Grupo Português
Génito - Urinário

XXVIII Workshop
Urologia Oncológica

UM CARCINOMA DE CÉLULAS CLARAS COM METASTIZAÇÃO TIROIDEIA

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Conflitos de interesse

- Sem conflitos de interesse

Introdução e Métodos

- O Carcinoma de células claras representa 75-80% dos tumores renais;
- Em CCCR M0, em 20-30% dos casos, as recidivas ocorrem nos primeiros 5 anos.

Métodos: informação presente no processo clínico do doente.

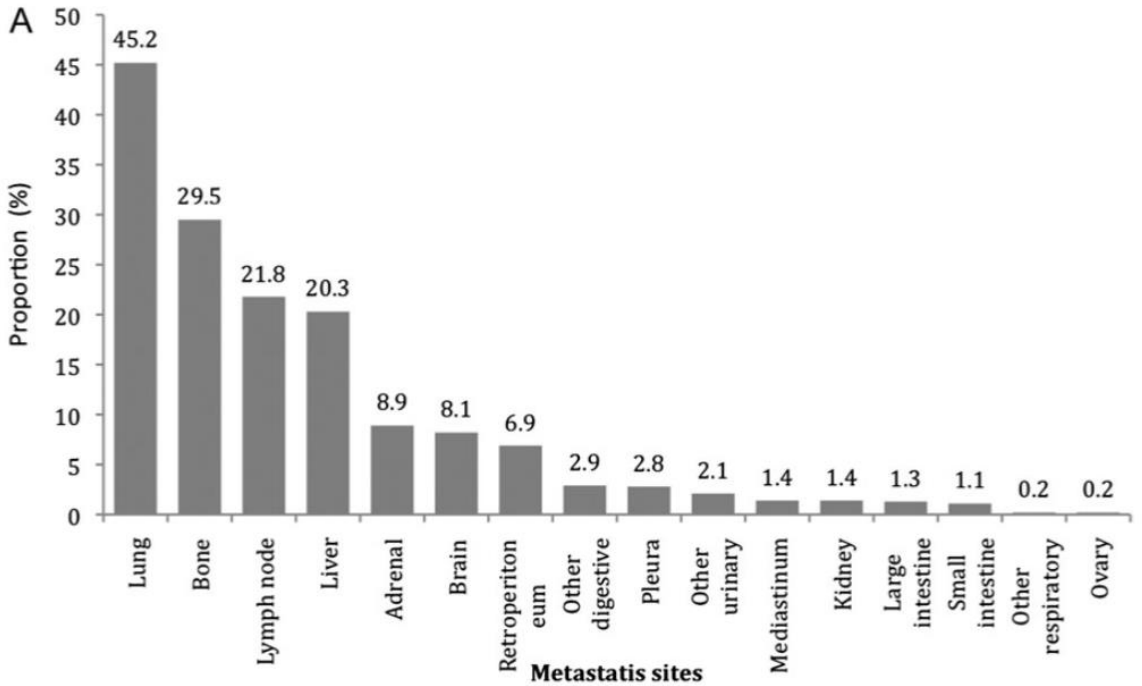
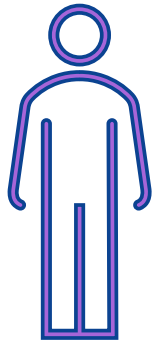
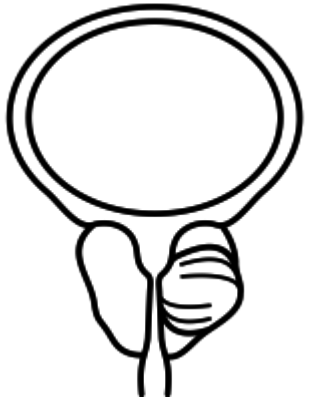


Figura 1 – Locais de Metastização de CCR, retirado de "Distribution of metastatic sites in renal cell carcinoma: A population-based analysis. *Annals of Oncology*"

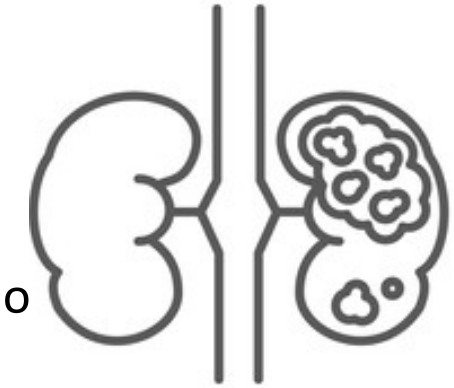
Caso Clínico



- Idade: 84 anos
- PS: ECOG 0
- Comorbilidades: DRC, HTA
- Medicação regular: Amlodipina, Levotiroxina



- Abril 2014
- Adenocarcinoma da Próstata
- Estadio IIb
- Radioterapia local + Hormonoterapia de longa duração
- Sob vigilância ativa, ultimo PSA 0,3ng/mL (estável)



- Setembro 2015
- Carcinoma de células renais claras
- Nefrectomia radical
- Estadio pT3a(5,5cm)NxM0R0
- Fuhrman Grau 3
- SSIGN Score 5 – Risco Intermédio
- Sob vigilância ativa com exames de imagem periódicos

Caso Clínico

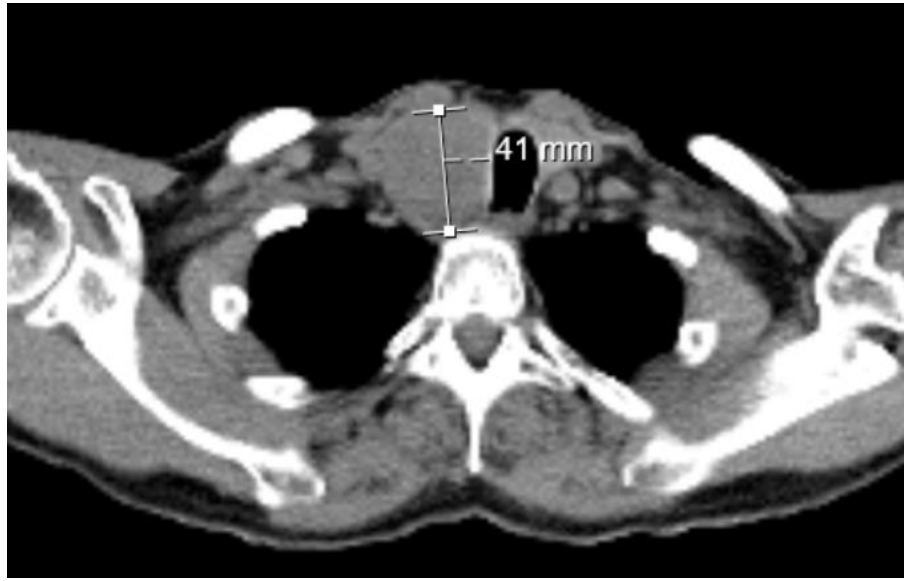
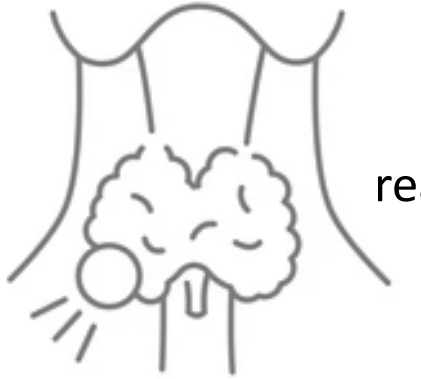


Fig. 2 - Outubro de 2022 – em TC de vigilância nódulo de novo de 41mm a nível da tiroide

Fig. 3 -PET-CT 18-FDG, Outubro 2022

Caso Clínico



Outubro 2022, realizada tiroidectomia total

- Metástase única de carcinoma de células renais claras
- 3 carcinomas papilares da tiróide, com dimensões <0,1mm

RE-ESTADIAMENTO

TC-TAP: Sem lesões de novo ou suspeitas

Conclusão: Recidiva tardia de Ca de Células claras, de risco intermédio, IDMC 5, que se manifesta por metástase única a nível tiroideu

Discussão

Model	Outcome	C-index	Features
Kattan (2001)	RFS[a]	0.74	Symptoms (incidental, local, systemic symptoms), Histology (chromophobe, papillary, clear cell), Tumor size, 1997 pT-stage[2]
UISS (2001)	OS[b]	ND[e]	1997 TNM Stage, Fuhrman grade, ECOG performance status[11]
SSIGN (2002)	CSS[c]	0.84	1997 T stage, N stage, M stage, Tumor size, Fuhrman grade, Necrosis[13]
Leibovich (2003)	MFS[d]	0.819	Tumor Stage, Regional lymph node status, Tumor Size, Fuhrman grade, Necrosis[8]
Sorbellini (2005)	RFS	0.82	Size, 2002pT, Fuhrman grade, Necrosis, Vascular invasion, Presentation (incidental, local symptoms, systemic symptoms)[14]
Karakiewicz (2009)	CSS	ND	Age, Gender, Symptoms (no, local, systemic), Tumor Size, T-stage, Metastasis[12]
Leibovich (2018)	RFS	0.83	Constitutional symptoms (yes, no), WHO/ISUP 2016 tumor grade, Necrosis, Sarcomatoid differentiation, Tumor size, Perinephric or renal sinus fat invasion, Tumor thrombus level, Extension beyond kidney, Nodal involvement[15]

Fig. 5 – Modelos de predição de risco de recidiva de CCR – retirado de "A three-feature prediction model for metastasis-free survival after surgery of localized clear cell renal cell carcinoma. *Scientific Reports*, *11*."

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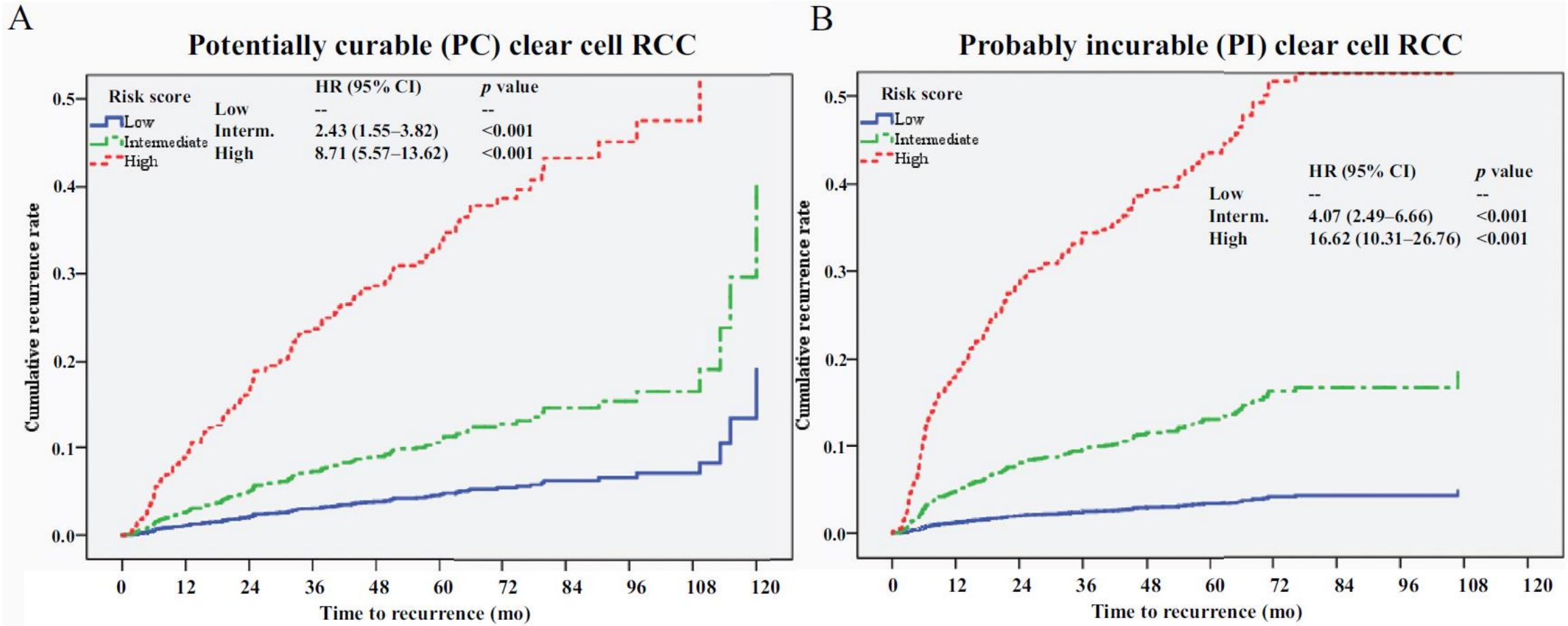

Fig. 5 – Taxa de recidiva de CCR, retirado de "Long-term outcomes of follow-up for initially localised clear cell renal cell carcinoma: Recur database analysis. *European Urology Focus"*

Discussão

	3m	6m	12m	18m	24m	30m	36m	>3A	>5A
Risco Baixo		TC		TC		TC		TC de 2 em 2 anos	
Risco Intermédio		TC	TC		TC		TC	TC anualmente	TC de 2 em 2 anos
Risco Alto	TC	TC	TC	TC	TC		TC		

Fig. 6 – Recomendações de Follow-up pós nefrectomia com intuito curativo, com base no risco de recidiva, adaptado das Guidelines da EAU

Discussão

ESMO

- **Metastasectomy and other local treatment strategies** including whole-brain radiotherapy (WBRT), conventional radiotherapy (RT), stereotactic radiosurgery (SRS), stereotactic body radiotherapy (SBRT), CyberKnifeVR RT and hypofractionated RT **can be considered and carried out for selected patients after multidisciplinary review**.

- Regarding **the M1 NED population, systemic therapy** with programmed cell death protein 1 (PD-1)-based combination therapy is the standard of **care for patients who relapse within one year of nephrectomy** [I, A].

- Metastasectomy as an alternative to this systemic therapy in patients with synchronous or early oligometastatic disease is not usually recommended [I, D] and requires a multidisciplinary team decision.

- **Adjuvant pembrolizumab can be offered to these patients after complete resection of their oligometastatic disease [II, B]**.

Discussão

- *7.3.2.5 Adjuvant treatment in cM0 patients after metastasectomy*

Patients after metastasectomy and no evidence of disease (cM0) have a high risk of relapse. Recent attempts **to reduce RFS by offering adjuvant TKI treatment after metastasectomy did not demonstrate an improvement in RFS**. (…)

KEYNOTE-564 included a small percentage of patients who were treated by nephrectomy and **complete metastasectomy within one year after primary diagnosis** (…) **metachronous interval of < 1 year for recurrences following surgery with curative intent is a poor prognostic factor by IMDC classification. Systemic therapy based on immune combinations has stronger levels of evidence than surgery in this intermediate/advanced disease setting** (…). **DFS HR of 0.29** (95% CI: 0.12-0.69) in **favour of resection of M1 to NED plus pembrolizumab shows** that patients with subclinical, but **progressive disease who were subjected to metastasectomy had a benefit of adjuvant systemic therapy with pembrolizumab**.

Discussão - tratamento sistémico?

NCCN National Comprehensive Cancer Network®

- (…) **The panel also recommends adjuvant pembrolizumab for treatment of stage 4 ccRCC after metastasectomy with complete resection of disease, within a year of nephrectomy.** (…)

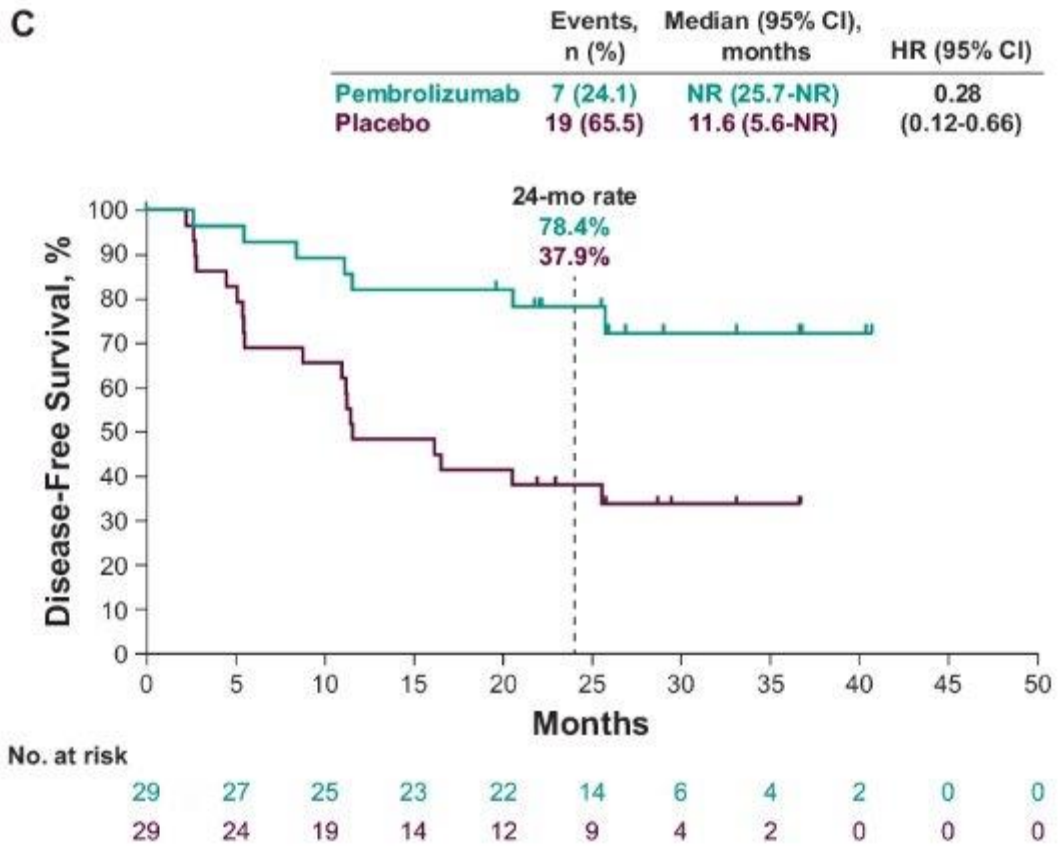

Fig. 7 – Taxa de sobrevivência sem doença nos doentes participantes no Trial KEYNOTE-564, com estadio M1 NED (sem evidência de doença) sujeitos a metastectomia e terapêutica adjuvante com Pembrolizumab, até 1 ano após nefrectomia. Retirado de "ASCO GU 2023: Adjuvant Pembrolizumab for Renal Cell Carcinoma (RCC) Across UCLA Integrated Staging System Risk Groups and Disease Stage: Subgroup Analysis from the KEYNOTE-564 Study"

Conclusões

- O carcinoma de células renais é uma patologia muito heterogénea;
- Apesar da imagiologia tiroidea não fazer parte da vigilância dos tumores renais, deverão ser valorizados nódulos de novo e considerada a hipótese de metastização.
- Não está definido quando se deve iniciar terapia sistémica nos casos de recidiva de CCR;
- Há benefício na realização de terapêutica adjuvante com Pembrolizumab em casos de recidiva metastática até 1 ano após nefrectomia.

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