Project on

“Review article on present scenario & current treatment option of stomach cancer”

[In the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy]

Submitted To

The Department of Pharmacy,

Faculty of Allied Health Sciences,

Daffodil International University

Submitted By

Student ID: **191-29-238**

Department of Pharmacy

Faculty of Allied Health Sciences

Daffodil International University

……..

April 2023

APPROVAL

This Project, **'Present scenario & current treatment option of stomach cancer'**, submitted to the Department of Pharmacy, Daffodil International University, has been accepted as satisfactory for the partial fulfilment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.

BOARD OF EXAMINERS

Professor Dr. Muniruddin Ahamed Head of the Department

Head

Department of Pharmacy

Faculty of Allied Health

Science

Daffodil International

University

---------- Internal Examiner-1

---------- Internal Examiner-2

---------- External Examiner

Supervisor

……

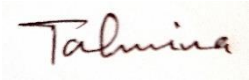
Ms Tahmina Afroz

Assistant Professor,Department of Pharmacy

DECLARATION

I hereby declare that this project report, **"Present scenario & current treatment option of stomach cancer".** I am declaring that this Project is my original work. I also declare that neither this project nor any part there of has been submitted elsewhere for the award of Bachelor or any degree.

Supervised By



…….

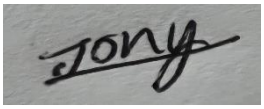
Ms. Tahmina Afroz

Assistant Professor

Department of Pharmacy

Faculty of Allied Health Science

Submitted By



……

Mohammad Shakil Jony

ID: 191-29-238

Department of Pharmacy

Faculty of Allied Health Sciences

Daffodil International University

Abstract

The fourth most prevalent cause of cancer-related deaths globally right now is gastric cancer. In the western world, it is most frequently discovered in an advanced state, after it has spread to far-off regions. Patients with advanced cancer (locally developed or metastatic), who have a poor prognosis with a median overall mortality of 10–12 months, are treated primarily with palliative chemotherapy. When compared with chemotherapy alone as first-line therapy, new methods that suppress the human epidermal growth factor receptor 2 (HER2) have demonstrated appreciable improvements in advancement-free and overall mortality in patients with HER2 overexpression. This condition has entered the age of molecular and personalized medicine with the development of medications that target vascular endothelial growth factor/vascular endothelial growth factors receptor. Immune check point inhibitors, such as anti-programmed cell death protein advancement/programmed death-ligand 1, have demonstrated tentative but positive clinical effectiveness in the management of gastric cancer. The introduction of new therapies for this condition, as well as the creation of new drugs, will heavily depend on molecular identification of patients.

Keywords: Gastric cancer, Treatment, Molecular medicine, Immunotherapy

- # Contents

List of figures

Chapter 1
Introduction

1. Introduction

Gastric cancer, also known as stomach cancer, starts in the muscle of the abdomen. More than 90% of stomach tumors are adenocarcinomas, with the remaining 10% being lymphomas and gastrointestinal stromal tissue. (sarcomas). Belly cancer continues to be one of the main causes of cancer-related fatalities globally, despite a steady decrease in incidence over the past few decades. Additionally, there are significant geographic differences on a global level. (1). However, the root causes of these disparities are not well known. Additionally, it is unclear what is causing the overall found a reduction in prevalence. The distal belly's gastric tumors are specifically linked to this decline. The proportion of gastric cancers that impact the gastroesophageal junction and proximal stomach appears to be steadily rising. A change in prior events or related environmental danger factors is most likely to blame as the pathogenesis of proximal and distal belly most cancers appears to vary. A minimum of one group will benefit from something, but not another. Long-standing theories point to nutritional factors as the main contributors to the risk of developing stomach cancer. nevertheless, research into the significance of preserved foods, a lack of fruit consumption, and other dietary components has produced mixed findings, and dietary components can only partially explain the difference in belly cancer risk. Since 1994, the gastric bacteria Helicobacter pylori has been recognized as a specific carcinogen for the development of stomach cancer. (2). Recent research demonstrates that this agent's role is much more crucial than previously believed. Tumors pointing in the opposite direction of the stomach are no longer linked to H. pylori infection; only distal malignancies remain so. In addition, some extremely high H. pylori contamination communities have low rates of stomach cancer (3), indicating that additional factors are also crucial. Undoubtedly, over the past 20 years, significant progress has been made in shedding light on the risk factors for stomach cancer. Yet, in order to develop effective cancer prevention tactics, it is still necessary to have a deeper understanding of the causes behind this serious cancer. This is especially important because the impacted patients' assessments continue to be grim. (4). Globally, the incidence of stomach cancer has sharply declined over the past 50 years. Regardless of this, gastric cancer continues to be a global health concern given that it ranks fifth in terms of frequency of occurrence and accounts for 0.33 of all cancer-related fatalities [5]. However, East Asia, Latin America, Eastern

Europe, as well as certain populations within the United States, have disproportionately high rates of gastric cancer incidence and mortality. Economic growth brought about improvements in sanitation, hygiene, clean water sources, food preservation, diversity, and access, all of which reduced the incidence of gastric cancer. In areas where the disease is currently frequently occurring, both primary and secondary preventive measures have helped to reduce the mortality rate for stomach cancer. [6].

1.1 Stomach Cancer Subtypes

Ninety-nine percent of all GI tumors are gastric adenocarcinomas, with the remainder being lymphoma, leiomyosarcoma, gastrointestinal stromal tumors, and neuroendocrine tumors [7]. Gastric adenocarcinoma is frequently perceived as a single organization, but it actually has two anatomic subtypes, cardia gastric cancers and non-cardia gastric cancers (henceforth referred to as belly cancers), each with unique scientific and epidemiological features. Heart-related gastric cancers are adenocarcinomas of the proximal stomach that are within five cm of and impact the gastroesophageal junction [8]. Obesity, chronic gastroesophageal reflux, and possibly smoking is all associated with cardiac gastric tumors. The majority of Caucasian men in the United States do not find it strange. The scientific path and epidemiology of cardiac cancer are similar to those of esophageal adenocarcinoma [9] and it has a lower long-term mortality rate than no cardiac gastric cancer [10]. The incidence of cardiac gastric cancers has stayed constant or risen inside a few subgroups [11]. Tumors that stand up equally far from the coronary heart are referred to as non-cardia stomach cancers, and they are linked to helicobacter pylori contaminants, smoking, and a high-sodium diet [12–13]. Each article relates to H. pylori contamination, which over time causes mucosal irritation, is seen as mucosal atrophy, and ultimately results in intraepithelial and superior neoplasia. Mucosal atrophy and metaplasia, which are malignant tumors, are linked to gastric cancer. These are easily detectable and demonstrable endoscopically using histopathology. E-cadherin expression loss is particularly associated with diffuse-type gastric cancers. The majority of diffuse-type cancers are linked to atrophic gastritis, but no clear precancerous tumor has been found. Signet ring adenocarcinoma is a sort of diffuse-kind gastric most cancers this is additionally connected to non-H. pylori-related hereditary gastric most cancers. [12]

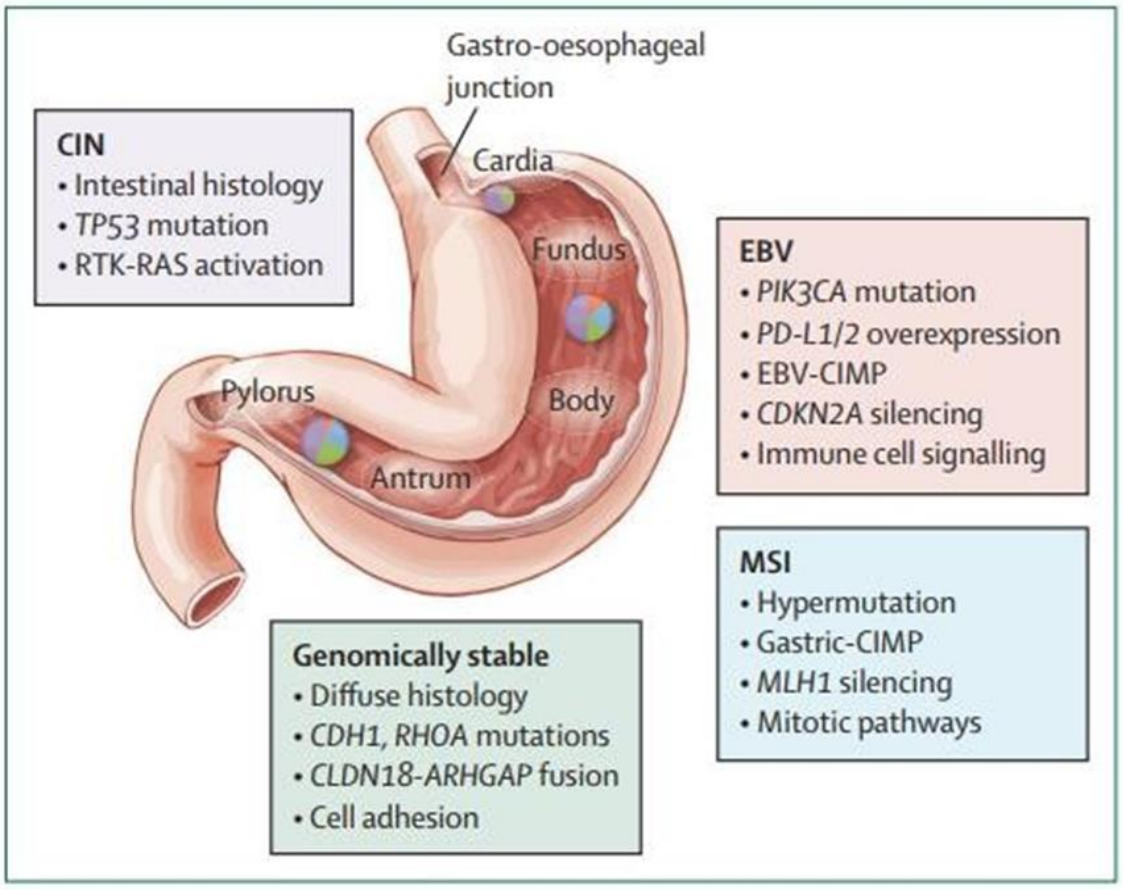


Figure 1: Molecular characterization of subtypes of gastric carcinomas [13]

1.2 Stomach Cancer Pathogenesis and Risk Factors

Most cases of stomach cancer are rare and associated with H. pylori infection. A class I carcinogen known as H. pylori is believed to be the cause of 89 percent of all cases of stomach cancer (at least 95 percent in evolution-incidence areas) [14, 15]. The virulence of H. pylori, modifications in the host's inflammatory response to infection, and specific environmental exposures all affect the chance of developing stomach cancer. stomach atrophy and stomach cancer have long been strongly associated [16]. The long-running investigation into the etiology of gastritis, which had long been connected to stomach atrophy and cancer, came to an end with the identification of H. pylori in 1983 and resulting confirmation that it was the main cause of the condition. H. pylori infections are most frequently contracted as children and can persist for a long time [17]. Dysplasia foci may develop within the grass of atrophic mucosa and progress into intrusive gastric neoplasia. There are much higher lifetime stomach cancer chances, which frequently exceed 10%, in

other countries like Japan, Korea, and some of China. The prevalence of and rate of development of atrophic gastritis are directly correlated with the likelihood of stomach cancer in a given nation or area [18]. The annual risk of developing stomach cancer increases to over 1% once atrophic gastritis has formed [19]. H. pylori infection is regarded as a required but insufficient cause of gastric cancer as there are other factors that can influence one's risk as well. In India and other tropical countries, for instance. The incidence of gastric cancer between men and females is 62 to 69/100,000 and 26/100,000 in Japan and China, accordingly, where H. pylori prevalence is equally high [20]. Although H. pylori virulence and the body's reaction to infection affect gastric cancer risk [12], nutrition is the most crucial environmental component [21]. Many studies have been conducted in an effort to identify the H. pylori virulence factors that increase the chance of gastric cancer. None have been reported, and the data points to the fact that all of the H. pylori virulence factors connected to gastric cancer share the same characteristic of raising the risk of gastric cancer [22]. The two H. pylori virulence factors that are most frequently identified are the vacuolating cytotoxin Vacca and the cytotoxin-associated protein Caged. The creation of stomach cancer and peptic ulcers has been related to H. pylori strains of all virulences; having one of the most virulent strains nearly doubles the risk [23]. Gastric cancer risk has been related to host factors associated with an augmented inflammatory reaction following infection. One illustration is the pro-inflammatory interleukin (IL)-1. While some IL-1 genotypes are associated with more inflammation and a higher chance of gastric cancer, others are not [23]. For instance, a pro-inflammatory IL-1 infection with a virulent H. pylori strain has been associated with an 87-fold greater probability of stomach cancer [24].

1.3 Etiology of stomach cancer

Inborn verbose gastric cancer accounts for 1% to 3% of cases of stomach cancer. In about 30% of hereditary gastric cancers, a germline mutation in one allele of the E-cadherin gene (CDH1) is discovered. [25] Through mutagenesis or hyper methylation, the second locus is rendered inactive. [26] Early genetic changes lead to diffuse stomach cancer development. Male carriers of the CDH1 gene had a lifetime risk of 67 percent gastric cancer and female carriers a lifetime risk of 83 percent. In families where at least two members have diffuse gastric cancer and one of those cases was discovered prior to the age

of 50, advancement analysis is recommended. [27] Protective gastrectomy remains that underwent histopathological analysis showed microscopic foci of signet ring cell invasion and development that were macroscopically undetectable. Mutation holders should think about prophylactic gastrectomy even though the clinical relevance of such foci is unclear. Two additional genetic disorders that raise the chance of gastric cancer are Lynch syndrome and Peutz-Jeghers syndrome (mutations in one of the mismatch repair genes) [28]. (STK11 mutation). [29] The precursor lesions (figure 1) [30] of the intestinal form of sporadic stomach cancer are brought on by H. pylori infection. [31-38]

1.4 Histopathology and molecular pathology

Most gastrointestinal cancers are well to poorly separated. On the other hand, solitary or tiny clusters of tumor cells without glandular structures characterize diffuse-type adenocarcinomas. On certain occasions, clear intracellular vacuoles can be seen. These advancement-producing cells have their nuclei moved to the cell periphery. (signet-ring-cell carcinoma). It can be difficult to distinguish specific tumor cells in typical hematoxylin and eosin sections because there is typically a lot of freshly produced stroma. Additional keratin labeling reveals the tumor's true size. Gastric cancer develops as a consequence of accumulating genetic damage that compromises essential cellular function [39] These changes could be caused by chromosomal fragility or microsatellite instability, two different kinds of genomic instability. As a new method of damaging DNA, the cag-pathogenicity-island-methylated phenotype has been identified. (CIMP) [40]. There are at present no such biomarkers accessible, despite the fact that understanding those pathways, likewise with the Tumor-Inhibiting genes and cancer genes that contribute to malignancy, has been proposed to be a way to find new therapeutic targets or forecast therapy reaction. About 15% of stomach carcinomas are attributed to a dysfunctional mismatch repair mechanism. [41] Base pair mismatches, which happen when a base is included or deleted through cell replication, are detected by this process. A collection of mismatch repair proteins, such as MLH1, MSH2, MSH6, and PMS2, eliminates the mismatched lesion and development the DNA prior the cell cycle is finished. The MLH1 protein silence caused by promoter hypermethylation is the most frequent factor in microsatellite instability in sporadic stomach cancer. [42] This leads to a higher change rate at the nucleotide level. Mutations cause oncogenes to become active, tumor suppressor genes to become inactive,

or both, giving cells an advantage in growth and intrusiveness. Microsatellite instability has been associated with clinical and pathological traits like intestinal cancer, antral location, fewer lymph node metastases, and extended life. [43] Although it has been extensively studied in colorectal cancer, it is unclear whether microsatellite instability plays a role in the tumor reaction to the fluorouracil. [44] The relationship among chemotherapy reaction and microsatellite instability in gastric cancer was only briefly examined in one advancement but the sample size was too small to make any definitive inferences [45] By complementary genomic hybridization, gains on chromosomes 3q, 7q, 8q, 13q, 17q, and 20q as well as declines on chromosomes 4q, 5q, 6p, 9p, 17p, and 18q are the numbers abnormalities that are most frequently found in cases of gastric cancer. Consistent high-level amplifications are present on chromosomes 7q, 8p, 8q, 17q, 19q, and 20q. [46] Clinically significant traits like tumor type, tumor growth, and lymph node spread have all been connected to specific chromosomal abnormalities. Several studies connect high-level chromosomal instability to a positive outcome from chemotherapy based on cisplatin and a poor outlook. [47] advancement-resolution array comparison genomic hybridization has advanced, but the exact genes involved in oncogenesis are still unidentified [48]. CIMP might represent a novel form of genetic instability. [49] Improved methylation may be an attractive approach for researching carcinogenesis since hyper methylation of gene promoters results in gene silencing. Since DNA methyltransferase antagonists can reverse methylation, reactivating genes, the presence of hyper methylation of significant genes may be therapeutically pertinent irrespective of whether CIMP is a distinct pathway in gastric carcinogenesis [50].

Chapter 2
Purpose of the study

2.1 Purpose of the study

Gastric cancer, also known as stomach cancer, is a cell development that begins in the stomach. The purposes of this review mentioned following points:

- The goals of this project are to get a comprehensive thoughtful of the medical problem being researched.
- To learn more about the variables that subsidize to the development of **stomach cancer** infection.
- To have a better grasp of the many diagnostic measures used to detect this ailment.
- To gain a systematic considerate of the bug, as well as its cause, signs and symptoms, consequences, and medical and nursing administration selections.
- The determination of this investigation was to identify more about **stomach cancer** infection in the world.
- Designate the epidemiology of **stomach cancer** infection.
- Review the demonstration of a patient sick with **stomach cancer** infection.
- To discovery out permitted beneficial practice for **stomach cancer** infection.
- Recapitulate the role of the inter-professional healthcare team in **stomach cancer** infection illness preclusion and control events.

Chapter 3
Methodology

3.1 Materials and Procedures

The methods employed in this investigation are discussed in this chapter. It is a explanation of the study environment. The study population, the study sample, the research equipment, the technique, and the data analysis are all factors to contemplate.

3.2 Research Methodology

This is a summary of prior studies on different clinical trials as a **stomach cancer** disease treatment.

3.3 Inclusion and Exclusion Criteria

All studies on Drug candidates in clinical trials for **stomach cancer** disease.

3.4 Data Collection Procedure

Data was gathered directly from prior study articles, while another portion was gathered through searching the internet for relevant information. The actions of many treatments were recorded.

Chapter 4
Results & Discussion

4.1 Association of Helicobacter pylori infection and gastric carcinoma

The second most prevalent cancer worldwide, gastric carcinoma, affects individuals all over the world. H. pylori remains the main pathogen producing a broad variety of gastro-duodenal diseases, based on numerous studies. [51] Epidemiological data show that stomach cancer incidence is increased by H. pylori infection. In a Bangladeshi community, the investigators looked to see if there was any correlation between H. pylori infection and stomach cancer. 151 people were engaged in this study overall. 101 people with different gastro-duodenal diseases served as the controls, while 50 patients with gastric carcinoma served as the cases. Males made up 74 (75.3%) of the 101 controls and 36 (72.0%) of the 50 cases. In cases and controls, the masculine to female ratios were 1:0.39 and 1:0.36, correspondingly. For H. pylori infection, sera from 40 of 50 cases (80.0%) and 62 of 101 controls (61.4%) were found to be positive. Both groups participating in the study had different levels of H. pylori infection, which was statistically significant (OR=2.516, p0.05). The results of this research suggest that stomach cancer and H. pylori infection may be related. [52]

4.2 Risk Factors of Stomach Cancer Bangladesh Perspective

In total, 300 people (in Bangladesh) were included in this research; half were in the case group and half were in the control group. Among the participants, males between the ages of 30 and 49 make up the largest percentage. Two charts are used to depict the entire analytical process in this instance, one of which contains a frequency distribution with P-value and the other of which consists the probability distribution with P-value. Major variables and the odds ratio have a relationship that has an interval of confidence. shows the frequency breakdown of patients with stomach cancer (case and control groups) with substantial variation in risk factors. Age (P0.001), BMI (P0.001), Education Level (P0.001), Working Status (P0.001), Monthly Income (P0.001), Family Person (P0.001), Blood Group (P0.001), Daily Food in Time (P0.001), Take Spicy and Salted Food (P0.001), and Take Green Vegetables (P0.001) are all factors that should be taken into consideration. (P0.001). The odds ratio (OR) test results, which assess different groups, have a 95% confidence interval. (CI). There are statistically significant associations between stomach cancer and the following factors: gender, body mass index (BMI), living area, level of education, monthly income, blood group, regular exercise, intake of spicy

and salty foods, excessive illness, skin color, previous stomach surgery, tarry stools, and menetrier disease. When it comes to gastric cancer, gender matters a lot. The odds ratio for guys who responded is 1.812, which indicates that men are 1.812 times more likely to experience stomach cancer than women. With a chance that is 139.462 times higher than that of those who have never had stomach cancer, "Skin Color" is a highly serious danger factor for stomach cancer. Similar results are found for the factors "Abdominal Pain," Naturally, an individual's capacity to fend off illness diminishes as they age [53]. However, people who are getting older often have one or more serious illnesses, like stomach cancer.

4.3 FIRST-LINE MANAGEMENT

Before beginning any systemic therapy for GC, the human epidermal evolution factor receptor 2 (HER2) status is confirmed. The management options for the 20% of patients with HER2-positive GC are enclosed in the part on beleaguered healing. The subsequent part goes over the numerous therapeutic options available to patients with HER2-negative GC. Chemotherapy is typically used as the first-line treatment for patients who have advanced GC and a good performance level. Results from controlled experimental judgments showed that palliative chemotherapy was statistically superior to best supportive care (BSC) in terms of symptom relief and better persistence for patients who had innovative GC [54]. Contrarily, the benefit of combination chemotherapy is considerably lower than that of single-agent chemotherapy: According to a meta-analysis from 2010, combination chemotherapy improved mortality over single-agent therapy by about 1.5 months. It's important to note that the "older" combination chemotherapy strategies utilized in this research (combinations of 5-FU and anthracyclines) may not have had the best efficacy [55].

4.4 Platinum derivatives - alternatives to cisplatin

Several recent studies investigated the possibility of substituting oxaliplatin for cisplatin in GC. The use of cisplatin-free regimens is an increasingly practical therapeutic strategy because it eliminates the need for excessive hydration and lowers the possibility of renal and ototoxicity from the drug, but at the expense of increased neurotoxicity. In the treatment of advanced GC, oxaliplatin was found to be comparable to cisplatin in two phase III studies and non-inferior in a third. In a controlled phase III study conducted in Japan,

the normal SP regimen (S-1 40 mg/m2 twice daily on days 1–21 and cisplatin 60 mg/m2 on day 8 for 5 weeks) was contrasted with SOX (S-1 40 mg/m2 twice daily on days 1–14 and oxaliplatin 100 mg/m2 on day 1 for 3 weeks). The study, which recruited 685 patients in total, achieved its main objective of showing SOX's non-inferiority in PFS. Patients receiving SP experienced more serious adverse effects than anticipated. (29.3 percent vs 37.9 percent). Additionally, in patients receiving SP medication, the incidence of therapy-related fatalities was twice as high (2.4 percent vs. 1.2 percent) [60]. Al-Batran et al. [61] contrasted oxaliplatin (FLO) or cisplatin with biweekly infusional fluorouracil and leucovorin. (FLP). the enhanced in this research, the tolerability of oxaliplatin was confirmed. Although there were no appreciable variations in the median OS (10.7 vs. 8.8 months) among the two groups, there was a tendency for the FLO patients to have longer PFS. Patients treated with oxaliplatin experienced fewer thromboembolic events than those treated with cisplatin (7.6% vs. 15%), in addition to the anticipated variations in toxicities among the two drugs [62]. A different approach platinum compound option that has been researched in several controlled trials is irinotecan. 2008 saw the presentation of the results of a phase III study that contrasted irinotecan/5-FU and cisplatin/5-FU by Dank et al [63]. even though the irinotecan/5-FU combination did not shorten the time to progression, it was better accepted, with a lower percentage of patients stopping their therapy due to toxicity (10% vs. 22%). This conclusion has been supported by additional randomized phase II studies [64]. Both oxaliplatin and irinotecan work well in place of cisplatin when combined with Fluoropyrimidines.

4.5 Role of Taxane in Gastric cancer

In the V-325 study, which was written up by Van Cutsem et al [64], cisplatin/5-FU with or without docetaxel was administered to 445 patients. Docetaxel was added, which improved the RR (37 percent vs 25 percent), time to progression (5.6 mo vs 3.7 mo), and 2-year OS rate (18 percent vs 9 percent), but the absolute advantage in terms of mortality was less than 4 weeks and was countered by a significant rise in grade 3–4 adverse events. As a result of the significant toxicities connected with this advancement especially in the elderly population, multiple advancement"modified DCF" regimens have been developed. A prime instance of a therapy plan that is performed every two cycles is FLOT (docetaxel 50

mg/m2, infusional 5-FU 2600 mg/m2, leucovorin 200 mg/m2, and oxaliplatin 85 mg/m2). Al-Batran et al [65] performed a controlled phase II study (n = 143) to determine whether supplementing the FLO combo with docetaxel is practical for healthy patients over the age of 65. There were no distinctions between the two groups in terms of serious side effects, toxicity-related removal, or evolution-related deaths, but the FLOT group experienced substantially more grade 1-4 adverse events, such as neutropenia, alopecia, and diarrhea [66]. Thus, in the selected healthy older patients, the FLOT regimen was found to be effective. In contrast, patients receiving FLOT had lower standards of life than those receiving FLO.

4.6 Agents targeting HER2

The human epidermal growth factors receptor is expressed in up to 30% of gastric tumors that are in an advanced phase. The expression of HER2 (also called ERBB2) gets amplified or excessive. When used in conjunction with fluoropyrimidine/platinum chemotherapy, the monoclonal antibody trastuzumab, which targets HER2, raised the median overall survival, or OS, of patients with HER2-positive gastric or GEJ cancer from 11.1 months (95 percent confidence interval [CI] 10-13 months to 13.8 months (95 percent CI 12-16 months) after initial therapy [68]. Since then, the new preferred treatment for HER2-positive metastatic gastric or GEJ cancer patients is trastuzumab combined with chemotherapy. nevertheless, there was no substantial improvement in OS in gastric cancer patients with HER2 amplification as identified by fluorescence in situ hybridization (FISH) when lapatinib, a small-molecule tyrosine kinase inhibitor (TKI) targeting HER2 and epithelial growth factor receptor (EGFR), was administered in combination with either primary (LOGiC) or second-line (TyTan) chemotherapies [69]. Trastuzumab and lapatinib trials used different patient selection parameters, which could be a contributing factor. Patients who obtained lapatinib in the TyTAN trial and whose tumors tested positive for HER2 by FISH or strongly positive (+++) by immunohistochemical (IHC) staining had a longer OS (hazard ratio [HR] 0.59, P = 0.0176), emphasizing the significance of evaluating the expression of proteins in addition to gene copy number in order to identify patients who are most likely to reap the rewards from HER2-targeting drugs [70]. Similar to the development of options for treatment for HER2-positive breast cancer, suitable synergistic combinations will likely be offered to HER2-positive gastric cancer in order to further improve therapy efficacy.

The phase III JACOB study is testing trastuzumab/first-line chemotherapy with or without pertuzumab, an anti-HER2 antibody with a different binding domain than trastuzumab that prevents HER2 dimerization with other HER family receptors. Trastuzumab emtansine (an antibody-drug combination composed of trastuzumab coupled to the cytotoxic chemical DM1) is compared to standard taxane medicine as second-line therapy in the GATSBY study. Additionally, phase II development is currently testing afatinib and other second-generation irreversible kinase inhibitors in patients with GEJ cancer who are trastuzumab-refractory and HER2-positive.

4.7 Agents targeting VEGF/VEGFR-2

The pathogenesis of gastric cancer is influenced by signaling and angiogenesis regulated by vascular endothelial growth factor (VEGF) and vascular endothelial growth factor receptor-2 (VEGFR-2). Bevacizumab, a monoclonal antibody that targets VEGFA, was tested in patients with metastatic stomach (and other) cancers who had never received chemotherapy. individuals with GEJ) cancer who are undergoing chemotherapy. Combining bevacizumab with chemotherapy was found to significantly increase the percentage of patients who experience an objective response and have a prolonged survival without any progression. (PFS).

4.8 Immunotherapies

It is well known that tumors can evade the host immune reaction through a number of different pathways, leading to immune effector resistance. One of these events is the growth of immunosuppressive cells in the tumor microenvironment, such as regulatory T (Treg) cells and myeloid-derived suppressor cells (MDSCs); another is the elevation of different cytokines and chemokines, such as transforming growth factor (TGF), indoleamine 2,3-dioxygenase (IDO), and interleukin (IL)-10; and a third is advancement-inhibit [71]. The use of immune checkpoint blockade in the treatment of gastrointestinal cancers, especially GEJ cancer, is currently being researched. A crucial T-cell activation suppressor is CTLA-4. It is inducible on activated T lymphocytes and monocytes and is expressed on the surface of Treg cells by default. Increased CTLA-4 expression also causes T cells to arrest in the G1 phase of the cell cycle and reduce levels of IL-2 and IL-2 receptor expression. On the surface of activated T, B, and myeloid cells, the advancement-inhibitory

receptor PD-1 interacts with its ligands to inhibit T-cell function. (PD-L1 and PD-L2). This checkpoint is inhibited by antibody-mediated suppression of PD-1 or PD-L1, which activates T cells and boosts their antitumor activity.

Chapter 5
Conclusion

5.1 Conclusion

Research and therapy for gastric cancer are evolving quickly. The field of precision medicine is beginning to apply to gastric cancer thanks to developments in molecular profiling and the development of tailored therapies. Despite the fact that second- and third-line chemotherapy, HER2-targeting medications, and ramucirumab have all been frequently administered to patients with progressive GC in current years, many phase III trials have produced disappointing results, and others have had to be prematurely closed because of unexplained toxicity. If certain chemotherapy regimens benefit some patient subsets more than others are one of the unanswered issues. Additionally, the ideal time frame for combination chemotherapy is unknown: should we keep going until disease progression or just sustain therapy? In addition, reliable biomarkers other than HER2 are required in GC molecularly defined subgroups to choose patients for therapeutic trials. The results of the KEYNOTE 12 trial have given a first sign of immunotherapy's effectiveness in advanced GC. To prove the effectiveness of immunotherapy, more studies are needed, especially those with long-term follow-up.