

Fig S1. Patient enrollment and sample selection flowchart

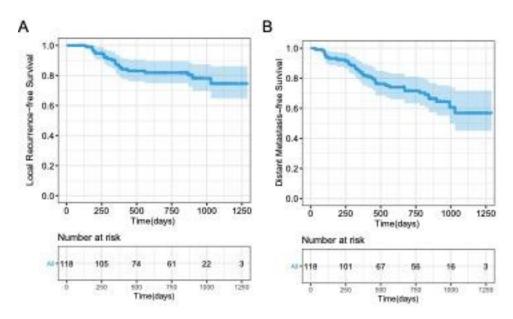


Fig S 2. Kaplan–Meier curve of locoregional recurrence-free survival (LRFS)(A) and distant metastasis-free survival (DMFS) (B) of all patients.

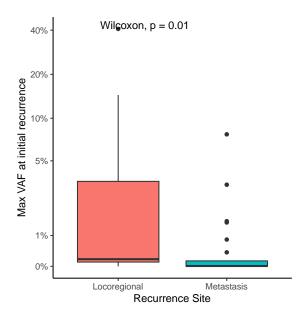


Fig S3. Comparison of ctDNA level at the time of initial recurrence between locoregional recurrence and metastasis only patients

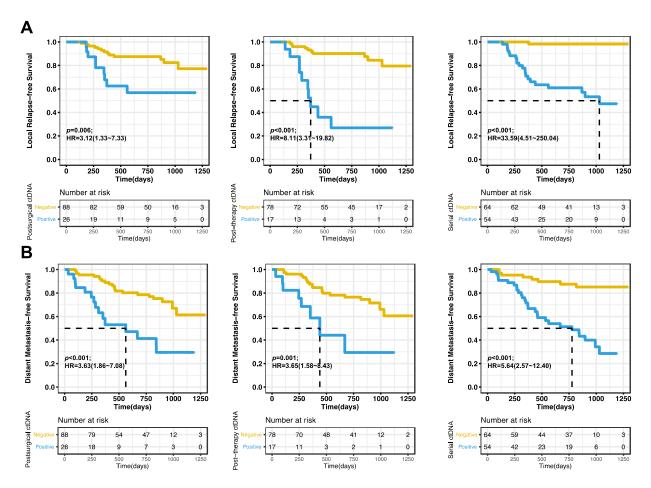


Fig S4. Kaplan–Meier curve of locoregional recurrence-free survival (LRFS)(A) and distant metastasis-free survival (DMFS) (B) in patients stratified by postsurgical ctDNA status, post-adjuvant therapy ctDNA status or longitudinal serial ctDNA status.

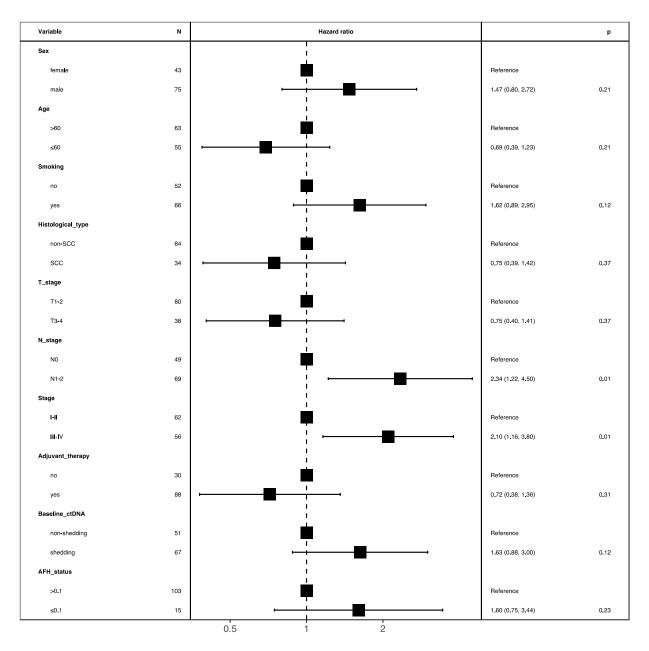


Fig S5A. Univariate cox regression analysis of baseline risk factor for disease-free survival (DFS)

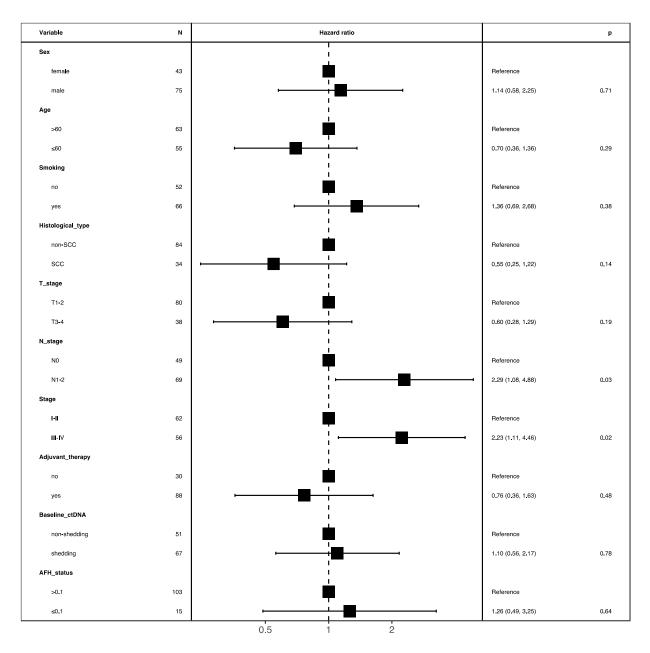


Fig S5B. Univariate cox regression analysis of baseline risk factors for distant metastasis-free survival (DMFS)

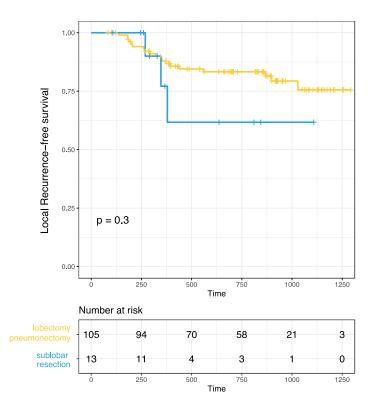


Fig S6A. Kaplan-Meier curve of LRFS in patients stratified by operative methods.

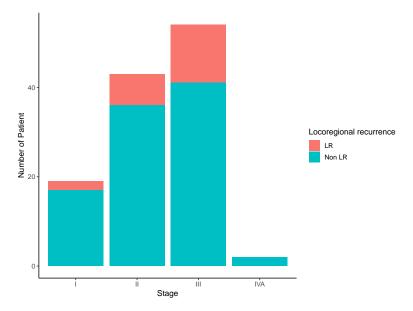


Fig S6B. Ratio of the locoregional recurrence in relation to the pathological stage.

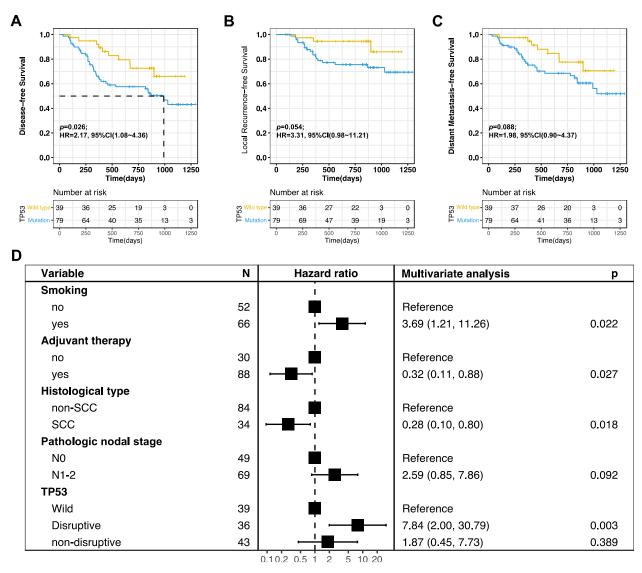


Fig S7. Kaplan–Meier curve of DFS (A), LRFS (B) and DMFS (C) in patients stratified by TP53 status. (D) Multivariate cox regression analysis of selected prognostic factors and TP53 mutation categories for LRFS

Variable	N	Hazard ratio	Multivariate analysis	р
Adjuvant therapy		l I		
No	30	L L L L L L L L L L L L L L L L L L L	Reference	
chemo/radio	75	⊢∎	0.36 (0.13, 0.95)	0.04
Targeted	13		0.46 (0.04, 5.73)	0.54
Histological type		I I		
non-SCC	84		Reference	
SCC	34		0.56 (0.22, 1.43)	0.23
Pathologic nodal stage				
NO	49		Reference	
N1-2	69	¦	3.48 (1.18, 10.33)	0.02
EGFR status		l l		
wild type	73	<b>H</b>	Reference	
mutant	45	·	0.19 (0.04, 0.86)	0.03

Fig S8. Multivariate cox regression analysis of selected prognostic factors and EGFR status for LRFS