

IMAGINE

Ischemia **M**anagement with **A**ccupril
post bypass **G**raft via **I**nhibition of
angiotensin co**N**verting **E**nzyme

Discussion

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Quinapril and Coronary interventions

- **QUIET (Quinapril Ischemic Event Trial)**
 - Multicenter randomized clinical trial
 - 1,750 patients undergoing *angioplasty*
 - RDZ to Quinapril 20 mg or Placebo
- **QUO VADIS (Effects of Quinapril on clinical outcome after CABG)**
 - 149 patients scheduled for *CABG*
 - RDZ to Quinapril 40 mg or Placebo 4 weeks before surgery
- **PARIS:**
 - ACE DD genotype stented patients
 - RDZ to Quinapril 40 mg or placebo

1- Am.J. Cardiol 2001;87:1058

2- Am. J.Cardiol 2001;87:542-546

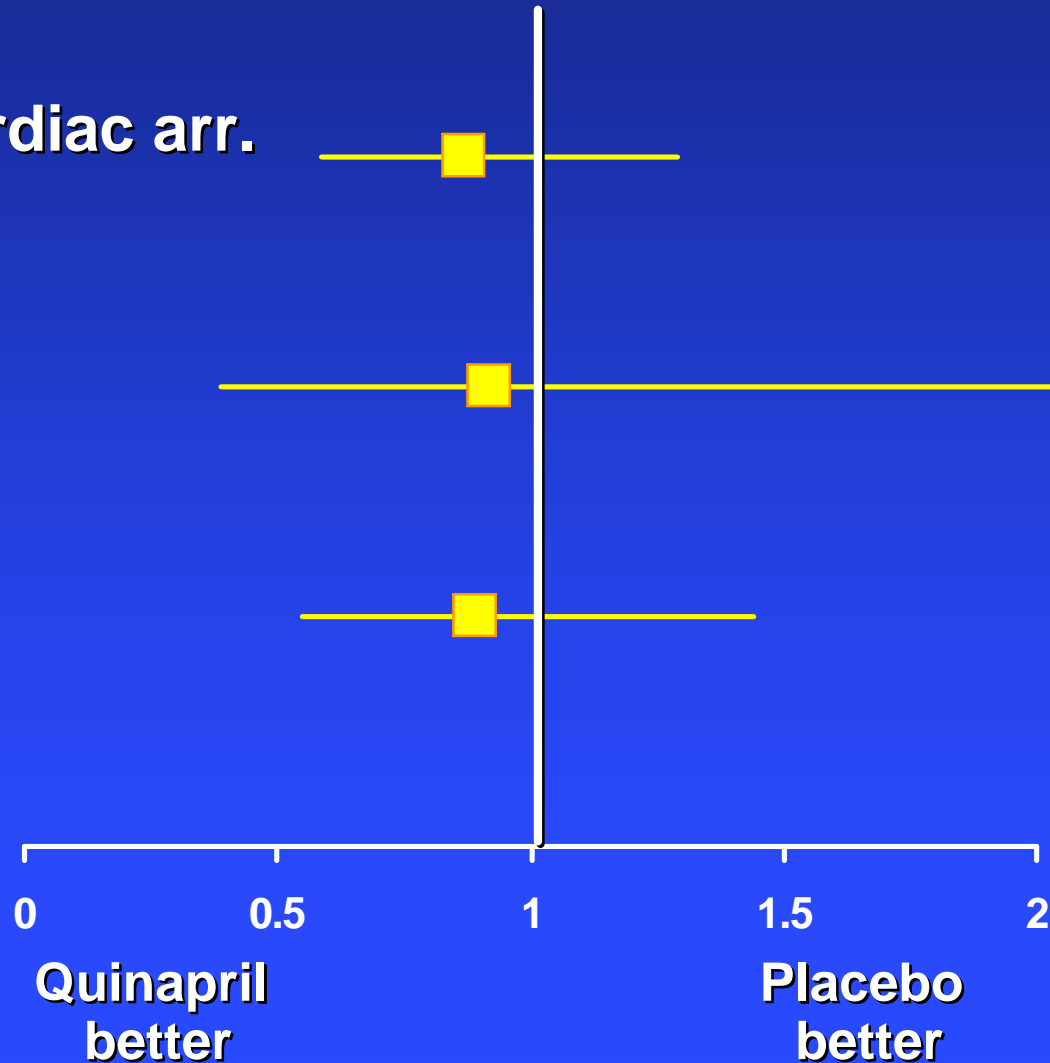
3- Lancet 2001;357:1321-24

QUIET trial: 1,750 pts undergoing PCI

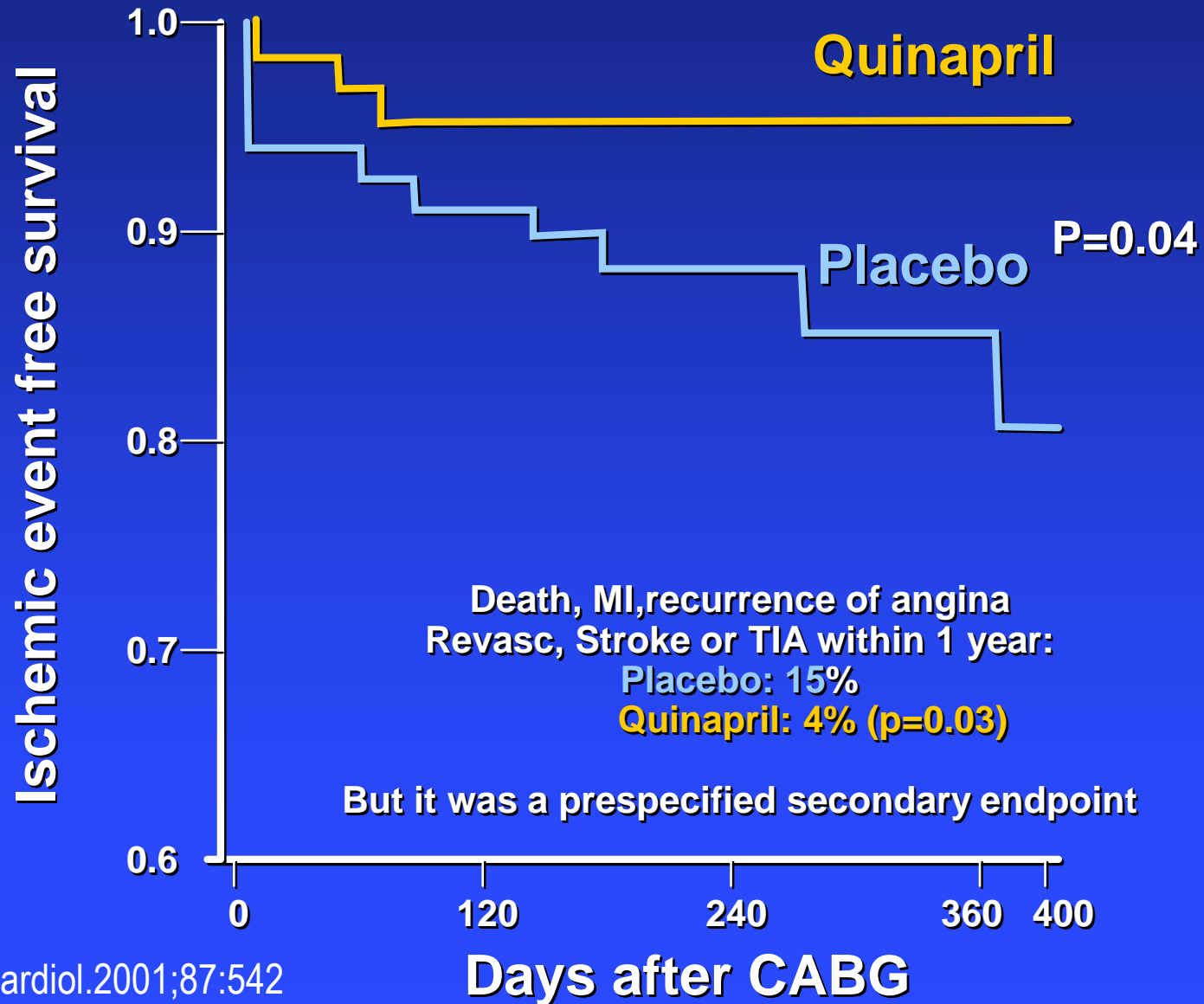
Cardiac death, MI, cardiac arr.
Revasc.Hosp for UA

Cardiac death

Non fatal MI

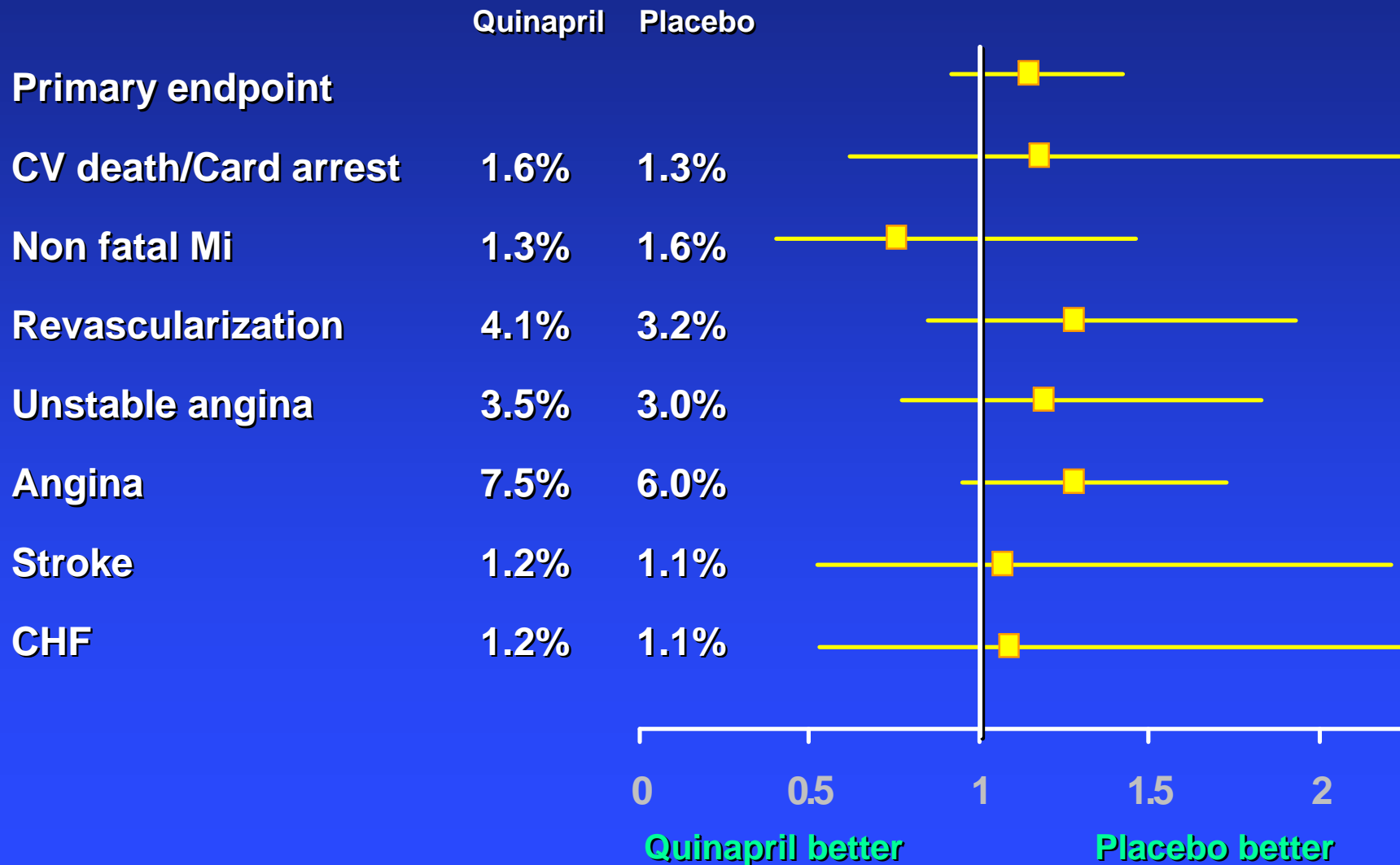


QUO VADIS: 149 pts RDZ 4 weeks before CABG





2,553 patients post CABG (< 7 days) RDZ to Quinapril (80 mg) or placebo



Strengths and limitations

■ Strengths

- Multicenter (57 centres-Europe & Canada), blinded, randomized study
- Representative of CABG population: (3 grafts /pt - >4 grafts in 39%)
- Adequate size (Power =80% level of significance 0.05): 2,060 pts to reach 325 pts with primary endpoint *
- Minimal number of lost FU patients
- Modern concomitant therapy

■ Limitations

- Relatively low risk population (History of MI: 39% - Diabetes: 10%)
- Complex primary endpoint : combination of 7 MACE
- High dose of ACE: Hypotension (12%), Cough (21%)

Explanations for (surprising) findings of IMAGINE ?

- Unrelated to study population characteristics
- Unrelated to concomitant therapy
- Probably not related to BP changes
- Relationship with ACE DD/genotype ?
- Time post CABG
- Quinapril – molecule specific effect ?
- Dose (High dose) ?

Time differences between CABG and randomization

CABG

HOPE
2399 pts
>4 yrs
RR: ↓ 11%

EUROPA
3587 pts
>6mo
RR ↓ 17%

PEACE
3232 pts
> 3 mo
RR: ↓ 4.7%

QUO VADIS
149 pts
<4weeks
RR: ↓ 77%

APRES
159 pts
Ramipril 10 mg
RR: ↓ 58%

IMAGINE
2553 pts
Quinapril 40 mg
RR: ↑ 15%

Years

Time

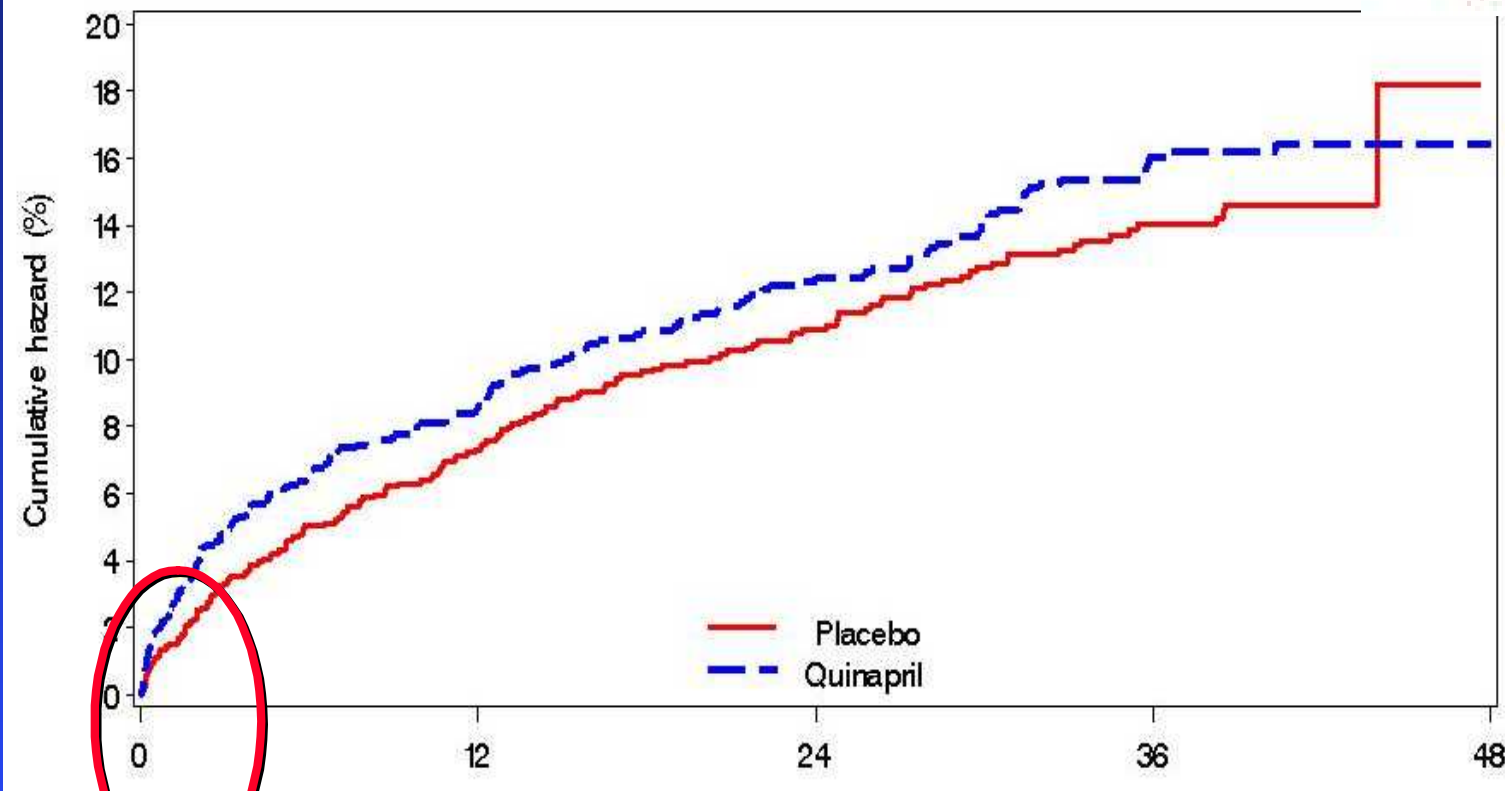
Weeks

Days

Primary endpoint



Hazard Ratio 1.15 (95% C.I. = 0.92 – 1.42) p=0.2124



Number at Risk

Quinapril

1280

1069

Months

776

504

43

155

Placebo

1273

1089

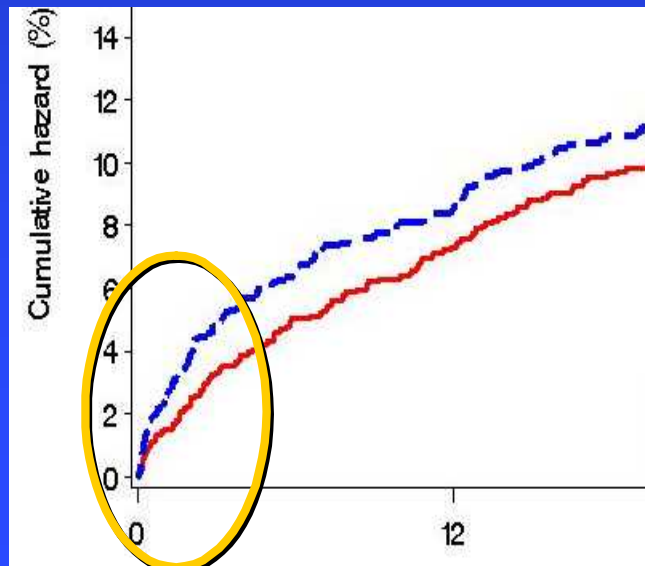
790

514

145

Speculations (1)

- High release of Bradykinine by High doses of ACE inhibitor :
 - Bradykinin is a mediator of inflammation
 - Stimulation of inflammation in the peri-operative period ?



Speculations (2)

- Molecule specific effect
 - Quinapril induced more MACE after interventions
 - IMAGINE (CABG)
 - PARIS (Stents in DD ACE genotype)
 - Restenosis Quinapril:36%
 - Placebo: 24%

Conclusions

- **IMAGINE does not question the good results obtained with ACE-I's (Ramipril & Perindopril) in secondary prevention of stable patients with CAD (HOPE & EUROPA)**
- **Owing to the number of patients undergoing intervention, further investigation should establish the optimal time to start ACE-I treatment after the procedure.**