Temporal trends of costs of nivolumab plus ipilimumab and pembrolizumab plus lenvatinib as first-line treatment for patients with advanced renal cell carcinoma

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*At the time of the analysis.

Background

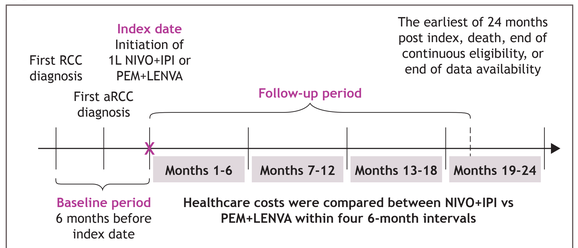
- Renal cell carcinoma (RCC) is a common malignancy in the United States (US) with approximately one-third of cases developing into advanced or metastatic disease[1]
- A total of 80,980 new cases and 14,510 deaths due to cancers of the kidney and renal pelvis are estimated in 2025[2]
- The first-line (1L) treatment landscape of advanced RCC (aRCC) has evolved due to combination immuno-oncology (IO) therapies demonstrating improved outcomes[3]
- Nivolumab plus ipilimumab (NIVO+IPI), pembrolizumab plus axitinib (PEM+AXI), NIVO plus cabozantinib, and pembrolizumab plus lenvatinib (PEM+LENVA) are 1L treatments in the US[3-7]
- Real-world evidence of the healthcare costs associated with 1L combination IO-based therapy in the US remains limited
- Temporal trends in real-world healthcare costs associated with NIVO+IPI and PEM+AXI as 1L treatment for aRCC were assessed in a previous study[8]
- This retrospective study similarly aims to evaluate and compare the all-cause and RCC-related healthcare costs and the temporal trends in baseline characteristics among patients with aRCC who received 1L NIVO+IPI vs PEM+LENVA

Methods

Study design

- Real-world US claims data were used from the IQVIA PharMetrics Plus with Mortality Database (January 2015 - December 2023). The database:
  - Includes pharmacy and medical claims for > 215 million enrollees
  - Covers inpatient, outpatient, emergency care, and mortality data
- Patients who received 1L NIVO+IPI or PEM+LENVA on or after the aRCC diagnosis date and the respective approval date of the combination therapy (NIVO+IPI, post-April 16, 2018; PEM+LENVA, post-August 10, 2021) were included in the study
- The index date was defined as the initiation date of the 1L treatment (ie, index treatment; **Figure 1**)

Figure 1. Data collection



- **Baseline period:** the 6-month period before the index date (exclusive)
- **Study period:** time from index date (inclusive) to the earliest of 24 months post index, end of continuous eligibility, or end of data availability
- **Follow-up period:** up to 24 months from the index date to the earliest occurrence of end of data availability, end of continuous eligibility, or death

Statistical analysis

- All-cause and RCC-related healthcare costs were compared between the NIVO+IPI and PEM+LENVA cohorts over the entire follow-up period
  - Unadjusted comparisons in healthcare costs were conducted using univariable generalized linear models with a log-link function and a Tweedie distribution
  - Incremental cost differences between the 2 cohorts are reported, along with the corresponding 95% confidence intervals (CIs) and *P* values, which were generated through deleted jackknifing with 90% random sampling over 500 iterations of the analytical sample
  - Multivariable models adjusted for baseline patient characteristics; covariates included in the model were selected based on clinical and statistical significance between cohorts in the baseline comparison results
- Univariable and multivariable models were also constructed to assess cost trends across four 6-month time intervals — 1-6 months, 7-12 months, 13-18 months, and 19-24 months from the index — to evaluate trends in monthly healthcare cost differences
  - Per-patient per-month costs were analyzed for each window and the entire follow-up period
  - Patients with ≥ 15 days of continuous enrollment in each window were included
- Statistical comparisons between the 2 treatment cohorts were conducted using Wilcoxon rank-sum tests for continuous variables and chi-squared tests for categorical variables

Results

Patients

- Baseline demographic and clinical characteristics were generally balanced between treatment arms
  - There was a higher proportion of commercially insured patients in the PEM+LENVA cohort (76.8%) vs the NIVO+IPI cohort (64.2%)
  - Among regions in the US, a higher uptake of PEM+LENVA (56.1%) vs NIVO+IPI (46.8%) was observed in the South

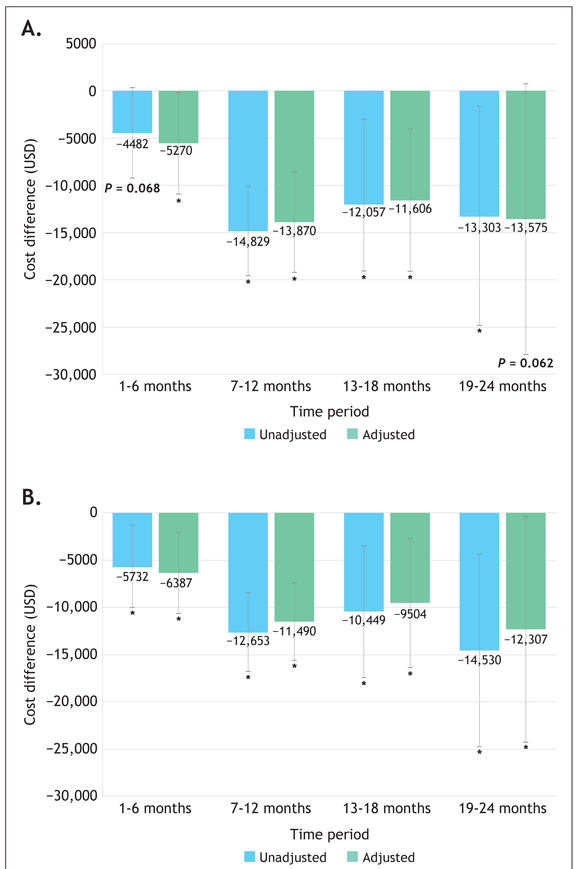
Temporal trends in healthcare costs

- Over the 24 months after index date, the monthly all-cause total healthcare costs (unadjusted) saw a larger reduction with NIVO+IPI vs PEM+LENVA
  - All-cause total healthcare costs for NIVO+IPI vs PEM+LENVA were $45,830 vs $50,312 at 1-6 months, $25,973 vs $40,803 at 7-12 months, $24,620 vs $36,677 at 13-18 months, and $25,395 vs $38,698 at 19-24 months, respectively
- Similar patterns were observed for the monthly RCC-related total healthcare costs

Temporal trends in cost difference between NIVO+IPI vs PEM+LENVA

- All-cause healthcare costs were lower with NIVO+IPI vs PEM+LENVA, and the cost difference between the 2 treatment arms increased over time (**Figure 2**)
  - At 1-6 months, NIVO+IPI had $4482 (unadjusted) and $5270 (adjusted) lower costs vs PEM+LENVA, a difference in cost savings that increased to $14,829 (unadjusted) and $13,870 (adjusted) by 13-18 months
- Similar trends were seen with RCC-related total healthcare costs, with significant unadjusted and adjusted cost differences observed over the four 6-month intervals

Figure 2. All-cause (A) and RCC-related (B) healthcare cost differences for NIVO+IPI vs PEM+LENVA

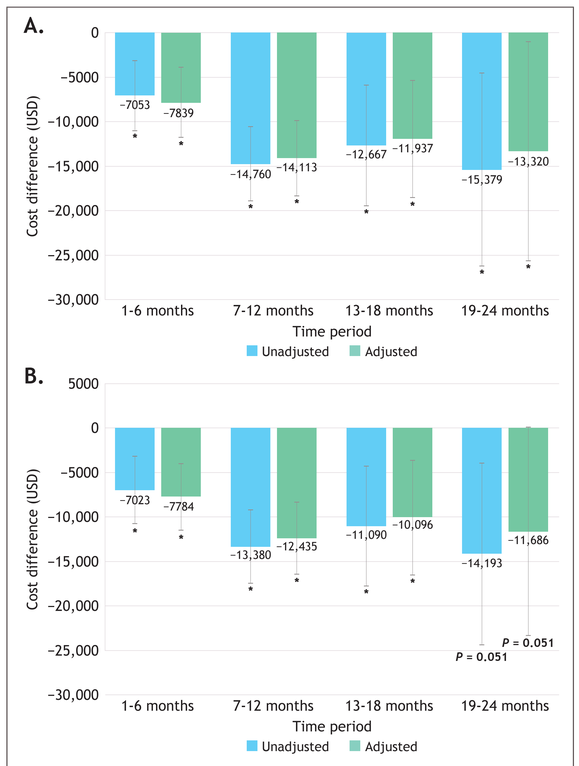


Total healthcare costs were calculated as the sum of total medical service costs and total drug costs.
Values are calculated as (NIVO+IPI − PEM+LENVA).
*$P < 0.05$.

Temporal trends in drug costs

- All-cause drug costs were significantly lower with NIVO+IPI vs PEM+LENVA over the four 6-month intervals, with greater savings seen in the midterm to long-term intervals (7-24 months; **Figure 3**)
  - The cost difference between NIVO+IPI vs PEM+LENVA was $7053 (unadjusted) and $7839 (adjusted) at 1-6 months, notably increasing to $14,760 (unadjusted) and $14,113 (adjusted) at 7-12 months, and $15,379 (unadjusted) and $13,320 (adjusted) at 19-24 months
- The unadjusted and adjusted cost differences in RCC-related total drug costs were mostly significant over the four 6-month intervals with the exception of adjusted cost difference at 19-24 months

Figure 3. All-cause (A) and RCC-related (B) drug cost differences for NIVO+IPI vs PEM+LENVA

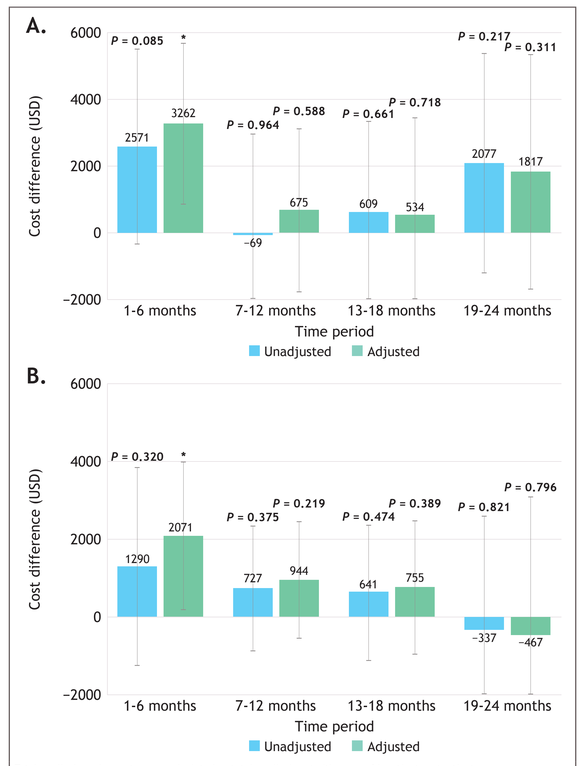


Total drug costs were calculated as the sum of total RCC treatment-related medical costs and total pharmacy costs.
*$P < 0.05$.

Temporal trends in medical service costs

- All-cause medical service costs were numerically higher with NIVO+IPI vs PEM+LENVA in the first 1-6 months (unadjusted, $2571; adjusted, $3262; **Figure 4**)
  - The cost difference decreased at 7-12 months (unadjusted, −$69; adjusted, $675) and 13-18 months (unadjusted, $609; adjusted, $534), then increased at 19-24 months (unadjusted, $2077; adjusted, $1817)
- Similar patterns were found for the unadjusted and adjusted RCC-related total medical service cost differences, but with very little cost difference at 19-24 months

Figure 4. All-cause (A) and RCC-related (B) medical service cost differences for NIVO+IPI vs PEM+LENVA



Total medical service costs were calculated as total medical costs (the sum of inpatient, outpatient, emergency room, and other medical service costs) with the costs associated with RCC treatment removed.
*$P < 0.05$.

Conclusions

- Results from this analysis reveal cost differences that consistently favor NIVO+IPI vs PEM+LENVA; a trend of initially high costs was observed with NIVO+IPI, followed by a decline and stabilization over time, with early costs reflective of intensive treatment with NIVO+IPI and significant sustained savings over time due to lower drug costs within the first 6-month assessment interval
- The cost trends were similar with PEM+LENVA, but with higher initial costs and less decline over time in all-cause and RCC-related healthcare costs compared with NIVO+IPI
- Higher medical service costs were incurred with NIVO+IPI vs PEM+LENVA, but drug cost savings offset these expenses, validating the economic potential of NIVO+IPI in real-world settings
- NIVO+IPI is a 1L treatment option for aRCC that offers long-term healthcare-related cost savings and sustainable economic value, largely driven by drug cost differences. Further research with a larger sample and longer follow-up is warranted
- Results from this analysis are consistent with previous findings evaluating temporal trends in real-world healthcare costs associated with NIVO+IPI and PEM+AXI,[8] and offer insights into long-term temporal trends of healthcare costs for aRCC that support payers, clinicians, and decision makers by providing critical cost-related data to optimize patient care and resource allocation

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