

MEDICINA

Področje: 3.01 – Mikrobiologija in imunologija



Področje mikrobiologije in imunologije je zelo široko raziskovalno področje, ki zajema povsem bazične biološke raziskave pogosto pa tudi raziskave, ki imajo neposredno in takojšnjo klinično uporabnost.

Veliko bazičnih raziskav se odvija v raziskovalnih skupinah, ki niso neposredno povezane s kliničnim okoljem. Kot najbolj produktivne v številu kvalitetnih objav pa so se izkazale skupine, ki so dobro povezale bazično in klinično raziskovanje. Praviloma te skupine dosegajo večje število objav in skrbijo tudi za širšo znanstveno podstat. Njihovo delo zajema od vrhunskih znanstvenih objav, skrb za vzgojo mladih raziskovalcev, poučevanja in tudi širokega vključevanja v mednarodne raziskave.

Samo na področju mikrobiologije in imunologije so bile v letu 2010 organizirane 3 svetovne znanstvene konference, ki jih organizatorji vedno zaupajo zgolj raziskovalnim skupinam, ki prej s svojimi mednarodnimi referencami zadostijo strogim kriterijem.

Kot zelo dobre lahko ocenimo skupine, ki se ukvarjajo s prirojeno imunostjo kakor tudi dve skupini, ki v kliničnem okolju združujeta bazično in klinično imunologijo na področju avtoimunskih bolezni in alergij. Zelo produktivne so tudi raziskovalne skupine, ki preučujejo široko paleto povzročiteljev infekcijskih bolezni in metode za njihovo dokazovanje.

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Dosežek 1: Jones G, Sebba A, Gu J, Lowenstein MB, Calvo A, Gomez-Reino JJ, Siri DA, Tomsic M, Alecock E, Woodworth T, Genovese MC. Comparison of tocilizumab monotherapy versus methotrexate monotherapy in patients with moderate to severe rheumatoid arthritis: the AMBITION study. *Ann Rheum Dis.* 2010 Jan;69(1):88-96. JCR=9,082 - najboljša revija na področju revmatologije

Comparison of tocilizumab monotherapy versus methotrexate monotherapy in patients with moderate to severe rheumatoid arthritis: the AMBITION study

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Accepted 19 February 2009
Published Online First
17 March 2009

ABSTRACT
Background: The anti-interleukin (IL) 6 receptor antibody tocilizumab inhibits signalling of IL6, a key cytokine in rheumatoid arthritis (RA) pathogenesis.

Objective: To evaluate through the AMBITION study the efficacy and safety of tocilizumab monotherapy versus methotrexate in patients with active RA for whom previous treatment with methotrexate/biological agents had not failed.

Methods: This 24-week, double-blind, double-dummy, parallel-group study, randomised 673 patients to either tocilizumab 8 mg/kg every 4 weeks, or methotrexate, starting at 7.5 mg/week and titrated to 20 mg/week within 8 weeks, or placebo for 8 weeks followed by tocilizumab 8 mg/kg. The primary end point was the proportion of patients achieving American College of Rheumatology (ACR) 20 response at week 24.

Results: The intention-to-treat analysis demonstrated that tocilizumab was better than methotrexate treatment with a higher ACR20 response (69.9 vs 52.5%, $p < 0.001$), and 28-joint Disease Activity Score (DAS28) < 2.6 rate (33.6 vs 12.1%) at week 24. Mean high-sensitivity C-reactive protein was within the normal range from week 12 with tocilizumab, whereas levels remained elevated with methotrexate. The incidence of serious adverse events with tocilizumab was 3.8% versus 2.6% with methotrexate ($p = 0.50$), and of serious infections, 1.4%

Tocilizumab is a humanised anti-IL6 receptor antibody that inhibits both soluble and membrane-expressed IL6 receptors (IL6R) limiting multiple IL6 proinflammatory activities through inhibition of the gp130 pathway.^{1,2} Tocilizumab has demonstrated efficacy in moderate to severe active RA with inadequate clinical response to disease-modifying antirheumatic drugs (DMARDs) or to tumour necrosis factor (TNF) inhibitors.³⁻⁸ Moreover, in a phase 3 study in Japan, more patients receiving tocilizumab 8 mg/kg monotherapy showed reduced radiographic progression than those receiving DMARDs.⁹ However, tocilizumab has not been studied in patients for whom DMARDs have not previously failed.

Methotrexate remains the most commonly used DMARD and is the recommended standard against which new DMARDs should be evaluated.¹⁰⁻¹⁸ To date, there is limited evidence that monotherapy with other treatments is better than methotrexate, as neither etanercept nor adalimumab monotherapy were statistically better than methotrexate in standard clinical efficacy parameters at 24 weeks in the ERA, TEMPO, and PREMIER trials.¹⁵⁻¹⁹ The objective of the AMBITION (A ctivemra versus Methotrexate double-Blind Investigative Trial in mO) study was to compare the efficacy and safety of tocilizumab monotherapy with that

V globalni klinični raziskavi so primerjali učinkovitost in varnost tocilizumaba v primerjavi z metotreksatom. V 24 tedensko raziskavo je bilo vključenih 673 bolnikov. Najpomembnejši rezultat raziskave je bila ugotovitev, da je Tocilizumab bolj učinkovit od metotreksata.

Neželeni učinki so bili primerljivi z izjemo nevtropenije in višjih koncentracij celokupnega holesterola pri bolnikih z tocilizumabom in višjih vrednosti transaminaz pri bolnikih z metotreksatom.

Skupina na področju klinične imunologije že vrsto let izvaja klinične in bazične raziskave, ki redno rezultirajo z objavami v vrhunskih znanstvenih revijah s področja imunologije.

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Dosežek 2: MITTERMANN, Irena, ZIDARN, Mihaela, ŠILAR, Mira, MARKOVIC-HOUSLEY, Zora, ABERER, Werner, KOROŠEC, Peter, KOŠNIK, Mitja, VALENTA, Rudolf. Recombinant allergen-based IgE testing to distinguish bee and wasp allergy. *J Allergy Clin Immunol*, 2010, letn. 125, št. 6, str. 1300-1307. JCR IF (2009) = 9.165. *Allergy* 1/21




Journal of Allergy and Clinical Immunology
Volume 125, Issue 6, June 2010, Pages 1300–1307.e3



Food, drug, insect sting allergy, and anaphylaxis

Recombinant allergen-based IgE testing to distinguish bee and wasp allergy

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Received 11 September 2009. Revised 8 February 2010. Accepted 15 March 2010. Available online 13 May 2010.

Eden od osnovnih problemov pri diagnostiki preobčutljivosti za kožekrilce in vitro je visok delež dvojno pozitivnih specifičnih IgE (na sistemu CAP je za ose in čebele 50 do 60 % dvojno pozitivnih). Avtorji so v raziskavi ugotovili pomembno izboljšanje diagnostične napovedne vrednosti z uporabo rekombinantnih neglikoziliranih antigenov.