

Grupo Português  
Génito - Urinário



# XXVIII Workshop

## Urologia Oncológica

• EPIC SANA Marquês Hotel  
LISBOA



# A distinct case of polycythemia in mRCC

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# DISCLOSURE OF INTEREST

- None



# CLINICAL CASE

- Male patient, 60 y.o.
- ECOG PS 0
- Medical history: vitiligo
- No usual medication
- No known allergies
- No smoking habits
  
- Family history: prostate, colon and lung cancer



# CLINICAL CASE

- Beginning July 2018 with painless macroscopic haematuria
- Sept 2018 presence of renal mass
- Oct 2018 - CT scan with lung metastatic lesions





- Cytoreductive left nephrectomy Nov 2018
  - Diagnosis of clear cell Renal Cell Carcinoma, pT3a
  - 01/2019 CT with disease progression (lymph nodes + lung)
  - International Metastatic RCC Database Consortium > intermediate risk
  
- Feb 2019
  - Transferred to HSM – CHLN

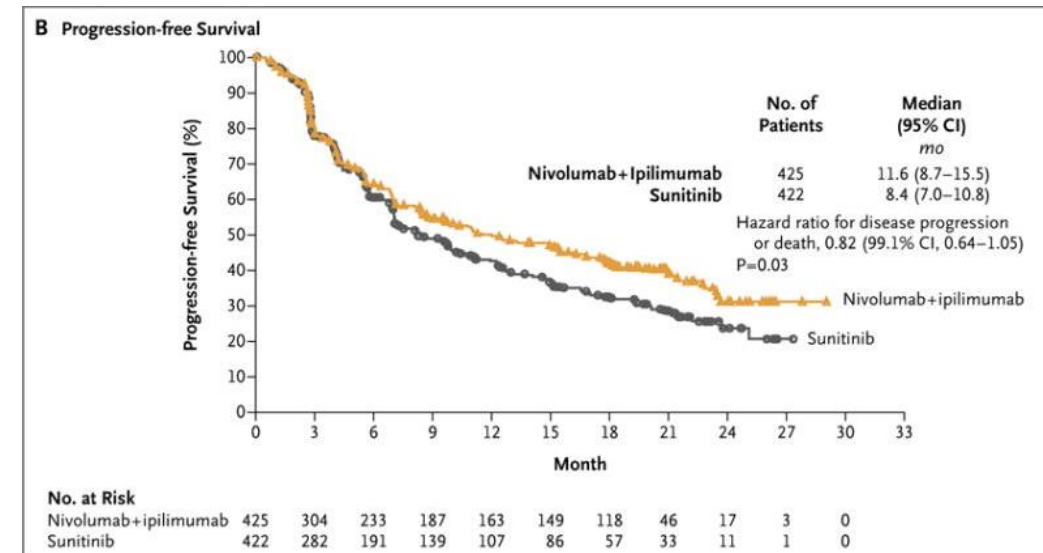
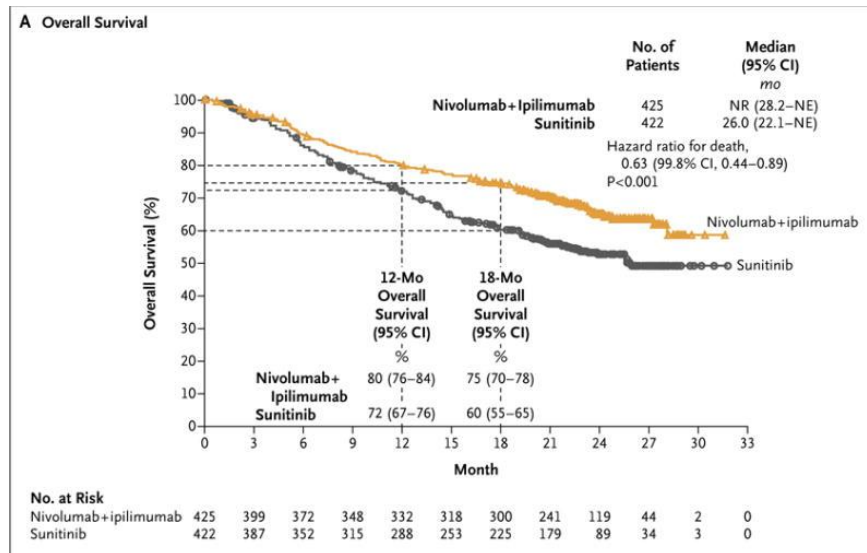




- Request to begin nivolumab/ipilimumab

Denied

- ✓ N Engl J Med 2018 CheckMate 214 - Overall survival and objective response rates were significantly higher with nivolumab plus ipilimumab than with sunitinib among intermediate- and poor-risk patients with previously untreated advanced RCC





- Started Sunitinib March 2019
  - Partial response with Sunitinib with reduction of lung metastatic lesions in size and number
  - March 2021 >> disease progression after 18 cycles
  - ❖ Side effects – hypertension controlled with medication

Nephrectomy  
Nov 2018

Sunitinib Mar 2019 – Mar 2021  
Partial Response

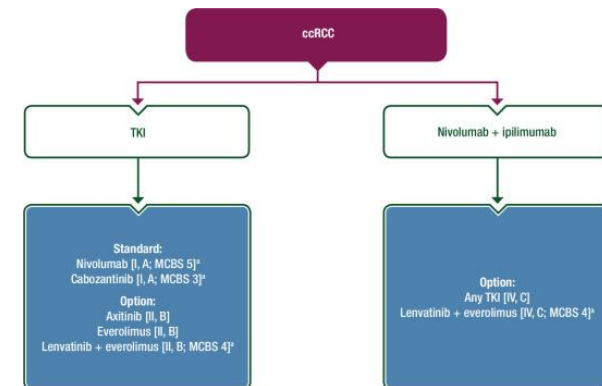


- Started Nivolumab 2L Apr 2021

- ✓ N Engl J Med 2017 Checkmate 025 – OS was longer and fewer grade 3 or 4 adverse events occurred for nivolumab versus everolimus in treatment-experienced patients with advanced renal cell carcinoma (who previously received 1-2 lines of anti-angiogenic therapy)

- No response > disease progression Sep 2021 (6 cycles)

- Side effects: aggravated vitiligo



SPECIAL ARTICLES | VOLUME 30, ISSUE 5, P706-720, MAY 2019  
Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Escudier et al. ESMO Guidelines Committee

Nephrectomy  
Nov 2018

Sunitinib Mar 2019 – Mar 2021  
Partial Response

Nivolumab  
Apr -Sep 2021

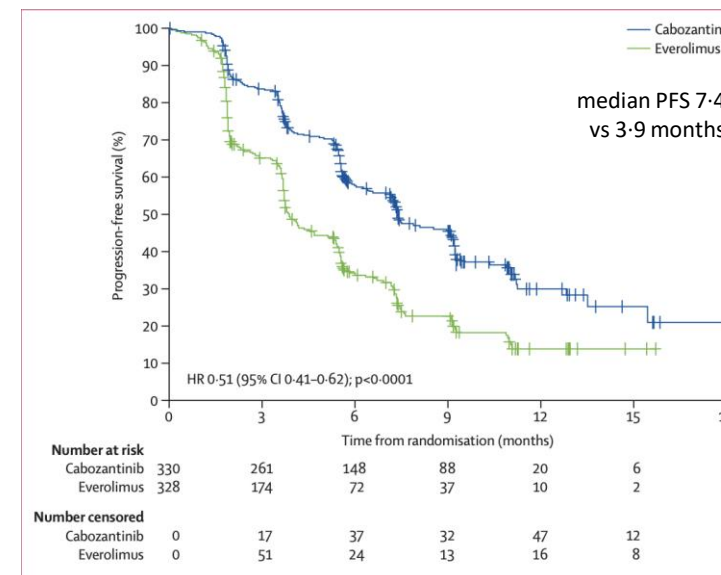
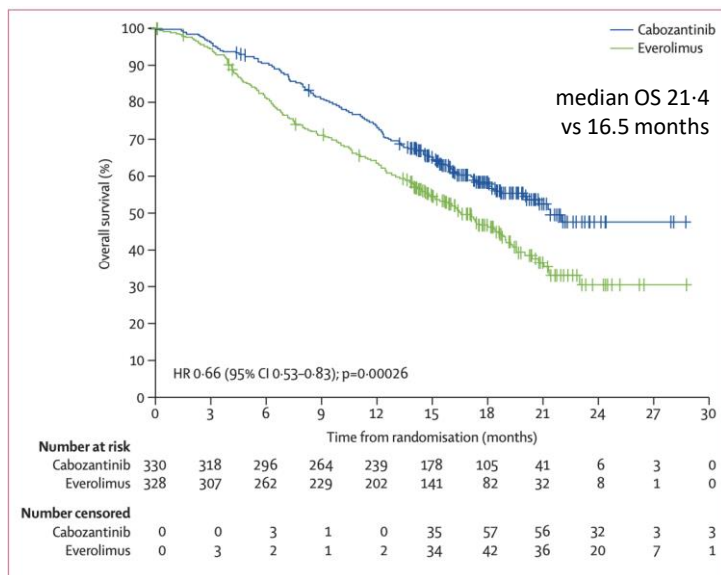




- Request to begin cabozantinib 3L

Denied

- ✓ Lancet Oncol 2016 METEOR trial - Cabozantinib increased OS, delayed disease progression, and improved the objective response compared with everolimus, in patients previously treated with one or more VEGFR tyrosine-kinase inhibitors





- Started everolimus 3L Nov 2021
  - Stable disease
  - ❖ Side effects: pneumonitis after 8 cycles with need to suspend everolimus and initiate corticotherapy
    - ✓ The Lancet 2008 RECORD-1 trial - Efficacy of everolimus in advanced renal cell carcinoma: a double-blind, randomised, placebo-controlled phase III trial > median PFS 4.0 vs 1.9 months
      - ❖ Adverse effects 8% pneumonitis

Nephrectomy  
Nov 2018

Sunitinib Mar 2019 – Mar 2021  
Partial Response

Nivolumab  
Apr -Sep 2021

Everolimus  
Nov 2021 –Aug 2022



- Started Cabozantinib 4L Oct 2022
  - ❖ Side effects: polycythemia during 1<sup>st</sup> cycle (Hb 15g/dL > 19.7g/dL; Htc 48.2% > 62.5%) with need to start therapeutic phlebotomies
    - No hyperviscosity symptoms
  - Aggravated polycythemia after 2 cycles (Hb 20.7g/dL, Htc 65.5%)
  - Therapeutic phlebotomies were done to reduce the hematocrit; cabozantinib was suspended for five weeks
    - (Hb 20.7g/dL > 18.5 g/dL > 15.9g/dL; Htc 65.5% > 58.7% > 51.0%)

Nephrectomy  
Nov 2018

Sunitinib Mar 2019 – Mar 2021  
Partial Response

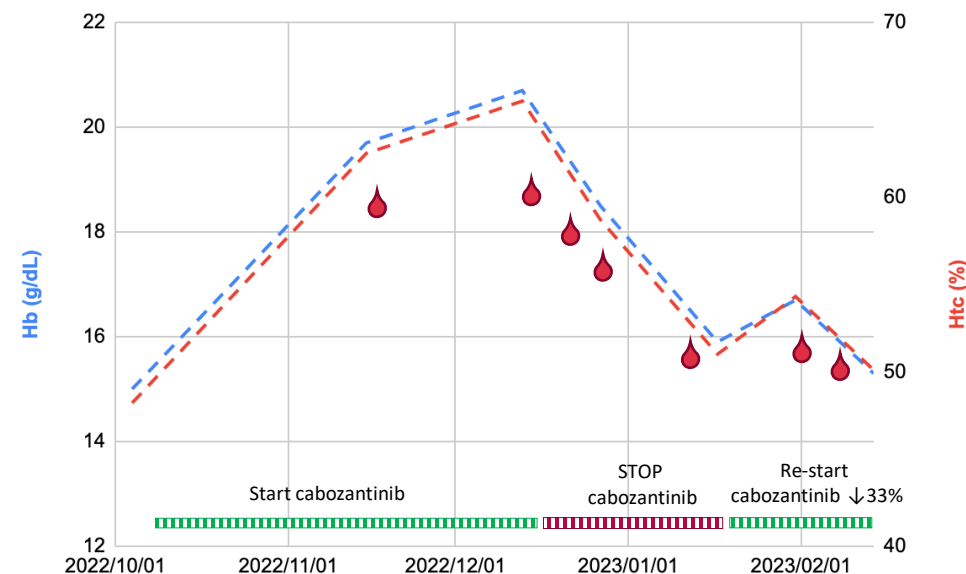
Nivolumab  
Apr -Sep 2021

Everolimus  
Nov 2021 –Aug 2022

Cabozantinib  
Oct 2022 ...



- Restarted Cabozantinib with reduced dose Jan 2023
  - After two weeks Hb 16.7g/dL (< 15.9g/dL), Htc 54.3% (< 51%)
- Maintain Cabozantinib and regular phlebotomies
  - Target Htc <55% and no hyperviscosity symptoms



Nephrectomy  
Nov 2018

Sunitinib Mar 2019 – Mar 2021  
Partial Response

Nivolumab  
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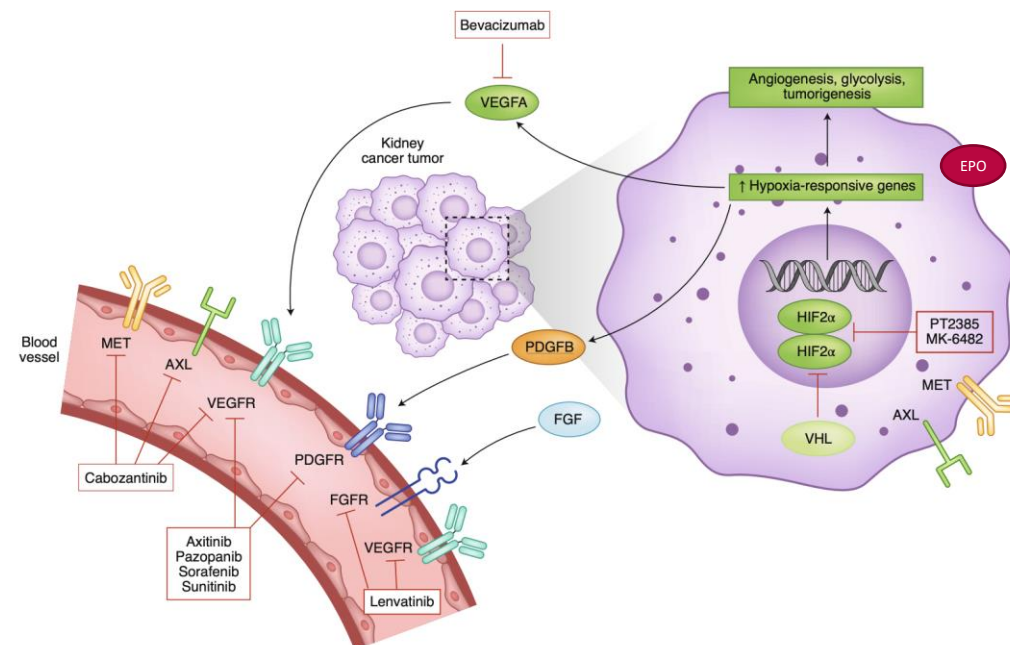


- Polycythemia is reported in VEGF Receptor Tyrosine Kinase Inhibitor Axitinib, but not yet reported in Cabozantinib

✓ In phase III study AXIS, axitinib vs sorafenib in 2L, 10% of patients treated with axitinib presented elevated haemoglobin (...) these increases appeared a few weeks after treatment initiation and seemed associated with better outcomes.

Molinier et al.. BMC Cancer. 2017

- Polycythemia is also a known paraneoplastic syndrome associated with Renal Cell Carcinoma



Adapted from Choueiri and Kaelin. Targeting the HIF2-VEGF axis in renal cell carcinoma. Nat Med 26, 1519-1530 (2020)

Nephrectomy  
Nov 2018

Sunitinib Mar 2019 – Mar 2021  
Partial Response

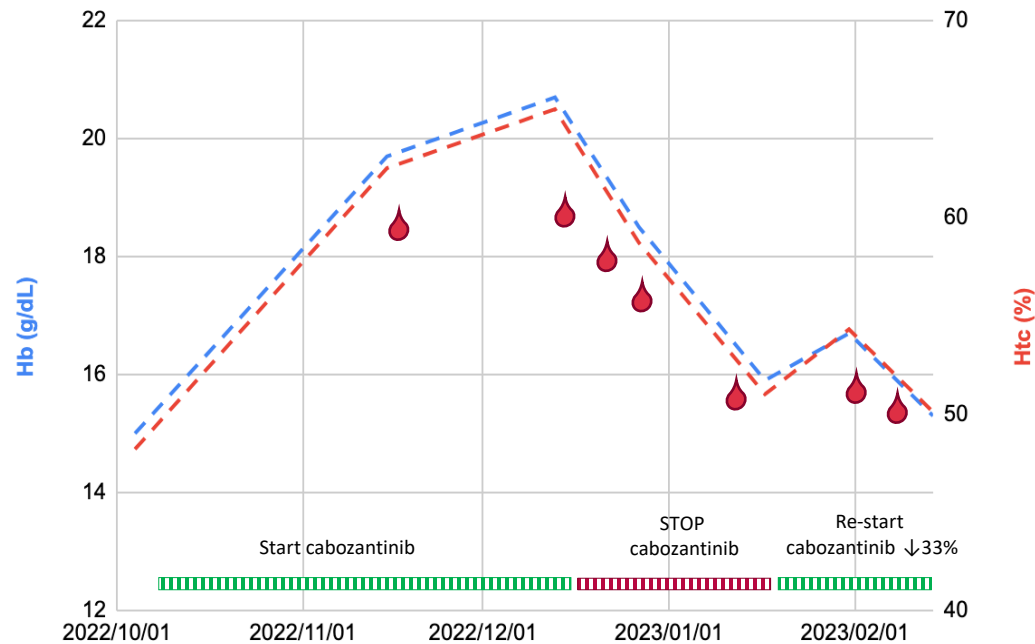
Nivolumab  
Apr -Sep 2021

Everolimus  
Nov 2021 –Aug 2022

Cabozantinib  
Oct 2022 ...



- Restart of Cabozantinib aggravated polycythaemia supporting the hypothesis of Cabozantinib induced polycythaemia



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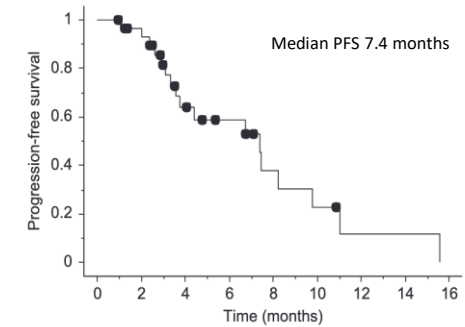
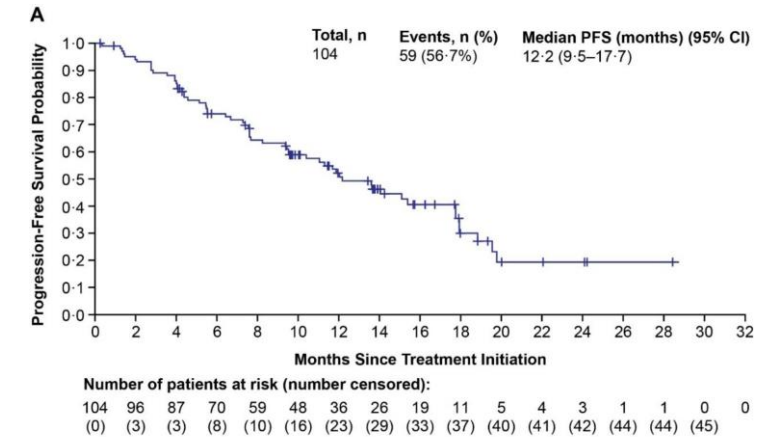
### • What's next?

#### • Pembrolizumab + Lenvatinib?

- ✓ Lee et al. Lenvatinib plus pembrolizumab in patients with either treatment-naive or previously treated metastatic renal cell carcinoma (Study 111/KEYNOTE-146): a phase 1b/2 study. *Lancet Oncol.* July 2021
- ✓ Polycythemia not reported as a side effect

#### • Pazopanib?

- ✓ Rautiola et al. Pazopanib after sunitinib failure in patients with mRCC. *Acta Oncologica* 2014
- ✓ Polycythemia reported as a rare side effect (0.03%)



Nephrectomy  
Nov 2018

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Obrigada