Acta Oncologica, 2010; 49: 837–843

informa
healthcare

ORIGINAL ARTICLE

Current and predicted cost of metastatic renal cell carcinoma in Finland

TIMO PURMONEN[1], PÄIVI NUTTUNEN[2], RIIKKA VUORINEN[3], SEPPO PYRHÖNEN[4], VESA KATAJA[5] & PIRKKO KELLOKUMPU-LEHTINEN[6]

[1]*Department of Social Pharmacy, Centre for Pharmaceutical Policy and Economics, University of Kuopio, Kuopio, Finland,* [2]*Department of Medicine, University of Kuopio, Kuopio, Finland,* [3]*Department of Medicine, University of Turku, Turku, Finland,* [4]*Department of Oncology, University of Turku and Turku University Hospital, Turku, Finland,* [5]*Departments of Oncology, Vaasa Central Hospital and Kuopio University Hospital, Finland and* [6]*Department of Oncology, University of Tampere and Tampere University Hospital, Tampere, Finland*

Abstract

Information on detailed treatment costs and the economic burden of renal cell carcinoma (RCC) is rare. The current study provides treatment costs and outcomes of patients with metastatic RCC (mRCC), as well as estimates of the future burden from the perspective of Finnish health care. These results offer a baseline against which the impact of emerging treatments may be evaluated. *Materials and methods.* Information on treatment modalities, survival, and the cost of treatment was retrospectively gathered from mRCC patients (n = 83) receiving first-line interferon-alpha (IFN). Predictions of the number of new cases, premature deaths, and productivity losses were made using local epidemiological data, which were projected to the future using population growth forecasts. The future costs of mRCC treatment and the budget impact of sunitinib were estimated through modeling. *Results.* Patients survived 11.9 months (median; 95% CI 9.2–14.7) after initiation of active IFN treatment, accruing an average total treatment cost of €32,951. Most of the treatment costs were due to hospitalization and active IFN treatment. The aging of the population leads to nearly a 2% increase in the absolute number of new diagnoses annually, while at the same time it results in declining productivity losses. The estimated five-year population cost of IFN-based treatment was €16M–€26M. Adding sunitinib to the first-line treatment protocol increased this cost by €13M–€41M. *Conclusions*. Despite the limited number of patients, metastatic renal cell carcinoma places a considerable economic burden on Finnish society. Treatment costs are likely to increase substantially due to the adoption of new and more expensive medications, the aging population, and enhanced survival times.

Renal cell carcinoma (RCC) accounts for 3% of all cancer deaths in Finland [1]. However, information on its burden on Finnish society and health care is scarce. The total annual cancer-related costs in Finland were €530 M in 2004, and the costs are estimated to double by 2015. The increase in costs is expected to be especially steep with respect to cancer medications, which are estimated to be more than fourfold by 2015 compared with 2004 [2].

Most RCC cases are diagnosed in age groups over 50 years, but RCC may occur at any age (Figure 1A) [3]. In many cases RCC is diagnosed incidentally during abdominal imaging, and it currently is often detected at an early stage [4]. However, diagnosis may be delayed due to a lack of early warning signs, and 25–30% of patients have metastases at diagnosis [5,6]. The average annual incidence of RCC in Finland has been 10.2/100 000 in men and 5.6/100 000 in women in 1995–2004. In 2004, 363 Finns died of RCC. The majority of new cases (57%) and deaths (56%) were in men (Figure 1) [3]. The incidence of RCC has been rising for several years [4,6,7], and there are approximately 209 000 new RCC cases and 102 000 deaths due to RCC per year worldwide [6].

Cytokines (interferon-α, Interleukin-2) have been widely used in first-line treatment of metastatic RCC (mRCC), and until recently they have been the standard of care for mRCC patients. Chemotherapy has a limited, if any, role in the treatment of mRCC. In addition, the response rates to cytokines have also

Correspondence: Mr. Timo Purmonen, Centre for Pharmaceutical Policy and Economics, Department of Social Pharmacy, University of Kuopio, P.O. Box 1627, 70211 Kuopio, Finland. Tel. +358 40 3553559. Fax. +358 17 162515. E-mail: Timo.Purmonen@uef.fi

(Received 12 November 2009; accepted 27 January 2010)

ISSN 0284-186X print/ISSN 1651-226X online
DOI: 10.3109/02841861003660049

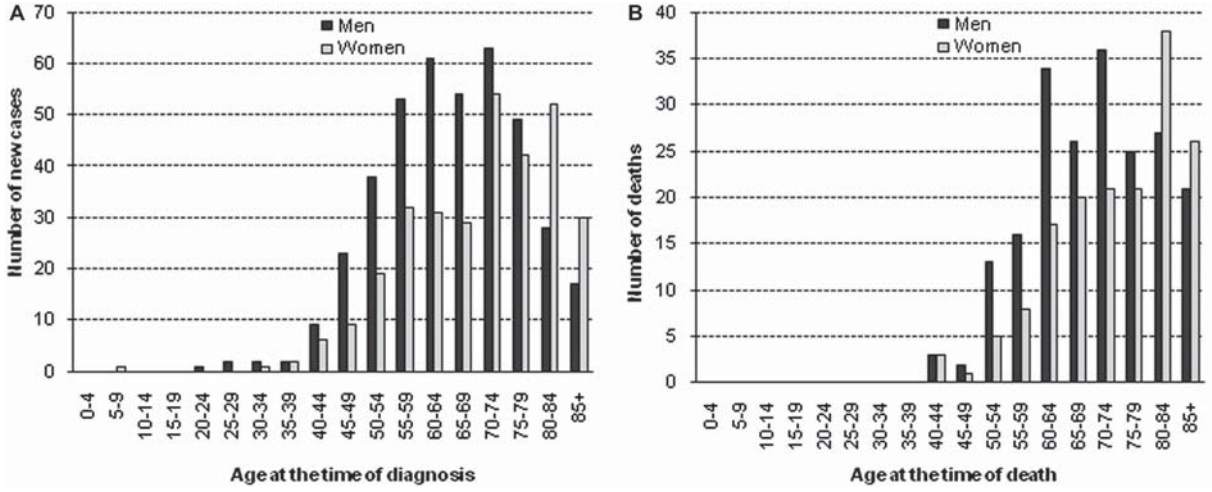

Figure 1. Number of new cases (A) and number of deaths (B) related to RCC in Finland in year 2004 [3].

been low (5 to 20%), and the effectiveness of these drugs is still controversial [4,8]. In Finland, interferon-α (IFN) has long been the standard first-line treatment of mRCC, and it still has its place in treatment of metastatic cases. Nevertheless, information on treatment modalities and the cost of treatment in different hospitals is scarce. In addition, despite its growing importance, data on the economic burden of RCC is sparse even globally [6,9].

The median overall survival period of patients treated with first-line cytokine-based therapy has been approximately one year [8]. However, an increased understanding of the underlying biological processes in renal cancer has led to advances in disease management. Novel targeted treatments, such as tyrosine kinase inhibitors, have shown their effectiveness and offer new treatment options for patients with mRCC. A median overall survival time of 26.4 months has already been reported [10].

Nevertheless, the economic consequences of these treatments have not been widely estimated. The introduction of new treatments has pressed the need for health economic evaluations, such as cost-effectiveness analyses. These will provide information on the costs of additional health benefits achieved with new medication compared with current care. In order to estimate the impact of new treatments, there has to be information on the current situation, which forms the basis for any analysis. The current study shows the costs and outcomes among patients with mRCC actively treated with first-line cytokine treatment. It also provides estimates of the future burden of renal cell cancer from the perspective of Finnish health care. We believe the results from the current study can be used as a baseline against which the impact of emerging treatments may be evaluated.

Materials and methods

The current study includes resource use and survival data from local patients, estimations based on available statistics, and model-based estimations (Table I). The empirical data are presented first, and they provide a background and basis for the modeling estimations. The study was conducted from a societal perspective.

Treatment cost and treatment times

Data from 83 mRCC patients who had received first-line cytokine-based therapy were gathered from the patient records of three Finnish university hospitals. The data were collected with a structured form in two phases (June-August 2006 and June-July 2007). The data were collected in each hospital from consecutive patients with mRCC. Consistent with the clinical practice at the time all eligible patients, who were diagnosed with metastatic disease, received first-line IFN treatment. Those with a very poor general condition and/

Table I. Study outcomes and the utilized information sources.

Study outcome	Source of information
IFN treatment costs and treatment times	Local patient data
Estimation on future RCC incidence	Expected population growth [1], New RCC-diagnoses [3]
Life-years lost due to RCC	Life expectancies [1], New RCC deaths [3]
Productivity loss due to mRCC	Expected population growth [1], New RCC diagnoses [3]
Future cost predictions of mRCC treatment	State-transition model (parameters from local data and literature [8,11])

or with contraindications to IFN treatment were treated in primary health care units and thus were not included in the study. The data collection process is described in more detail in a previous publication that included information about second-line mRCC treatment after active IFN treatment [11]. This data set from 2006 was extended in 2007 with 47 patients, from whom all data relating to health care resource use were extensively collected from initiation of active treatment until death. Thus, the detailed information on health care resource use during first-line IFN therapy is available only in the latter case (2007). The patient characteristics are presented in Table II. The patients died during 1996–2007; 86% of them in the 21st century. The treatment had remained similar during these years. One patient was alive at the end of the data collection. This case was included in the cost per follow-up day analysis but not in the survival estimates.

The collected resource use data included information on medication use, hospital stays, outpatient visits, radiotherapy, surgical procedures, nursing home stays, and diagnostics. Recommended Finnish unit costs, adjusted for regional price differences, were applied to all health care resource use [12]. Unit costs were real-valued to the year 2008 using the official health care price index [13]. The cost of medication was taken from the Finnish drug compendium Pharmaca Fennica [14]. Travel costs were not included. A statistical package (SPSS 14.0) and a spreadsheet (MS Excel) were used for data management and analyses. Kaplan Meier analysis was used in the survival estimates, and linear regression in defining the determinants of treatment costs.

Table II. Characteristics of the study population.

	Pooled data n=83	2007 data n=47	2006 data n=36
Sex, no. (%)			
Male	55 (66)	29 (62)	26 (72)
Female	28 (34)	18 (38)	10 (28)
Age at time of diagnosis (years)			
mean	63.6	63.1	64.4
median	65	64.5	65.6
range	38–83	38–80	44–83
Nephrectomy (%)			
Yes	66 (81)	36 (78)	30 (83)
No	16 (19)	10 (22)	6 (17)
Study site, No. patients (%)			
Hospital A	31 (37.5)	16 (34)	15 (42)
Hospital B	31 (37.5)	31 (66)	0 (0)
Hospital C	21 (25)	0 (0)	21 (58)
ALL	83 (100)	47 (57)	36 (43)

Estimation of future RCC incidence and life-years lost due to RCC

Estimations concerning the current and future burden of RCC were performed using available statistics. Epidemiological data were obtained from the Finnish Cancer Registry, which provided data on all RCC cases in Finland in 1994–2004. RCC was defined as cancer of the kidney, excluding cancer of the renal pelvis. Future estimations of RCC incidence were made using official population change projections up to 2020 [1]. At the same time, the relative age distribution of new RCC cases was assumed to remain constant (Figure 1A). Furthermore, the number of potentially lost life-years due to RCC were estimated using gender-specific expected lifetimes in every age group [1] and annual RCC deaths (Figure 1B) [3].

Estimation of productivity loss due to mRCC

Potential productivity loss due to metastatic RCC (mRCC) was estimated using the time from diagnosis to retirement, which in Finland begins at the age of 65 years. As a base case, we assumed that 30% of new RCC cases are metastatic, and that working-age patients (15–65 years) would not return to work at any point after the devastating diagnosis. The impact of a greater proportion of metastatic cases was tested in sensitivity analyses.

Future cost predictions of mRCC treatment

Modeling techniques were used to estimate the future cost of mRCC treatment and the budget impact of sunitinib in first-line treatment of mRCC. Sunitinib, one of the tyrosine kinase inhibitors, is the only targeted drug currently indicated for first-line treatment in Finland, and it was therefore chosen for our analysis. In budget impact analyses the treatment protocols, not only drug prices, are compared against each other in order to find out the net difference in treatment cost. An open cohort stage transition model was built to reproduce the natural history of mRCC. With this approach we were able to take into account the natural patient flow and to predict the prevalence of patients in different disease stages at a certain point in time. This method was chosen because mRCC is a rapidly progressing disease, and there are substantial differences in costs between active and symptomatic treatment. A similar approach has been previously utilized in budget impact analysis of cancer treatments [15]. The included disease stages in the model were "Diagnosed mRCC; active treatment", "Progressed disease; symptomatic treatment", and "Dead". Death was assumed to follow only after disease progression.

Table III. Survival times among local mRCC patients.

	n	mean	median
From IFN-start to death (months)			
Pooled	81	15.2	11.9
Hospital A	30	12.5	7
Hospital B	30	16.0	11.2
Hospital C	21	17.9	15.0
From IFN-end to death (months)			
Pooled	78	8.7	4.0
Hospital A	28	6.1	3.6
Hospital B	29	9.4	8.1
Hospital C	21	11.3	6.7

The model assumes that there are no seasonal changes in the diagnosis of new cases, and that patients enter the model steadily during every monthly cycle. We assumed that 30% of RCC patients would demonstrate with metastases at diagnosis, and that 50% of these patients would be eligible to receive sunitinib. As a sensitivity analysis, the proportion of metastatic cases was assumed to be 50%, which reflects the situation where additional patients eventually develop a metastatic disease. Transition probabilities between the model stages were derived from the local data (Table III) using the formula [1–(0,5)^(1/median)]. The length of IFN-α treatment was assumed to reflect the disease-free time among patients receiving interferon. In one scenario, sunitinib was assumed to prolong the median disease-free time by six months when compared with IFN-based treatment [8]. Possible effects on overall survival were not included.

The treatment costs are different between the modeled health stages. The collected, population-level, costs (Table IV) were used as the cost of active IFN-based treatment (€870 per month). These were also used as the cost of symptomatic care (€1 500 per month), and this was applied similarly in both groups after disease progression. The cost of active sunitinib-based treatment in the model was €4 000 per month, which included both the drug costs and other health care costs. This is parallel to that previously estimated in second-line sunitinib treatment in Finland [11]. It was assumed that the cost of sunitinib-based treatment is likely to be of similar magnitude also in first-line mRCC treatment. The model was built in MS Excel, which was also used in all the calculations.

Results

Survival and treatment times

The treatment paths of the hospitals were similar. The median time from diagnosis to nephrectomy was one month, and three months from diagnosis to the beginning of IFN treatment. The mRCC patients survived 11.9 months (median; 95% CI 9.2–14.7) after initiation of active IFN treatment (Table III). The median duration of IFN treatment was 5.6 months (95% CI 4.3–6.9); mean seven months (95% CI 5.6–8.4). Most patients had died soon after active treatment was finished. The median survival time after IFN treatment failure was four months (95% CI 1.2–6.7); mean 8.7 months (95% CI 6.8–10.6). The differences between hospitals were not statistically significant. There was a strong correlation between the length of IFN treatment and total survival time (Spearman correlation 0,689; $p<0.01$).

Treatment costs among patients

Costs were divided into medication costs and other treatment costs (Table IV). Other treatment includes hospital stays, outpatient visits, radiotherapy, surgical procedures, nursing home stays, and diagnostics (laboratory tests and imaging). Medication costs include IFN-α, other cancer medication, bisphosphonates,

Table IV. Treatment cost per day.

	Population	Patient-level results			
	mean (€)**	median (€)	mean (€)	range (€)	se	proportion of costs
During IFN treatment						
medication* (n=47)	18	23	24.5	1.5–65	2.23	60%
other treatment (n=47)	12	14	30.5	0.5–212	5.9	40%
total (n=47)	29	46.5	55	3.5–230	6.46	100%
After IFN treatment						
medication* (n=81)	3	2	4.5	0–40	0.81	6%
other treatment (n=81)	47	58	146	0–981	23.63	94%
total (n=81)	50	66	150	0–981	23.54	100%
During entire follow-up						
medication* (n=47)	12	15	15.5	1.5–45	1.63	27%
other treatment (n=47)	24	31.5	54	1.5–402	10.32	73%
total (n=47)	36	48.5	69.5	7–414	10.69	100%

*Medications administered during hospitalization are not included in medication costs.
**Sum of costs divided by sum of follow-up days.

and analgesics. The average total treatment cost from initiation of IFN treatment until death was €32,951 (median €27 938; n=46).

Treatment costs and their composition differed during and after active IFN treatment. Medication comprised 60% of total treatment costs during IFN treatment, whereas after disease progression it caused only 6% of all costs. Treatment after disease progression may be characterized as mainly symptomatic.

Hospital in-patient treatment caused most (79%) of the total non-medication costs. However, during active IFN treatment it was responsible for 70% of non-medication costs, and after disease progression the proportion increased to 80%. Other non-medication costs were due to outpatient visits (7%), radiotherapy (7%), and diagnostics (5%). A minority of the costs was caused by surgical procedures and nursing home stays. Only one patient had received treatment also outside public health care.

All the patients had received IFN-α as the cytokine of choice; both interferon-α2a and α2b were used. IFN treatment caused 89% (median per-patient-cost €7 130) of all medication costs during the entire follow-up. Other cancer treatment consisted of various agents (e.g. vinblastine, capesitabine, epirubicin, carmofur, vinorelbine, interleukin-2, and progestines), which were responsible for 6% of total drug costs. Approximately 20% of the patients had received bisphosphonates, which comprised 3% of all drug costs. Analgesics caused 2% of total medication costs. Medications administered during hospitalization were not included in medication costs, since their costs were allocated to hospital care costs.

The cost of medication, and specifically IFN-α, comprised most of the total costs during active treatment. However, due to the growing need for hospital treatment, the total cost per treatment day was more expensive after disease progression. Variation in treatment costs was great among patients. In an age- and sex-adjusted regression analysis (adjusted $R^2=0.254$), one additional survival month increased treatment costs by €783 (se 187; $p<0.0001$). The Spearman correlation between costs and survival was 0.569 ($p<0.01$).

Estimations of future disease burden

The aging of the population is likely to increase the future cancer burden. With respect to RCC, there would be nearly 960 new cases annually in Finland by 2020. This equals nearly a 2% increase in the absolute number of cancer cases each year, leading to an unadjusted incidence of 17.2 per 100 000 inhabitants in 2020.

RCC results in premature death. During 2004, renal cell cancer caused approximately 5 300 prematurely lost life-years in Finland. This equals an average of 14.7 years of life lost per-person-dying. Morbidity also leads to productivity losses. According to our estimations, in 2008 mRCC caused approximately 890 lost potential working years, and by 2020 the corresponding number will be 820. However, when 50% of the RCC cases are assumed to be metastatic, the results are 1 485 and 1 365 years, respectively. Due to the increasing number of retired people, productivity loss will start to decrease over time. Nevertheless, the results concerning productivity losses hold only when it is assumed that without mRCC, the patients would remain working until the age of 65 years, and that the patients would otherwise live a normal, healthy life. These measures reflect a possible productivity loss of €23.6 M in 2008, given that the average labor productivity cost in Finland is approximately €26 500 per year [12].

Predicted cost of IFN-based mRCC treatment and the budget impact of sunitinib

The future costs of mRCC treatment were estimated through modeling. With 227 annual patients, mRCC will cause €15.6 M in treatment costs, among patients entering the model during five years, when treated with IFN-α. When half of this population receives sunitinib instead of IFN-α, the additional cost will be, on average, €2.7 M per year. Inclusion of a population forecast increases these costs by 3–4%. If the additional health benefit obtained from sunitinib is included [8], the five-year budget impact of sunitinib is €24.4 M compared with IFN-based treatment (€40 M vs. €15.6 M). If, in addition, population changes are included, the estimated five-year budget impact rises to €25.2 M (€41.3 M vs. €16.1 M). In a scenario where 50% of annual RCC cases are metastatic, the five-year budget impact of sunitinib is €40.8 M (€66.8 M vs. €26 M) when neither population forecast nor increasing treatment effectiveness is included. In these estimations, only first-line mRCC treatment is taken into account.

Discussion

We estimated the economic consequences of mRCC for Finnish society, both currently and with future projections. Most of the treatment costs are caused by hospitalization and active drug therapy. New targeted treatments will inevitably lead to increasing costs in mRCC treatment, because previously available treatment options have been scant. In addition, the overall burden of renal cell cancer is likely to increase along with the aging population.

In order to effectively allocate finite health care resources, health care providers require estimates of the future cancer burden as well as treatment costs

[16]. Currently, there are only a limited number of studies on the cost of treatment and the burden of renal cell cancer. Nevertheless, there is an increasing information demand for more detailed patient-level costs related to specific diseases [9]. In the present study we have illustrated the costs per treatment day during different phases of treatment. We used official population forecasts and reliable incidence data from the Finnish Cancer Registry, which covers the vast majority of all cancer cases in the country [17]. Reliable population forecast and high-quality population-based data are considered to be the prerequisites for sensible predictions of cancer incidence [16].

However, there are a number of limitations in the current study. The first limitation relates to the size of the study population (n=83). However, due to the small number of inhabitants in Finland (5.3 M), this equals approximately 25 to 40% of annual mRCC cases in the country. The limited number of patients did not allow sufficient subgroup analyses. The treatment day costs were derived from natural variation of RCC patients, which reflects true clinical treatment practice at the time. Secondly, we did not have complete information on resource use during active IFN treatment from all the patients. Nevertheless, it was clear that IFN-α was the cost driver during that time period. The third limitation relates to the assumptions made during the study. The estimation of future burden was based on patient statistics from 2004. These were then projected to the future using population forecasts, which are predictions by nature, and thus include a source of error. Furthermore, a decrease in the incidence rates would balance the impact of aging, and thus there is a possibility of overestimation in the current study. Estimations concerning mRCC were based on the assumption that 30% or 50% of new cases would be metastatic, regardless of age at diagnosis. Furthermore, the proportion of new cases at each age was fixed to the 2004 level. However, it has been stated that age is the most important time-related variable that quantitatively influences the risk of cancer [16]. Finally, there was no information on patient status at the baseline. In addition, some of the differences in the observed survival times may be due to possible differences in the continuation of IFN treatment between hospitals.

Studies addressing the burden of mRCC are relatively sparse in the literature [6]. Gupta and colleagues have, in their review, presented a range of studies illustrating costs related to RCC and mRCC. Depending on the stage of the disease, included costs, and the perspective of the study, the per-patient cost ranged from US$12 500 to $64 900 [6]. The annual cost of distant RCC, prior to the launch of new treatments, has been estimated at US$28 271 per patient [18]. The monthly treatment cost for a patient with advanced renal cell cancer treated with bevacizumab, sorafenib, or sunitinib has been estimated to be US$13 351, $6 998, and $8 213, respectively. Intravenous bevacizumab was concluded to have similar therapeutic value as oral agents (sorafenib and sunitinib) but to be more costly [19]. In addition, in the treatment of mRCC bevacizumab is combined with IFN, which increases the total costs. In an Italian register-based study, mRCC treatment costs were €17 656 per patient for the total follow-up, and €13 692 for the first year. Hospitalization was responsible for 81% of total treatment costs during the total follow-up and 85% during the first year. The corresponding proportions for drug costs were 8% and 6%. The average monthly cost per patient was €1 400 [9]. These results differ from those obtained in our study. However, in this study by Mantovani and colleagues (2008), the cost of hospitalization was based on diagnostic-related groups, and drug costs were based on prescriptions dispensed to outpatients by community pharmacies. Nevertheless, the results from different studies are not fully comparable due to differences in health care systems, cost structures, and study designs. Country-specific data on costs and effectiveness of treatments are needed. In order to provide up-to-date information concerning first-line sunitinib treatment in Finland a prospective follow-up study has been initiated [20].

As to cancer treatment in Finland, the cost of medication and outpatient treatment has been estimated to increase the most in the near future. Due to the aging population, productivity losses are expected to increase less than other cancer-related costs [2]. Our estimates concerning prematurely lost life-years in the current study are close to those previously presented. Life-years lost due to cancer of the kidney and renal pelvis have been presented to be 15.7 years per-person-dying [6]. This parallels our estimate of 14.7 years for RCC only. The incidence of mRCC in Finland has earlier been estimated to be 8.0/100 000, with the assumption that 27.5% of RCC cases are metastatic at diagnosis. It was stated that these values may be underestimations, since patients with subclinical metastatic disease were not included. However, in the review Finland was inaccurately placed together with Australia and Asia instead of Europe [6]. Quality-of-life issues were not within the scope of the current study. Nevertheless, the mRCC burden related to the patient's quality of life has been studied using various measurement scales, and a review of this subject may be found elsewhere [6].

Sunitinib is currently seen as the new standard of care for first-line treatment of mRCC in good or intermediate risk clear cell renal carcinoma [4,21], and it is currently the only targeted treatment indicated for first-line treatment of mRCC in Finland. In poor risk clear cell renal carcinoma temsirolimus is recommended as the first-line treatment, sunitinib being an option [21]. The National Institute for Health and Clinical Excellence, the health authority in England and Wales, revised (August 2009) its recommendations for the

use of targeted drugs, concluding that sunitinib is their recommended first-line treatment option for mRCC [22,23]. Additional information on the costs and effectiveness of existing treatment options are still needed, while at the same time new treatments emerge. Targeted drugs are likely to be included more often in subsequent treatment lines, though knowledge about an optimal treatment strategy is lacking [21]. Lately, it has been stated that for patients whose disease progresses after treatment with targeted therapies everolimus should be regarded as the following treatment of choice [24]. Inevitably, progress in disease management will come with considerable costs. The issues related to the impact of novel treatments on the epidemiological and economic burden of mRCC are not yet adequately evaluated. The need for more research on the overall burden of mRCC has previously been recognized [4,6].

In conclusion, despite the limited number of patients, metastatic renal cell carcinoma places a considerable economic burden on Finnish society. Medication costs in the treatment of mRCC are likely to increase in the future due to more expensive medications, the aging population, and enhancement in survival times. Growing possibilities of offering subsequent treatment lines are also likely to have an impact on both treatment costs and survival. In order to enable more efficient health care planning, more attention should be paid to estimations of both costs and the epidemiological burden of specific indications.

Acknowledgements

Preliminary findings were presented in part at the International Society for Pharmacoeconomics and Outcomes Research 12th Annual European Congress (poster presentation); October 24–27, 2009; Paris, France. The data collection concerning local patients was supported by Pfizer Finland. However, all decisions related to the study were made on the basis of scientific issues with no editorial interference from the sponsor.

Declaration of interest: There are no conflict of interest regarding the current study. The study was conducted from scientific interest.

References

[1] Statistics Finland. Statistical yearbook of Finland 2008 – The official statistics of Finland, Helsinki; 2008.
[2] Mäklin S, Rissanen P. Cost of cancer – Treatment and productivity costs in 1996–2004 and forecast to year 2015. [In Finnish] Finnish Cancer Organizations Publication no. 67, Helsinki, Finland; 2006.
[3] Finnish Cancer Registry. (www.cancerregistry.fi) Information received 11.7.2006.
[4] Rini BI, Campbell SC, Escudier B. Renal cell carcinoma. Lancet 2009;373:1119–32.
[5] Motzer RJ, Bander NH, Nanus DM. Renal-cell carcinoma. N Engl J Med 1996;335:865–75.
[6] Gupta K, Miller JD, Li JZ, Russell MW, Charbonneau C. Epidemiologic and socioeconomic burden of metastatic renal cell carcinoma (mRCC): A literature review. Cancer Treat Rev 2008;34:193–205.
[7] Pantuck AJ, Zisman A, Belldegrun AS. The changing natural history of renal cell carcinoma. J Urol 2001;166: 1611–23.
[8] Motzer RJ, Hutson TE, Tomczak P, Michaelson MD, Bukowski RM, Rixe O, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. N Engl J Med 2007; 356:115–24.
[9] Mantovani L, Morsanutto A, Tosolini F, Mustacchi G, Esti R, Belisari A, et al. The burden of renal cell cancer: A retrospective longitudinal study on occurrence, outcomes and cost using an administrative claims database. Eur J Cancer 2008;(Suppl 6):46–51.
[10] Motzer RJ, Hutson TE, Tomczak P, Michaelson MD, Bukowski RM Oudard S, et al. Overall survival and updated results from sunitinib compared with interferon alfa in patients with metastatic renal cell carcinoma. J Clin Oncol 2009;27:3584–90.
[11] Purmonen T, Martikainen J, Soini EJ, Kataja V, Vuorinen R, Kellokumpu-Lehtinen P. Economic evaluation of sunitinib malate in second-line treatment of metastatic renal cell carcinoma in Finland. Clin Ther 2008;30:382–92.
[12] Hujanen T, Kapiainen S, Tuominen U, Pekurinen M. Health care unit costs in Finland in 2006 [In Finnish] Helsinki, Finland, Stakes publications; 2008.
[13] Statistics Finland and Local Finland: Price indexes 2008 [in Finnish] http://www.kunnat.net/k_perussivu.asp?path=1; 29;374;36984;10954;48923;52537 (accessed March 25, 2009).
[14] Pharmaca Fennica [Finnish drug compendium] Pharmaceutical Information Centre [in Finnish].
[15] Purmonen T, Auvinen P, Martikainen J. Budget impact analysis of trastuzumab in early breast cancer – a hospital district perspective. Int J Technol Assess Health Care 2010;26:163–169.
[16] Bray F, Møller B. Predicting the future burden of cancer. Nat Rev Cancer 2006;6:63–74.
[17] Teppo L, Pukkala E, Lehtonen M. Data quality and quality control of a population-based cancer registry. Experience in Finland. Acta Oncol 1994;33:365–9.
[18] Lang K, Danchenko N, Gondek K, Schwartz B, Thompson D. The burden of illness associated with renal cell carcinoma in the United States. Urol Oncol 2007;25:368–75.
[19] Duh MS, Dial E, Choueiri TK, Fournier AA, Antras L, Rodermund D, et al. Cost implications of IV versus oral anti-angiogenesis therapies in patients with advanced renal cell carcinoma: Retrospective claims database analysis. Curr Med Res Opin 2009;25:2081–90.
[20] Evaluation of the cost and effectiveness of sunitinib compared to interferon-alfa in Finland. ClinicalTrials.gov Identifier: NCT00980213.
[21] Escudier B, Kataja V. Renal cell carcinoma: ESMO clinical recommendations for diagnosis, treatment and follow-up. Ann Oncol 2009;20(Suppl 4):iv81–iv82.
[22] NICE technology appraisal guidance 169. Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma. http://www.nice.org.uk/TA169 (accessed July 1, 2009).
[23] NICE technology appraisal guidance 178. Bevacizumab (first-line), sorafenib (first- and second-line), sunitinib (second-line) and temsirolimus (first-line) for the treatment of advanced and/or metastatic renal cell carcinoma. http://www.nice.org.uk/TA178 (accessed October 2, 2009).
[24] Motzer RJ, Escudier B, Oudard S, Hutson TE, Porta C, Bracarda S, et al. Efficacy of everolimus in advanced renal cell carcinoma: A double-blind, randomized, placebo-controlled phase III trial. Lancet 2008;372:449–56.