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Datasheet for the decision of 6 November 2025

Case Number: T 0265/23 - 3.3.04

Application Number: 17165207.6

Publication Number: 3213750

IPC: A61K31/454, A61K31/498, A61P31/12

Language of the proceedings: EN

Title of invention:
Combination of two antivirals for treating Hepatitis C

Patent Proprietor:
AbbVie Inc.

Opponent:
Generics (U.K.) Limited

Relevant legal provisions:
EPC Art. 83, 56

Keyword:
Sufficiency of disclosure - (yes)
Inventive step - (yes)

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Case Number: T 0265/23 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 6 November 2025

Appellant: (Opponent)	Generics (U.K.) Limited Building 4, Trident Place Mosquito Way Hatfield Hertfordshire AL10 9UL (GB)
Representative:	Ter Meer Steinmeister & Partner Patentanwälte mbB Nymphenburger Straße 4 80335 München (DE)
Respondent: (Patent Proprietor)	AbbVie Inc. 1 North Waukegan Road North Chicago, IL 60064 (US)
Representative:	Mewburn Ellis LLP Aurora Building Counterslip Bristol BS1 6BX (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 29 November 2022 concerning maintenance of the European Patent No. 3213750 in amended form.**

Composition of the Board:

Chairman	M. Pregetter
Members:	R. Hauss
	M. Blasi

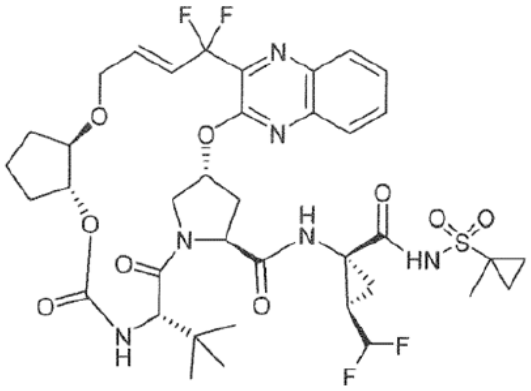
Summary of Facts and Submissions

I. European Patent No. 3 213 750 (patent in suit) was granted on application No. 17 165 207.6 (application as filed), which is a divisional of European patent application No. 14 719 977.2 (the earlier application, filed as an international application, published as WO 2014/152514 A1). The patent in suit was granted with a set of 15 claims.

II. The patent in suit was opposed under Article 100(a), (b) and (c) EPC on the grounds that the claimed subject-matter lacked inventive step within the meaning of Article 56 EPC, was not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art, and extended beyond the content of the application as filed and the earlier application as filed.

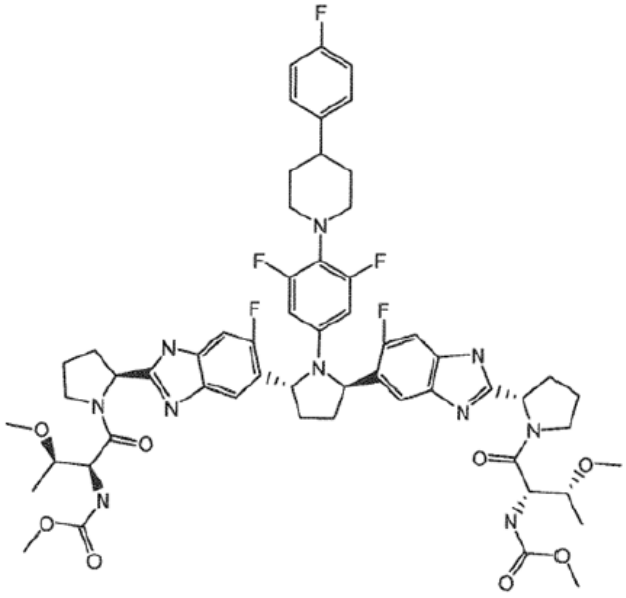
III. The patent proprietor requested that the opposition be rejected and, consequently, the patent be maintained as granted. It also filed amended sets of claims as auxiliary requests. Claim 1 of auxiliary request 1 is identical to claim 1 as granted and reads as follows:

> *"1. At least two direct acting antiviral agents (DAAs) for use in a method for treatment of HCV infection, said method comprising administering at least two DAAs to an HCV patient, wherein neither interferon nor ribavirin are administered to said patient during said treatment, and said treatment lasts for 16 weeks, and wherein said at least two DAAs comprise*



Compound 1

or a pharmaceutically acceptable salt thereof, and



Compound 2

or a pharmaceutically acceptable salt thereof."

IV. Compound 1 is an HCV (hepatitis C virus) protease inhibitor (see the patent in suit, paragraph [0016]) and is also known as glecaprevir. Compound 2 is an NS5A inhibitor (see the patent in suit, paragraph [0017) and is also known as pibrentasvir.

V. The documents cited in the proceedings before the opposition division included the following:

D2: Declaration Sven Mensing (15 June 2018)

D3: US 2013/0102526 A1 (25 April 2013)

D4: US 61/783,376 (priority document)

D6: US 2012/0070416 A1

D7: US 2012/0220562 A1

D8: MJA 196(10), 2012, 629-32

D9: Journal of Virology 81(6), 2007, 3005-8

D10: T. Ng et al., *"ABT-493, a Potent HCV NS3/4A Protease Inhibitor with Broad Genotype Coverage"*, Poster presented at the 21st Annual Conference on Retroviruses and Opportunistic Infections (CROI), Boston, MA, 3-6 March 2014

D11: Maviret, EPAR summary for the public, 2017

D16: Antiviral Research 14, 1990, 181-206

VI. The decision under appeal is the opposition division's interlocutory decision finding that the patent as amended in the form of auxiliary request 1 met the requirements of the EPC. The decision includes the following findings.

(a) The ground for opposition under Article 100(c) EPC prejudiced the maintenance of the patent as granted. The claim set of auxiliary request 1 complied with Article 76(1) and Article 123(2) EPC.

(b) The claims of auxiliary request 1 also met the requirements of Article 83 EPC regarding the active compounds and their suitability for the envisaged treatment of HCV infection.

(c) The claimed priority of the opposed patent was valid.

(d) Starting from the disclosure of document D6, which represented the closest prior art, two objective technical problems could be formulated:

(i) to provide improved treatment of HCV with compound 1 (applicable to HCV genotype 1b only),

(ii) to provide a pan-genotypic treatment of HCV

The claimed subject-matter was found to be inventive as none of the cited prior-art documents pointed to a combination of compound 1 with compound 2.

VII. The opponent (appellant) filed an appeal against this decision.

VIII. With its reply to the statement setting out the grounds of appeal, the patent proprietor (respondent) presented sets of claims of a main request and of auxiliary request 1. The set of claims of the main request is identical to that of former auxiliary request 1 found allowable in the decision under appeal. For the wording of claim 1, see point III. above.

IX. In a communication under Article 15(1) RPBA issued in preparation for oral proceedings, the board advised the parties of its preliminary view that the claimed subject-matter met the requirement of sufficiency of disclosure and that the question of whether the claimed priority was valid did not appear to be decisive for the outcome of the appeal case (see points 1.2 and 2.2 of the board's communication dated 17 March 2025).

X. Oral proceedings before the board took place on 6 November 2025. The debate focused on inventive step of the subject-matter defined in claim 1 of the main request. On sufficiency of disclosure, both parties relied on their written submissions. At the end of the

oral proceedings, the Chairwoman announced the board's decision dismissing the appeal.

XI. The appellant's arguments may be summarised as follows.

Sufficiency of disclosure

The optional antiviral agents that could be present in addition to the mandatory agents glecaprevir and pibrentasvir (as implied by the term *"at least two"* in granted claim 1) were defined only in functional terms as direct-acting antiviral (DAA) agents. It would be an undue burden for the skilled person to isolate and characterise all potential compounds or to test every known compound and every conceivable future compound for the desired activity.

The patent in suit did not disclose the suitability of the claimed DAA combination for the therapeutic application defined in claim 1. No clinical data were reported. Examples 1 and 2 did not demonstrate any effect of the combination of glecaprevir and pibrentasvir, let alone of a combination of these two compounds with further DAAs, on a metabolic mechanism directly involved in HCV infection. Also, the available data did not show the suitability of the combination treatment for a treatment duration of 16 weeks. It was not permissible for the respondent to rely, for its reasoning, on the disclosure of clinical modelling in D3 as this document did not represent common general knowledge.

Validity of the claimed priority

The claimed priority of 14 March 2013 was not valid due to lack of enablement.

Inventive step

The starting point for the assessment of inventive step should be the use of glecaprevir (disclosed in Example 6 of D6) in a combination treatment, as envisaged in D6 (paragraph [0249]). D6 also taught, at least implicitly, that the DAAs could be administered without co-administration of interferon and ribavirin.

The subject-matter of claim 1 differed from the disclosure in D6 only by the selection of pibrentasvir as the combination partner of glecaprevir and by the specified treatment duration of 16 weeks.

Like D6, the patent in suit did not disclose putting the clinical treatment of HCV infection into practice, so this was not a distinguishing feature.

The examples in the patent in suit did not provide evidence of any specific technical effect resulting from a feature that distinguished the claimed subject-matter from the disclosure of D6. The pan-genotypic activity of the combination alleged by the respondent could only be based on the predicted activity of glecaprevir against several genotypes as disclosed in Example 2 of the patent in suit. However, as glecaprevir was not a distinguishing technical feature over D6, this technical effect could not be taken into account for the formulation of the objective technical problem.

The synergistic effect alleged by the respondent (based on Figure 7 and paragraph [0054] in Example 2) had not been shown to be obtained across the ambit of claim 1, e.g. not for all HCV genotypes.

As a result, the only technical effect that could be taken into account for assessing inventive step was the provision of a new combination of active agents.

The objective technical problem to be solved was, accordingly, the provision of an alternative combination of antiviral agents for the treatment of HCV infection.

D6 disclosed in paragraph [0249] that HCV protease inhibitors such as glecaprevir could, *inter alia*, be combined with HCV NS5A inhibitors. The person skilled in the art, therefore, would have considered HCV NS5A inhibitors as potential combination partners, including pibrentasvir disclosed in D7.

D7 showed favourable *in vitro* data for HCV inhibition by pibrentasvir. Pibrentasvir, a pharmaceutical composition containing it, and a method of treating a patient infected with HCV with pibrentasvir were claimed individually in claims 3, 4 and 12 of D7. This showed that pibrentasvir was a particularly preferred compound.

In addition, the review article D8 mentioned a clinical study relating to an interferon-free dual DAA therapy of HCV in which a protease inhibitor was administered in combination with an NS5A inhibitor. A similar disclosure was found in D10.

It was also well known that strategies that combined compounds targeting different viral mechanisms could be expected to result in improved therapeutic efficacy (see D9: abstract).

For combination treatment based on DAAs, there was also a reasonable expectation of a short treatment duration. According to D8 (page 629, right-hand column), DAA therapy and the move towards interferon-free regimens were expected to provide short-duration (6 to 24 weeks) therapy with high efficacy.

For all these reasons, it would have been obvious for the person skilled in the art to consider pibrentasvir as a possible combination partner for glecaprevir and thereby arrive at the subject-matter of claim 1.

XII. The respondent's arguments may be summarised as follows.

Sufficiency of disclosure

The mandatory compounds of claim 1 (i.e. glecaprevir and pibrentasvir) were structurally well defined, and the person skilled in the art would have been enabled by the further information provided to put the method defined in claim 1 into practice. The examples in the patent in suit demonstrated the suitability of the claimed combination for the recited therapeutic use. This was confirmed by post-published evidence such as D11, disclosing that marketing authorisation had been obtained for a fixed-dose combination of glecaprevir and pibrentasvir for a treatment duration of 16 weeks. There were no serious doubts substantiated by verifiable facts that the optional addition of further DAAs would prejudice this suitability.

Mathematical clinical modelling (used in Example 1 and for the analysis shown in Figure 7, as described in D3 and D16) was an established method, based on scientifically justified assumptions and previously published or collected data, that was routinely used in antiviral research (see also the expert declaration D2, starting on paragraph [0021]).

Validity of the claimed priority

The issue of priority was irrelevant since the intermediate document D10 (which would be prior art under Article 54(2) EPC if the priority of the patent

were not valid) did not contain more pertinent information than the other prior-art documents on file.

Inventive step

Preferably, the starting point in D6 for the assessment of inventive step should be the established treatment methods according to paragraph [0006]. However, the respondent conceded that it was also a reasonable approach to start from the disclosure in D6 of a generic combination treatment with glecaprevir.

The claimed subject-matter differed from the disclosure of D6 in that

1) the DAA treatment envisaged in D6 was put into practice

2) glecaprevir was combined with pibrentasvir

3) the treatment duration was 16 weeks

4) interferon and ribavirin were not administered concomitantly

Four advantageous technical effects were relevant:

1) the treatment was consistently pan-genotypic

2) the claimed combination showed synergy

3) the treatment duration was short

4) undesirable side effects associated with interferon and ribavirin were avoided, resulting in improved patient compliance

These technical effects had been rendered credible by evidence provided in the patent in suit, supplemented by post-published evidence.

On this basis, the objective technical problem should be defined as the provision of an improved treatment for HCV infection.

The claimed subject-matter, in particular combining glecaprevir with pibrentasvir, would not have been obvious to the person skilled in the art seeking to solve the objective technical problem of improved treatment in the absence of any pointers to this combination in the prior art.

XIII. The parties' requests were the following.

- The appellant requested that the decision under appeal be set aside and that the patent be revoked.

- The respondent requested that the appeal be dismissed and that the patent in suit be maintained in amended form in accordance with the decision under appeal or, in the alternative, on the basis of the claim of auxiliary request 1 filed with the reply to the statement setting out the grounds of appeal.

Reasons for the Decision

1. Claim construction

1.1 Claim 1 of the current main request relates to a therapeutic application and is drafted as a purpose-related product claim in the format provided under Article 54(5) EPC.

1.2 According to claim 1, glecaprevir and pibrentasvir (where each of them may also be provided in the form of their pharmacologically acceptable salts) are the two mandatory pharmacologically active agents intended to treat HCV (hepatitis C virus) infection in a patient in a 16-week combination treatment. This is made clear by the wording:

> "said at least two DAAs comprise *[structure formula of glecaprevir]* Compound 1 or a pharmaceutically acceptable salt thereof, and *[structure formula of pibrentasvir]* Compound 2 or a pharmaceutically acceptable salt thereof."

Optionally, other DAA agents may be administered in addition, whereas the administration of interferon or ribavirin during this 16-week treatment is excluded.

1.3 Under the established case law of the boards, where, as in the case in hand, a therapeutic application is claimed in the format provided in Article 54(5) EPC, attaining the claimed therapeutic effect is regarded as a functional technical feature of the claim under consideration (see Case Law of the Boards of Appeal of the European Patent Office, 10th edn. 2022, I.C.7.2.1; G 2/08, OJ EPO 2010, 45, Reasons 5.10.9).

1.4 As provided in Article 54(5) EPC, such a feature may establish novelty. It also has to be taken into account in the assessment of sufficiency of disclosure (see G 1/03, OJ EPO 2004, 413, Reasons 2.5.2; G 2/21, OJ EPO 2023, A85, Reasons 77).

2. Amendments

The appellant did not contest the finding in the decision under appeal that former auxiliary request 1 (identical to the current main request; see point VIII. above) met the requirements of Articles 76(1) and 123(2) EPC. The board saw no reason to take up any issue under Articles 76(1) and 123(2) EPC.

3. Sufficiency of disclosure (Article 83 EPC)

3.1 The requirement of sufficiency of disclosure must be satisfied on the basis of the information provided in the patent application as filed and the common general knowledge then available to the person skilled in the art (see T 609/02, Reasons 8). Subsequently filed supplementary evidence may only be taken into account for confirmation but cannot be used as the only means to establish sufficiency.

3.2 As set out in point 1.3 above, attaining the claimed therapeutic effect is a functional technical feature of claim 1. To meet the requirement of sufficiency of disclosure, the suitability of the claimed combination for the claimed therapeutic indication must therefore be disclosed, unless this was already known to the person skilled in the art.

The question to be answered is whether the therapeutic efficacy of the claimed combination in the claimed therapeutic indication would have been considered credible on the basis of the information provided in

the patent application as filed and taking into account the common general knowledge available to the person skilled in the art at the time. This credibility has to be established across the entire scope claimed.

3.3 If the required credibility is not established on the basis of common general knowledge, the application as filed must provide appropriate experimental data or at least indicate a credible technical concept or mode of action such as information demonstrating that the claimed combination has a direct effect on a mechanism involved in the targeted pathology. Clinical data are not required if credibility can be established by other evidence.

3.4 The treatment defined in current claim 1 is the treatment of HCV infection in a patient. The claim furthermore requires that the treatment be performed in 16 weeks and without the administration of interferon or ribavirin.

3.5 The evidence presented in the examples of the patent in suit (paragraphs [0047] to [0056] and Figures 1 to 7) is also present in identical corresponding passages in the application as filed and the earlier application as filed (paragraphs [0070] to [0080] and Figures 1 to 7). The application as filed has the same paragraph numbering as the earlier application as filed.

3.6 The appellant contested that the suitability of the combination of glecaprevir with pibrentasvir for the therapeutic application defined in claim 1 had been rendered credible and that sufficient guidance had been provided regarding the selection of suitable optional further DAAs.

Efficacy of the mandatory DAA combination of glecaprevir and pibrentasvir

3.7 The (earlier) application as filed states that the two mandatory DAAs (glecaprevir and pibrentasvir) were known as potent HCV inhibitors and cites the pre-published documents D6 and D7 (see paragraphs [0022] and [0023]).

3.8 Both documents relate to new pharmacologically active compounds for treating HCV infection (see D6: paragraph [0003] and D7: paragraph [0002]). D6 relates to HCV serine protease inhibitors. Glecaprevir is disclosed in Example 6 of D6 (see paragraph [0425]). Pibrentasvir is disclosed in Example 3.52 on page 244 (see paragraph [1156]) of D7.

3.9 In addition to the compounds' synthesis, both documents also disclose *in vitro* bioassays for HCV inhibition, and both mention that inhibitory activity can be evaluated using a variety of assays known in the art (D6: Example 301 on pages 93 and 94; D7: paragraphs [1371], [1373] and [1374]).

3.10 In D6, EC_{50} values for a number of compounds, including glecaprevir (the compound according to Example 6 in D6) are provided for various HCV genotypes (see D6: page 94).

3.11 Pibrentasvir (the compound of Example 3.52 in D7) is listed in D7 (see paragraph [1371]) as one of a number of compounds having an EC_{50} value of less than 0.1 nM when tested using HCV 1b Con1 replicon assays in the presence of 5% FBS.

3.12 In addition, Example 2 in the (earlier) application as filed reports further *in vitro* data on HCV inhibition by glecaprevir which show inhibitory activity against

further genotypes (see Tables 2 and 3). Moreover, it reports inhibitory activity against certain common HCV genotype 1 NS3 resistance-associated variants in genotype 1b (Con-1) and potent activity against many NS5A inhibitor and NS5B inhibitor resistance-associated variants (see paragraph [0079]).

3.13 Figure 7 in the (earlier) application as filed shows results generated from test data (HCV inhibition as tested in HCV GT 1b Con-1 replication cells, see paragraph [0077]) with the help of a mathematical model of drug-drug interactions described in D16 (referenced in paragraph [0077]). The findings presented in Figure 7, which predict an additive or synergistic effect, may be taken as an indication that the desired anti-HCV activity will not be impaired by combining glecaprevir and pibrentasvir. No evidence to the contrary is on file.

3.14 Thus, it was known that DAA-based combination therapies and new therapeutic strategies were being developed for treating HCV (see also the overview presented in D8). Glecaprevir and pibrentasvir had been described previously and were known to have anti-HCV activity based on two different mechanisms (see the (earlier) application as filed, paragraphs [0022] and [0023]; D6; D7). On this basis, in combination with the further data provided in the (earlier) application as filed, and in the absence of evidence to the contrary, it would have been credible that the combination of these agents provides anti-HCV activity.

3.15 Example 1 relates to mathematical clinical modelling for interferon- and ribavirin-free combination therapy in conformity with claim 1. This was done according to a clinical simulation model described in D3, cited in paragraph [0070] of the (earlier) application as

filed (see D3: examples, in particular Example 6 starting in paragraph [0253]). Contrary to the appellant's argument, D3 does not have to be part of the common general knowledge since it is cross-referenced in the (earlier) application as filed as describing the model that was used in Example 1.

3.16 The respondent explained that modelling, based on experimental data and scientifically justified assumptions, is an established approach for predicting the efficacy of anti-HCV drugs (see also D2, paragraph [0021] and the following paragraphs). The approach described in full in D3 relates to treatment regimens for HCV comprising at least two DAAs, and in particular its application to 2-DAA treatment regimens (identified in D3 (paragraph [0255]) as being, e.g., a combination of a protease inhibitor and a NS5A inhibitor).

3.17 The (earlier) application as filed reports that in different scenarios that were evaluated in Example 1 for a 2-DAA combination of glecaprevir and pibrentasvir, administered at various once-daily dosages without interferon and ribavirin over a range of treatment durations to genotype 1 or genotype 3 treatment-naive subjects, the predicted sustained virological response rates for a treatment duration of 12 weeks were favourable (Example 1). The same information is provided for a duration of 16 weeks in the pertinent Figures 1 to 6.

3.18 For these reasons, the (earlier) application as filed contains sufficient evidence, going beyond mere verbal statements, of a mechanism and technical concept that supports the suitability of the combination of

glecaprevir and pibrentasvir for the therapeutic application defined in claim 1 as granted.

3.19 In this situation, post-published evidence may be taken into account for confirmation. D11 confirms the suitability of the combination of glecaprevir and pibrentasvir for HCV treatment with a duration of 16 weeks, as the European Medicines Agency recommended approval of the combination product "Maviret" (glecaprevir/pibrentasvir) for this use.

Further DAAs

3.20 With regard to the definition of the further optional DAA compounds for use in treating the HCV infection, the board observes that claim 1 does not require the identification and characterisation of every known and future compound suitable as a DAA agent as a precondition to its subject-matter being put into practice. The sufficiency requirement is met if a variety of suitable compounds can be readily identified.

3.21 This is the case since further specific examples of suitable compounds and compound classes were known and are mentioned as guidance in the (earlier) application as filed (paragraphs [0007], [0008] and [0045] to [0053]) and in the patent in suit (paragraphs [0009], [0010] and [0029] to [0037]). The compounds can be screened for activity with known methods (as mentioned in D6 and D7, see point 3.9 above).

3.22 No evidence was presented that the administration of further anti-HCV DAAs might compromise the efficacy of the two mandatory DAAs.

Conclusion

3.23 For these reasons, the claimed subject-matter meets the requirement of sufficiency of disclosure (Article 83 EPC).

4. Validity of the claimed priority (Article 87 EPC)

4.1 The appellant contested the validity of the patent's priority.

4.2 This issue would only have to be addressed if the disclosure of intermediate document D10, on which the appellant relied as a supplementary document in its reasoning on inventive step, could be decisive for the assessment of inventive step.

4.3 This is not, however, the case since there is no evidence that the identity and structures of the compounds designated in D10 as ABT-493 and ABT-530 were known before the filing date of the patent in suit. Thus, D10 teaches at most that it was envisaged, on the basis of encouraging *in vitro* data, that an unidentified HCV protease inhibitor (ABT-493) and an unidentified NS5A inhibitor (ABT-530) might be combined for the treatment of HCV infection and that interferon-free regimens were being considered. Without the knowledge that these two compounds are glecaprevir and pibrentasvir, this disclosure does not go beyond what was known from other documents such as D6, D7 or D8.

4.4 Since the disclosure of D10, if taken into account, could, in these circumstances, not have been critical for the issue of inventive step, no decision on priority was required.

5. Inventive step (Articles 52(1) and 56 EPC)

Patent in suit

5.1 The patent in suit seeks to provide a new therapy for HCV infection. The patent mentions several disadvantages associated with the known combination treatment with interferon and ribavirin (i.e. the then current standard of care), namely adverse effects, low efficacy and a typical treatment duration of 24 to 48 weeks (see paragraphs [0002] to [0004], [0018] and [0019]).

5.2 Claim 1 of the current main request (see point III. above) relates to a combination of at least two DAA agents for use in a method of treating HCV infection in which neither interferon nor ribavirin is administered to the patient and the treatment lasts for only 16 weeks. The two mandatory DAAs, defined in the claim by their chemical structures, are glecaprevir (compound 1) and pibrentasvir (compound 2) or their respective pharmaceutically acceptable salts (see point 1.2 above).

Starting point in the prior art

5.3 D6 relates to HCV serine protease inhibitors and suggests their use in the treatment of HCV infection (see D6: claims 17 to 19; paragraphs [0006], [0011], [0041] and [0528]). The mechanism is by inactivation of a virally coded enzyme essential for the replication of the virus (see D6: paragraph [0011]).

Example 6 in D6 discloses glecaprevir (see paragraph [0425]) as one of several highly preferred compounds (paragraph [0245] and following paragraphs).

Biological assays and *in vitro* data relating to the compounds' anti-HCV and inhibitory activity against

HCV genotypes 1a, 1b and 3a are found in Example 301 (paragraphs [0529] to [0545]). These include data on glecaprevir (i.e. the compound of Example 6 of D6), which was shown to be active *in vitro* against the tested HCV genotypes 1a, 1b and 3a.

D6 mentions that only two approved therapies for HCV infection were available at the time - interferon alone (involving a 3- to 12-month course of intravenous IFN-α) or in combination with general antiviral nucleoside mimics like ribavirin (see paragraph [0006]). Because of the poor tolerability and disappointing efficacy of existing therapies, D6 identifies a need for the development of effective antiviral agents for the treatment of HCV infection.

The protease inhibitors described and claimed in D6 can be administered either as the sole therapeutic agent or in combination with one or more other anti-HCV agents. Interferon, ribavirin or both can be included in the treatment or not (see D6: paragraphs [0249], [0250] and [0263]).

5.4 While mentioning general dosage ranges (for instance, in paragraphs [0322] and [0328]), D6 does not disclose clinical treatment with any of the claimed compounds and does not provide *in vivo* data on the safety and efficacy of glecaprevir or any specific combination of antiviral agents.

5.5 It was common ground that the assessment of inventive step was to be carried out starting from the disclosure of document D6 and that the generically envisaged combination treatment with glecaprevir (paragraph [0249]) could be taken as the starting point in D6.

5.6 This passage states that the compound of the invention of D6 can be administered alone or in combination with one or more other anti-HCV agents, such as HCV polymerase inhibitors, HCV protease inhibitors, HCV NS5A inhibitors, CD81 inhibitors, cyclophilin inhibitors, internal ribosome entry site inhibitors or any combinations of these. Interferon, ribavirin or both can also be included in the treatment.

Objective technical problem

5.7 As set out above, glecaprevir is a preferred HCV protease inhibitor of D6 (see paragraph [0245]), and it is generally disclosed that the HCV protease inhibitors of D6 can be administered in combination with one or more other anti-HCV agents. Thus, combination treatment of HCV infection with glecaprevir and a further anti-HCV agent is an option that is envisaged but not shown to be put into clinical practice in D6.

5.8 The subject-matter defined in claim 1 differs from this prior-art disclosure by the following technical features:

(a) the treatment of an HCV patient with a combination of glecaprevir and a further anti-HCV agent is put into clinical practice

(b) pibrentasvir is chosen as the further anti-HCV agent

(c) the treatment duration is 16 weeks

(d) the concomitant administration of interferon and ribavirin is excluded

5.9 Concerning feature (a), the appellant argued that the patent in suit and the application as filed did not disclose putting the claimed therapeutic application into clinical practice, either.

However, since attaining the claimed therapeutic effect in clinical practice is present as a functional technical feature in current claim 1 (see point 1.3 above), this feature has to be taken into consideration (see section 2. above for sufficiency of disclosure) as a distinguishing technical feature of claim 1 in comparison with the disclosure in D6.

5.10 Contrary to the appellant's view, feature (d) is also considered a distinguishing technical feature as it has to be selected in addition to the combination of features representing the starting point in D6. This starting point is the envisaged combination treatment of HCV infection with glecaprevir and a further anti-HCV agent (see point 5.7 above). D6 does not provide the specific disclosure that such combinations of glecaprevir should be administered without interferon/ribavirin.

The basis for assessing inventive step has to be a combination of technical features that is directly and unambiguously disclosed in the document chosen as the starting point. Features that have to be added to this combination by selection from the further teaching within that document are considered distinguishing features.

5.11 The technical effects linked to the distinguishing technical features identified above are:

- implementing the envisaged combination treatment of HCV infection with glecaprevir and a further anti-HCV agent in clinical practice (features (a) to (d))
- providing a combination of glecaprevir for the treatment of HCV infection (feature (b))
- avoiding treatment with interferon and ribavirin, which was known to have drawbacks (feature (d))

- providing a treatment with a short duration (features (b), (c) and (d))

5.12 The objective technical problem may thus be formulated as providing a combination of glecaprevir with a further anti-HCV agent for use in the treatment of HCV infection, while avoiding the disadvantages of interferon/ribavirin-based treatments.

Obviousness of the solution

5.13 According to D6 (see paragraph [0249]), interferon, ribavirin or both may be, but do not have to be, included in the treatment. D6 also mentions the known drawbacks of these drugs (paragraph [0006]), such as poor tolerability and low efficacy. In view of this teaching in D6, it would have been a possible consideration to test and implement DAA combination treatments without the co-administration of interferon and ribavirin. In the same vein, the review article D8, published about a year before the priority date, speculates that the ongoing rapid clinical development of numerous DAA agents might, at first, provide triple or quadruple combination therapies still including interferon and ribavirin combined with one or two DAAs but, ultimately, might result in dual DAA combination therapies without interferon and ribavirin.

5.14 The appellant pointed out that D8 also reports that a clinical study in patients with chronic HCV had been carried out with a combination of a protease inhibitor (BMS-650032) and an NS5A inhibitor (MBMS-790052)(see D8: page 631, right-hand column, second paragraph) and that it was common knowledge that compounds having different mechanisms of action may favourably complement each other in terms of efficacy and safety. D8 furthermore mentioned that before the end of the

decade, short-duration therapy with extremely high efficacy would be the norm (see D8: page 629, right-hand column, second paragraph). The appellant also mentioned D10 as showing synergy of a protease inhibitor (ABT-493) and an NS5A inhibitor (ABT-530).

5.15 The cited passage in D8 concerning the clinical study relates to different compounds, and, as mentioned above (see point 4.3), the identity of the compounds of D10 was not known. Thus, D8 and D10 only provide the information that compounds belonging to the classes of HCV protease inhibitors and NS5A inhibitors may be combined, which is already suggested in D6 (see D6: paragraph [0429] and point 5.6 above). Nothing about the expected behaviour of glecaprevir in combination with pibrentasvir can be inferred from the passages relied on by the appellant.

5.16 The more specific question that had to be answered in the case in hand was whether, in view of the available prior art, it would have been obvious for the person skilled in the art to choose pibrentasvir as the combination partner of glecaprevir to solve the objective technical problem. This includes whether there would have been a reasonable expectation of success for a viable combination treatment with glecaprevir and pibrentasvir that does not require the co-administration of interferon and ribavirin.

5.17 According to D6, the combination partner of the compound of D6 (an HCV protease inhibitor) may be an NS5A inhibitor, among several other possibilities (see D6: paragraph [0249] and point 5.6 above). D6 does not mention pibrentasvir.

5.18 Pibrentasvir is disclosed as one of over 150 exemplified anti-HCV agents in document D7 but is not

identified as an NS5A inhibitor. D7 mentions, however, that the compounds according to D7 may be combined with other anti-HCV agents such as, *inter alia*, HCV protease inhibitors (see D7: paragraphs [0006] and [1380]).

5.19 As to the obviousness of combining glecaprevir with pibrentasvir, the content of D6 and D7 (both published less than a year before the priority date) suggests that both compounds were still at an early stage of development. This is corroborated by the fact that neither compound is mentioned in D8, a review article giving an overview on emerging DAA therapies for HCV that was published around the same time. Based on the available information, it would thus appear that the individual therapeutic efficacy and safety of these compounds had yet to be assessed. Only *in vitro* data for the single compounds are provided in D6 and D7, and there is no teaching in either document about therapy duration or other potential details of a combination therapy to be administered to HCV patients.

5.20 There is also nothing in the prior art to suggest that the combination of glecaprevir and pibrentasvir would provide HCV treatment without interferon and ribavirin, thus avoiding the disadvantages associated with these drugs, and even providing the added benefit of a comparatively short treatment duration.

5.21 Under these circumstances, there was no direct route, at the effective date, that would have led to the development of the claimed combination with a reasonable expectation of success in solving the objective technical problem.

5.22 The appellant argued that predictive modelling as an established method in the art for predicting the efficacy of anti-HCV drugs would have led the person

skilled in the art to the claimed invention by a routine process, on the basis of the pertinent *in vitro* data for glecaprevir and pibrentasvir known from D6 and D7 (see also D2: paragraph [0022]).

5.23 The board did not arrive at the same conclusion, for the following reasons.

As D6 and D7 only indicate ranges (rather than specific values) for the EC_{50} data, it is doubtful that the person skilled in the art would have seriously considered the combination of the two specific active ingredients on this basis; see also points 5.16 to 5.21 on the expectation of success.

However, this can ultimately be left open, since the model used to perform the pertinent calculations according to the patent and the (earlier) application as filed (D3) did not form part of the common general knowledge and was, therefore, not accessible to the person skilled in the art without knowledge of the application/earlier application.

Consequently, even though modelling as such was undoubtedly common technical knowledge, it was not shown that the person skilled in the art would necessarily have arrived at the claimed subject-matter. The appellant did not show that other models or algorithms available to the person skilled in the art at the effective date, using the data points or ranges disclosed in D6 and D7, would have led to the same result.

5.24 For these reasons, the subject-matter of current claim 1 involves an inventive step within the meaning of Article 56 EPC. The same conclusion applies to the remaining claims, which are all dependent on claim 1.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

K. Boelicke M. Pregetter

Decision electronically authenticated