

Airway Inflammation in COPD after Long-term Withdrawal of Inhaled Corticosteroids

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Supplementary Tables

Supplementary Table 1: Fold change per year in inflammatory cells in bronchial biopsies during GL1, GL2 and difference between GL2 versus GL1. Data are presented as fold change per year with 95% confidence interval for patients who used 0-50% ICS during GL2. Data are calculated by taking the antilog of the estimates (data from the linear mixed-effect models) of natural log-transformed cells per 0.1mm² lamina propria and represent ratios. A factor greater than 1.0 implies an increase in the number of cells, a factor less than 1.0 implies a decrease in the number of cells.

* P≤0.05: slope change in bronchial inflammatory cells between GL2 minus GL1.

^q P≤0.05: slope change in bronchial inflammatory cells between original combined FS30/F30 groups compared to the original combined F6/placebo groups.

	GL1	GL2	GL2 - GL1
FS30/F30 groups			
CD3 ⁺ cells	0.55 (0.45 to 0.70)	1.50 (1.21 to 1.85)	2.68 (1.87 to 3.84) ^{*q}
CD4 ⁺ cells	0.60 (0.47 to 0.75)	1.14 (0.92 to 1.41)	1.91 (1.33 to 2.75) [*]
CD8 ⁺ cells	0.71 (0.55 to 0.91)	1.21 (0.96 to 1.52)	1.71 (1.15 to 2.53) ^{*q}
Mast cells	0.59 (0.48 to 1.36)	1.13 (0.94 to 1.37)	1.91 (1.36 to 2.68) ^{*q}
Neutrophils	1.27 (1.00 to 1.62)	1.07 (0.85 to 1.33)	0.84 (0.57 to 1.23)
Macrophages	0.76 (0.54 to 1.06)	1.17 (0.86 to 1.61)	1.51 (0.91 to 2.67)
Eosinophils	1.44 (0.93 to 2.23)	0.93 (0.62 to 1.39)	0.65 (0.33 to 1.28)
F6/placebo groups			
CD3 ⁺ cells	0.75 (0.65 to 0.86)	1.15 (1.05 to 1.26)	1.55 (1.27 to 1.89) [*]
CD4 ⁺ cells	0.69 (0.57 to 0.83)	1.07 (0.95 to 1.21)	1.56 (1.19 to 2.03) [*]
CD8 ⁺ cells	1.00 (0.80 to 1.25)	1.00 (0.86 to 1.15)	0.99 (0.72 to 1.36)
Mast cells	0.81 (0.72 to 1.09)	1.04 (0.96 to 1.13)	1.28 (1.07 to 1.53) [*]
Neutrophils	1.22 (0.99 to 1.50)	0.95 (0.83 to 1.08)	0.78 (0.58 to 1.05)
Macrophages	0.95 (0.75 to 1.21)	1.22 (1.04 to 1.42)	1.28 (0.91 to 1.81)
Eosinophils	1.21 (0.85 to 1.72)	1.21 (0.96 to 1.53)	1.01 (0.60 to 1.67)

GL1: first part of the GLUCOLD-study; GL2: follow-up study; F6/placebo: combination of original treatment groups with 6-month ICS (followed by 24-month placebo) and placebo group. FS30/F30: combination of original treatment groups with 30-month fluticasone with salmeterol and 30-month fluticasone.

Supplementary Table 2: Fold change per year in sputum inflammatory cells during GL1, GL2 and difference between GL2 versus GL1. Data are presented fold change per year with 95% confidence interval for patients who used 0-50% ICS during GL2. Data are calculated as the antilog of estimates (from the linear mixed-effect models) of natural log-transformed cells $\times 10^4$ per ml and represent ratios. A factor greater than 1.0 implies an increase in the number of cells, a factor less than 1.0 implies a decrease in the number of cells.

* $P \leq 0.05$ slope change in sputum cells between GL2 versus GL1.

^q $P \leq 0.05$: slope change in sputum inflammatory cells between original combined FS30/F30 groups compared to the original combined F6/placebo groups

	GL1	GL2	GL2 - GL1
FS30/F30 groups			
Total cells	0.60 (0.50 to 1.36)	1.15 (0.99 to 1.33)	1.90 (1.41 to 2.54) ^{* q}
Neutrophils	0.60 (0.49 to 1.34)	1.16 (0.99 to 1.36)	1.92 (1.39 to 2.65) ^{* q}
Macrophages	0.55 (0.45 to 0.68)	1.17 (1.00 to 1.36)	2.10 (1.55 to 2.86) ^{* q}
Lymphocytes	0.62 (0.50 to 0.77)	1.26 (1.07 to 1.47)	2.01 (1.46 to 2.78) ^{* q}
Eosinophils	0.75 (0.60 to 0.96)	1.03 (0.86 to 1.24)	1.36 (0.95 to 1.95)
F6/placebo groups			
Total cells	0.87 (0.72 to 1.05)	0.99 (0.88 to 1.11)	1.14 (0.87 to 1.49)
Neutrophils	0.87 (0.72 to 1.07)	0.99 (0.88 to 1.13)	1.14 (0.86 to 1.51)
Macrophages	0.88 (0.73 to 1.07)	0.98 (0.87 to 1.10)	1.11 (0.84 to 1.46)
Lymphocytes	0.90 (0.72 to 1.12)	1.04 (0.91 to 1.20)	1.16 (0.84 to 1.59)

Eosinophils	0.97 (0.76 to 1.23)	0.99 (0.86 to 1.15)	1.03 (0.73 to 1.44)
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GL1: first part of the GLUCOLD-study; GL2: follow-up study; F6/placebo: combination of original treatment groups with 6-month ICS followed by 24-month placebo and placebo group. FS30/F30: combination of original treatment groups with 30-month fluticasone with salmeterol and 30-month fluticasone.

Supplementary figures

Figure S1. Geometric mean cell counts per 0.1 mm² lamina propria in bronchial biopsies over time for all patients from the original combined treatment groups FS30/F30 and F6/placebo. Error bars represent 95% confidence interval. Data of bronchial CD3⁺ cells (Figure S1A), CD4⁺ cells (S1B), CD8⁺ cells (S1C) and mast cells (S1D) are presented. Data were calculated by taking the antilog of the means of natural log-transformed number of cells.

Figure S2. Geometric mean change in sputum cell counts ($\times 10^4$ per ml) over time for all patients from the original combined treatment groups FS30/F30 and F6/placebo. Error bars represent 95% confidence interval. Data of total sputum cells (Figure S2A), neutrophils (S2B), macrophages (S2C) and lymphocytes (S2D). Data were calculated by taking the antilog of the means of natural log-transformed number of cells.