# Patient-Reported Outcomes in Phase III Randomized Controlled Trials Evaluating First-Line Treatments in Advance/Metastatic Renal Cell Carcinoma: A Systematic Literature Review

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## Conclusion

Immunotherapy combinations, including targeted therapy, resulted in improved PROs in RCC. Further research is needed to validate and assess the impact of additional treatments on PRO

## Introduction

- Renal cell carcinoma (RCC) is the most common kidney cancer, with approximately 20 to 25% of cases of advanced disease[1,2]
- Patients with advanced renal cell carcinoma (RCC) typically carry a significant disease burden; Understanding patient-reported outcomes (PROs) is crucial for optimizing the well-being of RCC patients
- First-line treatment for advanced RCC has transitioned from tyrosine kinase inhibitors to include immuno-oncology agents[3]
- Evaluating the impact of first-line advanced RCC treatments on patient-reported outcomes (PRO) is essential for informed treatment decisions

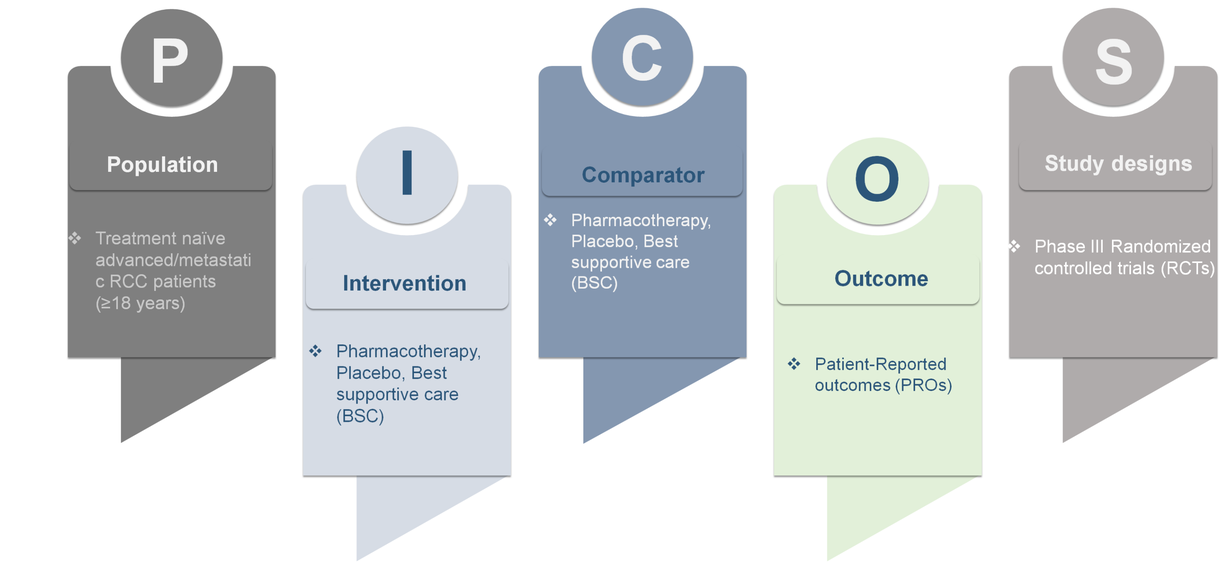
## Aim

- This research aimed to assess the PRO evidence among advanced/metastatic RCC patients receiving first-line systemic therapy

## Methods

- This review followed the standard methodology for conducting a systematic literature review (SLR) as per guidelines provided by the National Institute for Health and Care Excellence (NICE)
- Key biomedical databases (Embase®, MEDLINE®) were searched from database inception to May 2023 to identify relevant randomized controlled trials (RCTs) reporting PROs in advanced/metastatic RCC (Figure 1)
- The results of this review were reported as per Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines
- PRO assessments in RCC patients included the use of three generic instruments: the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQC30), the European Quality of Life Scale (EQ-VAS, EQ-5D index), as well as one disease-specific instrument, the Functional Assessment of Cancer Therapy – Kidney Symptom Index (FKSI)
- Two independent reviewers performed the screening and data extraction activities with conflicts resolved by a third independent reviewer; The risk of bias assessment was performed using Cochrane's RoB-2 tool for RCTs

**Figure 1: Prespecified PICOS eligibility criteria for selection of evidence**




## Results

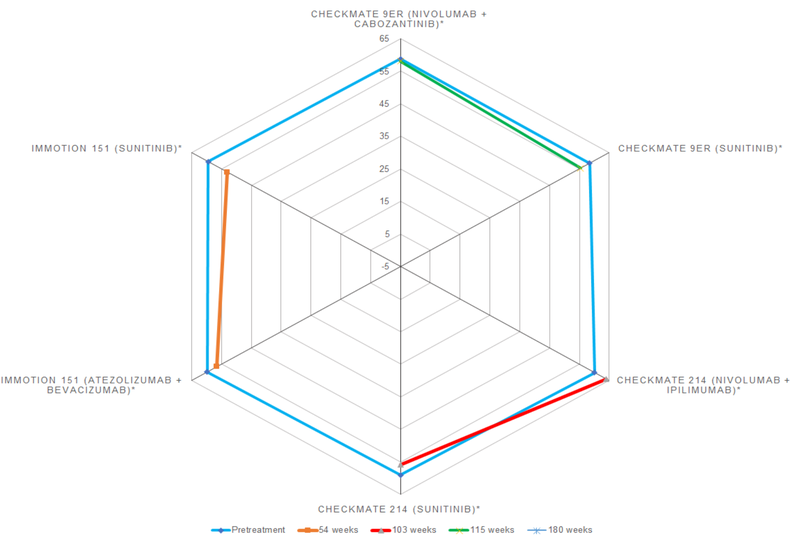
- A total of 13, phase III RCTs were included (Global=12, USA=1) (Figure 2)
- Nivolumab + cabozantinib, nivolumab + ipilimumab, atezolizumab + bevacizumab, and pazopanib, when compared to sunitinib, exhibited statistically significant improvements in FKSI total scores ($p<0.05$). This trend was consistent across the FKSI-DRS and FKSI-FWB domains, except for pazopanib (Figure 3)
- In the assessment of general measures, it was found that the combination of lenvatinib + pembrolizumab exhibited statistically significant improvements compared to sunitinib across all domains of the EORTC QLQ-C30 questionnaire ($p<0.05$). Conversely, sunitinib showed better results than lenvatinib + everolimus in symptom domains ($p<0.05$) (Figure 4)
- The analysis of EQ-5D-3L VAS and utility index scores showcased more favourable results with nivolumab + cabozantinib and nivolumab + ipilimumab in comparison to sunitinib. However, statistical significance was observed only with nivolumab + cabozantinib (Figure 5 and Figure 6)

**Figure 2: PRISMA diagram for the screening process**



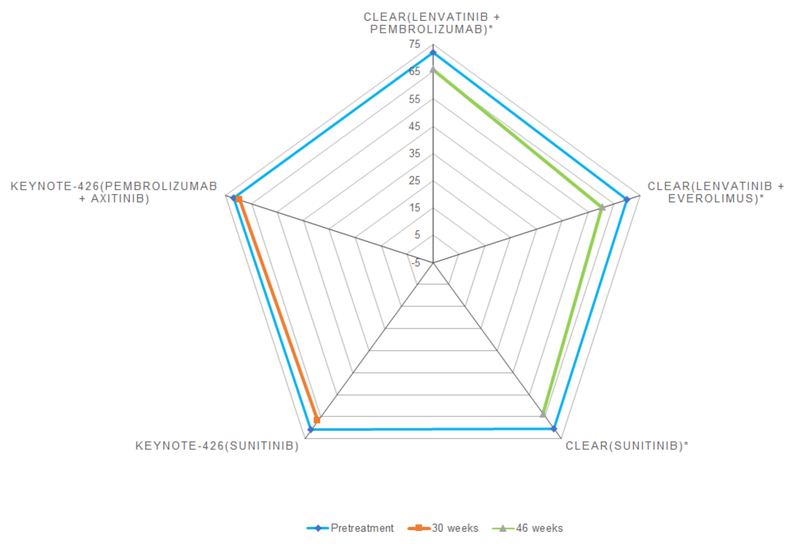

CA: Conference abstract; LOT: Line of therapy; PRO patient-reported outcomes

**Figure 3: Mean scores at pretreatment and post treatment timepoints on FKSI-total scale**



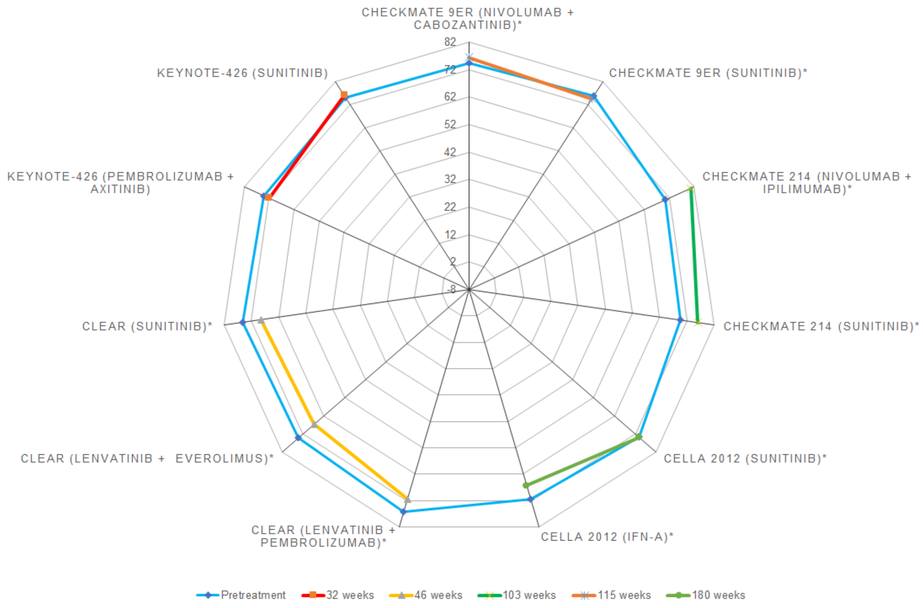

*The mean scores at post-treatment are calculated using 'baseline' and 'change from baseline' scores reported in the study

**Figure 4: Mean scores at pretreatment and post treatment timepoints on EORTC QLQ-30 scale**



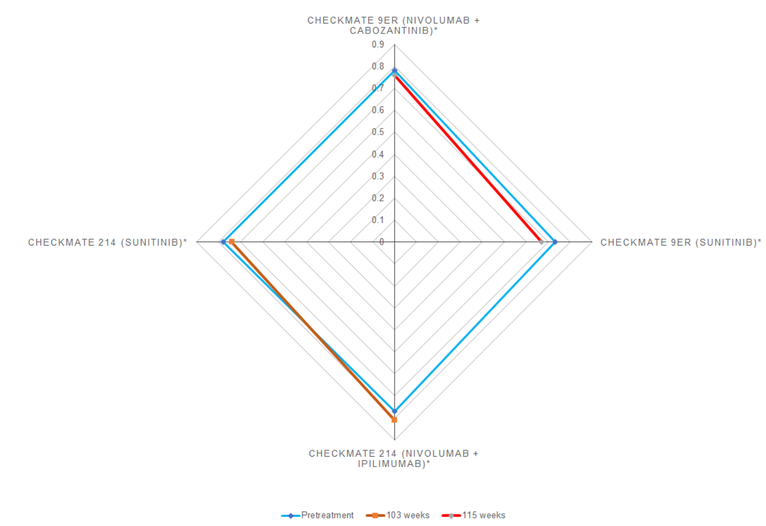

*The mean scores at post-treatment are calculated using 'baseline' and 'change from baseline' scores reported in the study

**Figure 5: Mean scores at pretreatment and post treatment timepoints on EQ-5D VAS scale**




*The mean scores at post-treatment are calculated using 'baseline' and 'change from baseline' scores reported in the study

**Figure 6: Mean scores at pretreatment and post treatment timepoints on EQ-5D utility index scale**




*The mean scores at post-treatment are calculated using 'baseline' and 'change from baseline' scores reported in the study

## Results

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3. Bedke J, et al. Updated European Association of Urology guidelines on renal cell carcinoma: Nivolumab plus cabozantinib joins immune checkpoint inhibition combination therapies for treatment-naïve metastatic clear-cell renal cell carcinoma. Eur Urol 2021; 79: 339–42.

## Disclosure

Barinder Singh, Pankaj Rai, and Ritesh Dubey, the authors, declare that they have no conflict of interest

## Sponsorship

The authors conducted this research independently, without any external collaboration.

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