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Review paper

Recommendations of the Polish Group of Experts for HCV for the treatment of hepatitis C in 2023

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Abstract

The recommendations define the principles of diagnosis and treatment of hepatitis C virus (HCV) infection according to the latest knowledge. The main goal of the treatment of HCV infection is to eliminate the virus from the body, which in turn leads to stopping the progression or causes the regression of previously formed changes in the liver. The current version of the guidelines prioritizes pangenotypic regimens and includes guidelines for special patient populations such as children, patients with cirrhosis, human immunodeficiency virus (HIV) and hepatitis B virus (HBV) infection, patients with renal failure, liver failure and lack of response to previous therapies as well as patients in the peri-transplant period.

Key words: therapy, liver, HCV, recommendations, viral hepatitis.

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Introduction

Liver disease caused by hepatitis C virus (HCV) infection is rarely diagnosed on the basis of the clinical picture, as it usually remains asymptomatic or oligosymptomatic for many years. Therefore, the identification of infection is often incidental or based on risk factor analysis, leading to the detection of anti-HCV antibodies. A separate group of patients consists of people with extrahepatic manifestations of HCV infection, in whom diseases of other organs or systems were the basis for serological tests. In recent years, in Poland, anti-HCV antibodies have been found in less than 1% of the population, while the presence of viral ribonucleic acid (HCV-RNA) indicating active infection has been found in about 0.4%. There is high variability in the occurrence of both indicators of infection depending on the study group. This may indicate that the estimated number of people infected with HCV in the Polish population reaches 140,000 [1-4].

Due to the influx of a significant number of refugees last year, both economic and, above all, as a consequence of the war in Ukraine, the total number of people infected in Poland may have increased significantly recently. The vast majority of infections among Polish citizens and other nationalities have not yet been diagnosed. The situation is not facilitated by the fact that the screening strategy for Poland should include population tests, and the identification of the so-called high-risk groups. An example of proper management

with features of population screening is anti-HCV testing in women of reproductive age as part of routine gynecological examinations, and not only examination of pregnant women, as is currently the case [4-6]. As research carried out under the EpiTer-2 project has shown, genotype (GT) 1b (82%) dominates in Poland; other genotypes are: GT3 (11.3%), GT4 (3.5%) and GT1a (3.2%). Infections with genotypes 2, 5 and 6 are diagnosed sporadically [1]. The distribution of genotypes in the Polish population changes slightly in successive years and shows some geographical variation.

It is believed that up to 40% of acute infections resolve spontaneously, and in the remaining patients, chronic HCV infection becomes apparent after many years, often at the stage of advanced changes in the liver. About 20% of chronically infected HCV patients will develop cirrhosis or hepatocellular carcinoma. HCV infection causes numerous extrahepatic syndromes, most commonly mixed cryoglobulinemia (often asymptomatic) and B-cell non-Hodgkin's lymphomas (especially diffuse large B-cell lymphoma [DLBCL] and marginal zone lymphoma [MZL]), as well as type 2 diabetes, autoimmune thyroiditis, chronic kidney disease, depression, and lichen planus. Moreover, it promotes the development of cardiovascular diseases [7, 8].

Treatment is aimed at eliminating HCV infection, and consequently stopping or reversing histological changes in the liver, reducing the risk of developing cirrhosis and hepatocellular carcinoma (HCC), and preventing new infections. HCV-infected people should be qualified for treatment as soon as possible. However, in patients with advanced, especially disseminated cancer, the decision to treat HCV infection should be made taking into account the life potential.

Course of HCV infection

Acute HCV infection

The only objective criterion for the diagnosis of acute hepatitis C is the presence of anti-HCV and/or HCV RNA in a previously seronegative person after documented exposure to HCV infection. In addition, the diagnosis of acute hepatitis C may be supported by high levels of alanine aminotransferase found in such cases. It should be remembered that HCV RNA is detected as early as 1-3 weeks after infection, and anti-HCV antibodies only after 4-10 weeks. When the first clinical symptoms appear, anti-HCV is present only in 50-70% of patients. Some of them do not have anti-HCV antibodies at all, so sometimes infection is diagnosed solely by the presence of HCV RNA in the blood [8, 9].

Patients with acute HCV infection should be treated after the initial diagnosis without waiting for the possible spontaneous elimination of the infection. The results of studies indicate the high effectiveness of interferon-free therapies; therefore patients diagnosed with acute hepatitis C should be immediately qualified for antiviral treatment in accordance with the principles described below [10, 11].

Chronic HCV infection

In about 20-40% of people with acute HCV infection, the virus is cleared spontaneously, and in the remaining patients, the infection becomes chronic. Chronic HCV infection can lead to chronic hepatitis, which in some patients results in cirrhosis and hepatocellular carcinoma, as well as the above-mentioned extrahepatic manifestations of HCV infection [11].

General recommendations

The decision on the choice of a therapeutic regimen must take into account the current availability, effectiveness and safety profile of antiviral drugs. The patient should be informed about the duration of therapy, the potential side effects of each drug, possible interactions with other medications in use and the importance of adherence to the prescribed treatment regimen, as well as the principles of continuation and discontinuation of therapy.

Detection of HCV infection

While implementing the goals set by the World Health Organization in the field of eliminating viral hepatitis as a threat to public health, it is necessary to strive for the maximum dissemination of screening tests detecting anti-HCV antibodies, with subsequent confirmation of infection activity by detecting HCV RNA as part of qualification for treatment [12]. Screening tests for anti-HCV should be carried out using both classical laboratory methods and rapid cassette tests, which already have a generally recognized diagnostic value.

Screening tests should be carried out primarily in:

- primary health care settings, due to accessibility for patients;
- hospital emergency departments (admission units), due to the high percentage of people who may have been exposed to infection in the past (multiple hospitalizations);
- prisons, due to the particularly high incidence of HCV infections.

Assessment of the stage of liver diseases

With the advent of pangenotypic drugs, the dosage of which does not depend on the stage of fibrosis, as was formerly the case, its assessment has lost importance. It seems that when qualifying for treatment, it is advisable to determine at most whether we are dealing with cirrhosis. On the other hand, a detailed assessment of the severity of liver disease should not be an absolutely required criterion when qualifying for treatment of HCV infections. However, it may still be useful in monitoring the patient after the end of treatment for the risk of developing cirrhosis and hepatocellular carcinoma, as well as the risk of liver failure and portal hypertension.

The severity of liver disease should be assessed using non-invasive methods to identify patients with a high probability of cirrhosis. The most effective method is dynamic elastography, which enables the measurement of hepatic tissue stiffness, expressed in kPa (SWE – shear wave elastography, TE – transient elastography, ARFI – acoustic radiation force impulse) [13]. However, it should be remembered that the stiffness of the liver tissue measured in this way is dependent not only on fibrosis, but also on inflammatory changes, blood supply and steatosis, as well as possible obesity or meals taken.

In the case of suspected coexistence of liver diseases of a different etiology, inconsistency between the result of a non-invasive examination and the patient's clinical condition, or discrepancies between the results of various non-invasive methods, it is advisable to perform a liver biopsy. Its result is then decisive.

If there are contraindications to both elastography and liver biopsy, or if it is impossible to evaluate the examination result, it is possible to use serum tests, based on which the patient can be qualified for treatment. The most accessible of these is APRI (aspartate aminotransferase/platelet ratio index), whose values below 1.0 make it possible to rule out advanced hepatic fibrosis with high probability. The next test is FIB-4, the result of which < 1.3 allows the exclusion of advanced fibrosis, while the value > 2.67 with high probability supports the diagnosis of advanced fibrosis [14].

Recommended medications

Table 1 presents the recommended direct acting antiviral (DAA) combination therapies registered by the European Medicines Agency (EMA). These include combination preparations containing the following active substances in tablets:

- glecaprevir (GLE), pibrentasvir (PIB),
- sofosbuvir (SOF), velpatasvir (VEL),
- sofosbuvir, velpatasvir, voxilaprevir (VOX),
- sofosbuvir, ledipasvir (LDV),
- elbasvir (EBR), grazoprevir (GZR).

Of those listed above, glecaprevir/pibrentasvir, sofosbuvir/velpatasvir, and sofosbuvir/velpatasvir/voxilaprevir are pangenotypic. On the other hand, sofosbuvir/ledipasvir and elbasvir/grazoprevir are genotype-specific drugs, the use of which should be limited to special situations where administration of pangenotypic drugs is impossible. Due to the contraindications regarding protease inhibitors, sofosbuvir/ledipasvir may be used in patients with decompensated cirrhosis infected with all genotypes except GT3. In turn, elbasvir/grazoprevir is the drug of choice in genotype 1 or 4-infected patients with renal failure, especially if glecaprevir/pibrentasvir is contraindicated due to drug interactions [15].

Treatment effectiveness assessment

To assess the effectiveness of treatment, it is necessary to determine the presence of HCV RNA at least 12 weeks after the end of treatment. Possible assessment of the response to treatment during its duration may be useful to assess the patient's adherence, but due to the short duration of interferon-free therapy, it is not useful in practice. It is also not recommended to test HCV RNA at the end of therapy, because even in the case of positive results, elimination of HCV infection is observed after a 12-week observation.

Treatment can be considered successful if no viral RNA (HCV RNA) is detected in the blood 12 weeks after treatment, which means a sustained virological response (SVR). In cases of dubious or low positive results in the quantitative test after 12 weeks, it is recommended to repeat the test. The effectiveness of therapy should be assessed using methods that ensure the detection level of HCV RNA ≤ 15 IU/ml [15]. The possibility of

Table 1. Currently recommended drugs in the treatment of HCV infection, divided into classes

Class	Drug	Dosage
NS3 (protease) inhibitors	Glecaprevir (GLE)	300 mg/day in 1 dose
	Voxilaprevir (VOX)	100 mg/day in 1 dose
	Grazoprevir (GZR)	100 mg/day in 1 dose
NS5B (polymerase) inhibitor	Sofosbuvir (SOF)	400 mg/day in 1 dose
NS5A inhibitors	Pibrentasvir (PIB)	120 mg/day in 1 dose
	Velpatasvir (VEL)	100 mg/day in 1 dose
	Elbasvir (EBR)	50 mg/day in 1 dose
	Ledipasvir (LDV)	90 mg/day in 1 dose

NS – non-structural

using the core antigen (HCVcAg) as an alternative to HCV RNA has been limited by the low prevalence of specialized equipment and the increasing availability of devices for rapid testing for HCV RNA using the polymerase chain reaction (PCR) technique. Nevertheless, the detection of viral core antigen (HCVcAg) may in some situations be used instead of HCV RNA testing, both for the purposes of qualification for treatment and assessment of its effectiveness [16, 17]. Such a strategy may be applicable in cases of limited access to PCR tests and in populations with expected lower adherence to treatment (prisons, addiction treatment institutions, long-term care facilities, etc.).

HCV infections in children

It is estimated that the number of children infected with HCV in the world is about 3.5 million. The main route of transmission of these infections in the youngest children is the vertical route with a frequency of 3-5%, and in adolescents taking psychoactive substances intravenously. All babies born to HCV-infected mothers should be routinely screened for HCV infection. Since anti-HCV antibodies cross the placenta and can persist in the blood of a child up to 18 months of age, diagnosis of vertical HCV infection in the first year of life requires PCR diagnostics. It is recommended that the first HCV RNA test be performed between the second and third month of life [18, 19].

It is recommended to treat HCV infections in all untreated children and those with previous therapy failure. Histological evaluation of the liver is not an obligatory criterion for qualifying for treatment. Therapy should be conducted in centers experienced in the treatment of children with chronic hepatitis C. The basic therapeutic regimen is interferon-free therapies, which can be used in children over 3 years of age, regardless of the severity of liver disease [15, 20].

In the treatment of HCV-infected children without cirrhosis or with compensated cirrhosis (Child-Pugh A), pangenotypic therapies, sofosbuvir/velpatasvir (SOF/VEL) or glecaprevir/pibrentasvir (GLE/PIB) are recommended. In adolescents over 12 years of age, these therapies are used in adult doses of SOF/VEL – 400 mg/100 mg, and GLE/PIB – 300 mg/120 mg, but in children aged 3-11 years in doses based on body weight, as shown in Table 2.

Cirrhosis and hepatocellular carcinoma

HCV infection poses a serious risk of developing HCC also in patients who are successfully treated. In HCV infections, HCC almost always occurs in patients with cirrhosis [21]. Therefore, they should systematically undergo liver ultrasound examinations and, possibly, additionally measurement of serum α-fetoprotein (AFP) concentrations. Ultrasound examinations should be performed obligatorily before starting therapy and no later than 12 weeks after its completion. In patients with mild fibrosis (F0-F2), repeated examinations may be considered in case of suspicion of other liver diseases, especially fatty liver disease. In patients with advanced liver disease, especially with cirrhosis, ultrasound should be performed every 24 weeks. Similar rules apply to patients with a history of HCC.

Patients with cirrhosis should also have regular endoscopic examinations of the upper gastrointestinal tract. Testing the AFP concentration at the time of detecting a focal lesion in ultrasound may be useful in determining the prognosis of already diagnosed cancer and in monitoring the effectiveness of therapy. If a neoplastic lesion is suspected, a four-phase contrast CT examination or magnetic resonance imaging with contrast is recommended. Contrast-enhanced ultrasound is not recommended for the routine diagnosis of HCC. Ultrasound, computed tomography and mag-

Table 2. Drugs used in the treatment of HCV infection in children

Age	SOF/VEL tablets – 200 mg/50 mg, granules – 50 mg/12.5 mg		GLE/PIB sachets 50 mg/20 mg served with a snack	
	Body weight (kg)	Dosage	Body weight (kg)	Dosage
Children 3-11 years	< 17	150 mg/37.5 mg (3 portions of granules)	12-19	150 mg/60 mg (3 sachets)
	> 17	200 mg/50 mg (tablet or 4 portions of granules)	20-29	200 mg/80 mg (4 sachets)
			30-44	250 mg/100 mg (5 sachets)
Teenagers 12-17 years	400 mg/100 mg			300 mg/120 mg

netic resonance imaging should be performed by specialists experienced in liver imaging [15, 22, 23].

Despite initial reports suggesting an increased risk of HCC after DAA therapy, studies conducted on large treated populations have ruled out this possibility in HCV-infected patients with no prior history of HCC [24, 25].

Coinfections with HBV or HIV

The treatment of HCV infection associated with hepatitis B virus (HBV) or human immunodeficiency virus (HIV) co-infection is the same as in HCV monoinfection, although antiretroviral drugs require a special analysis of the risk of drug interactions. Initially reported mainly in Asia, life-threatening emergencies from HBV reactivation in HCV co-infected individuals resulted from inadequate monitoring of HBV infection. Contemporary studies suggest that despite the relatively high frequency of previous exposure to HBV and latent hepatitis B in HCV-infected patients in Poland, the risk of HBV reactivation during DAA therapy in hepatitis B surface antigen (HBsAg) positive patients is relatively low, and in HBsAg(–)/anti-hepatitis B core (HBc) positive patients HBV reactivation seems to be limited to immunodeficient individuals [26].

HBV reactivation should be defined as a sudden increase in HBV deoxyribonucleic acid (HBV DNA) levels of at least 100-fold in patients with previously detectable HBV-DNA or the detection of previously undetectable (HBsAg) or HBV DNA in anti-HBc positive patients. The following measures should be considered to avoid the risk of HBV reactivation when treating HBV infection [27]:

1. Due to the particularly frequent cases of HBV reactivation during lamivudine treatment, this regimen should be avoided in patients scheduled for DAA therapy.
2. Patients eligible for HCV therapy who are already diagnosed with HBV but are not receiving nucleotide or nucleoside analogues (NUC) should receive entecavir (ETV), tenofovir disoproxil (TDF) or tenofovir alafenamide (TAF) for at least 4 weeks prior to DAA therapy, but the optimal time to start DAA should be when HBV DNA is undetectable. After completion of treatment of HCV infection, the patient should continue NUC therapy in accordance with the guidelines for the treatment of HBV infection.
3. Patients already treated for HBV infection who are unable to achieve viral suppression with their current regimen should be switched to alternative strong NUC therapy (ETV, TDF or TAF) or, if not possible, should be monitored more closely for deterioration of liver function during DAA therapy and for at least 24 weeks after the end of HCV treatment. After completion of DAA therapy, they should continue treatment of HBV infection.
4. Patients successfully treated with NUC who achieved viral suppression before starting HCV therapy should continue this regimen in parallel with DAA.
5. HBsAg testing should be performed in all patients not previously diagnosed for HBV infection with known HCV infection who are scheduled for DAA treatment. Additional anti-HBc tests should be performed in patients with immunodeficiencies resulting from a possible concomitant disease or immunosuppressive therapy. Persons with detectable HBsAg or HBsAg negative/anti-HBc positive with immunodeficiency should have a HBV DNA test before starting DAA treatment, and then during therapy they should have alanine transaminase (ALT) activities monitored according to the following scenarios:
   - In patients with undetectable HBV DNA and normal ALT activities prior to HCV treatment, in case of any increase in ALT during DAA therapy and within 12 weeks after its completion, HBV DNA testing should be performed with simultaneous administration of a strong NUC (ETV, TDF or TAF) in parallel to the DAA, without waiting for the HBV DNA test result.
   - In patients with undetectable HBV DNA but with elevated ALT activities that do not decrease during the first 4 weeks of DAA treatment, the HBV DNA test should be repeated during DAA therapy and 12 weeks after its completion; detection of HBV DNA should result in the administration of a strong NUC (ETV, TDF or TAF).
   - Patients with detectable HBV DNA should be mandatorily treated with NUC if they have advanced liver disease.

Renal failure

Patients with estimated glomerular filtration rate (eGFR) ≥ 30 ml/min/1.73 m^2 should be treated in accordance with the general principles of HCV therapy. The optimal therapy for infections of all genotypes in patients with severe renal impairment (eGFR < 30 ml/min/1.73 m^2), especially those undergoing hemodialysis, is GLE/PIB. In individual cases, especially those resulting from drug interactions, GZR/EBR therapy may also be used, but this option applies only to those infected with GT1 or GT4 [15]. In justified cases resulting

from drug interactions, and above all in patients with decompensated cirrhosis, the use of SOF/VEL may be considered, due to the proven safety of this therapy.

Patients with addictions

The presence of active addiction to alcohol or narcotic substances is not a contraindication to the treatment of HCV infection. This is due to the confirmation of the high effectiveness of DAA in cohorts of addicted people in numerous real-world experience studies. Antiviral treatment should be carried out in parallel with addiction therapy [28].

Prisons

Anti-HCV screening should be offered to all prisoners, preferably at the beginning of their sentence. Taking into account the numerous experiences from other countries and the well-known characteristics of available medication, in order to increase the availability of therapy, it is acceptable to refrain from HCV genotyping and disease staging when qualifying for pangenotypic treatment, as they do not change the treatment procedure [29]. In addition, with the exception of patients with decompensated cirrhosis, renal failure and after organ transplantation, it is acceptable to refrain from performing control laboratory and ultrasound examinations during and after treatment.

Liver transplantation

Effective antiviral treatment with a sustained virologic response is the most optimal form of protecting the transplanted liver against HCV reactivation. Patients with compensated cirrhosis and a Model of End-stage Liver Disease (MELD) score ≤ 18-20 should start antiviral therapy prior to transplantation. Clinical stabilization, maintenance of liver function, and possible partial regression of fibrosis, after achieving SVR, in selected cases allows permanent or temporary postponement of the decision to undergo transplantation [30].

Antiviral therapy in a patient with advanced hepatic insufficiency (Child-Pugh B and C), especially in the case of concomitant advanced renal insufficiency (eGFR < 30 ml/min), should be preceded by liver transplantation. Efficacy and safety of DAA in liver recipients make it possible to start antiviral therapy in the early period after transplantation, after confirmation of the presence of HCV viremia, optimally within a month after the transplantation procedure. If the transplant procedure was performed during antiviral therapy, the decision to interrupt or continue therapy should be considered on an individual patient basis. The choice of antiviral regimen, apart from the general rules, is dictated by potential drug interactions, including with immunosuppressive drugs. In patients after liver transplantation, the optimal therapeutic options are GLE/PIB or SOF/VEL. Calcineurin inhibitor concentrations should be monitored during and after antiviral therapy [31].

Patients with decompensated cirrhosis

In patients with a history of hepatic encephalopathy, ascites, classified into Child-Pugh class B or C, as well as patients after liver transplantation, therapy should be conducted under special supervision in centers experienced in the treatment of patients with decompensated cirrhosis. They should have the possibility of immediate hospitalization and qualification for liver transplantation. Patients with cirrhosis in Child-Pugh class C should primarily be qualified for liver transplantation [32]. There are currently no convincing data on the choice of therapeutic regimen in these cases, but drugs containing a protease inhibitor (GLE/PIB and SOF/VEL/VOX) are not recommended in class B hepatic failure and are contraindicated in patients with class C hepatic failure. This is due to the potential toxicity of protease inhibitors in patients with decompensated cirrhosis. Regimens based on SOF and an NS5A inhibitor (SOF/VEL or SOF/LDV) are recommended in these cases [33].

Drug interactions with DAA

Before starting treatment of HCV infection, it is necessary to check potential interactions with other drugs taken by the patient, which may affect the effectiveness, dosage or safety of therapy. If the risk of serious interactions is identified, the planned HCV infection therapy regimen should be changed, and if this is not possible, the previously used drugs should be replaced with safe ones or their dosage should be modified. Most doubts about drug interactions can be clarified using the website www.hep-druginteractions.org.

Detailed recommendations

So far, the basic criterion differentiating the therapeutic approach has been the HCV genotype test, the assessment of the severity of the liver disease and possible previous therapeutic failure. The emergence of pangenotypic drugs makes the assessment of the virus genotype less important, so it should not be absolutely required when qualifying for treatment. Genotyping

may be justified only when it is necessary to use a genotype-specific drug due to the presence of factors preventing or hindering the use of a pangenotypic drug (drug interactions, renal or hepatic failure, potentially HCV resistance profile). Its assessment may also be considered in the case of treatment failure, as part of the search for the causes of failure.

Pangenotypic regimens

Glecaprevir/pibrentasvir

One tablet contains 100 mg of glecaprevir and 40 mg of pibrentasvir. It is recommended to take three tablets a day with a meal. The duration of therapy is 8 weeks in all previously untreated patients and after treatment failure with pegylated interferon α + ribavirin (PegIFNa + RBV) ± SOF or SOF + RBV if they do not have cirrhosis and are infected with genotypes other than 3. In patients with compensated cirrhosis after failure of the aforementioned therapy, the duration of treatment should be extended to 12 weeks, and if they are infected with genotype 3, extended to 16 weeks both in patients with and without cirrhosis. After liver or kidney transplantation, GLE/PIB therapy should last 12 weeks, and if it was preceded by PegIFNa + RBV ± SOF or SOF + RBV failure, it should be extended to 16 weeks. The regimen is not recommended in patients with decompensated cirrhosis (Child-Pugh class B and C). GLE/PIB in the form of tablets can be administered over 12 years of age, and granules in sachets should be used in children between 3 and 12 years of age [34].

Sofosbuvir/velpatasvir

One tablet of the drug containing 400 mg of sofosbuvir and 100 mg of velpatasvir is given once a day independent of the meal for 12 weeks, regardless of the severity of the liver disease. Patients with previous failure of therapy containing NS5A inhibitors, as well as patients with decompensated cirrhosis (Child-Pugh class B or C) or compensated cirrhosis (Child-Pugh class A) but with previous episodes of decompensation should be treated for 24 weeks [35]. SOV/VEL in the form of tablets can be used in children weighing more than 17 kg, and in children with a lower body weight and at least 3 years of age, it is recommended in the form of granules.

Sofosbuvir/velpatasvir/voxilaprevir

One tablet of the drug contains 400 mg of sofosbuvir, 100 mg of velpatasvir, 100 mg of voxilaprevir. One tablet is taken daily with food. In patients without cirrhosis, previously untreated, the treatment duration is 8 weeks. Patients with compensated cirrhosis, as well as those undergoing retherapy after DAA failures, should receive SOF/VEL/VOX for 12 weeks. The use of the drug is not recommended in patients with decompensated cirrhosis (Child-Pugh class B or C) [36].

Genotype-specific regimens

Sofosbuvir/ledipasvir

One tablet of the drug, containing 90 mg of ledipasvir and 400 mg of sofosbuvir, is administered once a day without regard to food. In previously untreated patients without cirrhosis, therapy should last 12 weeks, but it may be shortened to 8 weeks if the severity of liver fibrosis does not exceed F2 in those infected with genotype 1b. Patients with cirrhosis and after liver transplantation should be treated with SOF/LDV for 24 weeks [37].

Grazoprevir/elbasvir

One tablet of the drug, containing 50 mg of elbasvir and 100 mg of grazoprevir, is taken once a day with or without food. In patients infected with GT1b, regardless of the severity of the disease, therapy should last 12 weeks. GZR/EBR is contraindicated in patients with decompensated cirrhosis (Child-Pugh class B or C) [38].

Retherapy of HCV infections

Patients after failure of treatment containing interferon (including triple therapy) should undergo interferon-free retherapy as soon as possible, according to the rules applicable to previously untreated patients. Infected patients after failure of interferon-free therapy can be treated with an effectiveness exceeding 90% with alternative interferon-free therapy, which has been confirmed both in relation to genotype-specific and pangenotypic therapies. However, the optimal therapeutic option after failure of interferon-free therapy is SOF/VEL/VOX [39, 40].

Disclosure

The authors declare no conflict of interest.

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