A health technology

assessment of the 2-nrti backbones available in Italy

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Introduction and Aim of the Study

- Recently, therapeutic strategies for HIV have had significant success in improving patients' quality of life. In particular, triple therapy with a 2-NRTI backbone, that is now considered the standard of care approach for HIV treatment.
- The introduction of emtricitabine/tenofovir alafenamide (FTC/TAF) and the shift to tenofovir disoproxil fumarate/emtricitabine (FTC/TDF), as an off-patent drug, is predicted to alter the HIV drugs market in Italy.
- As a consequence, this would have an impact on policy-making processes, disinvestment strategies, and re-allocation of economic resources.
- **The aim of the study was to analyse the effects of FTC/TAF introduction and emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) disinvestment**, using a multi-dimensional framework, similar to that proposed by EUnetHTA Core Model (EUNetHTA, 2016).

Methods

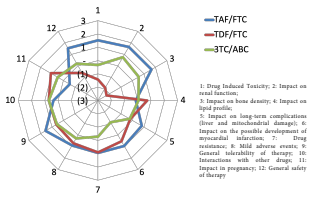
- In 2018, **a Health Technology Assessment (HTA)** was conducted, involving **18 Infectious Disease Departments across Italy**.
- The assessment compared the 2-NRTI backbones available in Italy: emtricitabine/tenofovir alafenamid (**FTC/TAF**), tenofovir disoproxil fumarate/emtricitabine (**FTC/TDF**), and abacavir/lamivudine (**ABC/3TC**).
- The HTA considered the 9 dimensions resulting from the European Network for Health Technology Assessment Core Model (EUNetHTA, 2016) and used an MCDA approach (Thokala et al., 2016).
10Systematic literature research was conducted to complete safety and efficacy dimensions. The validation of the evidence retrivied was carried out by 5 experts using the CASP Qualitative Checklist
- **Qualitative and quantitative data** were collected; in particular, clinicians perceptions, in terms of efficacy, safety, social aspects, equity, legal and organisational impacts were retrieved using validated **questionnaires** (with a 7 level Likert scale, from -3 to +3)
- A **Budget Impact Analysis** was performed: cost data inputs were derived from a process mapping analysis; considering the drug cost, the cost of pathway and the cost of adverse events. Information was evaluated in accordance with the Lombardy Region's outpatients and hospital admissions Reimbursement Tariffs and the NHS official drugs price list. The economic differences among the groups were studied using the ANOVA test.

Dimension	Prioritisation	Dimension	Prioritisation	Dimension	Prioritisation	Dimension	Prioritisation
Efficacy	1	Social and ethical impact	3	General relevance	5	Legal impact	7
Safety	2	Economic and finacial impact	4	Equity dimension	6	Organisation al impact	8

Table 1: Prioritisation of EUnetHTA Core Model dimensions

Literature evidence showed that **FTC/TAF ensures a higher percentage of virological and immunological control** compared with FTC/TDF and ABC/3TC. The perception of the clinicians confirmed (FTC/TAF: 1.36 vs FTC/TDF: 0.89 and ABC/3TC: 0.68; p-value: 0.023).

FTC/TAF also presents a better safety profile, in particular regarding **renal impairment and bone density**, compared with both FTC/TDF and ABC/3TC (0.93 vs -0.09 and 0.14 respectively; p-value: 0.04): the clinicians perceptions confirmed the safety evidence actually presented in literature.



From a social perspective,**FTC/TDF has a negative impact on social costs and patients' quality of life** (FTC/TDF: 0.98 vs FTC/TAF: 0.07 vs ABC/3TC: 0.23, p-value<0.001), caused by toxicities, and the worst overall impact of therapy on patient's satisfaction.

The total cost of HIV+ patients, assuming the 2-NRTI backbones, was evaluated.

- The Budget Impact analysis considered the Italian NHS perspective with 86,454 HIV+ patients assuming the backbone.
- Three scenarios were performed: i) basal, ii) the introduction of FTC/TAF, and iii) the introduction of FTC/TAF and FTC/TDF as an off patent drug.
- **The results revealed a 9% cost saving for the Italian NHS** with FTC/TAF introduction and FTC/TDF as an off patent drug.

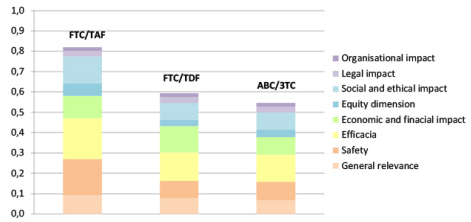
	BASAL SCENARIO (no FTC/TAF)			Total
	FIRST YEAR	SECOND YEAR	THIRD YEAR	
FTC/TAF	€ -	€ -	€ -	€ -
FTC/TDF	€ 619,594,357.98	€ 623,120,399.86	€ 626,667,941.99	€ 1,869,382,699.83
ABC/3TC	€ 245,292,807.85	€ 246,688,741.66	€ 248,093,187.26	€ 740,074,736.77
TOT	€ 864,887,165.83	€ 869,809,141.52	€ 874,761,129.24	€ 2,609,457,436.59
	INNOVATIVE SCENARIO (with FTC/TAF)			Total
	FIRST YEAR	SECOND YEAR	THIRD YEAR	
FTC/TAF	€ 452,562,491.84	€ 572,173,453.19	€ 671,336,102.19	€ 1,696,072,047.22
FTC/TDF	€ 119,152,761.15	€ 86,278,209.21	€ 77,128,362.09	€ 282,559,332.45
ABC/3TC	€ 245,292,807.85	€ 176,206,244.04	€ 106,325,651.68	€ 527,824,703.57
TOT	€ 817,008,060.84	€ 834,657,906.44	€ 854,790,115.96	€ 2,506,456,083.24
	INTRODUCTION OF FTC/TAF AND FTC/TDF OFF-PATENT DRUG			Total
	FIRST YEAR	SECOND YEAR	THIRD YEAR	
FTC/TAF	€ 383,600,588.32	€ 494,149,800.48	€ 584,149,595.41	€ 1,461,899,984.21
FTC/TDF	€ 143,193,933.30	€ 126,446,780.97	€ 127,166,666.38	€ 396,807,380.65
ABC/3TC	€ 245,292,807.85	€ 176,206,244.04	€ 106,325,651.68	€ 527,824,703.57
TOT	€ 772,087,329.47	€ 796,802,825.50	€ 817,641,913.47	€ 2,386,532,068.44

Collected data showed **that FTC/TAF decreases the burden of adverse events management,** thus increasing the accessibility of patients to healthcare providers (FTC/TAF: 0.85 vs FTC/TDF: 0.10 and ABC/3TC: 0.26, p-value: 0.016).

FTC/TAF was considered a valuable therapeutic approach also in terms of legal impact (FTC/TAF: 1.13 vs FTC/TDF: 0.65 and ABC/3TC: 0.73, p-value: 0.096) due to medico-legal issues in the prescription phase. It is important to note that all the 2-NRTI backbones in the study are mentioned in the Italian HIV National guidelines.

From an organisational perspective **FTC/TAF could simplify the overall management of drug complications for hospitals,** both in the short term (0.60 vs -0.13 [FTC/TDF] and 0.01 [ABC/3TC], p-value<0.001), and in the long term (0.65 vs -0.18 [FTC/TDF] and 0.03 [ABC/3TC], p-value<0.001). However, the introduction of FTC/TAF would require a little additional investment in training courses (5 days, on average, equal to € 3,300) and meetings (3.5 hours, on average).

After completing the steps of prioritisation and assessment of the dimensions, the final appraisal of technologies was conducted in order to give a unique and synthetic value that allows comparison of the 2-NRTI backbones.
The introduction of FTC/TAF was found to deliver improvements in efficacy, with a greater chance of virological control and safety compared with the older 2-NRTI backbones, FTC/TDF and ABC/3TC. Thus, a FTC/TDF disinvestment strategy would be cost saving for the Italian NHS.



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