Long Term Survival and Clinical Complete Responses of Various Prognostic Subgroups in 103 Relapsed/Refractory Acute Myeloid Leukemia (r/r AML) Patients Treated with Guadecitabine (SGI-110) in Phase 2 Studies

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On behalf of Study SGI-110-01 Investigators Team

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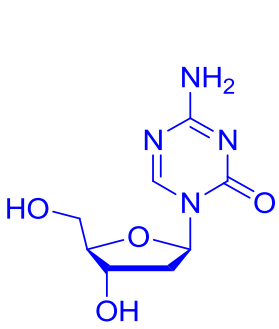
Guadecitabine in R/R AML
Guadecitabine: A Next Generation HMA

- **Decitabine (HMA agent) is FDA approved for MDS, and EU approved for treatment of elderly AML**
- **Rapid elimination by CDA shortens *in vivo* exposure limiting cell-cycle dependent efficacy (S-phase specific)**
- **SGI-110 increases *in vivo* exposure/potential efficacy of decitabine by incorporation into decitabine - deoxyguanosine dinucleotide**



Decitabine

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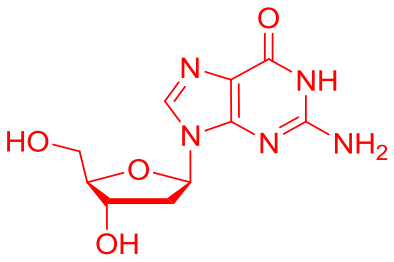
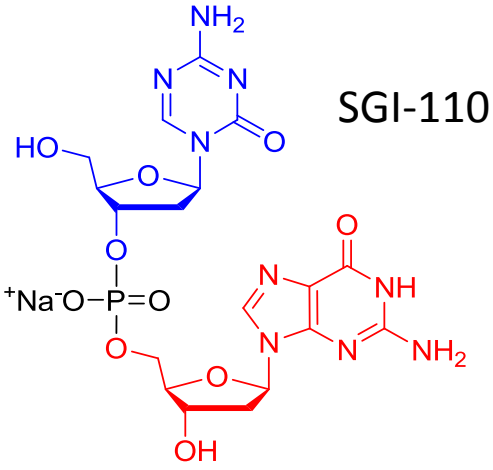
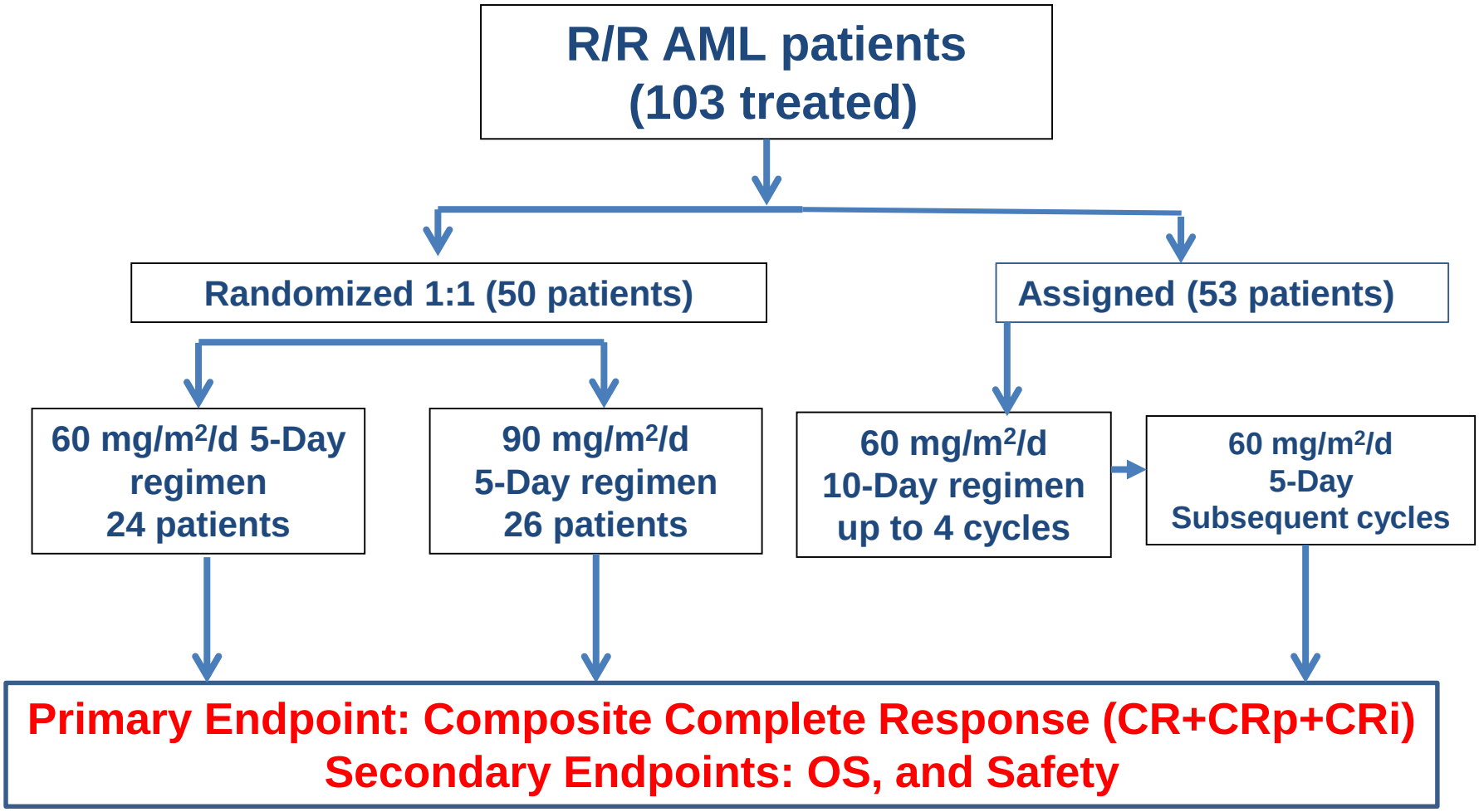


Deoxyguanosine



SGI-110

Guadecitabine in R/R AML
Study Design and Disposition



Guadecitabine in R/R AML
Patients' Characteristics

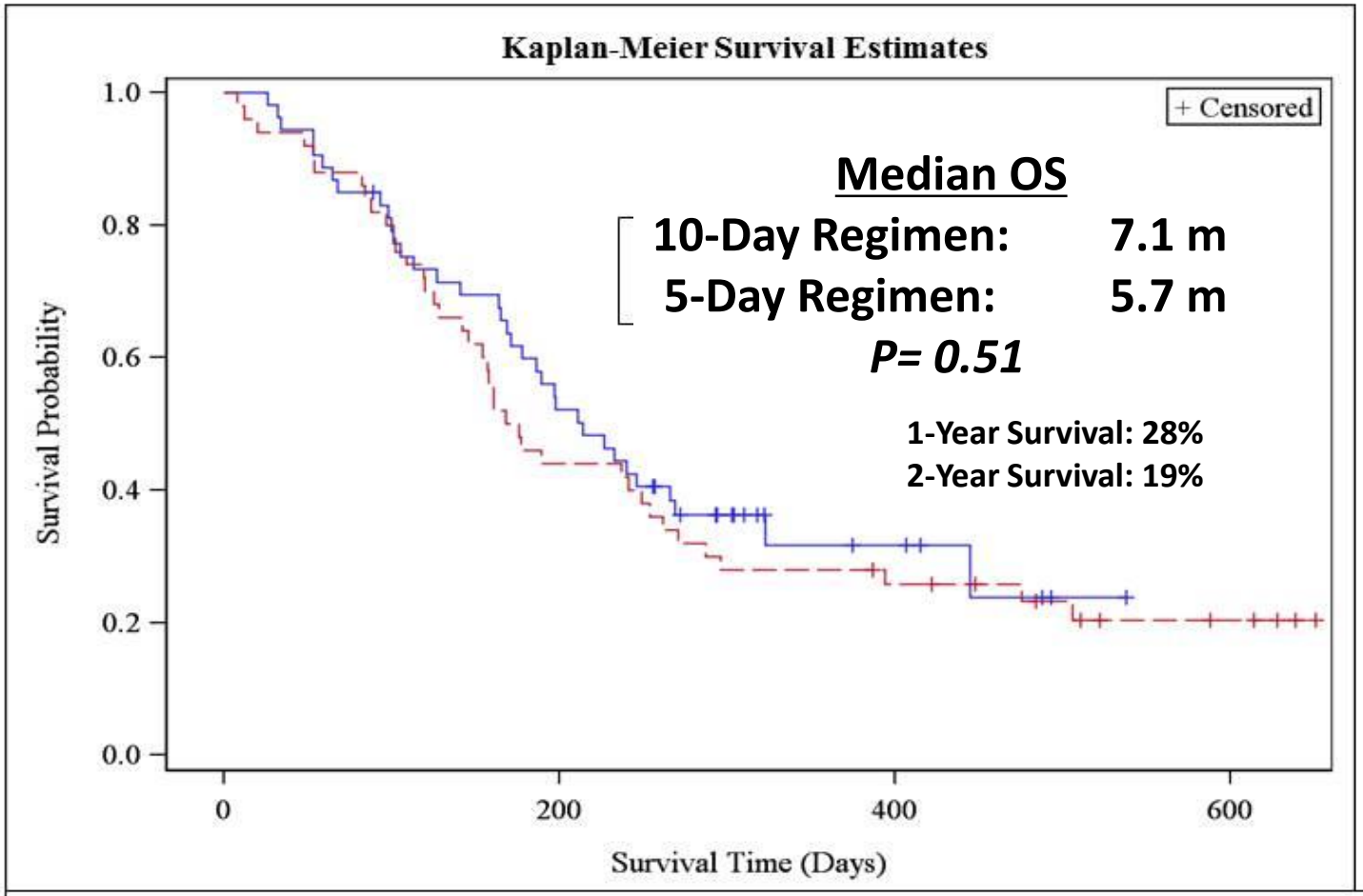
Characteristic		N (%)
Age (y) Median [range] (>60 years)		60 [22-82] 52 (50%)
ECOG PS 0-1		89 (86%)
Cytogenetics, Poor Intermediate Not done	 Diploid Miscellaneous	 42 (41%) 21 (20%) 31 (30%) 9(9%)
Prior HCT		19 (18%)
Prior Courses of Rx	Unknown 1 2 3-5 >5	3[3%) 27(26%) 31(30%) 39(38%) 2(2%)
Response to First Induction	 CR Primary Refractory	 55 (53%) 48 (47%)

Guadecitabine in R/R AML Responses

Response Category	Response rate (N=50) 5 Day (60 and 90 mg/m^2) N (%)	Response rate (N=53) 10 Day (60 mg/m^2) N (%)	*P* value
CR	3 (6%)	10 (19%)	0.074
CRp	1 (2%)	4 (7%)	
CRi	4 (8%)	2 (4%)	
CRc (CR + CRp + CRi)	8 (16%) (95% CI: 7, 29%)	16 (30%) (95% CI:18, 44%)	0.106

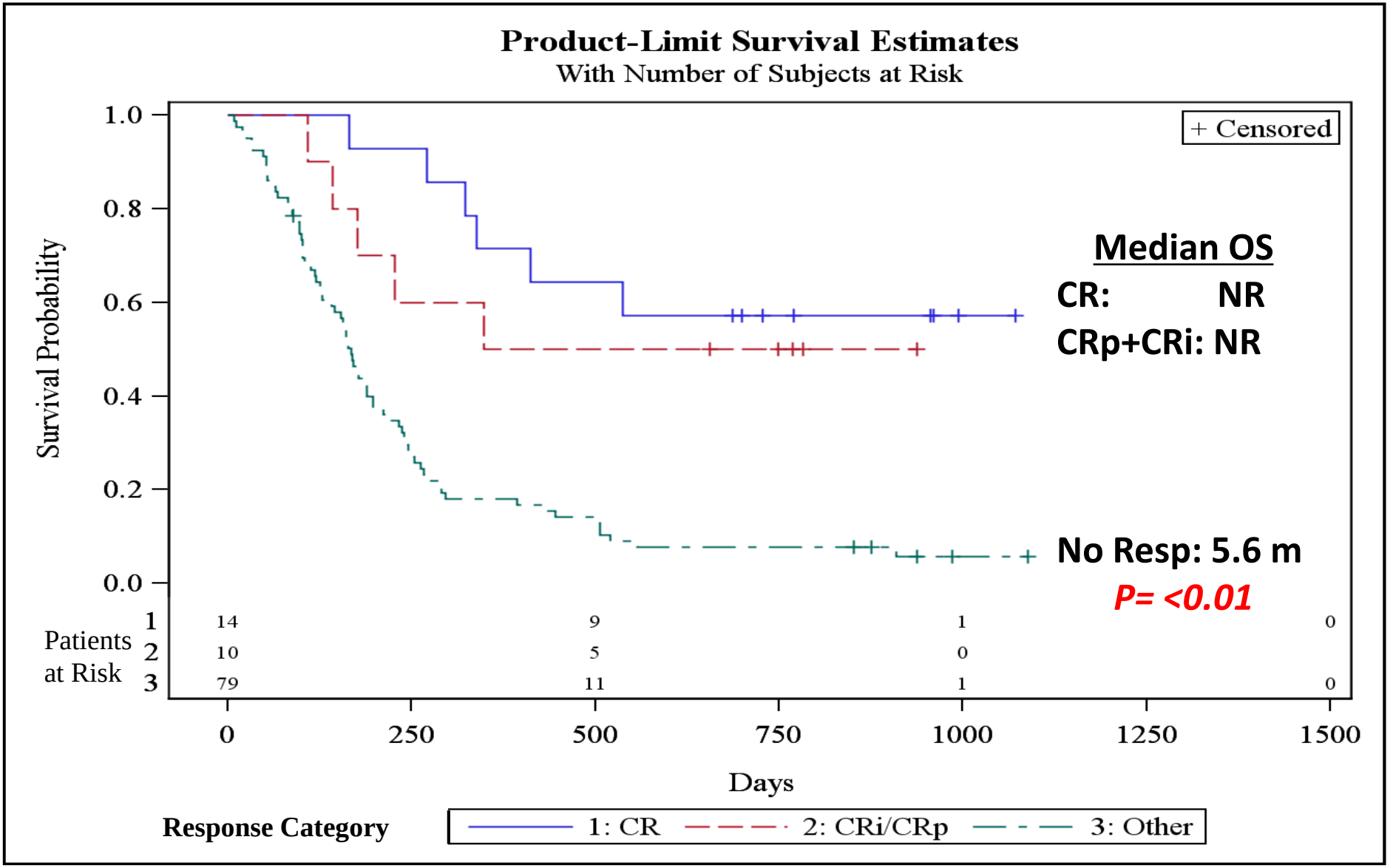
Trend of higher CR and CRc with the 10-Day regimen

Guadecitabine in R/R AML
Overall Survival by Regimen (n=103)

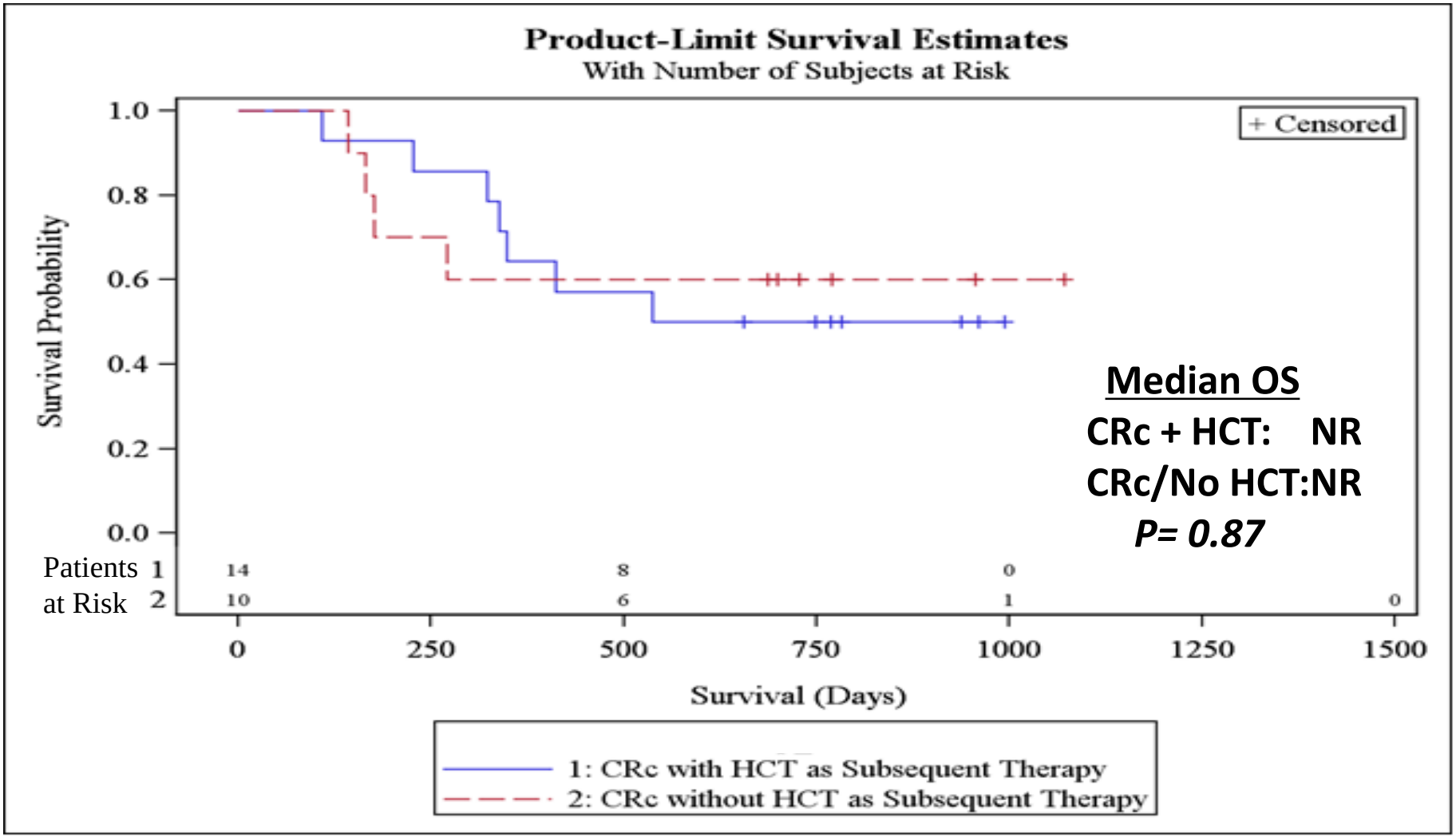


Slightly longer median OS for 10-Day regimen but not significant

Guadecitabine in R/R AML
Overall Survival by Response (n=103)



Guadecitabine in R/R AML
OS of Patients in CRc (n=24) by Subsequent HCT



Patients in CRc had good OS regardless of subsequent HCT

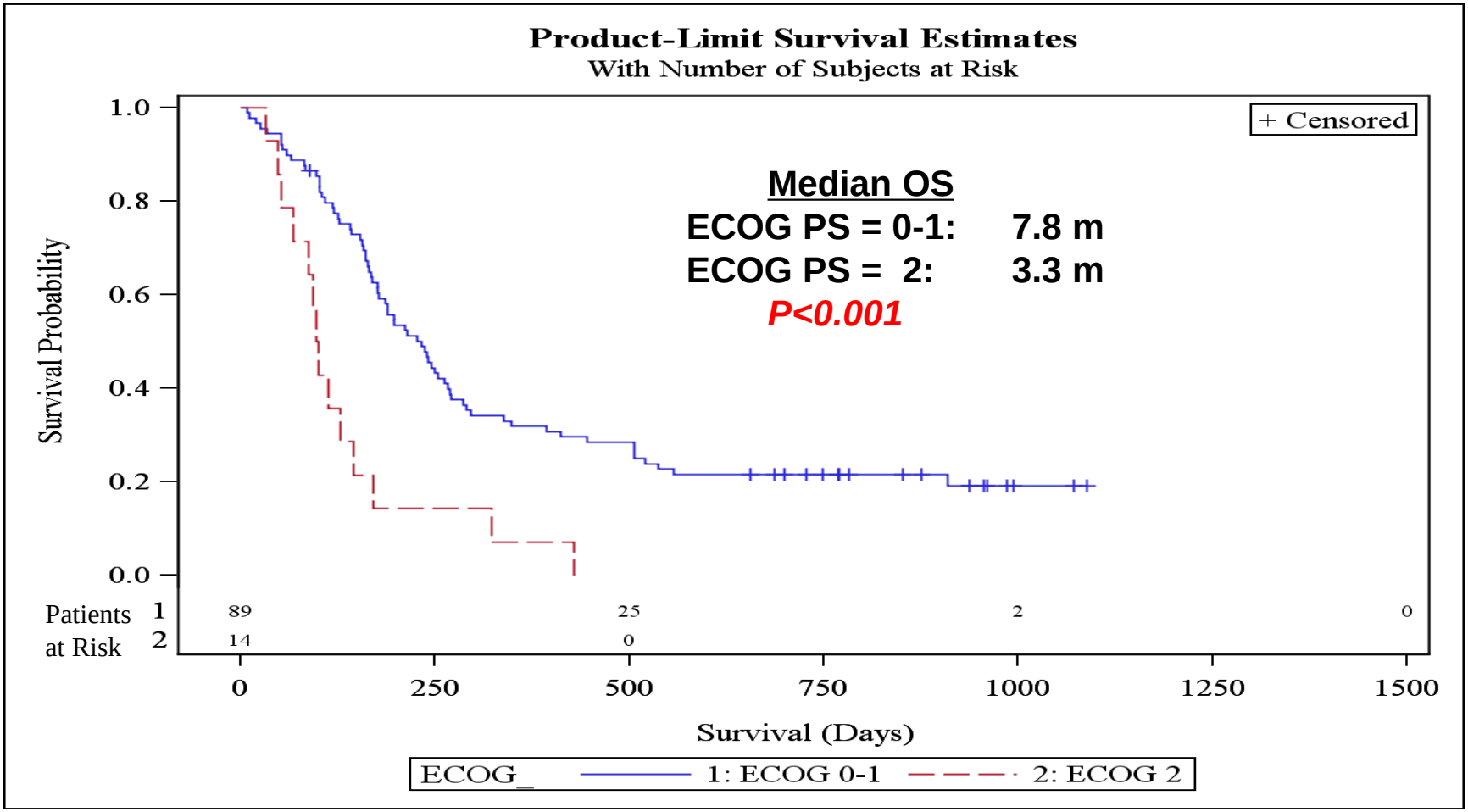
Guadecitabine in R/R AML
Clinical Response (CRc) Subgroup Analysis

Parameter	Category	N (%)	CRc N (%)	P value
Age	<65 ≥65	63 (61%) 40 (39%)	12 (19%) 12 (30%)	NS
ECOG PS	0-1 2	89 (86%) 14 (14%)	23 (26%) 1 (7%)	*P <0.001*
Cytogenetics	Adverse Diploid Others	42 (41%) 21(20%) 40 (39%)	8 (19%) 4(19%) 12 (30%)	NS
Prior HCT	Yes No	19 (18%) 84 (82%)	5 (26%) 19 (23%	NS
Response to induction	Refractory CR	48 (47%) 55 (53%)	12(25%) 8(15%)	NS
Time from Last Therapy	< 6 months ≥ 6 months	82 (80%) 20 (19%)	18 (22%) 6 (30%)	NS

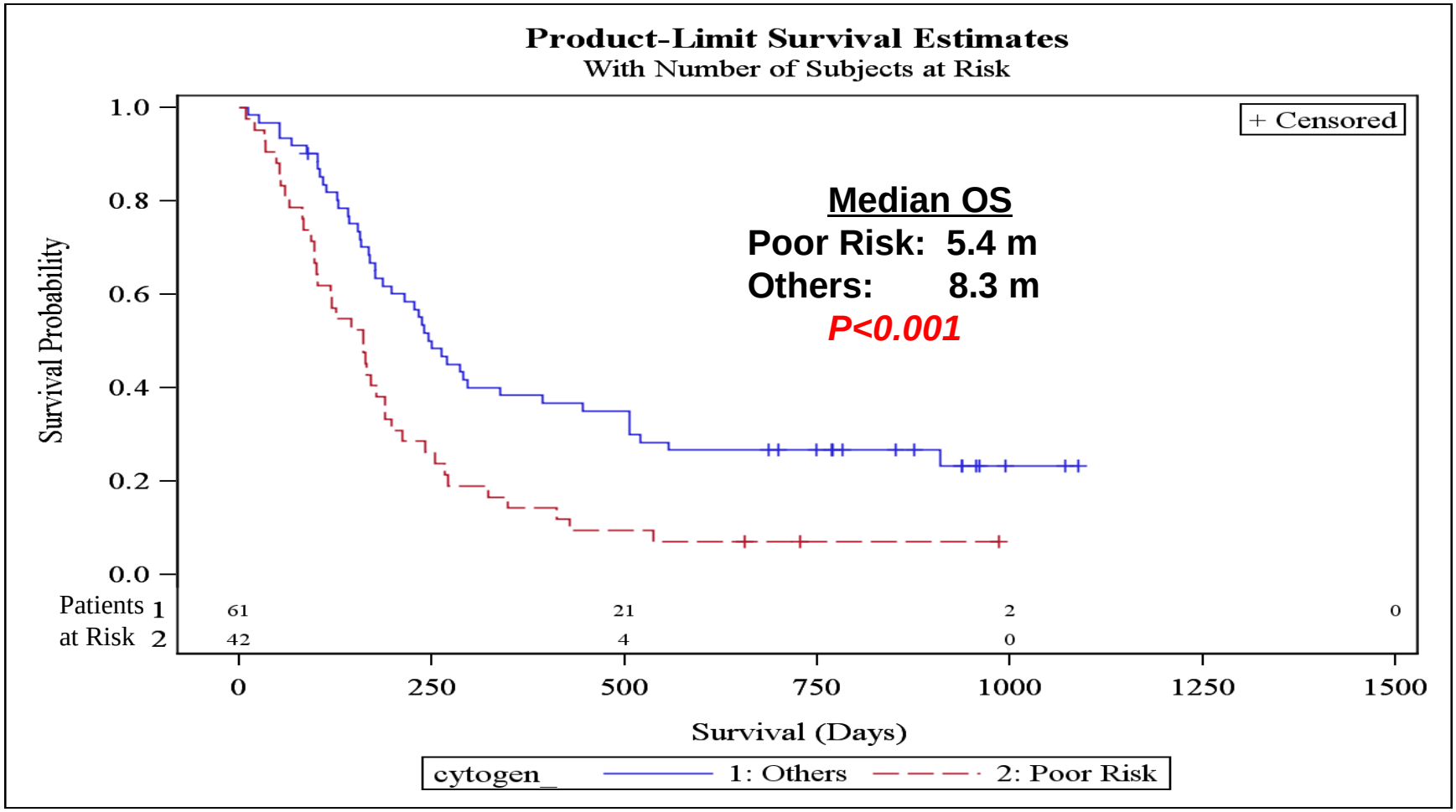
Guadecitabine in R/R AML
Overall Survival Subgroup Analysis

Subgroups		N (%)	Median OS (months)	P value
Age	< 65 years	63 (61%)	**6.6**	NS
	≥ 65 years	40 (39%)	**6.4**	
ECOG PS	0-1	89 (86%)	**7.8**	***P <0.001***
	2	14 (14%)	**3.3**	
Cytogenetics	Poor Risk	42 (41%)	**5.4**	
	Others	61 (59%)	**8.3**	***P <0.001***
Prior HCT	Yes	19 (18%)	**6.6**	NS
	No	84 (82%)	**6.3**	
Response to Initial Induction				
Refractory		48(47%)	**6.8**	NS
CR		55(53%)	**6.3**	
Time from Last Therapy				
< 6 months		82 (80%)	**5.9**	***P =0.015***
≥ 6 months		20 (19%)	**9.7**	

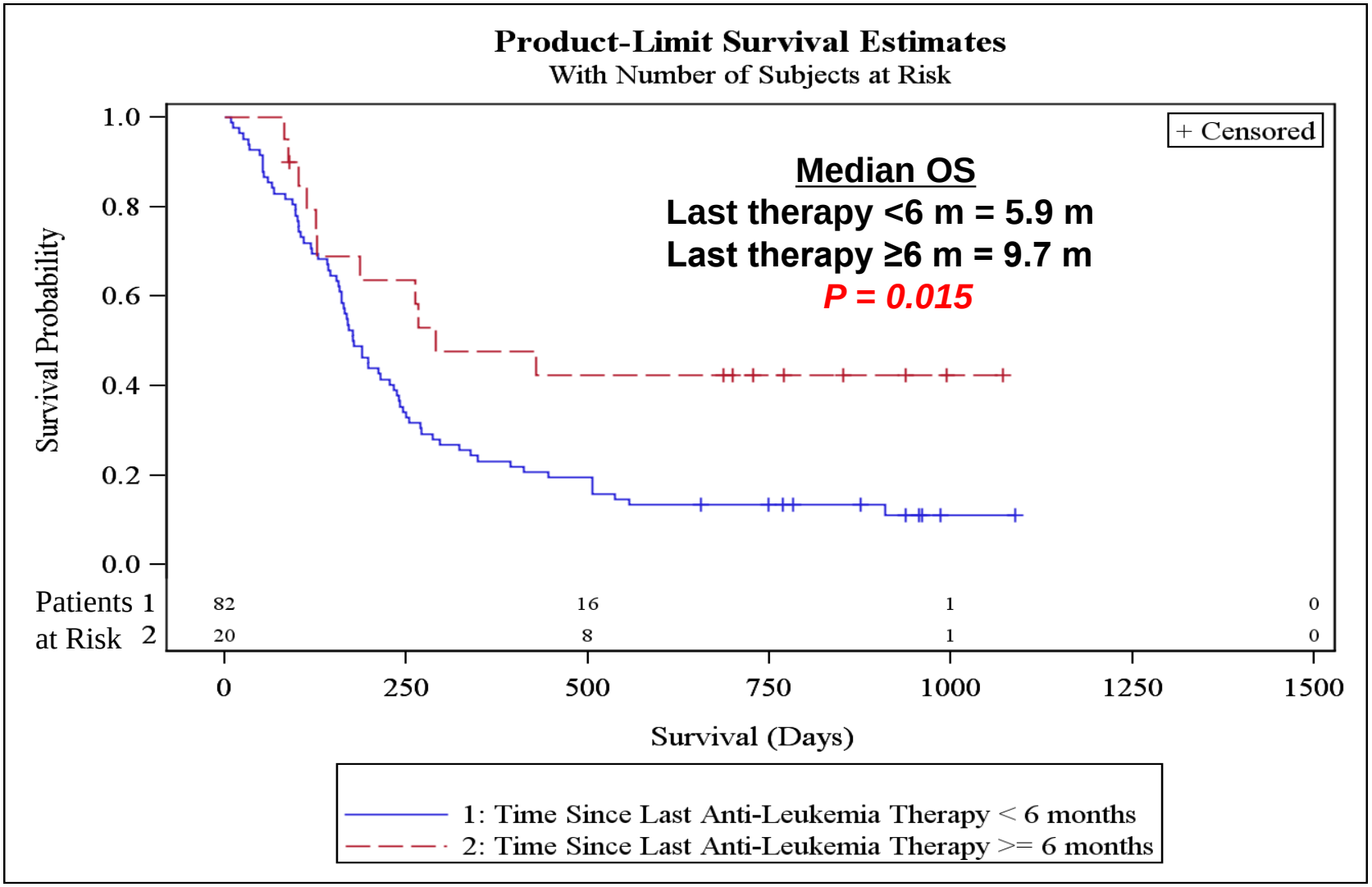
Guadecitabine in R/R AML
Survival by Performance Status



Guadecitabine in R/R AML
Survival by Cytogenetics Risk



Guadecitabine in R/R AML
Survival by Time from Last Therapy



Guadecitabine in R/R AML
AEs Gr ≥3 Regardless of Relationship

Adverse Event	N (%)
Febrile Neutropenia	62 (60%)
Pneumonia	37 (36%)
Thrombocytopenia	37 (36%)
Anemia	32 (31%)
Neutropenia	20 (19%)
Sepsis	16 (16%)

All Cause Early Mortality

30-Day	**4 (3.9%)**
60-Day	12 (11.7%)

Guadecitabine in R/R AML
Conclusions

- Guadecitabine has clinical activity in patients with r/r AML who relapsed or were refractory to prior induction Rx
- Trend of higher CRc and OS with initial 10-day regimen of guadecitabine
- Patients with CRc had significantly longer survival regardless of subsequent HCT
- Subgroup Results:
  - CRc was significantly lower in patients with ECOG PS 2, no other features impacted CRc rates
  - OS was significantly shorter in patients with ECOG PS 2; Adverse cytogenetics; and Time from last therapy < 6 months
  - Age, prior HCT, or prior response to induction did not impact OS
- Guadecitabine had acceptable safety with low early mortality
- Future Directions: Phase 3 Trial in r/r AML is being initiated