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Valsartan, Captopril, or Both in Myocardial Infarction Complicated by Heart Failure, Left Ventricular Dysfunction, or Both

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VALIANT

The VALIANT Cohort

Acute MI (0.5–10 days)—SAVE, AIRE or TRACE eligible
(either clinical/radiologic signs of HF or LV systolic dysfunction)

- **Major Exclusion Criteria:**
  - **BP <100 mm Hg**
  - **Serum creatinine >2.5 g/dL**
  - **Prior intolerance of an ARB or ACE-I**
  - **Nonconsent**

double-blind active-controlled

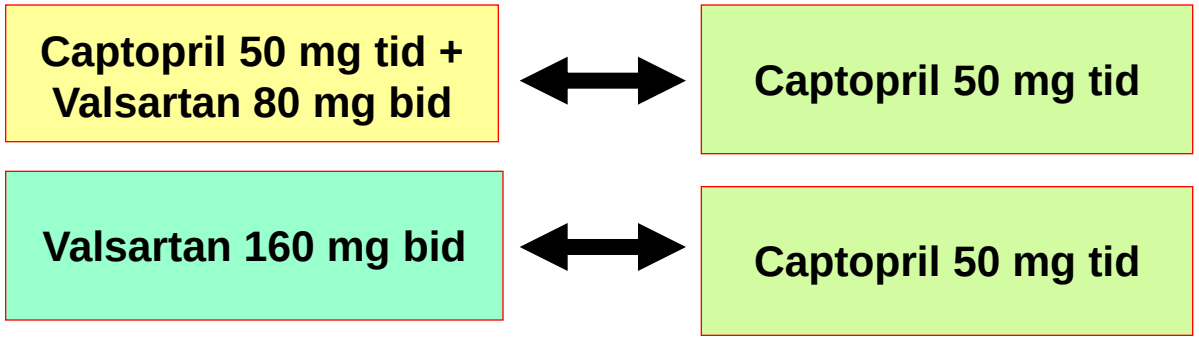
Captopril 50 mg tid (n = 4909)	Valsartan 160 mg bid (n = 4909)	Captopril 50 mg tid + Valsartan 80 mg bid (n = 4885)

- **median duration: 24.7 months**
- **event-driven**

Primary Endpoint:	**All-cause mortality**
Secondary Endpoints:	**CV death, MI, or HF**
Other Endpoints:	**Safety and tolerability**

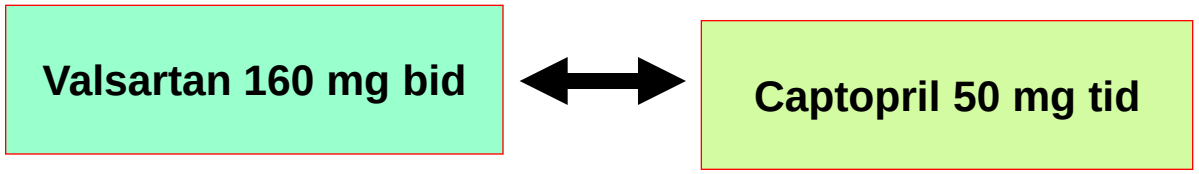
Primary Comparisons and Power consideration

Superiority



A total of 1700 primary events in the two treatment arms attains 85.9% power for detecting HR=0.85.

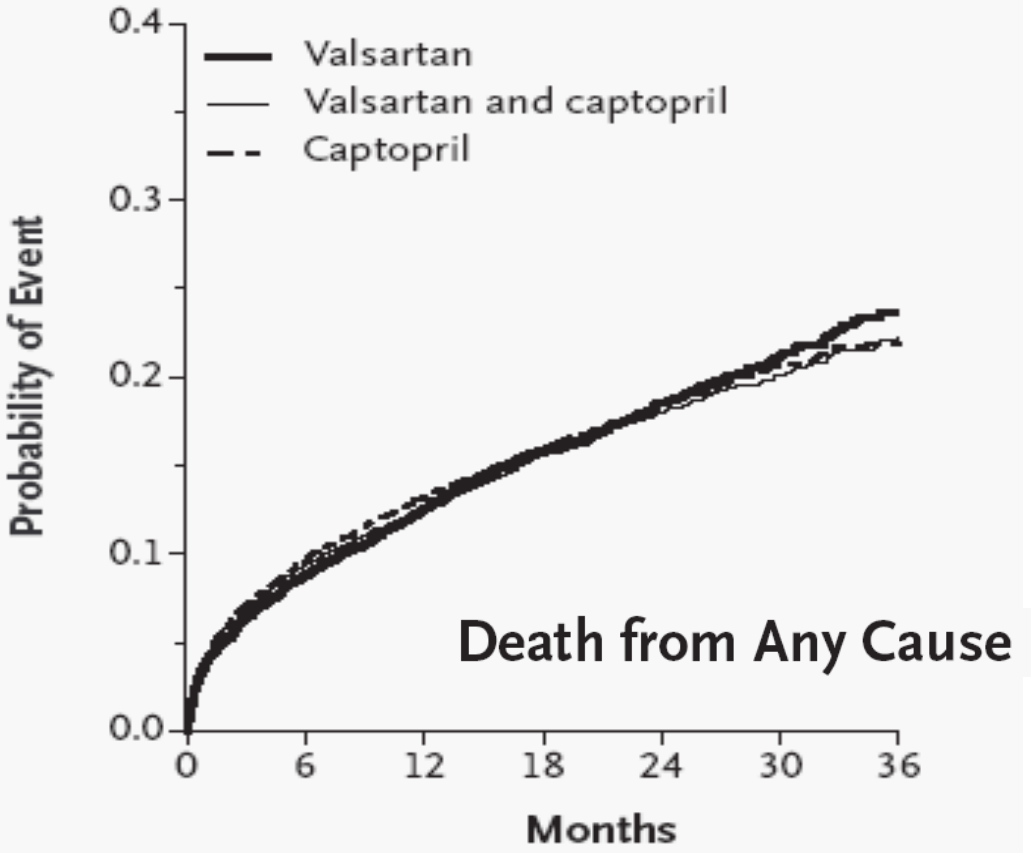
Non-inferiority



1850 primary events in these two treatment arms will provide 88.1% power if valsartan is actually 2.5% better than captopril

The total events = ½ (1700 + 1850 +1850) = **2700**

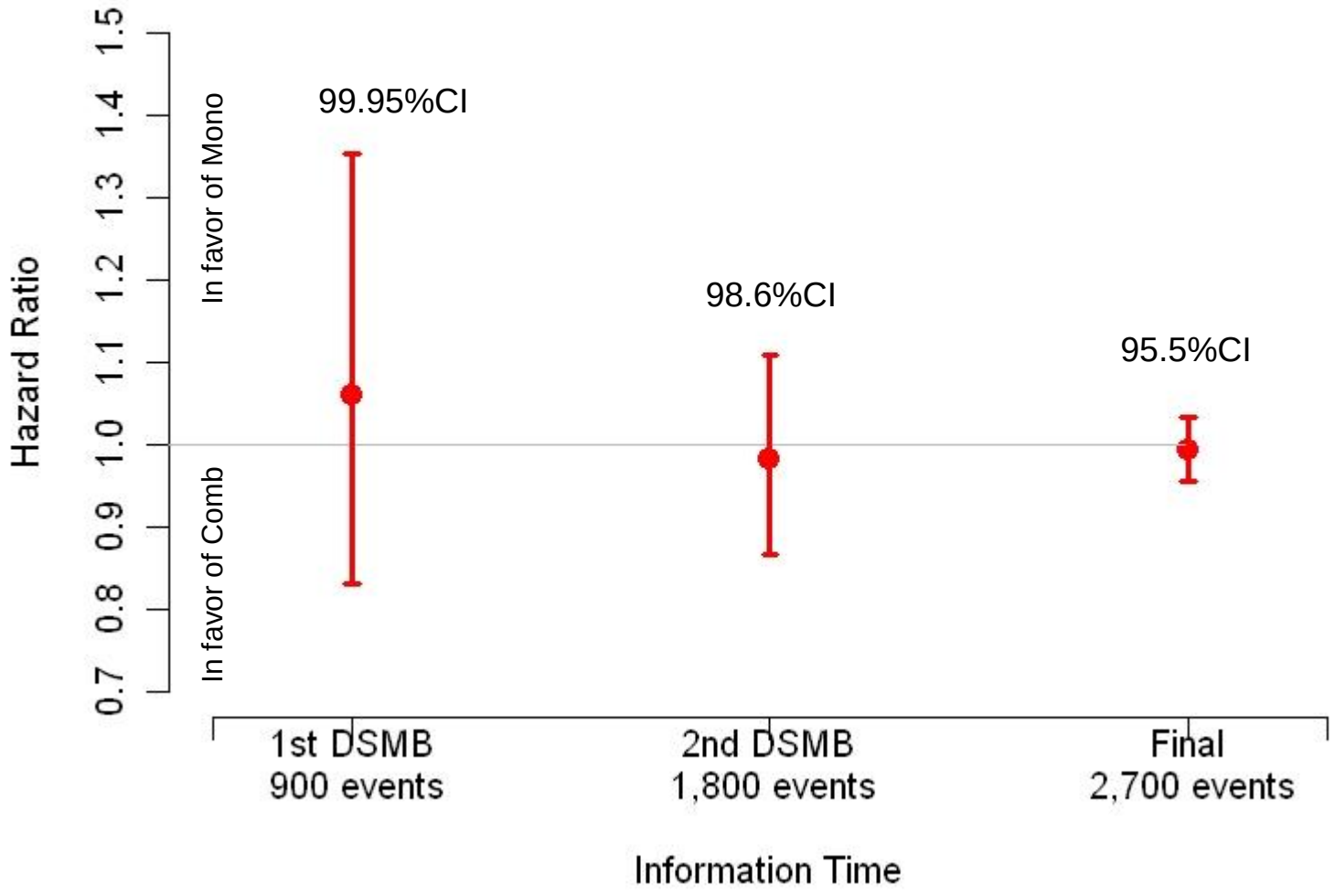
Final result of the VALIANT Study



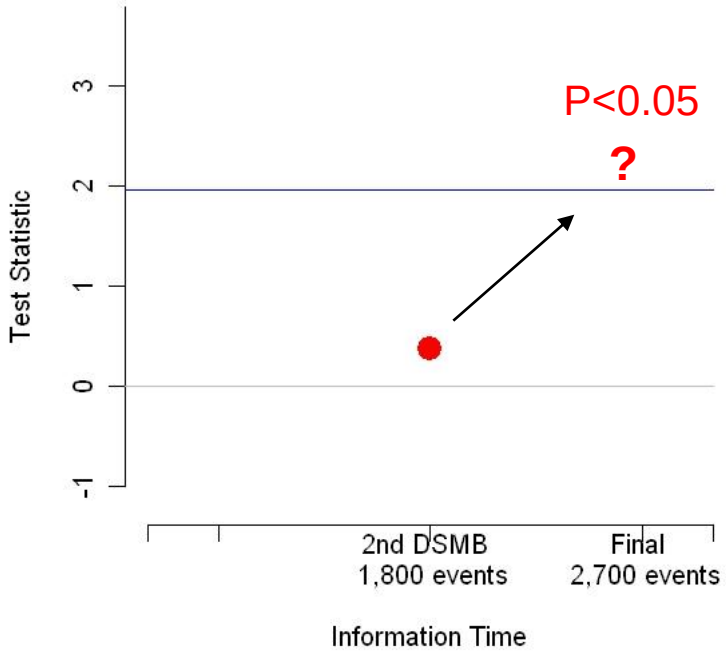
No. at Risk

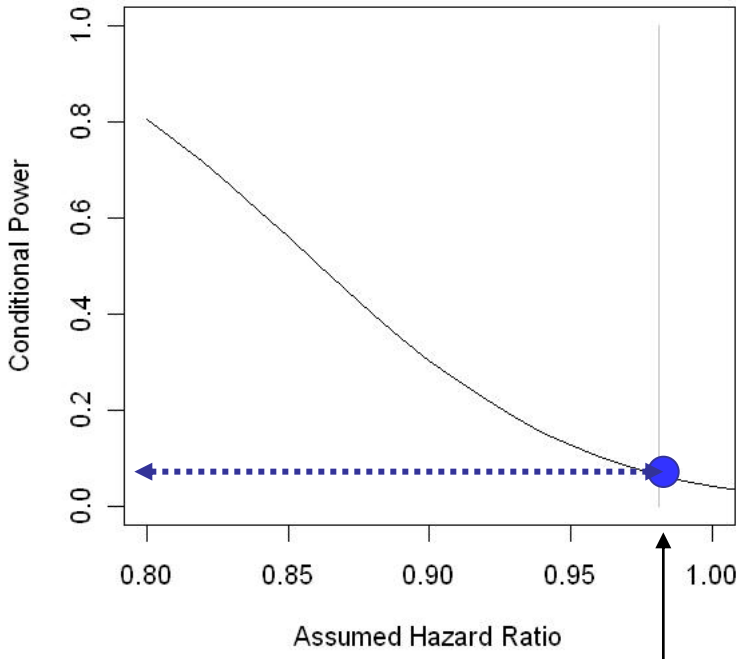
Valsartan	4909	4464	4272	4007	2648	1437	357
Valsartan and captopril	4885	4414	4265	3994	2648	1435	382
Captopril	4909	4428	4241	4018	2635	1432	364

Repeated Confidence Intervals



Conditional Power





Observed HR

With **8%** of chance, the significant result will be observed at the final.

Drawback of Conditional Power

What is going on with such a low chance?

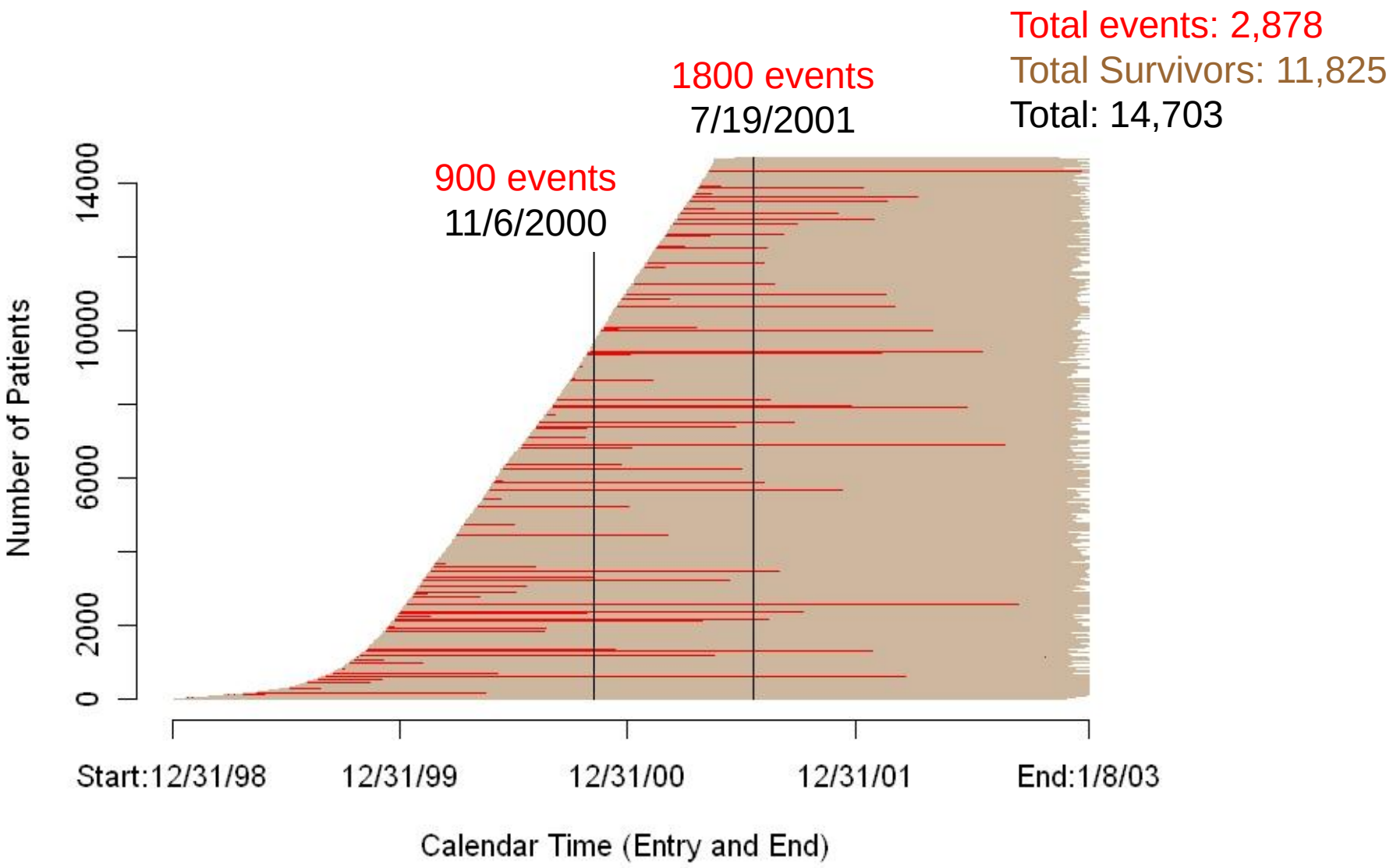
Conditional Power was 8%, because …

- Nothing is going on?
- Lack of the power?
- Or both?

But, Conditional Power does not provide enough information..

Predicted Intervals

Each Patient's Entry and Follow-up with calendar time



What this tool will give you.

Observed dataset at interim point

\+ Assumption of HR

Simulate future outcome

A **simulated complete** dataset at the end of the trial

Calculate the "final" result

95%CI

What this tool will give you.

DSMB: Dr. Evans

Observed dataset at interim point

\+ Assumption of HR

Simulate future outcome

A **simulated complete** dataset at the end of the trial

Repeat again

Calculate the "final" result

95%CI

What this tool will give you.

DSMB: Dr. Evans

Observed dataset at interim point

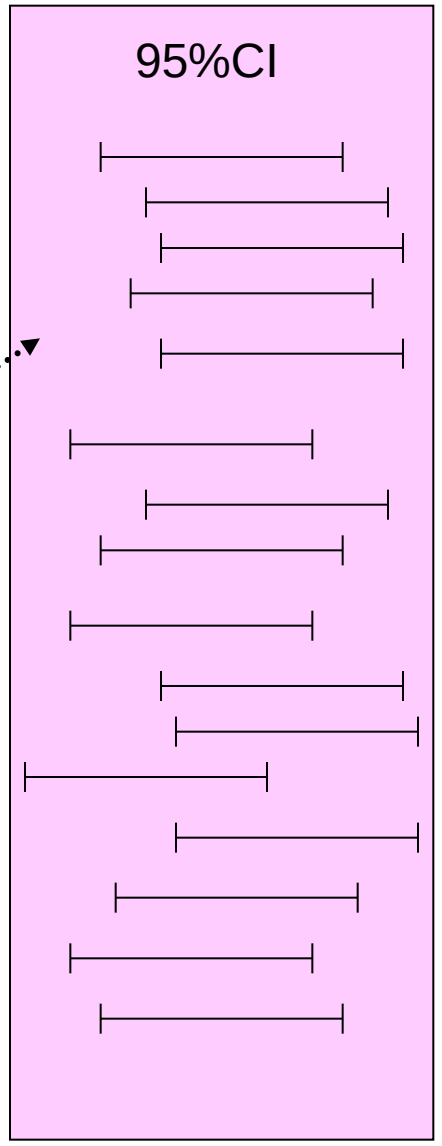
\+ Assumption of HR

Simulate future outcome

A **simulated complete** dataset at the end of the trial

Calculate the "final" result

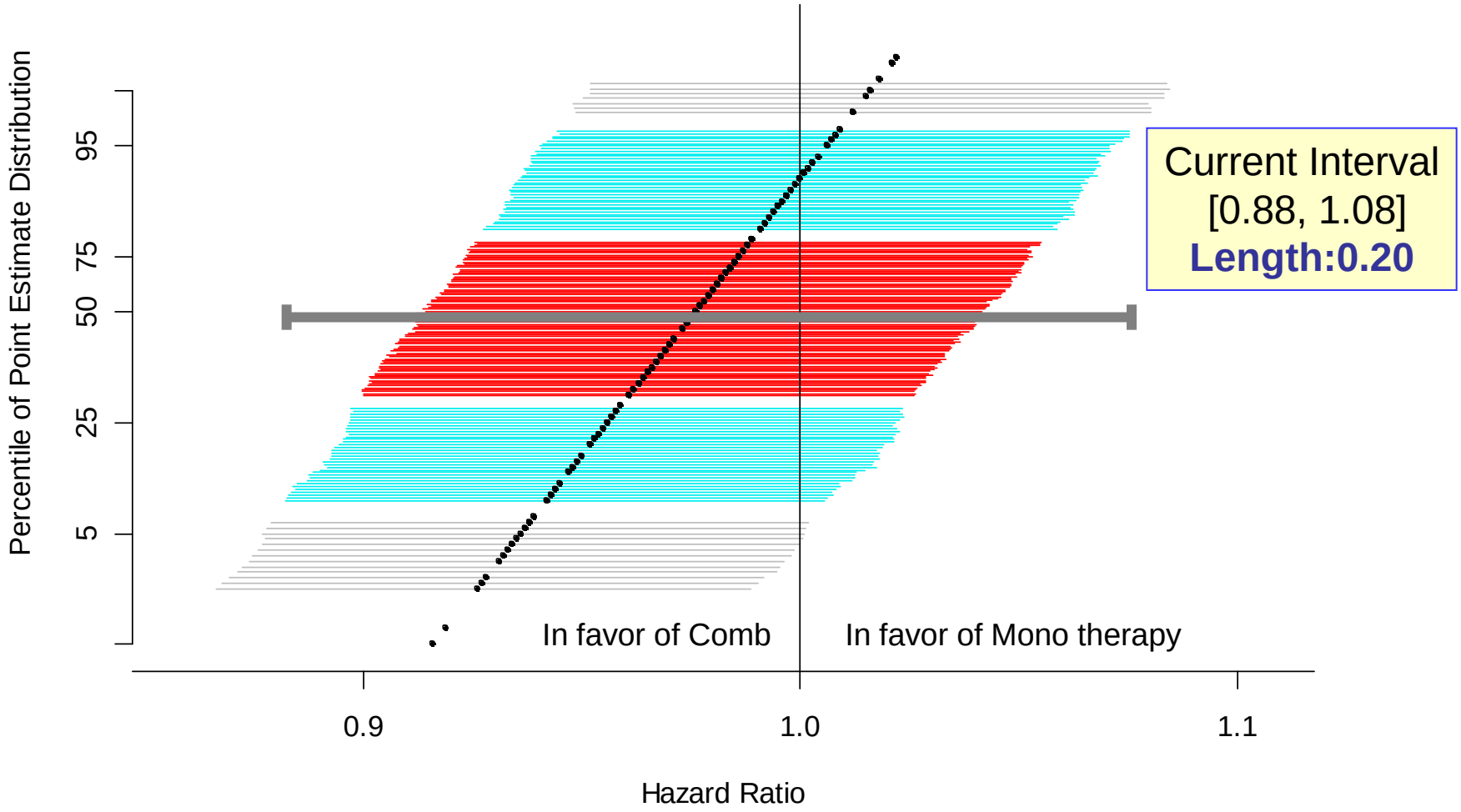
95%CI



Repeat this many times and get many 95%CIs

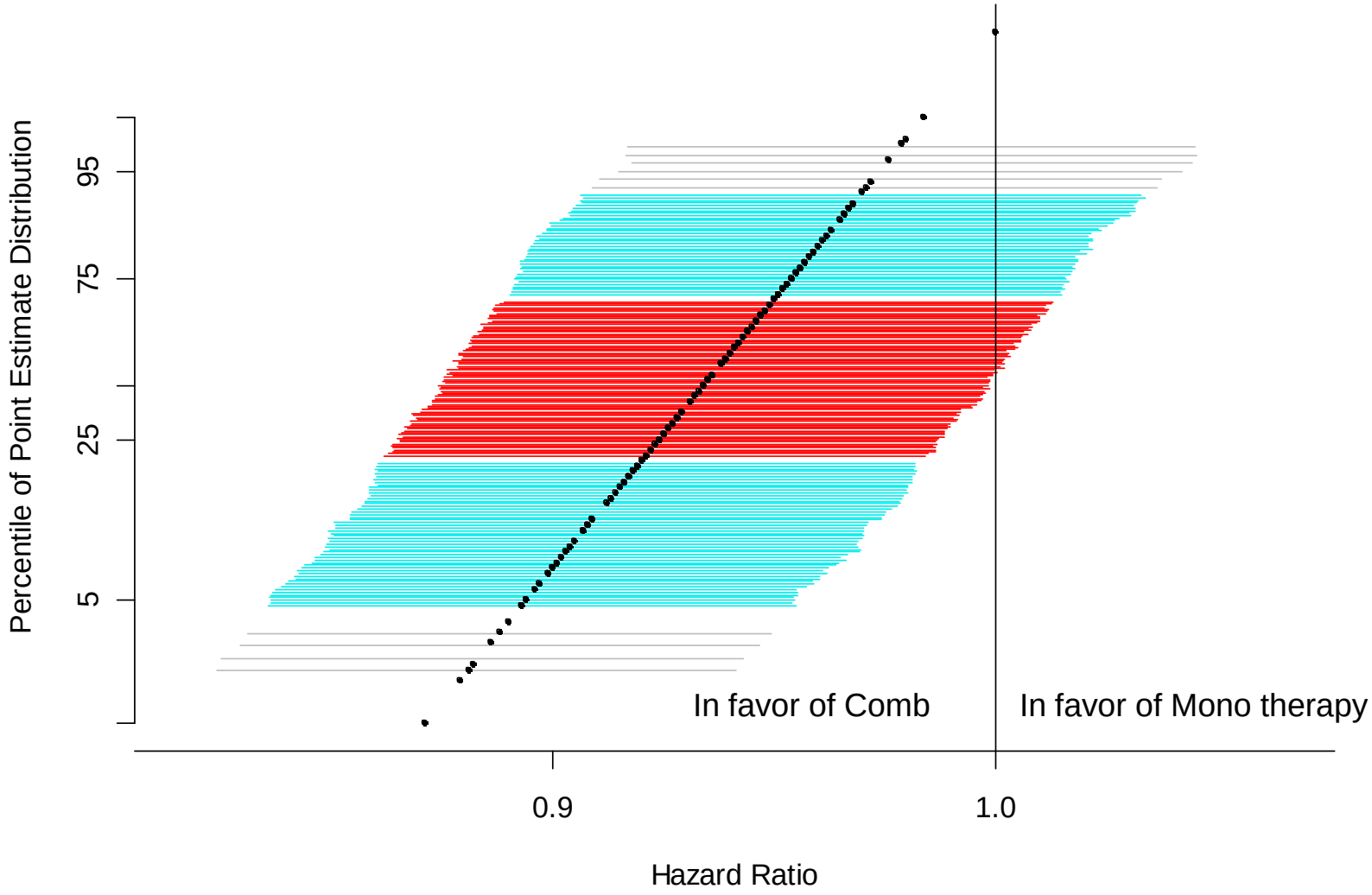
Predicted Interval Plot

18M after the 2nd interim analysis (4Y from the start) Assumed HR = 0.975.



Predicted Interval Plot

HR = 0.85 (original alternative hypothesized value)



Summary

- PIPs provides a useful quantitative information regarding effect sizes and associated precision.
- PIPs is useful for
  - Futility
  - Sample size re-adjustment
  - Re-adjustment of the duration of the follow-up
- PIPs is a useful tool of design and data monitoring.