

## In vivo Pharmacology: Lipopolysaccharide (LPS) Induced Pulmonary Neutrophilia in Mice

Species, strain, sex: mouse, Balb/c, male  
 No. of animals per group: n=8  
 Pharmacological control: azithromycin, clarithromycin, roflumilast  
 Routes of administration: IN, PO, IP, SC, IV, IM  
 Treatment mode: prophylactic, therapeutic  
 Duration of dosing: 1 day or upon request

After intranasal administration LPS, a constituent of the cell wall of Gram-negative bacteria, induces production of various inflammatory mediators (CXCL1, CXCL2, TNF $\alpha$ , IL-6, GM-CSF, CCL2, IL-1 $\beta$ ) and neutrophil accumulation in lung tissue.

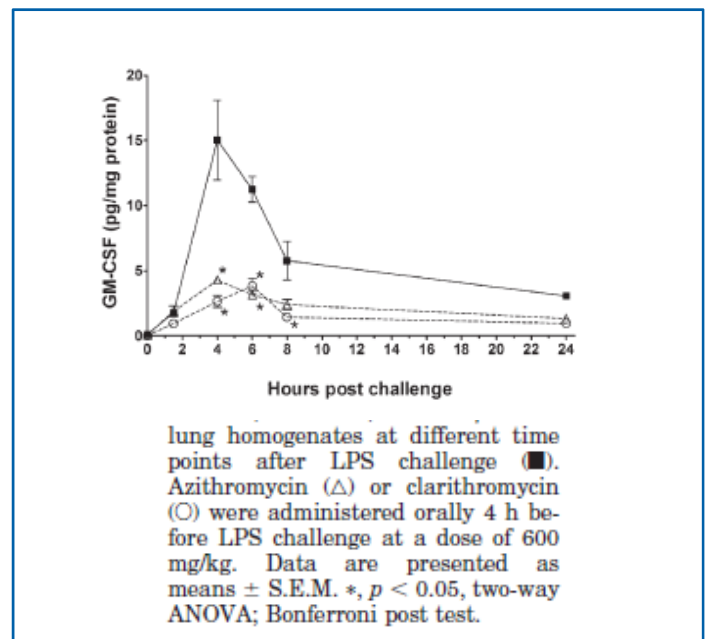
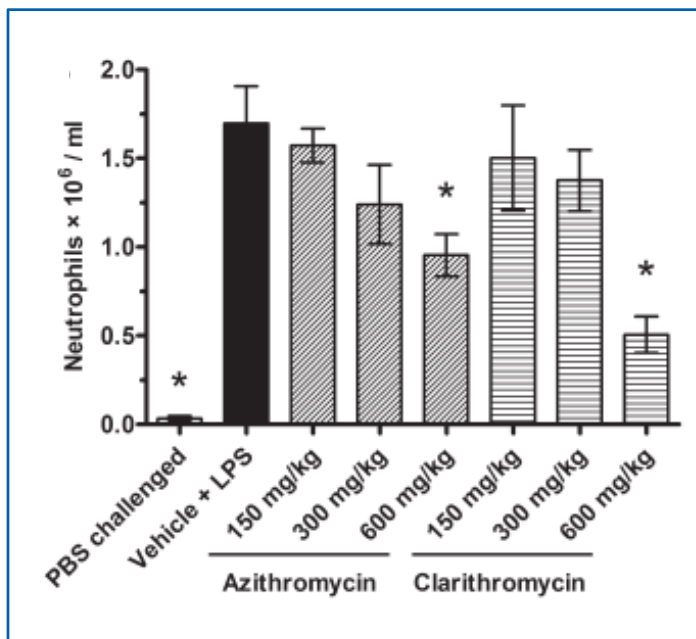
The anti-inflammatory activity of test compounds is evaluated 24h after LPS administration (main and facultative read-outs).

### Main read-outs:

- bronchoalveolar lavage fluid (BALF) analysis

### Facultative read outs:

- inflammatory mediators in lung homogenates
- histopathology
- immunohistochemistry



### References

Bosnar M, Bosnjak B, Snjezana C, Hrvacic B, Marjanovic N, Glojnaric I, Culic O, Parnham MJ, Erakovic V (2006) Azithromycin and clarithromycin inhibit lipopolysaccharide-induced murine pulmonary neutrophilia mainly through effects on macrophage-derived granulocyte-macrophage colony-stimulating factor and interleukin-1 $\beta$ . *JPET* (2006) 331: 104

Ivetic Tkalcovic V, Bosnjak B, Hrvacic B, Bosnar M, Marjanovic N, Ferencic Z, Situm K, Culic O, Parnham MJ, Erakovic V. Anti-inflammatory activity of azithromycin attenuates the effects of lipopolysaccharide administration in mice. *Eur J Pharmacol* (2006) 539: 131

Bosnar M, Čužić S, Bošnjak B, Nujić K, Ergović G, Marjanović N, Pašalić I, Hrvačić B, Polančec D, Glojnaric I, Eraković Haber V. Azithromycin inhibits macrophage interleukin-1 $\beta$  production through inhibition of activator protein-1 in lipopolysaccharide-induced murine pulmonary neutrophilia. *Int Immunopharmacol* (2011) 11:424