Supportive Care – Different Agents and Strategies in the Combat against Toxicities in Anticancer Therapy

Karin Jordan Juliane Brandt

Department of Hematology, Oncology and Rheumatology, University of Heidelberg, Heidelberg, Germany

*“Supportive care makes excellent cancer care possible”
(MASCC, Multinational Association of Supportive Care in Cancer)*

Depending on the diagnosis, cancer patients will receive different types and intensities of anticancer therapy. Along with antitumor treatment, in almost all patients, prevention and alleviation of side effects and toxicities associated with anticancer therapy are of utmost importance. This is one of the primary goals of supportive care. The European Society for Medical Oncology (ESMO) recently issued a position paper, advocating for holistic patient-centered care, including supportive and palliative care, to be personalized and integrated within anticancer treatment by a multidisciplinary team, from the time of diagnosis and throughout the continuum of the disease [1].

While prevention of chemotherapy-induced nausea and vomiting (CINV) has been revolutionized over the past 25 years [2], other therapy-associated side effects such as chemotherapy-induced polyneuropathy cannot be prevented as effectively. Chemotherapy-induced peripheral neurotoxicity (CIPN) is a severe and common side effect of patients with breast cancer caused by a variety of antineoplastic agents. Approximately 30 to 40% of patients treated with agents such as taxanes, nanoparticle albumin bound (nab)-paclitaxel, carboplatin, eribulin, or platinum derivatives will develop CIPN. In view of improved breast cancer survival outcomes, the prevention

and treatment of late effects of CIPN are an unmet need in these patients. The strategies currently employed as method of choice in this context are reviewed in this issue by Jordan et al. [3].

Skin toxicities have been a long-standing problem in the treatment of breast cancer and remain a challenge for supportive care [4]. Chemotherapeutic agents such as capecitabine, taxanes, and pegylated liposomal doxorubicin may cause significant skin reactions. Furthermore, the anticipated approval of immune checkpoint inhibitors in the treatment of metastatic breast cancer will add a new layer to the complexity of treatment-associated skin toxicities. The prophylaxis and management of these skin toxicities will be reviewed in this issue by Salzmann et al. [5], focusing on xerosis and pruritus, exanthema/rash, hand-foot-syndrome, nail toxicities, alopecia, and mucositis.

In 2015, the first-in-class cyclin-dependent kinase (CDK) 4/6 inhibitor palbociclib was approved by the FDA [6]. Nowadays, CDK4/6 inhibitors have become standard of care in the treatment of hormone receptor-positive, HER2-negative metastatic breast cancer. In the pivotal trials, neutropenia has been identified as a class side effect of the CDK4/6 inhibitors. Interestingly, the rate of CTCAE grade 3 and grade 4 neutropenia was considerably high, whereas the rate of febrile neutropenia did not exceed 2%. In his article “Management of Adverse Events due to CDK 4/6 Inhibitors” [7], Ettl reviews side

effects of this important antineoplastic drug class in patients with breast cancer and suggests specific management strategies.

Febrile neutropenia is one of the most important dose-limiting toxicities and can compromise the success of chemotherapy resulting, for example, in reduced dose intensity of chemotherapy or even death due to severe sepsis. The usage of G-CSF reduces the risk of neutropenic complications in high-risk cancer patients and is therefore recommended by clinical practice guidelines (S3 Guideline for Supportive Therapy) [8]. The potential improvement of disease control and survival through minimization of dose reductions and treatment delays is of particular importance for example in patients with breast

cancer in the adjuvant setting [9]. Furthermore, anemia, including iron deficiency, also represents a frequent complication in patients with breast cancer receiving antineoplastic agents and may be associated with fatigue and reduced quality of life. All these implications are discussed by Link in his review “Hematopoietic Growth Factors in the Management of Anemia and Febrile Neutropenia” [10].

Together with anticancer therapies, medical oncology should encompass patient-centered care by providing excellent supportive care. Therefore, our role as oncologists is not only to deliver the best quality anticancer treatment, but also to consider the impact of the disease and its treatment on each patient’s life.

References

- 1 Jordan K, Aapro M, Kaasa S, Ripamonti CI, Scotté F, Strasser F, et al. European Society for Medical Oncology (ESMO) position paper on supportive and palliative care. *Ann Oncol*. 2018 Jan;29(1):36–43.
- 2 Zhang L, Lu S, Feng J, Dechaphunkul A, Chang J, Wang D, et al. A randomized phase III study evaluating the efficacy of single-dose NEPA, a fixed antiemetic combination of netupitant and palonosetron, versus an aprepitant regimen for prevention of chemotherapy-induced nausea and vomiting (CINV) in patients receiving highly emetogenic chemotherapy (HEC). *Ann Oncol*. 2018 Feb;29(2):452–8.
- 3 Jordan B, et al. Prevention and Management of Chemotherapy-Induced Polyneuropathy. *Breast Care (Basel)*. 2019;14: <https://doi.org/10.1159/000499599>.
- 4 Gandhi M, Oishi K, Zubal B, Lacouture ME. Unanticipated toxicities from anticancer therapies: survivors’ perspectives. *Support Care Cancer*. 2010 Nov;18(11):1461–8.
- 5 Salzmann M, et al. Prophylaxis and Management of Skin Toxicities. *Breast Care (Basel)*. 2019;14: <https://doi.org/10.1159/000497232>.
- 6 Finn RS, Crown JP, Lang I, Boer K, Bondarenko IM, Kulyk SO, et al. The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomised phase 2 study. *Lancet Oncol*. 2015 Jan;16(1):25–35.
- 7 Ettl J. Management of Adverse Events Due to CDK 4/6 Inhibitors. *Breast Care (Basel)*. 2019;14: <https://doi.org/10.1159/000499534>.
- 8 Jordan K, Feyer P, Höller U, Link H, Wörmann B, Jahn F. Supportive Treatments for Patients with Cancer. *Dtsch Arztebl Int*. 2017 Jul;114(27-28):481–7.
- 9 Lyman GH, Yau L, Nakov R, Krendyukov A. Overall survival and risk of second malignancies with cancer chemotherapy and G-CSF support. *Ann Oncol*. 2018 Sep;29(9):1903–10.
- 10 Link H. Hematopoietic Growth Factors in the Management of Anemia and Febrile Neutropenia. *Breast Care (Basel)*. 2019;14: <https://doi.org/10.1159/000497408>.