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An Irreversible HIV-1 Protease inhibitor LB71350: Antiviral Activities, Resistance and Irreversibility Studies.

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LB71350, an irreversible HIV-1 (Human Immunodeficiency virus-1) protease inhibitor, inactivated the protease with time-dependent pattern and could efficiently block the replication of both the primary HIV-1 isolates and T-cell tropic HIV-1. We determined whether LB71350 had an advantage over the reported reversible protease inhibitors by analysis of the resistant HIV-1 variants as well as by irreversibility studies. To study resistance pattern for LB71350, we serially passaged the wild type HIV-1_{NL4-3} in MT-2 cells in the presence of increasing concentration of the inhibitor. After analyzing the genotype of the variants, recombinant viruses containing the mutation in the same genetic background were constructed and tested for the susceptibility against HIV-1 protease inhibitors. Drug susceptibility assay showed that all single mutations remained quite sensitive to LB71350, while accumulation of additional mutations increased the resistance. Furthermore LB71350 effectively blocked growth of recombinant viruses resistant to other protease inhibitors. Finally we examined whether the irreversible inactivation of the protease in HIV-1 infected cells could slow down emergence of infectious virions from the infected cells after removal of the inhibitor.

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Reassortant Rotavirus Vaccine - Live, Oral, Tetravalent

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Rotavirus is the leading cause of acute diarrhea in young children. All children are infected with rotavirus in their first four years, most get diarrhea, and in developing countries, this leads to an estimated 870,000 deaths per year. Each year in the United States, about 3 million cases of rotavirus diarrhea occur leading to an estimated 500,000 physician visits, 67,000 hospitalizations and 75 deaths. Because rotavirus affected rich and poor children alike, in both developed and developing contries, it seemed unlikely that traditional public-health measures aimed at improving waste, food or sanitation would alter the incidence of the disease. Attempt at prevention needed to be directed toward the development of safe and effective vaccines. The reassortant rotavirus vaccine now tested was developed from a rotavirus strain(serotype 3) originally isolated from a rhesus monkey with diarrhea. To broaden protection against the three other rotavirus serotypes commonly found in humans(types 1, 2 and 4), reassortant was composed of a single gene segment encoding the main outer capsid protein(VP7) responsible for viral neutralization of each of the three serotypes, with the remaining ten segments coming from the parent rhesus strain. Reassortant rotavirus vaccine(Live, Oral, Tetravalent) protected against 57 percent of all cases of rotavirual diarrhea. When ranked by severity of illness, reassortant rotavirus vaccine's effectiveness ranged from 49 percent protection for less serious cases to 82 percent for the most severe cases. Overall, the reassortant rotavirus vaccine protected against 92 percent of the diarrheal episodes lasting more than three days, and reduced by 78 percent the cases requiring medical visits. Licensed reassortant rotavirus vaccines may soon be with us and, given the incomplete protection of this vaccine against mild disease and the initial cost, the door is open to the next generation vaccines.