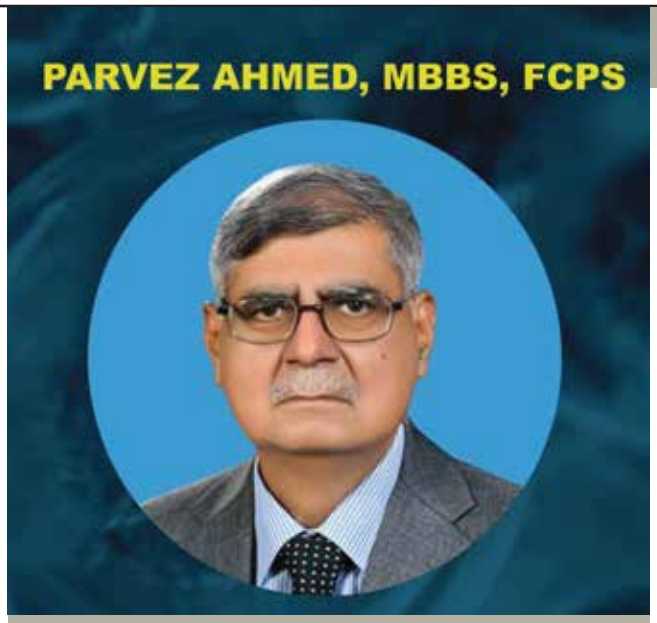
PATHWEL CENTER OF HEMATOLOGY
& BONE MARROW TRANSPLANT
A project of Pakistan Thalassaemia Welfare Society

PATHWEL *times*

BIMONTHLY NEWSLETTER 2026 | Jan - Feb | Vol 3.1



Global Recognition for Dr Parvez Ahmed: A Milestone for PATHWEL and Pakistan

On February 2, 2026, Dr Parvez Ahmed, MBBS, FCPS, received the Distinguished Service Award from the Center for International Blood and Marrow Transplant Research (CIBMTR) at the 2026 Tandem Meetings of American Society for Transplantation and Cellular Therapy (ASTCT) and CIBMTR®. The award recognizes his pioneering leadership in establishing and advancing clinical hematology and bone marrow transplantation in Pakistan.

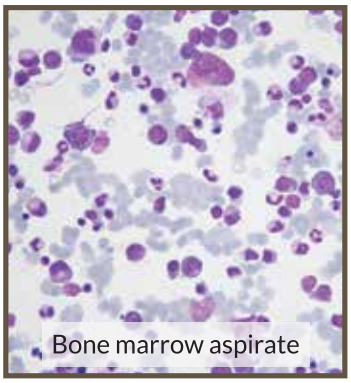
Dr Ahmed has played a central role in developing four transplant centers—three registered and in good standing with CIBMTR—and in strengthening national collaboration through the Pakistan Blood and Marrow Transplant (PBMT) group. His centers contribute data to global registries and collaborate with leading international organizations, ensuring Pakistan's active participation in worldwide transplant science.

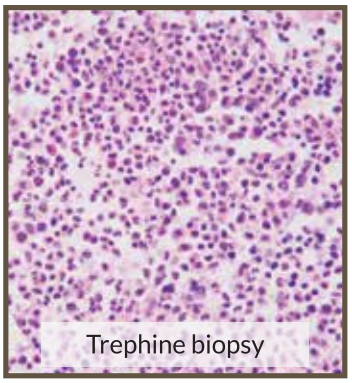
Currently serving at PATHWEL Center of Hematology and BMT and Quaid-e-Azam International Hospital, Dr Ahmed continues to champion excellence in patient care, education and research. This prestigious recognition is not only a personal milestone but a proud honor for PATHWEL and for Pakistan on the global stage. *(More on page three).*

Picture Quiz by Dr Laila Bahadur

A 21-year-old male presented with a history of chronic anemia since early childhood (from 2 years of age). His medical history was significant for progressive sensorineural hearing loss and insulin-dependent diabetes mellitus. On physical examination, he appeared pale, with no lymphadenopathy or hepatosplenomegaly. Complete blood count revealed a white blood cell count of 5.3 $\times 10^9$/L, hemoglobin was 6.7 g/dL, mean corpuscular volume (MCV) 104.2 fL, mean corpuscular hemoglobin (MCH) 31.2 pg, and platelet count 299 $\times 10^9$/L.

What is the most likely diagnosis? **(Answer on page 09)**


Bone marrow aspirate


Trephine biopsy

Two brand new ambulances generously donated by Askari Bank to PATHWEL Center of Hematology and Bone Marrow Transplant — strengthening our emergency response and ensuring safer, faster transport for patients in need.

Editor
Dr Syed Kamran Mahmood

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Mr. Muhammad Waseq Ayaz

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From Editor's Desk

If the Cure Exists, Why Not Here?

Across Pakistan, patients are asking a quiet but devastating question: if life saving treatments exist elsewhere, why are they unavailable here? A young man with relapsed cancer learns that his own immune cells could be engineered to fight his disease. Parents discover that a single gene therapy abroad might correct the mutation causing their child's suffering. These therapies are real. They are saving lives. Yet for most Pakistanis, they remain out of reach.

Families are told the same story—these treatments are too expensive, too complex, too technologically demanding. As a result, they fundraise desperately, sell property, seek visas, or resign themselves to limited options. Patients do not speak the language of regulatory frameworks or GMP facilities. They speak the language of hope.

Modern medicine has moved beyond managing disease to rewriting its course. Precision oncology now targets specific molecular mutations. CAR T cell therapy has produced durable remissions in relapsed leukemias and lymphomas, with long term survival in heavily pretreated patients. Gene therapies, including CRISPR based approaches, have achieved functional cures for disorders such as sickle cell disease and transfusion dependent thalassemia. More than 30 gene therapies are approved globally, with hundreds of trials underway.

Yet in Pakistan, access remains limited. Infrastructure gaps, regulatory hurdles, high costs, and a shortage of trained personnel are real barriers—but they are not destiny. When science advances but access does not, geography becomes fate. Should a passport determine survival?

Progress must begin with strengthening molecular diagnostics and genomics, training clinicians and scientists, and building phased infrastructure through regional and international collaboration. National policies must enable ethical clinical trials and public–private investment in biotechnology.

Above all, we must affirm a simple belief: our patients deserve the same opportunities as patients anywhere else. The medical revolution is already here. The question is whether Pakistan will be part of it.

From treating disease to rewriting destiny — the bridge to tomorrow begins today

Dr Parvez Ahmed: Honored by CIBMTR

Dr Parvez Ahmed was honored by CIBMTR in recognition of his longstanding contribution to transplant data integrity and global collaboration. In his acceptance remarks, he reflected on a journey that began in 2001 and emphasized that such achievements represent the collective efforts of clinicians, nurses, data teams, and patients alike. We are proud to share his words below.

"CIBMTR leadership, the members of the award committee, and colleagues from all over the world, I am deeply honored and humbled to receive this award and I feel a profound sense of gratitude for this recognition and trust.

And as we all know, such type of award can never be the work of an individual like me standing in front of you. It is the work of countless hours by visible and invisible workers, clinicians, nurses, lab scientists, data managers, coordinators, administrators, and many more people. And I'm grateful to all of them and to my patients and their families for this recognition.

I have been associated with CIBMTR since late 2001. At that time, it was IBMTR. And I was the first data manager of my center and we used to fill up the data forms manually and it was required to be faxed back to CIBMTR. And since then, that has transformed our setup. It has brought transparency, visibility, meticulous data management, patient track and follow-up, and we are grateful to CIBMTR. And I regard CIBMTR not as sort of a registry or just a scientific or research organization. It's a global hope for creating knowledge, knowledge that will translate into better patient care in our part of the world. And that's how we can collaborate and increase patient care in low and middle-income countries.

And I'm grateful to CIBMTR and all of you this afternoon for honoring me and may Allah bless you."

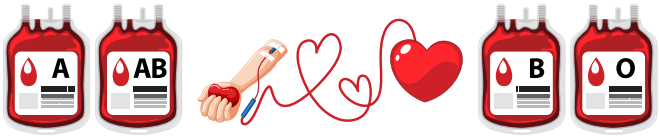
Farewell to Dr Hina Peter

After nearly two years of dedicated service, we bid a heartfelt farewell to Dr. Hina Peter, Consultant Clinical Hematologist at the PATHWEL Center of Hematology and Bone Marrow Transplant. Dr. Hina has been a valued member of our clinical team, known for her professionalism, compassion, and strong commitment to patient care. Her clinical expertise and supportive nature earned deep respect from colleagues and sincere appreciation from patients and their families. She contributed significantly to both clinical services and academic activities at PATHWEL. As she moves to the United Kingdom to continue her career in Clinical Hematology, we celebrate her professional growth while acknowledging that her presence will be greatly missed. We thank her for her dedicated service and wish her continued success ahead.

Farewell Luncheon Honoring Dr Hina Peter, Dr Sidra Barlas, and Dr Asad Ali Badshah

Blood Camps' Diary

By Ms Nigar Shah PRO & Camp Coordinator
Pakistan Thalassemia Welfare Society



A single donation can turn fear into hope and weakness into strength. Your blood is more than a gift — it is life flowing from one heart to another. Because of you, someone gets another sunrise to cherish.

Liaquat Bagh, Rawalpindi
22 November 2025

PATHWEL organized a blood donation camp in collaboration with The Blood Heroes at Liaquat Bagh, Rawalpindi, after obtaining approval from the Director of the Punjab Horticulture Authority (PHA). Volunteers from The Blood Heroes actively supported the activity throughout the camp. Dr. Gulalai, Founder of The Blood Heroes, also joined the team and motivated donors.

Liaquat Bagh, Rawalpindi
5 December 2025

Another blood donation drive was arranged at Liaquat Bagh due to winter vacations in universities and colleges. While institutions may close for holidays, patients suffering from thalassemia require regular blood transfusions without interruption. Keeping this critical need in view, PATHWEL continued organizing blood donation camps to help save the lives of thalassemia patients.

Allama Iqbal Park. Rawalpindi | 6 December 2025

PATHWEL is dedicated to regularly organizing blood donation camps at various public locations. A prominent example of this unwavering commitment is our consistent hosting of donation drives within community parks. The recent camp held at Allama Iqbal Park was specifically designed to help meet the critical and ongoing demand for life-saving blood transfusions for patients.

Ayub Park. Rawalpindi | 12, 13, and 14 December 2025

The Rawalpindi Chamber of Commerce and Industry (RCCI) recently organized a successful three-day Food Festival at Ayub Park, Rawalpindi, from December 12 to 14, 2025. Among the diverse participants, PATHWEL stood out by dedicatedly raising public awareness regarding thalassemia and the vital need for blood donation. A highlight of the event was the visit by RCCI President, Mr. Usman Shaukat, who formally honored the PATHWEL team with a certificate of appreciation for their noble efforts.

Health Services Academy, Islamabad
19 December 2025

On December 19, 2025, PATHWEL organized a blood donation drive at the Health Services Academy (HSA), Islamabad, following the signing of a Memorandum of Understanding. An awareness lecture on thalassemia, blood disorders, and the importance of blood donation was delivered by Maj Gen (R) Prof. Dr. Parvez Ahmed. The drive was supported by Director ORIC Dr. Babar Tasneem Sheikh, Dr. Aleeza Sana, and Dr. Gulalai, Founder of The Blood Heroes.

Bahria Phase 4, Green Valley, Rawalpindi
25-26 December 2025

PATHWEL organized a two-day awareness stall at an event arranged by Digital Nexus, Islamabad, where small businesses showcased their work. PATHWEL utilized this opportunity to spread awareness about thalassemia and blood donation. The event was inaugurated by Dr. Mehdi Tehri (Cultural Attaché, Embassy of Iran), who also visited the PATHWEL stall and appreciated the organization's efforts.

Kahuta Law College, Kahuta
29 December 2025

On December 29, 2025, PATHWEL organized a blood donation drive at Kahuta Law College with the kind approval of Mr. Uzair Hashmi, Chief Executive Officer (KLC). The event was coordinated by Mr. Jameel (Director Finance) and Mr. Shanazar (Director Administration). On this occasion, an awareness seminar was conducted to educate students about thalassemia, its prevention, and the importance of blood donation. Dr. Syed Kamran Mahmood, PATHWEL consultant physician, delivered the lecture, followed by an interactive question-and-answer session that reflected the students' keen interest.

PATHWEL at the 67th ASH Annual Meeting: Hope, Evidence, and a Global Platform

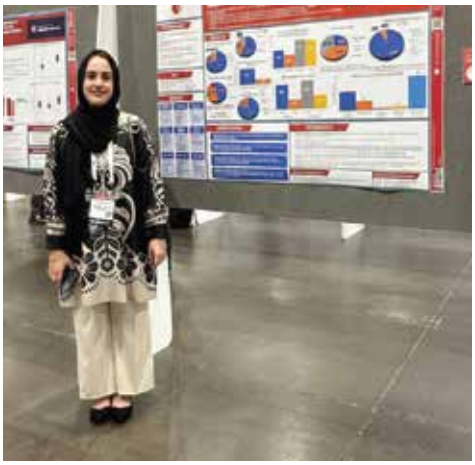
Report by: Dr Laila Bahadur

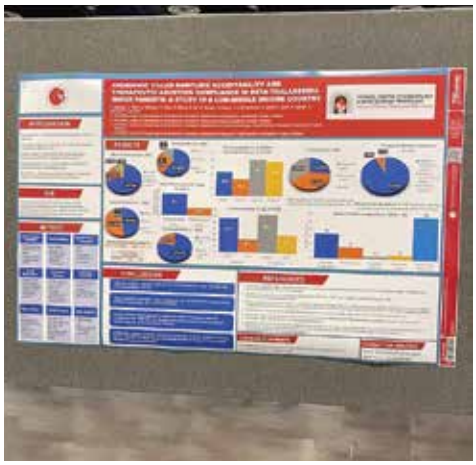
PATHWEL Center of Hematology and BMT was proudly represented at the 67th ASH Annual Meeting and Exposition, held from December 6–9, 2025, in Orlando, Florida. The four-day conference brought together thousands of physicians and researchers from across the world.

A competitively selected abstract from PATHWEL was presented as a poster at the ASH Annual Meeting titled, "Chorionic Villus Sampling Acceptability and Therapeutic Abortion Compliance in Beta Thalassemia Minor Parents: A Study in a Low-Middle-Income Country." This retrospective study spanning over a decade (2014–2024) included 266 high-risk mothers with a previously affected child with thalassemia major. The study found that acceptability of chorionic villus sampling was high (78%), particularly among educated, urban, and nuclear-family mothers. Therapeutic abortion compliance among fetuses diagnosed with thalassemia major was 93%, with refusals mainly due to procedure skepticism, family pressure, limited access to clinics and poor time management. The findings emphasize the need for targeted education, earlier referral, and improved access to timely CVS and authorized therapeutic abortion services in Pakistani healthcare setups.

Attending the ASH Annual Meeting provided an invaluable opportunity to engage with global leaders in hematology, showcase research at PATHWEL, and strengthen collaboration and knowledge exchange in the field. The experience reinforces our commitment to advancing hematology, cancer care and research both locally and internationally.

Rooted in community and guided by evidence, PATHWEL advances prevention where it matters most. From Pakistan to the global stage, its work speaks for families, futures, and hope.





Visit of MD Pakistan Bait-ul-Mal to PATHWEL

The Managing Director of Pakistan Bait-ul-Mal (PBM), Senator Capt. Shaheen Khalid Butt, visited the PATHWEL Center of Hematology and Bone Marrow Transplant on 13 January 2026 to review ongoing collaboration and support provided to patients suffering from serious blood disorders. He was accompanied by Dr. Sadia, Assistant Director, PBM.

During the visit, the delegation received a detailed briefing on the utilization of PBM funds allocated for underprivileged patients diagnosed with hematological diseases, including blood cancers and those undergoing bone marrow transplantation. The briefing emphasized the vital role of financial assistance in ensuring timely treatment, uninterrupted transplant procedures, and access to essential life-saving therapies for deserving patients.

Medical Director PATHWEL, Dr. Parvez Ahmed, expressed sincere appreciation for PBM's continued commitment to patient welfare, noting that sustained public-sector support is crucial for complex & resource-intensive treatments such as bone marrow transplantation.

The Managing Director also visited the Thalassemia Unit, where he distributed gifts among children receiving regular blood transfusions & interacted warmly with patients and their families. On this occasion, Senator Shaheen Khalid Butt reaffirmed PBM's continued support and announced an increase in grant allocation for eligible patients.

Visit of St. Mark's Cathedral High School

PATHWEL Center of Hematology and Bone Marrow Transplant warmly welcomed students and faculty from St. Mark's Cathedral High School, Rawalpindi, led by Principal Mr. Mubarik Daniel. The school generously donated a wheelchair to support patient mobility along with a cash contribution for patient care services. Students also presented flowers and small gifts to admitted patients, spreading joy and encouragement. Their thoughtful visit highlighted the importance of compassion, kindness, and community support in promoting hope and healing among patients.

Bridging Service and Science: MoU Between CUST–VIS & PATHWEL

On January 23, 2026, a delegation from the Volunteer in Service (VIS) Directorate of Capital University of Science & Technology visited the Pakistan Thalassaemia Welfare Society (PATHWEL) to strengthen institutional ties, witness ongoing services firsthand, and explore new avenues of collaboration in the fight against thalassaemia.

The delegation was led by Dr. Dur-e-Shehwar Sagheer, Director, Volunteer in Service Directorate. During the visit, the team was briefed on PATHWEL's comprehensive care programs, including transfusion services, patient support initiatives, and bone marrow transplantation facilities.

The visit culminated in the signing of a Memorandum of Understanding (MoU) between the VIS Directorate and PATHWEL . The agreement was formally signed by Parvez Ahmed, Medical Director, PATHWEL, marking a significant step forward in collaborative efforts focused on patient support, awareness campaigns, and community engagement.

This partnership reflects a shared commitment to advancing thalassaemia care and strengthening volunteer-driven initiatives to improve the lives of patients and their families.

Snippets Contributed by Ms. Nigar Shah, Public Relation Officer, Pakistan Thalassemia Welfare Society

Students of Rawalpindi Medical University visited PATHWEL and spent time with children receiving blood transfusions in the Thalassemia Unit. They also attended a lecture on blood diseases and blood transfusion.

Dr Aatika Ahmed Malik, Last day of observership

Students of Psychology dept, University of wah visited on 12th Jan 2026 and spent time with patients, played games, distributed gifts and deposited cash donation

On January 5, Riphah Radio (FM 102.2), in collaboration with Dr. Azhar Halim from the Social Welfare Department, hosted a special program at Riphah University featuring Dr Parvez Ahmed as the guest speaker.

A delegation from Blood Network Pakistan visited PATHWEL along with the Rawalpindi volunteer team supporting blood arrangements for patients.

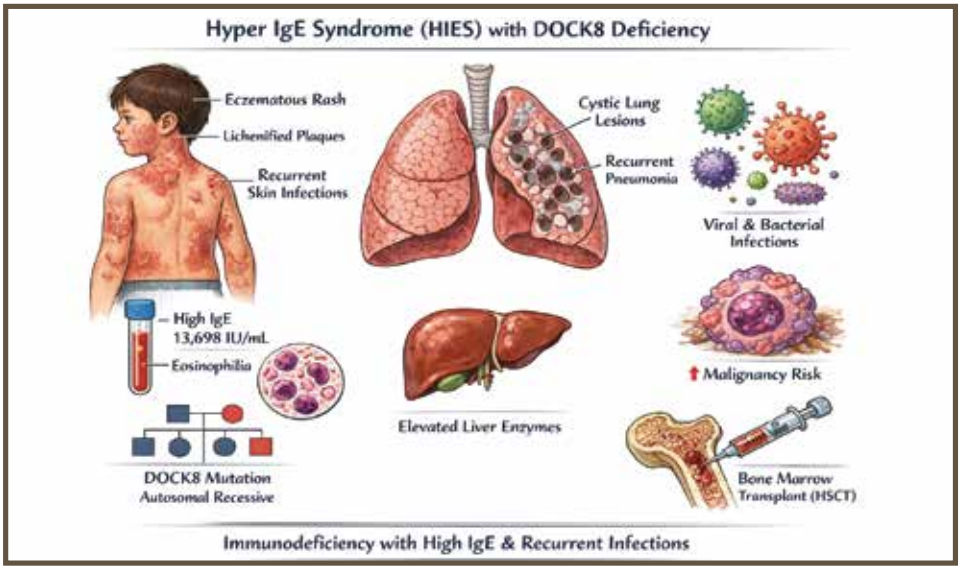
Grand Round

Reclaiming Immunity: A Child with DOCK8-Deficient Hyper IgE Syndrome

By Dr. Abdul Salam Khan, Resident Clinical Hematology, PATHWEL Center of Hematology & Bone Marrow Transplant

Case Presentation

We present a 9-year-old male child from Swat, a known case of Hyper IgE Syndrome (HIES), diagnosed in 2022, who was admitted in January 2026 for evaluation and preparation for allogeneic bone marrow transplantation. The child had a long history of severe eczema beginning in early childhood. His illness was characterized by recurrent maculopapular and exudative rashes, thickened lichenified plaques, and frequent secondary bacterial skin infections. Despite multiple consultations and repeated courses of systemic antibiotics, topical therapies, and antihistamines, only partial and temporary relief was achieved.



He also suffered from recurrent chest infections requiring frequent antibiotic therapy. Intermittent diarrhea had been present since the age of two years. Due to chronic respiratory symptoms in early childhood, he previously received anti-tuberculous treatment. His birth history was unremarkable (spontaneous vaginal delivery), developmental milestones were age-appropriate, and vaccinations were administered according to schedule.

On examination, he was small for age, with weight and height below the 3rd centile. Dermatologic findings included extensive eczematous plaques over the neck, axillae, genital region, & buttocks, with areas of serous discharge and lichenification. Occasional scattered crepitations were heard on chest examination. Mild hepatomegaly was present, while the remainder of systemic examination was unremarkable.

Laboratory evaluation revealed hemoglobin 10.3 g/dL, white blood cell count 18.2 $\times 10^9$/L, platelet count 710 $\times 10^9$/L, and eosinophils 30%. Liver function tests showed elevated ALT, markedly raised ALP, and elevated GGT. Serum IgE was markedly elevated at 13,698 IU/mL, while IgG, IgA, and IgM levels were within normal limits.

High-resolution CT scan of the chest demonstrated multiple thin-walled cystic lucencies of varying sizes in both lungs, consistent with structural damage secondary to recurrent infections, along with bronchial wall thickening.

Based on severe eczema, recurrent infections, extreme IgE elevation, and eosinophilia, Hyper IgE Syndrome was strongly suspected. Definitive diagnosis was established in June 2024 via NGS, which identified a DOCK8 mutation, confirming autosomal recessive Hyper IgE Syndrome (DOCK8 deficiency). HLA typing revealed a full high-resolution match with the father, making allogeneic transplantation a feasible curative option.

Case Discussion

Hyper IgE Syndrome is a rare primary immunodeficiency characterized by eczema, recurrent skin and sinopulmonary infections, eosinophilia, and markedly elevated serum IgE levels. Two main genetic forms exist: autosomal dominant (STAT3 mutation) and autosomal recessive (most commonly DOCK8 mutation). DOCK8 deficiency is associated with more severe disease, including recurrent bacterial and viral infections, progressive lung damage, increased malignancy risk, and higher mortality if untreated.

Unlike the autosomal dominant form, DOCK8 deficiency has a clear indication for hematopoietic stem cell transplantation as definitive therapy. In this patient, early-onset severe eczema, recurrent infections, markedly elevated IgE, and progressive pulmonary damage suggested an underlying primary immunodeficiency rather than simple atopic disease. Genetic confirmation allowed accurate classification and timely transplant planning.

Conclusion

This case emphasizes the importance of early recognition of primary immunodeficiency in children with persistent eczema and recurrent infections. Extremely elevated IgE levels should prompt comprehensive immunologic and genetic evaluation. For children with DOCK8 deficiency, allogeneic stem cell transplantation offers the possibility of immune restoration and prevention of long-term complications, including malignancy. Early diagnosis and multidisciplinary management remain essential to improving outcomes.

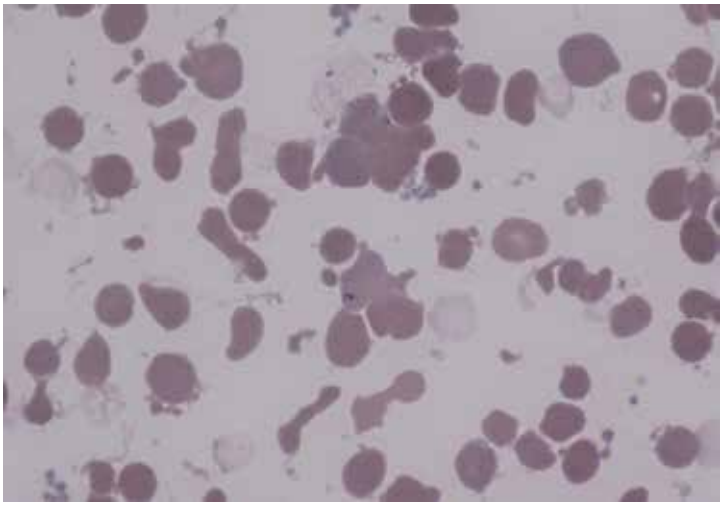
Morphology Updates

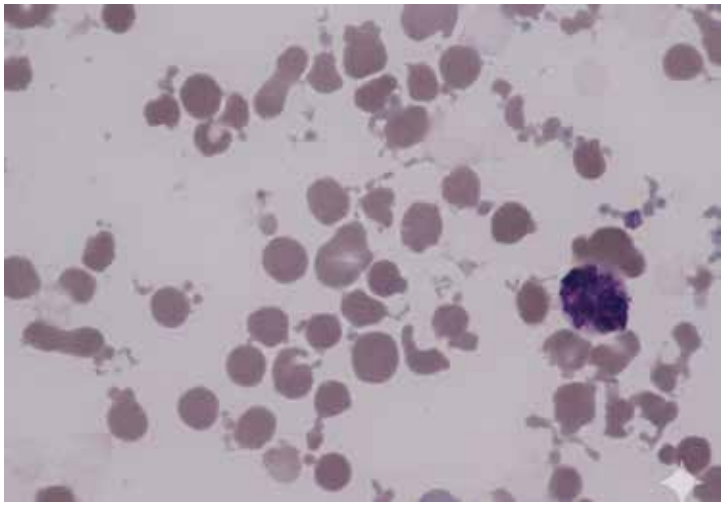
Can We Really Believe This Platelet Count?

James Manning[1] | Simona Deplano[1] | Ketan Patel[1] | Barbara J. Bain[2]

[1]Department of Haematology, Imperial College Healthcare NHS Trust, Hammersmith Hospital, London, UK | [2]Faculty of Medicine, Centre for Haematology, St Mary's Hospital Campus of Imperial College London, London, UK

A 64-year-old woman presented to the hematology clinic for follow up of refractory chronic cold agglutinin disease with hepatic iron overload secondary to a chronic red cell transfusion burden. Management had included single-agent rituximab and ciclosporin, to which the disease had proven refractory. She had recently received a first cycle of bendamustine and rituximab. On review preceding a second cycle, she was tired and lightheaded and scleral icterus was noted. A blood sample was taken urgently and conveyed to the laboratory for testing. Full blood count results, compared to results from three weeks earlier, are tabulated.





	Current	Previous
White blood cell count (WBC)×10⁹/L	35.6	4.2
Hemoglobin concentration (Hb) g/L	65	87
Mean cell volume (MCV) fL	80.6	95.2
Red cell distribution width (RDW) % [NR 10.0–15.9]	30.7	16.4
Platelet count×10⁹/L	1125	444

Given the unexpected abnormalities in the blood count, an urgent blood film was made. This showed only small red cell agglutinates (left image, ×100 objective) and did not confirm the apparent thrombocytosis. The most striking feature was the presence of numerous red cell fragments, many of which were spherical and some of which were budding from red cells (both images). There were small numbers of more angular fragments. The thrombocytosis was factitious and attributable to schistocytes being counted as platelets. The leucocytosis was also factitious and attributable to loose clumps of platelets and debris being counted as leucocytes. All neutrophils were cytologically abnormal with blurred nuclear and cytoplasmic outlines and increased granularity (right image). The findings were not suggestive of a microangiopathic hemolytic anemia since the schistocytes were not often angular but rather were often microspherocytes and could be seen budding from red cells. These findings suggest the effect of heat. These distinctive heat effects can be seen both in patients suffering fro burns and also when a blood sample has been inappropriately heated in vitro. Further investigation revealed that the phlebotomist had transported the patient's blood specimen to the laboratory in a mug of hot water.

Erroneous results of a blood count can result from preanalytical, analytical, or post-analytical errors. This is an example of an uncommon preanalytical error. It is important that when it is necessary to keep a blood specimen warm it is kept at a controlled temperature of 37°C.

Picture Quiz Answer

By Dr Laila Bahadur, Consultant Hematologist PATHWEL

Answer: Thiamine-responsive megaloblastic anemia (Rogers Syndrome).

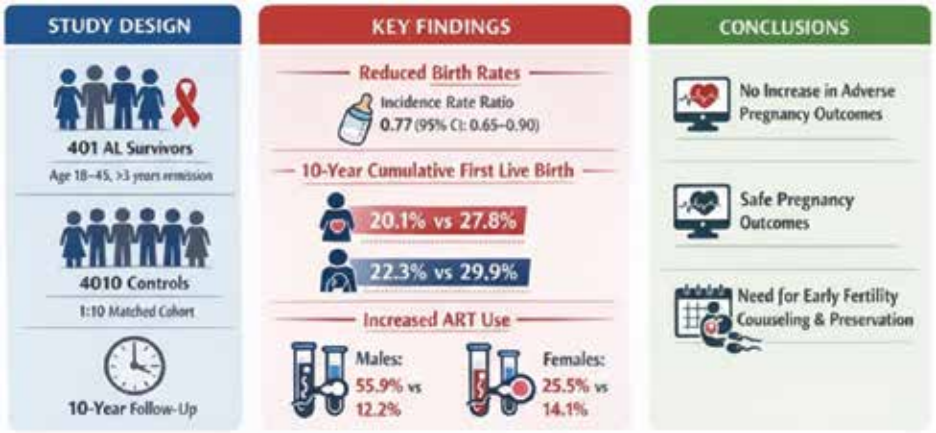
Thiamine-responsive megaloblastic anemia is characterized by the classical triad of megaloblastic anemia, type 1 diabetes mellitus, and sensorineural deafness. The condition typically manifests in early childhood. Targeted NGS panel testing identified two pathogenic variants in the SLC19A2 gene. SLC19A2 is associated with autosomal recessive thiamine-responsive megaloblastic anemia.

Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits

Reproductive patterns and birth rates in acute leukaemia survivors: A Danish population - based cohort study.

Nielsen et al., Br J Haematol; DOI: 10.1111/bjh.20238

In this Danish population-based cohort study, Nielsen et al. assessed long-term reproductive outcomes in 401 adult survivors of acute leukemia (AL) aged 18–45 years, matched 1:10 with population controls. Over a median follow-up of approximately 10 years, AL survivors demonstrated a significantly reduced birth rate compared with controls (incidence rate ratio 0.77; 95% CI 0.65–0.90).



The 10-year cumulative incidence of first live birth was lower among survivors in both sexes: 20.1% vs. 27.8% in women and 22.3% vs. 29.9% in men (both statistically significant). Use of assisted reproductive technology (ART) was markedly higher in survivors, particularly among men (55.9% vs. 12.2%) and women (25.5% vs. 14.1%), reflecting persistent treatment-related fertility impairment.

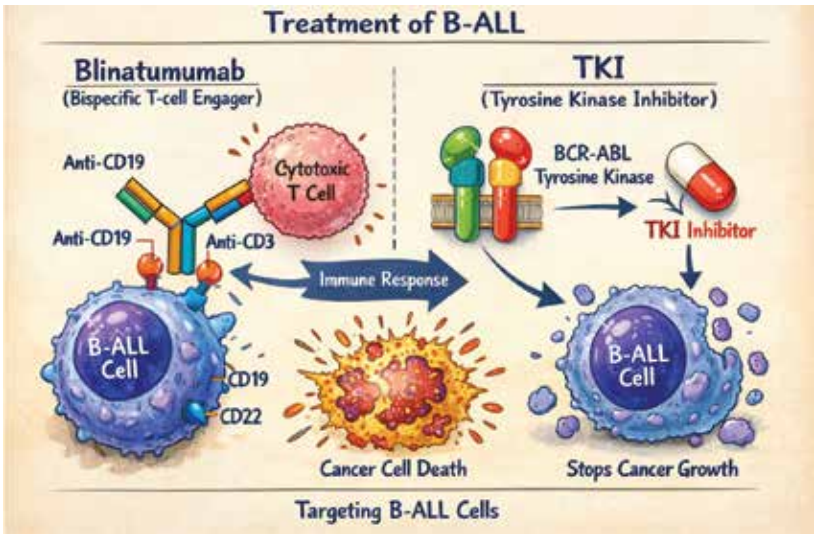
Reassuringly, among those who achieved pregnancy, no statistically significant increase in adverse pregnancy outcomes was observed compared with the general population.

Overall, the findings provide strong quantitative evidence that acute leukemia survivorship is associated with reduced fertility but preserved pregnancy outcomes, underscoring the need for early fertility counseling and preservation strategies as part of standard leukemia care.

Immunomodulatory effect of dasatinib plus blinatumomab versus ponatinib plus blinatumomab in newly diagnosed Ph+ acute lymphoblastic leukemia

Michela Ansuinelli, Nadia Peragine , Maria Stefania De Propris et al; Leukemia. 2026 Jan 22. doi: 10.1038/s41375-025-02855-5.

In Ph+ acute lymphoblastic leukemia, frontline dasatinib plus blinatumomab (dasa+blina) is associated with long-term survival rates of 75-80%. The phase III GIMEMA ALL2820 trial has explored ponatinib with blinatumomab (pona+blina). In the present study, the immune modulation induced by dasa+blina and pona+blina was investigated. Immune cells were analyzed at the end of induction (T0) and after 2, 4 and 5 blinatumomab cycles (T2, T4, T5).



Among 153 patients (43 dasa+blina, 110 pona+blina), the dasa+blina combination induced a significantly greater lymphocyte increase at T4 and T5 compared to pona+blina. The Treg counts decreased only in the dasa+blina treated patients. NK and NK-T cells increased significantly in the dasa+blina group, at all timepoints. Complete molecular responders (CMR) after dasatinib induction had significantly higher lymphocytes, T and NK cells compared to non-CMR patients. Bone marrow analyses showed higher activation (CD25, CD69) and lower exhaustion (PD1, TIM3) markers on NK and NK-T cells in dasa+blina treated patients.

Dasa+blina patients exhibited a significantly enhanced NK cell capacity compared to ponatinib treated patients. Patients remaining on dasatinib maintained elevated NK cells with a more mature phenotype, suggesting a durable effect. These results highlight the greater dasa+blina immune activation, supporting a potential synergistic effect of the drug combination.

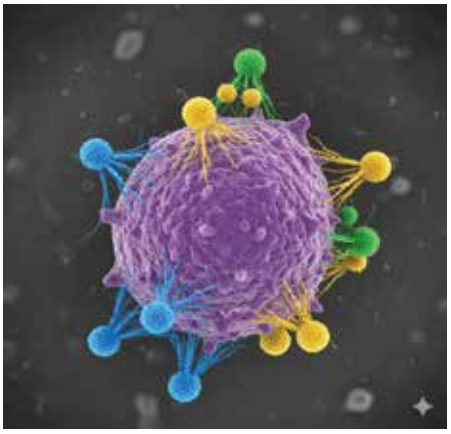
Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits

CAR T-cell therapy in patients with acute lymphoblastic leukemia: a systematic review and meta-analysis.

Victor Navarro et al: Bone Marrow Transplantation; https://doi.org/10.1038/s41409-026-02803-6

Chimeric antigen receptor (CAR) T-cell therapy has revolutionized the treatment landscape of relapsed/refractory (R/R) B-cell precursor acute lymphoblastic leukemia (B-ALL), with high remission rates across various CAR T-cell constructs. However, the durability of these responses remains a major challenge, with many patients experiencing relapse after an initial remission.

This systematic review and meta-analysis aimed to compare the efficacy and safety of different CAR T-cell constructs across 40 clinical trials, including a total of 1540 R/R B-ALL patients. We assessed the impact of patient demographics, prior treatment



exposure, and construct characteristics on treatment outcomes. The pooled complete remission rate (CRR) was 83.4% (I 2 = 49%), with a minimal residual disease-negative complete remission (MRDneg-CR/CRi) rate of 92.7% (I 2 = 48%). 4-1BB co-stimulatory domain constructs showed higher MRDneg-CR/CRi rates compared with CD28 (94.0% vs. 84.4%p = 0.048) and a lower incidence of immune effector cell-associated neurotoxicity syndrome. Additionally, CAR T-cell products targeting CD19 or CD19/CD22 patients presented higher MRDneg-CR/CRi rates than those targeting CD22 alone.

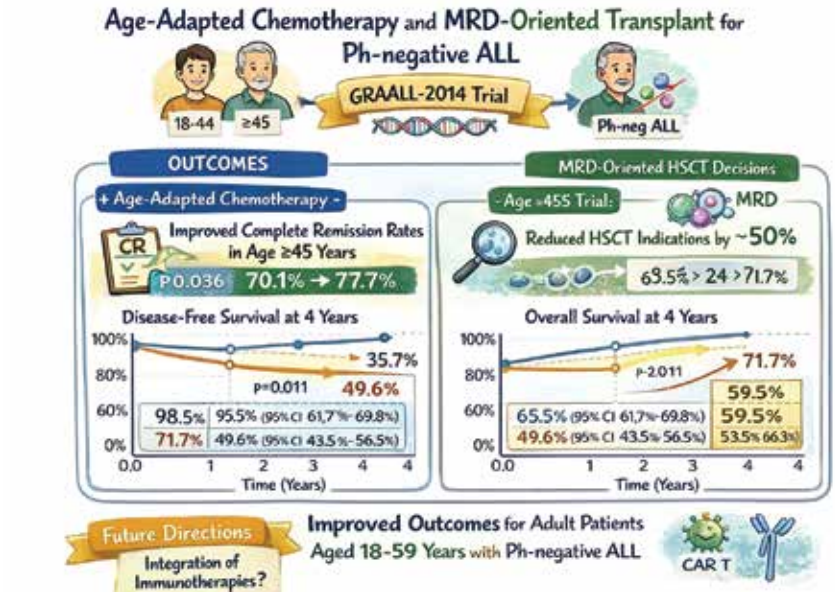
In conclusion, our findings suggest that 4-1BB-based CAR T-cell therapy targeting CD19 offers the best efficacy and safety profile in R/R B-ALL.

Age-adapted chemotherapy and MRD-oriented transplant for Ph-negative acute lymphoblastic leukemia -

GRAALL-2014 trial Nicolas Boissel, et al; https://doi.org/10.1182/blood.2025029611

The Group for Research in Adult Acute Lymphoblastic Leukemia (GRAALL)-2014 trial evaluated an intensive, age-adapted protocol for adults aged 18-59 years with Philadelphia chromosome-negative acute lymphoblastic leukemia (ALL). The GRAALL-2014 protocol aimed to reduce treatment-related toxicity in patients aged ≥45 years and to limit alloHSCT to patients with poor measurable residual disease (MRD) responses.

A total of 743 patients was included, and outcomes were compared to those of the GRAALL-2005 trial. The GRAALL-2014 demonstrated reduced early mortality and higher complete remission rates in patients aged ≥45 years. MRD-guided transplant decisions reduced alloHSCT indications by approximately 50%. While older patients experienced a higher cumulative incidence of relapse, no significant difference in disease-free survival (DFS) was observed compared to historical cohorts across age subgroups.



The overall 4-year DFS was 57.1% (95% CI, 53.4–61.1).Notably, 4-year overall survival improved significantly, from 65.5% (95%CI, 61.7-69.8) to 71.7% (95%CI, 67.7-76.0) in younger patients (p=0.031) and from 49.6% (95%CI, 43.5-56.5) to 59.5% (95%CI, 53.5-66.3) in older patients (p=0.011).

findings highlight the value of individualized treatment strategies, balancing efficacy and safety. Future studies should investigate the integration of immunotherapy to further reduce treatment intensity and improve outcomes.

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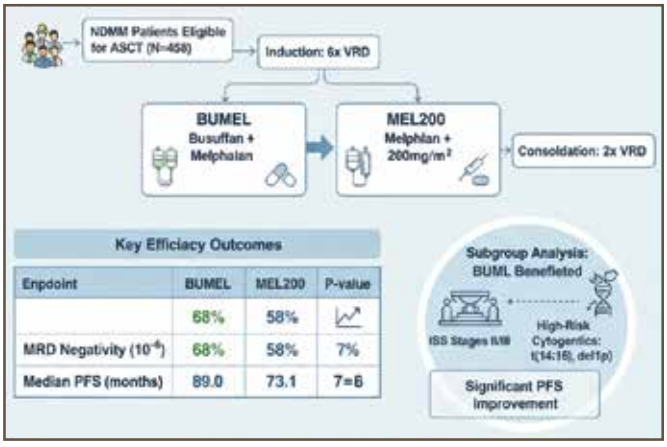
Autologous stem cell transplantation (ASCT) conditioning with high-dose busulfan-melphalan (BUMEL) vs melphalan (MEL200) and reinforced VRD for newly diagnosed multiple myeloma: a phase 3 GEM trial

Juan José Lahuerta, Jesús San-Miguel, Ana Jiménez-Ubieto et al; Blood (2025) 146 (15): 1747–1758. doi.org/10.1182/blood.2025028313



In retrospective studies, autologous stem cell transplantation (ASCT) conditioning with intravenous busulfan and melphalan (BUMEL) led to longer progression-free survival (PFS) than melphalan alone (MEL200). We compared long-term outcomes of BUMEL vs MEL200 in the context of intensified bortezomib, lenalidomide, and dexamethasone (VRD) induction and consolidation therapies.

GEM12 was a phase 3 trial for patients with newly diagnosed multiple myeloma (NDMM) eligible for ASCT including 6 reinforced bortezomib, lenalidomide, and dexamethasone (VRD) cycles followed by ASCT conditioned with BUMEL or MEL200 and 2 VRD consolidation cycles. The primary end point was PFS. Subgroup analyses were based on International Staging System (ISS) stages and high-risk genetic abnormalities. Patients were randomized with an open-label 2 × 2 factorial design and 1:1:1:1 allocation ratio to ensure the balance between the GEM12 & the subsequent phase 3 GEM14 trial.

Between 2013 and 2015, 458 patients were randomized (BUMEL, n = 230; MEL200, n = 228). The 10^6 MRD-negative rate was 63%, 68% for BUMEL vs 58% for MEL200 (odds ratio, 1.51; P = .035). The median PFS was 89 months for BUMEL and 73.1 for MEL200 (hazard ratio, 0.89 [95% confidence interval, 0.70-1.14]; P = .3). BUMEL showed benefit for patients with ISS stages II or III, t(14;16), and del(1p). For subcohorts ISS stages II or III treated with BUMEL and ISS I treated with MEL200 the median PFS was 96.5 months (95% confidence interval, 76 to not estimable). No safety concerns were observed. After a median follow-up of 8.4 years, GEM2012 demonstrated one of the longest PFS values reported in patients with NDMM, with significant differences favoring BUMEL in advanced ISS stages.

Treosulfan/fludarabine versus thiotepa/busulfan/fludarabine for allogeneic HCT in lymphoma in the post-transplant cyclophosphamide era: A GETH-TC study

Marta Peña, Lorenzo Lazzari et al; https://doi.org/10.1111/bjh.70367

Reduced-intensity conditioning regimens offer lower non-relapse mortality (NRM), however, relapse rates remain high, and optimal conditioning strategies in the setting of post-transplant cyclophosphamide (PTCy) prophylaxis remain undefined. In this retrospective, international multicentre study, the primary endpoint was NRM. We compared treosulfan/fludarabine (Treo/Flu) versus thiotepa/busulfan/fludarabine (TBF) in 178 adults with lymphoid malignancies undergoing first alloHCT with PTCy and peripheral blood grafts.

Three-year NRM was 14.0% with Treo/Flu versus 33.0% with TBF. On multivariate analysis, Treo/Flu was associated with significantly lower 3-year NRM (hazard ratio [HR] 0.44; 95% confidence interval [CI], 0.22–0.87; p = 0.018). Conditioning regimen was not independently associated with overall survival (OS) or progression-free survival (PFS), and relapse incidence was similar between regimens. Moderate to severe chronic graft-versus-host disease (GVHD) was higher with Treo/Flu (26.0% vs. 9.9%; HR 2.43; 95% CI, 1.09–5.43; p = 0.03), while GVHD-free/relapse-free survival (GFRS) was comparable.

Findings were consistent in a prespecified propensity score-matched sensitivity analysis. These findings support Treo/Flu as a potentially safer reduced-toxicity conditioning option than TBF in the context of PTCy-based GVHD prophylaxis for lymphoid malignancies and warrant prospective validation.

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Long-term benefits of autologous stem cell transplantation versus intensive chemotherapy consolidation for acute myeloid leukemia patients: A propensity score matching analysis from the PETHEMA AML registry

AA Pierola, DM Cuadrón, RR Veiga et al; Leukemia (2025) 39:2686–2696; https://doi.org/10.1038/s41375-025-02744-x

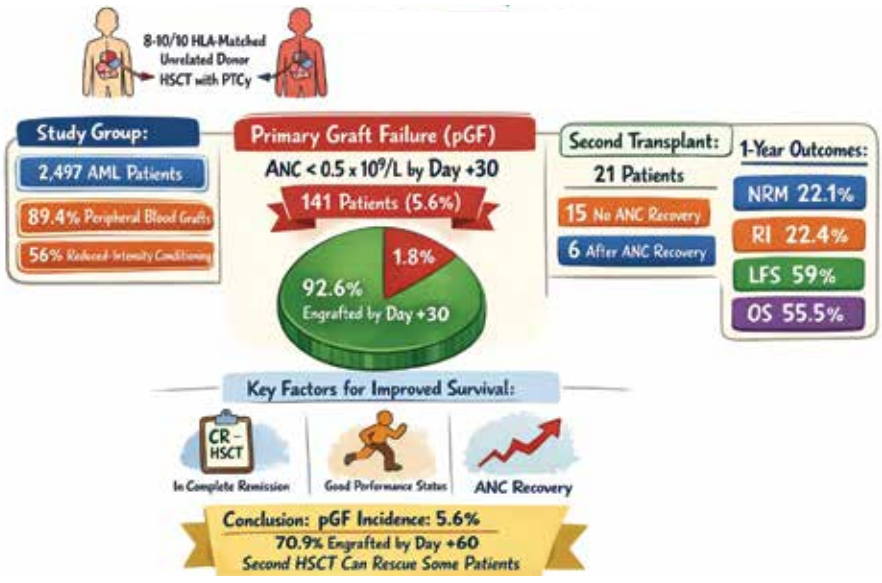
While allogeneic stem cell transplantation (allo-SCT) is the preferred consolidation for high and most intermediate-risk AML patients in first remission, the role of autologous SCT (auto-SCT) vs. chemotherapy (CT) when allo-SCT is not feasible or indicated, remains controversial. We conducted a real-world, retrospective cohort study using the PETHEMA AML registry to compare auto-SCT and CT. Multivariate Cox regression and propensity score matching (PS-matching) were used to adjust for confounding factors.

A total of 1272 patients in first remission and who received 2 consolidation courses were included (615 receiving additional CT cycles and 657 undergoing auto-SCT). Overall, 78.08% of auto-SCT patients were diagnosed before 2017, compared to 38.11% in the CT cohort (p< 0.001). In the overall cohort, auto-SCT was associated with significantly prolonged overall survival (OS) (HR: 0.73, p < 0.001) and relapse-free survival (RFS) (HR: 0.73, p < 0.001). This benefit was particularly evident in patients ≤65 years, those with normal karyotype, and FLT3-ITD negativity. In the PS-matched cohort, the RFS advantage persisted (HR: 0.80, p=0.092), but OS differences were not statistically significant (HR: 0.91, p = 0.563). The role of auto-SCT in the genomic and targeted agent era should not be discarded

Outcomes of primary graft failure in acute myeloid leukemia patients following unrelated transplantation with post-transplant cyclophosphamide: a study from the ALWP/EBMT.

Nagler, A., Galimard, JE., Kayser, S. et al. Bone Marrow Transplant (2025). https://doi.org/10.1038/s41409-025-02726-8

We assessed primary graft failure (pGF) in 2497 AML patients undergoing HSCT from 8-10/10 HLA-matched unrelated donor (UD) with post transplant cyclophosphamide (PTCy). pGF was defined as failure to achieve an ANC ≥ 0.5 × 109/L by day +30 after HSCT.



The day +30 cumulative incidence of ANC was 92.6% (95%CI: 91.5–93.6), and the incidence of death without ANC recovery was 1.8% (95% CI: 1.3%–2.3%), corresponding to 141 (5.6%) patients not achieving an ANC ≥ 0.5 × 109/L by day +30. Peripheral blood was the graft source in 89.4% of the patients, and 56% received reduced-intensity conditioning. Twenty one patients underwent a second HSCT (15 in the absence of ANC recovery and 6 after ANC recovery). 1-y NRM and RI post-pGF were 22.1% and 22.4%, respectively. 1-y LFS and OS post-pGF were 59% and 55.5%, respectively. ANC recovery evaluated as a time-dependent covariate, KPS ≥ 90, and being in CR at the time of HSCT were associated with improved OS. In conclusion, the incidence of pGF post-unrelated HSCT with PTCy was 5.6%. Of the patients who failed to engraft by day +30, 70.9% did so by day +60. A second transplant can save some of the patients with pGF.

Annual General Meeting of Hemophilia Patients Welfare Society Rawalpindi at Pakistan Sweet Home

Report by Ms. Hina Fatima

The Annual General Meeting (AGM) of the Hemophilia Patients Welfare Society (HPWS) Rawalpindi was held on 20 December 2025 at Pakistan Sweet Home, Islamabad, bringing together a diverse group of stakeholders including healthcare professionals, patients, caregivers, donors, volunteers and executive board members. A total of 113 participants attended the meeting, comprising 10 doctors, 57 patients, 11 patient relatives, 8 stakeholders and executive board representatives, 20 executive board members and volunteers and 7 staff members. The AGM served as a key platform to review the society's annual activities, discuss challenges in hemophilia care and define strategic priorities for improving patient services and sustainability.

The President of HPWS Rawalpindi presented the annual report, highlighting major achievements during 2025, including organizational development, legal and administrative progress, financial management, welfare programs and outreach initiatives conducted through the Hemophilia Treatment Centre (HTC). The report emphasized ongoing awareness campaigns, patient support programs and collaborations with national and international partners, alongside future plans to strengthen patient care delivery and expand advocacy activities.

A dedicated patient interaction session provided an opportunity for caregivers to share their experiences regarding financial assistance and treatment access. Mothers of hemophilia patients described their successful engagement with Pakistan Bait-ul-Mal for grants to procure clotting factor concentrates, demonstrating practical pathways for accessing government support. These testimonies served to encourage other families to seek institutional assistance and highlighted the importance of guidance and persistence in navigating healthcare funding systems.

Representatives from Pakistan Bait-ul-Mal reiterated their commitment to supporting hemophilia patients and emphasized the need to enhance annual financial grants to ensure sustainable access to lifesaving treatment. Contributions from private sector stakeholders were also highlighted, including financial donations and discussions regarding the establishment of a dedicated hemophilia center. Such commitments underscored the importance of public–private partnerships in strengthening hemophilia care infrastructure in Pakistan.

A detailed presentation on the history, projects and sustainability framework of HPWS Rawalpindi highlighted the organization's growth, operational model and fundraising strategies. The society's commitment to transparency and accountability was demonstrated through its annual financial contributions to the Hemophilia Foundation Pakistan and compliance with tax obligations. The role of volunteers and donors was acknowledged, with presentations describing how donations were utilized for clotting factor procurement, diagnostic services, patient welfare activities, and awareness programs.

The distribution of Save One Life (SOL) funds provided direct financial support to patients and families, alleviating treatment-related economic burdens and reinforcing the society's patient-centered approach. The meeting concluded with recognition of key contributors through certificates and shields, followed by a formal vote of thanks and group photograph. The AGM reaffirmed the collective commitment of clinicians, welfare organizations, donors, and patient communities to improving access to diagnosis, treatment, and comprehensive care for individuals living with hemophilia and other inherited bleeding disorders in Pakistan

Mr. Zamurad Khan, CEO of Pakistan Sweet Home and Advisor to HPWS Rawalpindi, attended the AGM as the Chief Guest continuing his longstanding annual participation and support for the hemophilia community. In his address, he appreciated the consistent efforts of HPWS in organizing awareness, welfare and support activities at Pakistan Sweet Home each year and acknowledged the organization's dedication to improving the lives of individuals with bleeding disorders. He reaffirmed his continued support for hemophilia patients and emphasized the importance of sustained collaboration between welfare organizations and patient groups.

Overall, the AGM reinforced HPWS Rawalpindi's role as a leading patient organization in Pakistan, highlighting the importance of annual stakeholder engagement, sustainable funding mechanisms and integrated care models to improve the quality of life for individuals living with hemophilia and other inherited bleeding disorders.

Turning Risk into Recovery: Successful Obstetric Outcome in Severe von Willebrand Disease

Introduction

von Willebrand disease (VWD) is the most common inherited bleeding disorder, resulting from quantitative or qualitative defects of von Willebrand factor and associated reduction in factor VIII activity. Women with severe VWD are at particularly high risk of peri-partum and postoperative hemorrhage. Delivery in such patients requires meticulous planning and close collaboration between hematology and obstetric teams to ensure adequate hemostatic coverage and favorable outcomes.

Case Report

Misbah Shaheen, a 27-year-old woman, known case of severe von Willebrand disease, presented at term pregnancy for delivery in Mother child Unit of PIMS Hospital. She was referred to our Hemophilia treatment center (HTC) for peri-operative hemostatic management. Her body weight was 65 kg. She was already a registered patient. This was her second Caesarean section and in the last pregnancy she was also managed by HTC. She had a previous history of mucocutaneous bleeding and menorrhagia and was under regular hematology follow-up.

Baseline laboratory investigations revealed hemoglobin of 8.1 g/dL, with prolonged coagulation parameters and low von Willebrand factor activity consistent with severe VWD. In view of anemia, she also received two units of packed red cell concentrate (RCC) pre-operatively.

As the attending hematologist, a multidisciplinary delivery plan was formulated in coordination with obstetrics and anesthesia teams. She was scheduled for elective lower segment cesarean section under adequate hemostatic cover. Pre-operatively, von Willebrand factor containing factor VIII concentrate was administered at a dose of 4000 IU(60 IU/kg VWF:RCo) according to body weight to raise factor levels to hemostatic range.Tranexamic acid was given at a dose of 15mg/kg (1000 mg x 8hrly) as adjunct antifibrinolytic therapy. Factor replacement therapy was provided by HTC post-operatively at dose of 3500 IU (50 IU/kg) for the next 3 days to maintain adequate von Willebrand factor and factor VIII levels, with close laboratory and clinical monitoring. Tranexamic acid was continued for several days postpartum.

The patient underwent an uncomplicated cesarean section and delivered a healthy baby boy. Intra-operative blood loss remained within acceptable limits. Postoperatively, she remained hemodynamically stable with no evidence of primary or secondary postpartum hemorrhage. Her recovery was uneventful, and she was discharged in stable condition with advice regarding postpartum bleeding precautions and scheduled hematology follow-up.
This case highlights the pivotal role of the hematologist in coordinating individualized hemostatic management. With appropriate factor replacement, blood transfusion support, and multidisciplinary care, cesarean section can be safely performed in patients with severe VWD, resulting in successful maternal recovery and favorable neonatal outcome

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