Contemporary Systemic Therapy for Urologic Malignancies in Geriatric Patients

Bo Zhao, MD[a], Petros D. Grivas, MD, PhD[b,*]

KEYWORDS

• Geriatric oncology • Urothelial carcinoma • Bladder cancer • Renal cell carcinoma • Kidney cancer • Prostate cancer • Systemic therapy • Geriatric assessment tools

KEY POINTS

- Geriatric patients represent a highly heterogeneous population; the life expectancy, functional status, and disease-related prognosis at a given age is highly variable among same-age individuals.
- Treatment decisions for geriatric patients with urologic (genitourinary) malignancies should be based on a comprehensive evaluation of several factors in addition to chronologic age, including clinical disease status and characteristics; life expectancy; medical comorbidities; organ function; performance, nutritional, cognitive, and emotional status; concomitant medications; psychosocial support; and patient preference, beliefs, goals, and expectations.
- Chronologic age alone should not be an absolute barrier or contraindication to systemic therapy.
- Validated assessment tools can be useful for the integrated evaluation of geriatric patients and can aid in the decision-making process; prospective evaluation of such tools in clinical trials is recommended.

INTRODUCTION

Aging is increasingly becoming a global issue, in both developed and developing countries. By 2050, the number of people older than 60 years is expected to be 2 billion worldwide.[1] In the United States, people greater than or equal to 65 years of age represented 12.4% of the population in the year 2000 but are expected to increase to 19% by 2030.[2] Aging is the single most important risk factor for developing

Disclosure: Dr. P.D. Grivas has done consulting with Genentech/Roche, and Valeant/Dendreon. Dr. B. Zhao has nothing to disclose.

[a] Department of Hematology/Oncology, Taussig Cancer Institute, Cleveland Clinic, Desk R30, 9500 Euclid Avenue, Cleveland, OH 44195, USA; [b] Department of Hematology/Oncology, Taussig Cancer Institute, Cleveland Clinic, Desk R35, 9500 Euclid Avenue, Cleveland, OH 44195, USA
* Corresponding author.
E-mail address: grivasp@ccf.org

Clin Geriatr Med 31 (2015) 645–665
http://dx.doi.org/10.1016/j.cger.2015.06.004 geriatric.theclinics.com
0749-0690/15/$ – see front matter

cancer, and numbers of older patients with cancer continue to increase.[3] Cancer is the leading cause of death among people greater than or equal to 65 years of age.[4] In the United States, urologic malignancies (cancers of the kidney, ureter, bladder, urethra, prostate, testes, and penis) account for 23% of all types of cancer and for more than 50,000 deaths in 2014.[5] Most of them were diagnosed in older individuals. The management of these patients becomes a major public health concern and clinical challenge. This article summarizes data regarding systemic therapy in geriatric populations with urologic malignancies, referencing data primarily from recently published clinical trials. When prospective evidence is not sufficient, retrospective data are included. Testicular cancer typically develops in young men, and penile cancer and other urinary tract cancers are rare, therefore this article focuses on prostate cancer, kidney cancer, and bladder cancer.

PROSTATE CANCER

Prostate cancer is the most common cause of nonskin cancer and the second leading cause of cancer death in US men. In 2014, there were an estimated 233,000 new diagnoses of prostate cancer and 29,480 deaths from the disease.[5] Prostate cancer is most frequently diagnosed among men aged 65 to 74 years, and the median age of diagnosis is 66 years. More than 55% of diagnoses occur in patients older than or equal to 65 years.[6] Prostate cancer is largely an androgen-driven disease, and androgen deprivation therapy (ADT) with medical or surgical castration remains part of the first-line therapy for metastatic prostate cancer. Despite tumor responses in 80% to 90% of treated patients and median response durations of 14 to 20 months, metastatic disease almost always eventually progresses in the form of castration-resistant prostate cancer (CRPC).[7] Data on ADT and agents currently approved for metastatic CRPC, including docetaxel, cabazitaxel, sipuleucel-T, abiraterone acetate, enzalutamide, and radium-223 are summarized later. Bone targeting agents, including zoledronic acid and denosumab, are not discussed, because these agents are generally well tolerated even in older individuals, but have not been shown to offer overall survival (OS) benefit.

Androgen Deprivation Therapy

Two recent large studies, NCIC-CTG PR.7 and SWOG-9346, have provided prospective data on quality of life (QoL) for patients receiving ADT. Both studies compared intermittent ADT (IAD) with continuous ADT (CAD); the former was conducted in patients with increasing prostate-specific antigen (PSA) levels after definitive radiotherapy,[8] and the latter was conducted in patients with newly diagnosed metastatic prostate cancer.[9] Although no age-specific outcomes were reported, both studies had enrolled primarily older patients: median age was 74 years in the NCIC-CTG study, the oldest patient was 89 years; median age of patients in the SWOG-9346 study was 70 years, and the oldest patient was 97 years. Common side effects of ADT, including sarcopenia, metabolic syndrome, and cardiovascular disease, were comparable in patients received IAD versus CAD in both studies. For QoL, hot flashes, libido, and urinary symptoms were better in the IAD arm in the NCIC-CTG study, as well as at 3-month and 9-month analyses in the SWOG-study[8,9] (**Table 1**). In the absence of OS benefit,[8] ADT should not be encouraged in patients with increasing PSA syndrome without detectable metastasis, unless progressive shortening of PSA doubling time predicts the impending emergence of overt metastases.[10] Primary ADT alone in older patients with localized disease should be discouraged because this practice has not been shown to improve survival.[11] When prolonged ADT is being