PRESS RELEASE


ARIA study shows superior efficacy of Triumeq® for treatment-naïve women living with HIV

London, UK and Durban, South Africa, 18 July 2016 – ViiV Healthcare today presented 48-week data from the phase IIIb, open-label, international, multi-centre ARIA study which showed superior efficacy for Triumeq® (dolutegravir/abacavir/lamivudine) compared with atazanavir boosted with ritonavir (ATV/r) plus tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) in 495 treatment-naïve women living with HIV. Results show statistically superior viral suppression (HIV-1 RNA <50 c/mL) rates at week 48: 82% versus 71% (adjusted difference 10.5%, 95% CI: 3.1%-17.8%, p=0.005) respectively. ARIA was a non-inferiority study with a pre-specified analysis for superiority. Both non-inferiority and superiority endpoints were met, with superiority being driven by lower rates of both virological failures and discontinuations due to adverse events (AEs) in the dolutegravir/abacavir/lamivudine group.

“Women account for over half of the almost 35 million adults living with HIV worldwide, yet unfortunately they are consistently under-represented in HIV clinical trials,” said John C Pottage, Jr, MD, Chief Scientific and Medical Officer, ViiV Healthcare. “For this reason, we are committed to ensuring that the specific treatment needs of women are investigated. This trial not only provides physicians with important additional information about Triumeq, it also builds on the strong body of evidence supporting the efficacy of dolutegravir-based regimens in a broad range of patient populations.”

The safety profile of dolutegravir/abacavir/lamivudine was favourable compared to ATV/r plus TDF/FTC, with fewer drug-related AEs reported on the dolutegravir/abacavir/lamivudine arm (33% vs 49%); there were also fewer AEs leading to discontinuation compared to those in the ATV/r plus TDF/FTC arm (4% vs 7%).

Drug-related AEs reported in the dolutegravir/abacavir/lamivudine arm included, nausea (31 individuals / 13%), diarrhoea (12 / 5%), headache (5 / 2%) and dyspepsia (4 / 2%). In the ATV/r plus TDF/FTC group, drug-related AEs included nausea (35 / 14%), diarrhoea (18 / 7%), ocular icterus (18 / 7%), dyspepsia (15 / 6%), headache (14 / 6%) and jaundice (13 / 5%).

There were fewer subjects meeting virologic non-response criteria (VL >50c/mL) in the dolutegravir/abacavir/lamivudine arm (6%) compared to the other group (14%) at week 48. Of the women that met protocol-defined virologic withdrawal criteria, none on the dolutegravir/abacavir/lamivudine arm had treatment-emergent resistance mutations to the components of dolutegravir/abacavir/lamivudine, compared with one in the comparator group.
About HIV
HIV stands for the Human Immunodeficiency Virus. Unlike some other viruses, the human body cannot get rid of HIV, so once someone has HIV they have it for life. There is no cure for HIV, but effective treatment can control the virus so that people with HIV can enjoy healthy and productive lives.²

About HIV in women
Globally, HIV/AIDS is the leading cause of death for women of reproductive age (15–44 years old)³ and infection rates in young women (aged 15–24) are twice as high as those seen in young men.⁴ Despite the scale of the challenge, women are routinely under-represented in HIV clinical trials.⁵ This may be in part due to lack of child-care services, exclusions from study protocols due to the potential for pregnancy and lack of support in the home.⁵ As a result there are gaps in our knowledge about issues regarding antiretroviral treatments that are particular to women.⁵

ARIA study design
ARIA is a phase IIIb randomised, open-label, international, multi-centre study designed to demonstrate the non-inferior antiviral activity of fixed-dose dolutegravir/abacavir/lamivudine (Triumeq) compared with atazanavir boosted with ritonavir (ATV/r) plus tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) in treatment-naïve adult women over 48 weeks.⁶ While ARIA is a non-inferiority study, there was a pre-specified analysis for superiority. ARIA also evaluated the safety and tolerability of dolutegravir/abacavir/lamivudine compared to ATV/r plus TDF/FTC arm.⁶ 495 treatment-naïve adult women were enrolled in the study.⁶

About Triumeq®
Triumeq is a once-daily dolutegravir-based regimen, containing the un-boosted integrase strand transfer inhibitor (INSTI) dolutegravir and the nucleoside reverse transcriptase inhibitors (NRTIs) abacavir and lamivudine.

Two essential steps in the HIV life cycle are replication – when the virus turns its RNA copy into DNA – and integration – the moment when viral DNA becomes part of the host cell’s DNA. These processes require two enzymes called reverse transcriptase and integrase. NRTIs and INSTIs interfere with the action of the two enzymes to prevent the virus from replicating. This decrease in replication will lead to less virus being available to cause subsequent infection of uninfected cells.

The latest data for Triumeq, including the ARIA data presented at IAC 2016,¹ build on existing clinical trial data demonstrating that dolutegravir-based regimens are efficacious and generally well-tolerated in a broad range of people living with HIV (PLHIV), including treatment-naïve, treatment-experienced and those who have developed resistance to multiple HIV drugs.⁷,⁸,⁹,¹⁰,¹¹

Triumeq is a registered trademark of the ViiV Healthcare group of companies.

Important Safety Information (ISI) for Triumeq® (abacavir, dolutegravir, and lamivudine) tablets¹²
Note: this is taken from the US label and local variations apply. Please refer to applicable local labelling.
FDA Indications and Usage: Triumeq is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection.

Limitations of Use:
Triumeq alone is not recommended in patients with:
- Current or past history of resistance to any components of Triumeq
- Resistance-associated integrase substitutions or clinically suspected INSTI resistance because the dose of dolutegravir in Triumeq is insufficient in these subpopulations. See full prescribing information for dolutegravir

BOXED WARNING: HYPERSENSITIVITY REACTIONS, LACTIC ACIDOSIS AND SEVERE HEPATOMEGALY, and EXACERBATIONS OF HEPATITIS B VIRUS (HBV):

Hypersensitivity Reactions:
- Serious and sometimes fatal hypersensitivity reactions have occurred with abacavir-containing products
- Hypersensitivity to abacavir is a multi-organ clinical syndrome
- Patients who carry the HLA-B*5701 allele are at a higher risk of experiencing a hypersensitivity reaction to abacavir; although, hypersensitivity reactions have occurred in patients who do not carry the HLA-B*5701 allele
- Triumeq is contraindicated in patients with a prior hypersensitivity reaction to abacavir and in HLA-B*5701-positive patients. All patients should be screened for the HLA-B*5701 allele prior to initiating therapy or reinitiation of therapy with Triumeq, unless patients have a previously documented HLA-B*5701 allele assessment
- Discontinue Triumeq as soon as hypersensitivity reaction is suspected. Regardless of HLA-B*5701 status, permanently discontinue Triumeq if hypersensitivity cannot be ruled out, even when other diagnoses are possible
- Following a hypersensitivity reaction to Triumeq, NEVER restart Triumeq or any other abacavir-containing product

Lactic Acidosis and Severe Hepatomegaly with Steatosis:
- Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues

Exacerbations of Hepatitis B:
- Severe acute exacerbations of HBV have been reported in patients who are co-infected with HBV and HIV-1 and have discontinued lamivudine, a component of Triumeq. Monitor hepatic function closely in these patients and, if appropriate, initiate anti-hepatitis B treatment

CONTRAINDICATIONS
Triumeq is contraindicated in patients:
- who have the HLA-B*5701 allele
- with prior hypersensitivity reaction to abacavir, dolutegravir, or lamivudine
- receiving dofetilide (antiarrhythmic)
• with moderate or severe hepatic impairment

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions to Dolutegravir:
• Hypersensitivity reactions have been reported and were characterized by rash, constitutional findings, and sometimes organ dysfunction, including liver injury. The events were reported in <1% of subjects receiving TIVICAY® in Phase 3 clinical trials
• Clinically, it is not possible to determine whether a hypersensitivity reaction with Triumeq would be caused by abacavir or dolutegravir. Discontinue Triumeq and other suspect agents immediately if signs or symptoms of hypersensitivity reaction develop

Effects on Serum Liver Biochemistries in Patients with Hepatitis B or C Co-infection:
• Patients with underlying hepatitis B or C may be at increased risk for worsening or development of transaminase elevations with use of Triumeq. In some cases the elevations in transaminases were consistent with immune reconstitution syndrome or hepatitis B reactivation, particularly in the setting where anti-hepatitis therapy was withdrawn
• Appropriate laboratory testing prior to initiating therapy and monitoring for hepatotoxicity during therapy with Triumeq are recommended in patients with underlying hepatic disease such as hepatitis B or C

Use With Interferon- and Ribavirin-based Regimens: Hepatic decompensation, some fatal, has occurred in HIV-1/hepatitis C virus (HCV) co-infected patients receiving combination antiretroviral therapy and interferon alfa with or without ribavirin. Patients receiving interferon alfa with or without ribavirin and Triumeq should be closely monitored.

Immune Reconstitution Syndrome: including the occurrence of autoimmune disorders with variable time to onset, has been reported.

Fat Redistribution or accumulation has been observed in patients receiving antiretroviral therapy.

Myocardial Infarction (MI):
• An observational study showed an increase in MI with abacavir; a sponsor-conducted, pooled analysis did not show increased risk. In totality, the available data are inconclusive
• The underlying risk of coronary heart disease should be considered when prescribing antiretroviral therapies, including abacavir, and action taken to minimize all modifiable risk factors (eg, hypertension, hyperlipidemia, diabetes mellitus, smoking)

Use With Certain Antiretroviral Products: Triumeq should not be administered concomitantly with other products containing abacavir or lamivudine.

ADVERSE REACTIONS: The most commonly reported (≥2%) adverse reactions of at least moderate intensity in treatment-naïve adults receiving Triumeq were insomnia (3%), headache (2%), and fatigue (2%).
DRUG INTERACTIONS

- Co-administration of Triumeq with certain inducers of UGT1A and/or CYP3A may reduce plasma concentrations of dolutegravir. Consult the full Prescribing Information for Triumeq for more information.
- Administer Triumeq 2 hours before or 6 hours after taking polyvalent cation-containing antacids or laxatives, sucralfate, oral supplements containing iron or calcium, or buffered medications. Alternatively, Triumeq and supplements containing calcium or iron can be taken with food.

USE IN SPECIFIC POPULATIONS

- **Pregnancy Category C**: Triumeq should be used during pregnancy only if the potential benefit justifies the potential risk. An Antiretroviral Pregnancy Registry has been established.
- **Nursing Mothers**: Breastfeeding is not recommended due to the potential for HIV transmission and the potential for adverse reactions in nursing infants.
- **Patients with Impaired Renal Function**: Triumeq is not recommended in patients with creatinine clearance <50 mL/min.
- **Patients with Impaired Hepatic Function**: If a dose reduction of abacavir, a component of Triumeq, is required for patients with mild hepatic impairment, then the individual components should be used.


About Viiv Healthcare

Viiv Healthcare is a global specialist HIV company established in November 2009 by GlaxoSmithKline (LSE: GSK) and Pfizer (NYSE: PFE) dedicated to delivering advances in treatment and care for people living with HIV. Shionogi (TYO: 4507) joined in October 2012. The company’s aim is to take a deeper and broader interest in HIV/AIDS than any company has done before and take a new approach to deliver effective and new HIV medicines, as well as support communities affected by HIV. For more information on the company, its management, portfolio, pipeline, and commitment, please visit www.viivhealthcare.com

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C. Orell et al. Superior efficacy of dolutegravir/abacavir/lamivudine (DTG/ABC/3TC) fixed dose combination (FDC) compared with ritonavir (RTV) boosted atazanavir (ATV) plus tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) in treatment-naïve women with HIV-1 infection (ARIA Study). Presented at the International AIDS Conference (IAC), 18-22 July 2016, Durban, South Africa. Abstract #10215.


