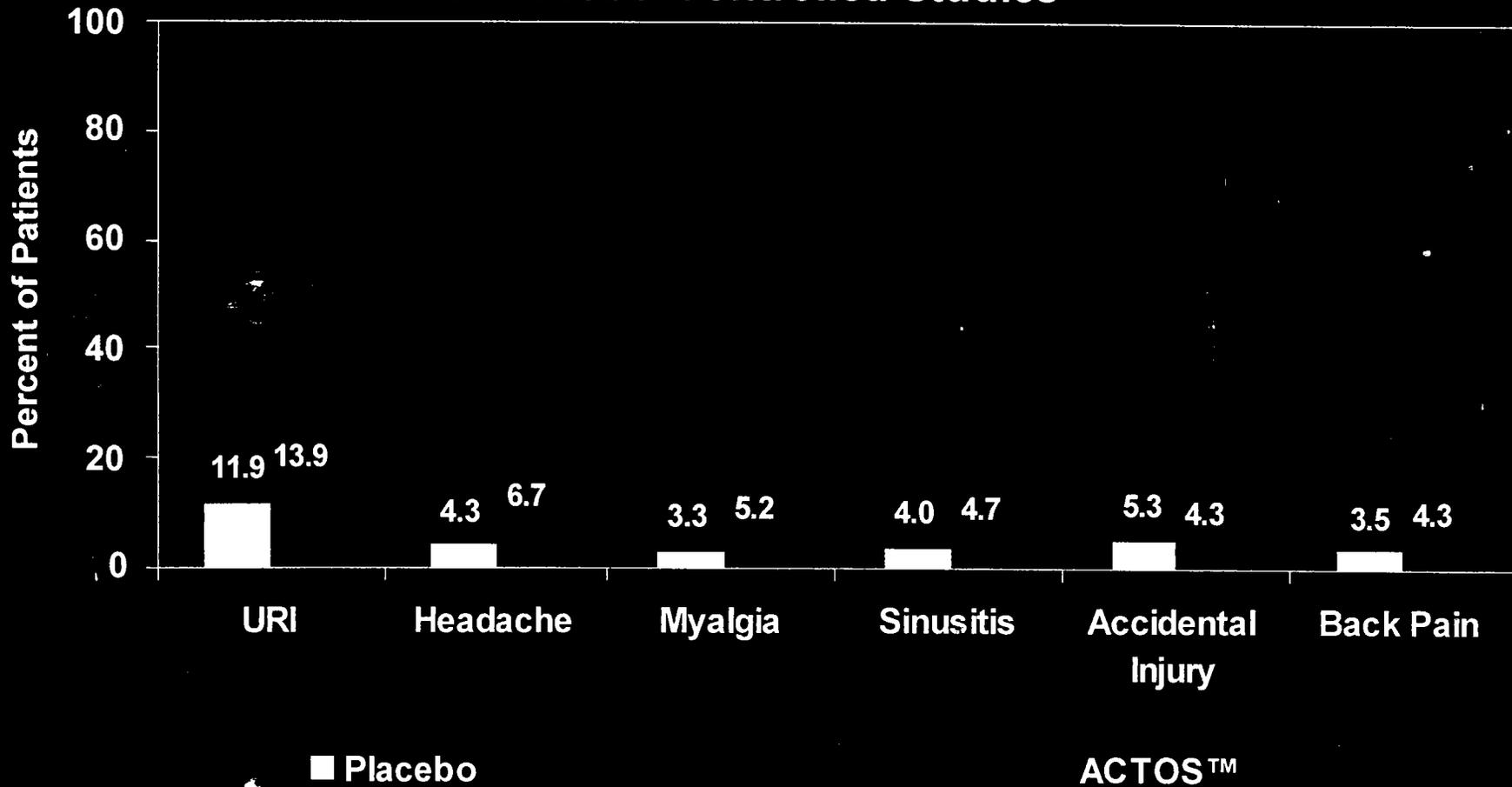


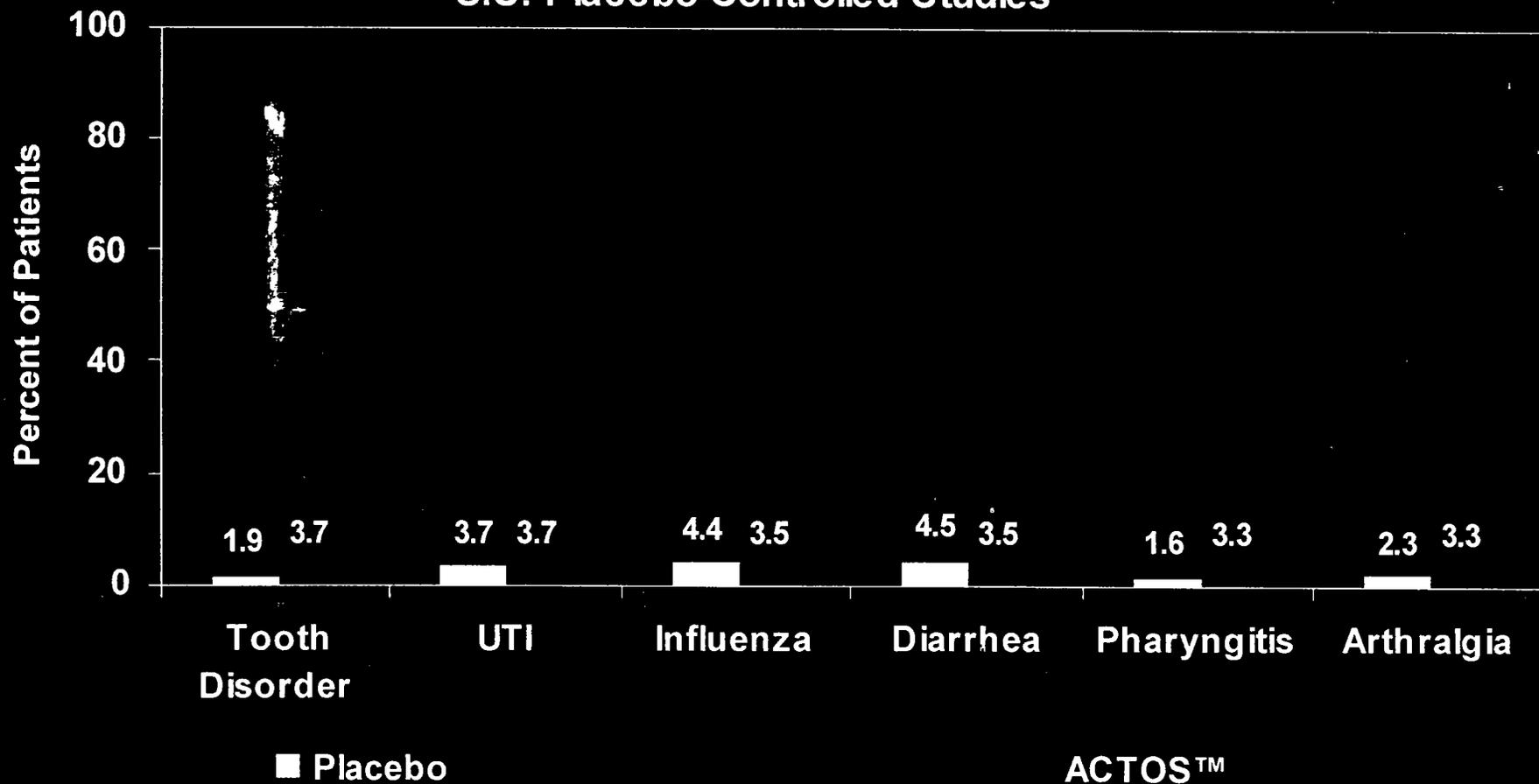
Most Frequently Reported Adverse Events

U.S. Placebo-Controlled Studies



Most Frequently Reported Adverse Events

U.S. Placebo-Controlled Studies





Other Safety Considerations

- Hypoglycemia
- Edema
- Hematology changes
- Cardiovascular assessment
- CPK
- Urinary cytology

Other Safety Considerations

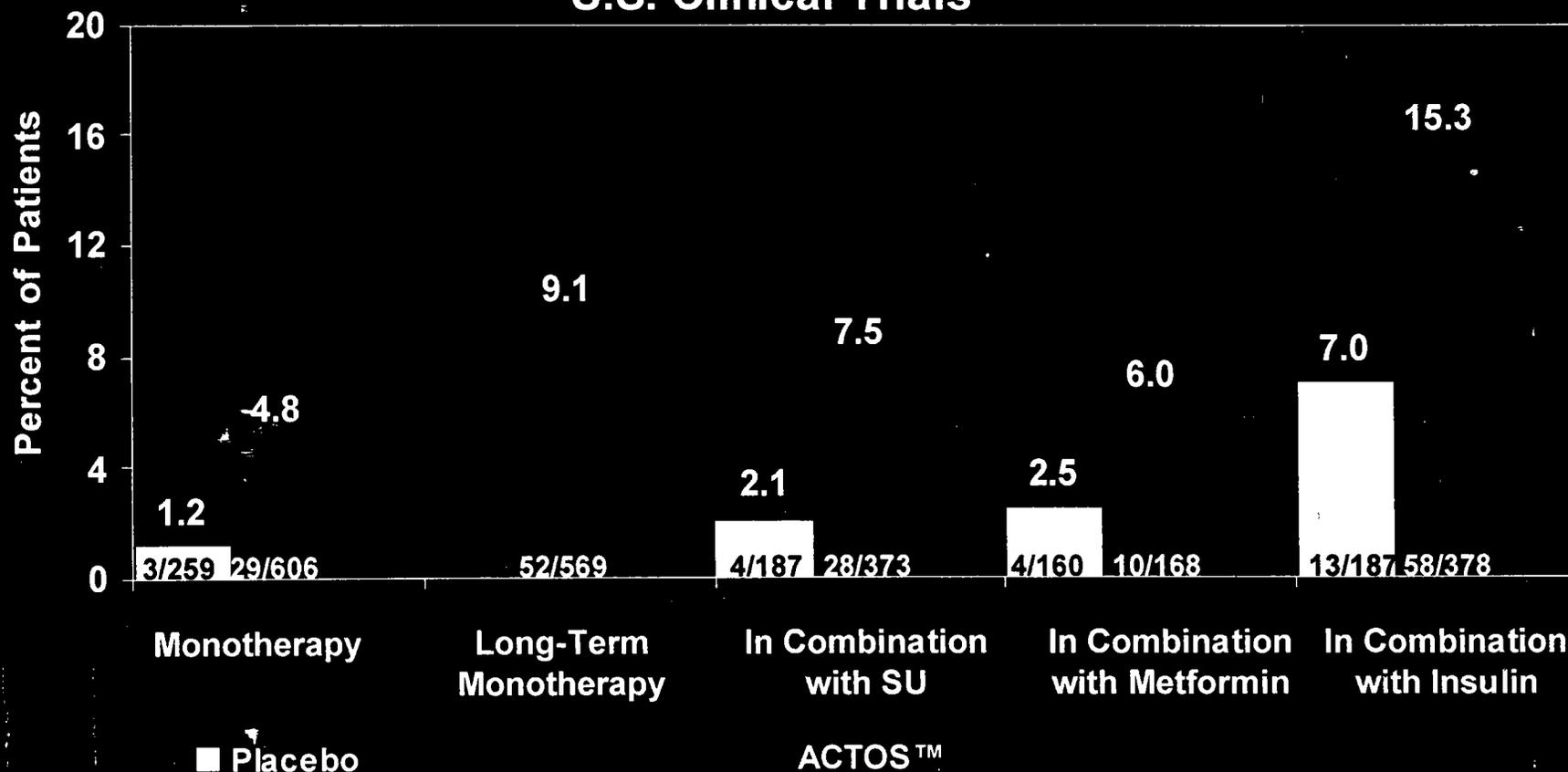
- Hypoglycemia

Other Safety Considerations

- Edema

Incidence of Edema

U.S. Clinical Trials



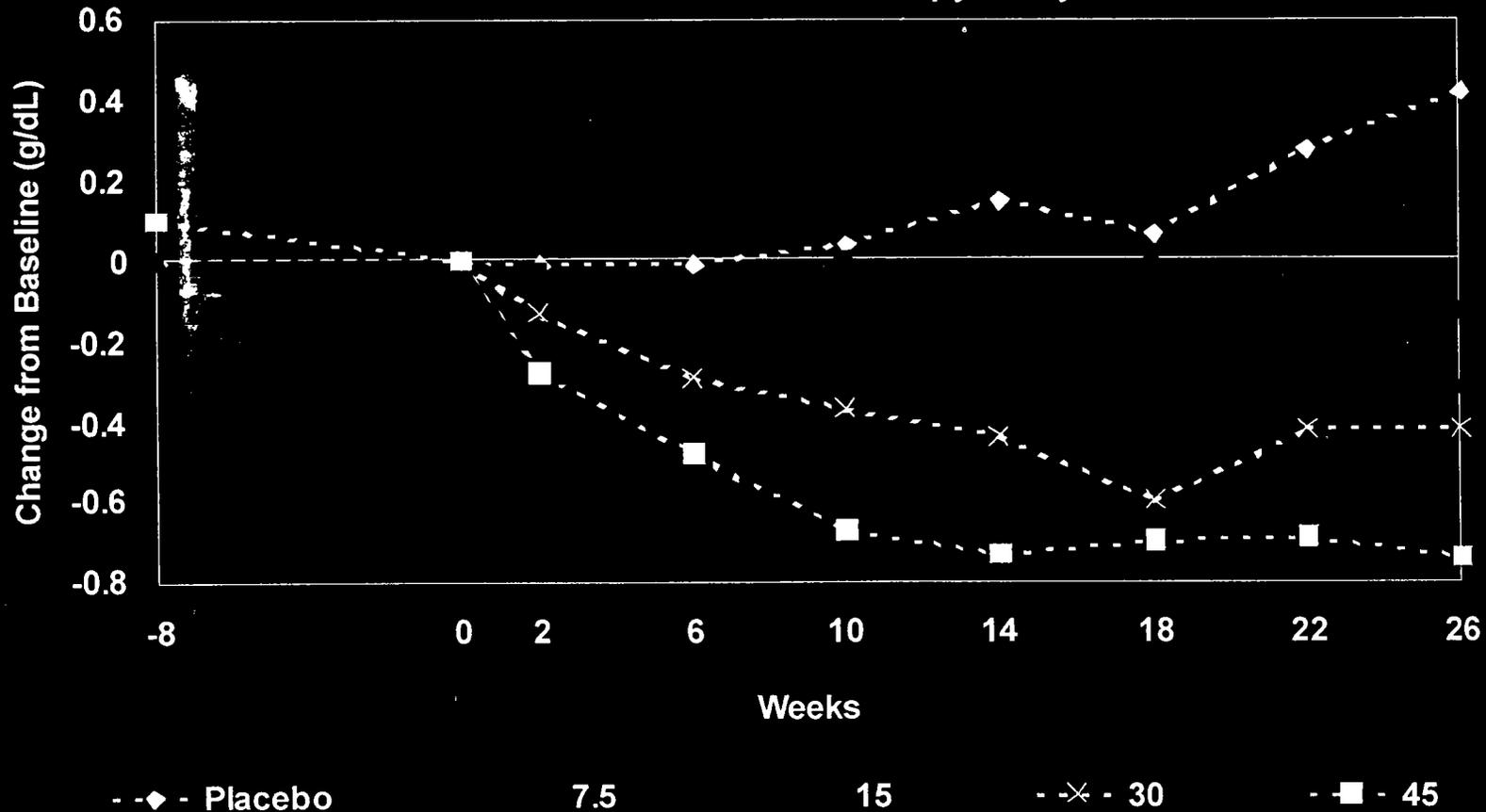
Two patients were withdrawn from combination therapy as a result of edema. All events were considered mild or moderate in intensity.

Other Safety Considerations

- Hematology changes

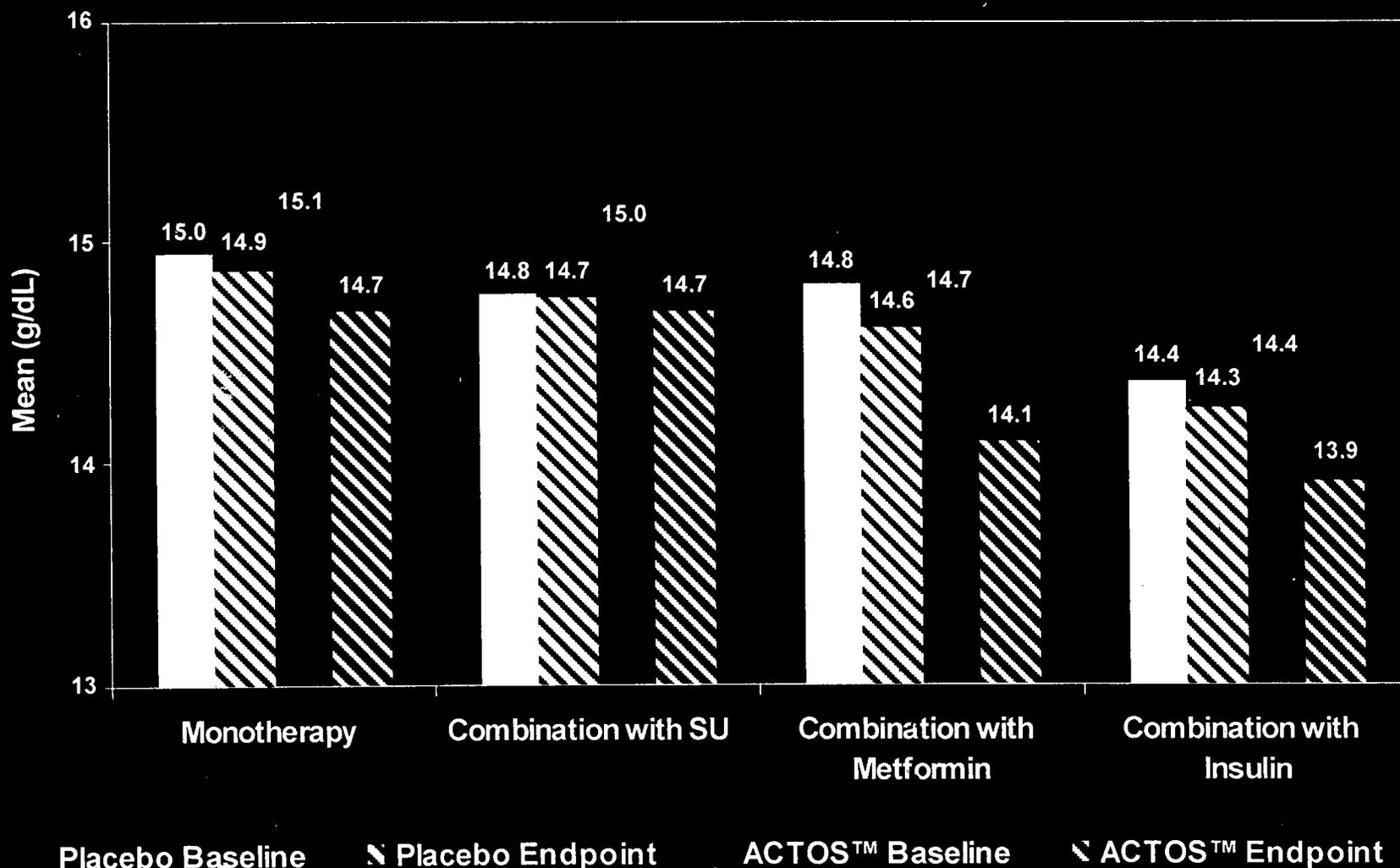
Hemoglobin

Placebo-Controlled Monotherapy Study 001



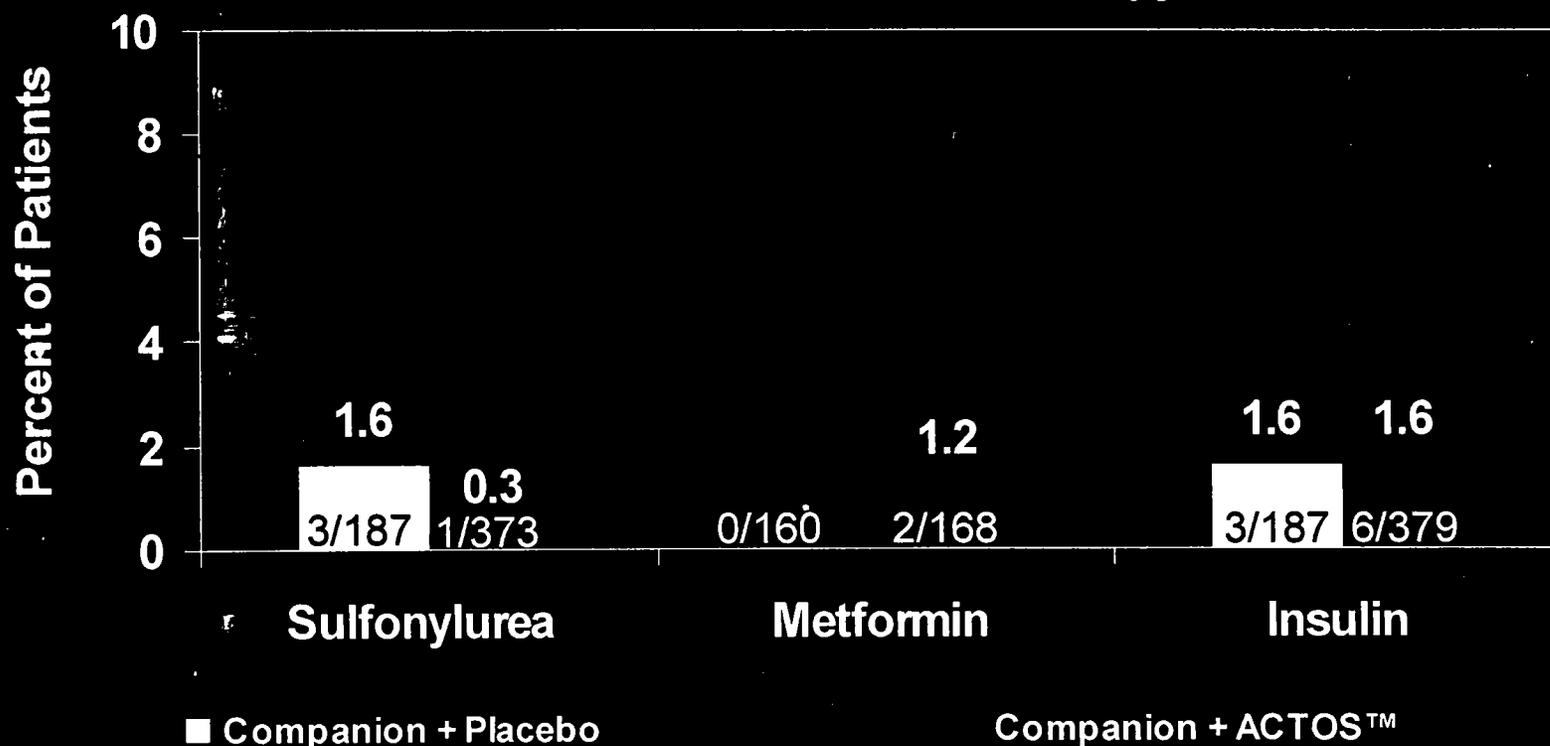
Hemoglobin

U.S. Placebo-Controlled Clinical Studies



Incidence of Anemia Reported as an Adverse Experience

U.S. Placebo-Controlled Combination Therapy Studies



No cases of anemia were reported in the placebo-controlled monotherapy studies or the long-term, open-label study

Other Safety Considerations

- Cardiovascular assessment

Cardiovascular Assessment

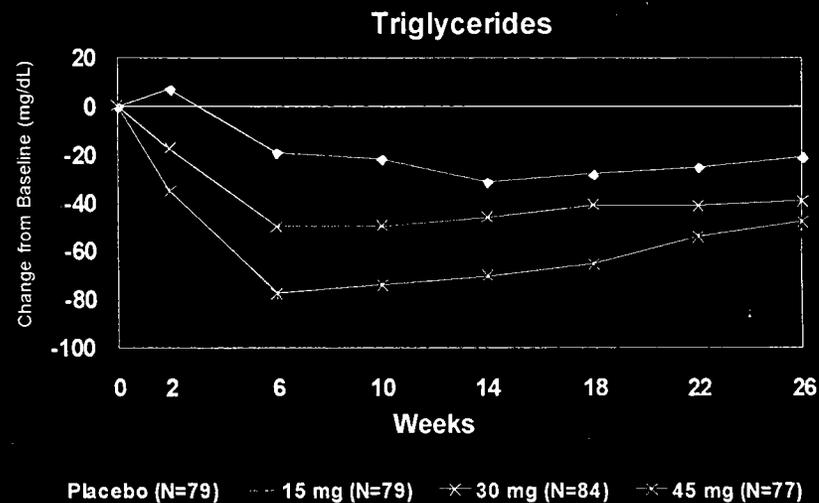
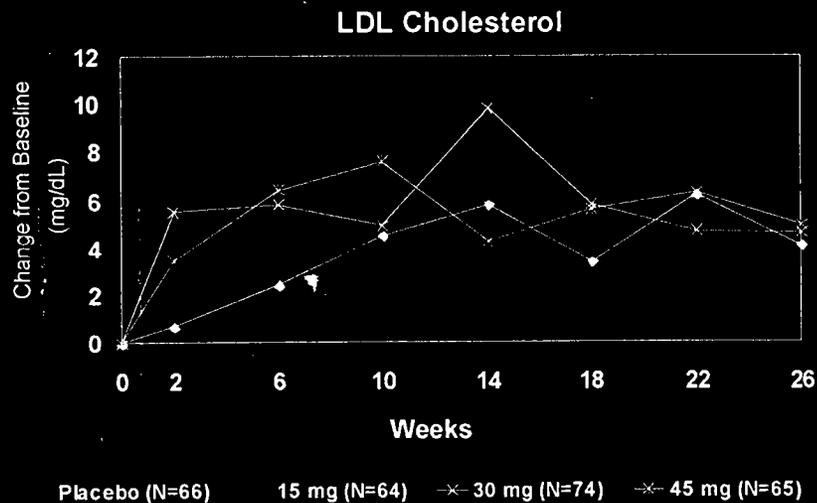
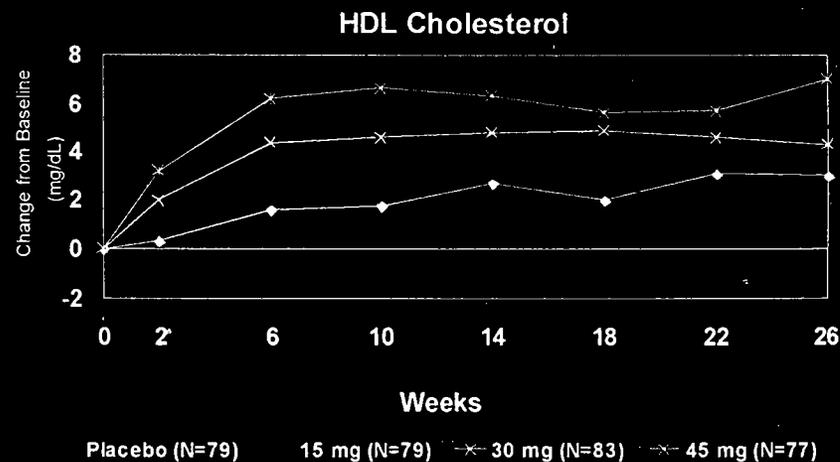
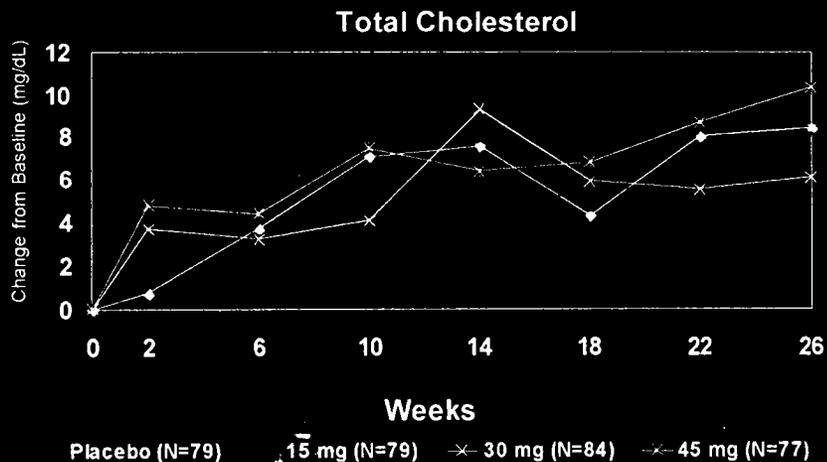
- Effects on serum lipid profile
- Cardiac adverse experiences
 - Overall
 - Most common
 - Findings of specific interest
 - Cardiomegaly by CXR
 - LVH by ECG
 - CHF
- Echocardiographic Evaluation

Effects on Serum Lipid Profile

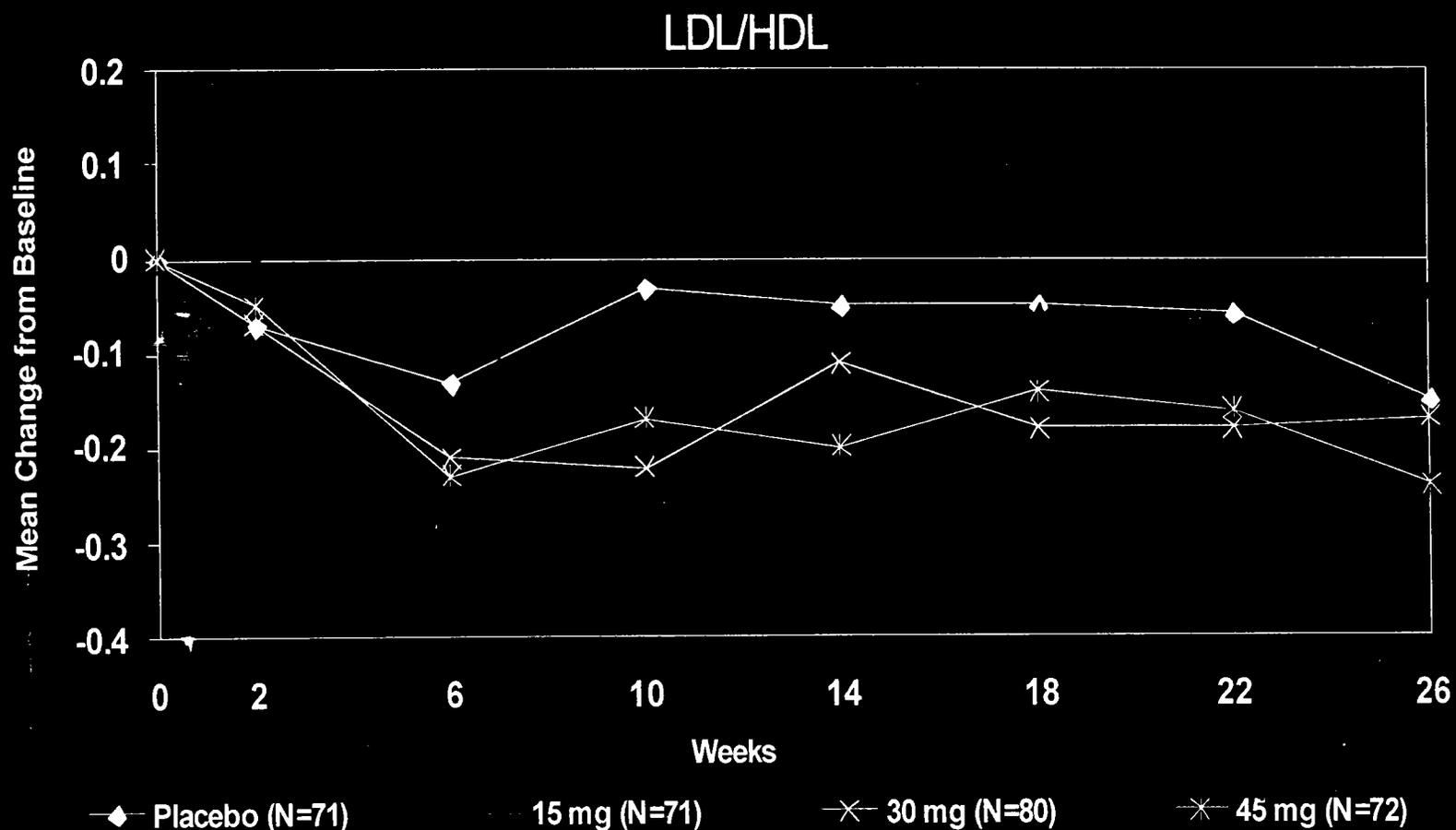
- Serum lipid levels were not adversely affected
- Ratios of total cholesterol to HDL and LDL to HDL were also not adversely affected
- Effects on lipids were consistent throughout the clinical program

U.S. Placebo-Controlled Monotherapy Studies

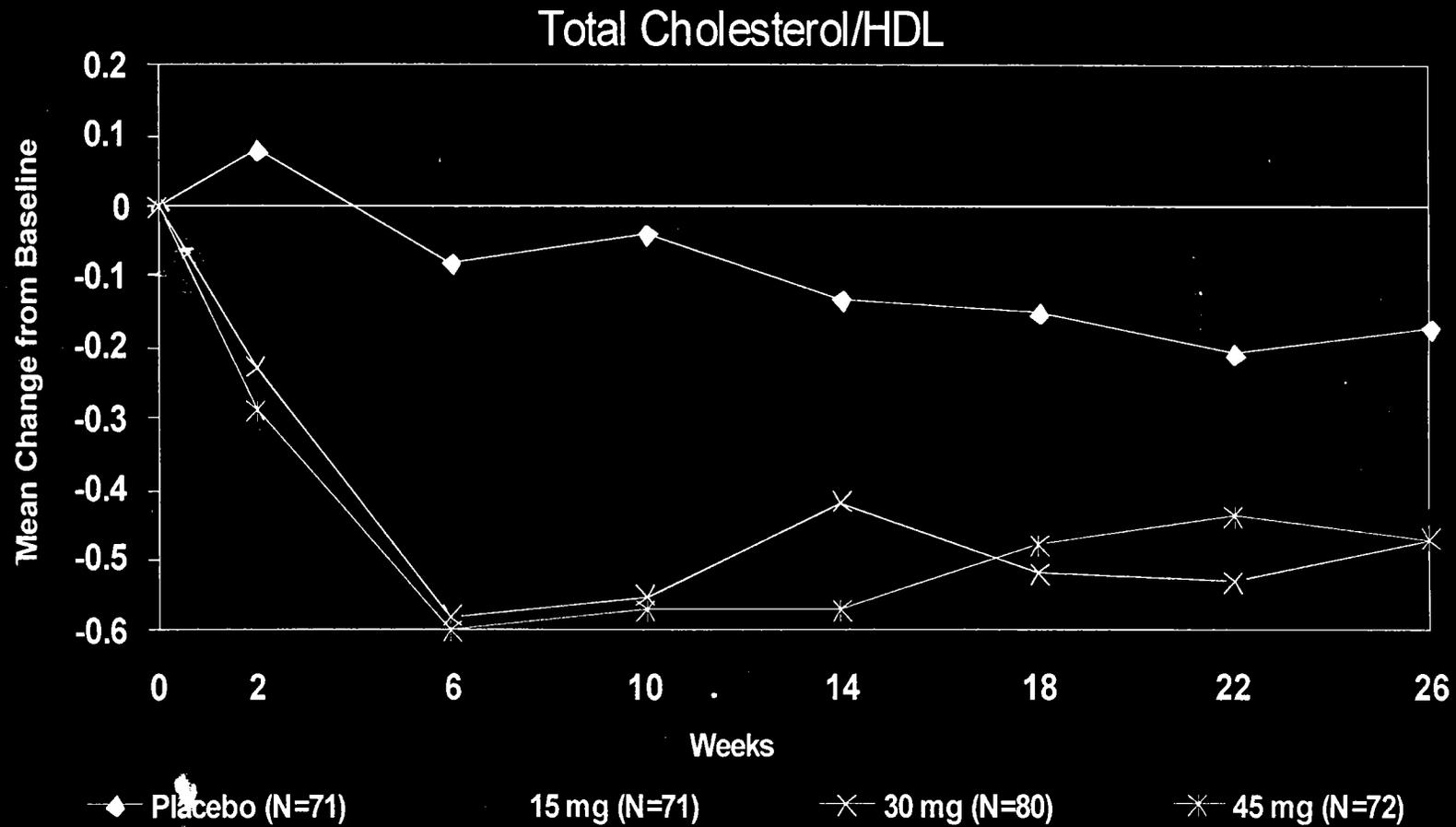
Study 001



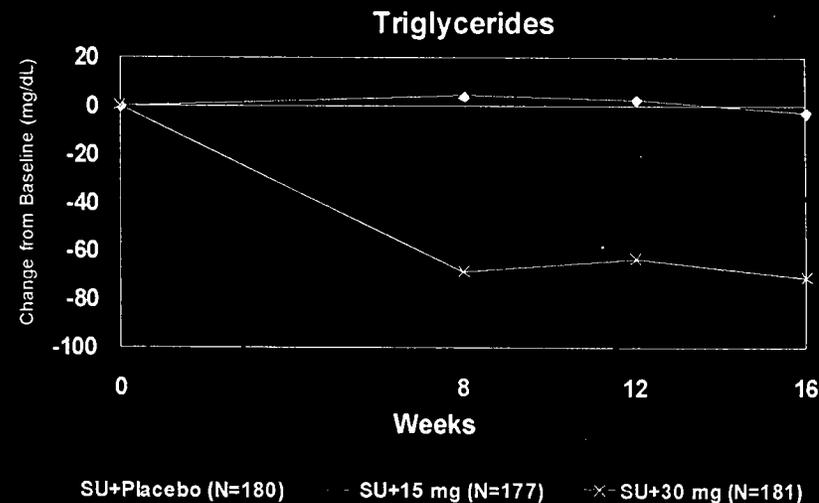
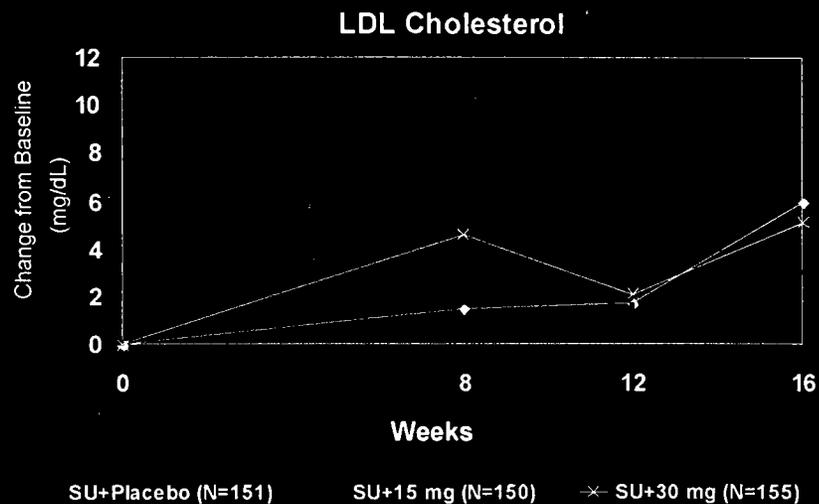
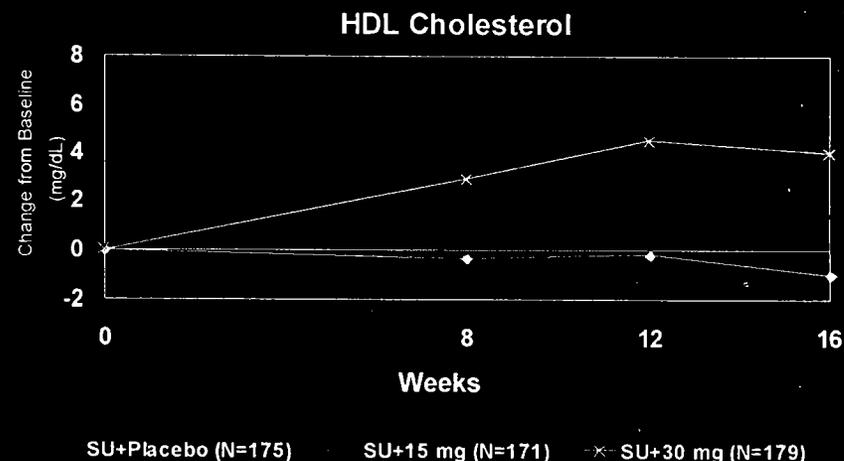
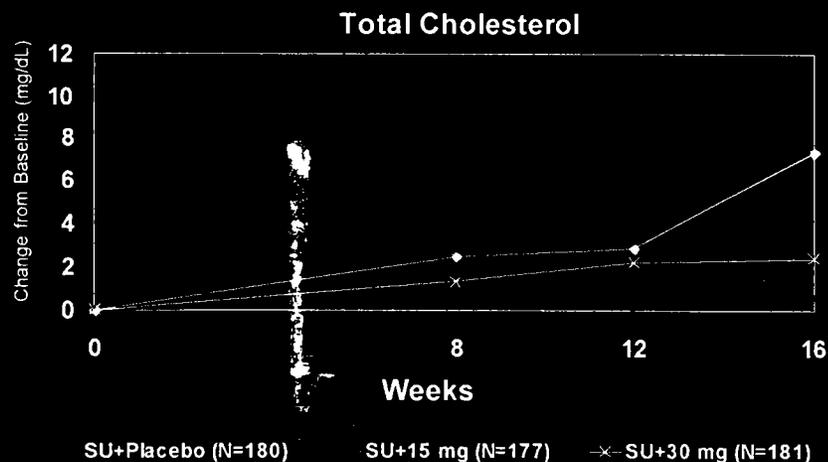
U.S. Placebo-Controlled Monotherapy Studies Study 001



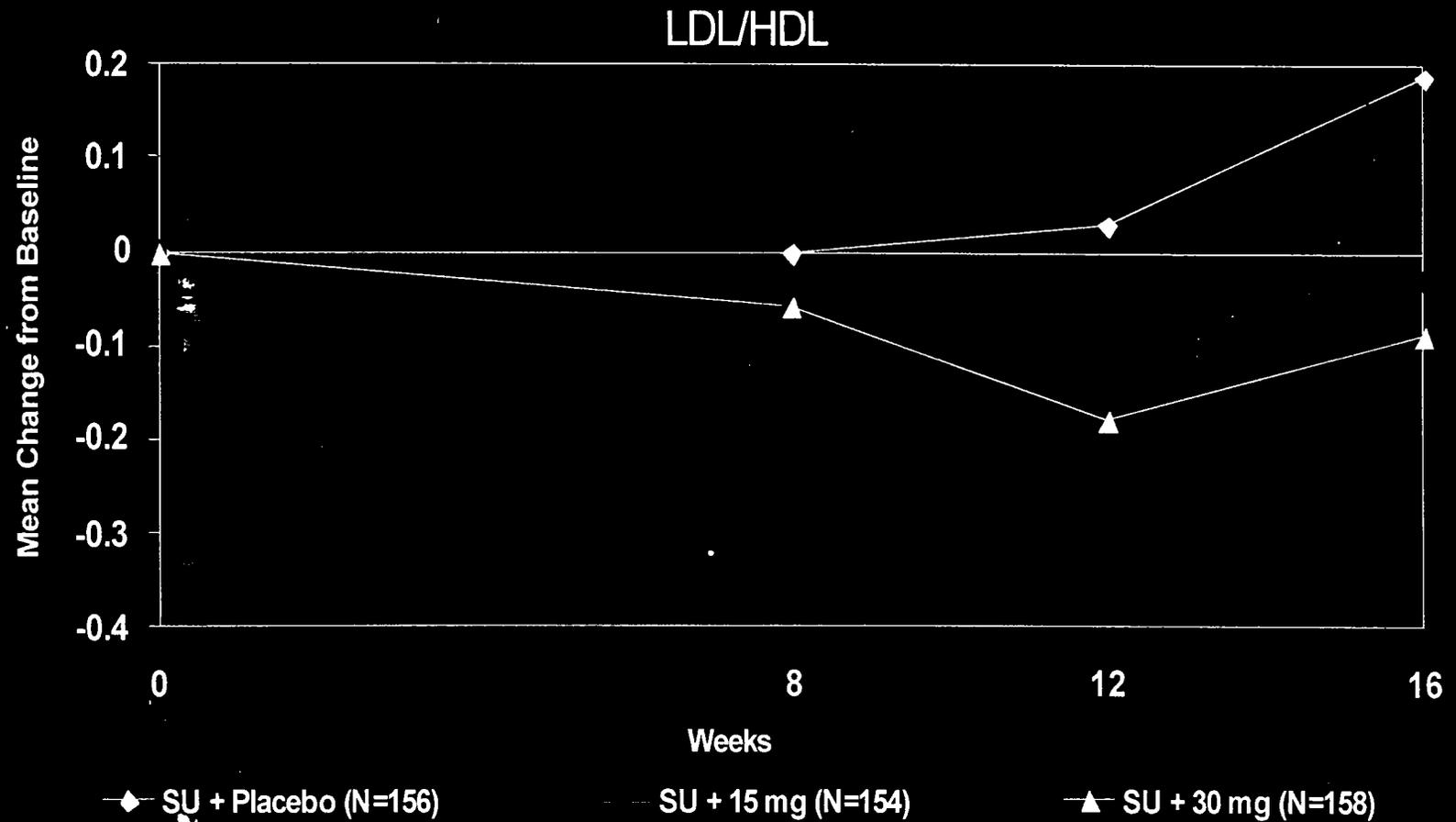
U.S. Placebo-Controlled Monotherapy Studies Study 001



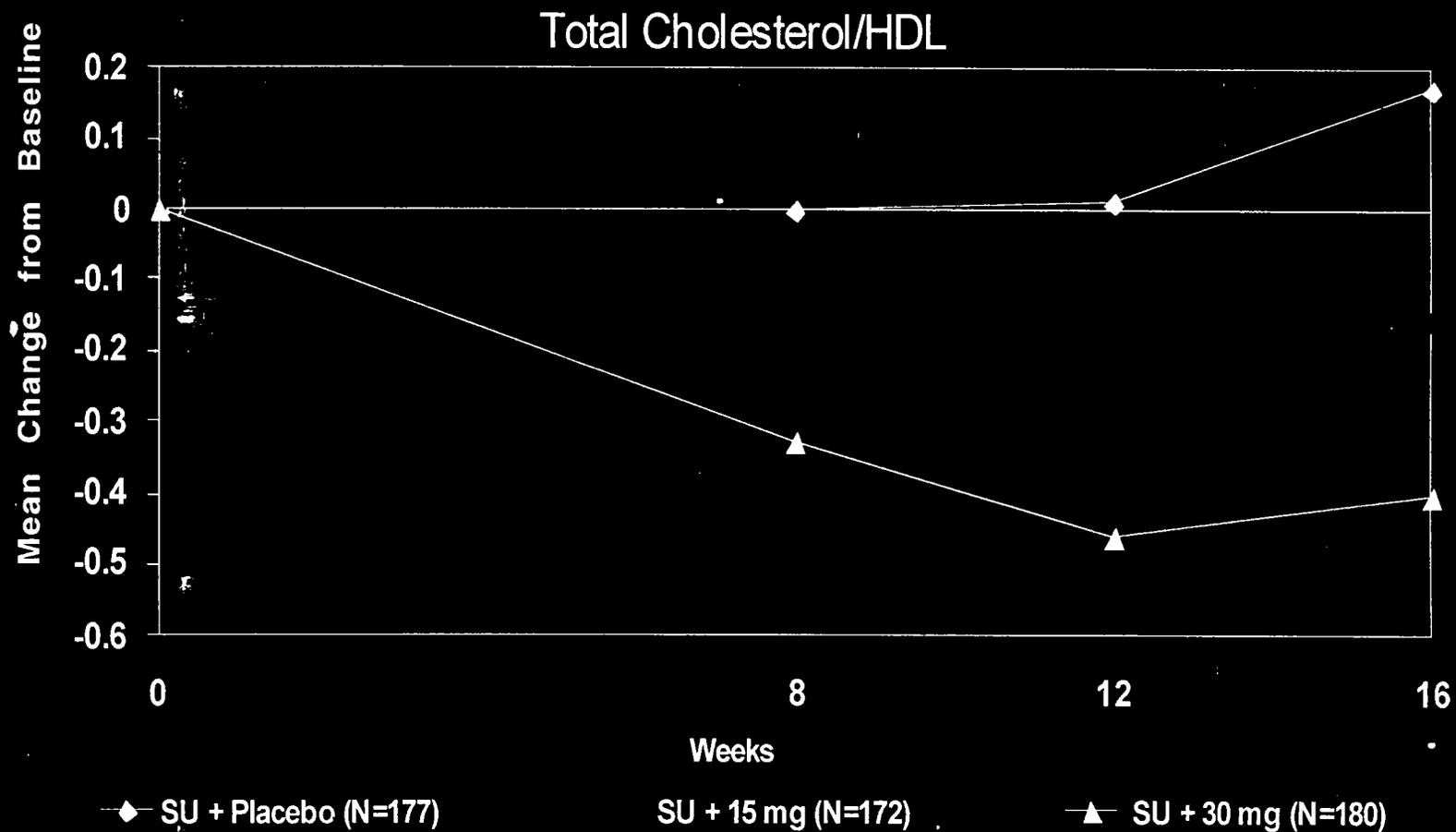
U.S. Placebo-Controlled Combination Therapy Studies Sulfonylurea



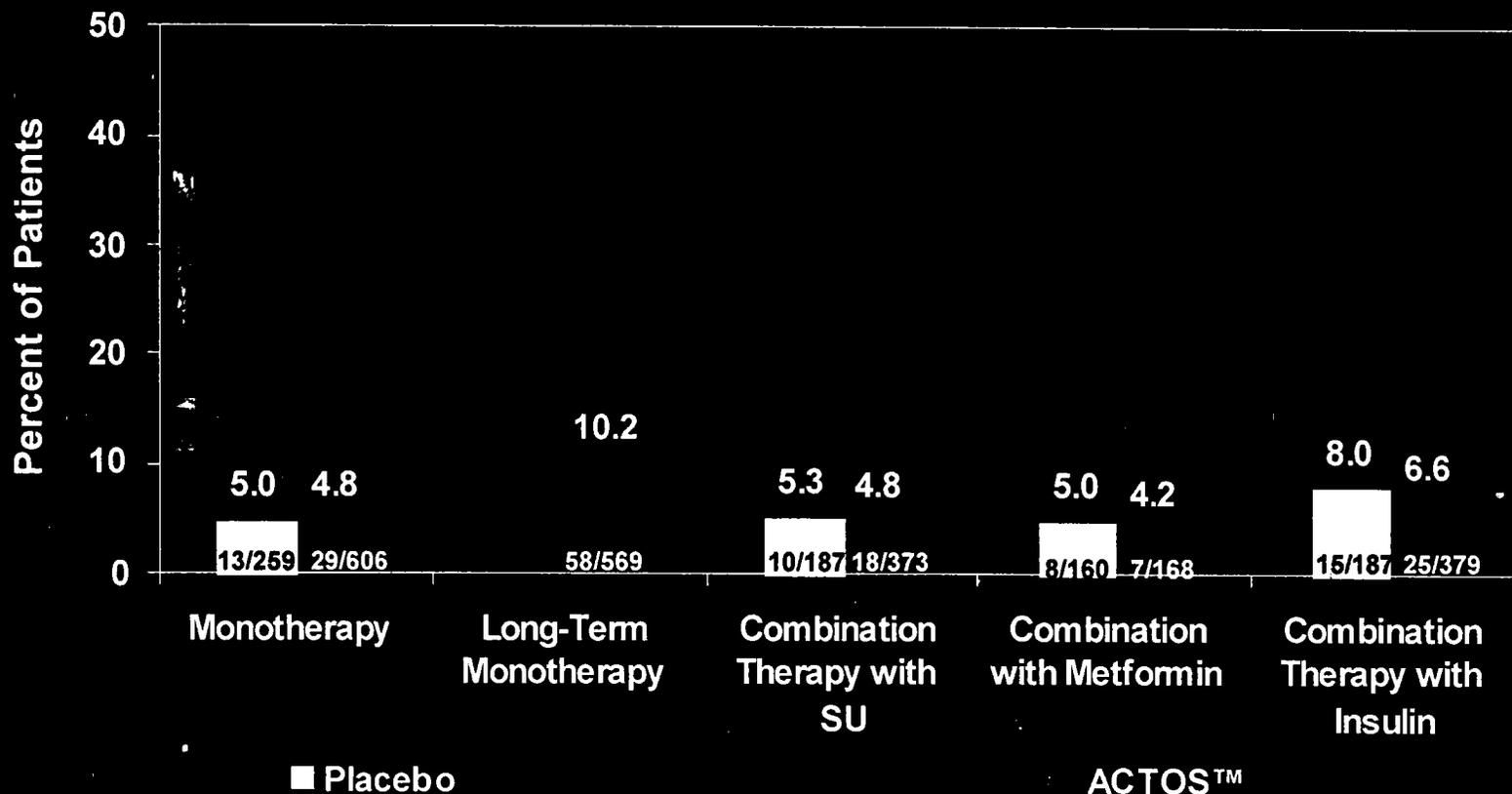
U.S. Placebo-Controlled Combination Therapy Studies Sulfonylurea



U.S. Placebo-Controlled Combination Therapy Studies Sulfonylurea



Cardiovascular Adverse Experiences



* Includes: All patients whose AE WHOART term coded to cardiovascular general, heart rate and rhythm or myocardial, endocardial, pericardial and valve disorder

Most Common CV Adverse Experiences

Monotherapy

	Placebo (N=259)		ACTOS™ (N=606)	
	N	%	N	%
ECG Abnormal	4	1.5	8	1.3
Hypertension	3	1.2	7	1.2
Coronary Artery Disorder*	5	1.9	3	0.5

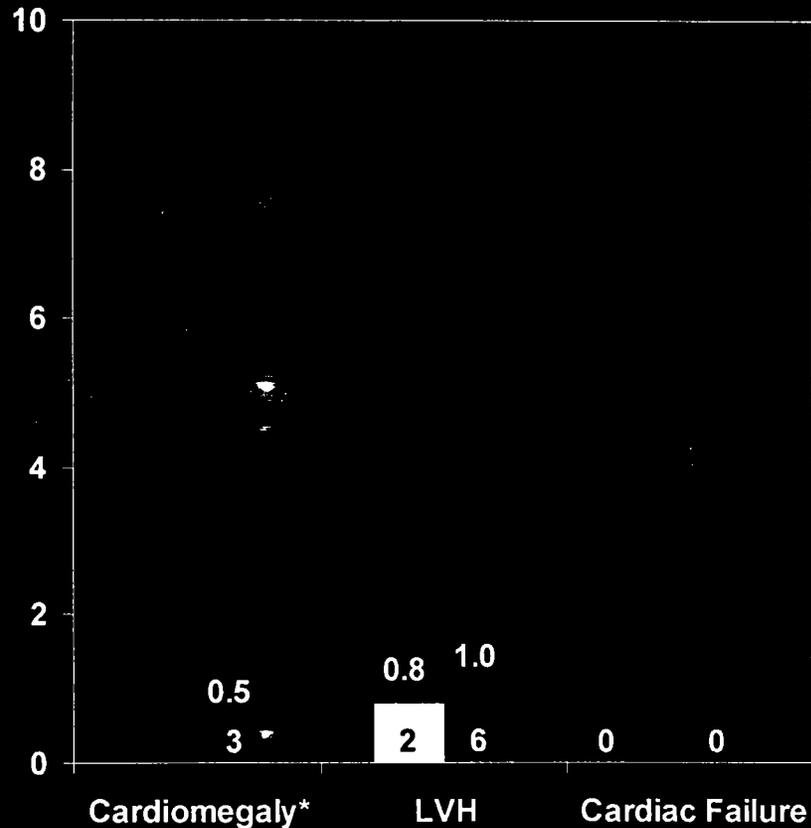
Combination Therapy

	Placebo (N=534)		ACTOS™ (N=920)	
	N	%	N	%
ECG Abnormal	8	4.5	11	2.9
Hypertension	1	0.5	3	0.8
Coronary Artery Disorder*	5	0.9	6	0.7

* Includes MI

CV Adverse Experiences of Specific Interest

Monotherapy

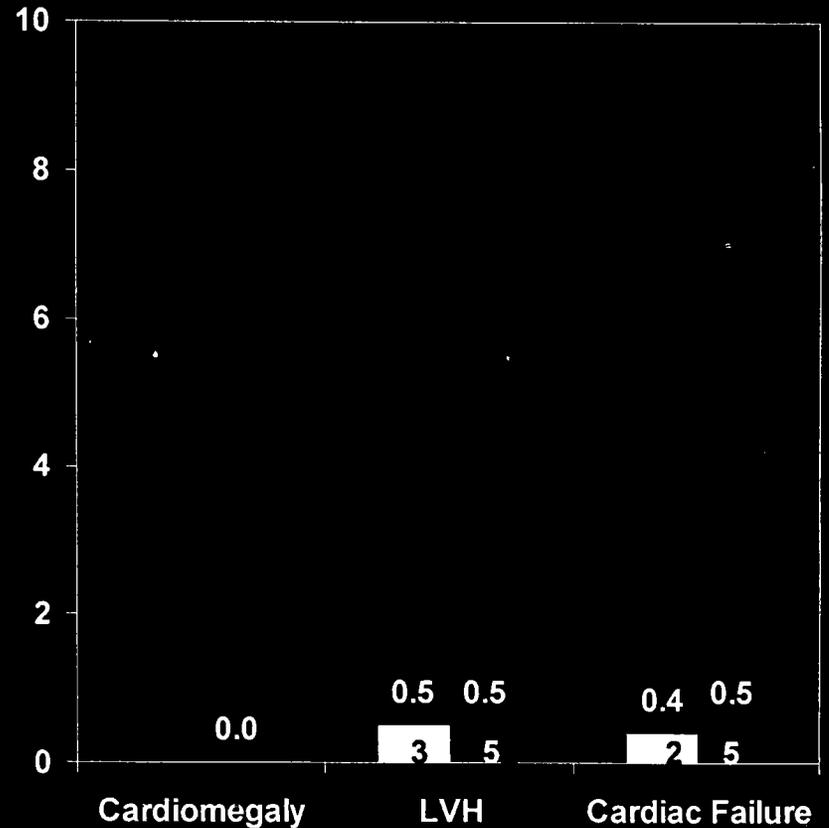


■ Placebo (N=259)

■ ACTOS™ (N=606)

*CXR diagnosis

**Combination Therapy
(SU, Metformin, Insulin)**



■ Placebo (N=534)

■ ACTOS™ (N=920)

Echocardiography Study Design

Study 001

Placebo, ACTOS™ 7.5 mg, 15 mg, 30 mg, 45 mg QD

26 w

Study 011

Rollover

ACTOS™ 7.5 mg, 15 mg, 30 mg, 45 mg, or 60 mg QD

New

ACTOS™ 7.5 mg, 15 mg, 30 mg, 45 mg, or 60 mg QD

Weeks

-8 -6

open-ended

Screen

Baseline

Treatment