

**A phase III study of Enoxaparin vs Aspirin as thromboprophylaxis for patients with newly diagnosed multiple myeloma treated with Lenalidomide-based regimens**

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# Disclosures

Research Support/P.	none
Employee	none
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Honoraria	Celgene, Janssen-Cilag
Scientific Advisory Board	none

**Presentation includes discussion of the off-label use of a drug or drugs**

# Lenalidomide regimens and VTE incidence

<b>Lenalidomide regimens</b>	<b>MM Phase</b>	<b>AGE (median)</b>	<b>VTE incidence (%)</b>	<b>Ref</b>
<b>Alone</b>	<b>Relapse</b>	<b>59</b>	<b>0-3</b>	Richardson PG Blood 2006
<b>+ Dexamethasone</b>	<b>Dia</b>	<b>66</b>	<b>12-26</b>	Rajkumar SV, Lancet Oncol 2010
<b>+ Dexamethasone</b>	<b>Relapse</b>	<b>64</b> <b>63</b>	<b>15</b> <b>11</b>	Weber DM NEJM 2007 Dimopoulos M NEJM 2007
<b>+ Melphalan</b>	<b>Dia</b>	<b>71</b>	<b>6</b>	Palumbo A JCO 2007
<b>+ Doxorubicin</b>	<b>Relapse</b>	<b>62</b>	<b>9</b>	Baz R Ann of Oncol 2006
<b>+ Bortezomib-Dexamethasone</b>	<b>Dia</b>	<b>58</b>	<b>6</b>	Richardson PG, Blood 2010
<b>+ Dexamethasone</b>	<b>Dia</b>	<b>65</b>	<b>6</b>	Zonder JA Blood 2010

Thromboprophylaxis was not mandatory

■ ASA thromboprophylaxis

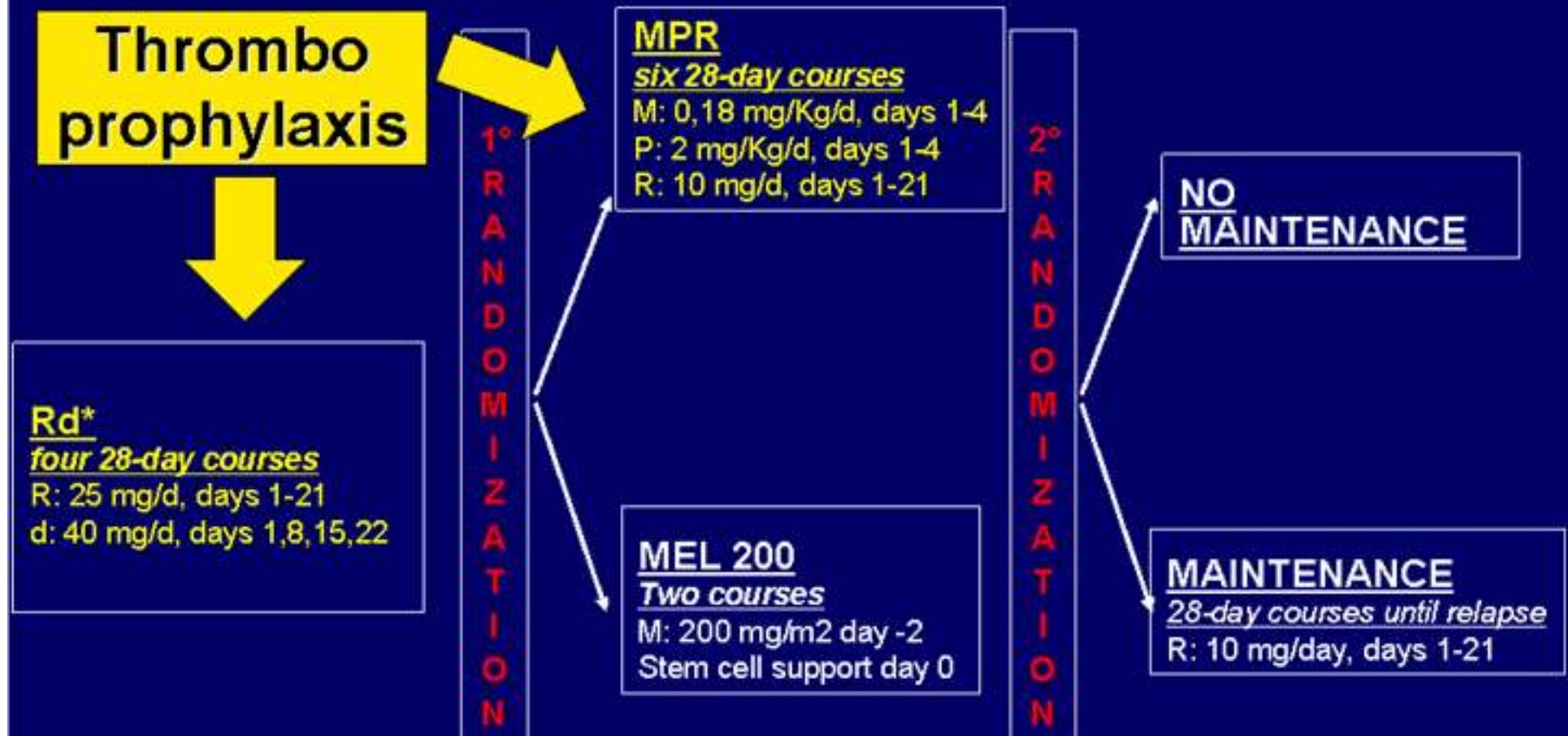
## ASCO Guidelines

“Prophylaxis with LMWH or WAR is recommended in MM patients receiving Thalidomide or Lenalidomide with chemotherapy and/or dexamethasone”

Randomized trials for Lenalidomide are still lacking

# Study Flowchart RV-MM-PI-209

- 402 patients (younger than 65 years) randomized from 62 centers
- Patients: symptomatic and measurable disease, with organ damage



# Study Endpoints

## Primary

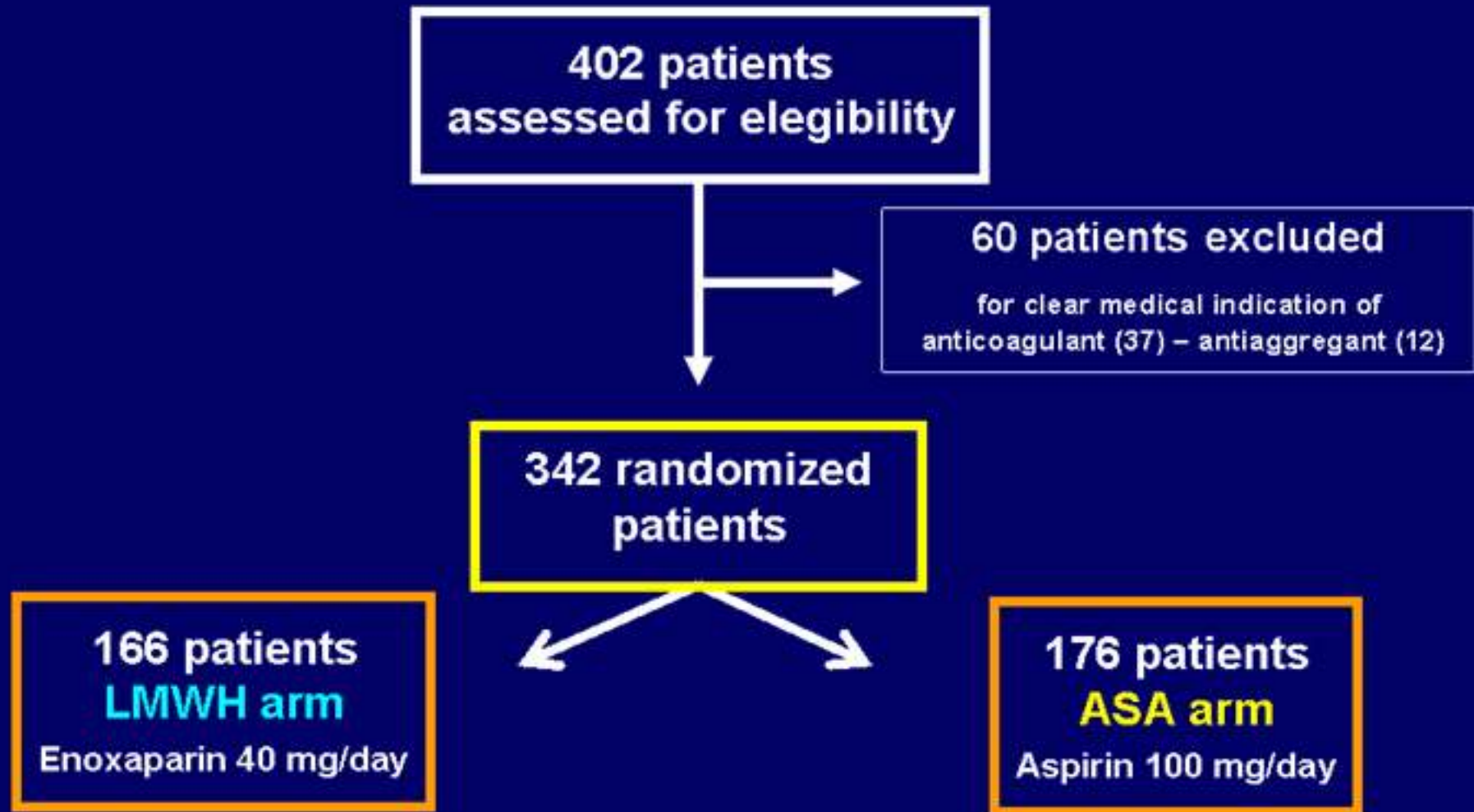
- deep vein thrombosis
- pulmonary embolism
- arterial thrombosis
- any acute cardiovascular event
- sudden, otherwise unexplained, death

## Secondary

- any bleeding complication
- any other complication related to thromboprophylaxis

# VTE Prophylaxis randomization

Patients enrolled from November 2007 to June 2009



# Patient characteristics

	ASA N=176	LMWH N=166
Age (median)	57	58
≥ 60 years	36 %	40 %
MPR	48 %	48 %
Mel 200 mg/m <sup>2</sup>	52 %	52 %
Cardiac disease	7 %	4 %
Diabetes	1 %	1 %
Inherited conditions	0 %	0 %
Concomitant rHuEpo	17 %	17 %
≥ 1 Risk factor	2 %	1 %



# Results

	<b>ASA N=176</b>	<b>LMWH N=166</b>	<b>Absolute difference, %</b>	<b>P-value</b>
<b>Efficacy analysis, n (%)</b>				
<b>Composite primary endpoint</b>	<b>4 (2.27)</b>	<b>2 (1.20)</b>	<b>1.07</b>	<b>0.452</b>
<b>Any grade 3/4 thromboembolic event, n (%)</b>	<b>4 (2.27)</b>	<b>2 (1.20)</b>	<b>1.07</b>	<b>0.452</b>
<b>Deep-vein thrombosis</b>	<b>2 (1.14)</b>	<b>2 (1.20)</b>	<b>-0.07</b>	<b>0.953</b>
<b>Pulmonary embolism</b>	<b>3 (1.70)</b>	<b>0</b>	<b>1.70</b>	<b>0.091</b>
<b>Arterial thrombosis</b>	<b>0</b>	<b>0</b>	<b>-</b>	<b>-</b>
<b>Acute cardiovascular events</b>	<b>0</b>	<b>0</b>	<b>-</b>	<b>-</b>
<b>Sudden deaths</b>	<b>0</b>	<b>0</b>	<b>-</b>	<b>-</b>

# VTE characteristics

Prophylaxis	Age	Sex	ISS	KPS	Risk Factors	VTE	Treatment
ASA	57	M	2	70	rHuEpo	PE	Rd
ASA	55	F	3	70	rHuEpo	PE	Rd
ASA	57	F	1	70	rHuEpo	PE	Rd
ASA	61	F	3	90	None	DVT	Rd
LMWH	52	M	1	100	None	DVT	Rd
LMWH	58	F	3	80	None	DVT	Rd

# Results

	ASA N=176	LMWH N=166	Absolute difference, %	P-value
<b>Safety analysis, n (%)</b>				
Minor bleeding	0	1 (0.60)	-0.60	0.302
Gastrointestinal	0	1 (0.60)	-	-

# Results: cumulative incidence of composite primary endpoint



# Conclusions

- **Thromboprophylaxis → low incidence of VTE**
- **Thromboembolic events → in early phase**
- **Thromboprophylaxis → first 4-6 months**

# Conclusions

**LMWH: standard prophylaxis  
for MM patients treated with Lenalidomide**

**ASA: possible alternative in**

- low-risk patients
- long term prophylaxis

# We Are Grateful to All Patients, Nurses and Physicians of the Participating Centers

1. ALESSANDRIA	Levis, Baraldi	39. GENOVA	Carella, Spriano	77. RIMINI	Pasquini, Fattori
2. ANCONA	Leoni, Offidani	40. GENOVA	Bacigalupo, Dominiotto	78. RIONERO VULTURE	Musto
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