석 사 학 위 논 문

The Real World Single Center Data of Decitabine Therapy in Patients with Myelodysplastic Syndrome

계 명 대 학 교 대 학 원
의 학 과
최 지 아
지도교수 도 영 록

2 0 2 0 년 8 월

The Real World Single Center Data of Decitabine Therapy in Patients with Myelodysplastic Syndrome

지도교수 도 영 록

이 논문을 석사학위 논문으로 제출함

2020년 8월

계 명 대 학 교 대 학 원

의 학 과

최 지 아

최지아의 석사학위 논문을 인준함

주 심 김 진 영

부 심 도 영 록

부 심 허 미 화

계 명 대 학 교 대 학 원

2 0 2 0 년 8 월

Acknowledgement

많은 분들의 도움 덕분에 이번 논문을 준비하였습니다. 바쁘신 일정 중에서도 많은 가르침을 주신 도영록 지도교수님과 심사위원을 맡아주신 김진영 교수님, 허미화 교수님께 진심으로 감사합니다.

항상 저를 격려해주고 응원해주시는 부모님과 많은 분들께도 고마운 마음을 전합니다.

2020년 8월

최 지 아

Table of Contents

List of Tables

List of Figures

1. Introduction

Myelodysplastic syndrome (MDS) is a heterogeneous group of myeloid neoplasms, which are characterized by morphologic dysplasia in hematopoietic cells and peripheral cytopenias and risk for progression to acute myeloid leukemia (AML). Patients are commonly stratified into lower-risk group and higher-risk group by grade of cytopenias, percentage of blasts, and cytogenetic risk. In lower-risk group, treatment approaches have been developed to improve cytopenias, while higher-risk group receives intensive (e.g., allogeneic hematopoietic cell transplantation [AlloSCT] or high-intensity combination chemotherapy) or non-intensive therapy (e.g., hypomethylating agents) to change the natural course of MDS and to induce hematologic remission (1).

Hypomethylating agents are nucleoside analogues inhibiting the DNA methyltransferases to activate expression of some tumor suppressor genes. Two hypomethylating agents, azacitidine and decitabine, are recommended for the treatment of MDS including chronic myelomonocytic leukemia (CMML). Hypomethylating therapy has been the standard of treatment in higher-risk MDS since phase III trials have reported that azacitidine could improve the overall survival of patients with higher risk MDS and decitabine could improve the time to AML progression or death (2, 3). For more than a decade, hypomethylating agents azacitidine and decitabine have been regarded as standard of treatment for MDS. Which of the 2 drugs has better efficacy is not clear. In 2013, two retrospective studies compared decitabine with azacitidine, the result found that there were no significant differences in overall response rates and survival advantage between these 2 drugs (4, 5). However, in patients who were elderly (≥ 65 years) or who had

poor performance status or MDS duration exceeding 1 year, azacitidine showed greater survival benefit.

Published results of hypomethylating agents-treated MDS patients in controlled trials indicate better outcomes compared with real-life data (6-8). This inconsistency may be due to differences in adherence to schedule, dose, and minimum number of cycles, as well as to the management of patients with severe comorbidities. Generally, it is obvious that the hypomethylating agents effect is transient, with responses maintained for 6 to 24 months. In our center, physicians preferred decitabine compared azacitidine because short days of treatment schedule. Our center have relatively many cases of patients who have been treated with decitabine as for single center. I report the results of decitabine therapy to patients with advanced MDS and analyze factors that affect survival of patients in real world data.

2. Materials and Methods

2.1. Patients:

This retrospective study included a total of 59 patients who were treated with decitabine for MDS between July 2009 and December 2019 in Dongsan Medical Center. Patients with CMML were excluded from this study. For study inclusion, patients needed to have an International Prognostic Scoring System (IPSS) lower risk score (IPSS low or intermediate-1) with significant cytopenia, or a higher risk score (IPSS intermediate-2 or high) (9). Patients with uncontrolled illnesses and who died within 2 weeks or who did not been followed up by 4 weeks were excluded. This study was approved from the respective Institutional Review Boards of the Keimyung University School of Medicine (No. 2020-05-067).

2.2. Treatment and evaluation:

All patients received intravenous infusion of decitabine 20 mg/m^2/day for 5 days. This regimen was repeated every 4 weeks. Decitabine treatment was continued until the patient experienced disease relapse, disease progression, unacceptable medication toxicity, or death. Bone marrow examination was performed after the initial 4-6 decitabine cycles and was repeated when either further clinical improvement or disease progression was noted. Treatment response to decitabine therapy was assessed using modified International Working Group (IWG) response criteria (10). Overall response rate included rates for complete

response (CR), partial response (PR), marrow CR (mCR), and stable disease (SD) with hematologic improvements (HI). In addition to IPSS, I also calculated scores for the revised version of IPSS (R-IPSS) (11), the revised WHO classification-based Prognostic Scoring System (R-WPSS) (12), and the prognostic index specifically developed for patients with IPSS lower-risk MDS by investigators at the MD Anderson Cancer Center, the Lower Risk Prognostic Scoring System (LR-PSS) (13). Adverse events were graded according to the Common Toxicity Criteria for Adverse Events version 4.0.

2.3. Statistical analysis:

Primary endpoints of this study were achievements of HI, overall response rate, and overall survival (OS). Survivals were calculated from the starting date of decitabine therapy to the date of death from any cause. AML progression was defined as increase of peripheral blood or bone marrow blasts over 20%. Data analyses were performed in statistical software (SPSS, version 25.0 for Windows; SPSS, Chicago, IL). For univariate and multivariate analyses, an extended Cox regression model was used according to the method of Andersen and Gill. Factors with a p value of less than 0.1 in the univariate analyses were entered in the multivariate analyses. Survival curves were drawn by using the Kaplan - Meier method, and differences in survival were tested for significance by employing the log-rank test and using censored data. P values of less than 0.05 were considered significant.

3. Results

3.1. Patients' characteristics:

The median age was 72 years (range, 45 - 89) at the time of decitabine therapy and 38 patients (64.4%) were male. The Eastern Cooperative Oncology Group (ECOG) performance status was 0-1 in 34 patients (57.6%), 2 in 19 patients (32.2%), and 3 in 6 patients (10.2%). MDS with multi-lineage dysplasia (MDS-MLD) was the most common subtype (49.2%) by the WHO classification (14). Fourteen patients had excess blast-2 (EB-2), 11 patients had excess blast-1 (EB-1), 7 patients with ringed sideroblast (RS), 4 patients with MDS with single-lineage dysplasia (MDS-SLD) and 1 patient had MDS-unclassified (MDS-U). The median values for hemoglobin, absolute neutrophil count (ANC), and platelet count at the time of decitabine therapy were 7.9 g/dL (range, 3.8-10.0), 800 /uL (range, 89-9,860), and 48 x 10^3 /uL (range, 2-475), respectively. The mean bone marrow blast percentage was 5.1% (range, 0-18.8%). The IPSS cytogenetic risk group was good in 34 (57.6%), intermediate in 12 (20.3%), and poor in 13 (22%). The IPSS risk category was intermediate-1 in 41 patients, intermediate-2 in 12 patients, and high in 6 patients. Oral antimicrobial and antifungal prophylaxis were used in 50 patients (84.7%).

3.2. Treatment response and toxicity:

Decitabine was administered for a median of 7 cycles (range, 1 - 32). Twelve patients (20.3%) were still being treated with decitabine at the

time of analysis. Overall response was achieved in 21 patients (35.6%) with the specific clinical responses being 7 CR (11.9%), 6 mCR (10.2%), 8 PR (13.6%). Median number of cycles to best hematologic response was 4 (range, 1 - 8). Among 13 patients with high-risk cytogenetics who received decitabine, 5 patients achieved hematologic improvements. Hematologic improvement (HI) with decitabine therapy was observed in 42 patients (71.2%); 1-lineage improvement in 7 (11.9%), 2-lineage improvement in 15 (25.4%) and 3-lineage improvement in 20 (33.9%). Median days to achieve HI-E, HI-P and HI-N was 84 (range, 15-305), 60 (range, 7-320), and 55 days (range, 20-289), respectively. The most common adverse events were cytopenia and cytopenia-related infection. Grade 3/4 neutropenia (76.3%), thrombocytopenia (49.1%), and anemia (35.6%) were observed frequently. In total, three episodes (5.1%) of grade 3 bleeding were observed. The grade 3 or higher non-hematologic toxicities were infrequent and reversible.

3.3. Overall survival and prognostic analysis:

With a median follow-up duration among surviving patients of 11.4 months (range, 0.6-92.3 months), 33 (55.9%) patients died and 7 (11.9%) progressed to AML. Median overall survival was 14.5 months (95% confidence interval [CI], 8.6-20.5 months). Two year overall survival rate was 18.6%. AlloSCT was performed in 6 patients (10.2%), and as of this analysis 4 patients of them were still alive. In lower risk MDS, the median overall survival was 14.5 months, while in higher risk MDS, it was 8.5 months. Univariate analyses demonstrated that female sex (hazard ratio [HR], 2.675; 95% CI, 0.937 - 7.642; $P < 0.1$), poor ECOG performance status (HR, 8.688; 95% CI, 3.035-24.87; $P < 0.05$), severe

neutropenia at decitabine treatment (HR, 1.815; 95% CI, 0.822-4.007; P < 0.1), IPSS higher risk (HR, 2.102; 95% CI, 0.933-4.734; P < 0.1), and no antibiotics prophylaxis (HR, 4.147; 95% CI, 1.239-13.880; P < 0.05) were prognostic factors for lower overall survival (Table 3). In multivariate analyses, poor ECOG performance status (HR, 7.887; 95% CI, 3.384-18.38; P < 0.05), severe neutropenia at decitabine treatment (HR, 2.007; 95% CI, 1.011-3.984; P < 0.05), and no antibiotics prophylaxis (HR, 3.174; 95% CI, 1.060-9.503; P < 0.05), were independent prognostic factors for lower overall survival.

Table 1A. Patient Characteristics

Characteristic	Number	Percent
Sex		
Male	38	64.4%
Female	21	35.6%
Age at Decitabine (median, years)	72	45-89
History of prior hematologic disease		
Yes	3	5.1%
No	56	94.9%
ECOG		
0-1	34	57.6%
2	19	32.2%
3	6	10.2%
WHO subtype		
RS	7	11.9%
MDS-U	1	1.7%
MDS-SLD	4	6.8%
MDS-MLD	22	37.3%
EB-1	11	18.6%
EB-2	14	23.7%
Hemoglobin at Decitabine (g/dL)	7.9	3.8-10.0
ANC at Decitabine (/uL)	800	89-9860
PLT at Decitabine (10^3/uL)	48	2-475
Percentage of bone marrow blasts	mean 5.1 (range, 0-18.8)	
< 2%	24	
2-10%	24	
> 10%	11	
IPSS Cytogenetics		
Good	34	57.6%
Intermediate	12	20.3%
Poor	13	22.0%
IPSS at Decitabine		
Int-1	41	69.5%
Int-2	12	20.3%
High	6	10.2%
R-IPSS at Decitabine		
low	9	15.3%
Int	20	33.9%
High	14	23.7%
Very high	16	27.1%
R-WPSS at Decitabine		
Low	4	6.8%
Int	22	37.3%
High	23	39.0%
Very high	10	16.9%

Table 1B. Patient Characteristics (Continued)

Characteristic	Number	Percent
LR-PSS at Decitabine (n=41)		
Category 1	0	0%
Category 2	9	15.3%
Category 3	32	54.2%

ECOG: Eastern Cooperative Oncology Group; RS: ringed sideroblast; MDS-U: MDS-unclassified; MDS-SLD: single-lineage dysplasia; MDS-MLD: multi-lineage dysplasia; EB-1: excess blast-1; EB-2: excess blast-2; ANC: absolute neutrophil count; PLT: platelet; IPSS: International Prognostic Scoring System; R-IPSS: revised International Prognostic Scoring System; R-WPSS: revised WHO Prognostic Scoring System; LR-PSS: Lower Risk Prognostic Scoring System.

Table 2. Decitabine Therapy Result

	Number	Percent
No. courses of Decitabine (median, months)	7	1-32
Reason for discontinuation of Decitabine		
No effect	13	22.0%
Primary progression	2	3.4%
Progression after initial response	15	25.4%
Prolonged cytopenia	9	15.3%
Excessive toxicity	3	5.1%
Proceeding to alloSCT	6	10.2%
Hematologic improvement		
Any HI	42	71.2%
HI-E	34	
HI-P	39	
HI-N	26	
Days of Decitabine for HI	**Days**	**Range**
Any HI	50	17-289
HI-E	84	15-305
HI-P	55	20-289
HI-N	60	17-320
Morphologic response	**Number**	**Percent**
CR	7	11.9%
mCR	6	10.2%
PR	8	13.6%
SD	19	32.2%
Failure	19	19.0%
Cytogenetic response		
Complete	7	11.9%
Partial	2	3.4%
Overall	17	28.8%
New clone	0	
Overall response to decitabine	21	35.6%
No. Decitabine courses for response(median, range)	4	1~8
Allogeneic stem cell transplantation	6	10.2%
Cause of Death		
Infection	23	39.0%
Hemorrhage	3	5.1%
Disease progression	6	10.2%
Others	3	5.1%
Unknown	2	3.4%

HI: Hematologic improvement; CR: complete response; mCR: marrow complete response; PR: partial response; SD: stable disease.

Table 3. Multivariate Prognostic Factor Analysis for Overall Survival

Variable	Univariate analysis			Multivariate analysis		
	HR	95% CI	P	HR	95% CI	P
Sex, male vs female	2.675	0.937-7.642	< 0.1	2.063	0.807-5.272	0.13
Age, ≥ 75	1.678	0.701-4.015	0.329			
ECOG, ≥ 2	8.688	3.035-24.870	< 0.05	7.887	3.384-18.380	< 0.05
ANC, < 800	1.815	0.822-4.007	< 0.1	2.007	1.011-3.984	< 0.05
Hb, < 7.9	0.912	0.430-1.936	0.81			
PLT, < 48,000	0.878	0.400-1.925	0.745			
BM blast, ≥ 5%	1.615	0.632-4.125	0.317			
Cytogenetic risk, Intermediate/poor vs good	1.378	0.592-3.211	0.457			
IPSS, Higher risk	2.102	0.933-4.734	< 0.1	1.998	0.947-4.217	0.069
Antibiotics prophylaxis, not use	4.147	1.239-13.880	< 0.05	3.174	1.060-9.503	< 0.05

HR: hazard ratio; CI, confidence interval: ECOG, Eastern Cooperative Oncology Group; ANC: absolute neutrophil count; Hb: hemoglobin; PLT: platelet; BM: bone marrow; IPSS: International Prognostic Scoring System.

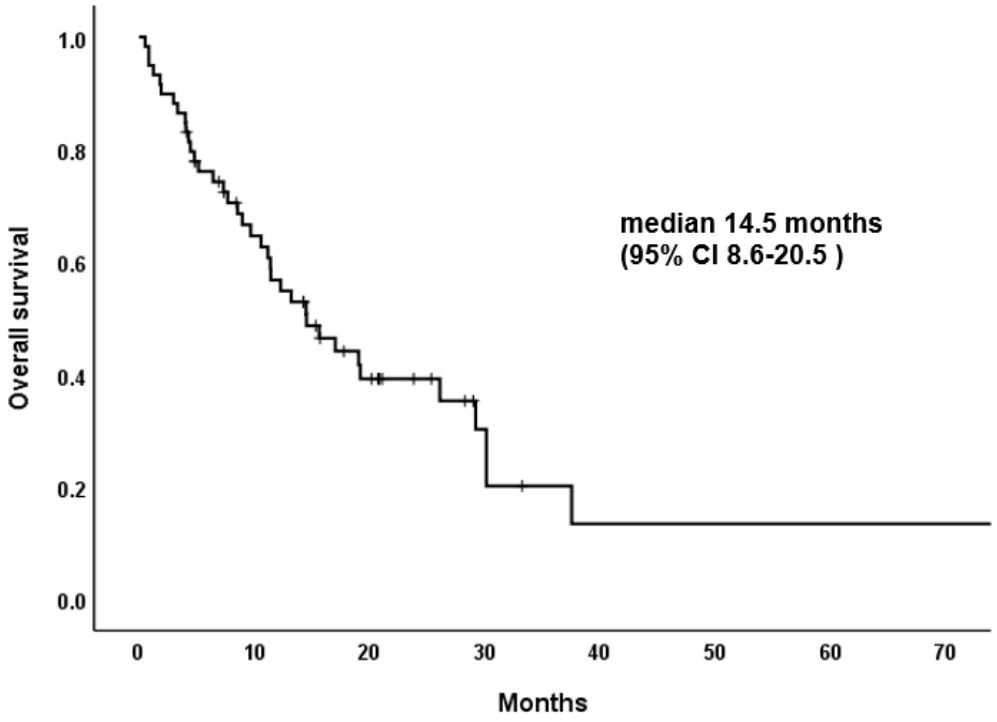

Figure 1. Overall survival curve of all patients. The median overall survival was 14.5 months (95% confidence interval 8.6-20.5).

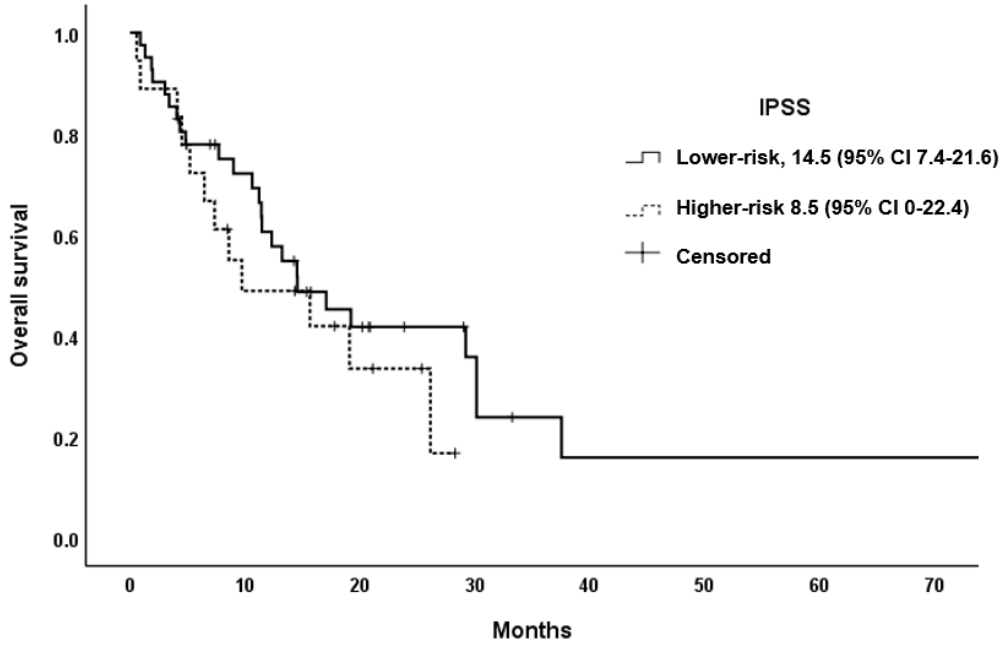

Figure 2. Overall survival curves in each risk group of International Prognostic scoring systems (IPSS). Lower-risk groups are low and intermediate-1 risk IPSS (overall survival was 14.5 months (95% confidence interval 7.4-21.6), higher-risk groups are intermediate-2 and high risk IPSS (overall survival was 8.5 months, 95% confidence interval 0-22.4).

4. Discussion

In this study, I retrospectively reviewed the response rate and survival outcome of decitabine therapy to patients with advanced MDS. Moreover, I analyzed the risk factors that affect survival outcome in MDS patients with decitabine therapy. In our study, 71.2% patients experienced any HI after decitabine therapy; 1-lineage improvement (11.9%), 2-lineage improvement (25.4%) and 3-lineage improvement (33.9%), and HI occurred during the first 2 courses of therapy in most patients. Overall response was achieved in 35.6% with the specific clinical responses; CR (11.9%), mCR (10.2%), and PR (13.6%). Despite promising HI and overall response, patients showed inferior survivals compared to the reports from prospective clinical trials (15, 16) and retrospective analysis studies (5, 17). It might reflect differences between randomized prospective clinical trials with relatively strict inclusion criteria and retrospective study with less selected, more real-life condition. However, other possible cause is that patients with older age, poor performance status and severe cytopenias at time of decitabine were included in this study. Although long-term outcomes for patients treated with decitabine showed an inferior survival results, decitaine treatment showed improving hematologic profile and response rates.

About the safety profile, patients with decitabine therapy experienced frequent grade 3 or 4 neutropenia (76.3%) and thrombocytopenia (49.1%). In this study, risk of death or AML transformation among patients with MDS was high despite decitabine treatment. Early discontinuation of decitabine was mainly due to hematologic complication (e.g., prolonged cytopenias, sepsis, and bleeding) and primary progression. Then there

are a couple of possibilities to change survival and prognostic factor according to follow up. AlloSCT should be considered when patients with high risk features do not respond to hypomethylating therapy, especially prior to AML evolution. AlloSCT is reported to be the only curative treatment of higher-risk MDS. Results from selected studies report prolonged disease free survival in about 30% to 50% of the patients (18). However, its use is mainly restricted to younger patients with an appropriate donor. In this study, transplantation was performed in 6 patients (10.2%) and 4 patients of them still alive. They were relatively younger age (range, 45-64 years old) and good performance status.

Multivariate analysis showed that the OS was affected by the poor ECOG performance status, severe neutropenia at decitabine treatment and no antibiotics prophylaxis. Decitabine and azacitidine were similarly effective in treating patients with MDS, there were some differences with regard to toxicities, response patterns, and the subgroups that showed more beneficial effects with one regimen. Decitabine is associated with a higher frequency of mCR than azacitidine, but it was also associated with a higher frequency of grade 3 or higher neutropenia (5). This suggest that frail patients were not candidate to treatment with decitabine because of its hematologic toxicities and possibility for infection.

This study has some limitations mainly due to retrospective nature of the study and limited numbers of patients. Second, I did not have genetic data of the patients. Third, many patients might receive inadequate decitabine treatment because treatment duration of a minimum of six courses is generally recommended before evaluating response, unless overt progression or unacceptable toxicity occurs.

5. Summary

In conclusion, decitabine treatment was effective in the treatment of patients with MDS. However, close observation for hematologic toxicity and proper use of antibiotics were necessary to treat older and frail MDS patients.

References

1. Montalban-Bravo G, Garcia-Manero G: Myelodysplastic syndromes: 2018 update on diagnosis, risk-stratification and management. American journal of hematology 2018; 93(1): 129-47.

2. Fenaux P, Mufti GJ, Hellstrom-Lindberg E, Santini V, Finelli C, Giagounidis A, et al: Efficacy of azacitidine compared with that of conventional care regimens in the treatment of higher-risk myelodysplastic syndromes: a randomised, open-label, phase III study. The Lancet Oncology 2009; 10(3): 223-32.

3. Kantarjian H, Issa JP, Rosenfeld CS, Bennett JM, Albitar M, DiPersio J, et al: Decitabine improves patient outcomes in myelodysplastic syndromes: results of a phase III randomized study. Cancer 2006; 106(8): 1794-803.

4. Lee YG, Kim I, Yoon SS, Park S, Cheong JW, Min YH, et al: Comparative analysis between azacitidine and decitabine for the treatment of myelodysplastic syndromes. British journal of haematology 2013; 161(3): 339-47.

5. Lee JH, Choi Y, Kim SD, Kim DY, Lee JH, Lee KH, et al: Comparison of 7-day azacitidine and 5-day decitabine for treating myelodysplastic syndrome. Annals of hematology 2013; 92(7): 889-97.

6. Dinmohamed AG, van Norden Y, van de Loosdrecht AA, Jongen-Lavrencic M: Effectiveness of azacitidine in higher-risk

myelodysplastic syndromes. Leukemia 2016; 30(8): 1795-6.

7. Bernal T, Martínez-Camblor P, Sánchez-García J, de Paz R, Luño E, Nomdedeu B, et al: Effectiveness of azacitidine in unselected high-risk myelodysplastic syndromes: results from the Spanish registry. Leukemia 2015; 29(9): 1875-81.

8. Zeidan AM, Stahl M, Hu X, Wang R, Huntington SF, Podoltsev NA, et al: Long-term survival of older patients with MDS treated with HMA therapy without subsequent stem cell transplantation. Blood 2018; 131(7): 818-21.

9. Greenberg P, Cox C, LeBeau MM, Fenaux P, Morel P, Sanz G, et al: International scoring system for evaluating prognosis in myelodysplastic syndromes. Blood 1997; 89(6): 2079-88.

10. Cheson BD, Greenberg PL, Bennett JM, Lowenberg B, Wijermans PW, Nimer SD, et al: Clinical application and proposal for modification of the International Working Group (IWG) response criteria in myelodysplasia. Blood 2006; 108(2): 419-25.

11. Greenberg PL, Tuechler H, Schanz J, Sanz G, Garcia-Manero G, Solé F, et al: Revised international prognostic scoring system for myelodysplastic syndromes. Blood 2012; 120(12): 2454-65.

12. Malcovati L, Della Porta MG, Strupp C, Ambaglio I, Kuendgen A, Nachtkamp K, et al: Impact of the degree of anemia on the outcome of patients with myelodysplastic syndrome and its integration into the WHO classification-based Prognostic Scoring System (WPSS).

Haematologica 2011; 96(10): 1433-40.

13. Garcia-Manero G, Shan J, Faderl S, Cortes J, Ravandi F, Borthakur G, et al: A prognostic score for patients with lower risk myelodysplastic syndrome. Leukemia 2008; 22(3): 538-43.

14. Arber DA, Orazi A, Hasserjian R, et al: The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood 2016; 127(20): 2391-2405. Blood 2016; 128(3): 462-3.

15. Steensma DP, Baer MR, Slack JL, Buckstein R, Godley LA, Garcia-Manero G, et al: Multicenter study of decitabine administered daily for 5 days every 4 weeks to adults with myelodysplastic syndromes: the alternative dosing for outpatient treatment (ADOPT) trial. Journal of clinical oncology: official journal of the American Society of Clinical Oncology 2009; 27(23): 3842-8.

16. Lübbert M, Suciu S, Baila L, Rüter BH, Platzbecker U, Giagounidis A, et al: Low-dose decitabine versus best supportive care in elderly patients with intermediate- or high-risk myelodysplastic syndrome (MDS) ineligible for intensive chemotherapy: final results of the randomized phase III study of the European Organisation for Research and Treatment of Cancer Leukemia Group and the German MDS Study Group. Journal of clinical oncology: official journal of the American Society of Clinical Oncology 2011; 29(15): 1987-96.

17. Lee BH, Kang KW, Jeon MJ, Yu ES, Kim DS, Choi H, et al: Comparison between 5-day decitabine and 7-day azacitidine for

lower-risk myelodysplastic syndromes with poor prognostic features: a retrospective multicentre cohort study. Scientific reports 2020; 10(1): 39.

18. Chang C, Storer BE, Scott BL, Bryant EM, Shulman HM, Flowers ME, et al: Hematopoietic cell transplantation in patients with myelodysplastic syndrome or acute myeloid leukemia arising from myelodysplastic syndrome: similar outcomes in patients with de novo disease and disease following prior therapy or antecedent hematologic disorders. Blood 2007; 110(4): 1379-87.

The Real World Single Center Data of Decitabine Therapy in Patients with Myelodysplastic Syndrome

Choi, Ji Ah

Department of Internal Medicine
Graduate School

Keimyung University

(Supervised by Professor Do, Young Rok)

(Abstract)

I analyzed the results of a decitabine therapy to patients with advanced myelodysplastic syndrome (MDS). The patients who were treated with decitabine for MDS in Keimyung University Dongsan Medical center from July 2009 to December 2019 were investigated. The study included 59 patients (64% male) with a median age at the time of decitabine therapy of 72 (24-89) years. The IPSS cytogenetic risk group was good in 34, intermediate in 12, and poor in 13. Complete response was observed in 7 patients (11.9%). With a median follow-up duration among surviving patients of 11.4 months, 33 patients died and 7 (11.9%) progressed to acute myeloid leukemia. Median overall survival was 14.5 months. In multivariate analyses, poor performance status, severe neutropenia at decitabine treatment, and no antibiotics prophylaxis, were

independent prognostic factors for lower overall survival. In conclusion, decitabine treatment was effective in the treatment of patients with MDS. However, observation for toxicity and proper antibiotics were necessary to treat older and frail MDS patients.

단일병원 골수형성이상증후군 환자에서 데시타빈 치료성적

최 지 아
계명대학교 대학원
의학과 내과학 전공
(지도교수 도 영 록)

(초록)

본 연구는 중증 골수형성이상증후군 환자에서 데시타빈 치료를 하였을 때 치료성적을 확인하고자 하였습니다. 계명대학교 동산의료원에서 2009년 7월부터 2019년 12월 기간 동안 골수형성이상증후군으로 데시타빈 치료를 받은 환자를 대상으로 하였습니다. 환자의 의무기록은 후향적으로 분석하였습니다.

총 59명의 환자(64% 남자)가 분석에 포함되었고, 데시타빈 투여 시 환자 나이의 중간값(24-89)은 72세였습니다. 세부진단은 MDS with multilineage dysplasia(MDS-MLD) 환자가 가장 많았습니다(49.2%). Decitabine 치료 시작 시점에 혈액학적 수치의 중간값은 헤모글로빈 7.9 g/dL(범위, 3.8-10.0), 호중구 800 /uL(범위, 89-9,860), 혈소판 48 x 10^3 /uL(범위, 2-475)이었습니다. 염색체 결과는 IPSS cytogenetic risk group를 기준으로 Good 37명(57.6%), Intermediate 12명(20.3%), Poor 13명(22%) 이었습니다. 데시타빈 투여횟수의 중간값은 7회였습니다(범위, 1-32).

치료를 받은 환자에서 Complete response는 7명(11.9%)에서 관찰되었고, 혈액학적 호전을 보인 환자는 42 명(71.2%)이었습니다; 1가지 계열에서 7명(11.9%), 2가지 계열에서 15명(25.4%); 3 가지 계열에서 20명(33.9%).

중간 추적기간 11.4개월(범위, 0.6-92.3 months)동안 33명이 사망하였고 7명이 AML로의 질병의 진행을 보였습니다. 전체 환자의 중간 생존기간은 14.5개월(95% confidence interval [CI], 8.6-20.5 months)이었습니다. 다변량 분석을 통해 불량한 수행상태, 데시타빈 투여시 중증 호중구감소증, 예방적 항생제의 미사용이 불량한 생존의 독립적인 예후인자 임을 확인하였습니다. 결과적으로 데시타빈 치료는 MDS환자에서 효과적이나, 전신상태가 불량한 고령의 환자에서는 혈액학적 독성에 대한 주의와 적절한 항생제의 사용이 필요합니다.