

**Phase I Study of CWP232291 in Patients with Relapsed or Refractory Acute Myeloid
Leukemia and Myelodysplastic Syndrome**

Je-Hwan Lee,^{*,1} Stefan Faderl,^{*,2} John M. Pagel,³ Chul Won Jung,⁴ Sung-Soo Yoon,⁵ Animesh
D. Pardanani,⁶ Pamela S. Becker,⁷ Howard Lee,⁸ Jeongeun Choi,⁹ Kyoungjune Lee,⁹
Minkyung Kim,⁹ and Jorge E. Cortes¹⁰

SUPPLEMENTARY DATA

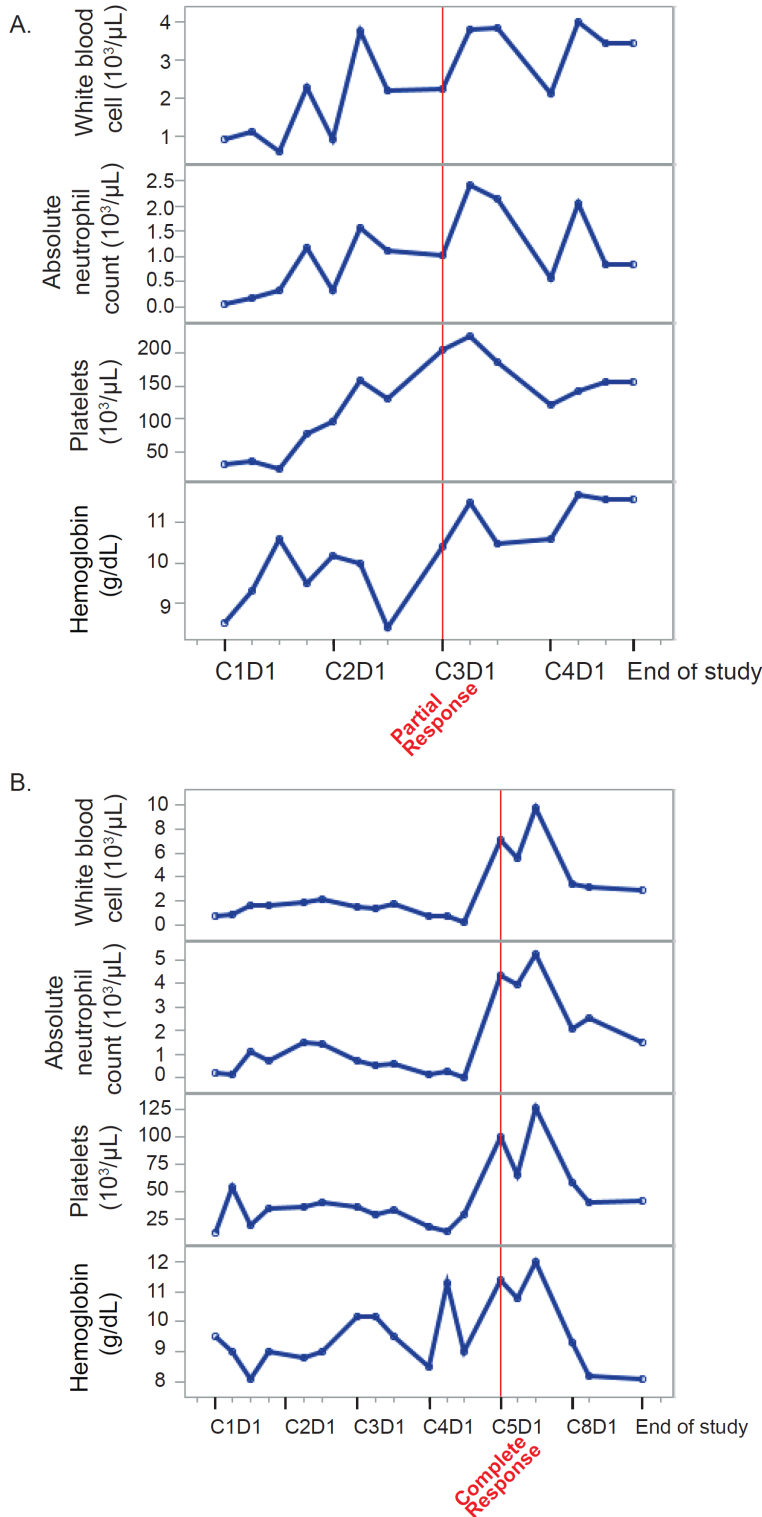
Supplementary Table 1. Dose limiting toxicity events

Event	Number of events	Cohort (Dose, mg/m²)
Nausea	1	54
Nausea	1	257 (2 h infusion)
Nausea	1	334
Abdominal pain	1	334
Anaphylactic reaction	1	198
Myalgia	1	334
Rash	1	153

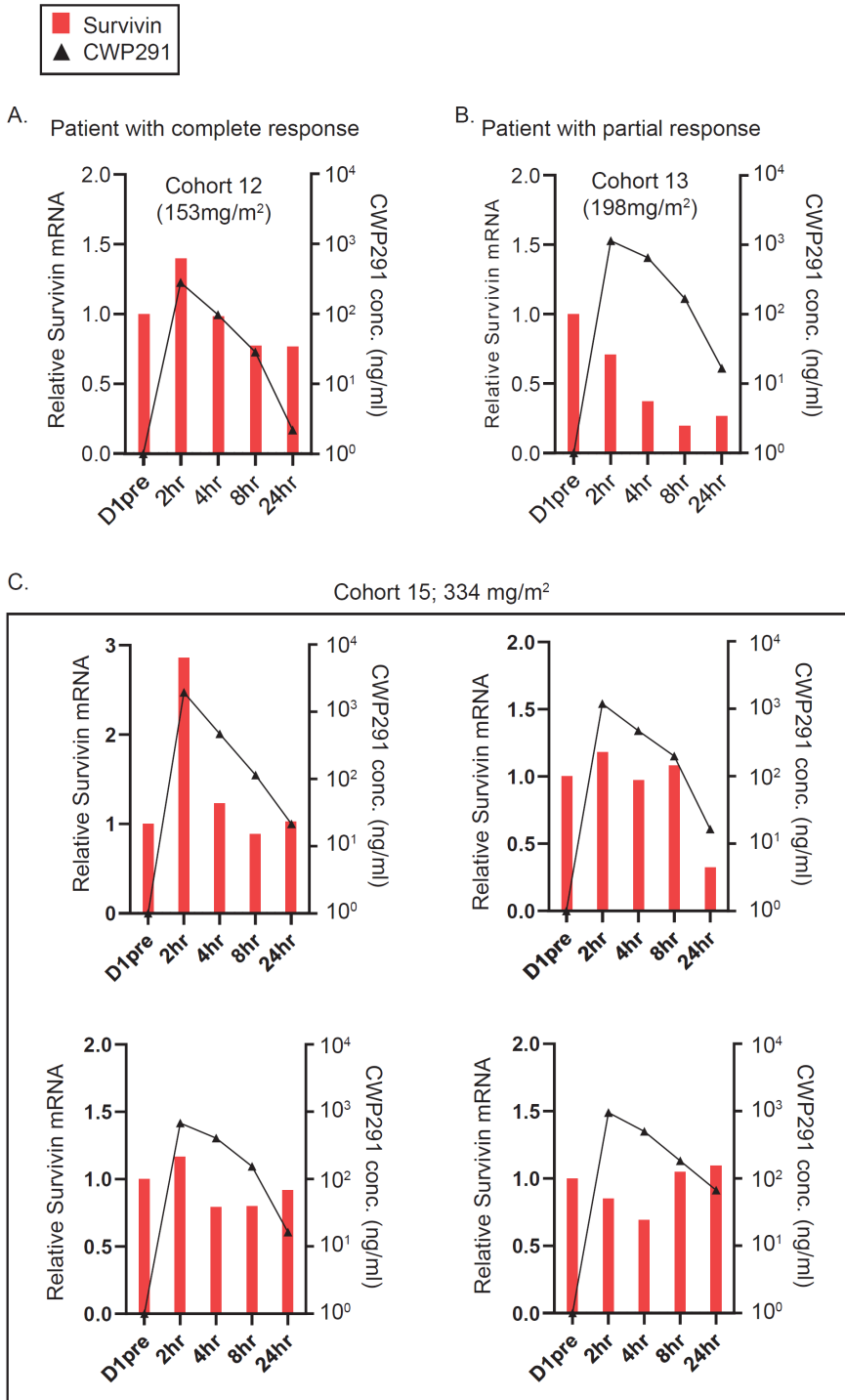
Supplementary Table 2. Pharmacokinetic parameters for CWP232204 at the maximum tolerated dose

Parameter	257 mg/m ² over 0.5 h (n=6)	257 mg/m ² over 2 h (n=6)
Day 1		
AUC ₀₋₂₄ (ng·h/mL)	4960 (2926 - 9368)	5750 (3424 - 7056)
AUC _{0-last} (ng·h/mL)	4810 (2795 - 9122)	5523 (3360 - 6958)
AUC _{0-∞} (ng·h/mL)	4953 (2892 - 9358)	5728 (3423 - 7045)
C _{max} (ng/mL)	5386 (1328 - 15036)	2959 (1949 - 3890)
t _{1/2} (h)	1.97 (1.46 - 2.27)	1.76 (1.19 - 2.51)
Day 7 (steady state)		
AUC ₀₋₂₄ (ng·h/mL)	5973 (4021 - 8311)	6663 (2961 - 11113)
AUC _{0-last} (ng·h/mL)	6147 (4012 - 9558)	7125 (3152 - 13275)
C _{max} (ng/mL)	5142 (3501 - 9814)	2964 (1432 - 3932)
t _{1/2} (h)	11.19 (3.28 - 15.83)	11.70 (6.11 - 19.29)

Supplementary Figure 1. Complete blood count (white blood, absolute neutrophil count, platelets, and hemoglobin) over time until end of study in patients with (A) partial response ($n=1$) and (B) complete response ($n=1$).

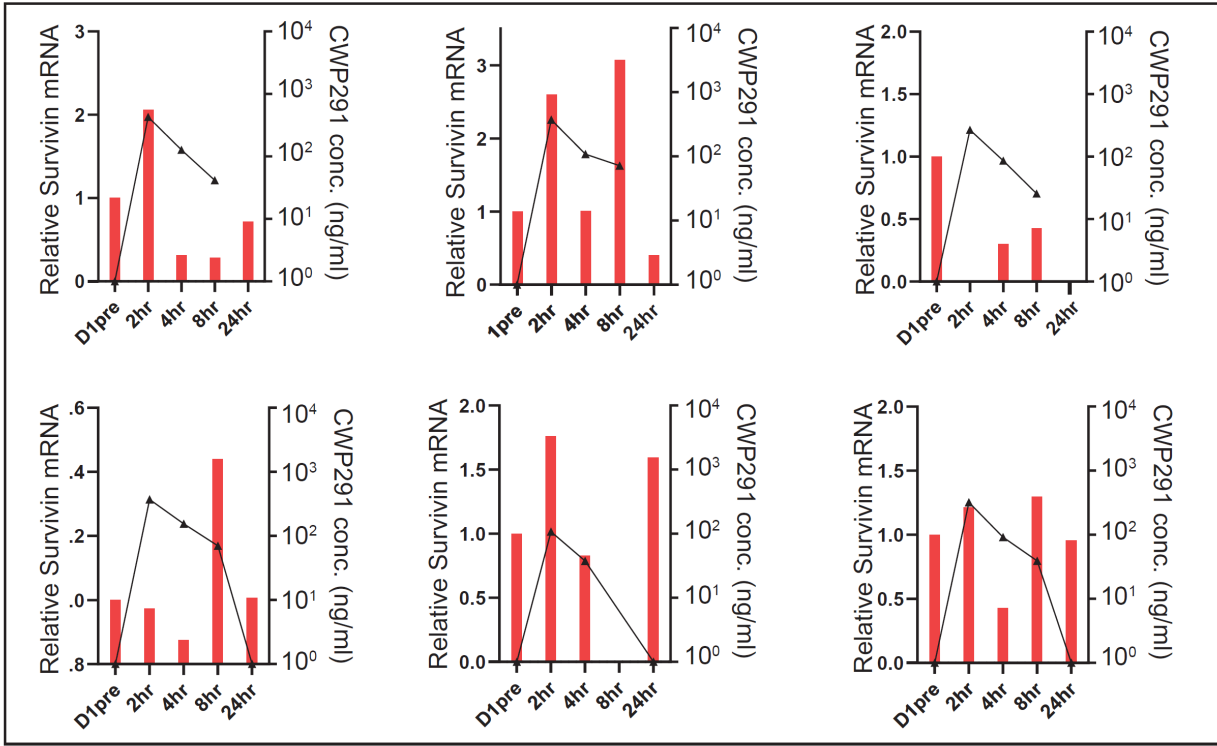


Supplementary Figure 2. Biomarker analysis for Wnt signaling pathway inhibition. Relative Survivin mRNA levels in plasma vs. time and CWP291 concentrations. PCR data was analyzed up to 24 hours vs. CWP291 plasma concentration. Data for responder patients: (A) CR, (B) PR. (X axis: time since CWP291 treatment). Patient individual data for (C) cohort 15, (D) cohort 14.1, (E) cohort 14, (F) cohort 13, (G) cohort 12.



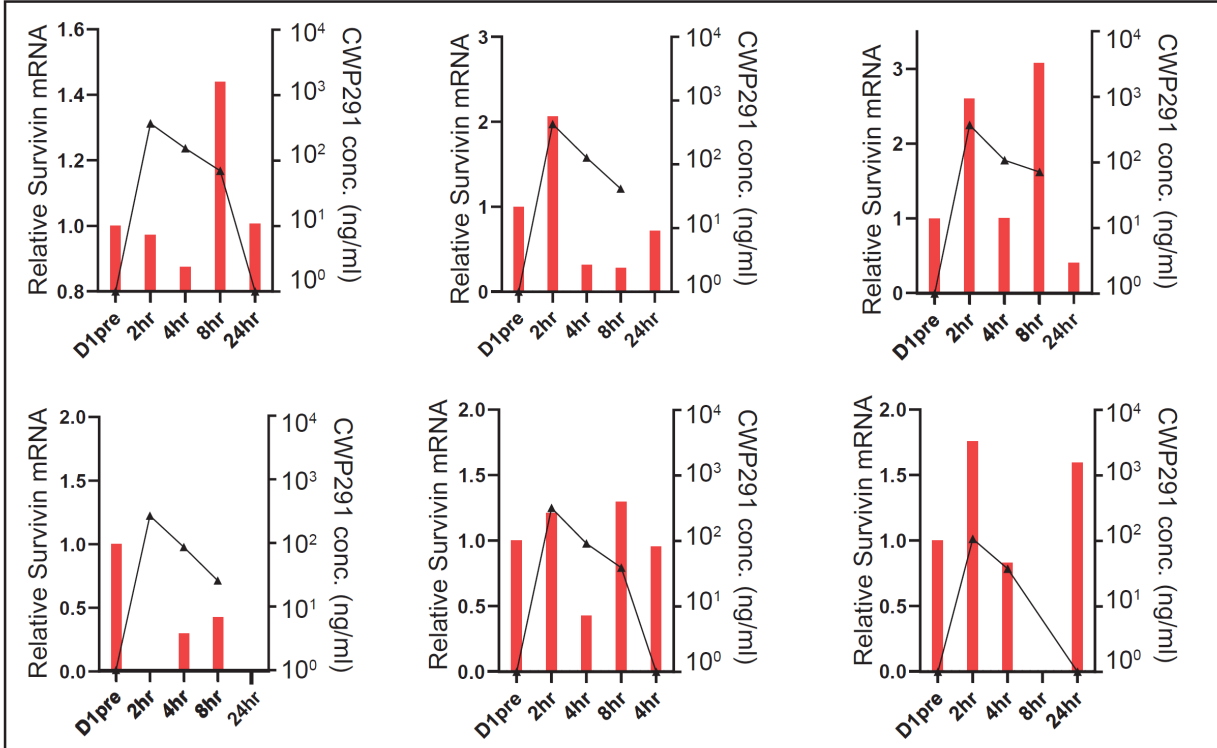
D.

Cohort 14.1; 257 mg/m²



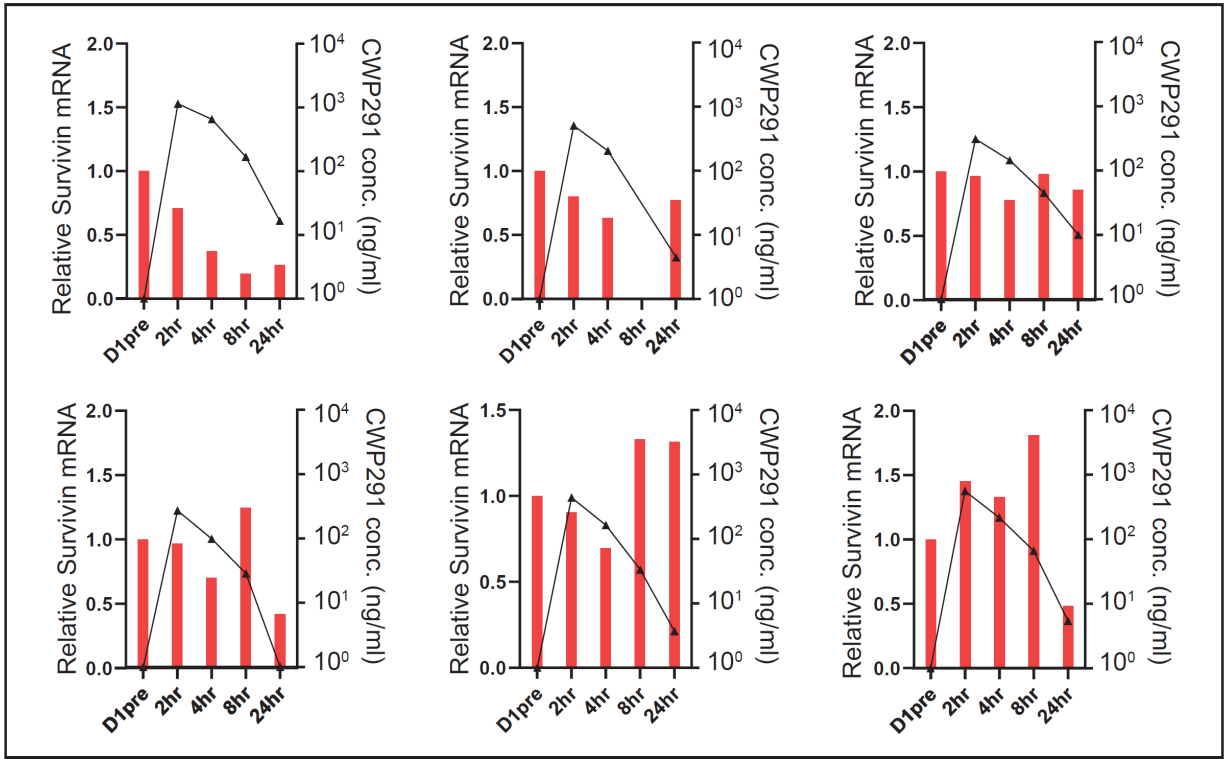
E.

Cohort 14; 257 mg/m²



F.

Cohort 13; 198 mg/m²



G.

Cohort 12; 153 mg/m²

