In the overall population and in each cohort, we primarily assessed association of gene sets from Hallmark (n=50), KEGG (n=186) and Reactome (n=197). We assessed RNA expression pathways and dynamics during neoadjuvant chemotherapy (with and without fulvestrant) using gene set enrichment analysis (GSEA) on pre-treatment and biopsies obtained pre and post-treatment [n=53/58 (91.4%)], at week 2 and surgery (p=0.001 and p=0.0006, respectively) (Figure 4B).

We assessed RNA-seq on core-biopsies obtained pre-treatment [n=53/58 (91.4%)], at week 2 [n=49/58 (84.5%)], and on residual disease at surgery [8X, n=42/45 (93.3%)].

We investigated curated gene sets from Halmann (n=50), KEGG (n=186) and Reactome (n=1520) at the single sample level.

In the overall population and in each cohort, we primarily assessed association of gene sets (biomarkers) with pCR or Ki67 down-regulation (centrally evaluated) at week 2 and at SX.

Significance defined by (biomarkers) with p<0.05. For all other tests: p<0.01.

Conclusions

- In ER+/HER2- BC, pre- and on-treatment expression of interferon, JAK/STAT and Toll-like receptor (TLR) related genes were associated with pCR. Metabolic pathways emerged as associated with both overall and pathologic complete response (pCR and RD patients).
- NOTCH signaling was associated with lower pCR rate and Ki67 rebound at SX, indicating a significant role of this pathway in resistance.

References

2. Gianni L ASCO 2018

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