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Thirteen-year analyses of medical oncology outpatient day clinic data: a changing field

Maximilian Marhold, Thais Topakian, Hermine Agis, Rupert Bartsch, Anna S Berghoff, Thomas Brodowicz, Thorsten Fuereder, Aysegül Ilhan-Mutlu, Barbara Kiesewetter, Michael Krainer, Gottfried J Locker, Christine Marosi, Gerald Prager, Manuela Schmidinger, Christiane Thallinger, Sabine Zöchbauer-Müller, Markus Raderer, Matthias Preusser, Wolfgang Lamm

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Division of Oncology, Department for Medicine I, Medical University of Vienna, Wien, Austria

Correspondence to
Dr Maximilian Marhold; maximilian.marhold@meduniwien.ac.at

ABSTRACT

Background Novel treatment modalities like targeted therapy and immunotherapy are currently changing treatment strategies and protocols in the field of medical oncology.

Methods Numbers of patients and patient contacts admitted to medical oncology day clinics of a large European academic cancer centre in the period from 2006 to 2018 were analysed using our patient administration system.

Results A patient cohort of 9.870 consecutive individual patients with 125.679 patient contacts was descriptively and retrospectively characterised. Mean age was 59.9 years. A substantial increase in both individual patients treated per year (+45.4%; 2006: 1.100; 2018: 1.599) and annual patient contacts (+63.3%; 2006: 8.857; 2018: 14.467) between 2006 and 2018 was detected. Hence and most interestingly, the ratio of visits per patient increased by approximately one visit per patient per year over the last 12 years (+12.4%; 2006: 8.0; 2018: 9.0). Further, a decrease of patient contacts in more prevalent entities like breast cancer was found, while contacts for orphan diseases like myeloma and sarcoma increased substantially. Interestingly, female patients showed more per patient contacts as compared with men (13.5 vs 11.9). Lastly, short-term safety data of outpatient day clinic admissions are reported.

Conclusions We present a representative and large set of patient contacts over time that indicates an increasing load in routine clinical work of outpatient cancer care. Increases observed were highest for orphan diseases, likely attributed to centralisation effects and increased treatment complexity.

Key questions

What is already known about this subject?

► Increases in approvals of cancer therapeutics, longer survival, centralisation effects and higher treatment complexity reshape the landscape of medical oncology treatment.

What does this study add?

► This study is the first to describe changes of characteristics of a large medical outpatient clinic patient cohort over time.

How might this impact on clinical practice?

► Our findings highlight the need to adapt to a novel era of medical oncology, that is defined by increases in patient numbers and visits as well as changes in cancer patient characteristics and entities.

INTRODUCTION

Cancer is the second-leading cause of death in industrialised countries. The economic burden of cancer for health insurances and care providers was reported to be increasing in recent years.[1] This observation is attributed to higher prevalence caused by more accurate diagnosis and longer survival of both incurable and hence chronically ill as well as curable patients with cancer.[2] Besides, potential pharmaceutical pricing policies as well as higher life expectancy within the general population and hence years at risk for the development of cancer may contribute to this finding. More accurate and earlier diagnosis was facilitated by the introduction of population-wide screening programmes such as colonoscopy and mammography plans and by creating awareness for cancer in the general population.[3] From a medical oncology point of view, prognosis and survival of cancer patients were ameliorated through the introduction of so-called 'targeted' agents, aiming at pharmaceutical inhibition of one specific molecular target,[4] the uprising of immunotherapeutic agents such as immune checkpoint inhibitors[5] and long-year efforts in combining and adopting of cytostatic therapeutic agents to more potent chemotherapy regimens. Besides, closer collaboration efforts with surgical specialties, radiation oncologists[6]

and the emergence of supportive care and rehabilitation programmes[7] can be seen as potential reasons for incremental patient survival and quality of life (QOL).

Many cancer entities have seen the approval of numerous new anticancer agents in the last 10 years, not only increasing survival, but also QOL of affected patients.[8] While in many cases these novel drugs are orally available and, in some cases, able to outcompete intravenous chemotherapy, 'chronification' of cancer in general leads to a higher burden for healthcare providers and insurance givers globally.[9]

As an example, in the entity of breast cancer (BCa) alone, the introduction of the first Her2-targeted therapeutic antibody trastuzumab, has led to an increase in 10-year overall survival rates of early Her2-positive breast cancer from 75% to 84%.[10] The addition of a second antibody targeting Her2 to trastuzumab, pertuzumab, has further increased disease-free survival in this population,[11] as has the addition of trastuzumab-emtansine (TDM-1) for patients not reaching pathological complete response prior to surgery.[12 13] Similar trends can be seen in metastatic BCa, where the approval of CDK4/6 inhibitors in the strictly hormone-dependent or luminal setting,[14 15] again use of trastuzumab and pertuzumab[16 17] as well as TDM-1[18] in Her2-positive BCa and most recently the addition of the immune checkpoint-inhibitor atezolizumab to chemotherapy in triple-negative breast cancer led to higher survival rates in cancer patient populations.[19]

In this study, we set to analyse and discuss changes in patient numbers at our academic hospital centre medical oncology outpatient wards and examine changes in prevalence of cancer entities over time. Further, we report short-term outcome measures for our study population and discuss the findings in light of relevant and recent literature.

METHODS

Our academic hospital is the largest tertiary healthcare centre in Austria. At our medical oncology department, which comprises of one inpatient ward and one outpatient day clinic, no changes in administrative routine or structures occurred since 2016, when two outpatient day clinics were fused and moved to another floor of the hospital. Tasks performed at the outpatient day clinic include but are not limited to intravenous therapy administration, administration of blood products, treatment of side effects and therapy complications, supportive care measures and performing thoraco- and paracenteses as well as bone marrow biopsies. Of note, patients receiving oral ambulatory therapies are not managed through our outpatient day clinic but through scheduled appointments in our outpatient ambulance and hence not registered in this analysis. Data were collected using our in-house patient administration system (AKIM) for the years 2006–2018 and exported as Microsoft Excel-files. Data for cancer entities and patient transfers/admissions to inpatient wards were available for the time frame of 10 years (2006–2015; 86.787 patient contacts, 6.044 individual patients) only, due to changes in software. Entity data were clustered for visualisation purposes. Data were anonymised and only one master file was kept by the first author. Individual patient determination was made using name and date of birth in order to exclude doublets. Only finalised patient contacts were included. Statistical analyses were performed using Microsoft Excel.

RESULTS

Descriptive results of a large tertiary cancer centre outpatient treatment patient cohort

Our study provides single-centre data on a large patient cohort of outpatient treatment visits over a time frame of 13 years (2006–2018). The total number of patients and patient contacts registered was 9.870 and 125.679, respectively. Mean age of the visiting patient was 59.9 years, with women being younger than men. 55.2% of contacts were accounted for by females, 44.8% by males. This is of interest as 5.149 and 4.271 individual patients registered were female and male respectively, meaning that women had–on average—approximately 1.5 more visits than men (13.5 vs 11.9; table 1). This difference was consistent after exclusion of gender-specific cancer entities (13.0 vs 11.8, online supplemental table 1).

Individual patient numbers as well as contacts per patient increase over time

Compared with 2006, the number of individual patients treated at our outpatient ward increased by 45.4% (figure 1A; 2006: 1.100; 2018: 1.599). This increase was gradual and consistent through all the years covered by our analysis. Strikingly, the number of patient contacts per year increased to an even greater extent by 63.3% (figure 1B;+63.3%; 2006: 8.857; 2018: 14.467) between 2006 and 2018. These findings translated into an increase of outpatient ward contacts per patient by approximately one contact per patient per year (figure 1C; 2006: 8.0; 2018: 9.0;+12.4%).

Table 1 Age, number of individuals treated, patient contacts and ratio of contacts per patient for male and female patients

	Mean age in years (SD)	Individual patients	Patient contacts	Contacts/Patient
Female	59.3 (12.6)	5.149	69.407	13.5
Male	60.7 (13.2)	4.721	56.272	11.9
Total	59.9	9.870	125.679	

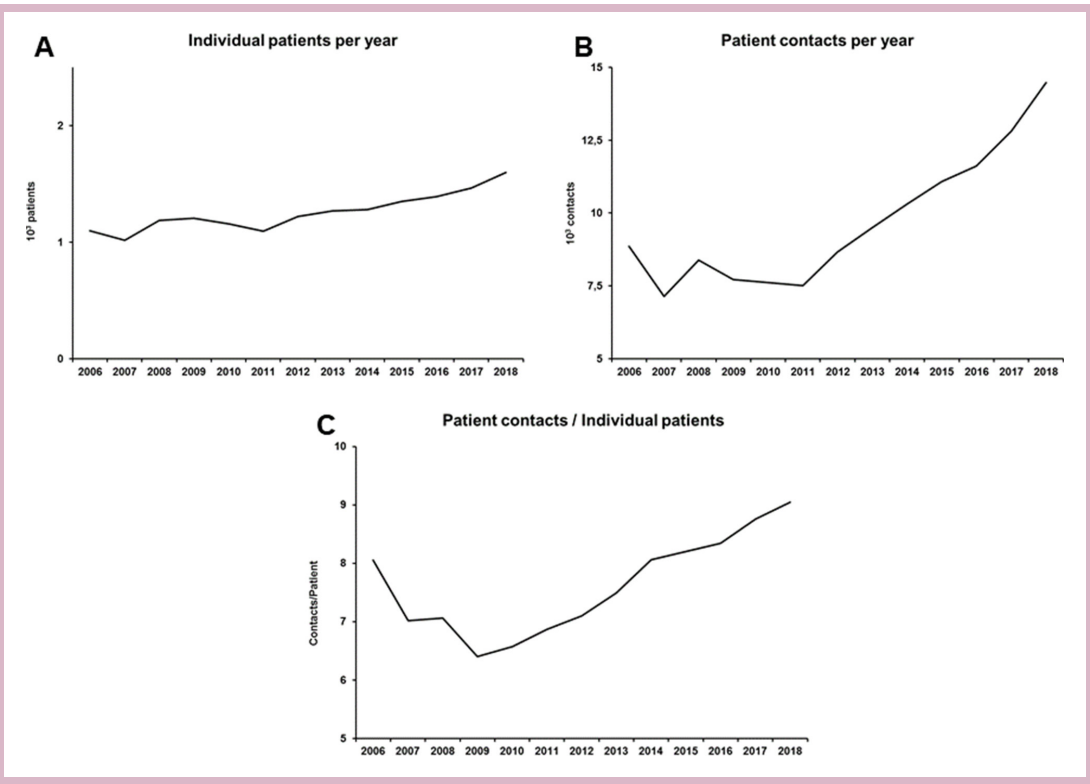

Figure 1 Development of patient numbers at a medical oncology outpatient day clinic in a large European tertiary cancer centre from 2006 to 2018. (A): Number of individual patients per year. (B): Number of patient contacts per year. (C): Ratio of patient contacts per individual patients per year.

Enhanced patient numbers caused by low-incidence cancer entities

Our department covers the treatment of all major solid tumours as well as selected haematological entities. Data available for the time frame 2006–2015 (86.787 patient contacts, 6.044 individual patients) showed a rise of patient contacts concerning the treatment of the relatively rare cancer entities multiple myeloma and sarcoma, while major entities like breast or gastrointestinal (GI) cancer lost when compared with the previously mentioned overall growth rate of patient contacts of 63.3% (figure 2A, table 2). Of note, myeloma and sarcoma were responsible for 62.2% of the increase seen in patient contacts between 2006 and 2015 (online supplemental table 2).

For entities causing 250–1000 patient contacts at our ward, we saw a decrease of gynaecological and urological cancers, while contacts with less frequent sarcoma patients increased disproportionally (figure 2B, table 2). Entities with fewer than 250 contacts per year showed marked increases for renal, upper GI (gastrointestinal) as well as CNS (central nervous system) cancer patient contacts, having said that yearly variations seemed high (figure 2C, table 2). When looking at historic data from individual patients in 2006 compared with the whole time frame of fully available data, we discovered changes in the composition of our patient collective reproducing the above-mentioned increases in lung cancer and smaller entities, and the relative decrease of patients suffering from breast, colorectal/pancreatic or gynaecological/urological cancers (figure 2D).

Low hospitalisation and high release rates indicate excellent safety of outpatient cancer treatment

Of 86.787 patient contacts at our outpatient ward from 2006 to 2015, 841 contacts (1.0%) led to admission to an inpatient ward of our hospital due to poor health status or treatment side effects. Of these patients, about one-third (n=305; 36.3%) were transferred to our own departments' wards and 23 patients (0.03%) were admitted to an intermediate/intensive care (IMC/ICU) units. No patient died while being admitted to the outpatient ward.

DISCUSSION

Our study represents a large descriptive single-centre analysis of medical oncology outpatient treatment, reporting data from 9.870 individual patients and 125.679 patient contacts. The results show interesting information about the excellent safety profile of ambulatory oncology treatment and an increase in patient numbers and contacts over time, as well as thought-provoking trends concerning changes in the patient population treated. The long time-frame and high patient as well as patient contact numbers are strengths of our study.

The prominent increase in patient contact numbers (figure 1A,B) is most likely attributed to centralisation effects on the national as well as international level. While

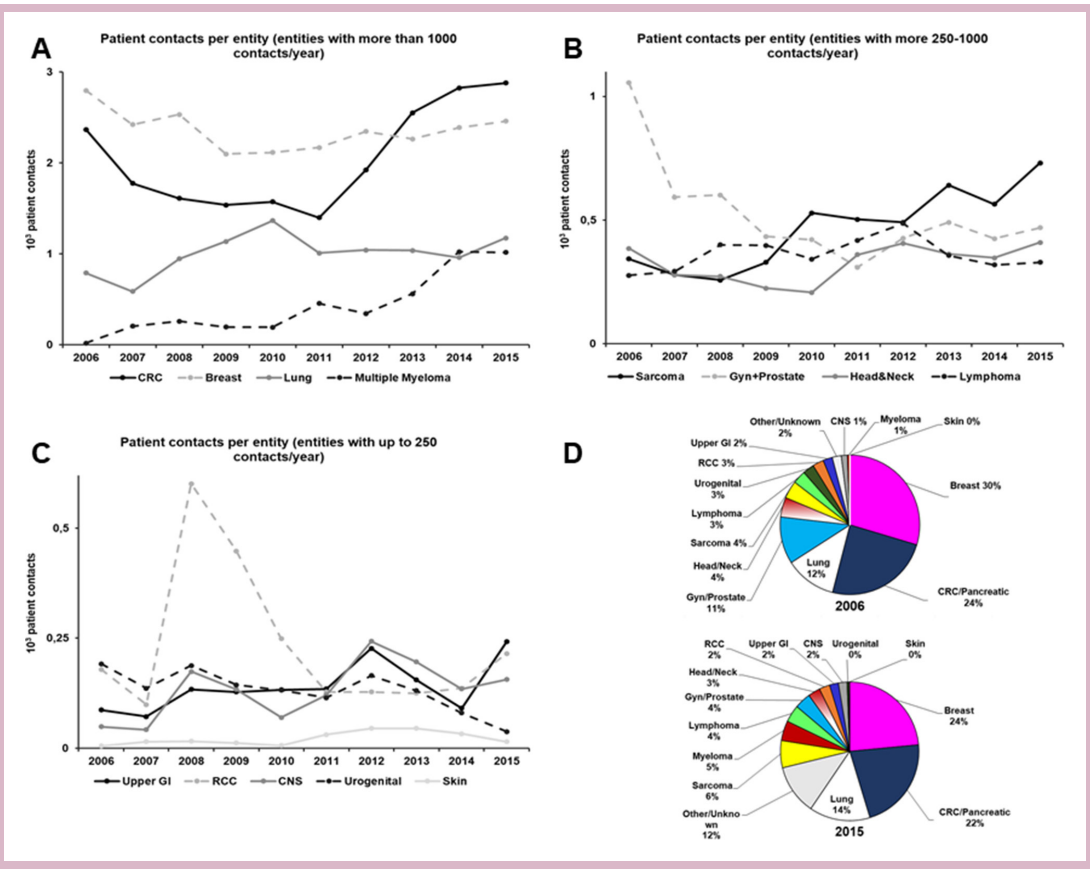

Figure 2 (A–C): Changes in patient contacts per entity over time (2006–2015). (D): Pie charts representing percentages of cancer entities of individual patients treated in 2006 (upper chart) and 2015 (lower chart). Upper GI, Upper Gastrointestinal Tract; RCC, Renal Cell Carcinoma; CNS, Central Nervous System.

Table 2 Patient contacts per year and entity from 2006 to 2015 and mean change (Δ) per year

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Δper year (%)
CRC/pancreatic	2365	1774	1609	1537	1571	1398	1920	2551	2823	2878	**+2.2**
Breast	2795	2421	2532	2098	2114	2168	2344	2263	2388	2459	**–1.2**
Lung	788	586	944	1135	1363	1007	1040	1037	959	1172	**+4.9**
Myeloma	19	203	259	194	193	453	343	559	1023	1016	**+53.47**
Sarcoma	343	279	257	329	529	503	491	641	564	731	**+11.3**
Gyn/prostate	1055	593	601	434	421	309	427	491	425	469	**–5.6**
Head/neck	385	278	272	224	207	360	406	363	347	409	**+0.6**
Lymphoma	276	293	400	397	342	418	486	357	319	329	**+1.9**
Upper GI	87	72	134	128	133	135	227	155	91	242	**+17.8**
RCC	179	99	601	448	249	128	128	125	136	215	**+2.0**
CNS	49	42	174	134	70	121	243	196	135	156	**+21.8**
Urogenital	192	136	188	144	132	115	165	131	80	38	**–8.0**
Skin	5	15	16	12	6	31	45	45	33	15	**+20.0**
Other/unknown	319	356	395	503	281	367	403	581	993	952	**+29.8**

Bold numbers mean annual change (%).

CNS, Central Nervous System; RCC, Renal Cell Carcinoma; Upper GI, Upper Gastrointestinal Tract.

centralisation in oncology can be helpful in ameliorating patient outcomes including survival, as shown by various groups in surgical oncology,[20 21] it causes higher administrative efforts and initial costs for the centres affected by higher patient numbers. This correlates with the established notion, that healthcare provider volume is a predictor of patient outcome for oncological procedures,[22] having said that data for medical oncology procedures such as chemotherapy administration are sparse compared with data reported for surgical procedures. Interestingly, from an administrative point of view, higher costs initially caused for centres affected by higher patient numbers do not outweigh the benefit in cost-effectiveness through centralisation, as described among others by Bristow *et al*.[23]

Moreover, we argue that gaining expertise as well as expert personnel over time for smaller entities additionally augmented centralisation effects within our centre. Offering expert treatment for orphan diseases, such as multiple myeloma, sarcoma or central nervous system tumours, directly influences the patient numbers seen for more underrepresented diseases in any single cancer centre, which in part explains the increases seen for these entities at our department (figure 2A, table 2).

The increase in patient numbers observed for multiple myeloma reflects the high number of newly approved therapeutic substances, their increasing use for this entity and better response/survival.[24] Blimark *et al*,[25] described a 50% increase of use of bortezomib, thalidomide and/or lenalidomide in the Swedish myeloma registry between 2008 and 2014 (31%–81% as part of first line treatment). Since administration of bortezomib and other novel therapeutics requires parenteral application, patient numbers at treatment administration facilities rise. Interestingly, Blimark *et al*[25] also highlighted the role of centralisation and treatment in academic cancer centres, with patients treated at such centres exhibiting better survival—confirming observations previously made by Go *et al*.[26]

Concordantly, we argue that approvals of novel cytostatic compounds drive the increase seen for patient visits per year as shown in figure 1C. For some entities, however, availability of novel orally available cytostatic compounds as well as intramuscular and subcutaneous therapies may decrease the number of patients seen at the outpatient day clinic, but increase patient contacts in our ambulance or elsewhere (eg, general practitioners offices). We were not able to register these contacts for this study. Examples for such phenomena could be the replacement of intravenous chemotherapy by CDK4/6 inhibitors for HR-positive/Her2-negative advanced breast cancer,[14] regorafenib or TAS-102 for metastatic colorectal cancer,[27 28] second generation antiandrogens for prostate cancer,[29 30] tyrosine kinase inhibitors for advanced renal[31 32] and EGFR- (Epidermal Growth Factor Receptor)mutated lung cancer[33] or antihormonal agents given through injections—such as somatostatin analogues for neuroendocrine tumours.[34]

In some instances, sharp increases and declines of patient contacts were caused by experimental testing of compounds in clinical trials (eg, increase in renal cancer patient contacts through the use of bevacizumab; figure 2C, years 2007–2009).[35]

Further, longer patient survival through more lines of therapy received creates an ageing patient population with more treatment-related comorbidities, again causing more complexity and more contacts per individual patient.[36] Interestingly, as shown in table 1, women had more visits when compared with men. This difference in patient contacts per individual patient between men and women was not driven by gender-specific cancer entities, as it remained stable after their exclusion (online supplemental table 1). This result potentially reflects longer life expectancy and the fact that women show higher adherence to healthcare providers and seek medical consultation more often.[37 38] Whether this is also true for cancer patients receiving chemotherapy at our ward remains unknown, having said that patients visiting our ward are encouraged to visit whenever side effects or complications occur. Behavioural and social[39] as well as biological[40] factors might influence whether patients come early or wait for resolution of symptoms. Furthermore, our study did not correct for types and intervals of treatments administered, which are different between genders. Therefore, we highlight the great need for gender-specific studies further investigating this apparent difference.

Lastly, treatment safety at our outpatient day clinic shows excellent short-term outcome as 1.0% of patient contacts led to patients not leaving the hospital the same day after having received therapy and 0.03% of patient contacts to transfer to IMC/ICU. Data from a smaller study by Markert *et al*[41] present a similar rate of chemotherapy-related severe adverse events (SAEs) of 0.8% per chemotherapy order, although various methodological differences between the studies and administrational and geographical differences between the centres hinder precise comparison. Please note that admissions at our outpatient day clinics examined are not limited to treatment administration and that endpoints of admission to inpatient ward and rates of SAEs should not be compared. Causes for admissions to inpatient wards, types and severity of adverse events[42] as well as further patient outcomes were not documented or analysed during this study. Also, prescription errors, previously shown to drive SAEs/admissions/readmissions of patients receiving ambulatory chemotherapy,[43 44] could not be assessed. Because of these two weaknesses of our study and due to its retrospective and single-centre design, comparing our outcome results to other centres remains challenging, especially for centres that are not within Europe and might have inferior access to therapies.

Concludingly, our work describes remarkable increases of patient numbers and contacts for ambulatory cancer patients receiving systemic therapy and

supportive care measures at one of the largest European academic cancer centres. Interestingly, increases observed were highest for orphan diseases, most likely attributed to centralisation effects. Higher treatment complexity possibly caused by higher number of newly approved therapies and longer survival of patients exhibiting higher rates of treatment-related morbidities resulted in more contacts per patient per year. Of note, more contacts per individual patient were observed for women.

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Patient consent for publication Not required.

Ethics approval Analyses and data acquisition were approved by our institutional ethics committee (vote number 1131/2020).

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ORCID iDs
Maximilian Marhold http://orcid.org/0000-0001-8439-3312
Hermine Agis http://orcid.org/0000-0002-1125-0211
Anna S Berghoff http://orcid.org/0000-0003-0767-6241
Aysegül Ilhan-Mutlu http://orcid.org/0000-0001-8291-0873
Barbara Kiesewetter http://orcid.org/0000-0002-5490-2371
Gerald Prager http://orcid.org/0000-0002-4751-6595
Manuela Schmidinger http://orcid.org/0000-0002-2567-2749
Matthias Preusser http://orcid.org/0000-0003-3541-2315

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