Paul Gauguin. *Little Breton Shepherd*, 1888. Oil on canvas.

The highly individual aging process must be considered in determining optimal treatment for elderly patients with cancer.

Guidelines for the Treatment of Elderly Cancer Patients

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Background: *The management of elderly patients with cancer is influenced by several factors that can vary widely among aging individuals. As the proportion of elderly individuals increases, the need for specific care guidelines for this population is critical. The National Comprehensive Cancer Network (NCCN) has developed guidelines to address these factors when formulating optimal treatment regimens for elderly patients and to avoid significant toxicity and maintain their quality of life.*

Methods: *Factors that influence the appropriate treatment choices for the elderly, such as functional status, comorbidity, polypharmacy, and the presence of anemia, are reviewed, and the guidelines developed by the NCCN for treatment elderly patients are discussed.*

Results: *The guidelines address these factors when defining the goal of therapy and formulating individualized treatment approaches for the elderly to provide optimal care for these patients, avoid significant toxicity, and maintain their quality of life.*

Conclusions: *The goal of therapy must be clearly defined, whether survival, remission, cure, or palliation of symptoms. Enrollment of elderly cancer patients onto clinical trials is encouraged so the guidelines can be validated.*

Introduction

Guidelines have recently been formulated for the treatment of older patients with cancer (Tables 1-3).[1] They have been developed under the auspices of the National Comprehensive Cancer Network (NCCN)[2] to provide adequate treatment of elderly patients and to avoid significant toxicity and maintain quality of life for this patient population. They include geriatric assessment as well as therapeutic guidelines.

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The fastest-growing segment of the US population is composed of individuals over the age of 65 years. This age group will account for an estimated 20% of Americans by the year 2030. Increasing age is directly associated with increasing rates of cancer, corresponding to an 11-fold greater incidence in persons over the age of 65 years vs those under age 65. The over-75-year-old group will triple by 2030, and the over-85-year-old will double in the same period.[3] Currently, the average life expectancy for a 75-year-old individual is 11.3 years, and for an 85-year-old it is 6.3 years.[4] Together, these statistics outline an increasingly older cancer population that will require specific management for various cancers.[3,5]

Despite the increasing incidence of cancer with the aging of the population, only a minority of elderly patients have been entered onto clinical trials.[6] Limited information is available on single-agent chemotherapy and combinations.[7,8] The European Organization of Research and Treatment of Cancer (EORTC) conducted

Table 1. — Proposed Screening Tests for Relevant Comorbid Conditions in Elderly Cancer Patients

Realm	Screening	Confirmatory Test
Mental status	Serial Threes: Tell patient, "I am going to name three objects (pencil, truck, book) and I am going to ask you to repeat them now and a few minutes from now"	Folstein Mini-Mental Status If score <24, institute workup for dementia
Emotional status/depression	Ask patient, "Do you often feel depressed or sad?"	Geriatric Depression Scale If positive (score >10), workup for depression
Activities of daily living	Ask patient, "Can you dress yourself? Do you need help to go to the bathroom? Do you wet yourself? Can you eat without help? Can you move from one place to another without help? Do you need help taking a bath or shower?"	Formal Katz Activities for Daily Living Scale
Instrumental activities of daily living	Ask patient, "Do you drive? Are you able to use public transportation? Do you prepare your own meals? Do you go shopping? Do you do your own checking? Can you call somebody with the telephone? Do you remember to take your medications?"	Formal Instruments of Daily Living scale
Home environment	Ask patient, "Do you have trouble with stairs inside and outside the house? Do you trip often on rugs?"	
Social support	Ask patient, "Who would be able to help you in case of emergency?"	If no caregiver, try to arrange for a caregiver; if the caregiver is a spouse, a sibling, or a friend of the same age as the patient, assess independence of the caregiver
Comorbidity	Evaluate the presence of the following conditions from review of systems: congestive heart failure, coronary artery disease, valvular heart disease, chronic lung disease (obstructive or restrictive), cerebrovascular disease, peripheral neuropathy, chronic renal insufficiency, hypertension, diabetes, coexisting malignancies, collagen vascular diseases, incapacitating arthritis	Confirm the presence of the condition and grade the seriousness
Nutrition	Weigh patient, measure height, inquire about weight loss	Mini-Nutritional Assessment
Polypharmacy	Review number and type of medications	If more than three medications, look for duplications, interactions, and compliance

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Table 2. — Guidelines for Geriatric Assessment in Cancer Patients

1. All patients aged 70 years and older should receive some form of geriatric assessment.

2. A time-consuming geriatric assessment is not recommended. Instead, it is recommended that all patients aged 70 years and older undergo a number of screening questions. Based on the answers to those questions, further investigations may be indicated. The screening instrument is one proposed by Lachs and colleagues[93] (see Table 1). Others may be substituted at the discretion of the clinician.[94] The instrument is comprehensive and can be completed by the patient, and it can be complemented by the nursing interview before the physician visit.

3. The results of the Screening Geriatric Assessment (SGA) should be reported on the patient's chart and, in a separate paragraph, in the history and physical section.

4. The SGA does not need to be repeated by the oncologist's office if it was already performed by the referring physician.

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Table 3. — Guidelines for the Amelioration of Complications From Therapy in Older Patients Receiving Cytotoxic Chemotherapy

1. Routine prophylactic use of hematopoietic growth factors (G-CSF, GM-CSF) in persons aged 70+ years receiving treatment with CHOP or a drug combination of similar dose intensity (CAF, FEC100, CA).

2. Routine prophylactic use of hematopoietic growth factors (G-CSF, GM-CSF) for patients aged 60+ years receiving induction or consolidation chemotherapy for acute myelogenous leukemia.

3. Maintenance of hemoglobin levels of ≥12 g/dL, with an erythropoietic preparation in older individuals receiving cytotoxic chemotherapy.

4. Aggressive treatment of mucositis in older individuals, with fluid resuscitation as soon as the patient becomes unable to eat or when diarrhea develops.

5. Consider dose adjustment to the measured glomerular filtration rate of drugs excreted through the kidneys. It is important to recognize that the pharmacokinetics of antineoplastic drugs are unpredictable to some extent. Thus, drug doses should be escalated or de-escalated according to the degree of toxicity developed. Particular attention should be paid to the use of cytarabine in high doses. Older patients are particularly susceptible to the toxicity of this regimen for two reasons: decreased renal excretion of the toxic metabolite ara-uridine and increased vulnerability of the cerebellum.

6. Consider less toxic alternatives to doxorubicin, when equal effectiveness has been demonstrated, in patients aged 70+ years.

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an analysis of European trials[9] in which 22% of the patients were 65 years of age or older and 8% were 70 years and older. Older patients underwent surgery, radiotherapy, and chemotherapy less often. Also, more elderly patients experienced a delay in the dose administration or a dose reduction compared with younger patients. With the exception of oral toxicity, there was no difference in toxicity in the older patients compared with the younger patients; this may be due to the increase in dose reductions and delays. There may have also been a bias toward positive selection, which may increase with patient age. The EORTC investigators as well as others advocate that the elderly should be candidates for all phases of clinical trials and that they should not be excluded on the basis of age. Traditionally, patient selection has been based on good clinical practice, consisting of clinical judgment with performance status and organ function parameters. There seems to be a need for a more comprehensive tool of pretreatment assessment so that the potential problems in treating elderly patients can be predicted and avoided.[9] Since aging is the result of highly individualized processes, an assessment should be made of each patient to adequately plan therapy. However, since not all patients could or should undergo an extensive geriatric assessment, screening has been recommended to determine which patients require more extensive evaluation.[1]

Comorbidity and Functional Status

Comorbidity and functional status are important factors in determining therapy. Patients with poor function are at increased risk of toxicity. Comorbidity is a key factor in the overall survival of patients as well as the benefits and toxicity of therapy. The role of comorbidity in survival has been evaluated by Charlson et al[10] who determined that the number and severity of comorbid illnesses can predict survival in general medical patients admitted in an inpatient unit. The effect of comorbidity on survival of patients with colorectal cancer and breast cancer has been extensively evaluated. The comorbid conditions included common general medical conditions such as any form of heart disease, hepatobiliary disease, and renal dysfunction. The increase in the degree of comorbidity observed is an independent predictor of survival.[11,12]

Functional status is also a significant consideration in the elderly.[13] Functional status is usually determined by two common geriatric scales, Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL). The ADL scale is a measure of simple functions (transfer, bathing and grooming, toileting, dressing, feeding, appropriate behavior). The IADL scale requires more complexity and interaction with the external environment (cooking, cleaning, laundry, use of telephone, use of transportation, managing money, taking medications).[14] Comorbidity and functional status are independent factors in older cancer patients and need to be assessed independently. The traditional oncology measures such as the Karnofsky score and Eastern Cooperative Oncology Group performance scale are not effective predictors in the elderly. The degree of dependency and geriatric functional scores can predict survival in older patients.[13,15-17] These factors are important in clinical trial design in the elderly.

Aging and Cancer Chemotherapy

Aging is a highly individualized, multidimensional process. Chronologic age does not always predict the physiological decline in an individual, due in part to the effect of comorbidity on aging. It has been suggested that the process of aging is a functional continuum, with

frailty at the midpoint between independence and predeath.[18] In the primary health stage, activity if not significantly limited and functional reserve is minimally reduced. During the aging process, many individuals become somewhat vulnerable, with a critical reduction in functional reserve that causes some functional limitations. Reversibility of some of these conditions is possible. The stage of frailty is characterized by severe limitations with no significant recovery of functional reserve.

There is no one standard definition of frailty, but most investigators agree that the definition should include dependence in one or more activities of daily living, three or more comorbid conditions, and one or more geriatric syndromes (including dementia, delirium, depression, incontinence, falls, osteoporosis, failure to thrive, gait disturbances, pressure ulcers, and sleep disorders). A phenotype of frailty with a simple clinical assessment has been published.[19] Cancer chemotherapy needs to be tailored according to the individual, taking into consideration these phases of aging, functional status, and comorbidity. In general, evaluations of functional status/frailty and measures of clinical assessment have not included a large cancer patient population. General management of the elderly can be based on the independence or frailty of the patient and on life expectancy relative to the patient's cancer survival. Frail patients are probably best suited for palliative treatment only. The patients in whom potential life expectancy exceeds predicted survival from cancer without therapy should receive standard treatment to potentially prolong survival.[1]

Clinical Pharmacology

Elderly patients are the largest users of pharmaceutical agents, incurring 30% of the total drug costs. Half of all drugs marketed will have some use in treating problems of the elderly.[20,21] However, most studies are conducted on patients younger than age 55 years.[22] This can complicate decision making, particularly in regards to dosing, and may contribute to some degree to the increased incidence of drug toxicity with age. These toxicity differences are also the result of age-related changes in pharmacokinetics and pharmacodynamics. Basic knowledge of these parameters will assist in the prevention and amelioration of toxicity.

Pharmacokinetics

Absorption

Drug absorption can be affected by a number of changes in the digestive system, including increased mucosal atrophy and decreases in gastrointestinal motility, splanchnic blood flow, or secretion of digestive enzymes.[22,23] These changes can result in reduced absorption rate (ie, in the amount of drug absorbed in the unit of time). Since most chemotherapy drugs are administered parenterally, absorption abnormalities do not usually affect chemotherapy.

Distribution

The volume of distribution of drugs is a function of body composition and the concentration of circulating plasma proteins such as serum albumin and red blood cell concentration.[23-25] Fat content doubles in the elderly from 15% to 30% of body weight, and intracellular water decreases to 33% in the average 75-year-old compared with 42% in the average 25-year-old. This results in a decrease in volume of distribution of more polar drugs that primarily distribute to body water, while that of the lipid soluble drugs increases. This can lead to a lower peak concentration and prolonged terminal half-life.[23,24] As an individual ages, plasma albumin may decrease by 15% to 20% or more, especially with chronic illness, malnutrition, and frailty. There is often a reduction of red blood cell concentration. Anemia can be particularly relevant for treatment with anthracyclines, taxanes, and epipodophyllotoxins that are heavily bound to red blood cells. Of particular benefit to older individuals is the correction of anemia, since it is the only component of volume of distribution that can be manipulated.[26-28]

Metabolism

The liver is the main site of drug metabolism. Although there is lack of agreement regarding the effects of age-related changes in hepatic drug metabolizing capacity, there is consensus that liver size decreases with age.[24] Liver blood flow is reduced at a rate of 0.3% to 1.5% per year after age 25. This may lead to lower clearances of drugs that are dependent on blood flow for elimination. Phase 1 metabolism occurs primarily via the cytochrome P450 (CYP) microsomal system, which consists of a number of isoenzymes. Phase 2 reactions are primarily conjugation reactions.

Cytochrome P450

These heme-based enzymes are located primarily in the liver, with additional locations in the small bowel, kidneys, lungs, and brain to a lesser extent. Despite large numbers of various enzymes, genetic variability accounts for differing levels of enzyme activity through various pathways that may lead to clinically important pharmacodynamic differences among individuals.[29-31] The potential for drug interactions is rela-

tively high in the elderly due to polypharmacy. This is important in the CYP3A4 enzyme, which is inhibited or induced by a variety of commonly prescribed medications and is involved in the metabolism of a variety of anticancer agents. Cyclophosphamide, ifosfamide, paclitaxel, etoposide, teniposide, vincristine, vinblastine, busulfan, and tamoxifen are all substrates of CYP3A4 and may be significantly affected by common enzyme inhibitors of this enzyme.[32]

Age-related declines in these systems have been reported in animal studies and some human trials. CYP1A2 has shown a decrease of 20% to 25% in clearance in healthy elderly individuals compared with their younger counterparts.[33,34] Most of the decrease in clearance can be explained by the age-related decrease in liver mass rather than a decrease in the intrinsic activity of the cytochrome CYP1A2. Phase 2 reactions appear unaffected by age.[35] The biliary excretion of drugs has been studied, but no age-related alterations have been reported.[35]

Excretion

Age-related changes also occur in excretory function, including a gradual loss in renal mass and a decline in function with age. Glomerular sclerosis produces loss of capacity to perform ultrafiltration of plasma, which leads to a decrease in the glomerular filtration (GFR) rate by approximately 1 mL per minute for every year over 40 years of age.[36-38] The importance of this decline was first emphasized in a study of dosages based on renal function leading to a higher therapeutic index.[39] The reduction in glomerular filtration rate is not reflected by an increase in serum creatinine levels because of the simultaneous loss of muscle mass that occurs with age. Serum creatinine is often not an adequate indicator of renal function in elderly patients.[40]

To facilitate the estimation of glomerular clearance, various equations have been evaluated to calculate creatinine clearance based on the serum creatinine and other factors. The two most common equations clinically used are the Cockcroft-Gault and Jellife equations.[41,42] The equations are less accurate in the elderly and in patients with severe renal failure or decreased muscle mass. Inaccuracies in measured creatinine clearance in elderly patients have also been demonstrated.[43] Estimations of creatinine clearance in the elderly may lead to errors in dosing.[44] A comparison of the accuracy of the formulas have shown that the recently described Wright formula may be the most accurate, precise, and least biased formula in the calculation of glomerular filtration rate in an elderly population.[45,46]

The decline in glomerular filtration rate with age translates into pharmacokinetic alterations of drugs or their active metabolites that are excreted by the kidneys. Due to the physiologic decline in renal function with age, chemotherapy, which is primarily renally excreted, must be used with care in the elderly. Standard doses may be too toxic, particularly in the frail elderly. Dosing modifications for these physiologic declines have been suggested.[47,48]

The formulas by Calvert et al[49] and Chatelut et al[50] can be used to calculate the dose of carboplatin for the desired area under the curve (AUC) based on patient age and the serum creatinine level. Other drugs can be dose-adjusted according to Kintzel and Dorr.[51] They provide general guidelines to adjust doses of renally excreted or nephrotoxic anticancer drugs in patients who present with altered renal function. The dosage adjustments for renal impairment were calculated using a formula to determine the fraction of the normal dose. The formula is:

$$\text{fraction of normal dose} = (\text{normal dose}) \times f(k_f - 1) + 1$$

In this formula, f = fraction of the original dose excreted as active or toxic moiety, and k_f = patient's creatinine clearance (mL/min) / 120 mL per min.

Compliance

The recent emphasis on oral therapy makes drug compliance an important issue in treatment.[52] Patient noncompliance is a potential major obstacle for orally formulated chemotherapy. Incomplete treatment in the adjuvant treatment of breast cancer results in a markedly inferior disease-free survival.[53] Factors associated with higher rates of noncompliance include lower socioeconomic status and treatment in a community-based setting, as well as number of doses required per day.[54]

In elderly patients, noncompliance can lead to a higher risk of hospitalization. In their study of hospitalized older patients, Col et al[55] reported that factors statistically associated with this risk were female gender, poor recall of the medication regimen, involvement of numerous physicians, medium income category, use of several medications, and belief that medications are expensive.[55] Pharmacokinetic analysis showed actual compliance was less than half that suggested by patient self-report. Compliance increased nearly threefold when measures designed to increase compliance, including patient education, home psychologic support, and exercises in pill taking, were utilized.[52,56]

Noncompliance with oral chemotherapy may influence survival.[57] A number of studies have evaluated compliance with regard to oral chemotherapy regimens[58-62] and have identified several risk factors in adherence to prescribed oral medication regimens.[62] To overcome problems of compliance in the elderly, simple dosage regimens should be prescribed for all medications (preferably 1 or 2 doses daily). Providers can also assist with compliance by suggesting cues (eg, time of day, mealtimes, other daily rituals) to help patients remember to take medications, by providing devices such as medication boxes, and by regularly monitoring compliance.

Anemia

Anemia is common in older patients and is a marker of early mortality.[63,64] The NCCN guidelines suggest that a hemoglobin level of 12 g/dL is a reasonable goal in older patients to avoid toxicity. The perception of what constitutes a normal hemoglobin level may not be appropriate for an elderly population. Chaves et al[64] showed a consistent trend of improvement in performance-based scores with increasing hemoglobin levels from <12 g/dL, 12 to 13 g/dL, and 13 to 14 g/dL. They proposed two hypotheses: (1) hemoglobin currently perceived as "mildly low" and even "low-normal" might have an independent adverse effect on mobility function, and (2) hemoglobin of 12 g/dL might be a suboptimal criterion for defining anemia in older women. Formal testing of these hypotheses might prove relevant for anemia-related and mobility disability-related clinical decision making. Therefore, in a more dependent and weaker cancer patient population, a hemoglobin level of 12 g/dL may be a reasonable goal, but this remains to be validated. Although hemoglobin level was significant even after adjusting for age, comorbid illnesses, and other markers of disability, this remains to be validated prospectively in cancer patients and in men and subsequently after correction of anemia with erythropoietin. Several studies have examined quality of life in cancer patients after improving hemoglobin levels and reducing transfusion requirements, the largest being a study by Littlewood and colleagues.[65] However, these studies did not report procedures to minimize bias and did not prospectively define the minimum differences in quality of life scores that would be considered clinically significant. Many studies removed randomized patients from outcome assessment due to missing data and were not performed on an intention-to-treat analysis. Because of these significant shortcomings, the joint panel of experts from the American Society of Hematology and the American Society of Clinical Oncology did not place strong weight on quality of life outcomes to make recommendations for the use of erythropoietin in patients with cancer and a hemoglobin level of ≤10 g/dL (and possibly <12 g/dL based on clinical circumstances) but rather on evidence for improvements in hemoglobin and decreases in blood transfusions.[66] This has been confirmed by a meta-analysis.[67]

Other benefits of correcting anemia in a cancer population include the prevention of functional dependency, or at least its delay.[68] A direct relationship exists between hemoglobin increases during epoetin alfa therapy and corresponding quality of life improvements in a general cancer patient population receiving chemotherapy. This was found across the hemoglobin range of 8 to 14 g/dL. The maximal incremental gain in quality of life occurred when hemoglobin was in the range of 11 to 13 g/dL.[69]

Anemia can also affect the pharmacokinetics and pharmacodynamics of chemotherapy. In addition to renal excretion, the most consequential change in pharmacokinetic parameters involves the volume of distribution (Vd). The Vd is a function of body composition, serum albumin, and red blood cell concentration. With aging, the Vd of water-soluble drugs decreases as a result of decline in total body water; a drop in albumin and hemoglobin concentration may further restrict the Vd of these agents and enhance their toxicity.[68] Part of this relationship stems from the fact that many drugs are bound to red blood cells in the circulation and a drop in red blood cell mass is associated with increased concentration of free drug. A number of studies have shown that hemoglobin concentration is an independent risk factor for myelotoxicity caused by the anthracyclines, epipodophyllotoxins, and camptothecins.[28]

Myelotoxicity

Whether the risk of myelotoxicity increases with age remains a controversial issue. Some retrospective analyses do not show a statistically significant difference in neutropenic fever but do show increase in duration of neutropenia. One study showed twice the frequency of life-threatening neutropenia in elderly patients, and the only drug-related septic deaths were in elderly patients.[70] A number of trials have failed to demonstrate this increased tendency.[7,39,71] However, these studies have been limited. Older persons were underrepresented; those over age 70 comprised only 10% to 15% of the total patient population, while 40% of all malignancies occur in this age group. The oldest old (ie, patients 80 years of age and older) were virtually absent. Patients were highly selected in terms of performance status and comorbidity; they all had been treated according to cooperative groups or major cancer center

protocols. The dose intensities of most chemotherapy regimens were lower than those of current regimens.[1] Prospective studies on non-Hodgkin's lymphoma using CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) and CHOP-like regimens with similar therapeutic intensity suggest the prophylactic use of hematopoietic growth factors decreases the incidence and severity of myelosuppression.[72-74] Evidence for this is supported by the fact that the risk of myelosuppression increases substantially by age 70 years, that the risk is reduced by 75% with growth factors, and that the incidence of neutropenic-related mortality in persons aged 70+ years varies from 5% to 30%.[1,74] The use of growth factors is also encouraged by data indicating that dose reductions compromise the effectiveness of the therapy by reducing the risk of febrile neutropenia and documented infection associated with malignancies and dose-intensive treatment regimens.[73] Randomized trials comparing chemotherapy with or without granulocyte colony-stimulating factor support in older patients (at least 60 to 65 years of age) with non-Hodgkin's lymphoma.[75,76] These studies demonstrated a significant reduction in neutropenia and infections during neutropenia or in days of treatment with antibiotics, or both. However, they did not demonstrate an improvement in complete remission rates, overall survival, or disease-free survival. Recommendations for the use of colony-stimulating factors have been published by the American Society of Clinical Oncology.[77]

Mucositis and Diarrhea

The guidelines also emphasize control of mucositis and diarrhea. Elderly patients are most susceptible to the toxic effects of fluoropyrimidines and methotrexate. The drug 5-fluorouracil (5-FU) has been infused over a multitude of schedules with little difference in efficacy. In older patients, 5-FU has often been associated with increased toxicity.[78] In a trial of 5-FU and folinic acid, patients over 70 years of age experienced more grade 3/4 mucositis than the younger group (11% vs 19%; P=.02).[79] However, in an analysis of a series of weekly 5-FU regimens, there was no difference in toxicity between younger and older patients.[80] A meta-analysis of adjuvant therapy regimens demonstrated no increased toxicity in older patients except for leukopenia.[81] From these publications it appears that increased toxicity in the elderly is dependent on performance status and the dosing schedule of 5-FU.[82] Methotrexate toxicity is most clearly related to renal function. Dose modifications have been extensively reported.[83]

Diarrhea can be particularly troublesome as it can rapidly lead to volume depletion and cardiovascular collapse if not treated aggressively. The current NCI Common Toxicity Criteria[84] lists the grading of diarrhea as follows: grade 2 = increase of 4 to 6 stools per day or nocturnal stools; grade 3 = increase of >7 stools per day or incontinence, or need for parenteral support for dehydration; grade 4 = physiologic consequences requiring intensive care, or hemodynamic collapse. Several publications emphasize grade 3/4 toxicity. Many elderly patients would consider grade 2 toxicity as significantly distressing. Future studies in elderly patients should document all grades of toxicity in order to make toxicity measures more relevant for these patients. Diarrhea has been intensively studied in patients receiving irinotecan. Retrospective analysis found that delayed diarrhea increased in patients with advanced age. Pharmacokinetic parameters such as mean plasma levels of irinotecan, the active metabolite SN-38, the inactive glucuronidase SN-38G, C_{max}, and $AUC_{0\text{-}24}$) in patients 65 years of age or older were within 3% of those in younger patients. In addition, the response rates do not vary based on age.[85,86] It is recommended that patients over age 70 or those with prior pelvic irradiation or poor performance status begin the drug use at reduced doses.[87] The typical therapy for delayed diarrhea has been loperamide and diphenoxylate. Other pharmacologic interventions including octreotide, neomycin, thalidomide, and celecoxib have been studied.[88-91]

Conclusions

The NCCN guidelines can be utilized to minimize toxicity. The most important aspect of these guidelines is the individualization of cancer treatment. Treatment-related decision-making involves a combination of biological and tumor-related factors.[92] The relative balance of these factors provides the overall guideline for treatment. The most significant element is the goal of therapy in context of the overall condition of the patient. This goal, whether it is prolongation of survival, remission, cure, or palliation of symptoms, must be clearly defined. This provides the patient and family with a view of the expectations of treatment and allows short- and long-term planning. The aggressiveness of the tumor and the availability of effective treatment are other aspects of planning. The balance of these factors for a frail patient with metastatic renal cell carcinoma, where no significant therapy exists, would differ from an elderly woman with asymptomatic bone metastases from a hormonally responsive breast cancer.

The effective management of cancer requires some skills for the general assessment of geriatric patients. Medical oncologists need to be aware of new data and ideas regarding the biology of aging and the aspects of various treatment programs relevant to older patients. A partnership needs to develop between geriatricians

and the physicians responsible for the treatment of cancer patients. Prospective clinical trials in the elderly are critical to assess these guidelines and to develop relevant data that clinicians can apply to optimize treatment of older patients.

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