Classical Lit

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The latest experimental-treatment buzz is all about Merck's vaccine and the new outside-the-cell weapons called entry inhibitors and integrase inhibitors (see "Seattle Rattle," *POZ*, May 2002). But don't let these innovations distract you from the progress made in the classic classes of NNRTIs and protease inhibitors (PIs). Given resistance and side effects, the need for smarter, gentler versions of the 16 HAART drugs currently available could not be clearer. Luckily there are 98 promises in the pipeline, and some are even nearing the 2004 finish line: Two second-generation NNRTIs -- Tibotec-Virco's **TMC 125** and Bristol-Myers Squibb's **DPC 083** -- have been designed to disarm virus that has already developed resistance to older non-nukes. In the recently completed Phase II clinical trials, TMC 125 dramatically decreased viral loads in the NNRTI-resistant as well as in the NNRTI-naïve. Let's hope the current dose of 18 pills twice daily also dramatically decreases if and when TMC 125 hits shelves. DPC 083, in Phase II, is also ruthless in overcoming NNRTI-resistant virus.

Bristol-Myers Squibb's **atazanavir** (Zrivada) is the first once-daily PI. In studies of previously untreated HIVers, 48-week data showed that the drug didn't max out lipids (cholesterol and triglycerides) as do the first-generation PIs, leading to cardio side effects. Look for atazanavir to be up and at 'em as soon as late 2003. Boehringer Ingelheim's **tipranavir** is the first non-peptidic PI. It boasts an increased ability to bind to a drug-resistant virus more readily than to unmutated HIV. Phase II studies showed that tipranavir, with a little boost from fellow PI ritonavir (Norvir), picked up the slack by KO'ing viral loads even in those whose second PI regimen had failed.

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