



## Impacts of Treatment Delays on Individuals With Breast Cancer During COVID-19 (April, 2020)

In these uncertain times, individuals diagnosed with breast cancer and currently undergoing or awaiting treatment across the country and around the world are concerned about how their care may be impacted by the current coronavirus pandemic. A number of guidelines and recommendations for managing patients have been issued by the oncology community to address this situation. NBCC wants to ensure that advocates are well-informed about the changes in treatment recommendations and the evidence underlying them.

### Background

Current pandemic related recommendations by the oncology community involve delaying certain procedures and modifying traditional treatment protocols to help minimize the risk of an individual's exposure to the coronavirus, and in some instances, to free up hospital space and healthcare workers. In that context, we reviewed some of the key breast cancer literature published prior to COVID-19 on the impact of timeliness of care. There is little published evidence of the effect of delays in standard breast cancer treatments. We then reviewed the more recent medical organization guidelines now being recommended during the pandemic that would result in delayed/modified care. They are listed at the end of this statement.

While there may be a risk in delaying breast cancer treatment, this has to be balanced on a personal level with the risk of developing COVID-19. There really is no evidence of how to balance this risk, and there is no strong evidence of the impact of treatment delays. Patients should consider the short- and long-term implications of these delays in care when discussing treatment plans with their oncology team.

Below we discuss what evidence there is. The evidence includes published information in the neoadjuvant (before surgery), surgery, adjuvant (shortly after surgery), and metastatic settings.

### Adjuvant Setting

A recent review by Bleicher (2018) summarizes the available medical literature on the relationship between breast cancer treatment times and outcomes. Times to surgery, chemotherapy, and radiotherapy following diagnosis all may have measurable impacts on outcomes, among them disease-free survival, disease-specific survival, and overall survival. Optimal times to treatment according to this review are for (a) **surgery**, no longer than 90 days after diagnosis, (b) **chemotherapy**, no more than 120 days from time of diagnosis, and (c) for **radiation therapy (RT)**, no more than 365 days if receiving chemotherapy prior to initiation of RT. If chemotherapy is not indicated as part of the treatment, RT should start within 20 weeks.

Other literature identified by NBCC highlighted certain subtypes of breast cancer based on estrogen receptor (ER), progesterone receptor (PR), and HER2 receptor status and how delays in treatment might affect the overall outcomes. A 2018 study indicated that for individuals with **hormone-receptor negative (ER, PR negative)** breast cancer, a delay in chemotherapy of more than 6 weeks could lead to an adverse effect on survival (Abdel-

Rahman, 2018). Another study found that for individuals with **HER2+ breast cancer** a delay in the receipt of trastuzumab (Herceptin) could have an impact on disease-free survival and overall survival. The findings suggest that trastuzumab (Herceptin) should be started no more than 8 weeks after surgery (Gullo et al., 2018).

For individuals with **triple-negative breast cancer** who had undergone breast-conserving surgery (lumpectomy with or without sentinel node or axillary node sampling), a delay in chemotherapy of more than 30 days after surgery had a negative impact on survival (Heeg et al., 2019).

### Neoadjuvant Setting

While most of the research NBCC found focused on adjuvant chemotherapy, one study did indicate that in regards to neo-adjuvant chemotherapy (starting chemotherapy before surgery), a delay in treatment of up to six months after diagnosis did not have a negative impact on long-term outcomes. This study only included individuals whose breast cancers were either triple-negative or HER2 positive, excluding ER or PR positive, HER2 negative (Livingston-Rosanoff et al., 2019).

### Metastatic Setting

For individuals with metastatic breast cancer, one study demonstrated that delays of over 12 weeks in receiving treatment were related to adverse survival outcomes measured from initiation of first treatment. (Jung, et al., 2011)

### Conclusion

There are not many published studies of the effect of breast cancer treatment delays. The available literature indicates that there are some time frames to keep in mind when thinking about how treatment delays might affect your health outcomes. When reviewing this information and discussing your treatment with your oncology team, it is important also to evaluate your risk of developing and dying of COVID-19 based on your personal health history (e.g., age, heart disease, diabetes and asthma) and how prevalent the coronavirus is in your area. Whenever possible, a multidisciplinary team should review your situation when developing a treatment plan.

As the coronavirus pandemic continues, the health care communities' response will remain fluid and constantly adapting. NBCC will update this information as we learn more.

## Guideline Resources

[COVID-19 Pandemic Breast Cancer Consortium \(Updated April 7, 2020\)](#) – The consortium is made up of representatives from the National Accreditation Program for Breast Centers, Commission on Cancer, the American Society of Breast Surgeons and National Comprehensive Cancer Network. They compiled preliminary guidelines for prioritization, treatment, and triage of breast cancer patients during the COVID-19 pandemic. Recommendations are broken down into priority categories based on patient condition.

[American Society of Clinical Oncologists \(ASCO\)](#) – Coronavirus resources to support clinicians, the cancer care delivery team, and patients with cancer. ASCO invited members to submit questions and has posted answers to frequently asked questions. This information is being updated as new questions emerge, and additional information is available.

[U.S. Food and Drug Administration \(FDA; Updated April 2, 2020\)](#) – Guidance on the conduct of clinical trials of medical products during COVID-19 pandemic. The FDA outlined general considerations to assist sponsors in assuring the safety of trial participants, maintaining compliance with good clinical practice (GCP), and minimizing risks to trial integrity during the pandemic.

## References

Abdel-Rahman O. Impact of timeliness of adjuvant chemotherapy and radiotherapy on the outcomes of breast cancer; a pooled analysis of three clinical trials. *Breast*. 2018 Apr;38:175-180.

Bleicher RJ. Timing and Delays in Breast Cancer Evaluation and Treatment. *Ann Surg Oncol*. 2018 Oct;25(10):2829-2838.

Gullo G, Walsh N, Fennelly D, Bose R, Walshe J, Tryfonopoulos D, O'Mahony K, Hammond L, Silva N, McDonnell D, Ballot J, Quinn C, McDermott EW, Evoy D, Prichard R, Geraghty J, Armstrong J, Crown J. Impact of timing of trastuzumab initiation on long-term outcome of patients with early-stage HER2-positive breast cancer: the "one thousand HER2 patients" project. *Br J Cancer*. 2018 Aug;119(3):374-380.

Heeg E, Marang-van de Mheen PJ, Van Maaren MC, Schreuder K, Tollenaar RAEM, Siesling S, Bos MEMM, Vrancken Peeters MTFD. Association between initiation of adjuvant chemotherapy beyond 30 days after surgery and overall survival among patients with triple-negative breast cancer. *Int J Cancer*. 2019 Nov 12.

Jung SY, Sereika SM, Linkov F, Brufsky A, Weissfeld JL, Rosenzweig M. The effect of delays in treatment for breast cancer metastasis on survival. *Breast Cancer Res Treat*. 2011 Dec;130(3):953-64.

Livingston-Rosanoff D, Hanlon B, Marka N, Vande Walle K, Stankowski-Drengler T, Schumacher J, Greenberg CC, Neuman H, Wilke LG. Time to initiation of neo-adjuvant chemotherapy for breast cancer treatment does not influence patient survival: A study of US breast cancer patients. *Breast J*. 2019 Sep 12.