



**GRCI
2021**



La science pour la santé
From science to health



Inflammation dans les pathologies cardiovasculaires : de la physiopathologie aux études d'intervention

Pr François Roubille

Cardiology Intensive Care Unit
francois.roubille@gmail.com



MONTPELLIER UNIVERSITÉ D'EXCELLENCE



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Conflits d'intérêt

Affiliation/Financial Relationship

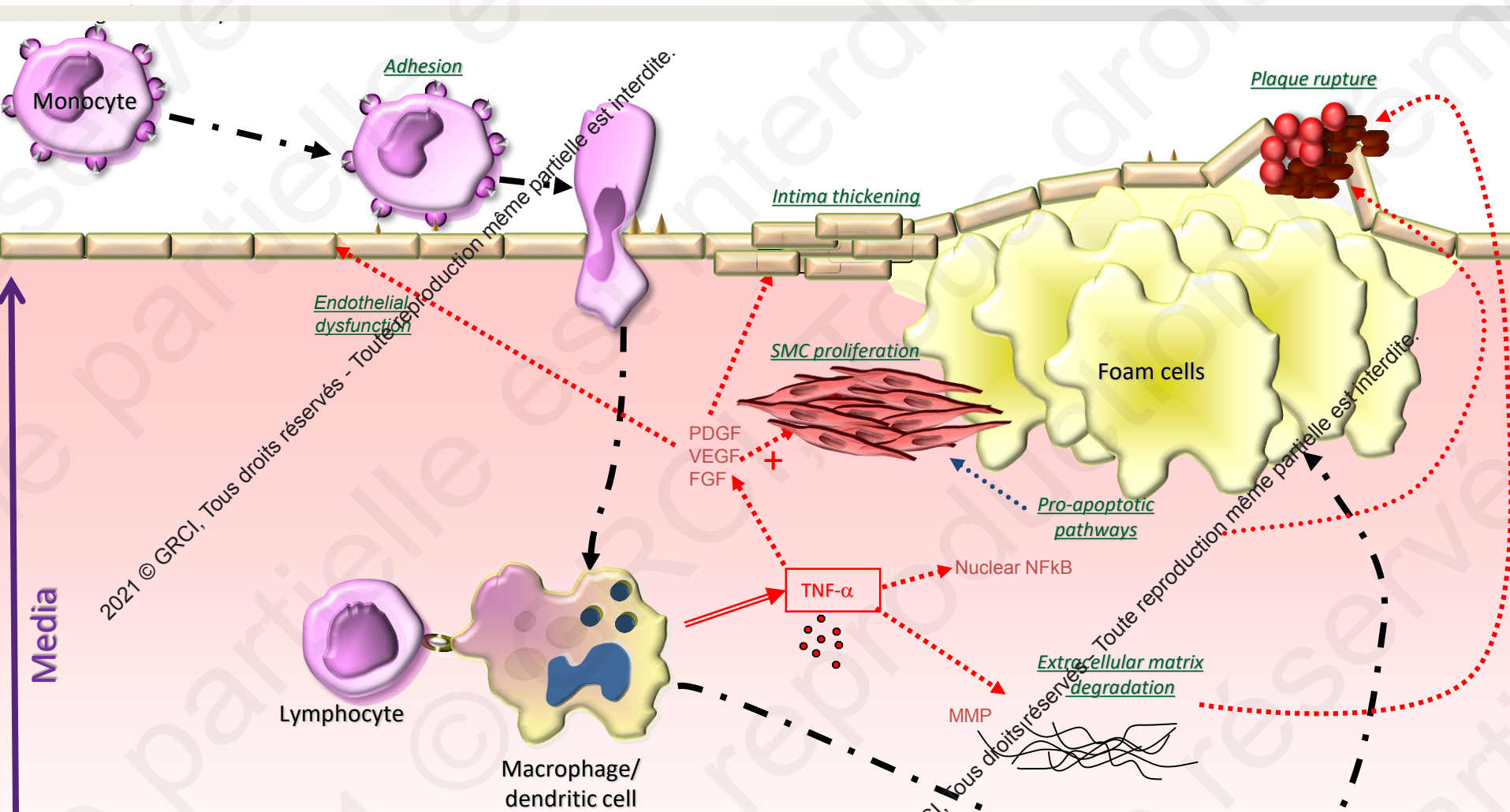
Company

- | | |
|----------------------------------|---|
| • Grant/Research Support | • Servier, Medtronic, Astra-Zeneca, LVL, Eole Santé, dir |
| • Consulting Fees/Honoraria | • liquide , Resmed, ISIS |
| • Major Stock Shareholder/Equity | • Medtronic, Novartis , AZ, MSD, Actelion, Abbott |
| • Royalty Income | • 0 |
| • Ownership/Founder | • 0 |
| • Intellectual Property Rights | • 0 |
| • Other Financial Benefit | • 0 |

PharmScience has provided both colchicine and placebo for the trial. No conflict of interest regarding this study.

Public grants (federal government of Canada and Quebec).



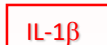







Atherosclerosis is at least partly an **inflammatory** disease...



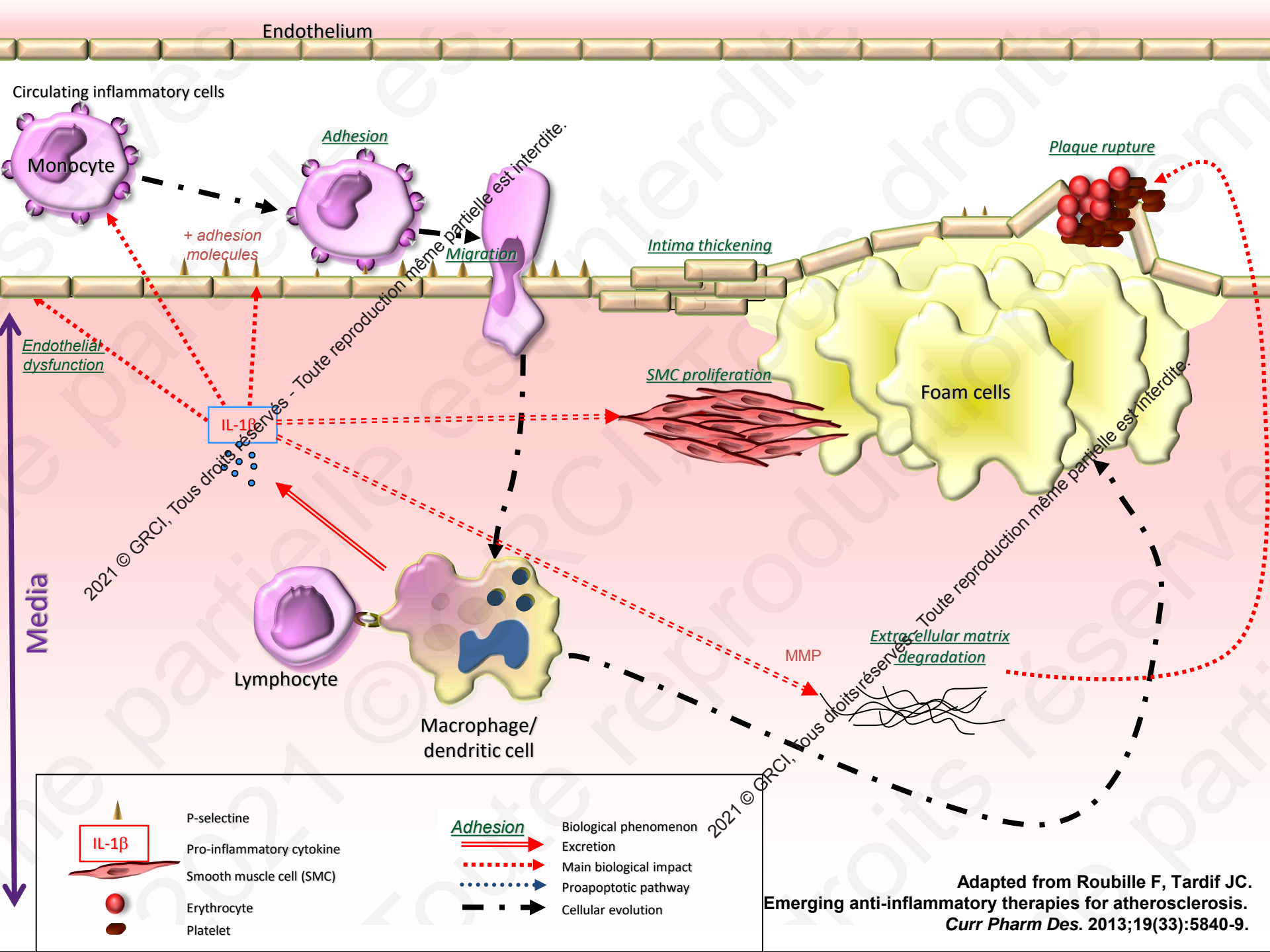
Media

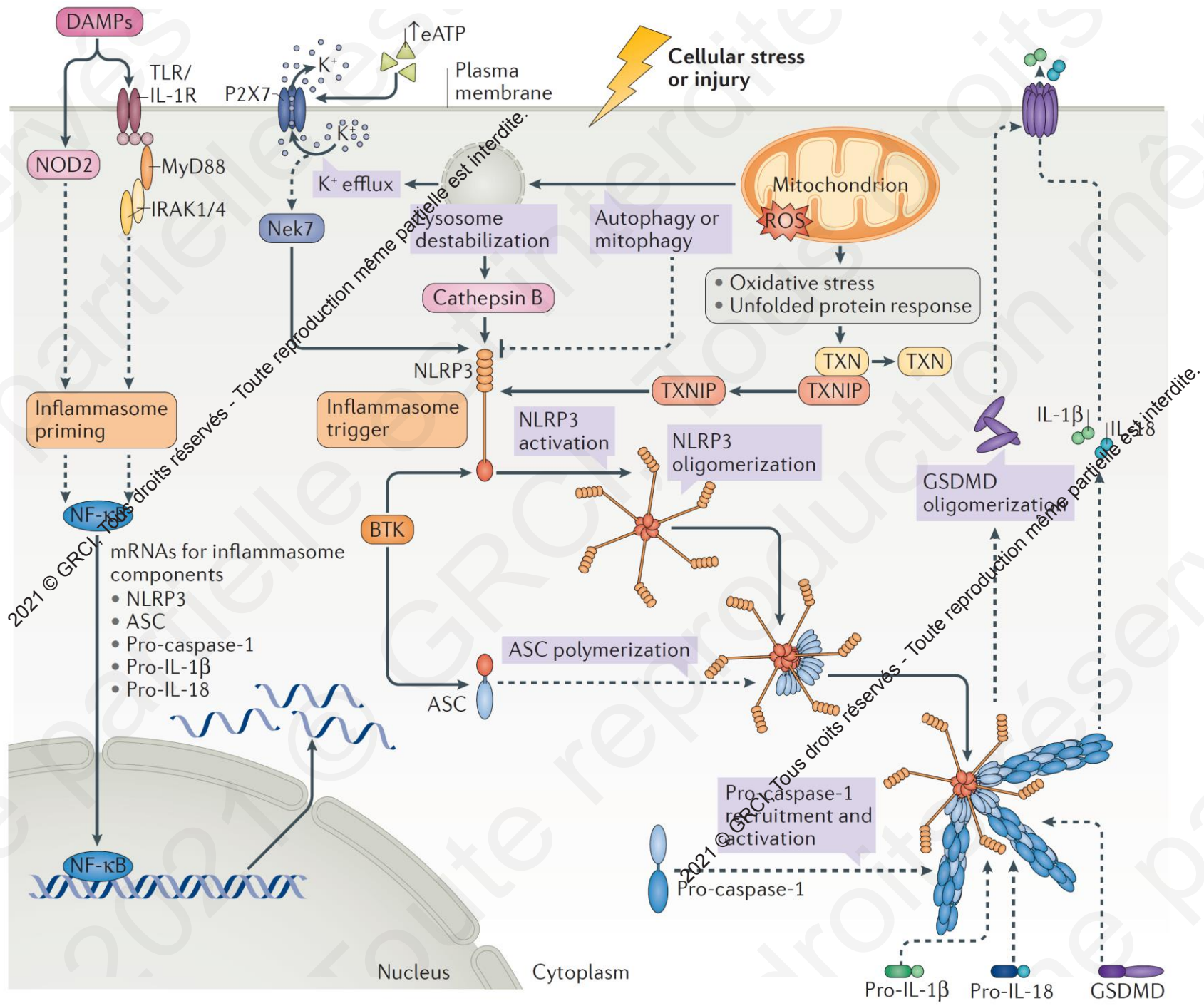
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	P-selectine		Biological phenomenon
	Pro-inflammatory cytokine		Excretion
	Smooth muscle cell (SMC)		Main biological impact
	Erythrocyte		Proapoptotic pathway
	Platelet		Cellular evolution

Adapted from Roubille F, Tardif JC.
Emerging anti-inflammatory therapies for atherosclerosis.
Curr Pharm Des. 2013;19(33):5840-9.







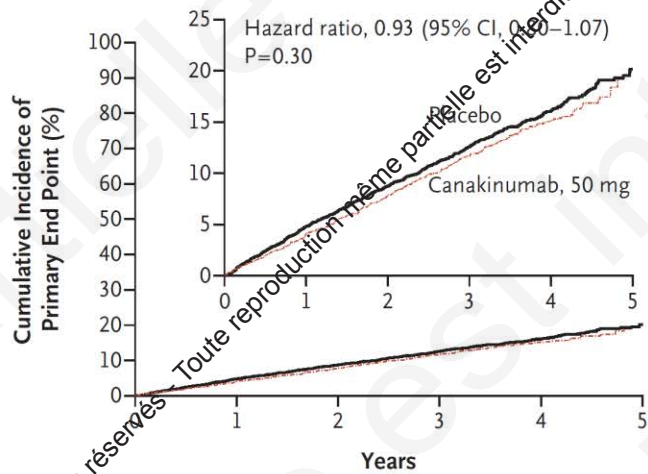
ORIGINAL ARTICLE

Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease

P.M. Ridker, B.M. Everett, T. Thuren, J.G. MacFadyen, W.H. Chang, C. Ballantyne, F. Fonseca, J. Nicolau, W. Koenig, S.D. Anker, J.J.P. Kastelein, J.H. Cornel, P. Pais, D. Pella, J. Genest, R. Cifkova, A. Lorenzatti, T. Forster, Z. Kobalava, L. Vida-Simiti, M. Flather, H. Shimokawa, H. Ogawa, M. Dellborg, P.R.F. Rossi, R.P.T. Troquay, P. Libby, and R.J. Glynn, for the CANTOS Trial Group*

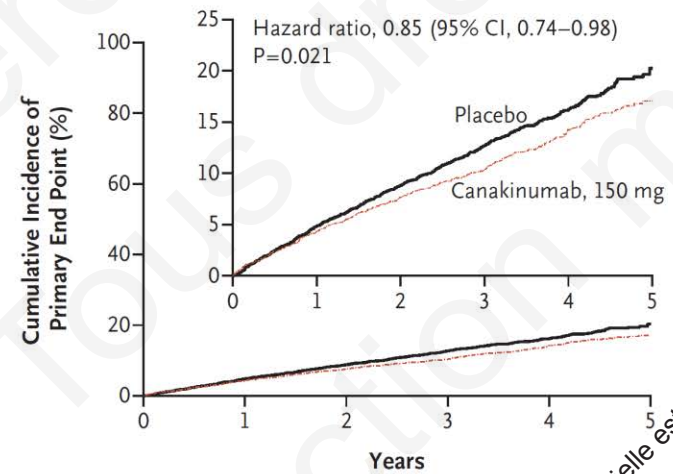
CANTOS: results

A Primary End Point with Canakinumab, 50 mg, vs. Placebo



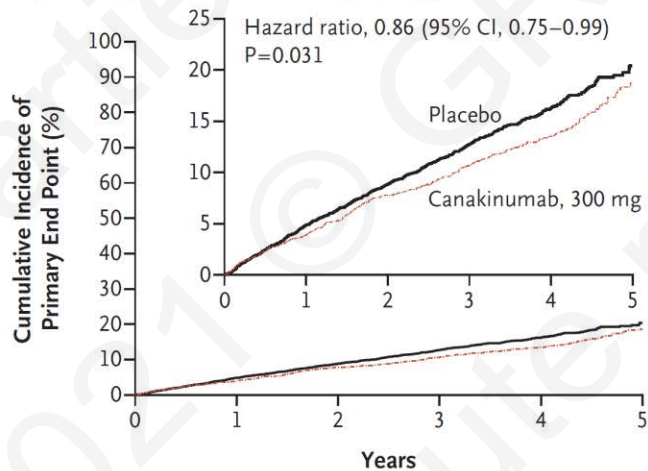
No. at Risk						
Placebo	3344	3141	2973	2632	1266	210
Canakinumab	2170	2057	1950	1713	762	47

B Primary End Point with Canakinumab, 150 mg, vs. Placebo



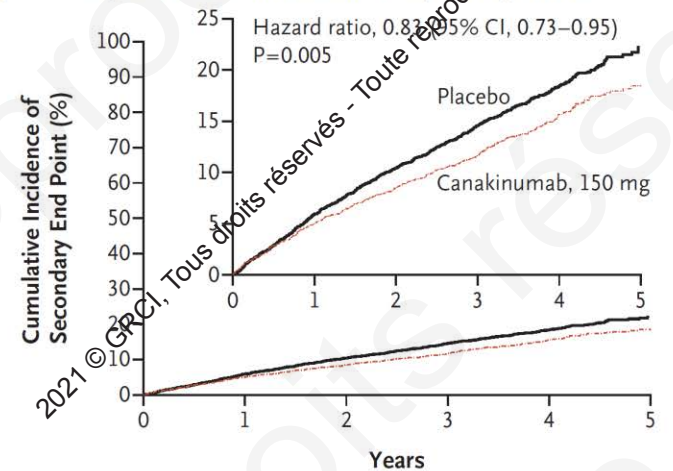
No. at Risk						
Placebo	3344	3141	2973	2632	1266	210
Canakinumab	2284	2151	2057	1849	707	207

C Primary End Point with Canakinumab, 300 mg, vs. Placebo



No. at Risk						
Placebo	3344	3141	2973	2632	1266	210
Canakinumab	2263	2149	2038	1819	938	199

D Key Secondary End Point with Canakinumab, 150 mg, vs. Placebo



No. at Risk						
Placebo	3344	3107	2921	2578	1238	206
Canakinumab	2284	2135	2039	1824	892	201

Ridker PM, et al.

Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease.
N Engl J Med. 2017 Sep 21;377(12):1119-1131.

CANTOS: adverse effects

Table 3. Incidence Rates and Numbers of Serious Adverse Events and Selected Safety Laboratory Data During Treatment, Stratified According to Trial Group.*

Adverse Event or Laboratory Variable	Placebo Group (N = 3344)	Canakinumab				P Value	
		50-mg Group (N = 2170)	150-mg Group (N = 2284)	300-mg Group (N = 2263)	All Doses (N = 6717)	For Trend across Doses vs. Placebo	For Combined Dose Groups vs. Placebo
Event — incidence rate per 100 person-yr (no. of patients with event)							
Any serious adverse event	11.96 (1202)	11.41 (741)	11.71 (812)	12.33 (836)	11.82 (2389)	0.43	0.79
Any serious adverse event of infection	2.86 (342)	3.03 (230)	3.13 (258)	3.25 (265)	3.14 (753)	0.12	0.14
Cellulitis	0.24 (30)	0.24 (19)	0.37 (32)	0.41 (35)	0.34 (86)	0.02	0.09
Pneumonia	0.90 (112)	0.94 (74)	0.94 (80)	0.99 (84)	0.95 (238)	0.56	0.62
Urinary tract infection	0.22 (27)	0.18 (14)	0.24 (21)	0.20 (17)	0.21 (52)	0.84	0.78
Opportunistic infection†	0.18 (23)	0.16 (13)	0.15 (13)	0.20 (17)	0.17 (43)	0.97	0.78
Pseudomonas aeruginosa	0.03 (4)	0.13 (10)	0.05 (4)	0.12 (10)	0.10 (24)	0.13	0.03
Fatal infection or sepsis	0.18 (23)	0.31 (25)	0.28 (24)	0.34 (29)	0.31 (78)	0.09	0.02
Any cancer‡	1.88 (231)	1.85 (144)	1.69 (143)	1.72 (144)	1.75 (431)	0.31	0.38
Fatal cancer‡	0.64 (81)	0.55 (44)	0.50 (44)	0.31 (27)	0.45 (115)	<0.001	0.02
Other adverse event							
Injection-site reaction†	0.23 (29)	0.27 (21)	0.28 (24)	0.30 (26)	0.28 (71)	0.49	0.36
Arthritis	3.32 (385)	2.15 (164)	2.17 (180)	2.47 (201)	2.26 (545)	0.002	<0.001
Osteoarthritis	1.67 (202)	1.21 (94)	1.12 (95)	1.30 (109)	1.21 (299)	0.04	<0.001
Gout	0.80 (99)	0.43 (34)	0.35 (30)	0.37 (32)	0.33 (96)	<0.001	<0.001
Drug-induced liver injury†	0.18 (23)	0.15 (12)	0.13 (11)	0.05 (4)	0.11 (27)	0.004	0.05
Leukopenia	0.24 (30)	0.30 (24)	0.37 (32)	0.52 (44)	0.40 (100)	0.002	0.01
Neutropenia	0.06 (7)	0.05 (4)	0.07 (6)	0.18 (15)	0.10 (25)	0.01	0.17
Any hemorrhage	4.01 (462)	3.33 (249)	4.15 (327)	3.82 (301)	3.78 (877)	0.94	0.31
Thrombocytopenia	0.43 (53)	0.56 (44)	0.54 (46)	0.70 (60)	0.60 (150)	0.02	0.03
Hepatic variable — percent of patients with condition (no.)							
Alanine aminotransferase >3× normal value	1.4 (46)	1.9 (42)	1.9 (44)	2.0 (45)	2.0 (131)	0.19	0.06
Aspartate aminotransferase >3× normal value	1.1 (36)	1.5 (32)	1.5 (35)	1.5 (34)	1.5 (101)	0.30	0.11
Alkaline phosphatase >3× normal value	0.4 (15)	0.5 (11)	0.4 (10)	0.5 (12)	0.5 (33)	0.67	0.82
Bilirubin >2× normal value	0.8 (26)	1.0 (21)	0.7 (15)	0.7 (15)	0.8 (51)	0.34	0.83

Ridker PM, et al.

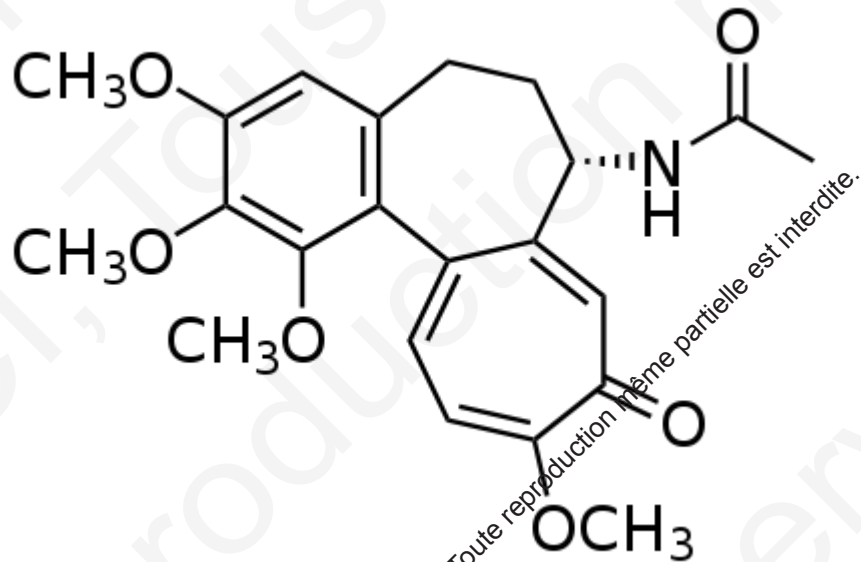
Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease.

N Engl J Med. 2017 Sep 21;377(12):1119-1131.

Colchicine: an old wine in a new bottle?



Colchicum autumnale



Chemical structure of colchicine

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COLCOT

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THE NEW ENGLAND
JOURNAL of MEDICINE

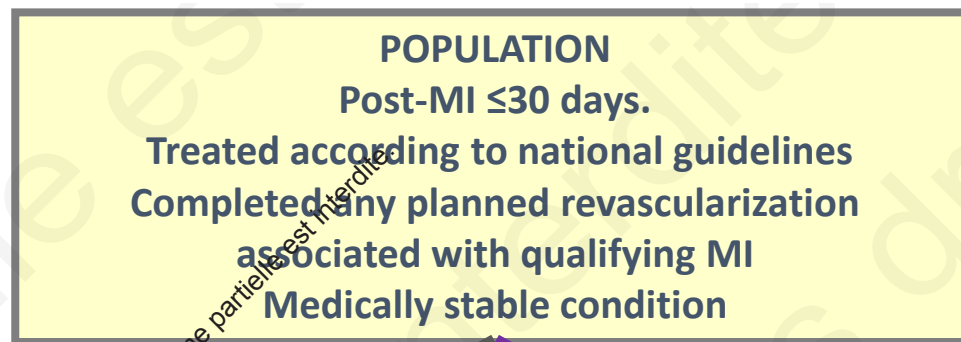


ORIGINAL ARTICLE

Efficacy and Safety of Low-Dose Colchicine after Myocardial Infarction

Jean-Claude Tardif, M.D., Simon Kouz, M.D., David D. Waters, M.D.,
Olivier F. Bertrand, M.D., Ph.D., Rafael Diaz, M.D., Aldo P. Maggioni, M.D.,
Fausto J. Pinto, M.D., Ph.D., Reda Ibrahim, M.D., Habib Gamra, M.D.,
Ghassan S. Kiwan, M.D., Colin Berry, M.D., Ph.D., José López-Séndon, M.D.,
Petr Ostadal, M.D., Ph.D., Wolfgang Koenig, M.D., Denis Angoulvant, M.D.,
Jean C. Grégoire, M.D., Marc-André Lavoie, M.D., Marie-Pierre Dubé, Ph.D.,
David Rhoads, Ph.D., Mylène Provencher, Ph.D., Lucie Blondeau, M.Sc.,
Andreas Orfanos, M.B., B.Ch., Philippe L. L'Allier, M.D.,
Marie-Claude Guertin, Ph.D., and François Roubille, M.D., Ph.D.

COLCOT: Design.



Placebo QD

Randomization
1:1

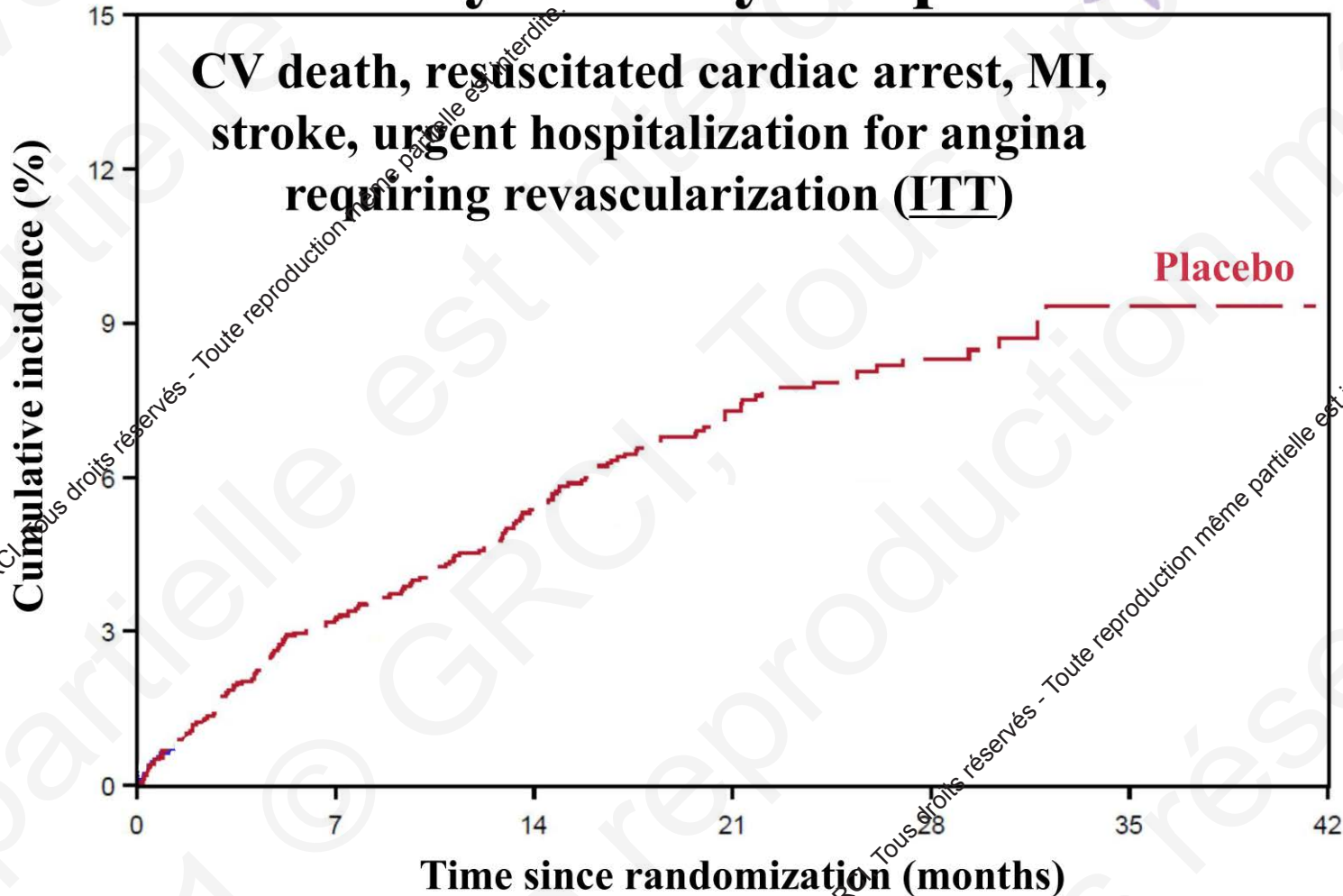
Colchicine 0.5 mg QD

Primary endpoint: CV death, resuscitated cardiac arrest, MI, stroke or urgent hospitalization for angina requiring coronary revascularization

Secondary endpoints: Components of primary; total mortality; composite of CV death, resuscitated cardiac arrest, MI and stroke

Exploratory endpoints: Deep Venous Thrombosis or Pulmonary Embolus, Atrial Fibrillation, Heart Failure Hospitalization, Coronary revascularization

Primary efficacy endpoint



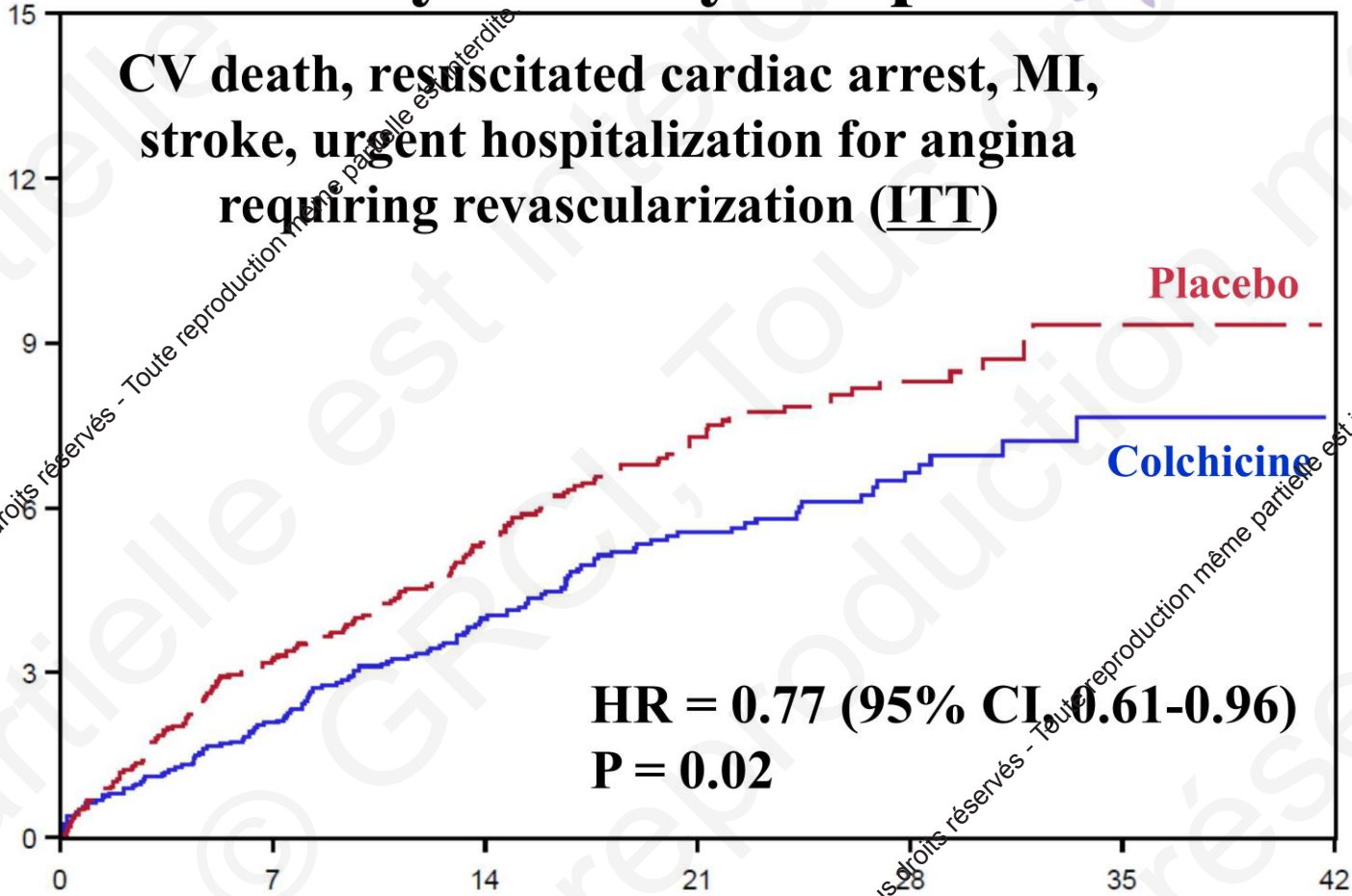
No. at Risk

Colchicine	2366	2284	1868	1230	628	153	0
Placebo	2379	2261	1854	1224	622	144	0

Primary efficacy endpoint

CV death, resuscitated cardiac arrest, MI, stroke, urgent hospitalization for angina requiring revascularization (ITT)

Cumulative incidence (%)



HR = 0.77 (95% CI 0.61-0.96)
P = 0.02

No. at Risk

Colchicine 2366
Placebo 2379

2284
2261

1868
1854

1230
1224

628
622

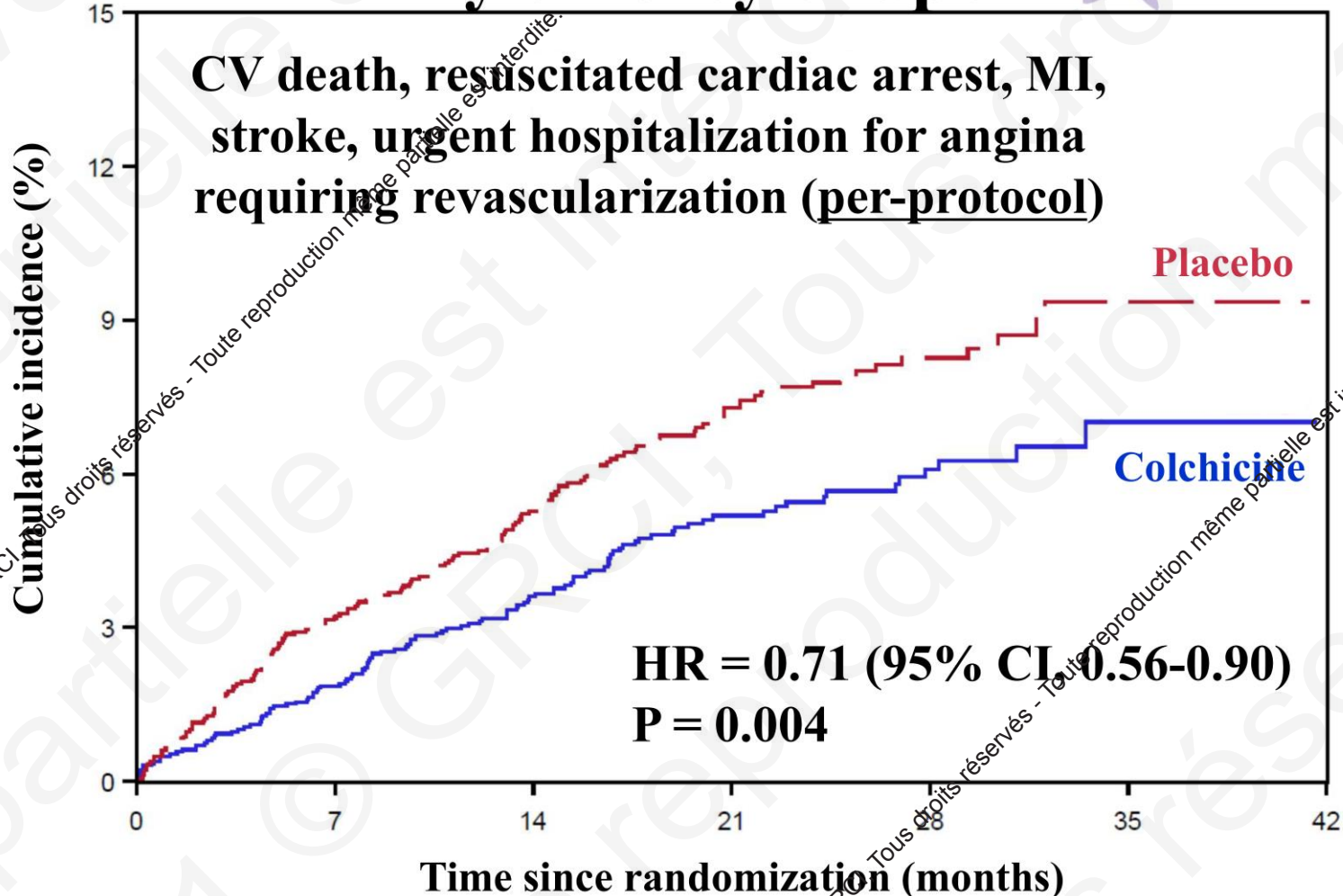
153
144

0
0

Major Clinical Outcomes

Clinical Outcome	Colchicine	Placebo	Hazard Ratio	P
Intent-to-treat population	N=2366	N=2379	(95% CI)	Value
<u>Primary composite endpoint</u> - no. (%)	<u>131 (5.5%)</u>	<u>170 (7.1%)</u>	<u>0.77 (0.61-0.96)</u>	<u>0.02</u>
CV death - no. (%)	20 (0.8%)	24 (1.0%)	0.84 (0.46-1.52)	
Resuscitated cardiac arrest - no. (%)	5 (0.2%)	6 (0.3%)	0.83 (0.25-2.73)	
Myocardial infarction - no. (%)	89 (3.8%)	98 (4.1%)	0.91 (0.68-1.21)	
Stroke - no. (%)	5 (0.2%)	19 (0.8%)	0.26 (0.10-0.70)	
Urgent hospitalization for angina requiring revascularization - no. (%)	25 (1.1%)	50 (2.1%)	0.50 (0.31-0.81)	
<u>Secondary composite endpoint</u> - no. (%)	<u>111 (4.7%)</u>	<u>130 (5.5%)</u>	<u>0.85 (0.66-1.10)</u>	
Death - no. (%)	43 (1.8%)	44 (1.8%)	0.98 (0.64-1.49)	
DVT or pulmonary embolus - no. (%)	10 (0.4%)	7 (0.3%)	1.43 (0.54-3.75)	
Atrial fibrillation - no. (%)	36 (1.5%)	40 (1.7%)	0.93 (0.59-1.46)	

Primary efficacy endpoint



No. at Risk

Colchicine 2260
Placebo 2270

2197
2169

1791
1778

1169
1173

601
596

140
135

0
0

Total (First + Recurrent)

Primary Endpoint Events (ITT)

Endpoint / Model		Colchicine N=2366	Placebo N=2379	Hazard / Rate Ratio (95% CI)
Total number of primary endpoint events		154	223	
Rate of primary endpoint events per 100 patient-months		0.29	0.42	
Negative binomial model				0.66 (0.51; 0.86)
Andersen-Gill model				0.69 (0.54; 0.88)
Wei-Lin-Wessfeld model	1 st event			0.77 (0.61; 0.96)
Wei-Lin-Wessfeld model	2 nd event			0.73 (0.48; 1.11)
Wei-Lin-Wessfeld model	3 rd event			0.64 (0.37; 1.10)
Wei-Lin-Wessfeld model	Average			0.77 (0.61; 0.96)

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Adverse events



Safety population	Colchicine (N=2330)	Placebo (N=2346)	P Value
Any related AE - no. (%)	372 (16.0%)	371 (15.8%)	0.89
Any SAE - no. (%)	383 (16.4%)	404 (17.2%)	0.47
Gastro-intestinal AE - no. (%)	408 (17.5%)	414 (17.6%)	0.90
Gastro-intestinal SAE - no. (%)	46 (2.0%)	36 (1.5%)	0.25
Diarrhea AE - no. (%)	225 (9.7%)	208 (8.9%)	0.35
Nausea AE - no. (%)	43 (1.8%)	24 (1.0%)	0.02
Flatulence AE - no. (%)	15 (0.6%)	5 (0.2%)	0.02
GI haemorrhage AE - no. (%)	7 (0.3%)	5 (0.2%)	0.56
Infection SAE - no. (%)	51 (2.2%)	38 (1.6%)	0.15
Pneumonia SAE - no. (%)	21 (0.9%)	9 (0.4%)	0.03
Septic shock SAE - no. (%)	2 (0.1%)	2 (0.1%)	0.99
HF hospitalization - no. (%)	25 (1.1%)	17 (0.7%)	0.21
Cancer - no. (%)	43 (1.8%)	46 (2.0%)	0.77
Anemia - no. (%)	14 (0.6%)	10 (0.4%)	0.40
Leukopenia - no. (%)	2 (0.1%)	3 (0.1%)	0.66
Thrombocytopenia - no. (%)	3 (0.1%)	7 (0.3%)	0.21

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LoDoCo2

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Protocol

Patients aged 35 – 82 years with proven coronary disease Clinically stable ≥ 6 months

No advanced renal disease, heart failure or severe valvular heart disease

30-day open label run-in of colchicine 0.5mg daily

Tolerant, clinically stable and willing

Colchicine

Placebo

Primary endpoint: Composite of CV death, MI, ischemic stroke or ischemia-driven coronary revascularization

Planned to begin close-out 12 months after the last participant had been randomized*

** If 331 primary events had accrued – sufficient to detect a 30% effect of therapy with 90% power*

6528

Enrolled

91.3% Tolerated open label therapy

5522

Randomized

Followed for a median of 29 months (12-64 months)

90.3% in each arm continued their trial medication

3.4% in each arm ceased due to perceived effects

5521

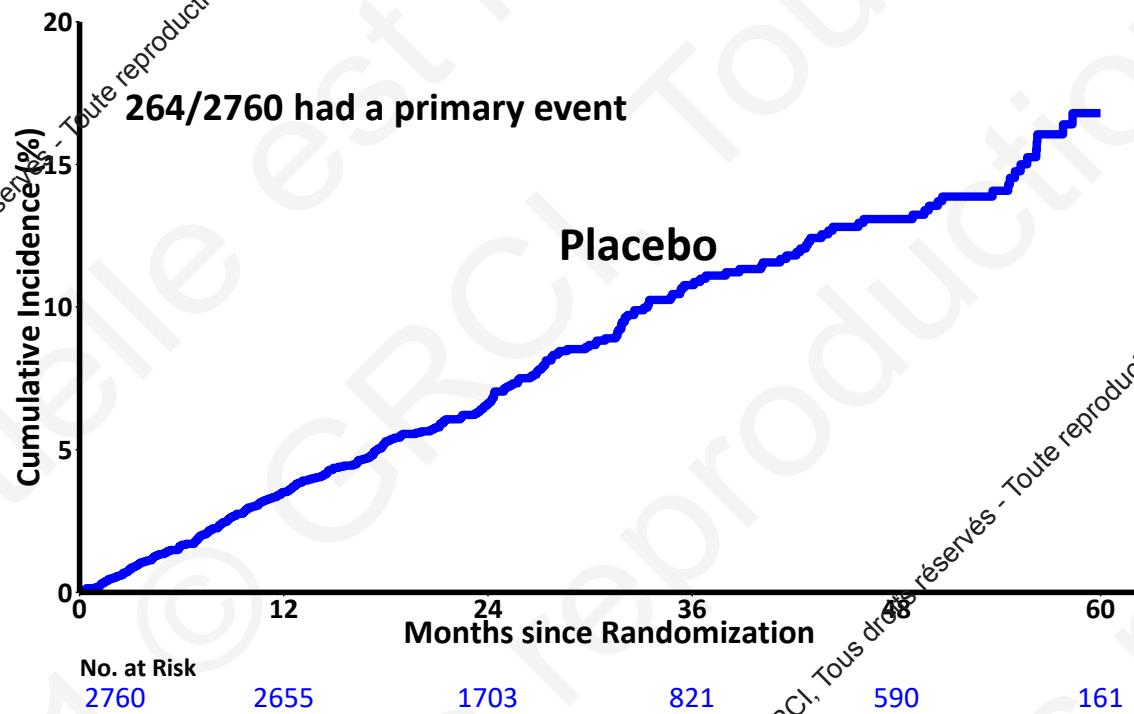
Close-out

Began on December 4, 2019; Ended February 17, 2020

99.9% Final, end point status known

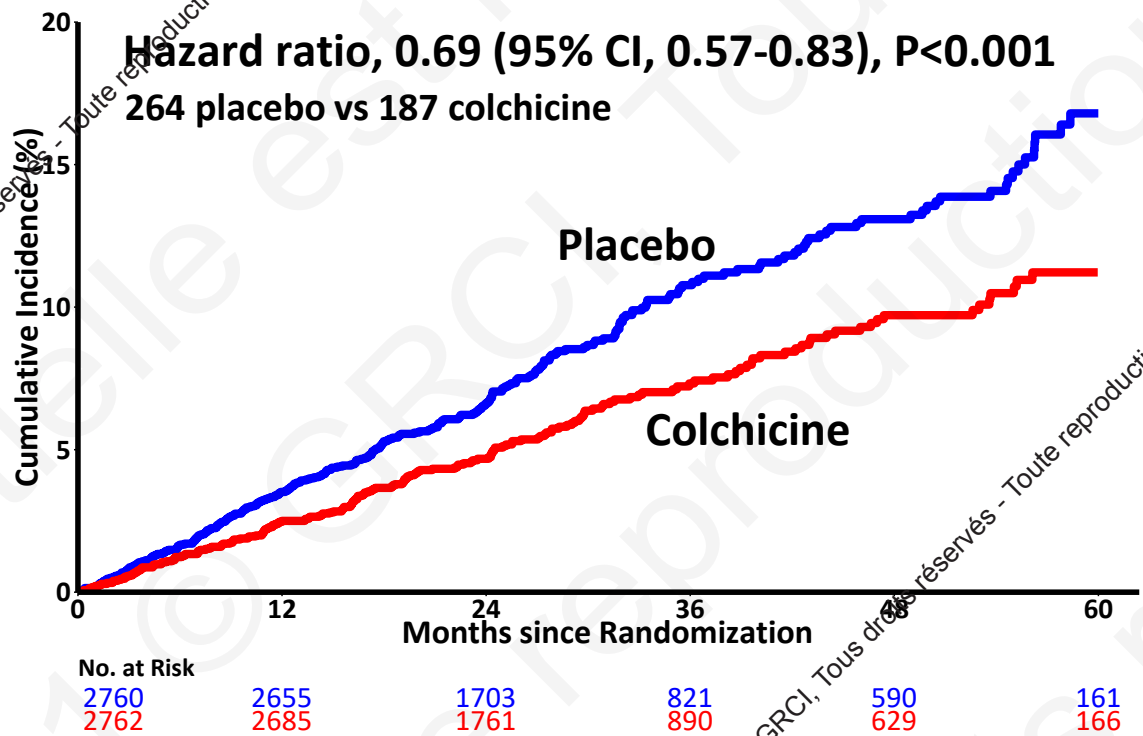
Primary endpoint

Cardiovascular death, myocardial infarction, ischemic stroke or ischemia-driven coronary revascularization



Primary endpoint

Cardiovascular death, myocardial infarction, ischemic stroke or ischemia-driven coronary revascularization



Serious adverse events

	Colchicine (N = 2762)	Placebo (N = 2760)
Non-cardiovascular death	53(1.9)	35(1.3)
Diagnosis of new cancer	120(4.3)	122(4.4)
Hospitalization for infection	137(5.0)	144(5.2)
Hospitalization for pneumonia	46(1.7)	55(2.0)
Hospitalization for gastro-intestinal reason	53(1.9)	50(1.8)
Neutropenia	3(0.1)	3(0.1)
Myotoxicity	4(0.1)	3(0.1)

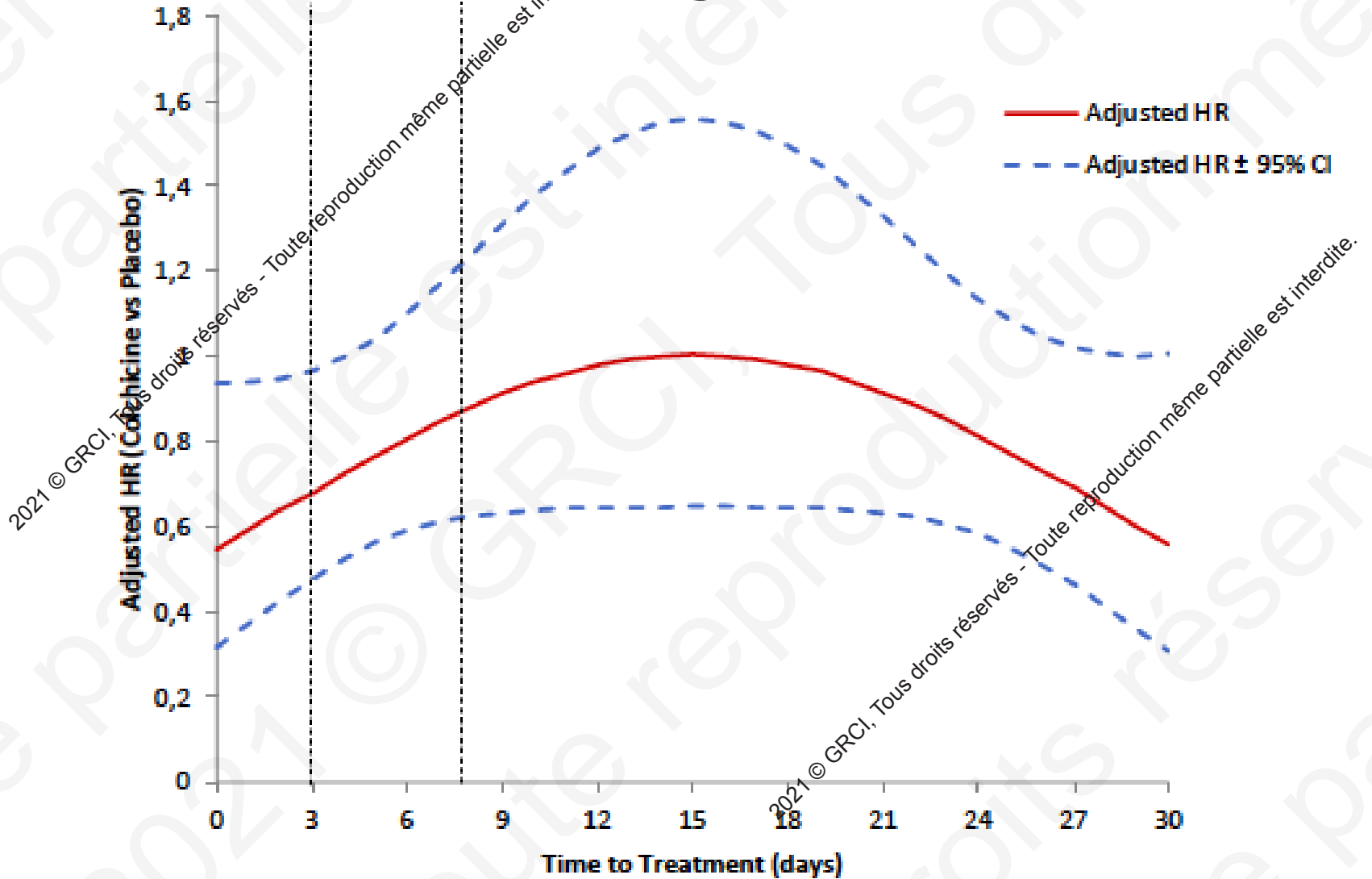
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COLCOT

Mieux vaut traiter tôt en cas de SCA

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Primary efficacy endpoint according to TTI



Quadratic model

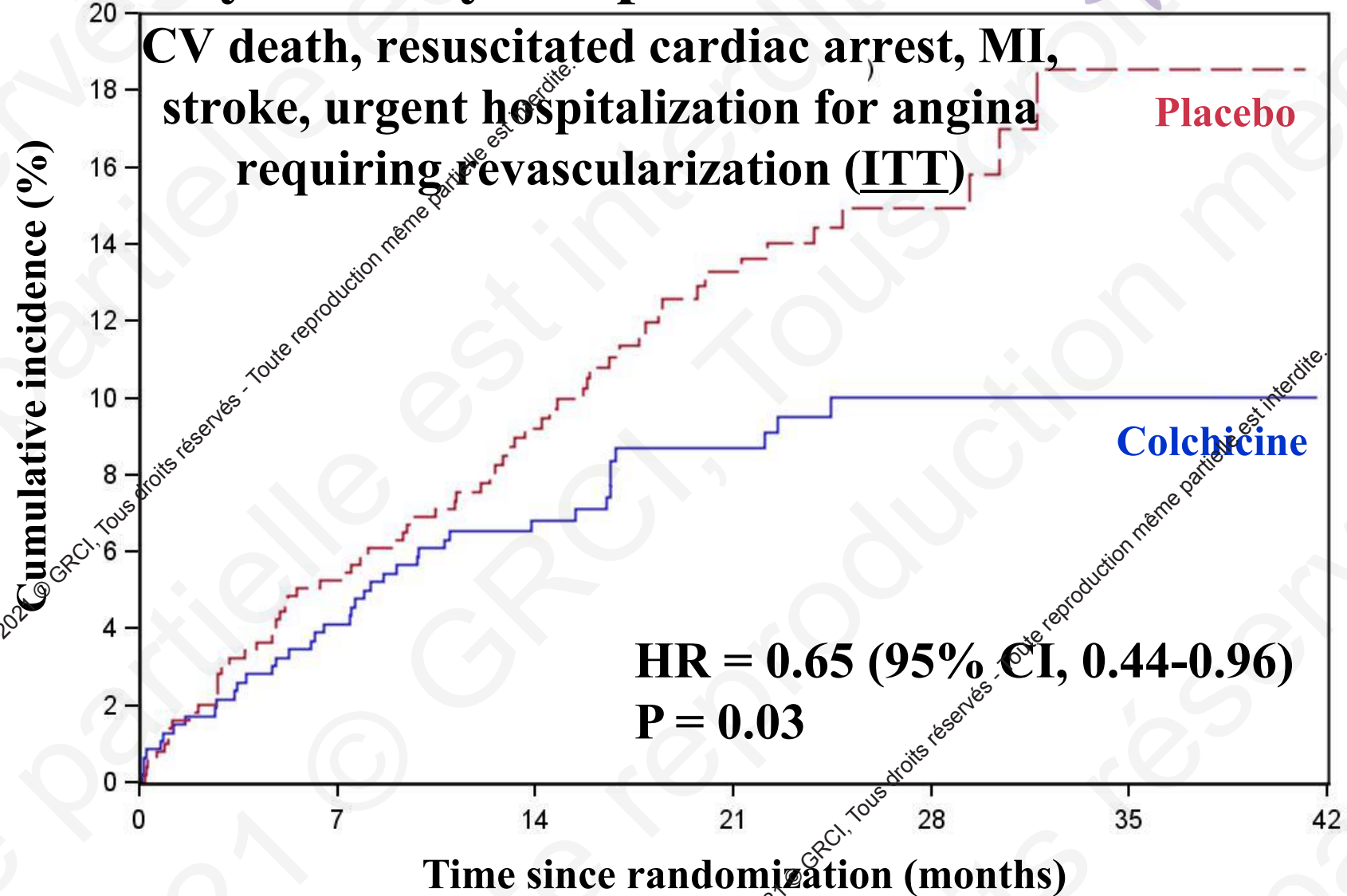
COLCOT

**Les patients avec profil inflammatoire
en tirent encore plus profit**

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Primary efficacy endpoint (DIABETES)



No. at Risk

	0	7	14	21	28	35	42
Colchicine	462	439	343	236	126	34	0
Placebo	497	464	366	241	123	22	0

COLCOT-T2D – Study design



**Type 2 Diabetes (n=10,000 patients)
without known coronary disease**

Treated according to national guidelines

**Colchicine 0.5 mg
daily**

**Placebo
daily**

Primary composite endpoint: Time to first of CV death, cardiac arrest, MI, stroke, or urgent hospitalization for angina requiring coronary revascularization

Secondary endpoints: Cancers; cognitive impairment and dementia; components of primary; total mortality; CV death, cardiac arrest, MI or stroke

ESC guidelines August 2021

Recommendation for anti-inflammatory therapy

Recommendation	Class ^a	Level ^b
Low-dose colchicine (0.5 mg <i>o.d.</i>) may be considered in secondary prevention of CVD, particularly if other risk factors are insufficiently controlled or if recurrent CVD events occur under optimal therapy. ^{85,86}	IIb	A

CVD = cardiovascular; *o.d.* = *omni die* (once a day).

^aClass of recommendation.

^bLevel of evidence.

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La colchicine pour quels patients?

Patients SCA ou coronariens stables

0,5 mg par jour voire moins, au long cours

Contexte micro-inflammatoire: diabète, maladie inflammatoire?

Absence de contre-indication à la colchicine

Patients récidivants, témoignant d'un risque résiduel élevé.



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Y a-t-il une alerte sur la mortalité non CV?

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Circulation

EDITORIAL

Colchicine for Secondary Cardiovascular Prevention in Coronary Disease

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Roubille F, Tardif JC.
Colchicine for Secondary Cardiovascular Prevention in Coronary Disease.
Circulation 2020;142:1901-1904.

Randomization group	COLCOT				COPS				LoDoCo2			
	N=4745		Hazard ratio (95% CI)	P value	N=795		Hazard ratio (95% CI)	P value	N=5522		Hazard ratio (95% CI)	P value
	Colchicine n=2366	Placebo n=2379			Colchicine n=396	Placebo n=399			Colchicine n=2762	Placebo n=2760		
Age, y	≥ 18				18–85				35–82			
Acute coronary syndrome	< 30 days postmyocardial infarction				yes†				Stable CAD No event in the past 6 mo			
Coronary artery disease	Myocardial infarction				≥30% luminal stenosis in epicardial vessel of >2.5 mm diameter by angiographic assessment				Invasive or CT coronary angiography Coronary artery calcium score > 400 U			
Median follow-up, mo	22.6				12				28.6			
Components of the primary end point	cardiovascular death, myocardial infarction, stroke, or urgent hospitalization for angina requiring coronary revascularization				death, acute coronary syndrome, ischemia-driven urgent revascularization, or stroke				cardiovascular death, myocardial infarction, ischemic stroke, or ischemia-driven coronary revascularization			
Primary efficacy end point, n (%)	131 (5.5)	170 (7.1)	0.77 (0.61–0.96)	0.02	24	38	0.64 (0.38–1.09)	0.09	187 (6.8)	264 (9.6)	0.69 (0.57–0.83)	<0.001
Mortality												
All-cause mortality death, n (%)	33 (1.8)	44 (1.8)	0.98 (0.64–1.49)		8	1	8.2 (1.03–65.61)	0.047	73 (2.6)	60 (2.2)	1.21 (0.86–1.71)	
CV death, n (%)	20 (0.8)	24 (1.0)	0.84 (0.46–1.52)		3	1	3.1 (0.32–29.71)		20 (0.7)	25 (0.9)	0.80 (0.44–1.44)	
Non CV death, n (%)	23 (1.0)	20 (0.8)			5	0		0.023	53 (1.9)	35 (1.3)	1.51 (0.99–2.31)	
Components of the composite primary end point, ITT population												
Deaths due to any cause	Not included among primary end point				8	1	8.2 (1.03–65.61)	0.047	Not included among primary end point			
CV death, n (%)	20 (0.8)	24 (1.0)	0.84 (0.46–1.52)		Not included among primary end point				20 (0.7)	25 (0.9)	0.80 (0.44–1.44)	
Resuscitated CA, n (%)	5 (0.2)	6 (0.3)	0.83 (0.25–2.73)		Not included among primary end point				Not included among primary end point			
MI, n (%)	89 (3.8)	98 (4.1)	0.91 (0.68–1.21)		Not included among primary end point				83 (3.0)	96 (4.2)	0.70 (0.53–0.93)	0.01
ACS	Not included among primary end point				11	20	0.56 (0.27–1.18)	0.13	Not included among primary end point			
Stroke, n (%)	5 (0.2)	19 (0.8)	0.26 (0.10–0.70)		2	5	0.41 (0.08–2.10)	0.28	16 (0.6)	24 (0.9)	0.66 (0.35–1.25)	0.20
UHARCR or unplanned revascularization, n (%)	25 (1.1)	50 (2.1)	0.50 (0.31–0.81)		3	12	0.26 (0.07–0.92)	0.37*	135 (4.9)	177 (6.4)	0.75 (0.60–0.94)	0.01
Selected secondary end points												
DVT or PE, n (%)	10 (0.4)	7 (0.3)	1.43 (0.54–3.75)		NA				17 (0.6)	16 (0.6)	1.06 (0.53–2.10)	
Atrial fibrillation (and flutter in LoDoCo2), n (%)	36 (1.5)	40 (1.7)	0.93 (0.59–1.46)		NA				126 (4.6)	148 (5.4)	0.84 (0.66–1.07)	

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Randomization group	COLCOT				COPS				LoDoCo2			
	N=4745		Hazard ratio (95% CI)	P value	N=795		Hazard ratio (95% CI)	P value	N=5522		Hazard ratio (95% CI)	P value
	Colchicine n=2366	Placebo n=2379			Colchicine n=396	Placebo n=399			Colchicine n=2762	Placebo n=2760		
Age, y	≥ 18				18–85				35–82			
Acute coronary syndrome	< 30 days postmyocardial infarction				yes†				Stable CAD No event in the past 6 mo			
Coronary artery disease	Myocardial infarction				≥30% luminal stenosis in epicardial vessel of >2.5 mm diameter by angiographic assessment				Invasive or CT coronary angiography Coronary artery calcium score > 400 U			
Median follow-up, mo	22.6				12				28.6			
Components of the primary end point	cardiovascular death, cardiac arrest, myocardial infarction, stroke, or urgent hospitalization for angina requiring coronary revascularization				death, acute coronary syndrome, ischemia-driven urgent revascularization, or stroke				cardiovascular death, myocardial infarction, ischemic stroke, or ischemia-driven coronary revascularization			
Primary efficacy end point, n (%)	131 (5.5)	170 (7.1)	0.77 (0.61–0.96)	0.02	24	38	0.64 (0.38–1.09)	0.09	187 (6.8)	264 (9.6)	0.69 (0.57–0.83)	<0.001
Mortality												
All-cause mortality death, n (%)	43 (1.8)	44 (1.8)	0.98 (0.64–1.49)		8	1	8.2 (1.03–65.61)	0.047	73 (2.6)	60 (2.2)	1.21 (0.86–1.71)	
CV death, n (%)	20 (0.8)	24 (1.0)	0.84 (0.46–1.52)		3	1	3.1 (0.32–29.71)		20 (0.7)	25 (0.9)	0.80 (0.44–1.44)	
Non CV death, n (%)	23 (1.0)	20 (0.8)			5	0		0.023	53 (1.9)	35 (1.3)	0.71 (0.99–2.31)	
Components of the composite primary end point, I11 population												
Deaths due to any cause	Not included among primary end point				8	1	8.2 (1.03–65.61)	0.047	Not included among primary end point			
CV death, n (%)	20 (0.8)	24 (1.0)	0.84 (0.46–1.52)		Not included among primary end point				20 (0.7)	25 (0.9)	0.80 (0.44–1.44)	
Resuscitated CA, n (%)	5 (0.2)	6 (0.3)	0.83 (0.25–2.73)		Not included among primary end point				Not included among primary end point			
MI, n (%)	89 (3.8)	98 (4.1)	0.91 (0.68–1.21)		Not included among primary end point				83 (3.0)	116 (4.2)	0.70 (0.53–0.93)	0.01
ACS	Not included among primary end point				11	20	0.56 (0.27–1.18)	0.13	Not included among primary end point			
Stroke, n (%)	5 (0.2)	19 (0.8)	0.26 (0.10–0.70)		2	5	0.41 (0.08–2.10)	0.28	16 (0.6)	24 (0.9)	0.66 (0.35–1.25)	0.20
UHARCR or unplanned revascularization, n (%)	25 (1.1)	50 (2.1)	0.50 (0.31–0.81)		3	12	0.26 (0.07–0.92)	0.037*	135 (4.9)	177 (6.4)	0.75 (0.60–0.94)	0.01

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In conclusion, colchicine at a dose of 0.5 mg once daily reduces inflammasome activation and neutrophil degranulation and lowers the risk of ischemic cardiovascular events both in patients with a recent MI and in those with stable chronic coronary artery disease. In the postMI setting, initiation of colchicine within the first 3 days after the event, before hospital discharge, appears to provide even greater benefits.⁵ In patients with chronic coronary disease, colchicine should not be administered with strong cytochrome P450 3A4 inhibitors. The addition of colchicine to standard of care has been shown to be an economically dominant strategy that generates cost savings.¹² Given that it reduces non-fatal cardiovascular events without affecting all-cause mortality, low-dose colchicine could be considered for patients with coronary disease and no severe renal dysfunction to reduce the considerable related cardiovascular morbidity.

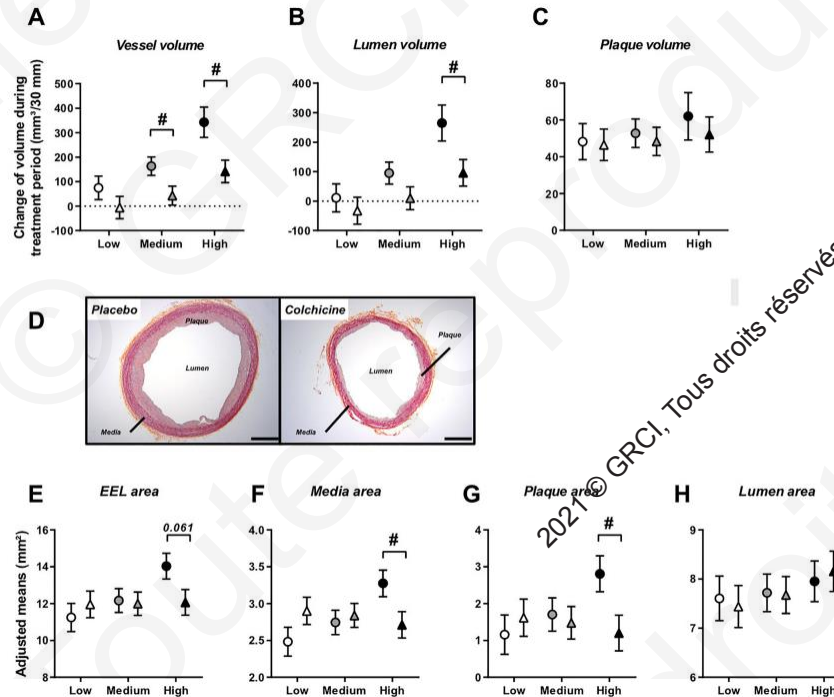
Colchicine reduces atherosclerotic plaque vulnerability in rabbits

François Roubille ^a, Nolwenn Merlet ^a, David Busseuil ^a, Marine Ferron ^a, Yanfen Shi ^a, Teodora Mihalache-Miram ^a, Mélanie Mecteau ^a, Geneviève Brand ^a, Daniel Rivas ^a, Mariève Cossette ^c, Marie-Claude Guertin ^c, Eric Rhéaume ^{a,b}, Jean-Claude Tardif ^{a,b,*}

^a Montreal Heart Institute, Montreal, Quebec, Canada

^b Department of Medicine, Université de Montréal, Montreal, Quebec, Canada

^c Montreal Health Innovations Coordinating Centre (MHICC), Montreal, Canada



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ORIGINAL ARTICLE

Pharmacogenomics of the Efficacy and Safety of Colchicine in COLCOT

Marie-Pierre Dubé, PhD , Marc-André Legault, BSc , Audrey Lemaçon, PhD , Louis-Philippe Lemieux Perreault, PhD , René Fouodjio, MSc, David D. Waters, MD , Simon Kouz, MD , Fausto J. Pinto, MD, PhD , Aldo R. Maggioni, MD , Rafael Diaz, MD , Colin Berry, MD, PhD , Wolfgang Koenig, MD , Jose Lopez-Sendon, MD , Habib Gamra, MD, Ghassan S. Kiwan, MD , Géraldine Asselin, MSc , Sylvie Provost, MSc, Amina Barhdadi, PhD, Maxine Sun, MSc , Mariève Cossette, MSc, Lucie Blondeau, MSc, Ian Mongrain, MSc , Anick Dubois, PhD , David Rhainds, PhD , Nadia Bouabdallaoui, MD , Michelle Samuel, MPH, PhD , Simon de Denus, BPharm, PhD , Philippe L. L'Allier, MD, Marie-Claude Guerin, PhD, François Roubille, MD, PhD , and Jean-Claude Tardif, MD 

Review in translational cardiovascular medicine

Colchicine and myocardial infarction: A review Colchicine et infarctus du myocarde : revue

Mariama Akodad ^{a, b, c, d, e}, Pierre Sicard ^b, Jérémy Fauconnier ^b, François Roubille ^{a, b}

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Circulation

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EDITORIAL

Colchicine for Secondary Cardiovascular Prevention in Coronary Disease

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Role of IL-1 β in acute myocardial infarction in a murine model:

Lost in translation? The COVERT-MI trial

Primary Endpoint

COVERT - MI

No significant reduction of IS at 5 days by CMR

P=0.87

Infarct Size (grams)

100
75
50
25
0

26.0 grams
(IQR, 16.0-44.0)

Colchicine

28.4 grams
(IQR 14.0-40.0)

Placebo

Short Communication

For reprint orders, please contact: reprints@future-science.com



Low-dose colchicine prevents sympathetic denervation after myocardial ischemia-reperfusion: a new potential protective mechanism

Fabien Huet^{1,2}, Jérémy Fauconnier^{1,2}, Marion Legall², Pierre Sicard², CatherineLozza², Alain Lacampagne^{1,2} & François Roubille^{1,2,*}¹Department of Cardiology, Montpellier University Hospital, Montpellier, Occitanie, France²University of Montpellier, CNRS, INSERM, CHRU Montpellier, Montpellier, France

*Author for correspondence: Tel.: +33 0467332501; fhuet@chu-montpellier.fr

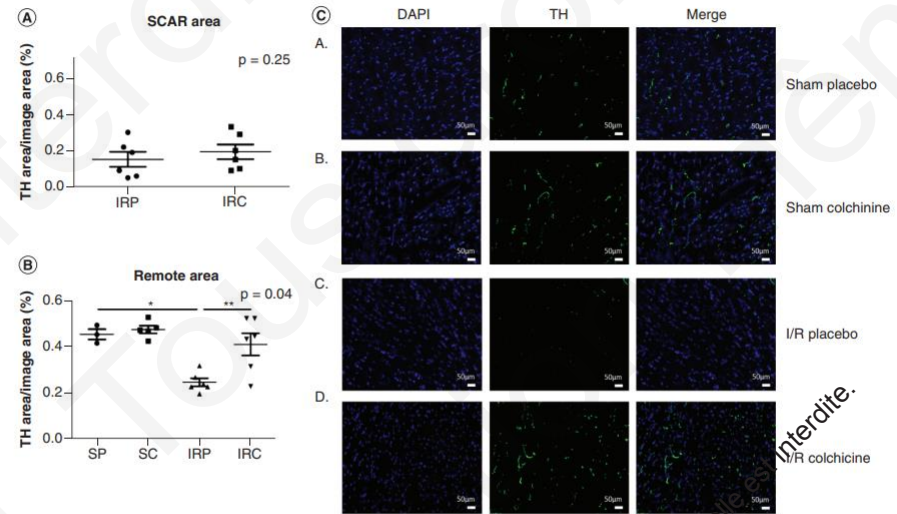
[†]Authors contributed equally[‡]Authors contributed equally

Figure 2. Sympathetic nerves quantification in the scar (A) and remote (B) areas of ischemic hearts on immune-fluorescence, with a typical example of remote area immunofluorescence (C). SP: Sham placebo; SC: Sham colchicine; IRP: IR placebo; IRC: IR colchicine; TH: THrosine hydroxylase.

*p < 0.05.

IRC: IR colchicine; IRP: IR placebo; SC: Sham colchicine; SP: Sham placebo; TH: THrosine hydroxylase.



Study Protocol

Colchicine to Prevent Sympathetic Denervation after an Acute Myocardial Infarction: The COLD-MI Trial Protocol

Fabien Huet^{1,†}, Quentin Delbaere^{1,2,†}, Sylvain Aguilhon¹, Valentin Dupasquier¹, Delphine Delseny¹, Richard Gervasoni¹, Jean-Christophe Macia¹, Florence Leclercq¹, Nidal Jammoul¹, Sandra Kahlouche¹, Sonia Soltani¹, Fanny Cardon³, Anne-Marie Dupuy⁴, Jean-Paul Cristol⁴, Denis Mariano-Goulart⁵, Myriam Akodad^{1,2}, Nicolas Nagot³ and François Roubille^{1,2,*}

Fig. 1

From: [Cardioprotection—Time to Take Into Account Clinical Complexity: The Case of Antiplatelet Agents](#)

