

Terapie Alzheimerovy nemoci: *výhledy*

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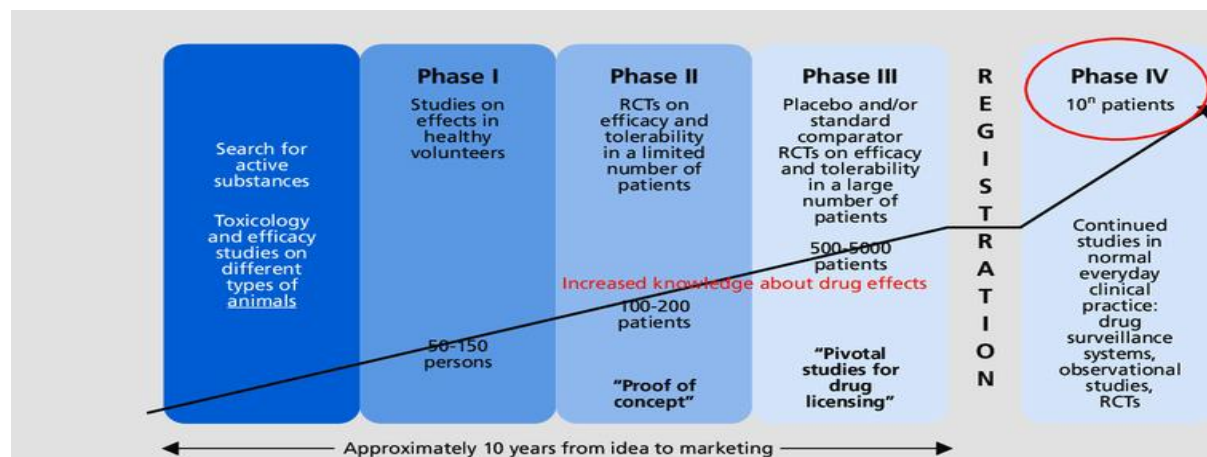
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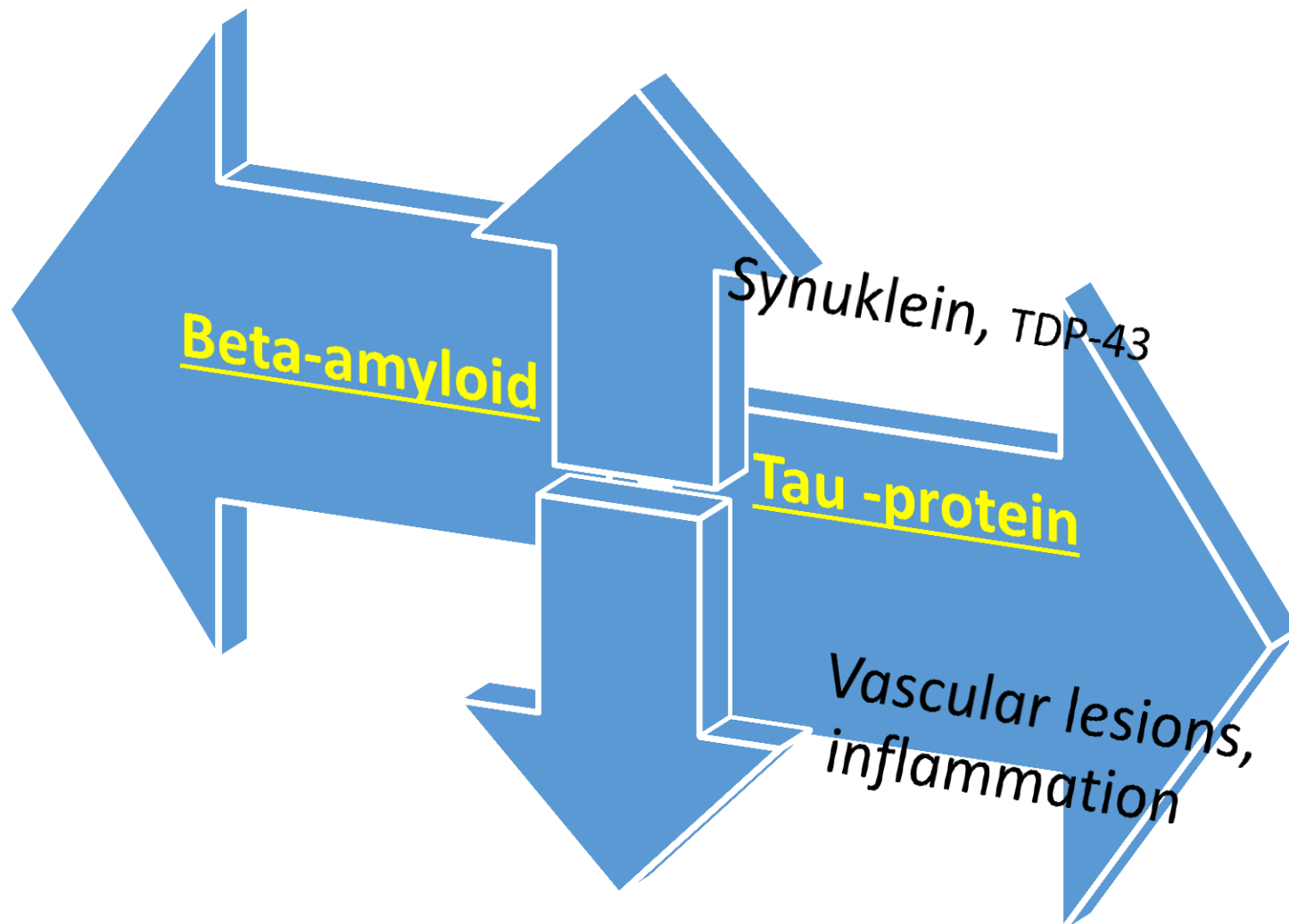


?

Velké množství studií na AN – 2428 podle clinicaltrials.gov

- z toho aktivních 456 intervenčních (klinických) studií
- fáze 4 – 15 studií, pouze symptomatická terapie (jiné formy iAChE, dále např. lithium, methylfenidát)
- **fáze 3 – 47 studií**
- cca 40% se zaměřením na amyloid, cca 20% na tau, zbytek ostatní mechanismy (neuroprotektiva, protizánětlivé léky, metabolické léky)

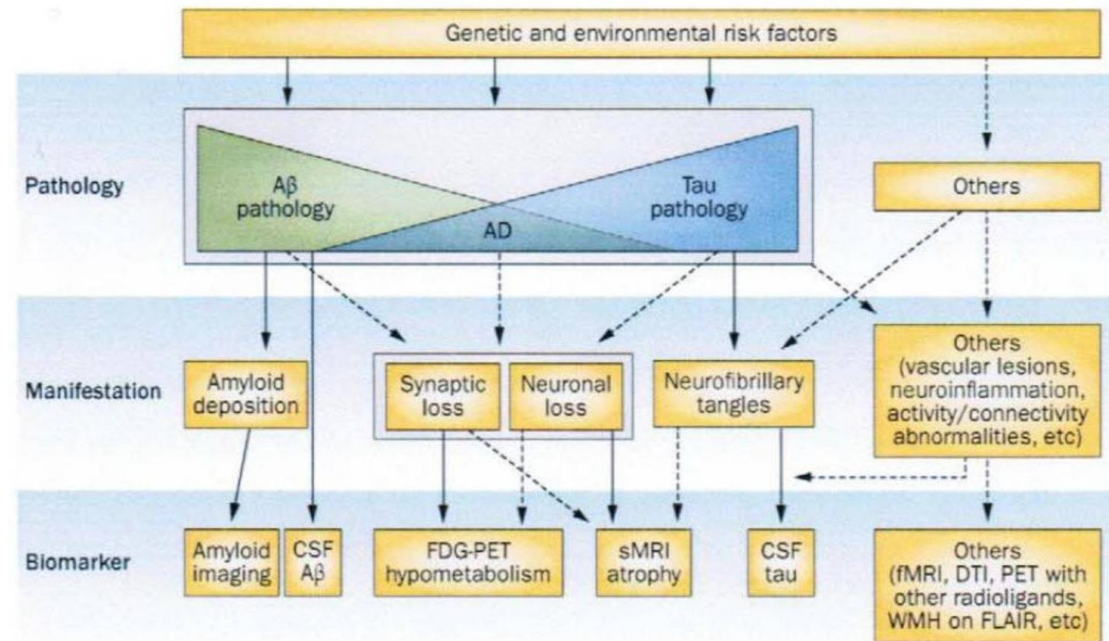




REPLY

The amyloid cascade is not the only pathway to AD

Gaël Chételat

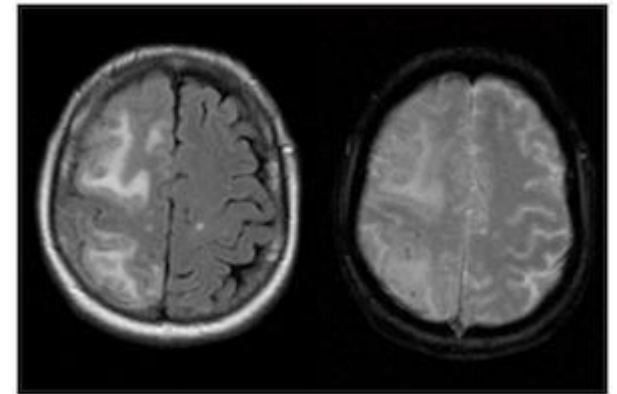


Beta amyloidové studie

1) Protilátky proti beta-amyloidu (IgG1 PL)

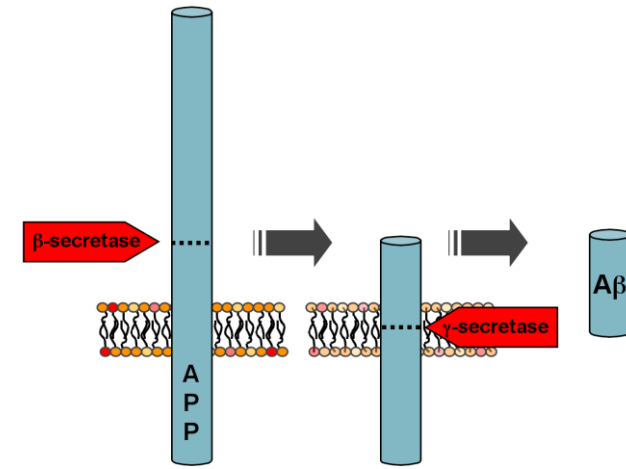
- **Aducanumab**
- Gantenerumab
- BAN 2401

- nežádoucí účinky: ARIA (amyloid related imaging abnormalities)



2) Inhibitory beta-sekretázy (BACE1-i)

- Elenbecestat - fáze 3 předčasně ukončena v min. roce





Non-Amyloid Approaches to Disease Modification for Alzheimer's Disease: An EU/US CTAD Task Force Report

*S. Gauthier¹, P.S. Aisen², J. Cummings³, M.J. Detke⁵, F.M. Longo⁶, R. Raman², M. Sabbagh⁴, L. Schneider⁷, R. Tanzi⁸, P. Tariot⁹, M. Weiner¹⁰, J. Touchon¹¹, B. Vellas¹² and the EU/US CTAD Task Force**

Anti – tau terapie (17 přípravků):

- jenom 1 aktuálně ve fázi 3 – redukována forma methylenové modři (TAI – tau aggregation inhibitor)
- gosuranemab, semorinemab – fáze 2 + řada preklinických studií
- *gantenerumab* – snižoval i hladiny tau, p-tau i NFL

Modulátory neutrophinového receptoru – molekula LM11A-31 (fáze 2)

Anti-mikrobiální a protizánětlivé strategie

- kromoglykát sodný + ibuprofen (ALZT – OP1)
- Atuzagingistat (COR388) – inhibitor gingipain proteázy





- **Prevence** vaskulárních změn, životní styl a další nefarmakologické přístupy (např. neurostimulační techniky)
- **FINGER** (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability) „*Findings from this large, long-term, randomised controlled trial suggest that a multidomain intervention could improve or maintain cognitive functioning in at-risk elderly people from the general population*“ Lancet, 2015

REVIEW

Open Access

Beyond synuclein neurodegeneration

Naomi P. Visanji

SCIENTIFIC
REPORTS

nature research



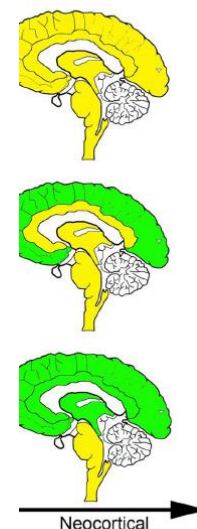
Targeting alpha synuclein and amyloid beta by a multifunctional, brain-penetrant dopamine D2/D3 agonist D-520: Potential therapeutic application in Parkinson's disease with dementia

Deepthi Yedlapudi¹, Liping Xu¹, Dan Luo¹, Gregory B. Marsh², Sokol V. Todi² & Aloke K. Dutta^{1*}

a-Synuclein in Parkinson's disease



Fig. 3 Predicted overlap (yellow) of aSyn in PD (green) with deposition patterns for amyloid-β in Alzheimer's disease (red) in the brainstem, limbic (e.g. amygdala, hippocampus, anterior cingulate) and subcortical areas (e.g. basal ganglia) and neocortical areas. According to the Thal Phases the deposition of amyloid-β follows a neocortical to limbic/subcortical to brainstem path [102], which is opposite to that seen for aSyn according to the Braak stages of Lewy pathology [97]



a-Synuclein in Parkinson's disease



Fig. 4 Predicted overlap (yellow) of aSyn in PD (green) with deposition patterns for tau in Alzheimer's disease and primary age-related tauopathy (red) in the brainstem, limbic (e.g. amygdala, hippocampus, anterior cingulate) and subcortical areas (e.g. basal ganglia) and neocortical areas. According to the Braak stages of neurofibrillary tau pathology [98] the deposition of tau follows a similar involvement of anatomical systems (i.e. brainstem to limbic/subcortical to neocortex) as seen for aSyn for Lewy pathology [97]

Alzheimer's disease: expedition into the unknown

Kombinované terapie

Lék zasahující klíčové procesy s modulací vícero patologických mechanismů (např. současně A-beta i tau)



Editorial

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Next-generation Alzheimer's Therapeutics: Leveraging Deep Biology

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Prevence

Děkuji za pozornost

- <https://www.alz.org>
- <https://www.alzforum.org>
- <https://en.wikipedia.org>

