



**Kantonsspital
Baselland**

«Impact of a pharmaceutical intervention to improve adherence of inhaled medication in asthma and COPD patients»

Baseline data from a randomized controlled trial

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Clinical relevance of medication adherence

- On average, adherence to long-term therapy is estimated to be around 50%¹
- Poor adherence to long-term therapies may result in poor health outcomes and increased health care costs²
 - Effectiveness of treatment is compromised
 - Negative effect on quality of life
- Despite the significant progress in pharmacological and non-pharmacological treatment in recent years, symptom control and management in asthma and COPD remain suboptimal
- Increased risk for recurrent exacerbations, which lead to massive costs for the health-care system (50-75% of the costs are caused by exacerbations³)
- Previous literature is limited to refill adherence and some retrospective studies based on pharmacy record databases

¹ World Health Organisation, Adherence to Long-term Therapies- Evidence for Action, *online*, (2003)

² Hughes et al., The impact of non-adherence on the cost-effectiveness of pharmaceuticals: a review of the literature, *Health Econ.*(2001)

³ Celli et al., Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *The European respiratory journal* (2004).

Aims

- To investigate the adherence of patients with asthma or COPD to prescribed long-term inhaled medication with specific electronic devices which provide data about the timing of inhaler action
- To assess the effects of an acoustic reminder and close supervision by a pharmacist on adherence with these medications and diseases outcomes

Study design

- On-going prospective single-blind randomized interventional trial
- Recruitment of at least 154 asthma and COPD patients
 - 70 subjects for each study group
 - +14 subjects for drop outs (+10%)
- Since January 2014, recruitment of in- and outpatients from several hospitals in the Basel region
- Inclusion criteria :
 - Clinical diagnosis of asthma or COPD
 - At least one exacerbation during the past 12 months
 - At least one inhaled medication, which is inhaled on a daily basis
- Exclusion criteria:
 - Severe comorbidities
 - Pregnant or lactating women
- Investigation of the adherence over the period of 6 months
 - 4 clinical visits (lung function tests, questionnaires and evaluation of inhalation techniques)

Intervention and control group

- Random assignment to either the intervention or control group
- Patients are not explicitly informed to which group they had been randomized
- Intervention group:
 - Monitoring of adherence with Audio-Reminder
 - Support calls when:
 - Use of rescue medication doubles
 - Inhaled medication is not taken as prescribed for more than 2 consecutive days
 - Feedback on adherence at each visit
- Control group:
 - Monitoring of adherence without Audio-Reminder
 - No support calls
 - No feedback on adherence

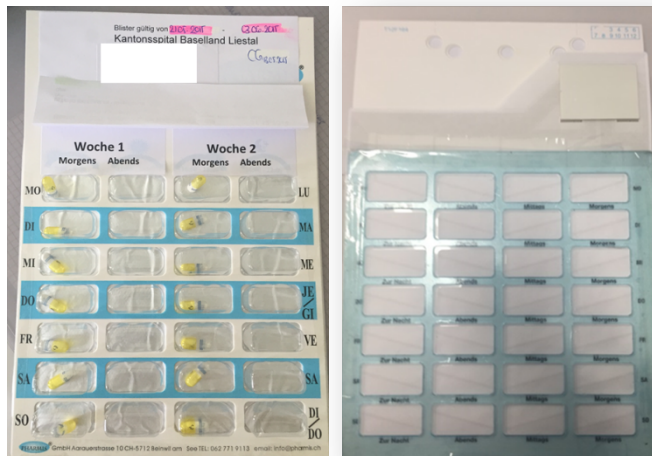
Adherence-Measurements

- Measurements of puff inhalers: Smartinhalers



- Electronic monitor for MDI, Diskus, Turbohaler
- Plastic casing into which a standard inhaler can be inserted
- Each actuation (depression of the canister, turning off the device) is recorded with date and time

- Measurements of inhalation powder capsules :
“Polymedication Electronic Monitoring System (POEMS)”



- Electronic film technology for inhaled medication with capsule system
- Self-adhesive polymer film with loop of conductive wires → Date and time are recorded when a loop is broken

Current status of the study

169 enrolled patients:

- 148 patients: completed the study
- 1 patient: ongoing

20 drop outs:

- 1 patient died after the 2nd visit
- 6 patients had to stop because of worsening health status
- 13 patients stopped for other reasons

Baseline data (n=149)

Patients' characteristics	
Age [yrs]	68 ± 8 (range: 29-87)
Gender	Male: n=96 (64%)
Diagnoses	
COPD	n=77 (52%)
Asthma	n=46 (31%)
Asthma-COPD overlap	n=26 (17%)
COPD Classification (n=103)	
GOLD I (FEV1 ≥ 80% predicted)	n=8 (7%)
GOLD II (50% ≤ FEV1 < 80% predicted)	n=44 (43%)
GOLD III (30% ≤ FEV1 < 50% predicted)	n=40 (39%)
GOLD IV (FEV1 < 30 % predicted)	n=11 (11%)
Smoking status:	
Non-smokers	n=32 (22%)
Ex-smokers	n=87 (58%)
Current smokers	n=30 (20%)

Baseline data (n=149)

Medication:	
Short-acting β 2-agonists (SABA)	n=63 (22%)
Long-acting β 2-agonists (LABA)	n=18 (6%)
Long-acting anticholinergics (LAMA)	n=69 (24%)
Inhaled corticosteroids (ICS)	n=13 (4%)
Combination of LAMA+SABA/LABA	n=20 (7%)
Combination of LABA+ICS	n=106 (37%)
Asthma Control Test (ACT) (n=72)	
Sum score	19.5 \pm 4.3
Well-controlled (20-25)	n=45 (63%)
Not well-controlled (16-19)	n=13 (18%)
Poorly controlled (5-15)	n=14 (19%)
COPD Assessment Test (CAT) (n=103)	
Sum score	16.0 \pm 6.9
Low impact (0-10)	n=21 (20%)
Medium impact (11-20)	n=54 (53%)
High impact (21-30)	n=25 (24%)
Very high impact (31-40)	n=3 (3%)

Taking adherence over the first 30 days

Taking adherence for puff inhalers

	Intervention group (n=56)*	Control group (n=58)
Correct dosing days (mean±SD)	24.0±5.5 (range:9-30)	19.4±8.5 (range:0-30)

* p<0.01 intervention vs. control group

Taking adherence for inhalation powder capsules

	Intervention group (n=38)	Control group (n=46)
Correct dosing days (mean±SD)	27.8±4.6 (range:4-30)	26.2±5.9 (range:5-30)

Taking adherence for powder capsules vs. puff inhalers

	Powder capsules (n=84)*	Puff inhalers (n=53)
Correct dosing days (mean±SD)	26.9±5.4 (range:4-30)	20.7.2±7.4 (range:1-30)

* p<0.001 intervention vs. control group

Taking adherence for once daily dosage vs multiple doses per day

	Once daily dosage (n=105)*	Multiple doses per day (n=93)
Correct dosing days (mean±SD)	26.6±5.4 (range:4-30)	20.8.2±7.7 (range:0-30)

* p<0.001 intervention vs. control group

Conclusions

- The results of our study suggest a beneficial effect of a regular reminder on adherence to long-term medication for treatment of asthma or COPD
- Adherence appears to be better when devices allowing the administration of predefined dose regimens (capsule inhalers) are used compared to devices that have to be loaded by the patient (puff inhalers)
- Adherence with once-daily dosage regimens appears to be higher than adherence observed in treatment plans urging the inhalation of multiple doses per day



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**THANKS FOR YOUR
ATTENTION**




Backup Slides

Overview of the study structure

Schulung	Tag 1 (Erste Visite)	Tag 2-59	Tag 60 (zweite Visite)	Tag 61-119	Tag 120 (dritte Visite)	Tag 121-179	Day 180 (vierte Visite)		
Primäres Ziel:	Eintrittsgespräch	Adherence Messung durch elektronische Messgeräte und Intervention in der Interventionsgruppe	Gespräch	Adherence Messung durch elektronische Messgeräte und Intervention in der Interventionsgruppe	Gespräch	Adherence Messung durch elektronische Messgeräte und Intervention in der Interventionsgruppe	Abschluss- gespräch		
Korrekte Anwendung der Inhalations- geräte mit dem Ziel, dass alle Teilnehmer bei Studienbeginn auf demselben Wissensstand sind und dass sie alle wissen wie sie ihre Inhalations- geräte richtig anwenden	**		**		**		**	**	**
	Schwangerschafts- test bei gebärfähigen Frauen		Lungenfunktion- Messungen		Lungenfunktion- Messungen		Lungenfunktion- Messungen	Lungenfunktion- Messungen	
	**		**		**		**	**	
	Lungenfunktion- Messungen		Beurteilung der Inhalations- technik		Beurteilung der Inhalations- technik		Beurteilung der Inhalations- technik	Beurteilung der Inhalations- technik	
	**		**		**		**	**	
	Beurteilung der Inhalations-technik		Fragebögen		Fragebögen		Fragebögen	Fragebögen	
	**		**		**		**	**	
	Fragebögen	Teilauswertung der registrierten Daten	Teilauswertung der registrierten Daten	Teilauswertung der registrierten Daten	Teilauswertung der registrierten Daten				
	**								
	Abgabe und Erklärung der Geräte						Auswertung der registrierten Daten		


Smartinhaler → Datatransfer

Patient 1




SmartTurbo Smartphone

Patient 2



SmartTurbo Smartphone

Patient 3



SmartTurbo Smartphone


Nexus6
Cellular
Data


Nexus6
Cellular
Data


Nexus6
Cellular
Data



smartinhalerlive™

14-Day Medication Use for GarthAsthma
From 06 Apr 2011 to 19 Apr 2011

Date	Daily usage (Dose)	Insp. (ppm)
06 Apr 07 Apr	2.5	1000
08 Apr 09 Apr	2.5	1000
10 Apr 11 Apr	2.5	1000
12 Apr 13 Apr	2.5	1000
14 Apr 15 Apr	2.5	1000
16 Apr 17 Apr	2.5	1000
18 Apr 19 Apr	2.5	1000

Nexus6
SmartinhalerLive.com

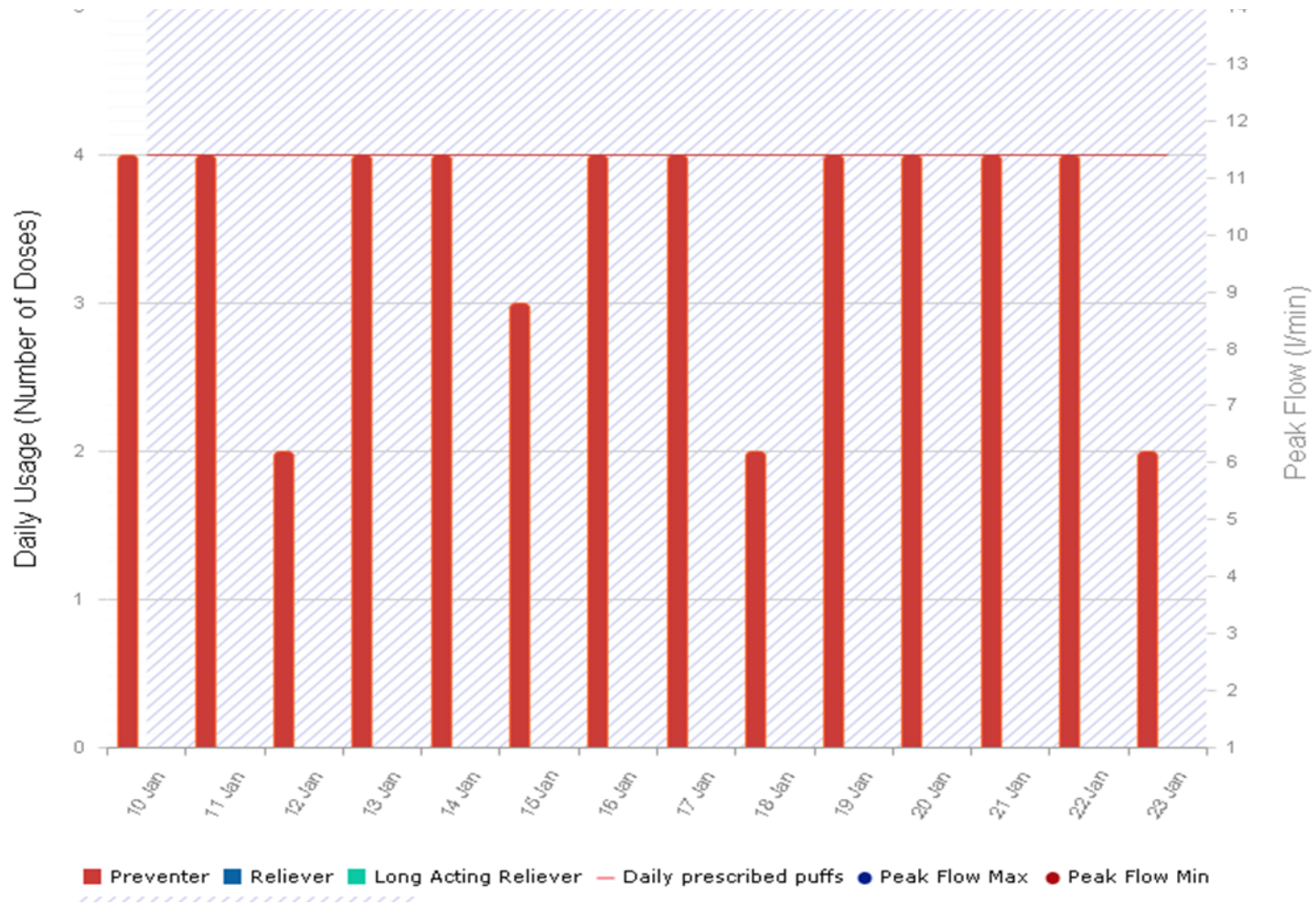


Investigator 1

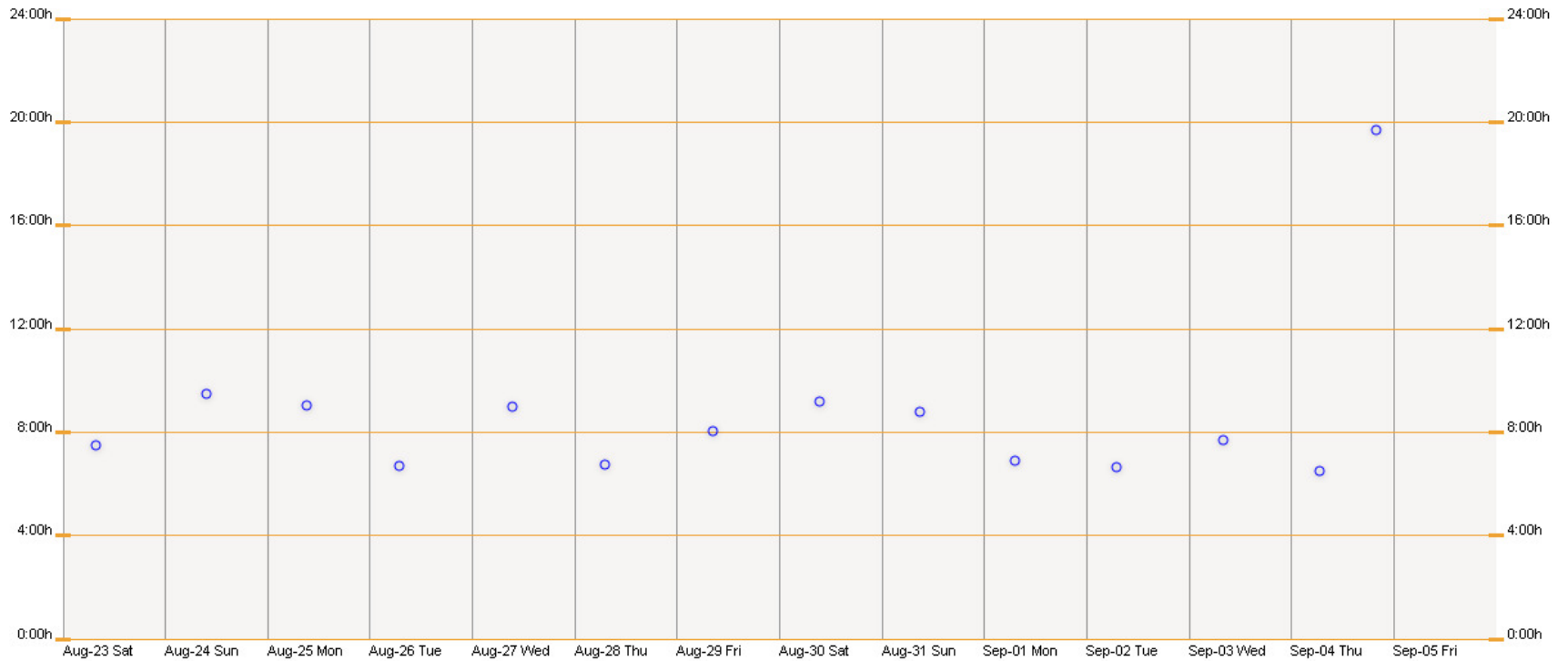


Investigator 2

Smartinhaler output



POEMS output



Stepwise approach for asthma treatment

	Stufe 1	Stufe 2	Stufe 3	Stufe 4	Stufe 5: zusätzlich zu 4
Patientenschulung, Kontrolle von Risiko- und Umweltfaktoren					
Bedarfsmedikation (Reliever):					
	SABA		SABA ODER Low-dose ICS + Formoterol		
Langzeitmedikation (Controller):					
Primäre Therapiewahl	Low-dose ICS	Low-dose ICS + LABA	Medium oder High-dose ICS + LABA	Anti-IgE bei IgE induziertem Asthma	
	ODER		ODER	ODER	
Alternative Therapiewahl	LRA	Medium oder High-dose ICS	High-dose ICS + LRA	Low-dose ICS	
	ODER				
Alternative Therapiewahlen	Low-dose ICS + LRA				
	ODER				
	Theophyllin				
SABA: short acting B2-agonist; ICS: inhaled corticosteroid;					
LABA: Long-acting beta2-agonist; LRA: Leukotrien-rezeptor-Antagonist					

Modified according to GINA-Guidelines (www.ginasthma.org)

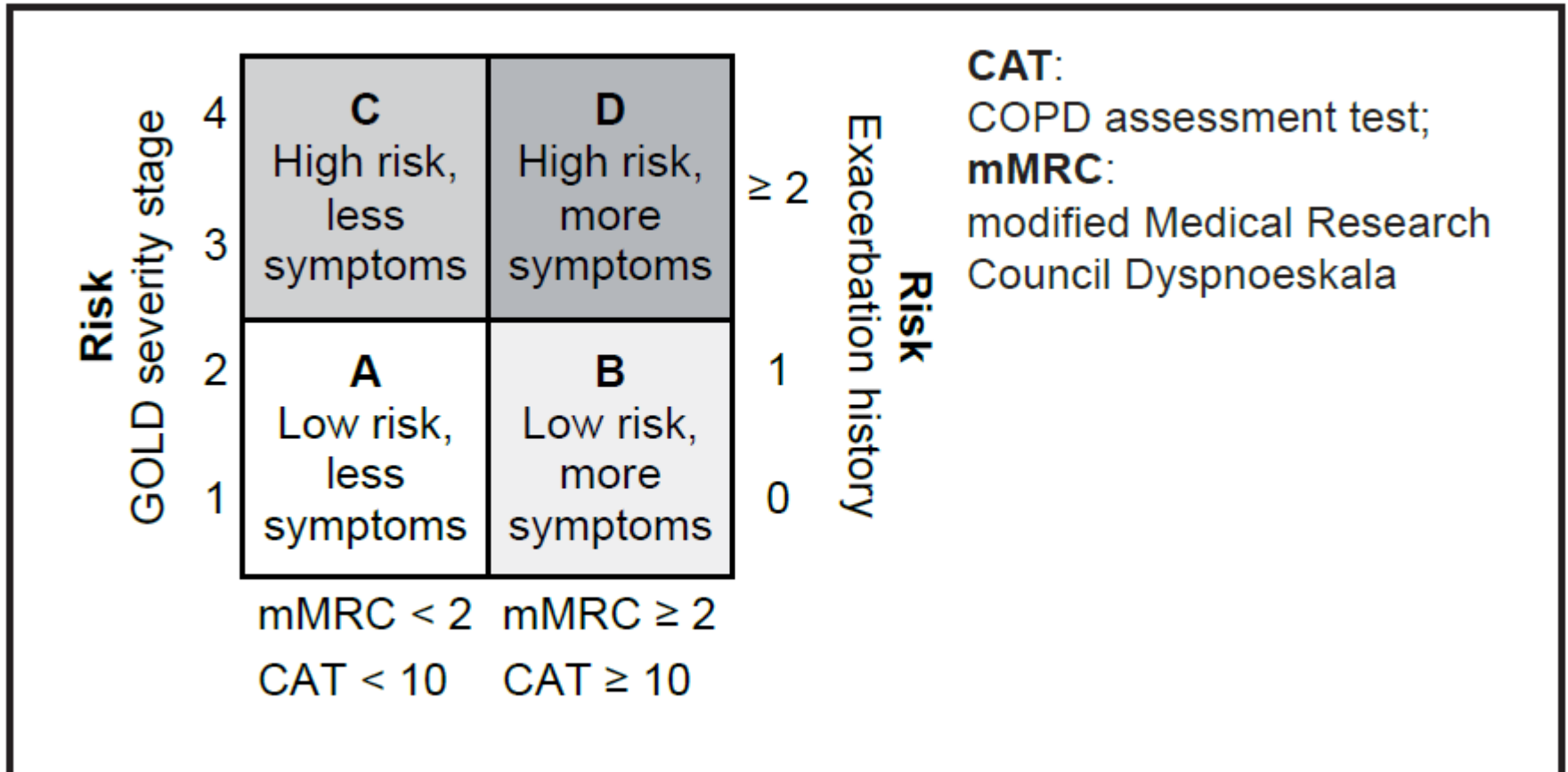
COPD Treatment Guidelines

Risiko- gruppe	Primäre Therapiewahl	Alternative Therapiewahl	Weitere Therapie- möglichkeiten
A	SAAC ODER SABA	LAAC ODER LABA ODER SABA + SAAC	Theophyllin
B	LAAC ODER LABA	LAAC + LABA	Theophyllin + SABA +/oder SAAC
C	ICS + LABA oder LAAC	LAAC + LABA ODER LAAC + PDE-4 Inhibitor ODER LABA + PDE-4 Inhibitor	Theophyllin + SABA +/oder SAAC
D	ICS + LABA +/oder LAAC	ICS + LABA + LAAC ODER ICS + LABA + PDE-4 Inhib. ODER LAAC + LABA ODER LAAC + PDE-4 Inhibitor	Theophyllin + Carbocystein + SABA +/oder SAAC

SABA: short acting B2-agonist; **LABA:** long acting B2-agonist;
SAAC: short acting anticholinergic; **LAAC:** long acting anticholinergic;
ICS: inhaled corticosteroids; **PDE-4:** Phosphodiesterase-4

Modified according to GOLD-Guidelines (www.goldcopd.org)

Classification of COPD patients into risk groups A-D



Modified according GOLD-Guidelines (www.goldcopd.org)