

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

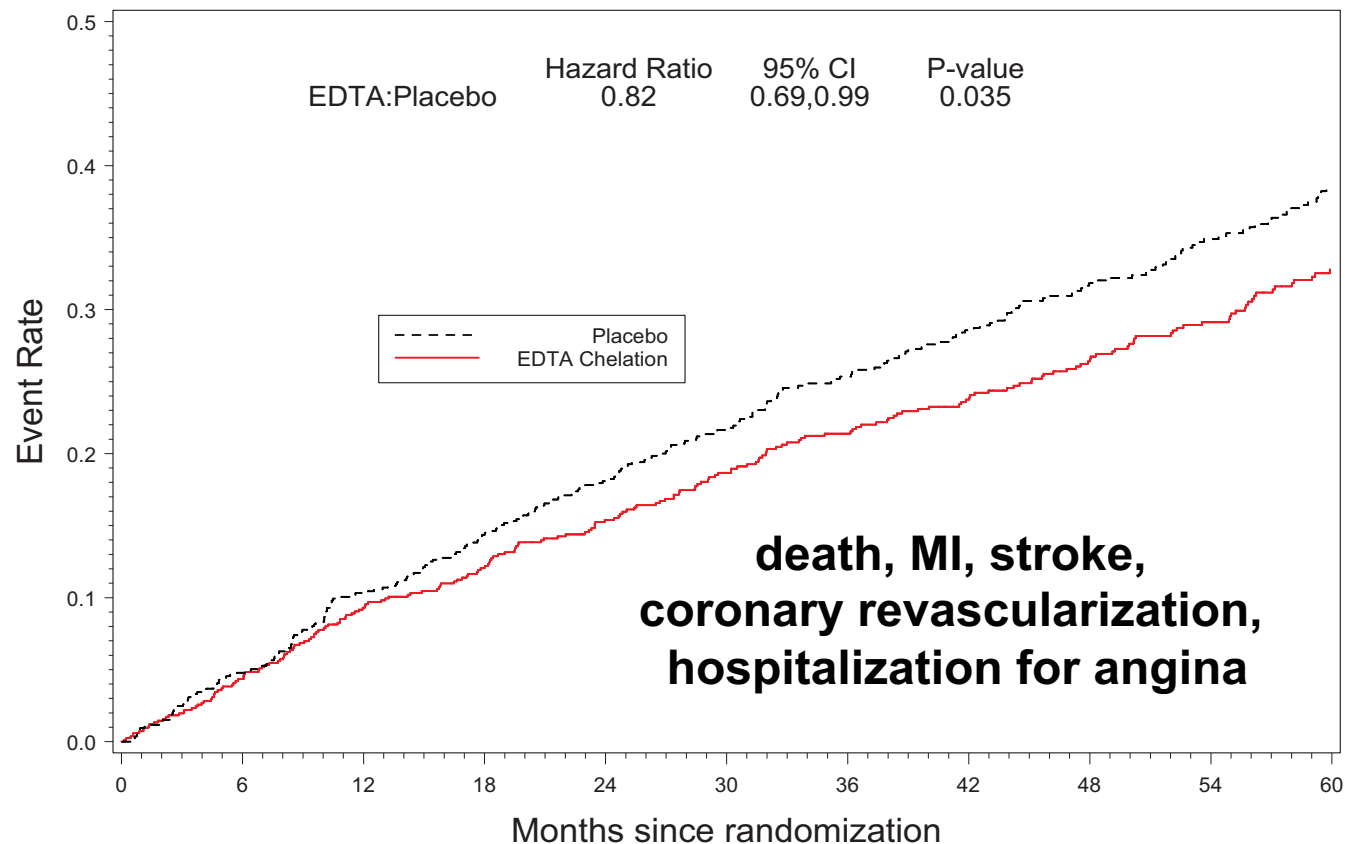
Chelation + high-dose vitamins	Chelation placebo + high-dose vitamins
Chelation + vitamin placebo	Chelation placebo + vitamin placebo

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											
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

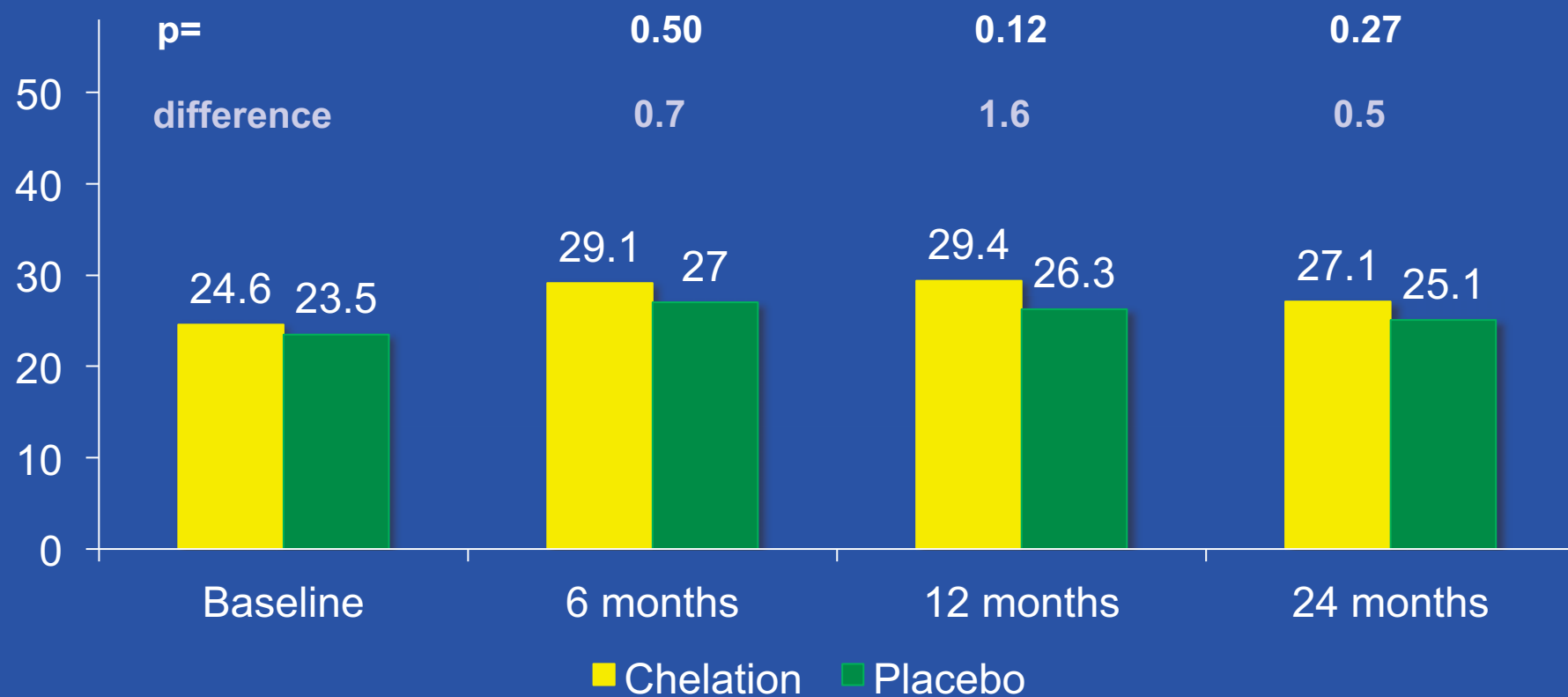
- All primary comparisons by intention to treat
- Follow-up QOL comparison p values adjusted for vitamin group and baseline QOL scores
- No adjustment was made in significance levels for multiple comparisons.

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%

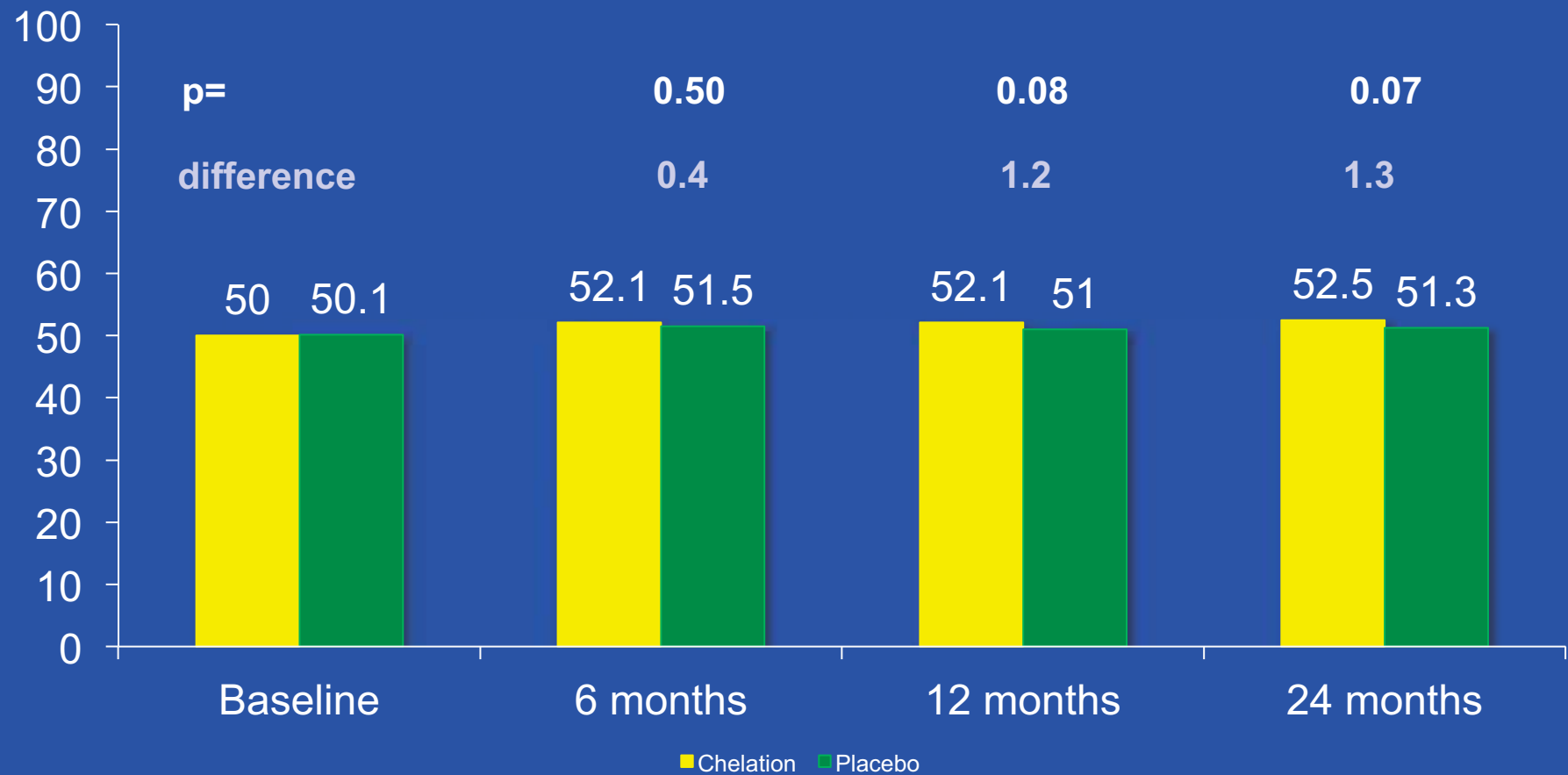
TACT QOL Outcomes DASI

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



TACT QOL Outcomes

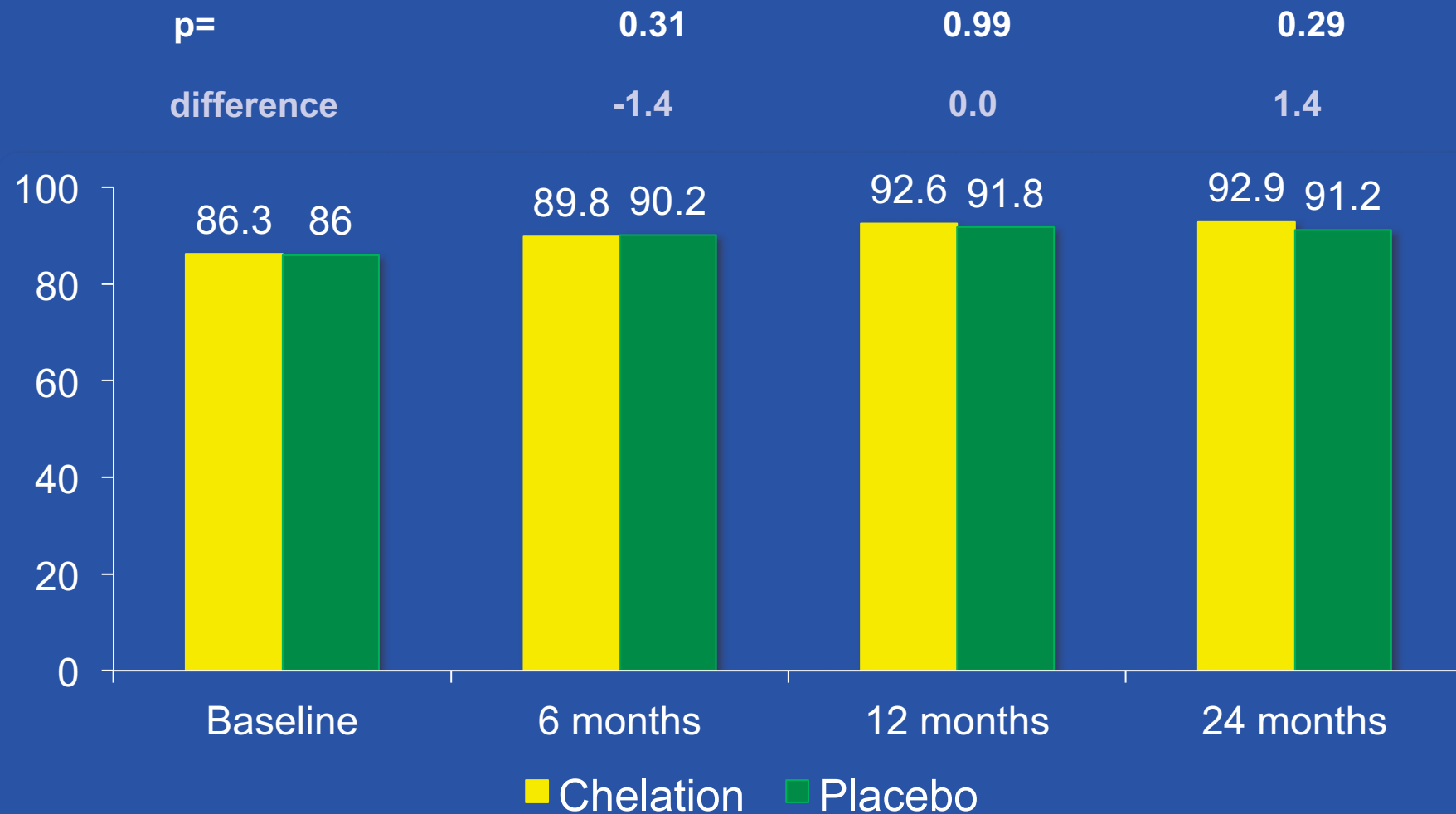
SF-36 MHI-5



Scaled to a norm of 50, SD 10

TACT QOL Outcomes

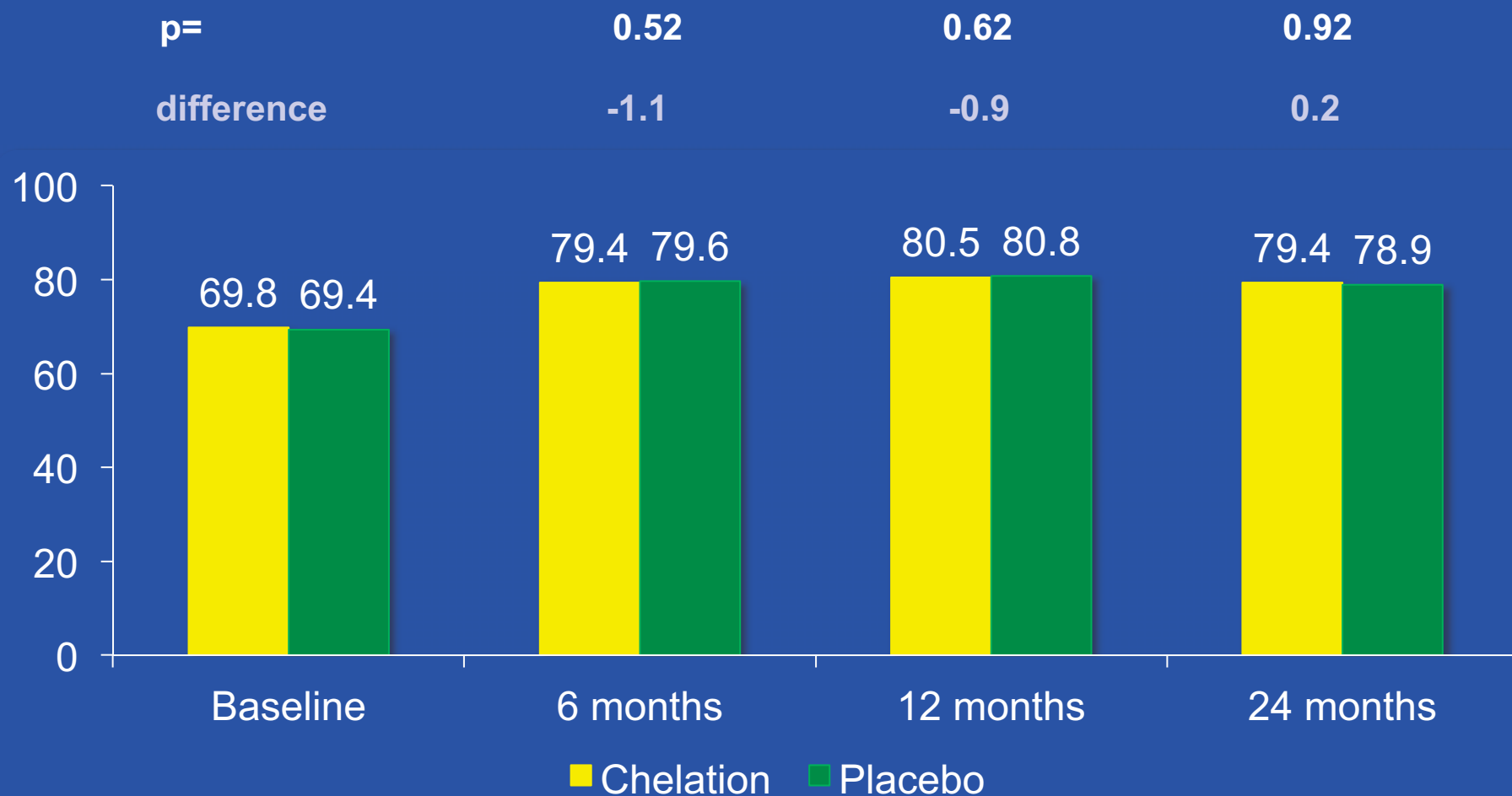
Seattle Angina Questionnaire – Anginal Frequency



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

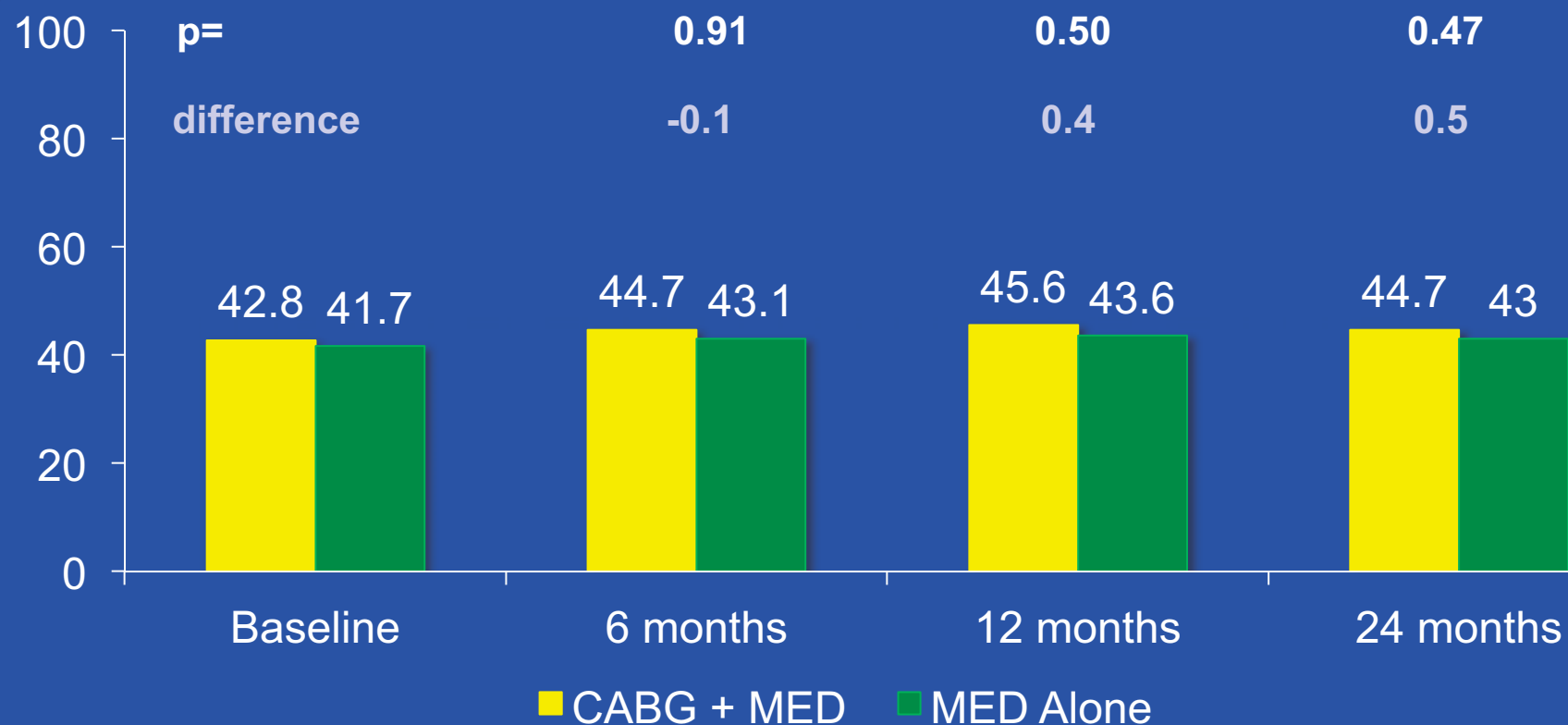
TACT QOL Outcomes: Summary

- **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

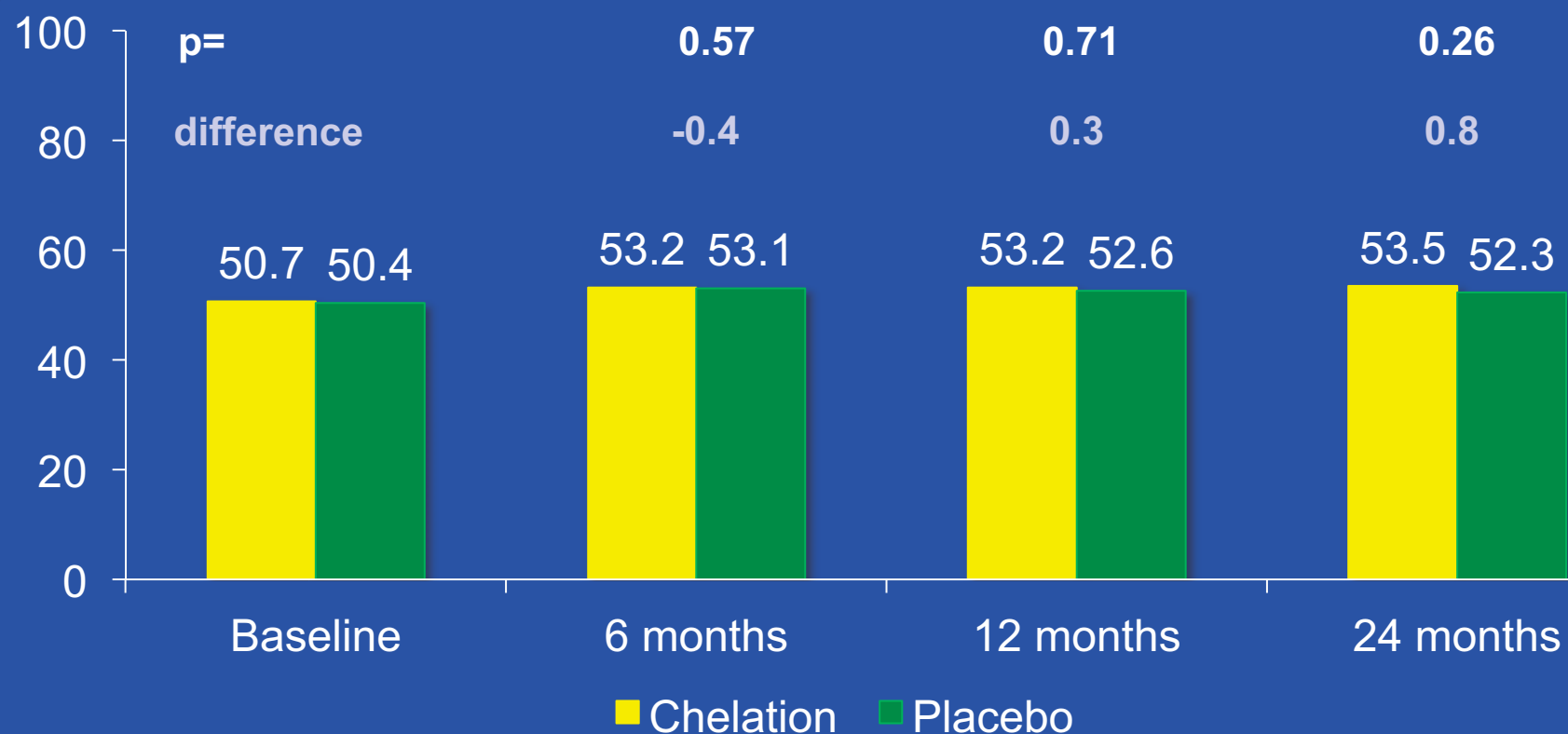
SF-36 Physical Component Summary



Scaled to a norm of 50, SD 10

TACT QOL Outcomes

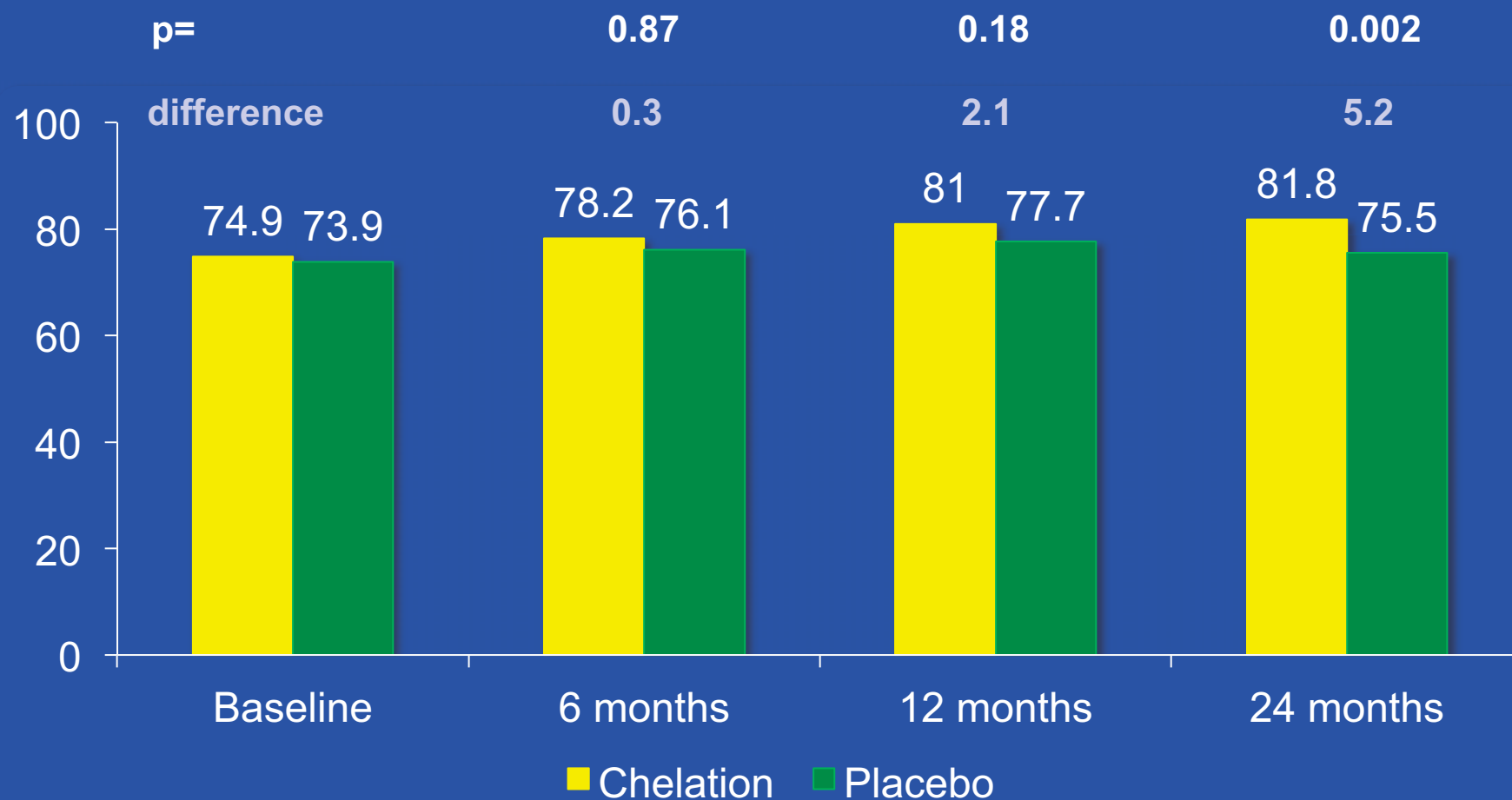
SF-36 Mental Component Summary



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

