

Targeted therapy for metastatic renal cell carcinoma

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Abstrak

In the past 10 years, recent development of targeted therapy in metastatic renal cell carcinoma (mRCC) has provided a new hope and significantly enhanced the prognosis of the disease. Three class of targeted therapy were developed, including multi-targeted tyrosine kinase inhibitors (TKI), the mammalian target of rapamycin (mTOR) complex-1 kinase inhibitors, and the humanized antivascular endothelial growth factor (VEGF) monoclonal antibody. Hence, the objective of this article was to critically examine the current evidence of targeted therapy treatment for patients with mRCC. In the majority of trials evaluating targeted therapy, patients were stratified according to Memorial Sloan Kattering Cancer Center (MSKCC) risk model and the recommendation of targeted treatment based on risk features. In first-line setting (no previous treatment), sunitinib, pazopanib, or bevacizumab plus IFN- were recommended as treatment options for patient with favorable- or intermediate- risk features and clear cell histology. Patients who progressed after previous cytokine therapy would have sorafenib or axitinib as treatment options. Clear-cell mRCC with favorable- or intermediate- risk features and failure with first-line TKI therapy might be treated with sorafenib, everolimus, temsirolimus or axitinib. However, the current evidence did not show the best treatment sequencing after first-line TKI failure. In patients with poor-risk clear-cell and non-clear cell mRCC, temsirolimus was the treatment option supported by phase III clinical trial. In addition, several new drugs, nowadays, are still being investigated and waiting for the result of phase II or III clinical trial, and this might change the standard therapy for mRCC in the future.

.....ada sepuluh tahun terakhir, perkembangan terapi target pada karsinoma sel renal bermetastasis menjadi harapan baru dan mampu meningkatkan prognosis penyakit tersebut. Terdapat tiga terapi target yang telah dikembangkan termasuk multi-targeted tyrosine kinase inhibitors (TKI), penghambat mammalian target of rapamycin (mTOR) complex-1 kinase, dan antibodi monoklonal humanized antivascular endothelial growth factor (VEGF). Tujuan artikel ini secara kritis menelaah studi terkini terapi target untuk tatalaksana pasien tersebut. Pada sebagian besar uji klinis yang mengevaluasi terapi target, pasien distratifikasi berdasarkan model yang dikembangkan oleh Memorial Sloan Kattering Cancer Center (MSKCC) dan rekomendasi terapi berdasarkan tingkat resiko pasien. Terapi target lini pertama (belum pernah mendapatkan terapi sistemik sebelumnya), sunitinib, pazopanib, atau bevacizumab ditambah IFN- merupakan pilihan terapi dengan tingkat resiko menguntungkan dan sedang serta gambaran histologi sel jernih. Pasien yang mengalami progresifitas pasca terapi sitokin, sorafenib atau axitinib adalah pilihan yang direkomendasikan. Karsinoma sel ginjal bermetastasis tipe sel jernih dengan tingkat resiko menguntungkan dan sedang yang gagal pada terapi target lini pertama dapat ditatalaksana dengan sorafenib, everolimus, temsirolimus atau axitinib. Akan tetapi, studi saat ini menunjukkan tidak ada pilihan terapi sekuensial terbaik pasca kegagalan terapi lini pertama. Pasien dengan tingkat risiko buruk dan gambaran histologi bukan sel jernih, temsirolimus merupakan terapi target yang didukung oleh uji klinis fase III. Saat ini, beberapa obat baru masih dalam tahap uji klinis fase II dan III dan hasil uji klinis tersebut mungkin dapat mengubah terapi standar pasien karsinoma sel ginjal bermetastasis di masa yang akan datang.