KURZPROTOKOLL
WISARD

Öffentlicher Titel	Dolutegravir und Rilpivirine bei HIV-1 und K103N Mutation
Wissenschaftl. Titel	The effect of switching to Dolutegravir and Rilpivirine combination therapy in patients with HIV-1 and the K103N mutation
Kurztitel	WISARD
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, offen/unverblindet, Pharma-Studie, zweiarmig
Studienphase	Phase III/IV
Erkrankung	Infektionen: Virusinfektionen: HIV
Einschlusskriterien	- Is male or female aged 18 years or over - Has documented HIV-1 infection - Is capable of giving informed consent - Is willing to comply with the protocol requirements - Virologically suppressed (plasma HIV-RNA <50 copies/mL) and on a stable regimen for >24 weeks - Subjects are required to have a history of the K103N mutation (acquired or selected). Subjects who at any time have had the mutations 100I, 101E/P, 106A/M, 138K/G/Q, 181C/I/V, 188L, 190A/S/E/Q, 230L mutations are to be excluded. Other NNRTI region variants can be included. All PI and NRTI mutations are acceptable. Study sites may ask the coordinating centre for advice as required - Subjects must have never failed INSTI (2 x VL >200 >2 weeks apart) but current regimen can include INSTI - A female, may be eligible to enter and participate in the study if she: is of non-child-bearing potential defined as post-menopausal (12 months of spontaneous amenorrhea without an alternative medical cause and >= 45 years of age); A high follicle stimulating hormone (FSH) level consistent with postmenopausal status may be used to confirm a post- menopausal state in women who are not using hormonal contraception) or hormonal replacement therapy at the discretion of the PI. However, in the absence of 12 months of amenorrhea, a single FSH measurement alone is insufficient OR is physically incapable of becoming pregnant with documented tubal ligation, hysterectomy or bilateral oophorectomy OR is of child-bearing potential with a negative pregnancy test at Screening (& baseline visit) and agrees to use one of the following methods of contraception to avoid pregnancy: True abstinence from penile-vaginal intercourse from 2 weeks prior to administration of IP, throughout the study, and for at least 2 weeks after discontinuation of all study medications (When this is in line with the preferred and usual lifestyle of the subject) (Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods), and withdrawal are not acceptable methods of contraception]; Any intrauterine device (IUD) with published data showing that the expected failure rate is <1% per year (not all IUDs meet this criterion, see Appendix 3 for an example listing of approved IUDs); Male partner sterilisation confirmed prior to the female subject's entry into the study, and this male is the sole partner for that subject; Approved hormonal contraception (see appendix 4 for a listing of examples of approved hormonal contraception); Any other method with published data showing that the expected failure rate is <1% per year; Any contraceptive method must be used consistently and for at least 2 weeks after discontinuation of IP - If a heterosexually active male, he is using effective birth control methods and is willing to continue practising these birth control methods during the trial and until follow-up visit - Subjects currently receiving DTG or RPV, but not both, can be included
Ausschlusskriterien	- Infected with HIV-2 - Detectable HIV-1 RNA at screening (HIV-1 RNA measurement >=50 c/mL)

- Subjects requiring regular dosing doing with H2 or PPI antacid medications or a history of achlorhidria or drug known to interact with RPV or DTG
- Use of medications that are associated with Torsades de Pointes
- Corrected QT interval (QTc [Bazett]) >450 milliseconds or QTc (Bazett) >480 milliseconds for participants with bundle branch block. The QTc is the QT interval corrected for heart rate according to Bazett's formula (QTcB)
- Unstable health conditions (i.e. opportunistic infections, cancers, unstable liver disease etc)
- Any evidence of an active Centres for Disease Control and Prevention Category C disease. Exceptions include cutaneous Kaposi's sarcoma not requiring systemic therapy and historic CD4+ lymphocyte counts of <200 cells/millimeter^3
- History or presence of allergy to the study drugs or their components or drugs of their class
- Ongoing malignancy other than cutaneous Kaposi's sarcoma, basal cell carcinoma, or resected, non- invasive cutaneous squamous cell carcinoma, or cervical intraepithelial neoplasia; other localised malignancies require agreement between the investigator and the Study medical monitor for inclusion of the subject prior to randomisation
- Any pre-existing physical or mental condition which, in the opinion of the Investigator, may interfere with the subject's ability to comply with the dosing schedule and/or protocol evaluations or which may compromise the safety of the participants. Subjects considered to pose a significant risk of suicide should be excluded
- Any condition which, in the opinion of the Investigator, may interfere with the absorption, distribution, metabolism or excretion of the study drugs or render the subject unable to take oral medication
- Using any concomitant therapy disallowed as per the reference safety information and product labelling for the study drugs. Specifically, co-administration with the following medicinal products is not allowed: dofetilide or pilsicainide; fampridine (also known as dalfampridine); carbamazepine, oxcarbazepine, phenobarbital, phenytoin; rifampicin, rifapentine; proton pump inhibitors, such as omeprazole, esomeprazole, lansoprazole, pantoprazole, rabeprazole; systemic dexamethasone, except as a single dose treatment; St John's wort (Hypericum perforatum)
- Has acute viral hepatitis including, but not limited to, A, B, or C
- Active hepatitis B/ Hep B non-immune subjects who have failed vaccination (antibody concentration < 10 international units). (If local practice does not include vaccination of low risk patients, then the patients without HBsAb are not excluded – this must be clearly documented in the medical records and eCRF). Note: subjects can be re screened if they receive vaccination and subsequently meet eligibility criteria
- Evidence of Hepatitis B virus (HBV) infection based on the results of testing at Screening for Hepatitis B surface antigen (HBsAg), Hepatitis B core antibody (anti-HBc), and Hepatitis B surface antibody (HBsAb) as follows: Participants positive for HBsAg are excluded; Participants positive for anti-HBc (negative HBsAg status) and negative for HBsAb are excluded (if local practice does not include vaccination of low risk patients, then the patients without HBsAb are not excluded – this must be clearly documented in the medical records and eCRF). Note: Subject positive for anti-HBc (negative HBsAg status) and positive for HBsAb are immune to HBV and are not excluded
- Participants with an anticipated need for any Hepatitis C virus (HCV) therapy during the Early Switch Phase and for interferon-based therapy for HCV throughout the entire study period
- Any investigational drug within 30 days prior to the trial drug administration

	- Any evidence of viral resistance different to the one described in the inclusion criteria i.e. not meeting inclusion criteria or having different mutation at K103 - Dialysis or renal insufficiency (creatinine clearance < 50ml/min) - History of decompensated liver disease (Alanine aminotransferase (ALT) >= 5 times the upper limit of normal (ULN), OR ALT >= 3xULN and bilirubin >= 1.5xULN (with >35% direct bilirubin) - Unstable liver disease (as defined by the presence of ascites, encephalopathy, coagulopathy, hypoalbuminemia, esophageal or gastric varices, or persistent jaundice), cirrhosis, known biliary abnormalities (with the exception of Gilbert's syndrome or asymptomatic gallstones) - Subjects with severe hepatic impairment (Class C) as determined by Child-Pugh classification (see appendix 4) - Opportunistic infection within 4 weeks prior to first dose of DTG plus RPV - Clinical decision that a switch of antiretroviral therapy should be immediate
Alter	18 Jahre und älter
Prüfzentren	**Innere Medizin 2** (Rekrutierung beendet) Infektiologie Theodor-Stern-Kai 7 60590 Frankfurt am Main Prof. Dr. med. Christoph Stephan c.stephan@em.uni-frankfurt.de
Sponsor	European AIDS Treatment Network Infectious Disease Foundation (NEAT ID)
Registrierung in anderen Studienregistern	EudraCT 2017-004040-38