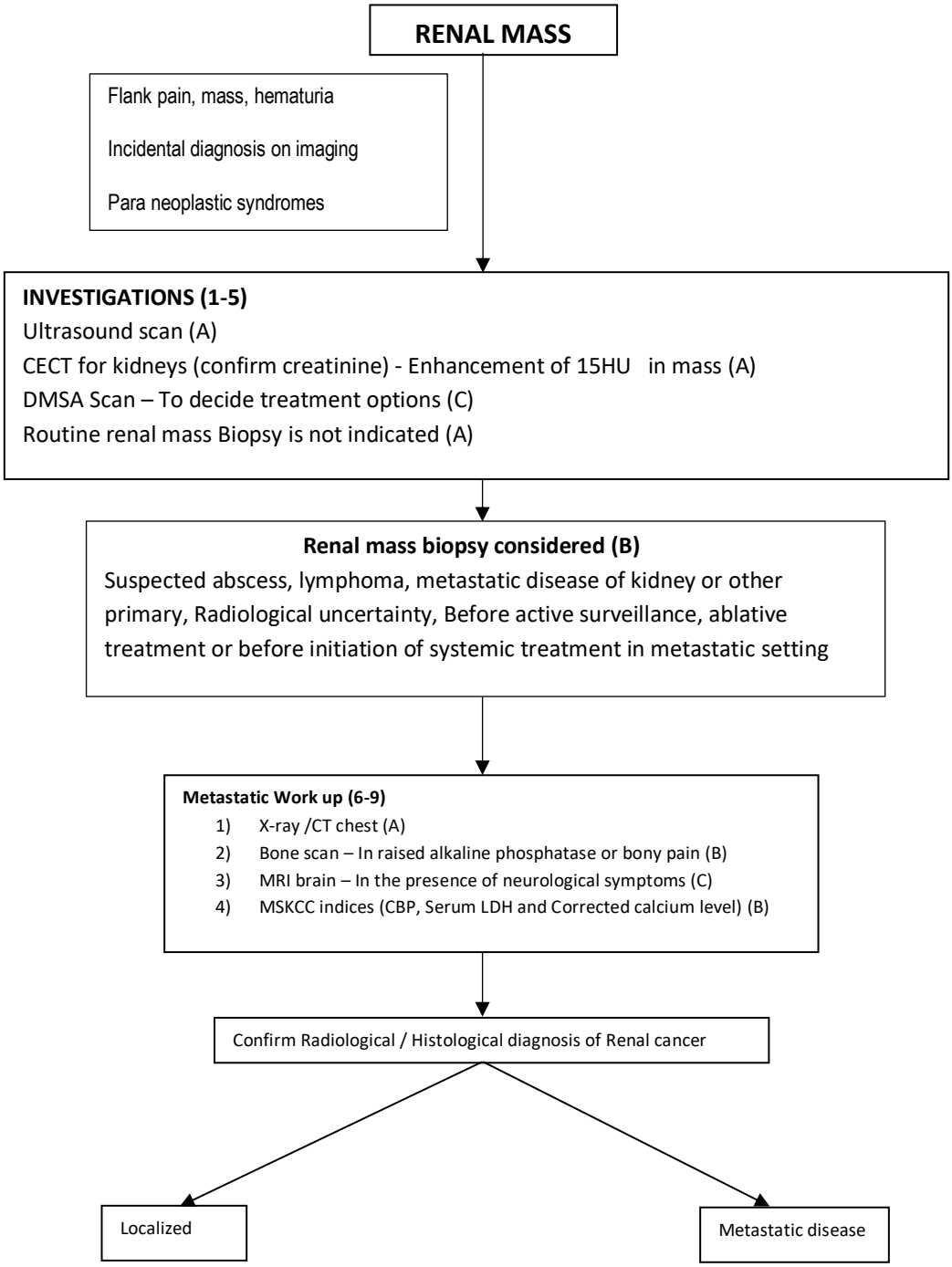
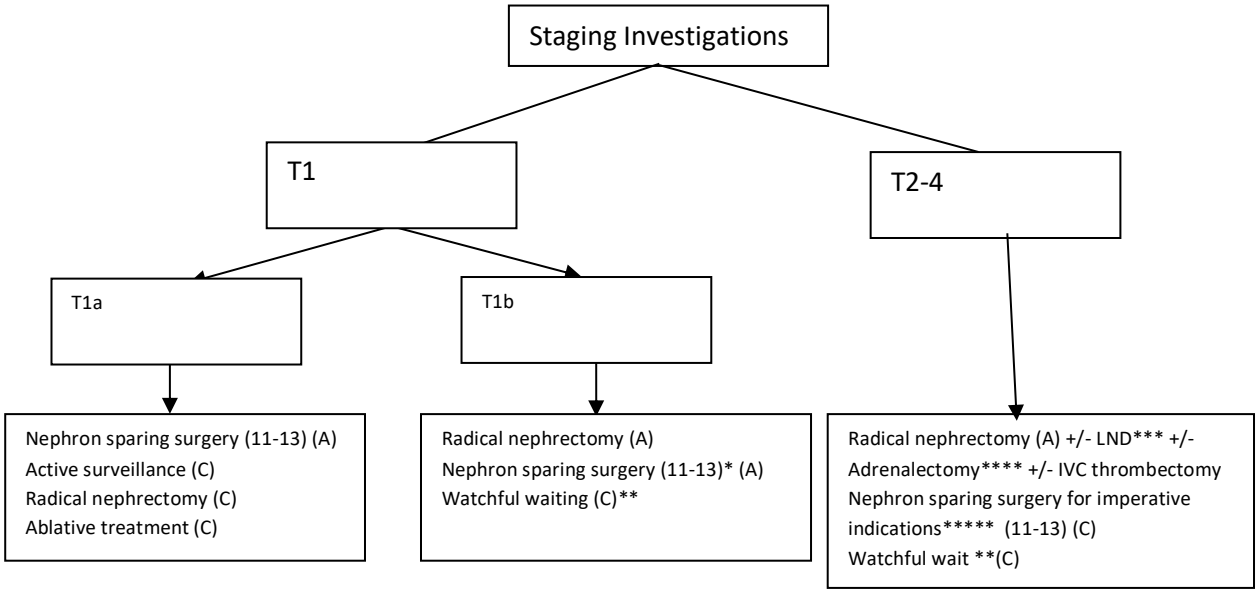
Investigational Pathway for Renal cell carcinoma



Treatment pathway for localized disease



Surgical approach - Open/ Laparoscopic / robotic-Individual surgeon discretion

*Nephron sparing surgery when technically feasible

**Watchful waiting: In patient with poor Performance status, significant comorbidity, asymptomatic, poor renal function

***LND – Lymph Node Dissection (18,19)

In patients of cT3-4, cN+, Intraoperative N+

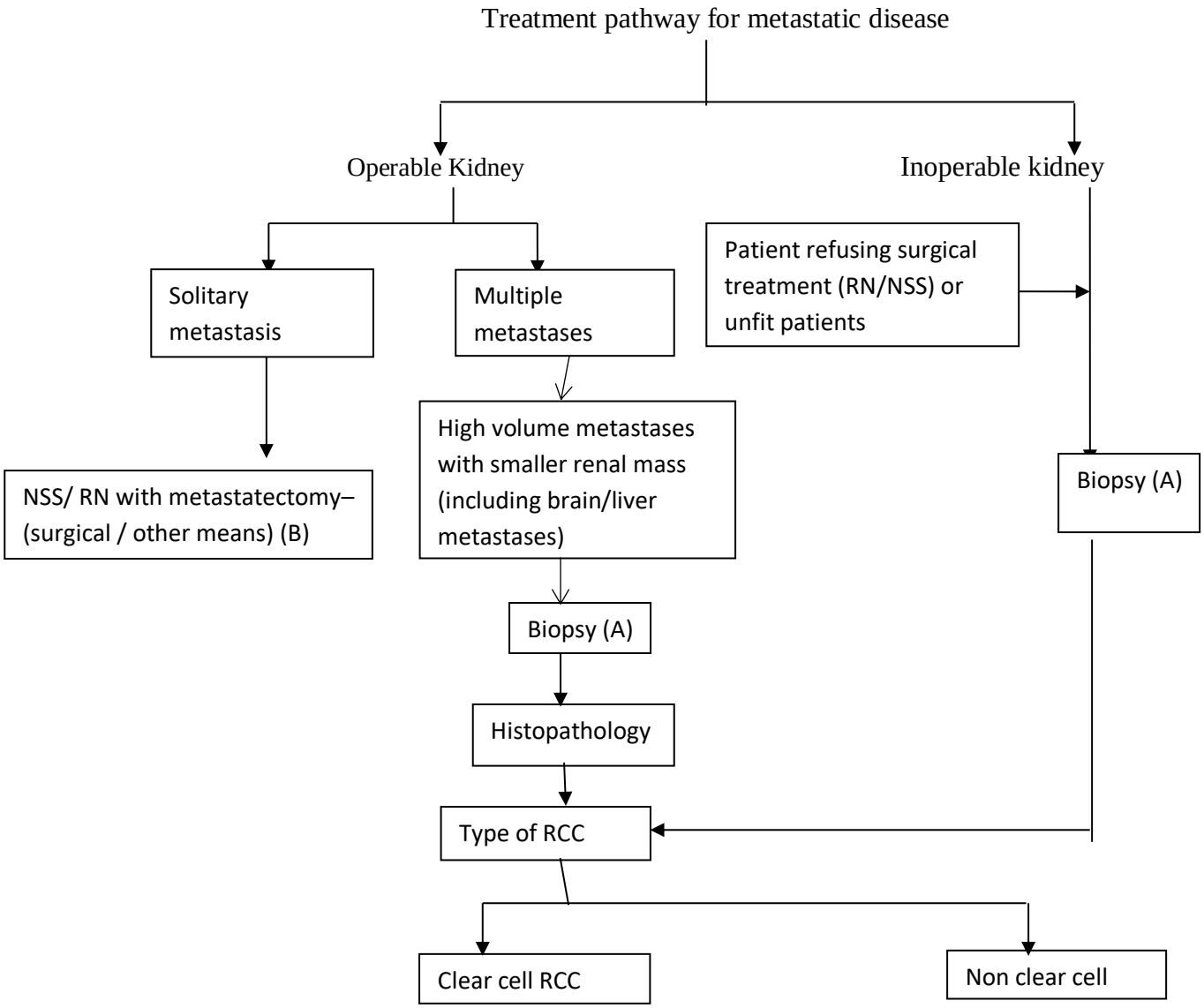
Rt side extent – Hilar, precaval, retrocaval, interaortocaval

Lt side extent – hilar, paraaortic, retroaortic, interaortocaval

****Adrenalectomy – only if contagious involvement

CT shows on abnormal adrenal gland,intra-operative findings suggest intra-adrenal metastatic spread or large upper pole tumour

***** Nephron sparing surgery when technically feasible in young patients who have bilateral disease, borderline renal function, multiple tumours.

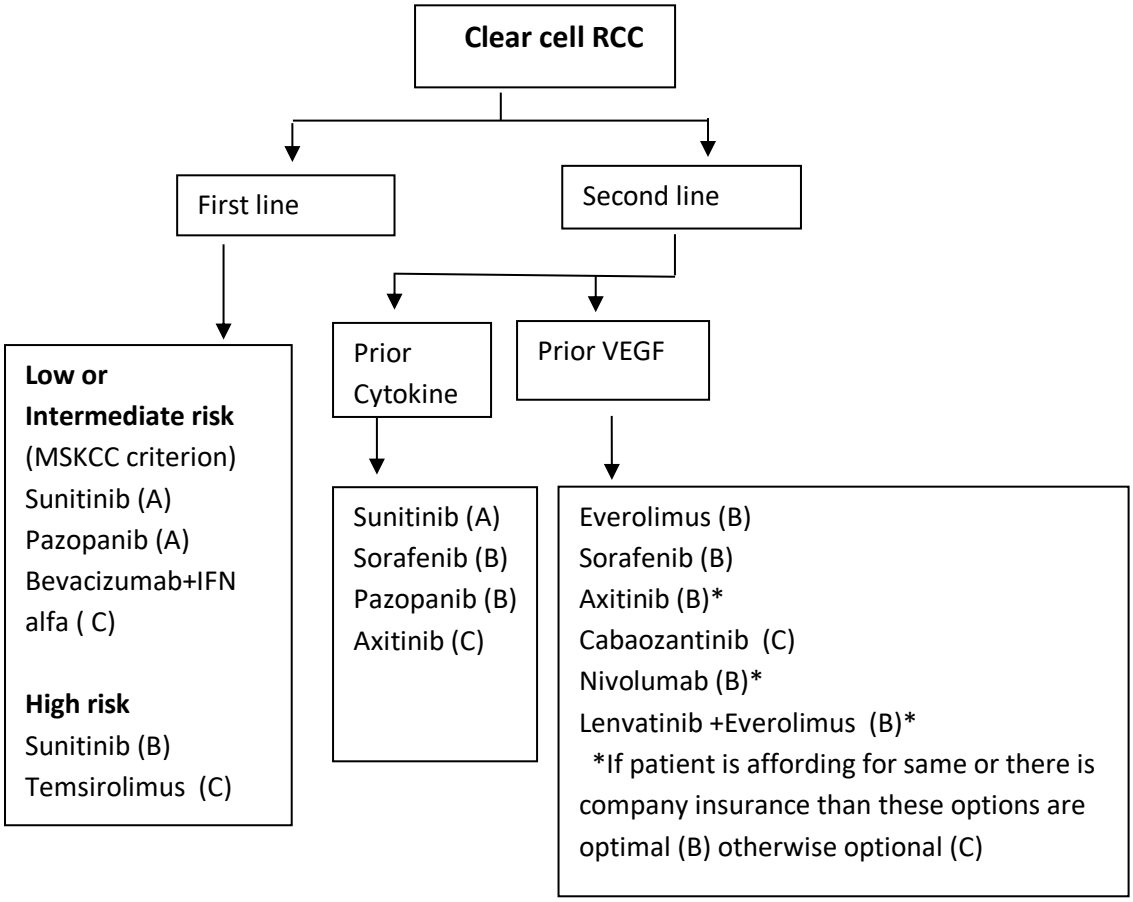


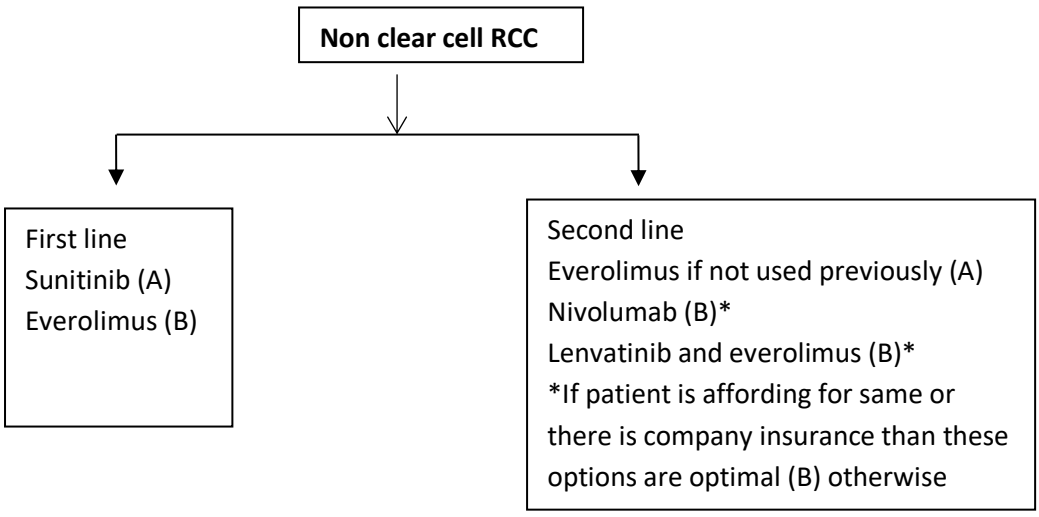
Surgery of primary renal mass in presence metastatic disease if planned for TKIs: As per MSKCC risk criteria: (B)

GOOD RISK: Primary renal mass surgery to be considered

INTERMEDIATE RISK: may or may not Individualized approach

POOR RISK: Primary renal mass surgery not to be done


Clear cell RCC
First line
Second line
Low or Intermediate risk
(MSKCC criterion)
Sunitinib (A)
Pazopanib (A)
Bevacizumab+IFN alfa (C)
High risk
Sunitinib (B)
Temsirolimus (C)
Prior Cytokine
Prior VEGF
Sunitinib (A)
Sorafenib (B)
Pazopanib (B)
Axitinib (C)
Everolimus (B)
Sorafenib (B)
Axitinib (B)*
Cabaozantinib (C)
Nivolumab (B)*
Lenvatinib +Everolimus (B)*
*If patient is affording for same or there is company insurance than these options are optimal (B) otherwise optional (C)


Non clear cell RCC
First line
Sunitinib (A)
Everolimus (B)
Second line
Everolimus if not used previously (A)
Nivolumab (B)*
Lenvatinib and everolimus (B)*
*If patient is affording for same or there is company insurance than these options are optimal (B) otherwise

Proposed surveillance schedule following treatment for RCC, taking into account patient risk profile and treatment efficacy (26-28)

		Surveillance						
Risk profile	Treatment	6 mo	1yr	2yr	3yr	4yr	5yr	>5yr
Low	RN/PN only	US	CT	US	CT	US	CT	Discharge
Intermediate	RN/PN/cryo/RFA	CT	CT	CT	US	CT	CT	CT once every 2 years
High	RN/PN/cryo/RFA	CT	CT	CT	CT	CT	CT	CT once every 2 years

- Blood test must include sr creatinine, blood urea nitrogen, electrolytes, sr calcium, alkaline phosphatise, and a liver function panel

SUGGESTED REFERENCES:

1. Davidson AJ, Hartman DS, Choyke PL, Wagner,BJ. Radiologic assessment of renal masses:implications for patient care. Radiology 1997;202:297-305

2. Bosniak MA. Renal-cell carcinoma. N Engl J Med. 1997 Mar 13; 336(11):810.

3. Zagoria RJ: Imaging of Small Renal Masses: AMedical Success Story. AJR Am J Roentgenol 2000,175, 945–955

4. Herts BR & Remer EM: Role of percutaneousbiopsy in the evaluation of renal and adrenal mass.AUA Update Series 2000, Vol 19, Lesson 36.

5. Li G, Culleron M, Gentil-Perret A, Tostain J: Characteristics of image-detected small renal masses: Implications for optimal treatment. Int J Urol 2004, 11, 63-67.

6. Campbell-Walsh Urology 10th edition: 2012; Elsevier.

7. Bechtold RE, Zagoria RJ. Imaging approach to staging of renal cell carcinoma. UrolClin North Am ,1997;24(3):507-22.

8. Koga S, Tsuda S, Nishikido M, et al. The diagnostic value of bone scan in patients with renal cellcarcinoma. J Urol 2001 Dec;166(6):2126-8.

9. Marshall ME, Pearson T, Simpson W, et al. Low incidence of asymptomatic brain metastases in patients with renal cell carcinoma. Urology 1990 Oct;36(4):300-2.

10. Sobin LH, Gospodariwicz M, Wittekind C (eds). TNM classification of malignant tumors. UICC International Union Against Cancer. 7th edn. Wiley-Blackwell, 2009: pp. 255-257.

11. Nieder AM and Taneja SS: The role of partial nephrectomy for renal cell carcinoma in contemporary practice. UrolClin North Am 2003;30, 529-42.

12. Hafez KS, Fergnay AF, Novick AC: Nephron sparing surgery for localized renal cell carcinoma: impact of tumour size on patient survival, tumour recurrence and TNM staging. J Urol 1999, 162, 1930-33.

13. P. Pelechano, m. Barrios benito, M. Ramírez, Backhaus, J. Rubio Briones, E. SolsonaNarbón, Nephrometry scores: A radiologist´s guide; European society of radiology: EPOS; 10.1594/ecr2013/C-2372

14. Robson CJ, Churchill BM, Anderson W. The results of radical nephrectomy for renal cell carcinoma. J Urol 1969; 101 : 297–301

15. Zini L, Perrotte P, Jeldres C, Capitanio U, Duclos A, Jolivet-Tremblay M, et al: A population-based comparison of survival after nephrectomy vs nonsurgical management for small renal masses.BJU Int. 2009 Apr;103(7):899-904

16. Volpe A, Panzarella T, Rendon RA, et al. The natural history of incidentally detected small renal masses. Cancer 2004 Feb;100(4):738-45.

17. Vitaly Margulis et al, International Consultation on Urologic Diseases and the European Association of Urology International Consultation on Locally Advanced Renal Cell Carcinoma; EUROPEAN UROLOGY 6 0 (2 0 1 1) 6 7 3 – 6 8 3

18. Leibovich BC and Blute ML: Lymph node dissectionin the management of renal cell carcinoma. UCNA2008, 35, 673-78.

19. O'Malley RL, Godoy G, Kanofsky JA, Taneja SS. The necessity of adrenalectomy at the time ofradical nephrectomy: a systematic review.J Urol. 2009, 181(5):2009-17.

20. Motzer RJ, Mazumdar M, Bacik J, et al. Survival and prognostic stratification of 670 patients with advanced renal cell carcinoma. J Clin Oncol,1999;17:2530–40.

21. Flanigan RC, Mickisch G, Sylvester R, et al. Cytoreductive nephrectomy in patients with metastatic renal cancer: a combined analysis. J Urol 2004 Mar;171(3):1071-6.

22. Murthy SC, Kim K, Rice TW, Rajeswaran J, Bukowski R, DeCamp MM, Blackstone EH. Can we predict long-term survival after pulmonary metastasectomy for renal cell carcinoma? AnnThorac Surg. 2005 Mar; 79(3):996-1003.

23. Escudier, B. et al. (2012) Treatment selection in metastatic renal cell carcinoma: expert consensus, Nat. Rev. Clin. Oncol. doi:10.1038/nrclinonc.2012.59

24. Jean-Jacques Patard et al, ICUD-EAU International Consultation on Kidney Cancer 2010:Treatment of Metastatic Disease; EUROPEAN UROLOGY 6 0 (2 01 1) 6 8 4 – 6 9 0

25. Robert J. Motzer et al, Treatment Outcome and Survival Associated With Metastatic Renal Cell Carcinoma of Non–Clear-Cell Histology; Journal of Clinical Oncology, Vol 20, No 9 (May 1), 2002: pp 2376-2381

26. Skolarikos, A., et al. A review on follow-up strategies for renal cell carcinoma after nephrectomy.EurUrol, 2007. 51: 1490.

27. Chin, A.I., et al. Surveillance strategies for renal cell carcinoma patients following nephrectomy.Rev Urol, 2006. 8: 1.

28. European association of Urology Guidelines 2016 edition available from: http://uroweb.org/guideline/renal-cell-carcinoma/#8 accessed on 23.12.2016

29. Adjuvant Sunitinib in High-Risk Renal-Cell Carcinoma after Nephrectomy. Ravaud A, Motzer RJ, Pandha HS, George DJ.N Engl J Med. 2016 Dec 8;375(23):2246-2254.

30. Motzer RJ, Escudier B at al.Nivolumab versus Everolimus in Advanced Renal-Cell Carcinoma. N Engl J Med. 2015;373(19):1803

31. Motzer et al:Lenvatinib, everolimus, and the combination in patients with metastatic renal cell carcinoma: a randomised, phase 2, open-label, multicentre trial. Lancet Oncol. 2015 Nov;16(15):1473-1482.

32. Arnaud Méjean, Alain Ravaud,et al;Sunitinib Alone or after Nephrectomy in Metastatic Renal-Cell Carcinoma;N Engl J Med 2018; 379:417-427