

# Clinical Study on Patients with Bone Metastases – A Twelve Year Follow-up

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## Abstract

A clinical study on patients with metastatic bone cancer studied in 2003, comparing the results of treatment using clodronate (a bisphosphonate) and a herbal formula BBYNG. Detailed study extended for 72 weeks, after which some patients continued taking the herbal treatment while others were just kept connected.

12 years after the start of the clinical study, 8 patients were surviving well, 7 of them belonged to the herbal group. Working back on the 5 years survival since 2003, it is observed that the herbal group compared with the clodronate group was 69.4% vs 30.6%. The twelve years' follow-up might indicate that the herbal formula might have given better sustenance effects.

**Keywords:** Metastatic Cancer; Bone Secondaries; Herbal Treatment; Bisphosphonate

## Introduction

Bone metastases are common for malignant tumours, 40-80% of which are affected. Bone metastases, apart from being an indication for poor prognosis, is notorious for complications like fractures, severe pain, and bone marrow suppression [1,2].

Currently although there is no cure for bone metastasis, supportive treatment for pain control, fracture prevention and maintenance of survival are very much desirable. However, the lack of perfect results would warrant an enthusiastic exploration for complementary alternative treatment [1,3].

## Methods

In 2003 a PhD Student interested at cancer treatment using Traditional Chinese Medicine started a research project "Clinical Observation and Experimental Study on the Efficacy of a Chinese Medicine Formula on Malignant tumour bone metastases" [4]. Clinical recruitment started in July 2003 and the study was completed in November 2005. Patients with bone metastases arising from the spread of malignant tumours were referred to the Orthopaedic Department because of fracture complication or bone pain. A total of 99 patients were recruited and the primary cancers were mainly from breast, lung, prostate and nasopharynx. Bone secondaries were mainly affecting the spinal segments and pelvis [2,5,6].

Since bone metastasis is considered a late presentation of cancer when conventional therapy has not achieved its desirable results, the treatment offered in the Orthopaedic department is limited to the care of complications (like fractures) and to relieve pain arising from the secondaries. The use of bisphosphonates which is originally prescribed for the treatment of osteoporosis has also been used to minimize bone destruction, probably through their osteoclast suppression effects [7-9].

This study therefore is designed to compare the benefits of a bisphosphonate viz. clodronate against an innovative Chinese Medicine Formula (BBYNG) consisting of 5 herbs, viz. *Herba Hedyotis diffusae* 15g (Anti-angiogenesis), *Fritus Ligustri Lucidi* 10g (Bone building), *Rhizoma Rhizoma Drynariae* 10g (promotes blood circulation and strengthen bones), *Herba Epimedii* 10g (strengthens bones

and muscles), *Psoralea corylifolia* 5g (improve general vitality). Hedyotidis is known to control cancer cell growth and angiogenesis whereas the other four herbs have been used for the control of osteoporosis [10-19].

The survival time was analyzed by using Kaplan-Meier methods. Statistical analyses were performed using SPSS for windows, version 22.0 (SPSS, Inc). P-values <0.05 (2-sided test) were considered statistically significant.

### Results

Recruitments from the Orthopaedic Department were initially well supported for obvious reasons. However, keeping the compliance of follow-up visits and continuous medication were particularly difficult for this category of patients who suffered from intense pain, fear of fractures and were mostly desperate about their future outlook.

99 patients were recruited initially but only 59 completed 72 weeks of follow-up (Table 1).

Moreover, mortality was also affecting the study. A careful scrutiny on the mortality of the first five years related to the study indicated a 5 years survival of 69.4% for the BBYNG group and 30.6% in the clodronate group (Figure 1).

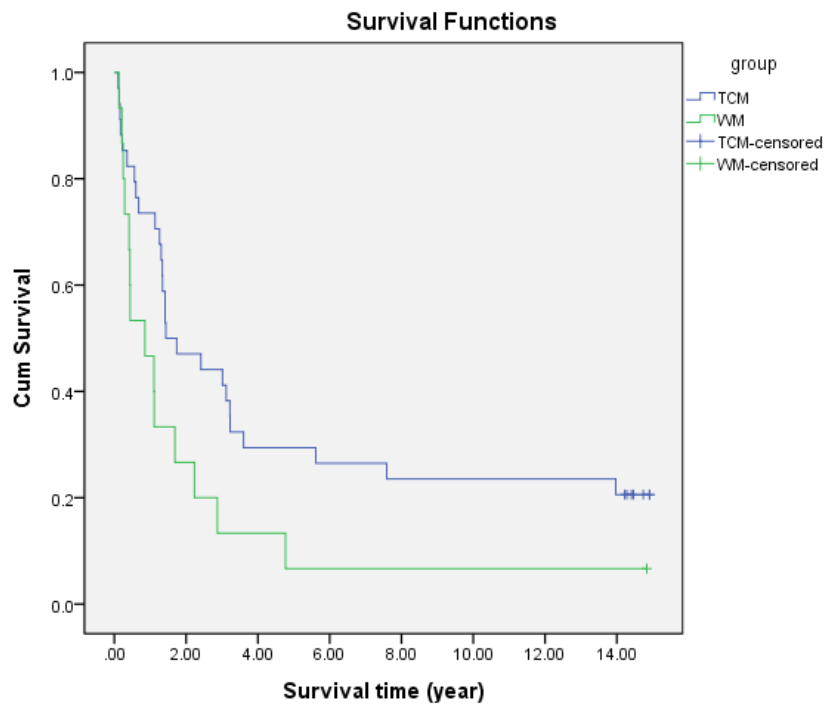


Figure 1: Survival Plot for Two Treatment Groups

	OSTAC	BBYNG	Total
No. of Patients recruited	39	47	86
No. of Patients completed study in 72 weeks	25	34	59

Table 1: Patients recruited and completed study

Other clinical parameters studied included Quality of life (QoL), pain severity, and radiological changes. The small number of cases and complexity of pain did not allow a reliable assessment. The short duration of follow up again did not allow a useful assessment of radiological changes. In the QoL assessment, the general state, especially the walking ability, appeared to be better in the BBYNG group.

### Extended Follow-up of Study Groups

Since some patients in the BBYNG group, on completion of the study, requested that they will be allowed to continue taking the herbal formula, 7 patients were given this privilege and up to today, 12 years after their diagnoses of bone secondaries they were still surviving well. This prompted us to give a general investigation of the patients from the two groups about their survivals.

Details of the survival state of the 86 patients are given in the following table (Table 1).

Long term follow-up on refractory cancer patients is uncommon for obvious reasons. We have this group of patients suffering from bone secondaries with expected short life expectancies. To our great surprise 8 of them are surviving with reasonably good quality of life, 12 years after their diagnosis of bone metastases. 7 of these patients have been taking BBYNG ever since they joined the trial. One patient did not take any herb treatment at all. Table 2 gives some details of the surviving 8 patients after 12 years (Table 2).

BBYNG group															
No	Sex/ Age	Primary Cancer	Conventional Rx Received					BBYNG			Other Rx	Current condition			
			Bone 2° sites	Surg	Chemo	RT	Others	Start date	End Date	No. of years	Including TCM	Independent	Wheel chair	Bed ridden	
1	F//0	Ovary	Multiple bones	x	x			Jul 2003	Jan 2005	1.5	Coriolus vesicolor	x			
2	M/56	NI-C	Cervical Spine				x	Jul 2003	Jan 2005	1.5	None	x			
3	M/85	Left Renal Cell	Left Femur	x			x	Sep 2003	April 2005	1.5	None		x		
4	FM	Right Breast	CSpine	x			x	Dec 2003	June 2005	1.5	Coriolus vesicolor				
5	M/91	Prostate	Pelvic & Spine	x				Jan 2004	continued	14	Coriolus vesicolor	x	Walk with clutches		
6	M/85	Prostate	Multiple bones	x				Mar 2004	continued	14	Coriolus vesicolor			x	
7	F//4	Rectum	Pelvic	x				Sep 2003	continued	14.5	Coriolus vesicolor	x			
No BBYNG group															
No	Sex/ Age	Primary Cancer	Conventional Rx Received					WM/Conn-o1			Other Rx	Current condition			
			Bone 2° sites	surg	Chemo	RT	Others	Start date	End Date	No. of years	Including TCM	Independent	Wheel chair	Bed ridden	
1	F/59	Left Breast	Left Prox Femur	x				x HT	Aug 2003	Feb 2005	1.5	Coriolus vesicolor	x (walk with a stick)		

HT: Hormonal Therapy

**Table 2:** Details of 8 patients surviving 12 years

No conclusion should be drawn from this interesting observation. The survival of these patients should be related to their primary cancer, the extensiveness of the metastases and the therapeutic measures together with their responses. The apparently favourable few patients could have some other unique features, either innate or environmental, that could have favourably affected their survival.

On the other hand, in view of the fact that there is yet no available effective means of treating refractory cancer patients, and target orientated therapy obviously will not give good effects in view of the refractory, late situations, alternative treatments like herbal medicine deserve to be seriously studied. The holistic approach of Traditional Chinese Medicine would be a logical approach to supplement standard treatment for cancer.

Indeed, some medicinal herbs have been researched and proven effective in the different areas of pathogenesis of cancer: viz. apoptosis, anti-angiogenesis, immunological defense and anti-metastasis. These herbs could be used together in a combined formula to give a comprehensive, holistic control to the aggressive cancer activities [20].

## Protocol of Future Study

The interesting results of the bone metastases study and the apparent better survivals observed in the BBYNG group, have prompted the planning of a study protocol for similar refractory cases of cancer.

Based on our past investigations on the anti-tumour, anti-angiogenesis, anti-metastases bone protection and immune-supportive effects of a number of Chinese Medicinal herbs, four items have been selected to form an innovative herbal formula. They are *Andrographis paniculata*, *Acanthopanax senticosus*, *Ganoderma lucidum*, and *Hedyotis diffusa*. The anticancer efficacies of the formula will be evaluated in metastatic breast cancer mice and other in-vitro platforms. In addition, chemotherapeutic effects with metronomic doses will be explored when used together with the herbal formula [21,22].

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