

HIGHLIGHTS FROM THE
**2010 American Society of
Hematology Annual Meeting**

*A Summary of Abstracts for Patients with
Paroxysmal Nocturnal Hemoglobinuria (PNH)
and their Caregivers*

 **Aplastic Anemia & MDS**
INTERNATIONAL FOUNDATION

The Aplastic Anemia & MDS International Foundation, Inc. (AA&MDSIF) is an independent non-profit organization. Our mission is to support patients, families, and caregivers coping with:

- ◆ Aplastic anemia
- ◆ MDS (myelodysplastic syndromes)
- ◆ PNH (paroxysmal nocturnal hemoglobinuria)
- ◆ Related bone marrow failure diseases

This booklet offers summaries of abstracts presented at the 52nd Annual Meeting of the American Society of Hematology (ASH) in December 2010. It provides some of the most up-to-date information about new research into the biology and treatment of paroxysmal nocturnal hemoglobinuria (PNH). Although the information in this booklet has undergone a thorough, independent medical review to insure its accuracy, this information is not intended to be a substitute for the advice of your doctor. You should always seek medical advice from a qualified physician.

For more information, call us at (800) 747-2820, or visit us online at www.AAMDS.org.

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Dear Patient or Caregiver,

The purpose of this booklet is to provide you with the most up-to-date information about new research into the biology and treatment of paroxysmal nocturnal hemoglobinuria (PNH), as presented at the 52nd Annual Meeting of the American Society of Hematology (ASH) in December 2010.

The ASH Annual Meeting is the world's largest professional gathering of hematologists and hematological oncologists—i.e., doctors who care for patients with blood disorders or blood and bone marrow cancers. This conference is where many major findings in the field of blood and marrow disorders are first announced to attendees, the larger medical and scientific community, and the media. New information that researchers hope is important enough to be presented at this meeting is submitted a few months ahead of the conference in the form of an “abstract”— i.e., a brief summary of the study and its results—and authors of the most interesting and noteworthy abstracts are asked by ASH to present their research in more detail, either in the format of a tacked-up printed poster or an oral (podium) presentation.

We selected the ASH abstracts in this summary because we feel they are the most relevant and important for people living with PNH to know about. By reviewing the information presented in the booklet, we hope you will:

- ◆ Learn how ongoing research on PNH may affect the diagnosis, treatment, and prognosis of patients in the near term as well as the more distant future
- ◆ Understand how researchers are approaching the most promising areas of PNH therapy
- ◆ Learn about the importance of clinical trials in identifying novel therapies for PNH
- ◆ Know the most important issues about PNH which you may want or need to understand and to ask your health care providers about as part of your ongoing treatment

Please note that the research results discussed at the ASH Annual Meeting sometimes involve experimental drugs that are not approved for general use by the Food and Drug Administration (FDA) or investigation of potential new uses of previously approved treatments. By providing summaries of the research presented, we do not intend to recommend or endorse any particular medication or treatment approach. Our goal is simply to inform you about current news and trends in healthcare related to PNH.

If you are interested in participating in research studies such as those discussed in this booklet, we encourage you to speak to with your doctor about clinical trials or to visit **www.clinicaltrials.gov**.

As always, please contact AA&MDSIF if you have questions about these summaries or any aspect of managing your disease.

Carlos M. De Castro, III, M.D.

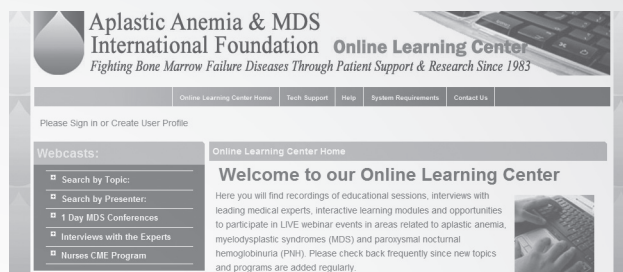
Duke University Medical Center

Member, AA&MDSIF Medical Advisory Board

The abstracts summarized in this booklet may be viewed on the American Society of Hematology Web site at <http://ash.confex.com/ash/2010/webprogram/start.html>. You may type in the abstract number or title in the search box. Any conflicts of interest or other relevant disclosures by the study authors are noted in each abstract.

Research Update on PNH Diagnosis and Treatment Now Available on the Online Learning Center (OLC): www.AAMDS.org/Learn

In April 2011, AA&MDSIF conducted a live webinar titled, PNH Clinical Update for Patients: Important Findings from the 2010 American Society of Hematology Annual Meeting. During this webinar, Ilene Weitz, MD, discussed the latest PNH diagnosis and treatment research as reported at the 52nd Annual Meeting of the American Society of Hematology (ASH). This webinar is now archived and posted on the Online Learning Center and is available for on-demand viewing.



To view this and other archived webinars, visit our Online Learning Center at www.AAMDS.org/learn and choose Archived Webinars.

The Online Learning Center (OLC) is your comprehensive information source on all aspects of bone marrow failure diseases. Created expressly for patients and their families, caregivers and advocates, all OLC content is free and available to anyone with access to a computer and a high-speed Internet connection. In addition to archived webinars, here is what else you will find on the OLC:

- Live webinars conducted by the nation's leading experts
- Innovative interactive learning modules
- Interviews with experts on aplastic anemia, MDS and PNH
- Webcasts of pre-recorded presentations

More than 80 programs are now available, and more are being added all the time. Here are just a few:

- Beating Fatigue
- PNH: Long-Term and Post-Treatment Issues
- Complementary and Alternative Therapies: Myths, Realities and Opportunities
- Fundamentals of Hematology and Bone Marrow Failure Diseases
- Growth Factors: Examining the Risks and Benefits
- Thrombosis in PNH: Debates in Prevention and Treatment

Read what one patient had to say about the AA&MDSIF Online Learning Center:

The live and archived webinars, interviews with experts, and interactive learning modules are an invaluable source of information about bone marrow failure diseases such as mine. Whenever I have questions, the Aplastic Anemia and MDS International Foundation is always my "go to" source for answers. Thank you so very much for the knowledge and support you provide.

-Charles (PNH patient)

AA&MDSIF Online Learning Center: www.AAMDS.org/Learn



Don't have Internet access? Go to your public library or local community center, or ask a friend or family member to help you the next time you visit.

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RESULTS FROM THE PNH REGISTRY

The PNH Registry is a worldwide study that is collecting data on treatment safety and effectiveness, as well as quality of life, in patients with PNH. The ultimate goal of the registry is to provide researchers with information that will help facilitate diagnosis and optimize treatment of PNH. The PNH Registry remains open to accepting information on patients (pnhregistry@iconplc.com). As of August 2010, there were 657 persons living with PNH enrolled in the PNH Registry. Speak with your doctor if you think you are interested in being enrolled. The following two abstracts from the last ASH meeting used the PNH Registry data to analyze outcomes.

1525 Evaluation of Paroxysmal Nocturnal Hemoglobinuria Disease Burden: The Patient's Perspective. A Report from the International PNH Registry

Petra Muus, M.D., Ph.D., Jeffrey Szer, M.B.B.S., FRACP, Hubert Schrezenmeier, M.D., Robert A. Brodsky, M.D., Monica Bessler, M.D., Ph.D., Gérard Socié, Alvaro Urbano-Ispizua, M.D., Jaroslaw P. Maciejewski, M.D., Ph.D., FACP, Wendell F. Rosse, M.D., Yuzuru Kanakura, M.D., Ph.D., Gus Khursigara, Ph.D., Anders Karnell, M.D., Ph.D., Camille L. Bedrosian, M.D., and Peter Hillmen, M.B.Ch.B., FRCP, FRCPath, Ph.D.

The goal of this study was to describe the impact of PNH on patients' quality of life. The study included 377 patients with PNH from 16 countries around the world who had enrolled in the PNH Registry. To be included in the study patients must have completed a questionnaire about their quality of life, fatigue, missed work and hospital stays due to PNH. This group of 377 patients represented 57% of the 657 patients currently enrolled in the registry. The authors noted that patients with a larger clone size were less likely to complete the questionnaire, and thus less likely to be included in the study.

Key Findings:

- ◆ On average, the quality-of-life scores in patients with PNH were 10% lower and fatigue levels were 16% more severe than in the general population.
- ◆ Men with PNH tended to feel better emotionally, physically, and socially and have less fatigue than women with PNH.
- ◆ One quarter of study participants had been admitted to a hospital and almost one-third of those with a job had missed work due to PNH in the past 6 months.
- ◆ Many patients who had missed work had stomach pain or hemoglobinuria (hemoglobin in the urine).
- ◆ Patients with thrombosis (blood clot in a vein or artery), chest or stomach pain, or hemoglobinuria were most likely to have been hospitalized or have poorer quality of life.

2241 Use of Blood Transfusions in Paroxysmal Nocturnal Hemoglobinuria Patients with and without Aplastic Anemia Enrolled in the Global PNH Registry

Hubert Schrezenmeier, Robert A. Brodsky, M.D., Petra Muus, M.D., Ph.D., Monica Bessler, M.D., Ph.D., Jeffrey Szer, MBBS, FRACP, Jaroslaw P. Maciejewski, M.D., Ph.D., FACP, Gérard Socié, Alvaro Urbano-Ispizua, M.D., Yuzuru Kanakura, M.D., Ph.D., Britta Hoehsmann, Wendell F. Rosse, M.D., Gus Khursigara, Ph.D., Anders Karnell, M.D., Ph.D., Camille L. Bedrosian, M.D., and Peter Hillmen, M.B.Ch.B., FRCP, FRCPath, Ph.D.

Patients with PNH, or with both PNH and aplastic anemia, sometimes need red blood cell transfusions to treat anemia. The authors studied red blood cell transfusions to treat anemia in patients with PNH. Some of these patients also had aplastic anemia, a disorder where the bone marrow is empty and does not make enough blood cells. Other patients had another bone marrow failure disease with a PNH clone.

The goal of this study was to understand the red blood cell transfusion needs of PNH patients with and without aplastic anemia. The study included data on 655 patients (53% female, median age 43) enrolled in the PNH Registry.

Key Findings:

- ◆ About half of the patients (56%) had needed at least one transfusion in the previous year, regardless of whether they also had aplastic anemia.
- ◆ Patients with larger PNH clones were more likely to need a transfusion.
- ◆ Patients with both PNH and aplastic anemia received more red blood cell units than patients with other bone marrow disorders.

LONG-TERM ECULIZUMAB RESULTS

Ecuzumab (also known as Soliris®) is a drug that reduces hemolysis, or the breakdown of red blood cells, in persons with PNH. People with PNH who undergo ecuzumab treatment need fewer blood transfusions. Ecuzumab can also improve quality of life and prevent some of the most serious symptoms of PNH, including blood clots, high blood pressure in the lung arteries and chronic kidney problems. The long term effects of ecuzumab including its effect on survival are unknown.

639 Long Term Treatment with Ecuzumab in Paroxysmal Nocturnal Hemoglobinuria (PNH): Sustained Efficacy and Improved Survival

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The goal of this study was to evaluate ecuzumab's effectiveness and impact on survival over the long term. The researchers collected data on 79 patients with PNH who had been treated with ecuzumab for an average of 39 months at the Leeds PNH Center in the United Kingdom, between May 2002 and July 2010. This included 40 men and 39 women who were treated for a average of 39 months. The median age at diagnosis was 37 years and the median age at the start of ecuzumab was 46 years.

Key Findings:

- ◆ The patients in this study had many fewer blood clots in an artery or vein, after starting ecuzumab treatment, with 34 blood clot episodes being recorded before treatment and 2 after.
- ◆ Twenty one patients were able to stop taking Coumadin® (warfarin) to prevent thromboses (blood clots in arteries or veins).
- ◆ Two-thirds of patients who had been on ecuzumab for at least a year stopped needing blood transfusions.
- ◆ Patients who still needed transfusions required fewer units of blood after starting ecuzumab treatment.
- ◆ Survival in patients with PNH on ecuzumab was similar to that of sex- and age-matched people in the general population without PNH.

Conclusions:

- ◆ The authors concluded that ecuzumab has few side effects and can reduce PNH symptoms.
- ◆ The therapy can also prevent blood clots; and eliminate or reduce patients' need for blood transfusions.
- ◆ The drug substantially improves survival.

4237 Long Term Safety and Efficacy of Sustained Eculizumab Treatment in Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH)

Robert A. Brodsky, M.D., Carlos de Castro III, M.D., Hubert Schrezenmeier, M.D., Antonio M. Risitano, M.D., Ph.D., Joerg Schubert, M.D., Jaroslaw P. Maciejewski, M.D., Ph.D., FACP, Ulrich Duehrsen, M.D., Lucio Luzzatto, M.D., FRCP, FRCPath, Petra Muus, M.D., Ph.D., Jeffrey Szer, BMedSc, M.B.B.S., FRACP10, Gérard Socié, M.D., Ph.D., and Peter Hillmen, M.B.Ch.B., FRCP, FRCPath, Ph.D.

This international group of researchers studied the safety and outcomes of long-term eculizumab treatment in patients with PNH. The study included data on 195 patients who had undergone eculizumab treatment for 29 months, on average, in three clinical trials. The median age of patients was 40 years old with 54% being female, 29% with a history of aplastic anemia, and 1.5% with history of myelodysplasia. Of the patients studied, 32% had reported having blood clots before starting eculizumab treatment.

Key Findings:

- ◆ Patients in the study experienced much less hemolysis and many fewer thrombotic events (blood clots) after starting eculizumab treatment.
- ◆ Patients who were taking anticoagulant medications to prevent blood clots were able to stop these treatments without developing thromboses.
- ◆ Rates of chronic kidney disease were much lower than before eculizumab treatment.
- ◆ Most patients no longer needed blood transfusions.
- ◆ Patients tolerated eculizumab well, with few side effects.

Conclusions:

- ◆ While other studies have shown that patients experience beneficial effects soon after starting eculizumab, this study showed that the drug continues to relieve PNH symptoms over the long term, reducing the risk of blood clots and improving kidney function.
- ◆ As a result, this drug may increase the life expectancy of people with PNH.

PNH AND BONE MARROW TRANSPLANT

3505 Long-Term Follow-up of Reduced Intensity Allogeneic Hematopoietic Stem Cell Transplantation for Severe Paroxysmal Nocturnal Hemoglobinuria

Jeremy Pantin, M.D., Xin Tian, Nancy Geller, Ph.D., Catalina Ramos, CRN, Lisa Cook, C.R.N., Sophia Grasmeder, C.R.N., Philip Scheinberg, M.D., Neal S. Young, M.D., Sumithira Vasu, M.D., Theresa Donohue, M.H.S., PA-C, and Richard Childs, M.D.

This group of researchers from the National Heart, Lung and Blood Institute of the National Institutes of Health had previously shown that transplantation of hematopoietic stem cells, or cells that can turn into all types of blood cells, can cure PNH. Reduced intensity hematopoietic stem cell transplant (HSCT) is a new method that tries to lower the amount of chemotherapy that a patient receives prior to receiving the transplant, therefore lowering the toxicity from the procedure. In this abstract, the authors present the results of a long-term follow-up study of 16 patients who received a reduced intensity hematopoietic stem cell transplant between May 1999 and January 2007.

Key Findings:

- ◆ Within 100 days of HSCT, analyses of blood samples showed no signs of PNH in all of the patients in the study.
- ◆ More than half of the patients developed graft-versus-host disease (GVHD), a common complication of stem cell transplantation. GVHD is caused when the donated stem cells (the graft), now in the patient, begin to see the patient's body (the host) as foreign causing an immune response. It can be mild to severe.
- ◆ After an average of almost 6 years, 14 patients had survived with no signs of PNH. These patients no longer needed blood transfusions or anticoagulant medications.
- ◆ Two patients died, one from complications related to acute GVHD, and one from complications related to peptic ulcer disease.

Conclusions and Recommendations:

- ◆ The authors concluded that reduced intensity HSCT can cure PNH over the long term and can produce excellent, long-lasting survival in patients with severe PNH.
- ◆ They recommend reduced intensity HSCT for patients with PNH who are not candidates for eculizumab treatment and who may not be able to tolerate a full intensity stem cell transplant.

NOTE: It is important to note that, while a stem cell transplant can cure PNH, it is not a perfect cure. It carries a number of risks including long-term illness with GVHD and death. If you are thinking about undergoing a stem cell transplant speak with your doctor and a transplant specialist to understand all the risks and benefits for your individual case.

2231 Paroxysmal Nocturnal Hemoglobinuria (PNH) in Pediatric Patients: Review of a Single Center Series

Kevin J. Curran, M.D., Nancy A. Kernan, M.D., Susan E. Prockop, M.D., Andromachi Scaradavou, M.D., Trudy N. Small, M.D., Hugo Castro-Malaspina, M.D., David Araten, M.D., Donna DiMichele, M.D., Richard J. O'Reilly, M.D., and Farid Boulad, M.D.

PNH is rare in children. When children develop PNH, they tend to have different symptoms than adults. The researchers described 11 children aged 11–17 years who had received a PNH diagnosis since 1993 at a New York City hospital. Most of these children also had bone marrow failure, meaning that their bone marrow was not making enough healthy blood cells, at diagnosis. This bone marrow failure rate was higher in these children than in adults with PNH.

Key Findings:

- ◆ About half the children developed thrombosis, or a blood clot in a vein or artery.
- ◆ Only one patient had hemoglobinuria (hemoglobin in the urine) at initial presentation. This is a much lower hemoglobinuria rate than in adults with PNH.
- ◆ Two of the four the patients who underwent stem cell transplant and two of three patients treated with eculizumab were still alive and free of disease at the time of the analysis.
- ◆ Two children had died from complications of thrombosis, and two had stable disease but needed red blood cell transfusions.

Conclusions and Recommendations:

- ◆ The authors concluded that children with certain bone marrow failure disorders, such as aplastic anemia and myelodysplastic syndrome, and those with unexplained hemolysis or thrombosis should be tested for PNH.
- ◆ Doctors should start eculizumab treatment promptly in children with PNH because of their high risk of hemolysis and thrombosis.
- ◆ A hematopoietic stem cell transplant, also called a bone marrow transplant, is the only cure for PNH in children but doctors and families must balance the risks of this treatment with the severity of the child's PNH.

4241 Association between Elevated Hemolysis at Diagnosis and Early Mortality and Risk of Thrombosis in Paroxysmal Nocturnal Hemoglobinuria (PNH) Patients with Cytopenia

Jin Seok Kim, M.D., Ph.D., Jong Wook Lee, M.D., Ph.D., Sung-Soo Yoon, M.D., Ph.D., Je-Hwan Lee, M.D., Ph.D., Deog-Yeon Jo, M.D., Ph.D., Jun-Ho Jang, M.D., Ph.D., Yeo-Kyung Kim, M.D., Ph.D., Jooseop Chung, M.D., Ph.D., and Sang Kyun Sohn, M.D., Ph.D.

Thrombosis, or blood clots in veins or arteries, is the main cause of death in patients with PNH. Many patients with PNH have stomach pain, and these patients have a higher risk of thrombosis and death.

A group of researchers from South Korea analyzed data from 286 patients with PNH in the National Data Registry in South Korea. The median patient age was 37 years, and the median PNH time since diagnosis was 7.8 years. Their goal was to assess and compare the relationship between PNH symptoms and complications in patients with and without cytopenias, also called low blood cell counts.

Key Finding:

- ◆ Patients who had hemolysis, or a breakdown of red blood cells, when they were first diagnosed with PNH had a higher risk of having blood clots, poor quality of life, and death.
- ◆ Patients with PNH and a low blood count experienced a similar prevalence of hemolytic symptoms and death compared to PNH patients with no evidence of a low blood count.
- ◆ Blood clots were seen in about the same percentage of PNH patients with and without a low blood count.

Conclusions and Recommendations:

- ◆ The authors concluded that hemolysis at diagnosis is a risk factor for life-threatening complications in patients with PNH, regardless of whether these patients also have cytopenias.
- ◆ Doctors should select treatments for patients that control both hemolysis and low blood counts.

Chronic intravascular hemolysis, or the breakdown of red blood cells in the veins and arteries, is a hallmark of PNH. The hemolysis in PNH is due to a lack of two proteins, CD55 and CD59, on red blood cells. The lack of these proteins interferes with the body's ability to regulate complement proteins, which normally protect red blood cells. The complement system and complement proteins are a natural part of the body's immune system. They help white blood cells to fight infection. When blood cells lack certain proteins on their surface, as in PNH, they are more vulnerable to destruction by the complement system.

Eculizumab can stop C5, a complement protein, from interfering with the body's ability to protect red blood cells. However, eculizumab can also result in the accumulation of C3 complement protein fragments on the surface of red cell which may lead to extravascular hemolysis, or hemolysis outside the veins and arteries, in some patients. Some studies suggest that this may explain, at least in part, why some patients continue to have low level hemolysis while on eculizumab therapy.

637 C3-Mediated Extravascular Hemolysis in Paroxysmal Nocturnal Hemoglobinuria: An In Vitro Model to Dissect Complement C3 Activation Comparing the Effects of Complement Inhibitors Eculizumab, 3E7 and TT30 on C3 Fragment Processing and Hemolysis of PNH Erythrocytes

Antonio M. Risitano, M.D., Ph.D., Caterina Pascariello, Luigi Del Vecchio, M.D., Christopher J. Horvath, D.V.M., M.S., D.A.C.V.P., Masha Fridkis-Hareli, Ph.D., V. Michael Holers, M.D., Margaret A. Lindorfer, Ph.D., and Ronald P. Taylor, Ph.D.

The authors evaluated the effects of monoclonal antibodies (proteins that target different C3 fragments) on C3 fragment accumulation and hemolysis in red blood cells from patients with PNH. The study also included compounds that inhibit complement, such as eculizumab. This study approach allowed the researchers to assess the roles of drugs and the body's own mechanisms to regulate complement in PNH and to study the potential role of these drugs in stopping both the hemolysis from PNH and the hemolysis from C3 coating of red cells.

Key Findings:

- ◆ Three of the monoclonal antibodies tested bound to the red blood cells.
- ◆ PNH cells exposed to eculizumab dramatically reduced hemolysis, although some hemolysis was still occurring.
- ◆ Two novel complement inhibitors, TT30 and 3E7, bound to the red blood cells and completely stopped hemolysis. These compounds prevented the earliest phases of the process that stops the body from regulating complement proteins.

Conclusion:

- ◆ The results have led the authors to suggest that TT30 should be evaluated clinically in patients with PNH and ongoing hemolysis. (Also see abstract 638 on page 16).

EXTRAVASCULAR HEMOLYSIS

4240 Low Level Residual Extravascular Haemolysis is Common Following Eculizumab Treatment in Paroxysmal Nocturnal Haemoglobinuria (PNH), but Does Not Affect Transfusion Requirement

Austin G. Kulasekararaj, Dupe Odunsi, Pramila Krishnamurthy, Hayden Janet, Ibrahim Momoh, Ghulam J. Mufti, D.M., FRCP, FRCPath, Judith C. W. Marsh, M.D. and Modupe Elebute, M.B.B.S., M.D., M.R.C.P., FRCPath

The goal of this British study was to evaluate the role of the C3 protein in making blood cells more susceptible to destruction by the body's immune cells. The study included 26 patients with PNH who had been treated with eculizumab and 22 non transfusion dependant patients who had not received eculizumab treatment.

Key Findings:

- ◆ Most patients on eculizumab and very few patients not on eculizumab had positive direct antiglobulin test (DAT) results, measuring an increased amount of C3 protein on blood cells. This accumulation of C3 complement protein fragments on the surface of red cell which may lead to extravascular hemolysis, or hemolysis outside the veins and arteries, in some PNH patients.
- ◆ Most patients treated with eculizumab who had a positive DAT test result had received at least two red blood cell transfusions.
- ◆ Patients on eculizumab with a negative DAT result had received no transfusions.
- ◆ In general, patients on eculizumab needed fewer transfusions after starting treatment, regardless of their DAT test results.

Conclusion:

- ◆ The authors concluded that the positive DAT results in patients on eculizumab reveal the presence of C3 protein fragments on red blood cells that play a role in extravascular hemolysis.
- ◆ This C3-mediated extravascular hemolysis is not entirely responsible for the ongoing hemolysis and continuing need for blood transfusions that is seen in some PNH patients on eculizumab.

4239 Thrombolytic Therapy for Reversal of Thrombosis in Paroxysmal Nocturnal Hemoglobinuria (PNH)

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Thrombosis, or a blood clot in a vein or artery, is the main cause of death in patients with PNH. Anticoagulation therapies, drugs that reduce the ability of the blood to clot, and anticomplement therapies, drugs that reduce complement system activation, can prevent or treat blood clots but are not appropriate for all patients with PNH. A few small studies have shown that tissue plasminogen activator (tPA), a clot-busting drug, can treat blood clots in some patients with PNH. tPA is given as an infusion through a vein and must be administered at a hospital or other treatment center.

In this study, the authors collected data on the use of tPA in 9 patients with PNH who had potentially life-threatening blood clots. During the study period these patients had a total of 15 hospital stays when they were treated for blood clots.

Key Findings:

- ◆ Most patients needed several 24-hour infusions of tPA and several needed tPA during at least two hospital stays.
- ◆ During all 15 total hospital stays when the patients were treated with tPA, the treatment reversed the blood clot.
- ◆ Three patients had serious bleeding complications.
- ◆ At the last follow up visit, three of the patients had died. The tPA treatment might have contributed to one patient's death from a bleeding-related complication.
- ◆ The authors believe that tPA saved the lives of three patients.

Conclusion:

- ◆ Thrombosis increases the risk of death and other serious complications in patients with PNH. Therefore, even though tPA is associated with serious bleeding, tPA can be a useful thrombosis treatment in patients with PNH.

NEW THERAPIES

638 TT30, a Novel Human Complement Inhibitor in Development for Paroxysmal Nocturnal Hemoglobinuria and Other Hemolytic Disorders, Demonstrates Red Blood Cell Surface Targeting and Retention in a Model of Complement Alternative Pathway-Mediated Hemolysis

Masha Fridkis-Hareli, Ph.D., Michael Storek, Ph.D., Antonio M. Risitano, M.D., Ph.D., Ante S. Lundberg, M.D., Christopher J Horvath, D.V.M., M.S., DACVP, and V. Michael Holers, M.D.

Chronic intravascular hemolysis, or the breakdown of red blood cells in the veins and arteries, is a hallmark of PNH. The hemolysis in PNH is due to a lack of two proteins, CD55 and CD59, on red blood cells, which interferes with the body's ability to regulate complement proteins. Complement proteins normally protect red blood cells. When the bone marrow does not produce enough complement proteins, red blood cells are more vulnerable to destruction.

Eculizumab can stop C5, a complement protein, from interfering with the body's ability to protect red blood cells. However, eculizumab can also result in the accumulation of C3 complement protein fragments and extravascular hemolysis, or hemolysis outside the veins and arteries.

Researchers at the University of Naples, Italy, have studied the novel complement inhibitor TT30. This treatment appears to take on the role of CD55, stopping the accumulation of C3 fragments on red blood cells. The authors studied TT30's ability to prevent hemolysis in human blood samples. They found that TT30 stops hemolysis.

Key Finding:

- ◆ The TT30 was detectable on red blood cells for at least 24 hours, and the amounts of bound TT30 were proportional to the amounts of accumulated C3 fragments.

Conclusion:

- ◆ TT30 might be useful to treat human diseases in which complement proteins play a role, including PNH.

MORE WAYS TO GET HELP

The Aplastic Anemia & MDS International Foundation (AA&MDSIF) is here to help. We provide the following services:

- ◆ Personalized support from patient educators
- ◆ Free educational materials on many topics related to PNH
- ◆ Online Learning Center
- ◆ Patient and family conferences
- ◆ Peer Support Network
- ◆ Print and electronic newsletters with important information and updates
- ◆ Clinical trials information

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Remember – you are not alone. We are standing by to support you in any way we can.



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