blood advances

Celebrating a year of clinical and translational research in *Blood Advances*

With the close of 2022, we wanted to take stock of the sixth year for *Blood Advances*. This has been another fantastic year for the journal. We continue to receive an impressive number of submissions both cascaded from our sister journal *Blood* and submitted directly to *Blood Advances*. In 2022, our impact factor increased to 7.637, which now ranks us in the top 20% of hematology-based journals.

This year showed growth not only in terms of our impact factor but also in our editorial team. It was with great excitement and appreciation that Andrew Weyrich accepted the role of deputy editor-in-chief of the journal. In addition, we welcomed 4 new associate editors to the team: Georg Lenz, Shannon Maude, Olatoyosi Odenike, and Alisa Wolberg. In addition, Rayne Rouce accepted the position as our new commissioning editor. We would also like to take this opportunity to profoundly thank our entire editorial team which includes our other associate editors: Michael DeBaun, Geoffrey Hill, Leslie Kean, Claudia Lengerke, Ryan Morin, Nikhil Munshi, Margaret Ragni, Wendy Stock, and Constantine Tam.

The clinical guidelines, which are developed by expert committees supported by the American Society of Hematology (ASH), continue to be among our most highly cited articles. This emphasizes how important such guidelines are to our readership along with the systematic reviews that support the recommendations. To that end, more guidelines are planned for next year along with updates to the current guidelines. Given this strong clinical interest by our readership, this editorial serves to highlight some of our highest cited articles that had a clinical/translational research focus spanning all spectrums of the field, including both malignant and classical hematology.

Selected papers: malignant hematology

Two of the highly cited malignancy-focused papers focused on immunotherapy in B-cell acute lymphoblastic leukemia (B-ALL). Specifically, an article by Fabrizio et al[1] entitled "Optimal fludarabine lymphodepletion is associated with improved outcomes after CAR T-cell therapy" details whether optimal fludarabine exposure could improve outcomes in patients with B-ALL after CD19 chimeric antigen receptor (CAR) T-cell therapy. The authors found that patients with suboptimal fludarabine exposure had higher rates of relapse, relapse/B-cell aplasia, and death than patients with optimal fludarabine exposure, suggesting that future studies are warranted to prospectively investigate lymphodepletion regimens and exposures across different disease types. In addition, Locatelli et al[2] report the final analysis of the RIALTO expanded-access study of blinatumomab for children with relapsed/refractory Ph^- $CD19^+$ ALL in their article, "Blinatumomab in pediatric relapsed/refractory B-cell acute lymphoblastic leukemia: RIALTO expanded access study final analysis." The authors showed that blinatumomab treatment was associated with a low incidence of grade 3 to 4 cytokine release syndrome and neurologic events. As a secondary assessment, blinatumomab response was independent of genetic abnormalities, and the best outcome was observed in patients with minimum residual disease–negative complete remission followed by allogeneic hematopoietic stem cell transplant.

Broadening from ALL to acute myeloid leukemia (AML) but staying within the immunotherapy theme, an article by Kinoshita et al,[3] "Outcome of donor-derived TAA-T cell therapy in patients with

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high-risk or relapsed acute leukemia post allogeneic BMT," evaluates the safety and clinical outcomes after administration of a donor-derived T-cell therapy that targeted 3 tumor-associated antigens (TAA-T) in adult and pediatric patients with acute leukemia (ALL and AML) who relapsed or were at a high risk of relapse after allogeneic bone marrow transplant (BMT). The investigative team showed that the ex vivo expanded TAA-T cells were safe and well-tolerated, and they also observed sustained continued complete remissions in high-risk and relapsed patients in whom persistence of the adoptively transferred TAA-T cells lasted up to at least 1-year after infusion.

Also focused on the post-BMT/acute leukemia population, the article by Qayad et al[4], "Abatacept for GVHD prophylaxis can reduce racial disparities by abrogating the impact of mismatching in unrelated donor stem cell transplantation," details a post hoc comparison in the mismatched unrelated donor (MMUD) vs matched unrelated donor (MUD) setting. Specifically, recipients who received an MMUD graft and received the costimulation blockade agent, cytotoxic T-cell lymphocyte-4-immunoglobulin (abatacept) with standard calcineurin inhibitor and methotrexate graft-versus-host disease (GVHD) prophylaxis (CNI/MTX), were compared with recipients who received an MUD hematopoietic cell transplant (HCT) with CNI/MTX/placebo (MUD/placebo). Overall, the report suggests that adding abatacept to standard CNI/MTX mitigates the disadvantages of donor mismatching by markedly reducing the risks of severe acute GVHD and nonrelapse mortality without increasing the risk of relapse.

It is unknown in the pediatric AML field whether body composition changes in children during the course of treatment, and if alterations in body mass index (BMI) are associated with adverse outcomes. To address this knowledge gap, in an article entitled "Changes in body mass index, weight, and height in children with acute myeloid leukemia and the associations with outcome," Iijima et al[5] longitudinally assessed the association of weight, height, and BMI with adverse outcomes in more than 200 pediatric patients with AML. The investigators identified several correlations between body composition changes and clinical outcomes in children with AML, including an association of a decreased weight Z-score during induction therapy that tracked with gastrointestinal, hepatic, and infection toxicities in subsequent treatments and with death in remission. The study highlights the importance of closely monitoring weight during the initial treatment approach and the relevance of a close follow-up of weight and height, as well as an endocrine evaluation, after completion of therapy.

Moving from acute to chronic leukemia, the article "Up to 8-year follow-up from RESONATE-2: first-line ibrutinib treatment for patients with chronic lymphocytic leukemia (CLL)" from is the latest update on RESONATE 2, the pivotal study that led to approval of ibrutinib for first-line CLL.[6] With an 8-year follow-up, the median progression free survival (PFS) has still not been reached. However, only 42 patients still remain on ibrutinib with the major reason for discontinuation being adverse events. Overall, the authors conclude that this study demonstrates sustained benefit for patients with CLL (including those with high-risk genomic features) receiving ibrutinib as first-line treatment.

The remaining 2 selected articles that are focused on malignant disease again have an immunotherapy focus. In the article "Polatuzumab vedotin plus bendamustine and rituximab in relapsed/refractory DLBCL: survival update and new extension cohort data," an international group of lymphoma investigators report additional follow-up on patients enrolled in a randomized phase 1b/11 trial of polatuzumab bendamustine-rituximab (Pola-BR) vs bendamustine-rituximab (BR) that led to accelerated approval for the triplet in a third line by the Food and Drug Administration (FDA) and second line by European Medicines Agency (EMA).[7] The group now reports the outcomes for a large expansion cohort of the polatuzumab BR arm and confirm the previously reported high complete response rate and a subset of relatively durable responses in this very high-risk patient population. Finally, the article "Langerhans dendritic cell vaccine bearing mRNA-encoded tumor antigens induces antimyeloma immunity after autotransplant" describes the use of a dendritic cell–based vaccine involving Langerhans dendritic cells electroporated with 3 prominent myeloma-associated antigens administered post-transplant with an assessment of immunologic and clinical immunologic efficacy.[8] The study describes the immunologic analysis, including evaluating the expansion of antigen specific T cells and the clonotypic analysis of the T-cell repertoire. The data support a robust vaccine-induced immunologic response particularly in the CD4 compartment and interestingly, the vaccine arm showed an improved PFS compared to the control cohort.

Selected papers: classical hematology

Within the collection of the classical hematology–focused clinical trial papers, this year has continued to stimulate the submission of COVID-19–related manuscripts to *Blood Advances*. One highly cited article that we selected entitled, "COVID-19 vaccination in patients with immune thrombocytopenia," evaluates postvaccine platelet counts in patients with immune thrombocytopenia vs healthy controls who received the SARS-CoV-2 vaccination.[9] Interestingly, platelet counts decreased by 6.1% after vaccination with no difference in decreases between the groups.

In addition to manuscripts focused on COVID-19, *Blood Advances* received a growing number of reports focused on sickle cell disease (SCD). Among these is the article "Deferiprone vs deferoxamine for transfusional iron overload in SCD and other anemias: a randomized, open-label noninferiority study," demonstrating that chronic transfusion of deferiprone is a useful treatment for patients with SCD and that the safety profile of the treatment was tolerable and similar to previous reports in patients with thalassemia syndromes.[10] This study provided a much needed contribution on how to treat transfusional iron overload in SCD.

The treatment of hemophilia also gained momentum, as evidenced by the report highlighted here. "Efanesoctocog alfa for hemophilia A: results from a phase 1 repeat-dose study" found that 4 once-weekly doses of efanesoctocog alfa were well-tolerated and safe while providing highly sustained factor VIII activity.[11] These findings indicated that efanesoctocog alfa may improve bleeding in patients with hemophilia A, and the results formed the basis for drug dosing that is being used for a current phase 3 study.

When it comes to phasing out classical drugs, we witnessed a study in the article "Apixaban compared with warfarin to prevent thrombosis in thrombotic antiphospholipid syndrome: a randomized trial" showing that apixaban may not be routinely substituted for warfarin to prevent recurrent thrombosis among patients with thrombotic antiphospholipid syndrome.[12] Although the randomized trial ended prematurely, enough information was collected to show that stroke occurred in 6 of 23 patients randomized to apixaban compared with 0 of 25 patients randomized to warfarin.

In summary, we are enormously proud of the continued upward trajectory of *Blood Advances* that has increased our prominence in the field of hematology since its inception in 2016. We thank you for the honor and privilege of leading this journal. We are sincerely grateful to all of our authors and reviewers without whom none of the journal's success would be possible. In addition, we extend our gratitude and appreciation to the many people at ASH who work tirelessly behind the scenes and have also been so instrumental in shaping the journal into what it is today. Please remember, we are here to serve you, our readership of the entire ASH/hematology community and beyond. To that end, this is your journal, and it is only with your loyal support that we can continue to thrive. We thank you so much for your ongoing support and welcome your suggestions regarding content that may be of interest to you and the field.

Conflict-of-interest disclosure: C.M.B. is a scientific cofounder and scientific advisory board member for Catamaran Bio and Mana Therapeutics and also serves on the board of directors of Caballetta Bio and the data and safety monitoring board for SOBI and has stock in Neximmune and Repertoire Immune Medicine. A.W. declares no competing financial interests.

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