HIGHLIGHTS FROM THE

2011 American Society of Hematology Annual Meeting

A Summary of Abstracts for Patients with Aplastic Anemia and their Caregivers
The Aplastic Anemia & MDS International Foundation (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 53rd Annual Meeting of the American Society of Hematology (ASH) in December 2011. It provides some of the most up-to-date information about new research into the biology and treatment of aplastic anemia. 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.
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 aplastic anemia, as presented at the 53rd Annual Meeting of the American Society of Hematology (ASH) in December 2011.

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 aplastic anemia to know about. By reviewing the information presented in the booklet, we hope you will:

- Learn how ongoing research on aplastic anemia 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 aplastic anemia therapy
- Learn about the importance of clinical trials in identifying novel therapies for aplastic anemia
- Know the most important issues about aplastic anemia 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 aplastic anemia.

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.

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The abstracts summarized in this booklet may be viewed on the American Society of Hematology Web site at http://ash.confex.com/ash/2011/webprogram/keywordindexm.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.
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Hematopoietic Stem Cell Transplant

Hematopoietic stem cell transplant (HSCT) has the potential to cure aplastic anemia. This procedure involves the infusion of healthy blood-forming (hemapoietic) stem cells from a healthy donor. The donor’s stem cells (known as a graft) enter the bone marrow, where they form healthy blood cells. The transplant is allogeneic when the cells come from a donor who is not the patient. HSCT is most successful when the donor is a family member whose blood has the same human leukocyte antigen (HLA) markers, or proteins on the surface of white blood cells and other cells, as the patient.

Doctors use drugs—such as cyclophosphamide and antithymocyte globulin (ATG) or antilymphocyte globulin (ALG)—to weaken the patient’s immune system before the transplant. This procedure, known as conditioning, prevents the patient’s immune system from attacking the transplanted bone marrow cells and allows the donor’s bone marrow to make healthy blood cells.

Patients may develop graft-versus-host disease (GVHD) after the transplant. With GVHD, the donated stem cells (the graft) in the patient treat the patient’s body (the host) as something foreign, and attacks certain tissues with an immune system response.

831 Allogeneic Bone Marrow Transplantation from HLA Mismatched Family Donors in Children with Aplastic Anemia

Hideki Muramatsu, M.D., Ph.D., Hiromasa Yabe, M.D., Ph.D., Ryoji Kobayashi, M.D., Ph.D., Akira Kikuchi, Kazuko Kudo, M.D., Ph.D., Keisai Kawa, Koji Kato, M.D., Ph.D., Ritsuro Suzuki, M.D., Yoshiyuki Takahashi, M.D., Ph.D., Jiro Inagaki, Masami Inoue, and Seiji Kojima, M.D., Ph.D.

The first-line treatment for severe aplastic anemia (SAA) in children is an allogeneic HSCT from a family member with the same HLA (immune system) markers as the patient. When the family member’s blood does not have the same HLA markers they are called mismatched family donors. In this case, the patient receives immunosuppressive treatment, which stops the immune system from attacking bone marrow cells. The alternative is an unrelated, HLA-matched donor.

A group of researchers in Japan, analyzed the outcomes of allogeneic HSCT in 578 children (325 boys and 253 girls) under age 20 treated between 1990 and 2009. The median age at transplant was 11 years. Of the children in the study, 312 received an HLA-matched transplant from a related donor, 53 from a related donor whose blood matched 3 to 5 of the patient’s 6 HLA markers, and 213 from an HLA-matched, unrelated donor.

Key Findings:
- Patients who received a graft from a partially mismatched related donor showed a 27% higher risk of developing GVHD than in those who received a graft from a matched related donor (5%).
- About 93% of patients survived for at least 5 years after a transplant from a relative with fully matched blood or a relative whose blood matched 5 of the patient’s 6 HLA markers.
- The 5-year survival rate was 79% in patients who received a graft from a related donor whose blood matched 3 or four 4 the patient’s 6 HLA markers and 67% in those who received stem cells from an unrelated donor with HLA-matching blood.
- The likelihood of surviving for at least 5 years did not improve between 1990–1999 and 2000–2009. But survival rates did rise from 67% to 86% in patients who received a transplant from an unrelated, HLA-matched donor.
Conclusions: HSCT can create an opportunity for many of these children to live 5 years or more. A related donor provides the better outcomes than unrelated donors. Children receiving HSCT from unrelated donors saw significantly better results after 2000.

52 National, Retrospective, Multi-Centre Comparison of Alemtuzumab-Versus ATG-Based Conditioning Regimens in Hematopoietic Stem Cell Transplantation for Aplastic Anemia: A Study from the British Society for Blood and Marrow Transplantation (BSBMT) (CTCR 09-03)

Judith C. W. Marsh, Rachel M Pearce, Mickey B Koh, Daniel Tang, ZiYi Lim, Antonio Pagliuca, Ghulam J. Mufti, M.D., John Snowden, Ajay J Vora, Brenda Gibson, Maria H Gilleece, Julia Lee, Keiren Kirkland, and Gordon Cook

The purpose of this study was to compare conditioning regimens which prepare patients for stem cell transplant (HSCT). They looked at the results of people who received ATG versus those who received alemtuzumab (Campath®). Alemtuzumab attaches to and kills a subset of lymphocytes, a type of white blood cell that attacks bone marrow stem cells in patients with aplastic anemia. The researchers analyzed data from 159 patients with aplastic anemia who had had an HSCT in the United Kingdom between 1999 and 2009. Median patient age was 20 years, and 86 patients were male. Of the 159 patients, 103 (65%) were conditioned with alemtuzumab, 55 (35%) with ATG, and 1 patient with both.

Key Findings:
- Eighty-five percent of patients survived for at least 10 years after their HSCT.
- 1-year survival rates were similar in patients conditioned with alemtuzumab (91%) and ATG (84%).
- Twenty-three patients (16%) whose data could be evaluated developed GVHD more than 100 days after their HSCT.
- In 15 patients (9%), the transplanted cells failed to grow and start making healthy blood cells.

Conclusions: Overall survival at 10 years following HSCT was achieved by 85% of individuals with either conditioning treatment. The 2 year survival rate is 50% in patients who are older than 50. Use of alemtuzumab showed a 2 year survival of 83% with an unrelated donor and 95% with a related donor.

4090 Long-Term Follow-up of Allogeneic Hematopoietic Stem Cell Transplantation in Patients with Severe Aplastic Anemia after Cyclophosphamide plus Antithymocyte Globulin Conditioning Regimen

Johanna Konopacki, M.D., Raphael Porcher, Marie Robin, Sabine Bieri, Jean Michel Cayuela, M.D., Ph.D., Jérome Larghero, Alineur Xhaard, Anna-Lisa Andreoli, M.D., Nathalie Dhedin, M.D., Anna D. Petropoulou, M.D., Paula Rodriguez-Otero, M.D., Ph.D., Patricia Ribaud, Helene Moins, M.D., Ph.D., Maryvonnix Carmagnat, Antoine Toubert, M.D., Ph.D., Yves Chalandon, M.D., Gérard Socié, and Régis Peffault de Latour

In the past, many patients with severe aplastic anemia (SAA) underwent conditioning treatment with radiation before their HSCT. These patients had a higher risk of developing cancer. This study looks at the results of using ATG or cyclophosphamide as conditioning treatment in preparation for HSCT instead of radiation. A group of researchers in France reported on the long-term outcomes of 61 patients with SAA who had an HSCT between 1991 and 2010 from an HLA-identical, related donor after conditioning with ATG and cyclophosphamide. Median patient age was 21 years, and 41 of the patients were adults. On average, patients had been diagnosed with SAA 3 months before undergoing HSCT.
Key Findings:
- The stem cells engrafted (accepted by the patient’s body) in 59 patients (97%).
- Fifty-three patients (87%) survived for at least 6 years after HSCT.
- Only 9% showed a secondary cancer 6 years after HSCT.

Conclusions:
The researchers conclude that HSCT from HLA-identical, related donors after conditioning with ATG and cyclosporine is curative for SAA and patients' long-term outcome is excellent.

Immunosuppressive Therapy

53 Comparison of Clinical Outcome between Children with Aplastic Anemia and Refractory Cytopenia of Childhood who Received Immunosuppressive Therapy with Antithymocyte Globulin and Cyclosporine

Asahito Hama, M.D., Ph.D., Hideki Muramatsu, M.D., Ph.D., Masafumi Ito, M.D., Ph.D., Masahiro Tsuchida, M.D., Ph.D., Hiroshi Sakaguchi, M.D., Sayoko Doisaki, M.D., Makito Tanaka, M.D., Ph.D., Akira Shimada, M.D., Ph.D., Yoshiyuki Takahashi, M.D., Ph.D., Ryoji Kobayashi, M.D., Ph.D., Etsuro Ito, M.D., Ph.D., Hiromasa Yabe, M.D., Ph.D., Shouichi Ohga, M.D., Ph.D., Akira Ohara, M.D., Ph.D., and Seiji Kojima, M.D., Ph.D.

Refractory cytopenia of childhood (RCC) is a type of myelodysplastic syndrome (MDS). Children with this condition have a shortage of blasts, or immature white blood cells in the bone marrow. Doctors often have trouble telling whether a patient has RCC or aplastic anemia.

The purpose of this study was to learn about the differences of aplastic anemia and RCC who received ATG and cyclosporine in children. 117 patients were reviewed. 58 (50%) had aplastic anemia, 47 (40%) had RCC, and 12 (10%) had or refractory cytopenia with multi-lineage dysplasia (RCMD). Patients with RCMD have a shortage of neutrophils (a type of white blood cell) or platelets as a result of abnormal blood-forming cells in their bone marrow. Median ages were 9 years in patients with aplastic anemia, 8 years in those with RCC, and 10 years in those with RCMD.

Key Findings:
- Patients with aplastic anemia or RCC tended to have severely underdeveloped bone marrow cells. Patients with RCMD had normal or only slightly underdeveloped bone marrow cells.
- Response rates 6 months after immunosuppressive treatment were 65% in patients with aplastic anemia, 70% in those with RCC, and 58% in those with RCMD.
- Twenty-five children (14 with aplastic anemia, 9 with RCC, and 2 with RCMD) received HSCT.
- Survival rates were similar for children with each disease.

Conclusion:
RCMD evolves in a similar way to MDS and should be considered childhood MDS. Overall survival did not differ among the three groups. The researchers suggest that newer evaluation methods such as whole exome (DNA sequencing of all expressed genes) analysis may help identify differences.

1346 Long-Term Outcome of Immunosuppressive Therapy with Rabbit Antithymocyte Globulin (rATG) for Childhood Severe Aplastic Anemia for 15 Years

Dae-Chul Jeong, M.D., Ph.D., Nack Gyun Chung, M.D., Ph.D., Jae Wook Lee, M.D., Pil-sang Jang, M.D., Ph.D., Bin Cho, M.D., and Hack-Ki Kim, M.D., Ph.D.
About 60 or 70% of children with severe aplastic anemia respond to immunosuppressive treatment with cyclosporine and horse antilymphocyte globulin (ALG). Rabbit ATG (rATG) has a stronger effect on the immune system than horse ALG. But previous studies have found that children do not respond as well to immunosuppressive treatment with rabbit ATG as with horse ATG, and their survival is shorter.

The authors analyzed data on 112 children with SAA, 58 of whom received rATG. The children had been diagnosed with aplastic anemia between 1991 and 2005 and they did not have an HLA-matched HSCT donor. Thirty of the children (52%) were boys, and median age at diagnosis was 9 years. Eleven of the children (19%) had very severe aplastic anemia.

Key Findings:
- Response rates increased gradually over time to 55% at 9 months after immunotherapy. But response rates did not increase substantially after 9 months.
- About a third of the children (31%) had a relapse within a median of 22 months.
- Among the children, 43% developed serum sickness, similar to an allergic reaction.
- About 80% of the children survived for at least a year after finishing their treatment. The factors that had the biggest impact on survival were aplastic anemia severity and whether the children had a relapse.

Conclusions:
Response rates to rATG in children with SAA in this study were similar to responses in past studies to horse ALG. More research is needed to determine if a different dose of rATG would improve effectiveness.

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2399 Different in Vivo Effects of Horse and Rabbit Antithymocyte Globulin in Patients with Severe Aplastic Anemia
Xingmin Feng, Ph.D., Phillip Scheinberg, M.D., Angelique Biancotto, Ph.D., Olga Rios, R.N., Sarah Donaldson, Colin O. Wu, Ph.D., Haiyun Zheng, Kazuya Sato, J. Philip McCoy Jr., Ph.D., and Neal S. Young, M.D.

The authors recently reported the results of the first prospective, randomized study to compare horse and rabbit ATG in patients who had never had treatment for aplastic anemia before. In that earlier study, rabbit ATG was noticeably less effective than horse ATG in improving blood counts and survival.

The purpose of the current analysis was to explain the different outcomes of horse and rabbit ATG in the earlier study. The authors evaluated blood collected from 54 patients before, during, and after horse and rabbit ATG treatment in their randomized study. Of these patients, 26 were treated with rabbit ATG and 28 with horse ATG.

Key Findings:
- ATG concentrations in blood from both horse and rabbit ATG were high within 2 days of administration. The concentrations then dropped gradually.
- Concentrations dropped by 77% within a month after rabbit ATG treatment, compared to 49% after horse ATG treatment.
- Both types of ATG resulted in massive but temporary release of cytokines within 2 days of treatment. Cytokines affect cell growth in the bone marrow to make blood cells. By the second week, levels of several cytokines were much higher in patients treated with rabbit ATG than those who underwent horse ATG treatment.
Both types of ATG immediately decreased the numbers of lymphocytes, a type of white blood cell, dramatically. But lymphocytes recovered much more quickly in patients treated with horse ATG (within 2 weeks) than those treated with rabbit ATG (within about 6 months).

Conclusions:
Horse and rabbit ATG have very different effects in the body, especially on certain lymphocytes and the release of cytokines. These differences might help explain why the effectiveness of horse and rabbit ATG is so different in suppressing the immune system and restoring blood counts in patients with aplastic anemia.

2400 Antithymocyte Globulin (ATG), Cyclosporine (CyA), and Danazol versus ATG and CyA as Treatment for Children with Aplastic Anemia: Result of Matched-Pair Analysis
Kazuko Kudo, M.D., Ph.D., Ryoji Kobayashi, M.D., Ph.D., Yoshiyuki Kosaka, M.D., Ph.D., Masahiro Tsuchida, M.D., Ph.D., Hideo Mugishima, M.D., Ph.D., Akira Ohara, M.D., Ph.D., Hiroshi Yagasaki, M.D., Ph.D., Hiromasa Yabe, M.D., Ph.D., Akira Morimoto, M.D., Ph.D., Yoshiyuki Takahashi, M.D., Ph.D., Shouichi Ohga, M.D., Ph.D., Tatsutoshi Nakahaha, M.D., Ph.D., and Seiji Kojima

Some patients with aplastic anemia have very short telomeres. Telomeres are located at the ends of chromosomes and help keep chromosomes stable. Previous research showed that androgen, increases the activity of telomerase, an enzyme that maintains telomere length, in cells. Adding androgens to immunosuppressive therapy could increase the response rate in certain patients with aplastic anemia.

The purpose of this study was to compare the effects of using danazol, a synthetic androgen (Danocrine®) in the treatment of aplastic anemia. 530 children were treated in multiple health care centers with horse ATG, cyclosporine, and methylprednisolone, a steroid hormone (Medrol®) between 1992 and 2009. Half the children were also treated with danazol. The researchers compared pairs of patients who shared certain characteristics, such as age, sex, and disease severity.

Key Findings:
• At 6 months, 68% of children in the danazol group had responded to treatment, compared to 57% of children who did not receive danazol.
• About 94% of children in the danazol group and 83% of those who were not treated with danazol survived for at least 10 years.
• Seventy percent of patients with very severe aplastic anemia in the danazol group responded to treatment, compared to 47% of patients not treated with danazol.
• Similar proportions of patients with severe aplastic anemia who were or were not treated with danazol survived for at least 10 years.

Conclusions:
These children, with aplastic anemia, had a better response to treatment when danazol was used.

2406 Cyclosporine Taper Does not Prevent Relapse in Severe Aplastic Anemia
Phillip Scheinberg, M.D., Olga Nunez, R.N., Priscila Scheinberg, M.S., CCRP, Barbara Weinstein, R.N., Colin O. Wu, Ph.D., and Neal S. Young, M.D.

About 60–70% of patients with aplastic anemia have normal blood counts after immunosuppressive treatment with horse ATG and cyclosporine. About a third of these patients have a relapse, and up to 15% develop MDS, sometimes years after their treatment.
The purpose of this study was to find out whether gradually reducing the cyclosporine dose after immunosuppressive treatment for 6 months could prevent relapses and progression to MDS in patients with aplastic anemia. Between 1989 and 2003, patients with aplastic anemia who participated in studies at the National Institutes of Health Clinical Center were treated with horse ATG for 4 days and cyclosporine for 6 months. After 6 months, the cyclosporine treatments stopped. Starting in 2003, patients with aplastic anemia were still treated with horse ATG for 4 days and cyclosporine for 6 months, but the cyclosporine dose was lowered gradually after that, by 25% every 3 months, over the next 18 months. These groups results were compared.

Key Findings:
• Three years after the patients began their treatment with ATG and cyclosporine, relapse was reduced slightly from 32% to 29%.
• Progression to MDS was the same in both groups.

Conclusions:
These results show that gradually reducing the cyclosporine dose after 6 months of immunosuppressive treatment is not beneficial in patients with aplastic anemia. Cyclosporine is difficult to tolerate and affects the liver, heart function and presents the anticipated risks of immunosuppression. Shorter exposure to cyclosporine provides more benefit to the patient.

Severe Aplastic Anemia Working Party (RATGAA07)
Judith C Marsh, Gérard Socié, Hubert Schrezenmeier, M.D., Andre Tichelli, Antonio M. Risitano, Jakob R. Passweg, M.D., Carlo Dufour, M.D., Mahmoud Aljurf, M.D., Hazza A Al-Zahrani, Rosi Oneto, Philip Sedgwick, Barrois Alain, Shahram Kordasti, Modupe Elebute, Ghulam J. Mafti, M.D., and Andrea Bacigalupo

Horse ATG (hATG) with cyclosporine used to be the standard immunosuppressive treatment for people with aplastic anemia who were not eligible for HSCT. Rabbit ATG (rATG) was used only for patients who had not responded or who had had a relapse after treatment with horse ATG. But horse ATG was taken off the market in European, Asian, and Latin American countries a few years ago.

The authors compared the effects of rabbit ATG and cyclosporine in 35 patients treated between 2008 and 2010 at 10 centers in Europe and Saudi Arabia and of horse ATG and cyclosporine in 105 patients who had been treated earlier. The patients treated with rabbit ATG were not eligible for HSCT from a matched sibling. Six of these patients had very severe aplastic anemia, 20 had severe aplastic anemia, and 9 had non-severe aplastic anemia. Median patient age was 46 years.

Key Findings:
• At 6 months, 7% of patients treated with rabbit ATG had a complete response (no signs of their aplastic anemia), and 32% had a partial response.
• Sixty-three percent of patients treated with rabbit ATG had an infection, 29% had a high liver enzyme level (showing liver damage), and 23% had developed a rash.
• Twenty-nine percent died after treatment with rabbit ATG, compared to 18% after horse ATG treatment.

2408 Prospective Phase II Pilot Study of Rabbit Antithymocyte Globulin (ATG, Thymoglobuline) with Ciclosporin for Patients with Acquired Aplastic Anemia and Matched Pair Analysis with Patients Treated with Horse ATG (Lymphoglobuline) and Ciclosporin: A Study from the EBMT
Two years after starting treatment, 56% of patients treated with rabbit ATG were still alive, compared to 78% of those treated with horse ATG.

Conclusions:
Responses were much poorer and survival was much lower after treatment with rabbit ATG than horse ATG.

**3430 The Efficacy of Rabbit Antithymocyte Globulin (Thymoglobulin®) with Cyclosporin as First-Line Treatment in Aplastic Anemia**

Seung-Hwan Shin, Seung-Ah Yahng, Sung-Eun Lee, Byung-Sik Cho, Ki-Seong Eom, Yoo-Jin Kim, Hee-je Kim, Seok Lee, Chang-Ki Min, Seok-Goo Cho, Dong-Wook Kim, Woo-Sung Min, Chong-Won Park, and Jong-Wook Lee

Since horse ATG became unavailable in South Korea in 2006, rabbit ATG has been the only ATG preparation available. Horse ATG had a response rate of 60-75% in 4 months. Limited information is available on the effectiveness of rabbit ATG as first-line treatment for patients with aplastic anemia.

A group of researchers studied the outcomes of immunosuppressive therapy using rabbit ATG with cyclosporine as first-line treatment in 58 patients with aplastic anemia. The patients were treated between March 2006 and April 2010. Of these patients, 31% had very severe aplastic anemia and 40% had severe aplastic anemia.

Key Findings:
- The proportion of patients who responded to the treatment increased from 28% at 3 months to 57% at 18 months.
- Complete response rates (no signs of aplastic anemia) increased over time, from 1% at 3 months to 21% at 18 months. The median time to achieve a complete response was just over a year (381 days).
- Among the 53% of patients who responded to the treatment, 32% had a relapse. The median time between response and relapse was 396 days.
- Eighty-six percent of patients were still alive 3 years after their rabbit ATG treatment.
- Patients were more likely to survive and respond to the treatment if they were younger than 45.

Conclusions:
This team reports rATG to be less effective alternative than hATG in treating aplastic anemia. It took longer to achieve the response (up to 18 months) and had a high number of serious infections.

**Transfusion Dependence**

**54 Eltrombopag Can Stimulate Trilineage Hematopoiesis with Transfusion Independence in Patients with Refractory Severe Aplastic Anemia: Results from a Phase II Trial**

Matthew J. Olnes, M.D., Ph.D., Phillip Scheinberg, M.D., Katherine Calvo, M.D., Ph.D., Yong Tang, Susan Soto, R.N., Xingmin Feng, Ph.D., Ronan G. Desmond, M.D., MRCP, FRCPath, Jay N. Lozier, M.D., Ph.D., Neal S. Young, M.D., and Cynthia E. Dunbar, M.D.

Most patients with severe aplastic anemia do well after HSCT or immunosuppressive treatment. But a suitable donor isn’t available for all patients, and some patients do not respond well to immunosuppressive therapy.

Eltrombopag (Promacta®) is a drug that stimulates thrombopoietin, a hormone that controls platelet production in the bone.
Iron Chelation

1344 Hematologic Responses in Patients with Aplastic Anemia Treated with Deferasirox: A Post-Hoc Analysis from the EPIC Study

Jong Wook Lee, M.D., Ph.D., Sung-Soo Yoon, M.D., Ph.D., Zhi Xiang Shen, M.D., Arnold Ganser, M.D., Hui-Chi Hsu, M.D., Ali El-Ali, M.D., Dany Habr, M.D., Bernard Roubert, Ph.D., and John B. Porter, M.D. on behalf of the EPIC study investigators

Patients with aplastic anemia who have had many red blood cell transfusions often develop high levels of iron, known as iron overload, because red blood cells carry iron and the body has difficulty releasing excess amounts. Iron overload can damage the body’s tissues and organs. Studies have shown that iron chelation drugs can remove the excess iron from the body. The purpose of this study was to examine the effects of deferasirox (Exjade®) treatment on blood counts in aplastic anemia patients being treated for iron overload.

The researchers looked at information about 72 patients with aplastic anemia who had enrolled in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. These patients needed regular blood transfusions and high levels of iron. The patients were treated with 20 mg/kg deferasirox each day. Doses were increased by 5 or 10 mg/kg per day up to 40 mg/kg daily, depending on the amount of iron in each patient’s blood and whether the patient had any side effects. Immunosuppressive treatments can affect patient responses to iron chelation treatment. 67% of these patients received at least one immunosuppressive treatment while they were on deferasirox treatment.

marrow. This process increases the number of platelets and decreases bleeding risk. Patients take this drug by mouth once a day.

The authors conducted a non-randomized, pilot Phase II study of eltrombopag in patients with severe aplastic anemia who had had severe thrombocytopenia, or shortage of platelets, for at least 6 months after at least one round of immunosuppressive treatment. Patients received 50 mg of eltrombopag each day, and the investigators increased their doses every 2 weeks to a maximum of 150 mg a day. At the time of the ASH meeting, the researchers had evaluated the responses of 22 patients. Their median age was 45 years.

Key Findings:
• Blood counts improved in 41% of patients for at least 8 weeks.
• Seven patients (32%) had higher platelet counts and 9 patients (27%) had higher counts of hemoglobin (a protein in red blood cells) for at least 8 weeks.
• Four patients who had needed regular red blood cell transfusions before the study stopped needing transfusions.
• The bone marrow of three of four patients who responded to the treatment for at least a year continued to make healthy blood cells throughout the year.

Conclusions:
These results offer the first evidence that stimulating thrombopoietin can increase the number of blood-forming stem cells in people. The study showed that eltrombopag helped a small number of patients with aplastic anemia reduce the need for blood transfusions in a clinical trial setting.
Key Findings:
• 67% of patients had better blood counts within a median of 42 days of starting the deferasirox. All of these patients stopped needing regular blood transfusions.
• Of those who received immunosuppressive treatment during their deferasirox treatment, 19 (40%) had better blood counts following iron chelation treatment.
• Iron levels in blood dropped more in patients who did not have immunosuppressive therapy during the study and who responded at least partially to iron chelation than in those who did not respond.

Conclusions:
Deferasirox is effective in reducing excess iron and improves blood counts in some patients with aplastic anemia.

3424 Hematologic Improvement with Iron Chelation Using Therapy Deferasirox in Patients with Aplastic Anemia: A Subgroup Analysis of KAM0112 Prospective Study
Yoo-Hong Min, Sung-Soo Yoon, M.D., Ph.D., Hyeoung Joon Kim, Kyoo-Hyung Lee, Jae Hoon Lee, M.D., Jong Ho Won, Jae Yong Cho, Hyeok Shim, M.D., Ho Young Kim, M.D., Chu-Myang Seung, Chul Soo Kim, Mark Hong Lee, M.D., Ph.D., Jooseop Chung, M.D., Ph.D., Myung Soo Hyun, Deog-Yeon Jo, M.D., Ph.D., Chul Won Jung, Sang Kyun Sohn, Hwi-Joong Yoon, M.D., Ph.D., Byung Soo Kim, Young-Don Joo, and June-Won Cheong, M.D., Ph.D.

Only limited data are available on the effects of iron chelation therapy on hematopoiesis, or the bone marrow’s ability to make healthy blood cells. In this multi-center study, a group of researchers in South Korea evaluated the effectiveness of iron chelation therapy with 20 mg/kg of deferasirox each day for at least 6 months in 54 patients with aplastic anemia and iron overload.

Key Findings:
• Ferritin levels in blood (a marker of how much iron the body is storing for later use) dropped about 25%.
• Iron levels in the liver were reduced from 20 mg/g to 8 mg/g.
• Patients starting with a low hemoglobin level showed significant improvement with the average hemoglobin level rising from 6.1 g/dl to 8.2 g/dl after treatment. This contributes to increased energy.
• Patients whose platelet count was low also showed improvement with the average platelet count rising from 12.5/ml to 22.2/ml. This means their blood is able to clot more effectively and decreases their risk of excessive bruising and bleeding.
• White blood cell counts showed some improvement increasing slightly, from 2.1 to 2.3/ml.
• Patients’ need for red blood cell transfusions decreased also.

Conclusions:
Iron chelation treatment with deferasirox can improve anemia and thrombocytopenia (low platelet count) in patients with aplastic anemia who have excess iron as a result of blood transfusions.
MORE WAYS TO GET HELP

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 MDS
- Online Learning Center
- Patient and family conferences
- Peer Support Network
- Print and electronic newsletters with important information and updates
- Clinical trials information

Contact us today. Here’s how:

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Email us:
info@aamds.org

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