Effectiveness of bictegravir compared with dolutegravir, raltegravir, and efavirenz as initial antiretroviral therapy

650

Isaac Núñez[1,2], Yanink Caro-Vega[2], Conor Macdonald[3], Juan Luis Mosqueda[4], **Alicia Piñeirúa-Menéndez[5]**, Anthony A. Matthews[3]

[1]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, [2]Universidad Nacional Autónoma de México, Mexico City, Mexico, [3]Karolinska Institutet, Stockholm, Sweden, [4]High Specialty Regional Hospital Bajio, León, Mexico, [5]Consorcio de Investigación en Salud (CISIDAT), Cuernavaca, Morelos, Mexico.

BACKGROUND

Bictegravir and dolutegravir based antiretroviral therapy are first-line HIV treatments. However, no trial has recruited enough participants to estimate the most effective treatment, and there is little evidence on the comparative effectiveness of bictegravir and other available antiretrovirals, like efavirenz and raltegravir.

METHODS

- We emulated a four-arm target trial to determine the effectiveness of bictegravir in reaching undetectable viral load (<50 copies/mm^3) by 3 and 12 months compared with dolutegravir, efavirenz, and raltegravir based-antiretroviral therapies.
- We first specified the protocol of a target trial and then we emulated it as closely as possible using national routinely collected data from Mexico.
- The eligibility criteria of the target trial were people with HIV that were treatment naïve with viral load >500 copies/mm^3, without tuberculosis, who were not pregnant, and started either bictegravir, dolutegravir, efavirenz or raltegravir-based antiretroviral therapy between July 2019 and September 2021. The same criteria were used in the target trial emulation, except individuals with tuberculosis were included according to a modified dose regime compatible with this diagnosis (e.g. double dose dolutegravir).
- The outcomes were the probability of undetectable viral load at 3 and 12 months, which was estimated using an adjusted logistic regression model, with assignment assumed to be random within levels of relevant baseline covariates (viral load, CD4 cell count [linear and quadratic], living in a prison, state within Mexico, year of initiation of antiretroviral, gender, and age [linear and quadratic]).
- A secondary analysis was performed for the outcome of viral load <1000 copies/mm^3. The estimated probabilities were compared via differences and non-parametric bootstrapping was used to calculate 95% confidence intervals.

Several sensitivity analyses (as inverse probability weighted analysis, including people labelled in the database as pregnant) were performed.

Bictegravir has comparable effectiveness to dolutegravir as initial antiretroviral therapy but is more effective than raltegravir and efavirenz.

RESULTS

20,285 individuals with HIV were eligible for the observational emulation of the target trial (Figure).

Single tablet regimes were started in 816 (55.5%) of people on dolutegravir (dolutegravir/abacavir/lamivudine) and in 1314 (97.1%) of people on efavirenz (efavirenz/emtricitabine/tenofovir disoproxil fumarate).

The majority were men, except in the raltegravir arm. The raltegravir arm had a higher proportion of individuals with baseline viral load <100,000 copies/mm^3 (76.1%) compared with those who received bictegravir (57.8%), dolutegravir (51.3%), and efavirenz (51.6%).

Median baseline CD4 cell count was higher in the raltegravir arm (242 cells/mm^3) compared with the bictegravir (221), dolutegravir (138), and efavirenz (170) arms.

Main results are shown in Table 1. Results of the sensitivity analyses and secondary analyses were very similar to those of the main analysis.

Figure 1. Flowchart of individuals eligible for an emulation of a target trial of initiation bictegravir vs dolutegravir vs efavirenz vs raltegravir in antiretroviral therapy naïve individuals with HIV.

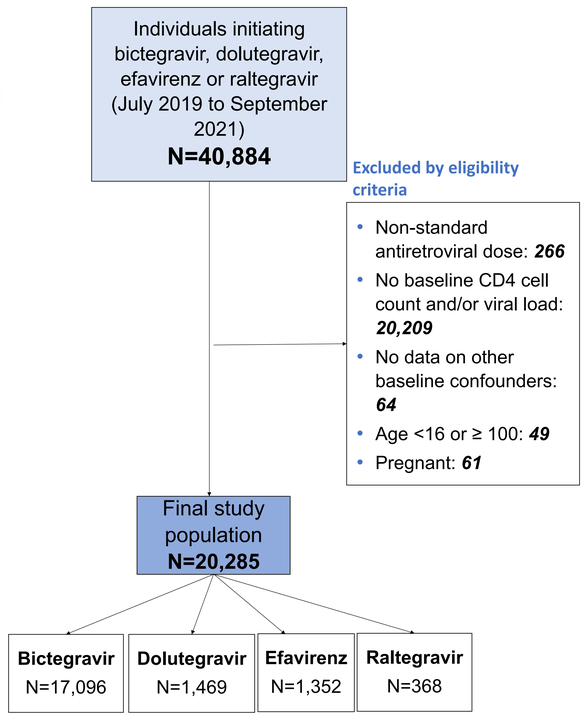


Table 1. Adjusted proportion and differences of undetectable viral load at 3 and 12 months after initiation of bictegravir, dolutegravir, efavirenz, or raltegravir.

	Adjusted proportion, % (95% CI)	Difference, % (95% CI)
Viral load <50 copies/mm^3 at 3 months		
Bictegravir	79.4 (78.6, 80.2)	ref
Dolutegravir	78.5 (76.2, 81.1)	-0.8 (-3.5, 1.9)
Efavirenz	63.9 (60.6, 67.7)	-15.5 (-19, -11.7)
Raltegravir	69.8 (63.8, 76.1)	-9.6 (-15.9, -3.3)
Viral load <50 copies/mm^3 at 12 months		
Bictegravir	87.7 (86.5, 88.9)	ref
Dolutegravir	85.9 (81.6, 89.3)	-1.9 (-6, 1.8)
Efavirenz	83.3 (78.9, 87.1)	-4.2 (-9, -0.2)
Raltegravir	80.3 (71.3, 88.5)	-7.6 (-16.5, 0.6)

CONCLUSIONS

Our results show that bictegravir achieves similar viral load suppression to dolutegravir by three and twelve months.

Additionally, we found that that bictegravir was superior to efavirenz and raltegravir as initial antiretroviral treatment in reaching viral load suppression at three months, which was less evident at twelve months.

Importantly, differences in reaching a non-transmissible viral load (<1000 copies/mm^3) were smaller than those of reaching undetectable viral load (<50 copies/mm^3) at three months and turned negligible at one year. Thus, while bictegravir and dolutegravir based antiretroviral therapies are still the preferred choice as the main first line treatment in treatment naïve individuals with HIV, efavirenz and raltegravir based antiretroviral therapies are still effective and can be used when no other drug is available.

Contact Information:
Isaac Núñez; isaac.nunezs@incmnsz.mx

Acknowledgements:
Isaac Núñez thanks Sergio Iván Valdés-Ferrer for general support and the Fundación para la Salud y la Educación Dr. Salvador Zubirán, A.C. for funding. The authors acknowledge CENSIDA staff and specially Dr. Alethse de la Torre for their contribution with databases for this analysis.