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Original Research Article

Clinical outcomes of neoadjuvant dual HER2 blockade with pertuzumab/Sigrima and trastuzumab/Vivitra biosimilars: real-world evidence in HER2-positive breast cancer in India

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ABSTRACT

Background: HER2-positive breast cancer is an aggressive subtype with a high risk of recurrence. Neoadjuvant chemotherapy (NACT) combined with dual HER2 blockade improves pathological complete response (pCR) rates in clinical trials; however, real-world evidence on biosimilars Sigrima™ and Vivitra™ in India remains limited.
Methods: This retrospective study analysed 571 HER2-positive breast cancer patients enrolled in the ANAYA Care programme. All patients received dual HER2 blockade with Sigrima™ (petuzumab biosimilar) and Vivitra™ (trastuzumab biosimilar), with 495 undergoing NACT. Data on demographics, disease stage, treatment setting, financial assistance, pCR outcomes, and adverse events were collected. pCR was evaluable in 242 patients.
Results: Most patients were aged 46-60 years, with stage II disease being most common, followed by stage III and stage I. The majority were treated in private hospitals, with additional representation from government and trust centres. Financial assistance supported chemotherapy access in 194 patients. Among evaluable patients, 182 achieved pCR, yielding a rate of 75.2%. Treatment was well tolerated, with ~90% reporting no adverse events. Observed toxicities were primarily mild to moderate, including nausea, fatigue, stomatitis, cytopenias, and liver enzyme abnormalities; serious events were rare.
Conclusions: Dual HER2 blockade with Sigrima™ and Vivitra™ demonstrated high efficacy and favourable tolerability in this real-world Indian cohort. These findings support their use as a practical and effective neoadjuvant treatment option in routine clinical practice.

Keywords: Biosimilars, HER2-positive breast cancer, India, Neoadjuvant therapy, Pathological complete response, Real-world evidence

INTRODUCTION

Human epidermal growth factor receptor 2 (HER2)-positive breast cancer accounts for approximately 15-20% of all breast cancer cases and represents a biologically aggressive subtype characterised by high proliferative rates, increased risk of recurrence, and poorer survival outcomes compared with HER2-negative disease.[1] Historically associated with an unfavourable prognosis, the therapeutic landscape of HER2-positive breast cancer has undergone a paradigm shift with the advent of HER2-targeted therapies, leading to substantial and sustained improvements in survival outcomes across disease stages.[2]

In contemporary clinical practice, the management of early and locally advanced HER2-positive breast cancer is centred on the neoadjuvant approach, wherein dual HER2 blockade with trastuzumab and pertuzumab in combination with chemotherapy is widely accepted as the standard of care.[3] Beyond facilitating tumour downstaging and improving surgical outcomes, neoadjuvant therapy provides a unique in vivo platform to evaluate tumour

biology and treatment responsiveness. In this context, pathological complete response (pCR) has emerged as a clinically meaningful surrogate endpoint, strongly associated with improved long-term outcomes, particularly in HER2-positive disease.[4]

Landmark clinical trials have firmly established the efficacy of dual HER2 blockade in achieving superior pCR rates. The NeoSphere trial demonstrated that the addition of pertuzumab to trastuzumab-based chemotherapy significantly improved pCR outcomes.[5] The TRAIN-2 study further showed that comparable efficacy can be achieved with anthracycline-free regimens, supporting treatment optimisation strategies aimed at minimising toxicity without compromising efficacy.[6] Similarly, the KRISTINE trial provided important insights into alternative HER2-targeted approaches, although conventional chemotherapy-based regimens remain the preferred strategy for maximising pCR.[7] These findings are complemented by the APHINITY trial, which demonstrated the long-term benefit of dual HER2 blockade in the adjuvant setting, thereby reinforcing its role across the continuum of care.

In the metastatic setting, the CLEOPATRA trial established the combination of trastuzumab, pertuzumab, and docetaxel as the standard first-line therapy, demonstrating significant and durable improvements in progression-free and overall survival.[8] Collectively, these data underscore the sustained clinical benefit of dual HER2 inhibition and its central role in treatment paradigms across disease stages.[2]

Despite robust evidence from randomised controlled trials, translating these outcomes into routine clinical practice remains a key challenge. Real-world evidence (RWE) studies have highlighted variability in outcomes due to differences in patient characteristics, treatment adherence, and healthcare infrastructure.[9] This gap is particularly pronounced in low- and middle-income countries such as India, where access to optimal cancer care is often constrained by economic and systemic factors.[10]

Indian-specific data further underscore distinct disease patterns, including younger age at presentation, more advanced stage at diagnosis, and variability in access to standard-of-care therapies, all of which can influence treatment outcomes.[11-16] Additionally, healthcare delivery models and reimbursement mechanisms, such as government-supported insurance schemes, play a pivotal role in determining access to advanced therapies.[17] Real-world observational studies from India also demonstrate heterogeneity in treatment patterns and clinical outcomes, emphasising the need for context-specific evidence to guide therapeutic decision-making.[18]

In this context, biosimilars have emerged as a critical enabler of access, offering cost-effective alternatives to innovator biologics without compromising efficacy or safety.[11] The economic implications of biosimilars are particularly relevant in India, where affordability remains a major determinant of treatment uptake.[12] National guidelines, including those from the National Cancer Grid, increasingly advocate for cost-effective strategies to optimise cancer care delivery in resource-constrained settings.[14]

Sigrima® (pertuzumab biosimilar) and Vivitra® (trastuzumab biosimilar) are being progressively integrated into routine oncology practice in India as part of this evolving therapeutic landscape. However, robust real-world evidence evaluating their combined use in the neoadjuvant setting remains limited. The ANAYA Care Programme, a patient assistance initiative, provides a unique platform to assess treatment accessibility, adherence, and clinical outcomes in patients receiving dual HER2-targeted therapy.

In this context, the present study aimed to generate real-world evidence on the effectiveness of biosimilar-based dual HER2 blockade in the neoadjuvant setting among patients with HER2-positive breast cancer. By bridging the gap between clinical trial efficacy and real-world effectiveness, this analysis seeks to provide clinically meaningful insights to inform treatment strategies and improve access to standard-of-care therapies in resource-constrained settings.

METHODS

Study design and data source

This retrospective, observational cohort analysis was conducted using data from patients registered under the ANAYA Care Programme. The programme is a structured patient support initiative developed by Zydus Lifesciences Ltd. (Ahmedabad, India) to facilitate access to oncology biologics across diverse healthcare settings in India. Clinical and treatment-related data were analysed as recorded during routine patient care, with no intervention or protocol-driven treatment assignment between June 2024 to June 2025.

Patient population

The study population comprised patients with confirmed HER2-positive breast cancer who were enrolled in the ANAYA Care Programme and received treatment with Sigrima® (pertuzumab biosimilar) in combination with Vivitra® (trastuzumab biosimilar). Patients receiving this combination in the neoadjuvant setting constituted the primary cohort for evaluation. Eligibility for inclusion was based on documented receipt of dual HER2 blockade prior to definitive surgery.

Data collection

Demographic, clinical, and treatment-related variables were extracted from programme records. Collected parameters included patient age at initiation of therapy,

disease stage at diagnosis, tumour laterality, and type of treating institution (private, government, or trust-based hospital). Information on payment status and receipt of chemotherapy-related assistance was also captured. Efficacy assessment focused on pathological complete response (pCR), while safety evaluation included documentation of treatment-emergent adverse events observed during neoadjuvant therapy.

Pathological complete response was defined as the absence of residual invasive carcinoma in both the breast tissue and axillary lymph nodes on post-surgical histopathological examination.

Statistical analysis

Data were analysed using descriptive statistical methods. Patient characteristics, treatment patterns, pCR outcomes, and safety findings were summarised using frequencies and percentages for categorical variables. No inferential statistical comparisons were planned, given the observational nature of the study.

RESULTS

Patient characteristics

A total of 571 patients diagnosed with HER2-positive breast cancer were included in the overall analysis. Among these, 495 patients received neoadjuvant treatment with the combination of Sigrima® and Vivitra® and formed the primary cohort for outcome evaluation (Figure 1). Most patients (50%) were between 46 and 60 years of age at the time of treatment initiation. Stage II disease was the most frequently observed at diagnosis (n=135), followed by Stage III (n=70), while a smaller proportion of patients presented with stage I disease (n=6).

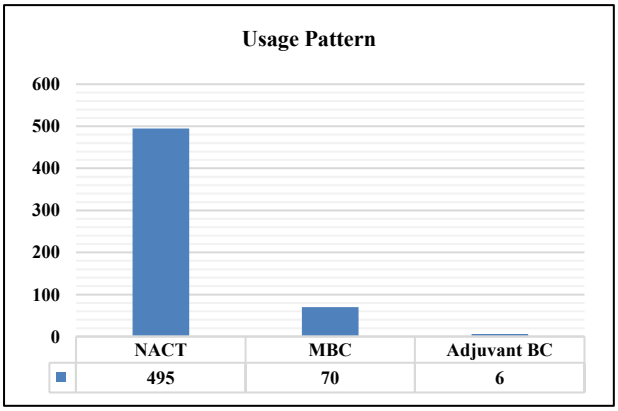

Figure 1: Utilization pattern of Sigrima.

With respect to tumour laterality, left-sided breast involvement was documented in 168 patients, right-sided disease in 150 patients, and bilateral involvement in 10 patients. Treatment was delivered predominantly in private healthcare facilities (n=400), with the remainder managed in government hospitals (n=100) and trust-based institutions (n=71), illustrating the heterogeneity of real-world oncology practice across India (Figure 2).

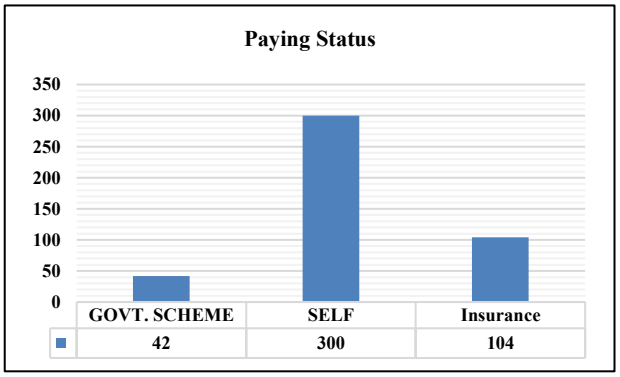

Figure 2: Paying status of the patients.

Treatment access and support

Financial and treatment-related assistance for chemotherapy was provided to 194 patients through the programme. Supported regimens most commonly included agents such as Zytax® (docetaxel), Biocarb® (carboplatin), Pegstim® (pegfilgrastim), and Petaxel® (paclitaxel). These findings underscore the contribution of patient assistance initiatives in facilitating access to comprehensive neoadjuvant therapy aligned with standard treatment guidelines in routine clinical settings.

Efficacy outcomes

Surgical pathology data following neoadjuvant therapy were available for 242 patients. Of these, 182 patients achieved a pathological complete response, yielding a pCR rate of 75.2% (Figure 3). This substantial response rate indicates robust real-world effectiveness of dual HER2 blockade using biosimilar pertuzumab and trastuzumab in the neoadjuvant treatment of HER2-positive breast cancer.

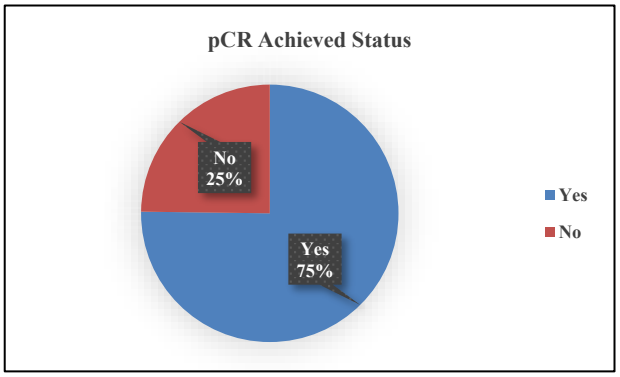

Figure 3: pCR rates observed among patients.

Safety outcomes

Treatment was generally well tolerated across the cohort. The majority of patients (approximately 90%) did not report any treatment-emergent adverse events during the

neoadjuvant phase. When adverse events did occur, they were predominantly mild to moderate in severity and included symptoms such as nausea, fatigue, stomatitis, hyperglycaemia, transient elevations in liver enzymes, cytopenias, and skin rash. Severe adverse events were infrequently observed (Figure 4).

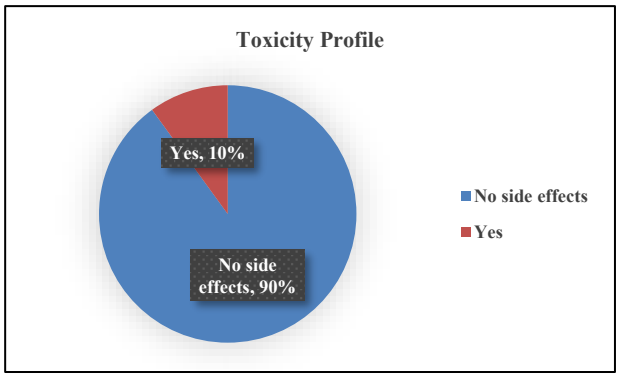

Figure 4: Toxicity profile of the patients.

DISCUSSION

The present real-world analysis from India demonstrates that neoadjuvant dual HER2 blockade using a biosimilar combination of pertuzumab (Sigrima®) and trastuzumab (Vivitra®) is associated with high pathological complete response (pCR) rates in patients with HER2-positive breast cancer. The observed pCR rate of 75.2% reflects robust antitumour activity in routine clinical practice and aligns with outcomes reported in controlled clinical trial settings.[5] Notably, this high response rate may reflect a combination of favourable tumour biology, adherence to guideline-concordant therapy, and improved treatment access facilitated through structured patient support programmes.

The consistency of these findings with pivotal clinical trial outcomes supports the translational effectiveness of biosimilar-based dual HER2 blockade, suggesting that clinical benefits observed in trial settings can be reliably reproduced in real-world Indian populations.[5] This is particularly relevant given the differences in patient characteristics, healthcare infrastructure, and treatment delivery outside controlled trial environments.

While pCR served as the primary endpoint, the magnitude of response observed in this cohort reinforces its clinical relevance as an indicator of favourable long-term outcomes in HER2-positive breast cancer.[4] When interpreted within the broader therapeutic landscape, the high pCR rates observed in this study may be expected to translate into meaningful survival benefits, consistent with the established continuum of HER2-directed therapy across early and advanced disease settings.[8,13]

A key strength of this study lies in its ability to capture real-world oncology practice across diverse healthcare settings, including private, government, and trust-based institutions. This heterogeneity enhances the generalisability of the findings and reflects the realities of cancer care delivery in India. Observations from major Indian centres have similarly demonstrated that meaningful clinical outcomes can be achieved despite variations in disease stage at presentation, access to therapy, and resource availability.[15,16]

In addition, healthcare financing mechanisms and patient support programmes play a crucial role in enabling access to systemic therapies. Population-level data and real-world analyses from India highlight the importance of such frameworks in improving treatment uptake, adherence, and continuity of care.[17,18] The ANAYA Care Programme exemplifies this integrated approach, supporting both access and delivery of evidence-based therapy.

The safety profile observed in this study was favourable and consistent with the known tolerability of dual HER2 blockade. The majority of patients did not experience significant adverse events, and no new safety signals were identified, supporting the routine clinical use of these biosimilars.

Importantly, these findings demonstrate that guideline-recommended neoadjuvant therapy can be effectively delivered using biosimilar formulations in routine practice.[14] Within the Indian healthcare context, where access to innovator biologics is often limited, biosimilars offer a pragmatic and scalable solution to bridge the gap between evidence-based standards and real-world treatment delivery.[11,12] The observed outcomes further highlight the synergistic role of biosimilars and patient assistance programmes in reducing treatment barriers and improving access to optimal care.

Taken together, these findings provide compelling real-world evidence supporting the effectiveness, safety, and accessibility of biosimilar-based dual HER2 blockade in the neoadjuvant setting. Beyond clinical outcomes, this study underscores a broader shift towards more equitable cancer care, demonstrating that high-quality, guideline-concordant treatment can be achieved in resource-constrained settings through cost-effective therapeutic strategies.

This analysis should be interpreted in light of certain limitations inherent to its design. As a retrospective observational study, the findings are subject to potential selection bias and reliance on routinely collected programme data. Availability of surgical pathology information was incomplete, resulting in pCR assessment for a subset rather than the entire neoadjuvant cohort. In addition, long-term clinical endpoints such as disease-free survival and overall survival were not evaluated. Treatment approaches, including chemotherapy backbones and supportive care, were determined by treating physicians and were not uniformly standardised across participating centres. Despite these constraints, the large sample size and inclusion of patients from diverse

healthcare settings across India strengthen the relevance of the findings and provide meaningful insight into real-world use of biosimilar-based dual HER2 blockade.

CONCLUSION

In this large real-world cohort from India, neoadjuvant treatment with dual HER2 blockade using the pertuzumab biosimilar Sigrima® and the trastuzumab biosimilar Vivitra® was associated with high clinical effectiveness and favourable tolerability. A pathological complete response rate of 75.2% was observed, consistent with the magnitude of benefit reported in pivotal randomised trials of innovator biologics. These results support the use of biosimilar-based dual HER2 therapy as an effective and pragmatic neoadjuvant option for patients with HER2-positive breast cancer in routine clinical practice. Importantly, the findings highlight the potential of biosimilars to expand access to guideline-recommended care and improve treatment equity in resource-constrained healthcare environments.

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