

Praktické odporúčania genetického testovania vo vzťahu k antiamyloidnej terapii

Monoklonálne protilátky proti beta amyloidu (lecanemab a donanemab) otvárajú novú éru v terapii Alzheimerovej choroby. Napriek množstvu kontroverzií, s ktorými sú spojené, predstavujú zásadný míľnik, ktorý má celospoločenský presah. Genetické testovanie APOE genotypu bude mandatórnou podmienkou indikovania liečby. V prípade lecanemabu je liek indikovaný u ApoE4 nenesiteľov a ApoE4 heterozygotov. ApoE4 homozygoti by mali byť z liečby vylúčení pre vysoké riziko ARIA fenoménu. V prípade donanemabu sa uvažuje o vylúčení akýchkoľvek nositeľov

ε4 alely, takže je možné, že bude indikovaný len pre relatívne úzku kohortu pacientov. Každopádne genetické testovanie APOE genotypu bude musieť byť dostupné v každom centre, ktoré bude indikovať liečbu.

Záver

Alzheimerova choroba a demencia s Lewyho telieskami sú dve najfrekvencovanejšie neurodegeneratívne demencie. Sú to prekrývajúce sa množiny, pričom platí, že čím viac patológií v mozgu konkomitantne prebieha, tým je klinický priebeh rýchlejší. Každá z týchto demencií má svoje špecifické genetické pozadie, pričom niektoré gény sú vysoko špecifické pre dané ochorenie, iné sú zdieľa-

né medzi oboma entitami. Je predpoklad, že v budúcnosti sa na základe vedomostí z GWAS a MPS (*massive parallel sequencing*) rozšíri repertoár génov zapojených do patogenézy oboch neurodegeneratívnych demencií. Význam genetiky nespočíva len v identifikácii príčiny ochorenia, ale stáva sa podkladom na triedenie pacientov na špecifickú terapiu. Napríklad lecanemab aj donanemab (monoklonálne protilátky na liečbu AD), ako už bolo spomenuté, sa ukazujú ako nevhodné pre ApoE4/4 homozygotov. Víziou budúcnosti je personalizovaná medicína, ktorá bude pri výbere terapie zohľadňovať genotyp, fenotyp a množstvo ďalších faktorov s cieľom dosiahnuť optimálny efekt.

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