

# Comparison of the Efficacy and Safety of 5-day and 10-day schedules of SGI-110, a novel subcutaneous (SC) hypomethylating agent (HMA), in the treatment of relapsed/refractory Acute Myeloid Leukemia (r/r AML)

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## On Behalf of the SGI-110 Investigators

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# Disclosures

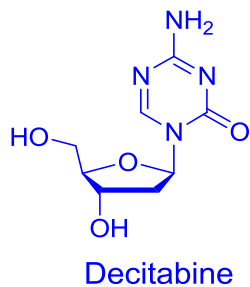
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# Relapsed/Refractory AML 2014

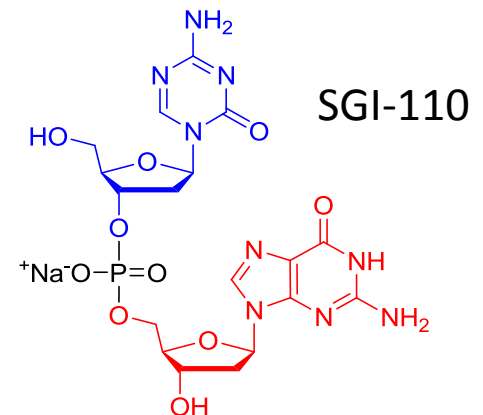
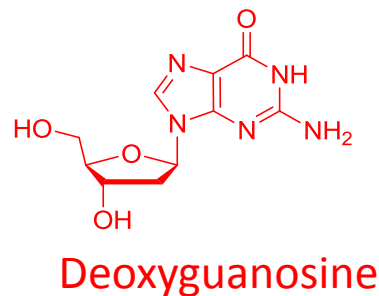
- Most AML patients relapse and die of disease
- Cytarabine-based intensive salvage regimens produce CR in selected pts, mostly younger and with > 1 year CR1
- Duration of CR2+ is only months unless allotransplant
- Recent international randomized trial of elacytarabine vs. investigator's choice 7 control arms: RR  $\approx$ 20%, OS  $\approx$ 3 months, lowest 30-day mortality with HMA (Roboz et al, J Clin Oncol 2014)
- Weill Cornell decitabine X 10 days CR 16%, OS  $\approx$ 6 months (Ritchie et al, Leuk Lymph, 2013)

# SGI-110, A Second Generation Hypomethylating Agent

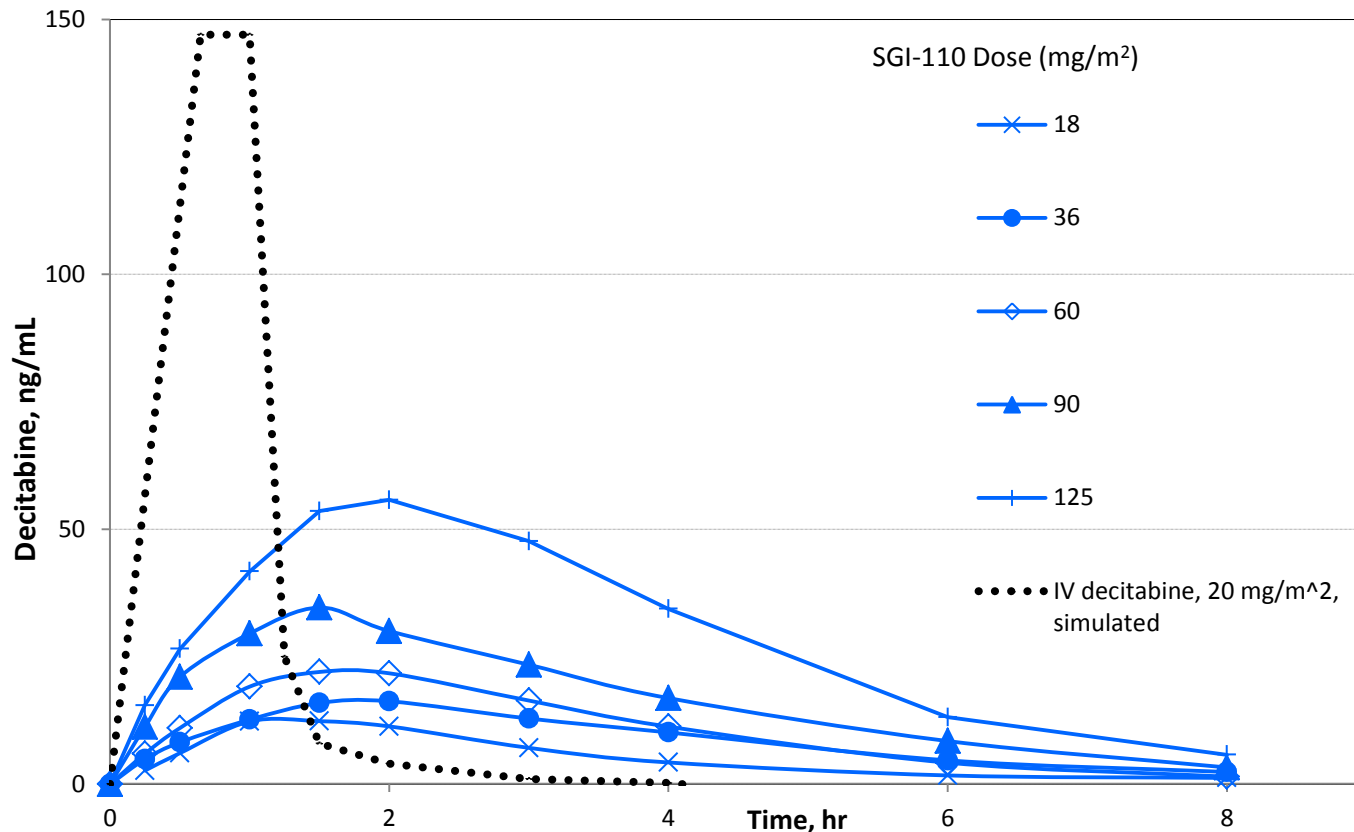
- Decitabine is rapidly eliminated by Cytidine Deaminase, limiting drug exposure time to cancer cells *in vivo*
- SGI-110 is a Dinucleotide of Decitabine and Deoxyguanosine that prolongs the *in vivo exposure* of decitabine by protecting it from deamination
- SGI-110 is given as a small volume (~1ml) SC injection



+

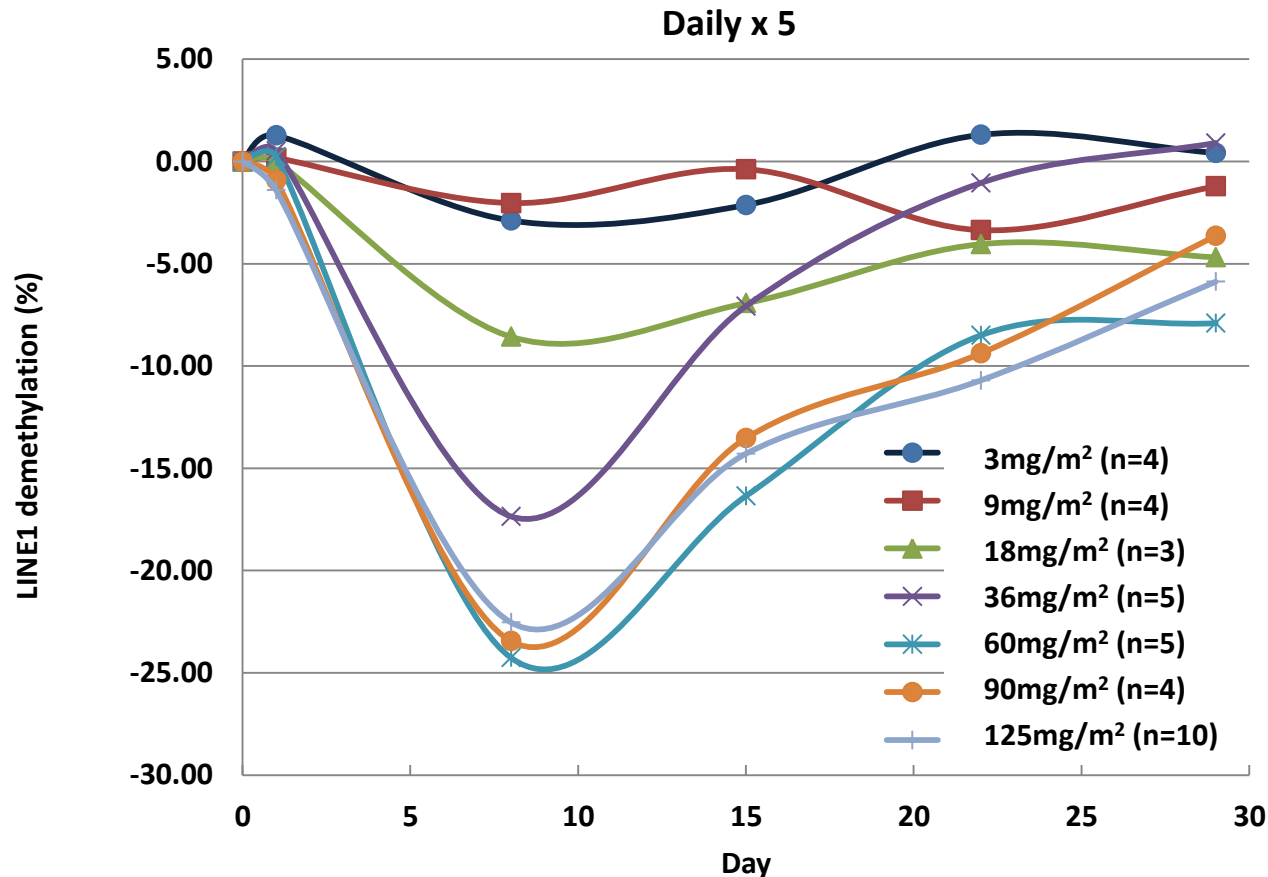


# SGI-110 SC results in prolonged Exposure Window to active metabolite decitabine



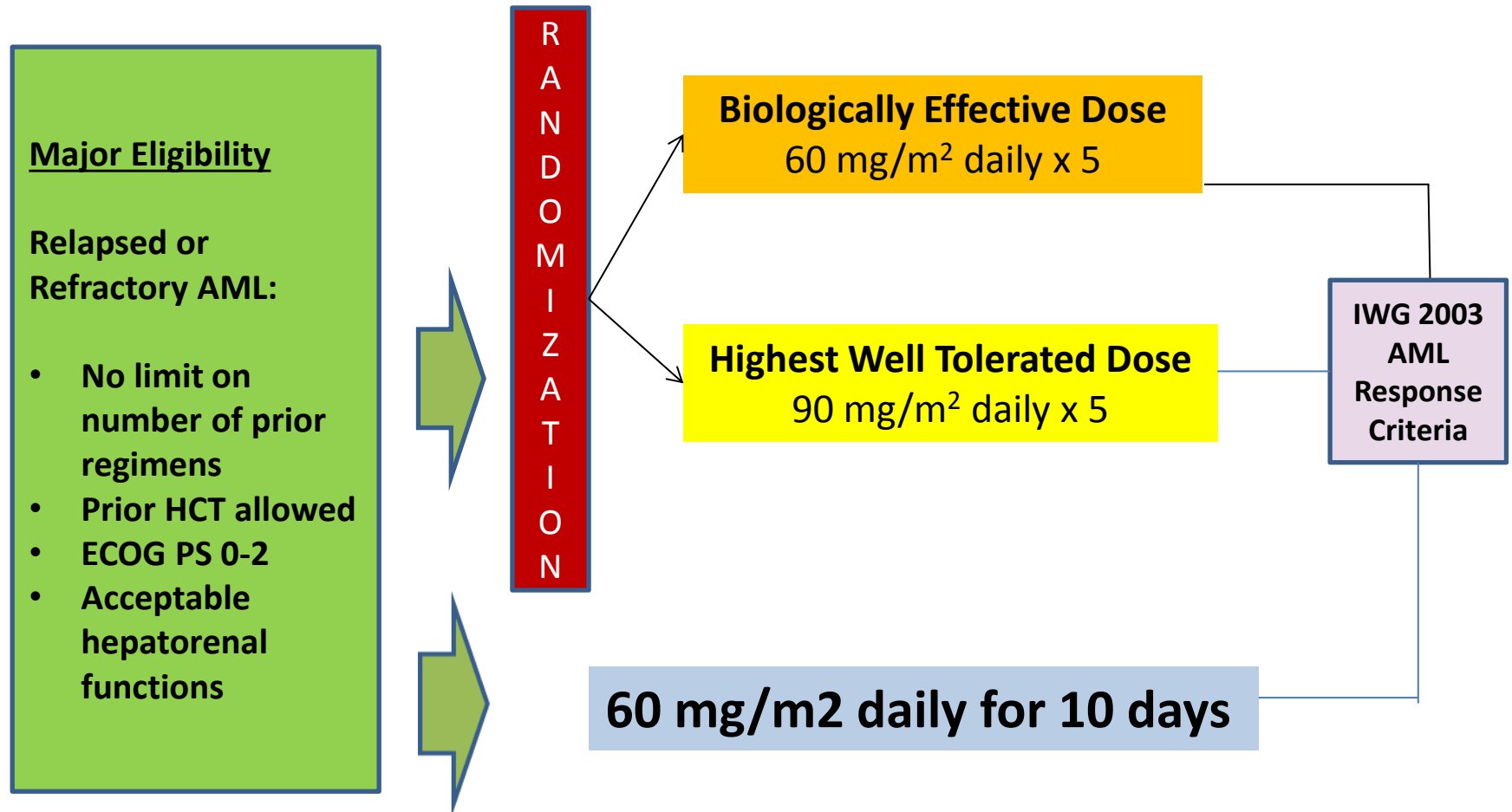
- Decitabine exposure window after SC SGI-110 is more than double (8hr+) compared to 20 mg/m<sup>2</sup> 1-hr IV infusion (simulated)
- Prolonged decitabine  $t_{1/2}$  (up to 2 hr vs 0.25-0.5 hr) due to protracted release from SGI-110
- Similar decitabine AUC achieved at much lower  $C_{max}$

# SGI-110 LINE1 DNA Demethylation in Cycle 1



- LINE-1 demethylation increased with dose in the dailyx5 regimen Q 28 days
- Maximum demethylation reached at 60 mg/m<sup>2</sup> SC dailyx5

# SGI-110 Phase 2 Study Design in r/r AML



- **Primary Endpoint: Overall composite CR rate (CRc): CR + CRp + CRi**
- **Secondary Endpoints: LINE-1 demethylation, overall survival, and Safety**

# SGI-110 10-Day regimen in r/r AML

Minimum 6 cycles

Up to 4 Cycles

Continue Till Progression or  
Unacceptable Toxicity

**10-Day Cycle (28 days)**

← SGI-110 → No treatment

D1-5

D8-12

D13-28

**5-Day Cycle (28 days)**

SGI-110

No treatment

D1-5

D6-28

**SGI-110 was given as 60 mg/m<sup>2</sup>/d SC days 1-5 and 8-12 Q28 days for up to 4 cycles followed by treatment on days 1-5 Q28 days for a total of at least 6 cycles**



# r/r AML 5-day and 10-day regimens

## Patients Characteristics

Patient Characteristics	5 Day (60 or 90 mg/m <sup>2</sup> /d) (n=50)	10 Day (60 mg/m <sup>2</sup> /d) (n=53)
Median Age, (range)	62 (22 – 81)	57 (29-82)
Gender, M (%)	35 (70%)	27 (51%)
ECOG PS (%)		
0	6 (12%)	9 (17%)
1	39 (78%)	35 (66%)
2	5 (10%)	9 (17%)
Median BM Blast % (range)	35 (2 – 94)	32 (4-95)
Median WBC (10 <sup>9</sup> /L) (range)	1.7 (0.3 – 18.7)	2.1 (0.2-75.5)
Secondary AML (%)	8 (16)	9 (17)
Prior HCT (%)	10 (20)	9 (17)
Median # Prior Regimens, (range)	2 (1 – 10)	2 (1-7)
# at 60 mg/m <sup>2</sup>	24	53
# at 90 mg/m <sup>2</sup>	26	0

# r/r AML 10-day regimen cycles administered

## Distribution of 10-day and 5-day cycles

Treatment Cycle	10-day dosing (N)	5-day dosing (N)
1	53	0
2	45	3
3	27	7
4	16	6
5	7	4
6	2	0
7	0	1
Total # of cycles (%)	150 (88%)	21 (12%)

- About half of patients (27/53) received 3 cycles of SGI-110 10-day treatment before continuing on 5-day cycles
- 88% of cycles were given as 10-day cycles

# SGI-110 5-day and 10-day Regimens Clinical Responses in r/r AML

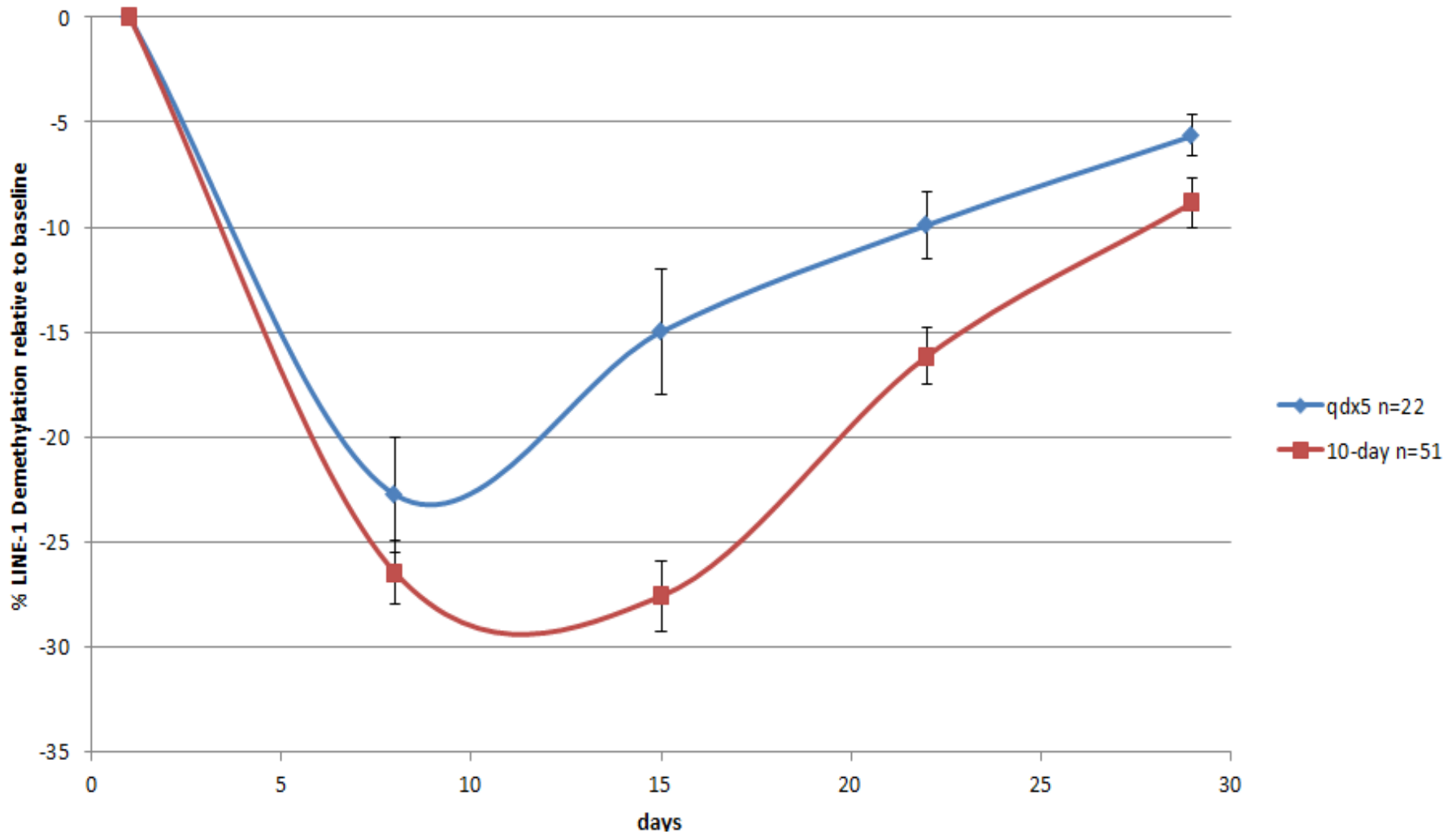
Response Category <sup>1</sup>	Response rate (N=50) 5 Day (60 and 90 mg/m <sup>2</sup> ) N (%)	Response rate (N=53) 10 Day (60 mg/m <sup>2</sup> ) N (%)	P value
<b>CR</b>	<b>3<sup>2</sup> (6%)</b>	<b>10 (19%)</b>	<b>0.074</b>
CRp	1 (2%)	4 (7%)	
CRi	4 (8%)	2 (4%)	
<b>CRc (CR + CRp + CRi)</b>	<b>8<sup>3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

<sup>1</sup> International Working Group 2003 AML Response Criteria

<sup>2</sup> 2 CR on 60 mg/m<sup>2</sup> and 1 CR on 90 mg/m<sup>2</sup>

<sup>3</sup> 3 CRc on 60 and 5 on 90 mg/m<sup>2</sup>

# r/r AML LINE-1 Demethylation 60 mg/m<sup>2</sup> 5-day vs 10-day in Cycle 1



***P value <0.001***

# Most Commonly Reported Grade $\geq 3$ AEs Regardless of Relationship ( $\geq 10\%$ )

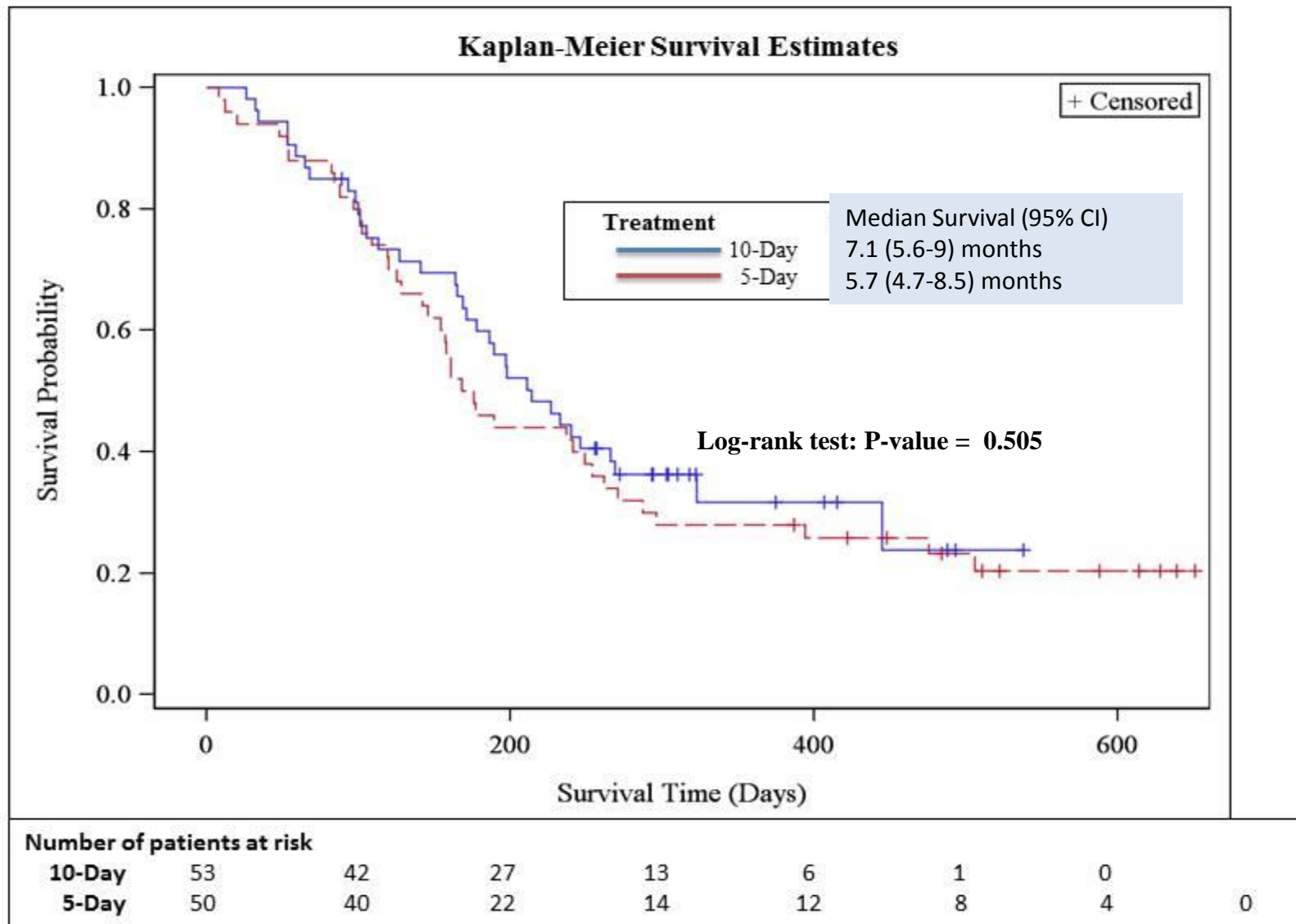
	60 or 90 mg/m <sup>2</sup> (5-d) (n=50) (%)	60 mg/m <sup>2</sup> (10-d) (n=53) (%)	P value
Febrile neutropenia	60%	59%	1.000
Thrombocytopenia	20%	38%	0.054
Anaemia	18%	36%	0.049
Pneumonia	24%	28%	0.660
Neutropenia	8%	15%	0.360
Hypokalemia	16%	11%	0.572
Leukopenia	12%	4%	0.153
Cellulitis	6%	13%	0.321
Sepsis	4%	11%	0.271

## All-Cause Early Mortality

Dose	N	30 day Mortality N (%) p value	60 day Mortality N (%) P value
60 or 90 mg/m <sup>2</sup> (5-Day)	50	3 (6.0)	6 (12.0)
60mg/m <sup>2</sup> (10-Day)	53	1 (1.9) (P = 0.353)	6 (11.3) (P = 1.000)

# SGI-110 5-day and 10-day regimens

## Overall Survival in r/r AML

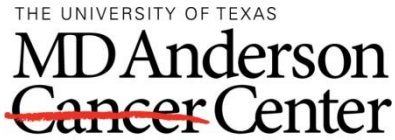


# SGI-110 5-d vs. 10-d regimens in r/r AML

## Conclusions

- SGI-110 is clinically active with good safety profile in heavily pretreated AML patients
- SGI-110 10-day regimen achieved significantly more potent and longer demethylation and a trend for better CR and CRc
- Median Overall Survival with 10-day regimen (7.1 months) is longer than expected median OS in this population (OS  $\approx$ 3 months)
- Safety of SGI-110 10-day regimen acceptable with no increase in early mortality compared to 5-day regimen

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