3.86: Lenvatinib plus Pembrolizumab or Everolimus for Advanced RCC with Dr. Karine Tawagi

↗ Type	Plenary Session

We Discuss:

Plenary Session 3.86 Show Notes

Overview

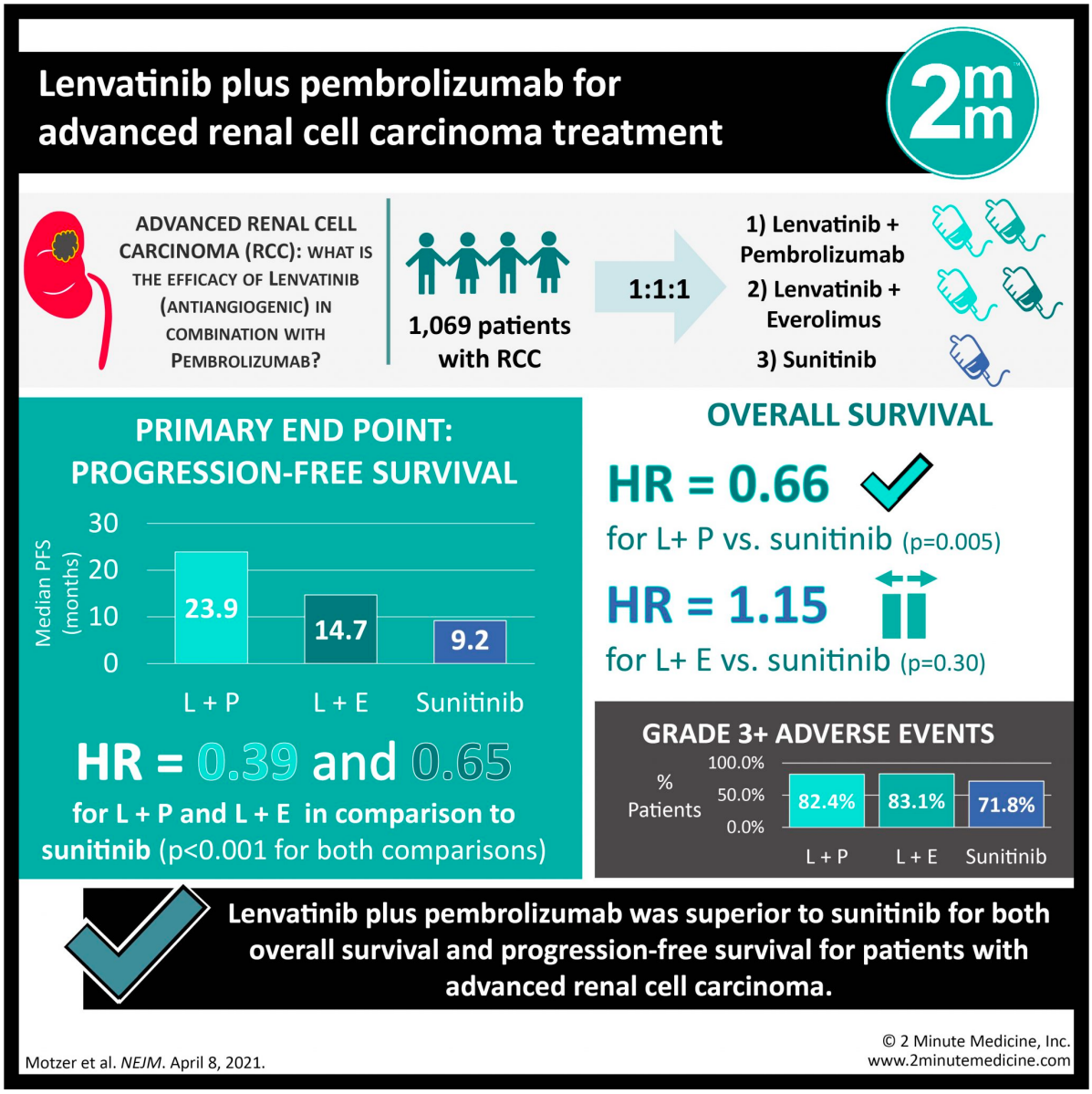
Conversation with Dr. Karine Tawagi [1:06]

- **YouTube**
  - Watch this conversation on youtube
- **Introduction**
  - Dr. Tawagi earned her M.D. from St. George’s University School of Medicine

- She completed her residency at St. Joseph Mercy Hospital Program
    - She is now Chief Fellow at Ochsner Medical Center in New Orleans, LA
- Follow on her on Twitter @DrKarineTawagi

Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma [1:20]

- **Published in the NEJM**



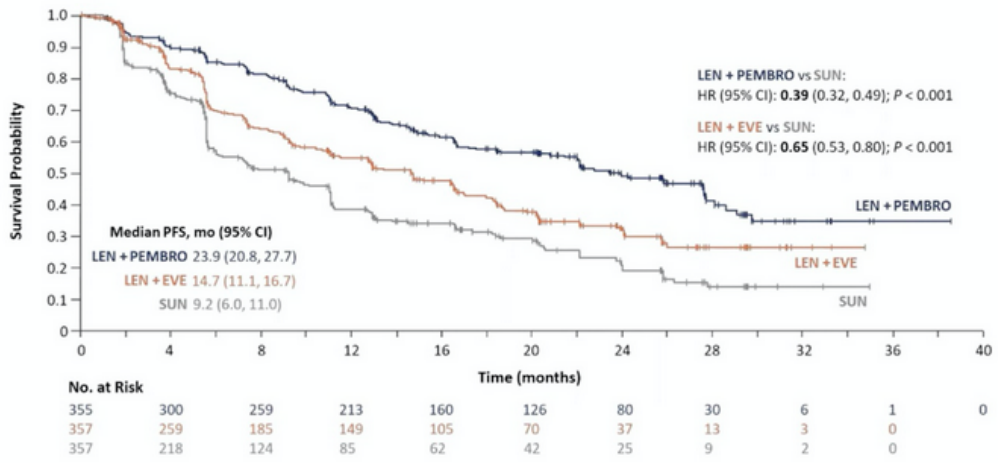
Source

- **Design**
  - Phase 3 trial (1:1:1)
    1. Lenvatinib (20 mg orally once daily) + pembrolizumab (200 mg intravenously once every 3 weeks)
    2. Lenvatinib (18 mg orally once daily) + everolimus (5 mg orally once daily)
    3. Sunitinib (50 mg orally once daily, alternating 4 weeks receiving treatment and 2 weeks without treatment)
  - Population
    - Patients with stage IV renal cell carcinoma
      - Inclusion criteria
        - Karnofsky Performance Scale of more than 70
        - Controlled blood pressure
        - Adequate organ function
      - Exclusion criteria
        - Untreated brain mets
        - Radiation within 3 weeks
        - Long term steroids
        - Particular management of other diseases
  - Endpoints
    - Primary endpoint → PFS
    - Secondary endpoint → OS, Safety
  - <u>Sunitinib versus Interferon Alfa in Metastatic Renal-Cell Carcinoma</u>
    - Motzer et al., NEJM

> *"The primary end point was progression-free survival. Secondary end points included the objective response rate, overall survival, patient-reported outcomes, and safety." - Motzer et al.*

- **Results [8:08]**
  - PFS

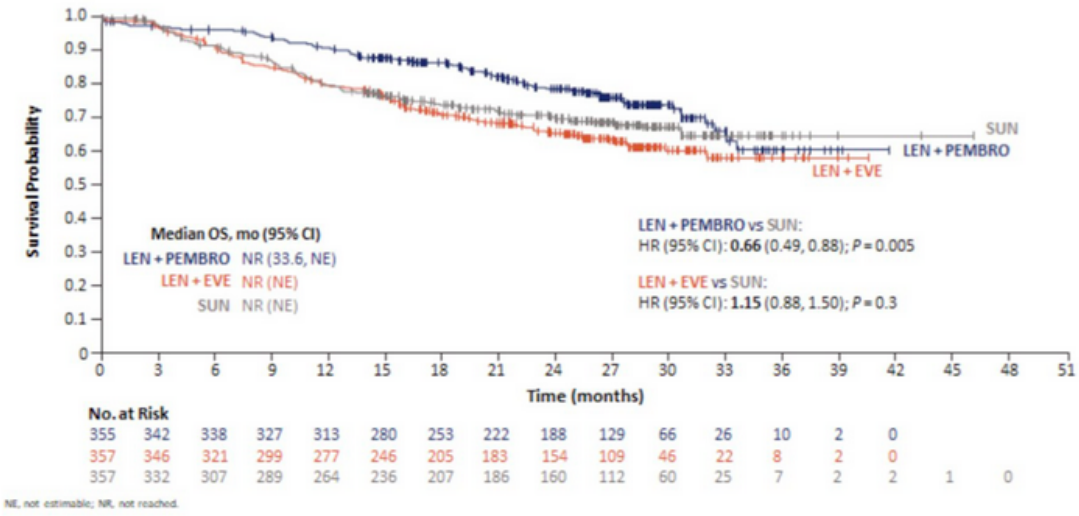
> *"Progression-free survival was longer with lenvatinib plus pembrolizumab than with sunitinib (median, 23.9 vs. 9.2 months; hazard ratio for disease progression or death, 0.39; 95% confidence interval [CI], 0.32 to 0.49; P<0.001) and was longer with lenvatinib plus everolimus than with sunitinib (median, 14.7 vs. 9.2 months; hazard ratio, 0.65; 95% CI, 0.53 to 0.80; P<0.001)." - Motzer et al.*



Source

  - OS

> *"Overall survival was longer with lenvatinib plus pembrolizumab than with sunitinib (hazard ratio for death, 0.66; 95% CI, 0.49 to 0.88; P=0.005) but was not longer with lenvatinib plus everolimus than with sunitinib (hazard ratio, 1.15; 95% CI, 0.88 to 1.50; P=0.30)." - Motzer et al.*



Source

- ORR
  - Lenvatinib + pembrolizumab
    - ORR 71%; complete response [CR] 16%
  - Lenvatinib + everolimus
    - ORR 54%; CR 10%
  - Sunitinib
    - ORR 36%; CR 4%

- **Post-protocol [13:00]**
  - In the lenvatinib + pembrolizumab group, 55% of patients went on to second line therapy after of which:
    1. Half had anti-angiogenic therapy
    2. 13% had a PD-1 or PD-1 one inhibitor

3. 3% mTOR inhibitor
4. 3% CTLA-4 inhibitor

- **Limitations [15:00]**
  1. Open-label design
  2. No QoL or PROs
  3. They should have included a higher number of poor risk patients
  4. No rate race breakdown
- **Dr. Prasad's thoughts [21:26]**
  - Here's the study you do:
    - Control arm:
      - Let cooperative group doctors pick any of the doublets that are on the market
    - Intervention arm:
      - Pembrolizumab (3 doses then discontinue) + Sunitinib
- **Water cooler talk [24:00]**
  - This study doesn't really answer a new clinical question or, or offer a significantly better treatment for patients
- **Other literature mentioned:**
  - Study of Cabozantinib in Combination With Nivolumab and Ipilimumab in Patients With Previously Untreated Advanced or Metastatic Renal Cell Carcinoma (COSMIC-313)
  - Comparative effectiveness of axitinib versus sorafenib in advanced renal cell carcinoma (AXIS): a randomised phase 3 trial
    - Rini et al., The Lancet
  - Oral anticancer drugs: how limited dosing options and dose reductions may affect outcomes in comparative trials and efficacy in patients
    - Prasad et al., JCO

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