Urology CHEAT SHEETS by RAEU GRUPO DE RESIDENTES Y JÓVENES UROLOGOS José Agustín López-González @Jose_Agustn

METASTATIC RENAL CARCINOMA

INTRODUCTION: 2-3 % of all renal cell cancer.
Incidence 60-70 yo. 1.5:1 (male : female)
-Most RCC diagnosed by abdominal US or CT performed for other reason.
-Most common symptoms: hematuria, low back pain and palpable mass.
-Metastasis: lung 45%, Bones 30%, LNs 22%, Liver 20%.

PROGNOSTIC MODELS FOR RCC:

Stratifies patients into risk groups based on risk scores obtained from clinical and laboratory data. Assists clinicians in discussions about prognosis.

***MSKCC Score*:**
-Favourable Risk: 0 factors.
-Intermediate Risk: 1-2 factors.
-Poor Risk: 3-5 factors.

MSKCC CRITERIA	
FACTOR	**POOR PROGNOSTIC FACTOR**
Time from diagnosis to systemic treatment	< 12 months
Hemoglobin	< lower limit of normal
LDH	> 1.5 upper limit of normal
Calcium	> 10 mg/dL
Karnofsky Performance Status	< 80%

***International mRCC Database Consortium Risk Model* (*IMDC*):**
-Favourable Risk: 0 factors.
-Intermediate Risk: 1-2 factors.
-Poor Risk: 3-6 factors.

IMDC RISK MODEL	
FACTOR	**POOR PROGNOSTIC FACTOR**
Karnofsky Performance Status	< 80%
Time from diagnosis to systemic treatment	< 12 months
Hemoglobin	< lower limit of normal
Calcium	> upper limit of normal
Neutrophils	> upper limit of normal
Platelets	> upper limit of normal

DISEASE MANAGEMENT:

LOCAL: *1.Cytoreductive nephrectomy (CN).*

Standard-of-care before targeted therapy era. Overall Survival: Inmunotherapy (*IFN-α, IL-2*) vs inmunotherapy (*IFN-α, IL-2*) + *CN*: *CN* improved OS.
-*Sunitinib vs CN + sunitinib* (CARMENA): **sunitinib alone not inferior to CN followed by sunitinib in OS** (intermediate and MSKCC poor risk).
-Immediate *CN + sunitinib vs sunitinib* + deferred *CN + sunitinib* (SURTIME): **OS benefit** with **deferred CN approach** in ITT population.
Recommendations: perform immediate CN in patients with oligometastases when complete local treatment of the metastases can be achieved.
Do not perform CN in MSKCC poor-risk patients.

2.Embolisation. Patients unfit for surgery or with non-resectable disease. Symptomatic control.

3.Local therapy of metastases. Too heterogeneous data to meta-analyse. Benefit of complete metastasectomy in mRCC patients in terms of OS, CSS and delay of systemic therapy *(lung, liver, pancreas)* in retrospective comparative studies.
Bone metastases. Single-dose RT vs hypofractionated RT. Single-dose RT improves PFS.
Metastasectomy/curettage vs no surgery of solitary bone metastases. Higher CSS rate in the intervention group.
Brain metastases. Stereotactic radiosurgery (SRS) vs SRS + whole brain radiotherapy. Similar outcomes.

SYSTEMIC THERAPY:

1.Chemotherapy (*5-FU, gemcitabina, doxorrubicine*). **No chemotherapy as first line therapy in patients with clear-cell mRCC.**

2.Inmunotherapy.

IFN- α	IL-2	BEVACIZUMAB (*Monoclonal antibody against circulating VEGF*)
Moderate efficacy. Only effective in some groups. Increases response rates and PFS combined with *bevacizumab*.	Has been used since 1985 with response rates 7-27%. High **toxicity**.	***AVOREN*** (*Bevacizumab vs bevacizumab + IFN-α* in first-line): *B+IL-2* increases PFS. No differences in OS. No statistically significant benefit in OS. ***CALGB90206*** (*CN* + bevacizumab vs CN* + bevacizumab + IFN-α*): combined treatment with IFN-α increases PFS. No statistically significant benefit in OS. Side effects: *AHT (+AEC inhibitors), proteinuria, bleeding events, wound healing delay, pulmonary embolism…*

ANTI PD-1 AND ANTI CTLA-4 MONOCLONAL ANTIBODY.

NIVOLUMAB (*anti PD-1*)	IPILIMUMAB (*anti CTLA-4*)	PEMBROLIZUMAB (*anti PD-1*).
CHECKMATE 025 (*Nivolumab vs everolimus* after VEGF-targeted therapy): longer OS, better QoL and fewer adverse events with nivolumab.	**CHECKMATE 214** (*Nivolumab + ipilimumab vs sunitinib* in first-line): *N+I* significant advantage in OS, better in patients with ≥1% PD-L1 expression.	**KEYNOTE-426** (*Pembrolizumab + axitinib vs sunitinib* in first-line): *P+A* increases PFS and OS vs sunitinib among patients with previously untreated advanced RCC.

Side effects of immune checkpoint inhibitors: *fatigue, endocrine disorders, diarrhea, rash, hepatitis, pneumonitis…*

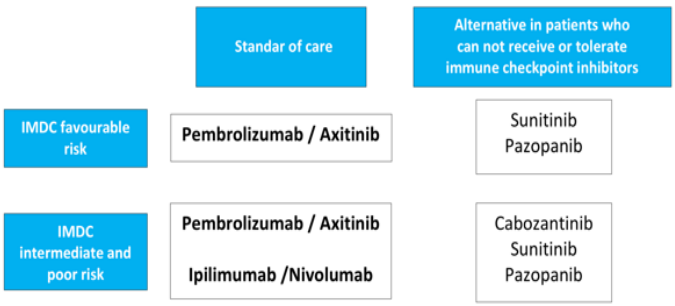
3.Tyrosine kinase inhibitors.

SORAFENIB	SUNITINIB	PAZOPANIB	CABOZANTINIB	AXITINIB
Not superior to *IFN-α* in untreated patients.	First-line monotherapy with *sunitinib* demonstrated longer PFS and OS vs *IFN-α*.	***VEG105192*** (*pazopanib vs placebo*): Improvement in PFS. ***COMPARZ*** (*Pazopanib vs sunitinib* in first-line): *pazopanib* not inferior PFS or OS compared to *sunitinib* *(well tolerated, **PISCES** trial).*	***METEOR*** (*Cabozantinib vs everolimus after VEGF-targeted therapies*): *cabozantinib* increased PFS and OS. ***CABOSUN*** (*Cabozantinib vs sunitinib* in first-line in intermediate- and poor-risk patients): *cabozantinib* increased median PFS, but not OS.	***AXIS*** (*Axitinib vs sorafenib* in second-line): PFS was greater for *axitinib*. ***KEYNOTE-426*** (*Pembrolizumab +axitinib vs sunitinib* in first-line): *P+A* increases PFS and OS.

Side effects of anti-angiogenic drugs: *asthenia, diarrhea, vomiting, hypertension, bleeding events, rash, pulmonary embolism…*

4.mTOR inhibitors.

-TEMSIROLIMUS.
ARCC (*Temsirolimus vs IFN-α vs temsirolimus + IFN-α* in first-line): median OS was higher in *temsirolimus* monotherapy group. *T+IFN-α* was not significantly superior. *IFN-α* toxicity was marked.
INTORSECT (*Temsirolimus vs sorafenib* in patients who had previously failed sunitinib): significant OS benefit for *sorafenib*.
-EVEROLIMUS.
RECORD-1 (*Everolimus vs placebo* in treatment of VEGF-refractory disease): *everolimus* increased PFS.
RECORD-3 (*Sunitinib* in first-line and *everolimus* in second-line vs *everolimus* in first-line and *sunitinib* in second-line): higher median PFS for first-line treatment in the *sunitinib* group.
Side effects of mTOR inhibitors: *asthenia, high serum glucose, dyslipidemia/hyperlipidemia, infections, mucositis, pneumonitis…*



Ljungberg B, et al. EAU GUIDELINES ON REANAL CELL CARCINOMA 2020. http://uroweb.org/guidelines/2020