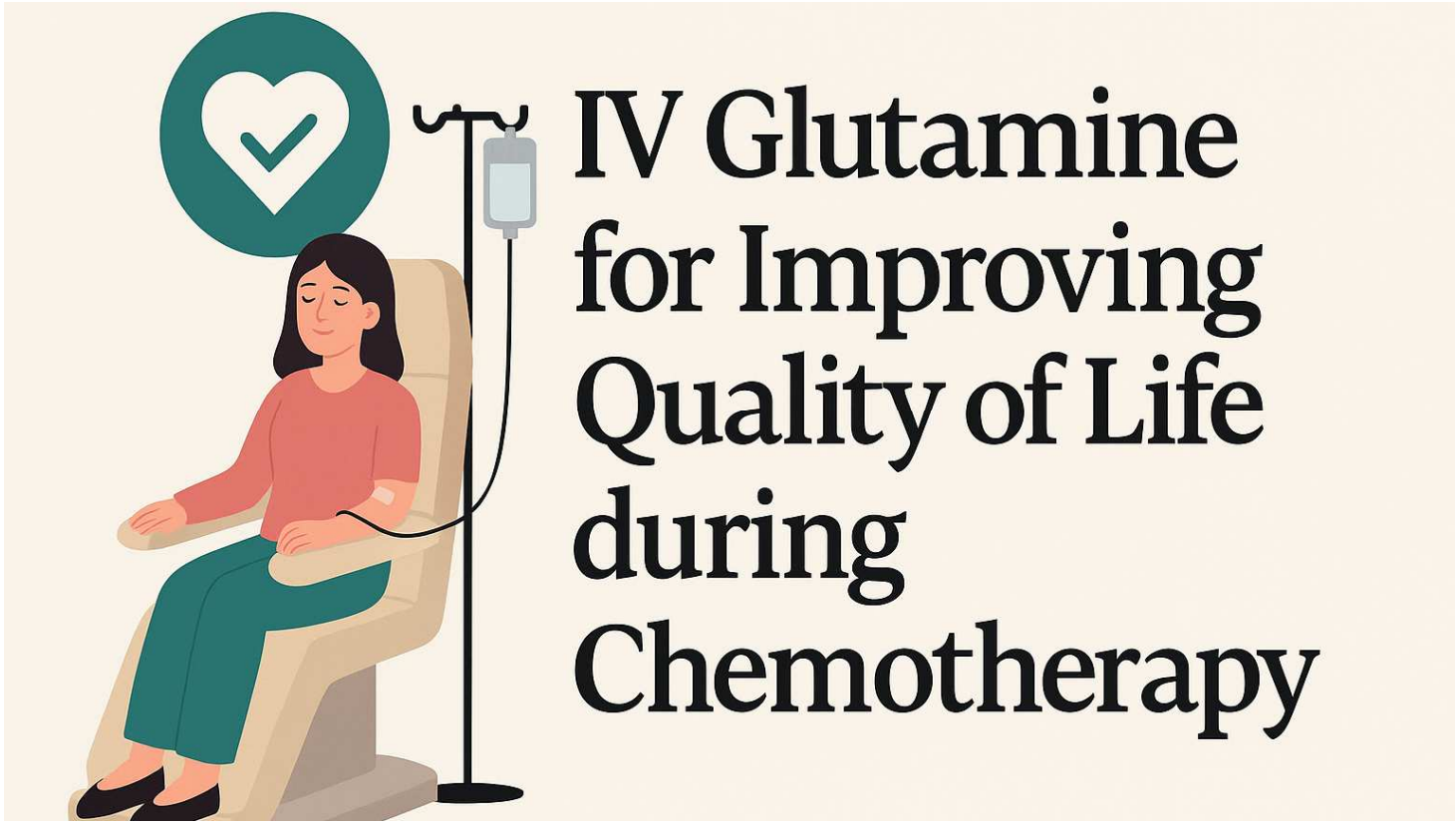

杜政勳
血液腫瘤內科
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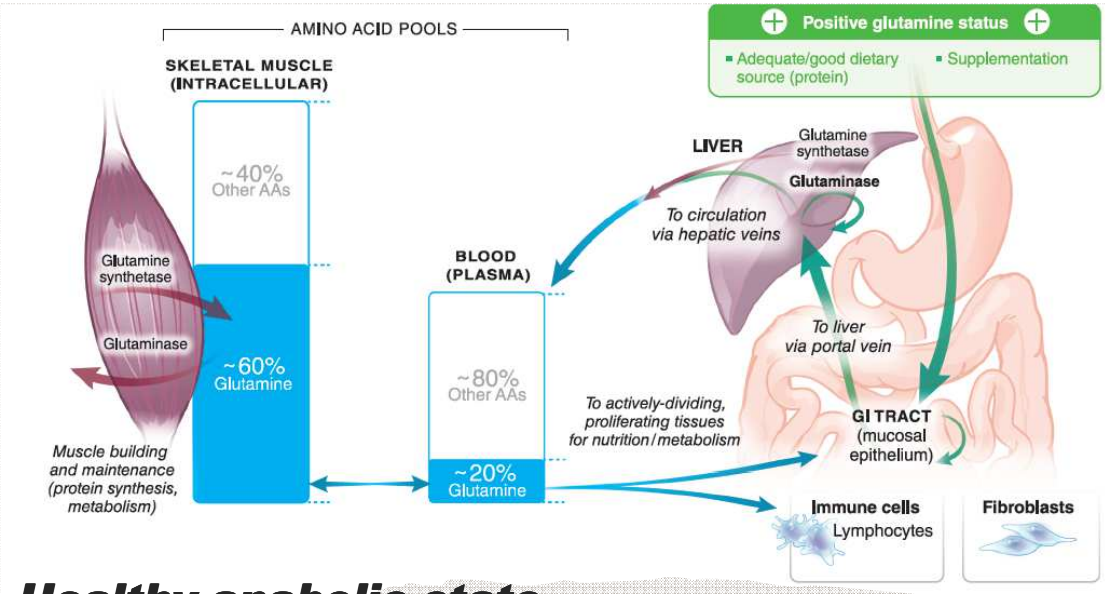
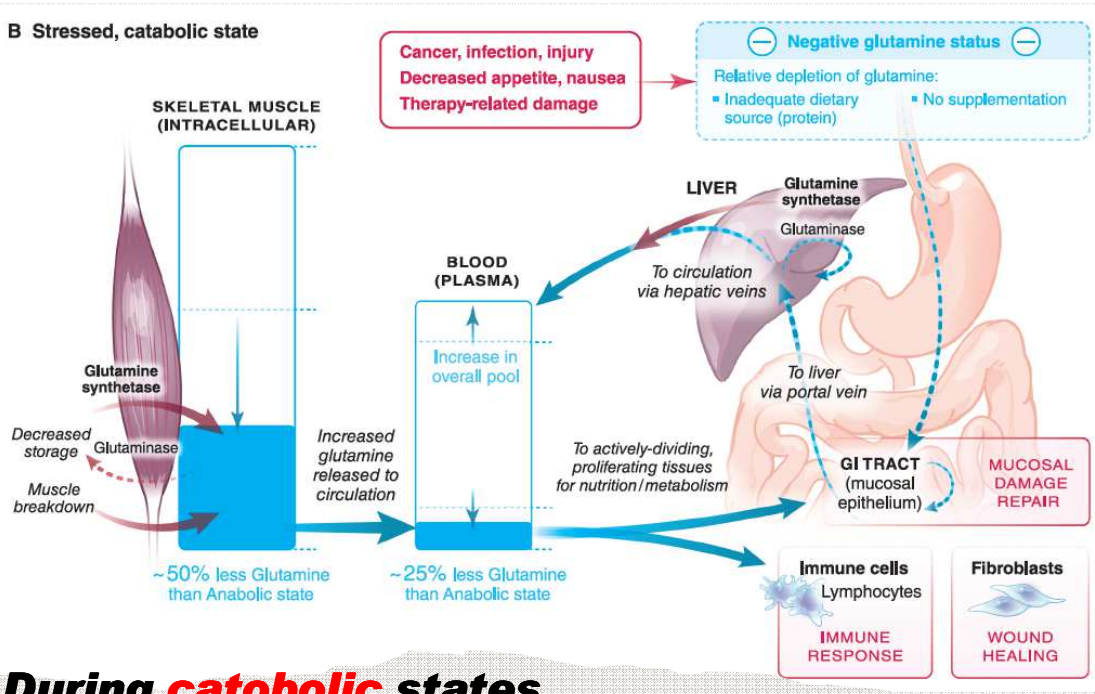
Outline

- The role of glutamine in cancer patients
- The Clinical benefit of Dipeptiven
- Cases sharing
- Myth of glutamine



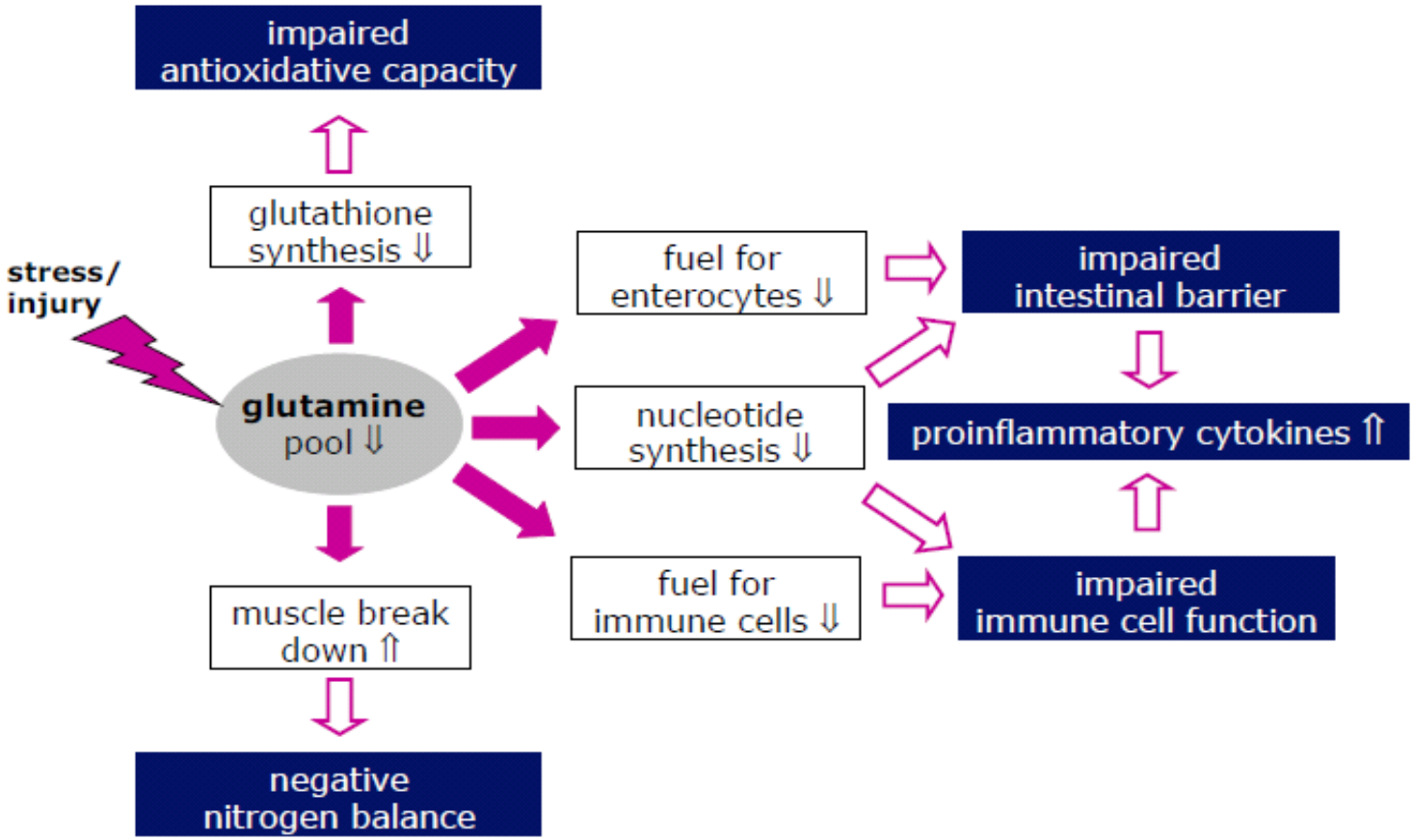
Healthy anabolic state

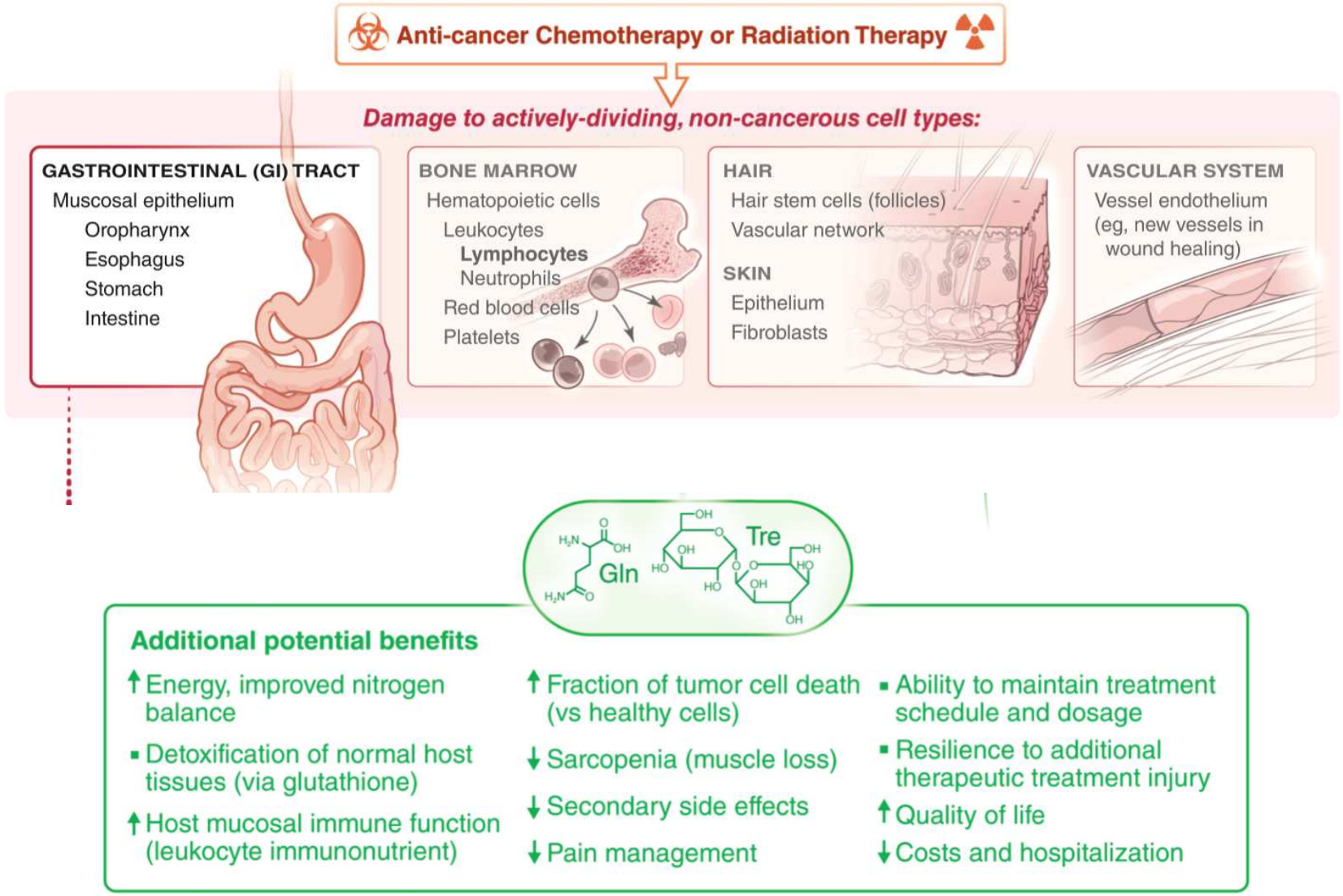


During catobolic states

The Pivotal Role of Glutamine

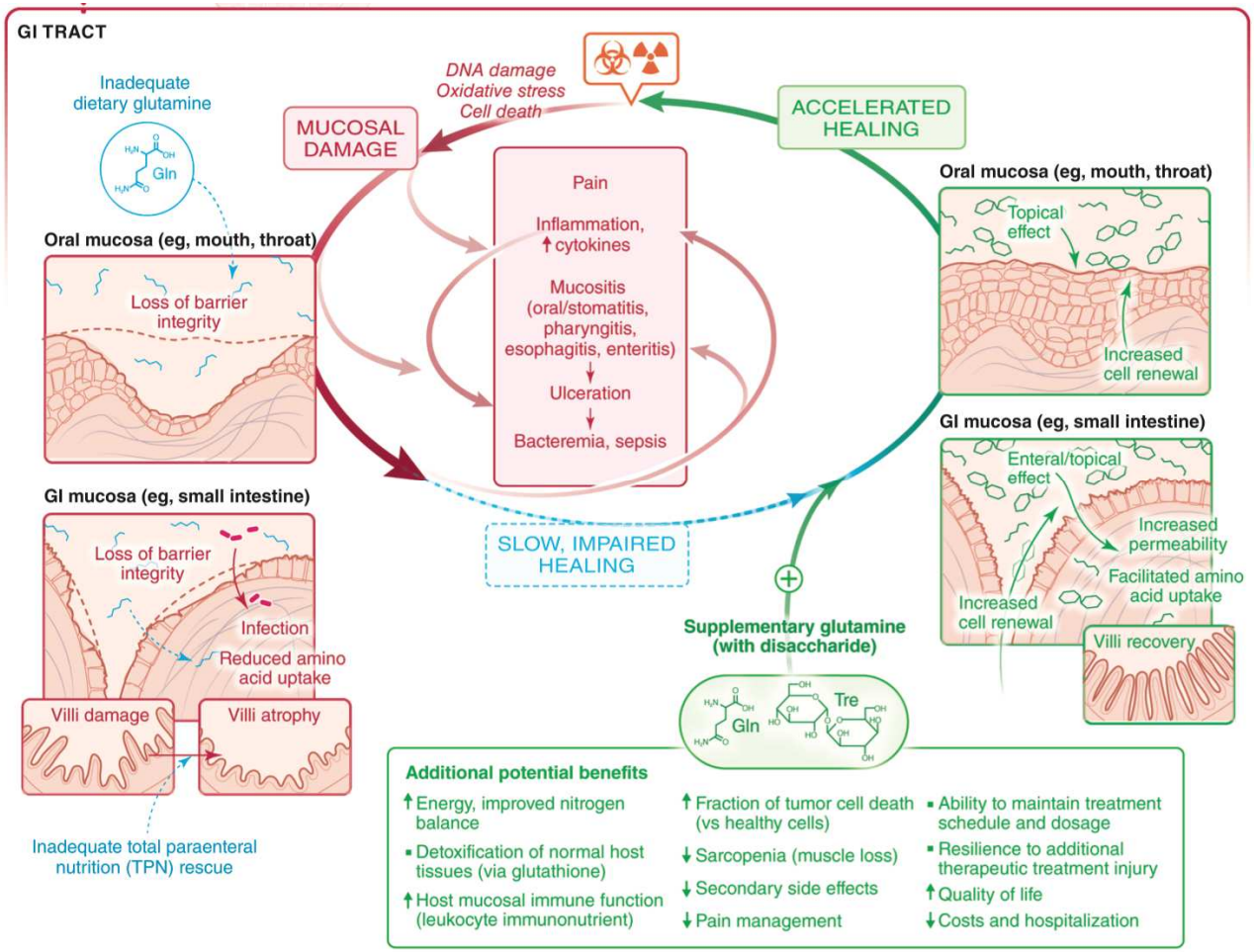
Detrimental consequences of glutamine depletion under catabolic stress



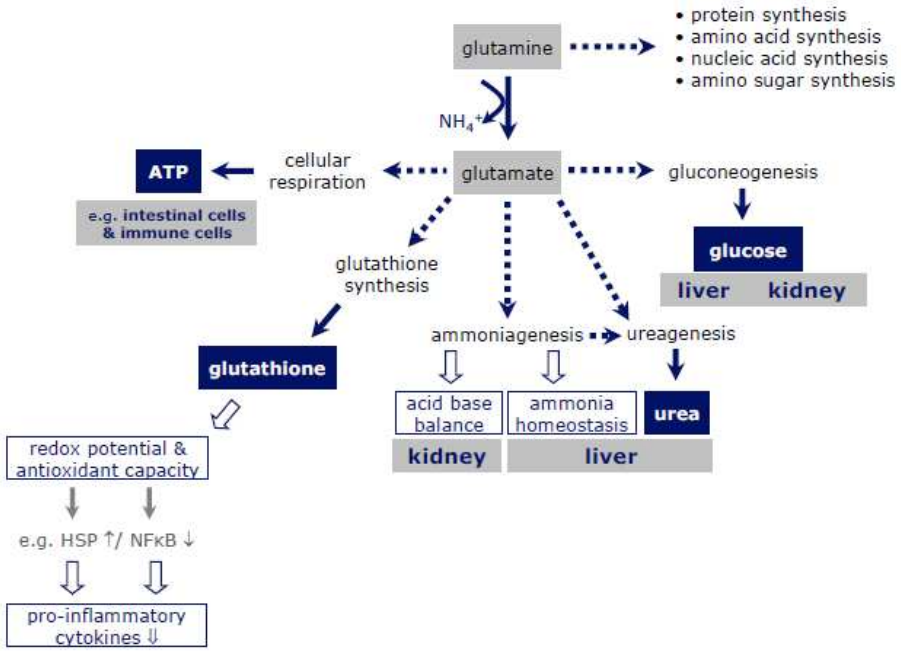


Peter M. Anderson et al. Nutrients 2020, 12, 1675

Glutamine Is Essential for Repair



Peter M. Anderson et al. Nutrients 2020, 12, 1675



麩醯胺 (glutamine) 的功能 (臨床益處)

- 修復黏膜組織 (口腔潰瘍)
- 維持腸胃道的完整性 (改善腹瀉)
- 強化免疫功能
- 降低感染發生率
- 促進細胞新生，加速傷口癒合
- 降低手術後的併發症
- 促進體內穀胱甘肽 (Glutathione) 的合成，減緩氧化壓力

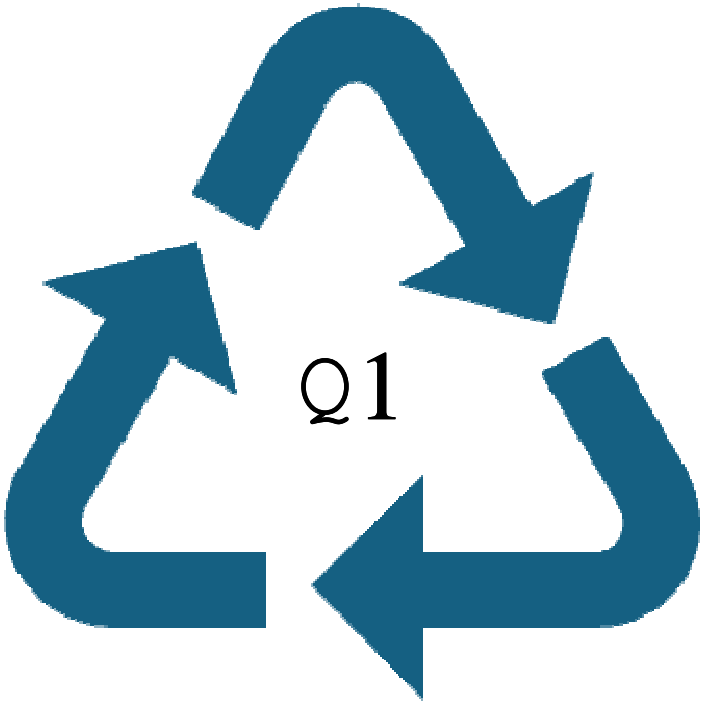
Glutamine 補充時機建議

在面對重大手術、化療、感染或外傷時，體內 glutamine 消耗迅速增加，而內源性合成速度無法即時補足

最快在24小時內，血漿 glutamine 即會下降

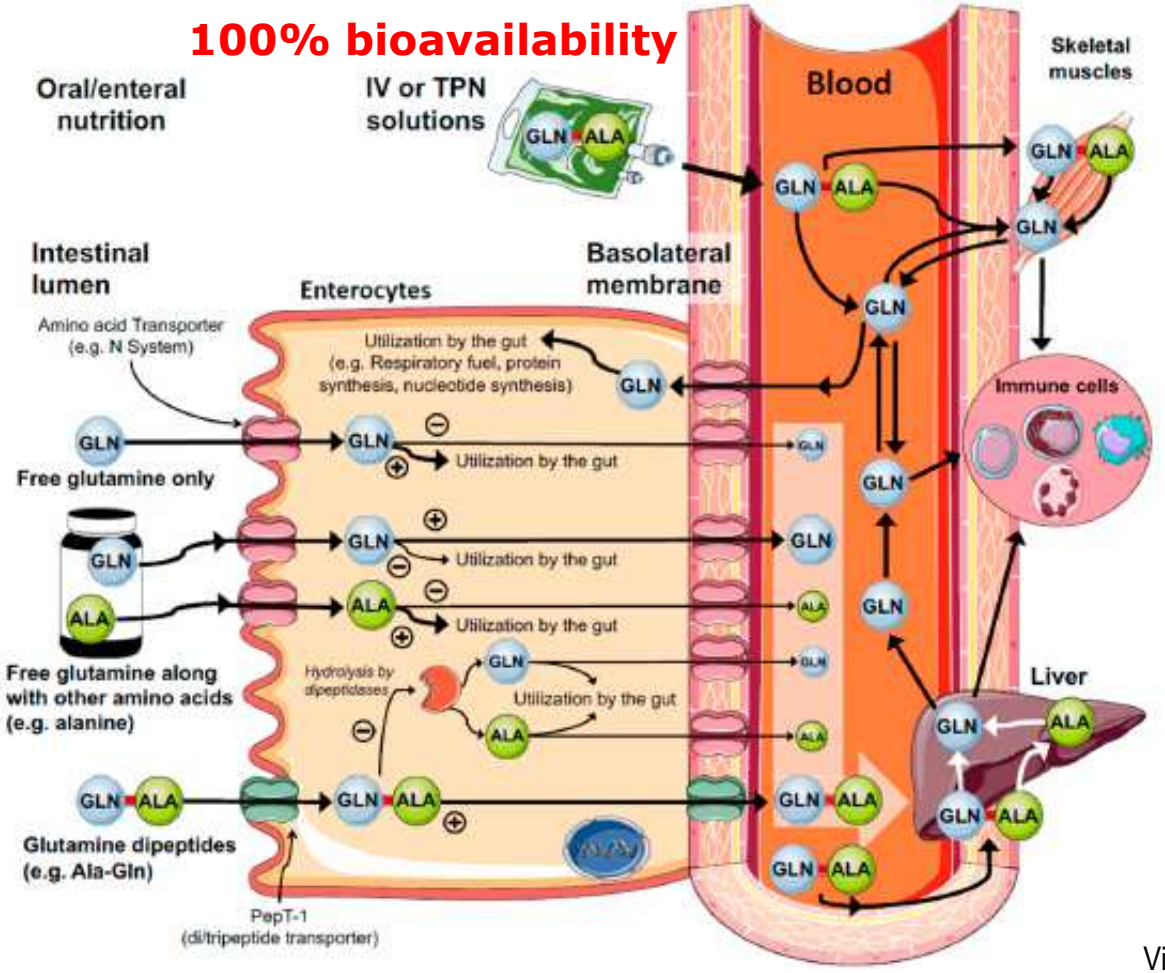
補充建議為 **早期、預防性、連續性**（通常連續補充數日到1-2週）

	建議補充時機	文獻依據或理由
重大手術或創傷後	24-48 小時內開始	Glutamine pool 在 24 小時內顯著下降；早期補充有助免疫、修復腸道屏障
化療或放療初期	治療開始前或當日	預防性補充可降低口腔炎、腹瀉等副作用
TPN（全靜脈營養）	同時添加 glutamine 補充劑	維持腸道與免疫細胞功能，避免肌肉分解



已經有在使用口服的glutamine，還需要使用靜脈注射的glutamine了？

Mechanisms of enteral and parenteral glutamine (GLN) supply



Vinicius Cruzat et al. Nutrients 2018, 10, 1564

IV glutamine increasing serum glutamine level than oral form

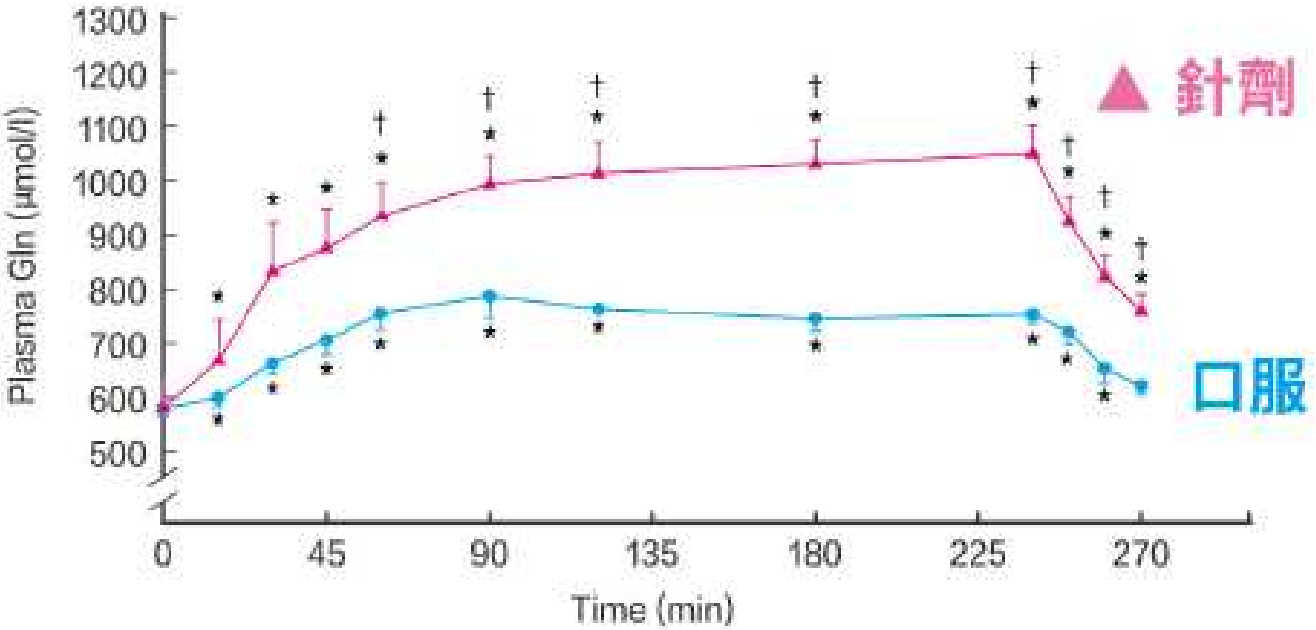


Fig. 2. Graphic illustration of plasma glutamine (Gln) response with parenteral (-▲-) or enteral (-●-) infusion of Ala-Gln. Mean value was significantly different from that at baseline (*$P<0.05$). Mean value for parenteral nutrition was significantly different from that for enteral nutrition (†$P<0.05$).[20]

British Journal of Nutrition (2005), 94, 19-26

Enteral vs. Parenteral Glutamine

	Parenteral(Dipeptiven)	Enteral
保險給付	醫療等級藥品類	屬營養食品
主成份	L-alanyl-L-glutamine, 經由靜脈給予入人體後,可快速完整的吸收	Glutamine
吸收率	100 %吸收	10-20 %
穩定性	穩定性良好,尤其在 1.高溫滅菌, 2.貯存時	不穩定 (亦受泡製之溶液溫度與攪拌速度影響)
Glutamine在腸道吸收的情形	Glutamine的量未受影響	Glutamine在肝臟代謝後加上腸道PH值影響, 腸道末端的黏膜細胞無法得到足夠Glutamine
經濟效益(每月)	1750X 5天=8750	9600X2/月=19200
在面臨疾病壓力下或受感染的病人 0.3~0.5g/kg/day	確保有較好的整體效果 (適合住院期間)完整足夠的補充	不足(適合居家保養)

The Clinical benefit of Dipeptiven

- Fatigue
- Mucositis
- Diarrhea
- Neuropathy
- Leukopenia

Fatigue

癌因性疲憊症之藥物治療

黃耆多醣注射劑有初步臨床試驗顯示可改善中重度癌因性疲憊症。 (Level IA, Grade A)	蔘類在臨床試驗顯示可以改善癌因性疲憊，但因中藥在使用上會因原料製備等影響，建議使用前應諮詢醫療團隊。 (Level IB, Grade B)
Methylphenidate 臨床研究顯示使用於疲憊程度或病情較嚴重的病人較具效果； 但在用藥前應審慎考量劑量、用藥時間、濫用風險、及病人個人疾病等臨床情形， 充分評估相關風險與效益。 (Level IA, Grade A)	Methylprednisolone、dexamethasone等類固醇藥物有臨床證據顯示可以改善癌症病人的疲憊和生活品質，但長期使用有安全風險， 故建議只用於癌症末期、合併疲憊與厭食症、或有腦部或骨骼轉移而疼痛的癌症病人。 (Level IB, Grade B)

Glutamine vs Cancer Fatigue

Clinical Nutrition 34 (2015) 1258–1265

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Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

Is glutamine deficiency the link between inflammation, malnutrition, and fatigue in cancer patients?☆

Marcus Schlemmer [a], Ulrich Suchner [b], Barbara Schäpers [c], Eva-Maria Duerr [a], Birgit Alteheld [d], Thomas Zwingers [e], Peter Stehle [d, *], Heinz-Gerd Zimmer [f]

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Serum glutamine vs Cancer Fatigue Scale (CSF)

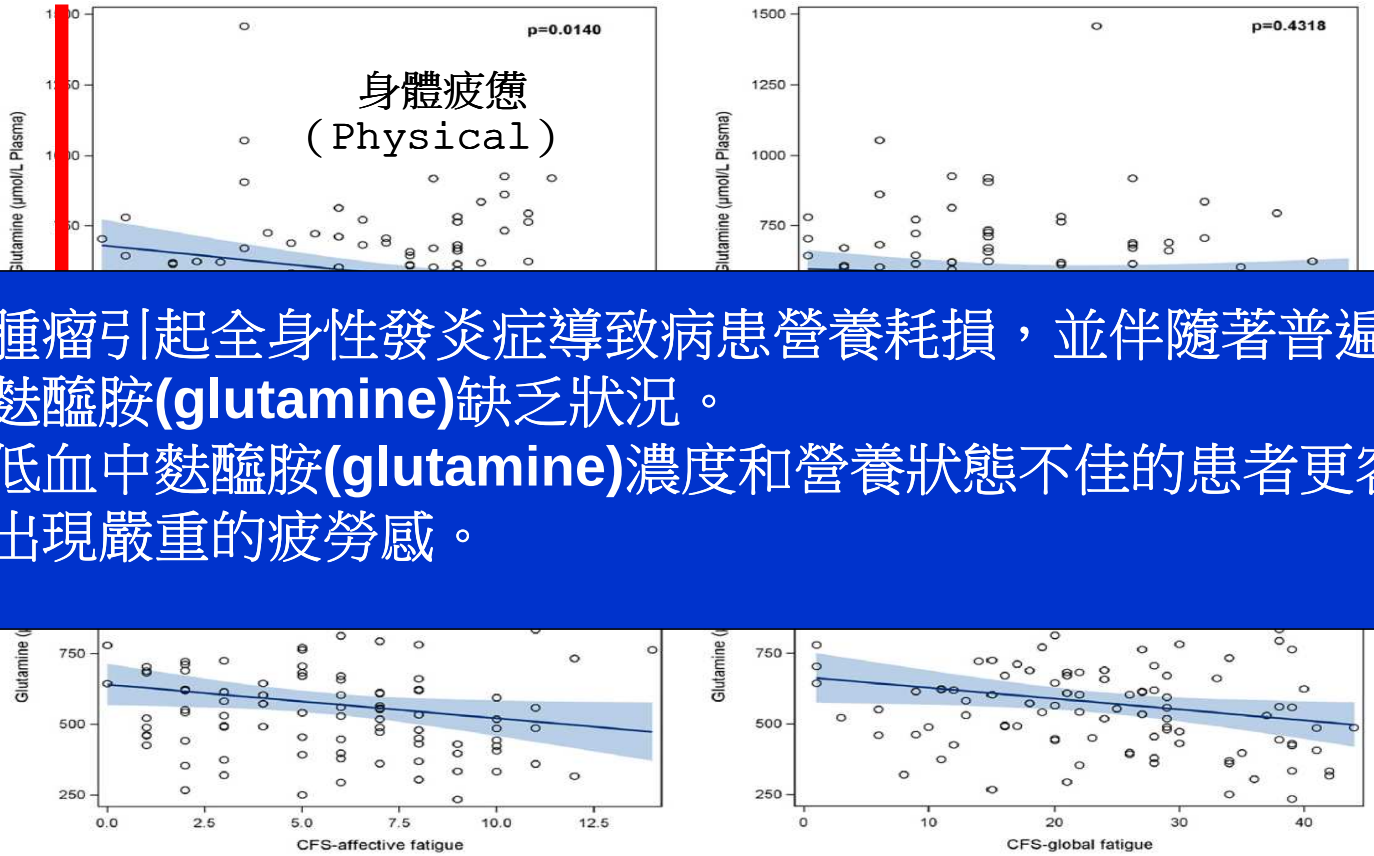

Fig. 3. Correlation between Cancer Fatigue Scale (CSF) including physical, affective, cognitive and global fatigue and the plasma levels of glutamine (µmol/l).

1. 腫瘤引起全身性發炎症導致病患營養耗損，並伴隨著普遍性麩醯胺**(glutamine)**缺乏狀況。
2. 低血中麩醯胺**(glutamine)**濃度和營養狀態不佳的患者更容易出現嚴重的疲勞感。

Serum glutamine level in TW colorectal cancer patients

Original Article

Relationship between pre-treatment nutritional status, serum glutamine, arginine levels and clinicopathological features in Taiwan colorectal cancer patients

Yi-Ping Pan BA[1], Pei-Hung Chang MD[2], Chung-Wei Fan MD[3], Wen-Ko Tseng MD[3], Jen-Seng Huang MD[2], Chih-Hung Chen MD[4], Wen-Chi Chou MD[5], Cheng-Hsu Wang MD, PhD[2], Kun-Yun Yeh MD, PhD[2]

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[4]*Division of Endocrinology and Metabolism, Department of Internal Medicine, Chang Gung Memorial Hospital, Keelung and Chang Gung University, College of Medicine, Taiwan*
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腫瘤引起全身性發炎症導致病患營養耗損，並伴隨著普遍性麩醯胺(glutamine)缺乏狀況，且腫瘤發展至愈晚期血中glutamine濃度愈低。

Table 1. Demographic and clinicopathologic data for 164 CRC patients

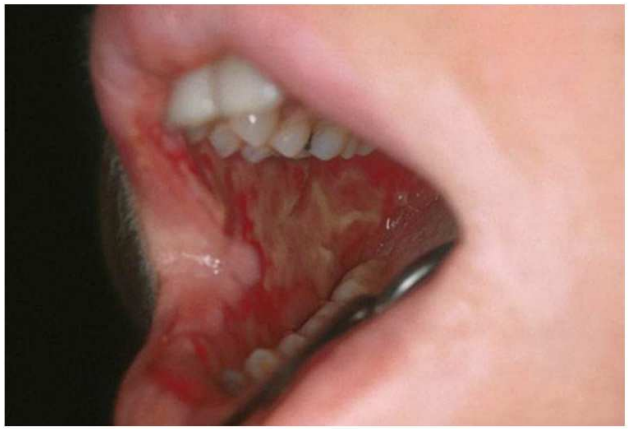
Variables expressed as number (%) or mean±SD	ALL	Stage I	Stage II	Stage III	Stage IV	*p* value*
Patient number (%)	164 (100)	37 (22.6)	45 (27.4)	56 (34.1)	26 (15.9)	
Sex						
Men	108 (65.9)	30 (81.1)	27 (60.0)	36 (64.3)	15 (57.7)	0.10
Women	56 (34.1)	7 (18.9)	18 (40.0)	20 (35.7)	11 (42.3)	
Age	64.9±13.7	62.8±10.5	67.6±15.8	64.1±13.9	65.0±13.5	0.42
Location						
Colon	109 (66.5)	29 (78.4)	34 (75.6)	32 (57.1)	14 (53.8)	0.05
Rectum	55 (33.5)	8 (21.6)	11 (24.4)	24 (42.9)	12 (46.2)	
Histologic grade differentiations						
1	50 (30.5)	19 (51.4)	14 (31.3)	12 (24.1)	5 (19.2)	0.02*
2	104 (63.4)	18 (48.6)	29 (64.4)	39 (69.6)	18 (69.2)	
3	10 (6.1)	0 (0)	2 (4.4)	5 (8.9)	3 (11.5)	
BH (cm)	161±8.8	162±9.3	159±8.3	162±8.2	161±9.9	0.41
BW before diagnosis (kg)†	61.8±11.2	63.8±11.8	60.8±11.6	62.0±10.2	60.1±11.7	0.55
BW at diagnosis (kg)	60.3±12.2	61.9±11.4	58.7±11.5	61.7±13.6	57.5±10.8	0.34
BMI before diagnosis (kg/m^2)†	23.9±3.9	24.3±3.6	23.9±4.6	24.0±3.4	23.2±4.1	0.77
BMI at diagnosis (kg/m^2)	24.4±14.1	23.5±3.5	23.3±4.6	26.8±23.5	22.2±3.5	0.46
WBC (cells/μL)	10,517±4,392	10,851±4,405	10,026±3,997	9,882±3,930	12,261±5,574	0.11
TLC (cells/mm^3)	1,424±733	1,618±850	1,399±369	1,434±721	1,174±696	0.13
Hb (g/dL)	12.0±1.9	12.5±2.2	11.5±1.9	12.2±1.9	11.9±1.3	0.08
Albumin (g/dL)	3.6±0.7	3.9±0.4	3.5±0.8	3.7±0.6	3.2±0.7	<0.0001*
CRP (mg/dL)	24.6±48.0	4.9±6.5	27.8±42.5	21.6±52.6	51.7±64.2	0.01*
AST (U/L)	27.6±22.9	26.7±6.7	27.3±13.8	23.1±9.2	40.9±55.2	0.04*
Glutamine (ng/mL)	94.6±121	123±134	105±130	96.2±119	29.9±53.1	0.04*
Arginine (ng/mL)	122±77.2	118±76.6	142±86.5	112±73.1	113±66.9	0.28
CEA (ng/mL)	1,425±733	2.3±2.1	6.0±9.8	7.9±10.9	298±1,313	0.08
Hospital stay after curative surgery (days)	19.2±17.6	13.5±7.8	18.9±13.2	23.1±23.6	NA	0.03*
3-year progression-free survival rate (%)	76.2	100	93.3	73.2	19.2	<0.001*

*p value was determined by ANOVA using Bonferroni adjustments (for age, BH, BW, BMI, WBC, TLC, Hb, albumin, CRP, AST, glutamine, arginine, CEA, and hospital stay) or chi-square test (for sex, stage, location, histologic differentiation, and progression-free survival rate) for multiple comparisons.
†BW or BMI of patients was obtained at 6 months before diagnosis.
AST: aspartate aminotransferase; BH: body height; BMI: body mass index; BW: body weight; CEA: carcinoembryonic antigen; CRC: colorectal cancer; CRP: C-reactive protein; Hb: hemoglobin; NA: not available; TLC: total lymphocyte count; WBC: white blood cell.

Stage↑ Albumin, Glutamine, Surrival rate↓, CRP↑

Mucositis

irinotecan, oxaliplatin, and 5-FU



Mucositis

Chemotherapy induced mucositis

Adverse event-	Grade 1	Grade 2	Grade 3	Grade 4
口腔黏膜炎	不痛或輕微疼痛	中度疼痛但不影響進食	嚴重疼痛而影響進食	危及生命
	傷口處理；按照標準化療評估與流程。(見附錄七)	傷口處理及止痛； 考慮調整劑量或更換藥物。(見附錄七)	傷口處理及止痛；營養支持; 建議停藥。(見附錄七)	傷口處理及止痛；營養支持; 建議停藥。(見附錄七)

Treatment: Morphine is the treatment of choice for pain control; cryotherapy or low level laser therapy was suggested for ulceration.

Chemotherapy-Induced Mucositis

類別	內容
基本口腔衛教	每日刷牙、漱口（如生理食鹽水或小蘇打水），避免刺激性食物
止痛	Topical: 2% viscous lidocaine, Benzydamine HClSystemic: Acetaminophen, Opioids (如 morphine mouthwash)
人工唾液/保濕劑	改善口腔乾燥，減緩疼痛
抗生素	若有二度感染：Chlorhexidine、nystatin 或 fluconazole
低能量雷射（LLLT）	可促進癒合與止痛，應用於高風險病人
Glutamine（口服或IV）	增加腸/黏膜細胞修復能力，減少 Grade ≥ 2 mucositis 發生率
冰療（Cryotherapy）	尤其在 5-FU、melphalan，治療期間口含冰塊可減少血流 → 減少毒性

DOUBLE-BLINDED, PLACEBO-CONTROLLED TRIAL ON INTRAVENOUS L-ALANYL-L-GLUTAMINE IN THE INCIDENCE OF ORAL MUCOSITIS FOLLOWING CHEMORADIOTHERAPY IN PATIENTS WITH HEAD-AND-NECK CANCER

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MARIBEL A. LUTTERAL, M.D.,† MONICA A. CASTRO, M.D.,* RICARDO KIRCHUK, M.D.,†
MARCELO BONOMI, M.D.,*‡ MARIA ESTHER CABALAR, M.D.,† BERTA ROTH, M.D.,‡
GRACIELA NEGRETTI, PHARM.D.,§ BEATRIZ SHEINKER, PHARM.D.,§ AND PATRICIA UCHIMA, PHARM.D.§

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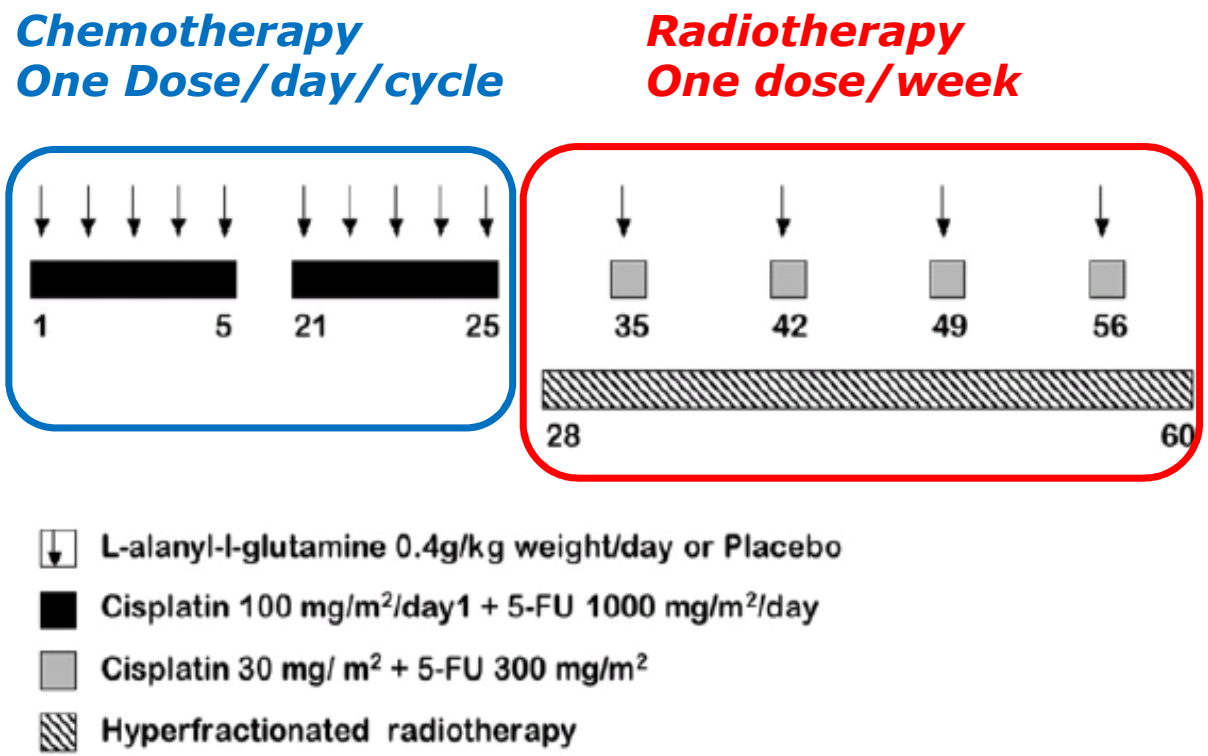
Purpose: We performed this double-blinded, placebo-controlled study to determine the safety and efficacy of L-alanyl-L-glutamine in the prevention of mucositis in patients with head-and-neck cancer.
Methods and Materials: Thirty-two patients with head-and-neck cancer were treated with chemoradiotherapy (CRT) (radiotherapy daily up to 70 Gy plus cisplatin/5-fluoruracil once a week) and were asked to participate. Twenty-nine patients received the CRT schedule and were double-blindly assigned to receive either intravenous L-alanyl-L-glutamine 0.4 g/kg weight/day or an equal volume of saline (placebo) during chemotherapy days.
Results: Fourteen patients received L-alanyl-L-glutamine and 15 received placebo. Mucositis was assessed by the Objective Mucositis Score (OMS) and the World Health Organization (WHO) grading system. There was a significant difference in incidence of mucositis developed in patients receiving placebo compared with those who received L-alanyl-L-glutamine ($p = 0.035$). The number of patients with severe objective mucositis (OMS >1.49) was higher in the placebo group compared with the L-alanyl-L-glutamine group (67% vs. 14%, $p = 0.007$). L-alanyl-L-glutamine patients experienced less pain (three highest Numeric Rating Scale scores of 1.3/10 vs. 6.3/10 respectively, $p = 0.008$) and need for feeding tubes (14% vs. 60% respectively, $p = 0.020$) compared with placebo patients. No adverse effects related to the drug or the infusions were noted in either group.
Conclusion: For patients with head-and-neck cancer receiving CRT, intravenous L-alanyl-L-glutamine may be an effective preventive measure to decrease the severity of mucositis.

Int. J. Radiation Oncology Biol. Phys., Vol. 65, No. 5, pp. 1330–1337, 2006

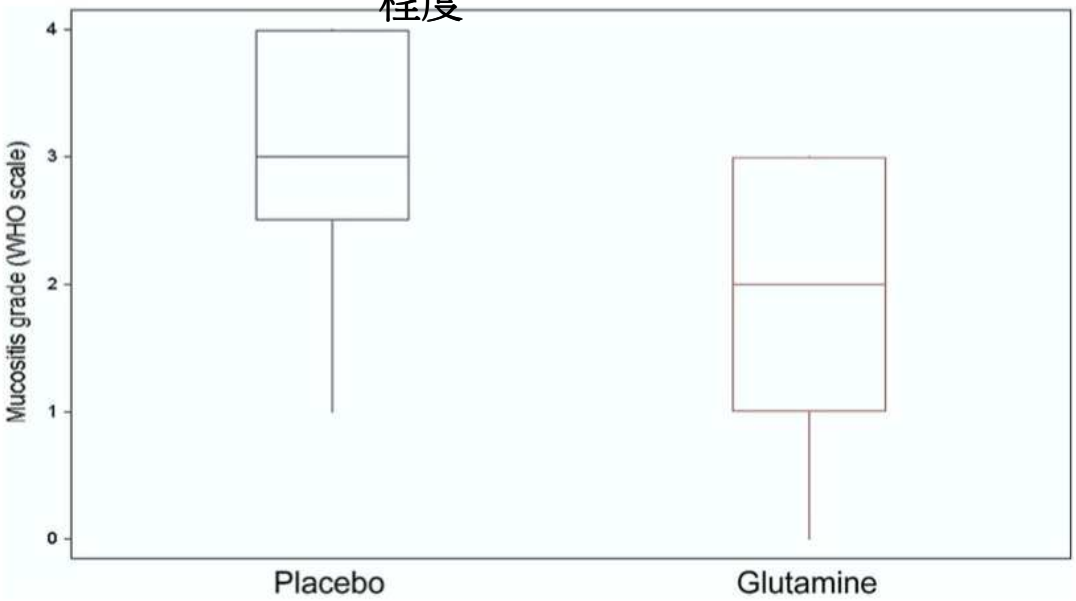
Schedule of the antineoplastic and intervention treatments



Int. J. Radiation Oncology Biol. Phys., Vol. 65, No. 5, pp. 1330–1337, 2006

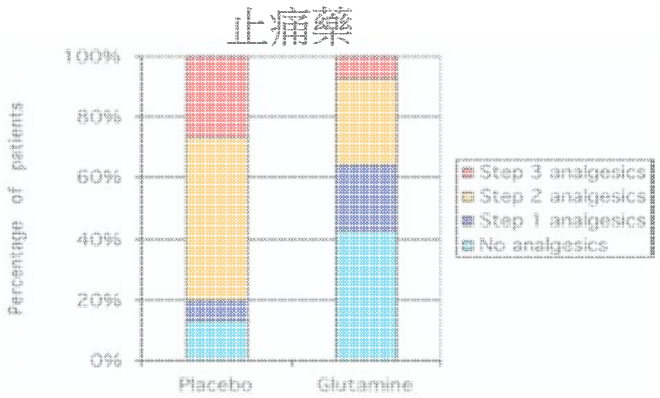
Mucositis & Pain Intensity

mucositis 嚴重程度



疼痛指數

止痛藥



Int. J. Radiation Oncology Biol. Phys., Vol. 65, No. 5, pp. 1330–1337, 2006

Effect of glutamine and free of severe mucositis

Table 2. Effect of glutamine on several outcomes

Endpoint	Placebo (n = 15)	Glutamine (n = 14)	p value
Intensity of objective mucositis developed (mean 3 highest OMS)	1.33 (± 0.4)	0.82 (± 0.3)	0.044†
Patients with severe objective mucositis (OMS >1.49)	10 (67%)	2 (14%)	0.007‡
Patients with mucositis WHO Grade 4*	5 (33%)	0 (0%)	0.042‡
Need for feeding tube	9 (60%)	2 (14%)	0.020‡
Body weight change, kg (mean)	−5.77 (± 2.2)	−3.3 (± 2.6)	NS§
Hospital admission due to severe mucositis	5 (33%)	1 (7%)	NS‡

Abbreviations: OMS = Objective Mucositis Score; WHO = World Health Organization.
* Oral alimentation not possible.
† Wilcoxon rank sum test.
‡ Fisher exact test.
§ t test.

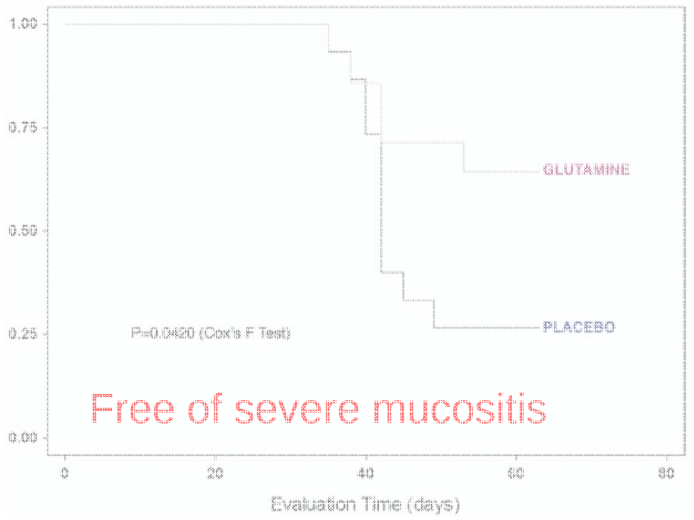


Fig. 6. Patients free of severe mucositis (World Health Organization score ≥3) (Kaplan-Meier survival curve).

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CLINICAL REVIEW

Glutamine for prevention and alleviation of radiation-induced oral mucositis in patients with head and neck squamous cell cancer: A systematic review and meta-analysis of controlled trials

Head & Neck. 2021;1-15.

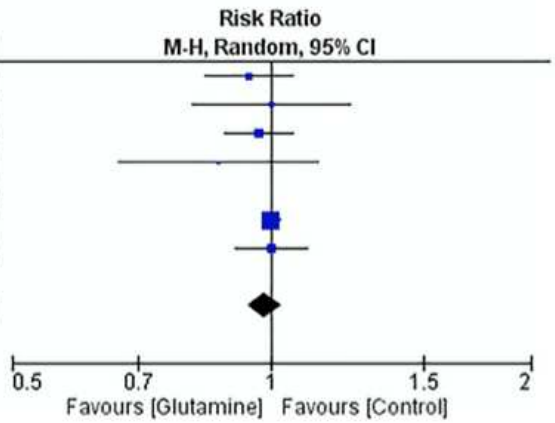
Any Grade mucositis

(B)

Study or Subgroup	Glutamine Events	Glutamine Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chattopadhyay 2014	32	35	34	35	12.1%	0.94 [0.84, 1.06]
Huang 2000	8	8	9	9	4.3%	1.00 [0.81, 1.24]
Huang 2019	29	30	29	29	17.1%	0.97 [0.88, 1.06]
Lopez-Vaquero 2017	19	25	21	24	2.8%	0.87 [0.66, 1.13]
Pachon Ibanze 2018	66	131	78	131		Not estimable
Pattanayak 2007	81	81	81	81	47.3%	1.00 [0.98, 1.02]
Tsujimoto 2015	20	20	20	20	16.5%	1.00 [0.91, 1.10]
Total (95% CI)		**199**		**198**	**100.0%**	**0.98 [0.94, 1.03]**
Total events	189		194			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 7.37$, $df = 5$ ($p = 0.19$); $I^2 = 32\%$

Test for overall effect: $Z = 0.72$ ($p = 0.47$)



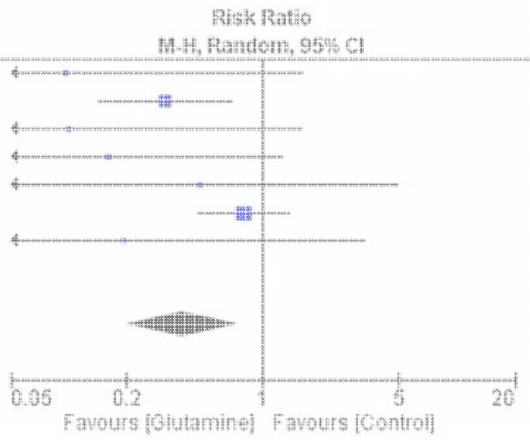
Grade 3-4 mucositis

(B)

Study or Subgroup	Glutamine Events	Glutamine Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Cerchietti 2006	0	14	5	15	5.0%	0.10 [0.01, 1.61]
Chattopadhyay 2014	6	35	19	35	30.1%	0.32 [0.14, 0.70]
Huang 2000	0	8	5	9	5.2%	0.10 [0.01, 1.58]
Huang 2019	1	30	6	29	8.7%	0.16 [0.02, 1.26]
Lopez-Vaquero 2017	1	25	2	24	7.0%	0.48 [0.05, 4.95]
Pachon Ibanze 2018	20	131	25	131	39.2%	0.80 [0.47, 1.37]
Sarumathy 2012	0	11	3	15	4.8%	0.19 [0.01, 3.35]
Tsujimoto 2015	19	20	20	20	0.0%	0.90 [0.76, 1.07]
Total (95% CI)		254		258	100.0%	0.38 [0.20, 0.74]
Total events	28		65			

Heterogeneity: $Tau^2 = 0.22$; $Chi^2 = 8.79$, $df = 6$ ($p = 0.19$); $I^2 = 32\%$

Test for overall effect: $Z = 2.85$ ($p = 0.004$)



Duration of Maximal Grade

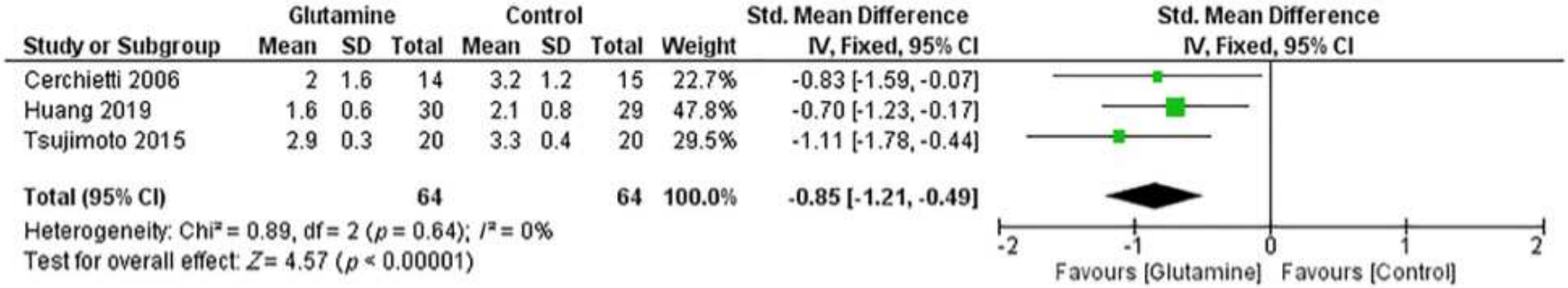


FIGURE 5 Forest plot showing the pooled standardized mean difference of the maximal grade of radiation-induced oral mucositis between glutamine and control groups [Color figure can be viewed at wileyonlinelibrary.com]

Duration of Grade 3-4

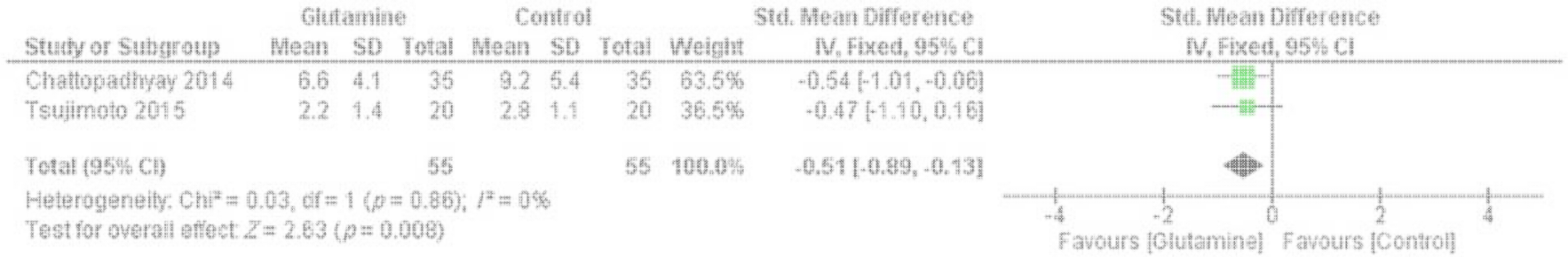


FIGURE 6 Forest plot showing the pooled standardized mean difference of the duration of severe (≥grade 3) radiation-induced oral mucositis sensitivity between glutamine and control groups [Color figure can be viewed at wileyonlinelibrary.com]

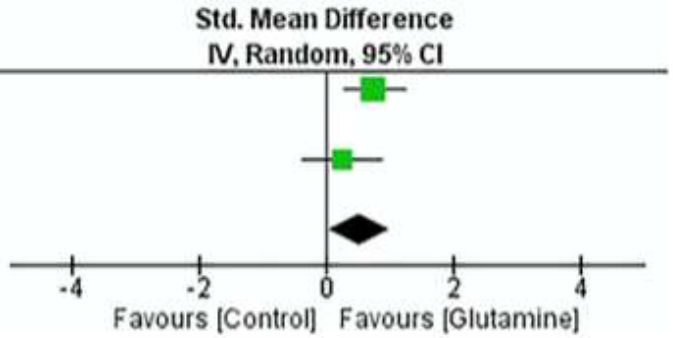
Onset of Mucositis

(B)

Study or Subgroup	Glutamine Mean	Glutamine SD	Glutamine Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Chattopadhyay 2014	16.5	13.6	35	7.1	11.2	35	57.9%	0.75 [0.26, 1.23]
Diwan 2018	32.68	4.61	30	17.06	3.47	30	0.0%	3.78 [2.92, 4.64]
Tsujimoto 2015	2.3	0.8	20	2.1	0.8	20	42.1%	0.25 [-0.38, 0.87]
Total (95% CI)			**55**			**55**	**100.0%**	**0.53 [0.05, 1.02]**

Heterogeneity: Tau² = 0.04; Chi² = 1.55, df = 1 (p = 0.21); I^2 = 35%

Test for overall effect: Z = 2.16 (p = 0.03)



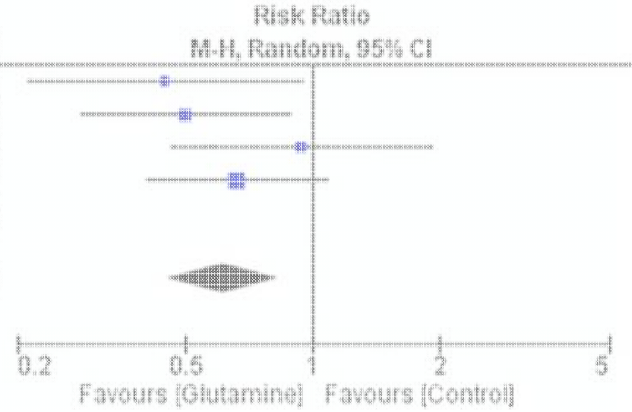
Opioid Use

(B)

Study or Subgroup	Glutamine Events	Glutamine Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Cerchietti 2006	5	14	12	15	16.1%	0.45 [0.21, 0.94]
Diwan 2018	10	30	20	30	28.1%	0.50 [0.28, 0.88]
Huang 2000	5	8	6	9	17.9%	0.94 [0.46, 1.90]
Huang 2019	13	30	19	29	37.9%	0.66 [0.41, 1.08]
Tsujimoto 2015	17	20	19	20	0.0%	0.89 [0.73, 1.10]
Total (95% CI)		82		83	100.0%	0.61 [0.45, 0.82]
Total events	33		57			

Heterogeneity: Tau² = 0.00; Chi² = 2.73, df = 3 (p = 0.44); I^2 = 0%

Test for overall effect: Z = 3.22 (p = 0.001)



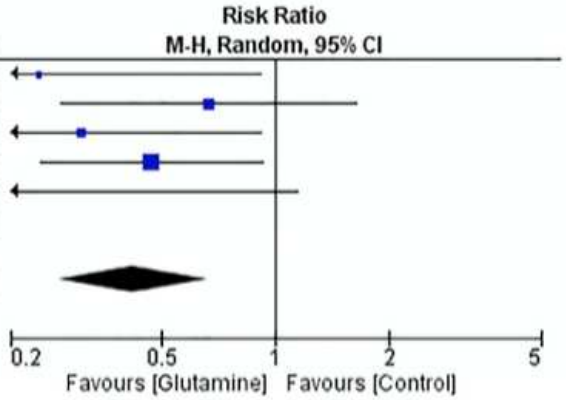
NG Feeding

(B)

Study or Subgroup	Glutamine Events	Glutamine Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Cerchietti 2006	2	14	9	15	11.1%	0.24 [0.06, 0.92]
Diwan 2018	6	30	9	30	24.9%	0.67 [0.27, 1.64]
Pachon Ibanze 2018	4	131	13	131	16.9%	0.31 [0.10, 0.92]
Pathak 2019	8	30	17	30	44.6%	0.47 [0.24, 0.92]
Pattanayak 2007	0	81	7	81	2.5%	0.07 [0.00, 1.15]
Tsujimoto 2015	16	20	19	20	0.0%	0.84 [0.66, 1.07]
Total (95% CI)		**286**		**287**	**100.0%**	**0.42 [0.27, 0.66]**
Total events	20		55			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 4.01$, $df = 4$ ($p = 0.40$); $I^2 = 0\%$

Test for overall effect: $Z = 3.76$ ($p = 0.0002$)

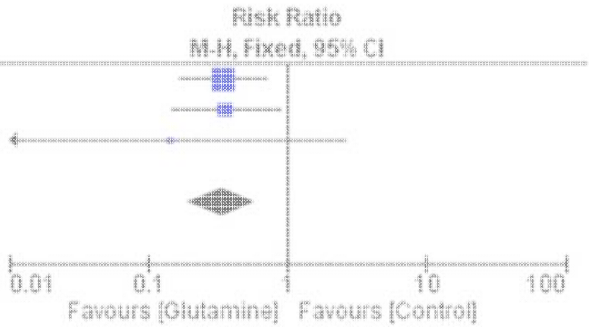


Treatment Interruption

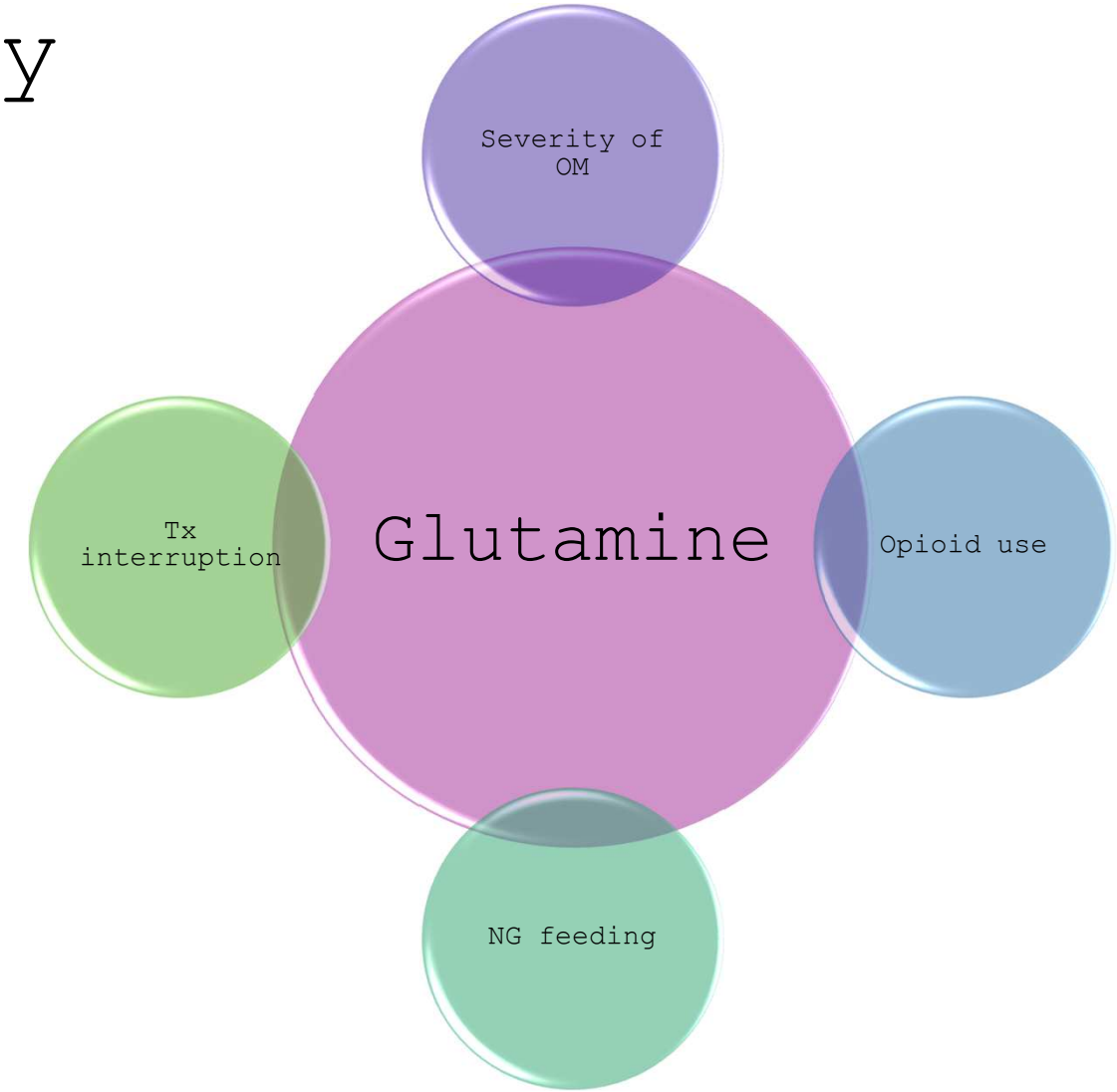
Study or Subgroup	Glutamine Events	Glutamine Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Pachon Ibanze 2018	9	131	26	131	59.8%	0.35 [0.17, 0.71]
Pathak 2019	5	30	14	30	32.2%	0.36 [0.15, 0.87]
Tsujimoto 2015	0	20	3	20	8.0%	0.14 [0.01, 2.60]
Total (95% CI)		**181**		**181**	**100.0%**	**0.33 [0.19, 0.58]**
Total events	14		43			

Heterogeneity: $Chi^2 = 0.36$, $df = 2$ ($p = 0.83$); $I^2 = 0\%$

Test for overall effect: $Z = 3.92$ ($p < 0.0001$)

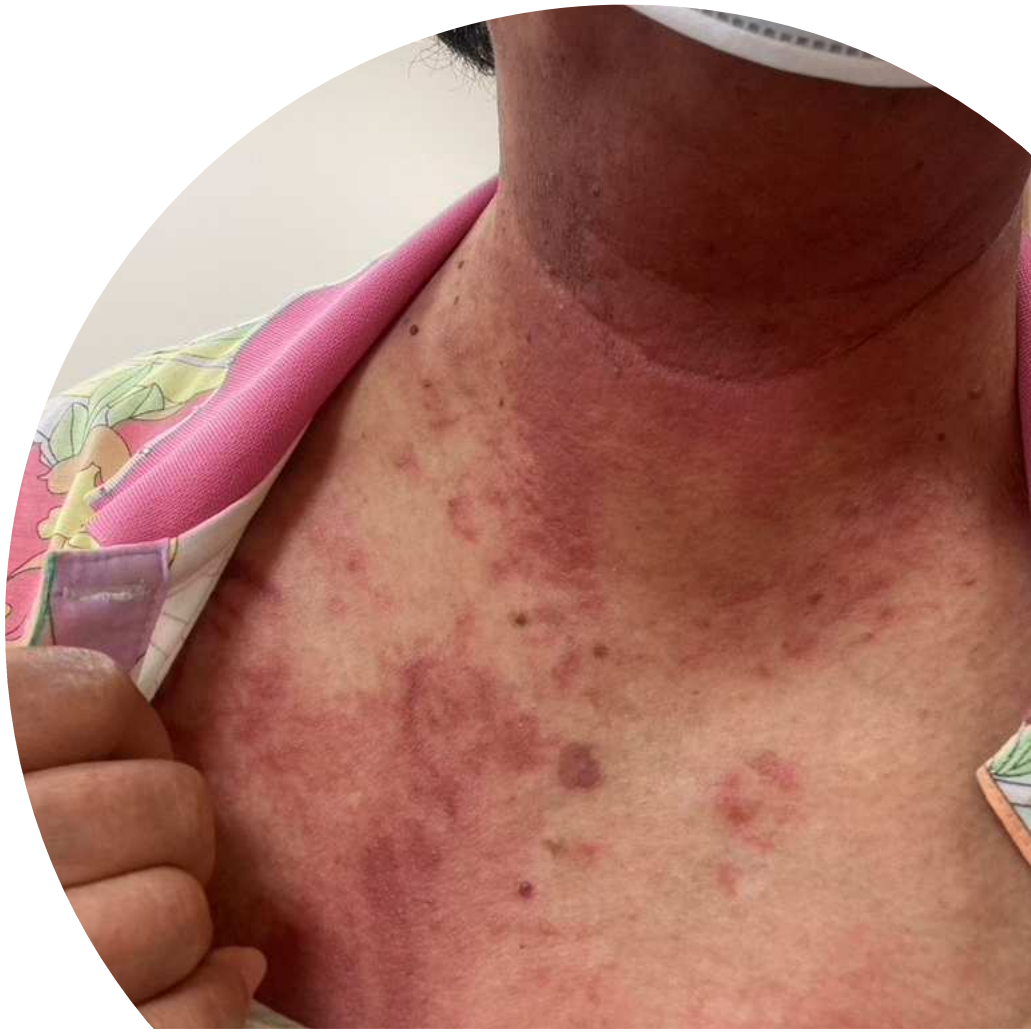


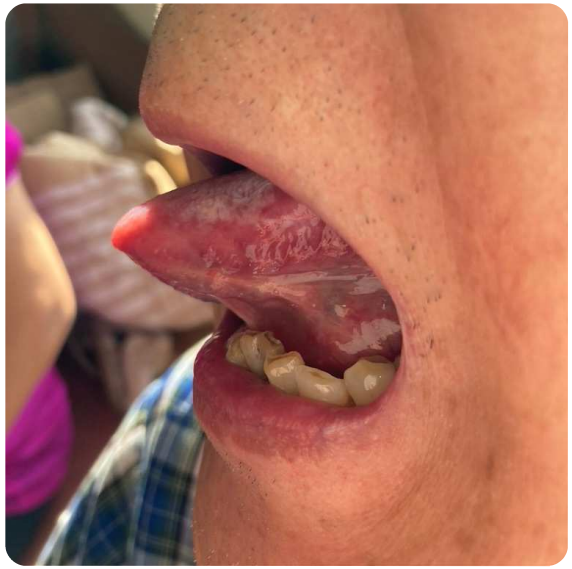
Summary

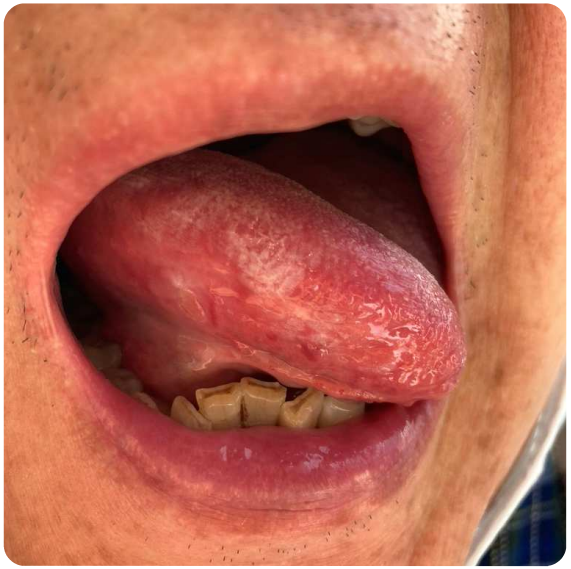

Severity of OM
Tx interruption
Glutamine
Opioid use
NG feeding

翁ＯＯ, 74F, cholangiocarcinoma, rycT1N0M1
-治療中使用Dipeptiven

- Recurrent of cholangiocarcinoma with lung metastesis, rycT1N0M1,STAGE：4
- Start Nivolumab/Gemzar/TS-1 since 2023/5/13
- Hold TS-1 on 2023/5/19 due to gr. 3 mucositis and skin eruption
- Restart C/T with NGS since 2023/5/30 with dipeptiven
- Gr.1 mucositis was noted since C2







洪ＯＯ/68M, Pancreatic cancer, pT2N0M0, stage 1 - 治療中使用 Dipeptiven

Pancreatic head ductal adenocarcinoma, grade 2, pT2N0M0, STAGE：1B

single-incision laparoscopic pancreatoduodenectomy on 2022/8/29

Adjunvant Chemotherapy with SLOG since 2022/11/2

Gr.2 mucositis after cycle 1 chemotherapy

No mucositis development after C2 with dipeptiven

Complete 12 cycles SLOG on 2023/4/13

Diarrhea


Managing Physical Side Effects:
Diarrhea
Cancer.Net
Doctor-Approved Patient Information from ASCO®

Chemotherapy induced diarrhea

Adverse event-	Grade 1	Grade 2	Grade 3	Grade 4
腹瀉	每天比正常多 **1~3次/24h**	每天比正常多 **4~6次/24h**	每天比正常多**7**次以上或肛失禁或其他症狀。	危及生命
	查找其他症狀;藥物治療;營養支持;協助病人緩解症狀。 (見附錄六)	查找其他症狀;藥物治療;營養支持;協助病人緩解症狀。 (見附錄六)	評估體重及尿量; 營養支持;建議停藥。 (見附錄六)	評估體重及尿量; 營養支持;建議停藥。 (見附錄六)

All patients with severe (grade 3 or 4) diarrhea are considered complicated. Patients with mild to moderate diarrhea (grade 1 or 2) with one or more complicating factors also are considered complicated (Cherny, 2008; Richardson & Dobish, 2007).

Chemotherapy-Induced Diarrhea (CID)

- 常見原因：
  - 藥物相關：5-FU, Capecitabine, Irinotecan（尤其 SN-38 代謝產物）
- 機轉：
  - 小腸上皮細胞破壞 → 黏膜屏障受損
  - 消化不良/腸道菌叢失衡
  - 胃腸排空加快 + 水分重吸收下降

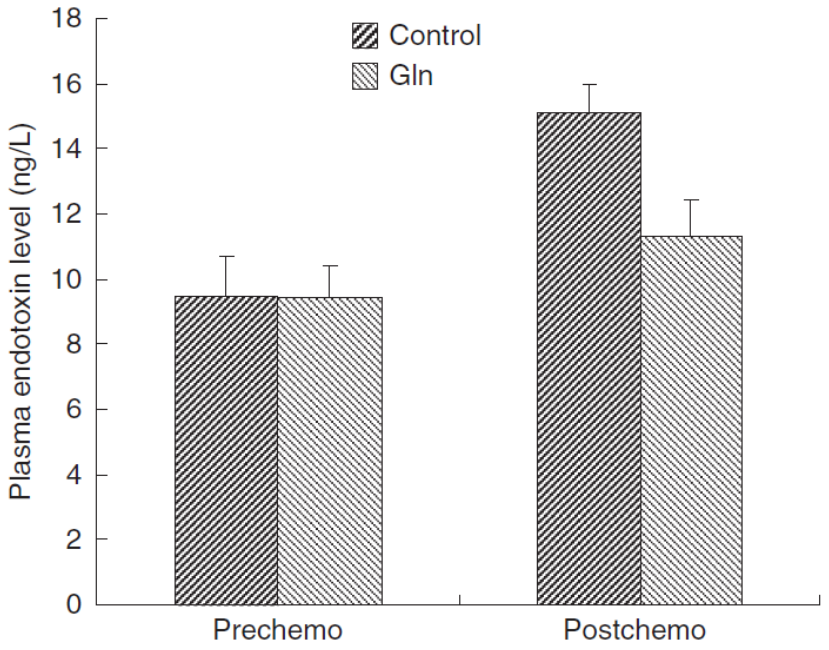
Dipeptiven® ?

治療類別	常用藥物/措施
一線： 止瀉劑	◆ Loperamide（Imodium®）：首選 – 起始 4 mg，之後每 4 小時 2 mg，最高一天 16-24 mg ◆ Diphenoxylate/Atropine（Lomotil）也可考慮
二線： Octreotide	對於 refractary diarrhea：起始 100-150 mcg SC，每 8 小時（或持續輸注）
水電解質補充	生理食鹽水、乳酸林格氏液；必要時靜脈補鉀
暫停化療	若 Grade ≥3，應暫停化療並進行 supportive care
飲食支持	清淡易消化、低渣飲食、避免乳糖、咖啡、辛辣食物
感染排除	若超過48小時未緩解，建議檢驗 Clostridium difficile、糞便培養等

Dipeptiven® Reduces GI Toxicity in Chemotherapy

- **44 gastric or colorectal cancer patients undergoing C/T**
- **Receiving 20 g of Dipeptiven®**
  - **Lower plasma endotoxin levels**
  - **Less severe GI adverse effects**

Control (n=22)	DIPEPTIVEN® (n=22)	P VALUE
Scale of Nausea/Vomiting		
2.63 ± 0.21	**1.18 ± 0.31**	< 0.05
Scale of Diarrhea		
2.82 ± 0.34	**1.31 ± 0.25**	< 0.05



Comparison of plasma endotoxin levels

Li Y et al. Aliment Pharmacol Ther 2009; 30:452-8.

medicina

MDPI

Article

Ameliorative Potential of L-Alanyl L-Glutamine Dipeptide in Colon Cancer Patients Receiving Modified FOLFOX-6 Regarding the Incidence of Diarrhea, the Treatment Response, and Patients' Survival: A Randomized Controlled Trial

Nesreen M. Sabry [1], Tamer M. Naguib [2], Ahmed M. Kabel [3,*], El-Sayed Khafagy [4,5], Hany H. Arab [6] and Walid A. Almorsy [1]

Table 3. The incidence of diarrhea in the studied groups.

	Glutamine Group (n=22)	Placebo Group (n=22)	p-Value
After Two Cycles			
No diarrhea	12 (54.55%)	8 (36.36%)	
Grade 1	8 (36.36%)	5 (22.73%)	0.066
Grade 2	2 (9.09%)	7 (31.82%)	
Grade 3	0 (0%)	2 (9.09%)	
After Four Cycles			
No diarrhea	8 (36.36%)	1 (4.55%)	
Grade 1	11 (50%)	2 (9.09%)	
Grade 2	2 (9.09%)	11 (50%)	<0.001*
Grade 3	1 (4.55%)	8 (36.36%)	
After Six Cycles			
No diarrhea	12 (54.55%)	1 (4.55%)	
Grade 1	6 (27.27%)	3 (13.6%)	
Grade 2	4 (18.18%)	9 (40.91%)	<0.001*
Grade 3	0 (0%)	5 (22.73%)	
Grade 4	0 (0%)	4 (18.18%)	

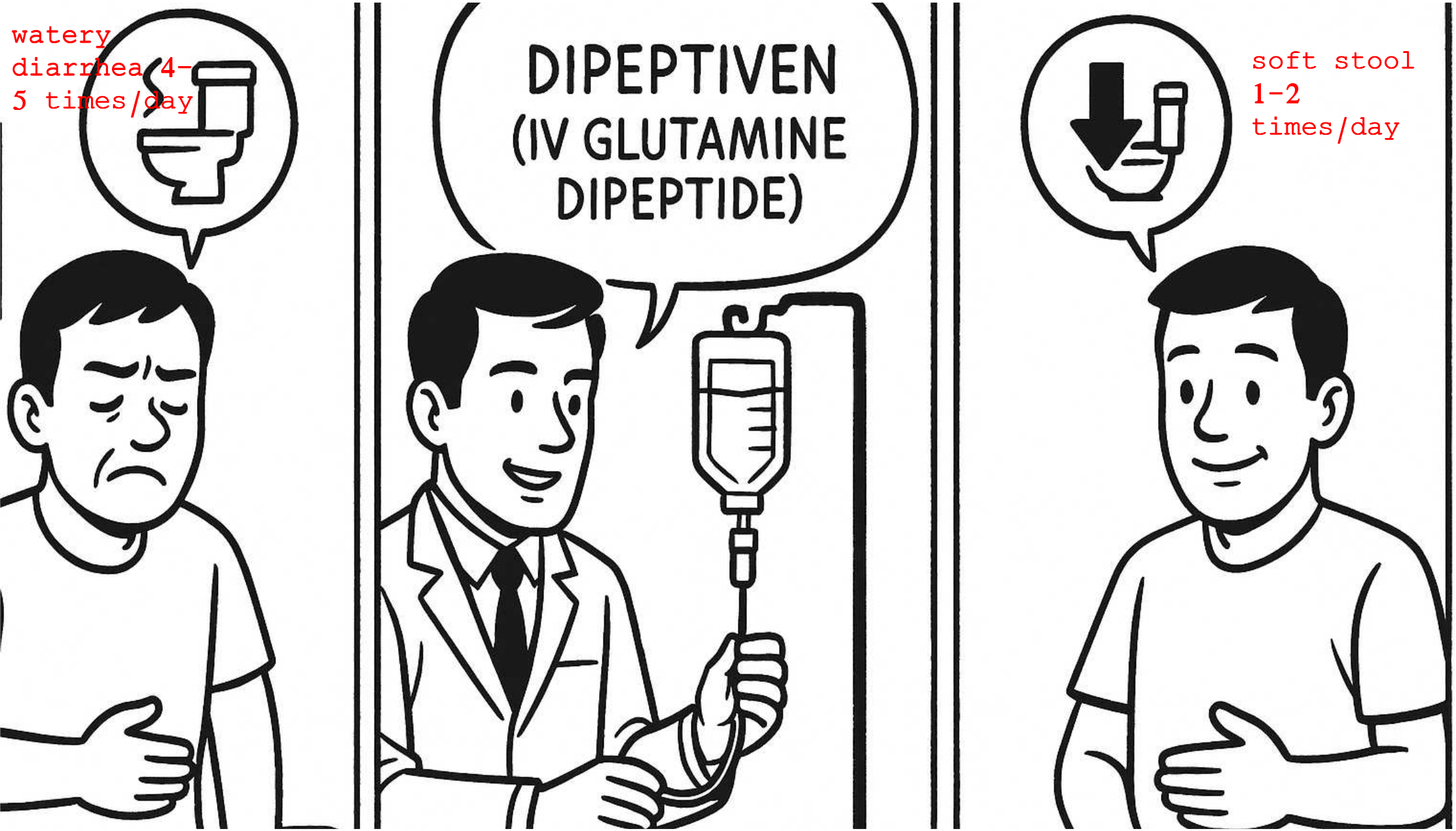
Data are presented as frequency (%), *: significant as p-value ≤ 0.05.

Patient Profile

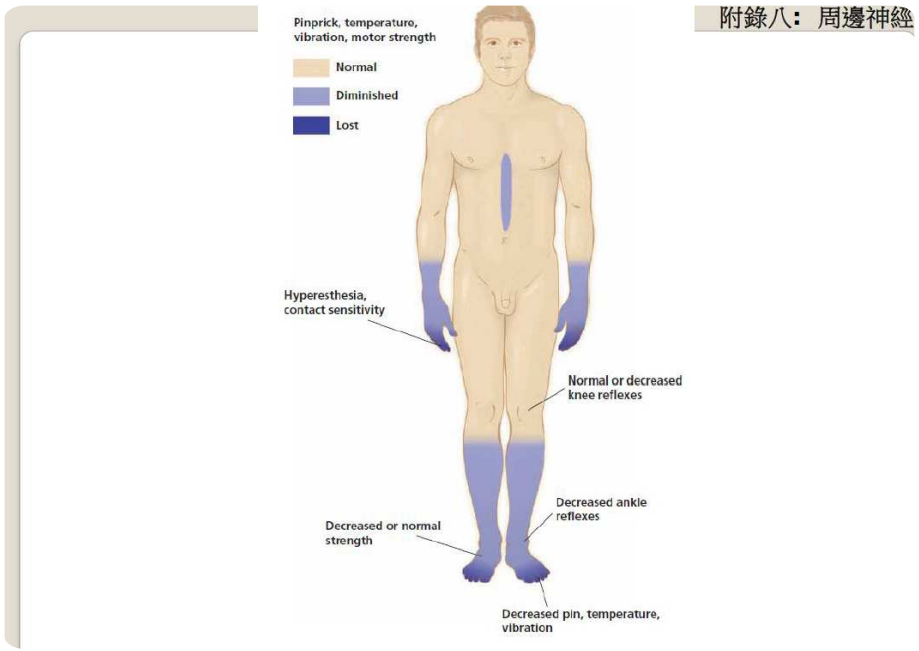
- Age/Sex: 58M
- Diagnosis: Pancreatic ductal adenocarcinoma, grade 2 (pT2N0, stage IB)
- Past procedures:
  - Whipple procedure + left venous port implantation on 2024/08/13
  - History of recurrent acute pancreatitis (grade C) and duodenal shallow ulcer
  - No surgical complications

Adjuvant Chemotherapy

- Gem/TS-1/oxaliplatin(SLOG) from 2024/9/23 to to 2025/3/6 with dipeptiven use before chemotherapy
- 2025/3/7 CT: suspicious soft tissue/infiltration around anastomosis/SMA region (possible PD).
- Tumor marker CA19-9: 1516 → 401 → 1300
- Subsequent Therapy
  - Onivyde (irinotecan微脂體注射劑) + 5-FU
    - C1 on 4/14
    - -> 4/24 OPD: watery diarrhea > 10 times per day
    - C2 on 5/6, -> add atropine, catilon (Otilonium bromide), imolex (Loperamide)
    - -> mild improving, but still watery diarrhea 4-5 times per day
    - C3 on 5/23 with pre-medications including atropine (0.25 amp) to reduce cholinergic symptoms, adding Dipeptiven


watery diarrhea 4-5 times/day
DIPEPTIVEN (IV GLUTAMINE DIPEPTIDE)
soft stool 1-2 times/day

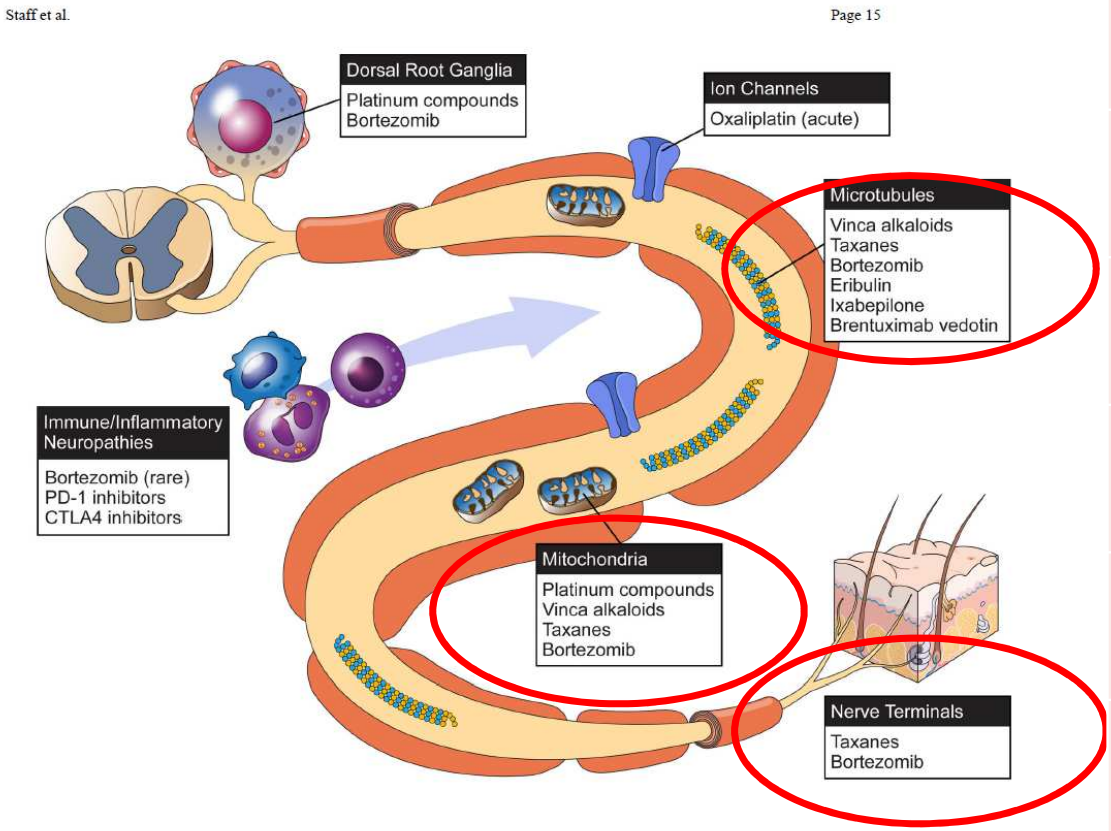
Neuropathy


附錄八：周邊神經
Pinprick, temperature, vibration, motor strength
Normal
Diminished
Lost
Hyperesthesia, contact sensitivity
Normal or decreased knee reflexes
Decreased ankle reflexes
Decreased or normal strength
Decreased pin, temperature, vibration

Chemotherapy induced peripheral neuropathy (CIPN)

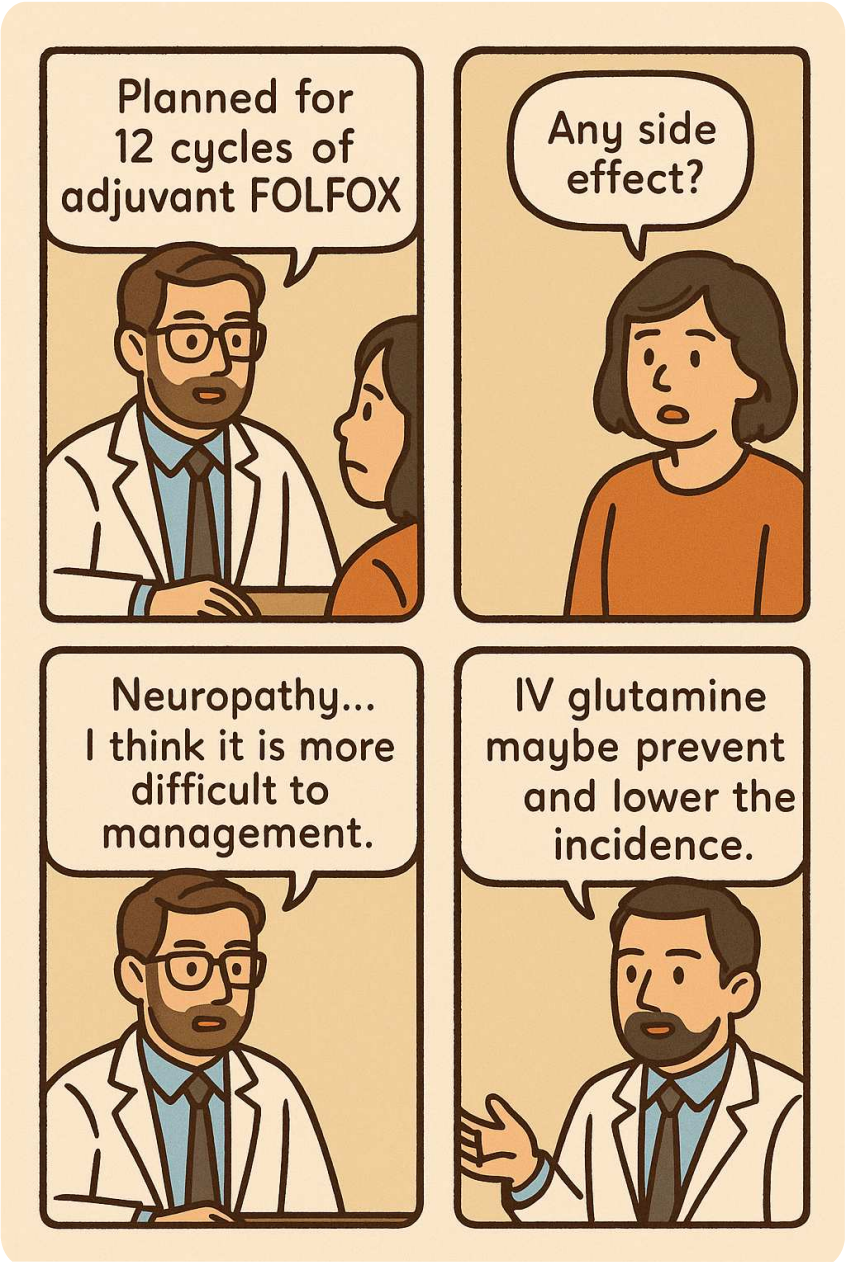
Adverse event-	Grade 1	Grade 2	Grade 3	Grade 4
周邊神經病變	輕微的感覺異常；深部肌腱反射損失	中度症狀致日常；深部肌腱反射消失;生活有困難	嚴重症狀影響自我照顧	呼吸抑制及癱瘓
ECOG	緩解病人症狀。 (見附錄八)	緩解病人症狀。 (見附錄八)	建議停藥或更換藥物。	建議停藥。

Neurotoxic chemotherapeutic agents target multiple aspects of CIPN



神經部位	影響藥物	臨床症狀
背根神經節（DRG）	Platinum 類（如 Cisplatin） Bortezomib	造成長期感覺異常，難以逆轉
離子通道(Ion Channels)	Oxaliplatin（急性）	急性冷感、觸電感，常見於 FOLFOX 初期
微管(Microtubules)	Vinca alkaloids, Taxanes, Eribulin, Ixabepilone 等	抑制軸突傳輸，導致神經退化
粒線體(Mitochondria)	Platinum, Taxanes, Vinca, Bortezomib	干擾能量代謝、氧化壓力加劇，造成神經損傷
神經終端（Nerve Terminals）	Taxanes, Bortezomib	引發四肢遠端麻木與疼痛
免疫神經毒性	PD-1、CTLA4 抑制劑	少見但可能引發自體免疫型神經炎

Nathan P. Staff et al. Ann Neurol. 2017 June ; 81(6): 772–781.



MS. Wu, 55-year-old woman with ascending colon cancer stage 3B, post-LAR

- Planned for 12 cycles of adjuvant FOLFOX.
- She was advised to consider IV glutamine during chemotherapy, but reported using oral glutamine instead.

Developed distal limb numbness worsened by cold starting from cycle 4, symptoms progressed through cycles 12, and persisted for 6 months post-treatment.

Oxaliplatin-induced peripheral neuropathy

- Patients typically begin experiencing peripheral neuropathy, often **after cumulative doses exceed ~540mg/m²** (commonly around cycle 4–6).
- Symptoms include acute **cold-triggered** dysesthesias (transient), which can evolve into chronic sensory neuropathy (tingling, numbness) with continued treatment.
- Neuropathy risk and severity increase with higher cumulative doses of oxaliplatin.


到底在哭什麼？

Scientific Research Publishing

Journal of Cancer Therapy, 2016, 7, 609-621
http://www.scirp.org/journal/jct
ISSN Online: 2151-1942
ISSN Print: 2151-1934

N(2)-L-Alanyl-L-Glutamine Dipeptide Preventing Oxaliplatin-Induced Neurotoxicity in Colorectal Cancer Patients

Adel Gabr[1], Ahmed A. S. Salem[2], Haisem Ahmed Samy[3], Shimaa Tmam[4], Anwar Mohammed Ali[5]

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[5]Department of Neurophysiology, Faculty of Medicine, Assiut University, Assiut, Egypt
Email: adelgabre@yahoo.com, ahmed_awad721@yahoo.com, shimaa@aun.edu.eg, haisamasa@yahoo.com, anwarmoh2006@yahoo.com

Background

- Oxaliplatin and infusional fluorouracil/leucovorin or capecitabine has emerged as important options in the adjuvant and palliative treatment of colorectal cancer.
- Severe Oxaliplatin induced neurotoxicity may require chemotherapy dose reduction or cessation.
- The incidence of oxaliplatin-induced neurotoxicity has varied from 12% - 18%.
- Several attempts have been proposed to prevent or treat oxaliplatin-induced neurotoxicity, but treatment of established chronic Oxaliplatin induced neurotoxicity is limited.

- Purpose:
  - To assess the efficacy of parenteral Glutamine dipeptide (L-Alanyl-L-Glutamine Dipeptide, 20 g·m/100ml, IV) for preventing of oxaliplatin induced neurotoxicity.
- Patients and Methods:
  - A pilot study was performed. 120 patients with metastatic colorectal cancer (mCRC) entered into the study. 60 patients randomly assigned to receive IV glutamine dipeptide (20 g·m IV) day 1-2 with FOLFOX-4 to be repeated every 15 days as a first line of treatment of metastatic colorectal cancer and 60 patients assigned to receive only FOLFOX-4 (control group). Neurotoxicity symptoms and signs were evaluated before each cycle.

Significantly reduced the incidence and severity of oxaliplatin induced neurotoxicity

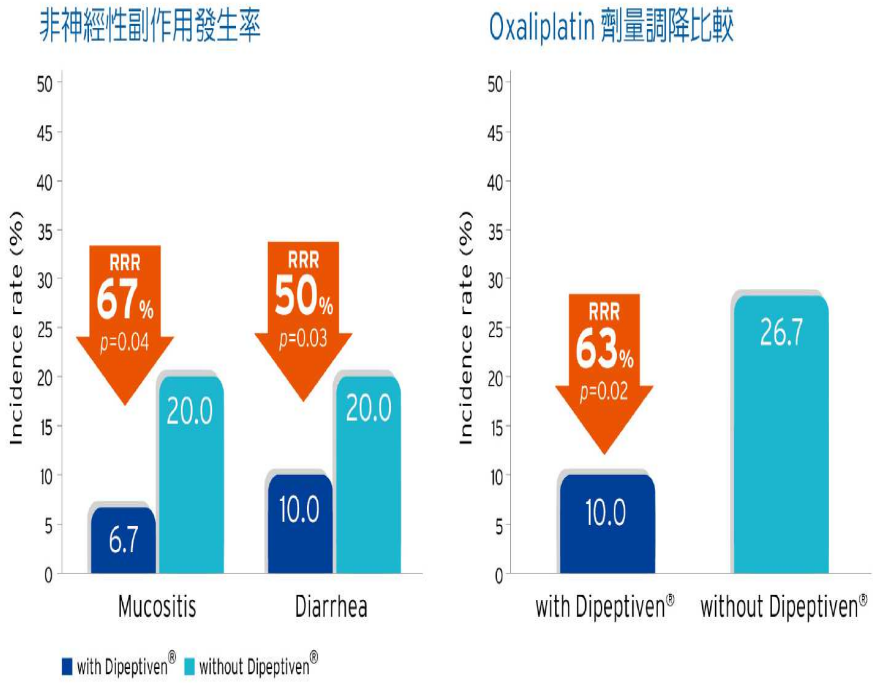
Table 4. Electrophysiological examination after 4 cycles in different group.

	Nerve	FOLFOX + Dipeptiven	FOLFOX	*P*
		Median ± SD	Median ± SD	
Median	Distance of latency	3.4 ± 0.4	3.6 ± 0.5	0.05
	Conduction velocity	45 ± 6	40 ± 6	0.05
Ulnar	Distance of latency	3.4 ± 0.5	3.5 ± 1.1	0.03
	Conduction velocity	43 ± 6	42 ± 8	0.05
Sural	Distance of latency	3.5 ± 3	3.7 ± 1.2	0.04
	Conduction velocity	45 ± 6	41 ± 8	0.04

Table 5. Electrophysiological examination after 6 cycles in different group.

	Nerve	FOLFOX + Dipeptiven	FOLFOX	*P*
		Median ± SD	Median ± SD	
Median	Distance of latency	3.4 ± 0.8	3.6 ± 0.7	0.02
	Conduction velocity	45 ± 6	39 ± 9	0.05
Ulnar	Distance of latency	3.3 ± 0.9	3.5 ± 1.5	0.03
	Conduction velocity	44 ± 6	42 ± 9	0.05
Sural	Distance of latency	3.5 ± 4	3.7 ± 1.2	0.002
	Conduction velocity	46 ± 6	41 ± 9	0.04

Dipeptiven® 亦能協助緩解 **50%** 以上在治療期間發生的腹瀉及口腔黏膜炎症狀，且減少因為藥物副作用而須調降 Oxaliplatin 劑量的發生率



Neutraceutical agents for prevention of the development of CIPN

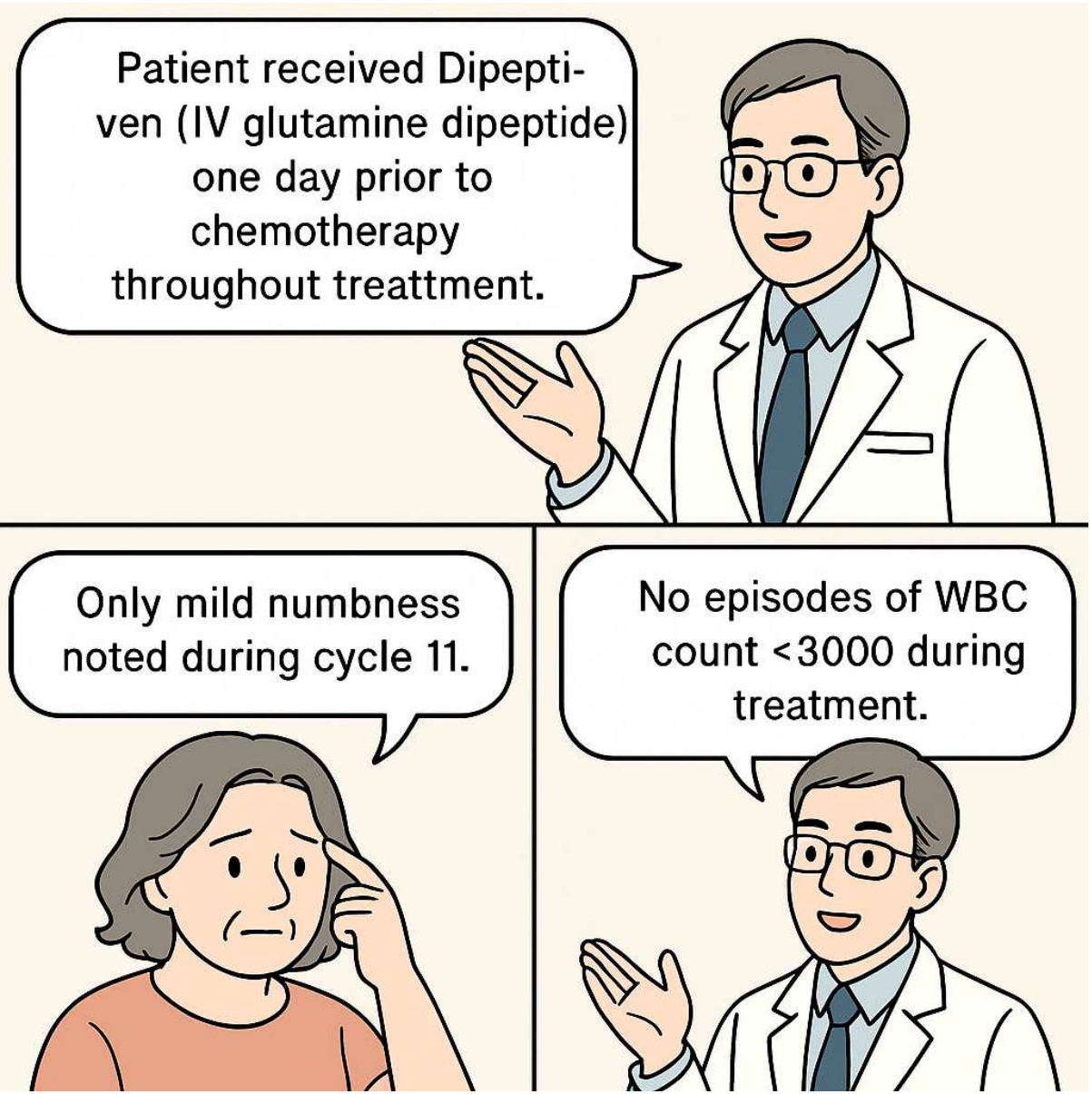
TABLE 1 | List of clinically used neutraceutical agents for prevention of the development of CIPN.

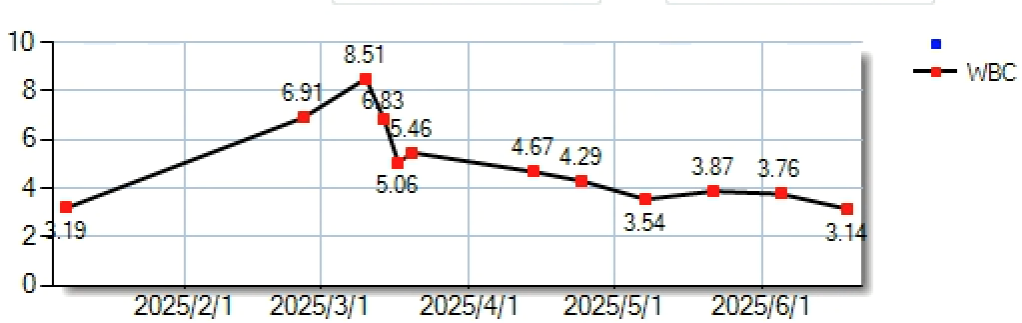
Nutraceutical agent	Class	Chemotherapy agent	Study outcome
NUTRACEUTICAL AGENTS			
Vitamin E	Vitamins	Cisplatin	+Decreased incidence and severity of peripheral neurotoxicity (Pace et al., 2003)
			+Reduced risk of developing neurotoxicity (Pace et al., 2010)
			+Neuroprotective effect (Argyriou et al., 2005)
		Oxaliplatin	−No significant decrease in the incidence of acute CIPN (de Afonseca et al., 2013)
		Paclitaxel	+Neuroprotective effect (Argyriou et al., 2005)
Glutamine	α-amino acid	Cisplatin	±Possible reduction of severity of CIPN symptoms (Huang et al., 2015)
		Vincristine	+Improvement in sensory function and self-reported overall quality of life (Sands et al., 2017).
		Oxaliplatin	±Possible reduction of severity of CIPN symptoms (Huang et al., 2015)
			+Reduction in incidence and severity of CIPN (Wang et al., 2007)
		Paclitaxel	±Possible reduction in the severity of CIPN (Vahdat et al., 2001)
			+Significant reduction of weakness, loss of vibratory sensation and toe numbness (Stubblefield et al., 2005)

Starobova H et al. (2017) Front. Mol. Neurosci. 10:174.

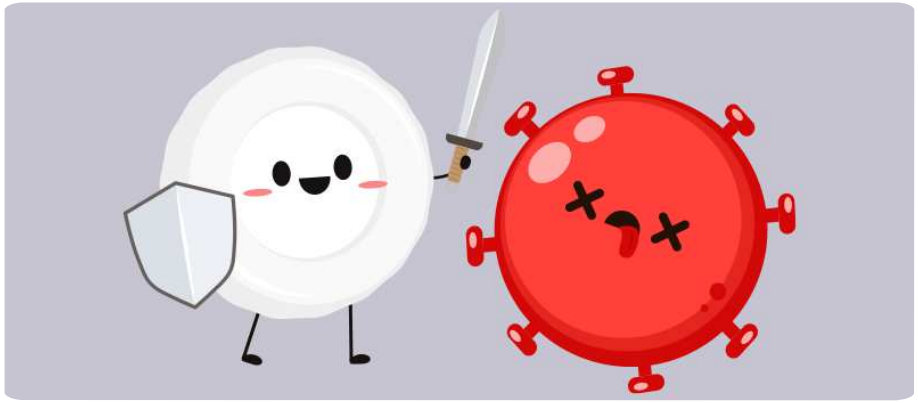
64F, Ascending colon cancer with pericolic invasion and regional metastatic lymph nodes (cT4aN1M0, stage IIIB)

- **9/10/2024:** Colonoscopy biopsy: grade 2 adenocarcinoma.
- **9/23/2024:** Laparoscopic exploration + ileostomy + port implantation.
- **IHC:** ERCC1/2 positive; MMR shows loss of MLH1/PMS2 (suggesting MSI pathway involvement → recommended MLH1 promoter methylation/BRAF testing). Codon 600 mutation (+).
- **FOLFOX chemotherapy:**
- C1-C6: 10/28/2024-1/7/2025
- **CT on 1/21/2025:** enlarged tumor
- **3/13/2025:** Right hemicolectomy → mucinous adenocarcinoma grade 3 (pT3N1a).
- **Refused immunotherapy.**
- Continued FOLFOX C7-C12 → completed 7/3/2025.
- **7/9/2025:** CT performed (pending detailed findings).


Patient received Dipepti-ven (IV glutamine dipeptide) one day prior to chemotherapy throughout treattment.
Only mild numbness noted during cycle 11.
No episodes of WBC count <3000 during treatment.


10
8
6
4
2
0
8.51
6.91
6.83
5.46
5.06
4.67
4.29
3.87
3.76
3.54
3.19
3.14
2025/2/1
2025/3/1
2025/4/1
2025/5/1
2025/6/1
WBC

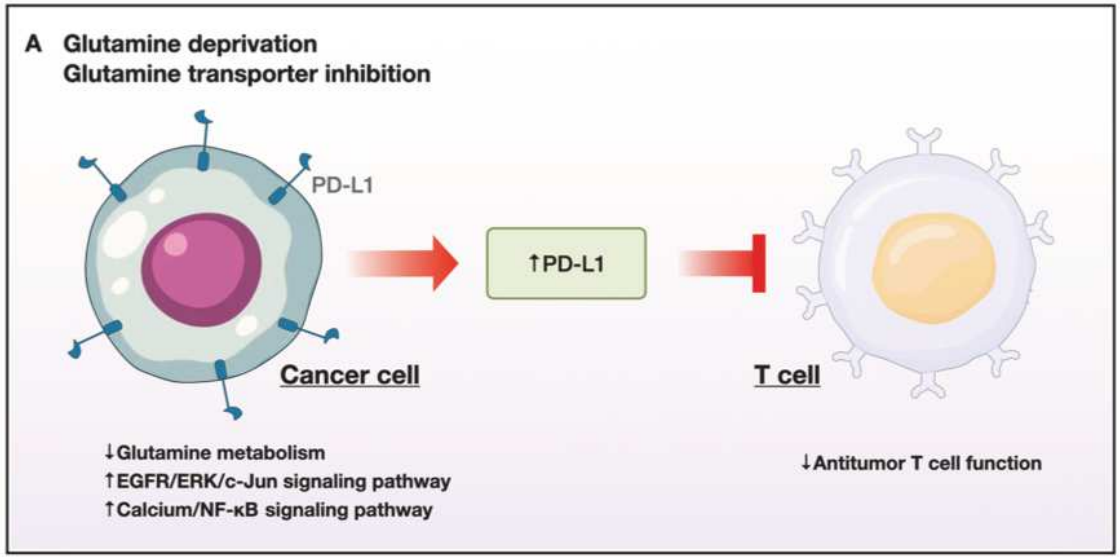
Leukopenia



CTCAE Grading for Leukopenia/Neutropenia

Grade	WBC (Leukopenia) / ANC (Neutropenia)	Clinical Description
1	WBC: below lower limit of normal (LLN) – 3,000/µLANC: LLN – 1,500/µL	Asymptomatic; no intervention needed
2	WBC: 2,999–2,000/µLANC: 1,499–1,000/µL	Mild to moderate; non-invasive intervention may be indicated ()
3	WBC: 1,999–1,000/µLANC: 999–500/µL	Severe; medically significant, may require hospitalization ()
4	WBC: <1,000/µLANC: <500/µL	Life-threatening; urgent intervention indicated ()

T-cell-mediated immune responses to glutamine-targeted treatment in cancer cells



Glutamine 缺乏時或抑制 Glutamine Transporter

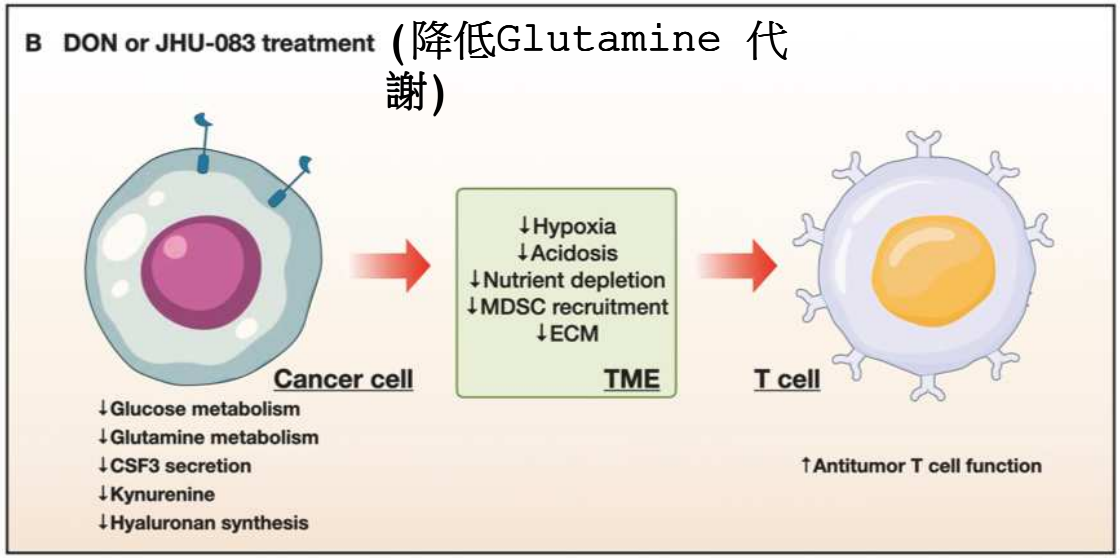
↓

Glutamine 代謝下降 → EGFR/ERK/c-Jun 與 NF-κB 路徑活化

↓

癌細胞表現 PD-L1，抑制免疫反應

降低 glutamine 代謝，可「改善腫瘤微環境」並「增強 T 細胞免疫反應」



Patient Profile

- 鄭○○, M/58
- Diagnosis:
  - Multiple myeloma, kappa light chain, International Staging System (ISS) stage II, Durie-Salmon stage III, post 4 courses VTD (velcade, thalidomide, dexamethasone) on 2019/01/10-2019/05/03
  - Autologous stem cell transplantation on 2019/10/16 (Day 0)
  - Conditioning regimen: Melphalan 200mg/m^2 on 2019/10/14 (Day -2)
- P.H.:
  - Chronic obstructive pulmonary disease
  - Hemorrhoid
  - Major depressive disorder, moderate
  - Hypertension

Clinical course

21 Oct. 2019

- (Day 5)
  - Grade 1 mucositis[oral rash]

22 Oct. 2019 - 28 Oct.

- (Day 6-Day 12)
  - Intermittent Fever
  - worsening mucositis, Grade 1 -> 3

26 Oct. 2019

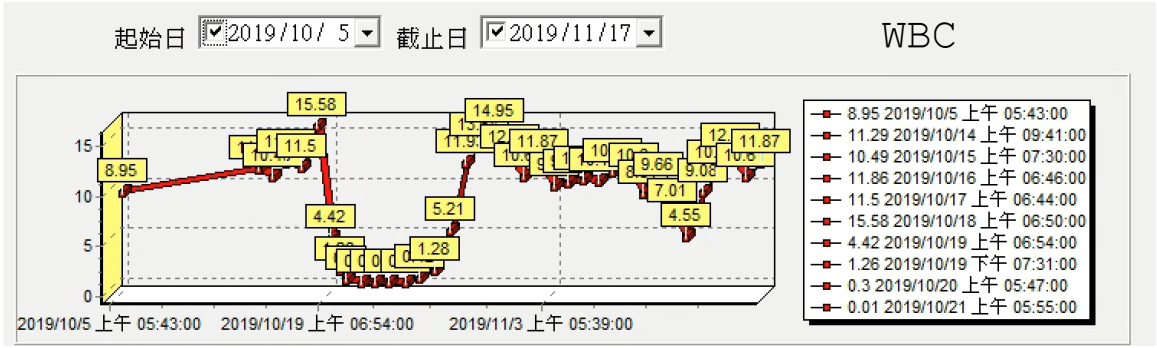
- (Day 10)
  - WBC: 1280/uL, persistent thrombocytopenia around 20000/uL
  - persistent grade 2-3 mucositis, poor oral intake
  - Refused NG, Add PPN for nutrition supplement

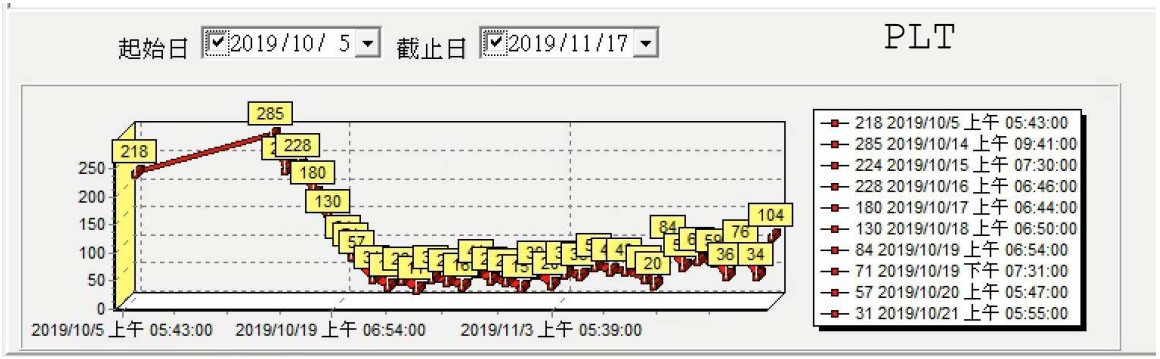
1 Nov. 2019

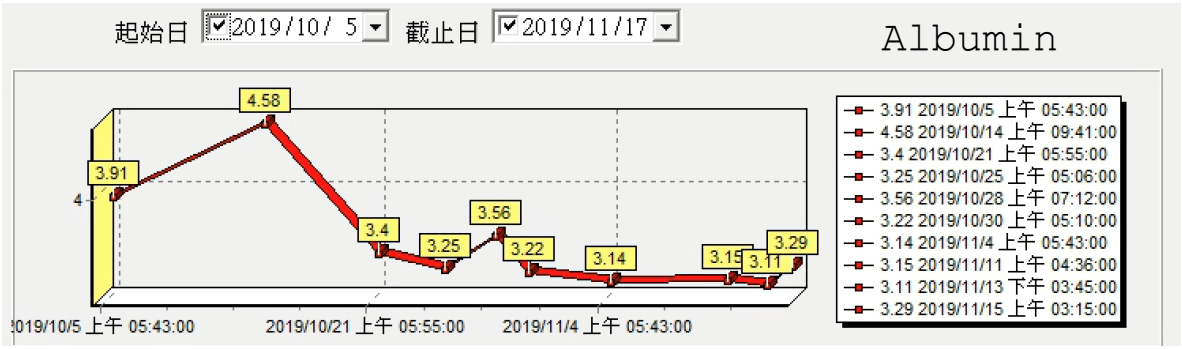
- (Day 16)
  - Diarrhea, grade2, clostridium difficile related

11 Nov. 2019

- (Day 26)
  - CMV viral load: 2836 -> add ganciclovir
  - persistent oral mucositis and poor oral intake, add NG







- Persistent oral mucositis and poor oral intake
- Recurrent pneumonia
- Persistent thrombocytopenia
- ICH, respiratory failure
- Expired on 2019/12/17

To our best

- 是不是不要移植就不會發生這樣的悲劇？
  - 以目前的治療，自體幹細胞移植對於疾病的控制有其療效
- 有什麼方式可以改善oral mucositis及使血小板正常生長?
  - Better nutrition supplement: TPN, NG feeding…….
  - Glutamine use

Patient Profile

莊○○, F/66

Diagnosis:

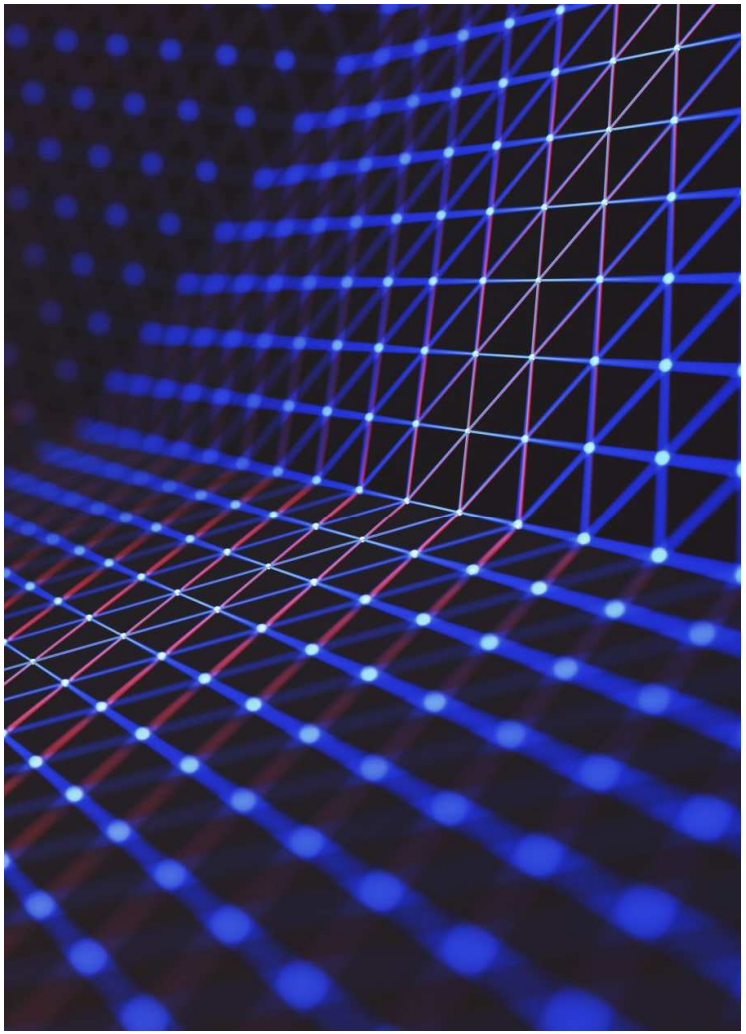
- Multiple meyloma, IgA kappa, ISS I, DSS stage I
- post 4 courses VTD (velcade, thalidomide, dexamethasone) on 2020/11/03-2021/02/23
- Autologous stem cell transplantation on 2021/07/01 (Day 0)
- Conditioning regimen: Melphalan 200mg/m^2 on 2021/06/29 (Day -2)

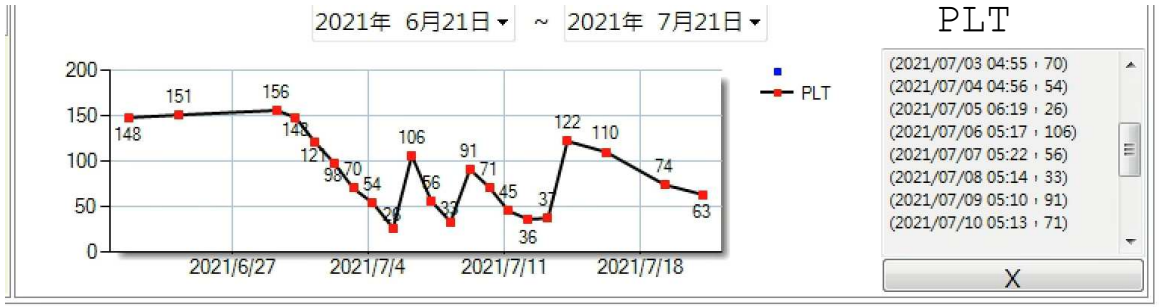
P.H.:

- HTN

Clinical course

29 June 2021 – 30 June	• Dipeptiven use for 2 days before and on the day of chemotherapy
29 June 2021	• (Day -2) • Conditioning regimen: Melphalan 200mg/m2
2021.07.01	• ASCT (Day 0)
10 July 2021	• (Day 9) • WBC: 3290/uL, PLT: 71000/uL





- No oral mucositis was noted when Day -2 to Day 9 and mild decreased oral intake
- No infection
- Grade 1 oral mucositis was noted on 7/7
  - Add Dipeptiven on 7/7-7/8
- MBD on 11/12

Patient Profile

游○○, F/40

Diagnosis:

- Multiple myeloma, Kappa light chain, ISS stage 1, DS stage 1
- post 4 courses VTD (velcade, thalidomide, dexamethasone) on 2021/02/09-2021/06/01
- Autologous stem cell transplantation on 2021/10/11 (Day 0)
- Conditioning regimen: Melphalan 200mg/m^2 on 2021/10/09 (Day -2)

P.H.:

- Chronic venous insufficiency with thrombosis in the bilateral calves, left iliac femoral veins
- Stress fracture at right femoral neck,suspect pathologic fracture
- Fatty liver related

Clinical course

8 Oct. 2021 - 10 Sep.

- Dipeptiven use for 2 days before and on the day of chemotherapy

9 Oct. 2021

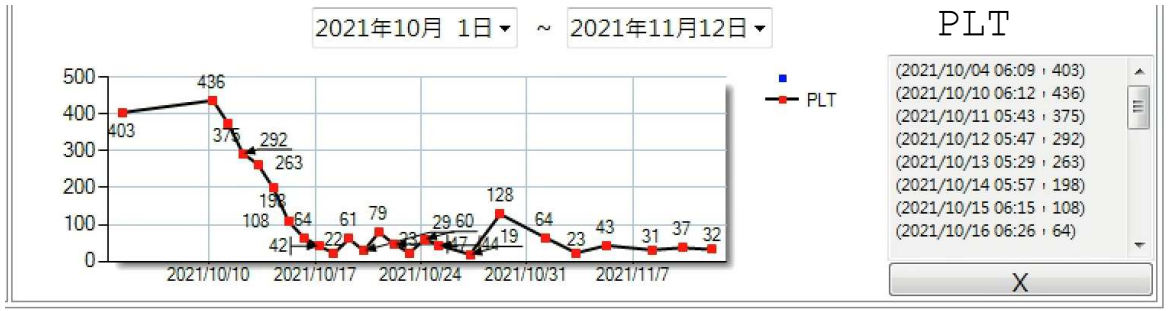
- (Day -2)
  - Conditioning regimen: Melphalan 200mg/m2

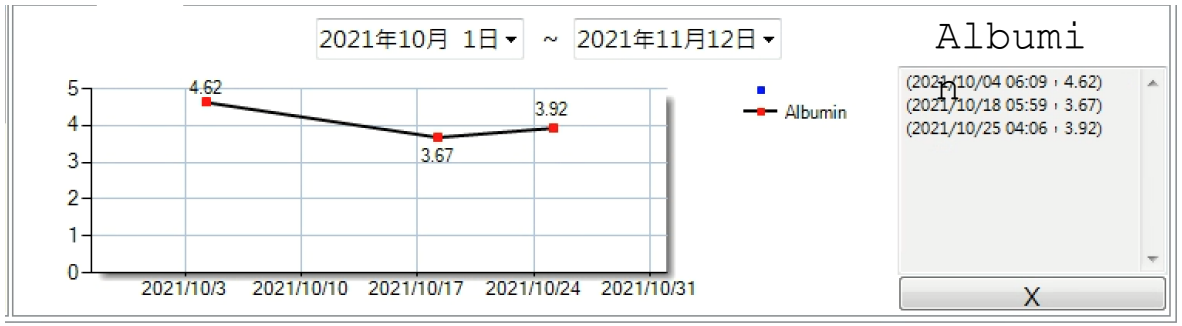
2021.10.11

- ASCT (Day 0)

20 Oct. 2021

- (Day 9)
  - WBC: 4620/uL, PLT: 32000/uL

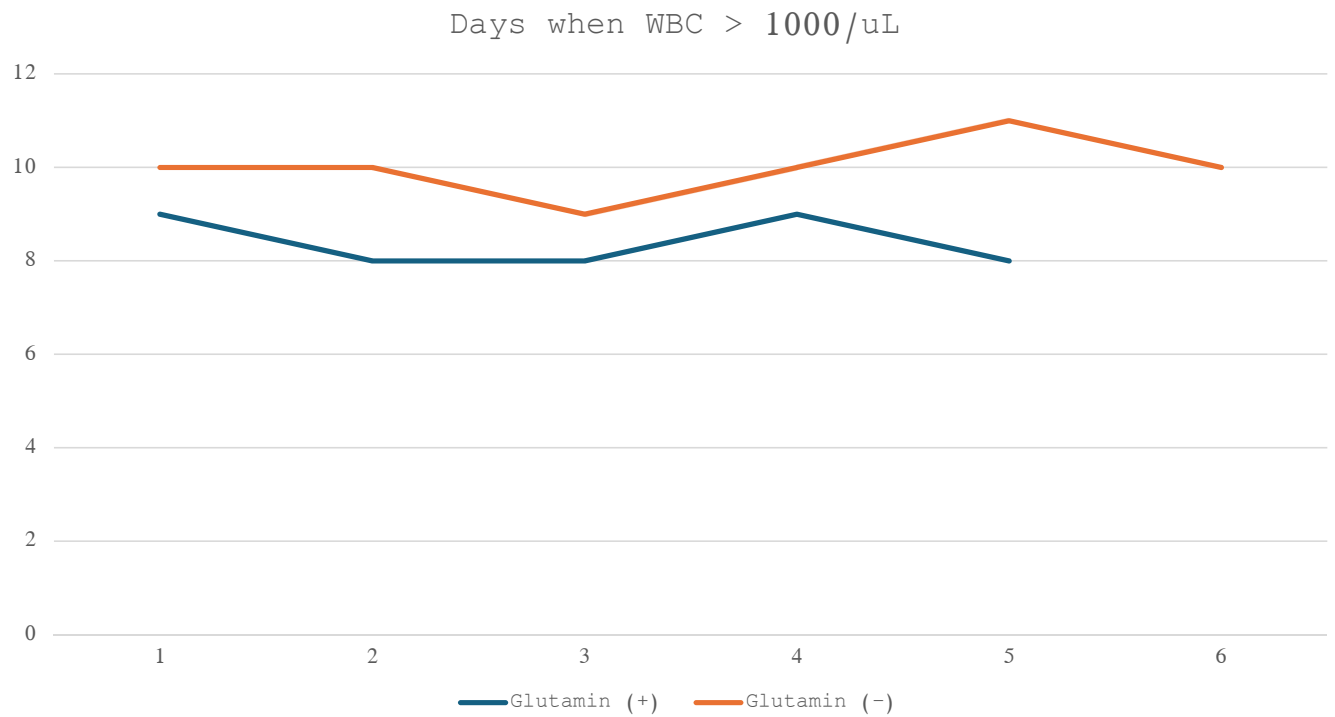




- No oral mucositis was noted when Day -2 to Day 9 and mild decreased oral intake
- No infection
- Prolong thrombocytopenia
- Grade 1 oral mucositis was noted on 10/12 and 10/18
  - Add Dipeptiven on 10/12-10/13, 10/18-10/19
- MBD on 11/12

From 2022/09/01-2023/6/30

- Multiple myeloma with ASCT
- Total 11 cases



Comparison of leukopenia/neutropenia risks in colon cancer chemotherapy

Regimen	Grade 3-4 Neutropenia	Febrile Neutropenia
FOLFOX-4	~35-47%	~4-6%
FOLFOX-6	~36%	(not specified)
FOLFIRI	24-71%	4-11%

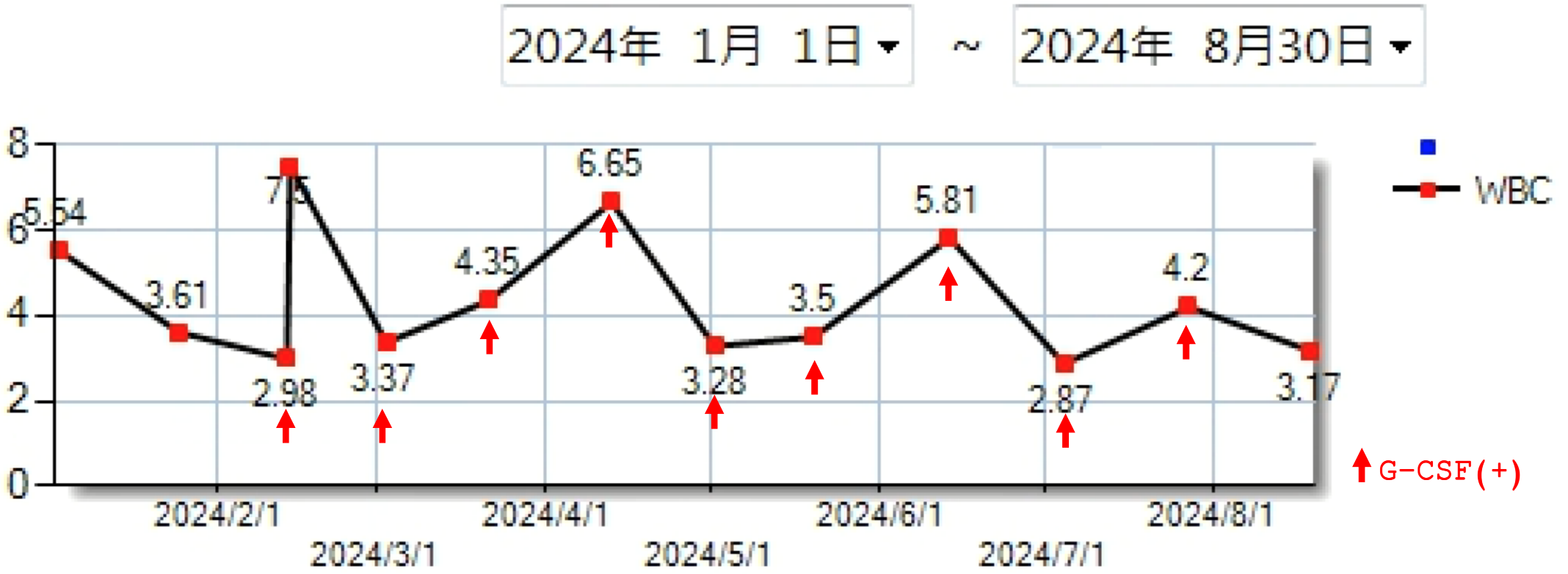
61-year-old man with descending colon adenocarcinoma, grade 2 (pT4aN2bM0, stage IIIC)

11/27/2023: Underwent laparoscopic anterior resection with side-to-side stapled anastomosis.

1/4/2024: Left infraclavicular venous port implanted.

1/5/2024: Began adjuvant FOLFOX6 chemotherapy; completed 12 cycles.

9/6/2024 – 5/9/2025: Received Tegafur + Uracil (UFUR)



Treatment course

- WBC dropped to **2980** around early March 2024 (cycle 2-3).
- G-CSF started at that point and used regularly after chemotherapy cycles.
- Subsequent WBC trends show fluctuations but generally stable counts, avoiding prolonged severe neutropenia.

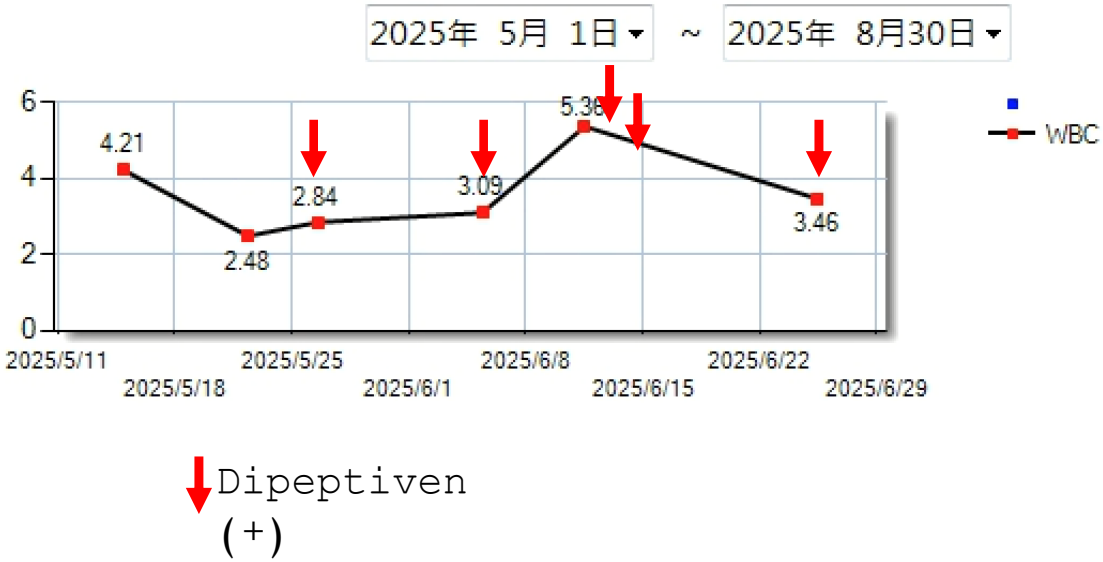
61M, colon ca with liver meta

- 4/14/2025: Abdominal CT showed new metastases in S7 and S8 of the liver.
- Gene tests: HER2 (-), NRAS (-), BRAF (-), KRAS (+).

- Treatment adjustment:
- Avastin + FOLFIRI (with IV glutamine prior to some cycles).
  - C1: 5/15-5/17
  - C2: 5/27 (glutamine given 5/26)
  - C3: 6/12
  - C4: 6/27

Treatment course

- **5/26:** Dipeptiven (IV glutamine dipeptide) administered; **no G-CSF support** given.
- WBC remained relatively stable post-treatment:
- 2.84 (5/26) → 3.09 (6/5) → 5.36 (6/11) → 3.46 (6/25).
- No severe or prolonged neutropenia observed despite lack of G-CSF.



Summary

	IV Glutamine	Oral Glutamine
Plasma Level	Achieves high/stable levels	Lower/variable levels
Mucositis	Strong evidence of reduced severity/duration	Some benefit
Diarrhea	Reduces duration by ~1 day (supported by RCTs/meta-analyses)	Mixed/inconsistent findings
Neuropathy	Pilot studies show reduced incidence/severity	Sparse, inconclusive data
WBC Recovery	Improves neutrophil recovery in studies	No clear evidence

Myth

癌細胞生長時需要Glutamine作為營養來源，那攝取Glutamine會不會更加速Cancer cell growth？

South African Journal of Clinical Nutrition 2017; 30(4):109–117
https://doi.org/10.1080/16070658.2017.1371467

SAJCN
ISSN 1607-0658 EISSN 2221-1268

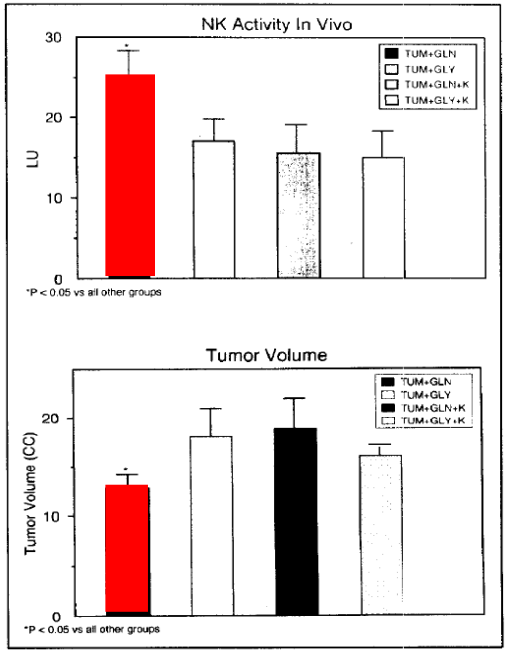
REVIEW ARTICLE

Glutamine and its use in selected oncology settings

Reinette Tydeman-Edwards[a*]

Tumour growth

Tumour cells use GLN in protein catabolism for tumour growth, depleting GLN in the skeletal muscles of cancer patients, leading to cachexia (Figure 1). It is believed that tumours become GLN traps and worsen GLN loss in cancer patients, but also that GLN has the potential to retard or halt tumour growth due to its immuno-modulatory action.[8] Various studies suggest that GLN supplementation suppresses tumour growth by restoring the function of natural 'killer' cells, improving protein metabolism,[3] and enhancing the effect of cancer therapy.[9,11,20,22] The review by Kuhn *et al.*[12] confirmed that GLN improves the clinical state of patients with a variety of malignancies without increasing tumour growth.

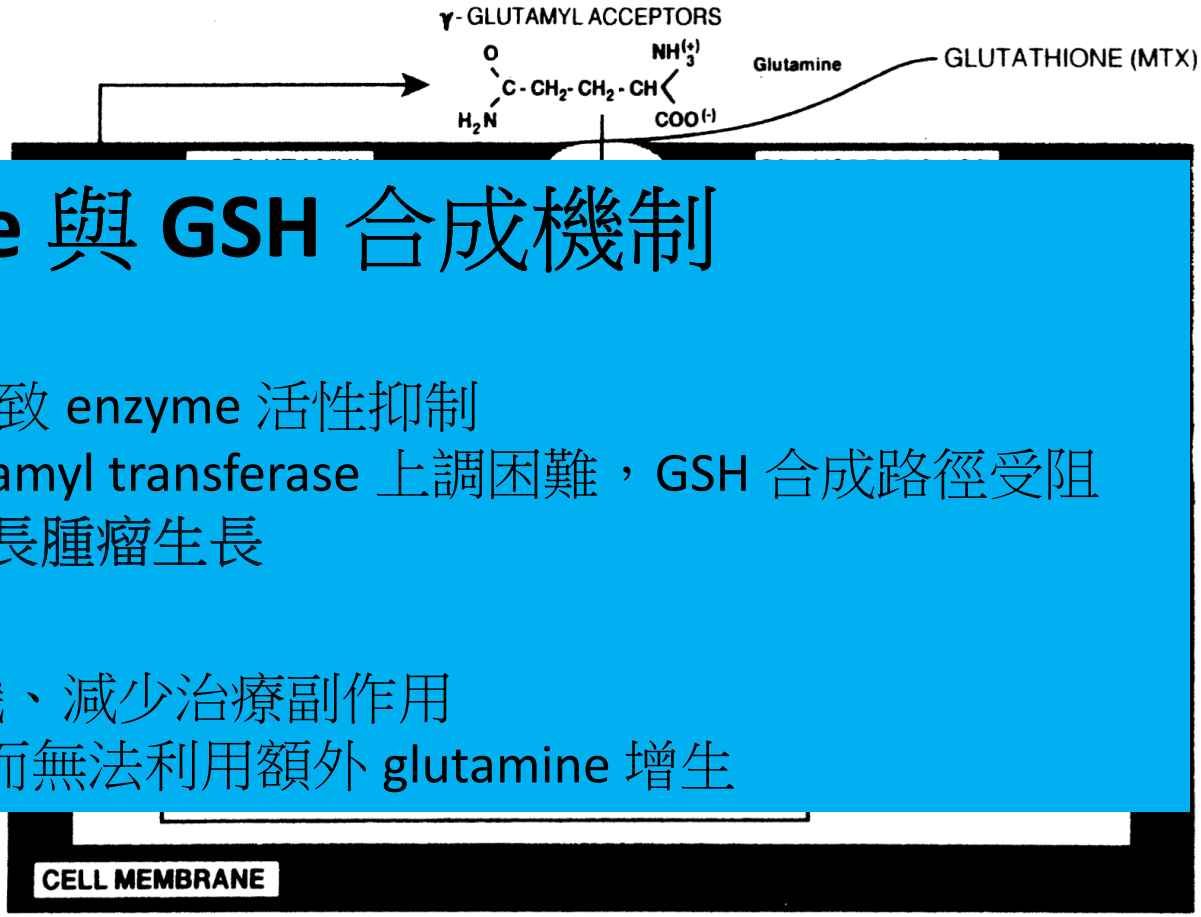


Tumor(TUM)+Glutamine(GLN)
Tumor(TUM)+Glycine(GLY)
Tumor(TUM)+Glutamine(GLN)+Ketamine(K)
Tumor(TUM)+Glycine(GLY)+Ketamine(K)

V. Suzanne Klimberg et al. J Surg. 1996;172:418-424

Proposed mechanism

- 在正常宿主組織中， Glutamine
  →GSH的代謝需要5-



Glutamine 與 GSH 合成機制

✦ 在腫瘤細胞內：

- 腫瘤環境常因缺氧而呈酸性導致 enzyme 活性抑制
- 即使補充 glutamine，因 γ-glutamyl transferase 上調困難，GSH 合成路徑受阻
- 補充 glutamine 並 不會直接助長腫瘤生長

✦ 臨床意義：

- 補充 glutamine 可保護正常組織、減少治療副作用
- 腫瘤細胞可能因代謝途徑阻斷而無法利用額外 glutamine 增生

CANCER TREATMENT REVIEWS 2003; 29: 501–513

Therapeutic indications & contraindications

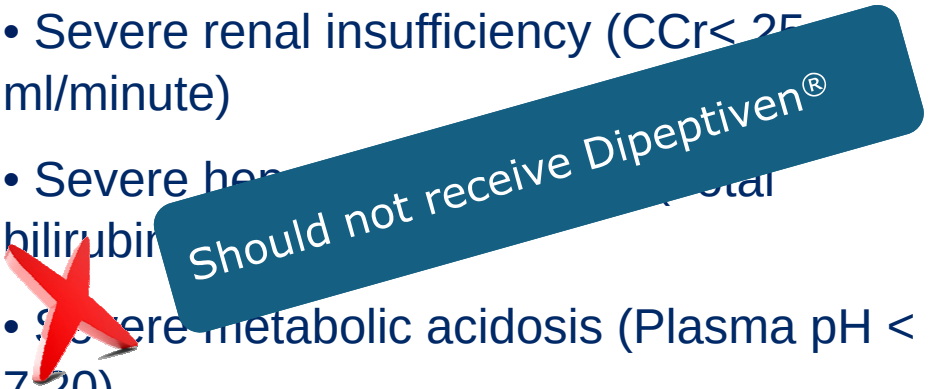
Indications

- For hypercatabolic and/or -metabolic states during clinical nutrition
- It should be given together with parenteral or enteral nutrition or a combination of both.

Contraindications

Patients, who suffer from …

- Severe renal insufficiency (CCr< 25 ml/minute)
- Severe hep… …otal bilirubi…
- Severe metabolic acidosis (Plasma pH < 7.20)
- Known hypersensitivity to the active substances or to any of the excipients



Take home Message

Dipeptiven® can reduce side effect of anti-cancer treatment which may lead to less treatment interruption and better survival

Dipeptiven® should be considered to administrate as soon as possible when patients received anti-cancer treatment