tions in *TP53* and the other genes of interest after allogeneic hematopoietic stem-cell transplantation.

Xiaolin Zhu, M.D., Ph.D.

University of Texas Southwestern Medical Center
Dallas, TX
xiaolin.zhu@alumni.duke.edu

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THE AUTHORS REPLY: In response to Fozza: we found no association between acute GVHD (<100 days after transplantation) and mutation clearance 30 days after transplantation with the use of a variant allele frequency threshold of 0.5% (P=0.64). Approximately 67% (95% confidence interval [CI], 52 to 79) of patients with a mutation with a maximum variant allele frequency of less than 0.5% at day 30 and approximately 59% (95% CI, 41 to 76) of patients with a mutation with a maximum variant allele frequency of at least 0.5% at day 30 had acute GVHD. Our analysis of chronic GVHD was limited by the availability of data for the cohort. A large prospective clinical trial incorporating detection of mutations after transplantation with uniform collection of standardized data on GVHD would be ideal to study this question.

In response to Zhu: we were unable to perform a stratified analysis because the sample sizes in the four groups defined by the presence or absence of mutations with a maximum variant allele frequency of at least 0.5% at day 30 and the presence or absence of a *TP53* mutation were too small to separately estimate the combinatorial effects of these two factors. However, several statistical models indicate that a mutation with a maximum variant allele frequency of at least 0.5% at day 30 provided a significantly better association with disease progression in our study than *TP53* mutation status. We used the likelihood ratio test to compare two univariate models (one with a mutation with a maximum variant allele frequency at day 30 and one with *TP53* mutation status as the sole predictors) with a bivariate model that included both variables. Results of the likelihood ratio test indicated that a mutation with a maximum variant allele frequency at day 30 alone provided as much information about disease progression as a mutation with a maximum variant allele frequency and *TP53* mutation status together. Although removal of *TP53* from the bivariate model had no detectable effect (P=0.14), removal of a mutation with maximum variant allele frequency resulted in a model that fit less well and contained less information about progression (P=0.002). These results, combined with our multivariable analysis, suggest that the persistence of any disease-associated mutation provides information about progression in addition to that provided by *TP53* mutation status.

Meagan A. Jacoby, M.D., Ph.D.
Kathryn Trinkaus, Ph.D.
Matthew J. Walter, M.D.

Washington University School of Medicine
St. Louis, MO
mjwalter@wustl.edu

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Heat-Stable Carbetocin to Prevent Postpartum Hemorrhage

TO THE EDITOR: Widmer et al. (Aug. 23 issue)[1] discuss the use of carbetocin versus oxytocin to prevent hemorrhage after vaginal birth. Carbetocin has the potential to be an important uterotonic contribution to the compendium of medicines administered to prevent postpartum hemorrhage. However, carbetocin cannot fully replace oxytocin but should instead be considered part of a suite of maternal medicines (including uterotonics and tranexamic acid) used in a collective strategy to reduce deaths from postpartum hemorrhage, which is still the leading cause of maternal death. The administration of carbetocin or oxytocin during the third stage of labor can prevent postpartum hemorrhage; when these medicines are not available, misoprostol is also effective. Either oxytocin or misoprostol can be used for induction, with misoprostol being the first-line medicine identified by the World Health Organization for use in low- and middle-income

countries. It is important to note that only oxytocin can be used for labor augmentation; carbetocin and misoprostol cannot be substituted for oxytocin for this purpose, in part because of their long half-lives. It is essential that clinicians, pharmacists, procurers, policymakers, program managers, and others be aware of and use this information regarding the key roles of these medicines to guide their work in counseling clients and procuring medicines.

Deborah Armbruster, C.N.M., M.P.H.

U.S. Agency for International Development
Washington, DC
darmbruster@usaid.gov

Thomas Burke, M.D.

Harvard Medical School
Boston, MA

Andrew Weeks, M.D.

University of Liverpool
Liverpool, United Kingdom

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Dr. Weeks reports being one of the inventors of a device used to treat postpartum hemorrhage and serving as scientific advisor to Azanta. No other potential conflict of interest relevant to this letter was reported.

1. Widmer M, Piaggio G, Nguyen TMH, et al. Heat-stable carbetocin versus oxytocin to prevent hemorrhage after vaginal birth. N Engl J Med 2018;379:743-52.

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THE AUTHORS REPLY: Our trial showed that heat-stable carbetocin is noninferior to oxytocin in preventing postpartum hemorrhage. Heat-stable carbetocin maintains its stability at 40°C for 6 months and at 30°C for more than 3 years[1] and is not associated with the concerns about quality attached to oxytocin and other uterotonics. It is for these reasons that the use of heat-stable carbetocin in settings without reliable cold-chain transport and storage could be of substantial benefit to women. We agree with Armbruster and colleagues that oxytocin has other indications for use in relation to childbirth. Policymakers should make efforts to secure adequate cold-chain transport and storage for oxytocin to ensure its quality regardless of the indication. Heat-stable carbetocin should be regarded as part of a suite of maternal medicines used collectively to reduce the risk of death from postpartum hemorrhage.

A. Metin Gülmezoglu, M.D., Ph.D.
Mariana Widmer, M.Sc.

World Health Organization
Geneva, Switzerland
gulmezoglum@who.int

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1. Malm M, Madsen I, Kjellström J. Development and stability of a heat-stable formulation of carbetocin for the prevention of postpartum haemorrhage for use in low and middle-income countries. J Pept Sci 2018;24(6):e3082.

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Case 28-2018: A Man with Epistaxis, Pain and Erythema of the Forearm, and Pancytopenia

TO THE EDITOR: In the Case Record, Iyasere et al. (Sept. 13 issue)[1] describe a patient who received a diagnosis of hairy-cell leukemia complicated by a bacterial infection. Hairy-cell leukemia commonly manifests with infection, an important cause of illness and potential death in patients with this form of cancer. We have some comments on the management of this condition. Although a 7-day course of cladribine is shorter than a course of pentostatin, myelosuppression can be profound and prolonged with both purine nucleoside analogues; recovery of the immune system is not shorter with cladribine than with pentostatin. In the initial trials of cladribine involving patients with hairy-cell leukemia, those with active infection were excluded from enrollment.[2,3]

In contrast to the recovery of the immune system associated with purine nucleoside analogues, the median time to neutrophil recovery in patients who have received the BRAF inhibitor vemurafenib is approximately 4 weeks.[4] Although vemurafenib is not approved for the treatment of hairy-cell leukemia, it has been used off-label in selected patients with hairy-cell leukemia and active infection as a bridge to neutrophil recovery and control of infection. Eradication of infection in these patients before the administration of myelosuppressive therapy is of prime impor-