Transcript Details
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Reaching HIV-1 Treatment Decisions Without a Patient's Medical Records

Announcer:
You are listening to ReachMD. Welcome to this week's industry feature sponsored by Janssen Therapeutics a Division of Janssen Products, LP: the marketer and distributor of SYMTUZA® (darunavir, cobicistat, emtricitabine, and tenofovir alafenamide) tablets, for oral use. See the full prescribing information including Boxed Warning for SYMTUZA® at www.SYMTUZA hcp.com. The following program is intended for US healthcare professionals only and is not certified for continuing medical education. Your host today is Dr. Matt Birnholz and your guest is Dr. Jason Leider who is a paid consultant for Janssen Therapeutics, Division of Janssen Products, LP.

Matt Birnholz, MD:
In our discussion today, we will focus on the clinical profile of SYMTUZA®. SYMTUZA® is indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (or HIV-1) infection in adults who have no prior antiretroviral treatment history or who are virologically suppressed (as in HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least 6 months and have no known substitutions associated with resistance to darunavir or tenofovir.

Joining me today is Dr. Jason Leider. Dr. Leider is Professor of Clinical Medicine at the Albert Einstein College of Medicine and the Medical Director of the North Bronx Health Care Network in Bronx, New York.

Dr. Leider, welcome to ReachMD.

Jason Leider, MD:
Thank you for having me here today.

Matt Birnholz, MD:
Before we discuss SYMTUZA®, let's review the boxed warning and contraindications.

Jason Leider, MD:
Yes - The boxed warning for SYMTUZA® is regarding severe acute exacerbations of hepatitis B that have been reported in patients who are coinfected with HIV-1 and hepatitis B and have discontinued products containing emtricitabine and/or tenofovir disoproxil fumarate and may occur with discontinuation of SYMTUZA®. You must closely monitor hepatic function with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and discontinue SYMTUZA®. If appropriate, anti-hepatitis B therapy may be warranted.

In addition, SYMTUZA® is contraindicated with certain medications due to the potential for serious and/or life-threatening events, or the loss of therapeutic effect and possible development of drug resistance.

Consult the full Prescribing Information at www.SYMTUZA hcp.com for potentially serious drug interactions prior to and during SYMTUZA® therapy.

Matt Birnholz, MD:
Now Dr Leider, normally when we're starting treatment in naive patients, we like to understand what agents they have sensitivity to because of the risk of transmitted drug resistance.

So, can you think of a patient that you've seen in the last few days where you didn't have their resistance records?

Jason Leider, MD:
Yes that's right, normally we do like to review their resistance testing records, but that's not always possible. I can actually tell you of a recent patient, whom I started treatment on a few days ago. He is a 29-year-old Caucasian MSM that had a viral load of 126,000 copies, CD4 count was 250 and serum creatinine was 0.75 and EGFR was 95 with no resistance records available.

He is a long-haul trucker and travels regularly throughout the U.S. and was apparently diagnosed with HIV-1 six months ago in an out-of-state clinic - no drug use.

Matt Birnholz, MD:
Dr. Leider, is it common that you have a patient who you need to treat but have never seen before or have no ARV treatment history?

How do you approach their treatment?

Jason Leider, MD:
Yes, I often treat many patients who are entirely "new to me" and their history and resistance testing records are incomplete, I'm waiting for them from another office or I just don't have them for this patient.

If the patient does not have resistance testing records available, I select a regimen containing Darunavir with a protective barrier to resistance with the goal of achieving and maintaining virologic suppression.

Matt Birnholz, MD:
And how did you treat this patient?

Jason Leider, MD:
I started him on SYMTUZA®. I also ordered hepatitis serology, liver function tests, urinalysis and resistance tests because these are required labs to have when initiating treatment with SYMTUZA® .

I also scheduled a follow-up appointment with the patient to assess him after starting therapy and to conduct laboratory monitoring as indicated.

Matt Birnholz, MD:
You have a lot of ARV options, why did you select SYMTUZA®?

Jason Leider, MD:
I select SYMTUZA® because it is indicated for patients with no prior ARV treatment history. As mentioned earlier, the patient did not have resistance testing records. In addition, given this patient's irregular lifestyle, being on the road as a truck driver, puts him at risk for suboptimal or poor adherence. Based on the DHHS guidelines, a darunavir-based regimen such as SYMTUZA®, is recommended in this type of patient type.

I have years of experience with darunavir. SYMTUZA® is the only STR that has the same barrier to resistance as other DRV containing regimens, that I have offered to my patients previously.

I also know that SYMTUZA® had less impact on bone and renal health vs an active control demonstrated in treatment naïve trial patients. This same study also demonstrated high rates of efficacy and only 2% of patients discontinuing treatment due to AEs at 48 weeks. We will discuss this more in a minute.

The efficacy and tolerability demonstrated in their clinical trial with naïve patients is impressive given how the study was designed.

Matt Birnholz, MD:
Tell me more about how SYMTUZA® was studied in treatment naïve patients?

Jason Leider, MD:
SYMTUZA® 's AMBER trial was a Phase 3 double-blind, active-controlled, international, multicenter, noninferiority study. assessing the efficacy and safety of SYMTUZA® in 362 treatment-naïve patients.

- This trial compared SYMTUZA® to darunavir/cobicistat + FTC/TDF in treatment-naïve patients. The SYMTUZA® arm of the study included, 6% of patients with CD4 count <200 cells/mm3 and 17% of patients with viral loads above 100,000 copies/mL. This is important because these patients are more difficult to treat.
- At Week 48, virologic response rates were 91% and 88% in the SYMTUZA® and control arms, respectively

- The virologic failure rate (≥50 copies/mL) was 4% in the SYMTUZA® arm vs 3% in the control arm

Matt Birnholz, MD:
I agree that those are noteworthy results but there are a lot of other ARV options that claim to have a high genetic barrier. Do you think that SYMTUZA® is different?

Jason Leider, MD:
Yes, as I mentioned before SYMTUZA® is the only STR containing the protective barrier of darunavir.

In AMBER, SYMTUZA® demonstrated a high genetic barrier to resistance with 0 treatment-emergent darunavir, primary PI or TAF mutations.

In addition, SYMTUZA® has been studied in patients who are virologically suppressed on a stable antiretroviral regimen for at least 6 months and have no known substitutions associated with resistance to darunavir or tenofovir.

Matt Birnholz, MD:
Good point but what do you think about the tolerability profile?

Jason Leider, MD:
I know there are some clinicians who may have concerns about darunavir's tolerability profile, so it's important to note that in treatment-naïve patients, the AMBER trial had a 2% discontinuation rate due to treatment-related adverse events in the SYMTUZA® arm and a 4% discontinuation rate for the control arm.

Most of adverse reactions during treatment with SYMTUZA® in treatment naïve patients, were mild to moderate in severity.

The most common clinical adverse reactions (of all grades) occurring in at least 2% of treatment-naïve patients were diarrhea, rash, nausea, fatigue, headache, abdominal discomfort, and flatulence. There were also Grade 2-4 lab abnormalities and mean changes from baseline lipid values which occurred in the AMBER study.

Many of my fellow colleagues were impressed to see that only 1 patient in the naive study and 1 patient in the virologically suppressed study discontinued due to diarrhea.

In my opinion, this is a tolerability profile that I'm comfortable with for my patients.

Of course, please refer to the full Prescribing Information for a complete list of adverse drug reactions.

Matt Birnholz, MD:
Dr. Leider, thank you for this case discussion and overview of SYMTUZA® .

Jason Leider, MD:
You're welcome. Thanks for having me here today.

Matt Birnholz, MD:
Thank you, Dr Leider.

Now, in addition to the Boxed Warning and contraindications, let's learn more Important Safety Information for SYMTUZA®.

Announcer:
The following is additional Important Safety Information for SYMTUZA®.

WARNINGS AND PRECAUTIONS

- **Hepatotoxicity:** Drug-induced hepatitis (e.g., acute hepatitis, cytolytic hepatitis) and cases of liver injury, including some fatalities, have been reported in patients receiving darunavir, a component of SYMTUZA®. Patients with pre-existing liver dysfunction, including chronic active hepatitis B or C, have an increased risk for liver function abnormalities, including severe hepatic adverse reactions.

  Action: Monitor liver function prior to initiating and during therapy, especially in patients with underlying chronic hepatitis, cirrhosis, or in patients who have pretreatment elevations of transaminases. Patients with evidence of new or worsening liver function should consider discontinuing SYMTUZA®. SYMTUZA® is not recommended in patients with severe hepatic impairment (Child-Pugh Class C).

- **Severe Skin Reactions:** In patients receiving darunavir, a component of SYMTUZA®, severe skin reactions may occur, including Stevens-Johnson syndrome, toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis. These include conditions accompanied by fever and/or elevations of transaminases.

  Action: Discontinue SYMTUZA® immediately if signs or symptoms of severe skin reactions develop. These can include but are not limited to severe rash or rash accompanied with fever, general malaise, fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis, hepatitis, and/or eosinophilia.

- **Risk of Serious Adverse Reactions or Loss of Virologic Response Due to Drug Interactions:** Consult the full Prescribing Information prior to and during treatment for potential drug interactions.

- **Immune Reconstitution Syndrome:** Patients receiving SYMTUZA® may develop new onset or exacerbations of immune reconstitution syndrome.

- **New Onset or Worsening Renal Impairment:** Renal impairment, including cases of acute renal failure and Fanconi syndrome, has been reported with the use of tenofovir prodrugs. In clinical trials of SYMTUZA®, there were no cases of proximal renal tubulopathy, including Fanconi syndrome, reported in the SYMTUZA® group through Week 48. SYMTUZA® is not recommended in patients with creatinine clearance below 30 mL per minute. Patients taking tenofovir prodrugs who have impaired renal function and those taking nephrotoxic agents including nonsteroidal anti-inflammatory drugs are at increased risk of developing renal-related adverse reactions.

  Action: Prior to initiating or during treatment, on a clinically appropriate schedule, monitor serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, also assess serum phosphorus. Discontinue SYMTUZA® in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome. Patients who experience a confirmed increase in serum creatinine of greater than 0.4 mg/dL should be closely monitored for renal safety.

- **Sulfa Allergy:** Darunavir contains a sulfonamide moiety. The incidence and severity of rash were similar in subjects with or without a history of sulfonamide allergy.

  Action: Monitor patients with a known sulfonamide allergy.

- **Lactic Acidosis/Severe Hepatomegaly With Steatosis:** Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including emtricitabine, a component of SYMTUZA®, and tenofovir disoproxil fumarate (TDF), another prodrug of tenofovir, alone or in combination with other antiretrovirals.

  Action: Discontinue SYMTUZA® in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity.

- **Diabetes Mellitus/Hyperglycemia:** New-onset or exacerbations of pre-existing diabetes mellitus and hyperglycemia have been reported in patients receiving protease inhibitors

  Action: Initiation or dose adjustments of insulin or oral hypoglycemic agents may be required

- **Fat Redistribution:** Redistribution and/or accumulation of body fat have been observed in patients receiving antiretroviral therapy.

- **Hemophilia:** Patients with hemophilia may develop an increase in bleeding events.

ADVERSE REACTIONS

- The most common clinical adverse reactions (all grades) occurring in at least 2% of treatment-naïve patients were diarrhea, rash,* nausea, fatigue, headache, abdominal discomfort, and flatulence.

* Includes pooled reported terms: dermatitis, dermatitis allergic, erythema, photosensitivity reaction, rash, rash generalized, rash macular, rash maculopapular, rash morbilliform, rash pruritic, toxic skin eruption, and urticaria.

Grade 2-4 laboratory abnormalities have been reported in patients receiving SYMTUZA®, including elevations in serum creatinine, liver function tests, triglycerides, total cholesterol, low-density lipoproteins, and glucose levels.

This is not a complete list of all adverse reactions reported with the use of SYMTUZA®. Please refer to the full Prescribing Information for a complete list of adverse drug reactions.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** SYMTUZA® is not recommended for use during pregnancy and should not be initiated in pregnant individuals because of substantially lower exposures of darunavir and cobicistat during pregnancy.

  Lactation: The Centers for Disease Control and Prevention recommends that HIV-infected mothers in the United States not breastfeed their infants to avoid risking postnatal transmission of HIV-1 Infection.

- Consult the full Prescribing Information for SYMTUZA® for additional information on the Uses in Specific Populations.

Please visit www.SymtuzaHCP.com for full Prescribing Information, including Boxed WARNING for SYMTUZA®.

Announcer:
This program was sponsored by Janssen Therapeutics a Division of Janssen Products, LP. If you missed any part of this discussion, visit www.ReachMD.com/HIVTreatment. This is ReachMD. Be part of the knowledge.

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