

# Comparison of Efficacy and Safety Results in 103 Treatment-Naïve Acute Myeloid Leukemia (TN-AML) Patients Not Candidates For Intensive Chemotherapy Using 5-day and 10-day Regimens of Guadecitabine (SGI-110), a novel Hypomethylating Agent (HMA)

On Behalf of the SGI-110 Investigative Team

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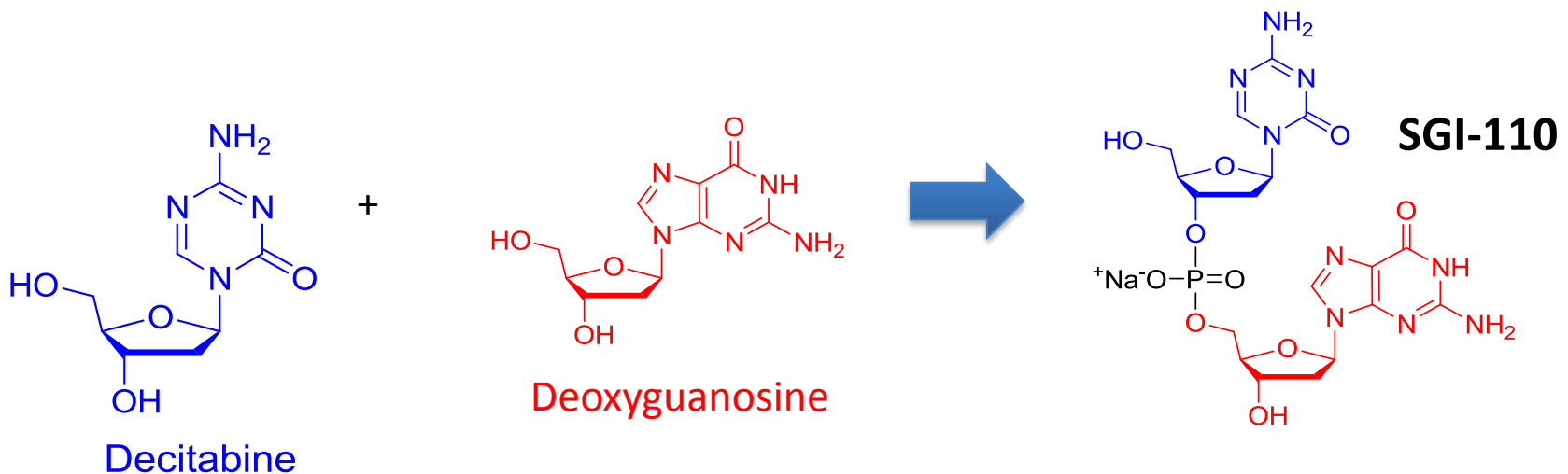
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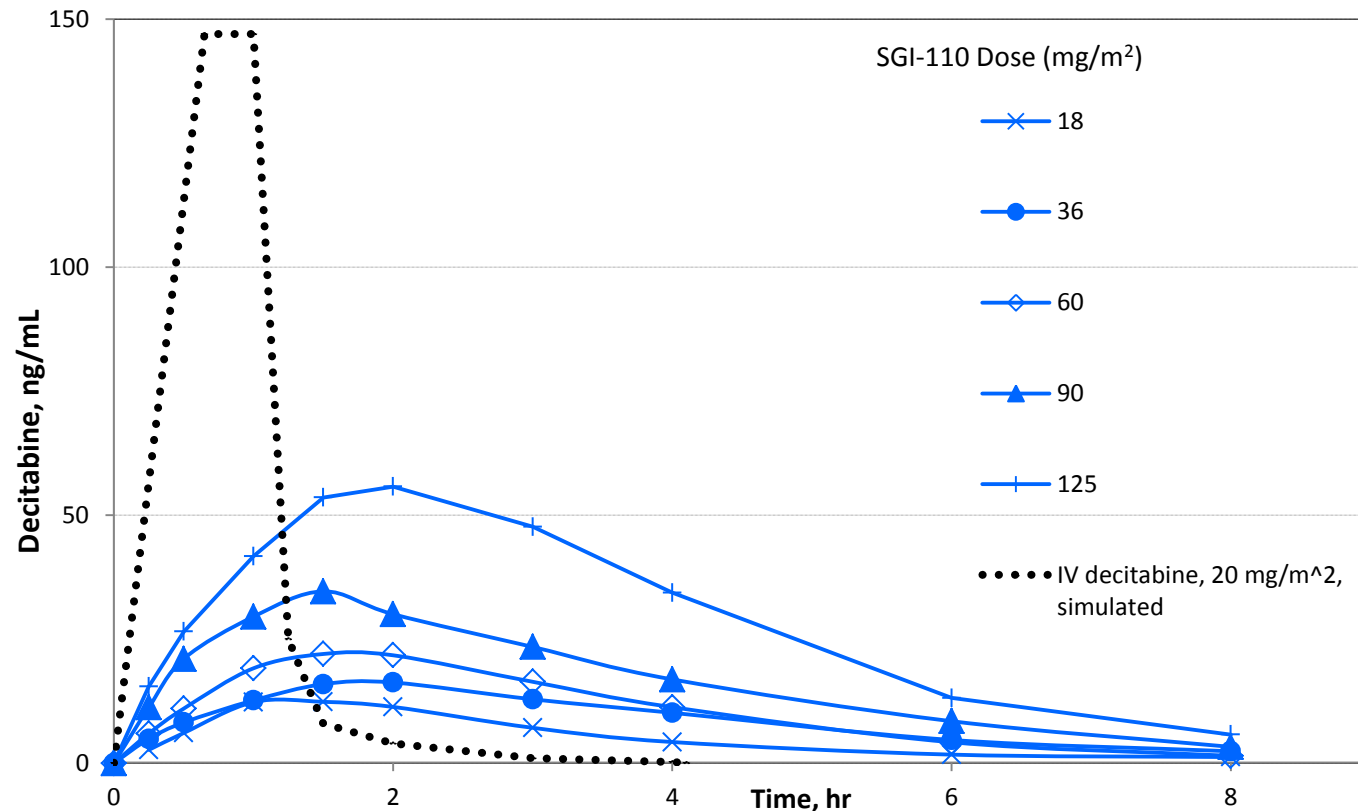
# Guadecitabine (SGI-110) - Background

- Next generation hypomethylating agents
- Dinucleotide of decitabine and deoxyguanosine=protects it from deamination=prolongs *in vivo* exposure of decitabine
- Prolonged decitabine exposure may translate into better efficacy



# Guadecitabine- Phase 1 Pharmacokinetics

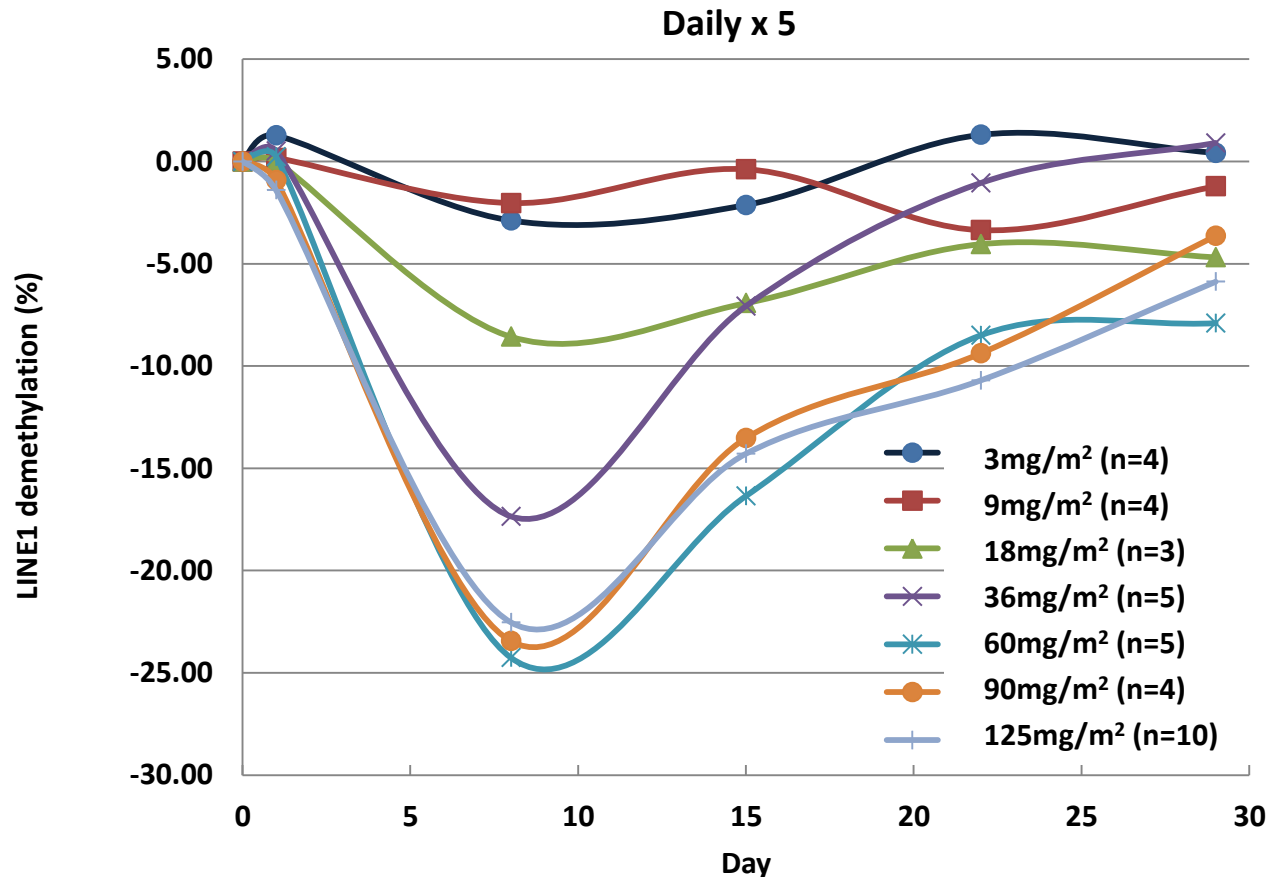
## Prolonged Exposure Time of Decitabine Compared to IV Decitabine



- Decitabine exposure window after SC SGI-110 increased (11-12 h) compared to decitabine 20 mg/m<sup>2</sup> 1-hr IV infusion (3-4h, simulated)
- Decitabine C<sub>max</sub> less than one third of IV decitabine
- 4-fold increase in half life over decitabine IV

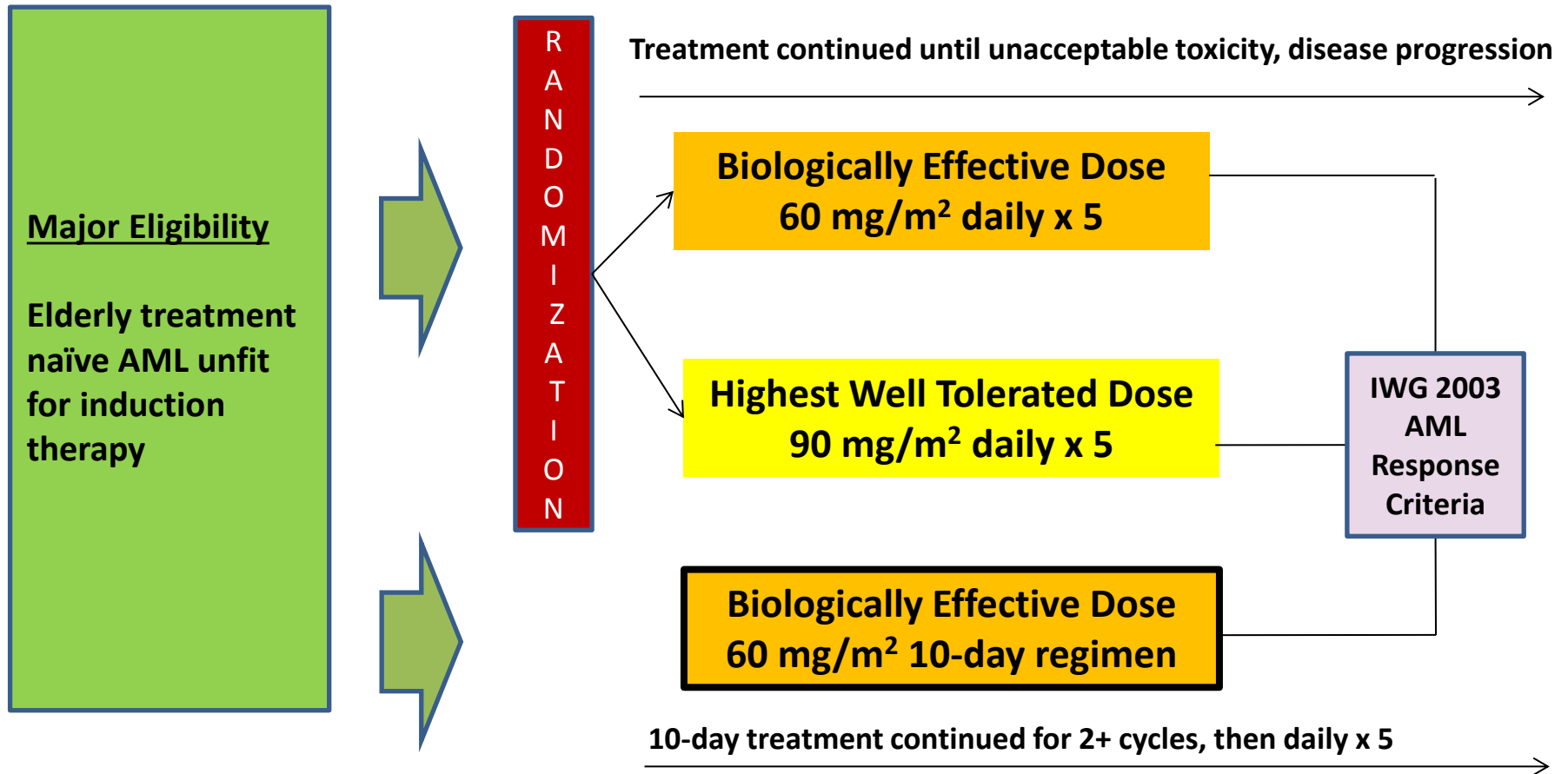
# Guadecitabine-Phase 1 Pharmacodynamics

## Potent Dose-dependent LINE-1 DNA Demethylation



- LINE-1 demethylation increased with dose up to 60 mg/m<sup>2</sup> Dailyx5
- Maximum demethylation at 60 mg/m<sup>2</sup> Dailyx5 (BED)

# Guadecitabine-Phase 2 Study in Rx-naïve AML



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

Data from randomized study previously presented (Yee et al EHA 2014)  
**consolidated as the 5-Day regimen**

# Guadecitabine - 10-day Regimen

Minimum 6 cycles

1-4 Cycles

10-Day Cycle (28 days)

← SGI-110 →

D1-5

D8-12

Continue Until Progression or  
Unacceptable Toxicity

5-Day Cycle (28 days)

SGI-110

D1-5

**SGI-110 60 mg/m<sup>2</sup>/d SQ Days 1-5 and 8-12, Q28 days for 1-4 cycles, followed by Rx on Days 1-5 Q28 days for a total of at least 6 cycles**

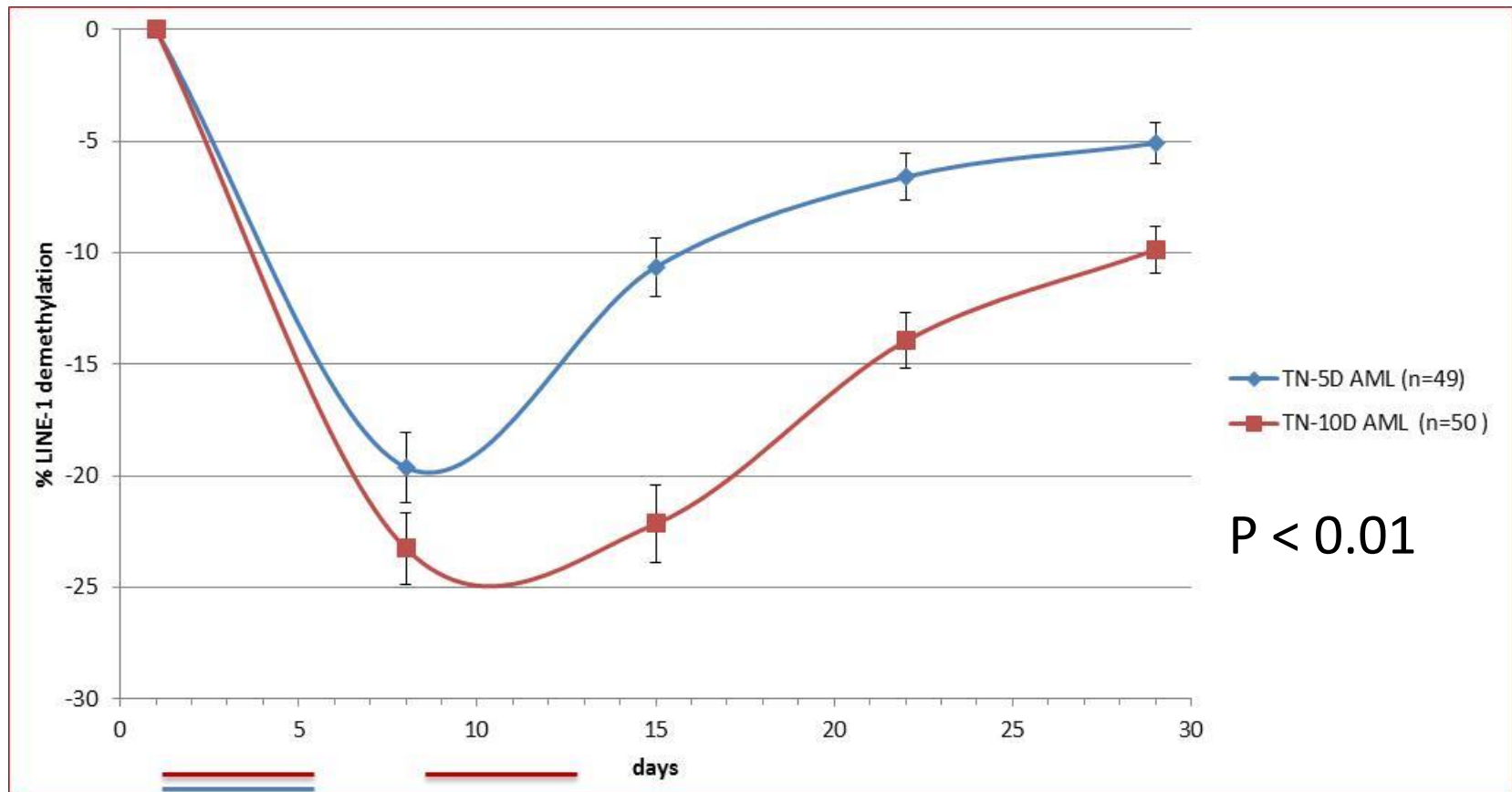
# Guadecitabine - Phase 2 5-day and 10-day Regimens

## Study Groups

Patient Characteristics	5-day (n=51)	10-day (n=52)
<b>Median age, (range)</b>	<b>78 (62-92)</b>	<b>77 (66-92)</b>
Gender M n (%)	30 (59)	34 (65)
F n (%)	21(41)	18(35)
ECOG PS, n(%)		
0	11 (22)	5 (10)
1	22 (43)	26 (50)
<b>&gt;2</b>	<b>18 (35)</b>	<b>21 (40)</b>
<b>Poor CG, n (%)</b>	<b>23 (45)</b>	<b>20 (38)</b>
<b>Secondary AML, n (%)</b>	<b>23 (45)</b>	<b>14 (27)</b>
Median BM % blast (range)	40 (13-94)	49.5 (16-98)
Median WBC (10 <sup>9</sup> /L) (range)	2.6 (0.7-50)	4.0 (0.5-87.7)

\* 5-day data consolidated for 60 and 90 mg/m<sup>2</sup> doses

# Guadecitabine - Phase 2 5-day and 10-day Regimens LINE-1 Demethylation in Cycle 1



**In Rx- naïve AML, 10-day schedule (Days 1-5 and 8-12) shows longer duration of LINE-1 demethylation compared to 5-day**



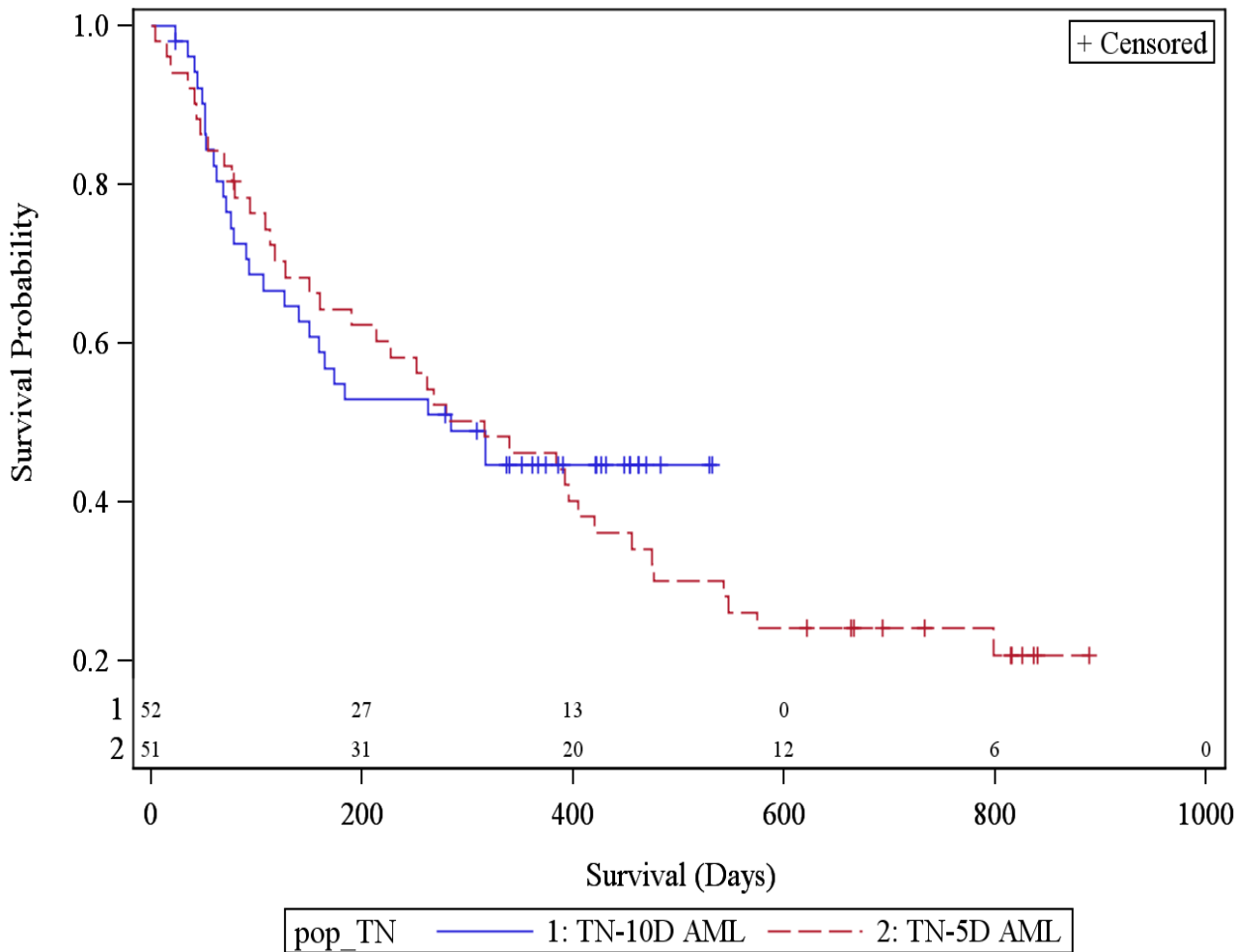
# Guadecitabine - Phase 2 5-day and 10-day Regimens Response

Response Category <sup>1</sup>	5-day (n=51)	10-day (n=52)	P value
	n (%)	n (%)	
CR	19 (37)	16 (31)	0.54
CRi	7 (14)	4 (8)	0.36
CRp	3 (6)	5 (10)	0.72
<b>Overall</b>	<b>29 (57)</b>	<b>25 (48)</b>	<b>0.43</b>

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

# Guadecitabine - Phase 2 Study 5-day and 10-day Survival by Regimen

**Product-Limit Survival Estimates**  
With Number of Subjects at Risk



**Median F/U (mo)**

**Dailyx5 30.1**

**10-day 16.8**

**Median Survival (mo)**

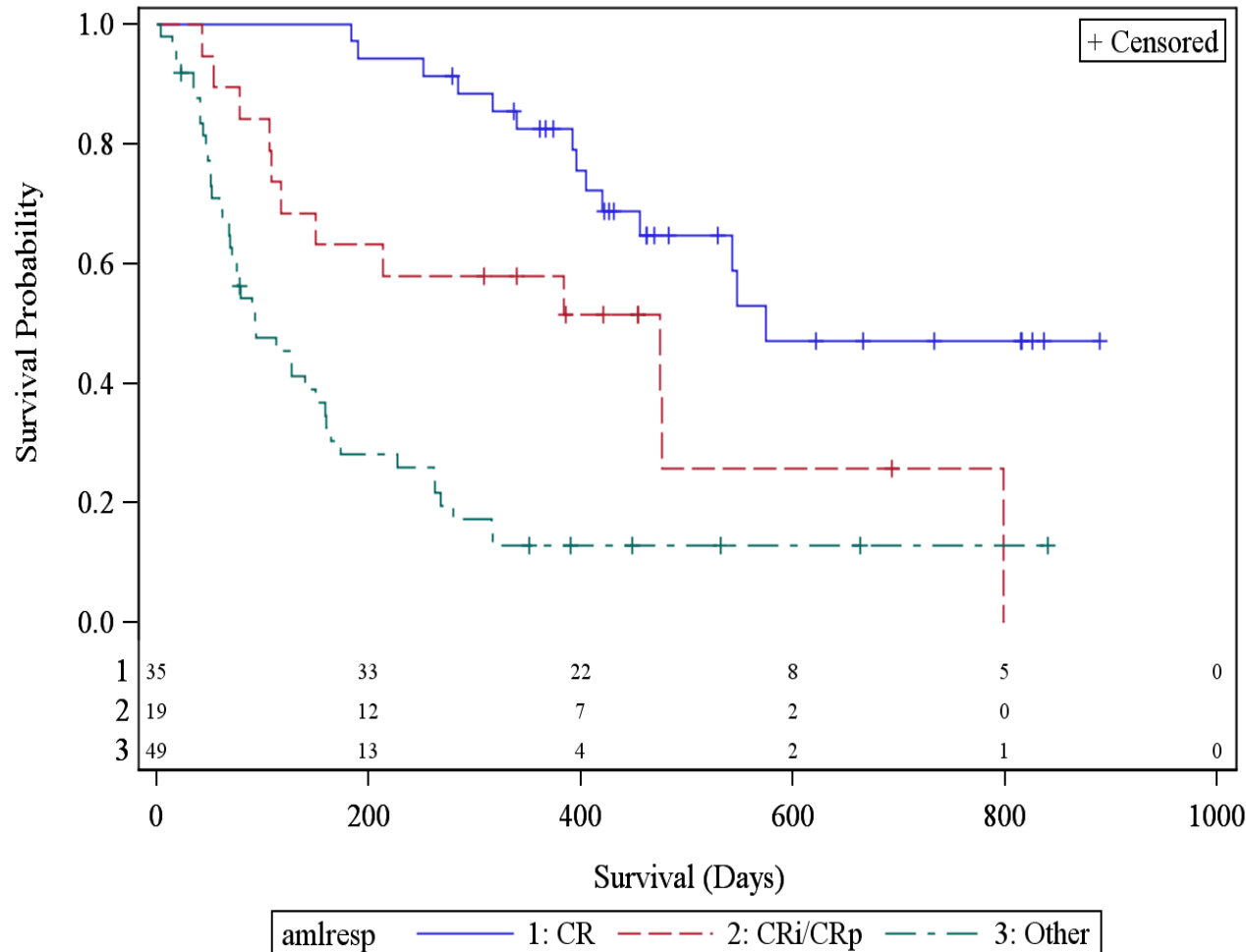
**5-day 10.5**

**10-day 9.5**

**Log-rank P = 0.70**

# Guadecitabine - Phase 2 Study 5-day and 10-day Survival by Response

Product-Limit Survival Estimates  
With Number of Subjects at Risk



## Median Survival (mo)

CR 19.1

CRp + CRi 15.8

Other 3.1

Log-Rank P < 0.0001

# Guadecitabine - Phase 2 Study 5-day and 10-day Adverse Events Grade $\geq 3$ in $\geq 10\%$ <sup>1</sup>

Adverse Event	5-day(n=51) Grade $\geq 3$ AEs %	10-day(n=52) <sup>2</sup> Grade $\geq 3$ AEs %
Febrile Neutropenia	61	63
Thrombocytopenia	49	40
Neutropenia	39	33
Pneumonia	24	35
Anemia	29	23
Sepsis	16	23
Bacteremia	10	17
Hypokalemia	14	12
Cellulitis	10	12

<sup>1</sup>Regardless of relationship to guadecitabine

<sup>2</sup> No significant differences between the 2 groups

# Guadecitabine - All-Cause Early Mortality

	<b>5-day (n=51)</b>	<b>10-Day <sup>1</sup> (n=52)</b>
<b>30-day n (%)</b>	<b>3 (5.9)</b>	<b>1 (1.9)</b>
<b>60-day n (%)</b>	<b>8 (15.7)</b>	<b>9 (17.3)</b>

<sup>1</sup> Differences not statistically significant between the 2 regimens

# Guadecitabine (SGI-110) - Conclusions

- Next generation HMA with prolonged in vivo exposure to decitabine
- Potent demethylation with both 5-day and 10-day regimens at the 60 mg/m<sup>2</sup>/d dose.
- Both regimens well-tolerated
- Promising activity in poor prognosis elderly Rx-naive AML unfit for intensive chemoRx - No significant efficacy differences
  - 37% CR and 57% CRc with 5-day
  - 31% CR and 48% CRc with the 10-day
- Survival
  - Median survival similar ~ 10 m in poor prognosis unfit patients
  - CR > CRi > Others p < 0.0001
- AML: ASTRAL-1 Phase 3 Trial in Rx-Naïve AML unfit for intensive chemoRx using 5-Day regimen underway

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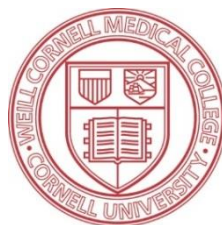
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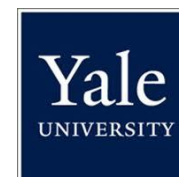
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