

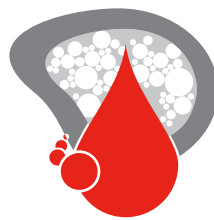
AAMDSIF MDS RESEARCH SUMMARY

2018

AMERICAN SOCIETY OF
CLINICAL ONCOLOGY (ASCO)

•
EUROPEAN HEMATOLOGY
ASSOCIATION (EHA)

*A Summary of Selected Scientific Abstracts for
Patients with Myelodysplastic Syndromes (MDS)
and Their Caregivers*



AA·MDS
INTERNATIONAL FOUNDATION

The Aplastic Anemia and MDS International Foundation (AAMDSIF) 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 summary of selected abstracts presented at the 2018 Annual Meetings of The American Society of Clinical Oncology (ASCO) and European Hematology Association (EHA). It provides some of the most up-to-date information about new research into the biology and treatment of myelodysplastic syndromes (MDS).

Although this information has undergone a thorough, independent medical review to insure its accuracy, this material 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 abstract summary is to provide you with the most up-to-date information about new research into the biology and treatment of myelodysplastic syndromes (MDS), as presented this year at the major hematology and oncology scientific meetings. American Society of Clinical Oncology (ASCO), and the European Hematology Association (EHA),

These are some of the world's largest meetings of hematologists and hematological oncologists and are 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. In presenting these research summaries, our goal is to simply inform you about current news and trends in research related to MDS.

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., summary of the study and its results. Authors of the most interesting and noteworthy abstracts are asked by conference organizers to present their research in more detail at the conference.

These abstract presentations are often considered early looks at study results, and these results may change when investigators publish them in full form, as a manuscript. We selected the abstracts in this summary because we feel they are the most relevant and important for MDS patients to know about. By reviewing the information presented in the booklet, we hope you will:

- Learn how ongoing research on MDS 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 MDS therapy
- Learn about the importance of clinical trials in identifying novel therapies for MDS
- Know the most important issues about MDS 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 these meetings often involve experimental drugs that are not yet approved for general use by the U.S. Food and Drug Administration (FDA) or investigations of potential new uses of previously approved treatments.

By providing summaries of the research presented, we do not intend to recommend or endorse any medication or treatment approach. If you are interested in participating in research studies such as those discussed here, we encourage you to speak to with your doctor about clinical trials or to visit www.clinicaltrials.gov.

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

Mikkael Sekeres, MD, MS

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AAMDSIF Medical Advisory Board*

Clone Size, Abnormal Chromosomes, and the Revised International Prognostic Scoring System

Omar Alkharabsheh, Salwa Shihadeh Saadeh, Mrinal Mahesh Patnaik, Hassan Alkhateeb, Naseema Gangat, Kebede Begna, William J. Hogan, Patricia T. Greipp, Rong He, Phuong L. Nguyen, Mark Robert Litzow, Aref Al-Kali

Doctors often use the Revised International Prognostic Scoring System (IPSS-R) to establish a prognosis and choose treatments for patients with MDS. One of the factors that this system considers when classifying a patient's MDS is abnormal chromosomes. However, the IPSS-R does not consider other factors that could affect prognosis in MDS, including abnormal clones, or copies of immature white blood cells.

A team from the Mayo Clinic reviewed records from 1,301 patients with MDS. The team collected information on chromosome abnormalities and clones in these patients.

Key findings:

- Of 637 patients who had an abnormal karyotype (collection of chromosomes), 372 (58%) had just one abnormal clone.
- Of patients with just one abnormal clone, 260 (70%) had just one abnormal chromosome.
- The outcomes of these patients were consistent with their IPSS-R scores.
- Overall survival was longer, at 54 months, in the 474 patients with a normal karyotype than in 121 patients with intermediate-risk MDS (30.5 months), 49 patients with poor-risk MDS (21.1 months), and 75 patients with very poor-risk MDS (8.7 months).
- Clone size had no effect on overall survival.

Conclusions:

- Clones did not affect overall survival in patients with MDS who had intermediate-risk or low-risk MDS according to the IPSS-R.
- The authors recommend considering abnormal chromosomes in prognoses using the IPSS-R for patients with MDS.

Phase I Clinical Trial of Ivosidenib in Patients with Acute Myelogenous Leukemia (AML) That Has Not Responded to Previous Treatment

Daniel Aaron Pollyea, Courtney Denton Dinardo, Stéphane de Botton, Eytan Stein, Gail J. Roboz, Alice S. Mims, Ronan T. Swords, Jessica K Altman, Robert Collins, Gabriel N. Mannis, Geoffrey L. Uy, William Bruce Donnellan, Arnaud Pigneux, Amir Tahmasb Fathi, Hua Liu, Bin Wu, Eyal C. Attar, Martin S. Tallman, Richard M. Stone, Hagop M. Kantarjian

About 3% of patients with MDS have a mutation in the IDH1 gene, as do 7–14% of patients with MDS. FT-2102 is an experimental drug that inhibits the activity of mutant IDH1.

Ivosidenib (Tibsovo) is a drug that inhibits the IDH1 mutation. This drug is being evaluated in a Phase I clinical trial in patients with advanced-stage blood cancers. This report describes the drug's efficacy and safety in this trial in 179 patients with AML that has not responded to previous treatment or that relapsed after treatment. These patients were treated with 500 mg once daily of ivosidenib.

Key findings:

- 42% of patients responded to the treatment.
- 24% of patients had a complete remission, meaning that they had no signs of AML.
- On average, complete remissions lasted 10.1 months.
- Patients tolerated the treatment well.
- The most common side effects were diarrhea, increased white cell counts, nausea, fever combined with low counts of some white blood cells, fatigue, and abnormal electrocardiogram findings.
- Most of these side effects were not severe and were not related to the treatment.

Conclusions:

- In high-risk patients with relapsed or refractory AML and an IDH1 mutation, ivosidenib led to durable remissions and was well tolerated.
- Studies are ongoing in patients with AML that has not been treated before.

Phase 1 Clinical Trial of FT-2102 for Acute Myeloid Leukemia (AML) or MDS

Justin M. Watts, Maria R. Baer, Sangmin Lee, Jay Yang, Shira Naomi Dinner, Thomas Prebet, Gary J. Schiller, Karen Seiter, Paul Brent Ferrell, Patrick Francis Kelly, Ping Li, Jennifer Sweeney, Courtney Watson, Hesham Mohamed, Jorge E. Cortes

About 3% of patients with MDS have a mutation in the IDH1 gene, as do 7–14% of patients with MDS. FT-2102 is an experimental drug that inhibits the activity of mutant IDH1.

The purpose of this Phase 1/2 clinical trial was to evaluate the safety and effectiveness of FT-2102 in 35 patients with AML or MDS who had the IDH1 mutation. Patients were treated with FT-2102 alone (22 patients) or in combination with azacitidine (Vidaza; 13 patients). At the time this report was written, 16 patients were still on treatment and had completed an average of 2 treatment cycles.

Key findings:

- Patients taking FT-2102 alone or with azacitidine tolerated the FT-2102 well.
- Most of the side effects caused by FT-2102 were mild.
- The most common side effects caused by the treatment were fatigue (34% of patients), nausea (29%), and white blood cell shortage with fever (23%).
- In the 16 patients treated with FT-2102 alone whose data could be evaluated, 2 (13%) had a complete remission, 4 (25%) had a complete remission but some of their blood cell counts did not recover, and 5 (31%) had stable disease for at least 8 weeks.
- In the 11 patients treated with FT-2102 and azacitidine whose data could be evaluated, 2 (18%) had a complete remission, 1 (9%) had a complete remission but not all their blood cell counts recovered, and 5 (45%) had stable disease for at least 8 weeks.

Conclusions:

- FT-2102 is safe and beneficial in patients with AML or MDS who have the IDH1 mutation.

Combination of Ivosidenib or Enasidenib with Azacitidine in Patients with Acute Myeloid Leukemia (AML)

Courtney Denton Dinardo, Anthony Selwyn Stein, Eytan M. Stein, Amir Tahmasb Fathi, Andre C. Schuh, Pau Montesinos Fernández, Olatoyosi Odenike, Hagop M. Kantarjian, Richard M. Stone, Robert Collins, Giovanni Martinelli, Montserrat Arnan, Bin Wu, Daniel O. Koralek, Jason Van Oostendorp, Jing Gong, Kyle J. MacBeth, Paresh Vyas

About 3% of patients with MDS have a mutation in the IDH1 gene, as do 7–14% of patients with MDS. Ivosidenib (Tibsovo) is a drug that inhibits the IDH1 mutation. About 2–13% of patients with AML have a mutation in another gene, IDH2, and enasidenib (IDHIFA) inhibits activity of this mutation.

This ongoing Phase 1b/2 study is evaluating the combination of ivosidenib and azacitidine (Vidaza) in patients with AML who have the IDH1 mutation. The study is also assessing the combination of enasidenib plus azacitidine in patients with AML and the IDH2 mutation.

As of this report, 11 patients (average age 76) had been treated with the ivosidenib/azacitidine combination, and 6 (average age 68 years) had been treated with the enasidenib/azacitidine combination.

Key findings:

- Ivosidenib/azacitidine combination:
 - Three pts stopped treatment, including two whose disease had progressed.
 - The most serious side effects were nausea (in 8 patients), constipation (6 patients), fatigue (5 patients) and diarrhea (4 patients).
 - These side effects were about as common as with azacitidine alone.
 - 8 patients (73%) responded, including 4 with a complete remission.
- Enasidenib/azacitidine combination:
 - The most common side effects were nausea (4 patients) and high levels of bilirubin in blood (4 patients).
 - Four patients (67%) responded, including two who had a complete remission.

Conclusions:

- Patients tolerated the combinations of ivosidenib or enasidenib with azacitidine well.
- The response rates to these treatments are encouraging.

Clinical Trial of Lenalidomide With or Without Epoetin for Lower-Risk MDS

Andrea Toma, Sylvie Chevret, Olivier Kosmider, Jacques Delaunay, Aspasia Stamatoullas, Christian Rose, Odile Beyne-Rauzy, Anne Banos, Agnes Guercy-Bresler, Eric Jourdan, Veronique Sardnal, Denis Caillot, Kamel Laribi, Benoit De Renzis, Dominique Bordessoule, Borhane Slama, Laurence Sanhes, Michaela Fontenay, Pierre Fenaux, Francois Dreyfus

Erythropoietin-stimulating agents (ESAs) are used to treat anemia in patients with lower-risk MDS and delay the need for red blood cell transfusions. But only 40–50% of patients respond to these drugs.

Lenalidomide (Revlimid) can help patients who don't respond to ESAs or who have a relapse after ESA treatment. About 25% of these patients stop needing regular red blood cell transfusions with lenalidomide treatment.

This open-label Phase II clinical trial included 132 patients with lower-risk MDS who did not have del(5q) MDS. The average age was 73, and 44 patients were women. All patients had needed transfusions with at least 4 red blood cell units during the previous 8 weeks, and all had either not responded to lenalidomide alone or had had a relapse after responding. Patients were treated with lenalidomide alone or lenalidomide plus epoetin beta, an ESA.

Key findings:

- Red blood cell counts rose in 15 patients (23%) treated with lenalidomide alone and 26 (40%) treated with lenalidomide and epoetin beta.
- Another 9 patients (14%) treated with lenalidomide alone stopped needing regular red blood cell transfusions, as did 16 (25%) of those treated with the combination.
- Side effects were similar in both groups.
- A mutation in the CRBN gene was associated with red blood cell responses in patients in both groups.

Conclusions:

- The combination of lenalidomide and epoetin beta had significantly better effects on red blood cell counts than lenalidomide alone in patients with lower-risk MDS who did not have del(5q) MDS and who had not responded to ESAs alone or had stopped responding to them.

New Clinical Trial of Venetoclax and Azacitidine in Patients with Higher-Risk MDS

Chun Yew Fong, Andrew H. Wei, Mark G. Frattini, Meagan Jacoby, Uma Borate, Katharina S. Gotze, Jacqueline Suen Garcia, Daniel Aaron Pollyea, Leanne Holes, Ying Zhou, Kaffa Mussumeh Fakouhi, Joel Levenson, Jason G Harb, Suresh K. Agarwal, Faraneh Attarchi, Mack H. Mabry, Wan-Jen Hong, Thomas Michael Jahn, Pierre Fenaux, Guillermo Garcia-Manero

Azacitidine (Vidaza) is the only drug shown in studies to prolong survival in patients with higher-risk MDS that has not been treated before. But about half of patients treated with azacitidine alone don't benefit from this treatment.

Venetoclax (VENCLEXTA) is a drug that inhibits the BCL-2 protein. Research has shown that the combination of venetoclax with azacitidine is safe and effective in older patients with acute myelogenous leukemia that has not been treated before.

These patients were not eligible for intensive chemotherapy.

This open-label, Phase 1b clinical trial has two parts. In the first part, about 24 patients with MDS will be treated with increasing doses of venetoclax and the standard azacitidine dose. In the second part, about 20 patients will be treated at the recommended venetoclax dose for Phase 2 clinical trials. The patients will not have had MDS treatment before. They will have intermediate-2-risk or high-risk MDS according to the International Prognostic Scoring System.

The study's main objectives are to assess the combination's safety and the recommended venetoclax dose for Phase 2 trials as well as the dosing schedule for the two treatments.

For more information about this clinical trial, see <https://clinicaltrials.gov/ct2/show/NCT02942290>.

New Phase 3 Clinical Trial of Azacitidine With or Without Pevonedistat for Higher-Risk MDS, Chronic Myelomonocytic Leukemia, or Acute Myelogenous Leukemia

Mikkael A. Sekeres, Robert J. Fram, Zhaowei Hua, Lionel Ades

Pevonedistat is a small-molecule inhibitor of the Nedd8 activating enzyme. Researchers believe that this drug encourages the death of abnormal clones, or copies of immature white blood cells, in people with bone marrow failure diseases.

A phase 1b clinical trial of a combination of pevonedistat and azacitidine appeared to be beneficial in patients with acute myelogenous leukemia (AML) that hadn't been treated before. These results justified the current Phase 3 clinical trial.

This new study will compare the efficacy and safety of pevonedistat with azacitidine with the efficacy and safety of azacitidine alone.

The study will include patients with higher-risk MDS, chronic myelomonocytic leukemia (CMML), or AML with low counts of blasts (immature white blood cells).

Plans call for the study to enroll about 450 adults who have not had treatment before for their MDS, CMML, or AML. These adults will not be eligible for intensive chemotherapy, stem cell transplantation, or both. Patients will be treated with azacitidine alone or a combination of pevonedistat and azacitidine in 28-day cycles until their disease progresses or they develop unacceptable side effects.

The study's main endpoints are overall response rate by the sixth cycle and survival without certain complications. The investigators will also assess overall survival, rates and duration of responses, time to AML transformation, rates and duration of independence from red blood cell transfusions, and health-related quality of life.

For more information about this study, see <https://clinicaltrials.gov/ct2/show/NCT03268954>.

A Phase II Clinical Trial of Guadecitabine for Untreated MDS

Guillermo Garcia-Manero, Prithviraj Bose, Yesid Alvarado, Gautam Borthakur, Naval Daver, Farhad Ravandi-Kashani, Elias Jabbour, Koichi Takahashi, Michael Andreeff, Tapan Kadia, Courtney DiNardo, Jorge Cortes, Steven Kornblau, Kiran Naqvi, Christopher Benton, Maro Ohanian, Marina Konopleva, Zeev Estrov, Guillermo Montalban Bravo, Sherry Pierce, Kristy Bodden, Hagop Kantarjian

Azacitidine and decitabine are the standard treatments for most patients with higher-risk MDS. Guadecitabine is a form of decitabine that releases the drug gradually, increasing the exposure to the drug of MDS cells. Studies have shown that guadecitabine is effective in acute myelogenous leukemia (AML) and MDS that has relapsed or hasn't responded to treatment.

This Phase II clinical trial assessed the safety and efficacy of guadecitabine in patients with MDS that has not been treated before. The investigators administered 60 mg/m² of the drug every day for five days in 28-day cycles. Patients were treated for an average of five cycles.

The study included 83 patients (median age 69 years) with higher-risk MDS. These patients had not been treated with chemotherapy for their MDS.

Key findings:

- Sixteen patients (23%) had a complete remission with guadecitabine.
- Another three patients (4%) had a complete remission but incomplete recovery of their platelet counts.
- In 26 patients (37%), blood counts increased.
- The most common side effect was infection.
- Only two patients (2%) died within the first 6 weeks of treatment, and patients have survived for a median of 14 months.

Conclusions:

- Guadecitabine is clinically active and safe in patients with higher-risk MDS.
- This study is continuing to enroll patients.

Imetelstat for Lower-Risk MDS

Pierre Fenaux, Azra Raza, Edo Vellenga, Uwe Platzbecker, Valeria Santini, Irina Samarina, Koen Van Eygen, María Díez-Campelo, Mrinal M. Patnaik, Laurie Jill Sherman, Libo Sun, Helen Varsos, Esther Rose, Aleksandra Rizo, David P. Steensma

Erythropoietin-stimulating agents (ESAs) are used to treat anemia in patients with lower-risk MDS and delay the need for red blood cell transfusions. Patients who don't respond to ESAs or who stop responding have few options.

Imetelstat could benefit these patients by targeting cells with short telomeres. Telomeres are the ends of chromosomes, and they help keep chromosomes stable. When telomeres get critically short, the cells die or the chromosomes become confused and allow the cells to keep dividing, resulting in more gene mutations and DNA damage. Telomeres can be very short in people with MDS.

This study is assessing the safety and efficacy of imetelstat in an ongoing Phase II/III clinical trial in patients with lower-risk MDS who needed regular red blood cell transfusions. These patients had not responded to ESAs or had stopped responding to them. They needed transfusions of at least four units of red blood cells in the 8 weeks before starting the study.

In the first part of the study, 32 patients (median age 68.5 years) were treated with 7.5 mg/kg imetelstat every 4 weeks. All had lower-risk MDS, and 88% had been treated with ESAs before.

Key findings:

- 38% of patients did not need any red blood cell transfusions for at least 8 weeks with this treatment.
- On average, patients stopped needing transfusions after 8 weeks of treatment, and they didn't need transfusions for a median of 23 weeks.
- 13 patients (41%) had not been treated with lenalidomide (Revlimid), azacitidine (Vidaza), or decitabine (Dacogen) or who did not have del(5q) MDS. Of these patients, 54% stopped needing red blood cell transfusions for at least 8 weeks.
- The most common side effects were low blood cell counts, especially low counts of white blood cells and platelets.

Conclusions:

- The side effects of imetelstat are predictable and manageable, and all can be treated successfully.
- The study has enrolled more patients to validate these initial findings.

Phase Ib/II Clinical Trial of APR-246 and Azacitidine for MDS or Acute Myelogenous Leukemia (AML) with a TP53 Mutation

David Sallman, Amy Dezern, Kendra Sweet, David Steensma, Thomas Cluzeau, Mikkael Sekeres, Guillermo Garcia-Manero, Gail Roboz, Amy McLemore, Kathy McGraw, John Puskas, Ling Zhang, Chirag Bhagat, Armin Graber, Najla Al Ali, Eric Padron, Roger Tell, Jeffrey Lancet, Pierre Fenaux, Alan List, Rami Komrokji

Outcomes are often poor in patients who have MDS or AML and a mutation in the TP53 gene. The standard MDS treatments, azacitidine (Vidaza) and decitabine (Dacogen), have a complete response rate of 20% to 30% in these patients. On average, patients with a TP53 mutation survive 6 to 12 months with these treatments.

This study evaluated the safety and efficacy of an experimental drug, APR-246, in combination with azacitidine in nine patients (67% female, median age 65 years). Of these patients, six had MDS and three had AML, and all had a TP53 mutation and higher-risk disease. The patients were treated with one of three doses of APR-246 (50, 75, or 100 mg/kg lean body weight) for 4 days and azacitidine for 7 days in 28-day cycles.

Key finding:

- Two patients in the 50 mg/kg group stopped treatment: one because of an infection who later died of sepsis that wasn't related to the treatment, and one because the patient's marrow showed no signs of disease after five cycles of treatment.
- Side effects in more than 3 patients included nausea (6 patients), low white blood cell counts (6 patients), infection (4 patients), and numbness or weakness (4 patients).
- None of the side effects were treatment related.
- Of the 5 patients whose responses could be evaluated, 4 had a complete response (no signs of the MDS or AML), and 1 had a complete response in the bone marrow.

Conclusions:

- Patients with MDS or AML and a TP53 mutation tolerated the combination of APR-246 and azacitidine well.
- All patients responded to the treatment.
- The maximum dose that patients can tolerate hasn't yet been reached.

Phase II Clinical Trial of Azacitidine Alone or in Combination with Lenalidomide for High-Risk MDS

Bengt Rasmussen, Lars Nilsson, Martin Jädersten, Magnus Tobiasson, Hege Garelius, Jan Maxwell Nørgaard, Ingunn Dybedal, Kirsten Grønbaek, Astrid Olsnes Kittang, Fryderyk Lorenz, Freja Eberling, Max FlogegårdClaus, Werenberg Marcher, Elisabeth Ejerblad, Annette Öster Fernström, Elsa Bernard, Gudrun Göhring, Elli Papaemmanuil, Leoni Saft, Eva Hellström-Lingberg, Lars Möllgård

Patients with 5q deletion MDS, also known as del(5q) MDS, have a deletion (loss) of the long (q) arm of chromosome 5. MDS with del(5q) has a poor prognosis. The usual treatment, azacitidine (Vidaza), has low response rates in this group of patients.

Lenalidomide (Revlimid) is an effective treatment for patients with lower-risk MDS who have del(5q). The researchers thought that a combination of azacitidine and lenalidomide might be more effective than azacitidine alone for those with higher-risk MDS and del(5q).

This randomized Phase II clinical trial included 72 patients (41% female, median age 72 years) from 12 centers in Sweden, Denmark, Norway, and Finland. Half the patients were treated with azacitidine only, and half with both azacitidine and lenalidomide. Most (75%) patients had MDS and 25% had AML. All had del(5q), and they were treated for up to six 28-day cycles.

Key findings:

- The response rates were 36% for patients treated with azacitidine alone and 28% for those treated with the combination of azacitidine and lenalidomide.
- 7 months after finishing the treatment, the median survival was 14 months for patients treated with azacitidine alone and 10 months for those treated with the combination.
- Rates of serious side effects were similar in the two groups.

Conclusions:

- Adding lenalidomide to azacitidine did not increase responses or prolong survival in patients with higher-risk MDS or AML with del(5q).

Phase II Clinical Trial of Luspatercept for Lower-Risk MDS

Uwe Platzbecker, Aristoteles Giagounidis, Philipp Kiewe, Ulrich Germing, Katharina Götze, Karin Mayer, Markus Radsak, Thomas Wolff, Joerg Chromik, Uta Oelschlägel, Joseph Reynolds, Carolyn Barron, Chris Rovaldi, Rajasekhar NVS Suragani, Xiaosha Zhang, Abderrahmane Laadem, Peter G Linde, Matthew L Sherman

In patients with MDS, immature red blood cells don't become healthy mature red blood cells. As a result, these patients develop anemia and other symptoms. Luspatercept is an investigational drug that helps the immature red blood cells become healthy mature cells in patients who have anemia due to MDS and other rare blood disorders.

This ongoing, Phase II, open-label clinical trial is evaluating the effects of luspatercept in patients with lower-risk MDS. The study is collecting data on such outcomes as the drug's long-term safety, red blood cell responses, whether patients stop needing red blood cell transfusions, and patient quality of life.

This report focuses on 88 patients whose data could be evaluated. Patients were treated with luspatercept every 3 weeks up to five times. They were eligible to continue treatment for up to five more years.

Key findings:

- Response rates were higher in patients whose erythropoietin levels were lower than 500 IU/L at the start of the study (62%, compared with 26% for those with higher erythropoietin levels). Erythropoietin is a hormone that helps the bone marrow form red blood cells.
- Response rates were also higher in patients with an SF3B1 mutation (72%) than in those without this mutation (36%).
- Responders tended to have lower ratios of myeloid to erythroid cells. Myeloid cells are immature cells that can turn into red blood cells, some types of white blood cells, or platelets. Erythroid cells are immature red blood cells.

Conclusions:

- The higher response rates in patients with lower ratios of myeloid to erythroid cells suggest that patients with more erythroid cells before treatment might be more likely to respond to luspatercept.
- This finding supports luspatercept's ability to help these immature red blood cells mature.
- Luspatercept might work in patients with different characteristics, including different genetic mutations.

Phase I Clinical Trial of Durvalumab in Patients with MDS After Treatment with Azacitidine or Decitabine

Guillermo Garcia-Manero, Manila Gaddh, Uwe Platzbecker, R. Coleman Lindsley, Sarah Larson, Lucy Godley, Jeanne Palmer, Fahd Quddus, Timothy Chevassut, Pierre Fenaux, Rami Komrokji, Roger Lyons, Gail Roboz, Charles Schiffer, Aref Al-Kali, Amer Zeidan, Nai Shun Yao, Bo Chao, Mei Tang, Chelsea Black, Joyson Karakunnel, John Bothos, Lewis R. Silverman

Some types of immune system cells make immune checkpoint proteins (such as PD-1 and its ligands PD-L1 and PD-L2) that help cancer cells escape the immune system. Patients with MDS sometimes have overly active PD-L1 proteins. PD-L1 expression (use of information in genes to control protein formation) on immature blood cells is common in MDS that progresses to acute myelogenous leukemia.

Durvalumab (Imfinzi) is a new type of drug known as a checkpoint inhibitor. These drugs stop immune system cells from making checkpoint proteins. When this happens, the immune system cells can do a better job of killing cancer cells.

This study evaluated the safety and efficacy of durvalumab in patients with MDS. The study included 40 patients (72% male, median age 73 years) who had MDS and had previously been treated with azacitidine (Vidaza) or decitabine (Dacogen). The patients had not responded to that treatment, had had a relapse afterward, or could not tolerate it. Patients were treated with durvalumab every 2 weeks for an average of 9 months.

Key findings:

- All patients had at least one side effect, and 12 (30%) had a serious side effect.
- The most common serious side effects related to durvalumab were decreased platelet count (2 patients, 5%), fluid around the lungs (2 patients, 5%), and inflammation in lung tissue (2 patients, 5%).
- Seven patients (18%) had a complete remission in their bone marrow, meaning that they had very low levels of blasts (abnormal white blood cells).
- Another 8 patients (20%) had stable disease.
- On average, survival was 24 months for patients with lower-risk MDS and 8 months for higher-risk MDS.

Conclusions:

- Durvalumab had little effect in patients previously treated with azacitidine or decitabine.
- Durvalumab's safety was similar to that of other checkpoint inhibitors.

How AAMDSIF Can Help You ...

Many FREE services and programs are available to anyone impacted by, or just interested in, bone marrow failure diseases:

- **Personalized Support** from Information Specialists at (800) 747-2820 or help@aamds.org
- **Educational Materials** on diseases and treatments at www.aamds.org/materials
- **Global Educational Materials** in Spanish, French, German, Italian, and Portuguese at www.aamds.org/global-education
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AAMDSIF relies on its growing team of local Ambassadors – volunteers who contribute their time and talent in many ways, such as becoming:

- **Online Supporters** who hold digital fundraisers in their community or workplace
- **Event Organizers** who plan “March for Marrow” fundraising walks or other events
- **Awareness Campaigners** who teach their community about bone marrow failure
- **Community Connections** leaders who coordinate local patient support groups

Learn more about
volunteering at
ambassadors@aamds.org
or (301) 279-7202 x122.



www.aamds.org



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