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Clinical Trial

Health-related quality of life in patients with locally recurrent or metastatic breast cancer treated with etirinotecan pegol versus treatment of physician's choice: Results from the randomised phase III BEACON trial

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Quality of life

Abstract ***Background:*** Health-related quality of life (HRQoL) enhances understanding of treatment effects that impact clinical decision-making. Although the primary end-point was not achieved, the BEACON (BrEAst Cancer Outcomes with NKTR-102) trial established etirinotecan pegol, a long-acting topoisomerase-1 (TOP1) inhibitor, as a promising therapeutic for patients with advanced/metastatic breast cancer (MBC) achieving clinically meaningful benefits in median overall survival (OS) for patients with stable brain metastases, with liver metastases or $\geq$ 2 sites of metastatic disease compared to treatment of physician's choice (TPC). Reported herein are the findings from the preplanned secondary end-point of HRQoL.
Patients and methods: HRQoL, assessed by European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core 30 (QLQ-C30) (version 3.0) supplemented by the breast cancer-specific Quality of Life Questionnaire (QLQ-BR23), was evaluated post randomisation in 733 of 852 patients with either anthracycline-, taxane- and capecitabine-pretreated locally recurrent or MBC randomised to etirinotecan pegol (n = 378; 145 mg/m^2 every 3 weeks (q3wk)) or single-agent TPC (n = 355). Patients completed assessments at screening, every 8 weeks (q8wk) during treatment, and end-of-treatment. Changes from baseline were analysed, and the proportions of patients achieving differences ($\geq$5 points) in HRQoL scores were compared.
Results: Differences were seen favouring etirinotecan pegol up to 32 weeks for global health status (GHS) and physical functioning scales ($P < 0.02$); numerical improvement was reported in other functional scales. The findings from HRQoL symptom scales were consistent with adverse event profiles; etirinotecan pegol was associated with worsening gastrointestinal symptoms whereas TPC was associated with worsened dyspnoea and other systemic side-effects. Analysis of GHS and physical functioning at disease progression showed a decline in HRQoL in both treatment arms, with a mean change from baseline of −9.4 and −10.8 points, respectively.
Conclusion: There was evidence of benefit associated with etirinotecan pegol compared with current standard of care agents in multiple HRQoL measurements, including global health status and physical functioning, despite worse gastrointestinal symptoms (e.g. diarrhoea). Patients in both arms had a decline in HRQoL at disease progression.
Study number: NCT01492101.

1. Introduction

While there are different treatment approaches for women with advanced/metastatic breast cancer (MBC) depending on the molecular phenotype, chemotherapy remains fundamental to the management of most patients. With advances in the treatment of MBC, more women are living longer with their disease [1–3]. Nevertheless, the treatment of MBC remains essentially palliative rather than curative, with more than 500,000 women dying annually from the disease worldwide [4–5]. The median survival of patients with MBC is approximately 24 months, but varies widely between prognostic subgroups [6–10].

The key aims in treating women with MBC are to prolong survival and maintain or improve QoL. As the focus of treatment is primarily palliative, the impact of both the disease and its treatment on patients' functional abilities has led to the incorporation of patient-reported clinical outcome (PRO) measures into clinical trials [11]. Health-related quality of life (HRQoL) incorporates domains related to physical, mental, emotional, and social functioning that go beyond the direct measures of health and focusses on the QoL consequences of health status [12]. Increasing evidence shows that overall outcomes for patients with MBC improve when therapy is not just focussed on the disease but also on minimising disease-related and treatment-related symptoms [13]. Despite PRO measures rarely being used for drug approval, the effect of an intervention on HRQoL is significant for both patients and clinicians [14–15].

The international phase III BEACON (BrEAst Cancer Outcomes with NKTR-102) trial randomly assigned patients with heavily pre-treated MBC either to etirinotecan pegol (NKTR-102), or to single agent treatment of physician's choice (TPC) comprising specific cytotoxics commonly used in this setting [16]. Etirinotecan pegol is a novel, long-acting polymer-engineered pegylated topoisomerase-1 (TOP1) inhibitor designed to provide continuous exposure to SN38, the active moiety of irinotecan, at the site of the tumour through altered pharmacokinetics and exploitation of the enhanced permeability and retention (EPR) effect [17]. Preclinical experiments and initial clinical studies have demonstrated a marked contrast in the pharmacokinetic profile of SN38 after treatment with