WHAT IS THE COST OF TREATING A TYPICAL HIV-CENTRE PATIENT COHORT, WITH EITHER A KALETRA (LPV/r)-, OR REYATAZ WITH NORVIR (ATV+RTV)-BASED REGIMEN IN THE UK?

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BACKGROUND

- An optimal strategy for the treatment of HIV should be primarily based upon potency, durability and freedom from side effects [1].
- Recently, the British HIV Association (BHIVA) suggest, that in the framework of medical ethics, the cost of treatment may also be a consideration [1]
- The two most commonly prescribed protease inhibitors (PI) in the UK are: Kaletra (lopinavir/ritonavir: LPV/r); and Reyataz (atazanavir: ATV) with Norvir (ritonavir: RTV) [2].

OBJECTIVES

- To compare the overall cost of implementing either an LPV/r- or ATV+RTV-based strategy, in a typical HIV-centre, from the perspective of the UK National Health Service (NHS). .

METHODS

- This analysis compared the total treatment costs associated with using either a LPV/r-, or a ATV+RTV-based regimen, in a typical UK HIV-centre population of treatment-experienced patients.
- Baseline characteristics and clinical outcomes of the HIV-centre population were derived from published data on the BMS AI424-045 trial [3-5], which was designed to evaluate the comparative safety and efficacy of LPV/r and ATV+RTV in experienced patients.
- The analysis considered direct costs to the HIV-centre over a 96-week period, to generate an average cost per patient.

TYPES OF TREATMENT COSTS CONSIDERED IN THE ANALYSIS (TABLE 1):

ANTI-RETROVIRAL THERAPIES (ART)

- LPV/r (400/100mg, twice daily) or ATV+RTV (300mg + 100mg, once daily)
- Tenofovir (TDF: 300mg, once daily)
- 1 x Nucleoside Reverse Transcriptase Inhibitor (NRTI) of:

didanosine (ddi:250mg, once daily) stavudine (d4T:40mg, twice daily)
abacavir (ABC:300mg, twice daily) zidovudine (AZT:300mg, twice daily); lamivudine (3TC:150mg, twice daily)

- Optimised ART following discontinuation of either a LPV/r- or ARV+RTV-based regimens

CONCOMITANT DRUGS

- Lipid-lowering agents
- Anti-diarrhoeal agent

RESOURCE UTILISATION

- HIV-centre personnel time and laboratory tests incurred during maintenance or discontinuation (virological or non-virological failure) of patients on either a LPV/r- or ARV+RTV-based regimen.

TABLE 1: Base case parameters and unit costs

PARAMETER	COST PER DAY	COST PER 48 WEEKS	COST PER 96 WEEKS
ELIGIBLE POPULATION: 550 TREATMENT-EXPERIENCED PATIENTS			
ANTIRETROVIRAL THERAPIES (ART)			
KALETRA (LPV/r)	£10.25	£3,443	£6,886
REYATAZ + NORVIR (ATV + RTV)	£11.65	£3,913	£7,826
VIREAD (TENOFOVIR: TDF)	£8.50	£2,856	£5,712
NRTI (average) [3-5]	£5.65	£1,898	£3,796
CONCOMITANT DRUGS			
ANTI-DIARRHOEAL AGENTS (loperamide, 2mg)	£0.04	£13	£26
LIPID-LOWERING AGENTS (average) [3-5]	£0.78	£263	£525
DRUGS FOLLOWING DISCONTINUATION			
OPTIMISED TREATMENT (3-5 ARTs) [6]	£22.70	£7,627	£15,254
RESOURCE UTILISATION [7]			
MAINTAINING ART	£1.88	£633	£1,266

- Resource costs incurred over a 0-48 or 48-96 week period, for a patient discontinuing their regimen for **virological** reasons was £1,420

- Resource costs incurred over a 0-48 or 48-96 week period, for a patient discontinuing their regimen for **non-virological** reasons was £1,167

EXAMPLE: Resource cost of a patient maintaining treatment from 0-48 weeks, followed by discontinuation (virological) during 48-96 weeks = £2,053 (£633 + £1,420) over a 96 week period

All drug prices: British National Formulary, September 2005

ASSUMPTIONS

Patient population

- Based on expert opinion, 550 treatment-experienced patients from St Mary's Hospital were identified as being representative of the BMS AI424-045 trial population.
- Baseline demographics of the St Mary's Hospital population was considered similar to that of the BMS AI424-045 study population [3] i.e. -No previous treatment experience of LPV/r, ATV, RTV or TDF
  -Failure of 2 or more prior Highly Active Anti Retroviral Therapy (HAART) regimens
- The cost of a strategy is based on all eligible patients (n=550) from St Mary's Hospital receiving LPV/r and ATV+RTV.
- Patient mortality was not disclosed in publications and was not taken into account in this analysis [3-5]

ARTs, lipid-lowering and anti-diarrhoeal treatment

- Choice and dose of ART were as defined in the BMS AI424-045 trial [3-5]
- Usage of: LPV/r-, or ATV/RTV-based regimes; optimised ART; lipid-lowering and anti-diarrhoeal agents were as reported at 0, 48 and 96-weeks timepoints in the BMS AI424-045 trial [3-5].
- All medication was taken continuously over the full 0-48 and/or 48-96-week analysis period, without any modification or losses.
- Averaged recommended dose of lipid-lowering agents (as per BMS AI424-045 trial [3]) and anti-diarrhoeal agents (loperamide 2mg,prn) used in the analysis were confirmed by expert opinion
- Discontinuation did not affect the relative use of lipid-lowering and anti-diarrhoeal agents.

ASSUMPTIONS CONTINUED…

Optimised ART following discontinuation

- The cost of optimised ART treatment (3-5 ARTs) following discontinuation of a LPV/r or ATV+RTV-based regimen was obtained from an audit of UK clinical practice [6]
- Patients discontinuing treatment received optimised ART either from week 0 (e.g. immediately), or from week 48 onwards.

Resource utilisation (*Medical personnel time and laboratory tests*)

- Patient discontinuation rates were as reported at 48- and 96-week timepoints in the BMS AI424-045 trial [3-5]
- Reasons for discontinuation were identified as virological (e.g. genotypic resistance) or non-virological (e.g. toxicity, adverse event, other), based on published data from the BMS AI424-045 trial.
- The resource utilisation (personnel time and laboratory tests incurred) and cost associated with patients maintaining or discontinuing treatment was identified from a survey of medical personnel at three HIV-centres and has previously been detailed elsewhere [7].
- HIV-centre personnel time included: Physicians, Nurses, Pharmacists, Physiotherapists, Health/Welfare Advisors and Psychologists.
- Laboratory tests included: standard blood / urine analysis, viral load, CD4 count, viral genotype/ virtual phenotype, and therapeutic dose monitoring
- The combined cost of medical personnel time and laboratory tests incurred for patients maintaining treatment was not considered different between LPV/r and ATV+RTV-based regimens.
- The cost of resources incurred during discontinuation, for virological or non-virological reasons, was assumed to be the same for patients treated with a LPV/r or an ATV+RTV-based regimen.
- All costs associated with treatment discontinuing were assumed to be completed by 96-weeks.
- Costs excluded from the analysis are: investigations (e.g. x-rays, non-routine blood tests), hospitalisations, building and building maintenance costs (e.g. heating / lighting); additional non-clinical personnel (administrators / cleaners etc), losses in patient work productivity or out-of pocket expenses.

Time frame

- The primary analysis was conducted over a 96-week period based on published data [3]
- A secondary analysis was also conducted over the 0-48 and 48-96 week period [4,5]

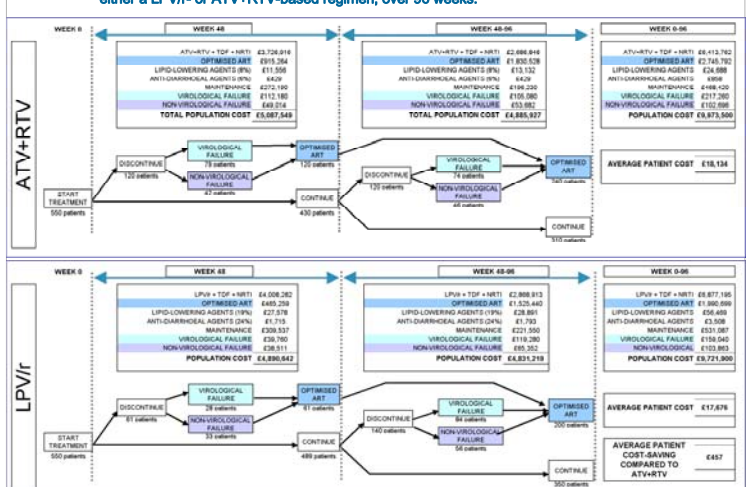
Analysis

- The analysis generated:
  i) Average cost difference per patient, between LPV/r- and ATV+RTV-strategies, over 96 weeks.
  ii) Total costs associated with treating a typical HIV-centre population with LPV/r and ATV+RTV.

RESULTS

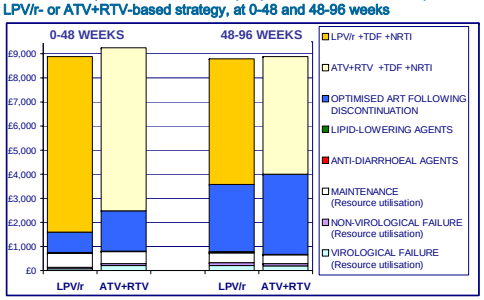
- The overall treatment cost to implement an ATV+RTV-based regimen in a typical HIV-centre population was £251,620 (£460 per patient) more expensive than a LPV/r-based regimen, over 96-weeks (FIGURE 1 and 2).

FIGURE 1: Total costs associated with treating 550 treatment-experienced patients from St Mary's hospital with either a LPV/r- or ATV+RTV-based regimen, over 96 weeks.



All patients immediately discontinue, receive optimised ART or concomitant drugs from week 0 or 48 onwards
Treatment costs are calculated to the nearest whole patient, over 96 weeks

FIGURE 2: Total and component treatment cost per patient associated with implementing either a LPV/r- or ATV+RTV-based strategy, at 0-48 and 48-96 weeks



Sensitivity Analysis

- A sensitivity analysis was conducted to examine the robustness of the results by varying the assumptions (TABLE 2).
- The following parameters were varied:
  - NRTI: from an average, to use of the highest (ABC: 300mg, BD) and lowest (ddi: 250mg, OD) cost only.
  - Lipid-lowering agent: from an average of treatments and doses, to use only of the highest cost (gemfibrozil: 600mg, BD); lowest cost (pravastatin: 10mg, OD), co-administration of an average of doses of statins+fibrates used in the BMS AI424-045 [3].
  - Optimised ART: from 3-5 ARTs6, to use of 3-5 ARTs + efuvirtide (Fuzeon: 90mg, BD).
  - The use of anti-diarrhoeal agents, lipid-lowering agents and optimised ART: from all patients starting treatment immediately (I.e. week 0 or week 48 onwards), to starting mid-way between 0-48, or 48-96 weeks onwards (i.e. at 24 or 72 weeks).

TABLE 2: Sensitivity analysis

PARAMETER	ORIGINAL VALUE (48 weeks)	ALTERNATIVE VALUE (48 weeks)	SAVING PER PATIENT OVER 96 WEEKS	% CHANGE FROM CENTRAL ESTIMATE
BASE-CASE ANALYSIS	-	-	£457	£0
NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS				
1 NRTI (Highest cost-ABC: 300mg, BD)	£1,898	£2,484	£352	-23%
1 NRTI (Lowest cost-ddi: 250mg,OD)	£1,898	£1,146	£593	30%
LIPID-LOWERING AGENTS				
Highest cost- gemfibrozil (Lopid, 600mg, BD)	£263	£427	£421	-8%
Lowest cost- benzofibrate (benzolip mono, 400mg, OD)	£263	£91	£495	8%
Co-administration (average of statin + average of fibrates)	£263	£549	£394	-14%
STARTING MEDICATION AT 24- OR 72-WEEKS ONWARDS				
Lipid-lowering agents (average cost of recommended doses)	£263	£131	£486	6%
Anti-diarrhoeal agent (Loperamide, 2mg, PRN)	£13	£6	£460	1%
50% optimised ART + 50% ATV+RTV- or LPV/r-based regimen	£7,627	£8,147 or £7,912	£663	45%
DRUGS FOLLOWING DISCONTINUATION				
Optimised ART + enfuvirtide	£7,627	£21,022	£2,869	527%

Optimised ART background treatment + enfuvirtide (T20, FUZEON). Based on an audit of UK clinical practice [6]

DISCUSSION

- This analysis demonstrates that there are additional costs associated with the treatment of HIV, beyond the cost of anti-retroviral medication.
- The costs associated with discontinuing treatment are significant and often overlooked in selecting HAART strategies.
- The implications of discontinuation rates should be considered alongside available service provision. Furthermore, an earlier discontinuation results in the patient progressing faster through a finite number of less effective therapeutic strategies [8,9].
- The combined cost of concomitant lipid-lowering and anti-diarrhoeal medication represents ~0.5% of total treatment cost associated with a LPV/r- or ATV+RTV-based strategy (FIGURE 1 and 2).
- Introducing efuvirtide into the optimised antiretroviral treatment of patients discontinuing a LPV/r- or ATV+RTV-based strategy, significantly increases the cost of an ATV+RTV-based strategy by £2,869 per patient compared to a LPV/r-based strategy (TABLE 2).

CONCLUSION

- This analysis provides a methodological framework for HIV-centres to determine the overall cost impact of HIV-treatment strategies for their patient populations.
- It can be concluded that LPV/r-based regimens are less expensive than ATV+RTV-based regimens.

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