Otsingu protokoll

Kliiniline küsimus nr 3: Kas ravinaiivsetel HIV-positiivsetel isikutel on esimese rea ravis efektiivsem 2 NRTI+INSTIga või 2 NRTI+efavirenz?

Kuupäev (pp.kk.aasta)	20.10.2019
Otsingu läbiviija	Kairit Linnaste
Andmebaas (koos vahendaja nimega Nt MEDLINE (Ovid))	Pubmed
Otsistrateegia (päring)	((((((HIV Infections[MeSH] OR HIV[MeSH] OR hiv[tiab] OR hiv-1[tiab] OR hiv-2*[tiab] OR hiv1[tiab] OR hiv2[tiab] OR hiv infect*[tiab] OR human immunodeficiency virus[tiab] OR human immune deficiency virus[tiab] OR human immuno-deficiency virus[tiab] OR human immune-deficiency virus[tiab] OR ((human immun*) AND (deficiency virus[tiab])) OR acquired immunodeficiency syndromes[tiab] OR acquired immune deficiency syndrome[tiab] OR acquired immuno-deficiency syndrome[tiab] OR acquired immune-deficiency syndrome[tiab] OR ((acquired immun*) AND (deficiency syndrome[tiab])) OR "sexually transmitted diseases, viral"[mh]) OR HIV[tiab] OR HIV/AIDS[tiab] OR HIV-infected[tiab] OR HIV[title] OR HIV/AIDS[title] OR HIVinfected[title]))) NOT ("Treatment Failure"[Mesh] OR Salvage therapy[Title/Abstract] OR Treatment-experienced[Title/Abstract] OR Antiretroviral experienced[Title/Abstract] OR ART-experienced[Title/Abstract] OR Experienced patients[Title/Abstract] OR treatment switch*[Title/Abstract]))) AND ((((((("HIV Reverse Transcriptase"[Mesh] OR "Reverse Transcriptase Inhibitors"[Mesh] OR "abacavir" [Supplementary Concept] OR "Zidovudine"[Mesh] OR "Emtricitabine"[Mesh] OR "Lamivudine"[Mesh] OR zidovudine[Title/Abstract] OR azidothymidine[Title/Abstract] OR Retrovir[Title/Abstract] OR abacavir[Title/Abstract] OR Ziagen[Title/Abstract] OR a699012[Title/Abstract] OR emtricitabine[Title/Abstract] OR

	Emtriva[Title/Abstract] OR Coviracil[Title/Abstract] OR a604004[Title/Abstract] OR lamivudine[Title/Abstract] OR 3TC[Title/Abstract] OR Zeffix[Title/Abstract] OR Heptovir[Title/Abstract] OR a696011[Title/Abstract] OR Epivir[Title/Abstract]))) AND (("Integrase Inhibitors"[Mesh] OR "HIV Integrase Inhibitors"[Mesh] OR "Raltegravir Potassium"[Mesh] OR Isentress[Title/Abstract] OR MK-0518[Title/Abstract] OR a608004[Title/Abstract] OR Elvitegravir[Title/Abstract] OR GS-9137[Title/Abstract] OR Vitekta[Title/Abstract] OR "bictegravir" [Supplementary Concept] OR bictegravir[Title/Abstract] OR GS-9883[Title/Abstract]))) AND ((((("HIV Reverse Transcriptase"[Mesh] OR "Reverse Transcriptase Inhibitors"[Mesh] OR "abacavir" [Supplementary Concept] OR "Zidovudine"[Mesh] OR "Emtricitabine"[Mesh] OR "Lamivudine"[Mesh] OR zidovudine[Title/Abstract] OR azidothymidine[Title/Abstract] OR Retrovir[Title/Abstract] OR abacavir[Title/Abstract] OR Ziagen[Title/Abstract] OR a699012[Title/Abstract] OR emtricitabine[Title/Abstract] OR Emtriva[Title/Abstract] OR Coviracil[Title/Abstract] OR a604004[Title/Abstract] OR lamivudine[Title/Abstract] OR 3TC[Title/Abstract] OR Zeffix[Title/Abstract] OR Heptovir[Title/Abstract] OR a696011[Title/Abstract] OR Epivir[Title/Abstract]))) AND (("efavirenz" [Supplementary Concept] OR efavirenz[Title/Abstract] OR Efavir[Title/Abstract] OR Sustiva[Title/Abstract] OR Stocrin[Title/Abstract] OR Efcure[Title/Abstract] OR Efferven[Title/Abstract] OR Estiva[Title/Abstract] OR Evirenz[Title/Abstract] OR Viranz[Title/Abstract] OR a699004[Title/Abstract]))))

Tulemuste arv	56
Andmebaasi filtrid	Humans, English
Ajaline piirang (ilmumisaeg)	01.01.2014-20.10.2019
Muud piirangud	
Märkused	

Ravijuhendisse kaasatakse neile kriteeriumitele vastavad allikad:

- uuringud, mis käsitlevad täiskasvanuid
- uuringud mis võrdlevad:
  1. 2 NRTI + raltegravir (RAL) versus 2 NRTI + efavirens (EFV)
  2. 2 NRTI + elvitegravir (EVG) versus 2 NRTI + efavirens (EFV)
  3. 2 NRTI + bictegravir (BIC) versus 2 NRTI + efavirens (EFV)
- Randomiseeritud kontrollitud uuringud; metaanalüüsid, mis põhinevad randomiseeritud kontrollitud uuringutel

Välja jäetakse neile kriteeriumitele vastavad allikad:

- uuringud, mis käsitlevad rasedaid

Sirveotsinguga (*hand search*) leitud artikleid: 0

Välja jäetud allikaid peale pealkirja/sisukokkuvõttega tutvumist: 54

Täistekstide põhjal raportist välja jäetud allikad: 0

Autor(id): Kairit Linnaste

Küsimus: Kas ravinaiivsetel HIV-positiivsetel isikutel on esimese rea ravis efektiivsem 2 NRTI+INSTIga või 2 NRTI+efavirenz?

Tõendatuse astme hinnang							Uuritavate arv		Mõju		Tõendatuse aste	Olulisus
Uuringute arv	Uuringukavand	Nihke tõenäosus	Tõenduse ebakõla	Tõenduse kaudsus	Tõenduse ebatäpsus	Muud kaalutlused	NRTI+INSTI	2 NRTI+efavirenz	Suhteline (95% CI)	Absoluutne (95% CI)		
aeg CD4/CD8 normaliseerumiseni läbilõikepunktides (>0,4; >1; >1,5;>2,0) (time to CD4/CD8 normalization at cut-offs >0,4; >1; >1,5; >2,0)												
1 [1]	randomiseeritud uuringud	suur [a]	väike	väike	väike [b]	puudub	raltegravir (n=281) efavirenz (n=282). Kahte rühma võrreldes ei esinenud statistiliselt olulist erinevust (P>0.05 by log-rank test) time to CD4/CD8 normalization at cut-offs of >1, >1.5 and >2.0. Statistiliselt oluline erinevus (P>0.048) time to CD4/CD8 normalization at cut-off >0.4 (5 a periood), raltegravir kasuks. 240.ndaks nädalaks, 5% patsientidest püsisid CD4/CD8 väärtused alla 0.4 ning rühmade vahel ei olnud statistiliselt olulist erinevust. (CD4/CD8 ratio at cut-off .0.4) - Oluliselt kiiremini normaliseerusid CD4/ CD8 väärtused raltegravir vs efavirenz rühmas (HR=1.23; 95% CI=1.03–1.46; P=0.02). Sama tulemust ei saadud CD4/CD8 ratio cut-offs >1, >1.5 ja >2.0 puhul. [c]		⊕⊕⊕◯ KESKMINE	
levels of soluble CD14 (sCD14) and soluble CD163 (sCD163), markers ofmonocyte activation; levels of soluble tumor necrosis factor α receptor I (sTNF-RI), interleukin 6 (IL-6), and high sensitivityC-reactive protein (hsCRP),markers of systemic inflammation; and the level of lipoprotein-associated phospholipase A2 (Lp-PLA2), a marker of vascular inflammation. (follow-up 48 months)												
1 [2]	randomiseeritud uuringud	väike	väike	väike	suur [d]	puudub	elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (EVG/c/FTC/TDF) vs efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/FTC/TDF). EVG/c/FTC/TDF vähendas rohkem sCD14, hsCRP, ja Lp-PLA2 väärtuseid vs EFV/FTC/TDF. [e,f]		⊕⊕⊕◯ KESKMINE	

CI: usaldusintervall

Selgitused

a. The studies included in this report were sponsored and funded by Merck, which manufactures raltegravir under the brand name ISENTRESSw. All randomized and treated patients in STARTMRK were included in thisexploratory post hoc analysis.

b. raltegravir (n=281) efavirenz (n=282)

c. Raltegravir was associated with higher rates of CD4/CD8 ratio normalization at the .0.4 cut-off (median time to normalization¼56 versus 84 days; P¼0.048 by log-rank test). A Cox proportional hazard model stratified based on baseline CD4 counts showed an association between raltegravir and higher rates of CD4/CD8 ratio normalization (HR¼1.23; P¼0.02).

d. n=100, n=100 mõlemas rühmas

e. From a random sample achieving an HIV type 1 RNA load of <50 copies/mL by week 48, changes over 24 and 48 weeks in levels of biomarkers of monocyte activation (soluble CD14 [sCD14] and soluble CD163 [sCD163]), systemic inflammation (soluble tumor necrosis factor α receptor I [sTNF-RI], interleukin 6 [IL-6], and high-sensitivity C-reactive protein [hsCRP]), and vascular inflammation (lipoprotein-associated phospholipase A2 [Lp-PLA2]) were compared.

f. tabel 2, lk 349

Viited

1. Serrano-Villar S, Zhou Y, Rodgers AJ, Moreno S. Different impact of raltegravir versus efavirenz on CD4/CD8 ratio recovery in HIV-infected patients. J Antimicrob Chemother 2017; 72: 235-239.

2. Hileman CO, Kinley B, Scharen-Guivel V, Melbourne K, Szwarcberg J, Robinson J, Lederman MM,Mccomsey GA. Differential Reduction in Monocyte Activation and Vascular Inflammation With Integrase Inhibitor-Based Initial Antiretroviral Therapy Among HIV-Infected Individuals. J Infect Dis 2015; 212: 345-54.