The updated EASL Recommendations on Treatment of Hepatitis C

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What was the purpose of the last update of the recommendations?

The European Association for the Study of the Liver (EASL) has just released the latest update of the "EASL Recommendations on Treatment of Hepatitis C". This will be the last update, which concludes a 6-year cycle during which the dynamic of publication of the 5 versions of the recommendations was carried out at a sustained pace, following the steady publication of new scientific data. The EASL recommendations have been the most followed throughout the world. Their impact on the management of hepatitis C patients has been and will remain major. This unprecedented collective effort is now coming to an end, as the development of new anti-HCV drugs has been completed and the field is stabilizing. The priority is no longer on the implementation of new therapeutic approaches, the current combinations being extremely effective, but on their implementation in order to reach the elimination targets set by the World Health Organization (WHO).

What is new in this final version of the recommendations?

First of all, clear recommendations for the diagnosis of the infection, as well as for screening in order to link-to-care as many infected subjects as possible. Classically, the diagnosis of the HCV infection is based on the detection of anti-HCV antibodies followed by confirmation of the presence of the virus by a molecular, generally polymerase chain reaction (PCR)-based, technique. HCV core antigen testing can be used as an alternative to RNA testing by PCR. For screening, the classical serum or plasma ELISA can be replaced by a whole-blood ELISA on dried blood spots, or by a rapid diagnostic test performed on serum, plasma, whole blood, or even saliva. Reflex testing for confirmation of replication is recommended to simplify and shorten access to treatment.

Once the diagnosis has been made, all subjects with recently acquired or chronic hepatitis C who are naïve to treatment or treatment-experienced (interferon, ribavirin and/or sofosbuvir) should be treated without delay. Pangenotypic combinations of two direct-acting antivirals (sofosbuvir/velpatasvir or glecaprevir/pibrentasvir) should be preferred in the therapeutic indication. Today, the majority of patients should have access to a simplified treatment, without prior determination of the HCV genotype and subtype.

What is required to start antiviral therapy of hepatitis C?

Only three pieces of information are necessary for treatment initiation: proof of viral replication (presence of RNA or core antigen), determination of the presence or absence of cirrhosis by a non-invasive test (possibly APRI or FIB-4,

which are easily accessible), and the study of possible drug-drug interactions. In this case, patients may be treated with sofosbuvir/velpatasvir for 12 weeks, or with glecaprevir/pibrentasvir for 8 weeks if they have no cirrhosis or if they have cirrhosis and are treatment-naïve, and 12 weeks if they have cirrhosis and a history of treatment failure. This simplified approach results in very high sustained virological response rates and, above all, easy access to treatment for a very large number of patients. It is a key option for achieving the WHO elimination targets.

In specialized departments, it remains interesting to perform HCV genotype and subtype determination in order to offer cirrhotic subjects infected with HCV genotype 3 an enhanced treatment to optimize their response rates. HCV genotype and subtype determination is also very important in regions where HCV subtypes inherently resistant to NS5A inhibitors are frequently found in infected subjects, or in industrialized countries in subjects originating from these regions. However, such determination should be based on sequence analysis (because hybridization-based assays cannot discriminate these subtypes), which is not available in many places. In the absence of reliable data with the most recent "pangenotypic" dual therapies for most of these subtypes, it is recommended to treat them with the triple combination sofosbuvir/velpatasvir/voxilaprevir as first-line therapy (subtypes 1l, 4r, 3b, 3g, 6u, 6v or any other subtype that naturally harbors polymorphisms conferring reduced susceptibility to NS5A inhibitors).

What is new on treatment of patients who failed previous antiviral therapy?

Retreatment of patients who failed to achieve viral eradication after an NS5A or protease inhibitor-containing regimen is based on a triple combination of sofosbuvir, velpatasvir and voxilaprevir. In the most difficult-to-cure patients (advanced cirrhosis, multiple treatment failures, presence of complex resistance-associated substitution profiles), the use of the combination of sofosbuvir plus glecaprevir/pibrentasvir provides a better barrier to resistance to NS5A inhibitors. Treatment can also be reinforced by adding ribavirin and/or extending its duration to 16 or 24 weeks in the most problematic subjects.

What do the updated recommendations means for the treatment of particular patient groups?

The treatment of many particular groups has been updated in this final version of the recommendations. An important novelty concerns pediatric treatments for which clear indications are given, pending the approval of the corresponding drug formulations. The treatment of adolescents is identical to that for adults. The treatment of hepatitis C during pregnancy is also discussed (but not recommended in the current state of knowledge). Other special groups that are discussed include patients with decompensated cirrhosis, those with hepatocellular carcinoma, solid organ (including liver) transplant recipients, patients who inject drugs and subjects under opioid substitution, and incarcerated subjects. The specific problem of certain co-morbidities (manifestations of hepatitis C related to the formation of immune complexes, patients with renal impairment, co-infection with the hepatitis B virus, hemoglobinopathies and coagulation disorders) is also covered.

What are your main reflections from the past 6 years of interaction with the EASL committee?

At the end of this collective adventure, what remains is the feeling of the work accomplished with the successive members of the panel, the reviewers and the members of the EASL Governing Board, and the satisfaction of a major contribution to the care and health of a part of humanity. It only remains for us, collectively, to make the best use of these latest EASL Recommendations on Treatment of Hepatitis C to bring the missing piece to the puzzle: the elimination of hepatitis C.