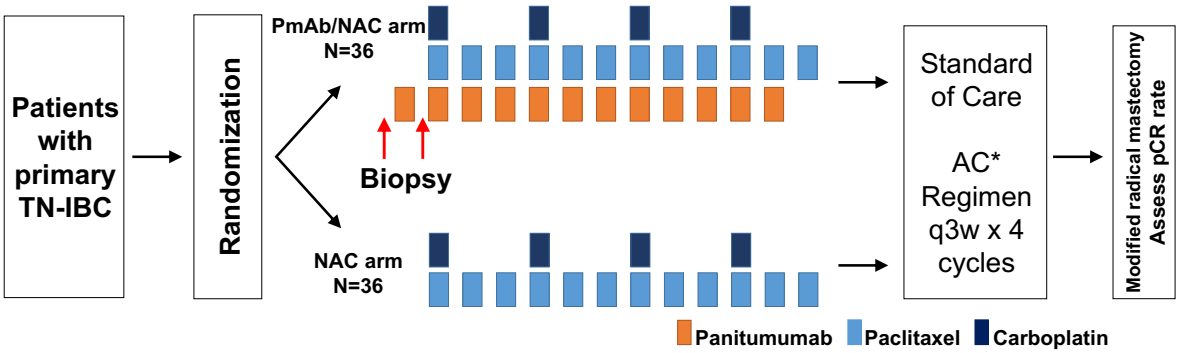
## Supplementary Table and Figures

**Supplementary Table 1. Baseline characteristics of 60 patients with TN-non-IBC**

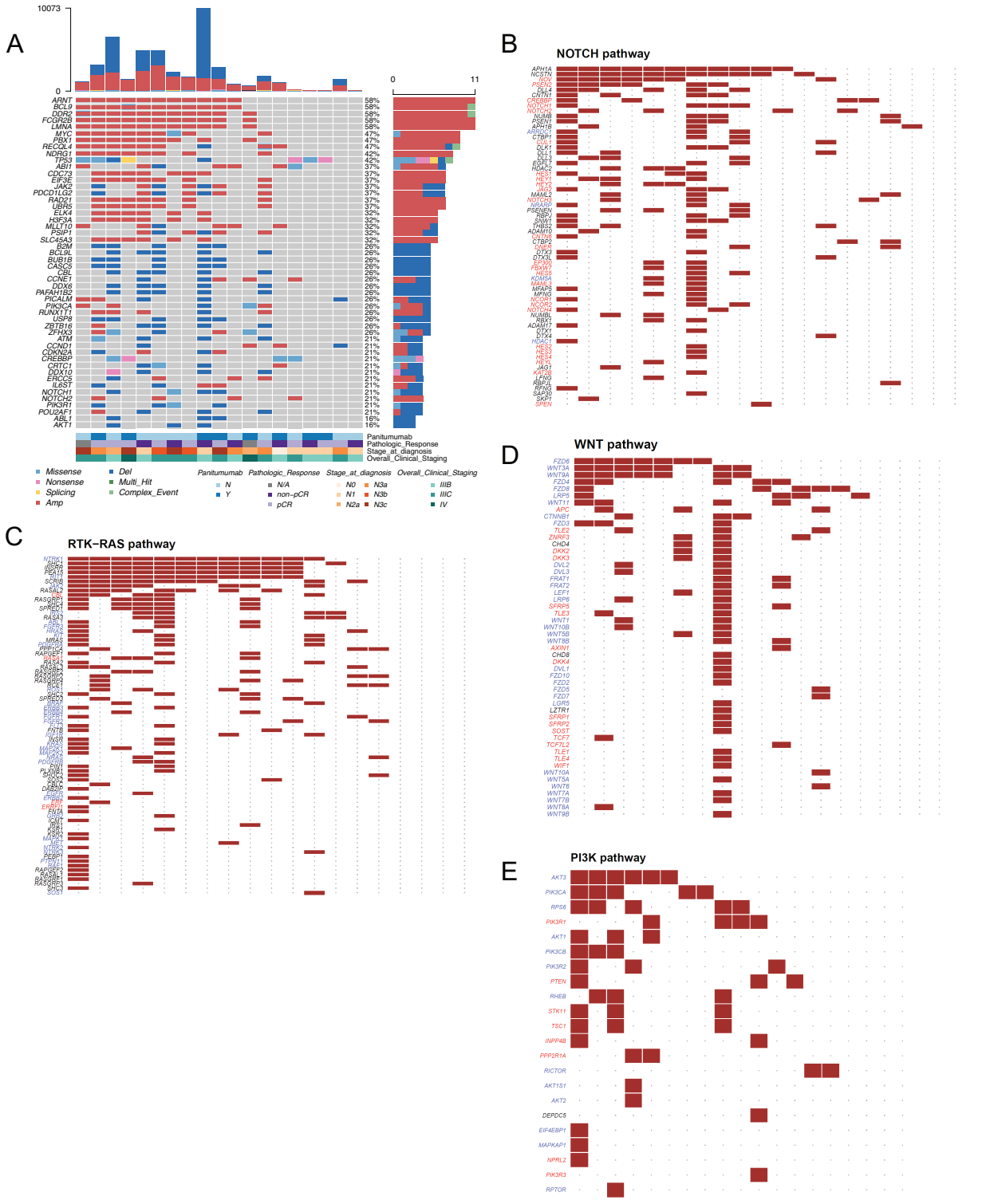
| Characteristic | Value |
|---|---|
| Age, mean (SD) range, y | 50.1 (12.9) 24-74 |
| BMI, mean (SD) range, kg/m$^2$ | 28.9 (6.3) 17.8-49.0 |
| TILs, mean (SD) range, % | 15.2 (19.1) 4-90 |
| Menopausal status, n (%) | |
| Premenopausal | 27 (45) |
| Postmenopausal | 31 (52) |
| Perimenopause | 1 (2) |
| Unknown | 1 (2) |
| Race, n (%) | |
| Asian | 6 (10) |
| Black or African American | 12 (20) |
| White or Caucasian | 42 (70) |
| Ethnicity, n (%) | |
| Hispanic or Latino | 13 (22) |
| Not Hispanic or Latino | 47 (78) |
| Clinical stage | |
| IIIA | 17 (28) |
| IIIB | 6 (10) |
| IIIC | 37 (62) |
| N category at diagnosis | |
| N0 | 4 (7) |
| N1 | 14 (23) |
| N2 | 5 (8) |
| N3 | 37 (62) |

**Supplementary Figure 1**




**Supplementary Figure 1. Trial design and genomic and transcriptomic data collection.** TN-IBC patients were recruited and randomized into PmAb/NAC and NAC arms. In the PmAb/NAC arm, patients received an initial dose of PmAb followed by weekly PmAb and paclitaxel and triweekly carboplatin for 4 cycles. Tissue biopsy was performed before and after the initial dose of PmAb. In the NAC arm, patients received weekly paclitaxel and triweekly carboplatin for 4 cycles. Tissue biopsy was performed only at baseline. Each cycle was defined as 21 days. PmAb, 2.5 mg/kg; paclitaxel, 80 mg/m$^2$; carboplatin, AUC 5. Standard-of-care chemotherapy (doxorubicin and cyclophosphamide) was administered after completion of PmAb/NAC or NAC. The doxorubicin and cyclophosphamide regimen consisted of 4 cycles repeated at 2- to 3-week intervals at the physician's discretion, assuming bone marrow recovery. Dose modification of doxorubicin and cyclophosphamide was based on standard practice guidelines. WES and RNA-seq data were collected on samples from 19 patients, 8 in the PmAb/NAC arm and 11 in the NAC arm.

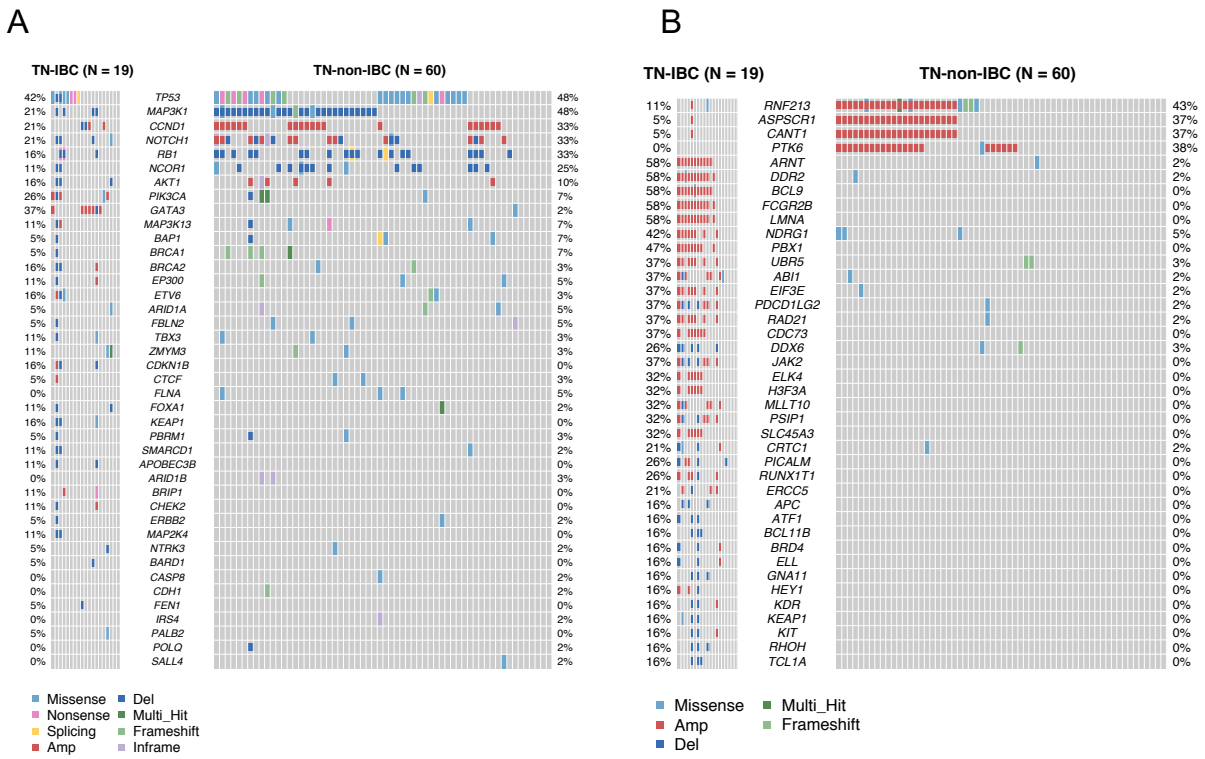
## Supplementary Figure 2




**Supplementary Figure 2. Somatic alterations identified in TN-IBC and comparison with TN-non-IBC. A.** Somatic alterations identified in the 50 most frequently altered cancer hallmark

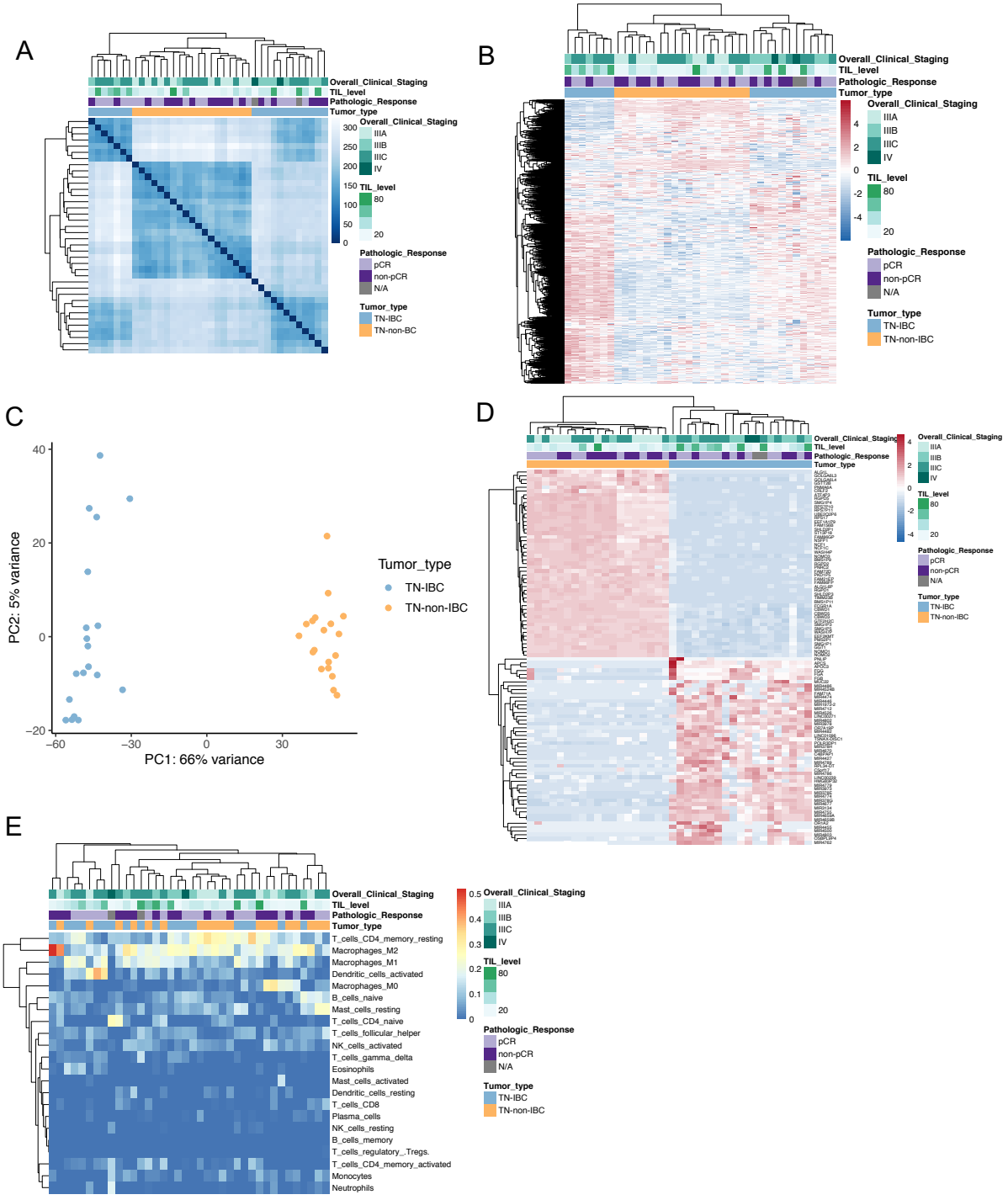
genes in TN-IBC. Top: bar graph defining the total number of somatic alterations in each patient; bottom: annotation for PmAb treatment, pathologic response, stage at diagnosis, and overall clinical stage. **B-E.** Somatic alterations of genes in the NOTCH (**B**), RTK-RAS (**C**), WNT (**D**), and PI3K (**E**) pathways.

## Supplementary Figure 3




**Supplementary Figure 3. Comparison of somatic alterations identified in TN-IBC and TN-non-IBC.** Summarized are somatic alterations of breast-cancer-associated genes (**A**) and cancer hallmark genes (**B**) identified in TN-IBC and TN-non-IBC. Gene names and relative frequency of mutations are reported in the double y-axis.

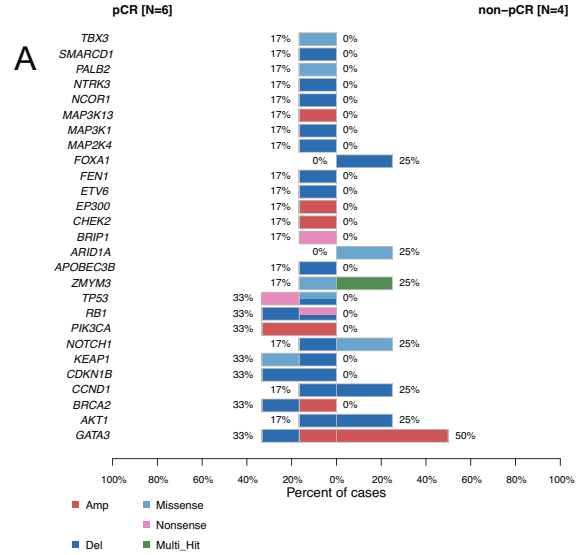
## Supplementary Figure 4

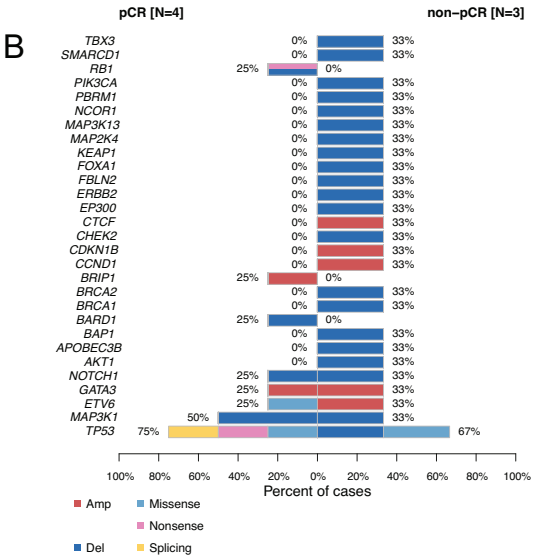


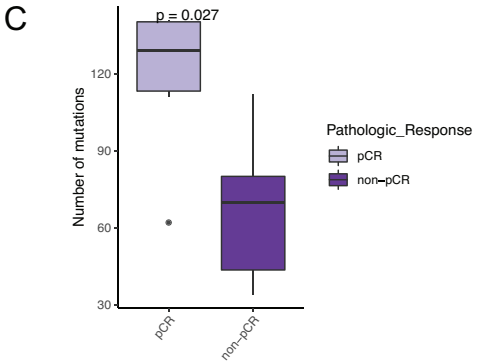

**Supplementary Figure 4. Comparison of transcriptomic profiles between TN-IBC and TN-non-IBC. A.** Heatmap of sample-to-sample distances between TN-IBC and TN-non-IBC samples. **B.** Heatmap of the expression of the 5000 most variable genes in TN-IBC and TN-non-IBC. **C.**

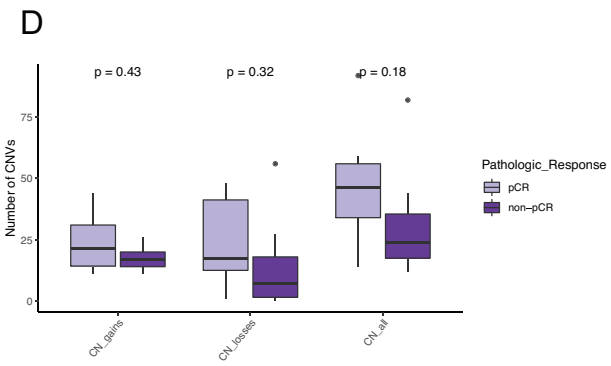
Principal component analysis shows the separation of TN-IBC and TN-non-IBC samples. **D.** Heatmap of the 50 most up-regulated and 50 most down-regulated genes in TN-IBC compared to TN-non-IBC samples. **E.** Heatmap of the composition of 22 types of immune cells in TN-IBC and TN-non-IBC samples analyzed by deconvolution analysis. The overall clinical stage, TIL level, pathologic response, and tumor type are annotated.

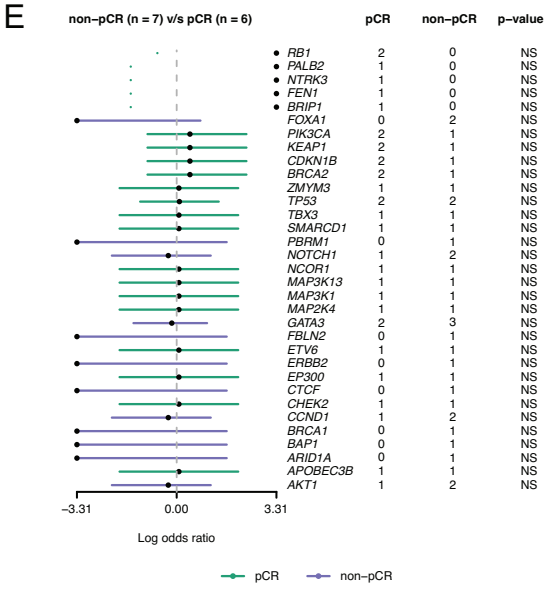
## Supplementary Figure 5



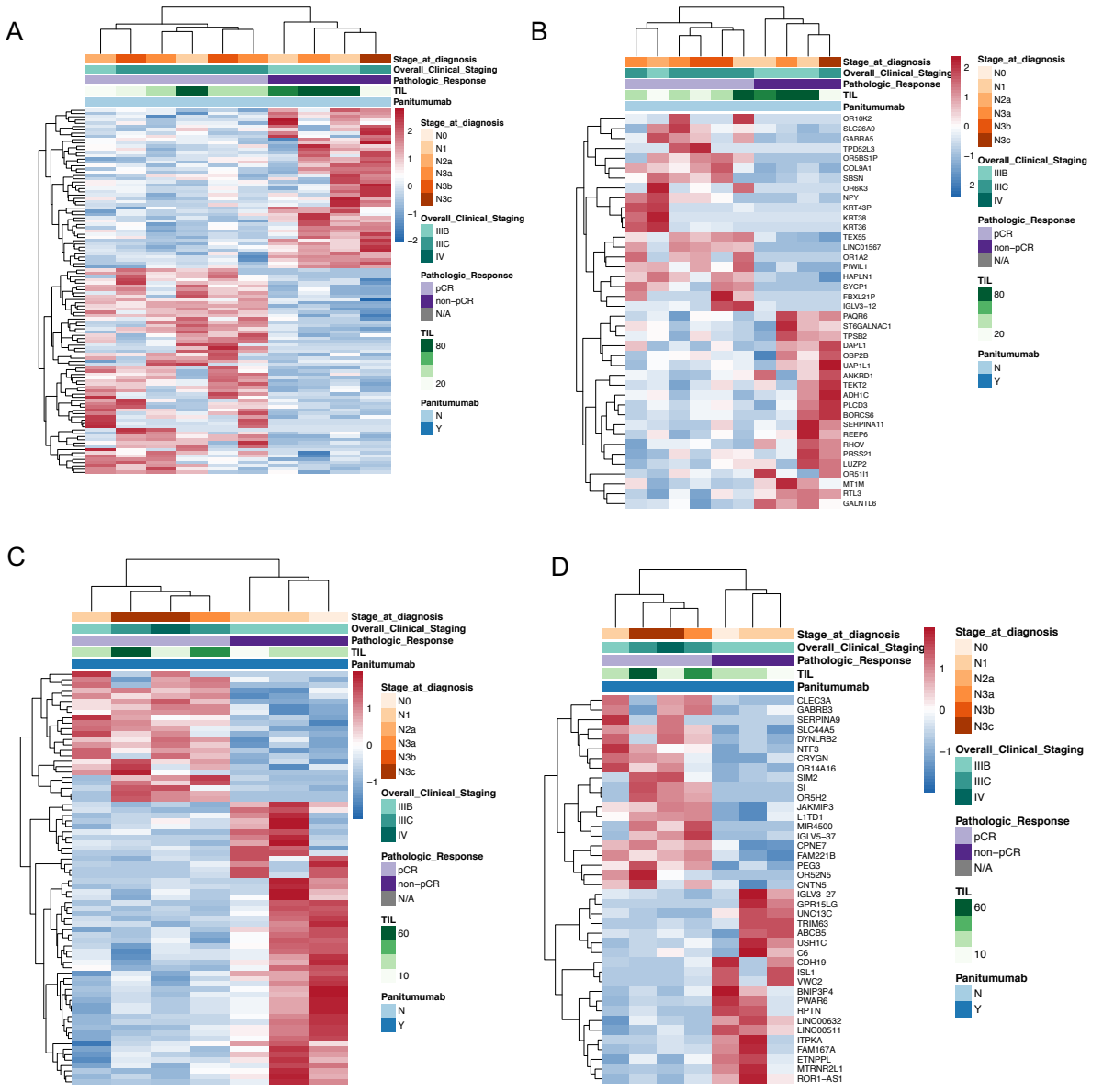



**Supplementary Figure 5. Comparison of somatic alterations between TN-IBC patients who did and did not have pCRs in the NAC and PmAb/NAC arms. A-B.** Comparison of somatic mutation frequency in TN-IBC patients who did and did not have pCRs in the NAC (**A**) and PmAb/NAC arms (**B**). **C-D.** Comparison of somatic mutation load (**C**) and CN gains, losses, and CNV load (**D**) between TN-IBC patients who did and did not have pCRs when combined both NAC and PmAb/NAC arms. **E.** Enrichment of genomic alterations between TN-IBC patients who did and did not have pCRs when combined both NAC and PmAb/NAC arms. NS, not significant.

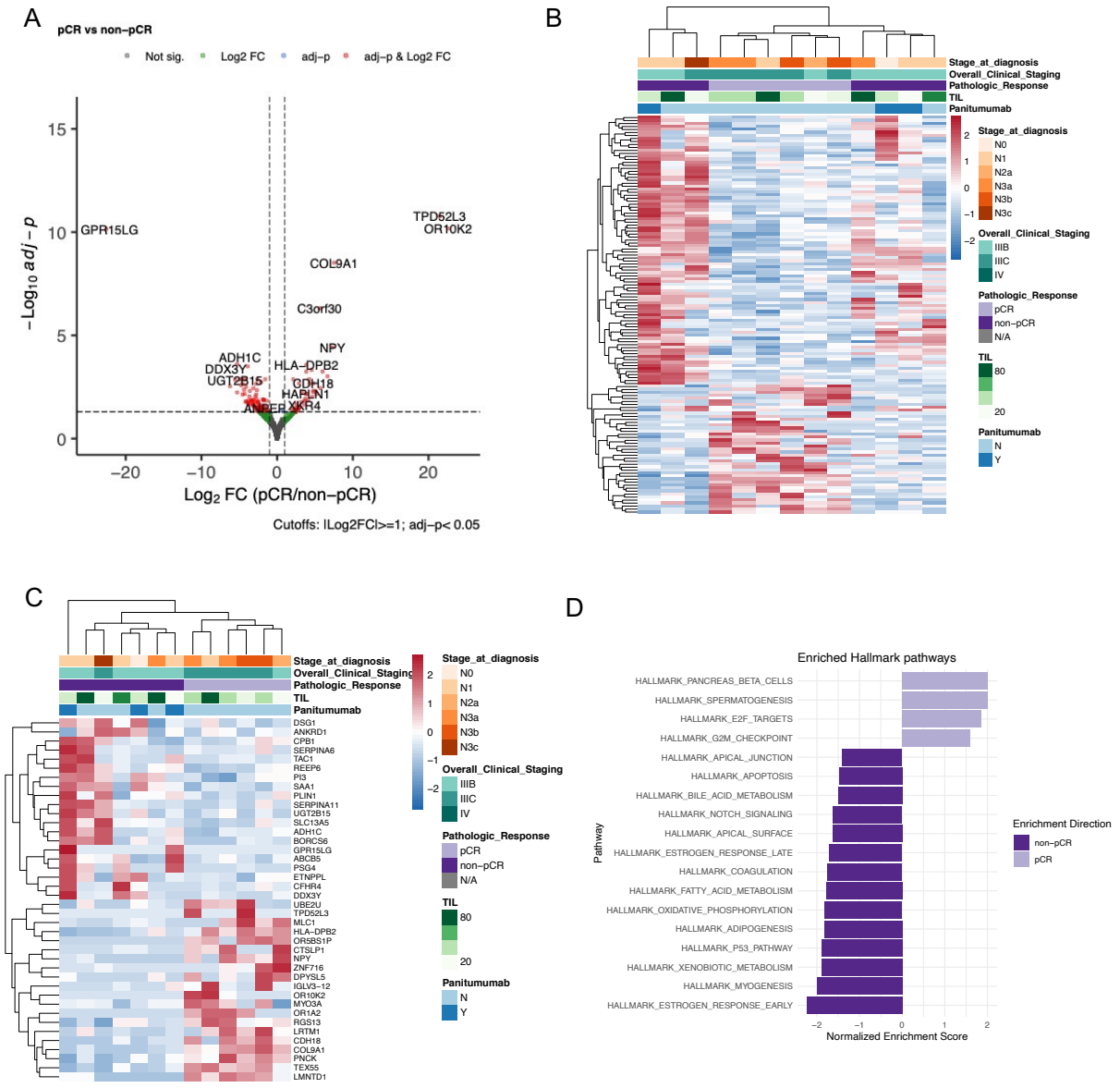
## Supplementary Figure 6




**Supplementary Figure 6. Comparison of gene expression between TN-IBC patients who did and did not have pCRs in the NAC and PmAb/NAC arms. A.** Heatmap of the 112 identified differentially expressed genes in the NAC arm, in which 63 genes are over-expressed in the pCR group and 49 are over-expressed in the non-pCR group. **B.** Heatmap of the top 20 up-regulated and 20 down-regulated genes in pCR vs non-pCR in the NAC arm. **C.** Heatmap of the 76 identified differentially expressed genes in the PmAb/NAC arm, in which 24 genes were over-expressed in the pCR group and 52 were over-expressed in the non-pCR group. **D.** Heatmap of the top 20 up-regulated and 20 down-regulated genes in pCR vs non-pCR in the PmAb/NAC arm. Stage at

diagnosis, overall clinical stage, pathologic response, TIL level, and PmAb treatment are annotated.

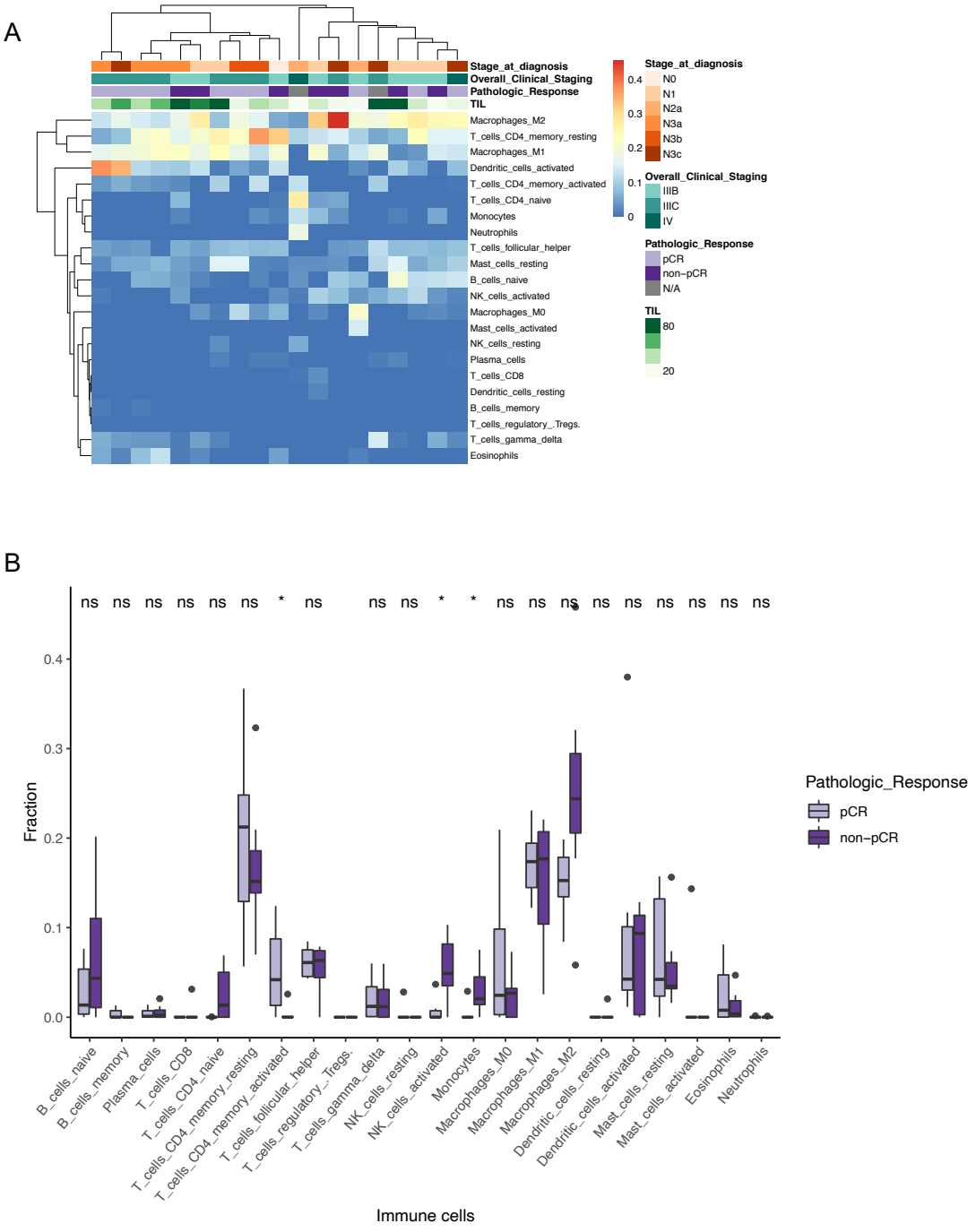
## Supplementary Figure 7




**Supplementary Figure 7. Comparison of gene expression between TN-IBC patients in the NAC arm who had pCRs and TN-IBC patients in the NAC and PmAb/NAC arms who did not have pCRs**. **A.** Volcano plot of differentially expressed genes with Log2FC ≥1 or ≤-1 and adj-*p*<0.05 in TN-IBC patients who did and did not have pCRs. **B.** Heatmap of the 133 differentially expressed genes, in which 41 genes are over-expressed in the pCR group and 92 are over-expressed in the non-pCR group. The stage at diagnosis, overall clinical stage, pathologic response, TIL level, and PmAb treatment are annotated. **C.** Heatmap of the 20 up-regulated and

20 down-regulated genes in TN-IBC patients who did and did not have pCRs. The stage at diagnosis, overall clinical stage, pathologic response, TIL level, and PmAb treatment are annotated. **D.** GSEA of the significantly enriched hallmark pathways in TN-IBC patients who did and did not have pCRs.

## Supplementary Figure 8




**Supplementary Figure 8. Estimation of immune cell fractions in TN-IBC patient samples by deconvolution analysis. A.** Heatmap of the composition of 22 types of immune cells in all TN-IBC patient tumor samples. The stage at diagnosis, overall clinical stage, pathologic response,

and TIL level are annotated. **B.** Comparison of the immune cell composition in TN-IBC patients who did and did not have pCRs in the combined NAC and PmAb/NAC arms. NS, not significant.

# CONSORT 2010 checklist of information to include when reporting a randomised trial*

| Section/Topic | Item No | Checklist item | Reported on page No |
|---|---|---|---|
| **Title and abstract** | | | |
| | 1a | Identification as a randomised trial in the title | N/A |
| | 1b | Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts) | 2 |
| **Introduction** | | | |
| Background and objectives | 2a | Scientific background and explanation of rationale | 3-4 |
| | 2b | Specific objectives or hypotheses | 4 |
| **Methods** | | | |
| Trial design | 3a | Description of trial design (such as parallel, factorial) including allocation ratio | 4 |
| | 3b | Important changes to methods after trial commencement (such as eligibility criteria), with reasons | 4-5 |
| Participants | 4a | Eligibility criteria for participants | 4-5 |
| | 4b | Settings and locations where the data were collected | 5 |
| Interventions | 5 | The interventions for each group with sufficient details to allow replication, including how and when they were actually administered | 5 |
| Outcomes | 6a | Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed | 5 |
| | 6b | Any changes to trial outcomes after the trial commenced, with reasons | N/A |
| Sample size | 7a | How sample size was determined | 4-5 |
| | 7b | When applicable, explanation of any interim analyses and stopping guidelines | N/A |
| Randomisation: | | | |
| Sequence generation | 8a | Method used to generate the random allocation sequence | 4-5 |
| | 8b | Type of randomisation; details of any restriction (such as blocking and block size) | 4-5 |
| Allocation concealment mechanism | 9 | Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned | N/A |
| Implementation | 10 | Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions | 4-5 |
| Blinding | 11a | If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how | N/A |
| | 11b | If relevant, description of the similarity of interventions | N/A |
| Statistical methods | 12a | Statistical methods used to compare groups for primary and secondary outcomes | 7-8 |
| | 12b | Methods for additional analyses, such as subgroup analyses and adjusted analyses | 6-8 |

| | | | |
|---|---|---|---|
| **Results** | | | |
| Participant flow (a diagram is strongly recommended) | 13a | For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome | 8 |
| | 13b | For each group, losses and exclusions after randomisation, together with reasons | N/A |
| Recruitment | 14a | Dates defining the periods of recruitment and follow-up | 5 |
| | 14b | Why the trial ended or was stopped | N/A |
| Baseline data | 15 | A table showing baseline demographic and clinical characteristics for each group | 22 |
| Numbers analysed | 16 | For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups | 8 |
| Outcomes and estimation | 17a | For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval) | 12 |
| | 17b | For binary outcomes, presentation of both absolute and relative effect sizes is recommended | N/A |
| Ancillary analyses | 18 | Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory | 8-15 |
| Harms | 19 | All important harms or unintended effects in each group (for specific guidance see CONSORT for harms) | N/A |
| **Discussion** | | | |
| Limitations | 20 | Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses | 19 |
| Generalisability | 21 | Generalisability (external validity, applicability) of the trial findings | N/A |
| Interpretation | 22 | Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence | N/A |
| **Other information** | | | |
| Registration | 23 | Registration number and name of trial registry | 4 |
| Protocol | 24 | Where the full trial protocol can be accessed, if available | N/A |
| Funding | 25 | Sources of funding and other support (such as supply of drugs), role of funders | 20 |

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.