Results Treatment of lipoxin A4 (100 nM) increased the apoptosis of neutrophils ($p = 0.0244$), and reduced the dead ($p = 0.0238$) and necrotic neutrophils ($p = 0.0358$) compared to control ($n = 8$). BALF from patients with ARDS suppressed efferocytosis of apoptotic neutrophils. The effects of BALF correlated with HMGB-1 levels in the BALF fluid. HMGB-1 decreased efferocytosis ($p < 0.05$) in a dose dependent manner, and reached a significant effect at 150 ng/ml ($p = 0.008$). Lipoxin A4 increased the efferocytosis ($p < 0.05$) of alveolar macrophages in a dose dependent manner, and reached the maximal effect at 100 nM ($p = 0.008$). Moreover, lipoxin A4 (100 nM) blocked the decreased efferocytosis response to HMGB-1 (150 ng/ml) ($p = 0.005$, $n = 8$). The lipoxin A4 beneficial effects were abrogated by ALX antagonist, BOC-2 ($p < 0.05$) and PI3K inhibitor ($p < 0.05$).

Conclusions Lipxin A_4*in vitro* promotes the apoptosis but not necrosis of neutrophils. In tandem it stimulates efferocytosis of alveolar macrophages. Elevated HMGB-1 in ARDS BALF suppresses efferocytosis. Lipoxin A_4 can block these effects of HMGB-1. The effect of lipoxin A4 increasing efferocytosis was through ALX–PI3K signalling pathways. Lipoxin A_4 may therefore have potential as a therapeutic agent to promote the resolution of neutrophilic inflammation in ARDS.

COPD outcomes

S103 NO LOSS IN EFFICACY FOLLOWING SWITCH FROM SALMETEROL/FLUTICASONE COMBINATION TO INDACATEROL MONOTHERAPY IN PATIENTS WITH MODERATE COPD: THE INSTEAD STUDY

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Introduction Many patients with low risk of COPD exacerbations receive twice-daily (*bid*) LABA/ICS, salmeterol/fluticasone (SFC), for maintenance treatment. This study evaluated the effect of switching these patients to a once-daily (*od*) LABA, indacaterol, monotherapy.

Methods INSTEAD was a 26-week double-blind, double-dummy study in patients aged ≥40 years, with moderate COPD (post-bronchodilator FEV_1 50–80% predicted) and no exacerbations in the past 12 months, who were receiving SFC 50/500 µg *bid* for ≥3 months prior to study entry. Patients were randomised (1:1) to continue with SFC 50/500 µg or to be switched (with no washout) to indacaterol 150 µg. The primary objective was to demonstrate non-inferiority of indacaterol to SFC, measured by trough FEV_1 after 12 weeks (non-inferiority margin: 60 mL). Trough FEV1 was also evaluated at 4, 8 and 26 weeks. TDI and SGRQ-C total scores were evaluated at Weeks 12 and 26; the annualised rate of exacerbations and safety were evaluated over 26 weeks.

Results A total of581 patients were randomised (indacaterol: 293; SFC: 288); 85.4% completed the study. The primary endpoint was met, with a LSM difference in trough FEV_1 between indacaterol and SFC of –9 mL (95% CI: –45 to 26 mL; p = 0·002 for NI). There were no significant differences between treatments in trough FEV_1 at any of the other visits (Baseline and Weeks 4, 8 and 26). The TDI and SGRQ-C total scores and their responder rates were similar between two treatments, at both Weeks 12 and 26 (Table 1). During the 26 week treatment period, 79.5% and 74.7% of patients in the indacaterol and SFC groups, respectively, experienced no exacerbations. There was no statistically significant difference between treatments in the rate of all COPD exacerbations per year, with rates of 0.57 vs 0.67, respectively (RR 0.86 [95% CI 0.62, 1.20]; p = 0.367). Adverse events (AEs) and serious AEs were comparable between the treatment arms.

Conclusion Indacaterol was non-inferior to SFC in terms of bronchodilation and showed similar efficacy in terms of breathlessness, health status, and exacerbation rate indicating that this group of patients can be switched from SFC to indacaterol 150 µg with no loss in efficacy.

S104 DOUBLE-BLIND MULTI-CENTRE RANDOMISED CONTROLLED TRIAL OF VITAMIN D3 SUPPLEMENTATION IN COPD (VIDICO)

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Introduction and objectives Inadequate vitamin D status is common in patients with COPD, and it associates with susceptibility to upper respiratory infection (URI) – a major precipitant of exacerbation. Multi-centre trials of vitamin D supplementation for prevention of exacerbation and URI in COPD are lacking. We therefore conducted a multi-centre double-blind randomised placebo-controlled trial of vitamin D supplementation for the prevention of moderate/severe exacerbation and URI in adults with COPD.

Methods Two hundred and forty patients were allocated to receive a 2-monthly oral dose of 3 mg vitamin D_3 or placebo for one year. Co-primary outcomes were time to first moderate/

Abstract S103 Table 1 TDI and SGRQ scores

	Week 12			Week 26		
	Indacaterol	SFC	Treatment difference (95% CI)	Indacaterol	SFC	Treatment difference (95% CI)
TDI total score	1.89 (0.499)†	1.69 (0.509)†	0.20 (-0.32, 0.72)	2.58 (0.543)†	2.70 (0.552)†	-0.12 (-0.71, 0.48)
SGRQ-C total score	32.8 (1.58)†	32.9 (1.61)†	-0.10 (-1.9, 1.8)	33.1 (1.87)†	33.5 (1.93)†	-0.40 (-2.5, 1.6)
TDI responder (≥1 unit),%	61.4	61.0	0.97 (0.65, 1.46)#	68.7	69.4	0.88 (0.58, 1.35)#
SGRQ-C responder (≥4 unit),%	44.7	42.4	1.12 (0.76, 1.63)#	49.6	48.8	1.03 (0.70, 1.52)#

†Data are LSM (SE): #odds ratio; LSM, least square means; TDI, transition dyspnoea index; SGRQ-C, St George Respiratory Questionnaire for COPD

severe exacerbation and time to first URI. Secondary outcomes included peak severity and area under the curve for exacerbation symptoms. A pre-specified sub-group analysis was conducted to determine whether effects of the intervention on co-primary outcomes were modified by baseline vitamin D status. This trial is registered with ClinicalTrials.gov (NCT00977873).

Results 122 participants were allocated to the intervention arm of the trial, and 118 to the control arm. Vitamin D supplementation did not influence time to first exacerbation (HR 0.86, 95% CI 0.60–1.24, p = 0.42) or time to first URI (HR 0.95, 95% CI 0.69–1.31, p = 0.75) in the study population as a whole, but it did reduce peak severity (p = 0.042) and area under the curve (p = 0.032) for exacerbation symptoms. Pre-specified sub-group analysis revealed that vitamin D supplementation was protective against moderate/severe exacerbation among the 148 participants with baseline serum 25-hydroxyvitamin D (25[OH]D) concentration < 50 nmol/L (aHR 0.57, 95% CI 0.35 to 0.92, p = 0.021), but not among the 92 participants with baseline serum 25(OH) D ≥ 50 nmol/L (aHR 1.45, 95% CI 0.81 to 2.62, p = 0.21; P for interaction = 0.021). Baseline vitamin D status did not modify the effect of vitamin D supplementation on risk of URI (P for interaction = 0.41).

Conclusions Vitamin D supplementation protected against moderate/severe exacerbation, but not upper respiratory infection, in COPD patients with baseline 25(OH)D < 50 nmol/L. It also modestly reduced peak severity and area under the curve for exacerbation symptom scores, irrespective of baseline vitamin D status.

Abstract S105 Table 1 Mean changes in, FVC, at IOS 5Hz andHz, FeNO and PWV after exposures began in Oxford Street (OS) and Hyde Park (HP)

	Healthy				COPD			
	OS	HP	Δd	p	OS	HP	Δd	p
Spirometry (difference%)								
FEV_1 1 h	0.78	3.46	-2.68	0.09	**-2.30**	**1.70**	**-4.00**	**0.01** *
FEV_1 2 h	0.49	2.38	-1.89	0.17	-1.43	-0.38	-1.05	0.39
FEV_1 6 h	**1.84**	**7.89**	**-6.05**	**0.01** *	1.68	2.08	-0.41	0.79
FEV_1 24h	**0.05**	**4.22**	**-4.17**	**0.01** *	1.85	0.92	0.93	0.65
FVC 1 h	0.00	1.81	-1.81	0.28	**-1.84**	**1.57**	**-3.41**	**0.02** *
FVC 2 h	-1.00	1.16	-2.16	0.32	-3.22	-0.11	-3.11	0.09
FVC 6 h	0.22	3.57	-3.35	0.17	1.38	1.60	-0.22	0.90
FVC 24h	-1.60	-2.84	1.24	0.68	1.60	2.54	-0.95	0.73
IOS 5hz (difference kPa/l/s)								
IOS 5hz 4 h	-0.01	-0.01	0.00	0.78	**0.03**	**-0.02**	**0.05**	**0.01** *
IOS 20hz 4 h	-0.01	-0.02	0.01	0.48	-0.01	-0.04	0.03	0.09
IOS 20hz (difference kPa/l/s)								
IOS 20hz 4 h	-0.01	-0.01	0.00	0.80	-0.72	-0.03	-0.68	0.35
IOS 20hz 24h	-0.01	-0.01	0.00	0.73	**0.00**	**-0.03**	**0.02**	**0.04** *
FeNO (difference ppb)								
3h	-5	-4	-1	0.75	-2	-4	2	0.71
5h	-4	-2	-2	0.37	-7	-7	-1	0.89
24h	-4	-1	-3	0.26	2	-6	8	0.09
PWV (difference m/s)								
3 h	-0.1	-0.2	0.2	0.47	**0.1**	**-0.6**	**0.8**	**0.03** *
6h	0.3	0.0	0.3	0.32	**0.2**	**-0.3**	**0.5**	**0.03** *
24 h	**0.6**	**-0.4**	**1.0**	**0.04** *	0.3	-0.4	0.7	0.32

* $p < 0.05$
Δ d Mean difference of difference between each exposure site

S105 THE EFFECTS OF REAL-WORLD EXPOSURES TO DIESEL TRAFFIC EMISSIONS ON CARDIO-RESPIRATORY OUTCOMES IN COPD : 'OXFORD STREET 2'

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Introduction and objectives We studied the changes in lung function and cardiovascular responses in healthy volunteers and patients with COPD exposed to the high pollution levels in a busy London street.

Methods Using a cross-over design, 37 healthy volunteers and 37 COPD patients (walked along Oxford Street (diesel only traffic) and, on a separate occasion, in Hyde Park (low or little traffic), London for two hours. Cardio-respiratory measurements were performed at baseline, and during and after each exposure, alongside personal particulate and gaseous exposure measurements.

Findings Compared to Hyde Park, mean exposures on Oxford Street had higher levels of black carbon (10.4 μm/m^3 vs. 1.2 μm/m^3, p < 0.001) and ultrafine particle counts (25472/cm^3 vs 5709/cm^3, p < 0.001).

In comparison with Hyde Park the healthy subjects had a mean fall in FEV_1 from baseline of6.05% (p = 0.01) 6 h and a fall of 4.17% (p = 0.01) 24 h after arrival in Oxford St. There was no associated drop in FVC. Arterial stiffness measured by pulse wave velocity (PWV) increased 24 h after arriving on Oxford Street.

In volunteers with COPD, there was a mean fall in FEV_1 of 4% (p = 0.01) with an associated drop in FVC of 3.4% (p = 0.02) one hour after the start of exposure on Oxford Street, compared to Hyde Park. Measurement of impulse oscillometry in volunteers with COPD demonstrated increased airway resistance at 5 Hz of 0.05 kPa/l/s (p = 0.01) four hours and at 20 Hz of 0.02 (p = 0.04) 24 h after exposure began on Oxford Street. PWV increased by 0.8 m/s and 0.5 m/s three hours and six hours after exposure started on Oxford street respectively.

There were no changes in FeNO in either group between the two sites.

Preliminary multivariate analysis has so far found no associations with individual particulate measurements.

Conclusions These findings show that airways obstruction occurred in both the healthy volunteers and COPD patients exposed to ambient levels of diesel pollution on a busy London Street. The associated vascular dysfunction was more prominent in COPD patients. Further analyses of markers of inflammation in the collected samples are now needed to ascertain the mechanistic cause of the pathophysiological findings.

S106 REVIEW OF EUROPEAN COPD AUDIT DATA: FACTORS AFFECTING LENGTH OF STAY

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