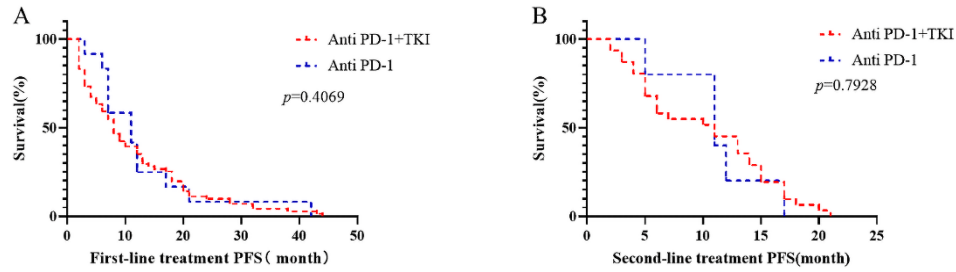
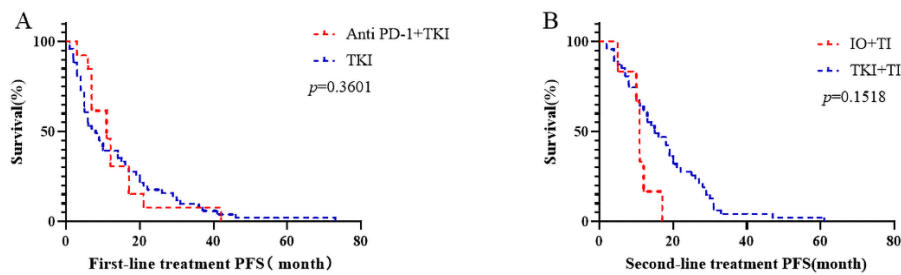


**Supplementary Figure1:** The progression-free survival (PFS) was compared between first-line targeted therapy combined immunotherapy and first-line immunotherapy alone. (TI:TKI combined Immunotherapy, IO: Immunotherapy).



**Supplementary Figure2:** A: PFS was compared between first-line immunotherapy and first-line targeted therapy; B: The PFS of targeted combined immunotherapy after progression on first-line immunotherapy and targeted combined immunotherapy after progression on first-line targeted therapy were compared. (IO: Immunotherapy).



Supplementary table 1. Adverse reactions

Treatment-related AEs		First-line Immunotherapy group		Second-line Immunotherapy group		<i>p</i> value
		NO(%)		NO(%)		
		first-line	second-line	first-line	second-line	
Bone marrow suppression						
Grade 1-2		45(53)	50 (59)	25(49)	32(63)	0.93
Grade 3		21(25)	19(23)	12(24)	10(20)	0.97
Grade 4		18(22)	15(18)	14(27)	9(17)	0.96
Elevated enzymes	liver					
Grade 1-2		30(36)	27(32)	16(31)	19(37)	0.88
Grade 3		4(5)	6(7)	3(6)	6(12)	0.82
Hypertension						
Grade 1-2		9(11)	11(13)	6(12)	7(14)	0.99
Grade 3		3(4)	4(5)	5(10)	5(10)	0.31
Proteinuria		17(20)	15(18)	12(24)	10(20)	0.96
Deep venous thrombosis						
Feeble		7(8)	8(10)	5(10)	5(10)	0.99
Hand-foot syndrome		11(13)	9(11)	6(12)	8(16)	0.85