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Review

Evaluation of treatment options for patients with advanced renal cell carcinoma: Assessment of appropriateness, using the validated semi-quantitative RAND corporation/University of California, Los Angeles methodology

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Abstract A diverse range of treatment options and interventions are available for the management of renal cell carcinoma (RCC), allowing clinicians to tailor therapy to best meet their patient's needs and situation. However, choosing from the plethora of options can be problematic. RCC treatment guidelines advise on the most efficacious agents based upon specific clinical trial populations, but these do not always take into account all the patient factors that influence the suitability of treatment options for individual patients.

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This study used the validated RAND/UCLA (RAND corporation/University of California, Los Angeles) 'appropriateness methodology' to integrate clinical efficacy data with expert opinion concerning the use of specific RCC treatment options for particular patient scenarios, in an attempt to facilitate the widespread implementation of patient-focussed treatment choices. Use of the methodology has allowed us to develop treatment algorithms for patients with locally-advanced RCC and for those with metastatic disease post-nephrectomy or with primary tumour *in situ*. The algorithms take into account patient-specific characteristics such as tumour histology, prior treatment and known risk factors to advise whether a particular treatment intervention is appropriate, not appropriate or of uncertain appropriateness.
Use of this methodology aims to develop a formalised process by which expert opinion can be integrated with clinical data and used as an additional source of information that can provide further guidance concerning difficult treatment decisions when data are absent or sparse.

1. Introduction

The development of therapies that target the vascular endothelial growth factor (VEGF) and mammalian target of rapamycin pathways (mTOR) have made a significant impact on the treatment of patients with advanced RCC. The targeted agents differ in terms of their biological effects, clinical efficacy, adverse event profiles and the patient populations in which they have been studied.[1] Treatment guidelines for RCC[2,3] have been developed based on clinical trial data but the appropriateness of a specific therapy to a particular situation depends in part on factors such as the extent and aggressiveness of the disease, prior treatment regimens and prognostic factors. Available RCC treatment guidelines may not always take into account these and other factors such as patient history which can have an important influence on clinical decision making. Another consideration is that guidelines can be either general or specific, and can be interpreted variably depending on the specialty of the treating physician (e.g. urologist, medical oncologist). There are many treatment choices available and it would be better if possible, to tailor therapy to meet the needs of each individual RCC patient based on the biology of their disease. A step towards tailoring therapy also requires that the available treatment options are prioritised to best suit the individual.[63]

Evidence is continually being developed with regards the efficacy and toxicity of new therapies. However, this evidence and the views of opinion leaders are not always rapidly transferred to community oncologists treating patients with advanced RCC. Collecting existing and emerging evidence and integrating it with expert opinion represents an important educational need. In 2006, Halbert et al.[4] reviewed the clinical evidence and integrated it with expert opinion, utilising the validated RAND corporation/University of California, Los Angeles (RAND/UCLA) appropriateness methodology,[5] to reach a consensus on the appropriateness of the available RCC treatment. The methodology has been utilised in oncology and applied to consider the applicability of treatments for breast cancer, melanoma,[6] colorectal cancer,[7,8] haematological malignancies and pancreatic cancer.[9]

In this study, we reviewed new evidence that has been published since the Halbert analysis and integrated the findings with the opinions of leaders in RCC treatment from across Europe, using the same RAND/UCLA methodology. This exercise becomes even more relevant given that the first randomized phase III trial with a targeted agent (Sorafenib) was published in 2005[67] and that almost each year since then an additional targeted agent has been approved by the FDA and EMA.

2. Methods

The consensus panel method developed by RAND/UCLA combines evidence-based review with the practical experience of clinicians and leaders in the field.

2.1. Literature review

Comprehensive literature review identified studies that assessed the use of systemic therapies in the treatment of metastatic RCC. The MEDLINE database was searched from February 2005 to July 2010 for English language articles using the search terms *kidney cancer*, *metastatic renal cell carcinoma*, *carcinoma renal cell* and *clinical trial*, as keywords; a search of the bibliographies of relevant articles and reviews identified additional publications. Abstracts from the websites of the American Society of Clinical Oncology, the European Society of Medical Oncology (ESMO) and the European Association of Urology (EAU) published to July 2010 were also reviewed. A broad perspective was taken, to include published evidence from non-randomised phase 1 and 2 studies. The literature review was used to identify data informing on the efficacy of RCC treatments and to support the development of patient scenarios for use in the RAND/UCLA assessment process.