50. COPD management

P244

Adherence of stable COPD patients to inhaled pharmacotherapy

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Since compliance to inhaled medications is related to a decreased risk of hospitalizations and death in COPD, we aimed to investigate the compliance of COPD patients to inhaled pharmacotherapy. We studied 208 COPD patients [age 63±8 years; 77 in stage II (37%); 112 in stage III (54%); and 19 in stage IV (9%)]. Non-compliance was defined as the incorrect use of the inhaler device, as a sporadic or prn use due to perception of no effect or due to wrong information, when patient or his caregiver declares non-compliance, and when medication is not prescribed regularly. Results are reported for Tiotropium (T), fixed combinations of either Salmeterol/Fluticasone (S/F) or Formoterol/Budesonide (F/B), and Salmeterol (S) or Formoterol (F) as single agents. Overall compliance to the above inhaled agents was 92%, 84%, 81%, 75% and 68% respectively. According to GOLD staging, compliance to T was 87% (st.II)-94% (st.III)-95% (st.IV), to S/F 78% (II)-84% (III)- 92% (IV), to F/B 78% (II)-79% (III)-100% (IV), to S 67% (II)-100% (III) and to F 61% (II)-86% (III). Major reasons for non-compliance to S/F was the incorrect technique to inhale from the Diskus (78%), to F/B the preception of no effect when inhaling from the Turbohaler (50%), while reasons for non-compliance to T were the incorrect technique of using Handihaler (36%), no purchase or prescription renewal (36%) and sporadic use (28%). We conclude that compliance rates were higher for Tiotropium and the fixed combination of Salmeterol/Fluticasone. There was an increasing compliance in relation to COPD severity, while the detected reasons of poor compliance should be tackled through a more effective contact between COPD patients and their physicians.

P245

Health-related quality of life (HRQL) and patient-reported outcomes (PRO) in COPD patients receiving add-on-therapy with EPs® 7630

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HRQL and PRO are important measures for treatment evaluation and assessment of health condition.

In an RCT (ISRCTN01681733) in patients with COPD stage II/III, add-on therapy with EPs® 7630, a herbal drug preparation from Pelargonium sidoides roots (Umckaloabo®; ISO Arzneimittel, Ettlingen, GER), significantly prolonged time to exacerbations and reduced their frequency. We also investigated HRQL and further PRO parameters assessed during the trial.

Patients with a standardised COPD baseline treatment according to GOLD were randomly allocated to a double-blind 24-week oral add-on therapy with 30 drops EPs® 7630 (n=99) or placebo (n=101) thrice daily. HRQL/PRO were assessed by St. George's Respiratory Questionnaire (SGRQ), EQ-5D, Integrative Medicine Patient Satisfaction Scale (IMPSS), Integrative Medicine Outcomes Scale (IMOS), patient-reported intensity score of cough, sputum production and sternal pain while coughing, and drug tolerability.

After 24 weeks, patients treated with EPs® 7630 reported a significantly more improved HRQL compared to placebo (SGRQ total score, $p<0.001$; EQ-5D VAS, $p<0.001$). For EPs® 7630, patient satisfaction with treatment was significantly

higher (IMPSS, p<0.001), patient-reported treatment outcome significantly better (IMOS, p<0.001) and the mean intensity score during exacerbations significantly lower (p=0.024). Incidence of adverse events was comparably low in both groups.
Conclusion: Add-on-therapy with EPs® 7630 led to a statistically significant and clinically relevant improvement of HRQL and other PRO (total score difference of SGRQ >4 points) including good long-term tolerability in patients with COPD stage II and III.

P246
Treatment with megestrol acetate and testosterone increases body weight and muscle mass in COPD cachexia
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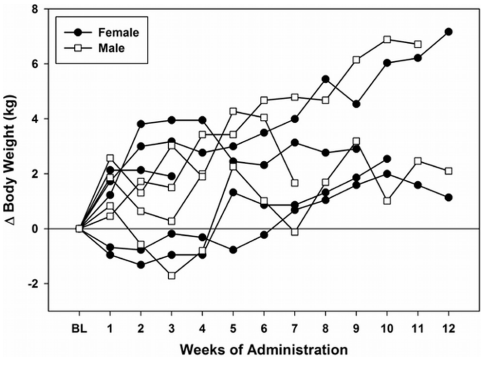
Underweight COPD patients with involuntary weight loss have a poor prognosis; no effective therapy is available. We conducted the first clinical trial determining whether combined therapy with an appetite stimulant and an anabolic steroid would have beneficial body composition effects.
We conducted a 12 week pilot study in which 4 men and 5 women (age 64±10y, FEV1%pred 31±9, BMI 18±3) with low testosterone (T) levels (average 490ng/dl in men and 12ng/dl in women) and weight loss >10lb over the previous year received 800mg megestrol acetate/day plus weekly testosterone enanthate injections initially 125mg in men and 40 mg in women, with doses subsequently adjusted targeting serum T levels of 850 and 300ng/dl, respectively.
Two women and two men had COPD exacerbations and did not complete the study. On treatment T levels were 334±72ng/dl in women and 670±98ng/dl in men. Body weight increased in all 9 subjects, with end-intervention weight gain of 3.1±2.2kg (p<0.005).



In the 5 subjects who completed, DEXA revealed 2.0±1.5kg lean mass and 2.5±2.0kg fat mass increase (both p<0.05). No adverse treatment effects were detected.
Combination therapy reversed involuntary weight loss and increased muscle mass in cachectic COPD patients. Though the interventions were apparently well tolerated, subject drop out rate was high. Larger randomized long-term studies with functional outcomes are needed.

P247
Efficacy of roflumilast in former and current smokers with COPD
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Background/Rationale: A history of smoking is common in COPD pts. Pooled data from four 1-year studies of the selective phosphodiesterase 4 inhibitor roflumilast (ROF) were analysed to investigate the effects of smoking history on response to ROF.
Methods: Two studies enrolled pts with severe COPD associated with chronic bronchitis and a history of exacerbations and two studies enrolled pts with or without bronchitis and exacerbations. Following a 4-week placebo run-in, pts received ROF 500µg or placebo (PBO) for 52 wks. Primary endpoints were change in exacerbation rate and FEV_1. We performed an analysis of these results according to smoking status.
Results: Mean age (SD) was 64.13 (9.17) yrs; 3440 (59.5%) pts were former smokers and 2337 (40.5%) pts were current smokers.
Conclusions: The efficacy of ROF vs PBO in reducing the rate of moderate or severe exacerbations and improving pre- and post-BD FEV_1 in pts with established COPD was independent of smoking history.

Abstract P247 – Table 1

	Former smokers		Current smokers	
	ROF (n=1700)	PBO (n=1740)	ROF (n=1164)	PBO (n=1173)
Mean age, yrs (SD)	66.46 (8.94)	66.39 (8.80)	60.83 (8.80)	60.71 (8.29)
Mean rate of moderate or severe exacerbations per patient per year (95% CI)	0.86 (0.79, 0.95)	1.05 (0.97, 1.14)	0.75 (0.68, 0.83)	0.91 (0.83, 1.0)
Rate ratio: ROF/PBO	0.82 (–17.9%, p=0.0003)		0.83 (–17.5%, p=0.0038)	
Frequency of patients with moderate or severe exacerbations (%)	673 (39.6%)	814 (46.8%)	451 (38.7%)	495 (42.2%)
Mean (SEM) pre-BD FEV1 (L)				
Baseline	0.97 (0.01)	0.97 (0.01)	1.05 (0.01)	1.07 (0.01)
52 wks	1.06 (0.01)	1.00 (0.01)*	1.12 (0.01)	1.09 (0.01)*
Mean (SEM) post-BD FEV1 (L)				
Baseline	1.08 (0.01)	1.08 (0.01)	1.16 (0.01)	1.17 (0.01)
52 wks	1.17 (0.01)	1.11 (0.01)*	1.23 (0.02)	1.19 (0.02)*

BD, bronchodilator. *p<0.0001.

P248
Impact of roflumilast treatment on the rate and duration of exacerbations and overall steroid load in patients with COPD
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Background/Rationale: Roflumilast (ROF), an oral, selective phosphodiesterase 4 inhibitor, reduces the rate of moderate and severe exacerbations. Oral steroids are frequently used to treat exacerbations, but whether ROF affects oral steroid exposure is not known. Using data pooled from two 1-year studies (NCT00297102 and NCT00297115), we investigated the effect of ROF on the need for oral steroids.
Methods: Patients with COPD and a history of exacerbations and chronic bronchitis were randomised to receive ROF 500µg once daily (n=1537) or placebo (PBO; n=1554) for 52 weeks. Rate of moderate or severe (leading to hospitalisation or death) exacerbations was a co-primary endpoint. Steroid use (dose/day and days of use) for the treatment of exacerbations was recorded.
Results: The mean rate of moderate or severe exacerbations in ROF- and PBO-treated patients (per patient/year) was 1.14 vs 1.37, respectively (reduction 16.9%, p=0.0003). The mean number of days on which patients had exacerbations was reduced with ROF vs PBO (moderate 23.7 vs 27.3; severe 21.5 vs 25.0). The mean duration (days) of exacerbations was also reduced with ROF vs PBO (moderate 13.4 vs 13.9; severe 17.4 vs 19.5). Patients receiving ROF had a lower mean daily steroid dose (3.9mg/day) than those receiving PBO (4.2mg/day).
Conclusions: In patients with COPD associated with chronic bronchitis, ROF significantly reduced the rate of moderate or severe exacerbations. ROF treatment also reduced the duration of exacerbations, particularly for severe exacerbations requiring hospitalisation. The overall steroid load and duration of steroid treatment needed to manage exacerbations was lower with ROF.

P249
Acupuncture improves nutritional status and BODE index in patients with chronic obstructive pulmonary disease: A randomized, placebo-controlled trial
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Introduction: Prognosis of COPD patients is influenced not only by pulmonary functions but also by nutritional status, exercise capacity and severity of dyspnea. Our previous study (Suzuki M et al. AJRCCM 2010; 181: A5420) showed that acupuncture improved significantly not only Modified Borg Scale at the end of 6-minute walk test (MBS), but also various general conditions of COPD patients including quality of life (SGRQ).
Aim and Objective: To determine whether acupuncture had any effects on nutritional status and BODE index of COPD patients in our previous study.
Methods: We conducted parallel-group randomized controlled multicentre trials involving 68 COPD patients. The participants were randomly assigned to real (RA, n=34) or placebo acupuncture (PA, n=34). Both group received real or placebo needling once a week for a total of 12 weeks. We evaluated not only change in

MBS, as primary endpoint, but changes in pre-albumin, BMI, MRC, 6MWD, and respiratory functions. BODE index was calculated by these data.
Results: Six (4 in RA, 2 in PA) withdrew during study. After 12 weeks, RA group showed significant improvements in pre-albumin [22.6 to 25.1mg/dl], BMI [21.2 to 22.6kg/m^2], MRC [3.3 to 2.3], 6MWD [373.2 to 436.7m] and%FEV1 [44.5 to 49.2%], as well as MBS [5.5 to 1.9] of primary endpoint. The BODE index decreased significantly in the RA (3.9 to 2.7, $p<0.01$), but not changed in the PA (3.3 to 3.3, $p>0.9$; mean difference [95%CI] between groups, -1.2 [-1.8 to -0.63]).
Conclusions: This study demonstrated that acupuncture may contribute to improvement of nutritional status and prognosis as well as DOE of the patients with COPD.

P250
Time to desaturation under 1 minute on the 6m walking test predicts chronic domiciliary oxygen therapy in COPD patients
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Introduction: Time to desaturation (T90) on the 6 minute walking test (WT6m) on chronic obstructive pulmonary disease (COPD) patients correlates with time of desaturation during 24 hours oximetry. But it is unknown the clinical evolution in time of these patients.
Objetive: To analise the gasometric parameters changes on copd patients with early desaturation on the WT6m 5 years later.
Material and Methods: We studied 83 patients with COPD and desaturation on WT6m under 1 minute. 73 men/10 women, average 66 years old, Fev1: 42% pred and PO2 66mmHg. We did spirometries, gasometries, WT6m every 6 months for 5 years. The patients who during the study needed domiciliary oxygen theraphy, were prescribed by their phYsicians who did not know the content of the study.
Results: 5 years later, 65% of patients with early desaturation- T90 under 1 minute- had chronic domiciliary oxygen therapy vs 11% of patients with desaturation after 1 minute (T90 > 1 min), $p< 0.001$.
Conclusions: Moderate-severe COPD patients desaturing before 1 min on the WT6m need oxygen therapy before 5 years opposed to patients with desaturation after 1 minute. Early desaturators need more clinical and gasometric controls.

P251
Tiotropium vs salmeterol in GOLD II and maintenance-naïve COPD patients: Subgroup analyses of POET-COPD™ trial
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Background: Chronic obstructive pulmonary disease (COPD) guidelines recommend long-acting bronchodilator (muscarinic antagonist or β_2-agonist) maintenance therapy from GOLD stage II (moderate) disease onwards.
Aims and objectives: Prespecified subgroup analyses of POET-COPD™ trial, evaluating exacerbation outcomes of tiotropium (18 µg qd) vs salmeterol (50 µg bid), in a) GOLD II and b) maintenance-naïve (not previously receiving maintenance therapy) COPD patients.
Methods: 1-yr randomized, double-blind, double-dummy, parallel-group, multicenter trial. Inclusion criteria: COPD, smoking history >10 pk-yrs, post-bronch forced expiratory volume in 1s (FEV_1) <70% pred, FEV_1/forced vital capacity (FVC) <0.7, history of ≥1 moderate or severe exacerbation in prior year. Primary endpoint: time to first exacerbation.
Results: Of 7376 patients randomized and treated, 3614 were GOLD II and 1343 maintenance naïve at randomization. GOLD II: 69.3% men, age 63.2 yrs, 37.3 pk-yrs. Maintenance naïve: 72.2% men, age 60.9 yrs, 34.6 pk-yrs. Tiotropium prolonged time to first exacerbation in both GOLD II and maintenance-naïve groups: hazard ratio (95% confidence interval [CI]), tiotropium vs salmeterol: 0.88 (0.79-0.99), *P*=0.028 and 0.79 (0.65-0.97), *P*=0.028. Exacerbation rates (per pt-yr), tiotropium vs salmeterol: GOLD II, 0.55 vs 0.60, rate ratio (RR) (95% CI) 0.91 (0.81-1.01), *P*=0.072; maintenance naïve, 0.38 vs 0.49, RR (95% CI) 0.77 (0.63-0.94), *P*<0.05.
Conclusion: Similar to overall cohort in POET-COPD™, tiotropium improved exacerbation outcomes vs salmeterol in GOLD II and maintenance-naïve subgroups of COPD patients with an exacerbation history.
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P252
Efficient deposition and absorption of orally inhaled indacaterol in the lungs
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Introduction: Indacaterol (IND) is an inhaled long-acting β2-agonist for the once daily treatment of COPD, delivered via single-dose dry powder inhaler (Onbrez® Breezhaler®). Study aims were 1) To determine absolute bioavailability (Fabs) of IND after oral inhalation compared with intravenous (IV) dosing and 2) To determine relative contributions of lung and gastrointestinal tract (GIT) absorption to systemic exposure of inhaled IND. To this end, inhaled IND was also administered concurrently with oral activated charcoal.
Method: A two-part randomized, open label, single-dose study in healthy volunteers (HV). In Part 1, 8 HV received an IV infusion of 200 µg IND and an inhaled dose of 300 µg IND in a 2-way, 2-sequence crossover design. In period 3 all 8 HV received an inhaled dose of 600 µg IND together with an oral dose of charcoal. Treatments were separated by washouts of ≥14 days. In Part 2, 4 other HV received oral doses of IND (600 µg) and charcoal. Blood samples were taken for PK analysis and IND was determined in serum by LC-MS/MS. PK parameters were determined by non-compartmental methods.
Results: The Fabs of inhaled IND was 45%. Oral activated charcoal was effective in blocking the oral absorption of IND. The relative bioavailability of inhaled IND with oral charcoal was 74% compared to inhalation without charcoal.
Conclusion: Almost 75% of the systemic exposure following inhalation of IND was due to lung absorption, and 25% was due to GIT absorption. Based on an Fabs of 45% for inhaled IND, the fraction of the inhaled dose deposited and absorbed in the lungs was estimated as 34% of the nominal IND dose, providing evidence of effective lung delivery of inhaled IND via Onbrez® Breezhaler®.

P253
Subclinical cardiac dysfunction in moderate to severe chronic obstructive pulmonary disease (COPD) patients
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Introduction: COPD is associated with chronic cardiovascular (CV) comorbidities. IL6 is a pro-inflammatory cytokine involved in COPD pathogenesis. PTX3 is a inflammatory marker that might have role in systemic inflammation associated with COPD and comorbidities.
Objective: To investigate the relationship between circulating IL6 and PTX3 and COPD, we assessed cardiac function in COPD patients clinically free of CV disease and association among IL6 and PTX3, COPD severity, right (RV) and left (LV) ventricle function.
Methods: In 70 COPD (GOLD diagnosis) outpatients, ≥10 p/y, ≥50 yrs, we assessed Charlson Comorbidity Index, BODE index and echocardiography. LV systolic dysfunction was defined as LV ejection fraction (EF) <40%. Tricuspid Annular Plane Systolic Excursion (TAPSE) and RV function are according to JASE guidelines 2010. IL6 and PTX3 levels were measured by sandwich enzyme-linked immunosorbent assay. Associations were assessed by a linear regression model.
Results: We analyzed 70 COPD pts (52 M), mean age 68 yrs, mean p/y 45. COPD severity was GOLD I in 10 pts, II in 34, III in 26. Mean Charlson Index was 4 (range 2-8), mean BODE index 2.3, mean±SD DL_{CO}/Va 73±28, mean±SD LVEF 70±7. Mild RV diastolic dysfunction was found in 40/70 pts (57%). Interestingly, positive significant association (β=4.1,p=0.001) was found between TAPSE and DL_{CO}. Positive significant association (β=0.08,p=0.03) was also found between age and PTX3.
Conclusions: COPD pts with reduced DL_{CO} have reduction of TAPSE suggesting a subclinical RV systolic dysfunction. In this population, IL6 and PTX3 levels were not associated with cardiac dysfunction and COPD severity. By contrast, PTX3 is associated with aging.

P254
Effects of ambulatory oxygen on exercise capacity and vital parameters in patients with COPD
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Introduction: Ambulatory oxygen is defined as supplemental oxygen during exercise. Candidates for ambulatory oxygen are either already on long term oxygen therapy (LTOT) or show evidence of exercise desaturation.
Aim: The aim of this study is to evaluate the effects of ambulatory oxygen on exercise capacity and vital parameters in patients with COPD who didn't fulfill the criteria for LTOT.

Method: 45 patients with moderate to very severe COPD were included in our study. Six minute walk test was performed twice, while breathing room air (without oxygen cylinder) and oxygen at 2 l/min (while carrying oxygen cylinder). Six minute walk distance (6MWD), vital parameters, borg dyspnea and fatigue scores were recorded.
Results: Oxygen resulted in a significant increase in 6MWD for all patients. The results of SaO2, borg dyspnea and fatigue scores were same as 6MWD, all parameters were significantly improved while breathing oxygen and these improvements were significantly prominent in severe and very severe groups than the moderate group.

Improvments in 6MWD and Dyspnea

		Stage 2	Stage 3	Stage 4
Room Air	6MWD (m)	422,2	321,9	290
	Borg Dyspnea Score	2,71	3,96	4,86
Oxygen 2 l/min	6MWD (m)	432,6§	373,9§	346,2§
	Borg Dyspnea Score	1,29§	1,61§	2§

§p<0.001.

Conclusion: Oxygen significantly improved not only subjective complaints such as dyspnea and fatigue but also objective parameters such as 6MWD and saturation. Improvement of 6MWD in severe and very severe groups were over 10% which is a critical limit used in guidelines about ambulatory oxygen prescription. Thus our findings indicate that ambulatory oxygen therapy is an effective treatment modality for severe and very severe group COPD patients.

P255
Time required for PaO2 equilibration in patients with severe COPD
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Adjusting the inspired oxygen level in patients with COPD can be time consuming. Typically 30 minutes are waited before drawing an arterial sample to verify the PaO2 level. Consensus does not exist as to whether 30 minutes is a necessary period. Sherter et al. (Sherter, CB et al. Chest 1975; 67:259-261) showed that 20 minutes were required to return to baseline PaO2 after increased O2 in spontaneously breathing patients with COPD. In contrast, Sasse et al. (Sasse, SA et al. Am J Respir Crit Care Med 1995; 152(1):148-52) showed that 7 minutes were required to reach 90% of baseline PaO2 after an increase in O2 in mechanically ventilated patients with COPD. To the authors knowledge no study has investigated PaO2 equilibrium time following clinically relevant de- and increases in O2 in spontaneously breathing patients with COPD.
This study investigated PaO2 equilibration time in 5 patients with severe COPD in stable state (mean FEV1% 26, mean MRC-score 4.2), by analysis of consecutively drawn ABG samples. The initial PaO2 level was measured by 2 ABG's at the patient's LTOT level (1-2 l/min). Hereafter, LTOT was discontinued or reduced. Blood samples were drawn after 1, 2, 4, 8, 12, 17, 22, 32, and 33 minutes to analyse the reduction in PaO2. Hereafter LTOT was set to the initial level and increase in PaO2 was analysed at the same time periods. The 90% equilibrium times for PaO2 were 5.3 (±2.8) min for the decrease and 5.4 (±0.4) min for the increase in O2.
These results show a faster response to changes in FiO2 than seen previously, with similar response times for de- and increase in O2. Results indicate that it may be possible to reduce the time waited before evaluating ABG following changes in inspired oxygen.

P256
Determinants of dyspnea in stable COPD patients
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Background: Dyspnea is a major symptom in COPD, but its determinants remain poorly understood, with usually moderate correlation with clinical and lung function characteristics.
Aim of study: To analyse in a multivariate model the correlates of dyspnea in a large COPD cohort, including both clinical and resting lung function data.
Methods: Dyspnea was evaluated by the mMRC scale and the baseline dyspnea index (BDI) in 239 patients from the multicenter French COPD cohort Initiatives BPCO. A logistic ordinal regression (with stepwise ascending and descending analysis) was performed with the following variables: age, sex, BMI, FEV1, FVC, GOLD stage, IC, IC/TLC ratio, anxiety and depression scores (HAD; significant if ≥ 10), number of exacerbations, cardiac failure, history of venous thrombo-embolism
Results: For MRC score, the following variables were significant contributors to the model: BMI, FEV1, thrombo-embolic history, exacerbation rate, heart failure, HAD depression score. Estimated r^2 of the model was 0,33. For the BDI scale, only HAD depression, FEV1, exacerbation rate and heart failure were significant contributors. Estimated r^2 of the model was 0,29.
Conclusion: Dyspnea correlates in COPD include FEV1, HAD depression score, exacerbation frequency and heart failure. MRC and BDI were explained by slightly different contributors. Contrary to what could be expected, sex, age, and resting hyperinflation did not contribute significantly to dyspnea intensity.

P257
Screening for malnutrition in outpatients with pulmonary diseases
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Background: Malnutrion has negative effects on patient outcome, in particular in patients with COPD. Recognition of malnutrition in an early phase might be beneficial for patients and screening for malnutrition in an outpatient setting might, therefore, be worthwhile.
Aim: To determine the extent of malnutrition in outpatients with pulmonary diseases using different methods.
Methods: All patients visiting our outpatient department of pulmonary diseases for the first time (period Oct. 2010 - Febr. 2011) were screened for malnutrition. Different methods were used to screen for malnutrition: body mass index (bmi), Short Nutritional Assessment Questionnaire (SNAQ), and a fat free mass measurement (FFM; bio-impedance by Bodystat® 1500).
Results: Data of 121 outpatients (mean age 59, 49% male, 29% COPD) were analysed. Obesity (bmi > 30) was found in 26% of patients and underweight (bmi < 21 in COPD, and respectively <18.5 or <20 in non-COPD, aged ≤65 or >65 yrs) was found in 7 patients. The SNAQ score detected 9 and 3 patients being severely or moderately malnourished. FFM revealed 17 patients (14%) with malnutrition. Combining SNAQ and bmi resulted in detection of 17 malnourished patients. However, different patients are detected (Table 1).

Table 1. Malnutrition: FFM vs. SNAQ + bmi

	FFM	
SNAQ + bmi	low	normal
No	8	96
Moderate	0	2
Severe	9	6

A low FFM was found more often in patients with COPD (23%) and in females (21%).
Conclusion: This study revealed malnutrition in 6 to 14% of outpatients with pulmonary diseases. Measurement of bmi only seems to underestimate nutritional problems. The discrepancies in detecting different patients emphasise the need for determining a gold standard for defining and measuring malnutrition.

P258
Comparison of costs of community-acquired pneumonia (CAP) treatment at patients with and without bronchial obstruction
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With purpose to estimate economical costs of treatment of CAP at the patients with COPD and without it the comparison of therapeutic expenses of CAP at 33 inpatients against a background COPD (basic group – BG) and 33 patients without COPD (control group - CG) was performed by case-control method. Patients were represented by age and gender (main age- 63,5±14,3 years, 54,4% male). Average duration of hospitalization was similar: BG - 11,55±2,39 days, CG - 10,91±2,65 days (p>0,1). Pneumonia severity index (PSI) was higher in BG (81,53±3,8 score) than in CG (64,27±26,9 score). Half of patients of both groups had concomitant cardiovascular diseases (51,5% Ta 45,5%, p>0,1). Average costs of treatment for patient in BG was 1229,54±46,77 UAN, but for patient of CG – 789,25±32,43 UAN (p<0,001). Due to obstruction, severe respiratory failure, slower improving CAP symptoms in BG therapy of these patients was more intensive. 30,3% from BG were needed change of initial antibiotic to alternative, but nobody from CG. Duration of antibiotic therapy was longer in BG than in CG (12,5±2,3 days vs 8,4±1,9 days, (p<0,05)). Portion of expenses for antibiotics were higher in BG than CG (59,1% and 44,3% agreeably (p<0,05)). Treatment of bronchial obstruction and respiratory failure caused increasing costs for BG at the mean 389,45±34,76 UAN. Costs of treatment of cardiovascular diseases were similar in the both group: 10,1% in BG and 9,7% in CG (p>0,1) from total sum. More severe CAP at patients with COPD requires more intensive treatment with involving bigger therapeutic and diagnostic resources. It considerably increases costs of medical care for this group of patients.

P259
Comorbidities in stage IV COPD patients
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Introduction: Chronic Obstructive Pulmonary Disease (COPD) is associated with

many comorbidities, however the prevalence of these diseases varies in different studies.
Aim: To determine the prevalence of various comorbidities in stage IV COPD patients (pts), followed in a respiratory outpatient clinic of an Universitary Hospital.
Methods: A questionnaire was designed and applied to stage IV COPD pts in order to characterize the disease and its comorbidities. Data were supplemented by consulting clinical files.
Results: We included 89 pts (87% male), with a mean age of 68±9 years, 79% were ex-smokers. Mean FEV_1 was 38% of predicted and all of them had chronic respiratory failure. Thirty five pts (39%) were frequent exacerbators (≥2 exacerbations in the last year).
Thirty-seven pts (42%) had at least one admission because of their respiratory disease in the last year and 66 patients (74%) in the last 5 years.
Most pts had at least one comorbidity (97%), with an average of 4 comorbidities by patient and a mean Charlson index of 2.
The most frequent comorbidities were cardiovascular diseases (70%), erectile dysfunction (48%), sleep apnea syndrome (43%), dyslipidemia (35%), cataracts (31%), gastroesophageal reflux (29%) and diabetes (20%).
Frequent exacerbators were associated with a 5-fold increase in the odds ratio of having 2 or more comorbidities.
Frequent exacerbators had more gastroesophageal reflux (p=0,006) and more admissions in the last year and in previous 5 years (p<0,001).
Conclusion: This study confirms the high prevalence and association of comorbidities in stage IV COPD pts and its influence on exacerbations and admissions, justifying the need of a complete and integrative treatment approach.

P260
Fenspiride as complementary anti-inflammatory agent in therapy of patients with chronic obstructive pulmonary disease
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The aim of our study was to study the efficacy of fenspiride (F) in the complex therapy of patients with chronic obstructive pulmonary disease (COPD).
Study population: COPD pts with I-II stages (n=20) were observed on an extent 6-month treatment period. Among them were 13 males (65%). Mild age 49,02±11,32 year, duration of COPD 13,03±4,76. 1st gr. (10 pts) – combined therapy with F (160 mg/day) and fenoteroly/ipratropium bromide (F+I) (200+80 mcg dayly). 2nd gr. (10 pts) – monotherapy with F+I.
Methods: Spirometry and pneumotonometry were performed on days 1, 90 and 180 by means MasterScreen Body/Diff (“Jaeger”, German). Functional status was accessed by six-minute walk distance (6MWD) test and Borg dyspnea scale. The St. George’s Respiratory Questionnaire (SGRQ) data were determined before and after treatment period.
Results: Significant increase in all of the SGRQ domains in pts of 1st gr (p<0,01) was observed. Essential increase of the 6MWD test result has been established (on 25,15±5,5 meters) in the 1st gr. Perceived dyspnea severity and leg fatigue severity were reduced in 1st gr (p<0.05). Reduction of bronchial obstruction was less considerable and was comparable in both groups (p1=0,04 & p2=0,038). We didn’t received significant increases in the respiratory muscle strength (p>0.05).
Conclusion: The study demonstrated greater efficacy of long-term complex therapy with fenspiride and fenoterol/ipratropium bromide compared with fenoterol/ipratropium bromide alone in patients with COPD. This combination regimen can be recommended for the reduction of inflammation and prevention of disease progression in COPD patients.

P261
What are the factors related to misdiagnosis of COPD?
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Background: The factors for COPD misdiagnosed by physicians are not known.
Objective: To determine the factors associated with COPD misdiagnosed.
Methods: This research was part of the Canadian Cohort Obstructive Lung Disease (CanCOLD). Subjects were recruited (population-based sampling) from 9 cities. Physician-diagnosed COPD was based on patient self-reported. COPD was confirmed by spirometry, i.e., post-BD FEV_1/FVC <0.70.
Results: This analysis included 2132 subjects from 5 cities. Of 163 with physician-diagnosed COPD, 79 were confirmed to have COPD by spirometry while 84 didn’t have COPD, 333 had COPD confirmed by spirometry but were undiagnosed, 910 were at risk (ever smoker) and 726 were healthy (never smoker). Among those with physician-diagnosed COPD as compared to undiagnosed COPD, diagnosed subjects were more likely to be current smokers (36% vs 20%, p<0.0001), to have chronic bronchitis (32% vs 12%, p<0.0001), wheezing (64% vs 38%, p<0.0001), dyspnea ≥3/5 MRC (22% vs 9%, p<0.0001), diagnosis of asthma (47% vs 23%, p<0.0001), and lower health status. Similar characteristics were present for physician-diagnosed COPD whether or not the diagnosis was confirmed by spirometry. Predictors of physician-diagnosed COPD included current smoking (OR: 1.86, 95% CI: 1.09-3.18), chronic cough (2.04, 1.13-3.69), chronic bronchitis (2.70, 1.45-5.04), and reduced physical health “SF-12” (0.96, 0.96-0.99).
Conclusions: Misdiagnosis and underdiagnosis of COPD is common. Current smoking, respiratory symptoms and reduced health seems to trigger physician to make diagnosis of COPD. The absence of these factors may result in underdiagnosis.
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