Question 2

Squares to the left of the vertical line indicate a reduction in asthma exacerbations, showing benefit from the treatment. Otherwise, squares to the right of the no effects line suggest an increase in asthma exacerbations, indicating harm from the treatment. Most studies demonstrate decreased asthma exacerbations except for one study in the low blood eosinophil counts subgroup that showed increasing asthma exacerbations after receiving the treatment. The diamond for the high blood eosinophil counts subgroup is further from the line of no effect, indicating a greater reduction in asthma exacerbations for patients with high blood eosinophil levels after undergoing the treatment. The treatment will be more beneficial for patients in this subgroup.

Both subgroups and the overall study have statistically significant p-values (below 0.1), indicating the presence of heterogeneity. The p-value for the test of group differences is also below 0.1, so there is also heterogeneity between groups.

Confidence intervals within both subgroups all overlap each other. The confidence interval of the overall study’s summary estimate also overlaps with the confidence interval of both subgroups’ summary estimate. These overlap of confidence intervals suggests no statistically significant heterogeneity within subgroups or the overall study. However, some studies’ confidence intervals, like the SOURCE study from low eosinophil subgroup and the NAVIGATOR study from high eosinophil subgroup, do not overlap. Therefore, heterogeneity may be present between two subgroups.

The I2 value tells us the amount of heterogeneity present in the study. The low and high eosinophil subgroups have I2 values of 69.47% and 43.18% respectively. This indicates moderate heterogeneity within both subgroups. However, considerable heterogeneity is observed in the overall study (I² = 78.75%).

To conclude, the forest plot suggests that the anti-epithelial-derived cytokines treatment may effectively reduce asthma exacerbation, especially in patients with high blood eosinophil counts. However, there is statistically significant heterogeneity between subgroups in this systematic review and the overall study. Moderate heterogeneity is also found within subgroups. This statistical heterogeneity may be due to differences in treatment and patient characteristics (clinical heterogeneity) or study design features and quality (methodological heterogeneity). Therefore, the heterogeneity must be considered when making treatment decisions. Clinicians should tailor treatment decisions based on patient’s characteristics, preferences and risk profiles. Lastly, there are less than 10 studies included in the systematic review. Performing subgroup analysis may not be an appropriate approach as the heterogeneity may be due to chance alone.