Real-world treatment patterns and outcomes of patients with HER2+ advanced breast cancer

Chapter 9

Scientific impact

Impact paragraph

Scientific impact

Retrospective and prospective observational studies use real-world data to reveal the outcomes and tolerance of treatment used in daily practices. They give insight into patients' health status, current practices, and the impact of chosen treatment. The data are usually collected from electronic health records or insurance databases with only a few inclusion and exclusion criteria. Randomized controlled trials have strict in- and exclusion criteria and are conducted in controlled settings to provide the most reliable assessment of the efficacy of new treatment. Combined with randomization, the strict in- and exclusion criteria avoid bias by reducing baseline differences between the control and treatment arms. Although randomized controlled trials are crucial in comparative assessments, the design lacks evidence on the impact on patients with comorbidities or more severe disease. In addition, they are time-limited, which restricts the evidence on long-term efficacy and tolerance. Also, the control arm does not always reflect the most preferred or used current treatment in clinical practice, making it difficult to compare to daily practice[1].

The SONABRE registry was one of the first real-world studies that provided data on the survival of metastatic breast cancer in the Netherlands, with the first results published in 2013[2]. It showed the median overall survival per receptor subtype and metastatic site and the importance of individualized therapy. The studies in this thesis, using data from the SONABRE registry, have strengthened the insights about the heterogeneity in patients diagnosed with HER2+ advanced breast cancer and the impressive improvement in progression-free and overall survival with new targeted therapies. These results have been published in several international scientific peer-reviewed journals. Additionally, the results have been presented at (inter)national conferences and meetings: GROW Science Day 2018 and 2019 (Maastricht University Medical Centre), Science Day 2018 and 2019 (Maastricht University Medical Centre), European Society of Medical Oncology (ESMO) 2019 and 2022 (Spain). The results from this thesis have also been directly presented to the physicians from all participating hospitals. During this yearly reflection meeting, we present the number of patients included in the database, disease characteristics, received treatments, and outcomes. Since this concerned their own patient population, there was much interest in treatment patterns and outcomes. The observation of a significant use of first-line endocrine therapy in HR+/HER2+ disease instead of first-line pertuzumab-based therapy as advised in the guideline recommendations fuelled the discussion on the best treatment option in which situation. We have also identified areas of improvement in daily practice, such as the slow implementation rate of new agents and low biopsy rates of metastatic sites. These findings were acknowledged, and changes have been discussed to improve daily care.

It is important to note that real-world studies also have limitations; they have a potential for introducing biases and confounding by indication, missing data, and the time burden to collect and process/interpret the data. Nevertheless, the call for more real-world studies is increasing. The ASCO and the ESMO have published a statement explaining that real-world data is a valuable source of information[3,4]. All in all, the evidence generated from randomized controlled trials and real-world studies are complementary to each other regarding efficacy, tolerance, prognosis, comparative assessment, and other research questions[5].

Societal impact

The diagnosis of cancer and its treatment significantly impacts physical and psychological health, healthcare resources, budgets, and overall quality of life[6]. One-third of patients with a new diagnosis of advanced breast cancer are under the age of fifty years and play an active role in society[2]. The data from the SONABRE registry provide insights into treatment options based on disease characteristics, adverse effects, and probable prognosis. On request by the Dutch breast cancer association (Borstkanker vereniging Nederland, BVN), the data from the SONABRE registry and the Netherlands Cancer Registry were combined to inform a factsheet including figures on the statistics and prognosis of patients with advanced breast cancer in the Netherlands. The Dutch national patient organization for breast cancer (BVN) has advised patients to use the factsheet to better understand the disease and possible outcomes[7]. The substantial burden of breast cancer on patients and society has led to more research on prevention, pathophysiology, early detection, and effective new agents[6]. The most promising development in cancer treatment is driven by precision /personalized medicine, such as immuno- and targeted therapy[8,9]. The development of these agents is time-consuming and costly, and introducing new and more tailored immuno- and targeted therapy is expected to place a heavy burden on the healthcare system. The healthcare system must be adapted to ensure that the best possible therapy and tools remain available without putting a higher financial strain on the patients. Therefore, the Ministry of Health of the Netherlands has introduced the 'integrated healthcare agreement' (IZA)[10]. The agreements list for new and expensive drug consist of:

- Improving cost-effectiveness ratio by adjusting assessment criteria.
- Negotiating price agreements with the pharmaceutical company on a European level.
- Periodically monitoring how new interventions are implemented and reassessing the efficacy and side effects.

To monitor and improve the management of new and expensive treatments, the IZA needs real-world data, such as the SONABRE registry, that can provide information on implementation, outcomes, and cost-effectiveness of new drugs to keep healthcare accessible and affordable for the future.

References

1. Chodankar D. Introduction to real-world evidence studies. Perspect Clin Res 2021;12(3):171-174.
2. Lobbezoo DJ, van Kampen RJ, Voogd AC, Dercksen MW, van den Berkmortel F, Smilde TJ, et al. Prognosis of metastatic breast cancer subtypes: the hormone receptor/HER2-positive subtype is associated with the most favorable outcome. Breast Cancer Res Treat 2013;141(3): 507-514.
3. Giordano SH, Franzoi MAB, Temin S, Anders CK, Chandarlapaty S, Crews JR, et al. Systemic Therapy for Advanced Human Epidermal Growth Factor Receptor 2–Positive Breast Cancer: ASCO Guideline Update. J Clin Oncol 2022;40(23):2612-2635.
4. Cardoso F, Senkus E, Costa A, Papadopoulos E, Aapro M, Andre F, et al. 4th ESO-ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 4)dagger. Ann Oncol 2018;29(8):1634-1657.
5. Erin Hammers Forstag BK, Amanda Wagner Gee, and Carolyn Shore. Examining the Impact of Real-World Evidence on Medical Product Development. Washington (DC): National Academies Press (US); 2019 2019 Feb 6.
6. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71(3):209-249.
7. Uitgezaaide borstkanker in Nederland. The Netherlands: Borstkanker vereniging; 2021.
8. Khalil DN, Smith EL, Brentjens RJ, Wolchok JD. The future of cancer treatment: immunomodulation, CARs and combination immunotherapy. Nat Rev Clin Oncol 2016;13(5):273-290.
9. Wang J, Xu B. Targeted therapeutic options and future perspectives for HER2-positive breast cancer. Signal Transduct Target Ther 2019;4(1):34.
10. Integraal Zorgakkoord (IZA) : Samen werken aan gezonde zorg. Nederland: Ministerie van Volksgezondheid. Welzijn en Sport; 16-09-2022.