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Datasheet for the decision of 22 October 2024

Case Number: T 1390/22 - 3.3.07

Application Number: 13773463.8

Publication Number: 2897611

IPC: A61K31/4184, A61P31/14

Language of the proceedings: EN

Title of invention:
METHODS FOR TREATING HEPATITIS C

Patent Proprietor:
AbbVie Inc.

Opponent:
Luigi, Rumi

Headword:
Treating Hepatitis C/ABBVIE

Relevant legal provisions:
EPC Art. 54(5), 56, 83
RPBA 2020 Art. 13(2)

Keyword:

Novelty - main request (yes) - novelty of use - second (or further) medical use - implicit disclosure (no)
Inventive step - main request (yes) - reasonable expectation of success (no)
Sufficiency of disclosure - main request (yes)
Amendment after notification of Art. 15(1) RPBA communication - taken into account (no)

Decisions cited:

G 0002/08, T 2056/17, T 1491/14

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Case Number: T 1390/22 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 22 October 2024

Appellant: (Patent Proprietor)	AbbVie Inc. 1 North Waukegan Road North Chicago, IL 60064 (US)
Representative:	Mewburn Ellis LLP City Tower 40 Basinghall Street London EC2V 5DE (GB)
Respondent: (Opponent)	Luigi, Rumi Ter Meer Steinmeister & Partner Nymphenburger Strasse 4 80335 Munich (DE)
Representative:	Ter Meer Steinmeister & Partner Patentanwälte mbB Nymphenburger Straße 4 80335 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 25 March 2022 revoking European patent No. 2897611 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman	A. Usuelli
Members:	M. Steendijk
	Y. Podbielski

Summary of Facts and Submissions

I. European patent 2 897 611 ("the patent") was granted on the basis of nineteen claims.

Claim 1 as granted defined:

"Methyl{(2S,3R)-1-[(2S)-2-{5-[(2R,5R)-1-{3,5-difluoro-4-[4-(4-fluorophenyl)piperidin-1-yl]phenyl}-5-(6-fluoro-2-{(2S)-l-[N-(methoxycarbonyl)-O-methyl-L-threonyl]pyrrolidin-2-yl}-lH-benzimidazol-5-yl)pyrrolidin-2-yl]-6-fluoro-lH-benzimidazol-2-yl} pyrrolidin-l-yl]-3-methoxy-l-oxobutan-2-yl}carbamate (Compound 1) or a pharmaceutically acceptable salt thereof for use in a method of treatment for HCV, comprising administering an effective amount of Compound 1 or a pharmaceutically acceptable salt thereof to an HCV patient, regardless of the specific HCV genotype(s) that the patient has, wherein said patient is not genotyped for said treatment."

Compound 1 is also known as pibrentasvir.

II. The grant of European patent was opposed on the grounds that its subject-matter lacked novelty and inventive step and that the claimed invention was not sufficiently disclosed.

The patent proprietor filed the appeal against the decision of the opposition division to revoke the patent.

The decision was based on the main request and auxiliary requests 1-3 all filed on 18 November 2021.

Claim 1 of the main request was identical to claim 1 as granted. The amendments in the main request concerned the deletion of claims 2-6, 11-17 and 19 as granted.

Claim 1 of auxiliary request 1 was identical to claim 1 of the main request. Claim 1 according to auxiliary requests 2 and 3 additionally defined with respect to claim 1 of the main request that compound 1 is co-administered with an HCV protease inhibitor".

The opposition division cited *inter alia* the following documents:

D1: Liver International, 2012, 88-102 (first published 29 December 2011)
D2: US 2012/004196 A1
D3: Fachinformation Marivet®, February 2018, Rote Liste Service GmbH,
D4: Nature, 2010, Vol. 465, 96-102
D5: Journal of Virology, 2011, 85(13), 6353-6368
D6: Gastroenterology & Hepatology, 2012, 8(7), 464-466
D7: Curr. Opin. Virol., 2011, 1(6), 607-616
D8: Journal of Hepatology, 2010, Vol. 52, S14-S15, Abstract 33
D9: Conference Reports of NATAP, 2011, "Dose-Ranging Trial of PPI-461, a Potent New Pan-Genotypic HCV NS5A Inhibitor, in Patients with HCV Genotype-1 Infection" (http://www.natap.org/2011/AASLD/AASLD_10.htm)
D10: i-base, Pipeline report, 21 July 2012, "Hepatitis C drug development goes from pony ride to rocket launch" (https://i-base.info/htb/16961)
D12: Antimicrobial Agents and Chemotherapy, 2017, 61(5), e02558-16
D16: Journal of Hepatology, 2014, Vol. 60, 392-420

D19: Journal of Hepatology, 2011, Vol. 55, 245–264
D20: Am J Gastroenterol, advance online publication, 24 April 2012; doi:10.1038/ajg.2012.48

The opposition division arrived at the following conclusions:

(a) The patent presented experimental results in examples 1 and 2 which supported a pan-genotypic effect of pibrentasvir against HCV and which thereby indicated that the genotyping conventionally performed in HCV treatment could be avoided.

The patent thereby sufficiently disclosed the invention as claimed in accordance with the main request.

Document D2 described the potent *in vitro* activity of pibrentasvir against HCV replicons of a variety of genotypes, including variants containing NS5A mutations.

The claimed subject-matter differed from the disclosure in document D2 in the feature that the patient is not genotyped for the intended treatment.

The objective technical problem in view of document D2 concerned the provision of an effective treatment of HCV regardless of the specific genotype of the patient.

The claimed solution was obvious, because document D2 already indicated the pan-genotypic effect of pibrentasvir against HCV by interacting

with NS5A, in view of which the skilled person could reasonably expect its efficacy in treating HCV without the need for HCV genotyping. In addition, the pan-genotyping activity of NS5A inhibitors was in view of document D10 part of the common general knowledge.

The subject-matter of the main request and auxiliary request 1 did therefore not involve an inventive step.

(b) The subject-matter of claim 1 in auxiliary requests 2 and 3 did also not involve an inventive step in view of document D2 as closest prior art.

III. With the statement setting out the grounds of appeal the patent proprietor maintained and re-filed the main and auxiliary requests 1-3 on which the decision under appeal was based.

IV. In its communication under Article 15(1) RPBA the Board indicated that the main request seemed to comply with the requirements of sufficiency of disclosure and novelty. The Board further indicated that the subject-matter of claim 1 of the main request did not seem obvious in view of document D2 by itself or in combination with documents D1, D4, D7, D8, D9 or D10, but referred to the apparent relevance of document D5.

V. In its letter of 27 September 2024 the patent proprietor contested the relevance of document D5 and filed the following document which was cited in document D5:

D21: Journal of Virology, 2010, 84, 482-491

VI. Oral proceedings were held on 22 October 2024.

VII. The arguments of the patent proprietor relevant to the present decision are summarized as follows:

(a) Admittance of document D21

Document D21 was relevant, because it demonstrated that the data on which document D5 relied did not support the assertion in document D5 that NS5A inhibitors generally exhibit pan-genotypic activity. Document D21 was only filed after the Board's communication under Article 15(1) RPBA, because in its preliminary opinion the Board newly raised the issue of the relevance of the pan-genotype activity for NS5A inhibitors mentioned in document D5, whereas in the decision under appeal the opposition division relied on document D10 for its conclusion concerning the pan-genotypic activity of NS5A inhibitors in general.

(b) Novelty

Documents D16, D19 and D20 indicated that at the relevant date the standard of care in the treatment of patients suffering from HCV infection required the assessment of the HCV genotype for the determination of the dose of the medication and the duration of the treatment.

Claim 1 of the main request defined the use of pibrentasvir in the treatment of HCV in which the genotyping of the patient is omitted. The patent demonstrated for pibrentasvir consistent inhibitory activity against HCV genotypes 1-6 as well as mutants thereof within a narrow concentration range, which

therefore allowed the omission of the assessment of the HCV genotype before treatment.

Document D2 described the utility of pibrentasvir in the treatment of HCV infection, but did not explicitly disclose that in such treatment the assessment of the HCV genotype could be omitted. Document D2 described the improved activity of pibrentasvir relative to ombitasvir with respect to a subset of HCV genotypes and mutants, but failed to disclose for pibrentasvir a consistent inhibitory activity against a relevant spectrum of HCV genotypes. Document D2 did therefore also not implicitly disclose that in the treatment with pibrentasvir the HCV genotyping could be omitted.

(c) Inventive step

The standard of care in the treatment of HCV at the relevant date involved the assessment of the HCV genotype of the infected patient. The consistent inhibitory activity of pibrentasvir against HCV genotypes 1-6 as well as mutants thereof within a narrow concentration range as demonstrated by the experimental data in the patent allowed the omission of the conventional genotyping prior to the administration of pibrentasvir. The post-published document D12 confirmed this quantitatively consistent pan-genotypic activity of pibrentasvir activity without raising concerns regarding the more recently identified HCV genotype 7. Document D3 only recommended a longer duration of treatment with pibrentasvir in case of infection with HCV genotype 3 as compared to other genotypes in a subgroup of patients in which prior treatment with sofosbuvir had failed. Document D3 did thereby not require actual genotyping in this subgroup of patients.

Accordingly, the difference of the subject-matter of claim 1 of the main request with the teaching of document D2, namely the omission of the genotyping, represented a significant simplification in the treatment of HCV allowing for the treatment of HCV regardless of the specific HCV genotype.

Document D2 described pibrentasvir as a member of a group of examplified compounds with enhanced activity against various HCV genotypes and mutants thereof as compared to the activity of ombitasvir. However, document D2 did not distinguish pibrentasvir within this group of compounds and did not disclose the quantitatively consistent activity of pibrentasvir across the spectrum of HCV genotypes and mutants thereof required for treatment of patients infected with HCV without the need for genotyping.

Documents D1, D4 and D6-D9 only indicated the pan-genotypic activity against HCV of certain specific NS5A inhibitors. Any suggestion from documents D5 and D10 that NS5A inhibitors in general exhibit pan-genotypic activity against HCV was not supported by the available experimental data. Moreover, such pan-genotypic activity of NS5A inhibitors did not imply their quantitatively consistent activity allowing the treatment without the need for genotyping.

(d) Sufficiency

The patent presented experimental data demonstrating the consistent inhibitory activity of pibrentasvir against HCV genotypes 1-6 as well as mutants thereof within a narrow concentration range and thereby disclosed the suitability of pibrentasvir in the

treatment of patients infected with HCV without the need for the assessment of the specific HCV genotype. The opponent had not raised any serious doubt regarding the relevant efficacy of pibrentasvir against the more recently identified HCV genotype 7 or the Y93H mutant of HCV genotype 1a. The efficacy against the Y93H mutant of HCV genotype 1a was actually demonstrated in the post-published document D12. This document did furthermore not raise any concern regarding the efficacy of pibrentasvir against the HCV genotype 7. Document D3 did not require HCV genotyping in the subgroup of patients in which prior treatment with sofosbuvir had failed, but only recommended in such patients a longer duration of treatment with pibrentasvir in case of infection with HCV genotype 3 as compared to other genotypes.

VIII. The arguments of the opponent relevant to the present decision are summarized as follows:

(a) Admittance of document D21

No exceptional circumstances justified the admittance of document D21. The argument that document D5 indicated pan-genotype activity for NS5A inhibitors in general had already been raised by the opponent during the first instance proceedings. Moreover, with the argument that the mention of the pan-genotypic activity of NS5A inhibitors in document D5 was not supported by the data in document D21 the patent proprietor attempted to introduce a complex new issue, which should not be admitted after the Board issued its communication under Article 15(1) RPBA.

(b) Novelty

Document D2 described compounds of a general formula for inhibiting HCV replication indicating their activity against NS5A, which represented a critical component of HCV replication and which was believed to exert multiple functions at various stages of the viral life cycle. Document D2 specifically described pibrentasvir as an example of general formula I_B (example 3.52) having enhanced activity compared to ombitasvir (reference example 37) against the HCV genotypes 1a, 2a, 3a and 6a as well as NS5A mutants L31V, M28T, M28V, Q30E, Q30R, Y93C, Y93H and Q30H of HCV genotype 1a. The document specifically indicated that accordingly the compounds of formula I_B are suitable for treating patients infected with HCV genotype 1a, 1b, 2a, 2b, 3a, 4a, 5a or 6a or one of the mentioned variants.

Document D2 thereby explicitly disclosed the utility of pibrentasvir in treatment of HCV regardless of whether the patient was infected with HCV genotype 1, 2, 3, 4, 5 or 6 or the described NS5A mutants thereof. In line with the considerations in T 1491/14 document D2 thus described the utility of pibrentasvir in the treatment of the same patient group as defined in claim 1 of the main request regardless of the specific HCV genotype in the patient to be treated.

Document D16 was published after the filing date for the patent and did therefore not indicate the standard of care at the relevant date. Documents D16 and D19 anyway concerned the use of ribavirin, not the use of pibrentasvir in the treatment of HCV. Moreover, document D19 only referred to the assessment of the HCV genotype, not subtypes or mutations thereof.

Document D2 reported improved activity of pibrentasvir with respect to the pan-genotypic inhibitor BMS790052 known from document D4 as well as ombitasvir and did not indicate that genotyping was required for the use of pibrentasvir in the treatment of HCV. The pan-genotypic activity of pibrentasvir as described in document D2 actually implied that the use of pibrentasvir in the treatment of HCV infection did not require genotyping, especially in view of the consideration that document D2 substantiated the outstanding activity of pibrentasvir with respect to the most prevalent HCV genotypes and even mutants thereof. The feature in claim 1 of the main request that the patient is not genotyped for the treatment with pibrentasvir did therefore not distinguish the claimed subject-matter from the teaching in document D2.

The omission of genotyping in treatment of HCV did anyway not qualify as a distinguishing feature within the framework of the possible features of a specific therapeutic use recognized in G 2/08 and jurisprudence following therefrom, in particular T 2056/17.

(c) Inventive step

If the omission of the genotyping was considered to represent a distinguishing feature, the claimed subject-matter could anyway not be considered to involve an inventive step starting from document D2 as closest prior art.

Document D3 indicated that patients with HCV genotype 3 in which treatment with sofosbuvir had failed required

a different duration of treatment with pibrentasvir than patients infected with other HCV genotypes. Since according to the patent proprietor the suitability to treat patients regardless of genotype required that the same dosage regimen could be prescribed to all patients, it had to be concluded that pibrentasvir could not be prescribed without genotyping. Moreover the patent did not substantiate any efficacy of pibrentasvir against HCV genotype 7 or the particularly problematic Y93H mutant of HCV genotype 1a. The problem of providing effective treatment of HCV regardless of the specific genotype of the patient was therefore not credibly solved, at least not over the whole scope of the claim.

Insofar the claimed subject-matter provided effective treatment of HCV regardless of the specific genotype of the patient, the omission of the genotyping would seem obvious to the skilled person in view of the improved pan-genotypic activity against HCV of halo-substituted benzimidazole derivatives, in particular pibrentasvir, as already described in document D2. The pan-genotypic activity against HCV of NS5A inhibitors was indeed already well known in the prior art as evidenced by documents D1 and D5-D10. The circumstance that document D2 also described improved activity against HCV for three further examples could in this context not render the choice of pibrentasvir less obvious.

Whilst the patent provided no data regarding mutants of the most prevalent HCV genotype 1a, document D2 indicated the efficacy of pibrentasvir against mutants of HCV genotype 1a, including the Y93H mutant, which conferred according to document D12 resistance against conventional NS5A inhibitors. If the skilled person would consider on the basis of the data in the patent

that in treatment of HCV with pibrentasvir the genotyping could be omitted, the skilled person would on the basis of similar considerations regard this omission already obvious in view of document D2.

(d) Sufficiency

The patent did not provide any efficacy data of pibrentasvir against the Y93H mutant of HCV genotype 1a, which conferred according to document D12 resistance against conventional NS5A inhibitors. The patent further failed to substantiate the activity of pibrentasvir against HCV subtype 7. Moreover, document D3 indicated that patients with HCV genotype 3 in which treatment with sofosbuvir had failed required a longer duration of treatment with pibrentasvir than patients infected with other HCV genotypes. The patent did therefore not credibly disclose the suitability of pibrentasvir in treatment of HCV regardless of the specific HCV genotype.

IX. The appellant-patent proprietor requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request or one of auxiliary requests 1-3 as filed on 18 November 2021 and re-submitted with the statement of grounds of appeal.

The patent proprietor furthermore requested that document D21 be admitted into the appeal proceedings should D5 become relevant for the assessment of inventive step.

X. The respondent-opponent requested that the appeal be dismissed. The opponent furthermore requested that document D21 not be admitted into the proceedings.

Reasons for the Decision

1. Admittance of document D21

1.1 Document D21 was filed by the patent proprietor after the Board had issued its communication under Article 15(1) RPBA. In accordance with Article 13(2) RPBA the admittance of this document in the appeal proceedings is to be denied unless there are exceptional circumstances which have been justified with cogent reasons by the patent proprietor.

1.2 According to the patent proprietor the content of document D21 demonstrated that the assertion in document D5 regarding the pan-genotypic activity of NS5A inhibitors in general was not supported by the data relied upon in document D5.

The patent proprietor justified the filing of document D21 at the late stage of the proceedings in view of the issue of the relevance of document D5 which the Board would have newly raised the communication under Article 15(1) RPBA.

1.3 The Board considers that the patent proprietor raised a complex new issue with the filing of document D21, namely the question whether the mention of the pan-genotypic activity of NS5A inhibitors in document D5 was supported by the data in document D21.

The argument that document D5 indicated pan-genotype activity for NS5A inhibitors in general had already been presented by the opponent during the first instance proceedings (see decision under appeal, page 13, section 5.1.2). Moreover, this argument was

maintained by the opponent in its reply to the appeal (see page 13). Contrary to the suggestion by the patent proprietor, the Board did thus not raise a new issue by referring to the possible relevance of document D5 in its communication under Article 15(1) RPBA.

The Board does therefore not recognize any exceptional circumstances that could justify the late introduction of the new issues with the filing of document D21.

Accordingly, the Board has not admitted this document into the appeal proceedings.

2. Novelty - main request

2.1 The assessment of the HCV genotype in treatment of HCV prior to the administration of antiviral therapy was standard practice at the time of the priority date for the patent. Document D19 indicates that such assessment formed part of the standard of care in order to select the appropriate type of antiviral therapy, including the dose of the medication and the duration of the treatment (see D19, page 250, section 4.4.5). Moreover, document D20 explicitly qualified the assessment of the HCV genotype in patients with chronic HCV infection as necessary (see D20, page 3, Table 2). The intentional omission of the HCV genotyping as defined in claim 1 of the main request therefore represents a technically meaningful characteristic of the defined therapeutic treatment.

It follows from the considerations in G 2/08 (see Reasons 5.10.9), which refer to the wording "any specific use" in Article 54(5) EPC and confirm the seamless fit between the exclusion from patentability of methods of treatment by therapy and the special

provisions regarding the novelty of a substance or composition for use in such a method, that this technically meaningful characteristic of the defined therapeutic treatment involving the use of pibrentasvir is suitable to characterize the claimed subject-matter in terms of a specific use as intended in Article 54(5) EPC.

Contrary to the opponent's argument the considerations in G 2/08 do not imply any limited framework in terms of the type of technical features of a method of treatment by therapy that may characterize a specific use as intended in Article 54(5) EPC. The opponent's argument regarding such a limited framework does also not find support in T 2056/17. In T 2056/17 (see reasons 2.6) the deciding Board concluded that a pharmaceutical combination for a defined therapeutic use lacked novelty in view of the known use of that combination for the same therapeutic purpose in the same patients by the same route of administration and with the same dosage regimen. In line with the considerations in G 2/08 the deciding Board in T 2056/17 held that the definition of the co-marketing or co-promoting of the individual compositions in the combination was not a technical feature characterizing the defined therapeutic use, because the definition of the co-marketing or co-promoting does not change the clinical situation nor contribute to the therapeutic effect.

2.2 Document D2 describes the non-structural HCV protein NS5A as a critical component of HCV replication which is believed to exert multiple functions at various stages of the viral life cycle which represents a promising target for treating HCV (see D2, paragraph [0004]). In this context document D2 presents compounds

of the general formula I and I_A-I_G for inhibiting HCV replication indicating their activity against NS5A (see D2, paragraph [0005]).

Document D2 describes pibrentasvir (see D2, page 259, example 3.52) as an example of an advantageous halogenated benzimidazole derivative of general formula I_B and as a member of a group of four examples (examples 3.48, 3,52, 4.38 and 5.1) which exhibit improved activity relative to the activity of ombitasvir (see D2, page 16, reference example 37 from US 2010/0317568) against the replication of the HCV genotypes 1a, 2a, 3a and 6a as well as NS5A mutants L31V, M28T, M28V, Q30E, Q30R, Y93C, Y93H and Q30H of HCV genotype 1a (see D2, paragraph [0181]):

> "*For instance, when tested against HCV replicons of different genotypes in stable cell lines (in the presence of 5% FBS), and as compared to Example 37 of U.S. Patent Application Publication No. 2010/0317568, the EC50 values ofthe compounds of Examples 3.48,3.52, 4.38, and 5.1 were at least about 6-fold less than that of Example 37 against genotype 1a, at least about 3-fold less against genotype 3a, at least about 50-fold less against genotype 6a, and significantly less against genotype 2a. In addition, when tested against HCV genotype 1a replicons containing certain NS5A mutations in transient transfection assays, and as compared to Example 37 of U.S. Patent Application Publication No. 2010/0317568, the EC50 values of the compounds of Examples 3.48, 3.52, 4.38, and 5.1 were at least about 130-fold less than that of Example 37 against the L31V variant, at least about 7,500 fold less against the M28T variant, at least about 80-fold less against the M28V variant, at*

least about 500-fold less against the Q30E variant, at least about 300-fold less against the Q30R variant, at least about 800-fold less against the Y93C variant, at least about 1,500-fold less against the Y93H variant, and significantly less against the Q30H variant.
Likewise, when tested against HCV genotype 1b replicons containing certain NS5A mutations in transient transfection assays, and as compared to Example 37 of U.S. Patent Application Publication No. 2010/0317568, the EC50 value of the compound of Example 5.1 was at least about 10-fold less than that of Example 37 against the Y93H variant."

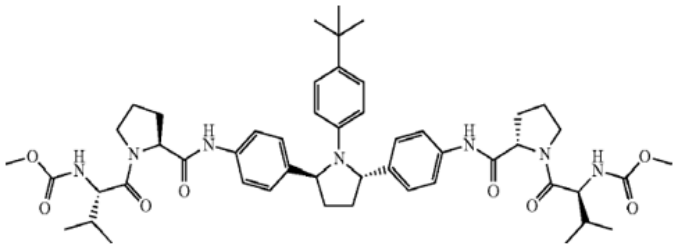
Document D2 concludes in this context that accordingly the compounds of formula I_B are suitable for treating patients infected with HCV genotype 1a, 1b, 2a, 2b, 3a, 4a, 5a or 6a or one of the described variants (see D2, paragraph [0181]).

2.3 Document D2 does not explicitly disclose the utility of pibrentasvir in treatment of HCV in which the assessment of the HCV genotype is intentionally omitted as defined in claim 1 of the main request.

Moreover, whilst document D2 describes compounds of formula I_B to be suitable for treating patients infected with HCV genotype 1a, 1b, 2a, 2b, 3a, 4a, 5a or 6a and identifies pibrentasvir as an advantageous example thereof, document D2 does not describe any absolute activity data for pibrentasvir. The reported activity data for pibrentasvir and the three further examples are only expressed in terms of factors by which the EC_{50} values of these examples for the different HCV genotypes and mutants thereof are at least reduced with respect to the EC_{50} values of

ombitasvir. Meanwhile, document D2 presents for ombitasvir only limited and partly approximate EC_{50} values (see D2, page 16):

EC_{50} (nM in the presence of 40% HP)		EC_{50} (nM in the absence of HP)			
1a	1b	2a	2b	3a	4a
0.2	0.1	≤0.05	≤0.05	≤0.05	≤0.05



(Example 37 of U.S. Patent Application Publication No. 2010/0317568)

Contrary to the opponents argument, document D2 does therefore not disclose any quantitatively consistent activity of pibrentasvir against a spectrum of HCV genotypes and mutants that might imply that in treatment of HCV patients with pibrentasvir the HCV genotyping could be omitted.

2.4 Accordingly, the Board considers that document D2 does not disclose the intentional omission of the HCV genotyping, and that this omission represents a technically meaningful feature of therapeutic use distinguishing the subject-matter of claim 1 of the main request from the teaching of D2.

In view of this distinguishing technical feature of the defined therapeutic use the opponent's argument that according to the criteria applied in point 2.2 of T 1491/14 claim 1 of the main request does not define

the treatment of a new patient group remains without consequence. In this context it is noted, however, that in the case of T 1491/14 the deciding Board acknowledged the novelty of the claimed subject-matter in view of criteria proposed by the patent proprietor that were not contested by the opponent, but also explicitly indicated that the jurisprudence of the Boards of Appeal does not seem to provide fixed criteria for the definition of a new patient group (see T 1491/14, reasons 2.2).

2.5 Accordingly, the Board concludes that the subject-matter of claim 1 of the main request is new in view of the prior art (Article 54 EPC).

3. Inventive step - main request

3.1 The starting point in the prior art

It was not in dispute that document D2 represents the closest prior art.

As explained in section 2 above the intentional omission of the genotyping of the patient in the treatment for HCV as defined in claim 1 of the main request distinguishes the claimed subject-matter from the teaching in document D2.

3.2 The objective technical problem

The patent (see paragraph [0069]) reports in Table 2 experimental results concerning the mean IC_{50} values of pibrentasvir for HCV genotypes 1a, 1b, 2a, 2b, 3a, 4a, 5a and 6a which range from 1.4 to 4.3 pM. Moreover the patent (see paragraph [0071]) presents in Table 3 additional average IC_{50} values of pibrentasvir for HCV

wild type genotypes 2a, 2b, 3a, 4a, 5a and 6a as well as a variety of mutants of each of these wild types, including the Y93H mutant of genotype 3, which are all within the range from 0.8 to 4.3 pM. In addition, Table 3 of the patent provides a comparison of the IC_{50} values for pibrentasvir with the IC_{50} values for ombitasvir. The reported IC_{50} values of ombitasvir range from 0.4 to 80 pM for the HCV wild type genotypes 2-6 and are significantly increased for the mutants thereof showing a greatly increased variability depending on the particular mutation. The reported EC_{50} value of ombitasvir for the Y93H mutant of genotype 3 even exceeds 100.000 pM.

As pointed out in section 2 above, the assessment of the HCV genotype was conventionally required in therapy of HCV in order to determine the appropriate dose for the antiviral treatment. With the reported quantitatively consistent inhibitory activity of pibrentasvir against HCV genotypes 1-6 and mutants thereof the patent credibly demonstrates that in the treatment of HCV an appropriate dose of pibrentasvir should be effective regardless of the specific genotype of the HCV infection.

The opponent's objection that the patent does not demonstrate the efficacy of pibrentasvir against the more recently discovered HCV genotype 7 and mutants of the more prevalent HCV genotype 1a, including the problematic Y93H mutant, is not considered convincing. In view of the extensive efficacy data in the patent the skilled person had no reason to doubt that pibrentasvir would be similarly effective against HCV genotype 7 and mutants of HCV genotype 1a. Moreover, the post-published document D12 confirms the required efficacy of pibrentasvir against HCV genotype 1a

mutants, including the Y93H mutant (see D12, page 4, Table 4) and raises no concern regarding the efficacy of pibrentasvir against the more recently identified HCV genotype 7.

The opponent's further objection that document D3 indicates for the use of pibrentasvir in the treatment of HCV patients in which prior therapy with sofosbuvir had failed a longer duration in case of infection with HCV genotype 3 than in case of infection with HCV genotypes 1-2 and 4-6, and that the treatment of HCV with pibrentasvir therefore still requires genotyping at least for this subgroup of patients, is also not considered convincing. Document D3 recommends for the treatment of patients infected with HCV genotypes 1-6 the same dose of pibrentasvir and in general also the same duration of treatment irrespective of the specific HCV genotype (see D3, page 1, section 4.2, Table 1). Only in the case of patients in which prior therapy with sofosbuvir had failed does document D3 recommend a longer duration of treatment if the patients are infected with HCV genotype 3 (see D3, page 1, Table 2). In these patients the recommended effective dose of pibrentasvir remains according to document D3 unchanged. The mere variation in the recommended duration of treatment with an established effective dose of pibrentasvir does not indicate any necessity for the assessment of the specific HCV genotype, because when the effectiveness of the dose is not in question the effective duration of such treatment follows from the observable effects of the treatment on the HCV infection irrespective of the involved specific HCV genotype.

The intentional omission of the genotyping distinguishing the subject-matter of claim 1 of the

main request is therefore associated with the utility of pibrentasvir in treatment of HCV regardless of the HCV genotype. Accordingly, the objective technical problem underlying the subject-matter of claim 1 of the main request may be seen in the provision of an effective treatment of HCV regardless of the HCV genotype, which evidently represents a significant simplification in the conventional treatment of HCV.

3.3 The assessment of the solution

3.3.1 Document D2 itself describes pibrentasvir as an example of compounds of a general formula I_B having utility in the treatment of infection by HCV genotypes 1-6 which forms part of a group of four exemplified compounds with enhanced activity against various HCV genotypes and mutants thereof as compared to the activity of ombitasvir (see D2, paragraphs [0181]-[0182]). However, as explained in sections 2.2 and 2.3 above, document D2 does not distinguish the activity of pibrentasvir within this group of examples nor disclose any absolute activity data for pibrentasvir. Document D2 does therefore not provide the skilled person with any information that pibrentasvir exhibits effective inhibitory activity against HCV across a wide spectrum of HCV genotypes and mutants within a narrow concentration range that would allow for the treatment of HCV without the need for genotyping.

From the information in document D2 itself the skilled person could therefore not derive any reasonable expectation that pibrentasvir would be suitable for treatment of patients infected with HCV irrespective of the specific HCV genotype without the need for genotyping.

In this context the Board considers the opponent's argument that if the skilled person could on the basis of the data in the patent conclude that in treatment of HCV with pibrentasvir the assessment of the HCV genotype may be omitted, the omission of this assessment in treatment of HCV with pibrentasvir would already be obvious in view of document D2, not convincing, because document D2 does not describe the quantitatively consistent activity of pibrentasvir against a wide spectrum of HCV genotypes disclosed in the patent.

3.3.2 Documents D1, D4, D6 and D7 describe the specific NS5A inhibitor BMS-790052, also known as daclastavir, to exhibit activity against a broad spectrum of HCV genotypes (see D1, page 91, left column; D4, page 97, left column; D6, page 466, right column; D7, page 3). Document D4 presents for this specific compound EC_{50} values against HCV genotypes 1-6 ranging from 9-146 pM (see D4, page 97, Table 1).

Documents D8 and D9 describe the specific NS5A inhibitor PPI-461 to exhibit pan-genotypic antiviral against HCV (see D8, under "Results"; D9, title). Document D8 reports for this specific compound EC_{50} values for the HCV genotypes 1a and 1b of 0.2 and 0.01 nM and for genotypes 2-7 EC_{50} values ranging from 0.1-19 nM.

Document D5 states that NS5A inhibitors demonstrate pan-genotypic activity against HCV in general (see D5, page 6354, left column, lines 2-3). A similar statement is found in document D10 (see page 3, under "NS5a Inhibitors").

As is evident from the broad ranges of the EC_{50} values reported for the specific NS5A inhibitors in documents D4 and D8, the qualification of NS5A inhibitors as pan-genotypic does not imply that these specific NS5A inhibitors, let alone NS5A in general, exhibit effective inhibitory activity against HCV across a wide spectrum of HCV genotypes and mutants within a narrow concentration range that would allow their use for the treatment of HCV without the need for genotyping.

Documents D1 and D4-D10 do therefore not provide the skilled person with any additional information allowing for a reasonable expectation that pibrentasvir would be suitable for treatment of patients infected with HCV irrespective of the specific HCV genotype without the need for genotyping.

3.4 Accordingly, the Board concludes that the subject-matter of claim 1 of the main request involves an inventive step (Article 56 EPC).

4. Sufficiency - main request

4.1 As pointed out in section 3.2 above the patent credibly discloses on the basis of the quantitatively consistent inhibitory activity of pibrentasvir against HCV genotypes 1-6 and mutants thereof that in the treatment of HCV a suitable dose of pibrentasvir should be effective regardless of the specific genotype of the HCV infection. The Board therefore considers that the patent sufficiently discloses the claimed utility of pibrentasvir in the treatment of HCV regardless of the specific HCV genotype wherein the patient is not genotyped for the treatment.

4.2 The opponent's objection that the patent does not disclose the efficacy of pibrentasvir against the more recently discovered HCV genotype 7 and mutants of the more prevalent HCV genotype 1a, including the problematic Y93H mutant, is not considered convincing for similar reasons as set out in section 3.2 in the context of the assessment of inventive step. In particular, the Board considers that in view of the extensive efficacy data in the patent the opponent has not raised serious doubts concerning the efficacy against HCV genotype 7 or mutants of HCV genotype 1a.

The opponent's further objection that document D3 indicates for the use of pibrentasvir in the treatment of HCV patients in which prior therapy with sofosbuvir had failed a longer duration in case of infection with HCV genotype 3 than in case of infection with HCV genotypes 1-2 and 4-6, and that the treatment of HCV with pibrentasvir therefore still requires genotyping at least for this subgroup of patients, is also not considered convincing for similar reasons as set out in section 3.2 in the context of the assessment of inventive step. In particular, the Board considers that the mere variation in the recommended duration of treatment with an established effective dose of pibrentasvir does not indicate any necessity for the assessment of the specific HCV genotype, because when the effectiveness of the dose is not in question the effective duration of such treatment follows from the observable effects of the treatment on the HCV infection irrespective of the involved specific HCV genotype.

4.3 Accordingly, the Board concludes that the main request complies with the requirement of Article 83 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent on the basis of claims 1-6 of the main request filed with the statement setting out the grounds of appeal and a description to be adapted thereto if necessary.

The Registrar: The Chairman:

S. Sánchez Chiquero A. Usuelli

Decision electronically authenticated