To the editor:

The revised IPSS is a powerful tool to evaluate the outcome of MDS patients treated with azacitidine: the GFM experience

The International Prognostic Scoring System (IPSS), which is based on cytogenetics, BM blast percentage, and number of cytopenias, has played a major role in prognosis assessment in myelodysplastic syndrome (MDS) since its publication in 1997. The recently published revised IPSS (IPSS-R),[1] which uses the same parameters as the original except for using 5 rather than 3 cytogenetic subgroups,[2] new cutoff values for cytopenias and BM blast percentages, and different weighing of parameters, refines the original IPSS prognostic value. However, like the original IPSS, the IPSS-R was also established in patients who had received no disease-modifying drugs. We previously reported that peripheral blast percentages, performance status, RBC transfusion requirement, and original IPSS cytogenetic risk independently predicted overall survival (OS) in 282 IPSS high-risk and intermediate 2–risk MDS patients treated with azacitidine (AZA) in a compassionate patient-named program.[3] In that series (Table 1), cytogenetics could be reclassified using IPSS-R cytogenetic groups in 265 patients: 1% very good, 37% good, 18% intermediate, 12% poor, and 32% very poor. A total of 18%, 48%, and 34% of patients had hemoglobin < 8, 8-10, and > 10 g/dL, respectively; 43%, 32%, and 25% had baseline platelets < 50, 50-100, and > 100 G/L, respectively. The absolute neutrophil count was < 0.8 G/L in 45% patients. Finally, the BM blast percentage was $\leq 2\%$, 3%-5%, 5%-10%, and $> 10\%$ in 2%, 3%, 18%, and 77% of the patients, respectively. IPSS-R risk score could be calculated in 259 patients and was found to be low in 1 patient, intermediate in 11%, high in 34%, and very high in 55%. The single patient in the low-risk group was excluded from further analysis.

Table 1. Characteristics and outcome of MDS patients treated with AZA according to IPSS-R parameters

Variable	Percentage	Response according to IWG 2006[4]	*P*	OS, mo	*P*
Hemoglobin, g/dL					
< 8	18%	44%	.948	8.1	.06
8-10	48%	42%		15.3	
> 10	34%	44%		14.1	
Absolute neutrophil count, $\times 10^9$/L					
< 0.8	45%	45%	.465	15.3	.4
> 0.8	54%	40%		12.2	
Platelet count, $\times 10^9$/L					
< 50	43%	40%	.10	20.3	.0001
50-100	32%	42%		15.1	
> 100	25%	50%		9.7	
BM blasts, %					
≤ 2	2%	60%	.287	16.1	.12
3-5	3%	70%		8.1	
5-10	18%	44%		15.9	
> 10	77%	41%		14.1	
Cytogenetic group					
Very good	1%		.646		.0001
Good	37%	46%		21.8	
Intermediate	18%	39%		12.3	
Poor	12%	45%		15.1	
Very poor	32%	38%		7.1	
IPSS-R classification					
Low	$< 1\%$		.463		.0001
Intermediate	11%	46%		30.7	
High	34%	47%		17.6	
Very high	55%	39%		10	

With the classic IPSS score, high-risk and intermediate 2–risk patients treated with AZA had significantly different responses (37% vs 49%, $P = .05$) and OS (median 9.4 vs 16 months, $P = .004$).

Using the IPSS-R, 46%, 47%, and 39% of patients responded (complete response, partial response, or hematologic improvement) to AZA in the intermediate-, poor-, and very-poor-risk groups, respectively ($P = .463$). Individual IPSS-R parameters, including cytogenetics ($P = .646$), hemoglobin ($P = .948$), platelets ($P = .10$), absolute neutrophil count ($P = .465$), and BM blast percentage stratified according to IPSS-R ($P = .287$) had no significant impact on response (Table 1).

According to IPSS-R cytogenetics, the median OS was 21.8, 12.3, 15.1, and 7.1 months in the good-, intermediate-, poor- and very-poor-risk groups, respectively (overall $P < 10^{-4}$). Finally, according to overall IPSS-R, the median OS was 30.7, 17.6, and 10 months in the intermediate-, high-, and very-high-risk groups, respectively ($P < 10^{-4}$; Figure 1 and Table 1).

The 55% of patients with very-high-risk IPSS-R scores could be further subdivided by our AZA scoring system[3] into 3%, 67%, and 30% low-, intermediate-, and high-risk patients with significantly different OS (median not reached at 12.7 and 5.9 months, respectively, $P < 10^{-4}$). Similarly, the 34% of patients with high-risk IPSS-R scores could be further subdivided by our AZA scoring system into 6%, 80%, and 14% low-, intermediate-, and high-risk patients, respectively, with significantly different OS (median not reached at 17.3 and 6.1 months, $P < 10^{-4}$). We conclude that the IPSS-R has strong prognostic value for survival

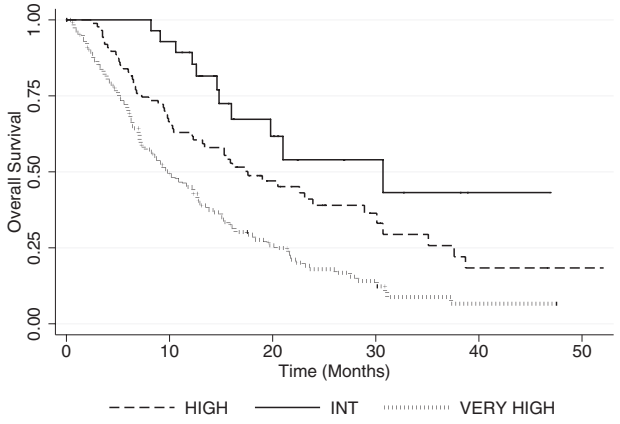

Figure 1. OS according to IPSS-R score in MDS patients treated with AZA with a median follow-up time of 41.4 months.

in MDS patients treated with AZA. Its prognostic value may be further improved by specific scoring systems established for AZA treatment such as the one we described previously.[3]

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Contribution: M.L., R.I., S.T., B.Q., F.D., O.B.R., P.T., N.V., C.R., C.D., L.L., J.D., S.V., A.S., and L.A. collected the data; M.L. and S.R. collected the cytogenic data and reviewed the analysis; M.L., P.F., and L.A. designed the study and wrote the manuscript; and L.A. performed the statistical analysis and wrote the manuscript.

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To the editor:

CD8$^+$ T cells far predominate over CD4$^+$ T cells in healthy immune response to Epstein-Barr virus infected lymphoblastoid cell lines

Infection with EBV is normally kept in check by cellular immunity,[1,2] which, if disrupted, may contribute to the important role of EBV in the pathogenesis of certain malignancies[3] and possibly chronic autoimmune diseases such as multiple sclerosis and systemic lupus erythematosus.[4] It is therefore essential that the aggregate T-cell response to EBV can be measured accurately to