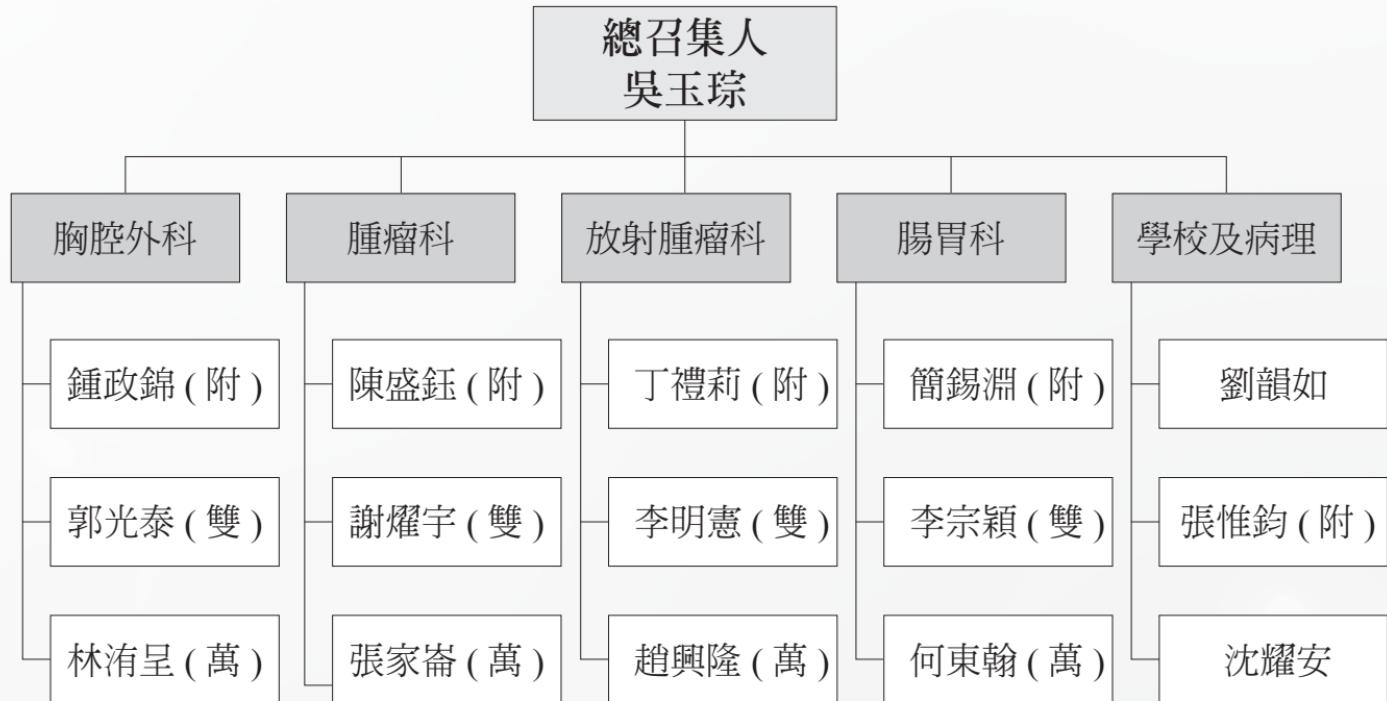




食道癌診療準則

食道團隊成員



Pretreatment Workup

WORKUP

- H &P
- Upper GI endoscopy and biopsy
- Chest / abdomen CT with oral and IV contrast
- Pelvic CT with contrast as clinical indicated
- PET-CT evaluation (skull base to mid-thigh) if no evidence of M1 disease
- CBC and Chemistry profile
- Endoscopic ultrasound(EUS), if no evidence of M1 un-resectable disease
- Endoscopic resection (ER) is recommended for the accurate staging of early- stage cancers(T1a or T1b). Early-stage cancer can be best diagnosed by ER
- Biopsy of metastatic disease as clinically indicated
- Universal testing for microsatellite instability (MSI) by PCR/next-generation sequencing (NGS) or MMR by IHC is recommended in all newly diagnosed patients
- Programmed death ligand 1 (PD-L1) testing if advanced / metastatic disease is documented/suspected
- HER2-neu testing if metastatic adenocarcinoma is documented/ suspected
- Next-generation sequencing (NGS) may be considered
- Bronchoscopy, if tumor is at or above the carina with no evidence of M1 disease
- Assign Siewert category
- Nutritional assessment and counseling
- Smoking cessation advice, counseling, and pharmacotherapy as indicated
- Screen for family history

Pretreatment Workup

CLINICAL STAGE

Stage I-IVA(Locoregional disease, except T4b or unresectable N3)

- Squamous cell carcinoma
- Adenocarcinoma



Multidisciplinary evaluation
 - Consider enteric feeding tube*
 for preoperative nutrition support
 - Laparoscopy(optional)
 If no evidence of M1 disease and
 tumor is at EGJ

Squamous cell Ca
 (See Esophageal cancer
 guideline -2)

Adenocarcinoma
 (See Esophageal cancer
 guideline -10)

Squamous cell Ca
 (See Esophageal cancer
 guideline -6)

Adenocarcinoma
 (See Esophageal cancer
 guideline -6)

Stage IVA(including T4b or unresectable N3) & IVB(metastatic disease)

- Squamous cell carcinoma
- Adenocarcinoma

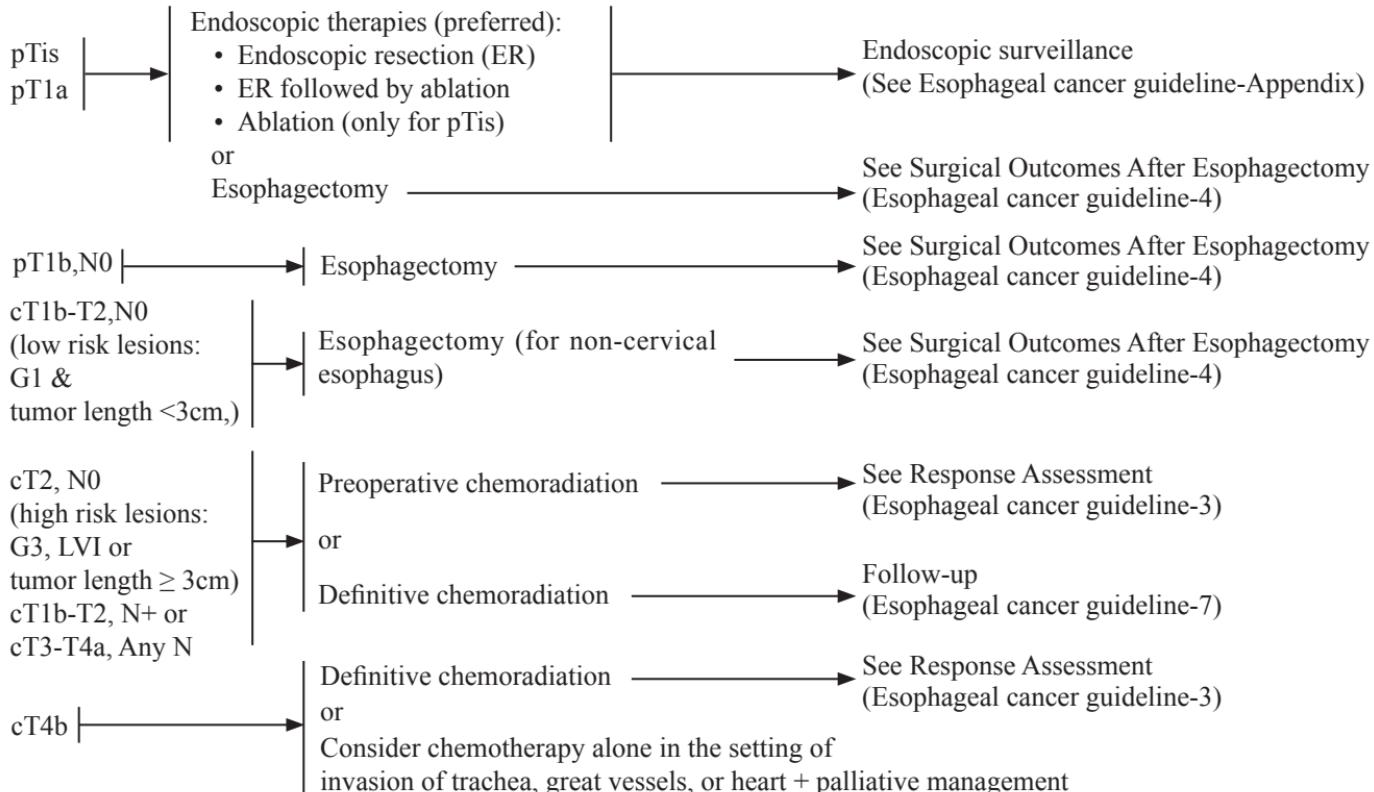


(See Esophageal cancer
 guideline -8)

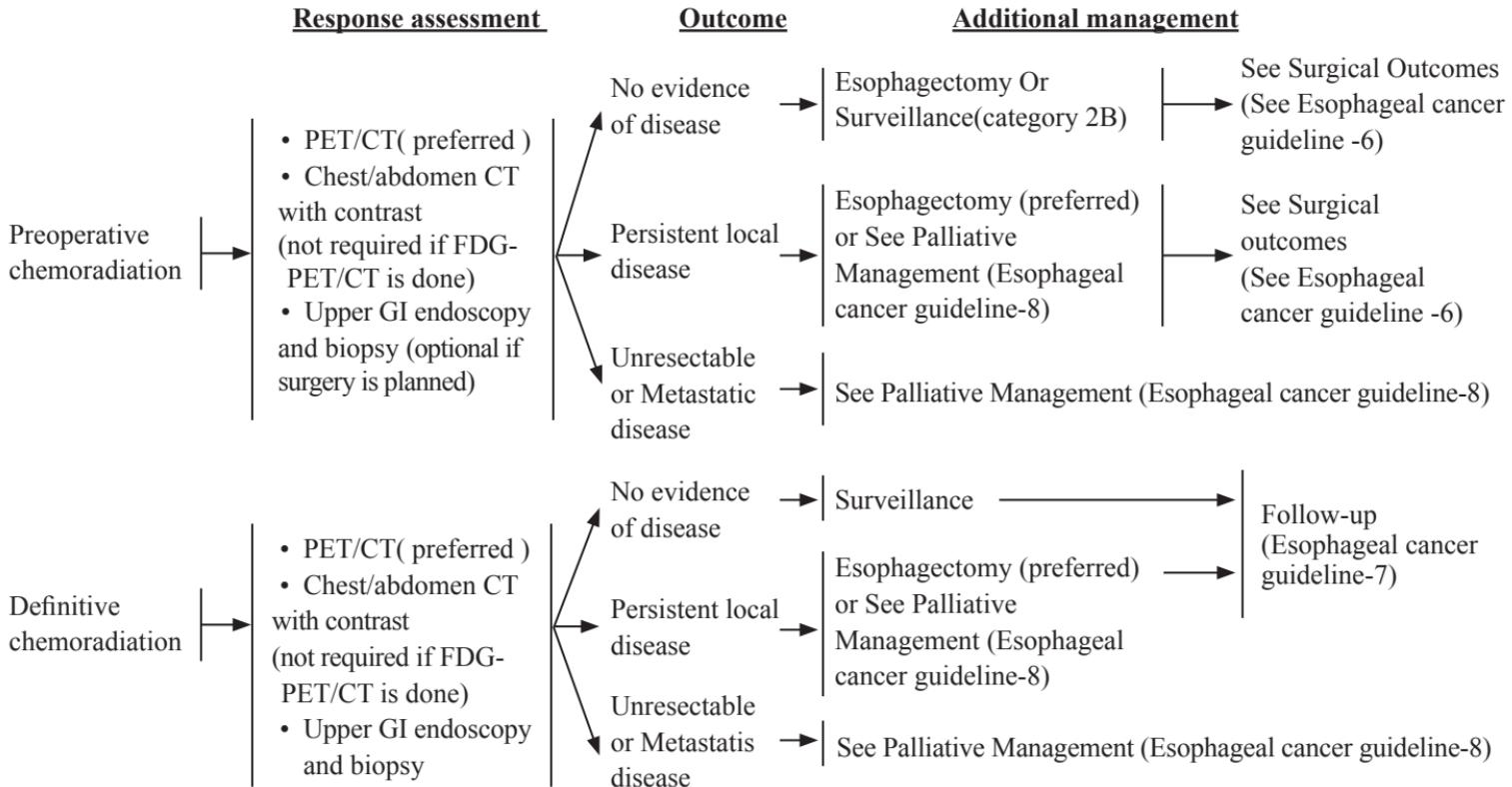
* Percutaneous gastrostomy tube (PCG) may be considered for patient with cervical esophageal tumors receiving definitive chemoradiation or for patients with marginally resectable disease.

『Esophageal cancer guideline-2』

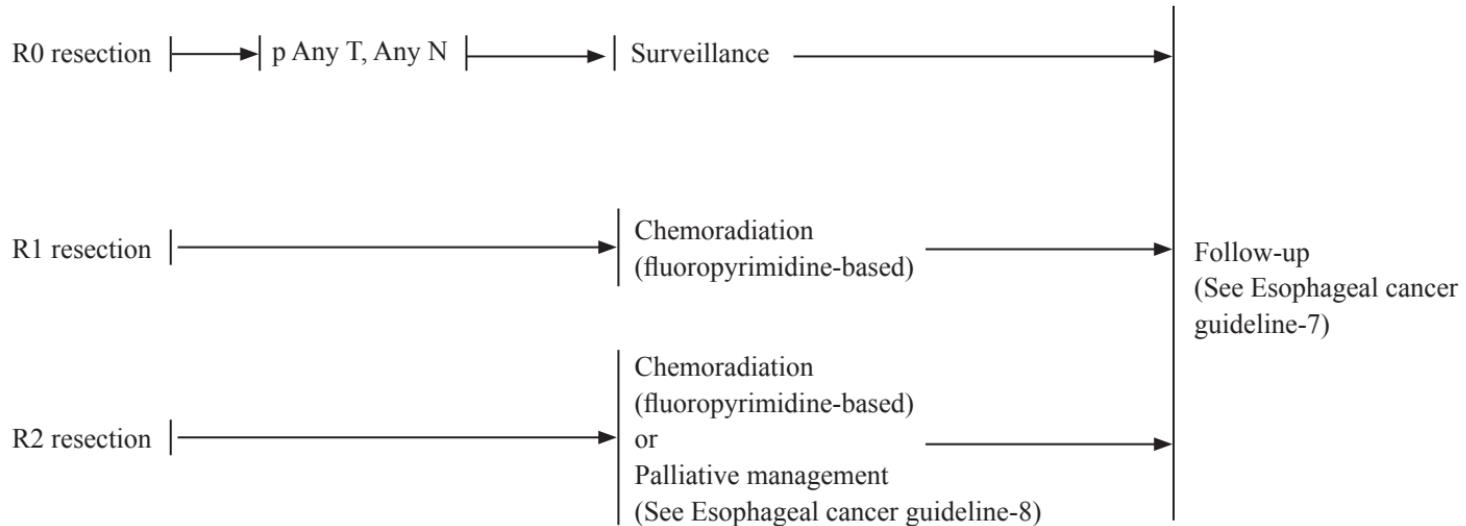
Squamous cell carcinoma: primary treatment options for medically fit surgery patients



Squamous cell carcinoma: response assessment

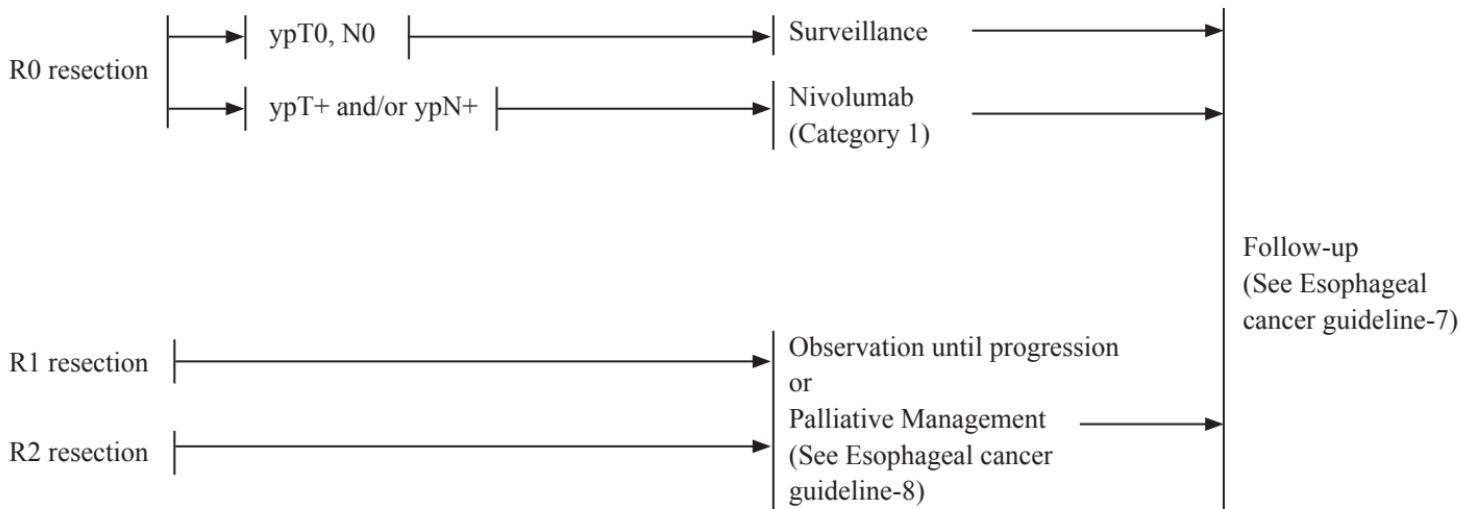


『Esophageal cancer guideline-4』

Squamous cell carcinoma: surgical outcomesPatients Have Not Received Preoperative Chemoradiation

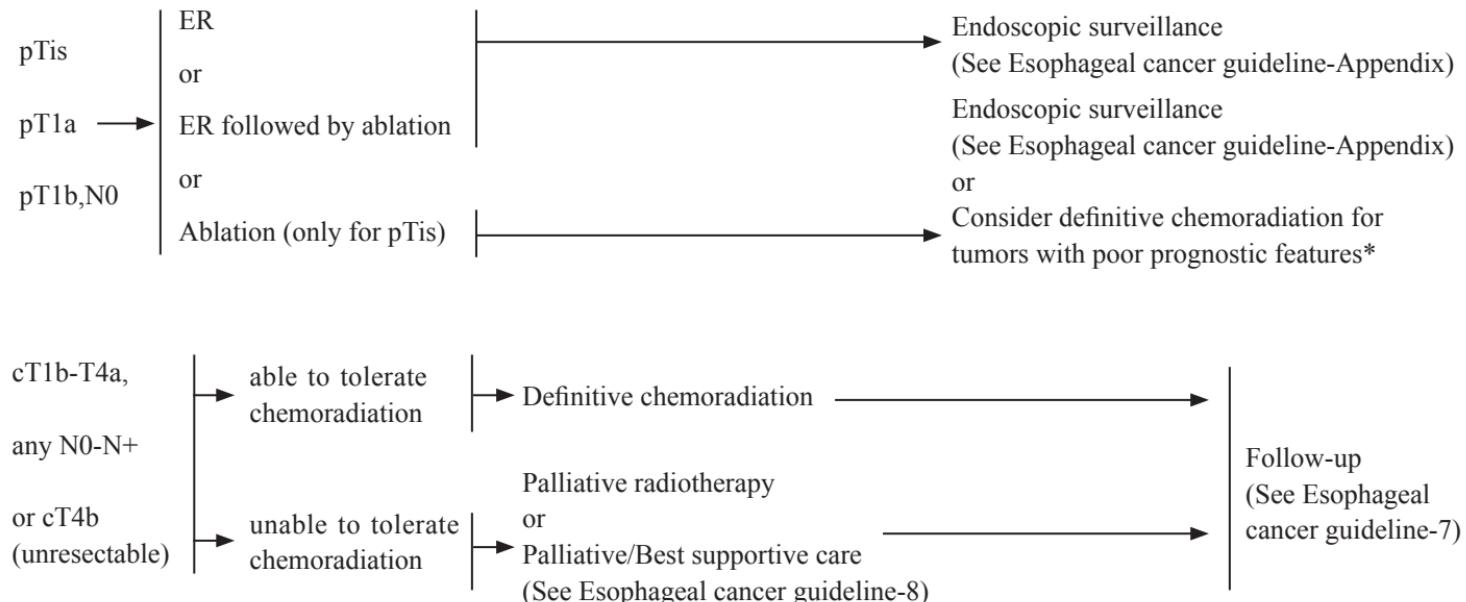
Squamous cell carcinoma: surgical outcomes

Patients Have Received Preoperative Chemoradiation



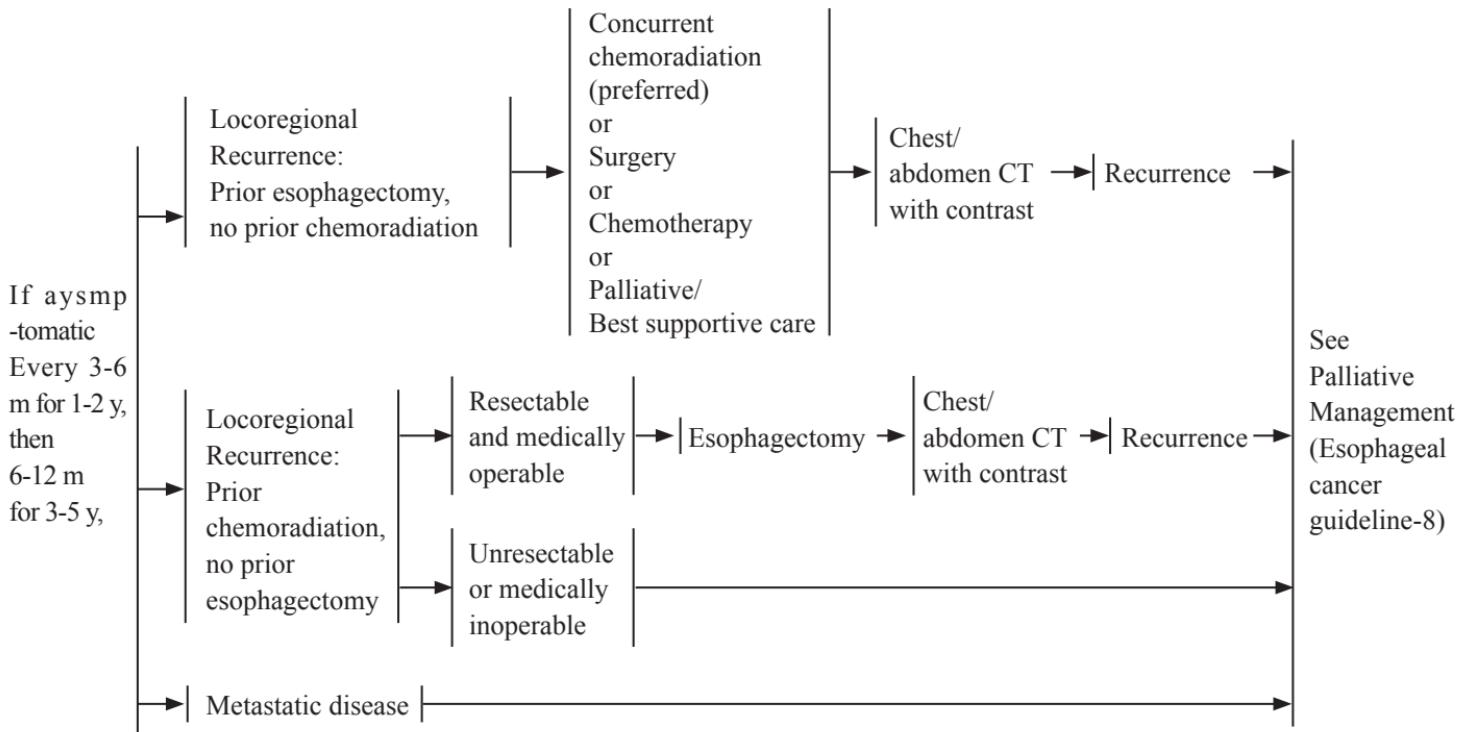
《Esophageal cancer guideline-6》

Squamous cell carcinoma & adenocarcinoma : non-surgical candidate



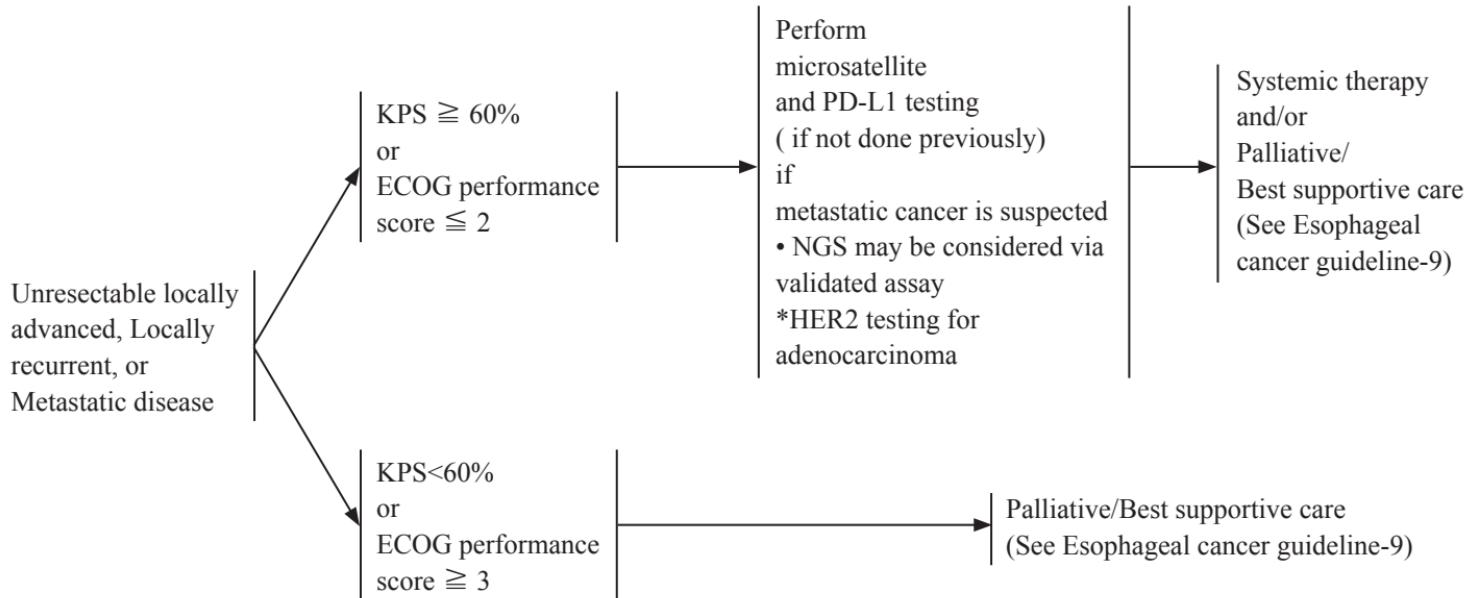
* Poor prognostic features: positive margin(s), max. tumor diameter > 2cm, G2/3, LVI or more

Squamous cell carcinoma & adenocarcinoma follow up – recurrence – palliative management



《Esophageal cancer guideline-8》

Squamous cell carcinoma & adenocarcinoma : unresectable locally advanced, locally recurrent, or metastatic disease



Principles of Palliative/Best Supportive Care

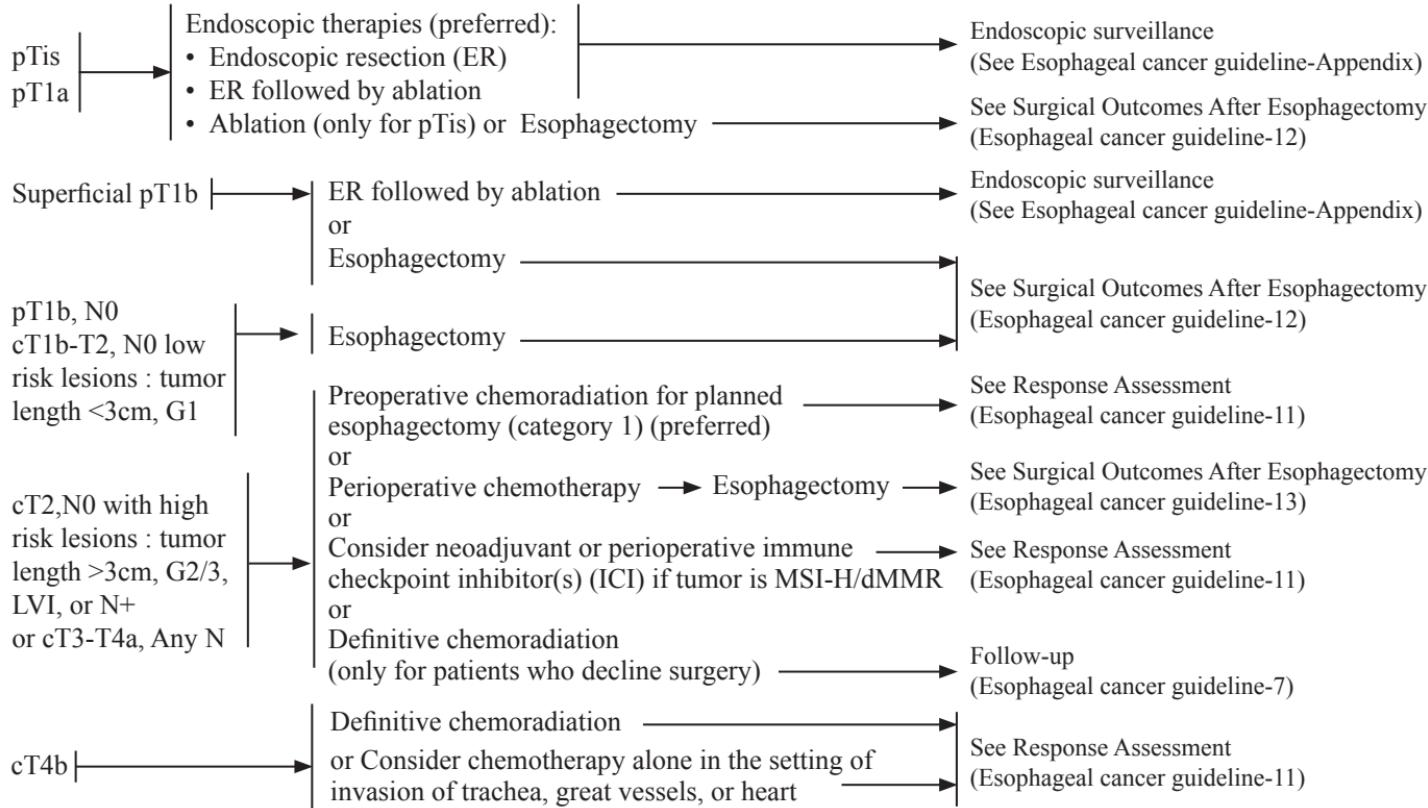
最佳支持性療護的目標是預防和減輕痛苦，無論疾病處於哪個階段或是否需要其他治療，都要為病患及其家人提供盡可能最佳的生活質量。對於食道癌，緩解主要症狀的介入措施可能會顯著延長餘命。採取跨多專科團隊的醫療模式更顯得重要。因此，鼓勵採取多專科團隊的醫療模式對食道癌患者進行安寧療護。

Dysphagia

- Assess the extent of disease and the functional degree of swallowing impairment, preferably through a standardized scoring scale and confirm the etiology of dysphagia
- Dysphagia grading scale
 - Grade 0: Able to eat solid food without special attention to bite size or chewing
 - Grade 1: Able to swallow solid food cut into pieces less than 18 mm in diameter and thoroughly chewed
 - Grade 2: Able to swallow semisolid food (consistency of baby food)
 - Grade 3: Able to swallow liquids only
 - Grade 4: Unable to swallow liquids or saliva
- Dysphagia arising from esophageal cancer most often is due to obstruction, but on occasion may be primarily due to tumor-related dysmotility.
- Patients with dysphagia who are not candidates for curative surgery should be considered for palliation of their dysphagia symptoms, based on symptom severity. This can be achieved through multiple modalities, although placement of an esophageal stent is most commonly utilized. In contrast, stent placement is generally not advised in patients who may undergo curative surgery in the future due to concerns that stent-related adverse events may preclude curative surgery in the future.

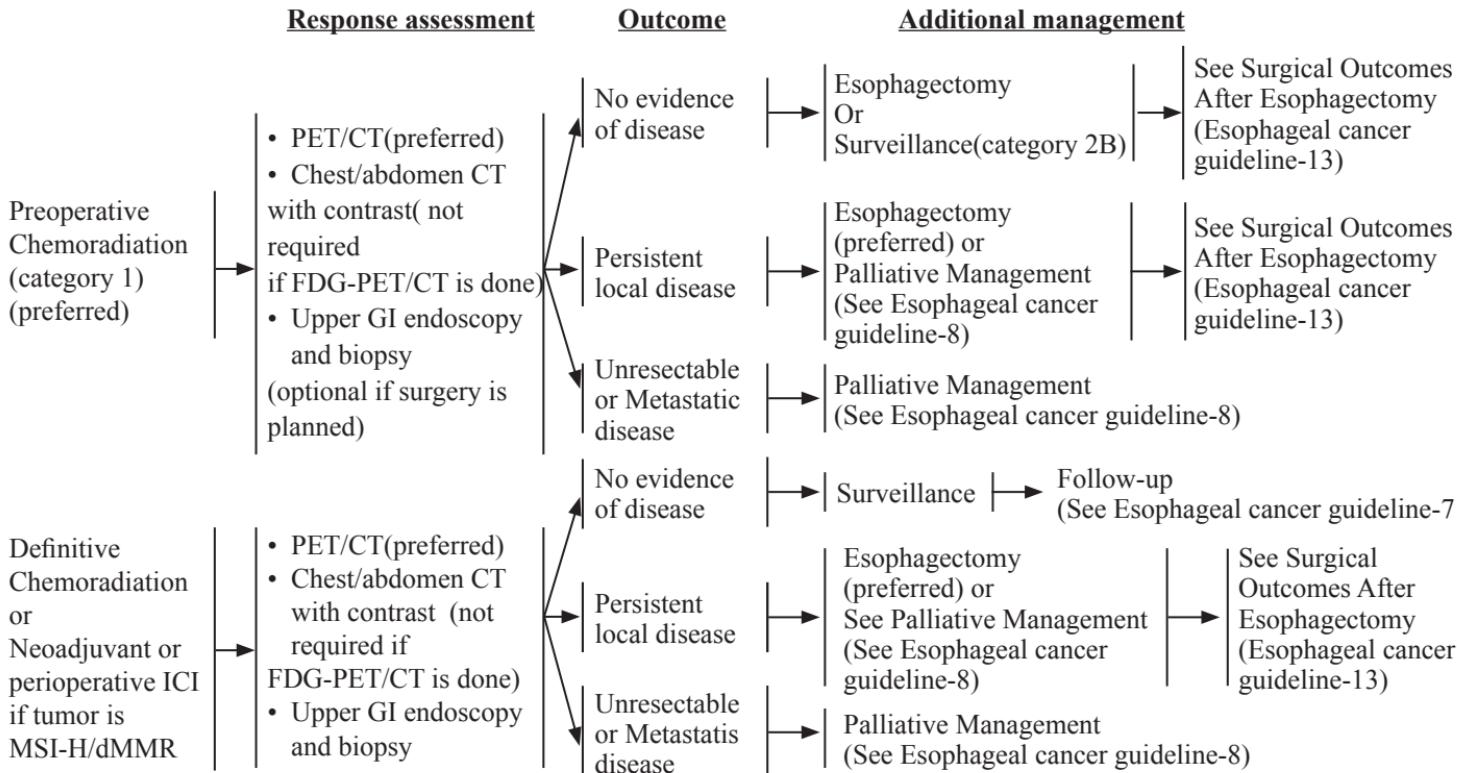
《Esophageal cancer guideline-10》

Adenocarcinoma: primary treatment for medically fit surgery patients



《Esophageal cancer guideline-11》

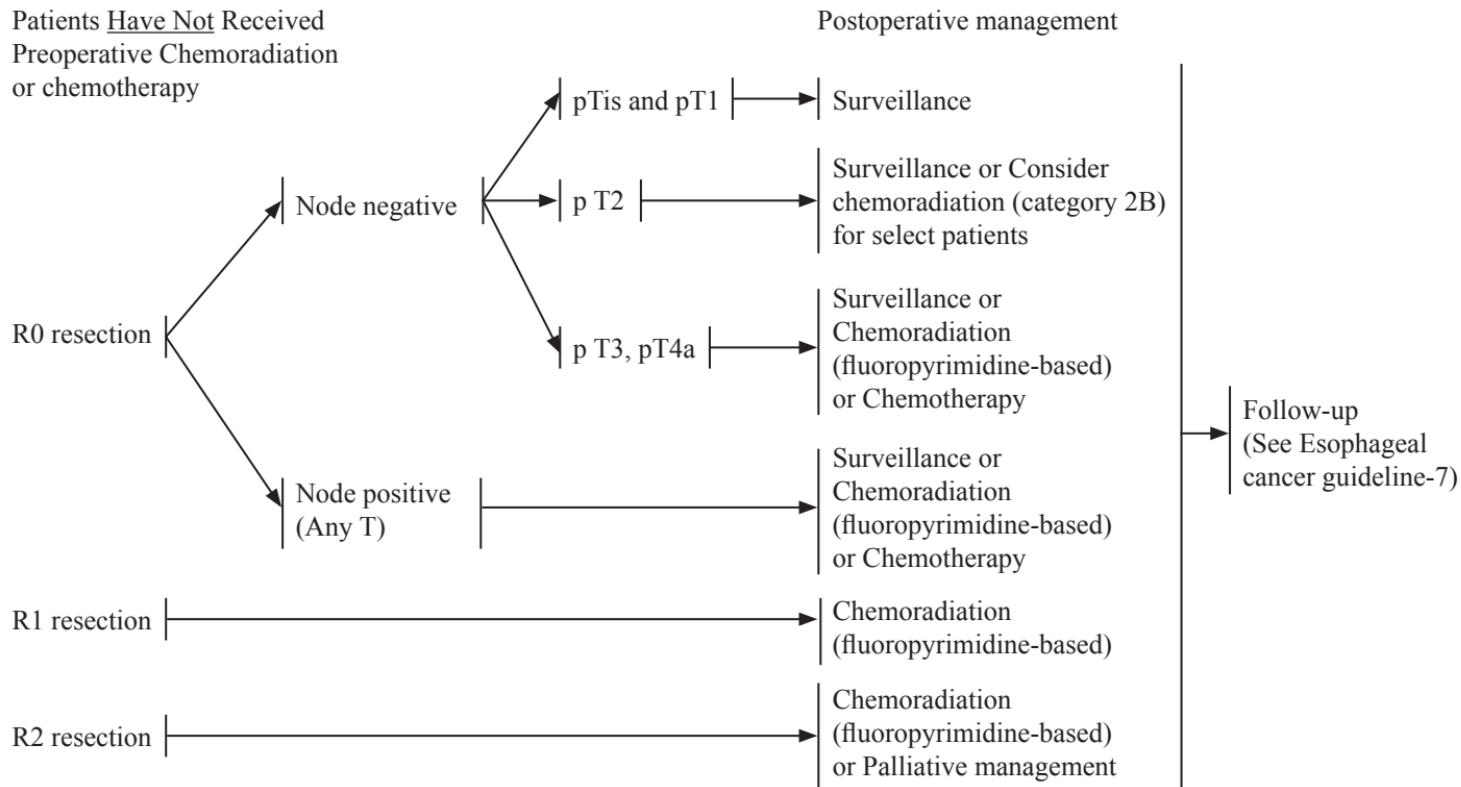
Adenocarcinoma: response assessment



『Esophageal cancer guideline-12』

Adenocarcinoma: surgical outcomes

Patients Have Not Received
Preoperative Chemoradiation
or chemotherapy

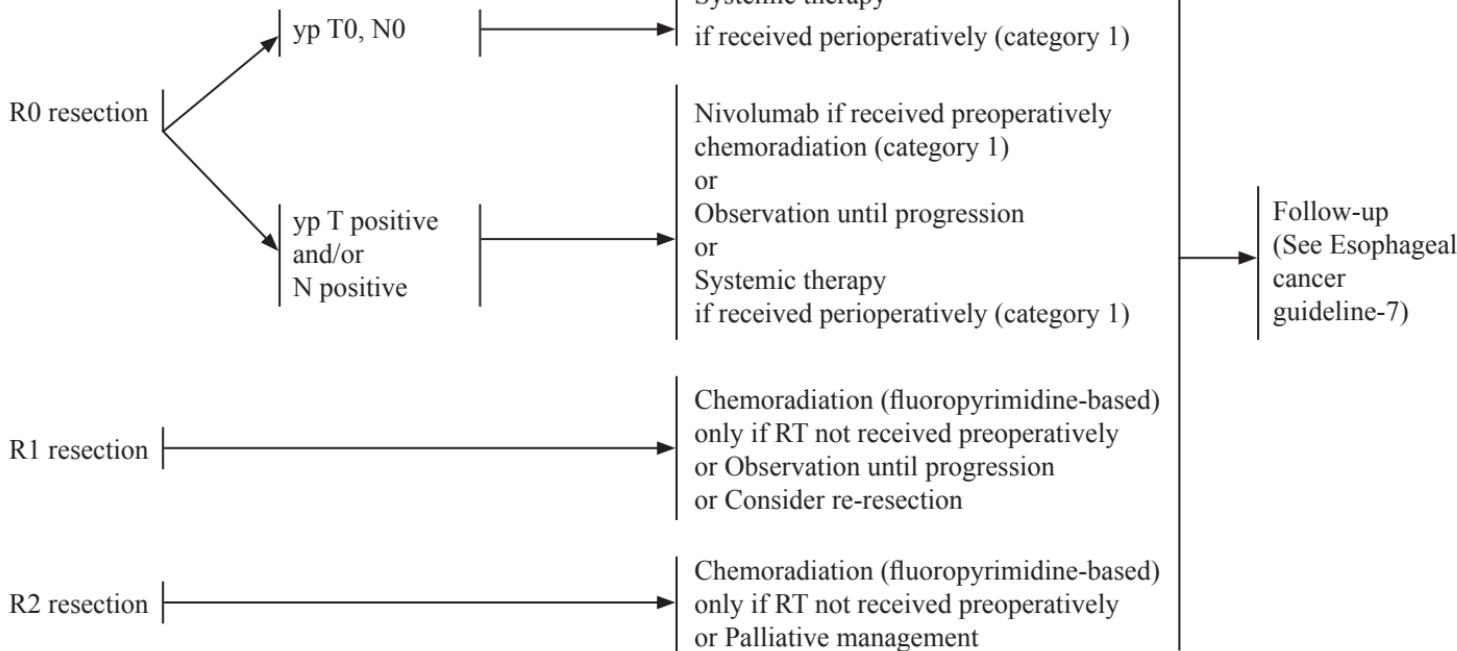


《Esophageal cancer guideline-13》

Adenocarcinoma: surgical outcomes

Patients Have Received

Preoperative Chemoradiation
or chemotherapy



《Esophageal cancer guideline-Appendix》

Principles of Endoscopic Staging and Therapy

Treatment of Symptoms

- Esophageal dilation can be performed with the use of dilating balloons or bougies to temporarily relieve obstruction from tumors, or treatment-related strictures. Caution should be exercised to avoid overdilation, to minimize the risk of perforation.
- Long-term palliation of dysphagia can be achieved with endoscopic tumor ablation by Nd:YAG laser, PDT and cryoablation, or endoscopic and radiographic-assisted insertion of expandable metal or plastic stents.
- Long-term palliation of anorexia, dysphagia, or malnutrition may be achieved with endoscopic or radiographic-assisted placement of feeding gastrostomy or jejunostomy. The placement of a gastrostomy in the preoperative setting may compromise the gastric vasculature, thereby interfering with the creation of the gastric conduit in the reconstruction during esophagectomy and should be avoided.

Post-Treatment Surveillance

- Consider deferring assessment endoscopy with biopsy to 6 weeks or later after completion of preoperative therapy in patients whom avoidance of surgery is being considered.
- EUS exams performed after chemotherapy or radiation therapy have a reduced ability to accurately determine the present stage of disease. Similarly, biopsies performed after chemotherapy or radiation therapy may not accurately diagnose the presence of residual disease.
- Endoscopic surveillance following definitive treatment of esophageal cancer requires careful attention to detail for mucosal surface changes, and multiple biopsies of any visualized abnormalities. Strictures should be biopsied to rule out neoplastic cause. EUS-guided FNA should be performed if suspicious lymph nodes or areas of wall thickening are seen on cross-sectional imaging.
- Endoscopic surveillance after ablative therapy or ER of early-stage esophageal cancer should continue after completion of treatment. Biopsies should be taken of the neosquamous mucosa even in the absence of mucosal abnormalities as dysplasia may occasionally be present beneath the squamous mucosa.
- Endoscopic surveillance should also include a search for the presence of Barrett esophagus and four-quadrant biopsies to detect residual or recurrent dysplasia. The ablation of residual or recurrent high-grade and low-grade dysplasia using RFA or cryoablation should be considered.
- Patients who have received therapeutic ER should have endoscopic surveillance.

Principles of Pathologic Review

- Pathology review 的目的包括：
 - Classification of tumor
 - Determine the extent of invasion
 - Establish status of cancer involvement of surgical margins
- 所有手術病理報告都應該依照食道癌 WHO 分類
- 所有手術病理報告都應該依 AJCC/UICC TNM 8th edition 分期
- 手術病理報告應包括下列項目
 - Histologic type
 - Histologic grade (G1: well differentiated; G2: moderately differentiated; G3: poorly differentiated)
 - Microscopic tumor extension
 - Margin status

Principles of Pathologic Review

病理報告根據標本的不同應包括下列項目：

- Biopsy: invasion, if present; high-grade dysplasia in Barrett esophagus; histologic type; Grade; Presence or absence of Barrett esophagus; Universal testing for MSI by PCR/NGS or MMR by IHC is recommended in all newly diagnosed patients
- Endoscopic resection (ER): include all elements as for biopsy specimen plus the depth of tumor invasion; lymphovascular invasion (LVI), and the status of mucosal and deep margins; Universal testing for MSI by PCR/NGS or MMR by IHC is recommended in all newly diagnosed patients
- Esophagectomy, without prior chemoradiation: include all elements as for ER specimen plus the location of the tumor midpoint in relation to the EGJ, whether the tumor crosses EGJ, lymph node status, and the number of lymph nodes recovered; Universal testing for MSI by PCR/NGS or MMR by IHC is recommended in all newly diagnosed patients, if not previously performed
- Esophagectomy, with prior chemoradiation :
 - the tumor sites should be thoroughly sampled, with submission of entire EGJ or ulcer/tumor bed for specimens without grossly obvious residual tumor
 - For pathology report, include all elements as for esophagectomy without prior chemoradiation, plus assessment of the treatment effect
 - Assessment treatment effect: 術前治療反應與預後相關。目前採用 The modified Ryan scheme in the CAP Cancer Protocol for Esophageal Carcinoma

Description	Tumor Regression Score
No viable cancer cells (complete response)	0
Single cells or rare small groups of cancer cells (near complete response)	1
Residual cancer with evident tumor regression, but more than single cells or rare small groups of cancer cells (partial response)	2
Extensive residual cancer with no evident tumor regression (poor or no response)	3

Principles of Biomarker Testing

- HER2 狀態，微衛星不穩定性（MSI）狀態的分子測試，程序性死亡配體 1（PD-L1）表達和 NTRK 基因融合檢測被用於預測局部晚期，不可切除或轉移性食道癌和 EGJ 癌的臨床治療用藥選擇
- Assessment of overexpression or amplification of Her2 in Esophageal and EGJ Cancer
 - For patients with inoperable locally advanced, recurrent, or metastatic adenocarcinoma of esophagus or EGJ for whom trastuzumab therapy is being considered
 - Immunohistochemical criteria for scoring HER2/neu expression

	Surgical Specimen Expression Pattern, Immunohistochemistry	Biopsy Specimen Expression Pattern, Immunohistochemistry	HER2 Overexpression Assessment
0	No reactivity or membranous reactivity in <10% of cancer cells	No reactivity or no membranous reactivity in any cancer cell	Negative
1+	Faint or barely perceptible membranous reactivity in ≥10% of cancer cells; cells are reactive only in part of their membrane	Cluster of five or more cancer cells with a faint or barely perceptible membranous reactivity irrespective of percentage of cancer cells positive	Negative
2+	Weak to moderate complete, basolateral or lateral membranous reactivity in ≥10% of cancer cells	Cluster of five or more cancer cells with a weak to moderate complete, basolateral, or lateral membranous reactivity irrespective of percentage of cancer cells positive	Equivocal
3+	Strong complete, basolateral, or lateral membranous reactivity in ≥10% of cancer cells	Cluster of five or more cancer cells with a strong complete, basolateral, or lateral membranous reactivity irrespective of percentage of cancer cells positive	Positive

- HER2 IHC is performed first, followed by FISH methods in cases showing 2+ (equivocal) expressions by IHC. Cases with HER2:CEP17 ratio >=2 or an average HER2 copy number >=6.0 signals/cell are considered positive by FISH.

Principles of Biomarker Testing

◆ *Microsatellite Instability (MSI) or Mismatch Repair (MMR) Testing:*

- 所有新診斷的食道癌和食道胃結合部癌應透過聚合酶鏈反應 (PCR)、NGS 或 IHC MMR 進行 MSI 通用檢測。根據 CAP DNA 錯配修復生物標記報告指南，結果被解釋為 MSI 高 (MSI-H) 或錯配修復缺陷 (dMMR)。測試只能在臨床實驗室改進修正案 (CLIA) 批准的實驗室中進行。MSI-H 或 dMMR 腫瘤患者應轉診至遺傳學顧問，以在適當的臨床背景下進行進一步評估。
- MMR Interpretation
 - ◊ No loss of nuclear expression of MMR proteins: No evidence of dMMR (low probability of MSI-H)
 - ◊ Loss of nuclear expression of one or more MMR proteins: dMMR
- MSI Interpretation
 - ◊ MSI-stable (MSS)
 - ◊ MSI-low (MSI-L)
 - 1%–29% of the markers exhibit instability
 - 1 of the 5 National Cancer Institute (NCI) or mononucleotide markers exhibits instability
 - ◊ MSI-H
 - ≥ 30% of the markers exhibit instability
 - 2 or more of the 5 NCI or mononucleotide markers exhibit instability

◆ *PD-L1 Testing:*

- PD-L1 IHC testing may be considered on locally advanced, recurrent, or metastatic esophageal and EGJ cancer in patients who are candidate for treatment with PD-1 inhibitors
- Assessment of PD-L1 Protein Expression
 - Pembrolizumab as a second-line treatment option for esophageal SCC with PD-L1 expression levels by combined positive score (CPS) of >=10, and as a third-or subsequent-line treatment option for EGJ adenocarcinoma with PD-L1 expression levels by CPS >=1, as determined by an FDA-approved companion diagnosed test
 - CPS is determined by

$$CPS = \frac{\# \text{ of PD-L1-positive cells} \text{ (tumor cells, lymphocytes, macrophages)}}{\text{Total } \# \text{ of tumor cells}} \times 100$$

Principles of Biomarker Testing

◆ 次世代定序 (Next-Generation Sequencing, NGS):

- 目前，多種標靶治療藥物例如：trastuzumab, pembrolizumab/nivolumab, and entrectinib/larotrectinib, selpercatinib, and dabrafenib / trametinib, 已被 FDA 核准用於食道癌和食道胃結合部癌。Tratuzumab 基於 HER2 過度表現測試。選擇免疫節點抑制劑的使用是基於 PCR 檢測 MSI 或 IHC 檢測 NGS/MMR、PD-L1 免疫組織化學表達或 NGS 檢測高腫瘤突變負荷 (TMB)。FDA 核准使用選定的 TRK 抑制劑治療 NTRK 基因融合陽性實體瘤，並核准使用 selpercatinib 治療 RET 基因融合陽性腫瘤。Dabrafenib/trametinib 已被批准用於治療具有 BRAF V600E 突變的腫瘤。當可用於測試的組織有限，或患者無法進行傳統的活檢時，單一生物標記的連續測試或使用有限的分子診斷面板可能會很快耗盡樣本。在這些情況下，透過在 CLIA 批准的實驗室中進行的經過驗證的 NGS 檢測進行全面的基因組分析可用於識別 HER2 擴增、MSI 狀態、MMR 缺陷、TMB、NTRK 基因融合、RET 基因融合和 BRAF V600E 突變。應先考慮使用 IHC/ISH/ 靶向 PCR，然後視情況進行 NGS 檢測。

◆ Liquid Biopsy:

- The genomic alterations of solid cancers may be identified by evaluating circulating tumor DNA (ctDNA) in the blood, hence a form of “liquid biopsy.” Liquid biopsy is being used more frequently in patients with advanced disease, particularly those who are unable to have a clinical biopsy for disease surveillance and management. The detection of mutations/alterations in DNA shed from esophageal and EGJ carcinomas can identify targetable alterations or the evolution of clones with altered treatment response profiles. Therefore, for patients who have metastatic or advanced esophageal/esophagogastric cancers who may be unable to undergo a traditional biopsy or for disease progression monitoring, testing using a validated NGS-based comprehensive genomic profiling assay performed in a CLIA-approved laboratory may be considered. A negative result should be interpreted with caution, as this does not exclude the presence of tumor mutations or amplifications.

Principles of Biomarker Testing

- Assessment of *NTRK* gene fusions:
 - The FDA granted approval for the use of select TRK inhibitors for *NTRK* gene fusion-positive solid tumors
 - A two-step approach is used, which includes IHC first and confirmation of any positivity detected with IHC by Next generation sequencing (NGS)
- TRK IHC as a screening tool:
 - IHC negative: No TRK expression
 - IHC positive: Detection of TRK expression, confirmation by NGS
- 若只有少量組織 (biopsy specimen) 可供檢測不同種類的 biomarker，建議臨床醫師開立檢測請在病理申請單註明，同一次病理組織切片除了 HE，應預留組織空白片，以避免因蠟塊多次處理，造成腫瘤細胞消耗。

Principles of Endoscopic Staging and Therapy

1. 食道鱗狀細胞癌病患，在初步確診時，必須由專精影像強化技術 IEE 的內視鏡醫師進行一次上消化道內視鏡精查，以確認是否同時存在其他源於黏膜的癌症及癌前病變。(work up)
2. 所有食道癌病患，在進行手術或 CCRT 前，應會診胃腸科醫師討論是否施行內視鏡或外科性胃腸造口，以顧全病患治療前後的營養狀態。(principle of surgery)
3. 食道癌在接受治療前，除了已明確證實為 M1 的病人外（如 CT scan、PET scan），應進行 EUS 診斷。(work up)
4. 關於早期食道癌：適用內視鏡切除的絕對適應症為腫瘤深度侷限在 m1、m2 層，且 LN(-)；相對適應症為腫瘤深度侷限在 m3、sm1 層，且 LN(-)；無法辨明情況下，可考慮行 diagnostic ESD。
5. 如果在上述測試完成後有足夠的組織可用，可以考慮用 NGS 做第二次檢測。
6. 食道癌病患若 EUS 發現 LN(+)，可選擇性加做 FNA/FNB。
7. 食道癌 CCRT 之後，可選擇性加做 EUS 做 re-staging。(optional)
8. 姑息性的內視鏡治療（例如：金屬支架擴張術、氫氣電漿凝固術局部消融…等），應於食道癌多科團隊會議中提出討論後執行。

註一：執行上消化道內視鏡精查時，應備有擴大型內視鏡、魯格爾試液 (Lugol's solution)、稀釋醋酸、影像強化光源（例如 NBI、BLI 等），由具早期癌判斷能力的內視鏡醫師執行並撰寫報告。

註二：巴瑞特氏食道病患，須例行接受上消化道內視鏡精查，以確認是否發生癌變，精查應由專精影像強化技術 IEE 的內視鏡醫師執行。（有 dysplasia 者至少每年一次，無 dysplasia 者至少每三年一次。）

註三：應由食道癌共識會議向三院相關癌症多科團隊提出診療建議「所有口腔癌（含舌癌）、頭頸癌、下咽癌、喉癌等病患，在初步確診時及術後至少每年，必須由專精影像強化技術 IEE 的內視鏡醫師進行一次上消化道內視鏡精查，以確認是否同時存有食道癌及癌前病變。」

Principles of Surgery

- 手術前之臨床分期應使用胸腹部電腦斷層，正子電腦斷層掃描 (PET-CT) 及內視鏡超音波，以評估可否切除
- 治療前所有病患皆需諮詢胸腔外科醫師，接受是否可以耐受食道切除之生理評估
- 所有生理狀態適合食道切除，且為局部可切除之胸腔 (超過環咽部 5 公分以下) 及腹腔食道癌患者，皆應考慮手術切除
- 食道交接處 (EGJ) 腺癌之病患皆應有 Siewert 分類
 - Siewert Type I: adenocarcinoma of the lower esophagus with the epicenter location located within 1cm to 5 cm above the anatomic EGJ
 - Siewert Type II: true carcinoma of the cardia with the tumor epicenter within 1 cm above and 2 cm below the EGJ
 - Siewert Type III: subcardial carcinoma with the tumor epicenter between 2 cm and 5 cm below the EGJ, which infiltrates the EGJ and lower esophagus from below
- Siewert type I 及 II 腫瘤應遵從食道癌及胃食道交接癌治療準則。Siewert type III 則視為胃癌，應遵從胃癌治療準則，然某些狀況下需增加部分食道切除，以獲取適當的之切除距離
- 腹腔內視鏡可以偵測放射線影像檢查無法找到之潛伏轉移病灶 (Occult metastatic disease) 尤其是 Seiwert type II 及 III 腫瘤
- 腹膜積液細胞學檢查陽性與不良預後相關，應視為 M1 疾患。患者若為進展期之腫瘤，臨床分期 T3 或 N+ 疾患，應考慮接受腹腔內視鏡腹膜沖洗分期檢查 (laparoscopic staging with peritoneal washings)。
- 頸部食道癌或不超過環咽部 (cricopharyngeal) 5 公分以上之食道癌應該以決定性放射化療 (definitive chemoradiation) 治療

Principles of Surgery

- 可切除的食道癌 Stage I-IVA(Locoregional disease, except T4b or unresectable N3)
 - Tis or T1a 腫瘤 (可考慮 EMR+Ablation 或手術)
 - T1b 腫瘤
 - T1-T3 腫瘤，即使局部淋巴腺已經轉移，多區域 (multi-station) 淋巴腺或巨大 (bulky) 淋巴腺轉移為手術切除之 relative contraindication，可否切除尚應考慮，如年齡、體能狀態、或治療反應等其他因素
 - T4a 腫瘤，侵犯至肋膜、心包膜或橫隔膜
- 不可切除的食道癌 Stage IVA(including T4b or unresectable N3) & IVB(metastatic disease)
 - cT4b 腫瘤：侵犯心臟、大血管、氣管、或鄰近器官包括肝、胰、肺及脾臟
 - 多區域 (multi-station) 淋巴腺或巨大 (bulky) 淋巴腺侵犯，大多數應視為不可切除，然而淋巴侵犯可否切除尚應考慮，如年齡、體能狀態、或治療反應等其他因素
 - EJG 腫瘤患者合併鎖骨上淋巴轉移應視為不可切除
 - 轉移第 IV 期之食道癌 (包括非區域淋巴腺 non-regional lymph node 轉移)
- 食道切除方式之選擇取決於腫瘤位置、可選擇重建之器官，手術者之經驗及喜好，以及病患之喜好
- 病患在術前引導期間無法經口進食以維持營養者可考慮食道擴張或空腸造瘻 (J-tube)，優於胃造瘻術 (會妨礙往後胃重建手術時胃管之健全)

Principles of Surgery

- 可接受之食道及胃交接腫瘤切除術式

- Ivor Lewis esophagogastrectomy (開腹及右側開胸)
- McKeown esohagogastrctomy (右側開胸、開腹及頸部吻合)
- Minimally invasive Ivor Lewis esophagogastrectomy (腹腔鏡及微創右側開胸)
- Minimally invasive McKeown esophagogastrectomy (胸腔鏡、微創開腹 / 腹腔鏡及頸部吻合)
- Transhiatal esophagogastrectomy (開腹不經胸腔及頸部吻合)
- Robotic minimally invasive esophagogastrectomy (機器手臂輔助微創術式)
- Left transthoracic or thoracoabdominal approaches with anastomosis in chest or neck(左側開胸或胸腹聯合術式、胸腔或頸部吻合)

- 可接受之食道重建取代物

- 胃（優先選擇）

- 大腸

- 空腸

- 可接受之淋巴擴清方式

- 標準方式

- 擴展方式（整體 En-bloc 方式）

- 至少需移除或評估 15 個以上之淋巴結以達到適當的淋巴分期，若術前接受過放射化學治療，雖適切需移除或評估之淋巴結數量仍然未知，仍建議移除或評估 15 個以上之淋巴結

- 患者經過決定性放射及化學治療後，仍有可切除之局部腫瘤，且沒有遠端轉移，可以考慮食道切除

- 食道切除，內視鏡食道黏膜切除，及其他燒灼術式，應在高容量之食道治療中心由有經驗的外科醫師或內視鏡醫師執行

Reference for principles of surgery

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6. Wang BY, Liu CY, Lin CH, Hsu PK, Hsu WH, Wu YC, Cheng CY. Endoscopic Tumor Length Is an Independent Prognostic Factor in Esophageal Squamous Cell Carcinoma. *Ann Surg Oncol*. 2012;19:2149-58. (SCI)
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8. Hsu PK, Wang BY, Chou TY, Huang CS, Wu YC, Hsu WH. The total number of resected lymph node is not a prognostic factor for recurrence in esophageal squamous cell carcinoma patients undergone transthoracic esophagectomy. *J Surg Oncol*. 2011;103:416-20. (SCI)
9. Wang BY, Goan YG, Hsu PK, Hsu WH, Wu YC. Tumor length as a prognostic factor in esophageal squamous cell carcinoma. *Ann Thorac Surg*. 2011;91:887-93. (SCI)

Follow-up

- 病史和身體檢查
 - 每 3 到 6 個月一次，維持 1 到 2 年。
 - 然後，每 6 到 12 個月一次，維持 3 到 5 年。
- 臨床檢查
 - 依臨床指示，生化檢驗及全套血液檢查。
 - 依臨床指示安排影像學檢查。
 - 根據臨床需求進行上消化道內視鏡檢查和組織切片。
 - 針對食道手術吻合口狹窄處進行擴張術治療。
 - 安排營養評估與諮詢。

《食道癌抗癌藥物治療指引》

Preoperative Chemoradiation Therapy of Esophageal Cancer Preferred Regimens

Paclitaxel + Carboplatin

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Paclitaxel	50	1	QW	5	1
Carboplatin	AUC 2	1	QW	5	

Cisplatin + Fluoropyrimidine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Cisplatin	75	1	Q4W	2(RT) + 2	2
5-FU	1000*	1-4	Q4W	2(RT) + 2	

* Continuous infusion for 24 hours

藥品名 *	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Cisplatin	15	1-5	Q3W	2	5
5-FU	800*	1-5	Q3W	2	

* Continuous infusion for 24 hours

藥品名 *	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Cisplatin	30	1	QW	5	43
Capecitabine	800 PO BID	1-5	QW	5	

Oxaliplatin + Fluoropyrimidine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q2W	3(RT) + 3	2
Leucovorin	400	1	Q2W	3(RT) + 3	
5-FU	400	1	Q2W	3(RT) + 3	
5-FU	800*	1-2	Q2W	3(RT) + 3	

* Continuous infusion for 24 hours

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1, 15, 29		For 3 doses	42
Capecitabine	625 PO BID	1-5	QW	5	

Other Regimens

Cisplatin + Fluorouracil

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Cisplatin	100	1, 29	Q35D	1	4
5-Fu	1000	1-4, 29-32	Q35D	1	

Irinotecan + Cisplatin

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Irinotecan	65	1, 8, 22, 29		1	6
Cisplatin	30	1, 8, 22, 29		1	

Paclitaxel + Fluoropyrimidine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Paclitaxel	45	1	QW	5	7
5-FU	300*	1-5	QW	5	

* Continuous infusion for 24 hours

Perioperative Chemotherapy (Include EGJ)
Preferred Regimens
ECF medications

藥品名 *	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Epirubicin	50	1	Q3W	6*	9
Cisplatin	60	1	Q3W	6*	
Capecitabine	625 PO BID	1-21	Q3W	6*	

*3(pre-op) + 3(post-op)

藥品名 *	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Epirubicin	50	1	Q3W	6*	9
Oxaliplatin	130	1	Q3W	6*	
Capecitabine	625 PO BID	1-21	Q3W	6*	

*3(pre-op) + 3(post-op)

Oxaliplatin + Fluoropyrimidine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q2W	6 [#]	22
Leucovorin	400	1	Q2W	6 [#]	
5-FU	400	1	Q2W	6 [#]	
5-FU	1200*	1-2	Q2W	6 [#]	

* Continuous infusion for 24 hours #3 (pre-op) + 3 (post-op)

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q2W	6 [#]	19
Leucovorin	200	1	Q2W	6 [#]	
5-FU	2600*	1	Q2W	6 [#]	

* Continuous infusion for 24 hours #3 (pre-op) + 3 (post-op)

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Oxaliplatin	130	1	Q3W	6 [#]	23
Capecitabine	1000 PO BID	1-14	Q3W	6 [#]	

#3 (pre-op) + 3 (post-op)

Oxaliplatin + Fluoropyrimidine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Docetaxel	50	1	Q2W	8 [#]	8
Oxaliplatin	85	1	Q2W	8 [#]	
Leucovorin	200	1	Q2W	8 [#]	
5-FU	2600*	1	Q2W	8 [#]	

* Continuous infusion for 24 hours [#]4 (pre-op) + 4 (post-op)

Other Regimens

Cisplatin + Fluorouracil

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Cisplatin	100	1	Q4W	6 [#]	9
5-Fu	800*	1-5	Q4W	6 [#]	

* Continuous infusion for 24 hours [#]2-3 (pre-op) + 3-4 (post-op)

Preoperative Chemotherapy

(Only for adenocarcinoma of the thoracic esophagus or EGJ)

Cisplatin + Fluorouracil

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Cisplatin	80	1	Q3W	2 [#]	10
5-Fu	1000*	1-4	Q3W	2 [#]	

* Continuous infusion for 24 hours [#]2(pre-op)

Definitive Chemoradiation (Non-Surgical) Preferred Regimens

Oxaliplatin + Fluoropyrimidine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q2W	6 [#]	5
Leucovorin	400	1	Q2W	6 [#]	
5-FU	400	1	Q2W	6 [#]	
5-FU	800*	1-2	Q2W	6 [#]	

* Continuous infusion for 24 hours #3 (RT) + 3 (post-RT)

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1, 15, 29		For 3 doses	42
Capecitabine	625 PO BID	1-5	QW	5	

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1, 15, 29			3
5-FU	180	1-33			

Paclitaxel + Carboplatin

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Paclitaxel	50	1	QW	5	1
Carboplatin	AUC 2	1	QW	5	

Other Regimens

Cisplatin + Fluoropyrimidine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Cisplatin	75	1	Q4W	2~4#	11
5-FU	1000*	1-4	Q4W	2~4#	

* Continuous infusion for 24 hours #2 (RT) + 2

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Cisplatin	30	1	QW	5	41
Capecitabine	800 PO BID	1-5	QW	5	

Taxane + Cisplatin

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Paclitaxel	60	1, 8 , 15, 22		1	12
Cisplatin	75	1		1	

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Docetaxel	60	1, 22		1	13
Cisplatin	80	1, 22		1	

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Docetaxel	30	1	QW	5	14
Cisplatin	30	1	QW	5	

Irinotecan + Cisplatin

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Irinotecan	65	1, 8, 22, 29		1	6
Cisplatin	30	1, 8, 22, 29		1	

Paclitaxel + Fluoropyrimidine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Paclitaxel	45-50	1	QW	5	7
5-FU	300*	1-5	QW	5	

* Continuous infusion for 24 hours

Postoperative Chemoradiation (Including EGJ)

5-FU (bolus) + Leucovorin

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Lecovorin	20	1-5	Q4W	1 st , 3 rd , 4 th #	15, 44
5-FU	425	1-5	Q4W	1 st , 3 rd , 4 th #	
Lecovorin	20	1-4, 31-33	Q5W	2 nd (with RT)	
5-FU	400	1-4, 31-33	Q5W	2 nd (with RT)	

#Cycle 1st (pre-RT), and cycle 3rd, 4th (post-RT)

5-FU + Leucovorin modifications

1 cycle before + 2 cycle after chemoradiation

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Capecitabine	1000 PO BID	1-14	Q4W	1 + 2	45

2 cycle before + 4 cycle after chemoradiation

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Leucovorin	400	1	Q2W	2 + 4	58
5-FU	400	1	Q2W	2 + 4	
5-FU	1200*	1-2	Q2W	2 + 4	

*Continuous infusion for 24 hours

With radiation

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
5-FU	200*	1-5 or 1-7	QW	5 with RT	46

*Continuous infusion for 24 hours

藥品名 *	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Capecitabine	825 PO BID	1-5 or 1-7	QW	5 with RT	47

Postoperative Chemotherapy**Preferred Regimens****Nivolumab only after preoperative chemoradiation with R0 resection and residual disease**

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Nivolumab	240 mg	1	Q2W	8	49
Followed by					
Nivolumab	480 mg	1	Q4W	For max 1 year	

Other Recommended Regimens**Oxaliplatin + Capecitabine**

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Oxaliplatin	130	1	Q3W		16
Capecitabine	1000 PO BID	1-14	Q3W		

Oxaliplatin + Fluorouracil

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q2W		22
Leucovorin	400	1	Q2W		
5-FU	400	1	Q2W		
5-FU	1200*	1-2	Q2W		

* Continuous infusion for 24 hours #3 (RT) + 3 (post-RT)

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q2W		19
Leucovorin	200	1	Q2W		
5-FU	2600*	1	Q2W		

* Continuous infusion for 24 hours #3 (RT) + 3 (post-RT)

Neoadjuvant or Perioperative Immunotherapy
Nivolumab and Ipilimumab followed by Nivolumab (MSI-H/dMMR)

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Nivolumab	240 mg	1	Q2W	Pre-OP X 6	54
Ipilimumab	1 mg/kg	1	Q6W	Pre-OP X 2	
Followed by surgery					
Nivolumab	480 mg	1	Q4W	Pre-OP X 9	

Pembrolizumab (MSI-H/dMMR)

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Pembrolizumab Followed by surgery	200 mg	1	Q3W	Pre-OP X 2	55, 56
Pembrolizumab	200 mg	1	Q3W	Pre-OP X 5	

Tremelimumab + Durvalumab (MSI-H/dMMR) (for neoadjuvant therapy only)

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Tremelimumab	300 mg	1	Q12W	Pre-OP X 1	57
Durvalumab	1500 mg	1	Q4W	Pre-OP X 3	

Systemic therapy for metastatic or locally advanced cancer**(where local therapy is not indicated)****First-line Therapy****Trastuzumab (with chemotherapy)**

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Trastuzumab	8 → 6 mg/kg	1	Q3W		17, 53

Trastuzumab (with chemotherapy)

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Trastuzumab	6 → 4 mg/kg	1	Q2W		17

Preferred Regimens
± Nivolumab + Oxaliplatin + Capecitabine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
± Nivolumab	360 mg	1	Q3W		51
Oxaliplatin	130	1	Q3W		23
Capecitabine	1000 PO BID	1-14	Q3W		

For adenocarcinoma (PD-L1 CPS: 1-4, category 2B; ≥ 5, category 1) or Squamous cell carcinoma.

*2023 NCCN & 團隊共識

± Nivolumab + Oxaliplatin + 5Fu

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
± Nivolumab	240 mg	1	Q2W		50
Oxaliplatin	85	1	Q2W		22
Leucovorin	400	1	Q2W		
5-FU	400	1	Q2W		
5-FU	1200*	1-2	Q2W		

For adenocarcinoma (PD-L1 CPS: 1-4, category 2B; ≥ 5, category 1) or Squamous cell carcinoma.

* Continuous infusion for 24 hours

Nivolumab + 5FU + Cisplatin

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Nivolumab	360 mg	1	Q3W	Max 2 years	50
Cisplatin	80	1	Q3W	Max 2 years	54
Capecitabine	850~1000* PO BID	1-14	Q3W	Max 2 years	

*2023 NCCN & 團隊共識

Pembrolizumab + Oxaliplatin + Capecitabine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Pembrolizumab	200 mg	1	Q3W	Up to 2 years	51
Oxaliplatin	130	1	Q3W	6	
Capecitabine	1000 PO BID	1-14	Q3W	6	

*2023 NCCN & 團隊共識

Pembrolizumab + Oxaliplatin + 5Fu

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Pembrolizumab	200 mg	1	Q2W	Up to 2 years	51
Oxaliplatin	85	1	Q2W	9	
Leucovorin	400	1	Q2W	9	
5-FU	400	1	Q2W	9	
5-FU	1200*	1-2	Q2W	9	

* Continuous infusion for 24 hours

Pembrolizumab + Cisplatin + 5Fu

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Pembrolizumab	200 mg	1	Q3W	Up to 2 years	51
Cisplatin	80	1	Q3W	6	
5-Fu	800*	1-5	Q3W	6	

* Continuous infusion for 24 hours

Pembrolizumab + Cisplatin + Capecitabine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Pembrolizumab	200 mg	1	Q3W	Up to 2 years	51
Cisplatin	80	1	Q3W	6	
Capecitabine	1000 PO BID	1-14	Q3W	6	

*2023 NCCN & 團隊共識

Fluoropyrimidine + Cisplatin

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Cisplatin	100	1	Q4W		18
5-FU	1000*	1-4	Q4W		

* Continuous infusion for 24 hours

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Cisplatin	50	1	Q2W		19, 20
Leucovorin	200	1	Q2W		
5-FU	2000*	1	Q2W		

* Continuous infusion for 24 hours

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Cisplatin	80	1	Q3W		21
Capecitabine	1000 PO BID	1-4	Q3W		

*2023 NCCN & 團隊共識

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Nivolumab	3 mg/kg	1	Q3W	Max 2 years	53
Ipilimumab	1 mg/kg	1	Q6W		

Fluoropyrimidine + Oxaliplatin

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q2W		19
Leucovorin	200	1	Q2W		
5-FU	2600*	1	Q2W		

* Continuous infusion for 24 hours

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Oxaliplatin	85	1	Q3W		47
Capecitabine	625 PO BID	1-14	Q3W		

MSI-H/dMMR tumors (independent of PD-L1 status)

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Pembrolizumab	200 mg	1	Q3W		55

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Pembrolizumab	400 mg	1	Q6W		56

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Nivolumab	1 mg/kg	1	Q3W	4	57
Ipilimumab	3 mg/kg	1	Q3W	4	
Followed by					
Nivolumab	240 mg	1	Q2W	Max 2 years	

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Nivolumab	240 mg	1	Q3W	4	57
Ipilimumab	1 mg/kg	1	Q3W	4	
Followed by					
Nivolumab	240 mg (480 mg)	1	Q2W (Q4W)	Max 2 years	

Other Regimens
Paclitaxel + Cisplatin/Carboplatin

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Paclitaxel	200	1	Q3W		24
Cisplatin	75	2	Q3W		

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Paclitaxel	90	1	Q2W		25
Cisplatin	50	1	Q2W		

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Paclitaxel	200	1	Q3W		26
Carboplatin	AUC 5	1	Q3W		

Docetaxel + Cisplatin

藥品名*	劑量 mg/m ² *	給藥日	頻率	週期	參考文獻
Docetaxel	75-85	1	Q3W		27, 28
Cisplatin	70-75	1	Q3W		

Fluoropyrimidine

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Leucovorin	400	1	Q2W		20
5-FU	400	1	Q2W		
5-FU	1200*	1-2	Q2W		

* Continuous infusion for 24 hours

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
5-FU	800*	1-5	Q4W		29

* Continuous infusion for 24 hours

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Capecitabine	1250 PO BID	1-14	Q3W		30

Taxane

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Docetaxel	100	1	Q3W		31, 32

藥品名 *	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Paclitaxel	250	1	Q3W		33

藥品名 *	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Paclitaxel	80	1	QW		34

Irinotecan + 5-FU (only for adenocarcinoma)

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Irinotecan	180	1	Q2W		35
Leucovorin	400	1	Q2W		
5-FU	400	1	Q2W		
5-FU	1200*	1-2	Q2W		

* Continuous infusion for 24 hours

藥品名	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Irinotecan	80	1	QW	6 + 2(off)‡	48
Leucovorin	500	1	QW	6 + 2(off)‡	
5-FU	2000*	1	QW	6 + 2(off)‡	

* Continuous infusion for 24 hours ‡6 weeks treatment, followed by 2 weeks off

ECF

藥品名*	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Epirubicin	50	1	Q3W		38
Cisplatin	60	1	Q3W		
5-Fu	200*	1-21	Q3W		

* Continuous infusion for 24 hours

ECF modifications

藥品名*	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Epirubicin	50	1	Q3W		39, 40
Oxaliplatin	130	1	Q3W		
5-Fu	200*	1-21	Q3W		

* Continuous infusion for 24 hours

藥品名*	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Epirubicin	50	1	Q3W		39, 40
Cisplatin	60	1	Q3W		
Capecitabine	625 PO BID	1-21	Q3W		

藥品名*	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Epirubicin	50	1	Q3W		38
Oxaliplatin	130	1	Q3W		
Capecitabine	625 PO BID	1-21	Q3W		

DCF modifications

藥品名*	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Docetaxel	40	1	Q2W		36
Leucovorin	400	1	Q2W		
5-FU	400	1	Q2W		
5-FU	1000*	1-2	Q2W		
Cisplatin	40	3	Q2W		

* Continuous infusion for 24 hours

藥品名*	劑量 mg/m ²	給藥日	頻率	週期	參考文獻
Docetaxel	50	1	Q2W		37
Oxaliplatin	85	1	Q2W		
5-FU	1200*	1-2	Q2W		

* Continuous infusion for 24 hours

*三院有個別版本

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《食道癌放射治療共識》

一、治療範圍

1. 食道腫瘤或腫瘤原發部位
2. 淋巴轉移病灶
3. 高風險淋巴轉移範圍

二、治療劑量 / 次數

▲輔助性放射治療 (手術後)

1. 總劑量
 - (a) 殘餘腫瘤 / 腫瘤原發部位 : 50Gy(50~50.4Gy) *
 - (b) 高風險範圍 : 48Gy(45~50.4Gy)
 - (c) 照射次數 : 27 次 (25~30 次)

▲根治性放射治療 (無手術)

1. 總劑量
 - (a) 腫瘤 : 50Gy(50~50.4Gy) *
 - (b) 高風險範圍 : 48Gy(45~50.4Gy)
 - (c) 照射次數 : 27 次 (25~30 次)

* 上段食道癌可考慮增加劑量至 60~66 Gy；中下段食道癌可考慮增加劑量至 60 Gy。

▲前導性放射治療 (手術前)

1. 總劑量
 - (a) 腫瘤 : 48Gy(45~50.4Gy)

- (b) 高風險範圍：48Gy(45~50.4Gy)
- (c) 照射次數：27 次 (25~30 次)

或是

- 2. 總劑量
 - (a) 腫瘤：41.4Gy
 - (b) 高風險範圍：41.4Gy
 - (c) 照射次數：23 次

三、治療方式：

使用強度調控放射治療技術，包含弧形及螺旋放射規畫，可考慮搭配影像導引治療，治療選擇可使用同步照射高與低危險部位的方式或先給予整個照射部位部份劑量照射後，再針對高危險部位加強劑量。

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