

**Rutherford Chronic Limb  
Ischemia Classification  
System Stratifies Risk in  
Patients Undergoing  
Lower Extremity  
Revascularization:  
Insights from VOYAGER  
PAD**



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# Background

- Risk stratification for patients with PAD is important for both medical and surgical care
- Novel medical therapies such as aggressive lipid lowering therapy, antiplatelets, anti-thrombotics, are being used to mitigate progression of disease and adverse limb events (amputation, acute limb ischemia)

# Rutherford Chronic Limb Ischemia Classification

- **Designed in 1986 to grade severity of peripheral artery disease**
- **Widely accepted for risk stratification in trials and registries**

Rutherford Stage	Signs and Symptoms
0	Asymptomatic
1	Mild claudication
2	Moderate claudication
3	Severe claudication
4	Rest pain
5	Ischemic ulcers of digits
6	Severe ischemic ulcers or gangrene

# Objective

- **Primary Objective: examine the risk of amputation post lower extremity revascularization (LER) stratified by baseline Rutherford Chronic Limb Ischemia Stage**
- **Determine the risk of other limb events based on Rutherford Stage**
- **Examine utility of low dose rivaroxaban in each Rutherford Stage**

## Trial Design

NCT02504216

6,564 Patients with Symptomatic Lower Extremity PAD\* Undergoing Peripheral Revascularization

*\*Ankle Brachial Index < 0.90 and Imaging Evidence of Occlusive Disease*

*ASA 100 daily for all Patients  
Clopidogrel at Investigator's Discretion*

Randomized 1:1 Double Blind

Rivaroxaban 2.5 mg  
twice daily

*Stratified by  
Revascularization Approach  
(Surgical or Endovascular)  
and Use of Clopidogrel*

Placebo

Follow up Q6 Months, Event Driven, Median f/u 28 Months

Primary Efficacy Endpoint: Acute limb ischemia, major amputation of vascular etiology, myocardial infarction, ischemic stroke or cardiovascular death

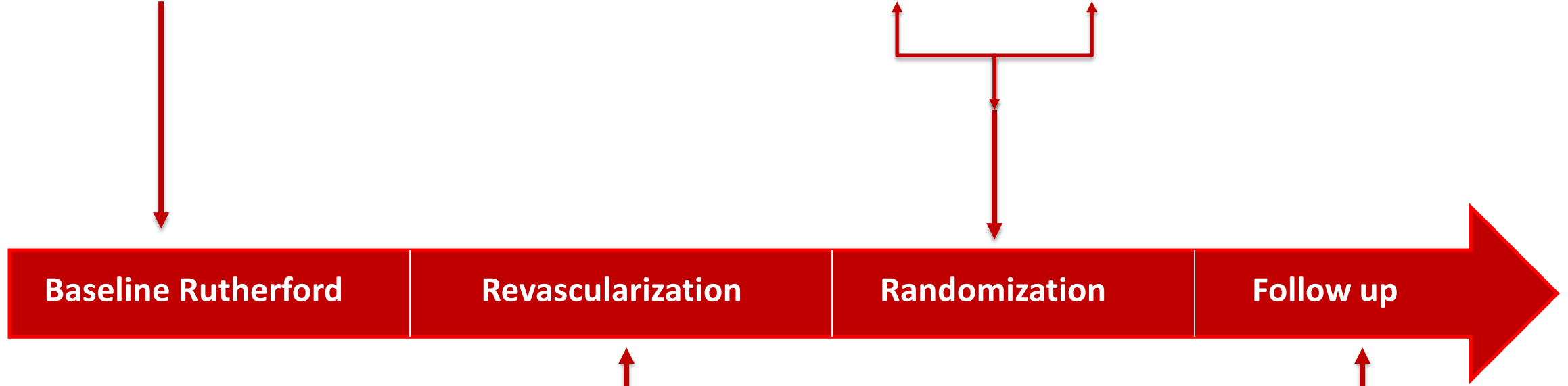
Principal Safety Outcome: TIMI Major Bleeding

# Methods

- **VOYAGER PAD patients were categorized by baseline Rutherford Chronic Limb Ischemia Stage**
  - Rutherford 1 and 2 are combined due to trial protocol
- **Amputation incidence (major, minor and major) at one year and three years were determined**
- **Incidence of the composite of Major amputation + Acute Limb Ischemia at each baseline Rutherford Stage were determined; comparisons between Rivaroxaban and placebo were made**

**Rutherford Chronic  
Limb Ischemia Stage  
Determined**

**Rivaroxaban      Placebo**



**Baseline Rutherford**

**Revascularization**

**Randomization**

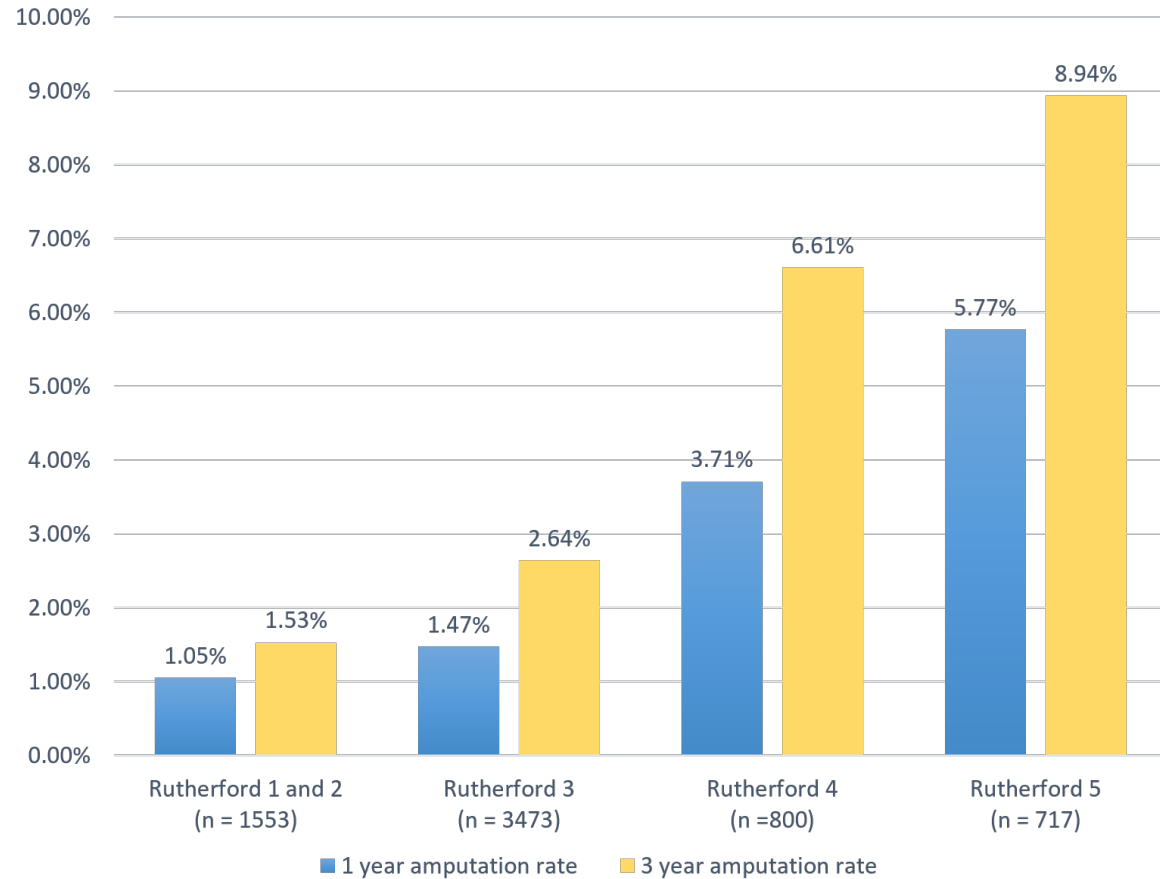
**Follow up**

**Open/Endo**

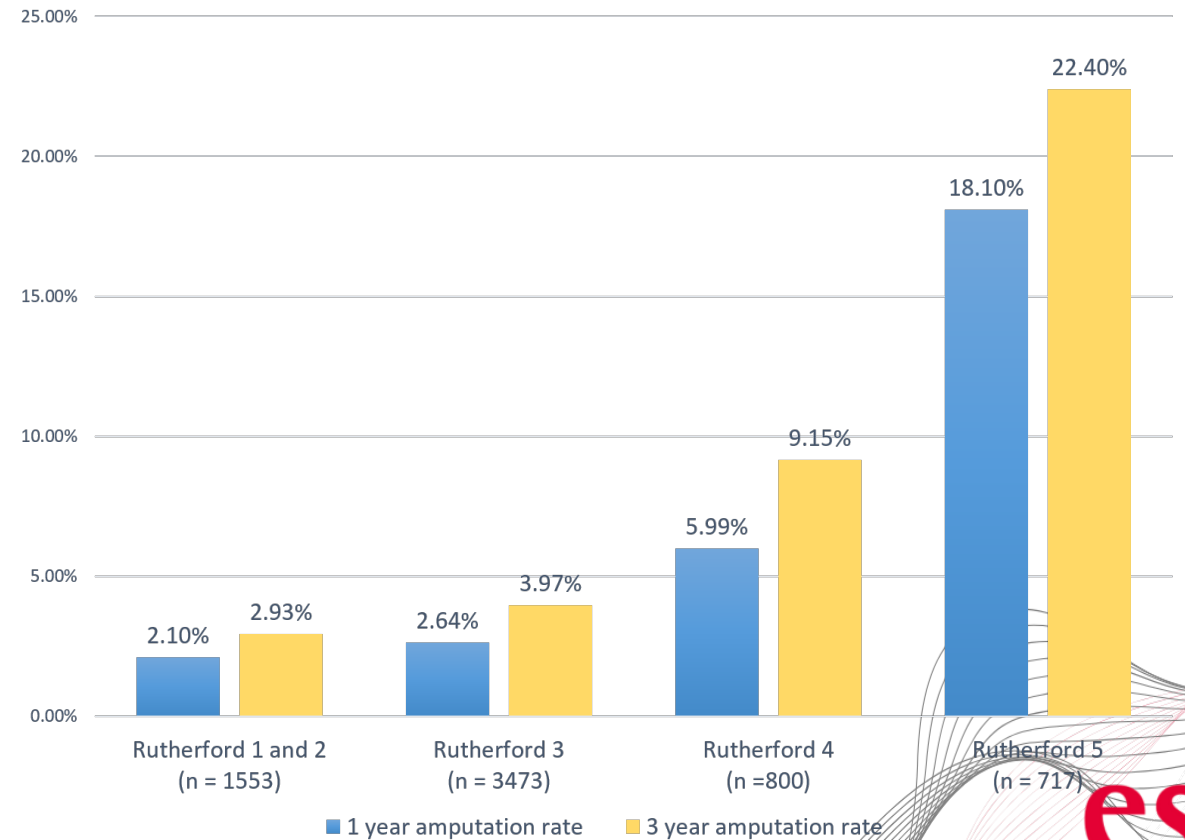
**Median 28 months**

# Results- Amputation Events

Panel A: Major Amputation Rate Post LER at Year 1 and Year 3  
( $p < 0.0001$ )



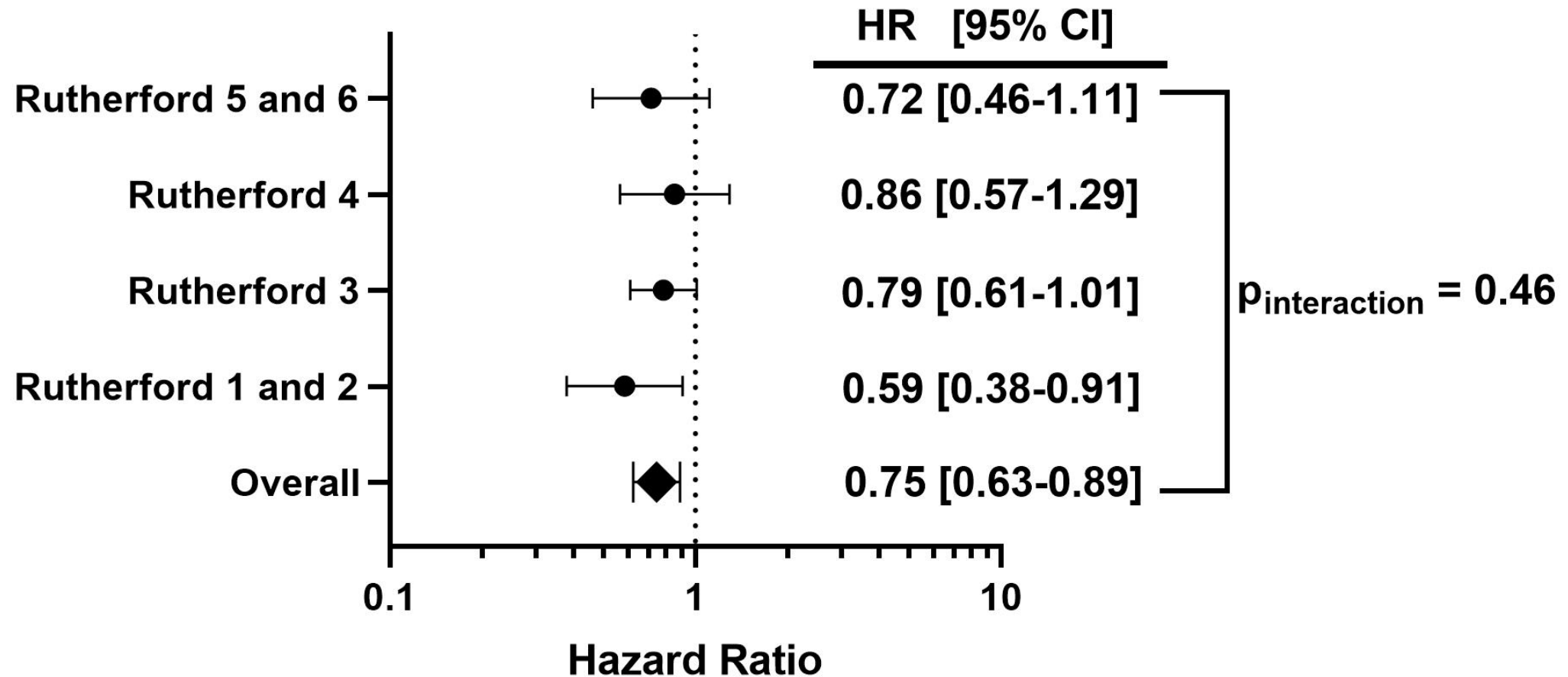
Panel B: Major and Minor Amputation Rate Post LER at Year 1 and Year 3  
( $p < 0.0001$ )





# Results- Composite of Major Amputation and ALL: Rivaroxaban vs. Placebo

## 3 Year Incidence of Amputation/ALI Rivaroxaban vs. Placebo



# Conclusion

- **Baseline pre LER Rutherford Chronic Limb Ischemia Stage provides risk stratification for amputation events**
- **There is a significant association between Rutherford Stage and outcomes, even after successful LER suggesting other drivers of limb events**
- **These data are useful when risk stratifying patients or predicting limb event rates in PAD post LER clinical trials**
- **Rutherford remains relevant in the modern era of PAD**