U-BIOPRED asthma cohort: inflammatory markers and corticosteroid use

### Background:
The Unbiased Biomarkers for the Prediction of Respiratory Disease Outcomes (U-BIOPRED) consortium is a pan-European public-private collaboration funded by the Innovative Medicines Initiative (IMI) of the European Union and EFPIA. U-BIOPRED aims to identify subphenotypes and patient groups with severe refractory asthma by using an innovative systems medicine approach. (http://www.unbiasedpredictiveasthma-lungfoundation.org)

### Hypothesis:
The inflammatory response in severe asthma is variable and influenced by oral corticosteroid (OCS) use.

### Methods (cont.):
- A sub-set of patients undergoing fibrobronchoscopic (n=194).
- Severe asthma cohorts are followed up longitudinally from 12 to 18 months and in some, an additional exacerbation visit.

#### Results:

- In the adult severe cohort:
  - Sputum eos % weakly positively correlated with FENO (Plots 2).
  - Sputum eos % negatively correlated with sputum neutrophil % (Plots 3).
  - Maintenance oral corticosteroid use was associated with higher sputum eosinophils, raised FENO, a greater prevalence of nasal polyps and greater requirements for nebuliser use and theophylline.

#### Methods:
- Severe asthma was defined according to IMI criteria (Thorax 2011; 66:910-7: patients on high-dose inhaled corticosteroids (≥1000mg FP), and uncontrolled according to GINA criteria of >3 exacerbations/year or used oral corticosteroids.
- 15 recruiting centres from 12 European countries participated.
- A baseline visit included an assessment of current health status, atopy, pulmonary function, sputum, HRCT scans (n=179), questionnaires (QOL, anxiety/depression, adherence) together with blood and urine tests, exhaled air VOCs and induced sputum; with biobanking of samples for lipidomic, transcriptomic, proteomic and immunohistochemistry analyses.

### Results (cont.):

#### Table 4: Adult severe asthmatics according to daily OCS use

<table>
<thead>
<tr>
<th>OCS N (%)</th>
<th>Yes</th>
<th>No</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>95 (50.0)</td>
<td>73 (47.0)</td>
<td>0.007</td>
</tr>
<tr>
<td>Ex</td>
<td>71 (31.7)</td>
<td>70 (44.6)</td>
<td>0.03</td>
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<tr>
<td>BMI</td>
<td>28.9 (29.4 - 34.2)</td>
<td>27.0 (24.0 - 32.7)</td>
<td>0.007</td>
</tr>
<tr>
<td>FEV1 (%)</td>
<td>78 (43.7 - 165.2)</td>
<td>78 (43.7 - 165.2)</td>
<td>0.41</td>
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<tr>
<td>FENO (ppb)</td>
<td>43.9 (13.2 - 215)</td>
<td>21.0 (20.3 - 22.2)</td>
<td>0.007</td>
</tr>
<tr>
<td>eos</td>
<td>48 (9.2)</td>
<td>48 (9.2)</td>
<td>0.41</td>
</tr>
<tr>
<td>FVC (%)</td>
<td>0.9</td>
<td>0.9</td>
<td>0.41</td>
</tr>
</tbody>
</table>

#### Conclusions:
- The OCS-dependent severe patient is characterised by high sputum eosinophilia and raised exhaled NO levels.
- This may reflect increased disease severity and a decreased response to corticosteroidal therapy.
- Analysis of the entire cohort is being undertaken incorporating integrative ‘omics’ analysis to form a definitive ‘handprint’ of severe asthma in terms of corticosteroid use.