

## Otsingu protokoll

**Kliiniline küsimus nr 4:** Kas HIV-positiivsetel isikutel, kes saavad INSTI-t sisaldavat ARV ravi, on lühi- ja pikaajalisi kõrvaltoimeid vähem võrreldes INSTI-t mitte sisaldavate raviskeemidega?

Kuupäev (pp.kk.aasta)	09.10.19
Otsingu läbiviija	Bruno Saar
Andmebaas (koos vahendaja nimega Nt MEDLINE (Ovid))	PubMed
Otsistrateegia (päring)	((("hiv infections"[MeSH Terms] OR "hiv"[MeSH Terms] OR hiv[tiab] OR hiv-1[tiab] OR (hiv 2[tiab] OR hiv 2,2[tiab] OR hiv 21[tiab] OR hiv 213[tiab] OR hiv 2287[tiab] OR hiv 25[tiab] OR hiv 27[tiab] OR hiv 273[tiab] OR hiv 27924a[tiab] OR hiv 2a[tiab] OR hiv 2ab[tiab] OR hiv 2ali[tiab] OR hiv 2alt[tiab] OR hiv 2b[tiab] OR hiv 2ben[tiab] OR hiv 2cam2[tiab] OR hiv 2cam4[tiab] OR hiv 2cbl23[tiab] OR hiv 2cbl24[tiab] OR hiv 2d194[tiab] OR hiv 2d205[tiab] OR hiv 2deltavpx[tiab] OR hiv 2eho[tiab] OR hiv 2env[tiab] OR hiv 2eu[tiab] OR hiv 2hom[tiab] OR hiv 2in[tiab] OR hiv 2infection[tiab] OR hiv 2isy[tiab] OR hiv 2kr[tiab] OR hiv 2mic97[tiab] OR hiv 2mir[tiab] OR hiv 2mjc97[tiab] OR hiv 2nep[tiab] OR hiv 2nihz[tiab] OR hiv 2pei2[tiab] OR hiv 2rod[tiab] OR hiv 2rod9[tiab] OR hiv 2s[tiab] OR hiv 2sbl[tiab] OR hiv 2sbl6669[tiab] OR hiv 2sew[tiab] OR hiv 2st[tiab] OR hiv 2uc1[tiab] OR hiv 2uc12[tiab] OR hiv 2uc14[tiab] OR hiv 2uc1mc[tiab] OR hiv 2uc2[tiab] OR hiv 2uc2mc[tiab] OR hiv 2uc3[tiab] OR hiv 2uc7[tiab]) OR hiv1[tiab] OR hiv2[tiab] OR (hiv infect[tiab] OR hiv infectability[tiab] OR hiv infectable[tiab] OR hiv infecte[tiab] OR hiv infected[tiab] OR hiv infecteds[tiab] OR hiv infectibility[tiab] OR hiv infectid[tiab] OR hiv infecting[tiab] OR hiv infection[tiab] OR hiv infection,[tiab] OR hiv infectioned[tiab] OR hiv infectioning[tiab] OR hiv infections[tiab] OR hiv infections,[tiab] OR hiv infectious[tiab] OR hiv infectiousness[tiab] OR hiv infective[tiab] OR hiv infectives[tiab] OR hiv infectivity[tiab] OR hiv infectors[tiab] OR

hiv infects[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 immune[All Fields] OR human immunoglobulin[All Fields] OR human immunoglobuline[All Fields] OR human immunoglobulinen[All Fields] OR human immunisation[All Fields] OR human immunity[All Fields] OR human immunization[All Fields] OR human immuno[All Fields] OR human immunoassay[All Fields] OR human immunoassays[All Fields] OR human immunobiology[All Fields] OR human immunocompetence[All Fields] OR human immunocontraception[All Fields] OR human immunocytes[All Fields] OR human immunodeficiencies[All Fields] OR human immunodeficiency[All Fields] OR human immunodeficient[All Fields] OR human immunogammaglobulin[All Fields] OR human immunogen[All Fields] OR human immunogenetics[All Fields] OR human immunogenicity[All Fields] OR human immunoglobin[All Fields] OR human immunoglobins[All Fields] OR human immunoglobulin[All Fields] OR human immunoglobuline[All Fields] OR human immunoglobulinen[All Fields] OR human immunoglobulines[All Fields] OR human immunoglobulins[All Fields] OR human immunoglogulins[All Fields] OR human immunohistochemical[All Fields] OR human immunohistochemistry[All Fields] OR human immunoinfertility[All Fields] OR human immunologic[All Fields] OR human immunological[All Fields] OR human immunology[All Fields] OR human immunome[All Fields] OR human immunomodulators[All Fields] OR human immunopathologies[All Fields] OR human immunopathology[All Fields] OR human immunophenotyping[All Fields] OR human immunoprophylaxis[All Fields] OR human immunoproteasome[All Fields] OR human immunoregulation[All Fields] OR human immunorepertoires[All Fields] OR human

immunornase[All Fields] OR human  
 immunosenescence[All Fields] OR human  
 immunosuppression[All Fields] OR human  
 immunosystem[All Fields] OR human  
 immunotherapeutics[All Fields] OR human  
 immunotherapy[All Fields] OR human  
 immunotoxicity[All Fields] OR human  
 immunotoxicological[All Fields] OR human  
 immunotoxicology[All Fields] OR human  
 immunotoxin[All Fields] OR human  
 immunovirology[All Fields] OR human  
 immuntoxischer[All Fields]) AND deficiency  
 virus[tiab]) OR acquired immunodeficiency  
 syndromes[tiab] OR acquired immune deficiency  
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 syndrome[tiab] OR acquired immune-deficiency  
 syndrome[tiab] OR ((acquired immune[All  
 Fields] OR acquired immunities[All Fields] OR  
 acquired immunity[All Fields] OR acquired  
 immunodeficiencies[All Fields] OR acquired  
 immunodeficiencies[All Fields] OR acquired  
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 immunogenicity[All Fields] OR acquired  
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 immunoglobulins[All Fields] OR acquired  
 immunoreactivity[All Fields] OR acquired  
 immunosuppression[All Fields] OR acquired  
 immunotoxicity[All Fields]) 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]) 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  
 emtricitabine[Title/Abstract] OR  
 Emtriva[Title/Abstract] OR  
 Coviracil[Title/Abstract] OR

lamivudine[Title/Abstract] OR  
 3TC[Title/Abstract] OR Zeffix[Title/Abstract]  
 OR Heptovir[Title/Abstract] OR  
 Epivir[Title/Abstract]) AND ("Integrase  
 Inhibitors"[Mesh] OR "HIV Integrase  
 Inhibitors"[Mesh] OR "Cobicistat"[Mesh] OR  
 "dolutegravir"[Supplementary Concept] OR  
 "Raltegravir Potassium"[Mesh] OR  
 cobicistat[Title/Abstract] OR GS-  
 9350[Title/Abstract] OR Tybost[Title/Abstract]  
 OR dolutegravir[Title/Abstract] OR  
 Tivicay[Title/Abstract] OR  
 S?GSK1349572[Title/Abstract] OR  
 GSK1349572[Title/Abstract] OR  
 Elvitegravir[Title/Abstract] OR GS-  
 9137[Title/Abstract] OR Vitekta[Title/Abstract]  
 OR raltegravir[Title/Abstract] OR  
 Isentress[Title/Abstract] OR MK-  
 0518[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  
 emtricitabine[Title/Abstract] OR  
 Emtriva[Title/Abstract] OR  
 Coviracil[Title/Abstract] OR  
 lamivudine[Title/Abstract] OR  
 3TC[Title/Abstract] OR Zeffix[Title/Abstract]  
 OR Heptovir[Title/Abstract] OR  
 Epivir[Title/Abstract]) AND  
 ("efavirenz"[Supplementary Concept] OR  
 efavirenz[Title/Abstract] OR  
 Sustiva[Title/Abstract] OR  
 Stocrin[Title/Abstract] OR  
 Estiva[Title/Abstract])) AND (Randomized  
 Controlled Trial[PT] OR "randomized controlled  
 trials as topic"[MeSH Terms] OR (randomized  
 controlled trial[tiab] OR randomized controlled  
 trial,[tiab] OR randomized controlled trials[tiab]  
 OR randomized controlled trials,[tiab]) OR  
 (randomized control trial[tiab] OR randomized  
 control trial,[tiab] OR randomized control

trials[tiab]) OR (Clinical Trial[PT] AND ("random allocation"[MeSH Terms] OR (random[tiab] OR random'[tiab] OR random1[tiab] OR randomly[tiab] OR randomaized[tiab] OR randomly[tiab] OR randomaly[tiab] OR randomamplified[tiab] OR randoman[tiab] OR randomand[tiab] OR randomate[tiab] OR randombalance[tiab] OR randombased[tiab] OR randomboost[tiab] OR randombred[tiab] OR randombreeds[tiab] OR randomcoil[tiab] OR randomcommittee[tiab] OR randomcontrol[tiab] OR randomdata[tiab] OR randomdigit[tiab] OR randomdock[tiab] OR randomdot[tiab] OR randomdouble[tiab] OR randome[tiab] OR randomed[tiab] OR randomeffect[tiab] OR randomeffects[tiab] OR randomely[tiab] OR randomer[tiab] OR randomesque[tiab] OR randomezed[tiab] OR randomferns[tiab] OR randomforest[tiab] OR randomforest'[tiab] OR randomforest4life[tiab] OR randomforestclassifier[tiab] OR randomforests[tiab] OR randomforestsrc[tiab] OR randomforrest[tiab] OR randomfrog[tiab] OR randomglm[tiab] OR randomi[tiab] OR randomiazed[tiab] OR randomic[tiab] OR randomically[tiab] OR randomicaly[tiab] OR randomiced[tiab] OR randomicity[tiab] OR randomico[tiab] OR randomided[tiab] OR randomied[tiab] OR randomifzed[tiab] OR randomil[tiab] OR randomily[tiab] OR randomin[tiab] OR randomined[tiab] OR randomingly[tiab] OR randominization[tiab] OR randominzed[tiab] OR randomirrespective[tiab] OR randomis[tiab] OR randomisable[tiab] OR randomisaion[tiab] OR randomisation[tiab] OR randomisation'[tiab] OR randomisations[tiab] OR randomisationsecondary[tiab] OR randomisaton[tiab] OR randomisd[tiab] OR randomise[tiab] OR randomised[tiab] OR randomised'[tiab] OR randomisedbhc[tiab] OR randomisedclinical[tiab] OR randomisedcontrolled[tiab] OR randomisedrandomised[tiab] OR randomisee[tiab] OR randomisees[tiab] OR randomisely[tiab] OR randomisert[tiab] OR randomiserte[tiab] OR randomises[tiab] OR randomisiert[tiab] OR randomisierte[tiab] OR

randomisierten[tiab] OR randomisierter[tiab] OR  
randomisierung[tiab] OR randomising[tiab] OR  
randomized[tiab] OR randomisly[tiab] OR  
randomised[tiab] OR randomiz[tiab] OR  
randomizability[tiab] OR randomizable[tiab] OR  
randomizacao[tiab] OR randomizad[tiab] OR  
randomizadas[tiab] OR randomizadely[tiab] OR  
randomizado[tiab] OR randomizados[tiab] OR  
randomizaion[tiab] OR randomization[tiab] OR  
randomization'[tiab] OR randomization's[tiab]  
OR randomizationin[tiab] OR  
randomizations[tiab] OR randomizations'[tiab]  
OR randomizationstudies[tiab] OR  
randomizd[tiab] OR randomize[tiab] OR  
randomize'[tiab] OR randomized[tiab] OR  
randomized'[tiab] OR randomized1[tiab] OR  
randomized150[tiab] OR  
randomizedcontrolled[tiab] OR  
randomizedcontrolledclinicaltrialstif20[tiab] OR  
randomizedcontrolledtrial[tiab] OR  
randomizedcontrolledtrials[tiab] OR  
randomizedcontroltrials[tiab] OR  
randomizedcrossover[tiab] OR  
randomizedd[tiab] OR randomizeddouble[tiab]  
OR randomizedduring[tiab] OR  
randomizedinto[tiab] OR randomizedly[tiab] OR  
randomizedphase[tiab] OR  
randomizedrandomised[tiab] OR  
randomizedsequence[tiab] OR  
randomizedstudies[tiab] OR randomizedto[tiab]  
OR randomizedtrial[tiab] OR randomizely[tiab]  
OR randomizer[tiab] OR randomizer'[tiab] OR  
randomizers[tiab] OR randomizes[tiab] OR  
randomized[tiab] OR randomizing[tiab] OR  
randomizing'[tiab] OR randomizingly[tiab] OR  
randomizowanych[tiab] OR randomized[tiab]  
OR randomizzati[tiab] OR randomizzato[tiab]  
OR randomjungle[tiab] OR randoml[tiab] OR  
randomlike[tiab] OR randomlly[tiab] OR  
randomly[tiab] OR randomly'[tiab] OR  
randomly'assign[tiab] OR  
randomlyallocated[tiab] OR randomlyand[tiab]  
OR randomlyassigned[tiab] OR  
randomlychosen[tiab] OR randomlydivided[tiab]  
OR randomlyequally[tiab] OR  
randomlyinserted[tiab] OR randomlyn[tiab] OR  
randomlyselected[tiab] OR randomlysplit[tiab]

	<p>OR randomlyuniformly[tiab] OR  randonmess[tiab] OR randommethacrylic[tiab]  OR randommized[tiab] OR randommobility[tiab]  OR randomnes[tiab] OR randomness[tiab] OR  randomness'[tiab] OR randomnesses[tiab] OR  randomnicity[tiab] OR randomniized[tiab] OR  randomnized[tiab] OR randomnly[tiab] OR  randomomized[tiab] OR randomosed[tiab] OR  randomoutcross[tiab] OR randompairs[tiab] OR  randompattern[tiab] OR randompf[tiab] OR  randomphase[tiab] OR randompod[tiab] OR  randompolypeptides[tiab] OR randompower[tiab]  OR randomrecommendation[tiab] OR  randoms[tiab] OR randoms'[tiab] OR  randomsample[tiab] OR randomsamples[tiab]  OR randomsampling[tiab] OR randomsed[tiab]  OR randomselection[tiab] OR  randomsequences[tiab] OR randomsied[tiab] OR  randomsource[tiab] OR randomspot[tiab] OR  randomsurvivalforest[tiab] OR  randomsymmetric[tiab] OR randomtree[tiab] OR  randomvariables[tiab] OR randomwalk[tiab] OR  randomwalkrestartmh[tiab] OR  randomwalksat[tiab] OR randomy[tiab] OR  randomyl[tiab] OR randomyly[tiab] OR  randomzed[tiab] OR randomzied[tiab] OR  randomzing[tiab]) OR "double-blind  method"[MeSH Terms] OR (double blind[tiab]  OR double blindcrossover[tiab] OR double  blinde[tiab] OR double blinded[tiab] OR double  blindedly[tiab] OR double blindedness[tiab] OR  double blindfold[tiab] OR double  blindfolded[tiab] OR double blinding[tiab] OR  double blindly[tiab] OR double blindness[tiab]  OR double blinds[tiab] OR double  blindsight[tiab] OR double blindtrial[tiab]))))  AND (("2014/01/01"[PDAT] :  "2019/10/09"[PDAT]) AND "humans"[MeSH  Terms] AND English[lang])</p>
Tulemuste arv	27
Andmebaasi filtrid	Human, English
Ajaline piirang (ilmumisaeg)	01.01.2014–09.10.2019
Muud piirangud	Ilmunud enne 2015a

Märkused	
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Ravijuhendisse kaasatakse neile kriteeriumitele vastavad allikad:

- On uuritud NRTI + INSTI *versus* NRTI + efavirenz ravi korral esinevaid kõrvaltoimeid
- Uurib kõrvaltoimete profiili ravinaiivsetel patsientidel

Välja jäetakse neile kriteeriumitele vastavad allikad:

- Ei ole uuritud NRTI + INSTI *versus* NRTI + efavirenz ravi korral esinevaid kõrvaltoimeid
- Uurib kõrvaltoimete profiili ravikogenud patsientidel (pärast *switchi*)

Sirveotsinguga (*hand search*) leitud artikleid: 0

Välja jäetud allikaid peale pealkirja/sisukokkuvõttega tutvumist: 23

Täistekstide põhjal raportist välja jäetud allikad: 0



## Otsingu protokoll

**Kliiniline küsimus nr 4:** Kas HIV-positiivsetel isikutel, kes saavad INSTI-t sisaldavat ARV ravi, on lühi- ja pikaajalisi kõrvaltoimeid vähem võrreldes INSTI-t mitte sisaldavate raviskeemidega?

Kuupäev (pp.kk.aasta)	09.10.19
Otsingu läbiviija	Bruno Saar
Andmebaas (koos vahendaja nimega Nt MEDLINE (Ovid))	PubMed
Otsistrateegia (päring)	((("hiv infections"[MeSH Terms] OR "hiv"[MeSH Terms] OR hiv[tiab] OR hiv-1[tiab] OR (hiv 2[tiab] OR hiv 2,2[tiab] OR hiv 21[tiab] OR hiv 213[tiab] OR hiv 2287[tiab] OR hiv 25[tiab] OR hiv 27[tiab] OR hiv 273[tiab] OR hiv 27924a[tiab] OR hiv 2a[tiab] OR hiv 2ab[tiab] OR hiv 2ali[tiab] OR hiv 2alt[tiab] OR hiv 2b[tiab] OR hiv 2ben[tiab] OR hiv 2cam2[tiab] OR hiv 2cam4[tiab] OR hiv 2cbl23[tiab] OR hiv 2cbl24[tiab] OR hiv 2d194[tiab] OR hiv 2d205[tiab] OR hiv 2deltavpx[tiab] OR hiv 2eho[tiab] OR hiv 2env[tiab] OR hiv 2eu[tiab] OR hiv 2hom[tiab] OR hiv 2in[tiab] OR hiv 2infection[tiab] OR hiv 2isy[tiab] OR hiv 2kr[tiab] OR hiv 2mic97[tiab] OR hiv 2mir[tiab] OR hiv 2mjc97[tiab] OR hiv 2nep[tiab] OR hiv 2nihz[tiab] OR hiv 2pei2[tiab] OR hiv 2rod[tiab] OR hiv 2rod9[tiab] OR hiv 2s[tiab] OR hiv 2sbl[tiab] OR hiv 2sbl6669[tiab] OR hiv 2sew[tiab] OR hiv 2st[tiab] OR hiv 2uc1[tiab] OR hiv 2uc12[tiab] OR hiv 2uc14[tiab] OR hiv 2uc1mc[tiab] OR hiv 2uc2[tiab] OR hiv 2uc2mc[tiab] OR hiv 2uc3[tiab] OR hiv 2uc7[tiab]) OR hiv1[tiab] OR hiv2[tiab] OR (hiv infect[tiab] OR hiv infectability[tiab] OR hiv infectable[tiab] OR hiv infecte[tiab] OR hiv infected[tiab] OR hiv infecteds[tiab] OR hiv infectibility[tiab] OR hiv infectid[tiab] OR hiv infecting[tiab] OR hiv infection[tiab] OR hiv infection,[tiab] OR hiv infected[tiab] OR hiv infectioning[tiab] OR hiv infections[tiab] OR hiv infections,[tiab] OR hiv infectious[tiab] OR hiv infectiousness[tiab] OR hiv infective[tiab] OR hiv infectives[tiab] OR hiv infectivity[tiab] OR hiv infectors[tiab] OR hiv infects[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 immune[All Fields] OR  
human immunoglobulin[All Fields] OR human  
immunoglobuline[All Fields] OR human  
immunoglobulinen[All Fields] OR human  
immunisation[All Fields] OR human  
immunity[All Fields] OR human  
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immuno[All Fields] OR human immunoassay[All  
Fields] OR human immunoassays[All Fields] OR  
human immunobiology[All Fields] OR human  
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immunocontraception[All Fields] OR human  
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immunomodulators[All Fields] OR human  
immunopathologies[All Fields] OR human  
immunopathology[All Fields] OR human  
immunophenotyping[All Fields] OR human  
immunoprophylaxis[All Fields] OR human  
immunoproteasome[All Fields] OR human  
immunoregulation[All Fields] OR human  
immunorepertoires[All Fields] OR human  
immunornase[All Fields] OR human  
immunosenescence[All Fields] OR human

immunosuppression[All Fields] OR human immunosystem[All Fields] OR human immunotherapeutics[All Fields] OR human immunotherapy[All Fields] OR human immunotoxicity[All Fields] OR human immunotoxicological[All Fields] OR human immunotoxicology[All Fields] OR human immunotoxin[All Fields] OR human immunovirology[All Fields] OR human immuntoxischer[All Fields]) 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 immune[All Fields] OR acquired immunities[All Fields] OR acquired immunity[All Fields] OR acquired immunodeficiencies[All Fields] OR acquired immunodeficiencies[All Fields] OR acquired immunodeficiency[All Fields] OR acquired immunodeficient[All Fields] OR acquired immunodepression[All Fields] OR acquired immunogenicity[All Fields] OR acquired immunoglobulin[All Fields] OR acquired immunoglobulins[All Fields] OR acquired immunoreactivity[All Fields] OR acquired immunosuppression[All Fields] OR acquired immunotoxicity[All Fields]) 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]) 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 emtricitabine[Title/Abstract] OR Emtriva[Title/Abstract] OR Coviracil[Title/Abstract] OR lamivudine[Title/Abstract] OR 3TC[Title/Abstract] OR Zeffix[Title/Abstract]

OR Heptovir[Title/Abstract] OR  
 Epivir[Title/Abstract]) AND ("Integrase  
 Inhibitors"[Mesh] OR "HIV Integrase  
 Inhibitors"[Mesh] OR "Cobicistat"[Mesh] OR  
 "dolutegravir"[Supplementary Concept] OR  
 "Raltegravir Potassium"[Mesh] OR  
 cobicistat[Title/Abstract] OR GS-  
 9350[Title/Abstract] OR Tybost[Title/Abstract]  
 OR dolutegravir[Title/Abstract] OR  
 Tivicay[Title/Abstract] OR  
 S?GSK1349572[Title/Abstract] OR  
 GSK1349572[Title/Abstract] OR  
 Elvitegravir[Title/Abstract] OR GS-  
 9137[Title/Abstract] OR Vitekta[Title/Abstract]  
 OR raltegravir[Title/Abstract] OR  
 Isentress[Title/Abstract] OR MK-  
 0518[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  
 emtricitabine[Title/Abstract] OR  
 Emtriva[Title/Abstract] OR  
 Coviracil[Title/Abstract] OR  
 lamivudine[Title/Abstract] OR  
 3TC[Title/Abstract] OR Zeffix[Title/Abstract]  
 OR Heptovir[Title/Abstract] OR  
 Epivir[Title/Abstract]) AND ("Atazanavir  
 Sulfate"[Mesh] OR "Darunavir"[Mesh] OR  
 "Lopinavir"[Mesh] OR "Ritonavir"[Mesh] OR  
 "HIV Protease Inhibitors"[Mesh] OR  
 atazanavir[Title/Abstract] OR  
 Reyataz[Title/Abstract] OR BMS-  
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 OR atv1[Title/Abstract] OR atv10[Title/Abstract]  
 OR atv131[Title/Abstract] OR  
 atv300[Title/Abstract] OR atv399[Title/Abstract]  
 OR atv40[Title/Abstract] OR  
 atv400[Title/Abstract] OR atv80[Title/Abstract]  
 OR atva[Title/Abstract] OR  
 atvab1[Title/Abstract] OR atvab2[Title/Abstract]

OR atvab3[Title/Abstract] OR  
atvabs[Title/Abstract] OR atvac[Title/Abstract]  
OR atval1[Title/Abstract] OR  
atvam2[Title/Abstract] OR  
atvam3[Title/Abstract] OR  
atvam3p[Title/Abstract] OR  
atvamp[Title/Abstract] OR  
atvamp71[Title/Abstract] OR  
atvamp711[Title/Abstract] OR  
atvamp725[Title/Abstract] OR  
atvamp727[Title/Abstract] OR  
atvamp7c[Title/Abstract] OR  
atvan[Title/Abstract] OR atvar[Title/Abstract]  
OR atvarious[Title/Abstract] OR  
atvarp[Title/Abstract] OR  
atvarying[Title/Abstract] OR atvb[Title/Abstract]  
OR atvbaha[Title/Abstract] OR  
atvbp1[Title/Abstract] OR atvc[Title/Abstract]  
OR atvccn1[Title/Abstract] OR  
atvco2[Title/Abstract] OR atvcs[Title/Abstract]  
OR atvdac[Title/Abstract] OR  
atvdac1[Title/Abstract] OR  
atvdac2[Title/Abstract] OR  
atvdac3[Title/Abstract] OR  
atvdac4[Title/Abstract] OR  
atvdacs[Title/Abstract] OR atvde[Title/Abstract]  
OR atvdelta25r[Title/Abstract] OR  
atvdelta57r[Title/Abstract] OR  
atvdi[Title/Abstract] OR atve[Title/Abstract] OR  
atveaieade[Title/Abstract] OR  
atveg[Title/Abstract] OR atvel[Title/Abstract]  
OR atven[Title/Abstract] OR  
atveo2[Title/Abstract] OR atvery[Title/Abstract]  
OR atvex1[Title/Abstract] OR  
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Tulemuste arv	63
Andmebaasi filtrid	English, Human
Ajaline piirang (ilmumisaeg)	01.01.2014-09.10.2019
Muud piirangud	
Märkused	

Ravijuhendisse kaasatakse neile kriteeriumitele vastavad allikad:

- On uuritud NRTI + INSTI *versus* NRTI + PI ravi korral esinevaid kõrvaltoimeid
- Uurib kõrvaltoimete profiili ravinaiivsetel patsientidel

Välja jäetakse neile kriteeriumitele vastavad allikad:

- Ei ole uuritud NRTI + INSTI *versus* NRTI + PI ravi korral esinevaid kõrvaltoimeid
- Uurib kõrvaltoimete profiili ravikogenud patsientidel (pärast *switchi*)

Sirveotsinguga (*hand search*) leitud artikleid: 0

Välja jäetud allikaid peale pealkirja/sisukokkuvõttega tutvumist: 62

Täistekstide põhjal raportist välja jäetud allikad: (arv põhjuste kaupa)

Autor(id): Bruno Saar

Küsimus: Kas HIV-positiivsetel isikutel, kes saavad INSTI-t sisaldavat ARV ravi, on lühi- ja pikaajalisi kõrvaltoimeid vähem võrreldes INSTI-t mitte sisaldavate raviskeemidega?

Tõendatuse astme hinnang							Uuritavate arv		Mõju		Tõendatuse aste	Olulisus
Uuringute arv	Uuringukavand	Nihke tõenäosus	Tõenduse ebakõla	Tõenduse kaudsus	Tõenduse ebatäpsus	Muud kaalutlused	INSTI sisaldav ARV ravi	INSTI mitte sisaldavate raviskeemidega	Suhteline (95% CI)	Absoluutne (95% CI)		

Luu ainevahetuse muutused - CTx (type 1 collagen cross-linked C-telopeptide) DTG+ABC+3TC vs. EFV+FTC+TDF (järelkontroll: keskmine 144 nädalat)

1 <sup>1</sup>	randomiseeritud uuringud	suur <sup>a</sup>	väike	väike	väike	puudub	SINGLE uuringusse kaasati 833 HIV-positiivset, ravinaivset patsienti (mediaanvanus 35a), kes randomiseeriti DTG/ABC/3TC (n=414) ja EFV/FTC/TDF (n=419) rühma. 48., 96. ja 144. ravinädalal määrati patsientide verest CTx (type-1 collagen cross-linked C-telopeptide), mis on surrogaatmarkeriks luu resorptsiooni intensiivsusele. Võrreldes DTG sisaldava rühmaga oli EFV-sisaldavas rühmas CTx tõusnud oluliselt enam kõikidel uuritud ravinädalatel (EFV/FTC/TDF vs DTG/ABC/3TC, muutus algtasemest %): 68 vs. 33 (48. ravinädalal, p<0,001); 56 vs. 27 (96. ravinädalal, p<0,001); 39 vs. 25 (144. ravinädalal, p<0,002).	⊕⊕⊕⊙ KESKMIINE	KRIITILINE
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Kõrvaltoimetega seotud ravikatkestused (TAF+FTC+DTG vs. TDF+FTC+DTG vs. TDF+FTC+EFV) (järelkontroll: keskmine 48 nädalat)

1 <sup>2</sup>	randomiseeritud uuringud	suur <sup>b</sup>	väike	suur <sup>c</sup>	suur <sup>d</sup>	puudub	ADVANCE uuringus randomiseeriti ≥12a vanused HIV-ravinaivsed patsiendid (n=1053) Lõuna-Aafrika Vabariigis kolme gruppi: TAF/FTC/DTG (n=351), TDF/FTC/DTG (n=351), TDF/FTC/EFV (n=351). Kõrvaltoimetega seotud ravikatkestusi esines 48.ravinädalaks vastavalt 1, 0 ja 10 patsiendil.	⊕⊙⊙⊙ VÄGA MADAL	KRIITILINE
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Kõrvaltoimed (any grade) (DTG vs. ATV/r ja DTG vs. DRV/r ja DTG vs. LPV/r ja DTG vs. EFV ja DTG vs. RPV) (järelkontroll: keskmine 48 nädalat)

38 <sup>3e</sup>	randomiseeritud uuringud	väike <sup>f</sup>	väike <sup>g</sup>	väike	väike	puudub	2019.a avaldud võrgustik meta-analüüs (VMA) võrreldi DTG efektiivsust ja ohutust teiste ARV ravimitega (ATV/r, DRV/r, LPV/r, EFV, RPV, RAL, EVG/c, BIC) HIV-ravinaivsete täiskasvanud patsientide seas. Meta-analüüsi kaasati 38 RCT-d, eraldi ei ole välja toodud kõrvaltoimete analüüsi kaasatud uuringute hulka. DTG ja muude ARV ravimite vahel ei esinenud olulist erinevust kõikide kõrvaltoimete (mistahes raskusega) esinemissageduses, v.a DTG vs LPV/r, kus DTG seostati oluliselt vähemate kõrvaltoimetega. DTG vs. ATV/r OR 0,52 (95% CrI 0,24; 1,20) NRTI kohandatud mudel DTG vs. ATV/r OR 0,73 (95% CrI 0,41; 1,28) NRTI mittekohandatud mudel DTG vs. DRV/r OR 0,85 (95% CrI 0,40; 1,72) NRTI kohandatud mudel DTG vs. DRV/r OR 0,97 (95% CrI 0,48; 1,90) NRTI mittekohandatud mudel DTG vs. LPV/r OR 0,33 (95% CrI 0,14; 0,73) NRTI kohandatud mudel DTG vs. LPV/r OR 0,43 (95% CrI 0,21; 0,82) NRTI mittekohandatud mudel DTG vs. EFV OR 0,51 (95% CrI 0,24; 1,12) NRTI kohandatud mudel DTG vs. EFV OR 0,69 (95% CrI 0,39; 1,19) NRTI mittekohandatud mudel DTG vs. RPV OR 0,68 (95% CrI 0,25; 1,84) NRTI kohandatud mudel DTG vs. RPV OR 0,92 (95% CrI 0,40; 2,09) NRTI mittekohandatud mudel	⊕⊕⊕⊕ KÕRGE	KRIITILINE
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Tõendatuse astme hinnang							Uuritavate arv		Mõju		Tõendatuse aste	Olulisus
Uuringute arv	Uuringukavand	Nihke tõenäosus	Tõenduse ebakõla	Tõenduse kaudsus	Tõenduse ebatäpsus	Muud kaalutlused	INSTI sisaldav ARV ravi	INSTI mitte sisaldavate raviskeemidega	Suhteline (95% CI)	Absoluutne (95% CI)		

kõrvaltoimetega seotud ravikatkestused (DTG vs. ATV/r ja DTG vs. DRV/r ja DTG vs. LPV/r ja DTG vs. EFV ja DTG vs. RPV) (järelkontroll: keskmine 48 nädalat)

38 <sup>3e</sup>	randomiseeritud uuringud	väike <sup>f</sup>	väike <sup>g</sup>	väike	väike	puudub	2019.a avaldud võrgustik meta-analüüsis (VMA) võrreldi DTG efektiivsust ja ohutust teiste ARV ravimitega (ATV/r, DRV/r, LPV/r, EFV, RPV, RAL, EVG/c, BIC) HIV-ravinaivsete täiskasvanud patsientide seas. Meta-analüüsi kaasati 38 RCT-d, eraldi ei ole välja toodud kõrvaltoimete analüüsi kaasatud uuringute hulka. DTG ja muude ARV ravimite vahel ei esinenud olulist erinevust kõrvaltoimete tõttu ravi katkestamise sageduses, v.a DTG vs ATV/r, DTG vs LPV/r ja DTG vs EFV, kus dolutegraviini seostati harvemate kõrvaltoimetest tingitud ravikatkestustega. DTG vs. ATV/r OR 0,21 (95% CrI 0,04; 0,67) NRTI kohandatud mudel DTG vs. ATV/r OR 0,31 (95% CrI 0,09; 0,89) NRTI mittekohandatud mudel DTG vs. DRV/r OR 0,41 (95% CrI 0,10; 1,65) NRTI kohandatud mudel DTG vs. DRV/r OR 0,53 (95% CrI 0,14; 2,33) NRTI mittekohandatud mudel DTG vs. LPV/r OR 0,17 (95% CrI 0,04; 0,62) NRTI kohandatud mudel DTG vs. LPV/r OR 0,25 (95% CrI 0,07; 0,86) NRTI mittekohandatud mudel DTG vs. EFV OR 0,21 (95% CrI 0,05; 0,69) NRTI kohandatud mudel DTG vs. EFV OR 0,32 (95% CrI 0,11; 0,95) NRTI mittekohandatud mudel DTG vs. RPV OR 0,61 (95% CrI 0,11; 2,62) NRTI kohandatud mudel DTG vs. RPV OR 0,90 (95% CrI 0,21; 4,02) NRTI mittekohandatud mudel	⊕⊕⊕⊕ KÕRGE	KRIITILINE
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Kaalutõus (TDF+XTC+DTG vs. TDF+XTC+EFV400) (järelkontroll: keskmine 48 nädalat)

1 <sup>4</sup>	randomiseeritud uuringud	suur <sup>b</sup>	väike	suur <sup>h</sup>	väike	puudub	NAMSAL ANRS 12313 uuringusse kaasati Kamerunist 613 ≥18a HIV-positiivset, ravinaivset patsienti, kes randomiseeriti TDF+XTC+DTG (n=310) ja TDF+XTC+EFV400 (n=303) gruppi. 48. ravinädalaks oli DTG grupis kehakaal võrreldes ravi alustamisel mõõdetud kehakaaluga tõusnud keskmiselt (mediaan, kg) oluliselt rohkem kui EFV 400 grupis: DTG +5,0 (IQR +1,0; +8,0) vs EFV400 +3,0 (IQR 0,0; +7,0), p<0,001	⊕⊕○○ MADAL	KRIITILINE
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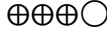
Luu ainevahetuse muutused - CTx (type 1 collagen cross-linked C-telopeptide) TDF+FTC+EVG/c vs. TDF+FTC+ATV/r (järelkontroll: keskmine 48 nädalat)

1 <sup>5</sup>	randomiseeritud uuringud	väike	väike	suur <sup>i</sup>	väike	puudub	WAVES on rahvusvaheline, topeltpimendatud RCT, milles randomiseeriti 575 HIV-positiivset ravinaivset naist kahte rühma: TDF+FTC+EVG/c (n= 289) ja TDF+FTC+ATV/r (n=286). Võrreldes EVG/c grupiga tõusis 48.ravinädalaks ATV/r grupis CTx võrreldes baasväärtusega enam. EVG/c vs. ATV/r, CTx (% mediaan): +15,4 (vahemik -2,9; +35,7) vs. +22,9 (vahemik +3,4; +39,3)	⊕⊕⊕○ KESKMINE	KRIITILINE
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Kõrvaltoimetega seotud ravikatkestused TDF+FTC+EVG/c vs. TDF+FTC+ATV/r (järelkontroll: keskmine 48 nädalat)

Tõendatuse astme hinnang							Uuritavate arv		Mõju		Tõendatuse aste	Olulisus
Uuringute arv	Uuringukavand	Nihke tõenäosus	Tõenduse ebakõla	Tõenduse kaudsus	Tõenduse ebatäpsus	Muud kaalutlused	INSTI sisaldav ARV ravi	INSTI mitte sisaldavate raviseemidega	Suhteline (95% CI)	Absoluutne (95% CI)		
1 <sup>5</sup>	randomiseeritud uuringud	väike	väike	suur <sup>i</sup>	väike	puudub	WAVES on rahvusvaheline, topeltpimendatud RCT, milles randomiseeriti 575 HIV-positiivset ravinaivset naist kahte rühma: TDF+FTC+EVG/c (n= 289) ja TDF+FTC+ATV/r (n=286). Võrreldes ATV/r grupiga oli 48.ravinädalaks kõrvaltoimetega seotud ravikatkestusi EVG/c grupis vähem. EVG/c vs. ATV/r, n(%): 5(2) vs. 19(7).		 KESKMINE		KRIITILINE	


Lüülsamba densitomeetriline luutihedus TDF+FTC+EVG/c vs. TDF+FTC+ATV/r (järelkontroll: keskmine 48 nädalat)

1 <sup>5</sup>	randomiseeritud uuringud	väike	väike	suur <sup>i</sup>	väike	puudub	WAVES on rahvusvaheline, topeltpimendatud RCT, milles randomiseeriti 575 HIV-positiivset ravinaivset naist kahte rühma: TDF+FTC+EVG/c (n= 289) ja TDF+FTC+ATV/r (n=286). Mõlemas grupis oli lüülsamba densitomeetriline luutihedus 48. ravinädalaks langenud, kuid gruppide vahel ei esinenud olulist erinevust. EVG/c vs. ATV/r, lüülsamba DXA % (vahemik): -3,23 (-5,13; -1,06) vs. -3,28% (-5,00; -1,14)		 KESKMINE		KRIITILINE
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Uus vertebraalne osteopeenia TAF+FTC+DTG vs. TDF+FTC+DTG vs. TDF+FTC+EFV (järelkontroll: keskmine 48 nädalat)

1 <sup>2</sup>	randomiseeritud uuringud	suur <sup>b</sup>	väike	suur <sup>c</sup>	väike	puudub	ADVANCE uuringus randomiseeriti ≥12a vanused HIV-ravinaivsed patsiendid (n=1053) Lõuna-Aafrika Vabariigis kolme gruppi: TAF/FTC/DTG (n=351), TDF/FTC/DTG (n=351), TDF/FTC/EFV (n=351). Gruppides mõõdeti 48. ravinädalal densitomeetriliselt vertebraalset luutihedust ning raporteeriti uued osteopeenia juhud. Uus vertebraalne osteopeenia - n/kogu n (%) TAF/FTC/DTG-grupp 37/203 (8) TDF/FTC/DTG-grupp 50/270 (23) TDF/FTC/EFV-grupp 45/202 (22)		 MADAL		KRIITILINE
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Kaalutõus TAF+FTC+DTG vs. TDF+FTC+DTG vs. TDF+FTC+EFV (järelkontroll: keskmine 48 nädalat)

1 <sup>2</sup>	randomiseeritud uuringud	suur <sup>b</sup>	väike	suur <sup>c</sup>	väga suur <sup>i</sup>	puudub	ADVANCE uuringus randomiseeriti ≥12a vanused HIV-ravinaivsed patsiendid (n=1053) Lõuna-Aafrika Vabariigis kolme gruppi: TAF/FTC/DTG (n=351), TDF/FTC/DTG (n=351), TDF/FTC/EFV (n=351). Kaalutõus 48. ravinädalal, võrreldes algse kehakaaluga: TAF/FTC/DTG, naised (n=158): +6,7kg TDF/FTC/DTG, naised (n=156): +3,4kg TDF/FTC/EFV, naised (n=137): +1,8kg TAF/FTC/DTG, mehed (n=109): +5,2kg TDF/FTC/DTG, mehed (n=156): +2,8kg TDF/FTC/EFV, mehed (n=137): +0,7kg		 VÄGA MADAL		KRIITILINE
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CI: usaldusintervall

## Selgitused

a. unblinded @ week 96

- b. open label
- c. Uuring läbi viidud Lõuna-Aafrika Vabariigis, > 99% uuritavatest ei olnud Euroopa rassist
- d. raporteeritud kõik kõrvaltoime juhud
- e. VMA kaasas kokku 38 RCT, aga pole raporteeritud, mitu katset oli kaasatud antud preparaatide võrdlusesse.
- f. autorid hinnanud uuringute kvaliteeti, enamus olid "strong" või "moderate" quality kvaliteedi hinnanguga
- g. uuringute heterogeensuse hinnang sisaldub üldise kvaliteedi hinnangus, mis oli "strong" või "moderate"
- h. uuritud Kameruni kohalikku populatsiooni
- i. Valimis ainult naissoost patsiendid
- j. Ei raporteeritud kaalu muutuse olemust (mediaan? aritmeetiline keskmine?) ega ka kaalu muutuse usaldusintervalle

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