Therapeutic Response to Montelukast in Asthma

BACKGROUND SCIENCE

Asthma causes the body to overreact to allergens or irritants in the air, constricting and inflaming the bronchial tubes so severely that breathing becomes difficult. In severe cases, asthma attacks can be fatal. Researchers do not know why the prevalence of asthma has been increasing in the United States and other developed countries for the past quarter century; more than one person in 10 is now diagnosed with the condition at some time during childhood. But most experts agree that a person's likelihood of developing the condition depends on a combination of genetic susceptibility and exposure to environmental factors such as air pollution, viral infections, allergens and psychological stress.

Two major classes of leukotriene modifiers, including leukotriene antagonists (e.g. montelukast) and lipoxygenase inhibitors (zileuton), are commonly prescribed for management of asthma symptoms. Montelukast targets the cysteinyl leukotriene receptors (CysLTRs) at the cell membrane to block binding of cysteinyl leukotrienes, whereas zileuton, a 5-lipoxygenase (5-LO) antagonist, exerts its effects upstream of montelukast through inhibition of 5-LO mediated leukotriene biosynthesis from arachidonic acid.

As with all asthma medications, therapeutic responses to montelukast are highly variable, with some patients responding preferentially to leukotriene modifiers vs. other medications, such as inhaled corticosteroids. However, 40-50% of patients do not respond to this class of medication and require additional therapeutic intervention. Mounting evidence suggests that this heterogeneity in treatment response to montelukast is due, in part, to patient genetics.

GENETICS & MONTELUKAST

Using genome-wide genotype and phenotypic data available from American Lung Association - Asthma Clinical Research Center (ALA-ACRC) cohorts, a study[1] evaluated 8-week change in FEV1 related to montelukast administration in a discovery population of 133 asthmatics. This study identified a genome-wide significant SNP, rs6475448, which is present within MLLT3. This SNP may represent a novel mechanism for differential responses to leukotriene modifying agents in asthma.

[1] Amber Dahlin, et al. "Genome-Wide Association Study Identifies Novel Pharmacogenomic Loci For Therapeutic Response to Montelukast in Asthma"

YOUR RESULTS

Gene	Your results	Effects
MLLT3	GG	Lower response to Montelukast

CONCLUSION : Based on your genetic profil, you may have a lower response to Montelukast.

Close