Population-Based Patterns of Care in the 1st Line Treatment of Patients with Advanced Esophagogastric Adenocarcinoma in Germany

Populations-bezogene Behandlungsrealität in der 1st line Therapie von Patienten mit fortgeschrittenem Adenokarzinom des Ösophagus oder Magens in Deutschland

Ralf-Dieter Hofheinz[1], Salah-Eddin Al-Batran[2], Karsten Ridwelski[3], Christian Görg[4], Klaus Wehle[5], Matthias Birth[6], Sebastian Fetscher[7], Harald Scheiber[8], Nadine Lukan[1], Florian Lordick[9]

[1]TagesTherapieZentrum (TTZ) am Interdisziplinären Tumorzentrum Mannheim (ITM) & III. Medizinische Klinik, Universitätsmedizin Mannheim; [2]Klinik für Onkologie und Hämatologie am Krankenhaus Nordwest, Frankfurt; [3]Chirurgische Klinik, Klinikum Magdeburg; [4]Klinik für Innere Medizin, Schwerpunkt Hämatologie, Onkologie und Immunologie, Universitätsklinikum Marburg; [5]Niederrheinklinik, Abteilung Hämatologie und Onkologie, Korschenbroich; [6]Chirurgische Klinik, Hanse-Klinikum Stralsund; [7]Klinik für Hämatologie/Onkologie, Sana-Kliniken, Lübeck; Klinik für Strahlentherapie und Radioonkologie, [8]Klinikum Ansbach; [9]Medizinische Klinik III, Klinikum Braunschweig, Medizinische Hochschule Hannover, Germany.

Correspondence

Prof. Dr. med. Ralf-Dieter Hofheinz

TagesTherapieZentrum am Interdisziplinären Tumorzentrum Mannheim

Universitätsmedizin Mannheim

Universität Heidelberg

68167 Mannheim

Phone: + 49-621-383-2855

Fax.: + 49-621-383-2488

e-mail: ralf.hofheinz@umm.de

Short title: 1st line treatment of patients with advanced esophagogastric adenocarcinoma in Germany

Keywords: Chemotherapy, metastatic gastric cancer.

Schlüsselwörter: Chemotherapie, metastasiertes Magenkarzinom

Therapiemonitor® was supported by grants of Sanofi-Synthelabo, Berlin, and Roche Pharma AG Grenzach-Wyhlen, Germany.

Abstract

Background: Randomized studies proved the efficacy of new drugs for the systemic treatment of advanced gastric cancer in the past 5 years. But little is known about the use of 1st line chemotherapy in clinical practice in patients with advanced or metastatic adenocarcinoma of the esophagogastric junction (AEG) and the stomach. We investigated temporal trends in therapy, and factors influencing treatment decisions for these patients during a four-year period.

Patients and methods: 1058 patients (median age 67 years) with advanced AEG or gastric cancers undergoing treatment decisions were documented with the Therapiemonitor® in 2006 – 2009. Therapiemonitor® collects population-based data regarding treatment decisions and strategies. Time trends of drug use and intensity in the 1st line treatment were analysed in the entire patient group and according to age (cut-off 65 years) and Karnofsky performance status (KPS; cut-off 80%).

Results: Over time the use of oxaliplatin and docetaxel as well as capecitabine increased, while cisplatin and irinotecan use slightly declined. The use of chemotherapy triplets rose from 10.1% in 2006 to 47.0% in 2009. Treatment patterns significantly varied by age and KPS: Older patients were significantly less likely to receive chemotherapy triplets, cisplatin and docetaxel but tended to receive more often oxaliplatin. Likewise, triplets, cisplatin and docetaxel were less frequently used in patients with KPS < 80%, while capecitabine and irinotecan were significantly more often used in this patient group.

Conclusion: A clear tendency towards the use of more intensive chemotherapy regimens in patients with AEG and gastric cancer was observed over time. Older or less fit patients were treated preferably with monotherapy or chemotherapy doublets during 2006 – 2009. Oxaliplatin and docetaxel use has substantially risen.

Abstract

Hintergrund: In den letzten 5 Jahren wurde die Effektivität neuer Zytostatika zur Behandlung des fortgeschrittenen Magenkarzinoms in randomisierten Studien belegt. Über die Verwendung von 1st-line Chemotherapie bei Patienten mit fortgeschrittenen oder metastasierten Adenokarzinomen des ösophagogastralen Übergangs (AEG) bzw. des Magens im klinischen Altag ist jedoch wenig bekannt. Wir untersuchten Zeit-Trends in der Therapie dieser Patienten und Faktoren, die Therapieentscheidungen beeinflussen innerhalb einer 4-Jahres-Periode.

Patienten und Methodik: 1058 Patienten (medianes Alter 67 Jahre) mit fortgeschrittenem AEG oder Magenkarzinom, bei denen Behandlungsentscheidungen getroffen worden waren, wurden zwischen 2006 und 2009 mit dem Therapiemonitor® dokumentiert. Im Therapiemonitor® werden Populations-bezogene Daten über Therapieentscheidungen und Behandlungsstrategien gesammelt. Analysiert wurden Zeit-Trends hinsichtlich des Einsatzes verschiedener Substanzen und der Behandlungsintensität in der 1st-line Therapie sowohl für die Gesamtgruppe als auch in Abhängigkeit von Alter (cut-off 65 Jahre) und Karnofsky Status (KPS; cut-off 80%).

Ergebnisse: Der Einsatz von Oxaliplatin, Docetaxel und Capecitabine hat über die Jahre zugenommen, während Cisplatin und Irinotecan weniger zum Einsatz kamen. Die Verwendung von Chemotherapie-Triplets (d.h. von drei aktiven Substanzen) stieg von 10,1% im Jahr 2006 auf 47,0% in 2009. Die Behandlungsstrategien unterschieden sich nach Alter und KPS des Patienten deutlich: Ältere erhielten signifikant seltener Triplets, Cisplatin und Docetaxel, aber tendentiell öfter Oxaliplatin. Auch Patienten mit einem KPS unter 80% wurden seltener mit Triplets, Cisplatin und Docetaxel behandelt, wohingegen Capecitabin und Irinotecan signifikant häufiger zum Einsatz kamen.

Zusammenfassung: Ein deutlicher Trend zum Einsatz intensiverer Chemotherapien wurde über die Jahre bei Patienten mit AEG und Magenkarzinom beobachtet. Ältere oder Patienten in weniger gutem Allgemeinzustand wurden im Dokumentationszeitraums 2006-2009 hauptsächlich mit Monotherapien und Zweifach-Chemotherapien behandelt. Der Einsatz von Oxaliplatin und Docetaxel hat deutlich zugenommen.

Introduction

Gastric cancer is the second most common cause of cancer death in the world [1]. In Germany, adenocarcinoma of the esophagogastric junction (AEG) and the stomach accounted for about 2.300 (AEG) and 11.000 (stomach) cancer deaths in 2006 and about 2.500 (AEG) and 19.000 (stomach) new cases are expected for 2010 [2]. Most patients present with locally advanced tumors or metastatic disease, and about 75% of all patients diagnosed with cancer of the AEG and the stomach will ultimately require palliative treatment.

Palliative chemotherapy was shown to prolong survival and to maintain quality of life [3]. Combination regimens with three active compounds have shown improved survival albeit at the price of higher treatment-related toxicity [3,4]. Palliative chemotherapy using 5-FU derivatives and platinum-compounds are widely accepted as standard of care but a reference regimen can not be defined. In Germany, weekly 24-hour infusional 5-fluorouracil (5-FU) in combination with folinic acid has frequently been used as backbone for the treatment for advanced gastric cancer [5]. During the past years several new drugs have been integrated in the treatment of metastastic gastric cancer: (i) Capecitabine was licensed to replace infusional 5-FU in combination regimens [6,7], (ii) oxaliplatin was shown to be at least as effective as cisplatin but advantageous with regard to toxicity (not licensed in Germany) [7,8]; (iii) docetaxel improved the activity of cisplatin and 5-FU combination at the price of higher toxicity but was able to maintain quality of life parameters for a longer time span [9]. Recently, trastuzumab was licensed for the treatment of metastatic adencarcinoma of the AEG and the stomach for patients with *HER-2* neu overexpressing tumors (IHC 3+ or IHC 2+ and FISH+) on the basis of the randomized ToGA phase-III trial showing a survival benefit of 4.2 months for these patients [10].

Notably, these studies were conducted in patient populations with a median age of 55-65 years. In contrast, median age at diagnosis of gastric cancer in Germany is 75 in women and 71 in men, while AEG is diagnosed a median of 5 years earlier (66 – 70 years) [2]. Little is known about the influence or the transferability of data from clinical trials on the treatment reality and practice patterns.

In this pooled analysis of data obtained with Therapiemonitor®, our aims were to evaluate treatment patterns in different institutions in Germany. We were especially interested to evaluate whether changes of drug use and treatment intensity over time and different drugs were used in elderly or less fit patients.

Material and Methods

Therapiemonitor®

Therapiemonitor® collects clinical and epidemiological data of patients with metastatic adenocarcinoma of the esophagogastric junction and the stomach who underwent treatment decisions within a defined time span in selected institutions (for instance during the third quarter of 2009; see examples in **Figure 1**). Physicians are asked to document current treatment decisions in individual patients along with demographic and tumor-related data, former medical and surgical treatment, insurance status etc. Therapiemonitor® does neither collect data on outcome parameters such as response rates, progression-free or overall survival nor toxicity data.

The case report forms contain several modules ("primary diagnosis", "primary therapy" [for instance perioperative treatment], "treatment in the metastatic setting"). The documentation is either internet-based (using EDC SecuTrial-system) or via paper case report form at the discretion of the reporting physician. Data are centrally monitored and checked for plausibility using original documents (e.g. histology report, doctor´s letter). In case of unclear or missing data query forms are provided. Onsite monitoring is not carried out. Data are handled with SPSS-database.

Selection of centers

The selection of centers for documentation of a representative series of patients with advanced AEG or gastric cancer is based on a two-step procedure which has been used for several years in a variety of malignant diseases such as colorectal cancer or multiple myeloma.

The apportioned and stratified random sample is based on an initial survey among all institutions dealing with the treatment of patients with advanced gastric cancer (medical oncologists, gastroenterologists, surgeons and radiotherapists): university hospitals, hospitals with or without oncological departments, private practices. Physicians are asked to participate in the Therapiemonitor® and to provide data on the prevalence of patients with advanced AEG or gastric cancer treated in their institution during the representative time of survey. A total of about 800 institutions are contacted per year including almost all institutions involved in oncological treatment in Germany. The response rate for this survey usually is between 15 and 20%.

According to this survey the "treated prevalence" of patients with advanced gastric cancer in Germany is as follows: university hospitals 15%, hospitals with oncological departments

55%, oncology private practice 20%, and hospitals without oncological department treating patients with gastric cancer 10%. According to this data a collective of patients with advanced gastric cancer was apportioned according to treatment center and distributed regionally according to population density.

Centers for documentation are selected usually according to date of response to the query. These selected treatment institutions are contacted again and asked to document their patients with advanced gastric cancer undergoing treatment decisions in the respective quarter.

Statistical analysis

The analyses presented in this paper are explorative. Differences in the treatment procedures or the use of cytostatic drugs in different sugroups were evaluated by means of a two-sided Chi-square test. A p-value of less then 0.05 was considered statistically significant. We were especially interested if different treatment strategies in elderly or les fit patients are were used.

Results

Patients and tumor characteristics

Patient and tumor charateristics are depicted in **Table 1**. A total of 1058 patients receiving 1st line chemotherapy were documented between 2006 and 2009. Taken all documentation periods together the median age is 67 years and 63.8% were male. 55.3% of the patients were older than 65 years. About ¾ of the patients had a Karnofsky performance status ≥80%. About 70% had metastatic disease at primary diagnosis with liver (50.1%), peritoneum (43.2%), lung (17.1%) and bone (8.5%) being the most frequently reported metastatic sites. Most of the patients were treated in non-university hospitals and private oncology practices. Remarkably, the patients´ and tumor characteristics remained comparable over the years of documentation.

Administered drugs – trends over time

Virtually all patients received fluoropyrimidine-based treatment in the 1st line treatment. The oral 5-FU derivative capecitabine has increasingly been used over time with a total of 17.1% of patients receiving capecitabine instead of 5-FU in 2009. **Table 2** provides an overview of the most frequently used cytotoxic drugs in the respective years. **Figure 2** illustrates the trends of the use of newly investigated drugs. It is noteworthy that epirubicin which is part of the ECF or EOX regimen considered a reference therapy in other countries like the United Kingdom was used in only about 10% of patients in Germany. Older drugs such as paclitaxel, etoposide or mitomycin have almost disappeared from the armamentarium of cytostatics used. With respect to time trends, an increase in the use of docetaxel, oxaliplatin and capecitabine has been observed during the past four years. For instance, docetaxel was used in 29.3% of patients and oxaliplatin in 36.3% of patients as part of the 1st line treatment regimen in 2009 (2006: docetaxel 13.1%, oxaliplatin 11.2%). The use of cisplatin has decreased from 57.6% in 2006 to values between 42.4% and 49.1% during the past two years, while oxaliplatin-use has risen.

Use of monotherapy, doublets or triplets – trends over time

The treatment intensity illustrated as the use of monotherapy, chemotherapy doublets and triplets over time is listed in **Table 3**. A total of 113 patients (10.7%) received monotherapy, 634 (59.9%) received chemotherapy doublets and 311 patients (29.4%) received chemotherapy triplets between 2006 and 2009. Of note, the percentage of patients receiving

chemotherapy triplets has constantly risen over time from 10.1% in 2006 to 47.0% in 2009 (see **Figure 3**). The rate of patients receiving monotherapy remained unchanged over the observation period in the range of 6 –15 %.

Treatment of patients aged >65 years: Administered drugs and treatment intensity

A total of 1054 patients could be analyzed for treatment intensity (i.e. the use of monotherapy, doublets or triplets) and drug-use with respect to age. A cut-off of 65 years was chosen for the analysis. In the present analysis, 585 patients (55.3%) were older than 65 years. The drugs administered along with treatment intensity provided for elderly in comparison to younger patients are listed in **Table 4**. Cisplatin, docetaxel and epirubicin were significantly more often used in younger patients, while oxaliplatin and irinotecan have been preferred for the treatment of elderly patients. The use of capecitabine did not differ between both age groups.

Concerning the use of chemotherapy triplets the rate of younger patients receiving three-drug regimens was almost twice as high as in the elderly patient group (40.2% versus 20.8%; $p < 0.0001$).

Treatment of patients with impaired Karnofsky perfomance status: Administered drugs and treatment intensity

A total of 1046 patients were evaluable for the analysis according to Karnofsky performance status (KPS). A cut-off of 80% was chosen. A total of 771 patients (72.9%) had a KPS ≥80%. Treatment according to KPS is listed in **Table 5**. Again, the greatest difference concerning drug use in favor of fitter patients was seen for cisplatin (57.2% versus 36.4% in patients with KPS <80%) followed by docetaxel (22.6% versus 15.3%). Capecitabine and irinotecan were statistically more often used in patients with lower KPS but the numeric differences are small. No differences were observed for oxaliplatin and epirubicin.

Concerning the administration of chemotherapy triplets the rate of fitter patients receiving three-drug regimens was 10.2% higher (30.2 versus 20.0%; $p = 0.001$).

Discussion

One major hurdle in transferring study results into clinical practice is the rigid patient selection made in clinical trials which usually does not reflect clinical reality. With respect to adenocarcinoma of the esophagogastric (AEG) junction and the stomach several recent studies exhibited new treatment options for these patients. It could be demonstrated that oxaliplatin may replace cisplatin, and that capecitabine may be used instead of infusional 5-FU. Docetaxel has significantly improved the results of cisplatin and 5-FU-based treatment. Yet, the median age of patients in these studies ranged between 55 and 65 years. Moreover, patients in reduced performance status are rarely included in clinical trials, while a total of 27.1% of the patients included in the present analysis had performance status of ≥2. Demographical data however indicate that the initial diagnosis of AEG or gastric cancer is made at about 66 – 75 years in Germany. Consequently, clinical studies for elderly or frail patients are of utmost interest albeit it could be shown in subgroup analyses, that elderly study patients fulfilling the criteria for clinical studies derive the same benefit as younger patients [11].

Threapiemonitor® was established to collect data on treatment reality in patients with malignant disease. It has been used in patients with colorectal cancer or multiple myeloma. Therapiemonitor® does neither collect outcome data such as progression-free or overall survial nor toxicity results. Physicians are asked to document their treatment decisions along with demographic data and tumor characteristics. Thus, Therapiemonitor® provides an interesting platform for evaluating real-life treatment.

The patient population reported here with a median age of 67 years in the 1st line setting compares with what is reported by tumor registries [2]. Like in the worldwide REGATE registry a male preponderance (64% compared to 65% in REGATE) was noticed and most patients had undifferentiated (G3) cancer (43% compared to 51% in REGATE) [12]. The reliability of the data presented here is strengthened by the fact that patient´s and tumor characteristics remained almost identical over the period of documentation.

With regard to the choice of 1st line treatment it is noteworthy that only 10% of all patients received a monotherapy. This percentage remained virtually identical between 2006 and 2009. This compares adequately with what was observed in a smaller cohort of 123 patients reported from a group in North-Eastern Germany (1st line monotherapy in 8% of patients) [13] and with a NCI patterns of care study published in 2008 by Cronin-Fenlon and coworkers [14]. Interestingly, the rate of patients receiving triplet chemotherapy has substantially

increased over the 4-year period from 10.1% in 2006 to 47.0% in 2009. One reason might be that the relatively toxic DCF triplet regimen as originally published in 2006 [4] has rapidly and succesfully been adopted to the German treatment reality by establishing more convenient and less toxic regimens using (bi-)weekly 24-hour infusional 5-FU and split-course docetaxel in combination with platinum derivatives [15,16].

The present analysis illustrates that the results of clinical studies have relatively quickly impacted treatment reality. For instance, the use of docetaxel and oxaliplatin has significantly increased over time, although oxaliplatin is not licensed in Germany for the treatment of advanced gastric cancer. In 2009 for example, about 35% of all patients received oxaliplatin as part of their 1st line treatment regimen. This trend of increased oxaliplatin use is paralleled by a decrease of cisplatin use by approximately 10%. Of interest, another potential alternative to cisplatin – irinotecan (like oxaliplatin not licensed for gastric cancer) – has not been adopted into clinical practice in a larger group of patients. Contrarily, docetaxel use has significantly increased. In 2009, 30% of patients received this drug in the 1st line setting.
Capecitabine was increasingly used, as well, but the acceptance among oncologists appears to be still lower than for docetaxel or oxaliplatin. Infusional 5-FU remained the 5-FU backbone regimen of choice also in 2009. The reasons are unclear, especially in view of the results of the Therapiemonitor® analysis in the elderly population. One could have speculated that the increase in capecitabine use was seen in the younger population due to difficulties with swallowing or renal toxicity when using capecitabine in elderly. Contrary to expectations the use of capecitabine was virtually identical in the age groups over and below 65 years (12.4% and 12.9%, respectively).
In contrast to capecitabine, significant disparities were found in the use of cisplatin and docetaxel in the different age groups. Elderly were significantly less likely to receive cisplatin or docetaxel, while oxaliplatin and irinotecan were used more often. Accordingly, older patients were significantly less exposed to three-drug regimens, maybe due to tolerability concerns. This reflects the above mentioned fact that very little data on three-drug regimens in elderly was at hand during the time span between 2006 and 2008.
Meanwhile, the FLOT65+ study has answered some of the questions how best to treat elderly, namely on the use of docetaxel in elderly [17]. FLOT65+ compared a doublet (FLO, i.e. bi-weekly infusional 24-h 5-FU, leucovorin and oxaliplatin) with a chemotherapy triplet (FLOT = FLO + bi-weekly docetaxel 50 mg/m²) in patients aged >65 years. FLOT was significantly superior to FLO regarding response rate and progression-free survival in the elderly

population (median age in FLOT65+ was 70 years). Survival and quality of life data are not yet mature. This study may have contributed to the increasing percentage of patients >65 years treated with docetaxel (and triplets) observed in the present analysis in 2009.
Comparable to what has been observed in the elderly population patients with Karnofsky performance status (KPS) < 80% received significantly less cisplatin and docetaxel as well as triplet chemotherapy regimens. Noteworthy, 18.5% of this patient group was treated with 5-FU monotherapy.This observation is difficult to interprete. If the reduced KPS was not due to comorbidity but due to tumor activity one would have expected to have a higher number of patients treated with the presumably more active triplet or with docetaxel.

The strength of the present analysis is that it reflects the transfer of study data into clinical practice. It could be demonstrated that the adoption of oxaliplatin and docetaxel has taken place quite rapidly, while capecitabine is still used to a lower extent in clinical practice. Therapiemonitor® may help to identify the medical needs, for instance the need for more data on triplets in elderly patients with a special focus on quality of life issues. The question how best to treat patients with lower performance status should be addressed in future trials as well.
A limitation of the Theapiemonitor® is that no outcome data are collected, i.e. that it can not be confirmed how the strategies implemented by the physicians impacted the outcome of the respective patient groups.
In summary, in the present analysis we found a relatively good adoption of study results in the younger patient group while there seems to be a need for more studies on the treatment of elderly or less fit patients and on quality of life issues. In addition to providing descriptive analyses of the treated prevalence of patients with AEG and gastric cancers, Theapiemonitor® may help to identify unmet medical needs and to establish study protocols in patient groups with presumably suboptimal current treatment patterns.

Acknowledgement: The authors are indoubted to Lenka Kellermann (Oncology information service [O.I.S.], Freiburg) who set-up and conducted the Therapiemonitor and is responsible for data aquisition and management. The authors would further like to thank all 106 participating institutions in the Therapiemonitor 2006 – 2009.

Disclosures. Therapiemonitor was supported by grants of Sanofi-Synthelabo, Berlin, and Roche Pharma AG Grenzach-Wyhlen, Germany. All authors received documentation fees from O.I.S.

Tables and Figures

Table 1: Patient and tumor characteristics of 1058 patients with advanced or metastatic adenocarcinoma of the esophagogastric junction and the stomach documented in the Therapiemonitor® 2006 – 2009.

	Total number of patients 2006 – 2009	2006	2007	2008	2009
Total number of patients receiving 1st line treatment (n)	1058	326	234	170	328
Gender [§]					
Male; n (%)	674 (63.8)	202 (62.2)	150 (64.1)	111 (65.3)	211 (64.3)
Female; n (%)	383 (36.2)	123 (37.8)	84 (35.9)	59 (34.7)	117 (35.7)
Age; median (years)	67	64	67	67	67
Patients aged < 65 years (%)	44.7	50.3	42.3	42.9	42.4
Patients with Karnofksy status ≥80% in 1st line treatment (%)	72.9	77.3	70.5	67.1	73.2
Patients with initial diagnosis of carcinoma in stage IV (%)	69.8	69.3	67.1	69.4	72.3
Histology					
Signet cell cancer (%)	14.5	12.9	13.3	13.7	17.4
Undifferentiated cancer (G3) (%)	43.5	45.1	38.9	49.8	42.0
Metastatic sites					
Liver (%)	50.1	47.9	51.7	50.0	51.5
Peritoneum (%)	43.2	44.2	40.6	48.2	41.4
Lung (%)	17.1	16.6	16.7	13.5	19.8
Bone (%)	8.5	9.2	10.3	3.5	9.1
Patients participating in clinical trials on 1st line chemotherapy (%)	10.1	14.4	9.0	2.4	10.7
Treatment institution[§§]					
University hospital	16.9	17.5	17.1	19.4	14.9
Other hospitals	59.7	77.7	57.7	47.6	49.7
Oncology practice	28.0	14.4	26.5	35.3	38.7
Insurance status					
State insurance (%)	91.7	91.9	92.1	91.8	91.1
Private insurance (%)	8.3	8.1	7.9	8.2	8.9

Note: [§] = Gender is missing in one patient. [§§] = Multiple answers were permitted.

Table 2: Anti-cancer drugs used in the 1st line treatment of patients with advanced or metastatic adenocarcinoma of the esophagogastric junction and the stomach in the Therapiemonitor® 2006 – 2009. Indicated is the number of patients receiving the respective drugs in the respective year. A total of 1053 patients were evaluable for this analysis.

	Overall 2006 – 2009 n (%)	2006 n (%)	2007 n (%)	2008 n (%)	2009 n (%)
Cisplatin	538 (51.1)	185 (57.6)	120 (51.3)	72 (42.4)	161 (49.1)
Oxaliplatin	251 (23.8)	36 (11.2)	48 (20.5)	48 (28.2)	119 (36.3)
Capecitabine	133 (12.6)	21 (6.5)	33 (14.1)	23 (13.5)	56 (17.1)
Docetaxel	216 (20.5)	42 (13.1)	42 (17.9)	36 (21.2)	96 (29.3)
Paclitaxel	6 (0.6)	2 (0.6)	1 (0.4)	3 (1.8)	0 (0.0)
Irinotecan	92 (8.7)	43 (13.4)	16 (6.8)	19 (11.2)	14 (4.3)
Epirubicin	107 (10.2)	8 (2.5)	27 (11.5)	22 (12.9)	50 (15.2)
Mitomycin C	12 (1.1)	7 (2.2)	5 (2.1)	0 (0.0)	0 (0.0)
Etoposide	45 (4.3)	19 (5.9)	9 (3.8)	8 (4.7)	9 (2.7)
Number of evaluable patients	**1053**	**321**	**234**	**170**	**328**

Table 3: Treatment intensity chosen for the 1st line treatment of patients with advanced or metastatic adenocarcinoma of the esophagogastric junction and the stomach in the Therapiemonitor® 2006 – 2009. A total of 1053 patients were evaluable for this analysis.

	Overall 2006 – 2009 (%)	2006 (%)	2007 (%)	2008 (%)	2009 (%)
Monotherapy	10.7	11.3	14.9	11.8	6.4
Chemotherapy doublet	59.9	78.5	54.3	57.7	46.6
Chemotherapy triplet	29.4	10.1	30.8	30.5	47.0

Note: Folinic acid is not considered an active drug and is consequently not included in this analysis.

Table 4: Anti-cancer drugs and treatment intensity chosen for the 1st line treatment of elderly versus younger patients with advanced or metastatic adenocarcinoma of the esophagogastric junction and the stomach in the Therapiemonitor® 2006 – 2009. A total of 1054 patients were evaluable for this analysis.

	Patients < 65 years n = 473	Patients ≥ 65 years n = 581	p-value χ-square-Test
Cisplatin (%)	61.1	42.9	p < 0.0001
Oxaliplatin (%)	21.4	25.8	p = 0.09
Capecitabine (%)	12.9	12.4	p = 0.81
Docetaxel (%)	27.5	14.8	p < 0.0001
Irinotecan (%)	7.2	10.0	p = 0.11
Epirubicin (%)	13.3	7.6	P = 0.002
Treatment intensity Monotherapy / doublet (%) Triplet (%)	 59.8 (8.0 / 51.8) 40.2	 79.2 (12.9 / 66.3) 20.8	 p < 0.0001

Table 5: Analysis of anti-cancer drug use and treatment intensity chosen for the 1st line treatment of patients with advanced or metastatic adenocarcinoma of the esophagogastric junction and the stomach in the Therapiemonitor® 2006 – 2009 according to Karnofsky performance status (KPS). A total of 1046 patients were evaluable for this analysis.

	Patients with KPS < 80 % n = 275	Patients with KPS ≥ 80 % n = 771	p-value χ-square-Test
Cisplatin (%)	36.4	57.2	p < 0.0001
Oxaliplatin (%)	26.2	23.0	p = 0.28
Capecitabine (%)	16.4	11.4	p = 0.034
Docetaxel (%)	15.3	22.6	p = 0.01
Irinotecan (%)	12.4	7.8	p = 0.02
Epirubicin (%)	9.8	10.1	p = 0.88
Treatment intensity Monotherapy / doublet (%) Triplet (%)	 80.0 (18.5 / 61.5) 20.0	 69.8 (7.0 / 62.8) 30.2	 p = 0.001

Legend to the Figures

Figure 1: *Therapiemonitor*®: All patients undergoing treatment decisions in the third quarter in 2009 (present example) are documented. Patient 2 for instance with a primarily metastatic cancer initiates 2nd line treatment after progression on 1st line therapy in the third quarter 2009, while patient 3 exhibits tumor recurrence after curative surgery and starts 1st line therapy.

Figure 2: Time trends in the use of platinum derivatives, capecitabine, docetaxel and irinotecan for the 1st line treatment of patients with advanced or metastastic adenocarcinoma of the esophagogastric junction and the stomach in the Therapiemonitor® 2006 – 2009. The bars indicate the percentage of drug use in the respective year.

Figure 3: Time trends in the use of monotherapy versus doublet or triplet chemotherapy for the 1st line treatment of patients with advanced or metastatic adenocarcinoma of the esophagogastric junction and the stomach in the Therapiemonitor® 2006 – 2009.

References

1 Ferlay J, Bray F, Pisani et al. GLOBOCAN 2002 – Cancer incidence, mortality and prevalenca worlwide, version 2.0. 2004

2. http://www.rki.de/cln_169/nn_205770/DE/Content/GBE/Gesundheitsberichterstattung/GBEDownloadsB/KID2010,templateId=raw,property=publicationFile.pdf/KID2010.pdf.

3. Wagner AD; Grothe W, Haerting J et al. Chemotherapy in advanced gasric cancer: a systematic review and meta-analysis based on aggregate data. J Clin Oncol 2006;24:2903-2909.

4. Van Cutsem E et al: Phase III study of docetaxel and cisplatin plus fluorouracil compared with cisplatin and fluorouracil as first-line therapy for advanced gastric cancer: a report of the V325 Study Group. J Clin Oncol 2006; 24: 4991–7

5. Lutz M, Wilke H, Wagener DJ, et al: Weekly infusional high-dose fluorouracil (HD-FU), HD-FU plus folinic acid (HD-FU/FA), or HD-FU/FA plus biweekly cisplatin in advanced gastric cancer: randomized phase II trial 40953 of the European Organisation for Research and Treatment of Cancer Gastrointestinal Group and the Arbeitsgemeinschaft Internistische Onkologie. J Clin Oncol 2007; 25: 2580–5

6. Kang YK, Kang WK, Shin DB, et al. Capecitabine/cisplatin versus 5-fluorouracil/cisplatin as first-line therapy in patients with advanced gastric cancer: a randomised phase III noninferiority trial. Ann Oncol 2009;20:666-73.

7. Cunningham D, Starling N, Rao S et al. Capeciatbine and oxaliplatin for advanced esophagogastric cancer. N Engl J Med 2008;358:36-46.

8. Al-Batran SE, Hartmann JT, Probst S, et al. Phase III trial in metastatic gastroesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft für Internistsiche Onkologie. J Clin Oncol 2008;26:1435-1442.

9. Ajani JA, Moiseyenko VM, Tjulandin S. Quality of life with docetaxel plus cisplatin and fluorouracil compared with cisplatin and fluorouracil from a phase III trial for advanced gastric or gastroesophageal adenocarcinoma: the V-325 Study Group. J Clin Oncol. 2007 Aug 1;25(22):3210-6.

10. Van Cutsem E, Kang YK, Chung HC et al. Efficacy results from the ToGA trial: A phase III study of trastuzumab added to standard chemotherapy (CT) in first-line human epidermal growth factor receptor 2 (HER2)-positive advanced gastric cancer (GC). J Clin Oncol 27:18s, 2009 (suppl; abstr LBA4509

11. Trumper M, Ross PJ, Cunningham D, et al. Efficacy and tolerability of chemotherapy in elderly patients with advanced oesophago-gastric cancer: A pooled analysis of three clinical trials. Eur J Cancer 2006;42:827-34.

12. Ter-Ovanesov MD, Bang Y, Yalcin S, Roth A, Zalcberg R, Soloviev V, Mallath MK, Ecstein-Fraisse EB, Wu C. Registry of gastric cancer treatment evaluation (REGATE): Baseline characteristics of 10,299 patients from 22 countries. J Clin Oncol 2009;27:15s (abstr 4575)

13. Leithäuser M, Wilhelm S, Kahl C, Eschenburg H, Jost K, Hilgendorf I, Junghanss C, Freund M, Palliative chemotherapy for advanced and metastatic gastric cancer in the community. Onkologie 2009;32(suppl 4),136(abstr).

14. Cronin-Fenton DP, Mooney MM, Clegg LX, Harlan LC. Treatment and survival in a population-based sample of patients diagnosed with gastroesophageal adenocarcinomaWorld J Gastroenterol. 2008 May 28;14(20):3165-73.2007.

15. Lorenzen S, Hentrich M, Haberl C, Heinemann V, Schuster T, Seroneit T, Roethling N, Peschel C, Lordick F. Split-dose docetaxel, cisplatin and leucovorin/fluorouracil as first-

line therapy in advanced gastric cancer and adenocarcinoma of the gastroesophageal junction: results of a phase II trial. Ann Oncol. 2007 Oct;18(10):1673-9.
16. Al-Batran SE, Hartmann JT, Hofheinz R, et al. Biweekly fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT) for patients with metastatic adenocarcinoma of the stomach or esophagogastric junction: a phase II trial of the Arbeitsgemeinschaft Internistische Onkologie. Ann Oncol 2008 ;19:1882-7.
17. Al-Batran SE, Homann N, Hartmann JT, et al. 5-Fluorouracil, leucovorin, oxaliplatin with or without docetaxel in older adult patients with esophagogastric cancer: preliminary results from the FLOT 65+ trial of the Arbeitsgemeinschaft Internistische Onkologie (AIO). Onkologie 2009; 32(suppl 4):1-254 (page 135).