14.4.1 Treatment-naive Studies

All three currently available STRs, EFV/FTC/TDF, FTC/RPV/TDF and EVG/COBI/FTC/TDF, have been approved for use in treatment-naive patients based on results from key clinical studies demonstrating the efficacy of these STRs in comparison with other DHHS-preferred ARV treatment regimens. Most recently, the newest STR EVG/COBI/FTC/TDF demonstrated non-inferior efficacy to two other standard-of-care regimens in two large Phase 3 studies in HIV-infected treatment-naive patients.[30,31] Study 102 was a prospective, randomized, double-blind 192-week trial comparing the efficacies of the EVG/COBI/FTC/TDF STR ($n = 348$) and the EFV/FTC/TDF STR ($n = 352$). The primary endpoint of the study was the proportion of subjects achieving HIV-1 RNA < 50 copies mL^{-1} at week 48 based on intention-to-treat (ITT) FDA snapshot analysis. The predefined criterion for non-inferiority was a lower bound of a two-sided 95% CI $> -12\%$. At week 48, 87.6% of patients on EVG/COBI/FTC/TDF achieved HIV-1 RNA < 50 copies mL^{-1} compared with 84.1% of patients in the EFV/FTC/TDF arm (treatment difference 3.6%; 95% CI –1.6 to 8.8%). The mean increase in CD4 cell count from baseline was significantly higher in the EVG/COBI/FTC/TDF arm than the EFV/FTC/TDF arm (239 *versus* 206 cells mm^{-3}; $p = 0.009$). In both arms, virologic failure (VF) rates were low with 2% of subjects developing primary resistance mutations.[30] Similarly, Study 103 was a prospective, randomized, double-blind 192-week trial comparing the efficacy of the EVG/COBI/FTC/TDF ($n = 353$) *versus* atazanavir (ATV) + ritonavir (RTV) + FTC/TDF ($n = 355$). The primary endpoint and criterion for non-inferiority were the same as described above for Study 102. At week 48, 89.5% of patients on EVG/COBI/FTC/TDF achieved HIV-1 RNA < 50 copies mL^{-1} compared with 86.8% of patients on ATV + RTV + FTC/TDF (treatment difference 3.0%; 95% CI –1.9 to 7.8%). Mean increases in CD4 cell count from baseline were similar in both the EVG/COBI/FTC/TDF and ATV + RTV + FTC/TDF treatment arms (207 *versus* 211 cells mm^{-3}). In both arms, VF rates were low. with 1% of subjects in the EVG/COBI/FTC/TDF arm and no subjects in the ATV + RTV + FTC/TDF arm developing primary resistance mutations.[31]

Figure 14.6 summarizes the efficacy data for the EVG/COBI/FTC/TDF and EFV/FTC/TDF STRs in treatment-naive patients from Studies 102 and 103.

Patients taking the EFV/FTC/TDF STR maintained virologic suppression through week 240 in the extension phase of Study 934. Study 934 was a randomized, open-label, 144-week study evaluating the non-inferiority of FTC/TDF + EFV *versus* AZT/3TC twice daily + EFV once daily in treatment-naive patients. Through 144 weeks, 64% (146/227) of patients on FTC/TDF + EFV achieved HIV-1 RNA < 50 copies mL^{-1} compared with 56% (130/231) of patients on AZT/3TC + EFV.[32] After week 144, a total of 160 patients in the FTC/TDF + EFV arm and 126 patients in the AZT/3TC + EFV arm switched to EFV/FTC/TDF STR. Among patients who switched to the STR, similar proportions had HIV-1 RNA < 50 copies mL^{-1} (83% switch from FTC/TDF + EFV *versus* 82% switch from AZT/3TC + EFV) at week 240 (96 weeks post-switch to EFV/FTC/TDF STR).[21]