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New Drug Update

Rytelo: a novel option for transfusion-dependent anemia in myelodysplastic syndromes

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ABSTRACT

Rytelo (Imetelstat), approved by the FDA in June 2024, offers a groundbreaking treatment for patients with transfusion-dependent anemia due to lower-risk myelodysplastic syndromes (MDS). Rytelo is a first-in-class telomerase inhibitor that targets telomerase, an enzyme that cancer cells use to maintain their telomeres and continue proliferating. By inhibiting telomerase, Rytelo induces apoptosis in malignant cells in the bone marrow, thus reducing the need for frequent blood transfusions. Administered intravenously every four weeks, clinical trials have shown Rytelo effectively lowers transfusion requirements and enhances patients' quality of life. However, common side effects such as neutropenia and thrombocytopenia require careful monitoring and dose adjustments to manage. Despite these challenges, Rytelo represents a significant advancement in treating transfusion-dependent anemia in MDS, providing a novel therapeutic option that addresses the underlying cause of the disease and improves patient outcomes.

Keywords: Rytelo, FDA, MDS

INTRODUCTION

Myelodysplastic syndromes (MDS) are a diverse category of hematologic malignancies distinguished by inefficient blood cell synthesis in the bone marrow. Patients with lower-risk MDS frequently develop comorbidities such as transfusion-dependent anemia, which have a substantial influence on their quality of life. The FDA approved Rytelo (imetelstat) in June 2024, ushering in a new age of treatment and providing hope to this specific patient population.[1]

RYTELO: MECHANSIM OF ACTION

Rytelo (imetelstat) operates as a first-in-class telomerase inhibitor, targeting the enzyme telomerase that maintains telomere length in cells.[2] Telomeres are DNA sequences at chromosome ends that shorten during cell division, and telomerase activity is typically upregulated in cancer cells, aiding their continued proliferation. By inhibiting telomerase, Rytelo disrupts the replicative potential of malignant hematopoietic cells in the bone marrow, leading to cellular apoptosis and decreased cancer cell viability.[2] This mechanism is particularly relevant in MDS, where ineffective hematopoiesis results in conditions such as transfusion-dependent anemia. The drug's ability to curb the overactive telomerase in MDS provides a targeted therapeutic strategy to reduce transfusion needs and improve patients' quality of life.[2,7]

PHARMACOKINETICS OF RYTELO

Rytelo is administered as an intravenous infusion, typically delivered over two hours every four weeks. The pharmacokinetic profile of imetelstat is characterized by its plasma half-life, distribution, metabolism, and excretion. Following infusion, imetelstat demonstrates a biexponential decline in plasma concentrations with a

terminal half-life allowing for sustained inhibition of telomerase.[7] The drug is extensively distributed in body tissues, and its clearance is mediated primarily through hepatic metabolism and renal excretion. Dose adjustments may be necessary for patients experiencing severe neutropenia or thrombocytopenia, common adverse effects associated with the drug. Monitoring blood counts and adjusting the dosing schedule are essential to managing these side effects and optimizing therapeutic outcomes.[7]

CLINICAL TRIAL PHASE

The approval of Rytelo stemmed from clinical trials demonstrating its efficacy in reducing transfusion burden. In a phase II clinical trial evaluating two imetelstat dose regimens, the 9.4 mg/kg dose administered every 21 days demonstrated a favorable response rate with regards to patient-reported symptoms.[3] The drug targets adult patients with lower-risk MDS experiencing transfusion-dependent anemia.[4] These patients require frequent red blood cell transfusions (four or more units over eight weeks) and have either not responded to, lost response to, or are ineligible for erythropoiesis-stimulating agents (ESAs), previously the mainstay of treatment for this specific situation.[4]

Rytelo is given as an IV infusion lasting 2 hours every 4 weeks. Studies such as merge experiment have yielded promising outcomes, with patients going without blood transfusions for extended periods of time (possibly longer than 24 weeks).[2] This results in significant increase in their quality of life, lowering reliance on healthcare interventions and related consequences.[4]

SIDE EFFECT

It is critical to recognize that Rytelo is not without adverse effects. Neutropenia (low neutrophil count) and thrombocytopenia (low platelet count) are typical problems that necessitate regular patient monitoring and possible dose changes.[6] Neutropenia weakens the immune system, making patients more susceptible to infections. Signs to watch for include fever, chills, and unusual fatigue. Thrombocytopenia increases the risk of bleeding, with easy bruising, nosebleeds, and bleeding gums being potential indicators.[7]

Table 1: Summary of Rytelo (Imetelstat) for treating transfusion-dependent anemia in MDS.

Category	Details
Drug name	Rytelo (Imetelstat)
Condition treated	Transfusion-dependent anemia in lower-risk MSD
Approval date	June 2024
FDA approval	Yes
Mechanism of action	Telomerase inhibitor
Function of telomerase	Maintains telomere length, often hyperactive in cancer cells
Impact of telomerase inhibition	Disrupts proliferation of malignant cells in the bone marrow
Clinical trial phase	Phase II and III
Effective dose	9.4 mg/kg every 21 days (Phase II)
Target patients	Adult patients with lower-risk MDS and transfusion-dependent anemia
Transfusion requirements for patients	Four or more units of red blood cells over eight weeks
Previous treatment options	Erythropoiesis-stimulating agents (ESAs)
Administration method	Intravenous infusion over two hours every four weeks
Efficacy	Extended periods (potentially >24 weeks) without need for transfusions
Quality of life improvement	Reduced transfusion dependence and healthcare interventions
Common side effects	Neutropenia (low neutrophil count), Thrombocytopenia (low platelet count)
Patient monitoring	Required for side effects, with potential dose adjustments
Ongoing research	Exploring efficacy in other hematologic malignancies

Table 1 summarizes some of the key facts about Rytelo.

CONCLUSION

Rytelo (imetelstat) marks a significant advancement in treating transfusion-dependent anemia in patients with lower-risk MDS. This first-in-class telomerase inhibitor offers a promising therapeutic option by targeting the underlying cause of disease and potentially reducing reliance on blood transfusions. Clinical trials have shown encouraging results, with patients experiencing extended transfusion-free periods and improved quality of life. However, it's important to acknowledge the potential side effects, particularly neutropenia and thrombocytopenia, which necessitate close monitoring and dose adjustments. With ongoing research exploring its application in other blood cancers, the Rytelo holds immense potential for improving the lives of patients with various hematologic malignancies.

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Ethical approval: Not required

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