



NUCLEOSIDE ANALOG REVERSE TRANSCRIPTASE INHIBITORS IN DEVELOPMENT

NOTE: several fact sheets describe drugs that are being tested against HIV:

- Fact sheet 430: non-nucleoside analog reverse transcriptase inhibitors (NNRTIs or non-nukes)
- Fact sheet 440: protease inhibitors
- Fact sheet 460: attachment and fusion inhibitors
- Fact sheet 470: new classes of antiviral drugs
- Fact sheet 480: immune therapies

These drugs have not been approved by the Food and Drug Administration (FDA) for use against HIV.

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These drugs stop HIV from multiplying by blocking the reverse transcriptase enzyme. This enzyme changes HIV's genetic material (RNA) into the form of DNA. This step has to occur before HIV's genetic code gets combined with an infected cell's own genetic codes. The nucleoside analogs (often called "nukes") mimic the building blocks used by reverse transcriptase to make copies of the HIV genetic material. These fake building blocks disrupt the copying.

NUCLEOSIDE ANALOGS (NUKES) IN DEVELOPMENT

Nucleoside analogs (nukes) in development include Apricitabine, DAPD, DOT, Elvucitabine, KP-1461, MIV-210 (FLG), and Racivir.

Apricitabine (AVX754) by Avexa (formerly **SPD754** by Shire Pharmaceuticals) has shown good activity against HIV that is resistant to 3TC (EpiVir). It is in Phase II studies. Apricitabine seems well tolerated.

DAPD (amdoxovir) is being developed by RFS Pharm. It is in Phase II studies. Some eye problems were detected in early studies and are being studied carefully.

DOT (Dioxolane thymidine) is being studied by the University of Georgia in Phase I trials.

Elvucitabine (ACH-126,443, Fd4C) by Achillion Pharmaceuticals is a once-daily drug with activity against HIV that is resistant to several other nukes. It is also effective against hepatitis B. It is in Phase II studies.

KP1461 by Koronis is a prodrug of Koronis KP-1212. It introduces mutations into HIV that become lethal. It is in Phase I trials.

MIV-210 (FLG) by GlaxoSmithKline and Medivir shows good activity against HIV with resistance to other nukes. It is in Phase I trials.

Racivir by Pharmasset Inc is active against HIV and hepatitis B in laboratory studies. In a Phase I/II study, Racivir showed anti HIV activity that lasted more than 2 weeks after the drug was stopped. The makers hope that Racivir can be used as a once-daily drug.

NUKES NO LONGER IN DEVELOPMENT

The following drugs are no longer being developed for use against HIV:

Adefovir dipivoxil (bis POM PMEA) by Gilead Sciences

Alovudine (MIV-310, FLT) by Boehringer Ingelheim and Medivir

DFC (Dexelvucitabine, formerly known as Reverset) by Incyte Corporation

dOTC (BCH-10652, BCH-10618) by BioChem Pharma

FddA (Beta-fluoro-ddA, Lodenosine®) by US Bioscience

GW420867X by GlaxoSmithKline

Lobucavir by Bristol-Myers Squibb
SPD756 by Shire Pharmaceuticals

Revised June 16, 2006