Klinikum rechts der Isar
Technische Universität München

ADEQUATE PLASMA LEVELS OF DOLUTEGRAVIR IN COMBINATION WITH RITONAVIR-BOOSTED DARUNAVIR: A PHARMACOKINETIC SUBGROUP-ANALYSIS OF THE DUALIS STUDY

S Weidlich[1], C Boesecke[2], J Schneider1, H F Klinker[3], A Zink[4], A Balogh[5], E Wolf[5], H Bidner[6], and C D Spinner[1] * on behalf of the DUALIS study team

1 Technical University of Munich, School of Medicine, University Hospital rechts der Isar, Department of Medicine II, Munich, Germany 2 Bonn University Hospital, Department of Medicine I, Venusberg-Campus, Bonn, Germany 3 University of Wuerzburg Medical Center, Department of Medicine II, Division of Infectious Diseases, Wuerzburg, Germany 4 Technical University of Munich, School of Medicine, University Hospital rechts der Isar, Department of Dermatology and Allergy, Munich, Germany 5 MUC Research, Clinical Research Organisation, Munich, Germany 6 Technical University of Munich, School of Medicine, University Hospital rechts der Isar, Munich Study Center, Clinical Research Organization, Munich, Germany

PEB0242

Background

A combination of dolutegravir (DTG) and ritonavir-boosted darunavir (DRV/r) demonstrated non-inferiority as switch-option in virologically suppressed people-living-with-HIV (PLWH).

Methods

We present a prespecified pharmacokinetic sub-analysis of a pharmacokinetic sub-study of the prospective, randomized, non-blinded DUALIS-study (Eudra-CT:2015-000360-34). Virologically suppressed PLWH were randomized and either remaining on DRV/r in combination with 2 NRTIs (3DR) or being switched to DTG 50 mg and DRV/r 800/100 mg once-daily (2DR). Samples for PK-analysis in the interventional 2DR arm were obtained after 4, 12 and 24 weeks at a single time-point. Plasma-levels were determined using high-performance-liquid-chromatography (HPLC).

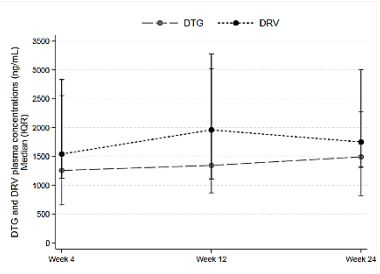

Figure 1. Median plasma concentrations (IQR) for dolutegravir (DTG) and darunavir (DRV) after week 4, 12 and 24.

Results

A total of 57 subjects (50 male, 7 female) with a median (IQR) age of 45 (37-51) years and a body-mass-index of 24.3 (22.6-26.2) were included in the sub-study. HIV RNA was <50 cps/mL in 98.1%, 96.3% and 96.3% at week 4, 12 and 24 respectively. Full treatment compliance was reported for DRV in 75.4%, 87.5% and 89.3% and DTG in 78.9%, 87.5% and 89.3% at week 4, 12 and 24, respectively. The median (IQR, interquartile range) differences between last intake of the study medication and sampling at weeks 4, 12 and 24 were 20.6 (8.1-24.0), 18.3 (5.8-23.5) and 18.3 (8.9-23.0) hours, respectively. Median (IQR) levels at weeks 4, 12 and 24 were 1543 (1123-2832) ng/mL, 1961 (1111-3279) ng/mL and 1751 (1314-3008) ng/mL for DRV and 1258 (662-2556) ng/mL, 1345 (870-3021) ng/mL and 1494 (816-2274) ng/mL for DTG (Figure 1). Plasma concentrations were 0-82 -fold (week 4), 3-79 -fold (week 12) and 4-98 -fold (week 24) above the protein-adjusted IC_{90} (64 ng/mL) for DTG and 0-45 -fold (week 4), 2-33 -fold (week 12) and 1-42 -fold (week 24) above the protein-adjusted EC_{90} (200 ng/mL) for DRV, respectively.

Table 1. Adherence and pharmacokinetic data

N=57	week 4	week 12	week 24
adherence to DTG by pill count (%)	78.9	87.5	89.3
adherence to DRV by pill count (%)	75.4	87.5	89.3
median (IQR) time difference between last intake of DTG/DRV (ng/mL)	20.6 (8.1-24.0)	18.3 (5.8-23.5)	18.3 (8.9-23.0)
median (IQR) plasma levels DTG (ng/mL)	1258 (662-2556)	1345 (870-3021)	1494 (816-2274)
median (IQR) plasma levels DRV (ng/mL)	1543 (1123-2832)	1961 (1111-3279)	1751 (1314-3008)

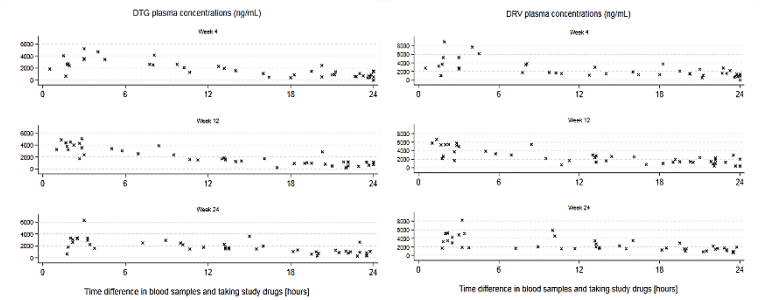

Figure 2. Distribution of plasma levels of DTG (left side) and DRV (right side) in hours after last reported intake at week 4, 12 and 24, each cross representing one subject.

Conclusions

The presented pharmacologic data support the suitability for the 2DR combination DTG plus DRV/r.

Acknowledgments

We thank all study sites and participants of the DUALIS STUDY as well as Münchner Studienzentrum (CRO) and MUC Research (CRO) for supporting this study.

This poster has been presented at 23rd International AIDS Conference from 6-0 July 2020 held as virtual).

Financial support for the conduct of the DUALIS study was provided by Janssen-Cilag & ViiV Healthcare.

The full manuscript has been accepted for publication in *J Antimicrob Chemother* and is available at: doi:10.1093/jac/dkaa234