Ombitasvir/Paritaprevir/Ritonavir

National Cancer Institute

Source

National Cancer Institute. Ombitasvir/Paritaprevir/Ritonavir. NCI Thesaurus. Code C123920.

An orally bioavailable combination agent containing ombitasvir, an inhibitor of the hepatitis C virus (HCV) non-structural protein 5A (NS5A) replication complex, paritaprevir, a synthetic acylsulfonamide inhibitor of the HCV protease complex comprised of non-structural protein 3 and 4A (NS3/NS4A), and the cytochrome P450 (CYP) 3A4 inhibitor ritonavir, with potential activity against HCV. Upon oral administration of ombitasvir/paritaprevir/ritonavir, ombitasvir, enters the cell and binds to and blocks the activity of the NS5A protein. This results in the disruption of the viral RNA replication complex, blockage of HCV RNA production, and inhibition of viral replication. After intracellular uptake, paritaprevir reversibly binds to the active center and binding site of the HCV NS3/NS4A protease and prevents NS3/NS4A protease-mediated polyprotein maturation. This disrupts both the processing of viral proteins and the formation of the viral replication complex, which inhibits viral replication in HCV genotype 1-infected host cells. Although ritonavir is not active against HCV, it strongly inhibits the activity of CYP3A4, thereby blocking the degradation of paritaprevir, which is a CYP3A4 substrate. This leads to an increased concentration and half-life of paritaprevir as compared to the administration of paritaprevir without ritonavir. NS5A, a zinc-binding and proline-rich hydrophilic phosphoprotein, plays a crucial role in HCV RNA replication. NS3, a serine protease essential for the proteolytic cleavage of multiple sites within the HCV polyprotein, plays a key role during HCV ribonucleic acid (RNA) replication. NS4A is an activating factor for NS3. HCV is a small, enveloped, single-stranded RNA virus belonging to the Flaviviridae family, and infection is associated with the development of hepatocellular carcinoma (HCC).