Background

Most individuals diagnosed with metastatic breast cancer (MBC) remain on treatment indefinitely. Many oncology drugs were developed under the maximum tolerated dose (MTD) premise that the higher the dose and toxicity, the greater the efficacy. The recommended starting dose (RSD) on package labelling is often based on the MTD. However, due to treatment-related toxicities, patients may require acute care, miss scheduled treatments, experience a degraded quality of life (QOL) and potentially face fewer treatment options. To understand the consequences of treatment-related side effects (SEs) and the strategies for alleviating them, the Patient-Centered Dosing Initiative (PCDI) conducted separate anonymous surveys of MBC patients and medical oncologists who treat individuals with MBC.

Discovery

86% of the 1,221 MBC Patient Survey respondents reported at least one bad treatment-related side effect. Of those, 20% visited the emergency room/hospital and 43% missed treatment.[1] In contrast, the 119 PCDI Medical Oncologist Survey respondents underestimated the prevalence of MBC patients' SEs (at 47%), acute care visits (15%), and missed treatments (37%).[2]

77% of patients reported being asked about SEs at every visit, whereas 100% of oncologists indicated that they inquire about SE's at each appointment. Despite this discordance, 98% of patients reported discussing SEs with their physician, and 82% obtained assistance. Of these, 66% received a reduced dose for mitigation and 83% subsequently felt better. Dose reduction ranked among the top three SE palliation strategies reported by respondents in both surveys. Notably, 59% of oncologists who initiated patients' treatment at a lower dose and 71% who prescribed dose reduction for SE mitigation indicated that patients felt better on the lower dose and that efficacy was similar to the RSD.

An overwhelming majority of oncologists (97%) and patients (92%) expressed willingness to collaboratively discuss flexible dosing options, and more than half of patients (53%) and most oncologists (85%) do not believe that a higher drug dose is always more effective than a lower dose.

Action

These PCDI study findings substantiate the importance of health care provider (HCP)-patient discussions about the optimal dose for the patient, at the start of each new treatment and thereafter, to enhance patients' QOL and ability to tolerate therapy.

To assist patients in raising discussions with their providers, the PCDI developed an informational flyer depicting SE alleviation strategies, patient attributes for consideration regarding dosage, and conversation starters. Combined, these provide a framework for collaborative decision-making.

Discussion

The PCDI's patient and oncologist survey results highlight the effectiveness of dose reduction to improve treatment tolerability and challenge the paradigm that "more is better."

This paradigm is likewise being questioned by the Federal Drug Administration's "Project Optimus,"[2] which espouses identifying dosages in early clinical trials that maximize efficacy, safety, and tolerability instead of routinely leveraging the MTD.[3]

It is essential that patients and HCPs become progressively aware of the importance of discussing flexible dosing options. To this end, the PCDI encourages leveraging its informational flyer to enhance patient understanding around this complex topic and facilitate focused HCP-patient conversations about treatment-related toxicities and patient-oriented dosing.

[1] Loeser AL, Peppercorn JM, Burkard ME, et al: Treatment-related side effects and views about dosage assessment to sustain quality of life: Results of an advocate-led survey of patients with metastatic breast cancer (MBC). JCO 39:1005–1005, 2021

[2] Loeser AL, Gao L, Bardia A, *et al.* Patient-centered dosing: oncologists' perspectives about treatment-related side effects and individualized dosing for patients with metastatic breast cancer (MBC). Breast Cancer Res Treat 196:549–563 (2022).

[3] US FDA: Project Optimus: Reforming the dose optimization and dose selection paradigm in oncology [Internet], 2022[cited 2022 Nov 27] Available from: https://www.fda.gov/about-fda/oncology-center-excellence/project-optimus