New drugs, wider range of genotypes, more cures

Hepatitis C virus (HCV) infection attacks the liver, causing inflammation of this organ. In the struggle between the immune system and HCV, the liver becomes injured as healthy tissue is gradually replaced with useless scar tissue. If HCV is left untreated, most of the liver becomes severely injured and scar tissue becomes predominant; at this stage, cirrhosis has developed. As the liver degrades and is unable to filter blood, other organs such as the kidneys and brain are affected and complications develop.

Many people who have HCV may not be aware that they carry the virus. HCV testing can help uncover hidden infection and can lead to discussion about treatment options.

As recently as six years ago, treatment of chronic HCV consisted of a long-lasting form of interferon and the antiviral drug ribavirin. Interferon activates the body’s antiviral defence system and ribavirin is an old drug with activity against different viruses. Interferon had to be injected weekly and caused side effects that at best would be considered highly unpleasant. The combination of both drugs had to be taken for 24 to 48 consecutive weeks and cure rates usually ranged between 60% and 75%.

About 12 years ago researchers created the first experimental direct-acting antiviral (DAA) called ciluprevir. However, in clinical trials HCV quickly developed resistance to this compound and it was abandoned. Pharmaceutical companies then began developing other DAAs.

By 2011 the first generation of more effective DAAs arrived—boceprevir and telaprevir—though they had to be used in combination with interferon and ribavirin. These DAAs could also have side effects and were not highly effective, with cure rates averaging between 65% and 75%.

Spurred by the relative recent success of DAAs, companies began making more potent all-oral drugs against HCV, including the following:

- Daclatasvir (Daklinza)
- Harvoni (sofosbuvir + ledipasvir)
- Holkira Pak (dasabuvir + ombitasvir +paritaprevir+ ritonavir)
- simeprevir (Galexos)
- sofosbuvir (Sovaldi and in Harvoni)
- Zepatier (elbasvir and grazoprevir)

As a group, these drugs are mainly effective against HCV genotype 1 (the most common strain of HCV), but some of these drugs or combinations of them can be used against other genotypes. However, all the leading pharmaceutical companies are now developing combinations of drugs that can treat all major HCV genotypes and can be taken once daily. Some of these regimens under development have shown to be sufficiently powerful that they can even cure some people whose previous regimens failed. More information about drugs under development for HCV appears later in this issue of TreatmentUpdate as well as in issue 216.

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