

Online Supplement

Early diagnostic BioMARKers in Exacerbations of Chronic Obstructive Pulmonary Disease: protocol of the exploratory, prospective, longitudinal, single-center, observational MARKED study

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Table 1. Overview of study measurements. · represents measurements that are part of routine clinical care at Cirro. + represents study-specific measurements.

	Assessment	Baseline assessment	Enrollment	Daily assessment	3x weekly assessment	Exacerbation assessment	Outcome assessment	
Demograph	Age	·						
	Sex	·						
	Race	·						
Clinical Measures & Patient History	Body length	·						
	Body weight	·					·	
	Body mass index	·					·	
	Fat-free mass (index)	·					·	
	Bone mineral density	·						
	Exacerbations last yr	·						
	Hospitalisations last yr	·						
	mMRC score	·					·	
	CAT score	·					·	
	EXACT-PRO			+	+		+	+
	Visual Analogue scale			+	+		+	+
	Oxygen use	·		+				

Assessment	Baseline assessment	Enrollment	Daily assessment	3x weekly assessment	Exacerbation assessment	Outcome assessment
NIV use	.	+				
Medical history	.	+			.	
Comorbidities	.	+				
Medications	.	+	+		.	.
Smoking history	.	+				
Blood pressure	.	+	+		.	+
Heart rate	.	+	+		.	.
Oxygen saturation	.	+	+		.	.
Temperature	.	+	+		.	+
Breathing frequency	.	+	+		.	+
Pre BD-spirometry		+	+		+	
Post BD-spirometry	.	+				.
Peakflow	.	+	+		+	.
WB-plethysmography	.					
Diffusing capacity	.					
Respiratory muscle strength	.					.
Arterial blood gas	.				.	
Six minute walking test	.					.
Resting ECG	.				.	
Peak cycle ergometry	.					
Submaximal cycle ergometry	.					.
Quadriceps muscle function	.					.
HADS scores	.					.

	Assessment	Baseline assessment	Enrollment	Daily assessment	3x weekly assessment	Exacerbation assessment	Outcome assessment
Microbiome	Chest X-ray					.	
	Chest HRCT §		+				
	Nasal swab		+		+	+	
	Spontaneous sputum		+		+	./ +	
	Stool		+			+	+
Clinic Labs	Genomic sequencing		+				
	Routine hematology	.					.
	Routine chemistry	.					.
	Inflammatory parameters, anti-bacterial titers and multi-omics		+		+	+	+
	ECV/exosome/cfDNA sequencing		+			+	+
	Exacerbation markers #					.	

§ no HRCT will be performed, only scans that were performed in the previous 12 months will be collected. # exacerbation markers include: leukocytes, eosinophils, high-sensitive C-reactive protein (hs-CRP), d-dimer, N-terminal pro b-type natriuretic peptide (NT-proBNP), troponin-T. Abbreviations: BD; bronchodilation, CAT; COPD assessment test, cfDNA; cell free DNA, DNA; deoxyribonucleic acid, ECG; electrocardiography, ECV; extracellular vesicle, EXACT-PRO; exacerbations of COPD tool patient reported outcome, HADS; hospital anxiety and depression scale, HRCT; high-resolution computer tomography, mMRC; modified medical research council, NIV; non-invasive ventilation, WB; whole body.