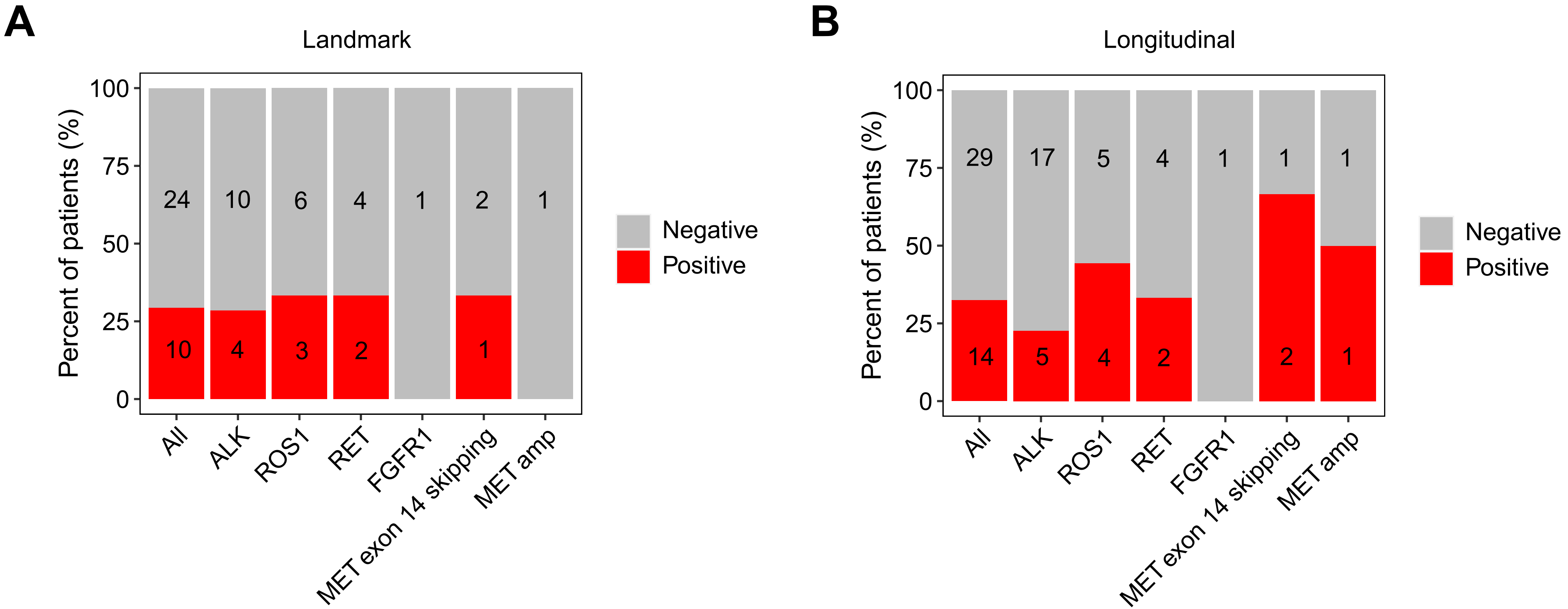
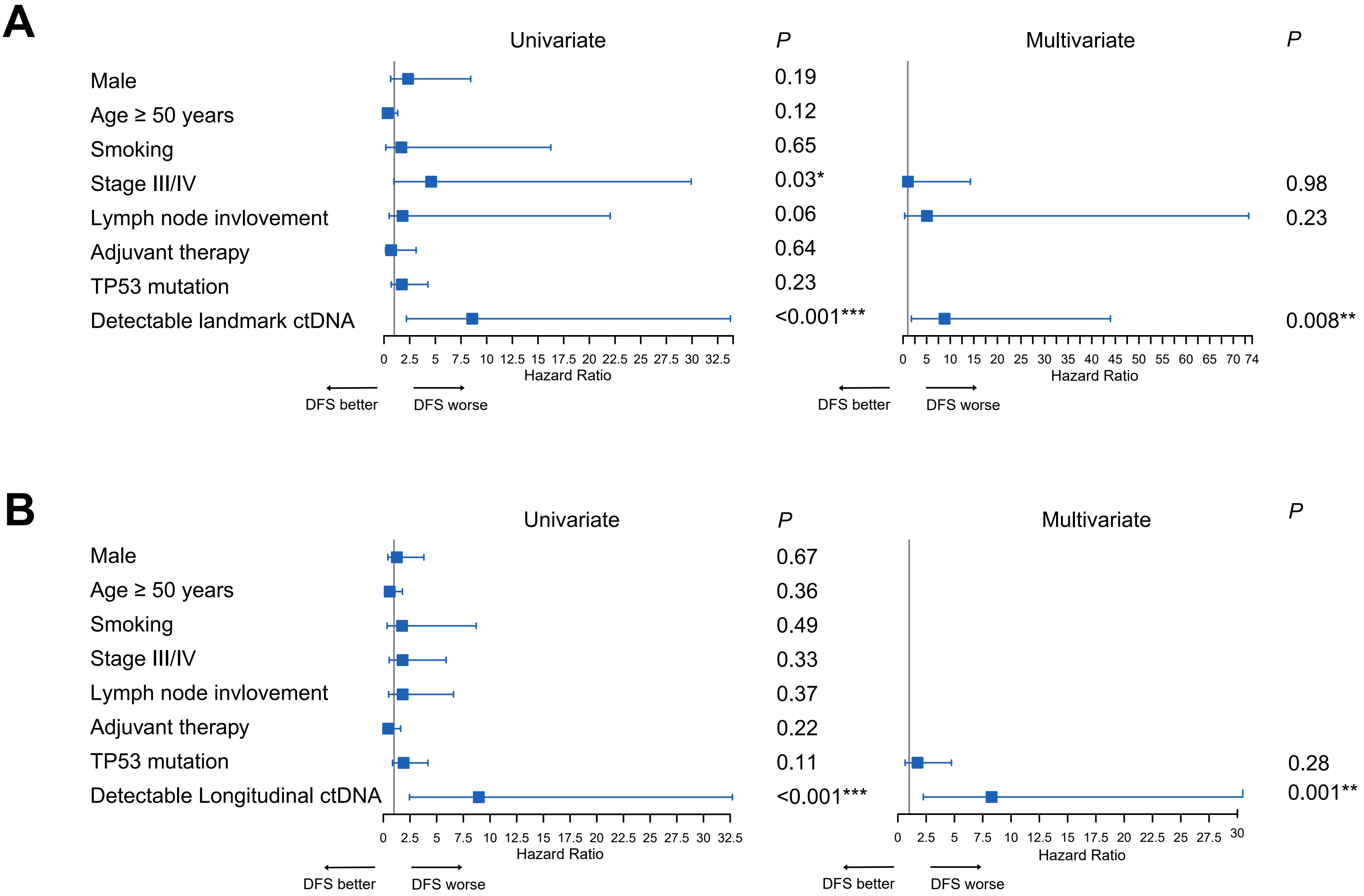
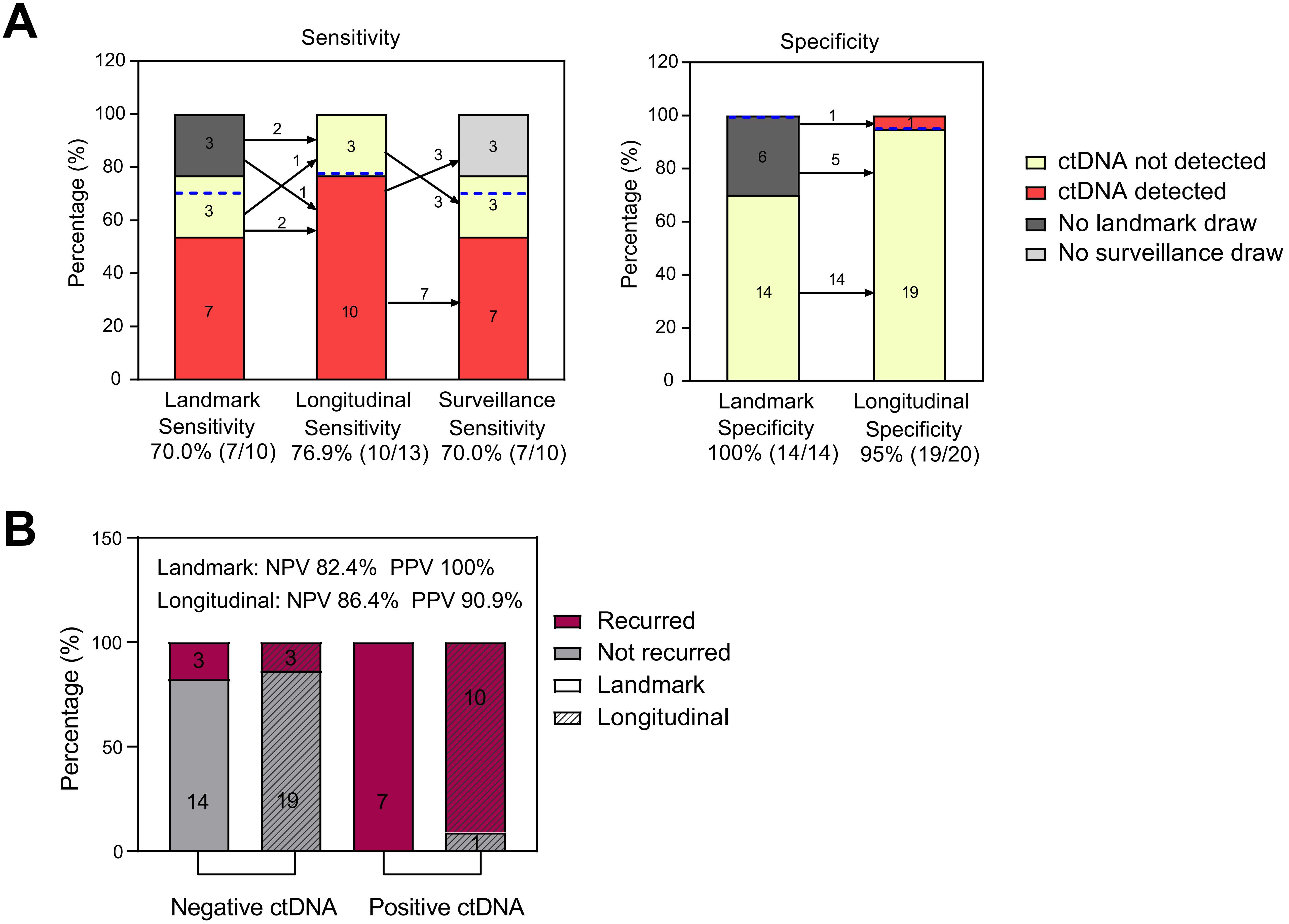

A
Landmark
Percent of patients (%)
100
75
50
25
0
24
10
6
4
1
2
1
10
4
3
2
1
All
ALK
ROS1
RET
FGFR1
MET exon 14 skipping
MET amp
Negative
Positive
B
Longitudinal
Percent of patients (%)
100
75
50
25
0
29
17
5
4
1
1
1
14
5
4
2
2
1
All
ALK
ROS1
RET
FGFR1
MET exon 14 skipping
MET amp
Negative
Positive


A
Univariate
P
Multivariate
P
Male
Age ≥ 50 years
Smoking
Stage III/IV
Lymph node invlovement
Adjuvant therapy
TP53 mutation
Detectable landmark ctDNA
0.19
0.12
0.65
0.03*
0.06
0.64
0.23
<0.001***
0.98
0.23
0.008**
0 2.5 5 7.5 10 12.5 15 17.5 20 22.5 25 27.5 30 32.5
Hazard Ratio
0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 74
Hazard Ratio
DFS better
DFS worse
DFS better
DFS worse
B
Univariate
P
Multivariate
P
Male
Age ≥ 50 years
Smoking
Stage III/IV
Lymph node invlovement
Adjuvant therapy
TP53 mutation
Detectable Longitudinal ctDNA
0.67
0.36
0.49
0.33
0.37
0.22
0.11
<0.001***
0.28
0.001**
0 2.5 5 7.5 10 12.5 15 17.5 20 22.5 25 27.5 30 32.5
Hazard Ratio
0 2.5 5 7.5 10 12.5 15 17.5 20 22.5 25 27.5 30
Hazard Ratio
DFS better
DFS worse
DFS better
DFS worse


A
Sensitivity
120
100
80
60
40
20
0
Percentage (%)
3
3
7
2
1
1
2
3
10
3
3
7
3
3
7
Landmark Sensitivity 70.0% (7/10)
Longitudinal Sensitivity 76.9% (10/13)
Surveillance Sensitivity 70.0% (7/10)
Specificity
120
100
80
60
40
20
0
Percentage (%)
6
14
1
5
14
1
19
Landmark Specificity 100% (14/14)
Longitudinal Specificity 95% (19/20)
ctDNA not detected
ctDNA detected
No landmark draw
No surveillance draw
B
150
100
50
0
Percentage (%)
Landmark: NPV 82.4% PPV 100%
Longitudinal: NPV 86.4% PPV 90.9%
3
14
3
19
7
10
1
Negative ctDNA
Positive ctDNA
Recurred
Not recurred
Landmark
Longitudinal

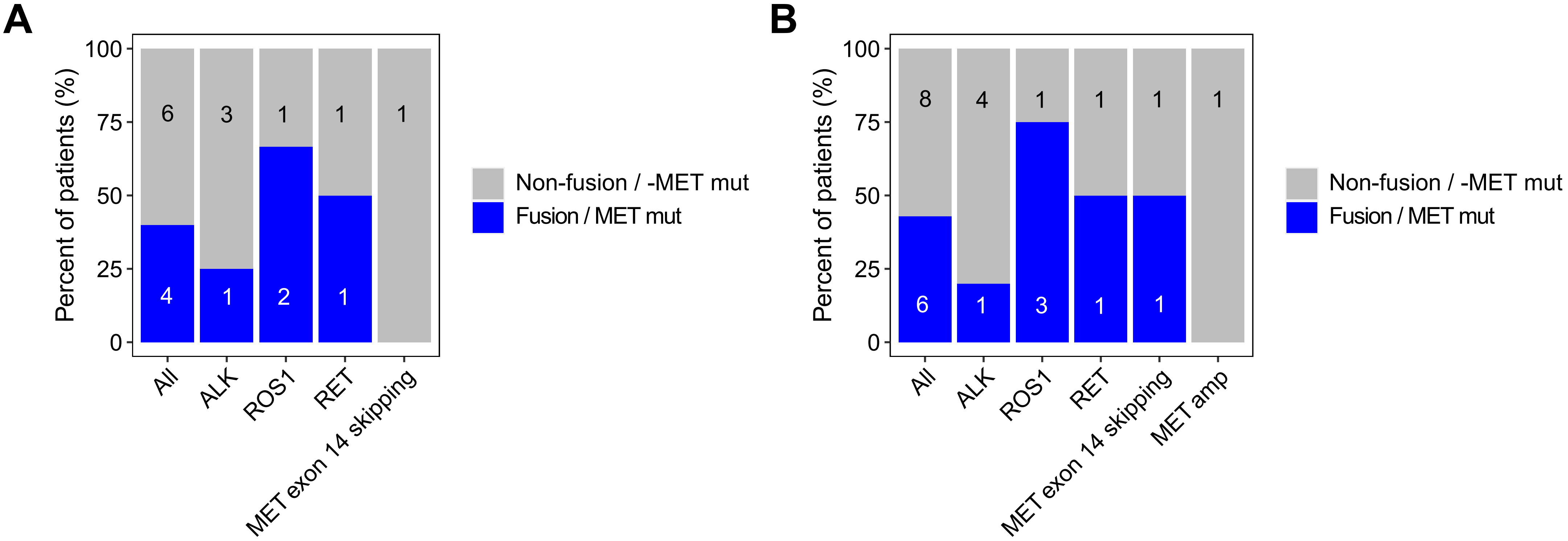

A
Percent of patients (%)
100
75
50
25
0
6
3
1
1
1
4
1
2
1
All
ALK
ROS1
RET
MET exon 14 skipping
Non-fusion / -MET mut
Fusion / MET mut
B
Percent of patients (%)
100
75
50
25
0
8
4
1
1
1
1
6
1
3
1
1
All
ALK
ROS1
RET
MET exon 14 skipping
MET amp
Non-fusion / -MET mut
Fusion / MET mut

Figure S1. The positive rate of ctDNA. The positive rate of landmark (A) or longitudinal ctDNA (B) in different groups classified by fusion/MET alterations.

Figure S2. Landmark and longitudinal detectable MRD is an independent predictor for disease recurrence. (A and B) Univariant and multivariate analysis for disease-recurrence prediction with multiple clinicopathological variables and landmark (A) or longitudinal positive ctDNA (B).

Figure S3. The sensitivity and specificity of postoperative MRD in predicting disease recurrence. (A) Sensitivity and specificity analysis of ctDNA detection at landmark, longitudinal or surveillance time points. (B) The negative and positive predictive value of ctDNA at landmark and longitudinal time points. NPV, negative predictive value; PPV, positive predictive value.

Figure S4. The detection rate of fusion/MET alterations in ctDNA. (A and B) The detection rate of fusion/MET alterations of detectable landmark (A) or longitudinal ctDNA (B) in different groups classified by fusion/MET alterations.