The “No Nukes” Movement

February 1, 1999 By Lark Lands, PhD

First the bad news. Some nuked-out PWAs pinning their hopes on abacavir (Ziagen), Glaxo Wellcome’s new contender in the class of nucleoside analog reverse transcriptase inhibitors (NRTIs), may be in for trouble. Several research groups have identified two different resistance phenonema that create cross-resistance among all the nukes, including just-out abacavir. Most forms of NRTI resistance result in a one-for-one switcheroo—the exchange of one of the reverse transcriptase (RT) enzyme’s amino-acid building blocks for another. Because such mutations usually allow the virus to resist only a specific drug, others in the nuke class may still work. But with these newly found hitches—identifiable on some genotypic (viral resistance) tests—that’s not the case.

In one—the so-called 69SSS amino acid insertion—the addition of two extra amino acid building blocks to the RT enzyme causes multi-nuke resistance. In the other—the Q151M complex—a specific combination of five mutations (test-takers, observe: A62V, V751, F77L, F116Y and Q151M) has the same unfortunate result. Virco researcher Brendan Larder, MD, reports significant abacavir resistance with either of these.

Now for the good news: In studies to date, these problems with nuke cross-resistance have only been seen in 1 percent or 2 percent of participants. And not to worry: the 69SSS insertion and Q151M complex do not create resistance to the nonnucleoside RTIs or to the protease inhibitors.

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