BJMS
www.batnajms.net

Batna Journal of Medical Sciences 2026;13(5):13
https://doi.org/10.48087/BJMS.2026.130513

ORIGINAL ARTICLE

Real-World Efficacy and Safety of the KEYNOTE-522 Protocol for Neoadjuvant Triple-Negative Breast Cancer: A Single-Center Experience

Assia BENSALEM[1], Khouloud BRAHIMI[1], Abdelaziz AMMARI[1], Sihem BENSALEM[2], Nour Djihane BOUATROUS[1], Meryem BOUDJERDA[1]

ABSTRACT

Triple-negative breast cancer (TNBC), defined by the absence of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) expression, is an aggressive subtype associated with a high risk of relapse and poorer overall survival compared with other breast cancer subtypes. The phase III KEYNOTE-522 trial demonstrated that the addition of pembrolizumab, a programmed death-1 (PD-1) inhibitor, to standard neoadjuvant chemotherapy significantly improves pathological complete response (pCR) rates in patients with high-risk early-stage TNBC. This study aimed to evaluate the efficacy and safety of this regimen in a real-world clinical practice setting. We conducted a retrospective study of patients with localized TNBC treated according to the KEYNOTE-522 protocol at the Medical Oncology Department of EH Didouche Mourad, Constantine (Algeria), between December 2022 and January 2024. Thirteen patients were included. The primary endpoints were the pCR rate and the incidence of treatment-related adverse events. The mean age was 46 years (range: 25–73), and comorbidities were present in 38.4% (n = 5) of patients. All patients (100%) completed neoadjuvant treatment and underwent definitive surgery. Among the 13 evaluable patients, 9 (69.2%) achieved a pCR. Treatment-related adverse events were observed in all patients; the most frequent were neutropenia (61.5%), hypothyroidism (30.8%), and generalized urticarial reactions (30.8%). In this real-world cohort, the addition of pembrolizumab to neoadjuvant chemotherapy demonstrated encouraging efficacy, with a pCR rate consistent with that reported in clinical trials. The safety profile was in line with known toxicities and was considered manageable. These findings support the feasibility and effectiveness of the KEYNOTE-522 regimen outside a clinical trial setting.

Keywords: Triple-negative breast cancer, TNBC, Pembrolizumab, Neoadjuvant therapy, Immunotherapy, Pathological complete response, pCR, Real-world evidence, Adverse events.

1- Medical Oncology Department, DIDOUCHE Mourad University Hospital, Faculty of Medicine, University Constantine 3, ALGERIA. 2- Endocrinology-Diabetology and Metabolic diseases, Regional University Military Hospital Commander Abdellali BENBAATOUCHE (HMRUC) Constantine, Faculty of Medicine, University Constantine 3, ALGERIA

Received: 10 Mar 2026
Accepted: 25 Apr 2026

Correspondance to: Abdelaziz AMMARI
E-mail: abdelazizammari@yahoo.fr

1. INTRODUCTION

For decades, triple-negative breast cancer (TNBC) has been considered the "therapeutic orphan" among breast cancer subtypes. Defined by the absence of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) expression, it is inherently unresponsive to endocrine or HER2-targeted therapies that have dramatically improved outcomes for other patients. This left cytotoxic chemotherapy as the sole systemic treatment option, a strategy often associated with suboptimal outcomes, a high risk of early relapse, and an inferior overall survival [1]. Consequently, TNBC represented a formidable clinical challenge and a major area of unmet need in oncology.

The therapeutic landscape for TNBC has been revolutionized in recent years, primarily by the advent of cancer immunotherapy. The high tumor mutational burden and frequent expression of programmed death-ligand 1 (PD-L1) in many TNBCs render them particularly susceptible to immune checkpoint inhibition. This breakthrough was first established in the metastatic setting, with the KEYNOTE-355 trial demonstrating a significant survival benefit for pembrolizumab combined with chemotherapy [2]. This success has logically translated into the neoadjuvant setting, where the goal is to eradicate micrometastatic disease and improve long-term cure rates. The phase III KEYNOTE-522 trial was a landmark study, demonstrating that adding pembrolizumab, a PD-1 inhibitor, to standard neoadjuvant chemotherapy significantly improved pathological complete response (pCR) rates and event-free survival in patients with high-risk, early-stage TNBC, marking a new standard of care [3].

While the KEYNOTE-522 trial provided robust evidence from a controlled clinical trial environment, confirming these results in real-world clinical practice remains essential. Real-world data can validate the applicability of trial outcomes across broader patient populations, including those with comorbidities or in different healthcare systems, and can provide critical insights into the practical management of treatment-related toxicities [4]. Therefore, this study aims to evaluate the real-world efficacy, as measured by pCR rates, and the safety profile of the KEYNOTE-522 protocol in a cohort of patients with early-stage TNBC treated at our institution.

2. MATERIALS AND METHODS

Study Design and Setting We conducted a retrospective, observational, single-center study designed to evaluate the outcomes of the KEYNOTE-522 protocol in a real-world clinical setting. This was not a clinical trial; patients received standard-of-care treatment, and no experimental interventions were performed beyond routine clinical practice. The study was performed at the Medical Oncology Department of the Hospital University Didouche Mourad, Constantine (Algeria). The study period encompassed patients who initiated neoadjuvant treatment between December 2022 and January 2024.

Patient Population We included all female patients (≥ 18 years) with histologically confirmed, early-stage (Stage II-III) triple-negative breast cancer (TNBC) who were treated with the neoadjuvant pembrolizumab plus chemotherapy regimen as per the KEYNOTE-522 protocol. A total of thirteen (13) patient records were identified and included in the final cohort.

Data Collection and Variables Data were systematically extracted from patient medical records. The following information was collected for analysis: baseline Characteristics: Age at diagnosis, body mass index (BMI), comorbidities, and family history of cancer; Tumor Characteristics: Clinical stage at diagnosis, determined according to the 8th edition of the AJCC TNM staging system; treatment Details: The neoadjuvant chemotherapy regimen was administered in accordance with the KEYNOTE-522 protocol, consisting of paclitaxel plus carboplitaxel followed by anthracycline-based chemotherapy, combined with pembrolizumab; surgical and Pathological Outcomes: Type of definitive surgery performed and final pathological response; and safety Data: All documented treatment-related adverse events (AEs) occurring during the neoadjuvant period.

Study Endpoints The primary efficacy endpoint was the rate of pathological complete response (pCR), defined as the absence of any residual invasive carcinoma in the breast and axillary lymph nodes (ypT0/Tis ypN0) on final pathological examination of the surgical specimen [5]. The primary safety endpoint was the incidence and severity of treatment-related adverse events, which were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 [6].

Ethical Considerations

This study was a retrospective analysis of anonymized patient data. As this was not an interventional clinical trial and involved no modification of standard patient care, formal review and approval by an institutional ethics committee were not required, in accordance with institutional and national guidelines for observational studies. All patient data were anonymized prior to analysis to protect confidentiality.

3. RESULTS

Patient Cohort and Baseline Characteristics A total of 13 patients with early-stage triple-negative breast cancer (TNBC) were included in this analysis. The mean age of the cohort was 46 years (range, 25–73 years). The baseline demographic and clinical characteristics of the patients are summarized in Table 1. Comorbidities were present in 38.4% (n=5) of patients, primarily hypothyroidism (23.0%, n=3) and hypertension (15.3%, n=2). A notable family history of cancer was reported by 69.2% (n=9) of patients, with nearly half (46.1%, n=6) having a first-degree relative with breast cancer. According to the 8th edition of the AJCC TNM classification, the majority of patients presented with stage II or III disease (76.9%, n=10).

Table 1: Baseline Demographic and Clinical Characteristics of the Cohort (N=13)

CHARACTERISTIC	N (%) OR MEAN ± SD (RANGE)
Age (years)	46 ± 15.6 (25-73)
Comorbidities	5 (38.4%)
Hypothyroidism	3 (23.0%)
Hypertension	2 (15.3%)
Diabetes Mellitus	1 (7.6%)
Family History of Cancer	9 (69.2%)
Breast Cancer	6 (46.1%)
Clinical Stage at Diagnosis (AJCC 8th Ed.)	
Stage IIA	3 (23.1%)
Stage IIB	5 (38.5%)
Stage IIIA	5 (38.5%)

Efficacy Outcomes Of the total cohort, the thirteen patients have undergone surgery. Among these patients, nine (69,2%) achieved a pathological complete response (pCR), defined as the absence of any residual invasive carcinoma in the breast and axillary lymph nodes (ypT0/Tis ypN0). The remaining four patients (30,7%) had residual invasive disease at the time of surgery.

Safety Outcomes Treatment-related adverse events (AEs) were observed in all patients throughout the neoadjuvant period. The most frequently reported AEs are summarized in Table 2. The most common toxicity was hematological, with neutropenia occurring in 61.5% (n=8) of patients. Endocrine toxicities, particularly hypothyroidism requiring hormone replacement, were also frequent, affecting 30.8% (n=4) of the cohort. Notably, generalized urticarial skin reactions occurred in four patients (30.8%); these were managed with antihistamines and corticosteroids and did not result in treatment delays or discontinuation of pembrolizumab.

Table 2. Most Frequent Treatment-Related Adverse Events (N=13).

Adverse Event	n (%)
Hematological	
Neutropenia (all grades)	8 (61.5%)
Endocrine	
Hypothyroidism (requiring substitution)	4 (30.8%)
Hyperthyroidism	1 (7.7%)
Dermatological	
Generalized urticaria	4 (30.8%)
Cardiac	
Asymptomatic troponin elevation	1 (7.7%)

4. DISCUSSION

Principal Findings and Comparison with the KEYNOTE-522 Trial The principal finding of this real-world cohort study is that the integration of pembrolizumab with neoadjuvant chemotherapy for early-stage triple-negative breast cancer (TNBC) is both feasible and effective, with an encouraging pathological complete response (pCR) rate. The pCR of 69.2% observed in our evaluable patients is remarkably consistent with the 64.8% pCR rate reported in the pembrolizumab arm of the pivotal KEYNOTE-522 phase III trial [3]. This concordance is highly significant, as it suggests that the impressive efficacy demonstrated in a highly controlled clinical trial environment is translatable and reproducible in routine clinical practice, even in a setting with different resource availability.

Furthermore, the safety profile observed in our cohort was consistent with the known toxicities of the protocol. The high incidence of hematological toxicity (neutropenia) and endocrine events (hypothyroidism, hyperthyroidism) mirrors the findings of the KEYNOTE-522 trial and other studies involving immune checkpoint inhibitors [7]. This consistency is reassuring for clinicians, confirming that the

adverse events are predictable and, as our data suggest, manageable with appropriate monitoring and intervention, such as routine thyroid function tests and prompt management of skin reactions.

Clinical Implications and Feasibility Our results provide valuable real-world evidence that supports the adoption of the KEYNOTE-522 protocol as a new standard of care for high-risk, early-stage TNBC. For clinicians, this study confirms that with adequate multidisciplinary support—including hematology monitoring for neutropenia and endocrinology collaboration for thyroid dysfunction—this intensive regimen can be safely delivered. The high pCR rate is particularly meaningful, as achieving a pCR is strongly correlated with improved long-term outcomes, including event-free survival, in patients with TNBC [5].

Strengths and Limitations

The strengths of our study include its focus on a real-world population and the prospective collection of data within a retrospective analysis. However, our study must be interpreted in light of several important limitations. The primary limitation is the small sample size, with thirteen patients evaluable for the primary endpoint of pCR at the time of analysis. This small number limits the statistical power. The single-center, retrospective design also introduces the potential for selection bias and limits the diversity of the population. Finally, the short follow-up duration means we could only assess pCR as a surrogate endpoint; we are unable to report on long-term outcomes such as event-free survival or overall survival, which are the ultimate measures of treatment success.

Despite its limitations, our study provides an early and encouraging real-world validation of the KEYNOTE-522 protocol. It demonstrates that the combination of pembrolizumab and chemotherapy can achieve pCR rates comparable to clinical trials, with a manageable safety profile in routine practice. These findings support the feasibility of this regimen and its role in transforming the prognosis for patients with high-risk, early-stage TNBC. Future research with larger, multi-center cohorts and long-term follow-up is warranted to definitively establish the impact of this regimen on survival outcomes in real-world settings.

5. CONCLUSION

This study provides compelling real-world evidence that the therapeutic revolution for early-stage triple-negative breast cancer (TNBC) is both effective and feasible beyond the confines of a clinical trial. Our findings demonstrate that the integration of pembrolizumab with neoadjuvant chemotherapy yields a pathological complete response rate of 69.2% in evaluable patients, a figure that closely mirrors the efficacy of the landmark KEYNOTE-522 trial. The safety profile, while notable, was consistent with established toxicities and was deemed manageable with routine monitoring and multidisciplinary care. These results collectively validate the KEYNOTE-522 protocol as a robust and translatable new standard of care in routine clinical practice. The significance of this work extends beyond a single-center experience. For years, TNBC was considered the "therapeutic orphan" of breast oncology. Our results contribute to the growing body of evidence that bridges the critical gap between clinical trial efficacy and real-world applicability. This successful implementation underscores the necessity of a well-equipped healthcare environment, including access to immunotherapy, pathology, and supportive care services to manage potential immune-related adverse events. For clinicians, our data offers practical reassurance; for patients, it represents tangible hope for improved long-term outcomes. Ultimately, this study heralds a new era in the management of a historically challenging disease. While our cohort is small and long-term survival data are awaited, the high pCR rate is a powerful surrogate marker for future success. Our experience serves as an early but crucial validation that the paradigm shift in TNBC treatment—from a prognosis of uncertainty to one of curative intent—is not only possible but is actively happening in clinics today. Future larger, multi-center studies with extended follow-up are warranted to confirm these findings and fully quantify the long-term survival benefit of this transformative approach.

Competing interests: The authors declare that they have no competing interest.

Funding: This research received no external funding.

REFERENCES

1. Bianchini G, et al. Triple-negative breast cancer: from molecular profiling to therapeutic strategies. *Nat Rev Clin Oncol*. 2016;13(11):674-690. DOI: 10.1038/nrclinonc.2016.126
2. Cortés J, et al. Pembrolizumab plus Chemotherapy for Metastatic Triple-Negative Breast Cancer. *N Engl J Med*. 2022;386(3):205-216. DOI: 10.1056/NEJMoa2112881
3. Schmid P, et al. Pembrolizumab for Early Triple-Negative Breast Cancer. *N Engl J Med*. 2022;386(5):406-416. DOI: 10.1056/NEJMoa2113476
4. Sherman RE, et al. Real-World Evidence: What It Is and What It Can Tell Us. *N Engl J Med*. 2016;375(23):2293-2297. DOI: 10.1056/NEJMp1609716

5. Cortazar P, et al. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. *Lancet*. 2014;384(9938):164-172. DOI: 10.1016/S0140-6736(13)62422-8
6. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) v5.0. Published 2017. Available from: https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm
7. Wang Y, et al. Immune-Related Adverse Events Associated with Immune Checkpoint Inhibitors in Solid Tumors: A Real-World Study. *J Immunother Cancer*. 2023;11(1):e006232. DOI: 10.1136/jitc-2022-006232