



# 中山醫學大學附設醫院

## 胃癌診療指引

本臨床指引參考國家衛生研究院胃癌臨床診療指引、NCCN、ESMO版本

胃癌多專科醫療團隊編修

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## 修訂內容

頁數	version16.0	version16.1
	<p>一、前言</p> <p>日本、南美、東歐、部份中東地區及中國地區為高罹患率地區。胃腺癌依組織型態學分為兩大類：腸型和瀰漫型。腸型源自胃癌前驅病灶如萎縮性胃炎或腸型化生，較常見於男性及年老病人，而且是胃癌流行地區主要的組織型態，其主要來自環境的影響。瀰漫型胃癌並未有前驅病灶現象，在胃癌非盛行地區為主要的胃癌組織型態，較常見於女性及年輕病人。此外因消化性潰瘍、慢性胃炎、息肉、外傷等而做過部份胃切除之殘餘胃，經過一段時間(10 年以上)，也有可能發生原發性殘胃癌。</p> <p>胃癌病人有較高的幽門螺旋桿菌感染率，但幽門螺旋桿菌和胃癌的關係尚待進一步研究證實。大部份研究胃癌形成的學者認為食用生鮮蔬菜、水果及高纖維麵包較不易得胃癌。相反的，食用多量動物蛋白質及脂肪、高複雜性澱粉、高鹽醃漬之肉類或魚類和飲用水內含硝酸鹽，得胃癌的危險性增加。食用富含維生素 A 和 C 以及 <math>\beta</math> 胡蘿蔔素的食物得胃癌的危險性較低。</p>	刪除前言文字敘述
	<p>二、臨床症狀</p> <p>由於胃癌病人沒有特定的臨床症狀，因此大部分病人被診斷出來時，已是晚期胃癌了。有些病人症狀類似消化性潰瘍，呈現出來的上腹疼痛，可被一般抗潰瘍藥物緩解；有些病人可能有體重減輕、食慾不振、疲倦、上腹部不適，甚至合併腹水，但這些無一為胃癌特定症狀。直至病況嚴重，引起吞嚥困難，持續性嘔吐等腸胃道阻塞症狀發生，才緊急就醫。根據醫學統計，胃癌細胞形成到臨床出現症狀其間，約長達</p>	刪除臨床症狀文字敘述



	<p>20 個月；而從有臨床症狀，到就醫做出正確的診斷，多半延誤 6-8 個月的時間；這段期間，若能提高警覺，儘早得到正確的診斷，多半會有很好的預後。</p>	
	<p>三、診斷方法</p> <p>上消化道 X 光攝影和胃內視鏡檢查是胃癌診斷的兩大利器，這兩種檢查互有利弊。上消化道 X 光攝影比內視鏡檢查，更能看到胃整體的結構，對於病灶的範圍及黏膜下的腫瘤易顯現，且比較便宜，病人接受度高；但是上消化道 X 光攝影不能作切片檢查，無法得到組織學確證，則是其缺點。胃內視鏡診斷胃癌，其敏感性和特異性都很高，若再加上胃生體切片檢查，正確診斷率可高達 95% 以上。腹部超音波、內試鏡超音波及電腦斷層檢查，對於胃癌手術前之分期、侵犯程度及有無轉移跡象亦有幫助。</p>	<p>刪除診斷方法文字敘述</p>
	<p>四、胃癌轉移常見部位</p> <p>胃癌的轉移分為四大種類，局部侵犯、淋巴腺轉移、腹膜轉移及血液轉移、局部侵犯可侵犯到附近的器官，包括肝臟、胰臟、橫結腸、食道或大動脈，造成手術切除的困難或變成不可切除；淋巴腺的轉移可能是局部性，也可能是全身性的淋巴腺；腹膜轉移也就是一般所謂的癌性腹膜炎；血液轉移最常見的還是肝臟、肺臟、骨頭等。</p>	<p>刪除胃癌轉移常見部位文字敘述</p>
	<p>五、胃癌之分期</p> <p>胃腺癌侵犯之深度與淋巴腺轉移的機會與病人的預後關係密切。依據腫瘤之侵犯深度，而分為早期癌(early cancer) 和進行性癌(advanced cancer)。早期癌僅侵犯胃壁之黏膜層(mucosa)或黏膜下層(submucosa)，根據日本內視鏡學會的分類標準，可分為三個基本型：第 I 型是指凸出型，具有表淺性明顯的隆起。第 II 型又分為 IIA、IIB 及 IIC 三種亞型，IIA 只有些微的隆起者；IIB 無任何隆起或陷凹；IIC 是略有凹陷</p>	<p>胃癌之分期刪除文字敘述</p>



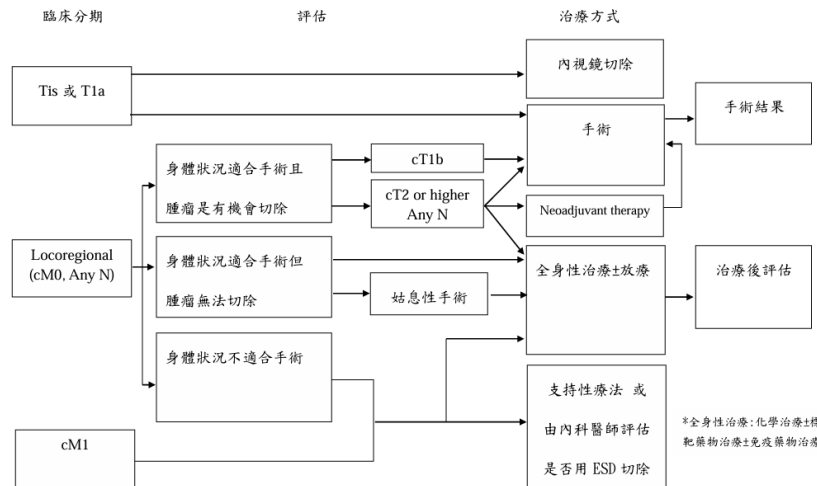
者。第 III 型是潰瘍型，但癌細胞僅侷限於潰瘍周邊黏膜。進行癌依肉眼外觀的形態分為四種基本類型：第 I 型是息肉型或凸出型；第 II 型是周圍具有隆起邊緣的潰瘍稱為凹陷型；第 III 型是潰瘍且其邊緣已有浸潤者；第 IV 型是廣泛性浸潤型，無明顯界限，向胃腔內凸出不明顯，黏膜可有潰瘍，胃壁增厚變硬，若擴及全胃時稱皮革胃。胃癌分期則是依據原始腫瘤大小 T，局部淋巴腺轉移的有無 N 以及遠處轉移的與否 M，分為 stage0 (原位癌)、I (又可分成 IA、IB)、II、III (又可分成 IIIA、IIIB)、IV 五級。

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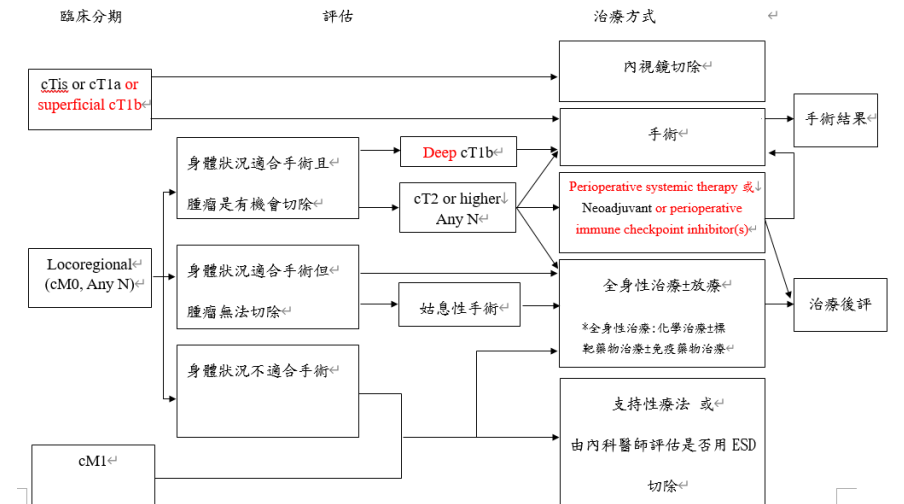
選擇性檢查新增： microsatellite instability (MSI) by polymerase chain reaction (PCR)/next-generation sequencing (NGS) or mismatch repair (MMR) by immunohistochemistry (IHC)

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### 七、胃癌治療



### 胃癌治療





<p>8</p>	<p>九、一開始無法手術的胃癌治療後的評估</p>	<p>五、一開始無法手術的胃癌治療後評估</p>
<p>16</p>	<p>FLOT + durvalumab (for PD-L1 CPS <math>\geq 1</math> or TAP <math>\geq 1\%</math>)</p>	<p>FLOT + durvalumab 新增備註：</p> <ol style="list-style-type: none"> <li>1. For PD-L1 CPS <math>\geq 1</math> or TAP <math>\geq 1\%</math> (category 1)</li> <li>2. For clinical node negative tumor</li> <li>3. For PD-L1 CPS <math>&lt; 1</math> or TAP <math>&lt; 1\%</math> (category 2B)</li> <li>4. For diffuse type (category 2B)</li> </ol> <p>* Category 2B :Based upon lower-level evidence, there is NCCN consensus (<math>\geq 50\%</math>, but <math>&lt; 85\%</math> support of the Panel) that the intervention is appropriate.</p> <p>* In the MATTERHORN trial, diffuse type gastric or EGJ adenocarcinoma showed no event-free overall survival advantage when durvalumab was added to FLOT</p>
<p>27.31.33</p>	<p>HER2 overexpression positive HER2 overexpression negative HER2 overexpression Negative, CLDN18.2 Positive</p>	<p>HER2 positive HER2 negative HER2 Negative, CLDN18.2 Positive</p>



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## 一、胃癌之分期－AJCC 8<sup>th</sup> T-N-M

Primary Tumor(T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ; intraepithelial tumor without invasion of the lamina propria,high grade dysplasia
T1	Tumor invades the lamina propria,muscularis mucosae, or submucosa
T1a	Tumor invades the lamina propria or muscularis mucosae
T1b	Tumor invades the submucosae
T2	Tumor invades muscularis propria
T3	Tumor penetrates subserosal connective tissue without invasion of visceral peritoneum or adjacent structures
T4	Tumor invades serosa (visceral peritoneum) or adjacent structures
T4a	Tumor invades serosa (visceral peritoneum)
T4b	Tumor invades adjacent structures/organs

Regional Lymph Nodes(N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1-2 regional lymph nodes
N2	Metastasis in 3-6 regional lymph nodes
N3	Metastasis in seven or more regional lymph nodes
N3a	Metastasis in 7-15 regional lymph nodes
N3b	Metastasis in 16 or more regional lymph nodes



Distant Metastasis(M)	
M0	No distant metastasis
M1	Distant metastasis

cT-N-M Stage Grouping							
Stage 0	Tis	N0	M0	Stage II B	T3	N0	M0
Stage I	T1	N0	M0		T4a	N0	M0
Stage I	T2	N0	M0	Stage III	T3	N1	M0
Stage II A	T1	N1	M0		T3	N2	M0
	T1	N2	M0		T3	N3	M0
	T1	N3	M0		T4a	N1	M0
Stage II A	T2	N1	M0		T4a	N2	M0
	T2	N2	M0		T4a	N3	M0
	T2	N3	M0	Stage IV A	T4b	Any N	M0
				Stage IV B	Any T	Any N	M1



pT-N-M				Stage Grouping			
Stage 0	Tis	N0	M0	StageIIIB	T1	N3b	M0
Stage I A	T1	N0	M0		T2	N3b	M0
Stage I B	T1	N1	M0		T3	N3a	M0
	T2	N0	M0		T4a	N3a	M0
Stage II A	T1	N2	M0	T4b	N1	M0	
	T2	N1	M0	T4b	N2	M0	
	T3	N0	M0	StageIIIC	T3	N3b	M0
Stage II B	T1	N3a	M0		T4a	N3b	M0
	T2	N2	M0		T4b	N3a	M0
	T3	N1	M0	T4b	N3b	M0	
StageIIIA	T4a	N0	M0	StageIV	Any T	Any N	M1
	T2	N3a	M0				
	T3	N2	M0				
	T4a	N1	M0				
	T4a	N2	M0				
	T4b	N0	M0				



## Post Neoadjuvant Therapy

ypT-N-M				Stage	Grouping		
Stage I	T1	N0	M0	Stage III	T4a	N1	M0
Stage I	T2	N0	M0		T3	N2	M0
Stage I	T1	N1	M0		T2	N3	M0
Stage II	T3	N0	M0		T4b	N0	M0
	T2	N1	M0		T4b	N1	M0
	T1	N2	M0		T4a	N2	M0
	T4a	N0	M0		T3	N3	M0
	T3	N1	M0		T4b	N2	M0
	T2	N2	M0		T4b	N3	M0
	T1	N3	M0		T4a	N3	M0
				Stage IV	Any T	Any N	M1

Histologic Grade(G)	
GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Undifferentiated



## 二、胃癌診斷

### 主要檢查:

- Upper G-I panendoscopy Biopsy
- CT of abdominal or MRI or ultrasound

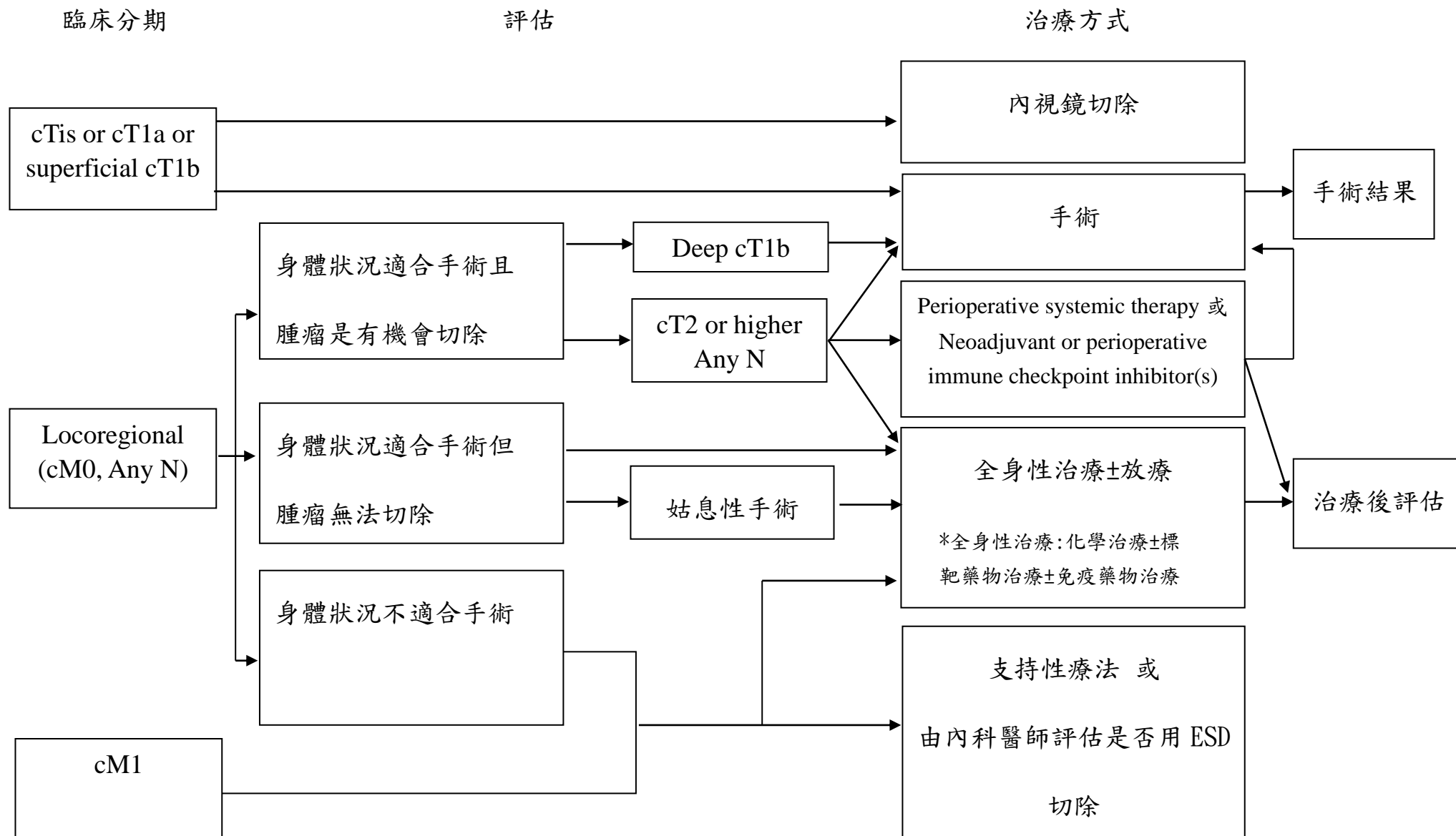
### 選擇性檢查:

- PET scan
- Endoscopic ultrasound (EUS)
- Universal testing for programmed death ligand 1 (PD-L1) is recommended in all newly diagnosed patients
- HER2 testing if advanced/metastatic disease is documented/suspected
- NGS should be considered
- CLDN18.2 testing if advanced/metastatic disease is documented/suspected
- microsatellite instability (MSI) by polymerase chain reaction (PCR)/next-generation sequencing (NGS) or mismatch repair (MMR) by immunohistochemistry (IHC)

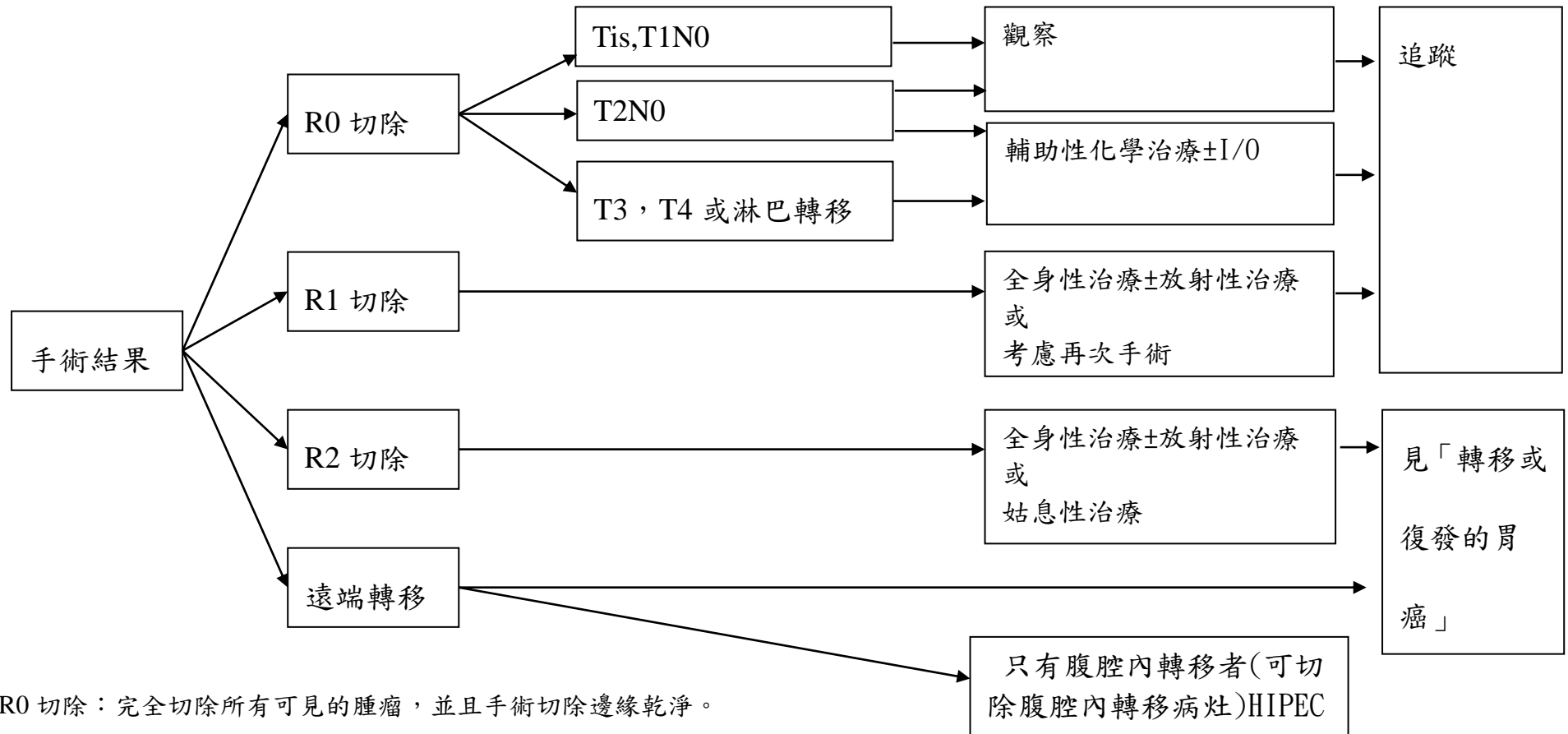
臨床分期



### 三、胃癌治療



## 四、胃癌手術結果

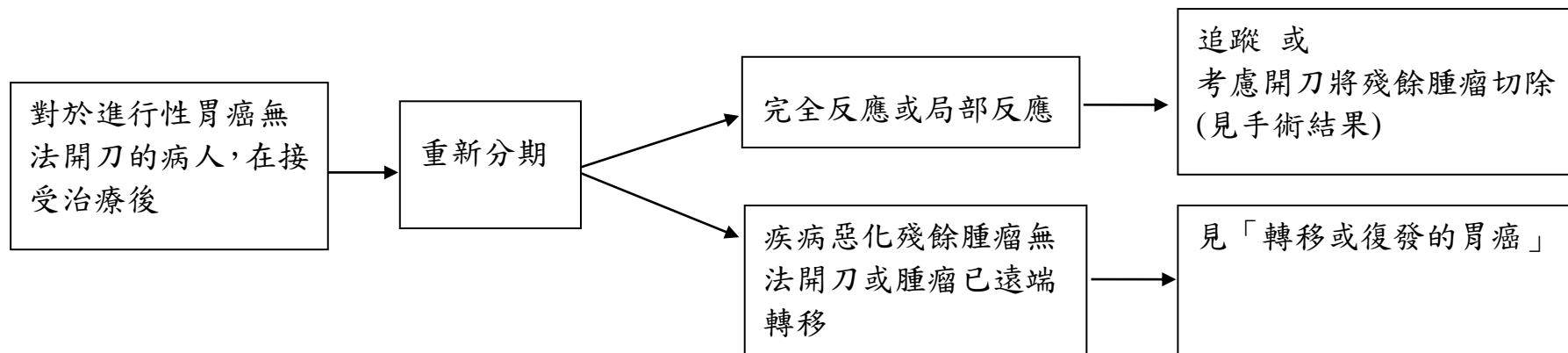


R0 切除：完全切除所有可見的腫瘤，並且手術切除邊緣乾淨。

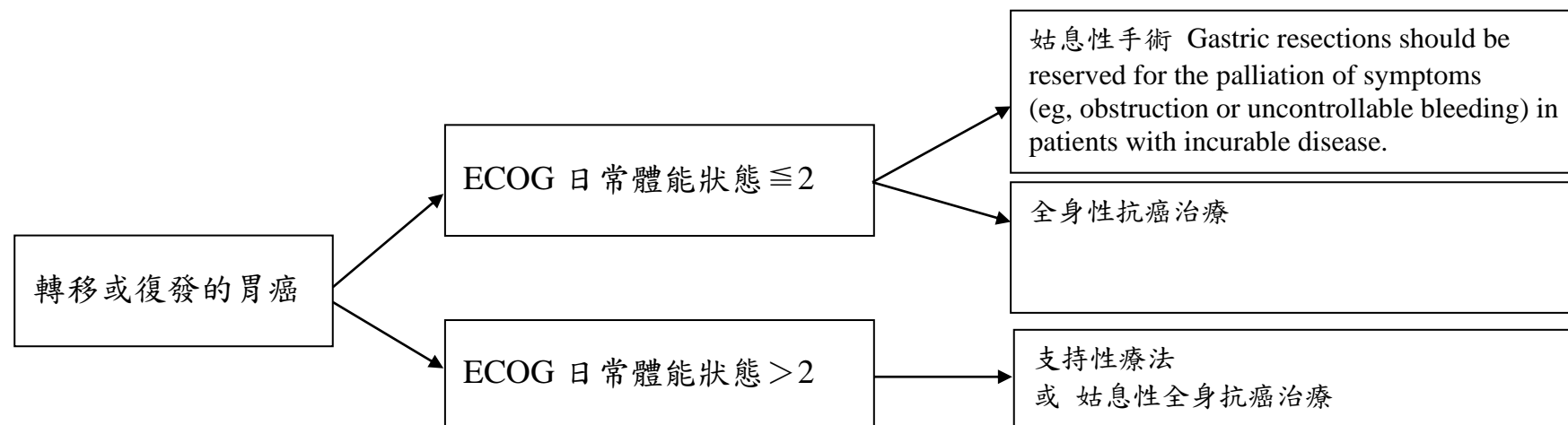
R1 切除：有顯微就可見的殘餘病灶

R2 切除：有肉眼可見的殘餘病灶

### 五、一開始無法手術的胃癌治療後評估



### 六、轉移或復發的胃癌(M1)



分數 ECOG

0 無症狀

1 有症狀，但是可以正常活動，對生活無影響

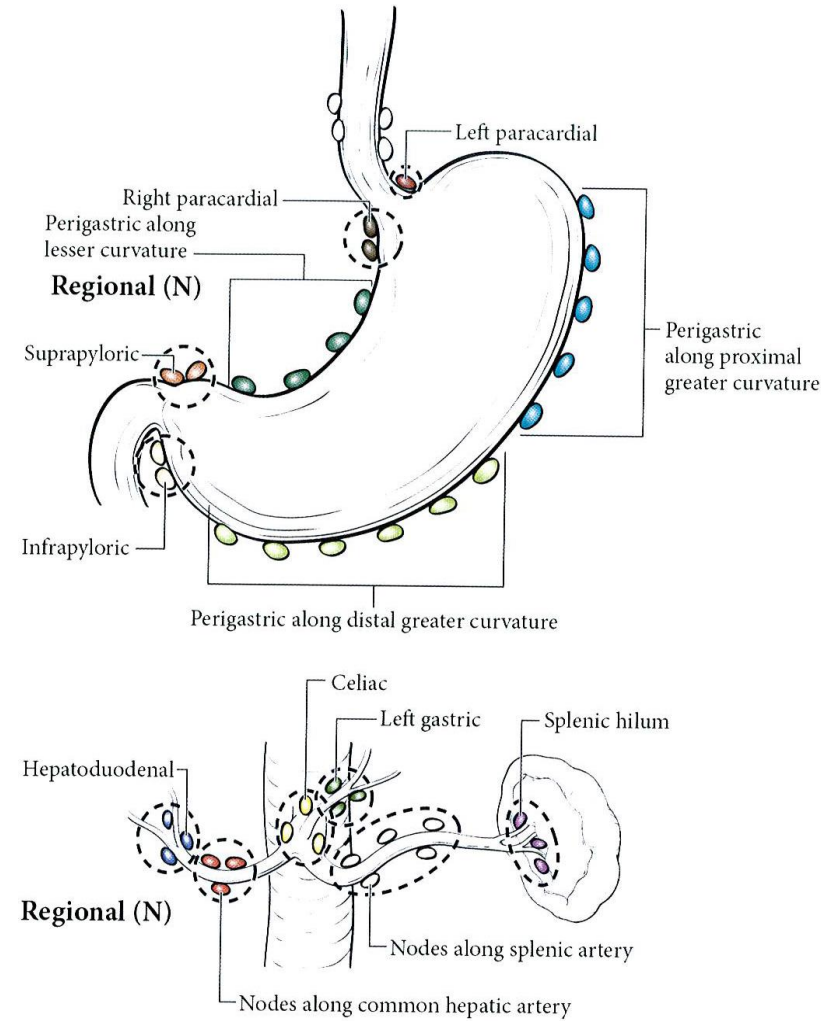
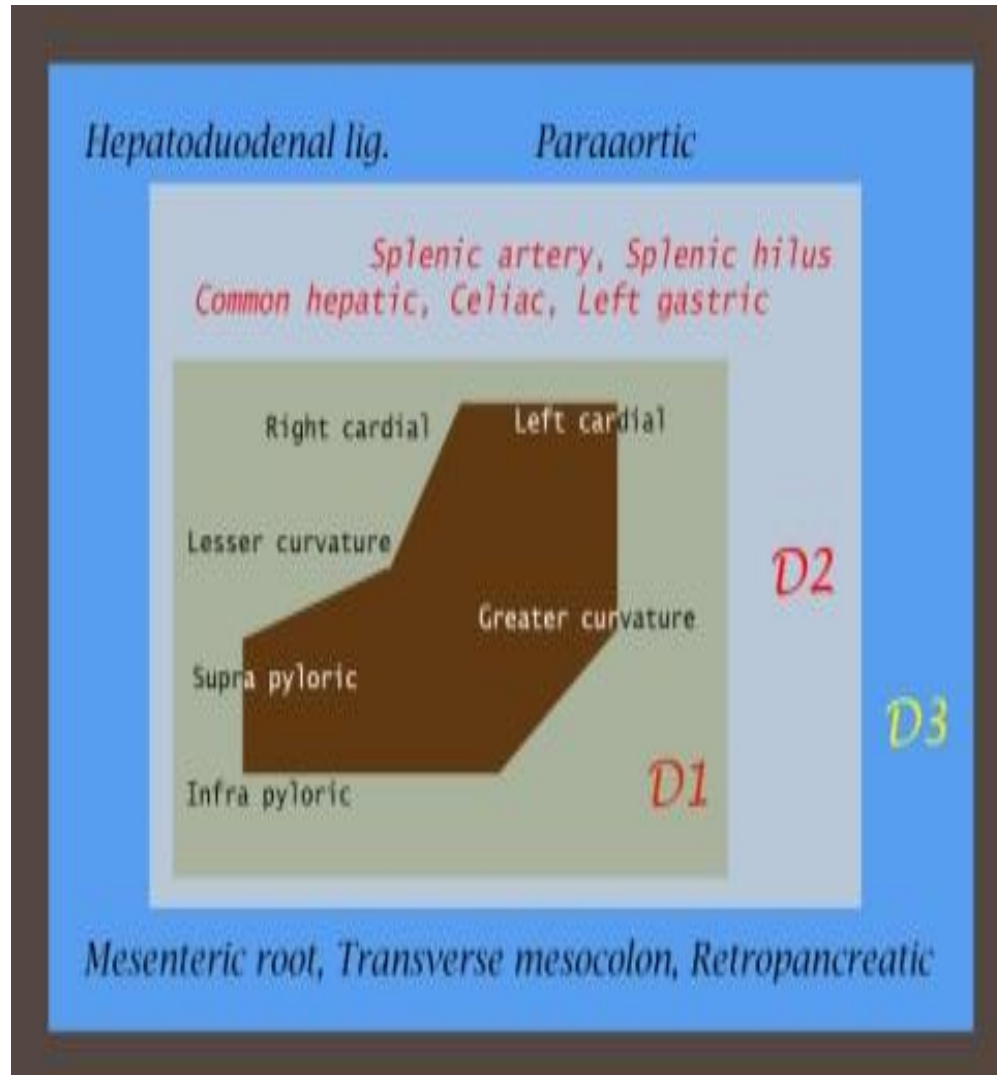
2 可以照顧自己但無法工作，躺在床上的時間 < 50% 的工作時間

3 躺在床上的時間 > 50% 的工作時間

4 長期臥病在床

5 死亡

## 七、胃部淋巴結位置



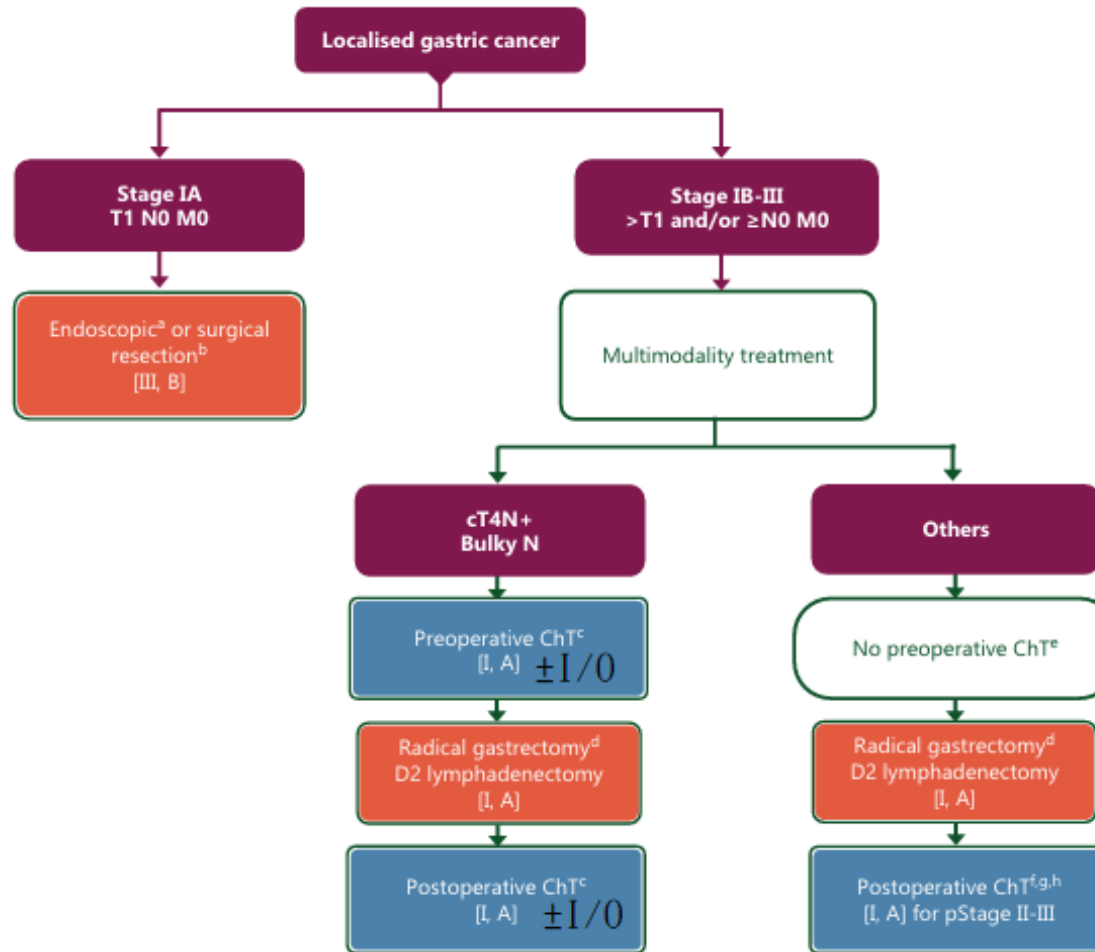
**Anatomical definitions of lymph node stations**

<b>Nr.</b>	<b>Definition</b>
1	Right paracardial LNs, including those along the first branch of the ascending limb of the left gastric artery
2	Left paracardial LNs including those along the esophagocardiac branch of the left subphrenic artery
3a	Lesser curvature LNs along the branches of the left gastric artery
3b	Lesser curvature LNs along the 2nd branch and distal part of the right gastric artery
4sa	Left greater curvature LNs along the short gastric arteries (perigastric area)
4sb	Left greater curvature LNs along the left gastroepiploic artery (perigastric area)
4d	Rt. greater curvature LNs along the 2nd branch and distal part of the right gastroepiploic artery
5	Suprapyloric LNs along the 1st branch and proximal part of the right gastric artery
6	Infrapyloric LNs along the first branch and proximal part of the right gastroepiploic artery down to the confluence of the right gastroepiploic vein and the anterior superior pancreaticoduodenal vein
7	LNs along the trunk of left gastric artery between its root and the origin of its ascending branch
8a	Anterosuperior LNs along the common hepatic artery
8p	Posterior LNs along the common hepatic artery
9	Coeliac artery
10	Splenic hilar LNs including those adjacent to the splenic artery distal to the pancreatic tail, and those on the roots of the short gastric arteries and those along the left gastroepiploic artery proximal to its 1st gastric branch
11p	Proximal splenic artery LNs from its origin to halfway between its origin and the pancreatic tail end
11d	Distal splenic artery LNs from halfway between its origin and the pancreatic tail end to the end of the pancreatic tail
12a	Hepatoduodenal ligament LNs along the proper hepatic artery, in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas

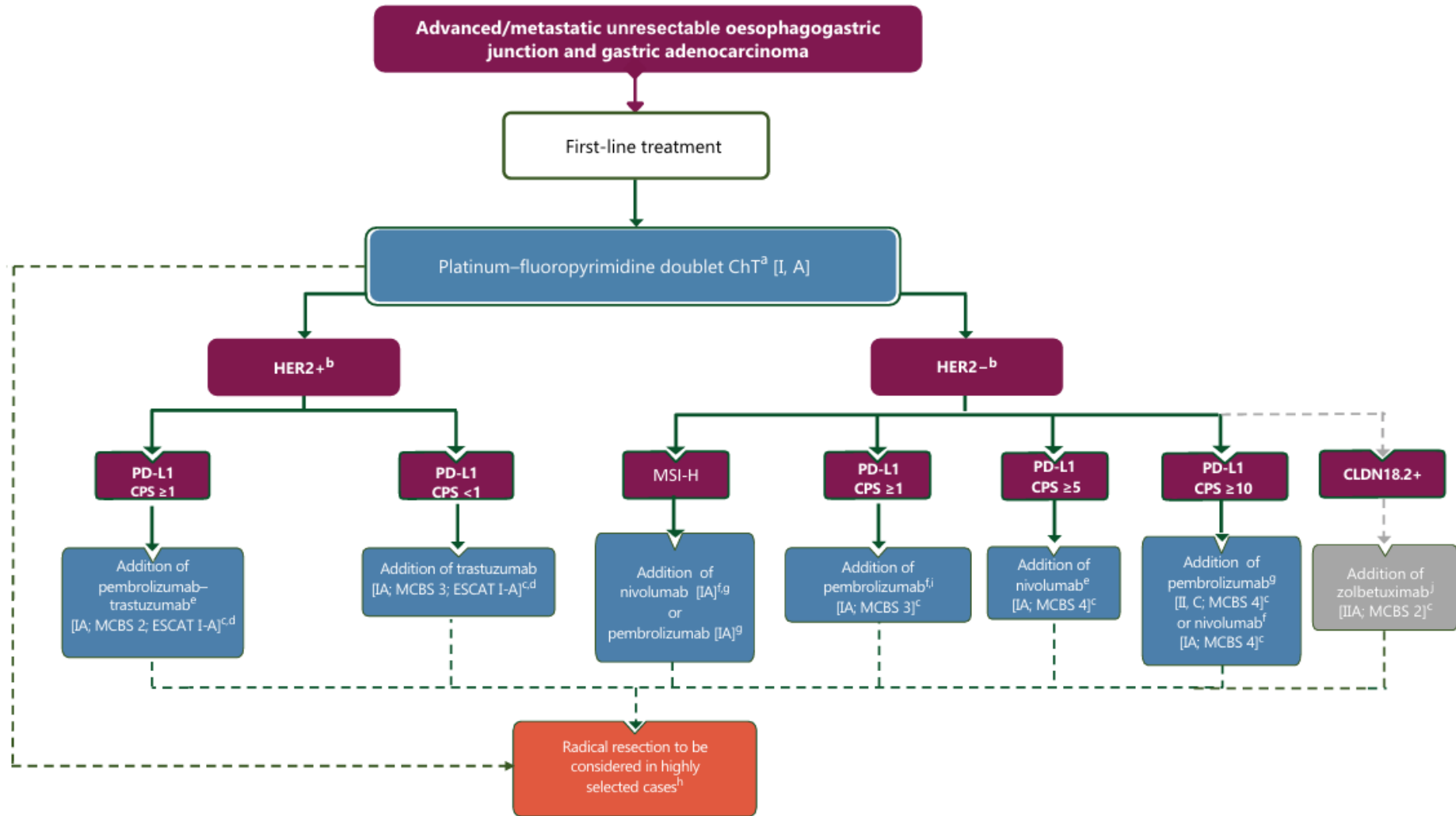


11p	Proximal splenic artery LNs from its origin to halfway between its origin and the pancreatic tail end
11d	Distal splenic artery LNs from halfway between its origin and the pancreatic tail end to the end of the pancreatic tail
12a	Hepatoduodenal ligament LNs along the proper hepatic artery, in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas
12b	Hepatoduodenal ligament LNs along the bile duct, in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas
12p	Hepatoduodenal ligament LNs along the portal vein in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas
13	LNs on the posterior surface of the pancreatic head cranial to the duodenal papilla
14v	LNs along the superior mesenteric vein
15	LNs along the middle colic vessels
16a1	Paraortic LNs in the diaphragmatic aortic hiatus
16a2	Paraortic LNs between the upper margin of the origin of the celiac artery and the lower border of the left renal vein
16b1	Paraortic LNs between the lower border of the left renal vein and the upper border of the origin of the inferior mesenteric artery
16b2	Paraortic LNs between the upper border of the origin of the inferior mesenteric artery and the aortic bifurcation
17	LNs on the anterior surface of the pancreatic head beneath the pancreatic sheath
18	LNs along the inferior border of the pancreatic body
19	Infradiaphragmatic LNs predominantly along the subphrenic artery
20	Paraesophageal LNs in the diaphragmatic esophageal hiatus
110	Paraesophageal LNs in the lower thorax
111	Supradiaphragmatic LNs separate from the esophagus
112	Posterior mediastinal LNs separate from the esophagus and the esophageal hiatus

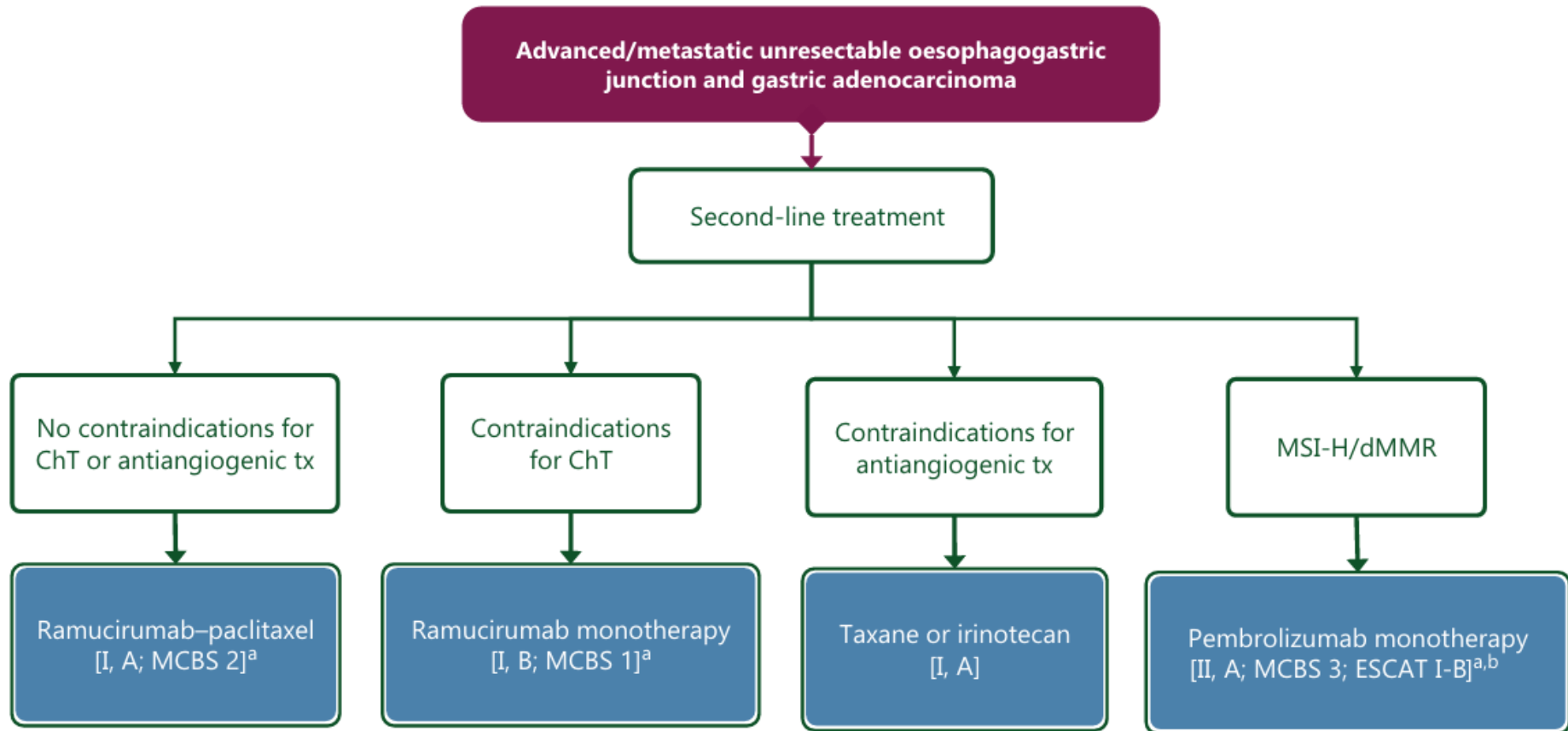
## 八、Pan-Asian adapted ESMO Clinical Practice Guidelines for the diagnosis, treatment and follow-up of patients with gastric cancer(2024)



圖一、Algorithm for the treatment of localised gastric cancer.



圖二、Algorithm for the first-line treatment of unresectable advanced or metastatic oesophagogastric junction and gastric cancers.



圖三、Algorithm for the second-line treatment of unresectable advanced or metastatic oesophagogastric junction and gastric cancers.



## 九、癌症藥物治療原則與處方

1. 對晚期食道胃腺癌和胃腺癌推薦的化療方案可以交換使用。
2. 化療方案應該根據病患體力狀態、合併症、毒性反應和 HER2-neu、Claudin 18.2 by immunohistochemistry 表現狀態做選擇。
3. 對晚期腫瘤患者應用三種藥物聯合處方前，應確定患者的身體狀況良好（ECOG PS 0~1），並能夠經常進行毒性評估。
4. 如果有證據支持毒性更低並且療效不受影響時可以優先選定 1 類方案的改良方案或使用 2A、2B 類方案。
5. 任何方案的劑量和用藥方案若不是來自 1 類證據，則只作為一種建議，應根據具體情況進行適當修改。
6. 允許基於是否能獲得的藥物、臨床指引中的喜好和禁忌證據改變細胞毒藥物的組合及用藥方案。
7. 靜脈滴注 5-FU 和口服 capecitabine 可互換使用（除非明確標示）。與 5-FU 注射相比，應選靜脈持續滴注 5-FU。
8. Cisplatin 和 Oxaliplatin 可以根據毒性反應互換使用。
9. 完成化療後，應該評估療效和晚期併發症。
10. 外科手術術中若為 R1 或 R2 切除病患給予腹腔內投藥 Cisplatin 100mg。



## Perioperative systemic therapy

Regimen	Fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT)				
Drug Combination	Dosage	Route of administration	Times	Frequency/ Duration	Notes
Fluorouracil	2600 mg/m <sup>2</sup>	IV	continuous infusion over 24 hours on Day 1	Cycled every 14 days	4 cycles preoperative and 4 cycles postoperative
Leucovorin	200 mg/m <sup>2</sup>	IV	continuous infusion over 24 hours on Day 1		
Oxaliplatin	85 mg/m <sup>2</sup>	IV	drip 90-120 mins, on Day 1		
Docetaxel	50 mg/m <sup>2</sup>	IV	drip 60 mins, on Day 1		
<b>Ref.</b>	<i>Al-Batran S-E, Homann N, Pauligk C, et al. Perioperative chemotherapy with fluorouracil plus leucovorin, oxaliplatin, and docetaxel versus fluorouracil or capecitabine plus cisplatin and epirubicin for locally advanced, resectable gastric or gastro-oesophageal junction adenocarcinoma (FLOT4): a randomised, phase 2/3 trial. Lancet 2019;393:1948-1957.</i>				

Regimen	FLOT + durvalumab				
Drug Combination	Dosage	Route of administration	Times	Frequency/ Duration	Notes
Durvalumab	1500 mg	IV	drip 30 mins, on Day 1	Cycled every 28 days (2 cycles preoperative and 2 cycles postoperative, 4 cycles total)	1. For PD-L1 CPS $\geq 1$ or TAP $\geq 1\%$ (category 1) 2. For clinical node negative tumor 3. For PD-L1 CPS
Fluorouracil	2600 mg/m <sup>2</sup>	IV	continuous infusion over 24 hours on Day 1 and 15		
Leucovorin	200 mg/m <sup>2</sup>	IV	continuous infusion over 24 hours on Day 1 and 15		
Oxaliplatin	85 mg/m <sup>2</sup>	IV	drip 90-120 mins, on Day 1 and		



			15	followed by	<1 or TAP <1%b
Docetaxel	50 mg/m <sup>2</sup>	IV	drip 60 mins, on Day 1 and 15	Durvalumab 1500 mg IV on Day 1 every 4 weeks for 10 additional cycles	(category 2B <sup>註 1</sup> ) 4. For diffuse type (category 2B) <sup>註 2</sup>
<b>Ref.</b>	<i>Janjigian YY, Al-Batran SE, Wainberg ZA, et al. Perioperative durvalumab in gastric and gastroesophageal junction cancer. N Engl J Med 2025;393:217-230.</i>				

註 1. Category 2B :Based upon lower-level evidence, there is NCCN consensus (≥50%, but <85% support of the Panel) that the intervention is appropriate.

註 2. In the MATTERHORN trial, diffuse type gastric or EGJ adenocarcinoma showed no event-free overall survival advantage when durvalumab was added to FLOT

Regimen	Fluoropyrimidine and oxaliplatin					
Drug Combination	Dosage	Route of administration	Times	Frequency/ Duration	Notes	
Oxaliplatin	85 mg/m <sup>2</sup>	IV	on Day1	Cycled every 14 days	4 cycles preoperative and 4 cycles postoperative	
Leucovorin	400 mg/m <sup>2</sup>	IV	on Day 1			
Fluorouracil	400 mg/m <sup>2</sup>	IV Push	on Day 1			
Fluorouracil	1200 mg/m <sup>2</sup>	IV	continuous infusion over 24 hours daily on Days 1			
or						
Oxaliplatin	85 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 14 days		
Leucovorin	200 mg/m <sup>2</sup>	IV	continuous infusion over 24 hours on Day 1			
Fluorouracil	2600 mg/m <sup>2</sup>	IV	continuous infusion over 24			



			hours on Day 1		
or					
Capecitabine	850-1000 mg/m <sup>2</sup> BID	PO	on Days 1–14	Cycled every 21 days	
Oxaliplatin	130 mg/m <sup>2</sup>	IV	drip 120 mins, on Day 1		
or					
Capecitabine	850-1000 mg/m <sup>2</sup> BID	PO	on Days 1–14	Cycled every 21 days	
Oxaliplatin	65mg/m <sup>2</sup>	IV	drip 90-120 mins, on Day 1, 8		
<b>Ref.</b>	<p>1. Al-Batran S-E, Hartmann JT, Probst S, et al. Phase III trial in metastatic gastroesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft Internistische Onkologie. <i>J Clin Oncol</i> 2008;26:1435-1442.</p> <p>2. Kim GM, Jeung HC, Rha SY, et al. A randomized phase II trial of S-1-oxaliplatin versus capecitabine- oxaliplatin in advanced gastric cancer. <i>Eur J Cancer</i> 2012;48:518-526.</p>				



## Neoadjuvant or perioperative Immunotherapy regimens ( MSI-H/dMMR tumors)

Regimen	<b>Nivolumab and ipilimumab followed by nivolumab</b>				
Drug Combination	Dosage	Route of administration	Times	Frequency/ Duration	Notes
Nivolumab	240 mg	IV	drip 30 mins, on Day 1	every 2 weeks	Ipilimumab(preoperative for at least 12 total weeks), followed by surgery and adjuvant nivolumab 480 mg IV every 4 weeks for 9 cycles
Ipilimumab	1mg/kg	IV	drip 30 mins, on Day 1	every 6 weeks	
<b>Ref.</b>	<i>Andre T, Tougeron D, Piessen G, et al. Neoadjuvant nivolumab plus ipilimumab and adjuvant nivolumab in localized deficient mismatch repair/microsatellite instability-high gastric or esophagogastric junction adenocarcinoma: The GERCOR NEONIPIGA phase II study. J Clin Oncol 2023;41:255-265.</i>				

Regimen	<b>Pembrolizumab</b>				
Drug Combination	Dosage	Route of administration	Times	Frequency/ Duration	Notes
Pembrolizumab	200 mg	IV	drip 30 mins, on Day 1	every 3 weeks for at least 12 total weeks	followed by surgery and adjuvant pembrolizumab 200 mg IV every 3 weeks x 16 cycles



<b>Ref.</b>	<i>Ludford K, Ho WJ, Thomas JV, et al. Neoadjuvant pembrolizumab in localized microsatellite instability high/deficient mismatch repair solid tumors. J Clin Oncol 2023;41:2181-2190.</i> <i>Liu L, Woo Y, D'Apuzzo M, et al. Immunotherapy-based neoadjuvant treatment of advanced microsatellite instability-high gastric cancer: A case series. J Natl Compr Canc Netw 2022;20:857-865.</i>
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<b>Regimen</b>	<b>Tremelimumab and durvalumab</b>				
<b>Drug Combination</b>	<b>Dosage</b>	<b>Route of administration</b>	<b>Times</b>	<b>Frequency/Duration</b>	<b>Notes</b>
Tremelimumab	300 mg	IV	on Day 1	once	for neoadjuvant therapy only
Durvalumab	1500 mg	IV	on Days 1, 29, and 57 for 12 weeks preoperatively for 1 cycle only	every 4 weeks x 3	
<b>Ref.</b>	<i>Kelly RJ, Lee J, Bang YJ, et al. Safety and efficacy of durvalumab and tremelimumab alone or in combination in patients with advanced gastric and gastroesophageal junction adenocarcinoma. Clin Cancer Res 2020;26:846-854.</i> <i>Pietrantonio F, Raimondi A, Lonardi S, et al. INFINITY: A multicentre, single-arm, multi-cohort, phase II trial of tremelimumab and durvalumab as neoadjuvant treatment of patients with microsatellite instability-high (MSI) resectable gastric or gastroesophageal junction adenocarcinoma (GAC/GEJAC). Journal of Clinical Oncology 2023;41:358- 358.</i>				

## Adjuvant Chemotherapy regimens

<b>Regimen</b>	<b>TS-1</b>				
<b>Drug Combination</b>	<b>Dosage</b>	<b>Route of administration</b>	<b>Times</b>	<b>Frequency/Duration</b>	<b>Notes</b>
Tegafur/potassium oxonate/gimeracil	BSA < 1.25 40mg bid BSA 1.25-1.5 50mg bid BSA ≥ 1.5 60mg bid	PO	4 weeks on/2 weeks off (or 2 weeks on/1 weeks off)	1 year	
<b>Ref.</b>	<i>Sakuramoto S, et al. Adjuvant chemotherapy for gastric cancer with S-1, an oral fluoropyrimidine. N Engl J Med. 2007;357:1810.</i>				



Regimen	Modified FOLFOX				
Drug Combination	Dosage	Route of administration	Times	Frequency/ Duration	Notes
Oxaliplatin	85 mg/m <sup>2</sup>	IV	drip 120 mins, on Day 1	Q2w x 6–12 cycles	
Leucovorin	200 mg/m <sup>2</sup>	IV	46 hours on Day 1		
5-FU	2600 mg/m <sup>2</sup>	IV	46 hours on Day 1		
<b>Ref.</b>	<i>Al-Batran S-E, Hartmann JT, Probst S, et al. Phase III trial in metastatic gastroesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft Internistische Onkologie. J Clin Oncol 2008;26:1435-1442.</i>				

Regimen	Fluorouracil and oxaliplatin				
Drug Combination	Dosage	Route of administration	Times	Frequency/ Duration	Notes
Oxaliplatin	85 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 14 days	
Leucovorin	400mg/m <sup>2</sup>	IV	on Day 1		
Fluorouracil	400 mg/m <sup>2</sup>	IV Push	on Day 1		
Fluorouracil	1200 mg/m <sup>2</sup>	IV	continuous infusion over 24 hours daily on Days 1		
or					
Oxaliplatin	85 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 14 days	
Leucovorin	200 mg/m <sup>2</sup>	IV	on Day 1		
Fluorouracil	2600 mg/m <sup>2</sup>	IV	continuous infusion over 24		



			hours on Day 1		
Ref.	<p>1. Enzinger PC, Burtness BA, Niedzwiecki D, et al. CALGB 80403 (Alliance)/E1206: a randomized phase II study of three chemotherapy regimens plus cetuximab in metastatic esophageal and gastroesophageal junction cancers. <i>J Clin Oncol</i> 2016;34:2736-2742.</p> <p>2. Al-Batran S-E, Hartmann JT, Probst S, et al. Phase III trial in metastatic gastroesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft Internistische Onkologie. <i>J Clin Oncol</i> 2008;26:1435-1442.</p>				

Regimen	XELOX(CAPOX)					
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes	
Capecitabine	850-1000 mg/m <sup>2</sup> BID	PO	on Days 1–14	Cycled every 21 days for 8 cycles	for patients who have undergone primary D2 lymph node dissection	
Oxaliplatin	130 mg/m <sup>2</sup>	IV	drip 120 mins, on Day 1			
or						
Capecitabine	850-1000 mg/m <sup>2</sup> BID	PO	on Days 1–14	Cycled every 21 days for 8 cycles		
Oxaliplatin	65 mg/m <sup>2</sup>	IV	drip 90-120 mins, on Day 1, 8			
Ref.	<p>Noh SH, Park SR, Yang HK, et al. Adjuvant capecitabine plus oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): 5-year follow-up of an open-label, randomised phase 3 trial. <i>Lancet Oncol</i> 2014;15:1389-1396.</p> <p>Kang YK, Kang WK, Shin DB, et al. Capecitabine/cisplatin versus 5-fluorouracil/cisplatin as first-line therapy in patients with advanced gastric cancer: a randomised phase III noninferiority trial. <i>Ann Oncol</i> 2009;20:666-673.</p>					

Regimen	TS-1+Oxaliplatin				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Tegafur/potassium oxonate/gimeracil	BSA < 1.25 40mg bid BSA 1.25-1.5 50mg bid BSA ≥ 1.5 60mg bid	PO	4 weeks on/2 weeks off (or 2 weeks on/1 weeks off)	Cycled every 21 days for 8 cycles	
Oxaliplatin	100mg/m <sup>2</sup>	IV	drip 2hrs, on day 1		



<b>Ref.</b>	<i>Namikawa, T., Maeda, H., Kitagawa, H., Oba, K., Tsuji, A., Yoshikawa, T., ... &amp; Hanazaki, K. (2018). Treatment using oxaliplatin and S-1 adjuvant chemotherapy for pathological stage III gastric cancer: a multicenter phase II study (TOSA trial) protocol. BMC cancer, 18(1), 186.</i>
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## Postoperative chemoradiation

Regimen	Fluorouracil					
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes	
2 cycles before and 4 cycles after chemoradiation. For cycles after chemoradiation, begin chemotherapy 1 month after chemoradiation.						
Leucovorin	400 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 14 days		
Fluorouracil	400 mg/m <sup>2</sup>	IV Push	on Day 1			
Fluorouracil	1200 mg/m <sup>2</sup>	IV	IV continuous infusion over 24 hours daily on Days 1			
With radiation						
Fluorouracil	200–250 mg/m <sup>2</sup>	IV	continuous infusion over 24 hours daily on Days 1–5	Weekly for 5 weeks		
<b>Ref.</b>	<i>Leong T, Joon DL, Willis D, et al. Adjuvant chemoradiation for gastric cancer using epirubicin, cisplatin, and 5-fluorouracil before and after three-dimensional conformal radiotherapy with concurrent infusional 5-fluorouracil: a multicenter study of the Trans-Tasman Radiation Oncology Group. Int J Radiat Oncol Biol Phys 2011;79:690-695.</i>					

Regimen	Capecitabine				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
1 cycle before and 2 cycles after chemoradiation.					



For cycles after chemoradiation, begin chemotherapy 1 month after chemoradiation.					
Capecitabine	750–1000 mg/m <sup>2</sup> BID	PO	on Days 1–14	Cycled every 21 days	
With radiation					
Capecitabine	625–825 mg/m <sup>2</sup> BID	PO	on Days 1–5	Weekly for 5 weeks	
<b>Ref.</b>	<i>Jansen EP, Boot H, Saunders MP, et al. A phase I-II study of postoperative capecitabine-based chemoradiotherapy in gastric cancer. Int J Radiat Oncol Biol Phys 2007;69:1424-1428.</i> <i>Lee HS, Choi Y, Hur WJ, et al. Pilot study of postoperative adjuvant chemoradiation for advanced gastric cancer: adjuvant 5-FU/cisplatin and chemoradiation with capecitabine. World J Gastroenterol 2006;12:603-607.</i>				

## Chemoradiation for unresectable disease

Regimen	Fluorouracil and oxaliplatin				
Drug Combination	Dosage	Route of administration	Times	Frequency/ Duration	Notes
Oxaliplatin	85 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 14 days for 3 cycles with radiation followed by 3 cycles without radiation	
Leucovorin	400 mg/m <sup>2</sup>	IV	on Day 1		
Fluorouracil	400 mg/m <sup>2</sup>	IV Push	on Day 1		
Fluorouracil	800 mg/m <sup>2</sup>	IV	IV continuous infusion over 24 hours daily on Days 1		
<b>Ref.</b>	<i>Conroy T, Galais MP, Raoul JL, et al. Definitive chemoradiotherapy with FOLFOX versus fluorouracil and cisplatin in patients with oesophageal cancer (PRODIGE5/ACCORD17): final results of a randomised, phase 2/3 trial. Lancet Oncol 2014;15:305-314.</i>				



Regimen	Capecitabine and oxaliplatin				
Drug Combination	Dosage	Route of administration	Times	Frequency/ Duration	Notes
Oxaliplatin	85 mg/m <sup>2</sup>	IV	on Days 1, 15, and 29	for 3 doses	
Capecitabine	625 mg/m <sup>2</sup> BID	PO	on Days 1–5	weekly for 5 weeks	
<b>Ref.</b>	<i>Javle MM, Yang G, Nwogu CE, et al. Capecitabine, oxaliplatin and radiotherapy: a phase IB neoadjuvant study for esophageal cancer with gene expression analysis. Cancer Invest 2009;27:193-200.</i>				

Regimen	Fluorouracil and cisplatin				
Drug Combination	Dosage	Route of administration	Times	Frequency/ Duration	Notes
Cisplatin	75–100 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 28 days for 2 cycles with radiation followed by 2 cycles without radiation	
Fluorouracil	750–1000 mg/m <sup>2</sup>	IV	continuous infusion over 24 hours daily on Days 1–4		
<b>Ref.</b>	<i>Minsky BD, Pajak TF, Ginsberg RJ, et al. INT 0123 (Radiation Therapy Oncology Group 94-05) phase III trial of combined-modality therapy for esophageal cancer: high-dose versus standard-dose radiation therapy. J Clin Oncol 2002;20:1167-1174.</i>				

Regimen	Capecitabine and cisplatin				
Drug Combination	Dosage	Route of administration	Times	Frequency/ Duration	Notes
Cisplatin	30 mg/m <sup>2</sup>	IV	on Day 1	Weekly for 5 weeks	
Capecitabine	800 mg/m <sup>2</sup> BID	PO	on Days 1–5		



<b>Ref.</b>	<i>Lee SS, Kim SB, Park SI, et al. Capecitabine and cisplatin chemotherapy (XP) alone or sequentially combined chemoradiotherapy containing XP regimen in patients with three different settings of stage IV esophageal cancer. Jpn J Clin Oncol 2007;37:829-835.</i>
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<b>Regimen</b>	<b>Paclitaxel and fluoropyrimidine</b>				
Drug Combination	Dosage	Route of administration	Times	Frequency/ Duration	Notes
Paclitaxel	45–50 mg/m <sup>2</sup>	IV	on Day 1 weekly	Weekly for 5 weeks	
Fluorouracil	300 mg/m <sup>2</sup>	IV	continuous infusion daily on Days 1–5		
or					
Paclitaxel	45–50 mg/m <sup>2</sup>	IV	on Day 1	Weekly for 5 weeks	
Capecitabine	625–825 mg/m <sup>2</sup> BID	PO	on Days 1–5		
<b>Ref.</b>	Ajani JA, Winter K, Okawara GS, et al. Phase II trial of preoperative chemoradiation in patients with localized gastric adenocarcinoma (RTOG 9904): quality of combined modality therapy and pathologic response. J Clin Oncol 2006;24:3953-3958.				



## SYSTEMIC THERAPY Advanced/Metastasis therapy

### 說明:

1. Infusional fluorouracil can be replaced with capecitabine or UFUR(Tegafur/Uracyl)
2. UFUR 每日 300-600mg，分 2-3 次服用，服用 3 週休 1 週
3. Systemic therapy regimen and dosing schedules 是根據已發表的文獻與臨床實務經驗加以推論而來。

### HER2 positive

Regimen	Trastuzumab with chemotherapy(Fluoropyrimidine and oxaliplatin)				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Trastuzumab	8 mg/kg IV loading dose on Day 1 of cycle 1, then 6 mg/kg	IV	drip 90 mins, then 60 mins, day 1	every 21 days	
or					
Trastuzumab	6 mg/kg IV loading dose on Day 1 of cycle 1, then 4 mg/kg	IV	drip 90 mins, then 60 mins, day 1	every 14 days	
Ref.	<i>Bang YJ, Van Cutsem E, Feyereislova A, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. Lancet 2010;376:687-697.</i>				
+					
Oxaliplatin	85 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 14 days	
Leucovorin	200 mg/m <sup>2</sup>	IV	continuous infusion over 24 hours on Day 1		



Fluorouracil	2600 mg/m <sup>2</sup>	IV	continuous infusion over 24 hours on Day 1		
or					
Capecitabine	850-1000 mg/m <sup>2</sup> BID	PO	on Days 1–14	Cycled every 21 days	
Oxaliplatin	130 mg/m <sup>2</sup>	IV	drip 120 mins, on Day 1		
or					
Capecitabine	850-1000 mg/m <sup>2</sup> BID	PO	on Days 1–14	Cycled every 21 days	
Oxaliplatin	65mg/m <sup>2</sup>	IV	drip 90-120 mins, on Day 1 and 8		
or					
Capecitabine	625 mg/m <sup>2</sup> BID	PO	on Days 1–14	Cycled every 21 days	
Oxaliplatin	85 mg/m <sup>2</sup>	IV	on Day 1		
<b>Ref.</b>	<p>1.Al-Batran S-E, Hartmann JT, Probst S, et al. Phase III trial in metastatic gastroesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft Internistische Onkologie. <i>J Clin Oncol</i> 2008;26:1435-1442.</p> <p>2.Kim GM, Jeung HC, Rha SY, et al. A randomized phase II trial of S-1-oxaliplatin versus capecitabine- oxaliplatin in advanced gastric cancer. <i>Eur J Cancer</i> 2012;48:518-526.</p> <p>3.Hall PS, Swinson D, Waters JS, et al. Optimizing chemotherapy for frail and elderly patients (pts) with advanced gastroesophageal cancer (aGOAC): the GO2 phase III trial. <i>J Clin Oncol</i> 2019;37:4006.</p>				

<b>Regimen</b>	<b>Trastuzumab with chemotherapy(Fluoropyrimidine and cisplatin)</b>				
Drug Combination	Dosage	Route of administration	Times	Frequency/ Duration	Notes
Trastuzumab	8 mg/kg IV loading dose on Day 1 of cycle 1, then 6 mg/kg	IV	drip 90 mins, then 60 mins, day 1	every 21 days	
or					



Trastuzumab	6 mg/kg IV loading dose on Day 1 of cycle 1, then 4 mg/kg	IV	drip 90 mins, then 60 mins, day 1	every 14 days	
<b>Ref.</b>	<i>Bang YJ, Van Cutsem E, Feyereislova A, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2- positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. Lancet 2010;376:687- 697.</i>				
+					
Cisplatin	75–100 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 28 days	
Fluorouracil	750–1000 mg/m <sup>2</sup>	IV	continuous infusion over 24 hours daily on Days 1–4		
or					
Cisplatin	50 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 14 days	
Leucovorin	200 mg/m <sup>2</sup>	IV	IV continuous infusion over 24 hours daily on Day 1		
Fluorouracil	2600 mg/m <sup>2</sup>	IV	IV continuous infusion over 24 hours daily on Day 1		
or					
Cisplatin	80 mg/m <sup>2</sup>	IV	daily on Day 1	Cycled every 21 days	
Capecitabine	850–1000 mg/m <sup>2</sup> BID	PO	on Days 1–14		
<b>Ref.</b>	<p><i>1.Lorenzen S, Schuster T, Porschen R, et al. Cetuximab plus cisplatin-5-fluorouracil versus cisplatin-5-fluorouracil alone in first-line metastatic squamous cell carcinoma of the esophagus: a randomized phase II study of the Arbeitsgemeinschaft Internistische Onkologie. Ann Oncol 2009;20:1667-1673.</i></p> <p><i>2.Al-Batran S-E, Hartmann JT, Probst S, et al. Phase III trial in metastatic gastroesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft Internistische Onkologie. J Clin Oncol 2008;26:1435-1442.</i></p> <p><i>Bouche O, Raoul JL, Bonnetain F, et al. Randomized multicenter phase II trial of a biweekly regimen of fluorouracil and leucovorin (LV5FU2), LV5FU2 plus cisplatin, or LV5FU2 plus irinotecan in patients with previously untreated metastatic gastric cancer: a Federation Francophone de Cancerologie Digestive Group Study-FFCD 9803. J Clin Oncol</i></p>				



	2004;22:4319-4328. 3.Kang YK, Kang WK, Shin DB, et al. Capecitabine/cisplatin versus 5-fluorouracil/cisplatin as first-line therapy in patients with advanced gastric cancer: a randomised phase III noninferiority trial. <i>Ann Oncol</i> 2009;20:666-673.	
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Regimen	Trastuzumab and pembrolizumab with fluoropyrimidine and oxaliplatin or fluoropyrimidine and cisplatin (for PD-L1 CPS ≥1)					
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes	
Trastuzumab	8 mg/kg loading dose on Day 1 of cycle 1, then 6 mg/kg	IV	drip 90 mins, then 60 mins, day 1	every 21 days		
Pembrolizumab	200 mg	IV	on Day 1	Cycled every 3 weeks		
Ref.	<p>1. Janjigian YY, Kawazoe A, Bai Y, et al. Pembrolizumab plus trastuzumab and chemotherapy for HER2-positive gastric or gastro-oesophageal junction adenocarcinoma: interim analyses from the phase 3 KEYNOTE-811 randomised placebo-controlled trial. <i>Lancet</i> 2023;402:2197-2208.</p> <p>2. Bang YJ, Van Cutsem E, Feyereislova A, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2- positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. <i>Lancet</i> 2010;376:687- 697.</p> <p>3. Janjigian YY, Kawazoe A, Yanez P, et al. The KEYNOTE-811 trial of dual PD-1 and HER2 blockade in HER2-positive gastric cancer. <i>Nature</i> 2021;600:727-730.</p>					
+						
Capecitabine	850–1000 mg/m <sup>2</sup> BID	PO	Days 1–14	Cycled every 21 days		
Oxaliplatin	130 mg/m <sup>2</sup>	IV	drip 120 mins, on Day 1			
or						
Capecitabine	850-1000 mg/m <sup>2</sup> BID	PO	on Days 1–14	Cycled every 21 days		
Oxaliplatin	65mg/m <sup>2</sup>	IV	drip 90-120 mins, on Day 1 and 8			



or					
Cisplatin	80 mg/m <sup>2</sup>	IV	daily on Day 1	Cycled every 21 days	
Capecitabine	850–1000 mg/m <sup>2</sup> BID	PO	on Days 1–14		
<b>Ref.</b>	<i>Kim GM, Jeung HC, Rha SY, et al. A randomized phase II trial of S-1-oxaliplatin versus capecitabine- oxaliplatin in advanced gastric cancer. Eur J Cancer 2012;48:518-526.</i> <i>Kang YK, Kang WK, Shin DB, et al. Capecitabine/cisplatin versus 5-fluorouracil/cisplatin as first-line therapy in patients with advanced gastric cancer: a randomised phase III noninferiority trial. Ann Oncol 2009;20:666-673.</i>				

**HER2 negative**

Regimen	Fluoropyrimidine (fluorouracil or capecitabine), oxaliplatin, and nivolumab for PD-L1 CPS ≥1 (category 1 for PD-L1 CPS ≥5)				
Drug Combination	Dosage	Route of administration	Times	Frequency/ Duration	Notes
Nivolumab	240 mg	IV	on Day 1 (per study maximum of 2 years)	Cycled every 14 days	
Oxaliplatin	85 mg/m <sup>2</sup>	IV	on Day 1		
Leucovorin	400 mg/m <sup>2</sup>	IV	on Day 1		
Fluorouracil	400 mg/m <sup>2</sup>	IV Push	on Day 1		
Fluorouracil	1200 mg/m <sup>2</sup>	IV	IV continuous infusion over 24 hours daily on Days 1		
or					
Nivolumab	360 mg	IV	on Day 1 (per study maximum of 2 years)	Cycled every 21 days	



Capecitabine	850–1000 mg/m <sup>2</sup> BID	PO	Days 1–14		
Oxaliplatin	130 mg/m <sup>2</sup> or 65mg/m <sup>2</sup>	IV	drip 90-120 mins, on Day 1 or on Day 1 and 8		
<b>Ref.</b>	<i>Janjigian YY, Shitara K, Moehler M, et al. First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma (CheckMate 649): a randomised, open-label, phase 3 trial. Lancet 2021;398:27-40.</i>				

Regimen	Fluoropyrimidine, oxaliplatin, and pembrolizumab for PD-L1 CPS ≥1 (category 1 for PD-L1 CPS ≥5)					
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes	
Pembrolizumab	200 mg	IV	every 21 days for up to 2 years	Cycled every 21 days for up to 6 cycles (total 18 weeks)		
Capecitabine	850–1000 mg/m <sup>2</sup> BID	PO	on Days 1–14			
Oxaliplatin	130 mg/m <sup>2</sup> or 65mg/m <sup>2</sup>	IV	drip 90-120 mins, on Day 1 or on Day 1 and 8			
or						
Pembrolizumab	200 mg	IV	every 21 days for up to 2 years	Cycled every 14 days for up to 9 cycles (total 18 weeks)		
Oxaliplatin	85 mg/m <sup>2</sup>	IV	on Day 1			
Leucovorin	400 mg/m <sup>2</sup>	IV	on Day 1			
Fluorouracil	400 mg/m <sup>2</sup>	IV Push	on Day 1			
Fluorouracil	1200 mg/m <sup>2</sup>	IV	IV continuous infusion over 24 hours daily on Days 1			
<b>Ref.</b>	<i>Rha SY, Oh DY, Yanez P, et al. Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for HER2-negative advanced gastric cancer (KEYNOTE-859): a multicentre, randomised, double-blind, phase 3 trial. Lancet Oncol 2023;24:1181- 1195.</i>					



Regimen	Fluoropyrimidine (fluorouracil or capecitabine), cisplatin, and pembrolizumab for PD-L1 CPS $\geq 1$ (category 1 for PD-L1 CPS $\geq 5$ )					
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes	
Pembrolizumab	200 mg	IV	every 21 days for up to 2 years	Cycled every 21 days for up to 6 cycles		
Cisplatin	80 mg/m <sup>2</sup>	IV	on Day 1			
Fluorouracil	800 mg/m <sup>2</sup>	IV	continuous infusion over 24 hours daily on Days 1–5			
or						
Pembrolizumab	200 mg	IV	every 21 days for up to 2 years	Cycled every 21 days for up to 6 cycles (total of 18 weeks)		
Cisplatin	80 mg/m <sup>2</sup>	IV	on Day 1			
Capecitabine	850–1000 mg/m <sup>2</sup> BID	PO	on Days 1–14			
<b>Ref.</b>	<i>Rha SY, Oh DY, Yanez P, et al. Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for HER2-negative advanced gastric cancer (KEYNOTE-859): a multicentre, randomised, double-blind, phase 3 trial. Lancet Oncol 2023;24:1181- 1195.</i>					

### HER2 Negative, CLDN18.2 Positive

Regimen	Fluoropyrimidine (fluorouracil or capecitabine), oxaliplatin, and zolbetuximab-clzb				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Zolbetuximab-clzb	800 mg/m <sup>2</sup> first-dose only, subsequent doses 400 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 14 days	



Oxaliplatin	85 mg/m <sup>2</sup>	IV	on Day 1(per study maximum of 12 doses)	
Leucovorin	400 mg/m <sup>2</sup>	IV	on Day 1	
Fluorouracil	400 mg/m <sup>2</sup>	IV Push	on Day 1	
Fluorouracil	1200 mg/m <sup>2</sup>	IV	IV continuous infusion over 24 hours daily on Days 1	
or				
Zolbetuximab-clzb	800 mg/m <sup>2</sup> IV first-dose only, subsequent doses 600 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 21 days
Oxaliplatin	130 mg/m <sup>2</sup>	IV	on Day 1 (per study maximum of 8 doses)	
Capecitabine	850–1000 mg/m <sup>2</sup> BID	PO	on Days 1–14	
or				
Zolbetuximab-clzb	800 mg/m <sup>2</sup> IV first-dose only, subsequent doses 600 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 21 days
Oxaliplatin	65mg/m <sup>2</sup>	IV	drip 90-120 mins, on Day 1 and 8	
Capecitabine	850–1000 mg/m <sup>2</sup> BID	PO	on Days 1–14	



<b>Ref.</b>	<p>1. Shitara K, Lordick F, Bang YJ, et al. Zolbetuximab plus mFOLFOX6 in patients with CLDN18.2- positive, HER2-negative, untreated, locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma (SPOTLIGHT): a multicentre, randomised, double- blind, phase 3 trial. <i>Lancet</i> 2023;401:1655-1668.</p> <p>2. Shah MA, Shitara K, Ajani JA, et al. Zolbetuximab plus CAPOX in CLDN18.2-positive gastric or gastroesophageal junction adenocarcinoma: the randomized, phase 3 GLOW trial. <i>Nat Med</i> 2023;29:2133-2141.</p>
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### MSI-H/dMMR tumors (independent of PD-L1 status)

<b>Regimen</b>	<b>Pembrolizumab</b>				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Pembrolizumab	200 mg	IV	on Day 1	Cycled every 21 days (up to 2 years)	
<b>Ref.</b>	Fuchs CS, Doi T, Jang RW, et al. Safety and efficacy of pembrolizumab monotherapy in patients with previously treated advanced gastric and gastroesophageal junction cancer: Phase 2 clinical KEYNOTE-059 trial. <i>JAMA Oncol</i> 2018;4:e180013.				

<b>Regimen</b>	<b>Nivolumab and ipilimumab</b>				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Nivolumab	240 mg	IV	on Day 1	every 2 weeks	For 16 weeks, followed by Nivolumab 240 mg



Ipilimumab	1 mg/kg	IV	on Day 1	every 6 weeks	IV every 2 weeks or Nivolumab 480 mg IV every 4 weeks (maximum of 2 years)
<b>Ref.</b>	<i>Janjigian YY, Shitara K, Moehler M, et al. First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma (CheckMate 649): a randomised, open-label, phase 3 trial. Lancet 2021;398:27-40.</i>				

Regimen	Fluoropyrimidine (fluorouracil or capecitabine), oxaliplatin, and nivolumab					
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes	
Nivolumab	360 mg	IV	on Day 1 (per study maximum of 2 years)	Cycled every 21 days		
Capecitabine	850–1000 mg/m <sup>2</sup> BID	PO	on Days 1–14			
Oxaliplatin	130 mg/m <sup>2</sup>	IV	on Day 1			
or						
Nivolumab	240 mg	IV	on Day 1 (per study maximum of 2 years)	Cycled every 14 days		
Oxaliplatin	85 mg/m <sup>2</sup>	IV	on Day 1			
Leucovorin	400 mg/m <sup>2</sup>	IV	on Day 1			
Fluorouracil	400 mg/m <sup>2</sup>	IV Push	on Day 1			
Fluorouracil	1200 mg/m <sup>2</sup>	IV	IV continuous infusion over 24 hours daily on Days 1			
<b>Ref.</b>	<i>Janjigian YY, Shitara K, Moehler M, et al. First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma (CheckMate 649): a randomised, open-label, phase 3 trial. Lancet 2021;398:27-40.</i>					



Regimen	Fluoropyrimidine, oxaliplatin, and pembrolizumab					
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes	
Pembrolizumab	200 mg	IV	every 21 days for up to 2 years	Cycled every 21 days for up to 6 cycles (total 18 weeks)		
Capecitabine	850–1000 mg/m <sup>2</sup> BID	PO	on Days 1–14			
Oxaliplatin	130 mg/m <sup>2</sup> or 65mg/m <sup>2</sup>	IV	drip 90-120 mins, on Day 1 or on Day 1 and 8			
or						
Pembrolizumab	200 mg	IV	every 21 days for up to 2 years	Cycled every 14 days for up to 9 cycles (total 18 weeks)		
Oxaliplatin	85 mg/m <sup>2</sup>	IV	on Day 1			
Leucovorin	400 mg/m <sup>2</sup>	IV	on Day 1			
Fluorouracil	400 mg/m <sup>2</sup>	IV Push	on Day 1			
Fluorouracil	1200 mg/m <sup>2</sup>	IV	IV continuous infusion over 24 hours daily on Days 1			
<b>Ref.</b>	<i>Rha SY, Oh DY, Yanez P, et al. Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for HER2-negative advanced gastric cancer (KEYNOTE-859): a multicentre, randomised, double-blind, phase 3 trial. Lancet Oncol 2023;24:1181- 1195.</i>					

Regimen	Fluorouracil and irinotecan				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Irinotecan	180 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 14 days	
Leucovorin	400 mg/m <sup>2</sup>	IV	on Day 1		
Fluorouracil	400 mg/m <sup>2</sup>	IV Push	on Day 1		



Fluorouracil	1200 mg/m <sup>2</sup>	IV	IV continuous infusion over 24 hours daily on Days 1		
<b>Ref.</b>	<i>Guimbaud R, Louvet C, Ries P, et al. Prospective, randomized, multicenter, phase III study of fluorouracil, leucovorin, and irinotecan versus epirubicin, cisplatin, and capecitabine in advanced gastric adenocarcinoma: a French Intergroup (Federation Francophone de Cancerologie Digestive, Federation Nationale des Centres de Lutte Contre le Cancer, and Groupe Cooperateur Multidisciplinaire en Oncologie) study. J Clin Oncol 2014;32:3520-3526.</i>				

Regimen	Paclitaxel with or without carboplatin or cisplatin					
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes	
Paclitaxel	175 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 21 days		
Carboplatin	AUC 5	IV	on Day 1			
or						
Paclitaxel	135–200mg/m <sup>2</sup>	IV	on Day 1	Cycled every 21 days		
Cisplatin	75 mg/m <sup>2</sup>	IV	on Day 1			
or						
Paclitaxel	90 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 14 days		
Cisplatin	50 mg/m <sup>2</sup>	IV	on Day 1			
or						
Paclitaxel	200mg/m <sup>2</sup>	IV	on Day 1	Cycled every 21 days		
or						
Paclitaxel	80 mg/m <sup>2</sup>	IV	on Days 1, 8, and 15	Cycled every 28 days		
<b>Ref.</b>	<i>1. Gadgeel SM, Shields AF, Heilbrun LK, et al. Phase II study of paclitaxel and carboplatin in patients with advanced gastric cancer. Am J Clin Oncol 2003;26:37-41.</i>					



	<p>2. Ilson DH, Forastiere A, Arquette M, et al. A phase II trial of paclitaxel and cisplatin in patients with advanced carcinoma of the esophagus. <i>Cancer J</i> 2000;6:316-323.</p> <p>3. Petrasch S, Welt A, Reinacher A, et al. Chemotherapy with cisplatin and paclitaxel in patients with locally advanced, recurrent or metastatic oesophageal cancer. <i>Br J Cancer</i> 1998;78:511-514.</p> <p>4. Ajani JA, Ilson DH, Daugherty K, et al. Activity of taxol in patients with squamous cell carcinoma and adenocarcinoma of the esophagus. <i>J Natl Cancer Inst</i> 1994;86:1086-1091.</p> <p>5. Hironaka S, Ueda S, Yasui H, et al. Randomized, open-label, phase III study comparing irinotecan with paclitaxel in patients with advanced gastric cancer without severe peritoneal metastasis after failure of prior combination chemotherapy using fluoropyrimidine plus platinum: WJOG 4007 trial. <i>J Clin Oncol</i> 2013;31:4438-4444.</p>
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Regimen	Docetaxel with or without cisplatin					
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes	
Docetaxel	60-72 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 21 days		
Cisplatin	70-75 mg/m <sup>2</sup>	IV	on Day 1			
or						
Docetaxel	60-75mg/m <sup>2</sup>	IV	on Day 1	Cycled every 21 days		
<b>Ref.</b>	<p>1. Ajani JA, Fodor MB, Tjulandin SA, et al. Phase II multi-institutional randomized trial of docetaxel plus cisplatin with or without fluorouracil in patients with untreated, advanced gastric, or gastroesophageal adenocarcinoma. <i>J Clin Oncol</i> 2005;23:5660-5667.</p> <p>Kim JY, Do YR, Park KU, et al. A multi-center phase II study of docetaxel plus cisplatin as first-line therapy in patients with metastatic squamous cell esophageal cancer. <i>Cancer Chemother Pharmacol</i> 2010;66:31-36.</p> <p>2. Ford ER, Marshall A, Bridgewater JA, et al. Docetaxel versus active symptom control for refractory oesophagogastric adenocarcinoma (COUGAR-02): an open-label, phase 3 randomised controlled trial. <i>Lancet Oncol</i> 2014;15:78-86.</p> <p>Albertsson M, Johansson B, Friesland S, et al. Phase II studies on docetaxel alone every third week, or weekly in combination with gemcitabine in patients with primary locally advanced, metastatic, or recurrent esophageal cancer. <i>Med Oncol</i> 2007;24:407-412.</p>					

Regimen	Fluoropyrimidine				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Leucovorin	400 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 14 days	



Fluorouracil	400 mg/m <sup>2</sup>	IV Push	on Day 1		
Fluorouracil	1200 mg/m <sup>2</sup>	IV	IV continuous infusion over 24 hours daily on Days 1		
or					
Capecitabine	850–1000 mg/m <sup>2</sup> BID	PO	on Days 1–14	Cycled every 21 days	
<b>Ref.</b>	<p>1. Bouche O, Raoul JL, Bonnetain F, et al. Randomized multicenter phase II trial of a biweekly regimen of fluorouracil and leucovorin (LV5FU2), LV5FU2 plus cisplatin, or LV5FU2 plus irinotecan in patients with previously untreated metastatic gastric cancer: a Federation Francophone de Cancerologie Digestive Group Study-FFCD 9803. <i>J Clin Oncol</i> 2004;22:4319-4328.</p> <p>2. Ohtsu A, Shimada Y, Shirao K, et al. Randomized phase III trial of fluorouracil alone versus fluorouracil plus cisplatin versus uracil and tegafur plus mitomycin in patients with unresectable, advanced gastric cancer: The Japan Clinical Oncology Group Study (JCOG9205). <i>J Clin Oncol</i> 2003;21:54-59.</p> <p>3. Hong YS, Song SY, Lee SI, et al. A phase II trial of capecitabine in previously untreated patients with advanced and/or metastatic gastric cancer. <i>Ann Oncol</i> 2004;15:1344-1347.</p>				

Regimen	Docetaxel, cisplatin or oxaliplatin, and fluorouracil				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Docetaxel	40 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 14 days	
Leucovorin	400 mg/m <sup>2</sup>	IV	on Day 1		
Fluorouracil	400 mg/m <sup>2</sup>	IV	on Day 1		
Fluorouracil	1000 mg/m <sup>2</sup>	IV	IV continuous infusion over 24 hours daily on Days 1		
Cisplatin	40 mg/m <sup>2</sup>	IV	on Day 3		
or					



Docetaxel	50 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 14 days	
Oxaliplatin	85 mg/m <sup>2</sup>	IV	on Day 1		
Fluorouracil	1200 mg/m <sup>2</sup>	IV	IV continuous infusion over 24 hours daily on Days 1		
<b>Ref.</b>	<p>1. Shah MA, Janjigian YY, Stoller R, et al. Randomized multicenter phase II study of modified docetaxel, cisplatin, and fluorouracil (DCF) versus DCF plus growth factor support in patients with metastatic gastric adenocarcinoma: a study of the US Gastric Cancer Consortium. <i>J Clin Oncol</i> 2015;33:3874-3879.</p> <p>2. Blum Murphy MA, Qiao W, Mewada N, et al. A phase I/II study of docetaxel, oxaliplatin, and fluorouracil (D-FOX) chemotherapy in patients with untreated locally unresectable or metastatic adenocarcinoma of the stomach and gastroesophageal junction. <i>Am J Clin Oncol</i> 2018;41:321-325.</p>				



## Second-line and subsequent therapy

Regimen	Ramucirumab and paclitaxel				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Ramucirumab	8 mg/kg	IV	on Days 1 and 15	Cycled every 28 days	
Paclitaxel	80 mg/m <sup>2</sup>	IV	on Days 1, 8, and 15		
<b>Ref.</b>	<i>Wilke H, Muro K, Van Cutsem E, et al. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial. Lancet Oncol 2014;15:1224-1235.</i>				

Regimen	Fam-trastuzumab deruxtecan-nxki				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Fam-trastuzumab deruxtecan-nxki	6.4 mg/kg	IV	on Day 1	cycled every 21 days	
<b>Ref.</b>	<i>Shitara K, Bang YJ, Iwasa S, et al. Trastuzumab deruxtecan in previously treated HER2-positive gastric cancer. N Engl J Med 2020;382:2419-2430.</i>				

Regimen	Taxane				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Docetaxel	60-75 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 21 days	
or					
Paclitaxel	135–175 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 21 days	
or					
Paclitaxel	80 mg/m <sup>2</sup>	IV	on Days 1, 8, and 15	Cycled every 28 days	



<b>Ref.</b>	<p>1. Ford ER, Marshall A, Bridgewater JA, et al. Docetaxel versus active symptom control for refractory oesophagogastric adenocarcinoma (COUGAR-02): an open-label, phase 3 randomised controlled trial. <i>Lancet Oncol</i> 2014;15:78-86.</p> <p>Albertsson M, Johansson B, Friesland S, et al. Phase II studies on docetaxel alone every third week, or weekly in combination with gemcitabine in patients with primary locally advanced, metastatic, or recurrent esophageal cancer. <i>Med Oncol</i> 2007;24:407-412.</p> <p>2. Ajani JA, Ilson DH, Daugherty K, et al. Activity of taxol in patients with squamous cell carcinoma and adenocarcinoma of the esophagus. <i>J Natl Cancer Inst</i> 1994;86:1086-1091.</p> <p>3. Hironaka S, Ueda S, Yasui H, et al. Randomized, open-label, phase III study comparing irinotecan with paclitaxel in patients with advanced gastric cancer without severe peritoneal metastasis after failure of prior combination chemotherapy using fluoropyrimidine plus platinum: WJOG 4007 trial. <i>J Clin Oncol</i> 2013;31:4438-4444.</p>
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<b>Regimen</b>	<b>Irinotecan</b>					
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes	
Irinotecan	150–180 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 14 days		
or						
Irinotecan	125 mg/m <sup>2</sup>	IV	on Days 1 and 8	Cycled every 21 days		
or						
Irinotecan	250–350 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 21 days		
<b>Ref.</b>	<p>1. Hironaka S, Ueda S, Yasui H, et al. Randomized, open-label, phase III study comparing irinotecan with paclitaxel in patients with advanced gastric cancer without severe peritoneal metastasis after failure of prior combination chemotherapy using fluoropyrimidine plus platinum: WJOG 4007 trial. <i>J Clin Oncol</i> 2013;31:4438-4444.</p> <p>Sym SJ, Hong J, Park J, et al. A randomized phase II study of biweekly irinotecan monotherapy or a combination of irinotecan plus 5-fluorouracil/leucovorin (mFOLFIRI) in patients with metastatic gastric adenocarcinoma refractory to or progressive after first-line chemotherapy. <i>Cancer Chemother Pharmacol</i> 2013;71:481-488.</p> <p>2. Fuchs CS, Moore MR, Harker G, et al. Phase III comparison of two irinotecan dosing regimens in second-line therapy of metastatic colorectal cancer. <i>J Clin Oncol</i> 2003;21:807-814.</p> <p>3. Thuss-Patience PC, Kretschmar A, Bichev D, et al. Survival advantage for irinotecan versus best supportive care as second-line chemotherapy in gastric cancer--a randomised phase III study of the Arbeitsgemeinschaft Internistische Onkologie (AIO). <i>Eur J Cancer</i> 2011;47:2306-2314.</p>					



Regimen	Fluorouracil and irinotecan				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Irinotecan	180 mg/m <sup>2</sup>	IV	on Day 1	Cycled every 14 days	
Leucovorin	400 mg/m <sup>2</sup>	IV	on Day 1		
Fluorouracil	400 mg/m <sup>2</sup>	IV Push	on Day 1		
Fluorouracil	1200 mg/m <sup>2</sup>	IV	IV continuous infusion over 24 hours daily on Days 1 and 2		
<b>Ref.</b>	<i>Sym SJ, Hong J, Park J, et al. A randomized phase II study of biweekly irinotecan monotherapy or a combination of irinotecan plus 5-fluorouracil/leucovorin (mFOLFIRI) in patients with metastatic gastric adenocarcinoma refractory to or progressive after first-line chemotherapy. Cancer Chemother Pharmacol 2013;71:481-488.</i>				

Regimen	Ramucirumab				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Ramucirumab	8 mg/kg	IV	on Day 1	Cycled every 14 days	
<b>Ref.</b>	<i>Fuchs CS, Tomasek J, Yong CJ, et al. Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): an international, randomised, multicentre, placebo-controlled, phase 3 trial. Lancet 2014;383:31-39.</i>				

Regimen	Irinotecan and cisplatin				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Irinotecan	65 mg/m <sup>2</sup>	IV	on Days 1 and 8	Cycled every 21 days	
Cisplatin	25–30 mg/m <sup>2</sup>	IV	on Days 1 and 8		



<b>Ref.</b>	<i>Enzinger PC, Burtness BA, Niedzwiecki D, et al. CALGB 80403 (Alliance)/E1206: a randomized phase II study of three chemotherapy regimens plus cetuximab in metastatic esophageal and gastroesophageal junction cancers. J Clin Oncol 2016;34:2736-2742. Ison DH. Phase II trial of weekly irinotecan/cisplatin in advanced esophageal cancer. Oncology (Williston Park 2004;18:22-25.</i>
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<b>Regimen</b>		<b>Fluorouracil and irinotecan + ramucirumab</b>			
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Ramucirumab	8 mg/kg	IV	on Day 1	Cycled every 14 days	
Irinotecan	180 mg/m <sup>2</sup>	IV	on Days 1		
Leucovorin	400 mg/m <sup>2</sup>	IV	on Day 1		
Fluorouracil	400 mg/m <sup>2</sup>	IV Push	on Day 1		
Fluorouracil	1200 mg/m <sup>2</sup>	IV	IV continuous infusion over 24 hours daily on Days 1 and 2		
<b>Ref.</b>	<i>Tabernero J, Yoshino T, Cohn AL, et al. Ramucirumab versus placebo in combination with second-line FOLFIRI in patients with metastatic colorectal carcinoma that progressed during or after first-line therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine (RAISE): a randomised, double-blind, multicentre, phase 3 study. Lancet Oncol 2015;16:499-508.</i>				

<b>Regimen</b>		<b>Irinotecan and ramucirumab</b>			
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Irinotecan	150 mg/m <sup>2</sup>	IV	on Days 1	Cycled every 14 days	
Ramucirumab	8 mg/kg	IV	on Day 1		
<b>Ref.</b>	<i>Sakai D, Boku N, Kodera Y, et al. An intergroup phase III trial of ramucirumab plus irinotecan in third or more line beyond progression after ramucirumab for advanced gastric cancer (RINDBeRG trial). J Clin Oncol 2018;36:TPS4138.</i>				



Regimen	Docetaxel and irinotecan				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Docetaxel	30 mg/m <sup>2</sup>	IV	on Days 1 and 8	Cycled every 21 days	
Irinotecan	50 mg/m <sup>2</sup>	IV	on Days 1 and 8		
<b>Ref.</b>	<i>Burtness B, Gibson M, Egleston B, et al. Phase II trial of docetaxel-irinotecan combination in advanced esophageal cancer. Ann Oncol 2009;20:1242-1248.</i>				

Regimen	TS-1+Docetaxel				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
TS-1	40mg- 60mg bid	PO	on Day1-10	every 2 weeks	
Docetaxel	40mg/m <sup>2</sup>	IV	on Day 1		
<b>Ref.</b>	<i>Yoshida, K., Kodera, Y., Kochi, M., Ichikawa, W., Kakeji, Y., Sano, T., ... &amp; Kaji, M. (2019). Addition of Docetaxel to Oral Fluoropyrimidine Improves Efficacy in Patients With Stage III Gastric Cancer: Interim Analysis of JACCRO GC-07, a Randomized Controlled Trial. Journal of Clinical Oncology,37(15), 1296-1304.</i>				

Regimen	Pembrolizumab(for MSI-H/dMMR tumors or TMB-H [≥10 mutations/megabase] tumors)				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Pembrolizumab	200 mg	IV	on Day 1	Cycled every 21 days	
<b>Ref.</b>	<i>Fuchs CS, Doi T, Jang RW, et al. Safety and efficacy of pembrolizumab monotherapy in patients with previously treated advanced gastric and gastroesophageal junction cancer: Phase 2 clinical KEYNOTE-059 trial. JAMA Oncol 2018;4:e180013.</i>				



Regimen	Dabrafenib and trametinib				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Dabrafenib	150 mg	PO	twice daily	twice daily	for BRAF V600E-mutated tumors
Trametinib	2 mg	PO	daily	daily	
<b>Ref.</b>	<i>Shin, J. E., An, H. J., Park, H. S., Kim, H., &amp; Shim, B. Y. (2022). Efficacy of dabrafenib/trametinib in pancreatic ductal adenocarcinoma with BRAF NVTAP deletion: A case report. Frontiers in Oncology, 12, 976450.</i>				

### Third-line therapy

Regimen	Trifluridine and tipiracil				
Drug Combination	Dosage	Route of administration	Times	Frequency/Duration	Notes
Trifluridine and tipiracil	35 mg/m <sup>2</sup> up to a maximum dose of 80 mg per dose (based on the trifluridine component) BID	PO	daily on Days 1–5 and 8–12	Repeat every 28 days	
<b>Ref.</b>	<i>Shitara K, Doi T, Dvorkin M, et al. Trifluridine/tipiracil versus placebo in patients with heavily pretreated metastatic gastric cancer (TAGS): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol 2018;19:1437-1448.</i>				



## Target therapy

## For NTRK gene fusion-positive tumors

<b>Regimen</b>	<b>Entrectinib</b>
<b>藥名(學名)</b>	Entrectinib 600 mg PO once daily
<b>Ref.</b>	<i>Doebele RC, Drilon A, Paz-Ares L, et al. Entrectinib in patients with advanced or metastatic NTRK fusion- positive solid tumours: integrated analysis of three phase 1-2 trials. Lancet Oncol 2020;21:271-282.</i>

<b>Regimen</b>	<b>Larotrectinib</b>
<b>藥名(學名)</b>	Larotrectinib 100 mg PO twice daily
<b>Ref.</b>	<i>Drilon A, Laetsch TW, Kummar S, et al. Efficacy of larotrectinib in TRK fusion-positive cancers in adults and children. N Engl J Med 2018;378:731-739.</i>

<b>Regimen</b>	<b>Repotrectinib</b>
<b>藥名(學名)</b>	Repotrectinib 160 mg PO Daily Days 1–14 of cycle 1 160 mg PO BID Days 15–28 of cycle 1 160 mg PO BID Days 1-28 of cycle 2 and beyond Cycled every 28 days
<b>Ref.</b>	<i>Solomon BJ, Drilon A, Lin JJ, et al. 1372P Repotrectinib in patients (pts) with NTRK fusion- positive (NTRK+) advanced solid tumors, including NSCLC: Update from the phase I/II TRIDENT-1 trial. Annals of Oncology 2023;34:S787-S788.</i>

**For BRAF V600E-mutated tumors**

<b>Regimen</b>	<b>Dabrafenib and trametinib</b>
<b>藥名</b>	Dabrafenib and trametinib Dabrafenib 150 mg PO twice daily Trametinib 2 mg PO daily <sup>68</sup>
<b>Ref.</b>	<i>Salama AKS, Li S, Macrae ER, et al. Dabrafenib and trametinib in patients with tumors with BRAF(V600E) mutations: Results of the NCI-MATCH trial subprotocol H. J Clin Oncol 2020;38:3895-3904.</i>

**For RET gene fusion-positive tumors**

<b>Regimen</b>	<b>Selpercatinib</b>
<b>藥名(學名)</b>	Selpercatinib Patients $\geq$ 50 kg: 160 mg PO twice daily Patients $<$ 50 kg: 120 mg PO twice daily
<b>Ref.</b>	<i>Subbiah V, Wolf J, Konda B, et al. Tumour-agnostic efficacy and safety of selpercatinib in patients with RET fusion-positive solid tumours other than lung or thyroid tumours (LIBRETTO-001): a phase 1/2, open-label, basket trial. Lancet Oncol 2022;23:1261-1273.</i>



## 十四、放射線治療原則

### Radiotherapy with external beam

1. Dose: 45-50Gy (1.8Gy per fraction, per day)
2. Treatment field:
3. Proximal one-third/Cardia/GE junction
  - A. Proximal: gastric lesion, 3~5 cm margin of distal esophagus, medial left hemidiaphragm and adjacent pancreatic body.
  - B. Nodal area: adjacent paraesophageal, perigastric, suprapancreatic, and celiac lymph nodes.
4. Middle one third/Body
  - A. Proximal: gastric lesion, pancreatic body.
  - B. Nodal area: adjacent perigastric, suprapancreatic, celiac, splenic hilar, porta hepatic and pancreatoduodenal lymph nodes.
5. Third one third/Antrum/Pylorus
  - A. Proximal: gastric lesion and head of pancreas. If gross lesion extent to gastroduodenal junction, 3~5 cm margin of duodenal stump.
  - B. Nodal area: Perigastric, suprapancreatic, celiac, porta hepatic and pancreatoduodenal lymph nodes.

## 十五、安寧緩和照護原則

若預期疾病難以治癒時，病人存活期小於 6 個月便適合安寧療護(Pomeranz & Brustman, 2005；Waldrop & Rinfrette, 2009)。若藉由症狀、檢驗數據、及確切的腫瘤診斷，證實臨床上該惡性腫瘤已經廣泛侵犯、或進展快速；功能分數(Palliative Performance Scale) 低於 70%；拒絕進一步腫瘤治癒性治療，或者在治療之下仍持續惡化者，即可轉介緩和醫療團隊（彭等，2006）。



## 十六、完治率定義

癌別	分期	治療方式	完治率定義
胃癌	原位癌、 第 I 期	OP(包含 ESD、EMR)	手術完成，即可算首次完成治療
	第 II 期	OP+輔助性化療	手術+輔助性化療滿 6 個月，即可算首次治療完成(治療中轉安寧，算完成治療)
	第 III 期	OP+輔助性化療	手術+輔助性化療滿 3 個月，即可算首次治療完成(治療中轉安寧，算完成治療)
	第 IV 期	Palliatiave OP	手術完成，即可算首次完成治療
		Palliatiave 化療 Palliatiave 化療+免疫	療程滿 3 個月就可算完成治療(治療中轉安寧，算完成治療)

備註:以上期別個案治療期間，因為疾病進展無法繼續治療，改採取安寧緩和治療，即可以算首次治療已完成



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