the rash eventually resolved. Atenolol and pantoprazole were reintroduced progressively along with zidovudine, lamivudine and nevirapine without recurrence of a rash. Unfortunately, repeat testing demonstrated a rebound of HBV DNA to 1930 pg/ml.

Tenofovir is generally well tolerated, with uncommon grade 3/4 clinical and laboratory adverse events, and low discontinuation rates in clinical trials. There have been several reports of nephrotoxicity with proximal renal tubular dysfunction [5,6].

We believe this is the first reported lichenoid drug eruption in response to tenofovir. However, in Gilead 907, a phase III study of tenofovir in treatment-experienced patients, the incidence of rashes described at 48 weeks was 7% in the tenofovir arm versus 1% in the placebo/crossover arm [7], suggesting that they may not be uncommon.

Further treatment of this HIV/HBV-co-infected patient is complicated by the development of a lamivudine-selected YMDD mutation in his HBV [8], for which tenofovir has been shown to have activity. Adefovir may be a potential treatment option, but there is potential cross-reaction between adefovir and tenofovir.

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Improved accuracy of HIV-1 genotypic susceptibility interpretation using a consensus approach

HIV-1 genotypic susceptibility testing has become an important tool in improving the efficacy of antiretroviral therapies. In clinical trials on patients who failed to suppress viral replication, patients whose physicians were provided with genotypic test information before making therapy changes had greater reductions in viral load than patients whose physicians were not provided with this information [1,2]. The benefit of these tests, however, is limited by the accuracy of the genotypic interpretation algorithms. Drug resistance is characterized by a complex series of resistance-inducing and compensatory mutational changes [3]. Different web-based interpretation systems [4–6] have been shown to give highly discordant results [7]. In this study, we show that the accuracy of HIV-1 protease genotypic susceptibility interpretation algorithms can be improved by using consensus results from different computational methods.

We retrieved 1792 HIV-1 protease isolates and their corresponding IC_{50} (the concentration of drug required to inhibit viral growth by 50%) values for six drugs (amprenavir, $n = 318$; lopinavir, $n = 90$; indinavir, $n = 348$; nelfinavir, $n = 357$; ritonavir, $n = 337$; saquinavir, $n = 342$) from the Stanford HIV Drug Resistance Database (http://hivdb.stanford.edu). We selected samples that were genotyped and phenotyped using ViroLogic's GeneSeqs and PhenoSense assays, respectively. All sequences were analysed by the linear regression method provided as part of the PIRSpred [4] server (http://protinfo.compbio.washington.edu/pirspred.html), the rule-based method provided at the Stanford HIV Drug Resistance Database [5], and the support vector machine method of Geno2Pheno [6] version 2.2 (http://195.37.60.133/cgi-bin/geno2pheno.pl). The websites were accessed between 15 December and 20 December 2003. Interpretations were based on the default cut-off values of each method for reduced susceptibility: a 2.5-fold increase in the IC_{50} value for phenotypic test (10-fold for lopinavir), a 2.5-fold increase in the IC_{50} value for the linear regression method (10-fold for lopinavir), a 'drug mutation score' of 30 for the rule-based method, and a 'cut-off score' of 3.5 for the support vector machine method. Samples with resistance scores equal to or higher than the cut-off were defined as having reduced susceptibility to a drug. Consensus predictions were then generated for sequences for which the three methods predicted the

Table 1. Accuracy of three HIV-1 resistance interpretation systems and their consensus.

	Protease inhibitors					
Interpretation system	Amprenavir (%)	Lopinavir (%)	Indinavir (%)	Nelfinavir (%)	Ritonavir (%)	Saquinavir (%)
Phenotypic susceptibility test	318	90	348	357	337	342
Linear regression	257 (80.8)	58 (64.4)	308 (88.5)	319 (89.4)	306 (90.8)	312 (91.2)
Rule based	246 (77.4)	65 (72.2)	310 (89.1)	322 (90.2)	312 (92.6)	298 (87.1)
Support vector machine	256 (80.5)	58 (64.4)	307 (88.2)	319 (89.4)	308 (91.4)	285 (83.3)
Agree (consensus)	291 (91.5)	83 (92.2)	319 (91.7)	336 (94.1)	317 (94.1)	321 (93.9)
Consensus correct	238 (81.8)	58 (69.9)	296 (92.8)	310 (92.3)	300 (94.6)	281 (87.5)
Disagree	27 (8.5)	7 (7.8)	29 (8.3)	21 (5.9)	20 (5.9)	21 (6.1)
Linear regression correct	17 (63.0)	0 (0)	13 (44.8)	9 (42.9)	8 (40.0)	4 (19.0)
Rule based correct	9 (33.3)	7 (100)	16 (55.2)	12 (57.1)	12 (60.0)	17 (81.0)
Support vector machine correct	17 (63.0)	0 (0)	13 (44.8)	9 (42.9)	8 (40.0)	4 (19.0)

same result. Predictions that matched the results of the phenotypic susceptibility test were classified as correct. The HIV-1 protease sequences, the IC_{50} values, and the interpretation results may be downloaded at http://software.compbio.washington.edu/misc/downloads/aids/.

Consensus predictions ranged from 91.5 to 94.1% of the total number of isolates evaluated for each of the six drugs, with accuracies of 81.8% (amprenavir), 69.9% (lopinavir), 92.8% (indinavir), 92.3% (nelfinavir), 94.6% (ritonavir) and 87.5% (saquinavir) (see Table 1). For the discordant predictions, the rule-based method had the highest accuracies for five drugs: 100% (lopinavir), 55.2% (indinavir), 57.1% (nelfinavir), 60.0% (ritonavir) and 81.0% (saquinavir).

We have analysed the individual performance of three web-based genotypic interpretation systems relative to predictions made using the consensus of the three methods for evaluating phenotypic susceptibilities to HIV-1 protease inhibitors. The results indicate that the consensus predictions generated from different genotypic interpretation algorithms have higher overall accuracies than any of the methods considered individually. This suggests that genotypic interpretations should not rely on a single system, and that decisions about therapeutic regimens may be undertaken with greater confidence when consensus results are obtained.

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Hepatitis C virus infection does not prevent autologous bone marrow transplantation in HIV-related non-Hodgkin's lymphoma

High-dose chemotherapy followed by peripheral blood stem cell transplantation (PBSCT) is the first choice treatment for HIV-negative patients with refractory or relapsed Hodgkin's and non-Hodgkin's lymphoma (NHL) [1,2]. The introduction of highly active antiretroviral therapy (HAART) has reduced the morbidity and mortality of AIDS [3]; but lymphomas still have a poor prognosis in this setting [4–7]; therefore, autolo-