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metabolized by CYP3A to improve their PK exposure. The efficacy of cobicistat versus ritonavir as a pharmacoenhancer for atrazanavir was studied in a randomized, placebo-controlled, double-blind, multicenter, 48-week Phase 3 study. In the trial, anti-retroviral treatment-naive HIV-1-infected adults received either cobicistat or ritonavir for 48 weeks; all patients also received atazanavir plus Truvada. At 48 weeks, the study found that 85% of patients on the cobicistat-containing regimen, compared with 87% of patients on the ritonavir-containing regimen, achieved the primary endpoint, with HIV RNA levels less than 50 copies mL^{-1}; 7% of the patients discontinued owing to adverse events in each arm of the study. The study found that an HIV regimen containing a cobicistat-boosted PI was non-inferior to a regimen containing a ritonavir-boosted PI at 48 weeks of therapy.[58] Currently, cobicistat is under regulatory review. If approved, cobicistat may be an effective option for boosting the potency of HIV regimens that are based on PIs.

Cobicistat has favorable physicochemical properties, especially high aqueous solubility, allowing it to be formulated as a tablet and co-formulated with other drugs as a tablet. It was co-formulated with the preferred, once-daily nucleoside/nucleotide reverse transcriptase backbone tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC), and also the integrase inhibitor elvitegravir (EVG 150 mg, COBI 150 mg, FTC 200 mg and TDF 300 mg) as a once-daily single-tablet regimen (STR), known as Quad. Quad is the first and only integrase inhibitor-containing single-tablet regimen. The other two single-tablet regimens available, Atripla® and Complera®, are based on a non-nucleoside reverse transcriptase inhibitor as the third agent. Two independent, fully powered Phase 3 non-inferiority trials have compared Quad with two current standard-of-care regimens for initial HIV treatment. One regimen contained the non-nucleoside reverse transcriptase inhibitor efavirenz and the other was based on the boosted protease inhibitor atazanzavir; both used Truvada as the backbone. Results at 48 weeks from these two Phase 3 studies have been published. The two Phase 3 studies show that Quad has high efficacy and a good tolerability profile, with the limitations of drug–drug interaction and a need to be taken with food. The primary endpoint for the study is to achieve HIV RNA (viral load) fewer than 50 copies mL^{-1} at 48 weeks. The top line results showed 88% of Quad patients *versus* 84% of Atripla® patients achieved the primary endpoint. Mean CD4+ T cell count from baseline in Quad was 239 cells mm^{-1} *versus* 206 cells mm^{-1} in Atripla®.[59] In the study comparing Quad with boosted atazanavir, 90% of Quad patients *versus* 87% of boosted atazanavir patients achieved the primary endpoint at 48 weeks.[60] Quad is statistically non-inferior to the two standard-of-care regimens. The FDA approved Quad (Stribild®) to treat HIV-1 infection in treatment-naive adults on 27 August 2012. It is expected that Quad will become an important complete regimen option for adult HIV-infected subjects.

With the availability of low dose and ease of formulation, cobicistat is also being co-formulated as a fixed-dose combination tablet with atazanavir and darunavir. It is expected to help further simplify the regimen and reduce the pill burden in boosted PI drug combinations. In addition, cobicistat may help