Plaque Regression and Endothelial Progenitor Cell Mobilization With Intensive Lipid Elimination Regimen (PREMIER)

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On behalf of PREMIER Trial Investigators

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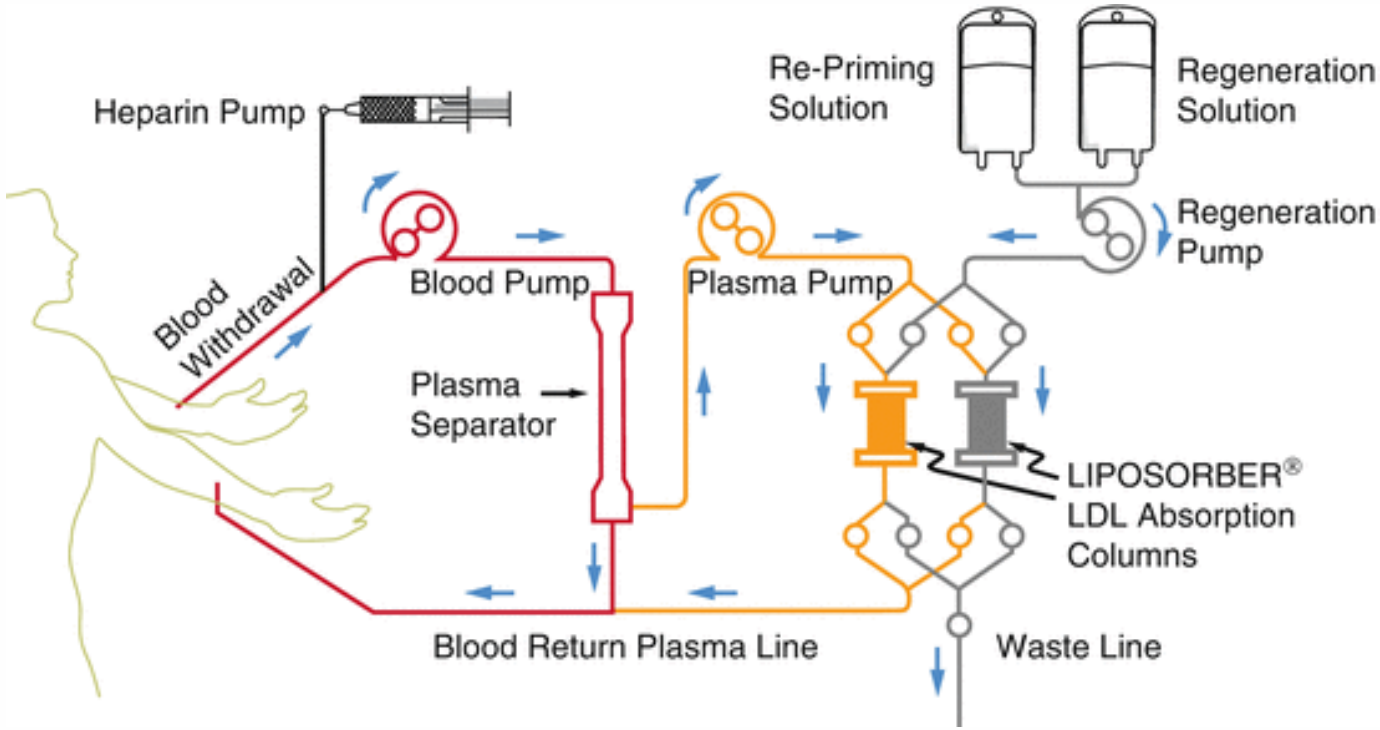
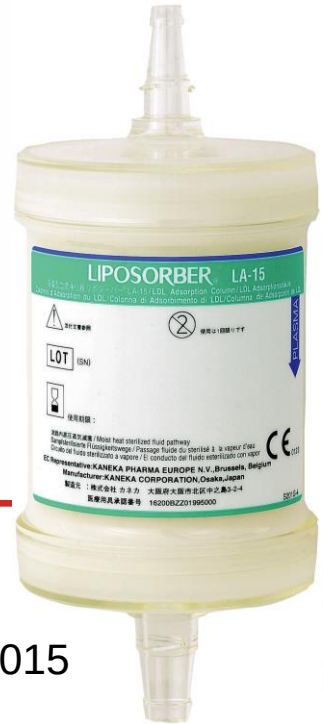
VA | U.S. Department of Veterans Affairs

LDL-Apheresis

Extracorporeal filtration of LDL from peripheral blood
First use in non-FH ACS (U.S. FDA IDE trial)



Dextran sulfate cellulose beads: selectively bind Apo-B lipoproteins; ↓PCSK9*



FH: familial hyperlipidemia

Plasma volume treated = 0.7 x kg body weight x Hct.

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Liposorber LDL-apheresis system
Kaneka Inc., New York, NY

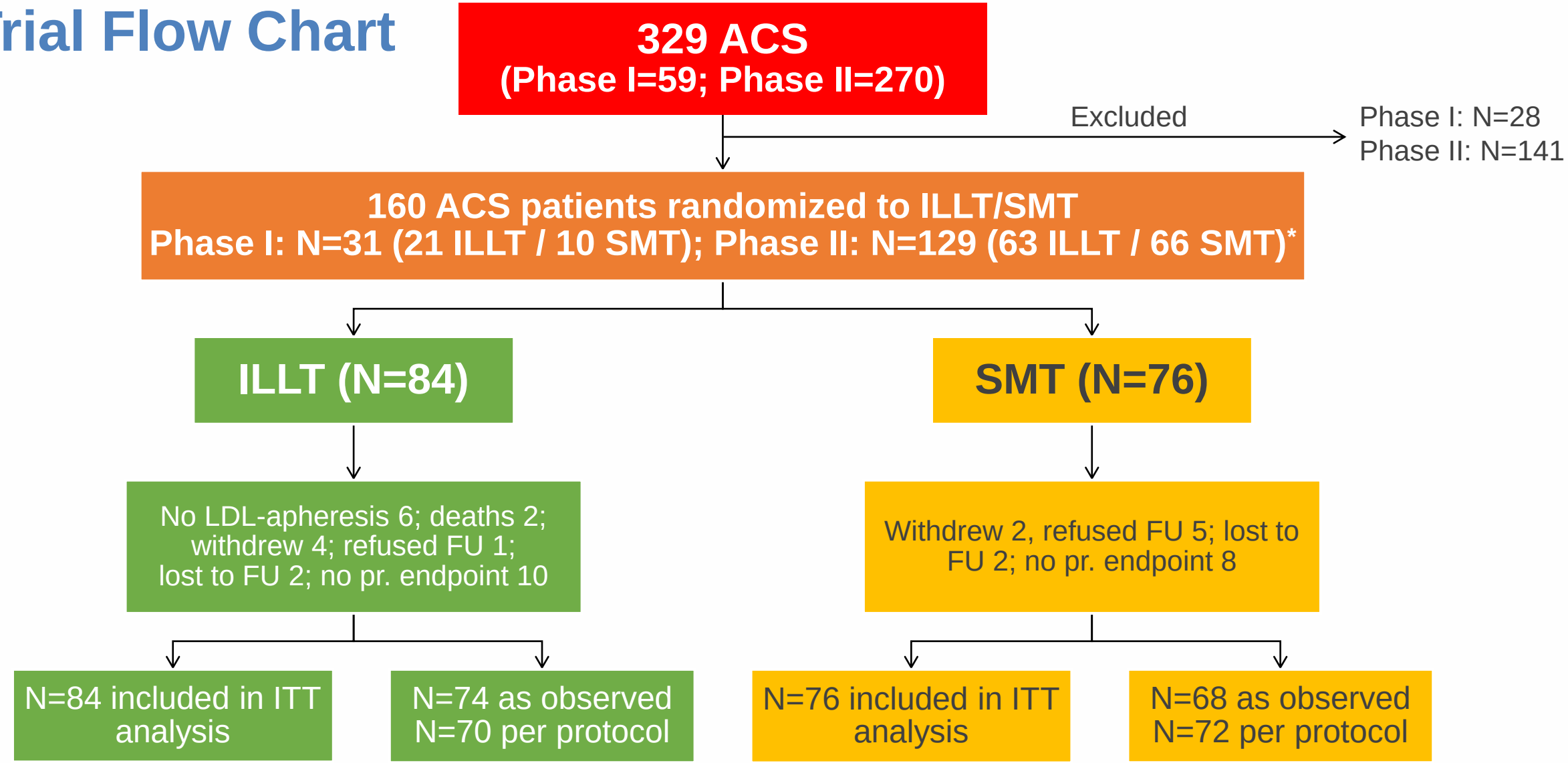
*Julius U *et al.* Atherosclerosis suppl. 2015

Endpoints

- **Primary safety endpoint:** Total number & percentage of patients with major peri-PCI procedure adverse events.*
- **Primary effectiveness endpoint:** Percent change in total plaque volume within a ≥20 mm target coronary artery at 90 days IVUS-VH follow-up.
- **Secondary safety endpoints:** Total number & percentage of patients with statin-related abnormal liver function test and muscle injury events.
- **Secondary effectiveness endpoints:** Change in EPC-CFU/ml of peripheral blood from baseline to 30 days & 90 days post-PCI, change (%) in necrotic core (NC) component of coronary plaque at 90 days & major adverse CV events (MACE)** at 90 days and six-month follow-up.

*Hypotension, angina, myocardial ischemia, myocardial infarction(MI), cerebrovascular event, vermicular tachycardia, bleeding (PCI access and/or apheresis cannulation sites), & all-cause death. **Death, MI, coronary revascularization & stroke.

Trial Flow Chart



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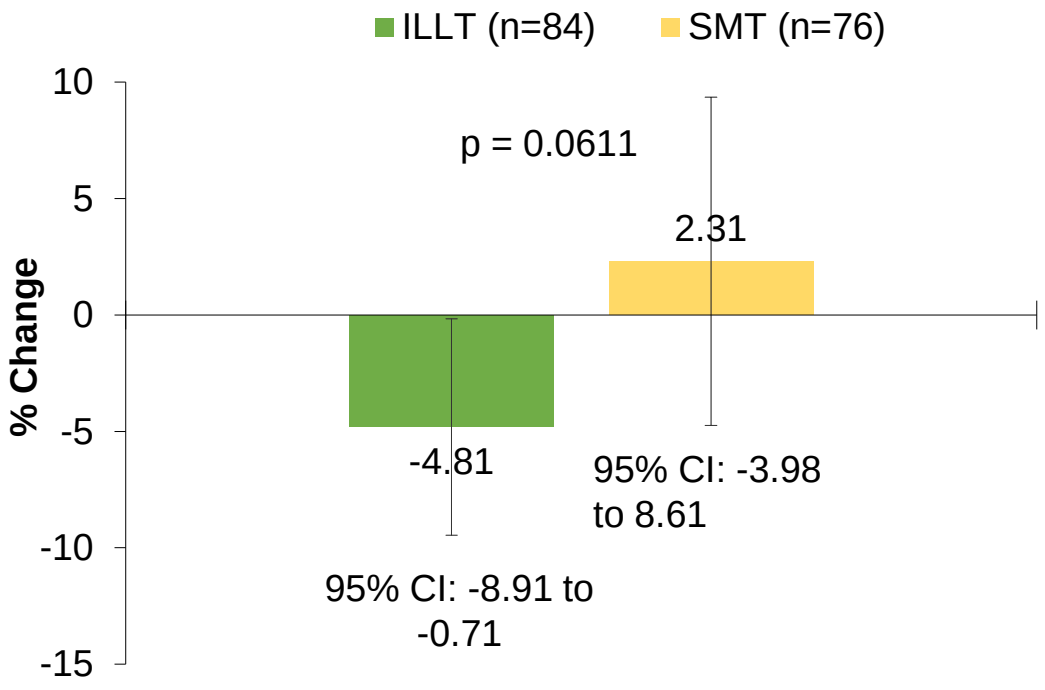
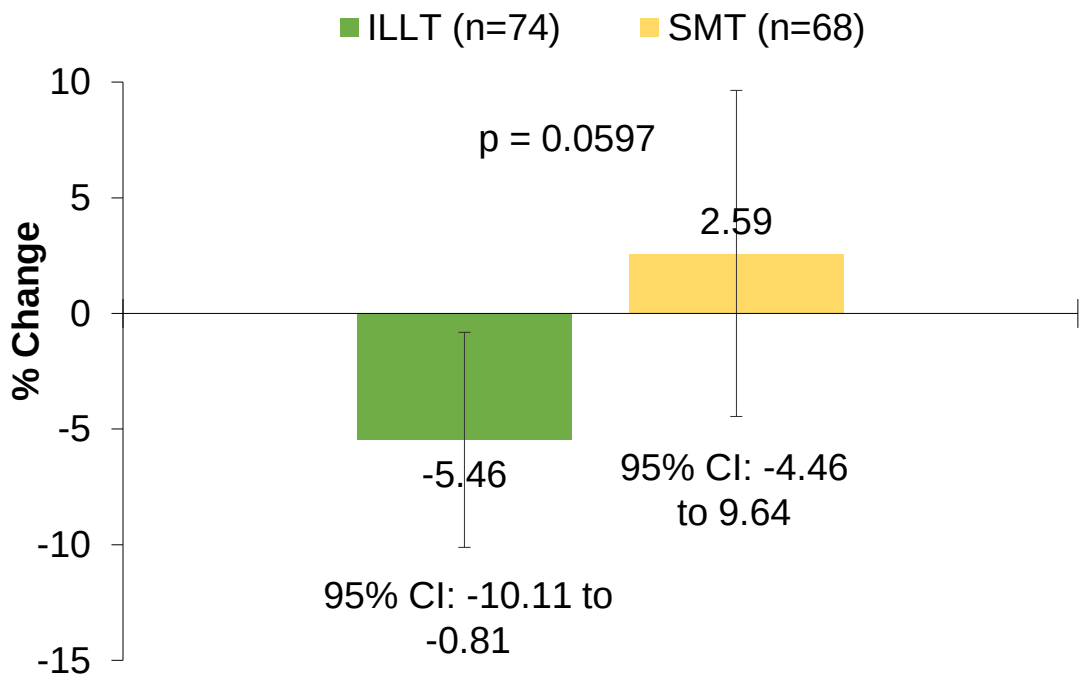
ILLT: Single LDL-apheresis + statins
SMT: Statin therapy alone
*Phase I: NCT01004406; Phase II: NCT02347098

Primary Effectiveness Endpoint

Percent Change in Coronary Plaque Volume (ITT analysis)

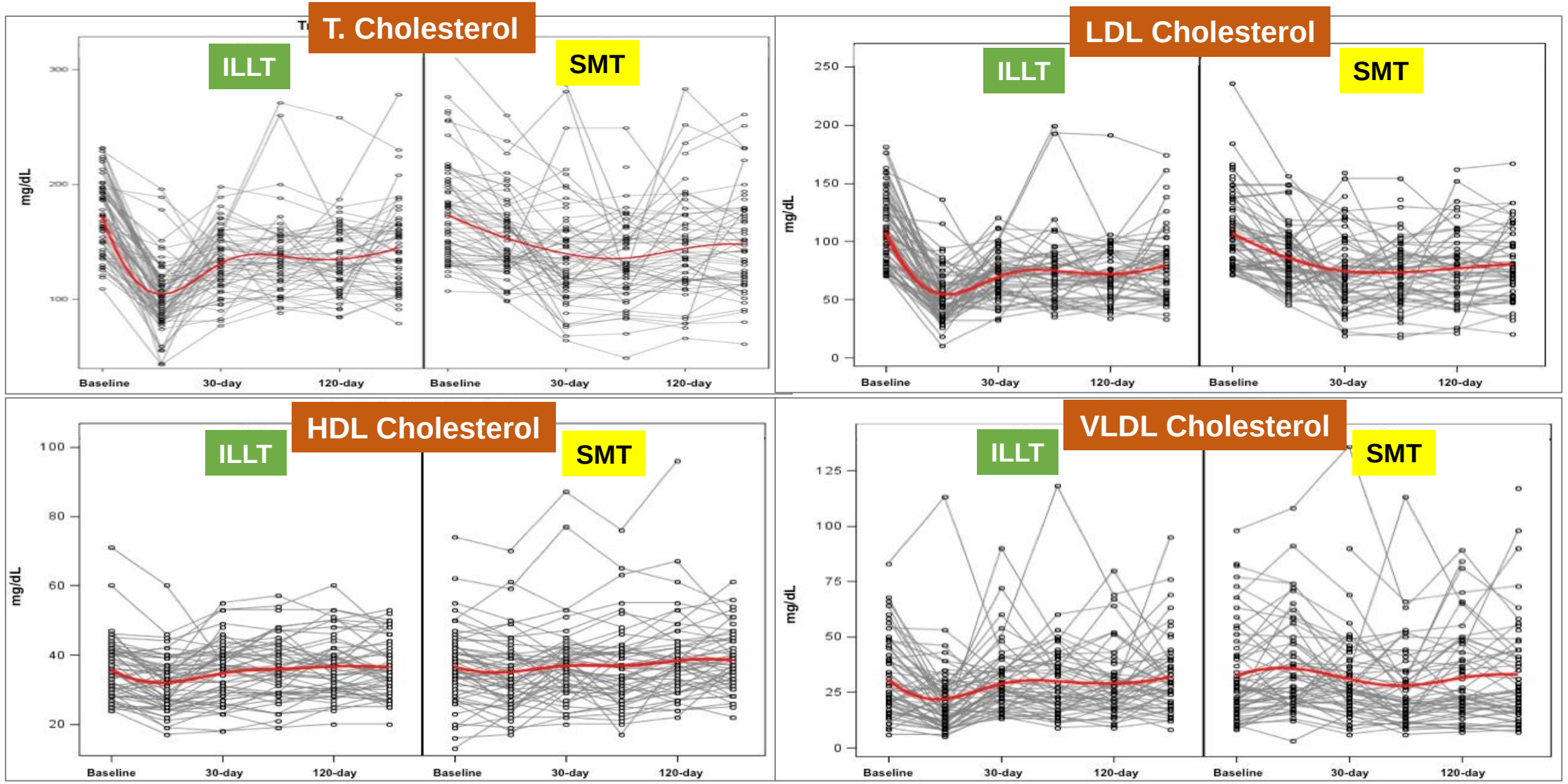


Percent Change in Coronary Plaque Volume (as observed)*



Safety Endpoints

	All	ILLT (N=84)	SMT (N=76)	p	Description
Major peri-PCI adverse events, (n events); **Primary Safety Endpoint**	3	3	0		3 hypotensive events in 2 ILLT patient treated with IV fluids.
All serious adverse events, (n events in % participants)	126	67 (45.2%)	59 (42.1%)	0.7505	
All peri-PCI adverse event events, (n events in % participants)	88	69 (46.4%)	19 (18.4%)	0.0002	Transient hypotension & flushing most common.
Death, n (6-month)	2	2	0	-	~2m post-enrollment, COPD; ~4m post-enrollment, CVA.
Myocardial infarction, n (6-month)	3	2	1	-	
Ischemic stroke, n (6-month)	2	1	1	-	
All adverse events, n (events)	318	165	153	-	



Lipoprotein Trends: ILLT & SMT

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PREMIER Trial: Conclusions

- First RCT to demonstrate safety of LDL-apheresis in non-FH ACS patients treated with PCI.
- LDL-apheresis reduced LDL more than medical Rx with strong trend for early coronary plaque regression.
- Use of LDL-apheresis in ACS patients needs further study.