



中山醫學大學附設醫院

院內通用抗癌藥物處方

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頭頸癌團隊	口腔癌	95/12/01 V1.0 96/05/23 V2.0 97/03/26 V3.0 98/12/09 V4.0 99/04/28 V5.0 99/11/24 V5.1 100/11/23 V6.0 101/12/05 V7.0 103/01/08 V8.0 103/2/17 V9.0 104/11/11 V10.0 105/11/09 V11.0 106/12/06 V12.0 107/11/14 V13.0 108/11/27 V14.0	第14版	108/11/27
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Concurrent chemoradiation for stage III, IVA and IVB cancer

Cisplatin

Cisplatin	35 mg/m ² iv
Qw, total > 200 mg/m ²	

Beckmann GK et al. Hyperfractionated accelerated radiotherapy in combination with weekly cisplatin for locally advanced head and neck cancer. *Head Neck* 2005;27:36.

UFT

Uracil-tegafur	250 – 300 mg/m ² po
7 days/week	

Yuzuru Nibe et al. Effectiveness of Concurrent Radiation Therapy with UFT or TS-1 for T2N0 Glottic Cancer in Japan. *Anticancer Res* 2007;27:3497.

Cisplatin+ UFT

Cisplatin	30-35 mg/m ² iv qw
Uracil-tegafur	250 – 300 mg/m ² po 7 days/week
Qw x 7 cycles	

A phase II study of concomitant boost radiation plus concurrent weekly cisplatin for locally advanced unresectable head and neck carcinomas. *Radiother Oncol.* 2006 Apr;79(1):34-8. Epub 2006 Apr 19.

CFHx

Cisplatin	20 mg/m ² iv	d1-4
5-FU	600 mg/m ² iv	d1-4
Hydrea(Hydroxyurea)	500mg/cap 1# BID po	d1-5
Q3w x 2-3 cycles		

Hu MH et al. Cisplatin-based chemotherapy versus cetuximab in concurrent chemoradiotherapy for locally advanced head and neck cancer treatment. *Biomed Res Int* 2014;2014:904341

Concurrent targeted-radiation therapy for stage III, IVA and IVB cancer

Cetuximab

Cetuximab loading dose	400 mg/m ² iv, then 250 mg/m ² iv qw
Cetuximab loading dose	400 mg/m ² iv, then 500 mg/m ² iv q2w

Bonner JA et al. Radiotherapy plus cetuximab for squamous cell carcinoma of the head and neck. *N Engl J Med* 2006; 354:567.

Neoadjuvant chemotherapy for stage III, IVA and IVB cancer

Modified TPF at CSMUH

Docetaxel	33 mg/m ² iv	d1, 8
Cisplatin	75 mg/m ² iv	d1
5-FU	750 mg/m ² /d civi	d1-4
Q3w x 3-4 cycles		

Vermorken JB et al. Cisplatin, fluorouracil, and docetaxel in unresectable head and neck cancer. *N Engl J Med* 2007; 357:1695.

Modified TPFL

Docetaxel	33 mg/m ² iv	d1, 8
Cisplatin	50 mg/m ² iv	d1
5-FU	3000 mg/m ² /d civi	46-48 hrs
Q3w x 3-6 cycles		

Jen-Tsun Lin et al. Chemotherapy with Modified Docetaxel, Cisplatin, and 5-Fluorouracil in Patients with Metastatic Head and Neck Cancer. *Adv Ther* (2012) 29(1):71-77.

Modified TP+DG

Docetaxel	20 mg/m ² iv	d1, 8
Cisplatin	50 mg/m ² iv	d1
5-FU	400 mg/m ² /d civi	d1
5-FU	1200 mg/m ² /d	46-48 hrs
Q2w x 4-6 cycles		

Cisplatin, fluorouracil, and docetaxel in unresectable head and neck cancer. *N Engl J Med*. 2007 Oct 25;357(17):1695-704.

PF

Cisplatin	70 - 80 mg/m ² iv	d1
5-FU	800 - 1000 mg/m ² /d civi	d1-4
Q3w x 3-4 cycles		

Al-Sarraf et al. Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: Phase III randomized intergroup study 0099. *J Clin Oncol* 1998 ; 16:1310.

Cisplatin + DG

Cisplatin	50 mg/m ² iv	d1
5-FU	400 mg/m ² /d civi	d1
5-FU	1200 mg/m ² /d civi	46-48 hr
Q2w x 3-4 cycles		

Platinum-based chemotherapy plus cetuximab in head and neck cancer. *N Engl J Med*. 2008 Sep 11;359(11):1116-27. doi: 10.1056/NEJMoa0802656

Adjuvant chemotherapy for stage III, IVA and IVB cancer

PF

Cisplatin	70 - 80 mg/m ² iv	d1
5-FU	800 - 1000 mg/m ² /d civi	d1-4
Q3w x 4 cycles		

Al-Sarraf et al. Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: Phase III randomized intergroup study 0099. J Clin Oncol 1998; 16:1310.

UFT

Uracil-tegafur	400 mg	till PD
5 days/week		

Yuzuru Nibe et al. Effectiveness of Concurrent Radiation Therapy with UFT or TS-1 for T2N0 Glottic Cancer in Japan. Anticancer Res 2007;27:3497.

Cisplatin+ UFT

Cisplatin	30 mg/m ² iv qw	
Uracil-tegafur	250 – 300 mg/m ² po 7 days/week	
Qw, 7 cycles		

A phase II study of concomitant boost radiation plus concurrent weekly cisplatin for locally advanced unresectable head and neck carcinomas. [Radiother Oncol](#). 2006 Apr; 79(1):34-8. Epub 2006 Apr 19.

Chemotherapy for recurrent, unresectable or stage IVC cancer

PF

Cisplatin	70 - 100 mg/m ² iv	d1
5-FU	800 - 1000 mg/m ² /d civi	d1-4
Q3w		

Al-Sarraf et al. Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: Phase III randomized intergroup study 0099. J Clin Oncol 1998; 16:1310.

Modified PFL at CSMUH

Cisplatin	50 mg/m ² iv	d1
5-FU	2400 - 3000 mg/m ² /d civi	d1
Leucovorin	200 mg/m ²	d1
Q2w		

Forastiere AA et al. Randomized comparison of cisplatin plus fluorouracil and carboplatin plus fluorouracil versus methotrexate in advanced squamous-cell carcinoma of the head and neck. J Clin Oncol 1992; 10:1245.

P-HDFL

Cisplatin	30 mg/m ² iv	d1, 8, 15
5-FU	2000 - 2600 mg/m ² /d civi	d1, 8, 15
Leucovorin	200 mg/m ² /d civi	d1, 8, 15
Q4w		

Chi KH et al. Elimination of dose limiting toxicities of cisplatin, 5-fluorouracil, and leucovorin using a weekly 24-hour infusion schedule for the treatment of patients with nasopharyngeal carcinoma. Cancer 1995;76:2186.

Paclitaxel

Paclitaxel	80 mg/m ²	d1, 8, 15
Q4w		

Grau JJ et al. Weekly paclitaxel for platin-resistant stage IV head and neck cancer patients. Acta Otolaryngol 2009;129:1294.

Modified Paclitaxel + PF at CSMUH

Paclitaxel	80 mg/m ² iv	d1, 8
Cisplatin	70 – 80 mg/m ² iv	d1
5-FU	750 mg/m ² /d civi	d1-4
Q3w		

Hitt R et al. Phase III study comparing cisplatin plus fluorouracil to paclitaxel, cisplatin, and fluorouracil induction chemotherapy followed by chemoradiotherapy in locally advanced head and neck cancer. J Clin Oncol 2005;23:8636.

Docetaxel

Docetaxel	30-40 mg/m ²	d1, 8, 15
Q4w		

Guardiola E et al. Results of a randomised phase II study comparing docetaxel with methotrexate in patients with recurrent head and neck cancer. Eur J Cancer 2004;40:2071.

Modified TPF at CSMUH

Docetaxel	33 mg/m ² iv	d1, 8
Cisplatin	75 mg/m ² iv	d1
5-FU	750 mg/m ² /d civi	d1-4
Q3w		

Vermorken JB et al. Cisplatin, fluorouracil, and docetaxel in unresectable head and neck cancer. N Eng J Med 2007; 357:1695.

Methotrexate +/- Cyclophosphamide

Methotrexate	30 - 40 mg/m ²	d1
Cyclophosphamide	200 mg/m ²	d1
Qw		

Forastiere AA et al. Randomized comparison of cisplatin plus fluorouracil and carboplatin plus fluorouracil versus methotrexate in advanced squamous-cell carcinoma of the head and neck. J Clin Oncol 1992; 10:1245.

Modified Ifosfamide +/- Doxorubicin

Doxorubicin	40 mg/m ²	d1
Ifosfamide	2000 - 3000 mg/m ² /day	d1, 2
Q2w		

Didem Sener Dede et al. Ifosfamide and Doxorubicin Combination Chemotherapy for Recurrent Nasopharyngeal Carcinoma Patients. *Asian Pacific J Cancer Prev* 2012;13:2225

Vinorelbine

Vinorelbine	25 - 30 mg/m ²	d1
Qw		

Degardin M et al. An EORTC-ECSG phase II study of vinorelbine in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck. *Ann Oncol* 1998;9:1103.

MEMOCLUB

Methotrexate	30 mg/m ²	d1
Epirubicin	30 mg/m ²	d1
Mitomycin-C	4 mg/m ²	d8
Vincristin	1 mg/m ²	d8
Cisplatin	25 mg/m ²	d8
Leucovorin	120 mg/m ²	d8
5-fluorouracil	1000 mg/m ²	d8
Bleomycin	10 mg/m ²	d8
Q2w		

Jin-Ching Lin et al. Experience of cetuximab in the salvage treatment for recurrent/metastatic oral squamous cell carcinoma. 2012 ASCO Annual Meeting. Abstract e16006

Targeted therapy for stage IVC cancer**Cetuximab +/- Chemotherapy**

Cetuximab loading dose 400 mg/m ² iv, then 250 mg/m ² iv qw
Cetuximab loading dose 400 mg/m ² iv, then 500 mg/m ² iv q2w

Hitt R et al. Phase II study of combination cetuximab and weekly paclitaxel in patients with metastatic/recurrent squamous cell carcinoma of head and neck (SCCHN): Spanish Head and Neck Cancer Group (TTCC). 2007 ASCO annual meeting. Abstract 6012.

Carboplatin

Carboplatin	AUC2-4	Cisplatin versus carboplatin
Q1W、Q2W、Q3W		

De Andrés L, Brunet J, López-Pousa A, et al. Randomized trial of neoadjuvant cisplatin and fluorouracil versus carboplatin and fluorouracil in patients with stage IV-M0 head and neck cancer. *J Clin Oncol* 1995; 13:1493.

食道癌

Neoadjuvant chemoradiation followed by surgery for resectable cancer

Cisplatin + 5-FU

5-FU	600 - 1000 mg/m ² /d civi	d1-4
Cisplatin	70 – 80 mg/m ² iv	d1
q3-4w x 2 cycles		

1. Bedenne L et al. Chemoradiation followed by surgery compared with chemoradiation alone in squamous cancer of the esophagus: FFCD 9102. J Clin Oncol 2007; 25:1160.
2. Herskovic A et al. Combined chemotherapy and radiotherapy compared with radiotherapy alone in patients with cancer of the esophagus. N Eng J Med 1992; 326:1593.

Cisplatin +/- Capecitabine (UFUR)

Cisplatin	25-30 mg/m ² iv	d1
Capecitabine	800 mg/m ² po bid	d1-5
UFUR	200-250mg/m ² /d po bid	d1-5
Qw x 12 cycles		

Lee SS 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.

Weekly PFL

Cisplatin	25 mg/m ² iv	d1
5-FU	2000 mg/m ² /d civi 46-48 hours	d1
Leucovorin	150-200 mg/m ² /d civi 46-48 hours	d1
Q2w x 6 - 12 cycles		

Bouche O 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--FFCD98.3. J Clin Oncol 2004;22:4319.

Perioperative chemotherapy for resectable adenocarcinoma

Cisplatin + 5-FU check Full paper

Cisplatin	70- 100 mg/m ² iv	d1
5-FU	750 -1000 mg/m ² /d civi	d1-4
Q3-4w total 6 cycles (2-3 cycles before operation)		

Boige V et al. Final results of a randomized trial comparing preoperative 5-fluorouracil (F) / cisplatin (P) to surgery alone in adenocarcinoma of stomach and lower esophagus (ASLE): FNLCC ACCORD07-FFCD 9703 trial. 2007 ASCO annual meeting. Abstract 4510.

Concurrent chemoradiation for locally advanced cancer

Cisplatin + 5-FU

5-FU	600 - 1000 mg/m ² /d civi	d1-4
Cisplatin	70 – 80 mg/m ² iv	d1
q3-4w x 4 cycles		

Herskovic A et al. Combined chemotherapy and radiotherapy compared with radiotherapy alone in patients with cancer of the esophagus. N Eng J Med 1992; 326:1593.

Cisplatin + Capecitabine (or UFUR)

Cisplatin	25-30 mg/m ² iv	d1
Capecitabine	800 mg/m ² po bid	d1-5
UFUR	200-250mg/m ² /d po bid	d1-5
Qw		

Lee SS 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.

Weekly PFL

Cisplatin	25 mg/m ² iv	d1
5-FU	2000 mg/m ² /d civi 46-48 hours	d1
Leucovorin	150-200 mg/m ² /d civi 46-48 hours	d1
Q2w x 6 - 12 cycles		

Bouche O 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--FFCD98.3. J Clin Oncol 2004;22:4319.

Chemotherapy for stage IV cancer

Cisplatin + 5-FU

Cisplatin	75- 100 mg/m ² iv	d1
5-FU	750 -1000 mg/m ² /d civi	d1-4
Q4w x 3 - 6 cycles		

Lorenzen S 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.

PFL

Cisplatin	50 mg/m ² iv	d1
5-FU	2400 - 3000 mg/m ² /d civi 46-48 hours	d1
Leucovorin	200 mg/m ² /d civi 46-48 hours	d1
Q2w x 6 - 12 cycles		

Bouche O 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--FFCD98.3. J Clin Oncol 2004;22:4319.

P-HDFL

Cisplatin	25-30 mg/m ² iv	d1, 8, 15
5-FU	2000 - 2600 mg/m ² /d civi	d1, 8, 15
Leucovorin	200 mg/m ² /d civi	d1, 8, 15
Q4w x 3 - 6 cycles		

Hung TC et al. Weekly 24-hour infusional 5-fluorouracil as initial treatment for advanced gastric cancer with acute disseminated intravascular coagulation. *Anticancer Res* 2008;28:1293.

Docetaxel (check weekly Docetaxel, 1, 8, q3w, 30-35mg/m²: 1, 8, 15, q4w; 22-25 mg/m²)

Docetaxel	60-75 mg/m ² iv	d1
Q3w x 4 - 6 cycles		

Albertsson M 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. *Med Oncol* 2007;24:407.

Paclitaxel

Paclitaxel	60 - 80 mg/m ² iv	d1, 8, 15
Q4w x 3 -6 cycles		

Ilson DH et al. Paclitaxel given by a weekly 1-h infusion in advanced esophageal cancer. *Ann Oncol* 2007;18:898.

Paclitaxel + Cisplatin

Paclitaxel	90 mg/m ² iv	d1
Cisplatin	50 mg/m ² iv	d1
Q2w		

Kornek, GV et al. Effective combination chemotherapy with paclitaxel and cisplatin with or without human granulocyte colony-stimulating factor and/or erythropoietin in patients with advanced gastric cancer. *Br J Cancer* 2002; 86:1858.

Ilson DH et al. Paclitaxel given by a weekly 1-h infusion in advanced esophageal cancer. *Ann Oncol* 2007;18:898.

Modified Paclitaxel + Cisplatin

Paclitaxel	60 - 80 mg/m ² iv	d1, 8, 15
Cisplatin	70-80 mg/m ²	d1
Q4w x 3 -6 cycles		

Kornek, GV et al. Effective combination chemotherapy with paclitaxel and cisplatin with or without human granulocyte colony-stimulating factor and/or erythropoietin in patients with advanced gastric cancer. *Br J Cancer* 2002; 86:1858.

Ilson DH et al. Paclitaxel given by a weekly 1-h infusion in advanced esophageal cancer. *Ann Oncol* 2007;18:898.

S-1 (TS-1)

Tegafur/potassium oxonate/gimeracil	BSA < 1.25	40mg bid
	BSA 1.25 - 1.5	50mg bid
	BSA ≥ 1.5	60mg bid
4 weeks on/2 weeks off (or 2 weeks on/1 weeks off), 1 year		

Sakuramoto S, et al. Adjuvant chemotherapy for gastric cancer with S-1, an oral fluoropyrimidine. *N Engl J Med*. 2007;357:1810.

S-1 Monotherapy as Second- or Third-Line Chemotherapy for Unresectable and Recurrent Esophageal Squamous Cell Carcinoma Akutsu Y. · Kono T. · Uesato M. · Hoshino I. · Narushima K. · Hanaoka T. · Tochigi T. · Semba Y. · Qin W. · Matsubara H. Department of Frontier Surgery, Graduate School of Medicine, Chiba University, Chiba, Japan

Pembrolizumab

(for second-line therapy for esophageal squamous cell carcinoma, esophageal adenocarcinoma, and EGJ adenocarcinoma with PD-L1 expression levels by CPS of ≥ 10 or for third-line or subsequent therapy for esophageal and EGJ adenocarcinoma with PD-L1 expression levels by CPS of ≥ 1)

Pembrolizumab 200 mg	IV	Day 1
Cycled every 21 days		

Kojima T, Muro K, Francois E, et al. Pembrolizumab versus chemotherapy as second-line therapy for advanced esophageal cancer: phase III KEYNOTE-181 study. J Clin Oncol 2019;37:2. 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.

胃癌

Adjuvant chemotherapy

Cisplatin + Capecitabine

Cisplatin	60 – 70 mg/m ² iv	d1
Capecitabine	1000 mg/m ² po bid	14 days
Q3w x 6 cycles		

Lee J et al. Phase III trial comparing capecitabine plus cisplatin versus capecitabine plus cisplatin with concurrent capecitabine radiotherapy in completely resected gastric cancer with D2 lymph node dissection: the ARTIST trial. J Clin Oncol. 2012;30:268.(stageII-III)

XELOX

Oxaliplatin	130 mg/m ² iv	d1
Capecitabine	1000 mg/m ² po bid	14 days
Q3w x 8 cycles		

or

Oxaliplatin	65 mg/m ² iv	d1, 8
Capecitabine	1000 mg/m ² po bid	14 days
Q3w x 8 cycles		

Bang YJ, et al. Adjuvant capecitabine and oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): a phase 3 open-label, randomised controlled trial. Lancet 2012;379:315. (stage II-IIIb)

TS-1

Tegafur/potassium oxonate/gimeracil	BSA < 1.25 40mg bid
	BSA 1.25 - 1.5 50mg bid
	BSA ≥ 1.5 60mg bid
4 weeks on/2 weeks off (or 2 weeks on/1 weeks off), 1 year	

Sakuramoto S, et al. Adjuvant chemotherapy for gastric cancer with S-1, an oral fluoropyrimidine. N Engl J Med. 2007;357:1810.

Tegafur/gimeracil/oteracil 複方製劑(如TS-1) (105/12/1) :

- (1)胃癌術後輔助性化療，用於罹患TNM Stage II (排除 T1) 、III A或III B 胃癌且接受過胃癌 根治性手術的成年患者，限用1年。
- (2)需經事前審查核准後使用。

TS-1+Docetaxel

TS-1 80mg/m ² on Day1-14 cycle 1 (3weeks)
Docetaxe 40mg/m ² on Day 1 and TS-1 Day1-14 cycle 2-7(every 3weeks)
TS-1 80mg/m ² on Day1-28 cycle ≥ 8 (3weeks)
3 weeks on/ 1 weeks off

Yoshida, K., Kodera, Y., Kochi, M., Ichikawa, W., Kakeji, Y., Sano, T., ... & 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.

- (1)適用晚期胃腺癌患者，包括胃食道接合處之腺癌

Fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT)

Fluorouracil 2600 mg/m ² IV continuous infusion over 24 hours on Day 1 Leucovorin 200 mg/m ² IV on Day 1 Oxaliplatin 85 mg/m ² IV on Day 1 Docetaxel 50 mg/m ² IV on Day 1 Cycled every 14 days

4 cycles preoperative and 4 cycles postoperative
--

Adjuvant chemoradiotherapy**5-FU + LV**

5-FU	425 mg/m ² /d iv	d1-5
Leucovorin	20 mg/m ² /d iv	d1-5
One month later		
5-FU	400 mg/m ² /d	d1-4 and last 3 days of RT
Leucovorin	20 mg/m ² /d iv	d1-4 and last 3 days of RT
One month after completion of RT		
5-FU	425 mg/m ² /d iv	d1-5 q4w x 2 cycles
Leucovorin	20 mg/m ² /d iv	d1-5 q4w x 2 cycles

Macdonald, JS et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med 2001; 345:725.

Chemotherapy for locally advanced unresectable and metastatic cancer**Modified FOLFOX at CSMUH**

Oxaliplatin	85 mg/m ² iv	d1
Leucovorin	150 - 200 mg/m ² civi	46-48 hours d1
5-FU	2400 - 3000 mg/m ² civi	46-48 hours d1
Q2w x 6 – 12 cycles		

P. C. Enzinger, et al. CALGB 80403/ECOG 1206: A randomized phase II study of three standard chemotherapy regimens (ECF, IC, FOLFOX) plus cetuximab in metastatic esophageal and GE junction cancer. J Clin Oncol 2010;28:15s.

XELOX

Oxaliplatin	130 mg/m ² iv	d1
Capecitabine	1000 mg/m ² po bid	14 days
Q3w x 4 -6 cycles		

or

Oxaliplatin	65 mg/m ² iv	d1, 8
Capecitabine	1000 mg/m ² po bid	14 days
Q3w x 4 -6 cycles		

Kim GM, et al. A randomized phase II trial of S-1-oxaliplatin versus capecitabine-oxaliplatin in advanced gastric cancer. Eur J Cancer 2012;48:518.

or

Oxaliplatin	85 mg/m2 iv	d1,
Capecitabine	1000 mg/m2 po bid	14 days
Q2w x 4 -6 cycles		

Yung- Chia Kou, et al. Modified Biweekly Oxaliplatin and Capecitabine for Advanced Gastric Cancer: A Retrospective Analysis from A Medical Center 2014;37:141-146. (stage II-IV)

Cisplatin + 5-FU

Cisplatin	75 - 100 mg/m2 iv	d1
5-FU	750 - 1000 mg/m2/d civi	d1-4
Q4w x 3 -6 cycles		

Lorenzen S, 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.

PFL

Cisplatin	50 mg/m2 iv	d1
5-FU	2400 - 3000 mg/m2/d civi 4	d1
Leucovorin	200 mg/m2/d civi	d1
Q2w x 6-12 cycles		

Al-Batran SE et al. Phase III trial of metastatic gastroesophageal adenocarcinoma with fluorouracil, leucovorin plus either oxaliplatin or cisplatin: a study of the Arbeitsgemeinschaft Internistische Onkologie. J Clin Oncol 2008; 26:1435

P-HDFL

Cisplatin	25-30 mg/m2 iv	d1, 8, 15
5-FU	2000 - 2600 mg/m2/d civi	d1, 8, 15
Leucovorin	200 mg/m2/d civi	d1, 8, 15
Q4w x 3-6 cycles		

Hung TC et al. Weekly 24-hour infusional 5-fluorouracil as initial treatment for advanced gastric cancer with acute disseminated intravascular coagulation. Anticancer Res 2008;28:1293.

Docetaxel +/- Cisplatin

Cisplatin	75 mg/m2 iv	d1
Docetaxel	66-75 mg/m2 iv	d1
Q3w		

Roth AD et al. Docetaxel, cisplatin; and fluorouracil; docetaxel and cisplatin; and epirubicin, cisplatin, and fluorouracil as systemic treatment for advanced gastric carcinoma: a randomized phase II trial of the Swiss Group for Clinical Cancer Research. J Clin Oncol 2007; 25:3217.

Add TS1 +/- Cisplatin in stage IV irinotecan in patients with previously untreated metastatic gastric cancer: a Federation Francophone de Cancerologie Digestive Group Study--FFCD 9803. J Clin Oncol 2004; 22:4319

Gemcitabine+Oxaliplatin+5FU+LV

Gemcitabine	1000mg/m ² iv	d1
Oxaliplatin	85mg/m ² iv 4-6hrs	d2
5FU	400mg/m ² iv 22hrs	d1 d2
LV	100 mg/m ²	d1 d2
Q2W		

Fulfaro Fet al. Gemcitabine (GEM) plus oxaliplatin, folinic acid, and 5-fluorouracil (FOLFOX-4) in patients with advanced gastric cancer. *Cancer Chemother Pharmacol.* 2005 Dec;56(6):563-8. Epub 2005 Jul 23.

Target therapy for locally advanced unresectable and metastatic cancer**Trastuzumab + Chemotherapy**

Trastuzumab 8 mg/kg iv over 90 min first wk followed by 6 mg/kg iv over 30 min q3w
Trastuzumab 6 mg/kg iv over 90 min first wk followed by 4 mg/kg iv over 30 min q2w

Bang YJ 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.

Gastric cancer stage IV dependent on prior therapy and patient performance status**Irinotecan**

Irinotecan	150-180 mg/m ² iv	d1
Q2w		

Hironaka S 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* 2013;31: 4438-4444.

Paclitaxel

Paclitaxel	60-80 mg/m ² iv	d1, 8, 15
Q4w		

Ilson DH et al. Paclitaxel given by a weekly 1 h infusion in advanced esophageal cancer. *Ann Oncol* 2007;18:898.

Ramucirumab +/- Paclitaxel

Ramucirumab	8 mg/kg iv	d1, 15
Paclitaxel	60-80 mg/m2 iv	d1, 8, 15
Q4w		

White H et al. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-esophageal junction adenocarcinoma: a double-blind, randomised phase 3 trial. Lancet Oncol 2014; 15:1224-1235.

Docetaxel

Docetaxel	66- 75 mg/m2 iv	d1
Q3w		

Irinotecan + Cisplatin

Irinotecan	65 mg/m2 iv	d1, 8
Cisplatin	25-30 mg/m2	d1, 8
Q3w		

Modified FOLFIRI at CSMUH

Irinotecan	150-180 mg/m2 iv	d1
Leucovorin	150 - 200 mg/m2 civi	46-48 hours d1
5-FU	2400 - 3000 mg/m2 civi	46-48 hours d1
Q2w		

HIPEC(Hyperthermic Intraperitoneal Chemotherapy)

Cisplatin 120 mg+Mitomycin 30mg each in 6000 ml of normal saline at 40-43°C for 60-90 min.		
Peritoneal carcinomatosis from gastric cancer		

Olivier Glehen et al. Peritoneal Carcinomatosis from Gastric Cancer: A Multi-Institutional Study of 159 Patients Treated by Cytoreductive Surgery Combined with Perioperative Intraperitoneal Chemotherapy (2010) 17:2370–2377
Xiao-Jun Yang et al. Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy Improves Survival of Patients with Peritoneal Carcinomatosis from Gastric Cancer: Final Results of a Phase III Randomized Clinical Trial (2011) 18:1575–1581

大腸癌

Adjuvant chemotherapy

Uracil-Tegafur

Uracil-Tegafur	250-300 mg/m ² /day po
7 days/week x 24 weeks	

Lembersky BC et al. Oral uracil and tegafur plus leucovorin compared with intravenous fluorouracil and leucovorin in stage II and III carcinoma of the colon: results from national surgical adjuvant breast and bowel project protocol C-06. J Clin Oncol 2006; 24:2059

Modified FOLFOX at CSMUH

Leucovorin	150 mg/m ² iv over 46 hrs	d1
5-FU	2400 -3000 mg/m ² iv over 46 hrs	d1
Oxaliplatin	85 mg/m ² iv	d1
Q2w x 12 cycles		

1.de Gramont A et al. Oxaliplatin/5FU/LV in adjuvant colon cancer: updated efficacy results of the MOSAIC trial, including survival, with a medium follow-up of six years. 2007 ASCO annual meeting. Abstract 4007
 2.Tournigand, C et al. FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: A randomized GERCOR study. J Clin Oncol 2004; 22:229

XELOX

Capecitabine	825mg/m ² po bid	d1-14
Oxaliplatin	50 mg/m ² iv	d1
Q2w		

Rodel C et al. Multicenter phase II trial of chemoradiation with oxaliplatin for rectal cancer. J Clin Oncol 2007; 25:110.

Palliative chemotherapy

Modified FOLFOX

Leucovorin	150 mg/m ² iv over 46 hrs	d1
5-FU	2400 -3000 mg/m ² iv over 46 hrs	d1
Oxaliplatin	85 mg/m ² iv	d1
q2w		

Tournigand, C et al. FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: A randomized GERCOR study. J Clin Oncol 2004; 22:229

FOLFIRI

Leucovorin	400 mg/m ² iv over 2 hrs before 5-FU	d1
5-FU	400 mg/m ² iv bolus d1, and then 2400 mg/m ² iv over 46 hrs	d1
Irinotecan	150 - 180 mg/m ² iv	d1
q2w		

1.Fuchs CS et al. Randomized, controlled trial of irinotecan plus infusional, bolus, or oral fluoropyrimidines in first-line treatment of metastatic colorectal cancer: results from the BICC-C study. J Clin Oncol 2007; 25:4779.
 2.Van Cutsem E et al. Randomized phase III study of irinotecan and 5-FU/FA with or without cetuximab in the first-line treatment of patients with metastatic colorectal cancer (mCRC): The CRYSTAL trial. 2007 ASCO annual meeting. Abstract 4000.

Modified FOLFIRI

Leucovorin	150 mg/m ² iv over 46 hrs	d1
5-FU	2400 - 3000 mg/m ² iv over 46 hrs	d1
Irinotecan	150 - 180 mg/m ² iv	d1
q2w		

1. Fuchs CS et al. Randomized, controlled trial of irinotecan plus infusional, bolus, or oral fluoropyrimidines in first-line treatment of metastatic colorectal cancer: results from the BICC-C study. J Clin Oncol 2007; 25:4779.
2. Van Cutsem E et al. Randomized phase III study of irinotecan and 5-FU/FA with or without cetuximab in the first-line treatment of patients with metastatic colorectal cancer (mCRC): The CRYSTAL trial. 2007 ASCO annual meeting. Abstract 4000.

Capecitabine

Capecitabine	1000-1250 mg/m ² po bid	14 days
q3w till disease progression		

Van Cutsem, E et al. Oral capecitabine compared with intravenous fluorouracil plus leucovorin in patients with metastatic colorectal cancer: Results of a large phase III study. J Clin Oncol 2001; 19:4097.

Modified Uracil-Tegafur

Uracil-Tegafur	250 - 300 mg/m ² /day	
7 days/week		

Hochster HS et al. Phase II study of uracil-tegafur with leucovorin in elderly (> 75 years old) patients with colorectal cancer: ECOG 1299. J Clin Oncol 2007; 25:5397.

FOLFOXIRI

Irinotecan	160→mg/m ² 60 min	d1
Oxaliplatin	65→ mg/m ² iv	d1
Leucovorin	400 mg/m ² iv over 46 hrs	d1
5-FU	2400→mg/m ² iv over 48hrs	d1
Q2w		

FOLFOXIRI plus bevacizumab versus FOLFIRI plus bevacizumab as first –line treatment of patients with metastatic colorectal cancer: updated overall survival and molecular subgroup analyses of the open-label, phase 3 TRIBE study Chiara Cremolini et al Vol 16. October 2015; 1308
註: 依病人狀況調整劑量

Target therapy for stage IV cancer

Bevacizumab + chemotherapy

Bevacizumab	5 mg/kg iv	d1
q2w		

1. Phase II, randomized trial comparing bevacizumab plus fluorouracil (FU)/leucovorin (LV) with FU/LV alone in patients with metastatic colorectal cancer. J Clin Oncol 2003; 21:60
2. Saltz LB et al. Bevacizumab (Bev) in combination with XELOX or FOLFOX4: efficacy results from XELOX-1/No 16966, a randomized phase III trial in the first-line treatment of metastatic colorectal cancer (MCRC). 2007 Gastrointestinal Cancers Symposium. Abstract 238.
3. Giantonio, BJ et al. Bevacizumab in combination with oxaliplatin, fluorouracil, and leucovorin (FOLFOX4) for previously treated metastatic colorectal cancer: Results from the Eastern Cooperative Oncology Group Study E3200. J Clin Oncol 2007; 25:1539.
4. Hurwitz, H et al. Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer. N Engl J Med 2004; 350:2335.

Cetuximab +/- chemotherapy (for patients with wild-type KRAS)

Cetuximab	400 mg/m ² iv d1, and then 500 mg/m ² iv over 1 hour
q2w	

1. Bokemeyer C et al. KRAS status and efficacy of first-line treatment of patients with metastatic colorectal cancer (mCRC) with FOLFOX with or without cetuximab: the OPUS experience. 2008 ASCO annual meeting. Abstract 4000.
2. Van Cutsem E et al. KRAS status and efficacy in the first-line treatment of patients with metastatic colorectal cancer (mCRC) treated with or without cetuximab: the CRYSTAL experience. 2008 ASCO annual meeting. Abstract 2.
3. Jonker DJ et al. Cetuximab for the treatment of colorectal cancer. N Engl J Med 2007; 357:2040.
4. Sobrero AF et al. EPIC: phase III trial of cetuximab plus irinotecan after fluoropyrimidine and oxaliplatin failure in patients with metastatic colorectal cancer. J Clin Oncol 2008; 26:2311.

Target therapy +/- chemotherapy

Target therapy(Optional)	STIVARGA (regorafenib) 400 mg/m² x4 po QD
	21 days/cycle

STIVARGA (regorafenib) tablets, oral. Wayne, N.J.:Bayer HealthCare Pharmaceuticals; 2018.

Target therapy(Optional)	ZALTRAP 4 mg/kg iv over 1 hour
	q2w

ZALTRAP® (ziv-aflibercept). Bridgewater, NJ:Regeneron Pharmaceuticals, Inc. / sanofi-aventis U.S. LLC; 2016.

TAS-102(Trifluridine+tipiracil) 20mg/tab(35 mg/m²) (Optional)

1. 建議劑量及療程: 每天給藥兩次，在第1~5天與第8~12天，每28天為一個療程。
2. 最大劑量不可超過82mg。

Bendell JC, Rosen LS, Mayer RJ, et al. Phase 1 study of oral TAS-102 in patients with refractory metastatic colorectal cancer. Cancer Chemother Pharmacol 2015;76:925-932

TS-1 (Tegafur) 20mg/cap(Optional)

1. 建議劑量如下表格:

體表面積	早餐後30分鐘	晚餐後30分鐘	一天總劑量
<1.25m ²	服用2顆20mg TS-1	服用2顆20mg TS-1	80mg/天
1.25m ² ~1.5m ²	服用2顆25mg TS-1	服用2顆25mg TS-1	100mg/天
1.5m ²	服用3顆20mg TS-1	服用3顆20mg TS-1	120mg/天

2. 服藥週期:連續服用28天(4周)，接著休息14天(2周)。
3. TS-1與Irinotecan合併使用於已使用含有Oxaliplatin化學療法失敗之轉移性大腸直腸癌患者。
4. TS-1與Irinotecan合併使用:Irinotecan的劑量為125mg/m²，靜脈輸注，每兩週給藥一次。TS-1的劑量根據病人體表面積，每天兩次，連續吃兩週，接著休息兩週，重複以上方式治療。

5.禁忌並用化療藥物(TS-1不可與下列藥品併用)，如下:

藥品名稱
fluoropyrimidine類抗惡性腫瘤劑 fluorouracil(5-FU) tegafur/uracil(UFT) tegafur(futrafur) doxifluridine(furtulon) capecitabine(Xeloda) carmofur(mifurof) 葉酸+tegafur-uracil合併治療 (UZEL/UFT) Levofolinate與fluorouracil合併治療(Isovorin/5-FU) fluoropyrimidine類抗真菌劑 Flucytosine(ancotil)

Zaltrap(Aflibercept) 25mg/vial (Optional)

- 1.建議劑量及療程: 4 mg/kg以靜脈輸注給藥，每2週一次，每次輸注時間超過1小時。
 - 2.與5-fluorouracil、leucovorin、irinotecan-(FOLFIRI) 合併使用，治療已使用含有oxaliplatin化學療法無效或惡化之轉移性大腸直腸癌病患。
- ZALTRAP® (ziv-aflibercept). Bridgewater, NJ:Regeneron Pharmaceuticals, Inc. / sanofi-aventis U.S. LLC; 2016.

CYRAMZA(ramucirumab) (Optional)

1. 建議劑量為 8mg/kg，每兩週靜脈輸注一次，每次輸注約 60 分鐘，在投予 FOLFIRI 之前。
- CYRAMZA (ramucirumab) injection. Indianapolis, IN:Eli Lilly and Company; 2018.

Trastuzumab+ pertuzumab (HER2-amplified and RAS WT) (Optional)

Trastuzumab can be given after completion of chemotherapy as well, loading dose 8mg/kg . followed by 6mg/kg . iv q3w

Trastuzumab can be given after completion of chemotherapy as well . loading Dose 840mg , followed by 420mg . iv q3w

Sartore-Bianchi A, Trusolino L, Martino C, et al. Dual-targeted therapy with trastuzumab and lapatinib in treatment-refractory, KRAS codon 12/13 wild-type, HER2-positive metastatic colorectal cancer (HERACLES): a proof-of-concept, multicentre, open-label, phase 2 trial.Lancet Oncol 2016;17:738-746.

Trastuzumab+ lapatinib (HER2-amplified and RAS WT) (Optional)

Trastuzumab can be given after completion of chemotherapy as well, loading dose 8mg/kg . followed by 6mg/kg . iv q3w

Lapatinib 1000mg PO daily.

Sartore-Bianchi A, Trusolino L, Martino C, et al. Dual-targeted therapy with trastuzumab and lapatinib in treatment-refractory, KRAS codon 12/13 wild-type, HER2-positive metastatic colorectal cancer (HERACLES): a proof-of-concept, multicentre, open-label, phase 2 trial.Lancet Oncol 2016;17:738-746.

直腸癌

Neoadjuvant chemoradiation for rectal cancer

Capecitabine

Capecitabine	750 - 825 mg/m ² po bid
7 days/week	

Krishnan S et al. Phase II study of capecitabine (Xeloda) and concurrent boost radiotherapy in patients with locally advanced rectal cancer. Int J Radiat Oncol Bio Phys 2006; 66:762.

Uracil-tegafur (UFT)

Uracil-tegafur	250 - 300 mg/m ² /day po
7 days/week	

C. H. Hsieh et al. Adjuvant CCRT for locally advanced rectal cancer: Uracil-tegafur? Or intravenous fluorouracil? J Clin Oncol 2006 ASCO Annual Meeting Proceedings; 24: 13584

XELOX

Capecitabine	825 mg/m ² po bid	d1-14
Oxaliplatin	50 mg/m ² iv	d1, 8
q3w		

Rodel C et al. Multicenter phase II trial of chemoradiation with oxaliplatin for rectal cancer. J Clin Oncol 2007; 25:110.

Adjuvant chemotherapy

Uracil-Tegafur

Uracil-Tegafur	250-300 mg/m ² /day po
7 days/week x 24 weeks	

Lembersky BC et al. Oral uracil and tegafur plus leucovorin compared with intravenous fluorouracil and leucovorin in stage II and III carcinoma of the colon: results from national surgical adjuvant breast and bowel project protocol C-06. J Clin Oncol 2006; 24:2059

Capecitabine

Capecitabine	1000 - 1250 mg/m ² po bid	d1-14
q3w x 8 cycles		

Twelves C et al. Capecitabine as adjuvant treatment for stage III colon cancer. N Engl J Med 2005; 352:2696.

Modified FOLFOX at CSMUH

Leucovorin	150 mg/m ² iv over 46 hrs	d1
5-FU	2400 -3000 mg/m ² iv over 46 hrs	d1
Oxaliplatin	85 mg/m ² iv	d1
Q2w x 12 cycles		

de Gramont A et al. Oxaliplatin/5FU/LV in adjuvant colon cancer: updated efficacy results of the MOSAIC trial, including survival, with a medium follow-up of six years. 2007 ASCO annual meeting. Abstract 4007

Tournigand, C et al. FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: A randomized GERCOR study. J Clin Oncol 2004; 22:229

CapeOX

Capecitabine	850 – 1000 mg/m ² po bid	14 days
Oxaliplatin	130 mg/m ² iv	d1
Q3w x 8 cycles		

Schmoll H et al. Phase III trial of capecitabine plus oxaliplatin as adjuvant therapy for stage III colon cancer: a planned safety analysis in 1,864 patients. J Clin Oncol 2007; 25:102.

mHDFL

Leucovorin	400 mg/m ² iv 2 hrs	d1
5-FU	2400 -3000 mg/m ² iv over 46 hrs	d1
Q2 w x 12 cycles		

A de Gramont, et al. Randomized trial comparing monthly low dose leucovorin and fluorouracil bolus with bimonthly high dose leucovorin and fluorouracil bolus plus continuous infusion for advanced colorectal cancer: a French intergroup study. J Clin Oncol 1997; 1:808.

McCleary NJ, et al. Impact of older age on the efficacy of newer adjuvant therapies in >12,500 patients (pts) with stage II/III colon cancer: Findings from the ACCENT Database. J Clin Oncol 2009; 27:15s.

Chemotherapy for stage IV cancer**Modified FOLFOX at CSMUH**

Leucovorin	150 mg/m ² iv over 46 hrs	d1
5-FU	2400 -3000 mg/m ² iv over 46 hrs	d1
Oxaliplatin	85 mg/m ² iv	d1
q2w		

Tournigand, C et al. FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: A randomized GERCOR study. J Clin Oncol 2004; 22:229

Modified FUOX at CSMUH

Leucovorin	500 mg/m ² iv over 2 hours	d1, 8, 15, 22
5-FU	2000 -2600 mg/m ² iv over 22 hrs	d1, 8, 15, 22
Oxaliplatin	50 mg/m ² iv	d1, 8, 15, 22
q5w		

Porschen R et al. Phase III study of capecitabine plus oxaliplatin compared with fluorouracil and leucovorin plus oxaliplatin in metastatic colorectal cancer: a final report of the AIO Colorectal Study Group. J Clin Oncol 2007; 25:4217 .

FOLFIRI

Leucovorin	400 mg/m ² iv over 2 hrs before 5-FU	d1
5-FU	400 mg/m ² iv bolus d1, and then 2400 mg/m ² iv over 46 hrs	d1
Irinotecan	150 - 180 mg/m ² iv	d1
q2w		

Modified FOLFIRI at CSMUH

Leucovorin	150 mg/m ² iv over 46 hrs	d1
5-FU	2400 - 3000 mg/m ² iv over 46 hrs	d1
Irinotecan	150 - 180 mg/m ² iv	d1
q2w		

Fuchs CS et al. Randomized, controlled trial of irinotecan plus infusional, bolus, or oral fluoropyrimidines in first-line treatment of metastatic colorectal cancer: results from the BICC-C study. J Clin Oncol 2007; 25:4779.

Van Cutsem E et al. Randomized phase III study of irinotecan and 5-FU/FA with or without cetuximab in the first-line treatment of patients with metastatic colorectal cancer (mCRC): The CRYSTAL trial. 2007 ASCO annual meeting. Abstract 4000.

CapeOX

Capecitabine	850 - 1000 mg/m ² po bid	d1-14
Oxaliplatin	50 - 70 mg/m ² iv	d1, 8
q3w		

Mayer RJ et al. Should capecitabine replace infusional fluorouracil and leucovorin when combined with oxaliplatin in metastatic colorectal cancer (Editorial). J Clin Oncol 2007; 25:4165.

Porschen R et al. Phase III study of capecitabine plus oxaliplatin compared with fluorouracil and leucovorin plus oxaliplatin in metastatic colorectal cancer: a final report of the AIO Colorectal Study Group. J Clin Oncol 2007; 25:4217.

Capecitabine

Capecitabine	1000-1250 mg/m ² po bid	14 days
q3w till disease progression		

Van Cutsem, E et al. Oral capecitabine compared with intravenous fluorouracil plus leucovorin in patients with metastatic colorectal cancer: Results of a large phase III study. J Clin Oncol 2001; 19:4097.

Modified Uracil-Tegafur

Uracil-Tegafur	250 - 300 mg/m ² /day
7 days/week	

Hochster HS et al. Phase II study of uracil-tegafur with leucovorin in elderly (> 75 years old) patients with colorectal cancer: ECOG 1299. J Clin Oncol 2007; 25:5397.

Irinotecan

Irenotecan	125mg/m ²	d1, 8
Q3w		

Fuchs CS et al. Phase III comparison of two irinotecan dosing regimens in second-line therapy of metastatic colorectal cancer. J Clin Oncol 2003; 21:807.

FOLFOXIRI

Irenotecan	150-165→mg/m ² 60 min	d1
Oxaliplatin	85→ mg/m ² iv	d1
Leucovorin	200 mg/m ² iv over 46 hrs	d1
5-FU	3200→mg/m ² iv over 48hrs	d1
Q2w		

FOLFOXIRI plus bevacizumab versus FOLFIRI plis bevacizumab as first –line treatment of patients with metastatic colorectal cancer:updated overall survival and molecular subgroup analyses of the open-label,phase3 TRIBE study Chiara Cremolini et al Vol 16.october 2015;1308註:依病人狀況調整劑量

Target therapy for stage IV cancer

Bevacizumab + chemotherapy

Bevacizumab	5 mg/kg iv	d1
q2w		

Phase II, randomized trial comparing bevacizumab plus fluorouracil (FU)/leucovorin (LV) with FU/LV alone in patients with metastatic colorectal cancer. J Clin Oncol 2003; 21:60

Saltz LB et al. Bevacizumab (Bev) in combination with XELOX or FOLFOX4: efficacy results from XELOX-1/No 16966, a randomized phase III trial in the first-line treatment of metastatic colorectal cancer (MCRC). 2007 Gastrointestinal Cancers Symposium. Abstract 238.

Giantonio, BJ et al. Bevacizumab in combination with oxaliplatin, fluorouracil, and leucovorin (FOLFOX4) for previously treated metastatic colorectal cancer: Results from the Eastern Cooperative Oncology Group Study E3200. J Clin Oncol 2007; 25:1539.

Hurwitz, H et al. Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer. N Engl J Med 2004; 350:2335.

Cetuximab +/- chemotherapy (for patients with wild-type KRAS)

Cetuximab	400 mg/m ² iv d1, and then 500 mg/m ² iv over 1 hour
q2w	

Bokemeyer C et al. KRAS status and efficacy of first-line treatment of patients with metastatic colorectal cancer (mCRC) with FOLFOX with or without cetuximab: the OPUS experience. 2008 ASCO annual meeting. Abstract 4000.

Van Cutsem E et al. KRAS status and efficacy in the first-line treatment of patients with metastatic colorectal cancer (mCRC) treated with or without cetuximab: the CRYSTAL experience. 2008 ASCO annual meeting. Abstract 2.

Jonker DJ et al. Cetuximab for the treatment of colorectal cancer. N Engl J Med 2007; 357:2040.

Sobrero AF et al. EPIC: phase III trial of cetuximab plus irinotecan after fluoropyrimidine and oxaliplatin failure in patients with metastatic colorectal cancer. J Clin Oncol 2008; 26:2311.

ZALTRAP +/- chemotherapy

Target therapy(Optional) 自費 ZALTRAP	4 mg/kg iv over 1 hour
	q2w

Target therapy(Optional)	STIVARGA (regorafenib) 400 mg/m ² x4 po QD
	21 days/cycle

Panitumumab(Vectibix)

1.建議劑量:6 mg/kg，每兩週一次。

2.與FOLFOX合併使用於治療K-RAS基因及N-RAS基因沒有突變之轉移性直腸結腸病患之第一線治療。

3.本藥品需事前審查核准後使用，每次申請事前審查之療程以12週為限，再次申請必須提出客觀證據(如:影像學)證實無惡化，才可繼續使用。

4.使用總療程以24週為上限。

5. Panitumumab(Vectibix)+ FOLFOX與EributxFOLFIRI 二者僅能擇依使用。微有再無法忍受化療(其副作用)時方可交換。

Rectal Cancer Neoadjuvant CCRT		
RT 5000~6000 cGy (2 Gy/day) /28 ~30Fx / 6 weeks to gross rectal tumor and 4500- 5040 cGy/ 25-28 Fx to pelvic lymph nodes by IMRT +concurrent chemotherapy regime	Regime n (1)	Capecitabine :Capecitabine 750 - 825 mg/m2 po bid 7 days/week
	Regime n (2)	Uracil-tegafur (UFT):Uracil-tegafur 250 - 300 mg/m2/day po 7 days/week
	Regime n (3)	XELOX: Capecitabine 825 mg/m2 po bid d1-14, Oxaliplatin 50 mg/m2 iv d1, 8 q3w
	Regime n (4)	5-FU + Oxaliplatin :5-FU 225 - 250 mg/m2/d civi throughout radiotherapy Oxaliplatin 50 - 60 mg/m2 iv qw
Surgery at 4~8 weeks after long course CCRT		
Post-surgery adjuvant chemotherapy follows the Colon-Rectal Cancer Adjuvant chemotherapy regimens.		

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Adjuvant Therapy First line

mFOLFIRINOX (Unresetable)

Oxaliplatin 85 mg/m ² ,IV,2hrs	d1
Leucovorin 400 mg/m ² ,IV,2hrs	d1
Irinotecan 150-180 mg/m ² ,IV,90mins	d1
5-FU 400 mg/m ² ,IV bolus	d1
5-FU 2400 mg/m ² ,IV,46hrs	2 weekly
Q2Wx6-12cycles (If clinical condition is indicated)	

Thierry Conroy et.al. N ENGL J MED 364;19 NEJM.ORG MAY 12, 2011;1817-1825

Gemcitabine + paclitaxel (Metastatic Disease)

Gemcitabine	1000 mg/m ² IV	D1, 8, 15 every 4 weeks
Paclitaxel	125 mg/m ² IV	D1, 8, 15 every 4 weeks
Q4Wx3cycles (If clinical condition is indicated)		

N Engl J Med 2013; 369:1691-1703 Von Hoff et al. ASCO 2013.

Gemcitabine+Oxaliplatin+Leucovorin +5-FU

Gemcitabine	800 mg/m ² IV
Oxaliplatin	85mg/m ² IV
Leucovorin	300mg/m ² IV
5-FU	3000mg/m ² IV
Q2W/4-6cycles	

Ch'ang HJ et.al Cancer Chemotherapy and Pharmacology 2009;64:1173-1179

Gemcitabine + Cisplatin (Locally Advanced /Metastatic Disease)

Gemcitabine	1000mg/m ² IV	D1, 15
Cisplatin	50 mg/m ² IV	D1, 15
Q2w x 4-6cycles		

Volker Heinemann et al. Randomized Phase III Trial of Gemcitabine Plus Cisplatin Compared With Gemcitabine Alone in Advanced Pancreatic Cancer. J Clin Oncol 24:3946-3952; 2006.

S-1+ Gemcitabine+Oxaliplatin+Leucovorin

S-1	35mg/m ² PO	BID D1-7
Gemcitabine	800mg/m ² IV	
Oxaliplatin	85mg/m ² IV	
Folinic acid	20mg/m ² PO	BID D1-7
Q2W/4-6cycles		

Chiang NJ et.al. 2016. TJCC

Gemcitabine +Erlotinib (Locally Advanced/Unresectable /Metastatic Disease)

Gemcitabine	1000mg/m ² IV 30min	D1, 8, 15, 22, 29, 36, 43days 1week off
Erlotinib	100/150 mg PO	days
Q4w x3-6cycles		

Moore MJ, et al. J Clin Oncol. 2007;25:1960-1966

Gemcitabine (R0 resection or Unresectable)

Gemcitabine	1000mg/m ² IV	D1, 8, 15, days
Q28days x6cycles		

Moore MJ, et al. J Clin Oncol. 2007;25:1960-1966

S-1 (R0 resection or Unresectable)

S-1	80, 100, 120mg* d1-28 PO Repeated every 6 wks
Q42dx3-6cycles	

Ueno et al, J Clin Oncol. 2013 May 1;31(13):1640-8

Gemcitabine+ S-1 (Unresectable)

Gemcitabine	1000mg/m ² IV 30min	D 1, 8,
S-1	60, 80, 100mg PO	D1-14
Q21d x3-6cycles		

Ueno et al, J Clin Oncol. 2013 May 1;31(13):1640-8

Second-line therapy (Locally Advanced/Unresectable/Metastatic Disease)

Onivyde+ Leucovorin+5-FU

Onivyde	60-80 mg/m ² IV	
Leucovorin	400 mg/m ² IV	
5-FU	2400 mg/m ² IV	46hrs
Q2w/cycles until progression		

LANCET 2015 v.387 n.10018 p.545-557

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Chemotherapy regimen for neoadjuvant and adjuvant therapy

[Indication: pathological IB (high-risk patients, 健保不給付), stage II and IIIA]

Published Chemotherapy Regimens	Schedule
Cisplatin 75mg/m ² day 1; oral Vinorelbine 60-80 mg/m ² days 1 + 8, or Vinorelbine 25 mg/m ² iv days 1 + 8	Every 21 days for 4 cycles ^a

Other Acceptable Chemotherapy Regimens (健保不給付)	Schedules
Cisplatin 75 mg/m ² on day 1 Gemcitabine 1250 mg/m ² on days 1, 8	Every 21 days for 4 cycles ^a
Cisplatin 75 mg/m ² Docetaxel 66 mg/m ² d1 or 33 mg/m ² d1 , 8	Every 21 days for 4 cycles ^a
Cisplatin 80 mg/m ² Docetaxel 22 mg/m ² d1 , 8 , 15	Every 28 days for 4 cycles ^a
Paclitaxel (160-175 mg/m ²)-d1 Cisplatin (60-75 mg/m ²)-d1	Every 21 days for 4 cycles ^a
Pemetrexed (500 mg/m ²) Cisplatin (60-75 mg/m ²)-d1	Every 21 days for 4 cycles ^a

※Note: Cisplatin 75 mg/m² q3w, Cisplatin 80 mg/m² for q4w no less than 60 mg/m²

Chemotherapy Regimens for patients with comorbidities or patients not able to tolerate cisplatin	Schedule
Gemcitabine 1000 mg/m ² on days 1, 8, Carboplatin AUC 5 on day 1	Every 21 days for 4 cycles ^f
Paclitaxel 175 mg/m ² on day 1 Carboplatin AUC 6 on day 1	Every 21 days for 4 cycles ^d
Pemetrexed 500mg/m ² d1 Carboplatin AUC 5 on day 1	Every 21 days for 4 cycles ^e

Chemotherapy Regimens for Adjuvant Therapy- Alternative

Cisplatin 若改成 Carboplatin, 劑量為 (CCr+25) x AUC, AUC = 4-6

*Paclitaxel+carboplatin regimen showed survival benefit in stage IB, > 4 cm

Chemotherapy Regimens for Adjuvant Therapy-non platinum based

(Indication: Adeno, pT2 and tumor size > 3 cm)

UFUR(for adeno)	300-600 mg as tegafur, divided by 2-3 times daily	2 years
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REFERENCES

a Winton T, Livingston R, Johnson D, et al. Vinorelbine plus cisplatin vs. observation in resected non-small-lung cancer. N Engl J Med 2005;352:2589-2597.

d Ohe Y, Ohashi Y, Kubota K, et al. Randomized phase III study of cisplatin plus irinotecan versus carboplatin plus paclitaxel, cisplatin plus gemcitabine, and cisplatin plus vinorelbine for advanced non-small-cell lung cancer: Four-Arm Cooperative Study in Japan. Ann Oncol 2007;18:317-323. Epub 2006 Nov 1.

e Fossella F, Pereira JR, von Pawel J, et al. Randomized, multinational, phase III study of docetaxel plus platinum combinations versus vinorelbine plus cisplatin for advanced non-small-cell lung cancer: the TAX 326 study group. J Clin Oncol 2003;21(16):3016-24. Epub 2003 Jul 1.

f Danson S, Middleton MR, O'Byrne KJ, et al. Phase III trial of gemcitabine and carboplatin versus mitomycin, ifosfamide, and cisplatin or mitomycin, vinblastine, and cisplatin in patients with advanced nonsmall cell lung carcinoma. Cancer 2003;98(3):542-55

Small cell lung cancer Limited stage

Cisplatin + Etoposide +/- R/T

PRIMARY OR ADJUVANT THERAPY FOR LIMITED STAGE SCLC:
Maximum of 4–6 cycles Planned cycle length should be every 21–28 days during concurrent RT. During systemic therapy + RT, cisplatin/etoposide is recommended (category 1). The use of myeloid growth factors is not recommended during concurrent systemic therapy plus RT (category 1 for not using GM-CSF).4
Preferred Regimens Cisplatin 60-80 mg/m ² day 1 and etoposide 60-80mg/m ² days 1,2, 31 Other Recommended Regimens Cisplatin 25 mg/m ² days 1, 2, 3 and etoposide 80 mg/m ² days 1, 2, 31 Carboplatin AUC 4.5 day 1 and etoposide 80mg/m ² days 1, 2, 3a,3
Q3-4w x 4 cycles

Minoru Takada et al. Phase III Study of Concurrent Versus Sequential Thoracic Radiotherapy in Combination With Cisplatin and Etoposide for Limited-Stage Small-Cell Lung Cancer: Results of the Japan Clinical Oncology Group Study 9104. J Clin Oncol 2002;14:3054.

Small cell lung cancer Extensive stage

Cisplatin (Carboplatin) + Etoposide

PRIMARY OR ADJUVANT THERAPY FOR EXTENSIVE STAGE SCLC:		
Maximum of 4–6 cycles		
Preferred Regimen Carboplatin AUC 4.5 day 1 and etoposide 80 mg/m² days 1, 2, 3 and atezolizumab 1,200 mg day 1 every 21 days x 4 cycles followed by maintenance atezolizumab 1,200 mg day 1, every 21 days (category 1, for all)b,c,5 Carboplatin AUC 4.5 day 1 and etoposide 80 mg/m² days 1, 2, 3 and durvalumab 1,500 mg day 1 every 21 days x 4 cycles followed by maintenance durvalumab 1,500 mg day 1 every 28 days (category 1 for all)b,c,36 Cisplatin 75mg/m² day 1 and etoposide 80 mg/m² days 1, 2, 3 and durvalumab 1,500 mg day 1 every 21 days x 4 cycles followed by maintenance durvalumab 1,500 mg day 1 every 28 days (category 1 for all)b,c,36 Other Recommended Regimens Carboplatin AUC 4.5 day 1 and etoposide 80 mg/m² days 1, 2, 3 Cisplatin 75 mg/m² day 1 and etoposide 80 mg/m² days 1, 2, 3 Cisplatin 80 mg/m² day 1 and etoposide 80 mg/m² days 1, 2, 3 Cisplatin 25 mg/m² days 1, 2, 3 and etoposide 80mg/m² days 1, 2, 3 Useful In Certain Circumstances Carboplatin AUC 5 day 1 and irinotecan 50 mg/m² days 1, 8, 15 Cisplatin 60 mg/m² day 1 and irinotecan 60 mg/m² days 1, 8, 15 Cisplatin 30 mg/m² days 1, 8 and irinotecan 65 mg/m² days 1, 8		
Q3-4w x 4 cycles		

Okamoto H et al. Randomized phase III trial of carboplatin plus etoposide vs split doses of cisplatin plus etoposide in elderly or poor-risk patients with extensive disease small-cell lung cancer: JCOG 9702. Br J Cancer 2007; 97:162.

Ihde DC et al. Prospective randomized comparison of high-dose and standard-dose etoposide and cisplatin chemotherapy in patients with extensive-stage small cell lung cancer. J Clin Oncol 1994; 12:2022.

Topotecan

Topotecan	1..25 mg/m ²	d1-4
Q3w		

von Pawel J et al. Topotecan versus cyclophosphamide, doxorubicin, and vincristine for the treatment of recurrent small-cell lung cancer. J Clin Oncol 1999;17:658.

Irinotecan

Irinotecan	100 mg/m ²	d1
Qw		

Masuda N et al. CPT-11: a new derivative of camptothecin for the treatment of refractory or relapsed small-cell lung cancer. J Clin Oncol 1992;10:1225.

PRINCIPLES OF SYSTEMIC THERAPY

Consider dose reduction or growth factor support for patients with PS 2.

SCLC SUBSEQUENT SYSTEMIC THERAPY:
Relapse $\leq$ 6 months PS 0-2
Preferred Regimens • Topotecan PO or IV • Clinical trial Other Recommended Regimens • Nivolumab $\pm$ ipilimumab • Pembrolizumab • Paclitaxel • Docetaxel • Irinotecan • Temozolomide • Cyclophosphamide/doxorubicin/vincristine (CAV)¹² • Oral etoposide • Vinorelbine • Gemcitabine • Bendamustine (category 2B)
Relapse $>$ 6 months
• Original regimen

化學治療和胸部放射線治療

Concurrent Chemotherapy/RT Regimens* Good PS
• Paclitaxel 45-50 mg/m² 2 weekly over 1 hour Carboplatin AUC = 2 mg/mL/min over 30 min weekly or cisplatin 25 mg/m² day 1,8,15,29, 36 and 42 over 1 hour weekly • Docetaxel 20 mg/m² 2 weekly over 1 hour Cisplatin 20-25 mg/m² over 1 hour weekly or Carboplatin AUC = 2 mg/mL/min over 30 min weekly day 1, 8,15, 29, 36 and 42 • Navelbine 15 mg/m² 2 iv D1, D8 Q3wks Cisplatin 30 mg/m² iv D1,8 Q3wks • Oral Navelbine 30- 40 mg/m² 2 D1, D8 Q3wks Cisplatin 30 mg/m² iv D1,8 Q3wks • Cisplatin 40 mg/m² on days 1,8,29, and 36; etoposide 40mg/m² days 1-5, 29-33; concurrent thoracic RTa 64-70 Gy/6-7wks (preferred)* • Cisplatin 80 mg/m² on days 1 and 29; vinblastine 5 mg/m²/weekly x 5; concurrent thoracic RTb 64-70 Gy/6-7wks (preferred) • Carboplatin AUC 5 on day 1, pemetrexed 500 mg/m² on day1 every 21 days for 4 cycles; • Cisplatin 75 mg/m² on days 1, pemetrexed 500 mg/m² on day1 every 21 days for 3 cycles; RT Regimens:*once-daily RT,higher doses of 60-70Gy. *on 45Gy(BID) in 3 weeks to 70Gy in 7 weeks

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aAlbain KS, Crowley JJ, Turrisi AT III, et al. Concurrent cisplatin, etoposide, and chest radiotherapy in pathologic stage IIIB non-small-cell lung cancer: A Southwest Oncology Group Phase II Study, SWOG 9019. J Clin Oncol 2002;20:3454-3460.

bCurran WJ Jr, Paulus R, Langer CJ, et al. Sequential vs. concurrent chemoradiation for stage III non-small cell lung cancer: randomized phase III trial RTOG 9410. J Natl Cancer Inst. 2011;103:1452-1460.

cGovindan R, Bogart J, Stinchcombe T, et al. Randomized phase II study of pemetrexed, carboplatin, and thoracic radiation with or without cetuximab in patients with locally advanced unresectable non-small-cell lung cancer: Cancer and Leukemia Group B trial 30407. J Clin Oncol 2011;29:3120-3125.

dVokes EE, Senan S, Treat JA, Iscoe NA. PROCLAIM: A phase III study of pemetrexed, cisplatin, and radiation therapy followed by consolidation pemetrexed versus etoposide, cisplatin, and radiation therapy followed by consolidation cytotoxic chemotherapy of choice in locally advanced stage III non-small-cell lung cancer of other than predominantly squamous cell histology. Clin Lung Cancer 2009;10:193-198.

*Randomized data supports full dose cisplatin over carboplatin-based regimens. Carboplatin regimens have not been adequately tested.

gScagliotti GV, Turrisi III AT: Docetaxel-based combined-modality chemoradiotherapy for locally advanced non-small cell lung cancer (review). The Oncologist 2003; 8:361-374

hVokes EE, Herndon II JE, Green MR, et al: Randomized Phase II Study of Cisplatin With Gemcitabine or Paclitaxel or Vinorelbine as Induction Chemotherapy Followed by Concomitant Chemoradiotherapy for Stage IIIB Non-Small-Cell Lung Cancer: Cancer and Leukemia Group B Study 9431 J Clin Oncol 2002; 20:4191-4198

iKrzakowski M, Provencio M, Riggi M, et al: Oral Vinorelbine and Cisplatin as Induction Chemotherapy and Concomitant Chemo-Radiotherapy in Stage III Non-small Cell Lung Cancer Final Results of an International Phase II Trial. J Thorac Oncol. 2008;3: 994–1002

Sequential Chemotherapy/RT Regimens

- Paclitaxel→ 175 mg/m² every 3 weeks over 3 hours, 2 cycles
Carboplatin AUC 6, 2 cycles or cisplatin 75- 80 mg/m²
- followed by thoracic RT 60~70 Gy/ 2 Gy per fractions c.d beginning on day 42 d Sterotatic Body Radrosurgery:SBRT, 10~12Gy×4 or other regimens in clinical trials.
- Cisplatin 80 mg/m² on days 1 and 29; vinblastine 5 mg/m²/weekly on days 1, 8, 15, 22,and 29; followed by RTb

REFERENCES

bCurran WJ Jr, Paulus R, Langer CJ, et al. Sequential vs. concurrent chemoradiation for stage III non-small cell lung cancer: randomized phase III trial RTOG 9410. J Natl Cancer Inst. 2011;103:1452-1460.

Concurrent Chemotherapy/RT Followed by Chemotherapy

- Paclitaxel 45-50 mg/m² weekly; carboplatin AUC 2, concurrent thoracic RT followed by 2 cycles of paclitaxel 175 mg/m² and carboplatin AUCe
- Cisplatin 40 mg/m² on days 1,8,29, and 36; etoposide 40 mg/m² days 1-5, 29-33; concurrent thoracic RT followed by cisplatin 40mg/m² and etoposide 40 mg/m² x 2 additional cycles (category 2B)a

c Belani CP, Choy H, Bonomi P, et al. Combined chemoradiotherapy regimens of paclitaxel and carboplatin for locally advanced non-small-cell lung cancer: a randomized phase II locally advanced multi-modality protocol. J Clin Oncol 2005;23(25):5883-5891.

d NCCN 2011,version 2

*This regimen can be used as neoadjuvant chemoradiotherapy. Cisplatin and etoposide is the preferred regimen. If weekly carboplatin and paclitaxel is used

because the patient is not able to tolerate concurrent full-dose cisplatin and radiotherapy, the treating physician should consider 2 cycles of full-dose platinum therapy after local treatment is completed.

eBelani CP, Choy H, Bonomi P, et al. Combined chemoradiotherapy regimens of paclitaxel and carboplatin for locally advanced non-small-cell lung cancer: a randomized phase II locally advanced multi-modality protocol. *J Clin Oncol*. 2005;23:5883-5891.

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Neoadjuvant /Adjuvant chemotherapy

AC

Doxorubicin	60 mg/m ² iv	d1
Cyclophosphamide	600 mg/m ² iv	d1
Q3w x 4 cycles or Q2W x 4 cycles (with GCSF support)		

Muss HB et al. Standard chemotherapy (CMF or AC) versus capecitabine in early-stage breast cancer (BC) patients aged 65 or older: results of CALGB/CTSU 49907. 2008 ASCO annual meeting. Abstract 507 .

Fisher, B et al. Treatment of axillary lymph node-negative, estrogen receptor-negative breast cancer: updated findings from National Surgical Adjuvant Breast and Bowel Project clinical trials. J Natl Cancer Inst 2004; 96:1823 .

EC

Epirubicin	75 - 100 mg/m ² iv	d1
Cyclophosphamide	600 mg/m ² iv	d1
Q3w x 4 cycles or Q2W x 4-6 cycles (with GCSF support)		

Piccart MJ et al. Phase III trial comparing two dose levels of epirubicin combined with cyclophosphamide with cyclophosphamide, methotrexate, and fluorouracil in node-positive breast cancer. . J Clin Oncol 2001; 19:3103.

LC(Liposomal doxorubicin-optional)

Liposomal doxorubicin	35- 50 mg/m ² iv	d1
Cyclophosphamide	600 mg/m ² iv	d1
Q3w x 4 cycles or Q4w x 4 cycles		

Pegylated Liposomal Doxorubicin as Adjuvant Therapy for Stage I-III Operable Breast Cancer.Lu YC, Ou-Yang FU, Hsieh CM, Chang KJ, Chen DR, Tu CW, Wang HC, Hou MF.In Vivo. 2016 Mar-Apr;30(2):159-63.

健保規範:Doxorubicin hydrochloride liposome injection(如Lipo-Dox、Caelyx)：用於單一治療有心臟疾病風險考量之轉移性乳癌患者。(93/11/1)

TC

Docetaxel	60 - 100 mg/m ² iv	d1
Cyclophosphamide	600 mg/m ² iv	d1
Q3w x 4 cycles or Q2W x 4 cycles (with GCSF support)		

Jones SE et al. Phase III trial comparing doxorubicin plus cyclophosphamide with docetaxel plus cyclophosphamide as adjuvant therapy for operable breast cancer. J Clin Oncol 2006; 24:5381.

健保規範: Docetaxel 1.局部晚期或轉移性乳癌。2.與anthracycline合併使用於腋下淋巴結轉移之早期乳癌之術後輔助性化學治療。(99/6/1)3.早期乳癌手術後，經診斷為三陰性反應且無淋巴轉移的病人，得作為與cyclophosphamide併用 doxorubicin的化學輔助療法4.除以上條件，其餘皆自費。

Docetaxel+ Cisplatin

Docetaxel	60 - 75mg/m2 iv	d1
Cisplatin	60- 75 mg/m2 iv	d1
Q3w x 4 cycles or Q2W x 4 cycles (with GCSF support)		

A randomized phase II trial of platinum salts in basal-like breast cancer patients in the neoadjuvant setting. Results from the GEICAM/2006-03, multicenter study. (Abstract in PubMed) Breast Cancer Res Treat (2012) 136:487–493

CMF po

Cyclophosphamide	100 mg/m2/d po	d1-14
Methotrexate	40 mg/m2 iv	d1, 8
5- FU	600 mg/m2 iv	d1, 8
Q4w x 6 cycles		

Muss HB et al. Standard chemotherapy (CMF or AC) versus capecitabine in early-stage breast cancer (BC) patients aged 65 or older: results of CALGB/CTSU 49907. 2008 ASCO annual meeting. Abstract 507.

CMF IV

Cyclophosphamide	600 mg/m2 iv	d1
Methotrexate	40 mg/m2 iv	d1
5-FU	600 mg/m2 iv	d1
Q3w x 6 cycles		

Weiss RB et al. Adjuvant chemotherapy after conservative surgery plus irradiation versus modified radical mastectomy. Analysis of drug dosing and toxicity. Am J Med 1987; 83:455.

FAC

5-FU	500 mg/m2 iv	d1
Doxorubicin	50 mg/m2 iv	d1
Cyclophosphamide	500 mg/m2 iv	d1
Q3w x 6 cycles		

Martin M et al. Doxorubicin in combination with fluorouracil and cyclophosphamide (i.v. FAC regimen d1, 21) versus methotrexate in combination with fluorouracil and cyclophosphamide (i.v. CMF regimen d1, 21) as adjuvant chemotherapy for operable breast cancer: a study by the GEICAM group. Ann Oncol 2003; 14:833.

FEC

5-FU	500 - 600 mg/m2 iv	d1
Epirubicin	50 - 100 mg/m2 iv	d1
Cyclophosphamide	500 - 600 mg/m2 iv	d1
Q3w x 6 cycles or Q2W x 4-6 cycles (with GCSF support)		

Bonneterre J et al. Epirubicin increase long term survival in adjuvant chemotherapy of patients with poor prognosis, node positive, early breast cancer: 10 years follow up results of the French Adjuvant Study Group 05 randomized trial. J Clin Oncol 2005; 23:2686.

AC/EC→Paclitaxel Qw (or Paclitaxel→AC/EC)

Paclitaxel	80 mg/m ² iv	d1
Qw x 12 cycles		

Sparano JA et al. Weekly paclitaxel in the adjuvant treatment of breast cancer. N Eng J Med 2008; 358:1663.

健保規範: Paclitaxel 腋下淋巴轉移之乳癌且動情素受體為陰性之患者，paclitaxel 可作為接續含doxorubicin在內之輔助化學治療。(91/4/1、94/1/1、98/8/1)

AC/EC→Docetaxel Q3w (or Docetaxel→AC/EC)

Docetaxel	60-100 mg/m ² iv	d1
Q3w x 4 cycles		

Sparano JA et al. Weekly paclitaxel in the adjuvant treatment of breast cancer. N Eng J Med 2008; 358:1663.

健保規範: Docetaxel 1.局部晚期或轉移性乳癌。2.與anthracycline合併使用於腋下淋巴結轉移之早期乳癌之術後輔助性化學治療。(99/6/1)3.早期乳癌手術後，經診斷為三陰性反應且無淋巴轉移的病人，得作為與cyclophosphamide併用doxorubicin的化學輔助療法4.除以上條件，其餘皆自費。

TAC

Docetaxel	50 - 75 mg/m ² iv	d1
Doxorubicin	50 mg/m ² iv	d1
Cyclophosphamide	500 mg/m ² iv	d1
Q3w x 6 cycles		

Martin M et al. Adjuvant docetaxel for node-positive breast cancer. N Eng J Med 2005; 352:2302 .

TEC

Docetaxel	50-75 mg/m ² iv	d1
Epirubicin	50-75 mg/m ² iv	d1
Cyclophosphamide	500 mg/m ² iv	d1
Q3w x 6 cycles		

P Piedbois et al. Dose-dense adjuvant chemotherapy in node-positive breast cancer: docetaxel followed by epirubicin/cyclophosphamide (T/EC), or the reverse sequence (EC/T), every 2 weeks, versus docetaxel, epirubicin and cyclophosphamide (TEC) every 3 weeks. AERO B03 randomized phase II study. Ann Oncol. 2007; 18: 52.

Cisplatin

Cisplatin	75 mg/m ² iv	d1
Q3w		

Caboplatin

Caboplatin	6 mg, AUC iv	d1
Q3w		

Silver DP et al. Efficacy of neoadjuvant cisplatin in triple negative breast cancer. J Clin Oncol 2010;28:1145.

Docetaxel+ Carboplatin

Docetaxel	60 - 75mg/m ² iv	d1
Caboplatin	6 mg, AUC iv	d1
Cycled every 21 days for 6 cycles		

von Minckwitz G, Schneeweiss A, Loibl S, et al. Neoadjuvant carboplatin in patients with triple-negative and HER2-positive early breast cancer (GeparSixto; GBG 66): a randomised phase 2 trial Lancet Oncol 2014;15:747-756.

Adjuvant Targeted therapy**Trastuzumab IV/SC +/- Chemotherapy**

Trastuzumab can be given after completion of chemotherapy as well , loading dose 8 mg/kg , followed by 6 mg/kg , iv q3w for a total of 1 year.
Trastuzumab 4 mg/kg loading dose followed by 2 mg/kg iv qw during chemotherapy , then 6 mg/kg iv q3w , for a total of 1 year
Trastuzumab 600mg , for a total of 1 year

Smith I et al. 2-year follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer: a randomized controlled trial. Lancet 2007; 369:29.

Romond EH et al. Trastuzumab plus adjuvant chemotherapy for operable Her2-positive breast cancer. N Eng J Med 2005; 353:1673

健保申請條件如下~1. 早期乳癌::(1)外科手術前後、化學療法(術前輔助治療或輔助治療)治療後，具HER2過度表現(IHC 3+或FISH+)，且具腋下淋巴結轉移但無遠處臟器轉移之早期乳癌患者，作為輔助性治療用藥。(2)使用至多以一年為限。

Pertuzumab -optional

loading dose 840 mg IV day 1 followed by 420 mg IV Cycled every 21 days to complete 1y of therapy q3w

Schneeweiss A, Chia S, Hickish T, et al. Pertuzumab plus trastuzumab in combination with standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer: a randomized phase II cardiac safety study (TRYPHAENA). Ann Oncol 2013;24:2278-2284.

Swain S, Kim S-B, Cortes J, et al. Confirmatory overall survival(OS) analysis of CLEOPATRA: a randomized, double-blind, placebocontrolled Phase III study with pertuzumab (P), trastuzumab (T), and docetaxel (D) in patients (pts) with HER2-positive first-line (1L)metastatic breast cancer (MBC). Cancer Research 2012;72:P5-18-26.

Baselga J, Cortes J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. N Engl J Med 2012;366:109-119.

Datko F, D'Andrea G, Dickler M, et al. Phase II study of pertuzumab, trastuzumab, and weekly paclitaxel in patients with metastatic HER2-overexpressing metastatic breastcancer [abstract]. Cancer Research 2012;72:Abstract P5-18-20.

Gianni L, Pienkowski T, Im YH, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer(NeoSphere): a randomised multicentre, open-label, phase 2 trial.Lancet Oncol 2012;13:25-32

Chemotherapy for Metastatic breast cancer

Doxorubicin

Doxorubicin	60-75 mg/m ² iv	d1
Q3w		

or

Doxorubicin	20 mg/m ² iv	d1
Qw		

Chan S et al. Prospective randomized trial of docotaxel versus doxorubicin in patients with metastatic breast cancer. J Clin Oncol 1999;17:2341.

Gasparini G et al. Weekly epirubicin versus doxorubicin as second line therapy in advanced breast cancer. A randomized clinical trial. Am J Clin Oncol 1991;14:38.

Epirubicin

Epirubicin	60-90 mg/m ² iv	d1
Q3w		

or

Epirubicin	20 mg/m ² iv	d1
Qw		

Bastholt L et al. Dose-response relationship of epirubicin in the treatment of postmenopausal patients with metastatic breast cancer: a randomized study of epirubicin at four different dose levels performed by the Danish Breast Cancer Cooperative Group. J Clin Oncol 1996;14:1146.

Gasparini G et al. Weekly epirubicin versus doxorubicin as second line therapy in advanced breast cancer. A randomized clinical trial. Am J Clin Oncol 1991;14:38.

Liposomal doxorubicin

Liposomal doxorubicin	35- 50 mg/m ² iv	d1
Q3-4w		

O'Brien ME et al. Reduced cardiotoxicity and comparable efficacy in a phase III trial of pegylated liposomal doxorubicin HCL versus conventional doxorubicin for first line treatment of metastatic breast cancer. Ann Oncol 2004;15:440.

健保申請條件:1.用於單一治療有心臟疾病風險考量之轉移性乳癌患者。2.除以上條件，其餘皆自費。

Cisplatin

Cisplatin	75 mg/m ² iv	d1
Q3w		

Caboplatin

Caboplatin	6 mg, AUC iv	d1
Q3w		

Silver DP et al. Efficacy of neoadjuvant cisplatin in triple negative breast cancer. J Clin Oncol 2010;28:1145.

Docetaxel

Docetaxel	60-100 mg/m ² iv	d1
Q3w		

or

Docetaxel	25 -40 mg/m ² iv	d1
Qw		

Harvey V et al. Phase III trial of comparing three doses of docetaxel for second-line treatment of advanced breast cancer. J Clin Oncol 2006; 24:4963.

Burstein, HJ et al. Docetaxel administered on a weekly basis for metastatic breast cancer. J Clin Oncol 2000; 18:1212.

Paclitaxel

Paclitaxel	80 mg/m ² iv	d1
Qw		

Bishop, JF et al. Initial paclitaxel improves outcome compared with CMFP combination chemotherapy as front-line therapy in untreated metastatic breast cancer. J Clin Oncol 1999; 17:2355.

Seidman AD et al. Randomized phase III trial of weekly compared with every-3-weeks paclitaxel for metastatic breast cancer, with trastuzumab for all Her-2 overexpressors and random assignment to trastuzumab or not in Her-2 nonoverexpressors: Final results of Cancer and Leukemia Group B Protocol 9840. J Clin Oncol 2008; 26:1642.

健保規範;Paclitaxel

限用於已使用合併療法(除非有禁忌症、至少應包括使用anthracycline)失敗的轉移性乳癌患者。(91/4/1、94/1/1)

Gemcitabine

Gemcitabine	800-1200 mg/m ² iv	d1, 8, 15
Q4w		

Carmichael, J et al. Advanced breast cancer: a phase II trial with gemcitabine. J Clin Oncol 1995; 13:2731.

健保規範;Gemcitabine (如Gemzar)

限用於Gemcitabine與paclitaxel併用，可使用於曾經使用過anthracycline之局部復發且無法手術切除或轉移性之乳癌病患。(94/10/1)

GT

Gemcitabine	800-1200 mg/m ² iv	d1, 8,
Paclitaxel	175 mg/m ² iv	d1,
following paclitaxel on day 1 Cycled every 21 days.		

GT

Gemcitabine	800 mg/m ² iv	d1, 8,
Paclitaxel	80 mg/m ² iv	d1, 8
Q4w		

Vinorelbine

Vinorelbine	20 - 25 mg/m ² iv 、 50-80 mg/m ² po	d1,8
Q3w		

Gasparini, G et al. Vinorelbine is an active antiproliferative agent in pretreated advanced breast cancer patients: a phase II study. J Clin Oncol 1994; 12:2094.

健保規範; Vinorelbine

晚期或無法手術切除之非小細胞肺癌及轉移性乳癌病患。本成分之口服劑型與注射劑型不得併用

Capecitabine

Capecitabine	800 - 1250 mg/m ² po bid	d1-14
Q3w		

Fumoleau, P et al. Multicentre, phase II study evaluating capecitabine monotherapy in patients with anthracycline- and taxane-pretreated metastatic breast cancer. Eur J Cancer 2004; 40:536.

1. capecitabine與docetaxel併用於治療對anthracycline化學治療無效之局部晚期或轉移性乳癌病患。
2. 單獨用於對taxanes及anthracycline化學治療無效，或無法使用anthracycline治療之局部晚期或轉移性乳癌病患。

UFT po

Uracil/Tegafur	270 mg/m ² /day po
7 days/week	

Y Park. Uracil-tegafur and tamoxifen vs cyclophosphamide, methotrexate, fluorouracil, and tamoxifen in post-operative adjuvant therapy for stage I, II, or IIIA lymph node-positive breast cancer: a comparative study. British Journal of Cancer (2009), 1 – 7

健保規範:Uracil-Tegafur

限轉移性胃癌、轉移性直腸癌、轉移性結腸癌、轉移性乳癌之病患使用
(89/10/1 、 97/12/1) 。

AC

Doxorubicin	60 mg/m ² iv	d1
Cyclophosphamide	600 mg/m ² iv	d1
Q3w		

Nabholtz JM et al. Docetaxel and doxorubicin compared with doxorubicin and cyclophosphamide as first-line chemotherapy for metastatic breast cancer: results of a randomized, multicenter, phase III trial. J Clin Oncol 2003;21:968.

EC

Epirubicin	75 mg/m ² iv	d1
Cyclophosphamide	600 mg/m ² iv	d1
Q3w , or Q2W(and GCSF support)		

Langley RE et al. Phase III trial of epirubicin plus paclitaxel compared with epirubicin plus cyclophosphamide as first-line chemotherapy for metastatic breast cancer: United Kingdom National Cancer Research Institute Trial AB01. J Clin Oncol 2005; 23:8322.

Eribulin

Eribulin	1.4mg/m ² iv	d1,8
Q3w		

Pooled analyses of eribulin in metastatic breast cancer patients with at least one prior chemotherapy.

Pivot X1, Marmé F2, Koenigsberg R3, Guo M4, Berrak E5, Wolfer A6. 2016

Aug;27(8):1525-31. doi: 10.1093/annonc/mdw203. Epub 2016 May 13.

健保規範: (如 Halaven) : (103/12/1、106/11/1) 1.用於治療轉移性乳癌患者且先前曾接受過 anthracycline 和 taxane 兩種針對轉移性乳癌之化學治療輔助性治療。2.每 3 個療程需進行療效評估, 病歷應留存評估紀錄, 無疾病惡化方可繼續使用。(106/11/1)

Ixabepilone

Ixabepilone	40mg/m ² iv	d1
Q3w		

1. Li J, Ren J, Sun W. Systematic review of ixabepilone for treating metastatic breast cancer. Breast Cancer. 2017 Mar;24(2):171-179. doi:

10.1007/s12282-016-0717-0. Epub 2016 Aug 4. Review. PubMed PMID: 27491426.

2. Puhalla, S., & Brufsky, A. (2008). Ixabepilone: a new chemotherapeutic option for refractory metastatic breast cancer. Biologics : Targets & Therapy, 2(3), 505–515.

3. Sparano, J. A., Vrdoljak, E., Rixe, O., Xu, B., Manikhas, A., Medina, C., ... Conte, P. (2010). Randomized Phase III Trial of Ixabepilone Plus Capecitabine Versus Capecitabine in Patients With Metastatic Breast Cancer Previously Treated With an Anthracycline and a Taxane. Journal of Clinical Oncology, 28(20), 3256–3263. <http://doi.org/10.1200/JCO.2009.24.4244>

Target therapy for Metastatic breast cancer

Trastuzumab IV/SC +/- Chemotherapy

Trastuzumab 8mg/kg iv over 90 min first wk followed by 6 mg/kg iv over 30 min q3w	
Trastuzumab 4 mg/kg loading dose followed by 2 mg/kg iv	qw
Trastuzumab 600mg for a total of 1 year	

Cobleigh, MA et al. Multinational study of the efficacy and safety of humanized anti-HER2 monoclonal antibody in women who have HER2-overexpressing metastatic breast cancer that has progressed after chemotherapy for metastatic disease. J Clin Oncol 1999; 17:2639.

健保規範:轉移性乳癌(1)單獨使用於治療腫瘤細胞上有HER2過度表現(IHC3+或FISH+), 曾接受過一次以上化學治療之轉移性乳癌病人。(91/4/1、99/1/1)(2)與paclitaxel或docetaxel併用, 使用於未曾接受過化學治療之轉移性乳癌病患, 且為HER2過度表現(IHC3+或FISH+)者(93/8/1、95/2/1、99/1/1)

(3)轉移性乳癌且HER2過度表現之病人, 僅限先前未使用過本藥品者方可使用; 但與pertuzumab及docetaxel併用時, 不在此限。

(99/1/1、108/5/1)

經事前審查核准後使用, 核准後每24週須檢附療效評估資料再次申請, 若疾病有惡化情形即不應再行申請(105/11/1)。

Pertuzumab +/- Chemotherapy

840 mg IV day 1 followed by 420 mg IV Cycled every 21 days to complete 1 y of therapy q3w

Schneeweiss A, Chia S, Hickish T, et al. Pertuzumab plus trastuzumab in combination with standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer: a randomized phase II cardiac safety study (TRYPHAENA). *Ann Oncol* 2013;24:2278-2284.

Swain S, Kim S-B, Cortes J, et al. Confirmatory overall survival(OS) analysis of CLEOPATRA: a randomized, double-blind, placebo-controlled Phase III study with pertuzumab (P), trastuzumab (T), and docetaxel (D) in patients (pts) with HER2-positive first-line (1L) metastatic breast cancer (MBC). *Cancer Research* 2012;72:P5-18-26.

Baselga J, Cortes J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *N Engl J Med* 2012;366:109-119.

Datko F, D'Andrea G, Dickler M, et al. Phase II study of pertuzumab, trastuzumab, and weekly paclitaxel in patients with metastatic HER2-overexpressing metastatic breast cancer [abstract]. *Cancer Research* 2012;72:Abstract P5-18-20.

Gianni L, Pienkowski T, Im YH, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer(NeoSphere): a randomised multicentre, open-label, phase 2 trial. *Lancet Oncol* 2012;13:25-32
健保規範:(108/05/01)

1. Pertuzumab 與 trastuzumab 及 docetaxel 併用於治療轉移後未曾以抗 HER2 或化學療法治療之 HER2 過度表現(IHC3+或 FISH+)轉移性乳癌病患。2. 須經事前審查核准後使用，核准後每18週須檢附療效評估資料再次申請，若疾病有惡化情形即不應再行申請，每位病人至多給付18個月為限。

Bevacizumab(自費) + Chemotherapy

Bevacizumab	10 mg/kg iv	d1
Q2w		

or

Bevacizumab	15 mg/kg iv	d1
Q3w		

Miller KD et al. Paclitaxel plus bevacizumab versus paclitaxel alone for metastatic breast cancer. *N Eng J Med* 2007; 357:2666.

Miles D et al. Randomized, double-blind, placebo-controlled, phase III study of bevacizumab (BV) with docetaxel (D) or docetaxel with placebo (PL) as first-line therapy for patients with locally recurrent or metastatic breast cancer (mBC): AVADO. 2008 ASCO annual meeting. LBA1011.

Lapatinib + Xeloda

Lapatinib	1250mg po	
Xeloda	2000mg/m ² po	d1-14

Lancet Oncol 2013 Jan;14(1):64-71.doi:10.1016/S1470-2045(12)70432-1.Epub 2012 Nov.

健保規範:lapatinib (如Tykerb)

1. 與capecitabine併用，使用於曾接受anthracycline,taxane以及trastuzumab治療後

病況惡化之轉移性乳癌併有腦部轉移，且為HER2過度表現(IHC3+或FISH+)患者。

2.每3個月需進行療效評估，病歷應留存評估紀錄，無疾病惡化方可繼續使用。
(106/11/1)

Capecitabine (如Xeloda)

1. Capecitabine與docetaxel併用於治療對anthracycline化學治療無效之局部晚期或轉移性乳癌病患。
- 2.單獨用於對taxanes及anthracycline化學治療無效，或無法使用anthracycline治療之局部晚期或轉移性乳癌病患。

BEEP

Bevacizumab	15 mg/kg iv	d1	
Etoposide	70 mg/m2/d	d2, 3, 4	Cisplatin
mg/m2	d2		70
Q3w			

Lu YS, et al. Bevacizumab preconditioning followed by etoposide and cisplatin (BEEP) is a highly effective treatment for brain metastases of breast cancer progressing from radiotherapy — result of a multi-center phase II study. ECC 2013:1878.

Everolimus

Everolimus	10mg po
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健保規範::Everolimus 5mg及10mg(如Afinitor 5mg及10mg)：

與exemestane併用，作為已無適當之化學治療可供選擇，而先前已使用過非類固醇類之芳香環酶抑制劑治療無效，而未曾使用exemestane之轉移性乳癌，屬於荷爾蒙接受體陽性、HER2受體陰性且尚未出現其他器官症狀之病人的第一線治療(104/9/1)。

限每日最大劑量為10mg。(108/10/1)

Bachelot T, Bourgier c, Cropet C, et al. TAMRAD: A GINECO randomized phase II trial of everolimus in combination with tamoxifen versus tamoxifen alone in patients (pts) with hormone-receptor positive, HER2 negative metastatic breast Cancer (MBC) with prior

exposure to aromatase inhibitors (AI) [abstract]. Cancer Res 2010;70(24 Supplement):

Yardley DA, Noguchi S, Pritchard KI, et al. Everolimus plus exemestane in postmenopausal patients with HR(+) breast cancer:

BOLERO-2 final progression-free survival analysis. Adv Ther 2013;30:870-884.

Baselga J, Campone M, Piccart M, et al. Everolimus in postmenopausal hormone-receptor-positive advanced breast cancer.

N Engl J Med 2012;366:520-529.

子宮頸癌

Adjuvant AND Neoadjuvant chemotherapy

Cisplatin

Cisplatin	40-50mg/m ² iv	d1
wk x 6wks		

Moore DH, Blessing JA, McQuellon RP, et al. Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2004;22:3113-3119.

Carboplatin

Carboplatin	AUC (4-6) iv	d1
wk x 6wks		

Weiss GR, Green S, Hannigan EV, et al. A phase II trial of carboplatin for recurrent or metastatic squamous carcinoma of the uterine cervix: a Southwest Oncology Group study. Gynecol Oncol 1990;39:332-336.

Paclitaxel(自費)

Paclitaxel	80mg/m ² iv	d1
wk x 6 cycles		

Kudelka AP, Winn R, Edwards CL, et al. An update of a phase II study of paclitaxel in advanced or recurrent squamous cell cancer of the cervix. Anticancer Drugs 1997;8:657-661.

Cisplatin +Paclitaxel(自費)

Cisplatin	40-50mg/m ² iv	d1
Paclitaxel	80mg/m ² iv	d1
wk		

- 1.Monk BJ, Sill MW, McMeekin DS, et al. Phase III trial of four cisplatin-containing doublet combinations in stage IVB, recurrent, or persistent cervical carcinoma: A Gynecologic Oncology Group Study. J Clin Oncol 2009;27:4649-4655.
- 2.Moore DH, Blessing JA, McQuellon RP, et al. Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2004;22:3113-3119.

Carboplatin+Paclitaxel (自費)

Carboplatin	AUC (4-6) iv	d1
Paclitaxel	80mg/m ² iv	d1
wk		

Moore KN, Herzog TJ, Lewin S, et al. A comparison of cisplatin/paclitaxel and carboplatin/paclitaxel in stage IVB, recurrent or persistent cervical cancer. Gynecol Oncol 2007;105:299-303.

Cisplatin+Taxol

Cisplatin	75-100 mg/m ²	iv	d1
Taxol	(135-175)mg/m ²	iv	d1
q3w			

- 1.Monk BJ, Sill MW, McMeekin DS, et al. Phase III trial of four cisplatin-containing doublet combinations in stage IVB, recurrent, or persistent cervical carcinoma: A Gynecologic Oncology Group Study. J Clin Oncol 2009;27:4649-4655.
- 2.Moore DH, Blessing JA, McQuellon RP, et al. Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2004;22:3113-3119.

Carboplatin+Taxol

Carboplatin	AUC (4-6)	iv	d1
Taxol	(135-175)mg/m ²	iv	d1
q3w			

Moore KN, Herzog TJ, Lewin S, et al. A comparison of cisplatin/paclitaxel and carboplatin/paclitaxel in stage IVB, recurrent or persistent cervical cancer. Gynecol Oncol 2007;105:299-303.

Cisplatin +Oncovin

Cisplatin	40-50mg/m ²	iv	d1
Oncovin	1mg/m ²	iv	d1
10days x 3 course			

Eddy GL, Bundy BN, Creasman WT, et al. Treatment of ("bulky")stage IB cervical cancer with or without neoadjuvant vincristine and cisplatin prior to radical hysterectomy and pelvic/para-aortic lymphadenectomy: a phase III trial of the gynecologic oncology group.Gynecol Oncol 2007;106:362-369. Available at:<http://www.ncbi.nlm.nih.gov/pubmed/17493669>.

Carboplatin+ Oncovin

Carboplatin	AUC (4-6)	iv	d1
Oncovin	1mg/m ²	iv	d1
10days x 3 course			

Eddy GL, Bundy BN, Creasman WT, et al. Treatment of ("bulky") stage IB cervical cancer with or without neoadjuvant vincristine and cisplatin prior to radical hysterectomy and pelvic/para-aortic lymphadenectomy: a phase III trial of the gynecologic oncology group.Gynecol Oncol 2007;106:362-369. Available at:<http://www.ncbi.nlm.nih.gov/pubmed/17493669>.

Cisplatin+Ifosfamide

Cisplatin	(75-100)mg/m ²	iv	d1
Ifosfamide	(3-5)g/m ²	iv	d1
q3w x 6 cycles			

Coleman RE, Harper PG, Gallagher C, et al. A phase II study of ifosfamide in advanced and relapsed carcinoma of the cervix. Cancer Chemother Pharmacol 1986;18:280-283. Available at:<http://www.ncbi.nlm.nih.gov/pubmed/3802384>.

Carboplatin+Ifosfamide

Carboplatin	AUC (4-6) iv	d1
Ifosfamide	(3-5)g/m ² iv	d1
q3w x 6 cycles		

Sutton GP, Blessing JA, McGuire WP, et al. Phase II trial of ifosfamide and mesna in patients with advanced or recurrent squamouscarcinoma of the cervix who had never received chemotherapy: a Gynecologic Oncology Group study. Am J Obstet Gynecol 1993;168:805-807. Available at:<http://www.ncbi.nlm.nih.gov/pubmed/8456884>.

Cisplatin+ Topotecan

Cisplatin	(75-100)mg/m ² iv	d1
Topotecan	(2.5-4)mg/m ² iv	d1
q3w		

1. Long HJ, 3rd, Bundy BN, Grendys EC, Jr., et al. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. J Clin Oncol 2005;23:4626-4633.
2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.
3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Carboplatin+ Topotecan

Carboplatin	AUC (4-6) iv	d1
Topotecan	(2.5-4)mg/m ² iv	d1
q3w		

1. M A Bookman, H Malmström, G Bolis, et al. Topotecan for the treatment of advanced epithelial ovarian cancer: an open-label phase II study in patients treated after prior chemotherapy that contained cisplatin or carboplatin and paclitaxel. JCO October 1998 vol. 16 no. 10 3345-3352
2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.
3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Bevacizumab (Avastin) (自費)

Bevacizumab	15mg/kg iv	d1
Repeat cycle every 3 weeks.		

1. NCCN Clinical Practice Guidelines in Oncology™. Cervical Cancer.v 1.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed February 13, 2012.
2. Monk BJ, Sill MW, Burger RA, Gray HJ, Buekers TE, Roman LD. Phase II trial of bevacizumab in the treatment of persistent or recurrent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2009;27:1069–1074.

Topotecan+/-paclitaxel

Topotecan	(2.5-4)mg/m ² iv	d1
Taxol	(135-175)mg/m ² iv	d1
q3w		

1. Long HJ, 3rd, Bundy BN, Grendys EC, Jr., et al. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. J Clin Oncol 2005;23:4626-4633.
2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.
3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

CCRT**Cisplatin**

Cisplatin	30-50mg/m ² iv	d1
wk x 6wks		

Moore DH, Blessing JA, McQuellon RP, et al. Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2004;22:3113-3119.

Carboplatin

Carboplatin	AUC (4-6) iv	d1
wk x 6wks		

Weiss GR, Green S, Hannigan EV, et al. A phase II trial of carboplatin for recurrent or metastatic squamous carcinoma of the uterine cervix: a Southwest Oncology Group study. Gynecol Oncol 1990;39:332-336.

Paclitaxel

Paclitaxel	80mg/m ² iv	d1
wk x 6 cycles		

Kudelka AP, Winn R, Edwards CL, et al. An update of a phase II study of paclitaxel in advanced or recurrent squamous cell cancer of the cervix. Anticancer Drugs 1997;8:657-661.

Second-Line Therapy**Bevacizumab (Avastin) (自費)**

Bevacizumab	15mg/kg iv	d1
Repeat cycle every 3 weeks.		

1. NCCN Clinical Practice Guidelines in Oncology™. Cervical Cancer.v 1.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed February 13, 2012.
2. Monk BJ, Sill MW, Burger RA, Gray HJ, Buekers TE, Roman LD. Phase II trial of bevacizumab in the treatment of persistent or recurrent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2009;27:1069–1074.

Docetaxel (Taxotere) (自費)

Docetaxel	100mg/m ² , iv administered over 1 hr.	d1
Repeat cycle every 3 weeks.		

- 1.NCCN Clinical Practice Guidelines in Oncology™. Cervical Cancer.v 1.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed February 13, 2012.
- 2.Garcia AA, Blessing JA, Vaccarello L, Roman LD; Gynecologic Oncology Group Study. Phase II clinical trial of docetaxel in refractory squamous cell carcinoma of the cervix: a Gynecologic Oncology Group Study. Am J Clin Oncol. 2007;30:428–431.

Gemcitabine (Gemzar) (自費)

Gemcitabine	800mg/m ² , iv administered over 30 min.	d1
Repeat cycle every 4 weeks.		

- 1.NCCN Clinical Practice Guidelines in Oncology™. Cervical Cancer.v 1.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed February 13, 2012.
- 2.Schilder RJ, Blessing J, Cohn DE. Evaluation of gemcitabine in previously treated patients with non-squamous cell carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. Gynecol Oncol. 2005;96:103–107.

Palliative**Bevacizumab (Avastin) (自費)**

Bevacizumab	15mg/kg iv	d1
Repeat cycle every 3 weeks.		

- 1.NCCN Clinical Practice Guidelines in Oncology™. Cervical Cancer.v 1.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed February 13, 2012.
- 2.Monk BJ, Sill MW, Burger RA, Gray HJ, Buekers TE, Roman LD.Phase II trial of bevacizumab in the treatment of persistent or recurrent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2009;27:1069–1074.

Cisplatin+Topotecan

Cisplatin	75-100 mg/m ² iv	d1
Topotecan	0.75mg/m ² iv	d1-d3
q3w		

- 1.Long HJ, 3rd, Bundy BN, Grendys EC, Jr., et al. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. J Clin Oncol 2005;23:4626-4633.
2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.
3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Cisplatin+ Topotecan

Cisplatin	75-100 mg/m ² iv	d1
Topotecan	(2.5-4)mg/m ² iv	d1
q3w		

1. HJ, 3rd, Bundy BN, Grendys EC, Jr., et al. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. J Clin Oncol 2005;23:4626-4633.
2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.
3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Carboplatin+Topotecan

Carboplatin	AUC (4-6) iv	d1
Topotecan	0.75mg/m ²	d1-d3
q3w		

1. Long HJ, 3rd, Bundy BN, Grendys EC, Jr., et al. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. J Clin Oncol 2005;23:4626-4633.
2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.
3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Carboplatin+ Topotecan

Carboplatin	AUC (4-6) iv	d1
Topotecan	(2.5-4)mg/m ² iv	d1
q3w		

1. N. R. Abu-Rustum, S. Lee, L. S. Massad. Topotecan for recurrent cervical cancer after platinum-based therapy. International Journal of Gynecological Cancer, Volume 10, Issue 4, pages 285–288, July/August 2000
2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.
3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Cisplatin +paclitaxel+Bevacizumab

paclitaxel	135-175mg/m ² iv	d1
Cisplatin	50-75mg/m ² iv	d1
Bevacizumab	15mg/kg iv	d1
21 days intervals		

Tewari KS, Sill MW, Long HJ 3rd, et al. Improved survival with bevacizumab in advanced cervical cancer. N Engl J Med. 2014 Feb 20;370(8):734-43.

Topotecan+paclitaxel+Bevacizumab

paclitaxel	135-175mg/m ² iv	d1
Topotecan	0.75mg/m ² iv	d1- d3
Bevacizumab	15mg/kg iv	d1
21 days intervals		

Tewari KS, Sill MW, Long HJ 3rd, et al. Improved survival with bevacizumab in advanced cervical cancer. N Engl J Med. 2014 Feb 20;370(8):734-43

Doxorubicin liposome

Doxorubicin liposome	(35-45)mg/ m ² iv	d1
q3w		

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol 2010;28:3323-3329.

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Adjuvant chemotherapy

Paclitaxel+Cisplatin

Paclitaxel	(135/175)mg/m ² iv	d1
Cisplatin	75mg/m ² iv	d1
q3w x 6wks cycles		

Homesley HD, Filiaci V, Gibbons SK, et al. A randomized phase III trial in advanced endometrial carcinoma of surgery and volume directed radiation followed by cisplatin and doxorubicin with or without paclitaxel: A Gynecologic Oncology Group study. Gynecol Oncol 2009;112:543-552.

Paclitaxel+Carboplatin

Paclitaxel	(135/175)mg/m ² iv	d1
Carboplatin	AUC (4-6) iv	d1
q3w x 6wks cycles		

Miller D, Filiaci V, Fleming G, et al. Randomized phase III noninferiority trial of first line chemotherapy for metastatic or recurrent endometrial carcinoma: a Gynecologic Oncology Group study [abstract]. Gynecol Oncol 2012;125:771.

Doxorubicin +Cisplatin

Doxorubicin	50mg/m ² iv	d1
Cisplatin	75mg/m ² iv	d1
q3w x 6 cycles		

Homesley HD, Filiaci V, Gibbons SK, et al. A randomized phase III trial in advanced endometrial carcinoma of surgery and volume directed radiation followed by cisplatin and doxorubicin with or without paclitaxel: A Gynecologic Oncology Group study. Gynecol Oncol 2009;112:543-552.

Doxorubicin +Carboplatin

Doxorubicin	50mg/m ² iv	d1
Carboplatin	AUC (4-6) iv	d1
q3w x 6 cycles		

Homesley HD, Filiaci V, Gibbons SK, et al. A randomized phase III trial in advanced endometrial carcinoma of surgery and volume directed radiation followed by cisplatin and doxorubicin with or without paclitaxel: A Gynecologic Oncology Group study. Gynecol Oncol 2009;112:543-552.

Cisplatin+Ifosfamide

Cisplatin	50-100mg/m ² iv	d1
Ifosfamide	3-5g/m ² iv	d1
q3w x 6 cycles		

Howard D. Homesley, Virginia Filiaci, Maurie Markman, et al. Phase III Trial of

Carboplatin+Ifosfamide

Carboplatin	AUC (4-6) iv	d1
Ifosfamide	3-5g/m ² iv	d1
q3w x 6 cycles		

A. Pawinski1, a, e, S. Tumolob, G. Hoeselc, A. Cervantesd, et al. Cyclophosphamide or ifosfamide in patients with advanced and/or recurrent endometrial carcinoma: a randomized phase II study of the EORTC Gynecological Cancer Cooperative Group. European Journal of Obstetrics & Gynecology and Reproductive Biology Volume 86, Issue 2, October 1999, Pages 179–183

Cisplatin + doxorubicin +paclitaxel (Taxol)

Doxorubicin 45mg/m ² IV + cisplatin 50mg/m ² iv	d1
Paclitaxel 160mg/m ² 3-hr iv	d2
Filgrastim 5mcg/kg SC.Repeat cycle every 3 weeks for max 7 cycles.	d3-12
Maximum BSA of 2.0 was used for calculations.	

1.NCCN Clinical Practice Guidelines in Oncology™. Uterine Neoplasms.v 2.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed February 24, 2012.

2.Fleming, GF, Brunetto VL, Cella D, et al. Phase III trial of doxorubicin plus cisplatin with or without paclitaxel plus filgrastim in advanced endometrial carcinoma: a Gynecologic Oncology Group Study. J Clin Oncol. 2004;22:2159–2166.

Ifosfamide (Ifex) + paclitaxel

Paclitaxel 135mg/m ² administered as a 3-hr iv	d1
Ifosfamide 1.6g/m ² /day iv (1.2g/m ² /day if patient received prior radiation).	d1-3
Repeat cycle every 3 weeks for 8 cycles.	

1.NCCN Clinical Practice Guidelines in Oncology™. Uterine Neoplasms.v 2.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed February 24, 2012.

2.Homesley HD, Filiaci V, Markman M, et al. Phase III trial of ifosfamide with or without paclitaxel in advanced uterine carcinosarcoma:a Gynecologic Oncology Group study. J Clin Oncol.2007;25:526–531.

Bevacizumab (Avastin)

Bevacizumab 15mg/kg iv	d1
Repeat cycle every 3 weeks	

1.NCCN Clinical Practice Guidelines in Oncology™. Uterine Neoplasms.v 2.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed February 24, 2012.

2.Aghajanian C, Sill MW, Darcy KM, et al. Phase II trial of bevacizumab in recurrent or persistent endometrial cancer: a Gynecologic Oncology Group study. J Clin Oncol. 2011;29(16): 2259–2265.

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Adjuvant chemotherapy

Epirubicin+Cisplatin

Epirubicin	60mg/m ² iv	d1	Cisplatin
60mg/m ² iv		d1	
q3w x 6wks cycles			

Lissoni1, A. Gabriele1, G. Gorga2, et al. Cisplatin-, epirubicin- and aclitaxel-containing chemotherapy in uterine adenocarcinoma. *Ann Oncol* (1997) 8 (10): 969-972

Epirubicin+Carboplatin

Epirubicin	60mg/m ² iv	d1	Carboplatin	AUC
(4-6) iv		d1		
q3w x 6wks cycles				

F. Calero, E. Asins-Codoñer, J. Jimeno, et al. Epirubicin in advanced endometrial adenocarcinoma: a phase II study of the grupo ginecologico Español para el tratamiento oncológico (GGETO). *European Journal of Cancer and Clinical Oncology*, Volume 27, Issue 7, July 1991, Pages 864–866

Paclitaxel+Cisplatin

Paclitaxel	(135/175)mg/m ² iv	d1	
Cisplatin	75mg/m ² iv	d1	
q3w x 6wks cycles			

Homesley HD, Filiaci V, Gibbons SK, et al. A randomized phase III trial in advanced endometrial carcinoma of surgery and volume directed radiation followed by cisplatin and doxorubicin with or without paclitaxel: A Gynecologic Oncology Group study. *Gynecol Oncol* 2009;112:543-552.

Paclitaxel+Carboplatin

Paclitaxel	(135/175)mg/m ² iv	d1	
Carboplatin	AUC (4-6) iv	d1	
q3w x 6wks cycles			

Miller D, Filiaci V, Fleming G, et al. Randomized phase III noninferiority trial of first line chemotherapy for metastatic or recurrent endometrial carcinoma: a Gynecologic Oncology Group study [abstract]. *Gynecol Oncol* 2012;125:771.

Doxorubicin +Cisplatin

Doxorubicin	50mg/m ² iv	d1
Cisplatin	75mg/m ² iv	d1
q3w x 6 cycles		

Homesley HD, Filiaci V, Gibbons SK, et al. A randomized phase III trial in advanced endometrial carcinoma of surgery and volume directed radiation followed by cisplatin and doxorubicin with or without paclitaxel: A Gynecologic Oncology Group study. *Gynecol Oncol* 2009;112:543-552.

Doxorubicin +Carboplatin

Doxorubicin	50mg/m ² iv	d1
Carboplatin	AUC (4-6) iv	d1
q3w x 6 cycles		

Homesley HD, Filiaci V, Gibbons SK, et al. A randomized phase III trial in advanced endometrial carcinoma of surgery and volume directed radiation followed by cisplatin and doxorubicin with or without paclitaxel: A Gynecologic Oncology Group study. *Gynecol Oncol* 2009;112:543-552.

Cisplatin+Ifosfamide

Cisplatin	50-100mg/m ² iv	d1
Ifosfamide	3-5g/m ² iv	d1
q3w x 6 cycles		

Howard D. Homesley, Virginia Filiaci, Maurie Markman, et al. Phase III Trial of Ifosfamide With or Without Paclitaxel in Advanced Uterine Carcinosarcoma: A Gynecologic Oncology Group Study. *JCO* February 10, 2007 vol. 25 no. 5 526-531

Carboplatin+Ifosfamide

Carboplatin	AUC (4-6) iv	d1
Ifosfamide	3-5g/m ² iv	d1
q3w x 6 cycles		

A. Pawinski1, a, e, S. Tumolob, G. Hoeselc, A. Cervantesd, et al. Cyclophosphamide or ifosfamide in patients with advanced and/or recurrent endometrial carcinoma: a randomized phase II study of the EORTC Gynecological Cancer Cooperative Group. *European Journal of Obstetrics & Gynecology and Reproductive Biology* Volume 86, Issue 2, October 1999, Pages 179–183

Doxorubicin (Adriamycin)

Doxorubicin 75mg/m ² iv bolus.	d1
Repeat cycle every 31 days OR 60mg/m ² –70mg/m ² iv typically dosed every 3 weeks.	

1. NCCN Clinical Practice Guidelines in Oncology™. Uterine Neoplasms.v 2.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed February 24, 2012.
2. Sarcoma Meta-analysis Collaboration (SMAC). *Cochrane Database Syst Rev*. 2000;4:CD001419.

Gemcitabine (Gemzar) +docetaxel (Taxotere) +granulocyte-colony-stimulating factor (G-CSF)

Gemcitabine 900mg/m ² iv over 90 min(自費),	d1
Docetaxel 100mg/m ² iv over 60 min,	d8
G-CSF 150mcg/m ² SC(自費)	d9-15
OR Pegfilgrastim 6mg SC.	d9 or d10
Repeat cycle every 3 weeks until disease progression or toxicity occurs.	
NOTE: Patients with prior pelvic irradiation received Gemcitabine 675mg/m ² iv and Docetaxel 75mg/m ² iv	

1.NCCN Clinical Practice Guidelines in Oncology™. Uterine Neoplasms.v 2.2012.

Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf.

Accessed February 24, 2012.

2.Hensley ML, Blessing JA, Mannel R, Rose PG. Fixed-dose rate gemcitabine plus docetaxel as first-line therapy for metastatic uterine leiomyosarcoma: a Gynecologic Oncology Group phase II trial. Gynecol Oncol. 2008;109:329–34.

Gemcitabine

Gemcitabine 1,000mg/m ² iv. (自費)	d1,8,15
Repeat cycle every 4 weeks.	

1.NCCN Clinical Practice Guidelines in Oncology™. Uterine Neoplasms.v 2.2012.

Available at: http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf.

Accessed February 24, 2012.

2.Look KY, Sandler A, Blessing JA, Lucci JA 3rd, Rose PG; Gynecologic Oncology Group (GOG) Study. Phase II trial of gemcitabine as second-line chemotherapy of uterine leiomyosarcoma: a Gynecologic Oncology Group (GOG) Study. Gynecol Oncol. 2004;92:644–647.

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GTD Chemotherapy Protocol 【Primary】

GTD-Low risk Methotrexate-FA

MTX	1mg/kg IM	d 1,3,5,7
Folinic acid	0.1mg/kg IM	d 2,4,6,8
qow		

1.McNeish IA, Strickland S, Holden L, Rustin GJ, Foskett M, Seckl MJ, Newlands ES. Low-risk persistent gestational trophoblastic disease: outcome after initial treatment with low-dose methotrexate and folinic acid from 1992 to 2000. J Clin Oncol. 2002 Apr 1;20(7):1838-44

2.Newlands ES, Bagshawe KD, Begent RH, Rustin GJ, Holden L. Results with the EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) regimen in high risk gestational trophoblastic tumours, 1979 to 1989. Br J Obstet Gynaecol. 1991 Jun;98(6):550-7.

GTD-Low risk Actinomycin-D

Actinomycin-D	1.25 mg/m ² iv	d1
q2w		

Newlands ES, Bagshawe KD, Begent RH, Rustin GJ, Holden L. Results with the EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) regimen in high risk gestational trophoblastic tumours, 1979 to 1989. Br J Obstet Gynaecol. 1991 Jun;98(6):550-7.

GTD-High EMA/CO

Etoposide	100 mg/m ²	d1
Actinomycin-D	0.5 mg	d1
MTX	100mg/m ² iv push	d1
MTX	200mg/m ² iv 12hrs	d1
Etoposide	100 mg/m ²	d2
Actinomycin-D	0.5 mg	d2
Folinic acid	15 mg P.O q12h*4	d2
Cyclophosphamide	60	d8

Newlands ES, Bagshawe KD, Begent RH, Rustin GJ, Holden L. Results with the EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) regimen in high risk gestational trophoblastic tumours, 1979 to 1989. Br J Obstet Gynaecol. 1991 Jun;98(6):550-7.

GTD Chemotherapy Protocol **【Resistant】**

GTD-Resistant EMA/PE

Etoposide	100 mg/m ²	d1
Actinomycin-D	0.5 mg	d1
MTX	100mg/m ² iv push	d1
MTX	200mg/m ² iv 12hrs	d1
Etoposide	100 mg/m ²	d2
Actinomycin-D	0.5 mg	d2
Folinic acid	15 mg P.O q12h*4	d2
Cisplatin	75~80 mg	d8

1. Newlands ES, Bagshawe KD, Begent RH, Rustin GJ, Holden L. Results with the EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) regimen in high risk gestational trophoblastic tumours, 1979 to 1989. Br J Obstet Gynaecol. 1991 Jun;98(6):550-7.

2. Randall ME, Filiaci VL, Muss H, et al. Randomized phase III trial of whole-abdominal irradiation versus doxorubicin and cisplatin chemotherapy in advanced endometrial carcinoma: a Gynecologic Oncology Group Study. J Clin Oncol 2006;24:36-44. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16330675>

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Neoadjuvant

Cisplatin+Paclitaxel

Cisplatin	(75-100)mg/m ² iv	d1
Paclitaxel	(135/175)mg/m ² iv	d1
q 3w		

Ignace Vergote, M.D., Ph.D., Claes G. Tropé, M.D., Ph.D., Frédéric Amant, M.D., Ph.D., et al. Neoadjuvant Chemotherapy or Primary Surgery in Stage IIIC or IV Ovarian Cancer. N Engl J Med 2010; 363:943-953 September 2, 2010

Carboplatin+Paclitaxel

Carboplatin	AUC(4-6) iv	d1
Paclitaxel	(135/175)mg/m ² iv	d1
q 3w		

Parmar MK, Ledermann JA, Colombo N, et al. Paclitaxel plus platinum-based chemotherapy versus conventional platinum-based chemotherapy in women with relapsed ovarian cancer: the ICON4/AGO-OVAR-2.2 trial. Lancet 2003;361:2099-2106.

Paclitaxel+ Doxorubicin liposome

Paclitaxel	(135/175)mg/m ² iv	d1
Doxorubicin liposome	(35-45)mg/m ² iv	d1
q 3w		

Eleftherios P. Mamounas, John Bryant, Barry Lembersky, et al. Paclitaxel After Doxorubicin Plus Cyclophosphamide As Adjuvant Chemotherapy for Node-Positive Breast Cancer: Results From NSABP B-28. JCO June 1, 2005 vol. 23 no. 16 3686-3696

Adjuvant

Cisplatin+Cyclophosphamide(For stage I,II)

Cisplatin	(75-100)mg/m ² iv	d1
Cyclophosphamide	750mg/m ² iv	d1
q3wx 6cycles		

McGuire WP, Hoskins WJ, Brady MF, et al. Cyclophosphamide and cisplatin compared with paclitaxel and cisplatin in patients with stage III and stage IV ovarian cancer. N Engl J Med 1996;334:1-6. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/7494563>.

Carboplatin+Cyclophosphamide(For stage I,II)

Carboplatin	AUC (4-6) iv	d1
Cyclophosphamide	(750-1000)mg/m ² iv	d1
q3w x 6 cycles		

Swenerton K, Jeffrey J, Stuart G, et al. Cisplatin-cyclophosphamide versus carboplatin-cyclophosphamide in advanced ovarian cancer: a randomized phase III study of the National Cancer Institute of Canada Clinical Trials Group. J Clin Oncol 1992;10:718-726.

Cisplatin+Paclitaxel(For stage <III ,自費)

Cisplatin	(75-100)mg/m ² iv	d1
Paclitaxel	(135/175)mg/m ² iv	d1
q 3w x 6 cycles		

Lesnock JL, Darcy KM, Tian C, et al. BRCA1 expression and improved survival in ovarian cancer patients treated with intraperitoneal cisplatin and paclitaxel: a Gynecologic Oncology Group Study. Br J Cancer 2013;108:1231-1237. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23462720>.

Carboplatin+Paclitaxel(For stage <III ,自費)

Carboplatin	AUC (4-6) iv	d1
Paclitaxel	(135/175)mg/m ² iv	d1
q 3w x 6 cycles		

1.NCCN Clinical Practice Guidelines in Oncology™. Ovarian Cancer including Fallopian Tube Cancer and Primary Peritoneal Cancer.v 2.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed May 11, 2012.

2.Ozols RF, Bundy BN, Greer BE, et al; Gynecologic Oncology Group. Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group study.J Clin Oncol. 2003;21:3194–3200.

Adjuvant second line therapy**Cisplatin**

Cisplatin	(75-100)mg/m ² iv	d1
wk x 6 wks		

Aghajanian C, Blank SV, Goff BA, et al. OCEANS: A randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. J Clin Oncol 2012;30:2039-2045.

Carboplatin

Carboplatin	AUC (4-6) iv	d1
q3w x 6 cycles		

Aghajanian C, Blank SV, Goff BA, et al. OCEANS: A randomized, double-blind, placebo-controlled phase III trial of chemotherapy with or without bevacizumab in patients with platinum-sensitive recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer. J Clin Oncol 2012;30:2039-2045.

Paclitaxel

Paclitaxel	(50-80)mg/m ² iv	d1
q3w x 6 cycles		

Markman M, Blessing J, Rubin SC, et al. Phase II trial of weekly paclitaxel (80 mg/m²) in platinum and paclitaxel-resistant ovarian and primary peritoneal cancers: a Gynecologic Oncology Group study. Gynecol Oncol 2006;101:436-440.

Doxorubicin liposome

Doxorubicin liposome	(35-45)mg/ m ² iv	d1
q3w x 6 cycles		

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. *J Clin Oncol* 2010;28:3323-3329.

Cisplatin+Ifosfamide

Cisplatin	(50-100)mg/m ² iv	d1
Ifosfamide	(3-5)g/m ² iv	d1
q3w x 6 cycles		

1.Markman M, Hakes T, Reichman B, et al. Ifosfamide and mesna in previously treated advanced epithelial ovarian cancer: activity in platinum-resistant disease. *J Clin Oncol* 1992;10:243-248. Available

at:<http://www.ncbi.nlm.nih.gov/pubmed/1732425>.

2.Kondagunta GV, Bacik J, Donadio A, et al. Combination of paclitaxel, ifosfamide, and cisplatin is an effective second-line therapy for patients with relapsed testicular germ cell tumors. *J Clin Oncol* 2005;23:6549-6555. Available

at:<http://www.ncbi.nlm.nih.gov/pubmed/16170162>.

Carboplatin+Ifosfamide

Carboplatin	AUC (4-6) iv	d1
Ifosfamide	(3-5)g/m ² iv	d1
q3w x 6 cycles		

1.Markman M, Hakes T, Reichman B, et al. Ifosfamide and mesna in previously treated advanced epithelial ovarian cancer: activity in platinum-resistant disease. *J Clin Oncol* 1992;10:243-248. Available

at:<http://www.ncbi.nlm.nih.gov/pubmed/1732425>.

2.Kondagunta GV, Bacik J, Donadio A, et al. Combination of paclitaxel, ifosfamide, and cisplatin is an effective second-line therapy for patients with relapsed testicular germ cell tumors. *J Clin Oncol* 2005;23:6549-6555. Available

at:<http://www.ncbi.nlm.nih.gov/pubmed/16170162>.

Doxorubicin liposome +Carboplatin

Doxorubicin liposome	(35-45) mg/ m ² iv	d1
Carboplatin	AUC (4-6) iv	d1
q3w x 6 cycles		

1.Mutch DG, Orlando M, Goss T, et al. Randomized phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in patients with platinum-resistant ovarian cancer. *J Clin Oncol* 2007;25:2811-2818.

2.Ferrandina G, Ludovisi M, Lorusso D, et al. Phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in progressive or recurrent ovarian cancer. *J Clin Oncol* 2008;26:890-896.

Paclitaxel+ Doxorubicin liposome

Paclitaxel	80mg/m ² iv	d1
Doxorubicin liposome	(35-45) mg/m ² iv	d1
wk x 6 wks		

Elizabeth M. Swisher, M.D., David G. Mutch, M.D., Janet S. Rader, M.D., et al. Topotecan in Platinum- and Paclitaxel-Resistant Ovarian Cancer. *Gynecologic Oncology*, Volume 66, Issue 3, September 1997, Pages 480–486

Topotecan(自費)

Topotecan	(0.5-1.25)mg/ m ² iv	d1
wk x 6 cycles		

1. Sehouli J, Stengel D, Harter P, et al. Topotecan weekly versus conventional 5-day schedule in patients with platinum-resistant ovarian cancer: A randomized multicenter phase II trial of the North-Eastern German Society of Gynecological Oncology Ovarian Cancer Study Group. J Clin Oncol 2011;29:242-248.

2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.

3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Topotecan(自費)

Topotecan	(0.75-1.25)mg/ m ² iv	d1
q3w x 6 cycles		

1. Gordon AN, Tonda M, Sun S, Rackoff W. Long-term survival advantage for women treated with pegylated liposomal doxorubicin compared with topotecan in a phase 3 randomized study of recurrent and refractory epithelial ovarian cancer. Gynecol Oncol 2004;95:1-8.

2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.

3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Cisplatin+ Topotecan

Cisplatin	100mg/m ² iv	d1
Topotecan	(2.5-4)mg/m ² iv	d1
10days x 3 course		

1. M A Bookman, H Malmström, G Bolis, et al. Topotecan for the treatment of advanced epithelial ovarian cancer: an open-label phase II study in patients treated after prior chemotherapy that contained cisplatin or carboplatin and paclitaxel. JCO October 1998 vol. 16 no. 10 3345-3352

2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.

3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Carboplatin+ Topotecan

Carboplatin	AUC (4-6) iv	d1
Topotecan	(2.5-4)mg/m ² iv	d1
10days x 3 course		

1. M A Bookman, H Malmström, G Bolis, et al. Topotecan for the treatment of advanced epithelial ovarian cancer: an open-label phase II study in patients treated after prior chemotherapy that contained cisplatin or carboplatin and paclitaxel. JCO October 1998 vol. 16 no. 10 3345-3352

2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.

3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Palliative

Gefitinib +Paclitaxel

Gefitinib(自費)	2pc	d1
Paclitaxel	80mg/m ² iv	d1

Fortunato Ciardiello², Rosa Caputo, Roberto Bianco, et al. Antitumor Effect and Potentiation of Cytotoxic Drugs Activity in Human Cancer Cells by ZD-1839 (Iressa), an Epidermal Growth Factor Receptor-selective Tyrosine Kinase Inhibitor¹ Clin Cancer Res May 2000 6; 2053

Etoposide

Etoposide	1pc(oral)1#
QD x 7 day ~ 28 day	

Rose PG, Blessing JA, Mayer AR, Homesley HD. Prolonged oral etoposide as second-line therapy for platinum-resistant and platinum-sensitive ovarian carcinoma: a Gynecologic Oncology Group study. J Clin Oncol 1998;16:405-410.

Cyclophosphamide

Cyclophosphamide	1pc (oral)1#
QD x 7 day ~ 28day	

Swenerton K, Jeffrey J, Stuart G, et al. Cisplatin-cyclophosphamide versus carboplatin-cyclophosphamide in advanced ovarian cancer: a randomized phase III study of the National Cancer Institute of Canada Clinical Trials Group. J Clin Oncol 1992;10:718-726.

Gemcitabine+ Doxorubicin liposome

Gemcitabine	650mg/m ² iv	d1
Doxorubicin liposome	15mg/m ² iv	d1
weekx3 rest 1 week x 6 cycles		

1.Mutch DG, Orlando M, Goss T, et al. Randomized phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in patients with platinum-resistant ovarian cancer. J Clin Oncol 2007;25:2811-2818.

2.Ferrandina G, Ludovisi M, Lorusso D, et al. Phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in progressive or recurrent ovarian cancer. J Clin Oncol 2008;26:890-896.

Bevacizumab (自費)+Cyclophosphamide

Bevacizumab	5-10mg/kg q2weeks iv	d1
Cyclophosphamide	1#(50mg) qd 5days iv	d1

1.Robert A. Burger, Michael W. Sill, Bradley J. Monk, et al. Phase II Trial of Bevacizumab in Persistent or Recurrent Epithelial Ovarian Cancer or Primary Peritoneal Cancer: A Gynecologic Oncology Group Study.JCO November 20, 2007 vol. 25 no. 33 5165-5171

2.Carol Aghajanian¹, Stephanie V. Blank, Barbara A. Goff,et al. OCEANS: A Randomized, Double-Blind, Placebo-Controlled Phase III Trial of Chemotherapy With or Without Bevacizumab in Patients With Platinum-Sensitive Recurrent Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Cancer.JCO June 10, 2012 vol. 30 no. 17 2039-2045

paclitaxel

Paclitaxel	80mg/m ² iv	d1
wk x 6 wks		

Markman M, Blessing J, Rubin SC, et al. Phase II trial of weekly paclitaxel (80 mg/m²) in platinum and paclitaxel-resistant ovarian and primary peritoneal cancers: a Gynecologic Oncology Group study. *Gynecol Oncol* 2006;101:436-440.

Doxorubicin liposome

Doxorubicin liposome	(35-45)mg/m ² iv	d1
q4w x 6 cycles		

1. Mutch DG, Orlando M, Goss T, et al. Randomized phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in patients with platinum-resistant ovarian cancer. *J Clin Oncol* 2007;25:2811-2818.

2. Ferrandina G, Ludovisi M, Lorusso D, et al. Phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in progressive or recurrent ovarian cancer. *J Clin Oncol* 2008;26:890-896.

Carboplatin(自費) + Doxorubicin liposome

Carboplatin	AUC (4-6) iv	d1
Doxorubicin liposome	(35-45) mg/m ² iv	d1
q4w x 6 cycles		

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. *J Clin Oncol* 2010;28:3323-3329.

Topotecan(自費)

Topotecan	2.5-4mg/m ² iv	d1
wk x 6 cycles		

1. Gordon AN, Tonda M, Sun S, Rackoff W. Long-term survival advantage for women treated with pegylated liposomal doxorubicin compared with topotecan in a phase 3 randomized study of recurrent and refractory epithelial ovarian cancer. *Gynecol Oncol* 2004;95:1-8.

2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.

3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. *Am J Health-Syst Pharm*. 2006;63:1172-1193.

paclitaxel

Paclitaxel	(50-80)mg/m ² iv	d1
Monthly		

Markman M, Blessing J, Rubin SC, et al. Phase II trial of weekly paclitaxel (80 mg/m²) in platinum and paclitaxel-resistant ovarian and primary peritoneal cancers: a Gynecologic Oncology Group study. *Gynecol Oncol* 2006;101:436-440.

Intraperitoneal for stage III

Paclitaxel+cisplatin

Paclitaxel	135mg/m ² iv	d1
cisplatin	100mg/m ² ip	d2
Q3w x 6 cycles		

David S. Alberts, M.D., P.Y. Liu, Ph.D., Edward V. Hannigan, M.D., et al.
 Intraperitoneal Cisplatin plus Intravenous Cyclophosphamide versus Intravenous
 Cisplatin plus Intravenous Cyclophosphamide for Stage III Ovarian Cancer. N Engl J
 Med 1996; 335:1950-1955 December 26, 1996

Ovary (Dysgerminoma ,Embryonal, endodermal sinus tumor, immature teratoma, or mixed histology)

BEP 3 day regimen			
Etoposide	165mg/m ²		Day1,2,3
Cisplatin	35 mg/m ²		Day1,2,3
± Bleomycin	30 U		Day1,8,15
21 days intervals x 3-4course			

BEP 5 day regimen			
Etoposide	100 mg/m ²		Day1-5
Cisplatin	20 mg/m ²		Day1-5
± Bleomycin	30 units		Per week
21 days intervals x 3-4course			

Patients who do not respond to BEP may benefit from the following as salvage therapy (TIP):			
Cisplatin	35 mg/m ²		Day1,2,3
Ifosfamide	2 gm/m ²		Day2,3,4
Taxol	135 mg/m ²		Day1

Alberta Provincial Gynecologic Oncology Tumour Team. Ovarian germ cell tumours.
 Edmonton (Alberta): CancerControl Alberta; 2013 Apr. 12 p. (Clinical practice
 guideline; no. GYNE-001).

攝護腺癌

Principles of chemotherapy

Docetaxel + Prednisolone

Docetaxel	75 mg/m ²	d1
Prednisolone	10mg/day	
Q3w		

Berthold DR et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer: updated survival in the TAX 327 study. J Clin Oncol 2008; 26:242 (link to the article).

Docetaxel + Prednisolone

Docetaxel	30 mg/m ²	d1,8,15,22,29
Prednisolone	10mg/day	
Q6w		

Tannock IF et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. N Eng J Med 2004; 351:1502.

Mitoxantrone + Prednisone

Mitoxantrone	12 mg/m ²	d1
Prednisolone	10mg/day	
Q3w		

Tannock IF et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. N Eng J Med 2004; 351:1502.

膀胱癌

Intravesical chemotherapy for Tis ,Ta 及 T1 cancer

Mitomycin (Miomycin-C) 30mg qw x6 and /or qm x3

Phamarubicin 30mg qw x6 and/or qm x3

BCG 81 mg qw (x6) since 2nd post-op week and/or qw (x3) since 3rd post-op month, qw (x3) since 6th post-op month, qw (x3) since 12th post-op month Intravesical chemotherapy

Neoadjuvant or adjuvant chemotherapy for stage II, III and non-metastatic stage IV cancer

MVAC

Methotrexate	30 mg/m ² iv	d1, 15 and 22
Vinblastine	3 mg/m ² iv	d2, 15 and 22
Doxorubicin	30 mg/m ² iv	d2
Cisplatin	70 mg/m ² iv or Carboplatin AUC 4-6	d1 or 2
Q4w x 3 cycles		

Grossman HB et al. Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. N Eng J Med 2003; 349:859

Gemcitabine (自費)+ Cisplatin (Carboplatin)

Gemcitabine	800 - 1000 mg/m ² iv	d1, 8 and 15
Cisplatin	70 mg/m ² iv or Carboplatin AUC 4-6	d1
Q4w x 3 cycles		

Von der Maase H et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin and cisplatin in advanced or metastatic bladder cancer: results of a large, randomized, multinational, multicenter, phase III study. J Clin Oncol 2000; 18:3068

CMV

Cisplatin	70 mg/m ² iv	d2
Vinblastine	4 mg/m ² iv	d1, 8
Methotrexate	30 mg/m ² iv	d1, 8
Q3w x 3 cycles		

International Collaboration of Trialists. Neoadjuvant cisplatin, methotrexate, and vinblastine chemotherapy for muscle invasive bladder cancer: a randomized controlled trial. Lancet 1999; 354:533

Concurrent chemoradiation for stage II, III and non-metastatic stage IV cancer

Cisplatin

Cisplatin	30-40 mg/m ² iv or Carboplatin AUC 2	d1
Q1w x 6 cycles		

Tunio MA et al. Bladder preservation by neoadjuvant chemotherapy followed by concurrent chemoradiation for muscle-invasive bladder cancer: experience at Sindh Institute of Urology & Transplantation (SIUT). J Pak Med Assoc 2011; 61:6.

Chemotherapy for metastatic cancer

MVAC

Methotrexate	30 mg/m ² iv	d1, 15 and 22
Vinblastine	3 mg/m ² iv	d2, 15 and 22
Doxorubicin	30 mg/m ² iv	d2
Cisplatin	70 mg/m ² iv or Carboplatin AUC 4-6	d1 or 2
Q4w x 6 cycles		

Han KS et al. Methotrexate, vinblastine, doxorubicin and cisplatin combination regimen as salvage chemotherapy for patients with advanced or metastatic transitional cell carcinoma after failure of gemcitabine and cisplatin chemotherapy. Br J Cancer 2008; 98:86.

Logothetis CJ et al. A prospective randomized trial comparing MVAC with CISCA chemotherapy for patients with metastatic urothelial tumors. J Clin Oncol 1990; 8:1050.

Gemcitabine + Cisplatin(Carboplatin)

Gemcitabine	800 - 1000 mg/m ² iv	d1, 8 and 15
Cisplatin	70 mg/m ² iv	d2
Q4w x 6 cycles		

von der Maase H et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin and cisplatin in advanced or metastatic bladder cancer: results of a large, randomized, multinational, multicenter, phase III study. J Clin Oncol 2000; 18:3068

Paclitaxel +/- Cisplatin(Carboplatin)

Paclitaxel	80 mg/m ² iv	d1, 8, 15
Cisplatin	70 mg/m ² iv or Carboplatin AUC 4-6	d1
Q4w x 6 cycles		

von der Maase H et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin and cisplatin in advanced or metastatic bladder cancer: results of a large, randomized, multinational, multicenter, phase III study. J Clin Oncol 2000; 18:3068

甲狀腺癌

化學治療處方(Chemotherapy Regimen)

Regimen	Agents/Dosages	Frequency
Paclitaxel (weekly)	60-90 mg/m ² IV	Weekly
Paclitaxel(triweekly)	135-200 mg/m ² IV	Every 3-4 weeks
Doxorubicin(weekly)	20 mg/m ² IV	Weekly
Doxorubicin(triweekly)	60-75 mg/m ² IV	Every 3 weeks

淋巴瘤

Hodgkin Lymphoma

Most common variants

ABVD : (doxorubicin、bleomycin、vinblastine、dacarbazine)

Doxorubicin (Adriamycin) 25 mg/m² iv D1 and 15

Bleomycin 10 U/m² iv D1 and 15

Vinblastine 6 mg/m² iv D1 and 15

Dacarbazine (DTIC) 375 mg/m² iv D1 and 15 Q4w

Second-Line or Subsequent Therapy Options

1. Brentuximab vedotin (only for CHL)

2. Involved-site Radiation Therapy (ISRT)

Dose:

(1) Combined Modality Therapy

Non-bulky disease (stage I-II): 20–30 Gy (if treated with ABVD), 30 Gy (if treated with Stanford V); 1.5-2.0 Gy per fraction

*Non-bulky disease (stage IB-IIB): 30 Gy; 1.5-2.0 Gy per fraction

*Bulky disease sites (all stages): 30–36 Gy; 1.5-2.0 Gy per fraction

(2) ISRT Alone (uncommon, except for NLPHL):

*Involved regions: 30–36 Gy (the dose of 30 Gy is mainly used for NLPHL); 1.5-2.0 Gy per fraction

*Uninvolved regions: 25–30 Gy; 1.5-2.0 Gy per fraction

★Brentuximab vedotin 1.8mg/kg 以30分鐘以上靜脈輸注方式給藥，每3週一次，若患者體重超過100kg，應以100kg 算所需劑量。持續治療直到疾病惡化(disease progression)或出現無法接受的毒性為止。達到病況穩定(stable disease)或改善的患者，應接受最少8個療程，最多至16個療程(約1年)的治療。

★健保給付原則：

Brentuximab vedotin (如Adcetris)，限用於成人患者：

1. 治療復發或頑固型CD30+何杰金氏淋巴瘤(HL)：(1)已接受自體幹細胞移植(ASCT)，或(2)無法使用ASCT或多重藥物化療，且先前至少已接受兩種治療。

2. 治療復發或頑固型全身性退化分化型大細胞淋巴瘤(systemic anaplastic large cell lymphoma；sALCL)。

3. 每次申請療程以4個療程為限，再申請應檢附前次治療結果評估資料。若病人病情已達完全緩解，得再給付4個療程。健保給付以16個療程為上限。

(Reference)

1. NCCN Clinical Practice Guidelines in Oncology. Hodgkin's Lymphomas V4. 2019
2. McKelvey EM. cancer 1976;38:1484-1493. Lenz G. J clin Oncol 2005;23:1984-1992. Hiddemann W. Blood 2005;106:3725-3732
3. Velasquez WS. Blood 1988;71:117-122.
4. Velasquez WS. J clin Oncol 1994;12:1169-1176.
5. Moskowitz CH. J clin oncol 1999;17:3776-3785.
6. Kewalramans T. blood 2004;103:3684-3688

7. Canellos GP et al. Chemotherapy of advanced Hodgkin's disease with MOPP, ABVD, or MOPP alternating with ABVD. N Eng J Med 1992; 327:1478.
 8. BLOOD, 19 MAY 2016 x VOLUME 127, NUMBER 20:2376

Additional Therapy Options(only for CHL)

1. Bendamustine
 2. Nivolumab (for patients previously treated with brentuximab vedotin)
 3. Pembrolizumab(for patients previously treated with brentuximab vedotin)
- Canellos GP et al. Chemotherapy of advanced Hodgkin's disease with MOPP, ABVD, or MOPP alternating with ABVD. N Eng J Med 1992; 327:1478.

Diffuse Large B-cell Lymphoma

	Regimen	*Dosage	Reference
First-line	RCHOP	Rituximab 375 mg/m ² i.v. on day 1 Cyclophosphamide 750 mg/m ² i.v. on day 1 Doxorubicin 50 mg/m ² i.v. on day 1 Vincristine 1.4 mg/m ² i.v. on day 1(maximum dose of 2 mg) Prednisone 100mg p.o. daily on day1-5	McKelvey EM. cancer 1976;38:1484-1493.Lenz G. J clin Oncol 2005;23:1984-1992. Hiddemann W.Blood 2005;106:3725-3732
	RCEOP	Rituximab 375 mg/m ² i.v. on day 1 Cyclophosphamide 750 mg/m ² i.v. on day 1 Epirubicin 50 mg/m ² i.v. on day 1 Vincristine 1.4 mg/m ² i.v. on day 1(maximum dose of 2 mg) Prednisone 100mg p.o. daily on day1-5	
	DA-EPOCH + Rituximab	Etoposide Prednisone Vincristine Cyclophosphamide Doxorubicin	
註: patients >80 of age with comorbidities R-mini CHOP			
Second-line	DHAP±Rituximab	Cisplatin 80-100 mg/m ² CIVI over 24 h on day 1 Cytarabine 2000 mg/m ² i.v. q12h x2 dose on day 2 Dexamethasone 40 mg/m ² p.o./i.v. daily on day 1-4 Repeat cycle every21-28 d	Velasquez WS. Blood 1988;71:117-122.
	ESHAP±Rituximab	Etoposide 40 mg/m ² i.v. daily on days 1-4 Methylprednisolone 500 mg/m ² i.v. daily on days 1-5 Cytarabine 2000 mg/m ² CIVI on day 5 Cisplatin 25 mg/m ² i.v. daily on days 1-4 Repeat cycle every21-28 d	Velasquez WS. J clin Oncol 1994;12:1169-1176.

	ICE±Rituximab	Ifosfamide 5000 mg/m ² CIVI over 24h on day 2 Mesna 5000 mg/m ² CIVI over 24h on day 2 Carboplatin AUC 5 i.v. on day 2(maximum dose of 800 mg) Etoposide 100 mg/m ² i.v. daily on days 1-3 ±rituximab 375 mg/m ² i.v. 48 h before start of cycle 1 and on day 1 of each cycle Repeat cycle every 14-15 d	Moskowitz CH0J clin oncol 1999;17:3776-3785. Kewalramans T. blood 2004;103:3684-3688
	RB	Rituximab 375 mg/m ² i.v. on day 1 Bendamustine 90-120mg/m ² day 1-2	

Follicular Lymphoma grade1-2

	Regimen	Dosage	Reference
First-line	RCHOP	Rituximab 375 mg/m ² i.v. on day 1 Cyclophosphamide 750 mg/m ² i.v. on day 1 Doxorubicin 50 mg/m ² i.v. on day 1 Vincristine 1.4 mg/m ² i.v. on day 1(maximum dose of 2 mg) Prednisone 100mg p.o. daily on day1-5	McKelvey EM. cancer 1976;38:1484-1493.Lenz G. J clin Oncol 2005;23:1984-1992. Hiddemann W.Blood 2005;106:3725-3732
	RCEOP	Rituximab 375 mg/m ² i.v. on day 1 Cyclophosphamide 750 mg/m ² i.v. on day 1 Epirubicin 50 mg/m ² i.v. on day 1 Vincristine 1.4 mg/m ² i.v. on day 1(maximum dose of 2 mg) Prednisone 100mg p.o. daily on day1-5	
	BR	Rituximab 375 mg/m ² i.v. on day 1 Bendamustine 90-120mg/m ² day 1-2	
	GB	Bendamustine 90-120mg/m ² day 1-2 Obinutuzumab maintenance (1000 mg every 8 weeks for 12 doses)	
	RCOP	Rituximab 375 mg/m ² i.v. on day 1 Cyclophosphamide 750 mg/m ² i.v. on day 1 Vincristine 1.4 mg/m ² i.v. on day 1(maximum dose of 2 mg) Prednisone 100mg p.o. daily on day1-5	
Second-line	DHAP±Rituximab	Cisplatin 100 mg/m ² CIVI over 24 h on day 1 Cytarabine 2000 mg/m ² i.v. q12h x2 dose on day 2 Dexamethasone 40 mg/m ² p.o./i.v. daily on day 1-4 Repeat cycle every21-28 d	Velasquez WS. Blood 1988;71:117-122.
	ESHAP±Rituximab	Etoposide 40 mg/m ² i.v. daily on days 1-4 Methylprednisolone 500 mg/m ² i.v. daily on days 1-5 Cytarabine 2000 mg/m ² CIVI on day 5 Cisplatin 25 mg/m ² i.v. daily on days 1-4 Repeat cycle every21-28 d	Velasquez WS. J clin Oncol 1994;12:1169-1176.

	ICE±Rituximab	Ifosfamide 5000 mg/m² CIVI over 24h on day 2 Mesna 5000 mg/m² CIVI over 24h on day 2 Carboplatin AUC 5 i.v. on day 2(maximum dose of 800 mg) Etoposide 100 mg/m² i.v. daily on days 1-3 ±Rituximab 375 mg/m² i.v. 48 h before start of cycle 1 and on day 1 of each cycle Repeat cycle every 14-15 d	Moskowitz CH0J clin oncol 1999;17:3776-3785. Kewalramans T. blood 2004;103:3684-3688
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Acute Lymphoid Leukemia

TPOG-ALL-2013 Continuation Therapy (1)

Week	VHR/HR	SR
1	DEX + EPI + VCR + 6MP + ASP	6MP + DEX + VCR
2	6MP + ASP	6MP + MTX
3	# 6MP + ASP	*6MP + MTX
4	DEX + EPI + VCR + 6MP + ASP	6MP + DEX + VCR
5	6MP + ASP	6MP + MTX
6	6MP + ASP	6MP + MTX
7	*(Reind I)DEXx8d+VCR+EPI+ASPx3	*(Reind)DEXx8d+VCR+EPI+ASPx3
8	(Reind I) VCR+EPI+ASPx3	(Reind) VCR+ASPx3
9	(Reind I)DEXx7d+VCR+ASPx3	(Reind)DEXx7d+VCR+ASPx3
10	6MP + ASP	6MP + MTX

TPOG-ALL-2013 Continuation Therapy (2)

Drug dosages, schedules and routes for continuation therapy weeks

DEX (dexamethasone)	12 mg/m ² (VHR/HR) or 8 mg/m ² (SR) PO daily (tid) x 5 days, Days 1-5
EPI (epirubicin)	30 mg/m ² IV, Day 1
VCR (vincristine)	2.0 mg/m ² IV push (max. 2 mg), Day 1 (0.05 mg/kg for patients < 1 year of age or < 10kg in weight)
6MP (6-mercaptopurine)	40 mg/m ² PO h.s.daily x 7 days (VHR/ HR), Days 1-7 50 mg/m ² PO h.s. daily x 7 days (SR), Days 1-7
ASP (L-asparaginase)	10,000 U/m ² IM, Day 1
MTX (methotrexate)	40 mg/m ² IV or IM, Day 1

TPOG-ALL-2013 Continuation Therapy (3)
Reinduction for SR ALL (3 weeks)

Agents	Dosages and routes	Doses	Schedules
Dexamethasone	10 mg/m ² /day PO (t.i.d.)	45	Days 1-8, 15-21
Vincristine	1.5 mg/m ² /week IV (max 2 mg)	3	Days 1, 8, 15
L-asparaginase	6,000 U/m ² thrice weekly IM	9	Days 3, 5, 7, 10,12,14,17,19,21
Epirubicin	30 mg/m ² /week IV	1	Day 1

TPOG-ALL-2013 Continuation Therapy (4)
Reinduction I for VHR/HR ALL excluding infant with MLL+(3 weeks)

Agents	Dosages and routes	Doses	Schedules
Dexamethasone	12 mg/m ² /day PO (t.i.d.)	45	Days 1-8, 15-21
Vincristine	1.5 mg/m ² /week IV (max 2 mg)	3	Days 1, 8, 15
Epirubicin	30 mg/m ²	2	Days 1,8
L-asparaginase	6,000 U/m ² /thrice weekly IM	9	Days 3, 5, 7, 10,12, 14,17,19,21
Methotrexate + hydrocortisone + ara-C	Age-dependent, IT	1	Day 1

TPOG-ALL-2013 Continuation Therapy (5)
Reinduction I for infant with MLL+

Agent	Dosage and Route	Doses	Schedule
Dexamethasone	8 mg/m ² /day (divided t.i.d)	45	Days 1-8; 15-21
Clofarabine	25 mg/m ² /day, 2-hour IV infusion	5	Days 1-5
Etoposide	100 mg/m ² /day, 2-hour IV infusion	5	Days 1-5
Cyclophosphamide	300 mg/m ² /day, 1-hour IV infusion	5	Days 1-5
L-asparaginase	6,000 U/m ² thrice weekly IM	9	Days 3, 5, 7, 10,12, 14, 17, 19, 21

For infants < 1 month of age, or for infants < 3 months of age born significantly prematurely, a 50% reduction in dosages of asparaginase, etoposide, cyclophosphamide, epirubicin, and clofarabine should be made.

TPOG-ALL-2013 Continuation Therapy (6)

Week	VHR/HR	SR
11	EPI + VCR + 6MP + ASP	6MP + MTX
12	*6MP + ASP	* 6MP + MTX
13	6MP + ASP	6MP + MTX
14	DEX + EPI + VCR + 6MP + ASP	6MP + DEX + VCR
15	6MP + ASP	6MP + MTX
16	6MP + ASP	6MP+ MTX
17	*(Reind II)DEXx8d+VCR+ASPx3	*6MP + DEX + VCR
18	(Reind II) VCR+ ASPx3	6MP + MTX
19	(Reind II)DEXx7d+VCR+ASPx3	6MP + MTX
20	6MP + MTX	6MP + DEX + VCR

TPOG-ALL-2013 Continuation Therapy (7)
Reinduction II for VHR/HR ALL including infant with MLL+(3 weeks)

Agents	Dosages and routes	Doses	Schedules
Dexamethasone	12 mg/m ² /day PO (t.i.d.)	45	Days 1-8, 15-21
Vincristine	1.5 mg/m ² /week IV (max 2 mg)	3	Days 1, 8, 15
L-asparaginase	6,000 U/m ² /thrice weekly IM	9	Days 3, 5, 7, 10,12,14,17,19,21
Methotrexate + hydrocortisone + ara-C	Age-dependent, IT	1	Day 1

TPOG-ALL-2013 Continuation Therapy (8)
Treatment (weeks 21 to end of therapy)

Week	VHR , HR	SR
21	6MP + MTX	6MP + MTX
22	6MP + MTX	6MP + MTX
23	Cyclo + Ara-C	6MP + MTX
24	*DEX + VCR	*6MP + DEX + VCR
25	6MP + MTX	6MP + MTX
26	6MP + MTX	6MP + MTX
27	Cyclo + Ara-C	6MP + MTX
28	*DEX + VCR	(*) 6MP + DEX + VCR

IT MHA for standard-risk cases, *TEL-AML1* fusion and hyperdiploidy (51-68) with WBC > 100,000/mm³, CNS-2 or traumatic lumbar puncture with blast.

TPOG-ALL-2013 Continuation Therapy (9)

6MP (6-mercaptopurine)	60 mg/m ² PO h.s. daily x 7 days, Days 1-7
MTX (methotrexate)	40 mg/m ² IV or IM (or PO, if parenteral route is not feasible), Day 1
Cyclo (Cyclophosphamide)	300 mg/m ² IV, Day 1 (VHR/HR)
Ara-C (Cytarabine)	300 mg/m ² IV, Day 1 (VHR/HR)
DEX (dexamethasone) (decreases to 6 mg/m ² beginning week 68)	12 mg/m ² (VHR/HR) or 8 mg/m ² (SR) PO daily (tid) x 5, Day 1-5
VCR (vincristine)	2.0 mg/m ² IV push (max. 2 mg), Day 1

The same treatment (weeks 21-28) will be repeated for a total of 6 times (until week 68). After week 68, cyclophosphamide and cytarabine will be replaced by daily 6MP and methotrexate; all patients will then receive daily 6MP and weekly MTX with pulses of dexamethasone and vincristine every 4 weeks until week 100, after which only 6MP and methotrexate will be given.

Non-Hodgkin's lymphoma

TPOG 10 ALCL: Chemotherapy Dose and Schedule in Each Course(administered every 3 wk)

Course and Drug	Dose and Schedule
Prephase	
Dexamethasone	5 mg/m ² on days 1 and 2; 10 mg/m ² on days 3 to 5
Cyclophosphamide	200 mg/m ² on days 1 and 2
Triple intrathecal injection	Day 1
Course A	
Dexamethasone	10 mg/m ² on days 1 to 5
Methotrexate	3 g/m ² in 3-hour infusion on day 1
Ifosfamide	800 mg/m ² on days 1 to 5
Cytarabine	150 mg/m ² x 2 on days 4 and 5
Etoposide	100 mg/m ² on days 4 and 5
Course B	
Dexamethasone	10 mg/m ² on days 1 to 5
Methotrexate	3 g/m ² in 3-hour infusion on day 1
Cyclophosphamide	200 mg/m ² on days 1 to 5
Doxorubicin	25 mg/m ² on days 4 and 5

* Leucovorin rescue (15 mg/m² every 6 hours) starting at 24 hours of start of MTX infusion and ending when the methotrexate level was < 0.15 µm/L.