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Modelling the long-term clinical outcomes of the novel single-tablet regimen bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in the UK

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Objective

- This research aimed to predict the long-term clinical and cost-effectiveness outcomes of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) versus alternative commonly used integrase strand transfer inhibitor (INSTI) regimens in the UK setting.

Background

- B/F/TAF combines the novel INSTI, bictegravir, with the guideline-recommended F/TAF backbone.
- B/F/TAF is highly efficacious, with a safety profile that may improve short-term tolerability and help reduce the long-term occurrence of non-AIDS related morbidities (NARMs).

Methods

- A cohort Markov model **(Figure 1)** was used to evaluate B/F/TAF versus other INSTI-based regimens (dolutegravir/abacavir/lamivudine [DTG/ABC/3TC], elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide [E/c/F/TAF], DTG+F/TAF and raltegravir+F/TAF [RAL+F/TAF]) for treating HIV in the UK setting. INSTI comparator regimens were chosen as they form the current standard of care in the UK.[1]
- The base case used a lifetime horizon and considered both treatment-naïve and treatment-experienced, virologically suppressed patients. Patients could receive up to two subsequent lines of therapy in the model, incorporated via mixed market baskets of regimens.
- The NARMs considered in the model were cardiovascular disease (CVD), chronic kidney disease (CKD) and bone fractures. Published hazard ratios were used to differentiate between treatments and HIV patient risk groups.[2–7]
- Central nervous system (CNS) and gastrointestinal (GI) treatment-related adverse events (TRAEs) were also considered in the model.
- UK-specific model inputs were informed by systematic literature reviews, network meta-analyses, targeted searches and discussion with expert clinicians using standard published sources where possible.
- A published hazard ratio (HR) for treatment discontinuation was applied to patients on multiple-tablet regimens (MTRs), as single-tablet regimens have demonstrated significantly greater persistence than MTRs.[8]
- To reflect confidential net price discounts commonly applied in HIV, treatment acquisition costs for B/F/TAF and comparators were decreased in regular intervals from list prices, to provide a range of plausible incremental cost-effectiveness ratio (ICER) results.

Results

- In the model base case, B/F/TAF was associated with a gain in quality-adjusted life years (QALYs), fewer comorbid events and cost savings associated with disease management, adverse events and NARMs versus all comparators.
- The results of deterministic sensitivity analyses (DSAs), where input values were varied by 20% or their standard deviation (where available), versus all comparators showed that treatment acquisition costs and HRs for NARMs were the primary drivers of cost-effectiveness results (**Figure 2** for results versus DTG/ABC/3TC).
- In the treatment acquisition cost scenarios **(Figure 3)**, B/F/TAF was estimated to have a cost-effective or dominant ICER in more than half of the tested scenarios at a willingness-to-pay threshold of £20,000/QALY.
- B/F/TAF was estimated to provide the equal longest time on first-line treatment (10.74 years) of the considered regimens alongside E/c/F/TAF.

Strengths and Limitations

- The model built upon approaches taken in other cost-effectiveness models of HIV to date, considering comparable number of NARMs and treatment lines.[9-12] A wide range of HIV regimens were included as subsequent therapies reflecting currently used treatment options in UK clinical practice.
- Due to a lack of available data, the model did not consider drug-drug interactions (DDIs). These are expected to differ in terms of frequency between treatment regimens, however were expected to have a minimal impact on model results.

Conclusion

- Due to increased first-line treatment persistence, enhanced tolerability and/or reduced occurrence of NARMs in both treatment-naive and treatment-experienced patients, B/F/TAF could offer benefits in short- and long-term clinical outcomes as well as reduced mortality compared to other INSTI-based regimens.[7] These benefits could help reduce the present and future burden that the management of HIV and associated comorbidities places on both patients and the NHS.

Figure 1. Model structure

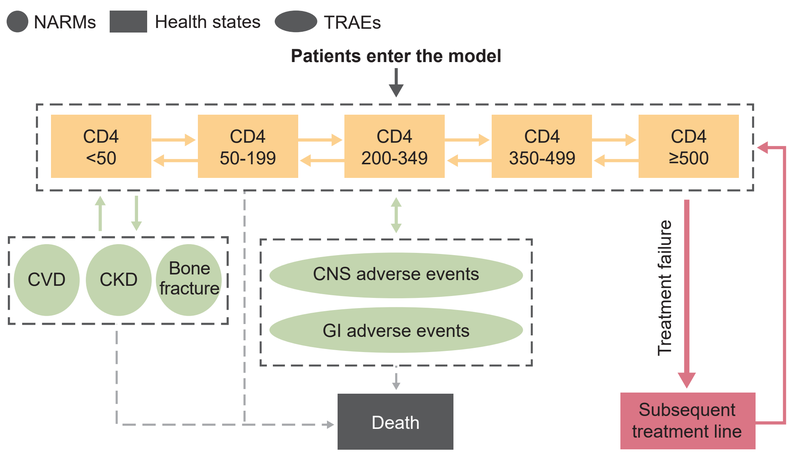

Figure 2. Tornado plot showing results of the ICER DSA (B/F/TAF versus DTG/ABC/3TC)

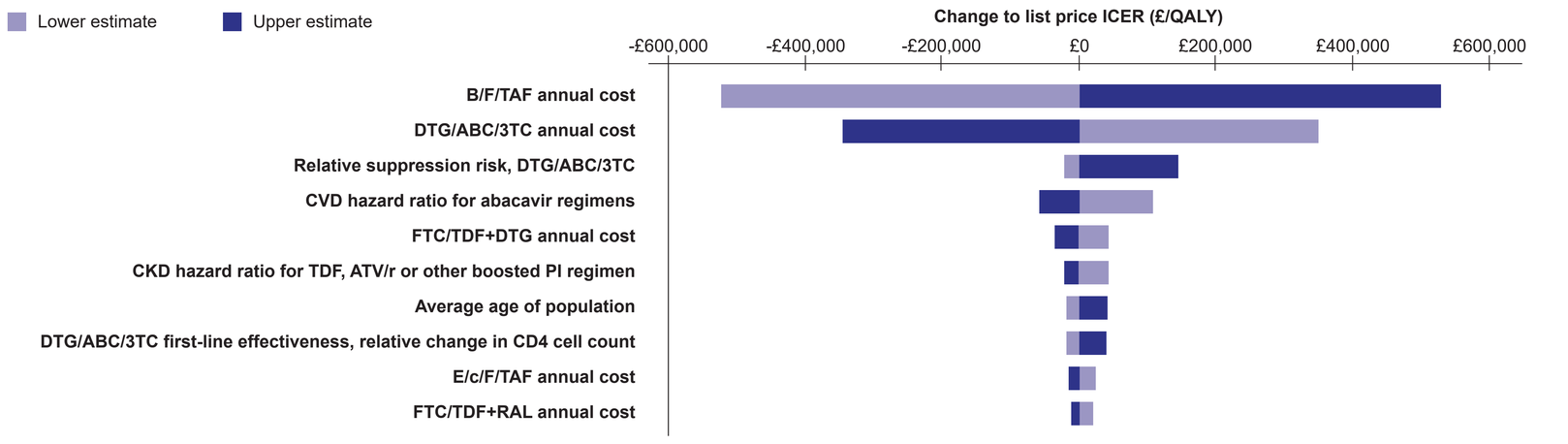

Figure 3. Scenario analysis of ICERs (£/QALY) for B/F/TAF versus comparator treatments

			DTG/ABC/3TC				DTG+F/TAF				E/c/F/TAF				RAL+F/TAF			
			Discount applied to list price				Discount applied to list price				Discount applied to list price				Discount applied to list price			
			0%	25%	50%	75%	0%	25%	50%	75%	0%	25%	50%	75%	0%	25%	50%	75%
B/F/TAF	Discount applied to list price	0%	£232,000	£665,000	£1,098,000	£1,531,000	£125,000	£675,000	£1,224,000	£1,774,000		£300,000	£1,245,000	£2,190,000				£126,000
		25%		£9,000	£442,000	£875,000			£167,000	£716,000			£93,000	£1,038,000				
		50%				£218,000												
		75%																

B/F/TAF dominant
B/F/TAF not cost-effective at a WTP threshold of £20,000/QALY
B/F/TAF cost-effective at a WTP threshold of £20,000/QALY

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Figure Abbreviations

ABC, abacavir; ATV, atazanavir; B, bictegravir; c, cobicistat; CKD, chronic kidney disease; CNS, central nervous system; CVD, cardiovascular disease; DTG, dolutegravir; E, elvitegravir; F, emtricitabine; FTC, emtricitabine; GI, gastrointestinal; ICER, incremental cost-effectiveness ratio; NARMs, non-aids related morbidities; PI, protease inhibitor; r, ritonavir; RAL, raltegravir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TRAEs, treatment-related adverse events; WTP, willingness-to-pay; 3TC, lamivudine.

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