

Figure S1. Kaplan-Meier curves of event-free survival. HR, hazard ratio; CI, confidence interval.

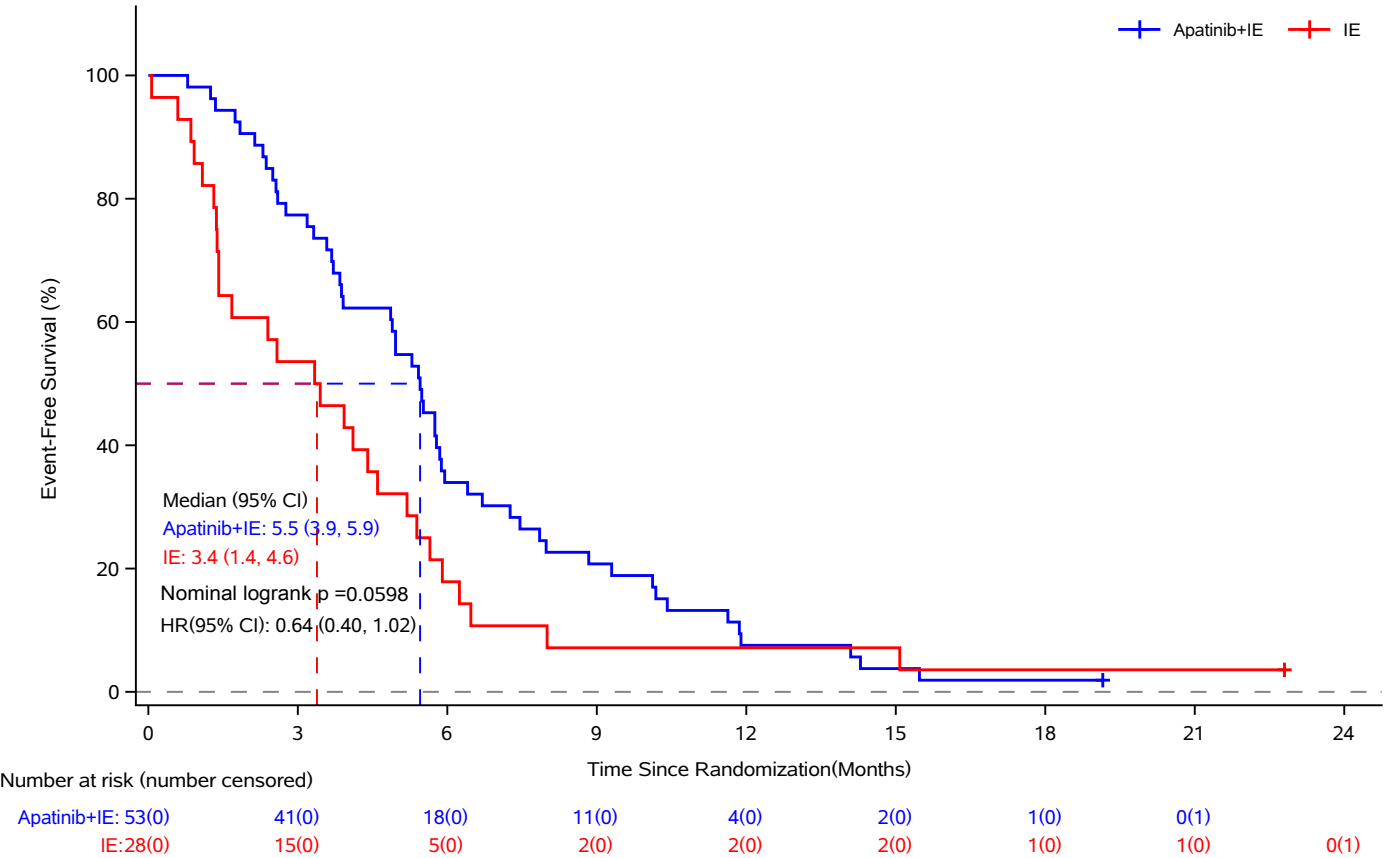


Figure S2. Tumor response. (A) The best percentage changes from baseline in target lesions; (B) treatment exposure and duration of response. CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; NE, not estimable.

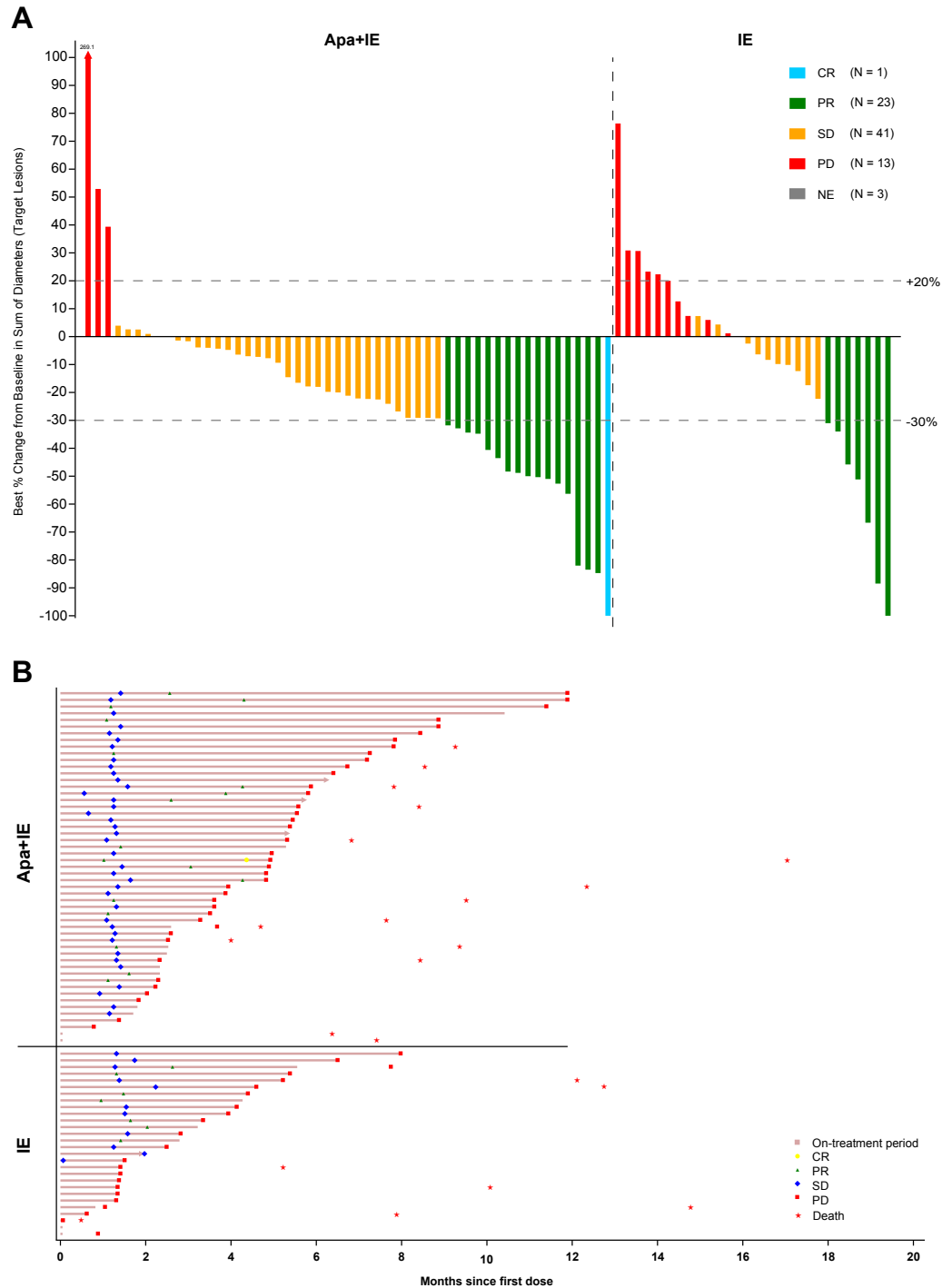


Figure S3. First-line chemotherapy regimens for osteosarcoma in mainland China. DOX: doxorubicin; CDDP: cisplatin; IFO: ifosfamide; HDMTX: high-dose methotrexate

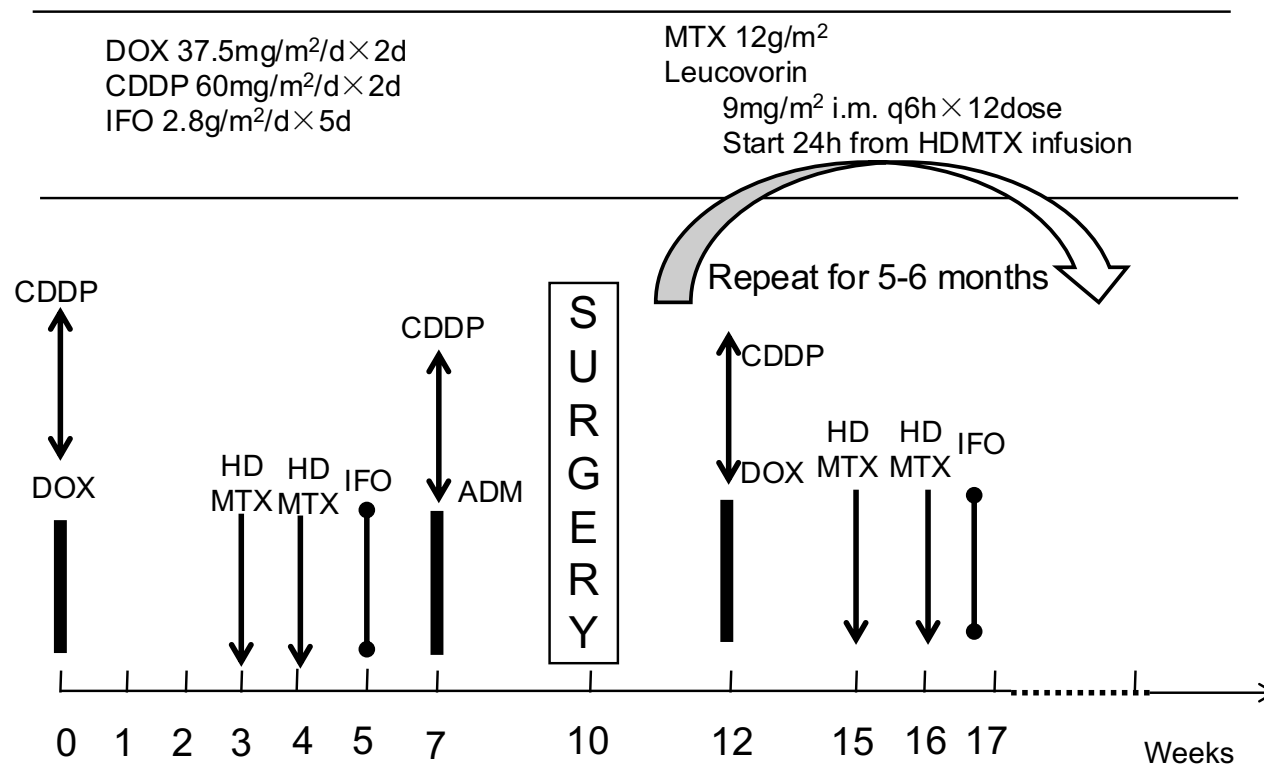


Table S1. Systemic therapy after disease progression

Therapy	Apa+IE group (n=53)	IE group (n=28)
No further treatment (OS event)	16 (30.2%)	5 (18.9%)
Chemotherapy plus TKI	10 (18.9%)	4 (14.3%)
Chemotherapy	9 (17.0%)	6 (21.4%)
TKI	5 (9.4%)	2 (7.1%)
Chemotherapy plus PD-1 inhibitor	4 (7.5%)	1 (3.6%)
ADC	1 (1.9%)	4 (14.3%)
PD-1 inhibitor	1 (1.9%)	3 (10.7%)
Chemotherapy, PD-1 inhibitor and TKI	1 (1.9%)	0
TKI plus PD-1 inhibitor	1 (1.9%)	0
Radiotherapy	1 (1.9%)	0
Other therapies	2 (3.8%)	2 (7.1%)
Unknown	2 (3.8%)	1 (3.6%)

OS, overall survival; TKI, tyrosine kinase inhibitor; PD-1, programmed cell death protein-1; ADC, antibody-drug conjugate

Table S2. Quality of life

Apa+IE group	Baseline (n/N=52/53)	C3 (n/N=41/47)	C5 (n/N=27/36)	C7 (n/N=23/28)	C9 (n/N=10/15)	P
Global health status	47.12±22.378	50.83±20.569	53.09±25.544	56.52±19.936	56.67±12.298	0.042
Functional scales						
Physical	58.21±26.309	59.72±22.286	57.90±26.168	58.26±24.636	59.33±15.219	0.549
Role	49.36±28.766	48.78±27.736	47.53±28.758	53.62±28.407	56.67±16.102	0.397
Emotional	72.92±19.587	72.15±16.203	67.28±25.833	70.53±22.202	65.00±17.916	0.116
Cognitive	81.73±18.453	82.93±19.180	77.78±25.737	74.64±28.369	80.00±20.488	0.946
Social	55.45±26.346	50.00±24.152	50.00±29.957	53.62±26.570	43.33±11.653	0.146
Symptom scales						
Fatigue	32.91±19.428	36.59±20.222	39.09±26.216	43.00±25.581	41.11±13.907	0.420
Nausea and vomiting	17.63±16.963	25.20±20.791	32.10±30.286	34.06±29.932	23.33±16.102	0.026
Pain	26.28±25.639	28.46±25.885	22.84±26.209	24.64±27.001	18.33±16.574	0.990
Dyspnoea	13.46±22.150	13.01±18.071	16.05±21.424	11.59±19.092	13.33±17.213	0.997
Insomnia	20.51±25.696	26.02±25.290	22.22±22.646	30.43±28.272	33.33±22.222	0.003
Appetite loss	28.85±21.922	30.08±26.672	38.46±30.829	43.48±30.871	36.67±24.595	0.493

Constipation	20.51±21.034	19.51±22.330	18.52±21.350	23.19±23.430	26.67±21.082	0.749
Diarrhoea	12.82±16.375	24.39±27.913	33.33±29.235	37.68±32.262	43.33±27.442	0.014
Financial difficulties	58.67±31.986	60.00±30.382	60.49±30.714	50.72±31.574	60.00±14.055	0.423
IE group	Baseline (n/N=25/28)	C3 (n/N=17/22)	C5 (n/N=6/13)	C7 (n/N=4/5)	C9 (n/N=2/3)	P
Global health status	55.90±26.521	67.16±24.908	72.22±20.184	45.83±22.048	29.17±17.678	0.678
Functional scales						
Physical	55.20±31.063	60.49±30.730	66.67±18.379	46.67±29.313	50.00±14.142	0.447
Role	49.33±37.106	53.92±32.021	50.00±29.814	33.33±45.134	8.33±11.785	0.605
Emotional	65.00±25.345	78.92±22.267	80.56±16.387	83.33±13.608	58.33±11.785	0.463
Cognitive	81.33±21.688	91.18±13.330	88.89±13.608	91.67±16.667	83.33±0.000	-
Social	47.33±35.901	59.80±33.364	58.33±39.087	37.50±43.833	16.67±23.570	0.822
Symptom scales / items						
Fatigue	40.00±24.003	36.60±18.743	35.19±16.355	33.33±24.003	38.89±7.857	0.911
Nausea and vomiting	24.00±23.114	18.63±21.150	5.56±8.607	8.33±9.623	58.33±35.355	0.500
Pain	30.67±27.504	19.61±26.507	19.44±22.153	12.50±15.957	25.00±11.785	0.257
Dyspnoea	16.00±21.773	11.76±20.211	5.56±13.608	16.67±19.245	33.33±0.000	-

Insomnia	21.33±25.240	15.69±23.914	16.67±18.257	16.67±19.245	50.00±70.711	0.522
Appetite loss	36.00±31.798	25.49±27.712	5.56±13.608	0.00±0.000	50.00±23.570	0.340
Constipation	22.67±24.944	11.76±20.211	5.56±13.608	16.67±19.245	33.33±0.000	0.530
Diarrhoea	10.67±15.870	7.84±14.575	5.56±13.608	16.67±19.245	0.00±0.000	0.502
Financial difficulties	69.33±34.588	56.86±38.666	50.00±40.825	66.67±47.140	83.33±23.570	0.835

n represents the number of patients who underwent assessment for each cycle, while N denotes the number of patients who were on treatment for each cycle.