Η εφαρμογή της θεραπευτικής αφαίρεσης στις δυσλιπιδαιμίες και διάφορα «ορφανά» νοσήματα

Π. Κρίκη

Νεφρολόγος , Π.Γ.Ν.Αλεξανδρούπολης

Σπάνια νόσος : όταν ο αριθμός των ασθενών που έχουν προσβληθεί από αυτή είναι < 5/10.000

RARE DISEASES by the NUMBERS

50%

of the people affected by rare diseases are children

Approximately

7,000

rare diseases & disorders have been identified

in the U.S. are living with rare diseases

in Europe are living with rare diseases

#DYK:

If all of the people with rare diseases lived in one country, it would be the

world's 3rd most populous country

Guidelines on the Use of Therapeutic Apheresis in Clinical Practice–Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Seventh Special Issue

ΚΑΤΗΓΟΡΙΑ I:
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ΚΑΤΗΓΟΡΙΑ II:
ΓΕΝΙΚΑ ΑΠΟΔΕΚΤΗ ΘΕΡΑΠΕΙΑ ΩΣ ΥΠΟΣΤΗΡΙΚΤΙΚΗ

N-METHYL-D-ASPARATE RECEPTOR ANTIBODY ENCEPHALITIS

Incidence: Rare		Procedure	Recommendation	Category
		TPE	Grade 1C	I
No. of reported patients: 100–300	**RCT**	**CT**	**CS**	**CR**
	0	0	5(221)	39(41)

- **Αυτοάνοση νευρολογική διαταραχή : Anti – NMDAR**
- **Αγωγή:**
  - ✓ 1ης γραμμής: CCS, IVIG, TPE (5-6ΜΠΜ)
  - ✓ 2ης γραμμής : Rituximab ± Cyclophosphamide

Technical notes

Volume treated: 1–1.5 TPV
Replacement fluid: Albumin
Frequency: Every other day

Scwartz et al, J Clin Apheresis 2016

Hyperlipidemia
Idiopathic thrombocytopenic purpura

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Εγκεφαλοπάθεια Hashimoto

Incidence: Rare		**Procedure** TPE	**Recommendation** Grade 2C	**Category** II
# of reported patients: < 100	**RCT** 0	**CT** 0	**CS** 0	**CR** 14(15)

- **Νευροψυχιατρική συνδρομή με αυξημένους τίτλους αντιθυρεοειδικών αντισωμάτων (πιθανώς ευθυρεοειδικοί οι ασθενείς)**

- **Αγωγή:**
  - ✓ 1ης γραμμής: CCS,
  - ✓ 2ης γραμμής : IVIG,Cyclophosphamide,AZA, TPE (3-9ΜΠΜ)

Technical notes

Volume treated: 1–1.5 TPV
Replacement fluid: Albumin
Frequency: Daily to every other day

Hyperlipidemia
Idiopathic thrombocytopenic purpura

Scwartz et al, J Clin Apheresis 2016

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ΜΗ ΤΕΚΜΗΡΙΩΜΕΝΗ ΕΝΔΕΙΞΗ

ΚΑΤΗΓΟΡΙΑ IV:
ΑΠΟΔΕΔΕΙΓΜΕΝΑ ΧΩΡΙΣ ΑΠΟΤΕΛΕΣΜΑ

Stiff man Syndrome

Incidence: 0.1/100,000		**Procedure**	**Recommendation**	**Category**
		TPE	Grade 2C	III
No. of reported patients: < 100	**RCT**	**CT**	**CS**	**CR**
	0	0	5(30)	13(14)

- **Νευρολογική αυτοάνοση διαταραχή : antiGlutamicAcidDecarboxylate (antiGAD)**
- **Αγωγή:**
  - ✓ Immune therapy, αντικαταθλιπτικά, μυοχαλαρωτικά, TPE (4-5 σε 8-14 μέρες)

Volume treated: 1–1.5 TPV	**Frequency:** Every 1–3 days
Replacement fluid: Albumin	

Scwartz et al, J Clin Apheresis 2016

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Δερματομυοσίτιδα/Πολυμυοσίτιδα

Incidence: 1/100,000/yr in adults, 0.4/100,000/yr in children		**Procedure**	**Recommendation**	**Category**
		TPE	Grade 2B	IV
		ECP	Grade 2C	IV
No. of reported patients: < 100	**RCT**	**CT**	**CS**	**CR**
TPE	1(39)	0	1(3)	2(2)

- **Ιδιοπαθής φλεγμονώδης μυοπάθεια ± δερματικές βλάβες**
- **Αγωγή:**
  - ✓ CCS ± AZA, Cyclophosphamide, IVIG, Rituximab
  - ✓ TPE;;;; Rescue therapy;;;
  - ✓ Αντισώματα: ANA, Anti-Ro, Anti-La, myositis specific antibodies..... Όχι ειδικά
  - ✓ RCT/CR

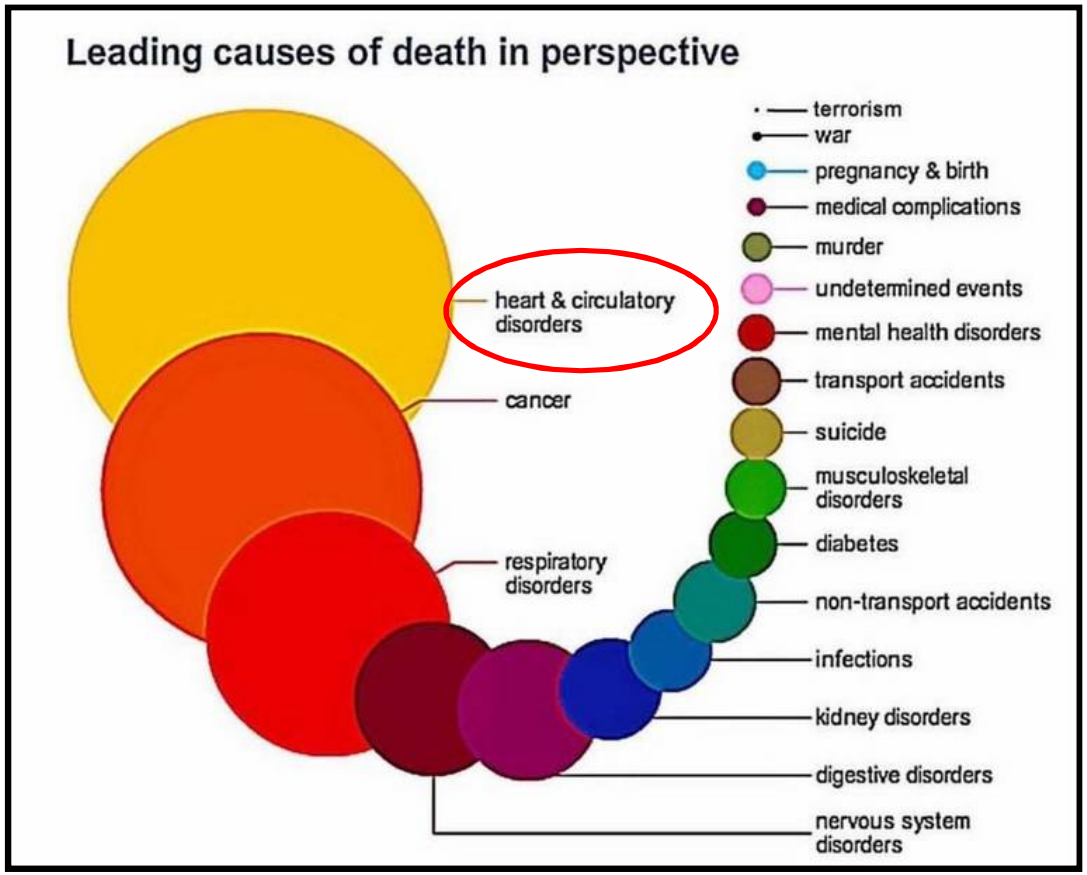
Scwartz et al, J Clin Apheresis 2016

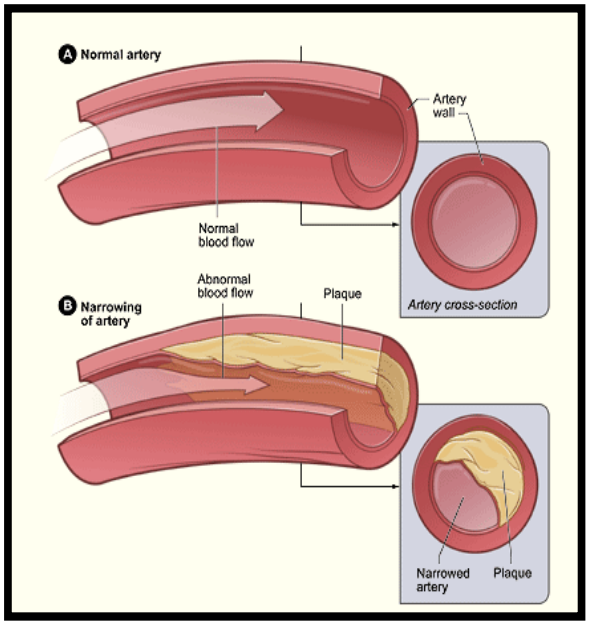
FAMILIAL HYPERCHOLESTEROLEMIA

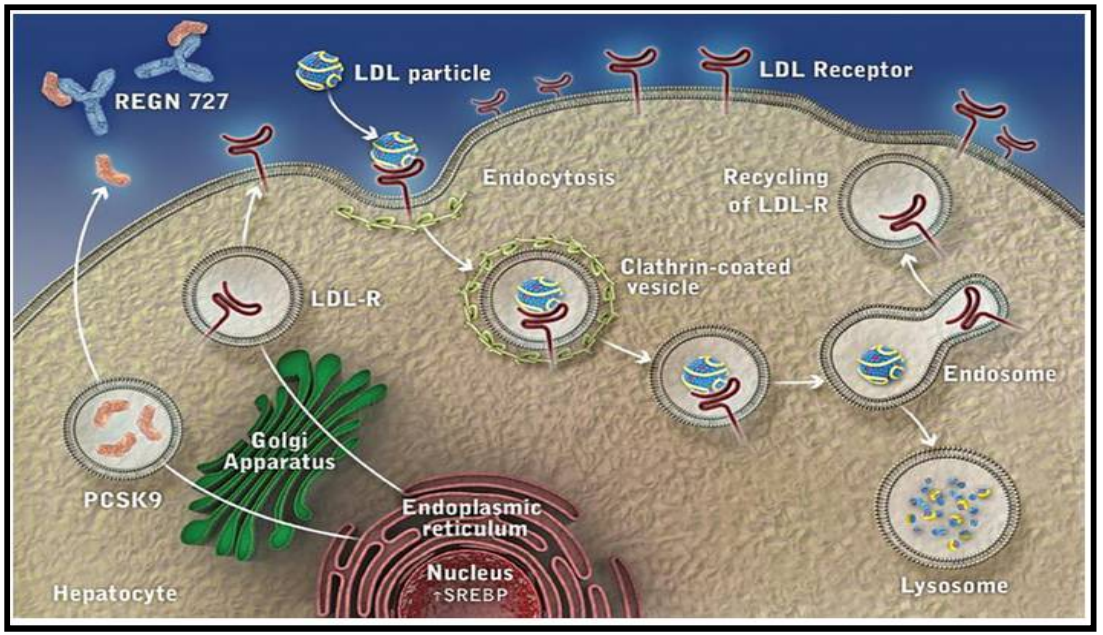
Incidence: Heterozygotes: 200/100,000/year; Homozygotes: 1/1,000,000/year	**Indication**	**Procedure**	**Recommendation**	**Category**
	Homozygotes[a]	LDL apheresis	Grade 1A	I
	Heterozygotes	LDL apheresis	Grade 1A	II
	Homozygotes with small blood volume[b]	TPE	Grade 1C	II
No. of reported patients: > 300	**RCT**	**CT**	**CS**	**CR**
LDL apheresis	6(228)	15(308)	22(401)	NA
TPE	0	1(5)	14(62)	NA

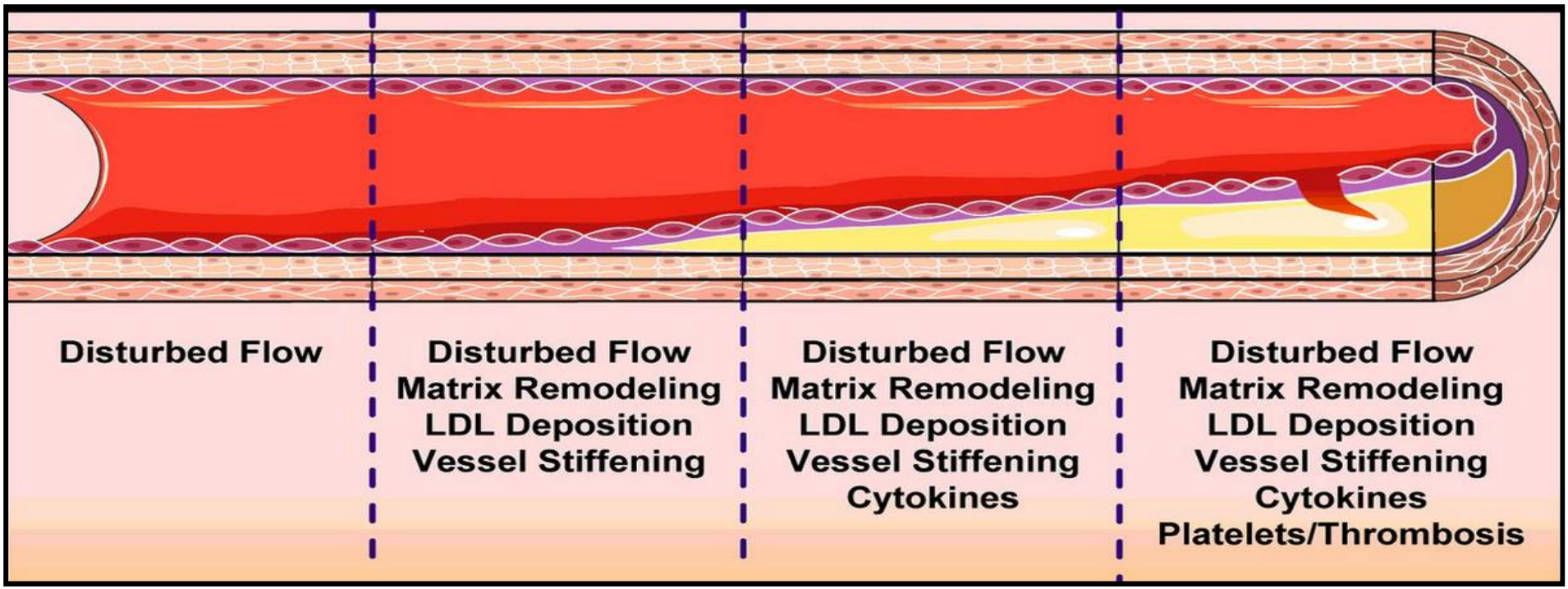
[a]Approved indications vary among countries, see technical notes below. [b]Relative to manufacturers' recommendation for available selective removal devices.

World Health Organization




A Normal artery
Artery wall
Normal blood flow
Artery cross-section
B Narrowing of artery
Abnormal blood flow
Plaque
Narrowed artery
Plaque


REGN 727
LDL particle
LDL Receptor
Endocytosis
Recycling of LDL-R
Clathrin-coated vesicle
LDL-R
Endosome
Golgi Apparatus
PCSK9
Endoplasmic reticulum
Nucleus
↑SREBP
Hepatocyte
Lysosome


Disturbed Flow
Disturbed Flow
Matrix Remodeling
LDL Deposition
Vessel Stiffening
Disturbed Flow
Matrix Remodeling
LDL Deposition
Vessel Stiffening
Cytokines
Disturbed Flow
Matrix Remodeling
LDL Deposition
Vessel Stiffening
Cytokines
Platelets/Thrombosis

Δίαιτα

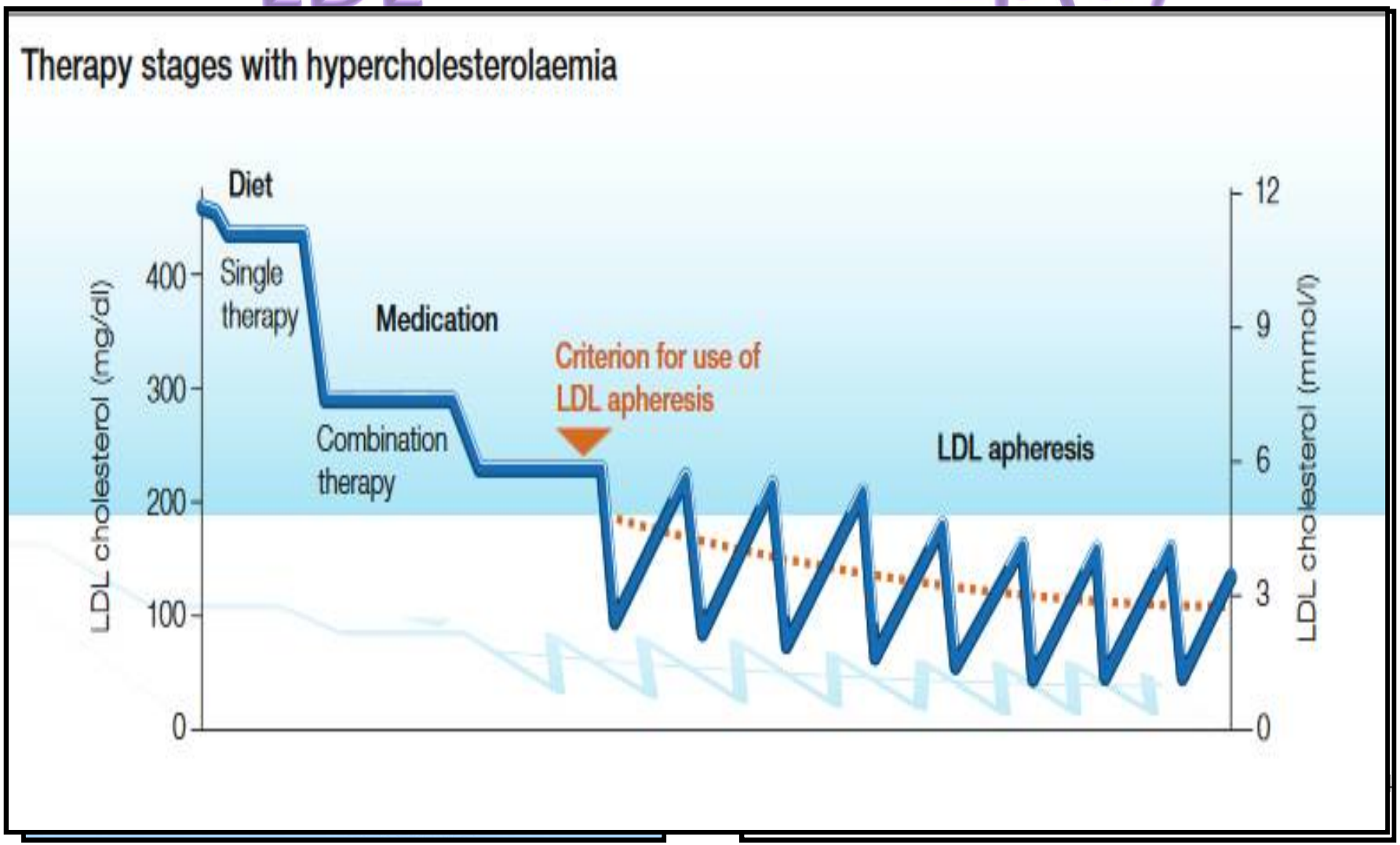
Φαρμακευτική αύξηση του μεταβολισμού

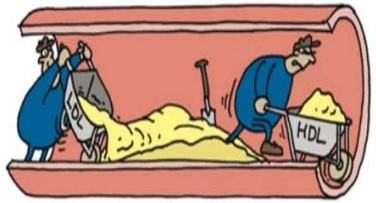
Αναστολή σύνθεσης

Απομάκρυνση από τον ενδαγγειακό χώρο

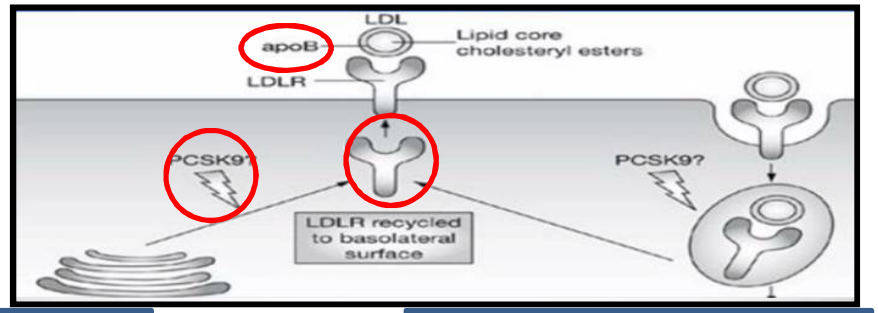
LDL

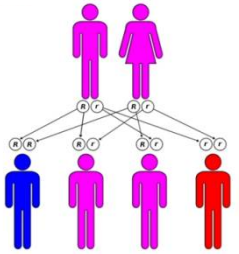
Lp(a)





Οικογενής υπερχοληστερολαιμία



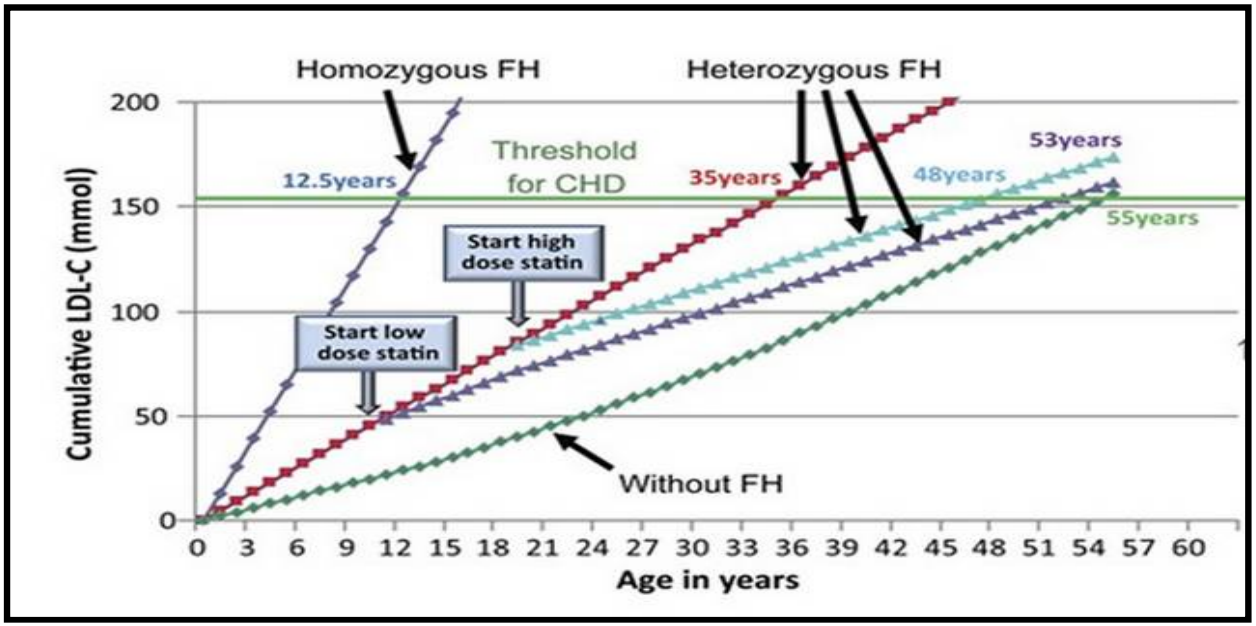


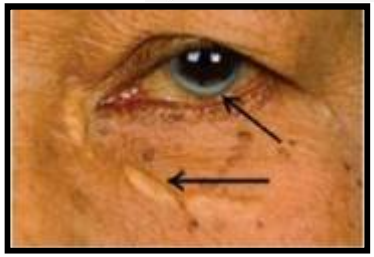
HoFH

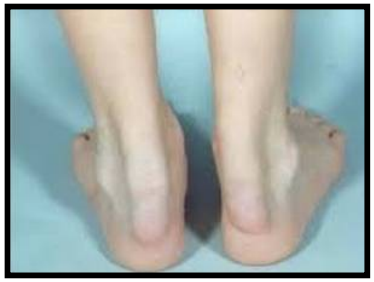
1/1000000
LDL : 650-1000mg/dl
Ξανθώματα 4 ετών
20 ετών

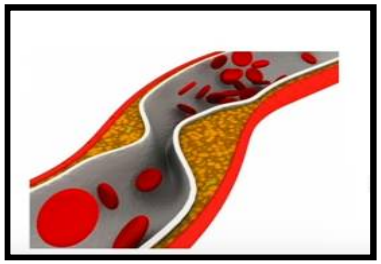
HeFH

1/1500
LDL : 250-550 mg/dl
Ξανθώματα 20 ετών
Αθηρωματική νόσος 30









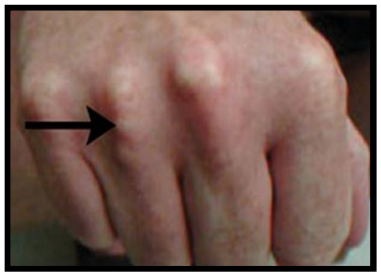


Table 1. Dutch Lipid Clinic Network criteria for the diagnosis of heterozygous familial hypercholesterolemia (hFH).[33,34]

Criteria		Score
Family history	First-degree adult relative with	
	• Premature coronary and/or vascular disease (male < 55 years; female < 60 years)	1
	• LDL-C > 95th percentile for age and gender	1
	• Tendon xanthomata and/or arcus cornealis	2
	First-degree relative < 18 years with LDL-C > 95th percentile for age and gender	2
Clinical history	Patient with premature IHD (ages as above)	2
	Patient with other premature vascular and/or cerebrovascular disease (ages as above)	1
Physical examination	Tendon xanthomata	6
	Arcus cornealis prior to age 45	4
Laboratory analysis	LDL-C (mmol/L)	
	• ≥8.5	8
	• 6.5–8.4	5
	• 5.0–6.4	3
	• 4.0–4.9	1
DNA analysis	Genetic test results confirming functional mutation in *LDLR*, *APOB*, or *PCSK9* gene	8

LDL-C = low-density lipoprotein cholesterol; IHD = ischemic heart disease; *LDLR* = low-density lipoprotein receptor; *APOB* = apolipoprotein B-100; *PCSK9* = proprotein convertase subtilisin/kexin9

SIMON BROOME DIAGNOSTIC CRITERIA FOR FAMILIAL HYPERCHOLESTEROLEMIA[1]

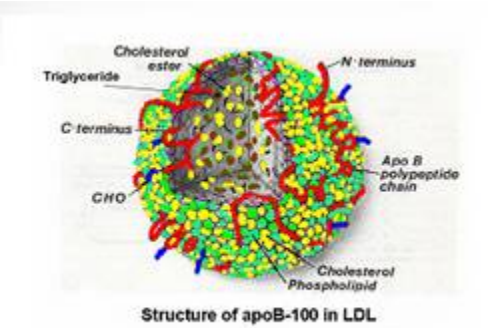
Point	Criteria
1	Total cholesterol levels > 290mg/dL (7.5 mmol/L) or LDL-C > 190 mg/dL (4.9 mmol/L) in adults. Total cholesterol levels > 260 mg/dL (6.7 mmol/L) or LDL-C > 155 mg/dL (4.0 mmol/L)
2	Tendon xanthomas in the patient or tendon xanthomas in a first or second degree relative.
3	DNA-based evidence of an LDL-receptor mutation, familial defective apo B-100, or a PCSK9 mutation.
4	Family history of myocardial infarction before age 50 years in a second degree relative or before age 60 years in a first degree relative.
5	Family history of elevated total cholesterol > 290 mg/dL (7.5 mmol/L) in an adult first or second-degree relative. Family history of elevated totacl cholesterol > 260 mg/dL (6.7 mmol/L) in a child, brother, or sister 16 years or younger.

DIAGNOSIS

Definite familial hypercholesterolemia = 1+2 or 3

Possible familial hypercholesterolemia = 1+4 or 5

1. Austin MA, Hutter CM, Zimmern RL, Humphries SE. Genetic causes of monogenic heterozygous familial hypercholesterolemia: a HuGE prevalence review. *American journal of epidemiology*. 2004;160:407-420.

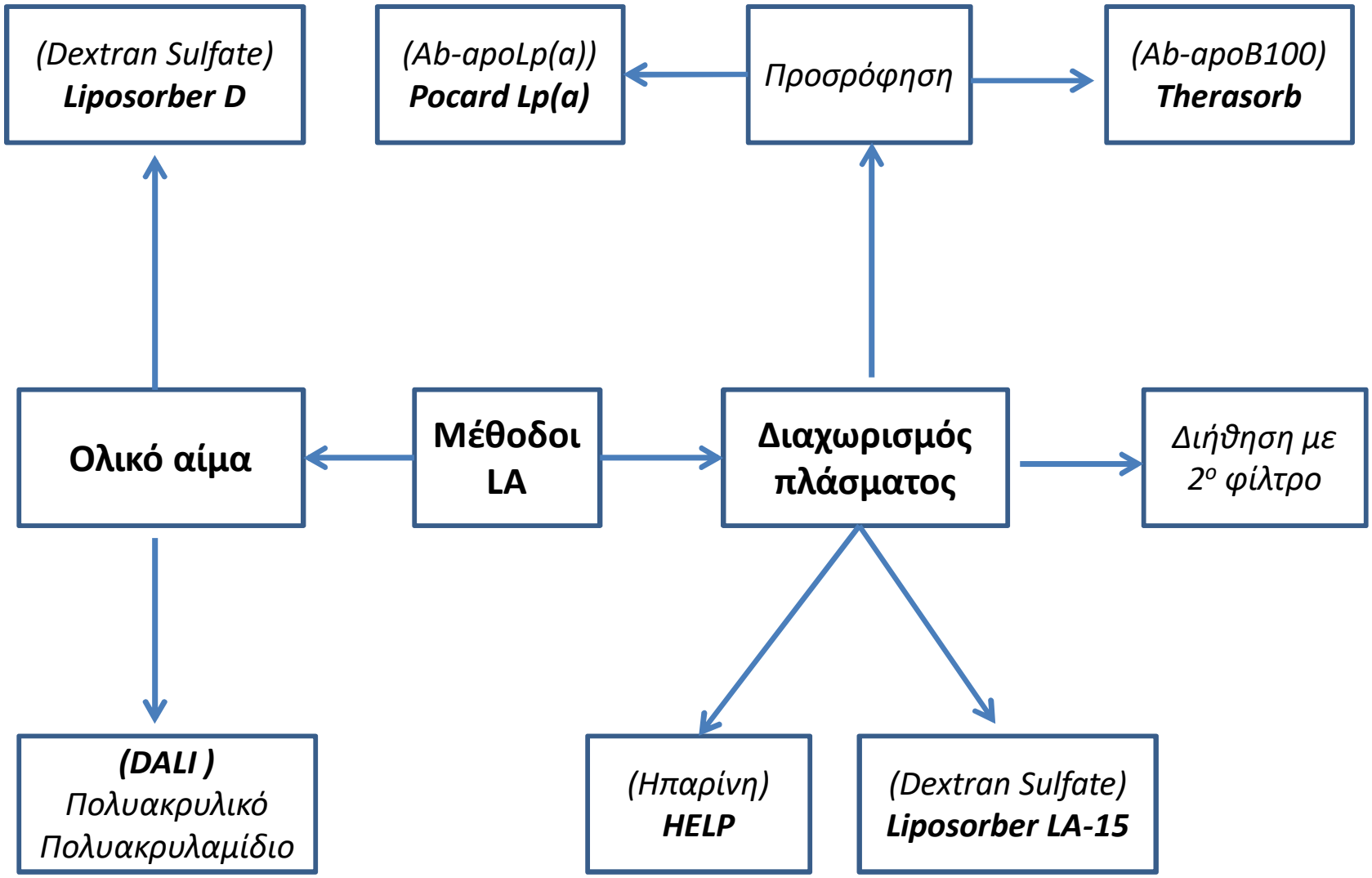


Structure of apoB-100 in LDL

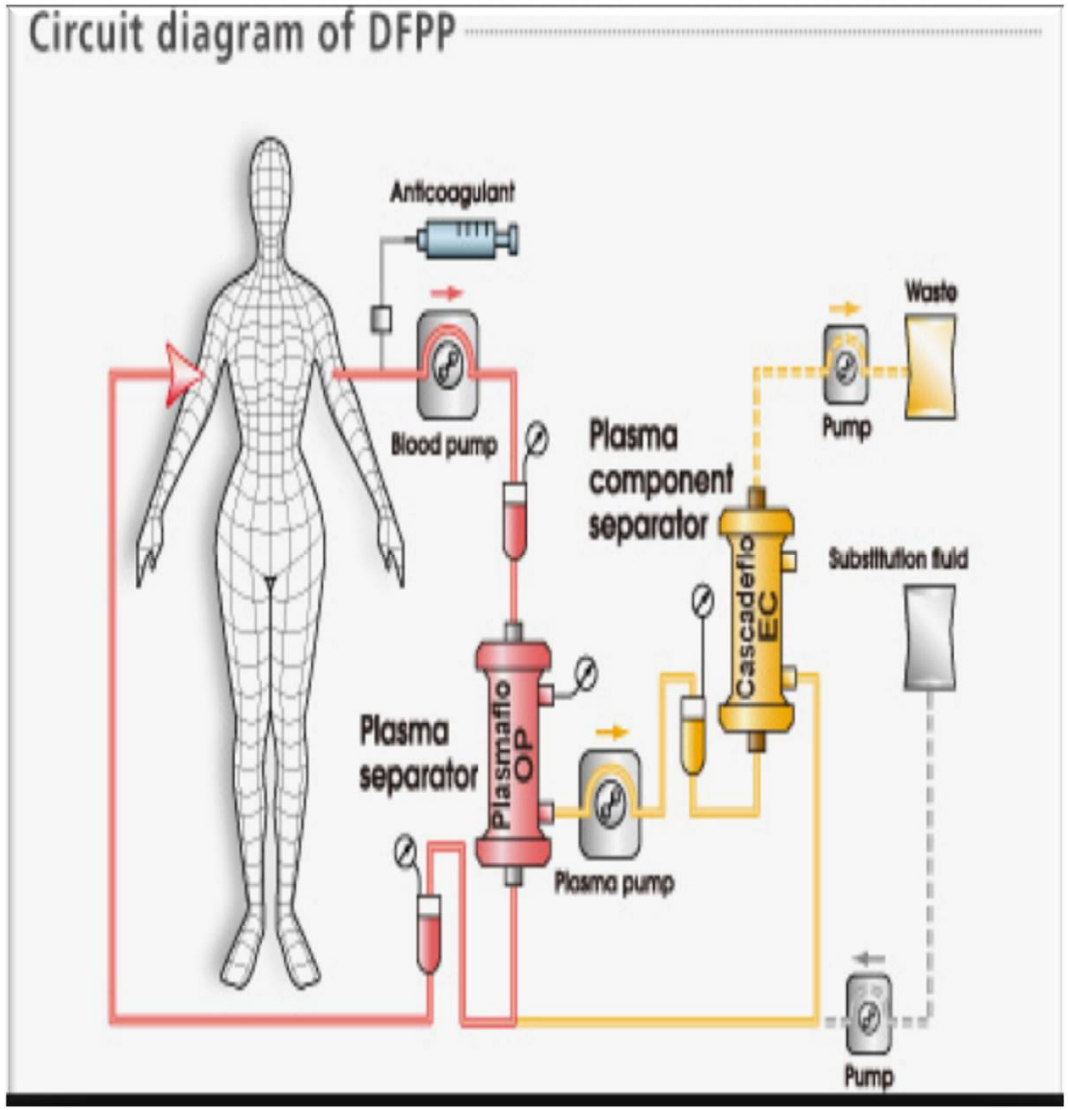
LDL-αφαίρεση
λιποπρωτεϊνική αφαίρεση

Year	Authors	Method	Advantage	Disadvantage
1967	De Gennes et al. [2]	Plasmapheresis	Quick and well-tolerated elimination of pathologic substances	Unselectivity, danger of infection, bleeding, and risks of human albumin
1975	Thompson et al. [3]	Plasmapheresis		
1980	Agishi et al. [4]	Cascade filtration	Semiselectivity	Danger of infection and low effectiveness
1981	Stoffel and Demant [5]	Immunoadsorption	Selectivity, effectiveness, regeneration, and reusability	Expensive technology
1983	Borberg et al. [6]	Immunoadsorption		
1983	Wieland and Seidel [7]	Heparin-induced LDL precipitation (HELP)	Selectivity and effectiveness	Expensive technology
1985	Nose et al. [8]	Thermofiltration	Selectivity and effectiveness	Outdated technology, behavior of macromolecules under heat unknown and not available
1985	Antwiller et al. [9]	Dextransulfate-induced LDL precipitation	Selectivity and effectiveness	Expensive technology and not available
1987	Mabuchi et al. [10]	Dextransulfate LDL adsorption (liposorber-LA 15)	Selectivity and effectiveness	Expensive technology
1993	Bosch et al. [11]	LDL hemoperfusion (DALI)	Selectivity, effectiveness, and simple technology	Unknown
2003	Otto et al. [12]	LDL hemoperfusion (liposorber D)	Selectivity, effectiveness, and simple technology	Unknown

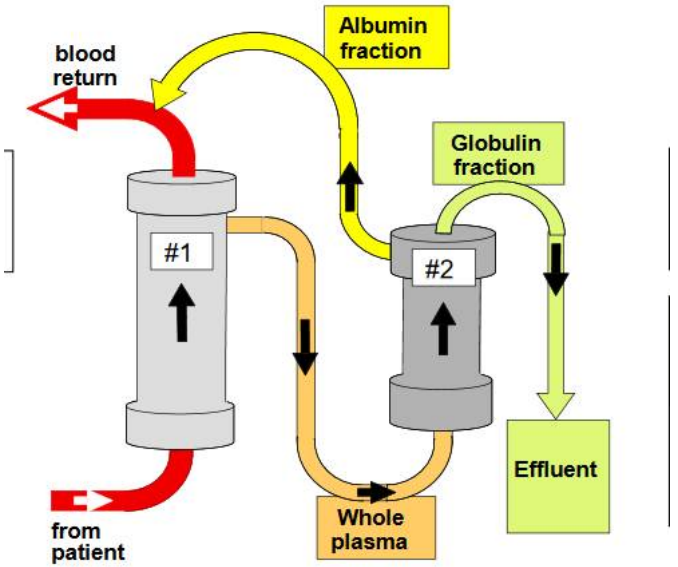
Bambauer et al, The Scientific World Journal 2012


(Dextran Sulfate)
Liposorber D
(Ab-apoLp(a))
Pocard Lp(a)
Προσρόφηση
(Ab-apoB100)
Therasorb
Ολικό αίμα
Μέθοδοι LA
Διαχωρισμός πλάσματος
Διήθηση με 2ο φίλτρο
(DALI)
Πολυακρυλικό Πολυακρυλαμίδιο
(Ηπαρίνη)
HELP
(Dextran Sulfate)
Liposorber LA-15

Cascade filtration

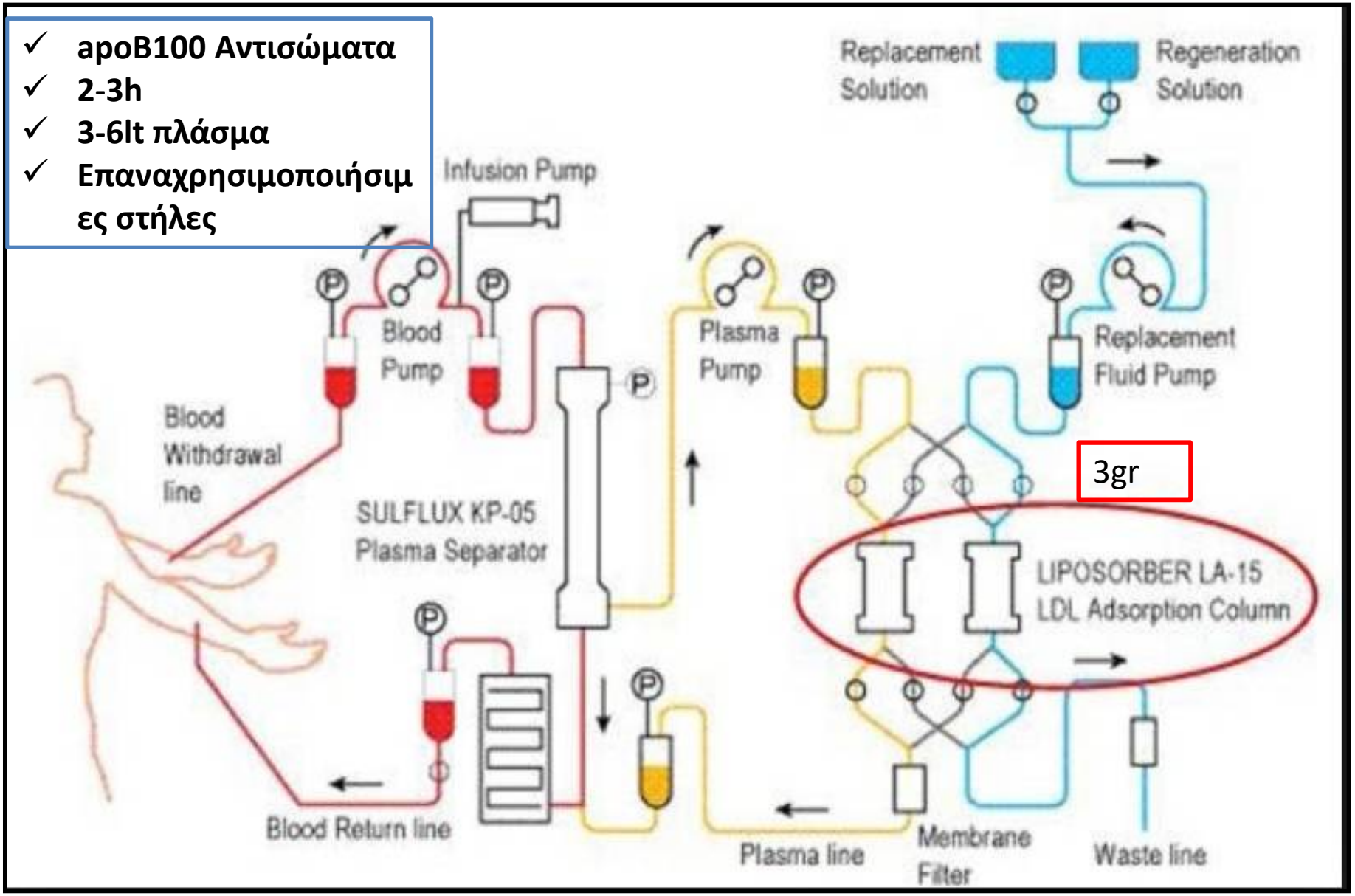


- ✓ 10^6d
- ✓ LDL – $2{,}3 \times 10^6$
- ✓ Απομακρύνονται ινωδογόνο, HDL, ανοσοσφαιρίνες



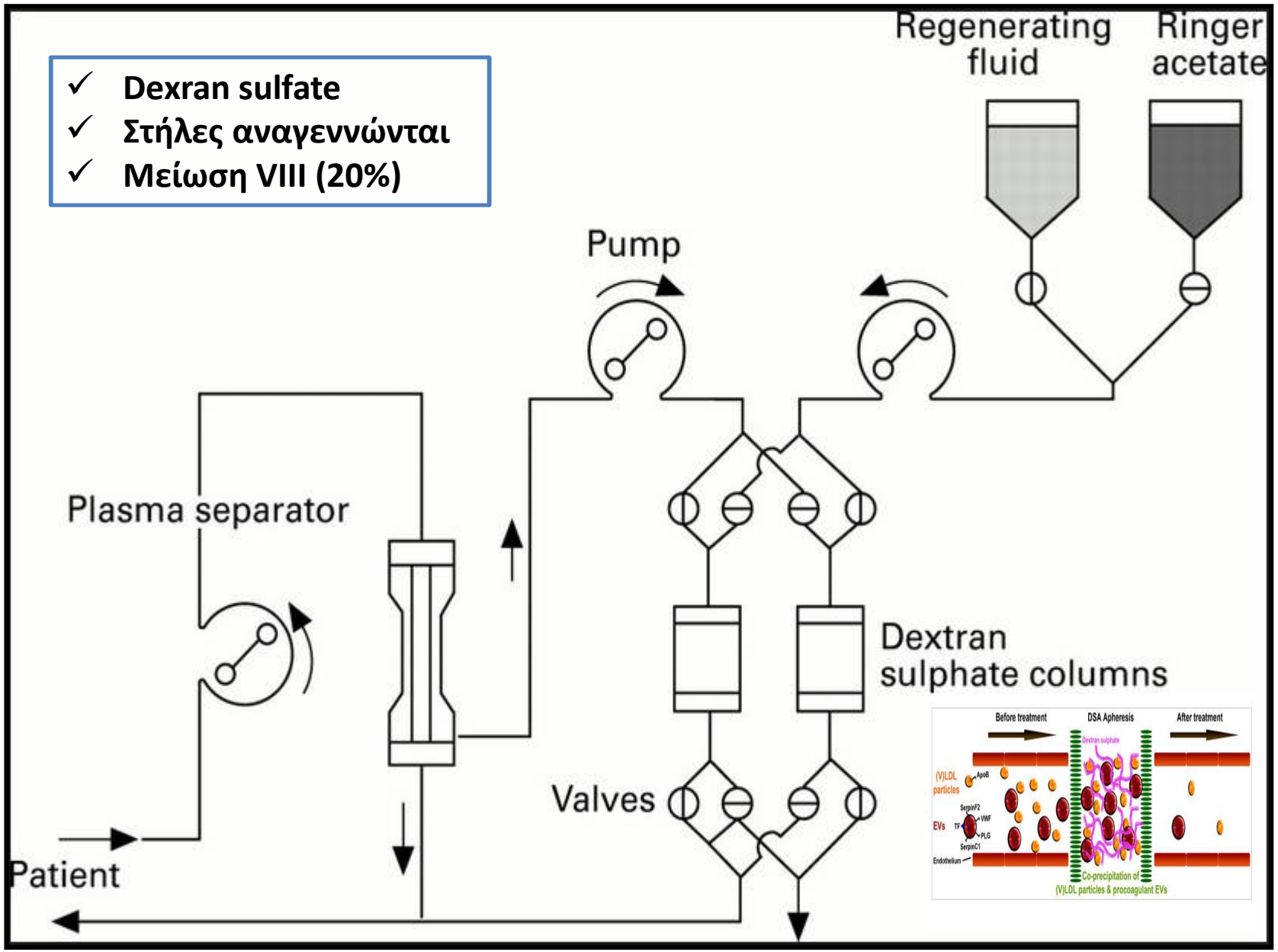
Προσρόφηση

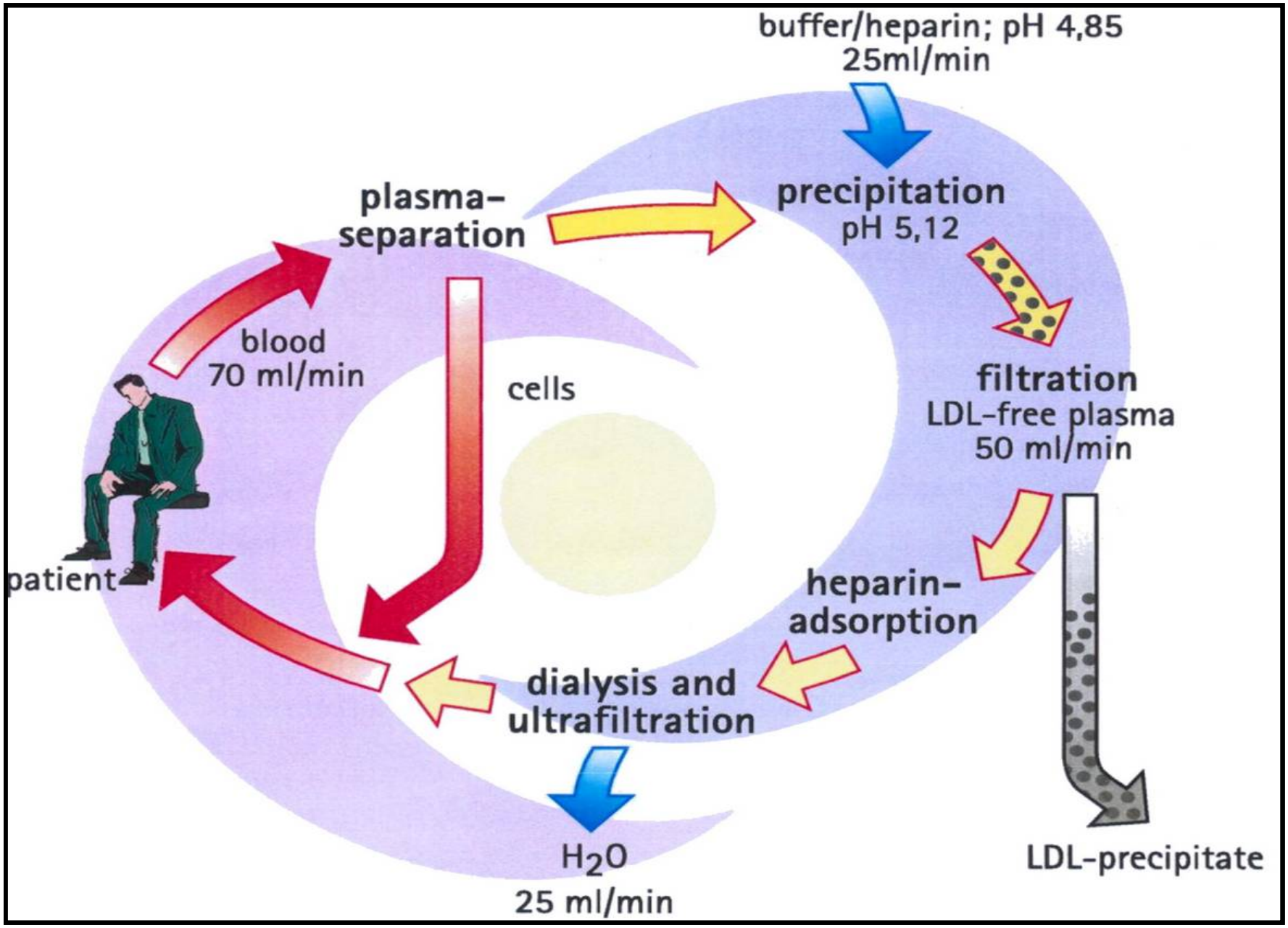
- ✓ **apoB100 Αντισώματα**
- ✓ **2-3h**
- ✓ **3-6lt πλάσμα**
- ✓ **Επαναχρησιμοποιήσιμες στήλες**



Προσρόφηση

- ✓ Dexran sulfate
- ✓ Στήλες αναγεννώνται
- ✓ Μείωση VIII (20%)




buffer/heparin; pH 4,85
25ml/min
plasma-
separation
precipitation
pH 5,12
blood
70 ml/min
cells
filtration
LDL-free plasma
50 ml/min
patient
heparin-
adsorption
dialysis and
ultrafiltration
H_2O
25 ml/min
LDL-precipitate

Καθίζηση

- ✓ **Απομάκρυνση C3-C4, ινωδογόνου και πλασμινογόνου**
- ✓ **3 L**

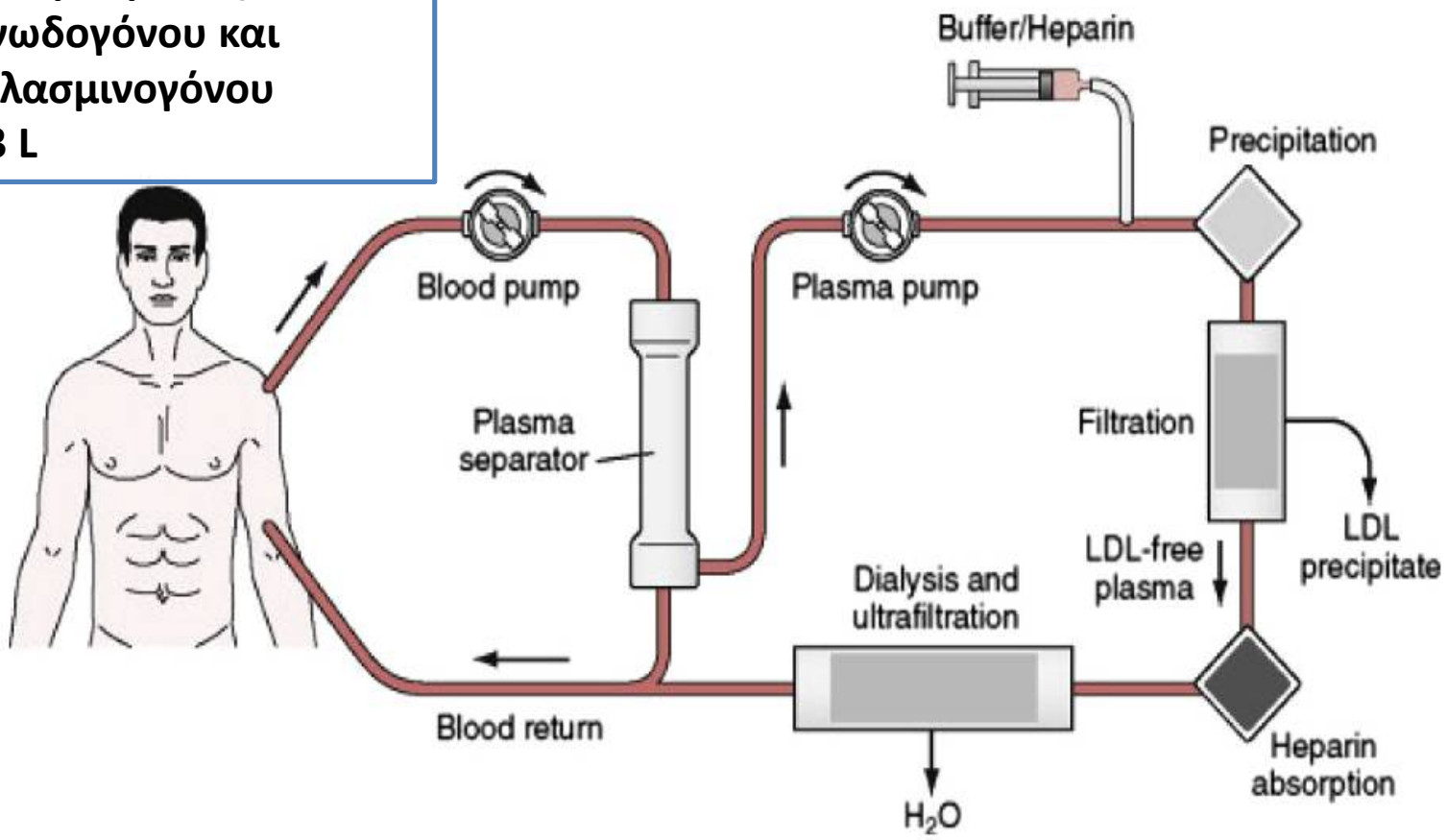


Fig. 1. HELP (Futura). (From Moriarty PM. Low-density lipoprotein apheresis. In: Ballantyne CM, editor. Clinical lipidology: a companion to Braunwald's heart disease. Philadelphia: Saunders Elsevier; 2009. p. 365; with permission.)

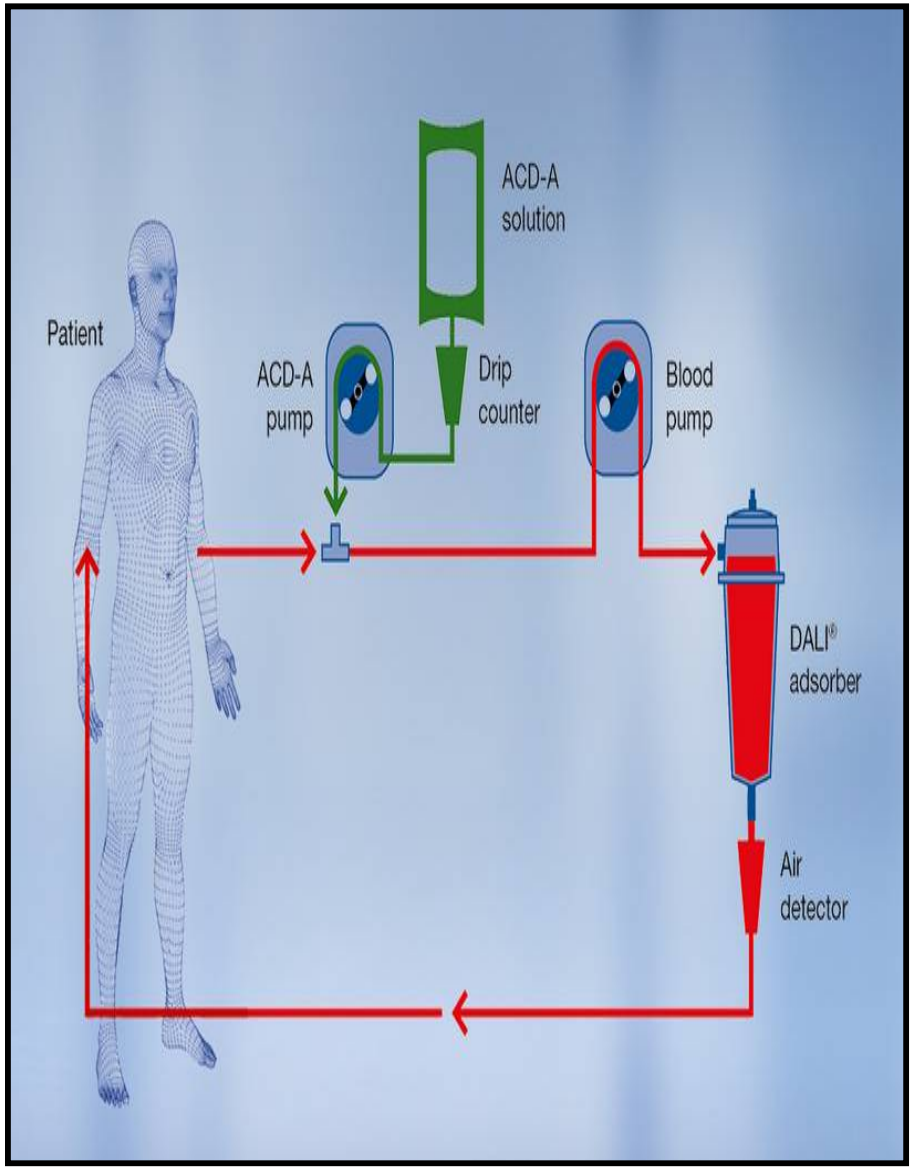
DALI (ολικό αίμα)

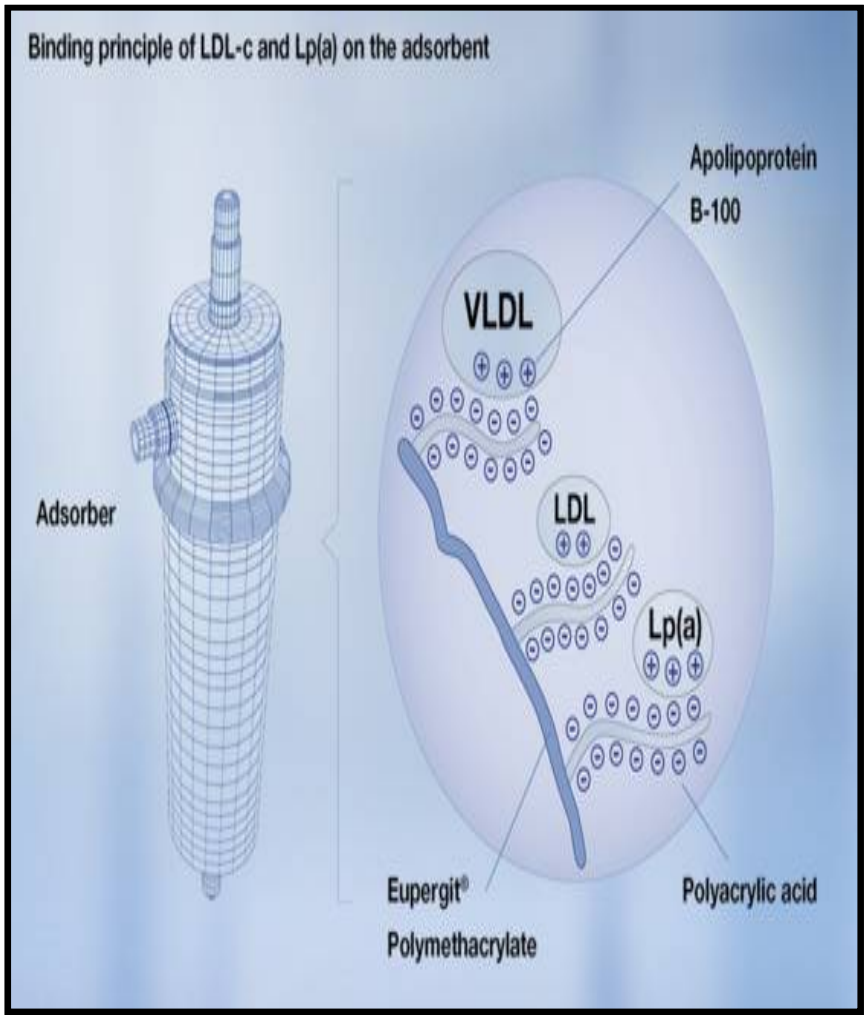
Reductions up to:

80 % LDL-ch

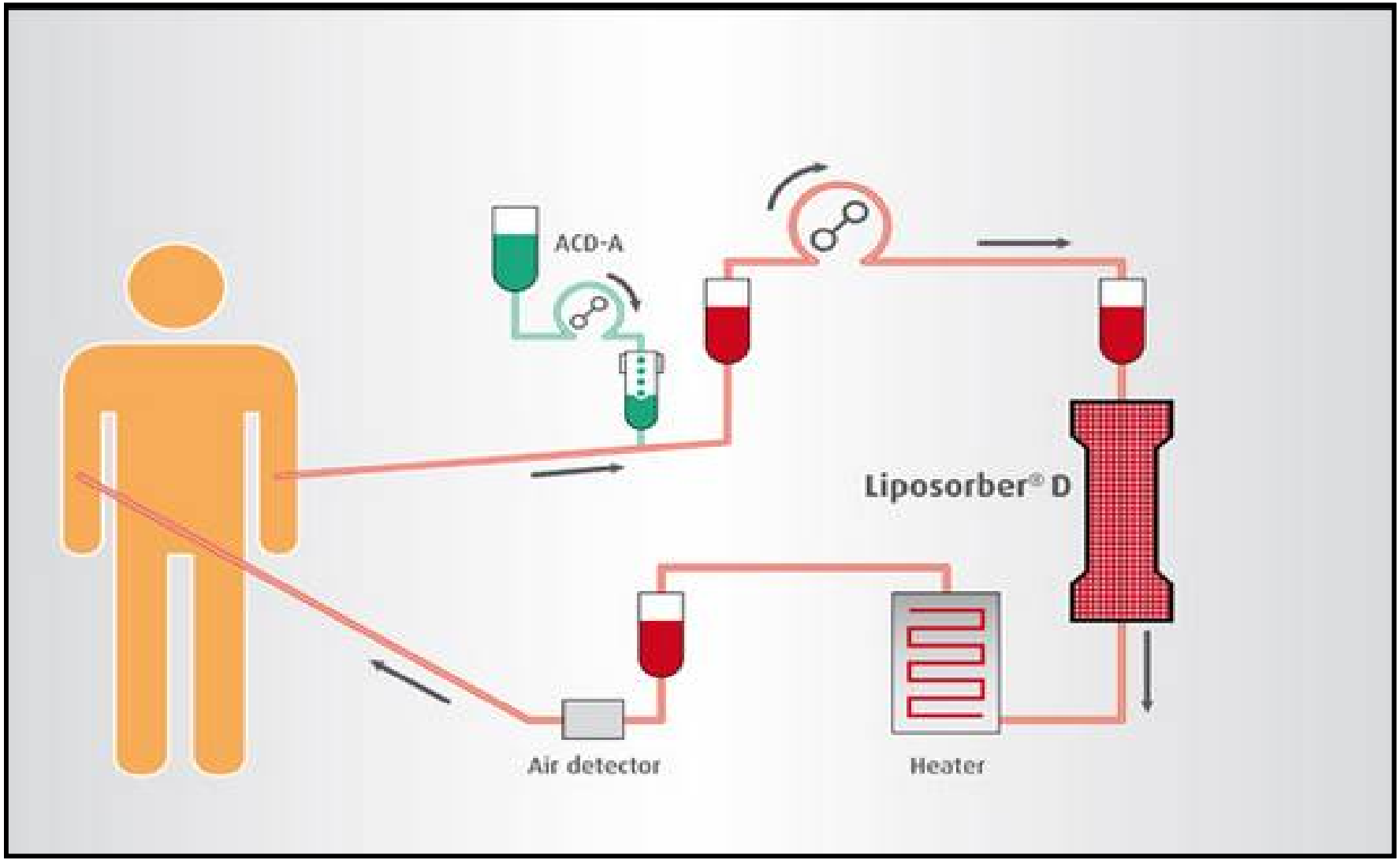
75 % lipoprotein (a)

50 % trigycerides

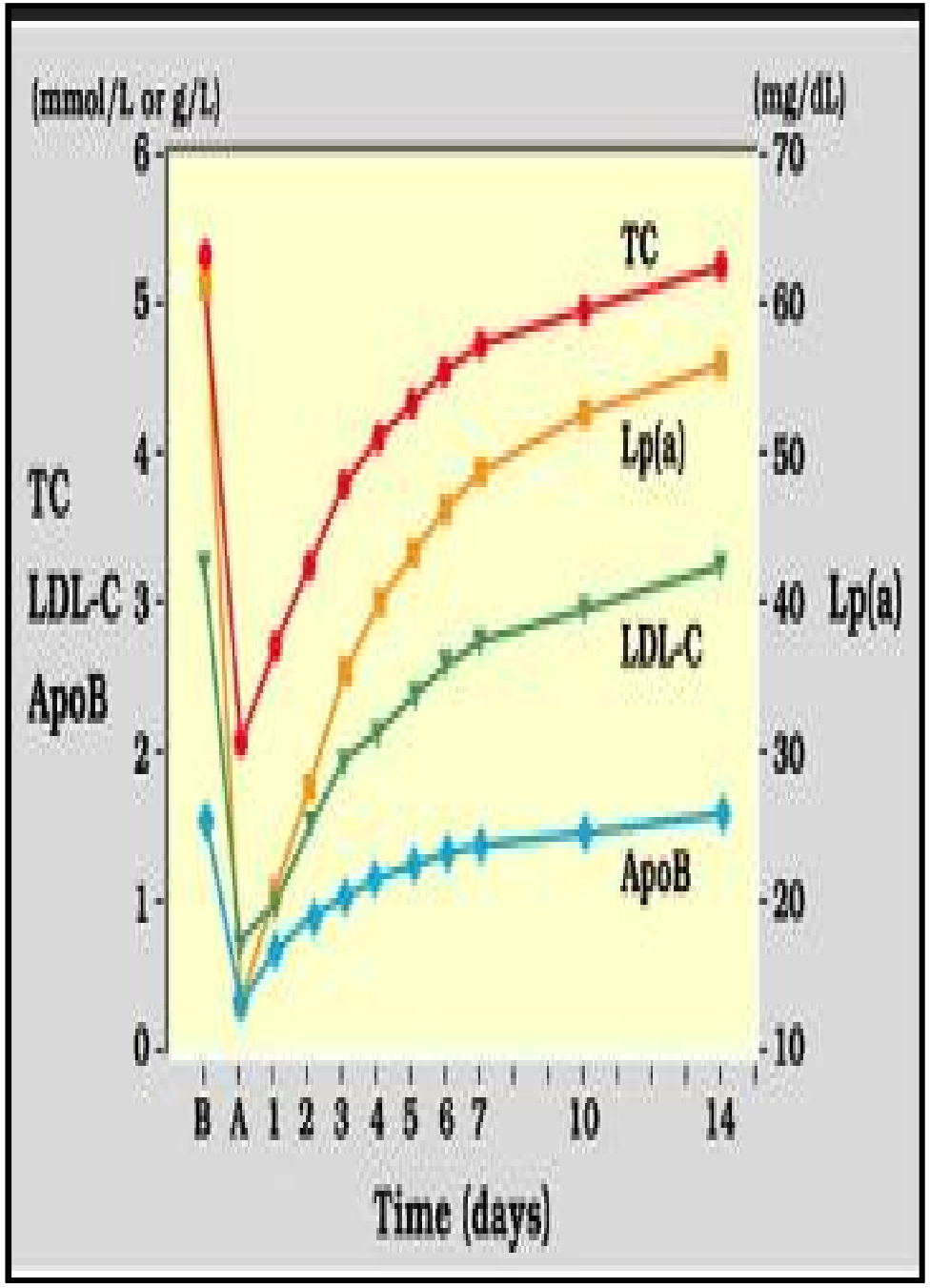


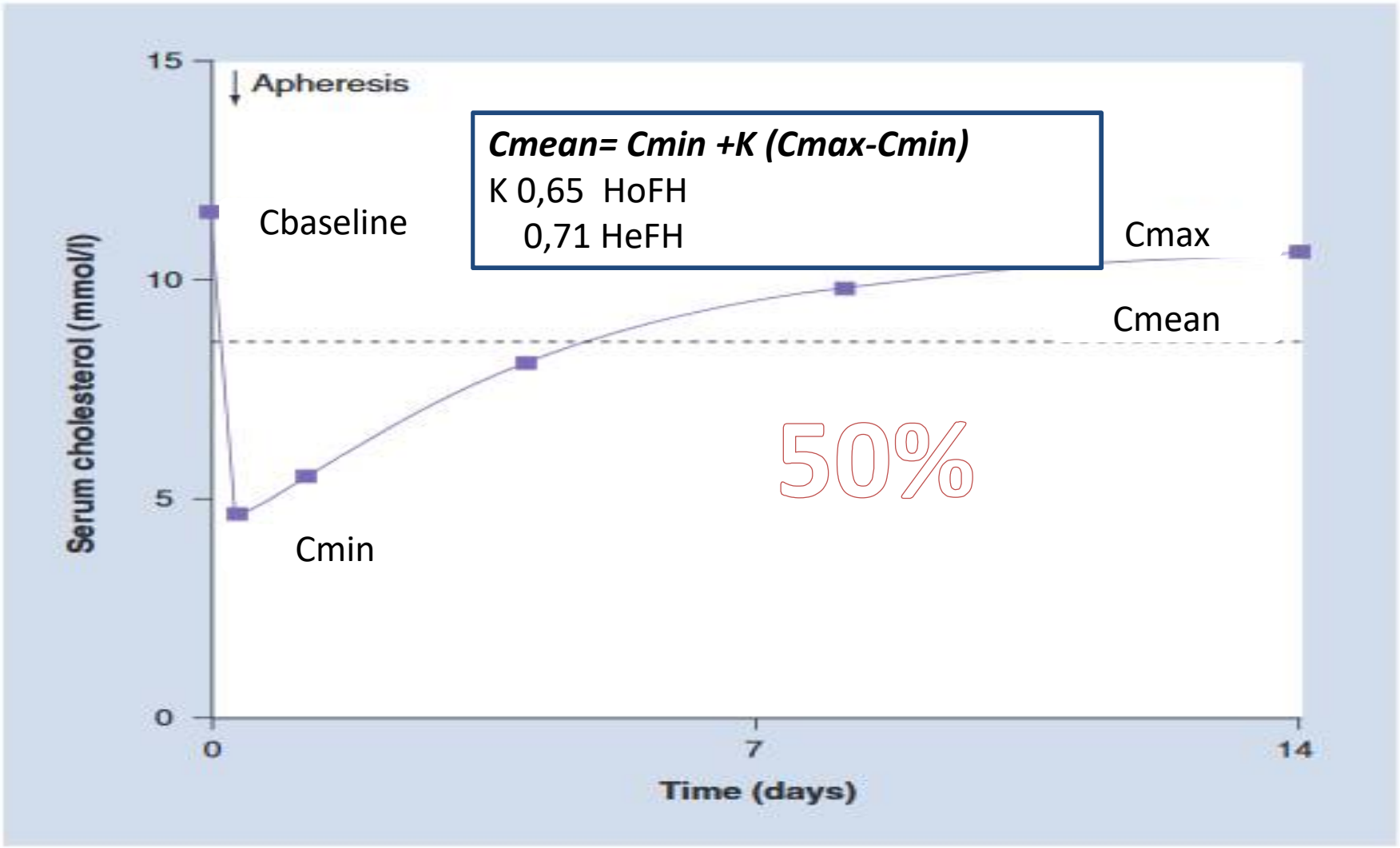


Liposorber D (ολικό αίμα)



- ✓ **Επεμβατικές μέθοδοι**
- ✓ **2 φλέβες… αρτηριοφλεβική αναστόμωση**
- ✓ **1,5-4 ώρες**
- ✓ **Αντιπηξία**
- ✓ **Όγκος πλάσματος αίματος**





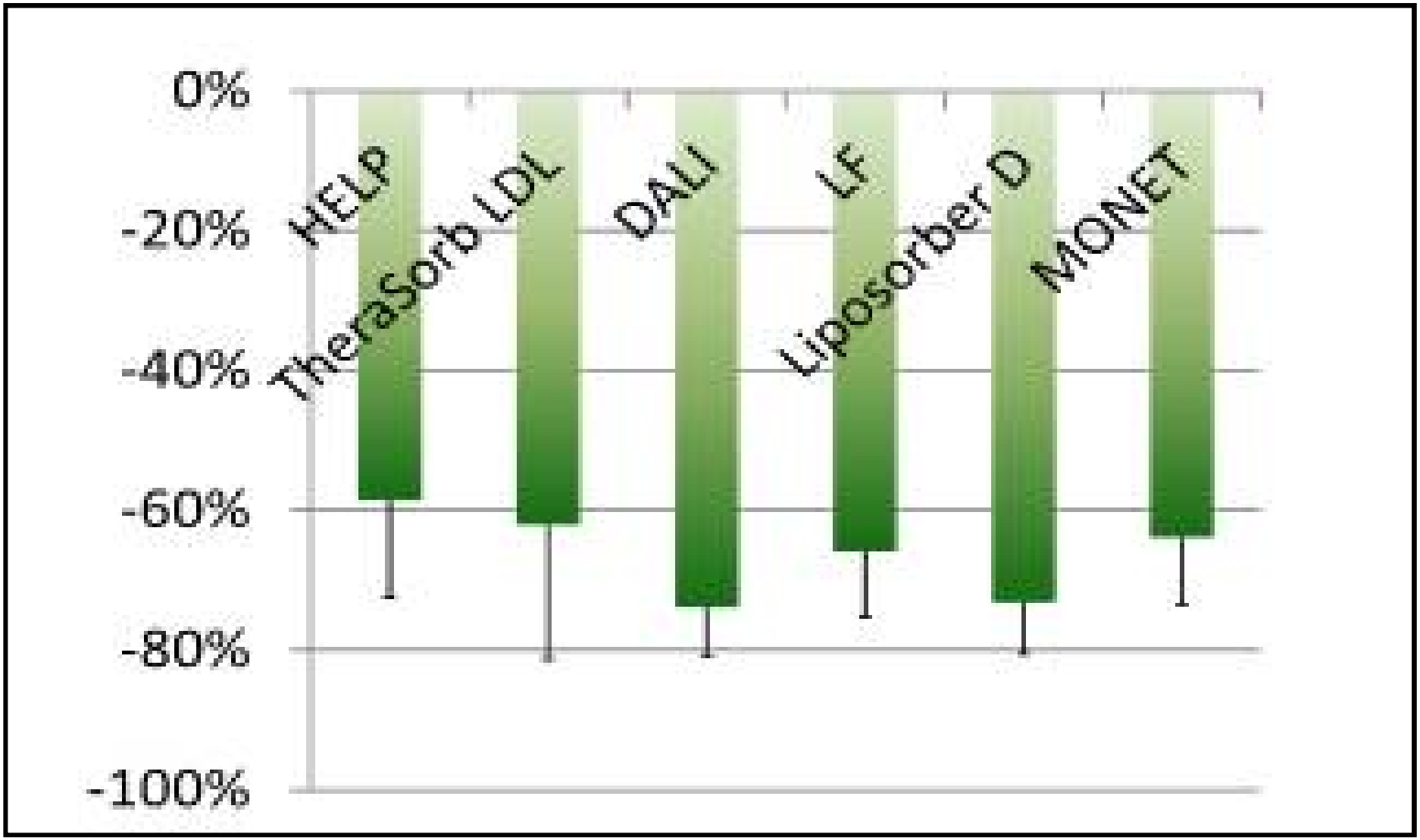
Cmean= Cmin +K (Cmax-Cmin)

K 0,65 HoFH

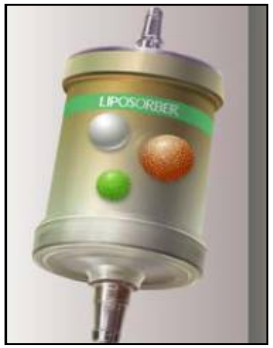
0,71 HeFH

Figure 1. Parameters of the rebound in serum cholesterol during the 2 weeks following an apheresis procedure. C_{mean} is the best index of the average lipoprotein level between consecutive procedures.
$C_{baseline}$: Baseline value; C_{max}: Maximum value; C_{mean}: Interval mean; C_{min}: Minimum value.

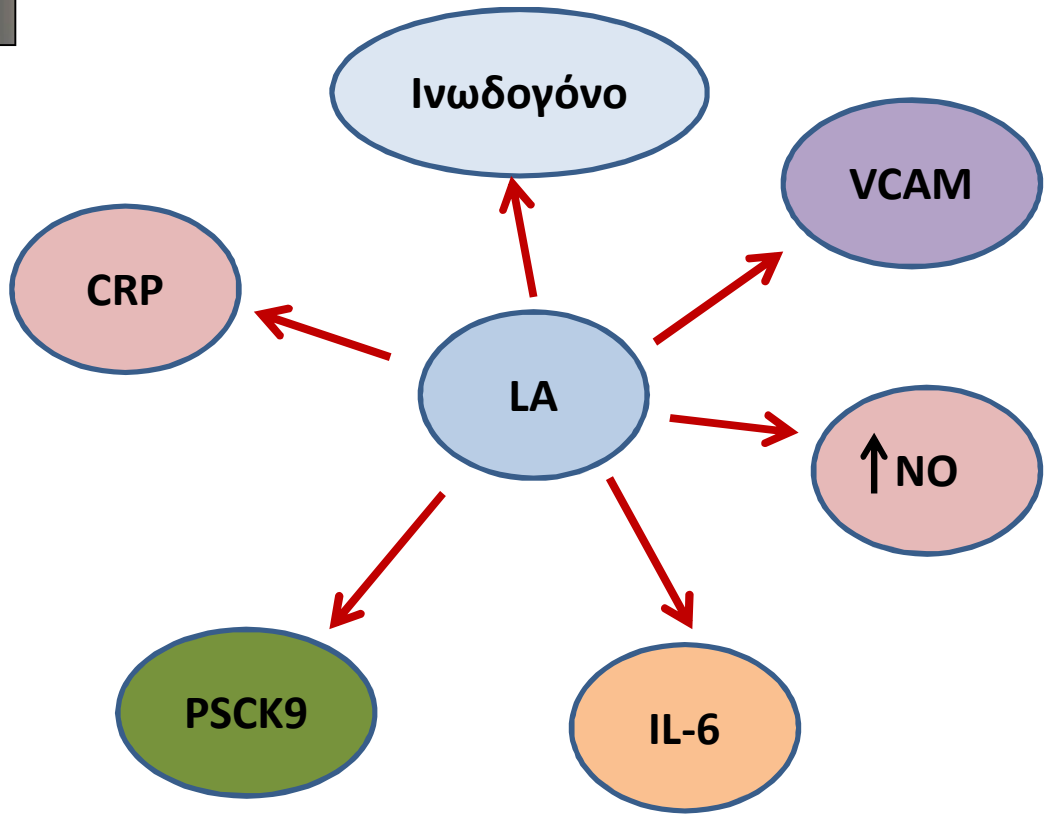
Μείωση LDL



Julius et al, Therapeutic Apheresis and Dialysis 2013



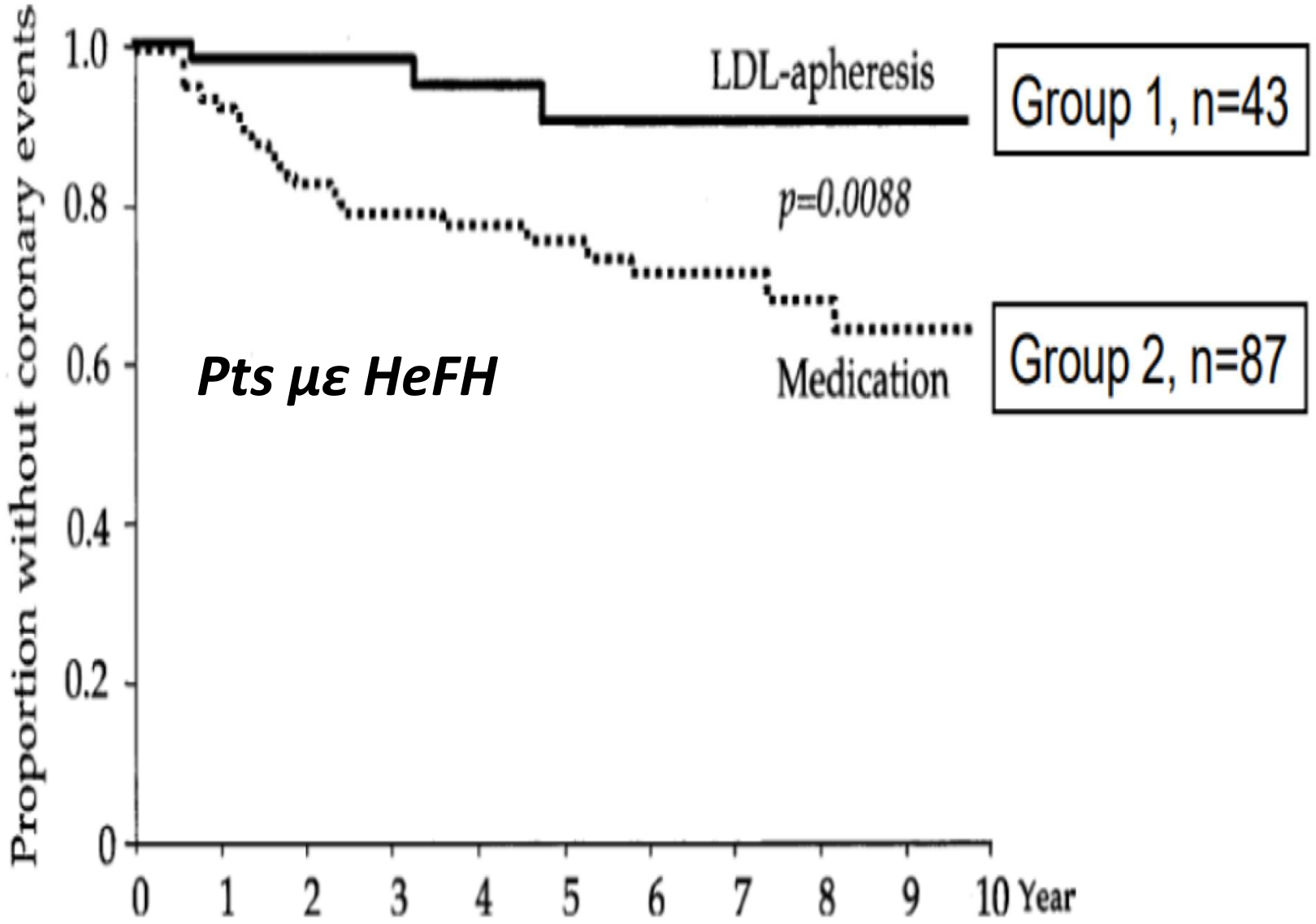
Πλειοτροπικές δράσεις της LA



- ✓ **Βελτίωση της αιματικής ροής**
- ✓ **Θετική επίδραση στο ενδοθήλιο**

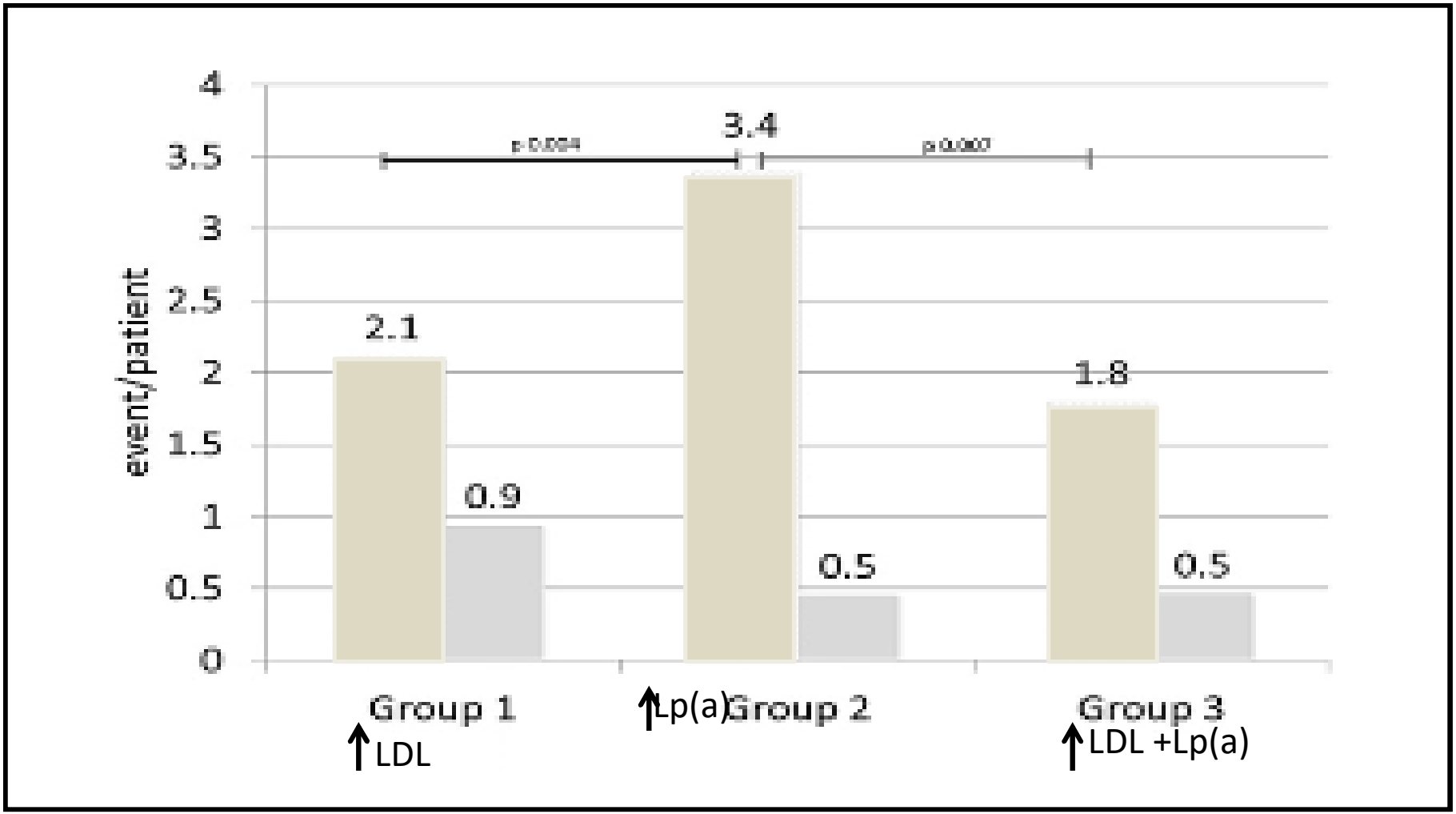
Βελτίωση κλινικών εκδηλώσεων αθηρωμάτωσης;

Stefanutti et al, J Clinical Lipidology 2018



Mabuchi et al, Atherosclerosis 1987

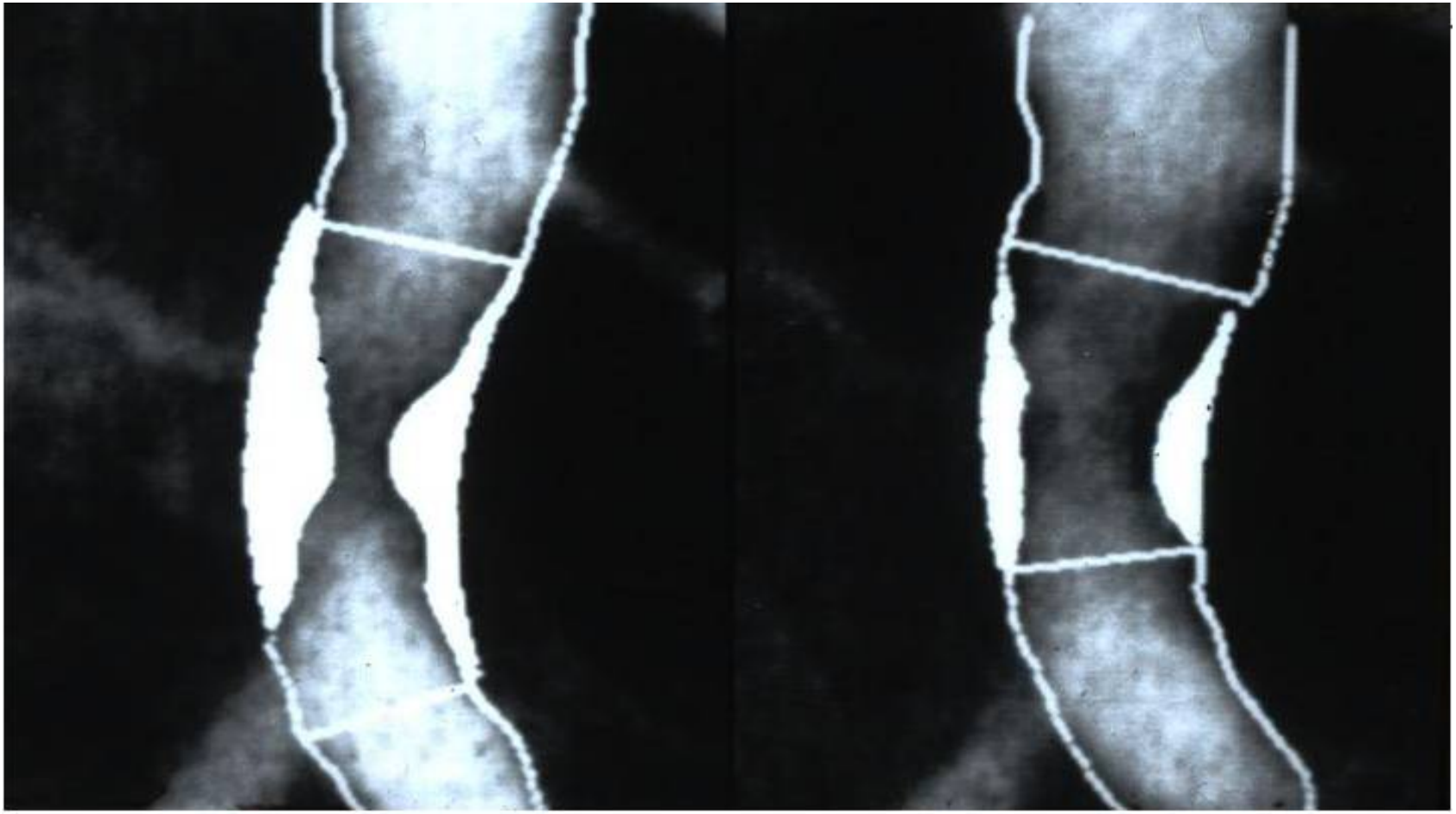
Differences in the atherogenic risk of patients treated by lipoprotein apheresis according to their lipid pattern



Von Dryander et al, Atheroscl Suppl 2013

Αγγειογραφικά δεδομένα

Μελέτη	Ασθενείς	Μέθοδος	Αποτελέσματα
L-CAPS	25pts HeFH 11 pts	LA+ Simvastatin Simvastatin	Εξέλιξη: 8%vs 64% Σταθεροποίηση: 76% vs 36% Υποστροφή: 16% vs 0
LARS	37pts 7HoFH 25HeFH 5 HCH	Dextran Sulfate LIPOSORBER-LA15	Εξέλιξη :14% Σταθεροποίηση: 38% Υποστροφή: 38%
HELP-Study Group	39/51	HELP	Διατήρηση βλαβών : 57,8% Εξέλιξη βλαβών : 15,5% Υποστροφή : 26,7%
LAARS	42 2 ομάδες	LA Φαρμακευτική αγωγή	Σταθεροποίηση των βλαβών και στις δύο ομάδες

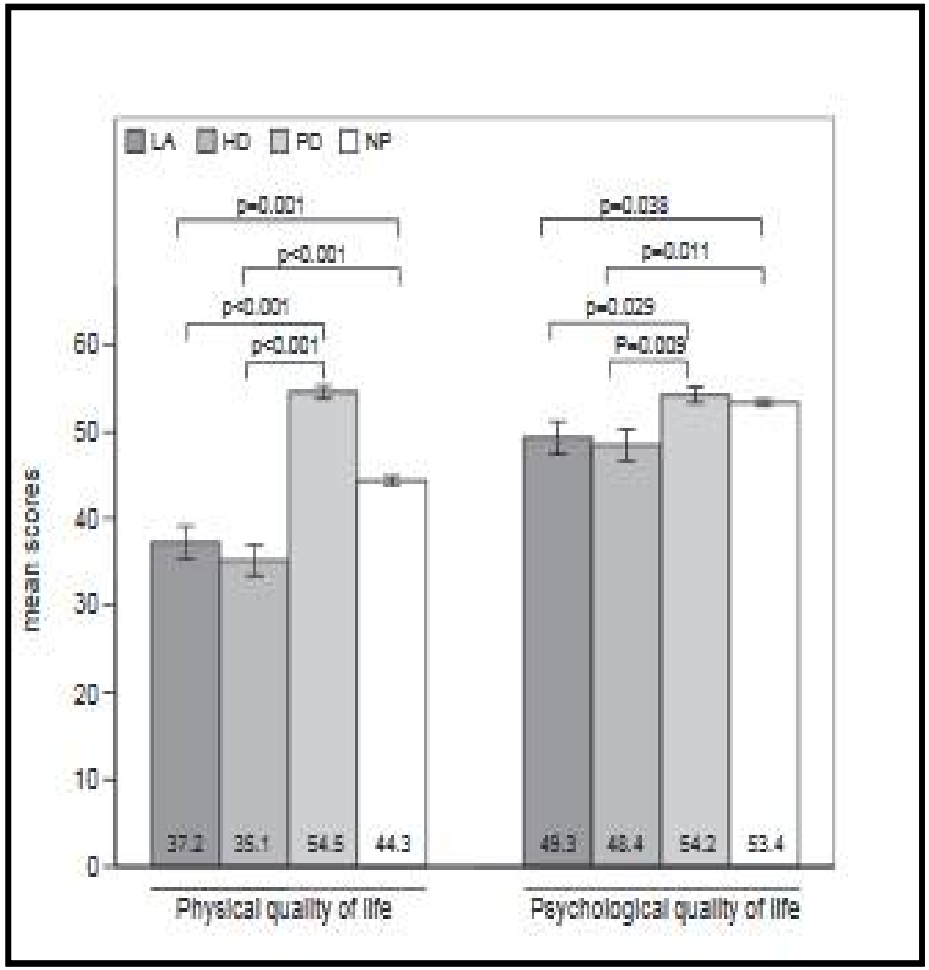


Βελτίωση αιματικής ροή, μείωση του επιπέδου ασβεστοποίησης, βελτίωση περιφερικής αγγειοπάθειας, υποστροφή ξανθωμάτων και των στενώσεων των καρωτίδων και καθυστέρηση της εξέλιξης της αορτικής στένωσης

LA

Αντενδείξεις διενέργειας LA

- ✓ Αδυναμία αγγειακής προσπέλασης
- ✓ Σοβαρή καρδιακή ανεπάρκεια
- ✓ Ανθεκτική υπέρταση
- ✓ Μη συμμόρφωση
- ✓ Μικρό προσδόκιμο επιβίωσης
- ✓ Κακοήθεια
- ✓ Ψυχιατρική διαταραχή



Stasiewski et al, Atheroscl Suppl 2015

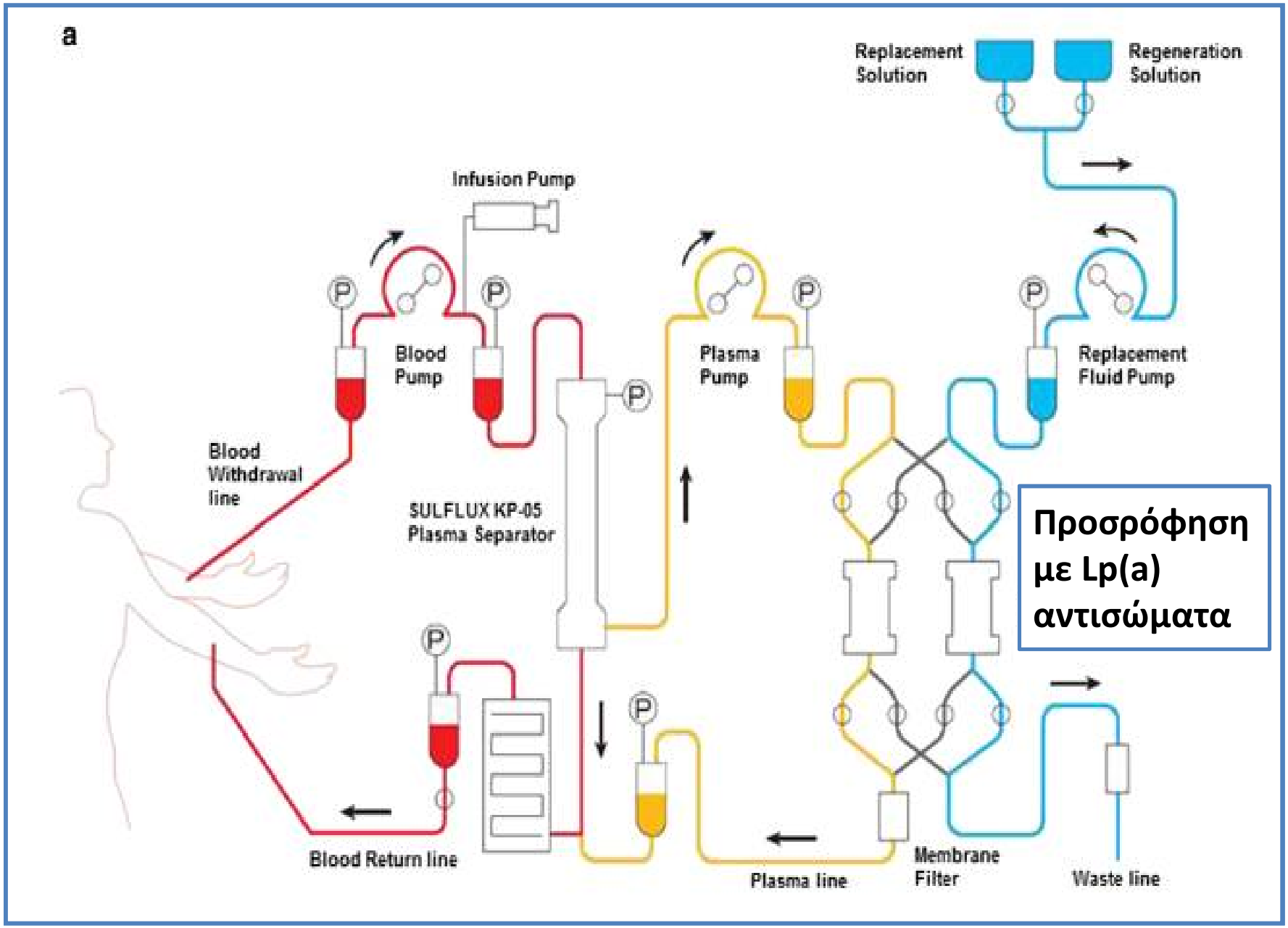
FDA	Heart UK	Γερμανία	Ιταλία
✓HoFH με LDL> 500 mg/dl ✓HeFH με LDL≥300 mg/dl *χωρίς ιστορικό καρδιαγγειακής νόσου* ✓HeFH με LDL ≥200 mg/dl *με ιστορικό καρδιαγγειακής νόσου*	✓HoFH με αδυναμία μείωσης της LDL >50% με συμβατική αγωγή ή CHOL >350 ✓HeFH ή σοβαρή HCH με προοδευτική επιδείνωση ΣΝ και LDL≥ 194 mg/dl ή μείωση <40% με αγωγή	✓HoFH ✓Σοβαρή HCH χωρίς βελτίωση με μέγιστη αγωγή για ένα χρόνο	✓HoFH με LDL≥300 mg/dl ✓HeFH με LDL ≥ 300 mg/dl ✓HeFH με LDL ≥200 mg/dl και στεφανιαία νόσο ✓HCH με δύο από τα παρακάτω: 1. Μη ανταπόκριση στη θεραπεία 2. Νέα επειδόσιο αγγειοπλαστικής 3. Μεταμόσχευση καρδιάς 4. Σοβαρή αθηροσκλήρυνση

+ Lipoprotein(a) + Heart disease

1 in 14 heart attacks and 1 in 7 cases of aortic valve disease are due to Lipoprotein(a) cholesterol.

Μελέτες για Lp(a)- αφαίρεση

Μελέτη	Pro(a)LiFe, Leebmann et al. 2013	Jaeger et al. 2009	Rosada et al. 2014
Περίοδος μελέτης	LA 2008–2010	LA > 3m	LA μεταξύ 1995–2010
Κριτήρια	Lp(a) > 60mg/dl και εξέλιξη καρδιαγγειακής βλάβης παρά τον έλεγχο LDL	Lp(a) > 60mg/dl και εξέλιξη καρδιαγγειακής βλάβης παρά τον έλεγχο LDL	Lp(a) > 60mg/dl με ιστορικό CVE και τουλάχιστον ένα ακόμα επεισόδιο παρά τον έλεγχο LDL
Μείωση CVE	Από 0,42 επεισόδια ανά ασθενή / έτος σε 0,09	Από 0,45 επεισόδια ανά ασθενή / έτος σε 0,10	Από 0,35 επεισόδια ανά ασθενή / έτος σε 0,08

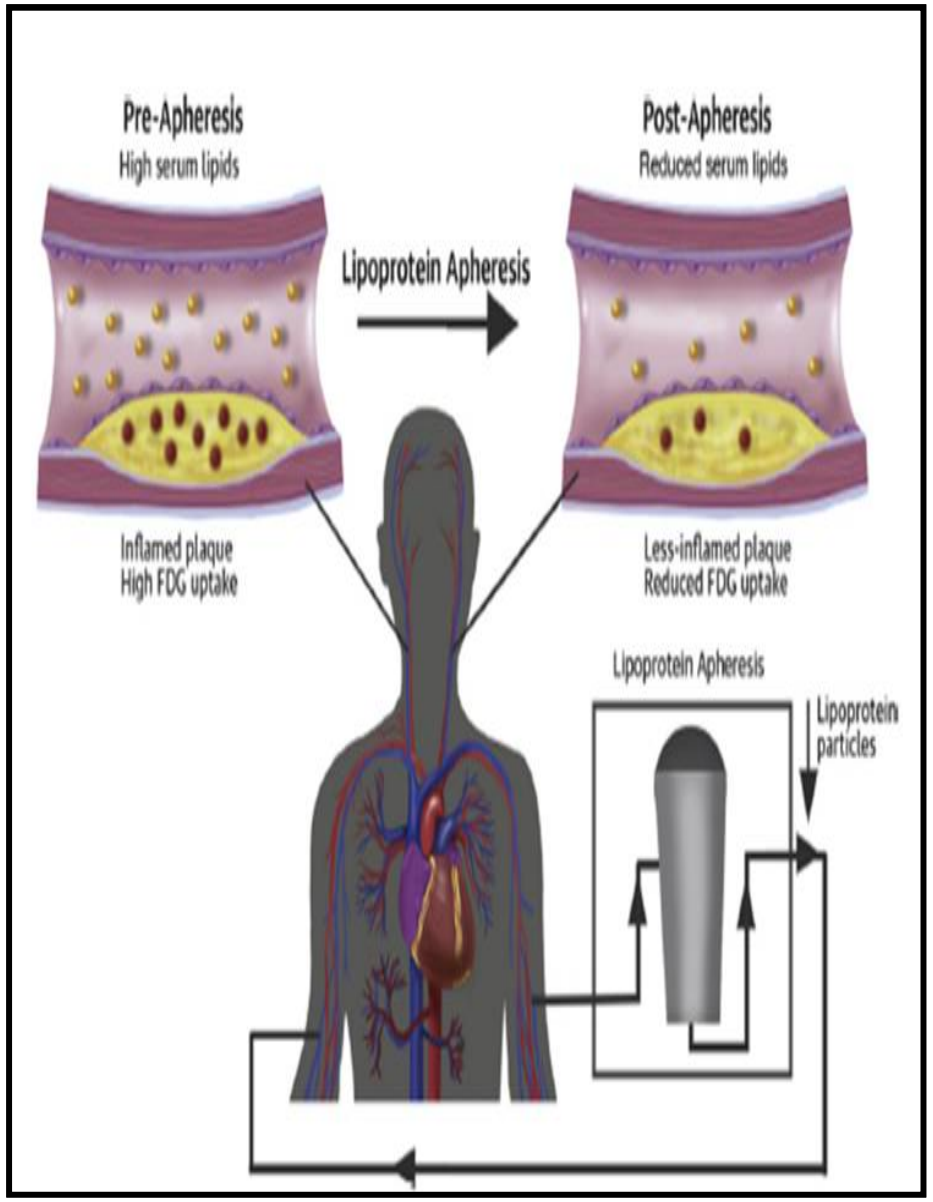

a
Replacement Solution
Regeneration Solution
Infusion Pump
Blood Pump
Plasma Pump
Replacement Fluid Pump
Blood Withdrawal line
SULFLUX KP-05 Plasma Separator
Blood Return line
Plasma line
Membrane Filter
Waste line
Προσρόφηση με Lp(a) αντισώματα

Γερμανία	**12/10^6**
Σουηδία	**3/10^6**
Ιταλία/ Γαλλία	**2/10^6**
Αγγλία	**0,6/10^6**
ΗΠΑ	**1,3/10^6**

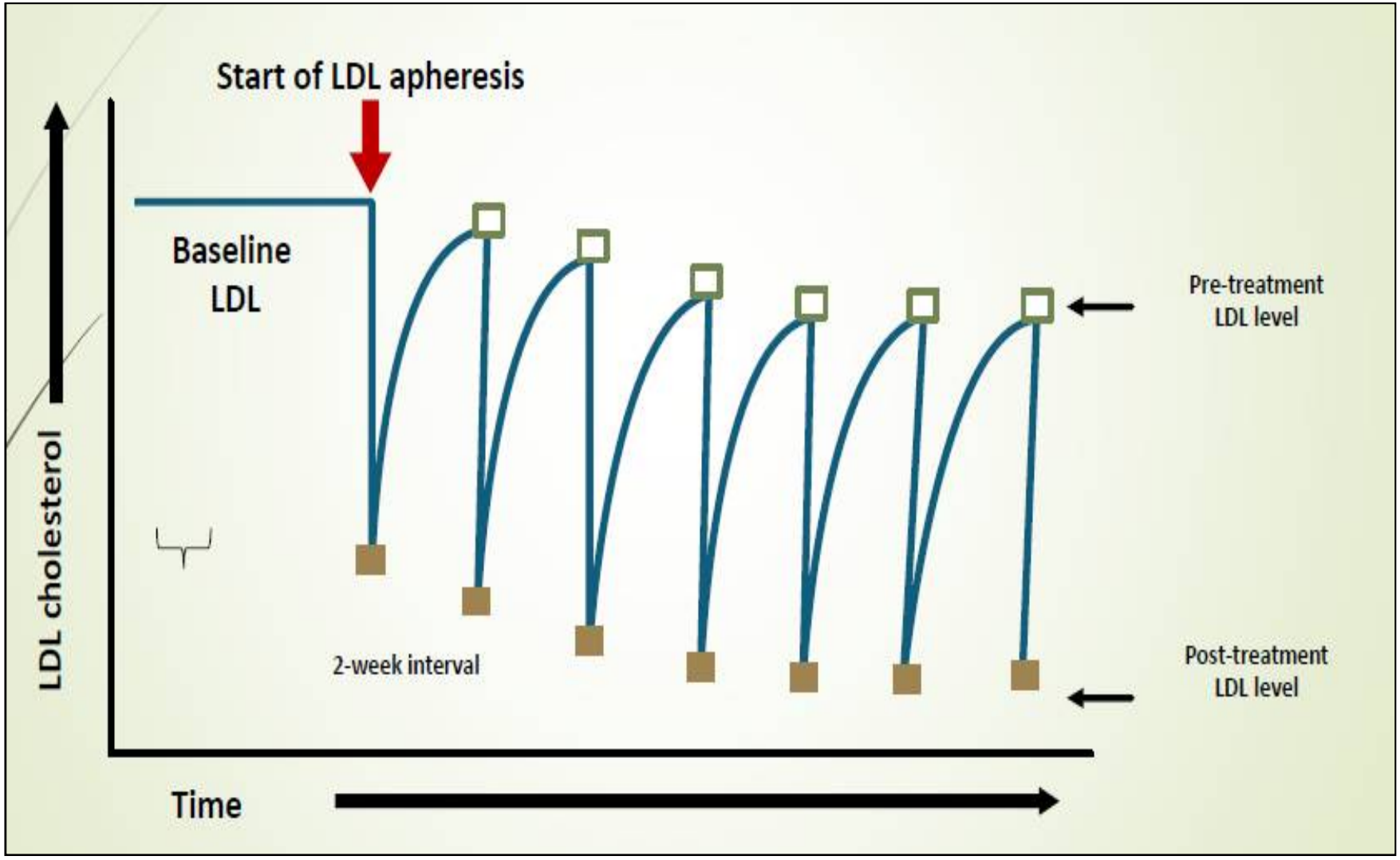
Table 3 LA centers, physicians, and patients in Germany in 2013–2015

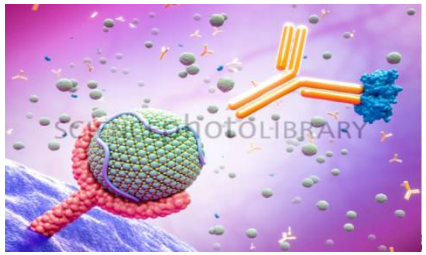
	2013[a]	2014[a]	2015[b]
Centers	218[a]	325[a]	378[b]
Physicians	962[a]	1,096[a]	Not known
Patients	2,161[a]	2,546[a]	3,197[b]

Notes: [a]Data from Quality report of the National Association of Statutory Health Insurance Physicians (KBV).[19,49] [b]Preliminary data (personal communication, 2015).
Abbreviation: LA, lipoprotein apheresis.

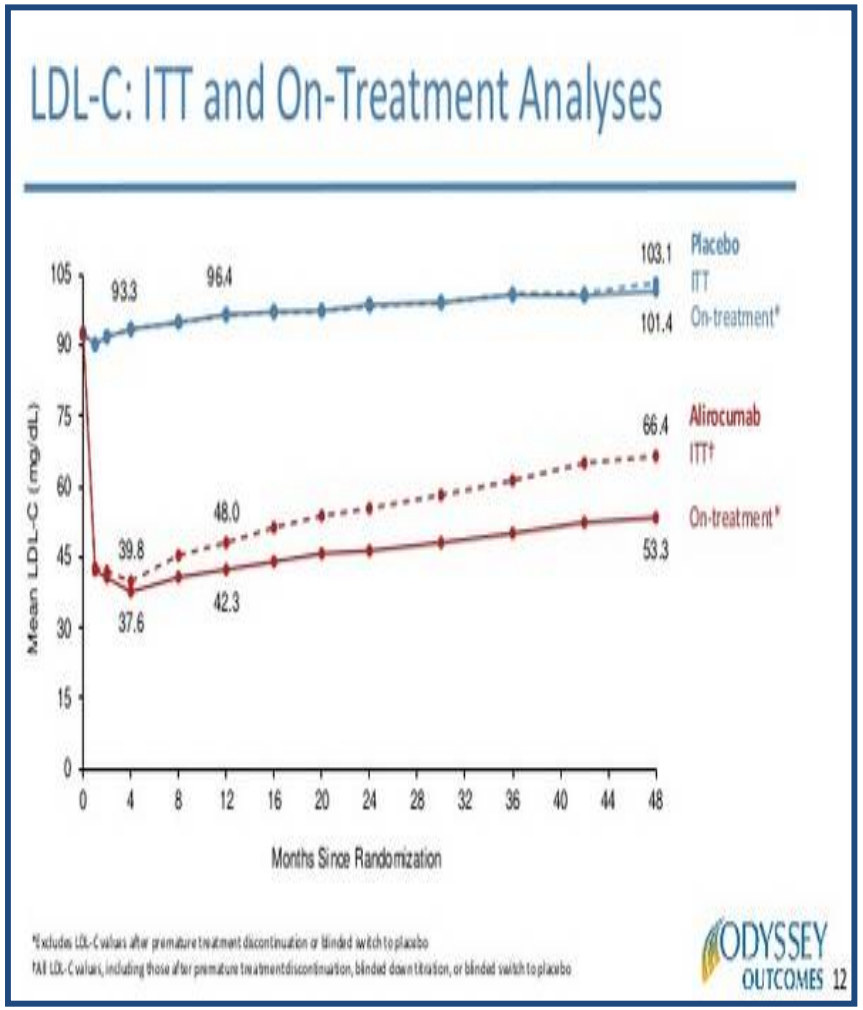


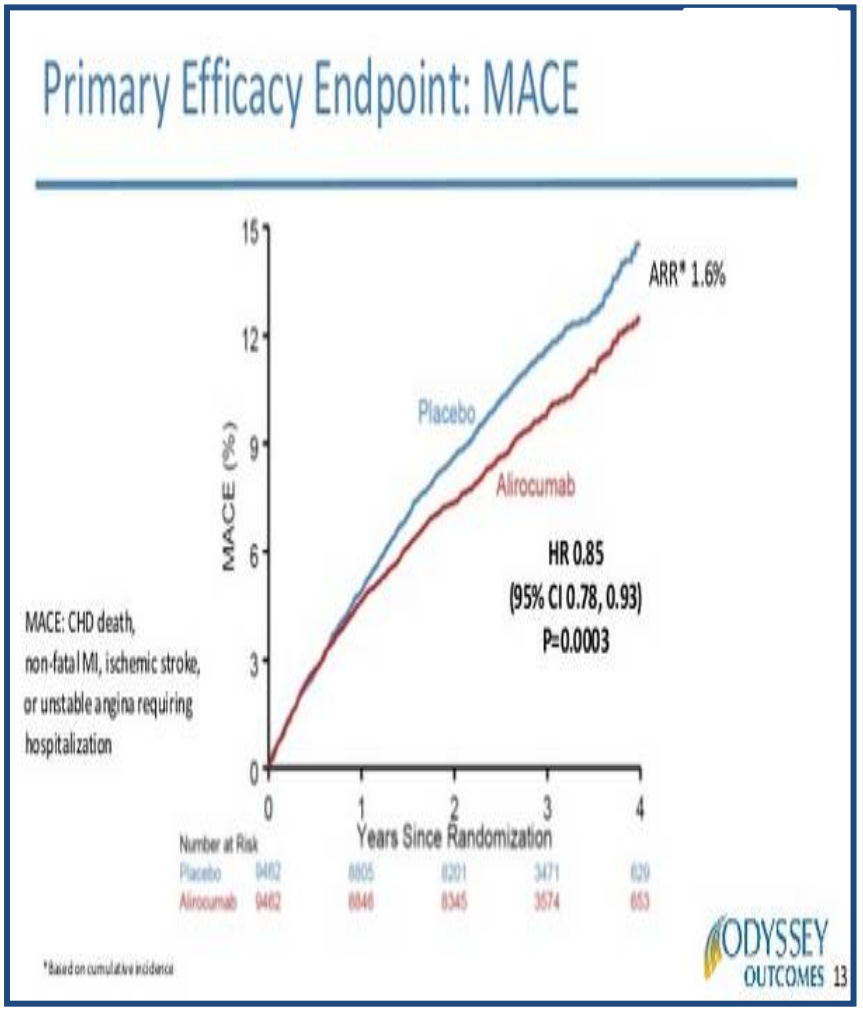
Κόστος

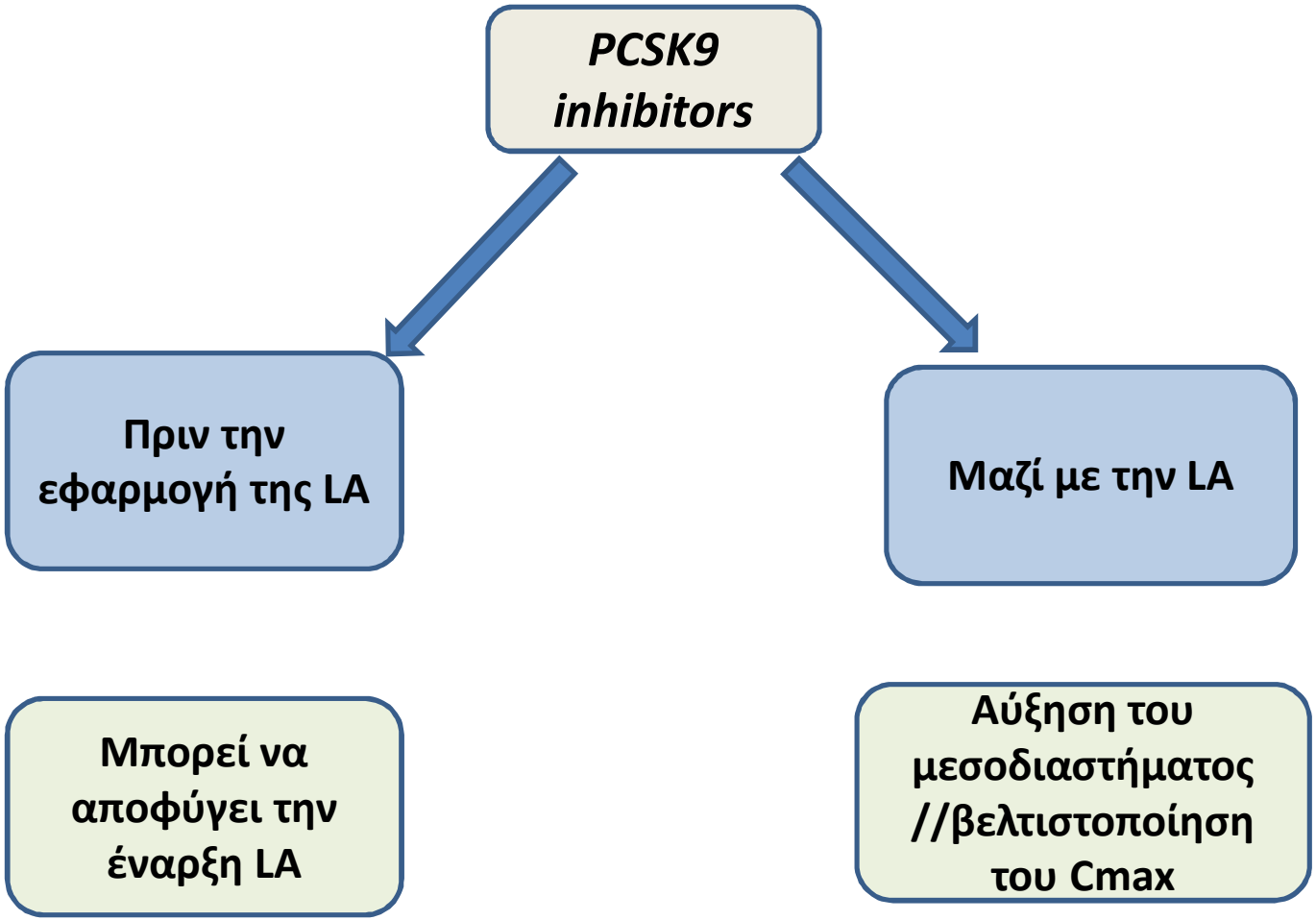

Start of LDL apheresis
Baseline
LDL
Pre-treatment
LDL level
LDL cholesterol
2-week interval
Post-treatment
LDL level
Time



PCSK9 inhibitors

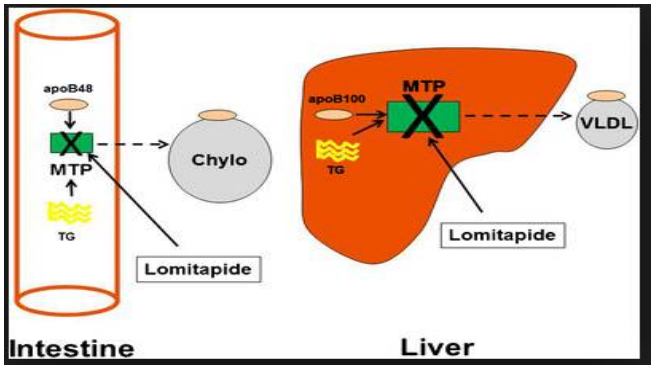




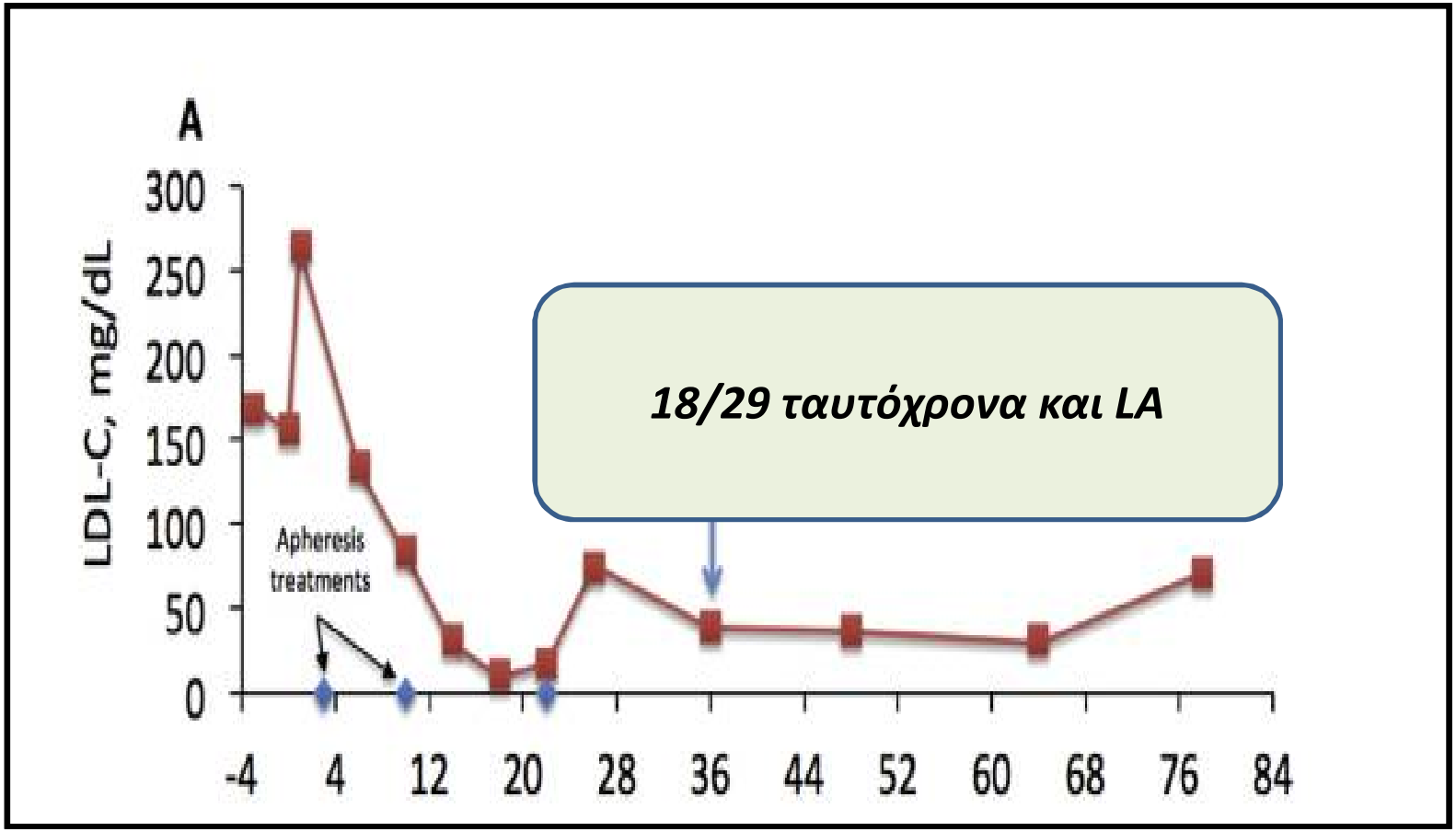


PCSK9 inhibitors και LA σε σοβαρή HCH

Harangi et al, Vessel Plus 2017

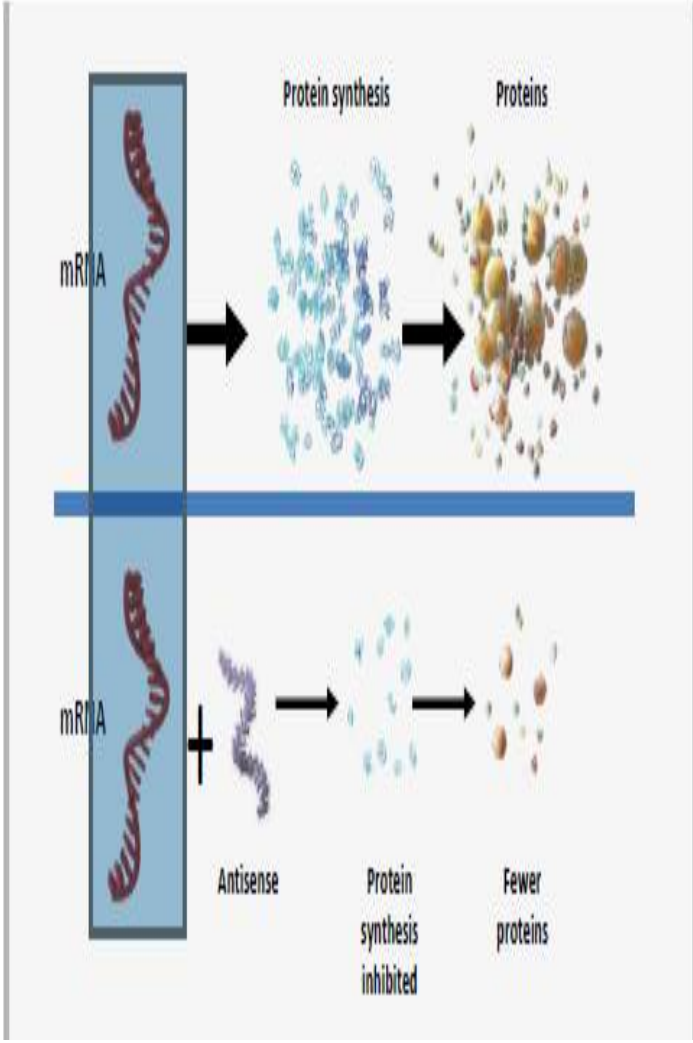


Microsomal Transfer Protein inhibitors (lomitapide)



Cachel et al, J Lancet 2013

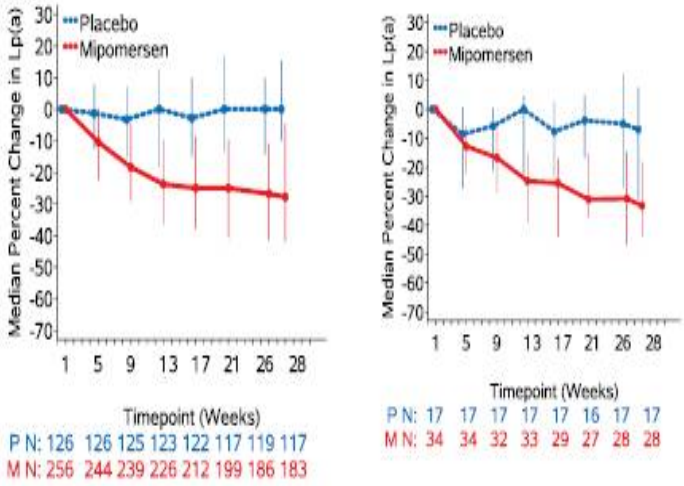
Antisense Oligonoucleotide against apo(a) (mipomersen)



Mipomersen, an Antisense Oligonucleotide to Apolipoprotein B-100, Reduces Lipoprotein(a) in Various Populations With Hypercholesterolemia

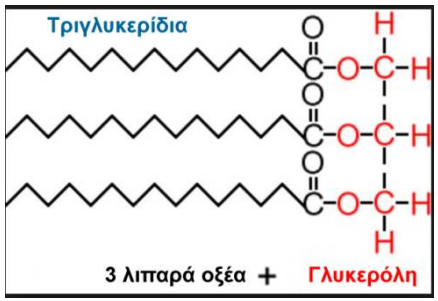
Results of 4 Phase III Trials

Raul D. Santos, Frederick J. Raal, Alberico L. Catapano, Joseph L. Witztum, Elisabeth Steinhagen-Thiessen, Sotirios Tsimikas



Pooled Population Homozygous FH

Santos RD et al. Arterioscler Thromb Vasc Biol. 2015;35:689-99.



Υπερτριγλυκεριδαιμία

Diseases	*Hereditary conditions*	*Medications*
· Uncontrolleddiabetes · Hypertension · CHD · Acute hepatitis · Hepatic disease · Hypothyroidism · Renal disease · Acromegaly · Lipo-dystrophies · Cushing'ssyndrome · Polycysticovary Syndrome (PCOS)	-Familialhypertriglyceridemia -Familialdysbetalipoproteinemia -Familiarlipoprotein lipase deficiency -Type IIIhyper-lipoproteinemia -TypeV hyper-lipoproteinemia	· Antiretroviraldrugs · Beta-blockers · Oralcontraceptives · Cyclosporine · Diuretics · Estrogenreplacement therapy · Glucocorticoids · Antipsychotics · Progesterone · Retinoids · Steroids · Tamoxifen

HYPERTRIGLYCERIDEMIC PANCREATITIS

Incidence: 18/100,000/yr		**Procedure** TPE	**Recommendation** Grade 2C	**Category** III
No. of reported patients: 100–300	**RCT** 0	**CT** 1(20)	**CS** 16(235)	**CR** 38(39)

TABLE 1. *Current available studies on the use of apheresis in the treatment of severe hypertriglyceridemia (sHTG) (only studies with patients* n ≥ *10)*

Reference	Patients included	Plasma exchange methods	Significant reduction of tryglicerides
Stefanutti et al. (34)	17	Albumin	By 61%
Yeh et al. (22)	18	FFP and albumin, double membrane filtration	By 66% (first setting) and by 83% (second setting)
Yeh et al. (21)	17	FFP and albumin	Significant reduction
Chen et al. (20)	94	FFP and albumin	n.a.
Gubensek et al. (22)	50	Albumin	Significant reduction
Kyriakidis et al. (6)	10	FFP	By 62%

FFP, fresh-frozen plasma; n.a., not available. Reproduced from Ewald and Kloer (20) with kind permission from Springer Science+ Business Media.

Κυτοκίνες
Αναπληρώνει την LpL

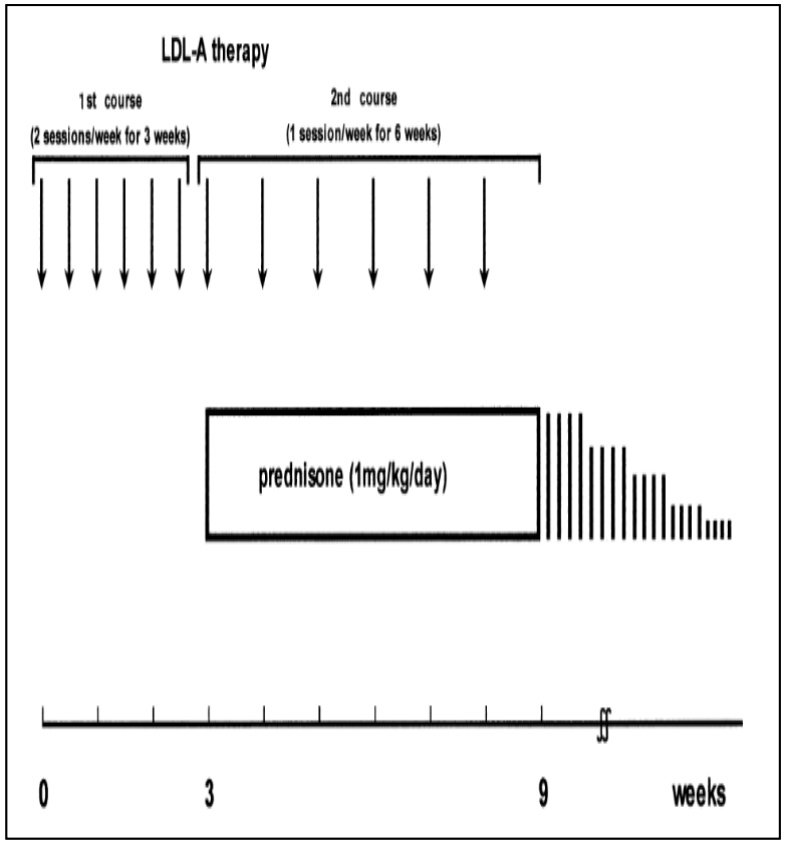
Δεν διαφοροποιεί τη θνητότητα

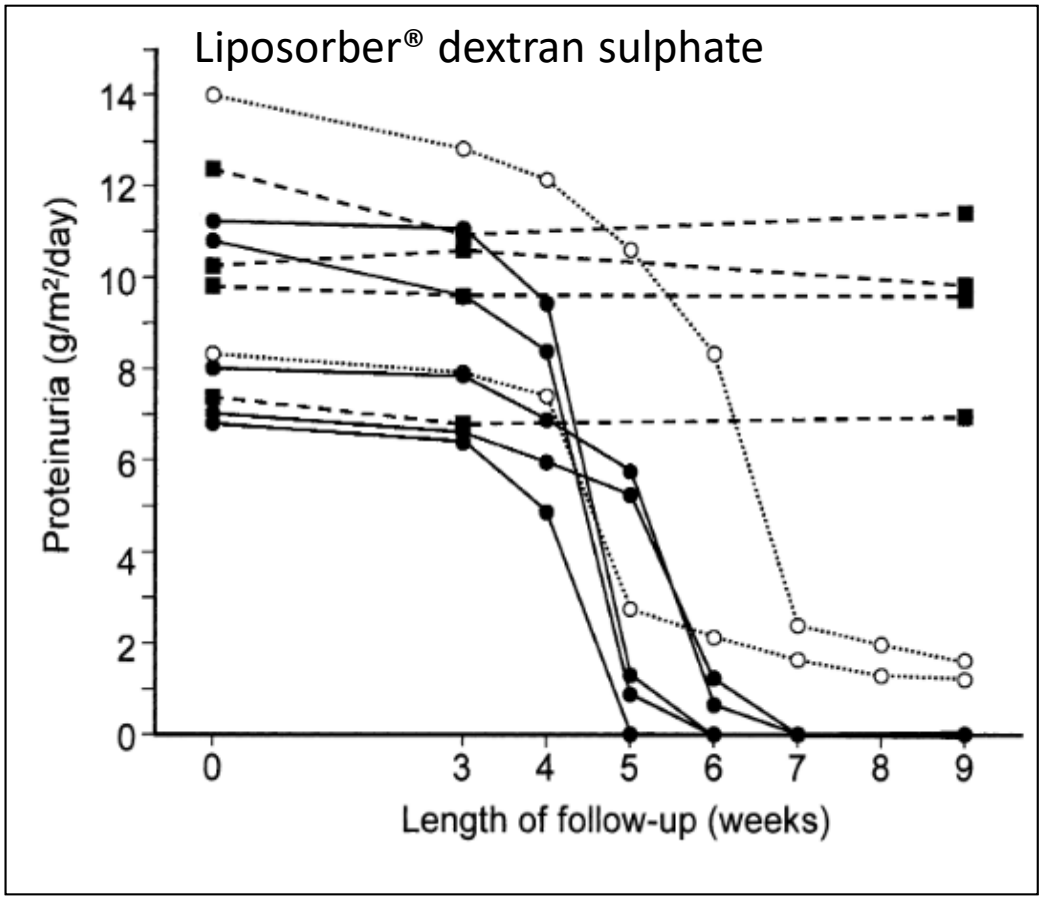
Volume treated: 1–1.5 TPV
Replacement fluid: Albumin, plasma

Frequency: Therapeutic: daily for 1–3 days depending upon patient course and TG level; Prophylactic: every 2–4 weeks to maintain TG level < 150 mg/dL

FOCAL SEGMENTAL GLOMERULOSCLEROSIS

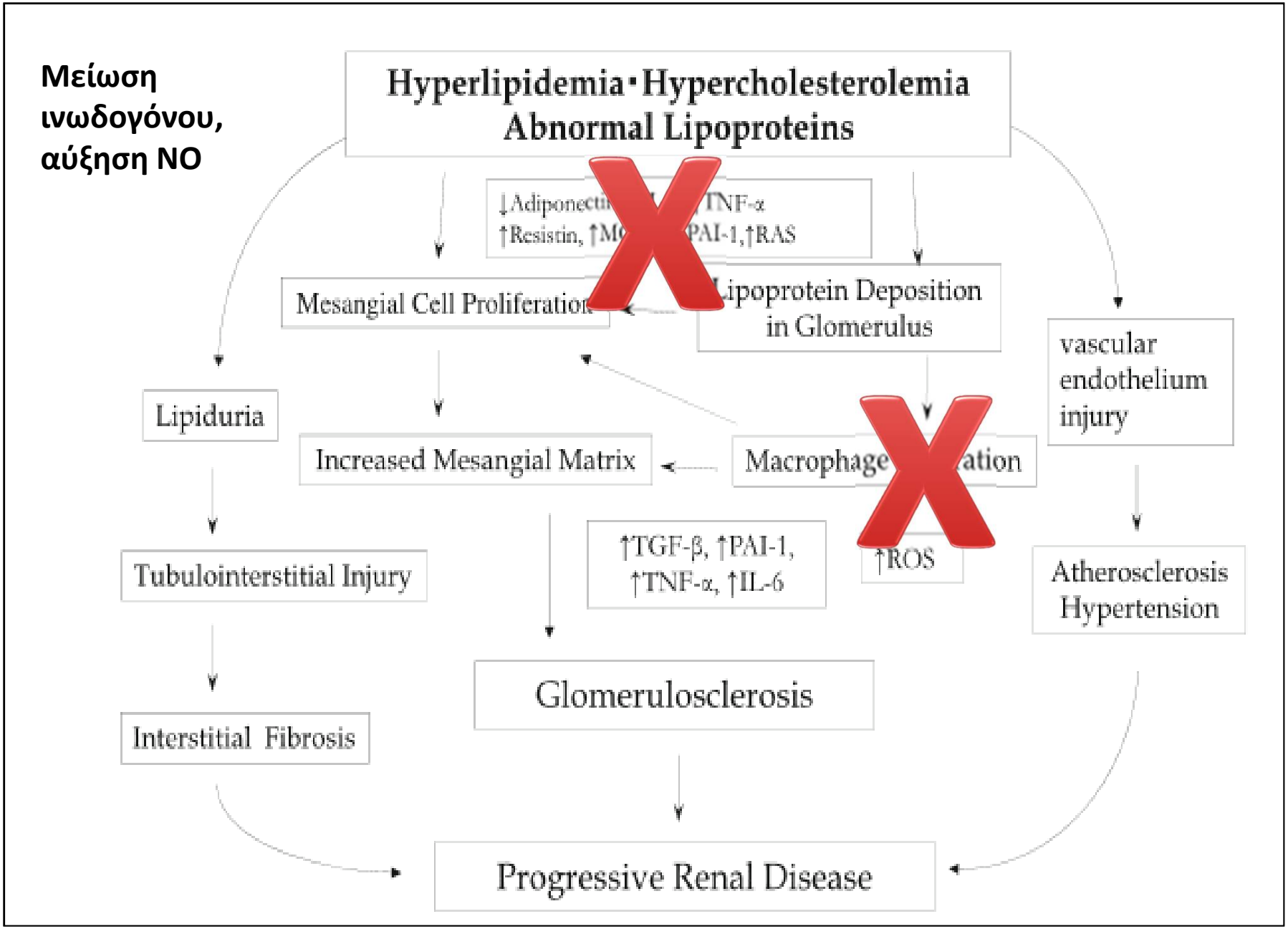
Incidence: 7/1,000,000	**Indication**	**Procedure**	**Recommendation**	**Category**
	Recurrent in transplanted kidney	TPE	Grade 1B	I
	Steroid resistant in native kidney	LDL Apheresis	Grade 2C	III
No. of reported patients: >300	**RCT**	**CT**	**CS**	**CR**
Recurrent in transplanted kidney	0	3(48)	49(224)	15(17)
Steroid resistant in native kidney	0	0	1(11)	4(4)





Hattori et al, Am J Kidney Dis 2003

Μείωση ινωδογόνου, αύξηση NO



Muso Clin Exp Nephrol 2013

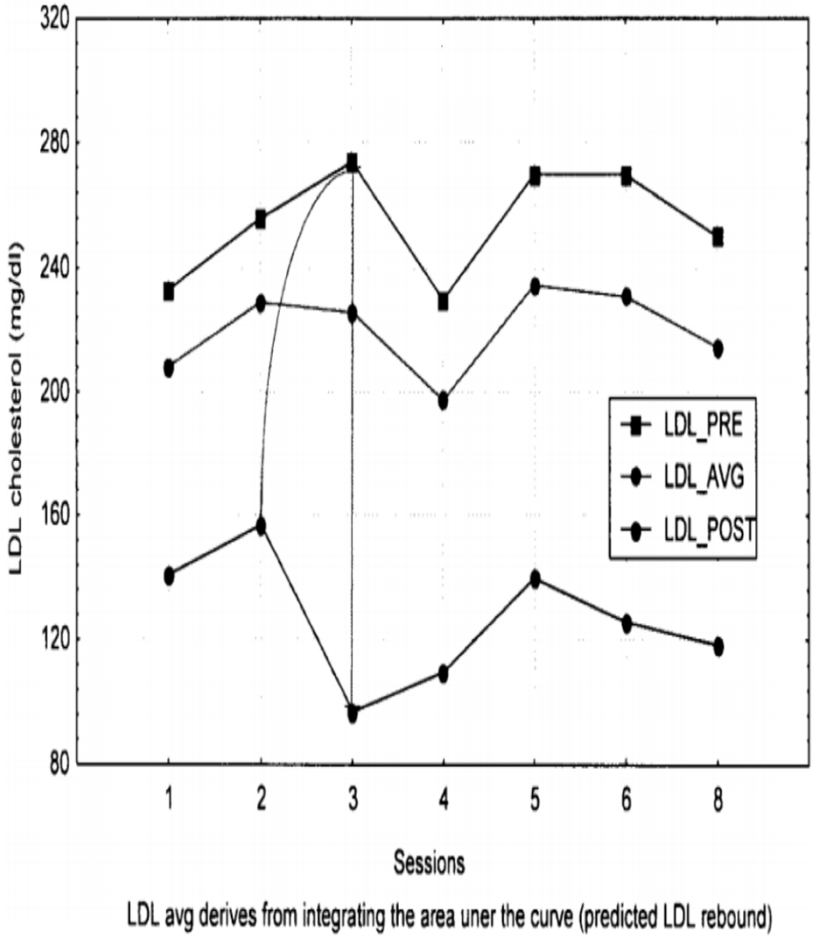
Table 2 Clinical efficacy of LDL-apheresis for nephrotic syndrome (Summary of Clinical Studies before 2007)

	Muso et al. Nephron 2001 89 408–415	Stenvinkel et al. Eur J Clin Invest 2000 30 866–870	Yokoyama et al. Clin Nephrol 1998 50 1–7	Muso et al. NDT 1994 9 2257-264	Sakai et al. Jin To Touseki 1994 33 321–328	Hattori et al. Am J Kidney Dis 42 1121–1130
Study design	Study Group: prospective	Prospective	Retrospective	Retrospective	Prospective	Retrospective
No. of cases (control group)	Control group: retrospective 17 (10)	7 (none)	14 (none)	8 (none)	16 (none)	11 (none)
Primary disease (no. of cases)	FSGS (14/9) MCNS(3/1)	MN (3) MCNS(2) IgAGN (1)	FSGS (14) PSL resistant	FSGS(6) MCNS (1) MN + FSGS (1)	FSGS (13) MN (3)	FSGS (11) PSL, CyA resistant
No. of Treatment	2/w × 3 1/w × 6 Total 12	2/w × 3 1/w × 7 Total 13	2/w × 3 Total 6	2-13 7.3 (average)	2/w × 3 Total 6	2/w × 3 1/w × 6 Total 12
Concomitant treatment (no. of cases)	PSL 1.0 mg/kg	none (4) PSL(1) PSL + CyA (2)	PSL 0.8 mg/kg	PSL/pulse 1.0 mg/kg	PSL (14) immunosuppressant (10)	PSL 1.0 mg/kg
Clinical efficacy	Remission 9 Partial remission 4 no effect 4	Remission 2 Partial remission 4 no effect 1	Responded 8 no effect 6	Remission 4 Partial remission 1 no effect 3	Improved 7 Unchanged 3 Worsened 3 unjudgemental 3	Remission 5 Partial remission 2
Efficacy rate	76 %	86 %	57 %	63 %	FSGS 54 %	76 %
Summary	Reduced remission induction period	Increased serum albumin	Increased serum albumin Effective in younger age	Amelioration of ApoB deposition in glomerulus 5 in 6 cases	>50 % reduction of proteinuria in 9 cases	Effective in PSL resistant juvenile patients

LDL apheresis in the treatment of a patient with resistant nephrotic syndrome

Antonoglou C, Passadakis P, Kriki P, Paraschou A, Giannatos V, Kantartzi C, Panagoutsos S, Vargemezis V
Division of Nephrology, Democritus University of Thrace, Alexandroupolis

3 sessions/wk
5 sessions/2wk
2 sessions/3wk
1session after 4wks



LDL avg derives from integrating the area uner the curve (predicted LDL rebound)


"Rare diseases are rare, but rare disease patients are numerous"
The Future
NEXT EXIT