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American Heart Association.

Professional Heart Daily

NEWTON 2

Randomized, Double-Blind, Placebo-Controlled Study Of EG-1962 In Adults With Aneurysmal Subarachnoid Hemorrhage

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for the NEWTON 2 Investigators

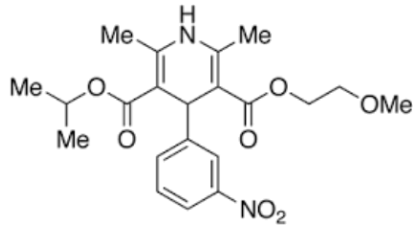




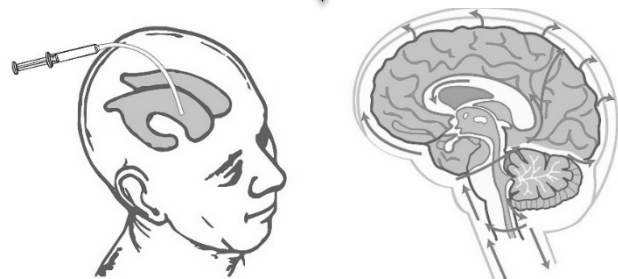
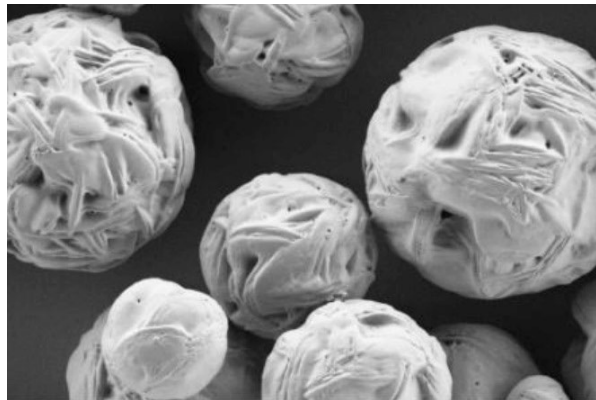
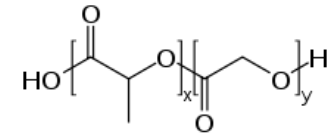
- Idorsia – Consulting fee
- Edge Therapeutics – Consulting fee



Nimodipine



PLGA

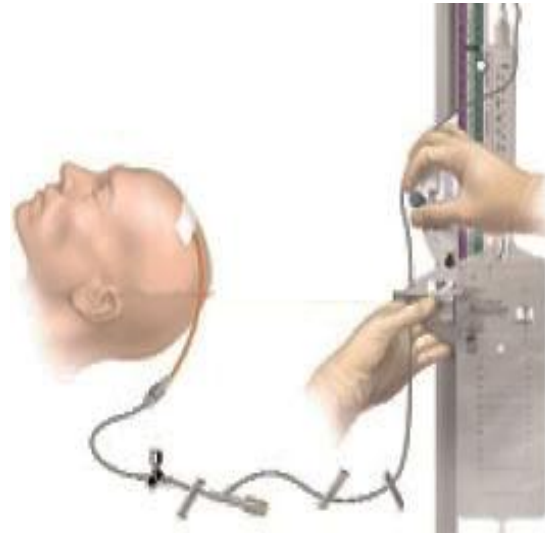
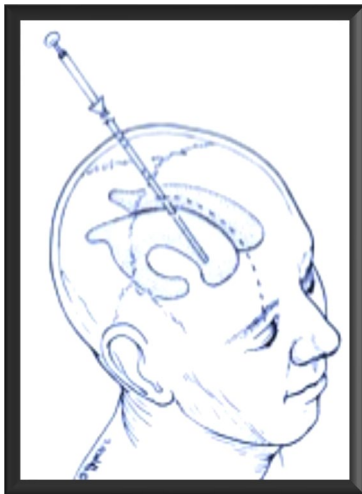


- 10 - 200 μm microparticles
- Biodegradable polymer
- Sodium hyaluronate diluent
- Single intraventricular injection
- Sustained-release formulation
- Nimodipine release for 21 days
- 600 mg nimodipine

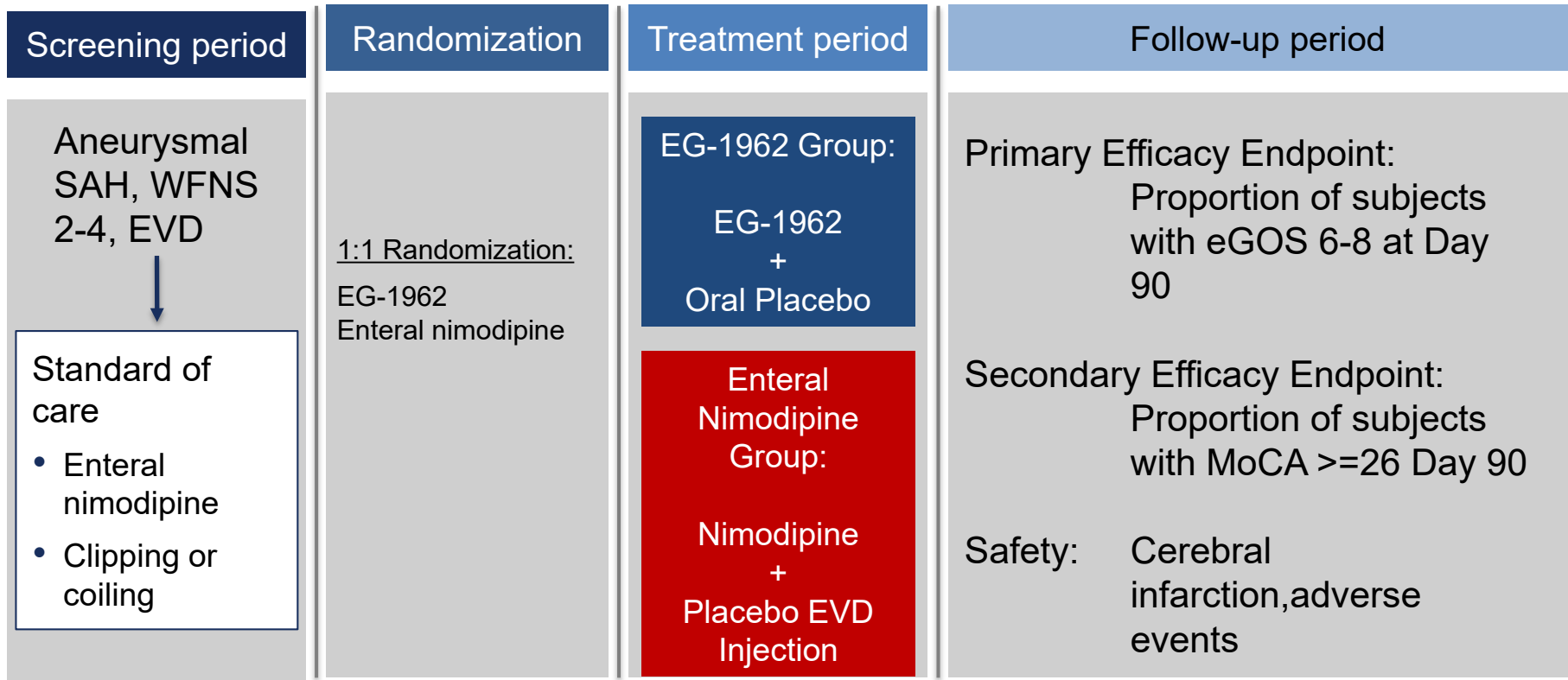
Background



External Ventricular Drain



NEWTON 2 Design



Day 0

Day 1 – 21

Day 90

374 subjects to detect a 15% difference in proportion of favorable outcome with EG-1962 compared to placebo



- 65 centers in 11 countries
- First subject randomized – July, 2016
- Preplanned interim analysis after 210 subjects had 90 day follow-up for sample size re-estimation
- Independent Data Monitoring Committee reviewed (safety data) 210 subject data
- March 27, 2018 – Stop the study because of a low likelihood of meeting the primary endpoint
- Final number of subjects - 282

Results: Baseline Characteristics



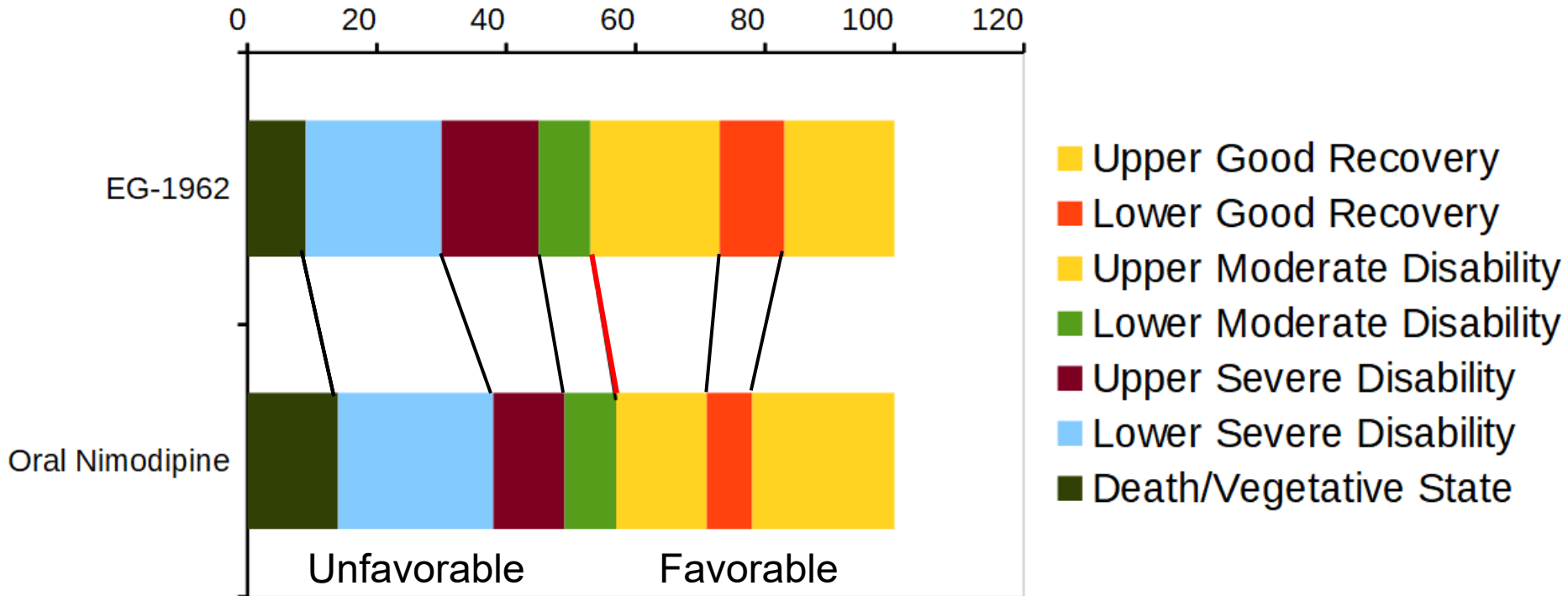
	EG-1962 (n = 138)	Oral nimodipine (n = 144)
Age	56 +/- 10	57 +/- 11
Female	95 (69%)	102 (71%)
WFNS 2	76 (55%)	67 (47%)
WFNS 3 + 4	62 (45%)	77 (53%)

Results: Angiographic Vasospasm



Factor	EG-1962 (n = 138)	Oral Nimodipine (n = 144)	2-sided P value
Any vasospasm	77 (56%)	101 (70%)	0.013
Angiographic vasospasm	69 (50%)	91 (63%)	0.025
Vasospasm as adverse event	53 (38%)	69 (48%)	0.11
Delayed cerebral ischemia	32 (23%)	40 (28%)	0.38

Results: Primary Outcome



EG-1962: 46% Favorable Outcome (7% mortality)

Oral Nimodipine: 43% Favorable Outcome (10% mortality)

Results: MoCA Day 90



	EG-1962 (n = 138)	Oral Nimodipine (n = 144)	2-sided P value
Raw score (mean)	23 +/- 7	22 +/- 8	0.33
Favorable MoCA > =26	44%	46%	0.66

Results: Prespecified Subgroups

Proportion subjects EGOS 6-8



Factor	Category	EG-1962 (n = 138)	Oral Nimodipine (n = 144)	2-sided P value
WFNS Grade	2	32 (46%)	38 (55%)	0.19
	3 + 4	32 (46%)	24 (32%)	0.09
Region	USA	46 (57%)	38 (45%)	0.17
	Non-USA	18 (32%)	24 (41%)	0.24
Age	< 60	46 (55%)	42 (53%)	0.88
	>= 60	18 (33%)	20 (31%)	0.75

Safety



Factor	EG-1962 (n = 138)	Oral Nimodipine (n = 144)	2-sided P value
Any rescue therapy	37 (27%)	50 (35%)	0.15
Hypotension	9 (7%)	14 (10%)	
Any treatment emergent SAE	63 (46%)	69 (48%)	
Hydrocephalus (CSF shunt)	36 (26%)	31 (22%)	
Bacterial meningitis	4 (3%)	3 (2%)	
Aseptic meningitis	6 (4%)	6 (4%)	



- EG-1962 significantly reduced angiographic vasospasm and any vasospasm
- Overall clinical outcome
 - EG-1962 = standard of care oral nimodipine
- No safety signals
- Subgroup analyses
 - WFNS 3+4 – EG-1962 trend toward improved outcome
 - WFNS 2 – EG-1962 trend towards worse outcome

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