

# Contents

- x Editors' Message
- xi Reviewers
- xii Continuing Medical Education Information

## Ham-Wasserman Lecture

- 1 Thrombotic anti-PF4 immune disorders: HIT, VITT, and beyond**  
ANDREAS GREINACHER AND THEODORE E. WARKENTIN

## Acquired Hemophilia A Diagnosis and Management

- 11 Diagnosis and laboratory monitoring of hemophilia A**  
SEAN PLATTON, SUTHESH SIVAPALARATNAM, AND PRIYANKA RAHEJA
- 19 Immunotherapy of acquired hemophilia A**  
ANDREAS TIEDE
- 24 The role of emicizumab in acquired hemophilia A**  
JACQUELINE POSTON AND REBECCA KRUSE-JARRES

## Alphabet Soup: Challenging Consults on the Pediatric Units

- 31 Inflamed—HLH, MAS, or something else?**  
ASHISH KUMAR, EILY COURNOYER, AND LEONARD NAYMAGON
- 37 Too many white cells—TAM, JMML, or something else?**  
ALEXANDRA SATTY, ELLIOT STIEGLITZ, AND NICOLE KUCINE
- 43 Where have all the platelets gone? HIT, DIC, or something else?**  
ROHITH JESUDAS AND CLIFFORD M. TAKEMOTO

## Are We Personalizing MDS Therapy in 2023?

- 51 How to classify risk based on clinical and molecular modeling: integrating molecular markers in the risk assessment of myelodysplastic syndrome**  
RENA R. XIAN
- 59 Next-generation therapy for lower-risk MDS**  
MARIE SÉBERT
- 65 Frontline treatment options for higher-risk MDS: can we move past azacitidine?**  
DAVID A. SALLMAN AND ZHUOER XIE
- 73 EVIDENCE-BASED MINIREVIEW**  
**Mutational screening to improve the transplantation decision-making process in MDS**  
ALESSIA CAMPAGNA AND MATTEO G. DELLA PORTA

### CAR T Cells in ALL: Bridge or Definitive Therapy?

- 77 Long-term follow-up of CD19-CAR T-cell therapy in children and young adults with B-ALL**  
REBECCA EPPERLY AND NIRALI N. SHAH
- 84 Stem cell transplantation for ALL: you've always got a donor, why not always use it?**  
DAVID SHYR, KARA L. DAVIS, AND ALICE BERTAINA
- 91 Preventing relapse after CD19 CAR T-cell therapy for pediatric ALL: the role of transplant and enhanced CAR T cells**  
AIMEE C. TALLEUR, SWATI NAIK, AND STEPHEN GOTTSCHALK

### Energizing the Red Cell: Pyruvate Kinase Activators for Treatment of Hereditary Hemolytic Anemias

- 97 Pyruvate kinase activators for treatment of pyruvate kinase deficiency**  
RACHAEL F. GRACE
- 107 Pyruvate kinase activators: targeting red cell metabolism in sickle cell disease**  
JULIA Z. XU AND GREGORY M. VERCELLOTTI
- 114 Pyruvate kinase activators: targeting red cell metabolism in thalassemia**  
KEVIN H.M. KUO
- 121 EVIDENCE-BASED MINIREVIEW**  
**When should gene therapy be considered for transfusion-dependent  $\beta$ -thalassemia patients?**  
CHERYL MENSAH AND SUJIT SHETH

### Goldilocks and Transplant Timing in Inherited Marrow Failure Syndromes: Too Early, Too Late, Just Right?

- 125 Clonal evolution in inherited marrow failure syndromes predicts disease progression**  
KRISTEN E. SCHRATZ
- 135 Minimal intensity conditioning strategies for bone marrow failure: is it time for "preventative" transplants?**  
SUNEET AGARWAL
- 141 Posttransplant complications in patients with marrow failure syndromes: are we improving long-term outcomes?**  
ZAHRA HUDDA AND KASIANI C. MYERS

### Graft-Versus-Host Disease: Is an Ounce of Prevention Worth a Pound of Cure?

- 149 Planning GvHD preemptive therapy: risk factors, biomarkers, and prognostic scores**  
JACOB ROZMUS, JOHN E. LEVINE, AND KIRK R. SCHULTZ
- 155 Novel approaches to acute graft-versus-host disease prevention**  
BENJAMIN WATKINS AND MUNA QAYED
- 164 Chronic GVHD: review advances in prevention, novel endpoints, and targeted strategies**  
IDOROENYI AMANAM, SALMAN OTOUKESH, MONZR M. AL MALKI, AND AMANDEEP SALHOTRA
- 171 EVIDENCE-BASED MINIREVIEW**  
**Should posttransplant cyclophosphamide be considered standard of care for pediatric transplantation of acute leukemia?**  
ERIN E. DOHERTY AND ROBERT A. KRANCE

### Have We Optimized Therapy Yet for Patients with AML?

- 175 Improving long-term outcomes with intensive induction chemotherapy for patients with AML**  
CHRISTOPH RÖLLIG
- 186 The approach of HMA plus VEN with or without BMT for all patients with AML**  
HEATHER J. MALE AND TARA L. LIN

- 192 The future paradigm of HMA + VEN or targeted inhibitor approaches: sequencing or triplet combinations in AML therapy**

SANGEETHA VENUGOPAL AND JUSTIN WATTS

### **Hematologic Toxicity of Immunotherapies**

- 198 Recognizing, defining, and managing CAR-T hematologic toxicities**

KAI REJESKI, MARION SUBKLEWE, AND FREDERICK L. LOCKE

- 209 Checkpoint inhibitors**

MICHAEL H. KROLL

- 216 Bispecific antibody therapies**

LUIZ HENRIQUE DE ASSIS, DANIEL EL FASSI, AND MARTIN HUTCHINGS

### **Hematologists and the Care of Pregnant Women**

- 223 Identifying and treating iron deficiency anemia in pregnancy**

ADAM K. LEWKOWITZ AND METHODIUS G. TUULI

- 229 Management of pregnant women who have bleeding disorders**

ANDRA H. JAMES, LUIS D. PACHECO, AND BARBARA A. KONKLE

- 237 Prevention, diagnosis, and management of PE and DVT in pregnant women**

BARRY KEVANE AND FIONNUALA NÍ ÁINLE

### **Hematologists as Lifesavers: Inpatient Hematology Emergencies**

- 248 How to avoid early mortality in acute promyelocytic leukemia**

OLUWATOBI ODETOLA AND MARTIN S. TALLMAN

- 254 How to manage ITP with life-threatening bleeding**

JEAN M. CONNORS AND STEVEN FEIN

- 259 Inpatient recognition and management of HLH**

ADI ZOREF-LORENZ, MARTIN ELLIS, AND MICHAEL B. JORDAN

### **Hemostasis in Patients with Severe Liver Disease**

- 267 How to assess hemostasis in patients with severe liver disease**

TON LISMAN

- 274 How to manage hemostasis in patients with liver disease during interventions**

LARA N. ROBERTS

- 281 How to manage splanchnic vein thrombosis in patients with liver disease**

NICOLETTA RIVA AND WALTER AGENO

- 289 EVIDENCE-BASED MINIREVIEW**

**Direct oral anticoagulants to treat deep venous thrombosis and pulmonary embolism in patients with cirrhosis: are we there yet?**

AMBER AFZAL AND JORDAN SCHAEFER

### **Hot Topics in Blood Donation: Donor Risks and Social Justice**

- 294 MSM and blood donation: shifting to individualized risk assessment**

MINDY GOLDMAN

- 299 Clonal hematopoiesis in frequent whole blood donors**

DARJA KARPOVA

- 305 T-cell lymphopenia in frequent volunteer platelet donors**

RICHARD M. KAUFMAN

### **How Can We Manage High-Risk Hematologic Malignancies in the Community?**

- 311 Acute leukemias and complicated lymphomas: pearls to optimize management when patients stay local**

DIPTI PATEL-DONNELLY AND MITUL GANDHI

**318 Multiple myeloma: a paradigm for blending community and academic care**

JESÚS G. BERDEJA

**324 Clinical research in the community**

RUEMU EJEDAFETA BIRHIRAY AND MAYA NICOLE BIRHIRAY

**How Do We Apply T-Cell Redirection Therapy for Multiple Myeloma? CAR T Cells and Bispecific Antibodies**

**332 Current use of bispecific antibodies to treat multiple myeloma**

HOLLY LEE, PAOLA NERI, AND NIZAR J. BAHLIS

**340 Current use of CAR T cells to treat multiple myeloma**

ROSS S. FIRESTONE AND SHAM MAILANKODY

**348 Managing side effects: guidance for use of immunotherapies in multiple myeloma**

EMILY C. LIANG AND SURBHI SIDANA

**How Do We Calibrate Cellular Therapy for Lymphoma in 2023?**

**357 CAR T-cell therapy in aggressive lymphomas—identifying prognostic and predictive markers**

ALBERTO MUSSETTI, NICOLE FABBRI, AND ANNA SUREDA

**364 Management of aggressive lymphoma after CAR T-cell therapy failure**

LORETTA J. NASTOUPIL AND SWETHA KAMBHAMPATI

**370 Selection of bispecific antibody therapies or CAR-T cell therapy in relapsed lymphomas**

AJAY MAJOR AND MANALI KAMDAR

**382 EVIDENCE-BASED MINIREVIEW**

**Barriers to accessing cellular therapy for patients receiving care in community practices**

CHIJOKE NZE AND CHRISTOPHER R. FLOWERS

**How Do We Enhance Results in Rare Hematologic Malignancies?**

**386 Langerhans cell histiocytosis: promises and caveats of targeted therapies in high-risk and CNS disease**

OUSSAMA ABLA

**396 Mastocytosis demystified**

SCOTT VEITCH AND DEEPTI H. RADIA

**407 Amyloid consults do not have to be vexing**

ANITA D'SOUZA

**How Do We Extend Survival for Patients with CLL in 2023?**

**413 MRD-directed therapy in CLL: ready for prime time?**

JOANNA M. RHODES, CARLOS A. LOPEZ, AND JACQUELINE C. BARRIENTOS

**421 Dual-targeted regimens for the frontline treatment of CLL**

CHAITRA UJJANI

**427 Richter transformation—is there light at the end of this tunnel?**

TOBY A. EYRE

**How Do We Improve Outcomes in Relapsed and Refractory Multiple Myeloma in 2023?**

**433 A rational approach to functional high-risk myeloma**

FRANCESCA GAY, GIUSEPPE BERTUGLIA, AND ROBERTO MINA

**443 Considerations for next therapy after anti-CD38 monoclonal antibodies used as first line**

MONIQUE HARTLEY-BROWN AND ATEH ZINKENG

**450 Options at the time of relapse after anti-BCMA therapy**

BEATRICE RAZZO, ALFRED L. GARFALL, AND ADAM D. COHEN

## How Do We Tackle Remaining Clinical Challenges in CML?

- 459 Accelerated-phase CML: de novo and transformed**  
NARANIE SHANMUGANATHAN AND TIMOTHY P. HUGHES
- 469 Resistance mutations in CML and how we approach them**  
SIMONA SOVERINI
- 476 Atypical CML: diagnosis and treatment**  
MASSIMO BRECCIA

## How Is the Management Paradigm Evolving for Hodgkin Lymphoma in 2023?

- 483 Hodgkin lymphoma treatment for older persons in the modern era**  
ANDREW M. EVENS, MARSHALL McKENNA, YUN KYOUNG RYU TIGER, AND JENICA N. UPSHAW
- 500 Management of limited-stage Hodgkin lymphoma**  
TAHA AL-JUHAISHI AND SAIRAH AHMED
- 510 The optimal management of relapsed and refractory Hodgkin lymphoma: post-brentuximab and checkpoint inhibitor failure**  
NATALIE S. GROVER, CHRISTOPHER DITTUS, ASTHA THAKKAR, AND ANNE W. BEAVEN

## Improving Outcomes for Individuals with Sickle Cell Disease: Are We Moving the Needle?

- 519 Using disease-modifying therapies in sickle cell disease**  
PARUL RAI AND KENNETH I. ATAGA
- 532 The range of haploidentical transplant protocols in sickle cell disease: all haplos are not created equally**  
ADETOLA A. KASSIM AND MICHAEL R. DEBAUN
- 542 Gene therapy for sickle cell disease**  
ALEXIS LEONARD AND JOHN F. TISDALE

## Inherited Bone Marrow Failure Syndromes: from Pediatrics to Adult

- 548 When to consider inherited marrow failure syndromes in adults**  
FERNANDA GUTIERREZ-RODRIGUES, BHAVISHA A. PATEL, AND EMMA M. GROARKE
- 556 Management of Fanconi anemia beyond childhood**  
TIMOTHY S. OLSON
- 563 Clinical manifestations of telomere biology disorders in adults**  
MARENA R. NIEWISCH, FABIAN BEIER, AND SHARON A. SAVAGE

## Not Kids Anymore and Not Adults Yet: How Do We Treat Adolescent and Young Adult (AYA) Patients with ALL?

- 573 Leveraging health care technology to improve health outcomes and reduce outcome disparities in AYA leukemia**  
JOHN C. MOLINA AND SETH ROTZ
- 581 Adolescents and young adults (AYAs) vs pediatric patients: survival, risks, and barriers to enrollment**  
SANYUKTA K. JANARDAN AND TAMARA P. MILLER
- 587 Acute lymphoblastic leukemia in young adults: which treatment?**  
ANNABELLE ANANDAPPA AND EMILY CURRAN

## Ongoing Challenges in the Management of VTE

- 593 The dos, don'ts, and nuances of thrombophilia testing**  
THITA CHIASAKUL AND KENNETH A. BAUER
- 600 Provoked vs minimally provoked vs unprovoked VTE: does it matter?**  
CECILIA BECATTINI AND LUDOVICA ANNA CIMINI

**606 How to diagnose and manage antiphospholipid syndrome**

ANNE HUBBEN AND KEITH R. McCRAE

**614 EVIDENCE-BASED MINIREVIEW**

**Should older patients with low weight and CKD receive full-dose DOACs for treatment of acute proximal DVT?**

NICOLAS GALLASTEGUI AND CAMILA MASIAS

**The Iron Revolution!**

**617 Sex, lies, and iron deficiency: a call to change ferritin reference ranges**

KYLEE MARTENS AND THOMAS G. DeLOUGHERY

**622 IV iron formulations and use in adults**

LAYLA VAN DOREN AND MICHAEL AUERBACH

**630 Intravenous iron therapy in pediatrics: who should get it and when is the right time?**

CLAY T. COHEN AND JACQUELYN M. POWERS

**636 EVIDENCE-BASED MINIREVIEW**

**Incidence, mechanism, and consequences of IV iron-induced hypophosphatemia**

KYLEE L. MARTENS AND MYLES WOLF

**Transfusion Support in Sickle Cell Disease**

**640 Managing pregnancy in patients with sickle cell disease from a transfusion perspective**

ANOOSHA HABIBI, ALEXANDRA BENACHI, AND EDOUARD LECARPENTIER

**646 Logistics, risks, and benefits of automated red blood cell exchange for patients with sickle cell disease**

SHANNON KELLY

**653 Alloimmunization and hyperhemolysis in sickle cell disease**

FRANCE PIRENNE AND CORINNE PONDARRÉ

**What Are the Advances in Myeloproliferative Neoplasms Affecting Management?**

**660 Cytoreduction for ET and PV: who, what, when, and how?**

DOUGLAS TREMBLAY

**667 Evolving landscape of JAK inhibition in myelofibrosis: monotherapy and combinations**

HARINDER GILL, GARRET M. K. LEUNG, AND YOK-LAM KWONG

**676 Are transplant indications changing for myelofibrosis?**

JEANNE PALMER

**What Are Treatment Options for Patients with Relapsed, Refractory, or Persistent AML?**

**682 Understanding differential technologies for detection of MRD and how to incorporate into clinical practice**

JACQUELINE CLOOS, LOK LAM NGAI, AND MICHAEL HEUSER

**691 Novel immunotherapies in the treatment of AML: is there hope?**

MARION SUBKLEWE, VEIT BÜCKLEIN, DAVID SALLMAN, AND NAVAL DAVER

**702 Novel therapies upon failure of HMA plus venetoclax**

ONYEE CHAN AND ALISON R. WALKER

**What Makes a Good Transplant Recipient? Putting the Puzzle Pieces Together**

**709 How old is too old? Frailty and geriatric assessments of older patients undergoing allogeneic HCT**

REENA V. JAYANI

**715 The sum of the parts: what we can and cannot learn from comorbidity scores in allogeneic transplantation**

RONI SHOUVAL AND JOSHUA A. FEIN

**723 Approaches to optimize outcomes in transplant recipients**

ASMITA MISHRA

**731 EVIDENCE-BASED MINIREVIEW**

**What makes a pediatric or young adult patient an appropriate transplant candidate?**

MONICA S. THAKAR AND MOHAMED L. SORROR

**Why Am I Getting Paged at 2 AM? Microangiopathic Emergencies**

**737 Labor and delivery: DIC, HELLP, preeclampsia**

JULIANA PEREZ BOTERO AND JENNIFER JURY McINTOSH

**745 Medical consult: aHUS, TTP? How to distinguish and what to do**

CHARLOTTE M. STORY, GLORIA F GERBER, AND SHRUTI CHATURVEDI

**754 Consumptive coagulopathy in the ICU**

ANDREW RETTER AND BEVERLEY J. HUNT