

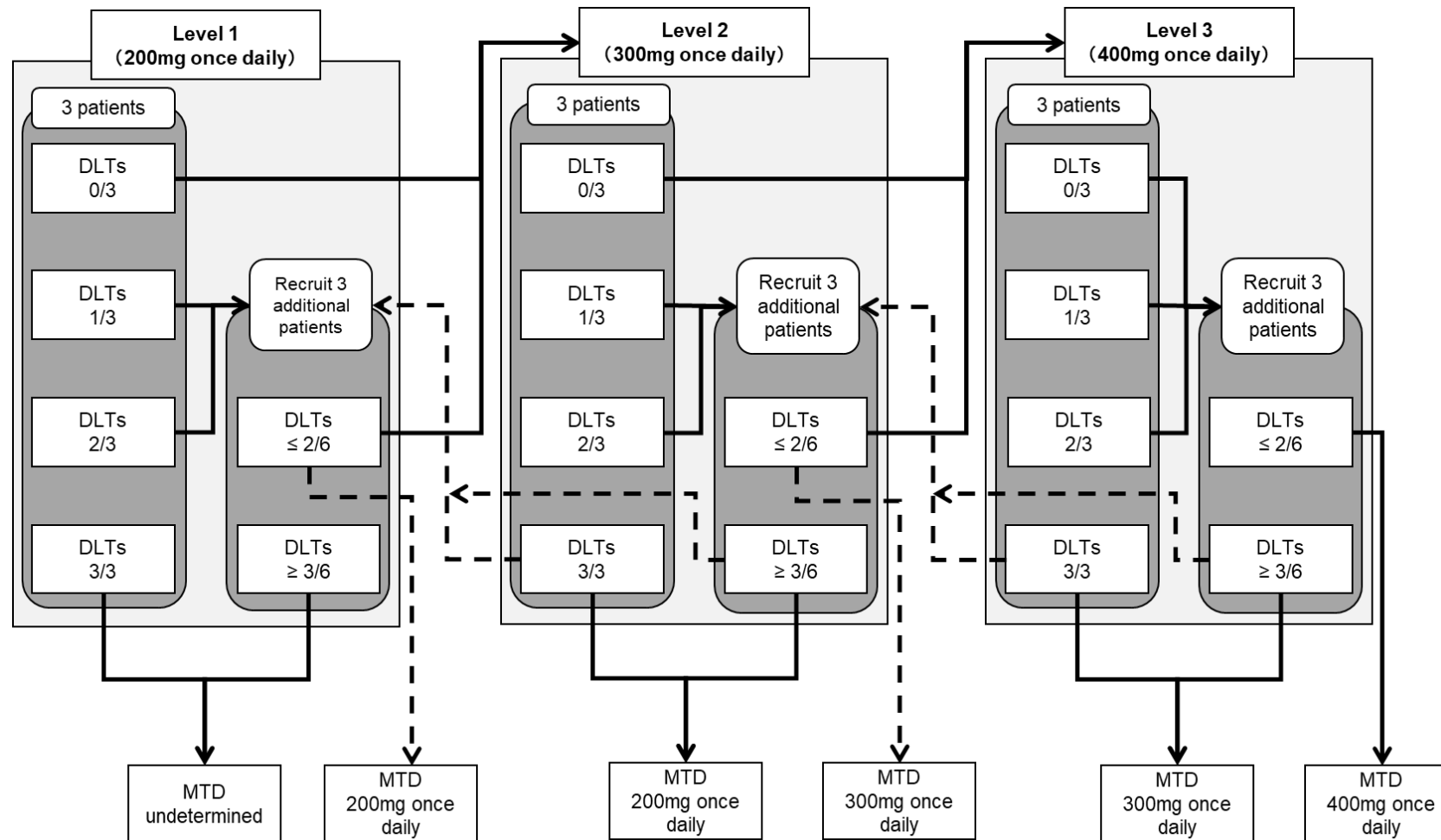
Supplementary table 2. Previous EGFR-TKI therapy

Level	Case	EGFR-TKIs		
1	VN-01	Gefitinib		
	VN-02	Erlotinib		
	VN-03	Gefitinib		
2	VS-01	Erlotinib	Gefitinib	Erlotinib
	VI-01	Erlotinib		
	VN-04	Gefitinib		
3	VK-01	Erlotinib	Gefitinib	Afatinib
	VK-02	Gefitinib	Erlotinib	
	VI-03	Erlotinib	Afatinib	
	VS-02	Gefitinib	Erlotinib	
	VN-05	Gefitinib	Osimertinib	
	VN-06	Gefitinib	Erlotinib	

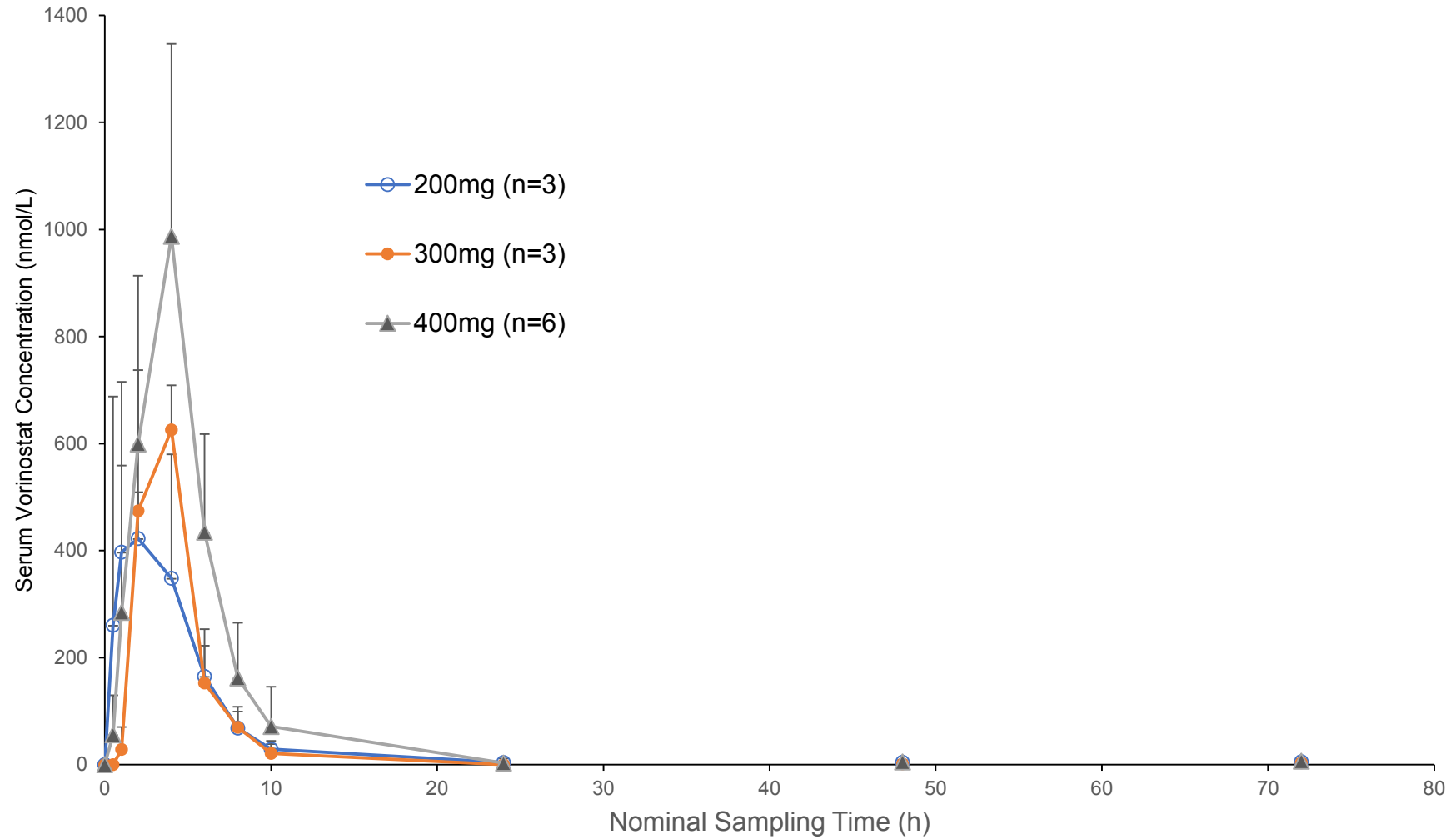
Supplementary table 3. Summary of pharmacokinetic and pharmacodynamic analysis

Level	Case	EGFR	BIM	BSA (m ²)	Acetylated histone H3	BIM _{EL}	Exon 3/4 changing rate (%)	Vorinostat		Gefitinib	
								C _{max} (nmol/L)	AUC _{inf} (nmol · h/L)	C _{max} (ng/mL)	AUC _{inf} (ng · h/L)
1	VN-01	Del 19	WT/Del	1.55	↑	↑	49.7±2.1	430	1500	295	5340
	VN-02	L858R	WT/Del	1.28	↑	→	30.9±3.0	762	2830	360	9320
	VN-03	Del 19	WT/Del	1.63	↑	→	26.7±1.4	615	2960	378	11400
2	VS-01	Del 19	WT/Del	1.58	↑	↑	52.3±2.4	643	2240	349	8270
	VI-01	L858R	WT/Del	1.79	↑	↑	28.6±4.7	641	2260	159	5250
	VN-04	Del 19	WT/Del	1.7	↑	↑	50.7±2.9	699	2950	211	8480
3	VK-01	Del 19	WT/Del	1.54	↑	→	49.3±2.5	1630	8650	802	23400
	VK-02	Del 19	WT/Del	1.72	↑	→	NE	1040	5270	161	NE
	VI-03	Del 19	Del/Del	2.27	→	→	66.5±2.1	789	4050	234	7560
	VS-02	Del 19	WT/Del	1.85	NE	NE	54.4±0.7	847	3420	159	8790
	VN-05	L858R	WT/Del	1.41	↑	↑	47.6±3.6	1040	4490	266	4730
	VN-06	L858R	WT/Del	1.94	↑	→	48±3.5	695	3010	148	3190

BSA : body surface area, Del 19: exon 19 deletion, WT: wild type, Del: deletion, NE : not evaluated, ↑ : increased, → : not discernibly changed.

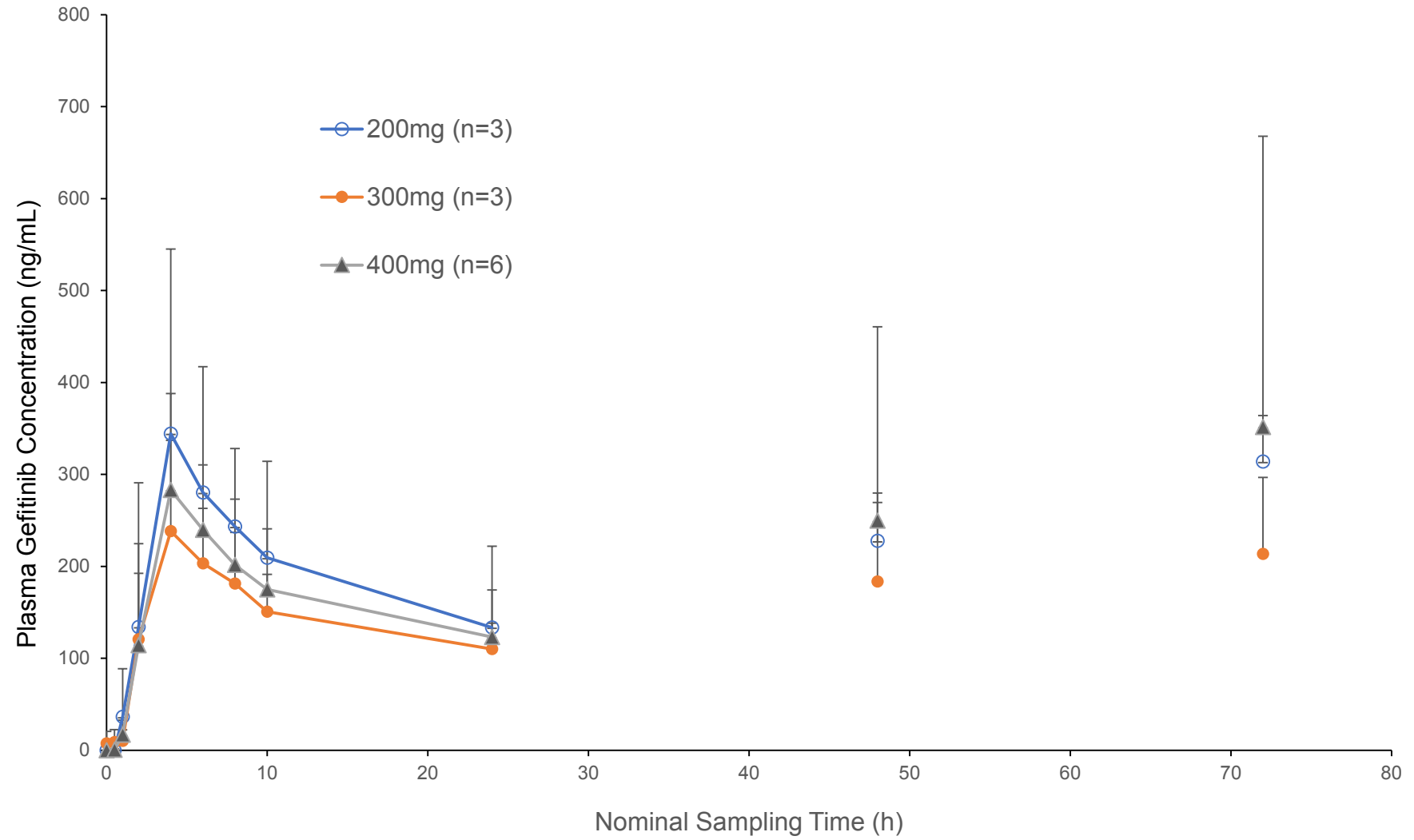


Supplementary figure 1. Study design. Dashed arrows; if no DLTs are observed in all of 3 patients at a lower dose level, an additional 3 patients are recruited. DLTs, dose-limiting toxicities. MTD, maximum tolerated dose. This figure was from the reference 22.



Supplementary figure 2. Kinetics of vorinostat concentration.

Mean (+SD) serum vorinostat concentration by each dose level.



Supplementary figure 3. Time kinetics of gefitinib concentration.
Mean (+SD) plasma gefitinib concentration by each dose level.