SWITCHING TO DOLUTEGRAVIR/LAMIVUDINE IS CLINICALLY NON-INFERIOR TO CONTINUING DOLUTEGRAVIR-BASED TRIPLE DRUG ANTIRETROVIRAL THERAPY: 1 YEAR RESULTS OF THE DUALING PROSPECTIVE MATCHED REAL-WORLD COHORT STUDY

Vasylyev, Marta[1]; Wit, Ferdinand [2]; Jordans, Carlijn [1]; Soetekouw, Robert [3]; van Lelyveld, Steven [3]; Kootstra, Gert-Jan [4]; Delsing Corine [4]; Ammerlaan, Heidi [5]; van Kasteren, Marjo [6]; Brouwer, Elisabeth [6]; Leyten, Eliane [7]; Claassen, Mark [8]; Hassing, Robert-Jan8;den Hollander, Jan [9]; van den Berge, Marcel [10]; Roukens, Anna [11]; Bierman, Wouter [12]; Groeneveld, Paul [13]; Lowe, Selwyn [14]; van Welzen, Berend [15]; Richel, Olivier [16]; Nellen, Jeannine [17]; van den Berk, Guido [18]; van der Valk, Marc [2]; Rijnders, Bart [1]; Rokx,Casper [1]

[1] Erasmus MC Universitair Medisch Centrum, Internal Medicine, Rotterdam, Netherlands ; [2] SHM, HIV Monitoring Foundation, Amsterdam, Netherlands; [3] Spaarne Gasthuis, Internal Medicine, Haarlem, Netherlands; [4]Medisch Spectrum Twente, Internal Medicine, Enschede, Netherlands; [5]Catharina Ziekenhuis Endhoven, Internal Medicine, Eindhoven, Netherlands; [6]Elisabeth Tweesteden Ziekenhuis, Internal Medicine, Tilburg, Netherlands; [7]Haaglanden Medisch Centrum, Internal Medicine, The Hague, Netherlands; [8]Rijnstate Ziekenhuis, Internal Medicine, Arnhem, Netherlands; [9]Maasstadziekenhuis, Internal Medicine, Rotterdam, Netherlands; [10]Admiraal de Ruyter Ziekenhuis, Internal Medicine, Vlissingen, Netherlands; [11] Leiden Universitair Medisch Centrum, Internal Medicine, Leiden, Netherlands; [12] Universitair Medisch Centrum Groningen, Internal Medicine, Groningen, Netherlands; [13] Isala Ziekenhuis, Internal Medicine, Zwolle, Netherlands; [14] Maastricht Universitair Medisch Centrum, Internal Medicine, Maastricht, Netherlands; [15] Universitair Medisch Centrum Utrecht, Internal Medicine, Utrecht, Netherlands; [16] Radboud Universitair Medisch Centrum, Internal Medicine, Nijmegen, Netherlands ;[17] Amsterdam Universitair Medisch Centrum, Internal Medicine, Amsterdam, Netherlands ; [18] Onze Lieve Vrouwe Gasthuis, Internal Medicine, Amsterdam, Netherlands;
on behalf of the ATHENA observational HIV cohort study

BACKGROUND

- Dolutegravir/lamivudine (DTG/3TC) is a recommended treatment option for treatment-naïve and experienced people with HIV (PWH).
- Real-world clinical efficacy data in PWH switching to DTG/3TC compared to well-matched controls continuing triple drug DTG-based regimens is scarce.

METHODS

- Prospective cohort study embedded within the Dutch ATHENA cohort
- Comparison treatment outcomes of switching from DTG-based triple antiretroviral therapy (ART) to DTG/3TC in well-suppressed PWH without prior virological failure (cases) with matched controls continuing DTG-based triple ART.
- Cases - selected from 9 HIV treatment centers that in 2019 had implemented a policy to actively recommend all eligible PWH to switch to DTG/3TC.
- Controls - recruited from the other 15 HIV treatment centers in the Netherlands.
- A formal sample size calculation, assuming a viral suppression rate of 95%, a control-to-intervention ratio of 2:1, and a non-inferiority margin δ = 0.05, resulted in a required sample size for the active arm of 390 cases in order to have 90% power to detect non-inferiority of the intervention arm.
- We matched the first 390 consecutive cases 1:2 to 780 controls by age, sex, HIV acquisition category, absent prior virological failure, pre-ART CD4 count (< or ≥ 200 cells/mm^3), and pre-ART viral load (< or ≥100.000 cps/mL).
- Follow-up for controls started at their clinic visit date closest to the start date of DTG/3TC of the matched case. The protocol-defined primary endpoint of the study was the 1-year virological outcome in the 'on-treatment' population with virological treatment failure being defined as
  - 2 consecutive viral loads >50 cps/mL, or
  - 1 viral load >50cps/mL directly followed by ART switch, death, or lost-to-follow-up.
- In the 'on treatment' analysis, individuals switching ART or becoming lost-to-follow-up while their viral load at the moment of switching was <50 cps/mL were censored.

Table 1

	Cases (n=390)	Controls (n=780)	P-value
Age, years	47.9 (37.4-56.9)	48.2 (38.0-56.8)	0.76
Male sex	88.2%	88.2%	0.99
HIV acquisition category			0.31
- Sexual transmission	93.0%	94.7%	
- Intravenous drug use	0.8%	0.3%	
- Other	1.3%	0.3%	
- Unknown	4.9%	4.7%	
NRTI backbone			
- 3TC	100%		
- ABC/3TC		76.9%	
- Tenofovir/FTC		23.1%	
CD4 prior to ART	330 (200-485)	310 (190-471)	0.14
Viral zenith, log10 cps/ml	4.9 (4.4-5.3)	4.8 (4.3-5.4)	0.99
Prior use of ART, years	4.9 (2.7-8.9)	7.5 (4.6-11.7)	<.001

RESULTS

- Between Nov 2014 and Dec 2020, 390 consecutive eligible individuals switched to DTG/3TC. The characteristics used for matching were well-balanced (Table 1).
- Ten (2.6%) cases and 18 (2.3%) controls became lost-to-follow-up while their last viral load was <50 cps/mL. Eighteen (4.6%) cases and 138 (17.7%) controls switched ART while their last viral load was <50 cps/mL. The remaining 362 cases and 624 controls constituted the 'on-treatment' population.
- Five (1.4%) cases and 6 (1.0%) controls experienced treatment failure (Fisher's exact test, p=0.54).
- One case and 2 controls experienced treatment failure because they switched ART while their last measured viral load was between 50-200 cps/mL.
- Four cases and 4 controls had treatment failure because of 2 consecutive viral loads >50 cps/mL. Of these 8 individuals, 2 controls had peak viremia >200 cps/mL (440 and 1120 cps/mL).
- Two in each group re-suppressed to <50 cps/mL without ART switch, and two in each group continued having low-level viremia without ART switch.
- The treatment failure risk difference for cases compared to controls was +0.42% (95%CI -1.01 to +1.85%), which is well within the non-inferiority limit of +5%.

Figure 1

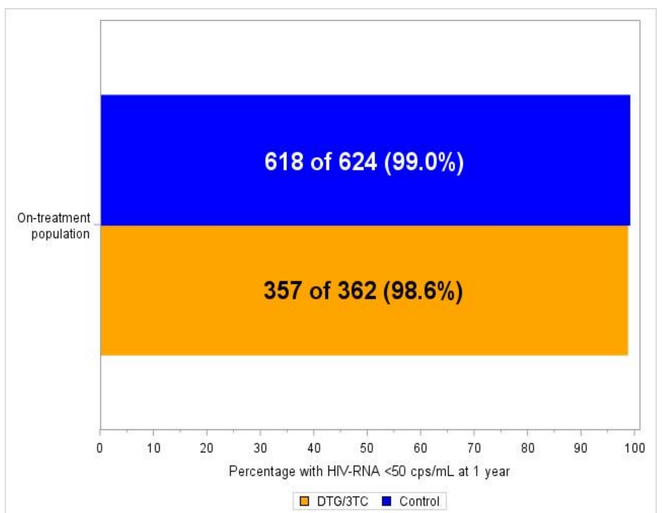
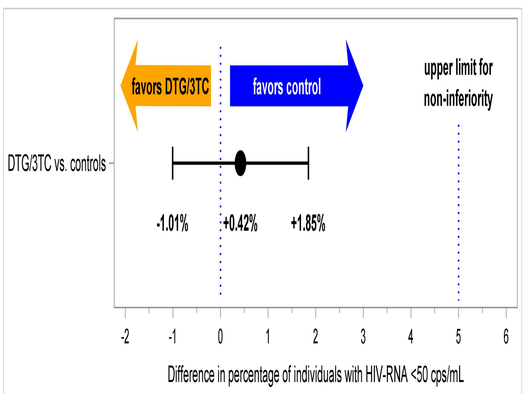


Figure 2



A sensitivity analysis, ignoring all ART switches with a last viral load <50 cps/mL in the control group only, showed virological treatment failure in 8 of 762 (1.05%) controls.

CONCLUSIONS

In a real-world setting, switching well-suppressed PWH from DTG-based ART to DTG/3TC was highly efficacious and non-inferior after 1 year compared to matched controls who continued DTG-based triple ART.

Funding: ViiV Healthcare

Contact
m.vasylyev@erasmusmc.nl c.rokx@erasmusmc.nl