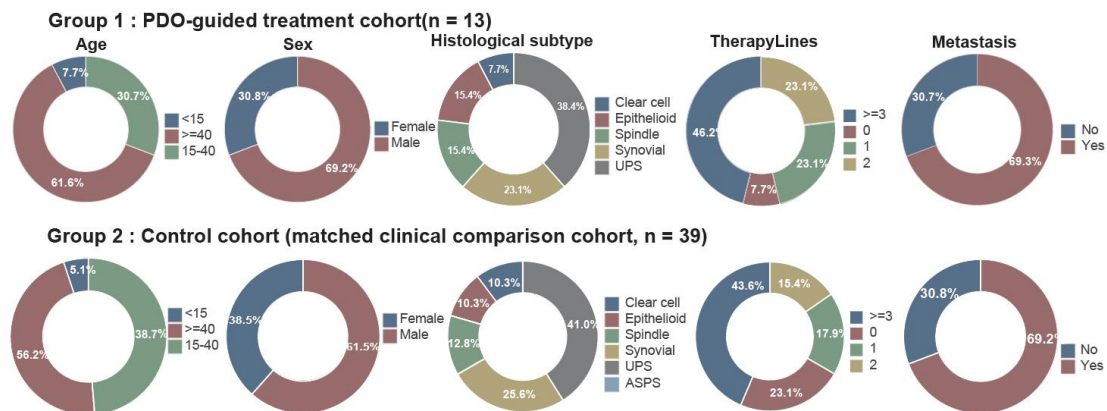




Supplementary Figure 1. Baseline characteristics of the PDO-guided treatment cohort and matched clinical comparison cohort.

Baseline clinical characteristics of patients included in the PDO-guided treatment cohort (n = 13) and the matched clinical comparison cohort (n = 39). Patient distributions are presented for age, sex, histological subtype, previous lines of systemic therapy, and metastatic disease status. Percentages are shown within each donut chart. The matched clinical comparison cohort was selected from patients receiving conventional treatment without PDO guidance.

Characteristic	Category	No. of Patients N=24 (%)
Age, years	Median (range)	42 (13–74)
	<15	1 (4.2)
	15–40	10 (41.6)
	≥40	13 (54.2)
Sex	Male	18 (75.0)
	Female	6 (25.0)
Histological subtype	UPS	7 (29.2)
	Synovial sarcoma	5 (20.8)
	Spindle cell sarcoma	4 (16.7)
	Clear cell sarcoma	3 (12.5)
	Epithelioid sarcoma	3 (12.5)
	ASPS	2 (8.3)
	Other	0 (0.0)
Previous lines of systemic therapy	0(treatment-naïve)	3 (12.5)
	1 line	5 (20.8)
	2 lines	6 (25.0)
	≥3 lines	10 (41.7)
Metastatic/recurrent disease at PDO establishment	Yes	16 (66.7)
	No	8 (33.3)
New metastatic/recurrent lesions after PDO sampling	Yes	7 (29.2)
	No	17 (70.8)
Specimen source for PDO	Surgical resection	12 (50.0)
	Biopsy	9 (37.5)
	Other	3 (12.5)
Tumor site used for PDO generation	Primary lesion	20 (83.3)
	Metastatic lesion	3 (12.5)
	Other	1 (4.2)

Supplementary Table 1. Baseline characteristics of patients undergoing PDO-based drug sensitivity testing .

Data are presented as median (range) for continuous variables and number (percentage) for categorical variables. Percentages were calculated based on the total number of patients (N = 24).

Cohort	No. of patients	Median cumulative PFS (months)	95% CI
Control	28	6.22	4.86–7.58
PDO-guided	9	18.88	0.00–44.36

Statistical comparison: Log-rank test, $\chi^2 = 5.780$, $P = 0.016$.

Supplementary Table 2. Cumulative progression-free survival analysis between PDO-guided and control cohorts.

Cumulative progression-free survival (PFS) was calculated based on the sum of progression-free survival durations across consecutive treatment lines. Survival curves were estimated using the Kaplan–Meier method and compared using the log-rank test.

Prior systemic therapy lines	No. of patients	Maximum PDO inhibition rate (%), median (IQR)
0	11	76.3 (62.4–83.3)
1	4	55.8 (52.1–69.4)
2	3	44.8 (26.5–61.9)
≥3	6	49.4 (38.8–61.0)

Supplementary Table 3. Maximum PDO inhibition rate stratified by prior systemic therapy line.

The maximum PDO inhibition rate represents the highest tumor inhibitory activity observed among all tested therapeutic regimens for each PDO model. Data are presented as median with interquartile range (IQR). Prior systemic therapy lines were defined according to the number of systemic treatment regimens received before PDO drug sensitivity testing. PDO, patient-derived organoid.

Components	Final Concentration	Source (Vendor)
Advance DMEM-F12	1×	Gibco
HEPES	10 mmol/L	Gibco
Glutamax	1×	Gibco
Penicillin Streptomycin	100 U/mL/100 µg/mL	Gibco
B27 Supplement	1 ×	Gibco
EGF	50 ng/mL	Peprtech
FGF-10	100 ng/mL	Peprtech
N2 Supplement	1 ×	Peprtech
Noggin	100 ng/mL	Peprtech
R-Spondin-1	500 ng/mL	peprtech
Forskolin	10 µmol/L	TOCRIS
A83-01	0.5 µmol/L	Tocris

Supplementary Table 4. Composition of culture medium used for TUD-derived PDO maintenance and expansion.

The listed components represent the final concentrations used for patient-derived organoid (PDO) culture.

Commercial sources of supplements and growth factors are indicated. PDO, patient-derived organoid; TUD, tumors of uncertain differentiation.

Components	Final Concentration	Source (Vendor)	Cat. No.
Gemcitabine	18.56 ug/ml	Topscience	T0251
Eribulin	0.52 ug/ml	Topscience	T13688
Cabozantinib	1.776 ug/ml	Topscience	T2586
Trabectedin	1.26 ng/ml	Topscience	T17155
Doxorubicin	543 ng/ml	Topscience	T1456
Ifosfamide	26.1 µg/mL	Topscience	T1055
Etoposide	11.1 µg/mL	Topscience	T0132
Vincristine	150 ng/ml	Topscience	T3S0209
Pazopanib	46 µg/mL	Topscience	T0097L
Pembrolizumab	91 µg/mL	Topscience	T9908
Toripalimab	83 µg/mL	Topscience	T77117
Dacarbazine	20 µg/mL	Topscience	T1120
Anlotinib	0.1 µg/mL	Coolpharm	KH-88104
Temozolomide	8 µg/mL	Topscience	T1178
Chidamide	0.2 µg/mL	Topscience	T4481
Regorafenib	2 µg/mL	Topscience	T1792
Fruquintinib	0.1 µg/mL	Topscience	T2656
Palbociclib	0.1 µg/mL	Topscience	T1785
Actinomycin D	0.02 µg/mL	Topscience	TN9827
Atezolizumab	150 µg/mL	Topscience	T9902
Adebrelimab	80 µg/mL	Topscience	T76899
Cadonilimab	100 µg/mL	Topscience	T76716
Crizotinib	0.2 µg/mL	Topscience	T1661
Epirubicin	1 µg/mL	Topscience	T69093
Docetaxe	2 µg/mL	Topscience	T0186
Selumetinib	0.2 µg/mL	Topscience	T6218
Olaparib	5 µg/mL	Topscience	T3015
Dasatinib	0.1 µg/mL	Topscience	T1448
Lenvatinib	0.05 µg/mL	Topscience	T0520
Paclitaxel	3 µg/mL	Topscience	T0968
Cisplatin	2 µg/mL	Topscience	T1564
Cyclophosphamide	20 µg/mL	Topscience	T0707L
Sorafenib	3 µg/mL	Topscience	T0093L
Apatinib	0.5 µg/mL	Topscience	T71204
Vorolanib	0.1 µg/mL	Topscience	T8491
Irinotecan	1 µg/mL	Topscience	T6228
Ivonescimab	100 µg/mL	Topscience	T77046
Ipilimumab	50 µg/mL	Topscience	T9906
Imatinib	2 µg/mL	Topscience	T6230
Durvalumab	100 µg/mL	Topscience	T11126
Utidelone	0.5 µg/mL	Topscience	TQ0202
Camrelizumab	80 µg/mL	Topscience	T37535
Vinorelbine	0.05 µg/mL	Topscience	T0190

Surufatinib	0.1 µg/mL	MedChemExpress	HY-12297
Everolimus	0.05 µg/mL	MedChemExpress	HY-10218
Cetuximab	150 µg/mL	TargetMol	T9905

Supplementary Table 5. Drugs and treatment conditions used for PDO-based drug sensitivity testing,

The table summarizes the therapeutic agents evaluated in PDO-based drug sensitivity assays, including drug names, final concentrations, manufacturers, and catalog numbers. Drug concentrations represent the final concentrations applied during ex vivo PDO treatment. Combination regimens were generated by combining individual agents at the indicated concentrations.