

高雄榮民總醫院

胃癌診療指引

2023年02月21日 第一版

胃癌醫療團隊共同擬訂

注意事項：這個診療原則主要作為醫師和其他保健專家診療癌症病人參考之用。假如你是一個癌症病人，直接引用這個診療原則並不恰當，只有你的醫師才能決定給你最恰當的治療。

修訂指引

- 本共識參考國家衛生研究院於2012年1月出版之胃癌臨床指引、JGCA及其他參考文獻，於2023. 2. 21由胃癌團隊成員共同討論後修訂。

會議討論

上次會議：2022/02/22

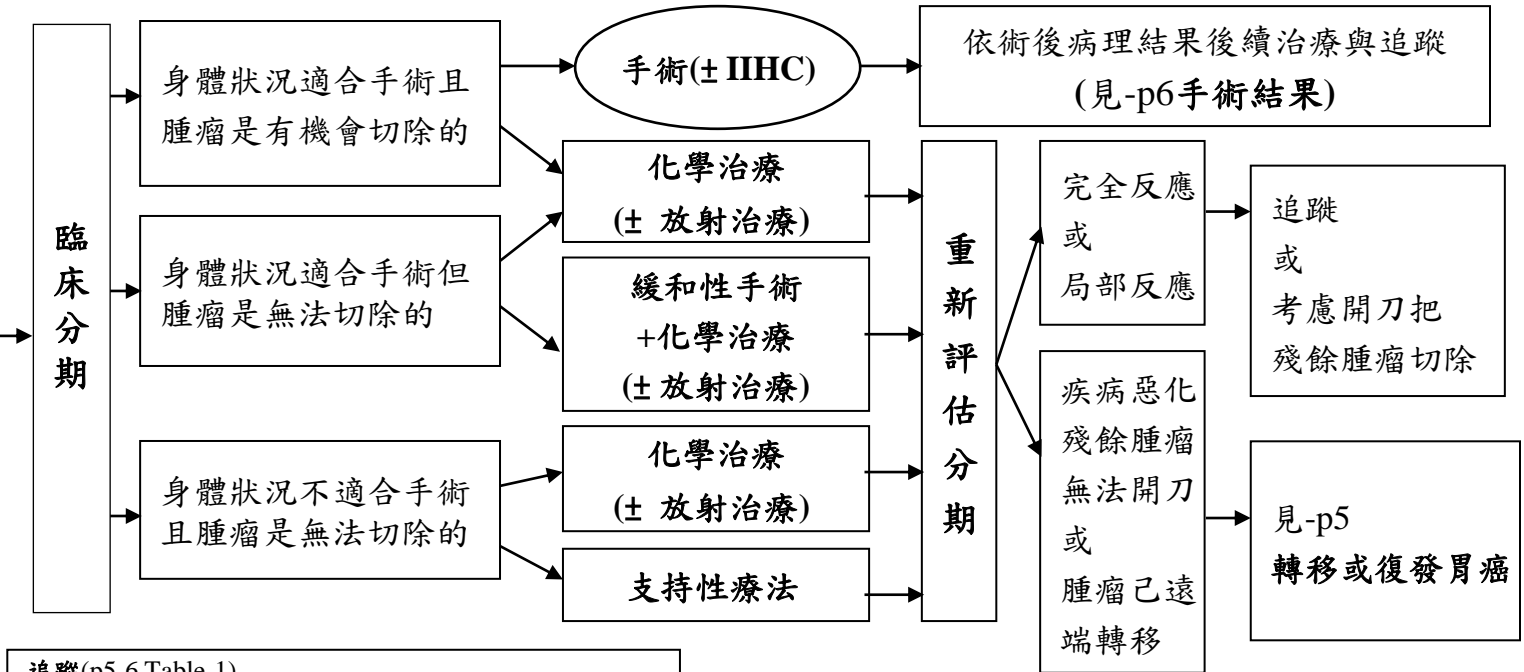
本共識與上一版的差異

| 上一版 | 新版 |
|-----|--|
| 無 | <ol style="list-style-type: none">1. 新增Her-2/neu immunostain、IHC:MMR、PD-L1評估選項。(page 4)2. 轉移或復發治療新增±免疫治療。(page 5) |

胃腺癌

| 評估 | 診斷 | 治療 | 追蹤 |
|----|----|----|----|
|----|----|----|----|

- 病史、理學檢查
 - 營養及日常體能狀態
 - 胸部X光
 - 血液常規
 - 電解質及肝腎功能
 - 腫瘤指標 (CEA, Ca19-9)
 - * 腹部(胃)電腦斷層攝影
 - 上消化道內視鏡及生檢 (Biopsy)
-
- 必要時評估→
 - * 正子攝影
 - * 內視鏡超音波
 - 腹腔鏡
 - 上消化道攝影
 - Her-2/neu immunostain
 - IHC: MMR、PD-L1
-
- * 與期別相關之主要檢查



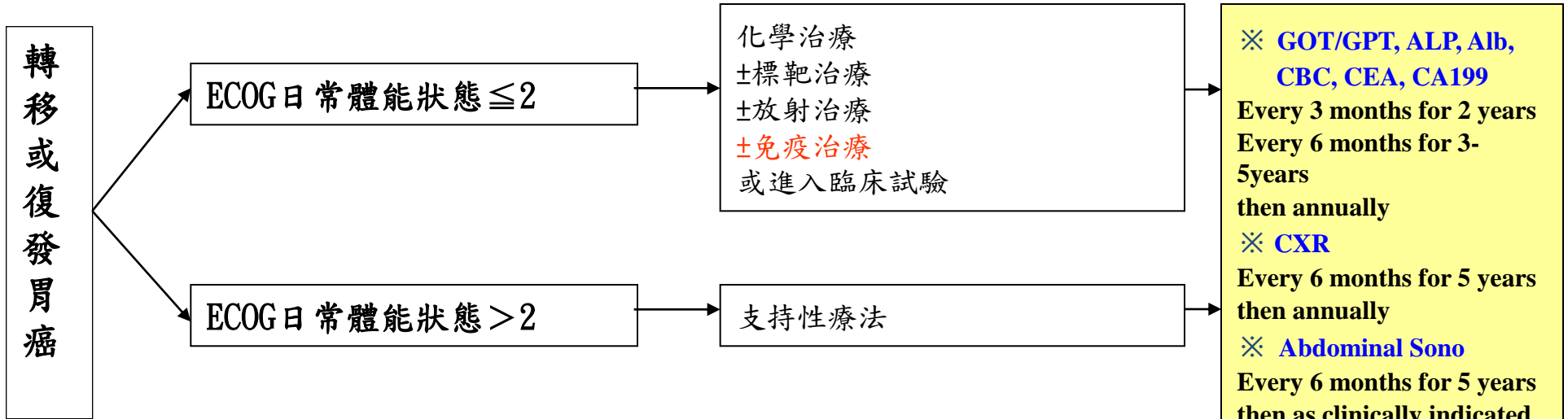
- 追蹤(p5-6 Table-1)
- 手術(p7-8 Table-2)
- IHC(p9 Table-3)
- 化學治療(p10-18 table-4.1、4.2、4.3、4.4、4.5、4.6)
- 標靶治療(p19 table-5)
- 免疫治療(p20 table-6)
- 放射治療(p21 table-7)
- 癌症藥物停藥準則(p22 table-8)

胃腺癌

高雄榮民總醫院
臨床診療指引

2023年第一版

| 評估 | 診斷 | 治療 | 追蹤 |
|----|----|----|----|
|----|----|----|----|



| 分數 | ECOG |
|----|--------------------------------|
| 0 | 無症狀 |
| 1 | 有症狀，但可以正常活動，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 | 長期完全臥床 |
| 5 | 死亡 |

| 評估 | 診斷 | 治療 | 追蹤 |
|--|---|--|--|
| <p>手術結果</p> <ul style="list-style-type: none"> R0切除 R1切除 R2切除 遠端轉移 | <ul style="list-style-type: none"> Tis, T1N0 T2, T3, T4 或淋巴轉移 化學治療 (±放射治療) 化學治療 (±放射治療) | <ul style="list-style-type: none"> 觀察 觀察或輔助性化學治療 (±放射治療) 見-p5 轉移或復發胃癌 | <ul style="list-style-type: none"> ※ GOT/GPT, ALP, Alb, CBC, CEA, CA199 Every 3 months for 2 years Every 6 months for 3-5 years then annually ※ CXR Every 6 months for 5 years then annually ※ Abdominal Sono Every 6 months for 5 years then as clinically indicated ※ Panendoscope Annually for 5 years then as clinically indicated ※ Abdominal CT Annually for 5 years then as clinically indicated |

Table-1 術後追蹤建議表

Table-2手術建議表(1)

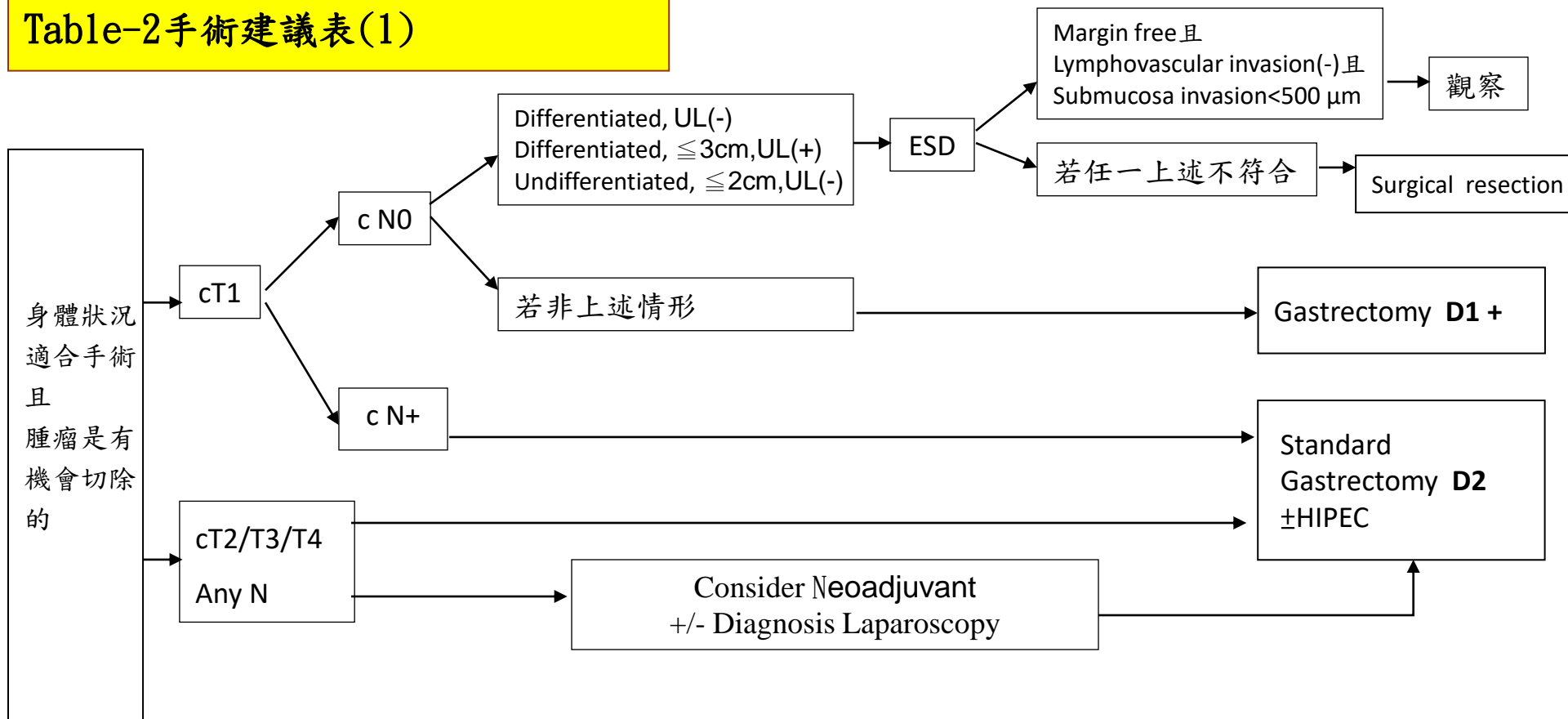


Table-2 手術建議表(2)

Type of Gastrectomy with lymph node dissection

| Gastrectomy | Extent of LN dissection | 圖表 |
|--------------------------------|--|----|
| Total gastrectomy | D1 :Nos 1-7 D1+:D1+Nos 8a,9,11p D2 :D1+Nos 8a,9,10,11p,11d,12a For tumor invading the esophagus D1+Includes No,110 ¹ . D2 includes Nos.19,20,110,and 111 | |
| Distal gastrectomy | D1 :Nos 1,3,4sb,4d,5,6,7 D1+:D1+Nos 8a, 9 D2 :D1+Nos 8a,9,11p,12a | |
| Pylorus-preserving gastrectomy | D1 :Nos 1,3,4sb,4d,6,7 D1+:D1+Nos 8a, 9 | |
| Proximal gastrectomy | D1 :Nos 1,2,3a,4sa,4sb,7 D1+:D1+Nos 8a, 9,11p | |

Table-3 IHC 適應症建議表

Hyperthermic IntraPeritoneal Chemotherapy (HIPEC)

※Indication : \geq T4a

※Regimen 1: (41-42°C for 20-60 minutes)

Cisplatin 90 mg 【IP-1】

Etoposide 90 mg

Mitomycin C 30 mg

Reference :No 4-7/strength of Evidence :Level I

※Regimen 2: (41-42°C for 20-60 minutes)

Paclitaxel 80mg/m² 【IP Paclitaxel, high dose】

Reference : No 28/strength of Evidence :Level IIB

Table-4.1 化學治療處方建議表：輔助化療

| Adjuvant chemotherapy | Schedule | Reference (No)/ strength of Evidence |
|---|--|---|
| TS-1 40-60mg , po, bid (ACTS-GC trial) (po 4 weeks on, 2 weeks off/or po 2 weeks on, 1 weeks off) BSA >1.5m ² : 60mg bid;1.25m ² -1.5m ² : 50mg bid;<1.25m ² : 40mg bid | Q42 d /cycle For 12 months | No.8 / Level I |
| UFUR 2#, po, bid (NSAS-GC trial) | For 16 months | No.9 / Level I |
| Oxaliplatin 130 mg/m ² , IV,D1 【XO】 (CLASSIC trial) Xeloda 2# po QAM,3# po QPM (Day1-14) (825-1000mg/m ² /次) | Q21 d x 8-12cycles | No.10 / Level I |
| Oxaliplatin 100mg/m ² , IV, D1 【SOX】 TS-1 40-60mg , po , bid , D1~14 BSA >1.5m ² : 60mg/bid ; 1.25-1.5m ² : 50mg/bid ; <1.25m ² : 40mg/bid | TS-1(2 weeks on, 1 weeks off) →SOX Q21 d x 8 cycles | No.31 / Level II |
| Docetaxel 50mg/m ² , IV, D1 【DOX】 Oxaliplatin 100mg/m ² , IV, D1 Xeloda 1.25#/m ² (625mg/m ²), po, bid , D1~14 | Q21d x 8 cycles | No.34 / Level IB |

Table-4.1 化學治療處方建議表：輔助化療

| Adjuvant chemotherapy | Schedule | Reference (No)/ strength of Evidence |
|---|---|---|
| Taxotere 50mg/m ² , IV, D1 【FLOT】 Oxaliplatin 85mg/m ² , IV, D1 Leucovorin 200mg/m ² , IV, D1 5-FU 2600mg/m ² , IV, D1 | Q14d x 4-8 cycles 術前4cycles 術後4cycles | No.35 / Level I |
| Oxaliplatin 85mg/m ² , IV, D1 【FOLFOX】 Leucovorin 400mg/m ² , IV, D1 5-FU 400mg/m ² , IV, D1 , 5-FU 2400-3000mg/m ² , IV, D1-2 | Q14d x 8-12cycles | No.36 / Level I |
| TS-1 + docetaxel *stage III 【DS】 Docetaxel 40mg/m ² , IV, D1 TS-1 80-120mg/day , po, bid , D1~14 BSA >1.5m ² : 60mg/bid ; 1.25- 1.5m ² : 50mg/bid ; <1.25m ² : 40mg/bid | Q21d x 8 cycles 1 st cycle TS-1 2 nd ~7 th TS-1+ docetaxel 8 th 起TS-1 up to 1year | No.37 / Level I |

Table-4.2 化學治療處方建議表：術前輔助化療

| Neoadjuvant chemotherapy | Schedule | Reference (No)/ strength of Evidence |
|--|---|---|
| Oxaliplatin 130 mg/m ² , IV,D1 【 XO 】 (CLASSIC trial) Xeloda 2# po QAM,3# po QPM (Day1-14) (825-1000mg/m ² /次) | Q21 d x 8-12cycles | No.10 / Level I |
| Docetaxel 50mg/m ² , IV, D1 【DOX】 Oxaliplatin 100mg/m ² , IV, D1 Xeloda 1.25#/m ² (625mg/m ²) PO, D1-14 | Q21d x 2-4 cycles | No.34 / Level IB |
| Taxotere 50mg/m ² , IV, D1 【FLOT】 Oxaliplatin 85mg/m ² , IV, D1 Leucovorin 200mg/m ² , IV, D1 5-FU 2600mg/m ² , IV, D1 | Q14d x 4-8 cycles 術前4cycles 術後4cycles | No.35 / Level I |
| Oxaliplatin 85mg/m ² , IV, D1 【FOLFOX】 Leucovorin 400mg/m ² , IV, D1 5-FU 400mg/m ² , IV, D1 , 5-FU 2400-3000mg/m ² , IV, D1-2 | Q14d /cycle | No.36 / Level I |

Table-4.3 化學治療處方建議表：轉移癌

| Chemotherapy for unresectable/recurrent disease | Schedule | Reference (No)/ strength of Evidence |
|---|-------------------------------|---|
| TS-1 40-60mg , po, bid (吃4周休2周或吃2周休1周) BSA $\geq 1.5\text{m}^2$: 60mg bid ; 1.25m^2 - 1.5m^2 : 50mg bid ; $<1.25\text{m}^2$: 40mg bid | Q42 d /cycle For 12 months | No.8 / Level I |
| UFUR 2# po bid | For 16 months | No.13 / Level I |
| Oxaliplatin 130 mg/m ² , IV,D1 【XO】 (CLASSIC trial) Xeloda 2# po QAM,3# po QPM (Day1-14) (825-1000mg/m ² /次) | Q21 d x 8- 12cycles | No.10 / Level I |
| Cisplatin 60-80 mg/m ² , IV, D1 【FP】 【FP-1】 5-FU 800-1000mg/m ² , IV, D1-5 | Q21 d x 8-12cycles | No.15 / Level II |

Table-4.3 化學治療處方建議表：轉移癌

| Chemotherapy for unresectable/recurrent disease | Schedule | Reference (No)/ strength of Evidence |
|--|---|---|
| Docetaxel 50mg/m ² , IV, D1 【D-FOX】 Oxaliplatin 85mg/m ² , IV, D1 5-FU 1100mg/m ² , IV, D1-2 | Q14d x 6-8 cycles /Until progression | No.30 /Level II |
| Docetaxel 50mg/m ² , IV, D1 【DOX】 Oxaliplatin 100mg/m ² , IV, D1 Xeloda 1.25#/m ² (625mg/m ²) po bid , D1-14 | Q21d x 6-8 cycles /Until progression | No.34 /Level IB |
| Docetaxel 40mg/m ² , IV, D1 【DS】 TS-1 80-120mg/day , po , bid , D1~14 | Q21d x 8 cycles/ Until progression | No.37 / Level I |
| Cisplatin 60mg/m ² , IV, D8 【SP】 TS-1 40-60mg/m ² , po , bid (吃3周休2周) | Q35day/cycle Until progression | No.40 / Level I |

Table-4.4 化學治療（二線）處方建議表

| Chemotherapy for unresectable/recurrent disease | Schedule | Reference (No)/ strength of Evidence |
|--|----------------------------------|---|
| Irinotecan 150 mg/m ² , IV, D1 | Q14d /cycle Until progression | No.20, 21 /Level I |
| Docetaxel 60 ~ 75 mg/m ² , IV, D1 | Q21d /cycle Until progression | No.21, 22 /Level I |
| Paclitaxel 80 mg/m ² , IV, D1, D8, D15 | Q28d/cycle Until progression | No.23 /Level I |
| Ramucirumab (8 mg/kg , IV, D1, D15) + Paclitaxel (80 mg/m ² , IV, D1, D8, D15) | Q28d/cycle Until progression | No. 25 /Level I |
| Docetaxel 50mg/m ² , IV , D1 【D-FOX】 Oxaliplatin 85mg/m ² , IV , D1 5-FU 1100mg/m ² , IV , D1 | Q14d /cycle Until progression | No.30 /Level II |

Table-4.4 化學治療（二線）處方建議表

| Chemotherapy for unresectable/recurrent disease | Schedule | Reference (No)/ strength of Evidence |
|--|---|---|
| Docetaxel 50mg/m ² , IV, D1 【DOX】 Oxaliplatin 100mg/m ² , IV, D1 Xeloda 1.25#/m ² (625mg/m ²) PO, bid, D1-14 | Q21d x 6-8 cycles /Until progression | No.34/Level IB |

Table-4.5 化學治療（三線）處方建議表

| Chemotherapy for unresectable/recurrent disease | Schedule | Reference (No)/ strength of Evidence |
|--|----------------------------------|---|
| Oral Lonsurf 35 mg/m ² , po, bid (D1-5 & D8-12) 前2週服用5天休2天，後2週休息 | Q28d/cycle /Until progression | No.38/ Level I |

Table-4.6 化學治療（NIPS）處方建議表：

| Neoadjuvant chemotherapy | Schedule | Reference (No)/ strength of Evidence |
|---|-------------------------|---|
| Paclitaxel 20mg/m²/week 【IP Paclitaxel, low dose】 | as clinically indicated | No 27/strength of Evidence :Level IIA |

Table-5 標靶治療處方建議表

| For unresectable/recurrent disease | Schedule | Reference (No)/ strength of Evidence |
|---|--|---|
| Trastuzumab 6-8mg/kg , IV, D1 使用條件： Her-2/neu免疫染色3+, 或2+且FISH positive for amplification | 8 mg/kg loading dose, 6 mg/kg every 3 weeks Until progression | No 41 / Level I |
| Trastuzumab 6-8mg/kg ,IV ,D1 CDDP 80mg/m ² ,IV ,D1 / Carboplatin AUC4-6mg ,IV ,D1 Xeloda 1000mg/m ² PO,BID ,D1~14 / 5-FU 800mg/m ² ,IV ,D1~5 使用條件： Her-2/neu免疫染色3+, 或2+且FISH positive for amplification | 8 mg/kg loading dose, 6 mg/kg every 3 weeks Until progression | No 16 / Level I |
| Ramucirumab 8 mg/kg, IV, D1 | Q14d/cycle Until progression | No. 24 / Level I |
| Ramucirumab (8 mg/kg, IV, D1, D15) + Paclitaxel (80 mg/m ² , IV, D1, D8, D15) | Q28d/cycle Until progression | No. 25 /Level I |

胃腺癌

高雄榮民總醫院
臨床診療指引

2023年第一版

Table-6 免疫治療處方建議表

| | | | | | |
|---------------|--------|----|-----|-------------------|------------------------|
| Nivolumab | 3mg/kg | D1 | Q2W | Until progression | (Ref. No 32/ Level II) |
| Pembrolizumab | 200mg | D1 | Q3W | Until progression | (Ref. No 33/ Level II) |

Table-7 放射治療處方建議表

| | |
|---|---|
| <p>※ Protocol of adjuvant chemoradiotherapy</p> | <p>※.For R0 resection \geq stage IIA ※ For R1 resection and R2 resection</p> |
| <p>Radiation therapy: Target volume: tumor/ gastric bed and pertinent nodal group Dose: 45-50.4 Gy /(1.8 Gy/day) Chemotherapy regimen: 5-FU (400 mg/m² per day) and leucovorin (20 mg/m² per day) on the first four and the last three days of RT. Reference :No 17/strength of Evidence :level 1</p> | |
| <p>※ Protocol of chemoradiation as the primary treatment</p> | <p>※ For medically fit patients but unresectable cancer without distant metastasis ※ For medically unfit patients without distant metastasis</p> |
| <p>Radiation therapy: Target volume: tumor/ gastric bed and pertinent nodal group Dose: 45-50.4 Gy /(1.8 Gy/day) Chemotherapy regimen: 5-FU (400 mg/m² per day) and leucovorin (20 mg/m² per day) on the first four and the last three days of RT. Reference :No 17/strength of Evidence :level 1</p> | |

Table-8 癌症藥物停藥準則

影像學檢查，腫瘤有變大或轉移變多，應停止或改變治療方式。

Reference

1. NCCN Clinical Practice Guideline in Oncology, Gastric cancer , Version 2.2022
2. 國家衛生研究院 胃癌臨床診療指引2012年第1版
3. 日本胃癌診療指引2010年第3版
4. Yan TD, Black D, Sugarbaker PH, et al. A systematic review and meta-analysis of the randomized controlled trials on adjuvant intraperitoneal chemotherapy for resectable gastric cancer. *Ann Surg Oncol* 2007;14:2702-2713.
5. Yonemura Y, de Aretxabala X, Fujimura T, et al. Intraoperative chemohyperthermic peritoneal perfusion as an adjuvant to gastric cancer: final results of a randomised controlled study. *Hepatogastroenterol* 2001; 48:1776–82.
6. Deng-Hai Mi , Zheng Li , Ke-Hu Yang et al. Surgery combined with intraoperative hyperthermic intraperitoneal chemotherapy (IHIC) for gastric cancer: a systematic review and meta-analysis of randomised controlled trials. *Int J Hyperthermia*. 2013;29(2):156-67
7. Kang LY et al. Intraoperative hyperthermic intraperitoneal chemotherapy as adjuvant chemotherapy for advanced gastric cancer patients with serosal invasion. *J Chin Med Assoc*. 2013 Aug;76(8):425-31.
8. Sakuramoto S, Sasako M, Yamaguchi T, et al. Adjuvant chemotherapy for gastric cancer with S-1, an oral fluoropyrimidine. *N Engl J Med*. 2007;357:1810–20.
9. T.Nakajima,T.Kinoshita,A Nashimoto et al:Randomized controlled trail of adjuvant uracil –tegafur versus surgery alone for serosa –negative ,locally advanced gastric cancer .*British Journal of Surgery* 2007, vol. 94:1468-1476.
10. Sung Hoon Noh, Sook Ryun Park, Han-Kwang Yang 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. *Lancet Oncol* 2014 Nov;15(12):1389-96
11. K Sumpter,C Harper-Wynne,D cunningham et al:Report of two protocol planned interim analyses in a randomised multicentre phase III study comparing capecitabine with fluorouracil and oxaliplatin with cisplatin in patients with advanced oesophagogastric cancer receiving ECF.*British journal of Cancer*2005, vol.92:1976-1983.
12. Wasaburo Koizumi,Hiroyuki Narahara,Takuo Hara et al:S-1 plus cisplatin versus S-1 alone for first-line treatment of advanced gastric cancer (SPIRITS trial):a phase III trial . *Lancet oncology* .2008 vol.3.215-221.

13. N.F.Aykan & E.Idlevich:The role of UFT in advanced gastric cancer .Annals of Oncology 2008 ,vol.19.1045-1052.
14. Kim GM, Jeung HC, Rha SY et al. A randomized phase II trial of S-1 oxaliplatin versus capecitabine-oxaliplatin in advanced gastric cancer. *Eu J Cancer* 2012;48:518-526.
15. Park SC and Chun HJ. Chemotherapy for advanced gastric cancer:Review and update of current practices. *Gut and Liver* 2013, vol 7. 385-393.
16. Yung-Jue Bang, Eric Van Cutsem, Andrea Feyereislova 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*.2012.vol.376.687-697.
17. Macdonald JS; Smalley SR; Benedetti J; Hundahl SA; Estes NC; Stemmermann GN; Haller DG; Ajani JA; Gunderson LL; Jessup JM; Martenson JA: Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction [Intergroup trial 0016]. *N Engl J Med* 2001 Sep 6;345(10):725-30.
18. Chikara Kunisaki, MD, PhD, Hirochika Makino, MD, PhD, Jun Kimura, MD et al. Impact of lymphovascular invasion in patients with stage I gastric cancer. *Surgery* 2010;147:204-11.
19. Chunyan Du . Ye Zhou . Kai Huang . Guangfa Zhao . Hong Fu . Yingqiang Shi. Defining a high-risk subgroup of pathological T2N0 gastric cancer by prognostic risk stratification for adjuvant therapy. *J Gastrointest Surg*(2011) 15:2153-2158.
20. Peter C. Thuss-Patience 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)*Eur J Cancer*. 2011 Oct;47(15):2306-14
21. Jung Hun Kang et al. Salvage Chemotherapy for Pretreated Gastric Cancer: A Randomized Phase III Trial Comparing Chemotherapy Plus Best Supportive Care With Best Supportive Care Alone. *J Clin Oncol* 30:1513-1518; 2012
22. Hugo E R Ford et al. Docetaxel versus active symptom control for refractory oesophagogastric adenocarcinoma (COUGAR-02): an open-label, phase 3 randomised controlled trial. *Lancet Oncol* 2014; 15: 78–86.

23. Shuichi Hironaka 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. *J Clin Oncol* 31:4438-4444; 2013.
24. Charles S Fuchs 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
25. Hansjochen Wilke 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: 1224–35.
26. 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.
27. Hironori Yamaguchi et al. Breakthrough therapy for peritoneal carcinomatosis of gastric cancer: Intraperitoneal chemotherapy with taxanes. *World Journal of Gastrointestinal Oncology* 2015;7(11):285-291.
28. Motohiro Imano et al, Phase II Study of Single Intraperitoneal Chemotherapy Followed by Systemic Chemotherapy FOR Gastric Cancer with Peritoneal Metastasis. *J Gasyrointest Surg* 2012;16:2190-2196.
29. Manish A. Shah 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. *Journal of clinical oncology* 2015;33:3874-3879.
30. Mariela A. Blum Murphy, MD 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. *American Journal of Clinical Oncology* 2018 ;41:321-325.
31. Kohei Shitara et al, Phase II study of adjuvant chemotherapy of S-1 plus oxaliplatin for patients with stage III gastric cancer after D2 gastrectomy. *Gastric Cancer*.2015 Dec 20(1)DOI:10.1007/s10120-015-0581-1
32. Yoon-Koo Kang et al, Nivolumab in patients with advanced gastric or gastro-oesophageal junction cancer refractory to, or intolerant of, at least two previous chemotherapy regimens (ONO-4538-12, ATTRACTION-2): a randomised, double-blind, placebo-controlled, phase 3 trial. *The Lancet* .2017 Dec 2;390(10111):2461-2471

33. Lola Fashoyin-Aje et al, FDA Approval Summary: Pembrolizumab for Recurrent Locally Advanced or Metastatic Gastric or Gastroesophageal Junction Adenocarcinoma Expressing PD-L1. *Oncologist*.2018 Aug 17 ; 2018-0221
34. E.Van Cutsem et al, Docetaxel plus oxaliplatin with or without fluorouracil or capecitabine in metastatic or locally recurrent gastric cancer: a randomized phase II study. *Annals of Oncology* 26: 149–156, 2015.
35. Al-Batran SE et al, Histopathological regression after neoadjuvant docetaxel,oxaliplatin, fl uorouracil, and leucovorin versus epirubicin,cisplatin, and fl uorouracil or capecitabine in patients with resectable gastric or gastro-oesophageal junction adenocarcinoma (FLOT4-AIO): results from the phase 2 part of a multicentre, open-label, randomised phase 2/3 trial. *Lancet Oncol*.2016 Dec;17(12):1697-1708.
36. Liu M,Hu G,Wang Y,Guo J,Liu L,Han X,Wang Z, Comparison of FOLFOX and DOF regimens as first-line treatment in East Asian patients with advanced gastric cancer. *OncoTargets and Therapy*.2018;11 Pages 375-381.
37. Kazuhiro Yoshida.et al, 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* 2019;37(15):1296-1304.
38. David H. Ilson, MD, PhD.et al, Efficacy and Safety of Trifluridine/Tipiracil Treatment in Patients With Metastatic Gastric Cancer Who Had Undergone Gastrectomy . *JAMA Oncol*. 2019 Oct 10;6(1):e193531.
39. Japanese gastric cancer treatment guidelines 2018(5th edition).*Gastric Cancer*.2021 Jan;24(1):1-21.
40. Koizumi W, Narahara H, Hara T, et al. S-1 plus cisplatin versus S-1 alone for first-line treatment of advanced gastric cancer (SPIRITS trial): a phase III trial. *Lancet Oncol*. 2008;9:215–21.
41. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2018 (5th edition). *Gastric cancer*. Epub 14 Feb 2020.