

**UNIVERSITI SAINS MALAYSIA
GERAN PENYELIDIKAN UNIVERSITI
PENYELIDIKAN
LAPORAN AKHIR**

**ASSOCIATION OF DEGREE OF EXPRESSION OF KI 67
PROLIFERATIVE CELL MARKER WITH AGGRESSIVE
GIANT CELL TUMOR OF THE BONE**

PENYELIDIK

PROF. MADYA DR. WAN FAISHAM NU MAN WAN ISMAIL

PENYELIDIK BERSAMA

**DR. AMINUDIN M SHAMSUDIN
DR. SALZIHAN MD SALLEH**

2013



LAPORAN AKHIR GERAN PENYELIDIKAN USM JANGKA PENDEK

TAJUK : THE ASSOCIATION OF DEGREE OF
EXPRESSION OF Ki67 PROLIFERATIVE
CELL MARKER WITH AGGRESSIVE
GIANT CELL TUMOUR OF THE BONE

NO. AKAUN : 304/PPSP/6131541

**PROF. MADYA DR. WAN FAISHAM
NUMAN B. WAN ISMAIL**



BAHAGIAN PENYELIDIKAN
Pusat Pengajian Sains Perubatan

SENARAI SEMAKAN UNTUK BUKU LAPORAN AKHIR GERAN USM JANGKA PENDEK
(untuk di isi oleh penyelidik)

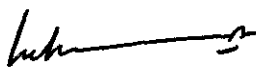
NAMA PENYELIDIK UTAMA	: Dr Wan Faisham Numan B Wan Ismail
NAMA CO-RESEARCHER	: Dr Aminudin M Shamsudin, Dr Salzihan Md Salleh
TAJUK GERAN	: The association of degree of expression of Ki67 proliferative cell marker with aggressive giant cell tumor of the bone
NO.AKAUN	: 304/PPSP/6131541

SENARAI SEMAKAN SEMASA PENYERAHAN BUKU LAPORAN AKHIR
(Sila Tandakan (✓) Pada Kotak Yang Berkenaan)

NO.	PERKARA	ADA	TIADA
1.	Borang Laporan Akhir Projek Penyelidikan USM Jangka Pendek	/	
2.	Borang Laporan Hasil Penyelidikan, PPSP	/	
3.	i) Salinan Menuskrip dan Salinan surat/email bukti penghantaran dan penerimaan manuskrip oleh mana-mana journal atau	/	
	ii)Kertas penerbitan disertakan	/	
4.	Penyata Perbelanjaan (Financial Statement) (Sila dapatkan daripada Jabatan Bendahari)	/	
5.	Laporan Komprehensif (termasuk kertas persidangan atau seminar dan penerbitan saintifik hasil daripada projek ini)	/	
6.	Surat pemakluman penghantaran Laporan Akhir ke Bhg. Penyelidikan	/	

Nota:

- 1) Sila buat 2 salinan buku laporan Akhir
- 2) No. 1- 5 - Perlu dimasukkan dalam Buku Laporan Akhir
- 3) No. 6 - Hantar terus Kepada Cik Noor Adnie Bajuri (RCMO) hanya salinan sahaja kepada Bhg. R&D, PPSP


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Jabatan Ortopedik
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Kampus Kesihatan
Universiti Sains Malaysia
16150 Kubang Kerian, Kelantan.
Updated July 2011 (ver.2)



LAPORAN AKHIR PROJEK PENYELIDIKAN JANGKA PENDEK
FINAL REPORT OF SHORT TERM RESEARCH PROJECT

Sila kemukakan laporan akhir ini melalui Jawatankuasa Penyelidikan di Pusat Pengajian dan Dekan/Pengarah/Ketua Jabatan kepada Pejabat Pelantar Penyelidikan

<p>1. Nama Ketua Penyelidik: <i>Name of Research Leader Wan Faisham Numan B Wan Ismail</i></p> <p> <input checked="" type="checkbox"/> Profesor Madya/ <i>Assoc. Prof.</i> <input type="checkbox"/> Dr./ <i>Dr.</i> <input type="checkbox"/> Encik/Puan/Cik <i>Mr/Mrs/Ms</i> </p>																																																			
<p>2. Pusat Tanggungjawab (PTJ): School of Medical Sciences <i>School/Department</i></p>																																																			
<p>3. Nama Penyelidik Bersama: <i>Name of Co-Researcher Dr Aminuddin M Shamsudin, Dr Salzihan M Daud</i></p>																																																			
<p>4. Tajuk Projek: <i>The association of degree of expression of Ki67 proliferative cell marker with aggressive giant cell tumor of the bone</i></p>																																																			
<p>5. Ringkasan Penilaian/Summary of Assessment:</p> <table border="1"> <thead> <tr> <th rowspan="2"></th> <th colspan="2">Tidak Mencukupi <i>Inadequate</i></th> <th rowspan="2">Boleh Diterima <i>Acceptable</i></th> <th colspan="2">Sangat Baik <i>Very Good</i></th> </tr> <tr> <th>1</th> <th>2</th> <th>3</th> <th>4</th> <th>5</th> </tr> </thead> <tbody> <tr> <td>i) Pencapaian objektif projek: <i>Achievement of project objectives</i></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>ii) Kualiti output: <i>Quality of outputs</i></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>iii) Kualiti impak: <i>Quality of impacts</i></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>iv) Pemindahan teknologi/potensi pengkomersialan: <i>Technology transfer/commercialization potential</i></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>v) Kualiti dan usahasama : <i>Quality and intensity of collaboration</i></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td>vi) Penilaian kepentingan secara keseluruhan: <i>Overall assessment of benefits</i></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </tbody> </table>						Tidak Mencukupi <i>Inadequate</i>		Boleh Diterima <i>Acceptable</i>	Sangat Baik <i>Very Good</i>		1	2	3	4	5	i) Pencapaian objektif projek: <i>Achievement of project objectives</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	ii) Kualiti output: <i>Quality of outputs</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	iii) Kualiti impak: <i>Quality of impacts</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	iv) Pemindahan teknologi/potensi pengkomersialan: <i>Technology transfer/commercialization potential</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	v) Kualiti dan usahasama : <i>Quality and intensity of collaboration</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	vi) Penilaian kepentingan secara keseluruhan: <i>Overall assessment of benefits</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
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6. Abstrak Penyelidikan

Stage III Campanacci giant cell tumour of the bone always exhibits high biological aggressiveness and has tendency for local recurrences and pulmonary metastases. We analyzed Ki-67 immuno-histochemistry of 31 cases of stage III giant cell tumour of the bone to determine the clinico-pathological correlation. The mean value of Ki-67 index obtained as a percentage of 1000 background cells was 8.15 with range from 1.00 to 20.00. There was no difference of indices in cases with recurrence and pulmonary metastasis. In conclusion, Ki-67 index is not useful as a prognostic marker for aggressive type of giant cell tumour of the bone.

7. Sila sediakan laporan teknikal lengkap yang menerangkan keseluruhan projek ini.

[Sila gunakan kertas berasingan]

*Applicant are required to prepare a Comprehensive Technical Report explaining the project.
(This report must be appended separately)*

Senaraikan kata kunci yang mencerminkan penyelidikan anda:

**Giant cell tumor
Stage III
Ki 67 index**

8. Output dan Faedah Projek

Output and Benefits of Project

(a) * Penerbitan Jurnal

Publication of Journals

Journal of experimental & clinical cancer research 2010 29:25

(b) **Faedah-faedah lain seperti perkembangan produk, pengkomersialan produk/pendaftaran paten atau impak kepada dasar dan masyarakat.**

1. Study behavior of GCT locally that have diferent characteristic compare to western population
2. Preliminary evaluation for future reseach on
 - a. Immunohistochemistry
 - b. Genetic

(c) **Latihan Sumber Manusia**
Training in Human Resources


i) Pelajar Sarjana:
Dr Aminuddin M Shamsuddin graduate MMed orthopedic 2009

ii) Lain-lain:
Follow up reseach – p53 in GCT of the bone on going reseach

9. **Peralatan yang Telah Dibeli:**

No

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Kampus Kesihatan
Universiti Sains Malaysia
16150 Kubang Kerian, Kelantan.



Tandatangan Penyelidik
Signature of Researcher

24/6/2013

Tarikh
Date

Komen Jawatankuasa Penyelidikan Pusat Pengajian/Pusat
Comments by the Research Committees of Schools/Centres

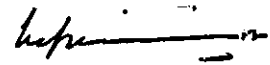
Tuduh Cerai

Dufin

24/8/13

TANDATANGAN PENERUSI
JAWATANKUASA PENYELIDIKAN
PUSAT PENGAJIAN/PUSAT
Signature of Chairman
[Research Committee of School/Centre]

Tarikh
Date


PROF. MADYA (DR) WAN FAISHAM NUMAN WAN ISMAIL
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UNIVERSITI SAINS MALAYSIA
JABATAN BENDAHARI
KUMPULAN WANG PENYELIDIKAN GERAN USM(304)
PENYATA PERBELANJAAN SEHINGGA 30 JUN 2012

Jumlah Geran:	RM	16,000.00	Ketua Projek:	DR WAN FAISHAM NUMAN WAN ISMAIL
Peruntukan 2007 (Tahun 1)	RM	7,900.00	Tajuk Projek:	Association of Degree of Expression of Ki 67 Proliferative Cell Marker with Aggressive Giant Cell Tumor of the Bone
Peruntukan 2008 (Tahun 2)	RM	0.00		
Peruntukan 2009 (Tahun 3)	RM	0.00	Tempoh:	01 Julai 07 - 30 Jun 09
			No.Akaun:	304/PPSP/6131541

Kwg	Akaun	PTJ	Projek	Donor	Peruntukan Projek	Perbelanjaan Kumpul Hingga Tahun Lalu	Peruntukan Semasa	Tanggung Semasa	Bayaran Tahun Semasa	Belanja Tahun Semasa	Baki Projek
304	11000	PPSP	6131541		-	-	-	-	-	-	-
304	14000	PPSP	6131541		-	-	-	-	-	-	-
304	15000	PPSP	6131541		-	-	-	-	-	-	-
304	21000	PPSP	6131541		-	-	-	-	-	-	-
304	22000	PPSP	6131541		-	-	-	-	-	-	-
304	23000	PPSP	6131541		250.00	-	250.00	-	-	-	250.00
304	24000	PPSP	6131541		-	-	-	-	-	-	-
304	25000	PPSP	6131541		-	-	-	-	-	-	-
304	26000	PPSP	6131541		1,000.00	-	1,000.00	-	-	-	1,000.00
304	27000	PPSP	6131541		5,650.00	-	5,650.00	-	-	-	5,650.00
304	28000	PPSP	6131541		-	-	-	-	-	-	-
304	29000	PPSP	6131541		1,000.00	-	1,000.00	-	-	-	1,000.00
304	32000	PPSP	6131541		-	-	-	-	-	-	-
304	35000	PPSP	6131541		-	-	-	-	-	-	-
					7,900.00	-	7,900.00	-	-	-	7,900.00

BORANG LAPORAN HASIL PENYELIDIKAN

PPSP

Tajuk geran: **The association of degree of expression of Ki67 proliferative cell marker with aggressive giant cell tumor of the bone**

Penyelidik: Dr Wan Faisham Numan B Wan Ismail

Jenis geran: Short Term

Tempoh geran: 2007-2009

Jenis laporan: Laporan Kemajuan Alatan di beli Ya:nyatakan.....

Laporan Akhir*: Tidak

OBJEKTIF SPESIFIK KAJIAN (sama spt dalam proposal asal)	SECARA RINGKAS TERANGKAN PENCAPAIAN/HASIL	OBJEKTIF TERCAPAI ATAU TIDAK
To determine the expression of Ki 67 proliferative marker in GCT of the bone amongst Malaysian population	8.15 in 1000 cell background	/
To determine the association between degree of expression of Ki 67 proliferative marker with the behaviour of GCT of the bone amongst Malaysian population.	Not significance	/
To determine the degree of Ki67 index in different stages of GCT of the bone amongst Malaysian population.	Not significance as index for evaluation behaviour	/
Conclusion	Ki67 is not useful as prognostic marker	/

- *Laporan Akhir perlu disertakan salinan manuskrip dan surat yang dihantar kepada mana-mana jurnal untuk penerbitan.*

Nama Penyelidik Utama (PI): Wan Faisham Numan B Wan Ismail



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RESEARCH

Open Access

Ki-67 immuno-histochemistry index in stage III giant cell tumor of the bone

Faisham W Ismail*¹, Aminudin M Shamsudin¹, Zulmi Wan¹, Salzihan M Daud² and Mutum S Samarendra²

Abstract

Background: Giant cell tumor is an infrequent and unpredictable bony lesion. Although numerous attempts have been made to predict the behaviour of GCT, there are no definite biological or histological parameters to determine the prognosis or aggressiveness of this lesion

Materials and methods: We analyzed Ki 67 immuno-histochemistry of 31 consecutive cases staged III giant cell tumor to determine the clinico-pathological correlation. There were 19 male patients compare to 12 females. The mean age was 33.8 years ranged from 18 to 59 years. Five cases presented with local recurrence prior to wide resection and one case had multiple recurrences there after. Six cases had pulmonary metastases. Expression of Ki 67 antigen was evaluated by immuno-histochemical staining techniques using the avidin-biotin peroxidase complex method using an LSAB2 kit (Dako, Glostrup, Denmark). The primary antibody used in this study was Ki-67 (MIB-1 clone, dilution 1:25; Dako).

Results: The mean value of Ki-67 index obtained as a percentage of 1000 background cells was 8.15 (ranged 1.00 - 20.0). The median Ki 67 index was 7.5 with standard deviation of 5.12. The Ki 67 index of recurrence tumor was 4.323 compared to 6.05 without recurrence and was not statistically significant (mean difference of 0.865 with p value in independent t test of 0.736). The Ki 67 index was also not statistically significant in the presence of pulmonary metastases with the mean value of metastases group of 6.681 compared to 2.890 without metastases (mean difference of 1.895 with p value in independent t test of 0.424).

Conclusion: Ki 67 index is not use-full prognostic marker for aggressive type of giant cell tumor of the bone.

Background

Giant cell tumor (GCT) of the bone is an infrequent and unpredictable bony lesion [1]. Although numerous attempts have been made to predict the behaviour of GCT, there are no definite biological or histological parameters to determine the prognosis or aggressiveness of this lesion [2]. Aggressive lesions (stage III Campanacci) are common in oriental population, and they have been shown to have higher risk of recurrence and pulmonary metastases [3-5].

Ki-67 represents a nuclear protein forming part of DNA replicase complex that provides a simple, rapid and reliable means of evaluating the growth fraction of neoplastic cell populations [6]. Ki-67 was shown to correlate with the biological behaviour and risk of pulmonary

metastases in a few reported cases of GCT of the bone [7]. However; there are no reported studies to identify the effectiveness of this marker to correlate with the aggressiveness and prognosis of the disease.

The aim of this study is to identify the effectiveness of Ki-67 as prognostic marker and in predicting the risk of local recurrence and pulmonary metastases for aggressive (stage III) GCT of the bone.

Methods

Thirty-one consecutive patients with histologically proven giant cell tumor, seen at our institution between January 1999 and December 2006, were included. The clinical and radiological records of all the patients were reviewed. Tissue diagnosis and immuno-histopathological study was obtained in all cases from the surgical specimen. Stage III or aggressive GCT in this study is defined as symptomatic, rapidly growing lesion. Bone scans showed intense activity that often extended beyond the

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