Insights from Phase III and Large-scale Phase IV Studies on Botanical Drug Astragalus Polysaccharides Lyo. Injection

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癌因性疲憊症之診療與照護指引

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

2023年 11月 第二版

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.

癌因性疲憊評估與治療

以VAS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

Rau KM, Shun SC, Hung SH, Chou HL, Ho CL, Chao TC, Liu CY, Lien CT, Hong MY, Wu CJ, Tsai LY, Jane SW, Hsieh RK. Management of cancer-related fatigue in Taiwan: an evidence-based consensus for screening, assessment and treatment. Jpn J Clin Oncol. 2022 Nov 9:hyac164. doi: 10.1093/jjco/hyac164.

癌因性疲憊症的藥物治療

此癌因性疲憊症指引，藥物治療的建議依實證強度排序，以利臨床人員評估運用。

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)

1

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)

4

Methylphenidate
臨床研究顯示使用於疲憊程度或病情較嚴重的病人較具效果；但在用藥前應審慎考量劑量、用藥時間、濫用風險、及病人個人疾病等臨床情形， 充分評估相關風險與效益。
(Level IA, Grade A)

2

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)

3

補氣藥之王：黃耆

《關於黃耆，你所不懂的》

鑑別	晉耆(紅皮耆)	北耆(白皮耆)
品種	多序岩黃耆	膜夾黃耆、蒙古黃耆
表皮	紅棕色	黃白色或黃褐色
甜味	甜味重	微甜
豆腥味	較淡或無	較重

資料提供：長庚紀念醫院中醫內兒科主治醫師王品涵

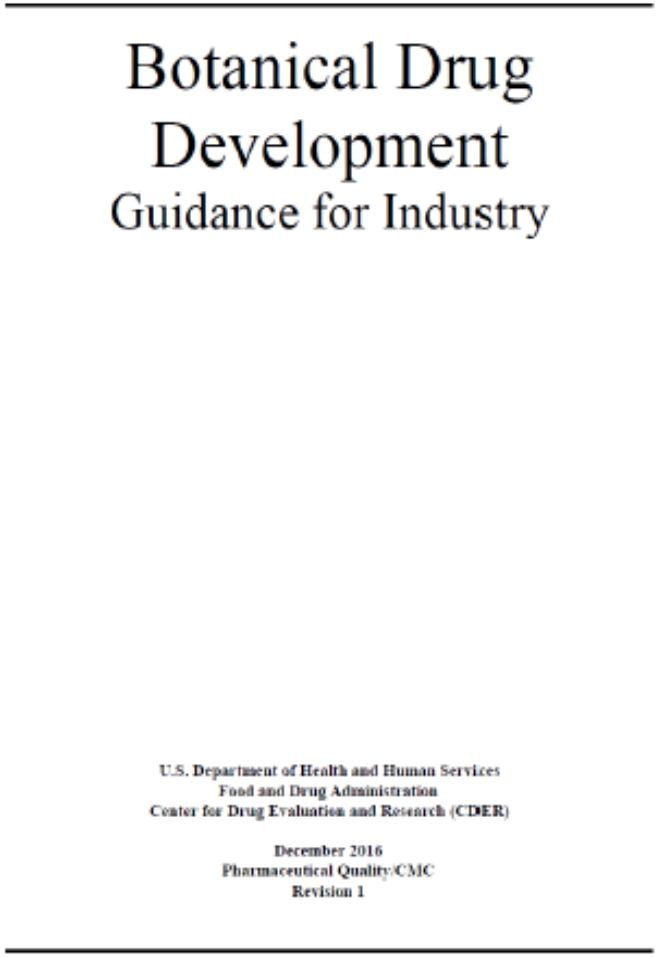
黃耆在中藥中被列為上藥，其功能為補氣升陽(增加元氣，提升能量)，益衛固表(提升免疫力)，利水消腫，托瘡生肌(肌肉增生)，為諸藥之長(中藥中的長老)，故名耆。

在各種類黃耆中，產地在蒙古北部的蒙古黃耆，又稱為北耆，所含的黃耆多醣效果最佳。

藥用黃耆品種：北耆 膜莢黃耆

FDA Guidance for Botanical Drug

- Further purification is not required
- Identification of active constituents is not essential
- FDA realizes botanical drug is a mixture, PK & PD data would be a challenge to obtain
  - Sizable percentage of the total ingredients, and a chemical fingerprint of the total ingredients
- Chemistry/Manufacturing/Controls is extended to raw materials
  - Original Species Control: DNA Fingerprinting
  - Planting Process Control: Good Agriculture Practices (GAP)


Botanical Drug Development
Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

December 2016
Pharmaceutical Quality/CMC
Revision 1

Center For Drug Evaluation and Research, FDA : Botanical Drug Development - Guidance for Industry - 2016

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

PG2® Injection: Phase II/III樞紐試驗

ORIGINAL RESEARCH

Hong-Wen Chen MD, PhD[1,2]
I-Hsin Lin MD, PhD[3]
Yu-Jen Chen MD, PhD[1]
Kao-Hwa Chang MD[1,4]
Meng-Hao Wu MD[1]
Wen-Hao Su MD[1,2]
Gwo-Che Huang MD[1]
Yuen-Liang Lai MD[1,5,6]

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[2] Mackay Medicine, Nursing and Management College, Taipei, Taiwan
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[6] Mackay Medical College, Taipei, Taiwan

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.

PG2® Injection: Pivotal Trial for indication & license approval

Title:

PG2 Treatment for Improving Fatigue among Advanced Cancer Patients under Standard Palliative Care

Objective:

This study is conducted to evaluate the **efficacy and safety** of PG2 **for relieving fatigue** among advanced cancer patients who are under standard palliative care (SPC) at hospice setting and have no further curative options available.

計畫書編號：PH-CP012
衛生署核准發文字號：衛署藥字第0960326352號 (申請案號：9608127)

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

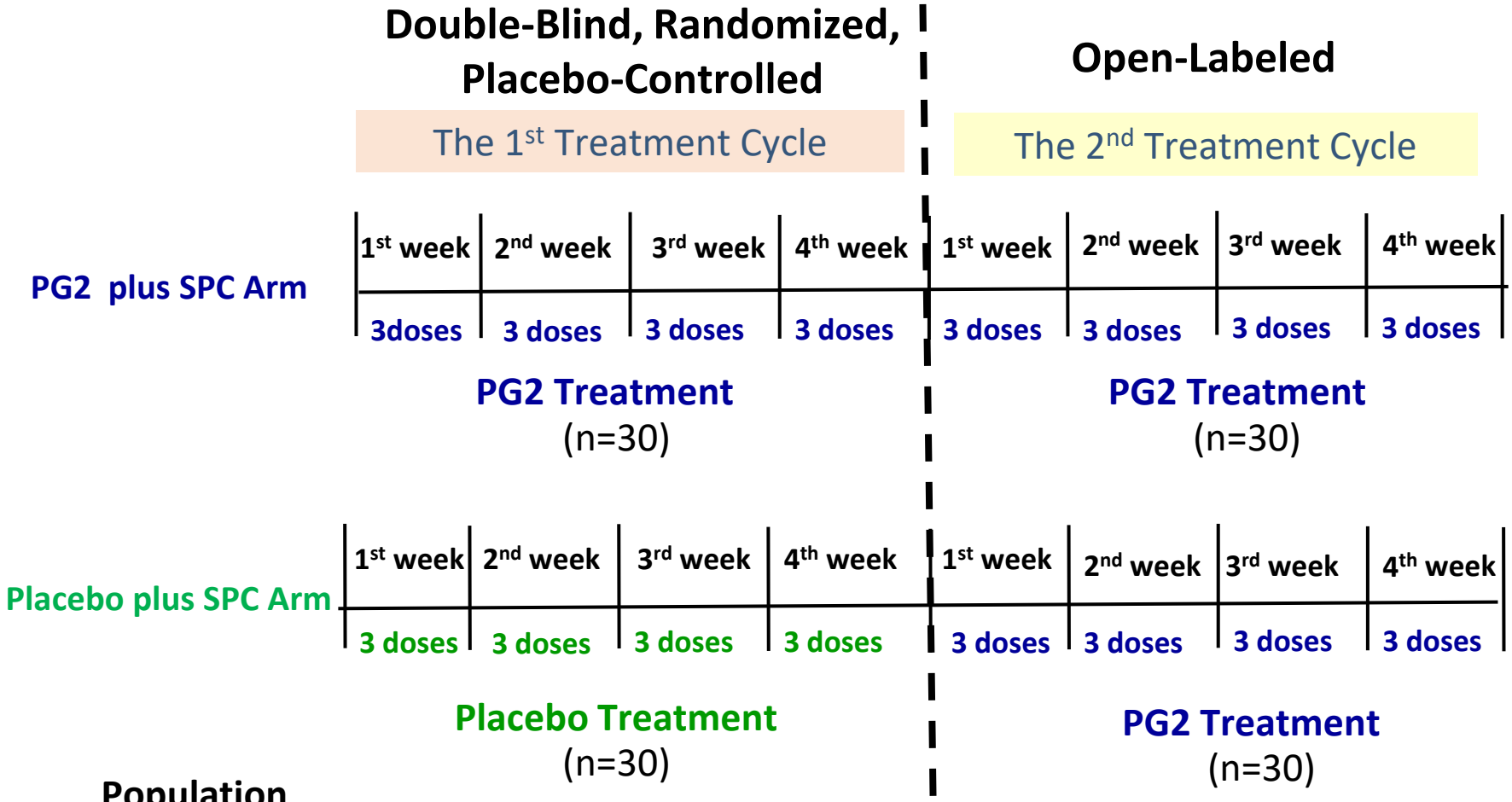
Inclusion Criteria

- 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

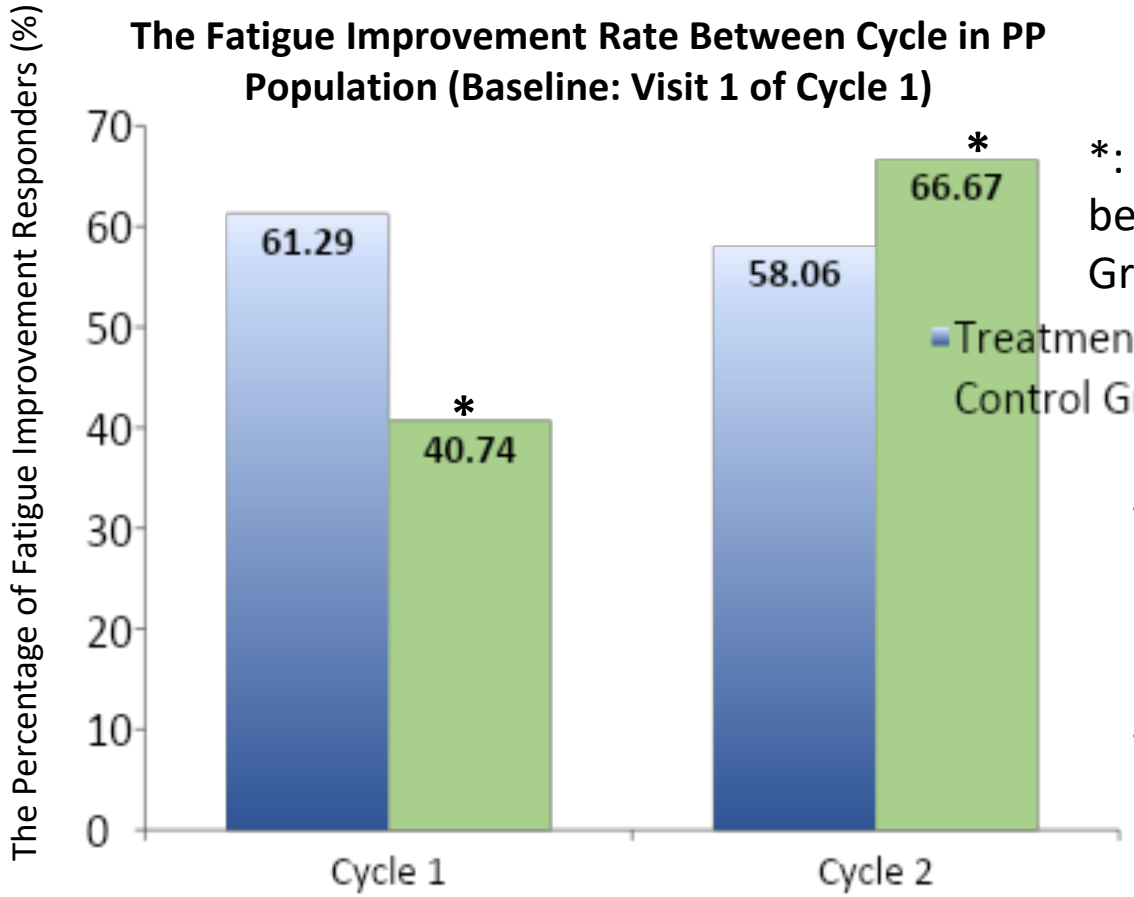
- Fatigue Improvement Response Rate (FIRR)

$$\frac{\text{Fatigue Improvement Responder}}{\text{Fatigue Improvement Responder + Non-Responder}} \times 100\%$$

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)

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

(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.

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

Baseline Disease Characteristics

Variable / Statistics	PG2 500 mg (N=111)	PG2 250 mg (N=103)
Lung cancer	20 (18.02%)	14 (13.59%)
Breast cancer	16 (14.41%)	12 (11.65%)
Colon cancer	13 (11.71%)	11 (10.68%)
Gastric cancer	10 (9.01%)	10 (9.71%)
Others	52 (46.85%)	56 (54.37%)

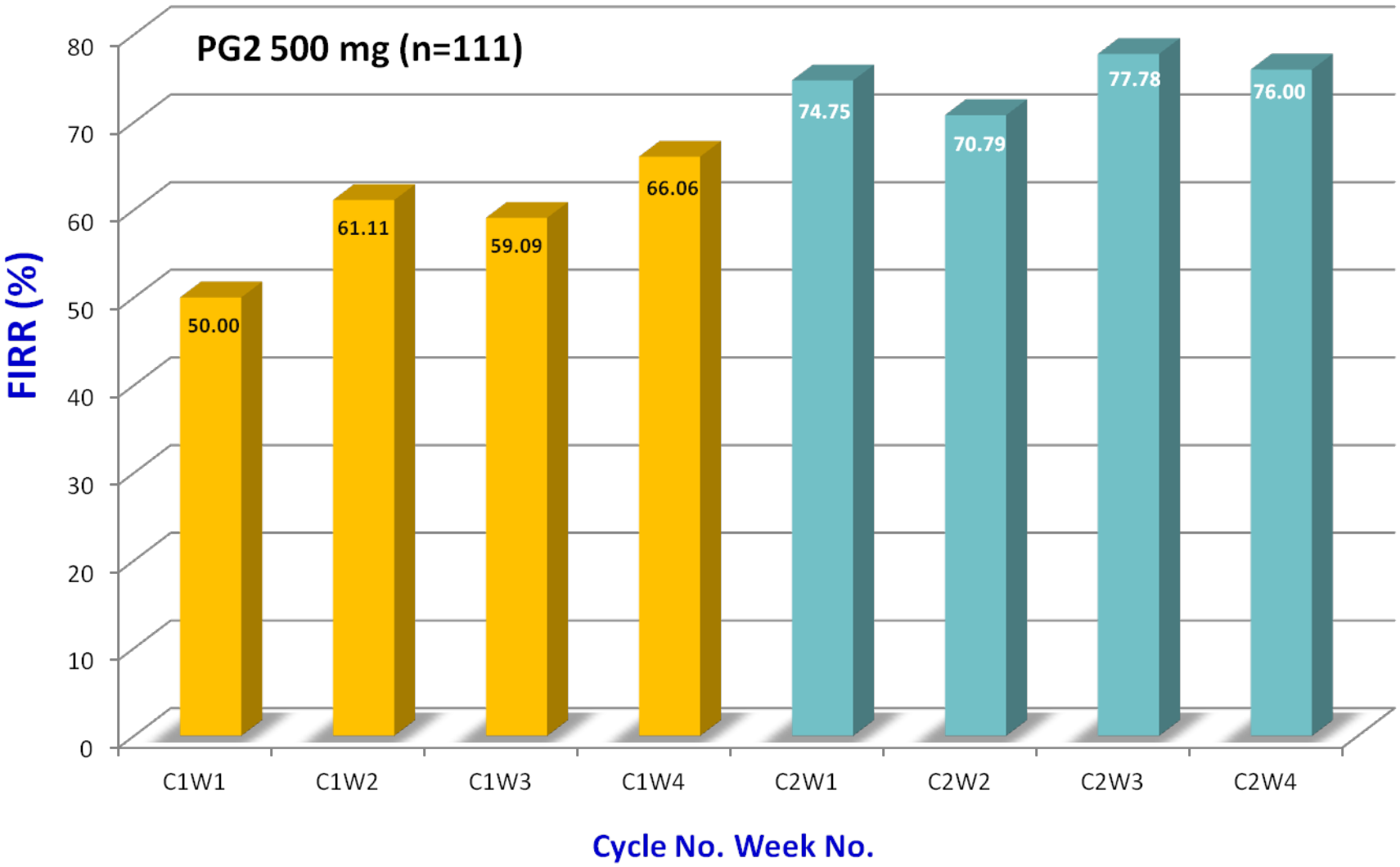
Baseline KPS and Baseline BFI

Variable / Statistics	PG2 500 mg (N=111)	PG2 250 mg (N=103)	Differences among Groups with 95% CI
Baseline KPS score			
n	111	103	
Mean (SD)	**64.50 (14.82)**	**66.65 (14.06)**	(-6.05, 1.75)
Median (min, max)	70 (30, 90)	70 (30, 90)	
95% CI	(61.72, 67.29)	(63.90, 69.40)	
Baseline BFI score			
n	111	103	
Mean (SD)	**6.80 (1.53)**	**6.76 (1.25)**	(-0.34, 0.42)
Median (min, max)	6.6 (4, 10)	6.9 (4.1, 9.4)	
95% CI	(6.51, 7.08)	(6.51, 7.00)	

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

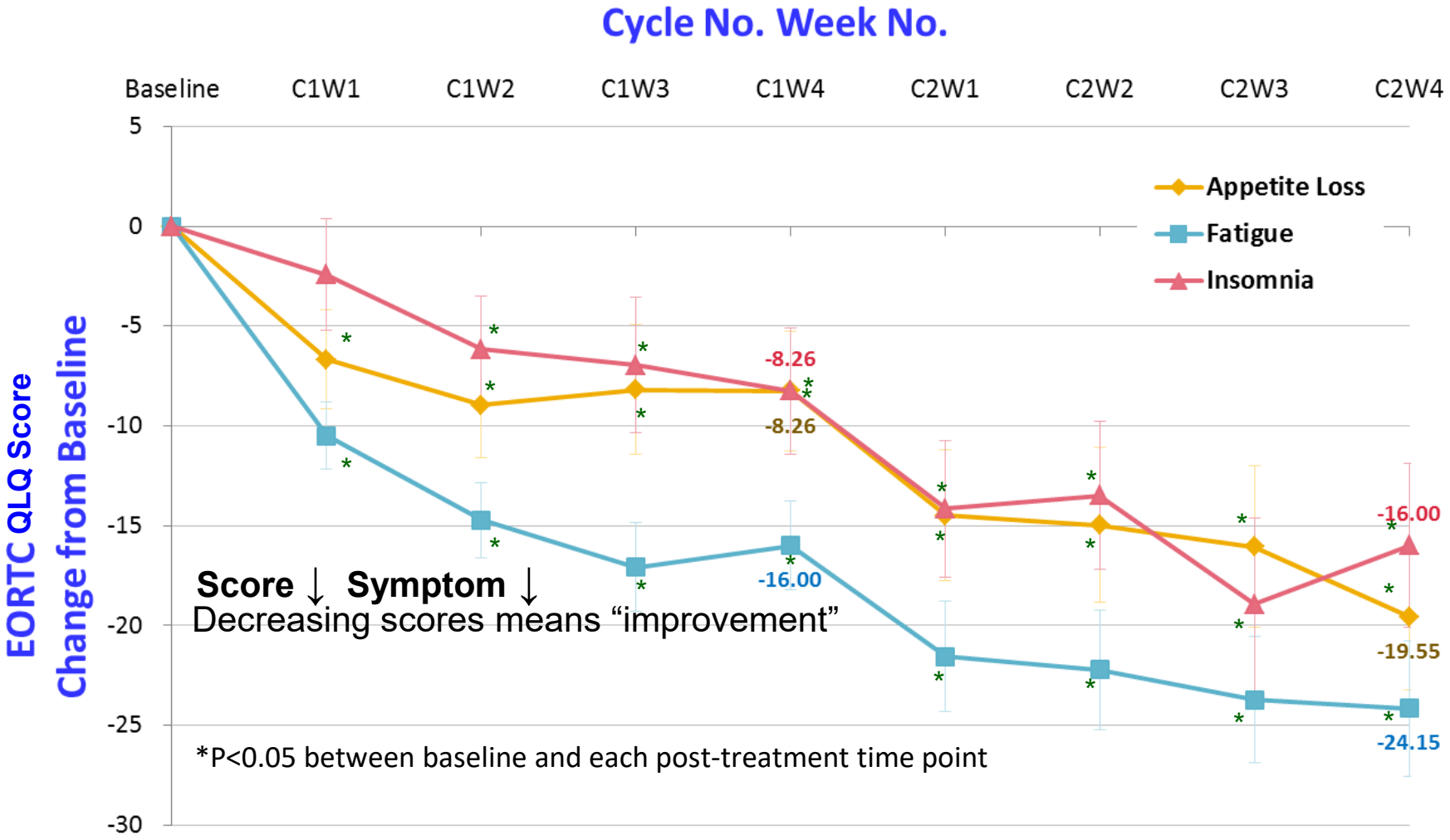
FIRR by Week during the Whole Study Period

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

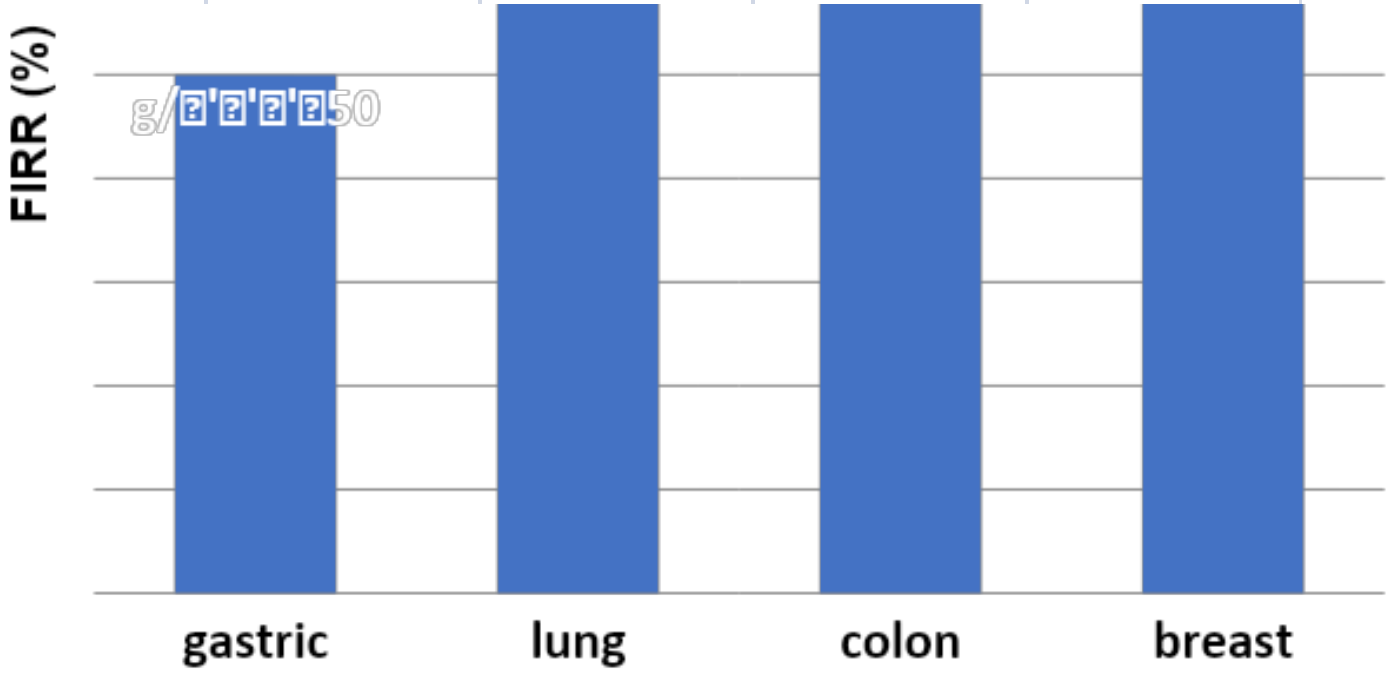


2018 MASCC e-Poster Presentation; J Clin Oncol 36, 2018 (suppl; abstr 10091); 2018 ASCO Annual Meeting, Poster Presentation Abstract #: 10091. PhytoHealth In-house Data

FIRR: Top 4 Types of Cancer

≥ 10% Improvement

	gastric	lung	colon	breast
FIR>10%	5	13	9	12
total	10	20	13	16
FIRR(%)	50.00	65.00	69.23	75.00



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

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,*]

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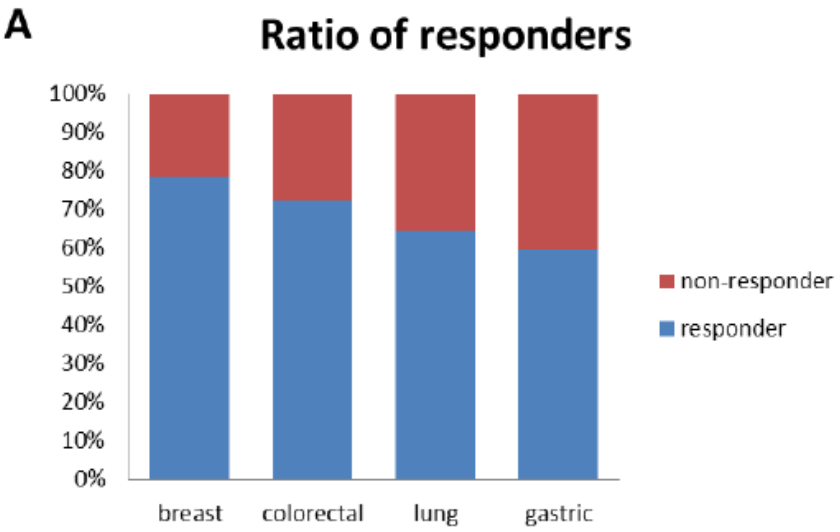
check for updates

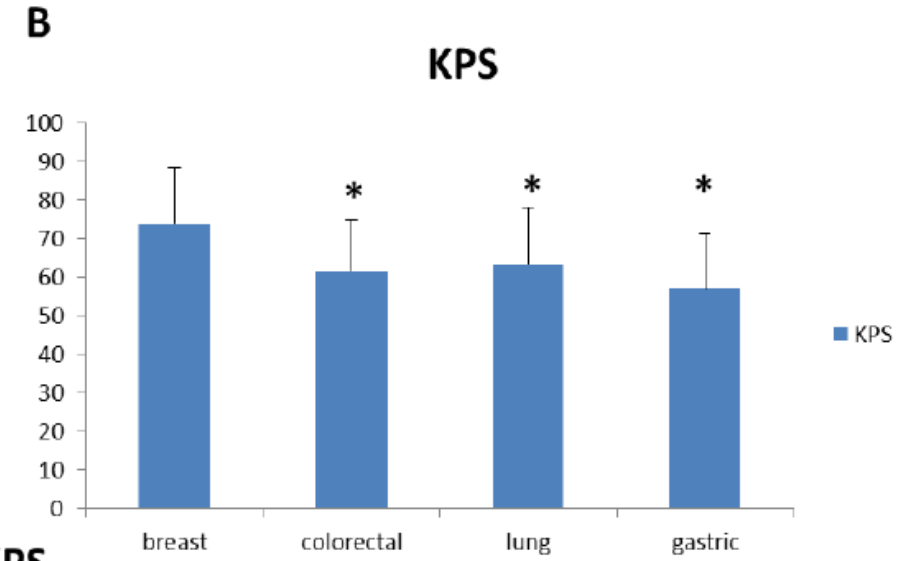
Cancers **2019**, *11*, 128; doi:10.3390/cancers11020128

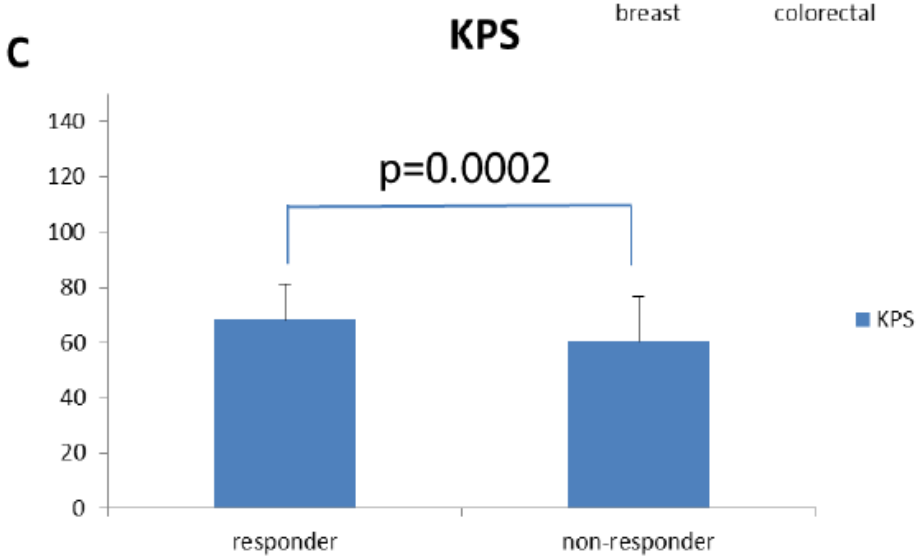
www.mdpi.com/journal/cancers

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

Responders vs. KPS







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

Multivariate analysis for responders and non-responders to 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 **
Age (years)					
n	140	74	0.3085 [W]	1.007 (0.978, 1.036)	0.6518
Mean (SD)	62.06 (11.28)	63.39 (10.66)			
Median (min, max)	62 (28, 91)	65 (22, 81)			
95% CI	(60.17, 63.94)	(60.92, 65.86)			
Gender					
Male	75 (53.57%)	46 (62.16%)	0.2279 [C]	0.774 (0.387, 1.546)	0.4677
Female	65 (46.43%)	28 (37.84%)			
Body mass index (BMI) (kg/m^2)					
<19	39 (28.26%)	27 (36.99%)	0.1935 [C]	0.724 (0.364, 1.440)	0.3570
≥19	99 (71.74%)	46 (63.01%)			
number of missing	2	1			
Body weight loss in previous 6 months					
<5%	63 (45.65%)	30 (40.54%)	0.4746 [C]	0.998 (0.512, 1.944)	0.9944
≥5%	75 (54.35%)	44 (59.46%)			
NA	2	0			
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%)			
Baseline BFI score					
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.

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

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 ****
Body mass index (BMI) (kg/m²)					
<19	39 (28.26%)	27 (36.99%)	0.1935 [C]	0.724 (0.364, 1.440)	0.3570
≥19	99 (71.74%)	46 (63.01%)			
number of missing	2	1			
Body weight loss in previous 6 months					
<5%	63 (45.65%)	30 (40.54%)	0.4746 [C]	0.998 (0.512, 1.944)	0.9944
≥5%	75 (54.35%)	44 (59.46%)			
NA	2	0			
Baseline KPS score					
30–50 **(42%)**	22 (15.71%)	31 (41.89%)	<0.0001 [C]	0.253 (0.126, 0.504)	<0.0001
60–90 **(73%)**	118 (84.29%)	43 (58.11%)			
Baseline BFI score					
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%)			

* 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.

Cancers (Basel). 2019 Jan 22;11(2).

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.

	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%)			

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.

Polysaccharides of Astragalus membranaceus (PG2 Lyo. Injection) 健保給付規定

第三節 代謝及營養劑 (自110年3月1日生效)

使用本藥品應符合下列各條件：

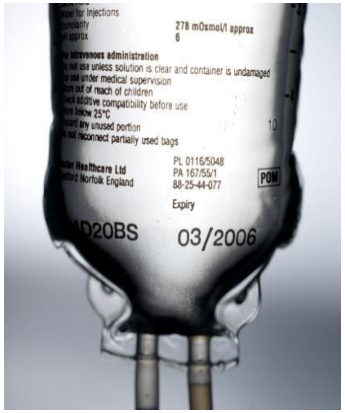
1. 用於**第四期**因疾病進展導致中重度疲憊之**乳癌**成人患者(不含住院安寧療護病患) 。
2. 臨床上需符合**ICD-10**診斷標準，病歷上應詳細記載疲憊分數≥4 (**BFI-T或 VAS**)，經其他處置無效之中重度癌因性疲憊症患者。
3. **ECOG**需為0-2之患者。
4. 每位病人終生給付**6支**為上限。
5. 需經**事先審查**核准後使用。

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

”Cure sometimes, treat often, comfort always“

Hippocrates

擊退癌疲憊、

癌症治療不delay

BACK UP

KPS vs. ECOG

ECOG		Karnofsky	
Normal activity fully ambulatory (無症狀)	0	100	Normal, no complaints(沒有任何抱怨，確定沒有疾病)
Symptoms, but nearly fully ambulatory (有症狀，但對生活無影響)	1	90	Able to carry on normal activities, Minor signs or symptoms of disease (可以正常活動，有一些疾病症狀)
		80	Normal activity with effort (可以稍微正常活動，已經有一些疾病的症狀)
Some bed time, but needs to be in bed less than 50% of normal daytime (躺在床上的時間<50%)	2	70	Cares for self. Unable to carry on normal activity or to do active work (需要自己照顧，無法從事正常活動)
		60	Requires occasional assistance, but able to care for most of his needs (有時需要別人幫助，能照顧患者大部分的需要)
Needs to be in bed more than 50% of normal daytime (躺在床上的時間>50%)	3	50	Requires considerable assistance, and frequent medical care (需要考慮別人幫助，經常給予醫療照顧)
		40	Disabled. Requires special care and assistance (傷殘，需要特別照顧及幫助)
Unable to get out of bed (長期臥床)	4	30	Severely disabled. Hospitalization indicated though death not imminent (嚴重傷殘，尚未有死亡的危險)
		20	Very sick. Hospitalization Necessary. Active supportive Treatment necessary (痛情嚴重，尚未有死亡的危險)
		10	Moribund (病況緊急，很快有死亡的危險)
Dead	5	0	Dead

012可化療

藥品輸注注意事項

輸注反應(Infusion Reaction)定義

- 注射針劑藥品在輸注過程中產生之不適症狀，統稱為輸注反應。
- 依據NCI-CTC(美國國家癌症組織)分級標準:
  (1)輕至中度反應(第1-2級)症狀包括: Flushing(發紅)、Rash(皮疹)、Fever(發燒)、Rigors(冷顫)、Chills(寒顫)、Dyspnea(呼吸困難)及Mild Hypotension(低血壓)。
  (2)嚴重反應(第3-4級)症狀包括: Bronchospasm(支氣管痙攣)、Hypotension requiring Treatment(需治療之低血壓)、Cardiac Dysfunction(心臟失能)及Anaphylaxis(嚴重衝擊性過敏反應)等。
- 生物製劑(如細胞激素、單株抗體等)及植物藥，其來源為生物體，藥品組成屬大分子蛋白質或複合性分子(M.W.>>1 kDa)，具有調控免疫系統作用，故可能導致輸注反應包括過敏反應(hypersensitivity reactions)及急性輸注反應。
- 輸注反應發生症狀通常不具特異性，故無法預測是否發生或是哪些患者較易發生，一般發生在輸注後2小時內，故對於首次輸注應加強監控。

懷特血寶® 凍晶注射劑-署核不良反應

- 懷特血寶®凍晶注射劑為一高度純化之大分子植物新藥，具有調控免疫系統作用，副作用並不常見，大多輕微且短暫，偶見**搔癢(2.38%)、皮疹(5.95%)及頭暈(2.38%)**。一般在注射後2~3小時即自然消除。也可在醫師給予對症處理後迅速獲得緩解。

  其他曾發生之不良反應包括：**Fever(發燒)，Chills(寒顫)**等，**皆屬輕至中度輸注反應**。

懷特血寶® 凍晶注射劑-輸注注意事項

- 為避免輸注過程因管路汙染及現存感染問題，影響輸注之安全性，建議：
  輸注前輸注管加強沖洗，並先以少量生理食鹽水輸注於病患，如生命體徵維持正常再開始施打。
- 輸注時間不宜太快，建議：
  每劑輸注需時3.5小時以上，並密切觀察病患是否有輸注反應的跡象，俾以即時處理。
- 可經由醫師評估病患狀況，建議：
  於輸注前投給藥物予以預防，如抗組織胺、類固醇及解熱劑等，或延長輸注時間降低輸注速率。
- 當發生輕至中度輸注反應時，建議：
  由醫師評估輸注反應嚴重程度，決定是否先行中斷輸注，或在嚴密監視下繼續輸注。
- 當輸注反應發生，建議：
  藉由連續輸注生理食鹽水，或使用抗組織胺、解熱劑或類固醇治療。一旦輸注反應症狀消退，可依醫師指示下以較慢的輸注速率下重新開始，完成輸注療程。