IQWiG Reports – Commission No. A16-73

Sofosbuvir/velpatasvir (chronic hepatitis C) –

Addendum to Commission A16-48[1]

Addendum

Commission: A16-73
Version: 1.0
Status: 8 December 2016

[1] Translation of addendum A16-73 *Sofosbuvir/Velpatasvir (chronische Hepatitis C) – Addendum zum Auftrag A16-48* (Version 1.0; Status: 8 December 2016). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

Publishing details

Publisher:
Institute for Quality and Efficiency in Health Care

Topic:
Sofosbuvir/velpatasvir (chronic hepatitis C) – Addendum to Commission A16-48

Commissioning agency:
Federal Joint Committee

Commission awarded on:
23 November 2016

Internal Commission No.:
A16-73

Address of publisher:
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Keywords: sofosbuvir, velpatasvir, hepatitis C – chronic, benefit assessment

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Abbreviation	Meaning
AE	adverse event
CHC	chronic hepatitis C
CSR	clinical study report
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
HCV	hepatitis C virus
HIV	human immunodeficiency virus
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
SOF	sofosbuvir
SVR 12	sustained virologic response 12 weeks after the end of treatment
VEL	velpatasvir

1 Background

On 23 November 2016, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to conduct supplementary assessments for Commission A16-48 (Sofosbuvir/velpatasvir – Benefit assessment according to §35a Social Code Book V [1]).

In its dossier, the pharmaceutical company (hereinafter referred to as "the company") had presented no data for the derivation of an added benefit for patients with chronic hepatitis C (CHC) and human immunodeficiency virus (HIV) coinfection. It had presented results of the one-arm study ASTRAL-5 on the basis of a congress presentation [2] as additional information.

In the framework of the commenting procedure on the dossier assessment the company sent supplementary information [3], which went beyond the information provided in the dossier on sofosbuvir/velpatasvir (SOF/VEL) [4], to prove the added benefit. This information also included the final clinical study report (CSR) of the ASTRAL-5 study, for which the dossier only contained the results from a presentation.

The G-BA commissioned IQWiG with further assessments. The data submitted by the company were to be assessed under the research question whether, under consideration of the final CSR of the ASTRAL-5 study, an added benefit for HIV-coinfected patients with genotype 1 to 6 can be determined, and to what extent a possible added benefit can be derived for the total population (both patients without coinfection and patients with HIV coinfection) in the respective genotypes.

The responsibility for the present assessment and the results of the assessment lies exclusively with IQWiG. The assessment is forwarded to the G-BA. The G-BA decides on the added benefit.

2 Assessment of the final clinical study report of the ASTRAL-5 study subsequently submitted (patients with HIV coinfection)

In the framework of the commenting procedure, the company subsequently submitted the final CSR of the ASTRAL-5 study [5]. The ASTRAL-5 study was a one-arm, open-label phase 3 study. Adult patients with CHC genotype 1 to 4 and HIV coinfection were included in the study. The patients received SOF/VEL over a period of 12 weeks. In its comment, the company presented a comparison of the rates of sustained virologic response 12 weeks after the end of treatment (SVR 12) in HIV-coinfected patients with the SVR 12 rates in hepatitis C virus (HCV)-monoinfected patients for the respective HCV genotypes (see Table 1 in Appendix A).

No patients with genotype 5 and 6 were included in the ASTRAL-5 study. Therefore no conclusions on these patients are possible.

The HIV-coinfected patients with HCV genotype 1 (N = 78) achieved similar SVR 12 results as the monoinfected patients. The company presented no comparison with the appropriate comparator therapy, however. In addition, it also presented no data on adverse events (AEs) for HIV-coinfected patients with genotype 1. In the dossier and in the CSR, the company only presented the results on AEs for the total population of the study. The added benefit cannot be assessed on the basis of the SVR 12 results under SOF/VEL alone.

Only very few HIV-coinfected patients with the HCV genotypes 2, 3 and 4 were included in the ASTRAL-5 study (N = 5 to 12). There was no information in comparison with the appropriate comparator therapy also for these patients and data on AEs were lacking. Due to the low number of patients, these data would have little informative value, however. The added benefit cannot be assessed also for this patient group.

In summary, no conclusions on the added benefit of SOF/VEL in patients with CHC and HIV coinfection are possible on the basis of the available data. Also, no conclusions can be drawn to what extent results of HCV-monoinfected patients are transferable to patients with CHC and HIV coinfection.

3 References

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5. Gilead. A phase 3, open-label study to investigate the efficacy and safety of sofosbuvir/GS-5816 fixed dose combination for 12 weeks in subjects with chronic Hepatitis C virus (HCV) and Human Immunodeficiency Virus (HIV)-1 coinfection; study GS-US-342-1202 (ASTRAL-5); final clinical study report [unpublished]. 2016.

Citations marked with * are unedited citations provided by the company.

Appendix A– SVR 12 rates

Table 1: Summary of the results for the outcome "SVR 12" presented by the company – HCV-monoinfected and HIV-coinfected patients

	SOF/VEL			
Outcome **Patient population**	**HCV-monoinfected patients[a]**		**HIV-coinfected patients (ASTRAL-5)**	
	N[b]	n (%)	N[b]	n (%)
SVR 12				
GT 1, without cirrhosis	301	297 (98.7)	78	74 (94.9)[c, d]
GT 1, with compensated cirrhosis	80	79 (98.8)		
GT 2	134	133 (99.3)	11	11 (100)
GT 3	277	264 (95.3)	12	11 (91.7)
GT 4, without cirrhosis	96	95 (99.0)	5	5 (100)[c, d]
GT 4, with compensated cirrhosis	27	27 (100)		

a: Results of the studies presented by the company in the dossier [4]. If several studies for one genotype were available, the company added up the number of randomized patients and of the patients with event for this presentation.
b: Number of randomized patients.
c: Data stratified by cirrhosis status were not available.
d: Discrepancy between the information provided by the company in the comment and the CSR of the ASTRAL-5 study. The data presented are from the CSR of the ASTRAL-5 study.
CSR: clinical study report; GT: genotype; HCV: hepatitis C virus; HIV: human immunodeficiency virus; N: number of randomized patients; n: number of patients with event; SOF: sofosbuvir; SVR: sustained virologic response; VEL: velpatasvir