Newsletter MDS Diagnosis *2017.01*

Recent MDS News and website updates

We would like to let you know that we have applied for CME accreditation by the European Board for Accreditation in Hematology (EBAH).

Continuing Medical Education (CME) is widely accepted as a means to encourage individual practitioners to maintain and develop professional knowledge and skills keeping up-to-date with latest developments within the field.
When spending valuable time at training events and tutorials, it is essential to ensure that one is attending a high-quality educational program.

The European Board for Accreditation in Hematology (EBAH) has been established as an independent accreditation body in response to this need, as accredited events are strictly reviewed by an independent review board and are of the highest quality standards.

Events are reviewed and only the high quality educational ones are granted accreditation.

We will let you know in upcoming Newsletters about our progress!

Don’t forget to provide us with your feedback and suggestions under the About us tab on Feedback - MDS Diagnosis

New in MDS

Sci Transl Med. 2017 Jan 25;9(374). pii: eaaj2025. doi: 10.1126/scitranslmed.aaj2025.

CD99 is a therapeutic target on disease stem cells in myeloid malignancies.

Chung SS, Eng WS, Hu W, Khalaj M, Garrett-Bakelman FE, Tavakkoli M, Levine RL, Carroll M, Klimek VM, Melnick AM, Park CY

Abstract

Acute myeloid leukemia (AML) and the myelodysplastic syndromes (MDS) are initiated and sustained by self-renewing malignant stem cells; thus, eradication of AML and MDS stem cells is required for cure. We identified CD99 as a cell surface protein frequently overexpressed on AML and MDS stem cells. Expression of CD99 allows for prospective separation of leukemic stem cells (LSCs) from functionally normal hematopoietic stem cells in AML, and high CD99 expression on AML blasts enriches for functional LSCs as demonstrated by limiting dilution xenotransplant studies. Monoclonal antibodies (mAbs) targeting CD99 induce the death of AML and MDS cells in a SARC family kinase-dependent manner in the absence of immune effector cells or complement, and anti-CD99 mAbs exhibit antileukemic activity in AML xenografts. These data establish CD99 as a marker of AML and MDS stem cells, as well as a promising therapeutic target in these disorders.

New in MDS

Leuk Res. 2017 Jan 5;55:6-17. doi: 10.1016/j.leukres.2017.01.008

Increase of IRF-1 gene expression and impairment of T regulatory cells suppression activity on patients with myelodysplastic syndrome: A longitudinal one-year study.

Perazzio AS, Oliveira JS, Figueiredo VL, Chauffaille ML

Abstract

Studies have demonstrated that abnormalities in interferon regulatory factor-1 (IRF-1) expression might develop myelodysplastic syndromes (MDS). IRF-1 was described as modulator of T regulatory (Treg) cells by suppressing Foxp3 on mice. We aimed to determine the role of Treg and IRF-1 in MDS. Thirty-eight MDS patients fulfilling WHO criteria and classified according to risk scores were evaluated at time 0 (T0) and after 12 months (T12) for: Treg suppression activity in coculture with T effector (Teff) cells; IRF-1 and Foxp3 genetic expression by qRT-PCR; IL-2, -4, -6, -10, -17, TNFα and IFNγ production by Cytometric Bead Array. No differences in Foxp3 expression (T0=0.06±0.06 vs T12=0.06±0.12, p=0.5), Treg number (T0=5.62±2.84×105 vs T12=4.87±2.62×105; p=0.3) and Teff percentage (T0=16.8±9.56% vs T12=13.1±6.3%; p=0.06) were observed on T12. Low risk MDS patients showed a higher number of Treg (5.2±2.6×105) versus high risk group (2.6±1.2×105, p=0.03). Treg suppression activity was impaired on T0 and T12.Cytokine production and IRF-1 expression were increased on T12. The correlation between IRF-1 and FoxP3 was negative (r2=0.317, p=0.045) on T0. These results suggest a hyper activity of the immune system, probably secondary to Treg suppression activity impairment. This state may induce the loss of tolerance culminating in the proliferation of MDS clones.

New in MDS

J Cancer Res Clin Oncol. 2017 Jan 20. doi: 10.1007/s00432-016-2331-0

Decitabine priming prior to low-dose chemotherapy improves patient outcomes in myelodysplastic syndromes-RAEB: a retrospective analysis vs. chemotherapy alone.

Ye L, Ren Y, Zhou X, Mei C, Ma L, Ye X, Wei J, Xu W, Meng H, Qian W, Mai W, Lou Y, Xu G, Qian J, Lou Y, Luo Y, Xie L, Lin P, Hu C, Jin J, Tong H

Abstract

Purpose:
The aim of this study was to examine whether decitabine priming prior to low-dose chemotherapeutic regimens could improve outcomes in patients with myelodysplastic syndromes-refractory anemia with excess of blasts (MDS-RAEB).

Methods:
The current retrospective analysis included all MDS-RAEB patients receiving idarubicin/cytarabine (IA) or aclacinomycin/cytarabine (AA), with or without decitabine priming during a period from February 2010 to May 2015. Treatment response and toxicity were compared between patients receiving decitabine priming and those who did not. A panel of 6 MDS-related genes was examined using bone marrow specimens.

Results:
A total of 81 patients were included in the analysis: 40 received decitabine priming prior to chemotherapy (decitabine priming group). The median follow-up was 10.9 months (IQR: 6.2-21.9). The rate of overall response (OR) and complete remission (CR) was significantly higher in the decitabine priming group than in the

chemotherapy group (OR: 75.0 vs. 51.2%, p = 0.027; CR: 55.0 vs. 29.3%, p = 0.019). Overall survival (OS) did not differ significantly between the two groups (19.5 vs. 14.7 months, p = 0.082). In a subgroup analysis that included only patients at < 60 years of age, the CR rate in the decitabine priming group was significantly higher than in the chemotherapy group (65.5 vs. 31.0%, p = 0.009). Survival benefit of decitabine priming was apparent in patients at < 60 years of age (22.4 months with 95% CI of 6.7-38.1 vs. 14.7 months with 95% CI of 11.4-18.0 months in the chemotherapy group, p = 0.028), patients with intermediate and unfavorable karyotypes (22.4 months with 95% CI of 15.1-29.7 vs. 11.9 months with 95% CI of 4.0-19.8 months in the chemotherapy group, p = 0.042), and patients with mutated splicing factor genes (35.3 months with 95% CI of 21.4-49.2 vs. 17.8 months with 95% CI of 13.8-21.8 months in the chemotherapy group, p = 0.039). Grade 3-4 hematological and non-hematological toxicities were not significantly different between the two groups.

Conclusions:
Decitabine priming prior to low-dose chemotherapy could improve treatment responses in patients with MDS-RAEB.