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Speaker: Dora Martinez, MD, FAAFP, AAHIVS

Topic: Dovato – Tango Clinical Trial

Dr. Martinez:
Hello, I'm Dr. Dora Martinez, the Chief Medical Officer of the Valley AIDS Council. As you may know, Dovato has been indicated as a complete regimen to treat HIV-1 infection in adults with no antiretroviral, ARV, treatment history, the indication for Dovato has been extended to include biologically suppressed adults on a stable ARV regimen with no history of treatment failure, and no known resistance to any component of Dovato.

Today, I'd like to share with you the 96-week data from the TANGO clinical trial, which is focused on using Dovato in virologically suppressed adults. In this presentation, we will review the TANGO study design and baseline characteristics, efficacy, resistance, and adverse events. Dovato is a complete once-daily, single pill, two-drug regimen for treatment-naive and virologically suppressed adult patients with HIV-1.

Before we get into the data, please take a moment to review the indication and important safety information including boxed warning for Dovato.

Male:
Indication: Dovato is indicated as a complete regimen to treat HIV-1 infection in adults with no antiretroviral treatment history, or to replace a regimen in those who are biologically suppressed on a stable regimen with no history of treatment failure or known resistance to the components of Dovato.

Important safety information: Dovato contains a boxed warning for patients who are coinfected with hepatitis B virus. All patients with HIV-1 should be tested for the presence of HBV prior to or when initiating Dovato. Emergence of HBV resistance has been reported with lamivudine-containing regimens. If Dovato was used in patients with HBV coinfection, additional treatment should be considered for the appropriate treatment of chronic HBV or use an alternative regimen. Additionally, if you're using Dovato in an HBV coinfected patient and discontinued treatment, severe acute exacerbation of their hepatitis B may occur. Closely monitor hepatic function.

Contraindications: Dovato is contraindicated in patients who have had a prior hypersensitivity reaction to dolutegravir or lamivudine or in patients who are receiving dofetilide.

Warnings and Precautions: Hypersensitivity reactions have been reported in persons taking dolutegravir-based regimens, and were characterized by the symptoms shown here. Discontinue Dovato immediately if a severe skin or

hypersensitivity reaction develops, as a delay may result in a life-threatening reaction. Monitor and appropriately treat the patient.

Hepatotoxicity: Hepatic adverse events, including hepatotoxicity, have been reported in patients taking dolutegravir-based regimens in persons with and without pre-existing hepatic disease. Patients with hepatitis B or C coinfection, or who have had a history of elevations in their LFTs may be at increased risk of worsening of their liver function. In some cases, increases in LFTs was consistent with IRS or HBV reactivation. Patients should be monitored for hepatotoxicity.

Embryo Fetal Toxicity: Assess the risk and benefits of Dovato, and discuss with the patient to determine if an alternative treatment should be considered at the time of conception through the first trimester of pregnancy, due to the risk of neural tube defects.

Lactic Acidosis and Severe Hepatomegaly with Steatosis: Discontinue Dovato if laboratory findings suggest lactic acidosis or severe hepatomegaly, including hepatomegaly with steatosis in the absence of marked transaminase elevations.

Adverse Reactions or Loss of Virologic Response due to Drug Interactions with concomitant use of Dovato may occur. Immune reconstitution syndrome including autoimmune disorders have been reported with Dovato.

Additional important safety information for Dovato will be presented later in this video. Please click the link accompanying this video to view the full prescribing information, including boxed warning for Dovato.

Dr. Martinez:
The TANGO clinical trial is a study to evaluate the efficacy and safety of a switch to dolutegravir 50 milligrams once daily, plus lamivudine 300 milligrams once daily in virologically suppressed adult patients living with HIV-1, versus remaining on an initial regimen of tenofovir alafenamide, TAF, and emtricitabine, FTC, plus an integrase strand transfer inhibitor, INSTI, a non-nucleoside reverse transcriptase inhibitor, NNRTI, or a protease inhibitor, PI.

This study is a phase 3 randomized, multicenter, non-inferiority switch study with 741 patients combined. The primary endpoint was the proportion of patients with HIV-1 RNA greater than or equal to 50 copies per mL at week 48 using the FDA Snapshot analysis with a 4% non-inferiority margin, proportion of patients with HIV-1 RNA less than 50 copies per mL at week 48 with a prespecified secondary endpoint.

The initial TAF-containing regimens included TAF FTC, plus a third agent; 79.6% or 296 patients included an INSTI in their initial regimen, 12.9% or 48 patients

included an NNRTI, and 7.5% or 28 patients included a PI. Baseline characteristics were similar between the two arms.

Dr. Martinez:
Did Dovato maintain virologic suppression as well as the TAF-containing regimens? By now you're probably wondering how Dovato performed in the trial compared to TAF-containing regimens. First, I want to mention that the primary endpoint for this study was the proportion of patients with HIV-1 greater than or equal to 50 copies per mL at 48 weeks. At 48 weeks, Dovato demonstrated no increased rate of virologic failure versus those who remained on TAF-containing regimens, with less than 1% of patients experiencing virologic failure across both treatment arms. The non-inferior treatment difference with 95% confidence interval was -0.3% with a range of -1.2% to 0.7%.

Now let's dive into the 96-week data. Efficacy results that 96 weeks were consistent with less than 1% and 1% of patients experiencing virologic failure in the devata arm and TAF-containing regimens are respectively. The non-inferior treatment difference with 95% confidence interval was -0.8% with a range of -2.0% to 0.4%. Dovato also demonstrated maintenance of virologic suppression versus TAF-containing regimens with 86% and 79% suppression for the Dovato arm and TAF-containing regimens arm, respectively. The number of patients with no virologic data at week 96 due to COVID-19 was a primary driver in the treatment difference.

Dr. Martinez:
I know what you're probably thinking; the efficacy data are great to have, but we also need to know about resistance. Through 96 weeks, there were zero cases of treatment emergent resistance. Resistance was evaluated in patients with confirmed virologic withdrawal, which was defined as one assessment with HIV-1 RNA greater than or equal to 200 copies per mL after day one, with an immediately prior HIV-1 RNA greater than or equal to 50 copies per mL. No patients in the Dovato arm were evaluated for treatment emergent resistance.

Dr. Martinez:
The most common adverse drug reactions grades 2 to 5 occurring in greater than or equal to 0.5% of patients receiving Dovato were depression, insomnia, constipation, weight increase, and flatulence.

Dr. Martinez:
So now that we reviewed all of the TANGO data, is there an appropriate virologically suppressed patient within your practice who could be ready for a switch to Dovato?

To summarize, we will now review the key takeaways from the TANGO study before returning to the remaining important safety information. Based on 96-week results from the study, Dovato demonstrated powerful durable efficacy. It was as effective as TAF-containing regimens at 96 weeks, and a high barrier to resistance based on zero cases of treatment emergent resistance at 96 weeks. Dovato also does not contain TAF, TDF, or abacavir.

I hope you found the content we covered today informative as you consider Dovato for your appropriate switch patients with HIV-1. To learn more visit Dovatohcp.com. Thanks for watching.

Male:
Important Safety Information.
Adverse reactions: The most common adverse reactions reported with Dovato include headache, nausea, diarrhea, insomnia, fatigue, and anxiety.
Drug Interactions. Please consult the full prescribing information for more information on potentially significant drug interactions. Dovato is indicated as a complete regimen. Coadministration with other ARV's for the treatment of HIV-1 is not recommended. Drugs that induce or inhibit CYP3A or UGT1A1 may affect levels of dolutegravir. Dovato should be administered two hours before or six hours after polyvalent cation, such as antacids, laxatives, and sucralfate. Alternatively, Dovato and supplements containing calcium or iron can be taken concomitantly if taken with food.

Use in Specific Populations.
Pregnancy: There are insufficient data on the use of Dovato during pregnancy to assess the risk for birth defects and miscarriage. Advise individuals of childbearing potential of the potential risk of neural tube defects.
Lactation: It is not recommended to breastfeed if you're HIV positive while taking Dovato.
Females and Males of Reproductive Potential: Pregnancy testing is recommended before initiation of Dovato. Counsel individuals of childbearing potential taking Dovato on the consistent use of effective contraception.
Renal Impairment: Dovato is not recommended for patients with creatinine clearance less than 30 milliliters per minute. Patients with a sustained creatinine clearance between 30 and 49 milliliters per minute should be monitored for hematologic toxicities.
Hepatic Impairment: Dovato is not recommended in patients with severe hepatic impairment.

Please see the link accompanying this video to view the full prescribing information including boxed warning for Dovato.