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ORIGINAL RESEARCH

Treatment Patterns Among Patients with Metastatic and/or Unresectable Gastric Cancer in Brazil

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Abstract

Purpose In Brazil, patients with gastric cancer have not been systematically followed-up and evaluated, thus data regarding patterns of care and outcomes are scarce or missing. The objective of this study was to evaluate patterns of care of advanced gastric cancer in standard practice in Brazil.

Methods This was an observational, multicenter, retrospective study, which included patients with metastatic and/or unresectable gastric cancer (MGC) who underwent at least one line of treatment.

Results We analyzed data on 155 patients diagnosed with MGC, most are men (57.4%), with mean age of 61.9 years at diagnosis, with 99 (63.9%) from the public healthcare system and 56 (36.1%) from the private setting. Platinum- and/or fluoropyrimidine-containing regimens prevailed as first-line therapy, while irinotecan was the most used regimen in the second and in the third lines. More than 40% of patients underwent only one line of systemic therapy, of which around 40% either died during the treatment or went on to best supportive care (BSC) only. The remaining patients received further treatment lines. A fifth of the patients in the study died within two months after discontinuation of the first-line treatment. Adverse events, use of concomitant medications, support procedures, outpatient visits, and hospitalizations were reported for most patients, especially in the first and second lines of treatment and during exclusive BSC.

Conclusions Survival during or after the first-line chemotherapy remains poor among patients with MGC. Adverse events and health resource use were common in the first and second lines of treatment and in exclusive BSC. These results suggest that there is space for improvement in the treatment of MGC in Brazil.

Keywords Gastric cancer · Metastatic/unresectable · Treatment patterns · Stomach neoplasm

Introduction

Gastric cancer is the fifth most common malignancy in the world and the third leading cause of cancer death in both sexes worldwide [1]. Its incidence is of approximately one million cases per year—more than 70% of these occurring in developing countries [1]. In Brazil, it is estimated a total of 20,520 new cases of gastric cancer for 2016 [2]. Although gastric cancer incidence and mortality have decreased in Brazil in the last decades, they are still higher than in most developed countries [3, 4]. According to Arregi et al., about 50% of the diagnosed Brazilian gastric cancer cases occurred between 55 and 74 years [5].

This disease is an aggressive malignancy often detected in late stages, which means that most patients are diagnosed in the metastatic phase [6]. Patients with metastatic and/or locally recurrent, unresectable gastric cancer (MGC) have a poor prognosis. Median overall survival (OS) reported in several studies on MGC was usually around 12 months [7–10]. Nevertheless, survival data vary among different countries, with median OS estimates as low as 8 months in a subset of patients in a study performed in Taiwan [8] and as high as

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26 months in a study from South Korea [11]. The former estimate refers to MGC patients that received best supportive care (BSC) only as second-line therapy [8].

The risk of developing gastric cancer increases with age, occurring most frequently between 55 and 80 years, and, in general, gastric cancer rates are twice as high in men as in women. Ingestion of smoked and salt-preserved food, smoking status, and *Helicobacter pylori* (*H. pylori*) infection contribute to gastric cancer incidence [12, 13]. Adenocarcinoma is the most common histological type of gastric cancer, affecting over 90% of all cases of the disease. Gastric lymphomas, sarcomas, gastrointestinal stromal tumor (GIST), and other rare tumors have distinct treatments and survival rates [14].

Few changes and advances in management and guidelines for the treatment of gastric cancer occurred during the past decades. Management of patients with MGC includes surgical approach for operable patients and/or palliative chemotherapy [15]. These patients may benefit from chemotherapy with potential improvement in OS and in quality of life [16, 17]. Trastuzumab with platinum and fluoropyrimidine-based chemotherapy is recommended for HER2-positive cases [15].

In Brazil, patients with gastric cancer have not been systematically followed-up and evaluated yet. Consequently, Brazilian data related to patterns of care and outcomes are scarce or missing. Different treatment strategies may be associated with different clinical and economical outcomes. Therefore, it is important to evaluate current management in order to define the impact of existing therapeutic strategies both with respect to clinical benefits to the patient and to direct healthcare costs.

The objective of this study was to evaluate treatment patterns of MGC in standard practice in Brazil. Understanding the current patterns of care will allow assessing the real value of available therapies for the management of disease burden, and such results may collaborate with the development of new handling strategies and guidelines for better care of these patients.

Methods

This was an observational, multicenter, retrospective cohort study to assess real-world treatment patterns of patients with MGC in Brazil. The primary endpoint was to describe treatment patterns of MGC in standard practice in selected institutions in Brazil. Treatment patterns were defined as the most frequently reported treatments for each therapy line, including best supportive care (BSC). Secondary endpoints included demographic and clinical characteristics of MGC, proportion of MGC patients that received systemic therapy during second-line of treatment, proportion of MGC patients that received BSC, OS of MGC patients, and healthcare resource use during the treatment of gastric cancer.

The study included patients aged 18 years and older with documented diagnosis of unresectable (IIIC) or metastatic (IV) gastric cancer (including gastroesophageal junction) between January 1, 2011, and December 31, 2014. Patients should have received first-line treatment with chemotherapy for unresectable or metastatic gastric cancer (e.g. cytotoxic agents or target agents) for at least one cycle, and medical records should have a follow-up of at least 3 months within the last administration (last date of administration documented) of the first-line treatment, except those with recording a documented death (those patients were included). Patients not having reliable data as per physician's opinion and patients with gastrointestinal stromal tumor (GIST), lymphoma, Krukenberg tumor, or any other non-adenocarcinoma tumor or malignant disease (with exception of non-melanoma skin cancer) were excluded from the study. Participation in any controlled clinical study for any disease other than gastric cancer during the data collection period was also an exclusion criterion. Participation in clinical trials for gastric cancer and death were not considered exclusion criteria; however, subjects who deceased needed to have had documented death or at least one follow-up visit between January 1, 2011, and December 31, 2014.

The chart review was performed retrospectively starting from the date the patient was included in the study. The follow-up interval included the entire unresectable or metastatic gastric cancer period. Prospective follow-up of patients was not performed in this study.

Sample Size

The primary objective of this study was to analyze descriptively the proportion of patients on the second line treatment for gastric cancer. Sample size was calculated based on the half-width of the 95% confidence intervals (CI) for the proportion of MGC patients who received a given treatment. A wide number of treatment options for first- and second-line therapy were foreseen; therefore, all possible proportions were considered for calculation of sample size. It was expected that about 30 and 50% of MGC patients from the public and the private healthcare system, respectively, would have received second-line therapy in the period from diagnosis to the last available evaluation. The maximum 95% CI around proportion estimates for a sample size of 155 subjects is ± 0.079, which can be considered a reasonable precision for the purpose of this study.

Statistical Analysis

All analyses were performed on the full analysis set, which comprised all subjects included in the study. Demographic data, disease-related information, reported outcomes, and

healthcare resource use were summarized. Data from patients who were considered screen failure were summarized according to the reported reason for screen failure.

There was no formal hypothesis in the study. Data reported as continuous variables (quantitative ones) were summarized by mean, standard deviation (SD), median, minimum, and maximum. Categorical variables were described by simple and cross-contingency tabulation, with absolute frequencies and percentages at 95% CIs.

The use of gastric cancer therapies, including the length of exposure and the number of different therapies per subject, was analyzed. Frequency of drug therapies according to the generic name and type/class (e.g. chemotherapy and targeted therapy) was summarized overall and by line of therapy. Furthermore, the most frequently reported treatments in each line of therapy were summarized.

In order to describe the OS after MGC diagnosis in relation to the variables of interest, Kaplan-Meier curves were performed for each studied variables to check whether there was evidence of differences between the curves using the log-rank test. Patients with loss of follow-up, missing data regarding living status, or patients still alive in the last contact were censored in the survival analyses.

The Cox proportional hazard model was used in order to identify possible independent prognostic factors and to relate the survival time with the variables of interest.

Subgroup analyses, considering public and private healthcare systems, were conducted.

Ethical Aspects

The study was retrospective and observational, meaning that no intervention was required in the study. Data were collected through chart review, and patients' personal data were de-identified and treated according to all laws and local applicable regulation. Only aggregated data are presented in the analyses. The study was approved by all institutional ethics committees from each participant institution before any study procedure.

Results

Study Population

Among 500 screened patients, 159 (31.8%) complied with all selection criteria. Four eligible patients did not have any other data (besides the eligibility form) available by the end of the study; therefore, the study population included 155 patients. The main reason for screen failure was diagnosis other than recurrent, unresectable (IIIC) or metastatic (IV) gastric cancer (including gastroesophageal junction), or diagnostic date not in the period between January 2011 and December 2014 (Fig. 1).

Baseline demographic and clinical characteristics of patients included in the study are presented in Table 1. Most of the patients were men (57.4%), with mean age at 61.9 years at

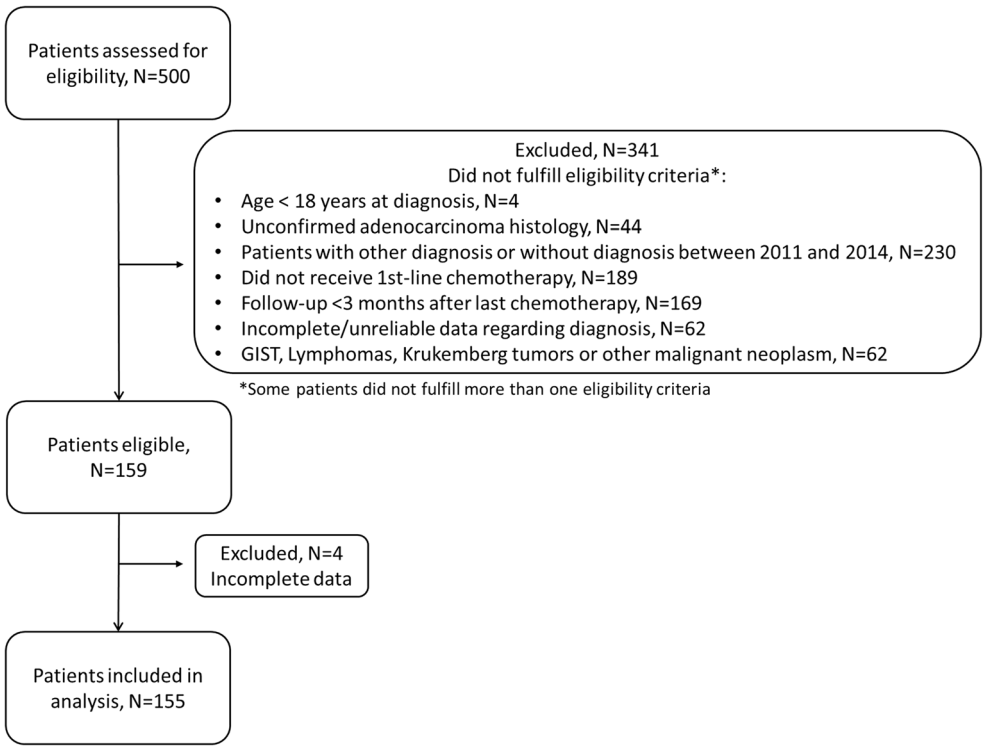

Fig. 1 Patient flow according to STROBE statement

Table 1 Patient's baseline demographics and clinical characteristics at diagnosis

	Patient's health care profile		
	Private $N = 56$	Public $N = 99$	Total $N = 155$
Age at MGC diagnosis (years)			
Mean (SD)	64.1 (13.9)	60.6 (12.7)	61.9 (13.2)
Median (range)	64.5 (27–87)	63 (30–83)	64.0 (27–87)
Male, *n* (%)	26 (46.4)	63 (63.6)	89 (57.4)
Ethnic group, n (%)			
Asian	0 (0)	2 (2)	2 (1.3)
Caucasian	6 (10.7)	36 (36.4)	42 (27.1)
Black	0 (0)	6 (6.1)	6 (3.9)
Other	0 (0)	8 (8.1)	8 (5.2)
Unknown	50 (89.3)	47 (47.5)	97 (62.6)
Family history of gastric cancer, n (%)			
No	19 (33.9)	45 (45.5)	64 (41.3)
Yes	18 (32.1)	19 (19.2)	37 (23.9)
Unknown	19 (33.9)	35 (35.4)	54 (34.8)
Degree of kinship, n (%)			
First level	12 (66.7)	13 (68.4)	25 (67.6)
Second level	5 (27.8)	4 (21.1)	9 (24.3)
Third level	1 (12.5)	2 (10.5)	3 (8.1)
Smoking history, n (%)			
Nonsmoker	22 (39.3)	35 (35.4)	57 (36.8)
Smoker	2 (3.6)	7 (7.1)	9 (5.8)
Former smoker	23 (41.1)	38 (38.4)	61 (39.4)
Unknown	9 (16.1)	19 (19.2)	28 (18.1)
Alcohol consumption, n (%)			
No alcohol user	19 (33.9)	37 (37.4)	56 (36.1)
Social drinker	18 (32.1)	10 (10.1)	28 (18.1)
Alcoholic	4 (7.1)	7 (7.1)	11 (7.1)
Former alcoholic	1 (1.8)	25 (25.3)	26 (16.8)
Unknown	14 (25.0)	20 (20.2)	34 (21.9)
Comorbidities, n (%)			
Hypertension	21 (37.5)	33 (33.3)	54 (34.8)
Obesity	4 (7.1)	5 (5.1)	9 (5.8)
Diabetes	10 (17.9)	11 (11.1)	21 (13.5)
Pernicious anemia	3 (5.4)	0 (0)	3 (1.9)
Other	29 (51.8)	10 (10.1)	39 (25.2)
History of Helicobacter pylori, n (%)	13 (23.2)	13 (13.1)	26 (16.8)

MGC, metastatic or locally recurrent, unresectable gastric cancer; *SD*, standard deviation

MGC diagnosis, and with no family history of gastric cancer (63.4%, excluding "unknown" answers). Regarding healthcare coverage, 99 (63.9%) patients were from the public healthcare system and 56 (36.1%) from the private setting. While a previous diagnosis of infection by *H. pylori* was reported in 16.8% of cases, this rate rises to 31.7% considering only patients with a known status.

Clinical characteristics are presented in Table 2. Stomach was the most frequent location of the tumor when gastric cancer was first diagnosed (40.6%), followed by cardia or gastroesophageal junction (23.9%), and fundus or body (17.4%). Stage IV was the most common stage (67.1%) at the primary gastric cancer diagnosis, and 42 patients (27.1%) presented recurrence. Regarding HER2, a positive result was assigned to 9 out of 46 patients (19.6%) with a known status.

Among the 42 patients who presented recurrence (21 from each healthcare setting), 20 (95.2%) patients from the private system and 12 (57.1%) patients from the public system underwent surgery prior to recurrence. Total gastrectomy was the most frequently performed surgery in these patients.

Systemic Therapy

The number of lines of systemic treatment received by MGC patients in each healthcare setting is described in Table 3. All patients included in the study should have received the first-line therapy. While 45.2% of patients received only one line of therapy, 36.8% received only two lines and 14.2% received a total of three lines. Among all cohorts, the rate of patients who received the second-, third-, fourth-, and fifth-line treatment was 54.8, 18.1, 4.5, and 1.3%, respectively.

Figure 2 shows the regimens administered to the MGC patients in all treatment lines and the number of patients who received them. Twenty-one regimens were reported, besides clinical trial regimens. The most frequently reported regimens for patients from the private health care system were fluorouracil + oxaliplatin + leucovorin (28.6%), followed by capecitabine + oxaliplatin (21.4%). Considering patients from the public health care system, capecitabine + oxaliplatin was the most frequently reported regimen (20.2%), followed by fluorouracil + cisplatin (12.1%) (Table 3). Trastuzumab was used in first-line treatment of only 5.4% patients from the private health care system and in no patients from the public setting. During the first-line treatment, patients received a median of six cycles (range 1–34) and three cycles (range 1–14) at the private and public system, respectively. The main criteria for selection of first-line therapy were hospital protocol/guidelines in the public setting and other than national or hospital guidelines, physician's clinical experience and patient's profile in the private setting.

Ten (6.4%) patients received BSC after the first-line therapy (Table 4), and 17 (11.0%) had "death" as reason for terminating therapy. Most patients managed in the private perspective completed the treatment according to the initial protocol, while disease progression was the most frequent reason for treatment discontinuation in the public setting. Of note, 29

Table 2 Disease and tumor characteristics

	Patient's health care profile		
	Private $N = 56$	Public $N = 99$	Total $N = 155$
Tumor location at diagnosis, n (%)			
Pyloric antrum	3 (5.4)	22 (22.2)	25 (16.1)
Cardia or gastroesophageal junction	10 (17.9)	27 (27.3)	37 (23.9)
Stomach NOS	32 (57.1)	31 (31.3)	63 (40.6)
Fundus or body	10 (17.9)	17 (17.2)	27 (17.4)
Lesser or greater curvature	1 (1.8)	2 (2)	3 (1.9)
T classification, n (%)			
T1	0 (0)	1 (1)	1 (0.6)
T2	5 (8.9)	2 (2)	7 (4.5)
T3	20 (35.7)	14 (14.1)	34 (21.9)
T4a	8 (14.3)	13 (13.1)	21 (13.5)
T4b	1 (1.8)	15 (15.2)	16 (10.3)
Tx	19 (33.9)	35 (35.4)	54 (34.8)
Unknown	3 (5.4)	19 (19.2)	22 (14.2)
N classification, n (%)			
N0	3 (5.4)	1 (1)	4 (2.6)
N1	13 (23.2)	10 (10.1)	23 (14.8)
N2	7 (12.5)	9 (9.1)	16 (10.3)
N3	5 (8.9)	10 (10.1)	15 (9.7)
Nx	25 (44.6)	50 (50.5)	75 (48.4)
Unknown	3 (5.4)	19 (19.2)	22 (14.2)
M classification, n (%)			
M0	20 (35.7)	24 (24.2)	44 (28.4)
M1	33 (58.9)	56 (56.6)	89 (57.4)
Unknown	3 (5.4)	19 (19.2)	22 (14.2)
More than one metastasis site, n (%)			
No	37 (66.1)	55 (55.6)	92 (59.4)
Yes	16 (28.6)	24 (24.2)	40 (25.8)
Unknown	3 (5.4)	20 (20.2)	23 (14.8)
Metastasis site, n (%)			
Liver	15 (45.5)	27 (48.2)	42 (47.2)
Peritoneum (carcinomatosis peritoneal)	13 (39.4)	25 (44.6)	38 (42.7)
Bone	1 (3)	1 (1.8)	2 (2.2)
Lymphonode	8 (24.2)	6 (10.7)	14 (15.7)
Lung	3 (9.1)	5 (8.9)	8 (9)
Central nervous system	0 (0)	1 (1.8)	1 (1.1)
Other	5 (15.2)	10 (17.9)	15 (16.9)
Tumor stage at the primary diagnosis (TNM AJCC 7th edition), n (%)			
Stage IB	1 (1.8)	0 (0)	1 (0.6)
Stage IIA	2 (3.6)	1 (1)	3 (1.9)
Stage IIB	3 (5.4)	1 (1)	4 (2.6)
Stage IIIA	5 (8.9)	1 (1)	6 (3.9)
Stage IIIB	3 (5.4)	2 (2)	5 (3.2)
Stage IIIC	0 (0)	7 (7.1)	7 (4.5)
Stage IV	36 (64.3)	68 (68.7)	104 (67.1)
Unknown	6 (10.7)	19 (19.2)	25 (16.1)
Recurrence, n (%)			
No	35 (62.5)	77 (77.8)	112 (72.3)
Yes	21 (37.5)	21 (21.2)	42 (27.1)
Unknown	0 (0)	1 (1)	1 (0.6)
HER2 status			
Negative	29 (51.8)	7 (7.1)	36 (23.2)
Positive (IHC 3+ or FISH +)	3 (5.4)	6 (6.1)	9 (5.8)
Inconclusive	1 (1.8)	0 (0)	1 (0.6)
Unknown	23 (41.1)	86 (86.9)	109 (70.3)

AJCC, American Joint Committee on Cancer; *NOS*, not otherwise specified; *SD*, standard deviation

patients (19%) died within two months after cessation of the therapy.

In the second-line therapy, 18 regimens were reported, besides clinical trial regimens. Irinotecan was by far the most frequently reported regimen in the private health care system (41.2%), followed by paclitaxel (14.7%). Among patients from the public setting, irinotecan (31.4%) and paclitaxel (21.6%) were also the main second-line regimens (Table 3). The median number of cycles in both settings was 3 (range 1–14). As in the first-line therapy, the main criteria for selection of regimen were hospital protocol/guideline in the public setting and "other" in the private setting. Disease progression was the main reason for treatment discontinuation in both settings. Among the patients who received this line of treatment, at least 9.4% died during its course and 10.6% went on to BSC.

Irinotecan was also the most used third-line regimen in the public setting (28.6% of patients), while paclitaxel was the main one as third- and fourth-line regimens in the private setting (40.0 and 60% of patients, respectively). Only one patient from the public setting received the fourth line of treatment, composed by fluorouracil, leucovorin, and oxaliplatin. Only two patients, both from the private healthcare system, underwent the fifth-line treatment, and both received irinotecan. Considering cases with known responses regarding reason for termination of therapy, disease progression prevailed in both settings in the last three lines of therapy, accounting for 62% of cases in the third line and for all cases in the fourth and fifth lines of treatment.

Time from MGC diagnosis to start systemic therapy was analyzed separately in the public and in the private

Table 3 All regimens used in gastric cancer treatment, according to treatment line and healthcare profile

Chemotherapy regimen	First line			Second line			Third line			Fourth line		Fifth line		
	Private *n* (%)	Public *n* (%)	Total *n* (%)	Private *n* (%)	Public *n* (%)	Total *n* (%)	Private *n* (%)	Public *n* (%)	Total *n* (%)	Private *n* (%)	Public *n* (%)	Total *n* (%)	Private *n* (%)	Total *n* (%)
Capecitabine	2 (3.6)	0 (0)	2 (1.3)	2 (5.9)	2 (3.9)	4 (4.7)	2 (13.3)	0 (0)	2 (7.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Capecitabine + oxaliplatin	12 (21.4)	20 (20.2)	32 (20.6)	2 (5.9)	2 (3.9)	4 (4.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cisplatin + Capecitabine	1 (1.8)	1 (1)	2 (1.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Docetaxel	0 (0)	1 (1)	1 (0.6)	0 (0)	0 (0)	0 (0)	2 (13.3)	1 (7.7)	3 (10.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Docetaxel + Cisplatin	1 (1.8)	5 (5.1)	6 (3.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Docetaxel + Cisplatin + Fluorouracil	2 (3.6)	3 (3)	5 (3.2)	1 (2.9)	0 (0)	1 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Docetaxel + Cisplatin + Fluorouracil + Leucovorin	3 (5.4)	0 (0)	3 (1.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Clinical trial	0 (0)	3 (3)	3 (1.9)	0 (0)	1 (2)	1 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Epirubicin + Cisplatin + Capecitabine	0 (0)	2 (2)	2 (1.3)	1 (2.9)	0 (0)	1 (1.2)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	1 (16.7)	0 (0)	0 (0)
Epirubicin + Cisplatin + Fluorouracil	2 (3.6)	0 (0)	2 (1.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Epirubicin + Oxaliplatin	0 (0)	1 (1)	1 (0.6)	0 (0)	1 (2)	1 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Epirubicin + Oxaliplatin + Capecitabine	7 (12.5)	7 (7.1)	14 (9)	1 (2.9)	1 (2)	2 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Epirubicin + Oxaliplatin + fluorouracil	2 (3.6)	1 (1)	3 (1.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Etoposide	0 (0)	0 (0)	0 (0)	0 (0)	3 (5.9)	3 (3.5)	0 (0)	3 (23.1)	3 (10.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Fluorouracil + Cisplatin	1 (1.8)	12 (12.1)	13 (8.4)	0 (0)	4 (7.8)	4 (4.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Fluorouracil + Cisplatin + Leucovorin	0 (0)	7 (7.1)	7 (4.5)	0 (0)	1 (2)	1 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Fluorouracil + Irinotecan + Leucovorin	0 (0)	0 (0)	0 (0)	3 (8.8)	0 (0)	3 (3.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Fluorouracil + Leucovorin	1 (1.8)	7 (7.1)	8 (5.2)	0 (0)	1 (2)	1 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Fluorouracil + Leucovorin + Etoposide	1 (1.8)	11 (11.1)	12 (7.7)	1 (2.9)	3 (5.9)	4 (4.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Fluorouracil + Oxaliplatin + Leucovorin	16 (28.6)	10 (10.1)	26 (16.8)	2 (5.9)	2 (3.9)	4 (4.7)	1 (6.7)	3 (23.1)	4 (14.3)	0 (0)	1 (100)	1 (16.7)	0 (0)	0 (0)
Irinotecan	3 (5.4)	4 (4)	7 (4.5)	14 (41.2)	16 (31.4)	30 (35.3)	4 (26.7)	4 (30.8)	8 (28.6)	1 (20)	0 (0)	1 (16.7)	2 (100)	2 (100)
Irinotecan + Cisplatin	2 (3.6)	1 (1)	3 (1.9)	1 (2.9)	0 (0)	1 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Irinotecan + Fluorouracil + Leucovorin	0 (0)	0 (0)	0 (0)	1 (2.9)	2 (3.9)	3 (3.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Paclitaxel	0 (0)	1 (1)	1 (0.6)	5 (14.7)	11 (21.6)	16 (18.8)	6 (40)	2 (15.4)	8 (28.6)	3 (60)	0 (0)	3 (50)	0 (0)	0 (0)
Paclitaxel + Carboplatin	0 (0)	2 (2)	2 (1.3)	0 (0)	1 (2)	1 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

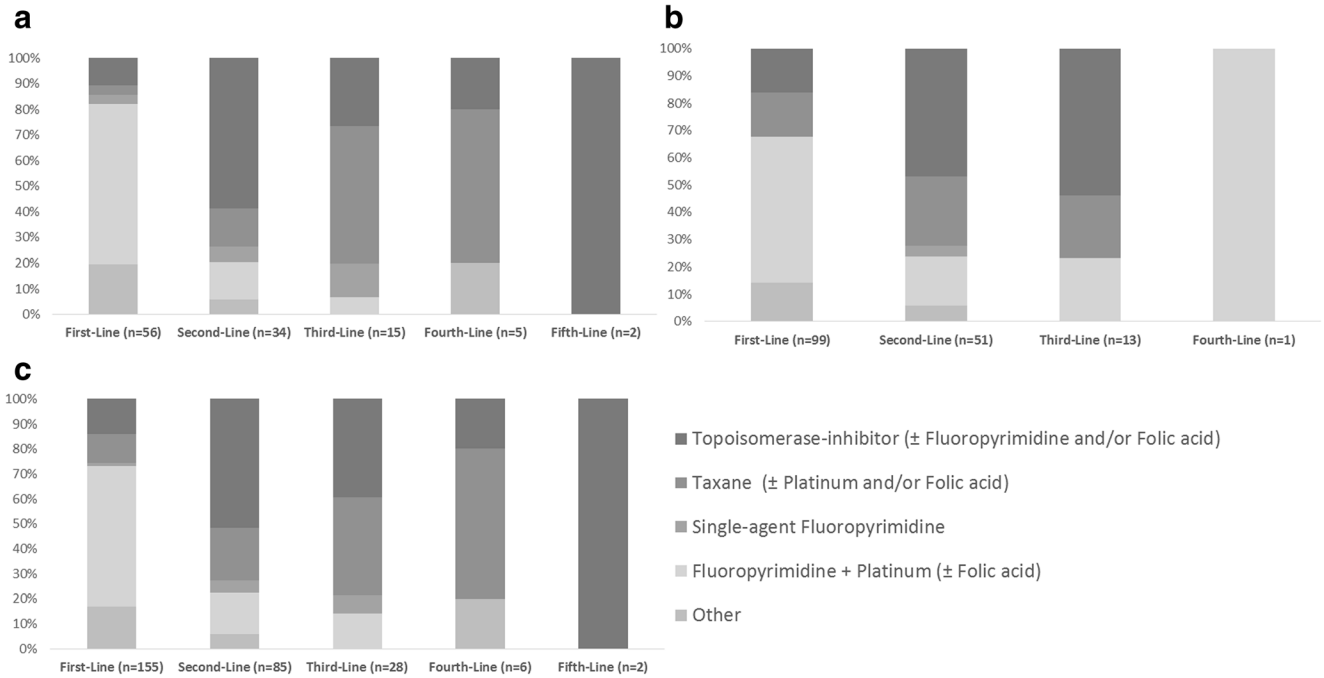

Fig. 2 Most commonly used chemotherapy regimens in private (**a**) and public (**b**) systems and overall (**c**)

settings and considering the whole population of patients. Median times to start first, second, third, and fourth lines of therapy in the whole study population were 2.8 (95% CI 2.4–3.4), 11.5 (95% CI 9.6–13.1), 15.1 (95% CI 13.0–19.3), and 20.2 months (95% CI 17.3–not reached), respectively. There was no significant difference in any of those times between the public and the private settings (p values of 0.54, 0.73, 0.89, and 0.95 for the first to the fourth line, respectively).

Table 4 Data on treatment lines, best supportive care, and radiotherapy and surgery performed at each treatment line by healthcare profile

Variable	Patient's healthcare profile		
	Private $N = 56$	Public $N = 99$	Total $N = 155$
Number of total of treatment lines			
1	22 (39.3)	48 (48.5)	70 (45.2)
2	19 (33.9)	38 (38.4)	57 (36.8)
3	10 (17.9)	12 (12.1)	22 (14.2)
4	3 (5.4)	1 (1)	4 (2.6)
5	2 (3.6)	0 (0)	2 (1.3)
Patients referred to BSC after each line			
First	2/22 (9.1)	8/48 (16.7)	10/70 (14.3)
Second	0/19	10/38 (26.3)	10/57 (17.5)
Third	4/10 (40.0)	3/12 (25.0)	7/22 (31.8)
Fourth	1/3 (33.3)	0/1	1/4 (25.0)
Fifth	0/2	0/0	0/2
Patients submitted to radiotherapy			
First	6 (10.7)	11 (11.1)	17 (11)
Second	2 (5.9)	1 (2)	3 (3.5)
BSC	–	1 (4.8)	1 (3.6)
Patients submitted to surgery			
First	10 (17.9)	11 (11.1)	21 (13.5)
Second	5 (14.7)	3 (5.9)	8 (9.4)

BSC, best supportive care

Radiotherapy

Radiotherapy was most frequently administered during the first-line treatment of MGC, accounting for 10.7% of patients from the private setting and 11.1% of patients from the public setting. Few patients underwent radiotherapy during the second-line therapy or as BSC (Table 4). Radiotherapy was administered as part of a chemoradiotherapy regimen in 38.1% of the cases. The median survival of MGC patients who underwent or not radiotherapy was 16.9 months (95% CI 10.4–not reached) and 17.8 months (95% CI 13.4–20.5) ($p = 0.90$), respectively.

Surgery

Surgeries were performed only during the first and second line of treatments, in 21 (13.5%) and in 8 (9.4%) of the patients, respectively. Not all surgeries were related to the primary tumor.

Best Supportive Care

The rate of patients who received exclusive BSC was 12.5% in the private setting and 21.2% in the public setting. Number

and rate of patients referred to BSC after each line of treatment are presented in Table 4. Most patients in both settings underwent three lines of treatment before being referred to BSC.

Clinical Outcomes and Survival Analysis

The best response to first-line treatment among most patients from the private and the public settings was partial response (39.0%) and disease progression (60.0%), respectively (considering cases with a reported response). The best response to second-line treatment among most patients in both private (80.0%) and public (73.9%) settings was disease progression (considering cases with a known response). Disease progression was also the best response to the last three lines of treatment in both settings.

Overall, median OS was 16.9 months (95% CI 13.6–20.5 months). Considering patients from the private and the public settings separately, median OS was 20.5 months (95% CI 15.3–27.5 months) and 14.9 months (95% CI 12.6–19.3 months), respectively ($p = 0.22$). The median OS of patients who underwent total or partial gastrectomy at some point of the treatment was 21.4 months (95 CI% 13.7–not reached), while the median OS of patients who did not undergo surgery was 16.8 months (95% CI 11.7–20.2) ($p = 0.03$) (Fig. 3a). Two other variables were associated with survival, namely primary tumor location and ECOG performance status (PS) (Fig. 3b,c, respectively). By multivariate analysis, all these variables except primary tumor location were selected as independent prognostic factors, as well as age (Table 5).

Healthcare Resource Use, Support Procedures, and Adverse Events

A total of 1416 concomitant medications were administered along all lines of systemic treatment considering patients with gastric cancer from both settings. They were used by 83.2% of patients with a known status in the first line of treatment and by 77.6, 64.3, and 33.3% of patients in the second, third, and fourth lines of treatment, respectively; in addition, they were used by all patients during the fifth line and BSC (Fig. 4). The median number of concomitant medications per patient was 5 (range 1–22), 3 (range 1–16), 3 (range 1–9), 3 (range 1–5), 2 (range 1–3), and 9 (range 1–28) during the successive lines of systemic treatment and BSC, respectively. Antiemetics and analgesics were among the main drug classes used during all lines of treatment. From 16.7 to 47.9% of the concomitant medications used along the first to the fourth line of therapy was related to adverse events (Table 6).

From 50 to 94.2% of patients underwent at least one outpatient visit during each line of systemic treatment and BSC. Most of the visits were consultation with a radiologist. Thirty-nine percent of patients in the first-line therapy underwent at least one hospitalization, while that rate was 29.4, 35.7, and 57.1% for patients in the second and third lines of treatment and in BSC, respectively. The main reasons for hospitalizations were chemotherapy and management of adverse events/toxicity. Hospitalization length of stay is described in Table 7. Considering patients from both the private and the public settings and with a known status regarding visits to emergency rooms, 45.6% of patients visited the emergency room during the first line of treatment, 38.5% during the second line, 26.9% during the third line, 16.7% during the fourth line, and 46.4% during BSC. The mean number of visits to the emergency room per patient varied from 1 to 2.6 along all lines of systemic therapy and BSC. Reasons other than adverse events/toxicity, management of pain, comorbidities, or disease symptoms prevailed during the first to the fourth line of systemic treatment. Within the period of BSC, management of disease symptoms was the main reason of visits to the emergency room (Fig. 5). About 2% of the patients with a known status underwent at least one backup hospitalization during the first line of treatment. No patient underwent backup hospitalizations during the other lines of treatment.

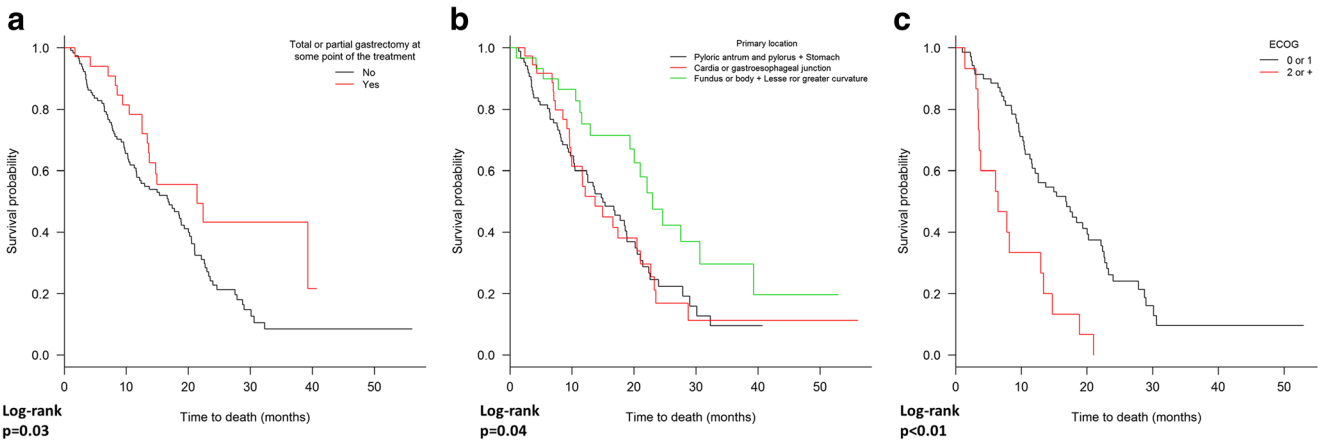

Fig. 3 Kaplan-Meier survival curves for gastrectomy (**a**), primary tumor location (**b**), and ECOG status (**c**)

Table 5 Multivariate analysis by Cox proportional hazard model, adjusted by age, of potential prognostic factors of overall survival

	HR (95% CI)	*p* value
Patient's healthcare profile		
Private	1.00	–
Public	0.45 (0.17–1.19)	0.11
Age at diagnosis of advanced gastric cancer		
< 50	4.34 (1.19–15.8)	**0.03**
> 50	1.00	–
Histologic grade		
G1	1.00	–
G2	1.1 (0.12–9.7)	0.93
G3	1.84 (0.21–16.32)	0.58
Primary tumor location		
Fundus or body + lesser or greater curvature	1.00	–
Cardia or gastroesophageal junction	1.33 (0.32–5.49)	0.70
Pyloric antrum + stomach	0.63 (0.21–1.92)	0.41
Peritoneal metastasis		
No	1.00	–
Yes	0.9 (0.32–2.53)	0.85
More than 1 distant metastasis at advanced diagnosis		
No	1.00	–
Yes	2.02 (0.82–5.02)	0.13
ECOG performance status		
0 or 1	1.00	–
2 or +	13.25 (3.36–52.23)	**<0.01**
Partial or total gastrectomy within treatment period		
No	3.28 (1.07–10.06)	**0.04**
Yes	1.00	–
Gender		
Feminine	1.00	–
Masculine	1.69 (0.78–3.66)	0.19
Radiotherapy		
No	1.47 (0.41–5.28)	0.55
Yes	1.00	–

CI, confidence interval; *HR*, hazard ratio

Regarding support procedures, 37.2, 28.9, 29.2, and 40.7% of patients underwent at least one support procedure while receiving the first, second, and third lines of treatment and BSC, respectively. Paracentesis and transfusion were the most common support procedures.

Exams were performed by 92.1% of patients during the first line of treatment, 93.8% during the second line, 85.7% during the third line, 16.7% during the fourth line, 100% during the fifth line, and 81.5% during BSC (Fig. 5 and Table 8).

The rate of patients that had at least one adverse event during each line of systemic treatment ranged from 33.3% (in the fourth line) to 94.8% (in the first line). Nausea/vomiting and diarrhea were the main adverse events reported for the first, second, and third lines of therapy, accounting together for 25.0, 23.7, and 23.3% of the events. Fatigue and asthenia, mucositis, and pain were also frequent, each of them accounting from 3.5 to 7.8% of the events in each of these lines of treatment (Fig. 4).

Discussion

This publication is a comprehensive study describing real-world treatment patterns and survival of MGC patients in Brazil. A wide range of chemotherapy regimens was reported by participating centers, mainly for first- and second-line therapy, as previously reported in studies with a similar design performed in Taiwan [8], South Korea [11], United States [10, 18], and France [19]. Gastric cancer lacks standard treatment strategies, especially following first-line therapy. Guidelines and drugs available for the treatment of gastric cancer vary among countries.

The population comprised mainly men with mean age around 61 years, stage IV disease, and no family history of gastric cancer, as in the studies in Taiwan, in South Korea, and in France [8, 11, 19]. Stomach not otherwise specified (NOS) prevailed as the primary tumor location, as in one of the USA studies. While the primary tumor location affected the OS according to the univariate analysis, this was not confirmed by multivariate analysis. On the other hand, ECOG PS in first-line therapy was confirmed as an independent prognostic factor by multivariate analysis, with PS 2 or 3 conferring a poorer prognosis than PS 0 or 1. Age at MGC diagnosis was also selected as an independent prognostic factor.

Platinum- and/or fluoropyrimidine-containing regimens were the most common practice as first-line therapy in this study. Indeed, these are the first-line regimens recommended by the National Comprehensive Cancer Network (NCCN) guidelines [20] and were also the predominant treatment in the real-world studies in MGC performed in Taiwan, South Korea, United States, and France [8, 10, 11, 18, 19].

Regarding second-line therapy, the studies performed in Taiwan and South Korea reported higher rates of patients who received it compared to this study (65 and 80% versus 55%, respectively) [8, 11]; on the other hand, studies conducted in United Kingdom, France, and United States reported rates varying from 29 to 55% [10, 18, 19, 21]. Of note, more Brazilian patients from the private healthcare system than from the public setting received second-line therapy (61 and 52%, respectively). The most common second-line treatments in this study, namely irinotecan and paclitaxel, are also in agreement with NCCN recommendations. Although there is not a highly prevailing drug/regimen used as second-line therapy among the real-world studies conducted so far, 5-fluorouracil alone or in combination with other agents,

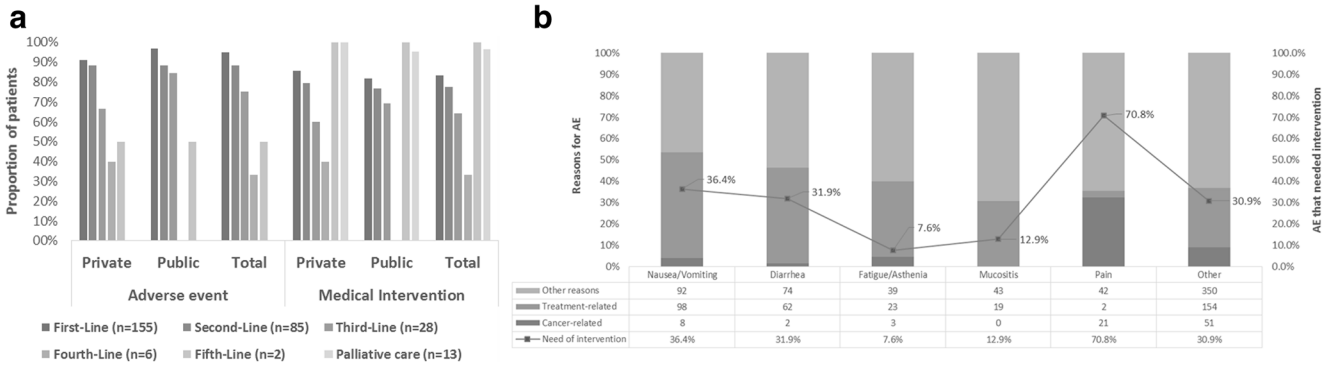

Fig. 4 **a** Proportion of patients who presented adverse events and who had any medical intervention. **b** Most commonly reported adverse events (AEs) in percentage of patients. In the secondary axis, the percentage of need for intervention (surgical or medical) for each AE

including irinotecan, are among the main options in most of them. A randomized study comparing BSC alone with irinotecan (left to the discretion of investigators) showed a benefit of irinotecan in OS of patients with advanced gastric cancer [22]. Similar results were observed in another randomized study comparing BSC alone with BSC plus chemotherapy with docetaxel or irinotecan (left to the discretion of investigators) [23]. In addition, a third randomized study suggests that both irinotecan and paclitaxel are reasonable options for second-line treatment of MGC, with no statistically significant difference found between them [24].

According to the recommendations of the NCCN, systemic therapy for advanced disease should be selected based on PS, medical comorbidities, and toxicity profile. Trastuzumab can

Table 6 Most commonly used supportive care procedures and visits to emergency room by treatment line and healthcare profile

Variable	First line			Second line		
	Private *N* = 56	Public *N* = 99	Total *N* = 155	Private *N* = 34	Public *N* = 51	Total *N* = 85
Supportive care						
Medical interventions, *n* (%)	48 (85.7)	81 (81.8)	129 (83.2)	27 (79.4)	39 (76.5)	66 (77.6)
Total number or procedures	255	515	770	81	232	313
Procedures per patient	5.3	6.4	6	3	5.9	4.7
Medications, *n* (%)						
Antiemetics	30 (11.8)	103 (20)	133 (17.3)	11 (13.6)	47 (20.3)	58 (18.5)
Analgesics	14 (5.5)	62 (12)	76 (9.9)	11 (13.6)	32 (13.8)	43 (13.7)
Laxative	3 (1.2)	31 (6)	34 (4.4)	2 (2.5)	16 (6.9)	18 (5.8)
Opioids	3 (1.2)	28 (5.4)	31 (4)	0 (0)	8 (3.4)	8 (2.6)
CSF	5 (2.0)	0 (0)	5 (0.7)	2 (2.4)	3 (1.3)	5 (1.6)
Other (% for each line)	173 (67.8)	257 (49.9)	430 (55.8)	48 (59.3)	115 (49.6)	163 (52.1)
Nutritional support, *n* (%)	4 (1.6)	21 (4.0)	25 (3.3)	2 (2.5)	7 (3.0	9 (2.9)
Visits to the emergency room						
Number of patients, *n* (%)	9 (16.1)	57 (57.6)	66 (42.6)	6 (17.6)	24 (47.1)	30 (35.3)
Reason for visit, *n* (%)						
Adverse event/toxicity	0 (0)	0 (0)	32 (18.5)	0 (0)	0 (0)	16 (29.6)
Pain	0 (0)	0 (0)	5 (2.9)	0 (0)	0 (0)	4 (7.4)
Comorbidity	0 (0)	0 (0)	2 (1.2)	0 (0)	0 (0)	0 (0)
Cancer symptoms	0 (0)	0 (0)	9 (5.2)	0 (0)	0 (0)	10 (18.5)
Other	0 (0)	0 (0)	125 (72.3)	0 (0)	0 (0)	24 (44.4)

CSF, colony-stimulating factor

Table 7 Number and length of stay of hospitalizations for each type of admission and healthcare profile

Type of admission	Private			Public			Total		
	Number of admissions	Length of stay (days)		Number of admissions	Length of stay (days)		Number of admissions	Length of stay (days)	
		Mean (SD)	Median (Min–Max)		Mean (SD)	Median (Min–Max)		Mean (SD)	Median (Min–Max)
Collective room	0	–	–	35	5.3 (2.8)	5 (2–13)	35	5.3 (2.8)	5 (2–13)
Private room	0	–	–	1	7 (–)	7 (7–7)	1	7 (–)	7 (7–7)
Intensive care unit	2	12 (5.7)	12 (8–16)	0	–	–	2	12 (5.7)	12 (8–16)
Semi-Intensive unit	1	15 (–)	15 (15–15)	0	–	–	1	15 (–)	15 (15–15)
Other	17	9.5 (9.3)	7 (4–43)	1	1 (–)	1 (1–1)	18	9 (9.2)	6.5 (1–43)
Total	**22**	**9.3 (8.6)**	**6.5 (2–43)**	**39**	**5.2 (2.8)**	**5 (1–13)**	**61**	**6.6 (5.9)**	**5 (1–43)**

SD, standard deviation

be added to cytotoxic regimen for HER2-neu-overexpressing adenocarcinoma. However, still according to the NCCN, preferred regimens for second-line therapy include docetaxel, paclitaxel, irinotecan, and ramucirumab alone or associated with paclitaxel. Selection depends on prior therapy and performance status [20].

Similarly, the Brazilian consensus for gastric cancer management, issued in 2013, recommends chemotherapy regimens and trastuzumab [14]. Among monoclonal antibodies, only trastuzumab associated with capecitabine or 5-fluorouracil plus a platinum-based agent has been approved as first-line treatment of gastric cancer in Brazil; to this date, there is no biological drug approved for second-line therapy. In this real world study, trastuzumab was used to treat only a few patients from the private healthcare system, since it is not available for patients managed in the public setting.

It is noteworthy that more than 90% of the patients receiving systemic treatment presented adverse events. Management of adverse events represented a burden associated with increased use of concomitant medications and support procedures during both systemic treatment and BSC. Furthermore, outpatient visits, visits to the emergency room, and hospitalizations were also very common. All these occurrences were especially frequent in the first and second lines of treatment as well as in BSC.

Surgery was the second most common treatment for MGC in this study, with a positive impact in OS in both univariate and multivariate analyses. A recent meta-analysis concluded that palliative gastrectomy may be associated with longer survival in patients with incurable advanced gastric cancer, especially for those at stage M1 [25]. The main international guidelines (NCCN) and the European Society for Medical

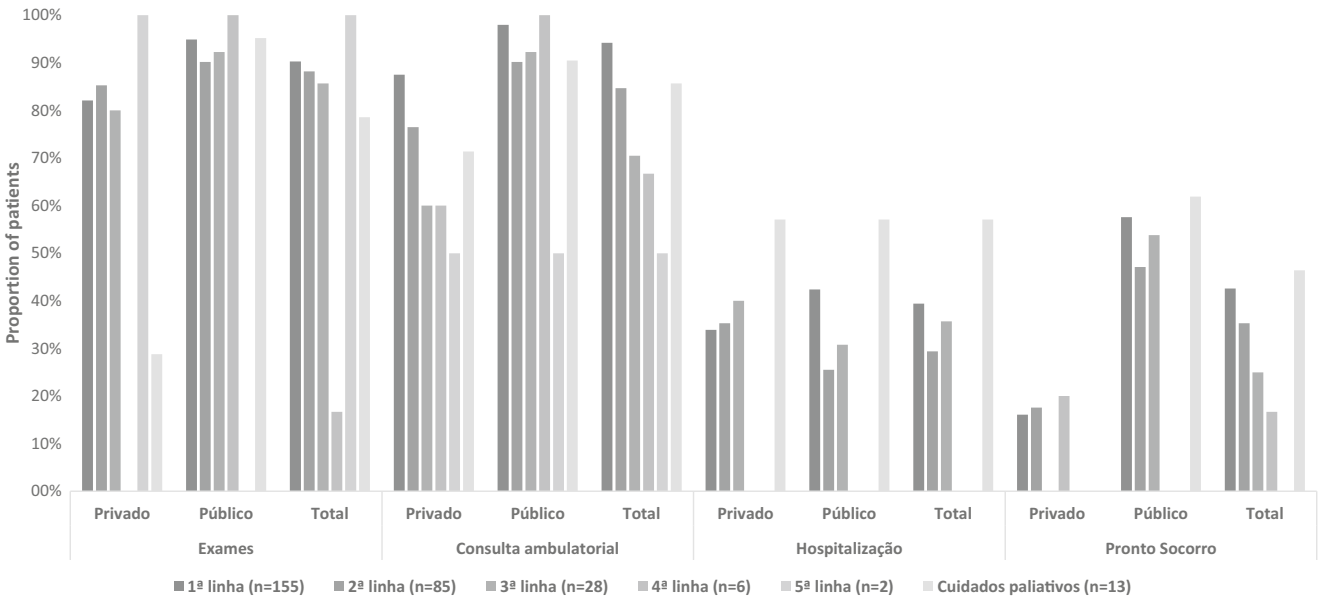

Fig. 5 Resource use regarding exams, outpatient, inpatient, and hospice unit admissions, by proportion of patients for each line

Table 8 Data on exams/laboratory tests performed by healthcare profile

Lab test/exams	Private			Public			Total		
	Number of patients (%)	Number of exams per patient		Number of patients (%)	Number of exams per patient		Number of patients (%)	Number of exams per patient	
		Mean ± SD	Median (Min–Max)		Mean ± SD	Median (Min–Max)		Mean ± SD	Median (Min–Max)
Blood calcium level test	14 (25)	2.4 ± 2.8	2 (1–12)	90 (90.9)	4.7 ± 4.3	3 (1–21)	104 (67.1)	4.4 ± 4.2	3 (1–21)
Total cholesterol and/or fractions	8 (14.3)	2 ± 1.4	1 (1–4)	27 (27.3)	3 ± 2	2 (1–8)	35 (22.6)	2.7 ± 1.9	2 (1–8)
Colonoscopy	–	–	–	1 (1)	1 ± −	1 (1–1)	1 (0.6)	1 ±	1 (1–1)
Creatinine	42 (75)	5.4 ± 5.6	3 (1–30)	96 (97)	8.1 ± 6.1	7 (1–25)	138 (89)	7.3 ± 6.1	6 (1–30)
Upper digestive endoscopy	15 (26.8)	1.3 ± 0.5	1 (1–2)	43 (43.4)	1.4 ± 1	1 (1–7)	58 (37.4)	1.4 ± 0.9	1 (1–7)
Phosphorus blood test	5 (8.9)	3 ± 4.5	1 (1–11)	25 (25.3)	2 ± 1.4	1 (1–6)	30 (19.4)	2.2 ± 2.2	1 (1–11)
Glycemia	31 (55.4)	4.8 ± 6	2 (1–29)	52 (52.5)	4.5 ± 4.1	3 (1–18)	83 (53.5)	4.6 ± 4.9	3 (1–29)
Complete blood count	47 (83.9)	7.3 ± 6.5	4 (1–30)	96 (97)	9.6 ± 7	9 (1–30)	143 (92.3)	8.8 ± 6.9	7 (1–30)
PET scan	3 (5.4)	1.3 ± 0.6	1 (1–2)	2 (2)	2 ± 1.4	2 (1–3)	5 (3.2)	1.6 ± 0.9	1 (1–3)
Potassium blood test	24 (42.9)	2.3 ± 1.4	2 (1–6)	77 (77.8)	4.8 ± 3.8	4 (1–16)	101 (65.2)	4.2 ± 3.5	3 (1–16)
X-ray	4 (7.1)	1.8 ± 1.7	1.5 (0–4)	25 (25.3)	1.6 ± 1.4	1 (1–7)	29 (18.7)	1.6 ± 1.4	1 (0–7)
NMR	10 (17.9)	1.7 ± 0.7	2 (1–3)	4 (4)	1.5 ± 0.6	1.5 (1–2)	14 (9)	1.6 ± 0.6	2 (1–3)
Sodium blood test	23 (41.1)	2.4 ± 1.9	2 (1–8)	76 (76.8)	5.2 ± 4.2	4 (1–19)	99 (63.9)	4.5 ± 4	3 (1–19)
T4 free and/or TSH	11 (19.6)	1.5 ± 0.8	1 (1–3)	2 (2)	1.5 ± 0.7	1.5 (1–2)	13 (8.4)	1.5 ± 0.8	1 (1–3)
ALT and/or AST	37 (66.1)	5.9 ± 10	4 (1–60)	92 (92.9)	7.7 ± 6.3	6 (1–36)	129 (83.2)	7.2 ± 7.5	5 (1–60)
Tomography	42 (75)	3.3 ± 3.2	2 (1–14)	72 (72.7)	3.5 ± 2.7	3 (0–15)	114 (73.5)	3.4 ± 2.9	2 (0–15)
Ultrasound	4 (7.1)	0.8 ± 0.5	1 (0–1)	12 (12.1)	1.6 ± 1.4	1 (1–5)	16 (10.3)	1.4 ± 1.3	1 (0–5)
Blood urea nitrogen	38 (67.9)	5.3 ± 5.7	3.5 (1–30)	95 (96)	7.6 ± 5.6	7 (1–22)	133 (85.8)	6.9 ± 5.7	5 (1–30)
Urinalysis	7 (12.5)	1.1 ± 0.4	1 (1–2)	23 (23.2)	1.4 ± 0.8	1 (1–4)	30 (19.4)	1.3 ± 0.8	1 (1–4)
Other	44 (78.6)	22 ± 25.5	13 (1–129)	86 (86.9)	23 ± 20.9	19 (1–116)	130 (83.9)	22.7 ± 22.5	18.5 (1–129)

ALT, alanine transaminase; *AST*, aspartate transaminase; *NMR*, nuclear magnetic resonance; *SD*, standard deviation; *TSH*, thyroid-stimulating hormone

Oncology/European Society of Surgical Oncology/European Society for Therapeutic Radiology and Oncology (ESMO-ESSO-ESTRO) recommend surgery as the primary treatment for gastric cancer. These guidelines emphasize that patients should be evaluated by a multidisciplinary team to consider surgery with curative intent in the early stages of the disease. In MGC, surgery may also be considered an option, depending on the general state of health of the patient [20]. The best surgery approach is determined according to the tumor's histological type and localization. The endoscopic submucosal resection is the preferred option for early stage gastric cancer, while for advanced disease, surgery followed by extended lymphadenectomy should be considered standard of care—although a large resection of D2 lymphatic chain can be related to higher perioperative rates of morbidity and mortality, it also shows a 5-year OS benefit in patients at stages T3 and T4 with splenic and pancreatic preservation [26].

Radiotherapy was not a very common practice to treat MGC in Brazil, and it was often administered as part of a chemoradiotherapy regimen. Conversely, two of the studies on real-world treatment patterns in advanced gastric cancer found that around 50% of patients received radiotherapy [10]. The median survival of patients who underwent radiotherapy in the current study was not significantly different than of those who did not undergo this procedure (18.4 versus 16.9 months; $p = 0.93$).

Time from diagnosis to initiation of systemic therapy showed no difference between the private and the public settings. Interestingly, a study by Elimova et al. [27] found that MGC patients with a delay in treatment longer than four weeks were more likely to be alive at 1 year than those who started treatment within four weeks of diagnosis, considering either the total study population or only the asymptomatic patients. Nevertheless, the great majority of patients in that study (around 88%) had a treatment delay less than 12 weeks, while only about half of the patients in the present study started the first-line chemotherapy within 12 weeks of the MGC diagnosis.

Based on this real-world study, outcomes related to MCG's management remain poor. More than 40% of patients underwent only one line of systemic therapy, and about 40% of them either died during the treatment or received BSC only

following the first line. Furthermore, a fifth of the patients in the study died within two months after discontinuation of the first-line treatment. Median OS among patients from the private (20.5 months) and the public (14.9 months) settings was not significantly different and was within the range of those reported for the studies in South Korea, Taiwan, and USA (12 to 27 months) [8, 10, 11, 18].

This study presents some limitations. The results do not allow conclusions for causal explanations due to the cohort study design. In addition, one important limitation of the retrospective studies is that the data are often incomplete. Individual or entire series of records can be missing, because either data were misplaced or data were not recorded. Additionally, treatment patterns represent only the practices of physicians who have agreed to participate in the study and may vary from non-responding physicians, i.e., those who refused study participation or failed to complete the study requirements on time and were excluded from the study.

Our findings indicate that there are variations in treatment for gastric cancer in the country. Survival following the completion of first-line chemotherapy remains poor in this population. Improved survival was observed among patients submitted to gastrectomy. Adverse events and resource use represented a burden mostly in the first and second lines of treatment and in exclusive BSC. These results suggest that there is space for improvement in the treatment of MGC in Brazil.

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Compliance with Ethical Standards

Conflict of Interest Diego Novick is an employee of Eli Lilly and Company Inc.; Eimy Minowa and Guilherme Silva Julian are employees of Kantar Health. The remaining authors declare that they have no conflicts of interest relevant to the manuscript submission.

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