Lung Cancer 114 (2017) 56–61

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

Research paper

Changing costs of metastatic non small cell lung cancer in the Netherlands

W.R. Keusters[a,b], V.A. de Weger[a], A. Hövels[b], J.H.M. Schellens[a,b], G.W.J. Frederix[c,*]

[a] Department of Clinical Pharmacology, The Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands
[b] Utrecht institute of Pharmaceutical Sciences (UIPS), Universiteitsweg 99, 3584 CG Utrecht, The Netherlands
[c] Julius Center for Health Sciences and Primary Care, University Medical Center, Universiteitsweg 100, 3584 CG Utrecht, The Netherlands

ARTICLE INFO

Keywords:
Cost of illness
Non-small cell lung cancer
Oncolytic drugs
Disease management
Healthcare policy

ABSTRACT

Objectives: The primary objective of this study was to identify the total intramural cost of illness of metastatic non-small cell lung cancer (NSCLC) in the Netherlands between 2006–2012. Secondary objective was to identify whether changes in cost patterns of metastatic NSCLC have occurred over the last years.
Methods: Patients diagnosed with metastatic NSCLC between 1-1-2006 and 31-12-2012, who had follow-up to death or the date of data cut-off and no trial participation were included. A structured chart review was performed using a case report form. Data collection started after diagnosis of metastatic NSCLC and ended at death or April first, 2015. Data regarding outpatient visits, clinical attendance, oncolytic drug use, imaging, lab tests, radiotherapy and surgery were collected.
Results: Sixty-seven patients were included with a median age of 67 years. The median follow-up was 234 days. On average patients had 28 outpatient visits and 11 inpatient days. Oncolytic drugs were administered to 76% of the patients. Mean per patient expenditures amounted up to €17,463, with oncolytic drugs (€6,390) as the main cost driver. In comparison with the time-period of 2003–2005 total per patient per year expenses decreased by 44%. The contribution to total yearly costs of oncolytic drugs increased from 18% to 35%, while costs for inpatient stay decreased from 52% to 28% of total expenditures.
Conclusion: Outcomes in this study demonstrate that average treatment costs for metastatic NSCLC in the Netherlands Cancer Institute amount to €17,463. Compared to a prior study the average cost for metastatic NSCLC over time in the Netherlands has decreased. A shift of main cost drivers seems to have occurred from inpatient stay, to oncolytic drugs as main contributor. The shift towards treatment cost might become more visible with the introduction of immunotherapy. These results mark the importance of up-to-date cost of illness studies.

1. Background

Lung cancer is the fourth most common cancer in the Netherlands [1]. With over 12,000 diagnoses in 2015, it accounts for over 10,000 annual deaths [1].

The treatment and prognosis of NSCLC depends on the stage of disease at diagnosis. Metastatic NSCLC (stage IV) is incurable and has a poor prognosis with a five-year overall survival (OS) rate of 4% [2]. Treatment guidelines for metastatic NSCLC consist of palliative treatment with oncolytic drugs, radiotherapy, surgery, a combination of these treatments or best supportive care [3,4].

Cancer treatment is currently highly discussed, because of expensive treatments involved; insight in the baseline costs is therefore essential to allow for highly valid cost-effectiveness calculations and decision-making. The treatment of metastatic NSCLC constitutes a large burden on healthcare in terms of costs [5–7], especially now expensive immunotherapy strategies become widely available.

In order to gain insight in the NSCLC healthcare burden, Pompen et al. (2009) conducted a retrospective by-chart-review cost of illness (COI) study in 102 patients diagnosed with advanced NSCLC during 2003–2005 in the Netherlands [6]. The estimated intramural healthcare burden of metastatic NSCLC amounted up to €32,386 per patient/year in this time period. Inpatient stay was the main contributor and oncolytic drugs were the second largest contributor [6].

Pompen et al. provided a useful insight in NSCLC costs for the period 2003–2005. Expenses on cancer treatment have however increased two-fold in the period of 2003–2011 as reported by Dutch authorities from 2.4 to 4.8 billion euros a year [8]. In the same time span, expenditures on oncolytic drugs in the Netherlands increased more than three-fold [9]. Relatively new oncolytic drugs for NSCLC i.e.

* Corresponding author at: Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Heidelberglaan 100, 3584 CG Utrecht, Room number. 7.155, The Netherlands.
E-mail address: G.W.J.Frederix@umcutrecht.nl (G.W.J. Frederix).

http://dx.doi.org/10.1016/j.lungcan.2017.10.005
Received 20 May 2017; Received in revised form 9 October 2017; Accepted 12 October 2017

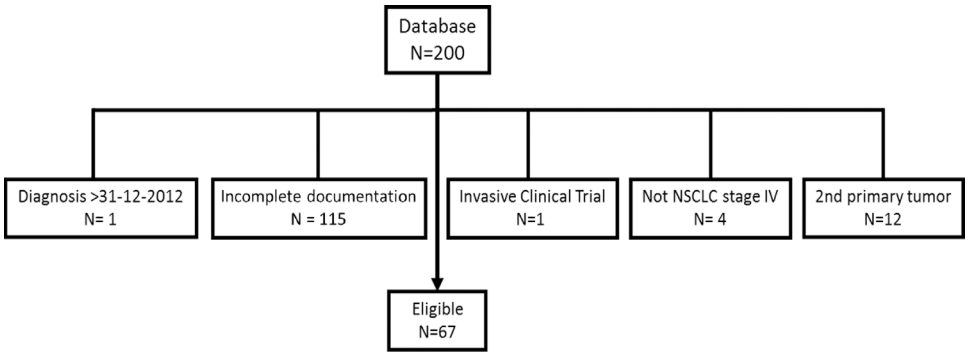

Fig. 1. Exclusion after individual assessment.

pemetrexed and new orally dosed tyrosine kinase inhibitors e.g. erlotinib, gefitinib and crizotinib all obtained marketing approval and were implemented in the standard of care [10].

These new oncolytic drugs have a substantially higher price per dose than older oncolytic drugs [11]. Data on the healthcare burden of metastatic NSCLC treatment in the Netherlands, have however not been reported since the study by Pompen et al.

Therefore, we aimed to determine total intramural COI in patients diagnosed with metastatic NSCLC in the period of 2006–2012. The secondary objective of this study was to identify changes in cost patterns over time.

2. Methods

2.1. Patient selection

Healthcare utilization data was obtained by a retrospective medical chart review. Charts were provided by the Netherlands Cancer Institute (NCI; a cancer referral center in Amsterdam). Patients were selected using a search combining data from the Electronic Patient Database (EPD) and the cancer registry database. The search included the following criteria: diagnosis of stage IV NSCLC between 1-1-2006 and 31-12-2012, according to the AJCC lung cancer staging version 7; follow-up in the NCI from diagnosis until death or until the data cut-off date of April first, 2015; no registered clinical trial participation in the NCI at any time during treatment for NSCLC.

2.2. Exclusion

All patient records retrieved from the search were individually assessed on in- and exclusion criteria. When during data collection the patient record was found to be incomplete or a patient was diagnosed with a secondary primary tumor in the follow-up period the patient record was excluded from the analyses.

2.3. Data collection

Data collection was standardized using an electronic Case Report Form (eCRF). Data was retrieved from the first visit after diagnosis of metastatic NSCLC, until death or end of data collection on April first, 2015. Data collected consisted of patients characteristics and healthcare utilization data.

Demographic characteristics: age, gender, date of birth, ECOG (Eastern Cooperative Oncology Group) performance score (PS), site of metastases, date of diagnose, date of disease progression and date of death were collected. When applicable, the reason for exclusion was recorded.

Healthcare utilization data consisted of: date and type of inpatient visit; date, type and length of outpatient visit; date, type and dose of oncolytic drugs; date and frequency of radiotherapy; number and type of laboratory tests; date and type of surgical procedures. Data concerning imaging was directly extracted from the Hospital Information System (HIS). Dates of all events were registered and all data were collected by one investigator (WK).

2.4. Unit costs

Unit costs were based on Dutch guidelines [11–13] or on available literature, if costs were not available in the guidelines [14]. If both sources did not provide sufficient information, unit costs were based on prices as determined by another academic hospital [15]. Because cost on surgical procedures were largely unknown, these costs were not considered in this analyses and were therefore accounted as being zero.

2.5. Cost comparison

Outcomes as published by Pompen et al. were extracted from the published article [8]. In this study Pompen and colleagues report on two patient populations: group A received best supportive care (BSC) and group B received second-line treatment in addition to BSC. The weighted mean cost/patient/year for both groups was considered the mean cost per patient for that population. In order to correct for differences in follow-up time, all cost outcomes, excluding cost for oncolytic therapy, from this study were converted from cost/patient into cost/patient/year, using the reported mean follow-up.

3. Results

In total 67 patients were found eligible for data collection. In 115 patients follow-up was incomplete and eighteen were not eligible for the study, an overview of reasons for exclusion of patients is shown in Fig. 1.

3.1. Patient Demographics

Of 67 eligible patients 30 were male (45%) and 37 female (55%), mean age at diagnosis was 67 for male patients and 55 years for female patients. Overall patients had a good PS of 0–2, only three patients with a PS greater than 2 were included in the study. The baseline characteristics are presented in Table 1.

Mean follow-up time was 348 days (median 234 days) and three patients were alive on the data cut-off date of April first 2015. Bone (37%) and brain metastases (24%) were the most frequent sites of distant metastases. Adenocarcinoma (51%) was the most common histological subtype, followed by large cell carcinoma (22%) and squamous cell carcinoma (19%). KRAS and EGFR mutations were found in 13% and 6% of patients, respectively.

3.2. Total costs

A detailed representation of mean cost per patient is provided in Table 2. Total mean cost per patient amounted to €17,463 (median:

Table 1
Patient characteristics of all included patients.

Patient Characteristics	N	%
Total		
Women	37	55
Men	30	45
Age (years)		
Men, median	67	
Range	33–89	
Women, median	55	
Range	24–76	
Performance status (ECOG)		
0–2	51	76
> 2	3	4
Unknown	13	19
Year of Diagnosis		
< 1-1-2010	25	37
> 31-12-2009	42	63
Site of Metastases		
Adrenal	9	13
Bone	25	37
Brain	16	24
Kidney	3	4
Liver	8	12
Lung	9	13
Lymfe	4	6
Mediastinal	2	3
Neck	5	7
Other	14	21
Follow-up (days)		
Mean	348	
Median	234	
Range	24–2829	
Histology		
Adenocarcinoma	34	51
Large Cell Carcinoma	15	22
Squamous Cell Carcinoma	13	19
Unknown Carcinoma	5	7
Mutations		
EGFR Mutation	4	6
KRAS Mutation	9	13
Unknown Mutation	54	81

Abbreviations: ECOGEastern Cooperative Oncology Group.

€14,824, range €624– €68,099). Oncolytic drugs (€6,390; 37%) were the most important cost driver followed by costs for inpatient stays (€4,766; 27%). Total cost of outpatient visits accounted for €3,156 and imaging costs amounted to €1,835. Costs of laboratory tests (€328) was the smallest contributor to healthcare resources used. Total cost per patient for radiotherapy was €987.

3.3. Utilization

The mean oncolytic drug use amounted up to 6.8 doses of Intravenously administered Oncolytic Drugs (IOD) and 21.3 doses (days) of Orally administered Oncolytic Drugs (OOD). The most frequently used healthcare utilization were outpatient visits. On average patients were seen 28 times. Medical specialist visits, medical specialist phone consults and day care visits were the most frequently used types of outpatient visits, respectively 15.3, 8.2 and 3.9 visits.

Patients had a mean of 11.1 inpatient days which was associated with 2.9 hospitalizations or ward transfers per patient. Most commonly used laboratory test was blood analyses which was used 15.1 times per patient. Chest X-ray and CT-scan were the most frequently used imaging methods, respectively 5.7 and 3.3 times per patient. In total a mean of 8.9 fractions of radiotherapy and 0.5 surgical procedures per patient were registered.

3.4. Incidence of treatment

Ninety-eight point five percent of patients visited the outpatient clinic (one patient was only treated during an inpatient stay). Oncolytic drugs were prescribed to 76.1% of patients. Imaging was performed in 98.5% of patients. Hospitalization occurred in 65.7% of patients. Laboratory tests were performed in 91.0% of patients. Radiotherapy was given to 80.6% of patients. Surgical procedures occurred in 23.9% of patients during the follow-up period.

3.5. Oncolytic drugs

A detailed overview of oncolytic drugs used is shown in Table 3. Cost for IOD was higher than cost for OOD, €4,924 and €1,466 respectively. Gemcitabine (2.1 doses) was the most frequently administered IOD. Pemetrexed, however was the largest contributor to the costs (€3,961) and was also the drug most frequently used (47.8% of patients). Of all OOD, erlotinib was the most prescribed. On average patients received 17.1 days of treatment with erlotinib. It was also the most frequently used (26.9%) and the biggest contributor to costs (€1,265) for OOD.

3.6. Cost comparison

Inclusion criteria differed slightly between this study and the study of Pompen et al. Here we only included patients diagnosed with stage IV NSCLC regardless of the PS. Pompen et al. included patients with stage IIIB or stage IV NSCLC and with a PS of ≤ 2. In result Pompen et al. reported a mean of 12.5 months follow-up in group A (BSC) (N = 74) and 14.4 months follow-up in group B (second-line treatment and BSC) (N = 28). Whereas average follow-up reported in this study was 11.4 months (348 days). The cost comparison is shown in Table 4. Compared to Pompen et al. (2003–2005) mean cost per year of NSCLC treatment decreased by 43% (from € 32,386 to € 18,010 per patient per year). Mean per patient per year expenses on all contributors decreased, except for expenses on oncolytic drugs and outpatient visits. Mean cost of inpatient stay decreased from €16,777 to € 5,001 per patient per year. Fig. 2 shows the comparison of the two studies on cost distribution data per patient per year. Mean per patient expenses on oncolytic drugs increased from 18% to 35%, while mean per patient per year expenses on inpatient stay decreased from 52% to 28%. Mean per patient per year expenses on outpatient visits increased from 8% to 18%.

4. Discussion

Our results show that the average mean intramural cost of metastatic NSCLC amounted up to €17,463 per patient in the period 2006–2012 in the NCI. The costs consisted mainly of expenses on oncolytic drugs and inpatient stays, which contributed to 37% and 27% respectively of the total treatment costs.

Compared to the period 2003-2005 total cost per patient per year of metastatic NSCLC in the Netherlands decreased, while expenses on oncolytic drugs and outpatient visits rose. The decrease in cost could mainly be attributed to a decrease in cost of inpatient stays. The reduction in hospitalizations can partially be attributed to less cisplatin administrations (1.2 doses versus 3.3 doses), since patients were not admitted to receive treatment. A second factor contributing to the reduced healthcare costs is the special referral role of the NCI, which biases our population to a more gradual disease course. This referral role could in addition result in unregistered care in local hospitals. In order to counteract this, patients treated in other hospitals were excluded from the study. However it is likely that some of the local care was not registered at the NCI and therefore unregistered in this study. Finally our population differed from the population by Pompen et al. as they included patients with stage IIIB and stage IV NSCLC (according to the AJCC lung cancer staging version 6, not reported), where this study

Table 2
Healthcare resource utilizations and costs.

Cost per healthcare resource	Unit Cost	Mean	Median	Range	Costs	% Treated
Oncolytic Drugs (OD)						
IOD	€ 727[11]	6.8	6	0–28	€ 4924	65.7
OOD	€ 69[11]	21.3	0	0–425	€ 1466	29.9
Total OD					€ 6390	76.1
Outpatient Visit						
Accident/Emergency	€ 151[12]	0.1	0	0–2	€ 9	4.5
Day Care	€ 159[12]	3.9	2	0–24	€ 615	59.7
Dietician	€ 27[12]	0.04	0	0–1	€ 1	4.5
Medical Specialist (MS)	€ 129[12]	15.3	11	0–51	€ 1970	97.0
Nurse	€ 28[12]	0.3	0	0–2	€ 8	0.3
Phone Consult MS	€ 65[12]	8.2	5	0–33	€ 529	88.1
Other Outpatient	€ 80[12]	0.3	0	0–7	€ 25	0.1
Total Outpatient		28.0	24	0–76	€ 3156	98.5
Inpatient Stay						
Inpatient Day	€ 218[12]	0.3	0	0–4	€ 71	20.9
Inpatient Night	€ 437[12]	10.7	5	0–47	€ 4694	64.2
Total Inpatient Days		11.1	5	0–49	€ 4766	65.7
Laboratory						
Blood Test	€ 16[13,14]	15.1	11	0–48	€ 236	89.6
Culture	€ 16[13,14]	4.0	0	0–68	€ 64	43.3
Mutation Analysis	€ 209[13]	0.01	0	0–1	€ 3	1.5
Pathology	€ 36 [13]	0.7	0	0–5	€ 25	43.3
Total Laboratory tests		19.8	14	0–95	€ 328	91.0
Imaging						
CTRT	€ 160[13,15]	1.3	1	0–5	€ 210	58.2
CT − scan	€ 202[13,15]	3.3	3	0–15	€ 675	76.1
ECG	€ 18[13]	0.9	0	0–6	€ 16	40.3
PET-scan	€ 1,300[13]	0.2	0	0–3	€ 252	13.4
X-Ray	€ 54[13,15]	5.7	4	0–24	€ 308	89.6
Ultrasound	€ 61[13,15]	0.8	0	0–4	€ 50	47.8
MRI	€ 198[13]	1.1	0	0–17	€ 210	46.3
MRRT	€ 196[13]	0.1	0	0–1	€ 12	6.0
Revision	€ 18[13]	0.1	0	0–1	€ 1	6.0
Scintigraphy	€ 133[13]	0.03	0	0–2	€ 4	1.5
Other imaging	€ 115[13]	0.9	0	0–8	€ 98	38.8
Total Imaging		14.3	14	0–44	€ 1835	98.5
Radiotherapy						
No. Fractions	€ 111[14]	8.9	8	0–33	€ 987	80.6
Total Radiotherapy		8.9	8	0–33	€ 987	80.6
Surgery						
Lobectomy	€ 0	0.01	0	0–1	€ 0	1.5
Pericardium Puncture	€ 0	0.01	0	0–1	€ 0	1.5
Peripheral Infusies	€ 0	0.1	0	0–3	€ 0	7.5
Pleurodesis	€ 0	0.2	0	0–4	€ 0	6.0
Puncture	€ 0	0.03	0	0–1	€ 0	3.0
Peripheral Catether	€ 0	0.03	0	0–1	€ 0	3.0
Resection Metastases	€ 0	0.01	0	0–1	€ 0	1.5
Diagnostic Pleural Puncture	€ 0	0.01	0	0–1	€ 0	1.5
Stent placement	€ 0	0.04	0	0–3	€ 0	1.5
Other surgery	€ 0	0.1	0	0–1	€ 0	7.5
Total Surgery		0.5	0	0–6	€ 0	23.9
Total					**€ 17,463**	**100.0**

IOD: Intravenous Oncologic Drugs, OOD: Oral Oncologic Drugs.

looked at stage IV disease according to the AJCC lung cancer staging version 7. As a result patients with pleural effusion were now scored as having stage IV disease rather than stage IIIB. A bias remains towards lower costs in our study, since no stage IIIB patients without pleural effusion were included.

Nevertheless the dramatic decrease in inpatient stays seems to confirm the hypothesis that new oncolytic drugs and treatments are successfully diminishing the number and the length of hospitalizations in this population.

Expenses on oncolytic drugs have increased significantly. This increase is even more notable since only 76.1% versus 100% of patients were treated with oncolytic drugs in this study and Pompen et al. respectively. The increase in cost of oncolytic drugs can be attributed to costs of the oncolytic drugs pemetrexed and erlotinib, these account for 82% of costs on oncolytic drugs. Drug prices of 2017 were used to correct for significant changes in drug pricing, for instance the patent of pemetrexed expired in 2016 [16]. However new immunotherapeutic drugs (e.g. nivolumab and pembrolizumab) have recently obtained marketing approval for the treatment of NSCLC. Therefore costs on oncolytic drugs are likely to increase further as these immunotherapeutic drugs are even more costly.

In order to put our results into perspective, cross validation was performed with other international COI studies. This is difficult as treatment standards for metastatic NSCLC differ between countries and hospitals. The most recent study [17] estimated mean hospital costs for 71 patients diagnosed in 2008 in Spain to be €15,044 [17], while other studies estimated mean hospital cost at €22,066 in Switzerland (1998) [18], and at 11,996 AUD in Australia (2005–2006) [19], which equals

Table 3
Detailed representation of oncolytic drugs utilization.

Cost of oncolytic drug use	Cost per mg	Mean Doses	Median Doses	Range	Mean Cost	% Treated
Intravenous Oncolytic Drugs (mean dose)						
Carboplatin (574 mg)	€ 0.33[11]	1.4	0	0–10	€ 267	41.8
Cisplatin (95 mg)	€ 0.47[11]	1.2	0	0–24	€ 53	29.9
Docetaxel (132 mg)	€ 5.49[11]	0.3	0	0–6	€ 217	7.5
Gemcitabine (2092 mg)	€ 0.09[11]	2.1	0	0–17	€ 398	32.8
Paclitaxel (150 mg)	€ 2.62[11]	0.01	0	0–1	€ 6	1.5
Pemetrexed (876 mg)	€ 2.66[11]	1.7	0	0–11	€ 3961	47.8
Other IOD[a]	€ 2.88[11]	0.03	0	0–2	€ 22	1.5
Total IOD		6.8	6	0–28	€ 4924	65.7
Oral Oncolytic Drugs (mean dose)						
Afatinib (280 mg)	€ 1.65[11]	0.2	0	0–14	€ 96	1.5
Erlotinib (144 mg)	€ 0.51[11]	17.1	0	0–425	€ 1265	26.9
Gefitinib (77 mg)	€ 0.35[11]	3.9	0	0–217	€ 105	4.5
Total OOD		21.3	0	0–425	€ 1466	29.9
Total					€ 6390	76.1

[a] Other IOD include multiple IOD with different prices per mg, a weighted mean is presented.

Table 4
Cost of illness per patient per year extracted from publication of Pompen et al. compared to outcomes (cost/patient/year) from this study.

Healthcare resource (cost/patient/year)	Pompen et al.	This study
Oncolytic Drugs (cost/patient)[a]	€ 5711	€ 6390
Outpatient Visit	€ 2502	€ 3312
Inpatient Stay	€ 16,777	€ 5001
Laboratory + Imaging	€ 4350	€ 2271
Radiotherapy	€ 3045	€ 1036
Surgery	€ 0	€ 0
Total Costs	€ 32,386	€ 18,010

[a] Cost of oncolytic drugs was expressed as costs per patient.

to approximately €8500. Based on literature data our findings of mean total cost of € 17,463 for metastatic NSCLC seem to be comparable to international series, but because of great differences in costs between countries no hard conclusions can be drawn. Differences in distribution of cost are more straightforward to compare. All studies reported by Kang et al. [19] reported inpatient stay to be the main cost driver in the United States, Canada, Ireland, Australia and the Netherlands [6]. The most recent study however, reported oncolytic therapy as the main cost driver in patients treated in Spain (2008) [17]. This is in line with our presumption that there might be a shift in cost distribution towards oncolytic drugs, which is mainly influenced by new expensive oncolytic drugs.

The observed differences in cost distribution and total costs per patient per year between 2003–2005 and 2006–2012 are striking. This indicates that COI studies are sensitive to the time period in which the study is conducted. NSCLC treatment with nivolumab today costs about €1500–€3000,- per dose [11] and patients received a median number of cycles ranging between 6 and 8 doses, depending on tumor histology [20]. This will most likely result in increased expenses on oncolytic drugs. This highlights further that COI studies reflect the current situation and that they are unreliable for long-term use. COI studies provide insights in cost patterns of a certain illness and are the basis for cost-effectiveness studies. Therefore transparent and up-to-date research on COI, is of critical importance to allow for high quality cost-effectiveness research.

Even though our study was carefully designed, the study has limitations. The NCI is actively participating in clinical trials in all stages of drug-development. A selection bias has therefore likely occurred, as patients included in trials are generally the ones with a good performance status and better survival. Secondly, the NCI is a tertiary hospital to which patients are referred to from general and academic hospitals in the Netherlands. This special role biases the population towards patient with more severe disease grade compared to the population that general and academic hospitals probably would have. The fact that our research was solely performed in de NCI could have influence the population and therefore treatment costs. Furthermore, the study period is quit long (2006 till 2012), which might have created a heterogeneous group. Though treatment guidelines did not change dramatically, though over the study period.

In our study more women were included at relatively young age, compared to men. This difference is not consistent with cancer incidence and mortality in the Netherlands, which reports a higher incidence of lung cancer in men [1,21]. The referral function of the NCI and an increase in smoking among females partially explain the higher number of female patients with NSCLC included in our trial.

Costs per patient were not normally distributed but skewed to the right. In addition the wide range of follow-up used in this study could potentially result in higher costs, as analysis showed that patients with longer follow-up tend to have a higher cost of treatment (R^2 = 0.177). Differences in study population and follow-up time between our study and Pompen et al. could explain some of the loss of costs. However, costs of treatment per patient do not divide equally over time and

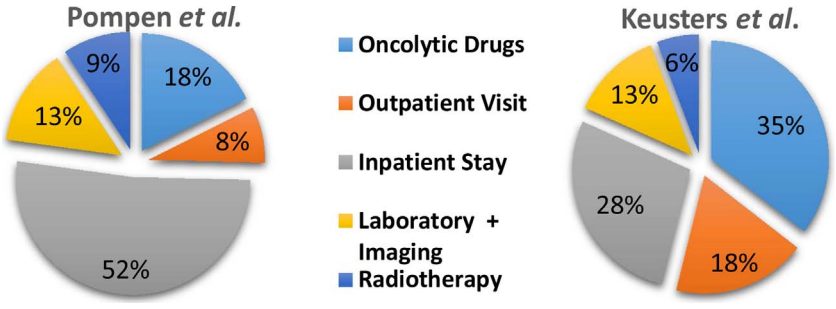

Fig. 2. Cost distribution extracted from Pompen et al. and cost distribution of this study. All cost are presented per patient per year, except for oncolytic drugs which was presented as cost per patient.

extrapolation could be a dangerous step in presenting real world outcomes. In extend, total costs of treatment are more relevant for interpretation of cost patterns, as survival is an important factor contributing to total costs, which should not be ignored when calculating treatment costs. Therefore correction for follow-up was only done in order to make comparison possible between our study and Pompen et al. and not to present real world costs.

Our research was solely focused on cost utilization. Real world COI studies also include extramural healthcare. In order to put intramural costs in perspective Pacolet et al. calculated that intramural costs accounted for 81% of the whole treatment cost of lung cancer in the Netherlands in 2005 [22]. If this is still the case in 2015, than our results could be used to perform a realistic estimation of total real world cost of metastatic NSCLC.

5. Conclusion

Mean intramural cost of treatment of metastatic NSCLC patients treated in our cancer referral center amounted to €17,463. Compared to 2003–2005 the average cost for metastatic NSCLC over time in the Netherlands has decreased. A shift of main cost drivers seems to have occurred from inpatient stay in 2003-2005, to oncolytic drugs as the main contributor. This shift is largely attributable to new expensive oncolytic drugs, as they raise oncolytic drug expenses. Meanwhile a decrease in hospital admissions costs occurred. However as a result of the referral function of the NCI, hospital admissions might be underestimated. Our results mark the importance of up-to-date COI studies as we showed that they are sensitive to new developments, this might become of higher importance as the expensive immunotherapeutic drugs are currently entering the market. We expect that the trend of decreasing costs over time will not be representative as immunomodulatory drugs will drive the trend into the opposite direction.

Conflict of interests

None.

References

[1] Integraal Kankercentrum Nederland. Nederlandse Kankerregistratie [Internet], (2014) [cited 2015 Mar 5]. Available from: http://www.cijfersoverkanker.nl/.

[2] K. Cetin, D.S. Ettinger, C. O'Malley, Survival by histologic subtype in stage IV nonsmall cell lung cancer based on data from the surveillance, epidemiology and end results program, Clin. Epidemiol. 3 (April) (2011) 139.

[3] UpToDate. Personalized Genotype Directed Therapy For Advanced Non Small Cell Lung Cancer [Internet], (2017) [cited 2015 Jul 15]. Available from: http://www.uptodate.com/contents/personalized-genotype-directed-therapy-for-advanced-non-small-cell-lung-cancer?source=see_link&anchor=H9880670#H9880670.

[4] C.G. Azzoli, S. Baker, S. Temin, W. Pao, T. Aliff, J. Brahmer, et al., American society of clinical oncology clinical practice guideline update on chemotherapy for stage IV non-small-cell lung cancer, J. Clin. Oncol. 27 (36) (2009) 6251–6266.

[5] S. Navaratnam, E.V. Kliewer, J. Butler, A.a. Demers, G. Musto, K. Badiani, Population-based patterns and cost of management of metastatic non-small cell lung cancer after completion of chemotherapy until death, Lung Cancer 70 (1) (2010) 110–115 Elsevier Ireland Ltd..

[6] M. Pompen, M. Gok, A. Novák, R. van Wuijtswinkel, B. Biesma, F. Schramel, et al., Direct costs associated with the disease management of patients with unresectable advanced non-small-cell lung cancer in The Netherlands, Lung Cancer 64 (2009) 110–116.

[7] J.J. Carlson, D.L. Veenstra, S.D. Ramsey, Pharmacoeconomic evaluations in the treatment of non-small cell lung cancer, Drugs 68 (8) (2008) 1105–1113.

[8] www.volksgezondheidenzorg.info. Cost of Illness Tool. [Internet]. [cited 2017 Feb 5]. Available from: https://kostenvanziektentool.volksgezondheidenzorg.info/tool/english/.

[9] KWF kankerbestrijding. Toegankelijkheid van dure kankergeneesmiddelen, Nu en in de toekomst [internet], (2017) [cited 2015 jun 19]. Available from: https://www.kwf.nl/sitecollectiondocuments/sck%20rapport%20toegankelijkheid%20van%20dure%20kankergeneesmiddelen.pdf.

[10] College ter Beoordeling van Geneesmiddelen. Geneesmiddeleninformatiebank [Internet], (2017) [cited 2015 Jun 19]. Available from: http://www.geneesmiddeleninformatiebank.nl/en.

[11] Zorginstituut Nederland. Medicijnkosten [Internet], (2017) [cited 2017 Sep 29]. Available from: http://www.medicijnkosten.nl/.

[12] L. Hakkaart- van Roijen, S.S. Tan, C.A.M. Bouwmans, Handleiding voor kostenonderzoek Methoden en standaard kostprijzen voor economische evaluaties [Internet], (2017) Available from: http://docplayer.nl/6361834-Handleiding-voor-kostenonderzoek-methoden-en-standaard-kostprijzen-voor-economische-evaluaties-in-de-gezondheidszorg.html.

[13] Nederlandse zorgautoriteit. Bijlage 2 bij Beleidsregel CU-2065 Tarieflijst Instellingen [Internet], (2012) Available from: https://www.nza.nl/1048076/1048155/BR_CU_2065_bijlage_2_Medisch_specialistische_behandelingen_en_tarieven_2012. xls.

[14] G.W.J. Frederix, J.L. Severens, A.M. Hövels, J.G.C. van Hasselt, M.J.J. Hooiveld, P. Neven, et al., Real world cost of human epidermal receptor 2-positive metastatic breast cancer patients: a longitudinal incidence-based observational costing study in the Netherlands and Belgium, Eur. J. Cancer Care 24 (3) (2015) 340–354.

[15] Universitair Medisch Centrum Groningen. Tarieven UMCG [Internet], (2013) Available from: http://docplayer.nl/12464280-Overzicht-tarieven-onderlinge-dienstverlening-umcg-per-1-januari-2013.html.

[16] Zorginstituut Nederland Beoordeling pemetrexed alimta [Internet], (2016) Available from: https://www.zorginstituutnederland.nl/binaries/content/documents/zinl-www/documenten/publicaties/geneesmiddelbeoordelingen/2016/1607-beoordeling-pemetrexed-alimta/Beoordeling+pemetrexed+(Alimta).pdf.

[17] J. Corral, J.A. Espinàs, F. Cots, L. Pareja, J. Solà, R. Font, et al., Estimation of lung cancer diagnosis and treatment costs based on a patient-level analysis in Catalonia (Spain), BMC Health Serv. Res. 15 (January) (2015) 70.

[18] K.J. Dedes, T.D. Szucs, S. Bodis, M. Joerger, A. Lowy, E.W. Russi, et al., Management and costs of treating lung cancer patients in a university hospital, Pharmacoeconomics 22 (January (7)) (2004) 435—444.

[19] S. Kang, E.-S. Koh, S.K. Vinod, B. Jalaludin, Cost analysis of lung cancer management in South Western Sydney, J. Med. Imaging Radiat. Oncol. 56 (April (2)) (2012) 235–241.

[20] J. Brahmer, K.L. Reckamp, P. Baas, L. Crinò, W.E.E. Eberhardt, E. Poddubskaya, et al., Nivolumab versus docetaxel in advanced squamous-cell non-small-cell lung cancer, N. Engl. J. Med. 373 (2) (2015) 123–135.

[21] F.I. Bray, E. Weiderpass, Lung cancer mortality trends in 36 European countries: secular trends and birth cohort patterns by sex and region 1970-2007, Int. J. Cancer 126 (March (6)) (2010) 1454–1466.

[22] J. Pacolet, A. Coninck De, De medische en niet-medische kosten van kankerpatiënten [Internet], (2017) available from: https://lirias.kuleuven.be/bitstream/123456789/320527/1/R1407.pdf.