improves outcomes as compared with less complete revascularization.2 However, our trial involved highly experienced interventional cardiologists and surgeons who attempted to maximize the completeness of revascularization. Substantially more complete PCI-based revascularization is therefore unlikely in other institutions.

Serruys and Farooq suggest that the SYNTAX score may have had a role in selecting patients in the FREEDOM trial in whom PCI may have been an appropriate procedure. In the group of patients with a low SYNTAX score, the incidence of the primary outcome of death, myocardial infarction, or stroke at 6 months was 6 percentage points lower in the CABG group than in the PCI group. In addition, the test for heterogeneity was nonsignificant and suggests that there was no significant interaction with the SYNTAX score in the comparison of PCI with CABG. Since the point estimates of all subgroups in Figure 2 of the article are trending in the same direction, the finding of the superiority of CABG is robust. Of course, subgroups can be defined for which inadequate power is available to fully study the question posed. Serruys and Farooq have defined such a subgroup.3 Even here, the data are consistent with the results in the full FREEDOM cohort.

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Since publication of their article, the authors report no further potential conflict of interest.


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Factor VIII Products and Inhibitors in Severe Hemophilia A

TO THE EDITOR: Gouw et al. (Jan. 17 issue)1 have provided a much-needed comparison of the risk of inhibitor development associated with different factor VIII molecules in previously untreated children with severe hemophilia A. We anticipate obvious concerns in the hemophilia community regarding the unexpected finding of a higher rate of inhibitor development for second-generation recombinant factor VIII, and we would like to comment on the strength of the association. The absence of a biologic hypothesis, a risk ratio of less than 2 (unadjusted lower limit, 0.91; adjusted, 1.09), and the omission of 20.4% of patients (74 eligible patients were excluded and 58 patients did not reach the study end point) leave the association weak and questionable. A sensitivity analysis comparing the first and second half of patients enrolled should be performed to determine whether in such a long study any temporal trends influenced recombinant concentrate use and outcome assessment. Comparing the recombinant concentrates produced in baby-hamster–kidney (BHK) cells and Chinese-hamster–ovary (CHO) cells would test a more plausible hypothesis2 than the “generation” effect. We strongly agree with the authors in recommending extreme caution in transferring these unexpected research results to decision making in clinical practice.

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The Authors Reply: We agree with Iorio et al. that our study findings should be interpreted with caution, but we want to emphasize that the increased risk of inhibitor development associated with the second-generation, full-length factor VIII product cannot be explained by any other plausible factor. We adjusted for all known confounders and included the 58 patients who had not yet reached the study end point; we believe that the reasons for the exclusion of the remaining 74 patients (11.4%) — including the absence of informed consent, unavailable data, and the fact that these patients had not yet been treated — render their exclusion highly unlikely to have caused selection bias. Temporal trend analysis, as suggested, is complicated by the later introduction of the third-generation product. Moreover, we adjusted for factors that could have changed over time, including the start of prophylaxis and dosage. We feel that no meaningful new information can be obtained by adding this analysis to the overall study. With respect to cell lines, only one company produced recombinant factor VIII products that were derived from BHK cells,1,2 which means that cell-line–based analysis would not have yielded different results.

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Abiraterone in Metastatic Prostate Cancer

To the Editor: In their article on the COU-AA-302 study, Ryan et al. (Jan. 10 issue) report improved progression-free survival with abiraterone–prednisone as compared with prednisone alone among patients with metastatic castration-resistant prostate cancer who had not received chemotherapy. It would be useful to know the views of the authors on clinical measurements (e.g., the Gleason score and pretrial prostate-specific antigen [PSA] doubling time) that could guide therapy and predict the response to abiraterone over prednisone alone or chemotherapy.

The prednisone-alone group in this study had a prolonged survival as compared with the survival reported in previous trials. Could such minimally symptomatic patients begin to receive prednisone alone initially, with the addition of abiraterone on disease progression? Moreover, the median duration of prednisone use was more than 2 years in the abiraterone group. Chemotherapy with a taxane, usually administered with prednisone, was subsequently administered to the majority of patients.

Hypogonadism from antiandrogen therapy and long-term glucocorticoid therapy increase the risk of osteoporosis and fractures among men.2,3 The authors should discuss the frequency of osteoporosis, avascular necrosis of the femoral head, and skeleton-related events such as pathologic fractures. Finally, initiation of bisphosphonates after randomization was precluded. Did the trial patients receive inhibitors of receptor activator of nuclear factor κB ligand or bisphosphonates when osteoporosis developed?

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To the Editor: Abiraterone extends life in patients with metastatic castration-resistant prostate cancer. We have treated a 63-year-old man whose