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Antiviral Agents

Updated: June 21, 2018.

OVERVIEW

The antivirals are a large and diverse group of agents that are typically classified by the virus infections for which they are used, their chemical structure and their mode of action. Most antiviral agents have been developed in the last 20 to 25 years, many as a result of the major research efforts to develop therapies and means of prevention of human immunodeficiency virus (HIV) infection and the acquired immunodeficiency syndrome (AIDS). Some of the agents developed to treat HIV infection, AIDS and its complications were found to also inhibit other viruses, and the novel approaches taken in development of antiretroviral therapy have been applied to develop therapies of other viral infections.

Antiretroviral Agents for HIV Infection. The antiretroviral agents include nucleoside analogues with reverse transcriptase activity (such as tenofovir, emtricitabine, lamivudine, abacavir, stavudine, didanosine, zidovudine), the nonnucleoside reverse transcriptase inhibitors (such as delavirdine, efavirenz, etravirine, nevirapine and rilpivirine), protease inhibitors (atazanavir, darunavir, indinavir, ritonavir, tipranavir and many others), and miscellaneous agents such as maraviroc that inhibits binding of the HIV virus its T cell receptor (CCR5 coreceptor antagonist), enfuvirtide that blocks the uptake of HIV into cells (fusion inhibitor), and integrase inhibitors (raltegravir, elvitegravir and dolutegravir) that block the integrase enzyme of HIV.

Hepatitis B Agents. The agents active against hepatitis B virus (HBV) include several nucleoside analogues that are also active against and used to treat HIV infection (tenofovir, emtricitabine, lamivudine), as well as agents that are poorly if at all active against HIV (adefovir, entecavir and telbivudine). Alpha interferon and peginterferon (its long acting pegylated form) are also active against hepatitis B, but are no longer commonly used for this indication.

Hepatitis C Agents. The agents active against hepatitis C virus (HCV) include interferon alfa (1992) and peginterferon (2000) which are used in combination with ribavirin, a nucleoside analogue that potentiates the effects of interferon against hepatitis C by unclearly defined mechanisms. Progress in treatment of hepatitis C began to accelerate in 2010 with the introduction of the first direct acting anti-HCV agents, two HCV-specific protease inhibitors: boceprevir and telaprevir. While combinations of these protease inhibitors with peginterferon and ribavirin yielded high response rates (60% to 75%), the regimens were poorly tolerated, expensive and prolonged (courses were typically for 48 weeks). Beginning in 2013, new direct acting anti-HCV agents with potent activity against different regions of the virus were introduced, which in combination obviated the need for interferon and yielded sustained response rates of greater than 90% with 12 to 24 weeks of treatment. The direct acting agents were directed against 3 components of HCV: HCV protease (NS3) inhibitors included simeprevir [2013], paritaprevir [2015], grazoprevir [2016] and glecaprevir [2017]); HCV RNA polymerase (NS5B) inhibitors included sofosbuvir [2013, a nucleoside analogue] and dasabuvir [2015, a non-nucleoside inhibitor]; and, HCV NS5A inhibitors included daclatasvir [2015], elbasvir [2016], lepidasvir [2014],

ombitasvir [2015], velpatsvir [2016] and pibrentasvor [2017]. Combinations of 2 or 3 of these achieve sustained response rates of greater than 90%, with relatively short courses of therapy (8, 12 to 16 weeks) and without the need of interferon and its difficult and dose-limiiting side effects. These combinations are available under brand names such as Harvoni, Technive, Viekira Pak, Zepatier, Epclusa and Mavyret. Newer agents and different combination products are likely to be developed in the near future. Many of the earlier combinations are likely to be discontinued as newer regimens are more effective, better tolerated and active against all genotypes and in patients with renal disease, HIV infection or cirrhosis.

Herpes Virus Agents. The agents active against various herpes viruses (herpes simplex, varicella zoster, cytomegalovirus) include acyclovir and related acyclic nucleoside analogues such as valacyclovir, cidofovir, famciclovir, ganciclovir and valganciclovir, and other miscellaneous agents such as foscarnet.

Influenza Agents. The agents active against influenza A virus include amantadine and rimantadine which act on viral uncapping, and three neuraminidase inhibitors osteomavir (oral), zanamivir (by inhalation) and peramivir (intravenous). These agents are used during influenza outbreaks, generally for a brief period only, but are effective in prevention as well as amelioration of influenza infection.

The following drug records are discussed individually:

Drugs for HIV Infection, in the Subclass Antiretroviral Agents

- Fusion Inhibitors (HIV)
  - Enfuvirtide, Maraviroc
- Integrase Inhibitors (HIV)
  - Bictegravir, Dolutegravir, Elvitegravir, Raltegravir
- Monoclonal Antibodies
  - Ibalizumab
- Nonnucleoside Reverse Transcriptase Inhibitors (HIV)
  - Delavirdine, Doravirine, Efavirenz, Etravirine, Nevirapine, Rilpivirine
- Nucleoside Analogues (HIV)
  - Abacavir, Didanosine, Emtricitabine, Lamivudine, Stavudine, Tenofovir, Zidovudine
- Protease Inhibitors (HIV)
  - Amprenavir, Atazanavir, Darunavir, Fosamprenavir, Indinavir, Lopinavir, Nelfinavir, Ritonavir, Saquinavir, Tipranavir

Drugs for Hepatitis B

- Alpha Interferon, Adefovir, Emtricitabine, Entecavir, Lamivudine, Telbivudine, Tenofovir

Drugs for Hepatitis C

- Interferon Based Therapies
  - Alpha Interferon and Peginterferon, Ribavirin
- HCV NS5A Inhibitors
  - Daclatasvir, Elbasvir, Ledipasvir, Ombitasvir, Pibrentasvir, Velpatasvir
- HCV NS5B (Polymerase) Inhibitors
  - Dasabuvir, Sofosbuvir
- HCV Protease Inhibitors
  - Asunaprevir, Boceprevir, Glecaprevir, Grazoprevir, Paritaprevir, Simeprevir, Telaprevir, Voxilaprevir
- Combination Therapies
  - Epclusa, Harvoni, Mavyret, Technive, Viekira Pak, Vosevi, Zepatier

Drugs for Herpes Virus Infections (HSV, CMV, others)

- Acyclovir, Cidofovir, Famciclovir, Foscarnet, Ganciclovir, Letermovir, Valacyclovir, Valganciclovir

Drugs for Influenza

- Amantadine, Baloxavir, Oseltamivir, Peramivir, Rimantadine, Zanamivir

ANNOTATED BIBLIOGRAPHY

References updated: 21 June 2018

Núñez M. Hepatic toxicity of antiviral agents. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2013, pp. 505-18.

(Review of hepatotoxicity of antiviral agents; mentions that risk of liver injury with different protease inhibitors is controversial, but that tipranavir, darunavir, lopinarivr and ritonavir are the leading causes in most case reports and reviews on the topic).

Flexner C. Antiretroviral agents and treatment of HIV infection. In, Brunton LL, Chabner BA, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New York: McGraw-Hill, 2011, pp. 1623-64.

(Textbook of pharmacology and therapeutics).

Available at: http://aidsinfo.nih.gov/guidelines

(Clinical guidelines on the use of antiretroviral agents in HIV-1 infected adults, adolescents and children).

(Clinical guidelines on the use of antiretroviral agents in HIV-1 infected adults, adolescents and children).

www.hcvguidelines.org

(Clinical guidelines on the diagnosis, management and therapy of hepatitis C from the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America, with regular updates).

(Clinical guidelines on the diagnosis, management and therapy of hepatitis C from the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America, with regular updates).

Antiviral drugs. Treat Guidel Med Lett 2013; 11 (127): 19-30. PubMed PMID: 23459414.

(Review of safety and efficacy of antiviral agents).

Antiviral drugs for influenza 2013-2014. Med Lett Drugs Ther 2014; 55 (1429): 6-8. PubMed PMID: 24457560.

(Concise summary of safety and efficacy of medications for influenza appropriate for the 2013-14 season mentions that adverse effects of oseltamivir include nausea, vomiting and headache; no mention of liver injury).

European Association for Study of Liver. EASL Recommendations on Treatment of Hepatitis C 2015. J Hepatol 2015; 63: 199-236. PubMed PMID: 25911336.

(Guidelines for the antiviral therapy of chronic hepatitis C from the European liver clinical, academic and research society).

AASLD/IDSA HCV Guidance Panel. Hepatitis C guidance: AASLD-IDSA recommendations for testing, managing, and treating adults infected with hepatitis C virus. Hepatology 2015; 62: 932-54. PubMed PMID: 26111063.

(Guidelines for the antiviral therapy of chronic hepatitis C from the US liver and infectious diseases research and academic societies).

Antiviral drugs for seasonal influenza 2016-2017. Med Lett Drugs Ther 2017; 59 (1511): 1-3. PubMed Citation
(Concise summary of safety and efficacy of medications for influenza appropriate for the 2016-17 season; discusses side effects of oseltamivir and zanamivir, but does not mention ALT elevations or hepatotoxicity).