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Background: In the SINGLE trial, dolutegravir (DTG) showed fewer adverse events than efavirenz (EFV) as first-line treatment, but no difference in virological suppression, quality of life or survival.[1] In switching studies (NEAT 022, SWORD, STRIVING), DTG led to significantly higher rates of adverse events and no virological benefit.[1] Yet, in upper-income countries such as UK, DTG costs £6,068 per year compared to £108 for EFV. There are other low-cost generic antiretrovirals which could be used as alternatives to DTG.

Method: Lowest prices of DTG and EFV in over 50 countries were collected from national price databases, reimbursement authorities and WHO Global Price Reporting Mechanism database. Median prices calculated for each income level group. We analysed the correlation between (1) DTG prices or (2) ratio of DTG to EFV (DTG/EFV) and Gross Domestic Product (GDP) per capita (2016) published by the World Bank. Prices were recorded in US\$ per person-year. Using clinical trial and actual cost inputs, we determined the cost savings of using a generic EFV-first step therapy via a cost-consequence analysis set in the UK.

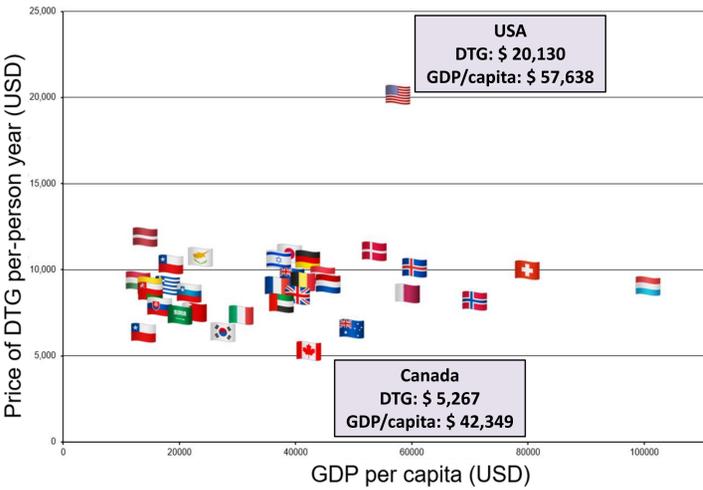
Results: DTG prices in high-income countries (HICs) and upper middle-income countries (UMICs) excluded from VL arrangements are substantially higher compared to low and lower middle-income countries (LMICs): median price in HICs \$9,045 ppy vs \$2,682 (UMICs) and \$60 (LMICs). The price in USA (\$20,130) is almost twice of Denmark (\$11,056), although their GDP per capita is comparable (USA: \$57,638 vs Denmark: \$53,579). In UMICs, we did not observe a correlation between DTG price and GDP per capita: In Bulgaria, DTG costs \$9,656 ppy compared to \$365 in Brazil, even though her GDP/capita is much lower (GDP/capita for Bulgaria: \$7,469 vs Brazil: \$8,650). There was also no relationship between DTG/EFV price ratio and GDP per capita. However, DTG prices were found to be much higher than EFV in UMICs (median DTG/EFV ratio= 6.9) compared HICs (ratio= 4.9). In LMICs, DTG prices were close to EFV prices (ratio = 1.8). A DTG-first step therapy may incur an additional £4,733 per person-year over a EFV-first approach.

Conclusions: Prices of DTG vary widely between countries, from <\$60 to over \$20,000 per person-year. Overall, we did not observe any correlation between DTG price and GDP per capita within income groups. In HICs and UMICs, the price of DTG is 4.9 to 6.9 times higher than EFV, despite limited clinical benefits. The cost-effectiveness of DTG versus EFV should be re-evaluated now that low-cost generic EFV has become widely available.

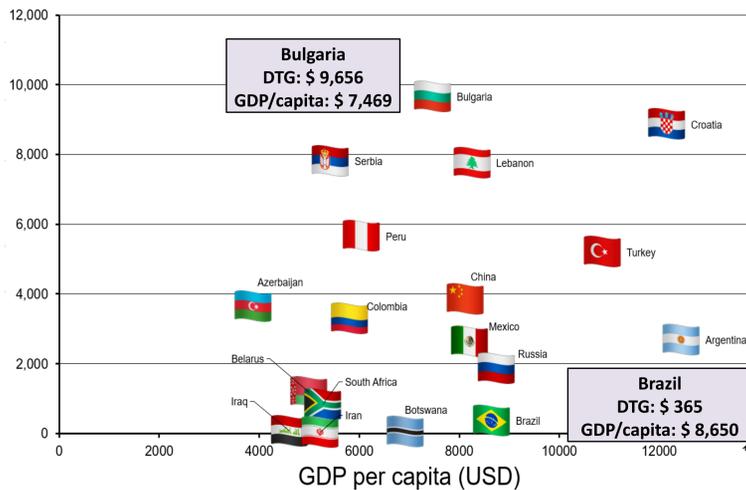
Country	Cost of DTG per person-year (US\$)
USA (H)	\$20,130
Latvia (H)	\$11,872
Denmark (H)	\$11,056
Japan (H)	\$10,908
Cyprus (H)	\$10,725
Israel (H)	\$10,559
Germany (H)	\$10,541
Czech Republic (H)	\$10,306
Iceland (H)	\$10,099
Switzerland (H)	\$9,972
Bulgaria (U)	\$9,656
Austria (H)	\$9,618
New Zealand (H)	\$9,548
Hungary (H)	\$9,343
Belgium (H)	\$9,282
Netherlands (H)	\$9,164
Greece (H)	\$9,083
France (H)	\$9,045
Lithuania (H)	\$9,040
Luxembourg (H)	\$9,020
Croatia (U)	\$8,867
Oman (H)	\$8,718
Slovenia (H)	\$8,630
Qatar (H)	\$8,598
U.K. (H)	\$8,379
Norway (H)	\$8,179
U.A.E (H)	\$8,033
Slovakia (H)	\$7,831
Serbia (U)	\$7,807
Lebanon (U)	\$7,765
Bahrain (H)	\$7,500
Saudi Arabia (H)	\$7,358
Italy (H)	\$7,350
Australia (H)	\$6,540
South Korea (H)	\$6,369
Chile (H)	\$6,338
Peru (U)	\$5,658
Canada (H)	\$5,267
Turkey (U)	\$5,204
Singapore (H)	\$4,911
China (U)	\$3,854
Thailand (U)	\$3,819
Azerbaijan (U)	\$3,645
Colombia (U)	\$3,285
Argentina (U)	\$2,682
Mexico (U)	\$2,629
Russia (U)	\$1,871
Belarus (U)	\$1,181
South Africa (U)	\$835
India (L)	\$538
Brazil (U)	\$365
Uganda (L)	\$269
Ukraine (L)	\$69
Cambodia (L)	\$60
Egypt (L)	\$60
Iraq (L)	\$60
Uzbekistan (L)	\$60
Cuba (L)	\$57
Armenia (L)	\$45
Botswana (U)	\$44
Iran (U)	\$36
Georgia (L)	\$27

Relationship between DTG Price and GDP per capita

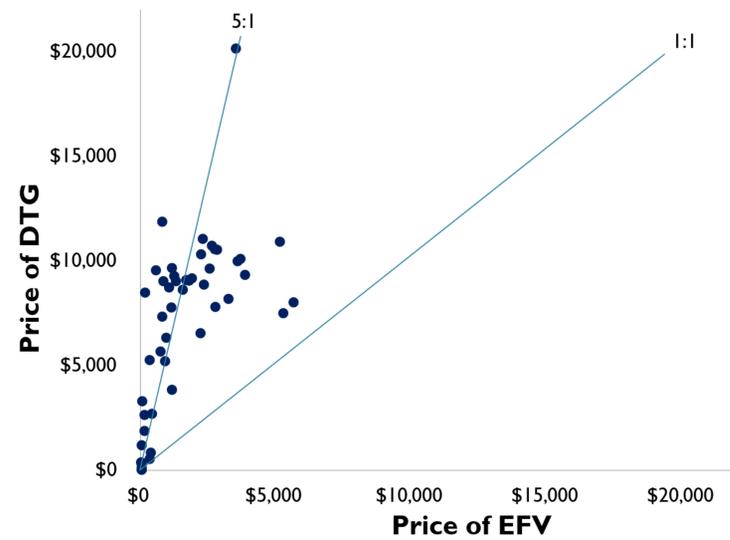
High-income countries (HICs)



Upper Middle-income countries (UMICs)

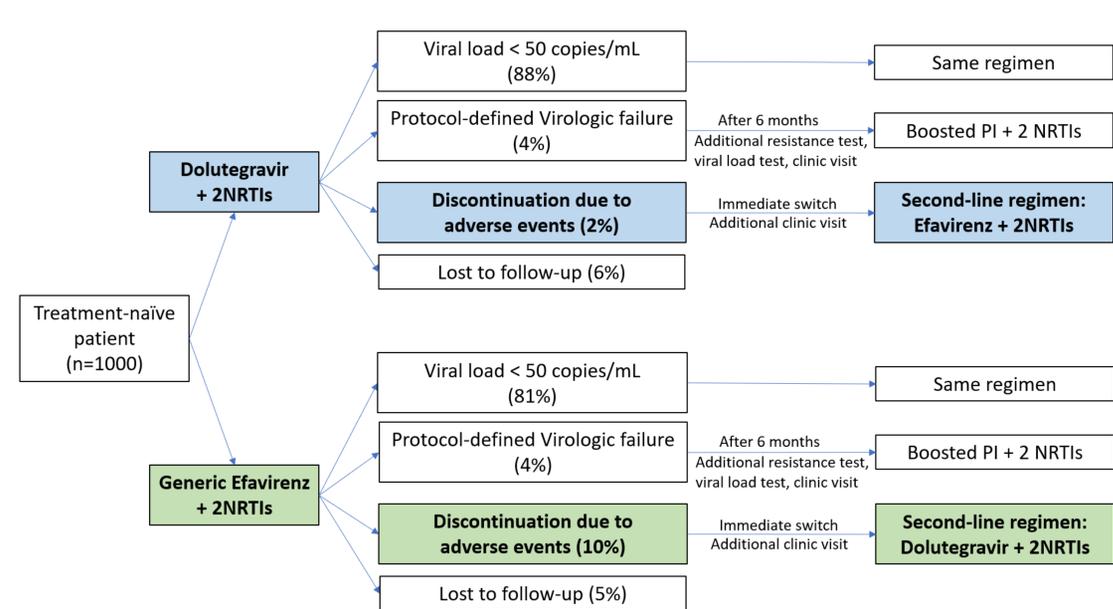


Price of DTG vs EFV



- Wide disparity in prices of DTG across countries, even when segregated by similar income levels
- Current price of DTG more than 500% higher than EFV (median EFV price: \$1,082) in more than half of the countries, regardless of income group
- Pattern of price difference between higher and lower-income countries consistent with findings from previous studies for several other classes of antiretrovirals such as PIs, NNRTIs and NRTIs

Cost-consequence analysis: DTG vs Generic EFV for First-line therapy in the UK



Cost inputs	Costs (£)
DTG (per person-year)	£ 5985
Generic EFV (per person-year)	£ 108
2nd-line boosted PI (per person-year)	£ 5064
Outpatient clinic visit	£ 324
HIV resistance test	£ 219
Viral load assay	£ 63

Prices of NRTIs assumed to be equal for DTG & EFV treatment.

Consequences (48-week data: SINGLE trial)	DTG (%)	EFV (%)
Viral suppression <50 c/mL	88	81
PDVF	4	4
Discontinuation due to AE	2	10
Loss to follow-up	6	5

Cost Implications for 1000 treatment-naïve patients for 1 year		
Findings	DTG-first	Generic EFV-first
Viral suppression	£5,266,800	£ 87,480
PDVF	£245,220	£ 127,680
Discontinuation (switch)	£18,435	£ 581,925
Total	£ 5,530,455	£ 797,085

DTG: Additional £4,733 per person-year

In UK: DTG should cost no more than £142 per person-year to be equivalent to EFV

This research has been supported by the International Treatment Preparedness Coalition (ITCP) and the Make Medicines Affordable Campaign

References: [1] Hill A et al. Meta-analysis of DTG for 7340 patients in 13 trials: effects of current HIV RNA suppression on efficacy and safety. HIV Medicine

Details of price sources / exchange rates can be found from: Sim et al. Is pricing of dolutegravir equitable? A comparative analysis of price and country income level in 52 countries. Journal of Virus Eradication 2018; 4: 230-237