PROSPECTIVE STUDY REGISTRY OF PERIPHERAL NEUROBLASTIC TUMOURS PRESENTING WITH SPINAL CANAL INVOLVEMENT (SCI)

Version 2.0 of May 22, 2015 (Version for Germany)

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ETHICAL COMMITTEE APPROVAL March 2014, Liguria Region, Italy

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SHORT STUDY TITLE NB with SCI

SUPPORTERS Hayim-Israel Parent Association and Italian Neuroblastoma Foundation

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Minimum Follow-up Five years

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BACKGROUND

About 15% of patients with peripheral neuroblastic tumour present with extradural SCI, of whom approximately 60% are symptomatic. Since SCI may progress to irreversible paraplegia, early diagnosis and prompt treatment is of critical importance.[1-3]

The treatment options include chemotherapy, neurosurgical decompression and radiation therapy. All may relieve epidural compression, but there is no consensus on which to use first in the individual patient. However, the choice of the treatment could be relevant in the perspective of reducing to the minimum the risk of long-term sequelae.[4]

Guidelines for the diagnostic work-up and treatment of SCI for SIOPEN neuroblastoma patients were already available in the LNESG1 Protocol, back in 1994,[5] although it is unknown how they were applied in the SIOPEN Centres. These guidelines have been reformulated in occasion of the recently activated LINES Protocol.

There are few publications addressing the diagnosis and treatment of SCI; most are retrospective studies, case reports, or reviews that may be affected by reporting bias.[1-9] Therefore new guidelines could be designed based on the information derived from a prospective data collection of newly diagnosed patients.

Pertinent literature data

Prior to 1980s, decompressive laminectomy was usually performed in an attempt to avoid progression to paraplegia.[7-8] However, laminectomy requires experienced surgeons and may carry an increased risk of late spinal deformities.[10-12] Radiation therapy reduces and alters the growth of vertebrae in the radiation field[10-12] and carries the risk of secondary malignancy.[13]

The use of chemotherapy was first reported in 1984 by Hayes et al.[6] Since then, several authors have confirmed that chemotherapy can successfully be used instead of neurosurgery or radiotherapy.

Following these reports studies have focused more on primary chemotherapy management of patients with SCI. Nevertheless, bias of treatment for patients with severe symptoms (paralysis) has always favoured a surgical approach.[4]

Publications focused on sequelae

In 1999, Hoover et al described long-term follow-up of 26 children diagnosed with symptomatic SCI. They focused mainly on orthopaedic sequelae and found that patients treated by laminectomy had more frequent deformities.[10]

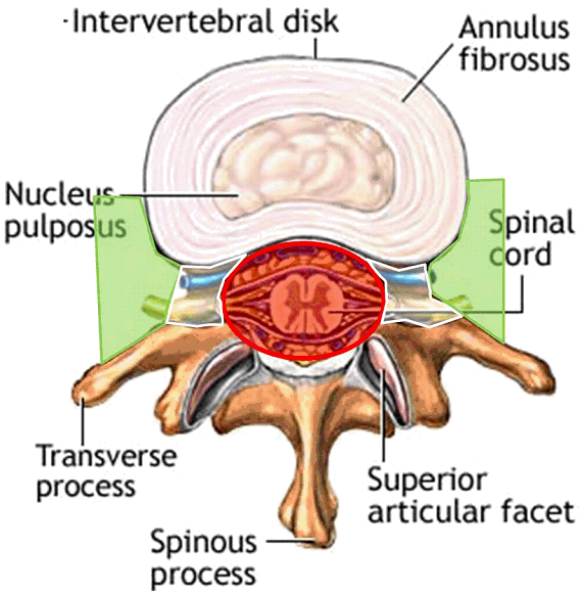
In 2011, Angelini et al described 98 patients followed for a median of 7.3 years, 58% of whom had one or more sequelae at last visit. 50/57 patients had motor deficit and 20/57 spinal deformities. Sequelae correlated with severity of motor deficit at presentation and neurosurgical treatment.[11]

In 2012, Simon et al described 122 patients followed for a median of 8 years. 72% of those evaluable had sequelae: motor deficit in 43%, scoliosis in 31%, impaired bladder function in 14%, growth delay in 14%, and constipation in 19%.[12]
Recently, De Bernardi et al have described 34 infants with symptomatic SCI. In their experience, neurosurgery and chemotherapy provided unsatisfactory results. Sequelae developed in 68% of the patients and were severe in 50%.[14]

DEFINITIONS

Spinal Canal Involvement (SCI)

Figure 1



For this study Spinal Canal Involvement (SCI) is defined when, referring to an axial plane of the spinal cord MR scan (Figure 1), the tumour extends into the vertebral canal and goes beyond a mentally drown ellipsoid (red circle) passing through the cortical bone of both anterior and posterior arches of the vertebra. This involvement is called “intraspinal” or, better, “intracanalar”.
Please note that lesions that affect only the paraspinal structures (i.e. extraforaminal, green spaces) and/or the bony canal formed by two contiguous vertebrae (foraminal grooves - white shapes), do not correspond to SCI.

Symptoms of SCI

SCI may be symptomatic or asymptomatic. Symptoms may be subtle or clearly manifest. The most frequently reported are motor deficit, sphincter dysfunction, back/radicular pain, sensory deficit, neurovegetative dysfunction

STUDY DESIGN

Multi-centre, observational, prospective study registry.

OBJECTIVES

Primary Objective

To describe the natural history of peripheral neuroblastic tumour presenting with SCI and evaluate the combined effects of different risk factors on the eventual neurologic and orthopaedic outcomes.

Secondary objectives

To correlate pathologic and biological characteristics with clinical features, response to therapy and sequelae

To share the diagnostic and therapeutic approaches adopted in the participating Centres

To increase the communication regarding patients with a peripheral neuroblastic tumour presenting with SCI

To develop common guidelines for the management of children with any peripheral neuroblastic tumour presenting with SCI

End Points

Response to therapy

Occurrence and severity of late effects

Occurrence of relapse

Survival

ELIGIBILITY CRITERIA

Inclusion criteria

Diagnosis of peripheral neuroblastic tumour – PNT (neuroblastoma, ganglioneuroblastoma, ganglioneuroma) presenting with SCI, symptomatic or asymptomatic, independent of disease extension (stage), and clinical course (first diagnosis or relapse/progression)

No previous chemotherapy, except steroids, in the last 6 months

Age <18 years

Minimal planned follow-up of 5 years

Parent/patient written informed consent

Exclusion criteria

Invasion of intervertebral foramina only

OVERALL TUMOR TREATMENT

According to institutional team decision

STUDY PROCEDURES AND REPORTING TIME POINTS

Registration (CRF 1.a and 1.b)

Patients with a documented SCI (see definition) associated to any paraspinal mass will be registered to the National Coordinator (NC) using CRF 1.a containing demographic information and a check list for eligibility criteria:

In case of the presence of all the eligibility criteria (i.e. diagnosis of peripheral neuroblastic tumor, age <18 y, no previous chemotherapy in the preceding 6 months, written informed consent), CRF1.b should also be completed containing information on the work-up examinations performed at diagnosis plus the SCI-oriented clinical evaluation stratified by age at diagnosis (age 0-35 or ≥36 months).

Patients 0-35 months at diagnosis. The clinical evaluation specific for this age range requires information on psychomotor and neuro-vegetative development, for both symptomatic and asymptomatic patients. In addition, symptoms of SCI ***(pain, dyspnoea, paraesthesia, upper motor neuron deficit, lower motor neuron deficit, bowel and bladder dysfunctions, decreased joint motion of cervical or lumbar spine, scoliosis, kyphosis and lordosis***) will be described in details using the relevant scales for patient age.

Patients ≥ 36 months at diagnosis. The clinical evaluation will include information for both symptomatic and asymptomatic patients. Symptoms of SCI (see above) will be described in details and will be evaluated using the relevant scales according to the patient age.

Together with the CRF1b copy (possibly on CD) of the neuro-imaging should also be sent to the National Coordinator. It is **responsability** of the NC to forward all the material to the Data Centre in Italy. The neuro-imaging sequencies should be at least triplannar T2 weighted, ideally covering the entire spine. In the case copy of neuroimaging is not available, that patient will not be included in the neuro-radiological revision.

The neuro-radiologists panel will then review all the cases and perform a volumetric evaluation of the intraspinal tumour. By taking into consideration the main neuro-radilogical features, a scoring system will be adopted to be considered for further validation.

The registration Forms should be sent within a maximum of 4 weeks since the diagnosis. (The early signalling of patients potentially eligible to this Study Registry is needed to avoid missing registration of patients who experience severe toxicity from therapy, including surgery-related deaths).

The NC will transmit the Forms to the Data Centre by fax or secured mail (for addresses, see page 6). After notification, the Data Centre will promptly assign the "Unique Patient Number" and transmit it to both Registering Physician and NC.

Clinical Response to therapy for SCI symptoms (72h to 2 months after therapeutic decision for SCI) CRF 2

The Clinical Response to therapy for SCI (CRF 2) is intended to report the clinical response at 72 hours, 1 week, 2 weeks, 4 weeks, and 2 months from therapeutic decision (either neurosurgery, or chemotherapy, or radiotherapy, or *wait-and-see*).

Treatment Summary (at stop of therapy) (CRF 3)

The Treatment Summary Form (CRF 3), collects information on:
Therapy administered (surgical approach, chemotherapy and radiotherapy).
Delayed neurosurgery, or resection of the extraspinal tumour, if performed.
Best response of intraspinal tumour at neuro-imaging (send, if possible, the copy of neuroimaging to the NC).
CRF 3 will be sent.
Together with CRF 2 for patients with localized disease receiving only two courses of chemotherapy
At the end of the overall treatment, for the remaining patients.

Follow-up (at 6 months and 1, 2, 3, 4, 5 and 10 years from diagnosis) (CRF 4.*a* & *b*)

The evolution of presenting symptoms (if present or developed after diagnosis), and the occurrence of functional and physical adverse events, have to been reported into the "Follow up" Form (CRF 4.*a* or *b* based on patient age at follow-up) at the following time points:
At 6 months from diagnosis
At 1, 2, 3, 4, 5 and 10 years from diagnosis
These time points are independent from the treatment for the tumour itself (i.e., some Forms may be filled in while the patient is on treatment).
There are two separate CRF 5 based on patient age at time of the evaluation (0-35 months, and ≥ 36 months), and symptoms will be described using the international CTCAE/FLACC/ASIA scores (Appendix 2).[15-16]
Forms have to be sent to the NC. Each evaluation form should be sent separately on real time.

STATISTICAL CONSIDERATIONS

This is a prospective observational study aiming to evaluate the combined effects of different risk factors on final neurologic and orthopaedic outcomes in children with peripheral neuroblastic

tumour and SCI. Given the binomial nature of the main outcome variable (presence/absence of occurrence of complication), it was decided to explore the relationship between the principal outcome and the different exposure factors by means of a classical multiple logistic regression model. Tests will be performed accepting an α error = 0.05; and a power of 80% (β = 0.20), after definition of the expected frequencies of the different outcomes and the estimated odds ratio (OR) between two different treatment approaches.

Sample Size

Sample size calculation was made using the formula for the multiple logistic regression model reported by Hsieh[17]. Since the outcomes of interest (binomial: i.e., yes/no) are several (e.g. scoliosis, paraplegia, incontinence) and the estimated OR between treatments might differ based on the specific outcomes, several calculations have been made [Table 1]. From Table 1, a number of patients ranging between 90 and 217 will be needed to demonstrate an OR between 1.5 and 2.0 for an outcome with a 40% proportion of events. Numbers modify if the proportion will be 30% (number of patients, 95-234).

Table 1

Alpha	beta	Power	Estimated OR	P (event proportion)	n	rho	N
0.05	0.20	80%	1.5	0.3 (or 0.7)	213	0.4	254
0.05	0.20	80%	1.5	0.4 (or 0.6)	182	0.4	217
0.05	0.20	80%	1.5	0.5	164	0.4	195
0.05	0.20	80%	2.0	0.3 (or 0.7)	86	0.4	102
0.05	0.20	80%	2.0	0.4 (or 0.6)	76	0.4	90
0.05	0.20	80%	2.0	0.5	70	0.4	83
0.05	0.20	80%	1.5	0.3 (or 0.7)	213	0.3	234
0.05	0.20	80%	1.5	0.4 (or 0.6)	182	0.3	200
0.05	0.20	80%	1.5	0.5	164	0.3	180
0.05	0.20	80%	2.0	0.3 (or 0.7)	86	0.3	95
0.05	0.20	80%	2.0	0.4 (or 0.6)	76	0.3	84
0.05	0.20	80%	2.0	0.5	70	0.3	77

Data storage and elaboration

In accordance with the directives 2001/20 Ethical Committee of the European Parliament and of the Council of April 4, 2001, and the corresponding national laws, all data will be handled strictly confidentially. Throughout documentation and analysis, participants into this Registry will be

identified only by the unique patient code. Identifying information will not be published. Submitted data will stored electronically into a specific database located at the Epidemiology-Biostatistics Unit of the Istituto Giannina Gaslini, Genova, Italy. Storing procedures will be provided by the local Data Manager under the Registry Coordinator supervision.

Study feasibility

This project is developed under the SIOPEN umbrella that recruits about 500 new peripheral neuroblastic tumour cases per year; moreover two other national groups will contribute to this study. Because of an expected frequency of SCI (symptomatic plus asymptomatic) in this population of about 10%, it is estimated that it is reasonable to collect information on about 150 SCI cases within two-three years.

ETHICAL CONSIDERATIONS

This prospective Study Registry will be conducted according to the principles of the Declaration of Helsinki (59th WMA General Assembly, Seoul, October 2008) and all its revisions, pertinent national laws and regulations, as well as the International Conference on Harmonization (ICH)'s Good Clinical Practice, taking into account the Directive 2001/20/EC of the European Parliament and of the Council April 2001.

The National Coordinating Centre is responsible, on behalf of the Sponsor, for ensuring that every participating institution within that country has gained approval for conducting the Prospective Study Registry from an appropriate EC/IRB. Copies of the approval should be sent to the Sponsor. Approval of the EC/IRB must be obtained before initiation of the study.

Patient data will be collected in pseudo-anonymized manner and will be stored in a secure system at the Epidemiology & Biostatistics Unit of the Istituto Giannina Gaslini, Genova, Italy. The storing procedure will be carried out by the local Data Manager under the supervision of the Registry Statistician

INFORMED CONSENT

The local Principal Investigator (PI) is responsible for the collection of the written informed consent from each parent/patient participating in the study, after clear explanation of the study objectives, design, methods, potential benefits and hazards, data protection/confidentiality. In addition, each parent/patient must have read and understood the Parent and Patient Information Leaflet (PIL) written in the language of the patient.

The Local PI must specify to parents/patient that they are free to refuse to participate in the study and can withdraw from the study at any time and for whatever reason, without any prejudice on the quality of care that the patient has the right to expect.

It is recommended that parents/patients should have adequate time between being given the information on the study and being asked to sign the Informed Consent Form (ICF).
The ICF must be dated and signed off by either the local PI and the patient (and/or their legal representative(s)) in duplicate. One copy of the ICF will be kept by the patient/parents and the original ICF will be kept by the local PI.

SPONSORSHIP

The Sponsor of this International Prospective Study Registry in the legal sense, as defined in the Directive 2001/20/EC of the European Parliament and of the Council April 2001 is the AIEOP (Associazione Italiana Ematologia-Oncologia Pediatrica). The Sponsor transfers its duties for every participating National Neuroblastoma Group to an authorised institution by a written agreement, which will be the National Coordinating Centre for that country. The National Coordinating Centre will fulfil the transferred duties for the sponsor and warrants the compliance with all the statutory provisions relevant for the Sponsor.

Financing: This is a collaborative clinical study which will be carried out in kind by the participating institutions. No payments will be made for participation in this Prospective Study Registry.

PUBLICATION POLICY

National results relevant to this study are not allowed to being published before study completion. Publications of single case reports are allowed.

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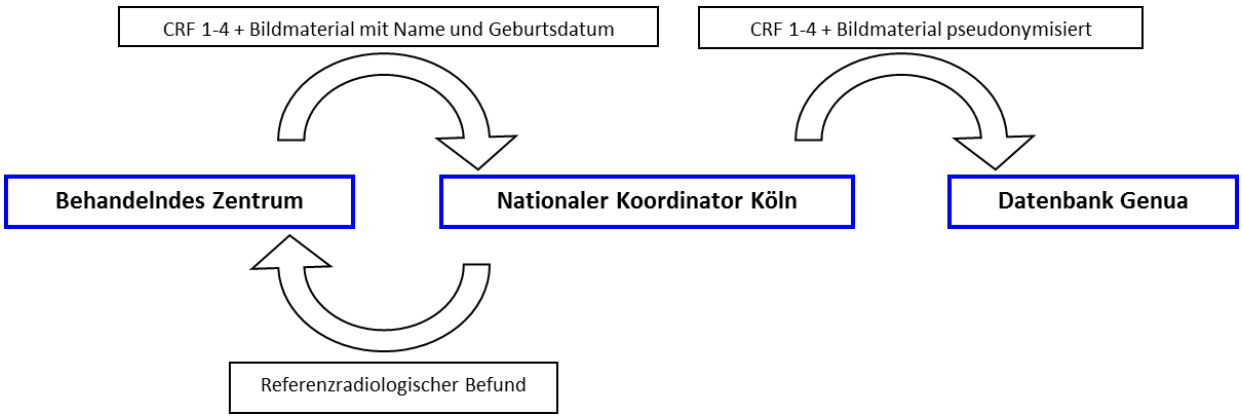
http.//ctep.cancer.gov. Published: May 28, 2009 (v4.02: Sept. 15, 2009)
Rosman Np, Gilmore HE. Spinal cord injury. In Swaiman KF, Ashwal S (editors): Pediatric Neurology: Principals and Practice (ed 3). St Louis, MO, Mosby, 1999:954-966
Hsieh FY. Sample size tables for logistic regression. Stat Med. 1989; 8:795-802.

APPENDIX 1

ORGANISATION DES REGISTERS IN DEUTSCHLAND

DATENSTROM



Alle Case Report Forms (CRF 1-4) und elektronische Kopien der bildgebenden Untersuchungen werden von der behandelnden Klinik an folgende Adresse gesandt:

Prof. Dr. Thorsten Simon
Pädiatrische Onkologie und Hämatologie
Klinik und Poliklinik für Kinder- und Jugendmedizin
Universitätsklinikum Köln
Kerpener Str. 62, 50924 Köln
Tel: +49 221 478 6853
Fax +49 221 478 6851
Email: neuroblastomstudie@uk-koeln.de

Referenzbeurteilung

Die bildgebenden Untersuchungen werden durch Frau Prof. Krug, Institut für Diagnostische und Interventionelle Radiologie, Universitätsklinikum Köln, referenzradiologisch beurteilt. Vom nationalen Studienzentrum in Köln aus werden die Aufnahmen in pseudonymisierter Form an die internationale Studienleitung weitergegeben.

Case Report Forms und Erfassung der Symptome:

Tabelle 2 (S. 20f) gibt einen Überblick über die vorgesehen Case Report Forms.
Die standardisierte Erfassung der Symptome zu den vorgegebenen Zeitpunkten erfolgt anhand von Skalen (s. S. 22) für Schmerz (FLACC), Motorik (ASIA) und Blasendysfunktion (normal vs. nicht normal) und Darmfunktion (normal vs. nicht normal).

Tabelle 2: Überblick über die Case Report Forms

CRF	Aktion	Zeitpunkt der Erfassung	Versand CRF
REGISTRATION (CRF 1a)	Bei peripherem neuroblastischem Tumor mit Beteiligung des Spinalkanals: Registrierung für das SCI-Register spätestens innerhalb 4 Wochen nach Diagnose an die nationale Studienzentrale bevorzugt via Fax: 0221 478 6851. *Über die nationale Studienzentrale Weitergabe der Registierung an das Datencenter in Genua, von dort Vergabe einer „Unique Patient Number", die der nationalen Studienzentrale in Köln und dem behandelnden Arzt mitgeteilt wird.*	Zur Diagnosestellung	Zeitnah, spätestens innerhalb 4 Wochen nach Diagnosestellung
WORK-UP AT DIAGNOSIS (CRF 1b)	Versand an die nationale Studienzentrale (Prof. Dr. T. Simon, Köln) zusammen mit der initialen spinalen Bildgebung *Referenzbefundung der Bildgebung über die nationale Studienleitung in Köln, von dort Weitergabe der Bildgebung (pseudonymisiert) an die internationale Studienleitung in Genua.*	Zeitraum erste Vorstellung bis erste Bildgebung Spinalkanal	Zeitnah, spätestens innerhalb von 4 Wochen nach Diagnosestellung
CLINICAL RESPONSE TO THERAPY (CRF 2)	In CRF 2 werden Symptom bzw. deren Änderung im Therapieverlauf anhand etablierter Skalen erfasst.	- innerhalb der ersten 72 h - 72 h – 1 Woche - 1 – 2 Wochen - 2 – 4 Wochen - 1 – 2 Monate nach der Entscheidung zur Therapiestrategie (Chemotherapie, Operation, Beobachtung)	Versand spätestens 2 Monate nach der Entscheidung zur Therapiestrategie

TREATMENT SUMMARY (CRF 3)	In CRF 3 werden Eckdaten zur Behandlung erfasst. Zusätzlich wird die BILDGEBUNG DES BESTEN ANSPRECHENS an die nationale Studienzentrale in Köln geschickt. *Referenzbefundung der Bildgebung über die nationale Studienleitung in Köln, von dort Weitergabe der Bildgebung (pseudonymisiert) an die internationale Studienleitung in Genua.*	Zum Abschluss der Therapie	
FOLLOW UP (CRF 4): CRF 4a für Patienten 0-35 Monate CRF 4b für Patienten ≥36 Monate	Neurologische Symptome Verlauf werden über das CRF FOLLOW UP erfasst (auch auszufüllen, wenn der Patient zum vorgesehenen Zeitpunkt noch therapiert wird)	- 6 Monate - 1 Jahr - 2 Jahre - 3 Jahre - 4 Jahre - 5 Jahre - 10 Jahre nach Diagnosestellung	

Alle Case Report Forms werden an die nationale Studienzentrale gesandt:

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APPENDIX 2

FLACC scale for pain (in children < 35 months of age)

Category	Score 0	Score 1	Score 2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, uninterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

Note: each of the five categories ***Face, Legs, Activity, Cry, Consolability,*** is scored from 0-2, which results in a
total score between zero and ten.

Reference. Merkel S *et al*.: The FLACC: A behavioral scale for scoring postoperative pain in young children. *Pediatr*
Nurse 1997;23:293-297.

ASIA Impairment Scale for motor deficit (modified)

Gade 0	Grade 1	Grade 2	Grade 3
normal	mild hyposthenia, movements possible against gravity	moderate hyposthenia, movements possible but not against gravity	severe hyposthenia with no spontaneous movements

Reference. Rosman NP, Gilmore HE: Spinal cord injury, in Swaiman KF, Ashwal S (eds): Pediatric Neurology: Principals
and Practice (ed 3). *St. Louis, MO, Mosby, 1999, pp 954-966.*

	Derived from ***"Common Terminology Criteria for Adverse Events v4.0 (CTCAE)"*** (modified) (http://ctep.cancer.gov)						
		0	**1**	**2**	**3**	**4**	**5**
	Pain	No symptoms	Pain Mild	Moderate pain; limiting instrumental ADL	Severe pain; limiting self care ADL		
	Dyspnea	No symptoms	Shortness of breath with moderate exertion	Shortness of breath with minimal exertion; limiting instrumental ADL	Shortness of breath at rest; limiting self care ADL	Life-threatening consequences; urgent intervention indicated	Death
	Paresthesia	No symptoms	Mild symptoms	Moderate symptoms	limiting instrumental ADL Severe symptoms; limiting self care ADL		
Bowel	**Fecal incontinence**	No symptoms	Occasional use of pads required	Daily use of pads required	Severe symptoms; elective operative intervention indicated		
Bowel	**Constipation**	No symptoms	Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or	Persistent symptoms with regular use of laxatives or enemas; limiting instrumental ADL	Obstipation with manual evacuation indicated; limiting self care ADL	Life-threatening consequences; urgent intervention indicated	Death
Bladder	**Urinary incontinence**	No symptoms	Occasional (e.g., with coughing, sneezing, etc.), pads not indicated	Spontaneous; pads indicated; limiting instrumental ADL	Intervention indicated (e.g., clamp, collagen injections); operative intervention indicated; limiting self care ADL		
Bladder	**Urinary retention**	No symptoms	Urinary, suprapubic or intermittent catheter placement not indicated; able to void with some residual	Placement of urinary, suprapubic or intermittent catheter placement indicated; medication indicated	Elective operative or radiologic intervention indicated; substantial loss of affected kidney function or mass	Life-threatening consequences; organ failure; urgent operative intervention indicated	Death

		0	1	2	3	4	5
Spine	**Joint range of motion decreased cervical spine**	No symptoms	Mild restriction of rotation or flexion between 60 – 70 degrees	Rotation <60 degrees to right or left; <60 degrees of flexion	Ankylosed/fused over multiple segments with no C-spine rotation		
	Joint range of motion decreased lumbar spine	No symptoms	Stiffness; difficulty bending to the floor to pick up a very light object but able to do athletic activity	Pain with range of motion (ROM) in lumbar spine; requires a reaching aid to pick up a very light object from the floor	<50% lumbar spine flexion; associated with symptoms of ankylosis or fused over multiple segments with no Lspine flexion (e.g., unable to reach to floor to pick up a very light object)		
	Scoliosis	No symptoms	<20 degrees; clinically undetectable	>20 - 45 degrees; visible by forward flexion; limiting instrumental ADL	>45 degrees; scapular prominence in forward flexion; operative intervention indicated; limiting self care ADL; disabling		
	Kyphosis	No symptoms	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Moderate accentuation; limiting instrumental ADL	Severe accentuation; operative intervention indicated; limiting self care ADL		
	Lordosis	No symptoms	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Moderate accentuation; limiting instrumental ADL	Severe accentuation; operative intervention indicated; limiting self care ADL		

For other symptoms, consult and follow the complete "Common Terminology Criteria for Adverse Events" :

http://www.acrin.org/Portals/0/Administration/Regulatory/CTCAE_4.02_2009-09-15_QuickReference_5x7.pdf

Universität zu Köln

Geschäftsstelle Ethikkommission • Universität zu Köln • 50931 Köln

Herrn
Prof. Dr. Thorsten Simon
Klinik und Poliklinik für Kinder- und Jugendmedizin
Uniklinik Köln

- im Hause -

Per Fax:
0221 478 6851

Unser Zeichen: 16-003

Prospective study registry of peripheral neuroblastic Tumours presenting with spinal canal involvement (SCI)

Köln, 31.10.2016

Sehr geehrter Herr Professor Simon,

hiermit bestätigen wir, dass Ihr Schreiben vom 17.10.2016 zum o. g. Vorhaben am selben Tag bei uns eingegangen ist.

Die in unserem Schreiben vom 03.02.2016 genannten Bedingungen sind nun hinreichend eingetreten bzw. erfüllt.

Es bestehen seitens der Ethik-Kommission keine berufsethischen noch berufsrechtlichen Bedenken. Wir wünschen Ihnen und allen Beteiligten viel Erfolg bei der Durchführung.

Mit freundlichen Grüßen

Prof. Dr. med. Alexander Drzezga Dipl.-Biol. Alice Kasprzik

Eingegangene Dokumente vom 17.10.2016:

- Anschreiben, 17.10.2016
- Information und Einwilligung für Sorgeberechtigte, Version 1.2 vom 05.10.2016
- Information und Einwilligung für Sorgeberechtigte, Version 1.2 vom 05.10.2016, tracked changes
- Information und Einwilligung für Jugendliche (14-18J), Version 1.2 vom 05.10.2016
- Information und Einwilligung für Jugendliche (14-18J), Version 1.2 vom 05.10.2016, tracked changes

Medizinische Fakultät der Universität zu Köln

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