

Preface

3. Definition of key terms

(1) Geriatric Patients (Older Patients)

In the present guidelines, except for certain clinical questions (CQs), geriatric patients (older patients) are not defined solely by their age but by age groups. Age groups were flexibly set while evaluating evidence and determining recommendations. The rationale is that the clinical relevance of “being old” varies depending on the purpose and details of treatment. Furthermore, the methods of stratification and sub-analysis differ between studies.

(2) Geriatric Assessment and Comprehensive Geriatric Assessment

Comprehensive geriatric assessment (CGA) has been adopted in the field of geriatric medicine, including interventions for identified issues. However, intervention is generally not anticipated in clinical oncology, although this area of study incorporates the concept of CGA and geriatric assessment (GA) is adopted in clinical oncology instead. Therefore, the present guidelines have adopted GA.

Introduction

(I) Organization and policy

2. Process of Guideline Creation

2.1. Orientation in Guideline Creation

The clinical backgrounds of geriatric patients vary, and the proportion of such patients in clinical studies is scarce. Therefore, evidence from clinical studies cannot be directly applied to geriatric patients in many real-world cases. Thus, it can be difficult to provide standard cancer treatment to geriatric patients. As the aging population grows in Japan, there has been increasing demand from physicians and other health professionals for practical guidelines for diagnosis and treatment. Given this background, we have created guidelines in accordance with Minds 2014. The guidelines are designed to provide detailed guidance for developing treatment plans based on multifaceted factors, such as evidence from clinical studies, the benefit-harm balance, and values unique to older patients. Clinical questions (CQs) in the guidelines reflect real-world situations in which health professionals encounter difficulties in making decisions and in which clinical outcomes can be improved. Recommendations for each CQs have been determined by the panel consisting of members who are in various decision-making positions.

Throughout the entire process of creating the present guidelines, unbiasedness and transparency were ensured.

2.2. Cautions When Using the Guidelines

Expected users of the present guidelines are physicians, pharmacists, and nurses who engage in cancer treatments for geriatric patients with cancer in Japan as well as for the patients themselves and their families.

2.3. Conflicts of Interest

Conflicts of interest have been voluntarily declared as per the guidelines for managing conflicts of interest and the managing rules of the Japanese Society of Medical Oncology. The voluntary declaration of conflicts of interest has been assessed by the committee for conflicts of interest of the Japanese Society of Medical Oncology. All members and associate members of the committee have confirmed that the present guidelines satisfy the requirements of the committee.

2.4. Funding for Creating the Guidelines

Funding was provided by the Japan Society of Clinical Oncology and the Japanese Society of Medical Oncology.

2.5. Organizational Structure

The creation of the present guidelines involved the guideline creation committee, an independent systematic review team, an associate committee consisting of nurses and pharmacists, and advisors from Minds.

2.6. Process of Guideline Creation

The guideline creation group was formed in April 2016, the initial meeting was held in July 2016, and systematic review committee members and associate committee members were selected in August 2016. The initial scope was determined by the guideline creation group, and comments from the associate committee members were reflected in it in November 2016. The scope was finalized in March 2017. A literature search was conducted, and a systematic review was commenced in May 2017. The systematic review was completed in December 2017. The recommendation panel meeting was held in January 2018. A mutual peer review of draft guidelines was conducted by the guideline creation committee members in May 2018, and the draft was completed in December 2018. External evaluation and public comments (from December 15, 2018 to December 28, 2018) were reflected in the draft. Subsequently, the guidelines were finalized in February 2019 and made public in July of the same year.

(II) Scope

1. Basic Characteristics of Cancer Pharmacotherapy for Geriatric Patients

1.1. Clinical Characteristics

In Japan, early-stage seniors are defined as those aged 65–74 years, and advanced-stage seniors are those aged 75 years or older. However, a patient's general condition is evaluated before a treatment plan is proposed in clinical settings, and the patient's age is considered as reference information. The cancer incidence rate among the older population is high, and certain types of cancer are more likely to develop in them. There are also issues specific to geriatric patients; for example, the proportion of patients who experience organ dysfunction and comorbidity is high among older individuals, they are susceptible to drug-induced adverse events as they use multiple drugs, and drug-induced adverse events can cause functional disorders, such as reduced physical function, in geriatric patients even if such adverse events are considered mild.

Additionally, older patients are often excluded from clinical studies even if there is no age limit in the eligibility criteria because of the issues mentioned above. In other words, the backgrounds of geriatric participants in a clinical study may be significantly different from those of many geriatric patients in actual clinical settings. Thus, it is extremely important to evaluate the general condition of a geriatric patient in actual clinical settings.

The measurement of physical functions (activities of daily living and instrumental activities of daily living), cognitive function, social factors, family environment, and other related factors in accordance with certain established evaluation techniques as well as disease evaluation techniques are referred to as geriatric assessment (GA). GA has been widely accepted as an established, basic approach to the consultation and treatment of general older patients in the field of geriatric medicine. Meanwhile, it is ideal to incorporate oncological concepts in the concepts of geriatric medicine and apply such a combination to the treatment of geriatric patients with cancer because factors specific to oncology can be observed in such a patient, including the sudden deterioration of general condition and the prolonged impact of surgery.

1.2. Epidemiological Characteristics

According to the 2016 version of the Annual Report on the Aging Society, the population of those aged 65 years or older in Japan has reached 33.92 million, which is the highest level ever. This population accounts for 26.7% of the total national population.

Moreover, the proportion of those aged 75 years or older relative to the national population is 12.9%. This indicates that Japan has a rapidly aging population. According to the Cancer Information Services of the National Cancer Center, the number of deaths from cancer in FY 2014 was approximately 370,000. Of these, 83.7% were aged 65 years or older, and 58.2% were aged 75 years or older. Cancer accounts for 40% of the total causes of death among older individuals.

1.3. Overall Process of Consultation and Treatment

In general, the eligibility criteria of most clinical studies include age, performance status (PS), and organ function. These factors are also considered while determining an appropriate treatment in actual clinical settings. However, geriatric patients have diverse backgrounds that differ from those of non-geriatric patients. Characteristics observed among geriatric patients include decreased organ and physical function due to physiological change, the presence of multiple diseases, the administration of multiple drugs, and reduced social function. In treating a geriatric patient, it is necessary to first identify risks associated with such characteristics and second propose a potentially optimal treatment method, including standard therapy, dose-reduction therapy, and symptomatic therapy.

The International Society of Geriatric Oncology (SIOG) recommends conducting GA for geriatric patients with cancer as they have diverse backgrounds. Items to be evaluated include physical function, cognitive function, psychological function, multiple diseases (multiple medications), nutrition, social circumstances, and geriatric syndrome. It has been reported that evaluating these items helps identify issues that have been overlooked through normal consultation as well as predict adverse events and prognoses.

The National Comprehensive Cancer Network Older Adult Oncology Guidelines (2016) delineates an approach for determining the treatment for geriatric patients while considering such diversity. It is important to propose a treatment appropriate for each patient by evaluating their life expectancy, decision-making capacity, treatment goals, values, and risks. It has been recognized that a multidisciplinary medical team consisting of professionals from various fields, including the geriatric field, plays an important role in such a process. However, such an approach is yet to be widely adopted in Japan.

Going forward, it is necessary to build a medical system in Japan that helps to provide potentially optimal support to patients with diverse backgrounds (including those with reduced cognitive function and reduced decision-making capacity) in making decisions.

Optimal healthcare for a patient can be achieved by respecting the patient's decisions, understanding their choices for treatment, and continuously providing them with support through consultations at various levels in which optimal healthcare can be discussed. It is imperative to broadly understand not only oncological concepts but also geriatric concepts in building a collaborative system.

2. Contents Covered in the Guidelines

2.1. Title

Chemotherapy and other drug therapies for older patients with cancer: JSMO-JSCO clinical practice guidelines

2.2. Purpose

To prolong life expectancy, alleviate side effects, and maintain quality of life

2.3. Topic

Chemotherapy and other drug therapies for older patients with cancer

2.4. Expected Users and Facilities

Physicians, pharmacists, and nurses in facilities where cancer treatment is provided as well as patients and their families

2.5. The Scope of the Guidelines

The guidelines are designed for geriatric patients who receive cancer pharmacotherapy. Except for certain CQs, geriatric patients are not defined by age but by age group. Age groups were set during evaluating evidence and determining recommendations such that the groups flexibly included patients of certain ages. Additionally, patients covered by the present guidelines are those who satisfy the basic criteria for drug therapy, have PS 0 or PS 1, have not been diagnosed with a cognitive disorder, and have no functional abnormalities in a main organ. Furthermore, prophylactic cranial irradiation (PCI) for small-cell lung cancer was selected as a clinically important CQ that is deeply related to drug therapy (CQ 7).

Diseases within the scope of the present guidelines are limited to primary malignant tumors of the main organs: respiratory organs, gastrointestinal organs, mammary glands, and hematopoietic organs. The guidelines are particularly focused on cancer pharmacotherapy in areas in which a large number of patients with cancer are treated in ordinary clinics, considering the experiences and skills of the members of the guideline creation team as well as the time and cost for creating the guidelines.

2.7. Relationship with Existing Guidelines

In Japan, there are no consultation/treatment guidelines that have been created from a cross-sectional perspective covering cancer pharmacotherapy for various organs of geriatric patients. Comprehensive guidelines for cancer pharmacotherapy for geriatric patients are available overseas. However, they differ from the present guidelines in that the present guidelines provide recommendations that have been determined by a recommendation panel consisting of those in various decision-making positions. The present guidelines are also based on multifaceted evaluation, including the body of evidence, the benefit-harm balance, and the patient's values.

Certain existing guidelines for specific organs describe cancer pharmacotherapy for geriatric patients. It is inevitable that there are duplications and discrepancies between the present and existing guidelines to a certain extent because the members of the creation team for the present guidelines are experts in limited areas; accordingly, there was a limitation in the scope of concepts to be adopted in the present guidelines. Regardless of such duplications and discrepancies, both the existing and present guidelines are important in that they provide various perspectives. Guidelines for consultation and treatment are aimed to help patients and health professionals make decisions.

3. Systematic Review

3.2 Literature Search for Evidence

The period of publications for literature search was from 1990 to March 2017 for all databases.

3.3. Inclusion and Exclusion Criteria for Literature Selection

Among the existing consultation and treatment guidelines that adopt the same clinical questions as those of the present guidelines, none have been created in accordance with Minds 2014. Therefore, a systematic review was conducted for all clinical questions. While conducting a systematic review, randomized comparative studies that satisfy the inclusion criteria were prioritized. When a sufficient number of such studies were not found, observational studies were also included. When no observational study that satisfied the inclusion criteria was found, a discussion was held between the guideline creation committee and the systematic review team and changes were made to the interpretation of clinical questions (CQs 10 and 12).

3.4. Methods of Evaluating and Integrating Evidence

The methods of evaluating body of evidence and expressing the strength of body of evidence were all in accordance with Minds2014. In principle, qualitative integration was conducted. However, quantitative integration (meta-analysis) was conducted for CQ 11 because multiple intervention studies were found that adopted similar designs.

4. Determination, Finalization, and Release of Recommendations

4.1. Basic Approach to Creating Recommendations

The basic approach to creating recommendations was in accordance with Minds2014. Particularly, great care was taken in setting up the recommendation panel to ensure that the perspectives of health professionals other than doctors would be incorporated. Therefore, the panel consisted of nurses, pharmacists, and patient advocates. The total number of members of the recommendation panel varied from 10 to 14. Members were responsible for the following areas: overview, hematopoietic organs, gastrointestinal organs, respiratory organs, and/or mammary glands. The breakdown of the members of each panel was as follows: seven or more people from the creation group, of whom at least two belong to the relevant area; two or more people from the associate committee who are nurses or pharmacists; and two people from the general public. In determining recommendations, a modified Delphi method was adopted. The recommendation panel conducted voting for up to three times for each draft recommendation created by area subleaders. A draft was accepted when two-thirds of panel members approved it. When a decision could not be made through voting, it was concluded that “there is no recommendation.” Furthermore, healthcare expenditure and the use of resources were not included in outcomes for CQs but were evaluated during the stage when recommendations were determined. The systematic review team members attended as jury members. They answered questions only from panel members. Recommendation panel meetings were held twice, on January 8 and 14, 2018.

In the recommendation panel meetings, decisions were made primarily based on the strength of evidence for overall outcomes (Table 1) and the benefit-harm balance. In doing so, the following factors were also considered in a comprehensive manner: the values, preferences, and burdens of patients, healthcare costs, and resources. The levels of recommendations were as follows: 1) strong recommendation and 2) mild recommendation (proposal). The strength of evidence was stated for each recommendation (Table 2). When it was not possible to make a clear recommendation,

this was indicated with the term “None.”

4.2. Finalization

In May 2018, creation committee members conducted a mutual peer review of the initial draft of the guidelines. In December 2018, external evaluation and public comments were reflected in the draft. The guidelines were finalized in February 2019 and were made public in July of the same year.

4.3. Methods of External Evaluation

The expert members of the Japan Geriatrics Society, the Japanese Society of Medical Oncology, and the Japan Society of Clinical Oncology, who were independent of the creation of the present guidelines, performed the external evaluation of the guidelines. In collecting public comments, email invitations were sent to the members of the Japan Society of Clinical Oncology and the Japanese Society of Medical Oncology. An announcement seeking public comments was also posted on the websites of these academic societies (from December 15, 2018 to December 28, 2018). The guideline creation group scrutinized the results of the external evaluation. The group amended the details of the guidelines based on these results. An agreement was made through an email meeting in February 2019.

4.4. Release

Following the completion of the external evaluation and responding to public comments, the guideline management committee made the final decision to release the guidelines.