NURAID II ™ (MLC 901)
PODPORA PRIRODZENEJ REGENERÁCIE MOZGU

DC. MUDR. GMITTEROVÁ KARIN, PHD.

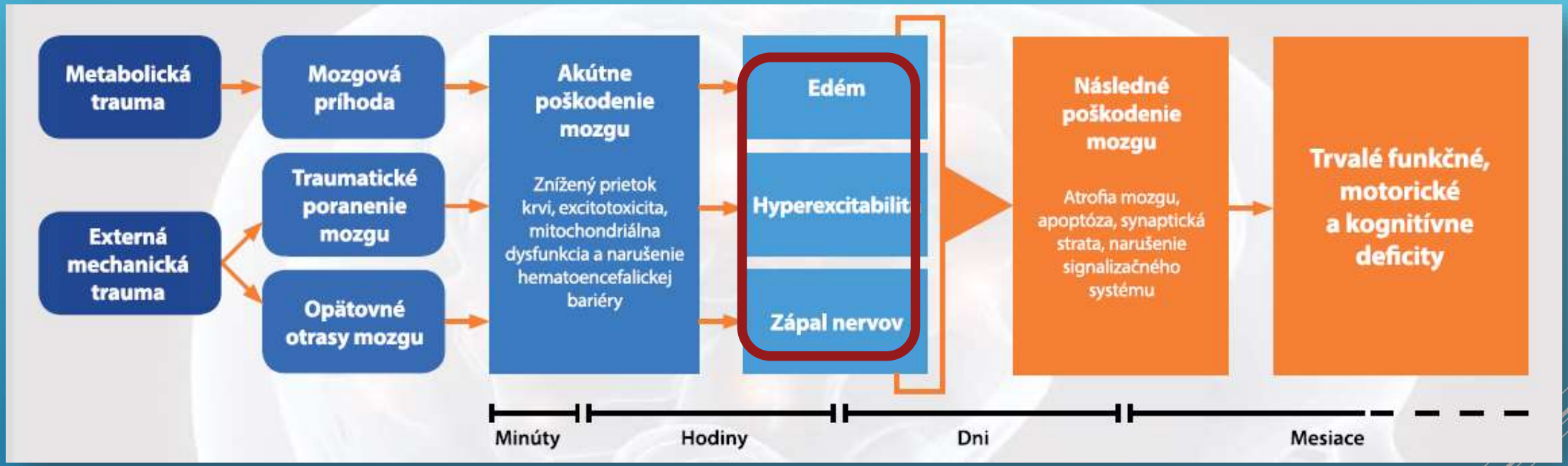
EPIDEMIOLÓGIA

Na Slovensku je približne 400 prípadov náhlych cievnych mozgových príhod a 200 prípadov TBI na 100 000 obyvateľov*

Štatistika CMP a TBI na Slovensku* - potenciál produktu NurAiD™II**

*National Registry of Neurological Diseases
**Data on file - Physicians survey

PODOBNOSTI MEDZI CMP A TBI



- CMP a TBI sú dve patologické udalosti s podobnými biologickými procesmi, ktoré vedú k poškodeniu mozgu a klinickým deficitom

Mozog má schopnosť prirodzenej reparácie po poranení.

<u>Reparácia však môže byť obmedzená a neúplná.</u>

NurAiD™II (MLC 901)

NurAiD™II je klinicky overený a bezpečný produkt, určený pre ľudí po CMP alebo po TBI.

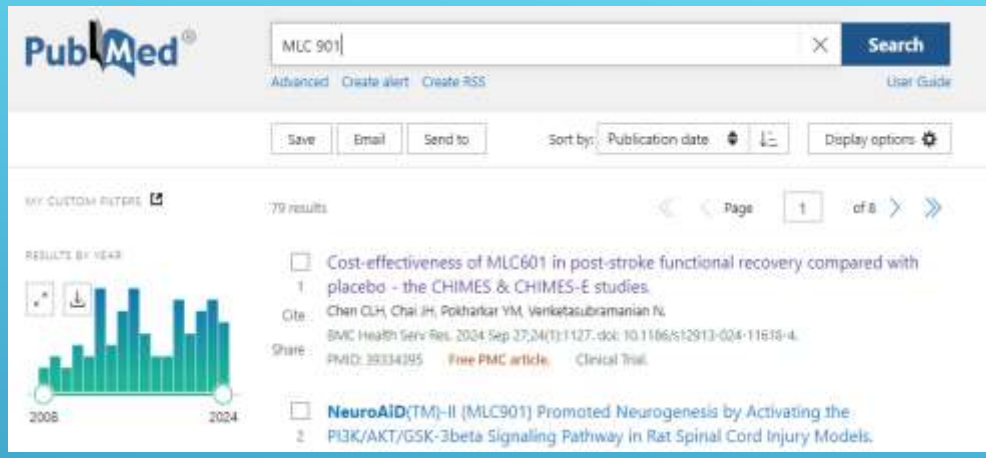
NurAiD™II obsahuje 9 zložiek rastlinného pôvodu, ktoré sú vybrané tak, aby zaistili účinnosť a zároveň bezpečnosť.

NurAiD™II (MLC 901)

Zoznam rastlinných zložiek (9)

- Koreň kozinca blanitého
- Koreň angeliky čínskej
- Koreň šalvie červenokorennej
- Koreň pivonky bielokvetej
- Koreň horčinky
- Koprníček čínsky
- Puškvorec tatrinov
- Jadro broskyne
- Sušený kvet požltu farbiarskeho

MLC 901 - NurAiD™II



- 41 publikácií v renomovaných vedeckých a odborných časopisoch týkajúcich sa mechanizmu účinku, bezpečnosti a účinnosti
- 79 klinicky orientovaných štúdií (pubmed)
- Registrovaný v 38 krajinách sveta
- SR 2013-2023 liečených **2500 pacientov**

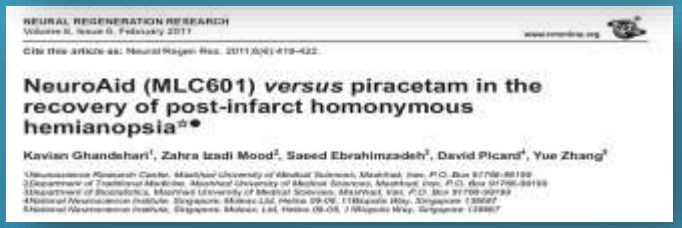
NurAiD™II je neustále vyvíjaný a jeho účinnosť je potvrdená klinickými štúdiami

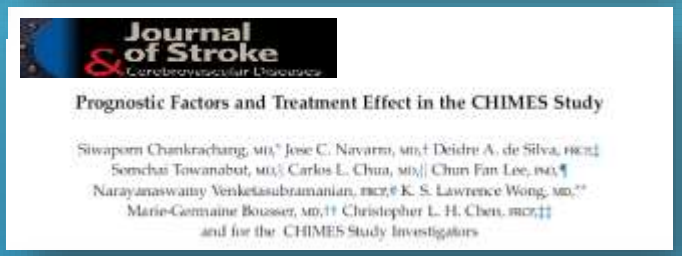

Stroke
American Stroke Association
A Division of American Heart Association
Danqi Piantang Jiannang (DJ), a Traditional Chinese Medicine, in Poststroke Recovery
Christopher Chen, N. Venketasubramanian, Robert N. Gan, Caroline Lambert, David Picard, Bernard P.L. Chan, Edwin Chan, Marie G. Boisser and Shi Xiaonin
Stroke published online Jan 22, 2009;
DOI: 10.1161/STROKEAHA.108.531616


Cerebrovascular Diseases
Efficacy and Safety of MLC601 (NeuroAiD™), a Traditional Chinese Medicine, in Poststroke Recovery: A Systematic Review
Fahad Javaid Siddiqui, Narayanaswamy Venketasubramanian, Edwin Shih-Yen Chan, Christopher Chen


International Journal of Stroke
Short report
Baseline characteristics and treatment response of patients from the Philippines in the CHIMES study
Jose C. Navarro, Herminigildo H. Gan, Annabelle Y. Lao, Alejandro C. Baroque II, John H. B. Hiyadan, Carlos L. Chua, Ma. Cristina San Jose, Joel M. Advincula, Chun Fan Lee, Marie-Germaine Bousser, Christopher L. H. Chen, for the CHIMES Study Investigators


Cerebrovascular Diseases
Original Paper
A Double-Blind, Placebo-Controlled, Randomized Phase II Pilot Study to Investigate the Potential Efficacy of the Traditional Chinese Medicine Neuroaid (MLC 601) in Enhancing Recovery after Stroke (TIERS)
Keng He Kong, Seng Kwee Wee, Chwee Yin Ng, Karen Chua, Kay Fei Chan, N. Venketasubramanian, Christopher Chen


NEURAL REGENERATION RESEARCH
NeuroAid (MLC601) *versus* piracetam in the recovery of post-infarct homonymous hemianopsia
Kavian Ghandehari, Zahra Izadi Mood, Saeed Ebrahimzadeh, David Picard, Yue Zhang


Journal of Stroke & Cerebrovascular Diseases
Prognostic Factors and Treatment Effect in the CHIMES Study
Siwaporn Chankrachang, Jose C. Navarro, Deidre A. de Silva, Somchai Towanabut, Carlos L. Chua, Chun Fan Lee, Narayanaswamy Venketasubramanian, K. S. Lawrence Wong, Marie-Germaine Bousser, Christopher L. H. Chen, and for the CHIMES Study Investigators


European Journal of Internal Medicine
The effect of NeuroAiD™ (MLC601) on cerebral blood flow velocity in subjects' post brain infarct in the middle cerebral artery territory


Stroke
American Heart Association | American Stroke Association
Chinese Medicine Neuroaid Efficacy on Stroke Recovery: A Double-Blind, Placebo-Controlled, Randomized Study
Christopher L.H. Chen, Sherry H.Y. Young, Herminigildo H. Gan, Rajinder Singh, Annabelle Y. Lao, Alejandro C. Baroque II, Hui Meng Chang, John Harold B. Hiyadan, Carlos L. Chua, Joel M. Advincula, Sombat Muengtaweeponsa, Bernard P.L. Chan, H. Anita de Silva, Somchai Towanabut, Nijasri C. Suwanwela, Niphon Poungvarin, Siwaporn Chankrachang, K.S. Lawrence Wong, Gaik Bee Eow, Jose C. Navarro, Narayanaswamy Venketasubramanian, Chun Fm Lee and Marie-Germaine Bousser for the CHIMES Study Investigators
Stroke. 2013;44:2093-2100: originally published online June 18, 2013;
doi: 10.1161/STROKEAHA.113.002055


JOURNAL OF EVIDENCE-BASED MEDICINE
ARTICLE
The value of patient selection in demonstrating treatment effect in stroke recovery trials: lessons from the CHIMES study of MLC601 (NeuroAiD)
Narayanaswamy Venketasubramanian, Chun Fan Lee, K. S. Lawrence Wong and Christopher L. H. Chen


Research Article
Safety and Efficacy of MLC601 in Iranian Patients after Stroke: A Double-Blind, Placebo-Controlled Clinical Trial
A. A. Harandi, R. Abolfazli, A. Hatemian, K. Ghraguzlee, M. Ghaffar-Pour, M. Karimi, S. Shahbegi, H. Pakdaman, M. Tabasi, A. L. Tabatabae, and A. Nourian

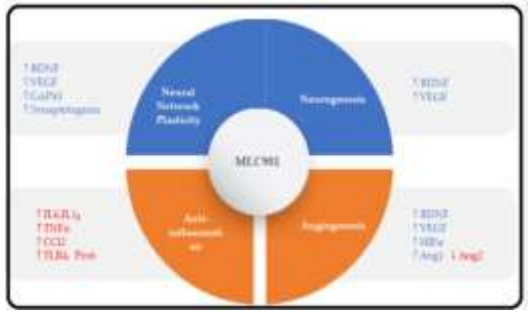

Stroke
American Heart Association | American Stroke Association
Effects of MLC601 on Early Vascular Events in Patients After Stroke: The CHIMES Study
Christopher L.H. Chen, Narayanaswamy Venketasubramanian, Chun Fan Lee, K.S. Lawrence Wong and Marie-Germaine Bousser
Stroke published online October 17, 2013;


Cerebrovascular Diseases
Original Paper
CHinese Medicine NeuroAiD Efficacy on Stroke Recovery – Extension Study (CHIMES-E): A Multicenter Study of Long-Term Efficacy
Narayanaswamy Venketasubramanian, Sherry H. Young, San San Tay, Thinagnanam Umapathi, Annabelle Y. Lao, Herminigildo H. Gan, Alejandro C. Baroque II, Jose C. Navarro, Hui Meng Chang, Joel M. Advincula, Sombat Muengtaweeponsa, Bernard P.L. Chan, Carlos L. Chua, Nirmala Wijekoon, H. Anita de Silva, John Harold B. Hiyadan, Nijasri C. Suwanwela, K.S. Lawrence Wong, Niphon Poungvarin, Gaik Bee Eow, Chun Fan Lee, Christopher L.H. Chen, for the CHIMES-E Study Investigators

Multimodálny potenciál účinku

Účinky výživového doplnku NurAiD™II sú dôležité ako pri cievnej mozgovej príhode, tak aj pri traumatickom poranení mozgu.

Plasticita neurónovej siete	» Zosilňuje expresiu mozgového neurotrofického faktora (BDNF), ktorý ovplyvňuje životaschopnosť buniek, posilnenie neurónovej siete, zlepšenie jej plasticity a neurogenézu. Stimuluje synaptogenézu a rast neuritov. [1,2]
Neurogenéza	» Zvyšuje tvorbu plne diferencovaných a funkčných neurónových buniek. [1,2]
Angiogenéza	» Zlepšuje a stabilizuje mikrocirkuláciu v odumretej oblasti. [3]
Modulácia zápalov	» Moduluje expresiu a aktivitu mediátorov činných pri neurónových zápaloch. [4]

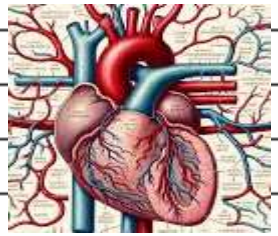


Vďaka svojmu multimodálnemu pôsobeniu NurAiD™II pomáha naštartovať proces obnovy.

Tento dokument poskytuje vedecké dáta a informácie určené len odborníkom v oblasti zdravotnej starostlivosti.

- **Plasticita neurónovej siete:** Zosilňuje sebaobranné a samoreparačné procesy mozgu (BDGF, synaptotagmín)
- **Neurogenéza:** Podporuje neurogenézu a zrenie nových buniek (BDGF)
- **Angiogenéza:** Stimuluje vznik nových ciev a podieľa sa tak na reparácii neurovaskulárnej jednotky (VEGF...)
- **Modulácia zápalu:** Reparuje vplyvom modulácie vrodenej imunity (TNF-a, TLR-4)

MLC901's Multimodal Mode of Action	MLC901 Ingredients
Effects on brain lesion recovery (1): brain tissue	
- Promotes neuroplasticity and prevents the loss of axons and synapses	*Radix Astragali*
- Promotes neurogenesis and slows down neurodegeneration	*Radix Astragali and Rhizoma Acori tatarinowii*
- Anti-inflammatory effect	*Radix Salviae miltiorrhizae and Carthamus tinctorius Semen persica*
- Improve hypoxia	*Radix Astragali, Radix Salviae miltiorrhizae, Radix Paeonia rubra, and Carthamus tinctorius*
Effects on brain lesion recovery (2): cerebral vascularization	
- Increases cerebral blood flow	*Rhizoma Chuanxiong and Semen persica*
- Improve microcirculation	*Rhizoma Chuanxiong, Radix Salviae miltiorrhizae, and Carthamus tinctorius*
- Protects the cardiovascular system	*Radix Astragali*
- Antithrombotic effect	*Radix Astragali, Rhizoma Chuanxiong, Radix Angelicae sinensis, Radix Paeonia rubra,and Semen persica*
- Anti-atherosclerotic properties	*Radix Salviae miltiorrhizaeand Carthamus tinctorius*
- Improves hemodynamics, reduces vascular resistance, and reduces blood viscosity	*Radix Salviae miltiorrhizae Rhizoma, Chuanxiong, Carthamus tinctorius, and Semen persica*
Effects on cognition and memory	
- Improves cognitive dysfunction	*Radix Polygalae and Rhizoma Acori tatarinowii*
- Attenuates memory deficits	*Radix Astragali, Radix Polygalae, Carthamus tinctorius, Semen persica, and Rhizoma Acori tatarinowii*
Cardiac protection	
- Protective effect on myocardial ischemia and increase in myocardial blood flow and oxygen supply	*Rhizoma Chuanxiong, Radix Angelicae sinensisRadix Salviae miltiorrhizae, and Carthamus tinctorius*
- Antagonizes arrhythmia	*Radix Astragali, Radix Salviae miltiorrhizaeCarthamus tinctorius, and Rhizoma Acori tatarinowii*
Protection against CV risk factors	
- Antihypertensive	*Rhizoma Chuanxiong and Radix Salviae miltiorrhizae*
- Lipid lowering	*Radix Astragali, Radix Salviae miltiorrhizae,and Carthamus tinctorius*
Effects on frequent diseases concomitant to brain lesions	
- Anti-infectious	*Radix Salviae miltiorrhizae, Radix Paeonia rubra, and Rhizoma Acori tatarinowii*
- Anticonvulsant	*Radix Paeonia rubra, Carthamus tinctorius, and Rhizoma Acori tatarinowii*

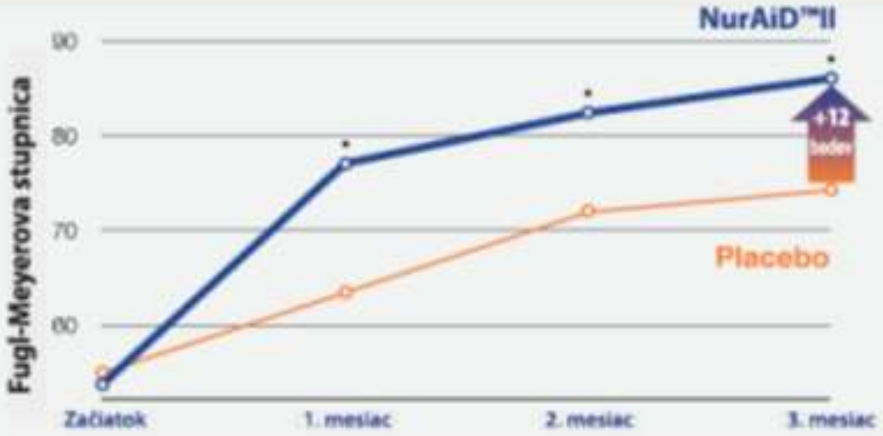


NurAiD™II Cievne príhody

- Zlepšuje **motorické funkcie** (metaanalýza)
- **Cerebrálny prietok** (CBF) vyšší voči placebu

Motorické funkcie

- Klinická štúdia s placebo kontrolnou skupinou so 150 pacientmi po ischemickej mozgovej príhode s deficitmi horných a dolných končatín s náborom do jedného mesiaca od mozgovej príhody.
- Podávanie NurAiD™II alebo kontrolného placeba po dobu 3 mesiacov.



- **Značné zlepšenie motorických funkcií bolo spozorované už v prvom mesiaci** terapie.
- **Účinky pretrvávajú počas celej doby** až do 3 mesiacov, **preukazujúc zrýchlenú a optimalizovanú obnovu.**

Štúdia CHIMES-E [7, 8]

- Medzinárodná multicentrická klinická štúdia s náhodným výberom a placebo kontrolnou skupinou (N=880) pacientov po ischemickej mozgovej príhode s náborom do 72 hod. po mozgovej príhode.
- NurAiD™II alebo kontrolné placebo podávané po dobu 3 mesiacov s kontrolami až do 2 rokov.
- Analýza 380 pacientov, ktorí boli rehabilitovaní po dobu 3 mesiacov.

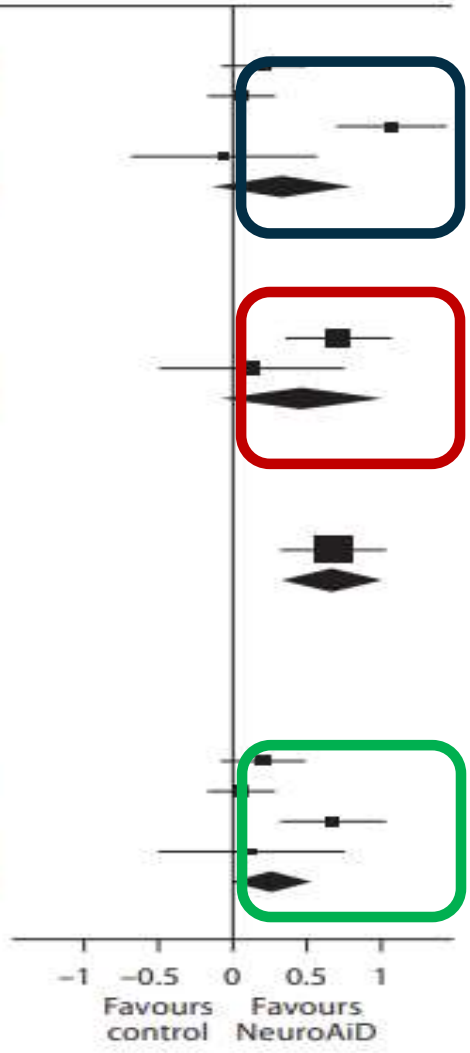
- **Zdvojnásobená šanca na dosiahnutie funkčnej samostatnosti** (definovaná ako mRS 0-1).
- **Pozitívne účinky pozorované už v 3. mesiaci** a pretrvávajúce až po dobu **2 rokov.**
- **Značné zlepšenie aktivít v každodennom živote** (Barthelov index

- **zlepšenie motorických funkcií už v 1. mesiaci**
- v kombinácii s RHB- **zdvojnásobenie šance na dosiahnutie funkčnej nezávislosti voči RHB samotnej**

Venketasubramanian N et al. Cerebrovasc Dis., 2015

NurAiD™II Cievne príhody

Study or subgroup	NeuroAiD mean	NeuroAiD SD	NeuroAiD total	Control mean	Control SD	Control total	Weight %	Standard mean difference IV, random (95% CI)
At 1 month								
China 01 [7]	1.44	1.83	100	1.04	1.97	100	27.1	0.21 (–0.07 to 0.49)
China 02 [7]	1.21	1.83	300	1.1	1.94	105	28.0	0.06 (–0.16 to 0.28)
Harandi [14]	23.44	14.03	100	8.4	13.89	50	25.4	1.07 (0.71–1.43)
Kong [15]	11.7	14.6	20	12.5	12.2	20	19.5	–0.06 (–0.68 to 0.56)
Subtotal			520			275	100.0	0.33 (–0.13 to 0.80)
Heterogeneity: $\tau^2 = 0.19$; $\chi^2 = 23.58$, d.f. = 3 ($p < 0.0001$), $I^2 = 87\%$								
Test for overall effect: Z = 1.41 (p = 0.16)								
At 2 months								
Harandi [14]	28.82	17.55	100	17.1	13.54	50	59.9	0.71 (0.36–1.06)
Kong [15]	16.7	19.6	20	14.5	14.2	20	40.1	0.13 (–0.49 to 0.75)
Subtotal			120			70	100.0	0.48 (–0.09 to 1.04)
Heterogeneity: $\tau^2 = 0.11$; $\chi^2 = 2.62$, d.f. = 1 ($p = 0.11$), $I^2 = 62\%$								
Test for overall effect: Z = 1.66 (p = 0.10)								
At 3 months								
Harandi [14]	32.53	21.61	100	19.4	13.23	50	100.0	0.68 (0.33–1.03)
Subtotal			100			50	100.0	0.68 (0.33–1.03)
Total events								
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.82 (p = 0.0001)								
At end of study								
China 01 [7]	1.44	1.83	100	1.04	1.97	100	29.0	0.21 (–0.07 to 0.49)
China 02 [7]	1.21	1.83	300	1.1	1.94	105	32.3	0.06 (–0.16 to 0.28)
Harandi [14]	32.53	21.61	100	19.4	13.23	50	25.0	0.68 (0.33–1.03)
Kong [15]	16.7	19.6	20	14.5	14.2	20	13.7	0.13 (–0.49 to 0.75)
Subtotal			520			275	100.0	0.27 (–0.02 to 0.55)
Heterogeneity: $\tau^2 = 0.05$; $\chi^2 = 8.77$, d.f. = 3 ($p = 0.03$); $I^2 = 66\%$								
Test for overall effect: Z = 1.85 (p = 0.06)								
Test for subgroup differences: $\chi^2 = 3.43$, d.f. = 3 ($p = 0.33$), $I^2 = 12.4\%$								



Venketasubramanian N et al. Biomolecules, 2024

NurAiD™II Cievne príhody

- Zlepšuje **funkčnosť** pacienta (metaanalýza)
- Vizuálny defekt (voči piracetamu)

Study or subgroup	NeuroAiD events	NeuroAiD total	Control events	Control total	Weight %	Risk ratio M-H, random (95% CI)
At 1 month						
China 01 [7]	20	100	6	100	48.9	3.33 (1.40–7.95)
China 02 [7]	30	300	6	105	51.1	1.75 (0.75–4.09)
Subtotal		400		205	100.0	2.40 (1.28–4.51)
Total events	50		12			
Heterogeneity: $\tau^2 = 0.02$; $\chi^2 = 1.08$, d.f. = 1 ($p = 0.30$); $I^2 = 8\%$						
Test for overall effect: $Z = 2.71$ ($p = 0.007$)						
At 3 months						
Shahripour [16]	2	36	1	32	100.0	1.78 (0.17–18.69)
Subtotal		36		32	100.0	1.78 (0.17–18.69)
Total events	2		1			
Heterogeneity: Not applicable						
Test for overall effect: $Z = 0.48$ ($p = 0.63$)						
At end of study						
China 01 [7]	20	100	6	100	45.7	3.33 (1.40–7.95)
China 02 [7]	30	300	6	105	48.0	1.75 (0.75–4.09)
Shahripour [16]	2	36	1	32	6.2	1.78 (0.17–18.69)
Subtotal		436		237	100.0	2.35 (1.31–4.23)
Total events	52		13			
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 1.14$, d.f. = 2 ($p = 0.57$), $I^2 = 0\%$						
Test for overall effect: $Z = 2.85$ ($p = 0.004$)						
Test for subgroup differences: $\chi^2 = 0.06$; d.f. = 2 ($p = 0.97$), $I^2 = 0\%$						

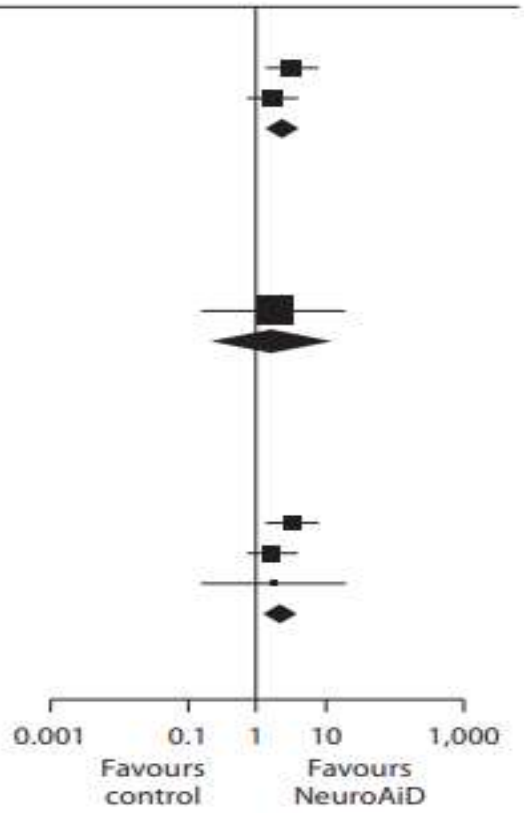


Fig. 3. Functional independence as measured by the BI (≥85) or DTER (≤2; comprehensive functions; item 8) among patients with stroke. M-H = Mantel-Haenszel method.

Venketasubramanian N et al. Biomolecules, 2024

NurAiD™II Cievne príhody

- Po 3 mesačnom užívaní, **je potvrdené 50% zníženie výskytu včasných kardiovaskulárnych príhod**(recidíva mozgovej príhody, akútne koronárne príhody....)

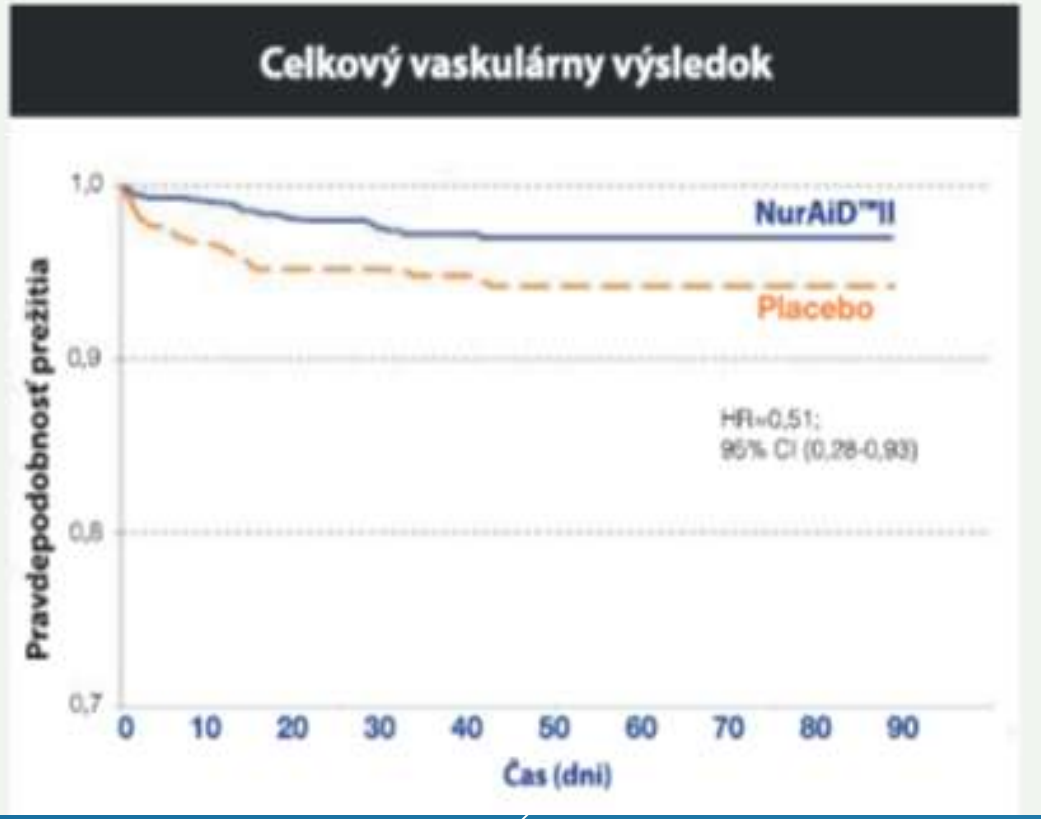
Post hoc analýza vykonaná na dátach štúdie CHIMES.

Medzinárodná, multicentrická klinická štúdia s náhodným výberom a placebo kontrolnou skupinou (N=1099) pacientov po ischemickej mozgovej príhode s náborom do 72 hod. po príhode.

Pacienti zapojení do štúdie užívali NurAiD™II alebo placebo po dobu 3 mesiacov s kontrolou až do 2 rokov.

Pri užívaní výživového doplnku NurAiD™II v 3-mesačnom cykle, je potvrdené značné (50%) zníženie výskytu včasných kardiovaskulárnych príhod u pacientov po ischemickej mozgovej príhode.

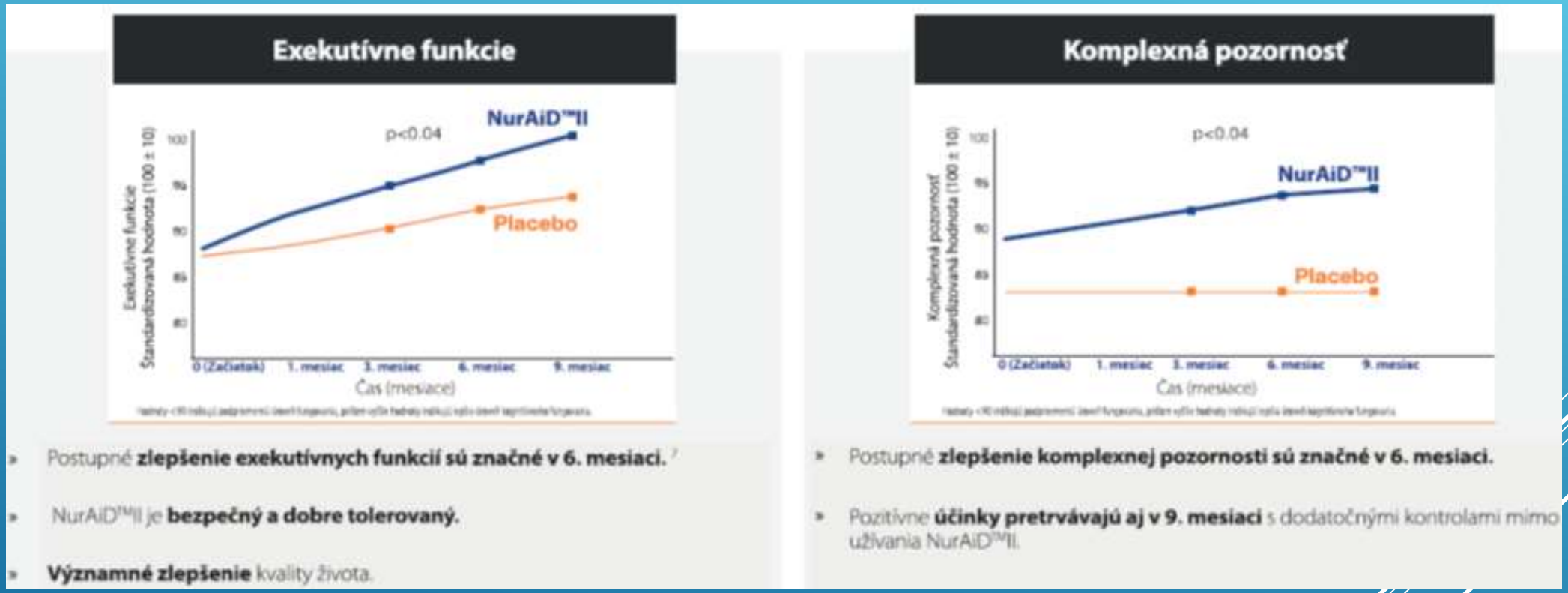
Včasné vaskulárne príhody sú definované ako opätovné mozgové príhody, akútne koronárne príhody a vaskulárna smrť (podľa stupnice FMA).



Suwanwela NC et al. Cerebrovasc Dis. 2018

NurAiD™II Traumatické postihnutie (TBI)

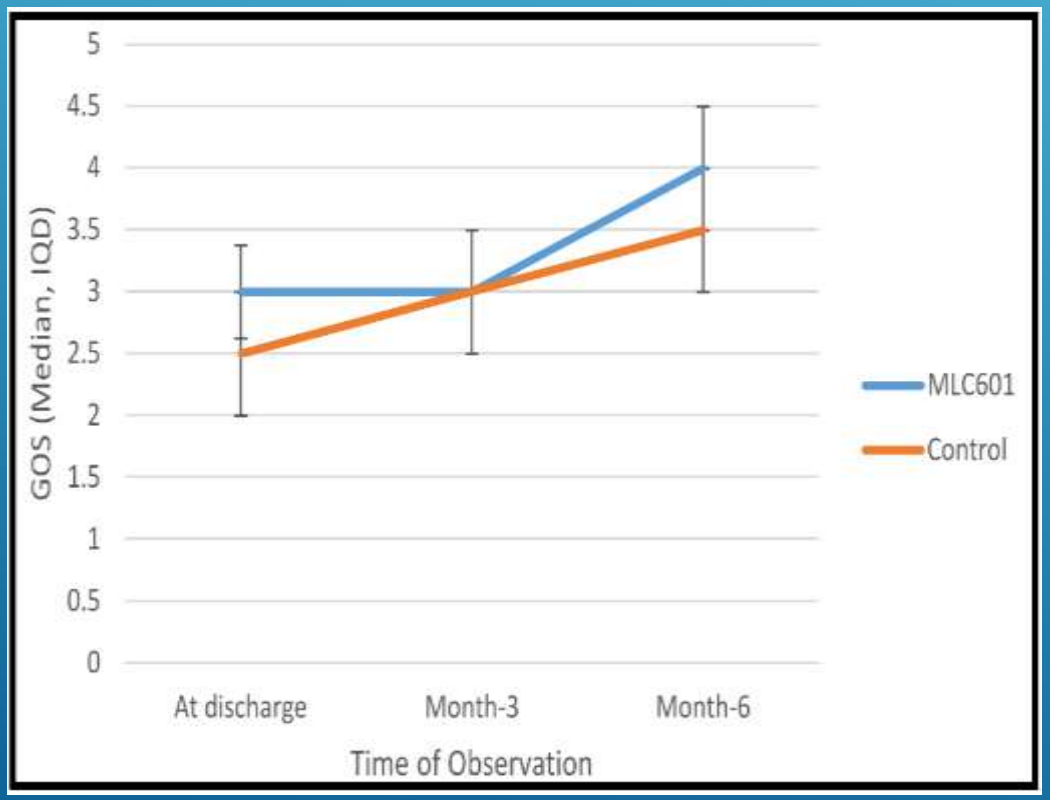
- **BRAINS štúdia** (6-mes) u ľahkej TBI (n = 36) **zlepšenie exekutívnych funkcií a komplexnej pozornosti, zlepšenie kvality života** (9 mes.)

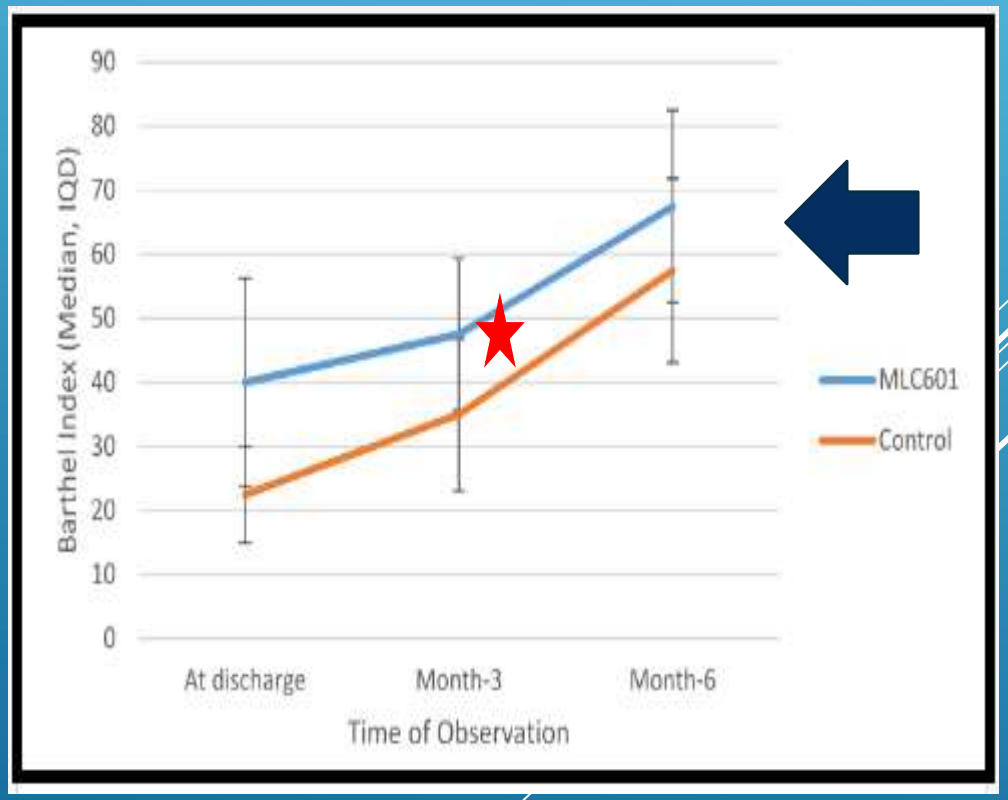


SAMURAI štúdia placebom kontrolovaná (6-mes) u ľahkej TBI (n = 92; placebo, n = 90) **bez efektu na kognitívne fungovanie** avšak **zlepšenie neurobehaviorálnych** schopností (úzkosť, depresia) a **kvality života**

NurAiD™II Traumatické postihnutie (TBI)

- **NEPTUN** (6-mes) u ľahkej/stredne ťažkej TBI (n = 16) **zlepšenie funkčnosti**, **bez nežiadúcich účinkov**





NEPTUN štúdia - Al Fauzi, A et al Brain Sci. 2020

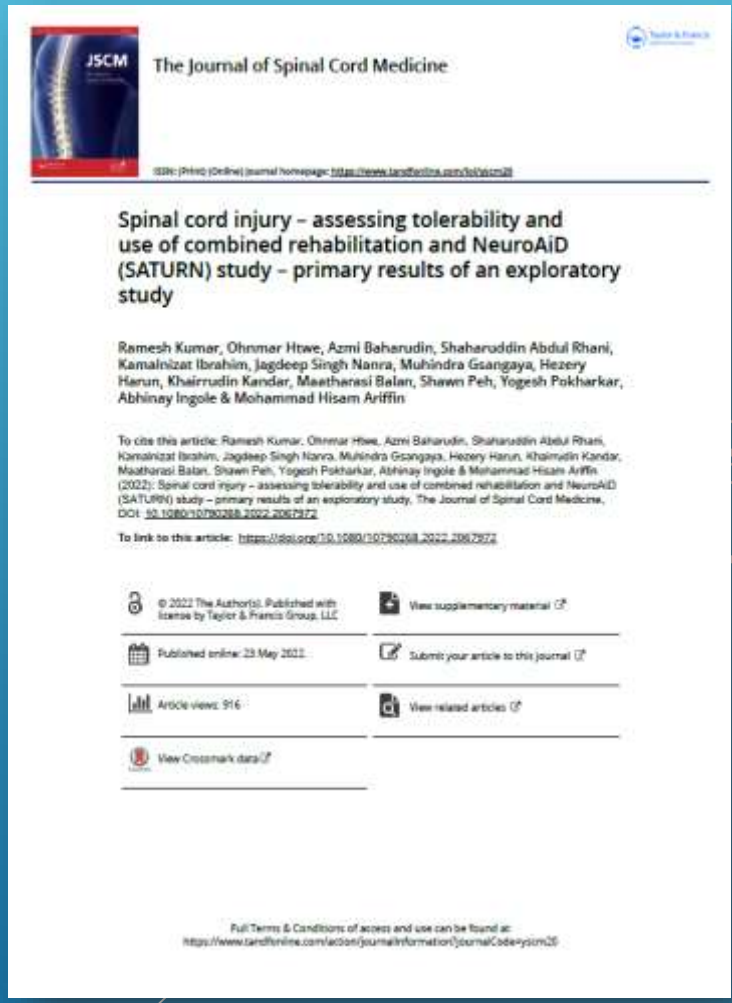
NurAiD™II Miešna trauma (SCI)

SATURN štúdia:

- Prospektívna kohortová štúdia (stredne ťažké a ťažké SCI
- Otvorená štúdia- liečba počas 6 mes.
  navyše k štandardnej starostlivosti
- Sledovanie 24 mesiacov
  Bezpečný u pacientov s ťažkým SCI
  - Stupeň zlepšenia v motorickom skóre

u liečených pacientov podporuje

Význam v liečbe pri ťažkej SCI



The Journal of Spinal Cord Medicine

Spinal cord injury – assessing tolerability and use of combined rehabilitation and NeuroAiD (SATURN) study – primary results of an exploratory study

Ramesh Kumar, Ohnmar Htwe, Azmi Baharudin, Shaharuddin Abdul Rhani, Kamalnizat Ibrahim, Jagdeep Singh Nanra, Muhindra Gsangaya, Hezery Harun, Khairrudin Kandar, Maatharasi Balan, Shawn Peh, Yogesh Pokharkar, Abhinay Ingole & Mohammad Hisam Ariffin

NurAiD™II - Benefit prídavnej liečby

- Zvyšuje šance dosiahnutia **funkčnej nezávislosti** **(2,5 x väčšia šanca).**
- Zlepšuje **obnovu motorických funkcií** **(70 % zníženie deficitu v oblasti motoriky už po 3 mesiacoch).**
- **Po 3 mesiacoch** môže dôjsť k významnému **zlepšeniu v motorických, rečových, zrakových a kognitívnych funkciách.**
- **Zabraňuje včasným kardiovaskulárnym príhodám a úmrtiam** po CMP a traumatickom poranení mozgu **až o 50 %.**
- **NurAiD™II v spojení s rehabilitáciou, zdvojnásobuje šance dosiahnuť funkčnú samostatnosť.**

Odporúčania

- Odporúča sa nasadiť ako **prídavná terapia** v ideálnom prípade u pacientov **v postakútnej* fáze, alebo do 6 mesiacov** od cievnej mozgovej príhody v prípade nedostatočného zotavovania sa.

- Zvyčajne je určený pre pacientov po **ischemickej alebo hemoragickej cievnej mozgovej príhode**, alebo po **traumatickom poranení mozgu (TBI).**

•Postakútna fáza je definovaná ako > 72 hodín, keď pacienti už viac nepotrebujú urgentné intervencie a intenzívne monitorovanie.

UŽÍVANIE a INTERAKCIE

- **2 kapsuly, 3 krát denne počas 3 mesiacov** a viac

  (CMP – najmenej 3 mesiace, TBI – najmenej 6 mesiacov)
- **1 kapsula, 3 krát denne** počas **3 mesiacov** a viac

  (DAT – 6 mesiacov)
- Kapsuly sa užívajú perorálne. Môžu sa otvoriť a ich obsah rozpustiť vo vode, alebo podávať výživovou sondou.
- Môžu sa používať popri bežnej inej liečbe.

Nie sú známe žiadne interakcie s inými liekmi (NOAK?)
Vedľajšie účinky (GIT dyskomfort, cefalea) sú zriedkavé, dočasné a mierne.

BEZPEČNOSŤ

- Má preukázanú bezpečnosť ako prídavná terapia.
- Odporúča sa v rámci sekundárnej prevencie a v rámci rehabilitačných programov.
- Výsledky závisia aj od rozsiahlosti postihnutia a taktiež od toho ako zavčasu je zahájené užívanie tohto produktu.

Study	n	Adverse events			Serious adverse events		
		MLC601 (n = 580)	control (n = 335)	total (n = 915)	MLC601 (n = 580)	control (n = 335)	total (n = 915)
China 01 and 02 [7]	605	2	0	2	0	0	0
Ghandehari [17]	40	2	2	4	0	1	1
Harandi [14]	150	7	0	7	0	0	0
Kong [15]	40	9	7	16	4	1	5
Shahripour [16]	80	2	4	6	0	0	0

Table 2. Distribution of serious and nonserious adverse events as reported in the included studies in different arms of the trials

Venketasubramanian N et al. Biomolecules, 2024

Chen *et al. BMC Health Services Research* (2024) 24:1127
https://doi.org/10.1186/s12913-024-11618-4

BMC Health Services Research

RESEARCH Open Access

Cost-effectiveness of MLC601 in post-stroke functional recovery compared with placebo - the CHIMES & CHIMES-E studies

Christopher Li Hsian Chen[1*], Jia Hui Chai[2], Yogesh Mahadev Pokharkar[2] and Narayanaswamy Venketasubramanian[3]

Abstract

Background Despite progress in stroke therapy (e.g., revascularisation interventions by thrombolysis and/or thrombectomy, organised stroke care), many stroke survivors will have impairment of neurological function. We aimed to compare the cost-effectiveness of an oral natural formulation, MLC601, versus placebo in functional recovery among subjects receiving standard of care after an ischemic stroke of intermediate severity assessed with NIH Stroke Scale at baseline (b-NIHSS 8–14).

Methods A Markov cohort model with a 2-year time horizon was developed to simulate patients from a published randomised placebo-controlled clinical trial of MLC601 in their post-stroke functional recovery assessed by modified Rankin Score (mRS), from a health system perspective. Transition probabilities were derived from a multi-centre clinical trial in South East Asia. As cost and utility data were not collected in the trial, therefore we extracted them from the published literature. The main outcomes were incremental cost, incremental quality-adjusted life-year (QALY) gained, and incremental cost-effectiveness ratio (ICER). Besides base-case and sensitivity analyses, we performed subgroup analyses to explore the heterogeneity of patients with poor-prognosis factors (b-NIHSS 10–14, stroke onset to treatment time > 48 h, rehabilitation during first 3 month). All costs are expressed in 2022 Euro and USD, with an annual discount rate of 3% applied to costs and QALYs.

Results Base-case analysis showed that MLC601 was cost-effective compared with placebo, with €5,080 saved and 0.45 QALY gained, resulting in an ICER of -€11,352.50 per QALY gained. Similarly, results from subgroup analyses indicated that the use of MLC601 was a dominant strategy in all subgroups with poor-prognosis factors. Sensitivity analyses revealed the results were robust.

Conclusion Compared with placebo on top of standard stroke care, MLC601 was cost-effective in post-stroke functional recovery over two years. Due to the lack of cost and utility data from the study population, the results might not be generalizable to other settings. Further studies with country-specific data are needed to confirm the results of this study.

NurAiD™II Neuroprotekcia

Open Access Meta-Analysis

Efficacy and safety of CDP-choline, cerebrolysin, MLC601, and edaravone in recovery of patients with acute ischemic strokes: a meta-analysis

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Cite this article: Abou Zaki SDB, Lokin JK. Efficacy and safety of CDP-choline, cerebrolysin, MLC601, and edaravone in recovery of patients with acute ischemic strokes: a meta-analysis. Explor Neuroprot Ther. 2023;3:398–408. https://doi.org/10.37349/ent.2023.00057

Abstract

Aim: Stroke is the second most common cause of mortality and disability worldwide with ischemic strokes being the predominant type. The advent of neuroprotectants brought hope of improved outcomes and quality of life, but current guidelines, despite numerous trials, have no strong recommendation advising their use. This meta-analysis aims to evaluate the degree of effect and safety of the neuroprotectants cytidine-5'-diphosphocholine (CDP-choline), cerebrolysin, edaravone, and MLC601 in the recovery of patients with cerebral infarcts.

Methods: An extensive literature search, through the databases of PubMed, PMC, Cochrane, and Ovid, was done with the keywords "CDP-choline", "cerebrolysin", "MLC601", and "edaravone" each combined with the term "acute ischemic stroke". Eligible studies included randomized controlled trials of these neuroprotectants administered to patients with acute ischemic strokes. A total of 2,025 studies were found, and after the application of screening criteria, 24 studies were eligible for analysis.

Results: The analysis showed that the functional outcome of patients with acute ischemic strokes improved significantly when receiving neuroprotectants *versus* placebo supported by an odds ratio = 0.29 (0.09–0.50) with a confidence interval of 95%. The *P*-values are 0.0022 for the one-tailed test, and 0.0030 for the two-tailed test which express the significant improvement of functional outcomes in patients with acute ischemic strokes taking neuroprotectants.

Conclusions: This study thus supports the use of neuroprotectants in patients with acute ischemic strokes to improve long-term functional outcomes and ultimately quality of life.

NurAiD™II
ALZHEIMEROVA CHOROBA

NurAiD: Nová možnosť pre Alzheimerovu chorobu

Dement Geriatr Cogn Disord Extra 2015;5:96–106
DOI: 10.1159/000375295
Published online: March 7, 2015
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www.karger.com/dee

Original Research Article

Effectiveness and Safety of MLC601 in the Treatment of Mild to Moderate Alzheimer's Disease: A Multicenter, Randomized Controlled Trial

Hossein Pakdaman[a] Ali Amini Harandi[a] Hamidreza Hatamian[c]
Mojgan Tabatabae[b] Hosein Delavar Kasmaei[a] Amirhossein Ghassemi[d]
Koroush Gharagozli[a] Farzad Ashrafi[a] Pardis Emami Naeini[e]
Mehrnaz Tavakolian[a] Darush Shahin[a]

[a]Department of Neurology, Shahid Beheshti University of Medical Sciences, and [b]Social Security, Tehran, [c]Department of Neurology, Rasht University of Medical Sciences, Rasht, [d]Social Security, Kerman, and [e]School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Clinical Trial

A Long-term Study of NeuroAid (MLC601, MLC901) in Patients with Alzheimer's Disease; An Extension 8-year Follow-up Study

Author(s): Hossein Pakdaman, Ali Amini Harandi*, Koroush Gharagozli, Fatemeh Siavoshi, Siavash Shirzadeh Barough, Ehsan Sharifipour, Akram Esfandani, Saba Ilkhani, Fatemeh Sadat Tabatabaei and Seyed Ali Sobhanian

Volume 16, Issue 3, 2023

Klinická štúdia

Multicentrick … **4 pacientov)**

Cieľom štúdie: … **ej až stredne ťažkej Alzheime**

- Donepezil
- Rivastigmine
- Galantamin

Dávkovanie: 1 …

V porovnar … **preukázal:**

Lepšia bezpečnosť a znášanlivosť

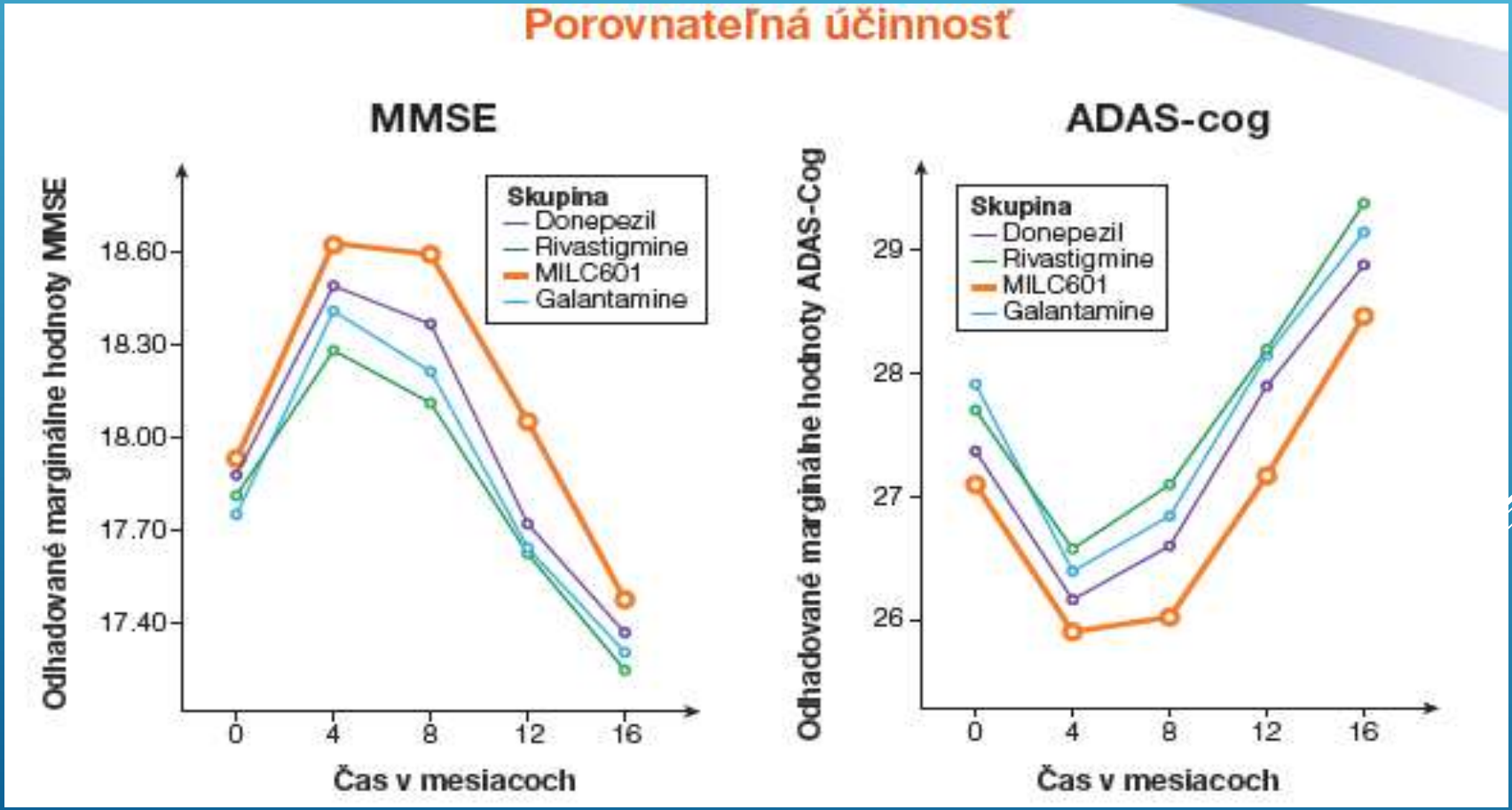
Vedľajší účinok	MLC601	Donepezil	Rivastigmine	Galantamine	p hodnota
Nevoľnosť	6 (9.1%)	14 (21.2%)	15 (22.7%)	21 (31.8%)	0.01*
Zvracanie	1 (1.5%)	4 (6.1%)	8 (12.1%)	10 (15.2%)	0.02*
Hnačka	3 (4.5%)	5 (7.6%)	9 (13.6%)	5 (7.6%)	0.28
Nechutenstvo	4 (6.1%)	15 (23.1%)	11 (16.7%)	17 (25.8%)	0.01*
Chudnutie	1 (1.5%)	4 (6.1%)	7 (10.6%)	3 (4.5%)	0.15
Nepohodlie v bruchu	0	3 (4.5%)	7 (10.6%)	9 (13.6%)	0.01*
Tenesmus	4 (6.1%)	4 (6.1%)	14 (21.2%)	4 (6.1%)	0.005*
Bolesť brucha	4 (6.1%)	8 (12.1%)	9 (13.6%)	10 (15.2%)	0.38
Žladna srdcová bolesť na hrudníku	3 (4.5%)	8 (12.1%)	7 (10.6%)	13 (19.7%)	0.08
Únava	3 (4.5%)	2 (3.0%)	9 (13.6%)	5 (7.6%)	11 (4.1%)
Slalorea	0	0	1 (1.5%)	4 (6.1%)	0.03*
Zápcha	0	9 (13.6%)	10 (15.2%)	6 (9.1%)	0.01*
Hyperhidróza	0	3 (4.5%)	3 (4.5%)	2 (3.0%)	0.37
Gastrointestinálne krvácanie	0	0	1 (1.5%)	2 (3.0%)	0.29
Srdcová arytmia	0	0	1 (1.5%)	0	0.39
Palpitácia	1 (1.5%)	5 (7.6%)	4 (6.1%)	5 (7.6%)	0.38
Točenie hlavy	2 (3.0%)	2 (3.0%)	8 (12.1%)	4 (6.1%)	0.09
Halucinácie	0	3 (4.5%)	3 (4.5%)	1 (1.5%)	0.26
Ospalosť	0	1 (1.5%)	5 (7.6%)	0	0.009*
Depresia	0	2 (3.0%)	5 (7.6%)	2 (3.0%)	0.11
Závraty	1 (1.5%)	4 (6.1%)	15 (22.7%)	8 (12.1%)	0.001*
Bolesť hlavy	1 (1.5%)	9 (13.6%)	14 (21.2%)	13 (19.7%)	0.004*
Nespavosť	0	11 (16.7%)	16 (24.2%)	8 (12.1%)	<0.0001*
Zmätok	0	5 (7.6%)	7 (10.6%)	5 (7.6%)	0.08

VÝSLEDKY – VPLYV NA KOGNÍCIU

Trendy kognitívnych zmien v priebehu času boli rovnaké medzi 4 skupinami

MMSE - Orientačný diagnostický test (mini mental test)

ADAS-cog - závažnosť kognitívnych symptómov demencie

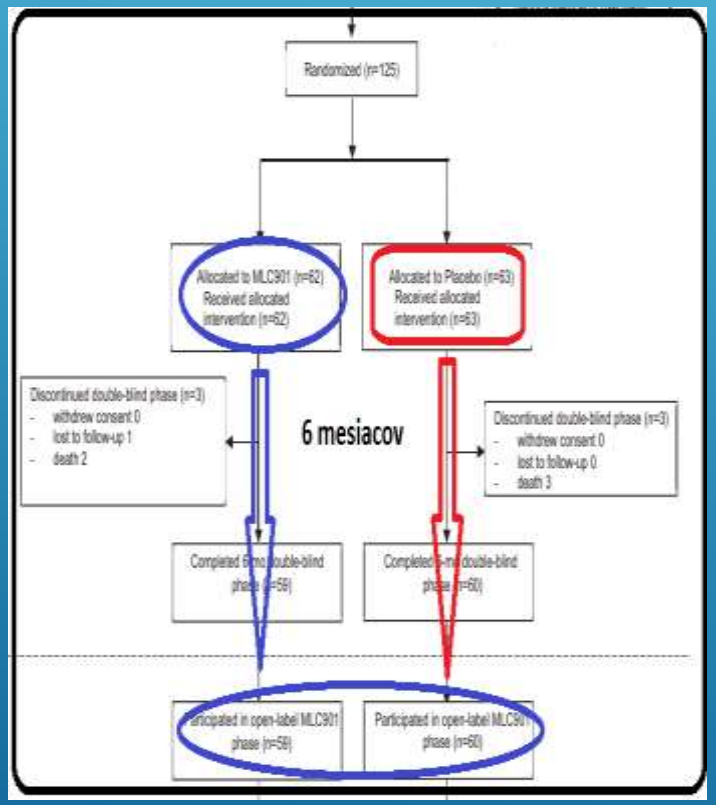


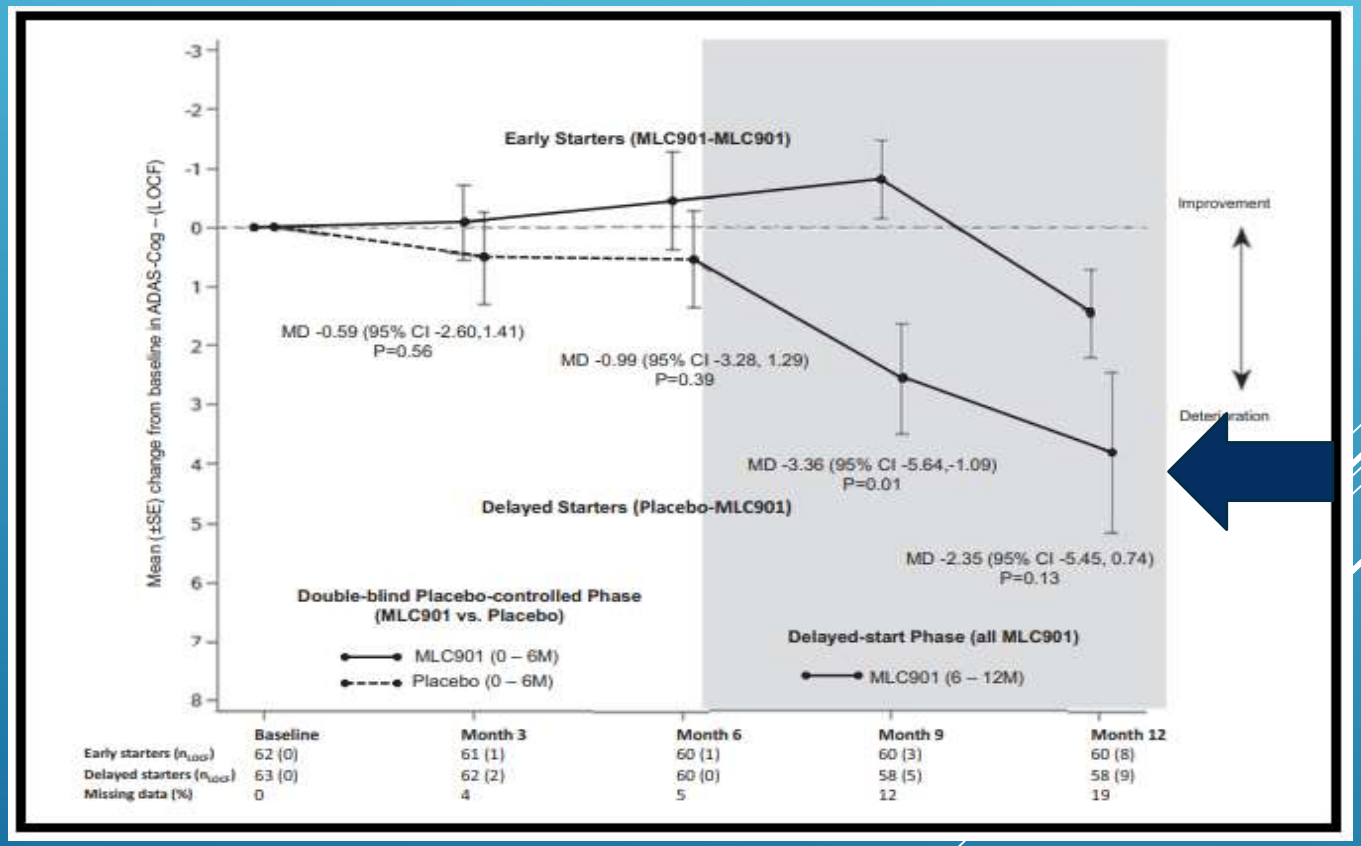
NurAiD™II Kedy a či vôbec?

Original Study

Alzheimer's Disease THErapy With NEuroaid (ATHENE): A Randomized Double-Blind Delayed-Start Trial

Christopher L.H. Chen BMBCh [a,b,*], Qingshu Lu PhD [c,d], Rajesh Babu Moorakonda MSc [c], Nagaendran Kandiah MBBS [d,e,f], Boon Yeow Tan MBBS [g], Steven Gayoles Villaraza MD [a], Jemelle Cano MD [a], Narayanaswamy Venketasubramanian MBBS [h]





Nedokázal sa rozdiel v ADAS-cog skóre (ani v NÚL)
Potenciál spomalenia progresie??

NurAiD™II

MILD COGNITIVE IMPAIRMENT

Received: 2 June 2020 | Revised: 5 December 2020 | Accepted: 6 January 2021 | Published online: 30 March 2021

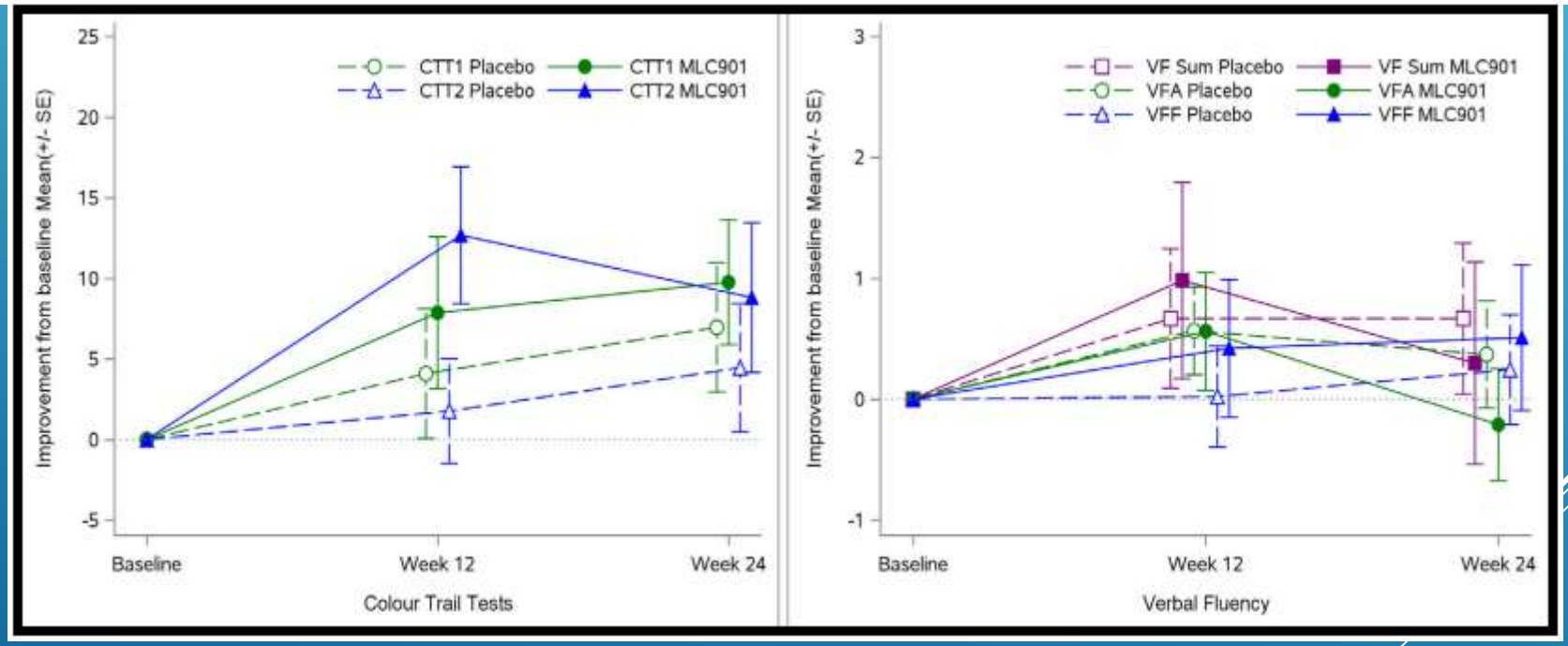
DOI: 10.1002/trc2.12161

RESEARCH ARTICLE

Alzheimer's & Dementia® Translational Research & Clinical Interventions

NEURoaid II (MLC901) in cognitively Impaired not demenTEd patientS (NEURITES): A pilot double blind, placebo-controlled randomized trial

Christopher L. H. Chen[1] | Trọng Hung Nguyen[2] | Simeon Marasigan[3,*] | Chun Fan Lee[4] | Qingshu Lu[5] | Nagaendran Kandiah[6] | Deidre de Silva[7] | Eddie Chong[8] | Narayanaswamy Venketasubramanian[9]



Nepreukázal sa efekt na exekutívne funkcie (porovnateľná bezpečnosť)

NurAiD™II

ALZHEIMEROVA CHOROBA??

Clinical Trial > Curr Aging Sci. 2023;16(3):234-239. doi: 10.2174/1874609816666230224111759.

A Long-term Study of NeuroAid (MLC601, MLC901) in Patients with Alzheimer's Disease; An Extension 8-year Follow-up Study

Hossein Pakdaman [1], Ali Amini Harandi [1], Koroush Gharagozli [1], Fatemeh Siavoshi [1], Siavash Shirzadeh Barough [1], Ehsan Sharifipour [1], Akram Esfandani [1], Saba Ilkhani [1], Fatemeh Sadat Tabatabaei [1], Seyed Ali Sobhanian [2]

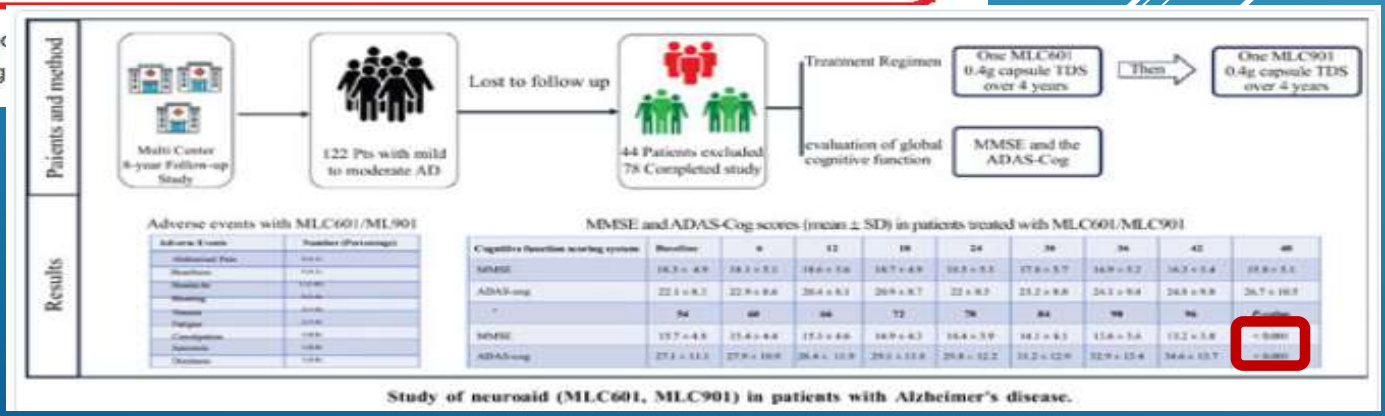
Abstract

Background: MLC601 and MLC901 showed neuroprotective and neuroregenerative properties and positive results in the treatment of dementia and cognitive impairment. This study aimed to investigate the long-term benefits of monotherapy with MLC601 and MLC901 in patients with Alzheimer's disease (AD).

Methods: In this study, patients with AD, diagnosed by DSM-IV criteria, were enrolled. Patients have received MLC601 for four years, and their regimen has changed to MLC901 for another four years. Recruited patients were followed to assess the efficacy and safety first of MLC601 and MLC901. Mini-Mental State Examination (MMSE) and Alzheimer's Disease Assessment Scale- Cognitive Subscale (ADAS-Cog) were used to assess cognitive function. Safety was evaluated by monitoring adverse events (AEs) and abnormal findings in physical examinations or lab tests.

Results: At the end of the trial, the changes in the mean (±SD) MMSE and ADAS-Cog scores were 5.1 (3.09) and 12.5 (10.89), respectively. Both scores showed a significant change in repeated measure analysis, with the ADAS-Cog score indicating a higher change than the MMSE score (P < 0.001).

Conclusion: For more than eight years, we studie
with AD. The study contributes further to the long



Study of neuroaid (MLC601, MLC901) in patients with Alzheimer's disease.

TAKE HOME

- Prídavná liečba CMP a TBI s preukázanou efektivitou na motorické a funkčné schopnosti pacientov
- Efektívny v rámci sekundárnej prevencie KV rizika a podpory efektu rehabilitačných programov
- Nová možnosť pre liečbu Alzheimerovej choroby („add on“)
- Výborný bezpečnostný profil a znášanlivosť
- Priaznivý pomer efektivita /cena

Klinické skúsenosti ????