Supplementary material; Prognostic significance of faecal eosinophil granule proteins in inflammatory bowel disease

Supplementary material

Prognostic significance of faecal eosinophil granule proteins in inflammatory bowel disease.

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1. Predictive value of baseline measurements

Model 1A includes baseline faecal concentrations of EDN and ECP, respectively, age, and sex. In model 1B, treatment options that might confound the effect of the faecal EDN and ECP levels are included as covariates in an extended Cox regression model.

No violation of proportional hazards assumption was found for covariates, and there was no statistically significant interaction found between baseline EDN/ECP and time. Since the effect of baseline EDN/ECP on relapse did not vary with time, interaction term between EDN/ECP and time was excluded in the following models.

Ulcerative colitis

Table 1 Data from extended Cox regression on predictors of clinical relapse in ulcerative colitis, based on log concentration of baseline faecal EDN.

| Predictors       | Model 1A - baseline EDN | Model 1B - baseline EDN |
|------------------|-------------------------|-------------------------|
|                  | HR  | 95% CI       | p-value   | HR  | 95% CI       | p-value   |
| Baseline EDN     | 1.20| 1.01-1.42    | 0.035     | 1.27| 1.04 - 1.54  | 0.018     |
| Age              | 0.99| 0.96-1.02    | 0.524     | 0.98| 0.94 - 1.03  | 0.437     |
| Sex              | 0.51| 0.20-1.29    | 0.152     | 0.74| 0.29 - 1.94  | 0.544     |
| 5ASA             | 0.40| 0.14 - 1.19  | 0.099     | 0.40| 0.14 - 1.19  | 0.099     |
| Salazopyrin      | 0.48| 0.11 - 2.04  | 0.316     | 0.48| 0.11 - 2.04  | 0.316     |
| Topical 5ASA     | 2.55| 0.65 - 10.05 | 0.181     | 2.55| 0.65 - 10.05 | 0.181     |
| Azathioprine/Methotrexate | 0.72| 0.23 - 2.21  | 0.564     | 0.72| 0.23 - 2.21  | 0.564     |

Remicade: no standard error available.
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Table 2 Data from extended Cox regression on predictors of clinical relapse in ulcerative colitis, based on log concentration of baseline faecal ECP.

| Predictors          | HR  | 95% CI     | p-value |
|---------------------|-----|------------|---------|
| Baseline ECP        | 1.13| 0.90 - 1.44| 0.298   |
| Age                 | 0.99| 0.96 - 1.02| 0.641   |
| Sex                 | 0.56| 0.21 - 1.45| 0.231   |

Model 1B - baseline ECP

| Predictors          | HR  | 95% CI     | p-value |
|---------------------|-----|------------|---------|
| Baseline ECP        | 1.11| 0.84 - 1.46| 0.471   |
| Age                 | 0.99| 0.95 - 1.03| 0.752   |
| Sex                 | 0.73| 0.27 - 2.00| 0.543   |
| 5ASA                | 0.41| 0.14 - 1.23| 0.111   |
| Salazopyrin         | 0.50| 0.11 - 2.21| 0.363   |
| Topical 5ASA        | 2.82| 0.64 - 12.48| 0.171  |
| Azathioprine/ Methotrexate | 0.90 | 0.28 - 2.85 | 0.858 |

Crohn's disease

Table 3 Data from extended Cox regression on predictors of clinical relapse in Crohn's disease, based on log concentration of baseline faecal EDN.

Model 1A - baseline EDN

| Predictors  | HR  | 95% CI     | p-value |
|-------------|-----|------------|---------|
| Log2 EDN    | 0.91| 0.71 - 1.15| 0.419   |
| Age         | 0.99| 0.96 - 1.03| 0.729   |
| Sex         | 0.77| 0.29 - 2.10| 0.614   |

Model 1B- baseline EDN

| Predictors          | HR  | 95% CI     | p-value |
|---------------------|-----|------------|---------|
| Log2 EDN            | 0.88| 0.69 - 1.13| 0.329   |
| Age                 | 1.02| 0.97 - 1.07| 0.446   |
| Sex                 | 0.82| 0.26 - 2.57| 0.734   |
| 5ASA                | 3.02| 0.60 - 15.22| 0.603  |
| Salazopyrin         | 0.80| 0.19 - 3.40| 0.761   |
| Azathioprine/ Methotrexate | 1.21 | 0.40 - 3.71 | 0.733 |

Topical 5ASA, Remicade: no standard error available.
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**Table 4** Data from extended Cox regression on predictors of clinical relapse in Crohn's disease, based on log concentration of baseline faecal ECP.

| Predictors       | HR   | 95% CI   | p-value |
|------------------|------|----------|---------|
| Model 1A - baseline ECP |      |          |         |
| Log2 ECP         | 1.14 | 0.85 - 1.52 | 0.392  |
| Age              | 1.00 | 0.97 - 1.04 | 0.875  |
| Sex              | 0.78 | 0.29 - 2.13 | 0.630  |

| Predictors       | HR   | 95% CI   | p-value |
|------------------|------|----------|---------|
| Model 1B - baseline ECP |      |          |         |
| Log2 ECP         | 1.12 | 0.84 - 1.50 | 0.450  |
| Age              | 1.03 | 0.98 - 1.07 | 0.296  |
| Sex              | 0.86 | 0.26 - 2.82 | 0.802  |
| 5ASA             | 2.70 | 0.49 - 14.96 | 0.255  |
| Salazopyrin      | 0.83 | 0.19 - 3.62 | 0.809  |
| Azathioprine/Methotrexate | 1.19 | 0.39 - 3.63 | 0.755  |

Topical 5ASA, Remicade: no standard error available.
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2. Predictive value of time-variant measurements

The analysis is based on all EDN/ECP measurements during the entire study period and model 2A includes time-variant faecal EDN/ECP levels, age and sex. Model 2B includes a sensitivity analysis by adding baseline treatment options as covariates in the extended Cox regression model.

No violation of proportional hazards assumption was found for covariates, and there was no statistically significant interaction found between EDN/ECP and time. Since the effect of EDN/ECP on relapse did not vary with time, interaction term between EDN/ECP and time was excluded in the following models.

**Ulcerative colitis**

*Table 5* Data from extended Cox regression on predictors of clinical relapse in ulcerative colitis, based on time-variant faecal EDN, age, sex; and extended model 2B, including time-variant EDN, age, sex and different treatment factors.

| Predictors        | HR   | 95% CI     | p-value |
|-------------------|------|------------|---------|
| Model 2A- EDN     |      |            |         |
| Log2 EDN          | 1.31 | 1.09 - 1.58| **0.004**|
| Age               | 0.99 | 0.96 - 1.02| 0.604   |
| Sex               | 0.48 | 0.19 - 1.25| 0.133   |

| Predictors        | HR   | 95% CI     | p-value |
|-------------------|------|------------|---------|
| Model 2B - EDN    |      |            |         |
| Log2 EDN          | 1.32 | 1.10 - 1.59| **0.003**|
| Age               | 1.00 | 0.96 - 1.03| 0.850   |
| Sex               | 0.59 | 0.22 - 1.56| 0.284   |
| 5ASA              | 0.77 | 0.26 - 2.22| 0.623   |
| Salazopyrin       | 0.38 | 0.08 - 1.90| 0.240   |
| Topical 5ASA      | 1.42 | 0.18 - 11.43| 0.743 |
| Azathioprine/     | 0.74 | 0.24 - 2.32| 0.605   |
| Methotrexate      |      |            |         |
| Remicade: no standard error available.
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**Table 6** Data from extended Cox regression on predictors of clinical relapse in ulcerative colitis, based on time-variant faecal ECP

| Predictors      | HR   | 95% CI       | p-value |
|-----------------|------|--------------|---------|
| Log2 ECP        | 1.27 | 1.00 - 1.61  | 0.046   |
| Age             | 0.99 | 0.96 - 1.03  | 0.728   |
| Sex             | 0.51 | 0.19 - 1.35  | 0.176   |

**Model 2B - ECP**

| Predictors      | HR   | 95% CI       | p-value |
|-----------------|------|--------------|---------|
| Log2 ECP        | 1.27 | 1.00 - 1.62  | 0.054   |
| Age             | 1.00 | 0.96 - 1.03  | 0.881   |
| Sex             | 0.57 | 0.21 - 1.54  | 0.269   |
| 5ASA            | 0.83 | 0.29 - 2.43  | 0.739   |
| Salazopyrin     | 0.46 | 0.09 - 2.24  | 0.338   |
| Topical 5ASA    | 1.81 | 0.22 - 15.14 | 0.582   |
| Azathioprine/   | 0.76 | 0.24 - 2.42  | 0.641   |
| Methotrexate    |      |              |         |

Remicade: no standard error available.

**Crohn's Disease**

**Table 7** Data from extended Cox regression on predictors of clinical relapse in Crohn's disease, based on time-variant faecal EDN

**Model 2A - EDN**

| Predictors      | HR   | 95% CI       | p-value |
|-----------------|------|--------------|---------|
| Log2 EDN        | 0.95 | 0.75 - 1.20  | 0.671   |
| Age             | 0.99 | 0.96 - 1.03  | 0.738   |
| Sex             | 0.81 | 0.29 - 2.23  | 0.682   |

**Model 2B - EDN**

| Predictors      | HR   | 95% CI       | p-value |
|-----------------|------|--------------|---------|
| Log2 EDN        | 0.94 | 0.73 - 1.21  | 0.627   |
| Age             | 1.01 | 0.97 - 1.06  | 0.533   |
| Sex             | 0.82 | 0.27 - 2.52  | 0.736   |
| 5ASA            | 2.78 | 0.51 - 15.24 | 0.240   |
| Salazopyrin     | 0.65 | 0.12 - 3.46  | 0.612   |
| Azathioprine/   | 1.14 | 0.34 - 3.81  | 0.828   |
| Methotrexate    |      |              |         |

Topical 5ASA, Remicade: no standard error available.
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**Table 8** Data from extended Cox regression on predictors of clinical relapse in Crohn's disease, based on time-variant faecal ECP

|                  | Model 2A - ECP | Model 2B - ECP |
|------------------|----------------|----------------|
| **Predictors**   | **HR**         | **95% CI**     | **p-value** |
| Log2 ECP         | 1.15           | 0.86 - 1.55    | 0.346       |
| Age              | 1.00           | 0.97 - 1.04    | 0.802       |
| Sex              | 0.74           | 0.27 - 2.03    | 0.564       |
| Log2 ECP         | 1.16           | 0.86 - 1.57    | 0.340       |
| age              | 1.03           | 0.98 - 1.07    | 0.283       |
| Sex              | 0.74           | 0.24 - 2.28    | 0.604       |
| 5ASA             | 2.31           | 0.40 - 13.36   | 0.349       |
| Salazopyrin      | 0.61           | 0.11 - 3.24    | 0.561       |
| Azathioprine/     | 1.32           | 0.43 - 4.07    | 0.624       |
| Methotrexate     |                |                |             |

Topical 5ASA, Remicade: no standard error available.