The New HIV Bouncers

When will entry inhibitors exit the pipeline to keep HIV from getting into your club?

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Unlike older drug classes—protease inhibitors (PIs), nukes, and non-nukes—that interfere with HIV after it hijacks CD4 immune cells, entry inhibitors (EIs) bar the virus from entering in the first place. This allows EIs to avoid many of the other meds' side effects. One EI type, coreceptor blockers, prevents HIV from hooking onto one of the receptors (CCR5, CXCR4 or, confusingly, CD4) on a CD4 cell's surface. Seven such blockers are in development, but none is expected to hit shelves before 2007. The other EI type, fusion inhibitors, blocks the final step of infection by preventing an HIV surface protein from fusing with the CD4 cell. Fuzeon, approved in 2003, is the lone drug in the fusion-inhibitor category.

Many AIDS experts agree with researcher John Moore, PhD, of Cornell University's Weill Medical College, that the upcoming EIs have "extremely high potential" for first-time treaters as well as for long-term HIVers with drug resistance.

Moore says test-tube studies suggest "you can get synergy" by combining a variety of EIs. They can also be mixed with PIs, nukes and non-nukes for a one-two punch at different points in HIV's life cycle. Other experts note that some EIs work for days after intake, possibly requiring fewer doses.

One possible red flag: Will drugs that block the CCR5 receptor, which HIV uses in the early stages of infection, kickstart the body to switch to CXCR4? Common in late infection, CXCR4 has been linked to rapid immune deterioration. But in trials so far, the few people whose virus switched have maintained good immune health.

Treatment activist Tim Horn warns that with all their promise, EIs will "by no means be a panacea" for those whose other drugs have failed. They provide "new pieces [of salvage therapy] for those with drug resistance," he says, but won't be sufficient alone. "We'll still need to piece together entire combinations" to keep HIV under wraps.

HIVers and docs alike hope that the new meds will perform well enough on the drug-development track to avoid getting bounced themselves.

The EI Front-Runners

In the lead are three CCR5 blockers, all pills—maraviroc (Pfizer), vicriviroc (Schering-Plough) and GSK-873,140 (GlaxoSmithKline). Each has cut viral loads significantly in short trials (10 to 14 days); all are entering larger trials.

Closing fast is AMD070 (AnorMED), a CXCR4 blocker. Only a short study of this IV drug in neggies has reported results; an HIVer trial is underway.

Bringing up the rear are three meds that block the CD4 receptor. TNX-355 (Tanox and Biogen Idec) suppressed virus for seven to 10 weeks in most HIVers in a trial, though some developed apparent resistance. PRO-542 (Progenics Pharmaceuticals) was potent in short studies. These two are IV drugs. BMS-378806 (Bristol-Myers Squibb), an oral med, is farther back in the process.

The finish line awaits—and so do we.
