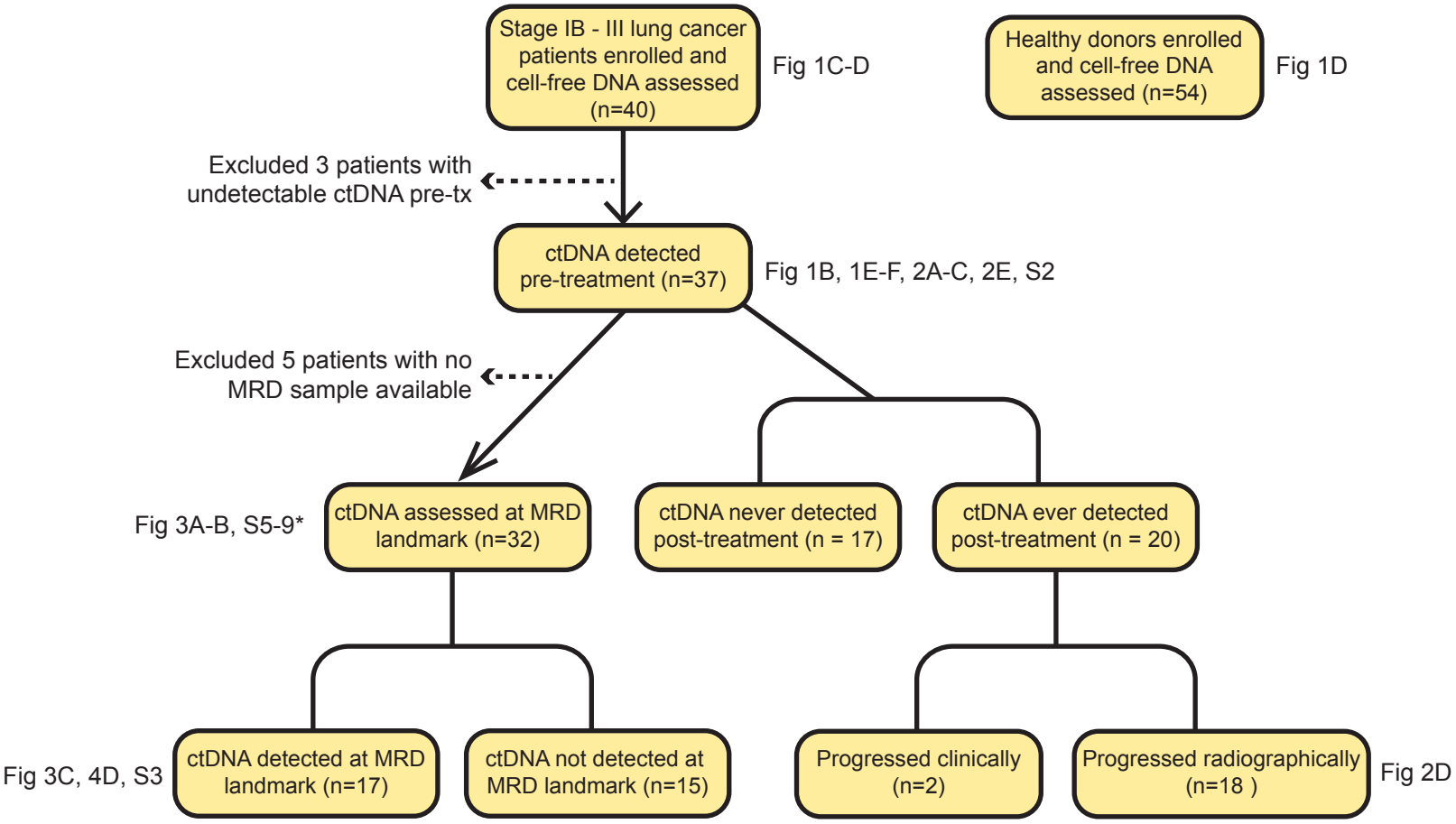
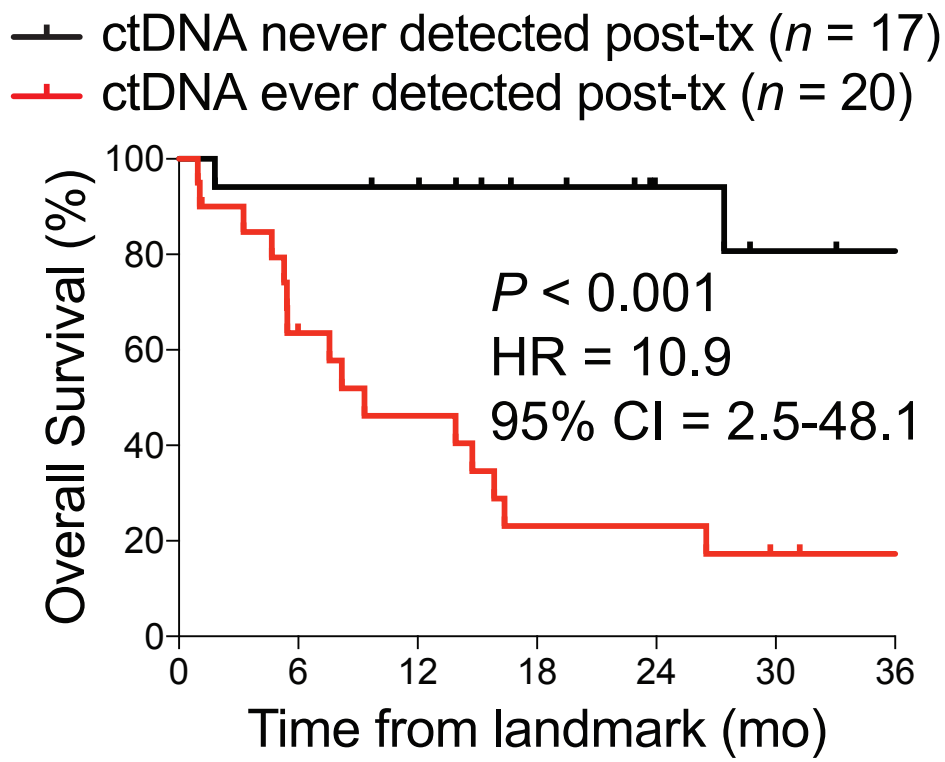
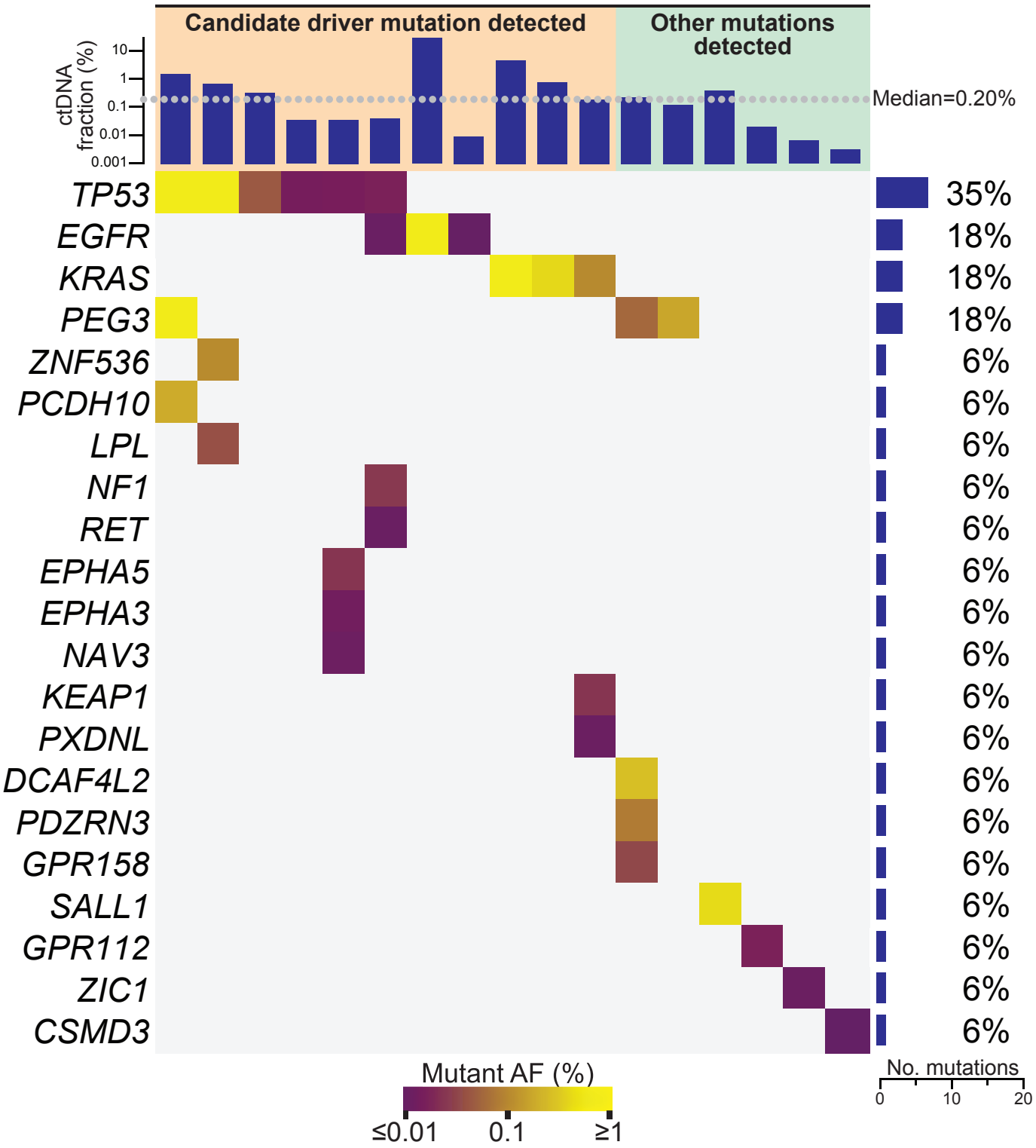


*For Fig S6, excluded 1 patient because CT scan was not performed at MRD landmark. For Fig S8, assessed 29 NSCLC patients. For Fig S9, analyzed 13 patients that were assessed at early MRD landmark (≤6 weeks post-treatment).

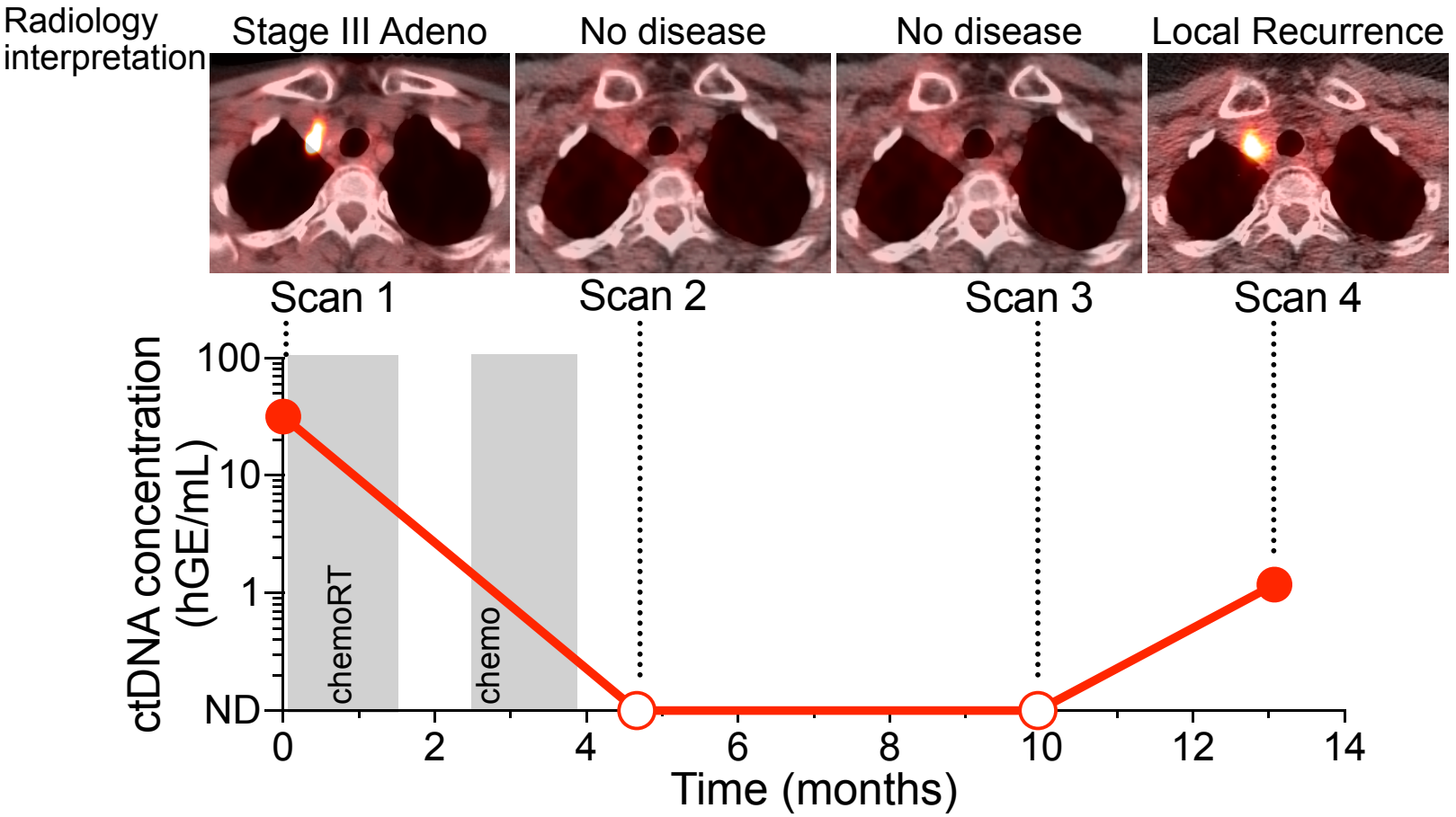
Supplemental Figure S1. Flow diagram. Number of patients analyzed per figure and table.



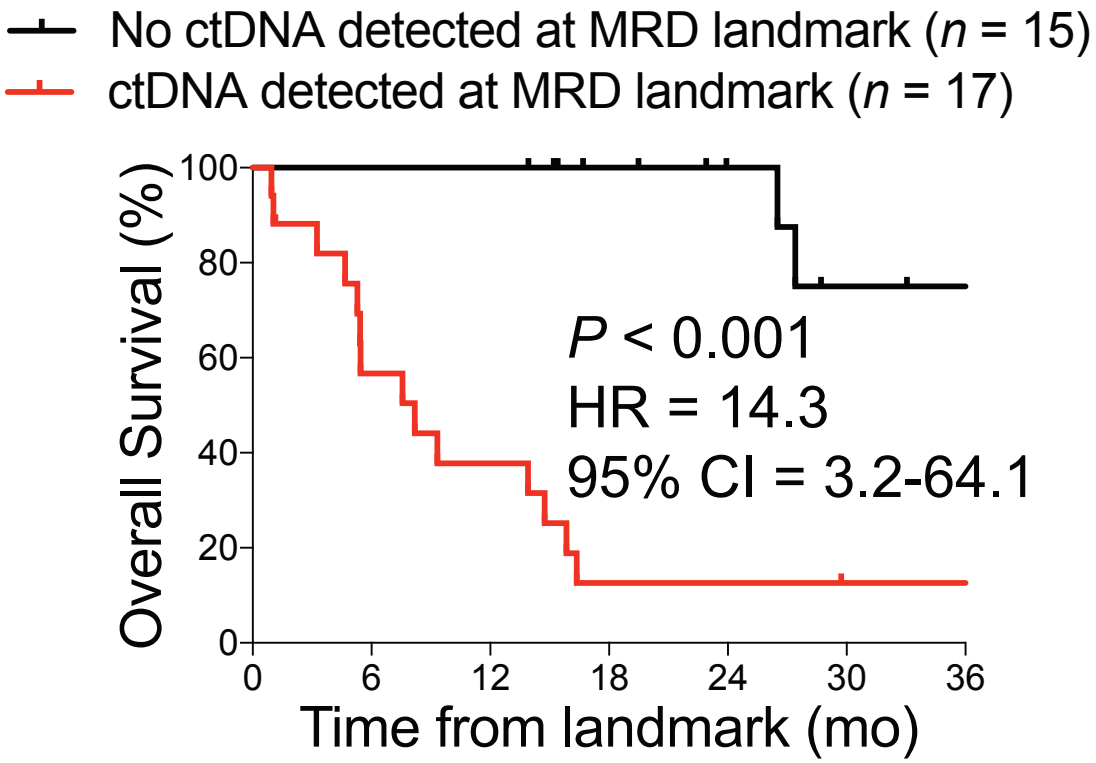
Supplemental Figure S2. Overall survival analysis based on ctDNA detection during post-treatment surveillance. Kaplan-Meier analysis stratified by ctDNA detection during post-treatment surveillance (ever detected vs. never detected). Landmark is first post-treatment blood draw. *P*-value was calculated by log-rank test and HR by Cox *exp(beta)* method.



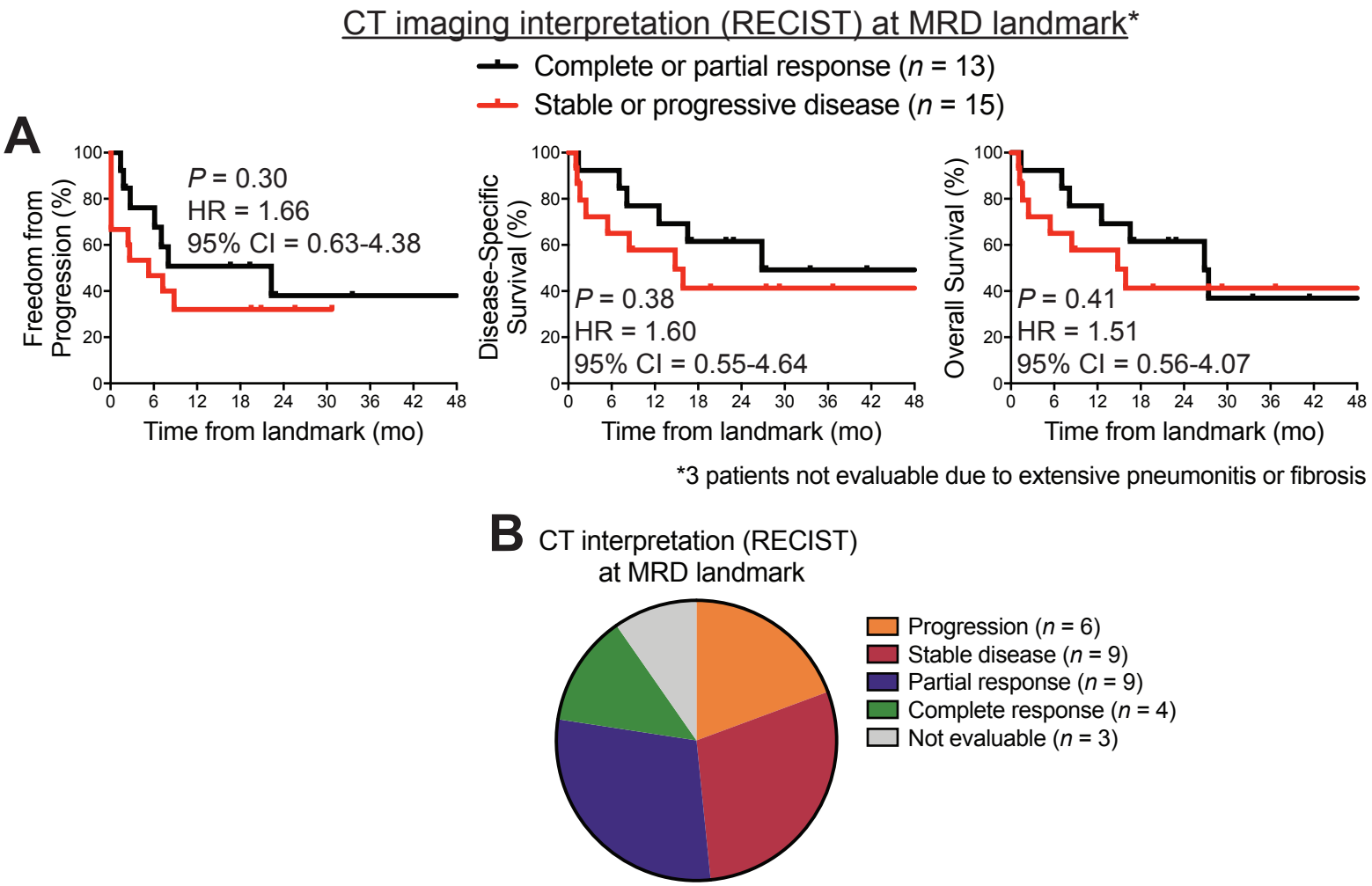
Supplemental Figure S3. Heat map depicting mutations detected in plasma at MRD landmark. Columns represent data from the first post-treatment blood sample from each patient with detectable ctDNA MRD (*n* = 17). Global mutant allele fraction is indicated by the upper bar graph. Cases in which candidate driver (*n* = 11) or only other (likely passenger) mutations (*n* = 6) were detected are shown. Heat map indicates allele fractions of individual mutations. Mutation recurrence rates are depicted by bar graph to the right.



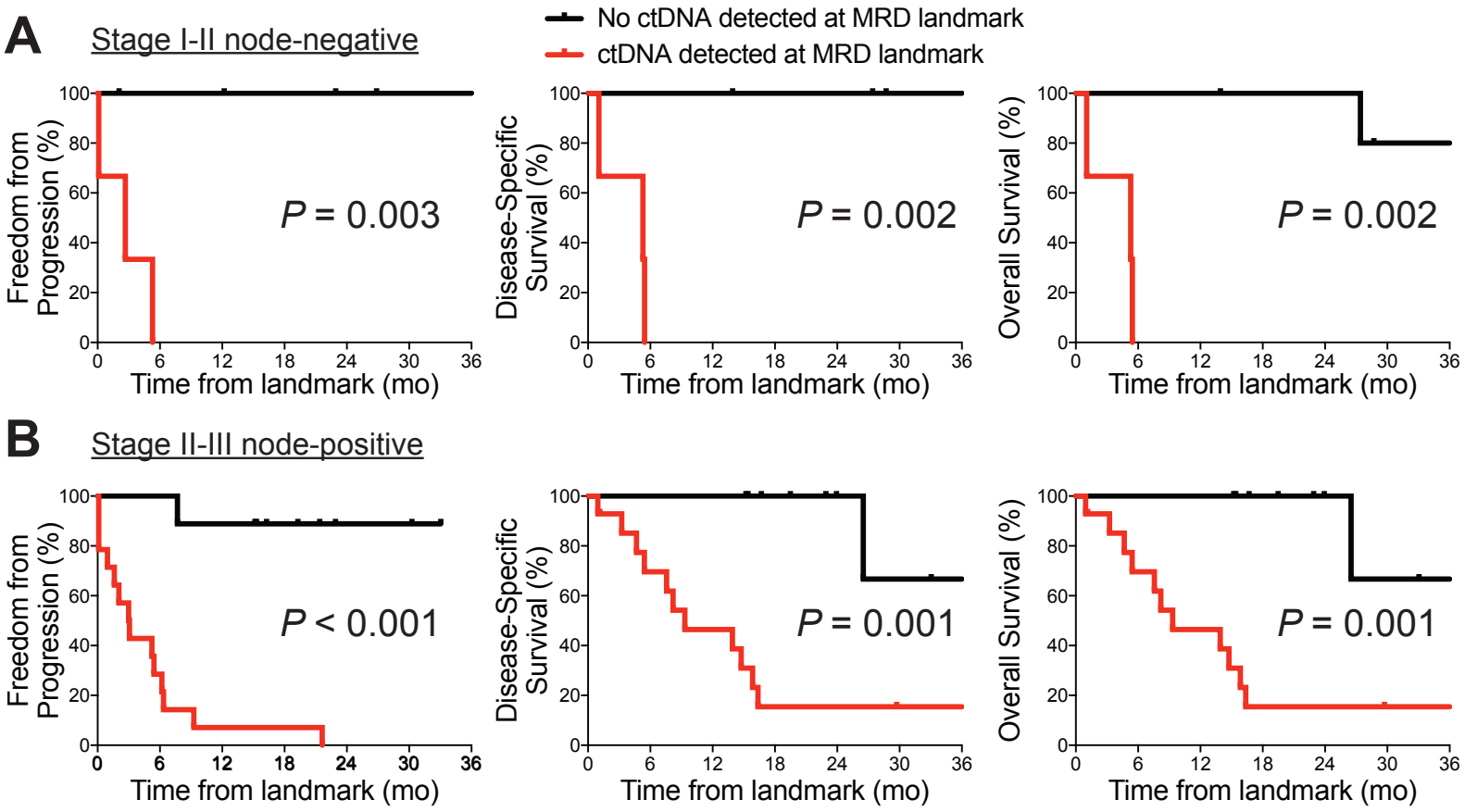
Supplemental Figure S4. Detection of ctDNA at time of local recurrence in a patient with Stage III NSCLC. For patient LUP26, post-treatment ctDNA was not detected (ND) at the MRD landmark but was detected at time of local recurrence.



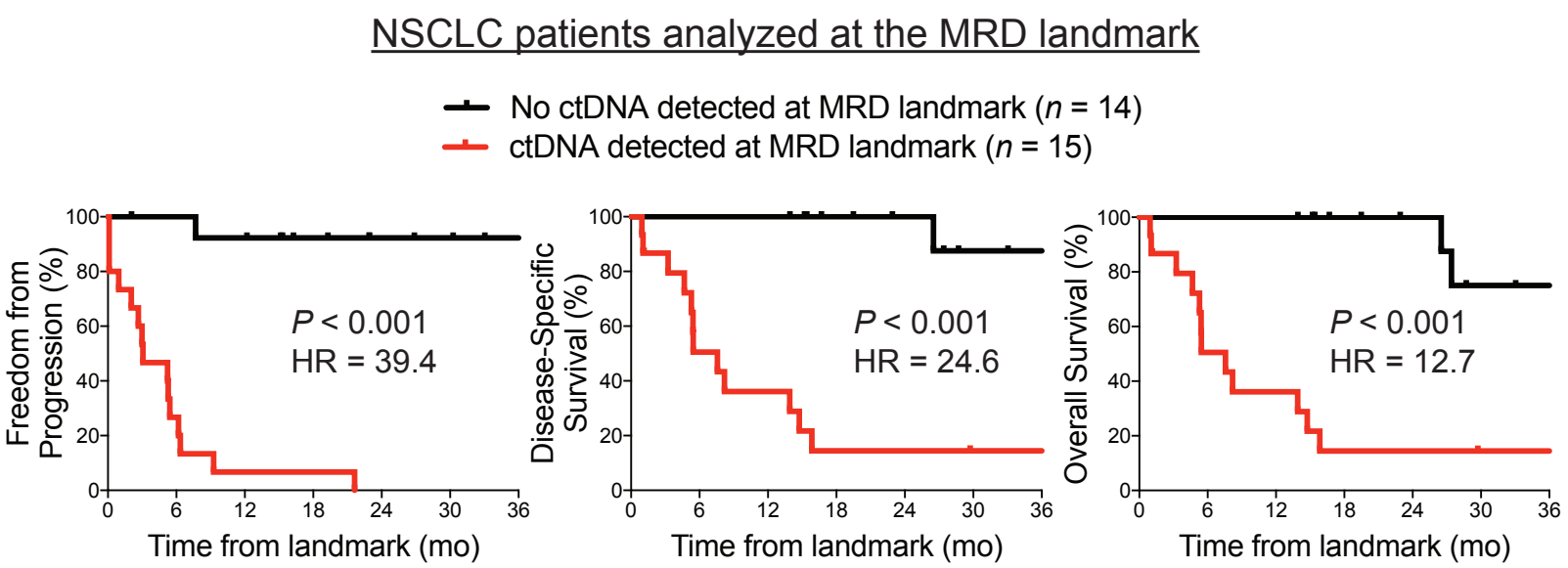
Supplemental Figure S5. Overall survival based on ctDNA detection at the MRD landmark. Kaplan-Meier analysis stratified by ctDNA detection at the MRD landmark. The MRD landmark was pre-specified to be ≤ 4 months after treatment completion. *P*-value calculated by log-rank test and HR by Cox *exp(beta)* method.



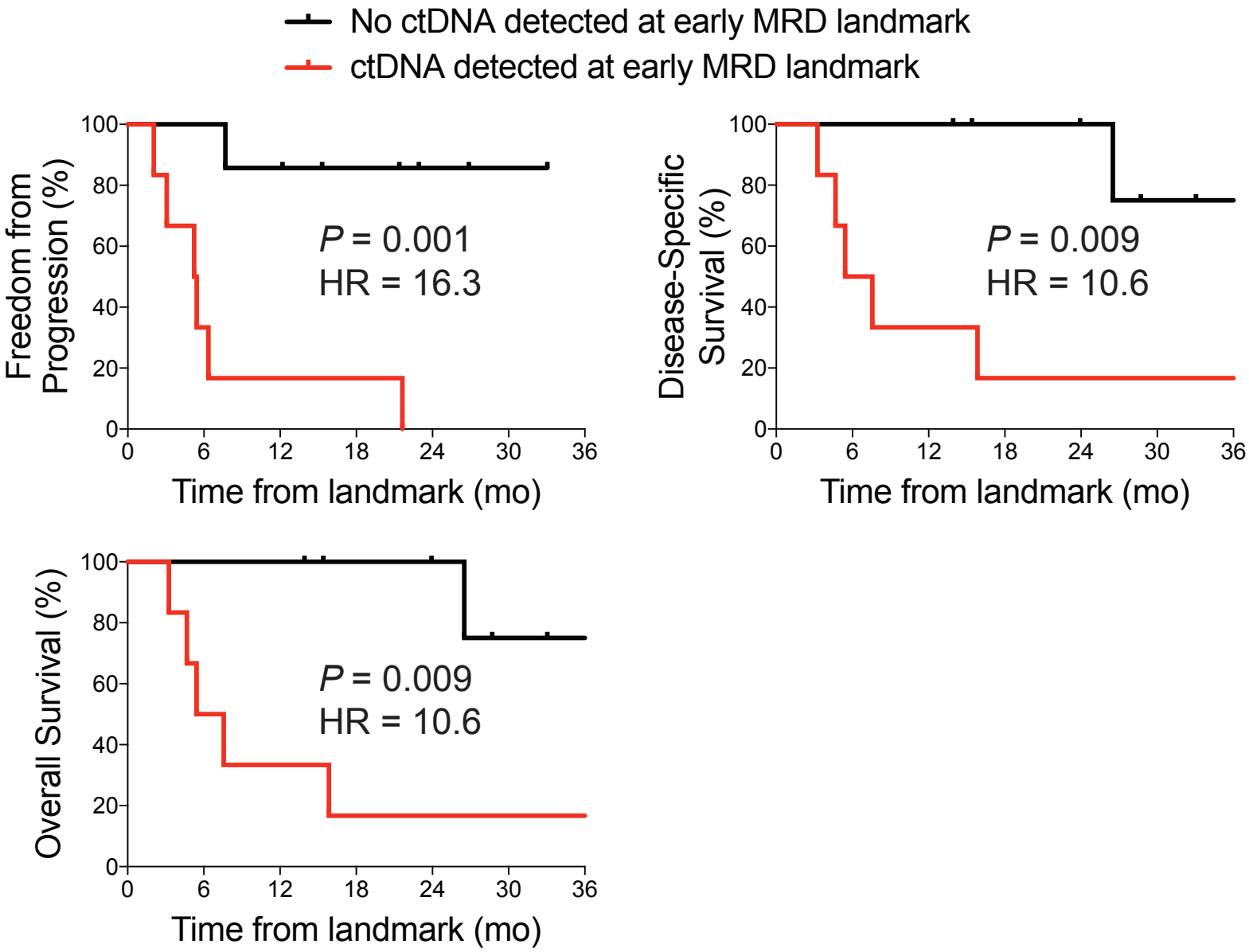
Supplemental Figure S6. CT imaging assessment at the MRD landmark. (A) Kaplan-Meier analysis stratified by CT scan RECIST interpretation at the MRD landmark (first post-treatment time-point within 4 months of treatment completion). **(B)** CT interpretation by RECIST criteria at the MRD landmark. One patient excluded from analysis because no CT scan performed within 4 months of treatment completion.



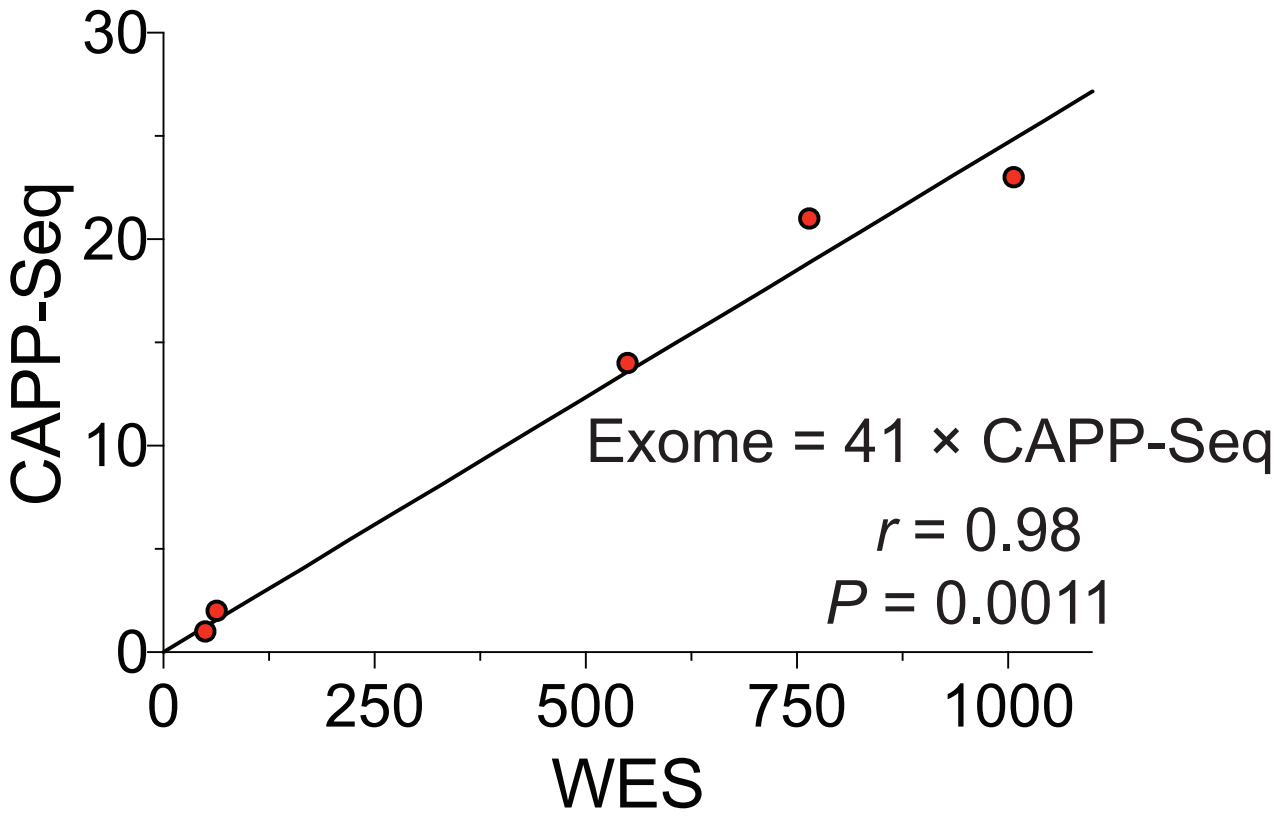
Supplemental Figure S7. ctDNA MRD is prognostic for node-negative and node-positive lung cancer patients. Freedom from progression, disease-specific survival and overall survival from MRD landmark in **(A)** stage I-II node-negative patients (*n* = 9), **(B)** stage II-III node-positive patients (*n* = 23). HR > 10 for all analyses.



Supplemental Figure S8. ctDNA MRD is prognostic for localized NSCLC patients. Kaplan-Meier analysis of NSCLC patients stratified by ctDNA detection at the MRD landmark after definitive intent treatment. *P*-value calculated by log-rank test and HR by Cox *exp(beta)* method.



Supplemental Figure S9. ctDNA detection is prognostic at early MRD landmark. Kaplan-Meier analysis stratified by ctDNA detection at early MRD landmark (≤ 6 weeks after completion of all treatment; *n* = 13). *P*-value calculated by log-rank test and HR by Cox *exp(beta)* method.



Supplemental Figure S10. Concordance between the number of non-synonymous mutations found using CAPP-Seq and whole exome sequencing. Non-synonymous mutation burden was independently measured by CAPP-Seq and whole exome sequencing (WES) using DNA from 5 NSCLC tumors.