Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

centrally managed (unintegrated) health programmes and have actively worked to integrate research and health care[10] and improve existing health programmes instead of developing parallel systems. This improvement requires long-term commitment and investment from partners to actively explore collaboration, and that funders, including governments, recognise the mutually beneficial value of research and health care. Engaging governments and other partners is essential to providing the necessary resources for the improvement of diagnostic services for the three diseases that are key to advancing haematology care in sub-Saharan Africa, and will also assist in collaborative research and establishment of networks to find newer and better ways of managing diseases that are a priority in the region.[11] Networks can achieve success in improving access and equity of medicines and vaccines through cost reduction within government programmes. The COVID-19 pandemic has highlighted the importance of manufacturing vaccines in Africa, emphasising the importance of producing non-high-profit medicines, such as hydroxyurea (hydroxycarbamide).

Important advances have been made in haematology in sub-Saharan Africa, as highlighted by these three conditions and blood transfusion as a core component. Nevertheless, opportunities for further learning, review, and progress in these and other areas of haematology remain. Furthermore, capitalising on available opportunities will require further elucidation of the crucial role of research and partnerships in eliciting meaningful improvements of haematological care in Africa.

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Antibody response after third BNT162b2 dose in recipients of allogeneic HSCT

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We previously reported a weak immune response after two doses of the vaccine against SARS-CoV-2 in 36 (41%) of 88 recipients of allogeneic hematopoietic stem-cell transplantation (HSCT).[1] Together with the poor prognosis of COVID-19 infection in recipients of HSCT[2,3] and solid-organ transplantation, this result prompted the French National Authority of Health to recommend the use of a third dose in patients who are immunosuppressed and who were not responding after a standard two-dose vaccination.[4]

Here, we report the humoral response in patients who were recipients of HSCT in the Haematolgy Department of the Henri Mondor University Hospital (Créteil, France) and who were given three doses of the BNT162b2 mRNA vaccine (Pfizer-BioNTech, Mainz, Germany) on the basis of their quantitated low titre of anti-spike glycoprotein-specific IgG (Spike protein-receptor-binding domain [S-RBD]) of less than 4160 AU/mL at 28 (SD 6) days after the second vaccine dose. This threshold of 4160 AU/mL is recommended by the manufacturer and is used as a surrogate

measure of vaccine protection because it corresponds to a 0·95 probability of obtaining an in-vitro plaque reduction neutralisation test.[1,5] In our department, vaccination was systematically offered to patients, whatever their transplantation date, starting from 3 months after HSCT. The first two doses were given 1 month apart, and the third dose was administered 51 (SD 22) days after the second dose. IgG (S-RBD) titres were quantitated at a mean of 26 (SD 6) days after the third vaccine dose, using the Abbott Architect SARS-CoV-2 IgG Quant II assay (Abbott, Sligo, Ireland). One patient who had transient facial paralysis after the second vaccine dose refused to receive a third vaccine dose, despite low titre of anti-spike IgG after vaccination. All patients aged older than 18 years receiving a third vaccine dose were eligible for the present study. Clinical and biological data were collected retrospectively from medical charts. According to French law, institutional review board approval was not required, because this was an anonymous retrospective study. Categorical variables were compared by Fisher exact tests. Comparisons of continuous variables means were done using Student's *t* tests. Multivariable analysis included risk factors with a significance of p<0·05 in univariate comparisons and used a logistic regression model. All tests were two-sided and the type 1 error rate was fixed at 0·05.

See Online for appendix

42 patients (median, 59 years [IQR 50–64]; 27 [65%] male, 15 [35%] female) were given three doses of the BNT162b2 mRNA vaccine. All patients received a transplantation for a haematological malignancy in remission, and vaccination was initiated in the first year after HSCT in 22 (52%) of 42 patients. The third dose led to a significant increase in anti-SARS-CoV-2 antibodies with IgG (S-RBD) increasing from 737 AU/mL (SD 1009; 2·9 Log, SD 3·0) to 11 099 AU/mL (SD 18 607; 4·05 Log, SD 4·3; p=0·00069; figure). However, only 20 (48%) of 42 patients reached the protective threshold of 4160 AU/mL or more.

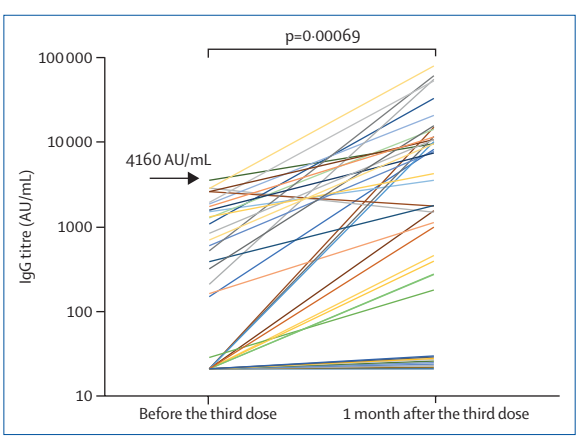

Figure: **Anti-SARS-CoV-2 antibodies in 42 patients who received HSCT**

In the univariate analysis, the two factors associated with the rise to the protective antibody threshold among the patient-associated and transplantation-associated factors were a B-cell count of more than 0·25 g/L in the peripheral blood at the time of the third vaccination (p=0·0032) and an IgG (S-RBD) concentration of more than 1000 AU/mL after the second vaccine dose (p=0·019). This IgG threshold was chosen on the basis of an independent study that used the same Abbott Architect SARS-CoV-2 IgG Quant II assay as in the present study, and which showed that a IgG (S-RBD) concentration of 1000 AU/mL is able to neutralise SARS-CoV-2 circulating variants of concern.[6] In a multivariable analysis, only a B-cell count of more than 0·25 g/L in the peripheral blood at the time of the third vaccination was associated with a humoral response (odds ratio 7·1 [95% CI 1·5–34·1], p=0·0016; appendix). We did not identify any transplantation-associated or disease-associated characteristics predicting the response to the booster third vaccine dose (appendix). Neither patient or donor age or sex, nor the interval between HSCT and the initiation of vaccination (less than or more than 12 months), were predictive in this primary analysis. With a median follow-up of 53 days (IQR 44·5–59·5) after the third vaccine dose, we did not observe any serious adverse event or COVID-19 infection within the vaccination schedule. We neither observed any case of graft-versus-host disease induction nor graft-versus-host disease worsening that could be associated with the vaccination schedule in this cohort.

This study showed that administration of a third dose of BNT162b2 improved the immunogenicity of the vaccine in recipients of HSCT, as reported in patients of solid-organ transplantation.[7,8] However, approximately half (52%) of the patients requiring a third dose still had low concentrations of anti-SARS-CoV-2 antibodies thereafter, emphasising the importance of barrier measures and the vaccination of relatives. Because the B-cell immune status at the time of vaccination is the main factor predicting a humoral response in these patients, further studies will be needed to evaluate the protective effect of delayed

vaccine doses given after the B-cell compartment has recovered.

One limitation of this study is the absence of assays for neutralising antibodies. However, the Abbott assay quantifies anti-S-RBD antibodies, which include most neutralising antibodies generated after a natural infection or vaccination. This assay has been tested and validated against the WHO international standard, because it showed excellent correlation with the results provided by the WHO standard. Another limitation is the absence of B-cell memory and T-cell functional responses. In the present study, time since HSCT did not affect the humoral response after the third vaccine dose. With regard to the response after two vaccine doses, we previously identified that an interval of more than 12 months between HSCT and vaccination correlated with protective IgG(S-RBD) titres in univariate analyses.[1] However, despite this time variable being predictive in the univariate analysis, it was not significant in the multivariable analysis, unlike the lymphocyte count in the peripheral blood at vaccination initiation and the systemic immunosuppressive drugs received within the 3 months before vaccination.[1] Similarly, in one large study of 885 patients with haematological malignancies, including patients who had and had not undergone transplantation, the treatments actively received at time of vaccination were the primary determinants of the antibody response.[9] Nine cases of breakthrough severe SARS-CoV-2 infections were reported in this previous study, which we did not observe in the present study, occurring in fully vaccinated patients who had mostly low anti-S-RBD IgG antibody titres.

The longevity of the vaccine-induced immunity will be a key variable in the protection against SARS-CoV-2 infections, in the general population and specifically in patients with cancer and who have undergone HSCT. Because long-term protection after other types of vaccination is known to be hard to obtain in patients who receive HSCT,[10] specific studies will be needed to address this question, with the aim of defining the best booster programme to provide a long-term protection against COVID-19.

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