

EARLY ACS – (TIMI 39)

Early (<8h) Eptifibatide in Pts with High-Risk ACS

n~10,000

- ≥ 2 of the following:**
- 1. ↑ MB or Tn**
 - 2. New STD ≥ 1mm**
 - 3. Age ≥ 60***

***Age 50-54 with hx of CAD & either ↑ MB or Tn or new STD can be enrolled**

Eptifibatide 180/2/180

Matching Placebo

Angiography > 12 Hrs Later

**Optional Study Drug in Cath Lab
Blinded Placebo / Eptifibatide**

**Primary Endpoint: D/MI/UR/TBO at 96h
Secondary Endpoint: D/MI at 30 days**



IMPROVE IT – (TIMI 40)

IMProved Reduction of Outcomes: Vytorin Efficacy International Trial

Patients stabilized post Acute Coronary Syndrome < 10 days
LDL \leq 125 mg/dL (or \leq 100 mg/dL if prior statin)

Double-blind

ASA + Standard Medical Therapy

n~18,000

Simvastatin 40 mg

Eze/Simva 10/40 mg

Follow-Up Visit Day 30, Every 4 Months

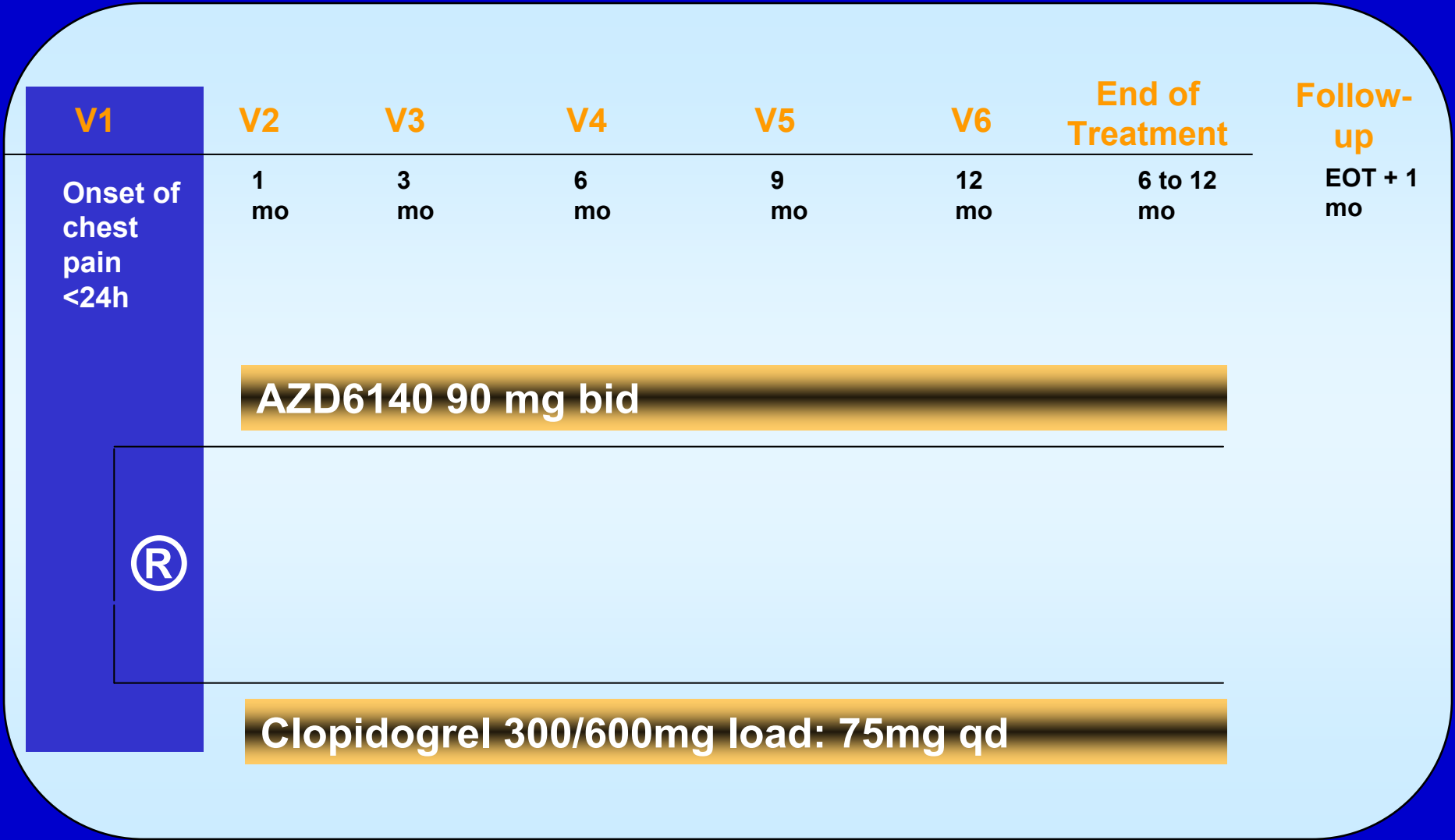
Duration: Minimum 2 1/2 year follow-up (>2955 events)

Primary Endpoint: CV Death, MI, Hospital Admission for UA, revascularization (> 30 days after randomization), or Stroke



PLATO – (TIMI 41)

A Study of PLAtelet inhibition and Patient Otcomes

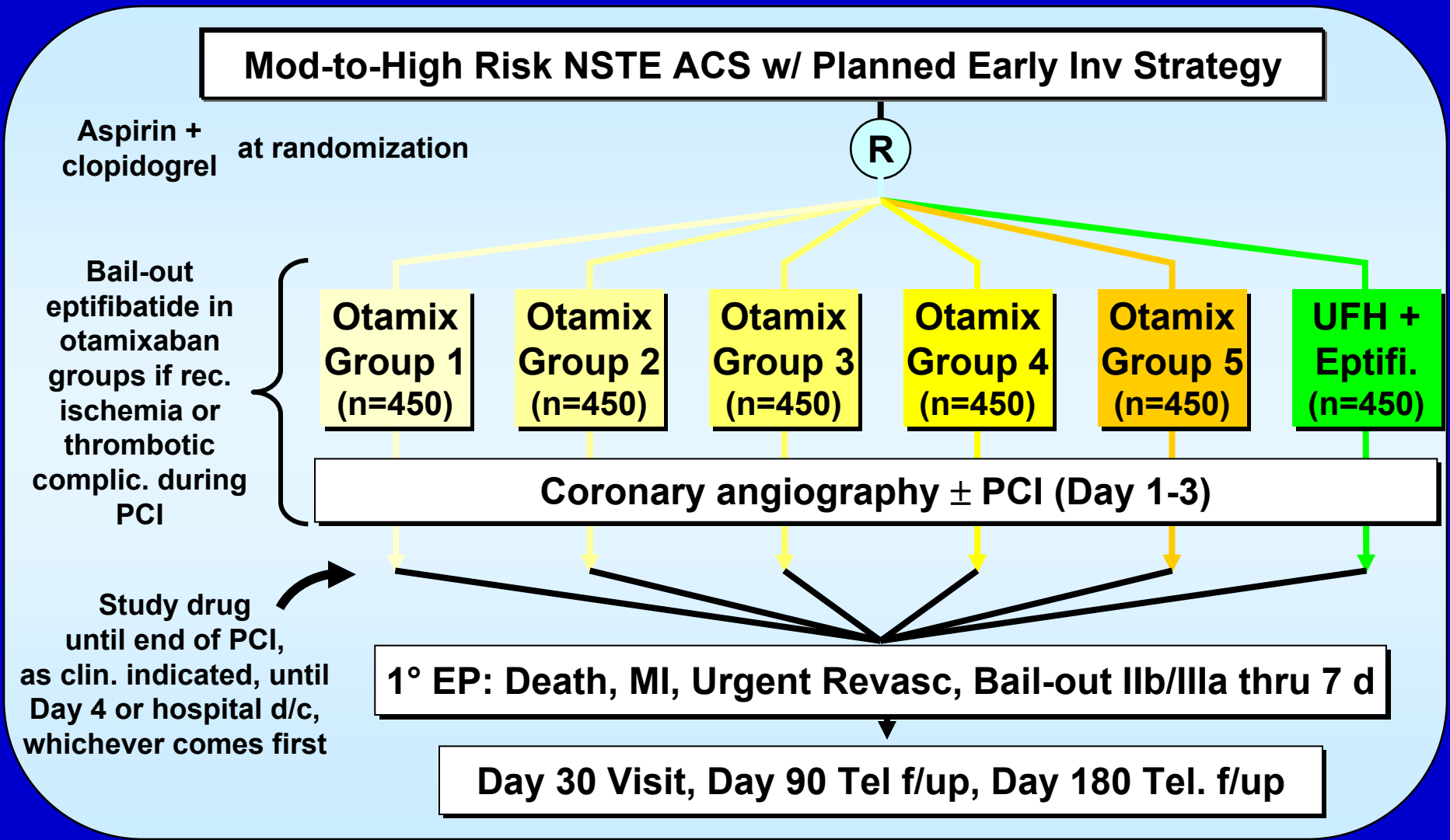




SEPIA-ACS 1 – TIMI 42



Dose Ranging Study of Otamixaban - a Novel, Intravenous, Direct Xa Inhibitor



AVANT GARDE – TIMI 43



Aliskiren and Valsartan to reduce NT-proBNP via renin-angiotensin-aldosterone-system blockade

Patients post ACS with ↑ natriuretic peptides

N= 1100

Blinded Therapy

Standard Medical Therapy

Valsartan

Aliskiren

Ali/Val

Placebo

NT-proBNP

4 wks

Dose up-titration over 2 wks

Dose up-titration of 2nd agent over 2 wks
(placebo in 3 arms and active in Combo arm)

NT-proBNP

4 wks

End of Study

Primary Endpoint - Δ NT-proBNP from baseline to week 8

NT-proBNP

VERIFY NOW – TIMI 45



Platelet Function Testing for Bleeding Management in Patients Treated with Clopidogrel and Undergoing Coronary Artery Bypass Grafting

**Enroll within 12 hrs of Angiography
Blood Draw for %P2Y12 Platelet Inhibition and Aspirin Responsiveness**

**Day 1
Blood Draw for % Platelet Inhibition**

**Day X
Blood Draw for % Platelet Inhibition**

**Pre-op Day
Blood Draw for % Platelet Inhibition**

**Day of CABG
Obtain Data from Procedure**

**Post-op Day
Follow Course for Complications**

PRIMARY OUTCOME

Correlation of % platelet inhibition immediately prior to surgery to the risk of major peri-operative bleeding.

ATLAS ACS – TIMI 46



N=3,491

**Recent ACS Patients
Stabilized 1-7 Days Post-Index Event**

NO

MD Decision to Treat with Clopidogrel

YES

STRATUM 1

Dose Levels
Stratum 1 – 5, 10, & 20 mg
Stratum 2 – 5, 10, 15, & 20 mg

STRATUM 2

PLACEBO

RIVA
QD

3 Dose Levels

RIVA
BID

3 Dose Levels

PLACEBO

RIVA
QD

3 Dose Levels

RIVA
BID

3 Dose Levels

Treat for 6 Months

Primary Safety Endpoint: TIMI Significant Bleeding
Primary Efficacy Endpoint: Death, MI, Stroke, or Ischemia Requiring Revascularization

RIVA = Rivaroxaban

IC-TITAN – TIMI 47



Intracoronary Treatment with Integrilin To Improve Angiographic Outcomes

**STEMI within 6 hours
Eligible for primary PCI**

**ASA 160-325 mg; Clopidogrel 300-600 mg
UFH; IV Eptifibatide (double bolus and infusion)**

Randomize

**Baseline angiography
Advance wire and balloon without crossing the lesion**

**IC Eptifibatide
90 µg/Kg bolus**

2 : 1

**IC saline
bolus**

Angiography (assess stenosis, flow and perfusion)

PCI

**Angiography
(assess epicardial flow and myocardial perfusion)**

**Primary Endpoint
Improvement in % diameter stenosis
pre and post Eptifibatide**

**Secondary Endpoint
Improvement in pre and post
Eptifibatide CTFC**

ENGAGE-AF-TIMI 48

A Study for Evaluation of DU-176b vs Warfarin in Subjects with AF

n~16,500

**AF on ECG \leq 12 mos
Intended oral A/C
CHADS₂ Score \geq 2**

Randomization Strata:
1. CHADS₂ 2-3 vs 4-6
2. Drug clearance

R

**Low Exposure
Strategy
DU-176b 30 mg QD
(n=5500)**

**High Exposure
Strategy
DU-176b 60 mg QD
(n=5500)**

**Active
Control
Warfarin
(n=5500)**

Median Duration of Followup 24 months

1° EP = Stroke or SEE (**Noninferiority Boundary HR 1.38**)
2° EP = Stroke or SEE or All-Cause Mortality
Safety EP's = Major Bleeding, Hepatic Function

Documented MI, CVA, or PAD

Standard care, including oral antiplt rx

RANDOMIZE 1:1 DOUBLE BLIND

SCH 530348
2.5 mg/d

Placebo

Follow-up
Min 1 yr; Avg 18-24 mo

Duration
Event driven

Follow up Visits
Day 30, Mo 4, Mo 8, Mo 12
Q6 months

Final Visit

Primary EP
**CV Death, MI, Stroke,
Urgent Coronary
Revascularization**