Buzz Back From ICAAC

Resistance was all the rage at one of the year's top AIDS research meetings -- but five new livers stole the show. Lark Lands reviews December's Interscience Conference on Antimicrobial Agents and Chemotherapy.

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One Major Loser

The long-awaited findings on **drug resistance** from HCSUS (the HIV Cost and Service Utilization Study) made us want to re-order that acronym as the more appropriate *SUCHS* (hard "K"). Researchers testing blood samples of 1,906 HIVers (some currently on meds, others not) found that only 36 percent had an undetectable viral load -- much lower than previously reported. And that's only for starters. When 1,080 of the samples were subjected to ViroLogic's **PhenoSense Assay** -- which directly measures HIV's ability to reproduce in the presence of antiretrovirals -- 78 percent with detectable viral load had developed resistance to one or more of the drugs -- and so could expect that the med has gone bust, or will. Here's the class analysis: 70 percent were resistant to one or more nukes, 42 percent to one or more protease inhibitors and 31 percent to one or more non-nukes. More than half had the big "R" to two classes, and -- ouch! -- 14 percent had a triple-class threat. Resistance was found in a whopping 87 percent of those currently on the cocktail (more than double last year's estimate), in 41 percent no longer on meds and in 20 percent who have *never* taken them -- and who are, therefore, presumably infected with already-resistant virus. All of this indicates a shrieking need for new drugs that disarm resistant bugs. Read on.

Two Up-&-Comers

In a promising -- albeit short and small --trial (seven days, 19 treatment-naïve folks), Tibotec-Virco's new non-nuke, called **TMC-125**, proved to pack a potent anti-HIV punch. Building on test-tube findings that the drug kills HIV that has developed resistance to the non-nuke class, the Belgian company is itching to test TMC-125 in that HCSUS 31 percent. But attracting volunteers may require a major drug reformulation -- the twice-daily regimen, 900 mg used in this study called for participants to take 36 capsules a day. Gulp.

As for protease-inhibitor resistance, Boehringer-Ingelheim's **tipranavir** -- previously shown to be an impressive test-tube force on that front -- was given with two nukes plus ritonavir to those failing their first PI-based regimen. Thirty-nine percent on the low-dose regimen (500 mg of tipranavir/100 mg of ritonavir, twice daily) achieved an undetectable viral load, compared to 40 percent given ritonavir/saquinavir (400 mg of each, twice daily) with the nukes. The experimental regimen performed better when tipranavir was given at a higher dose (1,250 mg tipranavir, twice

daily) -- 55 percent got the undetectable gold star. This may not exactly rock your boat, but note: 28 of the 63 volunteers, or almost half, had HIV that lacked PI mutations (even though their PI was failing) -- and researchers expect that those who have *multiple* PI mutations will do the best on the drug. That trial starts in the spring. So keep those fingers crossed.

Three Quick Takes

Bristol-Myers Squibb's new PI, **atazanavir**, provides hope for those in the cardiac-worried category. Researchers examining blood fats in those on once-daily combos with atazanavir (either 400 or 600 mg) saw triglycerides drop 25 percent; total cholesterol decreased 10 percent in those on 600 mg (and stayed the same in the 400-mg crowd).

Axxima Pharmaceuticals' **AXD-455** is aimed at a whole new target on HIV, blocking the activity of a chemical messenger (eIF-5A) used to help transport viral building blocks from the cell nucleus to the cytoplasm. If those materials don't get there, new HIV cells can't get made. Even better, in the test tube it works major mojo against resistant virus.

Best of show? The first-ever success of a series of **liver transplants** -- five HIVers coinfected with hepatitis B, C or both -- was announced. The fab five have survived for up to two years -- and remain healthy enough to take HAART. Bravo to them, the activists who fought to get them on transplant lists and the transplant teams who followed through!

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