



CLINICAL FRONTIERS

IN PEDIATRIC NEUROLOGY **2026**

October 22 & 23, 2026 Ljubljana, Slovenia

PROCEEDINGS

ORGANISED BY:

Slovenian Medical Association



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Zdravniško
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WELCOME ADDRESS

Dear Colleagues and Friends,

Welcome to Ljubljana and to the 6th Clinical Frontiers in Pediatric Neurology.

Over the next two days, CFPN brings together colleagues from Slovenia, the region and beyond to discuss current questions in pediatric neurology, exchange clinical experience and present new research.

This year's programme covers neonatal neurology, neuromuscular disorders, epilepsy, neurostimulation and a broad range of other topics relevant to everyday clinical practice. We are especially pleased to be joined by Prof. Linda de Vries, Prof. Floris Groenendaal and Prof. Mijna Hadders-Algra, who bring exceptional experience and expertise to the meeting.

For the first time, the congress also includes submitted abstracts in the conference proceedings, with selected contributions presented as oral presentations and posters. This gives CFPN an additional dimension and creates more space for participants to share their own work and discuss it with colleagues.

I hope the programme provides useful discussions, new ideas and opportunities for collaboration, but also time to meet colleagues and friends.

Thank you for being part of CFPN 2026, and I wish you an enjoyable and productive congress.



Prof. Damjan Osredkar, MD, PhD
Chair of the Symposium

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PROGRAMME

21 OCTOBER 2026 LOCATION: UMCL - Division of Pediatrics - P2 Lecture room, Ljubljana	
16:00 - 19:30	PRE-SYMPOSIUM WORKSHOP: Introduction to SINDA – Standardized Infant NeuroDevelopmental Assessment Welcome desk, participant materials
16:00 - 17:30	Introduction to SINDA, the Standardized Infant NeuroDevelopmental Assessment <i>Mijna Hadders-Algra (Netherlands)</i>
17:30 - 18:00	COFFEE BREAK
18:00 - 19:30	Scoring a video of SINDA's neurological scale SINDA's developmental and socio-emotional scales

22 OCTOBER 2026**LOCATION:**

Kosovel Hall, Cankarjev dom, Ljubljana

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09:00 - 9:10	OPENING ADDRESS
09:10 - 10:10	Early Diagnostics and Early Intervention in Neurodevelopmental Disorders <i>Mijna Hadders-Algra (Netherlands)</i>
10:10 - 10:55	Therapeutic Hypothermia Following Perinatal Asphyxia: What to Do? <i>Floris Groenendaal (Netherlands)</i>
10:55 - 11:25	COFFEE BREAK
11:25 - 11:45	Association Between Functional Brain Network Characteristics and Cognitive Deficits After Perinatal Stroke <i>Alja Kavčič, Aneta Soltirovska Šalamon (Slovenia)</i>
11:45 - 12:05	Impact of Congenital Heart Disease on Neurodevelopment in Childhood <i>Mojca Železnik, Tina Pahovnik, Jana Kodrič, Jana Lozar Krivec, Aneta Soltirovska Šalamon (Slovenia)</i>
12:05 - 12:50	Perinatal Stroke in the Term and Preterm Infant <i>Linda De Vries (Netherlands)</i>
12:50 - 13:10	Pharmacogenetics of Antiseizure Medication in Neonates with Seizures <i>Nika Morgan, Aneta Soltirovska Šalamon, Vita Dolžan, Tanja Blagus (Slovenia)</i>

13:10 - 13:30	Family-Centred Psychological Approaches in the Management of Neurology Diseases started in neonatal period <i>Sanja Zupančič (Slovenia)</i>
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14:50 - 15:10	Challenges in the Diagnosis of Hereditary neuropathies <i>Vedrana Milic Rasic, Ana Kosac (Serbia)</i>
15:10 - 15:30	Pediatric Neuromuscular Diseases: Diagnostic, Therapeutic, and Multidisciplinary Care Challenges — Insights from Montenegro <i>Nelica Ivanović Radović, Goran Banjac (Montenegro)</i>
15:30 - 15:50	Cardiac Monitoring Algorithm in Children and Adolescents with Neuromuscular Disorders Receiving Innovative Disease-Modifying Therapies <i>Vesna Miranović (Montenegro)</i>
15:50 - 16:10	Slovenian Experience With Treatment of DMD Patients With Givinostat <i>Tita Butenko, Tanja Loboda, Damjan Osredkar (Slovenia)</i>
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17:00 - 17:20	Early Manifestations, Diagnostic Pathways, and Epilepsy in Juvenile-Onset Huntington Disease: A Three-Patient Case Series and Systematic Review <i>Mirjana Perkovič Benedik, Tanja Loboda, Neli Bizjak (Slovenia)</i>
17:20 - 17:40	Hidden Morphometric Signals in Cranial Ultrasound: Associations With Neurodevelopmental Outcomes in Preterm Infants <i>Dorotea Drašković, Maja Zaninović, Koraljka Manestar Rukavina, Iva Bilić Čače (Croatia)</i>
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23 OCTOBER 2026

LOCATION:
Kosovel Hall, Cankarjev dom, Ljubljana

09:00 - 10:00	SESSION 4 — Epilepsies Chairperson: Maša Malenica
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09:20 - 09:40	How to Diagnose (Non)Epileptic Seizures? <i>Dimitrije Nikolić</i>
09:40 - 10:00	Epilepsy Beyond Seizures – Transitioning of Patients with DEE into Adulthood <i>Maša Malenica (Croatia)</i>
10:00 - 10:35	Swixx BioPharma Satellite Recent Advances and Emerging Trends in the Treatment of Gaucher Disease <i>Urh Grošelj (Slovenia)</i> Swixx BioPharma
10:35 - 11:05	COFFEE BREAK
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11:05 - 11:25	Non-Invasive Brain and Nerve Stimulation in Children and Adolescents: Indications, Safety, Protocols and Efficacy of TMS, VNS, taVNS and Related Methods <i>Jurij Bon (Slovenia)</i>
11:25 - 12:10	Transcutaneous Auricular Vagus Nerve Stimulation in Pediatric Neuropsychiatry: From Clinical Evidence to Precision Neuromodulation <i>Julian Koenig (Germany)</i>

12:10 - 12:30	Rewiring Development: Non-invasive Vagus Nerve Stimulation as a New Frontier in Pediatric Brain Health <i>Elisabetta Burchi</i>
12:30 - 13:05	Genesis Pharma Satellite How to integrate vamorolone in the standard care of patients with DMD <i>Damjan Osredkar (Slovenia)</i> 
13:05 - 14:00	LUNCH BREAK
14:00 - 15:20	SESSION 6 — Free Topics Chairperson: Nataša Šuštar, Tita Butenko
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14:20 - 14:40	Tubulinopathy: Marked Intrafamilial Phenotypic Variability <i>Alja Kavčič, Jernej Avsenik, Manca Velkavrh, Karin Writzl, Lana Stavber, Sara Bertok, Maruša Debeljak, Aleš Maver, Nataša Šuštar, Aneta Soltirovska Šalamon (Slovenia)</i>
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15:00 - 15:20	Body composition of Children with Spinal Muscular Atrophy: A Slovenian Retrospective Study <i>Doroteja Štrukelj, Matjaž Homan, Neža Lipovec, Damjan Osredkar, Evgen Benedik (Slovenia)</i>
15:20 - 15:30	CLOSING REMARKS

ACKNOWLEDGEMENTS

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SOCIAL PROGRAMME

SYMPOSIUM DINNER

23. october 2026 | 18:30

Venue: Zanolle
Rimska cesta 21, 1000 Ljubljana

OFFICIAL LANGUAGE

The official language of the Symposium is English. No simultaneous interpretation will be provided.

INTERNET

Wireless internet connection is available at Cankarjev dom. The name of the network is CD-guest. No login or password is needed.

SYMPOSIUM BADGE

A symposium badge will be included in the symposium materials provided upon registration. Participants are requested to wear their badge during all scientific sessions.

ATTENDANCE CERTIFICATE

A Certificate of Attendance will be sent by e-mail to all registered participants after the Symposium.

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Prvo in edino zdravljenje SMA v domačem okolju z dokazano učinkovitostjo pri odraslih, otrocih in dojenčkih.¹

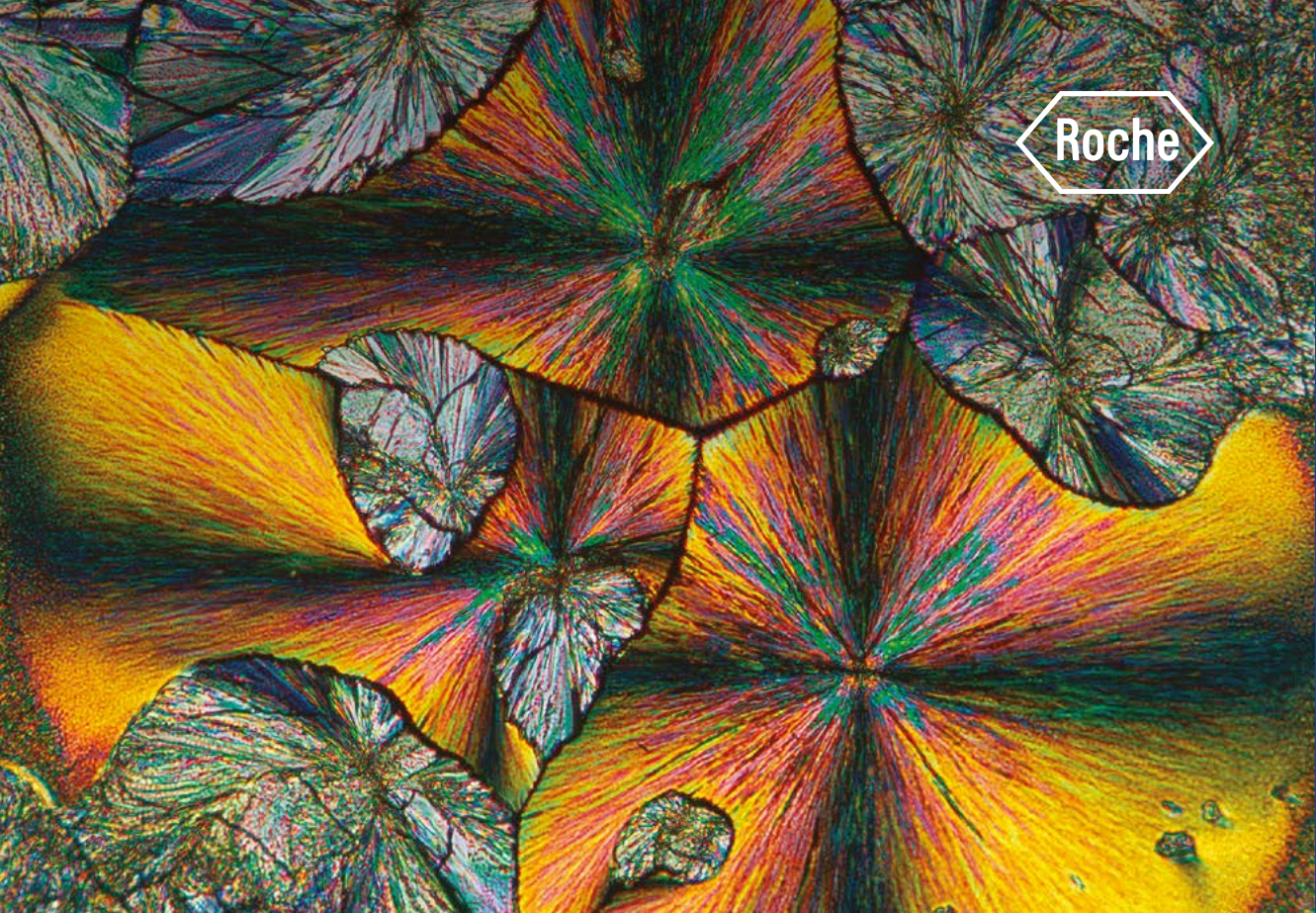
Zdravilo Evrysdi je indicirano za zdravljenje 5q spinalne mišične atrofije (SMA) pri bolnikih s klinično diagnozo SMA tipa 1, tipa 2 ali tipa 3 ali z eno do štirimi kopijami SMN2.¹

1. Evrysdi® Povzetek glavnih značilnosti zdravila Evrysdi. Dostopano na: https://www.ema.europa.eu/en/documents/product-information/evrysdi-epar-product-information_sl.pdf, dostopano 1.10.2026.

Ime zdravila: 0,75 mg/ml prašek za peroralno raztopino; Evrysdi 5 mg filmsko obložene tablete. **Kakovostna in količinska sestava:** Ena steklenička vsebuje 60 mg risdiplama v 2 g praška za peroralno raztopino. En mililiter pripravljene raztopine vsebuje 0,75 mg risdiplama; ena filmsko obložena tableta vsebuje 5 mg risdiplama. **Terapevtske indikacije:** Zdravilo Evrysdi je indicirano za zdravljenje 5q spinalne mišične atrofije (SMA) pri bolnikih s klinično diagnozo SMA tipa 1, tipa 2 ali tipa 3 ali z eno do štirimi kopijami SMN2. **Odmerjanje in način uporabe:** Priporočeni odmerek risdiplama enkrat na dan je treba določiti glede na starost in telesno maso (glejte Povzetek glavnih značilnosti zdravila). Zdravilo Evrysdi je treba jemati enkrat na dan s hrano ali brez nje, vsak dan ob približno istem času. Peroralna uporaba. Zdravilo Evrysdi prašek za peroralno raztopino mora pred izdajo bolniku pripraviti zdravstveni delavec. Uporabiti ga je treba s priloženo peroralno brizgo za večkratno uporabo. Zdravila Evrysdi se ne sme mešati z mlekom ali mlečnimi formulami. Zdravilo Evrysdi je treba vzeti takoj potem, ko se ga izvleče v peroralno brizgo. Če se zdravilo Evrysdi polije ali pride na kožo, je treba predel umiti z milom in vodo. Po zaužitju zdravila Evrysdi mora bolnik popiti nekaj vode, da zagotovi, da je zdravilo v celoti pogoltnil. Če bolnik ne more požirati, je mogoče zdravilo Evrysdi prašek za peroralno raztopino dati po sondi/stomi. **Tablete:** Priporočeni dnevni odmerek risdiplama v obliki filmsko obloženih tablet za bolnike, stare ≥ 2 leti, s telesno maso ≥ 20 kg, je 5 mg. Filmsko obložene tablete je treba pogoltniti cele ali pa jih raztopiti v majhni količini vode sobne temperature (glejte Navodilo za uporabo). Tablet ne žvečite, režite ali drobite. Če se zdravilo Evrysdi raztopi v vodi, ga je treba vzeti takoj. **Kontraindikacije:** Preobčutljivost na učinkovino ali katero koli pomožno snov. **Posebna opozorila in previdnostni ukrepi:** V študijah na živalih so opazili embrio-fetalno toksičnost. Bolnice in bolnike v obdobju plodnosti je treba seznaniti s temi tveganji. Uporabljati morajo visoko učinkovito kontracepcijo. Na podlagi opazanj v študijah na živalih med zdravljenjem in še 4 mesece po zadnjem odmerku risdiplama bolniki ne smajo darovati semen. Učinkov risdiplama na plodnost moških pri ljudeh niso raziskali. **Peroralna raztopina:** Zdravilo Evrysdi vsebuje izomalt. Bolniki z redko dedno intoleranco za fruktozo ne smejo jemati tega zdravila. Zdravilo Evrysdi vsebuje 0,375 mg natrijevega benzoata na mililiter. Natrijev benzoat lahko poveča tveganje za zlatenico pri novorojenčkih. **Medsebojno delovanje z drugimi zdravili in druge oblike interakcij:** Če se risdiplam uporabi sočasno z zaviralcem CYP3A, odmerka ni treba prilagoditi. Prilagoditev odmerka substratov CYP3A ni potrebna. Podatki in vitro kažejo, da lahko risdiplam v plazmi zviša koncentracijo zdravil, ki se odstranjujejo z MATE1 ali MATE2-K, npr. metformin. Če se sočasni uporabi ni mogoče izogniti, je treba bolnike spremljati glede morebitnih toksičnih učinkov in, če je treba, zmanjšati odmerek sočasno uporabljenega zdravila. **Neželeni učinki:** Pri bolnikih, pri katerih se je SMA začela v obdobju dojenčka, so bili v kliničnih študijah risdiplama najpogostejše opaženi neželeni učinki zvišana telesna temperatura, izpuščaji in driska. Pri bolnikih, pri katerih se je SMA začela pozneje, so bili v kliničnih študijah risdiplama najpogostejše opaženi neželeni učinki zvišana telesna temperatura, glavobol, driska in izpuščaji. Zgoraj navedeni neželeni učinki so se pojavili brez prepoznavnega kliničnega ali časovnega vzorca in so običajno kljub nadaljevanju zdravljenja minili tako pri bolnikih s SMA z začetkom v obdobju dojenčka kot s SMA s poznejšim začetkom. **Poročanje o domnevnih neželenih učinkih:** Poročanje o domnevnih neželenih učinkih zdravila po izdaji dovoljenja za promet je pomembno. Omogoča namreč stalno spremljanje razmerja med koristmi in tveganji zdravila. Od zdravstvenih delavcev se zahteva, da poročajo o katerem koli domnevnem neželenem učinku zdravila na: Javna agencija Republike Slovenije za zdravila in medicinske pripomočke, Sektor za farmakovigilanco, Nacionalni center za farmakovigilanco, Slovenčeva ulica 22, SI-1000 Ljubljana, Tel: +386 (0)8 2000 500, Faks: +386 (0)8 2000 510, e-pošta: h-farmakovigilanca@jazmp.si, spletna stran: www.jazmp.si. **Režim izdaje zdravila:** Rp/Spec. **Imetnik dovoljenja za promet:** Roche Registration GmbH, Emil-Barell-Strasse 1, 79639 Grenzach-Wyhlen, Nemčija. Za podrobnejše informacije glejte celoten Povzetek glavnih značilnosti zdravila. **Verzija:** 2.0/26

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Pre-Symposium Workshop: Introduction to SINDA – Standardized Infant NeuroDevelopmental Assessment

Introduction to SINDA, the Standardized Infant NeuroDevelopmental Assessment

Mijna Hadders-Algra¹

¹University Medical Center Groningen, Groningen, Netherlands

Background and Summary: SINDA is a novel neurodevelopmental assessment for infants of the corrected age of 6 weeks to 12 months. It has three scales: a neurological scale (28 dichotomous items – independent of infant age, taking less than 10 minutes), a developmental scale (15 dichotomous items/month, taking 5-7 (youngest ages) to 10-15 minutes (oldest ages)) and a socio-emotional scale (6 dichotomous items – independent of infant age, no extra time needed). The neurological scale aims to detect infants at high risk of cerebral palsy and/or intellectual disability; the developmental and socio-emotional scales primarily aim at caregiver counselling.

The course will address SINDA's design, its applicability and psychometric properties. It will primarily focus on the neurological scale. This scale assesses the infant's neurological condition in five domains: (1) spontaneous movements (8 items, including 7 items on the quality of the movements in terms of variation versus stereotypy); (2) cranial nerves (7 items); (3) motor reactions to postural stimulation (5 items); (4) muscle tone (4 items); (5) reflexes and reactions (4 items). The items are scored dichotomously as typical (score 1) or atypical (score 0) with age-independent criteria. The neurological scale has a good reliability and good predictive validity. An at risk score, defined as ≤ 21 points, predicted cerebral palsy in at risk infants with sensitivities of 91-100% and specificities of 81-91%. The predictive values of SINDA's neurological scale were similar to those of General Movement Assessment in at risk infants aged 3 months corrected age. SINDA is easy to learn, takes relatively little time and does not require expensive equipment. SINDA's predictive properties are similar to those of the Hammersmith Infant Neurodevelopmental Examination (HINE), but SINDA is easier to learn. These properties allow for SINDA's use in low resource settings, where it is increasingly used. The course will be richly illustrated by video-examples. It will include an interactive practice part (scoring of video examples) and it will allow ample time for discussion.

Keywords: early detection, cerebral palsy, intellectual disability, spontaneous movements

References

- Hadders-Algra M, Tacke U, Pietz J, Philippi H. SINDA: Standardized Infant NeuroDevelopmental Assessment – An instrument for early detection of neurodevelopmental disorders. London: Mac Keith Press, 2022 (also available in Croatian, Dutch and German; French translation forthcoming).
- Hadders-Algra M, Tacke U, Pietz J, Rupp A, Philippi H. Predictive value of the General Movements Assessment and Standardized Infant NeuroDevelopmental Assessment in infants at high risk of neurodevelopmental disorders . Dev Med Child Neurol. 2024, 113: 871-880.
- Hadders-Algra M. The developing brain: Challenges and opportunities to promote school readiness in young children at risk of neurodevelopmental disorders in low- and middle-income countries. Front Pediatr. 2022;10:989518.

Session 1 — Neonatal Neurology

Early Diagnostics and Early Intervention in Neurodevelopmental Disorders

Mijna Hadders-Algra¹

¹University Medical Center Groningen, Groningen, Netherlands

The young nervous system is characterized by high developmental activity. This is associated with challenges for early detection as the young nervous system (a) cannot express impairments in specific functions that first emerge at later age and (b) expresses dysfunctions in a different way than the adult nervous system does do. The high developmental activity also implies high neuroplasticity which offers opportunities for early intervention.

Spontaneous activity is a hallmark of neural activity. Brain activity and development is characterized by variation. Children develop by trying out the varied options and learn via trial and error to select for each situation efficient solutions and strategies, i.e., adaptive behaviour.

In the lecture the means of early detection of neurodevelopmental disorders by means of neurological, neuromotor and developmental tests is addressed. We gradually learned that neurological assessment should not only include the evaluation of muscle tone and reflexes and reactions, but also should pay attention to the quality of spontaneous movements, in particular in terms of variation in movements. General Movements Assessment (GMA) is entirely based on the assessment of the quality of spontaneous movements; the neurological scale of the Standardized Infant NeuroDevelopmental Assessment (SINDA) emphasizes the quality of spontaneous movements. GMA and SINDA well predict cerebral palsy and intellectual disability.

Early intervention in infants at high biological risk of neurodevelopmental disorders offers the means to families how they best can cope with the situation of having a young child with special needs and exploits the high neuroplasticity of the young brain. The presentation will underline the importance of ⁽¹⁾ family centred care; and ⁽²⁾ focusing on activities and participation.

Over the years we learned that no evidence is available that early intervention by means of NeuroDevelopmental Treatment or treatment according to Vojta is associated with a beneficial effect on child development and family well-being. We also learned that parental support is quintessential, both for child and family. Infants profit most from the intervention when they are challenged to explore by self-produced movements and trial and error the environment and the possibilities of their own body.

COPCA – COPing with and CARing for infants with special needs is a family centred early intervention programme. The programme's goal is to optimize child and family participation. COPCA has two components: ⁽¹⁾ the family; COPCA stresses family autonomy and therefore uses coaching of families as a major strategy; ⁽²⁾ the child; COPCA uses the principles of Neuronal Group Selection Theory which offer the keywords of exploration, variation, being challenged to self-produced movements, trial and error.

Therapeutic Hypothermia Following Perinatal Asphyxia: What to Do?

Floris Groenendaal¹

¹*Department of Neonatology, Wilhelmina Children's Hospital/University Medical Center Utrecht, Utrecht, Netherlands*

Therapeutic hypothermia (TH) has become an established therapy for term and near-term neonates with perinatal asphyxia and moderate-to-severe encephalopathy. Recent studies have been performed to examine several patient populations in which the safety and efficacy of TH have been less well established:

- Late preterms (33-35 weeks' gestational age)
- 'Later' TH, starting after 6 hours of birth
- Mild encephalopathy after perinatal asphyxia.
- Sudden unexpected postnatal collapse

Late preterms: Safety studies have demonstrated that low blood pressure is relatively more common in late preterm infants with TH, and is relatively more common at a lower gestational age. It is uncertain whether this is a direct effect of hypothermia or whether the perinatal asphyxia as such may result in more blood pressure problems. No other clinical issues have been reported consistently in late preterms. Efficacy is unproven, but abnormal brain MRI findings in late preterms are comparable to those in term infants, so neuroprotective effects are possible. Most paediatric societies recommend that TH is standard therapy ≥ 36.0 weeks' gestational age, and may be discussed with parents at a gestational age between 35+0 and 35+6 weeks. TH should not be used below 35+0 weeks, as risks may be larger than benefits⁽¹⁾.

'Later' TH: One trial compared TH initiated at 6 to 24 hours after birth with noncooling. Bayesian analysis showed a 76% probability of any reduction in death or disability, and a 64% probability of at least 2% less death or disability at 18 to 22 months. It was concluded that hypothermia initiated at 6 to 24 hours after birth may have benefit, but there is uncertainty of its effectiveness⁽²⁾.

Mild encephalopathy: Although there is a tendency to offer TH to infants with milder encephalopathy following perinatal asphyxia, no beneficial effect of TH has been demonstrated in this population, and TH should not be offered outside clinical trials⁽³⁾.

Sudden unexpected postnatal collapse: Many of these infants appear to have had a short, severe hypoxic-ischaemic insult resulting from acute airway obstruction after birth. Therefore, there is a theoretical plausibility for benefit from TH in such a context, and so it should be considered on an individual case basis⁽⁴⁾.

These aspects will be discussed in more detail during the presentation.

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Association Between Functional Brain Network Characteristics and Cognitive Deficits After Perinatal Stroke

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BACKGROUND: Functional brain networks, derived from graph-theoretical analysis of neurophysiological signals, offer insight into how the brain organizes and reorganizes across development and after early injury. High-density EEG-based connectomics in healthy children and in children after perinatal stroke remains underexplored, and its relationship to cognitive outcome is poorly understood.

AIM: To characterize age- and sex-related changes in EEG-derived functional brain networks during typical childhood and adolescence, and to determine how perinatal stroke alters these networks and relates to cognitive functioning.

METHODS: Resting-state high-density EEG was analysed in two cohorts: 113 typically developing children (5–18 years) and 24 children with perinatal stroke (12 ischemic, 12 hemorrhagic), who additionally undergone cognitive assessment. Functional connectomes were computed in different frequency bands and graph metrics (clustering coefficient, characteristic path length, global efficiency, small-worldness, modularity, interhemispheric strength) were compared using Bayesian statistics, with correlations to cognitive scores in the stroke cohort.

RESULTS: In typically developing children, the alpha band showed the most consistent age-related changes, reflecting brain network maturation. After perinatal stroke, networks showed higher segregation, reduced efficiency, and higher interhemispheric strength than controls, at both whole-brain and hemispheric levels, consistent with hypersynchrony and reorganization following injury. The perinatal stroke cohort also showed lower brain network modularity, which correlated with lower IQ and slower processing speed. In addition, increased interhemispheric strength after perinatal stroke correlated positively with impulsive decision-making.

DISCUSSION: Across the three studies, alpha-band connectivity was the most sensitive marker of both normal maturation and stroke-related reorganization. Hypersynchrony and increased interhemispheric connectivity after perinatal stroke may reflect compensatory reorganization but is also linked to less efficient brain network topology and specific cognitive vulnerabilities, particularly when it comes to processing speed and impulse control.

CONCLUSIONS: High-density resting-state EEG functional connectomics detects meaningful age-related network changes in healthy children and reveals clinically relevant brain network alterations after perinatal stroke that correlate with cognitive outcome, supporting its value as a non-invasive tool for studying brain network development and injury-related reorganization.

Impact of Congenital Heart Disease on Neurodevelopment in Childhood

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BACKGROUND: Congenital heart disease (CHD) is the most common congenital anomaly, affecting approximately 0.8% to 1.2% of live births, and represents the leading cause of infant mortality attributable to congenital anomalies. CHD encompasses a broad spectrum of conditions, ranging from relatively simple defects that may not require intervention to complex lesions requiring multiple surgical or catheter-based interventions during infancy and throughout the lifespan. Management therefore varies according to the severity of the defect, with most patients requiring pharmacological treatment and more than one-third requiring surgical repair or catheter-based intervention during early childhood. Patients with CHD requiring surgical or catheter-based intervention within the first year of life are considered to have critical CHD. Advances in surgical and intensive care have significantly improved survival among children with CHD, with approximately 85% surviving into adulthood. However, despite these advances in survival, more than 50% of children with CHD have neurodevelopmental impairment across a wide spectrum of domains.

AIM: To investigate neurodevelopmental outcomes and structural and functional brain network characteristics in children and adolescents with CHD.

METHODS: A narrative review of the literature was conducted using the PubMed, MEDLINE, PsycINFO and Web of Science databases. Relevant studies investigating neurodevelopmental outcomes and magnetic resonance imaging (MRI) findings, with a focus on structural and functional brain networks in children and adolescents with CHD, were identified and reviewed. The literature search focused on studies evaluating neurodevelopmental outcomes, structural brain alterations, white matter integrity, and functional connectivity, as well as the relationship between brain network characteristics and neurodevelopmental outcomes. Studies addressing the prenatal, preoperative, and postoperative periods were considered to provide an overview of neurodevelopmental vulnerability across the course of CHD.

RESULTS AND DISCUSSION: Despite improved survival, children with CHD remain at increased risk of neurodevelopmental impairment across several developmental domains, including motor, language, and cognitive function, as well as emotional, behavioral and psychosocial functioning. These difficulties may persist into adolescence and early adulthood, when deficits in higher-order cognitive domains may become more apparent. Importantly, MRI studies have demonstrated brain abnormalities before cardiac surgery, including white matter injury and altered brain development, suggesting that neurodevelopmental vulnerability may already be present before surgery. Quantitative structural MRI studies in adolescents and young adults with complex CHD have reported smaller cortical and subcortical gray matter volumes and microstructural alterations, particularly in association tracts and frontal regions. Resting-state fMRI studies have also demonstrated altered functional connectivity in neonates with complex CHD before cardiac surgery, particularly involving subcortical regions and their connections with the cerebral cortex. In youth with complex CHD, altered functional connectivity has been reported across widespread brain regions and networks, including the default mode, dorsal attention, and frontoparietal networks, and these alterations have been associated with differences in executive functioning.

CONCLUSIONS: A better understanding of brain network characteristics and their relationship with neurodevelopmental outcomes may help clarify the mechanisms underlying neurodevelopmental difficulties in children with CHD and support earlier recognition and appropriate follow-up.

Perinatal Stroke in the Term and Preterm Infant

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Perinatal stroke consists of different subtypes, the main ones being perinatal arterial ischemic stroke (PAIS), cerebral sinovenous thrombosis (CSVT), and perinatal hemorrhagic stroke (HS). In term infants the incidence is reported to be 1 in 1600 to 1 in 3000 live births in case of PAIS, and 1–12 per 100.000 livebirths in case of CSVT.¹ PAIS is caused by impaired cerebral artery flow due to factors as thrombosis, embolism, or vasospasm. Neonatal CSVT involves thrombus formation in the cerebral veins or dural sinuses, potentially causing venous hypertension, hemorrhage and ischemia, ultimately causing hemorrhagic parenchymal venous infarction and subsequent brain injury.

The diagnosis of PAIS is made, when the onset is between 20 weeks' gestation and 28 days after birth. The literature is mainly about PAIS in term infants, even though the incidence in a population-based study was 87 per 100.000 for those born before 34 weeks' gestation compared to 22 per 100.000 in infants born between 34 and 37 weeks.²

The majority of the term infants presents with seizures that are often focal clonic seizures. The preterm infants are often asymptomatic, as they more often have perforator strokes.³ Diagnosis and prediction of motor outcome can be reliably made using MRI within a week of onset, with diffusion weighting imaging (DWI) showing 'pre-Wallerian' degeneration in the corticospinal tracts in those who will develop a hemiparesis.⁴ Paying attention to the arterial territory allows better prediction of outcome in other domains (cognition, vision, epilepsy) as well. This will help when counselling parents and guide targeted rehabilitation, especially the use of constraint induced movement therapy (CIMT) with most benefit when started before 6 months of life.

Besides management of seizures, new therapies have been used in trials. A phase 1 trial administered nasal mesenchymal stromal cells in 10 term neonates.⁵ A phase 2 trial will be started early next year. In a recently completed randomized trial (RCT) 80 term infants were either given darbepoietine or a placebo. Enrollment is complete, and analyses are underway. At present, only term infants were eligible for the trials.

Most studies are about CSVT in term infants, but in the German population-based study 29.2% of their CSVT cases were born before 37 weeks.²

Term infants tend to present with seizures while the preterm infants are more often asymptomatic.³ The diagnosis of CSVT is best made using MRI/MRV (MR venography), even though the diagnosis can often be made using color Doppler ultrasound especially when the superior sagittal sinus or transverse sinus is thrombosed. Other sinuses are easier to visualize with MRV and more detailed information will be obtained regarding associated brain lesions. Prediction of outcome depends on the presence of associated brain lesions. In the term infant a thalamic hemorrhage is typically associated with thrombosis of the deep venous system and the straight sinus. Involvement of the medullary veins are also common and can be either hemorrhagic or ischemic. In preterm infants white matter involvement is more often present and this may be considered a PVL- mimic. In several outcome studies, moderate to severe impairment is reported to be as high as 45-50%. In infants with a thalamic haemorrhage there is a high risk of subsequent development of spike wake activity during sleep (SWAS).⁶

Besides management of seizures, anticoagulation therapy (ACT) is used in around 2/3 of the infants in both term as well as preterm infants. The aim is to prevent propagation of the thrombus that will occur in 20-25% of the cases and this carries a higher risk of associated brain lesions. Unfortunately, no proper RCT has been performed to prove that ACT is indeed associated with a better outcome.

Pharmacogenetics of Antiseizure Medication in Neonates with Seizures

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BACKGROUND: Neonatal seizures (NS) are the most common neurological emergency during the neonatal period and are associated with substantial mortality and long-term neurodevelopmental morbidity. Despite advances in diagnosis and neonatal intensive care, treatment remains challenging. Phenobarbital is still widely used as first-line therapy, although its efficacy is limited, while the optimal choice of second- and third-line antiseizure medications (ASMs) remains uncertain. Considerable interindividual variability exists in treatment response, drug exposure, and susceptibility to adverse drug reactions. Pharmacogenetics, the study of how genetic variation influences drug response, has emerged as a potential approach to explain some of this variability and support individualized treatment strategies through its effects on drug pharmacokinetics, pharmacodynamics, efficacy, and toxicity.

AIM:

METHODS: A literature review was performed to identify pharmacogenetic studies evaluating ASM treatment in neonates and to compare neonatal evidence with current pharmacogenetic knowledge in pediatric and adult epilepsy. The ClinPGx database was additionally searched for genetic variants associated with ASM metabolism, efficacy, and adverse drug reactions.

RESULTS: The literature review identified only three relevant neonatal publications: two original studies evaluating the association of cytochrome P450 (CYP) 2C19 and CYP2B6 polymorphisms with phenobarbital treatment and one case report describing carbamazepine exposure in a neonate with a poor-metabolizer CYP2C9 genotype. No pharmacogenetic studies were identified for other ASMs used in NS management. In contrast, numerous pharmacogenetic associations affecting ASM metabolism, efficacy, and toxicity have been described in older children and adults, with some already incorporated into clinical practice.

DISCUSSION: The available evidence highlights a striking discrepancy between advances in epilepsy pharmacogenetics and the limited data available in neonatal medicine. Interpretation of genetic effects in newborns is further complicated by rapidly changing developmental physiology, organ maturation, critical illness, inflammation, and co-medications, all of which may substantially influence drug disposition and response. Furthermore, developmental regulation of drug-metabolizing enzymes may limit the direct extrapolation of pharmacogenetic findings from older populations to neonates.

CONCLUSIONS: Current evidence is insufficient to support the routine use of pharmacogenetic testing for ASM selection or dosing in NS. The paucity of neonatal-specific data, together with the profound impact of developmental and clinical factors on drug disposition and treatment response, limits the transferability of pharmacogenetic knowledge derived from older populations. Future research should focus on defining the relative contribution of genetic variability in comparison with developmental pharmacology before pharmacogenetic-guided treatment can be meaningfully implemented in neonatal practice.

Family-Centred Psychological Approaches in the Management of Neurology Diseases started in neonatal period

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BACKGROUND: Neurological conditions beginning in the neonatal period can profoundly affect not only the developing child, but the entire family. Parents may face prognostic uncertainty, complex medical decisions, disruption of the expected transition to parenthood and significant psychological distress. Family-centred care therefore requires attention not only to the developing brain, but also to parents' psychological needs and their involvement as partners in care. Understanding families' experiences can help healthcare professionals provide appropriate support, build collaborative relationships and ultimately contribute to the best possible care for the child.

AIM: To describe key psychological processes experienced by families of children with neurological conditions beginning in the neonatal period and to highlight family-centred approaches that support adaptation, strengthen partnership between families and healthcare professionals and help ensure the best possible care for the child.

METHODS: This clinically oriented narrative synthesis integrates literature on family-centred care, rare neurological and genetic conditions and parental adjustment, together with clinical experience from a neonatal department and a rare diseases centre.

RESULTS: Across conditions, families may experience diagnostic and prognostic uncertainty, emotional distress, grief and a strong need to regain a sense of control and agency. Emotional responses may coexist or re-emerge as the child grows and new developmental challenges arise. Families benefit from clear, paced and trustworthy information, acknowledgement of uncertainty, continuity and coordination of care, emotional support and active involvement in decision-making. Responses perceived as resistance, indecision, conflict or an intensive search for additional treatment options may reflect fear, grief, helplessness and attempts to regain control. Psychological support can help families recognise and verbalise these experiences, tolerate uncertainty, strengthen their sense of agency, maintain family relationships and gradually integrate the child's condition into everyday life. Adaptation to life with the condition is ongoing and intense emotional responses may re-emerge throughout the child's development.

DISCUSSION: Understanding the psychological processes experienced by families is important because they can influence how parents process information, make decisions, communicate with healthcare professionals and participate in their child's care. A family-centred approach therefore extends beyond emotional support. It requires psychologically informed communication, coordinated multidisciplinary care and a collaborative relationship in which parents are recognised as partners. Recognising the emotions and needs underlying parents' responses can help healthcare professionals interpret challenging interactions with greater understanding and respond in ways that strengthen trust and cooperation. Family adaptation is not a one-time process; psychological needs may change and re-emerge as the child develops and families encounter new challenges, transitions and uncertainties.

CONCLUSIONS: Caring for a child with a neurological condition beginning in the neonatal period requires attention not only to the developing brain, but also to the developing relationships between the child, parents and healthcare professionals. Understanding families' psychological needs and working in partnership with them throughout uncertainty and change is an integral part of comprehensive care.

Session 2 — Neuromuscular Disorders

Challenges in the Diagnosis of Hereditary neuropathies

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BACKGROUND: Inherited neuropathies (HN) can manifest at any age, however disease onset most commonly occurs during the first two decades of life, most frequently in the form of autosomal dominant demyelinating neuropathy associated with a 17p11.2 duplication. More than 100 genes are known to be responsible for HN, with a large number of pathogenic variants

AIM: To demonstrate the importance of a well-defined phenotype for the appropriate choice of genetic method, as well as for distinguishing between inherited and acquired neuropathies.

METHODS: Analysis of patients with a strong genotype–phenotype correlation and patients with hereditary neuropathy whose phenotype resembles that of acquired neuropathies

RESULTS AND DISCUSSION: Intronic variants require whole-genome sequencing (WGS) after variants in the coding regions of DNA have been excluded. We present a phenotype that provides a sufficient clue for targeted analysis of a unique deep intronic variant in the CTD1 gene, responsible for autosomal recessive demyelinating neuropathy.

Variants in the coding regions of DNA may represent founder variants and may be associated with easily recognizable phenotypes. We present a typical phenotype of autosomal recessive axonal neuropathy associated with a unique founder variant in the HINT1 gene, especially in the population from Central and Southeastern Europe.

An acute or subacute onset of symptoms with a relapsing-remitting course is most suggestive of acquired neuropathies. However, this pattern may also occur in rare inherited neuropathies, including demyelinating forms such as HNPP, as well as in axonal neuropathies. We present a case of autosomal recessive axonal neuropathy associated with a variant in the SGPL1 gene.

CONCLUSIONS: Phenotypic analysis can significantly influence the planning of genetic testing, allowing a more targeted and rational diagnostic approach and reducing both diagnostic time and costs. Rapid genetic diagnosis may enable early implementation of preventive and therapeutic measures, as well as appropriate prenatal genetic counseling.

Pediatric Neuromuscular Diseases: Diagnostic, Therapeutic, and Multidisciplinary Care Challenges — Insights from Montenegro

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BACKGROUND: Pediatric neuromuscular diseases (NMDs), including spinal muscular atrophy (SMA) and Duchenne muscular dystrophy (DMD), require early recognition to enable timely intervention. SMA represents a particularly time-critical example, as disease-modifying therapies are most effective when initiated before irreversible motor neuron loss. While newborn screening (NBS) for SMA has been implemented in numerous European countries, Montenegro has not yet introduced this screening into its national NBS panel. This gap, together with limited awareness of SMA and other rare neuromuscular disorders among primary care providers, contributes to significant diagnostic delay. Care of these patients is further complicated by the absence of national clinical registries for rare diseases which hinder systematic follow-up, transition to adult care, and long-term outcome tracking.

AIM: To describe the diagnostic pathway, therapeutic management, and clinical characteristics of patients with neuromuscular diseases followed at Clinical Center of Montenegro and to highlight the impact of the absence of newborn screening, limited disease awareness, lack of national rare disease registries, and absence of formal multidisciplinary teams on diagnosis and care in Montenegro.

METHODS: A retrospective/descriptive analysis was conducted of pediatric and adult patients diagnosed with neuromuscular disease evaluated at our Center. Data collected included age at symptom onset, age at diagnosis, genetic findings, disease-modifying therapy, and availability of structured multidisciplinary follow-up.

RESULTS: Six pediatric patients with genetically confirmed SMA were identified: three with SMA type 1 and three with SMA type 3. One patient, previously treated with nusinersen followed by risdiplam, subsequently received gene therapy; two remain on nusinersen and three on risdiplam. Additionally, seven adult SMA patients are currently treated with risdiplam. All approved innovative disease-modifying therapies for SMA are accessible to patients in Montenegro. Eleven pediatric patients with Duchenne muscular dystrophy were identified, of whom four remain ambulatory; three of these, meeting eligibility criteria, have been receiving givinostat for almost one year. Corresponding data on adult DMD patients could not be obtained, reflecting the absence of clinical and national registries for rare diseases and the lack of systematic transition tracking.

DISCUSSION: Our cohort demonstrates that, despite full access to all approved disease-modifying therapies for SMA, and eligibility-based access to novel therapies such as givinostat for Duchenne muscular dystrophy, therapeutic availability alone does not offset the impact of delayed clinical recognition, particularly for SMA in the absence of newborn screening. The inability to report on adult DMD patients is itself a key finding, illustrating how the absence of a national rare disease registry directly limits visibility into long-term, cross-age disease burden and impedes structured transition from pediatric to adult neuromuscular care. These findings underscore that structural investment in registries, early detection, and care coordination, besides therapy access, represents the primary unmet need.

CONCLUSIONS: Montenegro provides full access to approved innovative therapies for patients with NMDs, yet diagnostic delay, absence of newborn screening, lack of a national rare disease registry, and absence of formally appointed multidisciplinary teams remain the leading structural barriers to optimal outcomes. Establishing newborn screening for SMA, registries, and formal multidisciplinary frameworks, alongside targeted awareness initiatives, should be prioritized as the next critical step.

Cardiac Monitoring Algorithm in Children and Adolescents with Neuromuscular Disorders Receiving Innovative Disease-Modifying Therapies

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BACKGROUND: Disease-modifying therapies have changed the survival and functional trajectory of several childhood neuromuscular disorders, but they have not removed disease-related cardiac risk. Systemic adeno-associated virus gene transfer has also introduced a distinct risk of myocardial injury and myocarditis. Cardiac surveillance must therefore address both the natural history of the underlying disorder and treatment-specific toxicity.

AIM: To define the evolving role of the pediatric cardiologist and propose a practical cardiac monitoring algorithm for children and adolescents receiving innovative neuromuscular therapies.

METHODS: This narrative review integrates major neuromuscular and pediatric cardiology guidance, contemporary consensus statements, regulatory prescribing information, and peer-reviewed clinical studies available through August 2026. Recommendations are organized by intrinsic cardiac phenotype, treatment platform, and response to abnormal findings.

RESULTS: Before disease-modifying therapy, pediatric cardiology was primarily responsible for baseline phenotyping, longitudinal detection of cardiomyopathy or conduction disease, preventive heart failure treatment, perioperative risk assessment, and management of advanced complications. In the current era, this role begins before treatment selection and includes risk stratification, creation of an interpretable cardiac baseline, optimization of cardiopulmonary status, protocol-specific toxicity surveillance, urgent adjudication of troponin or imaging abnormalities, and long-term pharmacovigilance.

DISCUSSION: Duchenne muscular dystrophy requires surveillance from diagnosis, generally at least annually, with cardiac magnetic resonance when feasible. Typical 5q spinal muscular atrophy usually requires phenotype-driven rather than routine intensive cardiac follow-up, although systemic gene transfer requires a product-specific safety overlay. Infantile-onset Pompe disease, LMNA-related muscular dystrophy, Emery-Dreifuss muscular dystrophy, sarcoglycanopathies, and myotonic dystrophy require disease-specific imaging and rhythm surveillance.

CONCLUSIONS: The safest model is a two-layer algorithm: a lifelong disease-risk pathway plus a temporary or persistent treatment-risk pathway. Product labeling and local regulatory requirements remain mandatory, while expert consensus is used to intensify monitoring in high-risk patients. Standardized baseline measurements, cardiac troponin I rather than troponin T in dystrophinopathy, early access to pediatric cardiology, and predefined escalation thresholds are central to safe implementation.

Session 3 — Free Topics

Cerebral Folate Deficiency in Siblings with FLO1R Pathogenic Variant – Spectrum of Clinical Presentation

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BACKGROUND: Cerebral folate deficiency syndrome (CFDS) is characterized with neuropsychiatric or developmental disorder due to decreased CSF folate levels in the presence of normal folate status outside the nervous system. There are five potential mechanisms underlying CFD: reduced transport of folates across the blood–brain barrier into CSF and across the ependymal into the brain; reduced folate storage and release from the intracellular folyl-polyglutamate pool; increased utilization and consumption of reduced folates within the nervous system leading to depletion of the folate pool; increased catabolism of reduced folates within the nervous system; metabolic conditions affecting folate metabolism within the nervous system.

AIM: The aim of this study was to comprehensively evaluate two siblings with CFDS due to same likely pathogenic variant in FLOR1 gene followed in our center.

METHODS: Clinical evaluation and follow-up, neuroimaging, neurophysiological and genetic analyses, laboratory analyses of the blood and CSF were performed in two siblings with suspicion to CFDS.

RESULTS: In both siblings, the same genotype was discovered – homozygous likely pathogenic variants FLOR1 gene (c.466T>G, p.Trp156Gly), while the phenotype is quite different. Clinical presentation in younger 7-year-old male sibling included drug - resistant seizures, ataxia, dysarthria, movement disorders, developmental delays, and developmental, neurological and cognitive regression. MRI showed severe white matter changes with slight improvement with treatment. The other sibling, 9-year-old-girl has very mild form of disease, with discrete cognitive difficulties, and no white matter changes on brain MRI. Both children are treated by folinic acid, although the boy with severe form required very high dosage of folinic acid, more than it was recommended in the literature, multiple antiseizure medication and treatment of movements disorders and motor agitation.

DISCUSSION: Diagnosis and the treatment of CFDS is very changeable and included wide spectrum of clinical presentation and different response to the treatment. Beyond ataxia, developmental delay and neurocognitive regression, the prominent problem in our patient is drug-resistant epilepsy with multiple seizure types.

CONCLUSIONS: CFDS is very rare disorder and there is limited experience and knowledge about clinical presentation and the treatment. This report illustrated very different phenotype in two siblings with the same genotype, and challenges in treatment approach depending on the clinical presentation.

Hidden Morphometric Signals in Cranial Ultrasound: Associations With Neurodevelopmental Outcomes in Preterm Infants

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BACKGROUND: Advances in perinatal and neonatal care have improved survival among preterm infants, yet neurodevelopmental impairment remains a major concern. Although major brain lesions detected by cranial ultrasound are established predictors of adverse outcomes, some preterm infants with normal or only mildly abnormal ultrasound findings subsequently develop neurodevelopmental difficulties. Sensitive, accessible, and reproducible markers extending beyond the detection of major structural injury are therefore needed. Standardized quantitative measurements obtained during routine cranial ultrasound may reveal subtle variations in brain growth and maturation that are not identified by conventional qualitative assessment.

AIM: To investigate the associations of standardized cranial ultrasound morphometric measurements obtained during the early neonatal period and at term-equivalent age, as well as head circumference, with Bayley Scales of Infant and Toddler Development, Fourth Edition (Bayley-4) outcomes and to explore their potential for early neurodevelopmental risk stratification.

METHODS: This exploratory observational study included 22 preterm infants admitted to a neonatal intensive care unit. Cranial ultrasound was performed according to a predefined standardized protocol within the first 72 hours after birth and at term-equivalent age (37–40 weeks postmenstrual age). Measurements included the Levene index, lateral ventricular width, third ventricle width, subarachnoid space, and interhemispheric fissure. Head circumference was included as an additional marker of postnatal brain growth. Neurodevelopment was assessed at 12–14 months corrected age using Bayley-4. Associations were examined using Spearman's rank correlation.

RESULTS: Significant associations were more frequent for measurements obtained at term-equivalent age than during the early neonatal period. Early ventricular measurements showed positive associations with motor outcomes, while early head circumference and third ventricle width were associated with receptive communication. At term-equivalent age, greater lateral ventricular width showed consistent negative correlations with motor and language outcomes, with particularly strong associations in motor domains ($p < 0.01$). Head circumference showed less consistent associations, reaching significance only for personal-social skills, whereas third ventricle width was associated with play and leisure activities.

DISCUSSION: The predominance of significant associations at term-equivalent age suggests that ultrasound morphometry at this stage may better reflect cumulative postnatal brain growth and maturation than measurements obtained shortly after birth. Importantly, the potential prognostic value of cranial ultrasound may extend beyond the detection of major brain injury. A normal or mildly abnormal qualitative ultrasound examination, when complemented by standardized quantitative measurements, may contain subtle morphometric markers associated with subsequent neurodevelopment. Ventricular parameters showed more consistent associations with neurodevelopmental outcomes than head circumference alone.

CONCLUSIONS: Standardized cranial ultrasound morphometry, particularly at term-equivalent age, may extend the prognostic value of routine ultrasound beyond the detection of major brain lesions. Quantitative measurements may reveal prognostically relevant differences even when conventional findings are normal or only mildly abnormal, potentially supporting earlier identification and targeted follow-up of infants at increased neurodevelopmental risk. This analysis represents the first step towards a multimodal predictive model integrating ultrasound-derived morphological markers with functional measures of brain activity obtained using amplitude-integrated electroencephalography. Larger prospective studies employing multivariable models and longer follow-up are required to confirm the independent predictive value of these markers.

Pediatric Intensive Care Unit-Acquired Polyneuromyopathy

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BACKGROUND: Pediatric intensive care unit-acquired weakness can be divided into three entities, that are usually overlapping: critical illness polyneuropathy (CIP), critical illness myopathy (CIM), and critical illness polyneuromyopathy (CIPNM) and is associated with intensive care stay. CIP typically manifests as a symmetrical, predominantly distal axonal polyneuropathy affecting the limb and respiratory muscles of critically ill children ^[1].

AIM: Recent evidence suggests CIPNM can affect up to 25.6% of pediatric intensive care unit (PICU) patients ^[1, 2].

The etiology is multifactorial, primarily driven by systemic inflammation, microcirculatory dysfunction leading to hypoxia, and metabolic stress. Key risk factors include sepsis, prolonged mechanical ventilation, neuromuscular blockage, corticosteroids, and multiorgan failure ^[1].

Clinical presentation occurs within the first ten days of admission, characterized by symmetrical limb weakness with diminished reflexes, and involves also the diaphragm, complicating ventilator weaning.

METHODS: Nerve conduction studies and electromyography (EMG) remain the gold standard for diagnosis. Simplified serial electrophysiological testing is increasingly utilized as a practical bedside screening tool to overcome diagnostic barriers ^[2].

RESULTS: The prognosis is generally favorable and potentially reversible, with most pediatric patients demonstrating spontaneous or therapeutically induced functional improvement over several months to two years ^[1]. Management focuses on avoiding well-known risk factors with strict glycemic control, optimized nutrition, and the avoidance of prolonged immobilization ^[3].

DISCUSSION: Early mobilization (EM) and early progressive exercise (EPE) are cornerstone therapeutic interventions. Incorporating structured EPE protocols, including passive and active locomotor physiotherapy, has been shown to safely slow muscle atrophy, and prevent contractures without increasing adverse events ^[4]. Furthermore, multidisciplinary consensus guidelines emphasize that developmentally appropriate EM should be integrated into standard PICU care bundles to diminish the risk of developing post-intensive care syndrome and speed-up neuromuscular recovery ^[5].

CONCLUSIONS: Pediatric intensive care unit-acquired polyneuromyopathy is a significant complication in critically ill children, caused primarily by systemic inflammation and prolonged immobility. Early recognition through combined clinical and electrophysiological assessments, alongside the prompt initiation of progressive rehabilitation with early mobilization and optimal metabolic management, are essential to improve long-term functional outcomes.

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Session 4 — Epilepsies

Neonatal Seizures Beyond the NICU

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BACKGROUND: Neonatal seizures are the most common neurological emergency in the neonatal period, yet their clinical significance extends far beyond seizure control in the NICU. Contemporary EEG monitoring has transformed seizure recognition, while advances in neuroimaging and genetic diagnostics have substantially improved etiological classification. However, the questions most relevant to the pediatric neurologist often arise only after discharge: Which infants will develop epilepsy? Who is at risk for adverse neurodevelopmental outcomes? How long should follow-up continue, and can early clinical, EEG, or imaging findings reliably identify those at greatest risk?

AIM: This presentation will critically address current controversies in prognostication, ASM discontinuation, prediction of post-neonatal epilepsy, and the optimal duration and intensity of neurodevelopmental surveillance. A risk-stratified, longitudinal approach integrating etiology, EEG, neuroimaging, and developmental trajectories may provide the most meaningful framework for care beyond the NICU.

DISCUSSION: Long-term outcome after neonatal seizures is highly heterogeneous and is predominantly determined by the underlying etiology and severity of brain injury. Nevertheless, seizure burden, neonatal status epilepticus, EEG background abnormalities, neurological examination, and neonatal-onset epilepsy provide additional prognostic information. Importantly, neurodevelopmental consequences may extend beyond motor and cognitive impairment to include language, behavioral, executive, and learning difficulties that may become apparent only later in childhood.

A major paradigm shift concerns antiseizure medication (ASM). Current evidence supports discontinuation of ASM before hospital discharge in most neonates after resolution of acute provoked seizures and in the absence of neonatal-onset epilepsy. Recent long-term data extending into school age further suggest that prolonged ASM treatment does not reduce subsequent epilepsy risk or improve cognitive or functional outcomes.

CONCLUSIONS: The challenge is therefore shifting from "How do we stop the neonatal seizure?" to "What does this seizure mean for the child's future?"

Epilepsy Beyond Seizures – Transitioning of Patients with DEE into Adulthood

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Epilepsy is often defined and treated through the lens of seizures. Yet for many people living with epilepsy, seizures represent only one part of a much broader and more complex disease burden. Cognitive and developmental difficulties, behavioural and psychiatric comorbidities, sleep disturbances, medication adverse effects, social isolation, educational and employment challenges, and the impact on families may persist even when seizures are well controlled.

This talk will explore what it means to move beyond seizures and towards a more holistic understanding of epilepsy and its treatment. Particular attention will be given to children and young people with rare and complex epilepsies, in whom neurodevelopment, behaviour, communication, independence and quality of life may be profoundly affected by the underlying disease and its treatment. The transition from paediatric to adult care further highlights the need to address the person's changing medical, psychosocial and developmental needs rather than simply transferring seizure management.

Beyond seizure freedom, meaningful outcomes should include cognition, development, mental health, functioning, participation, quality of life and the ability of patients and families to achieve their own goals. This requires multidisciplinary care, continuity across the lifespan, meaningful patient and family involvement, and clinical research that measures outcomes that matter to patients—not only outcomes that are easiest to count.

Ultimately, treating epilepsy should mean treating the person, not simply treating the seizures.

Session 5 — Neurostimulation (VNS / taVNS / TMS) for Treatment of Brain Disorders in Children

Non-Invasive Brain and Nerve Stimulation in Children and Adolescents: Indications, Safety, Protocols and Efficacy of TMS, VNS, taVNS and Related Methods

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BACKGROUND: Non-invasive neuromodulation is established in adult psychiatry and neurology, but its use in the developing brain raises distinct questions of dosing, safety and evidence. Regulatory decisions in 2019–2025 (transcranial magnetic stimulation for adolescent depression, trigeminal stimulation for ADHD, auricular and cervical nerve stimulators for abdominal pain and migraine) have moved several techniques into paediatric practice ahead of definitive trials.

AIM: To summarise, for paediatric neurologists and non-specialists, the mechanisms, indications, protocols, safety and efficacy of transcranial magnetic stimulation (TMS), vagus nerve stimulation (VNS), transcutaneous auricular VNS (taVNS) and related transcranial electrical and cranial-nerve techniques in children and adolescents.

METHODS: Narrative review of systematic reviews, meta-analyses, randomised trials, safety guidelines and regulatory documents published to September 2026, with mechanisms grouped by site of action: suprathreshold cortical induction (TMS), subthreshold cortical polarisation (tDCS, tRNS, tPCS) and bottom-up brainstem activation via vagal, trigeminal or median-nerve afferents.

RESULTS: Children differ from adults in motor threshold, intracortical inhibition, skull thickness and plasticity, so adult dose tables do not transfer directly ^[1,2]. Pooled paediatric data (>4,000 children; one centre alone >3.5 million pulses) show adverse-event profiles comparable to adults, with rTMS-related seizures at roughly 0.1% per session, clustered in medicated adolescents ^[1,3,4]. In adolescent depression, the pivotal monotherapy trial was negative ^[5], whereas adjunctive trials pooled to SMD -0.93 with NNT 10 ^[6], with effects markedly smaller against sham than against no stimulation ^[14]; the FDA cleared two rTMS systems for ages 15–21 (2024, 2025) on registry data, and accelerated theta-burst shows rapid but transient benefit ^[7]. Signals in ADHD, autism and Tourette syndrome are small to moderate and rest on few trials ^[8,9]. In drug-resistant focal epilepsy, low-frequency rTMS achieved >50% seizure reduction in 76% versus 12.5% with sham in the first paediatric RCT ^[10]. Implanted VNS yields ~55% responders in children, is approved from age 4 and improves with time, at the cost of surgical complications ^[11]. taVNS has no paediatric device and only pilot data (neonatal feeding failure, epileptic encephalopathy with spike-wave activation in sleep, anxiety in autism) ^[12]. Among peripheral devices, auricular field stimulation for adolescent functional abdominal pain and median-nerve stimulation for tics are supported by single positive RCTs, whereas trigeminal stimulation for ADHD, cleared in 2019, failed a 150-patient phase 2b replication ^[13].

DISCUSSION: Short-term safety is reassuring when individualised thresholds, hearing protection, pre-session seizure-risk screening and parental consent with child assent are applied. Efficacy evidence is heterogeneous, frequently unblinded and short, and regulatory clearance has repeatedly preceded robust efficacy data. Long-term neurodevelopmental follow-up is almost absent.

CONCLUSIONS: Non-invasive stimulation in minors should be delivered in specialist centres or trials, framed within multimodal care and accompanied by systematic adverse-event recording. Priorities are developmentally informed dosing, credible sham control, durability beyond three months and paediatric-specific devices, particularly for taVNS.

Transcutaneous Auricular Vagus Nerve Stimulation in Pediatric Neuropsychiatry: From Clinical Evidence to Precision Neuromodulation

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BACKGROUND: Transcutaneous auricular vagus nerve stimulation (taVNS) has emerged as a promising non-invasive neuromodulation approach with potential applications across neurological and psychiatric disorders. Its favorable tolerability, accessibility, and suitability for home-based treatment make taVNS particularly attractive for pediatric populations. However, despite increasing clinical interest, important questions remain regarding its therapeutic effectiveness, safety, and optimal application during neurodevelopment.

AIM: This keynote critically examines the current evidence for taVNS in pediatric neuropsychiatry, identifies fundamental barriers to clinical translation, and outlines emerging strategies toward mechanistically informed, evidence-based, and personalized neuromodulation.

METHODS: A narrative synthesis of clinical trials, systematic reviews, experimental human studies, and translational research is presented, integrating emerging developments in computational modeling and real-world assessment.

RESULTS: Available evidence suggests therapeutic potential across several neurological and psychiatric conditions, including epilepsy and depression, alongside a generally favorable short-term safety profile. Nevertheless, pediatric efficacy data remain limited, and considerable heterogeneity in study designs, stimulation parameters, and treatment regimens restricts the interpretation and generalizability of findings. Furthermore, the neurobiological mechanisms underlying therapeutic effects remain insufficiently understood.

DISCUSSION: Three interconnected challenges are particularly relevant for advancing taVNS toward evidence-based clinical application. First, the absence of sufficiently validated biomarkers of vagal target engagement limits the ability to determine whether stimulation reliably recruits the intended neural pathways and produces meaningful downstream physiological effects. Second, the mechanisms linking peripheral stimulation to central nervous system activity, autonomic regulation, and ultimately clinical improvement remain incompletely characterized. Third, stimulation settings, treatment duration, frequency, and timing are rarely established through systematic dose-response investigations, particularly in developing populations. Emerging research strategies offer promising opportunities to address these challenges. In-silico models may help characterize individual differences in current distribution and neural recruitment, while reverse-translational experimental approaches can support causal investigations of stimulation mechanisms. Complementary real-world assessments of device use, treatment adherence, safety, and clinical outcomes may provide the evidence needed to optimize treatment regimens beyond controlled research settings.

CONCLUSIONS: Realizing the clinical potential of taVNS in pediatric neuropsychiatry requires moving beyond proof-of-concept studies toward a mechanistic understanding of therapeutic action and systematic optimization of stimulation delivery. Integrating experimental, computational, and real-world evidence may pave the way for developmentally informed, personalized, and ultimately more effective neuromodulation interventions.

Session 6 — Free Topics

RLS Syndrome (Restless Leg) Misdiagnosed As Epilepsy – Case Report

Filip Duma

BACKGROUND A 7-year-old girl diagnosed with epilepsy was recently referred to our clinic with potential DRE, as AEDs could not stop her seizures. At 3-years-old, her brother was diagnosed with autism and had irregular sleep patterns. On initial exam, she was a bright and well-adjusted girl, who had reached all the expected milestones for her age. On inspection, everything was normal. Her neurological exam revealed no abnormalities.

The main complaint was involuntary leg movement during sleep, often accompanied by tingling sensations. She was frequently awakened by the movements and stayed conscious throughout the paroxysm. These episodes were accompanied by left side facial twitching and headaches. The episodes repeated nightly. The applied OXC was ineffective.

AIM: Verifying diagnosis of Epilepsy.

METHODS Sleep EEG scheduled before the exam with normal base activity, sleep spindles K-waves and without paroxysmal activity. Clinical observation: After the EEG, she was still sleepy. While we were making plans for the next steps with her parents, the paroxysm started. The presentation was with involuntary leg movement (closest to bike riding), she was scared but was able to answer questions, temporarily control the legs when asked.

RESULTS: Normal EEG, serum Iron slightly below normal. An MRI was initially planned, but was delayed following the episode of leg movement during the examination, suggesting a benign condition of RLS (restless leg) syndrome.

DISCUSSION RLS is a condition that can occur at any age and create discomfort and sleep disturbances.

While many cases may be genetic or have no known cause, RLS is frequently triggered or worsened by specific medical conditions, deficiencies, and medications.

AEDs were discontinued, iron supplements were introduced, we advised sleep time sibling separation, regular physical activities and a short-term Melatonin. Soon, everything was back to normal.

CONCLUSIONS Finally, in this case, there were clear clinical signs to rule out the diagnosis of epilepsy. While RLS is not rare in children, the diagnosis of epilepsy should be always carefully assessed, as there are many conditions that can lead to misdiagnosis and unnecessary treatments. Extra care is to be exercised, since one condition does not exclude the other.

Tubulinopathy: Marked Intrafamilial Phenotypic Variability

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BACKGROUND: Tubulinopathies are rare genetic disorders characterized by congenital brain malformations and a broad clinical spectrum. Inherited variants may be difficult to interpret when transmitting parents appear unaffected, making characteristic neuroimaging findings particularly valuable.

AIM: To describe intrafamilial phenotypic variability associated with a novel TUBB missense variant and highlight the contribution of neuroimaging to diagnosis and variant reclassification.

METHODS: We report a familial case series involving two sisters and their mother. Clinical and developmental findings were integrated with brain MRI, trio exome sequencing in the proband and parents, and targeted genetic analysis in the younger sibling. Variant classification was reassessed according to ACGS guidelines, incorporating familial segregation and neuroimaging findings.

RESULTS: The proband presented at 6 months with tonic seizures, hypotonia and motor developmental delay. She subsequently developed epileptic spasms, pharmacoresistant epilepsy, severe global developmental delay and microcephaly. The younger sister was identified in the neonatal period after cranial ultrasonography revealed ventricular asymmetry and dysmorphic basal ganglia. She has no developmental delay at 20 months and no seizures. Their mother had no known neurological disability. MRI in all three demonstrated abnormalities characteristic of tubulinopathy, including asymmetric lateral ventricles, dysmorphic basal ganglia and asymmetric brainstem or posterior fossa malformations. All three carried the heterozygous TUBB variant (c.873G>T, p.Gln291His), initially classified as a variant of uncertain significance. Characteristic MRI findings in the younger sibling and mother, together with familial segregation and additional variant evidence, supported reclassification as likely pathogenic.

DISCUSSION: The shared neuroimaging phenotype contrasted with marked clinical variability, demonstrating complete neuroradiological penetrance but variable clinical expressivity within this family. An apparently unaffected transmitting parent and a negative family history should not exclude tubulinopathy. Neuroimaging can reveal unrecognized manifestations and strengthen the interpretation of inherited variants.

CONCLUSIONS: This family expands the phenotypic spectrum associated with TUBB-related tubulinopathy. Integrating clinical assessment, neuroimaging and genetic testing is essential for recognizing familial disease and interpreting uncertain variants, particularly when clinical severity differs substantially among relatives.

Body composition of Children with Spinal Muscular Atrophy: A Slovenian Retrospective Study

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BACKGROUND: Spinal muscular atrophy (SMA) is a rare neuromuscular disorder that can significantly affect patients' nutritional status. The disease can therefore lead to changes in body composition (BC). Depending on the extent of functional impairment, patients may be at increased risk of both malnutrition and overnutrition. Excess body mass may result from a lower basal metabolic rate due to reduced fat-free mass (FFM), combined with lower levels of physical activity. A reduced proportion of FFM may often be masked by a higher proportion of fat mass (FM), meaning that nutritional status assessment based solely on growth charts may be insufficient.

AIM: The aim of the study was to assess the nutritional status and body composition of children with SMA.

METHODS: This retrospective study included children with SMA treated at the Division of Paediatrics, University Medical Centre Ljubljana, Slovenia. Nutritional status was evaluated using body weight, body height, body mass index (BMI), and dual-energy X-ray absorptiometry (DXA). Each child with SMA was matched by age and gender with a healthy control.

RESULTS: The study included 42 children aged 1–19 years (20 females, 22 males): 21 children with SMA (Type I, n=2; Type II, n=11; Type III, n=8) and 21 healthy controls. During the study, 19 children received nusinersen and 2 received risdiplam. Children with SMA had an absolute FM similar to controls ($p=0.397$), but their relative FM was nearly 12% higher ($p<0.001$). In contrast, lean mass, FFM, and muscle mass were significantly lower in children with SMA ($p=0.026$, $p=0.026$, and $p=0.029$, respectively). Children with SMA had a 0.13 g/cm^2 lower bone mineral density (BMD), though this difference was not statistically significant. However, their BMD z-scores were significantly lower ($p<0.001$), with a mean z-score below -2 . A BMD z-score < -2 was observed in 52% of children with SMA, while 33% had a z-score below -3 , indicating a high prevalence of reduced BMD in this population.

DISCUSSION: Our findings are consistent with published literature demonstrating increased FM and reduced FFM in children with SMA. Poorer motor function and reduced energy expenditure likely drive this altered phenotype, accelerating the accumulation of excess FM.

CONCLUSIONS: These findings underscore the importance of specialised dietetic support as an integral part of the treatment and multidisciplinary care of children with SMA. Individualised dietary intervention is essential to appropriately adjust energy intake, minimise excessive fat accumulation, and support the preservation of FFM.

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**Prinašamo inovativne
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Reference:

1. Povzetek glavnih značilnosti zdravila Duvyatz® (gvinostat). Dostopno na: https://www.ema.europa.eu/sl/documents/product-information/duvyatz-epar-product-information_sl.pdf. Zadnji dostop: oktober 2026 | 2. Evropska agencija za zdravila. Dostopno na: <https://www.ema.europa.eu/en/news/new-treatment-against-duchenne-muscular-dystrophy>. Zadnji dostop: oktober 2026 | 3. Advancing Health Through Innovation: New Drug Therapy Approvals 2024. Dostopno na: <https://www.fda.gov/media/184967/download>. Zadnji dostop: oktober 2026

SKRAJŠAN POVZETEK GLAVNIH ZNAČILNOSTI ZDRAVILA Duvyatz / gvinostat

Ime zdravila: Duvyatz 8,86 mg/ml peroralna suspenzija. **Sestava zdravila:** En ml vsebuje 8,86 mg gvinostata (v obliki hidroklorida monohidrata). **Terapevtske indikacije:** Zdravljenje Duchennove mišične distrofije (DMD) pri pokretnih bolnikih, starih 6 let in več, ob sočasnem zdravljenju s kortikosteroidi. **Odmerjanje in način uporabe:** Zdravljenje z gvinostatom mora uvesti zdravnik, ki ima izkušnje z zdravljenjem Duchennove mišične distrofije. **Odmerjanje:** Pred začetkom zdravljenja z gvinostatom je treba pridobiti in oceniti izhodiščno število trombocitov in trigliceridov. Gvinostata se ne sme začeti uporabljati pri bolnikih s številom trombocitov, manjšim od $150 \times 10^9/l$. Število trombocitov in trigliceridov je treba med zdravljenjem spremljati v skladu s priporočili, da se ugotovi, ali so potrebne spremembe odmerka. Poleg tega je treba pri bolnikih z osnovno boleznijo srca ali bolnikih, ki sočasno jemljejo zdravila, ki povzročajo podaljšanje intervala QT, ob začetku zdravljenja z gvinostatom, med sočasno uporabo in kot je klinično indicirano, opraviti EKG. Priporočeni odmerek gvinostata je odvisen od telesne mase in ga je treba jemati peroralno dvakrat na dan. Za priporočene odmerke glejte celoten Povzetek glavnih značilnosti zdravila. Odločitev o nadaljevanju zdravljenja pri bolnikih, ki ne morejo hoditi, mora zdravnik sprejeti po lastni presoji na podlagi splošne ocene koristi in tveganja. **Prilagoditev odmerka zaradi trombocitopenije, driske ali hipertrigliceridemije:** Zmanjšanje odmerka je potrebno pri bolnikih s: številom trombocitov $< 150 \times 10^9/l$, potrjeno z dvema meritvama v enotedenskem intervalu, zmerno ali hudo drisko (več kot 4 odvajanja na dan) ali vrednostjo trigliceridov na tešče $> 300 \text{ mg/dl}$, potrjeno z dvema meritvama v enotedenskem intervalu. Za spremembo odmerjanja zaradi neželenih učinkov glejte celoten Povzetek glavnih značilnosti zdravila. Glede na resnost teh neželenih učinkov je treba razmisliti o prekinitvi zdravljenja pred spremembo odmerka. Bolniki ne smejo vzeti dvojnega ali dodatnega odmerka, če so odmerek izpustili. **Pediatrična populacija:** Varnost in učinkovitost zdravila Duvyatz pri otrocih, mlajših od 6 let, nista bili dokazani. Podatki niso na voljo. **Način uporabe:** Pred uporabo je treba suspenzijo stresati vsaj 30 sekund z obračanjem plastenke za 180° približno 40 krat in vizualno preveriti homogenost suspenzije. Zaradi nepravilnega stresanja lahko pride do prevelikega ali premajhnega odmerjanja. Zdravilo Duvyatz je treba jemati takšno, kot je [tj. ne sme se redčiti z vodo ali drugimi tekočinami]. Suspenzijo je treba dajati s priloženo grauirano brizgo za peroralno dajanje, s katero se odmeri ustrezen volumen suspenzije, ki ustreza predpisnemu odmerku za bolnika. Zdravilo Duvyatz je treba jemati skupaj s hrano, da se ublaži grenak okus gvinostata. **Kontraindikacije:** Preobčutljivost na učinkovino ali katero koli pomožno snov. **Posebna opozorila in previdnostni ukrepi:** **Hematološki učinki:** Gvinostat je povezan s trombocitopenijo, povezano z odmerkom, in drugimi znaki mielosupresije, vključno z zmanjšano vrednostjo hemoglobina in nevotropenijo. Pred začetkom zdravljenja z gvinostatom je treba opraviti popolno krvno sliko. Število trombocitov je treba med zdravljenjem z gvinostatom skrbno spremljati, tj. vsaka dva tedna prva dva meseca zdravljenja, 3. mesec in nato vsake tri mesece. V primeru vztrajne trombocitopenije je treba odmerek gvinostata prilagoditi. Zdravljenje je treba prekiniti, če nepravilnosti še vedno vztrajajo. Pri bolnikih, pri katerih je bil odmerek povečan zaradi povečanja telesne mase, je treba v prvih dveh mesecih po povečanju odmerka skrbno spremljati število trombocitov vsaka dva tedna. **Povečana vrednost trigliceridov:** Gvinostat je povezan s povečanjem serumskih trigliceridov. Pred začetkom zdravljenja z gvinostatom je treba izmeriti raven trigliceridov. Trigliceride je treba spremljati vsaj v tretjem mesecu zdravljenja, šestem mesecu in nato vsakih 6 mesecev. Pri bolnikih z DMD, pri katerih se raven trigliceridov na tešče vztrajno povečuje ($> 300 \text{ mg/dl}$), je treba odmerek gvinostata prilagoditi. Zdravljenje z gvinostatom je treba prekiniti, če vrednosti trigliceridov kljub ustreznemu prehranskemu ukrepanju in prilagoditvi odmerka ostanejo povišani. **Prebavne motnje:** Driska in bruhanje sta bila zelo pogosta neželena učinka zdravila v kliničnih preskušanjih gvinostata pri bolnikih z DMD. Driska in bruhanje se običajno pojavita v prvih nekaj tednih po začetku zdravljenja z gvinostatom. Med zdravljenjem z gvinostatom se lahko razmisli o uporabi antiemetikov ali antiidiaroidov. Tekočino in elektrolite je treba po potrebi nadomeščati, da se prepreči dehidracija. V primeru zmerne ali hude driske (več kot 4 odvajanja na dan) je treba odmerek gvinostata prilagoditi. Zdravljenje je treba prekiniti, če nepravilnosti še vedno vztrajajo. **Podaljšanje intervala QTc:** Gvinostat lahko povzroči podaljšanje intervala QTc pri odmerkih, ki so 5-krat večji od priporočenega odmerka. Gvinostat je treba previdno uporabljati pri bolnikih s povečanim tveganjem za ventrikularne aritmije (vključno s torsades de pointes), bolnikih s prirojenim sindromom dolgega QT, koronarno boleznijo, motnjami elektrolitov ali sočasno uporabo drugih zdravil, za katera je znano, da povzročajo podaljšanje intervala QT. Pri teh bolnikih je treba ob začetku zdravljenja z zdravilom Duvyatz, med sočasno uporabo in kot je klinično indicirano opraviti EKG. Pri bolnikih s hipokaliemijo jo je treba odpraviti pred začetkom zdravljenja z gvinostatom in jo spremljati v primeru dehidracije zaradi diareje. Zdravilo Duvyatz je treba prekiniti, če je interval QTc $> 500 \text{ ms}$ ali če je sprememba glede na izhodiščno vrednost $> 60 \text{ ms}$. **Pomožne snovi z znanim učinkom:** Bolniki z dedno intoleranco za fruktozo (HFI) ne smejo vzeti tega zdravila. To zdravilo vsebuje 400 mg sorbitola v vsakem ml, kar je enako 40 mg/kg. Upoštevati je treba dodatni učinek sorbitola jemanja zdravil, ki vsebujejo sorbitol (ali fruktozo), in sorbitola (ali fruktoze), ki ga vnesemo s hrano. Količina sorbitola v zdravilih za peroralno uporabo lahko vpliva na biološko uporabnost drugih zdravil za peroralno uporabo, ki se jemljejo sočasno. To zdravilo vsebuje 4,4 mg natrijevega benzoata v vsakem ml, kar je enako 0,44 mg/kg. To zdravilo vsebuje manj kot 1 mmol (23 mg) natrija na odmerek, kar v bistvu pomeni »brez natrija«. **Medsebojno delovanje z drugimi zdravili in druge oblike interakcij:** Pri predpisovanju zdravila Duvyatz je potrebna previdnost, če ga uporabljamo sočasno z zdravili, za katera je znano, da podaljšujejo interval QT z znanim ali možnim tveganjem za torsades de pointes, npr. anestetiki (npr. sevofluran, propofol), antiaritmiki razreda III (npr. amiodaron, sotalol), antiemetiki (ondansetron), antibiotiki (azitromicin, klaritromicin, ciprofloksacin), antimitotiki (flukonazol), antipsihotiki (aripiprazol, risperidon) in antihistaminiki (npr. famotidin). Ta seznam je okviren in ni izčrpen. Učinek sočasne uporabe zdravila Duvyatz z antitrombotičnimi zdravili na število trombocitov ni znan. Zdravilo Duvyatz je treba previdno uporabljati pri bolnikih, ki sočasno jemljejo zdravila, za katera je znano, da povečujejo vrednosti trigliceridov, saj se lahko poveča tveganje za hipertrigliceridemijo. **Učinek gvinostata na farmakokinetiko drugih zdravil:** Šibko zaviranje CYP3A4, predvsem v črevesju, se je pokazalo v študiji o medsebojnem delovanju zdravil (DDI – Drug-Drug Interaction) pri ljudeh. Pri sočasni uporabi gvinostata z zdravili, ki so substrati CYP3A4 in imajo ozko terapevtsko območje, je potrebna previdnost. Ni mogoče izključiti možnosti zaviranja črevesnega prenašalnega proteina P-gp. Zdravila, za katera je znano, da so substrat prenašalca P-gp in imajo ozko terapevtsko območje, je treba z gvinostatom uporabljati previdno. Pri meritvah kreatinina so in vitro in v kliničnih preskušanjih z gvinostatom ugotovili šibko zaviranje ledvičnega privzemnega transporterja OCT2. Zdravila, za katera je znano, da so substrat transporterja OCT2 in imajo ozko terapevtsko območje, je treba z gvinostatom uporabljati previdno. **Neželeni učinki:** Spodaj so navedeni neželeni učinki, o katerih so v študiji EPIDYS poročali pri bolnikih, zdravljenih z gvinostatom, s pogostnostjo večjo kot 2 % v primerjavi z bolniki zdravljenimi s placebom. Zelo pogosti ($\geq 1/10$): trombocitopenija, hipertrigliceridemija, driska, bruhanje, bolečine v trebuhu, pireksija. Pogosti ($\geq 1/100$ do $< 1/10$): gastroenteritis, zmanjšan apetit, tesnoba, omotica, hematomi, konstipacija, eritem, izpuščaj, mialgija, artralgija, mišična oslabeledost, utrujenost, povečanje ščitnično stimulirajočega hormona v krvi. **Način in režim predpisovanja in izdaje zdravila:** Predpisovanje in izdaja zdravila je le na recept zdravnika specialista ustreznega področja medicine ali od njega pooblaščenega zdravnika. **Imetnik dovoljenja za promet:** Italfarmaco S.p.A., Viale F. Testi, 330, 20126 Milano, Italija. **Pred predpisovanjem, prosimo, preberite Povzetek glavnih značilnosti zdravila. Datum revizije besedila:** 06/2026.

▼ Za to zdravilo se izvaja dodatno spremljanje varnosti.

Tako bodo hitreje na voljo nove informacije o njegovi varnosti. Zdravstvene delavce naprošamo, da poročajo o katerem koli domnevnem neželenem učinku zdravila.



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Pri zdravljenju DMD šteje vsak dan



Zaviralec histonske deacetilaze (HDAC) – prvi te vrste za zdravljenje Duchennove mišične distrofije pri pokretnih bolnikih, starih 6 let in več, ob sočasnem zdravljenju s kortikosteroidi.¹⁻³

- **Edinstven mehanizem delovanja:** je zaviralec histonske deacetilaze (HDAC) razreda I in II, ki uravnava nenadzorovano aktivnost HDAC v distrofičnih mišicah.¹
- **Širok terapevtski učinek:** zmanjšuje poškodbe mišičnih vlaken, fibrozo, odlaganje maščob, kronično mišično vnetje in spodbuja biogenezo mitohondrijev.¹
- **Učinkovitost, neodvisna od mutacije:** učinkovit neodvisno od osnovne mutacije gena za distrofin, ki povzroča bolezen.¹
- **Dosežena primarna končna točka v študiji EPIDYS:** zdravilo Duvyzat® je pomembno zmanjšalo upad časa, potrebnega za prehod 4 stopnic, v primerjavi s placebom ($p = 0,035$).¹
- **Bolniku prijazna administracija zdravila:** peroralna suspenzija, ki se odmerja glede na telesno maso in jemlje dvakrat na dan skupaj s hrano.¹