Introduction

• The 2013 American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines for defining the HER2 receptor status of a breast cancer are utilized to determine who receives HER2 targeted therapy.

• There is substantial benefit to receiving HER2 targeted therapy for HER2 positive breast cancers.

• The benefit of HER2 targeted therapy is unclear for patients diagnosed with HER2 equivocal breast cancer, and the possible side effects of this therapy are not insubstantial, including cardiomyopathy.

• A core biopsy provides a limited amount of breast tissue. Could obtaining additional breast tissue with upfront surgery provide a more definitive HER2 diagnosis for patients diagnosed with HER2 equivocal breast cancer on core biopsy?

Methods and Materials

• Retrospective review of all HER2 equivocal core biopsies diagnosed and treated at Levine Cancer Institute from 2014 through 2017.

• HER2 equivocal specimens were defined using standards set forth by the 2013 ASCO/CAP guidelines: IHC 2+, single-probe FISH average HER2 copy number ≥4.0 and <6.0 signals/cell, or dual-probe HER2/CEP17 ratio <2.0 with an average HER2 copy number ≥4.0 and <6.0 signals/cell.

• Exclusion criteria included: positive or negative reflex test, positive or negative repeat test on a different core biopsy from the same specimen, patients with metastatic disease, patients not considered for surgery or chemotherapy for varying reasons, and biopsy at a site other than the breast.

Results

- 100% (n=9) patients were offered HER2 targeted therapy.
- 78% (n=40) of patients undergoing upfront surgery remained non-evaluable.
- 50% (n=20) of patients undergoing upfront surgery remained non-evaluable.
- The benefit of HER2 targeted therapy is unclear for patients diagnosed with HER2 equivocal breast cancer, and the possible side effects of this therapy are not insubstantial, including cardiomyopathy.
- A core biopsy provides a limited amount of breast tissue. Could obtaining additional breast tissue with upfront surgery provide a more definitive HER2 diagnosis for patients diagnosed with HER2 equivocal breast cancer on core biopsy?

Conclusions

• 49 patients HER2 equivocal on core biopsy.
  • 82% (n=40) received upfront surgery.
  • 50% (n=20) remained HER2 equivocal on surgical specimen.
  • 20% (n=4) of these patients received HER2 targeted therapy.

• 50% (n=20) patients were demonstrated to be either HER2 positive or negative on surgical specimen.
  • 45% (n=9) HER2 positive
  • 55% (n=11) HER2 negative

• 100% (n=9) patients were offered HER2 targeted therapy based on defined HER2 positive status of surgical specimen.
  • 78% (n=7) of these patients received HER2 targeted therapy.

• In 50% (N=20) of patients with a HER2 equivocal diagnosis based on core biopsy, obtaining a larger sample of breast tissue with upfront surgery provided patients with a definitive positive or negative HER2 diagnosis.

• Our institution was able to avoid the potential toxicities of HER2 targeted therapy in 55% (N=11) of patients found to be HER2 negative on final surgical specimen. Conversely, we were able to confidently offer HER2 targeted therapy for 45% (N=9) of patients found to be HER2 positive on final surgical specimen.

• Patients that could benefit were treated, and treating patients blindly without tumor biology knowledge was avoided.

• 50% (N=20) of patients undergoing upfront surgery remained HER2 equivocal on final surgical specimen and additional tissue did not resolve the dilemma of HER2 equivocal diagnoses.

References:
1. Long, Trusso, N.L., Levine, H. and Others. The New ASCO/CAP Guidelines: IHC 2+, single-probe FISH average HER2 copy number ≥4.0 and <6.0 signals/cell, or dual-probe HER2/CEP17 ratio <2.0 with an average HER2 copy number ≥4.0 and <6.0 signals/cell.