Supplemental Table

Selected human trials and animal stroke studies using agents targeting the immune system

	Human trials				Animal Studies			
Drug, Trial type	**Population, n (drug/ placebo or conventional tx)**	**Age**	**Time of initial dose**	**Outcomes, *comments (reference)**	**Model**	**Species and sex**	**Time of initial dose**	**Outcomes, *comments (reference)**
Anti CD11/CD18, Hu23F2G, Rovelizumab Phase III	Ischemic stroke >400	?	≤12 hours	Negative trial *study not published, data from news article (1)	Transient 2 hr proximal MCAO	Male NZ rabbits	20 min	smaller infarct (2)
					MCAO with fibrin-rich clot	Male Wistar Rats	2 hrs ± tPA	No benefit with or without tPA (3)
					MCAO with fibrin-rich clot	Male Wistar Rats	4 hrs ± tPA	No benefit alone, but improved infarct size and function when given with tPA (3)
anti-ICAM1 Enlimomab Phase II	Ischemic stroke 625(317/308)	20-99	≤6 hrs then 5d	More infection worse mRS *the murine antibody likely provoked an immune response (4)	Embolism	Rabbit, Not specified	15 or 30 min	no benefit unless with tPA (5)
UK-279,276 CD18 Antagonist Adaptive dose-response finding	Stroke 966(748/218)	36-96 (mean 72)	≤ 6hrs	stopped for futility *Well tolerated, did not alter change in SSS, (6)	Permanent proximal MCAO	Male Wistar rats	2 hrs	no benefit (7)
					Transient 2 hr proximal MCAO	Male Wistar rats	4 hrs	reduced infarct size, improved function (7)
Anakinra, Interleukin-1 receptor antagonist Phase II	Stroke 34(17/17)	61-77	≤ 6hrs, then for 72hrs IV	No adverse events, more 30d 0-1 mRS, more reduction from baseline NIHSS in patients with cortical infarcts only. *Reduced peripheral inflammation(8)	Transient 70 min proximal MCAO	Male Wistar rats	3 then 6 hr dose	smaller infarcts improved function (9)
					Transient 60 min proximal MCAO	Male Wistar rats	60 min	no difference in infarct size, improved recovery with 60 min (10)
					Transient 60 min proximal MCAO	Male Wistar rats	24 hrs	No benefit (10)

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Anakinra, Interleukin-1 receptor antagonist Phase II	Ischemic stroke, most with tPA 80(39/41)	Mean 72	≤5hrs, then bid for 3d sq	no clinical benefit *Reduced plasma IL-6, no change in CRP (11)	Transient 90 min proximal MCAO	Aged (15-16 month old) male lean and corpulent JCR rats	3 hrs	Smaller 24hr infarct volume, fewer infiltrating neutrophils (12)
					Transient 90 min proximal MCAO	Aged (13 month old) male lean and corpulent JCR rats	3 hrs	smaller infarcts improved function (9)
Minocycline Open label/ evaluator blinded	Ischemic stroke 152(74/77)	Mean 67	6-24hrs, then 5 days (mean 12.6 hrs)	Better function on mRS, BI, NIHSS out to 90d (13)	Embolic focal stroke	Male Wistar rats, type I diabetic	60 min	smaller infarcts (14)
					Transient 90 min proximal MCAO	Male C57BL/6J mice	30 min	smaller infarcts and better function (15)
					Transient 90 min proximal MCAO	Ovariect-omized female C57BL/6J mice	30 min	no benefit (15)
Minocycline Open label/ evaluator blinded	Ischemic stroke 53 (26/27)	Mean 67	6-24hrs, then 5 days	Males with improved NIHSS vs. ASA, females no effect (16)	Transient 60 min embolic stroke	Male SHR	tPA 6 hrs, mino-cycline at 4 hrs	reduced infarct, less hemor-rhagic conversion (17)
					Transient 90 min proximal MCAO	Male SD rats	4 hrs	Reduced Infarct size (18)
S1p inhibitor, FTY720, Fingolimod Open label / evaluator blinded	Ischemic stroke 22(11/11)	Mean 63	Mean 20 hrs, then daily for 3d	More reduction in NIHSS, more 0-1 90d mRS *case-control. By infarct size (19)	Embolic stroke, reperfusion at 30 min	Male C57BL/6J mice	30 min	Improved infarct size and function (20)
					Photothrombotic stroke	Male C57BL/6J mice	3 days	Improved function (21)
Fingolimod Open label	ACA or MCA strokes 47(25 tPA alone/22 fingolimod +tPA)	Mean 60	≤ 4.5 hrs, then daily for 3d	Less infarct growth, 0-1 90d mRS was better *randomized by coin toss (22)	Permanent distal MCAO	Male C57BL/6J mice	3 hrs	No benefit (23)
					Transient 2 hr proximal MCAO	male SD rats	2 hrs	decreased infarct, improved function (24)

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Anti-VLA-4 / CD49d Natalizumab Phase II	Ischemic stroke, 161(79/82)	18-85	≤9 hrs once	Infarct growth not different, more patients with mRS 0-1 at 30d *follow-up Phase IIb trial at ≤24hr dosing was negative (unpub) (25)	Permanent distal MCAO	Male C57BL/6J mice	3 hrs	infarct reduction, fewer leukocytes *multicenter preclinical (26)
					Transient 1 hr proximal MCAO	Male C57BL/6J mice	3 hrs	no benefit *multicenter preclinical (26)
					Transient 3hr proximal MCAO	Male Lewis Rats	2 hrs	Infarct reduction, better function (27)
					Transient 30 min proximal MCAO	Male C57BL/6J mice	3 hrs	Infarct reduction, fewer leukocytes (28)
					Transient 30 min proximal MCAO	Male C57BL/6J mice	3 hrs	No benefit (29)

Abbreviations: CRP: C reactive protein; MCAO: Middle Cerebral Artery Occlusion; SSS: Scandinavian Stroke Scale; SD: Sprague-Dawley; SHR: Spontaneously hypertensive rat

Legend: Selected human and animal stroke studies. Human studies were eliminated for being un-controlled, animal studies eliminated if the dosing regimen was not clinically applicable or if the outcome wasn't stroke size or animal function. Control is either placebo or conventional therapy for all human studies. For rodent trials, times are for first dose, and size means infarct reduction, function means improvement on some functional score or task. If an animal study was negative it is in red.

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