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RESPONSE TO VICRIVIROC IN HIV-INFECTED, TREATMENT-EXPERIENCED INDIVIDUALS USING AN ENHANCED VERSION OF THE TROFILE HIV CO-RECEPTOR TROPISM ASSAY [TROFILE (ES)]: REANALYSIS OF ACTG 5211 RESULTS

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BACKGROUND: Vicriviroc (VCV) demonstrated potent virological suppression in treatment-experienced patients with R5 virus at study screen by the standard Trofile assay (Monogram Biosciences, San Francisco, CA, USA). An enhanced sensitivity Trofile assay (Trofile [ES]), with improved ability to detect CXCR4-using minor variants, could optimize selection of patients who may benefit from CCR5 antagonists.

METHODS: We used Trofile (ES) to determine coreceptor usage at study screen and entry for the 118 individuals on ACTG 5211. We examined virological and immunologic responses by randomized treatment arm (VCV at 5, 10, 15 mg daily or placebo plus optimized background antiretrovirals at day 14) according to tropism results by Trofile (ES). All analyses were intent-to-treat.

RESULTS: Using Trofile (ES), 89 individuals had R5 virus at screening, 25 individuals with R5 virus by the standard assay were found to have dual/mixed (DM) virus and samples from four individuals were not available. Among VCV recipients, respective mean changes in HIV-1 RNA (log₁₀ copies/ml) at 14 days and 24 weeks were improved for individuals with R5 virus by Trofile (ES): -1.10 and 1.85 (5 mg), -1.31 and -2.09 (10 mg), and -0.93 and -1.75 (15 mg), compared with the original results for individuals with R5 virus by standard Trofile: -0.87 and -1.51 (5 mg), -1.15 and -1.86 (10 mg), and -0.92 and -1.68 (15 mg). No difference was found among placebo recipients. Amongst all VCV recipients and according to classification by Trofile (ES), greater reductions in log₁₀ HIV-1 RNA were observed in the 64 individuals with R5 virus at both screening and entry (group 1) compared with the five individuals with R5 virus at screening, but DM virus at study entry (group 2), and the 15 individuals with DM virus

at screening (group 3): at day 14, -1.15 versus -0.66 versus -0.09 and at week 24, -1.95 versus -1.20 versus -0.57 ($P>0.05$ comparing groups 1 and 2, and 2 and 3; $P<0.001$ comparing groups 1 and 3 for both endpoints).

CONCLUSIONS: Reanalysis of key study endpoints based on Trofile (ES) demonstrates improved antiretroviral activity of VCV and indicates that Trofile (ES) is an improved screening tool for determining patient eligibility for CCR5 antagonist therapy.

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