A phase I/II multicenter, open-label, dose escalation and randomized trial of BI 836858 in patients with low- or intermediate-1-risk myelodysplastic syndrome

Treatment for lower-risk myelodysplastic syndromes (MDS),[1] defined by the International Prognostic Scoring System as 'low-' and 'intermediate-1'-risk,[2] is aimed at managing symptomatic cytopenias.[3] Erythropoiesis-stimulating agents remain the first-line treatment for most patients, although lenalidomide is an established treatment option for patients with lower-risk MDS with deletion 5q and luspatercept has shown efficacy in transfusion-dependent MDS associated with ring sideroblasts and/or the *SF3B1* mutation.[4] Despite these advances, there remains a paucity of therapies for patients with lower-risk MDS that target the 'natural history' of the disease course. Myeloid-derived suppressor cells (MDSC) are a heterogeneous group of immature myeloid cells associated with immunosuppression, inflammation, and cancer. Aberrant accumulation of MDSC has been observed in the bone marrow of patients with MDS and is thought to play a pathogenic role in the suppression of hematopoiesis.[5-7] The myeloid differentiation antigen CD33, an established drug target in acute myeloid leukemia,[8-10] is highly expressed on MDSC isolated from patients with MDS, thus warranting assessment of CD33-targeted therapies as a means to 'suppress the suppressor' and thereby facilitate erythropoiesis.[5]

BI 836858 is a fully humanized IgG1 unconjugated anti-CD33 monoclonal antibody.[11] Preclinically, BI 836858 reduced MDSC by antibody-dependent cellular cytotoxicity and prevented immune-suppressive cytokine secretion.[12] Here, we report the findings of an open-label, phase I/II dose-escalation study of BI 836858 in patients with transfusion-dependent low- or intermediate-1-risk MDS (NCT02240706).

Details of the study methodology are available on request. Briefly, BI 836858 was administered as a rate-controlled intravenous infusion on days 1 and 15 of a 28-day treatment cycle without premedication. In phase I, the starting dose was 20 mg and, in the absence of dose-limiting toxicities, dose escalation up to 320 mg was planned. Patients were eligible to receive up to eight repeated administrations of BI 836858 and could continue treatment beyond four cycles if they showed clinical benefit and if tolerability was acceptable, until progressive disease or other withdrawal criteria occurred. In phase II, patients were to be randomized to BI 836858 plus best supportive care or best supportive care alone. However, phase II of this trial was not conducted due to a decision by the sponsor to terminate the study based on a lack of single-agent efficacy (hematologic response) in the dose-escalation phase.

The primary endpoints for the study were the maximum tolerated dose and number of patients with dose-limiting toxicities during the period of evaluation of maximum tolerated dose. Secondary endpoints included: red blood cell transfusion independency; neutrophil, platelet and erythroid hematologic improvement; time to the erythroid hematologic response; mean hemoglobin increase ≥1.5 g/dL; overall objective response; and duration of response. Thirty-six patients were enrolled and 27 patients were treated with BI 836858 (Table 1, *Online Supplementary Figure S1*). The median duration of treatment was 114 days (range, 1–811 days) and a median of five cycles were initiated (range, 1–29). Dose-limiting toxicities were observed in three of the 24 patients assessed during the period of evaluating the maximum tolerated dose (3 patients were excluded from evaluation of the maximum tolerated dose as they had <2 administrations in cycle 1 [1 patient in the 20 mg cohort and 2 patients in the 320 mg cohort]). One patient in the 80 mg group had a grade 3 decrease in neutrophil count and grade 4 sepsis during cycle 1, leading to a greater than 8-week delay in starting cycle 2. The patient recovered and received a reduced dose in cycle 2 (40 mg) but experienced recurrent grade 3 neutropenia and was unable to start cycle 3 and BI 836858 was discontinued in this patient. Two dose-limiting toxicities occurred during the phase I expansion cohort stage (320 mg): a grade 2 serious infusion-related reaction (IRR) leading to a dose reduction of BI 836858 and a grade 2 non-serious IRR leading to discontinuation of BI 836858. As only one dose-limiting toxicity was observed during dose escalation, the maximum tolerated dose was not determined.

No pharmacokinetic parameters were calculated. Individual plasma concentrations of BI 836858 were listed by dose group, cycle and day of treatment, as available. Bioanalytical results of further cycles were listed when available and all dose groups were represented in the lists. Table 2 shows a comparison of maximum plasma concentrations at day 1 and day 14 in cycle 1 and day 1 and day 14 in cycle 2. For the 20 mg dose group, the number of available bioanalytical results was not sufficient to calculate descriptive statistics at all time points. Maximum plasma concentrations increased in a more than dose-propor-

Table 1. Baseline demographics and characteristics of patients with low- or intermediate-1-risk myelodysplastic syndrome treated with BI 836858.

	BI 836858 dose					
Characteristic	**20 mg N=3**	**40 mg N=3**	**80 mg N=6**	**160 mg N=4**	**320 mg N=11**	**All patients N=27**
Male, N (%)	3 (100)	3 (100)	5 (83.3)	2 (50.0)	7 (63.6)	20 (74.1)
White race, N (%)	3 (100)	3 (100)	6 (100)	4 (100)	11 (100)	27 (100)
Age in years, median Aged <65 years, N (%) Aged ≥65 years, N (%)	70.0 0 3 (100)	77.0 0 3 (100)	79.5 1 (16.7) 5 (83.3)	67.0 2 (50.0) 2 (50.0)	76.0 0 11 (100)	76.0 3 (11.1) 24 (88.9)
ECOG PS, N (%) 0/1 2	 2 (66.7)/1 (33.3) 0	 1 (33.3)/2 (66.7) 0	 1 (16.7)/5 (83.3) 0	 2 (50.0)/2 (50.0) 0	 0/10 (90.9) 1 (9.1)	 6 (22.2)/20 (74.1) 1 (3.7)
IPSS category, N (%) Low/Int-1	 3 (100)/0	 1 (33.3)/2 (66.7)	 3 (50.0)/3 (50.0)	 2 (50.0)/2 (50.0)	 4 (36.4)/7 (63.6)	 13 (48.1)/14 (51.9)
Revised IPSS category, N (%) Very low Low Intermediate High Missing	 0 3 (100.0) 0 0 0	 1 (33.3) 1 (33.3) 0 0 1 (33.3)	 1 (16.7) 1 (16.7) 1 (16.7) 0 3 (50.0)	 1 (25.0) 0 1 (25.0) 1 (25.0) 1 (25.0)	 2 (18.2) 2 (18.2) 2 (18.2) 0 5 (45.5)	 5 (18.5) 7 (25.9) 4 (14.8) 1 (3.7) 10 (37.0)
Previous MDS therapy: yes, N (%)	2 (66.7)	2 (66.7)	6 (100)	3 (75.0)	11 (100)	24 (88.9)
N. of previous MDS therapies, median (range)	2.0 (1-3)	2.5 (2-3)	2.0 (1-7)	4.0 (4-6)	3.0 (1-5)	3.0 (1-7)

ECOG PS: Eastern Cooperative Oncology Group performance status; Int-1: intermediate-1; IPSS: International Prognostic Scoring System; MDS: myelodysplastic syndromes.

Table 2. Comparison of maximum plasma concentrations (C_{max}) of BI 836858 in cycles 1 and 2.

	Plasma concentrations			
	Cycle 1		Cycle 2	
Dose (mg)	**Day 1, 6 h (ng/mL)**	**Day 14, 6 h (ng/mL)**	**Day 1, 6 h (ng/mL)**	**Day 14, 6 h (ng/mL)**
20	-	-	1550	-
40	5270	5440	6160	6560
80	8310	12,400	14,900	16,700
160	43,600	56,200	57,300	67,100
320	64,200	82,700	88,700	91,900

tional behavior. Steady-state plasma concentration between cycles 1 and 2 was not proven with statistical significance for the 320 mg dose group, suggesting accumulation which may be expected with repeat IgG dosing, although pharmacokinetic assessments were not performed after cycle 2 to confirm achievement of steady state at later time points nor to confirm the half-life with this dosing regimen once every 14 days.

All treated patients experienced at least one adverse event; the most common adverse events were IRR (77.8%), decreased neutrophil count (29.6%), pyrexia (29.6%) and hyperglycemia (25.9%) (Table 3). Grade 3 and 4 adverse events were reported in 15 (55.6%) and six (22.2%) patients, respectively. There was no relationship between dose and incidence of adverse events. Twenty-four (88.9%) patients had adverse events considered related to BI 836858 (3 in the 20 mg cohort, 2 in the 40 mg cohort, 6 in the 80 mg cohort, 4 in the 160 mg cohort and 9 in the 320 mg cohort). The most common drug-related adverse events were IRR (77.8%), decreased neutrophil count

(22.2%), nausea (11.1%) and decreased white blood cell count (11.1%) (*Online Supplementary Table S1*). One patient (320 mg cohort) had an adverse event leading to dose reduction (grade 2 IRR, also reported as a dose-limiting toxicity). Five (18.5%) patients discontinued treatment due to adverse events: IRR and decreased white blood cell count in one patient, and IRR, decreased neutrophil count, non-cardiac chest pain and muscular weakness (each n=1). Serious adverse events were reported in 13 (48.1%) patients. Four serious adverse events were considered related to treatment (IRR [n=3] and sepsis [n=1]). There were no adverse events leading to death during the on-treatment period. IRR were generally mild, with only one patient (3.7%) reporting a grade 3 IRR (Table 3). IRR of grade 2 of higher occurred in 41% of patients.

No objective responses were reported. Furthermore, based on investigator assessment, hematologic improvement or red blood cell transfusion independence was not observed in any patients. One patient (160 mg cohort) had a mean hemoglobin increase of ≥1.5 g/dL; review of laboratory and transfusion data indicated that this patient likely qualified as having an erythroid hematologic response. This patient had received treatment for the longest period: 811 days.

The trial included a pharmacodynamic analysis of the impact of BI 836858 on CD33 expression on MDSC in bone marrow and peripheral blood by comparing levels of $CD33^{+}HLA\text{-}DR^{-}Lin^{-}$ MDSC to $CD33^{-}HLA\text{-}DR^{-}Lin^{-}$ leukocytes before and after treatment by fluorescence-activating cell sorting. While the absolute number of $CD33^{+}$ MDSC decreased with treatment in some patients (*Online Supplementary Figure S2*), $CD33^{-}$ leukocytes increased at the same time (*data not shown*), indicating that BI 836858 either masked or internalized CD33 molecules on MDSC but did not reduce the number of MDSC. Furthermore, natural killer (NK) cells are effector cells relevant for the

Table 3. All-cause adverse events, described by MedDRA preferred terms, and highest CTCAE grade in patients with low- or intermediate-1-risk myelodysplastic syndrome treated with BI 836858 (n=27). On-treatment period.

Adverse events	All grades, N (%)	Grade 1/2, N (%)	Grade 3, N (%)	Grade 4, N (%)
Total with adverse events	27 (100)	6 (22.2)	15 (55.6)	6 (22.2)
Infusion-related reaction	21 (77.8)	20 (74.0)	1 (3.7)	0
Neutrophil count decreased	8 (29.6)	0	5 (18.5)	3 (11.1)
Pyrexia	8 (29.6)	7 (25.9)	1 (3.7)	0
Hyperglycemia	7 (25.9)	4 (14.8)	3 (11.1)	0
Anemia	6 (22.2)	1 (3.7)	5 (18.5)	0
Dizziness	6 (22.2)	5 (18.5)	1 (3.7)	0
WBC count decreased	6 (22.2)	3 (11.1)	2 (7.4)	1 (3.7)
Diarrhea	5 (18.5)	5 (18.5)	0	0
Fatigue	5 (18.5)	5 (18.5)	0	0
Nausea	5 (18.5)	5 (18.5)	0	0
Peripheral edema	5 (18.5)	5 (18.5)	0	0
ALT increased	4 (14.8)	4 (14.8)	0	0
Cough	4 (14.8)	4 (14.8)	0	0
Fall	4 (14.8)	2 (7.4)	2 (7.4)	0
Headache	4 (14.8)	4 (14.8)	0	0
Iron overload	4 (14.8)	3 (11.1)	1 (3.7)	0
Muscular weakness	4 (14.8)	2 (7.4)	2 (7.4)	0
Platelet count decreased	4 (14.8)	2 (7.4)	2 (7.4)	0
Bone pain	3 (11.1)	3 (11.1)	0	0
Contusion	3 (11.1)	3 (11.1)	0	0
Decreased appetite	3 (11.1)	3 (11.1)	0	0
Dehydration	3 (11.1)	3 (11.1)	0	0
Dyspepsia	3 (11.1)	3 (11.1)	0	0
Upper respiratory tract infection	3 (11.1)	3 (11.1)	0	0
Vomiting	3 (11.1)	3 (11.1)	0	0

The adverse events shown are those occurring in >10% of patients for all grades. AE: adverse event; ALT: alanine aminotransferase; CTCAE: Common Terminology Criteria for Adverse Events; MedDRA: Medical Dictionary for Drug Regulatory Activities; MDS: myelodysplastic syndromes; WBC: white blood cell.

proposed BI 836858 mechanism of action. Accordingly, changes in NK cell numbers ($CD3^{-}CD16^{+}$ NK cells) and their activation status ($CD3^{-}CD16^{+}CD69^{+}$ NK cells) were also assessed. NK cell numbers were relatively low in all patients treated with BI 836858 and no increase in activated NK cells was observed (*Online Supplementary Figure S2*).

In summary, the maximum tolerated dose of BI 836858 was not reached at doses up to 320 mg in patients with low- or intermediate-1-risk MDS. The most common adverse event was IRR; the overall adverse event profile was consistent with that expected for patients with MDS. While the overall rate of IRR was high, the rate of grade 3 or higher IRR was consistent with that seen with the anti-CD33 agents gemtuzumab ozogamicin,[13] and lintuzumab.[13] No conclusions on the efficacy of BI 835858 in patients with MDS could be drawn due to premature termination of the trial; however, we observed an erythroid response in a single patient. A limitation of this study was the lack of enrollment of a diverse population of patients, with 100% Caucasian enrollment and imbalanced male/female representation (74% males/26% females). Nevertheless, in contrast to preclinical findings, pharmacodynamic analyses indicated that BI 835858 did not activate NK cells or reduce overall MDSC numbers in patients, despite a decrease in CD33 expression. These data do not support the proposed mode of action and are in line with the absence of clinical activity found in the study. The lack of activity in this lower-risk MDS population may reflect that other cell populations, in addition to MDSC, are implicated in the suppression of NK cells in MDS.[6] Moreover, MDSC are less predominant in lower-risk MDS than in higher-risk MDS, suggesting that they may play less of a role in the early stages of the natural history of the disease.[7]

BI 836858 was also assessed in a phase I dose escalation study in patients with relapsed or refractory acute myeloid leukemia (NCT01690624).[14] That study was also terminated prematurely. Consistent with our study, dose-limiting toxicity was not reached (although only doses up to 40 mg were assessed prior to trial termination) and BI 836858 had a predictable and manageable tolerability profile, with febrile neutropenia, nausea and IRR being among the most commonly reported all-cause adverse events. As with the current study, pharmacodynamic analysis suggested that there may be target engagement but BI 836858 did not increase activation of effector NK cells. This lack of effector cell function most likely underpins the lack of clinical activity. However, patients' outcomes may improve by targeting MDSC with targets other than CD33, or at an earlier stage of disease development rather than after failure of hypomethylating agents, as in this cohort, when poor outcomes are likely, even in patients with lower-risk MDS. Optimization of dosing in future studies may also contribute to improving hematopoesis in the setting of MDSC depletion.

In conclusion, evidence of $CD33^{+}$ MDSC target engagement in this study did not translate into a hematologic response and corresponding clinical efficacy. While development of BI 836858 has been discontinued, this trial demonstrates the feasibility and tolerability of MDSC-targeted approaches, using CD33, as applied in transfusion-dependent lower-risk MDS. It is unknown whether the lack of efficacy reflects a feature of the antibody itself, or whether targeting MDSC is insufficient to elicit an anti-tumor response. Alternative forms, differing from a 'naked' anti-CD33 antibody (e.g., antibody-drug conjugates or bispecific T-cell engaging antibodies) might be required to induce clinical efficacy. For example, recent preclinical data indicate that a bispecific CD33/CD3 antibody may confer anti-MDS activity.[15] Furthermore, given the complexity of the pathogenesis of lower-risk MDS, novel combination regimens incorporating anti-CD33 antibodies (e.g., with checkpoint inhibitors)[15] may be required to activate an immune response.

Authors

Rami S. Komrokji,[1] Hetty E. Carraway,[2] Ulrich Germing,[3] Martin Wermke,[4] Amer M. Zeidan,[5] Eric Fu,[6] Björn Rüter,[7] Ute Burkard,[7] Annika Osswald[7] and James M. Foran[8]

[1]Malignant Hematology Department, H Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; [2]Leukemia Program, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH, USA; [3]Department of Hematology, Oncology, and Clinical Immunology, Heinrich-Heine University Dusseldorf, Universitätsklinikum, Dusseldorf, Germany; [4]NCT/UCC-ECTU, Medical Faculty Carl Gustav Carus, Technical University, Dresden, Germany; [5]Department of Internal Medicine, Section of Hematology, Yale University School of Medicine, New Haven, CT, USA; [6]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; [7]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach/Riss, Germany and [8]Department of Hematology and Medical Oncology, Mayo Clinic, Jacksonville, FL, USA

Correspondence:
RAMI S. KOMROKJI - Rami.Komrokji@moffitt.org

https://doi.org/10.3324/haematol.2021.280500

Received: December 17, 2021.
Accepted: June 13, 2022.
Prepublished: June 23, 2022.

Disclosures

RSK reports a consulting or advisory role for Bristol Myers Squibb, Novartis, Daiichi Sankyo, Pfizer, Janssen, Agios, and Incyte; speakers' bureau fees from Novartis, Alexion Pharmaceuticals, and Jazz Pharmaceuticals; travel, accommodation, or expenses from Bristol Myers Squibb, Incyte, Alexion Pharmaceuticals, Novartis, Jazz Pharmaceuticals, and Daiichi Sankyo; and stock and other ownership interests in AbbVie. AZ reports honoraria from, and a consulting or advisory role for AbbVie, Otsuka, Pfizer, Bristol Myers Squibb, Jazz Pharmaceuticals, Incyte, Agios, Boehringer Ingelheim, Novartis, Acceleron Pharma, Astellas Pharma, Daiichi Sankyo, Cardinal Health, Taiho Pharmaceutical, Seattle Genetics, BeyondSpring Pharmaceuticals, Trovagene, Takeda, Ionis Pharmaceuticals, and Epizyme; research funding from Bristol Myers Squibb, AbbVie, Astex Pharmaceuticals, Pfizer, AstraZeneca/MedImmune, Boehringer Ingelheim, Trovagene, Incyte, Takeda, Novartis, Aprea Therapeutics, and ADC Therapeutics; and travel, accommodation, or expenses from Pfizer, Novartis, Bristol Myers Squibb, and Trovagene. HEC reports research funding for an investigator-initiated clinical trial from Celgene; sitting on advisory boards for Celgene, Agios, Bristol Myers Squibb, Daiichi, Jazz, Stemline, and Novartis; talks for Agios, Celgene, Agios, Jazz, Novartis, and Stemline; and sitting on an independent review committee for Abbvie, ASTEX, and Takeda. UG reports honoraria from Celgene, Novartis, and Jazz Pharmaceuticals; a consulting or advisory role for Celgene; and research funding from Celgene (institutional), and Novartis (institutional). MW reports honoraria from Bristol Myers Squibb; Merck, Roche, Novartis, Kite, Boehringer Ingelheim, and AstraZeneca; a consulting or advisory role for Bristol Myers Squibb, Novartis, Kite, Heidelberg Pharma, Roche, and Boehringer Ingelheim; and travel, accommodation, or expenses from Glenmark, Bristol Myers Squibb, and AstraZeneca. EF and BR report employment with Boehringer Ingelheim Pharmaceuticals, Inc. UB and AO report employment with Boehringer Ingelheim Pharma GmbH & Co. KG. JMF reports honoraria as a consultant for Revolution Medicines, Inc. and honoraria related to formal advisory activities from Bristol-Myers Squibb Company, Novartis AG, Pfizer Inc., and SERVIER. JMF's institution has received grant support related to research activities from AbbVie Inc., Actinium Pharmaceuticals, Inc., Aprea Therapeutics, Aptose Biosciences, Boehringer Ingelheim GmbH, H3 Biomedicine Inc., Kura Oncology, Inc., Takeda Oncology, Trillium Therapeutics Inc., and Xencor. The authors did not receive payment related to the development of the manuscript.

Contributions

RSK, EF, BR, UB, AO, and JMF designed the study. RSK, HEC, VG, MW, AZ, and JMF conducted the study. EF, BR, UB, and AO analyzed the data. The authors met criteria for authorship as recommended by the International Committee of Medical Journal Editors. All authors participated in manuscript development, approved the final version of the manuscript and agree to be accountable for all aspects of the work, which includes ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Acknowledgments

Medical writing assistance during the preparation of this manuscript was provided by Lynn Pritchard, of Ashfield MedComms, an Ashfield Health company, which was funded by Boehringer Ingelheim.

Funding

This work was supported and funded by Boehringer Ingelheim. Boehringer Ingelheim were given the opportunity to review the manuscript for medical and scientific accuracy as well as intellectual property considerations.

Data-sharing statement

To ensure independent interpretation of clinical study results, Boehringer Ingelheim grants all external authors access to relevant material, including participant-level clinical study data, as needed by them to fulfill their role and obligations as authors under the International Committee of Medical Journal Editors criteria. Clinical study documents and participants' clinical study data are available to be shared on request after publication of the primary manuscript in a peer-reviewed journal, and if regulatory activities are complete and other criteria met as per the BI Policy on Transparency and Publication of Clinical Study Data (see *https://www.mystudywindow.com/msw/datasharing*). *Bona fide*, qualified scientific and medical researchers are eligible to request access to the clinical study data with corresponding documentation describing the structure and content of the datasets. Upon approval, and governed by a legal agreement, data can be shared in a secured data-access system for a limited period of 1 year, which may be extended upon request. Prior to providing access, clinical study documents and data will be examined, and, if necessary, redacted and de-identified, to protect the personal data of study participants and personnel, and to respect the boundaries of the informed consent of the study participants. Researchers should use the *https://vivli.org/* link to request access to study data and visit *https://www.mystudywindow.com/msw/datasharing* for further information.

References

1. Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016;127(20):2391-2405.
2. Greenberg P, Cox C, LeBeau MM, et al. International scoring system for evaluating prognosis in myelodysplastic syndromes. Blood. 1997;89(6):2079-2088.
3. Hellstrom-Lindberg E, Tobiasson M, Greenberg P. Myelodysplastic syndromes: moving towards personalized management. Haematologica. 2020;105(7):1765-1779.
4. Fenaux P, Haase D, Santini V, et al. Myelodysplastic syndromes: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2021;32(2):142-156.

5. Chen X, Eksioglu EA, Zhou J, et al. Induction of myelodysplasia by myeloid-derived suppressor cells. J Clin Invest. 2013;123(11):4595-4611.
6. Carlsten M, Järås M. Natural killer cells in myeloid malignancies: immune surveillance, NK cell dysfunction, and pharmacological opportunities to bolster the endogenous NK cells. Front Immunol. 2019;10:2357.
7. Kittang AO, Kordasti S, Sand KE, et al. Expansion of myeloid derived suppressor cells correlates with number of T regulatory cells and disease progression in myelodysplastic syndrome. Oncoimmunology. 2016;5(2):e1062208.
8. Castaigne S, Pautas C, Terre C, et al. Effect of gemtuzumab ozogamicin on survival of adult patients with de-novo acute myeloid leukaemia (ALFA-0701): a randomised, open-label, phase 3 study. Lancet. 2012;379(9825):1508-1516.
9. Hills RK, Castaigne S, Appelbaum FR, et al. Addition of gemtuzumab ozogamicin to induction chemotherapy in adult patients with acute myeloid leukaemia: a meta-analysis of individual patient data from randomised controlled trials. Lancet Oncol. 2014;15(9):986-996.
10. Maakaron JE, Rogosheske J, Long M, Bachanova V, Mims AS. CD33-targeted therapies: beating the disease or beaten to death? J Clin Pharmacol. 2021;61(1):7-17.
11. Vasu S, He S, Cheney C, et al. Decitabine enhances anti-CD33 monoclonal antibody BI 836858-mediated natural killer ADCC against AML blasts. Blood. 2016;127(23):2879-2889.
12. Eksioglu EA, Chen X, Heider KH, et al. Novel therapeutic approach to improve hematopoiesis in low risk MDS by targeting MDSCs with the Fc-engineered CD33 antibody BI 836858. Leukemia. 2017;31(10):2172-2180.
13. Giles FJ, Cortes JE, Halliburton TA, et al. Intravenous corticosteroids to reduce gemtuzumab ozogamicin infusion reactions. Ann Pharmacother. 2003;37(9):1182-1185.
14. Vasu S, Altman JK, Uy GL, et al. A phase I study of the fully human, fragment crystallizable-engineered, anti-CD-33 monoclonal antibody BI 836858 in patients with previously-treated acute myeloid leukemia. Haematologica. 2021;107(3):770-773.
15. D'Souza S, Murata H, Jose MV, et al. Engineering of cell membranes with a bisphosphonate-containing polymer using ATRP synthesis for bone targeting. Biomaterials. 2014;35(35):9447-9458.