Newsletter | 2024 | Sep - Oct | Volume I/5

PATHWELtimes

BIMONTHLY NEWSLETTER

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

"Supporting the fighters Admiring the Survivors Honoring the taken and never, ever giving up hope"

PATHWEL Art Gallery

INSIDE THIS ISSUE

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Picture Quiz *by Dr Sidra Barlas*

A 23-year-old female presented with progressive pallor, jaundice, dizziness, and easy fatigability for the last 02 years. She was previously treated for iron deficiency anemia with iron supplements and showed no improvement in Hb. Lab studies showed hypochromic microcytic anemia with hemoglobin level of 7.8 g/dl. RBC morphology revealed anisocytosis, poikilocytosis, target cells, blister cells, polychromasia, and ovalocytes. Reticulocyte count was 8.5 %. Parents' blood counts are shown in the table.
Mutation for G6PD was negative. High performance liquid chromatography showed Hb A (92%) and Hb A2 (2%). An unknown significant peak was observed at 0.35 minutes of retention time with an area of 5.6 %. Look at the photographs of peripheral film and give your diagnosis.

	Father	Mother
WBC x 10^9/l	6.6	6.2
RBC	5.4	5.5
Hb g/dl	15	12
MCV	83	69
MCH	27.2	21.7
Platelets x 10^9/l	387	231

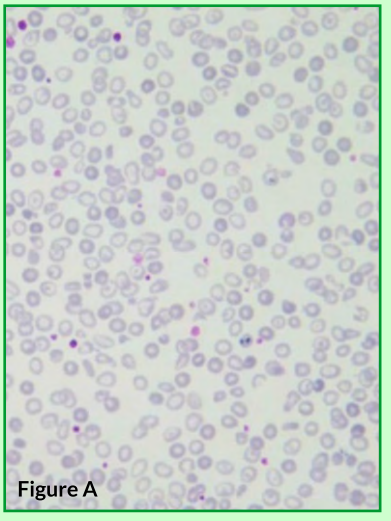


Figure A

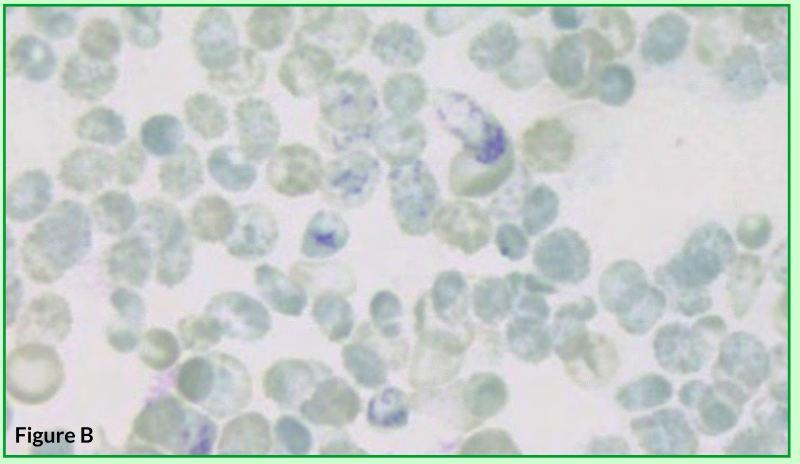


Figure B

Answer on page 9

BLOOD CANCER AWARENESS MONTH
SEPTEMBER

From Editor's Desk

Dear Readers,

As we enter a new era in hematology, the field finds itself at a transformative intersection of advanced research, innovative therapies, and a dedication to patient-centered care. Recent years have brought remarkable progress in understanding blood disorders, fundamentally changing treatment approaches and improving patient outcomes.

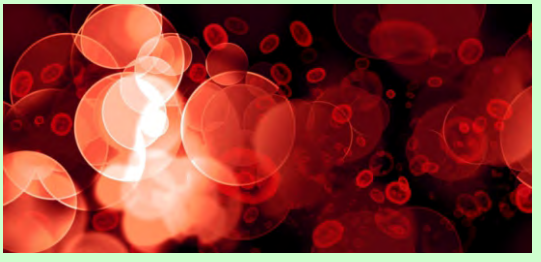
One of the most groundbreaking advancements has been in targeted therapies and immunotherapies for blood cancers like leukemia and lymphoma. Previously, options were largely confined to chemotherapy, often with challenging side effects and mixed success rates. However, precision medicine has now introduced therapies designed to target specific genetic mutations and abnormalities in cancer cells. CAR T-cell therapy, for example, has redefined treatment possibilities, offering new hope to patients once facing limited options.

Next-generation sequencing (NGS) is another innovation that has transformed hematology by enabling detailed genomic profiling, allowing for a more personalized approach to treatment. This individualized care not only enhances treatment effectiveness but also reduces unnecessary toxicity, sparing patients from ineffective therapies and side effects.

Progress is also evident in benign hematology, especially in managing sickle cell disease and hemophilia. Gene therapy, now showing promising results in clinical trials, offers a potential long-term solution for these chronic conditions, improving patients' quality of life by potentially altering the course of their diseases.

Despite these advances, challenges remain. Ensuring equitable access to these therapies is critical, particularly for underserved communities. Hematologists must advocate for wider availability of these life-saving treatments.

To embrace the future of hematology fully, ongoing education and interdisciplinary collaboration among healthcare professionals are essential. As we look forward, let us remain committed to compassionate, comprehensive care for every patient. Together, we can create a future where blood disorders are addressed with confidence, equipped with the most advanced tools and therapies available.



Take care.

Visit by Punjab Human Organ Transplantation Authority (PHOTA)

By Ms Nigar Shah

On 9 July 2024, a team of Punjab Human Organ Transplant Authority (PHOTA) visited PATHWEL. They carried out a detailed inspection. The PHOTA team appreciated the work done at our center and highlighted the areas which require further improvement.

The visit was part of the official registration process. At PATHWEL we are committed to providing efficient, effective, affordable, and safe health services to the patients suffering from blood diseases including blood cancers.

Blood Camps' Diary

By Ms Nigar Shah
PRO & Camp Coordinator, PTWS

In July and August we organized number of successful blood collection camps. We are very grateful to all the blood donors and facilitators who helped us in organizing these camps.

EOBI Tower, Islamabad | 1 July 2024
CEO Mr. Imran Khan Shinwari and Assistant Manager REM Mr. Muhammad Shehryar Zafar from Pakistan Real Estate Investment & Management Company Pvt Ltd (PRIMACO) arranged a successful blood donation camp. They were very supportive and motivated all those working in EOBI Tower to donate blood for the noble cause.

EOBI Plaza, Islamabad | 4 July 2024
Mr. Muhammad Muzammil (Sub Engineer) from Employees Old Age Benefit Institution, EOBI Plaza organized the blood donation camp. Tehzeeb Bakers, which was also located in the plaza, sent their staff to donate blood voluntarily for thalassemic patients.

NADRA Tower, Islamabad | 11 July 2024
DG NADRA RHO, Islamabad, Mr. Faheem Ahmed Khan organized a blood donation camp at NADRA Tower. Mr. Syed Azeem Hussain Rizvi (Asst. Director Admin) coordinated the camp and Ms. Tahira Naz (Superintendent) worked as a volunteer. She motivated her colleagues to donate blood. Lt Col (R) Omar Saeed (OIC M&E) from NADRA Headquarter team also donated blood and was a real inspiration for the rest of the donors.

Allama Iqbal Park, Rawalpindi | 26 July & 11 August 2024
Director Parks & Horticulture Authority, Rawalpindi, Mr. Sheikh Tariq was kind enough to approve establishment of blood collection camps by PTWS at public parks in Rawalpindi. This immensely helped our patients during summer vacations of educational institutions. Couple of such camps were organized at Allama Iqbal Park. The response of general public was very encouraging and a good number of people donated blood in this hot weather for the noble cause.

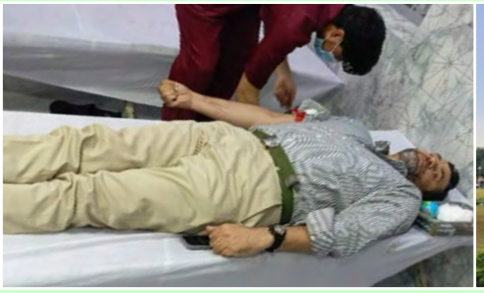
Lake View Park, Islamabad | 31 July & 11 August 2024

With the approval of Park Manager Islamabad, Mr. Ibrar Hussain, we arranged two blood donation camps in Lake View Park Islamabad. Although donations were less in number, people in the park took interest to know about thalassemia. Taking this opportunity our trained staff informed them about the disease and need to collect blood. Director Park Ms Saira Khan took personal interest to arrange a blood donation drive with the celebrations of Independence Day. Team Pathwel was very enthusiastic, and all team members wore green and white to mark the Independence Day spirit.



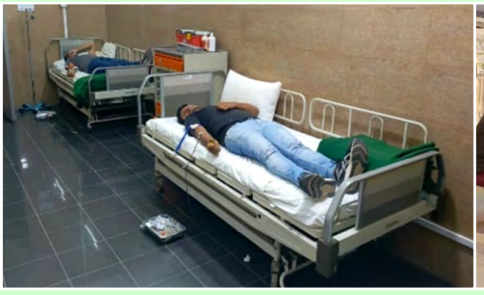
Evacuee Trust Complex, Islamabad | 27 August 2024

Deputy Administrator Mr. Imran Arif Janjua (Evacuee Trust) organized a blood donation camp in the building of Evacuee Trust Complex. The Pathwel staff was warmly received by Mr Fazal Ur Rehman (country representative) who took keen interest to know about our organization.




Giga Mall DHA Phase II Islamabad | 31 August 2024

Marketing department of Giga Mall arranged a blood donation drive and provided a Health and Safety Room for our camp activity. Moreover, Giga Mall team voluntarily helped us to motivate people for blood donation.


Leading from the front

31 July 2024

Chief Operating Officer, Pathwel, Col (R) Dr Kamran Mushtaq Pathwel also donated blood at the age of 68 on July 31, 2024 for Thalassemia patients. This is a real inspiration and motivation for all of us that everyone can donate blood with good Hb level.

PATHWEL Galaxy

Contributed by Dr Zohra J Wazir, Chief Medical Officer Thalassemia Wing

M Awais Abbas
Age: 3 years

Zoha Baber & Zainab Baber
Age: 4 years & 5 years

Abeha Umair
Age: 6 years

Shahanshah
He is in class 9th
Age: 18 years

Houzaima Mumtaz
Age: 3 years

Tanzeela Haider
She topped in class 1
Age: 5 years

Minahil Shehzadi
Age: 8 years

Our very talented patient Areesha Naeem (17 yrs). Her hobies are Stiching and Sketchting. We can see some of her art work.

PATHWEL Stars

A Case of Acute Myeloid Leukemia

By Dr. Khalil ur Rehman,
Junior Consultant and BMT specialist, PATHWEL

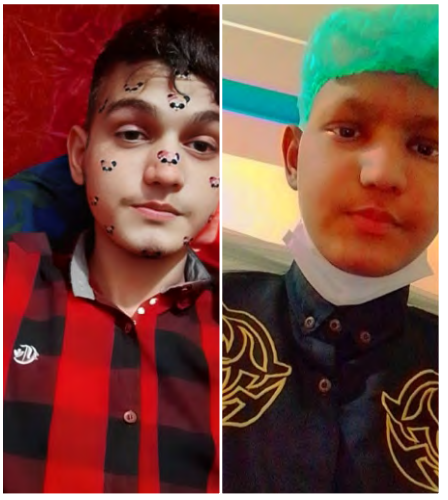
It was in November 2022 when Sahil, a 17-year-old student from Kotli, Azad Jammu and Kashmir, was referred to Pathwel with 2 weeks history of palpitations, headache, and fever. Before that he was fine and leading a normal life.

Upon examination, the patient was pale and had bilateral cervical lymphadenopathy and hepatomegaly. His CBC results revealed WBC: 188 x 109/l, Hb: 6.5 g/dl, and platelets 26 x 109/l. Peripheral blood film demonstrated 85% blast cells. Immunophenotyping suggested acute myeloid leukemia (AML), and cytogenetic analysis identified an abnormal karyotype with tetraploidy. PCR testing revealed PML-RARA fusion gene.

Sahil was given 2 cycles of induction chemotherapy with D3A7 along with ATRA. The bone marrow after the 2nd cycle was in morphological remission but PCR for PML-RARA was positive. The patient had an HLA matched sibling donor, and it was decided to take him to transplant.

Sahil underwent allogeneic bone marrow transplant (BMT) on 3 March 2023. There was no ABO mismatch. Conditioning regimen consisted of Bu12.8(IV), Cy120, and TG2.5. Stem cell source was three bags of primed bone marrow harvest, providing a total TNC dose of 6.1 x 109/kg and a CD34+ dose of 4.58 x 10^6/kg. GVHD prophylaxis was given with cyclosporine, mycophenolate mofetil, and a short course of methotrexate. Neutrophil engraftment was achieved by day +13, and platelet engraftment occurred by day +32.

The post-transplant course was complicated by grade IV mucositis, neutropenic fever, cyclosporine-induced hypertension, acute skin GVHD, and acute gut GVHD (which responded to steroid treatment). Sahil also experienced CMV reactivation, managed with valganciclovir, and TA-TMA, which necessitated switching from cyclosporine to tacrolimus. Immunosuppression was gradually



tapered from day +90 post-transplant and was discontinued on day +216. He subsequently experienced only mild oral and hepatic GVHD, which has resolved. Currently he is 18 months post-transplant, relapse free and maintaining stable blood counts with a good quality of life.

Zainab Raheem (30 years), MS (Software Engineering)

Zainab topped in MS in 2018 and achieved a gold medal from Bahria University. She was always an high achiever. Currently she is working as SQA engineer in a prestigious organization. She is always very vigilant about her blood transfusions and iron chelation so that's why her health is so preserved. God help those who help themselves.

Mr Muhammad Ali (50 years)

Our regular blood donor Muhammad Ali. He has donated blood for 56 times.

Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits

Exagamglogene Autotemcel for Transfusion-Dependent β-Thalassemia

F. Locatelli, P. Lang, D. Wall et al; N Engl J Med 2024;390:1663-76. DOI: 10.1056/NEJMoa2309673

Exagamglogene autotemcel (exa-cel) is a nonviral cell therapy designed to reactivate fetal hemoglobin synthesis through ex vivo CRISPR-Cas9 gene editing of the erythroid-specific enhancer region of BCL11A in autologous CD34+ hematopoietic stem and progenitor cells (HSPCs).

The authors conducted an open-label, single-group, phase 3 study of exa-cel in patients 12 to 35 years of age with transfusion-dependent β-thalassemia. Before the exa-cel infusion, patients underwent myeloablative conditioning with pharmacokinetically dose-adjusted busulfan. The primary end point was transfusion independence, defined as a weighted average hemoglobin level of 9 g per deciliter or higher without red-cell transfusion for at least 12 consecutive months.

A total of 52 patients received exa-cel and were included in this prespecified interim analysis; the median follow-up was 20.4 months (range, 2.1 to 48.1).

Neutrophils and platelets engrafted in each patient. Among the 35 patients with sufficient follow-up data for evaluation, transfusion independence occurred in 32 (91%; P<0.001 against the null hypothesis of a 50% response).

During transfusion independence, the mean total hemoglobin level was 13.1 g per deciliter and the mean fetal hemoglobin level was 11.9 g per deciliter, and fetal hemoglobin had a pancellular distribution (≥94% of red cells). The safety profile of exa-cel was generally consistent with that of myeloablative busulfan conditioning and autologous HSPC transplantation. No deaths or cancers occurred.

Decitabine in Older Patients with Acute Myeloid Leukemia (AML): Quality of Life Results of the EORTC-GIMEMA-GMDS-SG Randomized Phase 3 Trial

Fabio Efficace, Michal Kicinski, Corneel Coens,et al; Blood (2024) 144 (5): 541–551. doi.org/10.1182/blood.2023023625

ClinicalTrials.gov ID NCT02172872: 10-day decitabine versus conventional chemotherapy ("3+7") followed by allografting in AML patients ≥ 60 years

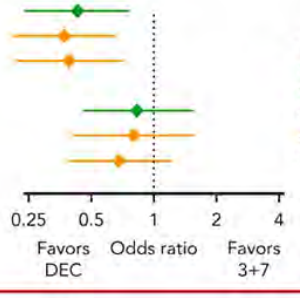
Between December 2014 and August 2019, 606 patients were randomized (303 in the DEC arm and 303 in the 3+7 arm)

Patient characteristics by treatment arm among those with a baseline health-related quality of life evaluation

	Treatment arm		
	DEC (N = 279) N (%)	3+7 (N = 270) N (%)	Total (N = 549) N (%)
Age, years			
N	279 (100.0)	270 (100.0)	549 (100.0)
60-64	66 (23.7)	65 (24.1)	131 (23.9)
65-69	119 (42.7)	112 (41.5)	231 (42.1)
≥70	94 (33.7)	93 (34.4)	187 (34.1)
Sex			
N	278 (99.6)	269 (99.6)	547 (99.6)
Male	149 (53.6)	169 (62.8)	318 (58.1)
Female	129 (46.4)	100 (37.2)	229 (41.9)

Health-related quality of life (HRQoL) deterioration by treatment arm: decitabine vs intensive chemotherapy

	Decitabine		3+7		
Deterioration at 2 months	N/Total	% (95% CI)	N/Total	% (95% CI)	OR (95% CI)
Main analysis	157/207	76 (69-82)	140/159	88 (82-93)	0.43 (0.24, 0.76)
Including discontinuation	199/248	80 (75-85)	210/229	92 (87-95)	0.37 (0.21, 0.65)
Excluding progression	143/194	74 (67-80)	135/154	88 (81-92)	0.39 (0.22, 0.70)
Deterioration at long-term					
Main analysis	231/258	90 (85-93)	216/237	91 (87-94)	0.83 (0.46, 1.52)
Including discontinuation	252/274	92 (88-95)	244/261	93 (90-96)	0.80 (0.41, 1.54)
Excluding progression	212/245	87 (82-91)	207/229	90 (86-94)	0.68 (0.39, 1.21)



The results of the main analyses are indicated in green on the plot. The results of the two sensitivity analyses are indicated in orange

Conclusion: The current findings on HRQoL indicate that decitabine may be a preferable treatment option for fit older patients with AML compared to intensive chemotherapy.

blood Visual Abstract

Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits

Blinatumomab for MRD-Negative Acute Lymphoblastic Leukemia in Adults

Mark R. Litzow, Zhuoxin Sun, Ryan J. Mattison et al; N Engl J Med 2024;391:320-333; DOI: 10.1056/NEJMoa2312948

Many older adults with B-cell precursor acute lymphoblastic leukemia (BCP-ALL) have a relapse despite having a measurable residual disease (MRD)–negative complete remission with combination chemotherapy. The addition of blinatumomab, a bispecific T-cell engager molecule that is approved for the treatment of relapsed, refractory, and MRD-positive BCP-ALL, may have efficacy in patients with MRD-negative remission.

In this phase 3 trial, authors randomly assigned patients 30 to 70 years of age with BCR::ABL1-negative BCP-ALL who had MRD-negative remission after induction and intensification chemotherapy to receive 4 cycles of blinatumomab in addition to 4 cycles of consolidation chemotherapy or to receive 4 cycles of consolidation chemotherapy alone. The primary end point was overall survival (OS), and relapse-free survival (RFS) was a secondary end point.

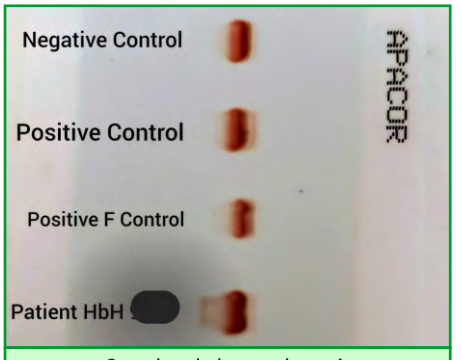
Complete remission with or without full count recovery was observed in 395 of 488 enrolled patients (81%). Of the 224 patients with MRD-negative status, 112 were assigned to each group. At a median follow-up of 43 months, an advantage was observed in the blinatumomab group as compared with the chemotherapy-only group with regard to OS (at 3 years: 85% vs. 68%; HR for death, 0.41; 95% CI, 0.23 to 0.73; P=0.002), and the 3-year RFS was 80% with blinatumomab and 64% with chemotherapy alone (HR for relapse or death, 0.53; 95% CI, 0.32 to 0.87). A higher incidence of neuropsychiatric events was reported in the blinatumomab group than in the chemotherapy-only group.

The addition of blinatumomab to consolidation chemotherapy in adult patients in MRD-negative remission from BCP-ALL significantly improved overall survival.

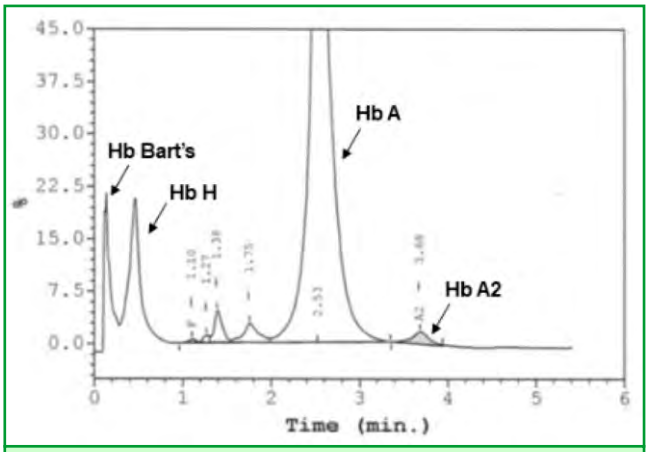
Picture Quiz Answer

Hemoglobin H Disease

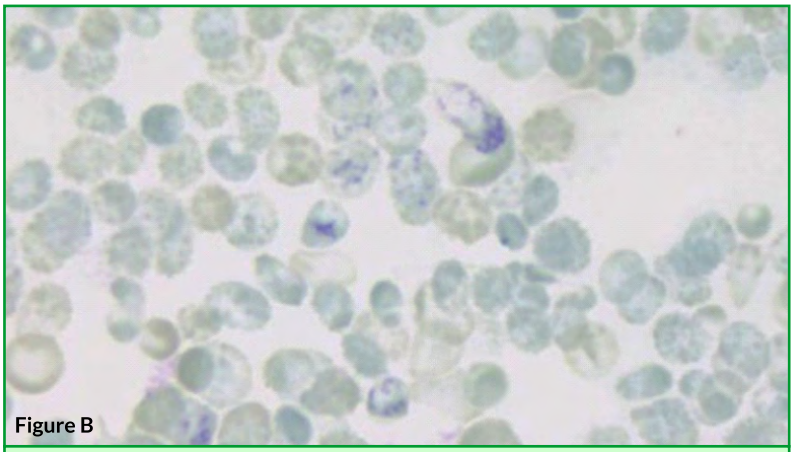
Hemoglobin H disease (HbH) is a form of alpha thalassemia in which moderately severe anemia develops due to reduced formation of alpha globin chains. As in the other forms of thalassemia, there is an imbalance of globin chains needed to form hemoglobin. Normally, there are four genes to produce alpha globin chains. When three out of four of these genes become inactive, there are too few alpha globin chains to combine with beta chains. The excess beta globin chains then combine with each other to form Hb H. While most individuals with HbH do not require transfusions, there is heterogeneity in the clinical course.



Starch gel electrophoresis



Typical hemoglobin analysis of patients with HbH



Reticulocyte stain using brilliant cresyl blue showing golf ball Inclusions

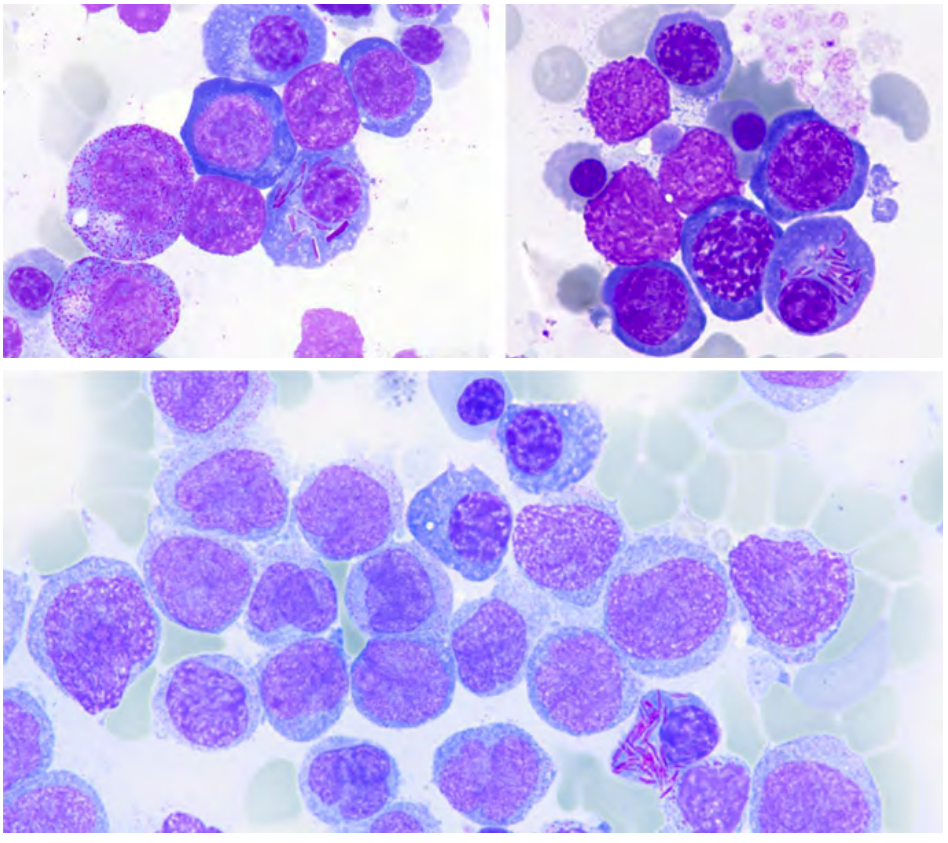
Morphology Updates

Plasma cells with Auer- rod- like inclusions in a patient with MGUS and acute myeloid leukaemia with NPM1 mutation

Janine Glanzmann[1], Christian Kalberer[1], Nicolas Bonadies[2], Giuseppe Colucci[1,3]
[1]Outer Corelab, Viollier AG, Allschwil, [2]Practice for Hematology and Oncology Hirslanden, Bern, [3]Department of Hematology, University of Basel, Basel, Switzerland *| DOI: 10.1111/bjh.19560*

A 76- year- old man with asymptomatic monoclonal gammopathy of undetermined significance (MGUS) type IgM kappa, presented with fever, joint pain, leucocytosis and monocytosis. On admission to hospital the blood count showed anaemia (haemoglobin concentration 102 g/L), leucocytosis with monoblasts (leucocytes 86.5 × 109 /L; monoblasts 48.5 × 109 /L) and thrombocytopenia (platelets 111 × 109 /L). A non- progressive paraprotein level of 3.5 g/L (IgM kappa) was confirmed.

Bone marrow aspirate showed hypercellularity with 85% blasts, and acute monocytic leukaemia was diagnosed. The other diagnostic procedures, including trephine biopsy, immunophenotyping, genetic studies and next- generation sequencing, allowed classification according to the WHO criteria as acute myeloid leukaemia (AML) with NPM1-Type A mutation, FLT3- ITD negative, with additional DNMT3A and PTPN11 mutations, but no chromosomal anomalies. The patient was treated with azacitidine 75 mg/m2 on days 1–5 and days 8–9, and with venetoclax 400 mg on days 1–14, achieving a complete remission after one cycle of chemotherapy. Bone marrow examination after two cycles of therapy showed a significant reduction of blasts (<2%).



Interestingly, plasma cells containing numerous intracellular Auer- rod- like, needle- shaped cytoplasmatic inclusions were observed (upper, plasma cells with and without intracytoplasmic inclusions, May–Grünwald–Giemsa stain, ×100 objective, total magnification ×1000). Retrospectively, the presence of rare plasma cells with the same cytoplasmatic inclusions were detected in the first bone marrow slide prepared at diagnosis of AML before chemotherapy (bottom, hypercellular bone marrow showing blasts and a single plasma cell with cytoplasmatic inclusions, May–Grünwald Giemsa stain, ×60 objective, total magnification ×600). No Auer rods were detected in the myeloid blasts in either bone marrow smears.

Cytoplasmatic inclusions that are sometimes indistinguishable from Auer rods have been described in B-cell, myeloid or plasma cell malignancies. This case of MGUS and AML with NPM1 mutation where 'bundled' Auer- rod- like structures were present in abnormal plasma cells of MGUS but not in blast cells emphasises the surprises that morphology can sometimes present.

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Trends in allogeneic transplantation for favorable risk acute myeloid leukemia in first remission: a longitudinal study of >15 years from the ALWP of the EBMT

Arnon Nagler, Myriam Labopin, Urpu Salmenniemi et al; Bone Marrow Transplantation (2024); DOI: 10.1038/s41409-024-02379-z

We assessed outcomes of allogeneic transplantation (HSCT) in favorable risk AML in CR1 over 3 time periods. 1850 patients were included, 2005 to 2009-222, 2010 to 2014 -392, and 2015 to 2021-1236; 526 with t (8:21), 625 with inv (16), and 699 with NPM1mutFLT3WT.

Patients transplanted in 2015–2021 were older (p<0.0001) with more patients ≥60 years of age (p<0.0001).

The most frequent diagnosis in 2015–2021 was NPM1mutFLT3WT vs. t (8:21) in the 2 earlier periods, (p<0001).

Haploidentical transplants increased from 5.9% to 14.5% (p<0.0001). Graft-versus-host disease (GVHD) prophylaxis with post-transplant cyclophosphamide (PTCy) was more frequent in 2015–2021 vs. the other 2 periods (p<0.0001).

On multivariate analysis, incidence of total chronic GVHD was reduced in HSCTs performed ≥2015 vs. those performed in 2005–2009, hazard ratio (HR)=0.74 (p=0.046) and GVHD-free, relapse-free survival (GRFS) improved for patients transplanted from 2010–2014 vs. those transplanted in 2005–2009, HR=0.74 (p=0.037). Other HSCT outcomes did not differ with no improvement ≥2015. LFS, OS, and GRFS were inferior in patients with t (8:21) with HR=1.32 (p=0.026), HR=1.38 (p=0.027) and HR=01.25 (p=0.035), respectively.

In conclusion, this retrospective analysis of HSCT in patients with favorable risk AML, transplanted over 16 years showed an increased number of transplants in patients ≥60 years, from Haplo donors with PTCy. Most importantly, 3-year GRFS improved ≥2010 and total chronic GVHD reduced ≥2015, with no significant change in other HSCT outcomes.

Comparative analysis of reduced toxicity conditioning regimens between fludarabine plus melphalan and fludarabine plus busulfex in adult patients with acute lymphoblastic leukemia

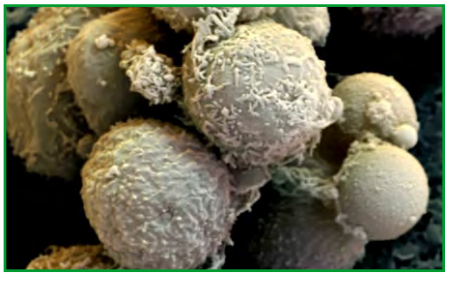
Jaehyun Ahn, Jae-Ho Yoon, Daehun Kwag et al; Bone Marrow Transplantation (2024); doi.org/10.1038/s41409-024-02363-7

Reduced-toxicity conditioning (RTC) regimens aim to mitigate regimen-related toxicity while maintaining anti-leukemic efficacy in allo-HSCT. We assessed outcomes of RTC regimens utilizing melphalan versus intravenous busulfan combined with fludarabine in adult acute lymphoblastic leukemia (ALL) patients.

A retrospective analysis was conducted with 149 consecutive adult ALL patients (median age 51, range 18–60) in remission undergoing allo-HSCT. Patients received either fludarabine 150mg/BSA plus 2 days of melphalan 70mg/BSA (FM140, n=76) from 2009 to 2015 or fludarabine plus 3 days of busulfan 3.2mg/kg (FB9.6, n=73) from 2016 to 2021.

At 5 years post-HSCT, FM140 demonstrated superior disease-free survival (53.4% vs. 30.5%, p=0.007) and lower cumulative relapse (27.4% vs. 46.8%, p=0.026) than FB9.6. Five-year overall survival and non-relapse mortality did not significantly differ. FM140 exhibited a higher incidence of acute graft-versus-host disease (GVHD) grades II-IV (49.3% vs. 30.3%, p=0.016), though rates of acute GVHD grades III-IV and chronic GVHD were similar.

Multivariate analysis identified Philadelphia chromosome and minimal residual disease positive status, and FB9.6 conditioning as predictors of increased relapse and poorer disease-free survival. FM140 RTC regimen displayed significantly reduced relapse and superior disease-free survival compared to FB9.6 in ALL patients undergoing allo-HSCT, highlighting its current clinical utility.



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Tacrolimus versus cyclosporine a combined with post-transplantation cyclophosphamide for AML In first complete remission: a study from the acute leukemia working party (EBMT)

Gesine Bug, Myriam Labopin, Alexander Kulagin et al; Bone Marrow Transplantation; https://doi.org/10.1038/s41409-024-02331-1

Choice of calcineurin inhibitor may impact the outcome of patients undergoing T-cell replete hematopoietic cell transplantation (HCT) with post-transplant cyclophosphamide (PT-Cy) and mycophenolate mofetil (MMF) for prophylaxis of graft-versus-host disease (GVHD). We retrospectively analyzed 2427 patients with acute myeloid leukemia (AML) in first remission transplanted from a haploidentical (n = 1844) or unrelated donor (UD, n = 583) using cyclosporine A (CSA, 63%) or tacrolimus (TAC, 37%) and PT-Cy/MMF.

In univariate analysis, CSA and TAC groups did not differ in 2-year leukemia-free or overall survival, cumulative incidence (CI) of relapse or non-relapse mortality. CI of severe grade III-IV acute GVHD was lower with TAC (6.6% vs. 9.1%, p = 0.02), without difference in grade II-IV acute GVHD or grade III-IV acute GVHD/severe chronic GVHD, relapse-free survival (GRFS). In multivariate analysis, TAC was associated with a lower risk of severe grade III-IV acute GVHD solely with haploidentical donors (HR 0.64 [95% CI, 0.42–0.98], p = 0.04), but not UD (HR 0.49 [95% CI, 0.2–1.21], p = 0.12). There was no significant difference for chronic GVHD.

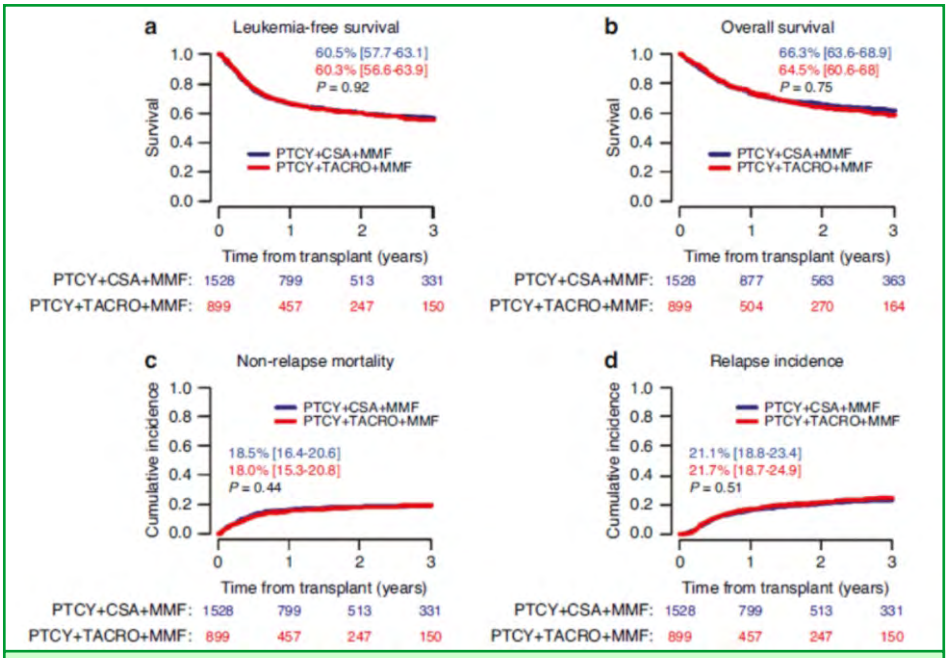

Fig: Outcome of patients according to graft-versus-host disease (GVHD) prophylaxis. a Leukemia-free Survival; b Overall Survival; c Nonrelapse Mortality; d Relapse Incidence.

In conclusion, PT-Cy/MMF-based GVHD prophylaxis resulted in favorable OS and GRFS, irrespective of the CNI added. In haploidentical HCT, TAC seemed to prevent severe acute GVHD more effectively than CSA without impact on other outcome parameters.

Definitions of SOS/VOD upon the modified Seattle criteria and the refined EBMT criteria 2023.

Hiroya Ichikawa, Kimikazu Yakushijin et al; Bone Marrow Transplantation (2024) 59:518–525; https://doi.org/10.1038/s41409-024-02215-4

	Refined EBMT criteria 2023		
Modified Seattle criteria	**Probable SOS/VOD**	**Clinical SOS/VOD**	**Proven SOS/VOD**
The presence of 2 or more of the following within 20 days (1) Bilirubin >2 mg/dL (2) Hepatomegaly and/or Right upper quadrant pain (3) Weight gain: >2%	The presence of 2 or more of the following (1) Bilirubin ≥2 mg/dL (2) Painful hepatomegaly (3) Weight gain: >5% (4) Ascites (5) Ultrasound and/or elastography suggestive of SOS/VOD	The presence of bilirubin ≥2 mg/dL and 2 or more of the following (1) Painful hepatomegaly (2) Weight gain: >5% (3) Ascites	The presence of either of the following (1) Histologically proven (2) Hemodynamically proven (HVPG ≥ 10 mmHg)

SOS/VOD sinusoidal obstruction syndrome/veno-occlusive disease, *EBMT* European Society for Blood and Marrow Transplantation, *HVPG* hepatic venous pressure gradient.

Hemophilia Patients Welfare Society Awareness Seminar

Report by Dr. Hina Fatima

Navigating Life with Bleeding Disorders Gynecological & Psychosocial Challenges for Women & Girls

Date: 6 July 2024
Venue: Rawalpindi Medical University
Attendees: Patients: 24, Staff members: 05, Doctors: 10.
Objective: The objective of the seminar was to provide a platform for women and girls with bleeding disorders to discuss gynecological issues and socioeconomic challenges, share experiences, and gain insights from experts to improve their overall health and quality of life.

General discussion about Hemophilia and Von Willebrand Diseases (VWD).
Sign, symptoms & management of VWD, RBD's & Hemophilia with special focus on HMB. Dr. Lubna Zafar answered various questions from the participants, such as: How to manage heavy menstrual bleeding? What are the treatment options for hemophilia and VWD? How can they improve their daily lives and prevent complications? What lifestyle adjustments can help manage these conditions?

Hormonal and non-hormonal therapies for managing HMB.
Dr. Humera Noreen provided an in-depth discussion on hormonal and non-hormonal therapies for managing menstrual bleeding in patients with (VWD). Use of Combined Oral Contraceptives (COCs) to regulate menstrual cycles, reduce menstrual flow, provide contraception, decrease the volume of menstrual blood loss, regulate, and predict menstrual cycles and reduce menstrual pain and cramps.

Dr. Humera emphasized the importance of personalized treatment plans based on the severity of the condition, individual patient needs, and medical history. She encouraged patients to maintain open communication with their healthcare providers. Regularly monitor their condition. Adhere to prescribed treatments and follow-up appointments. Seek support from patient advocacy groups and counseling services.

Psychosocial challenges
Dr. Umamia gave a presentation on managing daily life challenges, stress, and anxiety for women and girls with bleeding disorders. She gave details of how to manage life by coping with depression, anxiety, and tension. Importance of identifying specific triggers related to the bleeding disorder and daily life. Recognizing physical and emotional symptoms of stress and anxiety, such as headaches, irritability, and trouble in concentrating.

She explained the coping strategies including relaxation techniques and practicing deep breathing exercises, progressive muscle relaxation, and mindfulness meditation to reduce stress. Engaging in regular, moderate exercise to boost mood and reduce anxiety. Pursuing enjoyable activities to divert attention from stressors and enhance overall well-being.

Life story of patients Nazia and Alizey
Nazia shared her life story, offering another powerful source of inspiration for the seminar attendees. Nazia began her story by describing her childhood, where she often experienced unexplained bruises and frequent nosebleeds. It was not until her early teens that she was diagnosed with von Willebrand disease. This diagnosis brought both relief and fear, as she finally understood the cause of her symptoms but also faced the reality of living with a chronic condition. She highlighted the importance of self-care, seeking help when needed, and

staying informed about their condition. By implementing these strategies, she was able to lead fulfilling life and managed stress and anxiety effectively.

Alizey a student of 10th class also shared her story about the challenges she faced and how she overcame them to step forward towards a healthy lifestyle goal.

Donation by Nazia and Fauzia for HPWS.
In a heartwarming gesture, Nazia and Fauzia announced that they would provide funds to support patients with bleeding disorders. Nazia shared that her motivation to contribute funds stemmed from her own experiences and the challenges she faced growing up with a bleeding disorder. She expressed her desire to give back to the community and support others in similar situations. The purpose of her funds will be directed towards providing financial assistance for medical treatments, diagnostic tests, and necessary medications for patients who cannot afford them. She emphasized the importance of making healthcare accessible to all, regardless of their financial situation.

Conclusion
The seminar concluded with a commitment to continue these efforts, fostering a supportive and informed community for women and girls with bleeding disorders. The event was a reminder that, together we can overcome challenges and build a bright future for WGBDs.

Case Report

Laparoscopic Cholecystectomy in Hemophilia A - Effective Multidisciplinary Care

By Dr. Hina Fatima

A 17-year-old male with hemophilia A, resident of Abbottabad, presented with abdominal cramps, nausea, and vomiting over a two-day period. He was admitted to the Ayub Teaching Hospital in Abbottabad, where diagnostic imaging, including ultrasound and MRI, revealed cholelithiasis with multiple gallstones and a particularly large 13.5 mm stone impacted in the gallbladder neck.

A laparoscopic cholecystectomy was planned. To minimize surgical trauma and reduce the risk of bleeding, meticulous management of his bleeding risk was crucial. The patient was negative for inhibitors. A preoperative plan was carefully developed & shared with the Surgeons. This included starting tranexamic acid the night before the surgery & FVIII concentrates on the morning of the operation. A preoperative dose of 40 IU/kg of factor VIII was given. During the procedure, careful surgical techniques were employed, and factor VIII levels were closely monitored. Post-surgery, the FVIII dose was gradually reduced over a 2-week period. Tranexamic acid was continued for 10 days. Postoperative course was uneventful, and no signs of bleeding observed.

At the time of discharge, the patient was in stable condition. Detailed instructions were provided

regarding wound care, activity limitations, and signs of potential complications. Follow-up appointments were arranged to monitor recovery and adjust factor VIII dosing as needed.

This case illustrates the effective management of hemophilia A in a surgical context and highlights the successful coordination between the Hematology & Surgical teams to develop tailored factor VIII replacement protocol. The positive outcome underscores the importance of careful preoperative planning and postoperative care in achieving favorable results for patients with bleeding disorders.

PAKISTAN THALASSAEMIA
WELFARE SOCIETY (REGD)

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