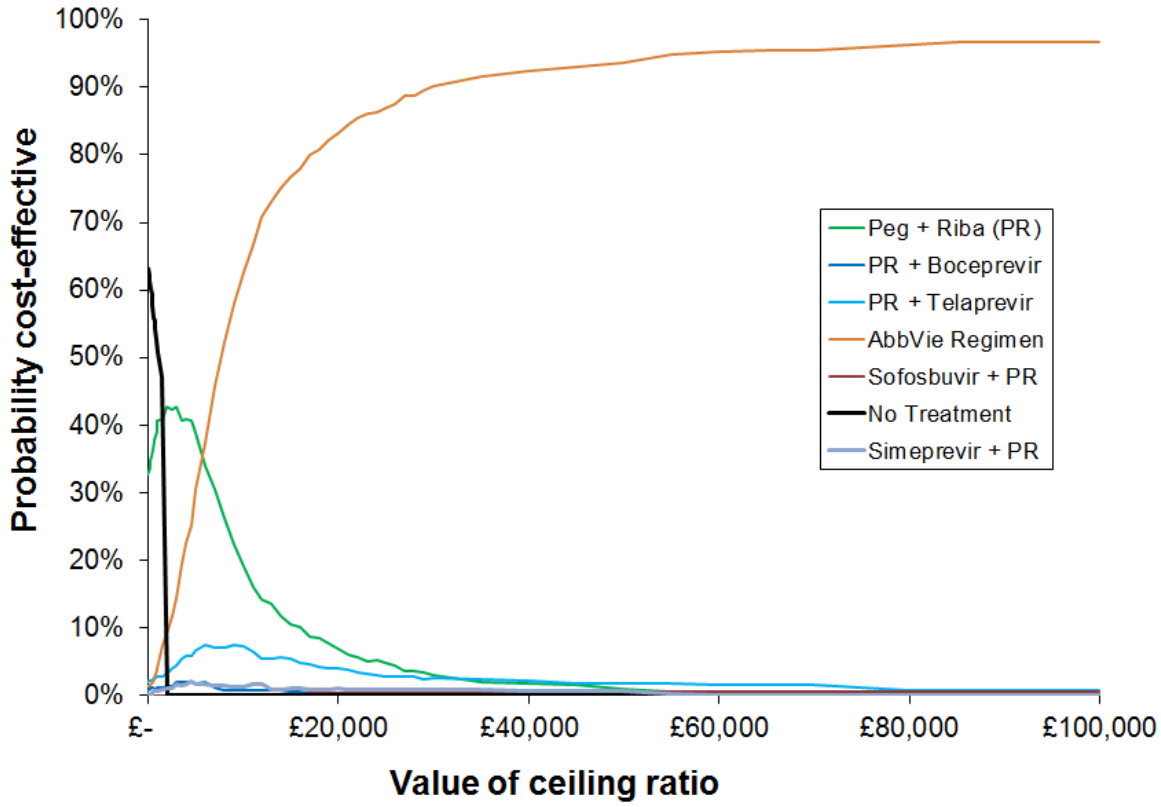


Figure 10. GT1, treatment-experienced (IFN-eligible) patients, any fibrosis stage

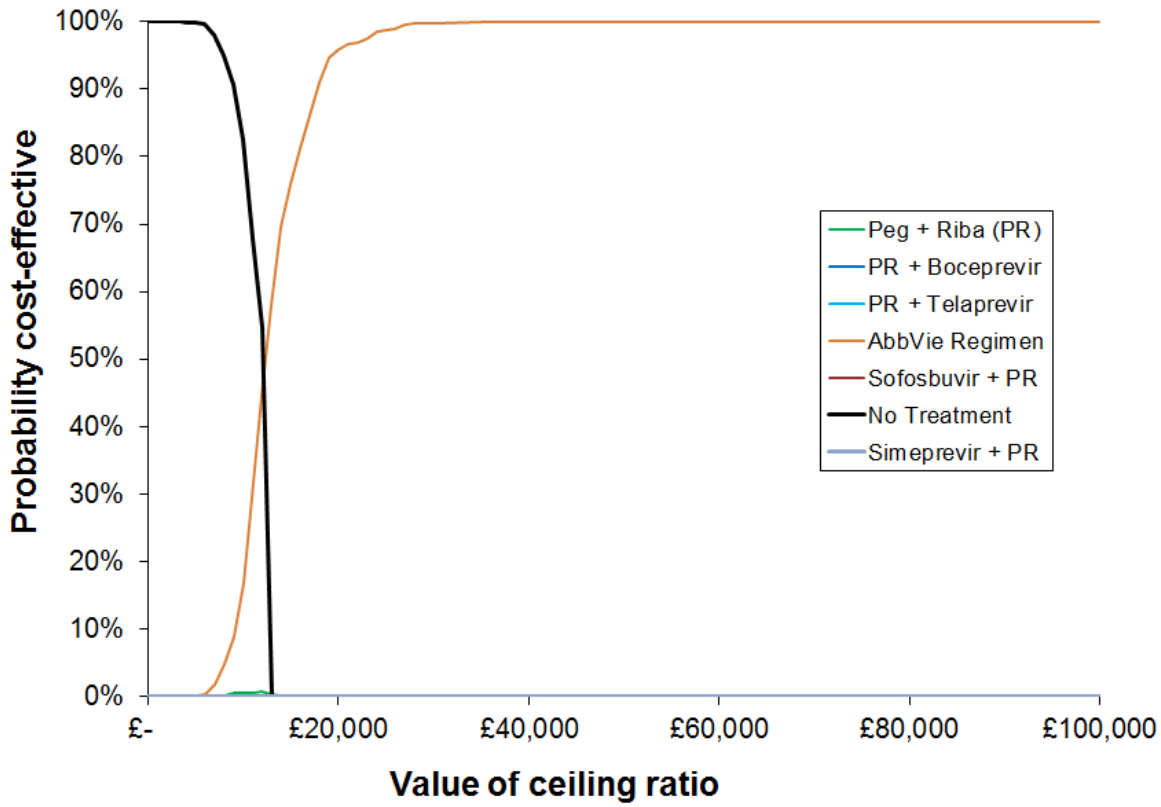


Figure 11. GT1, treatment-experienced (IFN-eligible) patients, non-cirrhotic only

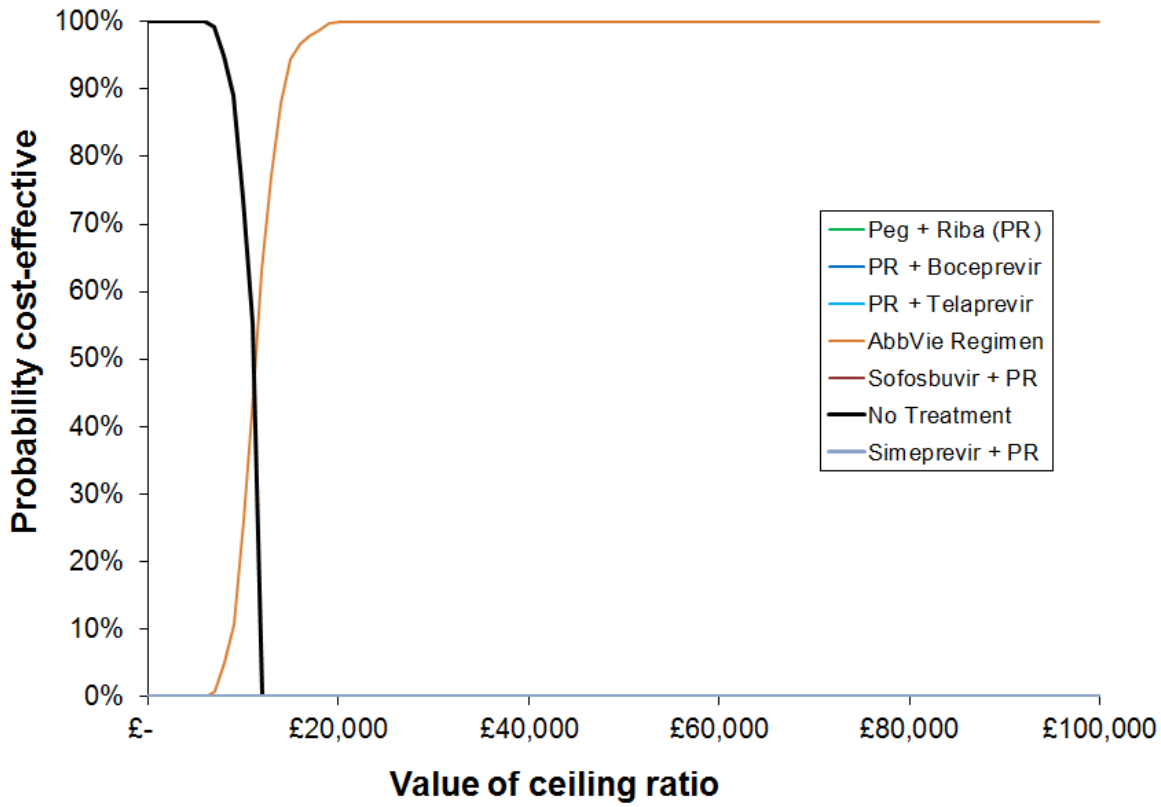


Figure 12. GT1, treatment-experienced (IFN-eligible) patients, cirrhotic only

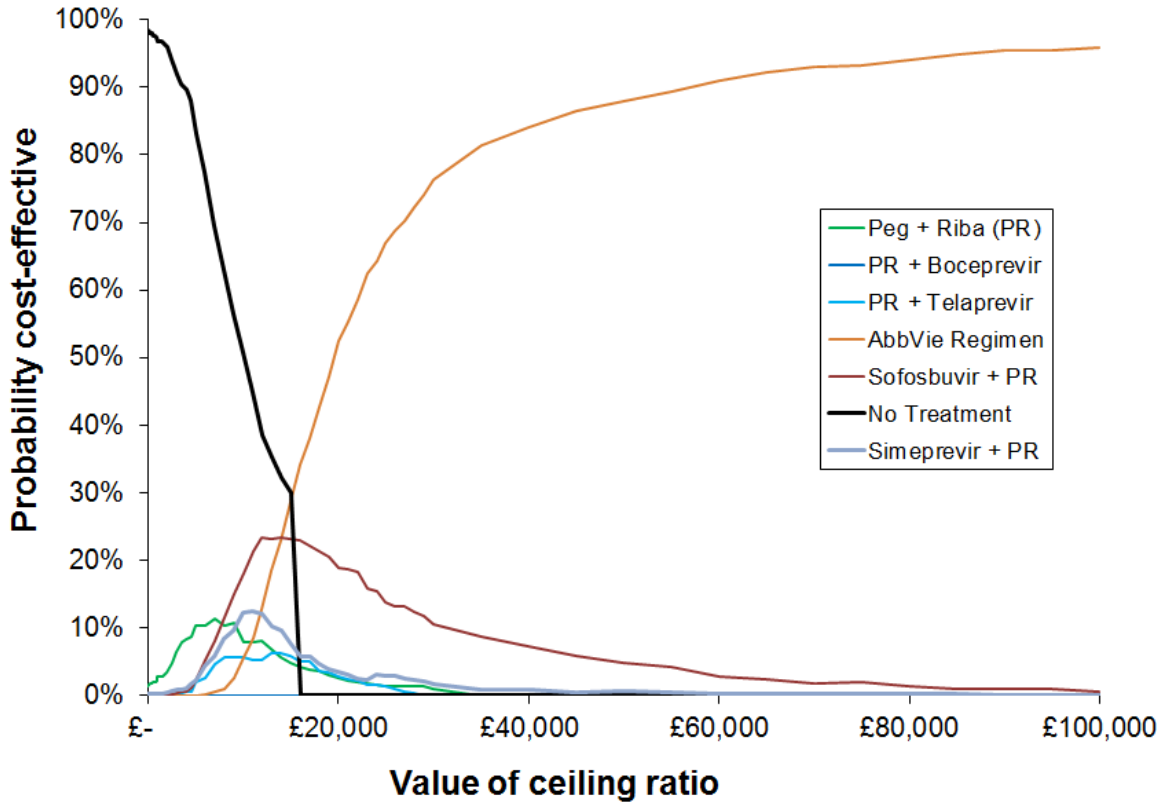


Figure 13. GT1a, treatment-experienced (IFN-eligible) patients, any fibrosis stage

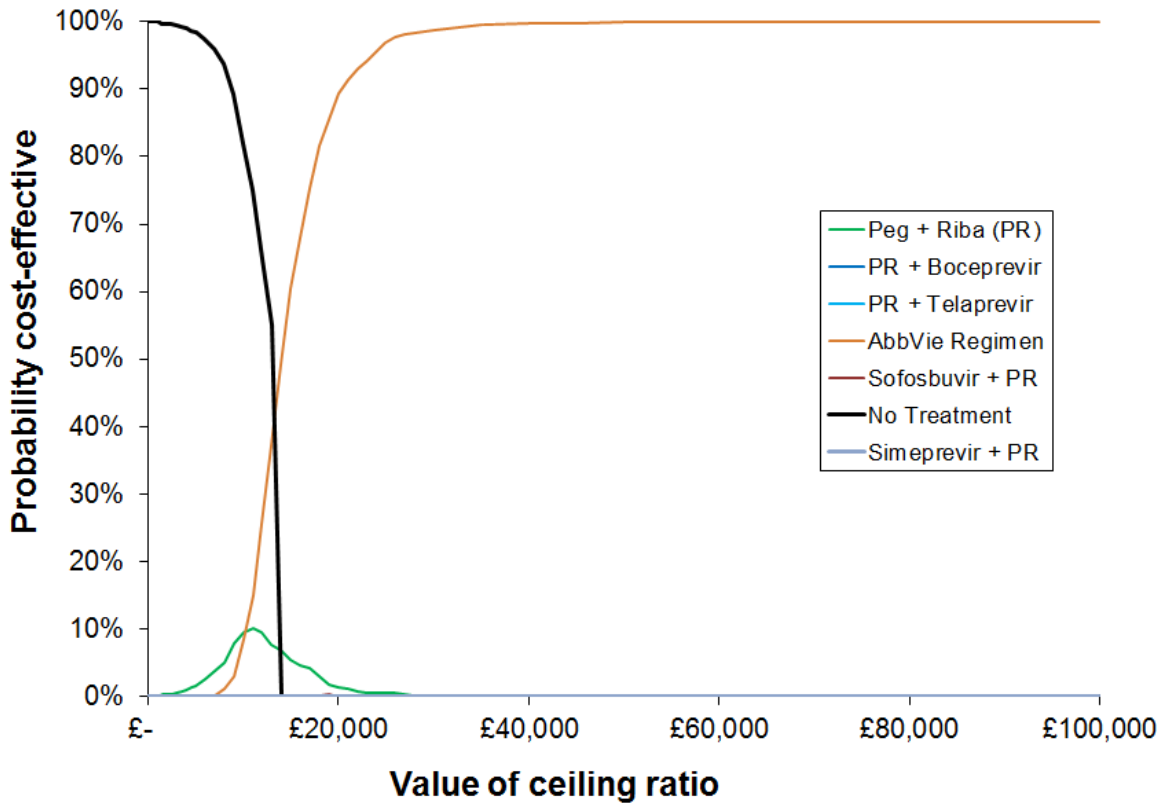


Figure 14. GT1a, treatment-experienced (IFN-eligible) patients, non-cirrhotic only

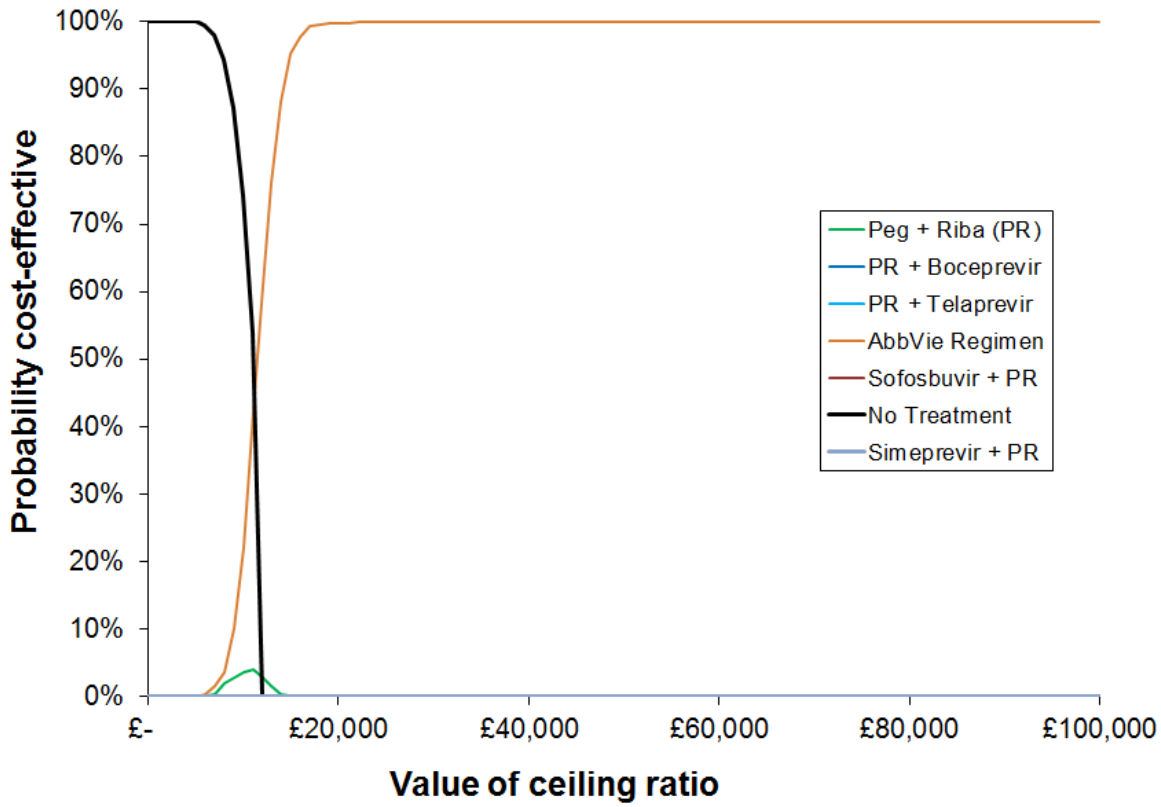


Figure 15. GT1a, treatment-experienced (IFN-eligible) patients, cirrhotic only

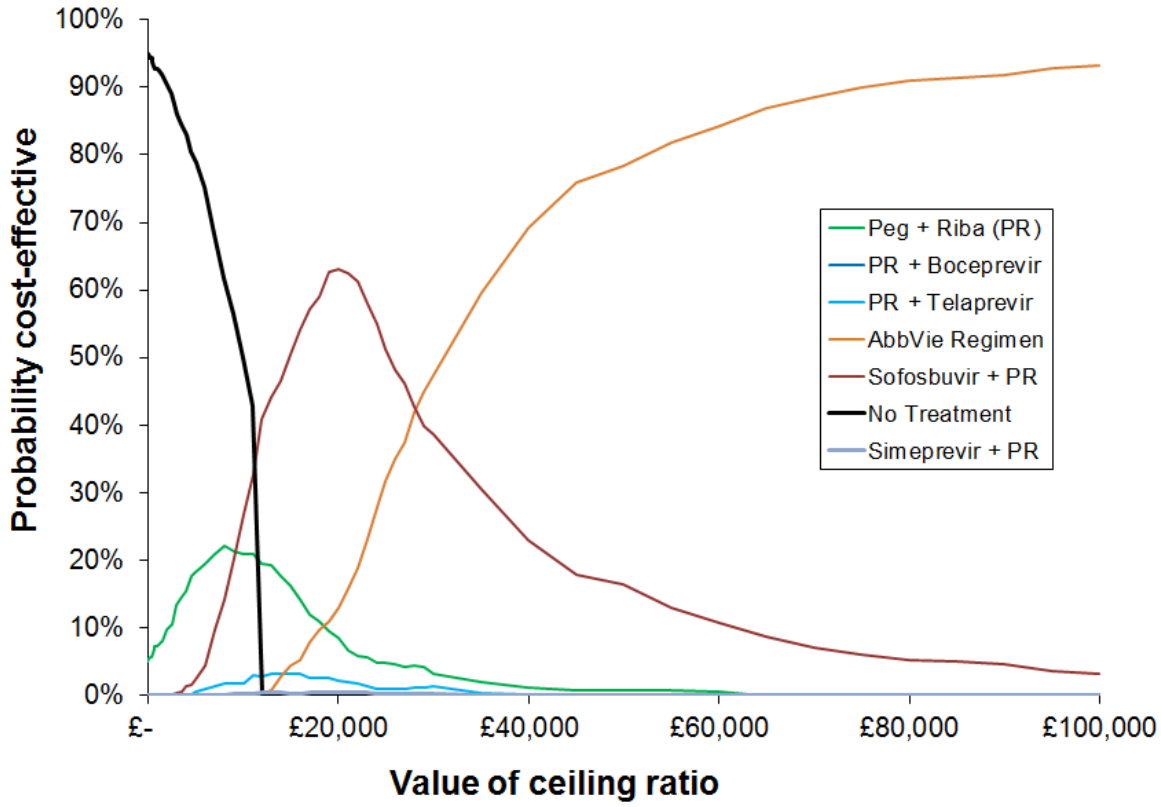


Figure 16. GT1b, treatment-experienced (IFN-eligible) patients, any fibrosis stage

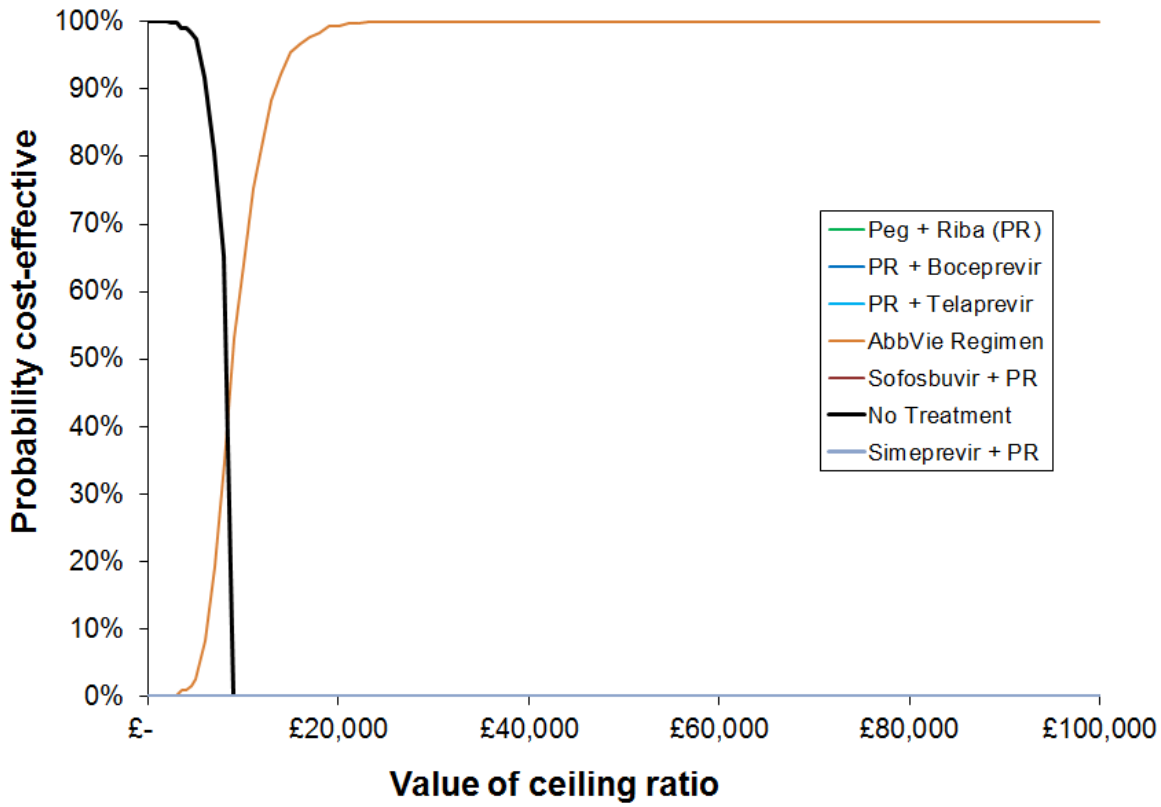


Figure 17. GT1b, treatment-experienced (IFN-eligible) patients, non-cirrhotic only

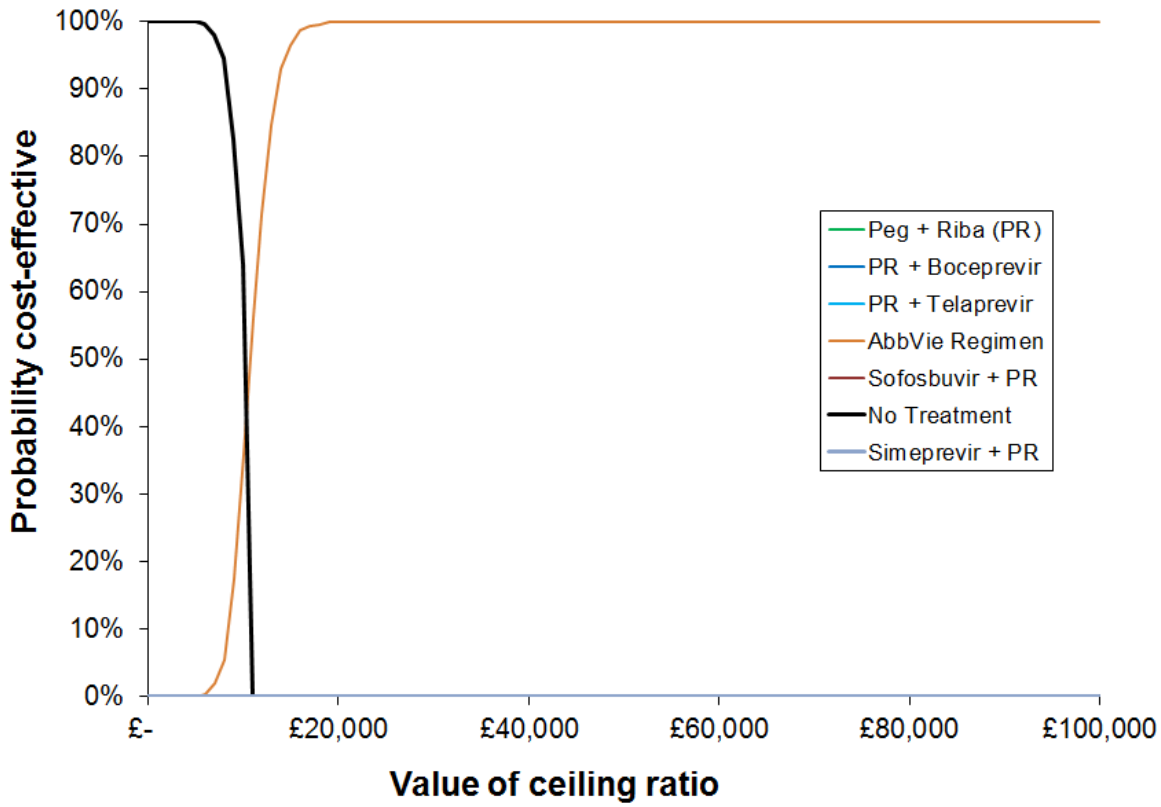


Figure 18. GT1b, treatment-experienced (IFN-eligible) patients, cirrhotic only

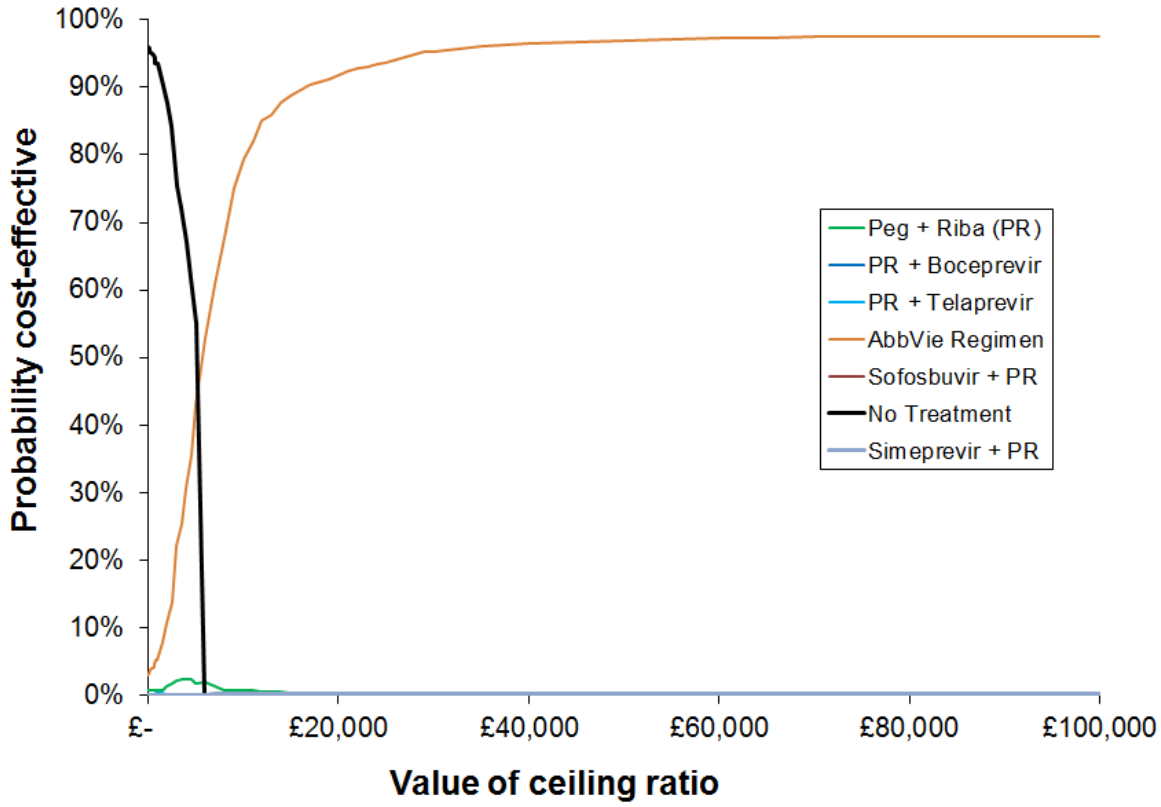


Figure 19. GT4, treatment-naïve (IFN-eligible) patients, any fibrosis stage

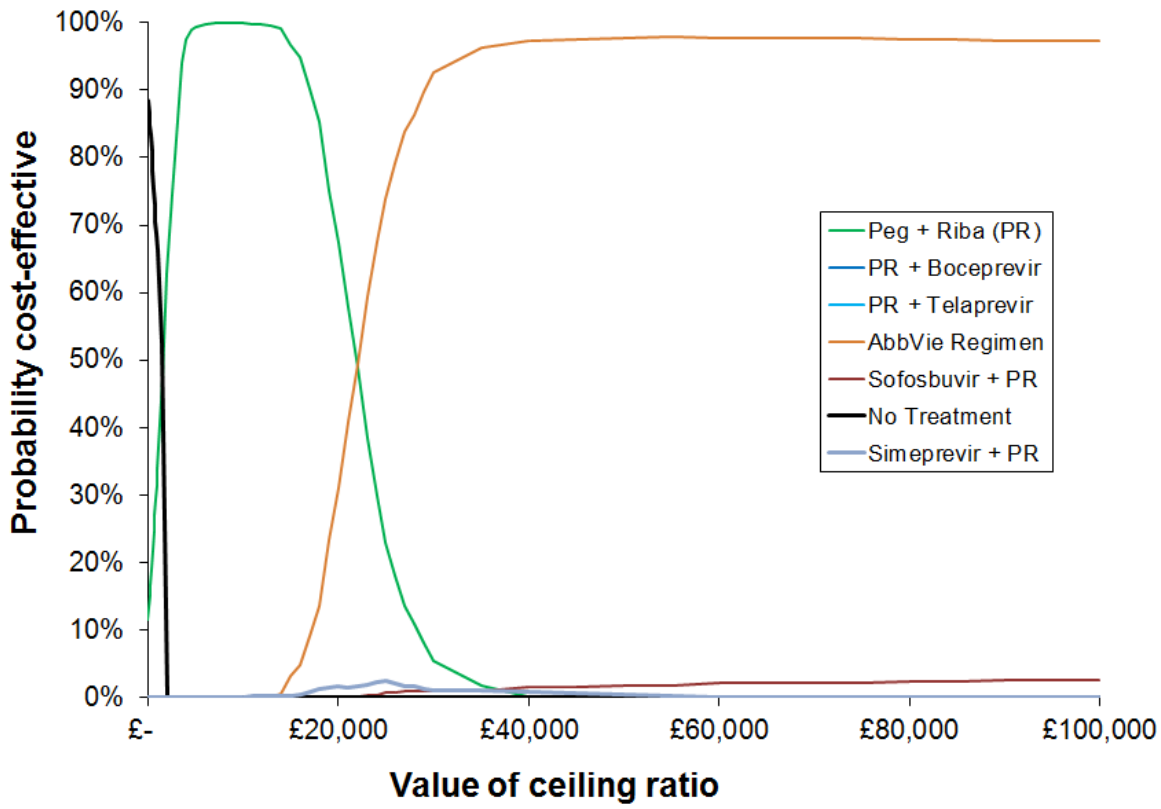


Figure 20. GT4, treatment-naïve (IFN-eligible) patients, non-cirrhotic only

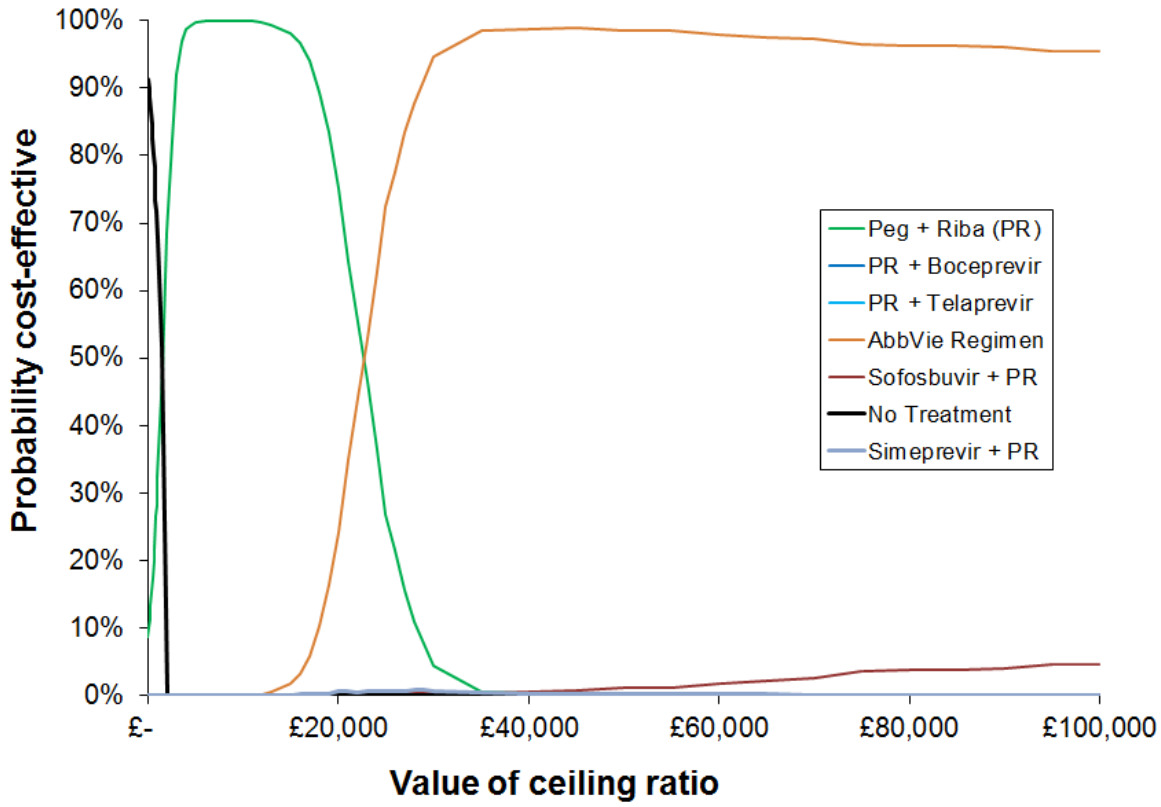


Figure 21. GT4, treatment-naïve (IFN-eligible) patients, cirrhotic only

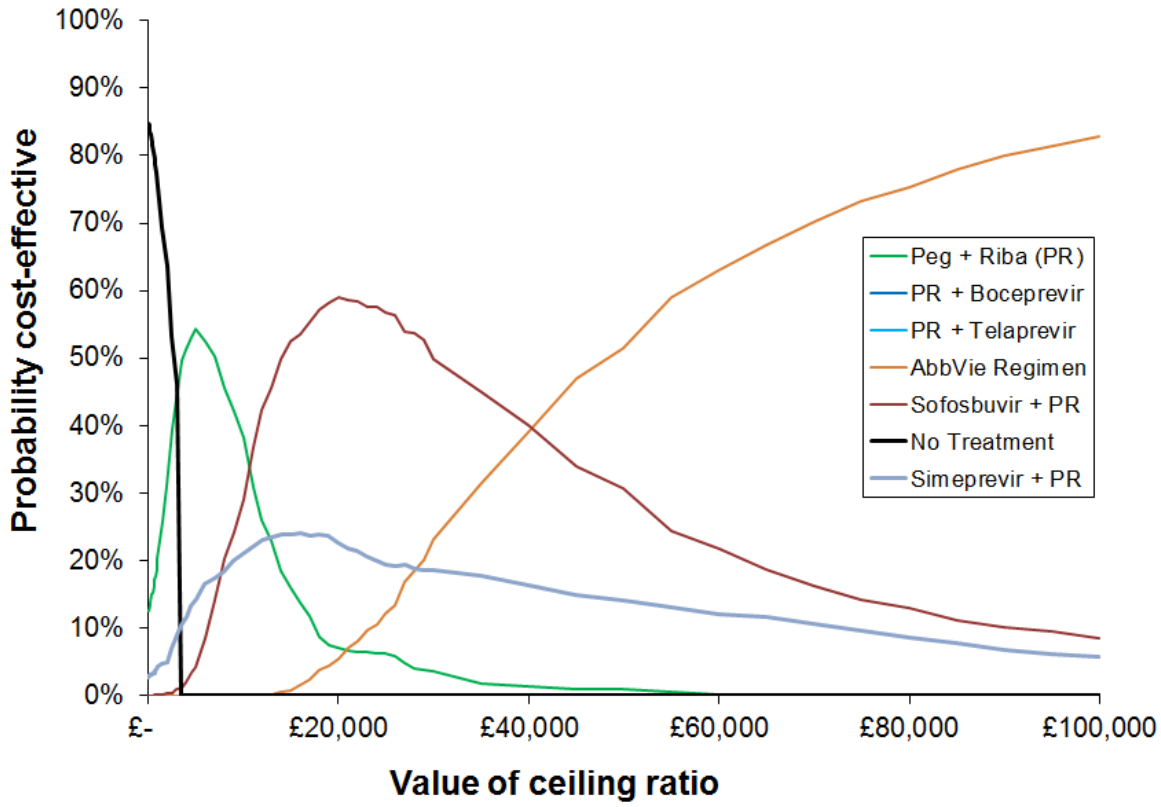


Figure 22. GT4, treatment-experienced (IFN-eligible) patients, any fibrosis stage

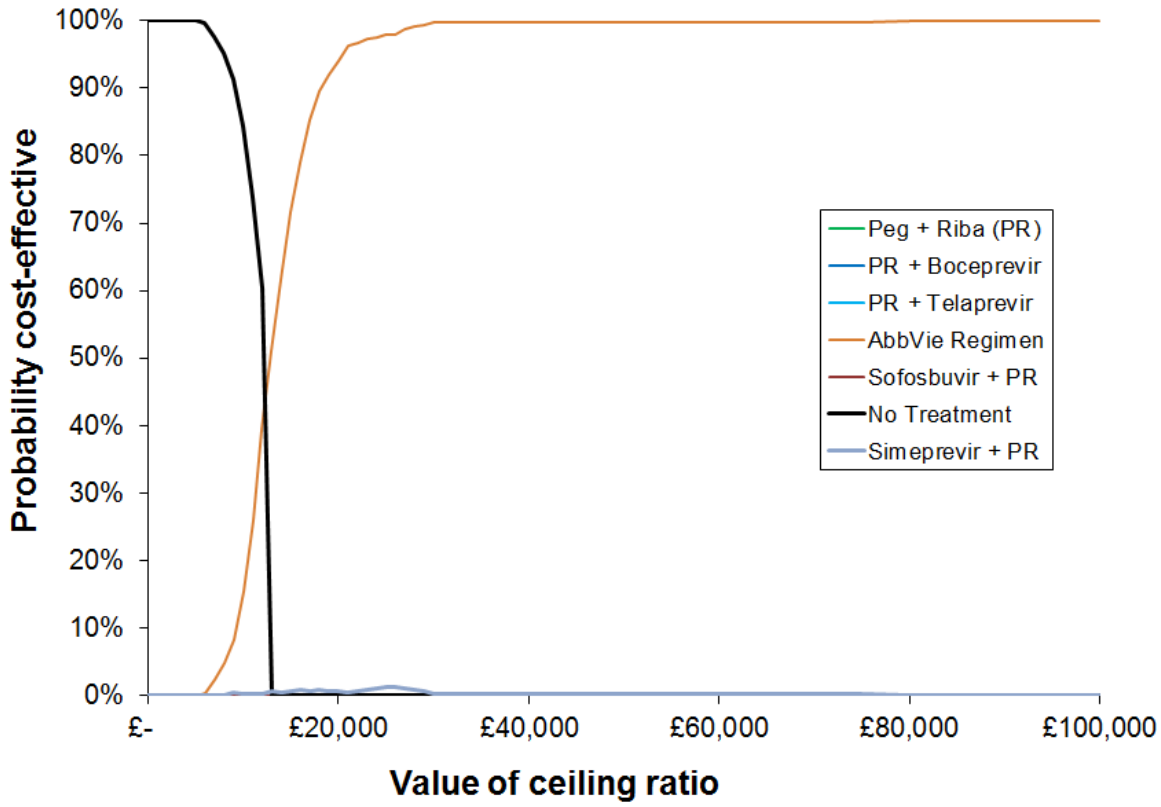


Figure 23. GT4, treatment-experienced (IFN-eligible) patients, non-cirrhotic only

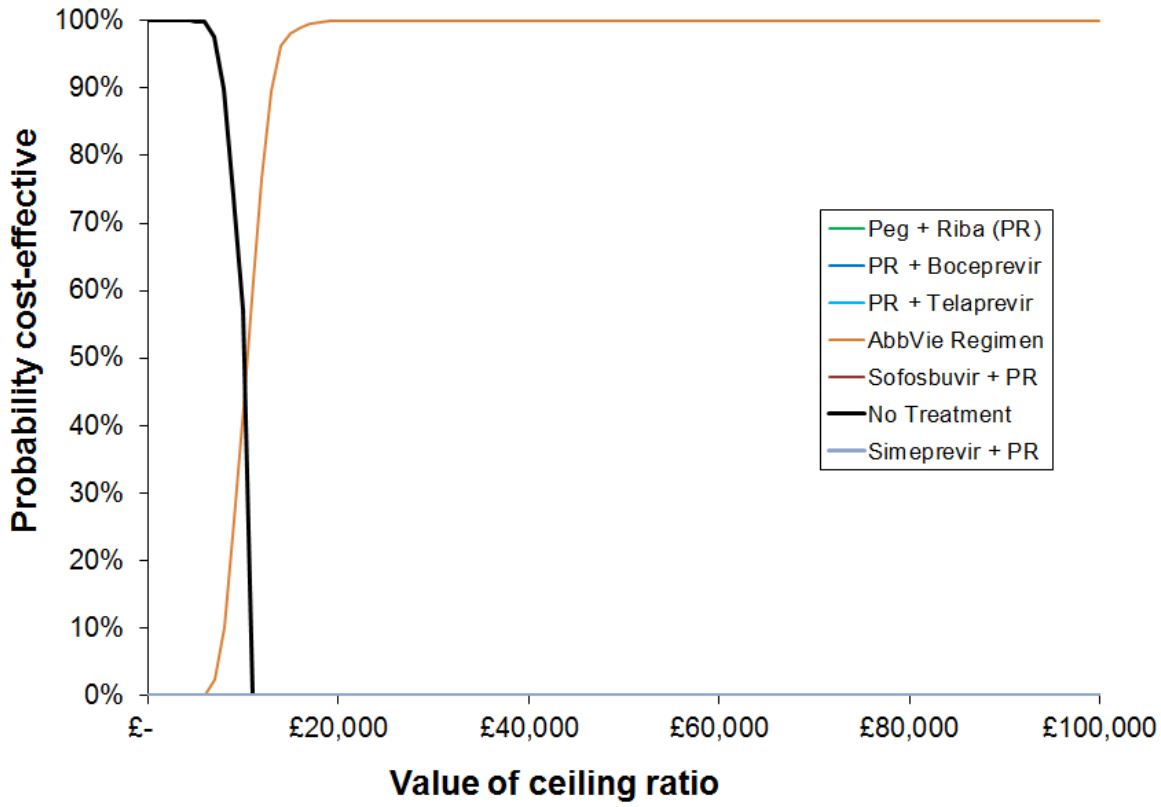


Figure 24. GT4, treatment-experienced (IFN-eligible) patients, cirrhotic only

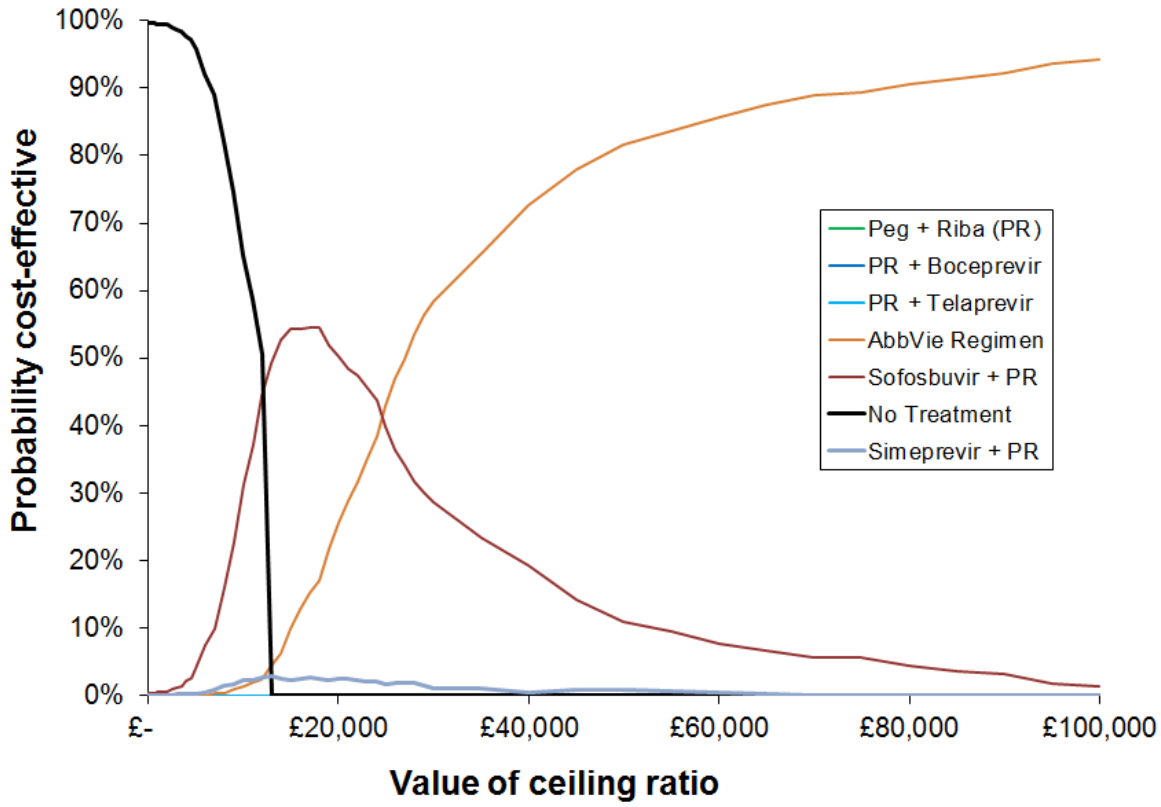


Figure 25. PSA, AbbVie Regimen versus No Treatment, GT1, treatment-naïve (IFN-unsuitable) patients, non-cirrhotic only

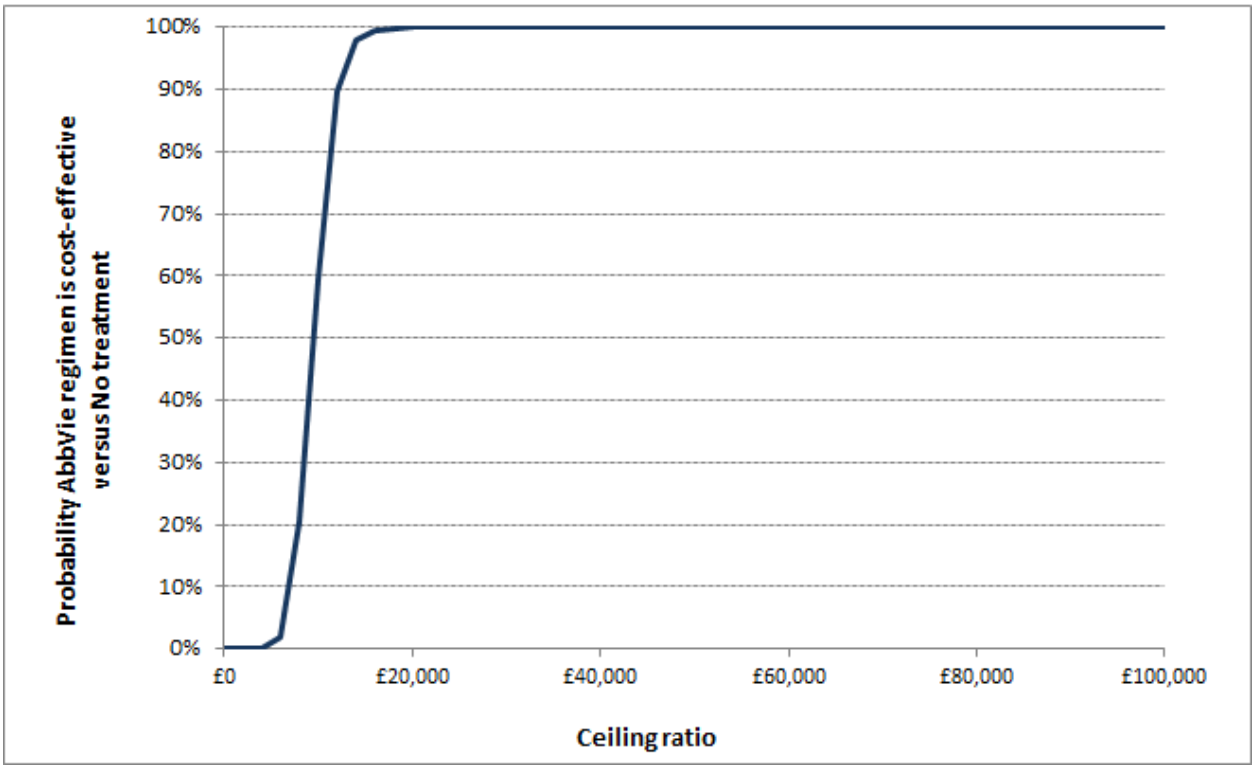


Figure 26. PSA, AbbVie Regimen versus No Treatment, GT1, treatment-naïve (IFN-unsuitable) patients, cirrhotic only

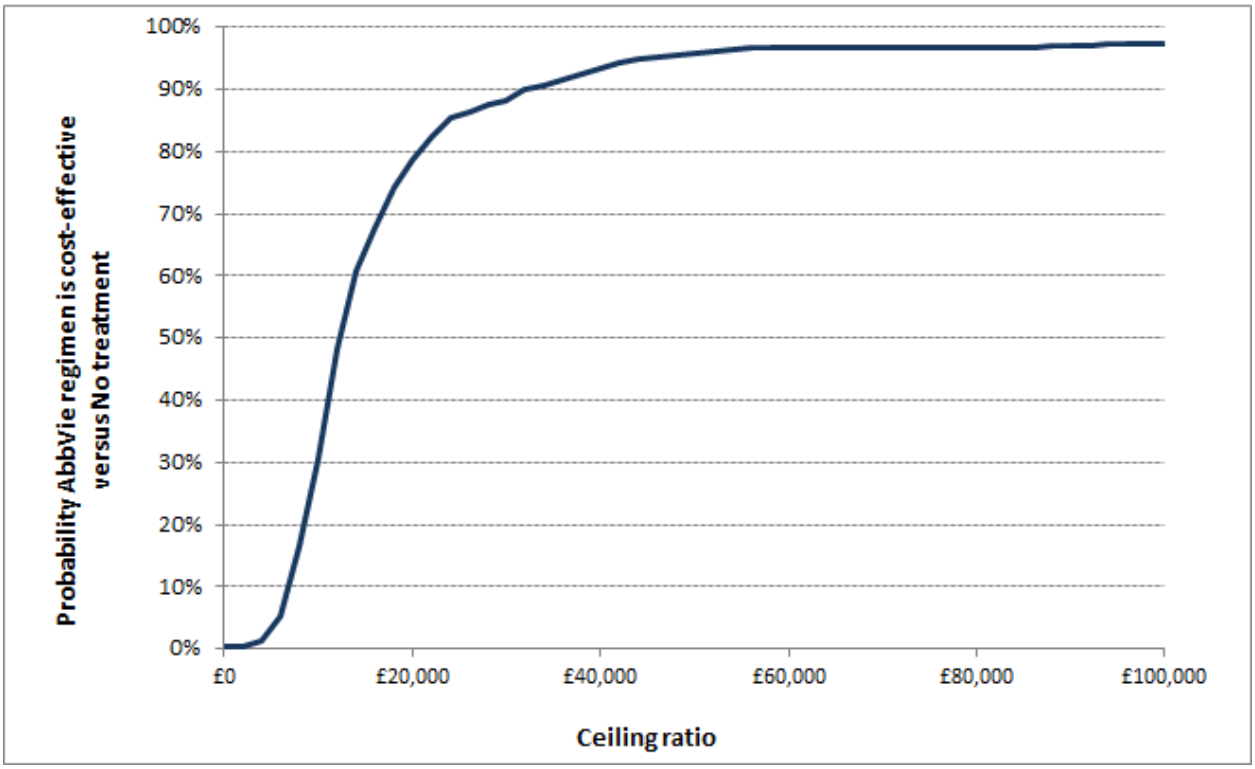


Figure 27. PSA, AbbVie Regimen versus No Treatment, GT1, treatment-experienced (IFN-unsuitable) patients, non-cirrhotic only

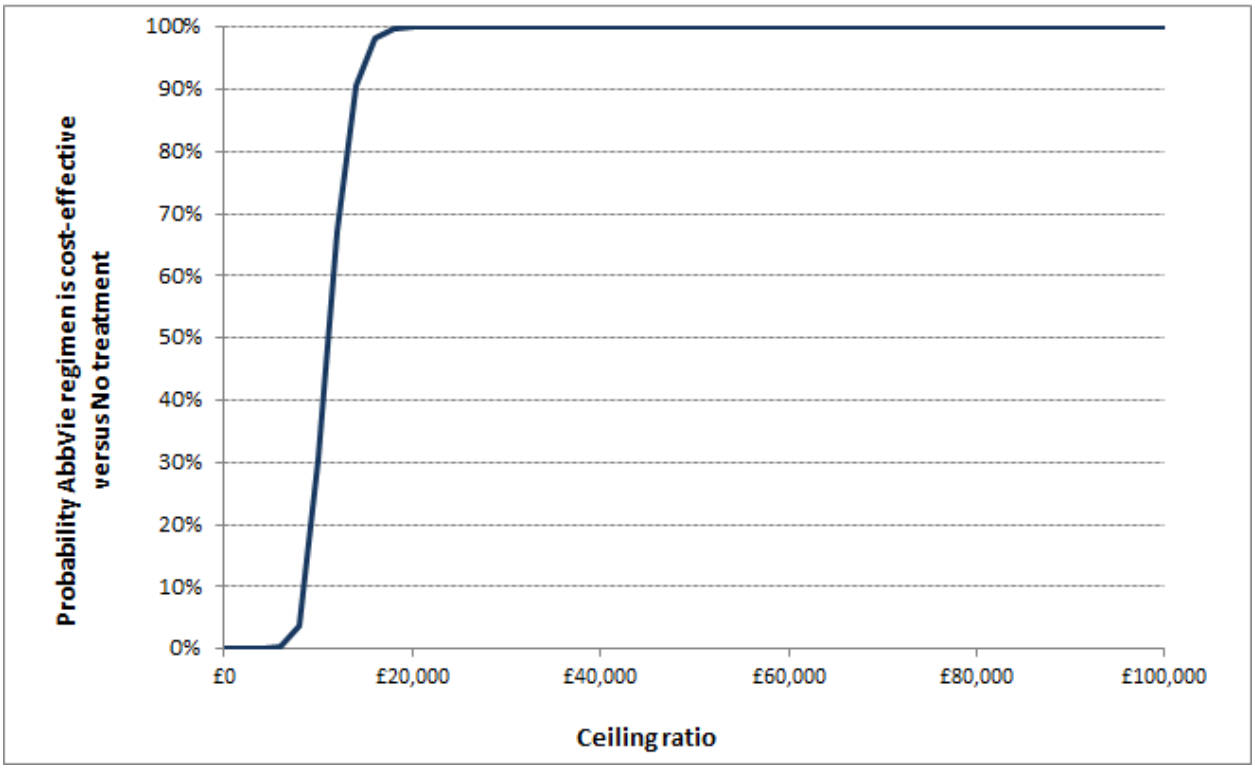


Figure 28. PSA, AbbVie Regimen versus No Treatment, GT1, treatment-experienced (IFN-unsuitable) patients, cirrhotic only

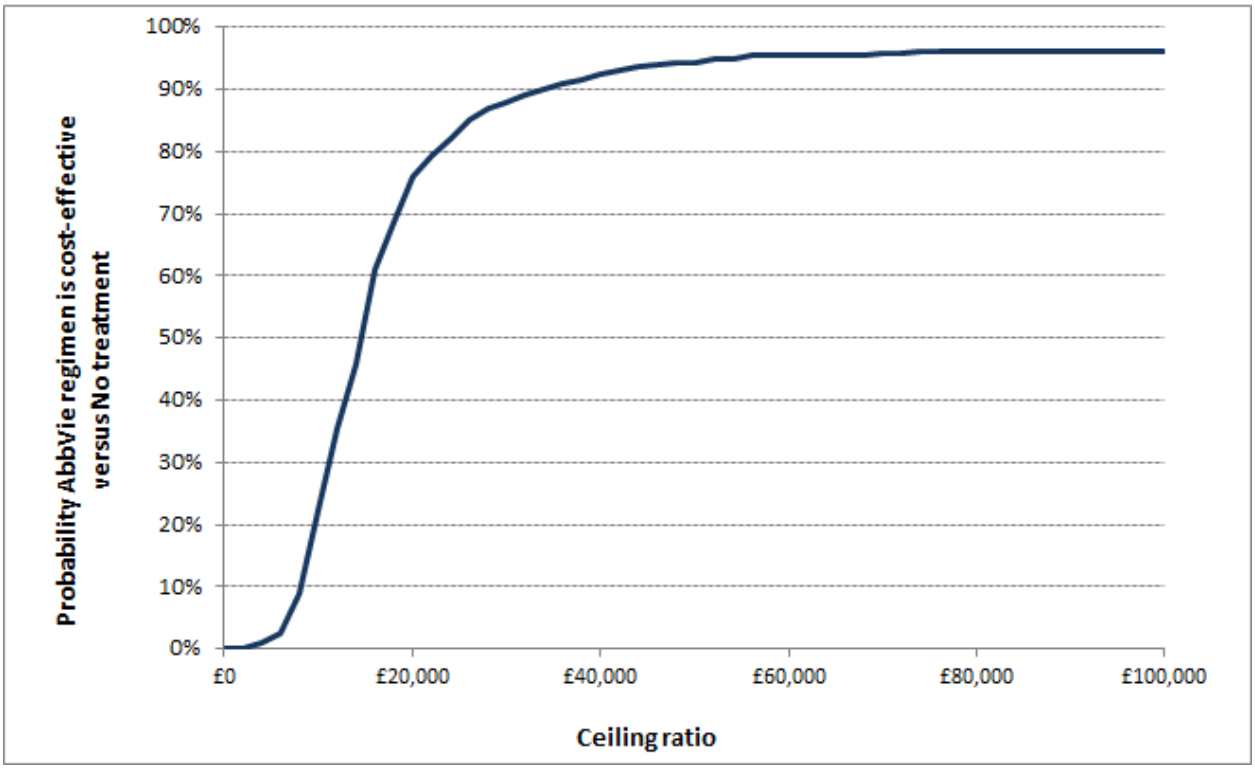


Figure 29. PSA, AbbVie Regimen versus No Treatment, GT4, treatment-naïve (IFN-unsuitable) patients, non-cirrhotic only

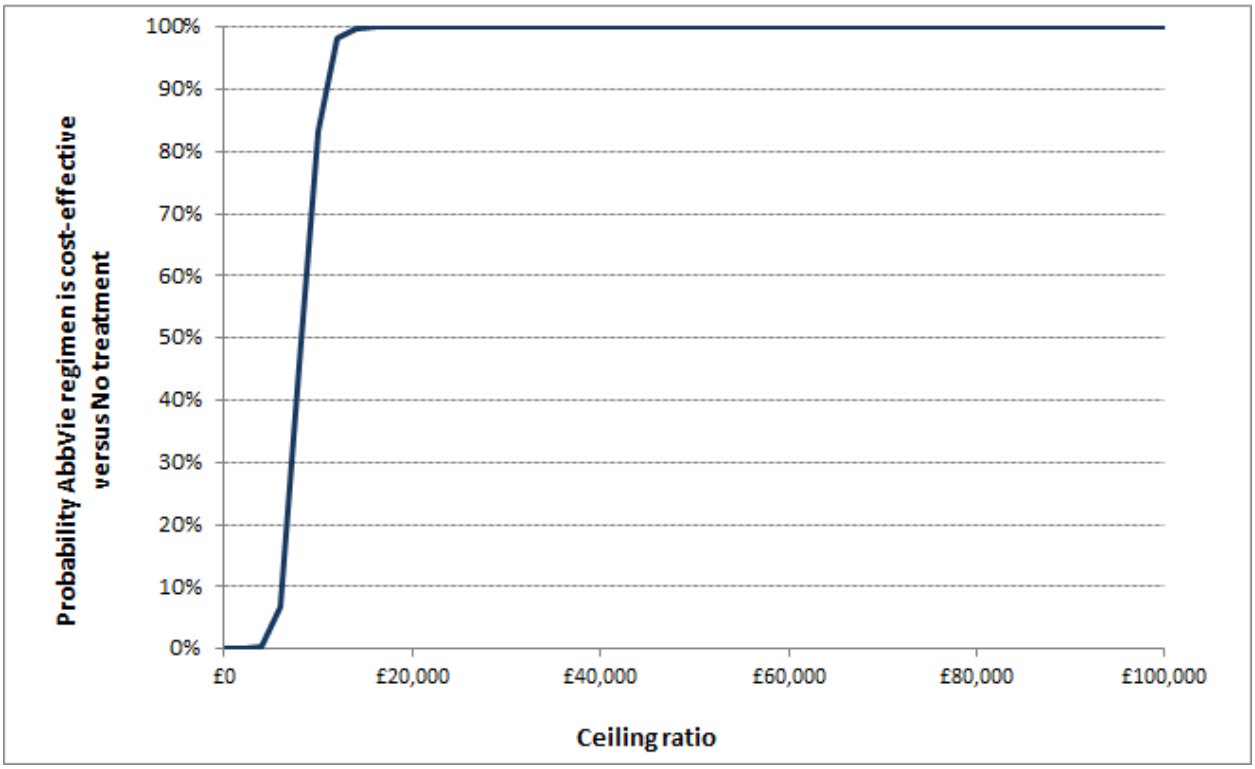


Figure 30. PSA, AbbVie Regimen versus No Treatment, GT4, treatment-naïve (IFN-unsuitable) patients, cirrhotic only

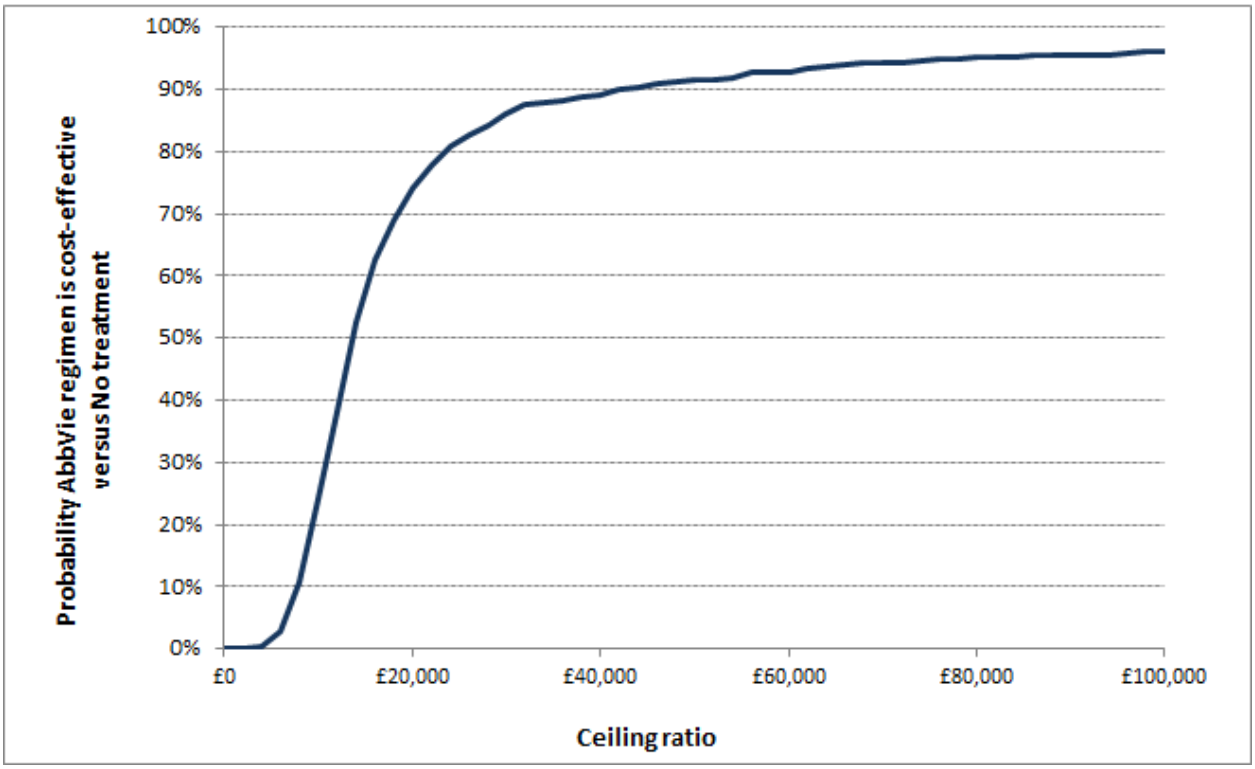


Figure 31. PSA, AbbVie Regimen versus No Treatment, GT4, treatment-experienced (IFN-unsuitable) patients, non-cirrhotic only

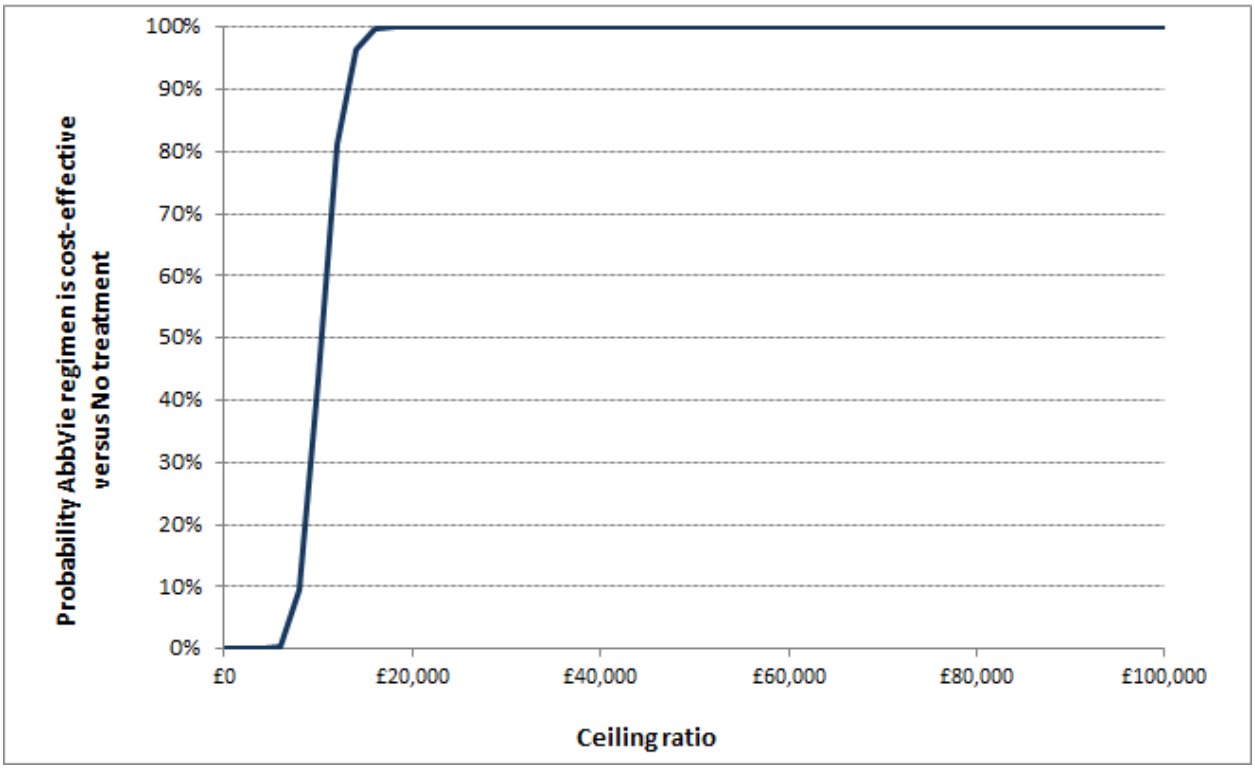
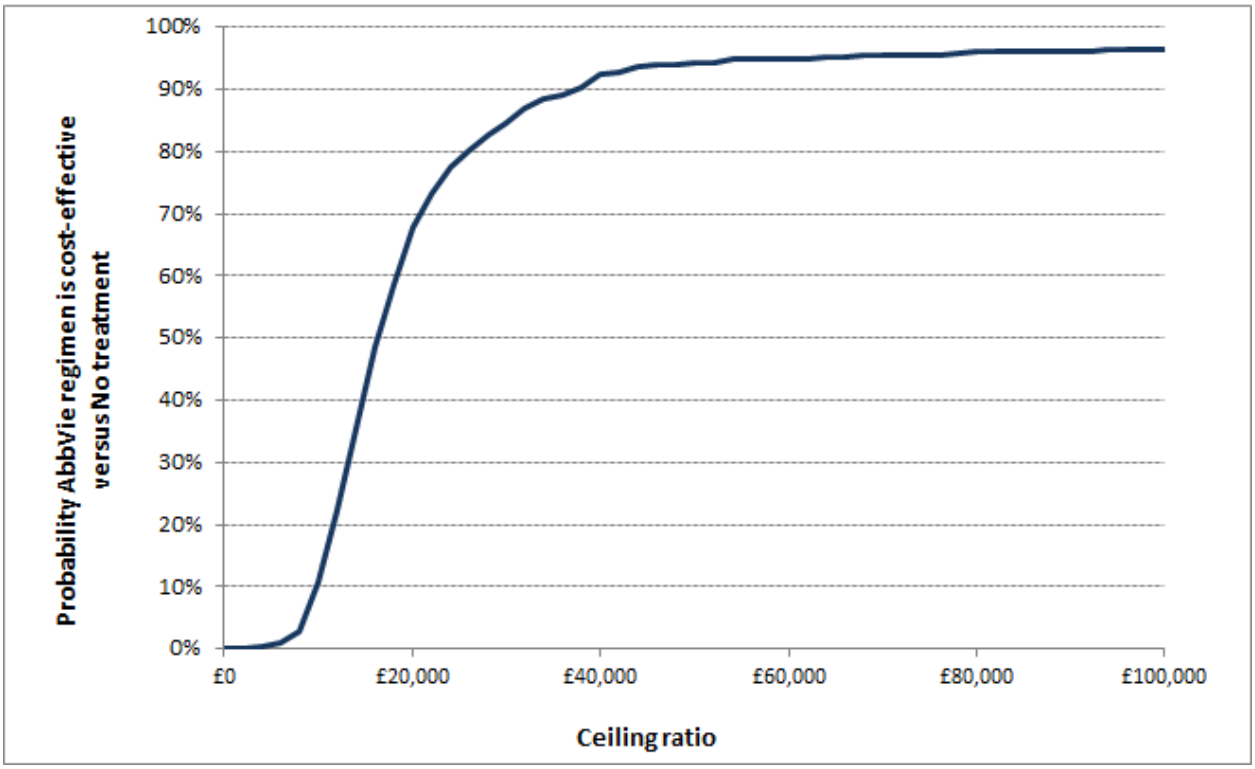



Figure 32. PSA, AbbVie Regimen versus No Treatment, GT4, treatment-experienced (IFN-unsuitable) patients, cirrhotic only