EJMI

DOI: 10.14744/ejmi.2023.71797
EJMI 2023;7(4):487–493

Research Article

Chemotherapy Efficacy and Tolerability in Metastatic Gastric Cancer Patients Aged 75 Years and Older

Yasin Sezgin,[1] Yonca Yilmaz Urun[2]

[1]Division of Medical Oncology, Department of Internal Medicine, Van Yüzüncü Yıl University Faculty of Medicine, Van, Türkiye
[2]Division of Gastroenterology, Department of Internal Medicine, Van Yüzüncü Yıl University Faculty of Medicine, Van, Türkiye

Abstract

Objectives: More than half of gastric cancer patients have no chance of resection at the time of diagnosis. In gastric cancer, which has increased frequency with age, chemotherapy efficacy and tolerability in metastatic gastric cancer aged 75 and over have been investigated due to the fact that the elderly patient population is not sufficiently involved in the studies.

Methods: In our study, the clinical and demographic characteristics of patients, treatment regimens and responses, prognostic factors, grad 3-4 toxicity, progression-free survival (PFS) and overall survival (OS) were examined.

Results: In the study involving 118 patients, PFS was 5.8 months and OS was 8.4 months. A disease control rate of 38.1% was achieved with chemotherapy.

Conclusion: Since the OS in this study was 10.5 months in patients with ECOG PS 0-1, 13.8 months in patients who received two lines or more, and the frequency of side effects was acceptable, we believe that this patient population should not be left untreated. Since there are acceptable survival values even with single-agent therapies, monotherapy can be recommended for patients with poor ECOG PS and combination therapies can be recommended for patients with good PS without comorbidities.

Keywords: Chemotherapy, elderly patients, gastric neoplasms, prognosis

Cite This Article: *Sezgin Y, Yilmaz Urun Y. Chemotherapy Efficacy and Tolerability in Metastatic Gastric Cancer Patients Aged 75 Years and Older. EJMI 2023;7(4):487–493.*

Although the incidence of gastric cancer has decreased with the preservation of food under more suitable conditions, the incidence is still increasing in the elderly population. Gastric cancer is the 5th most frequently common cancer worldwide and the 3rd most leading cause of malignancy-related deaths.[1-5] Despite the development of surgical, targeted therapies and combined chemotherapy treatments, 5-year overall survival (OS) rates are less than 30%.[3,6] Most patients with gastric cancer are diagnosed at an advanced stage.[3] The average age of diagnosis is 71 and the average age of death is 74.[4,5] More than half of patients have no chance of resection at the time of diagnosis.[7]

There are many studies in which multimodal treatment is recommended in the treatment of non-metastatic gastric cancer. In multimodal treatment, preoperative neoadjuvant treatment, followed by surgical treatment and then adjuvant treatment is recommended.[8-10] Treatment for metastatic gastric cancer is palliative. Chemotherapy has favorable OS than best supportive care (BSC) in metastatic gastric cancer.[11,12] In a meta-analysis comparing combina-

Address for correspondence: Yasin Sezgin, MD. Van Yuzuncu Yil Universitesi Tip Fakultesi, Ic Hastaliklari Anabilim Dali, Tibbi Onkoloji Anabilim Dali, Van, Türkiye
Phone: +90 532 658 15 24 **E-mail:** dr.yasin1982@hotmail.com

Submitted Date: August 23, 2023 **Accepted Date:** September 18, 2023 **Available Online Date:** September 20, 2023

©Copyright 2023 by Eurasian Journal of Medicine and Investigation - Available online at www.ejmi.org
OPEN ACCESS This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

tion chemotherapy regimens with monotherapy regimens in patients with metastatic gastric cancer, response rates were better in patients receiving combination therapy.[13] While a response rate of 35-45% can be achieved with combination therapies, this rate is 24% with single-agent docetaxel and 34% with single-agent capecitabine.[13-15]

Compared to the young patient population, survival rates are lower in elderly patients.[16] The lower survival rates are thought to be related to the inability of elderly patients to receive standard treatment. With advancing age, bone marrow reserve decreases, lean body mass decreases and some changes in organ function occur. As a result of these changes, drug pharmacokinetics and clearance are affected.[17,18] For these reasons, it becomes difficult for elderly patients to receive standard treatment. Another reason for the lower survival rates in elderly patients is thought to be due to the difference in tumor biology.[19,20] Rather than chronological age increase in this patient population; Factors such as biological age, comorbidities, physical life of the person and performance score were found to be more effective on drug tolerability.[21] Based on these data, a comprehensive geriatric assessment score has been created using parameters such as social life, comorbidities, cognitive impairment and functional impairment.[22] When the comprehensive geriatric assessment score is used in the treatment decision to the patient, the chemotherapy regimen to be given changes by 40-50%.[23,24] Therefore, comprehensive geriatric assessment rather than chronological age is recommended for treatment selection in the geriatric patient group.

Studies and guidelines in gastric cancer are generally based on young patient data.Elderly patients are generally not included in clinical trials. Since gastric cancer is more common in the elderly population and there are not enough guidelines on this subject, we aimed to investigate treatment response rates, treatment tolerability and side effect profile in elderly gastric cancer patients.

Methods

Our study is a retrospective study in which metastatic gastric cancer patients who were followed and treated at the Oncology Clinic of Van Yüzüncü Yıl University Faculty of Medicine, Dursun Odabaşı Medical Center between 2005 and 2016. Metastatic gastric cancer patients aged 75 and over who used at least two sessions of chemotherapy at the time of diagnosis took part in this study. Patients younger than 75 with a secondary malignancy and those out of follow-up were out of the study.In our trial, clinical and demographic characteristics of the patients, treatment regimens and responses, prognostic factors, grade 3-4 toxicity, progression-free survival (PFS) and OS were analysed. PFS was calculated as the time from diagnosis to the date of clinical or radiological progression, and OS was calculated as the time from diagnosis to death or last follow-up. Radiological assessments were performed every 3 months to patients. Treatment response was assessed according to RECIST 1.1.

Eastern Cooperative Oncology Group Performance Status of a patient (ECOG PS) and comorbid conditions were taken into account in the selection of the chemotherapy scheme. In this study, chemotherapy regimens with doublet and triplet cytotoxic agents were defined as combination therapy and single-agent regimens as monotherapy. Trastuzumab was not added to the number of drugs. Toxicity was graded based on haemogram, biochemistry, and medical history according to the National Cancer Institute consensus criteria. According to this; It was rated as 1: mild, 2: moderate, 3: severe, 4: very severe.

Statistical Analysis

Descriptive statistics were used for patient characteristics and parameter frequencies. The Kaplan-Meier test was used to estimate PFS and overall survival OS, and comparisons were made using the log-rank test.

Descriptive statistics for variables are expressed as mean, standard deviation, minimum and maximum values. Categorical variables are expressed as numbers and percentages. Chi-square test was used to analyse whether there was a significant difference between the distribution ratios of categorical variables according to the groups.In numerical data, the mean was used for normally distributed values, and the median for non-normally distributed values. A 95% confidence interval (CI) and a two-sided significance level of $p<0.05$ were used. The statistical software package SPSS (IBM, version 25) was used for the analysis of our study.

Results

A total of 118 patients took part in the study, of whom 82 (69.5%) are male and 36 (30.5%) are female. The median age of diagnosis of patients who took part in was 78 (75-90). The tumor was located in the cardia and antrum of most patients.

The most common site of metastasis was the liver (66.9%). The rates of use of single (27.1%), double (35.6%) and triple (37.3%) combination regimens were similar. 81.4% of patients received second-line therapy. The general characteristics of the patients are listed in Table 1. The chemotherapy regimens used by the patients are shown in Table 2. The response of the patients to the first series of chemotherapy is given in Table 3.

Table 1. Clinical and demographic characteristics of the patients

	Number of patients (n=118)	%
Gender		
Male	82	69.5
Female	36	30.5
ECOG PS		
0	18	15.3
1	46	39
2	51	43.2
3	3	2.5
Age		
75-79	78	66.1
≥80	40	33.9
Localization		
Cardia	45	38.1
Corpus	25	21.2
Antrum	38	32.2
Diffuse	10	8.5
Sites of metastasis		
Liver	39	66.9
Lung	21	17.8
Bone	6	5.1
Peritoneum	37	31.4
Lymph node	30	25.4
Pancreas	2	1.7
Other	4	3.3
Number of metastatic sites		
1	68	57.6
2	41	34.7
≥3	9	7.6
Number of chemotherapy cycles		
2-3	47	39.8
4-6	63	53.4
>6	8	6.8
Chemotherapy regimen		
Single agent	32	27.1
double agent	42	35.6
Triple agent	44	37.3
Second series of chemotherapy		
Yes	96	81.4
No	22	18.6
Current status		
Alive	2	1.7
Ex	116	98.3

ECOG PS: Eastern Cooperative Oncology Group performance status.

When all patients were evaluated, the median follow-up was 7 months (min-max: 1-60), PFS was 5.8 months, and OS was 8.4 months. In terms of response rates, a total of 25 (21.2%) patients achieved an objective response,

Table 2. Chemotherapy regimens given to patients in the first series

Treatment regimen used	Number of patients n (%)
Taxane + Platinum + Fluoropyrimidine	33 (28)
Trastuzumab combination regimens	4 (3.4)
Cisplatin + Floropirimidine	23 (19.5)
Platinum + Taxane	7 (5.9)
Taxane + Floropirimidine	1 (0.8)
Epirubicin + platinum + floropirimidine	7 (5.9)
Single agent (capecitabine, 5-FU, UFT)	32 (27.1)
FOLFOX/XELOX	11 (9.3)

XELOX: Capecitabine, oxaliplatine; FOLFOX: Oxaliplatine, folinic acide, fluorouracil.

including a complete response in 2 (1.7%) patients and a partial response in 23 (19.5%) patients. PFS was 7.2 months in patients with ECOG PS 0-1 and 4.5 months in patients with PS 2-3 (log rank p=0.011) (Fig. 1). OS was 10.5 months in patients with PS 0-1 and 6.2 months in patients with PS 2-3 (log rank p=0.039) and there was a statistically significant difference in both OS and PFS (Fig. 2). PFS was 7.2 months vs. 4.9 months (log rank p=0.22) and OS was 9 months vs. 6.5 months (log rank p=0.74) in patients with metastatic site 1 and patients with metastases in more than one organ, respectively. When comparing patients who received second-line therapy with those who did not, PFS was 8 months versus 5.3 months (log rank p=0.11) and OS was 13.8 months versus 7.7 months (log rank p=0.001) (Fig. 3). The most common treatment-emergent adverse events were neutropenia (17.8%), anaemia (17.8%) and nausea and vomiting (15.3%). Other adverse event rates are shown in Table 4. Dose changes were made during treatment in 33 (27.9%) patients. PFS and OS values according to patient risk groups are described in Table 5.

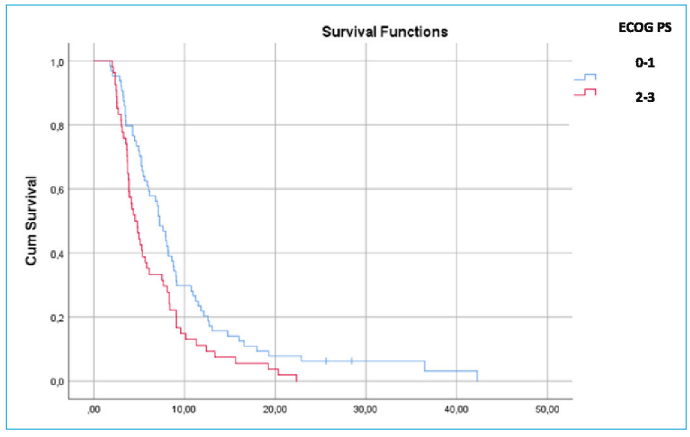

Figure 1. PFS comparison between ecog ps 0-1 and 2-3.

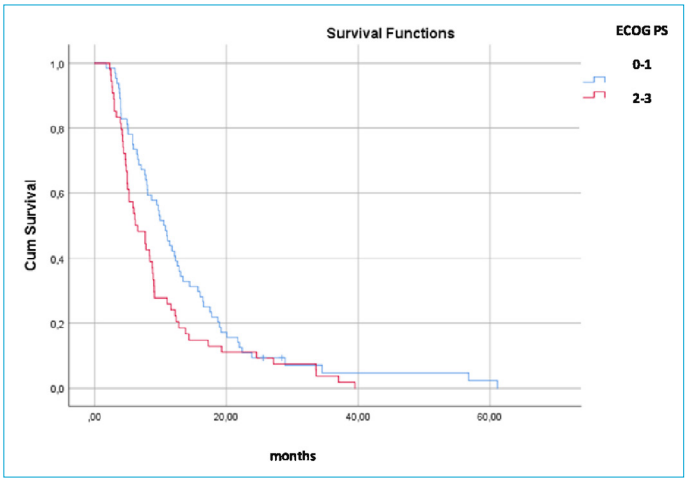

Figure 2. OS comparison between ecog ps 0-1 and 2-3.

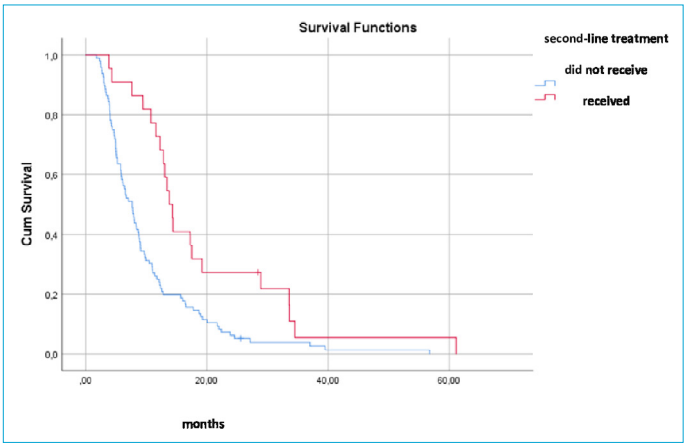

Figure 3. Comparison of OS in those receiving and not receiving second-line treatment.

Table 3. Patients' response to the first series of chemotherapy

Treatment response status	Number of patients (n=118)	%
Complet response	2	1.7
Partial response	23	19.5
Stable disease	20	16.9
Progressive disease	73	61.9

Table 4. Grade 3-4 toxicities

	Number of patients (n=118)	%
Hematologic toxicities		
Neutropenia	21	17.8
Anemia	21	17.8
Thrombocytopenia	1	0.8
Febrile neutropenia	2	1.7
Non-hematologic toxicities		
Mucositis	4	3.4
Diarrhea	11	9.3
Neuropathy	9	7.6
Nausea and vomiting	18	15.3
Allergic reaction	1	0.8
Thrombosis	5	4.2
Nephrotoxicity	7	5.9
Hepatotoxicity	0	0
Cardiotoxicity	1	0.8

Median PFS times with single, double and triple combination chemotherapy regimens were 5.3 months, 5.2 months and 7 months, respectively (log rank p=0.61). Median OS was 7.9 months, 8.8 months and 8.3 months, respectively (log rank p=0.96).

Table 5. PFS and OS times according to risk groups

Risk Groups	PFS (month)	p	OS (month)	P
All patients	5.8		8.4	
Age		0.53		0.98
75-80	6.1		8.3	
>80	5.3		7.8	
ECOG PS		0.011		0.039
0-1	7.2		10.5	
>1	4.5		6.2	
Metastasis site		0.22		0.74
1	7.2		9.0	
≥2	4.9		6.5	
Treatment received		0.64		0.98
Combination	5.9		8.6	
Monotherapy	5.3		7.9	
Second-line treatment		0.11		0.001
Received	8.0		13.8	
Did not receive	5.3		7.7	

PFS: Progression free survival; OS: Overall survival; ECOG PS: Eastern Cooperative Oncology Group performance status.

Discussion

Chemotherapy is a standard treatment for metastatic gastric cancer. The analysis of chemotherapy versus BSC (HR, 0.39, 95% CI: 0.28-0.52) and combination versus monotherapy, mainly 5-FU (HR, 0.83, 95% CI: 0.74- 0.93) showed a significant OS advantage in favour of both chemotherapy and especially combination chemotherapy.[13] As the elderly patient population was not included in most of the trials, the benefit of chemotherapy in elderly patients is not clearly known.Hence, it is difficult for physicians to plan treatment for elderly patients, and this group of patients is reluctant to being treated. To partially resolve this uncertainty, we conducted a study of

chemotherapy efficacy, tolerability and side-effect profile in metastatic gastric cancer patients over 75 of age.

PFS was 5.8 months and OS was 8.4 months, similar to previous studies.[13,15,25,26] When we compared patients with ECOG PS 0-1 to those with PS 2-3 in our study, there was a significant difference in both PFS and OS. In the study by Hayshi et al, survival in patients with ECOG PS 0, 1, 2, 3 was 599, 323, 193, 177 days, respectively.[27] In our study, PFS was 7.2 months in patients with ECOG PS 0-1 and 4.5 months in patients with PS 2-3 (log rank p=0.011), and OS was 10.5 months in patients with PS 0-1 and 6.2 months in patients with PS 2-3 (log rank p=0.039), and there was a statistically significant difference in both OS and PFS. We believe that the better survival in patients with good ECOG PS is related to the fact that these patients have fewer comorbidities and receive optimal treatment. The better the PS, the more likely they are to take combination treatment and the lower the incidence of side effects.

A meta-analysis by Wagner et al. compared patients who taking combination treatment with patients who taking monotherapy. According to this meta-analysis, OS was 1 month better in favour of those who received combined therapy and this was statistically significant.[13] In our study, OS was 8.6 months in those receiving combination therapy and 7.9 months in those receiving monotherapy, and there was no statistically significant difference.

When looking at studies on the efficacy and side effects of chemotherapy in elderly patients with gastric cancer, a study by Grazino et al. stands out. This was a phase 2 trial and 58 patients over the age of 65 were studied. Patients treated with cisplatin and 5-fluorouracil had a disease control rate of 43%. In the same study, grade 3-4 neutropenia was observed in 17% of patients.[28] In our study, 38.1% disease control was achieved. When comparing our study with this phase 2 study, the lower rate of disease control may be explained by the higher mean age of our patients.

The most common haematological toxicity in our study was neutropenia and anaemia with a rate of 17%, which is consistent with the literature.[13,28] Compared to monotherapy, the incidence of AEs is significantly higher in patients receiving combination therapy.[13] In our study, diarrhoea was observed in 2 patients taking monotherapy and anaemia in 2 patients, but no other adverse events developed. Side effects were most common in patients receiving combination therapy and were consistent with the literature. The reason for the higher incidence of side effects in older patients on combination therapies is thought to be related to their lower organ function reserves. As a result of low organ reserve, drug pharmacokinetics and drug clearance are affected.[17,18] Another issue to consider in elderly patients is that these patients use more medications due to comorbidities. Therefore, when adjusting chemotherapy drug doses in these patient groups, the drugs used by the patient should be listed, drug-drug interactions should be investigated, and dose reductions should be made if necessary.[29-31]

Although studies have shown that the incidence of chemotherapy intolerance and side effects is higher in elderly patients due to age-related comorbidities, many studies have shown that chemotherapy is effective and well tolerated in metastatic gastric cancer patients older than 65 years.[27,32-36] According to a study of metastatic gastric cancer patients over 75 years of age who received chemotherapy and were followed up with the BSC programme, OS was found to be 312 days in the chemotherapy arm and 43 days in the BSC arm.[27] According to this study, the OS of patients treated with chemotherapy was significantly longer than those who did not receive chemotherapy. Another study found that survival was better in patients who received neoadjuvant treatment and achieved a response.[37] In our study, although there was no comparator arm in the BSC programme, we believe that this patient population should not be left untreated because OS was 10.5 months in patients with ECOG PS 0-1, 13.8 months in patients receiving two lines or more, and the frequency of side effects was acceptable. As there are acceptable survival outcomes even with single-agent therapies, monotherapy should be recommended for patients with poor ECOG PS and combination therapies for patients with good PS without comorbidities.

Our study had limitations such as being single-centre, retrospective and not having a control group such as BSC. As our study included patients from 2016 and before, there were no patients who received immunotherapy treatment. This was also a limitation of the study. We believe that this study should be supported by prospective, multicentre studies with immunotherapy and chemotherapy and BSC arms.

Conclusion

The benefit of chemotherapy in patients with metastatic gastric cancer is clear. The efficacy of chemotherapy in elderly gastric cancer cases is still unclear, as the elderly patient population cannot be included in clinical trials.

As a result of increasing life expectancy and the aging of the world population, physicians will have to see and treat more elderly patients with gastric cancer in the coming years. In this respect, we believe that this study, in which examined the efficacy and tolerability of chemotherapy in metastatic gastric cancer aged 75 and over, is valuable. We recommend combination therapies for patients with good ECOG PS and no comorbidities, and single-agent regimens for patients with poorer PS and comorbidities.

Disclosures

Ethics Committee Approval: This study was conducted in accordance with the Declaration of Helsinki and approval was granted by the Ethics Committee of Van Yüzüncü Yıl University.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – Y.S.; Design – Y.S., Y.Y.U.; Supervision – Y.S.; Materials – Y.Y.U., Y.S.; Data collection &/or processing – Y.Y.U., Y.S.; Analysis and/or interpretation – Y.Y.U., Y.S.; Literature search – Y.Y.U.; Writing – Y.S.; Critical review – Y.S.

References

1. Kelley JR, Duggan JM. Gastric cancer epidemiology and risk factors. J Clin Epidemiol 2003;56:1–9.
2. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136:E359–386
3. National Cancer Institute. SEER Stat Fact Sheets: stomach cancer. Available at: https://seer.cancer.gov/statfacts/html/stomach.html.
4. Kitamura K, Yamaguchi T, Taniguchi H et al. Clinicopathological characteristics of gastric cancer in the elderly Br J Cancer 1996;73:798–802.
5. Kubota H, Kotoh T, Dhar DK et al. Gastric resection in the aged (> or = 80 years) with gastric carcinoma: a multivariate analysis of prognostic factors. Aust N Z J Surg 2000;70:254–7.
6. Ajani JA. Chemotherapy for gastric carcinoma: new and old options. Oncology (Williston Park) 1998;12:44–47.
7. Van Cutsem E, Haller D, Ohtsu A. The role of chemotherapy in the current treatment of gastric cancer. Gastric Cancer 2002; 5 (Suppl. 1):17–22.
8. Macdonald JS, Smalley SR, Benedetti J, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med 2001;345:725–730.
9. Buscariollo DL, Mamon HJ. Optimal management of resectable gastric adenocarcinoma. Expert Rev Anticancer Ther 2015;15:931–941.
10. Cunningham D, Allum WH, Stenning SP, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 2006;355:11–20.
11. Murad AM, Santiago FF, Petroianu A, Rocha PR, Rodrigues MA, Rausch M. Modified therapy with 5-fluorouracil, doxorubicin, and methotrexate in advanced gastric cancer. Cancer 1993;72:37–41.
12. Glimelius B, Hoffman K, Haglund U, Nyren O, Sjoden PO. Initial or delayed chemotherapy with best supportive care in advanced gastric cancer. Ann Oncol 1994;5:189–90.
13. Wagner AD, Grothe W, Haerting J, Kleber G, Grothey A, Fleig WE. Chemotherapy in advanced gastric cancer: a systematic review and meta-analysis based on aggregate data. J Clin Oncol 2006;24:2903–9.
14. Sulkes A, Smyth J, Sessa C et al. Docetaxel (taxotere) in advanced gastric cancer: results of a phase II clinical trial EORTC Early Clinical Trials Group. Br J Cancer 1994;70:380–3.
15. Hong YS, Song SY, Lee SI et al. A phase II trial of capecitabine in previously untreated patients with advanced and/or metastatic gastric cancer. Ann Oncol 2004;15:1344–7.
16. Coleman MP, Forman D, Bryant H, Butler J, Rachet B, Maringe C, et al. Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995–2007 (the International Cancer Benchmarking Partnership): an analysis of populationbased cancer registry data. The Lancet 2011;377(9760):127–38
17. Gridelli C, Perrone F, Gallo C et al. Chemotherapy for elderly patients with advanced non-small-cell lung cancer: the Multicenter Italian Lung Cancer in the Elderly Study (MILES) phase III randomized trial. J Natl Cancer Inst 2003;95:362–72.
18. 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.
19. Gaitonde SG, Fischer TD, Jones MS, Bandera B, Stern S, Goldfarb M. Young age, disparities, and survival in gastric adenocarcinoma: Implications for screening strategies. J Clin Oncol 2017;35(4_suppl):17.
20. Liang Y-X, Deng J-Y, Guo H-H, Ding X-W, Wang X-N, Wang B-G, et al Characteristics and prognosis of gastric cancer in patients aged ≥70 years. World J Gastroenterol 2013;19(39):6568–78.
21. Shahrokni A, Kim SJ, Bosl GJ, Korc-Grodzicki B. How we care for an older patient with cancer. J Oncol Practice 2017;13(2):95–102.
22. Extermann M, Hurria A. Comprehensive geriatric assessment for older patients with cancer. J Clin Oncol 2007;25(14):1824–31.
23. Chaibi P, Magne N, Breton S, Chebib A, Watson S, Duron JJ, et al. Influence of geriatric consultation with comprehensive geriatric assessment on final therapeutic decision in elderly cancer patients. Crit Rev Oncol/Hematol 2011;79(3):302–7.
24. Girre V, Falcou MC, Gisselbrecht M, Gridel G, Mosseri V, Bouleuc C, et al. Does a geriatric oncology consultation modify the cancer treatment plan for elderly patients? J Gerontol A Biol Sci Med Sci 2008;63(7):724–30.
25. Ohtsu A, Shimada Y, Shirao K et al. Randomized phase III trial of fluorouracil alone versus fluorouracil plus cisplatin versus uracil and tegafur plus mitomycin in patients with unresectable, advanced gastric cancer: the Japan Clinical Oncology Group Study (JCOG9205). J Clin Oncol 2003; 21: 54–9.
26. Kim NK, Park YS, Heo DS et al. A phase III randomized study of 5-fluorouracil and cisplatin versus 5-fluorouracil, doxorubicin, and mitomycin C versus 5-fluorouracil alone in the treatment of advanced gastric cancer. Cancer 1993;71:3813–8.
27. Hayashi Y, Nishida T, Tsutsui S, Ohta T, Yamaguchi S, Horimoto

M, et al. Efficacy of chemotherapy for older patients with gastric cancer: a multicenter retrospective cohort study. Int J Clin Oncol 2019;24(11):1377–1384.
28. Graziano F, Santini D, Testa E, Catalano V, Beretta GD, Mosconi S, et al. A phase II study of weekly cisplatin, 6S-stereoisomer leucovorin and fluorouracil as first-line chemotherapy for elderly patients with advanced gastric cancer. Br J Cancer 2003;89:1428–1432.
29. Maggiore RJ, Gross CP, Hurria A. Polypharmacy in older adults with cancer. Oncologist 2010;15:507–22.
30. Steinman M, Hanlon J. Managing medications in clinically complex elders: "There's got to be a happy medium". JAMA 2010;304:1592–601.
31. Scripture CD, Figg WD. Drug interactions in cancer therapy. Nat Rev Cancer 2006;6:546–58.
32. . Repetto L, Balducci L. A case for geriatric oncology. Lancet Oncol 2002;3:289–97.
33. Lichtman SM, Wildiers H, Chatelut E et al. International Society of Geriatric Oncology Chemotherapy Taskforce: evaluation of chemotherapy in older patients – an analysis of the medical literature. J Clin Oncol 2007;25:1832–43.
34. Catalano V, Bisonni R, Graziano F, Giordani P, Alessandroni P, Baldelli AM, et al. A phase II study of modified FOLFOX as first-line chemotherapy for metastatic gastric cancer in elderly patients with associated diseases. Gastric Cancer 2013;16(3):411–419.
35. Haghighi S, Kasbkar H, Esmaeilpour K, Yasaei M. Oxaliplatin, 5fluorouracil and leucovorin (FOLFOX4) as first line chemotherapy in elderly patients with advanced gastric cancer. Asian Pac J Cancer Prev 2016;17(7):3277–3280.
36. Muro K, Cho JY, Bodoky G, Goswami C, Chao Y, Dos Santos LV, et al. Age does not influence efficacy of ramucirumab in advanced gastric cancer: subgroup analyses of REGARD and RAINBOW. J Gastroenterol Hepatol 2018;33(4):814–824.
37. Sakin A, Şahis S, Sakin A, Aldemir MN, Bayram İ, Kotan Ç, The effect of obesity on response to neoadjuvant therapy in locally advanced gastric cancer Asian Pac J Cancer Prev 2020;21(9):2723-2731.