Peramivir

Medical name: Peramivir (Peramivirum, Peramivir-trihydrate [in pharmaceuticals], Rapivab [trade name], BCX-1812, RWJ-270201)

IUPAC-name: \((1S, 2S, 3R, 4R)-3-[(S)-1-acetamido-2-ethyl-butyl]-4-(diaminomethylideneamino)-2-hydroxy-cyclopentane-1-carboxylic acid\)

Formula: \(\text{C}_{15}\text{H}_{28}\text{N}_{4}\text{O}_{4}\) (molar mass=328.4 g/mol)

History

Peramivir is an antiviral drug for the treatment of influenza and was developed by BioCryst Pharmaceuticals. A study of using Peramivir in case of seasonal influenza in 2008 showed no effect compared to placebo, but in October 2009 Peramivir has shown life-saving effects in intravenous treatment of swine flu. Due to this, an Emergency Use Authorization has been established by the U.S. Food and Drug Administration (FDA), which says that Peramivir is allowed to be used in intravenous form for hospitalized patients if other methods of treatment are ineffective or unavailable. After this achievement the U.S. government supported the study of BioCryst Pharmaceuticals financially. In 2011 Phase 3 of this study revealed that one intravenous treatment with Peramivir is just as effective as a five-day oral treatment with Oseltamivir for people with seasonal influenza.

In June 2011 Peramivir has become very meaningful when a new variant of swine flu, with a genetic mutation, has emerged in Asia. The virus got resistant to Oseltamivir and Zanamivir because of this adaption, but not to Peramivir. According to this, BioCryst Pharmaceuticals proposed a motion for a new drug application for the intravenous treatment to the FDA.\(^1\)

Synthesis

![Synthesis of Peramivir.\(^2\)](Image)
Medical Use

The specific inhibitor of the enzyme neuraminidase is used for the treatment of influenza type A (for humans, birds, pigs, horses, etc.) and influenza type B (only humans). The drug is administered intravenously, which distinguishes it from Zanamivir, which is administered with a spray, and Oseltamivir, which is administered orally. Following a single administration of Peramivir the flu infection can be shortened up to one day, while the fever period can be shortened to about 12 hours. The drug's most common adverse effect is diarrhea. Rarely, there are fatal skin reactions and other hypersensitivity reactions such as the Stevens-Johnson syndrome. Furthermore, the drug raises the risk for hallucinations, delirium and abnormal behavior. [3, 4]

Biological Response

A virus is like a parasite which affects the body by using the host cells to propagate. There are different points of application for the antiviral drug: before and after the virus affects the cell and while the virus is synthesized. Neuraminidase inhibitors cannot operate in the cell, because the enzyme neuraminidase is only found on the outer membrane.

If a virus affects a host cell, it first sequesters to the cell. Then the virus is absorbed into the cell through the process of endocytosis. The genetic information of the virus are delivered to the cytoplasm as ribonucleic acid (RNA) and absorbed by the cell nucleus, where the RNA propagates. Due to this, new viruses emerged which are still hanging on the outer membrane, but by the enzyme neuraminidase the viruses are separate from the host cell. Peramivir operates at this point by inhibiting the neuraminidase, which prevents the separation and the exponential increase of the viruses. [5, 6, 7]

医疗应用

特异的神经氨酸酶抑制剂用于治疗流感型A（适用于人类、鸟类、猪、马等）和流感型B（仅适用于人类）。该药物通过静脉给药，这与zanamivir（通过喷雾给药）和oseltamivir（通过口服给药）不同。在接受peramivir单次给药后，流感感染可以缩短至一天，而发烧期可以缩短至12小时。该药物最常见的副作用是腹泻。罕见地，有致命的皮肤反应和其他过敏性反应，如斯蒂文斯-约翰逊综合症。此外，该药物会增加幻觉、谵语和异常行为的风险。[3, 4]

生物学反应

病毒就像寄生虫，通过利用宿主细胞来繁殖。抗病毒药物有三种不同的应用点：在病毒影响宿主细胞之前、之后和在病毒合成时。神经氨酸酶抑制剂不能在细胞内运作，因为神经氨酸酶只存在于细胞膜外。

如果病毒影响宿主细胞，它会首先被宿主细胞吸附。然后病毒通过内吞作用被宿主细胞吸收。病毒的遗传信息以RNA的形式被传递到细胞核，然后在细胞核内进行繁殖。由于这个原因，新的病毒出现了，它们仍然附着在细胞膜外，但通过神经氨酸酶的分离，病毒与宿主细胞分开。Peramivir在这一点上通过抑制神经氨酸酶，阻止了分离和病毒的指数增加。[5, 6, 7]
Literature