

# Prospective HLA-B\*5701 screening for abacavir hypersensitivity saves costs

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## Background

Avoiding abacavir (ABC) in HIV-patients tested positive for HLA-B\*5701 markedly reduces the risk of abacavir hypersensitivity reaction (ABC-HSR). Prospective HLA-B\*5701 screening prior to ABC use is generally recommended. However, implementation of genetic screening into therapeutic practice not only depends on improved clinical outcomes but also on cost-savings.

We estimated the average total costs per patient when implementing HLA-B\*5701 screening prior to using ABC/3TC fixed-dose combination (FDC) in comparison to initiating ABC/3TC FDC without genetic screening.

## Methods

### Decision tree model

A decision tree model was used to estimate total costs (=direct and indirect costs) of using ABC/3TC FDC with or without prospective HLA-B\*5701 screening.

### 5-centre (5C) study

To evaluate the costs related to an ABC-HSR, we performed a retrospective standardized assessment of all clinically suspected ABC-HSR cases at 5 German HIV-centres (3 private practices and 2 university hospitals).

### Inclusion criteria

- No HLA-B\*5701 screening
- symptoms (during the first 6 weeks of ABC use) which are associated with clinical diagnosis of ABC-HSR (acc. to the Kivexa Product Information).

### Input Parameters

- Resource utilisation** was valued with the outpatient fees of
  - the German social health insurance (EBM, Einheitlicher Bewertungsmaßstab)
  - or private health services GOÄ (Gebührenordnung für Ärzte)
 and the G-DRG (German Diagnosis Related Groups) system for inpatient services.
- Estimated private health insurance rates were based on the German-wide situation.
- The Lauer-Taxe was used for calculating the costs for antiretroviral and other drugs.
- Costs for HLA-B\*5701 screening were not considered in the analyses.
- Indirect costs (productivity loss)** were valued with age and sex specific labour costs.
- Length of inpatient hospital stay and period of disability derived from the 5C study.
- Rates of employed, unemployed and retired persons were extracted from the annual report of the Federal Statistical Office (Statistisches Bundesamt, Jahrbuch 2006).
- MICE, a module for indirect cost estimation, was used for the calculation of indirect costs. The module has been developed for disease-related hospitalizations at the University Hospital of Ulm<sup>1</sup>.
- Estimates for **HLA-B\*5701 prevalence in Germany, HSR incidence, and hospitalization rate** were based on clinical trials and cohorts<sup>2-4</sup> (see Table 1).

## 5C Study

- 32 ABC-HSR cases have been identified between 1998 and 2007.
- Mean time on drug until the first symptoms have been reported was 10.8 days. After the occurrence of the first symptoms it took 9.7 days (mean) until abacavir was discontinued.
- 22 patients received ambulant care (18/22 with grade 1-2 symptoms; as defined by the AIDS Clinical Trial Group)
- 10 patients were admitted to hospital (8/10 with grade 3-4 symptoms).
- Mean length of hospital stay was 20.8 days (range 1-58 days), mean number of days off due to sick certificate was 6.4 (hospitalizations excluded).
- On average, 53.7% of a monthly pack of ABC was discarded.

## References

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## Acknowledgement

This study was supported by GlaxoSmithKline, Germany.

## Base-Case Analysis

- Input parameters used in our model are shown in Table 1. Costs for discarding 53.7 % of a monthly pack of ABC/3TC FDC were calculated at € 407 per case. Overall mean direct costs per case were calculated at € 1.362. Indirect costs summed up to an average of 873 € per case. Including direct and indirect costs, the mean total costs per clinically suspected ABC-HSR were € 2,235 (Fig.1).
- The thresholds for cost-savings when implementing genetic screening were estimated at € 130 (direct costs only) and € 213 (total costs, Fig.1) per patient.

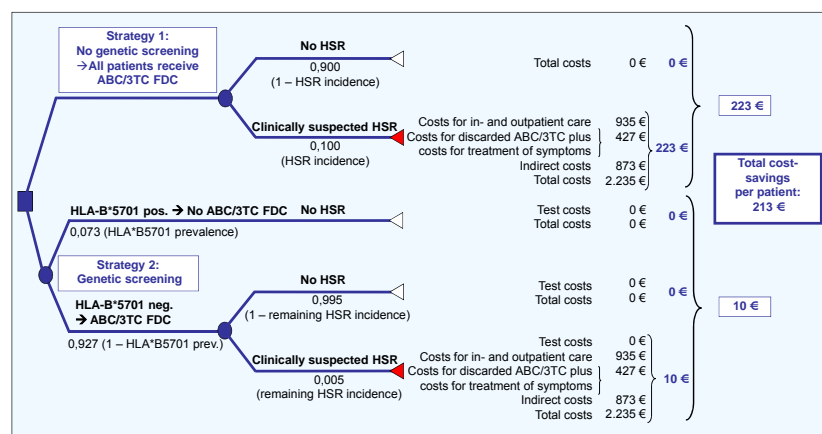
### Sensitivity analyses

- Total cost estimates remained relatively robust concerning extreme value analysis. When employing simultaneously extreme values of all variables (low or high cost scenarios), minimal total cost savings ranged from € 125 to 317. This was also true when considering only direct costs. The threshold for cost savings ranged from € 65 to 215 €.

**Table 1. Assumptions used for the base case analysis (using estimated average values) and for sensitivity analyses (using extreme values reflecting the cost outcomes in extreme case scenarios)**

	Base case	Reference	Extreme values for sensitivity analyses	
			Low HSR cost scenario	High HSR cost scenario
Percent discarded of a monthly pack of ABC/3TC FDC	53.7%	5C study	50 % assumption	56.3 % PREDICT-1 <sup>3</sup>
Costs for treatment of symptoms	20 €	5C study	*	*
Costs for outpatient care	73 €	5C study	*	*
Costs for inpatient care	6.904 €	5C study	4.623 € 5C study: lump sum for standard inpatient care (DRG-Code S63B)	8.436 € 5C study: mean hospital costs in 5-centre study when excluding hospital stays of only one day
Indirect costs	873 €	MICE module <sup>1</sup>	0	n.d.
Incidence of clinically suspected HSR	10.0 %	EPI-001 <sup>2</sup> + PREDICT-1 <sup>3</sup>	7.8 % PREDICT-1 <sup>3</sup>	12 % <sup>4</sup>
Prevalence of HLA-B*5701	7.3 %	EPI-001	5.6% PREDICT-1 <sup>3</sup>	9.5% EPI-001 (Eastern Europe ethnicity)
Negative predictive value of genetic HLA-B*5701 test	99.5 %	assumption	99 % assumption	100 % PREDICT-1 <sup>3</sup>
Hospitalization rate	12.0 %	GSK studies, data on file	10% GSK studies, data on file	15% GSK studies, data on file
Private health insurance rates	15 %	Single centre evaluation**	10 % (10 % of German population; according to the data of private insurances)	20% (20 % of German HIV-infected population; according to the data of private insurances)

\*Due to only minimal impact on cost outcomes, no sensitivity analyses performed; n.d. = not done; \*\*HIV Research and Clinical Care Centre Munich, priv. communication



**Figure 1. Decision tree comparing two alternative strategies.** Prospective HLA-B\*5701 screening prior to initiating ABC/3TC FDC versus initiation of ABC/3TC FDC without genetic screening. Analyses include total (direct and indirect) costs. Test costs for HLA-B\*5701 screening were not considered.

## Conclusions

According to our model, prospective HLA-B\*5701 screening prior to ABC/3TC FDC initiation results in cost-savings to the health care payer (considering only direct costs) and to the society (considering direct and indirect costs), if screening costs are below 130 € and 213 € per patient, respectively.

Irrespective of economic considerations, there is a clear medical benefit of prospective HLA-B\*5701 screening prior to ABC use.