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Initiation of low-dose colchicine early after myocardial infarction

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This commentary refers to the article 'Time-to-treatment initiation of colchicine and cardiovascular outcomes after myocardial infarction in the Colchicine Cardiovascular Outcomes Trial (COLCOT)', N. Bouabdallaoui *et al.*, doi:10.1093/eurheartj/ehaa659 and the discussion piece 'Colchicine administered early in acute MI: ready, set… go?', by D. Vrachatis *et al.*, doi:10.1093/eurheartj/ehab010; 'Colchicine and coronary artery disease: a virtuous adoption', by F. Angelini *et al.*, doi:10.1093/eurheartj/ehab008; and 'Lessons from COLCOT and LoDoCo2: colchicine for secondary prevention in coronary artery disease', by N. Bouabdallaoui *et al.*, doi:10.1093/eurheartj/ehab020.

We thank Vrachatis *et al.*[1] for their laudatory comments about the landmark COLchicine Cardiovascular Outcomes Trial (COLCOT). Myocardial infarction is associated with an acute exacerbation of inflammation superimposed on the chronic atherosclerosis-related inflammatory process. This intense inflammatory reaction has been linked to the pathogenesis of ventricular remodelling after myocardial infarction, and activation of the NLRP3 inflammasome appears to be a central player in this setting. As we hypothesized, inflammation reduction with colchicine started before hospital discharge following myocardial infarction in COLCOT resulted in a large decrease in ischaemic cardiovascular events when administered in addition to standard of care.[2,3] Indeed, patients in whom low-dose colchicine was initiated within 3 days post-infarction benefitted from relative and absolute risk reductions of 48% and 4% compared to placebo, respectively.[3] Colchicine initiated early after myocardial infarction also reduced the risk of the secondary composite endpoint of cardiovascular death, resuscitated cardiac arrest, myocardial infarction, and stroke by 45%.

Vrachatis *et al.*[1] expressed an interest in a sub-analysis of patients randomly assigned in COLCOT to colchicine or placebo within the first 3 days after myocardial infarction, further divided according to the time interval between this index event and randomization. This would have represented a smaller subgroup analysis of the initial subgroup, which would have been of limited value. This suggested analysis could also not be performed because of the manner in which the data were coded. Furthermore, this question is different than the hypothesis prospectively tested in COLCOT, in which low-dose colchicine clearly reduced the risk of ischaemic cardiovascular events when initiated within 30 days after a recent myocardial infarction.[2]

Regarding the consideration of the specific medication used to reduce inflammation and its dosage, the COLCOT and Low-Dose Colchicine-2 (LoDoCo2) trials have clearly shown that colchicine 0.5 mg once daily leads to a lower risk of an ischaemic cardiovascular event than placebo, both in patients with a recent myocardial infarction and those with chronic coronary disease.[2,4] A recent meta-analysis of studies in patients with coronary artery disease showed that low-dose colchicine reduces the incidence of myocardial infarction by 38%, that of stroke by 62% and of urgent coronary revascularization by 44% compared to placebo.[5] Given that it provides large benefits on cardiovascular events safely and in a cost-effective manner,[6] low-dose colchicine therapy should be considered for all patients with coronary disease and no severe renal dysfunction. When considering specifically patients in the post-myocardial infarction setting, initiation of colchicine within the first 3 days after the event provides marked cardiovascular benefits and represents a practical treatment strategy before hospital discharge.

Conflict of interest: N.B. reports personal fees from AstraZeneca, outside the submitted work; Dr. Tardif reports grants from Government of Quebec, grants from Canadian Institutes of Health Research, grants from Montreal Heart Institute Foundation, during the conduct of the study; grants from Amarin, grants and personal fees from Astra Zeneca, grants, personal fees and other from Dalcor, grants from Esperion, grants from Ionis, grants and personal fees from Sanofi, grants and personal fees from Servier, grants from RegenXBio, outside the submitted work; In addition, J.-C.T. has a patent Genetic markers for predicting responsiveness to therapy with HDL-raising or HDL mimicking agent pending, a patent Methods for using low dose colchicine after myocardial infarction pending to Invention assigned to the Montreal Heart Institute, and a

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patent Methods of treating a coronavirus infection using Colchicine pending.

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