Review Article
Management of primary gastric small cell carcinoma in China

Qin-Qin Wu1*, Wei-Guang Qiang2*, Feng Wang1, Ke-Jun Dai1, En-Ci Xu1, Ju-Dong Luo1, Qing Li3, Hua Tang1, Xi-Fa Zhou1, Xu-Jing Lu1
1Department of Radiation Oncology, The Tumor Hospital of Soochow University, Changzhou 213002, China; Departments of 2 Oncology, 3 Pathology, The Third Affiliated Hospital of Soochow University, Changzhou 213003, China. * Equal contributors.

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Abstract: Background: Primary gastric small cell carcinomas (GSCCs) are increasingly identified by endoscopy, and account for 15-20% of all gastric neuroendocrine tumors (NETs). GSCCs have the worst prognosis with the highest rate of metastases. Purpose: To provide useful information for clinicians and researchers to better manage patients with GSCC, we studied the clinical features of GSCC and explored the corresponding therapies and prognosis. Methods: A literature search was conducted through PUBMED, EMBASE, CNKI and WanFang Databases using search terms “stomach” or “gastric” and “small cell carcinoma” or “poorly differentiated neuroendocrine carcinoma”, for the period 1999 to 2012. And the cases reported were all from China. Relevant articles were identified through manual review. The reference lists of these articles were reviewed to include further appropriate articles. Results: Two hundred and five eligible cases were analyzed. The median age of patients was 62 years, with a male-to-female ratio of 5.4:1. Of the tumors, 53.17% were located in the upper stomach, 25.37% in the mid, 18.54% in the distal stomach, the remaining 2.93% were found in the total stomach. The mean size was 68mm in maximum diameter, with a range of 15-150mm. Of the one hundred and thirty-five patients, fifty appeared to be pure GSCCs, eighty-five were mixed. The median overall survival time of 195 patients was 18.50 months. The 1-, 2-, and 5-year average survival rates of 142 patients were 66.75%, 37.13%, and 20.15%, respectively. Conclusions: GSCC is a rare tumor and it is notoriously aggressive with a strong propensity for both regional and distant spread. Therapies including surgical resection, chemotherapy, and local radiotherapy, by itself or in combination with other treatment, have been used to treat GSCCs in China. To identify the most effective treatment modalities for GSCCs, we still need prospective, multicenter, randomized clinical researches.

Keywords: Small cell carcinoma, poorly differentiated neuroendocrine carcinoma, stomach, gastric

Introduction
Neuroendocrine tumors (NETs) are heterogeneous neoplasms, originating from different cells distributed in a large variety of anatomical locations throughout the body that share a common neuroendocrine phenotype [1]. Small cell carcinoma (SCC) is a group of the most aggressive and highly malignant NETs composed of small round or egg-shaped cells with little cytoplasm, which are found in various locations, but arises most frequently from the lung. Primary gastric small cell carcinoma (GSCC), first described in 1976, is an extremely rare neuroendocrine tumor that represents less than 0.1% of all gastric cancers [2, 3] and meanwhile accounts for 15-20% of all gastric NETs [4]. However, GSCC is notoriously aggressive with a strong propensity for both regional and distant spread [5, 6]. Prognosis is very poor for the patients without treatment, even just localized disease [7]. Due to the rareness of this disease, the majority of publications were only sporadic case-reports in the literature. It is for that very reason that the treatment protocols of GSCC have not been well established.

In recent years, the incidence of primary GSCCs in China has been increasing gradually because of the development of pathologically diagnostic techniques. In this report, we retrospectively analyzed the pathological characteristics, the clinical characteristics, the treatments and prognosis of GSCC.
Materials and methods

We systematically reviewed the Chinese- and English-language literature for the studies with primary data on GSCCs in China. We searched for publications in the Chinese medical literature using China National Knowledge Infrastructure (CNKI) and WanFang Databases that are two of the primary digital libraries providing most comprehensive access to full-text documents of publications in China. Using PUBMED and EMBASE, we performed additional searches for English-language literature, in which the patients reported were all from China. The original articles were identified with the keywords and topics related to “stomach” or “gastric” and “small cell carcinoma” or “poorly differentiated neuroendocrine carcinoma”, published during the period from 1999 to 2012. When cases were reported more than once, data of these cases from the most recent publication were used to analyze. All eligible cases were extracted according to a set of recorded features including age, gender, tumor site, histology (pure or mixed), tumor staging (Tumor-node-metastasis (TNM)), treatments, and follow-up. Local treatment consisted of radiotherapy and surgery, and systemic treatment consisted of adjuvant chemotherapy, neoadjuvant chemotherapy and somatostatin analogues.

The histological criteria for the diagnosis of GSCC was identical to that of pulmonary small cell carcinoma (SCLC) [8]. All eligible patients were required to have a histological diagnosis of GSCC according to the World Health Organization criteria (WHO, 6th edition). Histochemical and immunohistochemical staining were determined by argyrophilia and the direct or indirect presence of common neuroendocrine markers including NSE (neuron-specific enolase), Syn (synaptophysin), CgA (chromogranin A), and CD56.
Management of gastric small cell carcinoma

Currently, a revised consensus guideline of classification, staging and grading of NETs was recommended by both European and North American NET Societies (ENETS and NANETs) and WHO-2010 [9]. Limited studies retrospective studies have been used to validate the criteria. However, for all we know, no such review has been done in China. Because of this reason, the tumor-node-metastasis (TNM) system (6th edition, American Join Committee on Cancer (AJCC)) was adopted in present study [10]. The choice of employing different system may depend on the management algorithms applied. Follow-up was reported in terms of time. We computed the mean standard deviation of the continuous variables, where the differences were compared using the Mann-Whitney or Kruskal-Wallis test. Overall survival was calculated as the time from diagnosis to death or the last follow-up appointment for surviving patients. Statistical analyses were performed using the Fisher’s exact test by the SPSS 18.0.

Results

Patient characteristics

A total of 12 original articles on GSCC in China were published during the selected period in our study. Among these articles, there were only 9 eligible articles in which the studies covered 5 provinces and regions of China [5, 11-18], and the median time of patients collection was 12 years (range from 6 to 18.5 years).

Two hundred and five patients with gastric small cell carcinomas were admitted from these selected 9 articles. Among these 205 patients, 173 were males and 32 were females. The male-to-female ratio was 5.4:1 and the mean age was 62 years, with a range of 32-84 years. Among these 205 patients, 11 were lost to follow-up after the initial surgical operation [5, 11-18].

Pathological characteristics

GSCC’s characteristics under the microscope are essentially indistinguishable from their counterparts in the lung in histological and immunohistochemical features [7, 19], which are made up of round to spindle-shaped cells with very scant cytoplasm and small-sized oval nuclei with inconspicuous nucleoli (Figure 1A). Thirty-one patients were diagnosed by electron ic gastroscope and biopsy. Two hundred patients were further diagnosed with GSCC by postoperative histopathology and a part of patients were applied with immunohistochemical staining.

Table 1. Tumor clinical characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
</tr>
<tr>
<td>Gender (n=205)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>173</td>
</tr>
<tr>
<td>Female</td>
<td>32</td>
</tr>
<tr>
<td>Tumor length (mm) (n=200)</td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>68</td>
</tr>
<tr>
<td>Range</td>
<td>15-150</td>
</tr>
<tr>
<td>Tumor location (n=205)</td>
<td></td>
</tr>
<tr>
<td>Upper stomach</td>
<td>109</td>
</tr>
<tr>
<td>Middle stomach</td>
<td>52</td>
</tr>
<tr>
<td>Lower stomach</td>
<td>38</td>
</tr>
<tr>
<td>Total stomach</td>
<td>6</td>
</tr>
<tr>
<td>Histological component (n=135)</td>
<td></td>
</tr>
<tr>
<td>Pure type</td>
<td>50</td>
</tr>
<tr>
<td>Mixed type</td>
<td>85</td>
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<tr>
<td>Immunological marker</td>
<td></td>
</tr>
<tr>
<td>Syn</td>
<td>167</td>
</tr>
<tr>
<td>NSE</td>
<td>88</td>
</tr>
<tr>
<td>CgA</td>
<td>91</td>
</tr>
<tr>
<td>CD56</td>
<td>80</td>
</tr>
<tr>
<td>AE1/AE3</td>
<td>24</td>
</tr>
<tr>
<td>Pathological type (n=144)</td>
<td></td>
</tr>
<tr>
<td>Ulcerative type</td>
<td>83</td>
</tr>
<tr>
<td>Ulcer infiltrating type</td>
<td>26</td>
</tr>
<tr>
<td>Protruding/Fungating type</td>
<td>35</td>
</tr>
<tr>
<td>TNM staging (n=153)</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>6</td>
</tr>
<tr>
<td>II</td>
<td>19</td>
</tr>
<tr>
<td>III</td>
<td>103</td>
</tr>
<tr>
<td>IV</td>
<td>25</td>
</tr>
</tbody>
</table>

Abbreviations: Syn = synaptophysin, NSE = neuron-specific enolase, CgA = chromogranin A, CK = cytoeratin, CD56 = lymphocyte antigen 56, AE1/AE3 = Pan cytokeratins.
Carcinomas containing both SCC and non-SCC elements are designated “mixed” or “combined”. Approximately half of SCCs contain non-SCC elements. In previous literature reviews, the composite type accounts for 41.1-63.1% of all GSCC [3, 6], while in this study, the composite type accounts for 62.96% of all GSCC. And adenocarcinomas are the most common non-SCC elements in the GSCC (Figure 1B). Fifty of the tumors appeared to be pure GSCC, eighty-five were mixed, and the rest of the seventy patients did not mention this information in the articles.

Immunohistochemical staining of neuroendocrine markers, including Syn, CgA, NSE, AE1/AE3 and CD56, is usually positive [7, 20-22] (Figure 1C). Immunohistochemical information was available for 199 patients. Staining for the above five immunological markers (CgA, Syn, AE1/AE3, NSE and CD56) was performed on a part of the cases. Specifically, 83.92% (167/199) of the immunological reactivity of the samples were Syn, 63.31% (88/139) were NSE, 59.09% (91/154) were CgA, 48.19% (80/166) were CD56, and 37.50% (24/64) were AE1/AE3 [5, 11-18]. GSCCs had a high grade with a Ki67 (Figure 1D), ranging 30.0% to 95.5%, which was consistent with previous reports [22]. At present, the Ki67 index is used to determine prognosis and direct clinical management.

**Tumor characteristics**

Tumor characteristics were summarized in Table 1. In the present study, the tumor length was measured for most patients (97.6%, 200/205). The mean size, determined by endoscopy, radiological imaging, and gross measurements, was 68 mm in greatest dimension, with a range of 15-150 mm. Generally, the tumor location varied among the patients. For most patients (53.17%, 109/205), the tumors were located in the upper stomach. The tumors were found in the mid stomach for 52 patients (25.37%, 52/205), and in the distal stomach for 38 patients (18.54%, 38/205). In addition, the rest of the 6 cases with GSCC were found in the total stomach. Eighty-three of the tumors were described as ulcerative type, twenty-six as ulcer infiltrating type, and thirty-five as protruding/fungating type, and the other sixty-one patients were lack of the information in this regard.

Only a small part of the patients were pathologically confirmed to be malignant gastric tumor by electronic gastroscope and biopsy before operation. As this research showed, only 31 patients (15.12%, 31/205) were histologically diagnosed with GSCC before surgery. Lots of patients often misdiagnosed as adenocarcinoma or squamous cell carcinomas before operation [13, 14, 16, 17].

**Staging**

Most of tumors were staged according to the tumor-node-metastasis (TNM) staging system for gastric cancer (6th edition, American Joint Committee on Cancer (AJCC)), and the rests did not mention this information in the articles.

According to the AJCC TNM staging system, of 153 cases studied, there were 4 cases in stage Ib (2.61%, 4/153), 2 cases in stage I (1.31%, 2/153), 5 cases in stage IIa (3.27%, 5/153), 9 cases in stage IIb (5.88%, 9/153), 5 cases in stage II (3.27%, 5/153), 12 cases in stage IIIa (7.84%, 12/153), 41 cases in stage IIIb (26.80%, 41/153), 3 cases in stage IIIc (1.97%, 3/153), 47 cases in stage III (30.72%, 47/153), and 25 cases in stage IV (16.34%, 25/153) [5, 11, 13, 14, 16-18].

**Clinical Features**

We observed that the clinical features were often dominated by the advanced stage at diagnosis. Clinical symptoms of GSCC were similar.
to those of patients with carcinomas in the corresponding affected organ of the stomach, and no significant specificity was seen in computerized tomography (CT) imaging and electronic gastroscopy [23, 24]. Most of patients complained of upper epigastric discomfort (ranging from 47.83 to 80.00%) and/or dysphagia (ranging from 34.04 to 70.73%) as the major presenting symptoms. A large part of patients had anemia (ranging from 47.83 to 59.57%) and/or weight loss (ranging from 20.00 to 43.90%), a few patients might have anephthymia, nausea, vomiting, gastrointestinal haemorrhage and melena, etc. GSCC most often metastasizes to the liver, and patients may present with indications or symptoms related to disease metastasis. Paraneoplastic syndromes were not observed in our series. The duration of symptoms before diagnosis varied from 7 days to 13 months, with a mean time of 2.5 months.

**Treatment**

The standard treatment strategies for GSCC have not yet been established. Most oncologists have recommended using the same therapeutic strategies as those used for SCLC, because of the lack of adequate data, together with the apparent histological and clinical resemblance to the familiar SCLC. Modalities used to treat GSCC principally include surgery, chemotherapy, and radiotherapy [7]. Of the 205 patients studied, 200 patients received surgical resection, in which 166 patients underwent radical resection and 34 patients with palliative operation [5, 11-18]. The resection rate and radical resection rate were 97.56% (200/205) and 83.00% (166/200), respectively. Adjuvant chemotherapy was used in 136 cases, almost all of which with 2-6 courses of platinum-based combination chemotherapy, 3 cases with neoadjuvant chemotherapy, and only 2 cases with radiotherapy, respectively. Other 64 patients did not have the records of adjuvant chemoradiotherapy after surgery [5, 11-18]. 5 patients did not undergo surgery as a result of the presence of distant metastasis at diagnosis, in which 3 patients only received chemotherapy, other 2 patients did not receive any treatment [14, 16]. While the neuroendocrine features of GSCC might theoretically allow treatment with radiolabelled somatostatin analogues [7], but this approach had not been observed in this study. Table 2 showed our detailed analysis of the treatments for GSCC patients.

**Prognosis**

Usually, the prognosis of patients with GSCC is dismal even for the patients with apparently localized disease on account of early metastasis after surgery [3, 25, 26]. The prognosis is much more poor for patients who do not receive any treatment, with median survival measured in weeks, and no long-term survivors [7]. Of the 205 patients, the median survival time of 195 patients was 18.50 months [5, 12-18]. The median survival time of patients with and without surgery were 46.45 months (range, 10-63 months) and 7.65 months (range, 3-26 months), respectively [14, 16]. The patients tolerating systemic chemotherapy could obtain a more long-term survival. The median survival time of patients with and without adjuvant chemotherapy were 48.5 months (range, 5.2-228 months) and 19 months (range, 4.3-19 months), respectively [5]. The 1-, 2-, and 5-year average overall survival rates of 142 patients were 66.75% (range, 47.80-77.50%), 37.13% (range, 19.10-46.30%), and 20.15% (range, 4.30-36.60%), respectively [5, 14, 16-18].

**Discussion**

Primary GSCC is extremely rare, poorly differentiated, and highly malignant NETs. Yet regrettably, the exact pathogenesis is remaining largely unknown. Some researchers advocated a theory in which a pluripotent stem cell may be partially differentiated into squamous cell carcinoma and partially into adenocarcinoma or small cell carcinoma because of the stimulation of different carcinogenic agent [27, 28]. Similarly, we also found that GSCC were admixed with other histologic types of carcinoma such as adenocarcinoma or squamous cell carcinoma. In our results, of the 135 patients studied, 85 were composite type. Nevertheless, some investigators suggested that SCC elements may arise as a late-stage phenomenon in the genetic progression of carcinomas [8]. In addition, it has even been suggested that inflammatory cytokine gene such as IL-1B-511 and IL-1B-31 genotype may enhance the risks of gastric cancer [29]. But now, the correlation between inflammatory cytokine gene and GSCC is not clear. So far, it is almost impossible to identify whether such factors play a role in the pathogenesis of GSCC, but more investigations into their functions is imperative.
We observed the very low preoperative diagnostic rate, in which 84.88% cases were pathologically confirmed as undifferentiated adenocarcinoma or other types by preoperative electronic gastroscopy and biopsy. The following reasons may account for the misdiagnosis based on the biopsy: first of all, the small amount of tissues picked for endoscopic biopsy could be limited for the diagnosis and sometimes incur difficulties to differentiate GSCC from poorly differentiated adenocarcinoma. Secondly, in biopsy material, GSCC always becomes artificially distorted, producing the “crush” effects that frequently obscure the diagnosis [3, 7]. Consequently, resected specimens allow better evaluation of the histologic details. In addition, electron microscope, immunohistochemical and molecular findings are useful for the differential diagnosis. In the present study, we noted that the incidence for positive immunohistochemical reactivity for Syn, NSE and CD56 in GSCC were 83.92%, 63.31% and 59.09%, respectively, which was similar with previous reports [7, 21]. The existing reports regarding the role of newer imaging studies in GSCC, such as magnetic resonance imaging (MRI) and CT imaging, have rarely been described and have been non-specific. However, the available published data indicates that FDG PET/CT plays an important role in the staging and response assessment of SCC, while somatostatin-receptor scintigraphy is unlikely to provide any additional information [23].

The clinical features of GSCC with limited stage were similar to those of patients with carcinomas in the corresponding affected organ of the stomach [23, 24]. Systemic symptoms, such as anepithymia, anemia and weight loss, are common. Other presenting symptoms are site-specific. However, regardless of the precise location, epigastric discomfort, dysphagia, nausea, and melena are common. In our series, epigastric discomfort (ranging from 47.83 to 80.00%) and dysphagia (ranging from 34.04 to 70.73%) were observed in advanced patients, respectively, which were identical with the rate of gastric adenocarcinoma without significant difference. GSCC rarely secreted kinds of ectopic hormones such as vasoactive intestinal peptide, gastrin and so on [7, 30], which can result in paraneoplastic syndromes and even dominate clinical presentation. Paraneoplastic syndromes were not observed in our series. Even so, it is still necessary to evaluate paraneoplastic syndromes in the patients, especially when there is a clinical suspicion of GSCC. In clinical practice, GSCC arising from different locations of stomach shares similar pattern of spread. Most tumors are diagnosed with regional lymph node involvement and some have overt distant metastases [7]. GSCC most often metastasizes to the liver, followed by distant lymph nodes, bones, and bone marrow, and patients may present with signs or symptoms related to disease metastasis.

Currently, there were no randomized controlled trials which have been undertaken to establish the optimal therapy for GSCC because it’s very hard to get adequate numbers for a quality randomized controlled trial for its lower incidence rate and limited knowledge. However, the limited data in the literature is available describing the optimal treatment of patients with GSCC. Modalities including surgical resection, systemic chemotherapy, and local radiotherapy, by itself or in combination with other treatment, have been used to treat GSCC [5, 12-18].

Current guidance advocates that all GSCC should be treated with oncological resections without considering grade and stage [22]. Surgical resection undoubtedly remains the mainstay of the potentially curative treatment, which was widely performed to treat localized disease in patients with this disease. Of the 205 patients studied, 200 patients received surgical resection. The median survival time of patients with and without surgery were 46.45 months (range, 10-63 months) and 7.65 months (range, 3-26 months), respectively [14, 16]. Similarly, several cases treated by surgery alone could obtain a mean survival of 20 months [31]. In addition, in a review of 54 patients with GSCC, 3 patients without distant metastasis survived for more than 2 years after operation with dissection of regional lymph nodes [26, 32]. Taken together, these findings indicate that surgery may be considered as a standard treatment for limited disease of GSCC.

Systemic chemotherapy is now identified as the foundation of treatment for GSCC because of the high metastasis and recurrence rate [7]. Chemotherapy had improved the median survival to a range of 6-12 months, with occasional long-term survivors [33]. Our results demonstrated that postoperative chemotherapy significantly improved survival in patients with limited stage. Adjuvant chemotherapy was
used in 136 cases, almost all of which with two to six courses of platinum-based combination chemotherapy. Amazingly, the median survival of 48.5 months (range, 5.2-228 months) observed in patients with adjuvant chemotherapy, which is much better than the 19 months (range, 4.3-19 months) for the patients without it [5]. Analogously, Koide et al. reported a patient after surgery treated with chemotherapy experienced a more than 45 months of relapse-free survival [34]. Several studies have compared different regimens of chemotherapy [26, 34-37]. Unfortunately, there were no conclusions regarding which regimen was most effective on account of the sparse number of patients. Although the effectiveness of adjuvant chemotherapy is limited, it remains one of the most important strategies for treating GSCC.

Neoadjuvant chemotherapy is a modality of chemotherapy in the pre-operative setting in patients with resectable disease, which was verified to be an effective treatment against advanced gastric adenocarcinoma [38]. In recent years, it has begun to be used in GSCC, which was deemed to a feasible treatment in some literature [5, 39, 40]. It suggested that neoadjuvant chemotherapy should be recommended as standard treatment in patients with GSCC. However, the exact role of neoadjuvant chemotherapy remained controversial. In China, the application of neoadjuvant chemotherapy in GSCC was very scarce. Of the 205 patients studied, only 3 cases received neoadjuvant chemotherapy [5, 17]. Consequently, our research could not respond to the question about the role of neoadjuvant chemotherapy in limited stage.

In China, radiotherapy which was administrated in gastric small cell carcinomas was also rare. In this study, we showed that only 2 patients accepted radiotherapy [16]. Several trials and meta-analyses have shown that radiotherapy combined chemotherapy with could improve the curative effects [7], radiotherapy could provide locoregional control and subsequent long-term survival in isolated cases [24, 41]. Yet, we are still uncertain the accurate role of radiotherapy in GSCC. The exact role of radiotherapy in administrating GSCC needs further investigation with randomized controlled trials to establish long-term efficacy.

Theoretically, somatostatin analogue was regarded as a possible treatment against GSCC because of its neuroendocrine features. Nevertheless, this strategy has not been reported in China as yet. Similar to China, this kind of treatment applied in other countries was also quite rare [7]. However, there are no randomized controlled trials to determine whether somatostatin analogue was effective treatment for GSCC at present. Therefore, more studies are needed before this approach can be recommended to treat GSCC.

In spite of the application of multimodality treatment, the overall prognosis of GSCC is universally dismal with a mortality rate of 22-30% [3, 7, 42], even for patients with early-stage tumors as a result of high malignancy and early metastasis [3, 25, 26]. It’s our statistical fact that the median survival time of 195 patients was 18.50 months [5, 12-18], while some reports declared that they could obtain a mean survival of 20 months [31, 43]. The reason may be that the majority of patients in our group are late malignant tumor. Furthermore, the 1-, 2-, and 5-year average overall survival rates of 142 patients were 66.75%, 37.13% and 20.10%, respectively [5, 14, 16-18]. Collectively, our results demonstrate that the treatment of GSCC is still controversial and generally associated with a poor prognosis, which provide the impetus to develop more effective methods.

Conclusions

GSCC is a cancer characterized by high malignancy, early metastasis and poor prognosis. Normally, the most of reported cases come from East Asia where gastric cancer is more prevalent. This study is the first to summarize the cases of GSCC reported inside of China. It's difficult to conduct a randomized controlled clinical study in order to obtain the optimal therapeutic strategy because of the lower incidence rate. Though our comprehensive retrospective review cannot solve all problems, however, our results suggest that multimodal approaches may be an effective treatment for the treatment of GSCC and also disclose important aspects of the disease, such as its clinical features, its pathological features, prognosis and more. And still, prospective, multicenter, randomized clinical tests to identify the most effective treatment modalities for GSCC are warranted.
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Disclosure of conflict of interest

None.

Address correspondence to: Xi-Fa Zhou or Xu-Jing Lu, Department of Radiation Oncology, Tumor Hospital Soochow University, 1 Huaide North Road, Changzhou 213001, China. Tel: +86-519-86867830; Fax: +86-519-86867830; E-mail: zhouxifa@sina.com (XFZ); luxujing68@aliyun.com (XJL)

References


[22] Basu Roy, Srijanaskanthan R, Prachalias A, Quaglia A and Ramage JK. Review article: the investigation and management of gastric neu-
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