The following set of rules will be utilized within an inference system designed to guide patients in understanding their breast cancer treatment journey. While not exhaustive, these rules serve as a valuable reference for patients, sourced from the NCCN's guidelines for patient care concerning breast cancer.

Surgery

Rule 1:

- If a patient has invasive breast cancer, surgery is the primary treatment. Radiation therapy and systemic therapy are possible following surgery(If no preoperative therapy then this method of treatment)

Rule 3:

- There are two primary surgical options: lumpectomy (breast-conserving surgery) and total mastectomy.

Rule 4:

- Lumpectomy(Breast conserving surgery) may be followed by whole breast radiation therapy (WBRT) and possibly chemotherapy, depending on cancer type and lymph node status. Also regional node Irradiation might be added(If cancer is found in the axilllry lymph nodes[ALN's] and type of cancer)

Rule 5:

- Total mastectomy(The whole breast removed) may be followed by radiation therapy and/or systemic therapy, depending on lymph node status and tumor size.(if cancer was found in the axillary lymph nodes (ALNs), the number of lymph nodes that tested positive, and the size of the removed tumor)

Rule 6:

After Surgery:

Adjuvant systemic therapy(Drug treatment after surgery or radiation therapy is called adjuvant systemic therapy. It is given to kill any remaining cancer cells and to help reduce the risk of cancer returning.) may be given after surgery or radiation therapy to kill any remaining cancer cells and reduce the risk of cancer recurrence.

Rule 7:

- Adjuvant systemic therapy is based on tumor histology, hormone receptor (HR) status, and HER2 status. It may include endocrine therapy, HER2-targeted therapy, or chemotherapy.
- Note : Histology is the study of the anatomy (structure) of cells, tissues, and organs under a microscope

Rule 8:

- HR+ cancer, which includes estrogen receptor-positive (ER+) and/or progesterone receptor-positive (PR+) tumors, may receive endocrine therapy.

Rule 9:

- HER2+ cancer, with overexpressed HER2 receptors, may receive HER2-targeted therapy in addition to other treatments.

Rule 10:

- Triple-negative breast cancer (TNBC), which lacks HER2 and HR receptors, is typically treated with chemotherapy.

Rule 11:

- Favorable histology types of breast cancer may have a better prognosis and have less risk of returning and might receive specific treatments.
- . These tumor types are not high grade, are HER2-, and might respond better to treatment than other tumors
- Other systemic therapies are possible.

Favorable histology types include:

- Pure tubular
- Pure mucinous
- Pure cribriform
- Encapsulated or solid papillary carcinoma(SPC)
- Adenoid cystic and other salivary carcinomas
- Secretory carcinoma
- Rare low-grade forms of metaplastic carcinoma
- Other rare forms

Rule 12:

- Common histology types include ductal/no special type and lobular carcinoma, each with its potential treatments.

Common histology types include:

◦ Ductal/no special type (NST) (NST includes medullary pattern, cancers with neuroendocrine expression, and other rare patterns)

◦ Lobular

◦ Mixed

• Micropapillary

> Metaplastic (includes various subtypes)

Adjuvant treatment options for common histologies are described below Rule 13

Rule 13:

- HR+ with HER2+ cancer may receive specific HER2-targeted therapies, such as paclitaxel and trastuzumab.(Details in guide 4,5,6)

Rule 14:

- HR+ with HER2- cancer may receive different treatments, which might include endocrine therapy and chemotherapy.(Details page 60)

Rule 15:

- HR- with HER2+ cancer focuses on targeting HER2 receptors. Since the treatment is focused on treating HER2, HER2 ussually involves chemotherapy
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Rule 16:

- Triple negative breats cancer does not have HER2 receptors . Therefore HER2-therapy is not used Since no estrogen and progesterone hormone recptors endocrine therapy is not used . Adjuvalent treatment is chemotherapy for TNBC – Guide 5

Rule 18:

- Adjuvant endocrine therapy is used to treat HR+ breast cancer and may include tamoxifen or aromatase inhibitors.

Rule 19:

- The duration of endocrine therapy depends on menopausal status and other factors.

Rule 21:

- Follow-up care includes physical exams, genetic testing if needed, monitoring for lymphedema, mammograms, heart tests, and maintaining a healthy lifestyle.

Preoperative treatment

Rule 1: Identifying Stage 3 Breast Cancer:

- IF the cancer is large AND in the lymph nodes OR the cancer involves the skin or chest wall,
- THEN classify it as Stage 3 breast cancer.

Rule 2: Preoperative Therapy Options:

- IF the patient has Stage 3 breast cancer,
- THEN discuss preoperative therapy options, including systemic therapy or radiation therapy.

Rule 2 : Testing
If preoperative systemic therapy

then will have blood and imaging tests before starting treatment. These tests will determine if your cancer can be removed with surgery (operable) or cannot be removed with surgery at this time (inoperable).

Testing will include an axillary lymph node exam with ultrasound and biopsy of lymph nodes suspected of cancer.

Rule 3: Preoperative Testing:

- IF considering preoperative therapy,
- THEN conduct core biopsy of the breast, place clips or markers for surgical guidance, and perform an axillary lymph node exam.

Rule 4: Determining Operability:

- IF preoperative therapy is an option,
- THEN conduct blood and imaging tests to determine if the cancer can be surgically removed (operable) or not (inoperable).

Rule 5: Preoperative Systemic Therapy Options

Note - treatment before surgery is called preoperative therapy:

- IF opting for preoperative therapy and considering systemic(which is drug therpaty} therapy,
- THEN choose the therapy based on hormone receptor (HR) and HER2 status.

Rule 6: Benefits of Preoperative Systemic Therapy:

- IF considering preoperative systemic therapy,
- THEN its benefits:
- Help preserve the breast
- Shrink the tumor
- Shrink the tumor so it can be removed with a smaller surgery (lumpectomy)

• Provide important information about how your tumor responds to therapy, which is very helpful in those with triple-negative (TNBC) and HER2+ breast cancer

- Help choose adjuvant regimens in those with HER2+ and TNBC with residual disease
- Allow time for genetic testing
- Allow time to plan breast reconstruction in those choosing mastectomy
- Allow time for fewer lymph nodes to be removed at the time of surgery
- Allow time for you to decide about and prepare for surgery
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Rule 7: Monitoring Treatment Response:

- IF undergoing preoperative therapy,
- THEN schedule regular tests to monitor the tumor's response.

Rule 8: Postoperative Surgery Options:

- IF the tumor shrinks or the cancer burden is reduced after preoperative therapy,
- THEN consider surgery options, including lumpectomy or mastectomy, followed by systemic and radiation therapy.
- Else if tumor did not shrink enough to be removed with surgery
- Then more systemic therapy and /or radiation therapy

Rule 9: Adjuvant Treatment(tretament after surgery)

- IF cancer remains after surgery or if there's residual disease,
- THEN discuss adjuvant therapy based on tumor characteristics.

Rule 10: Pathologic Staging After Preoperative Therapy:

- IF the tumor responded to preoperative therapy,
- THEN restage the cancer after surgery and classify it using pathologic staging.

Rule 11: Hormone Receptor-Positive (HR+) Cancer Treatment:

- IF the cancer is HR+,
- THEN consider adjuvant endocrine therapy.

Rule 12: HER2-Positive (HER2+) Cancer Treatment:

- IF the cancer is HER2+,
- THEN discuss HER2-targeted therapy options, including trastuzumab and pertuzumab.

Rule 13: Triple-Negative Breast Cancer (TNBC) Treatment:

- IF the cancer is triple-negative (ER-, PR-, HER2-),
- THEN treat with chemotherapy and other systemic therapies found in Guide 9.

Rule 14: Treatment Order and Types

- IF considering preoperative therapy, perioperative therapy, or postoperative therapy,
- THEN follow the treatment order, including primary treatment, postoperative therapy, first-line therapy, and second-line therapy, as appropriate.

Rule 15: Follow-Up Care:

- IF treatment is completed,
- THEN enter follow-up care, which includes regular medical exams, imaging tests, and adherence to prescribed therapies.

Treatment after surgery :

Rule 16: Breast Reconstruction Options:
IF considering breast reconstruction after mastectomy,
THEN discuss the available options: volume displacement, flat closure, breast implants, flaps, or a combination of implants and flaps.

Rule 17: Volume Displacement Procedure:
IF a lumpectomy is needed and the breast may appear abnormal post-surgery,
THEN consider volume displacement or oncoplasty to reshape the breast using remaining tissue and fill the tumor-removed space.

Rule 18: Flat Closure Procedure:
IF opting for a total mastectomy without breast mound creation or implant addition,

THEN choose flat closure, where remaining skin is tightened and sewn together without breast reconstruction.

Rule 19: Breast Implant Reconstruction:
IF seeking breast reconstruction with implants,
THEN discuss options involving saline or silicone-filled implants, possibly preceded by tissue expansion using an expander device.

Rule 20: Flap Reconstruction:
IF considering breast reconstruction using tissue flaps from various body parts,
THEN evaluate the suitability of flap techniques and discuss risks associated with tissue removal and placement.

Rule 21: Nipple Remake Options:
IF interested in nipple reconstruction,
THEN explore options such as using surrounding tissues or tattooing, knowing that remade nipples won't have the sensation of real nipples.

Rule 22: Considerations for Reconstruction:
Consider the following factors when deciding on breast reconstruction:
◦ Desire for reconstruction or flat closure
◦ Health status and potential impact on healing and safety
◦ Tobacco use and its effect on surgical outcomes
◦ Breast size, shape, and available reconstruction options
◦ Body mass index (BMI) and its implications on infection risk and complications.

Rule 23: Smoking and Vaping Precautions:
IF considering surgery, including breast reconstruction,
THEN quit smoking or vaping to minimize surgery-related risks, improve wound healing, and enhance treatment effectiveness.

Rule 24: Nicotine Use and Surgery:
IF using nicotine through smoking, vaping, or other means,
THEN understand that it can negatively affect surgery outcomes, wound healing, cancer treatment, and may increase the risk of other cancers.

Rule 25: Nicotine Withdrawal Support:
IF using nicotine and considering quitting,
THEN seek counseling and medicinal support to overcome nicotine addiction, aiding in a smoother surgical and recovery process.

Reuccerence :

Rule 26: Identifying Breast Cancer Recurrence:
IF cancer reappears after initial treatment,
THEN it is termed a recurrence, categorized as local (breast), regional (axillary lymph nodes), or distant (metastatic breast cancer).

Rule 27: Recurrence Testing and Restaging:
IF experiencing a recurrence,
THEN undergo tests, including restaging and additional tests based on symptoms, to determine the extent of the recurrence, using guidelines provided in Guide 12.

Rule 28: Treatment Planning for Recurrence:
IF facing a recurrence,
THEN collaborate with the care team to devise a treatment plan based on the location of recurrence and previous treatments, potentially involving surgery, radiation therapy, and systemic therapy.

Rule 29: Hormone Receptor and HER2 Status:
IF experiencing a recurrence and considering treatment options,
THEN factor in hormone receptor (HR) and HER2 status to tailor systemic and endocrine therapy, along with assessing genetic markers.

Rule 30: Local Recurrence Treatment Options:
IF facing a local recurrence,
THEN the treatment depends on previous breast surgery (lumpectomy or mastectomy) and may involve additional surgery or alternative options if radiation therapy was administered previously.

Rule 31: Regional Recurrence Treatment Options:
IF encountering a regional recurrence,
THEN surgical removal of the tumor might be an option if the recurrence is in or near the armpit (axilla), possibly followed by radiation therapy and systemic therapy.

Rule 32: Locoregional Recurrence Treatment:
IF dealing with both local and regional recurrence (locoregional),
THEN consider surgery and radiation therapy, supplemented by systemic therapy if surgery is not feasible.

Rule 33: Treating Unresectable Recurrence:
IF facing an unresectable tumor,
THEN opt for systemic therapy as surgery is not possible, following guidelines outlined in NCCN Guidelines for Patients: Metastatic Breast Cancer.

Rule 34: Supportive Care for Recurrence:
IF experiencing a recurrence,
THEN receive supportive care to alleviate side effects and enhance the overall quality of life during the course of treatment.

Rule 35: Monitoring and Psychological Support:
IF dealing with breast cancer recurrence,
THEN undergo regular monitoring and psychological assessment to address distress and emotional well-being throughout the treatment journey.