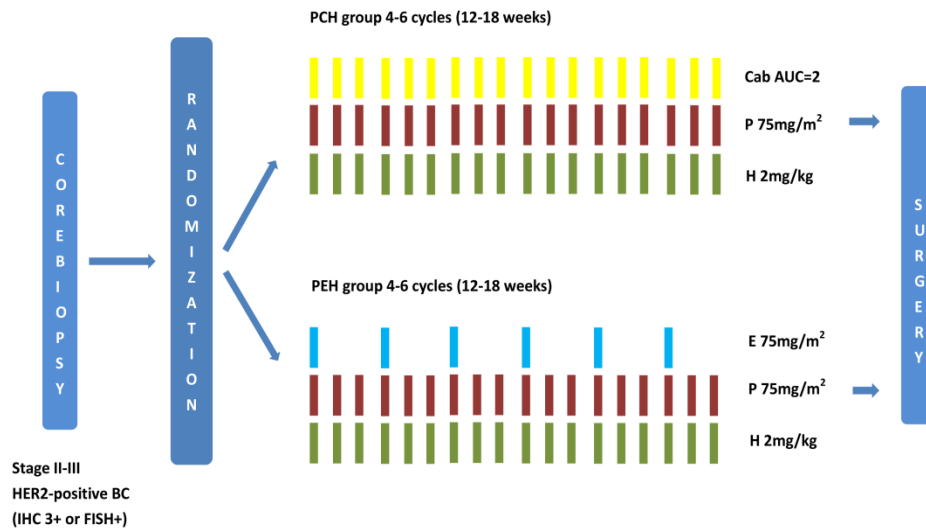


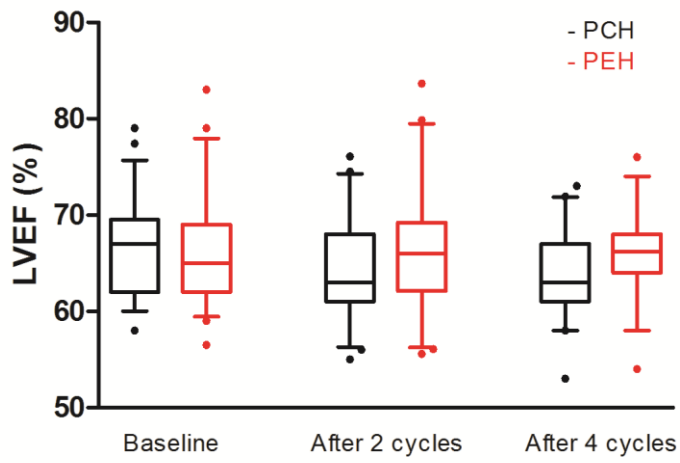
Efficacy and safety analysis of trastuzumab and paclitaxel based regimen plus carboplatin or epirubicin as neoadjuvant therapy for clinical stage II-III, HER2-positive breast cancer patients: a phase 2, open-label, multicenter, randomized trial

Supplementary Material



S.Figure 1: Treatment plan

Abbreviations: AUC, area under the concentration-time curve; BC, breast cancer; Car, carboplatin; FISH, fluorescence in situ hybridization; H, trastuzumab; IHC, immunohistochemistry; P, paclitaxel.



S.Figure 2: Left ventricular ejection fraction (LVEF) per treatment arm.

Central horizontal lines show medians, limits of shaded boxes show 50th percentile, horizontal lines outside

S.Table 1: Odds ratios for pathological complete response according to subgroups

| | Category | Univariable | | Multivariable | |
|----------------------------|------------------------|------------------------|---------|-------------------------|---------|
| | | Odds ratio (95% CI) | P value | Odds ratio (95% CI) | P value |
| Arm | PCH vs PEH | 1.481 (0.632-3.472) | 0.365 | 3.606 (1.153-11.274) | 0.027 |
| Age | <45y vs ≥45y | 1.218 (0.504-2.945) | 0.662 | 1.053 (0.338-3.279) | 0.930 |
| cT | cT1-2 vs cT3-4 | 0.490 (0.19q-1.258) | 0.135 | 0.407 (0.134-1.232) | 0.112 |
| cN | Negative vs positive | 0.721 (0.212-2.447) | 0.599 | 0.332 (0.054-2.057) | 0.236 |
| Ki67 | <14% vs ≥14% | 1.737 (0.479-6.295) | 0.397 | 2.483 (0.407-15.153) | 0.324 |
| HR status | Negative vs positive | 0.607 (0.259-1.426) | 0.251 | 0.550 (0.177-1.711) | 0.302 |
| Chemotherapy cycles | 4 cycles vs 5-6 cycles | 1.364 (0.583-3.190) | 0.474 | 2.671 (0.881-8.794) | 0.106 |
| FCGR2A | H/H vs H/R and R/R | 0.561 (0.224-1.406) | 0.216 | 0.330 (0.098-1.110) | 0.073 |
| FCGR3A | F/F vs F/V and V/V | 1.294 (0.521-3.214) | 0.578 | 1.348 (0.432-4.209) | 0.607 |
| PIK3CA | Wild type vs mutated | 0.799 (0.316-2.024) | 0.637 | 0.799 (0.250-2.550) | 0.705 |
| TP53 | Wild type vs mutated | 1.404 (0.558-3.533) | 0.471 | 0.813 (0.235-2.808) | 0.743 |
| PTEN | Normal vs Loss | 1.103 (0.378-3.219) | 0.857 | 0.694 (0.159-3.024) | 0.627 |

S.Table 2: Cardiac and most common adverse events reported as possibly, probably, or definitely related to treatment

| Adverse event | HPC group (N=50) | | HPE group (N=50) | |
|--------------------------|------------------|-----------|------------------|-----------|
| | Grade 1/2 | Grade 3/4 | Grade 1/2 | Grade 3/4 |
| Anemia | 30 | 7 | 33 | 5 |
| Febrile neutropenia | 0 | 4 | 0 | 7 |
| Neutropenia | 17 | 28 | 12 | 35 |
| Leucopenia | 14 | 4 | 15 | 13 |
| Thrombocytopenia | 10 | 3 | 5 | 1 |
| Granulocytopenia | 22 | 23 | 20 | 26 |
| ALP increased | 3 | 0 | 1 | 0 |
| Bilirubin increased | 26 | 1 | 23 | 2 |
| AST increased | 16 | 1 | 13 | 0 |
| ALT increased | 22 | 4 | 22 | 0 |
| Hand-foot syndrome | 3 | 0 | 9 | 0 |
| Diarrhea | 8 | 1 | 6 | 1 |
| Nausea | 29 | 0 | 31 | 0 |
| Vomiting | 23 | 0 | 21 | 0 |
| Fatigue | 24 | 0 | 22 | 1 |
| Peripheral neuropathy | 6 | 0 | 7 | 0 |
| Arthralgia/myalgia | 0 | 0 | 0 | 0 |
| Congestive heart failure | 0 | 0 | 0 | 0 |
| Palpitation | 4 | 0 | 5 | 0 |
| Lung infection | 1 | 1 | 1 | 1 |