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Predictors of laboratory spontaneous tumour lysis syndrome in children with high-grade tumours in Uganda

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Abstract

High-grade malignancy is endemic in sub-Saharan Africa and is prone to the spontaneous tumour lysis syndrome. However, data on spontaneous tumour lysis syndrome remain scanty in our setting. We sought to determine the prevalence and factors associated with laboratory spontaneous tumour lysis syndrome in children in Uganda. We conducted a cross-sectional study among children <18 years old with histologically confirmed high-grade malignancy between October 2013 and April 2014. Laboratory spontaneous tumour lysis syndrome was defined as the presence of ≥2 of each of hyperkalaemia, hypocalcaemia, hyperuricaemia and hyperphosphatemia prior to administration of chemotherapy when alternative diagnoses had been excluded. A $p < 0.05$ was considered statistically significant. Of 108 children, of median age 7.7 years, where boys outnumbered girls 2:1, high-grade, malignancy included Burkitt's lymphoma, acute lymphoblastic leukaemia, non-Hodgkin's lymphoma, acute myeloid leukaemia and Burkitt's leukaemia, with 14 suffering with laboratory spontaneous tumour lysis syndrome. Hypocalcaemia was its most common electrolyte imbalance; and four children died prior to commencement of chemotherapy. Bulky disease, lactate dehydrogenase levels ≥500 iu/l and serum creatinine levels >1.2 mg/dl were associated with laboratory spontaneous tumour lysis syndrome. However, only bulky disease was significantly predictive of laboratory spontaneous tumour lysis syndrome. Such children would benefit from routine screening.

Keywords

Tumour lysis syndrome, Burkitt's lymphoma, acute leukaemia, Uganda

Introduction

The recorded incidence of cancer has increased exponentially in the last few decades with up to 18 million new cases registered worldwide in 2018.[1] Of these, over 272,000 new cases and 100,000 deaths were among children aged 0–19 years.[1] Despite a global trend towards a decrease in cancer mortality, over 80% of cancer-related deaths occur in low- and middle-income countries.[2,3] In the United States, malignant neoplasms were the fourth most common cause of death among children <19 years, accounting for >9% (1853 cases) of all death cases.[4] Interestingly, most childhood cancers are now highly curable in the developed world which contributes less than 20% of the global burden as survival rates approach 80% due to improved supportive care and efficacy of treatment.[5]

In Africa, over 58,000 childhood cancers and over 18,000 deaths were recorded in 2018,[1] and >80% of these children still die without access to adequate treatment; in many reports, the five-year survival rates vary from as low as 5% to 70%.[6] The disparity in survival rates is compounded by barriers in all steps of

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cancer care from late presentation, co-morbidity (especially malnutrition), lack of affordability and restricted access to both supportive and empirical anti-cancer treatments.[6] Despite the widespread use of anti-retroviral therapy, human immunodeficiency virus (HIV)-associated cancers such as Burkitt's lymphoma (BL) and other non-Hodgkin's lymphoma (NHL), Kaposi's sarcoma are common among children living with HIV in sub-Saharan Africa (SSA).[6,7]

Spontaneous tumour lysis syndrome (STLS), a rare but life-threatening metabolic oncological emergency, is known to complicate high-grade tumours such as BL, NHL and the acute leukaemias.[8–10] This is noted to occur, however, in Malawi, Zimbabwe and Uganda, in >50% of these high-grade malignancies among African children.[11–13] However, there is paucity of data on the prevalence and factors associated with STLS in most SSA countries. STLS has obvious implications on immediate outcome, morbidity and mortality of patients.[14] Early recognition of risk factors, prophylaxis and treatment of STLS would avail patients the opportunity to receive appropriate therapy, particularly where appropriate chemotherapy regimens are curative, as is the case in up to 80%.[14]

Given that children routinely present with advanced local and metastatic disease, they are prone to STLS. However, the exact burden of this life-threatening condition and its predictors among children presenting with haematologic and solid-organ high-grade tumours in our setting is poorly understood.

Patients and methods

We conducted a hospital-based, cross-sectional study between October 2013 and April 2014 of patients from the Paediatric Haematology Unit of Mulago National Referral Hospital (MNRH), Kampala, Uganda and the Uganda Cancer Institute (UCI). MNRH is the largest hospital in the country and also acts as the teaching hospital for Makerere University College of Health Sciences, the oldest medical school in Uganda. Annually, MNRH admits approximately 20,000 children. The hospital has a total bed capacity of 1500 and an annual in-patient turnover of 120,000. All children are stabilised, reviewed by resident doctors and a paediatrician at the acute care unit prior to being sent to their respective wards based on the clinical diagnoses made. The haematology unit receives all children with suspected cancers, investigates and refers patients with suspected or confirmed malignancy to the UCI. On the other hand, UCI is an East African Centre of Excellence in Oncology and the only national referral and internationally renowned cancer treatment and research centre in Uganda. UCI admits about 400–500 new cases of paediatric malignancies per year, including those from surrounding countries (South Sudan, western Kenya, northern Tanzania, the Democratic Republic of Congo, Rwanda and Burundi).

We included all children aged <18 years with histological confirmation of a high-grade tumour admitted at any of the two study centres whose primary caregiver/parents provided informed consent and those >8 years who provided assent to participate in the study. Children with renal disease, cardiac disease, overt (clinical) tumour lysis syndrome (TLS) and those eventually discovered to have histologically low-grade tumours were excluded.

Using historical annual admissions of approximately 484 children with malignancies in the prior 12 months, an estimated prevalence of STLS of 10% among patients with acute myeloid leukaemia (AML) according to a Spanish study by Montesinos et al.,[15] at 95% confidence interval (95% CI) with a precision of 5%; a sample size of 108 children with high-grade cancers was arrived at using the OpenEpi Sample Size Calculator version 3.0 (see https://www.openepi.com/SampleSize/SSCohort.htm).

Within 24 h of admission, the investigators, with the help of trained research assistants, selected patients with probable high-grade tumours for possible inclusion into the study. Participants meeting the inclusion criteria were consecutively enrolled into the study until the required sample size was obtained. For patients who met the inclusion criteria, written informed consent and assent were obtained. All enrolled children were assigned a study number and evaluated by the investigators.

Using a semi-structured data collection tool, information on demographic characteristic, a thorough clinical history and a complete physical examination were recorded. Blood samples were taken for a full blood count, renal (including creatinine and uric acid levels) and liver function tests, electrolytes, lactose dehydrogenase (LDH) before any intravenous fluid was administered. Anthropometry, emergency assessment and vital signs were measured and recorded. Standard emergency care was offered for children with clinical or laboratory TLS according to protocol. The samples were run within 3 h of collection.

High-grade tumour was defined histologically as a fast growing poorly differentiated cancer that tends to be more aggressive and likely to spread quickly. For the purposes of our study, these were effectively BL, acute lymphoblastic leukaemia (ALL), AML and other high-grade NHL. Flow cytometry studies were performed to distinguish AML from ALL.

Bulky disease was defined as either a solid tumour mass >10 cm measured with a standard measuring tape or hepatomegaly ≥10 cm or splenomegaly ≥10 cm below the costal margin in a child diagnosed with

high-grade tumours odds ratio (OR) a white blood cell counts >25,000 μ/L in children with ALL or AML.

Laboratory STLS (LSTLS) was defined by >2 of the following: hyperuricaemia (level ≥ 476 μmol/l), hyperkalaemia (>6.0 mmol/l), hyperphosphataemia (>2.1 mmol/l) and hypocalcaemia (<1.5 mmol/l). This criterion had to be met prior to the start of chemotherapy in the absence of any other recognisable cause.

Collected data were crosschecked for completeness, sorted, coded and entered into the computer using Epi data version 3.1. The raw data were securely stored to maintain confidentiality. Data were analysed using STATA version 9.0.

Descriptive statistics were developed for demographic and baseline information, clinical history and physical examination findings, biochemical laboratory findings and prevalence of LSTLS among study participants. The Pearson's χ^2 or Fisher's exact tests were performed for categorical variables to establish whether an association existed between LSTLS and the rest of the explanatory variables. Multivariate analysis was done using the binary logistic regression to determine the factors independently associated with LSTLS. Variables with $p < 0.2$ on bivariate analysis and certain demographic characteristics were included in the multivariate analysis. Variables with cell counts <5 were eliminated from multivariate analysis. Analysis was performed using a stepwise logistic regression model. Results were presented as ORs and 95% CI. A $p < 0.05$ was considered statistically significant.

Approval to conduct the study was obtained from the Makerere University College of Health Sciences, School of Medicine Research Ethics Committee and the National Council for Science and Technology. Additional administrative clearance was obtained from MNRH and the UCI. Written informed consent/assent was obtained from all participants or caregivers.

Results

Of the total of 133 children with suspected high-grade screened, 108 fulfilled the inclusion criteria and were thus enrolled into the study. Of the 108 children studied, 69 (63.9%) were males, with a male: female ratio of 2:1. Their ages ranged from 18 months to 18 years with a median age (interquartile range) of 7.7 (5–12) years. Most participants (83, 76.8%) were from outside Kampala and Wakiso (the catchment area of the two centres). Just over half (56, 51.9%) were accompanied by their mothers. The majority had been admitted more than once for their current illness (65, 60.2%); 49 (45.4%) had BL, 26 (24.1%) ALL, 24 (22.2%) NHL, 6 (5.5%) AML and 3 (2.7%) Burkitt's leukaemia. Table 1 summarises their demographic and baseline characteristics.

Overall, 14 (13%; 95% CI: 9.8–0.16.2) participants had LSTLS. These had statistically significant hyperkalaemia, hyperuricaemia and hypocalcaemia. However, serum phosphate levels were similar across the two groups (Table 2).

Five had a combination of high uric acid and high phosphate levels. Four had elevated uric acid levels and hypocalcaemia, and another four had elevated potassium and uric acid levels. The prevalence of LSTLS was similar across the different histological diagnoses (Table 3).

More patients with LSTLS had bulky disease compared to those without (7/14 (50%) vs. 33/94 (35%), $p = 0.037$); eight (7.4%) were taking steroid therapy. Only three (2.7%) were found to be HIV-positive. Other findings are listed in Table 4.

Factors found to be significantly associated with LSTLS among the study participants included LDH ≥ 500 (OR = 8.07; 95% CI: 1.01–64.3; $p = 0.02$), bulky disease (OR = 3.3; 95% CI: 1.03–10.75; $p = 0.037$) and elevated serum creatinine (OR = 0.042; 95% CI: 0.982–14.54; $p = 0.042$) (Table 5).

Bulky disease was the only statistically significant predictor of LSTLS (adjusted odds ratio (aOR) = 4.5; 95% CI: 1.05– 9.29; $p = 0.043$). Age (aOR = 1.07; 95% CI: 0.31–3.73; $p = 0.92$) and sex (aOR = 0.63; 95% CI: 0.16–2.44; $p = 0.502$) were not statistically significant predictors.

Of the 14 children with LSTLS, 4 (28.6%) died prior to the initiation of chemotherapy (Table 6). Half the patients who had TLS had BL, and of these, six had abdominal masses and two had central nervous system disease. One child with T-cell lymphoma had a large mediastinal mass diagnosed on chest radiography and echocardiography (Case 14).

Discussion

STLS is a well-recognised medical emergency, noted to occur in patients with haematologic and solid-organ malignancies.[14] We found a 13% prevalence of LSTLS among children with high-grade tumours in Uganda. Data on pre-treatment STLS in Africa are limited to a few case reports and case series.[18,19] To the best of our knowledge, there is no published data on pre-treatment STLS among children in Uganda. This finding is similar to what other researchers have reported in high-grade tumours with large, rapidly growing, chemosensitive cells such as BL and ALL.[15,16]

BL was the most predominant histological diagnosis among the high-grade tumours, and it contributed the highest prevalence of LSTLS among our study participants. This finding is comparable to several studies in

Table 1. Demographic and baseline characteristics.

Characteristic	Category	Frequency (N = 108)	Percentage
Age (years)	≤5	23	21.3
	>5	85	78.7
Sex	Male	69	63.9
	Female	39	36.1
District of residence	Kampala	14	12.9
	Wakiso	11	10.2
	Others	83	76.8
Caretaker	Mother	56	51.8
	Father	39	36.1
	Others	13	12.0
Referral point	District hospital	33	30.6
	Private hospital	48	44.4
	Mulago hospital	27	25.0
Education status of caretaker	Tertiary	18	16.7
	Secondary	22	20.4
	Primary	50	46.2
	No formal education	18	16.7
Duration of symptoms	<1month	32	29.6
	1–2 months	52	48.2
	>2 months	24	22.2
No of admissions in past 12 months	1	30	27.8
	2	48	44.4
	>3	30	27.8
No of admissions for current illness	1	43	39.8
	2	56	51.9
	3	9	8.3

Table 2. Laboratory markers of spontaneous tumour lysis syndrome.

		LSTLS status	
Characteristic	Category	Present (n = 14): freq (%)	Absent (n = 94): freq (%)
Potassium	≥6 mmol/l	3 (21.4)	4 (4.3)
	<6 mmol/l	11 (78.6)	90 (95.7)
Uric acid	≥0.47 mmol/l	10 (71.4)	38 (40.4)
	<0.47 mmol/l	4 (28.6)	56 (59.6)
Calcium	≤1.5 mmol/l	12 (85.7)	28 (29.8)
	>1.5 mmol/l	2 (14.3)	66 (70.2)
Phosphate	≥2.1 mmol/l	7 (50.0)	34 (36.2)
	<2.1 mmol/l	7 (50.0)	60 (63.8)

LSTLS: laboratory spontaneous tumour lysis syndrome.

SSA that have found BL to be the most prevalent childhood tumour.[17,18] BL is a known fast proliferating tumour with a very high cell turnover that is associated with massive cell breakdown.[17,18] This results into an accelerated development of TLS when BL is compared with other well-demarcated tumours. Several studies have shown a distinct association between STLS and BL.[19,20] Notably, we enrolled children based on

Table 3. Laboratory spontaneous tumour lysis syndrome among the different histological diagnoses.

Histology result	Total N = 108	LSTLS status: Present (n = 14)	LSTLS status: Absent (n = 94)	OR	95% CI	p-value
BL	49	7 (14.3)	42 (85.7)	1.240	0.40–3.80	0.709
NHL	24	4 (16.7)	20 (83.3)	1.480	0.42–5.21	0.540
ALL	26	2 (7.7)	24 (92.3)	0.486	0.10–2.33	0.843
AML	6	1 (20)	5 (80)	1.369	0.14–12.66	0.781
Others	3	0 (0)	3 (100)	1.152	1.07–1.24	0.582

LSTLS: laboratory spontaneous tumour lysis syndrome; OR: odds ratio; CI: confidence interval; BL: Burkitt's lymphoma; NHL: non-Hodgkin's lymphoma; ALL: acute lymphoblastic leukaemia; AML: acute myeloid leukaemia.

Table 4. Clinical characteristics.

Variable	Category	LTLS status: Present (n = 14)	LTLS status: Absent (n = 94)	OR	95% CI	p-value
Fever	Yes	12	70	2.06	0.43–9.86	0.358
	No	2	24	–	–	
Nutritional status	Underweight	7	36	1.61	0.52–4.97	0.560
	≥Normal weight	7	58	–	–	
Excessive sweating	Yes	9	55	0.82	0.26–2.63	0.737
	No	5	38	–	–	
Convulsion	Yes	0	4	1.16	1.07–1.25	0.432
	No	14	90	–	–	
Dehydration	Yes	5	34	0.98	0.30–3.16	0.974
	No	9	60	–	–	
Pallor	Yes	8	46	1.39	0.45–4.32	0.567
	No	6	48	–	–	
Oedema	Yes	3	20	1.01	0.26–3.97	0.99
	No	11	74	–	–	
Hepatomegaly	Yes	8	51	1.12	0.36–3.49	0.84
	No	6	43	–	–	
Splenomegaly	Yes	8	53	1.03	0.33–3.21	0.957
	No	6	41	–	–	
Bulky disease	Yes	9	33	3.33	1.03–10.75	0.037
	No	5	61	–	–	
Allopurinol (on admission)	Yes	6	41	1.08	0.34–3.48	0.888
	No	7	52	–	–	
Steroids	Yes	0	8	1.16	1.07–1.26	0.257
	No	14	86	–	–	
Aminoglycosides	Yes	1	9	0.73	0.09–6.22	0.77
	No	13	85	–	–	
NSAIDS	Yes	1	3	2.33	0.23–24.10	0.465
	No	13	91	–	–	

LTLS: laboratory TLS; OR: odds ratio; CI: confidence interval; NSAIDS: non-steroidal anti-inflammatory drugs.

Table 5. Factors associated with laboratory spontaneous tumour syndrome.

Characteristic	Category	LSTLS status		OR	95% CI	p-value
		Present n = 14(%)	Absent N = 94 (%)			
Age (months)	<60	4 (17.4)	19 (82.6)	1.58	0.45–5.59	0.479
	≥60	10 (11.8)	75 (88.2)			
Sex	Male	9 (13.0)	60 (87)	1.02	0.32–3.29	0.974
	Female	5 (12.8)	34 (87.2)			
Spleen size	≥10 cm	8 (13.1)	53 (86.9)	1.03	0.33–3.27	0.957
	<10 cm	6 (12.8)	41 (87.2)			
Liver size	≥10 cm	8 (13.6)	51 (86.4)	1.12	0.36–3.49	0.840
	<10 cm	6 (12.2)	43 (87.8)			
WBC	≥25,000	3 (14.3)	18 (85.7)	1.15	0.29–4.56	0.841
	<25,000	11 (12.6)	76 (87.4)			
LDH levels	≥500 iu/l	13 (18.3)	58 (81.7)	8.07	1.012–64.3	**0.022**
	<500 iu/l	1 (2.8)	36 (97.2)	–	–	
Bulky disease	≥10 cm	9 (21.4)	33 (78.6)	3.33	1.03–10.75	**0.037**
	<10 cm	5 (7.6)	61 (92.4)	–	–	
Serum creatinine	Increased	4 (30.8)	9 (69.2)	3.78	0.98–14.54	**0.042**
	Reduced	10 (10.5)	85 (89.5)	–	–	

LSTLS: laboratory spontaneous tumour lysis syndrome; OR: odds ratio; CI: confidence interval; WBC: white blood cell; LDH: lactate dehydrogenase. Bold: Statistically significance

Table 6. Outcome of children with LSTLS prior to initiation of chemotherapy.

Case	Age (years)	Sex	Histological diagnosis	Stage	Creatinine (μmol/l)	Oedema	Wasted	LDH (iu/l)	Outcome
1	13	F	NHL	D	30.7	No	No	3254	Alive
2	8	F	BL	D	67	No	No	789	Alive
3	1.8	M	ALL	FAB L1	229.4	Yes	No	4738	Died
4	7	M	BL	D	189.6	No	Yes	922	Alive
5	4.5	M	BL	D	78	No	No	2613	Died
6	12	F	ALL	FAB L2	171.3	Yes	No	1382	Alive
7	6.2	M	AML	FAB M1	106	No	No	701	Alive
8	13	M	BL	C/D	54.6	No	No	1936	Alive
9	17	M	NHL	D	106	No	No	1640	Died
10	5	M	BL	D	83.5	No	No	2311	Alive
11	8	F	BL	C/D	44	No	No	586	Alive
12	4	F	BL	D	93.4	No	Yes	426	Alive
13	17.8	M	NHL	FAB L2	44	No	No	1890	Alive
14	5.4	M	NHL (T-cell)	D	151.4	Yes	No	2244	Died

BL: Burkitt's lymphoma; NHL: non-Hodgkin's lymphoma; ALL: acute lymphoblastic leukaemia; AML: acute myeloid leukaemia; F: female; M: male; FAB: French -American-British; LDH: lactate dehydrogenase.

histological diagnosis and not staging workup. However, more advanced stages of the disease are associated with more frequent and severe STLS.[15]

The main limitation of this study is the small sample size and our inability due to the study design to account for important confounders such as renal failure. However, these results provide an understanding of the magnitude of LSTLS among children with high-grade tumours prior to initiation of chemotherapy. Future well designed prospective studies could be modelled

based on our present findings. Also studies with larger sample size in other categories of tumours prevalent in Uganda may also allow for subgroup comparisons.

In conclusion, we found a high prevalence of pre-treatment LSTLS among children with high-grade tumours in Uganda. More than one-fourth of children with LSTLS died prior to commencement of chemotherapy. Bulky disease, elevated LDH levels $\geq$ 500 iu/l and serum creatinine were significantly predictors of LSTLS. Our findings suggest routine assessment and testing for LSTLS in children suspected or presenting with high-grade tumours.

Declaration of conflicting interests

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References

1. International Agency for Research on Cancer. GLOBOCAN 2020: estimated cancer incidence, mortality and prevalence worldwide in 2018. *Int Agency Res Cancer*, http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx (2020, accessed 12 July 2020).
2. Hashim D, Boffetta P, La Vecchia C, et al. The global decrease in cancer mortality: trends and disparities. *Ann Oncol* 2016; 27: 926–933.
3. Ferlay J, Shin H-R, Bray F, et al. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010; 127: 2893–2917.
4. Cunningham RM, Walton MA and Carter PM. The major causes of death in children and adolescents in the United States. *N Engl J Med* 2018; 379: 2468–2475.
5. Keegan THM, Ries LAG, Barr RD, et al. Comparison of cancer survival trends in the United States of adolescents and young adults with those in children and older adults. *Cancer* 2016; 122: 1009–1016.
6. Hadley LGP, Rouma BS and Saad-Eldin Y. Challenge of pediatric oncology in Africa. *Semin Pediatr Surg* 2012; 21: 136–141.
7. Menon MP, Coghill A, Mutyaba IO, et al. Association between HIV infection and cancer stage at presentation at the Uganda Cancer Institute. *J Glob Oncol* 2018; 4: 1–9.
8. Gupta A and Moore JA. Tumor lysis syndrome. *JAMA Oncol* 2018; 4: 895.
9. Criscuolo M, Fianchi L, Dragonetti G, et al. Tumor lysis syndrome: review of pathogenesis, risk factors and management of a medical emergency. *Expert Rev Hematol* 2016; 9: 197–208.
10. Jones GL, Will A, Jackson GH, et al. Guidelines for the management of tumour lysis syndrome in adults and children with haematological malignancies on behalf of the British Committee for Standards in Haematology. *Br J Haematol* 2015; 169: 661–671.
11. Wabinga HR, Nambooze S, Amulen PM, et al. Trends in the incidence of cancer in Kampala, Uganda 1991-2010. *Int J Cancer* 2014; 135: 432–439.
12. Banda LT, Parkin DM, Dzamalala CP, et al. Cancer incidence in Blantyre, Malawi 1994-1998. *Trop Med Int Heal* 2001; 6: 296–304.
13. International Agency for Research on Cancers. International Incidence of childhood cancer 3. *Int Agency Res Cancers*, https://iicc.iarc.fr/includes/results/registries/Africa/Africa_UGANDA_Kampala.pdf (2020, accessed 2 July 2020).
14. McBride A and Westervelt P. Recognizing and managing the expanded risk of tumor lysis syndrome in hematologic and solid malignancies. *J Hematol Oncol* 2012; 5: 75.
15. Montesinos P, Lorenzo I, Martín G, et al. Tumor lysis syndrome in patients with acute myeloid leukemia: identification of risk factors and development of a predictive model. *Haematologica* 2008; 93: 67–74.
16. Wilson FP and Berns JS. Tumor lysis syndrome: new challenges and recent advances. *Adv Chronic Kidney Dis* 2014; 21: 18–26.
17. Ferry JA. Burkitt's lymphoma: clinicopathologic features and differential diagnosis. *Oncologist* 2006; 11: 375–383.
18. Walusansa V, Okuku F and Orem J. Burkitt lymphoma in UGANDA, the legacy of Denis Burkitt and an update on the disease status. *Br J Haematol* 2012; 156: 757–760.
19. Cairo MS, Coiffier B, Reiter A, et al. Recommendations for the evaluation of risk and prophylaxis of tumour lysis syndrome (TLS) in adults and children with malignant diseases: an expert TLS panel consensus. *Br J Haematol* 2010; 149: 578–586.
20. Riccio B, Mato A, Olson EM, et al. Spontaneous tumor lysis syndrome in acute myeloid leukemia: two cases and a review of the literature. *Cancer Biol Ther* 2006; 5: 1614–1617.