

General AML

Can azacitidine be used as a pre-HSCT treatment in pediatric patients with advanced MDS?

 Cynthia Umukoro | Jan 04, 2017

Advanced Myelodysplastic Syndrome (MDS) in pediatric patients with an increased leukemia blast count in the Bone Marrow (BM) and/or in the peripheral blood is termed Refractory Cytopenia with Excess Blasts (RCEB). RCEB has a high probability of transforming into MDS-related Acute Myeloid Leukemia (AML) and the clinical outcome for RCEB in pediatric patients is poor. Hematopoietic Stem Cell Transplant (HSCT) is the current treatment used for RCEB and there is no established pre-HSCT treatment available for pediatric patients with RCEB.

Dr Nicolas Wasespe from [The Hospital for Sick Children](#), Toronto, Canada, and colleagues recently published their findings on the use of azacitidine (AZA), a hypomethylating agent, as a pre-HSCT treatment in pediatric patients with RCEB when compared to patients who did not receive AZA. The data were first [published](#) ahead of print on 19 August 2016 in [Haematologica](#).

Highlights:

- Twenty-two pediatric patients with RCEB were included in this study
- Eight patients received off-label AZA treatment
- In the AZA treated group: 50% achieved BM remission, 37% had partial BM response, 12.5% had stable and progressive disease
- Significant reduction in median BM blasts percentage at the start of AZA treatment and before HSCT; from 15% to 5%, $P = 0.02$
- Significant difference in estimated 4-year Event Free Survival (EFS) between AZA treated & control; 100% vs 45.4%, $P = 0.04$
- Estimated 4-year Overall Survival (OS) between AZA treated & control; 100% vs 69.3%, $P = 0.1$
- Adverse Events (AEs) included cytopenia ($n = 1$), infection ($n = 1$), nausea/vomiting ($n = 1$), and transient renal impairment ($n = 1$)

The authors highlighted that this study was the first to suggest that treatment with AZA prior to HSCT in pediatric patients with advanced MDS could decrease the percentage of BM blasts. They concluded that in pediatric patients with advanced MDS, AZA was well tolerated and led to a complete or partial BM response. These findings provide a platform for the use of AZA in pediatric patients with advanced MDS who do not readily have a BM stem cell donor.

Abstract

Advanced myelodysplastic syndrome harbors a high risk of progression to acute myeloid leukemia and poor prognosis. In children, there is no established treatment to prevent or delay progression to leukemia prior to hematopoietic stem cell transplantation. Azacitidine is a hypomethylating agent, which was shown to slow progression to leukemia in adults with

myelodysplastic syndrome. There is little data on the efficacy of azacitidine in children. We reviewed 22 pediatric patients with advanced myelodysplastic syndrome from a single center, diagnosed between January 2000 and December 2015. Of those, eight patients received off-label azacitidine before hematopoietic stem cell transplantation. A total of 31 cycles were administered and modification or delay occurred in four of them due to cytopenias, infection, nausea/vomiting, and transient renal impairment. Bone marrow blast percentages in azacitidine-treated patients decreased significantly from a median of 15% (range 9–31%) at the start of treatment to 5.5% (0–12%, $P=0.02$) before hematopoietic stem cell transplantation. Following azacitidine treatment, four patients (50%) achieved marrow remission, and none progressed. In contrast, three untreated patients (21.4%) had progressive disease characterized by >50% increase in blast counts or progression to leukemia. Azacitidine-treated patients had significantly increased 4-year event-free survival ($P=0.04$); predicted 4-year overall survival was 100% versus 69.3% in untreated patients ($P=0.1$). In summary, azacitidine treatment prior to hematopoietic stem cell transplantation was well tolerated in pediatric patients with advanced myelodysplastic syndrome, led to partial or complete bone marrow response in seven of eight patients (87.5%), and correlated with superior event-free survival in this cohort.

References

1. Waespe N. et al. Response to treatment with azacitidine in children with advanced Myelodysplastic Syndrome prior to hematopoietic stem cell transplantation. Haematologica. 2016 Dec; 101:1508–1515. DOI: [10.3324/haematol.2016.145821](https://doi.org/10.3324/haematol.2016.145821). Epub 2016 Aug 18.

© 2018 Scientific Education Support Ltd. This PDF is provided for personal use only. For wider or commercial use, please seek permission from secretariat@scientificeducationsupport.com and attribute the source as: <<http://www.amlglobalportal.com/medical-information/can-azacitidine-be-used-as-a-pre-hsct-treatment-in-pediatric-patients-with-advanced-mds>>