SURVIVAL AND RESOURCE USE IN THE TREATMENT OF METASTATIC RENAL CELL CARCINOMA - A RETROSPECTIVE ANALYSIS OF DATA FROM NATIONAL REGISTRIES

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INTRODUCTION

- Renal cell carcinoma (RCC) accounts for approximately 2% of all cancers worldwide[1]. In 2013, approximately 700 new cases of RCC were reported in Sweden, of which a majority were above 65 years of age[2].
- Many patients present with advanced or unresectable disease, and up to 30% of patients treated by nephrectomy for localized disease will eventually relapse[3]. Hormonal, chemotherapeutic, and radiation therapy approaches have failed to significantly improve clinical outcomes for patients with metastatic disease.
- With the invent of modern targeted therapies (TT) the prognosis of patients with metastatic RCC (mRCC) has improved, but the costs of drugs have also increased. Approved TTs for the treatment of mRCC as of today includes sunitinib, sorafenib, temsirolimus, bevacizumab+IFN, everolimus, pazopanib, axitinib, cabozantinib, lenvatinib, and nivolumab.
- This study is an update of the retrospective non-interventional RENal COMParison (RENCOMP) study that compared survival and resource use between 2002-2005 and 2006-2008[4]. The current update is motivated by an increased experience and use of available TTs as well as the introduction of new TTs.

OBJECTIVE

- The objective was to investigate the real world value of targeted therapies in patients diagnosed with mRCC by comparing survival and cost of care in three cohorts derived from Swedish national health registers.

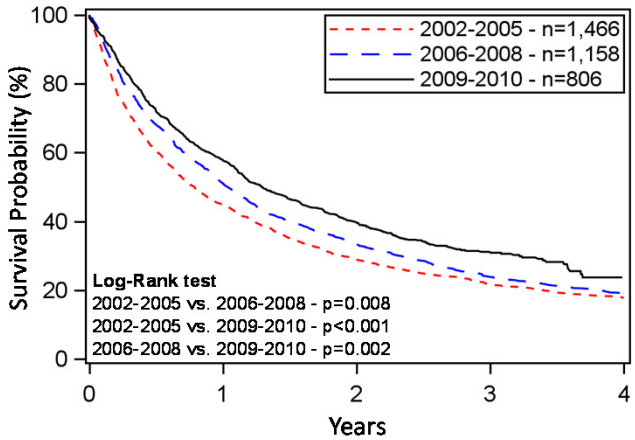
METHODS

- Patient-level data from Swedish health registers with total population coverage were extracted for all patients diagnosed with RCC between 2000 and 2010.
- Information on diagnosis and survival was retrieved from the Swedish Cancer Register while data on resource utilization was obtained through record linkage with the Prescribed Drug Register for prescription pharmaceuticals and the National Patient Register for inpatient- and specialized outpatient care.
- A predefined algorithm based on diagnosis of primary metastasis (M1 disease), diagnosis of secondary (malignant) tumor, and the first visit to an oncology clinic (whichever occurred first), was used to identify patients with mRCC between 2002 and 2010.
- Three patient cohorts were derived based on year of mRCC diagnosis; 2002-2005, 2006-2008, and 2009-2010 respectively. Initially only two cohorts, patients diagnosed 2002-2005 and 2006-2010, were derived to represent pre- and post TT introduction. However, as treatment experience and the number of new TTs increased over time, the latter cohort was divided into two; patients diagnosed 2006-2008 and 2009-2010.
- All included patients were followed from mRCC diagnosis until death or end of follow up. However, as data on resource utilization was only available until 31/12/2012, to enable cost comparisons across cohorts, maximum follow up was set to 4 years.
- Overall survival was estimated over 4 years using Kaplan-Meier methods.
- Expected resource utilization and cost was estimated following the Lin methodology to account for censoring[5]. Mean costs were estimated in three-month intervals. Information on prescription pharmaceuticals were only available from July 2005. Therefore, drug costs before July 2005 were imputed using data from 2005. Costs per in- and outpatient visit were derived from DRG (diagnose-related group) codes for the visits with RCC as the primary diagnosis. Costs were calculated in 2014 SEK (1 SEK=USD ($) 0.12).
- In many regions TTs were dispensed at hospital clinics and therefore not captured in the prescription register. The size of these costs were therefore estimated using regional sales data and these cost were included as a sensitivity analysis.

RESULTS

- In total 3,430 patients with mRCC were identified, of which 1,466 were diagnosed in 2002-2005, 1,158 in 2006-2008 and 806 in 2009-2010.
- Mean survival in years from mRCC diagnosis for the 2002-2005 cohort was 1.45 years; for the 2006-2008 cohort 1.62 years and for the 2009-2010 cohort 1.77 years (Table 1).
- Survival was signficantly higher in patients diagnosed in 2009-2010 compared to patients diagnosed in 2002-2005 and 2006-2008, respectively (Figure 1).

Figure 1 Kaplan–Meier estimates of survival in Swedish patients diagnosed with mRCC



- The estimated mean cost per patient in the three cohorts (2002-2005, 2006-2008, 2009-2010) over a period of 4 years were $16,894, $29,922 and $28,508, respectively (Table 1).

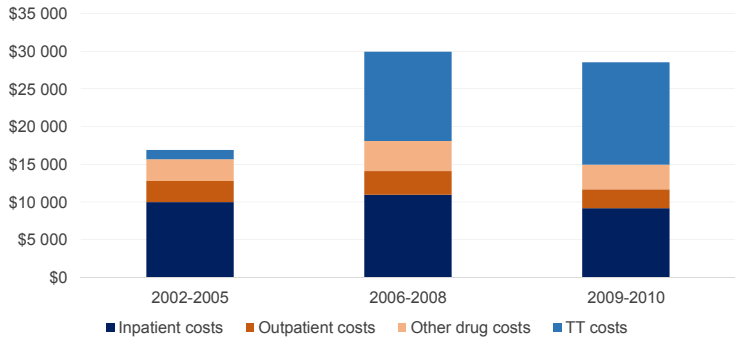
RESULTS (cont.)

Table 1 Estimated mean costs and life-years per patient

Cohort	2002-2005 N=1,466	2006-2008 N=1,158	2009-2010 N=806
Costs ($)			
Inpatient costs	9,978	10,948	9,165
Outpatient costs	2,802	3,157	2,512
Other drug costs	2,898	4,001	3,270
TT costs	1,217	11,817	13,561
Total costs	16,894	29,922	28,508
Life-years	1.45	1.62	1.77

- The mean cost per patient was higher in the 2006-2008 cohort compared to the 2002-2005 cohort, mainly explained by higher TT costs.
- In the 2009-2010 cohort the TT costs were higher compared to the other cohorts. However, the costs of both in- and outpatient care was lower.

Figure 2 Mean cost of care for Swedish patients with mRCC in the three cohorts



- The estimated cost per life-year gained was $78,656 when comparing the 2006-2008 and 2002-2005 cohorts and $36,228 when comparing the 2009-2010 and 2002-2005 cohorts (Table 2).
- When the 2009-2010 and 2006-2008 cohorts were compared, the former was dominant.

Table 2 Estimated incremental costs, life years gained, and cost per life year gained

	2006-2008 vs. 2002-2005	2009-2010 vs. 2002-2005	2009-2010 vs. 2006-2008
Costs ($)			
Inpatient costs	970	-813	-1,783
Outpatient costs	356	-289	-645
Other drug costs	1,103	372	-731
TT costs	10,600	12,344	1,744
Total costs	13,028	11,614	-1,414
Life years gained	0.17	0.32	0.15
Cost per life years gained	78,656	36,228	Dominant

- A sensitivity analysis, including the cost of TTs dispensed at hospitals, showed that total costs increased for each cohort; 2% (2002-2005), 15% (2006-2008), and 22% (2009-2010). Incremental cost per life-year gained was $103,171 when comparing (2006-2008) to (2002-2005), $54,328 when comparing (2009-2010) to (2002-2005), and $2,119 when comparing (2009-2010) to (2006-2008).

CONCLUSIONS

- By analyzing data from Swedish national health registers, we were able to provide real world evidence of a survival benefit over 4 years for patients diagnosed with mRCC after the introduction of TT.
- We also showed that patients diagnosed after the introduction of TT had higher drug costs, although these costs were partly offset by lower costs for in- and outpatient care.
- The study suggests that the real world value of TT in the Swedish mRCC population corresponds well to the investment made and that the value of invested money increases over time.

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