Meta-analyses from the Japanese Breast Cancer Society: clinical practice guidelines for breast cancer

The era of meta-analyses-based recommendations: how were the Japanese Breast Cancer Society Clinical Practice Guidelines for Systemic Treatment of Breast Cancer established?

Toshimi Takano¹

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The “Clinical Practice Guidelines for Breast Cancer” were established by the Japanese Breast Cancer Society (JBCS) in 2004, following the publication of the first edition of “Clinical Practice Guidelines for Systemic Treatment of Breast Cancer”. Evidence-based guidelines for systemic treatment, surgery, radiation therapy, “screening and diagnosis”, and “epidemiology and prevention” are periodically published since 2004. The JBCS Clinical Practice Guidelines for Systemic Treatment of Breast Cancer were updated in 2007, 2010, 2011, 2013, 2015, and 2018.

Although evidence-based data were used for all editions of these guidelines, the review processes were not necessarily standardized and could not be considered valid “systematic reviews” until the publication of the 2015 edition. The 2018 edition of “The JBCS Clinical Practice Guidelines for Systemic Treatment of Breast Cancer” [1] was significantly revised and strictly conformed to the Medical Information Network Distribution Service (MINDS) Handbook for Clinical Practice Guideline Development 2014 [2], the MINDS Manual for Guideline Development 2017 [3] and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [4]. MINDS is an information service established by the Japan Council for Quality Health Care and is financially supported by the Ministry of Health, Labor and Welfare of Japan as a assignment project. MINDS published a handbook for guideline development in 2014 [2], which is equivalent to the GRADE approach. The GRADE working group was launched in 2000 and has developed a common, sensible, and transparent

approach to grading the quality of evidence and strength of recommendations. The GRADE approach is now considered the standard in guideline development.

A “Systemic Treatment Sub-committee” consisting of 18 experts, established under the “Clinical Practice Guideline Committee” of the JBCS, was involved in publishing the 2018 edition. Dr. Hiroji Iwata served as the chairperson of the “Clinical Practice Guideline Committee” and Dr. Tatsuya Toyama as the chairperson of the “Systemic Treatment Sub-committee”. The sub-committee was subcategorized into five groups, and each group addressed approximately 10 clinical questions (CQs), background questions (BQs), or future research questions (FQs); a total of 27 CQs, 14 BQs, and 15 FQs were discussed. Where applicable, the sub-committee members performed systematic reviews and meta-analyses for the 27 CQs.

CQs are important for patients with breast cancer and their physicians because the results of meta-analyses are useful for optimal decision-making. However, among all CQs, we selected the following CQs that can be considered particularly important and requested the sub-committee members in charge of CQs to publish articles focusing on meta-analyses:

- a) CQ 11: “Is dose-dense chemotherapy recommended as adjuvant therapy for patients with breast cancer showing a high recurrence risk and adequate bone marrow function?” A meta-analysis reported by Yoshinami et al. [5] proved that dose-dense chemotherapy scored over conventional chemotherapy with regard to overall survival (OS) and disease-free survival. Based on these results, dose-dense chemotherapy is strongly recommended as adjuvant chemotherapy for patients with high recurrence risk and sufficient bone marrow function (strength of

✉ Toshimi Takano
toshimi.takano@jfc.or.jp

¹ Breast Medical Oncology Department, Cancer Institute Hospital of Japanese Foundation for Cancer Research, 3-8-31 Ariake, Koto-ku, Tokyo 135-8550, Japan

recommendation [SoR]: 1, the strength of evidence [SoE]: strong) [1].

- b) CQ 15: “Which is the preferred first-line endocrine therapy for hormone receptor-positive/human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer in postmenopausal patients?” Shimoi et al. [6] reported the results of two meta-analyses in this context; the first compared a combination of aromatase inhibitors (AI) and cyclin-dependent kinase (CDK) 4/6 inhibitors and AI monotherapy and the other compared anastrozole and fulvestrant 500 mg (details are discussed in the article). Based on these results, AI monotherapy, a combination of AI and CDK4/6 inhibitors, and fulvestrant 500 mg are all recommended in these cases (SoR: 1, SoE: strong) [1].
- c) CQ 20: “Is combination therapy with bevacizumab recommended as first- or second-line treatment for HER2-negative metastatic breast cancer?” A meta-analysis performed by Miyashita et al. [7] showed that progression-free survival was significantly longer in patients receiving combination chemotherapy concomitant with bevacizumab than in patients receiving chemotherapy alone. However, OS was not significantly different, and toxicity occurred more commonly in patients receiving combination therapy. Based on these results, combination chemotherapy concomitant with bevacizumab is weakly recommended as first- or second-line therapy for metastatic HER2-negative breast cancer (SoR: 2, SoE: moderate) (1).

Although several CQs and recommendations remain controversial, these issues can be discussed further based on evidence and meta-analyses following the availability of high-quality guidelines. Developing guidelines conforming strictly to the MINDS manual and GRADE approach is challenging and requires dedicated efforts and engagement of large numbers of personnel. However, currently,

“meta-analyses-based recommendations” are widely available, and it is necessary to continue to establish and revise evidence-based and meta-analyses-based guidelines to help patients and aid physicians in optimal treatment decision-making.

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