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Maraviroc

A Viewpoint by Jacob Lalezari

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The 24-week interim results of two phase III studies demonstrate that maraviroc is efficacious and well tolerated in highly treatment-experienced patients with HIV-1. Maraviroc, which binds to the CCR5 coreceptor of host T cells to block HIV-1 entry, is the first antiretroviral agent to show virological and immunological benefits as host-directed therapy in HIV-1-infected patients. Even against the stunning successes of HIV drug development over the last 10 years, this stands out as a milestone achievement.

That said, almost half of the treatment-experienced patients screened for the study with the Trofile™ assay (Monogram biosciences, Inc.), were excluded based on finding X4- or dual/mixed-tropic virus. A prior study of maraviroc in such patients demonstrated no clear benefit and, therefore, at least for now, maraviroc will only be indicated for patients with pure R5-tropic virus. Results from studies in antiretroviral-naive patients, in whom R5-tropic virus more consistently dominate the quasispecies, may one day expand the pool of patients who may potentially benefit from CCR5 coreceptor blockade.

The safety data, although preliminary, are encouraging although questions remain. The long-term consequences, if any, of CCR5 binding to host T cells may only become clear with longer-term follow-up. Moreover, the selection for X4-tropic virus in patients failing maraviroc treatment resulted in blunted T-cell responses compared with patients with R5-tropic virus failing treatment. As with long-term CCR5 binding, the clinical consequences, if any, of drug-selected emergence of X4-tropic virus remains to be determined.

The efficacy results from the phase III maraviroc studies demonstrate about a 1 log reduction in plasma HIV-1 RNA compared with placebo, and a doubling of response rates of patients achieving an undetectable viral load. The scale of this success is similar to that observed from studies of other novel agents like enfuvirtide, an HIV fusion inhibitor, and raltegravir, an HIV integrase inhibitor. Armed with these agents, which retain activity against multidrug-resistant virus, clinicians have renewed hope to achieve virological suppression in many of their most heavily pretreated patients. ▲