



NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS IN DEVELOPMENT

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

- Fact sheet 410: nucleoside analog reverse transcriptase inhibitors (nukes)
- Fact sheet 440: protease inhibitors
- Fact sheet 460: attachment and fusion inhibitors
- Fact sheet 470: new classes of antiretroviral drugs
- Fact sheet 480: immune therapies

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

NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS

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. Non-nucleoside reverse transcriptase inhibitors, called NNRTIs or non-nukes, physically prevent the reverse transcriptase enzyme from working.

NNRTIs IN DEVELOPMENT

BILR 355 BS by Boehringer Ingelheim is being developed against wild type virus and virus already resistant to NNRTIs. A Phase II study is in progress.

(+)-Calanolide A by Sarawak MediChem Pharmaceuticals was derived from a rain forest plant. It can easily cross the blood-brain barrier, and

seems to stay in the bloodstream for a long time. It is in Phase II human trials.

Etravirine (TMC125) by Tibotec is active against some strains of HIV that are resistant to other NNRTIs. It was approved in 2008. For more information, see fact sheet 434.

GSK 2248761 (was IDX899) by Idenix Pharma is being studied in Phase II studies. It is being developed by ViiV Healthcare*.

Lersivirine (UK 453,061) by ViiV Healthcare* has been studied in Phase II. It appears to be active against resistant strains of HIV, including HIV resistant to efavirenz.

MIV-150 by Medivir and Chiron shows good results in the laboratory against HIV that is resistant to other NNRTIs. It takes a long time for HIV to develop resistance to MIV-150. Phase II trials are in progress.

RDEA806 by Ardea has completed a Phase II trial. The drug is active against HIV that is resistant to efavirenz. Viral resistance does not develop easily.

Rilpivirine (TMC278) by Tibotec is active against some strains of HIV that are resistant to other NNRTIs. It is being developed as a once-daily medication. It is in Phase III trials. A slow-release formulation is being studied.

NNRTIs NO LONGER IN DEVELOPMENT

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

Ateviridine by Upjohn

Capravirine by Pfizer / Agouron Pharmaceuticals

Dapivirine (TMC120) by Tibotec was abandoned due to low blood levels. However, it may still be useful as a microbicide.

DPC083 by Bristol-Myers Squibb

Emivirine (Coactinon) by Triangle Pharmaceuticals

GW5634, GW678248 by GlaxoSmithKline

Loviride by Janssen Pharmaceuticals

HBY-097 by Hoechst-Bayer

PNU142721 by Pharmacia & Upjohn

TMC120 by Tibotec

*ViiV Healthcare is a new HIV company. It is a joint venture of Pfizer and GlaxoSmithKline.

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