

Quality of Life in the Catheter Ablation Versus Antiarrhythmic Drug Therapy for Atrial Fibrillation (CABANA) Trial



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MAYO CLINIC



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Declaration of interest

- Consulting/Royalties/Owner/ Stockholder of a healthcare company (Consulting - CeleCor)
- Research contracts (Eli Lilly & Company, AstraZeneca, Oxygen Therapeutics)
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CABANA Quality of Life Study: Background

- **Ablation for AF has been shown to improve QOL over drug therapy but evidence to date consists of studies with limited sample sizes, short follow-up (typically ≤ 1 year)**
- **A major secondary goal of the CABANA research program was to examine the long-term pattern of QOL with ablation versus drug therapy**

CABANA: Design Overview

2204 symptomatic pts w/ new onset or under-treated paroxysmal, persistent, or longstanding persistent AF

- ≥ 65 years of age or < 65 years of age with ≥ 1 CVA risk factor
- Eligible for ablation and ≥ 2 rhythm or rate control drugs

126 centers
(10 countries)

1:1 Randomization (open label)

Ablation Therapy

- Primary ablation (PVI, WACA)
- Ancillary ablation (Linear lesions, CFAE, GP)
- Guideline-based anticoagulation

Drug Therapy

- Rhythm control or
- Rate control
- Guideline-based anticoagulation

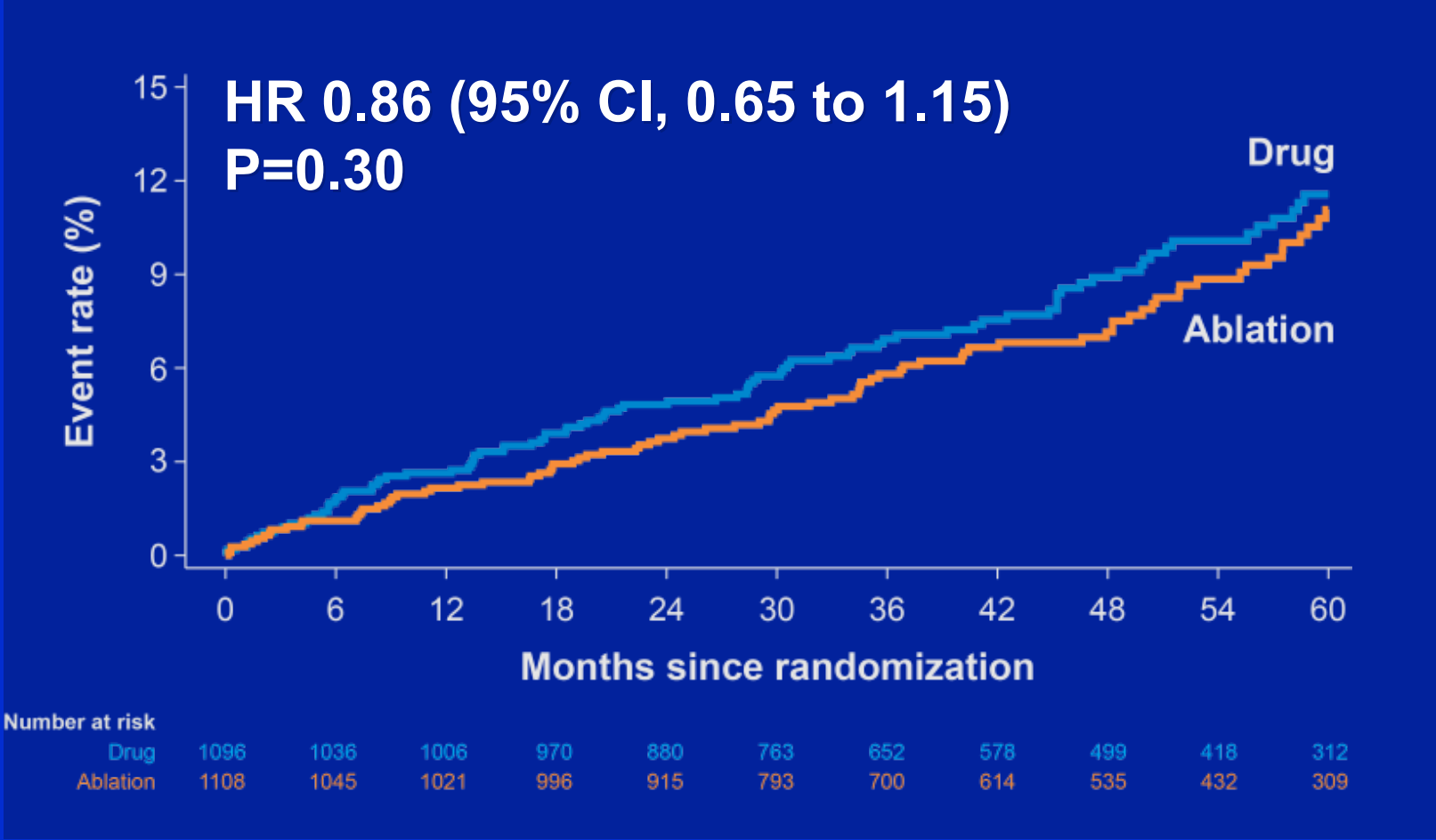
Median study follow-up 48.5 months

Clinical composite 1° endpoint: death, disabling stroke, serious bleeding, or cardiac arrest

2° endpoints incl.: quality of life outcomes

CABANA Primary Composite Endpoint: Death, Disabling Stroke, Serious Bleeding, or Cardiac Arrest

Intention to Treat (ITT)



Per Protocol (PP)
(Prespecified)
HR 0.73 (0.54,0.99)

As Treated
(Prespecified)
HR 0.67 (0.50,0.89)

CABANA Quality of Life (QOL) Study

Major Domains Assessed and Instruments Used

QOL Domains

- **AF symptoms**
- **AF-related QOL**
- **General health perceptions**
- **Physical functioning**
- **Psychological well-being**
- **Role and social functioning**

QOL Instruments

- **MAFSI**
 - **AFEQT**
 - **SF-36, EQ-5D**
 - **DASI, SF-36**
 - **SF-36 scales**
 - **SF-36 scales**
- Prespecified co-primary endpoints

CABANA Quality of Life Study

Data Collection

QOL Questionnaire Administration by Structured Interviews

- Enrolling sites did baseline interviews
- DCRI Call Center did follow-up telephone interviews in N. America
- Enrolling sites did follow-up interviews outside N. America

Data Completeness

- QOL data were collected for 92% of eligible patients at 12 months and 81% at 60 months

CABANA QOL Outcomes:

Analysis Methods

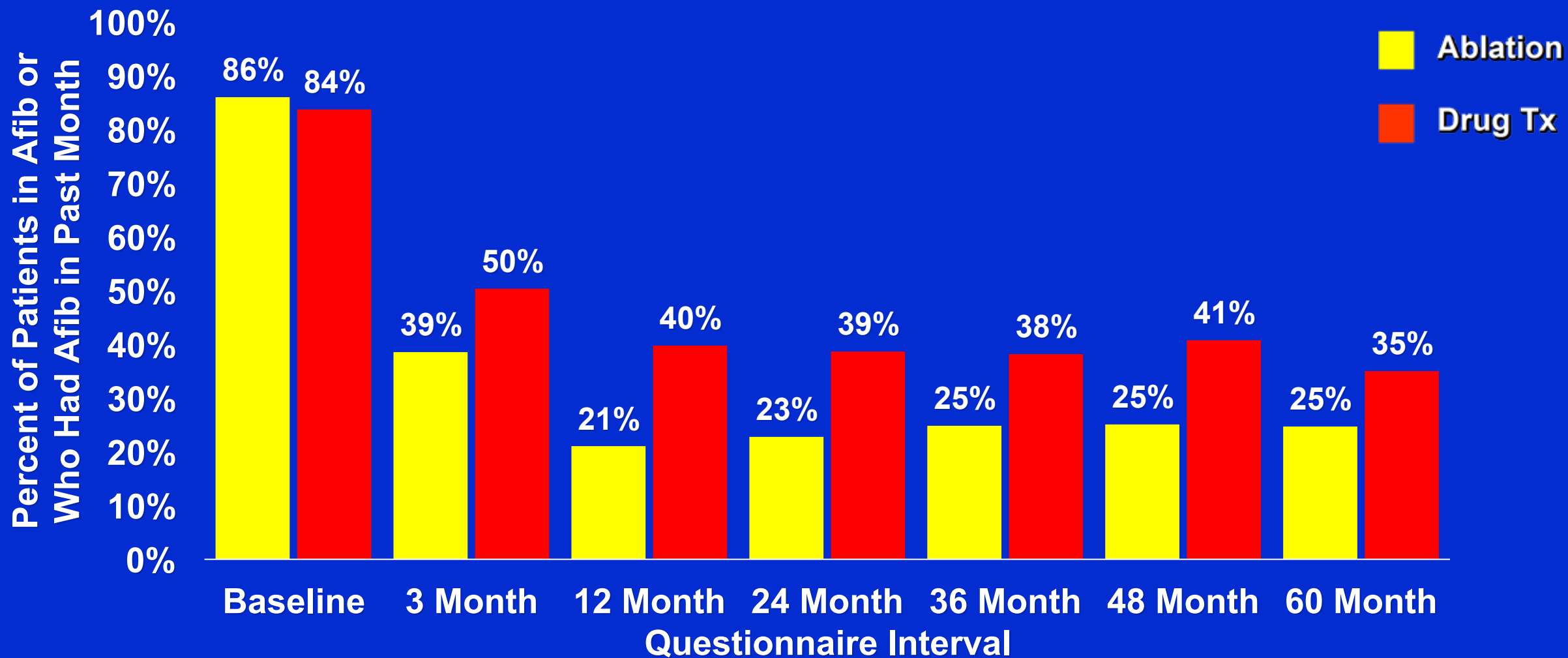
- **Primary comparisons using tx group assignment defined by intention-to-treat (ITT)**
- **Mixed-effects regression models used to account for repeated measures within a patient, adjusted for Rx group, time point (3 mos, 12 mos, 24 mos, 36 mos, 48 mos, 60 mos), baseline QOL**
- **MAFSI and AFEQT Overall Score at 12 months prespecified co-primary endpoints**

CABANA:

Select Baseline Characteristics

	Ablation (N=1108)	Drug Rx (N=1096)
Age, median (Q1, Q3)	68 (62, 72)	67 (62, 72)
Female	37%	37%
Minority	10%	10%
CHF	16%	15%
Prior CVA/TIA	11%	9%
AF		
Paroxysmal	42%	44%
Persistent	47%	47%
Longstanding Persistent	10%	9%
Years since AF onset, median (Q1, Q3)	1.1 (0.3, 4)	1.1 (0.3, 3.9)

% Pts In Afib “Now or Within the Past Month”: Patient Self-Report



Mayo AF-Specific Symptom Inventory (MAFSI): Overview

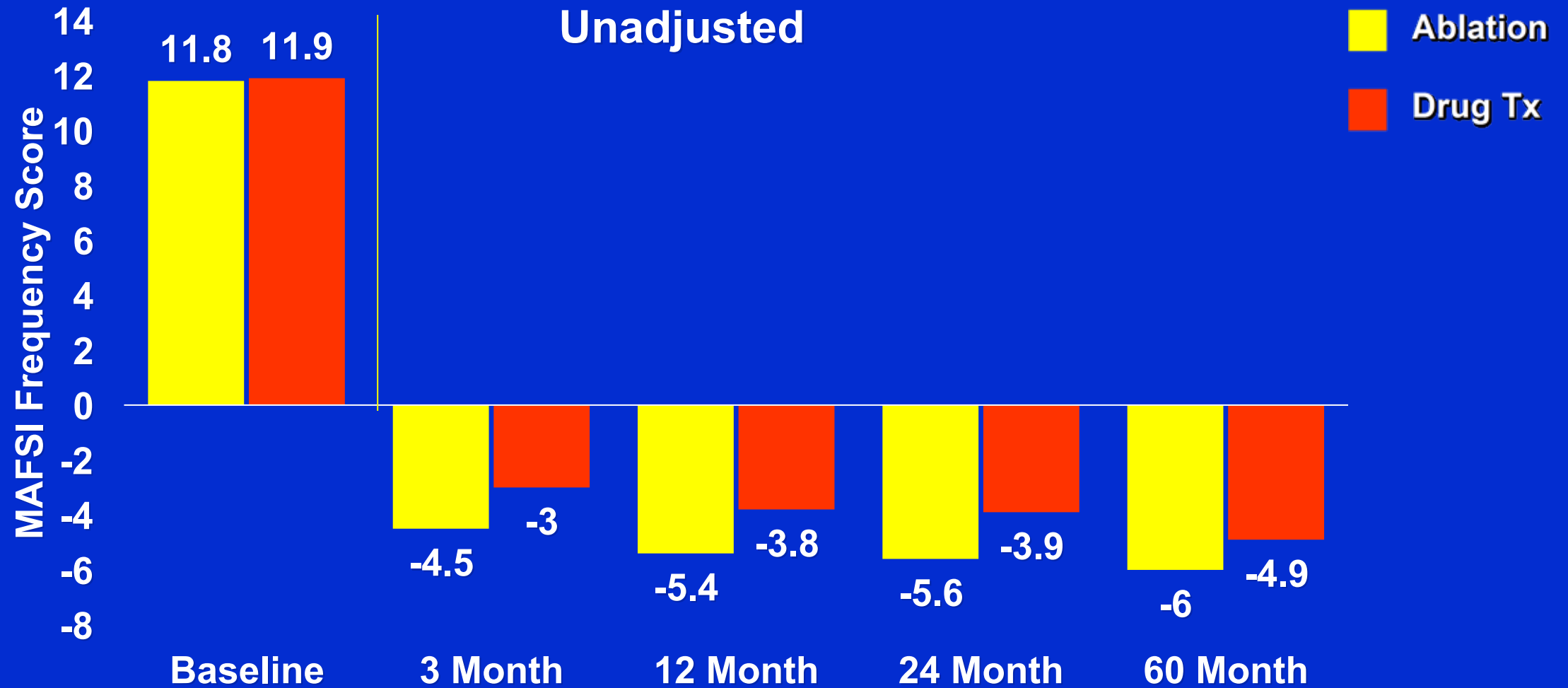
- Based on AF Symptom Checklist (Bubien and Kay, revised Jenkins 1993)
- 10 symptoms assessed “over past month” for frequency (never to always)
- Score: 0 (no AF sx) to 40 (worst)

Mayo AF Symptom Inventory (MAFSI) Worksheet

Think back over the past month. Please tell us how often you have had each symptom listed below:

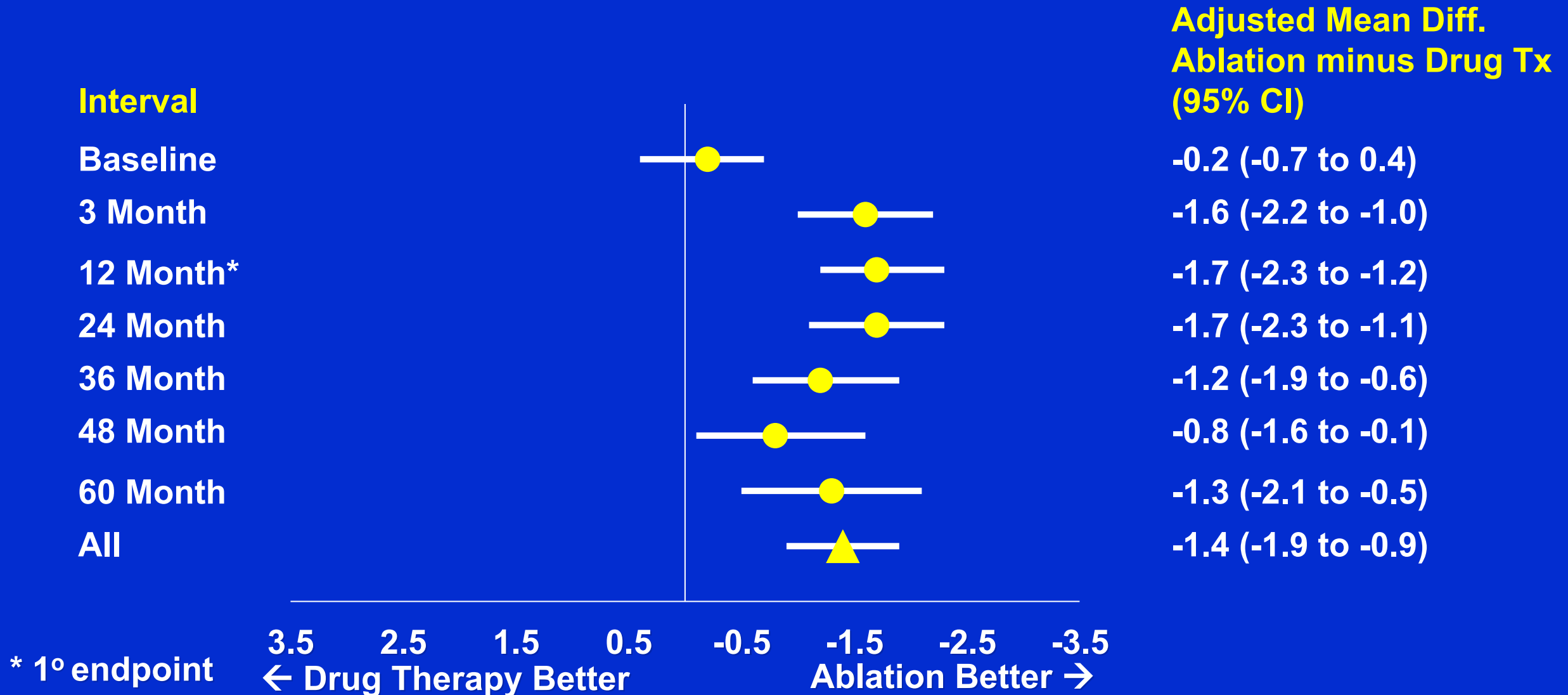
	How Often? (mark one)				
	Never	Rarely	Sometimes	Often	Always
Palpitations heart fluttering/racing	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Slow heart beat	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lightheadedness/dizziness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fainting/blackout/loss of consciousness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Chest pain, pressure or fullness WITHOUT palpitations	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Shortness of breath	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Unable to exercise	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Tired/lack of energy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Weakness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Feeling warm/flushed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

MAFSI Frequency Score: Baseline Values and Change from Baseline at Select Intervals



Mayo AF-Specific Symptom Inventory (MAFSI)

Frequency Score: Intention-to-Treat Analysis



Atrial Fibrillation Effect on Quality of Life (AFEQT): Overview

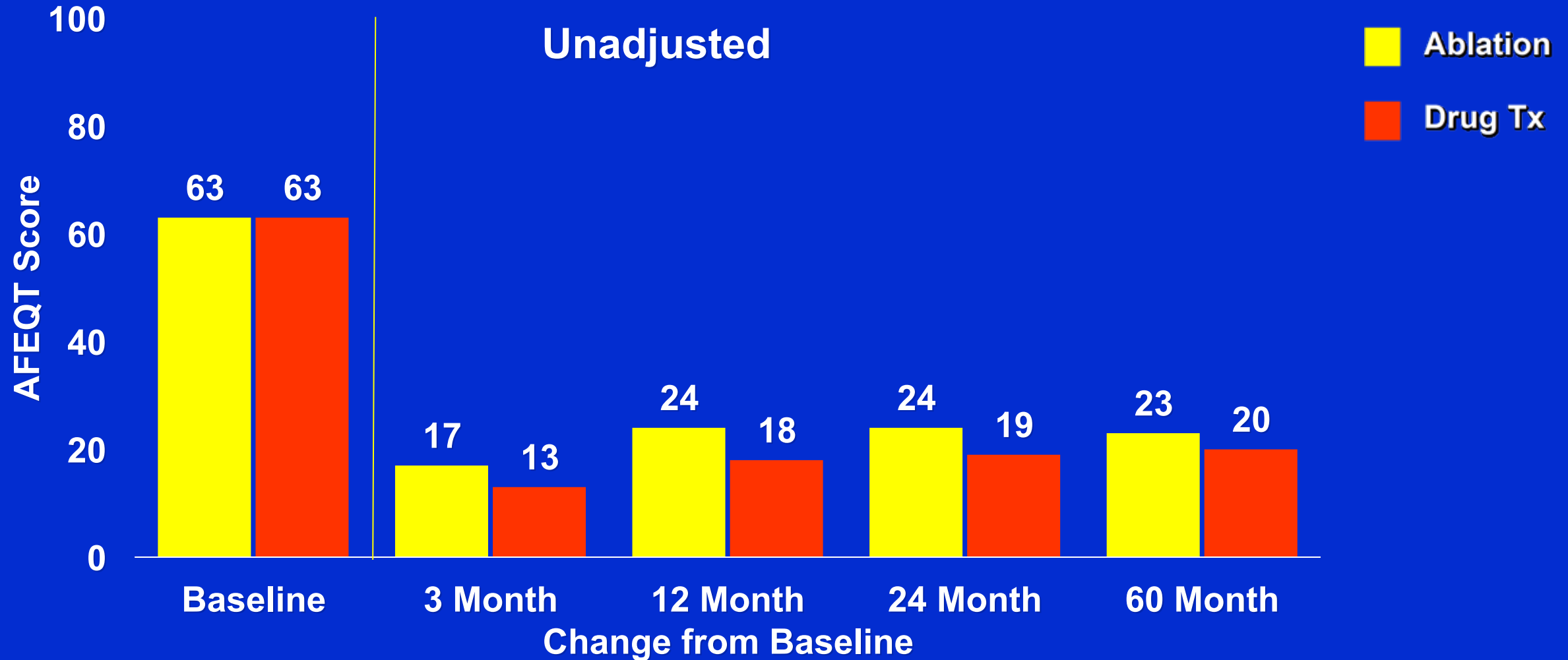
- Created in multi-step development and validation process in accord with US FDA draft recommendation for patient-reported outcomes

- Final instrument contained

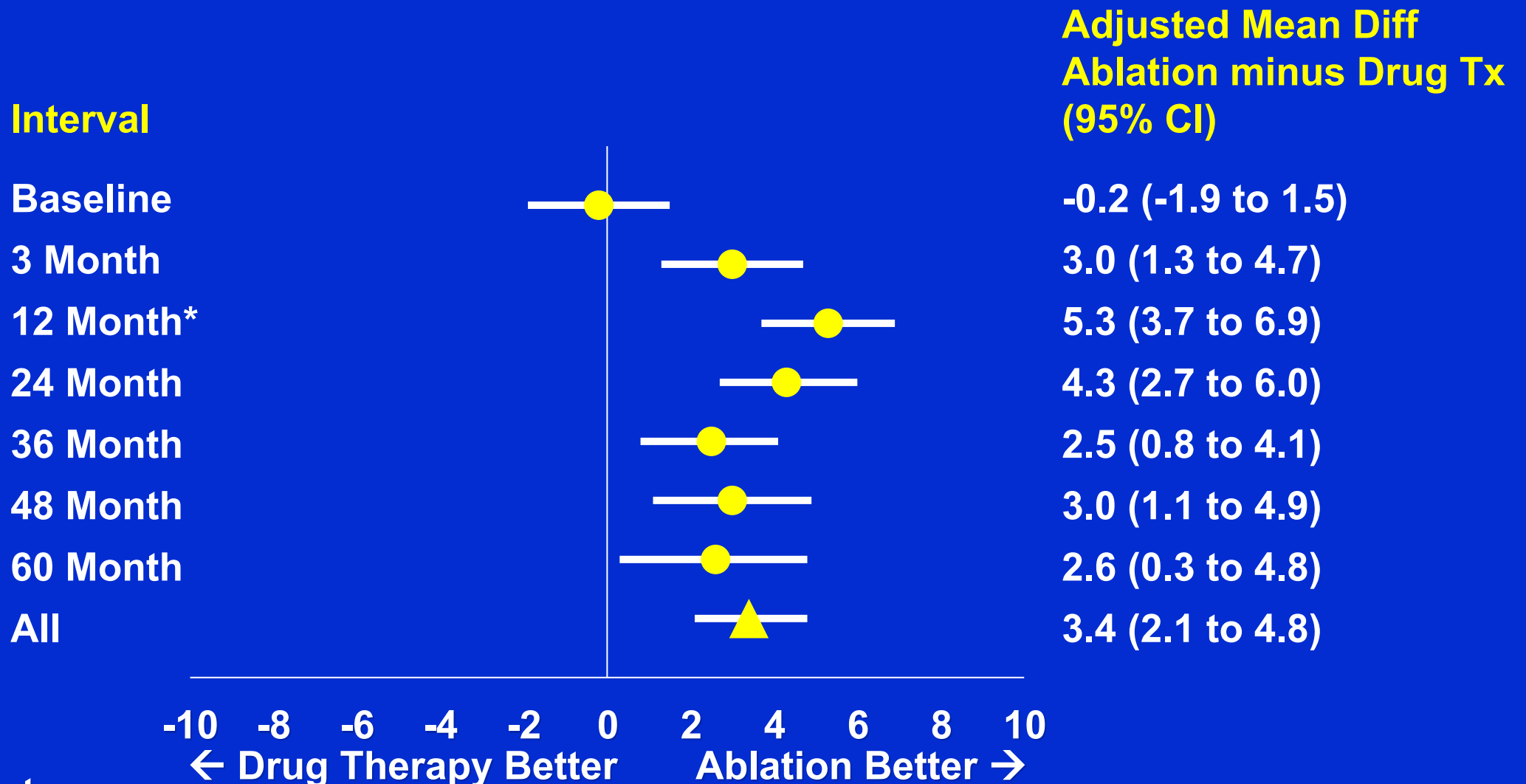
Symptoms	4 items
Daily Activities	8 items
Treatment Concerns	6 items
<hr/>	
Summary Score	18 items

- Each item assessed on 7-point Likert scale
- Final scores transformed to 0 (worst) to 100 (best) scale

AFEQT Overall Score: Baseline Values and Change from Baseline at Select Intervals

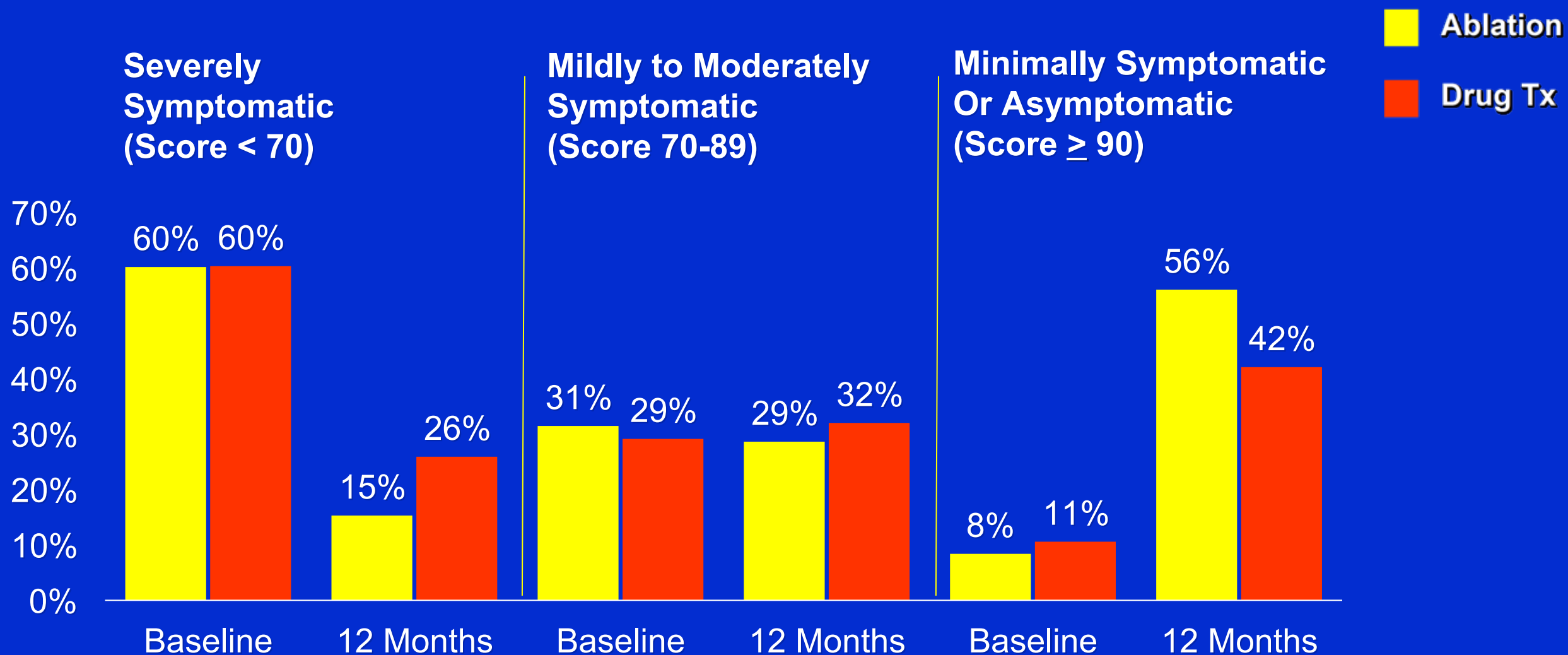


AFEQT Overall Score: Intention-to-Treat Analysis



* 1° endpoint

AF-Related Sx/Limitations at Baseline and 12 Mos: AFEQT Summary Score Illustrative Categories



CABANA QOL Study: Secondary QOL Outcomes

- **Secondary QOL measures (SF-36, DASI, EQ5D) showed similar patterns of Rx benefit for ablation but with smaller effect size estimates and/or less precision of the estimates (as would be expected for generic QOL measures relative to condition-specific ones)**

CABANA Quality of Life Study: Summary

- Ablation produced incremental, clinically meaningful and significant improvements in AF-related symptoms and QOL relative to drug tx that were sustained for 5 years.**
- In symptomatic AF patients enrolled into CABANA, both Rx groups showed substantial improvements over initial 12 months that were sustained for 5 years**

