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Review article

Current systemic therapies for metastatic renal cell carcinoma in older adults: A comprehensive review

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ABSTRACT

Physiological changes that occur during the aging process may impact drug metabolism and availability, consequently affecting treatment efficacy and tolerability. Despite being a disease of older adults, there is little data to guide treatment decisions for older patients with metastatic renal cell carcinoma (mRCC). The recent approval of many new agents for this disease poses a clinical challenge: how to best utilize these drugs in a population (older adults) who has been generally under-represented in clinical studies. Additionally, the presence of comorbid conditions, polypharmacy, frailty, and lack of social support place this group of patients in a very unique situation. In order to avoid under-treatment, international societies' guidelines recommend routine use of geriatric tools to assess patients' suitability for systemic treatments. Here we provide a thorough review of age-related metabolic differences, safety and efficacy data for each drug approved for mRCC, and cover specific considerations for the management of older adults with this disease.

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Contents

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1. Introduction

Renal cell carcinoma is the 8th most common malignancy diagnosed in men and women in the United States, with an incidence of 62,000 new cases in 2016. [1] A large proportion of renal cell carcinoma patients are older, with a median age at diagnosis of 65 years old and with 48% of patients being diagnosed beyond this age. [2,3] (See Fig. 1.)

Prior to 2005, systemic treatment options included interleukin-2 (IL-2) and interferon-alpha (IFN-α) with a median overall survival of 13 months. [4] However, these 2 drugs were rarely used in the older population since they are accompanied by considerable toxicities and consequently poor tolerability among patients with comorbidities. [4–7] Since 2005, however, treatment options have evolved dramatically, providing a multitude of new drugs approved for use in metastatic renal cell carcinoma (mRCC), including multi-targeted tyrosine kinase [MET, AXL, vascular endothelial growth factor (VEGF)] inhibitors, mammalian target of rapamycin (mTOR) pathway inhibitors, and immunotherapies (checkpoint inhibitors). [8–17]

Although tyrosine kinase inhibitors (TKIs) and checkpoint inhibitors have a more favorable toxicity profile compared to IL-2 and IFN-α, little data exists on the efficacy and tolerability of these novel agents in the older population given the unique age-related disease biology and drug metabolism. [18–20] While some reports have shown that the safety profile and efficacy of targeted drugs in the older population is comparable to younger patients,[21] others have suggested that this may not always be true. [22]

Unique challenges and barriers for treating older adults exist due to various factors, which influence treatment decisions and should be addressed in order to maximize results. In this context, the development of comprehensive geriatric assessment tools has been shown to predict clinical outcomes and risk of toxicities allowing tailored interventions.

Just as with younger adults, the optimal approach on utilizing treatment agents in RCC among older adults is unknown. In the current manuscript, we will discuss available data for each agent in older adults. We will provide a framework for utilization of these agents for practicing

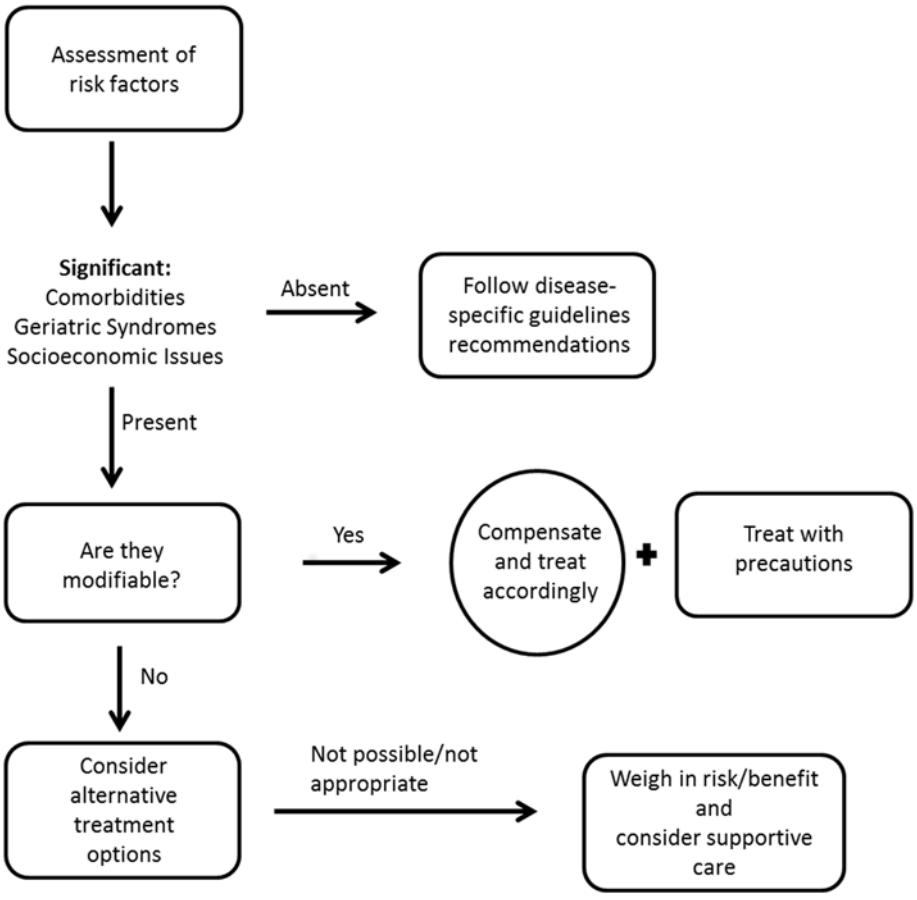

Fig. 1. Algorithm for treatment approach in mRCC older adults. Adapted from National Comprehensive Cancer Network. Older adult oncology (Version 2.2016). Available at http://www.nccn.org/professionals/physician_gls/pdf/senior.pdf.

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