Anemia in Myelodysplastic Syndrome 2024

ICER SNAPSHOT

Reviewed by: MDS Foundation

The MDS foundation is not responsible for the final contents of ICER's Report or Snapshot, nor should their review be assumed to support any part of ICER's findings.

The ICER Snapshot is a summary designed to help patients and the broader community learn about the key results and recommendations from ICER's 2024 Final Evidence Report on imetelstat for anemia in myelodysplastic syndrome.

The information included is up to date as of August 2024. New information about this therapy may become available, but is not captured here.

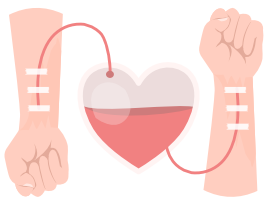
Let's Take a Look

What is Anemia in Myelodysplastic Syndrome?

Myelodysplastic syndromes (MDS) are disorders caused by a lack of healthy blood cells in the bone marrow, leading to an increased risk of blood or bone marrow cancer and a shorter lifespan. Anemia (low red blood cell counts) is common among patients with MDS. The most bothersome symptom for patients is severe fatigue, although they may also experience bleeding, bone pain, fever, weight loss, and infections.

Anemia
Low red blood cell counts

Bone Marrow
Soft spongy substance found in the center of bones where blood cells are made



Between 60,000 and 170,000 people are currently living with MDS in the United States and approximately 40% of lower-risk MDS patients become dependent on blood transfusions to treat their anemia. The financial burden of MDS is very high: annual medical costs may reach $220,000 for lower-risk MDS patients.

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Impact on Patients and Families

What ICER Learned from the Community

Anemia, which causes **fatigue** and **shortness of breath**, contributes to **poor quality of life** for patients. **Emotional distress** due to uncertainties and challenges of the MDS diagnosis also impacts quality of life.

The need for **frequent blood draws, blood transfusions, and doctors' visits** can be **overwhelming**. Patients feel unable to schedule vacations or outings with friends and family, sometimes resulting in a **lack of social life**.

There is an **enormous burden of receiving blood transfusions** which can require a full day or longer. Once patients have received many units of blood over time, they may **develop antibodies** to the available blood, making it harder and **harder to find safe blood** to transfuse.

Patients and caregivers found **patient support communities** and organizations to be of **tremendous value**. However, they had to connect with the organizations themselves and would have wanted a **list of local and national organizations shared with them at the time of diagnosis**.

Treatment of Focus

Imetelstat

Imetelstat, made by Geron Corporation, is a treatment administered through the vein as an infusion every 4 weeks.

How It Works

It works by destroying specific forms of cancer cells which then helps produce healthy blood cells in the bone marrow.

Imtetelstat (Rytelo™, Geron Corporation) was approved by the FDA on June 6, 2024 to treat anemia in lower-risk MDS patients who are dependent on blood transfusions and not eligible for or unresponsive to erythropoiesis-stimulating agents (*ESAs).

*ESAs are the standard treatment option for anemia in MDS that helps bone marrow to produce more red blood cells.

Helpful Clinical Terms

del(5q): Deletion of Part of Chromosome 5
10% of MDS patients have a deletion in chromosome 5. **Clinical trials for imetelstat only included MDS patients without this chromosome deletion**, since another treatment (lenalidomide) already exists for those with del(5q)

ESAs: Erythropoiesis-Stimulating Agents
ESAs are the standard treatment option for anemia in MDS that helps bone marrow to produce more red blood cells

Indirect Comparison
When there is no direct comparison of two treatments, this is a way to compare how well a treatment works by combining data from different studies

Luspatercept
Recently approved first-line treatment for lower-risk MDS patients with anemia, and for those who are unresponsive to ESAs or are RS+

Placebo
An inactive treatment intended to hide whether a patient received the studied drug

RS+/RS-: Ring Sideroblast Positive/Negative
35% of MDS patients have an abnormality in their red blood cells called ring sideroblasts (RS+). They are caused by iron deposits which create a "ring" shape in these blood cells. MDS patients without this abnormality are RS-

Transfusion Independence
Going at least 56 days (8 weeks) without receiving red blood cell or platelet transfusions

What Did Clinical Trials Show?

	IMerge	MEDALIST
TRIAL NAMES	IMerge	MEDALIST
PARTICIPANTS	Studied in 178 adults with lower risk MDS* without del(5q) (includes RS+ and RS- patients)	Studied in 229 adults with lower risk MDS* without del(5q) and RS+ only
TREATMENT GROUPS	Imetelstat vs. placebo	Luspatercept vs. placebo

*All MDS patients in both trials were dependent on blood transfusions and not eligible for/unresponsive to ESAs.

PATIENT OUTCOMES

Imetelstat vs. placebo:

ACHIEVED
At least 8 consecutive weeks of **Transfusion Independence**

In 40% of patients taking imetelstat vs. 15% taking placebo

Imetelstat vs. luspatercept:
(indirect comparison from IMerge and MEDALIST trials)

NO SIGNIFICANT DIFFERENCE IN 8-WEEK TRANSFUSION INDEPENDENCE

These represent some, but not all outcomes that were measured in the clinical trials.

Safety of Imetelstat

During the 18-month follow-up period, the IMerge trial showed a **high discontinuation** (stopping treatment) rate of 77% across both imetelstat and placebo groups. There was also no major reduction in death between groups.

Severe side effects like **low platelet count** and **low white blood cell count** were more frequent in the imetelstat group but were mostly managed within four weeks. Other common adverse events (harmful or negative outcomes) in the imetelstat group included **infections, bleeding, and anemia,** occurring more often than in the placebo group.

ICER's report findings are NOT recommendations that support the use of imetelstat. Patients and families should always talk with their doctors to make shared decisions about treatment for anemia in MDS.

Clinical Conclusions

Compared with placebo, **the overall benefit of imetelstat is promising, but not certain.** Imetelstat had clear benefits in the reduction in the need for red blood cell transfusions, but no significant improvement in fatigue and had substantially more severe adverse events. There is only one relatively small clinical trial, so the level of certainty is also small.

What We Still Don't Know...

- Why achieving transfusion independence with imetelstat does not have any significant impact on fatigue
- How patients and clinicians would manage the high rates of serious adverse events such as anemia, low white blood cell count, and low platelet counts
- How well imetelstat works in US patients
- How well imetelstat works compared directly to luspatercept with RS+ subgroups
- Whether imetelstat has any disease-modifying potential

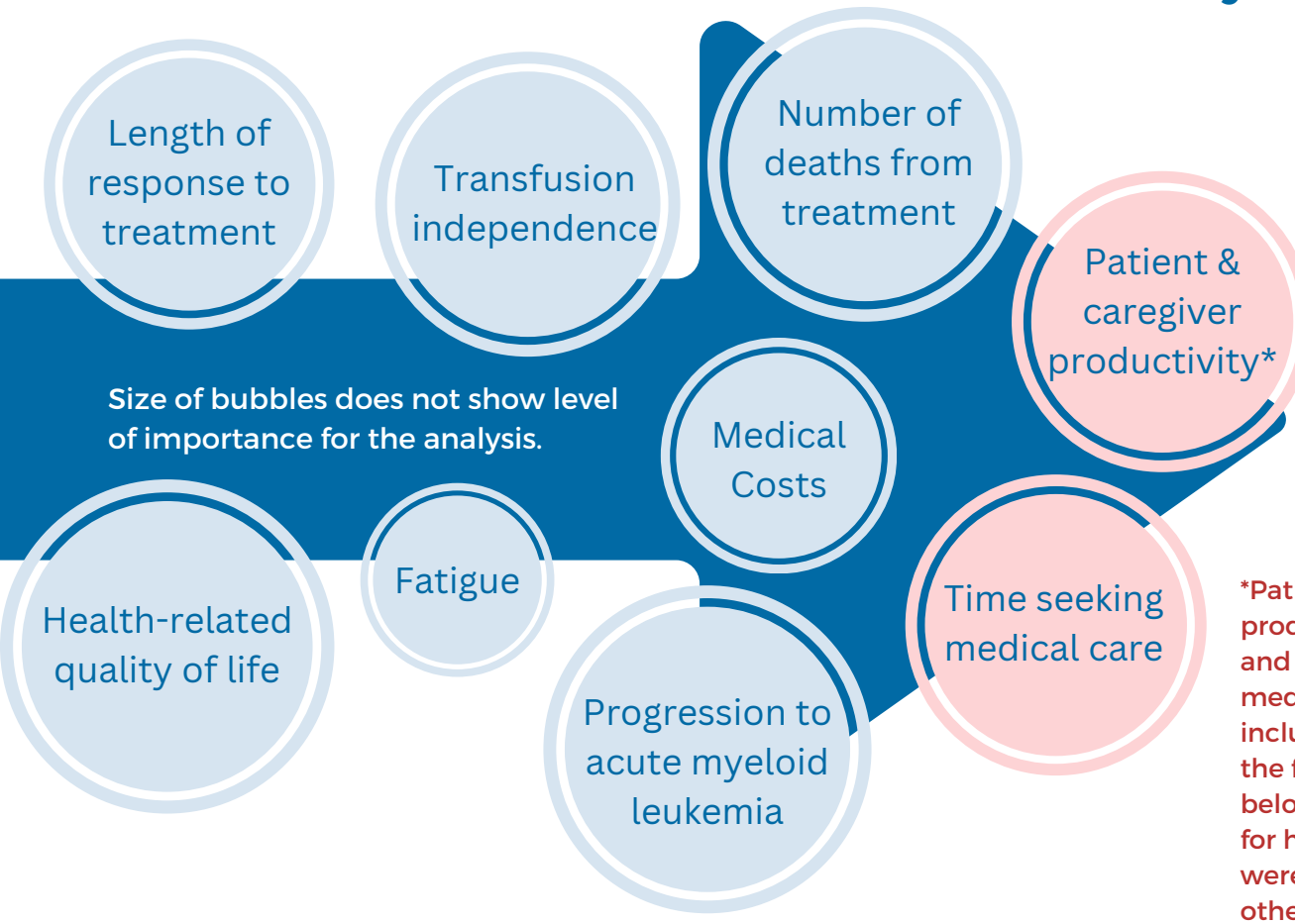
How Did ICER Calculate a Fair Price?

Using economic modeling, we calculated the cost-effectiveness of imetelstat based on transfusion burden compared to placebo. See below for what types of information ICER considered to calculate a fair price range for this treatment.

Populations

1. All MDS patients who were eligible for imetelstat and treated with imetelstat or placebo
2. RS+ MDS patients who were treated with imetelstat, luspatercept, or placebo

Factors Included in ICER's Economic Analysis



*Patient & caregiver productivity impacts and time seeking medical care were not included in calculating the fair price range below. See full report for how these inputs were factored into other economic results.

Fair Price Range for Imetelstat

$94,800 to $113,000 per year

Our economic analysis concluded that the **fair-price range for imetelstat** is between **$94,800 to $113,000 per year**. Imetelstat is **currently not cost effective** at its current annual price of $365,197. In patients with RS+, imetelstat was shown to be more expensive and less effective when compared to luspatercept.

Key Policy Recommendations

The Policy Roundtable at the ICER public meeting included a person living with MDS and informed several policy recommendations for pricing, access, guidelines, and future research in MDS. A few key recommendations are summarized below.

1 Patient groups should seek relationships with clinical specialty societies to advocate for fair drug prices justified by clinical benefit.

Patients often have significant co-pays for drugs requiring intravenous infusions like imetelstat. These costs often fall under Medicare Part B, with the patient required to pay 20% of the cost. **Patient groups and specialty organizations have an opportunity and responsibility to advocate for fair insurance access linked to fair prices for drugs.** Lower prices will lead to fewer restrictions on access to the drugs and less financial burden on patients. In addition, this will enhance more equitable access to effective therapies.

2 Measure the impact of treatment on caregiver burden.

The potential impact of effective therapy for anemia in MDS on caregiver burden was identified as an important potential benefit, but this is not explicitly measured in most clinical trials. Patient organizations have an important opportunity to **partner with researchers in developing measures of caregiver burden** and advocating to pharmaceutical companies and the FDA to include them in future trials of therapies like imetelstat.

3 Payers should establish site-of-service policies that cover home infusion or care at other low-cost sites when feasible.

Given the **reduced cost and increased convenience for patients when infusions are delivered at home** rather than at hospital-based infusion centers, payers should establish site-of-service policies that cover home infusion or care at other low-cost sites when feasible. Insurance policies should allow patients to have **lower cost sharing when lower-cost settings are used**.

4 Manufacturers should set prices that will foster affordability and good access for all patients.

In settings of substantial uncertainty regarding how well a new treatment works, as in the case of imetelstat for MDS, **initial drug pricing should err on the side of being more affordable**. This would allow more patients access and generate additional data. Imetelstat is priced well beyond its currently known clinical benefits. **The manufacturer should reduce the price of imetelstat to promote equitable access and reduce financial harm for patients.**

Impact of Patient Engagement

The Cancer Support Community shared **data on 150 MDS patients** from their "Cancer Experience Registry" which we **incorporated throughout the Patient and Caregiver Perspectives** chapter of the final report.

The MDS Foundation connected us with **3 patients with MDS and 3 caregivers** who participated in our small group interviews and **shaped our understanding of the lived experience.**

The Cancer Support Community's **feedback on ICER's policy recommendations** allowed us to emphasize that **MDS is commonly diagnosed in the non-Hispanic white population.**

The Institute for Clinical and Economic Review (ICER) is an independent nonprofit organization that does research on how well new treatments work and what a fair price should be. Patients and families should always talk with their doctor to make shared decisions about the best treatment option for them.

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