

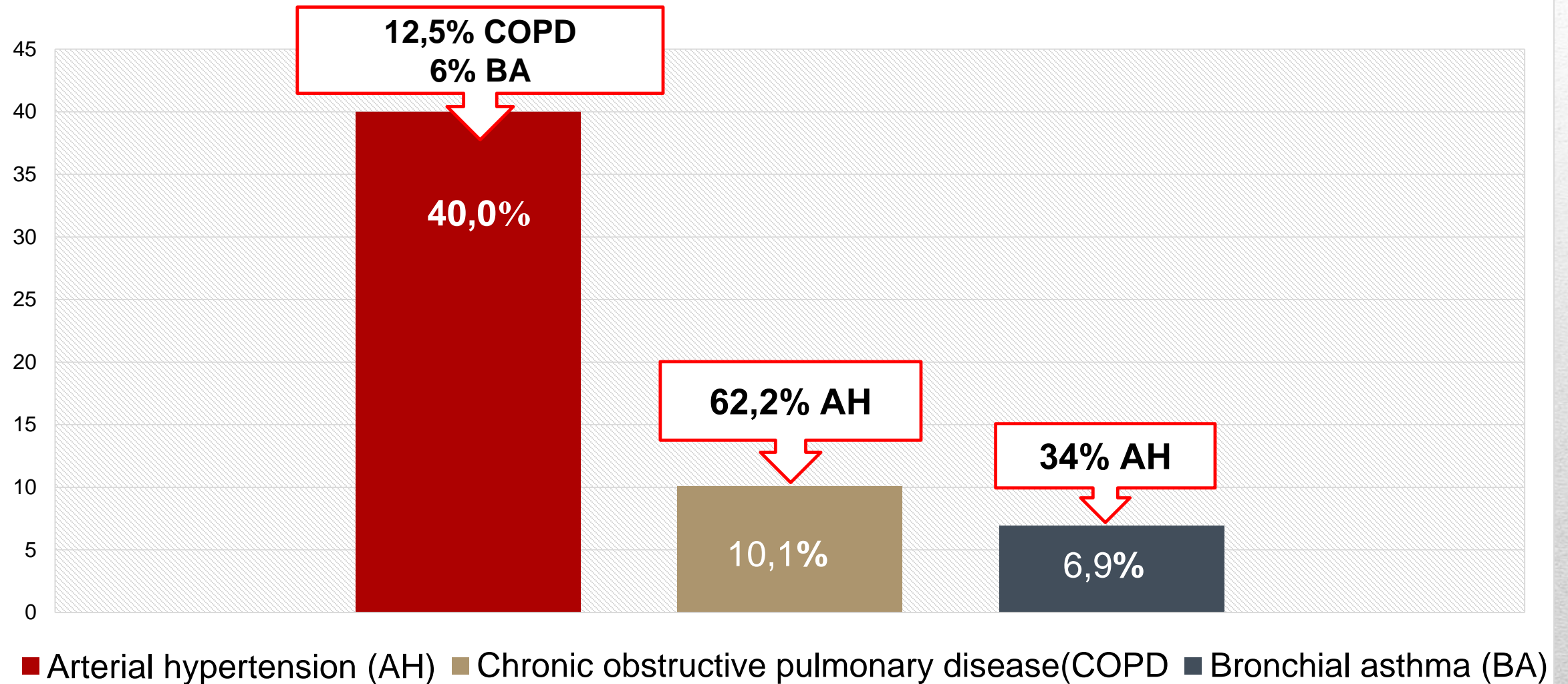


Differential effect of inhaled β 2-agonist on the characteristics of β 1- and β 2-adrenoreceptors in patients with cardiorespiratory pathology.

SMOLYAKOVA E.V.

National medical research center of cardiology
of the Ministry of healthcare of the Russian Federation

Incidence of cardiovascular disease (CVD) and bronchial obstruction disease (BOD)



Medications

CVD

Class of drugs
Thiazide diuretics
β1-blockers
Calcium antagonists
ACE inhibitors
Reninaldosterone blockers
Diuretics antagonists aldosterone

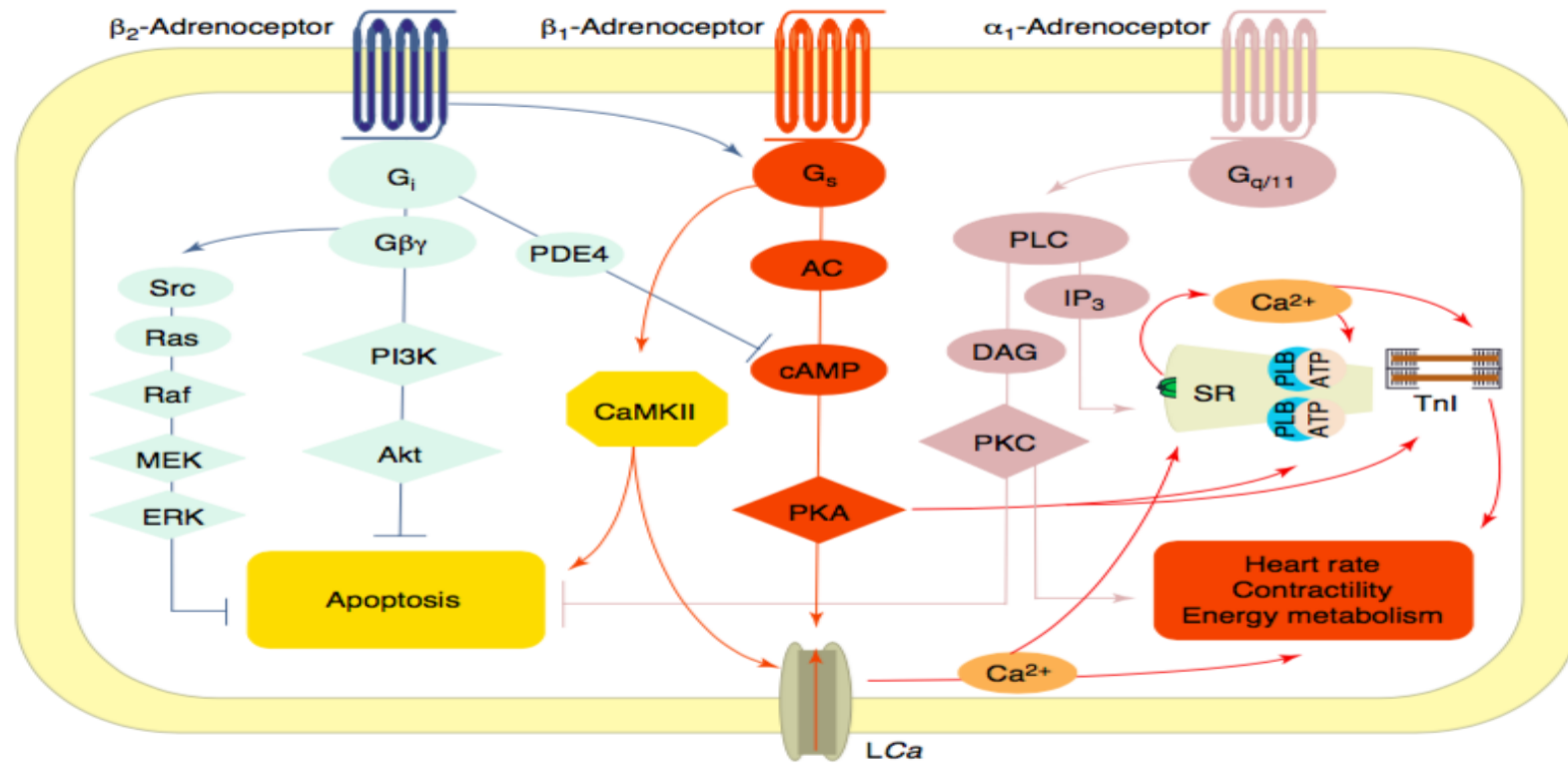
BOD

Class of drugs
β2-agonists
Anticholinergics
Methylxanthines
Inhaled glucocorticosteroids
Phosphodiesterase inhibitor-4

β -adrenoreceptors

The effect of β -agonists and β -blockers on the characteristics of β -adrenergic receptors

Item	Right atrium	Fat	Kidney	Lung	Liver
Competition by CGP 20712A (a β_1 -AR antagonist)					
β^1 -AR, %	50	35	32	27	18
β^2 -AR, %	50	65	68	73	82
K _d (nM)	1.3	0.7	1.1	0.0	3.8



Xiao RP et al. Subtype-specific α_1 - and β -adrenoceptor signaling in the heart
 TRENDS in Pharmacological Sciences Vol.27 No.6
 June 2006

The aim

- The aim of the study was to evaluate the changes of the characteristics of adrenoreceptors and spirometric parameters of patients with CVD (cardiovascular diseases) and BOD (bronchoobstructive diseases) after the initial administration of β 2-agonist (formoterol) with and without previous therapy with selective β 1-adrenoblocker (bisoprolol).

Methods

- Questionnaires: ACT, CAT, mMRC.
- Physical examination.
- ECG in 12 leads, Holter ECG Monitoring, Ambulatory blood pressure monitoring.
- Computer spirometry + bronchodilation test.
- Acute spirometric 4-hour test with selective beta1-blocker.
- Modified radioligand analysis on T-lymphocytes of peripheral human blood.

Modified radioligand analysis on T-lymphocytes of peripheral human blood

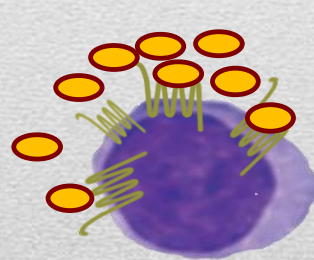
Activity binding of β -adrenoreceptors- this is a relative value that depends on:

- the number of receptors on the cell surface;
- the affinity of the receptor data;
- the availability of these receptors for a specific ligand

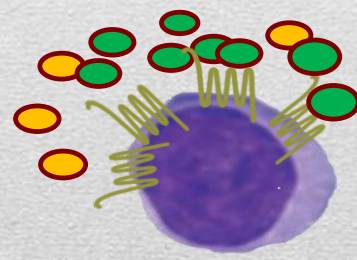
Nonspecifically ligand – [125 I]-cyanopindolol

Specifically β_1 - ligand - CGP 20712A

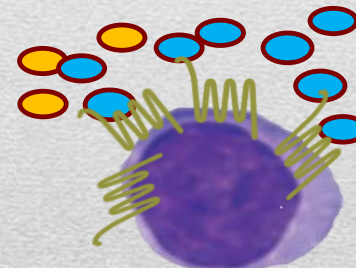
Specifically β_2 - ligand - ICI 118551



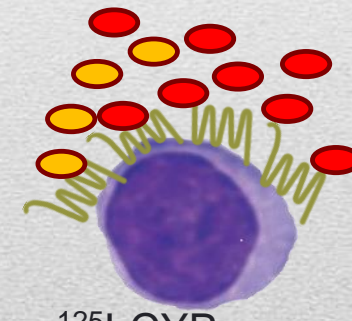
125 I-CYP



125 I-CYP + «non-radioactive»
CYP
(1000 times higher)

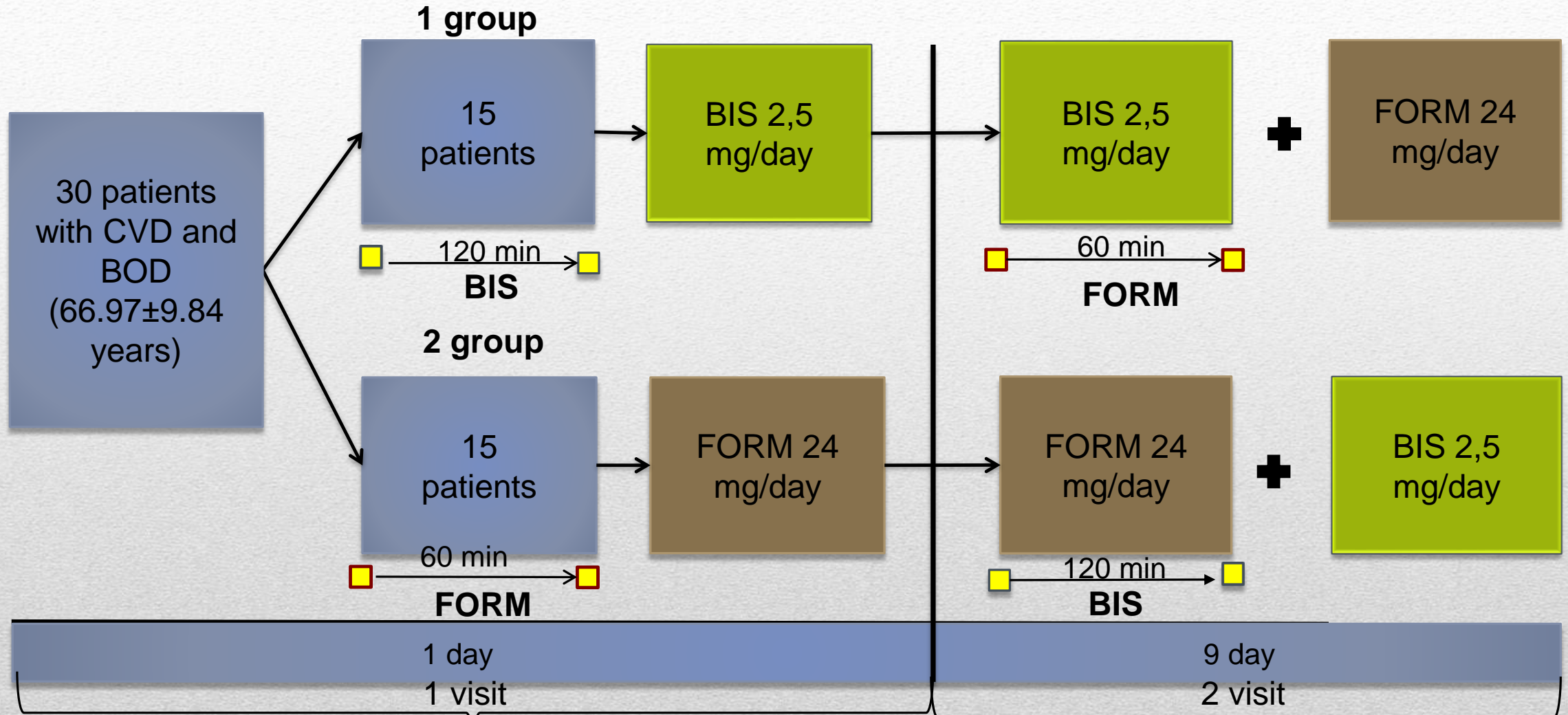


125 I-CYP +
 β_1 - ligand
(1000 times higher)



125 I-CYP +
 β_2 - ligand
(1000 times higher)

Study design



CVD – cardiovascular diseases.

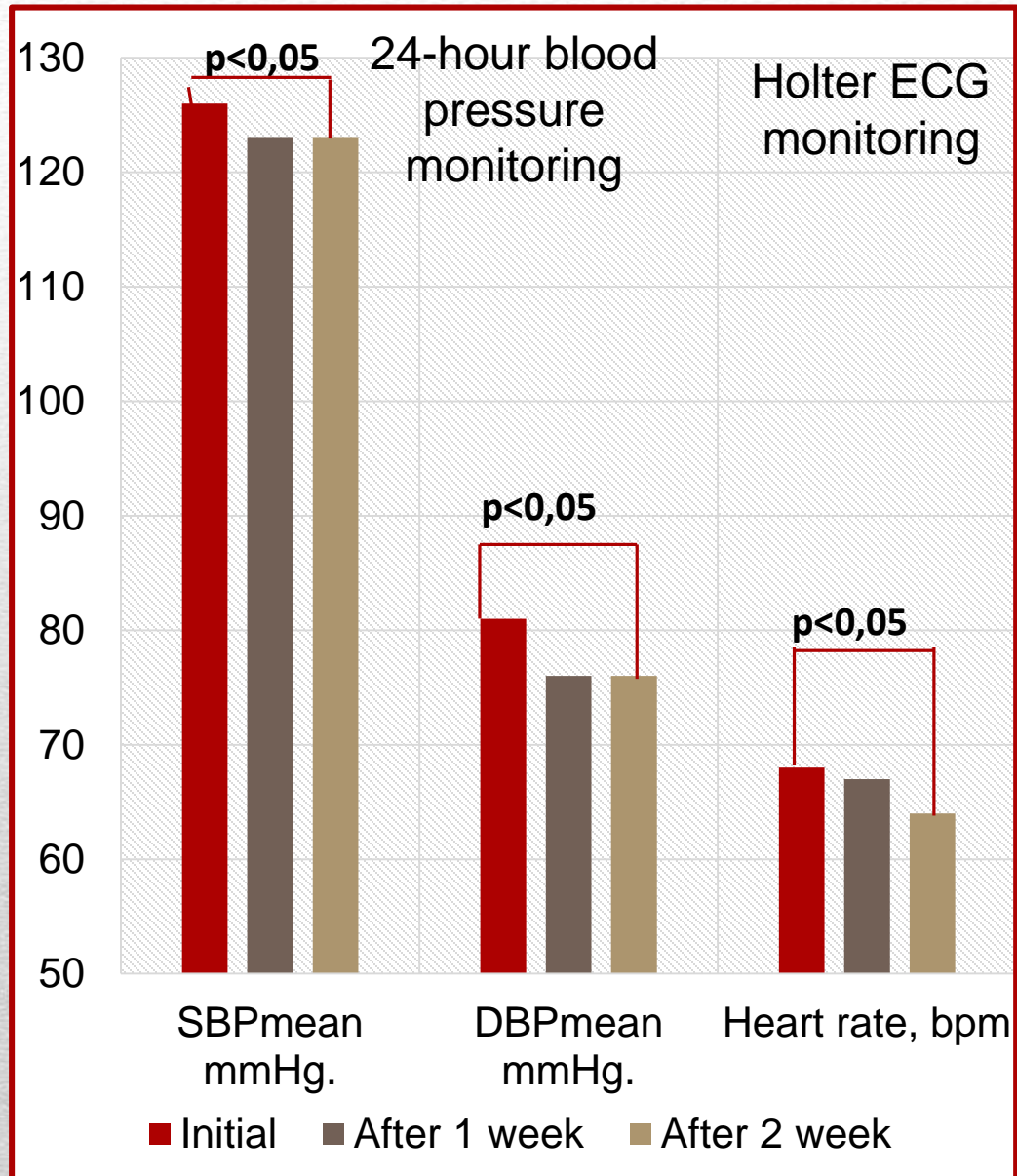
BOD – bronchial obstructive diseases.

■ - evaluate the index of specific binding o beta-adrenergic receptors

BIS – bisoprolol.

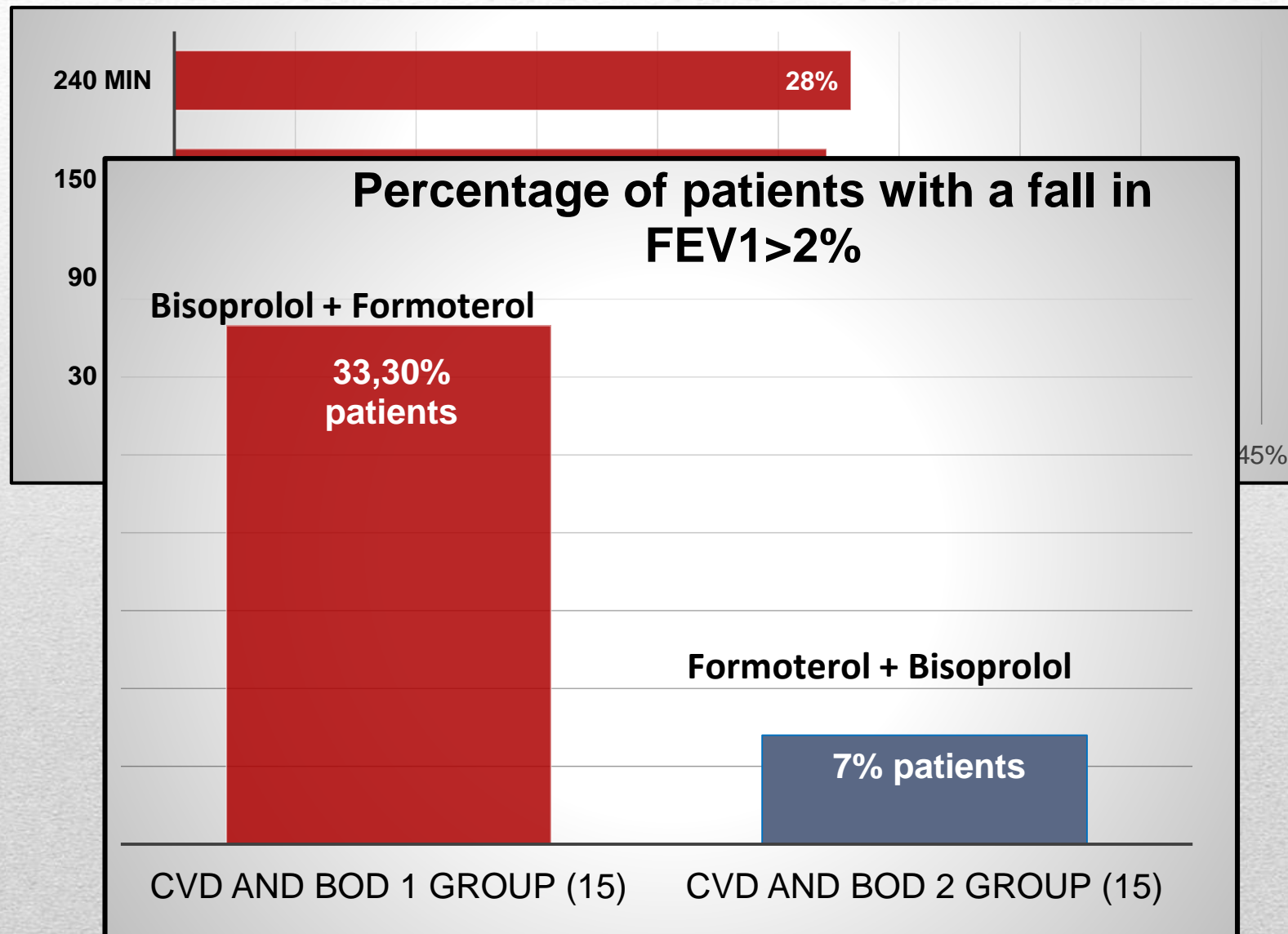
FORM – formoterol.

Clinical efficacy and safety of selective β 1-blocker and β 2-agonist in CVD and BOD

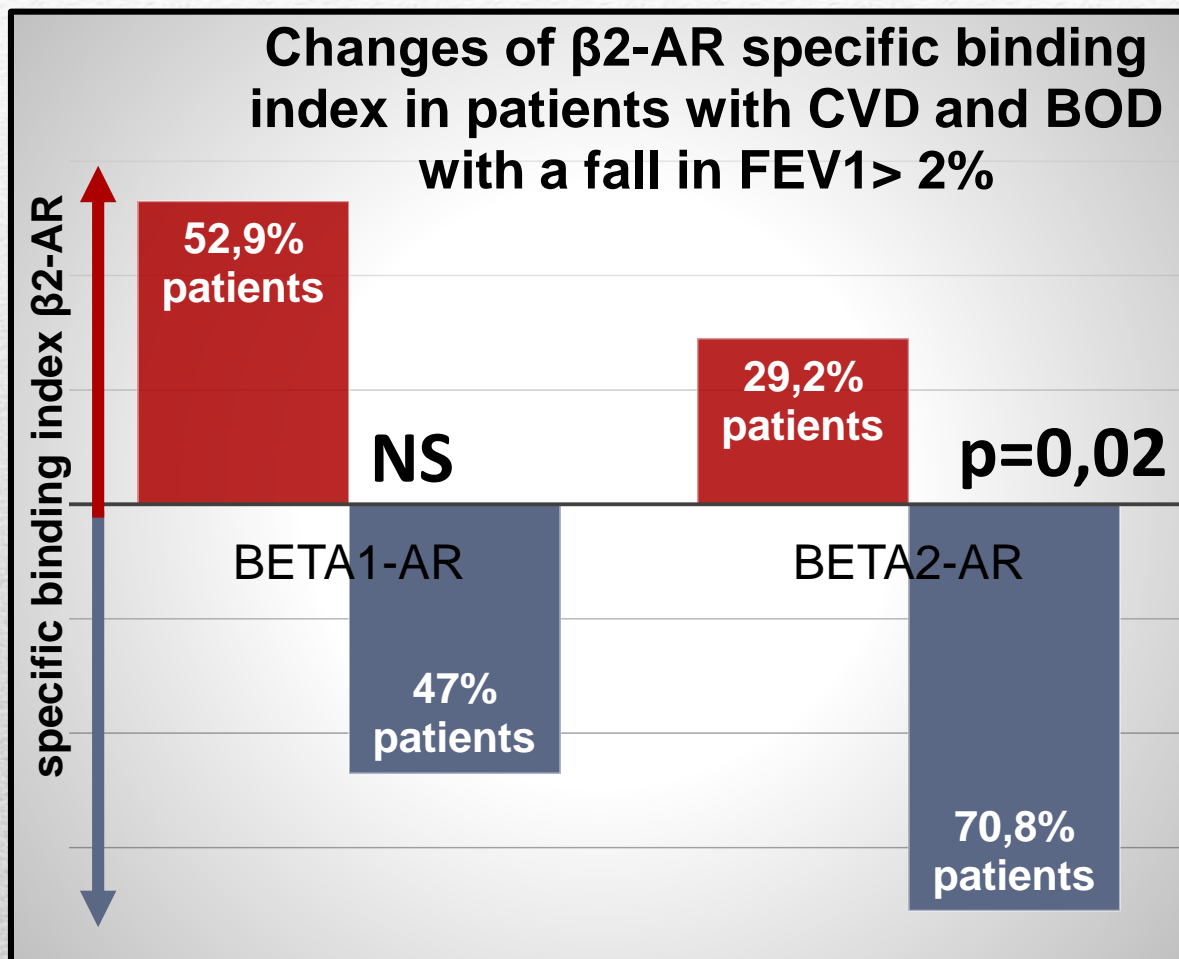


parameter	Baseline	After 1 week	After 2 week	p
ACT	17 [15,5;20]	20 [19; 23]	21,5 [20,25;24]	0,00
CAT	16 [14; 24]	13 [9;15]	8,5 [7;11,5]	0,00
mMRC	2 [1,5; 3]	1 [1; 2]	1 [0; 1]	0,00

The number of patients with the greatest fall in FEV1% at different time periods



The correlation between the parameters studied and the binding activity of β 2-AR in patients with CVD and BOD in patients receiving:



INCREASE

β 2-AR Specific Binding Index
FORMOTEROL + BISOPROLOL

Associated with **BETTER** Clinical Performance

- History of heart failure
- History of arrhythmia

Associated with **WORSE** clinical performance

- Heart rate
- BP
- CAT
- AH duration
- Inflammatory response
- Platelets

Conclusion

- With simultaneous administration of beta-agonists and beta-blockers, the order of prescription of drugs matters.
- A preliminary assignment of formoterol reduces the risk of bronchospastic effect of bisoprolol in patients with cardiorespiratory pathology that is accompanied by a decrease in specific binding of beta2-adrenergic receptors of peripheral blood lymphocytes.
- The phenomenon of decreasing of beta2-receptor's binding activity in patients treated with beta-blockers with the fall of FEV1 is worth attention for the conducting of further research. It needs to investigate whether the dynamics of beta-receptor's specific binding activity after the administration of beta-blockers and beta-agonists may be clinical biomarkers of future efficacy or possible side-effects of these drugs.

Thank you your attention !

