

# ATORVASTATIN (ATO) TREATMENT IS ASSOCIATED WITH A NON-SPECIFIC INCREASE IN MONOCYTE CD36 EXPRESSION IN HEMODIALYSIS (HD) PATIENTS

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## Objectives:

ATO may influence CD36 scavenger receptor directly or by improvement of serum lipid profile. To elucidate this problem, we examined monocyte CD36 expression during therapeutic lifestyle changes (TLC) or ATO treatment in HD patients.

## Methods:

### Dyslipidemic IHD patients

were selected according to the Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guidelines  
 LDL-Ch  $\geq$  100 mg/dL or  
 LDL-Ch < 100 mg/dL but TG  $\geq$  200 mg/dL and non-HDL-Ch  $\geq$  130 mg/dL  
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 Efficacy of interventions was evaluated by improvement of serum lipid profile.

### Controls

Individuals, age and gender matched to enrolled HD patients, which declared full health, but showing dyslipidemia according to criteria of HD patients, served as controls (n = 37).  
 Patients' results, if compared to controls, were adjusted for gender, age, pulse pressure, BMI, and cigarette smoking.

### Therapeutic lifestyle changes (TLC)

#### Lipid-lowering diet

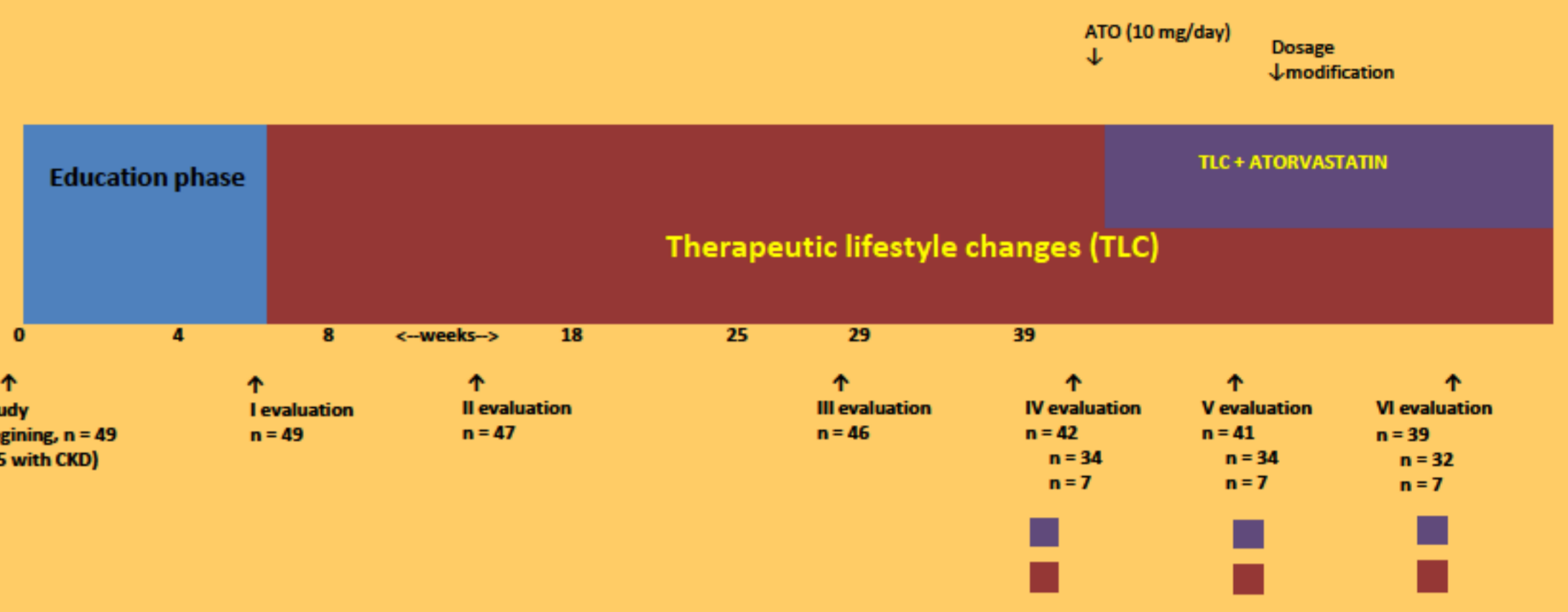
total calories app. 2,000/day,  
 7% of calories as saturated fat,  
 up to 10% of calories as polyunsaturated fat,  
 up to 20% of calories as monounsaturated fat,  
 a total fat of 25% to 35% of total calories,  
 complex carbohydrates of 50% to 60% of total calories,  
 fiber (20-30 g per day)  
 cholesterol (<200 mg/day).

#### Planned physical activity

10,000 steps per day  
 or 20-30 minute period of activity 3-4 times a week  
 or both interchangeably  
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### Laboratory analyses

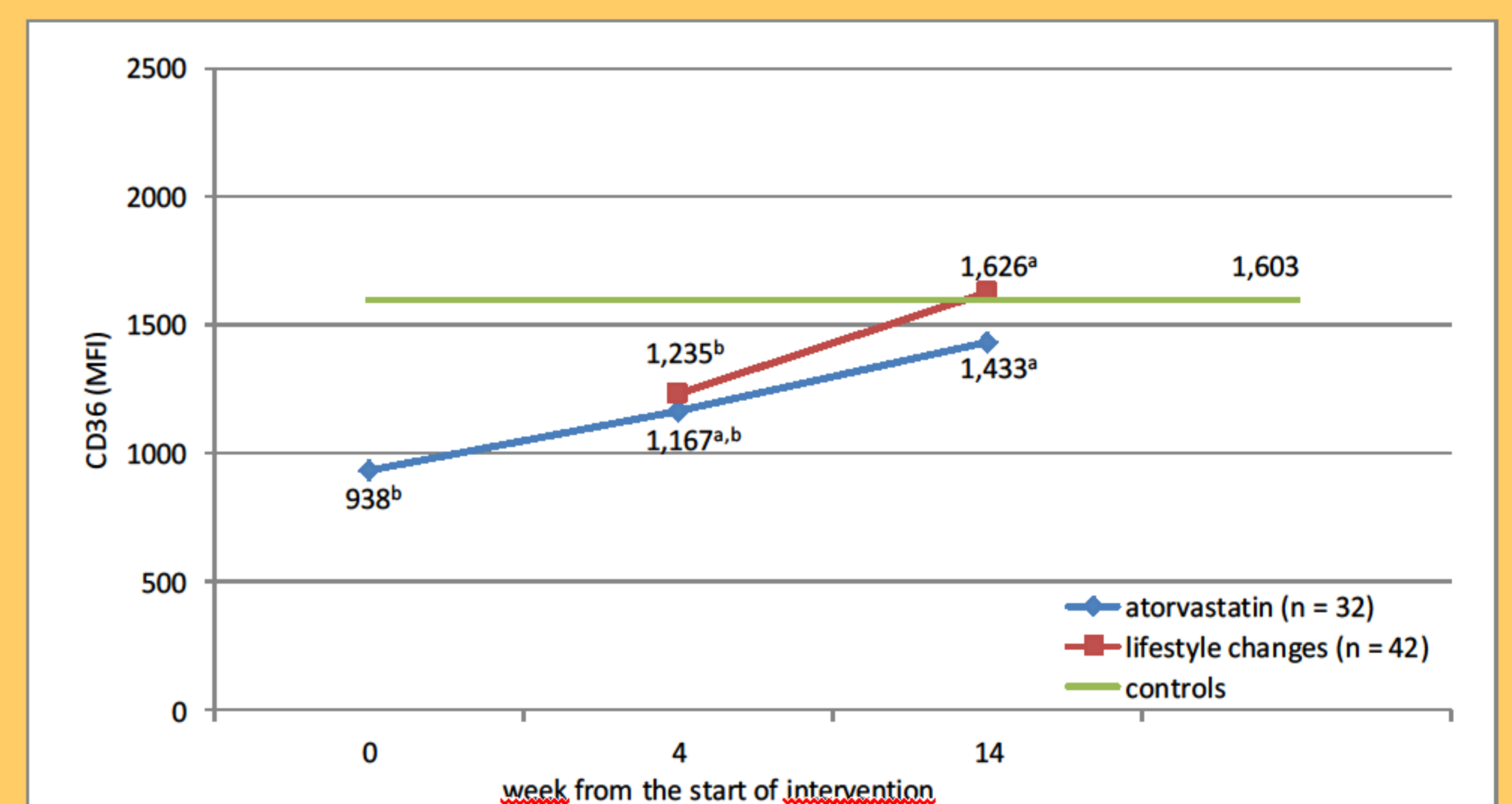
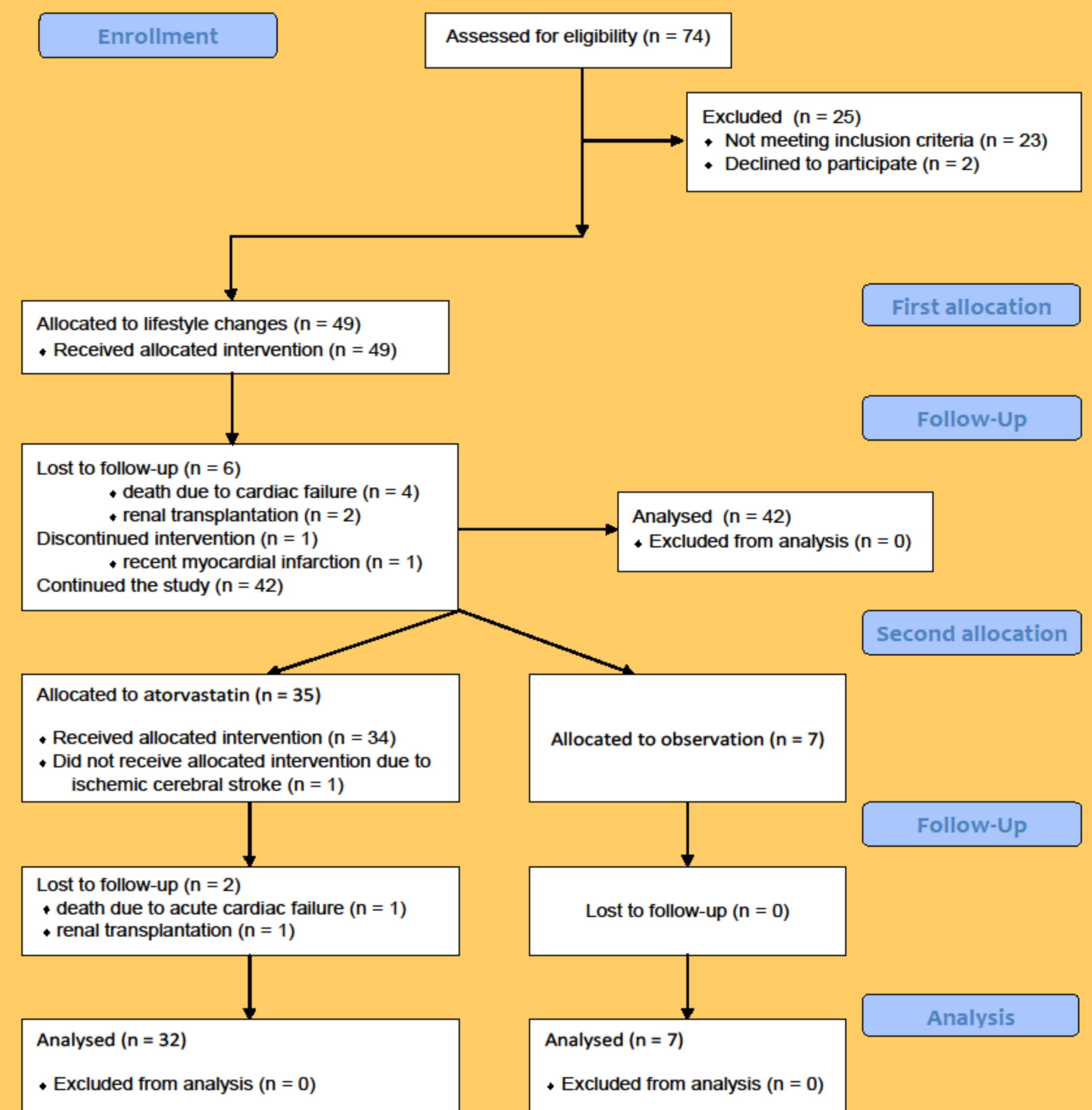
The level of expression of CD36 scavenger receptor density on monocyte surface was evaluated by flow cytometric analysis, using APC Mouse Anti-Human CD36 (BD Pharmingen, USA) and a mixture of fluorescein isothiocyanate-conjugated anti-CD45 and phycoerythrin-conjugated anti-CD14 (Simultest™ LeucoGATE™, USA). Mean fluorescence intensity (MFI) was used to measure expression of CD36 density.



## Results:

Parameter	Patients N = 49	Controls N = 37	P value
Caucasians (n, %)	49 (100)	37 (100)	-
Male gender (n, %)	28 (57.1)	19 (51.4)	0.664
Age (years)	65.0 ± 10.1	61.5 ± 9.9	0.112
Cigarette smoking >5 packs/year (n, %)	6 (12.2)	9 (24.3)	0.146
BMI (kg/m <sup>2</sup> )	30.6 ± 6.7	29.4 ± 4.7	0.583
Systolic blood pressure (mmHg)	134 ± 18	129 ± 13	0.092
Diastolic blood pressure (mmHg)	78 ± 8	79 ± 6	0.695
Mean arterial blood pressure (mmHg)	97 ± 10	96 ± 8	0.177
Pulse pressure (mmHg)	56 ± 14	49 ± 12	0.059
Hs-CRP (mg/L)	8.0 (4.0 – 143.0)	1.70 (0.10 – 9.30)	<0.0001
Fasting glucose (mg/dL)	125 ± 50	101 ± 10	0.182
Insulin (μIU/ml)	15.2 ± 13.2	8.8 ± 4.6	0.021
HOMA-IR	3.52 (0.35 – 37.0)	1.93 (0.66 – 5.55)	0.013
Fructosamine (μmol/L)	262 ± 63	233 ± 32	0.030
WBC (10 <sup>3</sup> /μL)	7.00 ± 2.44	6.30 ± 1.77	0.241
Hb (g/L)	115 ± 16	144 ± 10	<0.0001
E (10 <sup>6</sup> /μL)	3.81 ± 0.47	4.74 ± 0.38	<0.0001
PLT (10 <sup>3</sup> /μL)	219 ± 91	231 ± 47	0.030
ALT (U/L)	16.4 ± 8.6	26.2 ± 14.2	0.0001
AST (U/L)	15.0 ± 5.3	21.0 ± 5.8	<0.0001
Urea (mg/dL)	114 ± 38	30.4 ± 6.4	<0.0001
Creatinine (mg/dL)	7.49 ± 2.32	0.72 ± 0.12	<0.0001
Height (cm)	163.4 ± 8.4	165.3 ± 9.4	0.344
Waist circumference (cm)	105.4 ± 16.3	98.6 ± 11.4	0.035
Hip circumference (cm)	107.8 ± 14.6	107.2 ± 9.0	0.822
MUAC (cm)	33.4 ± 4.5	30.9 ± 2.9	0.003
MUAMC (cm)	29.6 ± 3.7	26.4 ± 3.9	0.0002
TSF (cm)	1.23 ± 0.71	1.46 ± 0.91	0.353
WHiR	0.98 ± 0.07	0.92 ± 0.08	0.0005
WHeR	0.65 ± 0.10	0.60 ± 0.07	0.017
Total cholesterol (mg/dL)	205 ± 31	238 ± 37	<0.0001
LDL-Ch (mg/dL)	143 ± 60	146 ± 31	0.927
MDA-OxLDL (μg/mL)	0.60 (0.05 – 9.20)	0.72 (0.05 – 13.09)	0.827
IgG anti-OxLDL (mU/mL)	147 (39 – 1,000)	205 (58 – 1,730)	0.098
HDL-Ch (mg/dL)	38.4 ± 10.5	64.1 ± 16.4	<0.0001
Non-HDL-Ch (mg/dL)	167 ± 31	174 ± 34	0.342
HDL-Ch/LDL-Ch ratio (%)	29.8 ± 12.0	45.2 ± 12.1	0.00003
Triacylglycerols (mg/dL)	187 ± 80	136 ± 71	0.003
White blood cell (10 <sup>3</sup> /μL)	7.08 ± 2.18	6.30 ± 1.77	0.059
Monocyte (cells/μL)	517 ± 233	376 ± 170	0.003
CD36 (cells/μL)	388 ± 174	332 ± 159	0.124
CD36 as percent of monocyte	77.0 ± 20.2	88.5 ± 10.2	0.003
CD36 expression (MFI)	1,400 ± 852	2,054 ± 1,413	0.002

The flowchart of hemodialysis patients



\* P value adjusted for gender, age, pulse pressure, body mass index, and cigarette smoking; § n = 47  
 Results are expressed as mean ± SD or median and range.  
 Significant differences are indicated using bold font.

## Conclusions:

Dyslipidemic HD patients show different serum lipid profile and lower CD36 MFI than dyslipidemic controls. Improvement in serum lipid profile in HD patients is associated with an increase in monocyte CD36 expression, independently whether this improvement is induced by TLC or ATO.

An increase in CD36 expression may be added to the non-specific effects of ATO treatment in dyslipidemic HD patients.

(ClinicalTrials.gov number, NCT01448174)

