copies/mL), virologic failure rates, and time to first regimen change. Regimen choices were determined by the primary provider. The Fischer exact test was used for qualitative variables, and the Kruskal-Wallis or Wilcoxon rank sum test was used for continuous variables. Groups were analyzed by initial regimen in an intention-to-treat analysis.

The cohort was 65% male, 69% black, and had a median age of 41 years (range, 34–47 years). Overall, the distribution of initial prescribed regimens for the 166 HIV-infected patients was as follows: 16 patients (9.6%) were prescribed a nonboosted-PI regimen, 46 patients (27.7%) were prescribed a boosted-PI regimen, and 104 patients (62.6%) were prescribed a non-NRTI (NNRTI) regimen. Baseline data on age, CD4+ cell count, and viral load were similar among groups. At 48 weeks of follow-up, the patients who received the PI-based regimens had a greater median increase in CD4+ cell count, and a higher percentage of these patients had a CD4+ cell count >200 cells/mm³. The median increase in CD4+ cell count was 268 cells/mm³ for patients who received the nonboosted-PI regimen, compared with 239 cells/mm³ for patients who received the boosted-PI regimen (P = .596) and 201 cells/mm³ for patients who received the NNRTI regimen (P = .540). The percentages of patients who had a CD4+ cell count >200 cells/mm³ were as follows: 67% of patients from the nonboosted-PI group, 60% of patients from the boosted-PI group, and 61% of patients from the NNRTI group (P = .99 among all groups).

At 48 weeks of follow-up, rates of viral suppression, although not statistically different, showed a trend toward superiority for the PI-based regimens, compared with the NNRTI regimens: 100% of patients who received the nonboosted-PI regimen, 81% of patients who received the boosted-PI regimen, and 68% of patients who received the NNRTI regimen experienced viral suppression (P = .155 among all groups). The boosted-PI regimens appeared to achieve viral suppression faster than did the nonboosted-PI regimens (P = .24) or the NNRTI regimens (P = .19), although this difference did not achieve statistical significance. Use of nonboosted-PI regimens ended after 2003, after which boosted-PI and NNRTI regimens were prescribed with similar frequency.

Similar to Khanna et al [1], we found that CD4+ T cell recovery did not differ by regimen type, although we had few subjects treated with nonboosted-PI regimens (n = 16). Rates of virologic suppression and failure were similar among all 3 groups and were relatively constant over time as the use of nonboosted-PI regimens was phased out, although, when compared with treatments started before 2003, those started after 2003 had a shorter time to viral load suppression. Our study is one of the few that compare results of all 3 types of ART regimens for ART-naive patients with advanced HIV infection and AIDS [2]. Data such as these are particularly relevant given the reality of late diagnosis of HIV infection [3]. In clinical practice, many HIV-infected persons are not diagnosed prior to developing AIDS, either by immunologic criteria (ie, a CD4+ cell count <200 cells/mm³) or by diagnosis of an opportunistic disease. Our findings differ from those of other studies, including those of the AIDS Clinical Trials Group 5142, in which differences were found among ART regimens in both the rate of virologic failure and the rate of CD4+ recovery [4]. This may be the result of differences in sample size, but it may also be due to the severity of immunosuppression in our cohort, as compared with the other studies in which a majority of subjects did not have advanced HIV infection.

Knowledge of treatment response rates for various currently available ART combinations provides guidance for patients and providers alike. Given similar virologic and immunologic responses to various ART combinations, providers may prescribe contemporary regimens based on other drug-related characteristics and tailor regimens to best suit individual patient needs. Such an approach may enhance adherence and maximize the potential for long-term success.

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References


Why We Need Statistical Inference

To the Editor—Several times during our teaching, we discuss the importance of
clinical significance versus statistical significance. That is, when evaluating efficacy, the magnitude of the difference in response rate between 2 therapies is at least as important as the P value derived from the formal statistical analysis and, thus, should be carefully examined for clinical importance. On the other hand, here we want to present our thoughts on an article published in Clinical Infectious Diseases, as an example that reminded us how important it is to also carefully interpret the type 1 error level before introducing a finding for the widespread use of clinicians.

Like anyone who has been interested in Crimean-Congo hemorrhagic fever during their career, we read the manuscript by Ergönül et al [1] with interest. This paper presented important results from the experience of a well-known hospital and research center in Turkey. The main finding presented in this manuscript is that ribavirin therapy was associated with a decrease in mortality among patients with Crimean-Congo hemorrhagic fever. This observation was based on the comparison of the point estimates of the overall case-fatality rate (involving patients with mild and severe disease) with the case-fatality rate among the patients with severe disease who did not receive ribavirin (case-fatality rate, 2.8% vs 4.5%).

The point estimate of 2.8% is clouded by the fact that it includes the patients with mild disease; for this comparison, the better estimate of 3.3% could have been used. More importantly, one can easily calculate that the observed difference of 1.2% in case-fatality rate will return a P value very close to 1.0 (P > .99). Furthermore, when the result of the Fisher’s test comparing proportions of patient fatalities is statistically analyzed (0 of 8 patients treated with ribavirin died vs 1 of 22 patients without ribavirin), it reminds us that, in real life, the risk of this therapy being ineffective may be as high as 100%, which is in direct contrast to the findings and interpretation of this study.

The design of the Ergönül et al [1] study was not as ideal as an epidemiologist would like; however, this is relatively acceptable given the nature of this disease and the circumstances surrounding the time at which the paper was published. Our main concern was to express that, although studies with small numbers of subjects may not necessarily have to use the conventional type 1 error level of 5% [2], we do have to carefully consider the effect of chance when presenting findings that will affect clinical practice. This study, which presents a main finding with a P value very close to 1.0, does not remove our concerns that, although ribavirin may be safe and possibly an option for the treatment of Crimean-Congo hemorrhagic fever, the seemingly increased efficacy of ribavirin therapy may still be totally attributable to chance.

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References


Ribavirin in Crimean-Congo Hemorrhagic Fever: Primum Non Nocere

To the Editor—We read the comment about our manuscript that was published 5 years ago, which was the first report on Crimean-Congo Hemorrhagic Fever (CCHF) from Turkey [1]. We hope to correct the point of view presented by Hayran and Aşçıoğlu, to avoid any misinterpretation.

Hayran and Aşçıoğlu criticized our manuscript because of the lack of statistical inference. In this study [1], we did not declare that the ribavirin was effective in the treatment of CCHF with statistical significance. However, it is known that type I error is closely related to the sample size of the study. Thus far, no studies of CCHF have had a sample size sufficient to reach statistical significance; in other words, the sample size has been such that the role of chance cannot be minimized to an acceptable level, such as a type I error level of 5% with a power of 80%. One of the earliest reports on the benefits of ribavirin in CCHF only included 3 severely diseased health care workers, and there was no control group [2]. The report of Mardani et al [3] supported the beneficial use of ribavirin. The results of our study [1] were also consistent with these previous reports.

In our study [1], we included 35 patients with CCHF; 30 cases were severe, and 5 were mild. The overall fatality rate was 2.8% (1 of 35 patients died). Among these, 27 patients were not given ribavirin, because the diagnosis of CCHF was not possible historically. Only 8 patients with severe CCHF received ribavirin. The group of patients who received ribavirin were compared to the group who did not in terms of fatality rate. To overcome the case-mix problem, we grouped the mild and severe cases separately; we did perform the comparison among patients with severe CCHF; then we compared fatality rate for the group that received ribavirin (0 [0%] of 8 patients died) with that for the group that did not receive ribavirin (1 [4.5%] of 22 patients died). We preferred not to provide a P value for this comparison because of small sample size and because there was only 1 outcome. The P