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Supplementary information

Therapeutic strategies targeting inflammation and immunity in atherosclerosis: how to proceed?

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Supplementary Table 1 | **Immunotherapies without beneficial effects on inflammation or event rates in cardiovascular disease in clinical trials**

Trial (year)	Drug	Drug target	Design	Patient cohort	Primary end point	Main outcomes	Ref.
CIRT (2019)	Methotrexate	Dihydrofolate reductase inhibitor	Phase III, randomized, double-blind, placebo-controlled	4,786 patients with previous MI or multivessel coronary artery disease who additionally had either T2DM or metabolic syndrome	Composite of nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death	No effect on cardiovascular events compared with placebo and did not reduce plasma IL-1β, IL-6 or CRP levels	[1]
SILENCE (2015)	Liposomal nanoparticle encapsulating prednisolone (LN-PLP)	Delivery to macrophages in atherosclerotic plaques	Phase II, randomized, double-blind, placebo-controlled	30 patients with documented history of CVD	FDG-PET CT to identify patients with marked arterial wall inflammation	Short-term LN-PLP treatment did not reduce arterial wall inflammation measured by FDG-PET CT	[2]
Bissonnette et al. (2017)	Adalimumab	Tumour necrosis factor antagonist	Phase II. randomized, double-blind, placebo-controlled	107 patients with psoriasis	Arterial inflammation detected by PET–CT	No difference in vascular inflammation after 16 weeks	[3]
GLACIER (2015)	MLDL1278A	Anti-oxidized-LDL antibody	Phase II, randomized, double-blind, placebo-controlled	147 patients with evidence of vascular inflammation, as quantified by FDG-PET–CT	Change in vascular inflammation, measured by FDG-PET–CT and hsCRP levels at 12 weeks	No difference in vascular inflammation on FDG-PET–CT and no significant differences in hsCRP levels with MLDL1278A versus placebo	[4]
Elkhawad et al. (2012)	Losmapimod	p38 inhibition	Phase II, randomized, placebo-controlled	99 patients with atherosclerosis who were receiving stable stain therapy	Vascular inflammation measured by FDG-PET–CT and hsCRP	No significant changes in vascular inflammation and hsCRP levels	[5]
SOLSTICE (2014)			Phase II, randomized, placebo-controlled	526 patients with NSTEMI	hsCRP and infarct size	hsCRP levels at 72 h were lower in the losmapimod group than in the placebo group but were similar at 12 weeks. No differences in infarct size	[6]
LATITUDE-TIMI 60 (2016)			Phase III, randomized, double-blind, placebo-controlled	3,505 patients with acute MI	Cardiovascular death, MI or severe recurrent ischaemia requiring urgent coronary revascularization	No reduction in the risk of major ischaemic cardiovascular events	[7]

ACS, acute coronary syndrome; FDG, fluorodeoxyglucose; hsCRP, high-sensitivity C-reactive protein; CVD, cardiovascular disease; LDL-C, LDL-cholesterol; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; T2DM, type 2 diabetes mellitus.

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