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Review paper

Recommendations for treatment of hepatitis C in 2026 from the Polish Group of Experts for HCV

Krzysztof Tomasiewicz[1], Robert Flisiak[2], Jerzy Jaroszewicz[3], Piotr Małkowski[4], Malgorzata Pawlowska[5], Anna Piekarska[6], Krzysztof Simon[7], Dorota Zarębska-Michaluk[8]

[1]Department of Infectious Diseases and Hepatology, USK-1, Medical University of Lublin, Poland
[2]Department of Infectious Diseases and Hepatology, Medical University of Bialystok, Poland
[3]Department of Infectious Diseases and Hepatology, Medical University of Silesia in Katowice, Poland
[4]Department of General, Transplantation and Liver Surgery, Medical University of Warsaw, Poland
[5]Department of Infectious Diseases and Hepatology, *Collegium Medicum* in Bydgoszcz, Nicolaus Copernicus University in Toruń, Poland
[6]Department of Infectious Diseases and Hepatology, Medical University of Lodz, Poland
[7]Department of Infectious Diseases and Hepatology, Wroclaw Medical University, Poland
[8]Department of Infectious Diseases and Allergology, Jan Kochanowski University of Kielce, Poland

Abstract

The recommendations outline the principles of diagnosis and treatment of hepatitis C virus (HCV) infection in accordance with the latest evidence. The primary goal of HCV treatment is to eliminate the virus from the body, which in turn can halt the progression or promote regression of liver lesions. The current version of the recommendations 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 those who do not respond to previous therapies, as well as patients in the peri-transplant period.

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

Address for correspondence:

Prof. Krzysztof Tomasiewicz, Department of Infectious Diseases and Hepatology, USK-1, Medical University of Lublin, Poland, e-mail: Tomaskdr@poczta.fm

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, whilst the presence of viral ribonucleic acid (HCV-RNA) indicating active infection has been found in approximately 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].

Since 2022, due to the influx of a significant number of refugees, primarily those arriving as a consequence of the war in Ukraine, as well as economic migrants, the total number of people infected in Poland may have increased substantially. 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-based testing, whereas the identification of so-called high-risk groups is of considerably lesser importance. An example of proper management bearing the characteristics of population screening is anti-HCV testing in women of reproductive age as part of routine gynaecological examinations, and not only examination of pregnant women, as is currently the case [4-6]. Research carried out under the EpiTer-2

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project showed that genotype (GT) 1b (82%) predominates in Poland, followed by 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 HCV infections resolve spontaneously, and in the remaining patients, chronic HCV infection may remain asymptomatic for many years, often becoming apparent only at an advanced stage of liver disease. Approximately 20% of chronically infected HCV patients will develop cirrhosis or hepatocellular carcinoma. HCV infection causes numerous extrahepatic syndromes, most commonly mixed cryoglobulinaemia (often asymptomatic) and B-cell non-Hodgkin's lymphomas (particularly 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 considered for treatment as soon as possible. The registration of glecaprevir/pibrentasvir for the treatment of patients with acute HCV infection will undoubtedly facilitate prompt treatment of patients with a confirmed diagnosis [9, 10].

In patients with advanced, particularly disseminated, malignant disease, the decision to treat HCV infection should be made on an individual basis, taking into account the patient's life expectancy and available oncological treatment options.

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 can be detected as early as 1-3 weeks after infection, whereas anti-HCV antibodies are detectable only after 4-10 weeks. When the first clinical symptoms appear, anti-HCV antibodies are present only in 50-70% of patients. Some patients do not develop detectable anti-HCV antibodies; therefore, HCV infection is sometimes diagnosed solely by the presence of HCV RNA in the blood [8, 11].

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; hence, patients diagnosed with acute hepatitis C should be considered for antiviral treatment without delay, in accordance with the principles described below [12, 13]. The direct-acting antiviral (DAA) therapy currently recommended for the treatment of acute hepatitis C is glecaprevir/pibrentasvir [9, 10].

Chronic HCV infection

In approximately 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 [13].

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 [14].

Detection of HCV infection

Whilst 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 promote widespread screening for anti-HCV antibodies, followed by confirmation of active infection by detecting HCV RNA before initiation of treatment [15]. It is now considered that population-based testing is the most cost-effective and organisationally efficient method of identifying individuals unaware of their HCV infection. It is recommended that testing for HCV infection be performed at least once in a lifetime in all adults in populations of countries where the prevalence of HCV RNA is at least 0.1%, a category to which Poland belongs. In particular, testing should be offered to all pregnant women during each pregnancy [16].

Additionally, testing for hepatitis C – regardless of age and the prevalence of HCV infection in the given population – should specifically include individuals with identified risk factors or exposure, including:

- persons infected with human immunodeficiency virus (HIV);
- persons who have ever used illicit drugs;
- persons with selected medical conditions, including those who have ever undergone haemodialysis;
- persons with persistently abnormal alanine aminotransferase (ALT) activity or other clinical or laboratory indicators of liver disease;
- persons who have previously received a blood transfusion or organ transplant, including those who received clotting factor concentrates before 1987, those who received a blood transfusion or blood components before 1992, those who underwent organ transplantation before 1992, and those who were notified that they received blood from a donor who subsequently tested reactive for HCV infection;
- healthcare workers, emergency medical services personnel, and public safety personnel at risk of exposure to biological material;
- persons detained in custodial institutions upon admission;
- children born to HCV-infected mothers.

If population-based testing, which is recommended as the most cost-effective and efficient approach, is not feasible, a one-off test is recommended in risk groups. Individuals in whom the above-mentioned risk factors persist may require repeated testing [16].

Any person who requests a test for hepatitis C should receive one, regardless of whether they disclose risk behaviour, as many people may be reluctant to reveal behaviours that could be stigmatising.

Screening tests for anti-HCV should be carried out using both classical laboratory methods and rapid cassette tests, which already have a generally recognised diagnostic value. It is also recommended that, wherever possible, the principle of so-called "reflex testing" be applied. This consists of the immediate testing for HCV RNA – often using point-of-care devices capable of returning results in approximately two hours – using the same blood sample in which anti-HCV antibodies were detected. By adopting this form of testing, the patient receives immediate, complete information as to whether HCV infection is active, and can be referred without delay for DAA therapy.

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 hospitalisations);
- prisons, due to the particularly high incidence of HCV infections.

Assessment of the stage of liver disease

With the advent of pangenotypic drugs, the dosage of which does not depend on the stage of fibrosis, as was formerly the case, assessment of fibrosis has become less important. When evaluating eligibility for treatment, however, it is advisable to determine whether cirrhosis is present. On the other hand, a detailed assessment of the severity of liver disease should not be an absolutely requirement for treatment eligibility in patients with 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) [17]. 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 aetiology, 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 the examination results cannot be adequately evaluated, it is possible to use serum tests, on the basis of which treatment eligibility can be assessed. In the era of pangenotypic therapies, serum tests are increasingly employed for the rapid assessment of newly diagnosed patients in whom HCV genotyping is not required and in whom there are no clinical signs of cirrhosis. The most accessible of these is APRI (aspartate aminotransferase/platelet ratio index), for which values below 1.0 make it possible to rule out advanced hepatic fibrosis with high probability. The next test is FIB-4, for which a value < 1.3 allows the exclusion of advanced fibrosis, whereas a value > 2.67 supports the diagnosis of advanced fibrosis with high probability [18].

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

Class	Medication	Dosage
NS3 (protease) inhibitors	Glecaprevir (GLE) Voxilaprevir (VOX)	300 mg/day in 1 dose 100 mg/day in 1 dose
NS5B (polymerase) inhibitor	Sofosbuvir (SOF)	400 mg/day in 1 dose
NS5A inhibitors	Pibrentasvir (PIB) Velpatasvir (VEL)	120 mg/day in 1 dose 100 mg/day in 1 dose

Recommended medications

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

- glecaprevir, pibrentasvir,
- sofosbuvir, velpatasvir,
- sofosbuvir, velpatasvir, voxilaprevir.

All of the above-listed medications have pangenotypic activity.

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 using the core antigen (HCVcAg) as an alternative to HCV RNA has been limited by the low prevalence of specialised 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 to evaluate eligibility for treatment and assess its effectiveness [19-21]. 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 globally is approximately 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%, whereas in adolescents, transmission is primarily associated with the intravenous use of psychoactive substances. All infants 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 [22, 23].

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 treatment eligibility. Therapy should be conducted in centres 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 [14, 24].

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, weight-based doses are used, as shown in Table 2.

Cirrhosis and hepatocellular carcinoma

HCV infection is associated with a residual risk of HCC even after successful antiviral treatment. In patients with HCV infection, HCC occurs predominantly in those with cirrhosis [25]. Therefore, they should systematically undergo liver ultrasound examinations and 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 being evaluated for DAA therapy eligibility, ultrasound and AFP testing are performed to exclude HCC. If a focal hepatic lesion or elevated serum

Table 2. Medications 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	Dosage	Body weight	Dosage
Children (age: 3-11)	< 17 kg	150 mg/37.5 mg (3 portions of granules)	12-19 kg	150 mg/60 mg (3 sachets)
	> 17 kg	200 mg/50 mg (1 tablet or 4 portions of granules)	20-29 kg	200 mg/80 mg (4 sachets) 250 mg/100 mg (5 sachets)
Teenagers (age: 12-17)		400 mg/100 mg		300 mg/120 mg

AFP is detected, multiphase contrast CT or MRI with contrast should be performed, assessed according to the LI-RADS scoring system [26-29]. If HCC is excluded, DAA therapy may be commenced. If HCC is confirmed, the patient should be referred for oncological treatment at a reference centre. In such a situation, DAA therapy should be initiated as soon as possible, but must not delay the treatment of HCC [30, 31].

In patients with mild fibrosis (F0-F2), repeated examinations may be considered in the event of suspected coexisting liver disease, particularly 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 on ultrasound, in patients following DAA therapy, 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, assessed according to the LI-RADS scoring system [26-31]. Contrast-enhanced ultrasound is not recommended for the routine diagnosis of HCC. Ultrasound, computed tomography and magnetic resonance imaging should be performed by specialists experienced in liver imaging [14, 32, 33].

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 [34, 35].

Coinfections with HBV and/or HIV

The treatment of HCV infection associated with hepatitis B virus (HBV) or 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 [36].

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 [37]:

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. During therapy, ALT levels should be monitored according to the following scenarios:
   - In patients with undetectable HBV DNA and normal ALT activities prior to HCV treatment, if ALT levels increase 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 haemodialysis, 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 [14]. 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 [38].

Prisons

Anti-HCV screening should be offered to all prisoners, preferably at the beginning of their sentence. Taking into account experience from other countries and the well-known characteristics of available medication, in order to increase the availability of therapy, fibrosis staging may be omitted when evaluating eligibility for pangenotypic treatment, as it does not change the treatment procedure, except in patients with decompensated cirrhosis [39]. In addition, except in patients with decompensated cirrhosis, renal failure and after organ transplantation, routine laboratory and ultrasound examinations may be omitted during and after treatment.

Liver transplantation

Effective antiviral treatment with a sustained virological 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 stabilisation, 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 [40].

Antiviral therapy in a patient with advanced hepatic insufficiency (Child-Pugh B and C), especially in the case of concomitant advanced renal insufficiency (GFR < 30 ml/min), should be preceded by liver transplantation. The 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 viraemia, optimally within a month after the transplantation procedure. This also applies to the majority of patients with HCC caused by HCV infection. Planned post-transplantation DAA therapy shortens the time spent on the waiting list and makes it possible to avoid potential tumour progression. Furthermore, according to American authors, this approach expands the pool of available donors to include HCV-infected individuals [41, 42].

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 [43].

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 centres experienced in the treatment of patients with decompensated cirrhosis. These patients should have the possibility of immediate hospitalisation and evaluation for liver transplantation. Patients with cirrhosis in Child-Pugh class C should primarily be considered for liver transplantation [44]. 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 [45].

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 evaluating eligibility 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.

Given that the first marketing authorisation for a DAA therapy (glecaprevir/pibrentasvir) for the treatment of acute hepatitis C has now been granted, differentiation of patients according to this criterion has become an important consideration.

Pangenotypic regimens

Glecaprevir/pibrentasvir (GLE/PIB)

One tablet contains 100 mg of glecaprevir and 40 mg of pibrentasvir. It is recommended to take three tablets a day with a meal [46]. The duration of therapy is 8 weeks in all previously untreated patients and after treatment failure with pegylated interferon α + ribavirin (PegIFNα + 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, it should be 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 PegIFNα + RBV ± SOF or SOF + RBV failure, it should be extended to 16 weeks. In patients with acute HCV infection, the same treatment duration is recommended as in patients with chronic HCV infection [9].

GLE/PIB in the form of tablets can be administered in patients over 12 years of age, and granules in sachets should be used in children between 3 and 12 years of age.

The regimen is not recommended in patients with decompensated cirrhosis (Child-Pugh class B and C).

Sofosbuvir/velpatasvir (SOF/VEL)

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 [47]. SOF/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 (SOF/VEL/VOX)

One tablet of the drug contains 400 mg of sofosbuvir, 100 mg of velpatasvir, and 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 retreatment 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) [48].

Retreatment of HCV infections

Patients who have failed treatment containing interferon alfa (including triple therapy) should undergo interferon-free retreatment as soon as possible, according to the principles applicable to previously untreated patients. Infected patients who have failed interferon-free therapy can be successfully treated with an alternative DAA regimen, with sustained virological response rates exceeding 90%. However, the optimal therapeutic option after failure of interferon-free therapy is SOF/VEL/VOX [49, 50].

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