

## Patient Resource:

# Treatment Options for Early-Stage Breast Cancer



The goals of this resource are as follows:

### PART 1

Provide information about early-stage breast cancer and help you identify what is important to you before engaging in conversations about your treatment options both before and after surgery to remove as much of the cancer as possible. Treatment before surgery is called neoadjuvant therapy and treatment after surgery is called adjuvant therapy. This section also will provide you with a few sample questions to ask your healthcare team.

### PART 2

Introduce standard definitions for the 3 major types of breast cancer—hormone receptor (HR) positive, HER2 positive, and triple-negative breast cancer (TNBC)—that are treated with different medicines. When doctors recommend treatments, they often look at many additional characteristics of the cancer along with your personal health history to individualize treatment as much as possible. Many of the questions below are about understanding these additional cancer characteristics.

### PART 3

The third section covers some possible patient scenarios with early-stage breast cancer that may be helpful to bring up and discuss with your healthcare professionals to help you select the most appropriate treatments for you. Example cases at the end of this document describe different subtypes of early-stage breast cancer diagnoses, including frequently seen characteristics that led to different treatment recommendations.

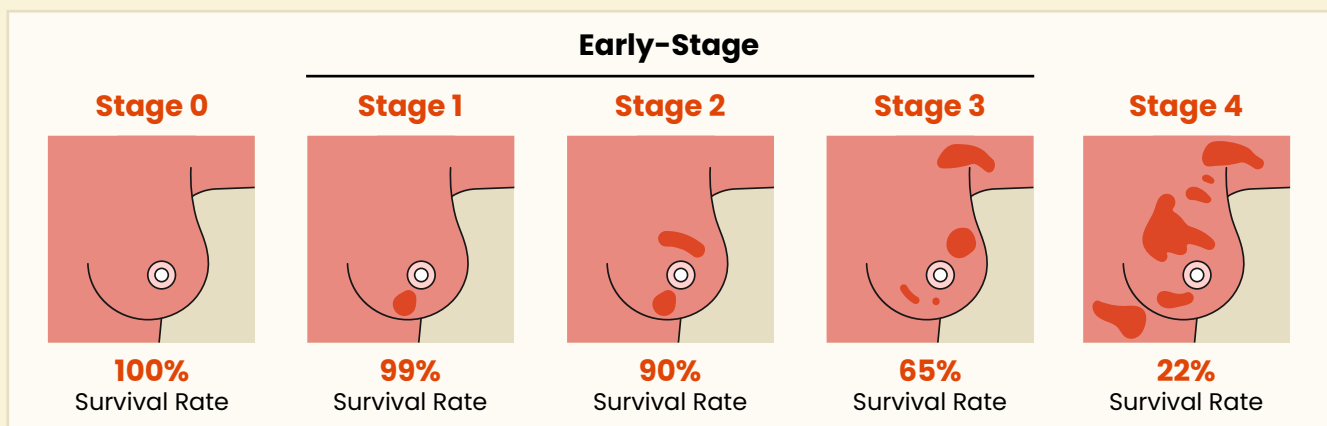
Understanding your diagnosis and treatment options, which depend on tumor subtype, stage/risk, actionable biomarkers, and prior treatment, will make it easier to partner with your oncology care team to make decisions that work for you.

*Before you begin, you'll want to have as much information as possible about your diagnosis. If you don't have all of the information listed below, ask your oncology care team to help you answer the questions.*



## PART 1 Early-Stage Breast Cancer Explained

**Early-stage breast cancer** usually means breast cancer that has not spread to distant parts of the body. This can include stage 0 to stage III disease, depending on the tumor size, lymph node involvement, and other features. Stage IV disease is known as metastatic disease and has spread to other distant sites in the body.



## Treatment Decisions and Your Quality of Life

### What Do You Need to Tell Your Doctor?

Information about the nature of your cancer isn't the only important factor in making decisions about your treatment. Treatments need to work for you and fit your lifestyle and priorities as much as possible. In other words, you should think about your preferences, needs, and priorities regarding treatment and share them with your care team.

According to younger patients with breast cancer:

*“You'll want to strike a balance between treatment priorities and your quality of life and being able to enjoy life with your family” and that “at some points in your journey, you may choose to give more weight to treatment, even if it affects your quality of life.”*

Knowing what you value will help you and your care team find this balance together.

*“When someone is newly diagnosed, they're often overwhelmed, scared, and trying to process so much information at once. Many of us don't even know what questions to ask until we're already in treatment or sometimes until it's too late.”*

To discover what is most important for you before discussing treatment, some questions you may want to ask yourself include:

- What upcoming events, activities, work responsibilities, or family situations should we keep in mind as we think about your treatment schedule? What kind of support do you have from family, friends, or others, and what additional help might you need at home during treatment?
- What other health conditions or medical issues do you think we should consider as we discuss treatment options?
- What side effects would feel most manageable for you, and which ones would be especially difficult or unacceptable? For example, some people may be okay with feeling tired but never want to feel pain.
- How do your travel patterns or time spent in different locations affect where you may need to receive treatment? Are there any possible moves or location changes coming up that could affect your treatment planning?
- How are conversations with loved ones going, and what support might be helpful as you talk with them about treatment?
- What are your concerns about costs? What other worries, fears, or concerns are on your mind as you think about treatment?
- What are your concerns about fertility, sexuality, or future family planning that are important to you?
- Do you have a plan for managing daily needs during treatment, such as transportation to appointments, paying bills, putting food on the table, preparing meals, childcare, or getting help if you're unable to work or care for yourself?
- How would a *BRCA1* or *BRCA2* mutation inform treatment options and outcomes?
- Who else do you want involved in helping you make treatment decisions?
- Are there financial assistance programs, transportation services, or other resources available if I need them?
- What side effects should I expect, and who should I contact if they become severe?
- How will treatment affect my quality of life, and what support services are available?

Make notes as you think about it and keep them up to date as time goes by. If anything about your priorities or your situation changes, it's important to let your care team know.

## PART 2

### Introducing the 3 Major Types of Breast Cancer: HR Positive, HER2 Positive, and TNBC

#### Patient–Provider Questionnaire: Describing Your Early–Stage Breast Cancer

To prepare for your treatment, fill out this questionnaire as much as you can, based on your diagnosis, past treatments or surgery (if applicable), and the test results you've received to date. If your answer to any question is “I don't know,” reach out to someone on your oncology care team to get the answer.

#### This patient tool kit starts by assuming that you:

- Have been diagnosed with early-stage breast cancer
- Have or have not undergone surgery
- Do not have any other health conditions or other traits that would affect the choice of treatment, besides those you describe when answering the questions in the tool



**1. Which of the following best describes your cancer's subtype?**

- ☐ HR positive
- ☐ HER2 positive
- ☐ HR negative/HER2 negative (meaning TNBC)
- ☐ I don't know

If the cancer is HER2 positive, please continue to question 7. If the cancer is TNBC, please continue to question 11.

HR-positive early-stage breast cancer has estrogen receptors, progesterone receptors, or both that fuel the growth of the cancer, and this matters because endocrine therapy can substantially reduce the risk that the cancer will come back by targeting these growth mechanisms. Treatment often includes medicines such as tamoxifen or an aromatase inhibitor, with the overall plan depending on characteristics including tumor size, lymph node involvement, genomic test results, menopausal status, and overall health.

**2. Which of the following best describes your breast cancer?**

- ☐ Tumors up to 2 cm in size and no cancer in any lymph nodes (node negative)
- ☐ Tumors larger than 2 cm and/or cancer in at least 1 lymph node (node positive)
- ☐ I don't know

**3. Which of the following neoadjuvant treatment regimens did you receive in addition to ovarian function suppression if you are premenopausal?**

- ☐ No therapy before surgery (neoadjuvant)
- ☐ Chemotherapy only
- ☐ Endocrine therapy (tamoxifen or aromatase inhibitor [AI])
- ☐ I don't know

**4. Did you have a pathologic complete response (or pCR; no cancer cells detected after neoadjuvant treatment)?**

- ☐ Yes
- ☐ No
- ☐ I don't know

**5. Have you tested positive for a germline *BRCA1* or *BRCA2* mutation, or both?**

- ☐ Yes
- ☐ No
- ☐ I don't know

**6. Do you fit the eligibility criteria for the HR-positive group in the OlympiA trial? (See the callout)**

- ☐ Yes
- ☐ No
- ☐ I don't know

**To be eligible for the HR-positive group in the OlympiA trial, you need to:**

- Be at least 18 years of age
- Test positive for a germline *BRCA1* or *BRCA2* mutation, or both
- Have HR-positive, HER2-negative primary breast cancer that is still at high risk for recurring after being treated with chemotherapy before or after surgery. HR-positive disease was considered high risk if you had surgery followed by chemotherapy and had cancer in at least 4 axillary lymph nodes; or if you were previously treated with chemotherapy followed by surgery, did not experience a pCR, and had a clinical and pathologic stage (CPS) + estrogen receptor status and histologic grade (EG) score of 3 or higher
- Have completed all treatments directed at the tumor itself, including surgery and radiation therapy, between 2 and 12 weeks before starting the trial
- Have completed 6 or more cycles of chemotherapy before or after surgery that included anthracyclines, taxanes, or both; this could include platinum chemotherapy

**The following questions are for cancers that are HER2 Positive**

HER2-positive breast cancers have "extra" HER2 protein or extra copies of the HER2 gene in the tumor cells. This matters because HER2-directed medicines can substantially change treatment recommendations. FDA-approved HER2-directed treatment options include monoclonal antibodies such as trastuzumab and pertuzumab, antibody-drug conjugates such as ado-trastuzumab emtansine (T-DM1) and fam-trastuzumab deruxtecan-nxki (T-DXd), and kinase inhibitors such as neratinib and tucatinib. Which option is appropriate depends on your cancer stage, prior treatments, test results, and overall health. If you do not know whether the cancer is HER2 positive, ask your oncology care team whether HER2 testing was done on the biopsy or surgery sample.

**7. Which of the following best describes the HER2-positive breast cancer?**

- ☐ Small tumor up to 2 cm and no cancer in lymph nodes
- ☐ Tumor larger than 2 cm, cancer in at least 1 lymph node, or locally advanced/inflammatory disease
- ☐ I don't know

**8. Did you receive treatment before surgery for HER2-positive breast cancer?**

- ☐ Chemotherapy plus trastuzumab and pertuzumab
- ☐ Chemotherapy plus trastuzumab only
- ☐ No, surgery with or without radiotherapy only
- ☐ I don't know

**9. If you received treatment before surgery, did you have a pathologic complete response (also known as pCR; no invasive cancer detected after treatment)?**

- ☐ Yes
- ☐ No, residual invasive cancer was found
- ☐ I don't know

**10. If the cancer is both hormone receptor positive and HER2 positive, has your doctor discussed endocrine therapy and whether extended HER2-directed therapy is appropriate after trastuzumab-based treatment? (See the callout)**

- ☐ Yes
- ☐ No
- ☐ I don't know

**HER2-positive treatment points to discuss with your care team**

- Small, node-negative HER2-positive cancers may be treated with surgery first and a shorter chemotherapy/HER2-directed therapy approach such as paclitaxel (a chemotherapy) plus trastuzumab (a HER2-directed therapy).
- Among patients with small, node-negative HER2-positive breast cancer treated in the single-arm phase II APT trial with adjuvant paclitaxel plus trastuzumab followed by trastuzumab to complete 1 year of therapy, the 10-year invasive disease-free survival rate was 91.3% (95% CI, 88.3%–94.4%); the 10-year recurrence-free interval was 96.3%.
- For tumors larger than 2 centimeters or node-positive disease, treatment before surgery is commonly used so the surgical pathology result can help guide adjuvant therapy.
- For HER2-positive stage II or III breast cancer, T-DXd followed by a combination of a taxane, trastuzumab, and pertuzumab is now FDA approved as a neoadjuvant treatment option based on the large DESTINY-Breast11 clinical trial.
- If cancer is still found in the breast or lymph nodes after treatment given before surgery, your care team may recommend more HER2-directed therapy after surgery. Options may include T-DM1 or, for some patients, T-DXd.
- In the phase III KATHERINE clinical trial, T-DM1 helped more patients remain free from invasive breast cancer coming back, a new invasive cancer developing, or death compared with trastuzumab.
- In the phase III DESTINY-Breast05 clinical trial, T-DXd helped more patients remain free from invasive breast cancer coming back, a new invasive cancer developing, or death compared with T-DM1.
- Pertuzumab is most relevant when the cancer has a higher risk of coming back, such as when cancer is found in the lymph nodes; neratinib may be discussed after trastuzumab-based therapy for selected HR-positive/HER2-positive disease; with this latter drug, diarrhea prevention and monitoring is important to discuss with your oncology care team.
- HER2-directed treatment may require heart monitoring. T-DM1 also requires monitoring for liver toxicity, low platelets, neuropathy, lung inflammation, and infusion reactions; T-DXd requires monitoring for lung inflammation, nausea, low blood counts, liver toxicity, heart effects, and infusion reactions. Be sure to ask your oncology care team about what to expect, when to call them, and a plan to manage side effects should they occur.

**The following questions are for cancers that are TNBC**

*Triple-negative early-stage breast cancer does not have estrogen receptors, progesterone receptors, or extra HER2 protein/gene copies, and this matters because treatment usually relies on chemotherapy rather than hormone therapy and HER2-directed therapy. Treatment may include chemotherapy before or after surgery, and for some higher-risk early-stage cancers, immunotherapy may be added depending on tumor size, lymph node involvement, overall health, and the treatment plan recommended by your oncology care team.*

**11. Which of the following best describes your breast cancer?**

- ☐ Tumors up to 2 cm in size and no cancer in any lymph nodes (node negative)
- ☐ Tumors larger than 2 cm and/or cancer in at least 1 lymph node (node positive)
- ☐ I don't know

**12. Which of the following neoadjuvant treatment regimens did you receive?**

- ☐ Chemotherapy plus pembrolizumab (together, this is known as the KEYNOTE-522 regimen)
- ☐ Chemotherapy only
- ☐ No neoadjuvant therapy
- ☐ I don't know

**13. Did you achieve a pCR (no cancer cells detected after neoadjuvant treatment)?**

- ☐ Yes  
☐ No  
☐ I don't know

**14. Have you tested positive for a germline *BRCA1* or *BRCA2* mutation, or both?**

- ☐ Yes  
☐ No  
☐ I don't know

**15. Do you fit the eligibility criteria for the TNBC group in the OlympiA trial? (See the callout)**

- ☐ Yes  
☐ No  
☐ I don't know

**To be eligible for the TNBC group in the OlympiA trial, you need to:**

- Be at least 18 years of age
- Test positive for germline *BRCA1* or *BRCA2* pathogenic mutation, or both
- Have HER2-negative primary breast cancer that is still at high risk for recurring after being treated with chemotherapy before or after surgery. TNBC is considered to be at a high risk for recurring if you had surgery followed by chemotherapy and either had cancer in at least 1 axillary lymph node, regardless of tumor size, or had no cancer in the axillary lymph nodes but had an invasive primary tumor larger than 2 cm; or if you were treated with chemotherapy before surgery and still had invasive cancer in the breast or axillary lymph nodes at surgery.
- Have completed chemotherapy, surgery, and radiation therapy, if radiation was indicated, at least 2 weeks and no more than 12 weeks before starting the trial
- Have completed 6 or more cycles of chemotherapy before or after surgery that included anthracyclines, taxanes, or both; this could include platinum chemotherapy

## **PART 3** Sample Cases and Expert Recommendations

### Using Case Studies to Help With Decision-making

To show how different breast cancer features can affect treatment recommendations, we have included a few example patient cases below. Please note that these examples are not exhaustive and reflect a general approach to managing early-stage breast cancer. Other factors, including your overall health, any other medical conditions you have, and your personal circumstances, can also guide treatment choices. Each of these example cases assumes the following 3 criteria are true:

1. Have early-stage breast cancer
2. Have or have not yet had surgery to remove the cancer
3. Have no other health conditions or other traits that would affect the choice of treatment

Each of these representative cases from a large physician tool includes recommendations from 5 highly regarded breast cancer experts on what systemic neoadjuvant or adjuvant therapy they think is most appropriate for patients in that situation. The experts also included a few caveats and special considerations with regard to the presence of common comorbidities observed in everyday clinical practice. In some patient scenarios included in this tool, the experts were not in complete agreement. This reflects the fact that there may be more than one reasonable treatment option, and the best choice for any individual patient can depend on factors such as cancer features, prior treatment, other health conditions, side effects, personal preferences, and life circumstances.

### The Experts

The experts providing recommendations were

▲ **Shipra Gandhi, MD, MS**, Associate Professor, Winship Cancer Institute of Emory University, Atlanta, Georgia

▲ **Tanya Gupta, MD**, Medical Oncologist, Palo Alto, California

▲ **Laura M. Spring, MD**, Breast Medical Oncologist, Mass General Brigham Cancer Center, Harvard Medical School, Boston, Massachusetts

▲ **Reshma L. Mahtani, DO**, Chief, Division of Breast Medical Oncology, Miami Cancer Center, Baptist Health South Florida, Miami, Florida

▲ **Erica L. Mayer, MD, MPH**, Director of Breast Cancer Clinical Research, Dana-Farber Cancer Institute, Boston, Massachusetts



## HR-Positive Early-Stage Breast Cancer Cases

### Case Scenario 1

The experts recommend the following neoadjuvant and adjuvant therapy for a patient who:

- Has early-stage breast cancer that is HR-positive, meaning the cancer uses hormones such as estrogen or progesterone to grow
- Has a small breast tumor, about 1 to 2 cm, with no cancer found in the lymph nodes and no biomarker result that would clearly point to a targeted treatment
- Has features that suggest a lower chance of the cancer coming back, including no lymph node involvement, a Ki-67 (cell proliferation) score of 10% to 15%, grade 1 cancer that is well differentiated, and an Oncotype DX score of 0 to 25. Ask your oncology team what these features mean for you.

All 5 experts preferred surgery first, followed by hormone-blocking treatment after surgery; they did not recommend treatment before surgery for this example.

| Expert 1 Recommendation                                                                                       | Expert 2 Recommendation                                  | Expert 3 Recommendation                                  | Expert 4 Recommendation                                  | Expert 5 Recommendation                                  |
|---------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|
| Tamoxifen + ovarian function suppression (OFS) if premenopausal or aromatase inhibitor (AI) if postmenopausal | Tamoxifen + OFS if premenopausal or AI if postmenopausal | Tamoxifen + OFS if premenopausal or AI if postmenopausal | Tamoxifen + OFS if premenopausal or AI if postmenopausal | Tamoxifen + OFS if premenopausal or AI if postmenopausal |

- Some experts noted that patients with an Oncotype DX score of 21 to 25 may want to discuss whether chemotherapy after surgery should be considered with their oncologist.

### Case Scenario 2

The experts recommend the following neoadjuvant and adjuvant therapy for a patient who:

- Has HR-positive early-stage breast cancer
- Has features that suggest a higher chance of the cancer coming back, defined as stage II-IIIa,  $\geq 5$  cm tumor size and/or  $\geq 4$  lymph nodes involved; or 1-3 nodes involved and fast-growing cancer features (Ki-67 index: 20% to 30%, grade 3; and Oncotype DX:  $\geq 26$ ). Ask your oncology team what these features mean for you.
- Tested negative for inherited (germline) *BRCA1* or *BRCA2* gene changes

All 5 experts preferred chemotherapy before surgery, specifically a dose-dense ACT regimen (ddACT), then surgery, followed by an AI with a CDK4/6 inhibitor (either abemaciclib for 2 years or ribociclib for 3 years) and OFS for those who were assigned female at birth and have not been through menopause.

| Expert 1 Recommendation                                   | Expert 2 Recommendation                                   | Expert 3 Recommendation                                   | Expert 4 Recommendation                                   | Expert 5 Recommendation                                   |
|-----------------------------------------------------------|-----------------------------------------------------------|-----------------------------------------------------------|-----------------------------------------------------------|-----------------------------------------------------------|
| ddACT, surgery then AI + CDK4/6i + OFS (if premenopausal) | ddACT, surgery then AI + CDK4/6i + OFS (if premenopausal) | ddACT, surgery then AI + CDK4/6i + OFS (if premenopausal) | ddACT, surgery then AI + CDK4/6i + OFS (if premenopausal) | ddACT, surgery then AI + CDK4/6i + OFS (if premenopausal) |

- For patients with significant gastrointestinal disease (such as inflammatory bowel disease), the experts indicated that ribociclib would be the preferred CDK4/6 inhibitor of choice over abemaciclib.
- If your breast cancer tested positive for pathogenic *BRCA1/2* mutations, the experts also opted for adding 1 year of olaparib as adjuvant therapy in patients with high-risk disease (if at least 4 lymph nodes involved) and/or residual disease following neoadjuvant chemotherapy

## HER2-Positive Early-Stage Breast Cancer

### Case Scenario 3

Experts would commonly consider the following treatment pathway for a patient who:

- Has HER2-positive early-stage breast cancer
- Has a tumor between 0.5 cm and 1.0 cm, no lymph node involvement, low to intermediate risk of disease recurrence, has had surgery, and is eligible for chemotherapy and HER2-directed treatment

All 5 experts preferred radiation therapy after surgery, followed by paclitaxel plus trastuzumab. Radiation therapy may be given around the same time as trastuzumab. After paclitaxel is completed, trastuzumab alone is continued to complete 1 year of HER2-directed treatment.

| Expert 1<br>Recommendation                                                                               | Expert 2<br>Recommendation                                                           | Expert 3<br>Recommendation                                                           | Expert 4<br>Recommendation                                                           | Expert 5<br>Recommendation                                                           |
|----------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| Radiation therapy (RT) followed by paclitaxel + trastuzumab ± RT, + trastuzumab alone to complete 1 year | RT followed by paclitaxel + trastuzumab ± RT, + trastuzumab alone to complete 1 year | RT followed by paclitaxel + trastuzumab ± RT, + trastuzumab alone to complete 1 year | RT followed by paclitaxel + trastuzumab ± RT, + trastuzumab alone to complete 1 year | RT followed by paclitaxel + trastuzumab ± RT, + trastuzumab alone to complete 1 year |

**Additional Expert Comments:** In patients with small disease that is <0.5 cm in size and with a low risk of recurrence, a conversation with patients about their goals and the benefits and risks of treatment is often had to determine whether adjuvant treatment is worth it. In patients with comorbidities (eg, heart disease, diabetes, kidney disease), the experts opted not to recommend systemic adjuvant treatment to patients with fully resected small tumors and a low-risk profile.

#### Case Scenario 4

Experts would commonly consider the following treatment pathway for a patient who:

- Has HER2-positive early-stage breast cancer
- Has a tumor larger than 2 cm and/or node-positive disease
- Has not yet had surgery
- Is eligible for chemotherapy and HER2-directed treatment, and has no comorbidities impacting treatment

All 5 experts preferred treatment before surgery with one of the following approaches: TCHP, which includes docetaxel, carboplatin, trastuzumab, and pertuzumab; THP, which includes paclitaxel or docetaxel with trastuzumab and pertuzumab; or T-DXd followed by THP. After this, they preferred surgery, followed by HP, which includes trastuzumab and pertuzumab, to complete 1 year of HER2-directed treatment.

| Expert 1<br>Recommendation                                                                    | Expert 2<br>Recommendation                                                                    | Expert 3<br>Recommendation                                                                    | Expert 4<br>Recommendation                                                                    | Expert 5<br>Recommendation                                                                    |
|-----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| Adjuvant TCHP or THP or T-DXd → THP, followed by surgery, then adjuvant HP to complete 1 year | Adjuvant TCHP or THP or T-DXd → THP, followed by surgery, then adjuvant HP to complete 1 year | Adjuvant TCHP or THP or T-DXd → THP, followed by surgery, then adjuvant HP to complete 1 year | Adjuvant TCHP or THP or T-DXd → THP, followed by surgery, then adjuvant HP to complete 1 year | Adjuvant TCHP or THP or T-DXd → THP, followed by surgery, then adjuvant HP to complete 1 year |

**Additional Expert Comments:** For patients not achieving a pCR or with lymph node involvement, experts would often consider adjuvant T-DXd if not previously received and not contraindicated (for example, no lung inflammation present); in patients with limited residual disease or no lymph node involvement, T-DMI is considered.

For patients with “frail” status, some experts would consider the short-STOP-HER2 trial if available. The ShortStop-HER2 trial is testing whether some patients who have an excellent response to treatment before surgery may safely receive 6 months, instead of 12 months, of HER2-targeted treatment such as trastuzumab, with or without pertuzumab. The choice between TCHP (not frail), THP (more frail), or T-DXd followed by THP per the DESTINY-Breast11 clinical trial (with higher-risk disease with unresectable status, ≥ T3, or >5 cm tumor size, or any size with node positive) depends on how likely the patient is to tolerate more intense chemotherapy.

#### Early-Stage TNBC Cases

##### Case Scenario 5

The experts recommend the following adjuvant therapy for a patient who:

- Has early-stage TNBC
- Has a tumor larger than 2 cm and/or any size tumor with node-positive disease (1 or more lymph nodes with cancer), and has not yet received any previous therapy

All 5 experts preferred the KEYNOTE-522 regimen before surgery, followed by surgery, then pembrolizumab after surgery. The KEYNOTE-522 regimen includes chemotherapy given together with pembrolizumab, an immunotherapy medicine that helps the immune system recognize and attack cancer cells. After surgery, pembrolizumab is continued as additional treatment to help lower the chance that the cancer will come back.

| Expert 1 Recommendation                                                | Expert 2 Recommendation                                                | Expert 3 Recommendation                                                | Expert 4 Recommendation                                                | Expert 5 Recommendation                                                |
|------------------------------------------------------------------------|------------------------------------------------------------------------|------------------------------------------------------------------------|------------------------------------------------------------------------|------------------------------------------------------------------------|
| KEYNOTE-522 regimen + surgery, then pembrolizumab for adjuvant therapy | KEYNOTE-522 regimen + surgery, then pembrolizumab for adjuvant therapy | KEYNOTE-522 regimen + surgery, then pembrolizumab for adjuvant therapy | KEYNOTE-522 regimen + surgery, then pembrolizumab for adjuvant therapy | KEYNOTE-522 regimen + surgery, then pembrolizumab for adjuvant therapy |

### Case Scenario 6

The experts recommend the following adjuvant therapy for a patient who:

- Has early-stage TNBC
- Has a tumor larger than 2 cm and/or any size tumor with node-positive disease (1 or more lymph nodes with cancer)
- Received the KEYNOTE-522 regimen then surgery but did not achieve a pCR, and tested negative on genetic testing for germline *BRCA1* and *BRCA2* mutations

All 5 experts preferred capecitabine plus pembrolizumab after surgery. Capecitabine is a chemotherapy pill, and pembrolizumab is an immunotherapy medicine that helps the immune system recognize and attack cancer cells. This approach was preferred for a patient who had chemotherapy plus pembrolizumab before surgery, still had cancer found at surgery, and did not have a germline *BRCA1* or *BRCA2* gene change.

| Expert 1 Recommendation      | Expert 2 Recommendation      | Expert 3 Recommendation      | Expert 4 Recommendation      | Expert 5 Recommendation      |
|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|
| Capecitabine + pembrolizumab | Capecitabine + pembrolizumab | Capecitabine + pembrolizumab | Capecitabine + pembrolizumab | Capecitabine + pembrolizumab |

### Case Scenario 7

The experts recommend the following adjuvant therapy for a patient who:

- Has early-stage TNBC
- Has a tumor larger than 2 cm and/or any size tumor with node-positive disease (1 or more lymph nodes with cancer) and received KEYNOTE-522 regimen then surgery but did not achieve a pCR and tested positive on genetic testing for a germline *BRCA1* or *BRCA2* mutation, or both

All 5 experts preferred chemotherapy after surgery, followed by olaparib. Olaparib is a targeted therapy pill for people with certain germline *BRCA1* or *BRCA2* gene changes; it helps block cancer cells from repairing DNA damage. The experts also said pembrolizumab may be considered as part of the treatment plan.

| Expert 1 Recommendation                                            | Expert 2 Recommendation                                            | Expert 3 Recommendation                                            | Expert 4 Recommendation                                            | Expert 5 Recommendation                                            |
|--------------------------------------------------------------------|--------------------------------------------------------------------|--------------------------------------------------------------------|--------------------------------------------------------------------|--------------------------------------------------------------------|
| Chemotherapy followed by olaparib<br>Consider adding pembrolizumab | Chemotherapy followed by olaparib<br>Consider adding pembrolizumab | Chemotherapy followed by olaparib<br>Consider adding pembrolizumab | Chemotherapy followed by olaparib<br>Consider adding pembrolizumab | Chemotherapy followed by olaparib<br>Consider adding pembrolizumab |

**Additional Expert Comments:** Olaparib for 1 year is recommended in patients who did not achieve a pCR. Adjuvant capecitabine for 6 months is also an option. However, choosing between capecitabine and olaparib or sequencing the 2 options has not been evaluated. Adjuvant olaparib would be favored given robust data from the OlympiA trial.

In patients with autoimmune disease, consider omitting pembrolizumab from the KEYNOTE-522 regimen in the neoadjuvant and adjuvant setting. In patients with mild or well-controlled autoimmune disease, shared decision-making with the patient is warranted regarding whether the benefits outweigh the risk of including immunotherapy.

### About Clinical Trials

Experts recommend considering enrollment in a clinical trial for any patient with early-stage breast cancer. Participation in a clinical trial should be discussed with all patients who may be eligible and interested.

It is always worth asking your care team the following questions:

- Is there a clinical trial available for my type and stage of breast cancer?
- Would a clinical trial change my treatment options?
- What are the possible risks, benefits, and time commitments of a clinical trial?