

**Challenges in data collection
for HABP/VABP trials:
Investigator's Perspective**

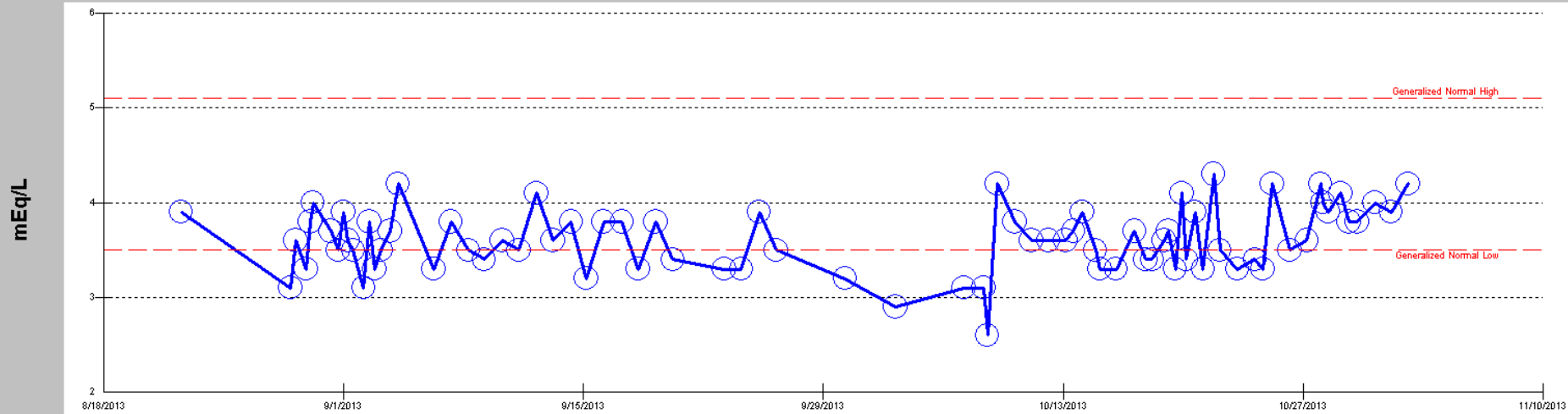
**Richard G. Wunderink MD, FCCP
Northwestern University Feinberg School of Medicine
Chicago, IL**

Challenges in data collection for HABP/VABP trials

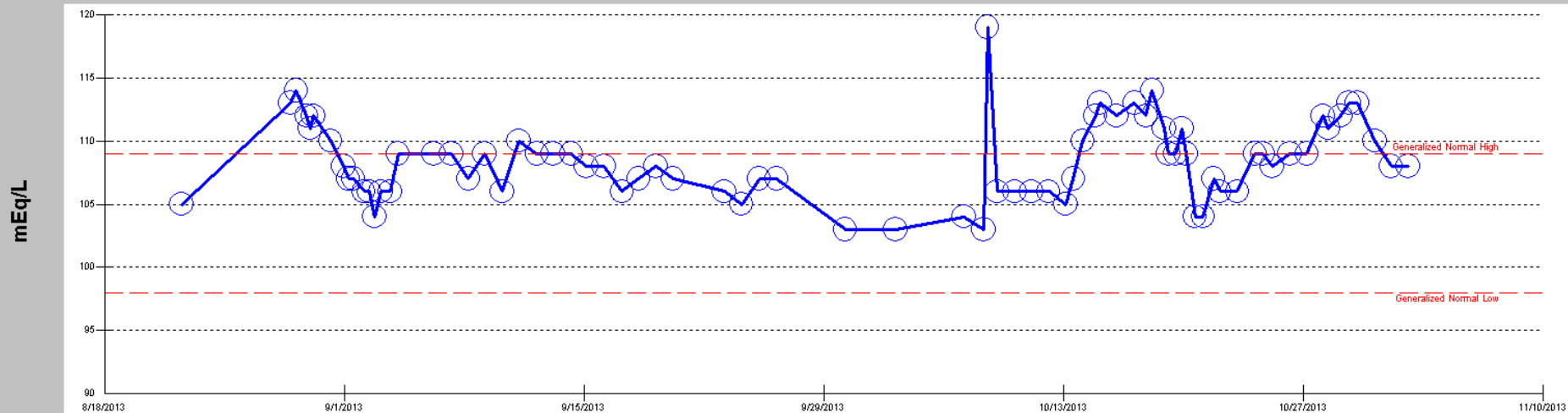
- ❖ **Excessive amount of irrelevant data collection**
- ❖ **ICU is unique environment**
 - **Expected complications/abnormalities**
 - **Rapid monitoring of therapeutic interventions**
 - **Excess of testing**

16 episodes of hypokalemia, 7 episodes of hyperchloremia

Potassium

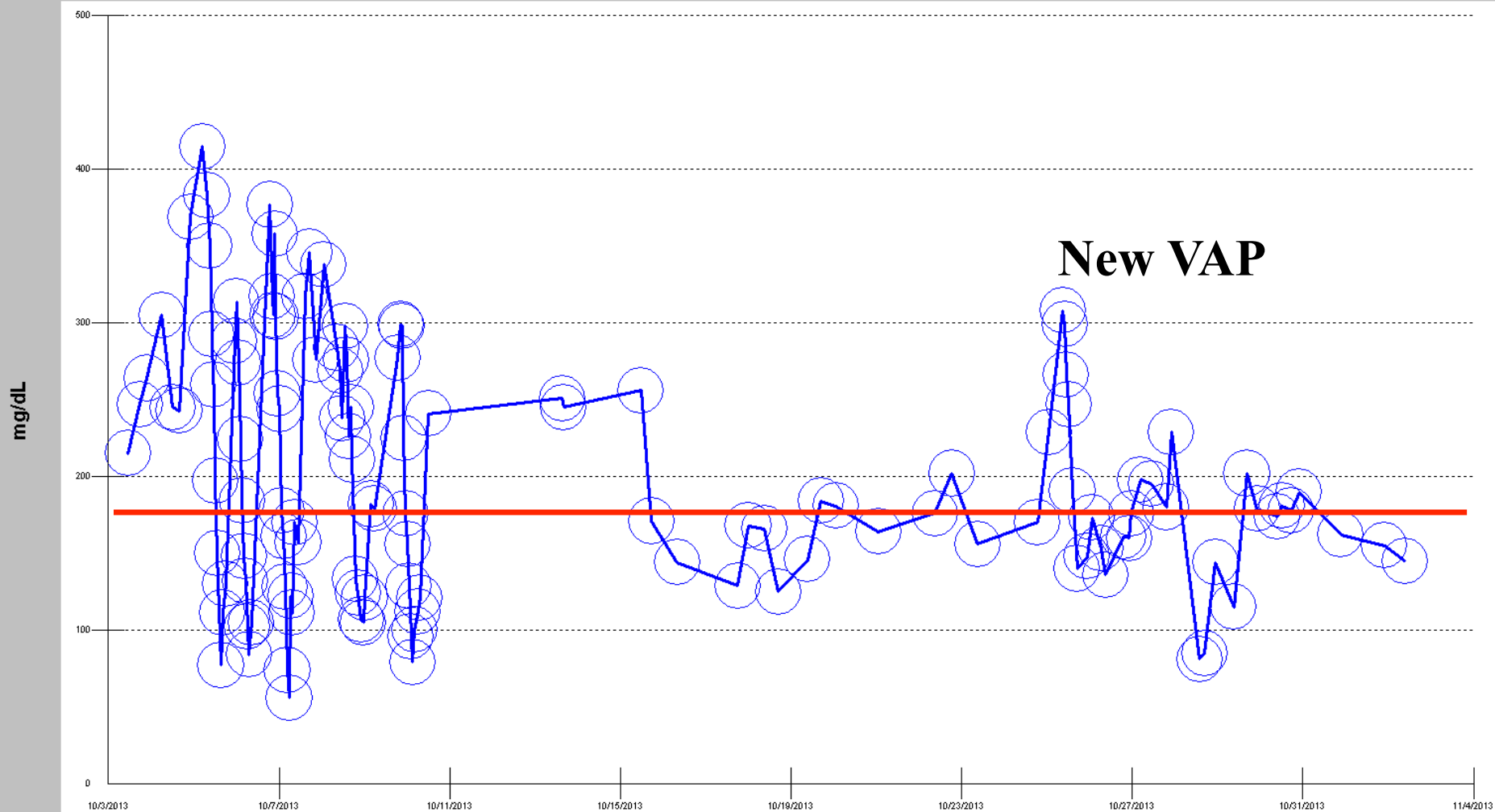


Chloride



Sepsis with DKA

Bedside Glucose



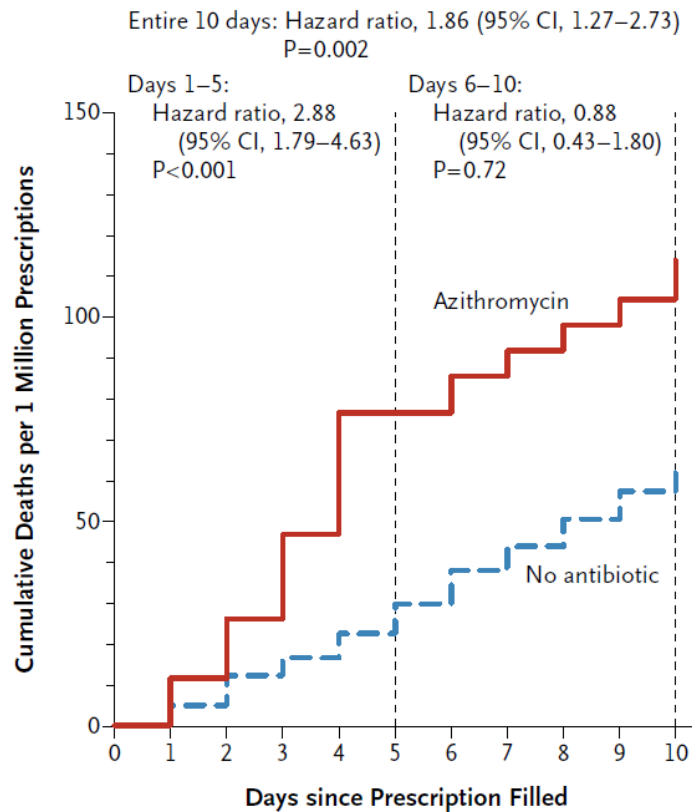
Challenges in data collection for HABP/VABP trials

- ❖ Excessive amount of irrelevant data collection
- ❖ ICU is unique environment
- ❖ Esoteric testing – external EKG analysis
 - Short term, no-cost lease agreement
 - Biomedical clearance
 - Collection of additional concomitant meds
 - Investigator review and sign offs

Azithromycin and the Risk of Cardiovascular Death

Wayne A. Ray, Ph.D., Katherine T. Murray, M.D., Kathi Hall, B.S., Patrick G. Arbogast, Ph.D., and C. Michael Stein, M.B., Ch.B.

A Cardiovascular Death

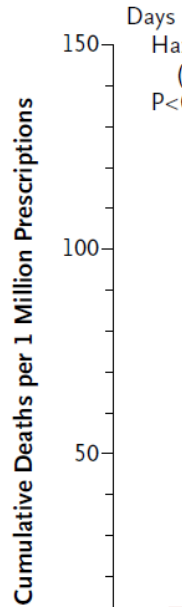


Azithromycin and the Risk of Cardiovascular Death

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A Cardiovascular Death

Entire 10 days: Hazard ratio, 1.86 (95% CI, 1.27–2.71); P=0.002



Analysis	Azithromycin (N=1,102,419)		Penicillin V (N=7,364,292)		Rate Ratio (95% CI)*	P Value†
	no. of events	no./1000 patient-yr	no. of events	no./1000 patient-yr		
Primary analysis	17	1.1	146	1.5	0.93 (0.56–1.55)	0.79
Subgroup analysis						
Sex						0.73
Male	9	1.7	87	2.3	0.86 (0.43–1.72)	
Female	8	0.8	59	1.0	1.03 (0.49–2.16)	
Age						0.50
18–44 yr	3	0.3	17	0.3	1.42 (0.41–4.90)	
45–64 yr	14	2.5	129	3.1	0.88 (0.51–1.53)	
History of cardiovascular disease‡						0.16
Yes	10	9.7	62	8.0	1.35 (0.69–2.64)	
No	7	0.5	84	0.9	0.65 (0.30–1.41)	

Use of Azithromycin and Death from Cardiovascular Causes

Henrik Svanström, M.Sc., Björn Pasternak, M.D., Ph.D., and Anders Hviid, Dr.Med.Sci.

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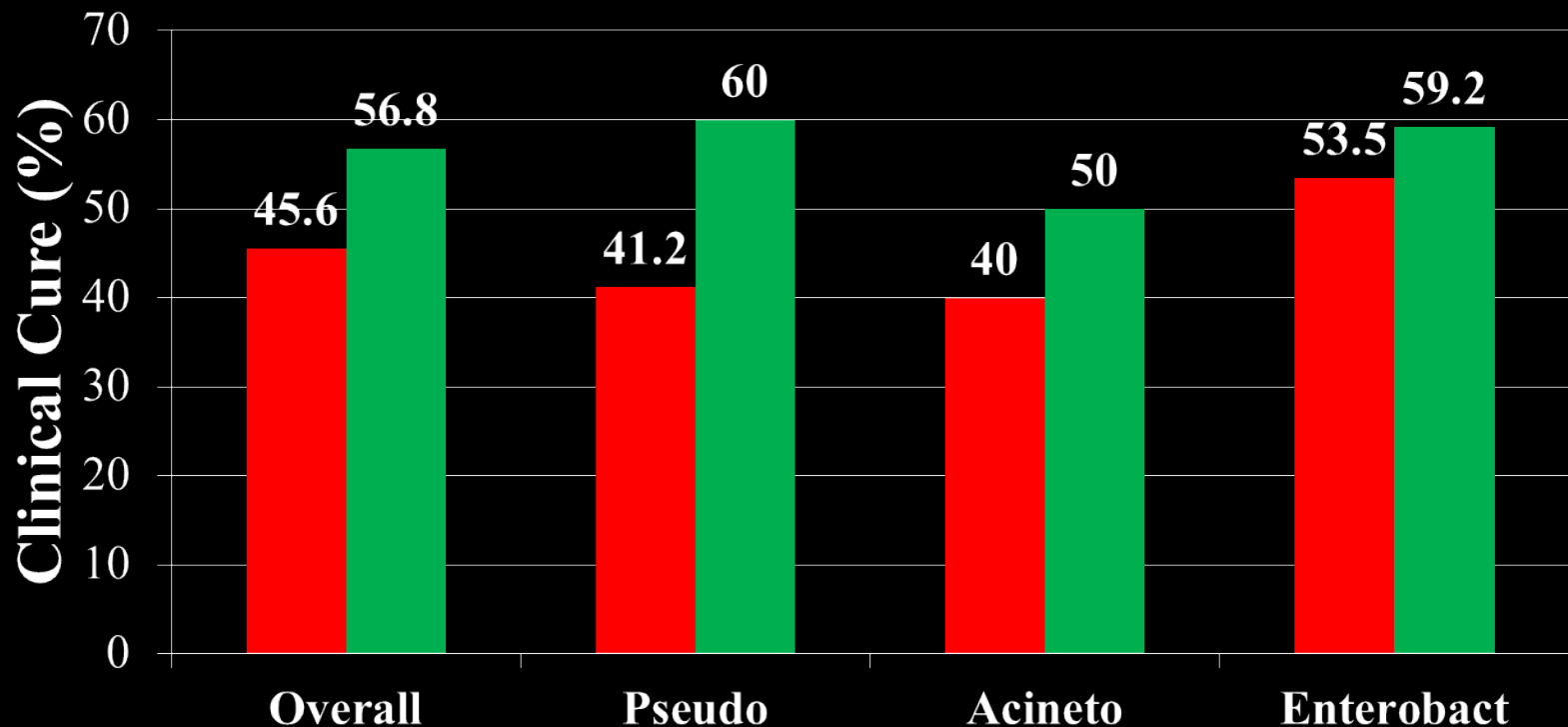
- ❖ Excessive amount of irrelevant data collection
- ❖ ICU is unique environment
- ❖ Esoteric testing – external EKG analysis
- ❖ **Excessive regulatory documentation**
 - Lot number, expiration date, signature of pharmacy preparer and saved vials/infusion bags for FDA-approved drugs taken from hospital stock
 - Training in general and drug-specific GCP for all RNs who may potentially infuse study drug
- Inadequate HIPPA standards



Clinical Response in Carbapenem VAP Trial

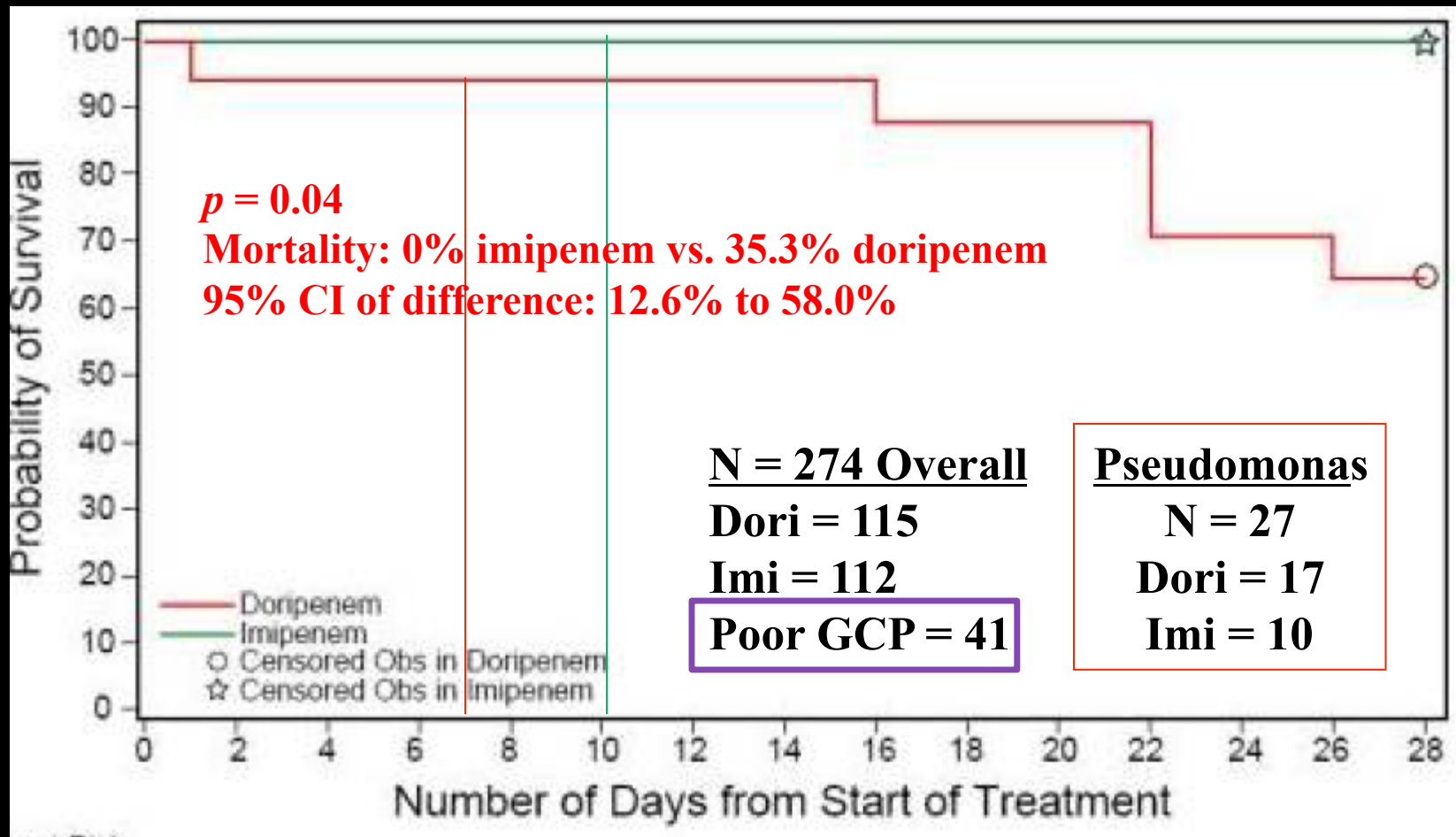
Kollef, Crit Care, 2012

■ Doripenem ■ Imipenem



Doripenem overall clinical cure rate difference was -11.2%, 95% CI of difference -26.3 to 3.8%

Pseudomonas Pneumonia Cases



Results

- ❖ **Excess time = excess cost**
- ❖ **Fatigue = loss of sites/patients**
 - **Investigator/ Research coordinator fatigue**
 - **Monitor fatigue = lose the forest for the trees**
- ❖ **Audit risk**
- ❖ **No clear patient benefit**
 - **? unexpected side effects detected by extensive data collection in Phase III trials**
 - **Most unusual side effects detected by post marketing surveillance**

**Humanity has but three great enemies:
Fever, famine, and war.
Of these, by far the greatest,
By far the most terrible, is fever.**

Sir William Osler