Effect of Complete Remission and Responses Less Than Complete Remission on Survival in Acute Myeloid Leukemia: A Combined Eastern Cooperative Oncology Group, Southwest Oncology Group, and M. D. Anderson Cancer Center Study

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A B S T R A C T

Purpose

It is known that complete remission (CR) prolongs survival in acute myeloid leukemia (AML). In 2003, less stringent response categories were introduced, most notably CR with incomplete platelet recovery (CRp). Although the significance of CRp for survival remains unclear, reports of AML trials frequently combine CR with CRp rather than considering CR as a separate entity.

Patients and Methods

This practice led us to retrospectively examine the effect of CR on outcome in newly diagnosed AML, by using data from 6,283 patients treated on Eastern Cooperative Oncology Group (ECOG) and Southwest Oncology Group (SWOG) protocols or at M. D. Anderson Cancer Center. This effect was then contrasted with the effect of CRp in the M. D. Anderson Cancer Center cohort.

Results

At least 94% of patients receiving cytarabine-based therapy and surviving for more than 3 or 5 years achieved a CR with either initial or salvage therapy; limited data suggest the same for patients receiving initial therapies that did not contain cytarabine. Patients with CR were more likely to live beyond 3 or 5 years than patients with CRp. The likelihood of achieving a CR rather than CRp was greater for patients with AML who had better prognosis. After adjustment for covariates, the relapse-free survival of patients achieving CR was longer than that of patients achieving CRp, whereas patients with CRp survived longer than those with resistant disease.

Conclusion

Our data indicate that CR is of unique clinical significance and should be reported as separate response in trials of newly diagnosed AML. Nonetheless, our findings validate CRp as a clinically meaningful response.

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INTRODUCTION

Almost 50 years ago, Freireich et al¹ demonstrated that patients with acute myeloid leukemia (AML) who achieve complete remission (CR) live longer than those who do not and that the difference in survival is accounted for by the time spent in CR.¹ For many years, response in AML, therefore, was classified as CR or not, which reflected this ability of CR to prolong survival.¹ Requirements for CR included the presence of less than 5% abnormal blasts in the bone marrow, the absence of extramedullary AML, and recovery of neutrophil and platelet counts to greater than 1,500/ μ L (more recently changed to > 1,000/ μ L) and greater than 100,000/ μ L in the

peripheral blood.^{2,3} In 2003, an International Working Group proposed a new category of presumably beneficial response, CR with incomplete blood count recovery (CRi).³ The criteria for CRi are most explicit for its subset, CR with incomplete platelet recovery (CRp). CRp requires fulfillment of all CR criteria except that the platelet count is less than 100,000/ μ L, provided that patients are platelet transfusion independent.³ CRp was originally used in studies of relapsed AML with the CD33-targeting immunoconjugate gemtuzumab ozogamicin (GO).⁴ However, subsequently, the term has been widely adapted together with CRi. Yet, some limited evidence suggests important differences between CR and CRp. For example, patients receiving GO

monotherapy who were not treated beyond initial induction had significantly longer survival if CR rather than CRp was achieved as best response.⁵ Although the results are based on small numbers of patients, de Greef et al⁶ and Etienne et al⁷ reported similar findings in adults given conventional chemotherapy for untreated AML. Analysis of potential survival differences between CR, CRp, and lesser degrees of response would have implications on AML trial design and reporting. Herein, we report such analyses that focus on 3- and 5-year survival as well as relapse-free and overall survival in a large number of patients with newly diagnosed AML other than acute promyelocytic leukemia.

PATIENTS AND METHODS

Study Population

Our analyses included 6,283 patients: 1,642 patients treated on 11 Southwest Oncology Group (SWOG) trials from 1985 to 2002 (trials S8326, S8522, S8561, S8600, S8706, S9031, S9126, S9333, S9500, S9918, and S0112); 2,413 patients treated on seven Eastern Cooperative Oncology Group (ECOG) trials from 1976 to 1999 (trials E1479, E2476, E3483, E3489, E3993, E3997, and E4995); and 2,228 patients treated at M. D. Anderson Cancer Center from 1980 to 2004, either on one of 65 protocols or off protocol. The charts for patients on SWOG trials who were reported as alive at 3 years without documentation of CR were reviewed to evaluate response by currently established criteria.³ Institutional review boards of participating institutions approved all protocols, and patients were treated in accordance with the Declaration of Helsinki.

Statistical Analyses

Survival rates at 3 and 5 years among patients achieving CR and those achieving CRp were compared with Fisher's exact test. Disease-free and overall survival were estimated by using the Kaplan-Meier method,⁸ and equality of survival distributions assessed with the log-rank test. To account for the differences in time required to achieve response, we compared survival by eventual response (ie, CR, CRp, resistant) among patients alive at 30 days and, in subsequent sensitivity analyses, among patients alive at 60 or 90 days. Cox proportional hazards analyses were performed for relapse-free and overall survival. Methods for assessing the goodness of fit of a model have been described previously. Computations were carried out by using StatExact (Cytel Software, Cambridge, MA) and SAS (SAS Institute, Cary, NC).

RESULTS

The 3- and 5-Year Survival Times in Newly Diagnosed AML Are Strongly Associated With Achievement of CR After Initial or Subsequent Chemotherapy

Previous studies have demonstrated a precipitous decline to less than 10% of the rate of recurrence or death when 3 years have elapsed from achievement of first CR, which thus defines a convenient time to consider patients potentially cured from AML.^{9,10} Therefore, we first examined the proportion of patients who achieved a CR with initial chemotherapy among those alive at 3 and 5 years after initial chemotherapy; the latter time point was chosen to account for some of the relapses that occurred beyond the third year. For these analyses, we used data from the 6,283 patients referred to in the Patients and Methods section (Table 1). Principal differences between the cohorts included the younger age of the patients on ECOG trials as well as the use of non-cytarabine-containing regimens as initial therapy in 9% of patients on M. D. Anderson Cancer Center treatments and in 10% of patients on SWOG trials but in no patients on ECOG trials. Although all ECOG protocols used anthracyclines, a variety of anthracycline-

free regimens that included fludarabine, clofarabine, topotecan, and cyclophosphamide were used at M. D. Anderson Cancer Center, and also higher doses of cytarabine during induction were used at that center. As expected, only 19% to 24% of all patients were alive at 3 years from start of cytarabine-containing therapy, and 14% to 20% were alive at 5 years; these proportions were even smaller for patients age 60 years and older (Table 2).

Approximately 90% of patients alive at 3 or 5 years achieved a CR with initial induction therapy. This proportion was independent of study cohort, age, and cytarabine dose. Certainly, it is an underestimate, because a small number of patients surviving beyond 3 or 5 years achieved a CR only with subsequent, rather than initial, therapy. Information on such salvage CRs is limited. Nonetheless, at least eight additional cytarabine-treated patients on M. D. Anderson Cancer Center regimens achieved a CR with salvage therapy. Likewise, a review of patients on SWOG trials alive at 3 years without achievement of CR after initial chemotherapy indicated that 12 achieved CR with salvage therapy. Thus, at least 253 of 273 cytarabine-treated patients on SWOG trials and 426 of 447 cytarabine-treated patients at M. D. Anderson Cancer Center alive at 3 years achieved CR with initial or salvage therapy (94.3%; similar data not available for ECOG). Limited data suggest that the significance of CR for long-term survival may extend beyond cytarabine-containing regimens. Specifically, 14 (82.4%) of 17 patients at M. D. Anderson Cancer Center initially given non-cytarabine-containing regimens and alive at 3 years achieved CR (ie, 10 patients with initial therapy and three patients with salvage therapy that consisted of cytarabine or stem-cell transplantation [SCT]). In addition, all 10 patients on SWOG trials alive at 3 years who were initially given non-cytarabine-containing regimens achieved CR with this initial therapy.

Records at both M. D. Anderson Cancer Center and SWOG indicate that some patients with best responses less than CR may survive 3 or 5 years after initial therapy. For example, the M. D. Anderson Cancer Center database shows that up to 5% of patients (ie, 24 of 464 patients) alive at 3 years did not achieve CR with either initial or salvage therapy. Eight of these patients achieved a CRp, but the remaining patients were recorded as resistant. Similarly, our review of SWOG records revealed 20 patients alive at 3 years who did not achieve CR with initial or salvage therapy. One of these 20 achieved a CRp, four achieved a partial response,³ and 15 had resistant disease as best response recorded. Data on responses less than CR were not available for patients on ECOG trials.

3 and 5-Year Survivals Are More Likely for Patients Achieving CR Than CRp

The observation that some patients alive at 3 and 5 years achieved only CRp increased the possibility that similar proportions of patients with CR and CRp were alive at these times, and that the predominance of CR merely reflected the larger number of CRs. Table 3 examines this possibility, with data limited to M. D. Anderson Cancer Center, because CRp responses were not routinely recorded by ECOG and SWOG. Patients achieving CR were more likely to be alive at 3, and particularly at 5, years than patients achieving CRp (relative risk for 5-year survival, 3.0; 95% CI, 1.0 to 9.0; $P < .02$). Only 5% of the patients with CR and 5% of the patients with CRp received an SCT, and patients who underwent transplantation constituted 6% of the patients with CR and CRp who were alive at 3 years. These data suggest that the use of SCT did not unduly influence our finding of a

Table 1. Demographic and Clinical Characteristics of the Study Population

Parameter	Study							
	ECOG (n = 2,413)		SWOG (n = 1,642)		MDA (n = 2,228)		Total (N = 6,283)	
	No.	%	No.	%	No.	%	No.	%
Age, years*								
Median	45.8		59.4		61			
Range	14-87		15-88		14-89			
≥ 60	538	22.3	790	48.1	1,116	50.1	2,444	38.9
Sex								
Male	1,293		894		1,272		3,459	
Female	1,116		748		956		2,820	
Unknown	4		0		0		4	
Cytogenetics								
Favorable	141	15.8	NA		218	9.8		
Intermediate	457	51.1	NA		1,346	60.4		
Unfavorable	296	33.1	NA		664	29.8		
Missing/unknown	1,519	63.0						
WBC, ×10 ³ /μL*								
Median	13.7		14.9		10.1			
Range	0.2-600		0.4-415.8		0.2-433.0			
Hemoglobin, g/dL*								
Median	9.2		9.2		8.3			
Range	0.2-39.5		3.0-27.7		2.5-16.1			
Platelets, ×10 ³ /μL*								
Median	52		55		49			
Range	1-1,660		2-3,000		1-2,292			
Peripheral blasts, %*								
Median	44		34		25			
Range	1-99		0-99		0-99			
Bone marrow blasts, %*								
Median	70		68		52			
Range	1-100		0-99		0-100			
Performance status*								
0	724	30	409	24.9	292	13.1	1,425	22.7
1	1,219	50.5	786	47.9	1,295	58.1	3,300	52.5
2	330	13.7	301	18.3	444	19.9	1,075	17.1
> 2	123	5.1	116	7.1	197	8.8	436	6.9
Missing/unknown	17	0.7	30	1.8	0	0	47	0.7
Patients treated with SD cytarabine	NA		1,121	68.3	285	12.8		
Patients treated with I/HD cytarabine	NA		354	21.6	1,756	78.8		
Patients treated without cytarabine	NA		167	10.2	187	8.4		
CR with initial therapy	1,426	59.1	797	48.5	1,309	58.8	3,531	56.2
Early deaths†	474	19.6	224	13.6	282	12.7	980	15.6
Median overall survival, months	11.9		9.3		10.3			
Median relapse-free survival, months	10.2		8.8		13.3			

NOTE. Other therapies included mitoxantrone/etoposide (n = 169), gemtuzumab ozogamicin ± interleukin-11 (n = 57), single-agent daunorubicin (n = 20), cloretazine/hydroxyurea (n = 18), decitabine or azacitidine ± valproic acid (n = 16), PKC-412 (n = 14), liposomal daunorubicin/topotecan ± thalidomide (n = 10), clofarabine (n = 10), vincristine/daunorubicin/dexamethasone (n = 9), axitinib (n = 9), imatinib (n = 1), histone deacetylase inhibitor monotherapy (n = 5), troxacitabine/darubicin (n = 5), R115777 (n = 3), bexarotene/rosiglitazone (n = 3), SU5416 (n = 2), idarubicin/all-trans retinoic acid (n = 1), ABT-751 (n = 1), or PR1 vaccine (n = 1).

Abbreviations: ECOG, Eastern Cooperative Oncology Group; SWOG, Southwest Oncology Group; MDA, M. D. Anderson Cancer Center; NA, not available; SD, standard dose; I/HD, intermediate/high dose; CR, complete remission.

*At diagnosis.

†Within 28 days of therapy initiation.

clinically relevant difference between CR and CRp with regard to long-term survival.

Likelihood of Achieving CRp Rather Than CR Is Associated With Cytogenetic Risk and Results in Inferior Overall and Relapse-Free Survival

Focus on 3 and 5-year survivals ignores overall survival. Therefore, we examined the effect of response on this outcome as well as on

relapse-free survival by using the 2,228 patients from M. D. Anderson Cancer Center. Overall, 1,321 (59.3%) of these patients achieved CR, 41 patients (1.8%) achieved CRp (Table 3), and the remaining 866 patients (38.9%) achieved neither (ie, resistant). The likelihood of achieving CRp rather than CR was greater for patients considered to have worse pretreatment prognoses. Specifically, although, there was one CRp for every 32 CR on average (ie, 1,321 CR, 41 CRp), this ratio was 1:64 for patients with favorable cytogenetics (193 CR, three CRp),

Table 2. Effect of Response With Initial Induction Chemotherapy on Probability of Long-Term Survival

Parameter	Patients by Study											Total
	ECOG (n = 2,413) All	SWOG (n = 1,642)					MDA (n = 2,228)					
		Conv Ara-C	I/HD Ara-C	All Ara-C	Other*	All	Conv Ara-C	I/HD Ara-C	All Ara-C	Other*	All	
Total No. of patients	2,413	1,121	354	1,475	167	1,642	285	1,756	2,041	187	2,228	6,283
Patients alive at 3 years†	586	210	63	273	10	283	68	379	447	17	464	1,333
Three-year survivors who obtained CR	513	181	60	241	10	251	64	354	418	10	428	1,191
% of patients	88	86	95	88	100	89	94	93	94	59	92	89
Patients alive at 5 years‡	481	146	53	199	5	204	53	257	310	3	313	998
Five-year survivors who obtained CR	430	126	52	178	5	183	50	244	294	2	296	909
% of patients	89	86	98	89	100	90	94	95	95	67	95	91
Age ≥ 60 years	538	539	103	642	148	790	91	848	939	177	1,116	2,444
Patients alive at 3 years	59	53	9	62	8	70	7	93	100	17	116	245
Three-year survivors who obtained CR	49	46	9	55	8	63	7	86	93	9	102	214
% of patients	83	87	100	89	100	90	100	93	93	53	88	87
Patients alive at 5 years	35	26	6	32	3	35	5	41	46	3	49	119
Five-year survivors who obtained CR	31	22	6	28	3	31	5	39	44	2	46	108
% of patients	89	85	100	88	100	89	100	95	96	67	94	91
Age < 60 years	1,875	582	251	833	19	852	188	908	1,096	16	1,112	3,839
Patients alive at 3 years	527	157	54	211	2	213	61	286	347	1	348	1,088
Three-year survivors who obtained CR	464	135	51	186	2	188	57	268	325	1	326	978
% of patients	88	86	94	88	100	88	93	94	94	100	94	90
Patients alive at 5 years	446	120	47	167	2	169	48	216	264	0	264	879
Five-year survivors who obtained CR	399	104	46	150	2	152	45	205	250	0	250	801
% of patients	89	87	98	90	100	90	94	95	95	0	95	91

Abbreviations: ECOG, Eastern Cooperative Oncology Group; SWOG, Southwest Oncology Group; MDA, M. D. Anderson Cancer Center; Conv Ara-C, conventional dose of cytarabine (≤ 70 -200 mg/m²/d); I/HD Ara-C, intermediate/high dose of cytarabine (> 200 mg/m²/d); CR, complete remission.

*Other = non-cytarabine-containing initial chemotherapy.

†At 3 years, a total of nine patients from ECOG, eight patients from SWOG, and 62 patients from MDA were lost to follow-up.

‡At 5 years a total of 20 patients from ECOG, 11 patients from SWOG, and 120 patients from MDA were lost to follow-up.

1:35 for patients with a normal karyotype (598 CR, 17 CRp), and 1:22 for patients with chromosome 5 and/or 7 abnormalities or with three or more chromosomal abnormalities (288 CR, 13 CRp). Likewise, these ratios were 1:118 for patients without history or antecedent hematologic disorder (AHD) or prior exposure to radiation or chemotherapy (828 CR, seven CRp) and 1:15 for patients with AHD of 1 month or greater duration (425 CR, 28 CRp), respectively. As shown in Figure 1A, relapse-free survival was longer for patients who obtained CR rather than CRp ($P = .001$). Similarly, overall survival was better for patients with CR than CRp ($P = .001$), whereas patients with CRp fared better than resistant patients, even when patients who died before day 30 were excluded ($P = .001$; Fig 1B). Of note, time to response was typically longer for patients whose best response was CRp rather than CR (Table 4). Therefore, to avoid giving patients with CRp a survival advantage as a result of the longer time needed

to enter CRp (ie, guarantee time), we performed additional analyses excluding patients who died before day 60 and day 90, and the findings of these were similar to the 30-day cutoff analysis; life expectancy was also longer for patients with CR than CRp when survival was dated from response date (data not shown).

Achievement of CR Rather Than CRp Is an Independent Predictor for Relapse-Free and Overall Survival

The association of CRp with worse prognosis cytogenetics and secondary AML increased the possibility that patients who achieved CR fared better simply because they had better underlying prognoses. We addressed this possibility by fitting a Cox model for relapse-free survival among 1,362 patients from M. D. Anderson Cancer Center

Table 3. Survival at 3 and 5 Years According to CR v CRp With Initial Or Salvage Therapy: 2,228 Patients From MDA With Known Outcomes at 3 and 5 Years

Best Response	Patients Overall		No. Evaluable for 3-Year Survival*	Alive at 3 Years		Dead by 3 Years		No. Evaluable for 5-Year Survival*	Alive at 5 Years		Dead by 5 Years	
	No.	%		No.	%	No.	%		No.	%	No.	%
CR	1,321	59.3	1,275	439†	34.4	836†	65.6	1,226	302‡	24.6	924‡	75.4
CRp	41	1.8	40	8†	20.0	32†	80.0	37	3‡	8.1	34‡	91.9

Abbreviations: MDA, M. D. Anderson Cancer Center; CR, complete remission; CRp, complete remission with incomplete platelet recovery.

*Excluded from analysis were patients who were alive with a follow-up of less than 3 or 5 years, respectively.

† $P = .0628$; relative risk, 1.722; 95% CI, 0.922 to 3.215.

‡ $P = .0185$; relative risk, 3.038; 95% CI, 1.022 to 9.031.

Fig 1. Kaplan-Meier survival analyses. (A) Probability of relapse-free survival of patients who eventually achieved either complete remission (CR) or CR with incomplete platelet recovery (CRp). (B) Probability of survival of patients who eventually achieved either CR, CRp, or neither CR nor CRp (ie, resistant) and who were alive on day 30 after initial induction chemotherapy for untreated acute myeloid leukemia.

who entered either CR ($n = 1,321$) or CRp ($n = 41$). Relapse corresponded to loss of CR or CRp unrelated to recovery of blood counts after administration of postremission therapy. We also fit a Cox model examining overall survival among the patients from M. D. Anderson Cancer Center who survived at least 30 days after initiation of therapy. Covariates included age at diagnosis, cytogenetics, prior chemotherapy, AHD, poor performance status, response (ie, CR, CRp) for

Table 4. Time to Response

Response	No. of Patients	Days to Response (percentiles)			
		25th	50th	75th	90th
CR	1,321	26	30	39	56
CRp	41	28	44	57	82

NOTE. Time to response was generally shorter for patients achieving CR than for those achieving CRp. For example, whereas $> 90\%$ of patients who entered CR had done so within 57 days, only 75% of CRp events had occurred by then. Abbreviations: CR, complete remission; CRp, complete remission with incomplete platelet recovery.

Table 5. Multivariate Cox Models for Relapse-Free and Overall Survival

Covariate	Hazard Ratio	95% CI	P
Relapse-free survival			
CR v CRp	0.695	0.506 to 0.954	.0243
Age	1.014	1.011 to 1.018	< .001
Prior chemotherapy	1.082	0.897 to 1.305	.4115
Antecedent hematologic disorder	1.154	1.021 to 1.304	.0219
Performance status 3 or 4	1.361	1.064 to 1.739	.0140
Favorable cytogenetics*	0.648	0.552 to 0.761	< .001
Unfavorable cytogenetics†	1.785	1.561 to 2.042	< .001
Overall survival			
CR v CRp	0.763	0.542 to 1.074	.1212
Resistant v CRp	2.309	1.636 to 3.258	< .001
Age	1.018	1.015 to 1.022	< .001
Prior chemotherapy	1.342	1.148 to 1.570	< .001
Antecedent hematologic disorder	1.006	0.903 to 1.122	.9075
Performance status 3 or 4	1.938	1.562 to 2.404	< .001
Favorable cytogenetics*	0.600	0.491 to 0.734	< .001
Unfavorable cytogenetics†	1.615	1.444 to 1.807	< .001

Abbreviations: CR, complete remission; CRp, complete remission with incomplete platelet recovery.

*Inv(16) or t(8;21).

†-5/-7, or three or more cytogenetic abnormalities.

relapse-free survival analysis, and the same covariates together with response (ie, CR, CRp, resistant) for overall survival analysis. The relapse-free survival analysis indicated that CR was independently associated with a longer relapse-free survival relative to CRp (hazard ratio [HR], 0.695; 95% CI, 0.506 to 0.954; $P = .02$; Table 5). CR was associated with a longer overall survival than CRp (HR, 0.763; 95% CI, 0.542 to 1.074; $P = .12$), whereas resistant disease was associated with higher mortality than CRp (HR, 2.309; 95% CI, 1.636 to 3.258; $P < .001$; Table 5).

DISCUSSION

Our data indicate that at least 90% to 95% of patients alive 3 or 5 years after receiving cytarabine-containing therapy achieved a CR with either initial or salvage therapy (Table 2). These findings were similar among ECOG, SWOG, and M. D. Anderson Cancer Center despite the use of different induction regimens. As noted in the Results, our inability to document that all such long-term survivors achieved CR could reflect the failure of each database to capture some patients who achieve CR later in the course of the disease. Nevertheless, both SWOG and M. D. Anderson Cancer Center data indicate that a small proportion of patients alive at 3 or 5 years will have only achieved a response less than CR, such as CRp. Although there were many more CR than CRp responses, the frequency of 3- and 5-year survivals were greater with CR than CRp (Table 3). CRp was relatively more common than CR in patients with poor prognostic features, including longer time to response,¹¹ which possibly accounts for some of the differences in outcome between these groups. However, our multivariate analyses suggest that, at least with respect to relapse-free survival, and likely also with respect to overall survival, patients with CR fare better than those with CRp. The observation that the HR for relapse-free survival, but not for overall survival, reached the statistical significance level of .05 for the comparison of CR versus CRp points to the possibility that a few patients with relapsed disease can undergo salvage treatment with

additional therapy. Still, our data indicate that achievement of CR has unique clinical significance for outcome of AML therapy and should be explicitly distinguished from other responses. Nonetheless, CRp is independently superior to resistant disease, even after exclusion of early deaths among the latter, which thus validates CRp as a clinically meaningful response.

A decrease in marrow blasts and/or an increase in blood counts may denote that a drug is active and worthy of additional investigation, even if this response does not meet the stringent criteria for CR. The need to recognize such biologic activity led the International Working Group to introduce response categories less than CR, most explicitly CRp.³ This group also recognized that achievement of CRp might be of value for patients who are candidates for subsequent SCT. However, unlike with CR, the linkage between responses less than CR and survival has, until now, remained unclear, particularly in patients who did not undergo SCT, such as the patients at M. D. Anderson Cancer Center who were analyzed here.

The major limitation of our study is the lack of complete data identifying responses less than CR. This was partially remedied for the SWOG database by a manual chart review. A second limitation is that the vast majority of our patients received cytarabine-containing therapy, which increased the possibility that other therapies, including targeted therapeutics, might convert AML into a chronic disease without need for CR. However, the M. D. Anderson Cancer Center and SWOG data, although sparse (ie, 24 of 27 patients given non-cytarabine-containing therapies as initial treatment and alive at 3 years achieved CR with either initial or salvage therapy), argue against this possibility. As a third limitation, it could be argued that our analyses are confounded because response to initial therapy (ie, CR v response less than CR) likely influences the choice and intensity of subsequent therapy. Thus, the longer survival of patients with CR may merely reflect more effective postinduction therapy. The postinduction therapy most likely to affect outcome is SCT. However, only a small minority (5%) of patients at M. D. Anderson Cancer Center underwent SCT in CR1 or CRp1, which suggests that this consolidation therapy did not significantly influence our analysis.

In summary, our data suggest that CR is a unique response in newly diagnosed AML, because it is independently associated with longer relapse-free survival; better 3- and 5-year survivals; and, most likely, im-

proved overall survival. Nevertheless, our data also suggest that CRp confers longer survival than inability to enter either CR or CRp, an observation analogous to that made with hematologic improvement after targeted therapy for AML or high-risk myelodysplastic syndrome.¹² We hope that our analyses encourage continued critical evaluation of the effect on survival of newer response categories in AML.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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