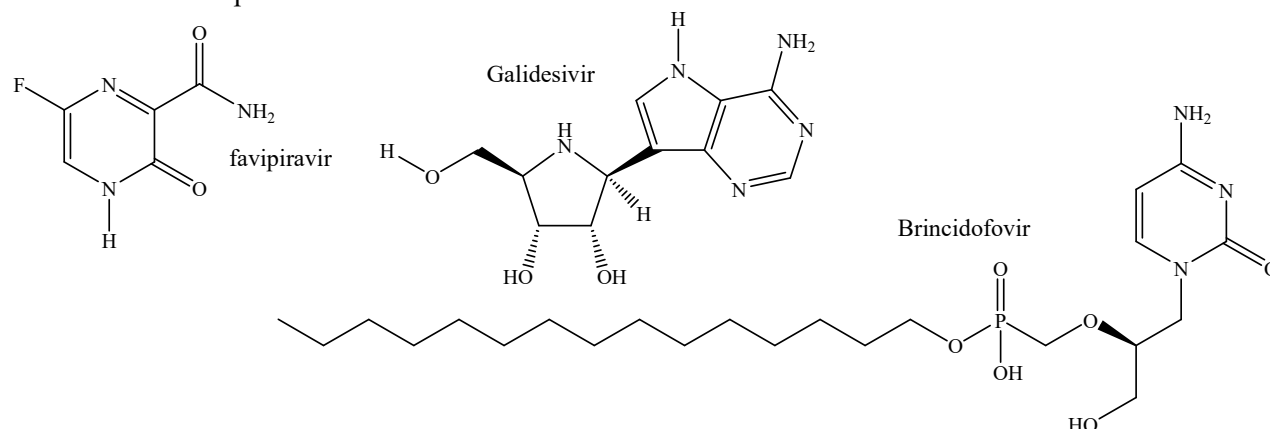


The Ebola virus is an RNA virus that was first discovered 40 years ago. Since the first recorded outbreak, 20 intermittent outbreaks have occurred. The most recent was in West Africa in 2013-2016, which was the largest one ever. There were over 28,000 cases and > 11,000 deaths, including > 500 healthcare workers. The Ebola virus persists in the blood for months and can be transmitted by bodily fluids. There has been much research on possible Ebola cures (vaccines or small molecule drugs). Three top drugs in clinical trials are shown below, but none have shown success in acute infections or persistent viral loads in the blood.



During the past several years over 1000 nucleosides (without the phosphorous) and nucleotides (with the phosphorous) drugs were screened against RNA virus targets that included Severe Acute Respiratory Syndrome (SARS) and MERS (Middle East Respiratory Syndrome), both of which are Corona viruses, like COVID-19. The drugs were also screened against mosquito born viruses (Dengue and Zika). The most promising candidate is the middle compound at the top of the page. The third compound at the top of the page is a prodrug. A prodrug is converted to the actual drug inside the body using the body's biochemistry. There are a couple of unusual details about this prodrug. First there is a carbon atom is attached at C1' position, whereas the usual DNA and RNA bases have a nitrogen atom and a hydrogen atom attached there (see adenosine nucleoside in the first structure). Another unusual detail is the nitrile (C≡N) group is also attached at C1' (where a hydrogen is usually attached) and the nitrile is essential for activity and lower toxicity. Additionally, the phosphorous atom is tetrahedral with 4 different groups (so it is chiral) and more active with the absolute configuration shown above (R or S?). There is no charge on the phosphoramidate prodrug so it can better cross nonpolar cell membranes. Once inside a cell the phosphamide side branch is cleaved off to the actual drug. In initial trials, nonhuman-primates were infected with the Ebola virus, and then given 10 mg / Kg body weight using iv treatment for 3-14 days, resulting in 100% survival rate. Phase 2 clinical trials were planned.

