RESULTS OF A RANDOMIZED MULTICENTER PHASE 2 STUDY OF A 5-DAY REGIMEN OF SGI-110, A NOVEL HYPOMETHYLATING AGENT, IN TREATMENT NAÏVE ELDERLY ACUTE MYELOID LEUKEMIA NOT ELIGIBLE FOR INTENSIVE THERAPY

Karen Yee, MD

Princess Margaret Cancer Center

On Behalf of the SGI-110 Investigative Team

Karen Yee[* 1], Naval Daver[2], Patricia Kropf[3], Raoul Tibes[4], Casey O'Connell[5], Gail Roboz[6], Katherine Walsh[7], Naveen Pemmaraju[2], Todd Rosenblat[8], Jesus Berdeja[9], Scott Lunin[10], Woonbok Chung[11], Jean-Pierre Issa[11], Sue Naim[12], Pietro Taverna[12], Yong Hao[12], Mohammad Azab[12], Hagop Kantarjian[2]

[1]Princess Margaret Cancer Center, Toronto, Canada, [2]University of Texas, MD Anderson Cancer Center, Houston, [3]Fox Chase Cancer Center, Philadelphia, [4]Mayo Clinic, Scottsdale, [5]USC Keck School of Medicine, University of Southern California, Los Angeles, [6]Weill Cornell Medical College, New York, [7]The Ohio State University, Columbus, [8]New York-Presbyterian/Columbia University Medical Center, New York, [9]Sarah Cannon Research Institute, Nashville, [10]Florida Cancer Specialist, Englewood, [11]Fels Institute, Temple University, Philadelphia, [12]Astex Pharmaceuticals Inc., Dublin, United States

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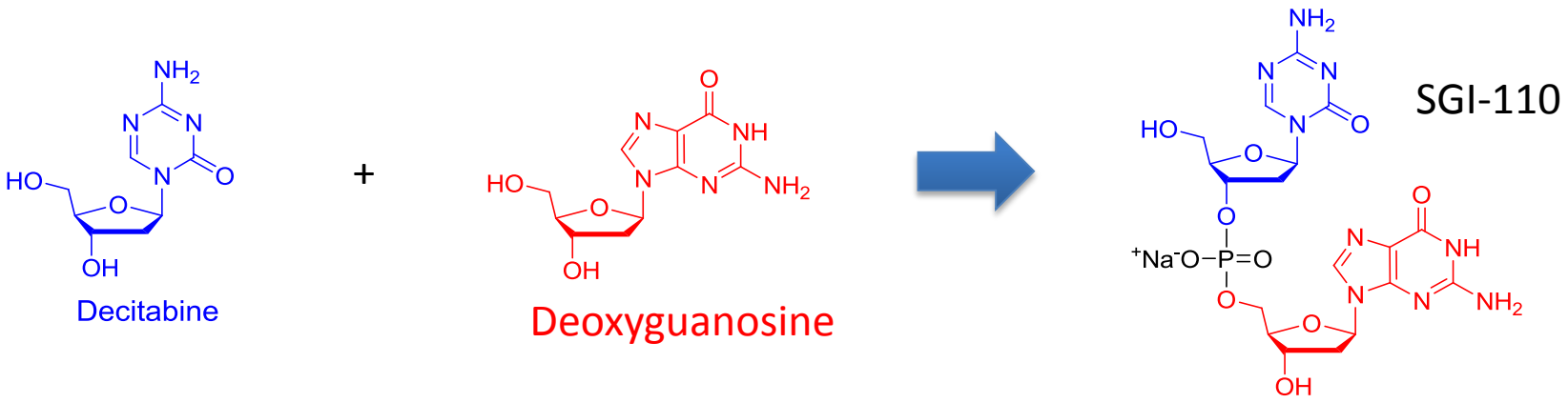
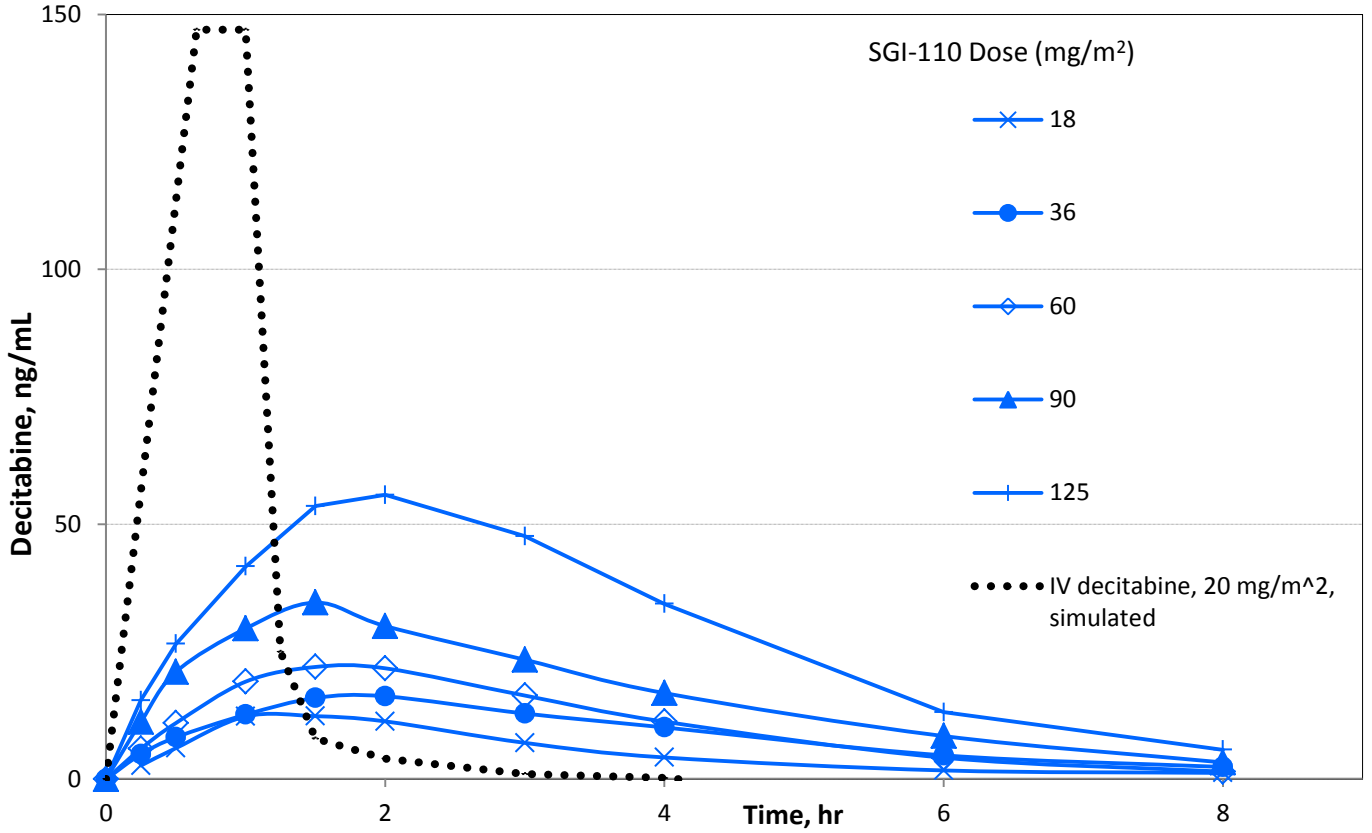
SGI-110, A Second Generation Hypomethylating Agent

- 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

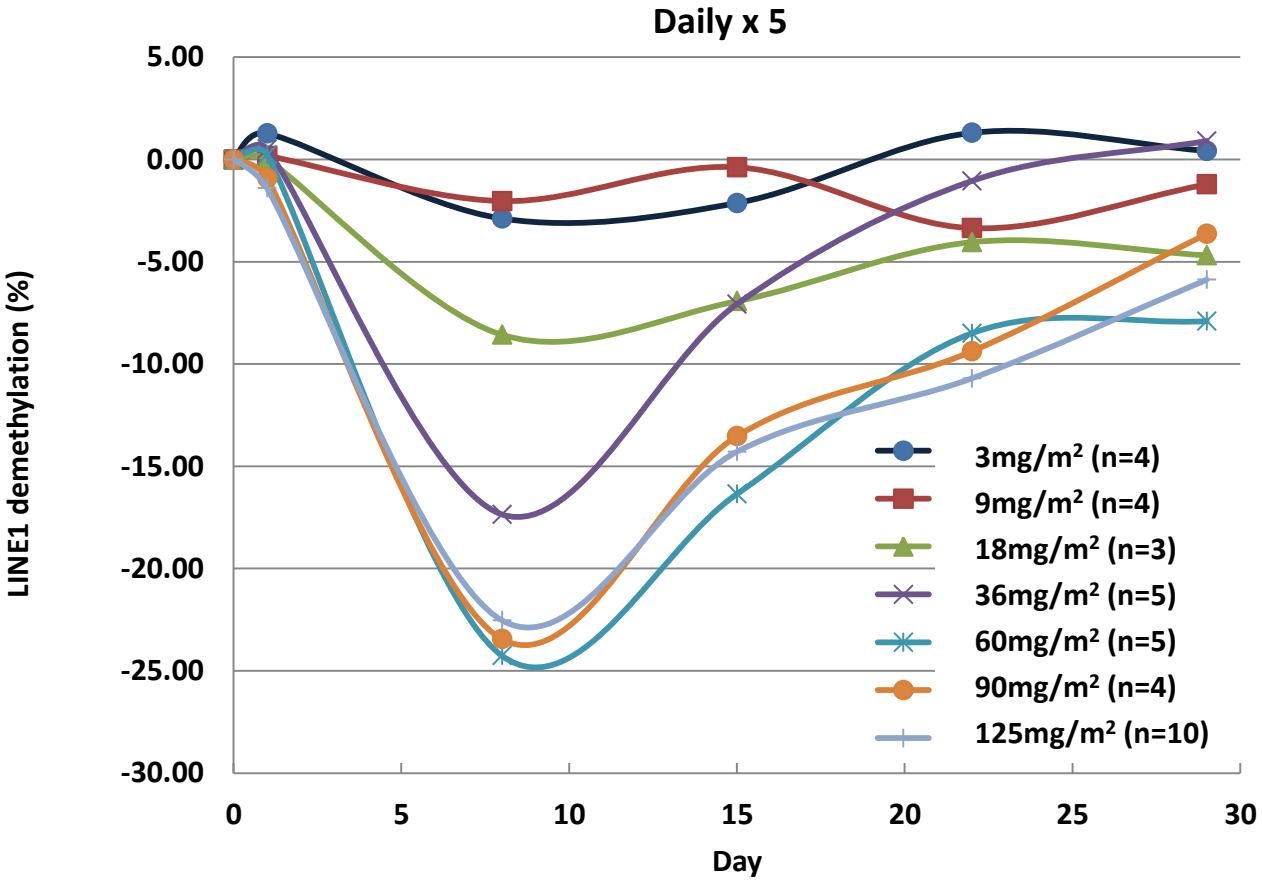


SGI-110 SC Provides More Effective Exposure Window to active metabolite decitabine in Phase 1 study



- Decitabine exposure window after SC SGI-110 is more than double (8hr+) compared to 20 mg/m^2 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 Phase I LINE1 DNA Demethylation in Cycle 1



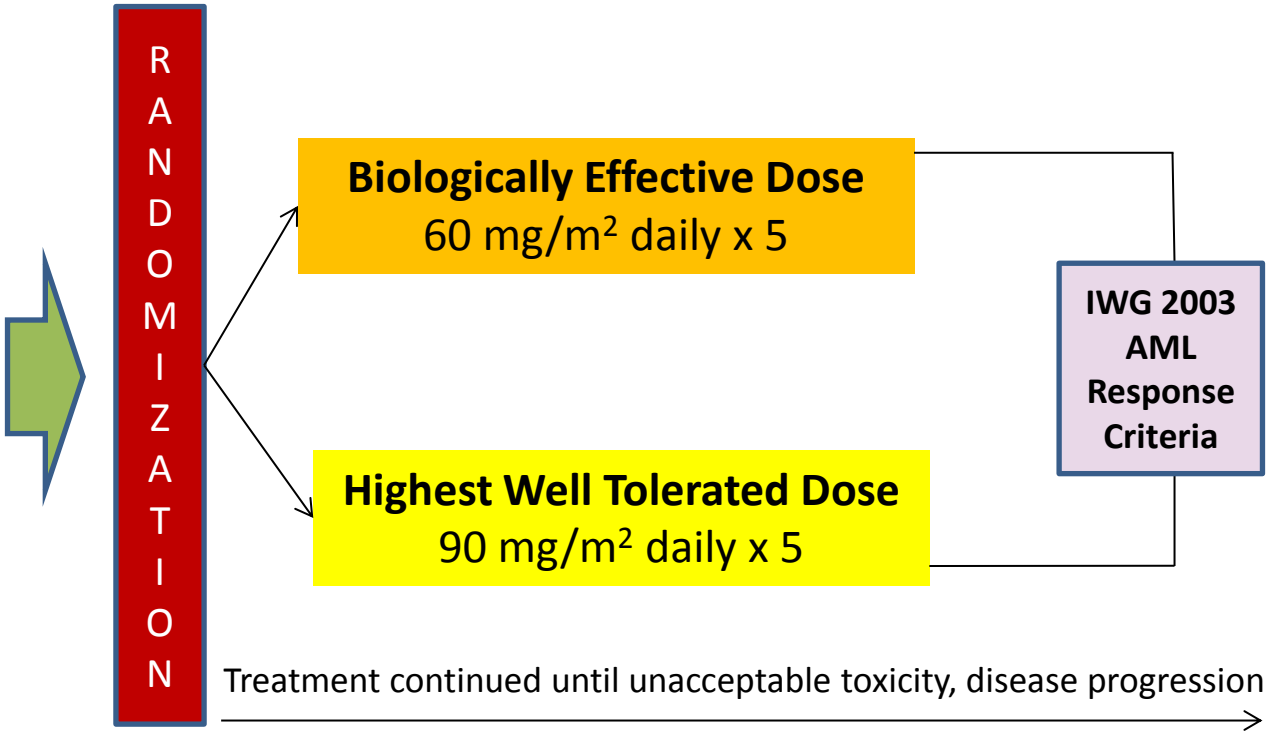
- LINE-1 demethylation increased with dose in the dailyx5 regimen Q 28 days
- Maximum demethylation reached at 60 mg/m2 SC dailyx5

Phase 2 Study Design in Treatment Naïve Elderly AML

Major Eligibility

Treatment Naïve Elderly AML ≥ 65 years with at least one of the following:

- Secondary AML
- Poor cytogenetics
- Pre-existing heart or lung co-morbidities
- ECOG PS 2



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

Patient and Disease Characteristics

Patient Characteristics	60 mg/m^2 QD x5 (n=24)	90 mg/m^2 QD x5 (n=27)	Total (n=51)
Median Age (range)	78 (62-92)	77 (66-92)	77 (62-92)
Gender M F	58% 42%	59% 41%	59% 41%
ECOG PS 0 1 2	13% 42% 46%	30% 44% 26%	22% 43% 35%
Secondary AML (%)	42%	48%	45%
Poor-risk Cytogenetics (%)	50%	46%	48%
Median BM Blast% (range)	40 (21-90)	46 (13-94)	40 (13-94)
Median WBC (10^9/L) (range)	2.5 (0.7-50.0)	2.9 (0.9-51.4)	2.8 (0.7-51.4)

31% of patients had more than one poor prognostic criteria in addition to age ≥ 65 years

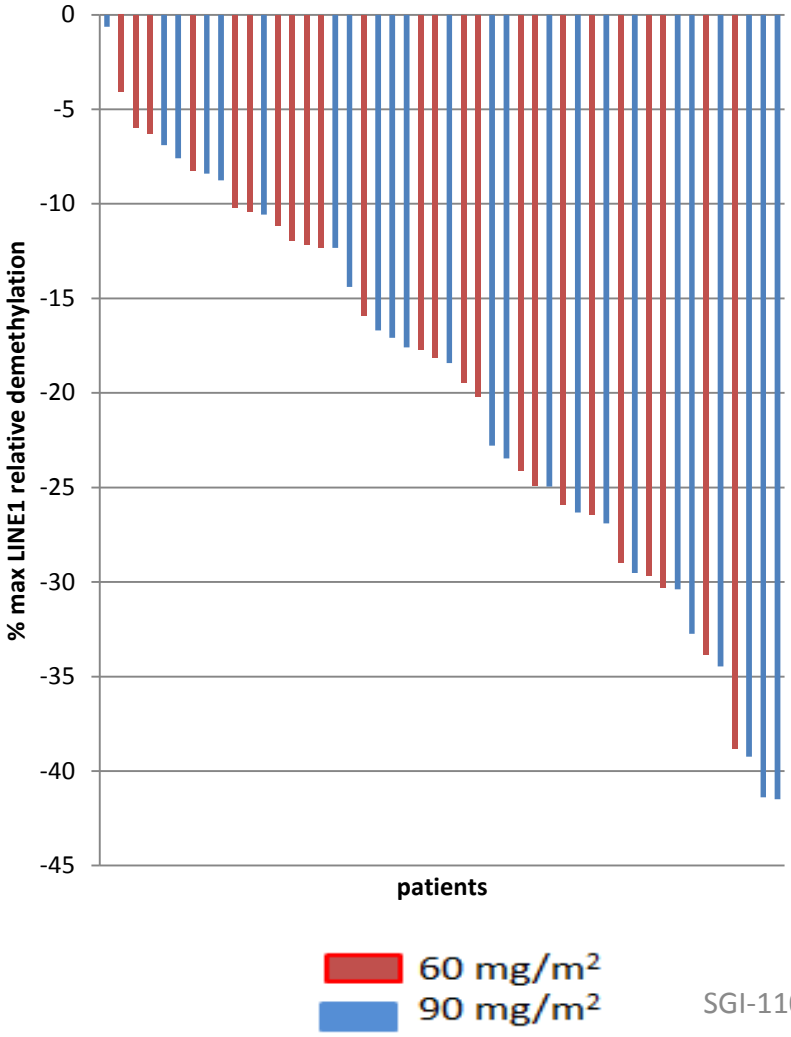
Clinical Response Summary

Complete Response Category	60 mg/m^2 QD x5 (n=24) N (%)	90 mg/m^2 QD x5 (n=27) N (%)	Total (n=51) N (%)
	Response rate (%)	**Response rate (%)**	**Response rate (%)**
CR	**8 (33%)**	**9 (33%)**	**17 (33%)**
CRi	5 (21%)	6 (22%)	11 (22%)
CRp	0	0	0
Overall CR Rate (CR+CRp+CRi)	**13 (54%)**	**15 (55%)**	**28 (55%)**

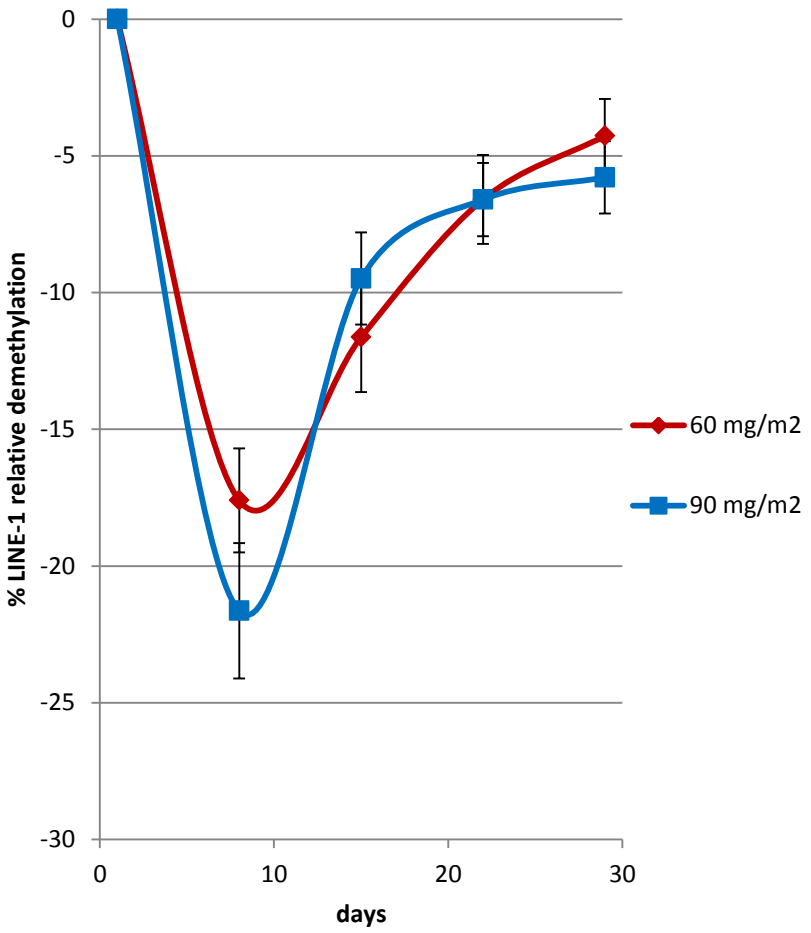
Median Duration of CR 147 days (Range: 55-273 days)

LINE-1 Demethylation in Cycle 1

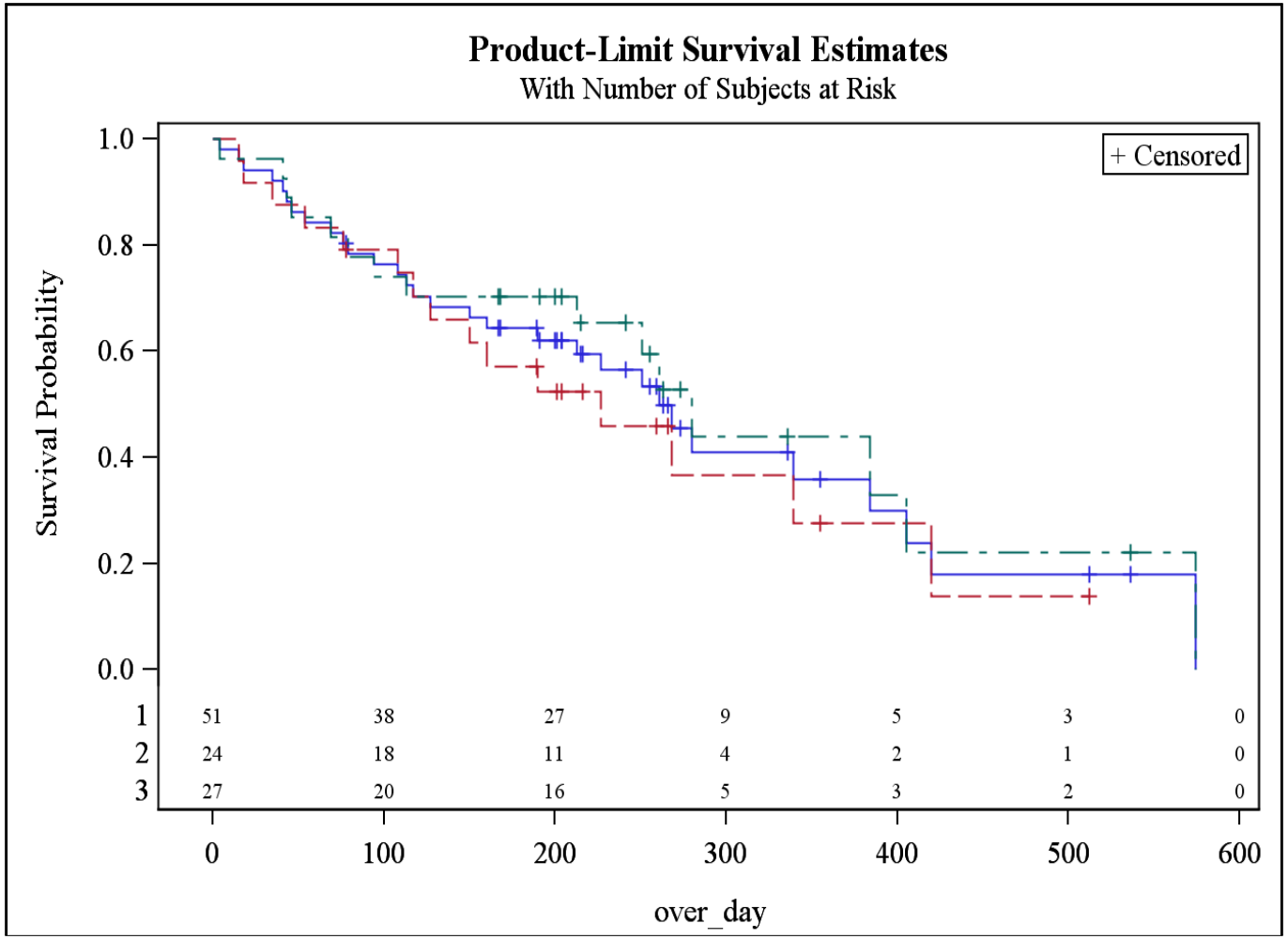
Extent of LINE-1 Demethylation



Duration of LINE-1 Demethylation



Overall Survival by Dose and Total Cohort

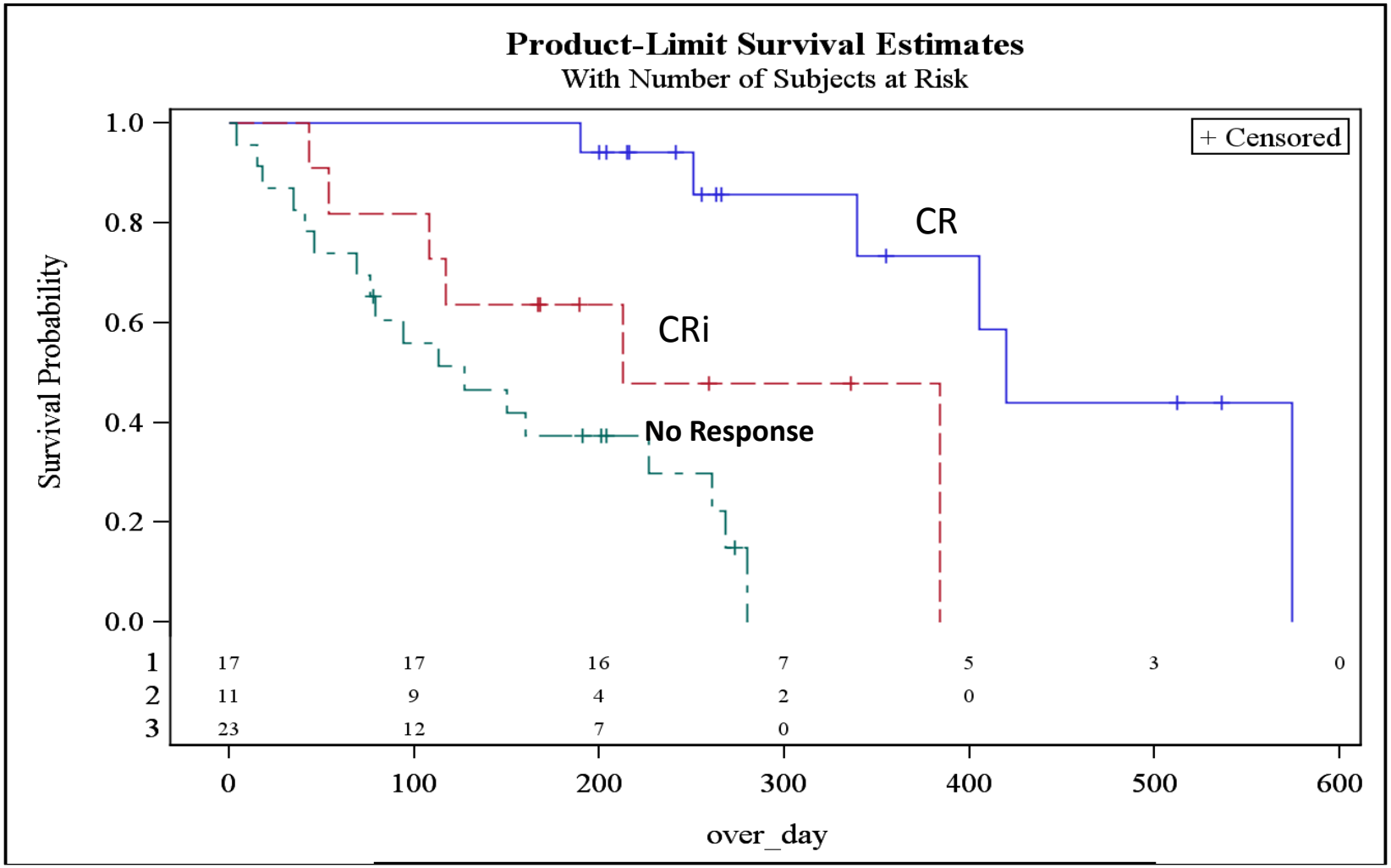


60 mg/m²
90 mg/m²
Total

Median Survival

- 60mg/m²: 7.6 m
- 90mg/m²: 9.3 m
- Total: 8.7 months

Overall Survival by Response



Overall Survival in CR patients > CRi > non-responders

Commonly Reported AEs Grade ≥ 3 Regardless of Relationship to SGI-110 (≥ 10%)

	60 mg/m² N=24	90 mg/m² N=27	Total N=51
Febrile neutropenia	54.2%	48.1%	51.0%
Thrombocytopenia	50.0%	37.0%	43.1%
Neutropenia	20.8%	44.4%	33.3%
Anaemia	29.2%	22.2%	25.5%
Leukopenia	20.8%	25.9%	23.5%
Pneumonia	20.8%	18.5%	19.6%
Hypokalemia	8.3%	18.5%	13.7%
Hypotension	8.3%	14.8%	11.8%

All-Cause Early Mortality

Dose	N	30 day Mortality (%)	60 day Mortality (%)
60 mg/m²	24	8.3%	16.7%
90 mg/m²	27	3.7%	14.8%
Total	51	5.9%	15.7%

SGI-110 dailyx5 results in Treatment-naïve elderly AML - Conclusions

- The study enrolled older patients (age ≥ 65 years) with one or more poor risk features who were not candidates for intensive chemotherapy
- High CR (33%) and Overall CR (55%) rates were achieved in this population
- No major differences in clinical responses, demethylation, overall survival, and safety between 60 and 90 mg/m^2 dailyx5
- Patient in CR or CRi had better Survival than non-responders
- The study is currently enrolling patients in an SGI-110 dailyx10 regimen
- The results support Phase 3 development of SGI-110 in this population

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