

**III KONGRES  
POLSKIEGO TOWARZYSTWA LIPIDOLOGICZNEGO**  
AKTUALNE REKOMENDACJE LECZENIA ZABURZEŃ LIPIDOWYCH

Warszawa, 11–12 października 2013 r.

# **Czy mamy dowody na pozalipidowe efekty stosowania statyn?**

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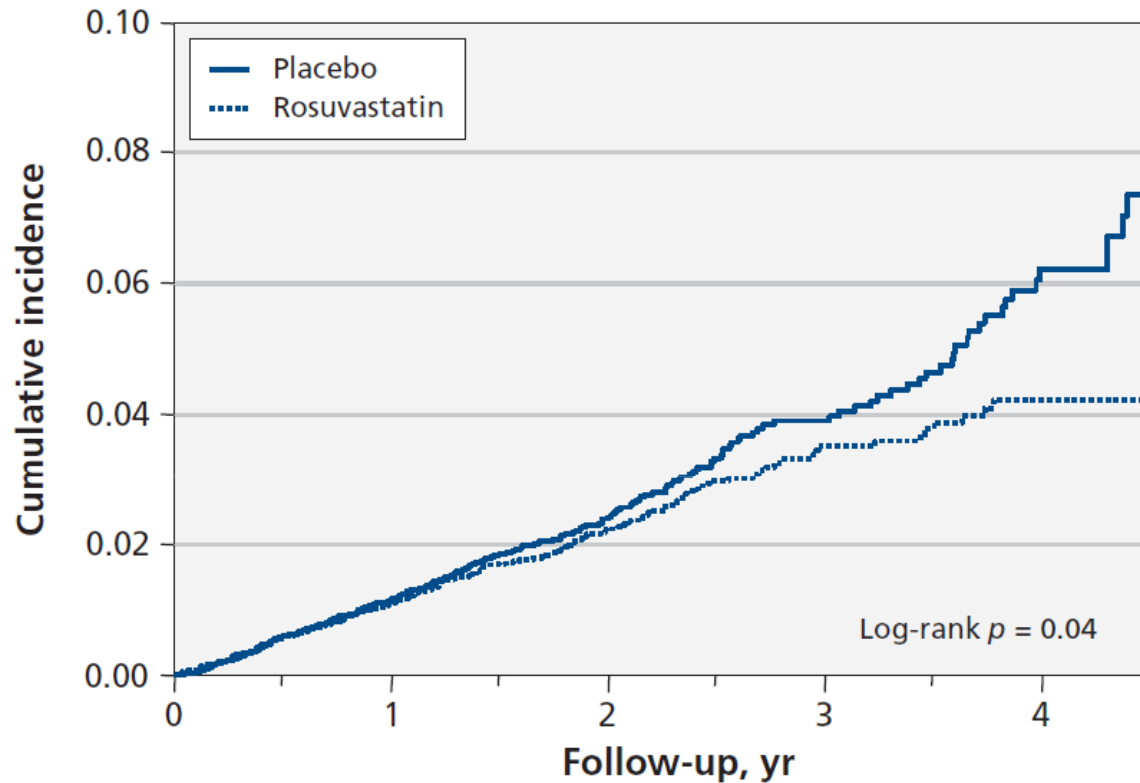
## Definicja

**Pleiotropia, pleiotropowość** – w biologii, zjawisko, w którym jeden czynnik ma więcej niż jeden efekt.

**Gen** pleiotropowy to gen, który wpływa na więcej niż jedną cechę fenotypową.

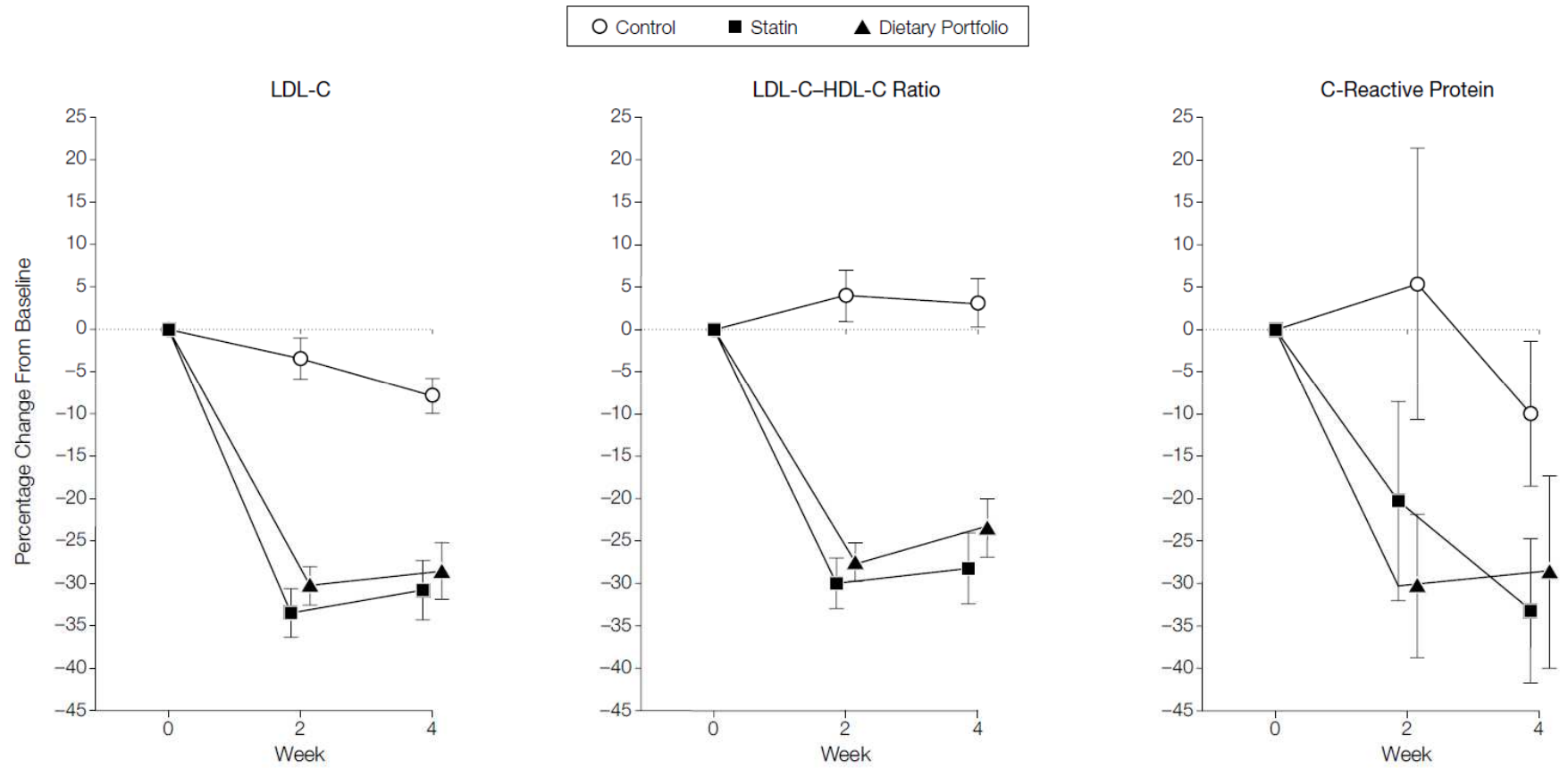
**Efekt** pleiotropowy to zjawisko w fizjologii, gdzie jeden czynnik posiada zdolność wielokierunkowego działania.

## Rosuvastatin treatment reduces the risk of incident pneumonia: results from the JUPITER trial

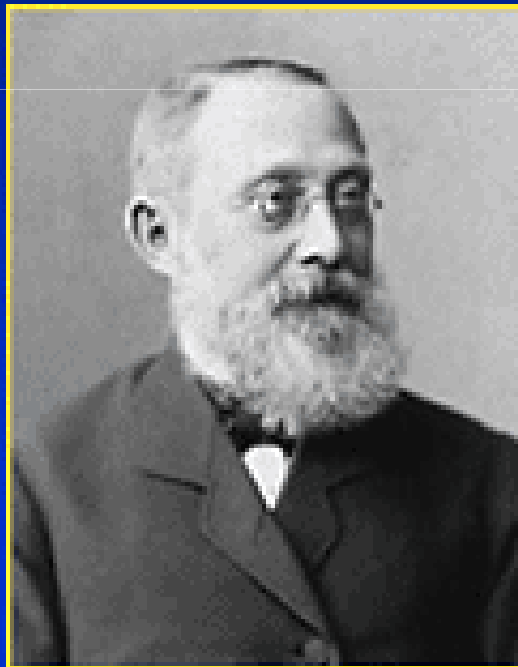


No. at risk	0	1	2	3	4	5	6	7	8	9
Rosuvastatin	8901	8609	8374	7050	4244	2104	1384	1007	587	187
Placebo	8901	8618	8352	7042	4216	2126	1385	979	567	198

# Similar effect of cholesterol reduction with statins and diet on CRP levels

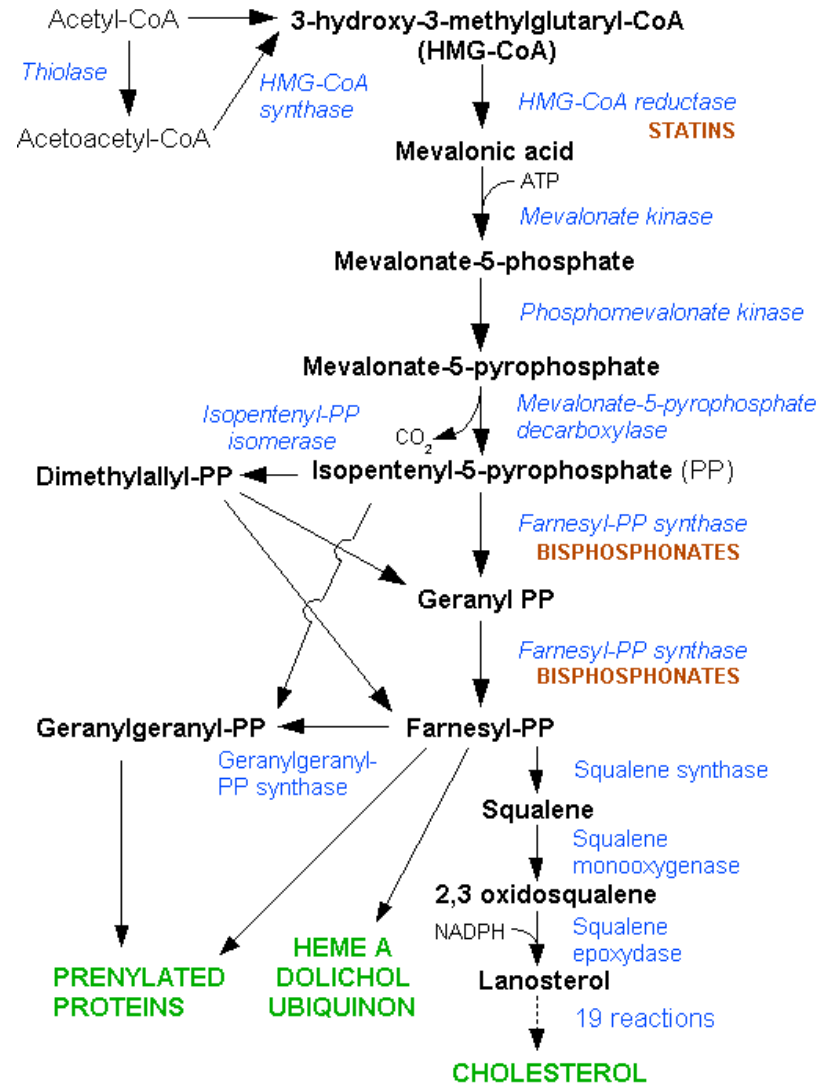


**Atherosclerosis is a chronic inflammation  
induced by cholesterol...**

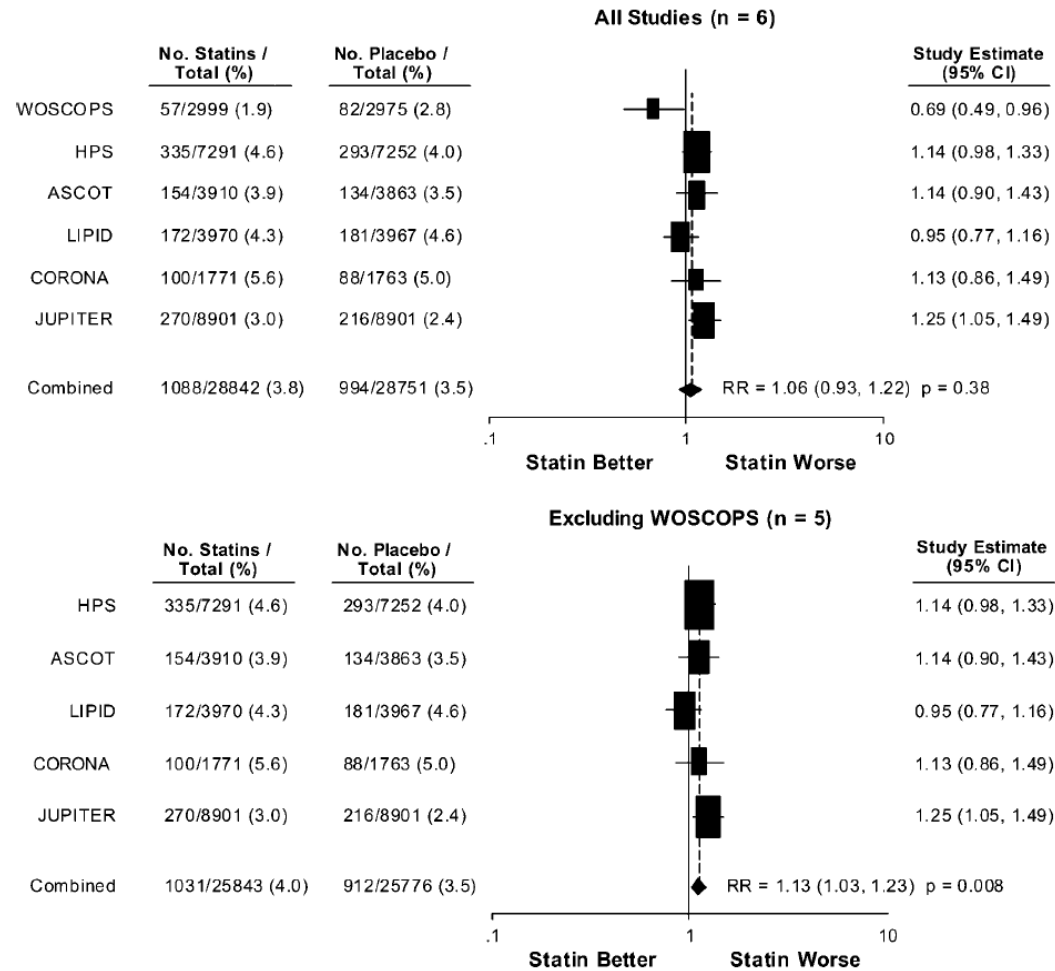


**Rudolf Virchow**

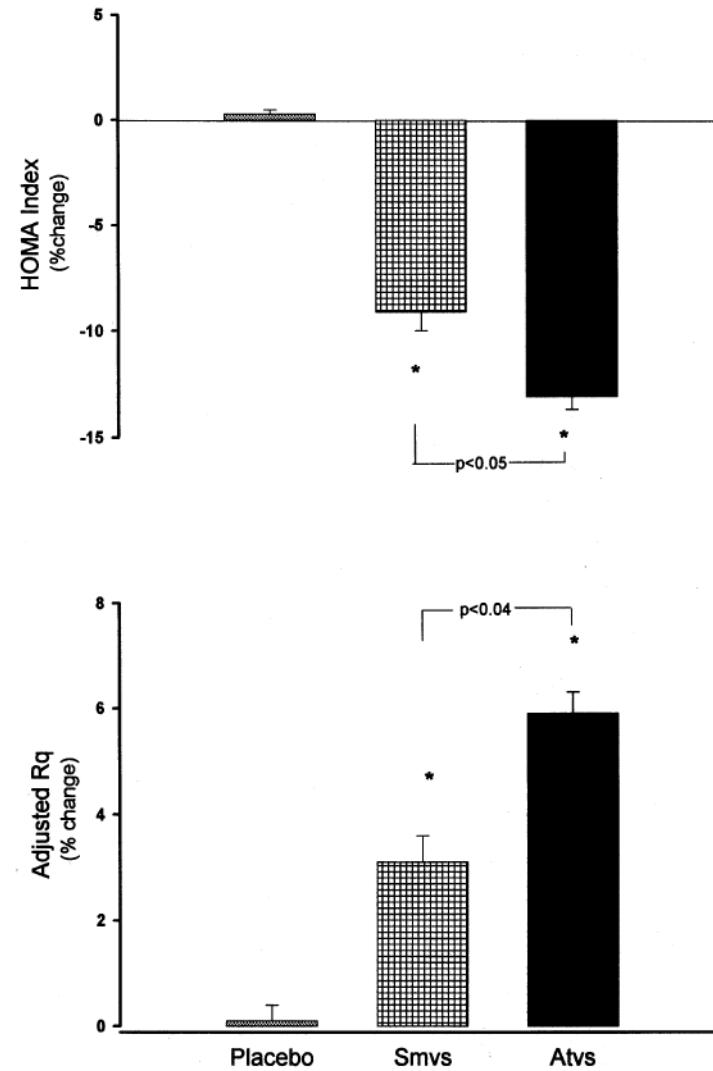
# Statins – mechanism of action



# Statin Therapy Increases the Risk of Developing Type 2 Diabetes

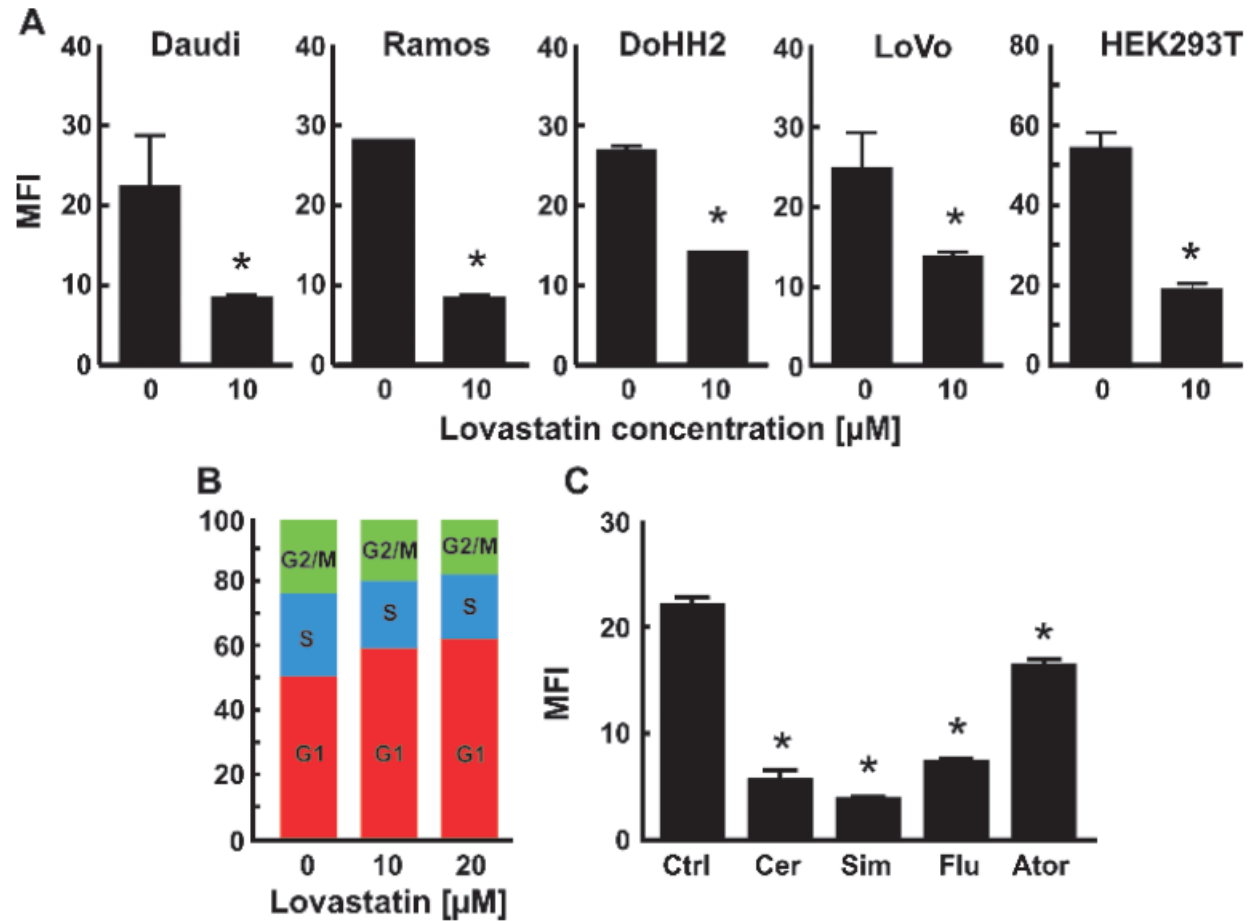


## Statins administration improves insulin resistance and respiratory quotient in aged dyslipidemic non-insulin dependent diabetic patients

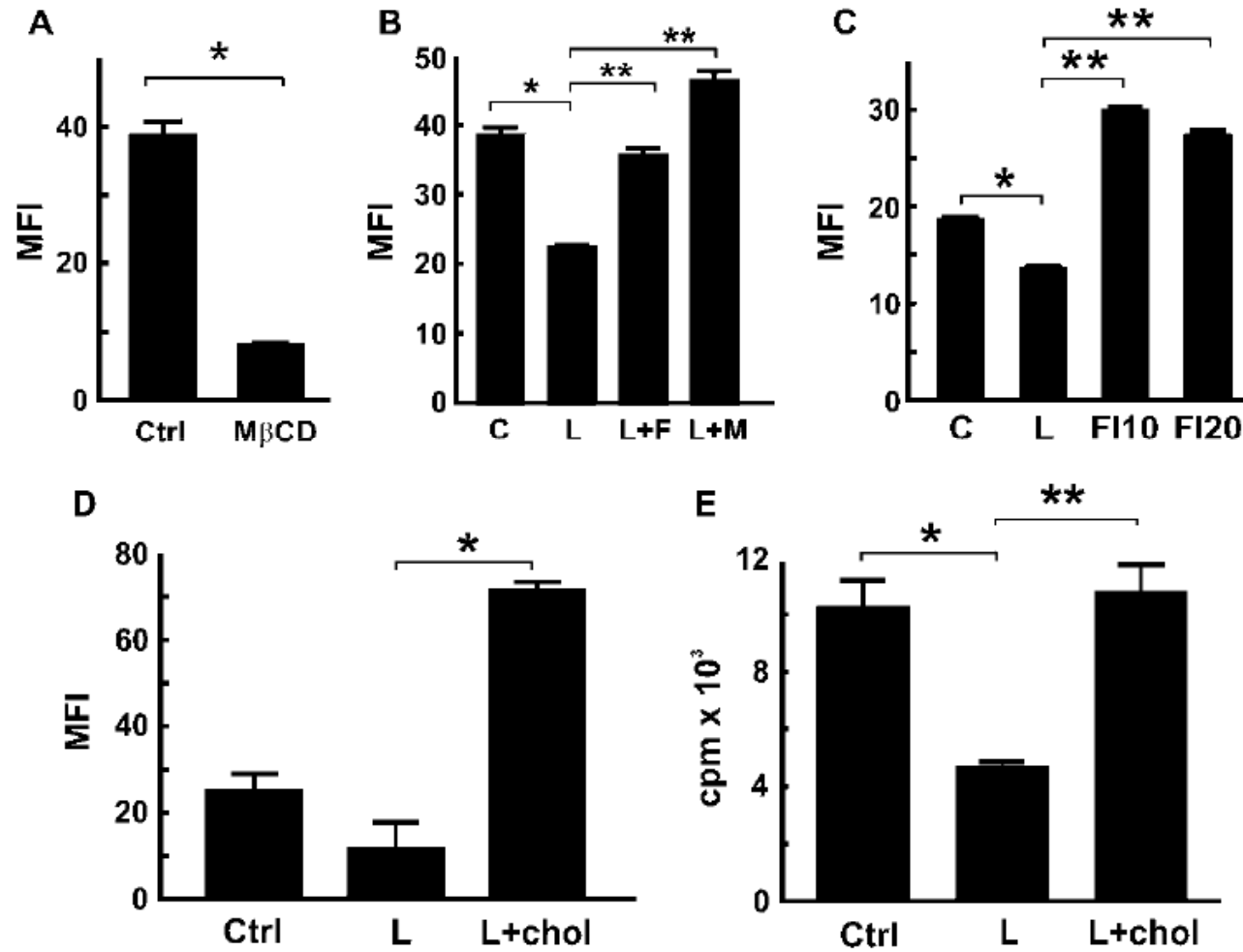




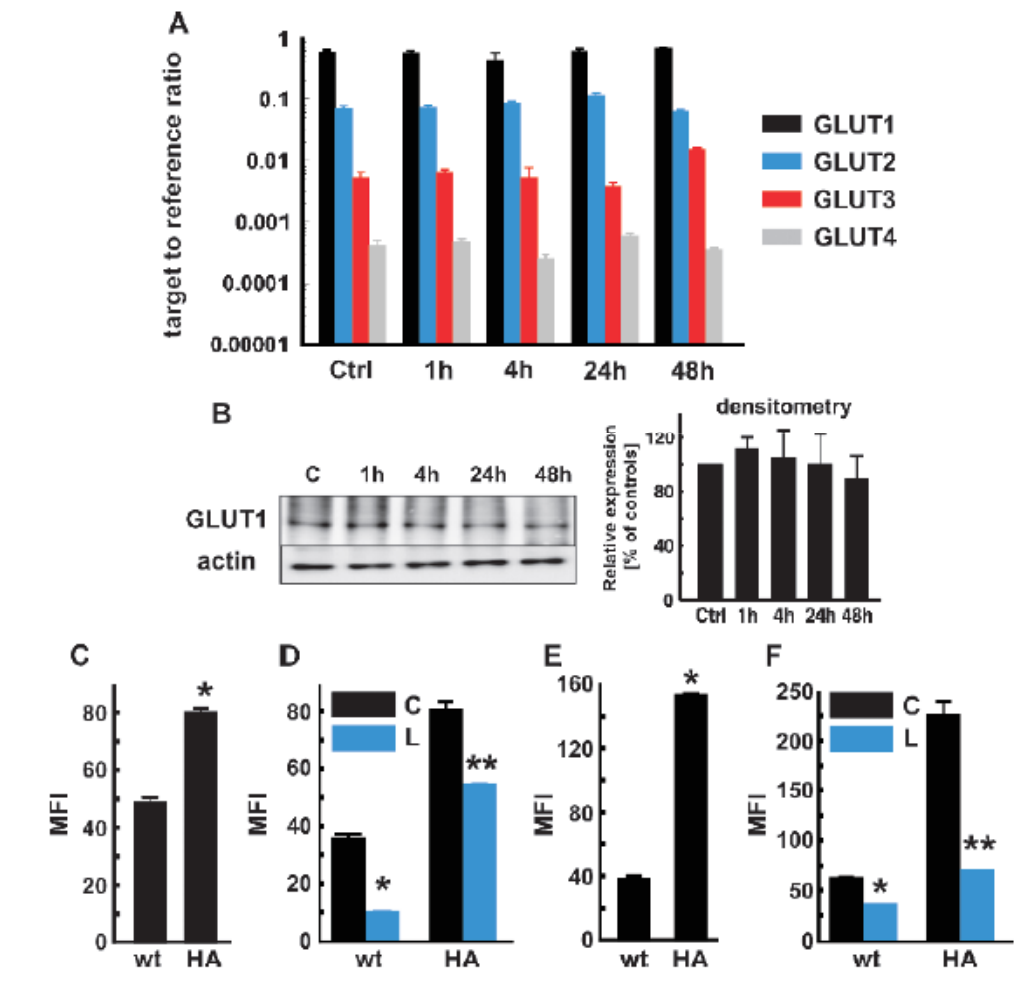
## Statins decrease glucose uptake in human malignant and nonmalignant cell lines



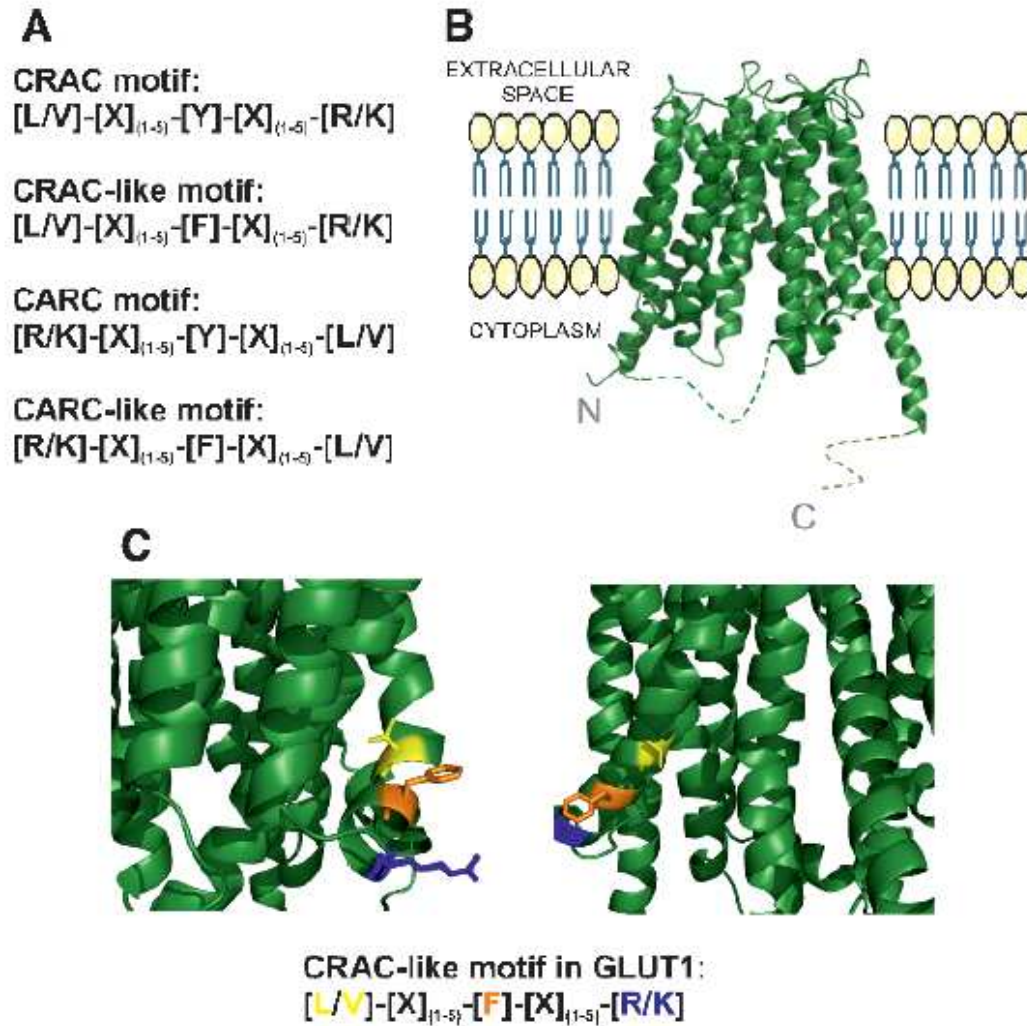
## Effects of lovastatin on glucose uptake depend on the cholesterol biosynthesis pathway



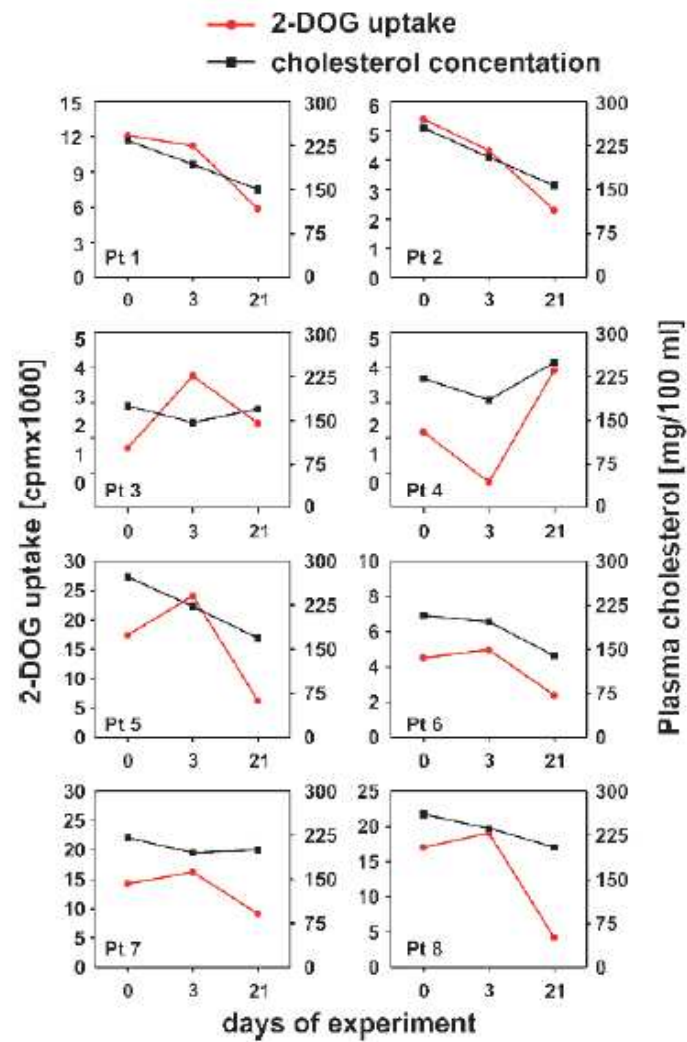
## Impaired glucose uptake by statins is not associated with changes in overall expression of GLUT 1, 2, 3, and 4



## Localization of putative cholesterol-binding motifs in the homology model of human GLUT1 protein

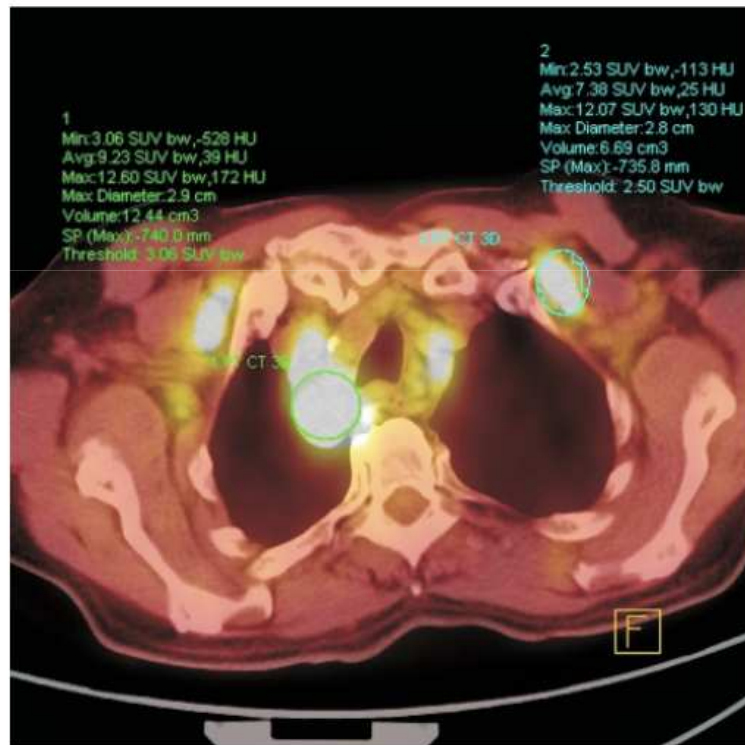


# Statins impair glucose uptake in PBMCs

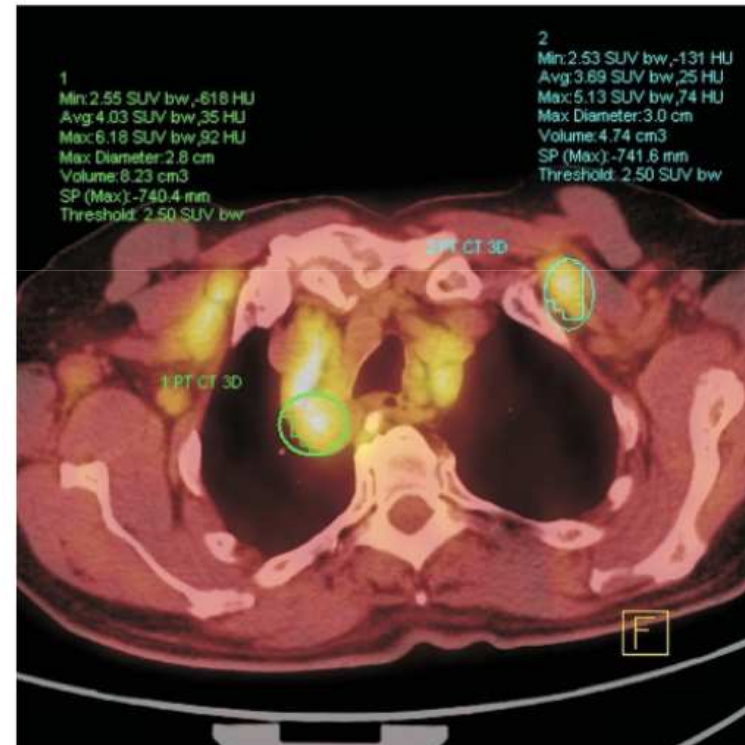


## Atorvastatin treatment significantly decreased 18F-FDG uptake in lymph nodes

A



B



*Expert Opin Drug Saf.* 2010 July ; 9(4): 603–621. doi:10.1517/14740331003662620.

## **Statin Use and Cancer Risk: A Comprehensive Review**

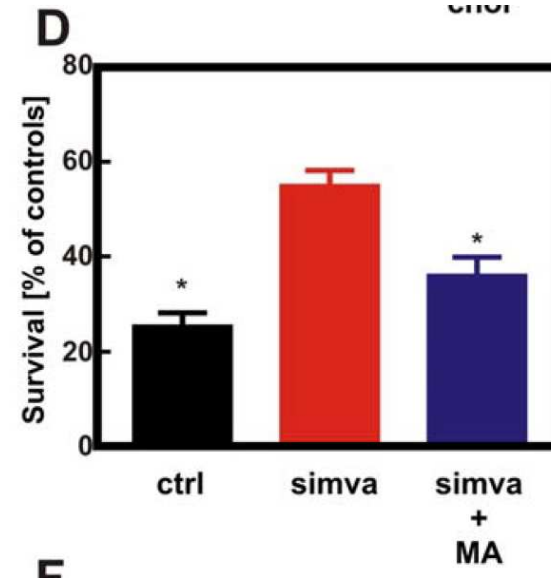
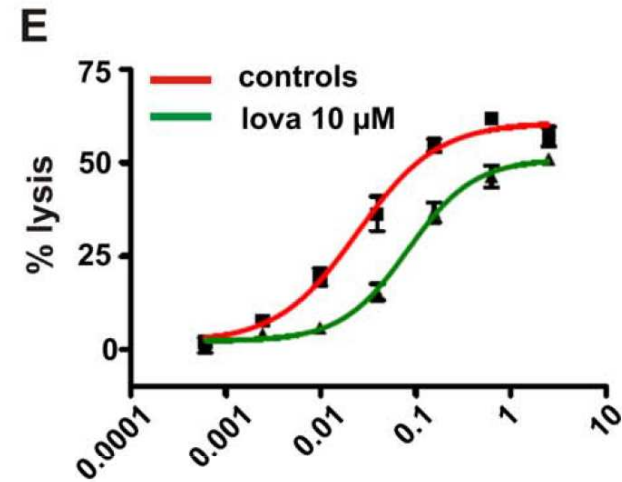
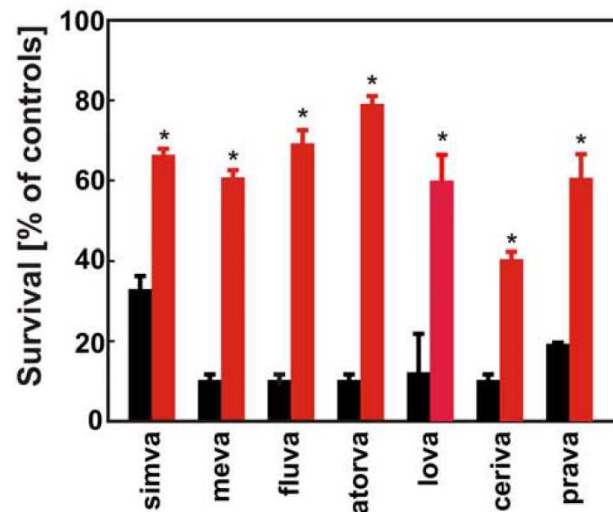
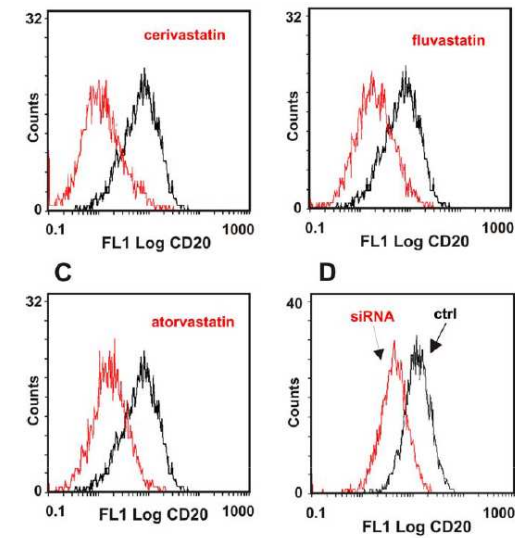
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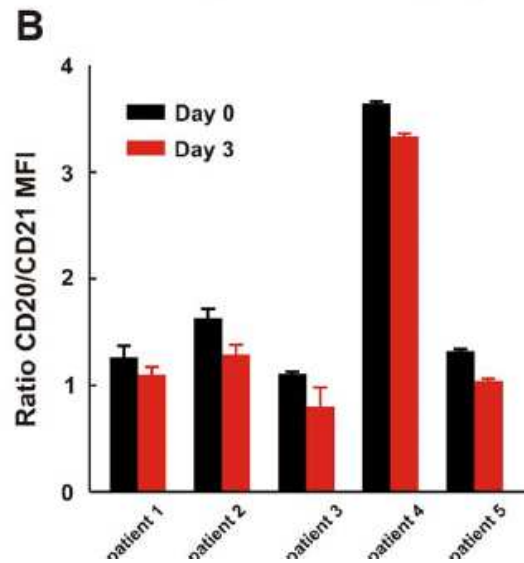
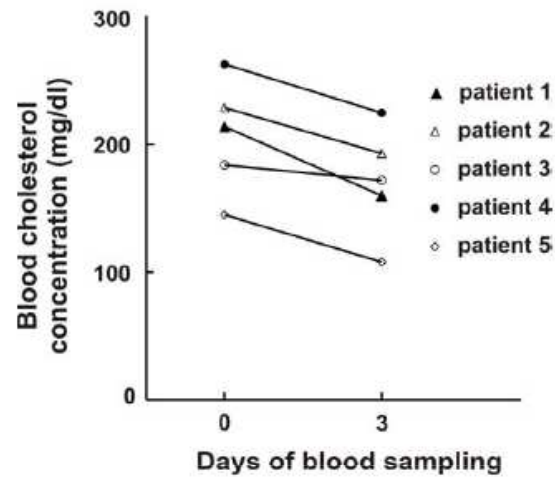


# Statins Impair Antitumor Effects of Rituximab by Inducing Conformational Changes of CD20

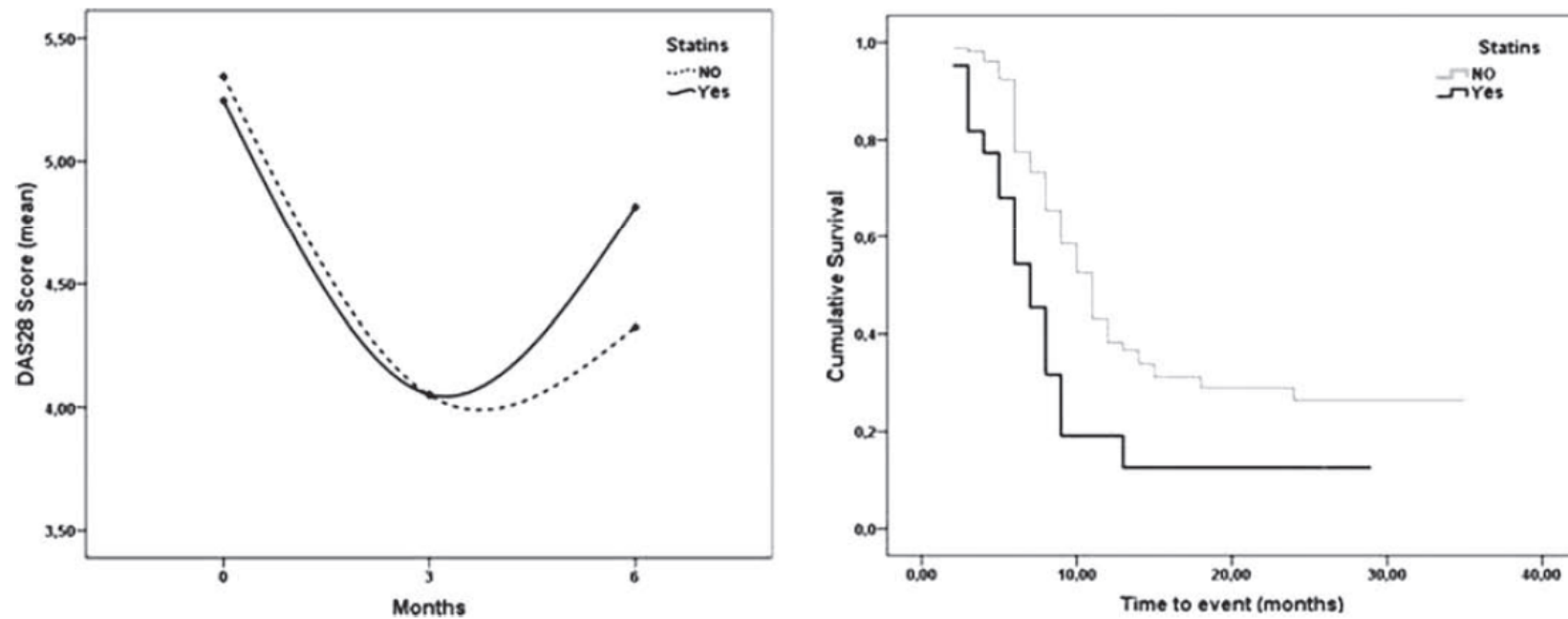




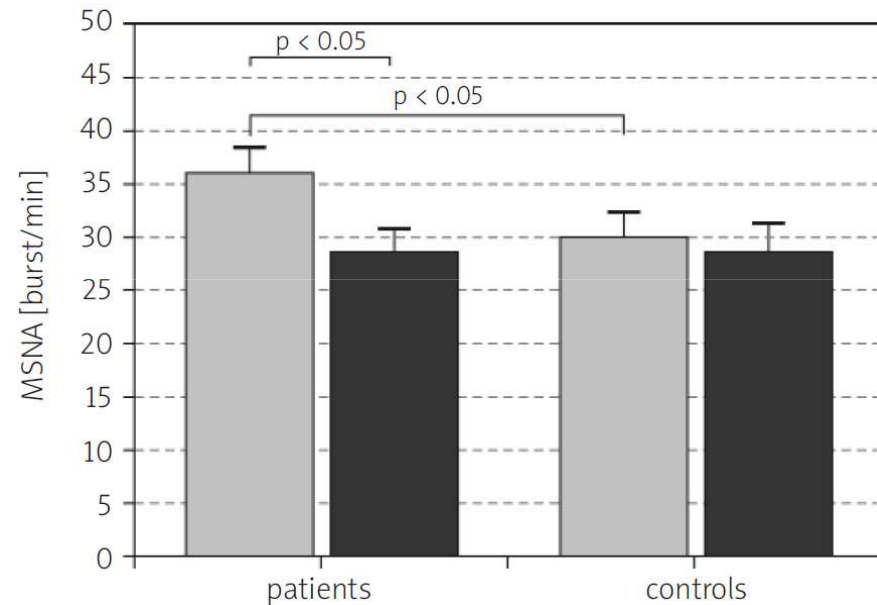
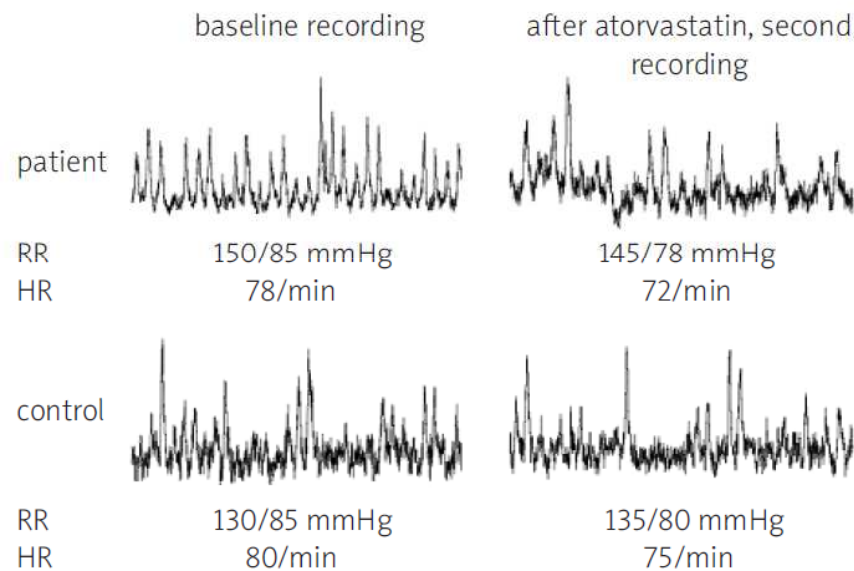
# Statins Impair Antitumor Effects of Rituximab by Inducing Conformational Changes of CD20



## Statins inhibit the antirheumatic effects of rituximab in rheumatoid arthritis: results from the Dutch Rheumatoid Arthritis Monitoring (DREAM) registry

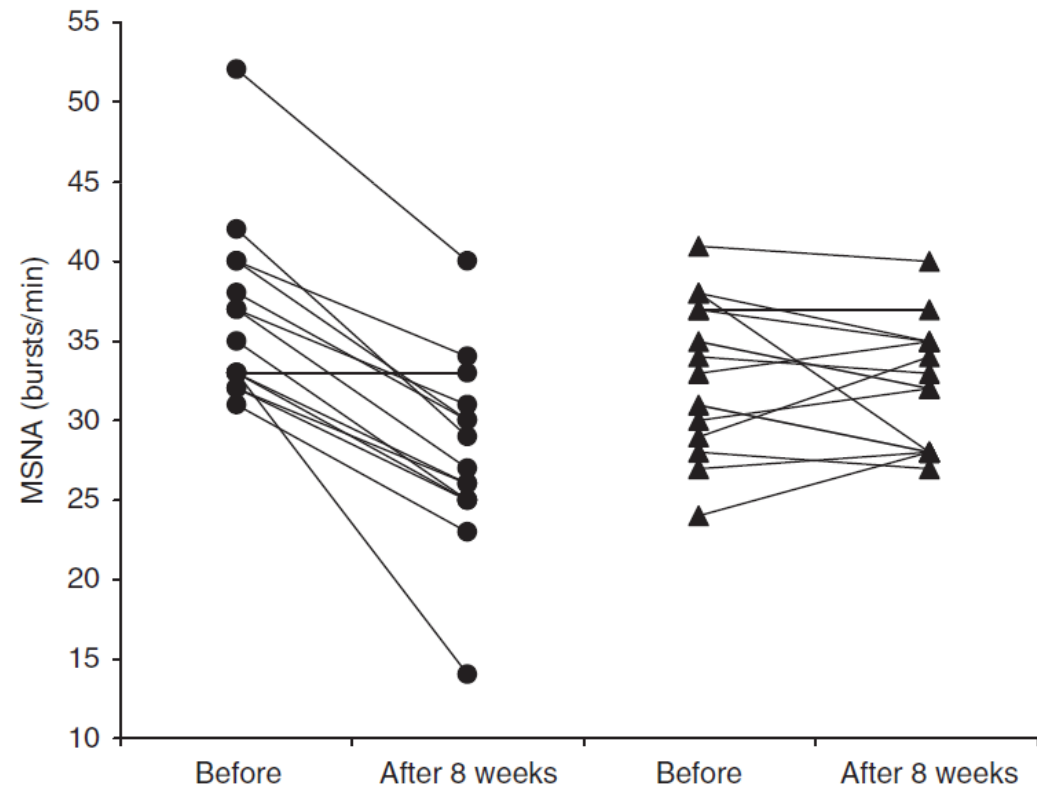


## Atorvastatin reduces sympathetic activity and increases baroreceptor reflex sensitivity in patients with hypercholesterolemia and hypertension



## Simvastatin reduces sympathetic activity in men with hypertension and hypercholesterolemia

Parameter	Simvastatin		Placebo	
	Baseline	After therapy	Baseline	After therapy
TCHOL (mg dl <sup>-1</sup> )	249 ± 30.6	184 ± 28.3**	232 ± 22.1	230 ± 26.2
LDL (mg dl <sup>-1</sup> )	169 ± 32.5	117 ± 31.2**	157 ± 29.1	150 ± 35.1
HDL (mg dl <sup>-1</sup> )	44 ± 1.6	44 ± 9.2	43 ± 12.0	45 ± 0.4
TG (mg dl <sup>-1</sup> )	156 ± 52.1	108 ± 33.2*	159 ± 52.0	161 ± 42.3



## Characteristic of subjects in simvastatin and placebo group at baseline (mean±SD)

	Simvastatin	Ezetimibe	P
Number of patients (M/F)	10/1	10/1	ns
Age, years	46.9±9.0	44.2±10.9	ns
Weight, kg	77.1±8.1	77.6±5.0	ns
Height, m	1.73±0.07	1.76±0.06	ns
BMI, kg/m <sup>2</sup>	25.7±1.1	25.2±2.8	ns
<b>Drugs</b>			
iACE	8	9	
ARB	3	2	
CaA	3	2	
BB	0	0	
Diuretics	2	3	
> 2 drugs	0	0	

## Effects of simvastatin and ezetimibe before and after 6 weeks of treatment (mean±SD)

Parameter	Simvastatin		Ezetimibe		Interaction Group x Time
	Baseline	After therapy	Baseline	After therapy	P
SBP, mmHg	147±5	147±6	149±4	150±8	0.9
DBP, mmHg	96±6	94±7	94±3	95±5	0.27
HR, beats/minute	78±7	74±5	75±7	73±5	0.12
TCHOL, mg/dL	254.1±33.3	196.0±28.0*	247.8±29.9	202.6±26.4**	0.16
LDL, mg/dL	170.4±27.9	117.7±24.2†	160.6±29.6	122.7±18.5††	0.09
HDL, mg/dL	52.7±15.1	55.0±14.3	49.8±11.5	51.8±10.4	0.92
TG, mg/dL	157.0±64.8	127.2±50.1*	181.7±54.2	165.6±64.5	0.1
BRS, ms/mmHg	15.1±2.7	25.0±5.0†††	14.3±2.2	11.5±1.0	0.01

\*p<0.0001 vs baseline

\* p<0.0006 vs baseline

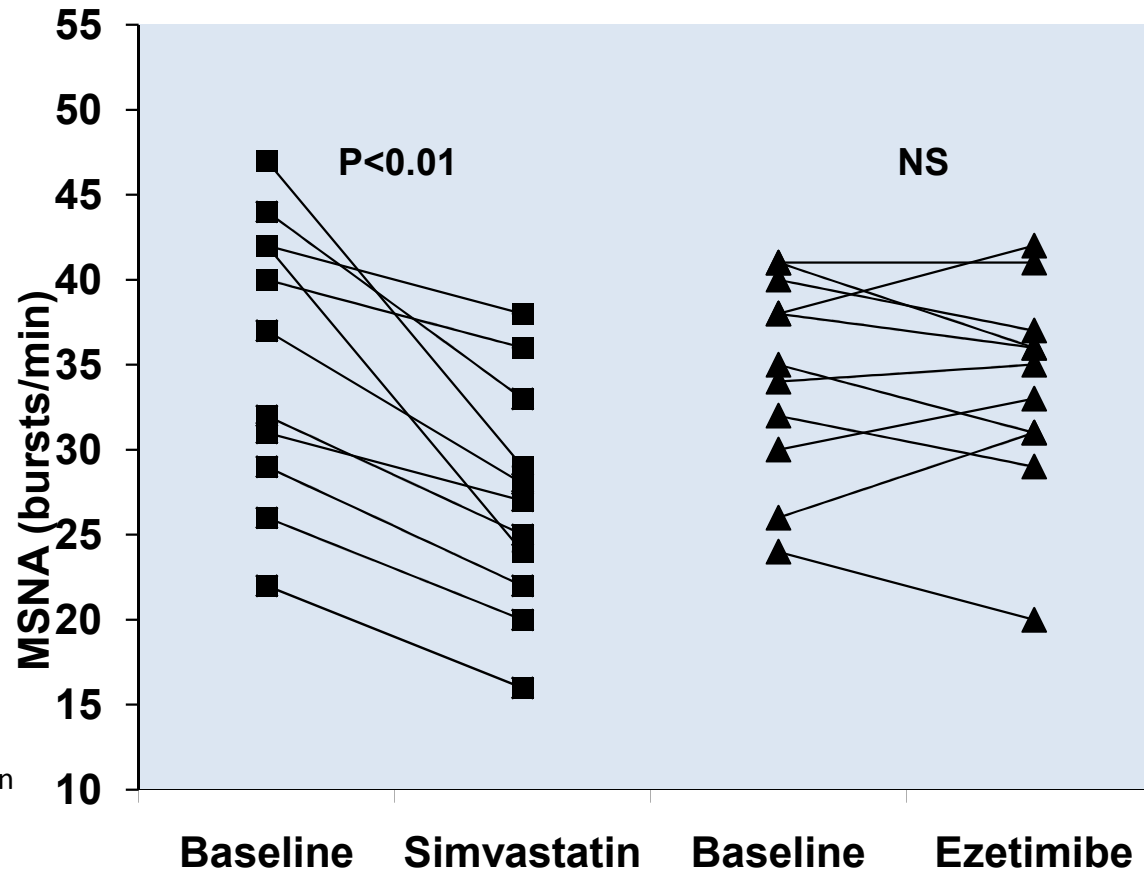
† p<0.0001 vs baseline

†† p<0.001 vs baseline

††† p<0.05 vs baseline

BRS – baroreceptor control of HR

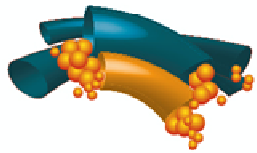
## MSNA – after therapy with simvastatin and ezetimibe (mean±SD)



p<0.01, † p<0.02 simvastatin vs baseline and ezetimibe

**Interaction  
Group x  
Time**

MSNA , burst/min	35.6±8.1	27.1±6.7*	34.5±5.9	33.7±6.1	0.001
MSNA, burst/100 heart beats	55.5±12.7	44.4±13.3†	56.7±12.6	57.2±14.1	0.01



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Brak przekonujących danych o efektach statyn niezwiązanych bezpośrednio z obniżeniem stężenia cholesterolu

Stosowanie statyn musi opierać się na określonych wartościach stężenia cholesterolu





## Statin treatment decreases cardiovascular risk also in subjects with very low cholesterol level (TNT trial)

