Nukelier Fusion

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The hope: Shed the side effects, complex dosing schedules and pill burden of protease inhibitors (PIs) by switching to kindler, gentler all-nucleoside-analogue regimens. The fear: popping three same-class compounds might not keep the bug at bay. Now two studies offer insight on who may be able to go wall-to-wall nukes. Among HIVers averaging 20 months on HAART, undetectable viral loads and no prior virological failure, Vancouver's Julio Montaner, MD, pitted 106 HAARTers who stayed on two-nuke, one-PI regimens against 105 who pitched the protease for the nuke abacavir (Ziagen) plus their other nucleosides. At 48 weeks, treatment failure -- virological failure or a therapy stop -- occurred in 26 PI-takers but only 13 who abaca-veered. That three times as many PI-poppers stopped their regimens because of side effects accounts for much of the difference. Viral rebound (two consecutive viral loads above 400) was low in both groups, appearing in only four all-nukers and two still on PIs. Abacavir-takers also reported more med-taking ease and treatment satisfaction and showed lower cholesterol and triglycerides trends.

So going nukelier might look tempting if you've never had drug failure. But the Swiss cohort's Simplified Maintenance Therapy (SMT) study yields important cautions. SMT was similar to Montaner's study -- HIVers could stay on PI-powered regimens or switch to abacavir and Combivir (AZT plus 3TC). But there was one key difference: 48 percent of those on PIs and 36 percent of switchers had a pre-HAART liaison with AZT. At a median 68 weeks, therapy failure for any reason (including virologic failure, treatment change, discontinuation or death) occurred in 29 percent of PI-poppers and 25 percent of abacavir-takers. But the virologic failure occurred in 15 percent of those on abacavir/Combivir and only 6 percent of PI-takers. Turns out that prior suboptimal AZT use quadrupled the odds of virologic failure. So if AZT was always used in successful HAART, switching to all nukes may be feasible. But with a mono- or dual-AZT past, sticking with a protease-spritzed cocktail may up the odds for keeping the virus down.

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