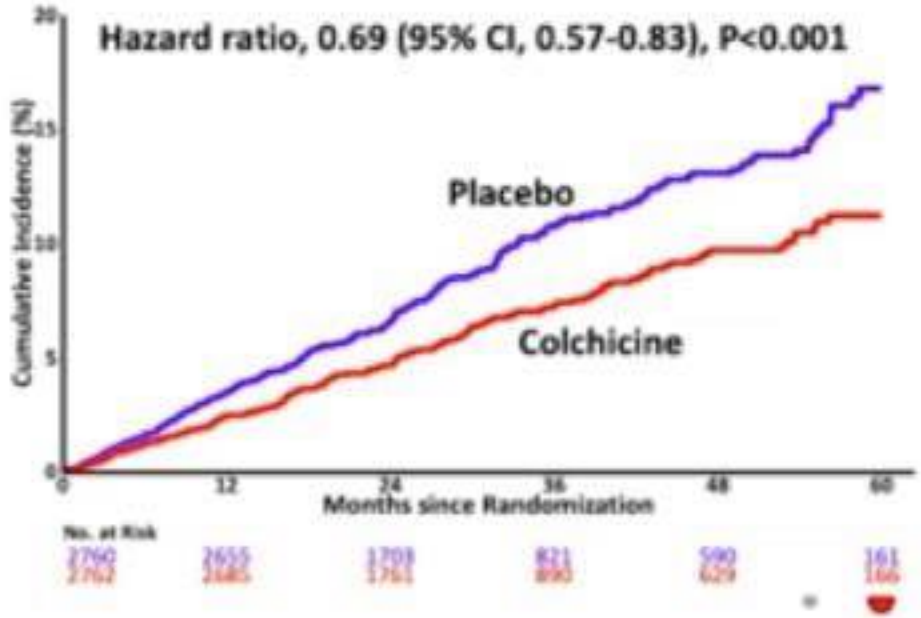

LoDoCo2

LoDoCo2: Colchicine, an old drug for a new CV indication (Chronic Coronary Syndromes)

- Double-blind, placebo-controlled RCT (5522 randomized pts)
- Setting: patients with stable CAD
- Intervention: colchicine 0.5mg/day (low dose, no loading) with a 30 day run-in of colchicine for tolerance (91% tolerated colchicine).
- Primary endpoint: CV death, MI, ischemic stroke, ischemia-driven coronary revascularization.



Median fw-up 29 months

Background

CANTOS proved that the specific anti-inflammatory effect of canakinumab reduced the risk of cardiovascular events in high risk patients with coronary disease.[1]

Colchicine has broad anti-inflammatory effects and is widely available

COLCOT proved that colchicine reduced the risk of cardiovascular events in patients following a recent myocardial infarction.[2]

Evidence to support the routine use of colchicine for secondary prevention in patients with chronic coronary disease is limited.

ESC Congress 2020
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1 - PM Ridker et al. 2017 NEJM
2 - JC Tardif et al. 2019 NEJM

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Colchicine in Patients with Chronic Coronary Disease


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Objective: To determine whether colchicine 0.5mg once daily prevents cardiovascular events in patients with chronic coronary disease.
Design: Investigator-initiated, double-blind, placebo-controlled, event-driven trial.
Enrolment: Began in Australia (GenesisCare) in August 2014. Expanded to The Netherlands, Dutch Network for Cardiovascular Research (WCN) in October 2016. Last enrolment: November 4, 201
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Table 1. Characteristics of the Trial Patients at Baseline.*

Characteristic	Colchicine (N = 2762)	Placebo (N = 2760)
Age — yr	65.8±8.4	65.9±8.7
Female sex — no. (%)	457 (16.5)	389 (14.1)
Country — no. (%)		
Australia	951 (34.4)	953 (34.5)
The Netherlands	1811 (65.6)	1807 (65.5)
Current smoker — no. (%)†	318 (11.5)	330 (12.0)
Hypertension — no. (%)	1421 (51.4)	1387 (50.3)
Diabetes — no. (%)		
Patients receiving any treatment for diabetes	492 (17.8)	515 (18.7)
Patients dependent on insulin	140 (5.1)	147 (5.3)
Renal function — no. (%)‡		
Stage 1 or 2	2614 (94.6)	2602 (94.3)
Stage 3a	148 (5.4)	158 (5.7)
Prior acute coronary syndrome — no. (%)	2323 (84.1)	2335 (84.6)
Time since last acute coronary syndrome — no. (%)		
≤24 mo	753 (27.3)	726 (26.3)
>24 mo	1570 (56.8)	1609 (58.3)
Prior coronary revascularization — no. (%)	2301 (83.3)	2320 (84.1)
Coronary-artery bypass grafting	319 (11.5)	391 (14.2)
Percutaneous coronary intervention	2100 (76.0)	2077 (75.3)
History of atrial fibrillation — no. (%)	332 (12.0)	317 (11.5)
History of gout — no. (%)	220 (8.0)	226 (8.2)
Medication use — no. (%)		
Single antiplatelet therapy	1849 (66.9)	1852 (67.1)
Dual antiplatelet therapy	638 (23.1)	642 (23.3)
Anticoagulant	342 (12.4)	330 (12.0)
No antiplatelet agent or anticoagulant	4 (0.1)	11 (0.4)
Statin	2594 (93.9)	2594 (94.0)
Ezetimibe	551 (19.9)	522 (18.9)
Any lipid-lowering agent	2670 (96.7)	2665 (96.6)
Renin–angiotensin inhibitor	1995 (72.2)	1965 (71.2)
Beta-blocker	1692 (61.3)	1735 (62.9)
Calcium-channel blocker	633 (22.9)	611 (22.1)

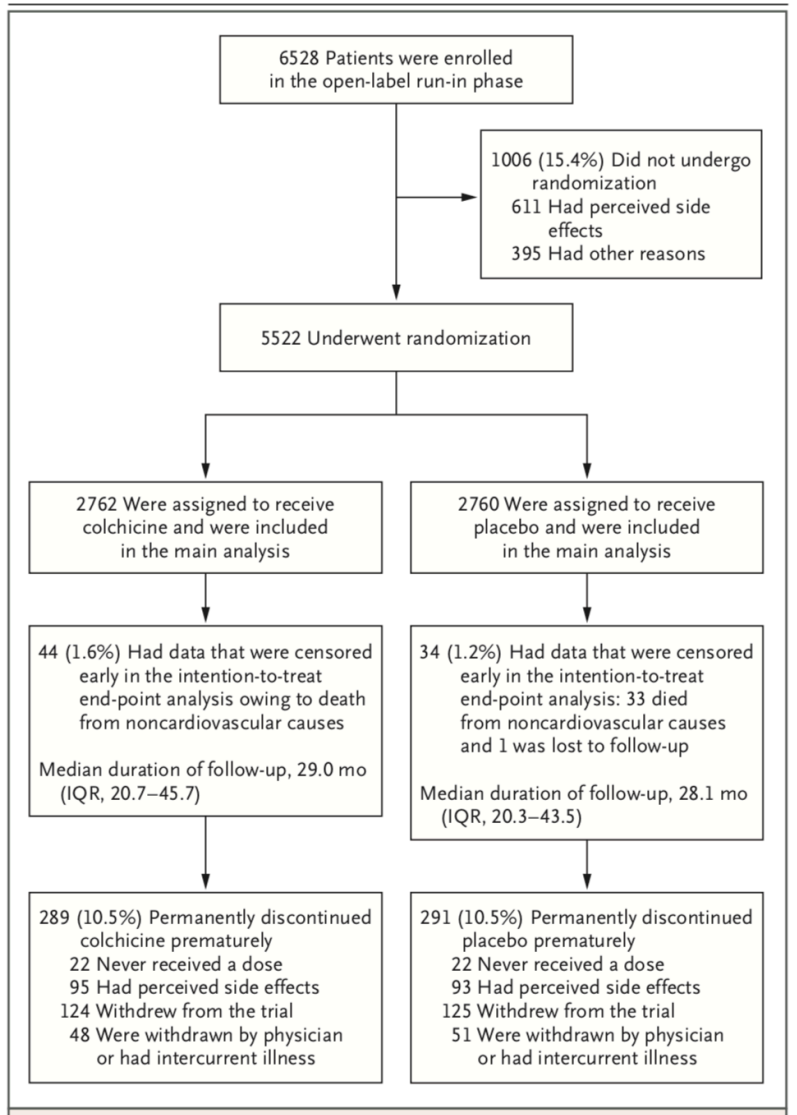
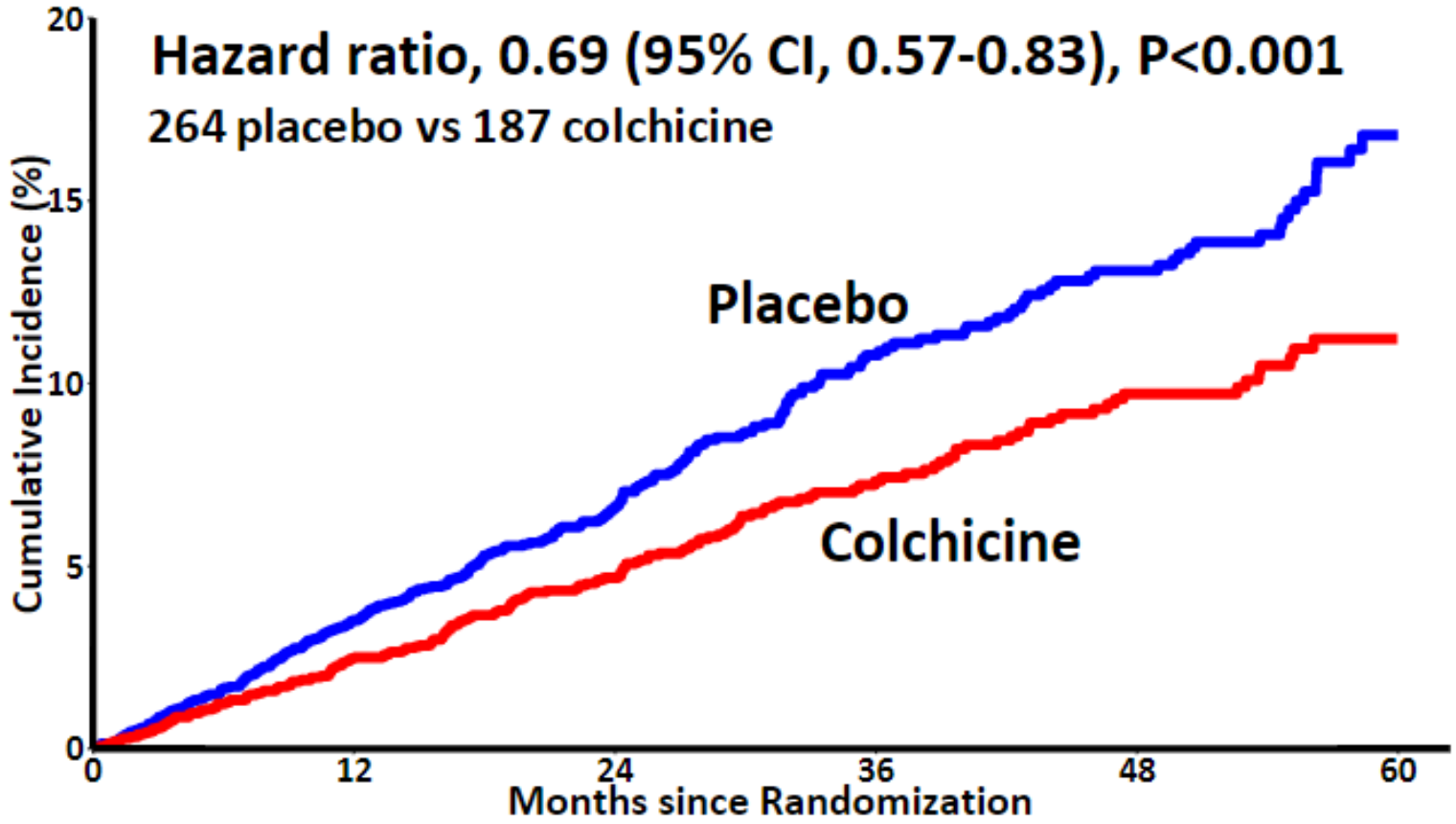


Figure 1. Enrollment, Randomization, and Follow-up.

Primary end point

Cardiovascular death, Myocardial infarction, Ischemic stroke or Ischemia-driven coronary revascularization

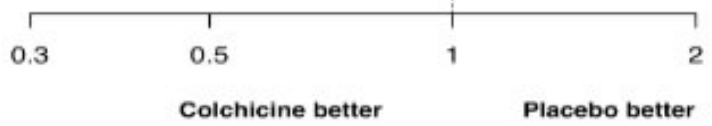


Ranked secondary end points

	Colchicine (N = 2762)	Placebo (N = 2760)	Hazard Ratio (95% CI)	P Value
1. Cardiovascular death, Myocardial infarction, or Ischemic stroke	115(4.2)	157(5.7)	0.72(0.57-0.92)	**0.007**
2. Myocardial infarction or Ischemia-driven coronary revascularization	155(5.6)	224(8.1)	0.67(0.55-0.83)	**<0.001**
3. Cardiovascular death or Myocardial infarction	100(3.6)	138(5.0)	0.71(0.55-0.92)	**0.010**
4. Ischemia-driven coronary revascularization	135(4.9)	177(6.4)	0.75(0.60-0.94)	**0.012**
5. Myocardial infarction	83(3.0)	116(4.2)	0.70(0.53-0.93)	**0.014**
6. Ischemic stroke	16(0.6)	24(0.9)	0.66(0.35-1.25)	0.198
7. Death from any cause	73(2.6)	60(2.2)	1.21(0.86-1.71)	
8. Cardiovascular death	20(0.7)	25(0.9)	0.80(0.44-1.44)	

Prespecified sub-groups

Subgroup	Colchicine (no. of events/no. of patients)	Placebo (no. of events/no. of patients)	Hazard Ratio (95% CI)
Total Cohort	181 / 2740	260 / 2738	0.68 (0.56-0.82)
Sex			
Male	154 / 2288	232 / 2352	0.67 (0.54-0.82)
Female	27 / 452	28 / 386	0.79 (0.46-1.33)
Age			
> 65 years	123 / 1533	164 / 1548	0.74 (0.59-0.93)
≤ 65 years	58 / 1207	96 / 1190	0.58 (0.42-0.80)
Smoking status			
Current	25 / 316	27 / 328	0.96 (0.56-1.66)
Former or never	156 / 2412	233 / 2401	0.65 (0.53-0.79)
Hypertension			
Yes	93 / 1413	137 / 1380	0.65 (0.50-0.85)
No	88 / 1327	123 / 1358	0.70 (0.54-0.93)
Diabetes			
Yes	53 / 488	65 / 511	0.85 (0.59-1.22)
No	128 / 2252	195 / 2227	0.63 (0.50-0.79)
Insulin dependent diabetes			
Yes	21 / 138	21 / 145	1.01 (0.55-1.85)
No	160 / 2602	239 / 2593	0.65 (0.53-0.79)
Renal function*			
Stage 1, 2	168 / 2593	249 / 2581	0.66 (0.54-0.80)
Stage 3a	13 / 147	11 / 157	1.19 (0.53-2.65)
Prior acute coronary syndrome			
Yes	147 / 2308	219 / 2317	0.66 (0.53-0.81)
No	34 / 432	41 / 421	0.79 (0.50-1.25)
Prior coronary revascularization			
Yes	148 / 2286	217 / 2302	0.67 (0.54-0.83)
No	33 / 454	43 / 436	0.72 (0.46-1.13)
Atrial fibrillation			
Yes	31 / 330	32 / 317	0.93 (0.57-1.53)
No	150 / 2410	228 / 2421	0.64 (0.52-0.79)
Statin therapy†			
High dose	108 / 1664	164 / 1715	0.66 (0.52-0.84)
Low-moderate	73 / 1076	96 / 1023	0.70 (0.51-0.95)
Ezetimibe			
Yes	36 / 549	44 / 520	0.75 (0.49-1.17)
No	145 / 2191	216 / 2218	0.66 (0.54-0.82)
Region			
Australia	74 / 932	144 / 935	0.49 (0.37-0.65)
The Netherlands	107 / 1808	116 / 1803	0.91 (0.70-1.18)



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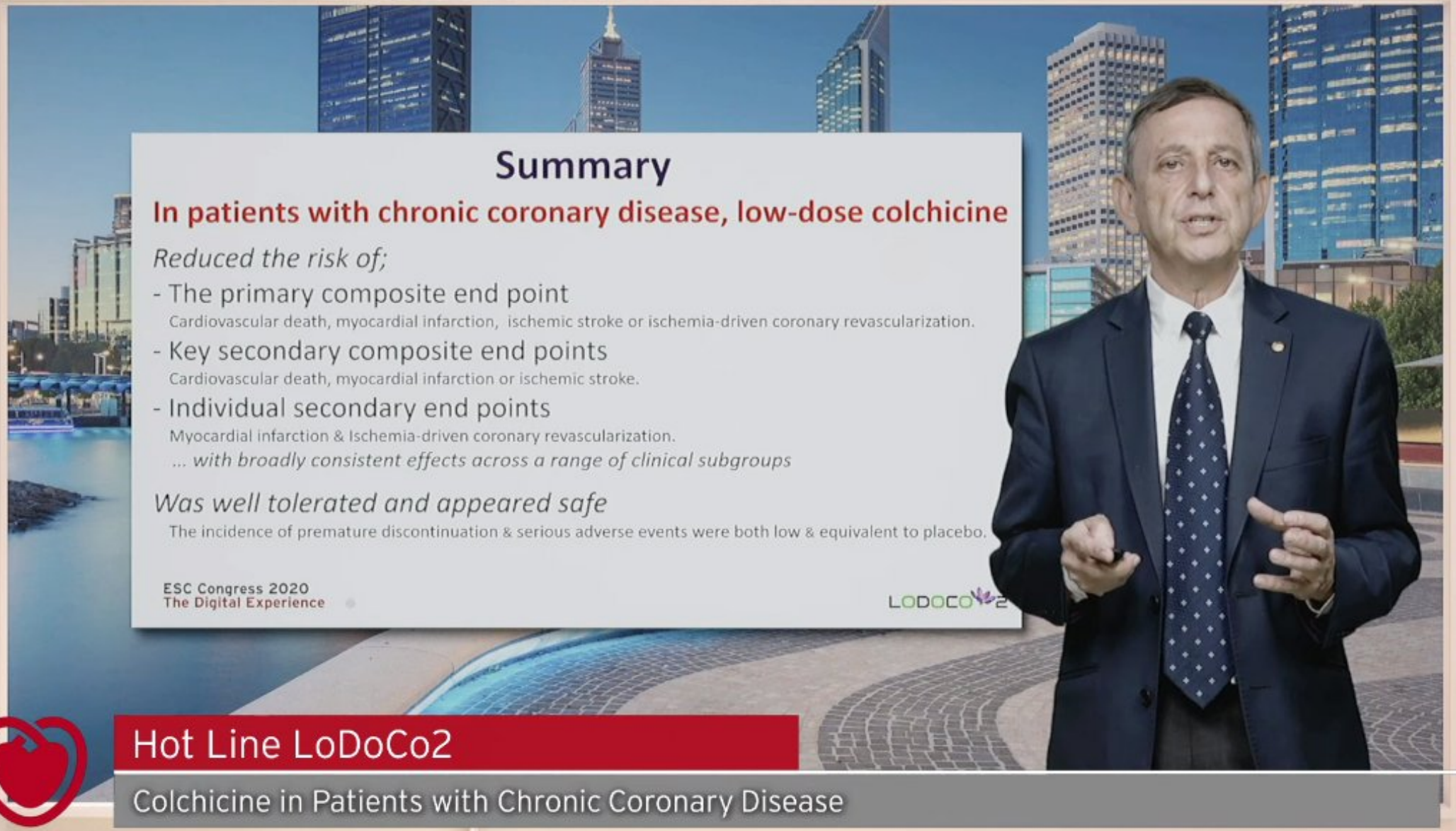
Serous adverse events

	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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