Title

A qualitative study to evaluate physician attitudes regarding omission of surgery among exceptional responders to neoadjuvant systemic therapy for breast cancer (NRG-CC006)

Journal

Breast Cancer Research and Treatment, 187(3)

ISSN

0167-6806

Authors

Gharzai, Laila A
Szczygiel, Lauren A
Shumway, Dean A
et al.

Publication Date

2021-06-01

DOI

10.1007/s10549-021-06172-0

Peer reviewed

HHS Public Access

Author manuscript

Breast Cancer Res Treat. Author manuscript; available in PMC 2021 December 06.

Published in final edited form as:

Breast Cancer Res Treat. 2021 June ; 187(3): 777–784. doi:10.1007/s10549-021-06172-0.

A Qualitative Study to Evaluate Physician Attitudes Regarding Omission of Surgery Among Exceptional Responders to Neoadjuvant Systemic Therapy for Breast Cancer (NRG-CC006)

Laila A Gharzai, MD, LLM[1,2], **Lauren A Szczygiel, PhD**[2], **Dean A Shumway, MD**[3], **Hanna Bandos, PhD**[4,5], **Thomas B. Julian, MD**[4,6], **Eleftherios P. Mamounas, MD, MPH**[4,7], **Julia White, MD**[4,8], **Jennifer F. De Los Santos, MD**[9], **Mark Basik, MD**[4,10], **Patricia A. Ganz, MD**[4,11], **Reshma Jagsi, MD, DPhil**[1,2]

[1.]Department of Radiation Oncology, University of Michigan, Ann Arbor, MI

[2.]Center for Bioethics and Social Sciences in Medicine, University of Michigan, Ann Arbor, MI

[3.]Department of Radiation Oncology, Mayo Clinic

[4.]NRG Oncology, Pittsburgh, PA

[5.]University of Pittsburgh, Pittsburgh, PA

[6.]Allegheny Health Network, Pittsburgh, PA

[7.]Orlando Health University of Florida Health Cancer Center, Orlando, FL

[8.]The Ohio State University Comprehensive Cancer Center, Columbus, OH

[9.]Grandview Medical Center, Birmingham, AL

[10.]Jewish General Hospital, Montreal, Quebec

[11.]Jonsson Comprehensive Cancer Center, University of California, Los Angeles, CA

Abstract

Corresponding author: Reshma Jagsi, MD, DPhil, Department of Radiation Oncology, University of Michigan, 1500 E. Medical Center Drive, Ann Arbor, MI 48109, P: 734-936-4300; F: 734-763-7370; rjagsi@med.umich.edu.

Declarations

Ethics Approval: Investigations were performed after approval from local Human Investigations Committees in accordance with assurances filed with and approved by the Department of Health and Human Services.

Consent to participate: After agreeing to participate, subjects were emailed an informed consent form and copy of the semi-structured interview guide. Interviews were conducted after verbally re-affirming consent.

Consent for publication: All authors provide their full consent for publication.

Availability of Data: Individual participant data are not available for sharing because of concerns about possible re-identifiability of subjects given the detailed transcript information and small number of participants in this qualitative study.

Code availability: Not applicable

CONFIDENTIAL

Not to be distributed or submitted without explicit permission of the NSABP Operations Office.

Conflict(s) of Interest

All other authors declare no other potential COIs.

Purpose: Accrual to clinical trials that challenge well-established treatment paradigms represents a unique challenge. Physician opinions on investigation of a novel approach to breast cancer treatment, in which patients with complete response to neoadjuvant chemotherapy are offered omission of lumpectomy, is unknown. NRG-CC006 sought to describe physician attitudes toward a novel approach to breast cancer treatment.

Methods: We recruited 18 participants in the fields of surgery, medical oncology, and radiation oncology to participate in semi-structured telephone interviews. Main outcomes are qualitative themes associated with omission of surgery.

Results: Of 18 interview participants, specialty and gender were evenly represented across surgery, medical oncology, and radiation oncology. Qualitative themes included general attitudes toward treatment de-escalation, stakeholder considerations, and trial/protocol considerations. The vast majority of participants expressed interest in investigation of omission of surgery, with all participants endorsing need for further investigation into treatment de-escalation. Stakeholder considerations in opening such a trial emphasized need for multidisciplinary involvement, and particularly, the unique role of surgeons as gatekeepers in breast cancer treatment. Finally, participants endorsed a need for further foundational studies to develop ways to predict complete pathologic response to chemotherapy without surgical intervention.

Conclusions: Physicians expressed interest in investigating a novel approach to breast cancer treatment that would omit surgery in complete responders to neoadjuvant chemotherapy. Multidisciplinary input, and specifically surgeon engagement, will be key to the success of future investigations. Ongoing work to develop approaches to predict pathologic complete response accurately is needed to achieve the promise of this idea.

ClinTrials #: BR005: NCT03188393 June 13, 2017

Keywords

qualitative; de-escalation; lumpectomy omission

INTRODUCTION

The introduction of neoadjuvant chemotherapy (NACT) in the treatment of breast cancer has altered the landscape of breast oncology. Patients are receiving effective systemic therapies with increasing rates of pathologic complete response (pCR), as high as 60% in HER2-positive disease;[1] it is well-recognized that pCR correlates inversely with recurrence rates[2] and directly with survival.[3] The occurrence of pCR after NACT challenges existing surgery-based treatment paradigms and invites new approaches to the treatment of breast cancer.

Treatment de-escalation to minimize side effects and overtreatment of patients who would have excellent outcomes even without additional therapy has been pursued by all fields of oncology. De-escalation has occurred in breast cancer through the identification of populations for whom radiotherapy can reasonably be omitted[4, 5] and with the use of genomic studies to identify patients who can safely omit adjuvant chemotherapy.[6] Key in these approaches is the identification of groups of patients for whom an entire treatment

modality can be safely omitted. Efforts to minimize the morbidity of surgery have centered on safely decreasing surgery in the axilla,[7, 8] however, no randomized efforts have explored the omission of surgery for breast-conserving therapy. It is unknown if surgical resection, with its associated morbidity, is necessary in patients with pCR to NACT when radiotherapy is planned.

A paradigm shift within breast cancer treatment exploring the potential of omitting surgery altogether requires several preliminary steps to lay the necessary groundwork. Patients' perceptions of any proposed clinical trial will, to some extent, reflect the perception of the clinicians who offer them that trial. Because the surgical intervention to be omitted in this context is the relatively limited outpatient procedure of breast-conserving surgery, it is possible that physicians might not consider this to be an area of interest or worth the risks associated with investigating novel approaches. Nevertheless, even what may seem to be a modest and limited intervention such as lumpectomy may have consequences for patients' quality of life; therefore, one of the necessary steps in establishing a clinical trial in this area involves research to explore physicians' perceptions in this regard.

Another challenge to de-escalating surgical management of the breast is that additional foundational work to identify ways to evaluate pCR non-surgically is required. As such, NRG Oncology opened BR005 in 2017 to study the potential omission of surgery. That phase II study was designed to assess the accuracy of tumor bed core needle biopsies in predicting pCR in patients who are exceptional responders, exhibiting both clinical and radiographic complete response. Given the important role of physicians in future study enrollment for a clinical trial testing omission of surgery, NRG-CC006 initiated a qualitative study to investigate physician attitudes toward surgical treatment de-escalation. NRG-CC006 is a companion study to NRG-BR005, with a focus on developing new information about physician perspectives toward omission of surgery as a precursor to a future randomized clinical trial.

METHODS

Investigations were performed after approval from local Human Investigations Committees in accordance with assurances filed with and approved by the Department of Health and Human Services.

Study Design and Participants

The NRG Oncology Statistics and Data Management Center provided the University of Michigan with a list of practicing surgeons, radiation oncologists, and medical oncologists (N=419) who enrolled patients to NRG Oncology trials. Physicians were stratified into cohorts based on specialty (surgery, radiation oncology, medical oncology), gender (male, female), and National Cancer Institute (NCI) site type. Site types were: Lead Academic Participating Sites (LAPS), representing academic sites; NCI Community Oncology Research Program (NCORP), representing community sites; and Main Members (Main), representing sites with considerable NRG clinical trial accrual history that was not part of the previous two groups. A 3×3×2 purposeful sampling table was created to randomly select

participants based on these characteristics. After selection, a research associate emailed physicians to invite them to participate in an audio-recorded telephone interview.

Interview Procedures

After agreeing to participate, subjects were emailed an informed consent form and copy of the semi-structured interview guide. Interviews were conducted after verbally re-affirming consent. Questions focused on willingness to enroll patients into a clinical trial investigating omission of surgery, influencing factors, and the role of imaging and biopsy results. All interviews were conducted by trained physician-researchers (LAG and DAS) from July-October 2019. Interviews were audio-recorded and transcribed verbatim by a professional transcription service.

Analysis

De-identified transcripts were analyzed using rigorous techniques of qualitative data analysis and are reported according to the Standards for Reporting Qualitative Research.[9–11] Interviews were independently reviewed and coded using standard techniques of thematic analysis[12] by two coders (LAG and LAS) using qualitative analysis software (Dedoose, v8.3.17[13]). For rigor, interviews were double-coded and compared for agreement. Disagreements were resolved by consensus. After coding, major themes were identified and analyzed for interpretive description by a diverse team of physicians and social scientists with expertise in qualitative research.[14] Results focused on dominant themes shaping physicians' attitudes toward evaluating pCR non-surgically and omitting lumpectomy in a subset of breast cancer patients.

RESULTS

A total of 18 physicians were interviewed. By design, gender was evenly distributed (9 males, 9 females). Physician specialty was evenly represented, with six in each of surgery, medical oncology, and radiation oncology. Practice type was evenly represented, with six in each of Main, LAPS, and NCORP. A wide range of years of practice were represented, with six in practice <10 years, and six >25 years (Table 1). Interviews lasted 25 minutes on average (range, 18–40 minutes).

Overall, physicians had positive sentiments toward investigation of omission of surgery, with 17/18 (94.4%) of all but one participants indicating interest or contingent interest in such an approach in node-negative patients. Enthusiasm waned for node-positive patients, with 13/18 (72.2%) participants indicating interest or contingent interest in enrollment in a trial investigating omission of surgery (Table 2). Reasons for contingencies included desire for more specific protocol information and the current lack of evidence supporting this novel approach. Categorization of physician responses investigating influencing factors resulted in three major themes: general attitudes toward de-escalation, stakeholder considerations in trial opening and enrollment, and protocol-specific considerations (Table 3).

General Attitudes Toward De-escalation

When asked about treatment de-escalation, all participants had a positive attitude toward treatment de-escalation in breast cancer management. Acknowledgment that our current treatment paradigm likely over-treats some patients was observed: “[W]e tend to treat maximally without knowing who will benefit versus the risk whether it’s surgery, radiation therapy, or chemotherapy, or endocrine therapy...” (surgeon). Additionally, there was acknowledgment of the toxicities and burdens associated with current treatments. There was interest in decreasing the amount of treatment that patients undergo without compromising outcomes: “I think as systemic therapies become more effective that that [lumpectomy omission] would be a natural progression, a natural evolution for some of our patients” (radiation oncologist).

Respondents expressed a general desire for additional research: “I’m in favor of finding appropriate populations who can safely [de-escalate] without comprising recurrence risk...” (medical oncologist). Physicians had a positive sentiment toward lumpectomy omission and felt that patients would also: “[I]n my experience the patients are already questioning, why do I have to now go and have surgery [after chemotherapy] if you’re telling me that everything looks like it’s gone” (radiation oncologist).

Concerns raised regarding omission of lumpectomy included potential for losing important prognostic pathologic information with omission of surgery, and specifically how this might impact additional therapeutic options available to patients: “...ensure that the medical oncologists don’t miss out on opportunities to recommended additional adjuvant therapies that we now know to be effective” (surgeon). There was also concern that inferior disease control could occur with de-escalation in the wrong subsets of patients who were ultimately at higher risk of recurrence, given that patients with aggressive histologies such as triple-negative and HER2-positive disease are more likely to achieve complete responses. Finally, there was a general perception that lumpectomy is a minimally morbid surgery and might not warrant further investigation of omission: “I would say that many women don’t perceive the lumpectomy to be a big deal” (surgeon).

Community, Personal, and Patient Factors Affecting Stakeholder Enthusiasm

Participants discussed factors affecting enthusiasm for enrollment in a trial investigating omission of surgery. Factors affecting the potential for trial enrollment included characteristics or traditions of the region, institution, or practice at large, attitudes of treating surgeons, and the multidisciplinary interactions among specialties. Some participants described negative sentiments toward such a novel approach at their institution or community level that were out of an individual physician’s control: “We have a very successful clinical trial unit, but [despite this participant’s interest in omission of surgery] I don’t think in this region where I live, out in the community setting, that I would have the ability to put enough patients on that kind of clinical trial” (medical oncologist).

The importance of surgeons in driving trial enrollment was acknowledged by half of the many participants. Given that the first physician seen by patients after diagnosis of breast cancer is typically a surgeon, surgeons are considered gatekeepers. Therefore, it was

acknowledged that most patients expected to have surgery which could represent a barrier to investigating omission of surgery: “I think most patients are expecting to have surgery... a lot of times they see the surgeon before they see us” (medical oncology). Additionally, there was concern about surgeon buy-in given the potential for omitting surgery to financially impact surgeons: “If they’re doing less procedures you know, they’re getting paid less, right? …breast cancer is their bread and butter” (medical oncologist).

Finally, the necessity of a multi-disciplinary approach to decision-making for any investigation omitting surgery was acknowledged: “It seems that opening a trial like this, it’s not like opening a trial of a systemic agent or a radiation trial. It’s really opening a multidisciplinary trial that you almost have to open it as an entire multidisciplinary clinic… that has to be from the beginning” (medical oncologist).

Participants were also asked about patient factors that would affect interest in such a trial. Again, participants acknowledged that patients’ preconceptions about the role of surgery as part of treatment could serve as a barrier to discussing omission of surgery: “They’re pretty much expecting surgery when they come to see me…I don’t think I can recall ever a patient who has asked to not have surgery for their cancer” (surgeon). Participants also acknowledged that different patients could have varying interest in receiving medical intervention. Therefore, whether patients were medical maximizers or minimizers was relevant[15]: “I have a group of patients who will say, ‘Well, I want everything done regardless. I don’t want to have any chance...’” (surgeon).

Considerations for a Future Trial Protocol

Participants were asked to comment on features of a potential future protocol investigating a non-surgical approach to breast cancer management, including patient eligibility, imaging considerations, and biopsy. First, participants discussed the types of patients that they wished to be the first cohort enrolled. Participants generally agreed that they wished to enroll patients who were at low risk of recurrence: “If I was starting a study like this, I would design it for patients who are extremely low risk” (radiation oncologist). Participants tended to define lower-risk patients in terms of older age, generally >50 years. There was polarization between the ideas of considering triple-negative and HER2-positive patients as traditionally at high risk of recurrence yet also acknowledging their higher rates of pCR, making this group more likely to be eligible for a trial predicated on the presence of clinical and radiographic complete response: “It’s a double-edged sword, right? Because the same histologies that are higher risk are also the ones that...have the potential higher pCR rate” (surgeon).

Participants were asked about follow-up imaging after the completion of a treatment regimen omitting surgery. Most endorsed more frequent imaging than currently endorsed by guidelines if such an approach were pursued. Participants were generally open to the inclusion of MRIs in post-treatment imaging. However, there was concern that the inclusion of MRIs in such an approach could cause financial distress for patients: “I would not want my patient to have to pay for it...the imaging part would have to be figured out, as far as who’s paying for it” (radiation oncologist). Specifically, there appeared to be less

enthusiasm for enrollment if there was a possibility that patients would have to shoulder this financial burden.

When asked about breast biopsy, all participants endorsed the need for a high level of biopsy accuracy, yet acknowledged the difficulty in assessing pCR after NACT without surgical excision at this time: “We need to... think about how we figure out, highly accurately, what’s happened at the end of neoadjuvant chemotherapy” (surgeon); “The chances of significant residual disease when a biopsy is negative would need to be...something on the order of 5% or less to correlate with continued very good outcomes for the overall treatment plan” (radiation oncologist). Some participants mentioned that they would be willing to accept some residual microscopic disease in the breast, understanding that radiation would be able to eradicate this minimal residual disease. There were concerns about biopsy technique and other factors that could confound the true assessment of response: “The problem is a needle biopsy isn’t really likely to give you the whole picture of what’s happened in the breast, but I do think it’s worth investigating” (medical oncologist). This concern reflected overall sentiments that additional research was needed in the area of treatment de-escalation in general and that building foundational knowledge would continue to move the field forward.

DISCUSSION

This study explores the perspectives of a group of physicians known to have enrolled patients on breast cancer clinical trials regarding a novel approach omitting surgery in the treatment of breast cancer. It is the first study to our knowledge to incorporate formal qualitative analysis of physician perspectives alongside a trial seeking to develop an accurate diagnostic approach, in order to inform a potential large-scale future clinical trial. These interviews demonstrate substantial support toward continued investigation on ways to safely de-escalate surgery in breast-conserving therapy. Three major themes emerged pertaining to: physicians’ general attitudes toward treatment de-escalation in breast cancer; community, personal, and patient factors affecting stakeholder enthusiasm; and considerations for a future trial protocol.

Many physicians were supportive about avenues to de-escalate surgery in the breast, believing that omission of lumpectomy in exceptional responders after NACT represented a goal worthy of further exploration. Others believed that omission of surgery could create unique challenges, including the possibility of inferior disease control if patients were inappropriately selected and of an inability to offer adjuvant chemotherapy in incomplete responders without accurate pathologic data. Despite these valid concerns, our results demonstrate considerable interest in investigation of non-surgical approaches to breast cancer treatment among a range of physician specialties.

Our analysis further suggests that the key to successful development and future enrollment of a novel surgical de-escalation trial will be to engage multi-disciplinary stakeholders. In this study, despite physicians from each specialty expressing interest, there was concern from non-surgical physicians that the role of the surgeon as the typical first contact in breast cancer treatment along with the potential impact of a non-surgical approach on surgeons could represent a hindrance to further investigation of this approach. This suggests

that engagement of multidisciplinary teams is essential. Future investigations should fully incorporate surgeon input in trial design and encourage leaders in surgery to promote trial participation among their colleagues.

Physicians in our study expressed opinions to inform a possible future trial of lumpectomy omission. Many were enthusiastic about enrolling HER2-positive and triple-negative patients, reflecting the known higher responses to NACT in these populations.[16] Others noted that traditional “low risk” patients, i.e. hormone-receptor positive patients, would likely not be eligible for enrollment on such a trial due to lower pCR in this population. This marks a notable change from the traditional selection paradigm of de-escalating therapy only in historically low-risk populations and may represent a barrier to enrollment on a future trial.

Participants interviewed in this study identified that the ability to accurately assess pCR based on imaging and biopsy alone is key to moving forward with omitting surgery. Many noted concerns with the current evidence supporting such an approach. Soon after the conduct of these interviews, NRG Oncology presented preliminary results from the BR005 study assessing biopsy accuracy after NACT with an unacceptably low negative predictive value of 77.5% (pre-specified threshold for success was >90%),[17] suggesting that we are not yet able to assess disease status accurately after NACT with an appropriate degree of certainty to support a clinical trial of this approach. Further efforts will need to center on improvements in assessment of pCR rates. Moving forward may require identification of more favorable subgroups based on consideration of multiple clinicopathologic or other characteristics, adoption of novel imaging techniques,[18] biomarker selection, and identification of modalities that may have differing levels of success in different breast cancer subtypes. For example, an exploratory analysis in another such small study[19] showed that in patients with residual imaging abnormalities of <2cm and with a minimum of six biopsy cores taken, negative predictive value of needle biopsy in predicting pCR was as high as 97.4%; another study in 40 patients showed an accuracy of 98%.[20]

Although challenges remain in setting the groundwork for omission of surgery, there is considerable interest in further investigation of this approach, not only as demonstrated in the current study but also in recent commentaries discussing challenges toward this approach.[21, 22] Omission of lumpectomy offers an important first target in assessing such an approach; in the future, efforts that consider omitting more morbid surgeries such as mastectomy may build on the foundation laid by the current study and future efforts to investigate lumpectomy omission. Additionally, investigating the impact of a lumpectomy omission approach in a fit patient population able to receive chemotherapy may offer insights into future efforts to expand such an approach in patient populations that may be less able to receive intensive chemotherapy and potentially at higher risk of complications from surgery due to underlying health issues. Importantly, patient perspectives toward omission of surgery remain underexplored.[23] Future qualitative studies assessing patient perceptions of the burdens of lumpectomy, willingness to undergo multiple biopsies, and acceptance of risk, are needed.

As further investigations continue to provide the foundation for omitting surgery in breast cancer treatment, qualitative studies such as ours offer a means to approach clinical trial design in this novel space by incorporating input from a variety of physician stakeholders who will ultimately determine the success of a future randomized trial. In the era of complex and expensive clinical trials, ensuring that physician concerns are heard during the design process will help to facilitate enrollment and optimize success for these novel trials.[24]

Limitations

The sample was drawn from physicians who participate within NRG Oncology's clinical trials network and may thus represent physicians who are biased toward enrollment on trials. However, because these physicians are the ones likely to open and support clinical trials, these are the physicians whose input is most essential for the success of future trials. Limitations of this study include its small sample size. Nevertheless, the data were collected from a purposefully diverse sample following rigorous qualitative methods, and interviews continued until thematic saturation, which is the standard approach favored in qualitative analysis for sampling. Although our sample size was small, physicians from multiple specialties encompassing the audience for an NRG sponsored trial were interviewed. Thematic saturation was reached, indicating that an in depth understanding of physician views and opinions was achieved. Additional verification of emerging themes identified in this study to determine generalizability within a larger population is needed to further ensure full appreciation of stakeholders' perspectives; to determine frequencies of the attitudes expressed by the subjects in this study, a future quantitative assessment of a survey study would be necessary. Finally, no patient input was solicited for this physician-directed study. Patient input and perspectives are an additional important component that should drive considerations for future clinical trial design, and additional work exploring patient perspectives is strongly needed.

Conclusions

Physicians expressed interest in investigating a novel approach to breast cancer treatment that omits surgery in appropriately selected patients and were most interested in a trial investigating this option in node-negative or possibly older, node-positive, breast cancer patients with triple-negative or HER2-positive disease. This was predicated on the development of an accurate means to assess pCR in the absence of surgery. Surgeon input and leadership will be particularly essential to the success of future investigations, given surgeons' key role as an important first contact in the treatment of breast cancer. Qualitative studies such as this can illuminate barriers and facilitators to enrollment on clinical trials and ensure success.

Acknowledgments:

The authors acknowledge the contributions of Wendy L. Rea, B.A., Editorial Associate, an employee of NSABP, who was not compensated beyond her normal salary for this work.

Funding: HHS | NIH | National Cancer Institute (NCI) Grants U10CA180868; UG1CA189867, and U10CA180822. The funders had no role in data collection, interpretation, reporting, or the decision to submit.

Sources of Funding

RJ has stock options as compensation for her advisory board role in Equity Quotient, a company that evaluates culture in health care companies; she has received personal fees from Amgen and Vizient and grants for unrelated work from the National Institutes of Health, the Doris Duke Foundation, the Greenwall Foundation, the Komen Foundation, and Blue Cross Blue Shield of Michigan for the Michigan Radiation Oncology Quality Consortium. She has a contract to conduct an investigator-initiated study with Genentech. She has served as an expert witness for Sherinian and Hasso and Dressman Benzinger LaVelle. She is an uncompensated founding member of TIME'S UP Healthcare, and a member of the Board of Directors of ASCO.

References

1. Schneeweiss A, Chia S, Hickish T, Harvey V, Eniu A, Waldron-Lynch M, et al. Long-term efficacy analysis of the randomised, phase II TRYPHAENA cardiac safety study: Evaluating pertuzumab and trastuzumab plus standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer. Eur J Cancer. 2018;89:27–35. [PubMed: 29223479]
2. Mamounas EP, Anderson SJ, Dignam JJ, Bear HD, Julian TB, Geyer CE, et al. Predictors of locoregional recurrence after neoadjuvant chemotherapy: results from combined analysis of National Surgical Adjuvant Breast and Bowel Project B-18 and B-27. J Clin Oncol. 2012;30(32):3960–6. [PubMed: 23032615]
3. Cortazar P, Zhang L, Untch M, Mehta K, Costantino JP, Wolmark N, et al. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. Lancet. 2014;384(9938):164–72. [PubMed: 24529560]
4. Hughes KS, Schnaper LA, Bellon JR, Cirrincione CT, Berry DA, McCormick B, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343. J Clin Oncol. 2013;31(19):2382–7. [PubMed: 23690420]
5. Kunkler IH, Williams LJ, Jack WJ, Cameron DA, Dixon JM, investigators PI. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial. Lancet Oncol. 2015;16(3):266–73. [PubMed: 25637340]
6. Sparano JA, Gray RJ, Makower DF, Pritchard KI, Albain KS, Hayes DF, et al. Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer. N Engl J Med. 2018;379(2):111–21. [PubMed: 29860917]
7. Krag DN, Anderson SJ, Julian TB, Brown AM, Harlow SP, Costantino JP, et al. Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol. 2010;11(10):927–33. [PubMed: 20863759]
8. Giuliano AE, Ballman KV, McCall L, Beitsch PD, Brennan MB, Kelemen PR, et al. Effect of Axillary Dissection vs No Axillary Dissection on 10-Year Overall Survival Among Women With Invasive Breast Cancer and Sentinel Node Metastasis: The ACOSOG Z0011 (Alliance) Randomized Clinical Trial. JAMA. 2017;318(10):918–26. [PubMed: 28898379]
9. Giacomini MK, Cook DJ. Users' guides to the medical literature: XXIII. Qualitative research in health care A. Are the results of the study valid? Evidence-Based Medicine Working Group. JAMA. 2000;284(3):357–62. [PubMed: 10891968]
10. Giacomini MK, Cook DJ. Users' guides to the medical literature: XXIII. Qualitative research in health care B. What are the results and how do they help me care for my patients? Evidence-Based Medicine Working Group. JAMA. 2000;284(4):478–82. [PubMed: 10904512]
11. O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for Reporting Qualitative Research: A Synthesis of Recommendations. Academic medicine : journal of the Association of American Medical Colleges. 2014;89(9).
12. Braun V, Clarke V. Using thematic analysis in psychology. Qualitative Research in Psychology. 2006;3(2):77–101.
13. Dedoose Version 7.0.23, web application for managing, analyzing, and presenting qualitative and mixed method research data Los Angeles, CA: SocioCultural Research Consultants, LLC; 2016 [Available from: www.dedoose.com.
14. Thorne S, Kirkham SR, O'Flynn-Magee K. The Analytic Challenge in Interpretive Description. International Journal of Qualitative Methods. 2004;3(1):1–11.

15. Scherer LD, Shaffer VA, Caverly T, DeWitt J, Zikmund-Fisher BJ. Medical Maximizing-Minimizing Predicts Patient Preferences for High- and Low-Benefit Care. Med Decis Making. 2020;40(1):72–80. [PubMed: 31975657]
16. Houssami N, Macaskill P, von Minckwitz G, Marinovich ML, Mamounas E. Meta-analysis of the association of breast cancer subtype and pathologic complete response to neoadjuvant chemotherapy. Eur J Cancer. 2012;48(18):3342–54. [PubMed: 22766518]
17. Basik M, Cecchini R, De Los Santos J, Umphrey H, Julian T, Mamounas E, et al. Primary analysis of NRG-BR005, a phase II trial assessing accuracy of tumor bed biopsies in predicting pathologic complete response in patients with clinical/radiological complete response after neoadjuvant chemotherapy to explore the feasibility of breast-conserving treatment without surgery.2019; (Prog #: GS5–05).
18. Lee HB, Han W, Kim SY, Cho N, Kim KE, Park JH, et al. Prediction of pathologic complete response using image-guided biopsy after neoadjuvant chemotherapy in breast cancer patients selected based on MRI findings: a prospective feasibility trial. Breast Cancer Res Treat. 2020;182(1):97–105. [PubMed: 32418044]
19. Tasoulis MK, Lee HB, Yang W, Pope R, Krishnamurthy S, Kim SY, et al. Accuracy of Post-Neoadjuvant Chemotherapy Image-Guided Breast Biopsy to Predict Residual Cancer. JAMA Surg. 2020:e204103. [PubMed: 33026457]
20. Kuerer HM, Rauch GM, Krishnamurthy S, Adrada BE, Caudle AS, DeSnyder SM, et al. A Clinical Feasibility Trial for Identification of Exceptional Responders in Whom Breast Cancer Surgery Can Be Eliminated Following Neoadjuvant Systemic Therapy. Ann Surg. 2018;267(5):946–51. [PubMed: 28549010]
21. Heil J, Kuerer HM, Pfob A, Rauch G, Sinn HP, Golatta M, et al. Eliminating the breast cancer surgery paradigm after neoadjuvant systemic therapy: current evidence and future challenges. Ann Oncol. 2020;31(1):61–71. [PubMed: 31912797]
22. Heil J, Pfob A, Kuerer HM. De-escalation towards omission is the tipping point of individualizing breast cancer surgery. Eur J Surg Oncol. 2020;46(8):1543–5. [PubMed: 32241595]
23. Caballero C, Piccart M. Important considerations prior to elimination of breast cancer surgery after neoadjuvant systemic therapy: Listening to what our patients want. Ann Oncol. 2020.
24. Lee SJC, Murphy CC, Geiger AM, Gerber DE, Cox JV, Nair R, et al. Conceptual Model for Accrual to Cancer Clinical Trials. J Clin Oncol. 2019;37(23):1993–6. [PubMed: 31166822]

Table 1.

Demographic Information

Characteristic	N (%)
Sex	
Female	9 (50%)
Male	9 (50%)
Specialty	
Surgery	6 (33.3%)
Medical Oncology	6 (33.3%)
Radiation Oncology	6 (33.3%)
Site Type	
Main Members	6 (33.3%)
LAPS	6 (33.3%)
NCORP	6 (33.3%)
Years of Practice	
≤5	4 (22.2%)
6–10	2 (11.1%)
11–15	3 (16.7%)
16–20	2 (11.1%)
21–25	1 (5.6%)
˃26	6 (33.3%)

LAPS indicates Lead Academic Participating Sites; NCORP indicates NCI Community Oncology Research Program.

Table 2.

Physicians' interest in enrolling patients in a trial that omits lumpectomy after neoadjuvant chemotherapy and stated reasons

Nodal Status	Interested in enrollment	Not interested in enrollment
	17	1
	Contingencies	*Reasons given*
	- Specifics of the protocol - Awaiting results from ongoing trials - Patient desires	- Not enough evidence - Current imaging not accurate enough
	13	5
	Contingencies	*Reasons given*
	- Age (prefer enrolling older patients) - Level of nodal involvement (would not enroll bulky axillary disease) - Comorbidities - Awaiting evidence from ongoing studies on axillary management after neoadjuvant chemotherapy	- Discordant to omit lumpectomy but still consider axillary surgery - Not enough evidence - Risk of recurrence too high - 'Just no'

Table 3.

Themes identified on qualitative thematic analysis

Theme	Subtheme	Categories
General Attitudes Toward De-escalation	Interest in treatment de-escalation	Perception that a subset of patients are receiving more treatment than necessary for cure
		Belief that current treatment options produce unwanted, difficult, or unpleasant side effects
		Interest in decreasing the amount of treatment patients undergo without compromising cure
		General desire for additional de-escalation research regarding treatment de-escalation
	Lumpectomy omission - Pro	General support for investigating lumpectomy omission
		Perception that patients would be interested in lumpectomy omission
	Lumpectomy omission - Con	Potential for losing important pathologic information with the omission of surgery
		Potential for inferior disease control with de-escalation in inappropriately selected patients
		Lumpectomy is considered a minimally morbid surgery and the benefit of its omission may not outweigh the risks
Community, Personal, and Patient Factors Affecting Stakeholder Enthusiasm	Community and individual physician factors	Belief that trial enrollment is affected by institution-or community-level concerns out of an individual physician's control
		Importance of surgeon endorsement and leadership as typical first-line providers at time of diagnosis
		Multi-disciplinary engagement and support of the protocol regimen
	Patient factors	Belief that some patients are more or less interested in receiving medical intervention than others (maximizers/minimizers)
		Belief that patients have preconceptions about the role of surgery as part of breast cancer treatment
Considerations for a Future Trial Protocol	Risk considerations	Belief that older patients are better candidates for trial enrollment (generally >50 years)
		Opinions on breast cancer subtypes that may be more suitable for a lumpectomy omission approach (HER2, triple-negative)
	Diagnostic assessment	Importance of a high level of biopsy accuracy after neoadjuvant treatment to consider trial enrollment
		Concern about various technical factors that could undermine confidence in biopsy results
	Imaging follow-up	Expectation of more frequent imaging posttreatment if lumpectomy is omitted
		MRI for follow-up is reasonable but not necessary if lumpectomy is omitted
		Addition of MRI to follow-up care may result in financial burdens for patients