Solo Shot

After years of HIV combo therapy, some are trying a boosted protease inhibitor—all by itself.

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A 2005 HIV diagnosis hasn't kept Houston's Ellen Foots, 52, a night-shift postal clerk and grandmother of seven, from playing three-card poker and slots. She's no slouch at keno, either: Recently,with only $125 of chips left, she won $800. "I bought some clothes,paid the bills and gave my children some money," says Foots.

About a year ago, when her lab reports said it was time to start HIV meds, Foots took another gamble. A three-drug combo has been the norm for a decade, because the triple punch seems best at keeping HIV undetectable. But Foots' doctor, Joseph Gathe, MD, of Baylor College of Medicine, invited her into his study of people taking only Kaletra—the protease inhibitor (PI) lopinavir with a built-in booster of the PINorvir (ritonavir). At the low booster dose, Norvir doesn't suppress HIV; thus lopinavir works on its own, making the regimen *monotherapy*.

Gathe first began presenting surprising results in 2003, showing that this therapy suppressed HIV in 21 patients—stabilizing or lifting CD4 counts as well. A year later, it was still working in all 21. Now, he says, "We're dead in the middle of these studies—and designing new ones" to evaluate the risk-benefit ratio. (Norvir-boosted Reyataz, which may suppress HIV on its own, hasn't been studied as monotherapy.)

Some HIV doctors aren't betting the benefit will outweigh the risk. Indeed, monotherapy may be running into resistance of its own. One small study recently found that after 90 weeks, some on Kaletra alone developed resistance to PIs, while none on Kaletra plus two nukes did. "It seems pretty clear that Kaletra monotherapy is not as effective as standard three-drug therapy," says Joel Gallant, MD, of Johns Hopkins School of Medicine in Baltimore. New York City's Howard Grossman, MD, former director of the American Academy of HIV Medicine says, "I'm still very hesitant about Kaletra monotherapy, although the results have been better than I expected."

Gathe says the recent study "hasn't dampened my enthusiasm: The percentage of resistance in the mono arm is still low and comparable to triple therapy studies with non-nukes." Meanwhile, a small Spanish study echoed Gathe's earlier monotherapy findings: little resistance at 48 weeks.

The conflicting results are keeping the debate alive. Since Gathe's original trial, several others—many funded by Abbott Laboratories, Kaletra's manufacturer—have produced similar

outcomes comparing monotherapy with three-drug regimens. In one, Kaletra monotherapy suppressed HIV as well as a combo of non-nuke Sustiva (efavirenz) plus two-nukes-in-one Combivir (AZT/3TC)—with less fat loss (lipoatrophy).

In the long term, Gathe says, “I don’t think you’ll see Kaletra mono winning against a three-drug regimen—it’s not a replacement for triple therapy.” So why try it at all? It’s all about the “real world” he says, “where we have to compromise because of cost and [side effects].”

Replacing three drugs with one to cut his patients’ copays, Gathe chose solo Kaletra because it mounts a fierce fight against HIV, with resistance prevailing only after many missed doses. “For the individual, drug costs drop by two thirds—and if they need the nuke, you can add it,” Gathe says. And eliminating nukes from combos may eliminate their side effects, such as fat loss and kidney and bone problems. Studies are now examining whether fat accumulation, often linked to PIs, occurs less in a nukeless PI regimen.

If monotherapy turns out to be safe for short periods of time but not in the long run, Gathe says, it could prove useful for people facing hep C treatment and needing an HIV regimen that won’t promote anemia (some nukes do), or for those with resistance to nukes and in need of a second combo. It’s also being studied for use during pregnancy, he says.

Gathe’s “real world” approach has some support among HIV doctors. Boston’s Cal Cohen, MD, who has a few patients doing well on Kaletra monotherapy, says the studies show that“not everyone needs the second or third [HIV drug] to maintain viral suppression—most don’t.” NYC’s Paul Bellman, MD, says he hopes that conventional wisdom won’t obscure monotherapy’s “potentially important place in treatment both here and globally.”

Other prominent HIV doctors say they wouldn’t prescribe the regimen in the U.S. “Why would you?” asks Washington, DC’s, Douglas Ward, MD, adding that Kaletra monotherapy must be taken a demanding twice a day.

Advocate Bob Huff of Treatment Action Group cites the studies in which monotherapy didn’t seem to keep people undetectable as consistently as three-drug combos, meaning it might not prevent HIV drug resistance in the long term. Grossman cautions that when such resistance does emerge, it may limit use of other PIs. And NYC’s Lloyd Bailey, MD, says, “I don’t think that sacrificing long-term success is currently worth the advantage of reducing cost or avoiding the toxicity of [nukes].”

As for Foots, her viral load remains undetectable and her CD4 count at about 800 after more than a year—with no side effects. She says she’ll stick with monotherapy as long as this trend continues. She’s not hedging her bets.

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