

Quality of Life Outcomes: The Trial to Assess Chelation Therapy

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(QOL) Research Team and the TACT Investigators

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TACT : Background

- **Disodium ethylene diamine tetra acetic acid (EDTA) binds divalent cations (e.g., lead, calcium) and permits renal excretion**
- **Treatment of lead toxicity with EDTA in 1951**
- **Report of treatment of angina in 1956 by Clarke with ↓ sx**
- **From 1956 to the present:**
 - **Use in atherosclerotic disease expanded**
 - **Evolution of a standardized protocol that included disodium EDTA, ascorbate, B-vitamins, and other components**
 - **Used clinically by chelation practitioners**
 - **Chelation discouraged by traditional professional societies**

TACT: Design Overview

1,708 post-MI pts

- Age ≥ 50
- MI ≥ 6 mos prior to randomization

134 sites
(US, CN)

double-blind 2x2 trial

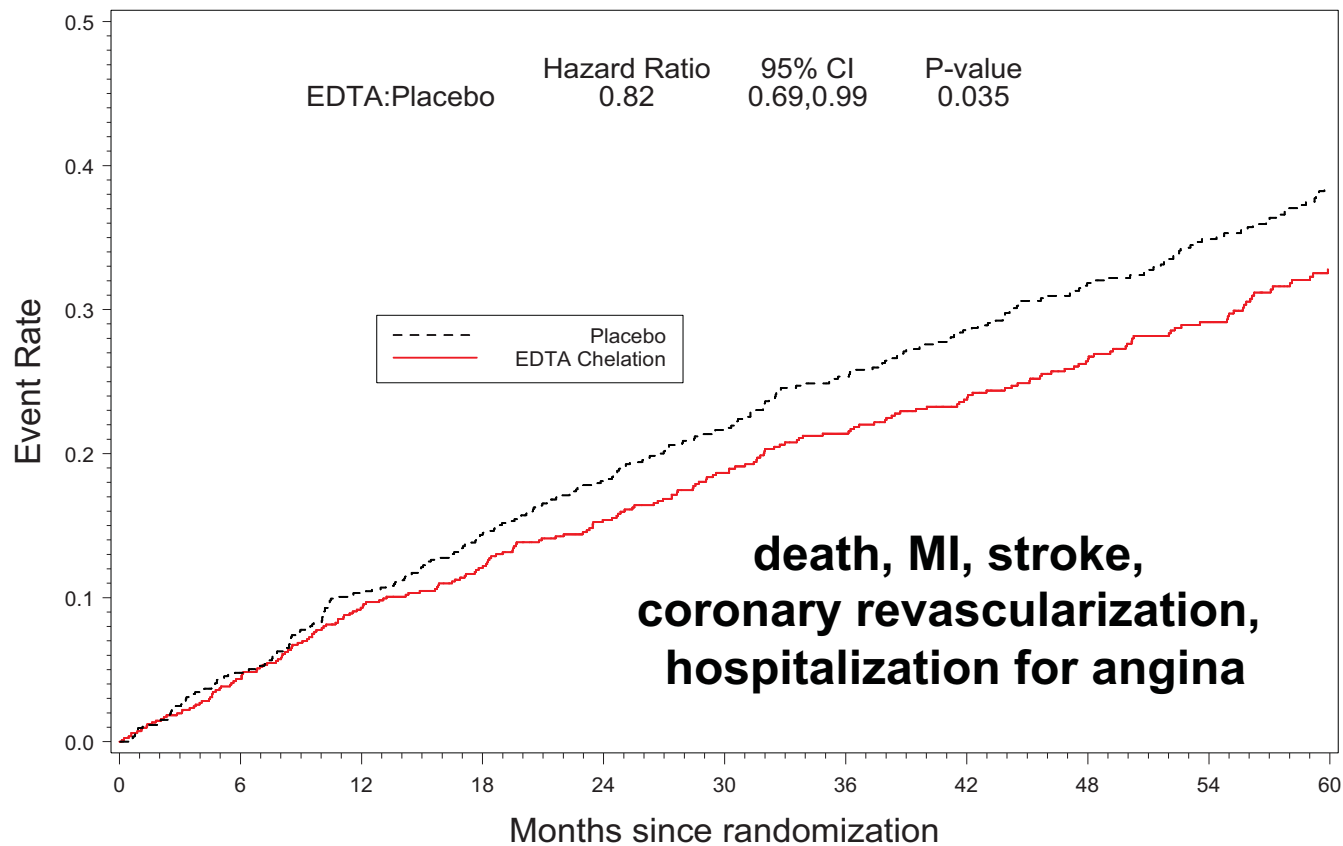
Chelation + high-dose vitamins	Chelation placebo + high-dose vitamins
Chelation + vitamin placebo	Chelation placebo + vitamin placebo

Mean study follow-up 55 mos

1° endpoint: composite of total mortality, recurrent MI, stroke, coronary revascularization, or hospitalization for unstable angina

2° endpoints incl.: **quality of life outcomes**

TACT 1° Clinical Endpoint



Number at Risk		0	6	12	18	24	30	36	42	48	54	60
EDTA Chelation	839	760	703	650	588	537	511	476	427	358	229	
Placebo	869	776	701	638	566	515	475	429	384	322	205	

TACT Quality of Life Study: Primary Objective

- **To determine whether chelation therapy significantly improves physical functioning and psychological well-being in stable CAD patients with a history of MI**

TACT QOL Study: Quality of Life (QOL) Methods Overview

- **911 (53%) of 1708 main TACT pts randomly selected for QOL substudy**
- **QOL structured interviews at baseline, 6 mos, 12 mos, and 24 mos**
- **All baseline questionnaires were collected by site coordinators who were trained by DCRI Outcomes Group**
- **Follow-up interviews were conducted via telephone by DCRI Outcomes Group**
- **97% of expected QOL contacts collected**

TACT QOL Substudy: Primary QOL Outcome Measures

- **DASI** - cardiac-related functional status.
 - Scores: 0 (worst) to 58 (best), reflect the ability of patients to do physical activities without difficulty or assistance in 12 domains.
 - For an individual pt, a clinically significant change is ≥ 4 points.
- **MHI-5** - psychological well-being, including both depression and anxiety.
 - Scores: normalized to 50 ± 10 .
 - A clinically significant change for an individual patient is approximately ≥ 2.5 points.
- **Other measures: SAQ (frequency, stability, QOL), SF-36, EQ-5D**

TACT QOL: Analysis Methods

- All primary comparisons by intention to treat
- Follow-up QOL comparison p values adjusted for vitamin group and baseline QOL scores
- No adjustment was made in significance levels for multiple comparisons.

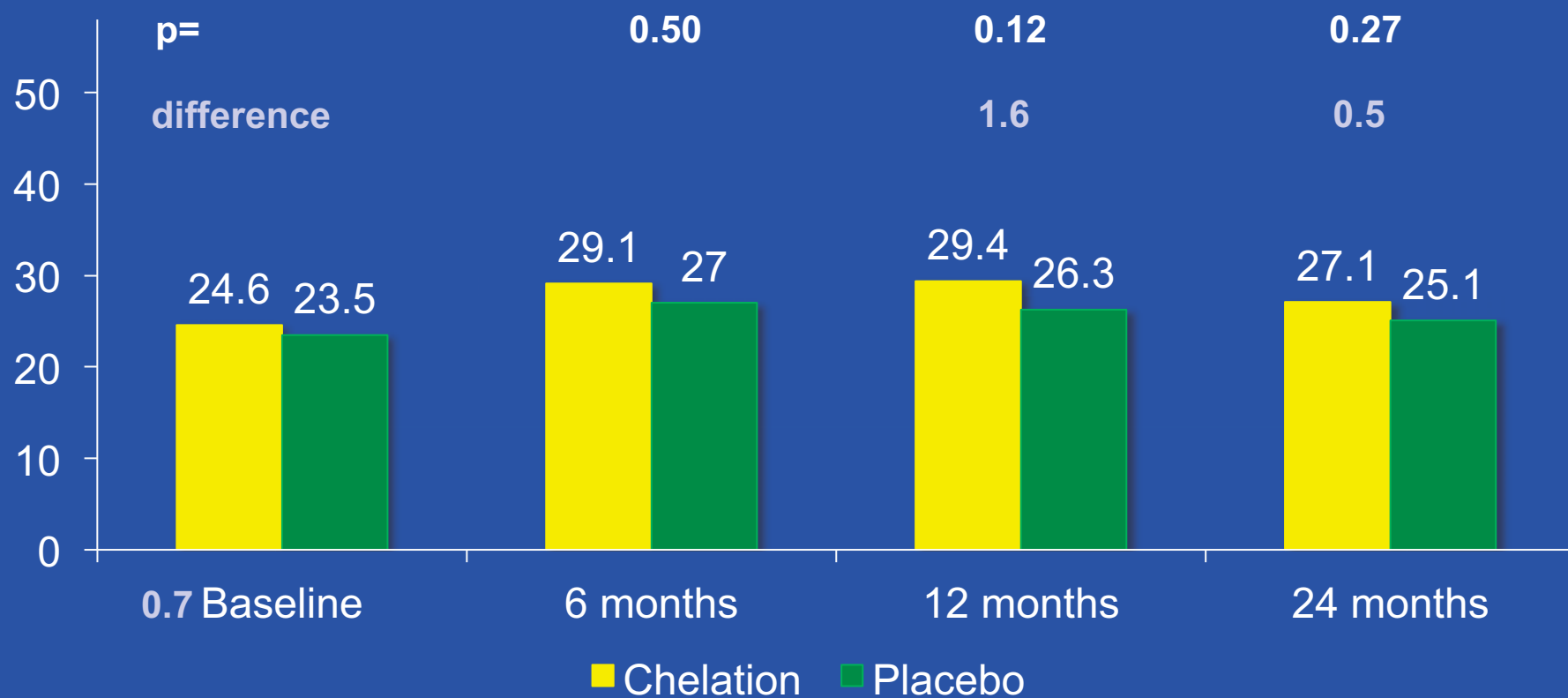
TACT QOL Baseline Characteristics

	Chelation (n=451)	Placebo (n=460)
Age (median)	64 (58 to 71)	65 (58 to 72)
Female	19%	19%
Race, nonwhite	6%	8%
Current NYHA Class		
None	80%	80%
I	12%	12%
II	7%	7%
III	1%	2%
Current CCS Angina Class		
None	79%	79%
I	10%	9%
II	7%	10%
III	3%	2%
IV	<1%	<1%
Diabetes	32%	35%

TACT QOL Outcomes

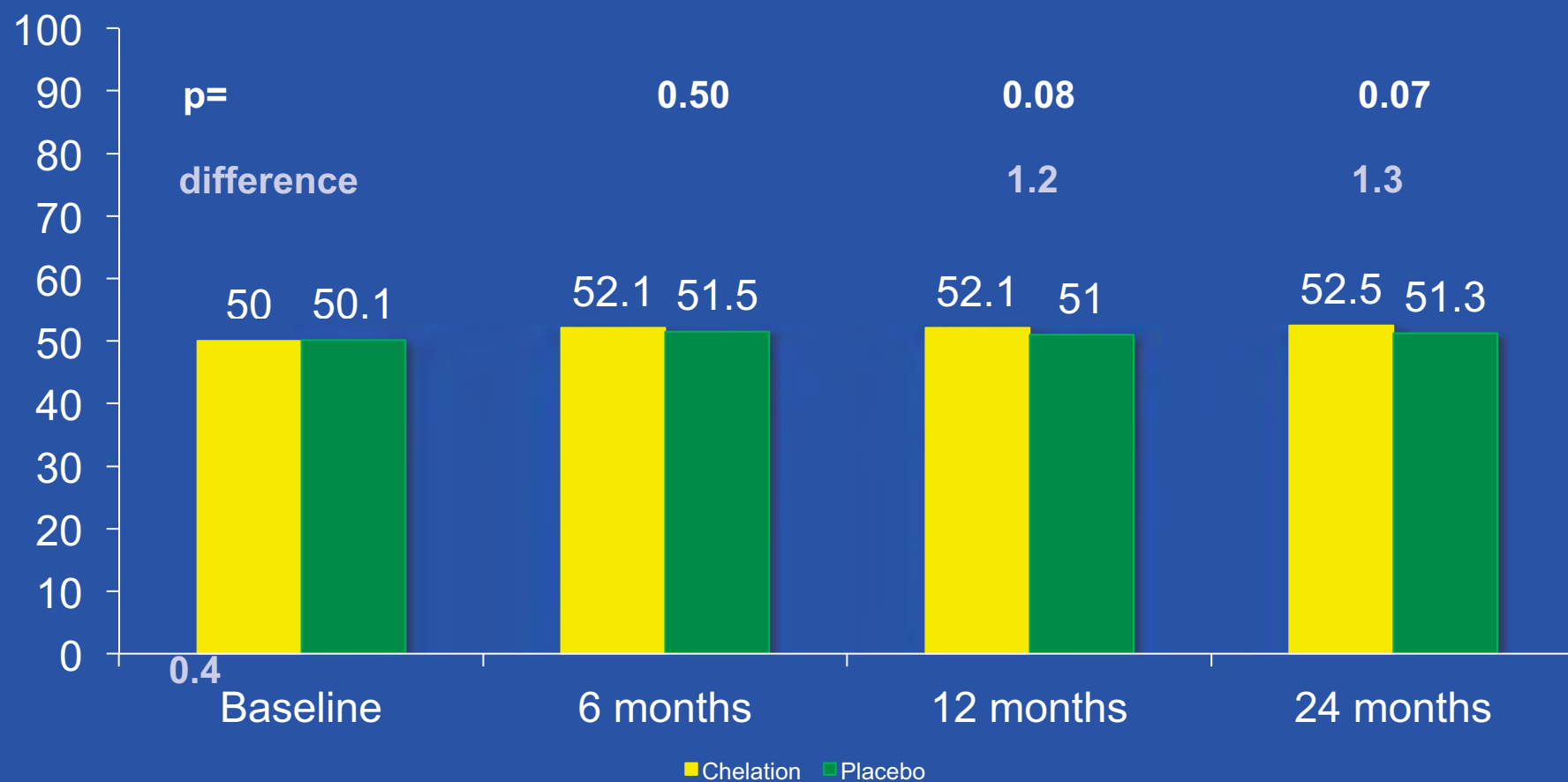
DASI

0-58 scale, with higher scores indicating more favorable cardiac physical functioning



TACT QOL Outcomes

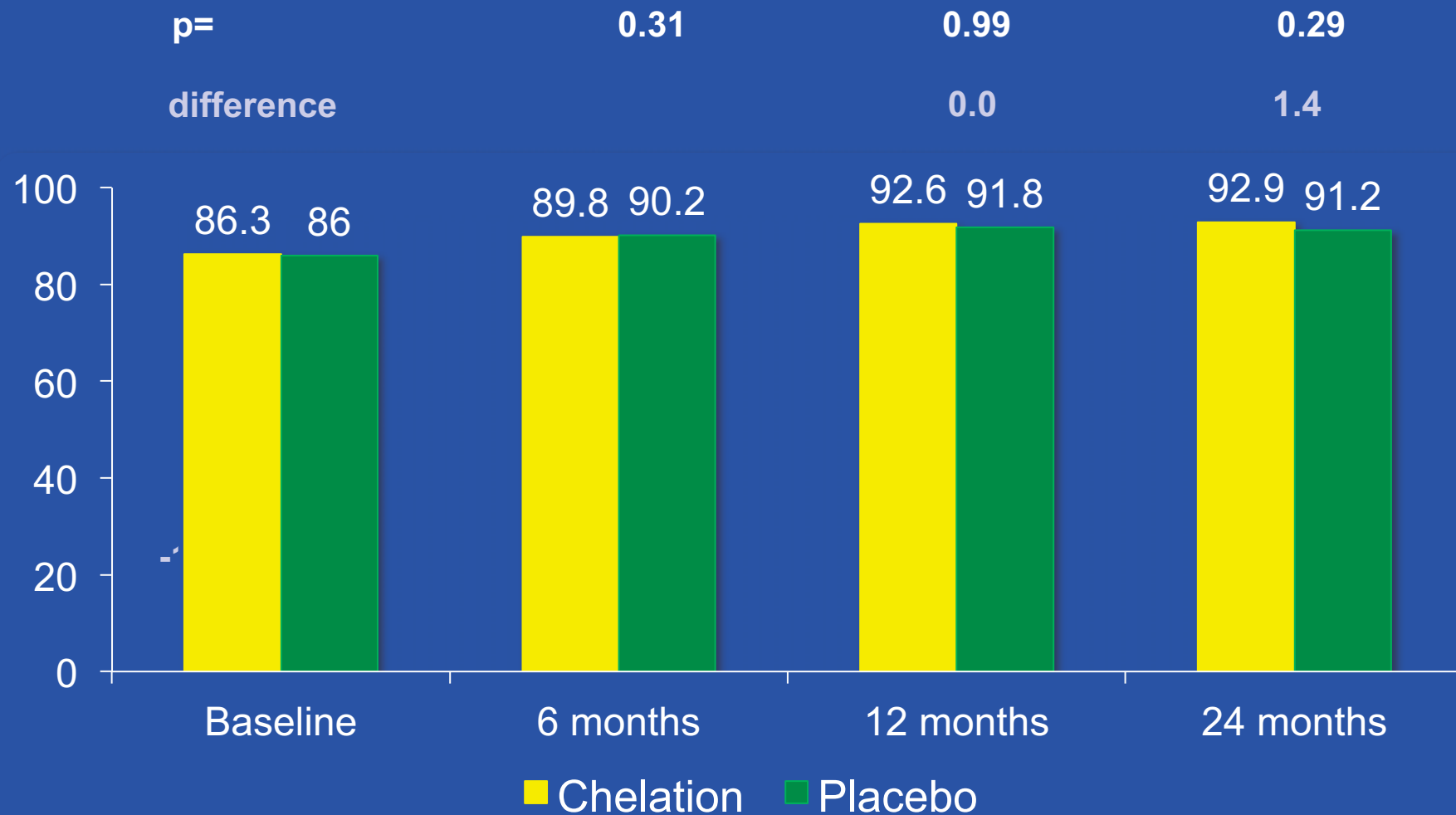
SF-36 MHI-5



Scaled to a norm of 50, SD 10

TACT QOL Outcomes

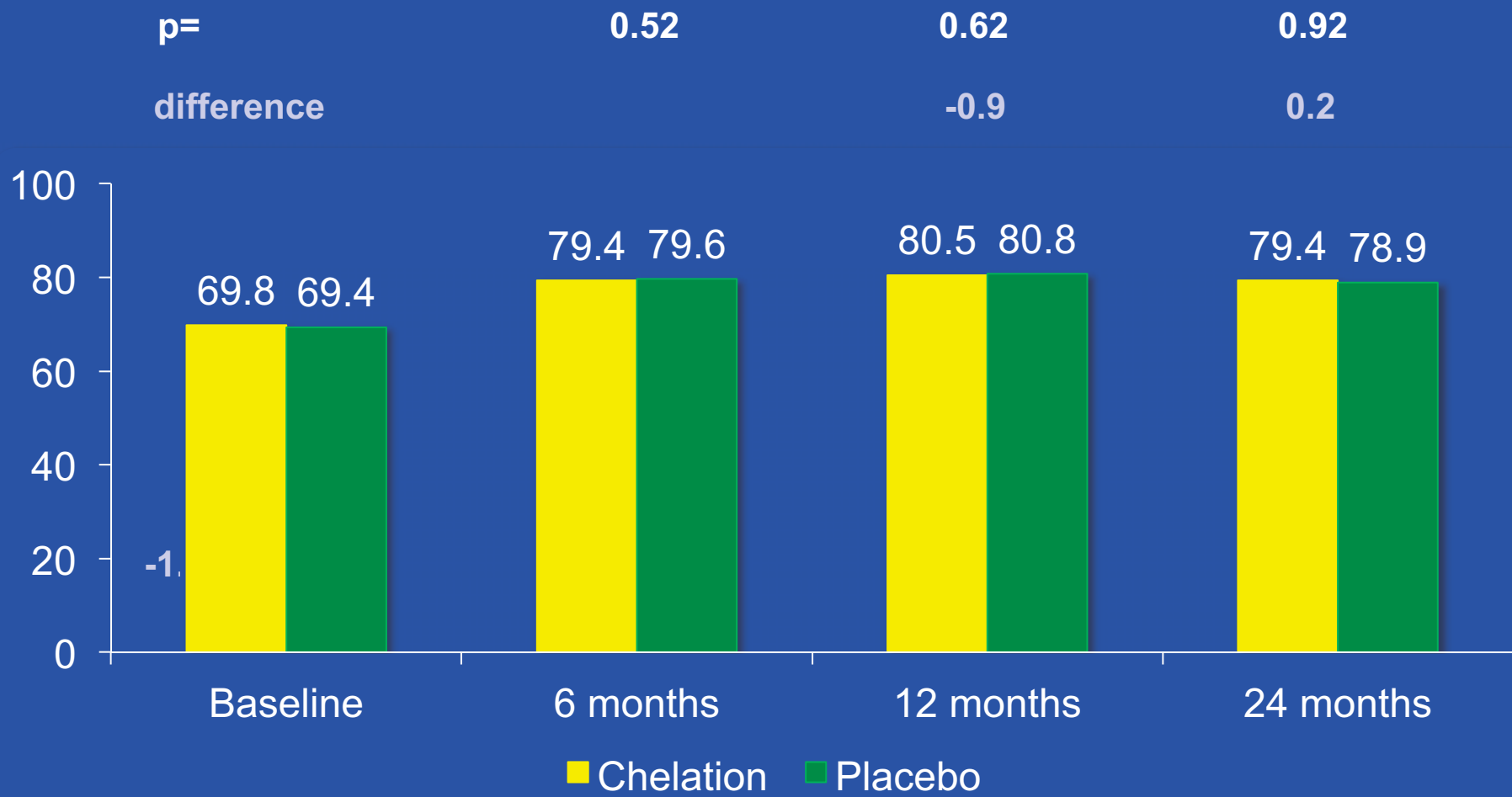
Seattle Angina Questionnaire – Anginal Frequency



Higher scores = less frequent angina

TACT QOL Outcomes

Seattle Angina Questionnaire – Quality of Life



Higher scores = better quality of life

TACT QOL Outcomes: Subgroup Analyses

- **None of the prespecified subgroups showed a treatment effect on QOL**
- **Pts with angina sx at baseline showed a tx effect at 1 year in favor of chelation therapy (4.99 points, $p=0.019$), but not at other time points or overall**
- **No tx effect was seen in pts with heart failure sx at baseline**

TACT QOL Outcomes: Caveats

- **Trial population was largely asymptomatic at baseline (ceiling effect for some measures incl. anginal QOL)**
- **QOL assessment follow-up was limited to 2 years, 1° clinical outcomes show continued divergence favoring chelation out to 5 years**

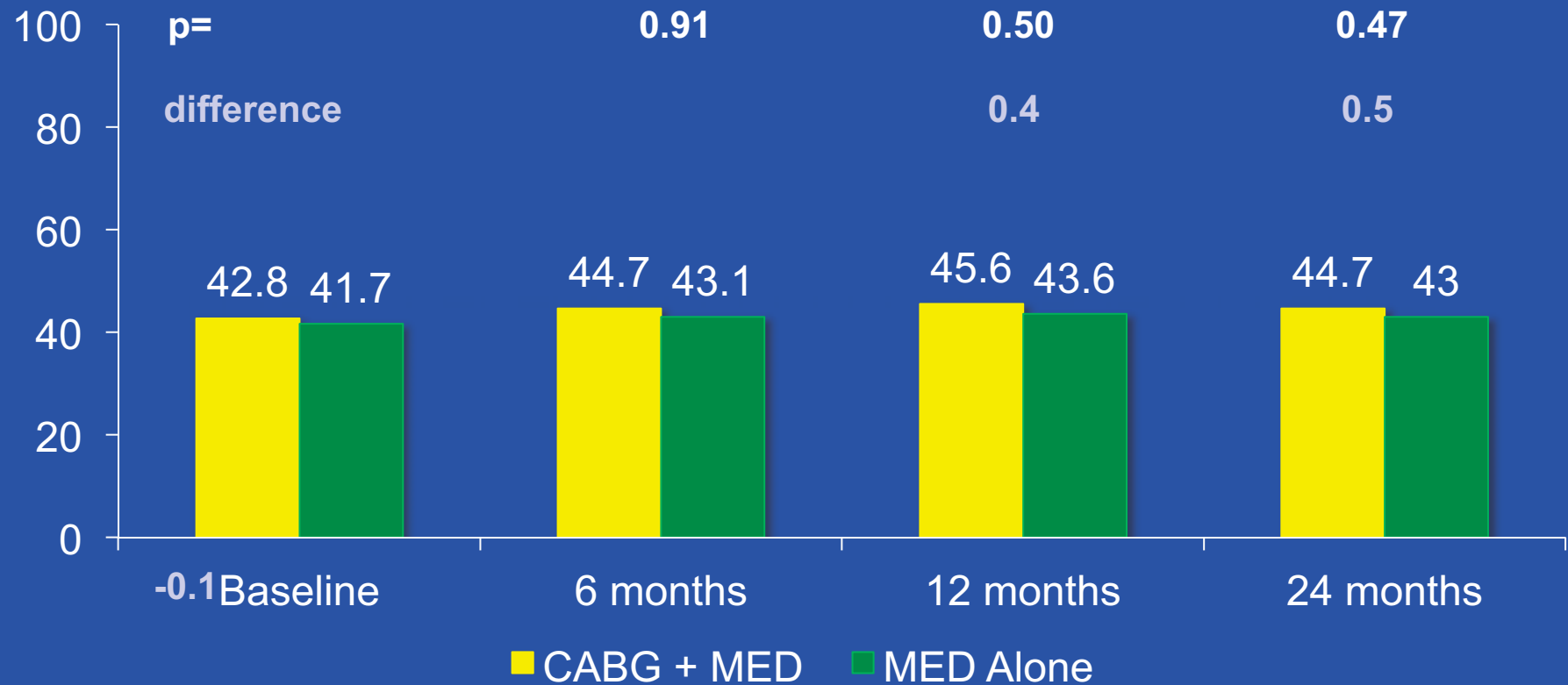
TACT QOL Outcomes: Summary

- **In a population of stable, predominantly asymptomatic CAD patients with a history of prior MI, the use of EDTA chelation therapy did not produce a consistent sustained improvement in any domain of health-related quality of life.**



TACT QOL Outcomes

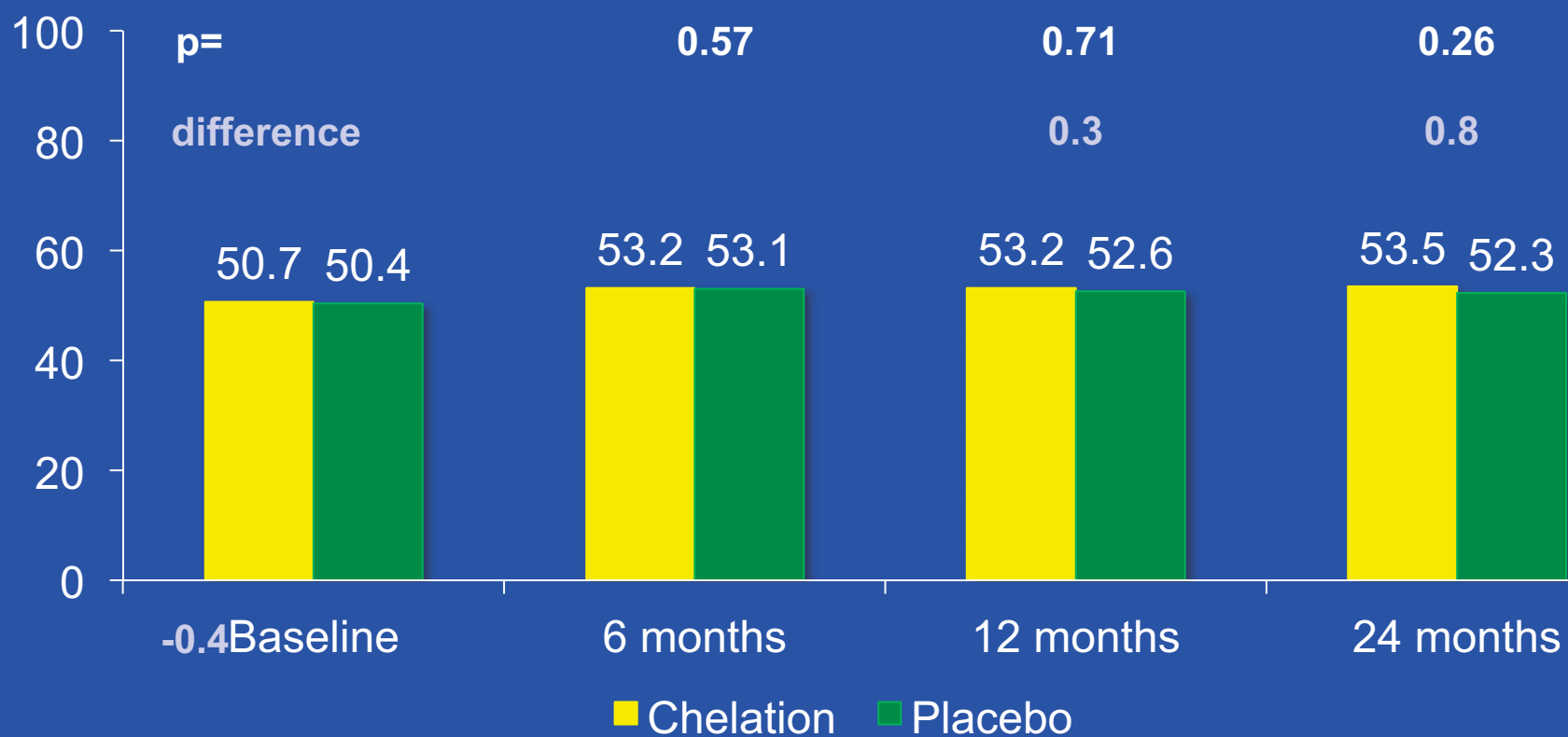
SF-36 Physical Component Summary



Scaled to a norm of 50, SD 10

TACT QOL Outcomes

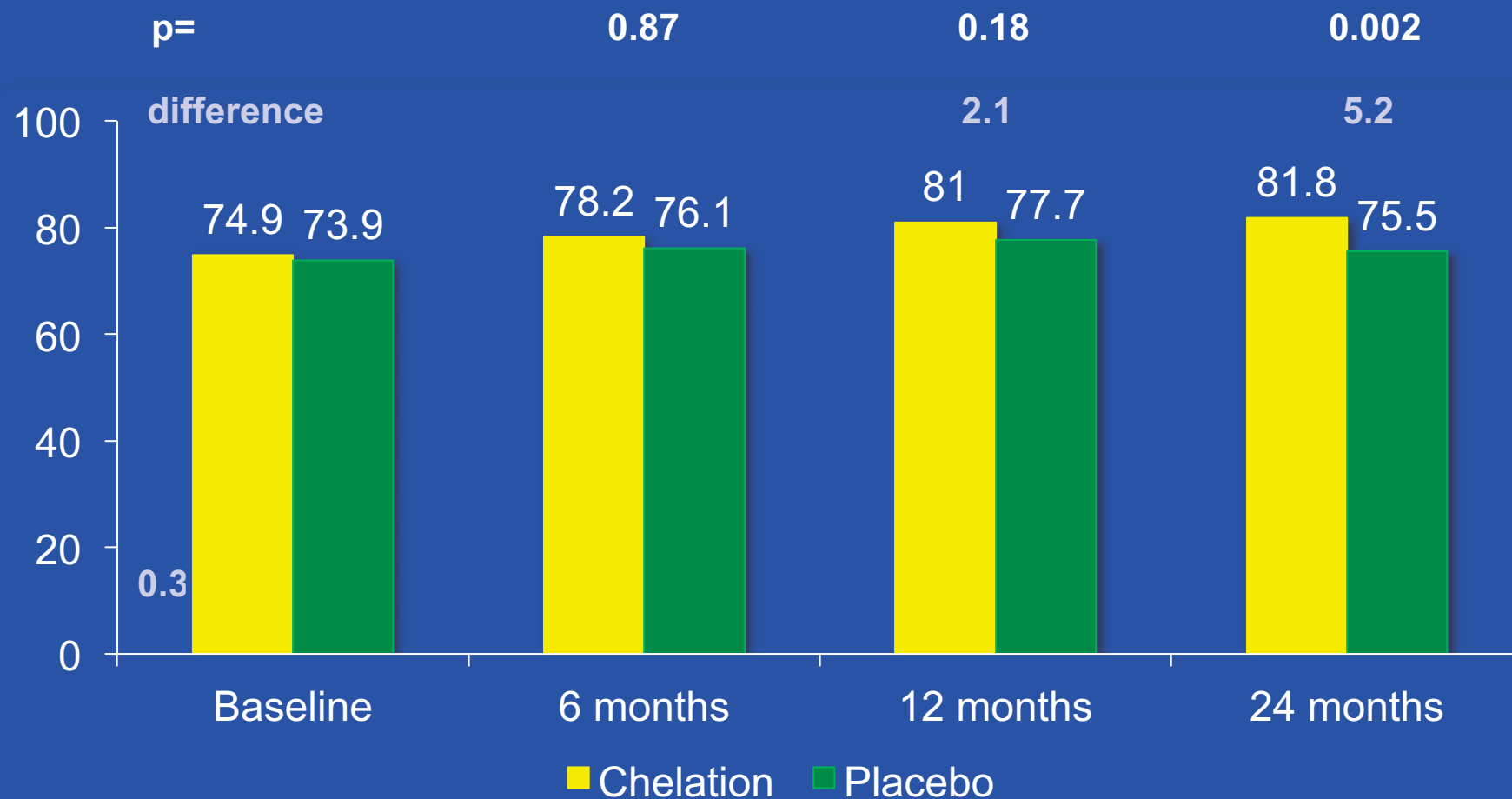
SF-36 Mental Component Summary



Scaled to a norm of 50, SD 10

TACT QOL Outcomes

EQ-5D Single Summary Index



Relative desirability of patient's current health status

TACT QOL Outcomes: Clinically Significant Improvement in DASI from Baseline

