Optimizing nutrition intervention during chemotherapy for cancer patients

優化營養介入於化療期間的癌症病患

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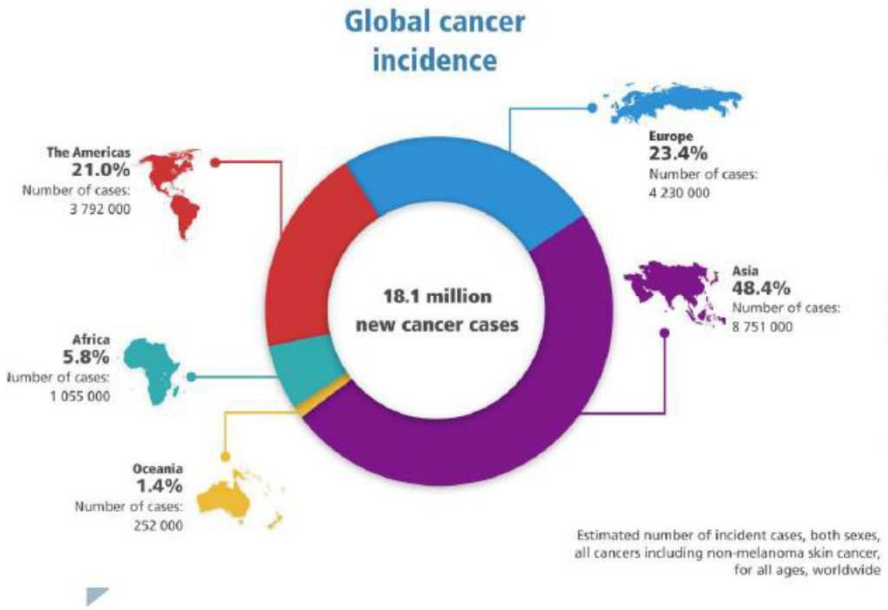
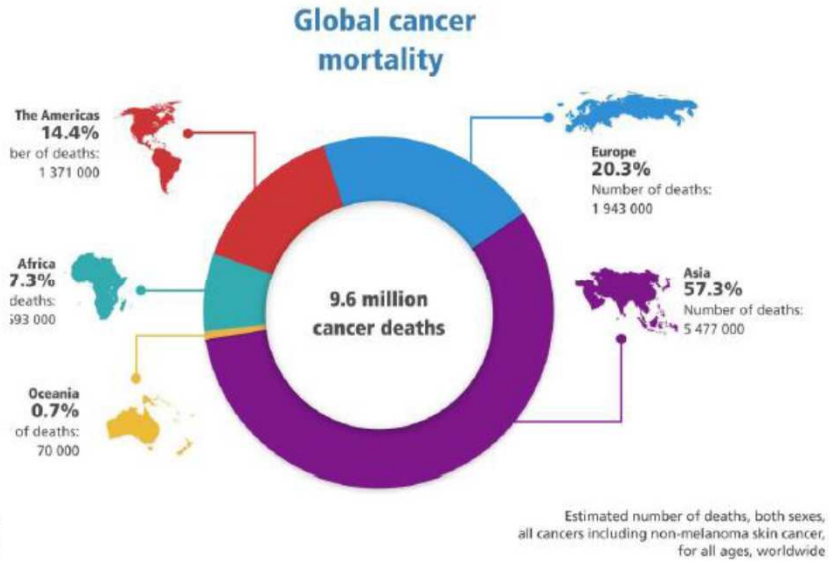
Outline: Nutrition intervention for cancer patients

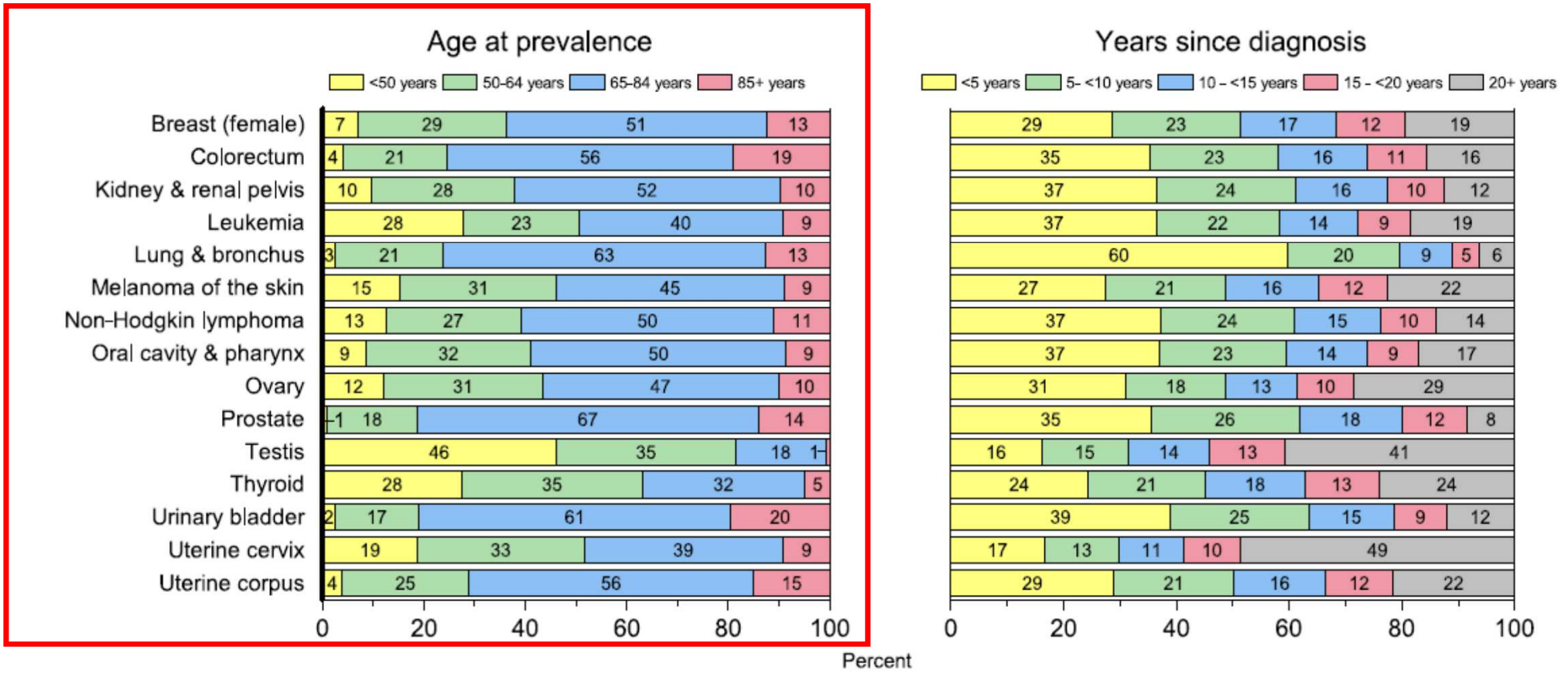
- Introduction
- Definition and Influence of cancer-related cachexia/malnutrition
- Nutrition strategies
  - Special for chemotherapy: IV glutamine
  - General concepts: Fish oil (n-3 PUFA)
  - Guidelines
- Conclusion

Burden of cancer: Global data

- Latest global cancer burden:
  - Cancer burden rises to 19.3 million new cases and 10.0 million cancer deaths in 2020. (IARC, 2020)







Prevalence **by Cancer Type, Years Since Diagnosis, and Age at Prevalence as of January 1, 2019, United States.**

CA CANCER J CLIN 2019;0:1–23

107年國人十大癌症發生人數，與106年比較

■ 排序同，除子宮體癌與食道癌互換(106年子宮體癌第11名、食道癌居第10名)

發生數序位	原發部位	107年				106年				107年發生人數增減值	107年發生率增減值
		個案數	標準化發生率	年齡中位數	標準化死亡率	個案數	標準化發生率	年齡中位數	標準化死亡率		
1	大腸	16,525	41.8	66	14	16,408	42.9	66	14.4	117	-1.1
2	肺、支氣管及氣管	15,345	38.8	66	22.8	14,282	37	67	23.1	1,063	1.8
3	女性乳房	14,217	78.9	56	12.5	13,965	78.9*1	55	12.6*1	252	0
4	肝及肝內膽管	11,342	28.6	66	20.3	11,225	29.3	66	21.6	117	-0.7
5	口腔、口咽及下咽	8,170	22.5	57	8.1	7,797	22	57	7.8	373	0.5
6	攝護腺	6,644	34.7	72	6.6	5,866	31.7*2	73	6.9*2	778	3
7	甲狀腺	4,445	14.3	50	0.5	4,053	13.1	50	0.5	392	1.2
8	皮膚	4,049	9.6	75	0.7	3,804	9.5	74	0.6	245	0.1
9	胃	3,798	9.3	68	5.5	3,703	9.4	68	5.6	95	-0.1
10	子宮體	2,787	15.5	55	2.0	2,695	15.1	56	1.7	92	0.4
	全癌症	116,131	309.8	63	121.8	111,684	305.4	63	123.4	4,447	4.4

註：
1. 發生序位係以癌症發生人數由高至低排序。
2 癌症發生人數增減情形：107年發生人數-106年發生人數。
3 .發生率資料來源：台灣癌症登記資料庫(不含原位癌)；死亡率資料來源：衛生福利部統計處死因統計。
4.標準化率係以西元2000年世界標準人口為標準人口計算(單位為每10萬人口)。
5., *1每10萬女性人口發生率及死亡率; *2每10萬男性人口發生率及死亡率。

Taiwan Dec. 2020

台灣人『上天堂』的10大原因（~2017）：癌症第一名

	死亡人數(人)		死亡率（每十萬人口）				標準化死亡率（每十萬人口）		
	106年	較上年增減%	105年順位	106年順位	106年	較上年增減%	順位	106年	較上年增減%
所有死亡原因	171,857	-0.3			729.6	-0.5		424.3	-3.4
癌症	48,037	0.6	1	1	203.9	0.4	1	123.4	-2.7
心臟疾病（高血壓性疾病除外）	20,644	-0.8	2	2	87.6	-1.0	2	48.5	-3.6
肺炎	12,480	2.2	3	3	53.0	2.1	4	26.5	-1.5
腦血管疾病	11,755	-0.8	4	4	49.9	-1.0	3	27.5	-3.8
糖尿病	9,845	-1.2	5	5	41.8	-1.4	5	23.5	-4.1
事故傷害	6,965	-3.3	6	6	29.6	-3.3	6	21.9	-5.2
慢性下呼吸道疾病	6,260	-7.8	7	7	26.6	-8.0	7	13.3	-11.9
高血壓性疾病	6,072	3.2	8	8	25.8	3.2	8	13.3	-1.5
腎炎、腎病症候群及腎病變	5,381	3.0	9	9	22.8	2.7	10	12.4	0.0
慢性肝病及肝硬化	4,554	-3.9	10	10	19.3	-4.0	9	12.6	-6.0

Chemo/radiotherapy

Surgery

Targeted therapy

Immunotherapy

Randomized Trial in Patients with Lung Cancer

150 patients within 8 weeks of diagnosis of metastatic NSCLC with an ECOG PS 0-2

- Integrated care
- Standard care

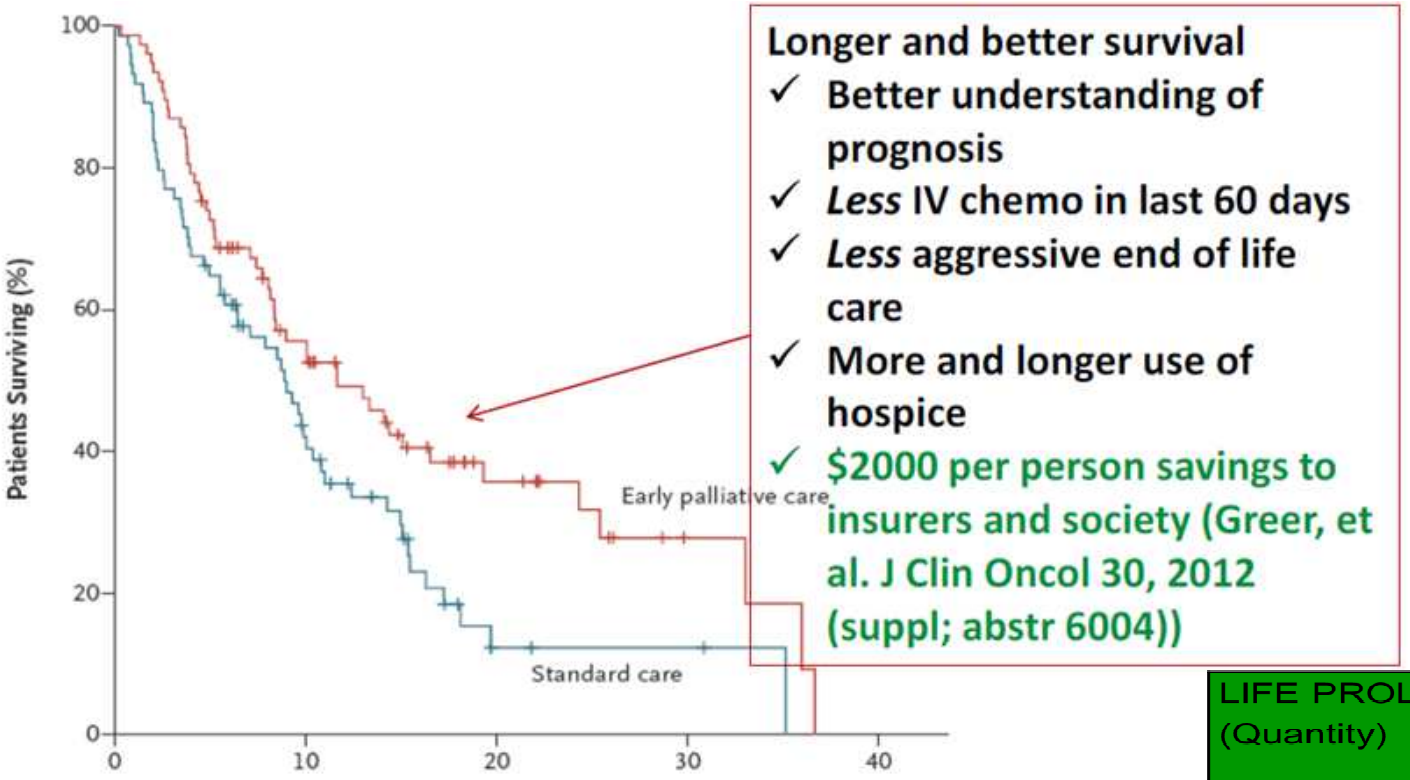
Outcome Measures

Patient-reported Outcomes
1. FACT Lung
2. HADS (mood)
3. PHQ-9 (depression)
4. Prognostic awareness

Health Service Utilization
1. Hospice referrals
2. Chemotherapy administration
3. Documentation of resuscitation preferences

Temel JS, Greer JA, Muzikansky A, et al. N engl J Med 2010;363:733-742.

Palliative care in addition to usual oncology care allowed lung cancer patients to live almost 3 months longer than those who got usual oncology care.



Longer and better survival

- ✓ Better understanding of prognosis
- ✓ *Less* IV chemo in last 60 days
- ✓ *Less* aggressive end of life care
- ✓ More and longer use of hospice
- ✓ $2000 per person savings to insurers and society (Greer, et al. J Clin Oncol 30, 2012 (suppl; abstr 6004))

Temel J, et al. NEJM 2010; Greer J, et al. JCO 2011

ASCO | GUIDELINES

Clinical Tools and Resources

Palliative Care Checklist

- ☐ Assess patient/caregiver medical literacy
- ☐ Assess patient/caregiver willingness to hear prognosis
- ☐ Assess patient/caregiver role preferences
  - o Patient prefers to share the decision with_____
  - o Patient prefers to decide him/herself after hearing the views of _____
  - o Patient prefers that someone else decides
  - o Patient prefers to decide on his/her own
- ☐ Assess patient/caregiver understanding of diagnosis, illness, and prognosis
- ☐ Offer clarification of treatment goals*
- ☐ Use standardized symptom assessment tools (Edmonton Symptom Assessment Scale or Condensed Memorial Symptom Assessment Scale)**
  - o Pain*
  - o Pulmonary symptoms (cough, dyspnea)*
  - o Fatigue and sleep disturbance*
  - o Mood (depression and anxiety)*
  - o GI (anorexia and weight loss, nausea and vomiting, constipation)*
- ☐ Screen for distress (with tool such as Distress Thermometer)
- ☐ Refer for or conduct psychosocial assessment
- ☐ Take a spiritual history***
- ☐ Refer for psychosocial support
- ☐ Refer to social work for practical issues (e.g. financial, caregiver, home health, transportation)
- ☐ For patients who are earlier in the disease course, consider referral for nutrition, physical and occupational therapy support.
- ☐ Identify care plan for future appointments*
- ☐ Document referrals to other care providers*/information and/or support sources
  - o Document referral to hospice
  - o Advanced Directive
  - o DNR
- ☐ Document new medications prescribed*
- ☐ Document patient/caregivers primary concerns and/or issues

*Adapted from Supplemental Table 1: Ambulatory Palliative Care Guidelines Supplement to: Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non–small-cell lung cancer. N Engl J Med 2010;363:733-42.

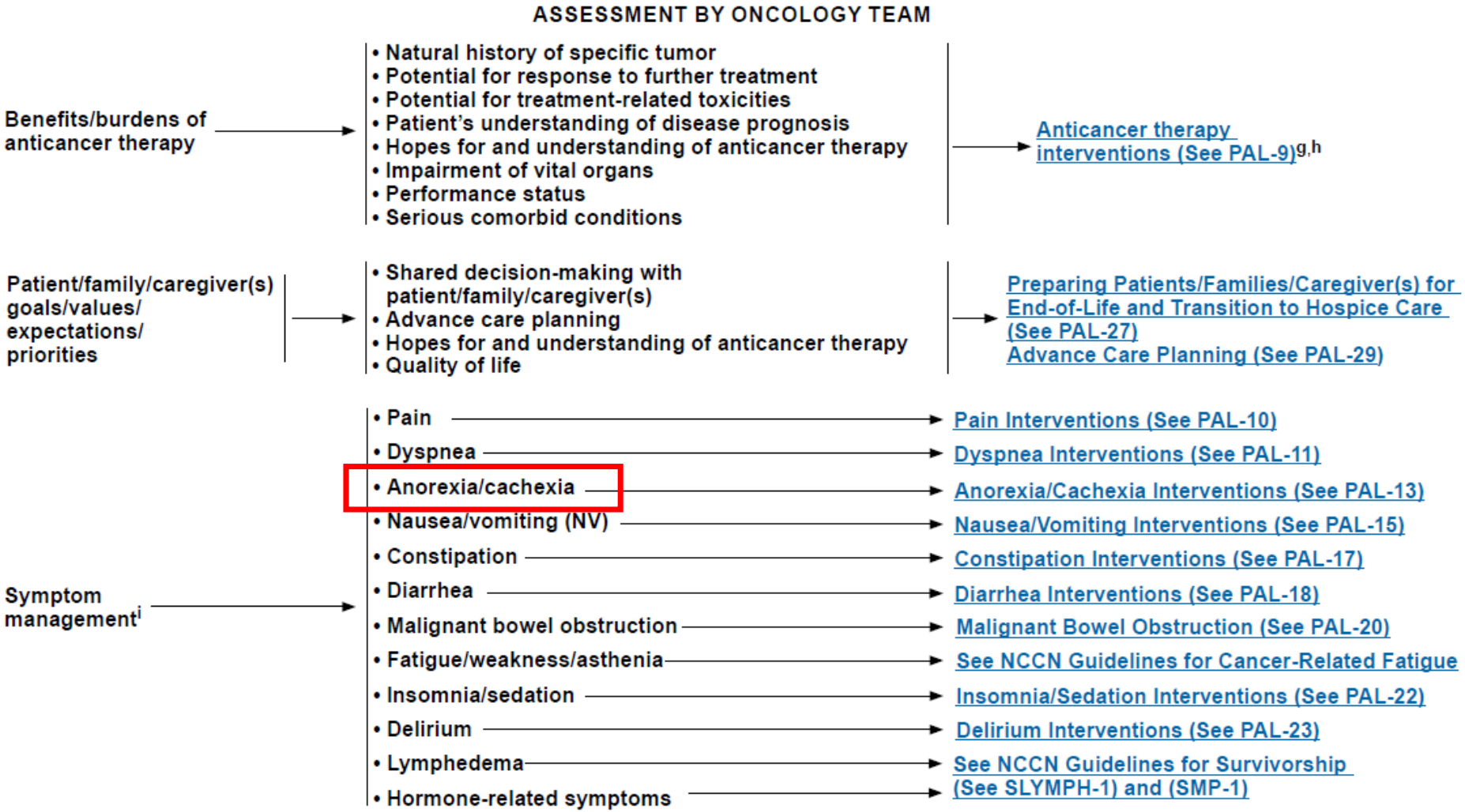
National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Palliative Care

Version 2.2021 — February 12, 2021

NCCN.org


ASSESSMENT BY ONCOLOGY TEAM
Benefits/burdens of anticancer therapy
• Natural history of specific tumor
• Potential for response to further treatment
• Potential for treatment-related toxicities
• Patient's understanding of disease prognosis
• Hopes for and understanding of anticancer therapy
• Impairment of vital organs
• Performance status
• Serious comorbid conditions
Anticancer therapy interventions (See PAL-9)g,h
Patient/family/caregiver(s) goals/values/ expectations/ priorities
• Shared decision-making with patient/family/caregiver(s)
• Advance care planning
• Hopes for and understanding of anticancer therapy
• Quality of life
Preparing Patients/Families/Caregiver(s) for End-of-Life and Transition to Hospice Care (See PAL-27)
Advance Care Planning (See PAL-29)
Symptom managementi
• Pain
Pain Interventions (See PAL-10)
• Dyspnea
Dyspnea Interventions (See PAL-11)
• Anorexia/cachexia
Anorexia/Cachexia Interventions (See PAL-13)
• Nausea/vomiting (NV)
Nausea/Vomiting Interventions (See PAL-15)
• Constipation
Constipation Interventions (See PAL-17)
• Diarrhea
Diarrhea Interventions (See PAL-18)
• Malignant bowel obstruction
Malignant Bowel Obstruction (See PAL-20)
• Fatigue/weakness/asthenia
See NCCN Guidelines for Cancer-Related Fatigue
• Insomnia/sedation
Insomnia/Sedation Interventions (See PAL-22)
• Delirium
Delirium Interventions (See PAL-23)
• Lymphedema
See NCCN Guidelines for Survivorship (See SLYMPH-1) and (SMP-1)
• Hormone-related symptoms

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Contents lists available at ScienceDirect

Clinical Nutrition

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

ESPEN Guideline

ESPEN practical guideline: Clinical Nutrition in cancer

Maurizio Muscaritoli [a, *], Jann Arends [b], Patrick Bachmann [c], Vickie Baracos [d], Nicole Barthelemy [e], Hartmut Bertz [b], Federico Bozzetti [f], Elisabeth Hütterer [g], Elizabeth Isenring [h], Stein Kaasa [i], Zeljko Krznaric [j], Barry Laird [k], Maria Larsson [l], Alessandro Laviano [a], Stefan Mühlebach [m], Line Oldervoll [n], Paula Ravasco [o], Tora S. Solheim [p], Florian Strasser [q], Marian de van der Schueren [r, s], Jean-Charles Preiser [t], Stephan C. Bischoff [u]

Outline: Nutrition intervention for cancer patients

- Introduction
- **Definition and Influence of cancer-related cachexia/malnutrition**
- Nutrition strategies
  - Special for chemotherapy: IV glutamine
  - General concepts: Fish oil (n-3 PUFA)
  - Guidelines
- Conclusion

Cachexia has detrimental consequences

1 in 5 patients with cancer dies from CACHEXIA

NOT FROM CANCER

TisdaleM.,*NatureRevCancer.*2002

Cancer Anorexia/Cachexia Syndrome (CACS)

- A complex metabolic syndrome, common among patients with cancer
- Anorexia:
  - Diagnosis: reduced appetite, early satiety, taste alterations and nausea
  - Often associated with reduced food intake
- Cachexia: physical wasting with loss of skeletal and visceral **muscle mass** resulting from negative protein and energy balance
- Characterized by loss of lean body mass and fat
- Anorexia contributes to cachexia.
- Cachexia can also occur independently from anorexia, as pro-inflammatory cytokines and tumor-derived factors directly lead to muscle proteolysis.

NCCN 2021

Weight Loss in CACS

- Very common among patients with cancer
- Often associated with inflammatory process, insulin resistance and increased tissue protein turnover rates
- Associated with poor tolerability of cancer treatment, progressive functional impairment, reduced quality of life and survival
- **Cannot be fully reversed by conventional nutritional support**

Tuca et al. (2013). Clinical evaluation and optimal management of cancer cachexia. Critical Reviews in Oncology/Hematology, 88:625-636. NCCN 2016.

Incidence of weight loss in cancers of different sites

Tumor site	Incidence of weight loss (%)
Pancreas	83
Gastric	83
Esophagus	79
Head and neck	72
Colorectal	55–60
Lung	50–66
Prostate	56
Breast	10–35
General cancer population	63

LAVIANO ET AL. NATURE CLINICAL PRACTICE ONCOLOGY 2005

Diagnosis and Assessment of CACS

- The amount of weight loss that indicates a risk of CACS is:
  - more than 10% in the last 6 months OR
  - 5% in less than one month
- A BMI of less than 20 kg/m2 is a criterion for malnutrition
- Biological values such as albumin, prealbumin, transferrin and C-reactive protein can provide valuable information about nutritional status
  - **Albumin** less than 3.2 g/dl indicates protein depletion and risk of malnutrition
  - Prealbumin-more sensitive than albumin. Prealbumin of <10 mg/dl indicates malnutrition
  - Transferrin decreased in CACS and a value of <100 mg/dl indicates severe malnutrition
  - **C-reactive protein** > 0.5 mg/dl

Tuca et al.(2013). Clinical evaluation and optimal management of cancer cachexia. *Critical Reviews in Oncology/Hematology,88:625-636.*

Stages of cancer-related cachexia

	Precachexia	Cachexia	Refractory Cachexia	
Normal				Death
	Weight loss ≤5% Anorexia and metabolic change	Weight loss >5% **or** BMI <20 and weight loss >2% **or** sarcopenia and weight loss >2%. Often reduced food intake Systemic inflammation	Cancer both procatabolic and not responsive to anticancer treatment Low performance score <3 months expected survival	

Fearon K, Strasser F, Anker S, et al. (2011). Definition and classification of cancer cachexia: an international consensus. *The Lancet Oncology*,12:489-495

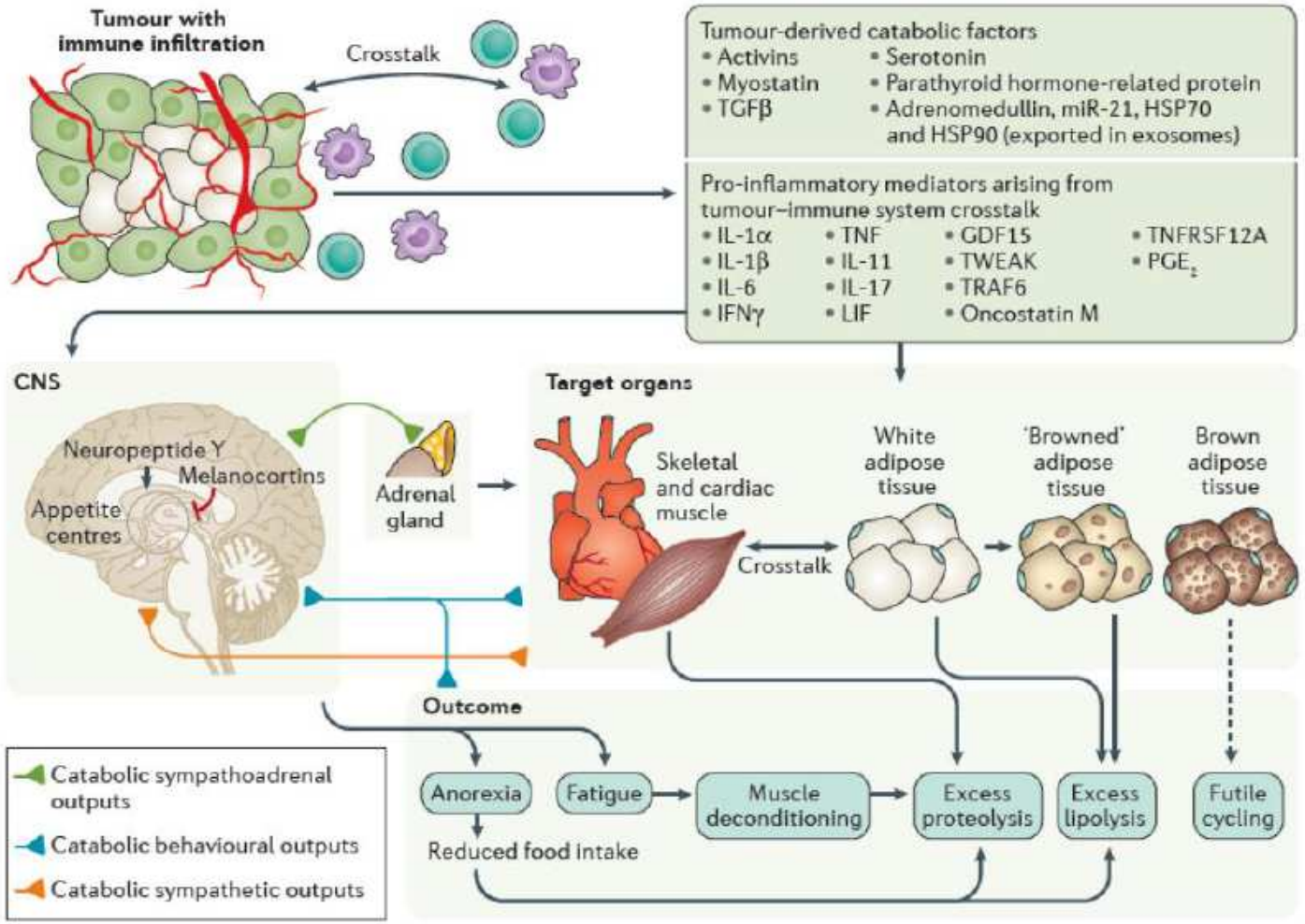
Epidemiology of CACS

- Overall prevalence of CACS:
  - 40% at diagnosis
  - 70-80% in late stages of disease
- Survival of patients with cachexia significantly shorter than those without cachexia –in stomach, pancreatic, prostate, colon, and breast cancer
- **Risk of CACS** higher when treated with radiotherapy and chemotherapy in esophageal, lung, and head and neck cancers due to swallowing disorders and mucositis
- CACS can be direct cause of death in more than 20% of patients with cancer

Muliawati et al. (2012). Cancer Anorexia-Cachexia Syndrome. Acta Medica Indonesiana. 44:153-162.

Cancer-associated cachexia

Vickie E. Baracos[1], Lisa Martin[2], Murray Korc[3], Denis C. Guttridge[4] and [1]Kenneth C. H. Fearon[5]



Nat Rev Dis Primer 2018; 4:17105

Cachexia

- Leads to asthenia (weakness), emaciation, immune system impairment, metabolic dysfunction, and autonomic failure
- Cachexia in the patient with cancer can lead to:
  - Failure of anti-cancer therapy
  - Increased toxicity from treatment
  - Delayed treatment initiation
  - Early treatment termination
  - Psychosocial distress
  - **Shorter survival**

NCCN 2021

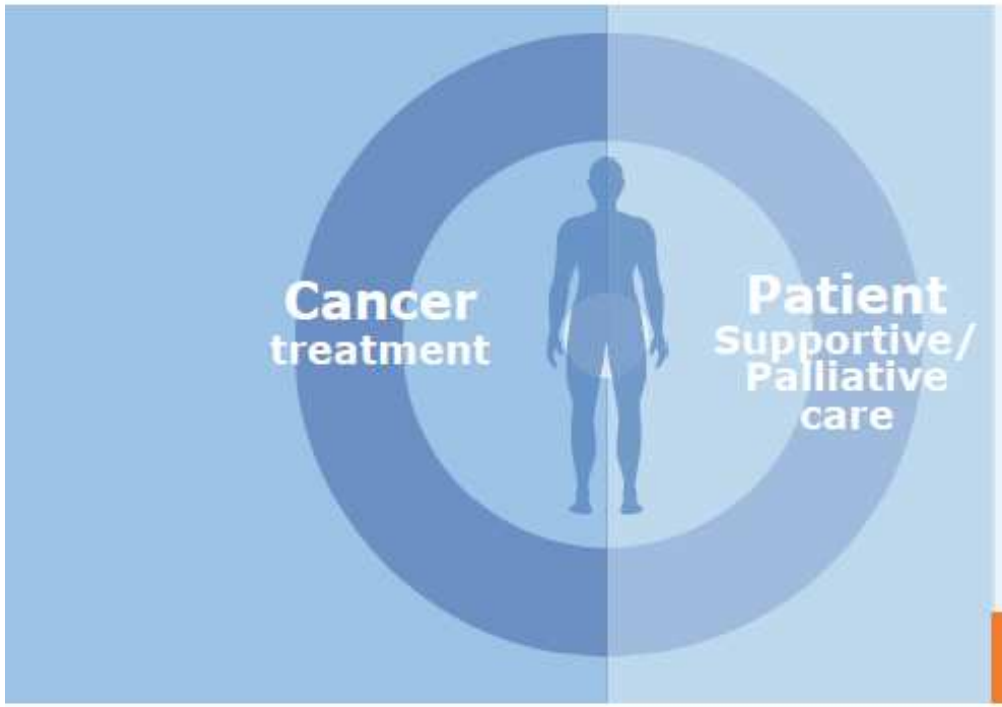
Treatment of CACS

- Treatment of CACS based on 3 factors:
  - Oncologic therapy
  - **Nutritional support**
  - Pharmacological treatment

Tucaet al. (2013). Clinical evaluation and optimal management of cancer cachexia. Critical Reviews in Oncology/Hematology, 88:625-636.

Treatment of cancer

Supportive/Palliative care



Prophylaxis/ treatment of side effects

- Nausea/vomiting
- Mucositis
- Anemia
- Neutropenia

Pain management

Psycho-oncological treatment

Exercise/physical activity

Nutritional support

- Oral nutritional supplements
- Enteral
- Parenteral

Nutrition is an integral component of supportive care.

Malnutrition: definition and impact

- Malnutrition is a condition that results from eating a diet which does not supply a healthy amount of one or more nutrients (Wikipedia).
- Malnutrition is a common feature in cancer patients and is the consequence of both the presence of the tumor and the medical and surgical anticancer treatments.
- Malnutrition negatively impacts on quality of life and treatment toxicities, and it has been estimated that up to 10-20% of cancer patients die due to consequences of malnutrition rather than for the tumor itself.
- **Thus, nutrition plays a crucial role in multimodal cancer care.**

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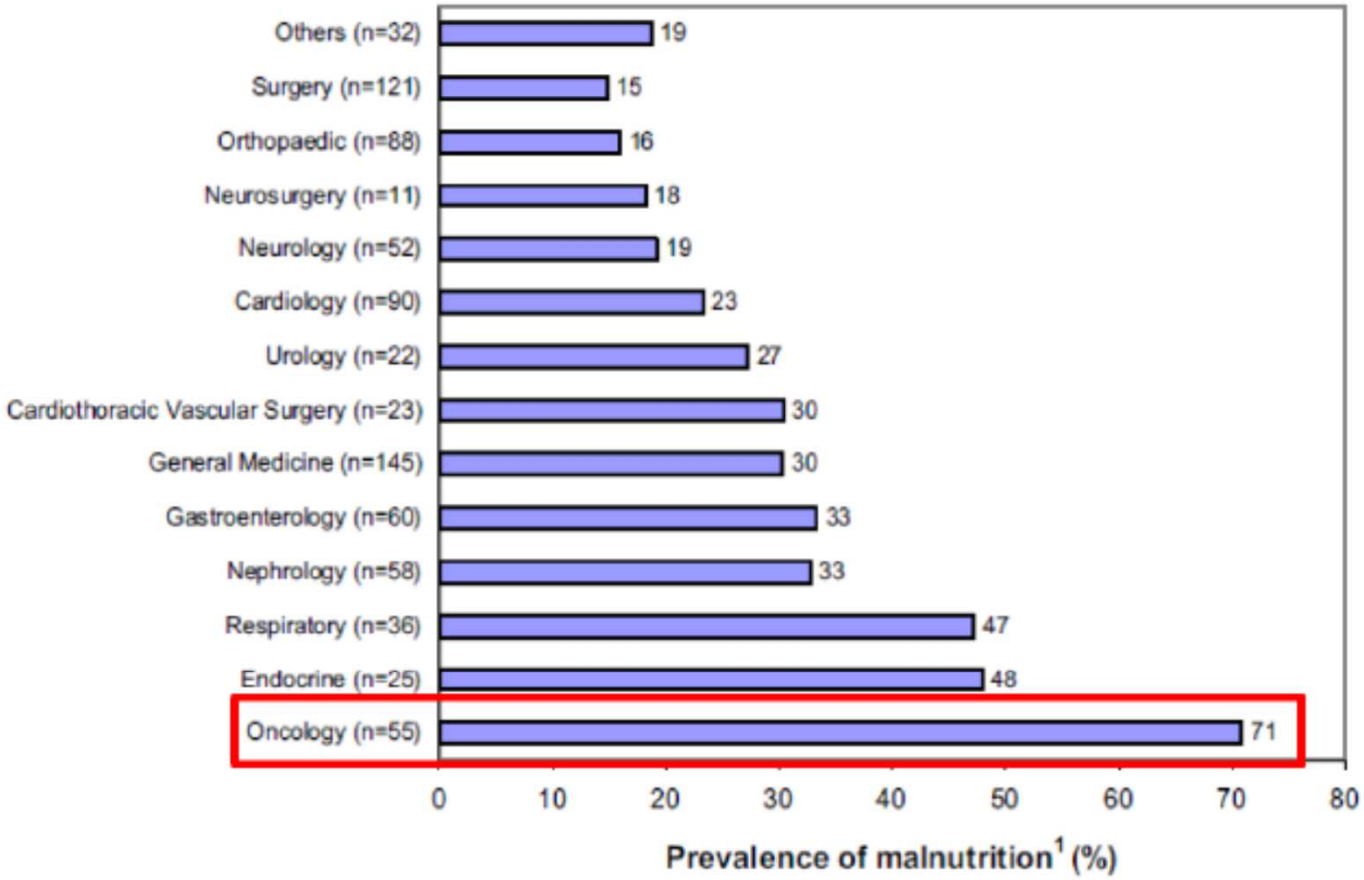
Prevalence of malnutrition

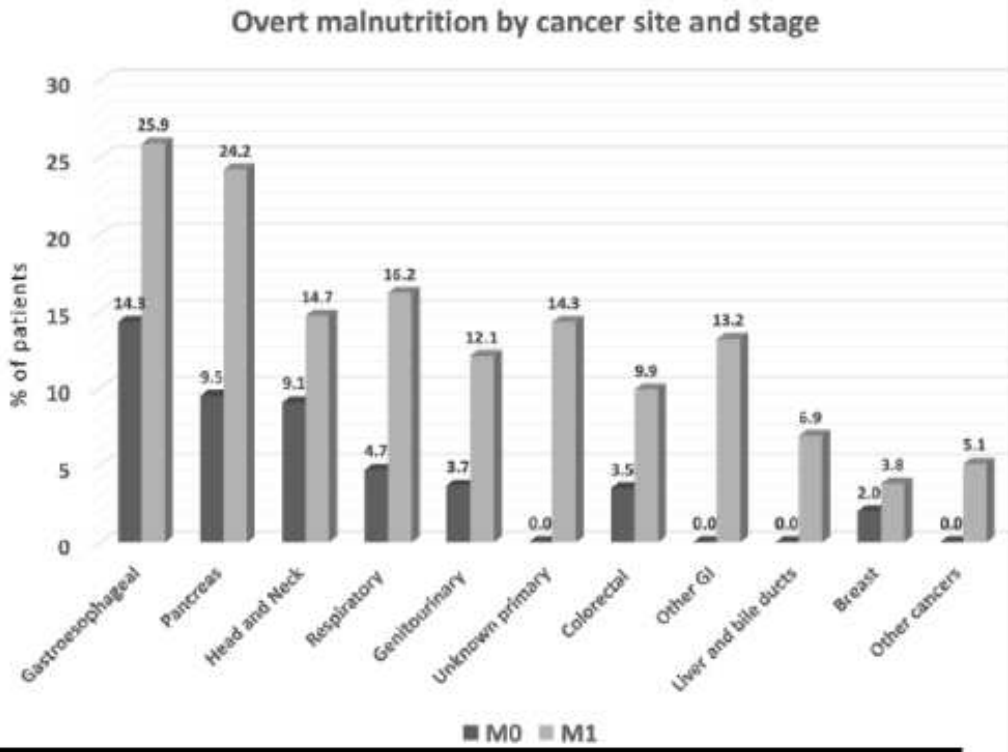


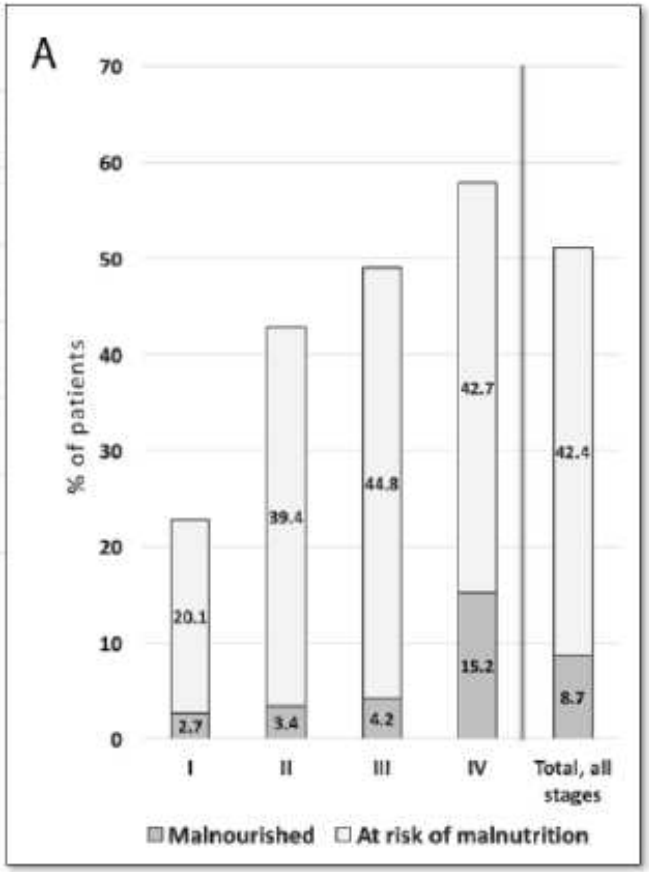
. Prevalence of malnutrition by specialties ($n = 818$). [1]Malnutrition was determined with Subjective Global Assessment within 48 h of hospital admission.

LimSL,etal,ClinicalNutrition.2012

Clinical Research Paper

Prevalence of malnutrition in patients at first medical oncology visit: the PreMiO study





Malnutrition, anorexia, and weight loss are common in cancer patients, even at their first visit to a medical oncology center

Muscaritoli M. et al. Oncotarget, 2017, Vol. 8, (No. 45), pp: 79884-79896

Malnutrition is the strongest independent risk factor for performance status

2373 men and 1382 women

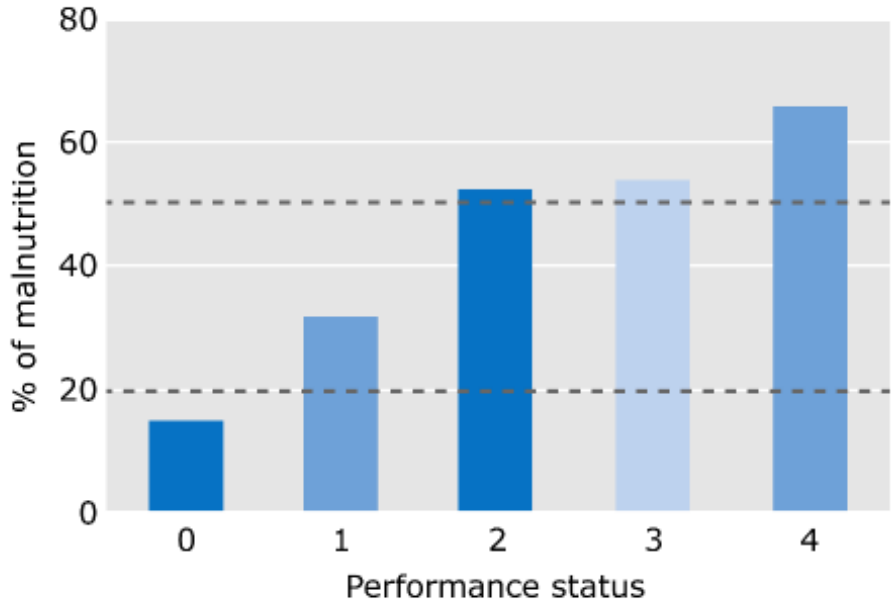
Risk factors	OR	[95%CI]	p value
Malnutrition SGA-C	22.6	11.6-44	0.000
Malnutrition SGA-B	3.3	1.8-5.9	0.000
Anemia Severe	3.5	1.7-7.5	0.000
Anemia Moderate	0.9	0.7-1.2	0.703
Low albumin	1.9	1.6-2.3	0.000
Low BMI	1.3	1.1-1.6	0.001
Old age	3.2	2.2-4.5	0.000

*Subjective Global Assessment (SGA)

Nair et al. ASCO Paper, JCO 2008;26:7S:A9628

Cancer associated malnutrition impacts performance status

Malnutrition is strongly associated with performance status and probably is the determining factor of its deterioration.



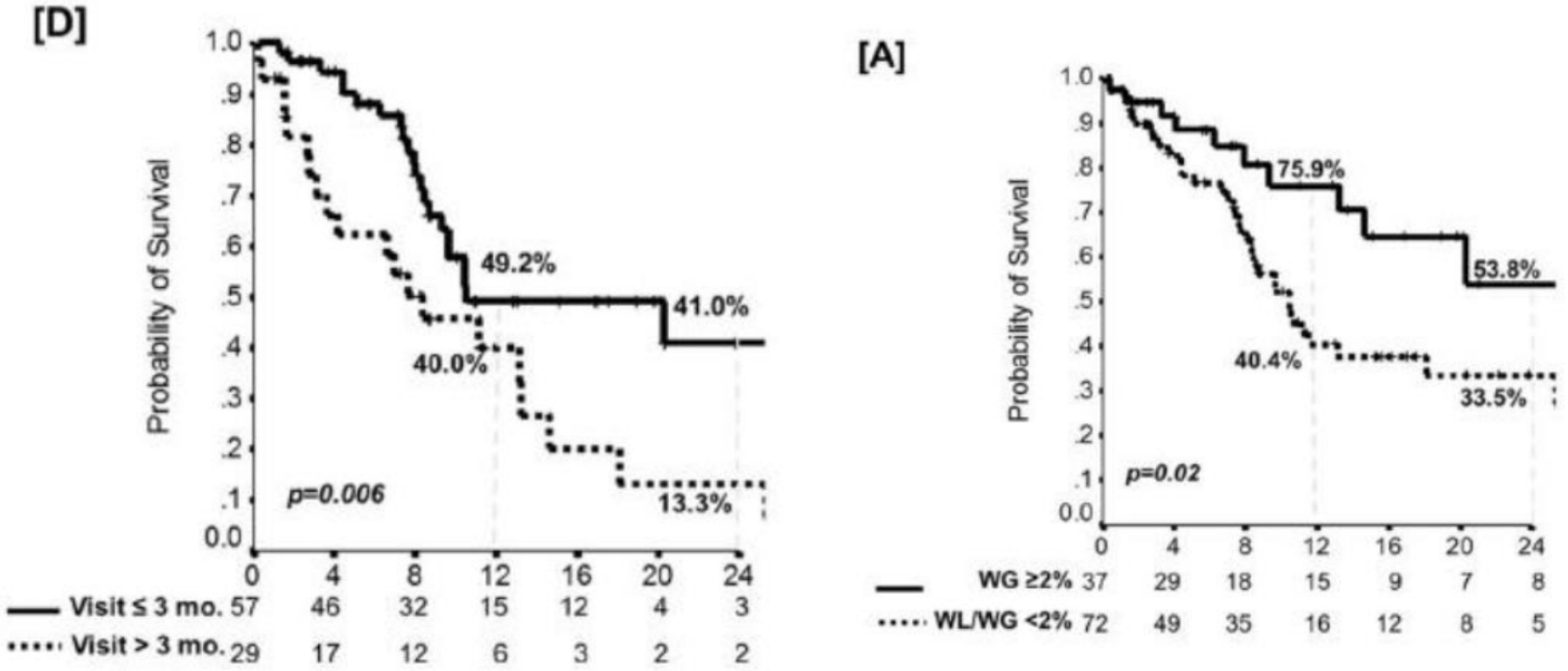
Prevalence of malnutrition in patients with performance status 0 to 4.

- Percentage of malnutrition highest in patients with PS 4 (~ 65 %) and PS 2-3 (~ 50 %).
- Even in the group of patients with PS 0-1, approximately 25 % are malnourished.

Modified from Cessot A et al.
Support Care Cancer 2011;19:869–870.

Evaluation of nutritional status should be part of the risk assessment prior to chemotherapy.

Prognostic impact of early nutritional support in patients affected by locally advanced and metastatic pancreatic ductal adenocarcinoma undergoing chemotherapy



Trestini I et al. Eur J Clin Nutr 2018

Published OnlineFirst June 11, 2018; DOI: 10.1158/1078-0432.CCR-18-0415

Clinical Trials: Immunotherapy

Clinical Cancer Research

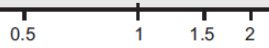
Pembrolizumab Exposure–Response Assessments Challenged by Association of Cancer Cachexia and Catabolic Clearance

David C. Turner[1], Anna G. Kondic[1], Keaven M. Anderson[1], Andrew G. Robinson[2], Edward B. Garon[3], Jonathan Wesley Riess[4], Lokesh Jain[1], Kapil Mayawala[1], Jiannan Kang[1], Scot W. Ebbinghaus[1], Vikram Sinha[1], Dinesh P. de Alwis[1], and Julie A. Stone[1]

OS HRs

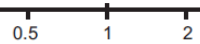
A Melanoma

Variable	HR	Point estimate (95% CI)
Baseline Sum of the Longest Diameter of the Target Lesions (BSLD)		1.3368 (1.1598–1.5407)
Tumor PD-L1 Expression Positivity (PDL1)		0.4700 (0.3263–0.6770)
Platelet Count (PLT)		1.3008 (1.1232–1.5064)
On-study Rate of Weight Change (WTRATE)		0.8033 (0.6950–0.9286)
Serum Albumin (ALB)		0.7929 (0.6559–0.9587)
$BRAF^{V600}$ Mutation Status (BRAF)		0.5950 (0.4103–0.8629)
ECOG Performance Status (ECOG)		1.4280 (0.9980–2.0432)



B NSCLC

Variable	HR	Point estimate (95% CI)
On-study Rate of Albumin Change (ALBRATE)		0.2793 (0.2117–0.3684)
Serum Albumin (ALB)		0.7030 (0.6207–0.7962)
On-study Rate of Weight Change (WTRATE)		0.7306 (0.6467–0.8254)
Lactate Dehydrogenase (LDH)		1.1697 (1.0941–1.2505)
Squamous Histology (SQUAM)		1.9428 (1.4454–2.6113)
Male Gender (MALE)		0.7094 (0.5450–0.9233)
Baseline Sum of the Longest Diameter of the Target Lesions (BSLD)		1.1551 (1.0188–1.3097)
ECOG Performance Status (ECOG)		1.2952 (0.9782–1.7149)



CCR 2018

Published OnlineFirst July 17, 2018; DOI: 10.1158/1078-0432.CCR-18-1847

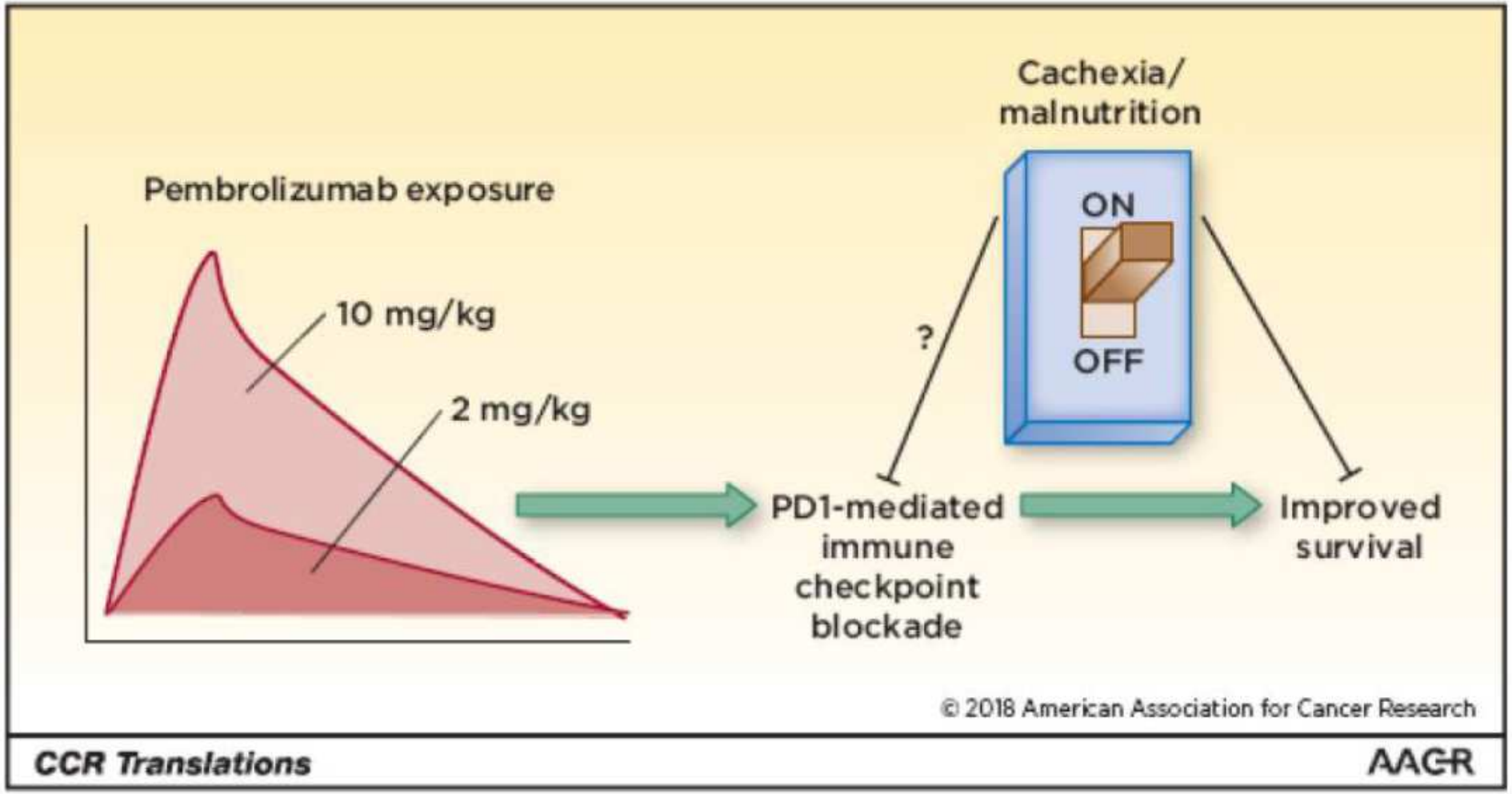
CCR Translations

Clinical Cancer Research

Cachectic Cancer Patients: Immune to Checkpoint Inhibitor Therapy?

Christopher C. Coss[1,2], Steven K. Clinton[2,3], and Mitch A. Phelps[1,2]

Cachectic cancer patients exhibit elevated pembrolizumab clearance and poor response, highlighting the immense therapeutic challenge posed by cancer cachexia. Clin Cancer Res; 24(23); 5787–9, 2018



Coss CC et al. Clin Cancer Res 2018

Outline: Nutrition intervention for cancer patients

- Introduction
- Definition and Influence of cancer-related cachexia/malnutrition
- Nutrition strategies
  - **Special for chemotherapy: IV glutamine**
  - General concepts: Fish oil (n-3 PUFA)
  - Guidelines
- Conclusion

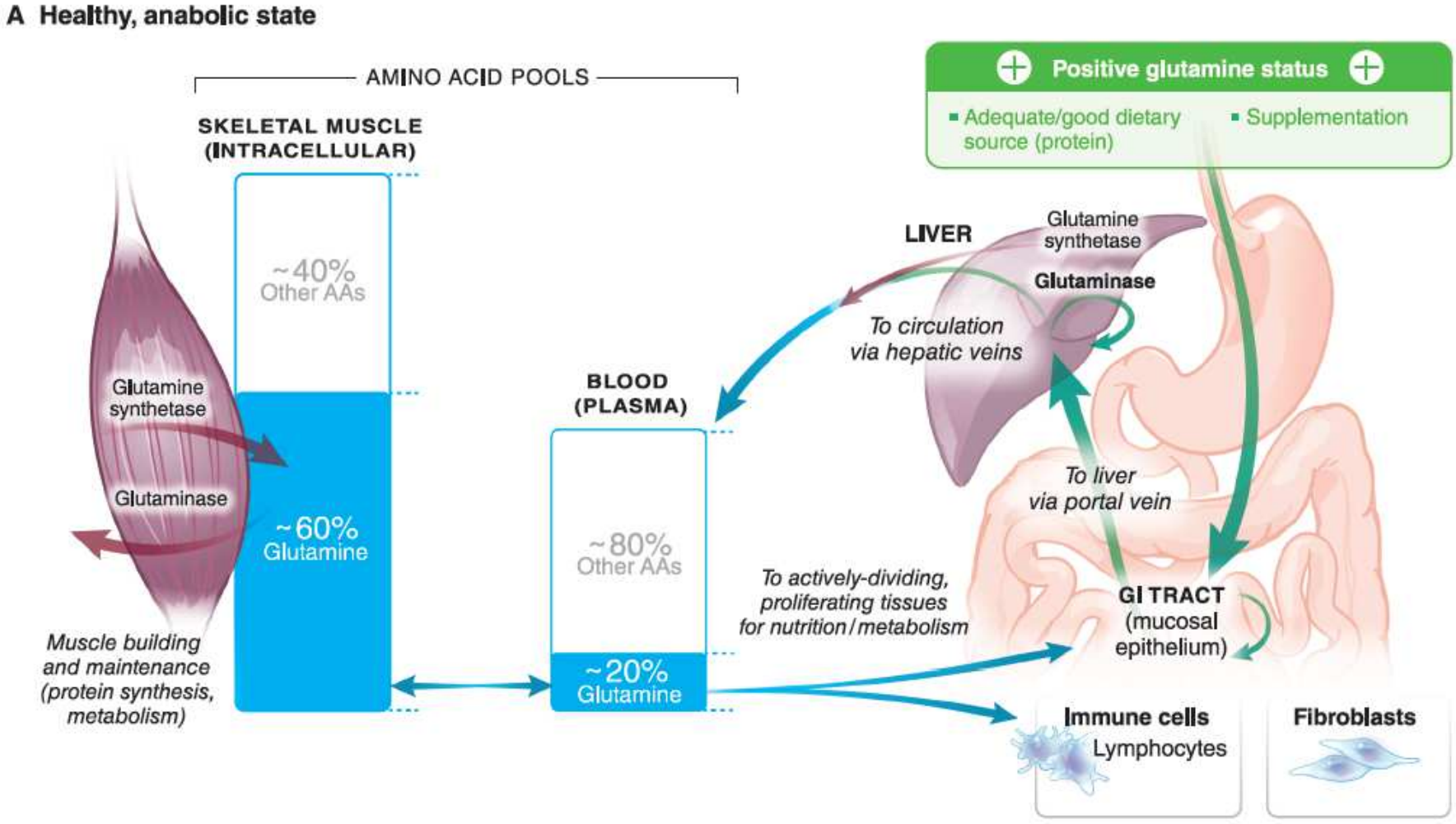
ESPEN practical guideline 2021 for glutamine

30) There are insufficient consistent clinical data to recommend glutamine to prevent radiation-induced enteritis/diarrhea, stomatitis, esophagitis or skin toxicity. (Recommendation C2-4; strength of recommendation none – Level of evidence low – strong consensus)

34) There are insufficient consistent clinical data to recommend glutamine supplementation during conventional cytotoxic or targeted therapy. (Recommendation C3-3; strength of recommendation none – Level of evidence low – strong consensus)

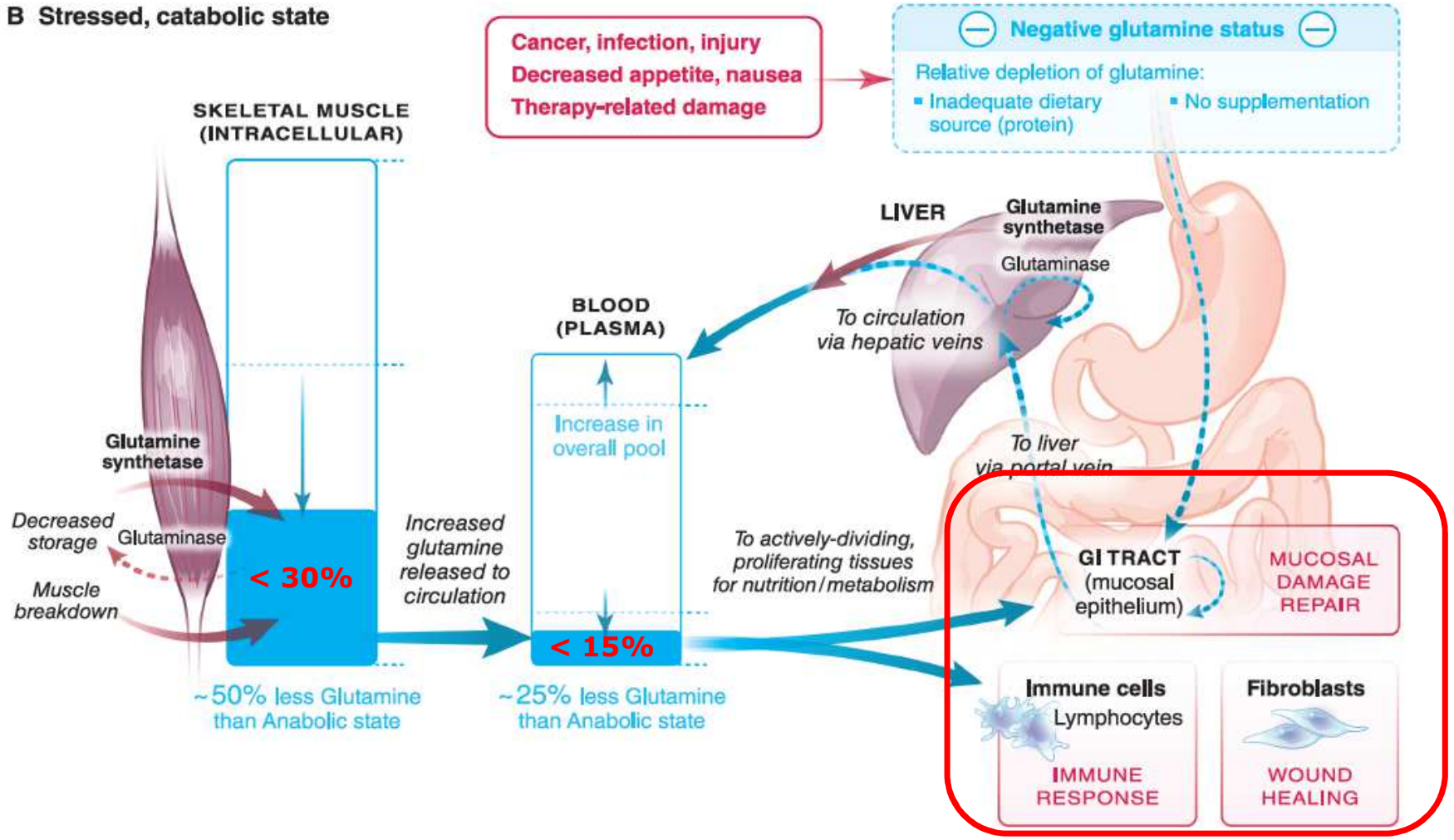
38) There are insufficient consistent clinical data to recommend glutamine to improve clinical outcome in patients undergoing high-dose chemotherapy and HSCT. (Recommendation C4-4; strength of recommendation none – Level of evidence low – strong consensus)

Healthly & Anabolic state of glutamine reserve



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

Catabolic state: glutamine level decreasing in muscle and blood



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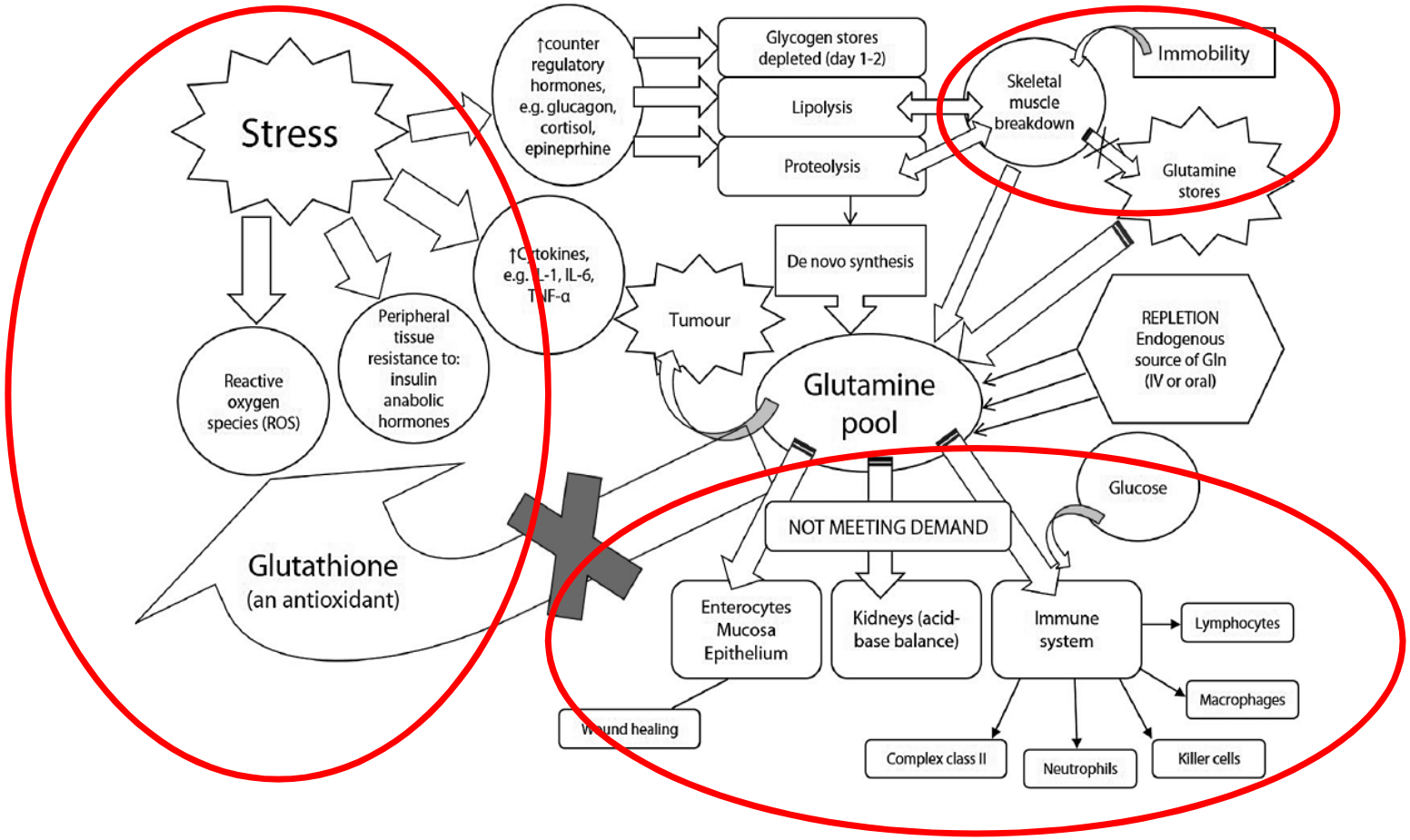
The depletion of GLN during stress, and its consequences



Reinette Tydeman-Edwardsa. South African Journal of Clinical Nutrition 2017; 30(4):109–117

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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[3]*Division of Colorectal Surgery, Chang Gung Memorial Hospital, Keelung and Chang Gung University, College of Medicine, Taiwan*
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[5]*Division of Hemato-oncology, Department of Internal Medicine, Chang Gung Memorial Hospital, Kweishan and Chang Gung University, College of Medicine, Taiwan*

Lower serum glutamine level in advanced colon cancer

腫瘤引發全身性發炎反應導致病患營養耗損，當腫瘤發展至愈晚期病患血中發炎指數CRP會愈高、Glutamine濃度愈低、Albumin也愈低[3]。

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*
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*
3-year progression-free survival rate (%)	76.2	100	93.3	73.2	19.2	<0.001

nutrients

MDPI

Article

Clinical Significance of Serum Glutamine Level in Patients with Colorectal Cancer

Hang Huong Ling [1], Yi-Ping Pan [2], Chung-Wei Fan [3], Wen-Ko Tseng [3], Jen-Seng Huang [1], Tsung-Han Wu [1], Wen-Chi Chou [4], Cheng-Hsu Wang [1], Kun-Yun Yeh [1] and Pei-Hung Chang [1,*]

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4 Division of Hemato-oncology, Department of Internal Medicine, Chang Gung Memorial Hospital, Linkou and Chang Gung University, College of Medicine, Taoyuan 333, Taiwan; wenchi3992@yahoo.com.tw

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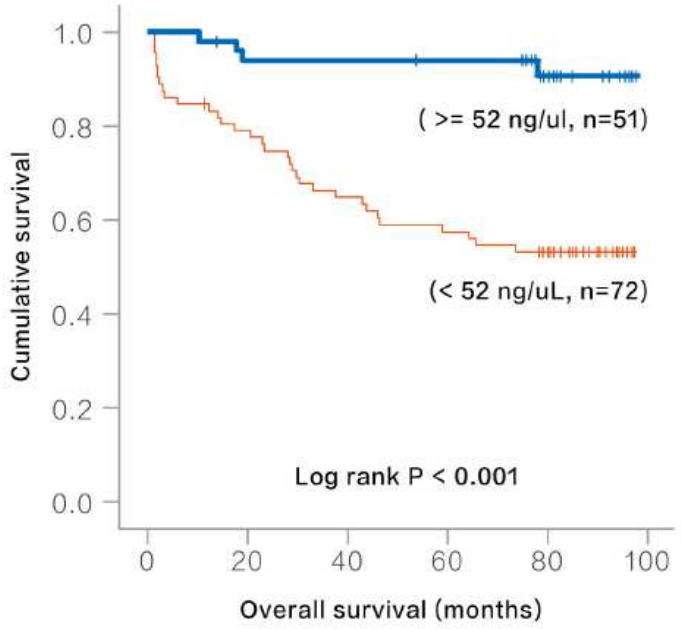
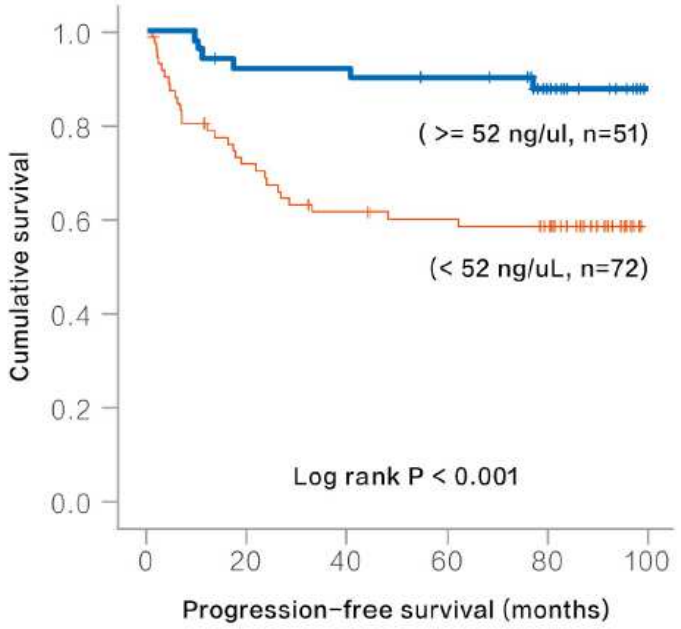
Glutamine level impact overall and progression-free survival

2019 Hang Huong Ling et al.的文獻進一步分析也發現，大腸直腸癌患者血中Glutamine濃度越低，五年整體存活率(57.7% vs. 94%) 及無疾病惡化存活率(60.1% vs. 90.1%)也愈低[4]



No. at risk:

High	51	47	47	46	17	0
Low	72	56	45	40	32	0



No. at risk:

High	51	46	46	44	16	0
Low	72	50	42	40	32	0

Dipeptiven: Product characteristics

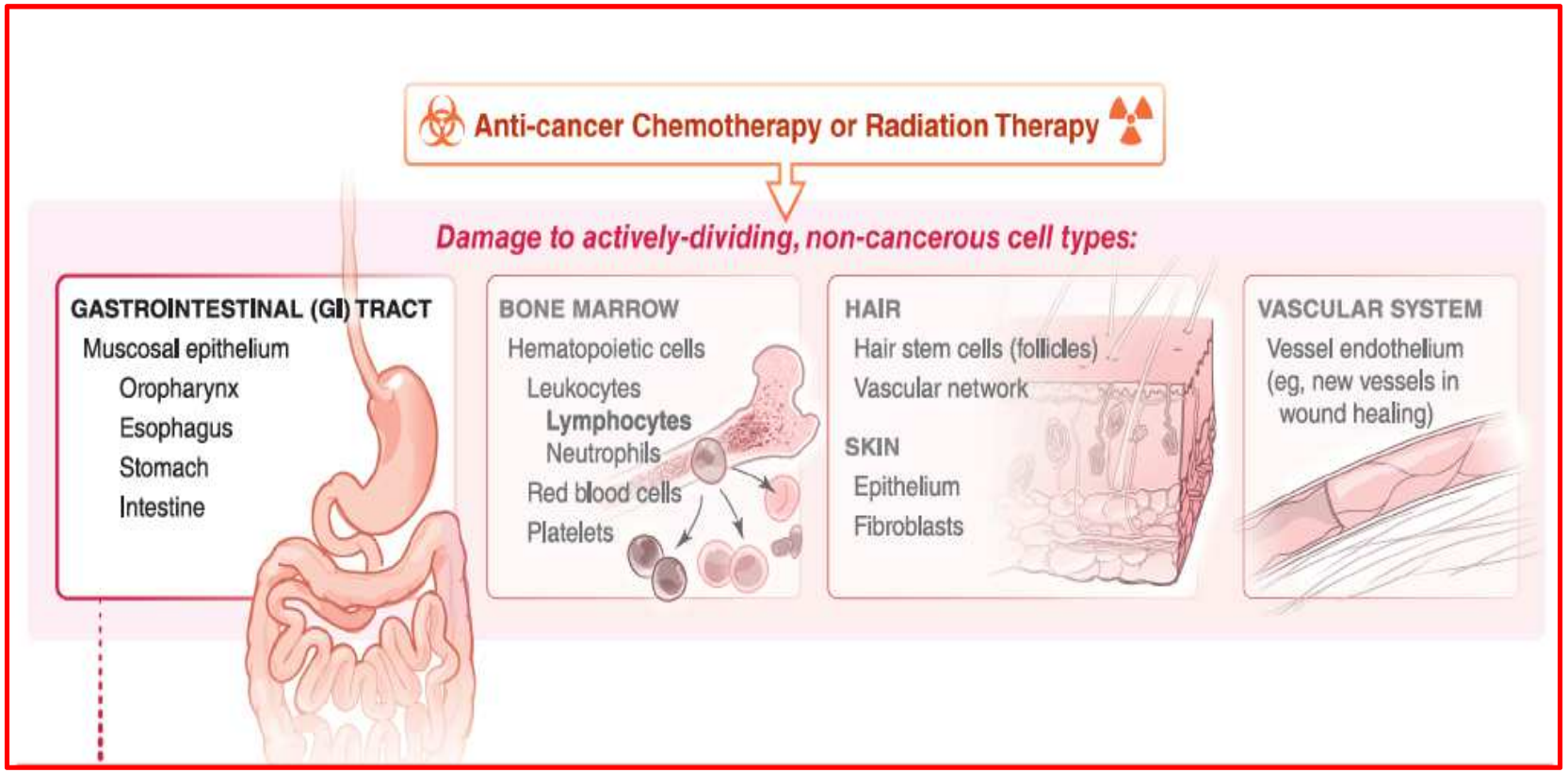
- **20%** infusion solution concentrate containing dipeptide alanyl-glutamine
- **100 ml contains:** 20 g N(2)-**L-alanyl-L-glutamine**

  = **13.46 g glutamine**, 8.20 g alanine
- A clear colorless solution
- Available in glass bottles of 50 ml and 100ml
- Solution for infusion after mixture with a compatible infusion solution.

IV glutamine (Dipeptiven)雙胜胺對外科病患臨床益處

- 提高術後血中麩醯胺濃度，減少傷口癒合時間。
- 促進正氮平衡、減少住院天數及死亡率。
- 改善術後病患營養狀態及恢復腸胃道正常功能。
- 提升病患前白蛋白(Prealbumin)及淋巴球細胞數量。

Chemotherapy Associated Mucositis during Cancer Therapy



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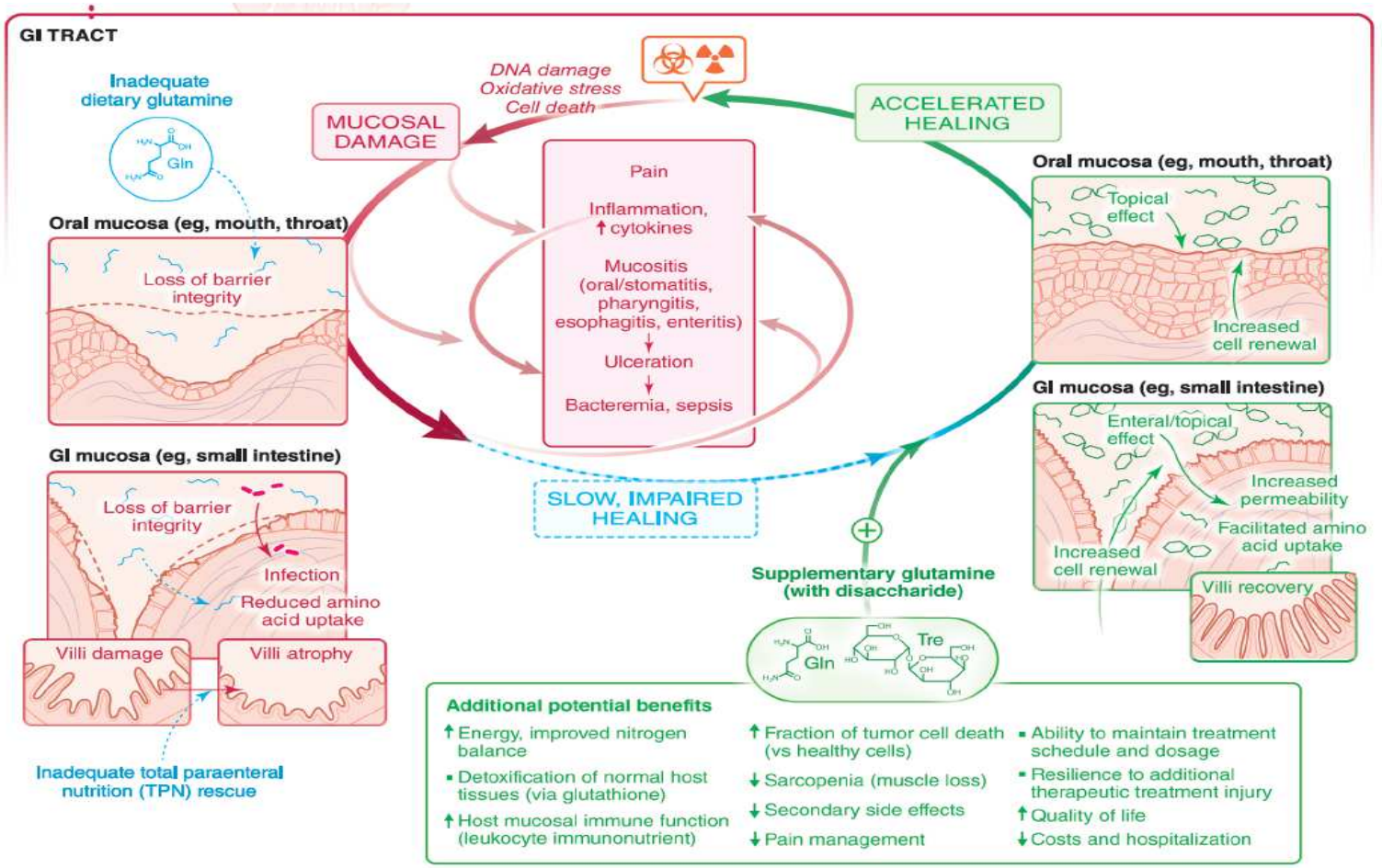
Supplementary glutamine may ameliorate these side effects of cancer therapy



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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

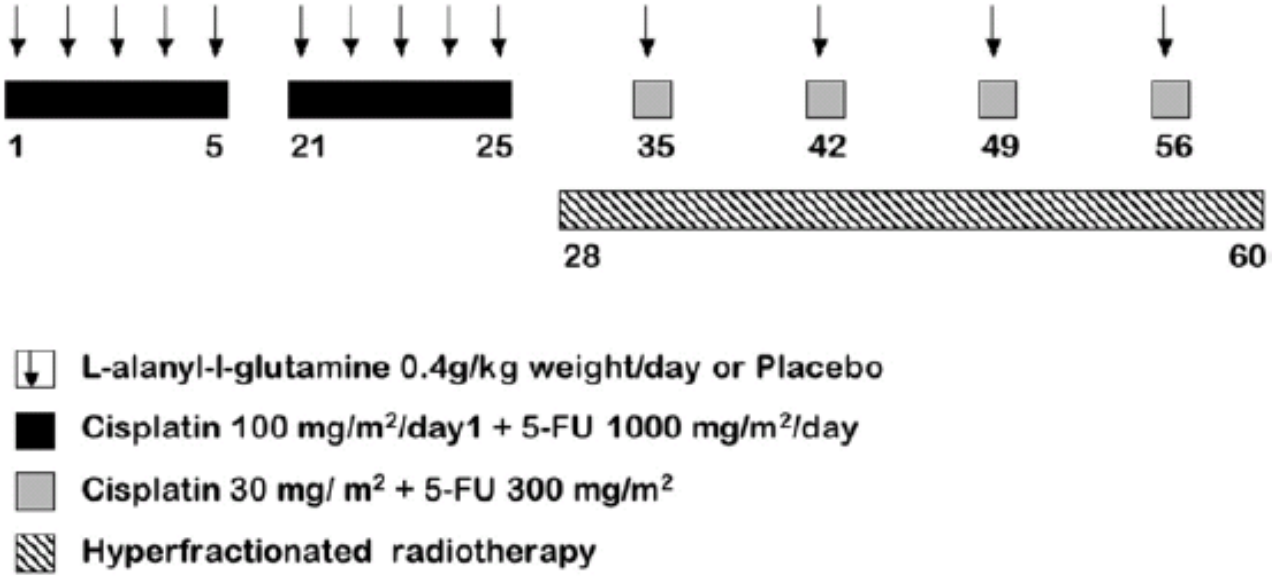
LEANDRO C. A. CERCHIETTI, M.D.,* ALFREDO H. NAVIGANTE, M.D., PH.D.,*†
MARIBEL A. LUTTERAL, M.D.,† MONICA A. CASTRO, M.D.,* RICARDO KIRCHUK, M.D.,†
MARCELO BONOMI, M.D.,*‡ MARIA ESTHER CABALAR, M.D.,† BERTA ROTH, M.D.,‡
GRACIELA NEGRETTI, PHARM.D.,§ BEATRIZ SHEINKER, PHARM.D.,§ AND PATRICIA UCHIMA, PHARM.D.§

*Translational Research Unit, †Internal Medicine Department, ‡Radiotherapy Department, §Pharmacy Department, Instituto de Oncologia Angel H. Roffo, Universidad de Buenos Aires, Buenos Aires, Argentina

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 Radiat Oncol Biol Phys. 2006 Aug 1;65(5):1330-7.

Schedule of the antineoplastic and intervention treatments (n=32)



Int J Radiat Oncol Biol Phys. 2006 Aug 1;65(5):1330-7.

Dipeptiven相較於安慰組能大幅降低45%因化放療引起嚴重口腔黏膜炎(WHO grade ≧ 3)發生率

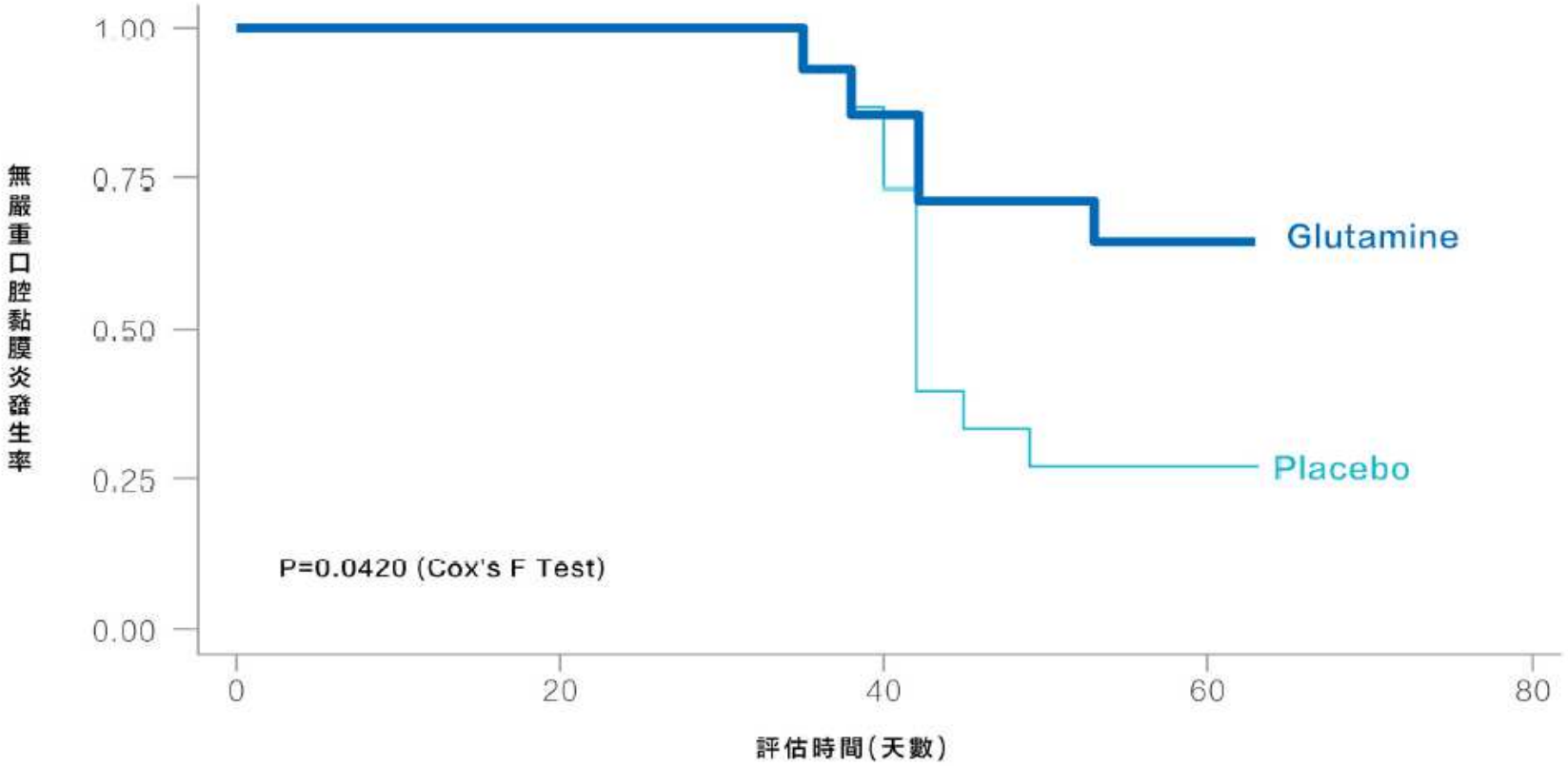


Fig. 6. Patients free of severe mucositis (World Health Organization score ≥3) (Kaplan–Meier survival curve).

Int J Radiat Oncol Biol Phys. 2006 Aug 1;65(5):1330-7

雙胜胺能緩解化療引起的口腔黏膜炎(Mucositis)[5]

Dipeptiven與化放療合併使用，相較於安慰組
能有效解緩病患疼痛感及減少使用止痛劑

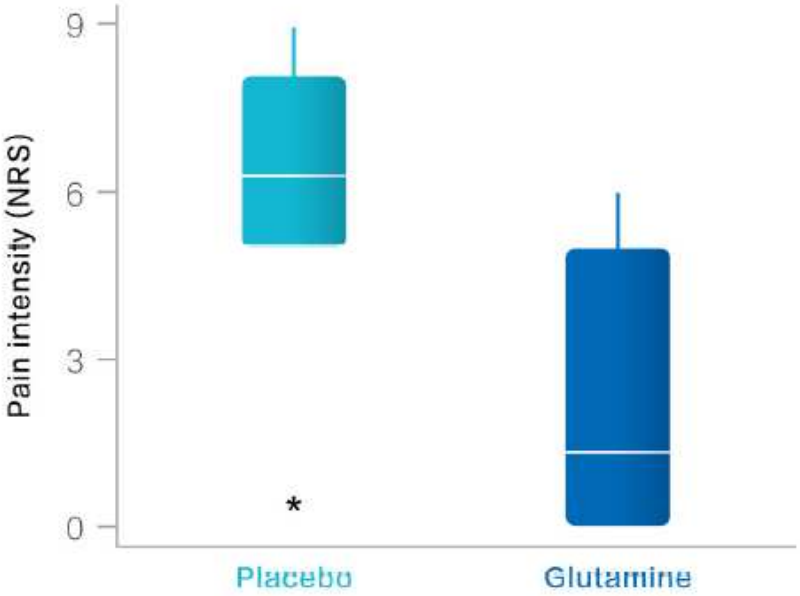


Fig. 4. Intensity of pain (mean of three highest Numeric Rating Scale [NRS] scores) in the glutamine and placebo groups.
p = 0.008, Wilcoxon rank sum test.

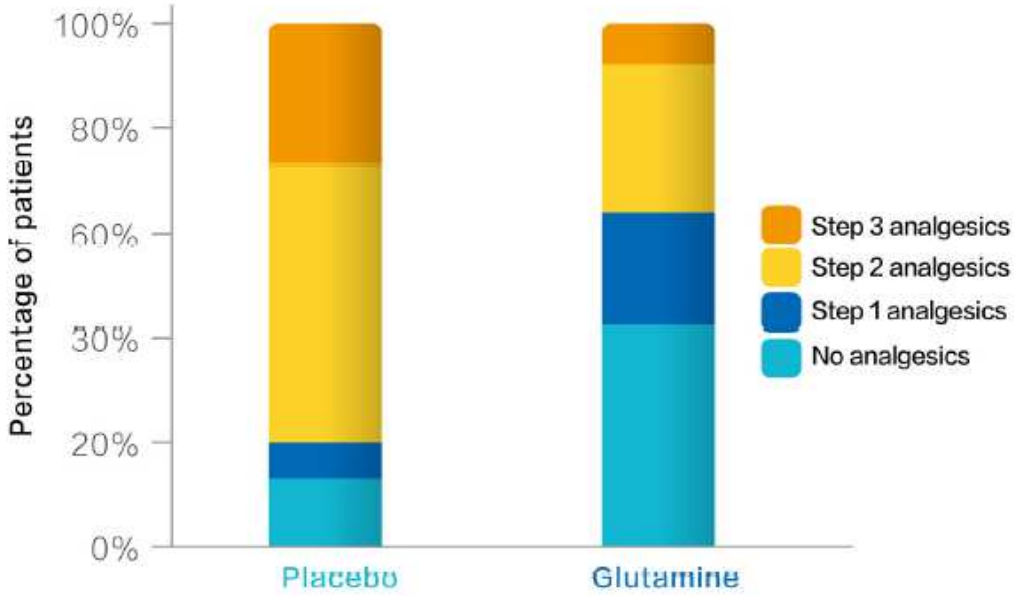


Fig. 5. Need for analgesia in the glutamine and placebo groups.
p= 0.025, Fisher exact test, for opioids (step 2 and step 3) vs. no analgesics or step 1 analgesics.

Int J Radiat Oncol Biol Phys. 2006 Aug 1;65(5):1330-7

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

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[2]Surgical Oncology Department, South Egypt Cancer Institute, Assiut University, Assiut, Egypt
[3]Diagnostic Radiology Department, South Egypt Cancer Institute, Assiut University, Assiut, Egypt
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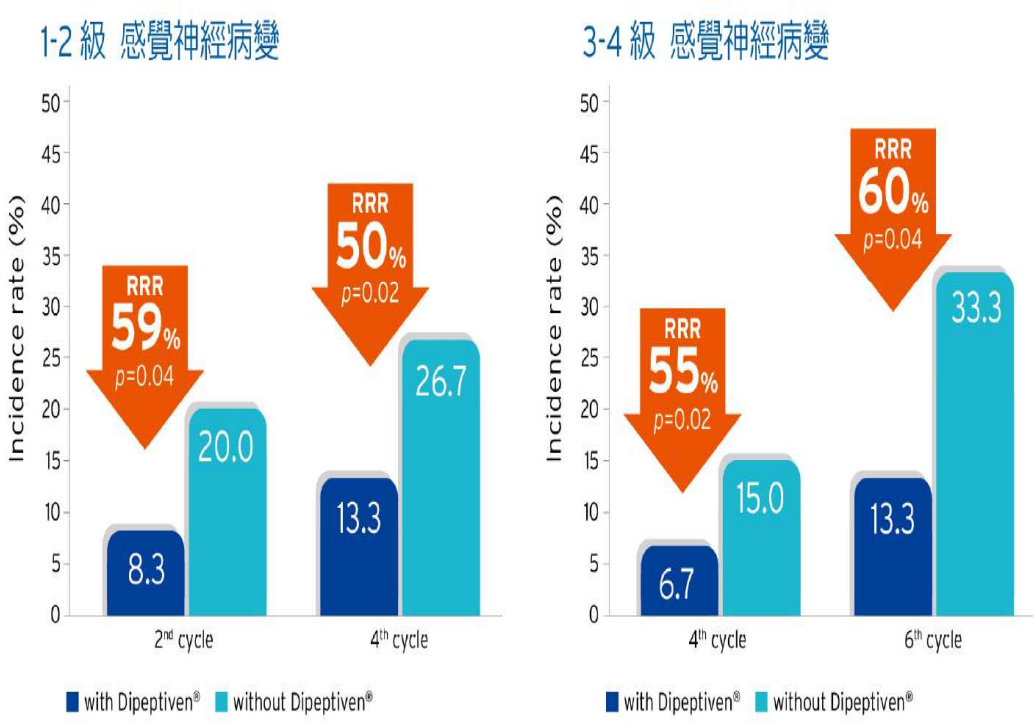
Purpose and Methods

- **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:**
  - 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.

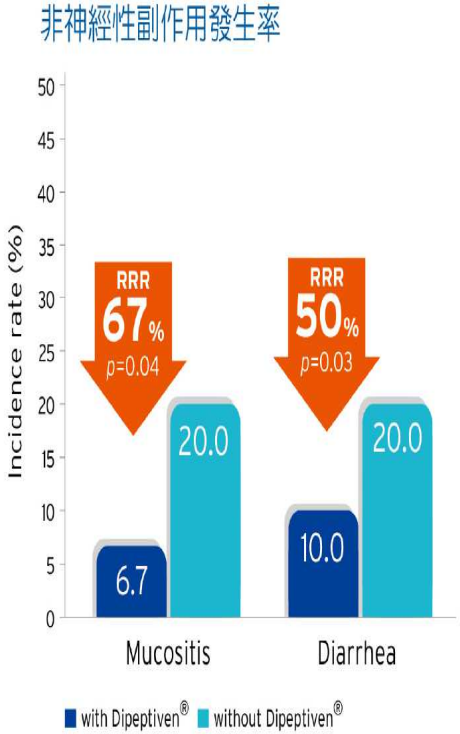
Journal of Cancer Therapy, 2016, 7, 609-621

Results

近期一項癌症*研究顯示，Oxaliplatin 化療療程配合使用 Dipeptiven®，能有效降低 **50%** 以上因化療藥物引起的神經毒性副作用



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

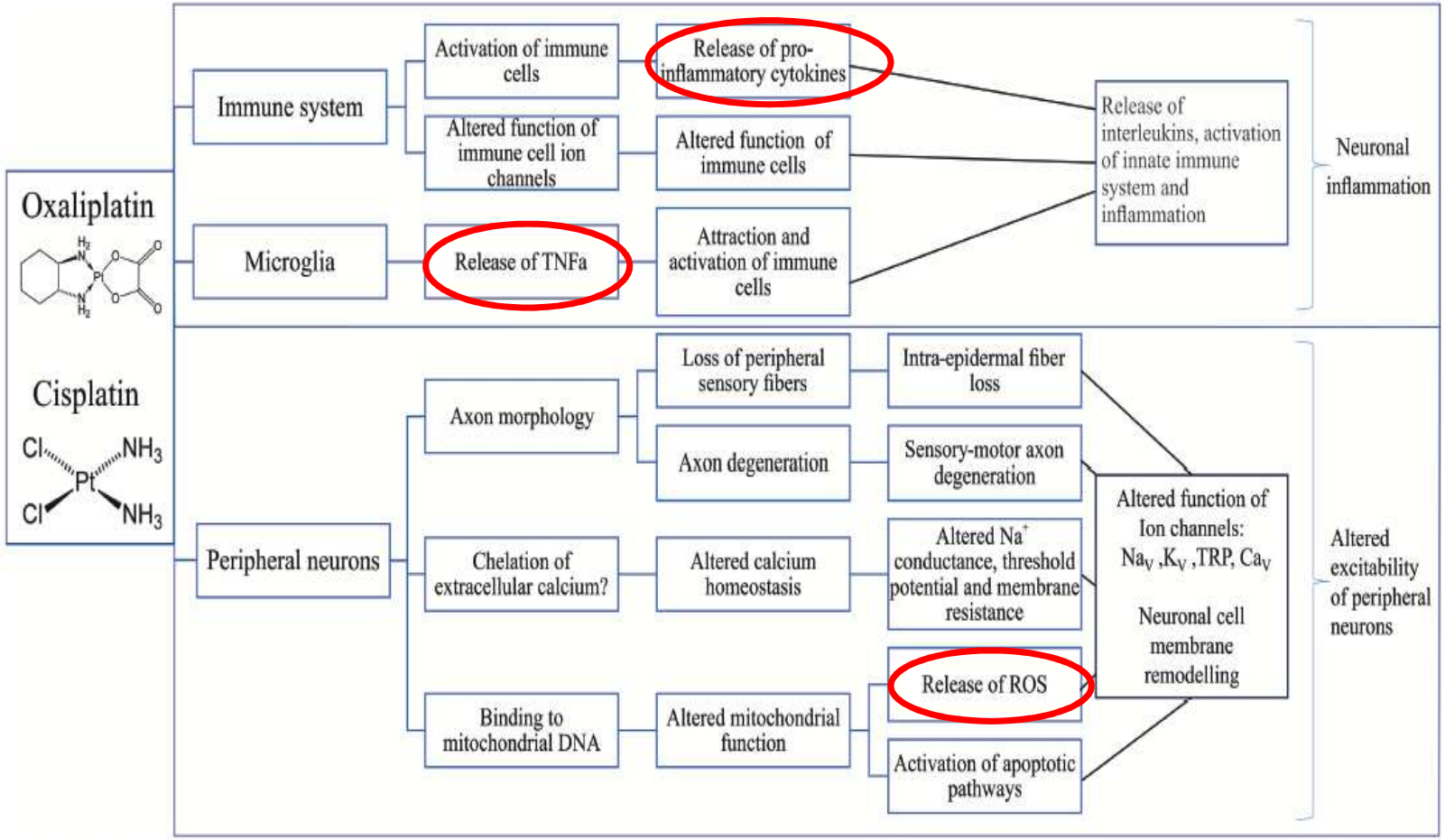


Journal of Cancer Therapy, 2016, 7, 609-621

奇美醫院大腸直腸病人接受FOLFOX-4 給予Dipeptiven研究得到類似神經毒性緩解

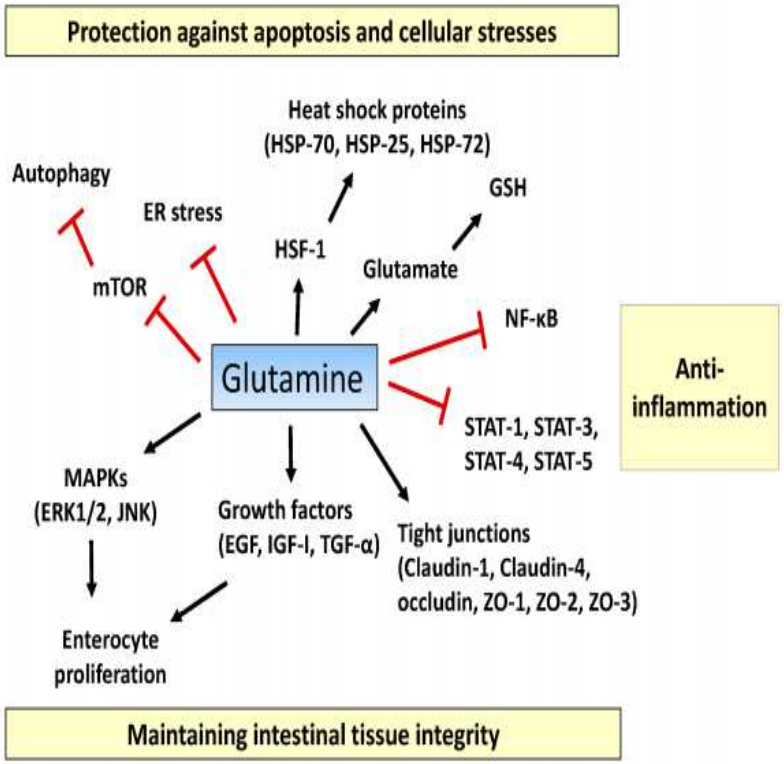
本篇出處	中華民國大腸直腸外科醫學會雜誌 30:4 2019.12[民108.12] 頁164-172
篇名	Use of N(2)-L-Alanyl-L-Glutamine Dipeptide in Stage III Colon Cancer Patients with Oxaliplatin-based Chemotherapy, Benefit or Harm?
作者	黃至豪；馮已榕；鄭立勤；田宇峯；周家麟
中文摘要	目的：在患有第三期大腸癌的患者中，奧沙利鉑在化療中扮演重要作用。但奧沙利鉑的毒性如神經毒性，嗜中性白血球低下症或血小板減少症可能導致治療過程中劑量減少甚至暫停化療。在先前的論文中報導了雙胜胺可預防神經毒性。本研究旨在討論雙胜胺對第三期結腸癌患者的臨床益處或危害。方法：2015年至2017年期間，奇美醫院大腸直腸外科共有74名患者診斷為第三期結腸癌患者接受FOLFOX-4治療。31位患者於每次15天的化療週期中有合併使用雙胜胺，另外43位則否。神經毒性症狀於每次化療週期前評估。其它毒性相關如化療劑量減少，疾病復發和進展等事件亦被記載。我們統計分析兩組間的臨床病理結果，神經毒性與非神經毒性，疾病復發或進展，及預後。結果：有使用雙胜胺之組別有著較低的神經症狀。經過4次及6次的FOLFOX治療後，雙胜胺組有較低的第一或二級神經症狀發生率。經過6個週期的治療後，雙胜胺組仍可有高達87%病人維持沒有神經症狀。在非神經毒性症狀如噁心、嘔吐、嗜中性白血球低下症或血小板減少症方面，兩組沒有顯著差異。與對照組相比，靜脈注射雙胜胺的患者粘膜炎發生率較低（3.23% 20.93% p=0.0382）。在整個化療過程中，靜脈注射雙胜胺組較能完成12次的FOLFOX療程記錄（p=0.0204）。以奧沙利鉑為基礎的化療，補充靜脈注射雙胜胺也不會增加癌症復發率和預後受損。兩組之間的總體存活率、，無疾病存活率和癌症特異性存活率無顯著差異。結論：在接受奧沙利鉑基底輔助化療的第三期結腸癌患者中，補充靜脈注射雙胜胺可以有效降低神經症狀發生率及嚴重程度。
英文摘要	Purpose. Oxaliplatin plays an important role in adjuvant chemotherapy but its toxicity often results in dose reduction or discontinuance. We evaluated the clinical benefits or harm of parenteral glutamine dipeptide (N2-LAlanyl-L-Glutamine Dipeptide, 20 g · m/100 ml, IV) for stage III colon cancer patients receiving oxaliplatin-based chemotherapy. Methods. Between January 2015 and December 2017, 74 stage III colon cancer patients who received FOLFOX-4 as adjuvant chemotherapy were enrolled and their data analyzed retrospectively. Among these patients, 31 had received IV glutamine dipeptide (20 g · m IV) days 1-2 with FOLFOX- 4 repeated every 15 days (glutamine dipeptide group), and 43 patients received only FOLFOX-4 (control group). Main measures were neurotoxicity symptoms and signs before each cycle, non-neurological toxicities and events (dosage reduction, disease recurrence or progression) and clinicopathologic features, neurotoxicity, disease recurrence, and prognosis. Results. Patients receiving glutamine dipeptide had significantly fewer neurologic symptoms than controls, including significantly lower incidence of grade 1-2 neuropathy after four and six cycles (6.45% vs. 32.56%, p = 0.0113; 6.45% vs. 51.16%, p < 0.001 respectively). No significant differences were found between groups in nausea, vomiting, neutropenia, and thrombocytopenia. Compared to controls, patients with intravenous glutamine dipeptide had less mucositis (3.23% verse 20.93%, p = 0.0382), a lower percentage of incomplete FOLFOX courses (p = 0.0204) and no increased recurrence rates or impaired prognosis. No significant differences were found in overall, disease-free, and cancer-specific survival between groups. Conclusion. Supplemental IV glutamine dipeptide significantly decreases the incidence and severity of oxaliplatin-induced neurotoxicity in stage III colon cancer.

Mechanisms of chemotherapy-induced peripheral neuropathy induced by platinum based drugs

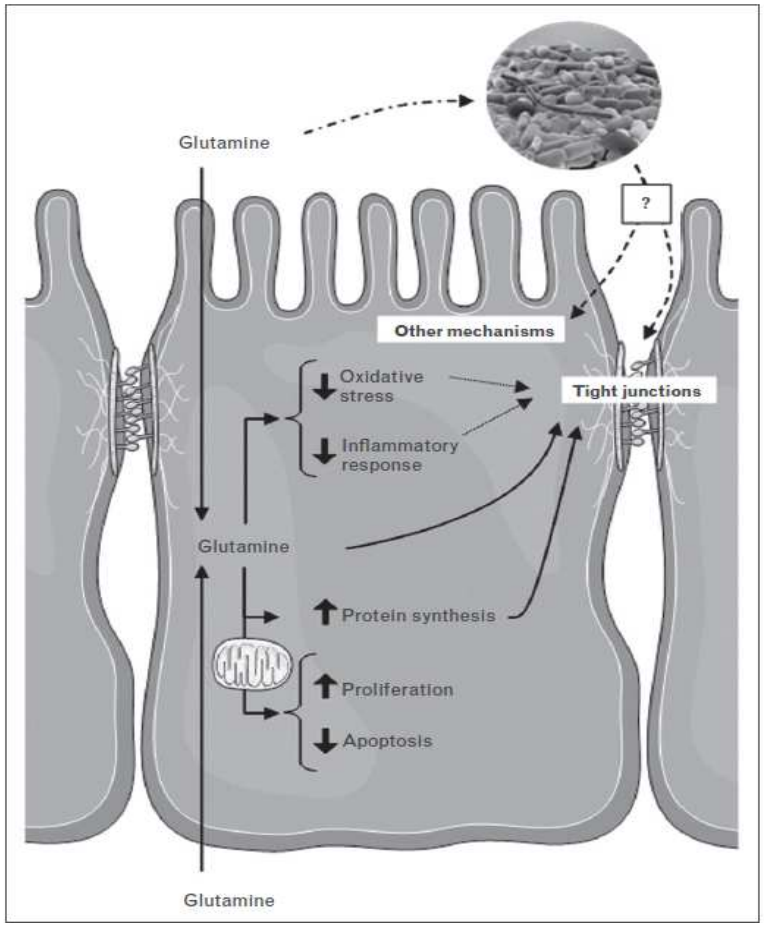


Starobova H et al. (2017) Front. Mol. Neurosci. 10:174.

Putative mechanisms of glutamine effects on gut barrier function

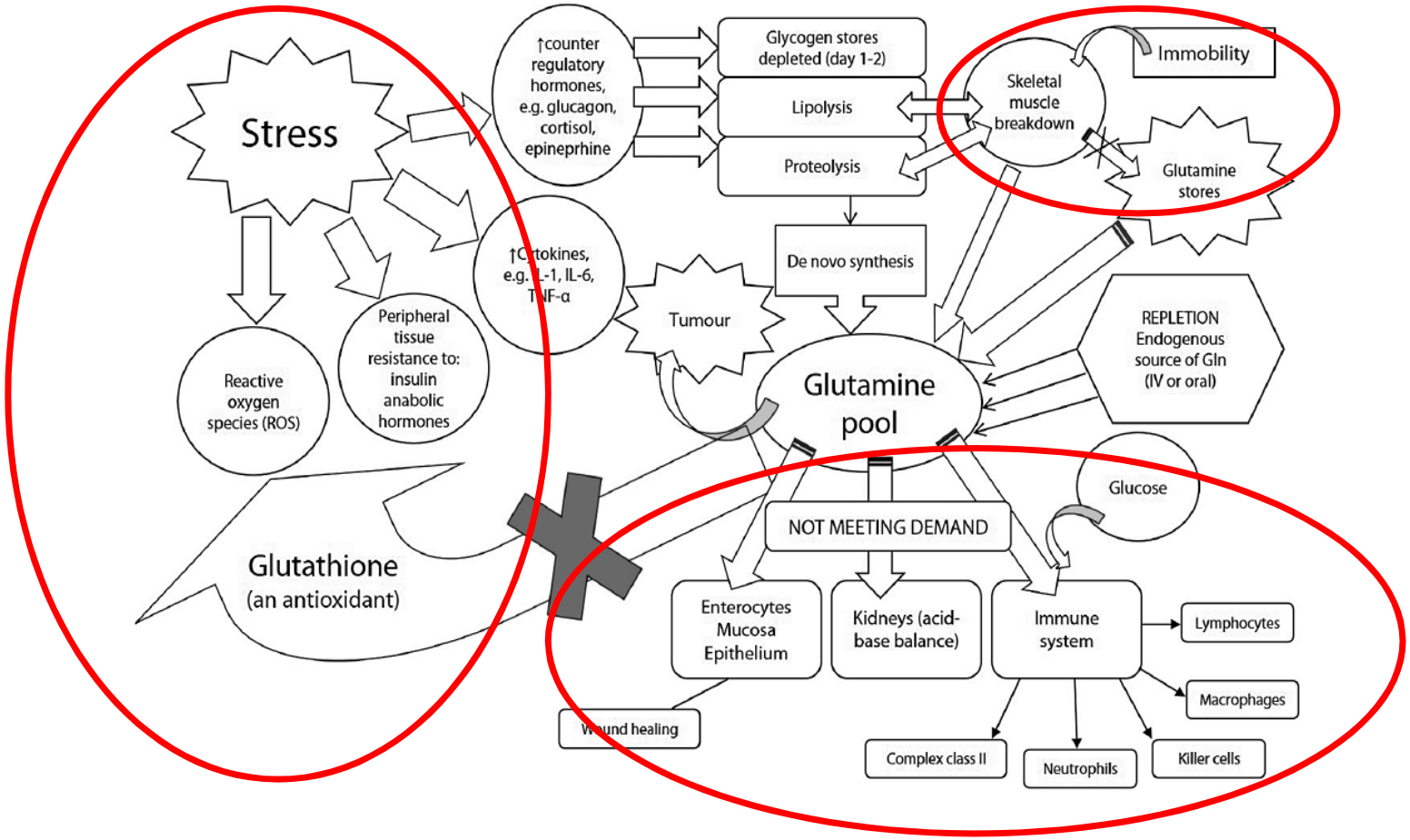


Min-Hyun Kim et al. Int. J. Mol. Sci. 2017, 18, 1051



Achamrah et al Curr Opin Clin Nutr Metab Care 2017, 20:86–91

The depletion of GLN during stress, and its consequences



Reinette Tydeman-Edwardsa. South African Journal of Clinical Nutrition 2017; 30(4):109–117

Does glutamine deprivation treat cancer?

Amino acid starvation strategies in cancer

Glutamine depletion	No specific glutamine depleting agent available, L-asparaginase acts as both L-glutamine and L-asparagine depleting agent
Glutamine transporter inhibition	Specific inhibitor not yet available, benzylserine may inhibit one of the glutamine transporter SLC1A5
Glutaminase inhibition	CB-839 (Glutaminase-1 specific)
	BPTES (Glutaminase-1 specific)
	BPTES nanoparticle
	DON (Target glutaminase-1, may also target glutamine fructose-6-phosphate amidotransferase)
	Alkyl benzoquinones, (Glutaminase-2 specific inhibitor)
	968 (Glutaminase-1 specific)

*L-asparaginase, ADI-PEG20 not included

Fung et al. Drug-induced amino acid deprivation as strategy for cancer therapy. Journal of Hematology & Oncology 2017

Jiun-I Lai, M.D. Ph.D

Amino acid starvation strategies in cancer

- The best developed small molecule is CB-839, a potent inhibitor of the mitochondrial glutaminase (GLS) and the only one that is currently used in clinical trials in cancer patients
- Since GLS catalyzes the conversion of glutamine to glutamate, it is anticipated that the treatment will deplete intracellular glutamate and block its further utilization in the TCA cycle, NEAA production and nucleotide biosynthesis.
- However, the physiological responses to glutaminase inhibition are likely to be different from glutamine deprivation in tumor cells

Jiang et al. Starve Cancer Cells of Glutamine: Break the Spell or Make a Hungry Monster? Cancers 2019

2021 ASCO ANNUAL MEETING

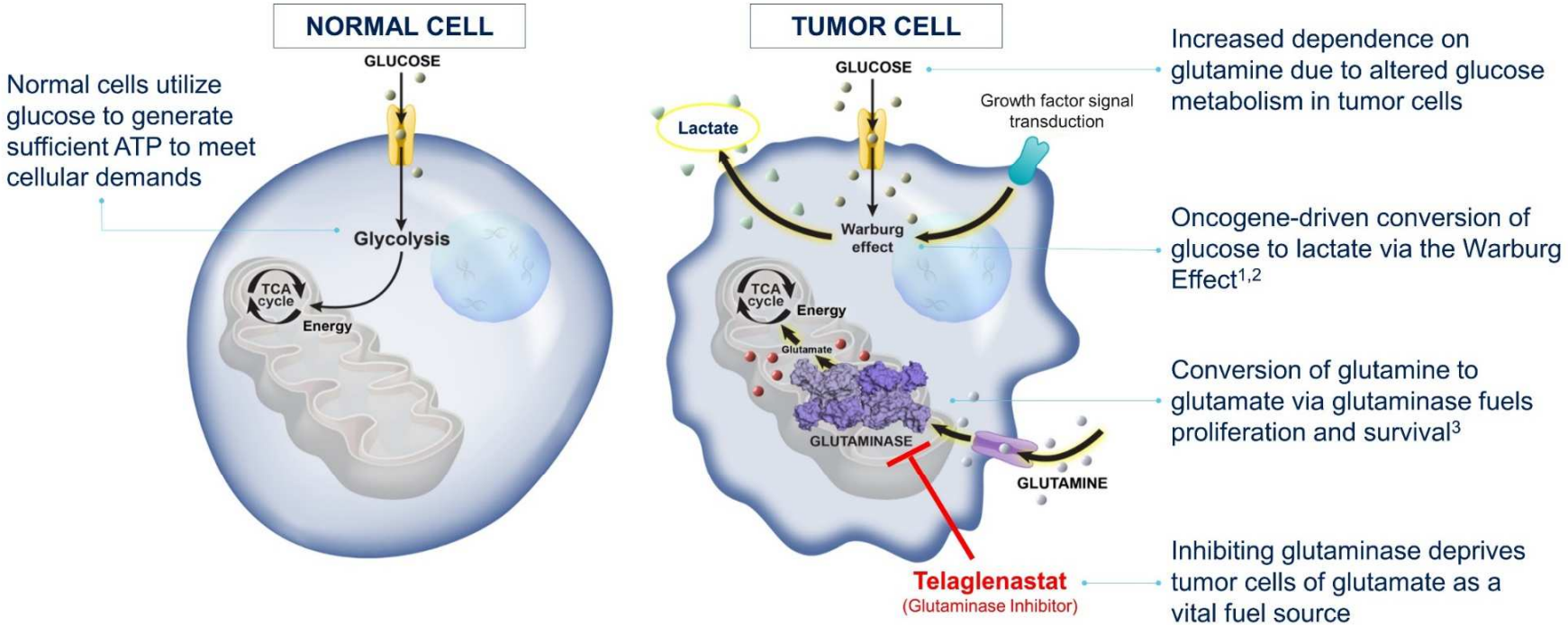
Abstract #4501

CANTATA: Primary Analysis of a Global, Randomized, Placebo-Controlled, Double-Blind Trial of Telaglenastat (CB-839) + Cabozantinib vs. Placebo + Cabozantinib in Patients With Advanced/Metastatic Renal Cell Carcinoma that Progressed on Immune Checkpoint Inhibitor or Anti-Angiogenic Therapies

Nizar M. Tannir[1], Neeraj Agarwal[2], Camillo Porta[3], Nicola J. Lawrence[4], Robert Motzer[5], Richard J. Lee[6], Rohit K. Jain[7], Nancy Davis[8], Leonard Appleman[9], Oscar Goodman, Jr.[10], Walter M. Stadler[11], Sunil Gandhi[12], Daniel M. Geynisman[13], Roberto Iacovelli[14], Begona Mellado[15], Robert Figlin[16], Thomas Powles[17], Lalith Akella[18], Keith Orford[18], Bernard Escudier[19]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; [3]University of Pavia, Pavia, Italy; [4]Auckland District Health Board, New Zealand; [5]Memorial Sloan Kettering Cancer Center, New York, NY; [6]Massachussetts General Hospital, Boston, MA; [7]H. Lee Moffitt Cancer & Research Institute, Tampa, FL; [8]Vanderbilt University Medical Center, Nashville, TN; [9]University of Pittsburgh Medical Center, Pittsburgh, PA; [10]Comprehensive Cancer Centers of Nevada, Las Vegas, NV; [11]University of Chicago, Chicago, IL; [12]Florida Cancer Specialists, Lecanto, FL; [13]Fox Chase Cancer Center, Philadelphia, PA; [14]Policlinico Universitario A. Gemelli, Rome, Italy; [15]Hospital Clínic, Provincial de Barcelona, Barcelona, Spain; [16]Cedars Sinai Medical Center, Samuel Oschin Comprehensive Cancer Institute, Los Angeles, CA; [17]St. Bartholomew's Hospital, Barts Health NHS Trust, London, UK; [18]Calithera Biosciences, Inc., South San Francisco, CA; [19]Gustave Roussy, Villejuif, France

Altered Tumor Metabolism in Tumor Cells



Normal cells utilize glucose to generate sufficient ATP to meet cellular demands

Increased dependence on glutamine due to altered glucose metabolism in tumor cells

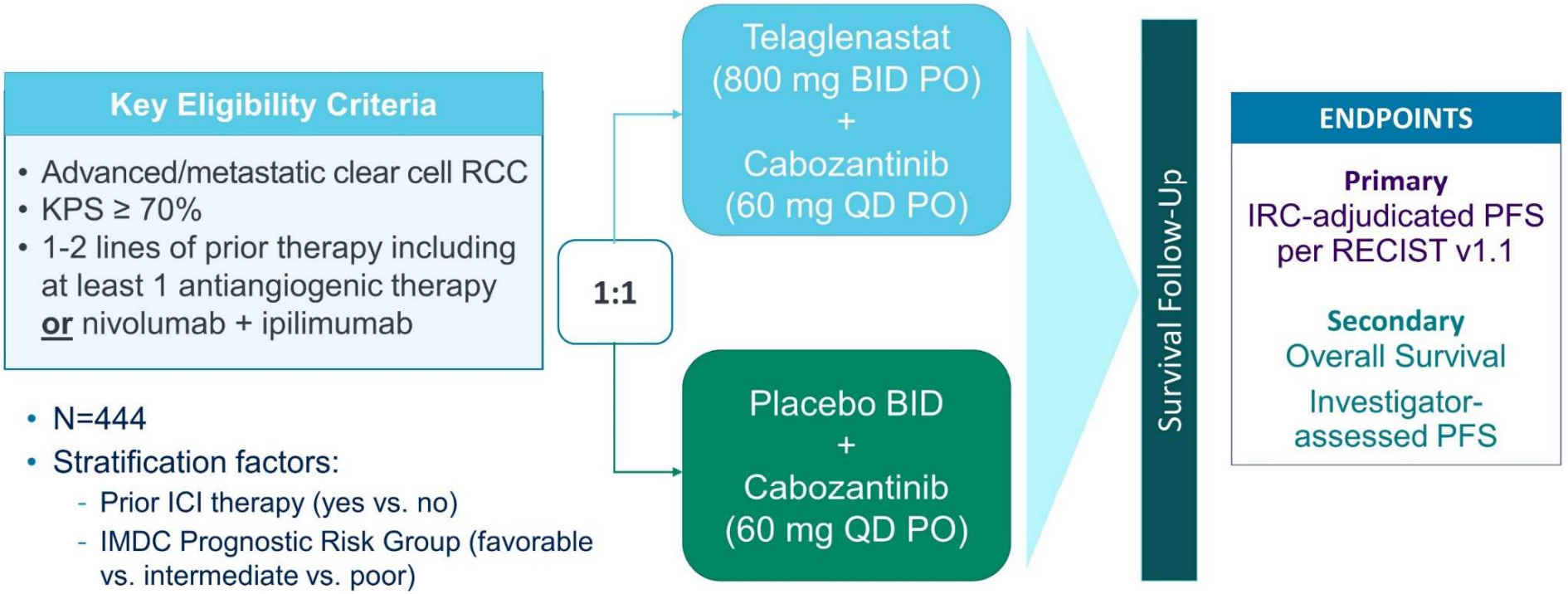
Oncogene-driven conversion of glucose to lactate via the Warburg Effect[1,2]

Conversion of glutamine to glutamate via glutaminase fuels proliferation and survival[3]

Inhibiting glutaminase deprives tumor cells of glutamate as a vital fuel source

[1]Warburg O. J Cancer Res. 1925;9(1):148-163; [2]Warburg O. Science. 1956;123(3191):309-314;
[3]Altman BJ et al. Nat Rev Cancer. 2016;16(10):619-634.

CANTATA Study Design



NCT03428217

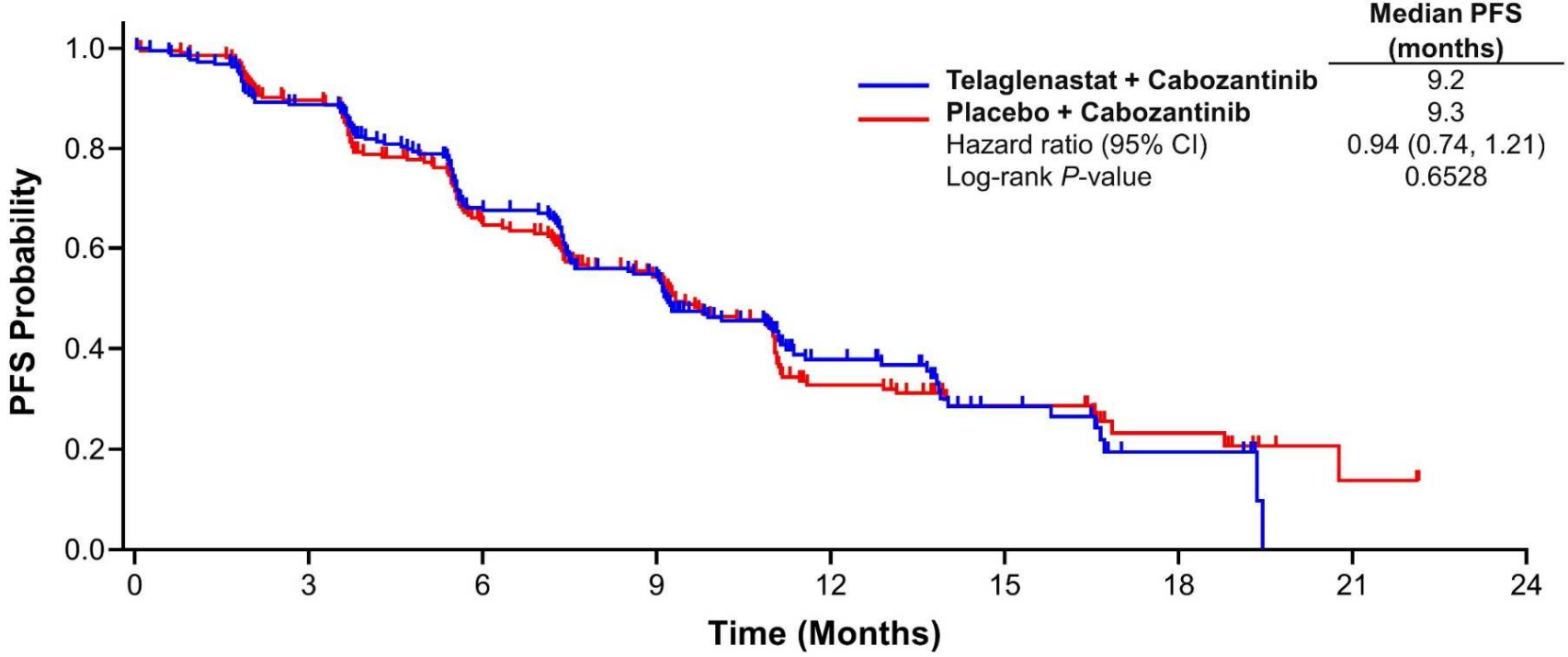
BID, twice daily; ICI, immune checkpoint inhibitor; IMDC, International Metastatic RCC Database Consortium; IRC, independent review committee; KPS, Karnofsky Performance Status; PFS, progression-free survival; PO, per os; QD, once daily; QOL, quality of life; RCC, renal cell carcinoma; RECIST, Response Evaluation Criteria in Solid Tumors

Efficacy (IRC-Assessed)

Parameter	Telaglenastat + Cabozantinib (n=221)	Placebo + Cabozantinib (n=223)
Progression-free survival (IRC)		
Median, months (95% CI)	9.2 (7.6, 11.1)	9.3 (7.6, 11.0)
Hazard ratio (95% CI)[a]	0.94 (0.74, 1.21)	
P-value	0.653	
Confirmed best responses, n (%)		
Complete response	2 (0.9)	2 (0.9)
Partial response	67 (30.3)	60 (26.9)
Stable disease	121 (54.8)	134 (60.1)
Progressive disease	19 (8.6)	19 (8.5)
Not evaluable/unknown	12 (5.4)	8 (3.6)
Overall response rate, n (%)	69 (31.2)	62 (27.8)

CI, confidence interval; CR, complete response; IRC, independent-review committee; PR, partial response.
NOTE: Hazard ratios based on stratified analyses for progression-free survival. Overall survival data not mature at data cutoff for primary analysis (August 31, 2020).
[a]Based on stratified analysis according to IMDC prognostic risk group (favorable/intermediate/poor).

IRC-Assessed Progression-Free Survival



	Median PFS (months)
Telaglenastat + Cabozantinib	9.2
Placebo + Cabozantinib	9.3
Hazard ratio (95% CI)	0.94 (0.74, 1.21)
Log-rank *P*-value	0.6528

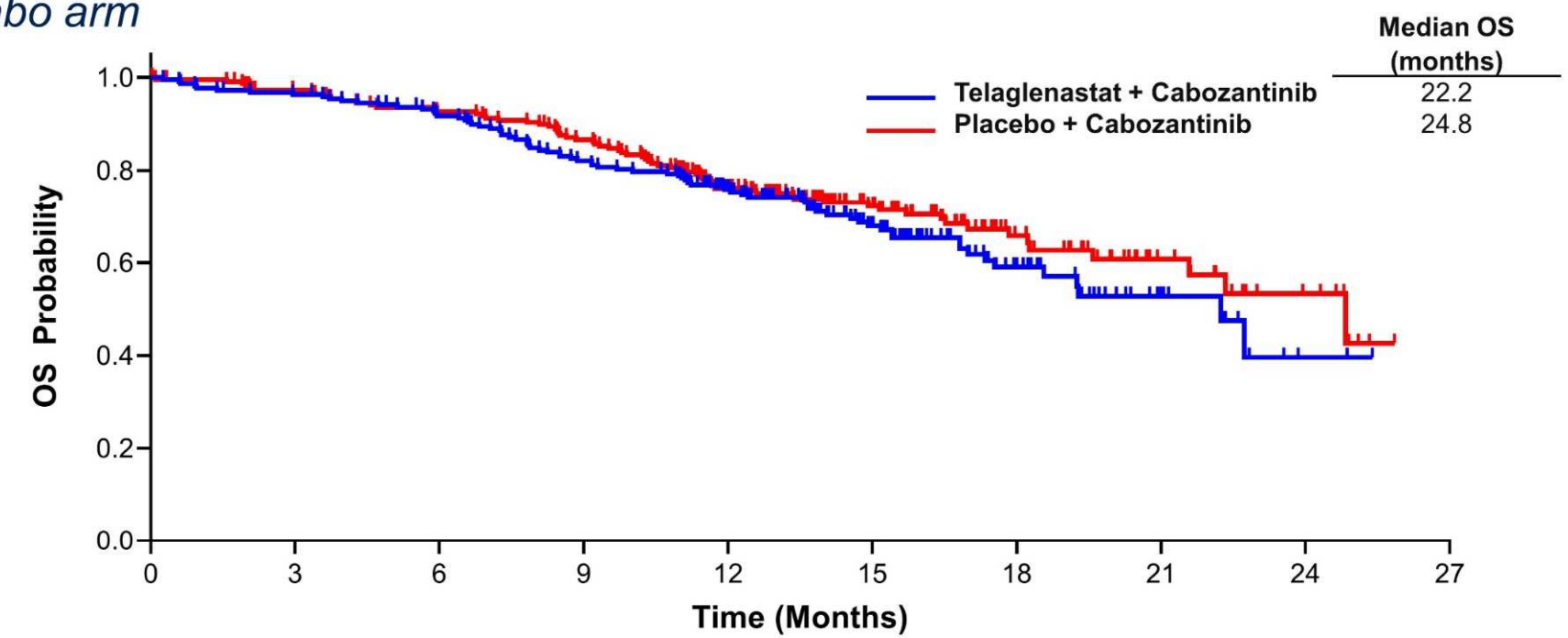
Number at risk

Telaglenastat + Cabozantinib:	221	185	131	97	37	15	6	0	0
Placebo + Cabozantinib:	223	184	117	90	40	21	9	2	0

CI, confidence interval; IRC, independent review committee; PFS, progression-free survival

Overall Survival

Not mature at data cutoff date: 77 deaths (34.8%) in tela+cabo arm, 69 deaths (30.9%) in pbo+cabo arm



Number at risk

Telaglenastat + Cabozantinib:	221	212	199	178	144	83	38	12	2	0
Placebo + Cabozantinib:	223	211	201	187	144	89	44	19	8	0

Cabo, cabozantinib; CI, confidence interval; OS, overall survival, pbo, placebo; tela, telaglenastat

Conclusions

- Addition of telaglenastat did not improve the efficacy of cabozantinib in patients with mRCC in this study
  - No significant difference in PFS between arms
- Telaglenastat plus cabozantinib was well tolerated, with AE profiles consistent with known risks of both agents
- Data in prior ICI subgroup may inform future development of telaglenastat
- This study provides valuable insight on efficacy outcomes of a contemporary population of patients with mRCC who receive cabozantinib in the 2/3L setting

AE, adverse event; ICI, immune checkpoint inhibitor; mRCC, metastatic renal cell carcinoma; OS, overall survival; PFS, progression-free survival

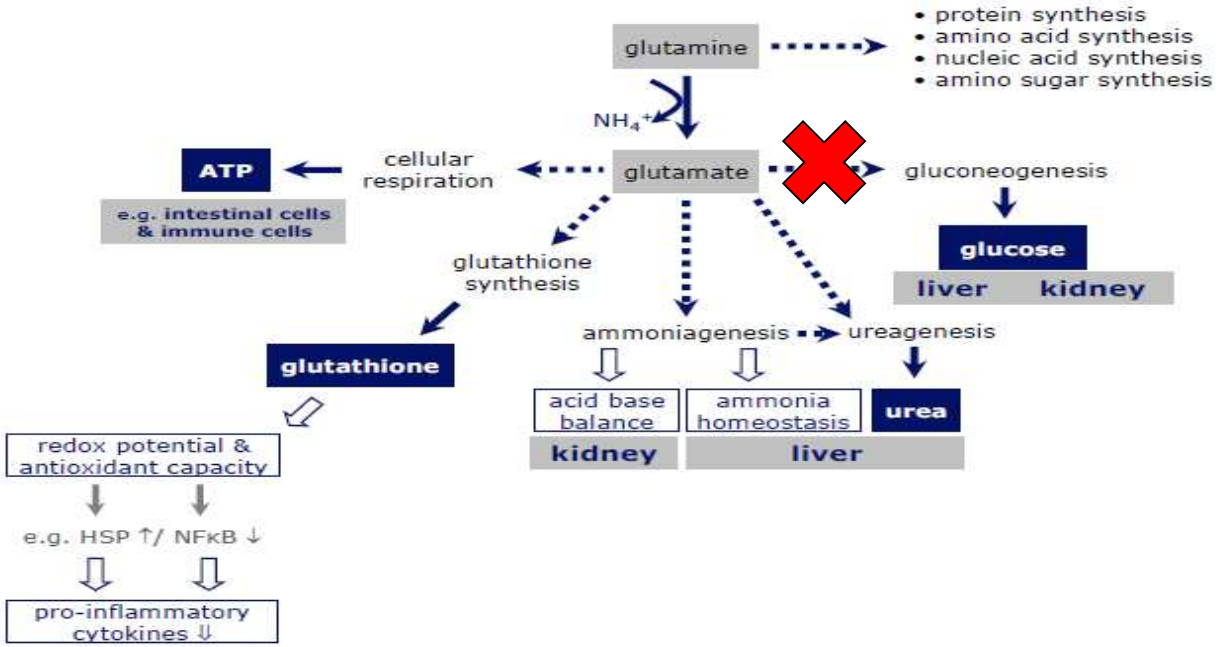
Dipeptiven: Product characteristics

- **20%** infusion solution concentrate containing dipeptide alanyl-glutamine
- **100 ml contains:** 20 g N(2)-**L-alanyl-L-glutamine**

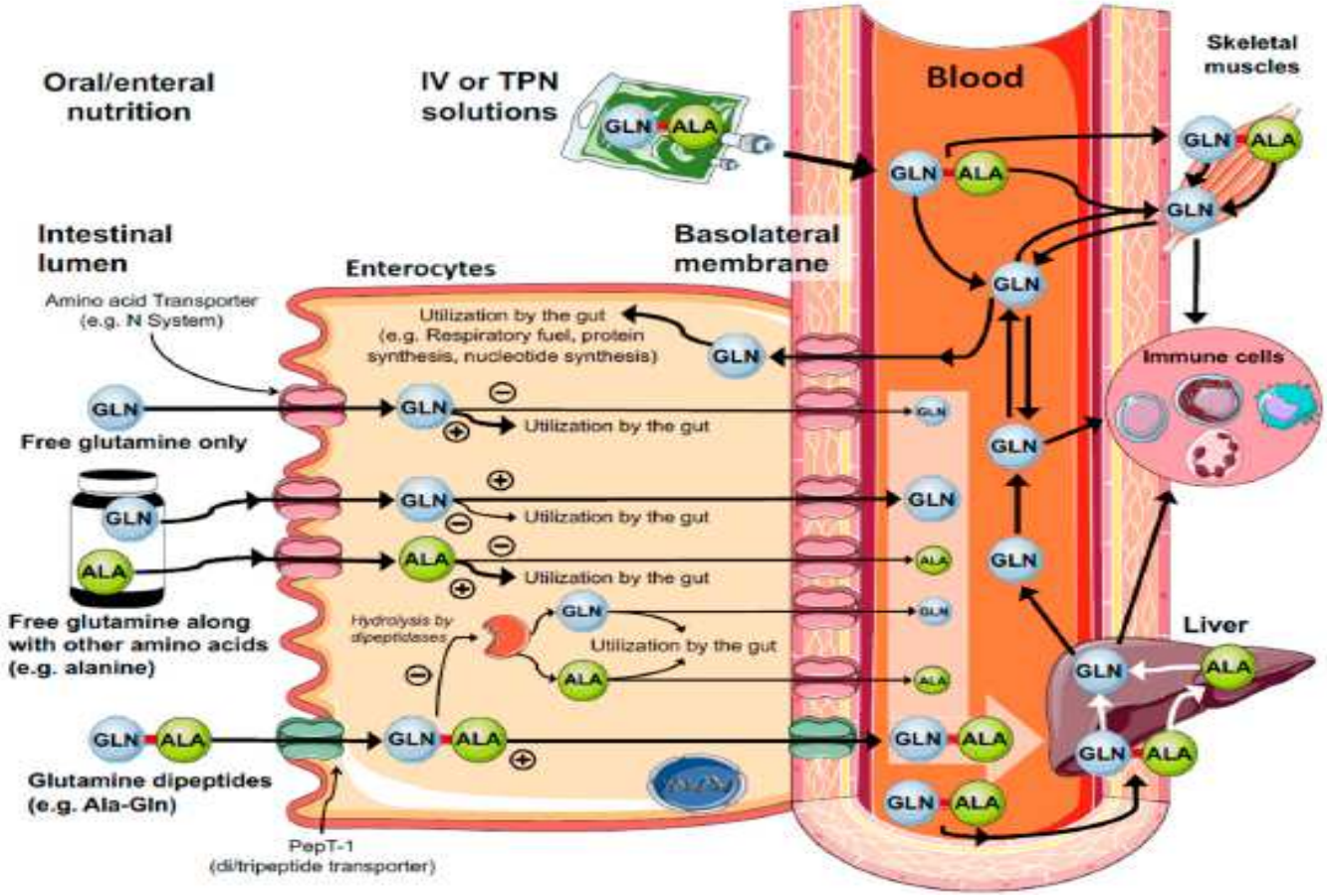
  = **13.46 g glutamine**, 8.20 g alanine
- A clear colorless solution
- Available in glass bottles of 50 ml and 100ml
- Solution for infusion after mixture with a compatible infusion solution.

Therapeutic 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.



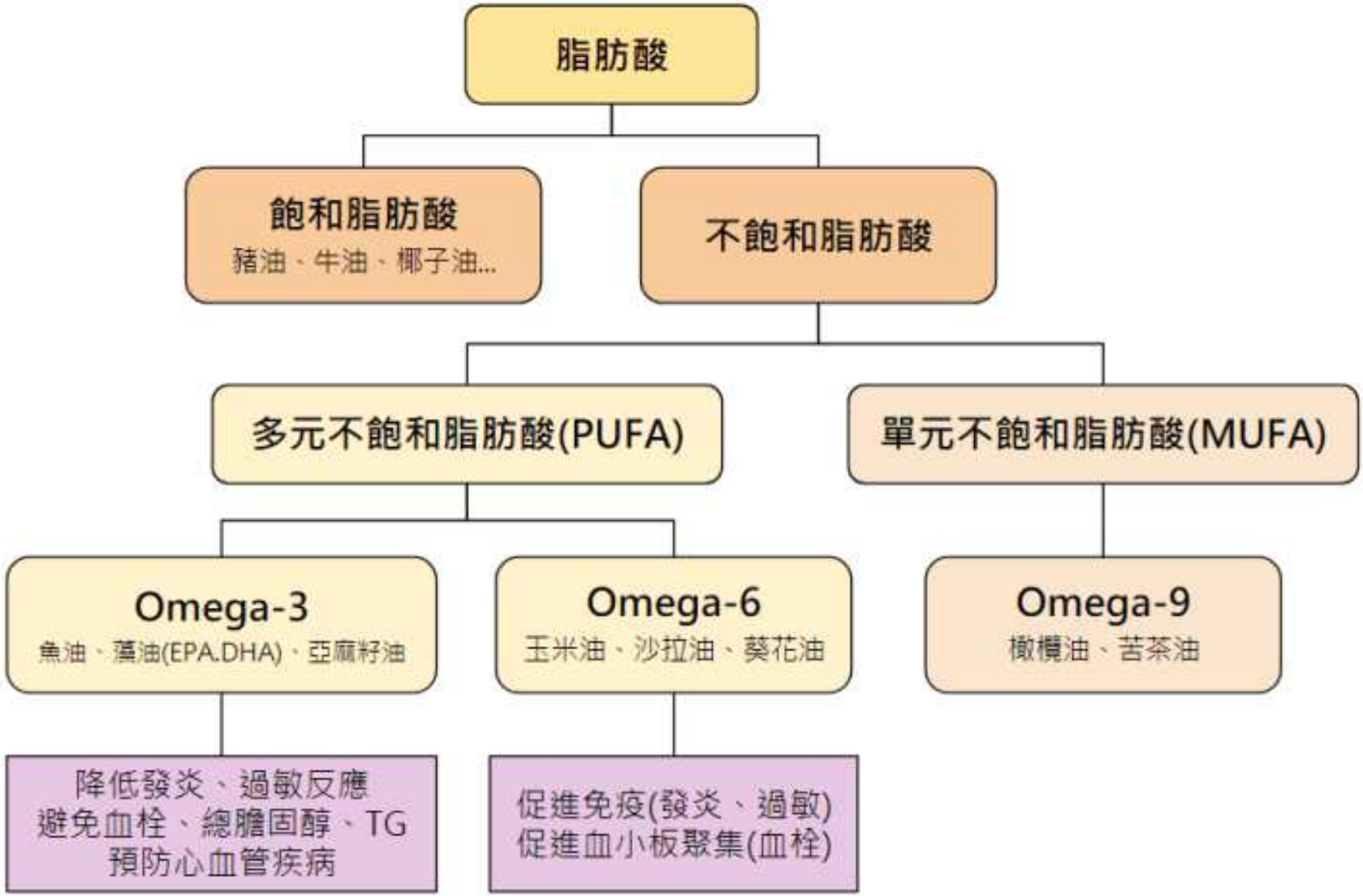
Mechanisms of enteral and parenteral glutamine (GLN) supply



Vinicius Cruzat et al. Nutrients 2018, 10, 1564

Outline: Nutrition intervention for cancer patients

- Introduction
- Definition and Influence of cancer-related cachexia/malnutrition
- Nutrition strategies
  - Special for chemotherapy: IV glutamine
  - **General concepts: Fish oil (n-3 PUFA)**
  - Guidelines
- Conclusion


脂肪酸
飽和脂肪酸
豬油、牛油、椰子油...
不飽和脂肪酸
多元不飽和脂肪酸(PUFA)
單元不飽和脂肪酸(MUFA)
Omega-3
魚油、藻油(EPA.DHA)、亞麻籽油
Omega-6
玉米油、沙拉油、葵花油
Omega-9
橄欖油、苦茶油
降低發炎、過敏反應
避免血栓、總膽固醇、TG
預防心血管疾病
促進免疫(發炎、過敏)
促進血小板聚集(血栓)

ω-3脂肪酸（Wikipedia）

- **ω-3脂肪酸**（Omega-3 fatty acids）又稱*n*−3脂肪酸，是一類不飽和脂肪酸，其中最重要的3種為：ALA（存在於植物中的油）、EPA和DHA（這二種發現存在於海洋動植物油中）。從脂肪酸分子中距離羧基最遠的甲基端（稱為ω端）的碳原子計數，這一類分子的倒數第三個與第四個碳原子之間為雙鍵（即倒數第三根鍵為雙鍵），因此稱為ω−3脂肪酸。含有較多ω−3脂肪酸的油脂包括：魚油、海藻油、雞蛋黃油、磷蝦油、沙棘果油、亞麻籽油、核桃油、奇亞籽油、南美印加果油、大麻籽油等。
- 重要的ω−3必需脂肪酸包括α－亞麻酸、二十碳五烯酸、二十二碳六烯酸，這三者均為多不飽和脂肪酸。人體內無法從頭合成ω−3脂肪酸，但可以使用十八碳的ω−3脂肪酸即α－亞麻酸（ALA）作為原料，通過人體內的酶延長碳鏈，合成二十碳的不飽和ω−3脂肪酸（即EPA），再由EPA合成二十二碳的不飽和ω−3脂肪酸（即DHA）。上述反應與ω-6脂肪酸的合成反應互為競爭反應，後者是從亞油酸衍生出的脂肪酸。ω−3與ω−6脂肪酸均為必須從食物中獲取的必需營養素。隨著人年齡的增長，體內由ALA合成DHA的能力隨之減退。因此，老年人可能存在DHA缺乏。

α-亞麻酸	alpha-Linolenic acid (ALA)	18:3 (*n*−3)	全-順-9,12,15-十八碳三烯酸
二十碳五烯酸	Eicosapentaenoic acid (EPA)	20:5 (*n*−3)	全-順-5,8,11,14,17-二十碳五烯酸
二十二碳六烯酸	Docosahexaenoic acid (DHA)	22:6 (*n*−3)	全-順-4,7,10,13,16,19-二十二碳六烯酸

魚油提供癌症病患有益的作用?

- 抑制致癌作用及癌細胞的生長
- 抑制:蛋白質分解誘導因子(proteolysis-inducing factor , PIF)
  抑制:脂肪移出因子(lipid mobilizing factor, LMF)
- 保護或增加瘦體組織
- 減低疲勞並增加生活品質
- 降低發炎性細胞激素的產生
- 增進化療的效果
- 減少化療所產生的副作用

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Clinical Nutrition xxx (2014) 1–7

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

Randomized control trials

Effects of an oral nutritional supplement containing eicosapentaenoic acid on nutritional and clinical outcomes in patients with advanced non-small cell lung cancer: Randomised trial☆

EPA

Karla Sánchez-Lara [a], Jenny G. Turcott [a], Eva Juárez-Hernández [a], Carolina Nuñez-Valencia [a], Geraldine Villanueva [a], Patricia Guevara [b], Martha De la Torre-Vallejo [a], Alejandro Mohar [c], Oscar Arrieta [a,d,*]

ProSure (Abbott Nutrition,Columbus, Ohio, USA).

SCIENTIFIC REPORTS

OPEN

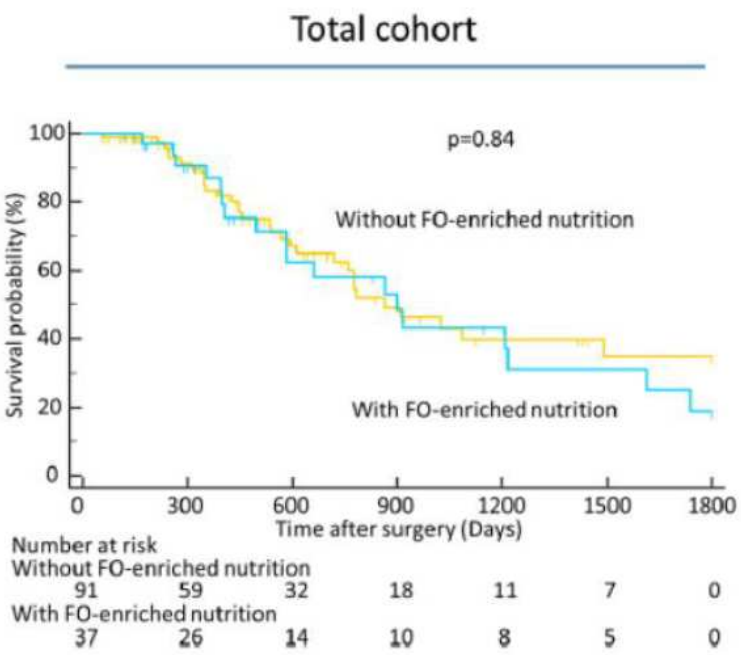
Fish oil-enriched nutrition combined with systemic chemotherapy for gastrointestinal cancer patients with cancer cachexia

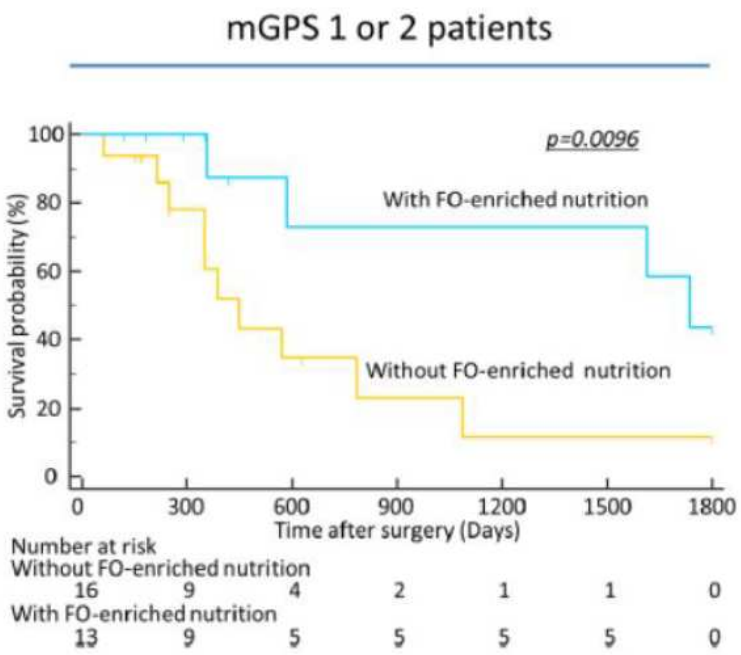
Received: 2 November 2016
Accepted: 26 May 2017
Published online: 06 July 2017

Yumiko Shirai[1], Yoshinaga Okugawa[2,3,4,5], Asahi Hishida[6], Aki Ogawa[7], Kyoko Okamoto[7], Miki Shintani[1], Yuki Morimoto[2], Ryutaro Nishikawa[2], Takeshi Yokoe[2], Koji Tanaka[2], Hisashi Urata[2], Yuji Toiyama[4], Yasuhiro Inoue[4], Motoyoshi Tanaka[3], Yasuhiko Mohri[4], Ajay Goel[5], Masato Kusunoki[4], Donald C. McMillan[8] & Chikao Miki[2]

Fish oil-enriched nutrition combined with systemic chemotherapy for gastrointestinal cancer patients with cancer cachexia

*mGPS (modified Glasgow prognostic score): Patients with elevated CRP (>0.5 mg/dl) were given a score of 1 or 2 depending on the absence or presence of hypoalbuminemia (<3.5 g/dl). Patients with a normal CRP and any albumin level were given a score of 0.





Shirai Y et al. Sci Rep 2017; 7:4826

SCIENTIFIC REPORTS

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Fish oil-enriched nutrition combined with systemic chemotherapy for gastrointestinal cancer patients with cancer cachexia

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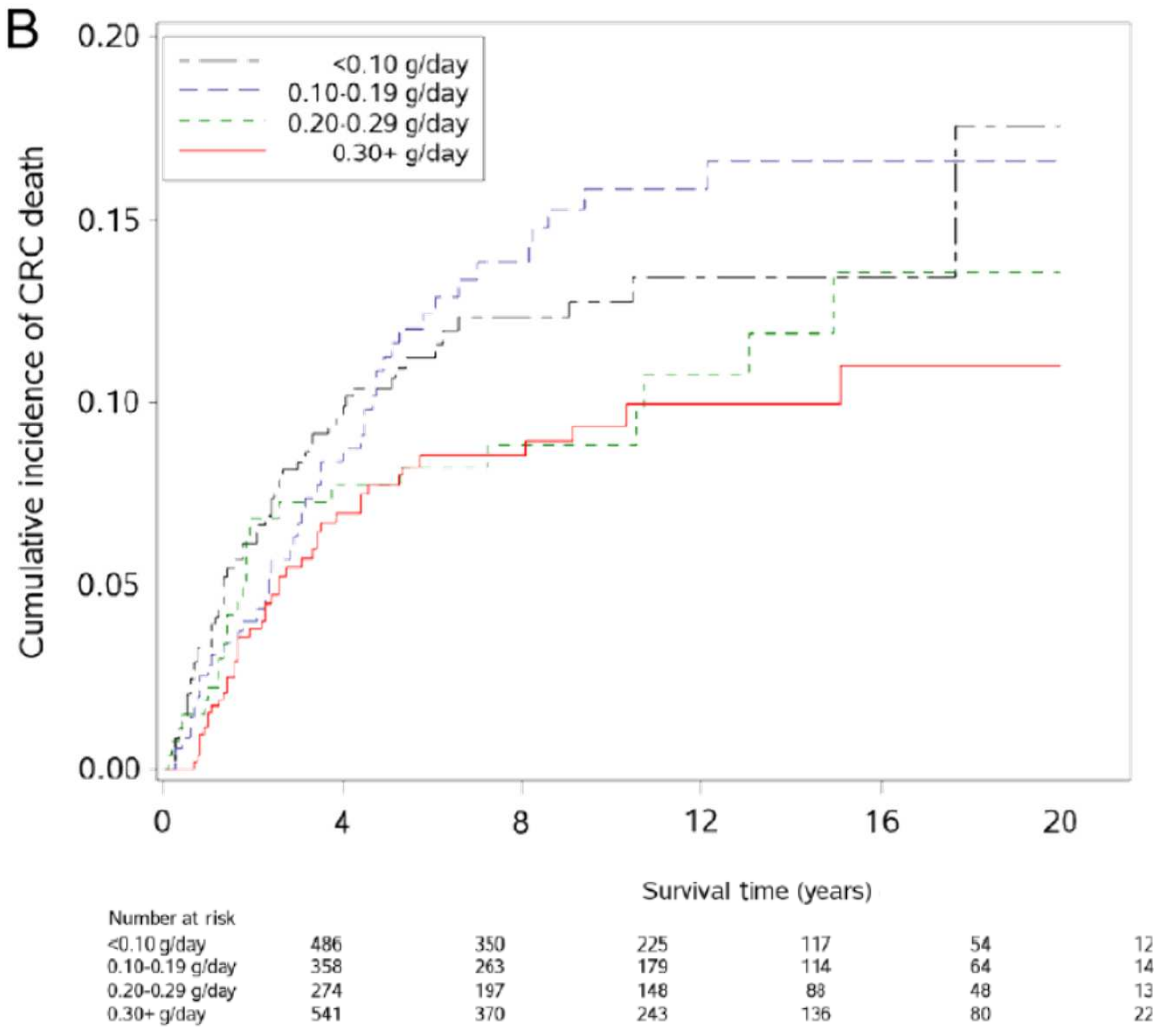
Yumiko Shirai[1], Yoshinaga Okugawa[2,3,4,5], Asahi Hishida[6], Aki Ogawa[7], Kyoko Okamoto[7], Miki Shintani[1], Yuki Morimoto[2], Ryutaro Nishikawa[2], Takeshi Yokoe[2], Koji Tanaka[2], Hisashi Urata[2], Yuji Toiyama[4], Yasuhiro Inoue[4], Motoyoshi Tanaka[3], Yasuhiko Mohri[4], Ajay Goel[5], Masato Kusunoki[4], Donald C. McMillan[8] & Chikao Miki[2]

Conclusion: FO-enriched nutrition may improve the prognosis of patients with cancer cachexia and systemic inflammation (i.e., those with a mGPS (modified Glasgow prognostic score) of 1 or 2.)

Marine ω-3 polyunsaturated fatty acid intake and survival after colorectal cancer diagnosis



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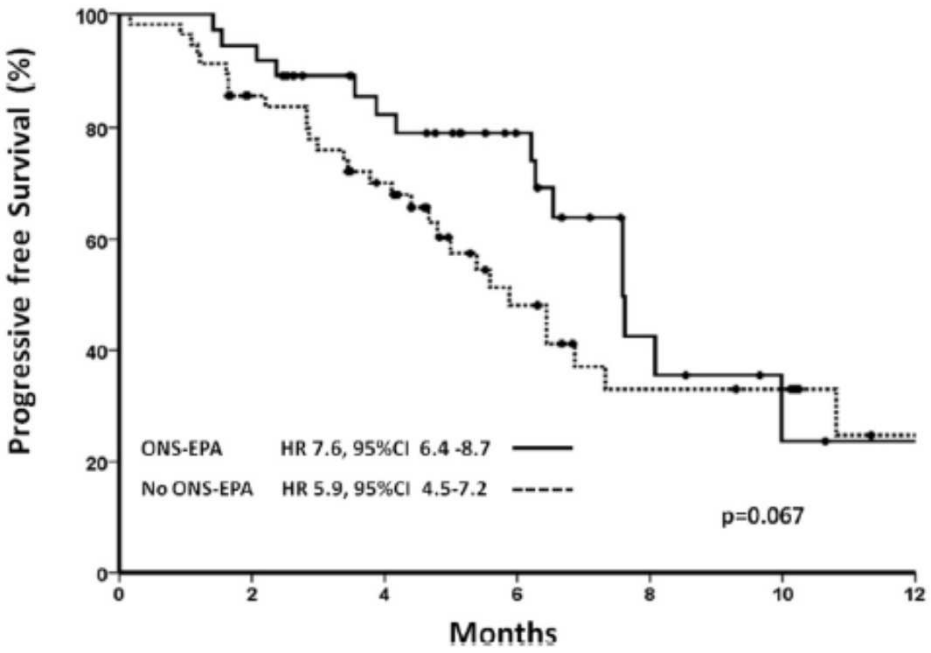


Fig. 2. Progression free survival Kaplan Meyer curves of ONS-EPA and C groups.

Table 5
Cox multivariate analysis of progression free survival adjusted by age, sex, functional status, stage, histopathology, smoking history, malnutrition and ONS-EPA intake.

		Hazard ratio (95% CI)	*p*
Age	≤60 vs > 60 years	1.32 (0.68–2.5)	0.417
Sex	Male vs Female	2.31 (1.04–5.1)	0.04
ECOG	0-1 vs 2	1.55 (0.88–2.7)	0.128
Stage	IIIB vs IV	3.3 (1.2–9.0)	0.02
Histopathology	Adenocarcinoma vs others	0.084 (0.94–2.4)	0.08
Smoking History	Absent/present	1.04 (0.52–2.0)	0.897
Malnutrition (SGA)	A vs B and C	1.12 (0.59–2.2)	0.716
ONS-EPA	Control vs Experimental	0.530 (0.27–1.0)	0.05

SGA = Subjective Global Assessment.
ONS-EPA = Oral nutritional supplement containing eicosapentaenoic acid.

Original Article

Effects of parenteral ω-3 fatty acid supplementation in postoperative gastrointestinal cancer on immune function and length of hospital stay: a systematic review and meta-analysis

Hao Bai MPH[1], Zhaoping Li MS[2], Yan Meng MS[2], Yue Yu MBBS[1], Huanhuan Zhang MBBS[1], Deqiang Shen MBBS[1], Liyong Chen MD[1,2]

[1]*Institute of Nutrition and Food Hygiene, School of Public health, Shandong University, Jinan, China*
[2]*Department of Nutrition, Shandong Provincial Hospital Affiliated to Shandong University, Jinan, China*

Conclusions: The results of this study suggest that parenteral ω-3 fatty acid supplementation is beneficial for gastrointestinal cancer patients, and is accompanied by improved postoperative immune function and satisfactory clinical outcomes.

Table 1. Characteristics of included studies in meta-analysis

First author	year	Country	Diagnosis of patients†	Number of participants (I/C)‡	Intervention measures		Intervention time (d)	Quality scores
					Intervention group	Control group		
Makay[14]	2013	Turkey	GC	14/12	ω-3 and ω-6 fatty acids (Omegaven, 0.2 g/kg/d; Lipovenoes 10%, 0.6 g/kg/d)	ω-6 fatty acid (Lipovenoes 10%, 0.8 g/kg/d)	5	4
Wei[25]	2014	China	GRC	26/20	ω-3 fatty acid (10% Omegaven, 0.2 g/kg/d, ω-3/ω-6 ratio was 1:4)	ω-6 fatty acid (20% Intralipid,1.0 g/kg/d)	6	4
Heller[23]	2004	Germany	GIC	24/20	0.8 g/kg/d soybean oil + 0.2 g/kg/d fish oil (ω-3/ω-6 ratio was 1:4)	1.0 g/kg/d soybean oil	5	6
Jiang[12]	2009	China	GIC	100/103	0.2 g/kg/d fish oil + 1.0 g/kg/d soybean oil (ω-3/ω-6 fatty acid ratio 1:3)	1.2 g/kg/d soybean oil	7	7
Zhu[22]	2012	China	CRC	29/28	0.2 g/kg/d fish oil + 1.0 g/kg/d soybean oil	1.2 g/kg/d soybean oil	7	7
Liang[21]	2008	China	CRC	20/21	0.2 g/kg/d ω-3 PUFA (ω-3/ω-6 ratio was 1:3)	0.8 g/kg/d soybean oil	7	7
Wachtler[24]	1997	Germany	CRC	19/21	MCT:LCT: fish oil, 5:3:2	MCT:LCT, 5:5	5	6

†CRC: colorectal cancer; GC: gastric cancer; GIC: gastrointestinal Cancer.
‡I: intervention Group; C: control group

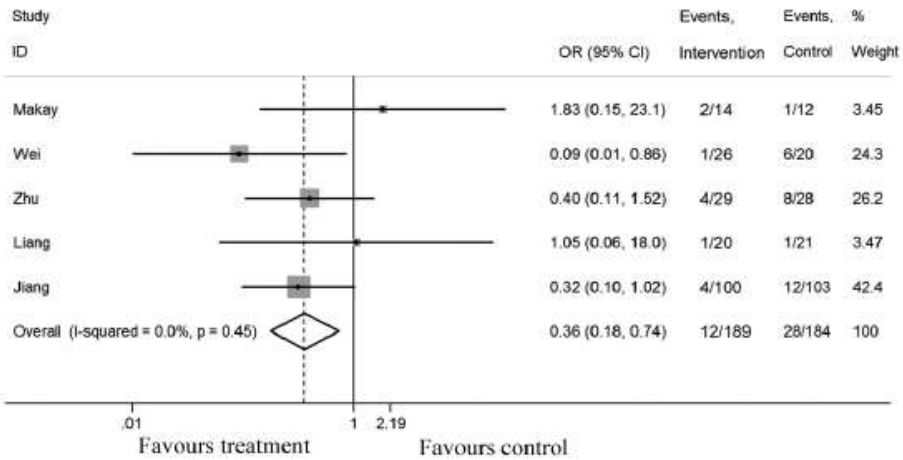


Figure 2. Effect of parenteral ω-3 fatty acid supplementation on infection complications

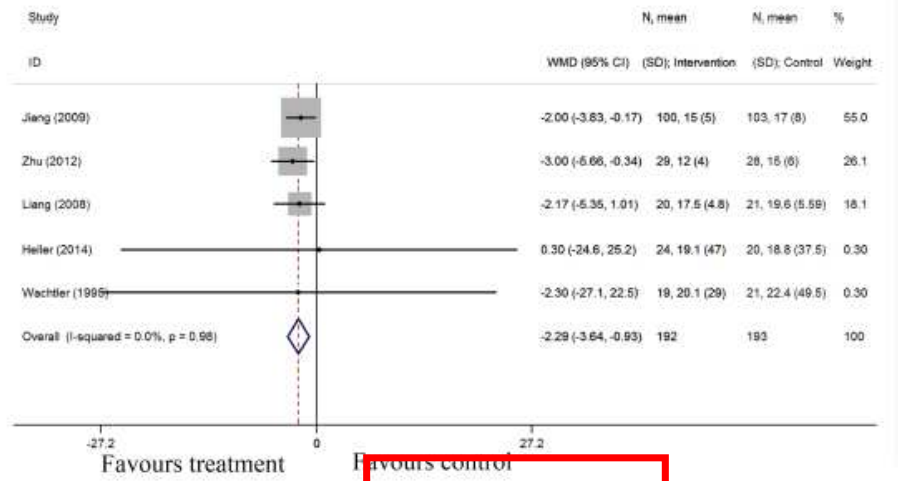


Figure 3. Effect of parenteral ω-3 fatty acid supplementation on length of hospital stay

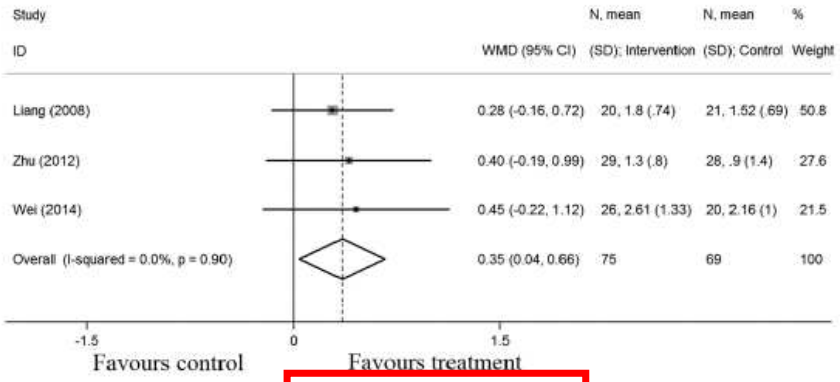


Figure 6. Effect of parenteral ω-3 fatty acid supplementation on CD4+/CD8+ ratio

The Effect of Supplementary Omegaven® on the Clinical Outcome of Patients With Advanced Esophagogastric Adenocarcinoma Receiving Palliative Epirubicin, Oxaliplatin, and Capecitabine Chemotherapy: A Phase II clinical trial

AMAR M. ELTWERI[1], ANNE L. THOMAS[2], WEN Y. CHUNG[1], BRUNO MORGAN[1], JOHN THOMPSON[3], ASHLEY R. DENNISON[1] and DAVID J. BOWREY[1,2]

Table I. *Demographic characteristics of the EOX plus fish oil (intervention) and EOX alone (historical control) groups.*

	Patient characteristics		
	EOX alone (n=37)	EOX + fish oil (n=21)	*p*-Value
Gender (male:female)	26:11	16:5	0.63
Median age in years (range)	66 (36-81)	67 (47-80)	
Number of patients aged over 60 years	8	16	<0.001
Performance status (0:1:2)	15:15:7	8:9:4	0.04
Median baseline weight in kg (range)	70.6 (43.1-105.7)	76.5 (49.0-110.6)	0.98
Tumour site			
Oesophagus: GEJ: Stomach	10:11:16	11:5:5	0.14
UICC stage (3:4)	3:34	3:18	0.46
Total number of chemotherapy cycles for all patients (median chemotherapy cycles per patient)	160 (5)	91 (6)	0.83
Number of patients completing 4 cycles (%)	23 (62%)	12 (60%)	0.70
Number of patients completing 6 cycles (%)	16 (43%)	11 (55%)	0.50

EOX, Epirubicin, Oxaliplatin, and capecitabine combination; GEJ, gastroesophageal junction; UICC, Union for International Cancer Control; WHO, World Health Organisation.

AMAR M. ELTWERI et al. ANTICANCER RESEARCH 39: 853-861 (2019)

Omegaven (lipid emulsion containing 10% fish oil with a high % of n-3 FA, esp., EPA+ DHA) with chemotherapy in esophageal cancer

Study design and sample size. This was a prospective, single-arm phase II clinical pilot trial. As this was a pilot/feasibility study, sample size was selected on pragmatic grounds to make an estimate of recruitment, retention, and drug toxicity, while not exposing too many participants to the full range of experimental procedures (14). Intervention. Participants received palliative chemotherapy with IV epirubicin (50 mg/m^2) and oxaliplatin (130 mg/m^2) every 21 days and oral capecitabine (1,250 mg/m^2) daily for 21 days (15). This is standard practice for care of these patients in the UK. As part of the trial, this regimen was coupled with intravenous infusion of omega-3 PUFAs as Omegaven® (Fresenius Kabi, Bad Homburg, Germany). Omegaven® was infused once weekly at a rate of 2 ml/kg body weight for 4 h (*i.e.*, 140 ml for 4 hours in a 70 kg patient). Omegaven® is a 10% fish oil lipid emulsion. Chemical analysis by gas chromatography revealed the contents of the batch used in the current study to be 2.0 g EPA and 2.3 g DHA/100 ml, respectively. Thus, patients received 0.04 and 0.046 g EPA and DHA/kg body weight for each 4-h infusion; in a 70 kg patient this would equate to 2.8 g EPA and 3.2 g DHA during each infusion. Omegaven® was administered through a peripheral venous line immediately after the chemotherapy treatment on day 1 of each cycle and then again on days 8 and 15 of the cycle (14). Blood samples were collected before and after each infusion for plasma cytokine analysis.

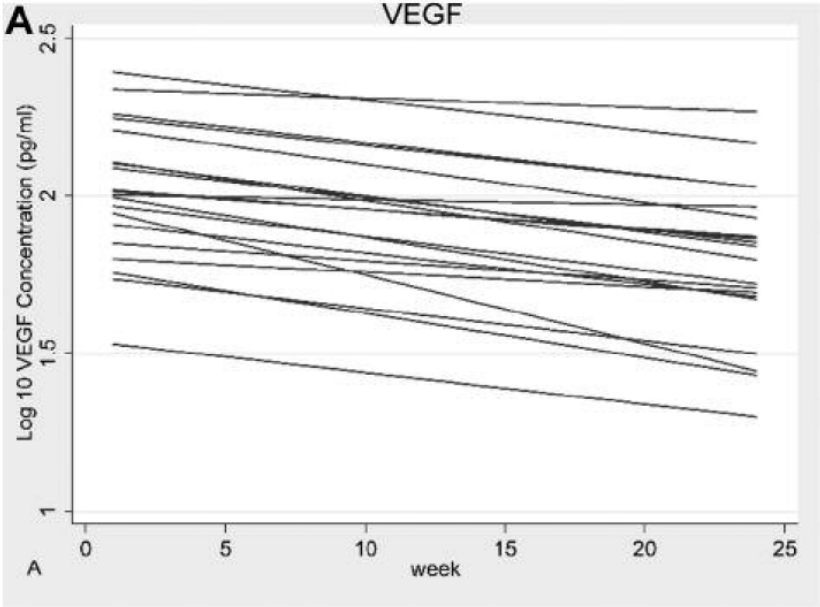
Table II. *Radiological tumour response at six months according to treatment received.*

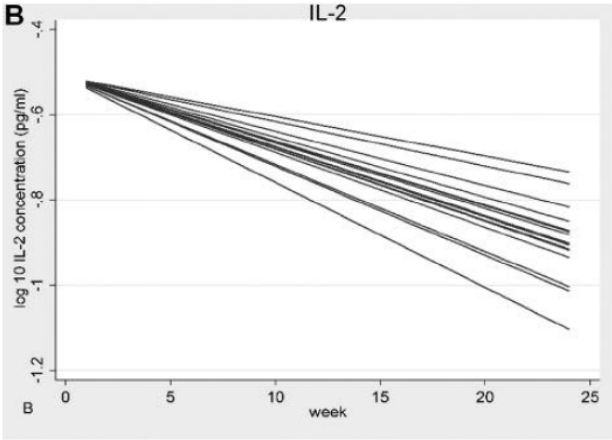
Response	EOX (n=28)	EOX plus fish oil (n=15)	*p*-Value
CR	1 (4%)	0 (0%)	0.47
PR	11 (39%)	11 (73%)	0.03*
SD	11 (39%)	3 (21%)	0.24
PD	5 (18%)	1 (7%)	0.34
Overall response			
CR + PR	12 (43%)	11 (73%)	0.05*
Disease control			
CR + PR + SD	23 (82%)	14 (93%)	0.31

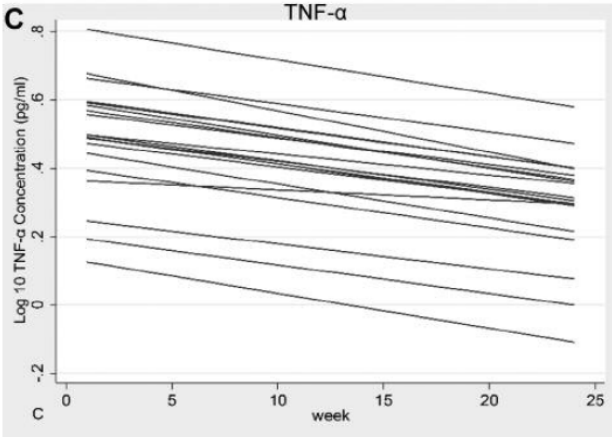
EOX, Epirubicin, oxaliplatin, and capecitabine combination; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease. *Statistically significant differences.

AMAR M. ELTWERI et al. ANTICANCER RESEARCH 39: 853-861 (2019)

Omegaven significant reductions IL-2 ,TNF-α and VEGF







AMAR M. ELTWERI et al. ANTICANCER RESEARCH 39: 853-861 (2019)

Clin Nutr Res. 2017 Jul;6(3):147-160
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cnr
CLINICAL NUTRITION RESEARCH

Review Article

Check for updates

Chemopreventive and Chemotherapeutic Effects of Fish Oil derived Omega-3 Polyunsaturated Fatty Acids on Colon Carcinogenesis

Ja Young Lee,[1] **Tae-Bu Sim**,[1] **Jeong-eun Lee**,[1] **Hye-Kyung Na**[1,2]

[1]Department of Food and Nutrition, College of Health and Wellness, Sungshin Women's University, Seoul 01133, Korea
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OPEN ACCESS

Therapeutic effects of long-chain n-3 PUFAs in colon cancer patients

Table 1. Therapeutic effects of dietary long-chain n-3 PUFAs in colon cancer patients

Type of n-3 PUFAs	Dose/period	Subjects	Effects	Reference
Fish oil	1.2 g/kg/day for 7 days	42 CRC patients undergoing radical resection	· Reduce the serum IL-6 levels · Increase the $CD4^+/CD8^+$ · Reduce the serum TNF-α levels · Increase the CD3 & CD4 lymphocyte percentage	[73]
Fish oil	2.0 g of fish oil containing 600 mg of EPA & DHA for 9 wk	23 CRC patients undergoing chemotherapy	· Reduce the C-reactive protein/albumin	[74]
Oral supplement of n-3 FAs	2.0 g of EPA & 1.0 g of DHA/day for 7 days before surgery	148 patients referred for elective CRC surgery	· Increase the production LTB_5 · Reduce the production of LTB_4 · Increase the neutrophil 5-HEPE production · Reduce the 5-HETE	[75]
Fish oil capsule	2.0 g fish oil containing 600 mg/ EPA + DHA/day for 9 wk	11 CRC patients undergoing chemotherapy	· Increase the body weight · Reduce the CRP/albumin	[76]
Fish oil capsule	2.0 g fish oil containing 1.4 g EPA & 1.0 g DHA/twice/day	51 patients requiring colon cancer surgery	· Increase the proportion of EPA in the mucosal lipids	[77]
Oral supplement of n-3 FAs	2.0 g of EPA & 1.0 g of DHA/twice/ day for 7 days before surgery	148 patients referred to colon cancer surgery	· Increase the DHA levels in colon tissue	[64]
Fish oil	6.1 g fat with 1.0 g of EPA/twice/ day for 12 wk	10 CRC patients (stage IV)	· Increase body weight · Enhanced quality of life	[78]
Fish oil	Fish oil supplements per day (12 mg EPA + 45 mg DHA/capsule) (total dose of 456 mg/day of EPA + DHA) for 2 yr	104 participants belong to experimental group	· Reduce the ratio of n-6 PUFAs/n-3 PUFAs · Reduce the colon cancer incidence	[79]

n-3, omega-3; FA, fatty acids; PUFAs, polyunsaturated fatty acids; CRC, colorectal cancer; IL, interleukin; TNF-α, tumor necrosis factor-α; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; LTB_4, leukotriene B4; LTB_5, leukotriene B5; HETE, hydroxyeicosatetraenoic acid; HEPE, hydroxy-eicosapentaenoic acid; CRP, C-reactive protein; n-6, omega-6.

Clin Nutr Res. 2017 Jul;6(3):147-160

Omega 3 fatty acid synergies chemotherapy

Table 2. Combination/synergistic effects of n-3 PUFAs with chemotherapeutic or chemopreventive agents

n-3 PUFAs	Chemicals	Models	Effects	Reference
DHA, EPA	Paclitaxel	Caco-2 cells	- Induce apoptosis	[80]
DHA	5-FU	Caco-2 cells	- Inhibit the cell growth through cell cycle arrest - Induce apoptosis	[39] [42]
DHA	Celecoxib	HCA-7 cell	- Induce apoptosis - Reduce the COX-2 expression	[43]
DHA, EPA	5-FU & OX	HT-29, HCT-116 SCID mice xenografts of CR	- Reduce the CSC/CSLC population - Suppression of tumor growth - Increase the phosphorylation of PTEN - Reduction of Akt phosphorylation - Normalization of β-catenin expression	[44]
Fish oil	5-FU & OX & IRI	HT-29 ($Bax^{-/-}$)	- Induce apoptosis via mitochondrial membrane depolarization	[81]
DHA	*p*-XSC	CaCo-2 cells	- Reduce the expression COX-2, INOS, cyclin D1, β-catenin, NF-κB - Inhibit the cell growth - Induce apoptosis	[46]
DHA, EPA	Doxorubicin	HT-29 cells, chemoresistant HT-29-dx cells	- Reduce the cholesterol synthesis & incorporation in the detergent resistant membrane - Reduced the amount of Pgp and MRP1 contained in detergent resistant membrane - Decreased the transporters activity - Restored the antitumor effects of different chemotherapeutic drugs - Restored a proper tumor-immune system recognition in response to chemotherapy in multidrug resistant tumor	[24]
Fish oil	Cisplantin	Xenografts with colon cancer cells	- Reduce the tumor weight	[82]
DHA	Butyrate	HCT-116 cells	- Reduce the methylation of pro-apoptotic genes	[50]
Fish oil	Butyrate	AOM-induced colon cancer model	- Reduce the aberrant crypt height and apoptosis - Induces apoptosis - Increase the p27 protein levels	[52]
Fish oil	Olive oil	DSS-induced colitis model	- Suppress the NO synthase expression - Reduce the colonic TNF-α and LTB_4 levels	[83]
Fish oil	Curcumin	DSS-induced colitis model	- Enhance the resolution of chronic inflammation - Suppress the NF-κB - Improve the repair of colonic epithelium	[56]
Fish oil	Quercitrin	DSS-induced colitis model	- Reduce the MPO & AP activities - Restore the colonic glutathione content - Reduce the colonic insult	[61]

n-3, omega-3; PUFAs, polyunsaturated fatty acids; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; 5-FU, 5-fluorouracil; COX-2, cyclooxygenase-2; OX, oxaliplatin; SCID, severe combined immunodeficiency; CR, complete response; CSC, cancer stem cell; CSLC, cancer stem-like cell; PTEN, phosphatase and tensin homolog; IRI, irinotecan; *p*-XSC, 1,4-phenylene*bis*(methylene)selenocyanate; INOS, inducible nitric oxide synthase; NF-κB, nuclear factor-kappa B; Pgp, p-glycoprotein; MRP1, multidrug resistance related protein 1; AOM, azoxymethane; DSS, dextran sulfate sodium; NO, nitric oxide; TNF-α, tumor necrosis factor-α; LTB_4, leukotriene B4; MPO, myeloperoxidase; AP, alkaline phosphatase.

Clin Nutr Res. 2017 Jul;6(3):147-160

Fish oil prevent colon carcinogenesis through multiple mechanisms

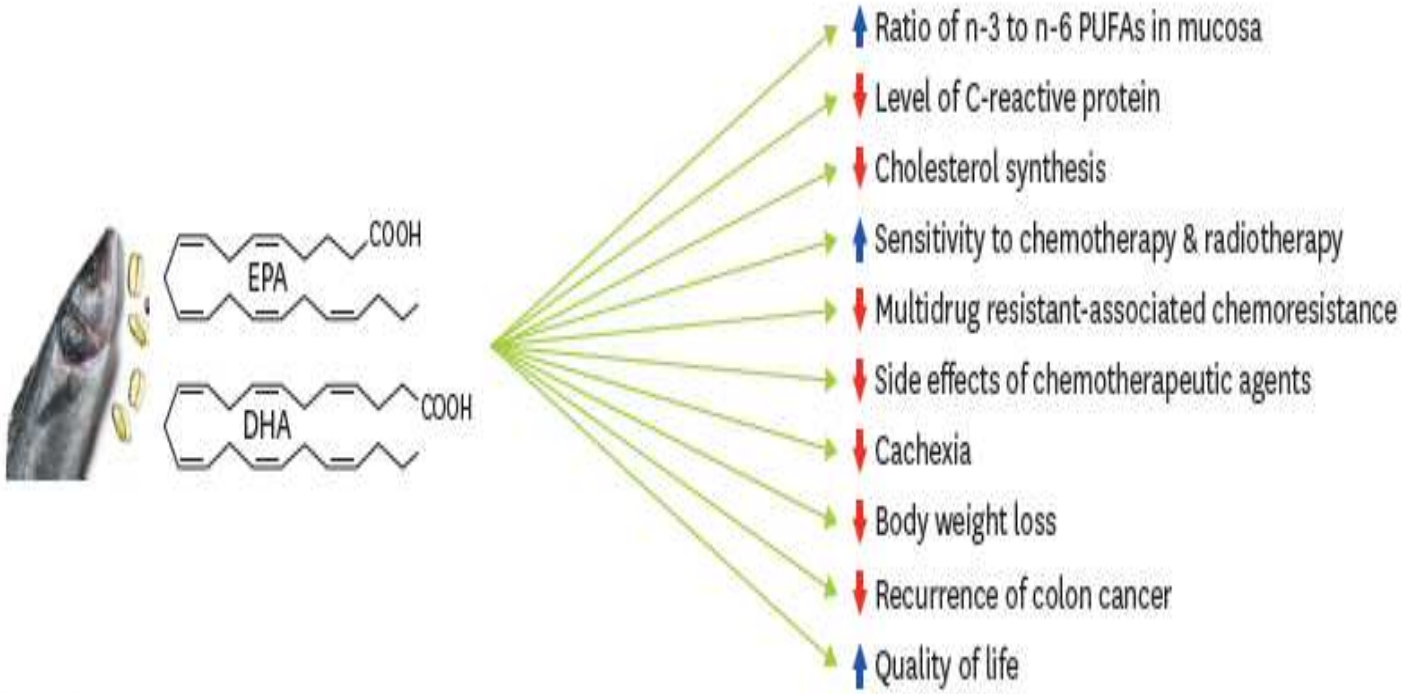
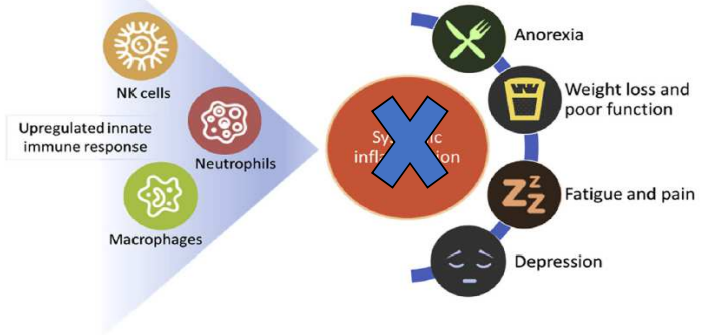


Figure 2. Chemotherapeutic effects of n-3 PUFAs on colon carcinogenesis.
n-3, omega-3; PUFAs, polyunsaturated fatty acids; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; n-6, omega-6.

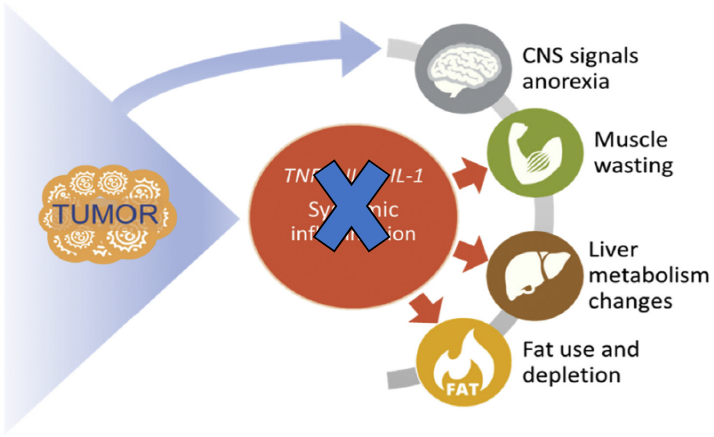
Clin Nutr Res. 2017 Jul;6(3):147-160

Fish oil down regulate the systemic inflammation

Association of immunologic, metabolic, and clinical phenomena in cancer



Pathophysiology and metabolism in the presence of a tumor: the mechanisms.



J. Arends et al. / Clinical Nutrition 36 (2017) 1187-1196

Omega-3 fatty acid block inflammatory pathway

Clinical Nutrition 36 (2017) 65–78

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Review

Potential applications of fish oils rich in omega-3 polyunsaturated fatty acids in the management of gastrointestinal cancer

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Keywords:
Cancer
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Inflammation

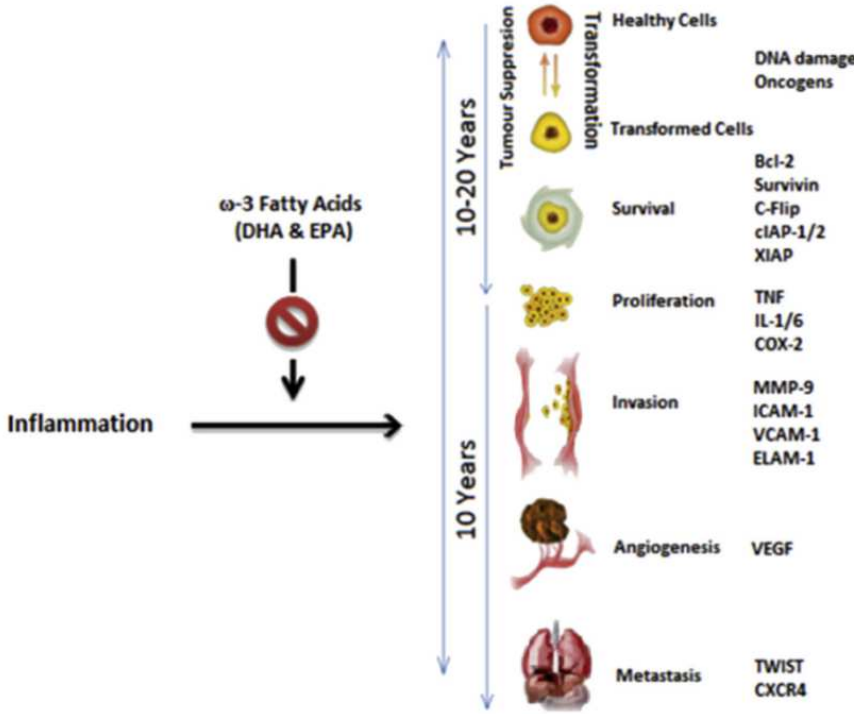
SUMMARY

Background & aims: Despite advances in chemotherapeutic agents and surgical approaches for its management, gastrointestinal cancer still accounts for 27% of new cancer cases and 35% of cancer related mortality worldwide. Omega-3 polyunsaturated fatty acids (PUFAs) specifically eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have anti-inflammatory and anticancer activities and are used as immuno-nutrients.

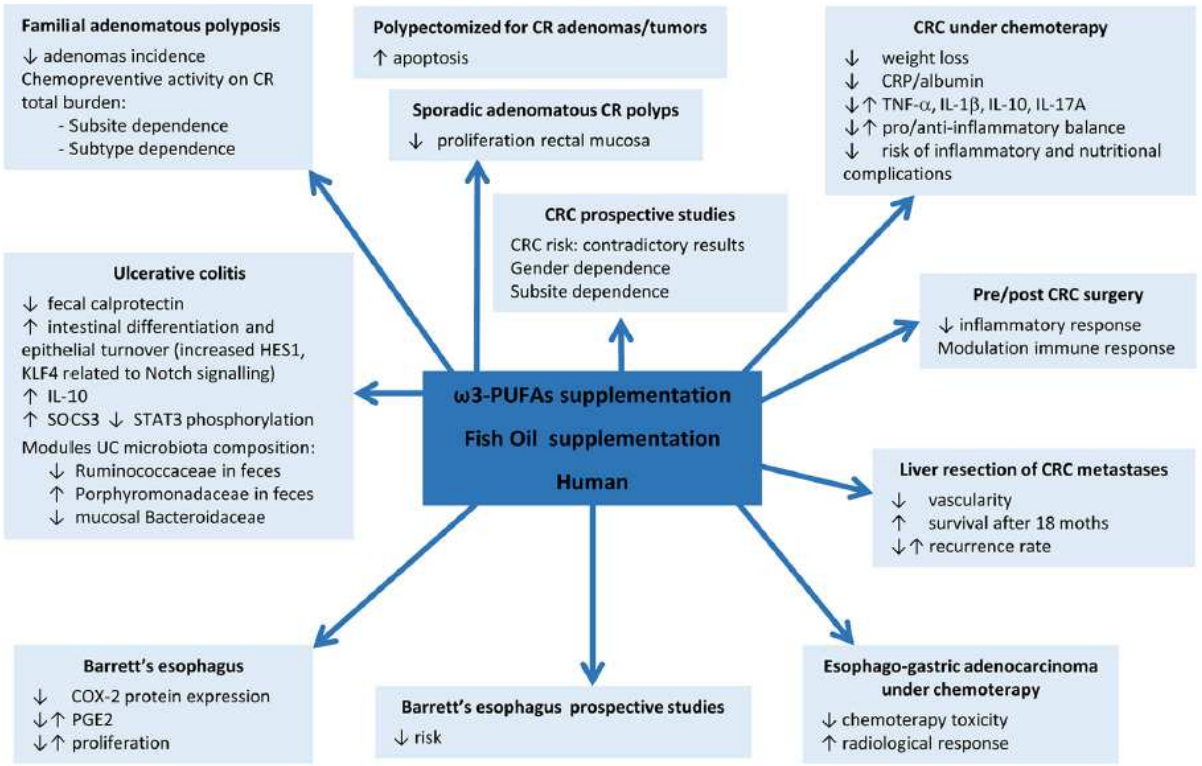
Methods: A literature search was conducted to identify primary research reporting on applications of the omega-3 PUFAs in gastrointestinal cancer.

Results: Reported laboratory studies indicate a clear role for omega-3 PUFAs in preventing cancer development at various stages including cancer cell proliferation, survival, angiogenesis, inflammation and metastasis. In clinical settings, omega-3 PUFAs have been reported to improve the immune response, maintain lean body mass, improve quality of life and improve overall survival in patients with colorectal and pancreatic cancer. In contrast to other GI cancers, there is a strong connection between inflammation and oesophageal cancer.

Conclusions: Little work has been done exploring the role for omega-3 PUFAs in oesophageal cancer prevention and management. The authors are conducting a clinical trial investigating the use of parenteral omega-3 PUFAs supplementary to the standard of care (epirubicin, oxaliplatin and capecitabine palliative chemotherapy) in patients with advanced oesophagogastric cancer as a promising new therapeutic approach.



Fish oil or ω3 polyunsaturated fatty acids (ω3-PUFAs) supplementation actions on gastrointestinal diseases in Human



Irún P,et al. Front. Pharmacol. 2019,10:852.

The Beneficial Effects of n-3 PUFAs in Skeletal Muscle

nutrients

MDPI

Review

Potential Roles of n-3 PUFAs during Skeletal Muscle Growth and Regeneration

Bill Tachtsis, Donny Camera and Orly Lacham-Kaplan *

Mary MacKillop Institute for Health Research, Exercise and Nutrition Research Program, Australian Catholic University, Melbourne, VIC 3000, Australia; bill.tachtsis@myacu.edu.au (B.T.); donny.camera@acu.edu.au (D.C.)
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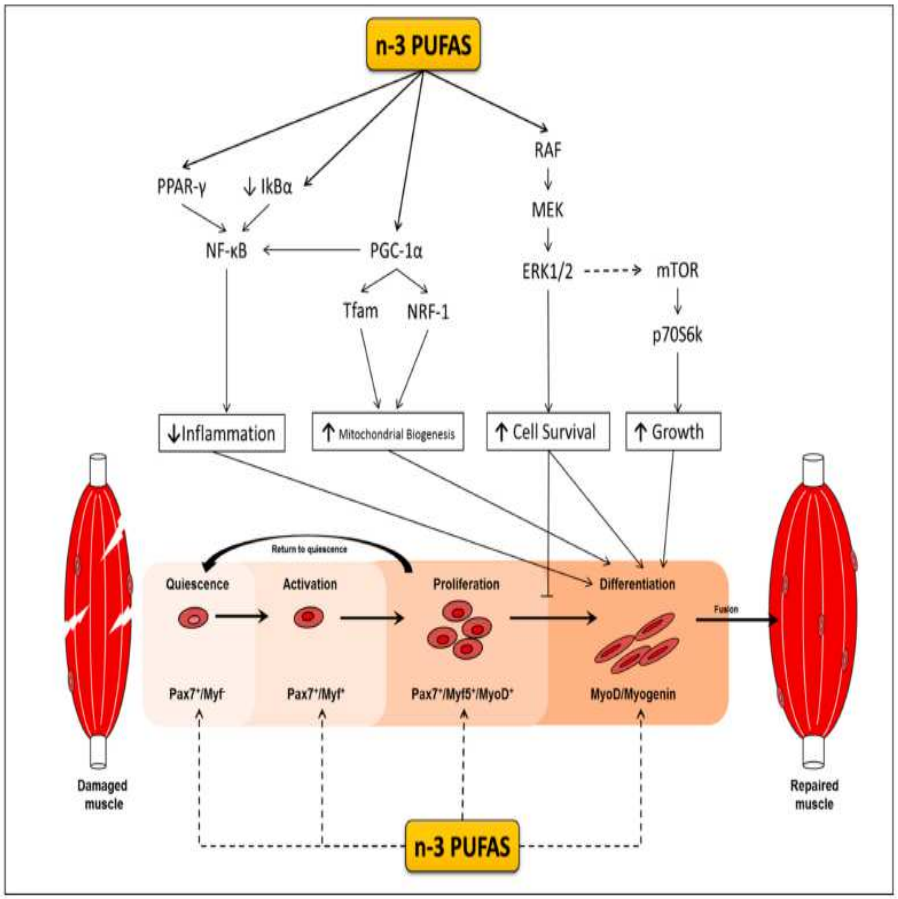
Received: 21 January 2018; Accepted: 2 March 2018; Published: 5 March 2018

Abstract: Omega-3 polyunsaturated fatty acids (n-3 PUFAs), which are commonly found in fish oil supplements, are known to possess anti-inflammatory properties and more recently alter skeletal muscle function. In this review, we discuss novel findings related to how n-3 PUFAs modulate molecular signaling responsible for growth and hypertrophy as well as the activity of muscle stem cells. Muscle stem cells commonly known as satellite cells, are primarily responsible for driving the skeletal muscle repair process to potentially damaging stimuli, such as mechanical stress elicited by exercise contraction. To date, there is a paucity of human investigations related to the effects of n-3 PUFAs on satellite cell content and activity. Based on current in vitro investigations, this review focuses on novel mechanisms linking n-3 PUFA's to satellite cell activity and how they may improve muscle repair. Understanding the role of n-3 PUFAs during muscle growth and regeneration in association with exercise could lead to the development of novel supplementation strategies that increase muscle mass and strength, therefore possibly reducing the burden of muscle wasting with age.



Bill Tachtsis et al. Nutrients 2018, 10, 309

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ESPEN Guideline

ESPEN practical guideline: Clinical Nutrition in cancer

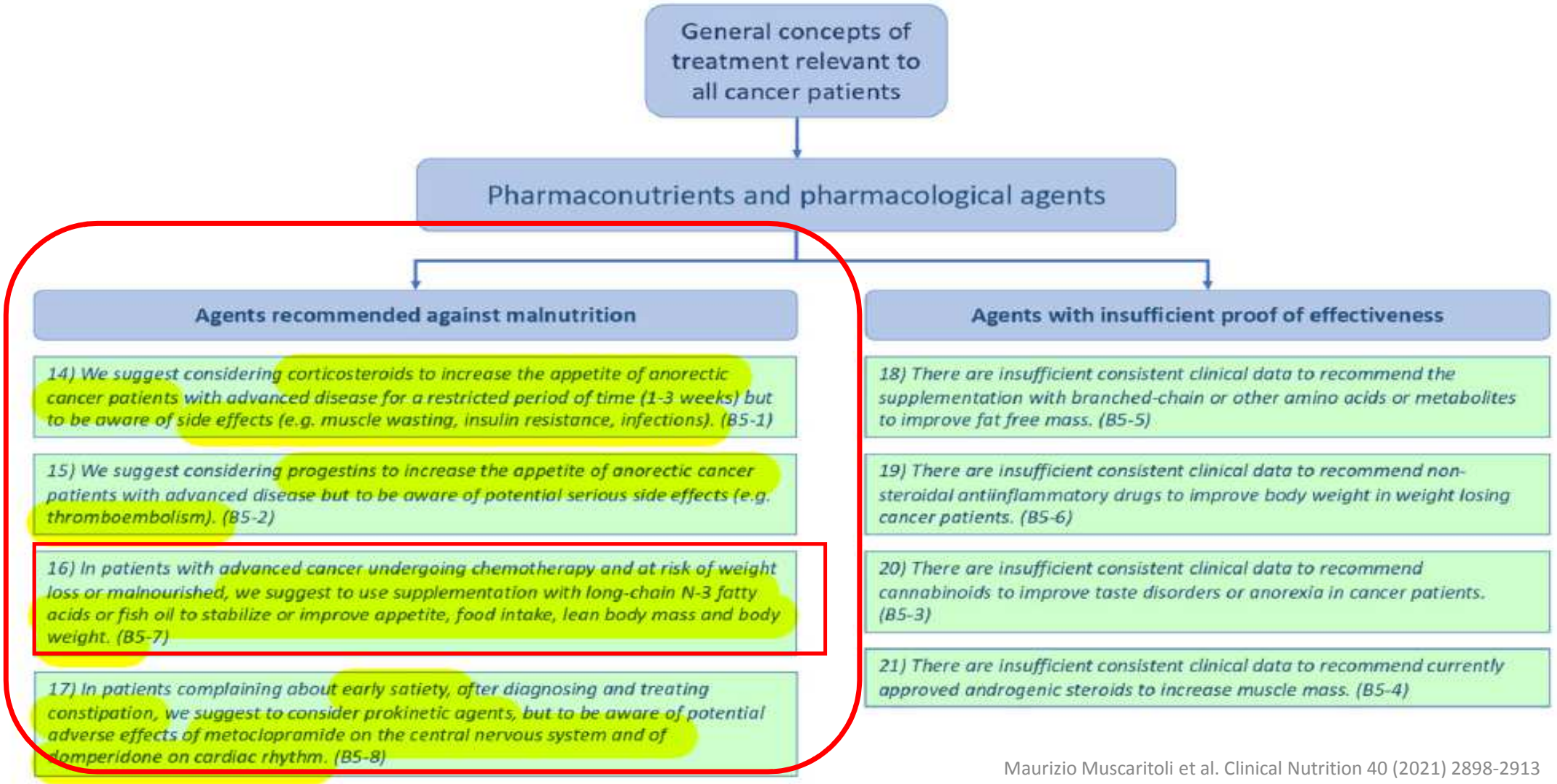
Maurizio Muscaritoli [a, *], Jann Arends [b], Patrick Bachmann [c], Vickie Baracos [d], Nicole Barthelemy [e], Hartmut Bertz [b], Federico Bozzetti [f], Elisabeth Hütterer [g], Elizabeth Isenring [h], Stein Kaasa [i], Zeljko Krznaric [j], Barry Laird [k], Maria Larsson [l], Alessandro Laviano [a], Stefan Mühlebach [m], Line Oldervoll [n], Paula Ravasco [o], Tora S. Solheim [p], Florian Strasser [q], Marian de van der Schueren [r, s], Jean-Charles Preiser [t], Stephan C. Bischoff [u]

Immuno-nutrients (arginine, N-3 fatty acids, nucleotides)

- **Improve lean body mass**
- **Reduces infectious complications**
- **Wound healing**
- **Prevent/ameliorate treatment related side effects like diarrhea,**
- **mucositis etc.**
- **Restore organ function**
- **Improve overall clinical outcomes**

- In upper GI cancer patients undergoing surgical resection in the context of traditional perioperative care, we recommend oral/enteral immunonutrition (arginine, n-3 fatty acids, nucleotides). (Recommendation C1-4; strength of recommendation strong - Level of evidence high - strong consensus)

Pharmaconutrients and pharmacological agents



Maurizio Muscaritoli et al. Clinical Nutrition 40 (2021) 2898-2913

2021 ESPEN guidelines on nutrition in cancer patients

- In patients with advanced cancer undergoing chemotherapy and at risk of weight loss or malnourished, we suggest using supplementation with long-chain N-3 fatty acids or fish oil to stabilize or improve appetite, food intake, lean body mass, and body weight. (Recommendation B5-7; strength of recommendation weak- Level of evidence low- strong consensus)

Maurizio Muscaritoli et al. Clinical Nutrition 40 (2021) 2898-2913

- Despite some systematic reviews, like Dewey et al. 2007, which concluded that there was insufficient evidence to support a recommendation for long-chain omega-3 fatty acids to treat cancer cachexia [51], two recent reviews demonstrate that long-chain fatty acids improved appetite, body weight, post-surgical morbidity, and quality of life in weight-losing cancer patients [52] and long-chain N-3 fatty acids in similar population during chemo and/or radiotherapy and reported beneficial effects when compared to a control arm, most prominently conservation of body composition [53]. Interestingly, there are several reports on the protective effects of fish oil on chemotherapy-induced toxicities like peripheral neuropathy [54,55]. When supplemented in usual doses fish oil and long-chain N-3 fatty acids are mostly well-tolerated. Mild GI effects were reported; the taste, a fishy aftertaste or fish belching, may impair compliance [56]. Recently ibrutinib has been associated with epistaxis in patients taking fish oil supplements; therefore, patients receiving ibrutinib should be counseled to avoid fish oil supplements. Due to the inconsistencies in the reported effects but with several positive trials published during the last few years reporting nutritional benefits, a plausible biological rationale, only mild side effects and no convincingly serious safety issues a weak recommendation for the use of fish oil and long-chain N-3 fatty acids has been made.

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Supportan® 倍速 專為癌症患者設計

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* 2017 ESPEN Guideline on Nutrition in Cancer Patients, Clinical Nutrition 36 (2017)11-48 符合 ESPEN三大營養素及魚油 EPA 攝取建議。

產品	三得利 魚油DHA&EPA	NU SKIN 深海鯊活魚油	NU SKIN 草飼鴨涎魚油	倍健 天然高濃縮魚油	OMACOR
等級	食品級				藥品級
EPA含量(mg)	25	150	150	300	460
DHA含量(mg)	75	100	100	200	380
魚油總量(mg)	400	1000	1000	1000	1000
EPA/DHA濃度	25%	25%	25%	50%	84%

Outline: Nutrition intervention for cancer patients

- Introduction
- Definition and Influence of cancer-related cachexia/malnutrition
- Nutrition strategies
  - Special for chemotherapy: IV glutamine
  - General concepts: Fish oil (n-3 PUFA)
  - **Guidelines**
- Conclusion

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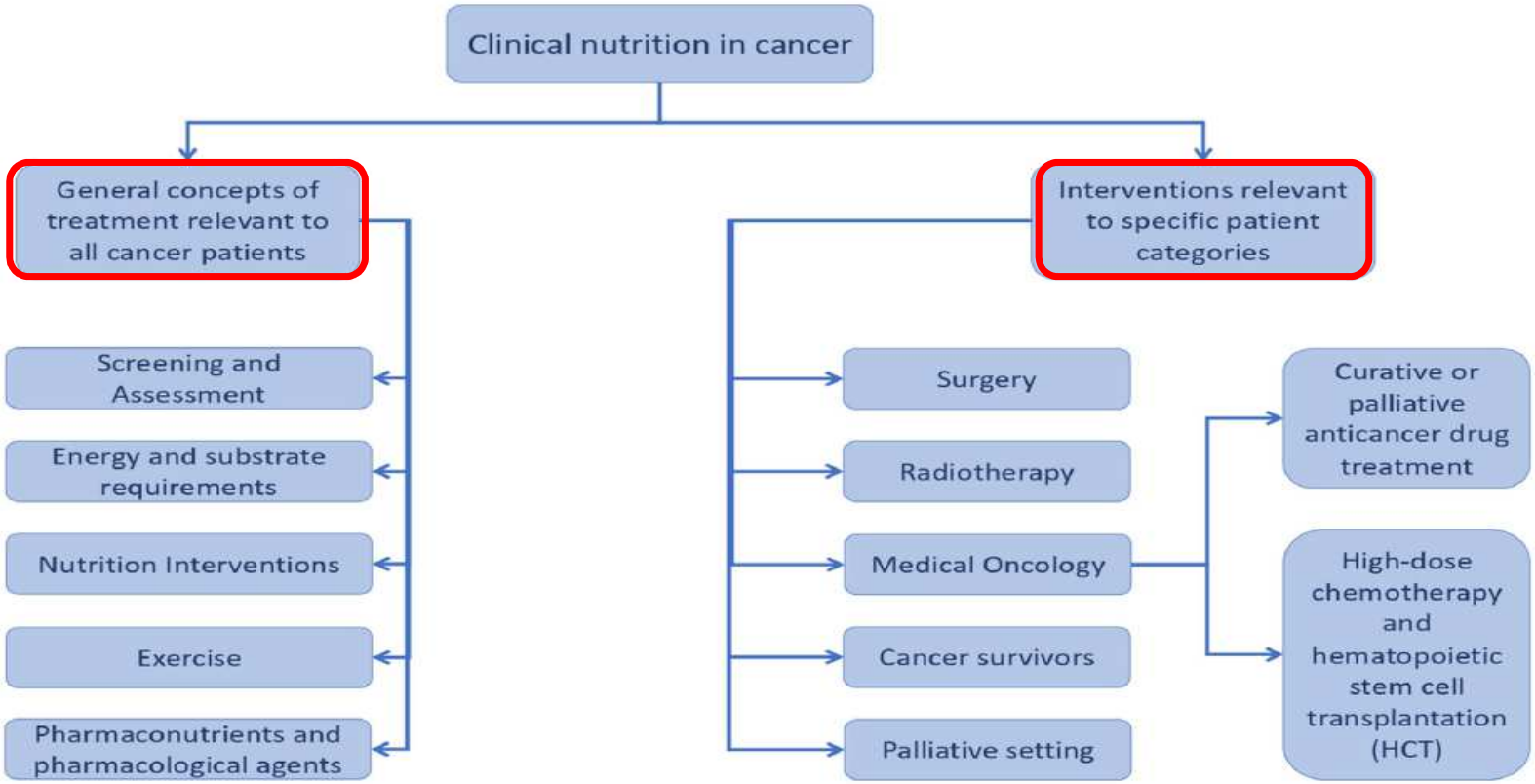
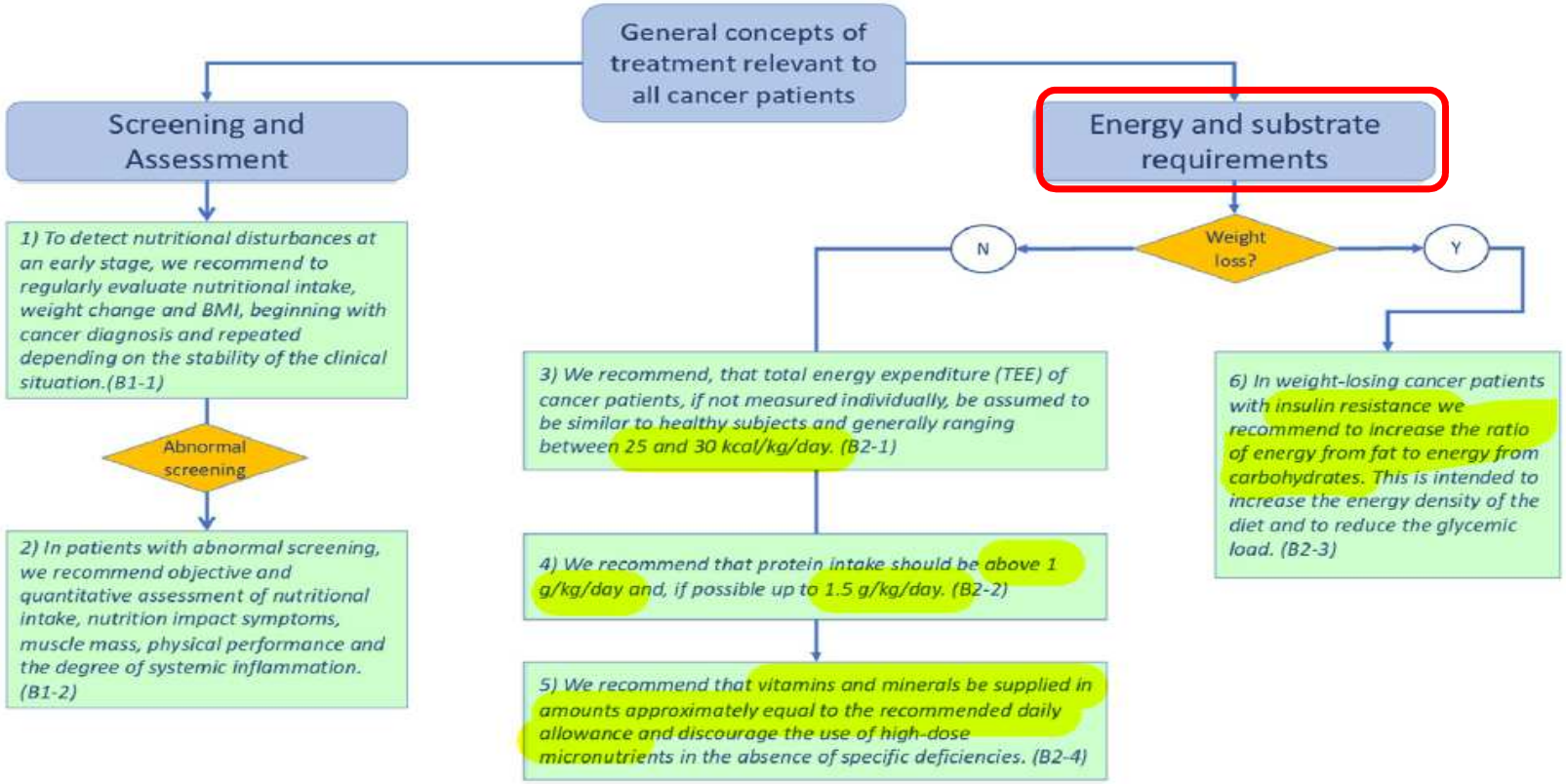
Structure of the ESPEN practical guideline: “Clinical nutrition in cancer”



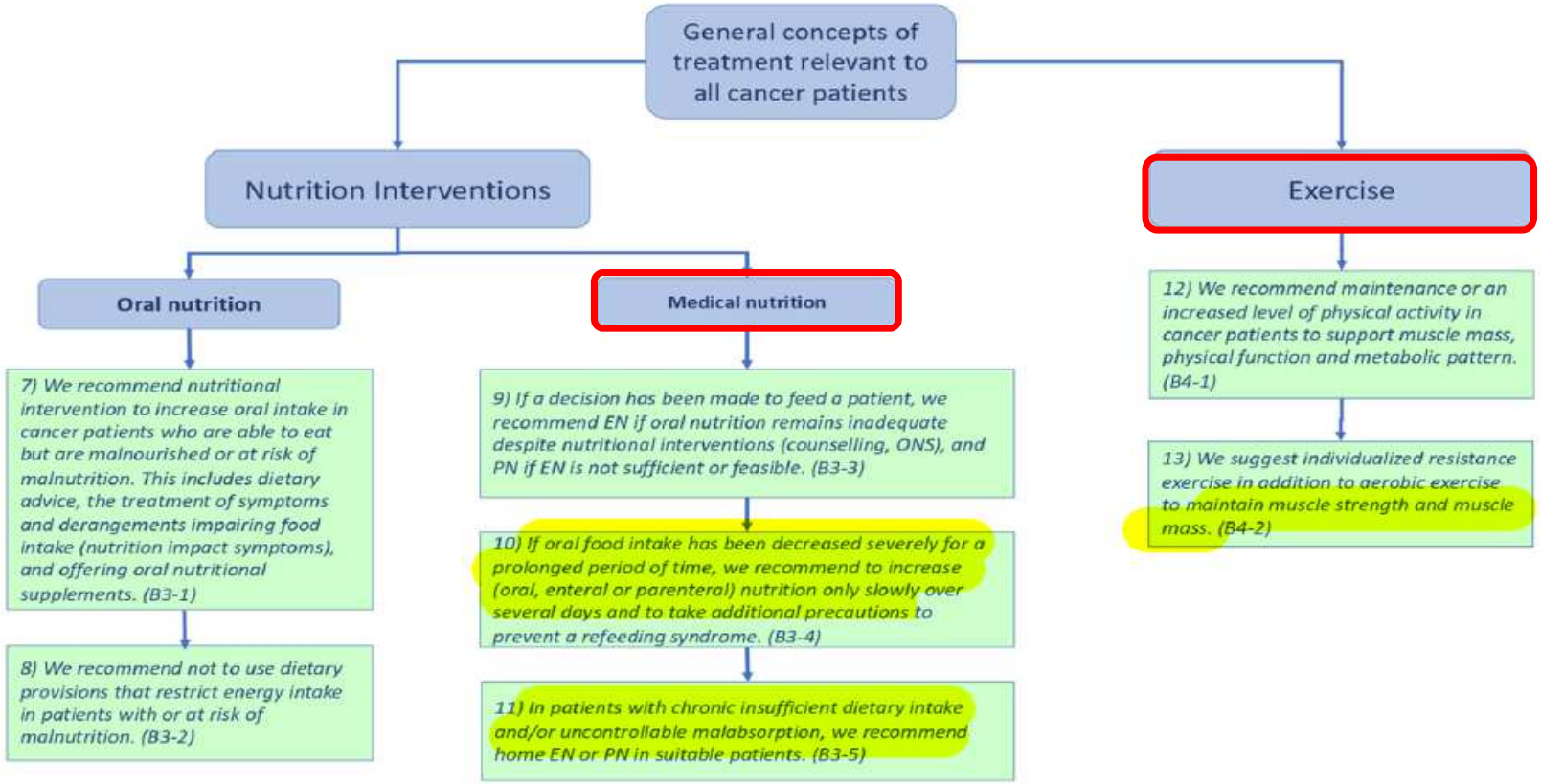
Maurizio Muscaritoli et al. Clinical Nutrition 40 (2021) 2898-2913

General concepts of treatment relevant to all cancer patients



Maurizio Muscaritoli et al. Clinical Nutrition 40 (2021) 2898-2913

Types of nutrition intervention and Exercise



Maurizio Muscaritoli et al. Clinical Nutrition 40 (2021) 2898-2913

Therapeutic Advances in Medical Oncology

Review

From guidelines to clinical practice: a roadmap for oncologists for nutrition therapy for cancer patients

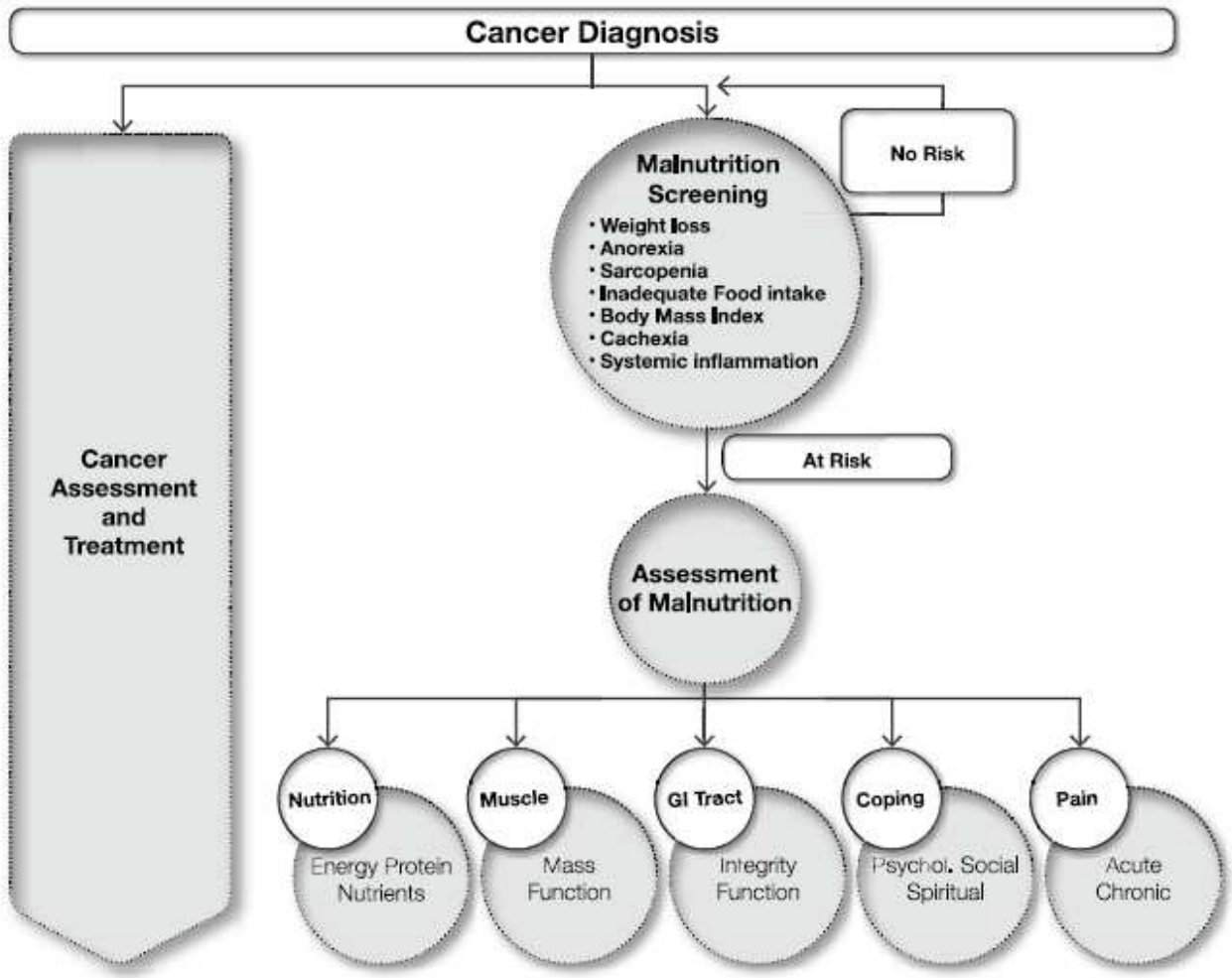
Maurizio Muscaritoli, Jann Arends and Matti Aapro

Ther Adv Med Oncol

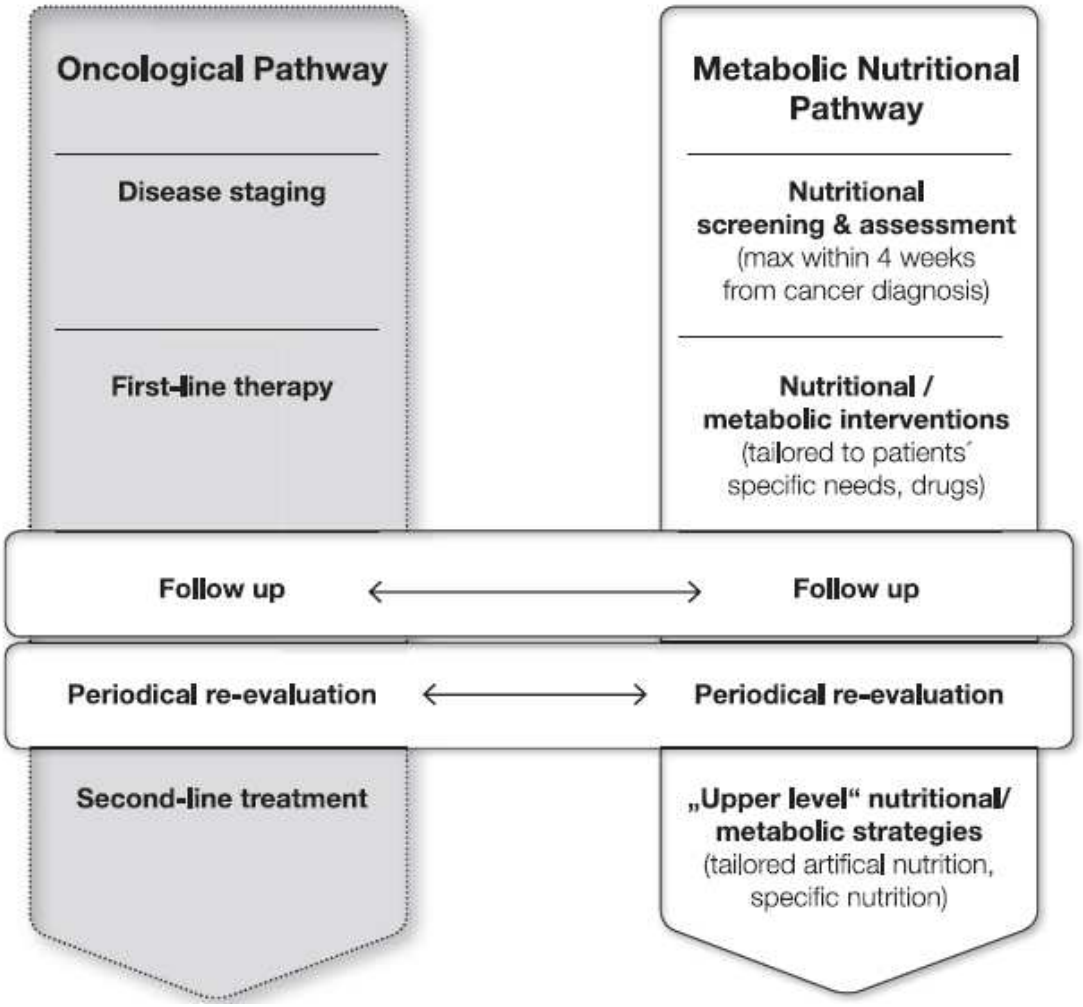
2019, Vol. 11: 1–14

DOI: 10.1177/1758835919880084

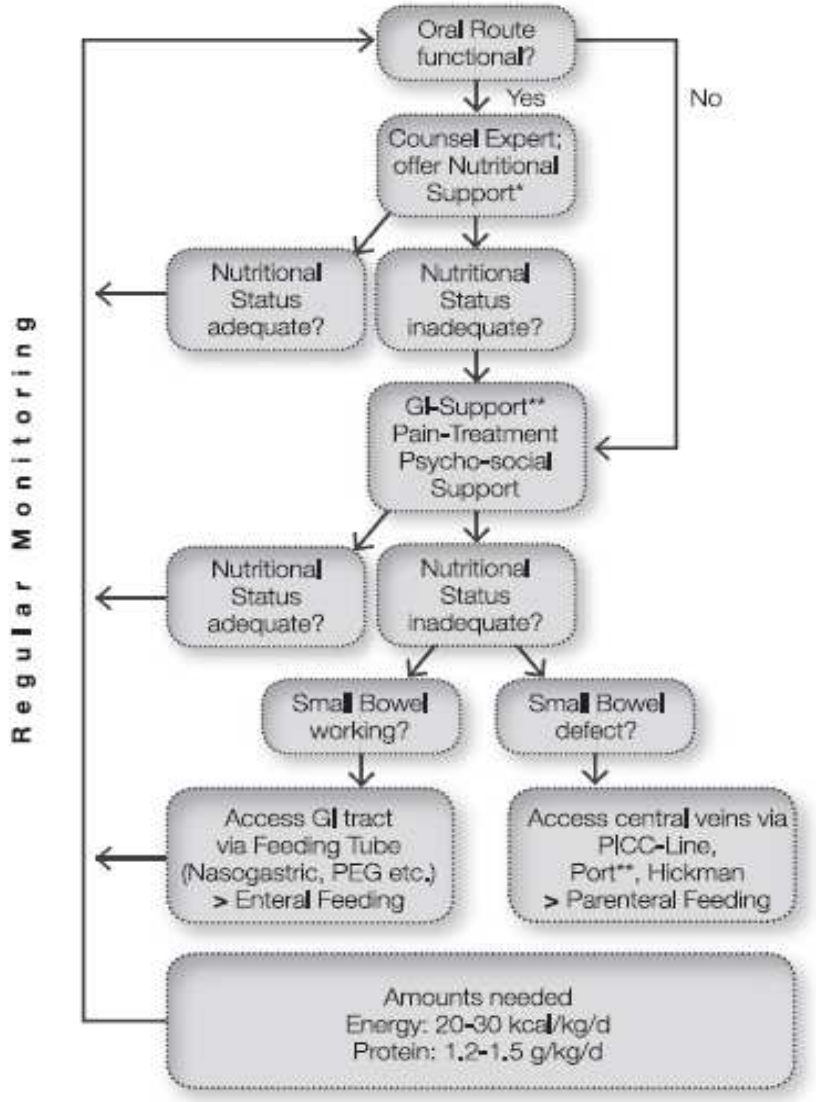
Tackling malnutrition in oncology as a multidisciplinary team approach



Continuum of care for the cancer patient: the parallel pathway in oncology



Proposed treatment algorithm incorporating the nutritional status in oncology



Nutritional goals in cancer treatment

Nutritional Intakes	Amount
Energy	20–25 kcal/kg/d for bedridden patients 25–30 kcal/kg/d for ambulatory patients
Protein	>1 g/kg/day and, if possible, up to 1.5 g/kg/day
Micronutrients, i.e. vitamins and essential trace elements	Vitamins and minerals to be supplied in amounts approximately equal to the RDA. Use of high-dose micronutrients in the absence of specific deficiencies is discouraged

RDA, recommended daily allowance.

Outline: Nutrition intervention for cancer patients

- Introduction
- Definition and Influence of cancer-related cachexia/malnutrition
- Nutrition strategies
  - Special for chemotherapy: IV glutamine
  - General concepts: Fish oil (n-3 PUFA)
  - Guidelines
- **Conclusion**

Goals of oncology-specific nutrition

- *Maintain/ increase body weight*
- *Preserve/ improve muscle mass & function*
- *Reduce inflammation*
- *Improve immunity*
- *Improve tolerance to multimodal cancer therapy*

High protein, High energy (esp. Lipid)
Consider Omega – 3FA +/- Glutamine

Take home message

- Anorexia/cachexia and malnutrition in oncology patients is a very frequent problem.
- Oncology patients are in very high risk of malnutrition and therefore increasing the risk of complications, length of hospital stay, and poor quality of life.
- Nutritional support started early helps in completing treatments and improving many outcomes.
- Nutrition strategies:
  - Modulate or reduce cachexia
  - Improve quality of life, oncology treatment tolerance and survival in cancer.

(Frida Kahlo)

Frida Kahlo (芙烈達·卡蘿,墨西哥女畫家)