

Presenter Disclosure Information

Andrew M. Tonkin, MD
Discussant: The JUPITER Trial

FINANCIAL DISCLOSURE:

Grants/Research Support: AstraZeneca, Bristol-Myers Squibb

Speakers Bureau: AstraZeneca, Pfizer, Schering Plough

UNLABELED/UNAPPROVED USES DISCLOSURE:

None

JUPITER

Screened 89,892:
53%/37% excl. by LDL-c/CRP

Hypothesis: Those 'healthy' with elevated hs-CRP (inflammation) will benefit from statin therapy.

Power calculations

- RRR 25%
- Placebo event rate based on AFCAPS

Randomised
17,802 without CVD or diabetes
LDL <130 mg/dl, hs-CRP > 2
Males > 50y, Females > 60y

(Cohort BMI 28.4 kg/m², 38% female, >25% minorities)

Rosuvastatin 20 mg

Placebo

Baseline characteristics balanced

At 12M, ↓ in LDL to 55mg/dl, hs-CRP to 2.2 mg/L

Drop-outs 25%
Presumably no drop-ins

Primary Outcome
Composite MCVE, 1.9y

0.77 per 100 person yrs

Primary Outcome
Composite MCVE, 1.9y

1.36 per 100 person yrs

Early termination

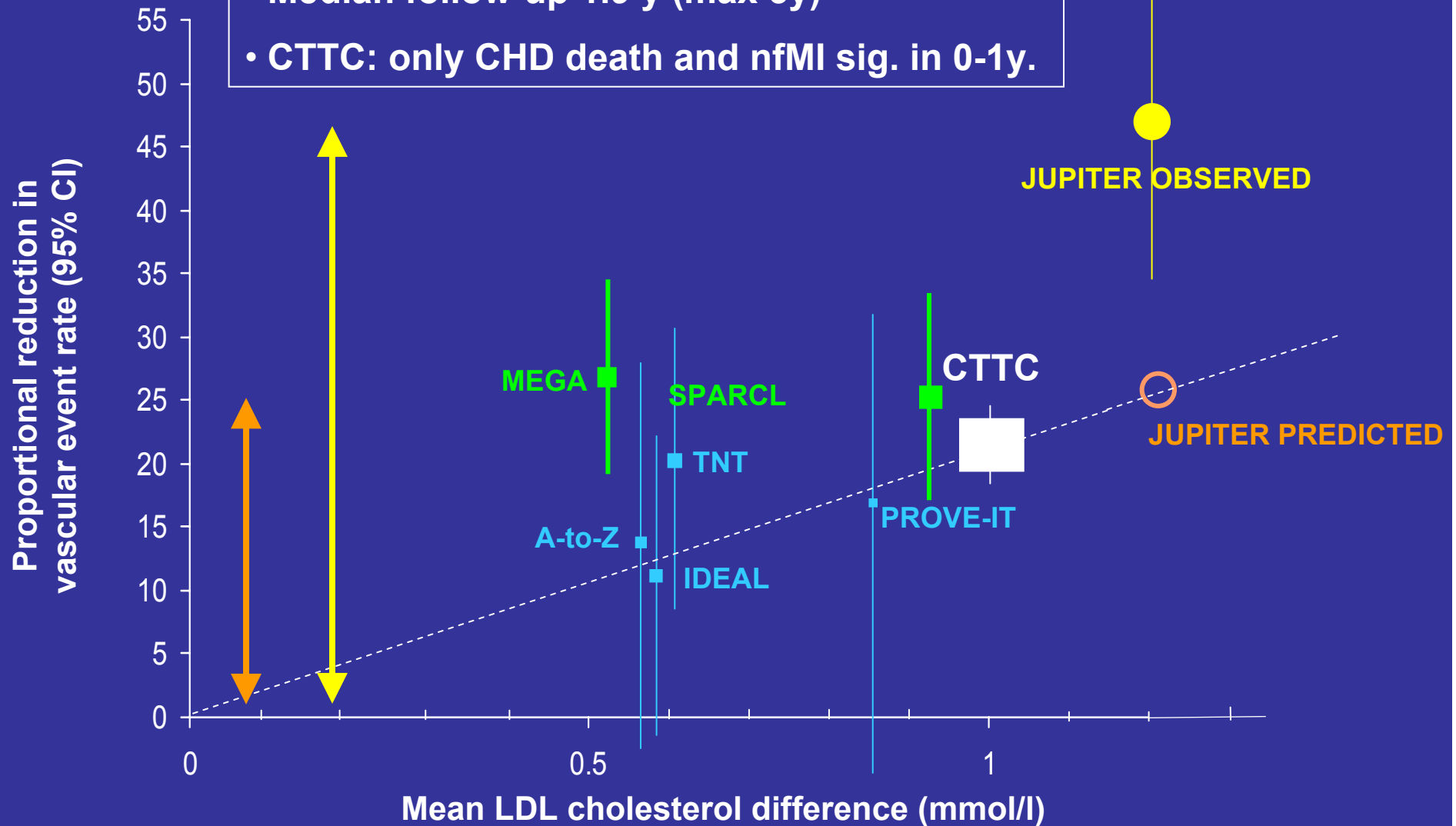
NNT (extrapolated to 5 years) = 25

- Secondary outcomes incl. 20% RRR in all-cause mortality. No safety concerns
- Robust data (RRR) in subgroups, incl. BMI < 25, non-smokers, FHS < 10%/10yrs

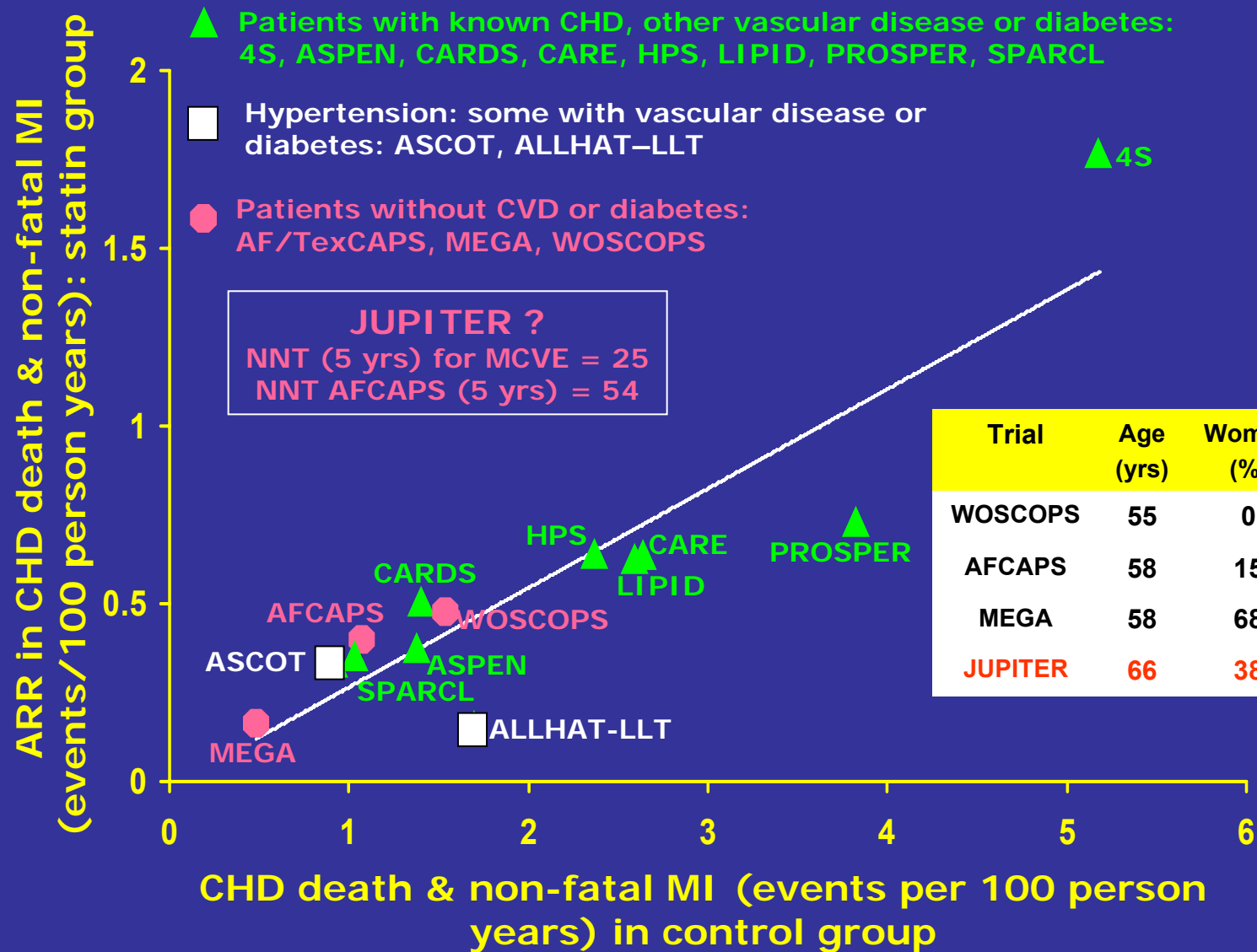
CTTC, JUPITER and Other Trials: The Impact of LDL-c Reduction

Considerations for Absolute Risk Reduction

- Median follow-up 1.9 y (max 5y)
- CTTC: only CHD death and nfMI sig. in 0-1y.



The Importance of Absolute Risk and Absolute Risk Reduction



Trial	Age (yrs)	Women (%)	Diabetes (%)	LDL-C (mg/dl)
WOSCOPS	55	0	1	192
AFCAPS	58	15	6	150
MEGA	58	68	21	156
JUPITER	66	38	0	108

CONCLUSIONS and IMPLICATIONS

- Benefits of rosuvastatin clearly proven when hs-CRP > 2mg/L and LDL-c < 130mg/dl, even if otherwise low risk
- Relative importance of effects of rosuvastatin on LDL-c and/or inflammation (hs-CRP) unclear. Other analyses (e.g. time-updated, covariate-adjusted models) may help clarify.
- No safety concerns: 12 months LDL-c 55mg/dl (IQR 44,72)
- No information whether hs-CRP a marker or mediator. Genetic epidemiology is uncertain. Ultimately tested by specific interventions, eg CRPi (or low dose MTX, etc)
- Guidelines concerning hs-CRP in risk assessment and statin treatment in primary prevention of CVD should be reviewed

CONCLUSIONS AND IMPLICATIONS (2)

- Need to consider whether hs-CRP should be incorporated in absolute risk equations (Reynolds Risk Score, FHS analyses online in Circulation)
- A possible simplified algorithm for statin treatment if no CVD or diabetes
 - a. If high absolute risk – treat
 - b. If hs-CRP > 2mg/L – treat, depending on analyses and caveats:
 - Exploration of treatment effect of rosuvastatin
 - Age in JUPITER cohort (hs-CRP increases with age)
 - ARR in subgroups and cost- effectiveness analyses vital
 - Considerations for detection of elevated hs-CRP
 - c. Study not designed to specifically test targets (?LDL-c 70)
- **Implementation in family practice:** Universal screening inappropriate at present. Predictive algorithms may inform who tested. Screening costs need to be included in C-E analyses to support systems enabling translation of the study results to the usual clinical environment