The Breast 40 (2018) 60–66

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

Outcomes of systemic therapy for advanced triple-negative breast cancer: A single centre experience

Nicolò Matteo Luca Battisti [a, *], David Okonji [a], Thubeena Manickavasagar [a], Kabir Mohammed [b], Mark Allen [a], Alistair Ring [a]

[a] Department of Medicine – Breast Unit, The Royal Marsden NHS Foundation Trust, Downs Road, Sutton, Surrey SM2 5PT, United Kingdom
[b] Research and Development Department, The Royal Marsden NHS Foundation Trust, Downs Road, Sutton, Surrey SM2 5PT, United Kingdom

ARTICLE INFO

Article history:
Received 8 January 2018
Received in revised form
17 March 2018
Accepted 16 April 2018

Keywords:
Breast cancer
Triple-negative
Advanced stage
Chemotherapy
Systemic therapy

ABSTRACT

Background: Prognosis is worse for advanced triple-negative breast cancer (aTNBC) compared to other disease subtypes. Trials describe treatment outcomes in single specified lines of therapy; but few data describe treatment outcomes across the whole treatment pathway, which is critical in determining when patients should be referred for trials and to inform discussion. We evaluated treatment outcomes for aTNBC (overall response rate [ORR], median progression-free survival [mPFS] and median overall survival [mOS]) in patients treated largely outside of clinical trials.

Methods: We retrospectively identified 268 patients diagnosed with aTNBC from 01/12/2011 to 30/11/2016 from our electronic records and recorded patients' and tumour characteristics and treatment outcomes. Chi-squared/Fishers exact test and Kaplan-Meier statistical methods were utilised.

Results: 186 patients treated with ≥1 line of systemic treatment were eligible and had median age of 55 (range 26–91). 53.8% had ECOG Performance Status 0 and 69.9% visceral involvement. 38.6% had disease-free interval (DFI)≤12 months following surgery or adjuvant chemotherapy completion and 14.0% had de-novo advanced disease. 11.4% carried a BRCA mutation. 64.5% received two lines of therapy, 37.6% three and 21.5% four.

ORR and mPFS were 43.9% and 3.7 months for first-line therapy, 40.2% and 3.5 months for second-line, 28.8% and 2.5 months for third-line and 25.0% and 2.1 months for fourth-line. In first line, DFI>12 months was associated with higher ORR and longer PFS compared DFI ≤12 months.

Conclusions: The observed response rates are consistent with literature. However, PFS is short, and early consideration of clinical trials can be justified in these patients.

Introduction

Triple-negative breast cancer (TNBC) lacks expression of the oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) [1,2]. It accounts for up to 20% of all breast cancer prevalence, with an annual incidence of 200,000 new patient diagnoses worldwide [3].

Compared to other disease subtypes, TNBC has an inherently aggressive behaviour and a poorer prognosis with higher rates of recurrence and shorter progression-free survival (PFS) and overall survival (OS) [4]. Therapeutic decisions are based on individual patient and disease characteristics and previous treatments. However, TNBC is a highly diverse group of cancers with six molecular subtypes identified based on gene expression [5]. Despite extensive ongoing research for biomarkers and new drugs, only two potential molecular targets have been identified in TNBC. First, targeting the androgen receptor with anti-androgen receptor or anti-androgen synthesis drugs has demonstrated anti-tumour efficacy in advanced disease in three prospective trials [6–8]. Second, targeting homologous recombination deficiency in patients with BRCA1 or 2 mutations with inhibitors of the enzyme poly ADP ribose polymerase (PARP) has also shown promising clinical

* Corresponding author. Department of Medicine – Breast Unit, The Royal Marsden NHS Foundation Trust, Downs Road, Sutton, Surrey SM2 5PT, United Kingdom.
E-mail addresses: nicolo.battisti@rmh.nhs.uk, nicolo.battisti@gmail.com (N.M.L. Battisti), david.okonji@rmh.nhs.uk (D. Okonji), thubeena.manickavasagar@rmh.nhs.uk (T. Manickavasagar), kabir.mohammed@rmh.nhs.uk (K. Mohammed), mark.allen@rmh.nhs.uk (M. Allen), alistair.ring@rmh.nhs.uk (A. Ring).

https://doi.org/10.1016/j.breast.2018.04.014
0960-9776/

activity in metastatic disease [9,10]. However, cytotoxic chemotherapy still remains the standard of care in the management of early- and advanced-stage disease [11]. In the metastatic disease setting, systemic treatment options aim at extending survival and palliating symptoms [12]. Response duration to chemotherapy is usually short-lived [13] and, depending on different therapeutic regimens, overall response rates (ORR) range from 10% to 35% with a median PFS of approximately 3 months [14–16].

There are a large number of clinical trials in patients with metastatic TNBC. However, the outcomes in clinical trial populations do not necessarily reflect those in day-to-day clinical practice. Furthermore, clinical trials focus on a single line of therapy (usually first line for TNBC) and do not examine outcomes across the whole treatment pathway involving subsequent lines of therapy [17–19].

Discussing prognosis and potential treatment outcomes is an essential part of shared decision-making [20,21] and helps contextualize therapeutic goals. This retrospective analysis aims to provide better insight into the efficacy of different lines of systemic therapy for advanced TNBC in terms of ORR, median PFS and median OS to better inform discussion with patients, clinical decision-making and referral for clinical trials.

Materials and methods

We retrospectively identified and reviewed the medical records of 268 patients diagnosed with advanced TNBC and treated with any line of systemic therapy from 01/12/2011 to 30/11/2016 at The Royal Marsden NHS Foundation Trust. These time limits were chosen to ensure adequate data quality and potential follow-up. Patients' and tumour characteristics (including age, performance status, BRCA mutational status, stage and grade at diagnosis, sites of metastatic involvement, early and advanced stage treatment history, and enrolment within clinical trials) were extracted from our electronic medical records, along with systemic treatment outcomes.

TNBC was defined as ER-negative (Allred score ≤ 2), PR-negative (Allred score ≤ 2) and HER2-not amplified (score ≤ 1 on

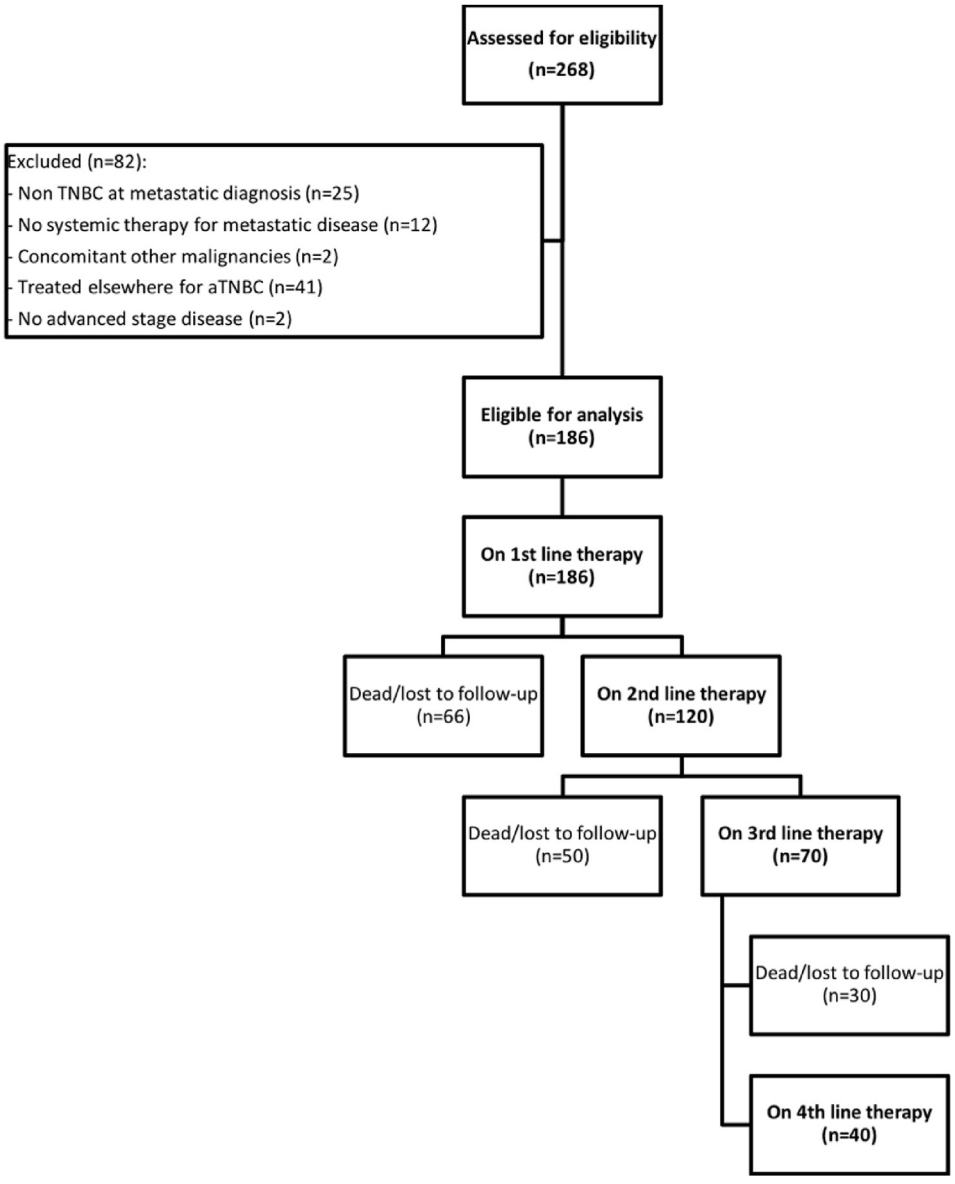

Fig. 1. CONSORT diagram.