

RE-ALIGN: Dabigatran in Patients With a Mechanical Heart Valve

**Randomized, phase II study to Evaluate the sAfety
and pharmacokinetics of oraL dabIGatran etexilate
in patients after heart valve replacemeNt**

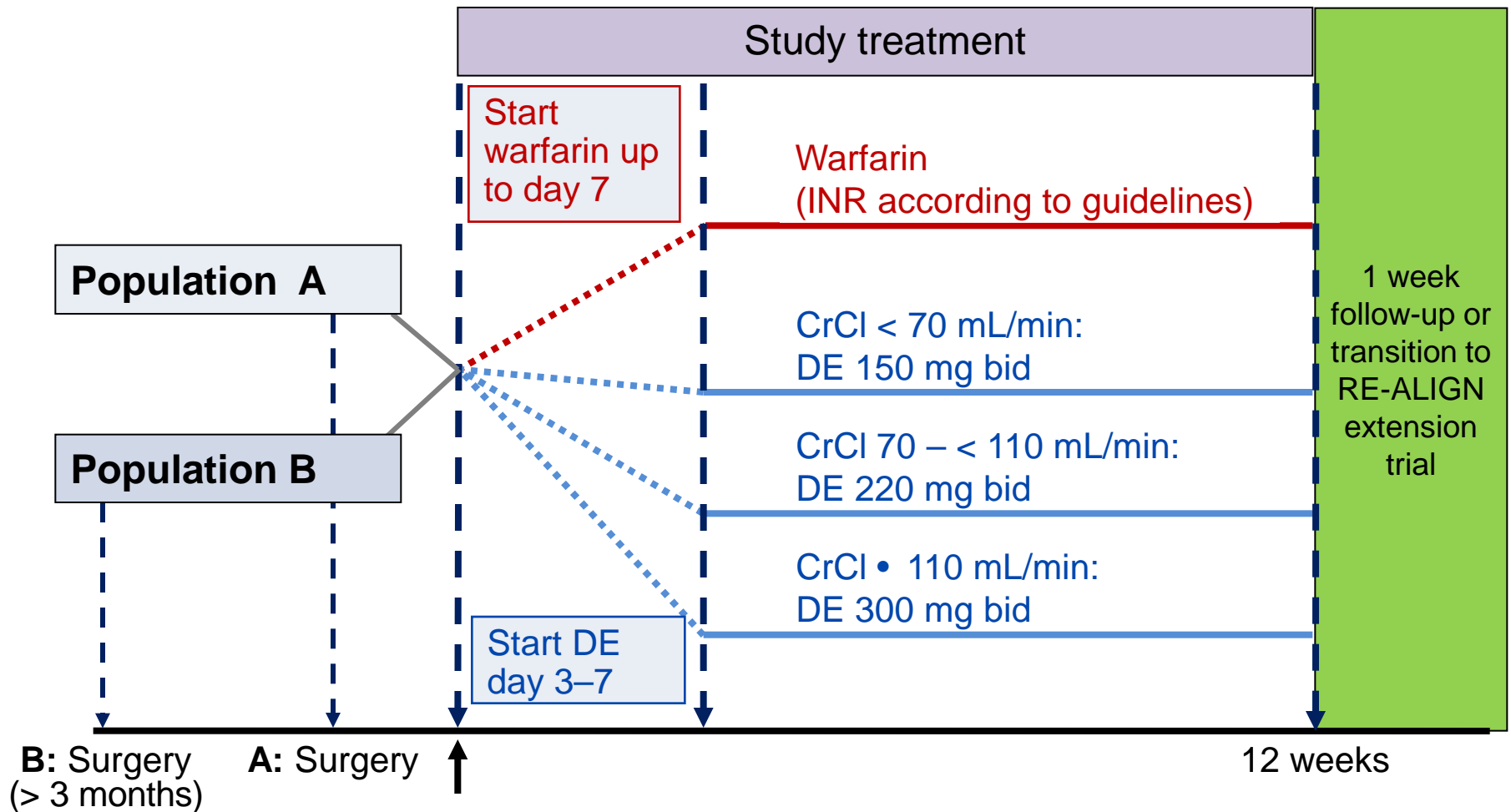
DECLARATION OF INTEREST

- Research contracts
- Consulting/Royalties/Owner/ Stockholder of a healthcare company

Background

- Vitamin K antagonists provide effective protection against thrombosis in patients with a mechanical valve but require food, alcohol and drug restrictions and coagulation monitoring
- Dabigatran 150 mg bid is superior to warfarin in non-valvular atrial fibrillation (RELY)
- Encouraging preclinical data with dabigatran in porcine mechanical valve models

Study design of RE-ALIGN



- Increase dose if dabigatran trough plasma level < 50 ng/mL (by Hemoclot®)
- Discontinue dabigatran (switch to nonstudy VKA) if < 50 ng/mL with 300 mg bid after 2 measurements

Adjudicated efficacy outcomes

	Population A		Population B		All patients	
	Dabigatran (n = 133)	Warfarin (n = 66)	Dabigatran (n = 35)	Warfarin (n = 18)	Dabigatran (n = 168)	Warfarin (n = 84)
Death, n (%)	1 (1)	2 (3)	0	0	1 (1)	2 (2)
Stroke, n (%)	9 (7)	0	0	0	9 (5)	0
SE, n (%)	0	0	0	0	0	0
TIA, n (%)	2 (2)	2 (3)	1 (3)	0	3 (2)	2 (2)
MI, n (%)	1 (1)	0	2 (6)	0	3 (2)	0
Valve thrombosis without symptoms	2 (2)	0	3 (9)	0	5 (3)	0
Death/stroke/SE/ MI, n (%)	11 (8)	2 (3)	2 (6)	0	13 (8)	2 (2)
Death/stroke/TIA/ SE/MI, n (%)	12 (9)	4 (6)	3 (9)	0	15 (9)	4 (5)

Adjudicated safety outcomes

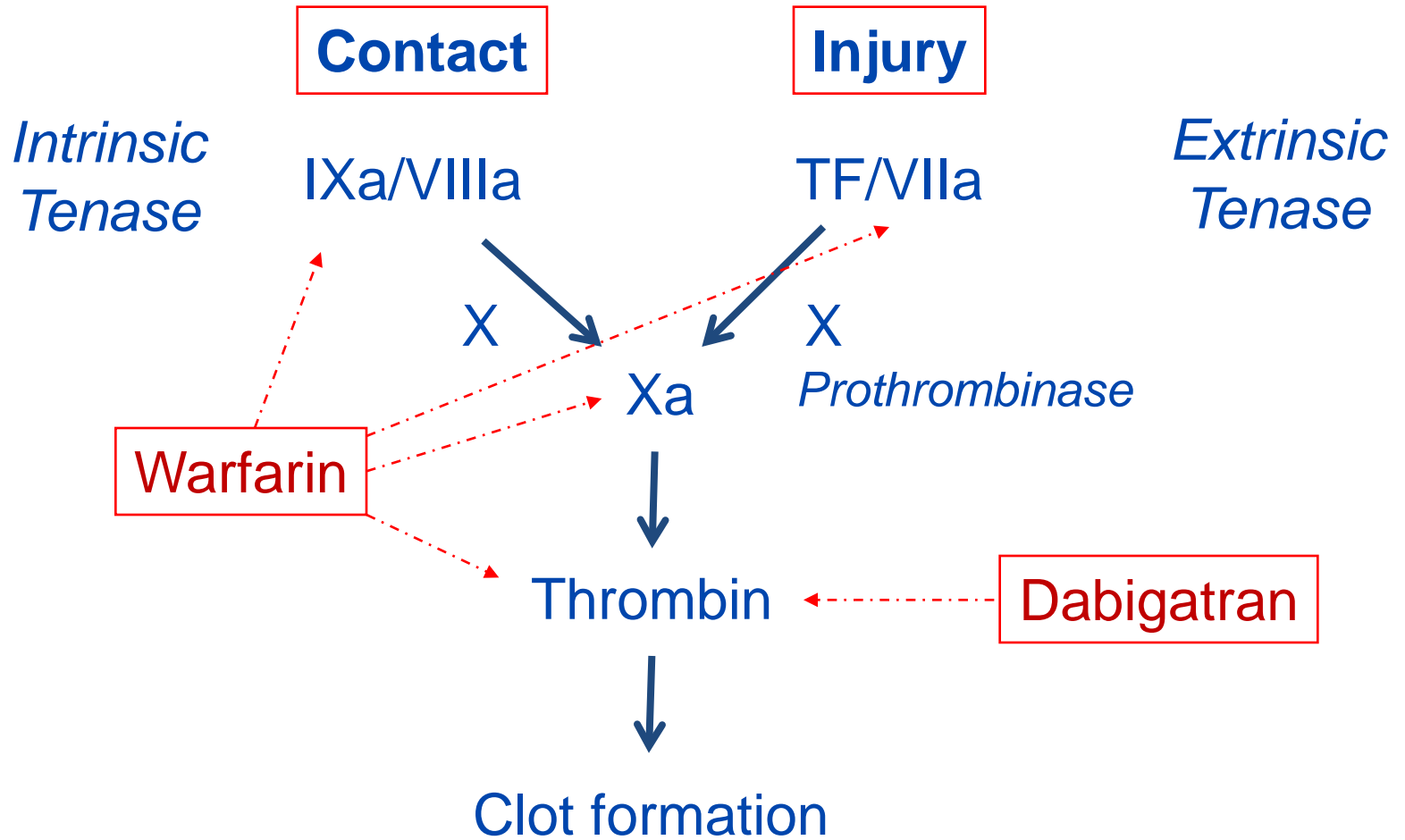
	Population A		Population B		All patients	
	Dabigatran (n = 133)	Warfarin (n = 66)	Dabigatran (n = 35)	Warfarin (n = 18)	Dabigatran (n = 168)	Warfarin (n = 84)
Major bleeding, n (%)	7 (5)	2 (3)	0	0	7 (4)	2 (2)
Major bleeding with pericardial location, n (%)	7 (5)	2 (3)	0	0	7 (4)	2 (2)
Any bleeding, n (%)	35 (26)	8 (12)	10 (29)	2 (11)	45 (27)	10 (12)

Possible explanations for negative study results

- Inadequate blood levels of dabigatran
- Play of chance with relatively few events seen in the warfarin arm
- Differences in the mechanism of action of dabigatran compared with warfarin
 - e.g., the inability of dabigatran to suppress activation of coagulation that occurs when blood is exposed to the artificial surface of prosthetic valves

Prosthetic valves and contact activation

Dabigatran vs. Warfarin



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ORIGINAL ARTICLE

Dabigatran versus Warfarin in Patients with Mechanical Heart Valves

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