

Multidisciplinary management for esophageal and gastric cancer

Megan M Boniface¹
Sachin B Wani²
Tracey E Schefter³
Phillip J Koo⁴
Cheryl Meguid¹
Stephen Leong⁵
Jeffrey B Kaplan⁶
Lisa J Wingrove⁷
Martin D McCarter¹

¹Section of Surgical Oncology, Division of GI, Tumor and Endocrine Surgery, Department of Surgery,

²Division of Gastroenterology and Hepatology, Department of Therapeutic and Interventional Endoscopy, ³Department of Radiation Oncology, ⁴Division of Radiology-Nuclear Medicine, Department of Radiology, ⁵Division of Medical Oncology, ⁶Department of Pathology, University of Colorado Denver, ⁷Department of Food and Nutrition Services, University of Colorado Hospital Cancer Center, Aurora, CO, USA

Abstract: The management of esophageal and gastric cancer is complex and involves multiple specialists in an effort to optimize patient outcomes. Utilizing a multidisciplinary team approach starting from the initial staging evaluation ensures that all members are in agreement with the plan of care. Treatment selection for esophageal and gastric cancer often involves a combination of chemotherapy, radiation, surgery, and palliative interventions (endoscopic and surgical), and direct communication between specialists in these fields is needed to ensure appropriate clinical decision making. At the University of Colorado, the Esophageal and Gastric Multidisciplinary Clinic was created to bring together all experts involved in treating these diseases at a weekly conference in order to provide patients with coordinated, individualized, and patient-centered care. This review details the essential elements and benefits of building a multidisciplinary program focused on treating esophageal and gastric cancer patients.

Keywords: tumor board, upper gastrointestinal malignancies, patient centered

Introduction

In 2015, the National Cancer Institute estimates that 16,980 new diagnoses of esophageal cancer and 24,590 new diagnoses of gastric cancer will occur in the US. Together these cancers account for ~3% of all new cancer cases.^{1,2} Although there have been notable improvements in survival over the past 35 years, overall 5-year survival rates still hover ~20% for esophageal cancer and 30% for gastric cancer.^{1,2} Unfortunately, ~50% of patients present with unresectable or locally advanced disease at the time of diagnosis.^{1,2} These sobering facts have inspired efforts for more individualized and aggressive treatment in order to improve long-term outcomes. Consequently, treatment of these diseases has evolved to use a multispecialty approach.^{3,4}

Accurate diagnosis, staging, and treatment for esophageal and gastric cancer requires a team of specialists including gastroenterologists, pathologists, radiologists, oncologists, radiation oncologists, surgeons, and robust support services, including registered dietitians and social workers. Traditionally, this has been a fragmented approach where the patient is seen separately by each specialist over several appointments at different office locations, often contributing to treatment delays and uncoordinated care. In addition to the untimely and inconvenient manner of this process, a lack of timely and accurate communication between specialists often frustrates patients and providers, resulting in suboptimal care.

The implementation of multidisciplinary cancer clinics has become increasingly more common in other disease processes such as pancreas, breast, and head and neck

Correspondence: Megan M Boniface
University of Colorado, 1665 Aurora
Court, Anschutz Cancer Pavilion
Room 5330, Aurora, CO 80045, USA
Tel +1 720 848 0405
Fax +1 720 848 5245
Email megan.boniface@ucdenver.edu



malignancies. While change in management associated with improved outcomes has been documented for patients treated at breast and pancreas multidisciplinary clinics, there is a paucity of data for esophageal and gastric cancer. Several studies have documented change in clinical decision for upper gastrointestinal (GI) malignancies discussed in a tumor board setting, but there is a lack of data examining patients with esophageal and gastric cancer formally seen and treated at a multidisciplinary clinic.^{5,6}

In August 2013, the Esophageal and Gastric Multidisciplinary Clinic (EGMDC) at the University of Colorado Hospital (UCH) was established to bring together the above-mentioned specialists who treat these cancers and create a patient-centered experience. The goal is to provide patients a one-stop comprehensive evaluation, including all of the necessary diagnostic imaging and/or procedures and have an individualized treatment plan in place by the end of the visit. The multidisciplinary clinic affords patients an expedited, coordinated approach and provides the highest level of comprehensive care. The purpose of this manuscript is to describe the essential elements of developing a multidisciplinary team and program to treat esophageal and gastric cancer.

The multidisciplinary model

Overview

The EGMDC team at UCH consists of surgical oncologists, thoracic surgeons, medical oncologists, radiation oncologists, gastroenterologists, radiologists, pathologists, otolaryngologists, a physician assistant, registered dietitians, speech and swallow pathologists, and social workers. It is a weekly clinic that runs over a 2-day period. On day 1, patients undergo history and physical examination with the clinic coordinator followed by completion of necessary radiographic imaging, endoscopic procedures, and laboratory studies. On day 2, the multidisciplinary conference is held early in the morning during which each patient's case is individually presented with imaging and pathology review. The multidisciplinary team discusses and decides on treatment recommendations for each patient. Immediately following the conference, patients meet with the specialists who will be involved in their care to discuss results from the conference and their personalized management plan.

The clinic structure

Intake and staging

A full-time advanced practice provider (APP) is the coordinator and main contact for the program. Referring providers and patients speak directly with the APP who is

able to appropriately triage the patient. Outside medical records, imaging and pathology slides are obtained for internal review (prior to and during the conference). If a patient is deemed more suitable for another clinic (eg, medical oncology), they are triaged to the oncology nurse navigator to schedule as appropriate. For patients who would benefit from a multidisciplinary evaluation, outside studies are reviewed by the experienced APP who determines what additional work-up will be necessary to complete each patient's staging evaluation. The coordinator communicates these needs and the reasoning for each test to the patient, and an email or letter is sent to them with the relevant details.

Prognosis for esophageal and gastric cancer is strongly associated with the tumor stage. Following initial diagnosis using upper endoscopy and tissue biopsy, radiographic imaging and endoscopic ultrasonography (EUS) are used to designate patients into T (tumor), N (nodal), and M (metastasis) categories following the American Joint Committee on Cancer staging criteria.^{7,8} Treatment selection is based on these TNM classifications and again highlights the importance of accurate results. In concordance with National Comprehensive Cancer Network (NCCN) guidelines, computed tomography (CT) of the chest, abdomen, and pelvis is done first to assess the extent of locoregional disease and to evaluate for distant metastasis.^{9,10} If CT is negative or equivocal for metastatic disease, positron emission tomography–computed tomography (PET/CT) with fluorodeoxyglucose (FDG) is often used as a more sensitive tool in detecting stage IV disease in addition to assessing malignant involvement of any lymphadenopathy detected on CT.^{7,11,12} Newly diagnosed patients without previous outside imaging typically receive a CT scan during their EGMDC evaluation, which provides physicians with essential staging information to make informed treatment recommendations. Those patients who are felt to benefit from further imaging with FDG PET/CT after their initial evaluation are scheduled in a timely fashion under the coordination and guidance by the APP.

Following NCCN guidelines, patients without evidence of metastatic disease undergo EUS, which provides detailed images of the primary tumor and its relationship within the walls of the esophagus or stomach. This also allows for assessment of regional lymph node involvement and otherwise clinically occult metastatic disease (eg, liver lesions and ascites), which can be sampled using fine needle aspiration.^{9,10} EUS has been found to be the most reliable technique for assessing tumor depth (T-stage) with an accuracy of 80%–90% and is vital in guiding treatment decisions.^{12,13}

Receipt of EUS has been associated with improved survival for patients with esophageal cancer, likely related to accurate staging and thus appropriate treatment.¹⁴ The accurate assessment of submucosal invasion is pivotal in those with early (T1) disease by discerning which patients may be candidates for endoscopic mucosal resection.¹²⁻¹⁴

Through collaboration with our radiology and gastroenterology colleagues, our clinic has three dedicated imaging and endoscopic time slots each week for both imaging and EUS. The established relationship within these departments allows for priority scheduling if additional tests are needed. This allows our patients expedited access to complete and thorough staging that could otherwise take multiple visits spread out over days or weeks. In addition, the radiologists and gastroenterologists who perform and interpret these examinations are then present at the conference to discuss the findings and have an open dialogue with the other members of the team.

The multidisciplinary conference structure

An hour-long conference is held on the morning of day 2 for each weekly EGMD. The multidisciplinary conference is held weekly to ensure that patients are seen in a timely manner from the time of the first contact by the patient or referring physician. The conference room is set up with a picture archive and viewing system, microscope, and air-media capabilities, which enable direct viewing for meeting attendees on large display screens. Conference capabilities include video and audio access with our colleagues off location, allowing for collaboration with remote members of our team. Tables are arranged into a U-shaped configuration around the room in order to facilitate open dialogue with fellow attendees.

In order to reduce the burden on any one individual and provide opportunities for multiple specialists to participate, there is a rotating physician schedule for each specialty to delineate which providers will staff the clinic each week. However, all providers are invited to participate weekly. All team members are emailed a handout created by the clinic coordinator the day before the conference, which provides pertinent information for each patient including demographics, medical history, and test results. Distributing the handout for review prior to conference allows for review and individual preparation of imaging, slides, and endoscopic images in order to improve workflow during conference. Handouts are also provided upon arrival to the conference for all attendees.

The multidisciplinary conference is led by the APP who is intimately aware of any extenuating circumstances and presents each patient's case to the team. Imaging, pathology slides, and endoscopic images are then reviewed by the respective specialists. Having the results of diagnostic tests reviewed by the specialist helps minimize any misinterpretation that may occur otherwise. Treatment recommendations are then discussed in a collaborative group setting. Participation in clinical trials is an important mission of our academic medical center, and this comprehensive review allows for a rapid and efficient determination of trial eligibility. Once a consensus is reached, the treatment plan is summarized by the coordinator who reviews which specialists will be seeing the patient that day. Appointments are created in the scheduling system for each provider by an Intake and Access Coordinator who attends conference and serves as the APPs main programmatic support. Patients return to the same clinic space on the morning of day 2 and are seen immediately following conference by the previously specified physicians and support services where recommendations for treatment are discussed in detail.

Treatment decisions

Multimodality therapy has become the foundation for treatment for the majority of patients with esophageal and gastric cancer. Tumors are classified as esophageal or gastric cancer depending upon their location in reference to the esophago-gastric junction (EGJ). Following the latest TNM staging manual, tumors arising at the EGJ or in the stomach within 5 cm of the EGJ extending into the EGJ or esophagus are staged as esophageal tumors. Tumors arising within 5 cm of the EGJ but without extension into the EGJ or esophagus are staged as gastric cancers.⁷

Esophageal cancer

For patients who have early esophageal tumors with disease limited to the mucosa (T1a), endoscopic eradication therapy is recommended given comparable outcomes between endoscopic and surgical therapies.¹⁵ Endoscopic eradication therapy involves endoscopic resection of the area that harbors neoplasia followed by ablation of remaining Barrett's segment to reduce the risk of metachronous cancer.¹⁵ The resection specimen can then provide a more accurate assessment of depth of invasion and need for additional therapy. Patients with tumors that invade deeper through the muscularis mucosa into the submucosa and no lymph node involvement (T1bN0) are candidates for esophagectomy secondary to the risk of subclinical lymph node metastases.¹⁶⁻²⁰

For the small subset of patients who present with clinical stage T2N0 esophageal cancer, we tend to follow NCCN guidelines and prefer initial chemoradiotherapy followed by surgical resection, although treatment in this particular population is disputable. Our recommendation stems from inaccuracies in preoperative staging with one study citing ~49% of patients who underwent initial surgery as understaged by EUS.^{10,21} The majority of patients present with disease that extends through the submucosa with nodal involvement (T2N1 or higher) and are treated with a combination of chemotherapy, radiation, and surgery to provide the best chance for cure.⁴ At UCH, esophagectomies are performed utilizing a two surgeon team to combine the expertise of the surgical oncologist and thoracic surgeon for this complex operation.

Unfortunately, as previously mentioned, the majority of patients present with incurable disease (locally advanced unresectable, metastatic, or poor surgical candidates), and the goal of treatment is to palliate symptoms and prolong survival.^{1,22} Optimal care in this subset of patients also involves a multidisciplinary approach utilizing chemotherapy, radiation therapy, and endoscopic interventions such as esophageal stents/dilations, feeding tubes, and palliative surgery.^{17,22}

Gastric cancer

Similar to early esophageal tumors, patients with gastric cancer limited to the mucosa without evidence of nodal involvement (T1N0) may be amenable to endoscopic resection. Those patients with mucosal disease but findings consistent with lymph node metastases (T1N1 or higher) are considered for neoadjuvant therapy and surgery.²³ Expert pathologic review is critical in making the best treatment decision.

Perioperative chemotherapy is recommended for patients with T2 disease or higher without evidence of distant metastatic disease. This approach utilizes neoadjuvant chemotherapy, which allows for the assessment of tumor biology and response. In rare cases, the tumor is found to be metastatic upon reimaging. Patients without metastatic disease after preoperative treatment are taken for surgical resection by a surgical oncologist, which is generally followed by adjuvant chemotherapy.³

Individuals with distant metastatic disease, invasion of major vasculature, or distant lymph nodes are typically unresectable. Mainstays of treatment are symptom palliation and perhaps some prolongation of survival. Here a multimodality approach is often beneficial since surgical, endoscopic, or radiation therapies may be used for symptom control in

addition to systemic chemotherapy.²⁴ The palliative care team is available for both esophageal and gastric cancer patients seen in the EGMDC upon request.

Outcomes of the treatment conference

Changes in recommended therapy

Appropriate treatment selection relies on the accuracy of the initial staging, thus why a comprehensive multidisciplinary evaluation is essential in arriving at the best treatment decision for the patient. The active involvement of radiologists, gastroenterologists, and pathologists at each conference allows for direct communication with the treating physicians to discuss findings. Review of outside pathology specimens by our expert GI pathologists often results in a change or refinement in diagnosis. Precise pathologic review can have a major impact on patient care. For example, pathologic over-read may differentiate a patient eligible for a less invasive endoscopic resection versus a surgical esophagectomy. Interventional gastroenterologists with expertise in endoscopic resection allow patients access to experienced noninvasive treatment techniques.

Patients with locoregional disease who undergo neoadjuvant therapy are brought back to the multidisciplinary clinic for their restaging evaluation. This is typically 4 weeks following the completion of their upfront treatment to assess response with CT or FDG PET/CT. The multidisciplinary model allows for coordination of imaging along with clinical assessment in this collaborative setting. For instance, some patients may benefit from another intervention such as feeding tube placement for profound weight loss in order to optimize nutrition status prior to surgery. Another example would be those patients who are found to have metastatic disease upon reimaging thus avoiding an unnecessary operation and shifting care to a palliative approach.

Global benefits for patients and providers

The multidisciplinary model offers many advantages for patients with esophageal and gastric cancer. A dedicated APP as the main contact for the clinic gives patients direct access to an experienced provider who is able to appropriately guide their care and navigate the complex health care system. At UCH, we are fortunate to have five GI multidisciplinary clinics, which are all run by a dedicated APP with a corresponding lead physician for each clinic. The APPs are able to provide cross-coverage for one another when needed to ensure patients are continuously provided with the highest level of care.

The APP reviews outside records ahead of time to determine what additional testing will be necessary with their visit, allowing patients to leave with a personalized treatment plan. Instead of multiple visits and appointments that would typically be necessary for staging and treatment recommendations, this is accomplished in a 2-day period. Understanding the anxiety associated with a new cancer diagnosis, the goal of the EGMDC is to schedule patients for the upcoming clinic (eg, the following Wednesday–Thursday). This means patients are potentially scheduled as quickly as 1–2 days from the time of the initial referral. We have dedicated Intake and Access Coordinators who are trained to assist with expeditious record and data acquisitions. The established relationship with gastroenterology and radiology enables expedited access for our patients to undergo necessary imaging and procedures to complete staging. The average time between referral and EGMDC visit is <1 week.

A single visit approach is especially advantageous for patients who live remotely. By bringing together the specialists who treat these cancers, the treatment plan for each patient is determined with input from each discipline and eliminates any variance that may otherwise stem from separate visits. This reduces frustration for both patients and providers. Furthermore, if the patient's stage or condition changes during or after treatment, there is a team in place with knowledge of the patient who are ready to assume care as needed. This facilitates ongoing care and reduces the need to establish with a new provider every time their condition changes.

Providers who refer to the multidisciplinary clinic appreciate the prompt evaluation of their patients and close follow-up to discuss treatment recommendations. Since many patients live remotely, care that can be provided closer to home is encouraged when appropriate. The APP helps to facilitate and coordinate management to ease the burden on the patient and referring provider. Patients are able to receive chemotherapy closer to home and then return to the EGMDC when needed for more specialized care such as endoscopic resection or surgery.

The multidisciplinary model also has many benefits for the physicians who treat patients with esophageal and gastric cancer. Having a dedicated APP to order and coordinate appropriate testing and perform a detailed history and physical examination ahead of time provides physicians with the clinical information necessary to make treatment decisions. This significantly minimizes the time physicians would spend reviewing records, ordering tests, and waiting

on results. In addition, esophageal and gastric cancer patients frequently present with dysphagia, early satiety, or difficulty eating often associated with substantial weight loss. Upfront knowledge of these findings is important as it allows for group discussion of additional interventions that may be required or may even become the first step in treatment. Metastatic or unresectable patients also benefit from a multidisciplinary approach as it facilitates clinical trial eligibility and offers patients and providers access to resources for symptom palliation including radiation therapy and stent or feeding tube placement.

Team approach and the opportunities for quality improvement and research

The EGMDC forms the nucleus for quality improvement and research for esophageal and gastric cancer at our center. We are able to offer patients access to clinical trials, and weekly conferences are attended by clinical trial coordinators to ensure optimal enrollment for eligible patients. In November 2014, our team implemented a Comprehensive Unit-Based Safety Program for our inpatient esophagectomy patients. The main goal of this program is to examine opportunities for improvement in patient safety and outcomes during hospitalization. The concept is to include all providers and staff involved in treating post-esophagectomy patients. Following the example and success of this program, in early 2015 our outpatient team developed a quality improvement initiative intended for our preoperative patients aimed at improving the overall status of those patients presenting for esophagectomy. In addition, our team is actively involved in a multicenter study evaluating outcomes related to endoscopic eradication therapies in patients with Barrett's esophagus-related neoplasia.

Creating a multidisciplinary clinic specifically for patients with esophageal and gastric cancer facilitates data collection for research. Currently, we see an average of four patients per week in the EGMDC. Since inception we have seen substantial growth with a 23% increase in patients seen during our second year. Patients are consented for tissue collection and tumor banking. In addition, tracking these patients allows for assessment of clinic growth and changes in patient care secondary to the multidisciplinary evaluation. For example, for esophageal and gastric patients seen in our multidisciplinary clinic, we have seen a 19% change in diagnosis or therapeutic recommendation based on the collaboration of expert services our team is able to provide (eg, patients referred for surgical resection are able to undergo endoscopic resection). In addition, the collaborative approach

encourages greater standardization of care and adherence to evidence-based guidelines.

Conclusion

The complexity of treating esophageal and gastric cancer necessitates the need for a multimodality approach. In order to appropriately stage and treat these patients, multiple specialists are required including surgeons, medical oncologists, radiation oncologists, gastroenterologists, radiologists, pathologists, and support services. The EGMDC at the UCH brings together this group of experts and provides patients a comprehensive diagnostic evaluation and treatment plan within a 2-day period. The goal is to offer patients a well-coordinated and individualized treatment plan. This approach improves satisfaction for patients and the providers involved in the patient's care. Through the description of essential elements detailed here, we hope that our method of implementing a multidisciplinary clinic for esophageal and gastric cancer patients proves useful to others treating this complex population.

Disclosure

The authors report no conflicts of interest in this work.

References

1. NIH [webpage on the Internet]. SEER Cancer Statistics Review, 1975–2012. 2014. Available from: http://seer.cancer.gov/csr/1975_2012/. Accessed September 25, 2015.
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin*. 2015;65(1):5–29.
3. Cunningham D, Allum WH, Stenning SP, et al; MAGIC Trial Participants. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. *N Engl J Med*. 2006;355(1):11–20.
4. van Hagen P, Hulshof MC, van Lanschot JJ, et al; CROSS Group. Preoperative chemoradiotherapy for esophageal or junctional cancer. *N Engl J Med*. 2012;366(22):2074–2084.
5. Pawlik TM, Laheru D, Hruban RH, et al; Johns Hopkins Multidisciplinary Pancreas Clinic Team. Evaluating the impact of a single-day multidisciplinary clinic on the management of pancreatic cancer. *Ann Surg Oncol*. 2008;15(8):2081–2088.
6. van Hagen P, Spaander MC, van der Gaast A, et al; Rotterdam Oesophageal Tumour Study Group. Impact of a multidisciplinary tumour board meeting for upper-GI malignancies on clinical decision making: a prospective cohort study. *Int J Clin Oncol*. 2013;18(2):214–219.
7. Edge S, Byrd DR, Compton CC, et al. *AJCC Cancer Staging Manual*. 7th ed. New York: Springer; 2010.
8. Rice TW, Rusch VW, Ishwaran H, Blackstone EH; Worldwide Esophageal Cancer Collaboration. Cancer of the esophagus and esophagogastric junction: data-driven staging for the seventh edition of the American Joint Committee on Cancer/International Union Against Cancer Staging Manuals. *Cancer*. 2010;116(16):3763–3773.
9. National Comprehensive Cancer Network [webpage on the Internet]. NCCN Clinical Practice Guidelines in Oncology – Gastric Cancer (Version 3.2015). Available from: http://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed February 2, 2016.
10. National Comprehensive Cancer Network [webpage on the Internet]. NCCN Clinical Practice Guidelines in Oncology – Esophageal and Esophagogastric Junction Cancers (Version 3.2015). Available from: http://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf. Accessed February 2, 2016.
11. Chen J, Cheong JH, Yun MJ, et al. Improvement in preoperative staging of gastric adenocarcinoma with positron emission tomography. *Cancer*. 2005;103(11):2383–2390.
12. van Vliet EP, Heijnenbroek-Kal MH, Hunink MG, Kuipers EJ, Siersema PD. Staging investigations for oesophageal cancer: a meta-analysis. *Br J Cancer*. 2008;98(3):547–557.
13. Mocellin S, Pasquali S. Diagnostic accuracy of endoscopic ultrasonography (EUS) for the preoperative locoregional staging of primary gastric cancer. *Cochrane Database Syst Rev*. 2015;2:CD009944.
14. Wani S, Das A, Rastogi A, et al. Endoscopic ultrasonography in esophageal cancer leads to improved survival rates: results from a population-based study. *Cancer*. 2015;121(2):194–201.
15. Wani S, Drahos J, Cook MB, et al. Comparison of endoscopic therapies and surgical resection in patients with early esophageal cancer: a population-based study. *Gastrointest Endosc*. 2014;79(2):224–232. e221.
16. Barbour AP, Jones M, Brown I, et al. Risk stratification for early esophageal adenocarcinoma: analysis of lymphatic spread and prognostic factors. *Ann Surg Oncol*. 2010;17(9):2494–2502.
17. Coia LR, Soffen EM, Schultheiss TE, Martin EE, Hanks GE. Swallowing function in patients with esophageal cancer treated with concurrent radiation and chemotherapy. *Cancer*. 1993;71(2):281–286.
18. Merkow RP, Bilimoria KY, Keswani RN, et al. Treatment trends, risk of lymph node metastasis, and outcomes for localized esophageal cancer. *J Natl Cancer Inst*. 2014;106(7):dju133.
19. Merkow RP, Bilimoria KY, McCarter MD, Chow WB, Ko CY, Bentrem DJ. Use of multimodality neoadjuvant therapy for esophageal cancer in the United States: assessment of 987 hospitals. *Ann Surg Oncol*. 2012;19(2):357–364.
20. Sun F, Yuan P, Chen T, Hu J. Efficacy and complication of endoscopic submucosal dissection for superficial esophageal carcinoma: a systematic review and meta-analysis. *J Cardiothorac Surg*. 2014;9:78.
21. Hardacker TJ, Ceppa D, Okereke I, et al. Treatment of clinical T2N0M0 esophageal cancer. *Ann Surg Oncol*. 2014;21(12):3739–3743.
22. Harvey JA, Bessell JR, Beller E, et al. Chemoradiation therapy is effective for the palliative treatment of malignant dysphagia. *Dis Esophagus*. 2004;17(3):260–265.
23. Min YW, Min BH, Lee JH, Kim JJ. Endoscopic treatment for early gastric cancer. *World J Gastroenterol*. 2014;20(16):4566–4573.
24. 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(18):2903–2909.

Cancer Management and Research

Publish your work in this journal

Cancer Management and Research is an international, peer-reviewed open access journal focusing on cancer research and the optimal use of preventative and integrated treatment interventions to achieve improved outcomes, enhanced survival and quality of life for the cancer patient. The journal welcomes original research, clinical & epidemiological

Submit your manuscript here: <http://www.dovepress.com/cancer-management-and-research-journal>

studies, reviews & evaluations, guidelines, expert opinion & commentary, case reports & extended reports. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Dovepress