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Title: The effects of interferon beta on cold-induced asthma exacerbations

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Body: In vitro studies show that asthmatic bronchial epithelial cells produce insufficient interferon beta (IFNb) when infected with rhinovirus (RV), whilst exogenous IFNb restores their capability to stop viral replication. This has provided pre-clinical POC for innate immune deficiency in asthma and a rationale for a randomised placebo controlled clinical trial of aerosolised IFNb. The trial involved 21 centres and 147 asthmatics, with the sACQ (shortened Asthma Control Questionnaire) as the primary outcome. Patients commenced treatment at the onset of common cold symptoms and, following baseline assessment, were treated daily for 2 wks with IFNb (6MIU) or placebo.134 patients fulfilled the Jackson criteria for a cold (mITT population): in these, respiratory viruses were detected in nasal lavage by PCR in 63% of patients (68% RV+). In the placebo group, cold symptoms correlated strongly with those of asthma and only patients with difficult to treat asthma (BTS steps 4 and 5) had a clinically relevant (>0.5) increase in sACQ, whilst step 2 or 3 asthmatics did not. In the difficult to treat patients the difference in sACQ during the first week was 0.63 ($p=0.004$) in favour of treatment and the % experiencing an exacerbation was significantly ($p=0.012$) lower. Treatment with IFNb also resulted in significantly faster recovery of PEF and less use of b2-agonists ($p<0.05$). This trial suggests that treatment with inhaled IFNb significantly attenuates the adverse effects of the common cold in difficult to treat asthma patients whose needs for such treatment are greatest. The study provides rationale for follow on clinical trials. (The trial was funded by Synairgen plc and supported by NIHR).