

Retrospective analysis to determine the use of tissue genomic analysis to predict the risk of recurrence in early stage invasive breast cancer.

Goal of the study:

- 1.To assess whether patients at Truman Medical Center/Bloch Cancer Center are evaluated & treated according to evidence-based American Society of Clinical Oncology¹ and National Comprehensive Cancer Network (NCCN) guidelines².
- 2.To assess the use of precision oncology driven genomic panel in early stage, hormone positive, lymph node negative invasive breast cancer.

Introduction:

Among women breast cancer is the most commonly diagnosed cancer and the second most common cause of cancer related death. Around 250,000 new cases of breast cancer are estimated in 2017.³ Traditionally size of the tumor, grade, histology, molecular expressions of estrogen (ER), progesterone (PR)and epidermal growth factor receptor 2 (HER2) have been used to guide the specific type of adjuvant treatment in breast cancer. Majority of patients with breast cancer undergo surgical resection and afterwards receive following treatments concurrently or in sequential manner.

- Adjuvant Chemotherapy
- Post lumpectomy or mastectomy radiation
- Adjuvant endocrine therapies
- Adjuvant targeted therapies

Chemotherapy is used to control the systemic disease and prevent the local or distant recurrence. It is associated with many systemic side effects and due to our inability to figure out which patients will benefit from chemotherapy we end up over treating a group of patients who might be at very low risk of recurrent disease. There has been retrospective data to support the use of gene panels to help predict the risk of recurrence and guide adjuvant chemotherapy. In 2015, a prospective trial involving patients with hormone-receptor-positive, HER2-negative, axillary node-negative breast cancer supported the clinical validity of the 21-gene assay in identifying patients who may be safely spared of adjuvant chemotherapy.⁴

The NCCN guideline 2017 recommend any invasive breast cancer which is early stage with pathologically negative lymph nodes or only micro metastasis to axillary lymph nodes and size greater than 0.5 cm can be considered to undergo 21 gene panel to help guide the adjuvant chemotherapy.²

Methods:

We reviewed the electronic medical records of all the patients diagnosed with breast cancer in year 2016. We identified 69 new cases of breast cancer in year 2016. All of them were treated at Bloch Cancer Center in outpatient setting by a multidisciplinary team involving medical oncologists, breast surgeons, radiologists, pathologists, primary care physicians, pharmacists and psychologists. When needed, each case was discussed in a multispecialty tumor board. This quality improvement retrospective analysis was exempt from institutional review board approval.

Following variables were assessed among the cohort of 69 patients:

- Age
- Sex
- Race
- Stage
- Lymph node status
- Size of primary tumor
- ER/PR status
- HER2 status
- Histology
- Type of surgery
- OncotypeDX performed or not
- Chemotherapy received or not
- Endocrine therapy received or not

Results:

Majority of patients were females (n=68). Race distribution was diverse Total 69 patients were evaluated, 42% were black, 39% were white, 12 % were Hispanic, 4% were Middle Eastern and 3% were others, (figure1).

American Joint Committee on Cancer (AJCC) guidelines were used post operatively to assign the stage. Patients cohort included both early and advanced stage breast cancer patients, there were thirteen patients with stage 1A, Nine patients with stage 2a, Eight patients with stage 3a and seven patients with stage 4, (figure2).

There were eight patients who underwent 21 gene panel testing (oncotypeDX). Four patients were stratified as low risk and five were intermediate risk. All eight patients received adjuvant endocrine therapy and adjuvant chemotherapy was avoided on basis of their recurrence score and discussion with the patients.

On further analysis of data, ten patients were found to be eligible to undergo 21 gene panel testing, out of that only eight patients underwent testing, one patient refused to follow at all and one followed at different medical facility. (figure3)

We also looked into Her2 testing on pathological specimen, 100% patients were tested for Her2, and among them 61% were negative and hence ineligible for any Her2 based therapy. 23% patients were positive. 16% patients which are mentioned as unknown mainly include who didn't follow or transferred care to different facility. Similarly, we looked into estrogen receptor (ER) and progesterone receptor (PR) status and found seventy eight percent patients as hormone positive and twenty two percent patients as hormone negative. Hormone positive patients were prescribed appropriate treatments. Different molecular subtypes in the cohort are shown in figure 4 & 5. We also looked into type of surgical treatments patients received. (diagram 1)

Conclusion:

We found 80% (n=8) compliance to the current guidelines for oncotype Dx testing by American Society of Clinical Oncology¹ and National Comprehensive Cancer Network (NCCN) guidelines. In 20% (n=2) of cases, patient preference affected the decision making as one patient refused to undergo any further treatment or workup and one patient transferred care to different facility.

The findings clearly indicate the adherence to current practice guidelines. Further studies are required to expand the predictive value of tissue genomics to more advanced stages of breast cancer.

Moreover, over study showed 100% compliance with testing of pathological specimen for hormonal status and Her2 status. Patients received different surgical treatments that's is lumpectomy vs mastectomy depending upon disease stage and patient preference.

References:

1. Harris LN, Ismaila N, Mcshane LM, et al. JOURNAL OF CLINICAL ONCOLOGY Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-Stage Invasive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol.* 34:1134-1150. doi:10.1200/JCO.2015.65.2289.
2. NCCN - Evidence-Based Cancer Guidelines, Oncology Drug Compendium, Oncology Continuing Medical Education. <https://www.nccn.org/>. Accessed October 17, 2017.
3. Estimated numbers of new cancer cases for 2017, excluding basal cell and squamous cell skin cancers and in situ carcinomas except urinary bladder. <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2017/cancer-facts-and-figures-2017.pdf>. Accessed October 17, 2017.
4. Sparano JA, Gray RJ, Makower DF, et al. Prospective Validation of a 21-Gene Expression Assay in Breast Cancer. *N Engl J Med.* 2015. doi:10.1056/NEJMoa1510764.

Figure1

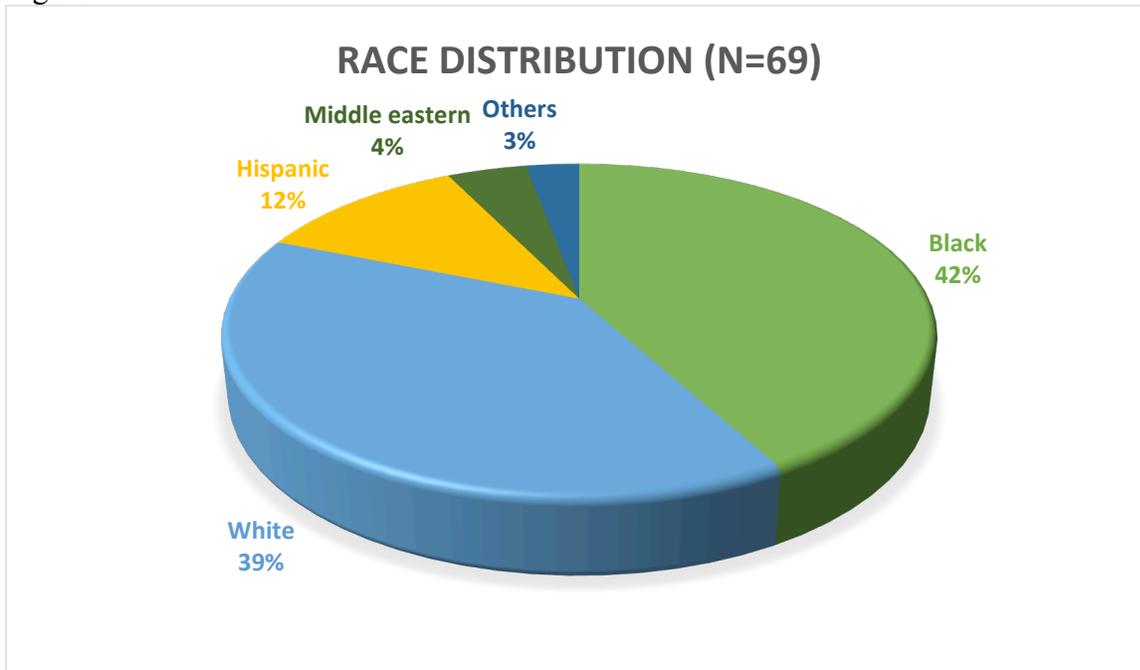


Figure2

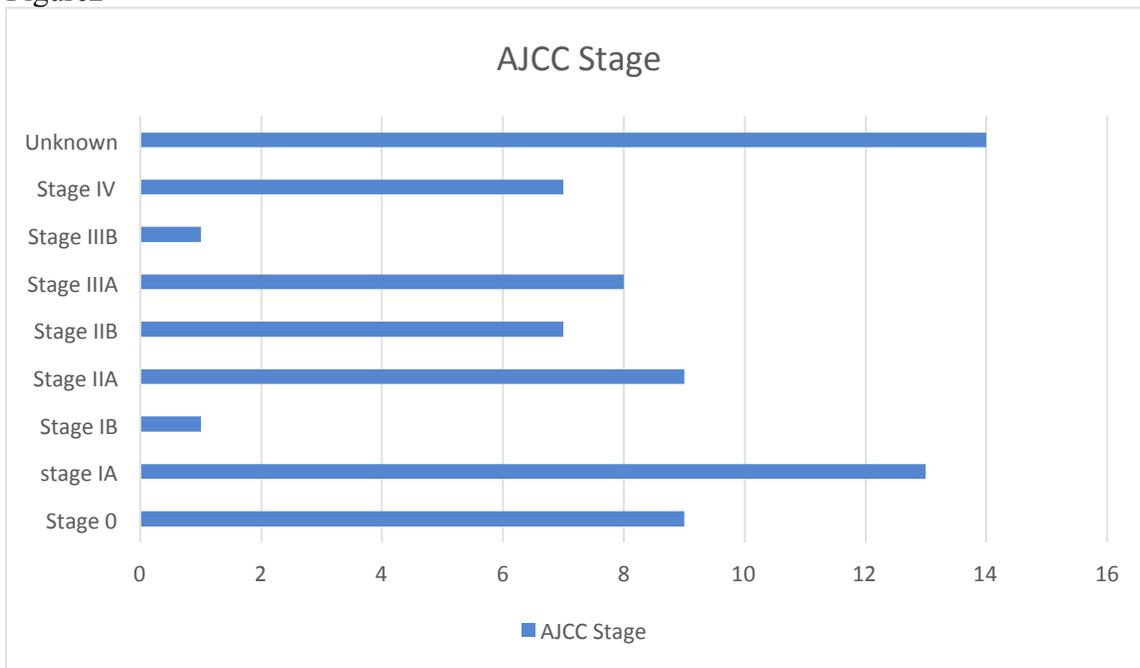


Figure3

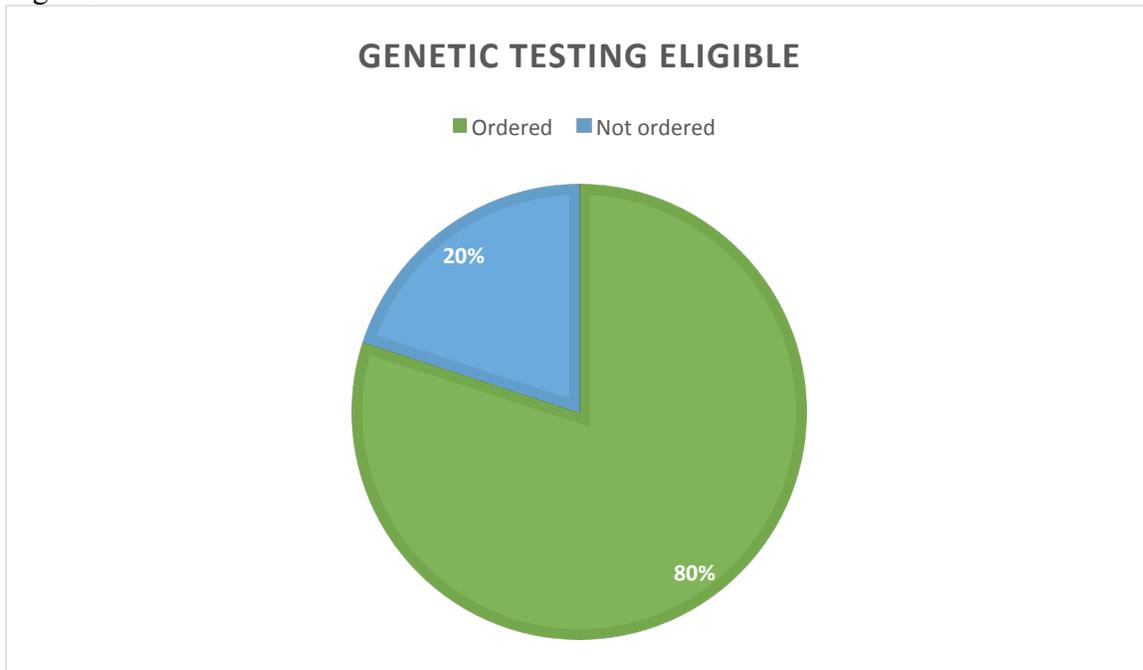


Figure4

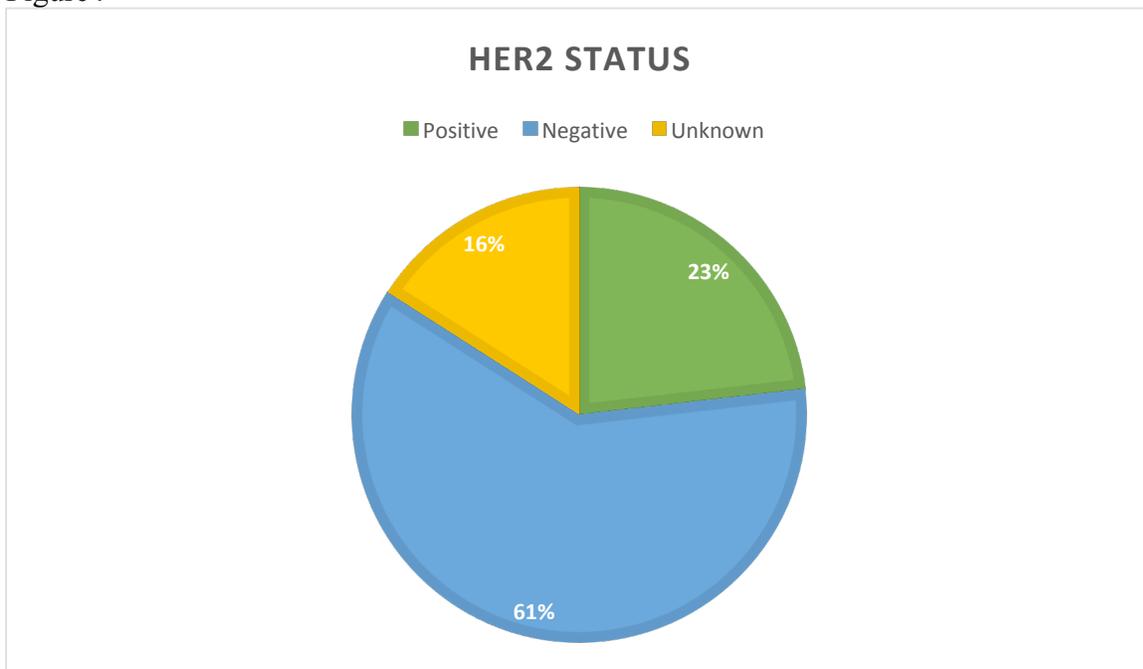
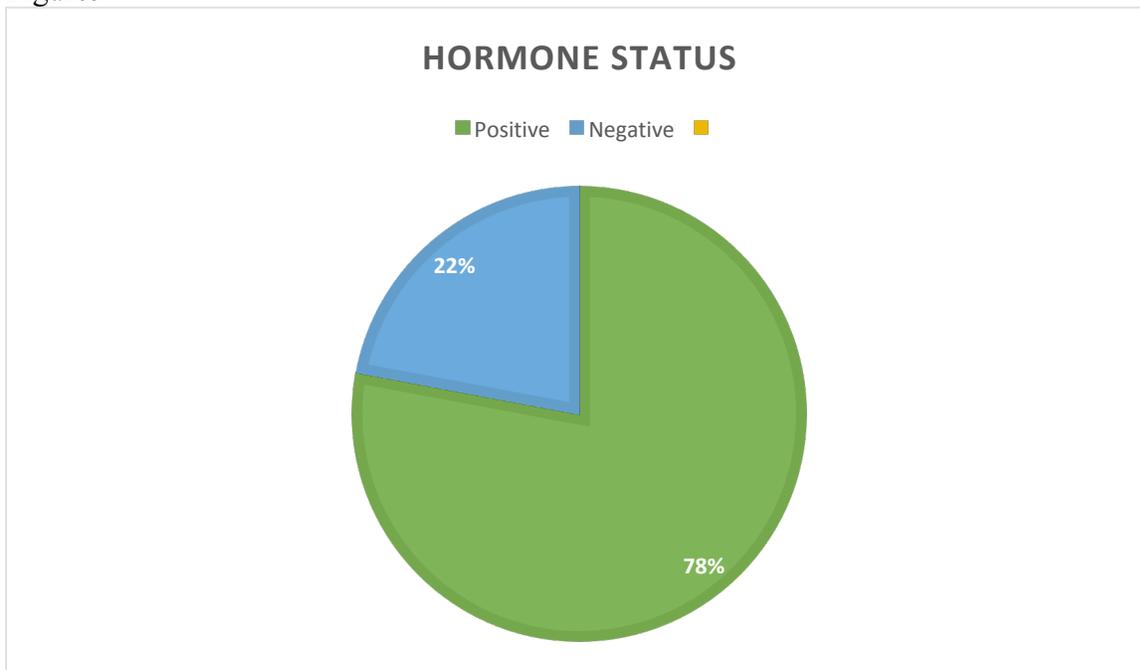
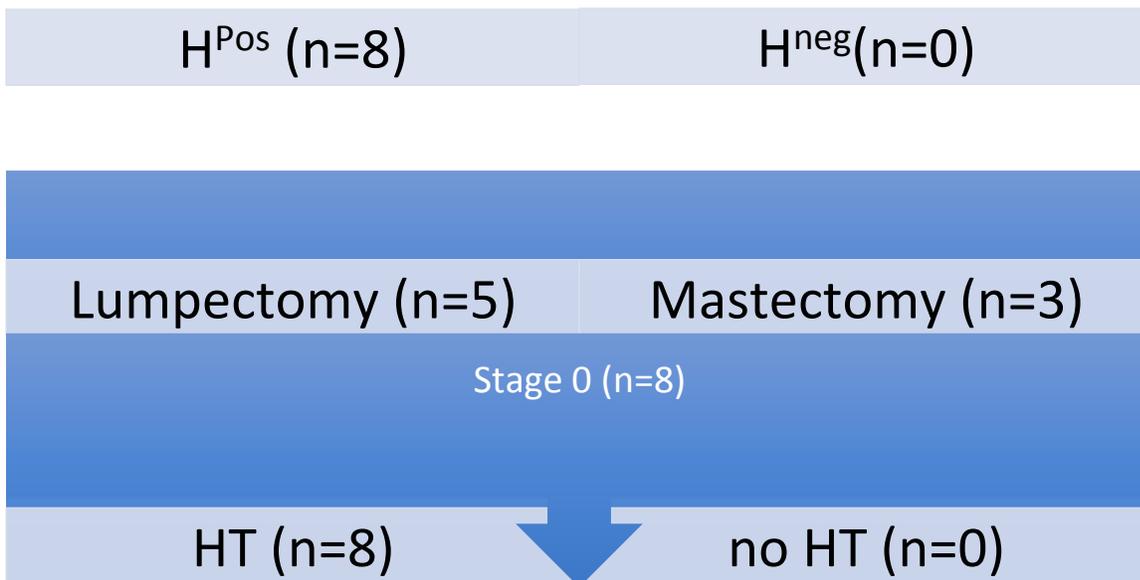
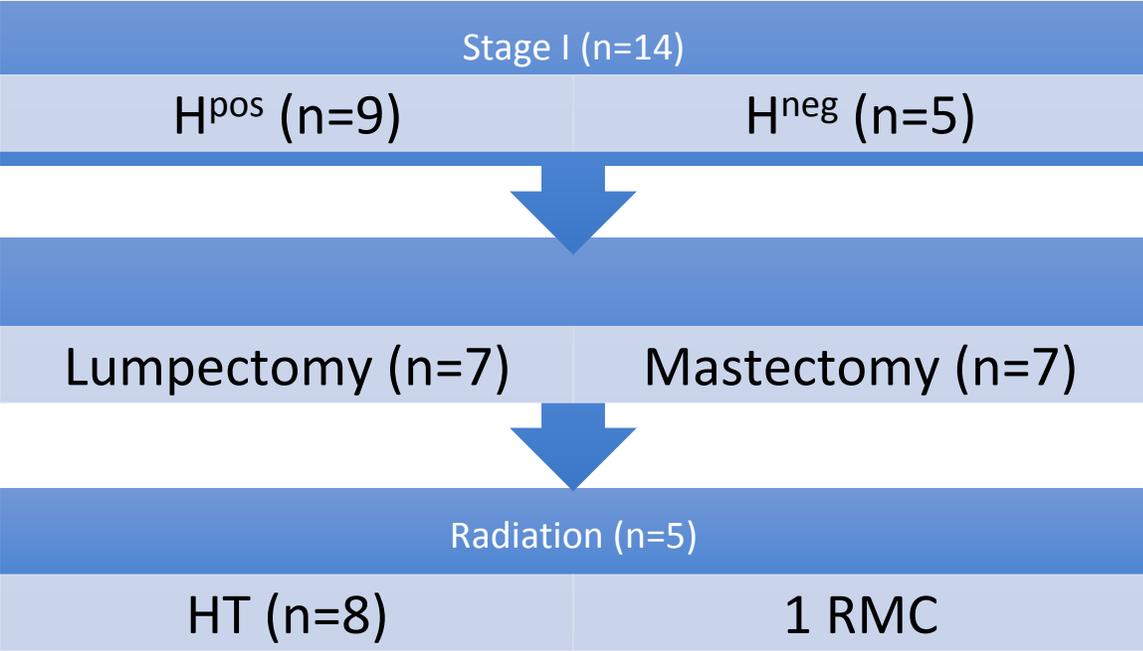


Figure5

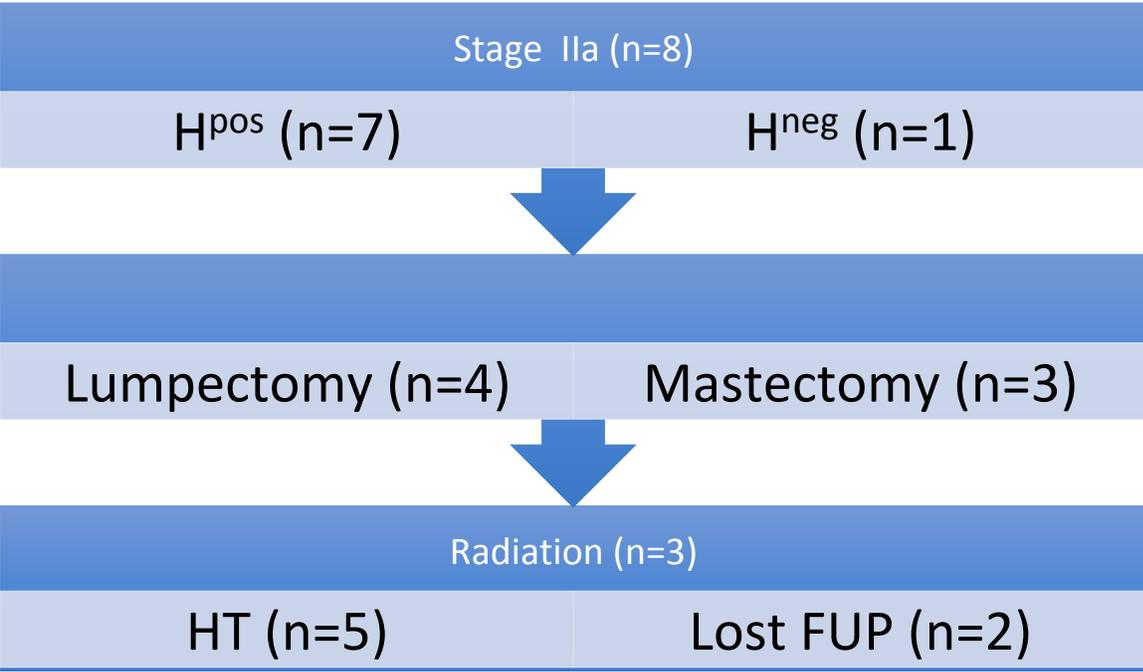


Stage 0 HT= Hormonal therapy, H= Hormone.

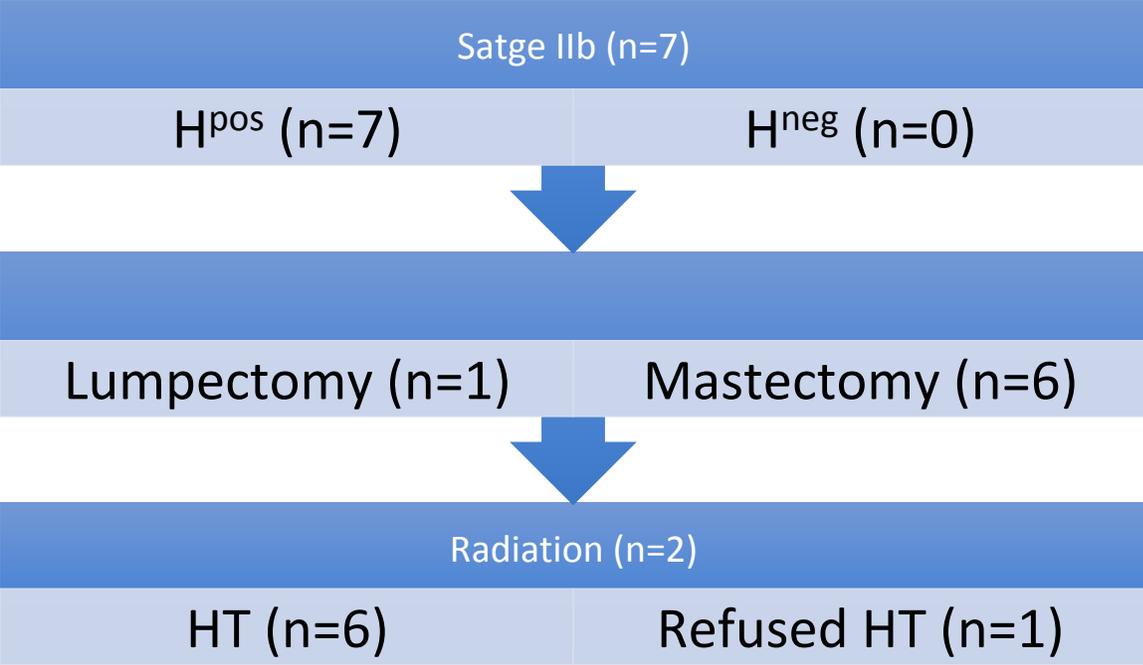




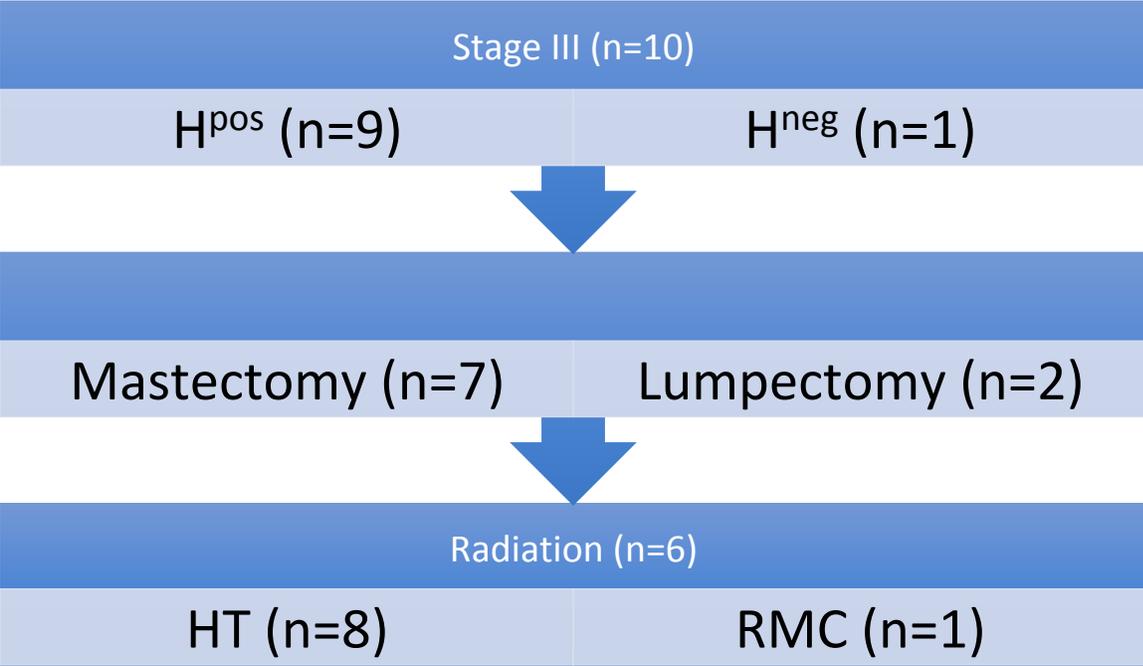
Stage I



Stage IIa



Stage IIb



Stage III

Diagram1