乳癌之癌因性疲憊症治療照護

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乳房外科

Cancer Treatment

”Cure sometimes, treat often, comfort always“

Hippocrates

因化療讓患者感到痛苦的事

Ranking #1: Fatigue

Ranking of adverse effect	1983[1]	1995[1]	2003[2]
1	Vomiting	Nausea	**Fatigue**
2	Nausea	Hair loss	Nausea
3	Hair loss	Vomiting	Sleep disturbance

1. De Boer-Dennert M, et al. Patient perceptions of the side-effects of chemotherapy: the influence of 5HT3 antagonists. Br J Cancer. 1997;76:1055-1061.
2. Hofman M, et al. Cancer Patients' Expectations of Experiencing Treatment-Related Side Effects. Cancer. 2004;101:851-857.

Fatigue in Different Adjuvant Chemotherapy Regimens Had the same pattern Over Time

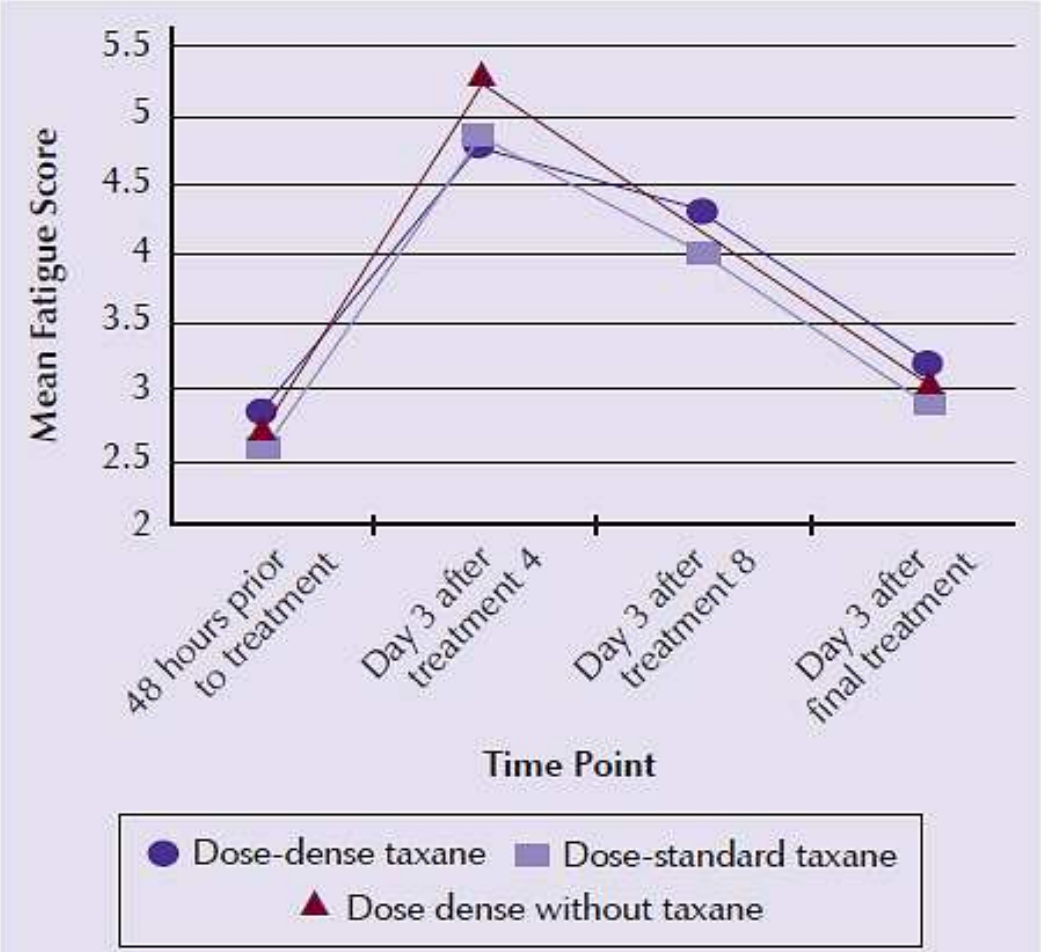


Figure 1. Patterns of Fatigue in Different Chemotherapy Regimens Over Time

- Participants rated their fatigue **highest at treatment 4**.
- Fatigue levels for all regimens **did not return to baseline levels by the 30-day measurement**.

Oncology Nursing Forum 2009; 36 (5): 563-569.

Fatigue is common at adjuvant chemotherapy for Breast Cancer

	Epirubicin, cyclophosphamide, and paclitaxel plus gemcitabine (n=1565)			Epirubicin, cyclophosphamide, and paclitaxel (n=1567)		
	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4
Neutropenia	397 (25%)	323 (21%)	204 (13%)	364 (23%)	212 (14%)	200 (13%)
Myalgia and arthralgia	1140 (73%)	200 (13%)	7 (<1%)	1147 (73%)	175 (11%)	11 (1%)
Fatigue	1254 (80%)	198 (13%)	9 (1%)	1287 (82%)	140 (9%)	12 (1%)
Infection	578 (37%)	194 (12%)	8 (1%)	601 (38%)	131 (8%)	10 (1%)
Vomiting	786 (50%)	134 (9%)	9 (1%)	736 (47%)	101 (6%)	7 (1%)
Nausea	1271 (81%)	132 (8%)	0	1255 (80%)	102 (7%)	0

Table 3. Frequency of Patient-Reported Adverse Events During Chemotherapy

	No. of Patients (%)									
	EC-D (n = 994)					DC (n = 1,006)				
Adverse Event	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	*P*
Nausea	103 (10)	465 (47)	340 (34)	71 (7)	7 (1)	255 (25)	552 (55)	182 (18)	11 (1)	4 (0)	< .001
Fatigue	8 (1)	255 (26)	427 (43)	249 (25)	48 (5)	33 (3)	290 (29)	436 (43)	225 (22)	20 (2)	< .001
Peripheral edema	387 (39)	464 (47)	110 (11)	25 (3)	—	334 (33)	463 (46)	181 (18)	26 (3)	—	< .001

J Clin Oncol. 2017 Aug 10;35(23):2639-2646.

Lancet Oncol. 2017 Jun;18(6):755-769.

隨著癌症多種合併治療的進行，可預測患者發生重度疲憊的風險更高

整合分析12,327位乳癌存活者，1/4病患在癌症治療後有重度疲憊

Table 3. Risk factors of severe fatigue in breast cancer survivors

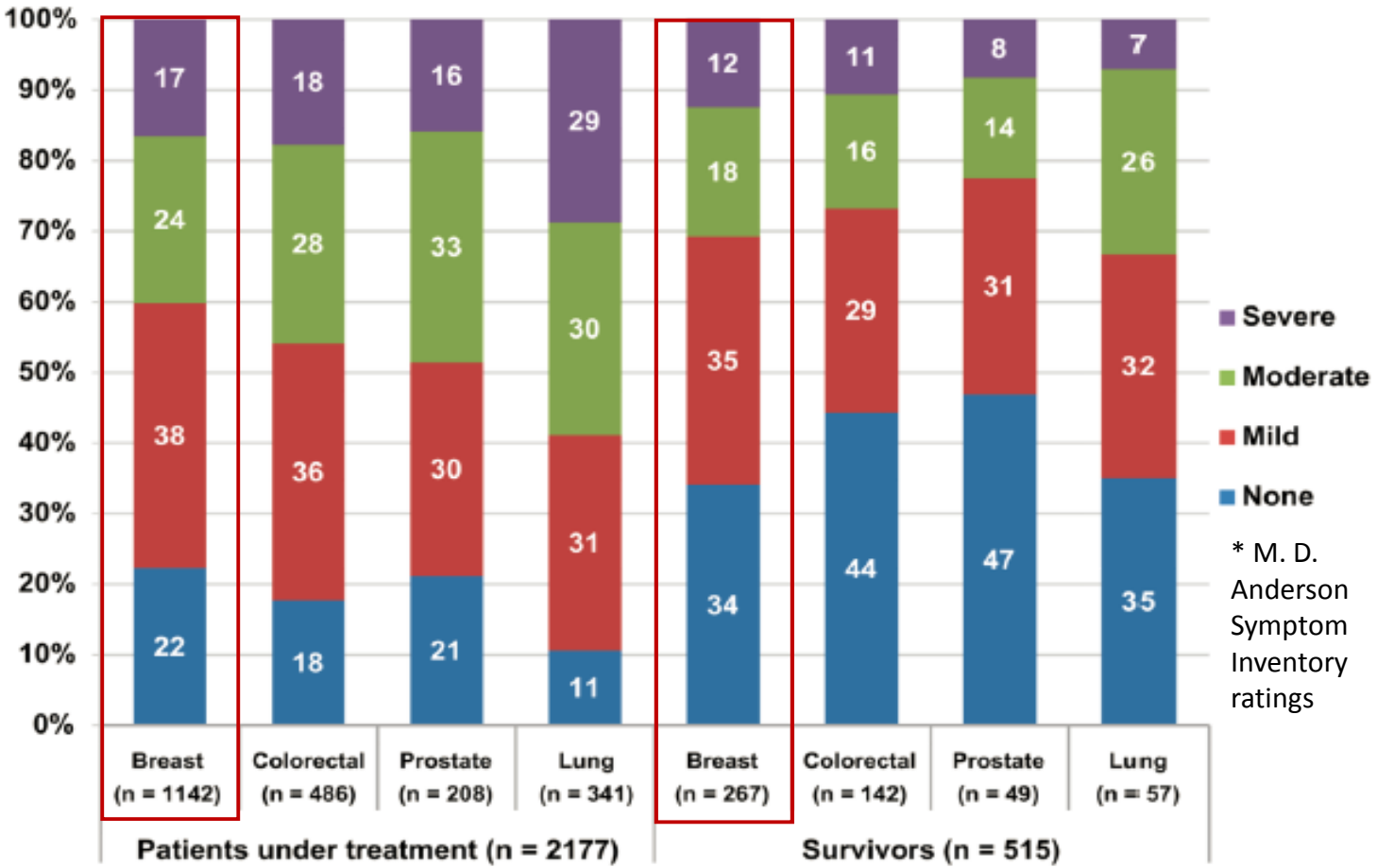
Variables	References	Number of studies	Sample size (*N*)	Risk ratio (CI)
Treatment combinations				
SU	[26, 38, 42, 45, 47, 56, 57]	6	3028	0.83 (0.70 to 0.98)*
SU + CT	[32, 38, 42, 47, 55–57]	7	3379	1.33 (0.97 to 1.82)
SU + RT	[26, 32, 38, 45–48, 50, 55–57]	11	4164	0.87 (0.78 to 0.96)*
SU + HT	[38, 42, 45–47]	4	981	0.83 (0.57 to 1.20)
SU + CT + RT	[26, 32, 38, 45–48, 55–57]	10	3882	1.18 (1.05 to 1.33)*
SU + CT + HT	[38, 42, 45–47]	4	981	0.99 (0.66 to 1.49)
SU + RT + HT	[26, 38, 45–48]	6	1264	0.89 (0.74 to 1.07)
SU + CT + RT + HT	[26, 38, 45–48]	6	1264	1.38 (1.15 to 1.66)*

*$P < 0.05$.

SU, surgery; CT, chemotherapy; RT, radiotherapy; HT, hormone therapy; SMD, standardized mean difference; SD, standard deviation.

Abrahams HJ et al. Risk factors, prevalence, and course of severe fatigue after breast cancer treatment: a meta-analysis involving 12 327 breast cancer survivors. Ann Oncol. 2016 Jun;27(6):965-74.

High prevalence of moderate/severe fatigue in both actively treated cancer patients & survivors



* M. D. Anderson Symptom Inventory ratings

Prevalence of fatigue by cancer type

Wang et al. Prevalence and characteristics of moderate-to-severe fatigue: a multicenter study in cancer patients and survivors. Cancer. 2014; 120(3): 425–432.

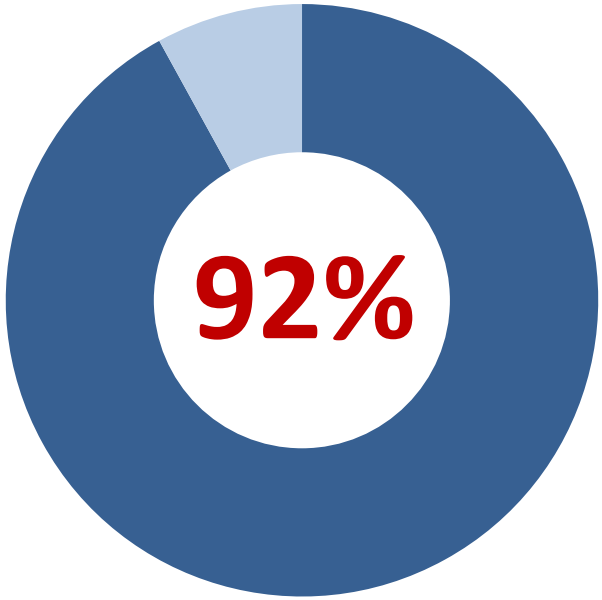
92% 台灣癌症患者罹癌期間有疲憊問題

- 第一次全台灣癌症病患「癌因性疲憊症」流行病學調查研究
  - 期間為2015年2月至5月
  - 共23家醫院進行研究
  - 共1,207病患參與調查
  - 問卷

    癌因性疲憊(BFI-T, ICD-10)

    生活品質量表(FACT-G7)

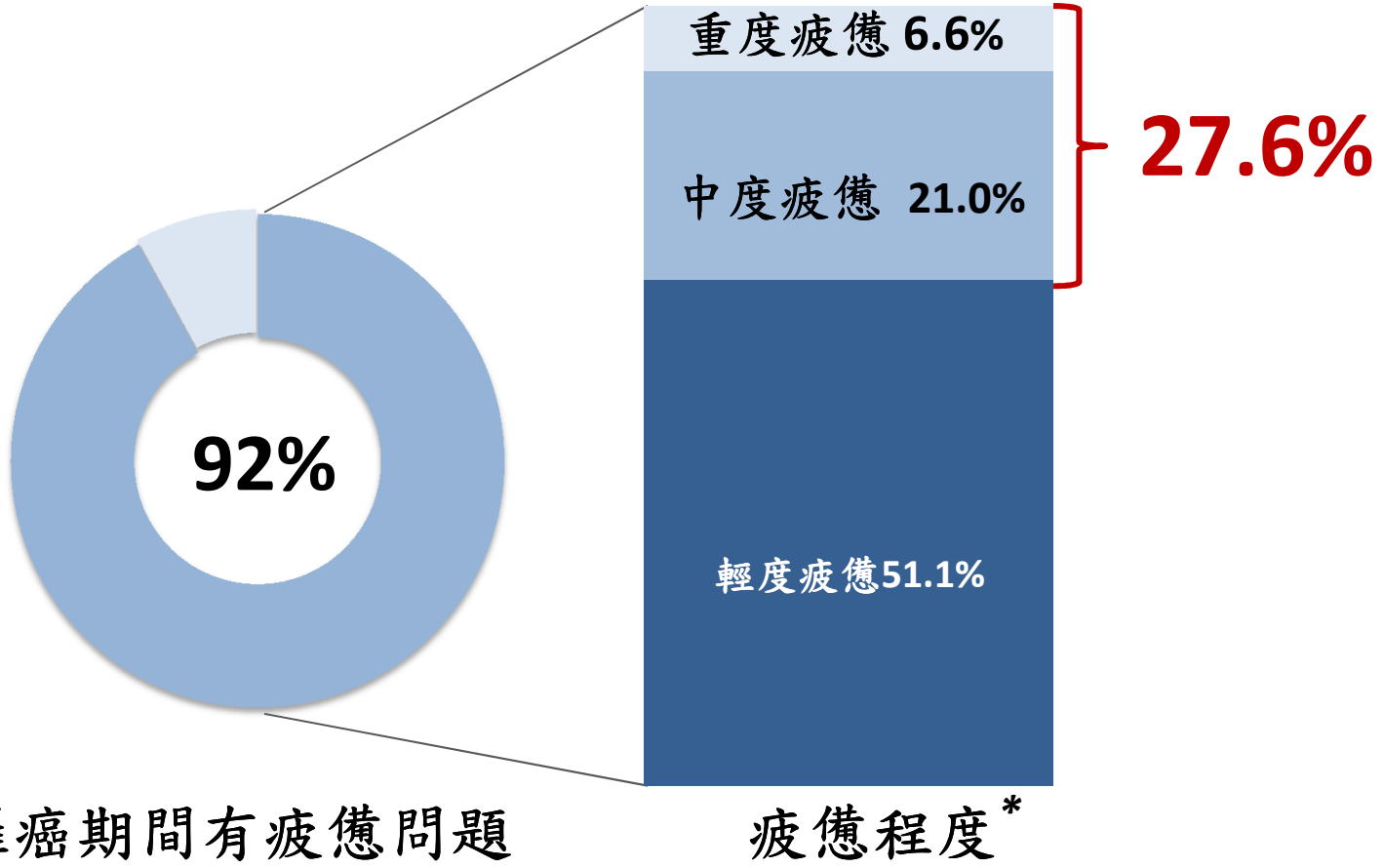
    癌症症狀困擾嚴重度量表



罹癌期間有疲憊問題

K. M. Rau et. Al., Japanese Journal of Clinical Oncology, 2020, 1–9
2015 Palliative Care in Oncology Symposium, Boston; Oct 9-10, 2015, Abstract # 155471. 2016 MASCC Poster # MASCC-0488.

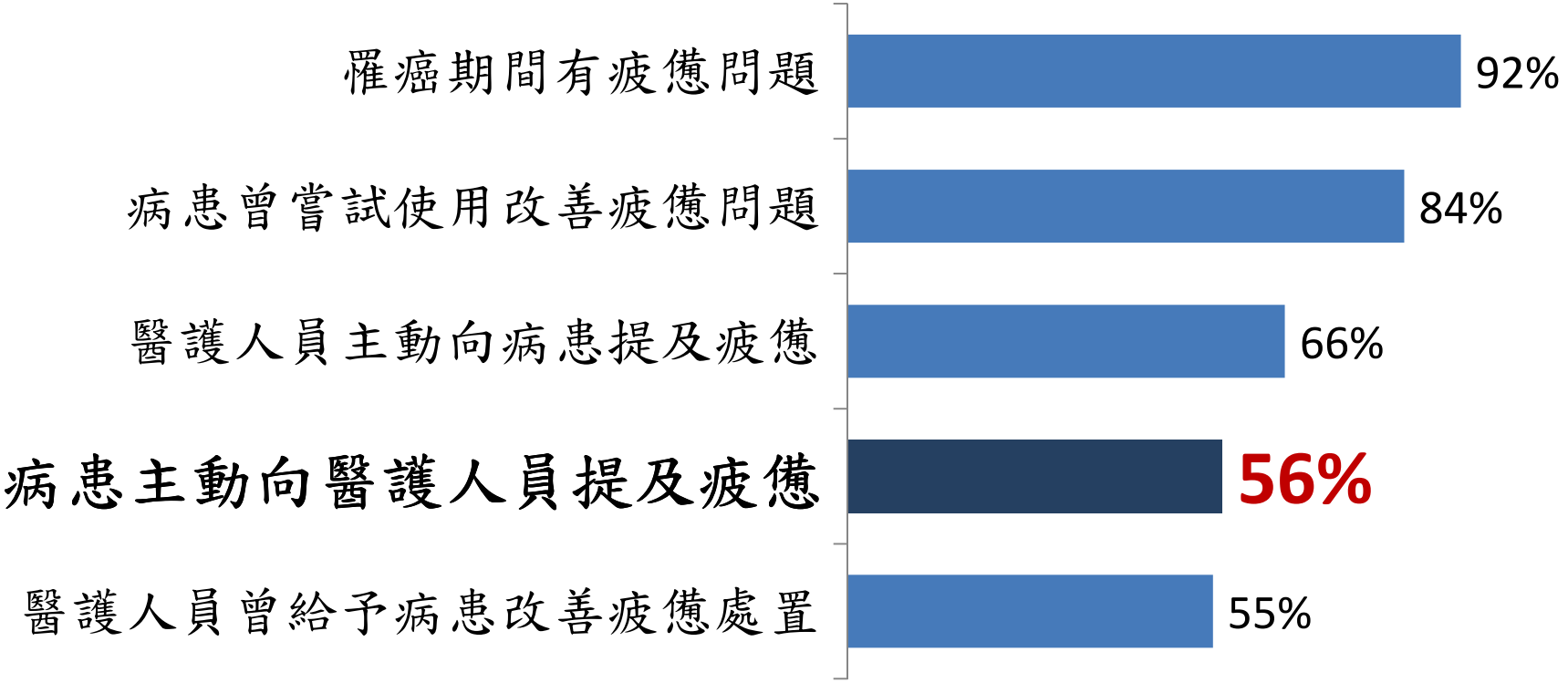
大於1/4 癌症病患有中重度疲憊



* The three groups were calculated from the average of nine items from BFI and categorize into mild (<4), moderate (4-6.99), Severe (≧7).

K. M. Rau et. Al., Japanese Journal of Clinical Oncology, 2020, 1–9
2015 Palliative Care in Oncology Symposium, Boston; Oct 9-10, 2015, Abstract # 155471. 2016 MASCC Poster # MASCC-0488.

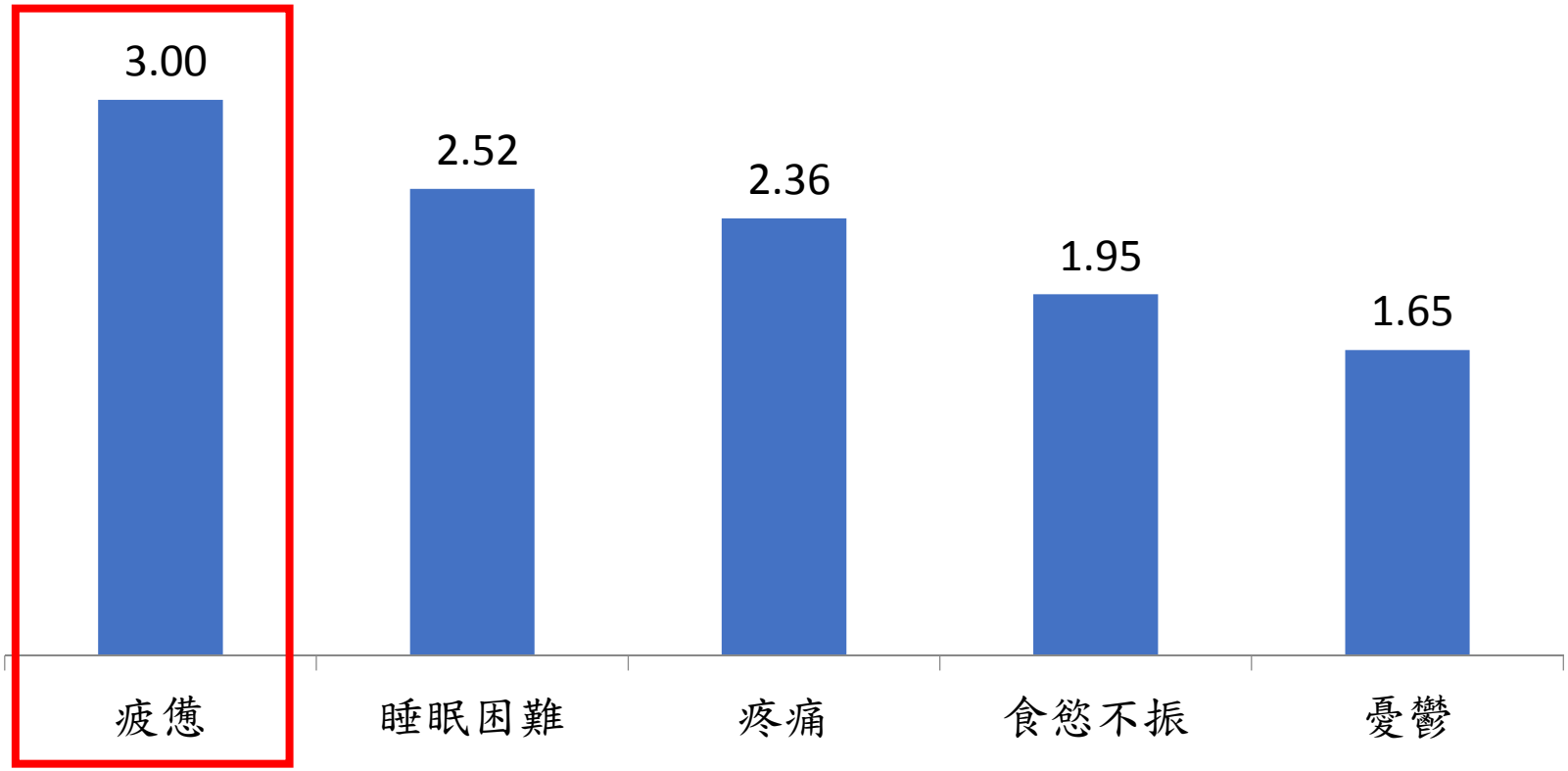
約一半癌症病患主動向醫護人員提及疲憊



K. M. Rau et. Al., Japanese Journal of Clinical Oncology, 2020, 1–9
2015 Palliative Care in Oncology Symposium, Boston; Oct 9-10, 2015, Abstract # 155471. 2016 MASCC Poster # MASCC-0488.

疲憊：最嚴重的症狀困擾

癌症症狀困擾嚴重度*

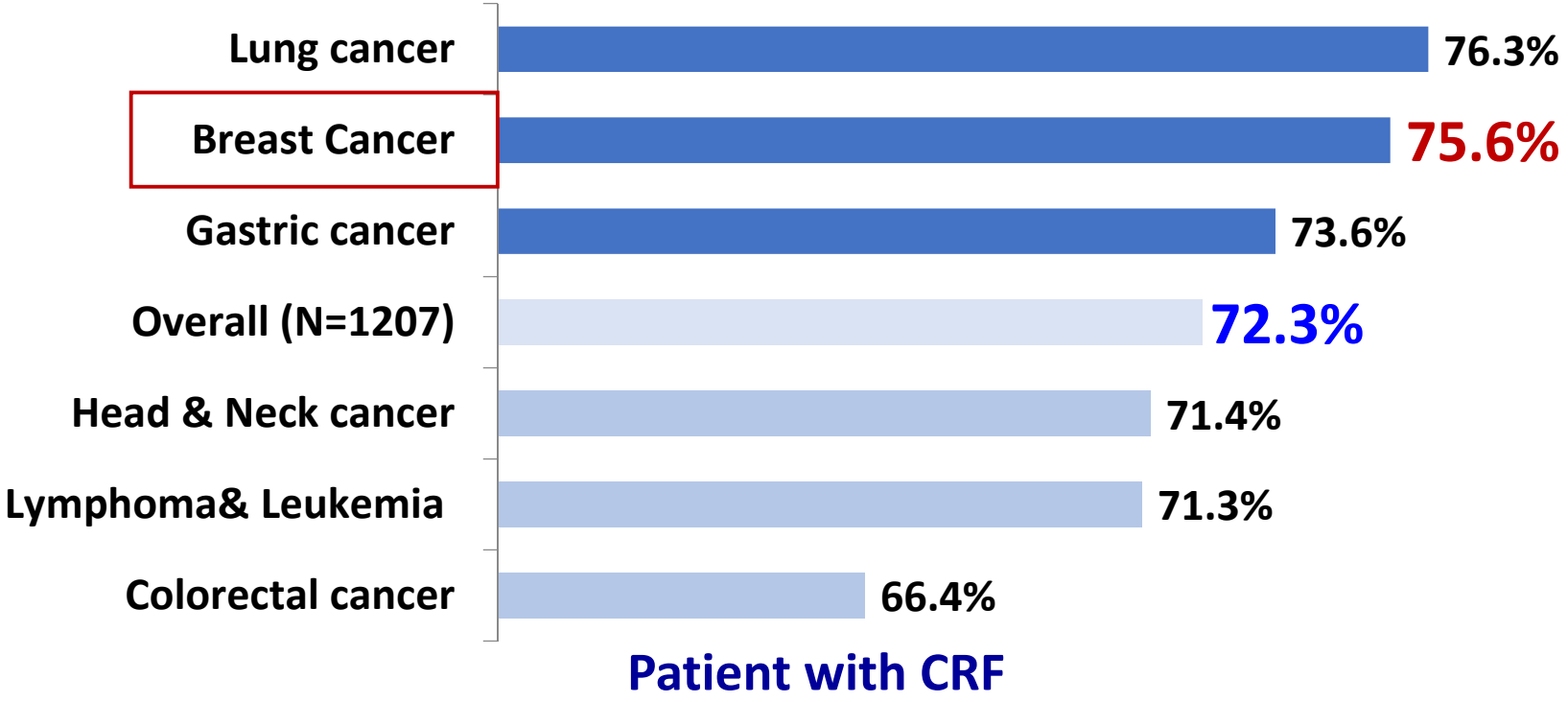


*Symptom distress scale in patients with cancer: ranging from 0 to 10, the higher score means the higher distress.

K. M. Rau et. Al., Japanese Journal of Clinical Oncology, 2020, 1–9
2015 Palliative Care in Oncology Symposium, Boston; Oct 9-10, 2015, Abstract # 155471. 2016 MASCC Poster # MASCC-0488.

經BFI-T評估，72%癌症患者有癌因性疲憊

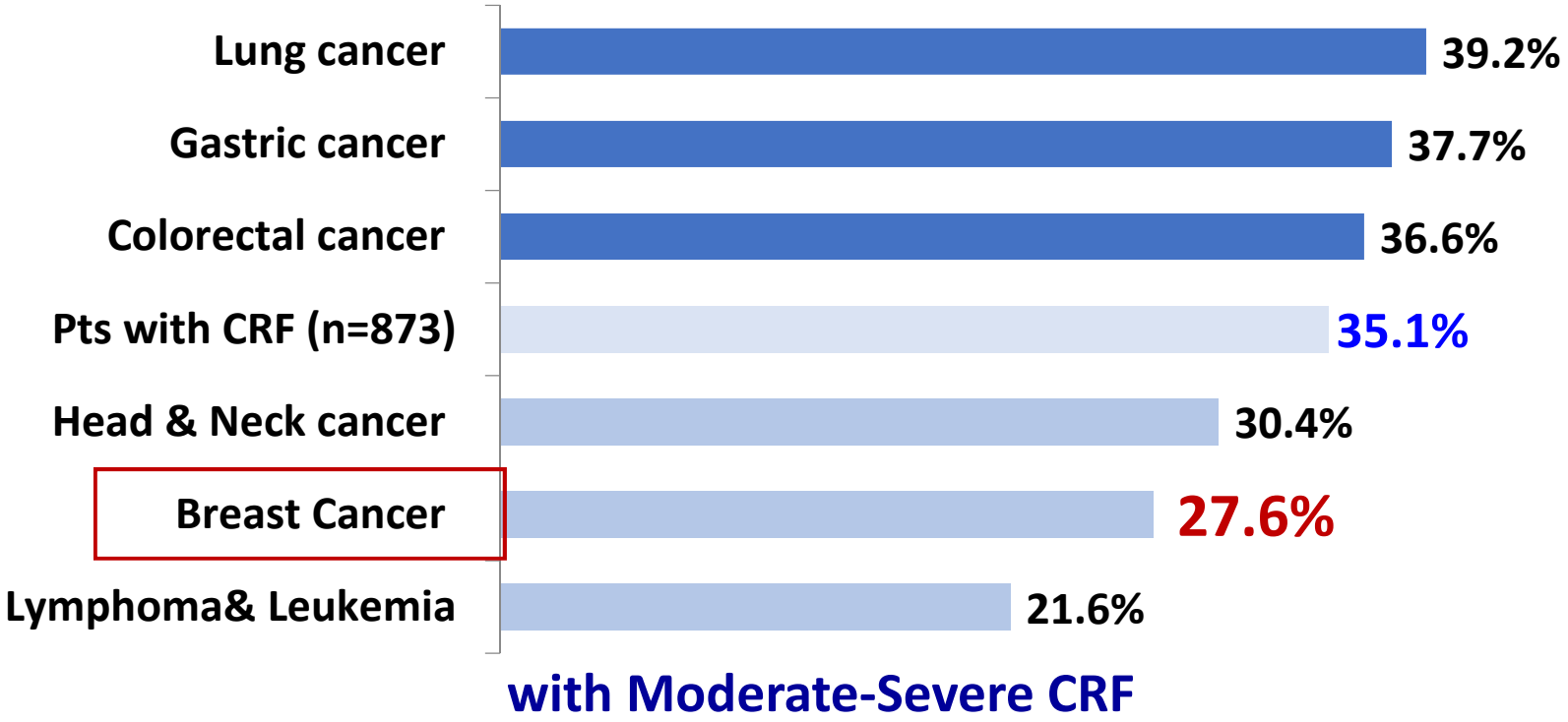
台灣乳癌患者，3/4有癌因性疲憊



K. M. Rau et. Al., Japanese Journal of Clinical Oncology, 2020, 1–9
2015 Palliative Care in Oncology Symposium, Boston; Oct 9-10, 2015, Abstract # 155471. 2016 MASCC Poster # MASCC-0488.

有癌因性疲憊的患者，35%為中重度疲憊

乳癌之癌因性疲憊症患者，約28%為中重度疲憊



**The severity was calculated from the average of nine items from BFI –T and categorized into mild (<4), moderate (4-6.99), Severe (≧7).*

K. M. Rau et. Al., Japanese Journal of Clinical Oncology, 2020, 1–9

2015 Palliative Care in Oncology Symposium, Boston; Oct 9-10, 2015, Abstract # 155471. 2016 MASCC Poster # MASCC-0488.

什麼是
CANER RELATED
FATIGUE ?

不一樣的累……疲憊！

正常人也會累，休息就可改善.....

癌症患者的累，無法藉由休息而改善！

- 累 (Tiredness): 發生在過度活動後，可透過充分休息或睡眠加以改善。
- **疲憊(Fatigue):** 感受異常的累，無法以休息或睡眠緩解，稱為疲憊症。

National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Cancer-Related Fatigue

Version 1.2021 — December 1, 2020

NCCN.org

Continue

DEFINITION OF CANCER-RELATED FATIGUE

Cancer-related fatigue is a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning.

與癌症或癌症治療相關而且和近期活動量不成比例的疲累感，具有持續、令人感到不適、而主觀的特性，且足以影響正常生活

1. NCCN. NCCN Clinical Practice Guidelines in Oncology: Cancer-Related Fatigue, Version 1.2021.
2. Yeh ET et al. BMC Cancer 2011; 11:387.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

癌因性疲憊的定義：NCCN, ICD-10

美國國家綜合癌症網絡[1] (National Comprehensive Cancer Network, NCCN)

與癌症或癌症治療相關而且和近期活動量不成比例的疲累感，
具有持續、令人感到不適、而主觀的特性，且足以影響正常生活

國際疾病分類第 10 版 (ICD-10)[2]

符合 A–D 四大要件

A. 症狀	B. 影響生活	C. 引起原因	D. 排除
最近一個月至少有連續兩週期間，每天或幾乎每天出現至少六項 A1–A11 的症狀 (A1 為必需)。	疲累不堪的感覺會干擾到職場工作、家務處理、或人際互動。	病歷、身體檢查、或生化檢查有記錄顯示疲憊症狀為癌症或癌症治療所引起。	疲憊不是由精神共病（如重度憂鬱、身體化疾患、心身症、或譫妄）所引起。

1. NCCN. NCCN Clinical Practice Guidelines in Oncology: Cancer-Related Fatigue, Version 2.2020.
2. Yeh ET et al. BMC Cancer 2011; 11:387.

癌因性疲憊的定義：ICD-10

A

最近**一個月至少有連續兩週**期間，每天或幾乎每天出現**至少六項 A1-A11 的症狀**（A1 為必需）

ICD-10 Code:
R53.0

國際疾病分類第10版 (ICD-10)[1]

A1 **感到明顯的疲累、缺少活力、或需要增加休息，且與近期活動程度不成比例**
A2 感到**全身**虛弱、沉重
A3 感到很**難集中精神**或注意力
A4 感到平常習慣做的事都變得**乏味**而不想去做
A5 感到**難以入睡**、睡得不安穩、早起有困難、或是睡得太多
A6 感到**睡覺起來還是覺得疲累**，精神沒有恢復
A7 感到做什麼事情都必須經過一番掙扎，**勉強**自己去做
A8 因為疲累而感到**悲傷**、失意、或煩躁
A9 因為疲累不堪而事情做一半就**做不下去**了
A10 感到**記性變差**
A11 只要做了**費力的事**就會**持續感到病懨懨、不舒服**

Yeh ET et al. BMC Cancer 2011; 11:387.

癌因性疲憊症之臨床治療指引

MANAGEMENT OF CANCER-RELATED FATIGUE – A GUIDELINE FOR TAIWAN –

2017年 11月 第一版

台灣癌症安寧緩和醫學會

台灣腫瘤護理學會

癌因性疲憊評估與治療

以NRS或BFI-T
評估疲憊

<4分
輕度疲憊

非藥物治療
運動、營養飲食、
認知行為治療、
睡眠衛生等

≥4分
中重度疲憊

加上藥物治療
- 癌因性疲憊適應症處方用藥
  PG2 Injection
- 其他用藥
  類固醇、中樞神經興奮劑

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(Ritalin) 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)

「藥品給付規定」修訂對照表

第 3 節 代謝及營養劑 Metabolic & nutrient agents

（自110年3月1日生效）

修訂後給付規定	原給付規定
3.3.20.Polysaccharides of Astragalus membranaceus(如 PG2 Lyo. Injection)：(110/3/1) 使用本藥品應符合下列各條件： 1.限用於第四期因疾病進展導致中重度疲憊之乳癌成人患者(不含住院安寧療護病患)。 2.臨床上需符合ICD-10診斷標準，病歷上應詳細記載疲憊分數≧4(BFI-T 或 VAS)，經其他處置無效之中重度癌因性疲憊症患者。 3.ECOG 需為 0-2 之患者。 4.每位病人終生給付 6 支為上限。 5.需經事前審查核准後使用。	無

備註：劃線部分為新修訂規定

癌因性疲憊治療適應症之處方用藥
PG2® Injection

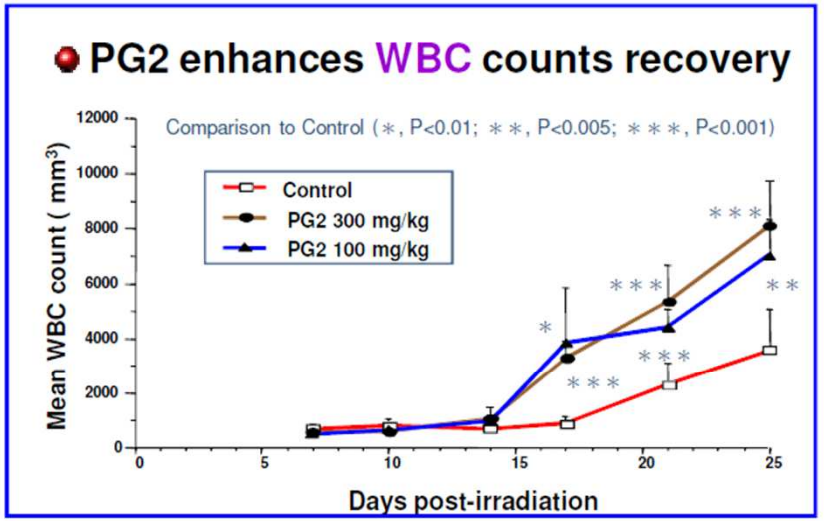
- 成份：黃耆多醣 (Polysaccharides of *Astragalus membranaceus)*
  萃取物 500 mg ，不含任何賦形劑。
  分子量約20,000~60,000 Da
- 適應症：**治療癌症療程中所導致的中、重度疲憊症**
- 機轉：增強免疫功能及刺激骨髓造血功能
- 用法及用量：
  - 成人每次劑量 500 mg，
    2.5 - 3.5 小時點滴靜脈滴注。
  - 每週2 - 4次，使用2 - 4週。

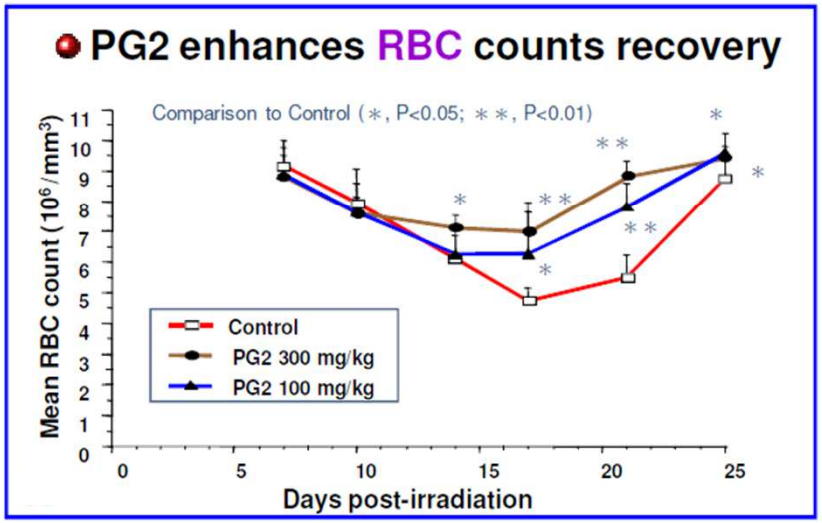
食品藥物管理署(TFDA)核准之第一個植物性處方用藥：**西藥藥證衛部藥製字第058837號**

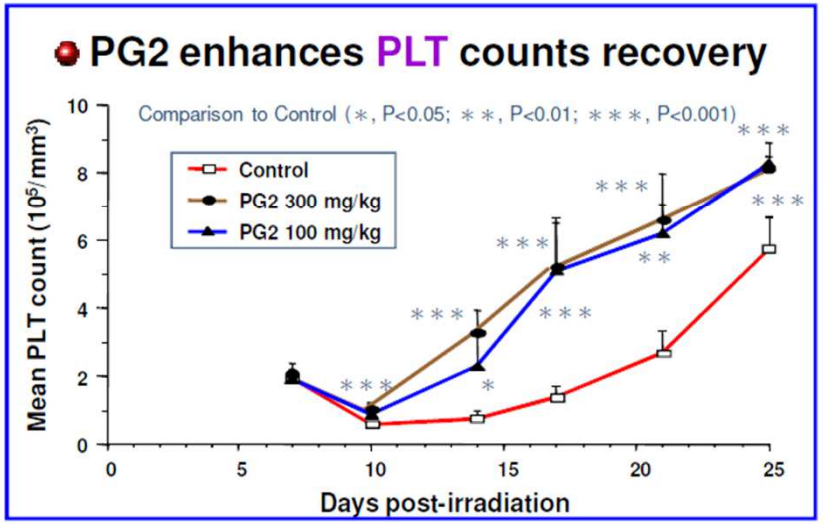
Hematopoietic activity of PG2

PG2 Regulated three-lineage WBC, RBC and Platelet counts in irradiated mice

Balb/c mice (n=6) were **sub-lethally irradiated** (425 cGy) on day 0 and different doses of **PG2 were given for 4 weeks**. Animals were bled twice weekly starting at day 7 post-irradiation.







PhytoHealth in-house data

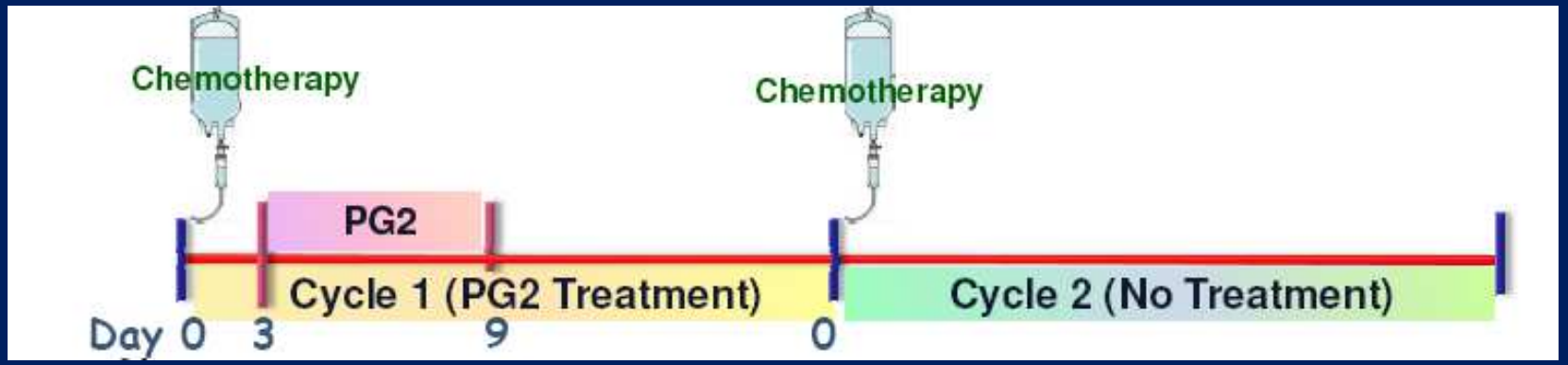
PG2 Phase I/II Trial

三軍總醫院血液腫瘤科執行

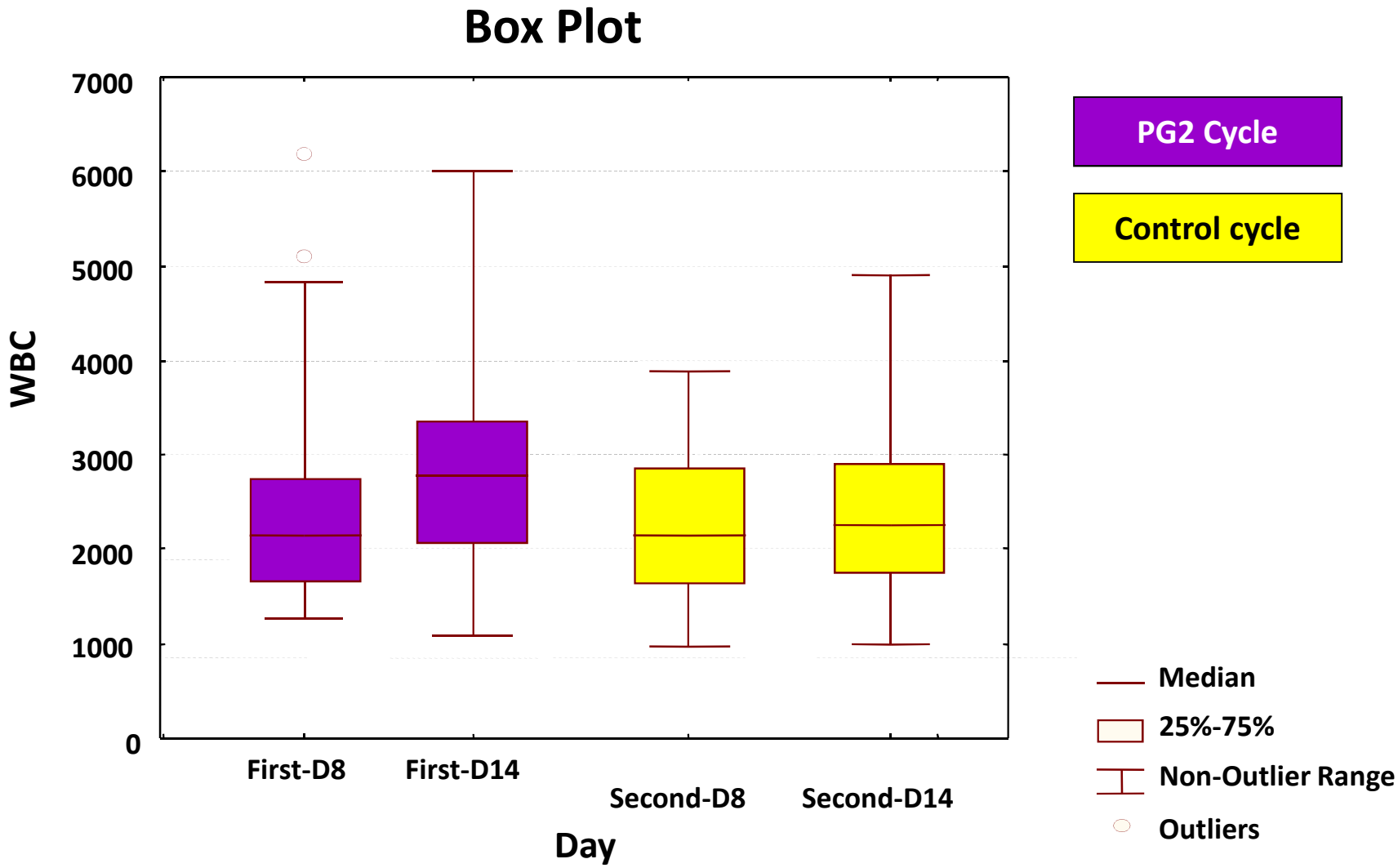
2001.12-2003.10

- Study Objective: Dose finding and safety
- Study Design
  - Phase I : Dose escalation trial (13 patients)

    125 mg: 4 patients, 250mg: 3 patients, 500 mg: 6 patients
  - Phase II : Up to a total of 20 patients at 500 mg/day
- All cancer types
- Self-Control

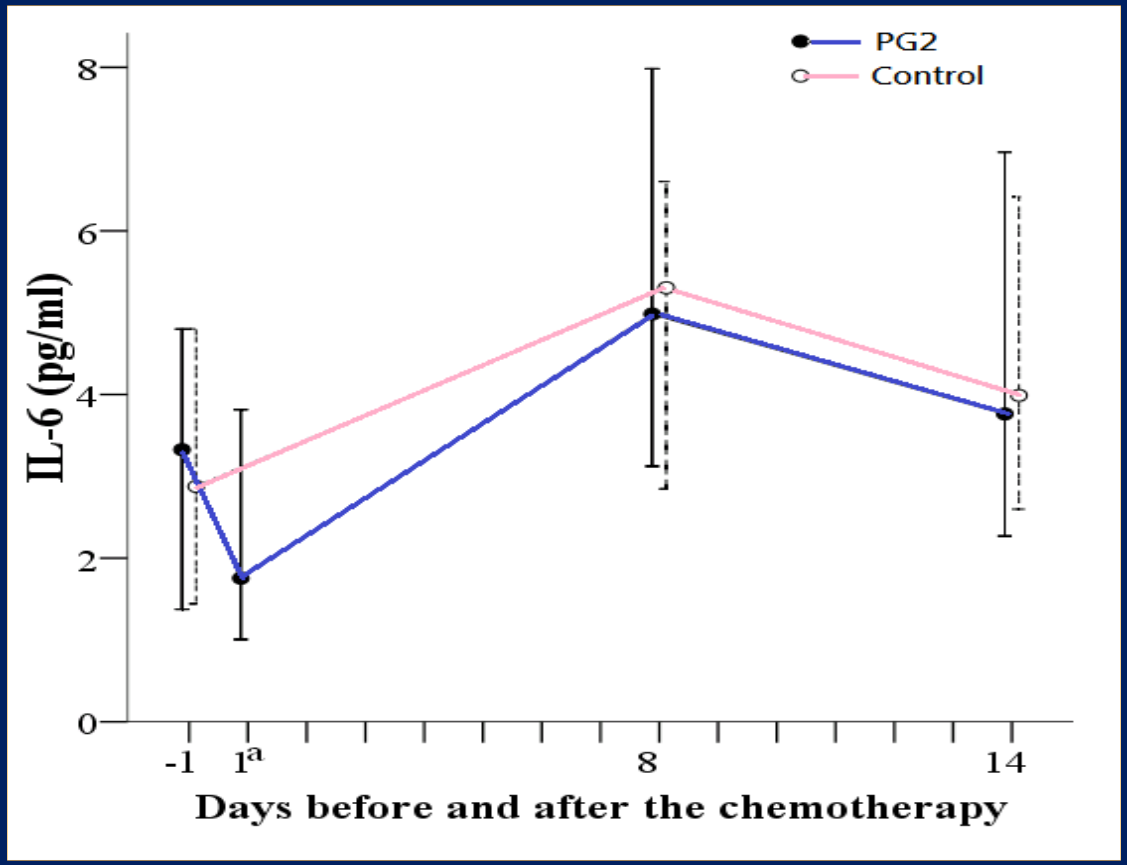


PG2 might reduce chemotherapy-induced myelosuppression



PG2 Phase I/II Clinical Trial Final Report

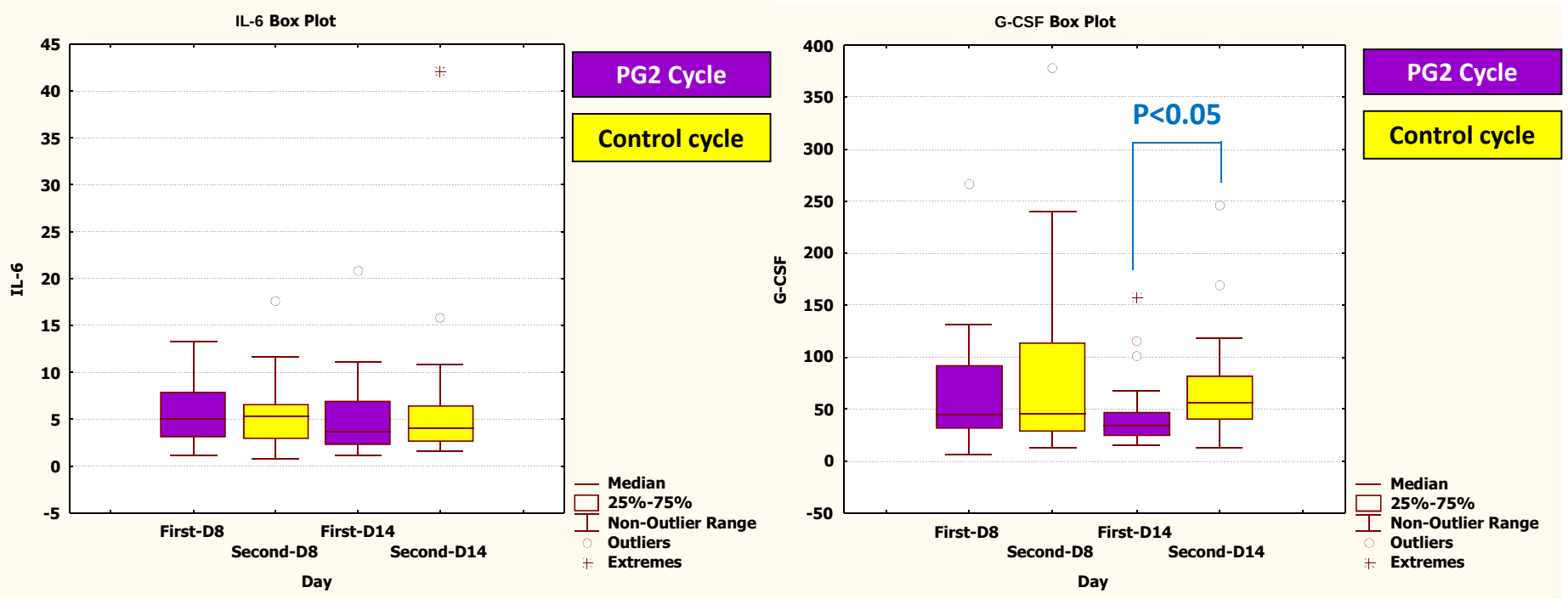
Cytokine Change



- **Relative lower IL-6 level from C/T on PG2 Treatment Cycle**
- **Significant positive correlations between CRF and IL-6 has been shown. (Brain, Behavior, and Immunity 2007;21:413–427)**

It supports that PG2 may improve CRF.

PG2 might reduce chemotherapy-induced myelosuppression



- Relative lower IL-6 and G-CSF change from pre-chemotherapy
- The cytokine results further support that PG2 can :
  - ✓ reduce the chemotherapy - induced myelosuppression
  - ✓ improve CRF

PG2 Phase I/II Clinical Trial Final Report

PG2® Injection: Phase II/III樞紐試驗

ORIGINAL RESEARCH

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A novel infusible botanically-derived drug, PG2, for cancer-related fatigue: A phase II double-blind, randomized placebo-controlled study

Abstract

Purpose: This study investigated the efficacy of the botanical-derived drug, PG2, a partially purified extract of *Astragalus membranaceus*, as a complementary and palliative medicine for managing cancer-related fatigue (CRF).

Methods: Patients with advanced cancer and moderate to severe CRF were randomized to receive either PG2 or a placebo (normal saline, NS) in the first treatment cycle (four weeks) in a double-blind manner; thereafter, on the next cycle (four weeks), all patients received open-label treatment with PG2.

Results: PG2 significantly improved CRF in the NS-primed group. In the first four week cycle, PG2 administration resulted in a greater fatigue-improvement response rate than seen with NS alone. In addition, approximately 82% of patients who reported an improvement of fatigue symptoms following the first cycle of PG2 experienced sustained benefits after administration of the second treatment cycle. Among patients treated with PG2 who did not report an improvement in symptoms throughout the first treatment cycle, approximately 71% showed significant improvement after the second treatment cy-

Chen HW et al. Clin Invest Med 2012; 35:E1-11.

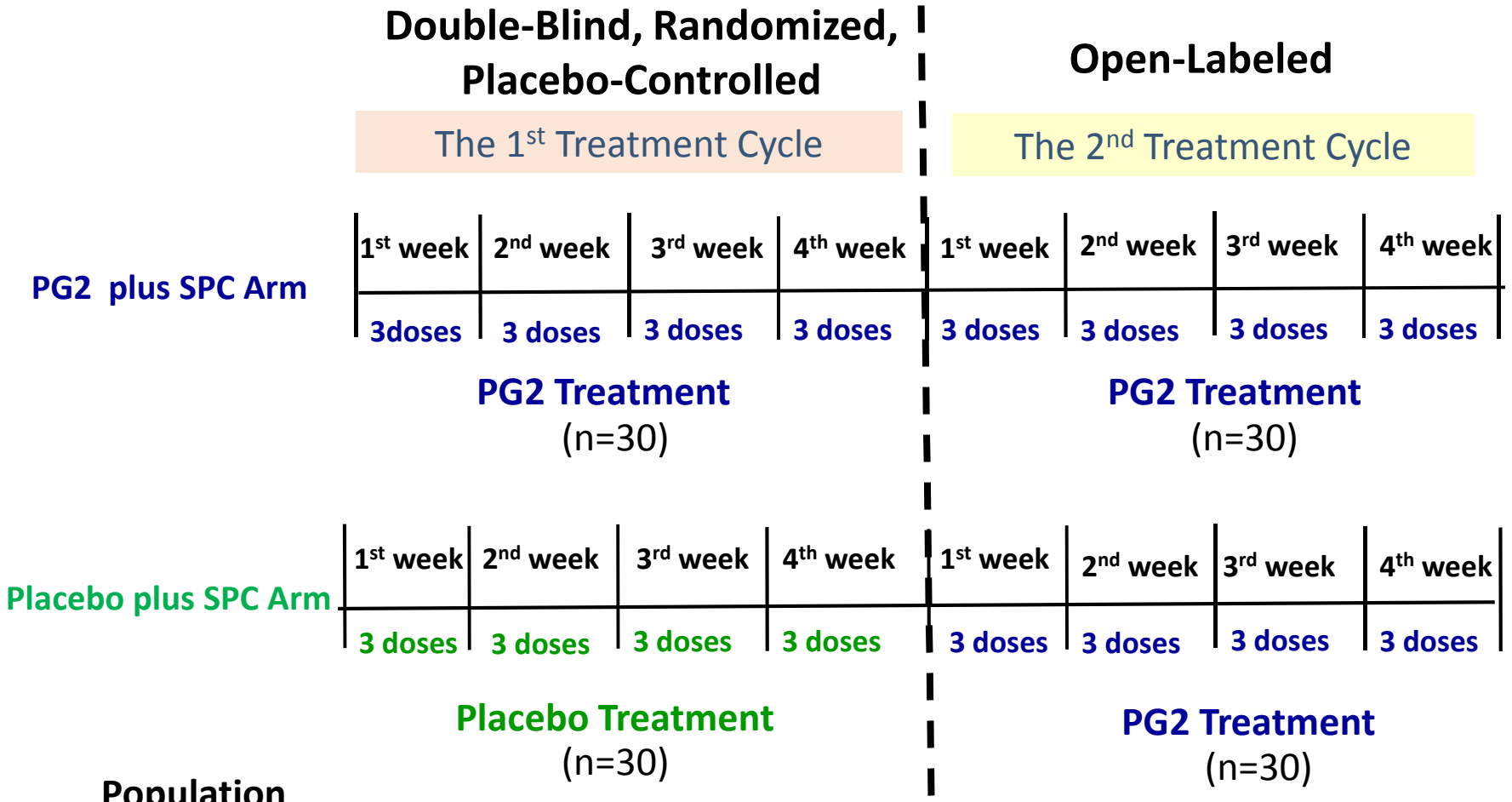
Inclusion Criteria

- Signed the informed consent form
- ≥ 20 years old
- **BFI Fatigue score ≥ 4**
- Have locally advanced or metastatic cancer or inoperable advanced cancer
- Under standard palliative care (SPC) at hospice setting and have no further curative options available
- Life expectancy of at least 3 months as determined by the investigator
- Willing and able to complete quality of life questionnaires

Chen HW et al. Clin Invest Med 2012; 35:E1-11.

黃耆多醣注射劑樞紐試驗設計

樞紐試驗研究設計



Population

- **Advanced progressive cancer patients**
- **Under standard palliative care (SPC) at hospice setting**
- **Have no further curative options available**

Chen HW et al. Clin Invest Med 2012; 35:E1-11.

Primary Endpoint

- Fatigue Evaluation:
  by **BFI-T**, 0-10 score, averaged by 9 questions

- Fatigue Improvement Responder (FIR) :
  - **Clinically effective: ≥ 10%** Improvement from baseline

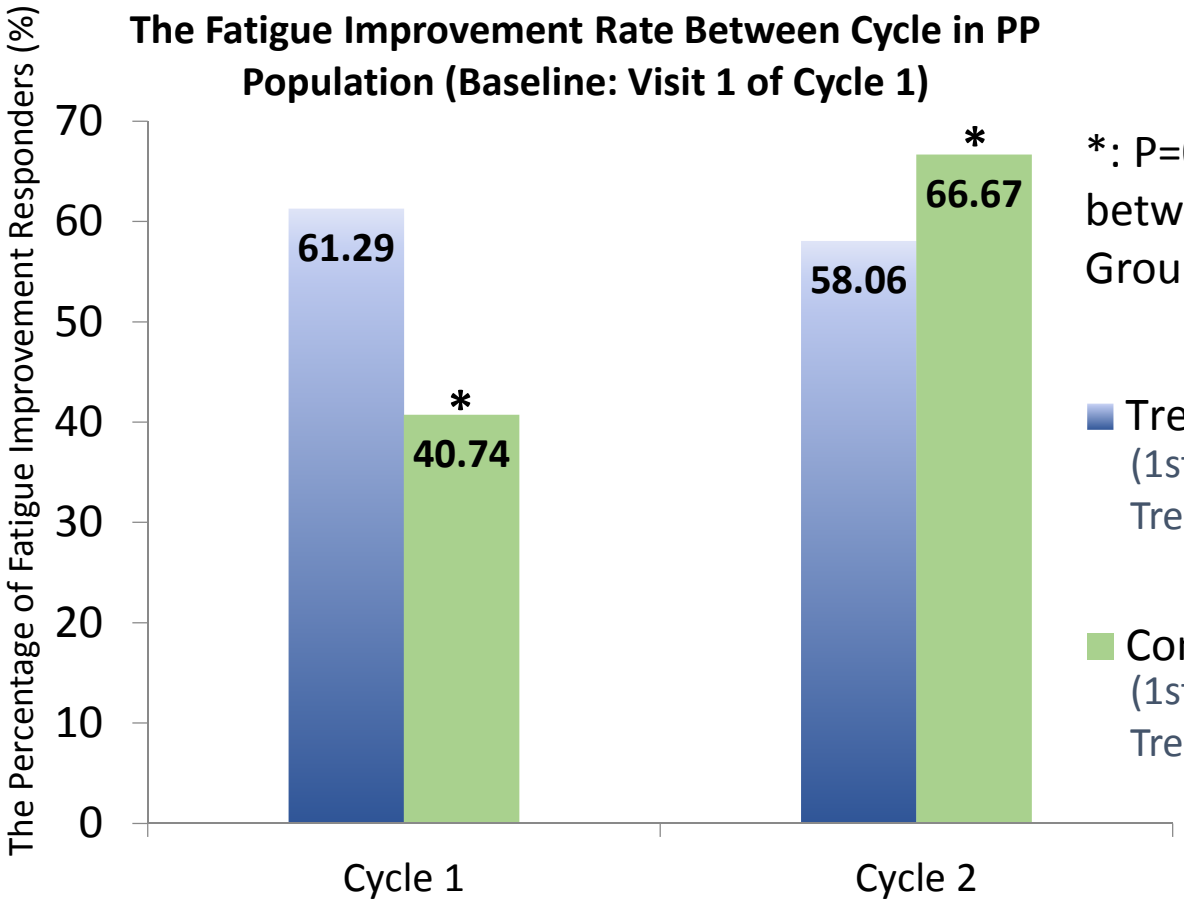
- Fatigue Improvement Response Rate (FIRR)

$$\frac{\text{Fatigue Improvement Responder}}{\text{Fatigue Improvement Responder + Non-Responder}} \text{X100\%}$$

Chen HW et al. Clin Invest Med 2012; 35:E1-11.

黃耆多醣注射劑可有效改善疲憊

Phase II/III樞紐試驗



*: P=0.020 (The comparison between two cycles in the Control Group by McNemar's test)

Treatment Group
(1st and 2nd Cycle PG2 and PG2 Treatment; n=31)

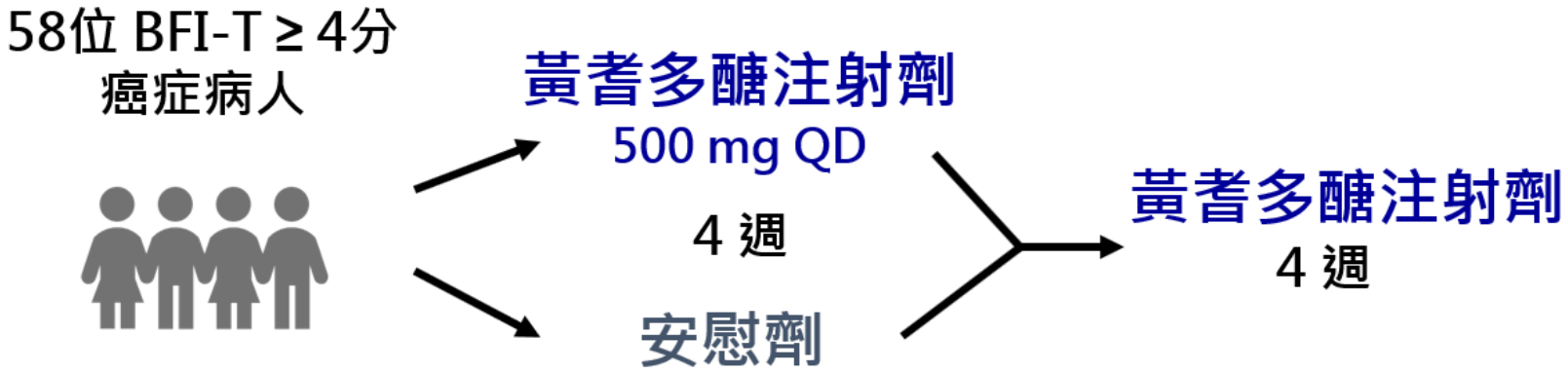
Control Group
(1st and 2nd Cycle Placebo and PG2 Treatment; n=27)

- 改善幅度最大的BFI-T項目為行走能力和情緒
- 黃耆多醣注射劑組的不良反應發生率或嚴重程度未明顯高於安慰劑組
- 主要不良反應為輕微的皮疹、濕疹、或搔癢症，多不須額外處置即恢復

Chen HW et al. Clin Invest Med 2012; 35:E1-11.

黃耆多醣注射劑樞紐試驗設計

Phase II/III樞紐試驗



- 試驗首週後，疲憊改善的病人比率在黃耆多醣注射劑組較高 (57% vs. 32%, P = 0.043)
- 雙盲階段結束時，有42.9%的黃耆多醣注射劑組達到BFI-T分數降低20%以上的改善幅度。
- 試驗結束後，82%的黃耆多醣注射劑組受試者之癌因性疲憊症明顯改善，顯示長達8週的療程對病人有正面效果。

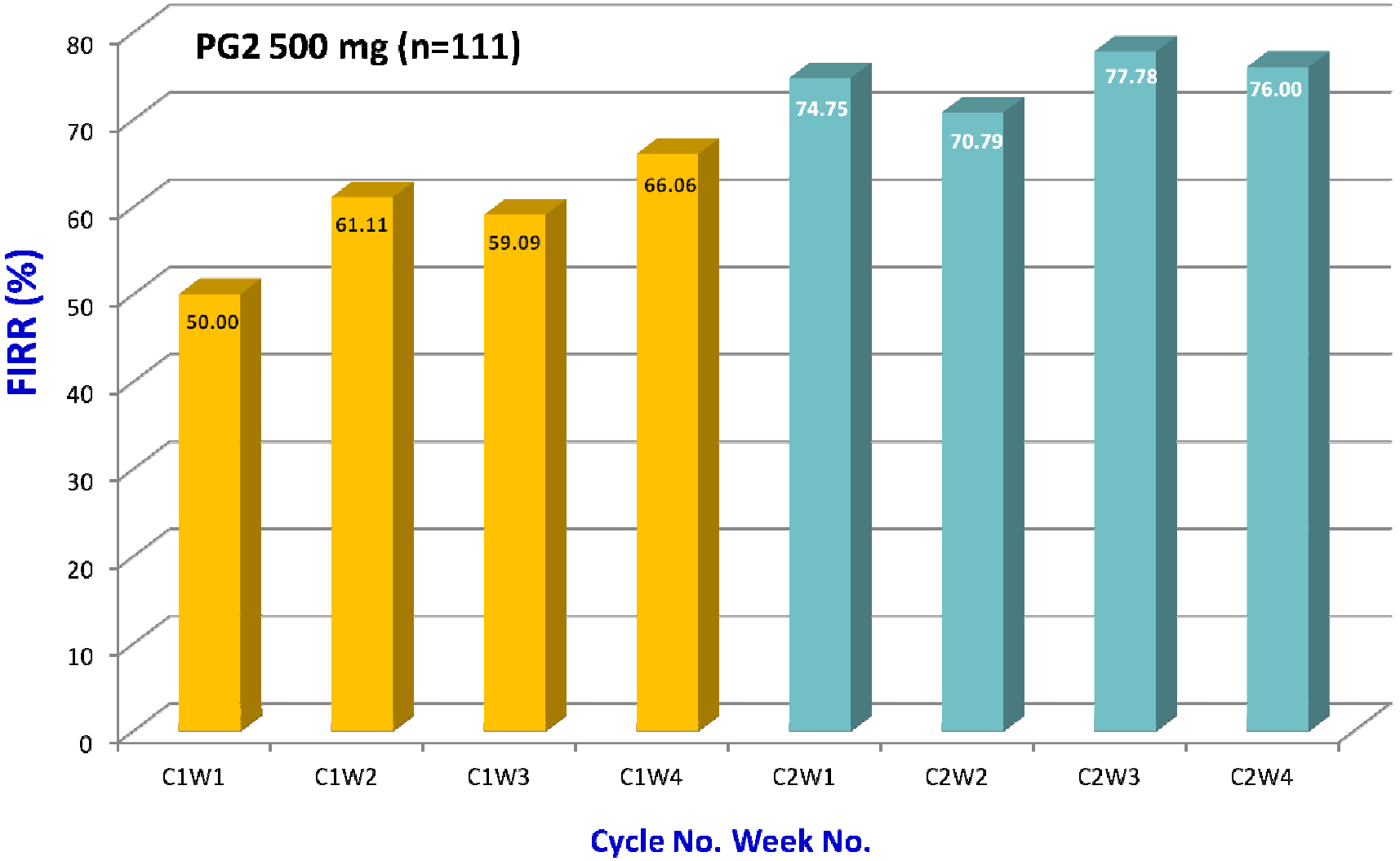
Chen HW et al. Clin Invest Med 2012; 35:E1-11.

PG2 Phase IV Trial

Center	馬偕，雙和，基隆長庚情人湖院區，三總，彰基，奇美柳營，中醫大，林口長庚，高雄長庚
Trial Objective	To evaluate the **efficacy and safety** of different doses of PG2 for relieving fatigue among advanced cancer patients who are under standard palliative care (SPC).
Blinding/ Randomization	Double-blinded/Randomized
Population	Advanced progressive cancer patients with moderate to severe fatigue (**BFI Fatigue score ≥ 4**) under palliative care.
Treatment Regimens	Two parallel arms: (1:1 ratio) 1. PG2 500 mg by IV infusion for 3 days per week 2. PG2 250 mg by IV infusion for 3 days per week
Study Period	8 weeks
Primary Endpoint	Fatigue Improvement Response Rate (FIRR)
Sample Size	Enrolled Patient No.: 323 Evaluable Patient No.: 214

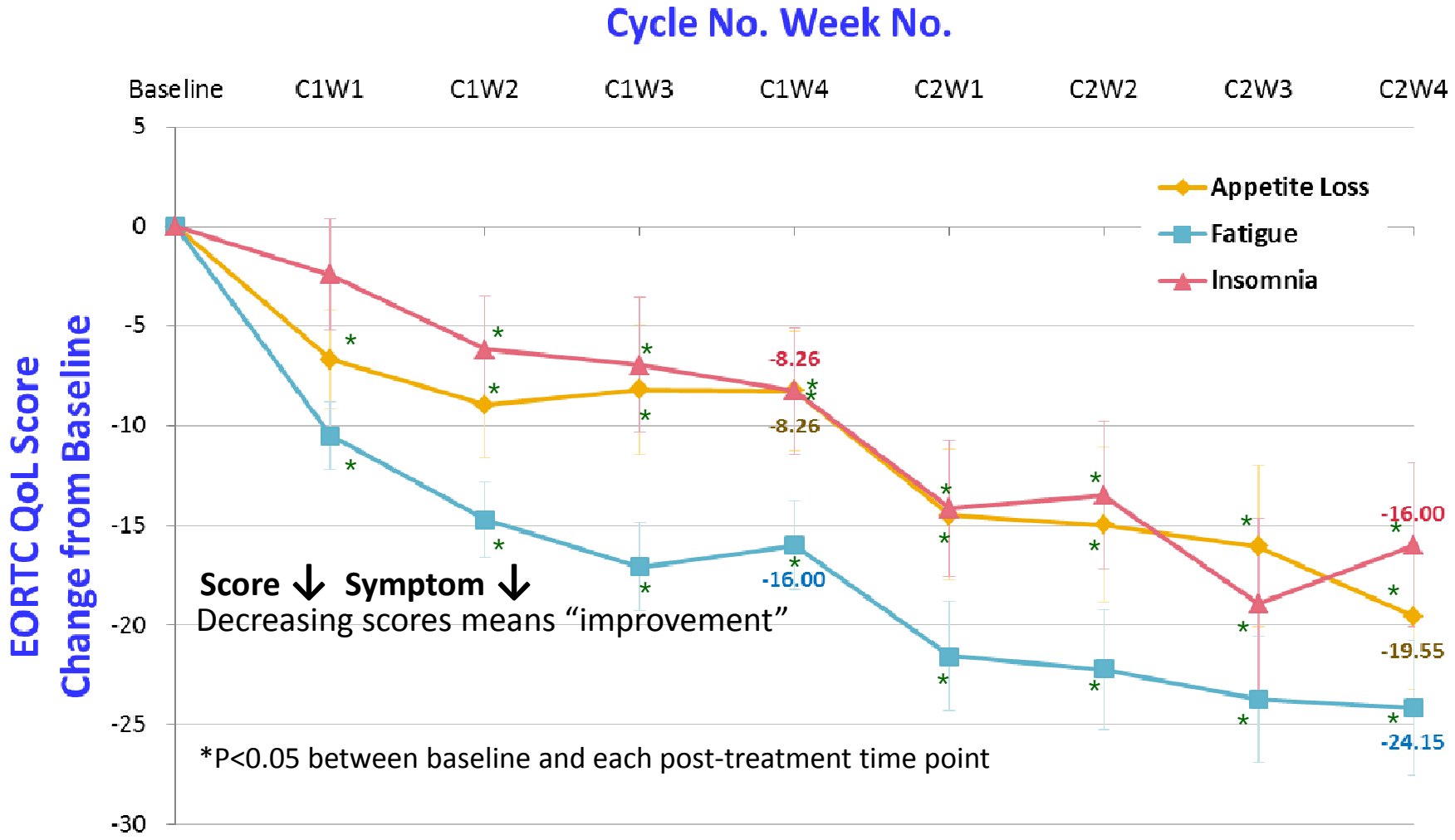
FIRR by Week during the Whole Study Period

Cut-off Point of FIR: 10 %



J Clin Oncol 36, 2018 (suppl; abstr 10091); 2018 ASCO Annual Meeting, Poster Presentation Abstract #: 10091. PhytoHealth In-house Data

Global Health Status: domains with significant improvement



2018 MASCC e-Poster Presentation; J Clin Oncol 36, 2018 (suppl; abstr 10091); 2018 ASCO Annual Meeting, Poster Presentation Abstract #: 10091. PhytoHealth In-house Data

cancers

MDPI

Article

Karnofsky Performance Status as A Predictive Factor for Cancer-Related Fatigue Treatment with Astragalus Polysaccharides (PG2) Injection—A Double Blind, Multi-Center, Randomized Phase IV Study

Cheng-Hsu Wang [1], Cheng-Yao Lin [2], Jen-Shi Chen [3,4], Ching-Liang Ho [5], Kun-Ming Rau [6,7,8], Jo-Ting Tsai [9,10], Cheng-Shyong Chang [11], Su-Peng Yeh [12], Chieh-Fang Cheng [13] and Yuen-Liang Lai [14,15,*]

Received: 22 October 2018; Accepted: 15 January 2019; Published: 22 January 2019

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Cancers **2019**, *11*, 128; doi:10.3390/cancers11020128

www.mdpi.com/journal/cancers

Cancers . 2019 Jan 22;11(2):128-140.

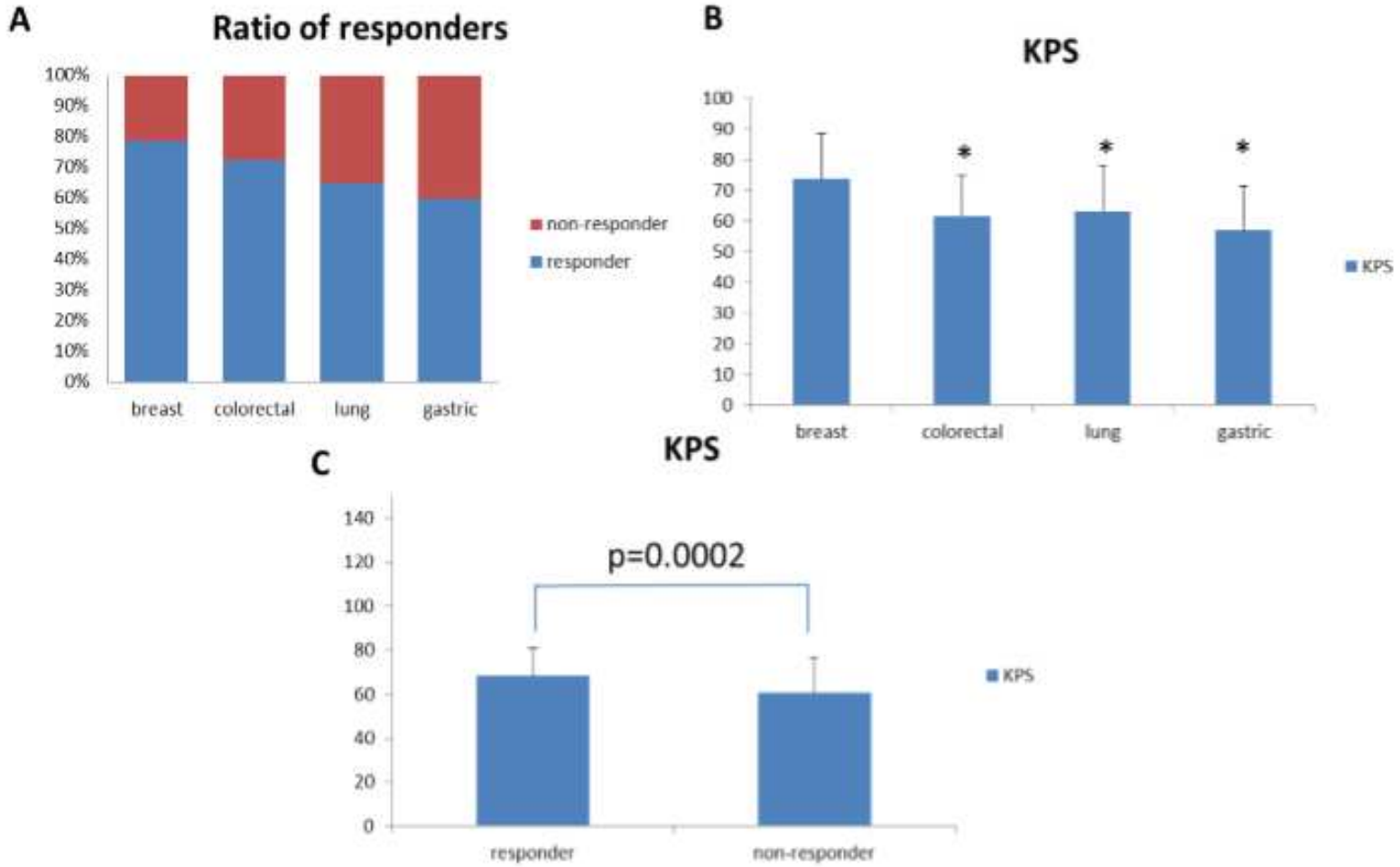

Figure 3. Fatigue Improvement Response Rate and KPS for patients with different cancer types. (**A**) Breast, colon, lung, and gastric cancer patients were selected for analysis. Fatigue improvement response rates for these patients were analyzed and compared. (**B**) KPS for breast, colon, lung, and gastric cancer patients were analyzed and compared. (**C**) KPS for responders and non-responders in the overall patient population. (* $p < 0.01$ versus breast cancer patients).

Cancers. 2019 Jan 22;11(2): 128-140.

Multivariate analysis for responders and non-responders to PG2

- Patients with **higher KPS** responded **better to PG2**.
- Identified **KPS as a promising predictive factor** for the therapeutic efficacy of PG2.

Table 3. Multivariate analysis for responders and non-responders to Astragalus Polysaccharides (PG2) injection.

All Subjects	Cut-off Points = 10%			Multivariate Analysis	
Variable/Status	Responder (*N* = 140)	Non-Responder (*N* = 74)	Univariate Analysis *p*-value *	Odds Ratio (95% CI)	*p*-value **
Baseline KPS score					
30–50	22 (15.71%)	31 (41.89%)	<0.0001 [C]	0.253 (0.126, 0.504)	<0.0001
60–90	118 (84.29%)	43 (58.11%)			
4–6	72 (51.43%)	41 (55.41%)	0.5794 [C]	0.885 (0.475, 1.647)	0.6998
7–10	68 (48.57%)	33 (44.59%)			
Cancer Type: three categories					
Lung cancer	22 (15.71%)	12 (16.22%)	0.2876 [C]		
Breast cancer	22 (15.71%)	6 (8.11%)		1.297 (0.343, 4.905)	0.7020
other	96 (68.57%)	56 (75.68%)		0.957 (0.414, 2.208)	0.9173
Albumin (g/dL)					
<3.0	20 (14.29%)	11 (14.86%)	0.9088 [C]	1.272 (0.518, 3.124)	0.5997
≥3.0	120 (85.71%)	63 (85.14%)			
Hemoglobin (g/dL)					
<10	48 (34.29%)	30 (40.54%)	0.3659 [C]	0.767 (0.405, 1.452)	0.4148
≥10	92 (65.71%)	44 (59.46%)			
Peripheral blood TLC (/μL)					
<700	46 (32.86%)	18 (24.32%)	0.1947 [C]	1.709 (0.846, 3.452)	0.1353
≥700	94 (67.14%)	56 (75.68%)			

* The Wilcoxon rank-sum test [W] was used to compare the difference between responders and non-responders for continuous variables; the Chi-squared test [C] was used to compare the difference between responders and non-responders for categorical variables. ** A logistic regression model was used to compare the differences between responders and non-responders.

Baseline KPS score	Responder %
30-50 (N=53)	22 (42%)
60-90 (N=161)	118 (73%)

Cancers. 2019 Jan 22;11(2): 128-140.

Summary of PG2® Phase IV Study

- **Fatigue improvement**

✓ PG2® treatment showed efficacy in relieving fatigue as early as the first week of treatment.

✓ Clinically meaningful fatigue improvement (≥ 10%) was observed in more than 65% of subjects receiving PG2® after the cycle 1 treatment when compared to baseline.

✓ Patients with higher KPS showed better chance to respond to PG2 treatment in BFI-T score.

J Clin Oncol 36, 2018 (suppl; abstr 10091); 2018 ASCO Annual Meeting, Poster Presentation Abstract #: 10091. Cancers. 2019 Jan 22;11(2): 128-140.

nutrients

MDPI

Article

Astragalus polysaccharides (PG2) Enhances the M1 Polarization of Macrophages, Functional Maturation of Dendritic Cells, and T Cell-Mediated Anticancer Immune Responses in Patients with Lung Cancer

Oluwaseun Adebayo Bamodu [1,2,†], Kuang-Tai Kuo [3,4,†], Chun-Hua Wang [5,6], Wen-Chien Huang [7,8], Alexander T.H. Wu [9], Jo-Ting Tsai [10,11], Kang-Yun Lee [12], Chi-Tai Yeh [1,2,13,*] and Liang-Shun Wang [3,4,*]

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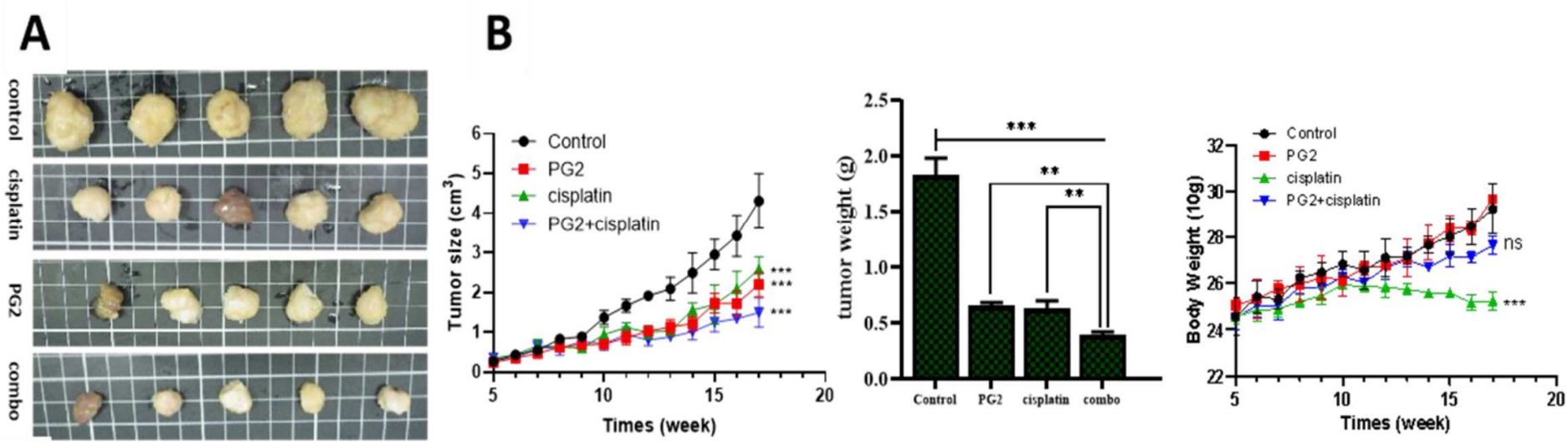
3 Division of Thoracic Surgery, Department of Surgery, Shuang Ho Hospital, Taipei Medical University, New Taipei City 235, Taiwan; doc2738h@gmail.com
4 Division of Thoracic Surgery, Department of Surgery, School of Medicine, College of Medicine, Taipei Medical University, Taipei City 110, Taiwan

Nutrients_2019(11)2264-2283.

Inhibited tumor growth & suppressed cisplatin-associated weight-loss



(A) Photo images show the anticancer effect of cisplatin and/or PG2 in syngeneic C57BL/6 mice inoculated with 1.5x103 LLC1 cells.

(B) Graphical representation of the effect of cisplatin and/or PG2 on the tumore size, tumor weight, and body weight in syngeneic C57BL/6 mice inoculated with 1.5x103 LLC1 cells.

*ns, not significant; **p < 0.01, ***p < 0.001;*

(17 weeks, and/or cisplatin in syngeneic LLC1 tumor-bearing C57BL/6 mice)

Nutrients_2019(11)2264-2283.

Suppression of tumor growth and metastasis

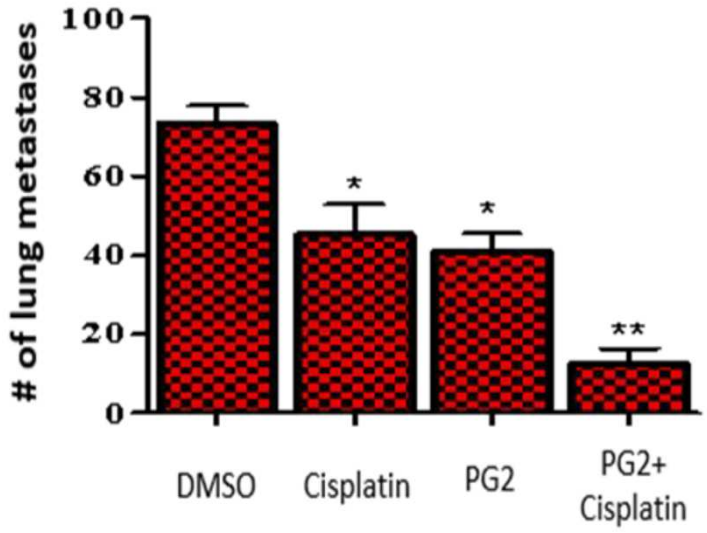


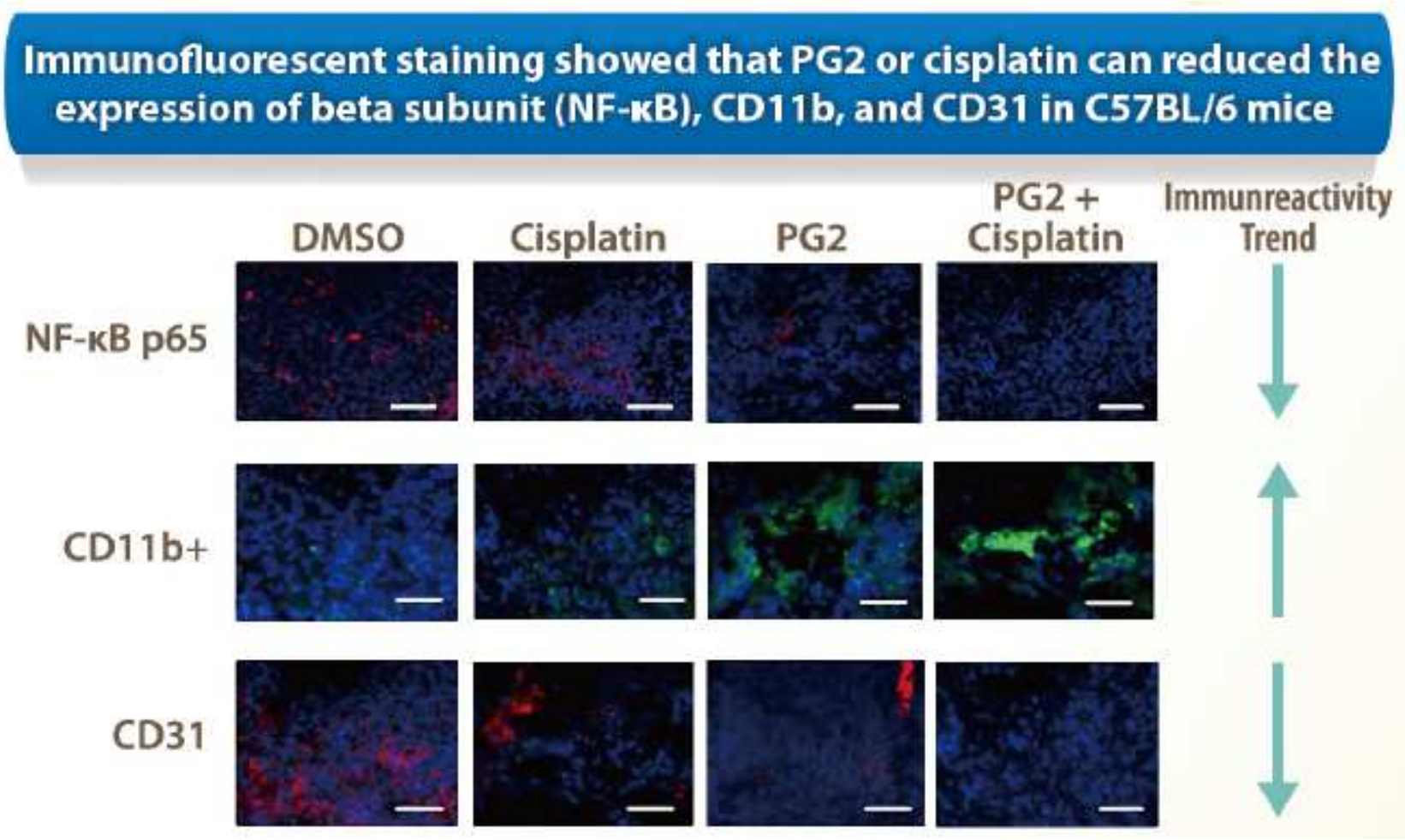
Photo images show the effect of cisplatin and/or PG2 on metastasis in syngeneic C57BL/6 mice inoculated with 1.5x103 LLC1 cells.

*ns, not significant; *p < 0.05, **p < 0.01; DMSO, dimethyl sulfoxide*

(17 weeks, and/or cisplatin in syngeneic LLC1 tumor-bearing C57BL/6 mice)

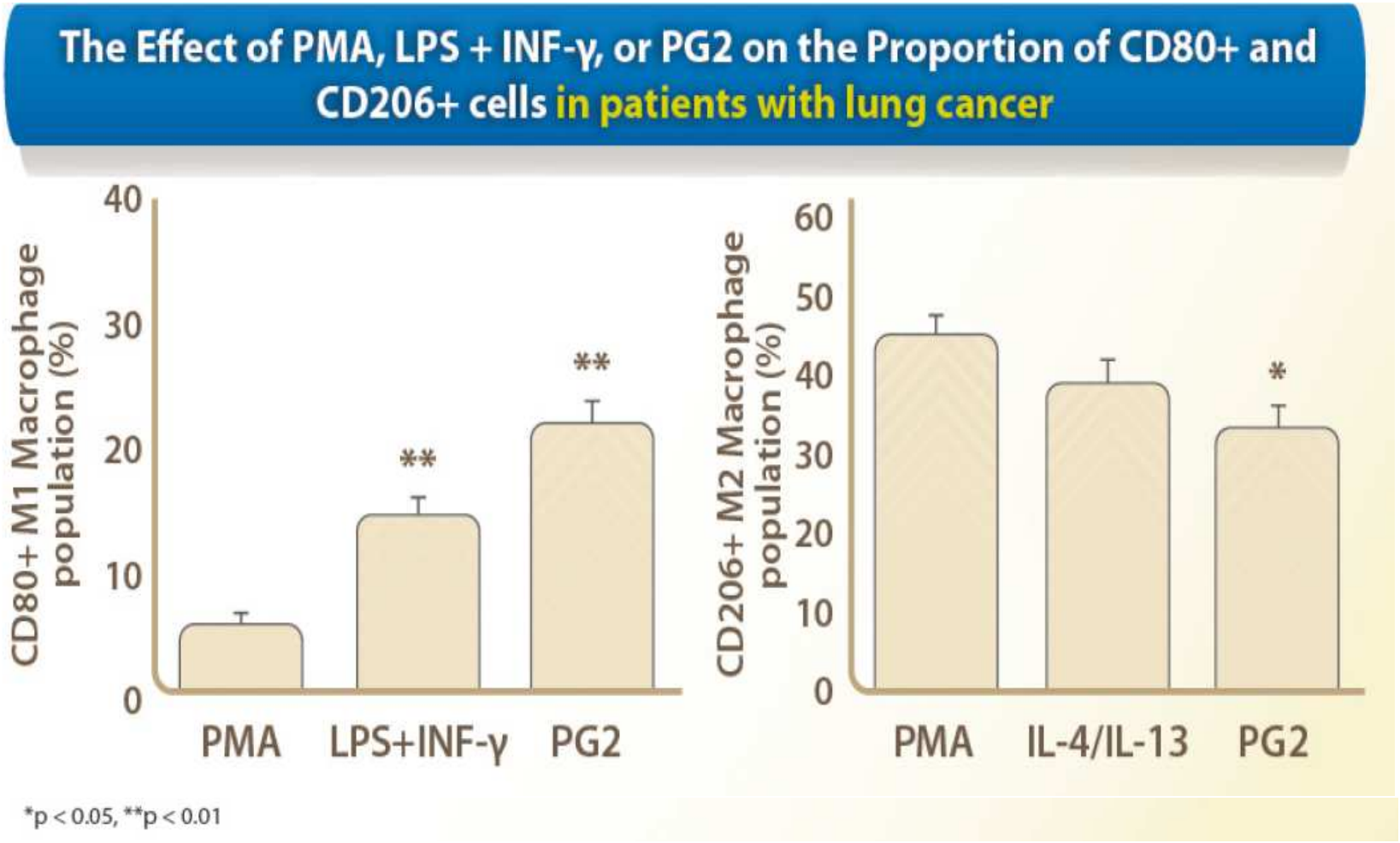
Nutrients_2019(11)2264-2283.

Regulating tumor micro-environment & suppressing tumorigenicity



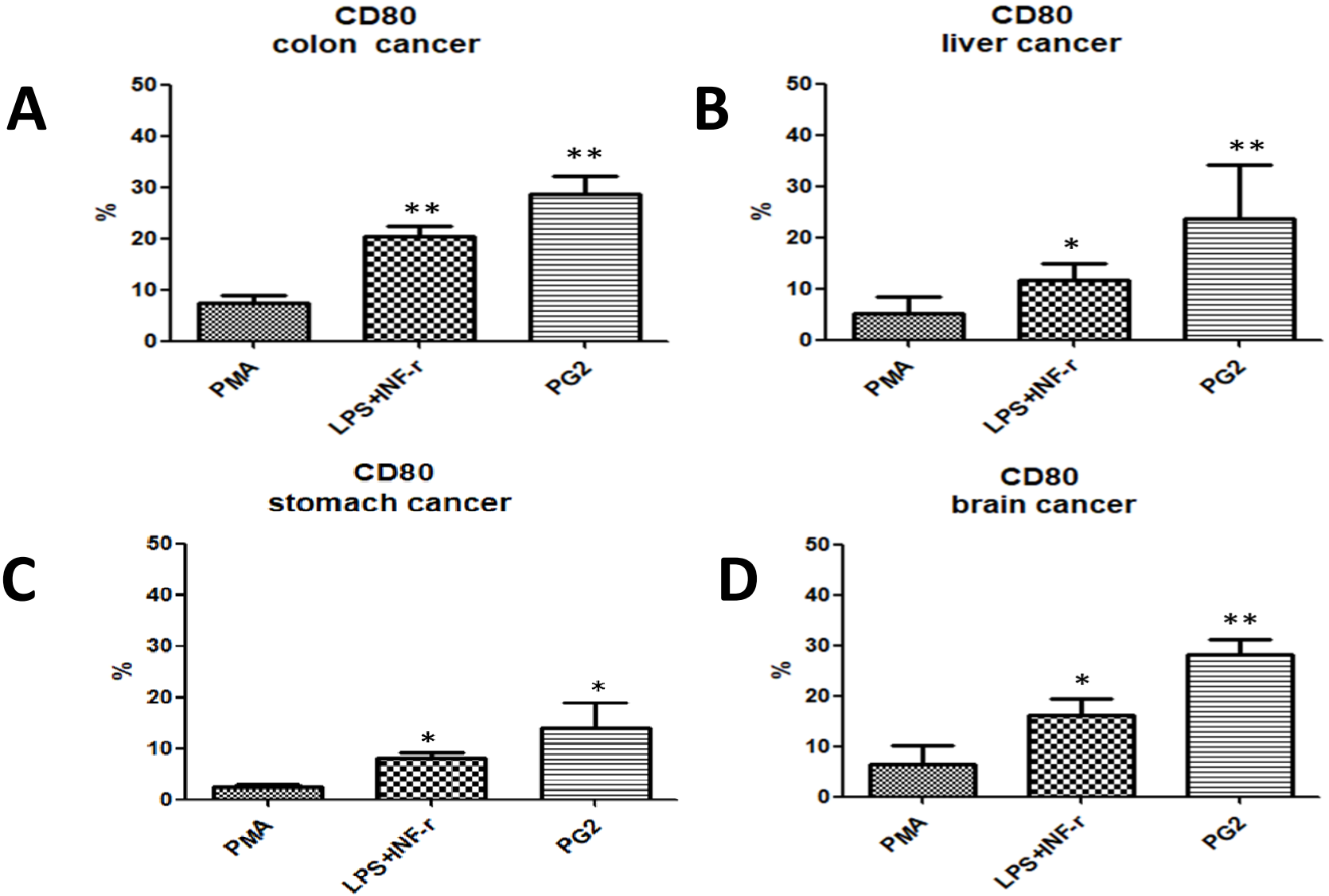
Nutrients_2019(11)2264-2283.

U.S. Patent. Patent No.: US 10,478,468 B2. Method for enhancing effect of immunotherapy for cancer



Nutrients_2019(11)2264-2283.

PG2 modulated the population of CD80+ M1 macrophages derived from PBMCs of different type of cancer patients



U.S. Patent. Patent No.: US 10,478,468 B2. Method for enhancing effect of immunotherapy for cancer

Nutrients_2019(11)2264-2283.

PG2®: beyond Cancer-related Fatigue Treatment

- **A therapeutically-relevant role for PG2 in modulating the M1/M2**
  - ✓ The treatment with PG2 elicited significant depletion of the tumor-associated M2 population.
- **Synergistically enhanced the anticancer effect of chemotherapeutic agent, cisplatin**
  - ✓ Inhibited tumor growth and metastasis.
  - ✓ In the presence of PG2, cisplatin-associated dyscrasia and weight-loss was markedly suppressed.

Nutrients_2019(11)2264-2283.

NLR: PG2 combine with IO in Lung Cancer

Integrative Cancer Therapies
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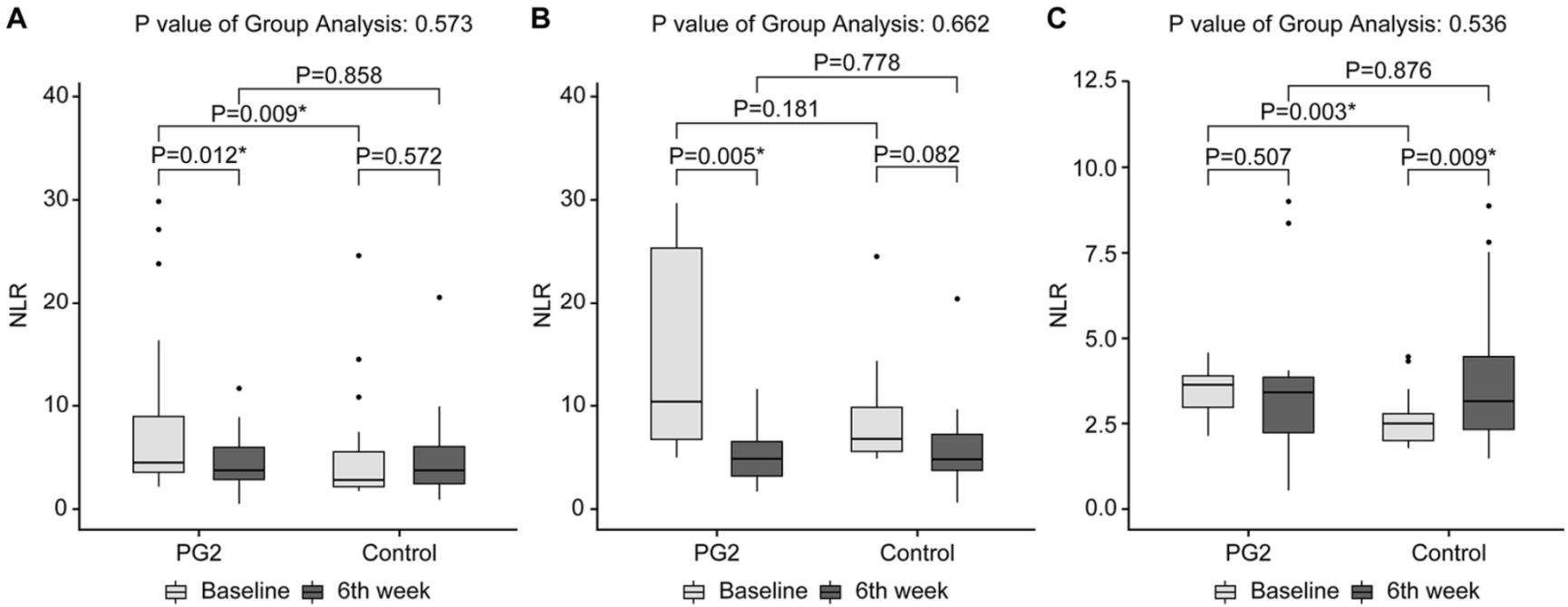
Astragalus Polysaccharide Injection (PG2) Normalizes the Neutrophil-to-Lymphocyte Ratio in Patients with Advanced Lung Cancer Receiving Immunotherapy

Shih Ming Tsao, PhD, MD[1], Tz Chin Wu, PhD, MD[1], JiZhen Chen, Msc[2], Feichi Chang, BS[1], and Thomos Tsao, PhD, MD[1]

Abstract

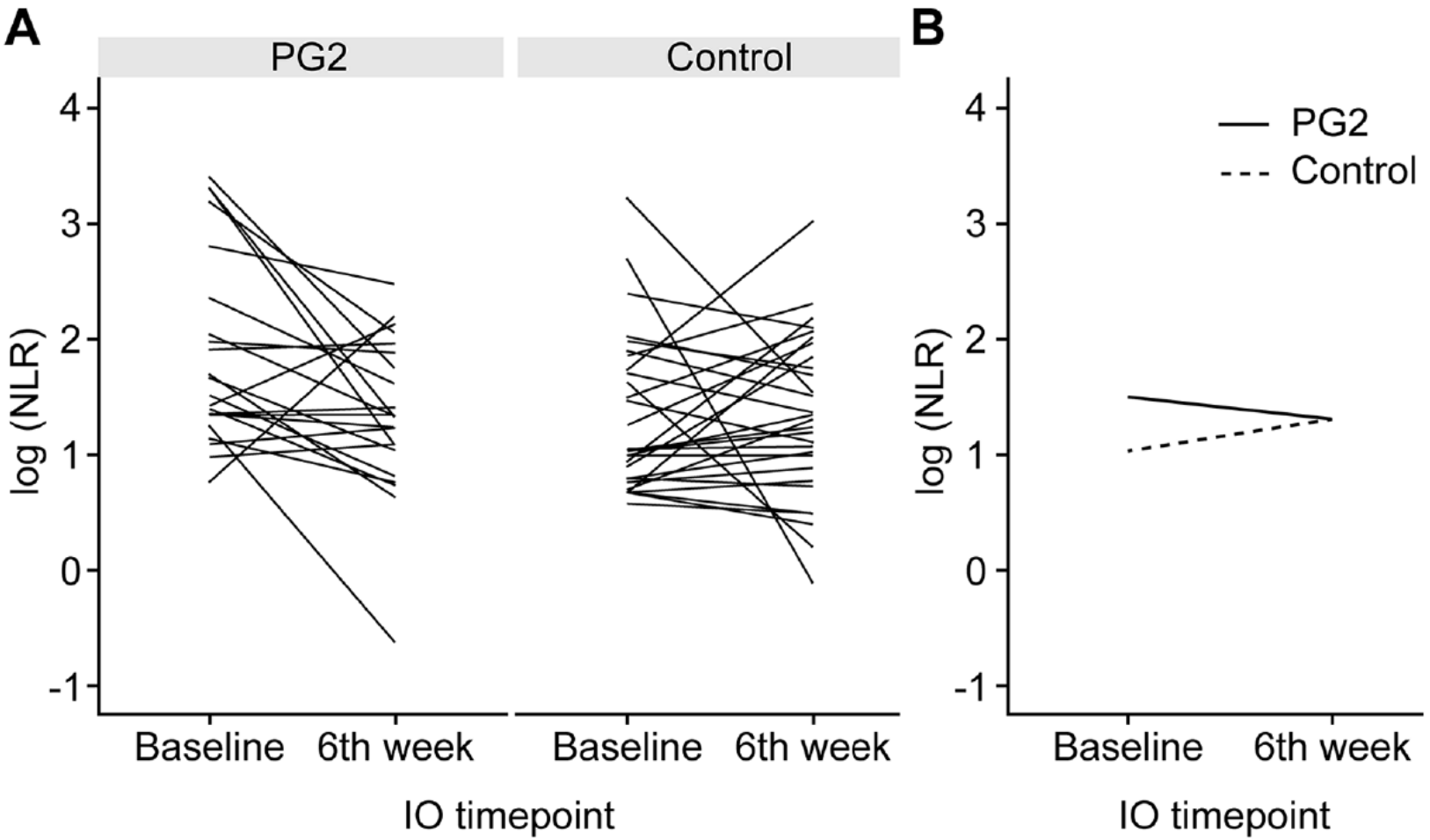
Objectives: The neutrophil-to-lymphocyte ratio (NLR) is a prognostic marker in patients with cancer receiving immunotherapy. Recent studies have shown that a high NLR was associated with a poor response and decreased survival. However, there is no intervention to reverse abnormally high NLR and improve clinical outcomes. Astragalus polysaccharide injection (PG2) is an immunomodulatory therapy for cancer-related fatigue. This study aimed to examine whether PG2 might normalize the NLR and affect the overall survival of patients with lung cancer treated with immunotherapy. **Materials and Methods:** We retrospectively examined the medical records of patients with lung cancer treated with immune checkpoint inhibitors (ICIs) between October 1, 2015 and November 30, 2019. All patients received ICI combination chemotherapies, and some similarly received PG2 (Control vs PG2). The NLR was assessed before treatment and 6 weeks after ICI initiation, and the survival data was collected at least 4 years after treatment initiation for the first enrolled patient. **Results:** Fifty-three patients were included. Six weeks after ICI initiation, 91.3% of the patients in the PG2 group exhibited a predefined "Decrease or no change" in the NLR, which was 28% higher than that in the Control group (63.3%) ($P = .028$). The NLR significantly decreased by 31.60% from baseline in the PG2 group ($P = .012$), whereas it increased by 5.80% in the Control group ($P = .572$). Six weeks after ICI treatment initiation, both groups had a median NLR of 3.73, and the overall survival was also similar (PG2 vs Control, 26.1 months vs 25.4 months, respectively); however, the PG2 group had a higher median baseline NLR than the Control group (PG2 vs Control, 4.51 vs 2.81, respectively). **Conclusion:** This study demonstrated that PG2 could normalize the NLR in patients with lung cancer receiving ICI combination treatments.

Ref. Integr Cancer Ther. Jan-Dec 2021;20:1534735421995256. doi: 10.1177/1534735421995256.



NLR at baseline and 6 after ICI initiation. (A) All patients. (B) Patients with a baseline NLR ≥ 5. (C) Patients with a baseline NLR <5. (Mann–Whitney tests: *P < .05.)

Abbrev. ICI, immune checkpoint inhibitor; NLR, neutrophil-to-lymphocyte ratio.

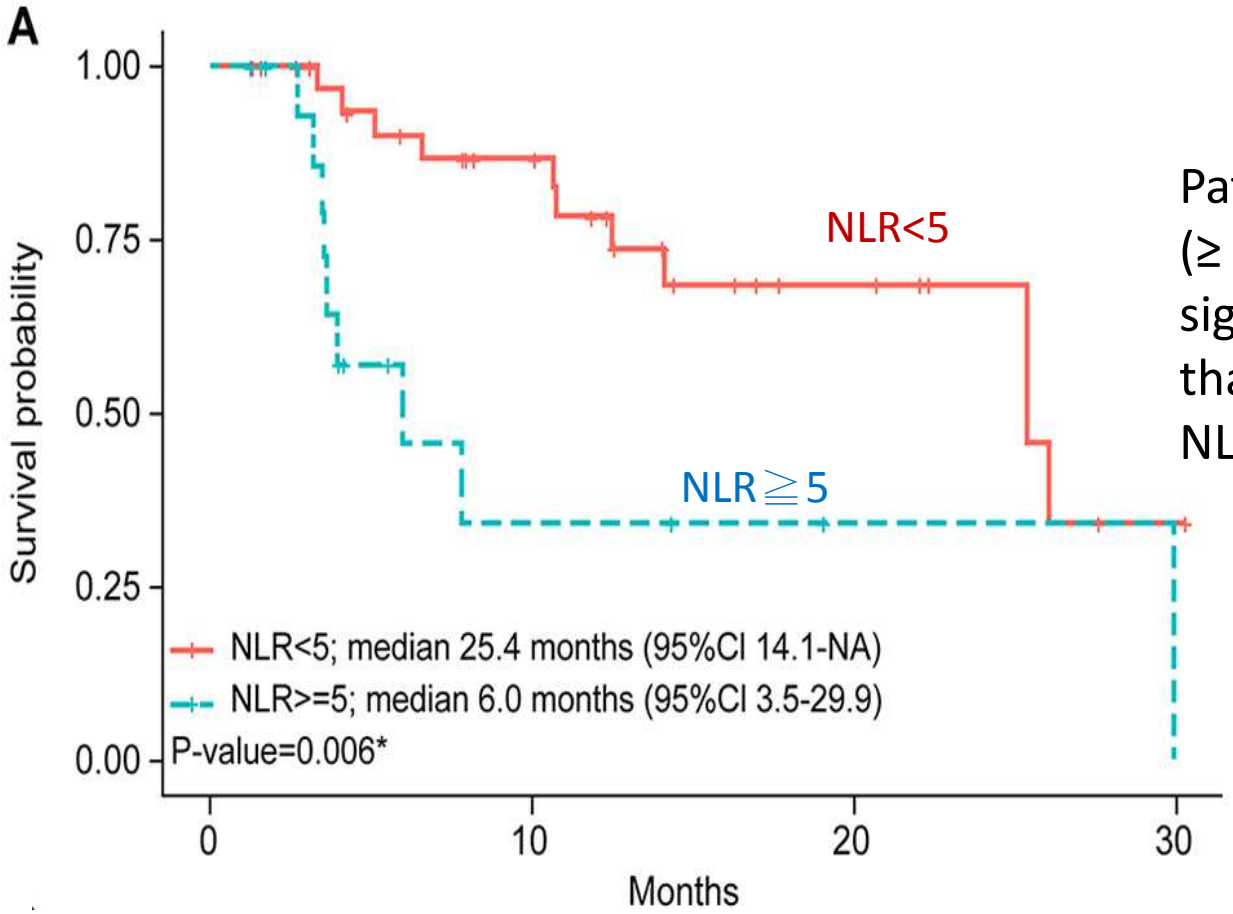


Change in the NLR before and 6 weeks after ICI initiation among all patients.
(A) Each line represents the data for an individual patient.
(B) The **median** of the 2 groups.

Abbrev. ICI, immune checkpoint inhibitor; NLR, neutrophil-to-lymphocyte ratio.

Ref. Integr Cancer Ther. Jan-Dec 2021;20:1534735421995256. doi: 10.1177/1534735421995256.

Overall survival：Patients with a baseline NLR ≥5 vs. <5.

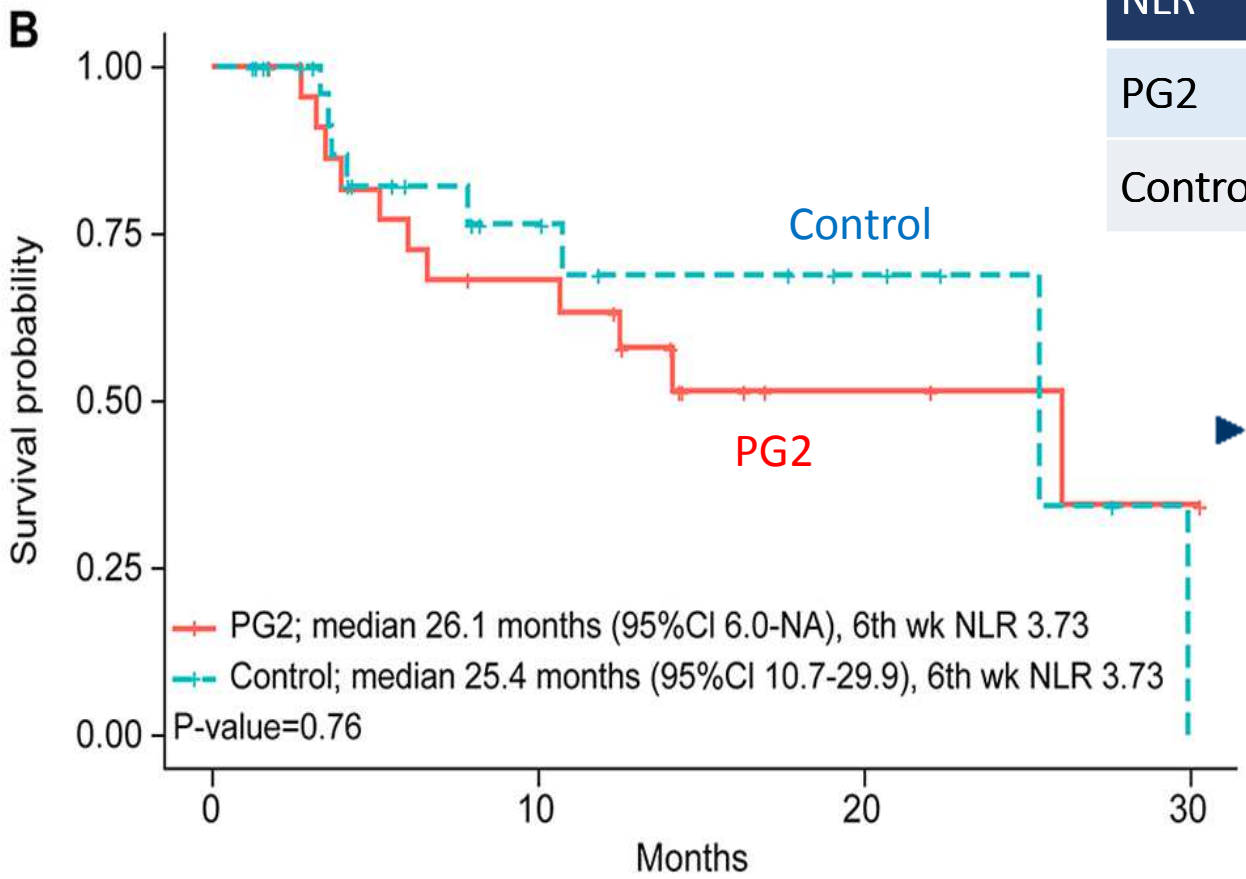


Patients with a high NLR (≥ 5) at 6 weeks had a significantly shorter OS than those with a low NLR (<5) (*p=0.009*).

As PG2 stabilizes or decreases the NLR, might promote the antitumor immune effect created by immunotherapy and then prolong survival.

Ref. Integr Cancer Ther. Jan-Dec 2021;20:1534735421995256. doi: 10.1177/1534735421995256.

Overall survival：Patients in PG2 vs. Control group



NLR	Baseline	6-wk	OS
PG2	4.51	3.73	26.1 M
Control	2.81	3.73	25.4 M

- There were no statistically significant differences between two group (p=0.76).

Ref. Integr Cancer Ther. Jan-Dec 2021;20:1534735421995256. doi: 10.1177/1534735421995256.

Results:

- Six weeks after ICI initiation:

"Decrease or no change" in the NLR (% of patient)	
PG2 group	**91.3% (P = .028 vs. control group)**
Control group	63.3%

NLR vs. baseline	
PG2 group	**decreased by 31.60% (P = .012)**
Control group	increased by 5.80% (P = .572)

Overall survival (both groups had a median NLR of 3.73)	
PG2 group	26.1 months
Control group	25.4 months

PG2 group had a higher median baseline NLR than the control group (PG2 vs Control, 4.51 vs 2.81, respectively).

Conclusion: This study demonstrated that PG2 could normalize the NLR in patients with lung cancer receiving ICI combination treatments.

Ref. Integr Cancer Ther. Jan-Dec 2021;20:1534735421995256. doi: 10.1177/1534735421995256.

懷特血寶注射劑 (PG2® Injection)
臨床用藥資訊

- 機轉：增強免疫功能及刺激骨髓造血功能
- 適應症：適用於癌症末期因疾病進展所導致中重度疲勞症狀之改善
- 用法及用量：

  成人每次劑量 500 mg，以 2.5 - 3.5 小時點滴靜脈滴注。

  每週2 - 4次，使用2 - 4週。
- 靜脈滴注溶液製備:
  - ✓ 從500 mL注射用生理食鹽水點滴瓶中抽取10mL，注入本品藥瓶中，充分混合至完全溶解後，注射回原500 mL生理食鹽水點滴瓶中，混合均勻，即完成製備。。

- 安全性:

  依據上市後第四期臨床試驗，懷特血寶注射劑常見的不良反應(>2%)包括皮疹(9.21%)、發燒(7.24%)、感覺冷(5.26%)、寒顫(2.63%)及過敏(2.63%)。預防輸注反應可考慮事先給予抗組織胺，及/或以較慢輸住速率，延長輸注時間完成輸注療程

幫助病患改善癌因性疲憊

- 92% 台灣癌症患者罹癌期間有疲憊問題，1/4 癌症病患有中重度疲憊
  - ✓ 癌因性疲憊症之ICD-10 code：**R53.0**
- 癌症病患應在初診和回診時，接受規律性疲憊評估
  - ✓ 住院患者為每日評估，門診患者則每次回診時評估
- 癌症病患依疲憊嚴重程度給予相對應的治療，治療後再評估疲憊程度
  - ✓ 輕度：非藥物治療，**VAS≧4**中重度：加上藥物治療
- 台灣癌因性疲憊症臨床指引建議：中度以上癌因性疲憊症之具適應症藥物為黃耆多醣注射劑(PG2)。
- 合併使用黃耆多醣注射劑(PG2)，可改善癌症患者之疲憊症，使癌症療程能順利完成，但不影響治療效果。

台灣癌症安寧緩和醫學會
Taiwan Society of Cancer Palliative Medicine

首頁 使用說明 網站導覽

關於學會 01 | 課程目錄 02 | 研討會 03 | 最新文獻資料 04 | 電子報 05 | 相關網站連結 06 | 聯絡我們 07

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嚴重特殊傳染性肺炎相...

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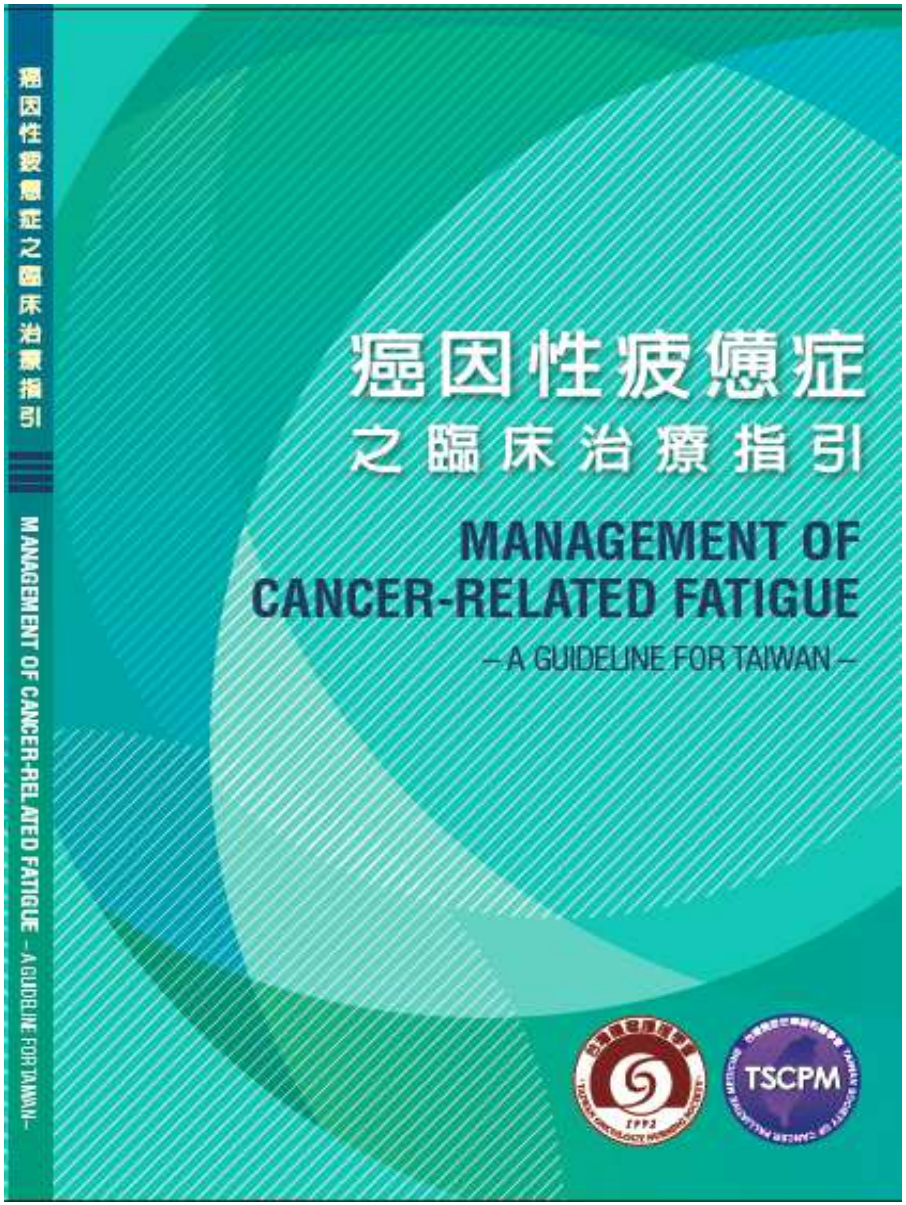
財團法人台灣癌症全人關懷基金會 TAIWAN TOTAL CANCER CARE FOUNDATION

癌症疼痛之藥物治療指引

HOPE 癌症希望協會 HOPE SOCIETY for CANCER CARE
希望 讓生命再現光彩



癌因性疲憊症之臨床治療指引電子版連結由此去

Thank You