

# Clinical Outcomes and Treatment-Related Complications in Triple-Negative Breast Cancer: A Review of 24 Case Reports from 2020 to 2025

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**Abstract:** Triple-negative breast cancer (TNBC) is clinically heterogeneous, and selected patients experience rare complications, unusual responses, or biomarker-discordant treatment trajectories that are not fully represented in aggregate trial evidence. This review aims to synthesize published case-report evidence on clinical outcomes and treatment-related complications in TNBC, with an emphasis on host vulnerability, tumor biology, biomarker-guided treatment, and therapy-associated toxicity. A descriptive review of PubMed-indexed case reports was performed for records published from January 1, 2020, to December 31, 2025. Two reviewers independently screened records, extracted data, and appraised the reporting quality using the CARE domains. Results were synthesized narratively without meta-analysis. Seventy-one records were screened, and 24 case reports were included. All patients were female, with a median age of 45 years (range 28–87 years). The cases consisted of 11 with metastatic or advanced disease, 10 with early or localized disease, 1 with a local recurrence, and 2 with unclear disease settings. Actionable or resistance-informative biomarker signals were described in 12 cases, and biomarker-matched therapy was reported in 11. Immunotherapy was used in 9 cases. Serious or clinically significant complications were reported in 10 cases, including two fatal treatment-related events. Favorable outcomes were reported in 17 cases, but these selected reports cannot be used to estimate response rates, survival, or the incidence of toxicity. TNBC case reports provide clinically instructive, hypothesis-generating evidence on rare toxicities, biomarker-guided treatment decisions, and individualized risk assessment.

**Keywords:** triple-negative breast cancer, case reports, treatment-related complications, immune checkpoint inhibitors, immune-related adverse events

## Introduction

Triple-negative breast cancer (TNBC) is an aggressive breast cancer subtype defined by the absence of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 (HER2) expression.<sup>1–4</sup> Because TNBC lacks the endocrine and HER2-directed therapeutic targets used in other breast cancer subtypes, systemic treatment has historically relied on cytotoxic chemotherapy.<sup>5,6</sup> Despite therapeutic advances, TNBC remains clinically challenging because of its early relapse pattern, high metastatic potential, frequent visceral dissemination, and poorer prognosis in advanced disease.<sup>4,7,8</sup>

TNBC accounts for approximately 10–20% of breast cancer cases worldwide, although reported prevalence varies across populations and regions.<sup>9–11</sup> Higher proportions have been reported in cohorts from India, Latin America, East Africa, and Barbados, suggesting that genetic ancestry, reproductive factors, health-care access, socioeconomic



determinants, and regional diagnostic patterns may influence the observed disease burden.<sup>12–15</sup> At the genomic level, TNBC is frequently associated with alterations in DNA damage response pathways and tumor suppressor genes, particularly BRCA1/2 and TP53, which contribute to genomic instability, therapeutic vulnerability, and the evolution of resistance.<sup>16–18</sup>

Beyond its receptor-negative definition, TNBC is biologically heterogeneous rather than a single uniform disease entity. Molecular classifications include luminal androgen receptor, immunomodulatory, basal-like immunosuppressed, and mesenchymal subtypes, each with distinct pathway dependencies, immune phenotypes, and treatment sensitivities.<sup>19,20</sup> TNBC also encompasses rare histological variants, including metaplastic breast carcinoma, adenoid cystic carcinoma, apocrine carcinoma, secretory carcinoma, neuroendocrine carcinoma, and rare lobular phenotypes, whose biological behavior may not be fully predicted by receptor status alone.<sup>21,22</sup> Among these, metaplastic breast carcinoma is clinically important because it is commonly triple-negative, morphologically heterogeneous, and frequently less responsive to conventional cytotoxic chemotherapy than non-metaplastic TNBC.<sup>23–25</sup> Molecular studies have shown that metaplastic breast carcinoma is enriched for alterations involving PI3K/AKT signaling, epithelial–mesenchymal transition, stemness-associated programs, and Wnt/β-catenin pathway dysregulation, all of which may contribute to intrinsic chemoresistance and aggressive clinical behavior.<sup>23,26</sup> This molecular and histological diversity helps explain why standardized treatment approaches may produce markedly different outcomes among patients with the same triple-negative receptor profile.<sup>21</sup>

The treatment paradigm for TNBC has therefore shifted from reliance on cytotoxic chemotherapy alone to multimodal, biomarker-guided strategies. Anthracyclines, taxanes, and platinum-based regimens remain important components of neoadjuvant, adjuvant, and metastatic treatment. However, early resistance and relapse continue to limit durable disease control in a subset of patients.<sup>27–31</sup> More recent therapeutic approaches include poly(ADP-ribose) polymerase inhibitors for selected patients with BRCA1/2 alterations and immune checkpoint inhibitors for selected clinical and biomarker-defined settings.<sup>32–34</sup> Although these approaches have expanded therapeutic options, treatment response remains heterogeneous, and intensified regimens may introduce clinically significant toxicity requiring individualized risk assessment.

Large clinical trials are essential for defining population-level efficacy and common safety profiles. Still, they may not fully capture rare, high-severity complications, unusual metastatic presentations, complex comorbidity-related risks, diagnostic mimics of progression, or exceptional responses to biomarker-guided therapy.<sup>35–38</sup> Published case reports provide complementary evidence by documenting granular clinical trajectories that are often under-represented in aggregate trial data. In TNBC, such case-level evidence is particularly relevant when reports describe rare immune-related adverse events, severe treatment-limiting complications, or outcomes shaped by uncommon genetic and clinical vulnerabilities. Examples include atezolizumab-associated posterior reversible encephalopathy syndrome and fatal therapy-related myelodysplastic syndrome in a patient with Bloom syndrome.<sup>39,40</sup>

Accordingly, this review focuses on published case reports of TNBC therapy rather than estimating population-level treatment efficacy or adverse event incidence. The objective was to synthesize case-level evidence on clinical outcomes and treatment-related complications in TNBC, with emphasis on three clinically relevant domains: patient-specific vulnerabilities, tumor histology and molecular biomarkers, and therapy-associated toxicities. By analyzing 24 published case reports from 2020 to 2025, this review aims to clarify how individualized interactions among host factors, tumor heterogeneity, biomarker-guided treatment selection, and complication management may shape TNBC outcomes. The intended contribution is to identify clinically instructive patterns and hypothesis-generating signals that may support individualized risk assessment, toxicity surveillance, and multidisciplinary treatment planning.

## Materials and Methods

### Study Design

A PRISMA-informed descriptive review of PubMed-indexed case reports was conducted to synthesize published case-level evidence on clinical outcomes and treatment-related complications in TNBC.<sup>41</sup> The review was designed as a descriptive case-report synthesis rather than a comparative effectiveness review or meta-analysis. This approach was

selected because eligible reports described heterogeneous individual patients, disease stages, therapeutic regimens, biomarker profiles, follow-up durations, and adverse-event reporting formats. No pooled estimate of treatment efficacy, toxicity incidence, or comparative treatment effect was planned. Frequencies and percentages were used only to summarize patterns within the included published case reports. The protocol was not prospectively registered.

## Search Strategy and Data Sources

A formal literature search was performed in PubMed because this database provides structured biomedical indexing through Medical Subject Headings (MeSH), publication-type filters, and broad coverage of peer-reviewed clinical case reports. The final search was documented on January 31, 2026, with publication-date limits from January 1, 2020, to December 31, 2025. The PubMed search strategy was: Triple Negative Breast Neoplasms/therapy [MeSH] AND “Case Reports”[Publication Type].

The MeSH term “Triple Negative Breast Neoplasms/therapy” was selected to retrieve records indexed for therapeutic management of TNBC. At the same time, the “Case Reports” [Publication Type] restriction limited the search to individual clinical reports. Additional eligibility restrictions were applied during screening rather than as database search terms. These included English-language publication, full-text availability, confirmed TNBC phenotype, and extractable information on treatment, outcome, and treatment-related toxicity or complications. The search was intentionally focused on clinically detailed case reports rather than all TNBC therapeutic publications. No restrictions were applied by country, patient age, disease stage, metastatic status, treatment setting, or therapeutic modality. Grey literature, conference abstracts, preprints, and non-indexed reports were not included. Reference lists of eligible reports and relevant review articles were screened for additional case reports. No additional eligible records were added.

## Study Selection and Screening Process

All records identified through PubMed were screened using a standardized PRISMA 2020-informed workflow.<sup>41</sup> After duplicate removal, titles and abstracts were screened independently by two reviewers (AD and RMF). Records judged potentially eligible by either reviewer were retrieved for full-text assessment. Full-text eligibility assessment was also performed independently by the same two reviewers. Disagreements regarding study inclusion or exclusion, or data interpretability, were resolved through discussion and, when needed, arbitration by a third reviewer (EH).

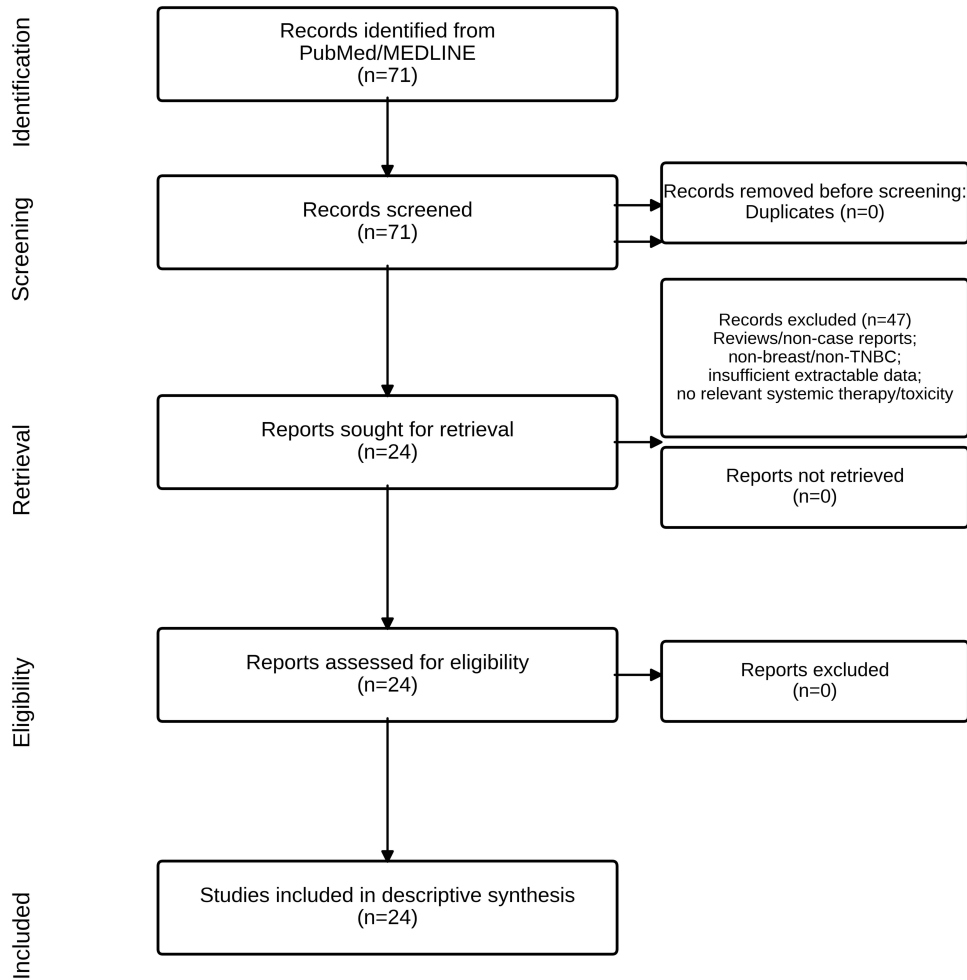
The database search identified 71 records. No duplicates were identified, and all 71 records underwent title and abstract screening. Forty-seven records were excluded during screening because they were review articles, cross-sectional or observational studies, focused on cancer types other than breast cancer or non-TNBC breast cancer, lacked extractable patient-level data, or described cancer treatment without relevant chemotherapy or systemic anticancer therapy. Twenty-four reports were retrieved and assessed for full-text eligibility. All 24 reports met the final eligibility criteria and were included in the descriptive synthesis (Figure 1).

## Eligibility Criteria

Studies were eligible for inclusion if they met all of the following criteria: peer-reviewed case report, English-language publication, publication date between 2020 and 2025, full-text availability, individual patient-level data, primary diagnosis of breast cancer with a triple-negative phenotype, and confirmation of TNBC by immunohistochemistry, defined by absence of estrogen receptor, progesterone receptor, and HER2 expression or HER2 amplification according to the criteria reported in the source article. Eligible reports were also required to describe at least one therapeutic intervention and provide extractable information on clinical outcome, treatment response, disease progression, survival status, treatment-related toxicity, or clinically relevant complications. Reports that included synchronous malignancies or complex comorbidities were retained only when TNBC-specific treatment, outcome, and complication data could be separately extracted.

## Data Extraction and Operational Definitions

Data extraction was performed independently by two reviewers (AD and RMF) using a standardized extraction form. Extracted variables included author and year of publication, patient age and sex, disease stage, TNM classification when



**Figure 1** PRISMA 2020 flow diagram of study identification, screening, eligibility assessment, and final inclusion of 24 TNBC case reports.

reported, metastatic sites, histological subtype, baseline receptor status, Ki-67 index, PD-L1 status, BRCA1/2 status, next-generation sequencing results, tumor mutational burden, homologous recombination deficiency markers, circulating tumor DNA or disseminated tumor cell findings, and other clinically relevant biomarkers. Host-related variables included comorbidities, viral carriage, hereditary cancer syndromes, pregnancy status, baseline organ dysfunction, and other patient-specific vulnerabilities that could influence treatment selection or toxicity risk.

Therapeutic data included treatment setting, treatment sequence, surgery, radiotherapy, chemotherapy, immunotherapy, targeted therapy, endocrine or androgen-directed therapy, where relevant, drug names, doses, number of cycles, duration, dose modifications, discontinuation, and subsequent treatment lines, when reported. Clinical outcome variables included complete response, partial response, stable disease, progressive disease, pathological complete response, near-pCR or major pathological response, no evidence of disease, disease-free status, recurrence, survival status, death, and duration of follow-up. Response categories were coded according to the definitions used by the original case-report authors. Treatment-related complications were extracted as reported by the original authors. They included hematologic toxicity, immune-related adverse events, hepatic toxicity, neurologic complications, infectious complications, treatment intolerance, therapy-related secondary malignancy, severe organ dysfunction, treatment discontinuation, hospitalization, and fatal adverse events. Missing or unreported variables were coded as “not reported” and were not imputed.

For descriptive synthesis, disease setting was categorized as early/localized, locally advanced, recurrent, metastatic/advanced, or unclear based on the source report. Outcomes were grouped descriptively as favorable, death/failure, or ongoing/unclear. Favorable outcomes included complete response, pathological complete response, near-pCR or major

pathological response, no evidence of disease, disease-free follow-up, or documented partial response/stable disease with clinically meaningful disease control. Death/failure included death attributed to disease progression or treatment-related toxicity, clear progressive disease, hyperprogressive disease, or absence of oncologic benefit. Ongoing/unclear outcomes were assigned when follow-up was insufficient to classify the final clinical trajectory.

## Quality Appraisal and Bias Evaluation

The reporting quality of the included case reports was appraised using the CARE guideline framework.<sup>42</sup> The appraisal focused on whether each report clearly described the case-report title and keywords, abstract or case uniqueness, patient information, diagnostic assessment, therapeutic intervention, follow-up and outcomes, adverse events, strengths or limitations, and take-away lessons.

Two reviewers independently assessed each report using a standardized CARE compliance matrix (MLNH and IR). Each domain was classified as “Yes” when the relevant information was adequately reported, “Partial” when the information was present but incomplete, and “NR” when the domain was not reported or could not be clearly identified. Disagreements were resolved through discussion, and a third reviewer adjudicated any remaining discrepancies. The CARE compliance matrix is provided as [Supplementary Table S1](#).

Because case reports are inherently susceptible to selective publication, incomplete follow-up, non-standardized outcome assessment, and limited causal attribution, the appraisal was interpreted qualitatively. Attention was given to whether treatment-related complications were explicitly described, whether adverse events were graded or clinically contextualized, and whether the authors acknowledged case-specific limitations. Reports lacking formal toxicity grading or explicit limitations were retained when they provided sufficient patient-level clinical, diagnostic, therapeutic, and outcome data for descriptive synthesis. The appraisal was used to contextualize the strength and interpretability of case-level evidence, not to generate pooled estimates of treatment efficacy or toxicity incidence.

## Data Synthesis

A descriptive narrative synthesis was performed due to substantial heterogeneity in patient characteristics, TNBC subtype, disease stage, biomarker profiles, treatment regimens, adverse event reporting, and follow-up duration. Extracted data were summarized in tables to compare baseline clinical characteristics, tumor biology, treatment sequence, response assessment, toxicity profile, and key biomarkers across the included cases. Counts and percentages were calculated only to characterize the 24 included reports. These values should not be interpreted as population-level incidence, prevalence, comparative efficacy, or real-world toxicity risk. The synthesis focused on clinically instructive patterns involving host vulnerability, tumor heterogeneity, biomarker-guided treatment selection, therapeutic response, and treatment-related complications.

## Results

A total of 24 case reports met the eligibility criteria and were included in the final descriptive synthesis ([Table 1](#)). All reported patients were female, with a median age of 45 years (mean 49.3 years; range, 28–87 years). In terms of disease setting, 11 cases (45.8%) were classified as metastatic or advanced disease, 10 cases (41.7%) as early or localized disease, one case (4.2%) as local recurrence, and two cases (8.3%) as unclear disease setting. These counts describe the composition of the included published case reports only and should not be interpreted as population-level frequencies of TNBC presentation.

The biomarker and genomic landscape were heterogeneous across the included reports. Among recurrently described findings, BRCA1/2 alterations and PD-L1 status were each reported in five cases (20.8%), followed by PIK3CA alterations and circulating tumor DNA/disseminated tumor cell-related findings in two cases each (8.3%). BRAF alteration and NTRK fusion were each reported in one case (4.2%). Overall, 12 cases (50.0%) contained an actionable or resistance-informative biomarker signal, and biomarker-matched therapy was reported in 11 cases (45.8%). Among these 11 cases, the source reports described objective response or at least transient disease stabilization in nine cases. This observation indicates that molecular or immune biomarker information frequently informed treatment selection in the

**Table I** Summary of Patient Demographics, Clinical Characteristics, Tumor Histology, and Key Baseline Biomarkers of the 24 Included Case Reports

| No. | Author (Year)                         | Stage                               | Metastatic Sites                                                   | Treatment Summary                                                                                                                                                                                                                                                                                  | Response Type    | Response Assessment   | Toxicity                                             | Key Biomarker                                             |
|-----|---------------------------------------|-------------------------------------|--------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|-----------------------|------------------------------------------------------|-----------------------------------------------------------|
| 1   | Chen et al (2025) <sup>43</sup>       | Stage IIA                           | Lung (multiple pulmonary metastases)                               | MRM+ALND; adjuvant AC→T (4 cycles AC + 2 cycles paclitaxel) → PD with lung mets; 2nd-line camrelizumab + GP ×6 → CR; sustained CR >5 months                                                                                                                                                        | CR               | Radiographic/clinical | NR                                                   | ER–; PR–; HER2 0; Ki-67 40%; PD-L1 (tumor 5%, immune 10%) |
| 2   | Al-Bitar et al (2025) <sup>44</sup>   | Localized (breast); pT3N1b (rectal) | Abdominal LNs (rectal)                                             | Planned NAC weekly paclitaxel+carboplatin + pembrolizumab q3w (stopped after 4 cycles due to HBV reactivation/transaminitis) → entecavir; right MRM+ALND; rectal resection + colostomy; adjuvant RT; disease-free at 3 years                                                                       | NED/disease-free | Clinical follow-up    | HBV reactivation with severe transaminitis           | ER–; PR–; HER2–; BRCA1 pathogenic mutation                |
| 3   | Yu et al (2024) <sup>45</sup>         | Stage IV                            | Lung; sternum; supraclavicular lymph node (later)                  | Prior surgery + multiple chemotherapies (regimens partly NR) + RT for sternal metastasis; gemcitabine +carboplatin; trial: SBRT + GM-CSF + thymosin α1 + camrelizumab → PR (abscopal effect), PFS 144 days; later vinorelbine then eribulin with cytopenias; new supraclavicular node metastasis   | PR               | Radiographic/RECIST   | Skin reaction plus myelosuppression/thrombocytopenia | ER–; PR–; HER2–; Ki-67 80%                                |
| 4   | Pellegrino et al (2024) <sup>46</sup> | Advanced / Metastatic               | Lung; mediastinal/pre-subcarinal lymph nodes                       | NAC → quadrantectomy + SLNB → RT; metastatic recurrence treated with atezolizumab + nab-paclitaxel (13 cycles) → PR; nab-paclitaxel stopped; atezolizumab maintenance → Sjögren syndrome after 4 cycles; managed with prednisone/pilocarpine/hydroxychloroquine while continuing atezolizumab → SD | PR               | Radiographic/clinical | Immune-related Sjögren syndrome                      | ER–; PGR–; HER2 0; MIB-1 70%                              |
| 5   | Bao et al (2024) <sup>47</sup>        | Local recurrence                    | Local recurrence (scar/chest wall); no distant metastasis reported | Pregnancy termination → NAC TE (epirubicin +docetaxel) ×3 → MRM → adjuvant chemo (docetaxel+pirarubicin) ×5; local recurrence treated with RT (50 Gy + boost) then paclitaxel+capecitabine ×3; follow-up: no recurrence/metastasis reported                                                        | NED/disease-free | Clinical follow-up    | No clinically significant toxicity reported          | ER–; PR–; HER2–                                           |



|    |                                   |                                |                                          |                                                                                                                                                                                                                                                                                                                                                       |                          |                       |                                                   |                                                                                                              |
|----|-----------------------------------|--------------------------------|------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|-----------------------|---------------------------------------------------|--------------------------------------------------------------------------------------------------------------|
| 6  | Wang et al (2022) <sup>48</sup>   | Stage IV (initially Stage IIA) | Lung, lymph nodes, adrenal gland, kidney | Mastectomy+ALND → adjuvant EC→docetaxel + RT + capecitabine; metastatic 1L vinorelbine+cisplatin (SD; PFS 7 mo) → 2L vemurafenib+nab-paclitaxel (mixed response; PFS 4.4 mo; grade 4 myelosuppression) → 3L bicalutamide (rapid PD); died of multiple organ failure (OS 12 mo from metastatic diagnosis)                                              | Mixed response           | Radiographic/clinical | Grade 4 myelosuppression with diarrhea/oral ulcer | ER–; PR–; HER2–; Ki-67 90%; BRAFV600E                                                                        |
| 7  | Feng et al (2021) <sup>49</sup>   | Stage IV (initially Stage III) | Liver                                    | Mastectomy+ALND → adjuvant AC-T (8 cycles); later liver mets → multi-line chemo (incl. vinorelbine +carboplatin; nab-paclitaxel+capecitabine; RFA); 3L gemcitabine+pembrolizumab → HPD after 2 cycles; 4L atezolizumab+nab-paclitaxel → PR >8 months; progressed Nov 2020                                                                             | PR                       | Radiographic/clinical | Hyperprogressive disease on pembrolizumab         | ER–; PR–; HER2– (FISH–); PD-L1: tumor 0%, immune 5% (22C3); TMB 5 muts/Mb; PIK3CA H1047R; MYCN amplification |
| 8  | Tan et al (2025) <sup>50</sup>    | Early-stage / Locally advanced | None (M0)                                | Neoadjuvant paclitaxel + pembrolizumab q3w (planned 4 cycles) → EC + pembrolizumab (planned 4); liver lesion detected after 6 cycles; cycle 7 EC only; achieved clinical CR; underwent modified radical surgery with pCR; adjuvant RT; adjuvant pembrolizumab postponed; liver lesion regressed after ICI discontinuation (sarcoidosis-like reaction) | pCR                      | Pathologic            | Hepatic sarcoidosis-like reaction                 | ER–; PR–; HER2–; Ki-67 80%; PD-L1 CPS 10%                                                                    |
| 9  | Farhat et al (2025) <sup>51</sup> | Stage III                      | Axillary lymph nodes                     | Neoadjuvant taxane/carboplatin (16 sessions) → right MRM+ALND; left subcutaneous mastectomy+SLND (benign contralateral lesion); adjuvant chemotherapy + radiotherapy; near-complete morpho-metabolic response; improved QoL; mild anemia only                                                                                                         | Near-pCR /major response | Radiographic/clinical | Mild anemia                                       | ER–; PR–; HER2–                                                                                              |
| 10 | Nahhat et al (2024) <sup>52</sup> | NR                             | Axillary lymph node                      | AC chemotherapy (doxorubicin + cyclophosphamide) ×6 → left modified radical mastectomy + ALND; pathology showed total burn-out tumor (pCR) and all 19 nodes negative; no recurrence at 1 year                                                                                                                                                         | pCR                      | Pathologic            | No clinically significant toxicity reported       | ER–; PR–; HER2–; Ki-67 <10%                                                                                  |
| 11 | Jinadasa (2024) <sup>53</sup>     | IIB                            | None (PET-CT negative)                   | NACT FEC-T + carboplatin with goserelin; mastectomy + SLNB; planned adjuvant RT; achieved pCR                                                                                                                                                                                                                                                         | pCR                      | Pathologic            | No clinically significant toxicity reported       | ER–/PR–/HER2–; Ki-67 50%; p53 aberrant; E-cadherin loss                                                      |

(Continued)

Table I (Continued).

| No. | Author (Year)                   | Stage                                     | Metastatic Sites                                           | Treatment Summary                                                                                                                                                                                                                                                                                      | Response Type            | Response Assessment         | Toxicity                                                           | Key Biomarker                                                                                                  |
|-----|---------------------------------|-------------------------------------------|------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|-----------------------------|--------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|
| 12  | Gürbüz (2024) <sup>40</sup>     | NR (early-stage)                          | None reported (PET-CT negative)                            | Adjuvant AC (doxorubicin/cyclophosphamide) ×4 → weekly paclitaxel ×12; IMRT 50 Gy (± boost); developed MDS-EB2 and died of sepsis                                                                                                                                                                      | NED/ oncologic control   | Clinical follow-up          | Therapy-related MDS-EB2 with pancytopenia/ sepsis                  | ER-/PR-/HER2-; Ki-67 60%; CA15-3 elevated                                                                      |
| 13  | Ge (2024) <sup>54</sup>         | NR                                        | None reported                                              | Breast-conserving surgery + SLNB; adjuvant epirubicin/cyclophosphamide ×8; radiotherapy; alive without recurrence                                                                                                                                                                                      | NED/disease-free         | Clinical follow-up          | No clinically significant toxicity reported                        | ER-/PR-/HER2-; Ki-67 95% (high-grade component)                                                                |
| 14  | Martorana (2023) <sup>55</sup>  | Initially Stage I (T1c N0)                | None reported (CT negative at 2021 recurrence)             | 2015 mastectomy + SLNB; 2016 local recurrence excision + chest wall RT; 2021 cutaneous recurrence treated with palbociclib+letrozole → oral vinorelbine (poor response) → everolimus+exemestane (temporary stabilization); NGS showed actionable mutations                                             | SD                       | Radiographic/ clinical      | Hematologic toxicity on vinorelbine                                | Initial: ER-/PgR-; AR 70%; HER2 1+; Ki-67 <1%. Recurrence (2021): ER 70%; PgR-; AR 70%; HER2 1+; Ki-67 10%     |
| 15  | Jacover (2023) <sup>56</sup>    | Locally advanced progressed to metastatic | NR                                                         | Multiple standard lines with rapid progression (incl. chemotherapy, pembrolizumab, olaparib, sacituzumab govitecan, RT); lymphodepleting cyclophosphamide +fludarabine → TIL adoptive cell therapy + IL-2; transient clinical benefit; death attributed to IL-2 toxicity                               | Symptomatic benefit only | Symptomatic/ clinical       | Cytokine release storm with shock/ myocarditis/renal failure       | BRCA1 germline pathogenic variant; tumor: loss of BRCA1 heterozygosity; TP53 mutations; MYC amplification      |
| 16  | Del Giglio et al (2023)         | Metastatic (lung); Localized (breast)     | Sentinel lymph node (micro-metastasis, 3 mm); otherwise NR | Olaparib for lung cancer (~30 months disease control) → new TNBC detected on PET/CT; quadrantectomy + sentinel lymph node biopsy; adjuvant breast radiotherapy; olaparib continued                                                                                                                     | Not evaluable/ unclear   | Not evaluable               | Severe fatigue                                                     | TNBC; BRCA2 frameshift + BRCA2 reversion mutation                                                              |
| 17  | Wang et al (2022) <sup>57</sup> | Stage IIA/IA progressed to Stage IV       | Lung; brain (left frontal lobe; right cerebellum)          | Surgery (breast-conserving + ALND) + RT + adjuvant cyclophosphamide/docetaxel (2011); contralateral surgery + adjuvant paclitaxel liposomes+carboplatin (2014); lung metastasectomy (2017) and brain surgery + RT; olaparib 300 mg BID from Sep 2017 with long-term disease-free survival (>40 months) | NED/disease-free         | Clinical/ imaging follow-up | Low-grade nausea/anemia; prior grade 3 neutropenia on chemotherapy | TNBC; HRD score 67; germline BRCA1 exon 2 deletion; somatic BRCA2-STAR13 rearrangement; RAD51 copy number loss |



|    |                                      |                               |                                                          |                                                                                                                                                                                                                                                                                                                                     |                          |                        |                                                          |                                                                                                        |
|----|--------------------------------------|-------------------------------|----------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|------------------------|----------------------------------------------------------|--------------------------------------------------------------------------------------------------------|
| 18 | Singh et al (2022) <sup>58</sup>     | Stage IV (Initially Stage IA) | Lung; pleura; hilar/ mediastinal/ retrocaval lymph nodes | Right mastectomy + SLNB for early disease; chest wall recurrence treated with docetaxel/ cyclophosphamide ×4 + chest wall RT; later pulmonary metastases monitored with alternative therapy; progression prompted repeat biopsy and NGS showing ETV6-NTRK3 → larotrectinib with partial response (>70% tumor reduction at 3 months) | PR                       | Radiographic           | No clinically significant toxicity reported              | ETV6-NTRK3 fusion (tissue); PD-L1 negative; ER low (1–10%); PR 0%; HER2–; low TMB                      |
| 19 | Saranti et al (2022) <sup>59</sup>   | Metastatic                    | Right ureter (intraluminal mass)                         | Primary: partial mastectomy (no SLNB) → adjuvant CMF ×6 + breast RT 45 Gy; Metastasis: ureteral stenting/biopsy → external beam RT to ureter 37.5 Gy/15 fractions with complete clinical remission at 12 months                                                                                                                     | CR                       | Clinical/ radiographic | Obstructive uropathy/ hematuria from ureteral metastasis | ER–; PR–; HER2–; Ki-67 20%; metastatic cells SOX10+, CK7 +, GATA3+                                     |
| 20 | Nel et al (2022) <sup>60</sup>       | Early-stage (cT1c cN0 cM0)    | None reported                                            | NACT EC ×4 (dose reduced) → weekly paclitaxel/ carboplatin planned ×12 but stopped after 5 cycles (intolerance) → lumpectomy + lymph node dissection with pCR → adjuvant radiotherapy 50.05 Gy; adjuvant clodronate 1040 mg/day for 2 years due to DTC positivity                                                                   | pCR                      | Pathologic             | Treatment intolerance/GI symptoms                        | ER–; PR–; HER2–; Ki-67 60%; DTC positive (85/4 million cells); ctDNA variants (CHEK2, PTEN, NF1, etc). |
| 21 | Kharel et al (2022) <sup>61</sup>    | Stage IIIC                    | None (M0)                                                | Neoadjuvant pembrolizumab + paclitaxel + carboplatin (KEYNOTE-522–based) → pembrolizumab + doxorubicin/cyclophosphamide ×4 → mastectomy + ALND → maintenance pembrolizumab; no recurrence at 9 months                                                                                                                               | pCR                      | Pathologic/ clinical   | Alopecia and grade I fatigue                             | ER–; PR–; HER2–; Ki-67 ~50%; PD-L1 CPS 20–30%                                                          |
| 22 | Kawaguchi et al (2022) <sup>62</sup> | NR (IBC; non-metastatic)      | None (no distant metastasis)                             | Prior: partial mastectomy + SLNB for pT1aN0 TNBC + RT; later bilateral IBC: neoadjuvant dose-dense epirubicin/cyclophosphamide ×4 → weekly paclitaxel ×12 → bilateral total mastectomy + ALND → RT to right chest wall; alive without recurrence at 1 year                                                                          | Near-pCR /major response | Pathologic/ clinical   | No clinically significant toxicity reported              | ER–; PR–; HER2–                                                                                        |

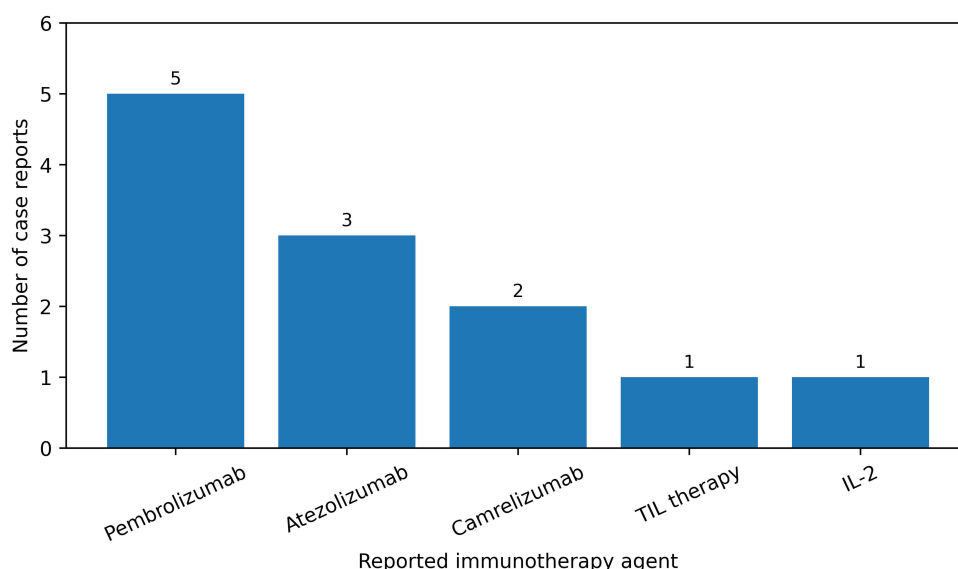
(Continued)

**Table I** (Continued).

| No. | Author (Year)                      | Stage                                          | Metastatic Sites                                 | Treatment Summary                                                                                                                                                                                                                                                                                                                                                                            | Response Type           | Response Assessment   | Toxicity                        | Key Biomarker                                |
|-----|------------------------------------|------------------------------------------------|--------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|-----------------------|---------------------------------|----------------------------------------------|
| 23  | Foulser et al (2022) <sup>39</sup> | Metastatic                                     | Bone; lymph nodes; cerebellum (brain metastasis) | Trial regimen ipatasertib (AKT inhibitor) + paclitaxel + atezolizumab for 4 months (paclitaxel stopped early due to neuropathy) → progression → capecitabine (PD at 9 weeks) → planned weekly carboplatin; developed severe hypertension with acute encephalopathy/visual symptoms and MRI-confirmed PRES; resolved with antihypertensive therapy; patient later died (per ethics statement) | PD/no oncologic benefit | Clinical/radiographic | PRES with severe hypertension   | Triple-negative receptors (ER –/PR –/HER2 –) |
| 24  | Bellon et al (2020) <sup>63</sup>  | Clinical Stage IIB; Pathological Stage ypT1bN1 |                                                  | Neoadjuvant ddAC → paclitaxel (ddACT) → bilateral mastectomy + SLNB with clipped node (residual disease) → completion ALND → adjuvant RT (chest wall + regional nodes) → adjuvant capecitabine                                                                                                                                                                                               | PR                      | Clinical/pathologic   | Chemotherapy-induced amenorrhea | ER –; PR –; HER2 – (FISH –)                  |

**Note:** The arrow symbol (→) indicates sequential treatment or clinical course transition.

**Abbreviations:** AC, doxorubicin/cyclophosphamide; ALND, axillary lymph node dissection; BID, twice daily; CR, complete response; ctDNA, circulating tumor DNA; DTC, disseminated tumor cell; EC, epirubicin/cyclophosphamide; GM-CSF, granulocyte-macrophage colony-stimulating factor; GP, gemcitabine/cisplatin; HBV, hepatitis B virus; HER2, human epidermal growth factor receptor 2; HPD, hyperprogressive disease; HRD, homologous recombination deficiency; IBC, inflammatory breast cancer; ICI, immune checkpoint inhibitor; IL-2, interleukin-2; IMRT, intensity-modulated radiotherapy; LN, lymph node; MDS-EB2, myelodysplastic syndrome with excess blasts 2; MRM, modified radical mastectomy; NAC/NACT, neoadjuvant chemotherapy; NED, no evidence of disease; NGS, next-generation sequencing; NR, not reported; pCR, pathological complete response; PD, progressive disease; PFS, progression-free survival; PR, partial response; PRES, posterior reversible encephalopathy syndrome; QoL, quality of life; RECIST, Response Evaluation Criteria in Solid Tumors; RFA, radiofrequency ablation; RT, radiotherapy; SBRT, stereotactic body radiotherapy; SD, stable disease; SLNB, sentinel lymph node biopsy; TIL, tumor-infiltrating lymphocyte; TMB, tumor mutational burden; TNBC, triple-negative breast cancer.



**Figure 2** Reported immunotherapy agents across the included TNBC case reports. Counts represent exposure frequencies within the reviewed case.

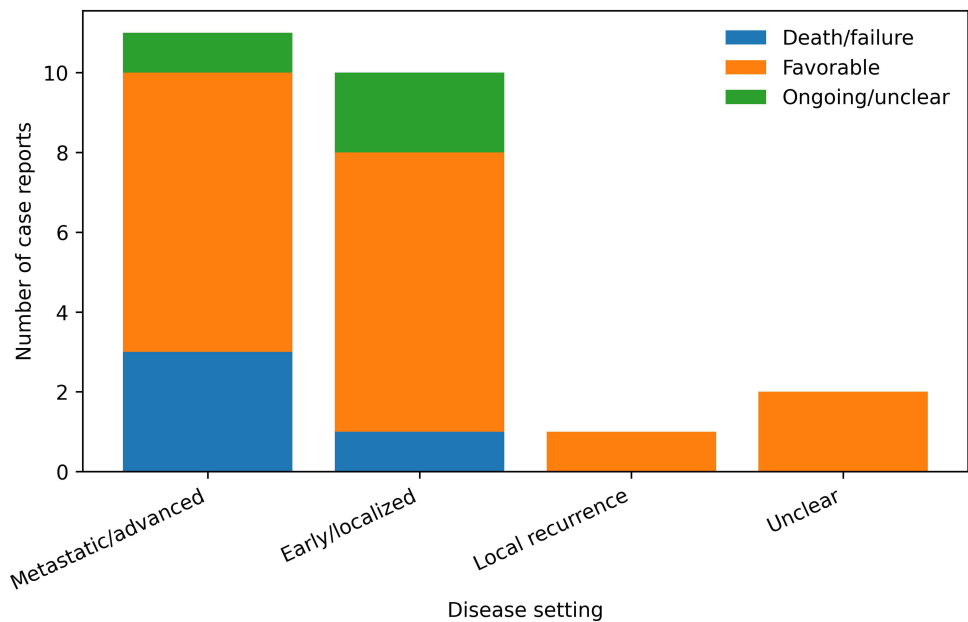
published cases. However, because these were selected case reports without control groups or standardized follow-up, these findings cannot establish predictive accuracy, treatment efficacy, or comparative benefit.

Treatment approaches were multimodal and commonly combined systemic chemotherapy with surgery, radiotherapy, immunotherapy, targeted therapy, or biomarker-guided treatment adaptation. Immunotherapy was reported in nine of 24 cases (37.5%). Pembrolizumab was the most frequently reported immune checkpoint inhibitor, appearing in five cases, followed by atezolizumab in three cases and camrelizumab in two cases. Tumor-infiltrating lymphocyte therapy and interleukin-2 were reported once in a highly refractory setting (Figure 2). These frequencies represent treatment exposures among the included published cases and do not indicate real-world utilization rates or comparative effectiveness.

Clinical outcomes varied across the included reports. Within this selected case-report dataset, 17 cases (70.8%) were categorized as favorable outcomes, four cases (16.7%) as death/failure, and three cases (12.5%) as ongoing or unclear outcomes (Figure 3). Favorable outcomes included complete response, pathological complete response, near-complete or major pathological response, no evidence of disease, disease-free follow-up, partial response, or stable disease with clinically meaningful disease control, as defined by the original case-report authors. Complete or near-complete disease eradication, including complete response, pathological complete response, no evidence of disease/disease-free status, or near-pCR/major response, was described in 14 cases (58.3%).

Treatment-related toxicity and clinically significant complications were central findings in the included reports. Serious toxicity or clinically significant complications were documented in 10 cases (41.7%), including two fatal treatment-related events (8.3%). Reported complications included hepatitis B virus reactivation with severe transaminitis, immune-related Sjogren syndrome, hepatic sarcoidosis-like reaction mimicking metastatic disease, posterior reversible encephalopathy syndrome, hyperprogressive disease after immune checkpoint inhibition, grade 4 myelosuppression, treatment intolerance, therapy-related myelodysplastic syndrome, and fatal inflammatory toxicity after adoptive cell therapy with interleukin-2. Because adverse-event grading and follow-up duration were inconsistently reported, these counts should not be interpreted as toxicity incidence. Instead, they identify clinically instructive patterns of complications that may inform individualized toxicity surveillance and multidisciplinary risk assessment.

Table 2 integrates these descriptive findings by summarizing the case-level factors that appeared to shape reported clinical outcomes and treatment-related complications across the included reports. The most clinically instructive patterns were not attributable to a single therapeutic modality, but reflected the interaction between patient-specific vulnerability, tumor histology, molecular biomarkers, treatment selection, and toxicity recognition. Patient-specific factors included germline DNA repair alterations, rare inherited vulnerabilities, viral carriage, and pregnancy-associated TNBC. Tumor-



**Figure 3** Outcome categories by disease setting among the included TNBC case reports.

level factors included rare histological subtypes, actionable or resistance-informative molecular alterations, receptor conversion, and biomarker-defined therapeutic opportunities. Treatment-related patterns included both favorable responses and clinically significant complications after immune checkpoint inhibitor-containing regimens, severe toxicity after intensive or experimental therapy, and diagnostic uncertainty caused by immune-related mimics of disease progression. Disease-monitoring findings, including ctDNA and DTC discordance with pathological response, further

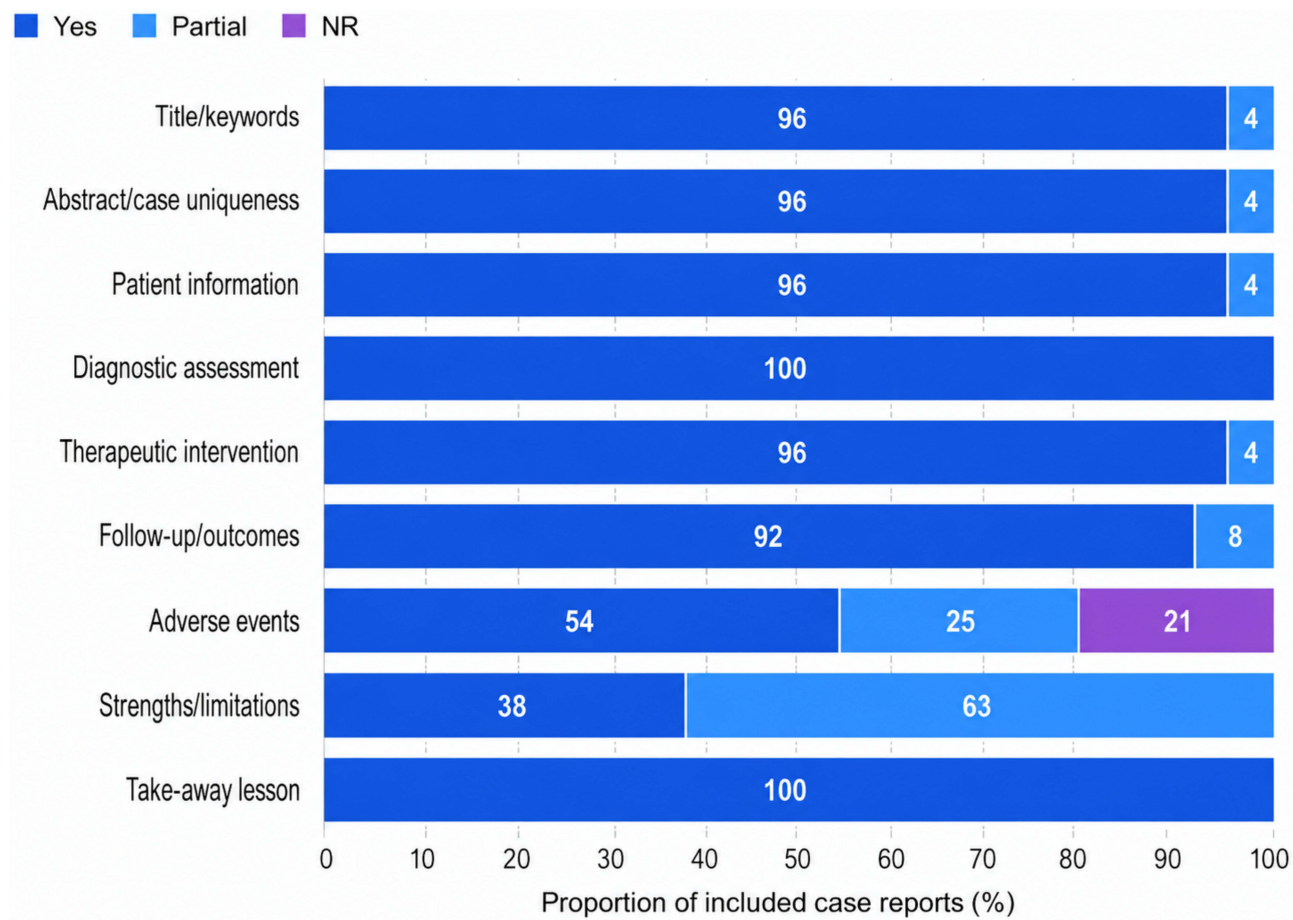
**Table 2** Case-Level Factors Associated with Reported Clinical Outcomes and Treatment-Related Complications in TNBC Case Reports

| Factor Category          | Specific Variable or Factor                                     | Case-Level Observation                                                                                                                                                                                                                                         | Representative Examples                                                                                        |
|--------------------------|-----------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|
| Patient-specific factors | Germline DNA-repair alterations, including BRCA1/2              | BRCA1/2 alterations informed platinum-based chemotherapy or PARP inhibition in selected reports. Favorable responses were described in some cases, but the case-report design does not establish predictive performance or treatment efficacy.                 | X. Wang et al (2022); <sup>57</sup> del Giglio et al (2023); <sup>64</sup> Jinadasa et al (2024) <sup>53</sup> |
| Patient-specific factors | Rare inherited vulnerability or clinically relevant comorbidity | Underlying host vulnerability modified treatment risk. Bloom syndrome was associated with fatal therapy-related myelodysplastic syndrome after DNA-damaging therapy, while hepatitis B virus carriage complicated systemic therapy through viral reactivation. | Gurbuz et al (2024); <sup>40</sup> Al-Bitar et al (2025) <sup>44</sup>                                         |
| Patient-specific factors | Pregnancy-associated TNBC                                       | Pregnancy created additional constraints around treatment timing, fetal risk, and systemic therapy sequencing, emphasizing individualized multidisciplinary decision-making rather than a generalizable treatment rule.                                        | Bao et al (2024) <sup>47</sup>                                                                                 |

(Continued)

Table 2 (Continued).

| Factor Category               | Specific Variable or Factor                                | Case-Level Observation                                                                                                                                                                                                                                                 | Representative Examples                                                                                                                                                                                                                        |
|-------------------------------|------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Tumor histology and biology   | Rare histological subtypes                                 | Rare TNBC-associated histologies showed heterogeneous diagnostic and therapeutic trajectories. Some reports described favorable responses after multimodal therapy, whereas others emphasized diagnostic complexity or molecular reclassification.                     | Chen et al (2025); <sup>43</sup> Farhat et al (2025); <sup>51</sup> Nahhat et al (2024); <sup>52</sup> Kharel et al (2022); <sup>61</sup> Ge et al (2024); <sup>54</sup> Jinadasa et al (2024); <sup>53</sup> Singh et al (2022) <sup>58</sup> |
| Tumor histology and biology   | Actionable or resistance-informative molecular alterations | NGS or other biomarker testing identified ETV6-NTRK3 fusion, BRAF V600E, homologous recombination deficiency, or BRCA2 reversion mutation. These findings influenced treatment selection or resistance interpretation, but clinical benefit varied across cases.       | Singh et al (2022); <sup>58</sup> L. Wang et al (2022); <sup>48</sup> X. Wang et al (2022); <sup>57</sup> del Giglio et al (2023) <sup>64</sup>                                                                                                |
| Tumor histology and biology   | Phenotypic plasticity and receptor conversion              | Serial biopsy and repeat biomarker testing altered clinical interpretation in a case with transition from LAR-positive TNBC to hormone receptor-positive recurrence and later molecularly characterized relapse.                                                       | Martorana et al (2023) <sup>55</sup>                                                                                                                                                                                                           |
| Therapeutic modalities        | Immune checkpoint inhibitor-containing therapy             | ICI-containing regimens were associated with both favorable responses and clinically significant immune-related or immune-associated complications in selected reports. These observations are descriptive and do not establish response probability or toxicity risk. | Chen et al (2025); <sup>43</sup> Kharel et al (2022); <sup>61</sup> Tan et al (2025); <sup>50</sup> Pellegrino et al (2024); <sup>46</sup> Feng et al (2021); <sup>49</sup> Foulser et al (2022) <sup>39</sup>                                 |
| Therapeutic modalities        | SBRT combined with immunomodulatory therapy                | One metastatic TNBC case described partial response with an abscopal pattern after SBRT combined with immune-based treatment. This remains a hypothesis-generating observation requiring prospective validation.                                                       | Yu et al (2024) <sup>45</sup>                                                                                                                                                                                                                  |
| Therapy-related complications | Immune-related adverse events and diagnostic mimics        | Immune-associated toxicities included Sjogren syndrome, hepatic sarcoidosis-like reaction, PRES, and hyperprogressive disease. Several events required careful differentiation from disease progression or metastasis.                                                 | Pellegrino et al (2024); <sup>46</sup> Tan et al (2025); <sup>50</sup> Foulser et al (2022); <sup>39</sup> Feng et al (2021) <sup>49</sup>                                                                                                     |
| Therapy-related complications | Toxicity from intensified or experimental therapy          | Severe toxicity was reported after intensive or experimental treatment, including fatal cytokine release syndrome, myocarditis, renal failure, and shock after adoptive TIL therapy with interleukin-2.                                                                | Jacover et al (2023) <sup>56</sup>                                                                                                                                                                                                             |
| Disease monitoring            | Liquid biopsy and residual molecular disease markers       | ctDNA and DTC findings did not always align with pathological response, suggesting that molecular residual disease assessment may provide additional information but remains difficult to interpret from single cases.                                                 | Nel et al (2022) <sup>60</sup>                                                                                                                                                                                                                 |



**Figure 4** Reporting completeness of the included triple-negative breast cancer case reports based on CARE appraisal.

emphasized that case-level TNBC outcomes may require interpretation beyond conventional response categories. These observations remain descriptive and hypothesis-generating, but they support the clinical relevance of individualized risk assessment, repeat pathological or molecular evaluation in selected cases, and multidisciplinary toxicity surveillance.

The CARE compliance assessment indicated generally adequate reporting quality across the 24 included case reports. Most reports described patient presentation, diagnostic work-up, therapeutic intervention, follow-up, and clinical outcome with sufficient clarity for descriptive synthesis. The strongest reporting domains were diagnostic assessment, treatment sequence, and case-specific clinical lessons. The least consistently reported domains were formal adverse-event grading, explicit discussion of limitations, and patient perspective (Figure 4). Reports focused on immune-related toxicity, experimental therapy, molecular resistance, or liquid-biopsy interpretation generally provided stronger discussion of clinical uncertainty and case-specific limitations.

## Discussion

The 24 TNBC case reports in this review underscore the clinical heterogeneity observed in treatment outcomes and complications. This review does not highlight the superiority of any single therapeutic strategy, but rather the significant influence of host vulnerability, tumor biology, treatment selection, and toxicity management on individual patient outcomes. These observations are consistent with the broader characterization of TNBC as an aggressive and biologically diverse subtype, marked by limited receptor-directed options, early relapse, and variable responses to systemic therapy.<sup>4,7,8</sup>

The reported cases encompassed a broad clinical spectrum, ranging from early-stage or localized disease to locally advanced, inflammatory, recurrent, and metastatic TNBC. Several cases described advanced disease with involvement of

the lung, liver, brain, mediastinal lymph nodes, bone, or rare metastatic sites such as the ureter.<sup>39,45,46,49,59</sup> Other reports emphasized complex host contexts, including pregnancy-associated TNBC, synchronous rectal adenocarcinoma, hepatitis B virus carriage, hereditary cancer susceptibility, and rare DNA-repair syndromes.<sup>40,44,47,53</sup> These findings indicate that TNBC management should not rely solely on receptor status or treatment regimen. Rather, patient-specific vulnerabilities and the broader disease context are central to determining which therapies are both feasible and safe.<sup>38</sup>

Contemporary TNBC therapy increasingly incorporates platinum chemotherapy, immune checkpoint inhibitors, PARP inhibitors, antibody-drug conjugates, and targeted approaches in selected clinical contexts.<sup>32–34</sup> Trial-level evidence remains the primary basis for treatment standards, response expectations, and safety profiles.<sup>65,66</sup> In contrast, the present review provides complementary case-level evidence. It captures rare or instructive clinical scenarios that are difficult to characterize in randomized trials, including severe toxicities, diagnostic mimics of disease progression, unusual metastatic patterns, rare histologies, and exceptional or discordant biomarker-associated responses.<sup>67–70</sup>

Several cases illustrate how baseline host factors influence therapeutic risk. Gurbuz et al (2024) reported that Bloom syndrome heightened vulnerability to DNA-damaging chemotherapy and radiotherapy, resulting in fatal therapy-related myelodysplastic syndrome and sepsis. While this case does not establish causality for all patients with DNA-repair disorders, it underscores the importance of identifying rare inherited vulnerabilities before initiating highly genotoxic treatments.<sup>40</sup> Similarly, Al-Bitar et al (2025) described TNBC management complicated by hepatitis B virus reactivation and synchronous rectal adenocarcinoma, demonstrating how viral carriage and concurrent malignancies can impact the safety and sequencing of systemic therapy.<sup>44</sup> Additionally, pregnancy-associated TNBC underscores the necessity for individualized treatment timing and multidisciplinary decision-making.<sup>47</sup> Building on earlier findings, TNBC management must account for patient-specific vulnerabilities and broader disease context rather than receptor status alone; host profiling should indeed extend beyond basic demographic factors. Real-world data on pembrolizumab illustrate that immune-related adverse events occur across heterogeneous patient backgrounds, emphasizing the need for comprehensive baseline assessment rather than relying on age or performance status alone.<sup>38</sup>

The reviewed cases confirm that TNBC comprises a heterogeneous group with distinct clinical and biological subtypes. While many patients presented with high-grade invasive ductal carcinoma, some exhibited rare or diagnostically challenging tumor types, such as metaplastic breast carcinoma, inflammatory breast cancer, acinic cell carcinoma, pleomorphic lobular carcinoma, and secretory breast carcinoma.<sup>43,51–54,58,61</sup> Given this diversity, thorough pathology review becomes essential whenever clinical presentation, morphologic features, biomarker patterns, or treatment responses deviate from expected TNBC behavior, as demonstrated by studies reporting diagnostic mimics, receptor conversion, misclassification, and discordant bilateral tumor responses.<sup>71–74</sup>

Molecular profiling influenced both interpretation and treatment selection in several cases. Next-generation sequencing or other biomarker testing identified actionable or resistance-informative alterations, including ETV6-NTRK3 fusion, BRAF V600E mutation, homologous recombination deficiency, BRCA1/2 alterations, and BRCA2 reversion mutation.<sup>48,57,58,64</sup> In certain cases, these findings guided targeted therapy or clarified mechanisms of resistance; however, clinical benefit varied among cases. Molecular actionability should not be presumed to guarantee a durable response. Martorana et al (2023) further demonstrated phenotypic plasticity, with receptor conversion under selective pressure, supporting repeat biopsy and reassessment of receptor and molecular status when disease biology appears to change.<sup>55</sup>

Immune checkpoint inhibitor-containing regimens were reported in several included cases, with outcomes ranging from complete or partial response to immune-related toxicity, hyperprogressive disease, and diagnostic uncertainty.<sup>43,46,49,50,61</sup> These cases are clinically instructive because immune checkpoint inhibitors can produce both antitumor activity and immune-mediated complications. However, this dataset cannot determine whether immune checkpoint inhibitors were independently responsible for response or toxicity because most cases involved multimodal treatment, chemotherapy combinations, radiotherapy, surgery, or sequential systemic therapy. Recent evidence in early-stage TNBC treated with pembrolizumab suggests an association between irAE development and pathological complete response, raising the possibility that selected toxicities may reflect immune activation related to treatment response.<sup>75</sup> In the present review, irAEs were observed in selected cases with variable outcomes, and the dataset was not designed to



test whether irAEs predict response. Therefore, irAEs should primarily be managed as clinically important toxicities, while their possible association with response should be considered hypothesis-generating and evaluated prospectively.

Treatment-related complications were clinically significant across the reviewed cases. Serious events included hepatitis B virus reactivation, immune-related Sjogren syndrome, hepatic sarcoidosis-like reaction, posterior reversible encephalopathy syndrome, hyperprogressive disease, grade 4 myelosuppression, treatment intolerance, fatal therapy-related myelodysplastic syndrome, and fatal toxicity following adoptive TIL therapy with interleukin-2.<sup>39,44,46,56</sup> These findings support several practical considerations for multidisciplinary TNBC care. First, host vulnerabilities should be assessed before treatment intensification. This is particularly relevant because DNA repair alterations and homologous recombination deficiency may influence both therapeutic vulnerability and toxicity risk. At the same time, immune checkpoint inhibitors may cause multisystem adverse events requiring coordinated recognition and management.<sup>76–78</sup> Second, biomarker and molecular testing may clarify treatment options in selected patients, particularly those with rare histology, refractory disease, discordant clinical behavior, or suspected actionable alterations involving PD-L1, BRCA1/2, HRD, TILs, TMB, or targetable gene fusions.<sup>78–81</sup> Third, serial biopsy or repeat molecular profiling should be considered when disease phenotype changes, when receptor status appears discordant, or when progression is inconsistent with expected tumor biology, because TNBC is characterized by genomic, transcriptomic, immune-microenvironmental, and treatment-driven heterogeneity.<sup>32,82–84</sup> However, given the limited number of reported cases and the absence of denominator populations, these considerations should not be interpreted as a validated clinical algorithm. Rather, they represent case-derived signals that support individualized risk assessment, early multidisciplinary consultation, and prospective evaluation of toxicity surveillance strategies in TNBC.

## Limitations

This review has several limitations. First, it was based on published case reports, which are intrinsically subject to publication bias, including exceptional responses, rare histologies, severe toxicities, unusual diagnostic dilemmas, or unexpected clinical trajectories compared with routine cases. Second, the reports were heterogeneous in disease stage, histology, biomarker testing, treatment regimen, follow-up duration, and documentation of adverse events. This heterogeneity precluded meta-analysis or comparative effectiveness assessment. Third, adverse-event grading was reported inconsistently, limiting cross-case comparisons of toxicity severity. Fourth, treatment attribution was often uncertain because many patients received multimodal or sequential therapy, including surgery, radiotherapy, chemotherapy, immunotherapy, targeted therapy, and supportive interventions. Finally, the search strategy was limited to PubMed-indexed sources, potentially excluding relevant reports from other databases.

## Conclusions

Published case reports on TNBC from 2020 to 2025 provide clinically instructive evidence on rare toxicities, unusual presentations, biomarker-guided treatment decisions, and individualized treatment risk. The reviewed cases support the importance of host-factor assessment, pathological and molecular reassessment in selected scenarios, careful evaluation of immune-related diagnostic mimics, and multidisciplinary toxicity management. However, these findings should be interpreted as descriptive and hypothesis-generating. They do not replace randomized or prospective evidence and cannot establish treatment efficacy, toxicity incidence, or causal risk. Future prospective studies should integrate standardized biomarker assessment, adverse-event grading, molecular residual disease monitoring, and longer follow-up to clarify which case-level signals are clinically generalizable.

## Abbreviations

AC, doxorubicin/cyclophosphamide; AciCC, acinic cell carcinoma; ALND, axillary lymph node dissection; BLIS, basal-like immunosuppressed; BRCA1/2, breast cancer gene 1/2; CMF, cyclophosphamide/methotrexate/fluorouracil; CR, complete response; CT, computed tomography; ctDNA, circulating tumor DNA; CTCAE, Common Terminology Criteria for Adverse Events; DTC, disseminated tumor cell; EC, epirubicin/cyclophosphamide; ER, estrogen receptor; FISH, fluorescence in situ hybridization; GM-CSF, granulocyte-macrophage colony-stimulating factor; HBV, hepatitis B virus; HER2, human epidermal growth factor receptor 2; HPD, hyperprogressive disease; HRD, homologous

recombination deficiency; IBC, inflammatory breast cancer; ICI, immune checkpoint inhibitor; IHC, immunohistochemistry; IL-2, interleukin-2; irAE, immune-related adverse event; LAR, luminal androgen receptor; MDS-EB2, myelodysplastic syndrome with excess blasts 2; MpBC, metaplastic breast carcinoma; MRM, modified radical mastectomy; NAC/NACT, neoadjuvant chemotherapy; NED, no evidence of disease; NGS, next-generation sequencing; NR, not reported; PARP, poly(ADP-ribose) polymerase; pCR, pathological complete response; PD, progressive disease; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PR, partial response; PRES, posterior reversible encephalopathy syndrome; RECIST, Response Evaluation Criteria in Solid Tumors; RT, radiotherapy; SBRT, stereotactic body radiotherapy; SD, stable disease; SLNB, sentinel lymph node biopsy; TIL, tumor-infiltrating lymphocyte; TMB, tumor mutational burden; TNBC, triple-negative breast cancer.

## Data Sharing Statement

All data analyzed in this review were extracted from the published case reports cited in the reference list. The extracted descriptive dataset is summarized in [Table 1](#) and [Supplementary Table S1](#).

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## Disclosure

The authors report no conflicts of interest in this work.

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