INTRODUCTION

- Endocrine therapies and cdk4/6 inhibitors have improved clinical outcomes and progression-free survival in metastatic hormone receptor positive (HR+), human epidermal growth factor 2 negative (HER2-) breast cancers (1).
- Early-stage breast cancer patients benefit initially from endocrine therapies, but most breast cancers eventually develop de novo or acquired resistance to cdk4/6i (2, 3).
- Mechanisms of cdk4/6i resistance in HR+ breast cancers are due mainly to endocrine therapy insensitivity (4).
- Multiple pathways involved in the development of resistance have been identified. However, improved clinical outcomes remain largely limited after development of resistance and disease progression.
- Focusing on clinical biomarkers contributing to resistance helps identify disease progression.
- Interleukin-6 promotes tumor survival and progression and could be investigated as a potential biomarker.

HYPOTHESIS

IL-6, a potential biomarker for endocrine therapy resistance, can be used to predict response to endocrine therapies in HR+, HER2- breast cancers. As an upregulator for tumor survival, IL-6 levels will increase during disease progression. Investigation into biomarkers will help determine additional therapies and give a better indication of metastatic HR+, HER2- breast cancer treatment response to cdk4/6i.

MATERIALS & METHODS

- Reagents: R&D Systems Quantikine Human IL-6 ELISA kit
- Patient Samples: Blood drawn from HR+, HER2- breast cancers at certain treatment timepoints and obtained through the clinic
- ELISA: Extracted plasma from patient blood samples to detect IL-6 levels throughout treatment timepoints

Additional Details:
- Blood samples were drawn from patients at baseline, timepoints at months 1, 4, 8, 12 and progression

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RESULTS & DISCUSSION

- Of the patients in the study who progressed, IL-6 levels at progression for those patients were higher than the IL-6 levels at baseline, even when IL-6 on-treatment trends were variable across patients
- Upon compiling all IL-6 measurements from metastatic or non-metastatic patients at baseline or progression, IL-6 levels in HR+, HER2- metastatic breast cancer patients who have progressed (post cdk4/6i) are significantly higher than IL-6 levels in metastatic patients at baseline (pre cdk4/6i) or early-stage non-metastatic patients.
- In addition, metastatic patients at baseline have significantly higher IL-6 plasma levels than the IL-6 levels of non-metastatic early-stage breast cancer patients.
- IL-6 levels did not exhibit significant change in on-treatment stages where the tumor was stable and had not yet developed therapeutic resistance.
- The sharp, significant increase in IL-6 levels during progression compared to baseline strongly suggests IL-6 is an important biomarker for resistance to endocrine therapies in HR+, HER2- breast cancers.
- Further focus on IL-6 and other potential biomarkers contributing to resistance would help better identify and predict disease progression, allowing determination of additional therapies and improved clinical outcomes.

REFERENCES

1) McAndrew NP. et al. Oncology & Hematology Rev 2020. DOI. 0.17925/OHR.2020.16.1.23
2) Lei JT. et al. Breast 2019. PMID. 31839155
3) Finn RS. et al. Lancet Oncology 2015. PMID. 25524798
4) Turner NC. et al. NEJM 2018. PMID. 30345905