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Table S1. Baseline characteristic of patients in Part 1

Characteristic	50 mg/m^2/d*5d (N=2)	75 mg/m^2/d*5d (N=7)	75 mg/m^2/d*7d (N=3)	Total (N=12)
Age, years, median (range)	60.5 (57, 64)	49 (38, 58)	51.0 (48, 62)	50.5 (38, 64)
BMI,kg/m^2, median (range)	23.50 (21.5, 25.5)	24.00 (20.6, 35.3)	21.80 (19.4, 27.7)	23.60 (19.4, 35.3)
Current clinical staging of tumors, n (%)				
Stage IV	2 (100.00)	7 (100.00)	3 (100.00)	12 (100.00)
Primary site of metastasis, n (%)	2 (100.00)	7 (100.00)	3 (100.00)	12 (100.00)
Bone	1 (50.00)	5 (71.43)	2 (66.67)	8 (66.67)
Brain	0	1 (14.29)	0	1 (8.33)
Lung	1 (50.00)	4 (57.14)	1 (33.33)	6 (50.00)
Liver	1 (50.00)	3(42.86)	2 (66.67)	6 (50.00)
Number of metastatic sites， n(%)				
<2	0	0	1 (33.33)	1 (8.33)
≥2	2 (100.00)	7 (100.00)	2 (66.67)	11 (91.67)
ECOG PS， n(%)				
0	1 (50.00)	1 (14.29)	0	2 (16.67)
1	1 (50.00)	6 (85.71)	3 (100.00)	10 (83.33)
Any prior history of anti-tumor drug treatment, n (%)				
Anthracycline or taxane	2 (100)	7 (100)	3 (100)	12 (100)
Targeted therapy	1 (50.00)	7 (100.00)	3 (100.00)	11 (91.67)
Endocrine therapy	1 (50.00)	6 (85.71)	2 (66.67)	9 (75.00)
Prior lines of treatment, median (min, max)				
< 3 prior lines of treatment, n (%)	/	3 (42.86)	2 (66.67)	5 (41.67)
≥ 3 prior lines of treatment, n (%)	2 (100.00)	4 (57.14)	1 (33.33)	7 (58.33)

Abbreviations: BMI, body-mass index; ECOG PS, Eastern Cooperative Oncology Group Performance Status. Patients were assigned to three UTD2 monotherapy dose cohorts: 50 mg/m²/day for 5 days, 75 mg/m²/day for 5 days, and 75 mg/m²/day for 7 days within 21-day cycles. Continuous variables are presented as median (range); categorical variables are reported as n (%).

Table S2. Overall response in full analysis population in Part 1

	50 mg/m^2/d*5d (N=2) n (%)	75 mg/m^2/d*5d (N=7) n (%)	75 mg/m^2/d*7d (N=3) n (%)	Total (N=12) n (%)
Best of Response				
CR	0	0	0	0
PR	1 (50.00)	0	1 (33.33)	2 (16.67)
SD	0	4 (57.14)	1 (33.33)	5 (41.67)
PD	0	3 (42.86)	1 (33.33)	4 (33.33)
NA	1 (50.00)	0	0	1(8.33)
Confirmed ORR，n (%) [95%CI]	1 (50.00) [1.26, 98.74]	0 [NE, NE]	1 (33.33) [0.84, 90.57]	2 (16.67) [2.09, 48.41]
DCR，n (%) [95%CI]	1 (50.00) [1.26, 98.74]	4 (57.14) [18.41, 90.10]	2 (66.67) [9.43, 99.16]	7 (58.33) [27.67, 84.83]

Abbreviations: CI, confidence interval; CR, complete response; DCR, disease control rate; NE, not estimable; ORR, objective response rate; PR, partial response; SD, stable disease; PD, progressive disease; NA, not assessable; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1.

Confirmed ORR was defined as the proportion of patients achieving confirmed CR or PR. DCR included patients with confirmed CR, PR, or SD. Values represent n (%), with 95% CIs calculated for ORR and DCR.

Table S3. Overall response in the full analysis population in Part 3

	UTD2 combined with capecitabine (N=50) n%
Best of Response	
CR	0
PR	23 (46.0)
SD	16 (32.0)
PD	7 (14.0)
NA	4 (8.0)
Confirmed ORR	23 (46.0)
[95%CI]	[31.8, 60.7]
DCR	39 (78.0)
[95%CI]	[64.0, 88.5]

Abbreviations: CI, confidence interval; CR, complete response; DCR, disease control rate; NA, not assessable; ORR, objective response rate; PR, partial response; PD, progressive disease; SD, stable disease; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1.

Confirmed ORR equals the proportion of patients with confirmed CR or PR. DCR equals the proportion of patients with confirmed CR, PR, or SD. Values represent n (%), with 95% CIs for ORR and DCR.

Table S4. Grade 3 or above Treatment-emergent adverse events in Part 1

	50 mg/m^2/d*5d (N=2) n(%)	75 mg/m^2/d*5d (N=7) n(%)	75 mg/m^2/d*7d (N=3) n(%)	Total (N=12) n(%)
Grade ⩾3 TEAEs	0	3(42.86)	3(100.00)	6(50.00)
Asthenia	0	0	2(66.67)	2(16.67)
Diarrhea	0	1(14.29)	1(33.33)	2(16.67)
Neuropathy peripheral	0	1(14.29)	0	1(8.30)
Insomnia	0	1(14.29)	0	1(8.30)
Neutropenia	0	1(14.29)	0	1(8.30)

Abbreviation: TEAE, treatment-emergent adverse event.

Adverse events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 5.0 (NCI-CTCAE v5.0). All listed events are treatment-emergent regardless of investigator-attributed causality to study drug. Values are n (%).

Table S5. Pharmacokinetic Parameters for a Single Dose of Utidelone Capsule (UTD2) and Utidelone Injection (UTD1; Part 2)

Drug	Parameters	C_{max} (ng/ml)	AUC_{0-t} (h•ng/ml)	AUC_{inf} (h*ng/mL)	T_{max} (h)	$t_{1/2}$ (h)	Cl (ml/h)	Vz (ml)
UTD2 (N=19)	mean	477.43	1708.862	2045.029	1.316	7.179	57845.590	631472.508
	SD	345.31	991.272	1093.858	0.807	2.081	25540.850	381066.536
UTD1 (N=19)	mean	943.00	3037.797	3235.806	1.448	7.983	16183.495	188310.339
	SD	444.75	1011.206	1003.428	0.385	1.894	4679.151	77261.810

Abbreviations: AUC_0-t, area under concentration-time curve to last quantifiable time point; AUCinf, area under the curve extrapolated to infinity; Cl, total clearance; Cmax, maximum plasma concentration; SD, standard deviation; Tmax, time to maximum concentration; $t_{1/2}$, terminal elimination half-life; Vz, volume of distribution.

Concentration is reported in ng/mL; exposure in ng*h/mL; time in hours; clearance and volume in mL.

Of the 20 enrolled patients, one patient did not undergo blood sampling following UTD1 administration, and one patient did not provide blood samples after UTD2 dosing. Accordingly, the evaluable sample size was 19 patients for both UTD1 and UTD2.

Table S6. The Absolute Bioavailability(F) for Utidelone Capsules (UTD2; Part 2)

	UTD2		UTD1		F %(90%CI)
	n	Geo-mean	n	Geo-mean	
C_{max}(ng/mL)	14	380.44	19	850.49	22.42(15.94，31.52)
AUC_{0-t}(h*ng/mL)	14	1524.28	19	2728.27	28.13(23.94，33.04)
$AUC_{0-\infty}$(h*ng/mL)	12	1870.48	18	2974.82	31.80(27.26，37.09)

Abbreviations: AUC_0-t, area under the plasma concentration-time curve up to last measurable concentration; AUC_0-∞, area under the plasma concentration-time curve extrapolated to infinity; Cmax, maximum observed plasma concentration; Geo-mean, geometric mean; UTD1, intravenous utidelone injection; UTD2, oral utidelone capsules; 90% CI, 90% confidence interval.

Absolute bioavailability (F%) of oral UTD2 was calculated relative to intravenousUTD1 using dose-normalized pharmacokinetic parameters. Geometric mean values are presented for Cmax, AUC_0-t, and AUC_0-∞. F% represents the ratio of dose-normalized geometric mean exposures for UTD2 versus UTD1. N values indicate number of evaluable participants for each parameter. Concentration units: ng/mL; exposure units: h·ng/mL.

For PK parameters of UTD2, among the 20 patients enrolled in Part 2, one patient had no blood sampling performed after UTD2 dosing, and five patients were excluded from the analysis due to uncertain fasting status. Therefore, geometric mean values for C_{max} and AUC_{0-t} were derived from data of 14 patients. Furthermore, one additional patient was excluded owing to an $AUC_{_\%Extrap}$ >20%, and PK data from another patient precluded reliable estimation of $AUC_{0-\infty}$; accordingly, geometric mean for $AUC_{0-\infty}$ was based on 12 patients.

For PK parameters of UTD1, of the 20 patients enrolled in Part 2, one patient did not undergo blood sampling following UTD1 administration. Thus, geometric mean values for C_{max} and AUC_{0-t} were calculated from 19 patients. In addition, one patient was excluded because of $AUC_{_\%Extrap}$ >20%, resulting in a sample size of 18 patients for the geometric mean of $AUC_{0-\infty}$.

Table S7. Effect of Food on Pharmacokinetic Parameters for Utidelone Capsules (UTD2): Comparison of Fed versus Fasting Administration (Part 2)

UTD2	C_{max} (ng/mL)		AUC_{0-t}(h*ng/mL)		AUC_{inf}(h*ng/mL)	
	Fed (N=15)	**Fasting (N=19)**	**Fed (N=15)**	**Fasting (N=19)**	**Fed (N=4)**	**Fasting (N=16)**
Mean	167.04	477.43	1565.197	1708.862	1508.633	2045.029
SD	98.63	345.31	888.736	991.272	169.391	1093.858
CV%	59.05	72.33	56.781	58.008	11.228	53.489
Geo-mean	142.51	370.92	1351.520	1475.745	1501.377	1812.294
CV%-GM	64.85	88.59	61.366	59.618	11.435	52.709

Abbreviations: AUC0-t, area under the plasma concentration-time curve up to last measurable concentration; AUCinf, area under the plasma concentration-time curve extrapolated to infinity; Cmax, maximum observed plasma concentration; CV%, coefficient of variation; CV%-GM, coefficient of variation based on geometric mean; Geo-mean, geometric mean; SD, standard deviation.

Pharmacokinetic parameters were summarized for participants receiving UTD2 under fasting and fed conditions. Concentration units: ng/mL; exposure units: ng*h/mL.

Under fasting conditions, among the 20 patients enrolled in Part 2, one patient had no blood sampling after UTD2 dosing. Analyses of for C_{max} and AUC_{0-t} were therefore derived from data of 19 patients. In addition, PK data from three patients precluded reliable estimation of $AUC_{0-\infty}$, thus, the analyses of for $AUC_{0-\infty}$ was based on 16 patients.

Under fed conditions, of the 20 patients enrolled in Part 2, five patients did not undergo post-dose blood sampling following UTD2 administration. Accordingly, analyses of for C_{max} and AUC_{0-t} were calculated from 15 patients. Furthermore, PK data from 11 patients prevented robust determination of $AUC_{0-\infty}$, resulting in a sample size of four patients for the analyses of $AUC_{0-\infty}$.

Table S8. Pharmacokinetic Parameters for a Single Dose of Utidelone Capsule (UTD2; Part 3)

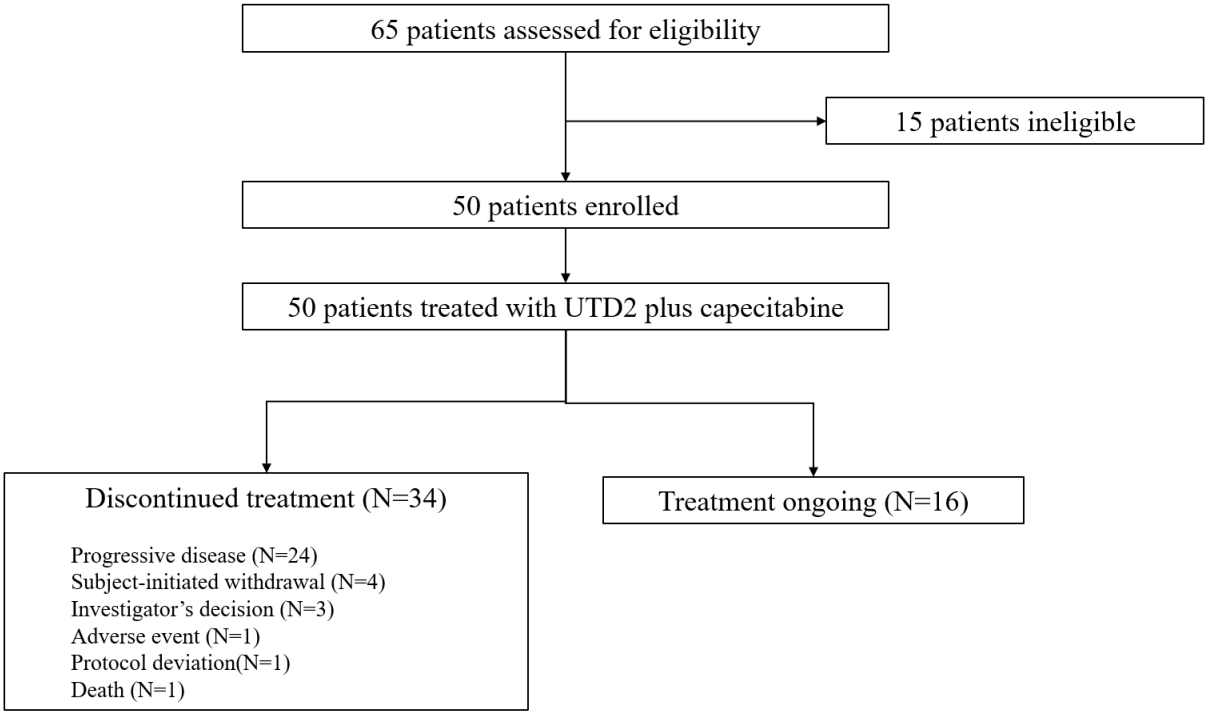
	C_{max} (ng/mL)	AUC_{0-t} (h*ng/mL)	AUC_{inf} (h*ng/mL)	T_{max} (h)	$t_{1/2z}$ (h)	CL/F (ml/h)	VZ/F (ml)
n	12	12	11	12	11	11	11
Mean	615.17	2003.717	2390.004	1.213	8.735	54635.038	708234.308
SD	404.11	1456.328	1653.335	0.910	1.411	26156.343	387528.268
CV%	65.7	72.7	69.2	75.0	16.2	47.9	54.7
Geo-mean	498.82	1663.939	2015.671	1.045	8.638	47638.693	593461.473
CV%-GM	81.3	65.9	63.2	53.8	15.7	65.4	77.0

Abbreviations: AUC0-t, area under concentration-time curve to last quantifiable time point; AUCinf, area under the curve extrapolated to infinity; Cl, total clearance; Cmax, maximum plasma concentration; SD, standard deviation; Tmax, time to maximum concentration; $t_{1/2}$, terminal elimination half-life; Vz, volume of distribution.

Concentration is reported in ng/mL; exposure in ng*h/mL; time in hours; clearance and volume in mL.

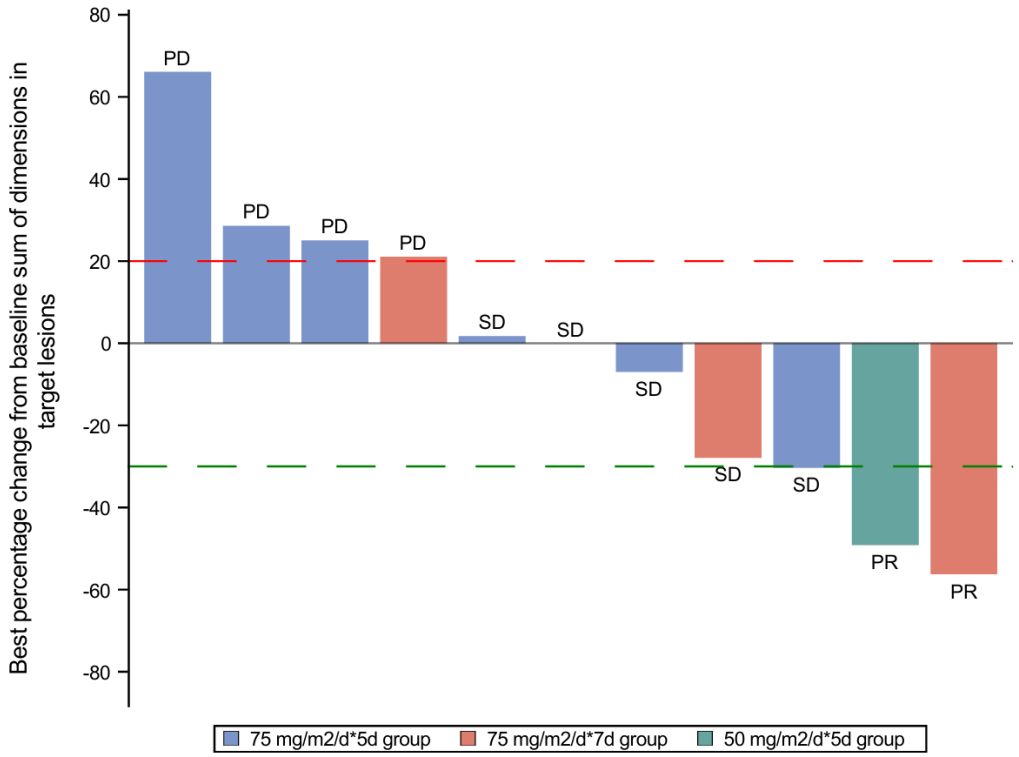
Among 12 patients with PK sampling in Part 3, data from 1 patient precluded reliable calculation of AUCinf, $t_{1/2}$z, CL/F, and Vz/F, leaving 11 patients available for analyses of these PK parameters.

Figure S1. Patient Flow Diagram in Part 3



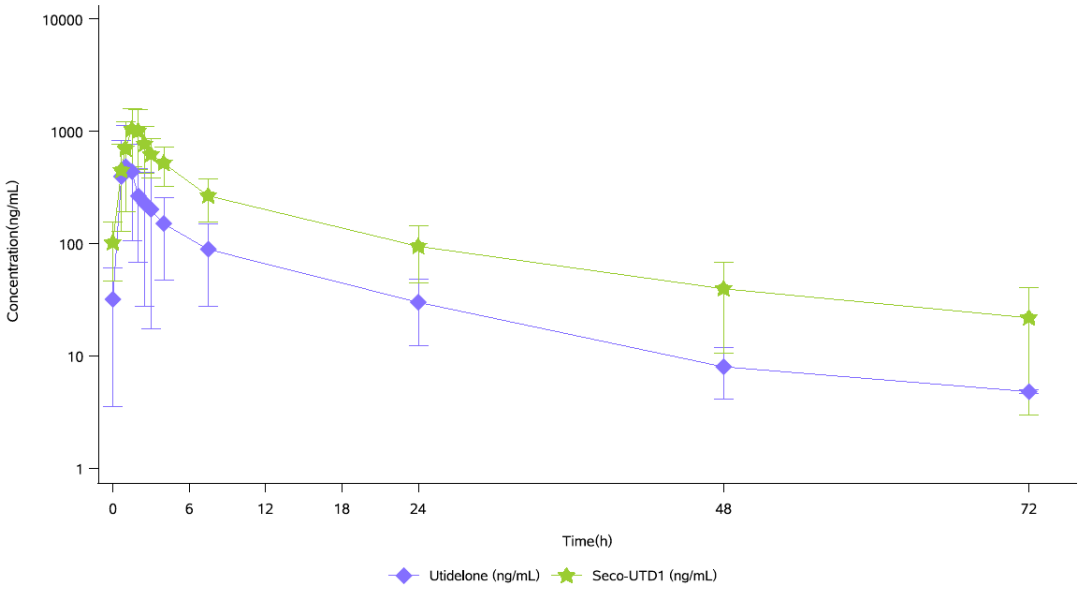
Of 65 patients assessed for eligibility, 15 patients were ineligible and 50 patients were enrolled in part 3 and received treatment with UTD2 plus capecitabine. Among treated patients, 34 patients discontinued treatment due to progressive disease (n=24), subject-initiated withdrawal (n=4), investigator's decision (n=3), adverse event (n=1), protocol deviation (n=1), and death (n=1). Sixteen patients remained on ongoing treatment.

Figure S2. Best percentage change from baseline sum of dimensions in target lesions in Part 1



Each bar represents one individual patient; bars are color-coded according to UTD2 dose cohort. Bars extending upward indicate tumor reduction, whereas bars extending downward indicate tumor increase. Horizontal dashed reference lines mark RECIST v1.1 thresholds: 30% reduction for partial response (PR) and 20% increase for progressive disease (PD). Tumor response status (PR, stable disease [SD], PD) is annotated for each patient.

Figure S3. Plasma Concentration-Time Curve of Utidelone Following Multiple Dosing (Part 3)



Error bars represent standard deviation. X-axis represents time in hours after drug administration; y-axis represents plasma concentration in ng/mL on a semi-logarithmic scale. Abbreviation: Seco-UTD1, seco-utidelone metabolite.