


# Efficacy and Safety of Neoadjuvant Stereotactic Body Radiotherapy (SBRT) Combined with Chemoimmunotherapy in Locally Advanced Breast Cancer: A Single-Center, Retrospective Pilot Study

Menglan Zhai<sup>1,\*</sup>, Jianping Bi<sup>1,\*</sup>, Zirui Ke<sup>2,3,\*</sup>, Min Hu<sup>4</sup>, Guoliang Pi<sup>1</sup>, Ying Li<sup>1</sup>, Hanping He<sup>1</sup>, Yanping Li<sup>1</sup>, Hongmei Zheng<sup>2,3</sup>, Xinhong Wu<sup>2,3</sup>, Vivek Verma<sup>5</sup>, Jun Shao<sup>2,3</sup>, Guang Han<sup>1</sup> 

<sup>1</sup>Department of Radiation Oncology, Hubei Cancer Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, People's Republic of China; <sup>2</sup>Department of Breast Surgery, Hubei Cancer Hospital, Tongji Medical College, Huazhong University of Science and Technology, National Key Clinical Specialty, Wuhan, Hubei, People's Republic of China; <sup>3</sup>Wuhan Clinical Research Center for Breast Cancer, Hubei Provincial Clinical Research Center for Breast Cancer, Wuhan, Hubei, People's Republic of China; <sup>4</sup>Department of Pathology, Hubei Cancer Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, People's Republic of China; <sup>5</sup>Department of Radiation Oncology, the University of Texas MD Anderson Cancer Center, Houston, TX, USA

\*These authors contributed equally to this work

Correspondence: Guang Han, Department of Radiation Oncology, Hubei Cancer Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, People's Republic of China, Tel +86-27-8767-0023, Email hg7913@hotmail.com; Jun Shao, Department of Breast Surgery, Hubei Cancer Hospital, Tongji Medical College, Huazhong University of Science and Technology, National Key Clinical Specialty, Wuhan, Hubei, People's Republic of China, Tel +86-27-8767-0051, Email 39390822@qq.com

**Purpose:** The combination of radiotherapy with immunotherapy holds synergistic potential, yet its role in the neoadjuvant treatment of breast cancer remains underexplored. This single-center, retrospective pilot study aimed to explore the preliminary efficacy and safety of integrating stereotactic body radiotherapy (SBRT) with chemoimmunotherapy as a novel neoadjuvant regimen for a small cohort of patients with high-risk, locally advanced breast cancer.

**Patients and Methods:** Between June 2023 and August 2025, 20 patients received neoadjuvant SBRT (18Gy/3 fractions for node-positive; 24Gy/3 fractions for node-negative disease) concurrently with chemoimmunotherapy (various anti-PD-1/bispecific antibodies plus chemotherapy), followed by surgery. Key endpoints were pathological complete response (pCR, ypT0/Tis ypN0), near-pCR (Residual Cancer Burden [RCB] class 0 or I), objective response rate (ORR), and safety.

**Results:** The cohort included triple-negative breast cancer (TNBC, 35%) and hormone receptor-positive/HER2-negative breast cancer of the Luminal B subtype (Luminal B/HER2-, 50%). Most had cT2 (75%) and node-positive (75%) disease. The median number of chemoimmunotherapy cycles were 8, with 80% receiving an AC-T backbone. The overall pCR rate was 45% (9/20). Efficacy varied by subtype: the pCR rate was 85.7% (6/7) in TNBC and 20% (2/10) in Luminal B/HER2- disease. Notably, 100% of TNBC and 40% of Luminal B/HER2- patients achieved near-pCR (RCB 0/I). ORR was 90%. Grade 3–4 adverse events occurred in 25% of patients, with no treatment-related mortality.

**Conclusion:** In this single-center, retrospective pilot study, early integration of SBRT with chemoimmunotherapy demonstrated promising antitumor activity, particularly high pCR rates in TNBC and induction of deep pathological responses (RCB 0/I) in Luminal B/HER2- disease, with a manageable safety profile. Observed in a heterogeneous cohort, these preliminary findings highlight potential efficacy but require cautious interpretation and warrant validation in larger, prospective trials.

**Keywords:** breast cancer, neoadjuvant therapy, stereotactic body radiotherapy, immunotherapy, pathological complete response

## Introduction

For locally advanced breast cancer, neoadjuvant chemotherapy (NACT) aims to downstage disease and improve surgical outcomes.<sup>1</sup> Pathological complete response (pCR) is a strong surrogate for improved long-term survival.<sup>2</sup> However, pCR rates with standard NACT remain modest, approximately 40–50% in triple-negative breast cancer (TNBC) and below 15% in hormone receptor-positive/HER2-negative (HR+/HER2-) disease,<sup>3–5</sup> underscoring the need for more effective strategies.

The integration of immune checkpoint inhibitors (ICIs) has improved pCR rates in both TNBC and high-risk HR+/HER2- breast cancer. Nonetheless, a significant proportion of patients, especially those with highly immunosuppressive or “immunologically cold” tumors such as luminal subtypes with high estrogen receptor expression, do not achieve a pCR.<sup>6–8</sup> This highlights the necessity to develop combinatorial approaches that can more effectively activate and sustain antitumor immunity. Radiotherapy, particularly stereotactic body radiotherapy (SBRT), can potentiate the effects of immunotherapy. SBRT is hypothesized to act as an *in situ* vaccine by inducing immunogenic cell death, releasing tumor antigens, and modulating the local tumor microenvironment, thereby synergizing with ICIs to overcome immune resistance.<sup>9,10</sup> Furthermore, dual targeting of the programmed cell death 1 (PD-1) and vascular endothelial growth factor (VEGF) pathways with a bispecific antibody (eg, ivonescimab) may concurrently alleviate immunosuppression and normalize tumor vasculature, potentially creating a more favorable environment for radiation-enhanced immune responses.<sup>11–14</sup> Based on this rationale, we hypothesized that the early integration of SBRT with a PD-1/VEGF bispecific antibody and chemotherapy could yield synergistic efficacy, potentially inducing deep pathological responses even in traditionally less immunoresponsive subtypes, such as Luminal B/HER2- breast cancer with high ER expression. While clinical trials have provided proof-of-concept for combining SBRT with ICIs,<sup>15–17</sup> clinical evidence for a triple-modality approach incorporating chemotherapy, SBRT, and novel immunotherapies such as bispecific antibodies remains scarce. This represents a critical knowledge gap. Therefore, we conducted this pilot study to explore this hypothesis. We selected a heterogeneous, high-risk locally advanced cohort (including a subset of HER2+ patients with inadequate response to prior therapy) to conduct an initial, broad evaluation of the efficacy and safety of this novel neoadjuvant strategy across different breast cancer subtypes.

## Patients and Methods

### Study Design and Patients

This was a single-center, retrospective pilot study conducted at Hubei Cancer Hospital. The study cohort comprised consecutive patients with high-risk, locally advanced breast cancer who were treated with a novel neoadjuvant protocol between June 2023 and August 2025. The primary objective was to explore the feasibility, safety, and preliminary efficacy of integrating SBRT with chemoimmunotherapy. Key inclusion criteria were: 1) histologically confirmed invasive breast carcinoma considered high-risk due to one or more of the following: cT3-T4 stage, clinically node-positive (cN+) disease, triple-negative or HER2-positive molecular subtype, or a high-risk Luminal B/HER2- profile based on large tumor size (>5 cm) and/or high-grade histology; 2) no evidence of distant metastasis (M0); 3) age  $\geq$  18 years with an ECOG performance status of 0–1; and 4) adequate hematologic, hepatic, and renal function. A unique inclusion criterion allowed for HER2+ patients with an inadequate response to initial standard anti-HER2 therapy to be switched to this salvage protocol. Exclusion criteria were active autoimmune disease, a history of other malignancies within 3 years (except non-melanoma skin cancer or carcinoma *in situ*), receipt of fewer than two cycles of protocol immunotherapy, or failure to proceed to definitive surgery.

### Ethics Approval and Consent

The study was conducted by the Declaration of Helsinki and approved by the Ethics Committee of Hubei Cancer Hospital of Huazhong University of Science and Technology (protocol code LLHBCH2025YN-060, approval date: August 11, 2025). All patients provided written informed consent.

### Neoadjuvant Therapy and Surgery

Stereotactic body radiation therapy (SBRT) was delivered using a linear accelerator equipped with volumetric modulated arc therapy (VMAT) or intensity-modulated radiation therapy (IMRT) capability. To ensure precision, daily image

guidance was performed using cone-beam computed tomography (CBCT) for accurate patient positioning prior to each fraction. Treatment planning was based on four-dimensional computed tomography (4D CT) simulation to account for intrinsic tumor mobility. The gross tumor volume (GTV), encompassing both primary and metastatic lesions, was initially defined on contrast-enhanced diagnostic CT or magnetic resonance imaging (MRI). This contour was then reviewed and adjusted on the maximum intensity projection (MIP) images derived from the 4D CT dataset to generate an internal gross tumor volume (IGTV), which incorporated the tumor's full respiratory motion. No additional expansion for a clinical target volume (CTV) was applied to the IGTV. The final planning target volume (PTV) was created by adding a uniform 5-mm isotropic margin to the IGTV. The prescription dose was stratified based on nodal involvement: For node-positive target volumes (primary tumor with involved lymph nodes), a total dose of 18 Gy was prescribed, delivered in 3 consecutive daily fractions of 6 Gy each. For node-negative target volumes (primary tumor only), 24 Gy was prescribed, delivered in 3 consecutive daily fractions of 8 Gy each. Dose was prescribed such that the 80% isodose line covered 100% of the PTV. The maximum dose (Dmax) within the PTV was constrained to be  $\leq$  (prescription dose / 0.8). All treatment plans strictly adhered to standard dose-volume constraints for relevant organs at risk.

Within 24 hours of completing SBRT, all patients initiated concurrent chemoimmunotherapy. Chemotherapy backbones were anthracycline- and taxane-based: either 4 cycles of dose-dense AC (doxorubicin 50 mg/m<sup>2</sup> + cyclophosphamide 600 mg/m<sup>2</sup>) every 3 weeks, followed by 4 cycles of a taxane (paclitaxel liposome 135 mg/m<sup>2</sup> or nab-paclitaxel 260 mg/m<sup>2</sup> every 3 weeks) with or without carboplatin (AUC 6 every 3 weeks); or 6 cycles of TCb (nab-paclitaxel 260 mg/m<sup>2</sup> or liposomal paclitaxel 135 mg/m<sup>2</sup> + carboplatin AUC 6 on day 1, every 3 weeks).

Immunotherapy was administered on day 1 of each chemotherapy cycle and consisted of one of the following agents: toripalimab (240 mg fixed dose), cadonilimab (6 mg/kg), or ivonescimab (20 mg/kg). For the three HER2+ patients included under the salvage criterion, initial treatment consisted of a median of 4 cycles of trastuzumab + pertuzumab + taxane-based chemotherapy. Upon demonstration of an inadequate response (no change in tumor as assessed by MRI), they proceeded to protocol SBRT followed by 3–5 cycles of chemoimmunotherapy as described above, without continued anti-HER2 therapy. Pegylated granulocyte colony-stimulating factor (G-CSF) was administered prophylactically per institutional guidelines. Definitive surgery was performed 2 to 6 weeks after the last cycle of neoadjuvant therapy, consisting of either breast-conserving surgery or mastectomy, combined with sentinel lymph node biopsy and/or axillary lymph node dissection as clinically indicated.

## Tumor Assessment

Clinical and radiological tumor response was assessed after 2–4 cycles and at completion of neoadjuvant therapy using breast MRI and physical examination, according to RECIST v1.1. The primary pathological endpoint was total pathological complete response (pCR), defined as the absence of invasive carcinoma in both the breast and axillary lymph nodes (ypT0/Tis ypN0) in the surgically resected specimen. Breast pCR (bpCR, ypT0/Tis) was a secondary endpoint. Residual Cancer Burden (RCB) and Miller-Payne (MP) grade were calculated as exploratory measures. All pathological assessments were performed independently by two dedicated breast pathologists blinded to the specific immunotherapy received. Discrepancies were resolved by consensus review. The Residual Cancer Burden (RCB) was derived from the pathological assessment of primary tumor dimensions, tumor bed cellularity, and axillary nodal disease burden. PD-L1 expression was evaluated on pre-treatment core biopsy specimens using the PD-L1 IHC 22C3 pharmDx assay on the DAKO Autostainer Link 48 platform. A Combined Positive Score (CPS)  $\geq 1$  was considered positive. Treatment-related adverse events (TRAEs) were graded using the National Cancer Institute Common Terminology Criteria for Adverse Events (version 5.0).

## Statistical Analysis

This was an exploratory, single-arm pilot study without a formal pre-specified sample size calculation. The cohort size was determined by the number of eligible patients treated with the novel protocol within the defined study period. Continuous variables are summarized as median and range, and categorical variables as frequencies and percentages. The pCR rate is reported with its 95% confidence interval (Clopper-Pearson exact method). Given the pilot, hypothesis-generating nature of the study and the limited sample size, no formal statistical hypothesis testing was performed;

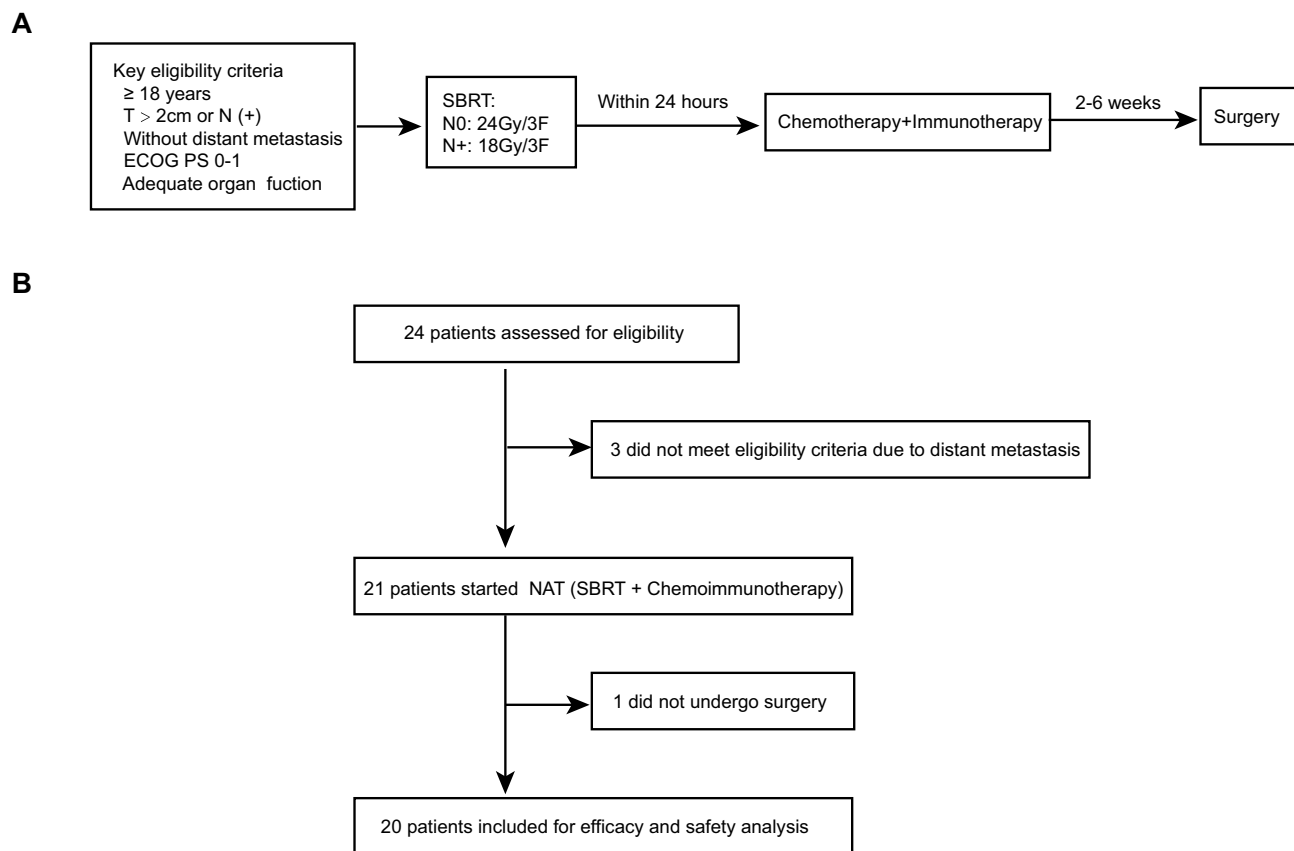
comparisons across subtypes are presented as descriptive and exploratory observations. Data visualizations were generated using the ggplot2 (version 3.5.2) and ggthemes (version 5.1.0) packages.

## Results

### Patient and Treatment Characteristics

The baseline characteristics of the 20 female patients (Figure 1) included in this analysis are summarized in Table 1. This was a heterogeneous, high-risk cohort: the majority presented with cT2 (75%) and clinically node-positive (cN+, 75%) disease, and 45% were diagnosed as stage III. Eighteen patients (90%) had an ECOG performance status score of 0. Molecular subtypes were: TNBC (35%, n=7), Luminal B/HER2- (50%, n=10), Luminal B/HER2+ (10%, n=2), and HER2+/non-luminal (5%, n=1) (Figure 2A). Among the 12 Luminal B patients, the median ER expression level was 90% (range: 40%-100%). PD-L1 status was assessed in eight patients, with six (75%) showing positivity (CPS  $\geq$ 1).

Detailed patient-level treatment data, including SBRT targets, chemotherapy regimens, and specific immunotherapy agents, are provided in Supplementary Table S1. Most patients (80%) received an AC-T-based chemotherapy backbone. The median of number of chemoimmunotherapy cycles administered was 8 (range: 3–8). As per protocol, three HER2+ patients with an inadequate response to initial anti-HER2 therapy were switched to salvage treatment involving SBRT followed by 3–5 cycles of chemoimmunotherapy. All underwent surgery (15% breast-conserving surgery, 85% mastectomy) at a median of 20 days (range: 14–27) after completing systemic therapy. All patients underwent surgical management in accordance with the initial treatment plan at diagnosis. One exception involved a patient with stage IIIA Luminal B/HER2- breast cancer, for whom the planned mastectomy was intraoperatively converted to breast-conserving surgery. Axillary lymph node dissection (ALND) was performed in 19 patients (95%).



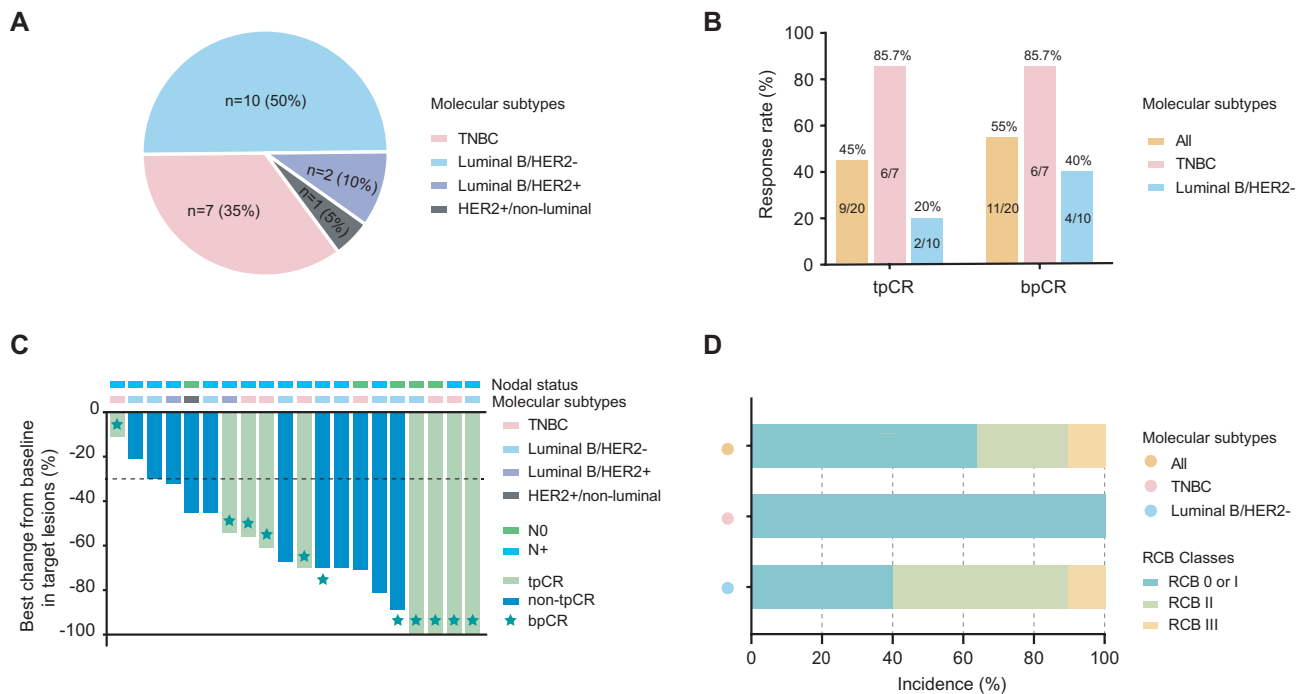
**Figure 1** Study design. (A) The flowchart of neoadjuvant therapy. (B) Flowchart for patient enrollment.

**Abbreviations:** ECOG, Eastern cooperative oncology group; PS, performance status; SBRT, stereotactic body radiotherapy; NAT, neoadjuvant therapy.

**Table 1** Demographic and Clinical Characteristics

Characteristic	N (%)
Median age (range), years	48 (31–63)
Tumor stage	
T2	15 (75)
T3-4	5 (25)
Clinical nodal status	
Negative	5 (25)
Positive	15 (75)
Clinical stage	
II	11 (55)
III	9 (45)
Tumor grade	
G2	11 (55)
G3	9 (45)
ER status	
Negative	8 (40)
Positive	12 (60)
HER2 status	
Negative	17 (85)
Positive	3 (15)
Ki-67 expression	
≤30%	6 (30)
>30%	14 (70)
Baseline PD-L1 status	
Negative	2 (10)
Positive	6 (30)
Unknown	12 (60)
Immunotherapy	
Toripalimab	10 (50)
Ivonescimab	7 (35)
Cadonilimab	3 (15)
Chemotherapy regimen	
AC-T	8 (40)
TCb-AC	7 (35)
TCb	5 (25)
Taxanes	
Nab-paclitaxel	14 (70)
Paclitaxel liposome	4 (20)
Paclitaxel liposome/ Nab-paclitaxel	2 (10)
Chemotherapy + Immunotherapy (range), cycles	8 (3–8)
Interval time from end of systemic therapy to surgery (range), days	20 (14–27)
Surgery	
Lumpectomy	3 (15)
Mastectomy	17 (85)
Axillary surgery	
SLNB	1 (5)
ALND	19 (95)

**Abbreviations:** ECOG, Eastern cooperative oncology group; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; PD-L1 positive is defined as a combined positive score of  $\geq 1$ ; AC, anthracyclines and cyclophosphamide; T, taxanes; Cb, carboplatin; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection.



**Figure 2** The efficacy of neoadjuvant therapy. **(A)** Distribution of molecular subtypes of breast cancer. **(B)** The rates of tpCR (ypT0/is ypN0) and bpCR (ypT0/is) compared by molecular subtype. **(C)** Waterfall plots of the best clinical response in efficacy evaluable set. **(D)** RCB by molecular subtype.

**Abbreviations:** tpCR, total pathological complete response; bpCR, breast pathological complete response; TNBC, triple-negative breast cancer; RCB, residual cancer burden.

## Overall Treatment Response

In this exploratory cohort, the total pathological complete response (pCR; ypT0/is ypN0) rate was 45% (9/20; 95% CI, 23.1–68.5). The breast pCR (ypT0/is) rate was 55% (11/20; 95% CI, 31.5–76.9, [Figure 2B](#)). According to RECIST v1.1, the objective response rate (ORR) was 90%, comprising a complete response in 4 patients (20%) and a partial response in 14 (70%). Stable disease was observed in the remaining 2 patients (10%), with no disease progression during neoadjuvant therapy ([Figure 2C](#)).

## Descriptive Analysis of Response by Subtype

Preliminary efficacy signals varied across subtypes. In the TNBC subgroup (n=7), a pCR was observed in 85.7% (6/7, [Figure 2B](#)) of patients, and all seven (100%) achieved a near-pCR (RCB 0/I, [Figure 2D](#)). In the Luminal B/HER2-subgroup (n=10), which had uniformly high ER expression, the pCR rate was 20% (2/10, [Figure 2B](#)) and the RCB 0/I rate was 40% (4/10, [Figure 2D](#)). Within the small HER2+ cohorts (n=3), one of two Luminal B/HER2+ patients achieved pCR, while the other had RCB-III disease; the single HER2+/non-luminal patient achieved RCB-I ([Supplementary Table S1](#)).

## Depth of Pathological Response and Radiographic Correlation

Overall, 65% of patients (13/20) achieved a near-pCR (RCB 0/I). Among the 11 patients who did not attain a pCR, Miller-Payne grading identified a major pathological response (MP 4–5) in 6 patients (55%), and a partial pathological response (MP 3) in the remaining 5 (45%). Among the 16 patients without a radiographic complete response (rCR), 11 (68.8%) had a major pathological response (MP 4–5) and 9 (56.3%) achieved near-pCR (RCB 0/I) ([Supplementary Table S1](#) and [Figure 2C](#)).

## Safety

The triple-modality regimen demonstrated a manageable toxicity profile, with detailed TRAEs summarized in [Table 2](#). The most common any-grade TRAEs were elevated alanine aminotransferase (70%), nausea (65%), elevated aspartate

**Table 2** Treatment-Related Adverse Events (N = 20)

Treatment-Related Adverse Events	Any Grades	Grade 3–4
<b>Haematological adverse events</b>		
Leukopenia	11 (55)	1 (5)
Neutropenia	8 (40)	1 (5)
Thrombocytopenia	2 (10)	0
Anemia	11 (55)	0
Elevated ALT	14 (70)	1 (5)
Elevated AST	12 (60)	1 (5)
Elevated creatinine levels	2 (10)	0
<b>Non-haematological adverse events</b>		
Nausea	13 (65)	0
Vomiting	10 (50)	1 (5)
Fatigue	9 (45)	0
Peripheral sensory neuropathy	9 (45)	0
Infusion reactions	1 (5)	0
<b>Potential immune-related AEs</b>		
Hypothyroidism/elevated TSH	3 (15)	0
Elevated CK	2 (10)	0
Rash	3 (15)	0

**Abbreviations:** ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase.

aminotransferase (60%), leukopenia (55%), anemia (55%), vomiting (50%), and fatigue (45%). Potential immune-related adverse events (irAEs) of any grade occurred in 8 patients (40%), including rash (n=3, 15%), hypothyroidism (n=3, 15%), and elevated creatine kinase (n=2, 10%); all were grade 1–2 in severity. Grade 3–4 TRAEs occurred in 5 patients (25%), including elevated transaminases (10%), neutropenia (5%), leukopenia (5%), and vomiting (5%). One patient experienced a grade 2 rash leading to omission of one immunotherapy cycle. No treatment-related deaths occurred. During the perioperative observation period, no cases of acute radiation pneumonitis, or symptomatic cardiotoxicity were identified, and no surgery was cancelled due to treatment-related toxicity.

## Follow-Up

Given the recent treatment completion for many patients, the post-surgery follow-up period was relatively short (median follow-up time 11.2 months, range: 8.2–28.2 months). No locoregional recurrences or distant metastases have been observed to date. Data on event-free and overall survival remain immature, and continued follow-up is ongoing to assess the durability of the pathological responses observed.

## Discussion

This single-center, retrospective pilot study describes preliminary efficacy and safety of a novel triple-modality neoadjuvant approach integrating SBRT with chemoimmunotherapy in a small, heterogeneous cohort of high-risk, locally advanced breast cancer. Given the inherent limitations, the findings must be interpreted as descriptive and hypothesis-generating.

Within the TNBC subgroup (n=7), we observed a pCR rate of 85.7%, with all patients achieving an RCB 0/1 response. While this rate is numerically higher than the 56.8–68.2% pCR rates reported in pivotal chemoimmunotherapy trials,<sup>5,18–20</sup> any direct comparison is invalid given the vast differences in trial design, scale, and patient selection. Our cohort was highly selected and small. This signal, however, aligns with the biological premise that SBRT may act as an in situ vaccine, potentially enhancing the efficacy of systemic immunotherapy by releasing tumor antigens and modulating the microenvironment.<sup>10</sup> This observation justifies formal evaluation in a dedicated, prospective setting.

The activity observed in Luminal B/HER2- breast cancer, a subtype typically characterized by an immunosuppressive microenvironment, is a key exploratory finding. All patients in this subgroup had high ER expression (median 90%, range 40% to 100%). The pCR rate of 20% (2/10) and the RCB 0/I rate of 40% (4/10) in our cohort represent meaningful pathological responses in a population where single-agent immunotherapy has shown limited benefit. For context, in the KEYNOTE-756 trial,<sup>7</sup> the pCR rate for patients with ER  $\geq$ 10% tumors in the pembrolizumab-chemotherapy arm was 22.5%. Our data, while not comparable in a statistical sense, suggest that the addition of SBRT may facilitate pathological responses of a similar magnitude in a comparable, high-ER population. This preliminary signal supports the hypothesis that radiotherapy might help overcome local immune resistance in “cold” tumors, a concept that requires rigorous validation. Several aspects of our regimen warrant consideration for future study. The sequencing of modalities (SBRT prior to chemoimmunotherapy) and the inclusion of metastatic lymph nodes in the radiation field differ from other pilot studies like PEARL<sup>17</sup>. The optimal spatiotemporal integration of these modalities is unknown and likely critical. Furthermore, a subset of our patients received the PD-1/VEGF bispecific antibody ivonescimab. The dual targeting of angiogenesis and immune checkpoints represents a theoretically synergistic partner for radiotherapy, which can also affect tumor vasculature.<sup>11</sup> The responses seen in some luminal patients who received this agent are intriguing, but cannot be attributed to it specifically in this unrandomized, multi-agent cohort. Its distinct contribution must be evaluated in randomized trials. An important interpretive consideration in our study is the heterogeneity of the immunotherapy agents used, which included conventional PD-1 inhibitors and bispecific antibodies targeting PD-1/CTLA-4 or PD-1/VEGF. While all agents modulate the PD-1 axis, their additional mechanisms (such as CTLA-4 inhibition or VEGF blockade) could theoretically lead to differential effects on the tumor microenvironment and clinical outcomes. The promising responses observed, particularly in some luminal patients who received the PD-1/VEGF bispecific antibody ivonescimab, are mechanistically intriguing given the potential synergy between anti-angiogenesis and radiotherapy. However, this pilot study was neither designed nor powered to compare the efficacy of different immunotherapies. Consequently, the observed efficacy signals should be interpreted as preliminary evidence for the class of PD-1-based immunotherapy combined with SBRT. Specifically, evaluating whether dual PD-1/VEGF targeting provides superior synergy with SBRT compared to PD-1 inhibition alone represents a compelling question for the next phase of clinical investigation.

We also note a significant discrepancy between radiographic and pathological assessment, with imaging frequently underestimating the degree of tumor regression. This underscores that surgical pathology remains the gold standard for evaluating response to novel neoadjuvant regimens and that clinical decisions should not be based solely on residual imaging findings.<sup>21,22</sup> Importantly, this analysis provides initial clinical evidence for a potential salvage strategy. The conversion of HER2+ patients with poor initial response to standard therapy to a regimen containing SBRT and chemoimmunotherapy resulted in a pCR in one case and a major pathological response in another. This concept merits exploration in dedicated studies of therapy-resistant disease.

The conclusions of this study are constrained by several important limitations, as follows. Firstly, the small, retrospective sample size from a single institution limits statistical power and generalizability. Secondly, the cohort was intentionally heterogeneous, including both treatment-naïve and previously treated (salvage HER2+) patients, which introduces confounding. Thirdly, the use of three different immunotherapy agents introduces unmeasured variability, although all targeted the PD-1 axis. Fourthly, the absence of a control group precludes any definitive assessment of the incremental value of SBRT or the specific choice of immunotherapy. Fifthly, a critical scientific gap is the lack of correlative biomarker studies. We cannot provide mechanistic data to link the observed clinical responses to immune activation or vascular changes. Lastly, the follow-up was short, and survival data remain immature; thus, the long-term clinical relevance of the observed pathological responses remains unknown. These limitations collectively underscore that our findings are preliminary and should be interpreted as hypothesis-generating only, rather than providing definitive evidence of efficacy.

## Conclusion

In conclusion, this pilot study provides preliminary, hypothesis-generating evidence that the novel integration of SBRT with chemoimmunotherapy is feasible and shows promising biological activity in high-risk breast cancer. Signals of deep pathological response were observed not only in TNBC but also, notably, in traditionally less immunoresponsive, high-

ER Luminal B/HER2- disease, with a manageable safety profile. While the inherent limitations of this small, retrospective analysis preclude definitive efficacy claims, the findings provide a robust rationale for prospective trials to validate this multimodal strategy and elucidate its mechanisms.

## Data Sharing Statement

The datasets generated during and/or analysed during the current study are available from the corresponding author (Guang Han) on reasonable request.

## Ethics Approval and Informed Consent

The study was conducted by the Declaration of Helsinki and approved by the Ethics Committee of Hubei Cancer Hospital of Huazhong University of Science and Technology (protocol code LLHBCH2025YN-060, approval date: August 11, 2025). All patients provided written informed consent.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

All authors declare no financial or non-financial competing interests in this work.

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