

**Dossier zur Nutzenbewertung  
gemäß § 35a SGB V**

*Colchicin (Colxi<sup>®</sup> 0,5 mg Filmtabletten)*

APONTIS PHARMA Deutschland GmbH & Co. KG

**Modul 4 A – Anhang 4-G**

*Prophylaxe von ischämischen kardiovaskulären  
Ereignissen nach vor kurzem stattgefundenem  
Myokardinfarkt*

Weitere Ergebnisse zu RCT mit dem zu bewertenden  
Arzneimittel

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**Hinweise**

Dieser Anhang zu Modul 4 A – Colchicin zur Prophylaxe von ischämischen kardiovaskulären Ereignissen nach vor kurzem stattgefundenem Myokardinfarkt enthält deskriptive Tabellen mit den qualifizierenden Ereignissen auf Ebene der einzelnen Endpunkte für den primären und sekundären kombinierten Endpunkt, Sensitivitätsanalysen für die Einzelkomponenten des primären kombinierten Endpunkts sowie Subgruppenanalysen für statistisch nicht signifikante Interaktionsterme.

Verwendete Abkürzungen werden im Abkürzungsverzeichnis des Moduls 4 A erläutert.

Die Ergebnisdarstellung erfolgt auf Englisch. Auf eine Übersetzung wurde verzichtet.

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## 4 RESULTS

### 4.1 Primary Outcome

#### 4.1.1 Primary Composite Outcome (Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization)

**Table 1:** Composite Outcome Composition for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization (ITT Population).

<b>Outcome</b>	<b>Colchicine + SoC (N = 2366)</b>	<b>Placebo + SoC (N = 2379)</b>
	e <sup>a</sup> /N <sup>b</sup>	e <sup>a</sup> /N <sup>b</sup>
<b>Acute Myocardial Infarction</b>	85/2366	92/2379
<b>Urgent Hospitalization for Angina Requiring Coronary Revascularization</b>	23/2366	47/2379
<b>Cardiovascular Death</b>	17/2366	13/2379
<b>Resuscitated Cardiac Arrest</b>	1/2366	1/2379
<b>Stroke or Transient Ischaemic Attack</b>	5/2366	17/2379

Database lock: 28-08-2019

<sup>a</sup>Number of events in the study population.  
<sup>b</sup>Number of participants in the study population.

Study: COLCOT

## 4.2 Secondary Outcomes

### 4.2.1 Secondary Composite Outcome (Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke)

**Table 2:** Composite Outcome Composition for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke (ITT Population).

<b>Outcome</b>	<b>Colchicine + SoC (N = 2366)</b>	<b>Placebo + SoC (N = 2379)</b>
	e <sup>a</sup> /N <sup>b</sup>	e <sup>a</sup> /N <sup>b</sup>
<b>Acute Myocardial Infarction</b>	88/2366	98/2379
<b>Cardiovascular Death</b>	17/2366	13/2379
<b>Resuscitated Cardiac Arrest</b>	1/2366	2/2379
<b>Stroke or Transient Ischaemic Attack</b>	5/2366	17/2379

Database lock: 28-08-2019

<sup>a</sup>Number of events in the study population.  
<sup>b</sup>Number of participants in the study population.

Study: COLCOT

### 4.3 Sensitivity Analyses for the Primary Composite Outcome Components

#### 4.3.1 Per-Protocol Analysis Set

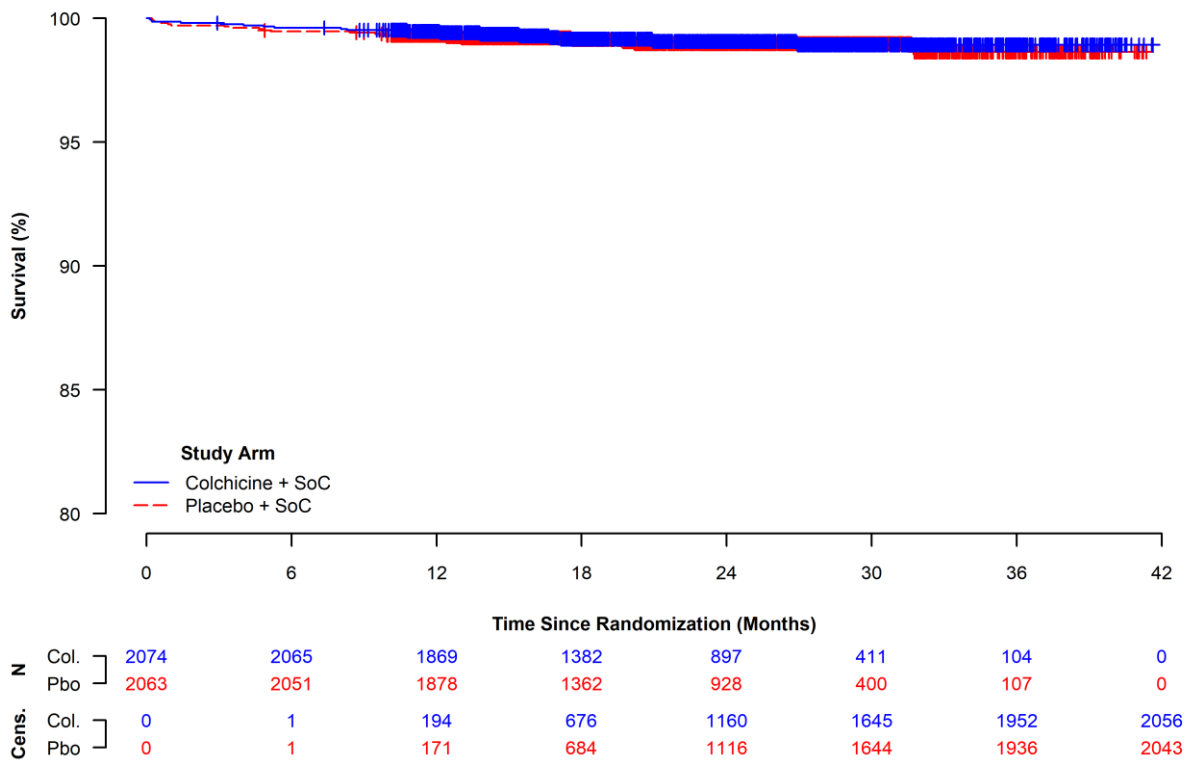
##### 4.3.1.1 Cardiovascular Death

**Table 3:** Proportion of Patients with Cardiovascular Death (Per Protocol Population).

Colchicine + SoC (N = 2,074)	Placebo + SoC (N = 2,063)	Colchicine + SoC vs. Placebo + SoC		
		RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)			
18/2,074 (0.9)	20/2,063 (1.0)	0.895 [0.475, 1.687] 0.7322	0.894 [0.472, 1.696] 0.7322	-0.102 [-0.683, 0.480] 0.7321
Database lock: 28-08-2019				
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC.				
Study: COLCOT				

**Table 4:** Time to Cardiovascular Death (Per Protocol Population).

<b>Colchicine + SoC (N = 2,074)</b>			<b>Placebo + SoC (N = 2,063)</b>			<b>Colchicine + SoC vs. Placebo + SoC</b>
n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
18/2,074 (0.9)	NE [NE, NE]	1.1 [0.5, 1.6]	20/2,063 (1.0)	NE [NE, NE]	1.4 [0.5, 2.2]	0.898 [0.475, 1.698] 0.7413
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC.						
Study: COLCOT						



**Figure 1:** Kaplan-Meier Curves for Cardiovascular Death (Per Protocol Population).

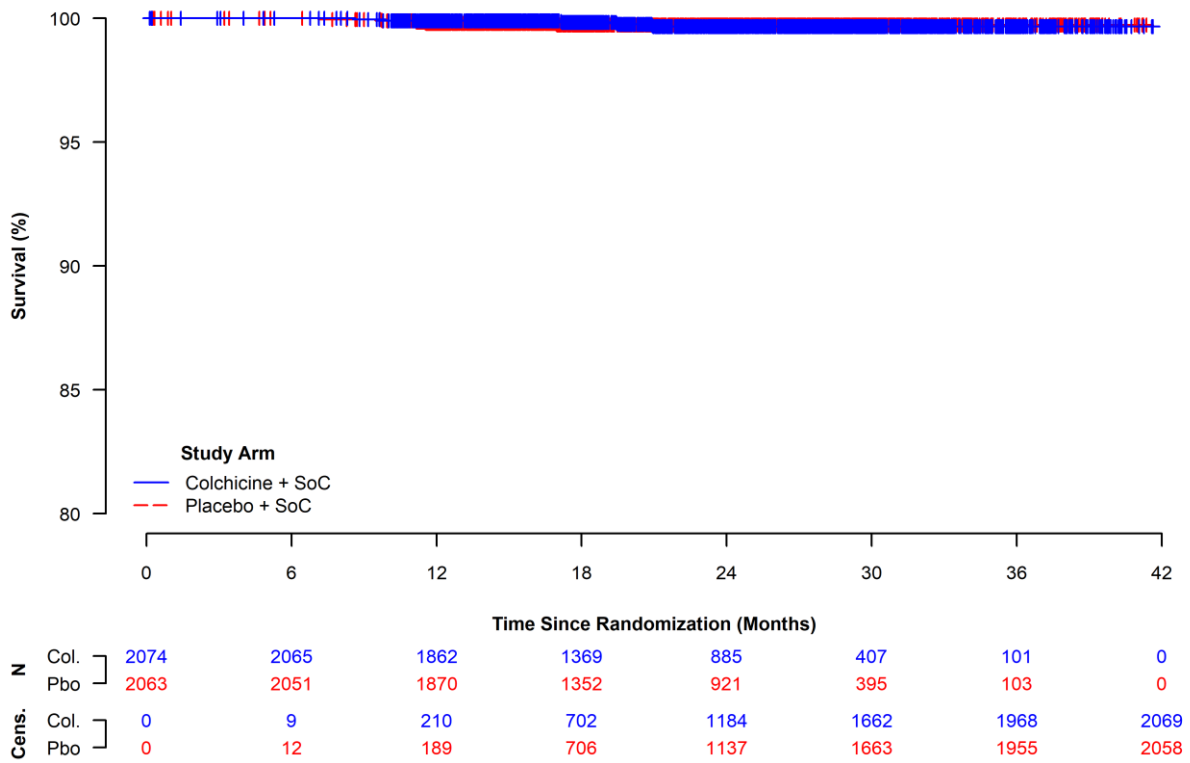
### 4.3.1.2 Resuscitated Cardiac Arrest

**Table 5:** Proportion of Patients with Resuscitated Cardiac Arrest (Per Protocol Population).

Colchicine + SoC (N = 2,074)	Placebo + SoC (N = 2,063)	Colchicine + SoC vs. Placebo + SoC		
		RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)			
5/2,074 (0.2)	5/2,063 (0.2)	0.995 [0.288, 3.431] 0.9933	0.995 [0.288, 3.441] 0.9933	-0.001 [-0.301, 0.298] 0.9933
Database lock: 28-08-2019				
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC.				
Study: COLCOT				

**Table 6:** Time to Resuscitated Cardiac Arrest (Per Protocol Population).

<b>Colchicine + SoC (N = 2,074)</b>			<b>Placebo + SoC (N = 2,063)</b>			<b>Colchicine + SoC vs. Placebo + SoC</b>
n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
5/2,074 (0.2)	NE [NE, NE]	0.3 [0.0, 0.6]	5/2,063 (0.2)	NE [NE, NE]	0.3 [0.0, 0.5]	0.997 [0.289, 3.443] 0.9957
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC.						
Study: COLCOT						



**Figure 2:** Kaplan-Meier Curves for Resuscitated Cardiac Arrest (Per Protocol Population).

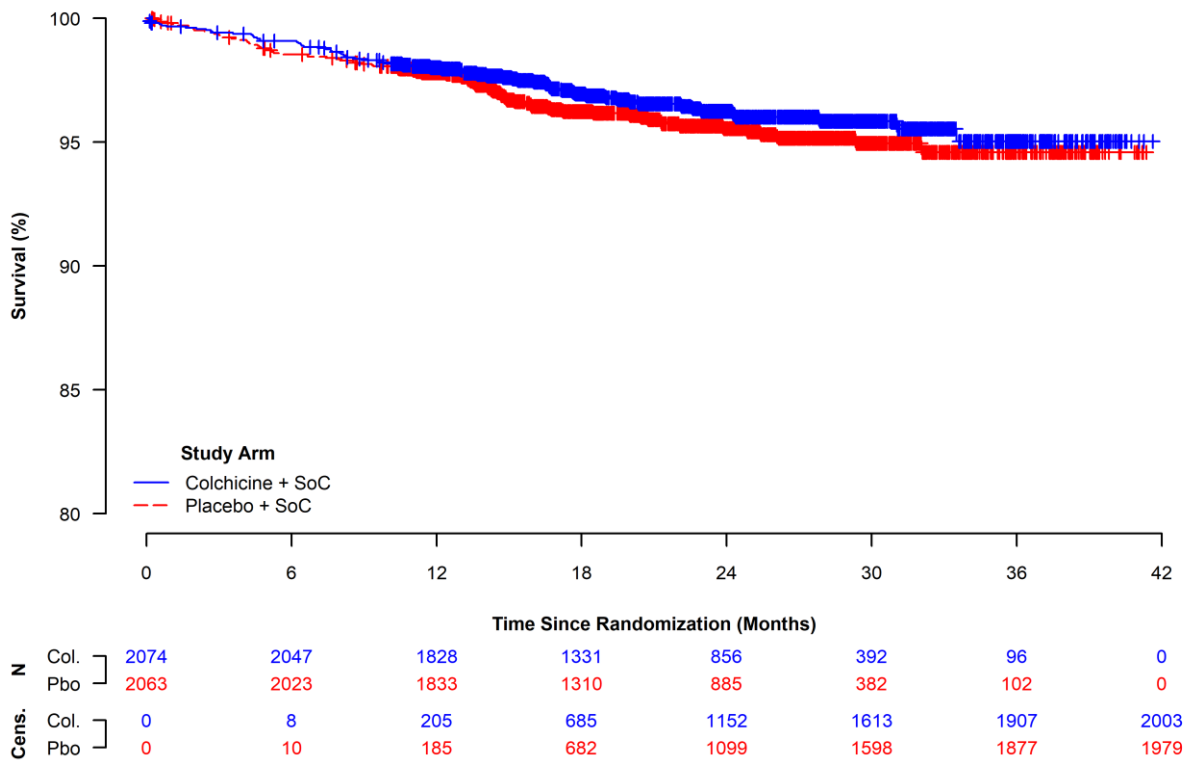
### 4.3.1.3 Acute Myocardial Infarction

**Table 7:** Proportion of Patients with Acute Myocardial Infarction (Per Protocol Population).

Colchicine + SoC (N = 2,074)	Placebo + SoC (N = 2,063)	Colchicine + SoC vs. Placebo + SoC		
		RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)			
71/2,074 (3.4)	84/2,063 (4.1)	0.841 [0.617, 1.146] 0.2728	0.835 [0.605, 1.152] 0.2728	-0.648 [-1.806, 0.509] 0.2722
Database lock: 28-08-2019				
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC.				
Study: COLCOT				

**Table 8:** Time to Acute Myocardial Infarction (Per Protocol Population).

Colchicine + SoC (N = 2,074)			Placebo + SoC (N = 2,063)			Colchicine + SoC vs. Placebo + SoC
n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
71/2,074 (3.4)	NE [NE, NE]	5.0 [3.4, 6.5]	84/2,063 (4.1)	NE [NE, NE]	5.4 [4.1, 6.8]	0.843 [0.614, 1.156] 0.2887
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC.						
Study: COLCOT						



**Figure 3:** Kaplan-Meier Curves for Acute Myocardial Infarction (Per Protocol Population).

#### 4.3.1.4 Stroke

**Table 9:** Proportion of Patients with Stroke (Per Protocol Population).

Colchicine + SoC (N = 2,074)	Placebo + SoC (N = 2,063)	Colchicine + SoC vs. Placebo + SoC		
		RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)			
2/2,074 (0.1)	17/2,063 (0.8)	0.117 [0.027, 0.506] 0.0041	0.116 [0.027, 0.503] 0.0040	-0.728 [-1.140, -0.315] 0.0005

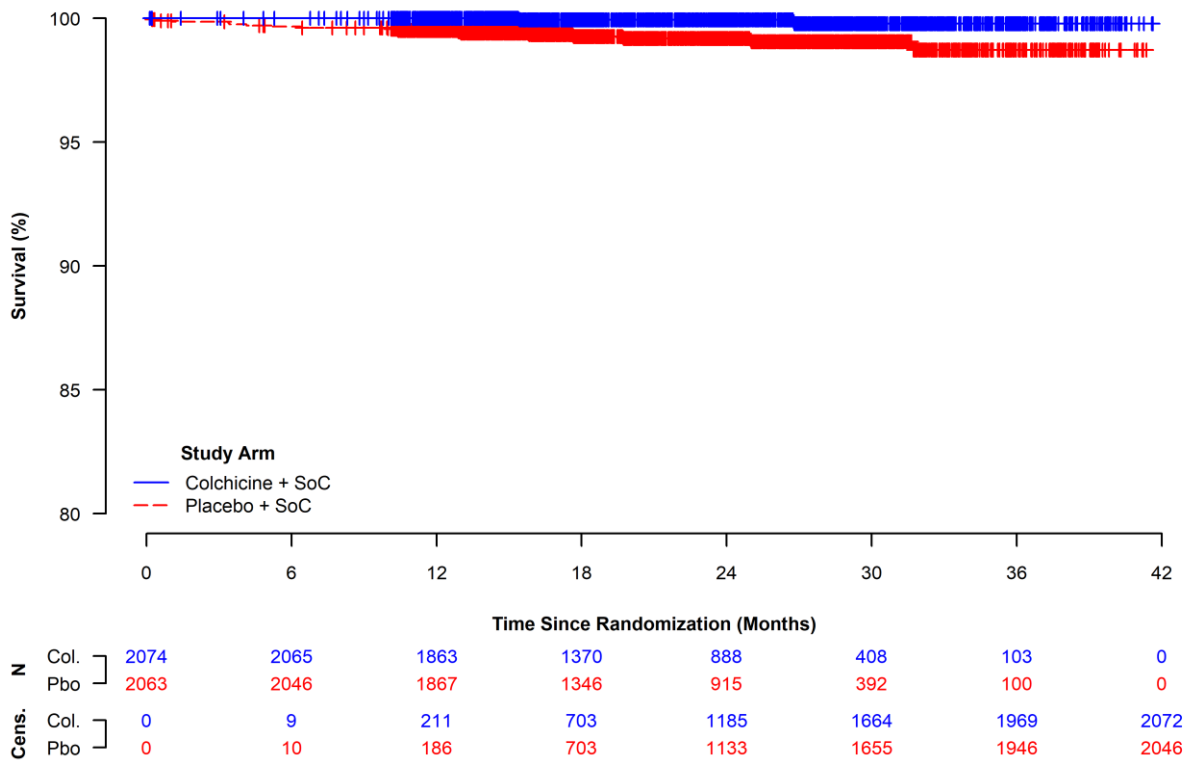
Database lock: 28-08-2019

<sup>a</sup>Number of patients with the event.  
<sup>b</sup>Number of patients in the study population.  
<sup>c</sup>OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC.

Study: COLCOT

**Table 10: Time to Stroke (Per Protocol Population).**

<b>Colchicine + SoC (N = 2,074)</b>			<b>Placebo + SoC (N = 2,063)</b>			<b>Colchicine + SoC vs. Placebo + SoC</b>
n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
2/2,074 (0.1)	NE [NE, NE]	0.2 [0.0, 0.5]	17/2,063 (0.8)	NE [NE, NE]	1.3 [0.4, 2.1]	0.117 [0.027, 0.508] 0.0042
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC.						
Study: COLCOT						



**Figure 4:** Kaplan-Meier Curves for Stroke (Per Protocol Population).

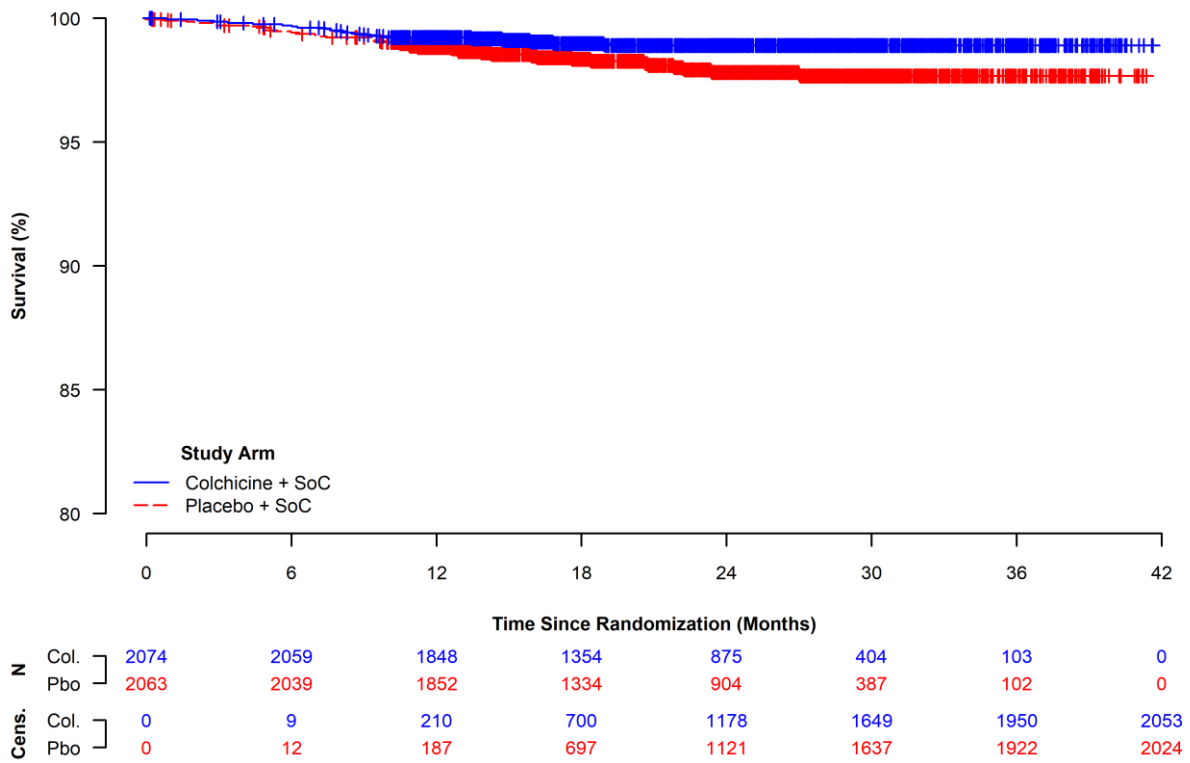
### 4.3.1.5 Urgent Hospitalization for Angina Requiring Coronary Revascularization

**Table 11:** Proportion of Patients with Urgent Hospitalization for Angina Requiring Coronary Revascularization (Per Protocol Population).

Colchicine + SoC (N = 2,074)	Placebo + SoC (N = 2,063)	Colchicine + SoC vs. Placebo + SoC		
		RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)			
21/2,074 (1.0)	39/2,063 (1.9)	0.536 [0.316, 0.907] 0.0202	0.531 [0.311, 0.906] 0.0201	-0.878 [-1.607, -0.149] 0.0182
Database lock: 28-08-2019				
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC.				
Study: COLCOT				

**Table 12:** Time to Urgent Hospitalization for Angina Requiring Coronary Revascularization (Per Protocol Population).

Colchicine + SoC (N = 2,074)			Placebo + SoC (N = 2,063)			Colchicine + SoC vs. Placebo + SoC
n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
21/2,074 (1.0)	NE [NE, NE]	1.1 [0.6, 1.6]	39/2,063 (1.9)	NE [NE, NE]	2.3 [1.6, 3.1]	0.536 [0.315, 0.911] 0.0213
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC.						
Study: COLCOT						



**Figure 5:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization (Per Protocol Population).

## 4.3.2 On Treatment Analysis Set

### 4.3.2.1 Cardiovascular Death

**Table 13:** Proportion of Patients with Cardiovascular Death (On Treatment Population).

Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
		RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)			
8/2,330 (0.3)	12/2,346 (0.5)	0.671 [0.275, 1.639] 0.3815	0.670 [0.273, 1.642] 0.3814	-0.168 [-0.542, 0.206] 0.3779
Database lock: 28-08-2019				
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC.				
Study: COLCOT				

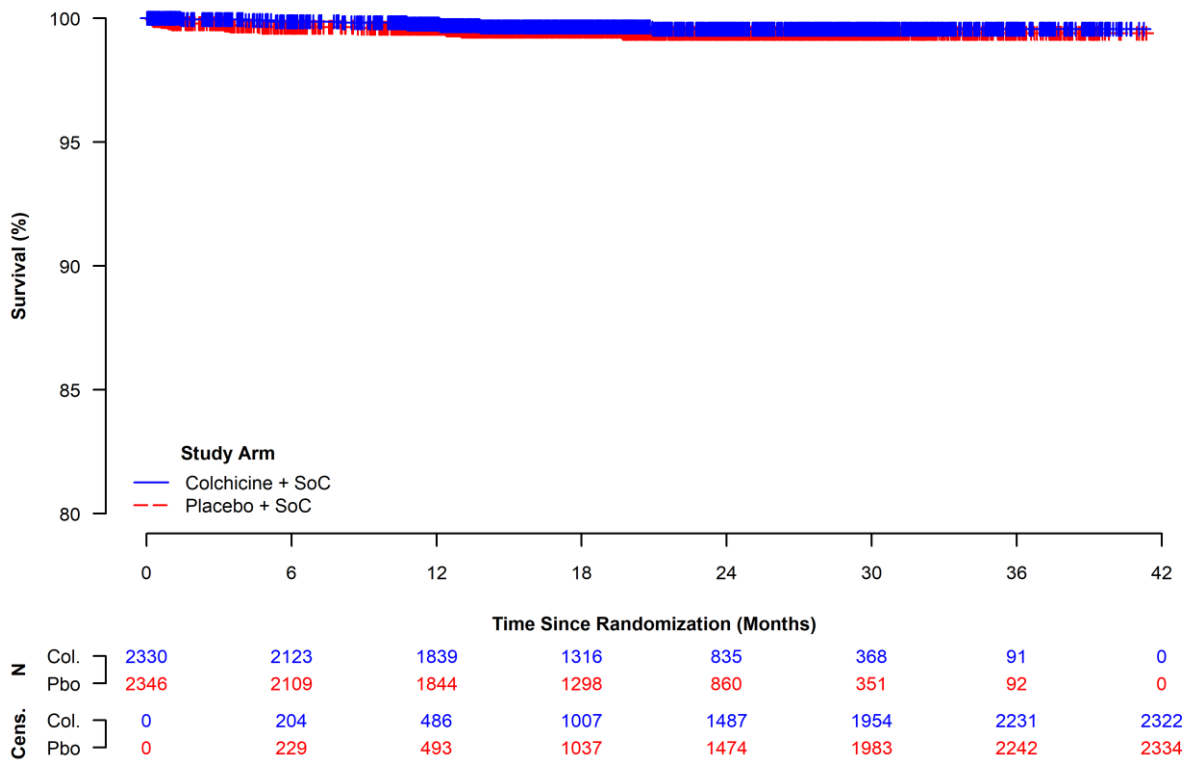
**Table 14: Time to Cardiovascular Death (On Treatment Population).**

<b>Colchicine + SoC (N = 2,330)</b>			<b>Placebo + SoC (N = 2,346)</b>			<b>Colchicine + SoC vs. Placebo + SoC</b>
n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
8/2,330 (0.3)	NE [NE, NE]	0.4 [0.1, 0.8]	12/2,346 (0.5)	NE [NE, NE]	0.6 [0.3, 1.0]	0.668 [0.273, 1.634] 0.3763

Database lock: 28-08-2019

<sup>a</sup>Number of patients with the event.  
<sup>b</sup>Number of patients in the study population.  
<sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  
<sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  
<sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC.

Study: COLCOT



**Figure 6:** Kaplan-Meier Curves for Cardiovascular Death (On Treatment Population).

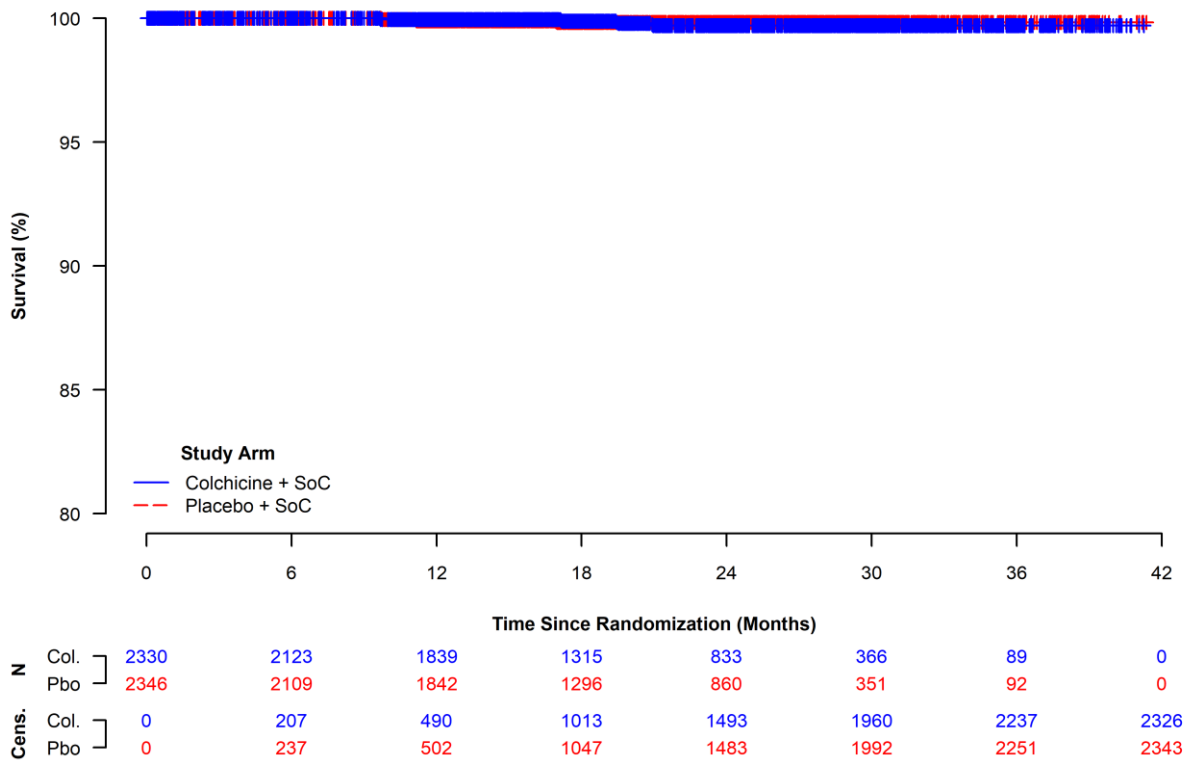
### 4.3.2.2 Resuscitated Cardiac Arrest

**Table 15:** Proportion of Patients with Resuscitated Cardiac Arrest (On Treatment Population).

Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
		RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)			
4/2,330 (0.2)	3/2,346 (0.1)	1.342 [0.301, 5.992] 0.6996	1.343 [0.300, 6.008] 0.6996	0.044 [-0.178, 0.266] 0.6987
Database lock: 28-08-2019				
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC.				
Study: COLCOT				

**Table 16:** Time to Resuscitated Cardiac Arrest (On Treatment Population).

Colchicine + SoC (N = 2,330)			Placebo + SoC (N = 2,346)			Colchicine + SoC vs. Placebo + SoC
n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
4/2,330 (0.2)	NE [NE, NE]	0.3 [0.0, 0.6]	3/2,346 (0.1)	NE [NE, NE]	0.2 [0.0, 0.4]	1.328 [0.297, 5.935] 0.7101
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC.						
Study: COLCOT						



**Figure 7:** Kaplan-Meier Curves for Resuscitated Cardiac Arrest (On Treatment Population).

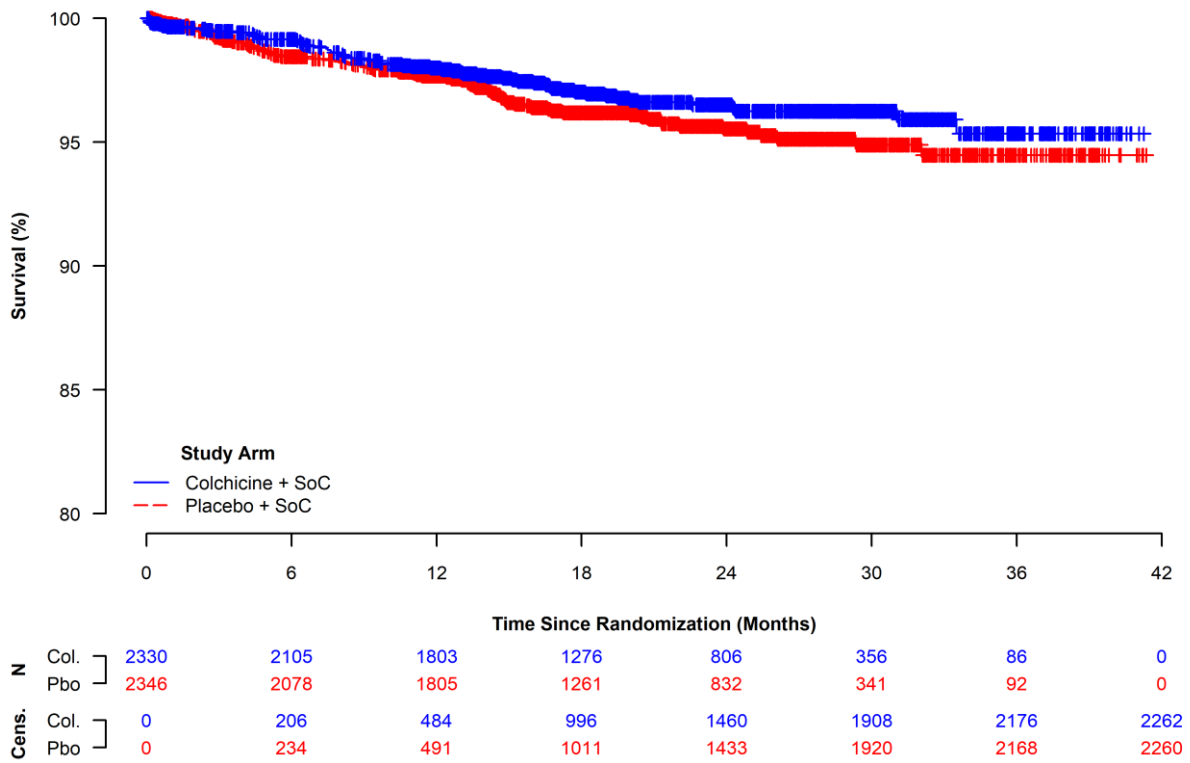
### 4.3.2.3 Acute Myocardial Infarction

**Table 17:** Proportion of Patients with Acute Myocardial Infarction (On Treatment Population).

Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
		RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)			
68/2,330 (2.9)	86/2,346 (3.7)	0.796 [0.582, 1.089] 0.1532	0.790 [0.572, 1.092] 0.1531	-0.747 [-1.770, 0.275] 0.1520
Database lock: 28-08-2019				
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC.				
Study: COLCOT				

**Table 18:** Time to Acute Myocardial Infarction (On Treatment Population).

Colchicine + SoC (N = 2,330)			Placebo + SoC (N = 2,346)			Colchicine + SoC vs. Placebo + SoC
n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
68/2,330 (2.9)	NE [NE, NE]	4.7 [3.1, 6.2]	86/2,346 (3.7)	NE [NE, NE]	5.5 [4.1, 6.9]	0.790 [0.575, 1.085] 0.1457
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC.						
Study: COLCOT						



**Figure 8:** Kaplan-Meier Curves for Acute Myocardial Infarction (On Treatment Population).

#### 4.3.2.4 Stroke

**Table 19:** Proportion of Patients with Stroke (On Treatment Population).

Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
		RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)			
2/2,330 (0.1)	16/2,346 (0.7)	0.126 [0.029, 0.547] 0.0057	0.125 [0.029, 0.545] 0.0056	-0.596 [-0.950, -0.243] 0.0010

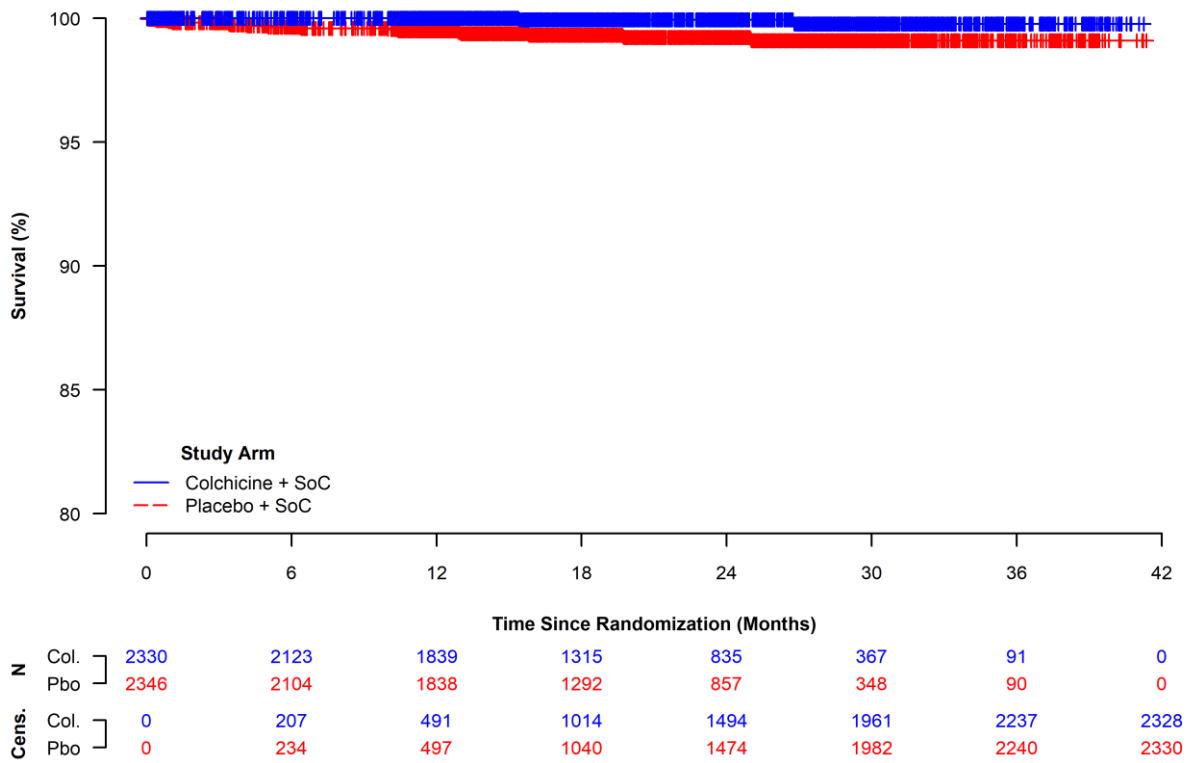
Database lock: 28-08-2019

<sup>a</sup>Number of patients with the event.  
<sup>b</sup>Number of patients in the study population.  
<sup>c</sup>OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC.

Study: COLCOT

**Table 20: Time to Stroke (On Treatment Population).**

<b>Colchicine + SoC (N = 2,330)</b>			<b>Placebo + SoC (N = 2,346)</b>			<b>Colchicine + SoC vs. Placebo + SoC</b>
n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
2/2,330 (0.1)	NE [NE, NE]	0.2 [0.0, 0.6]	16/2,346 (0.7)	NE [NE, NE]	0.9 [0.4, 1.4]	0.125 [0.029, 0.544] 0.0056
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC.						
Study: COLCOT						



**Figure 9:** Kaplan-Meier Curves for Stroke (On Treatment Population).

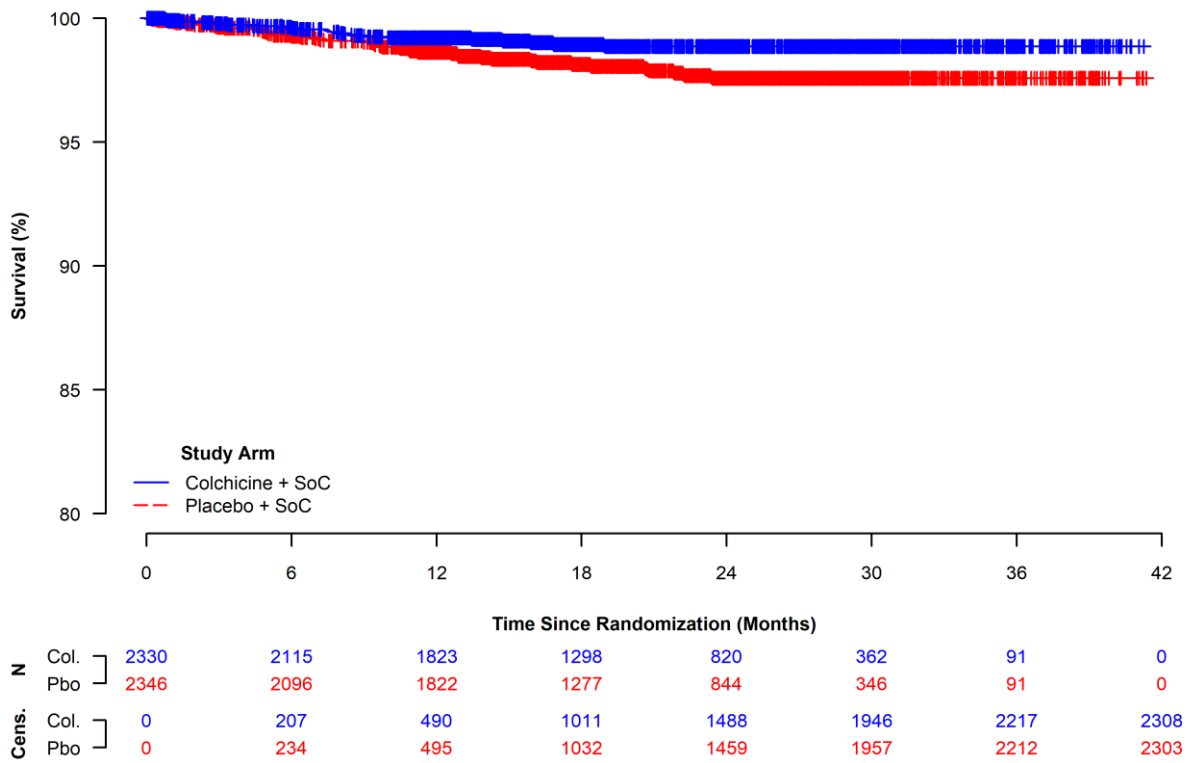
#### 4.3.2.5 Urgent Hospitalization for Angina Requiring Coronary Revascularization

**Table 21:** Proportion of Patients with Urgent Hospitalization for Angina Requiring Coronary Revascularization (On Treatment Population).

Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
		RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)			
22/2,330 (0.9)	43/2,346 (1.8)	0.515 [0.309, 0.858] 0.0109	0.511 [0.304, 0.856] 0.0108	-0.889 [-1.559, -0.219] 0.0093
Database lock: 28-08-2019				
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC.				
Study: COLCOT				

**Table 22:** Time to Urgent Hospitalization for Angina Requiring Coronary Revascularization (On Treatment Population).

Colchicine + SoC (N = 2,330)			Placebo + SoC (N = 2,346)			Colchicine + SoC vs. Placebo + SoC
n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
22/2,330 (0.9)	NE [NE, NE]	1.1 [0.7, 1.6]	43/2,346 (1.8)	NE [NE, NE]	2.4 [1.7, 3.2]	0.510 [0.305, 0.853] 0.0103
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC.						
Study: COLCOT						



**Figure 10:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization (On Treatment Population).

## 4.4 Subgroup Analyses

### 4.4.1 Mortality

#### 4.4.1.1 Total Mortality

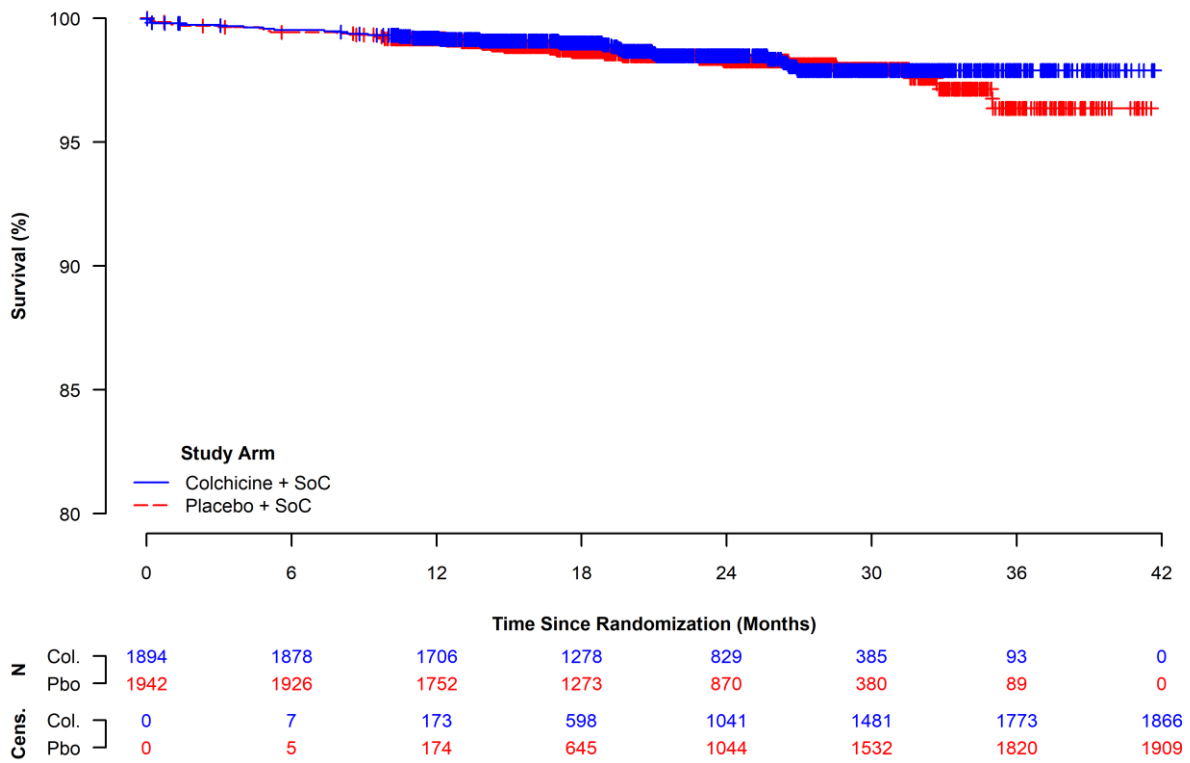
##### 4.4.1.1.1 Subgrouped by Sex

**Table 23:** Proportion of Patients with Total Mortality, Subgrouped by Sex (ITT Population).

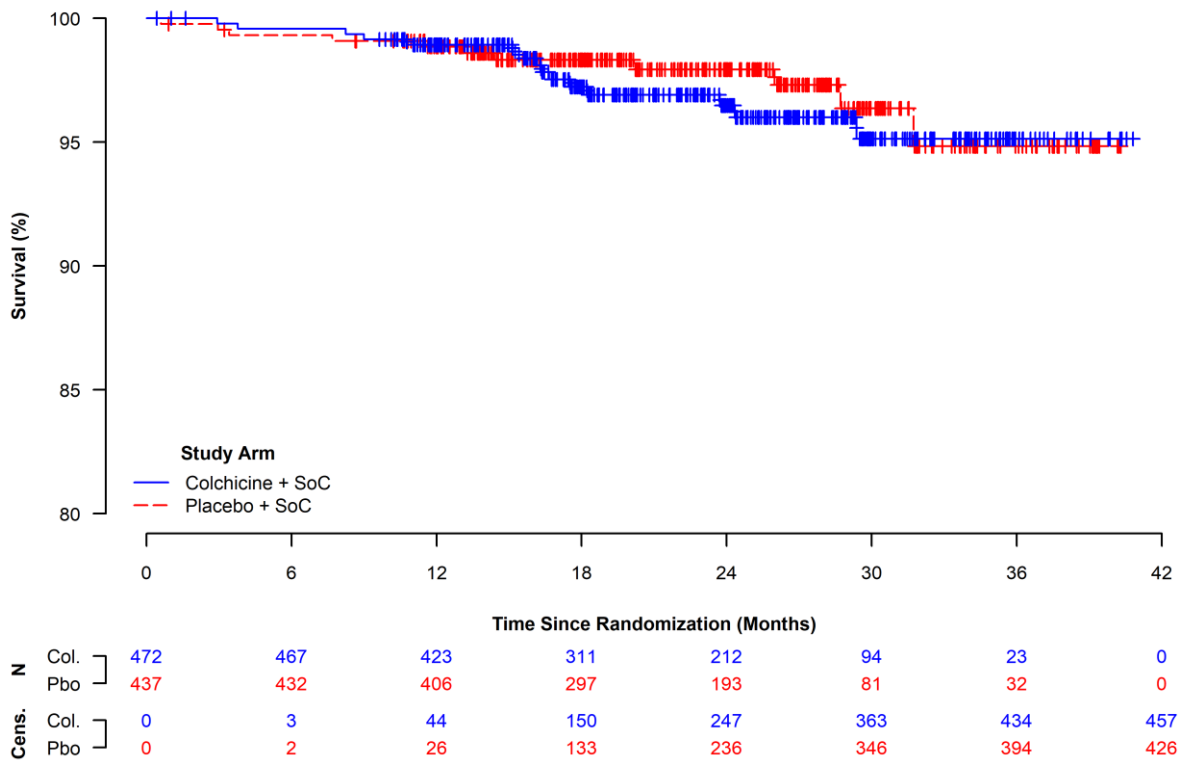
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Sex</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4237</b>					
<b>Male</b>	28/1,894 (1.5)	33/1,942 (1.7)	0.870 [0.528, 1.434] 0.5848	0.868 [0.522, 1.442] 0.5848	-0.221 [-1.012, 0.570] 0.5841
<b>Female</b>	15/472 (3.2)	11/437 (2.5)	1.263 [0.586, 2.719] 0.5514	1.271 [0.577, 2.798] 0.5513	0.661 [-1.498, 2.820] 0.5486
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 24:** Time to Total Mortality, Subgrouped by Sex (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.4178</b>							
<b>Male</b>	28/1,894 (1.5)	NE [NE, NE]	2.1 [1.3, 3.0]	33/1,942 (1.7)	NE [NE, NE]	3.6 [1.6, 5.6]	0.867 [0.524, 1.435] 0.5793
<b>Female</b>	15/472 (3.2)	NE [NE, NE]	4.9 [2.1, 7.5]	11/437 (2.5)	NE [NE, NE]	5.2 [1.1, 9.0]	1.271 [0.584, 2.767] 0.5464
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 11:** Kaplan-Meier Curves for Total Mortality, Within the Male Sex Subgroup (ITT Population).



**Figure 12:** Kaplan-Meier Curves for Total Mortality, Within the Female Sex Subgroup (ITT Population).

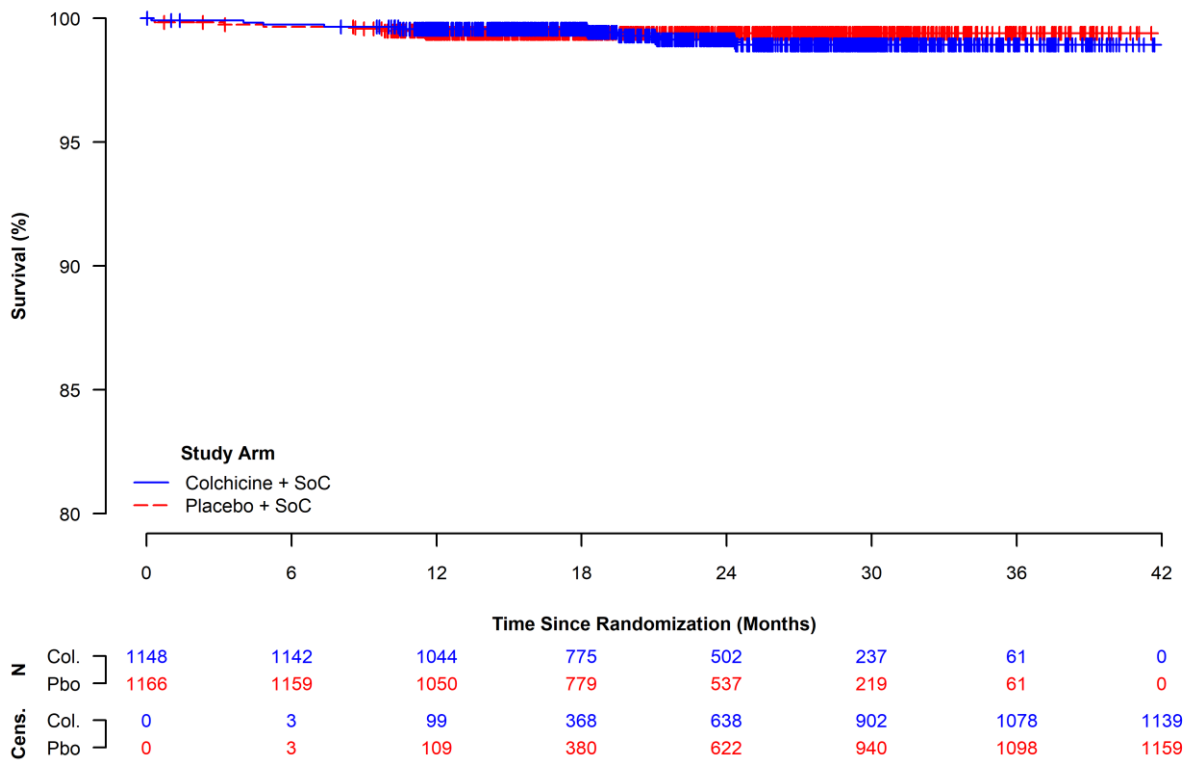
#### 4.4.1.1.2 Subgrouped by Age Group

**Table 25:** Proportion of Patients with Total Mortality, Subgrouped by Age Group (ITT Population).

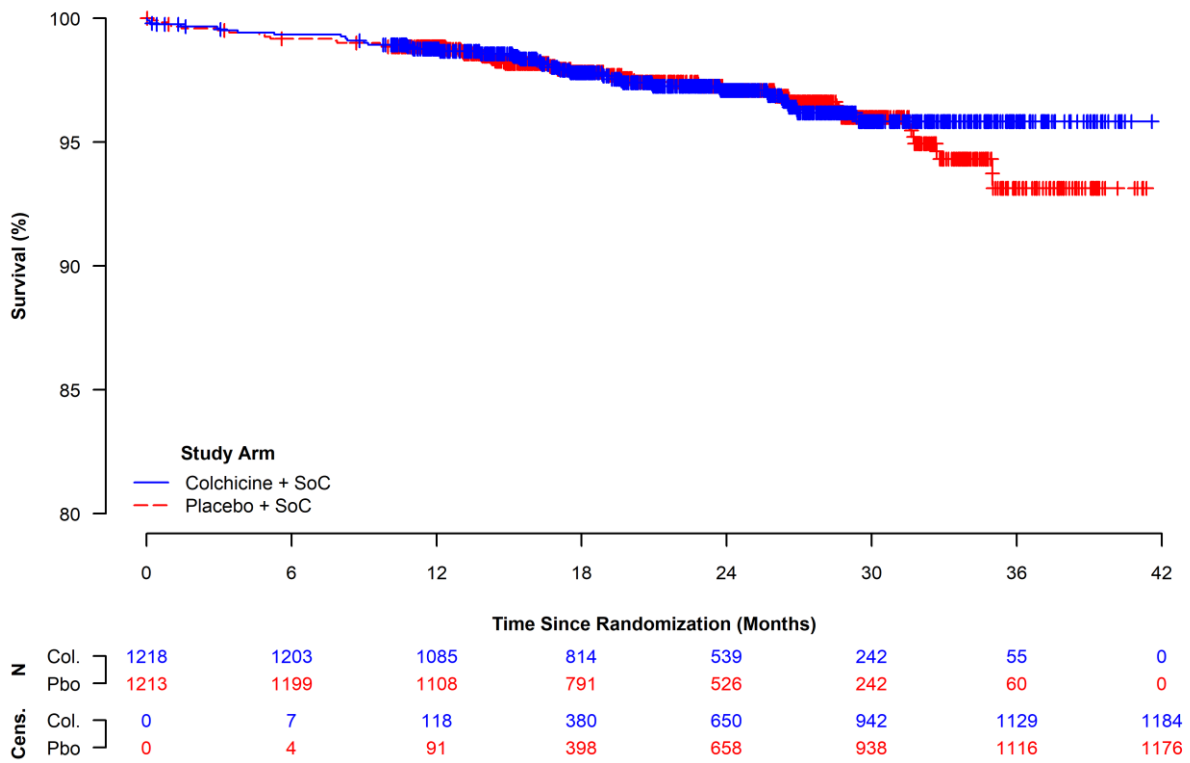
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Age</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.5189</b>					
< 60 Years	9/1,148 (0.8)	7/1,166 (0.6)	1.306 [0.488, 3.495] 0.5952	1.308 [0.486, 3.525] 0.5951	0.184 [-0.492, 0.860] 0.5944
≥ 60 Years	34/1,218 (2.8)	37/1,213 (3.1)	0.915 [0.578, 1.448] 0.7048	0.913 [0.569, 1.464] 0.7048	-0.259 [-1.598, 1.080] 0.7047
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 26:** Time to Total Mortality, Subgrouped by Age Group (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Age</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.5291</b>							
<b>&lt; 60 Years</b>	9/1,148 (0.8)	NE [NE, NE]	1.1 [0.3, 1.8]	7/1,166 (0.6)	NE [NE, NE]	0.6 [0.2, 1.1]	1.311 [0.488, 3.521] 0.5908
<b>≥ 60 Years</b>	34/1,218 (2.8)	NE [NE, NE]	4.2 [2.6, 5.7]	37/1,213 (3.1)	NE [NE, NE]	6.9 [3.5, 10.1]	0.918 [0.576, 1.462] 0.7179
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 13:** Kaplan-Meier Curves for Total Mortality, Within the Age 59 Years or Younger Subgroup (ITT Population).



**Figure 14:** Kaplan-Meier Curves for Total Mortality, Within the Age 60 Years or Older Subgroup (ITT Population).

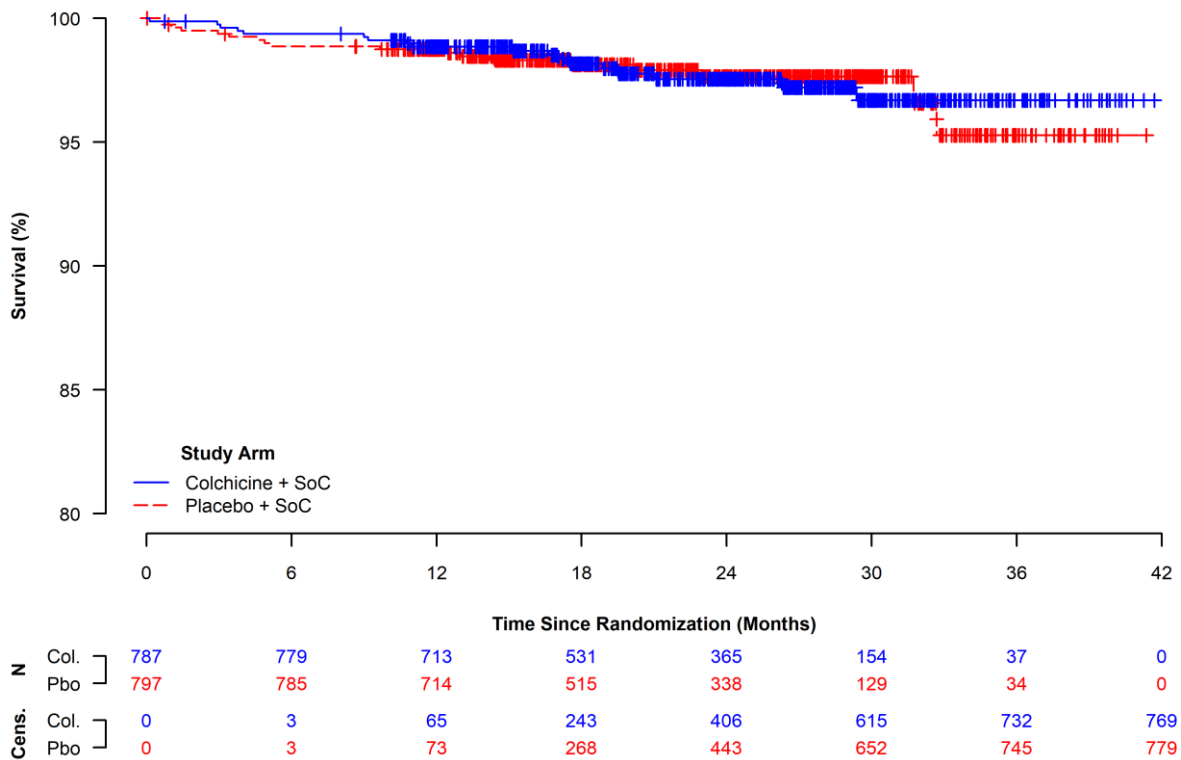
#### 4.4.1.1.3 Subgrouped by Smoking Status

**Table 27:** Proportion of Patients with Total Mortality, Subgrouped by Smoking Status (ITT Population).

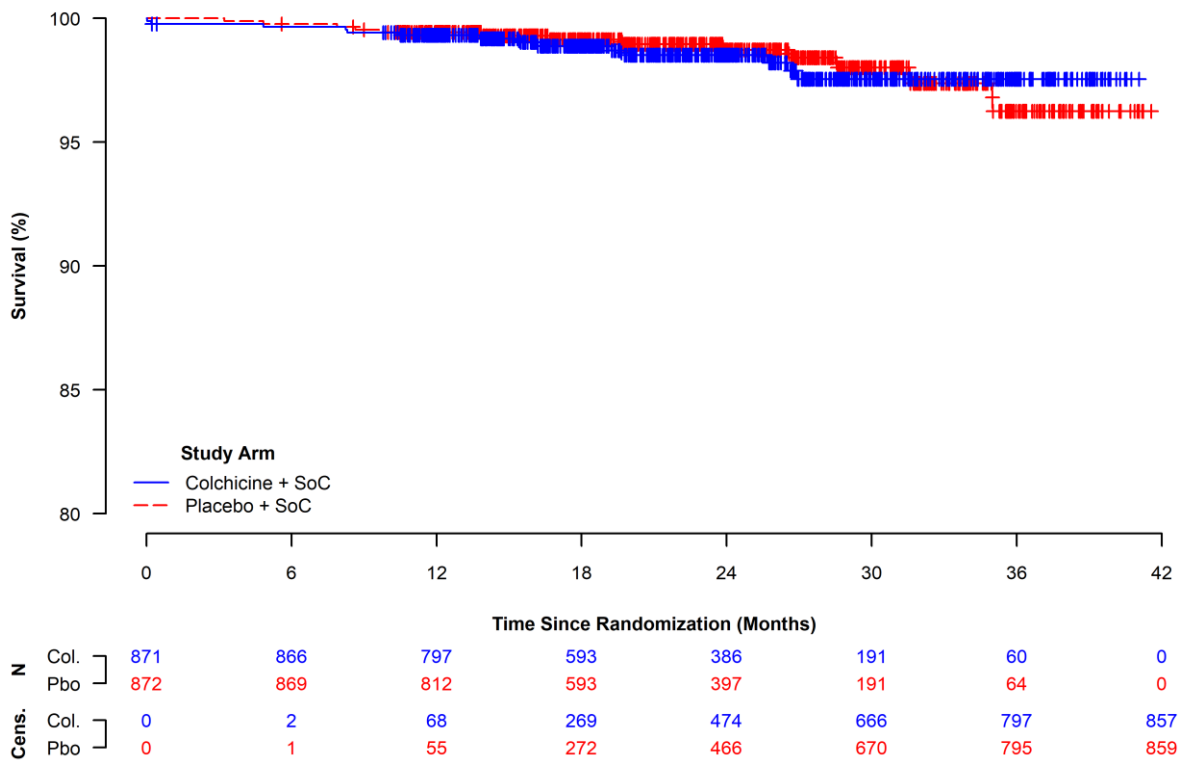
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,377)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Smoking Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.9034</b>					
<b>Non</b>	18/787 (2.3)	18/797 (2.3)	1.013 [0.531, 1.932] 0.9694	1.013 [0.523, 1.962] 0.9694	0.029 [-1.439, 1.497] 0.9694
<b>Ex</b>	14/871 (1.6)	13/872 (1.5)	1.078 [0.510, 2.280] 0.8439	1.079 [0.504, 2.310] 0.8439	0.117 [-1.043, 1.276] 0.8439
<b>Current</b>	11/708 (1.6)	13/708 (1.8)	0.846 [0.382, 1.876] 0.6809	0.844 [0.375, 1.896] 0.6809	-0.282 [-1.627, 1.062] 0.6805
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 28:** Time to Total Mortality, Subgrouped by Smoking Status (ITT Population).

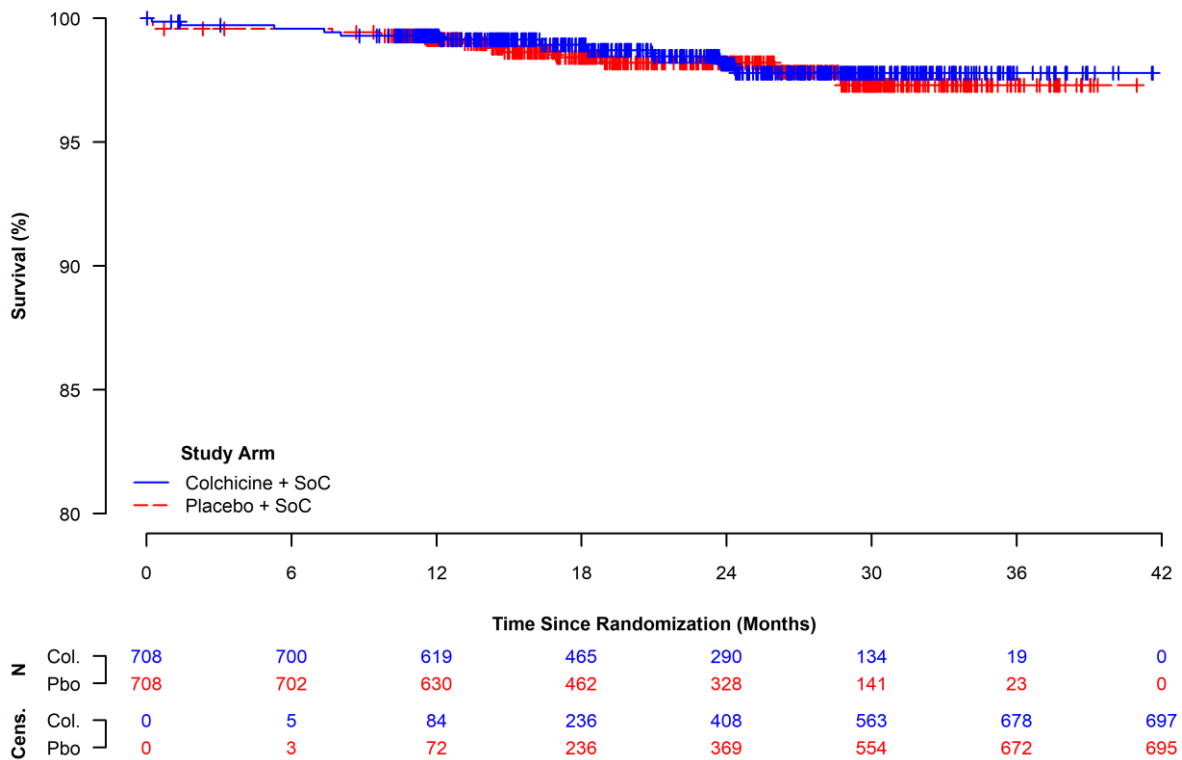
Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,377)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Smoking Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.9135</b>							
<b>Non</b>	18/787 (2.3)	NE [NE, NE]	3.3 [1.6, 5.0]	18/797 (2.3)	NE [NE, NE]	4.7 [1.2, 8.1]	0.984 [0.512, 1.892] 0.9625
<b>Ex</b>	14/871 (1.6)	NE [NE, NE]	2.5 [1.0, 3.9]	13/872 (1.5)	NE [NE, NE]	3.8 [0.9, 6.5]	1.098 [0.516, 2.335] 0.8088
<b>Current</b>	11/708 (1.6)	NE [NE, NE]	2.2 [0.8, 3.6]	13/708 (1.8)	NE [NE, NE]	2.7 [1.0, 4.3]	0.862 [0.386, 1.923] 0.7162
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 15:** Kaplan-Meier Curves for Total Mortality, Within the Non-Smoker Subgroup (ITT Population).



**Figure 16:** Kaplan-Meier Curves for Total Mortality, Within the Ex-Smoker Subgroup (ITT Population).



**Figure 17:** Kaplan-Meier Curves for Total Mortality, Within the Current Smoker Subgroup (ITT Population).

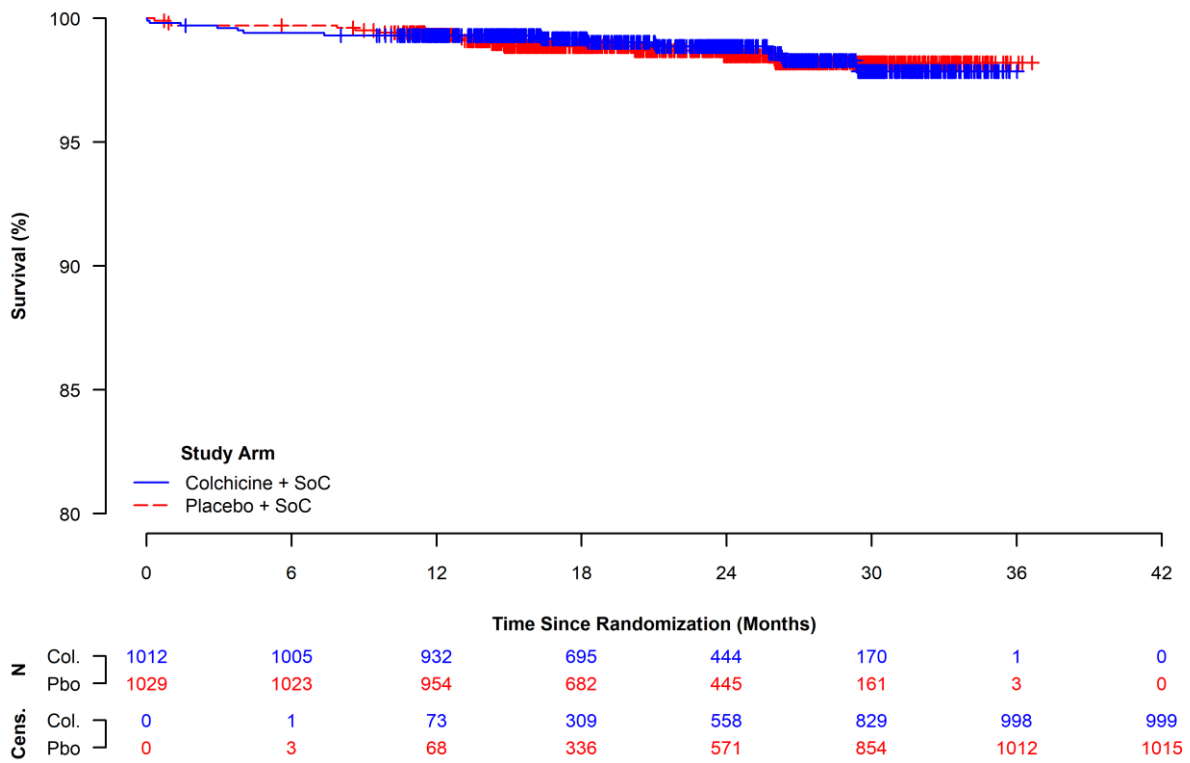
#### 4.4.1.1.4 Subgrouped by Region

**Table 29:** Proportion of Patients with Total Mortality, Subgrouped by Region (ITT Population).

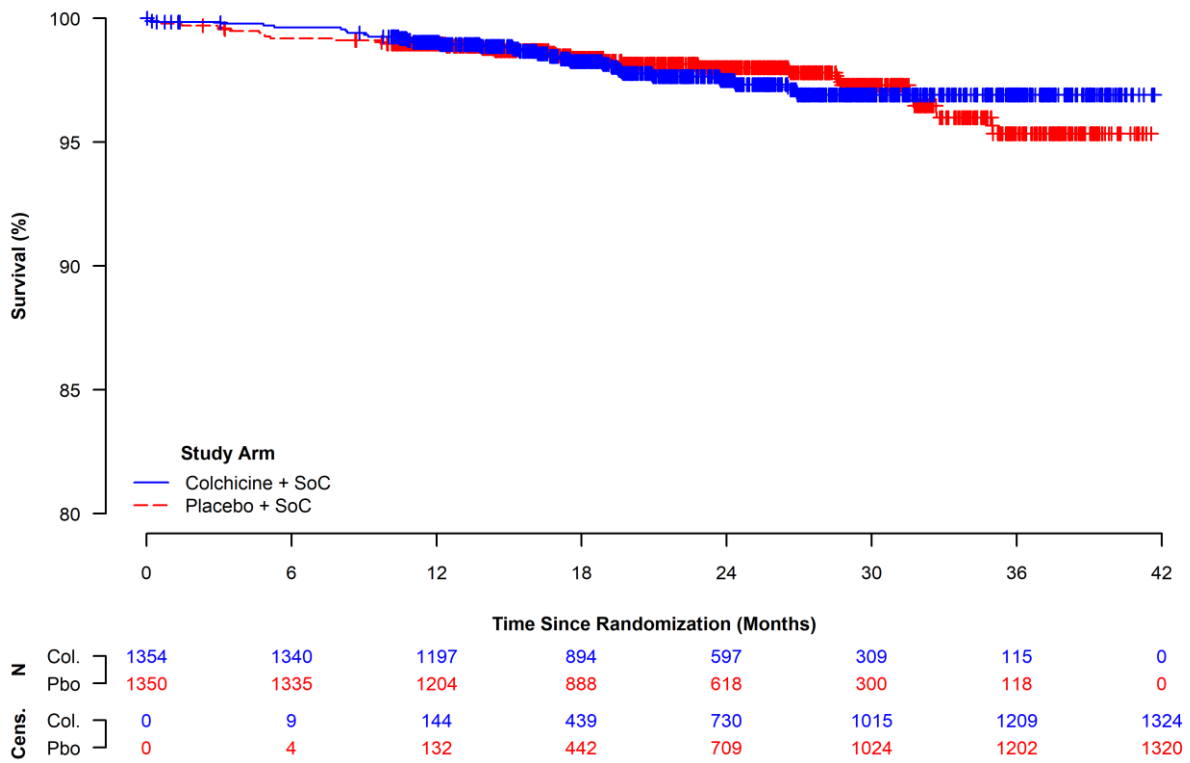
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Region</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.9060</b>					
<b>Europe</b>	13/1,012 (1.3)	14/1,029 (1.4)	0.944 [0.446, 1.999] 0.8806	0.943 [0.441, 2.017] 0.8806	-0.076 [-1.067, 0.915] 0.8806
<b>Non-Europe</b>	30/1,354 (2.2)	30/1,350 (2.2)	0.997 [0.604, 1.645] 0.9908	0.997 [0.598, 1.663] 0.9908	-0.007 [-1.117, 1.104] 0.9908
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 30:** Time to Total Mortality, Subgrouped by Region (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.8786</b>							
<b>Europe</b>	13/1,012 (1.3)	NE [NE, NE]	2.1 [0.8, 3.5]	14/1,029 (1.4)	NE [NE, NE]	1.8 [0.8, 2.8]	0.935 [0.439, 1.989] 0.8614
<b>Non-Europe</b>	30/1,354 (2.2)	NE [NE, NE]	3.1 [1.9, 4.3]	30/1,350 (2.2)	NE [NE, NE]	4.7 [2.4, 6.9]	1.002 [0.604, 1.662] 0.9939
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 18:** Kaplan-Meier Curves for Total Mortality, Within European Countries (ITT Population).



**Figure 19:** Kaplan-Meier Curves for Total Mortality, Within Non-European Countries (ITT Population).

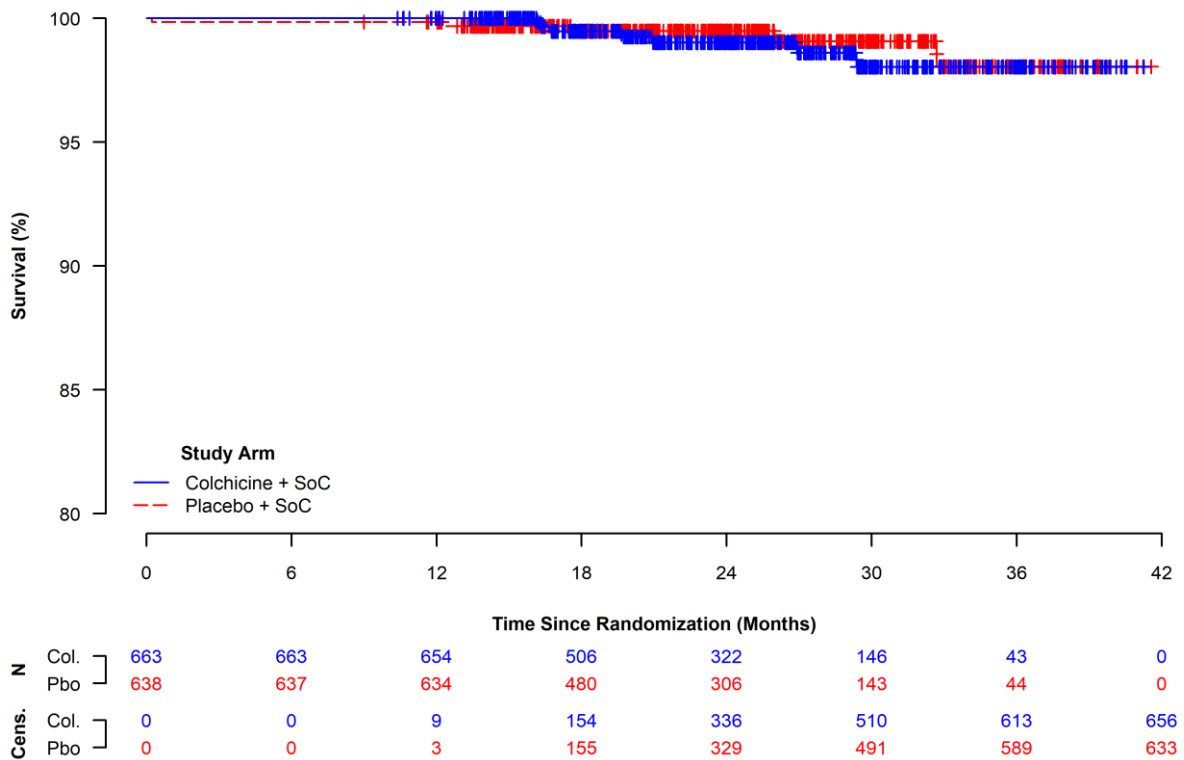
#### 4.4.1.1.5 Subgrouped by White Blood Cell Count

**Table 31:** Proportion of Patients with Total Mortality, Subgrouped by White Blood Cell Count (ITT Population).

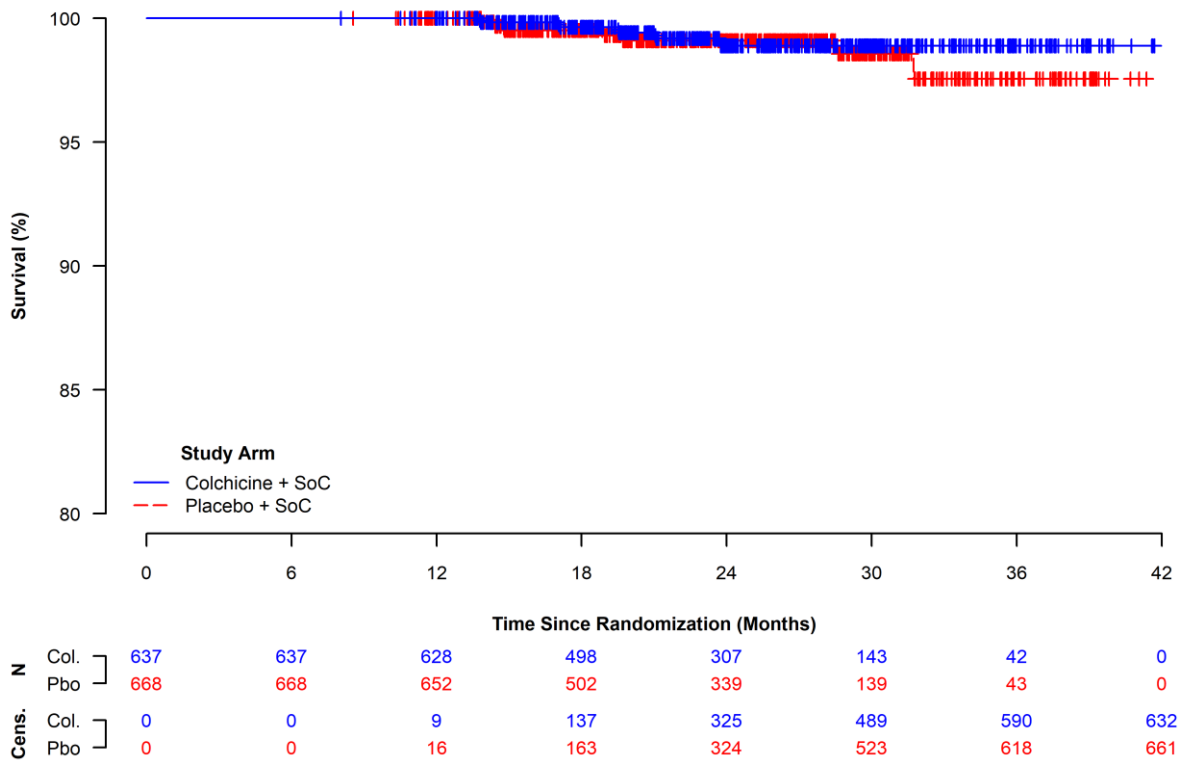
Subgroup	Colchicine + SoC (N = 1,300)	Placebo + SoC (N = 1,306)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4736</b>					
< 8.66 10 <sup>3</sup> /μL	7/663 (1.1)	5/638 (0.8)	1.347 [0.430, 4.223] 0.6091	1.351 [0.427, 4.279] 0.6091	0.272 [-0.764, 1.308] 0.6067
≥ 8.66 10 <sup>3</sup> /μL	5/637 (0.8)	7/668 (1.0)	0.749 [0.239, 2.348] 0.6201	0.747 [0.236, 2.366] 0.6200	-0.263 [-1.295, 0.769] 0.6176
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 32: Time to Total Mortality, Subgrouped by White Blood Cell Count (ITT Population).**

Subgroup	Colchicine + SoC (N = 1,300)			Placebo + SoC (N = 1,306)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.4659</b>							
< 8.66 10 <sup>3</sup> /μL	7/663 (1.1)	NE [NE, NE]	2.0 [0.3, 3.6]	5/638 (0.8)	NE [NE, NE]	2.0 [0.0, 4.2]	1.345 [0.427, 4.238] 0.6130
≥ 8.66 10 <sup>3</sup> /μL	5/637 (0.8)	NE [NE, NE]	1.1 [0.1, 2.1]	7/668 (1.0)	NE [NE, NE]	2.4 [0.1, 4.8]	0.737 [0.234, 2.323] 0.6028
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 20:** Kaplan-Meier Curves for Total Mortality, Within the Lower White Blood Cell Count Subgroup (ITT Population).



**Figure 21:** Kaplan-Meier Curves for Total Mortality, Within the Upper White Blood Cell Count Subgroup (ITT Population).

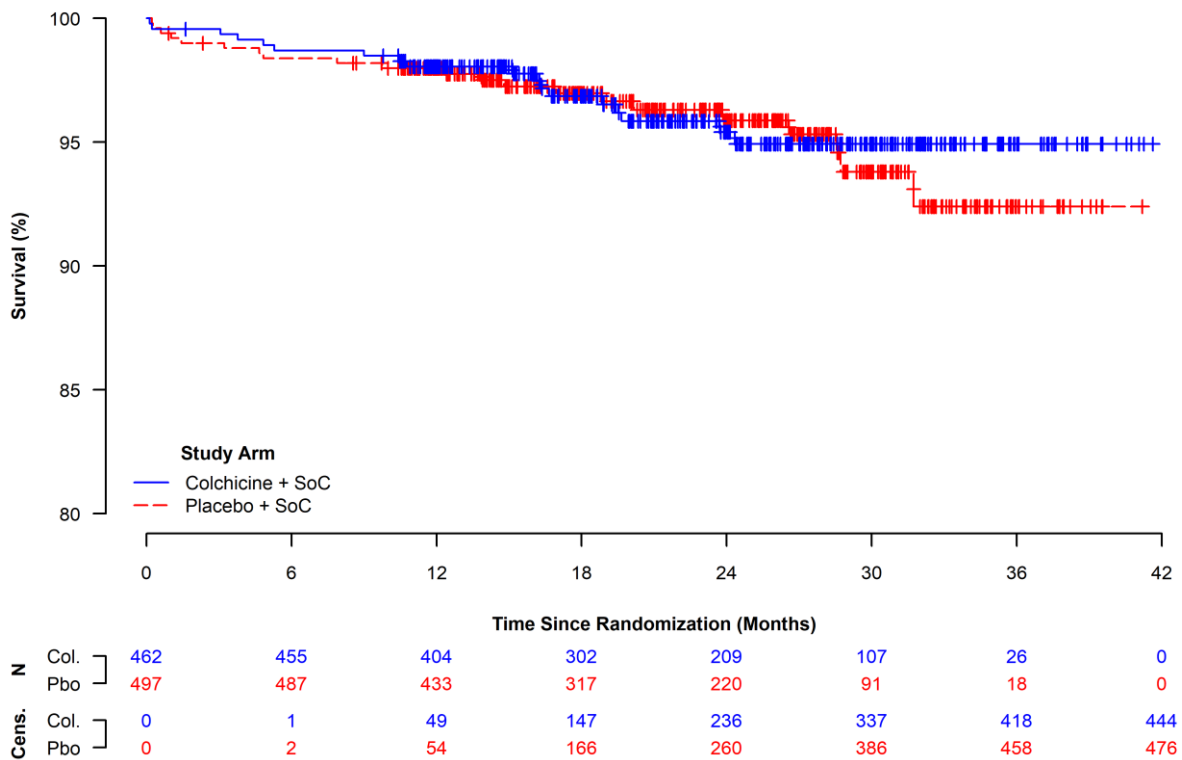
#### 4.4.1.1.6 Subgrouped by Diabetes Status

**Table 33:** Proportion of Patients with Total Mortality, Subgrouped by Diabetes Status (ITT Population).

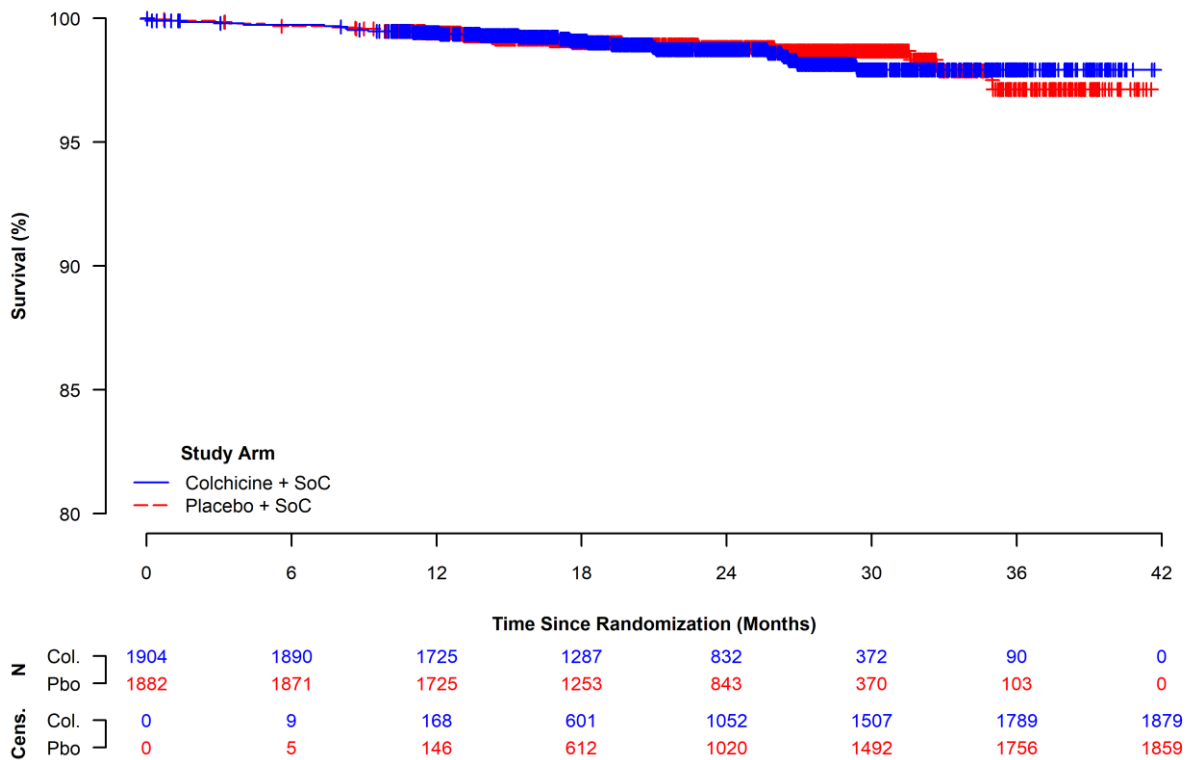
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7196</b>					
<b>Yes</b>	18/462 (3.9)	21/497 (4.2)	0.922 [0.498, 1.708] 0.7965	0.919 [0.483, 1.747] 0.7965	-0.329 [-2.827, 2.169] 0.7962
<b>No</b>	25/1,904 (1.3)	23/1,882 (1.2)	1.074 [0.612, 1.886] 0.8026	1.075 [0.608, 1.901] 0.8026	0.091 [-0.622, 0.804] 0.8025
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 34: Time to Total Mortality, Subgrouped by Diabetes Status (ITT Population).**

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.6800</b>							
<b>Yes</b>	18/462 (3.9)	NE [NE, NE]	5.1 [2.7, 7.4]	21/497 (4.2)	NE [NE, NE]	7.6 [3.5, 11.6]	0.906 [0.483, 1.701] 0.7598
<b>No</b>	25/1,904 (1.3)	NE [NE, NE]	2.1 [1.2, 3.0]	23/1,882 (1.2)	NE [NE, NE]	2.9 [0.9, 4.8]	1.079 [0.612, 1.900] 0.7930
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 22:** Kaplan-Meier Curves for Total Mortality, Within the Diabetic Subgroup (ITT Population).



**Figure 23:** Kaplan-Meier Curves for Total Mortality, Within the Non-Diabetic Subgroup (ITT Population).

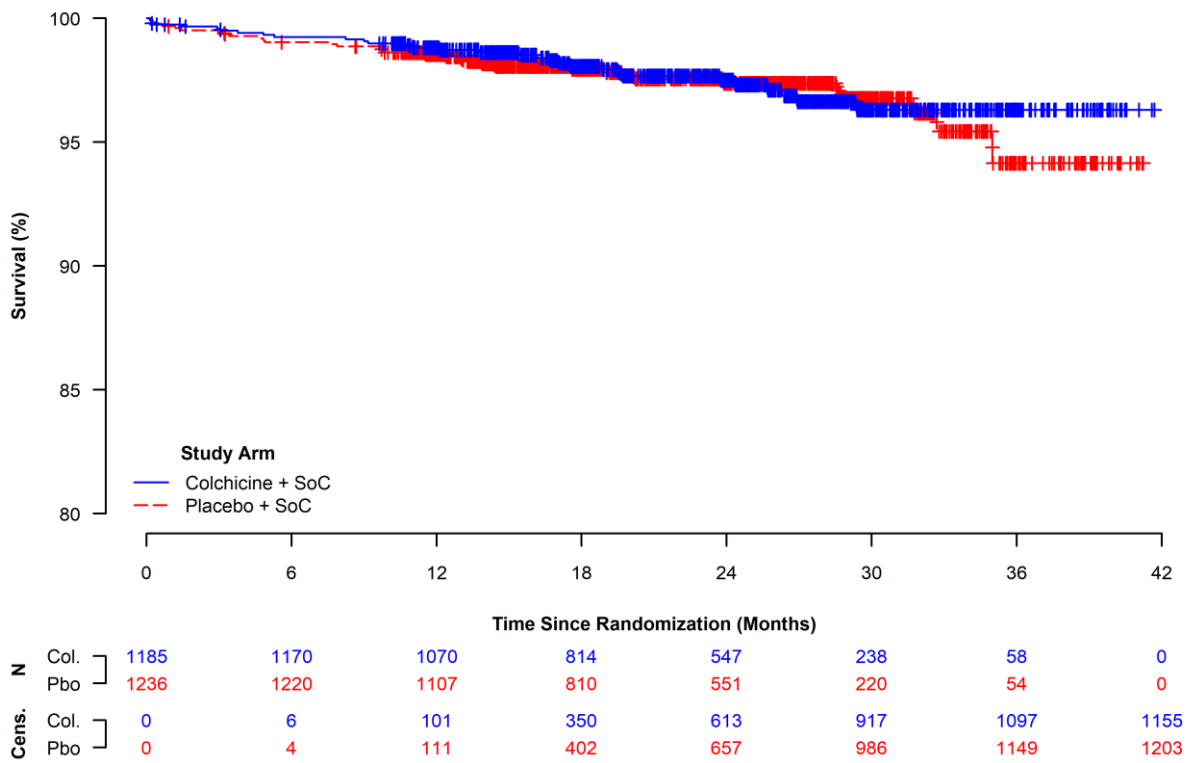
#### 4.4.1.1.7 Subgrouped by Hypertension Status

**Table 35:** Proportion of Patients with Total Mortality, Subgrouped by Hypertension Status (ITT Population).

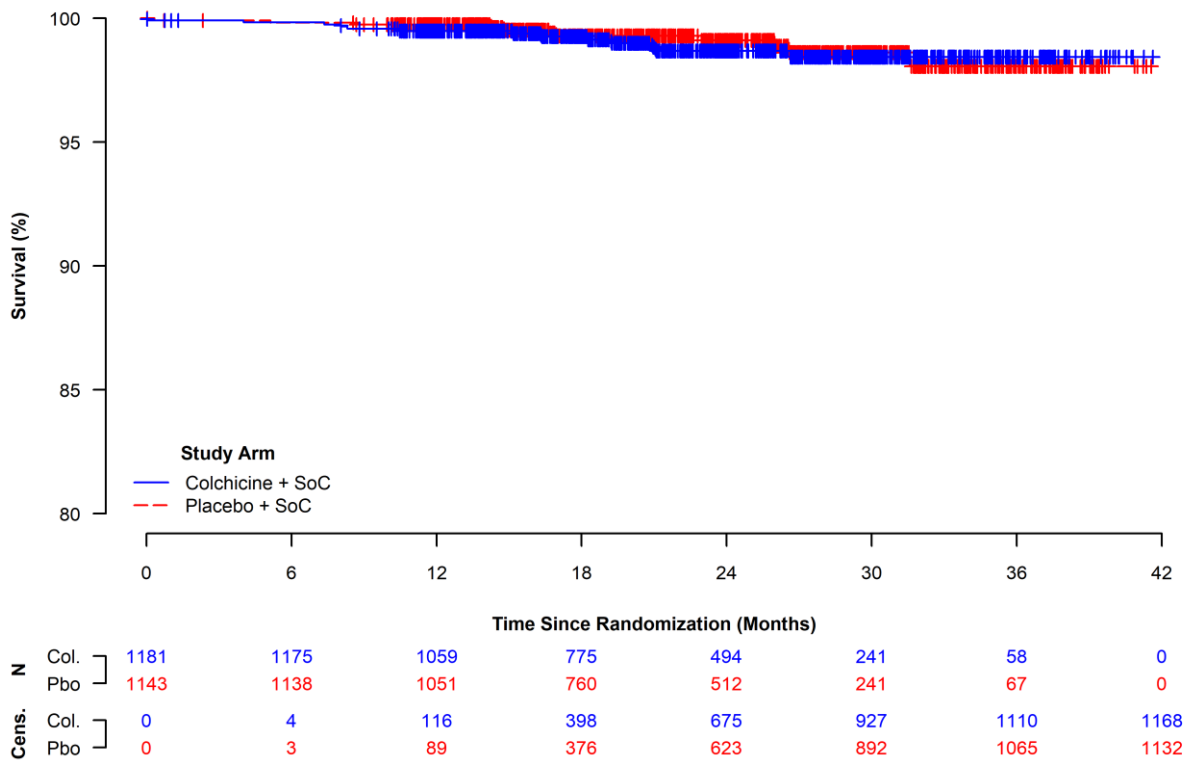
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.6942</b>					
<b>Yes</b>	30/1,185 (2.5)	33/1,236 (2.7)	0.948 [0.582, 1.545] 0.8309	0.947 [0.574, 1.563] 0.8309	-0.138 [-1.406, 1.130] 0.8308
<b>No</b>	13/1,181 (1.1)	11/1,143 (1.0)	1.144 [0.515, 2.543] 0.7417	1.145 [0.511, 2.567] 0.7417	0.138 [-0.683, 0.960] 0.7412
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 36:** Time to Total Mortality, Subgrouped by Hypertension Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.6340</b>							
<b>Yes</b>	30/1,185 (2.5)	NE [NE, NE]	3.7 [2.2, 5.1]	33/1,236 (2.7)	NE [NE, NE]	5.9 [2.4, 9.1]	0.929 [0.567, 1.523] 0.7705
<b>No</b>	13/1,181 (1.1)	NE [NE, NE]	1.6 [0.7, 2.5]	11/1,143 (1.0)	NE [NE, NE]	1.9 [0.5, 3.4]	1.171 [0.525, 2.614] 0.7002
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 24:** Kaplan-Meier Curves for Total Mortality, Within the Hypertensive Subgroup (ITT Population).



**Figure 25:** Kaplan-Meier Curves for Total Mortality, Within the Normotensive Subgroup (ITT Population).

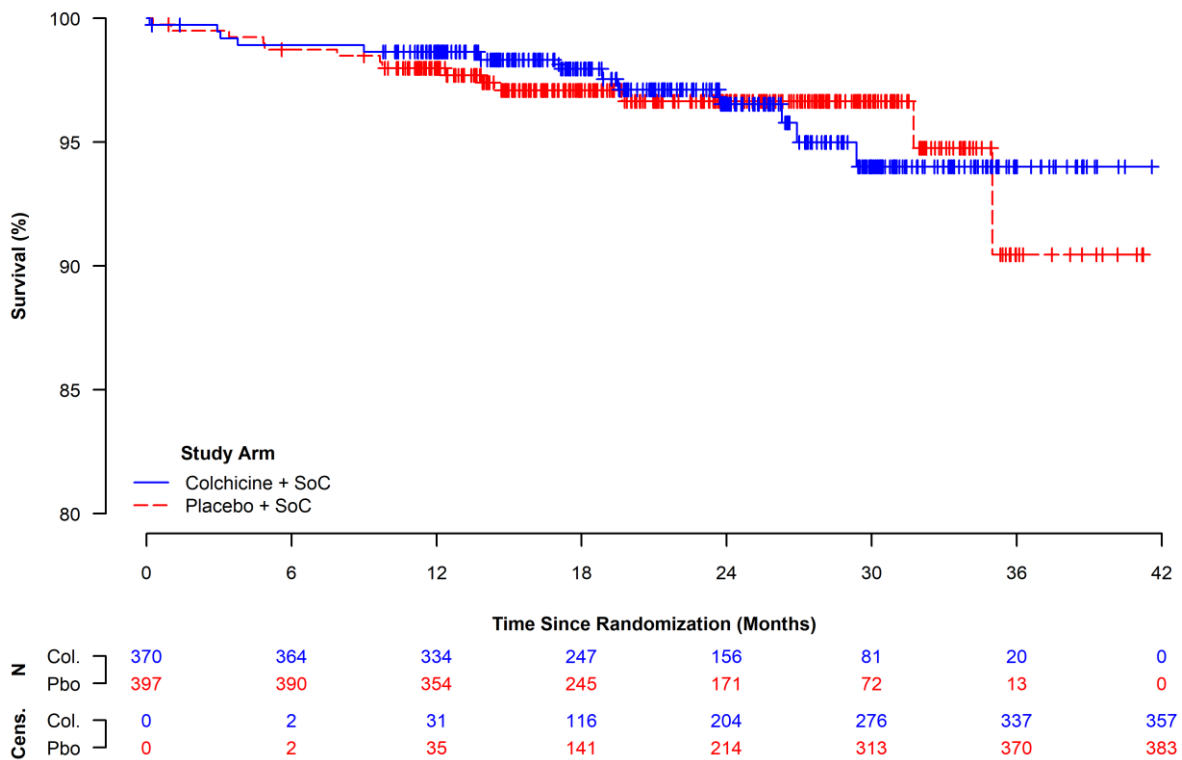
#### 4.4.1.1.8 Subgrouped by History of Myocardial Infarction

**Table 37:** Proportion of Patients with Total Mortality, Subgrouped by History of Myocardial Infarction (ITT Population).

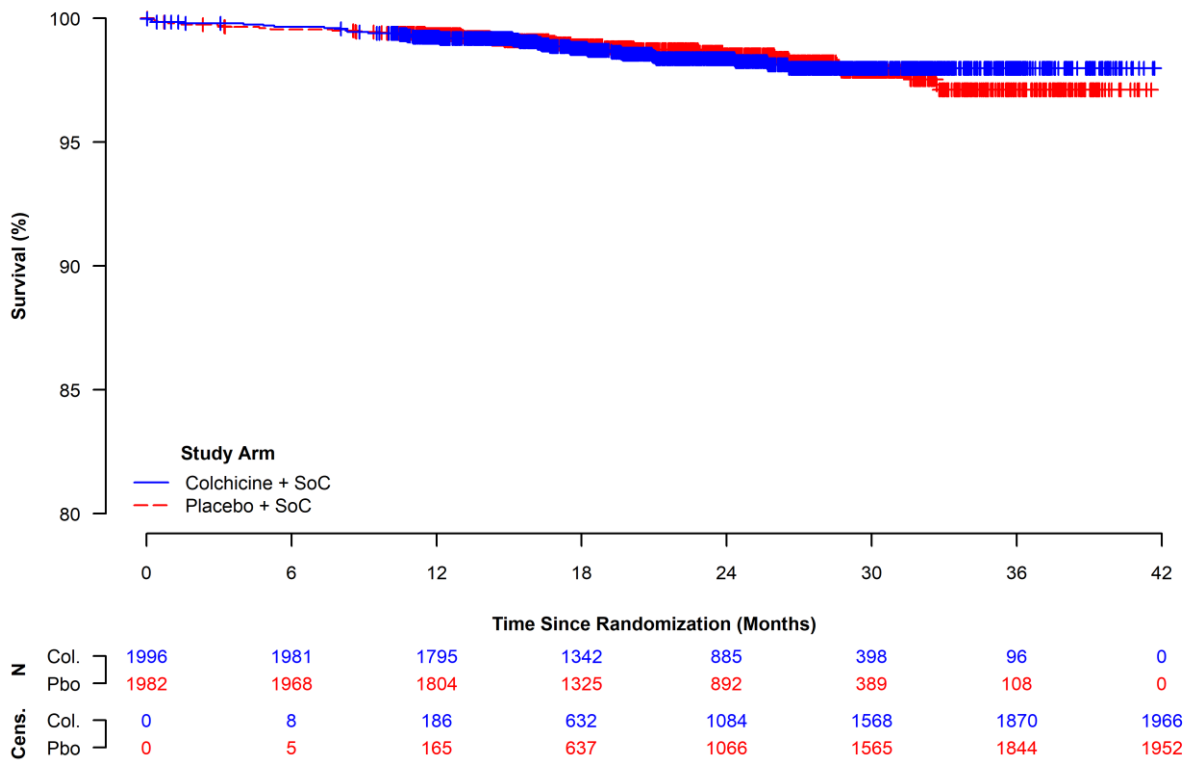
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of MI</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.9943</b>					
<b>Yes</b>	13/370 (3.5)	14/397 (3.5)	0.996 [0.475, 2.091] 0.9923	0.996 [0.462, 2.148] 0.9923	-0.013 [-2.623, 2.597] 0.9922
<b>No</b>	30/1,996 (1.5)	30/1,982 (1.5)	0.993 [0.601, 1.641] 0.9781	0.993 [0.596, 1.653] 0.9781	-0.011 [-0.768, 0.747] 0.9781
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 38:** Time to Total Mortality, Subgrouped by History of Myocardial Infarction (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of MI</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.9431</b>							
<b>Yes</b>	13/370 (3.5)	NE [NE, NE]	6.0 [2.4, 9.5]	14/397 (3.5)	NE [NE, NE]	9.6 [0.0, 18.2]	0.957 [0.450, 2.038] 0.9100
<b>No</b>	30/1,996 (1.5)	NE [NE, NE]	2.0 [1.3, 2.8]	30/1,982 (1.5)	NE [NE, NE]	2.9 [1.5, 4.2]	0.997 [0.601, 1.655] 0.9922
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 26:** Kaplan-Meier Curves for Total Mortality, Within the Subgroup With History of Myocardial Infarction (ITT Population).



**Figure 27:** Kaplan-Meier Curves for Total Mortality, Within the Subgroup Without History of Myocardial Infarction (ITT Population).

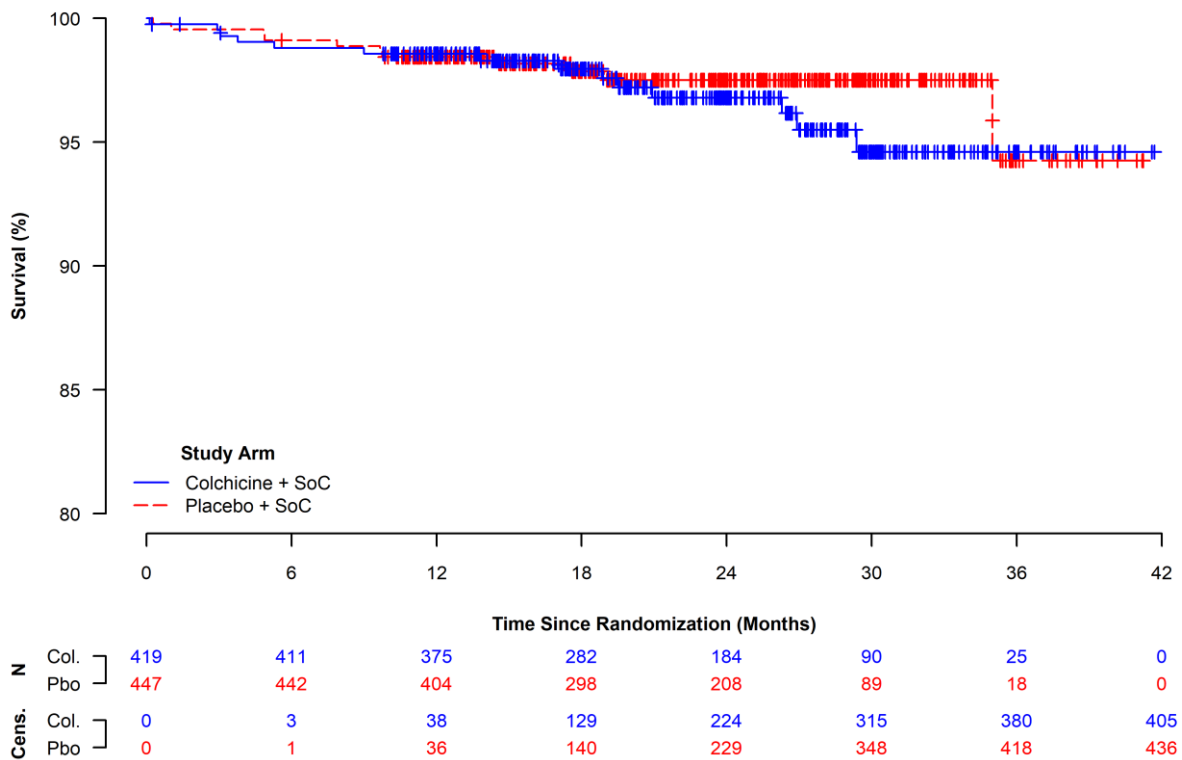
#### 4.4.1.1.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 39:** Proportion of Patients with Total Mortality, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

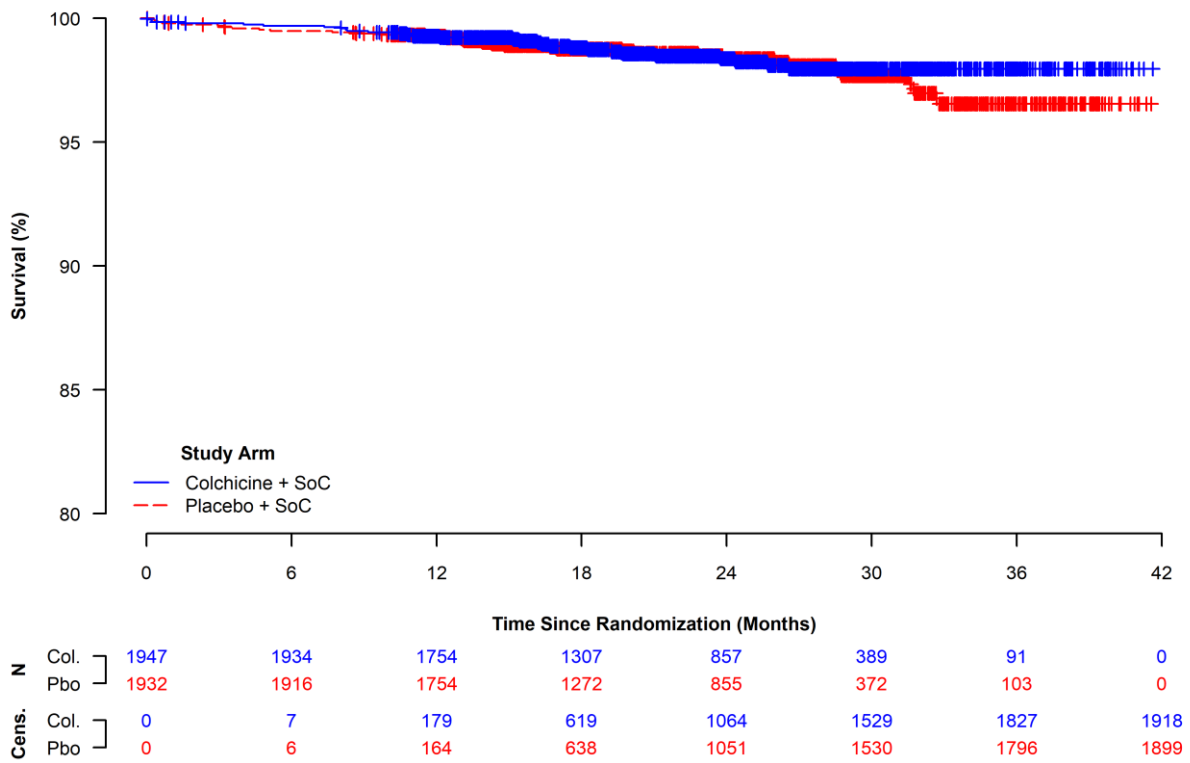
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.3452</b>					
<b>Yes</b>	14/419 (3.3)	11/447 (2.5)	1.358 [0.623, 2.957] 0.4412	1.370 [0.615, 3.053] 0.4411	0.880 [-1.361, 3.122] 0.4414
<b>No</b>	29/1,947 (1.5)	33/1,932 (1.7)	0.872 [0.532, 1.430] 0.5876	0.870 [0.526, 1.439] 0.5875	-0.219 [-1.008, 0.571] 0.5873
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 40:** Time to Total Mortality, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.3400</b>							
<b>Yes</b>	14/419 (3.3)	NE [NE, NE]	5.4 [2.2, 8.5]	11/447 (2.5)	NE [NE, NE]	5.8 [0.0, 12.0]	1.356 [0.616, 2.988] 0.4496
<b>No</b>	29/1,947 (1.5)	NE [NE, NE]	2.0 [1.3, 2.8]	33/1,932 (1.7)	NE [NE, NE]	3.5 [1.9, 5.0]	0.869 [0.528, 1.432] 0.5827
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 28:** Kaplan-Meier Curves for Total Mortality, Within the Subgroup With History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).



**Figure 29:** Kaplan-Meier Curves for Total Mortality, Within the Subgroup Without History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

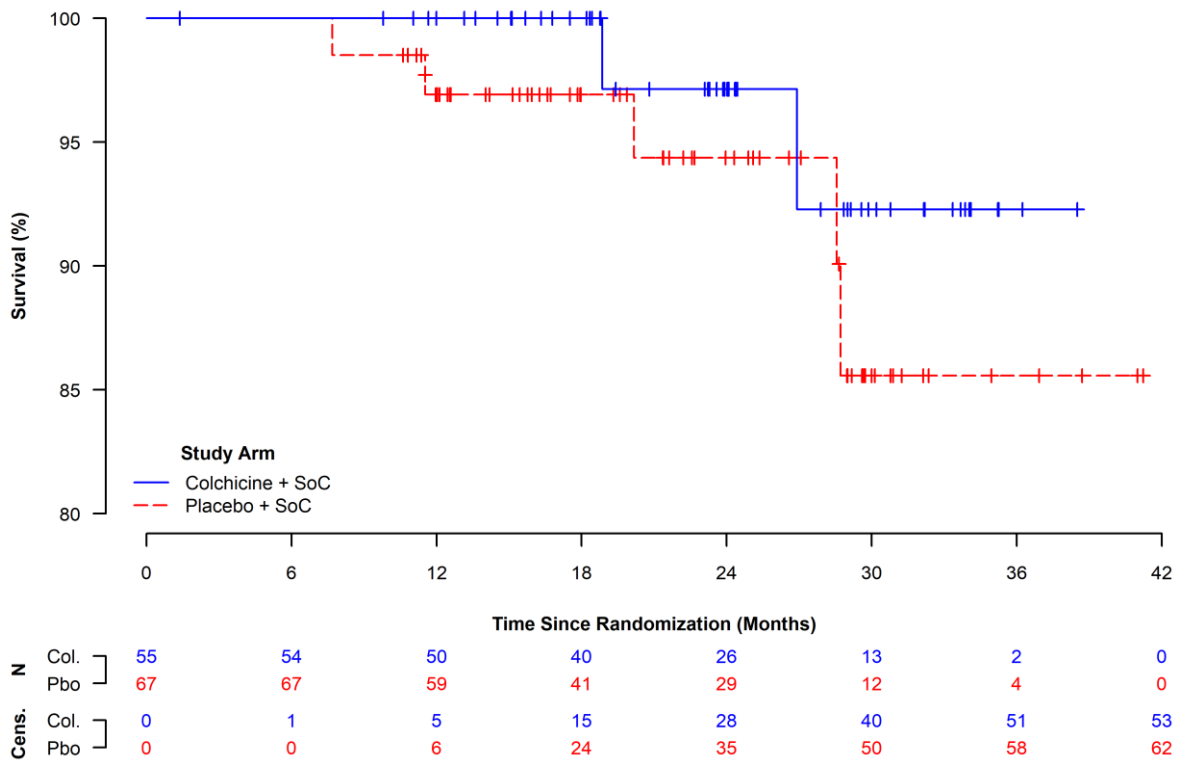
#### 4.4.1.1.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 41:** Proportion of Patients with Total Mortality, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

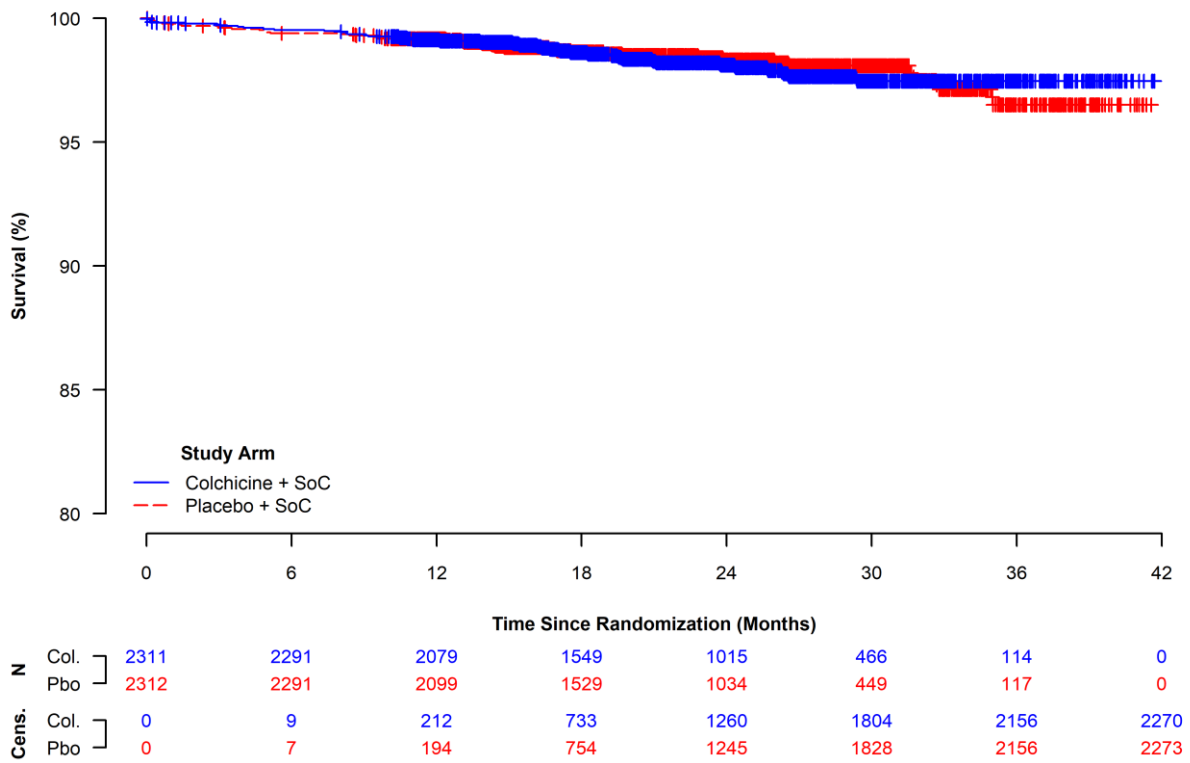
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.3423</b>					
<b>Yes</b>	2/55 (3.6)	5/67 (7.5)	0.487 [0.098, 2.415] 0.3787	0.468 [0.087, 2.511] 0.3757	-3.826 [-11.831, 4.178] 0.3488
<b>No</b>	41/2,311 (1.8)	39/2,312 (1.7)	1.052 [0.681, 1.624] 0.8200	1.053 [0.676, 1.638] 0.8200	0.087 [-0.665, 0.839] 0.8200
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 42:** Time to Total Mortality, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.3178</b>							
<b>Yes</b>	2/55 (3.6)	NE [NE, NE]	7.7 [0.0, 17.8]	5/67 (7.5)	NE [NE, NE]	14.4 [0.4, 26.5]	0.470 [0.091, 2.425] 0.3674
<b>No</b>	41/2,311 (1.8)	NE [NE, NE]	2.5 [1.7, 3.4]	39/2,312 (1.7)	NE [NE, NE]	3.5 [1.7, 5.2]	1.053 [0.679, 1.632] 0.8182
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 30:** Kaplan-Meier Curves for Total Mortality, Within the Subgroup With History of Stroke or Transient Ischaemic Attack (ITT Population).



**Figure 31:** Kaplan-Meier Curves for Total Mortality, Within the Subgroup Without History of Stroke or Transient Ischaemic Attack (ITT Population).

#### 4.4.1.2 Cardiovascular Death

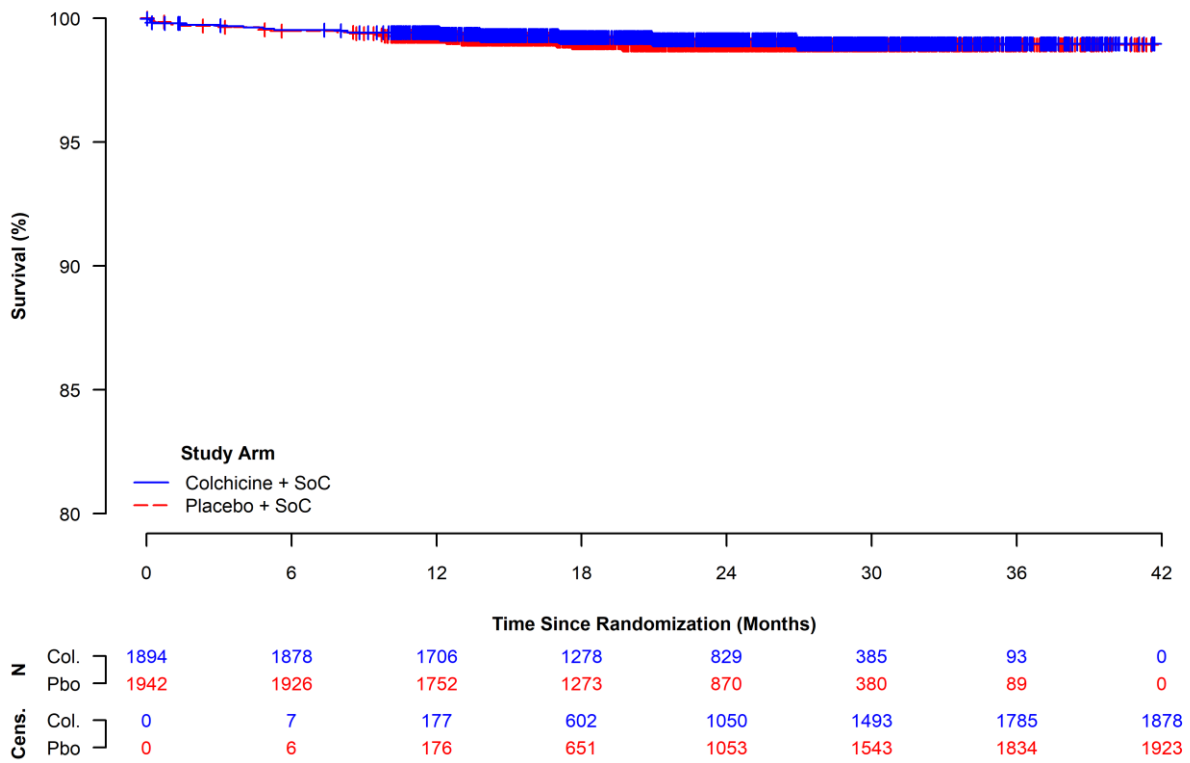
##### 4.4.1.2.1 Subgrouped by Sex

**Table 43:** Proportion of Patients with Cardiovascular Death, Subgrouped by Sex (ITT Population).

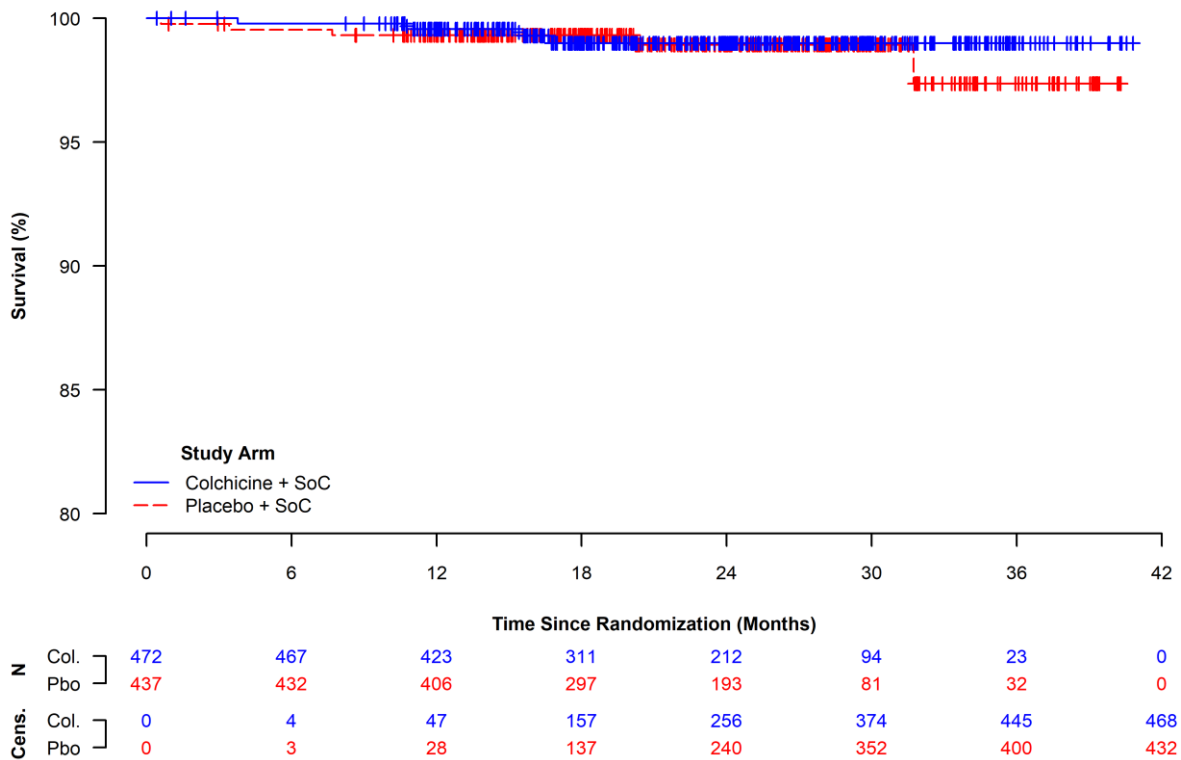
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Sex</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8372</b>					
<b>Male</b>	16/1,894 (0.8)	19/1,942 (1.0)	0.863 [0.445, 1.674] 0.6638	0.862 [0.442, 1.682] 0.6638	-0.134 [-0.735, 0.468] 0.6632
<b>Female</b>	4/472 (0.8)	5/437 (1.1)	0.741 [0.200, 2.741] 0.6529	0.738 [0.197, 2.768] 0.6529	-0.297 [-1.592, 0.999] 0.6535
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 44: Time to Cardiovascular Death, Subgrouped by Sex (ITT Population).**

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Sex</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.8506</b>							
<b>Male</b>	16/1,894 (0.8)	NE [NE, NE]	1.0 [0.5, 1.6]	19/1,942 (1.0)	NE [NE, NE]	1.1 [0.6, 1.6]	0.862 [0.443, 1.677] 0.6621
<b>Female</b>	4/472 (0.8)	NE [NE, NE]	1.0 [0.0, 2.0]	5/437 (1.1)	NE [NE, NE]	2.6 [0.0, 5.8]	0.752 [0.202, 2.800] 0.6706
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 32:** Kaplan-Meier Curves for Cardiovascular Death, Within the Male Sex Subgroup (ITT Population).



**Figure 33:** Kaplan-Meier Curves for Cardiovascular Death, Within the Female Sex Subgroup (ITT Population).

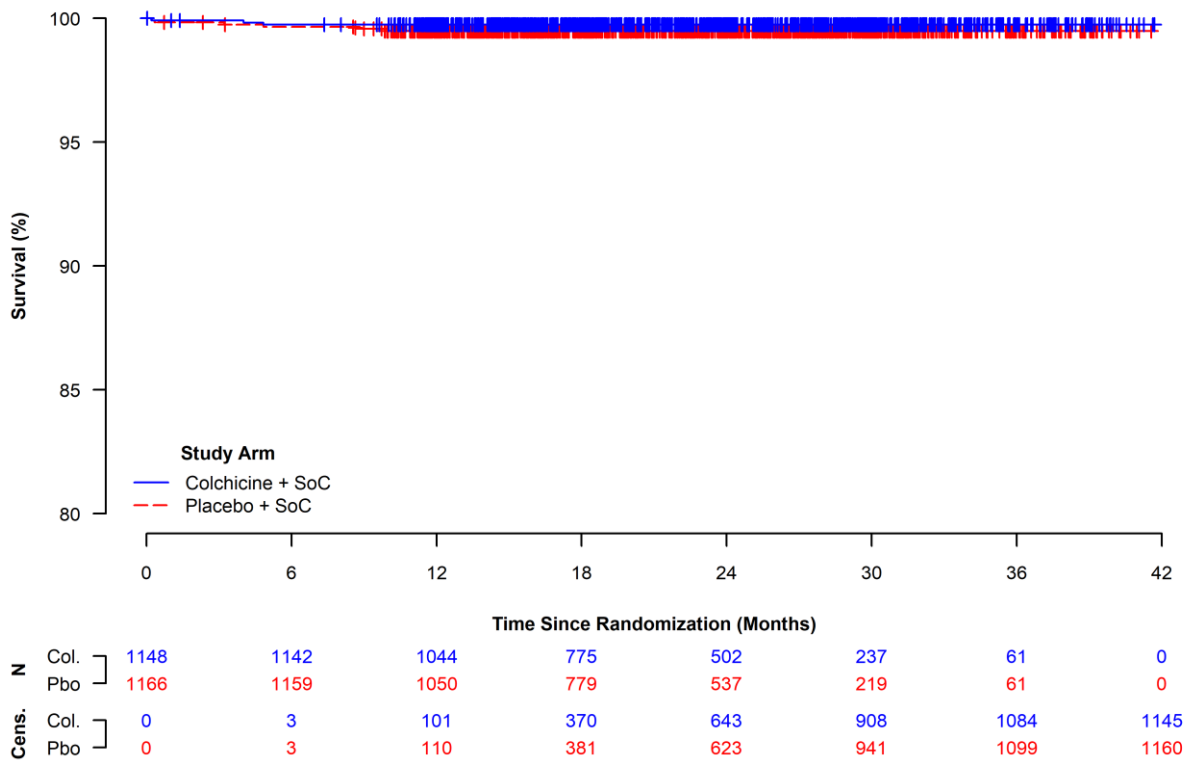
#### 4.4.1.2.2 Subgrouped by Age Group

**Table 45:** Proportion of Patients with Cardiovascular Death, Subgrouped by Age Group (ITT Population).

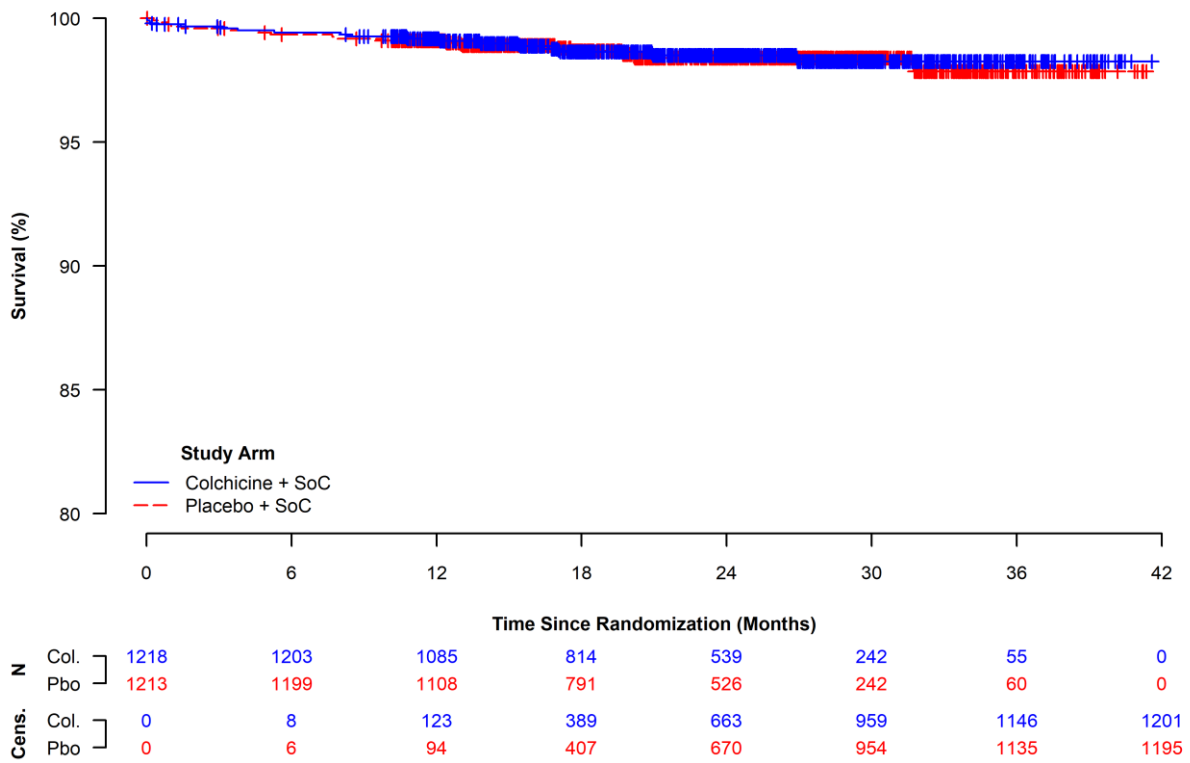
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Age</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4232</b>					
<b>&lt; 60 Years</b>	3/1,148 (0.3)	6/1,166 (0.5)	0.508 [0.127, 2.026] 0.3371	0.507 [0.126, 2.030] 0.3370	-0.253 [-0.759, 0.253] 0.3265
<b>≥ 60 Years</b>	17/1,218 (1.4)	18/1,213 (1.5)	0.941 [0.487, 1.816] 0.8552	0.940 [0.482, 1.832] 0.8552	-0.088 [-1.035, 0.859] 0.8552
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 46: Time to Cardiovascular Death, Subgrouped by Age Group (ITT Population).**

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.4160</b>							
< 60 Years	3/1,148 (0.3)	NE [NE, NE]	0.3 [0.0, 0.6]	6/1,166 (0.5)	NE [NE, NE]	0.5 [0.1, 0.9]	0.508 [0.127, 2.030] 0.3378
≥ 60 Years	17/1,218 (1.4)	NE [NE, NE]	1.7 [0.9, 2.6]	18/1,213 (1.5)	NE [NE, NE]	2.1 [0.8, 3.5]	0.946 [0.488, 1.836] 0.8698
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 34:** Kaplan-Meier Curves for Cardiovascular Death, Within the Age 59 Years or Younger Subgroup (ITT Population).



**Figure 35:** Kaplan-Meier Curves for Cardiovascular Death, Within the Age 60 Years or Older Subgroup (ITT Population).

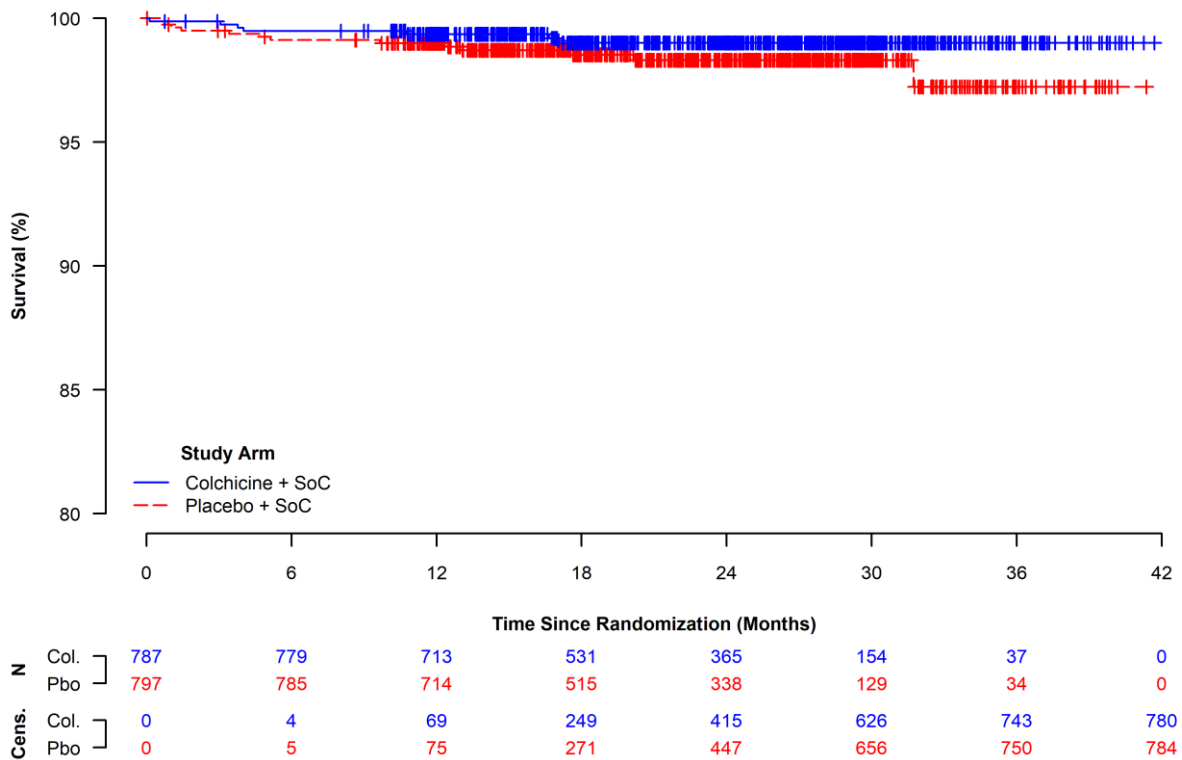
#### 4.4.1.2.3 Subgrouped by Smoking Status

**Table 47:** Proportion of Patients with Cardiovascular Death, Subgrouped by Smoking Status (ITT Population).

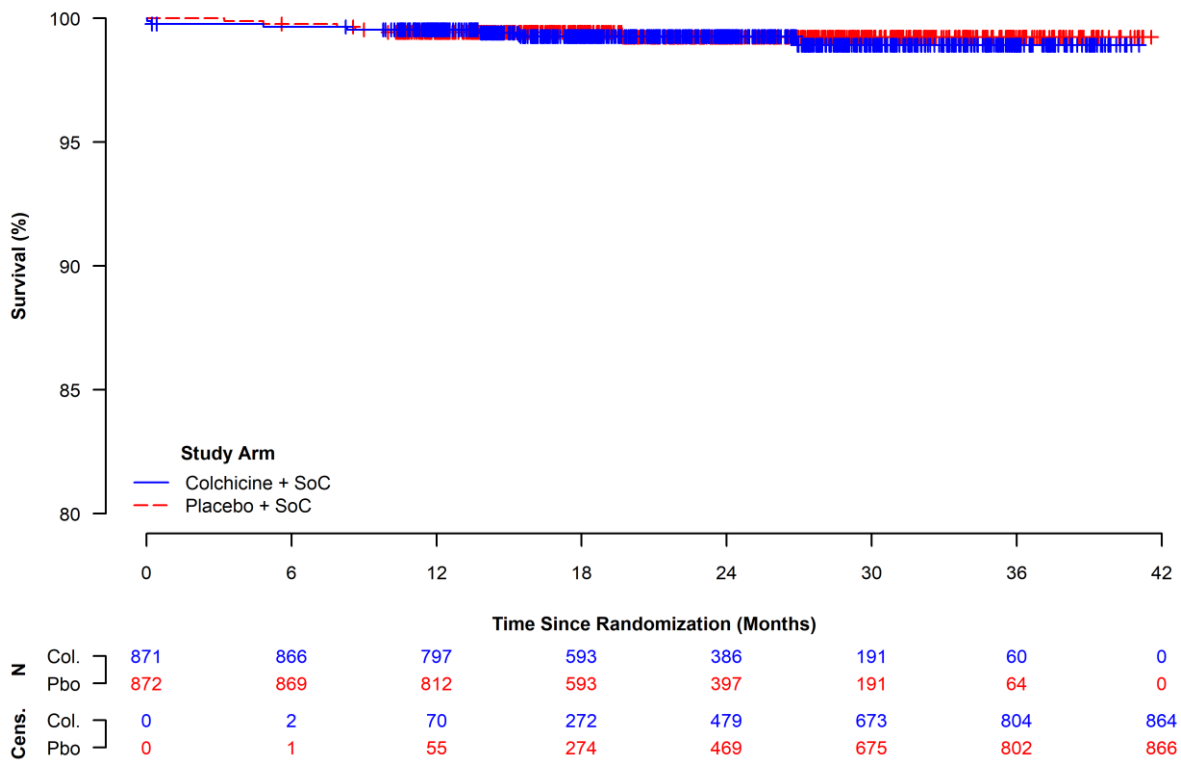
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,377)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Smoking Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4489</b>					
<b>Non</b>	7/787 (0.9)	13/797 (1.6)	0.545 [0.219, 1.360] 0.1933	0.541 [0.215, 1.364] 0.1929	-0.742 [-1.839, 0.355] 0.1852
<b>Ex</b>	7/871 (0.8)	6/872 (0.7)	1.168 [0.394, 3.461] 0.7793	1.169 [0.391, 3.494] 0.7793	0.116 [-0.692, 0.923] 0.7791
<b>Current</b>	6/708 (0.8)	5/708 (0.7)	1.200 [0.368, 3.914] 0.7625	1.202 [0.365, 3.956] 0.7624	0.141 [-0.773, 1.056] 0.7621
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 48:** Time to Cardiovascular Death, Subgrouped by Smoking Status (ITT Population).

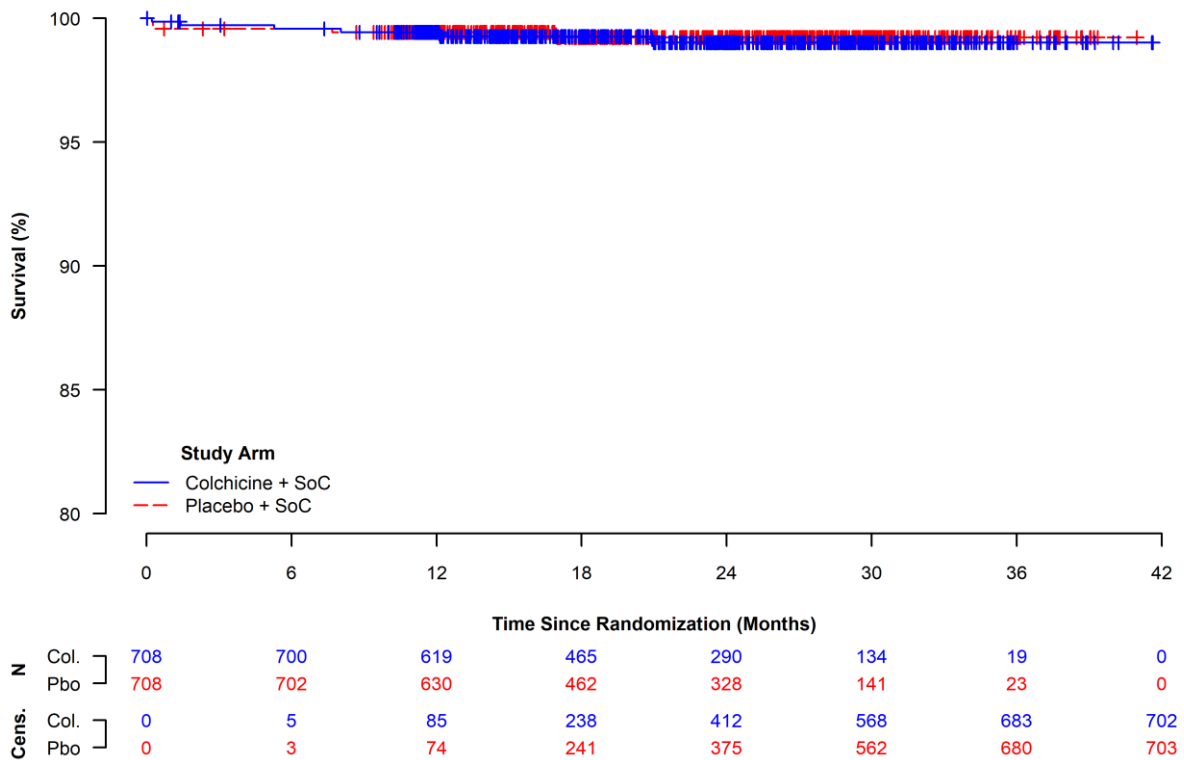
Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,377)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Smoking Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.4353</b>							
<b>Non</b>	7/787 (0.9)	NE [NE, NE]	1.0 [0.2, 1.7]	13/797 (1.6)	NE [NE, NE]	2.8 [0.4, 5.1]	0.537 [0.214, 1.347] 0.1855
<b>Ex</b>	7/871 (0.8)	NE [NE, NE]	1.1 [0.2, 2.0]	6/872 (0.7)	NE [NE, NE]	0.8 [0.1, 1.4]	1.178 [0.396, 3.506] 0.7682
<b>Current</b>	6/708 (0.8)	NE [NE, NE]	1.0 [0.2, 1.8]	5/708 (0.7)	NE [NE, NE]	0.8 [0.1, 1.4]	1.205 [0.368, 3.949] 0.7578
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 36:** Kaplan-Meier Curves for Cardiovascular Death, Within the Non-Smoker Subgroup (ITT Population).



**Figure 37:** Kaplan-Meier Curves for Cardiovascular Death, Within the Ex-Smoker Subgroup (ITT Population).



**Figure 38:** Kaplan-Meier Curves for Cardiovascular Death, Within the Current Smoker Subgroup (ITT Population).

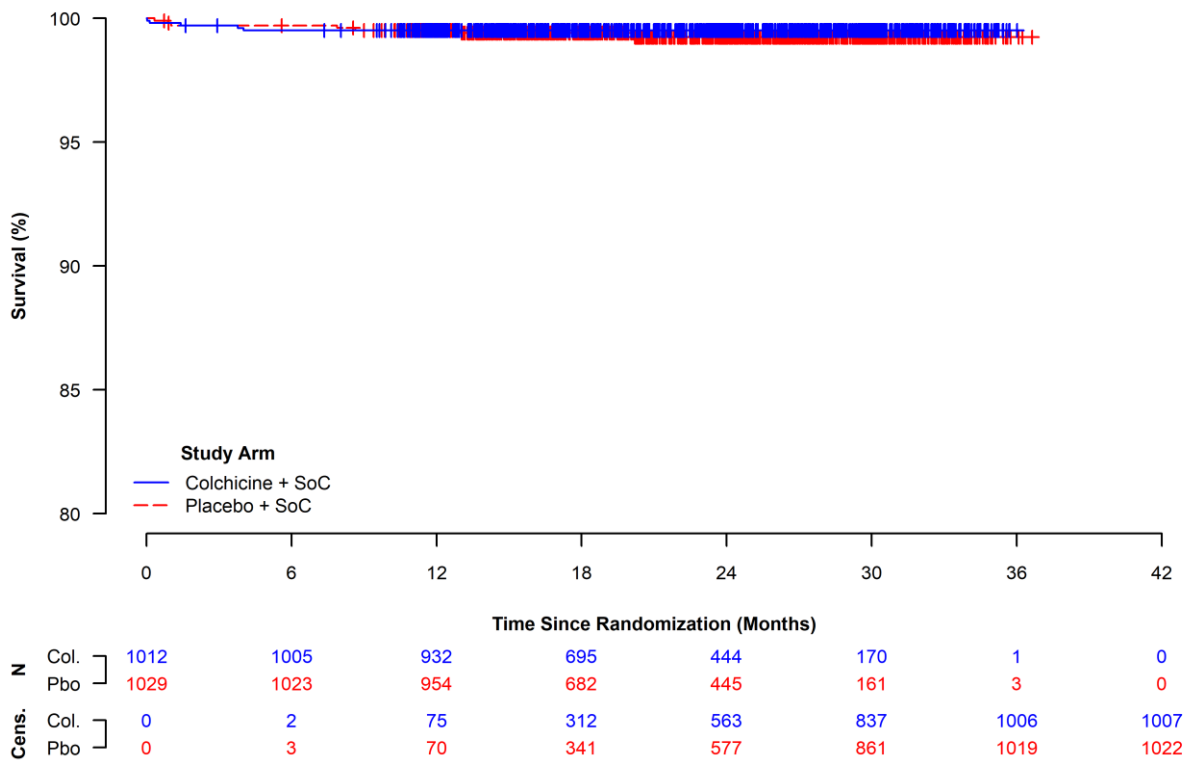
#### 4.4.1.2.4 Subgrouped by Region

**Table 49:** Proportion of Patients with Cardiovascular Death, Subgrouped by Region (ITT Population).

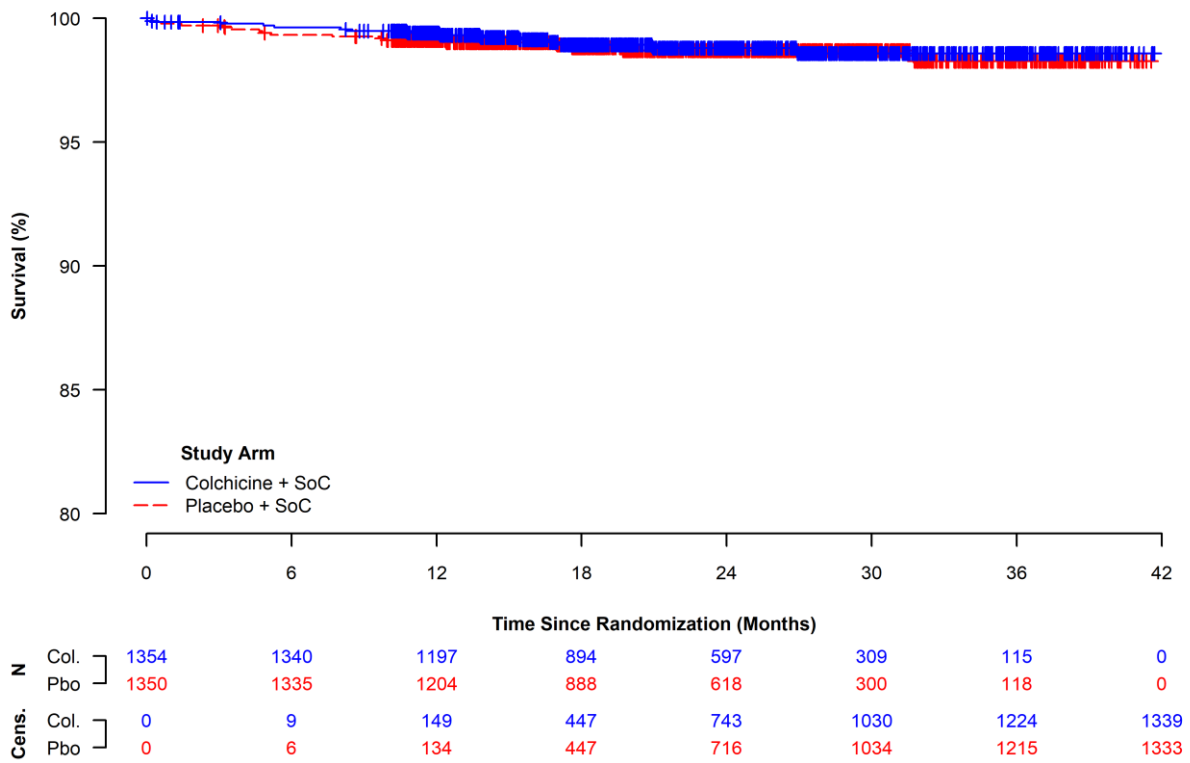
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Region</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7793</b>					
<b>Europe</b>	5/1,012 (0.5)	7/1,029 (0.7)	0.726 [0.231, 2.281] 0.5839	0.725 [0.229, 2.292] 0.5838	-0.186 [-0.849, 0.476] 0.5817
<b>Non-Europe</b>	15/1,354 (1.1)	17/1,350 (1.3)	0.880 [0.441, 1.754] 0.7160	0.878 [0.437, 1.766] 0.7160	-0.151 [-0.967, 0.664] 0.7158
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 50:** Time to Cardiovascular Death, Subgrouped by Region (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.7712</b>							
<b>Europe</b>	5/1,012 (0.5)	NE [NE, NE]	0.5 [0.1, 0.9]	7/1,029 (0.7)	NE [NE, NE]	0.8 [0.2, 1.3]	0.726 [0.230, 2.287] 0.5841
<b>Non-Europe</b>	15/1,354 (1.1)	NE [NE, NE]	1.4 [0.7, 2.2]	17/1,350 (1.3)	NE [NE, NE]	1.7 [0.7, 2.8]	0.883 [0.441, 1.769] 0.7259
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 39:** Kaplan-Meier Curves for Cardiovascular Death, Within European Countries (ITT Population).



**Figure 40:** Kaplan-Meier Curves for Cardiovascular Death, Within Non-European Countries (ITT Population).

#### **4.4.1.2.5 Subgrouped by White Blood Cell Count**

The requirements for performing subgroup analyses were not met, i.e., at least one subgroup contained fewer than ten patients and/or, in the case of binary data and time-to-event analyses, no subgroup had at least ten events.

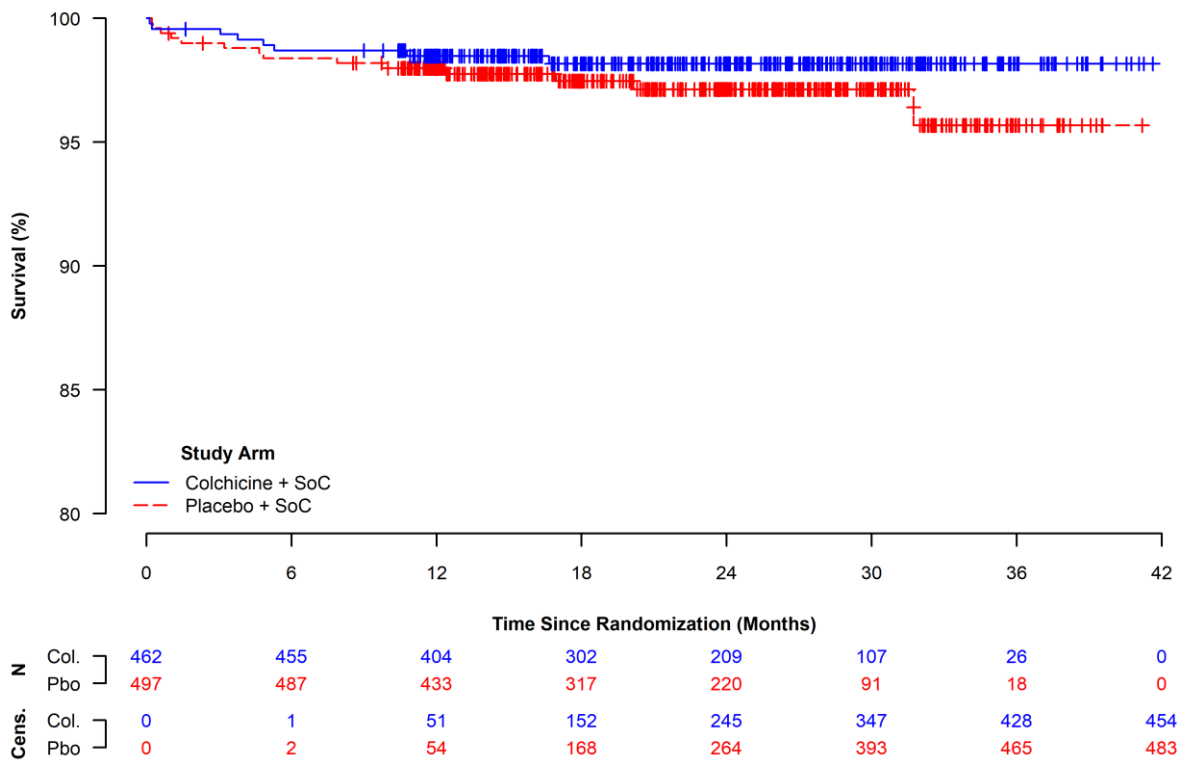
#### 4.4.1.2.6 Subgrouped by Diabetes Status

**Table 51:** Proportion of Patients with Cardiovascular Death, Subgrouped by Diabetes Status (ITT Population).

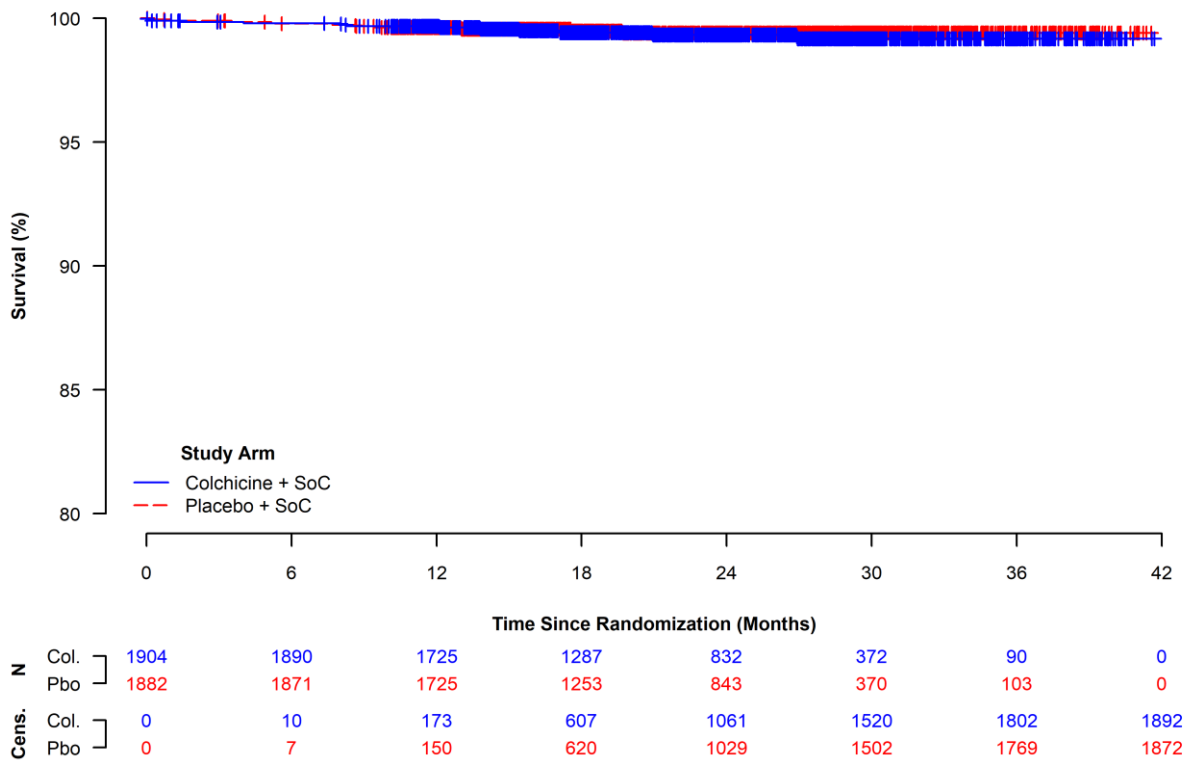
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2769</b>					
<b>Yes</b>	8/462 (1.7)	14/497 (2.8)	0.615 [0.260, 1.452] 0.2671	0.608 [0.253, 1.463] 0.2666	-1.085 [-2.964, 0.794] 0.2576
<b>No</b>	12/1,904 (0.6)	10/1,882 (0.5)	1.186 [0.514, 2.739] 0.6893	1.187 [0.512, 2.755] 0.6893	0.099 [-0.385, 0.583] 0.6888
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 52: Time to Cardiovascular Death, Subgrouped by Diabetes Status (ITT Population).**

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.2736</b>							
<b>Yes</b>	8/462 (1.7)	NE [NE, NE]	1.8 [0.6, 3.1]	14/497 (2.8)	NE [NE, NE]	4.3 [1.1, 7.5]	0.608 [0.255, 1.450] 0.2618
<b>No</b>	12/1,904 (0.6)	NE [NE, NE]	0.8 [0.3, 1.3]	10/1,882 (0.5)	NE [NE, NE]	0.6 [0.2, 1.0]	1.189 [0.514, 2.752] 0.6857
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 41:** Kaplan-Meier Curves for Cardiovascular Death, Within the Diabetic Subgroup (ITT Population).



**Figure 42:** Kaplan-Meier Curves for Cardiovascular Death, Within the Non-Diabetic Subgroup (ITT Population).

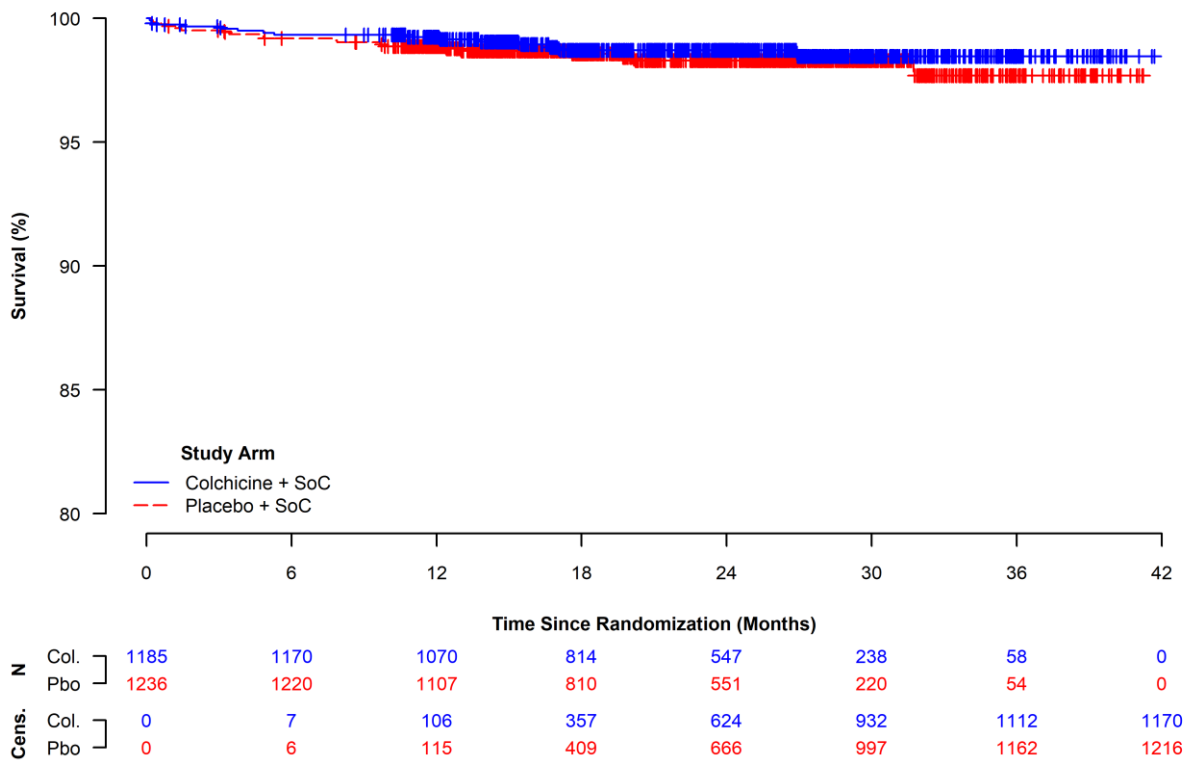
#### 4.4.1.2.7 Subgrouped by Hypertension Status

**Table 53:** Proportion of Patients with Cardiovascular Death, Subgrouped by Hypertension Status (ITT Population).

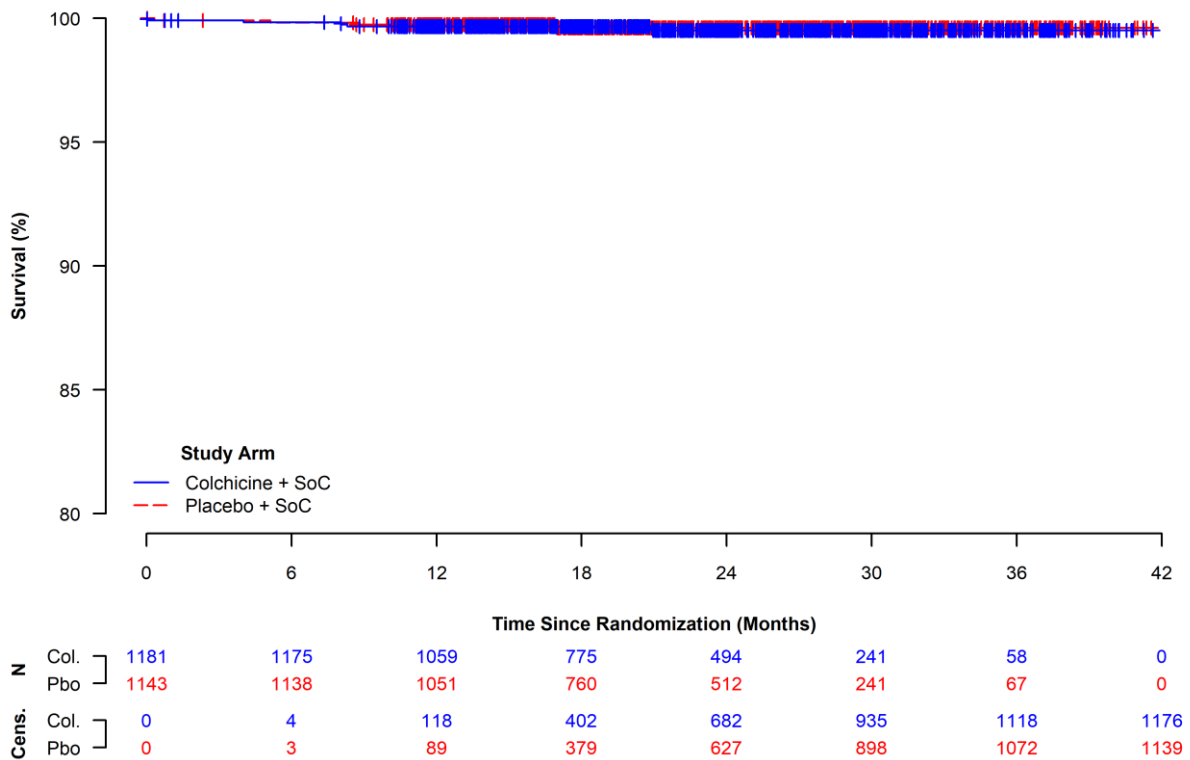
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.5584</b>					
<b>Yes</b>	15/1,185 (1.3)	20/1,236 (1.6)	0.782 [0.402, 1.521] 0.4690	0.779 [0.397, 1.530] 0.4690	-0.352 [-1.301, 0.596] 0.4667
<b>No</b>	5/1,181 (0.4)	4/1,143 (0.3)	1.210 [0.326, 4.494] 0.7761	1.211 [0.324, 4.520] 0.7761	0.073 [-0.431, 0.578] 0.7754
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 54:** Time to Cardiovascular Death, Subgrouped by Hypertension Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.5426</b>							
<b>Yes</b>	15/1,185 (1.3)	NE [NE, NE]	1.5 [0.7, 2.4]	20/1,236 (1.6)	NE [NE, NE]	2.3 [0.9, 3.7]	0.774 [0.397, 1.513] 0.4544
<b>No</b>	5/1,181 (0.4)	NE [NE, NE]	0.5 [0.0, 0.9]	4/1,143 (0.3)	NE [NE, NE]	0.4 [0.0, 0.8]	1.219 [0.327, 4.539] 0.7681
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 43:** Kaplan-Meier Curves for Cardiovascular Death, Within the Hypertensive Subgroup (ITT Population).



**Figure 44:** Kaplan-Meier Curves for Cardiovascular Death, Within the Normotensive Subgroup (ITT Population).

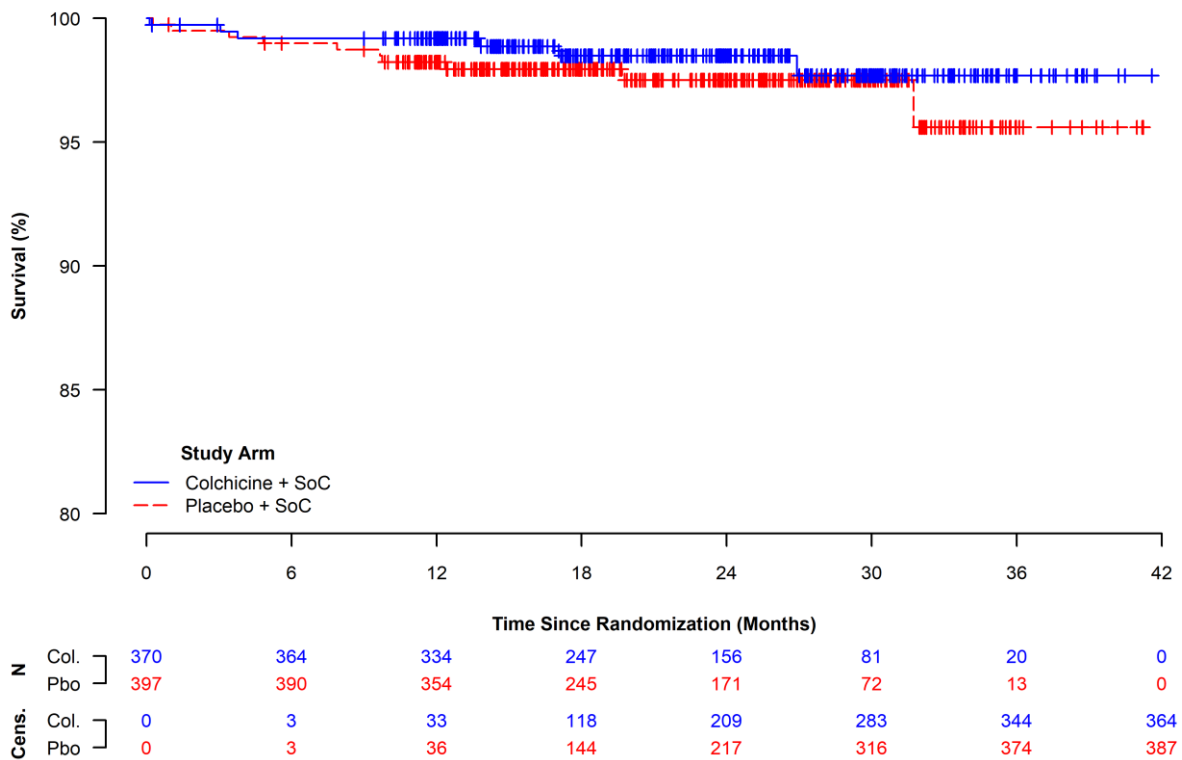
#### 4.4.1.2.8 Subgrouped by History of Myocardial Infarction

**Table 55:** Proportion of Patients with Cardiovascular Death, Subgrouped by History of Myocardial Infarction (ITT Population).

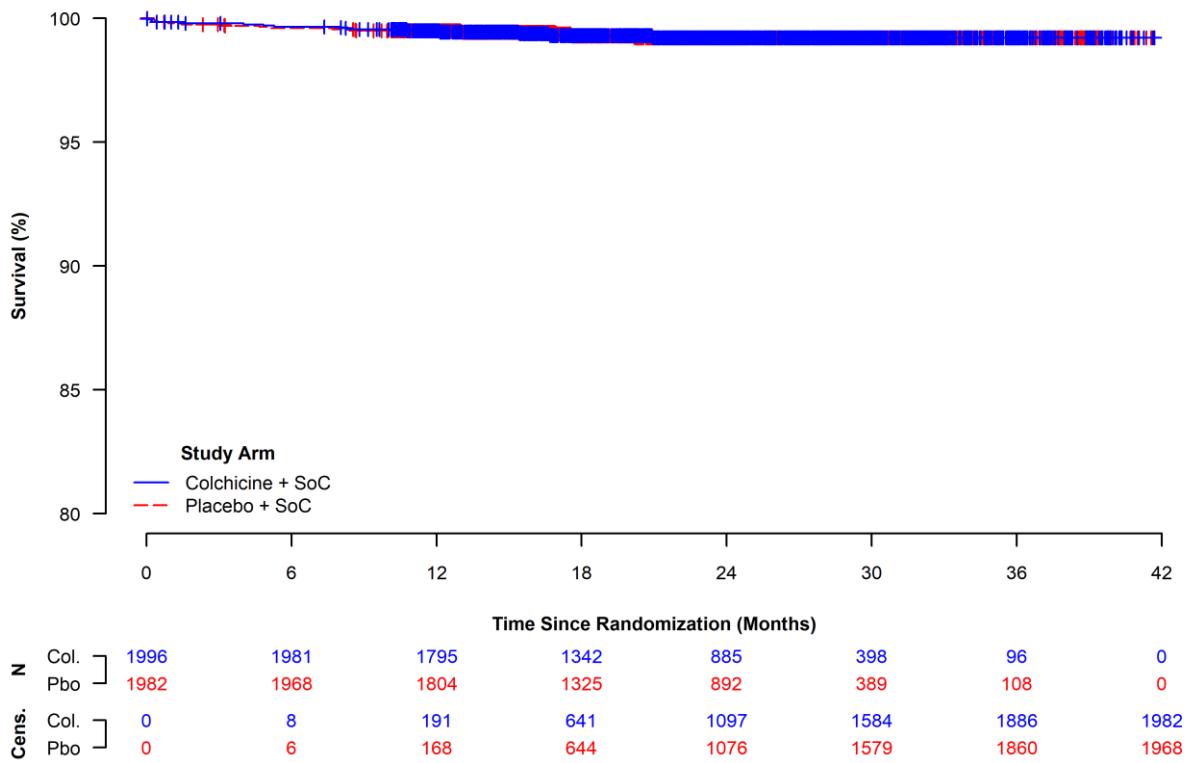
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of MI</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4899</b>					
<b>Yes</b>	6/370 (1.6)	10/397 (2.5)	0.644 [0.236, 1.754] 0.3891	0.638 [0.230, 1.773] 0.3887	-0.897 [-2.905, 1.111] 0.3811
<b>No</b>	14/1,996 (0.7)	14/1,982 (0.7)	0.993 [0.475, 2.077] 0.9851	0.993 [0.472, 2.088] 0.9851	-0.005 [-0.525, 0.515] 0.9851
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 56:** Time to Cardiovascular Death, Subgrouped by History of Myocardial Infarction (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of MI</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.4805</b>							
<b>Yes</b>	6/370 (1.6)	NE [NE, NE]	2.3 [0.2, 4.4]	10/397 (2.5)	NE [NE, NE]	4.4 [0.3, 8.4]	0.633 [0.230, 1.742] 0.3758
<b>No</b>	14/1,996 (0.7)	NE [NE, NE]	0.8 [0.4, 1.2]	14/1,982 (0.7)	NE [NE, NE]	0.8 [0.4, 1.2]	0.996 [0.475, 2.088] 0.9905
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 45:** Kaplan-Meier Curves for Cardiovascular Death, Within the Subgroup With History of Myocardial Infarction (ITT Population).



**Figure 46:** Kaplan-Meier Curves for Cardiovascular Death, Within the Subgroup Without History of Myocardial Infarction (ITT Population).

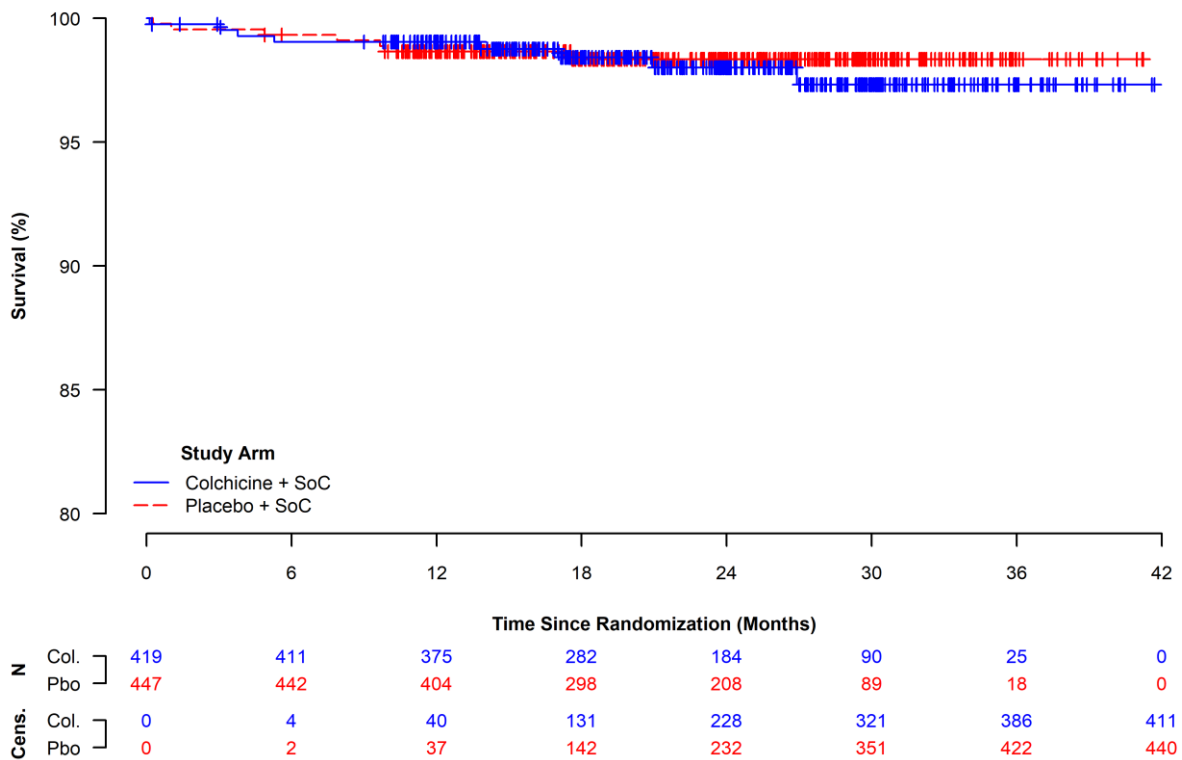
#### 4.4.1.2.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 57:** Proportion of Patients with Cardiovascular Death, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

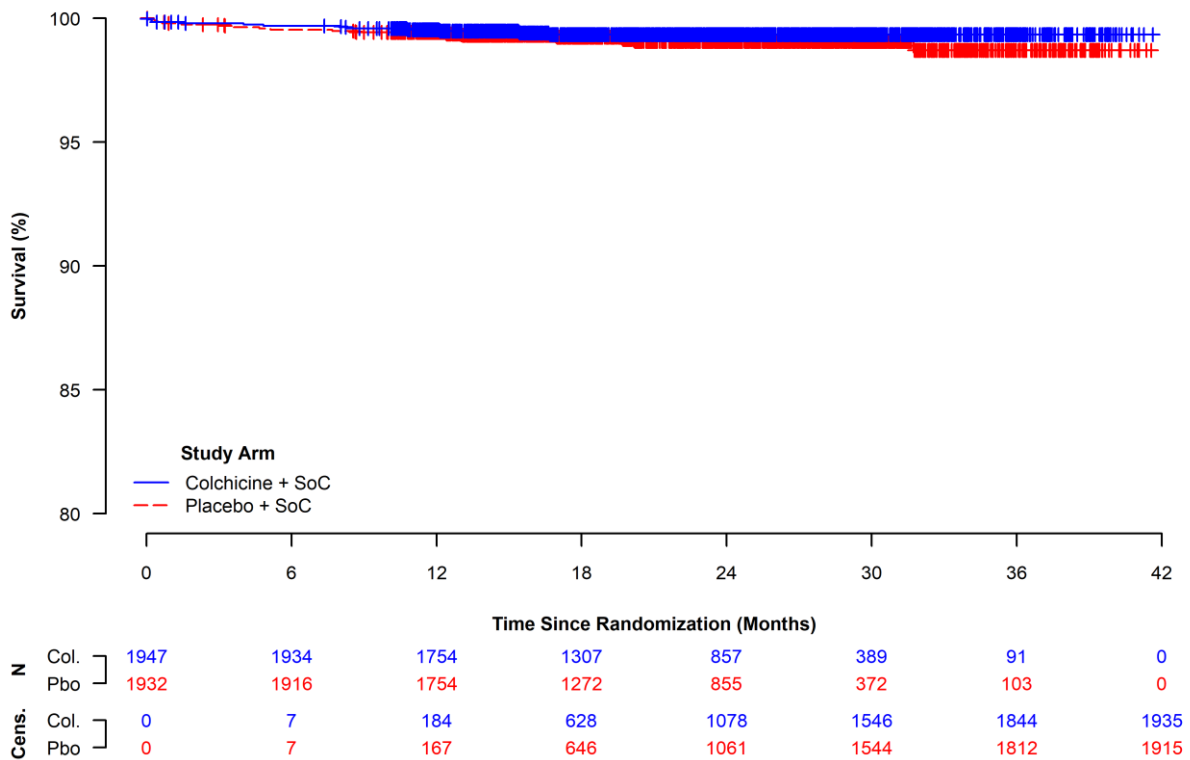
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>					
				<b>Interaction Test p-Value<sup>d</sup> = 0.3836</b>	
<b>Yes</b>	8/419 (1.9)	7/447 (1.6)	1.219 [0.446, 3.333] 0.6992	1.223 [0.440, 3.404] 0.6992	0.343 [-1.401, 2.087] 0.6996
<b>No</b>	12/1,947 (0.6)	17/1,932 (0.9)	0.700 [0.335, 1.463] 0.3433	0.699 [0.333, 1.467] 0.3432	-0.264 [-0.806, 0.279] 0.3409
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 58:** Time to Cardiovascular Death, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.3765</b>							
<b>Yes</b>	8/419 (1.9)	NE [NE, NE]	2.7 [0.7, 4.7]	7/447 (1.6)	NE [NE, NE]	1.7 [0.4, 2.9]	1.232 [0.447, 3.399] 0.6864
<b>No</b>	12/1,947 (0.6)	NE [NE, NE]	0.7 [0.3, 1.0]	17/1,932 (0.9)	NE [NE, NE]	1.3 [0.4, 2.1]	0.700 [0.334, 1.466] 0.3441
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 47:** Kaplan-Meier Curves for Cardiovascular Death, Within the Subgroup With History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).



**Figure 48:** Kaplan-Meier Curves for Cardiovascular Death, Within the Subgroup Without History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

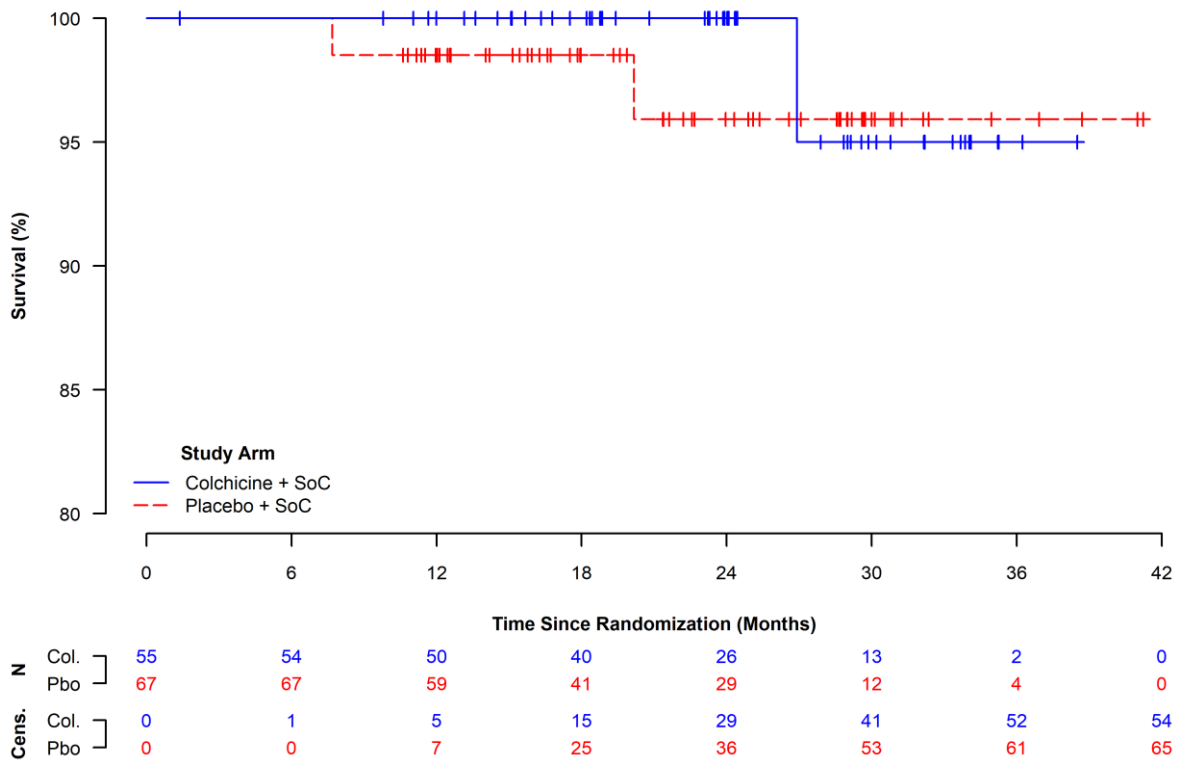
#### 4.4.1.2.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 59:** Proportion of Patients with Cardiovascular Death, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

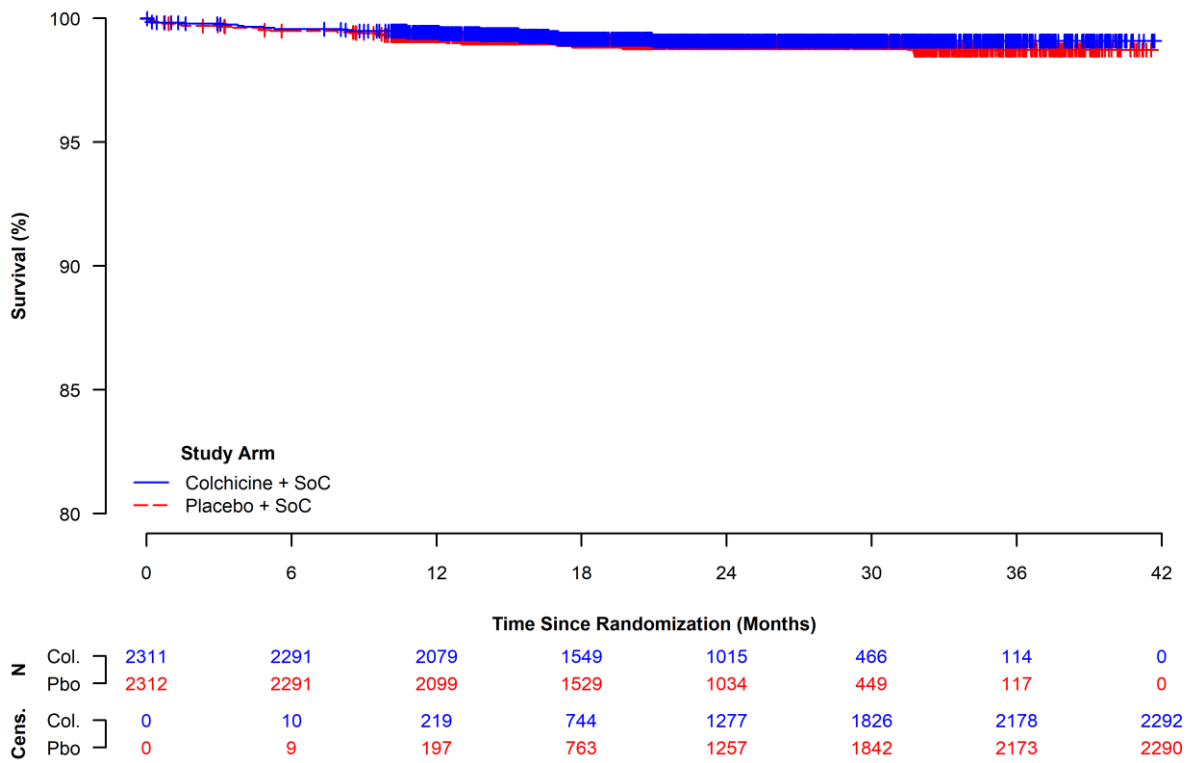
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7747</b>					
<b>Yes</b>	1/55 (1.8)	2/67 (3.0)	0.609 [0.057, 6.541] 0.6823	0.602 [0.053, 6.819] 0.6818	-1.167 [-6.559, 4.225] 0.6714
<b>No</b>	19/2,311 (0.8)	22/2,312 (1.0)	0.864 [0.469, 1.592] 0.6392	0.863 [0.466, 1.599] 0.6392	-0.129 [-0.670, 0.411] 0.6389
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 60:** Time to Cardiovascular Death, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.7569</b>							
<b>Yes</b>	1/55 (1.8)	NE [NE, NE]	5.0 [0.0, 14.1]	2/67 (3.0)	NE [NE, NE]	4.1 [0.0, 9.7]	0.590 [0.053, 6.507] 0.6665
<b>No</b>	19/2,311 (0.8)	NE [NE, NE]	0.9 [0.5, 1.3]	22/2,312 (1.0)	NE [NE, NE]	1.3 [0.6, 2.0]	0.865 [0.468, 1.598] 0.6436
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 49:** Kaplan-Meier Curves for Cardiovascular Death, Within the Subgroup With History of Stroke or Transient Ischaemic Attack (ITT Population).



**Figure 50:** Kaplan-Meier Curves for Cardiovascular Death, Within the Subgroup Without History of Stroke or Transient Ischaemic Attack (ITT Population).

## 4.4.2 Morbidity

### 4.4.2.1 Primary Composite Outcome (Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization)

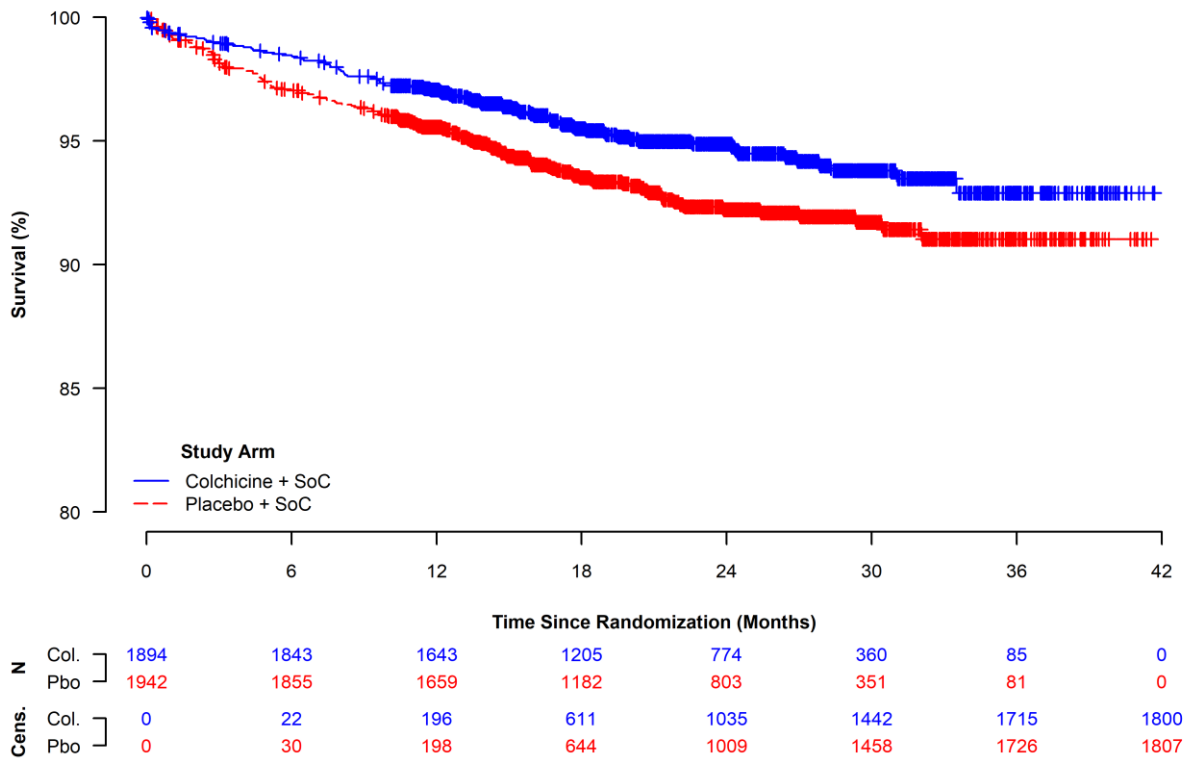
#### 4.4.2.1.1 Subgrouped by Sex

**Table 61:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Sex (ITT Population).

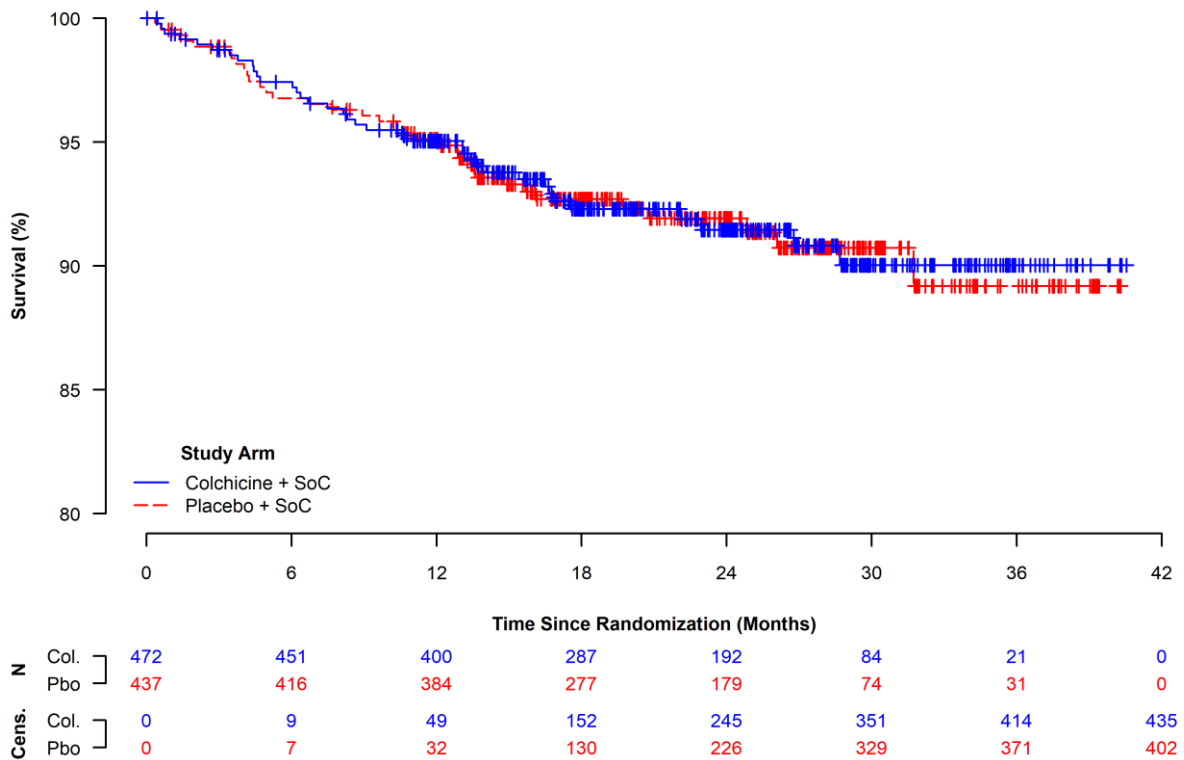
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Sex</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2350</b>					
<b>Male</b>	94/1,894 (5.0)	135/1,942 (7.0)	0.714 [0.553, 0.922] 0.0098	0.699 [0.533, 0.917] 0.0097	-1.989 [-3.484, -0.493] 0.0092
<b>Female</b>	37/472 (7.8)	35/437 (8.0)	0.979 [0.628, 1.525] 0.9244	0.977 [0.604, 1.581] 0.9244	-0.170 [-3.685, 3.345] 0.9244
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 62:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Sex (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Sex</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.2033</b>							
<b>Male</b>	94/1,894 (5.0)	NE [NE, NE]	7.1 [5.2, 8.9]	135/1,942 (7.0)	NE [NE, NE]	9.0 [7.2, 10.7]	0.703 [0.540, 0.915] 0.0087
<b>Female</b>	37/472 (7.8)	NE [NE, NE]	10.0 [6.5, 13.3]	35/437 (8.0)	NE [NE, NE]	10.8 [6.4, 15.0]	0.992 [0.625, 1.574] 0.9715
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 51:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Male Sex Subgroup (ITT Population).



**Figure 52:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Female Sex Subgroup (ITT Population).

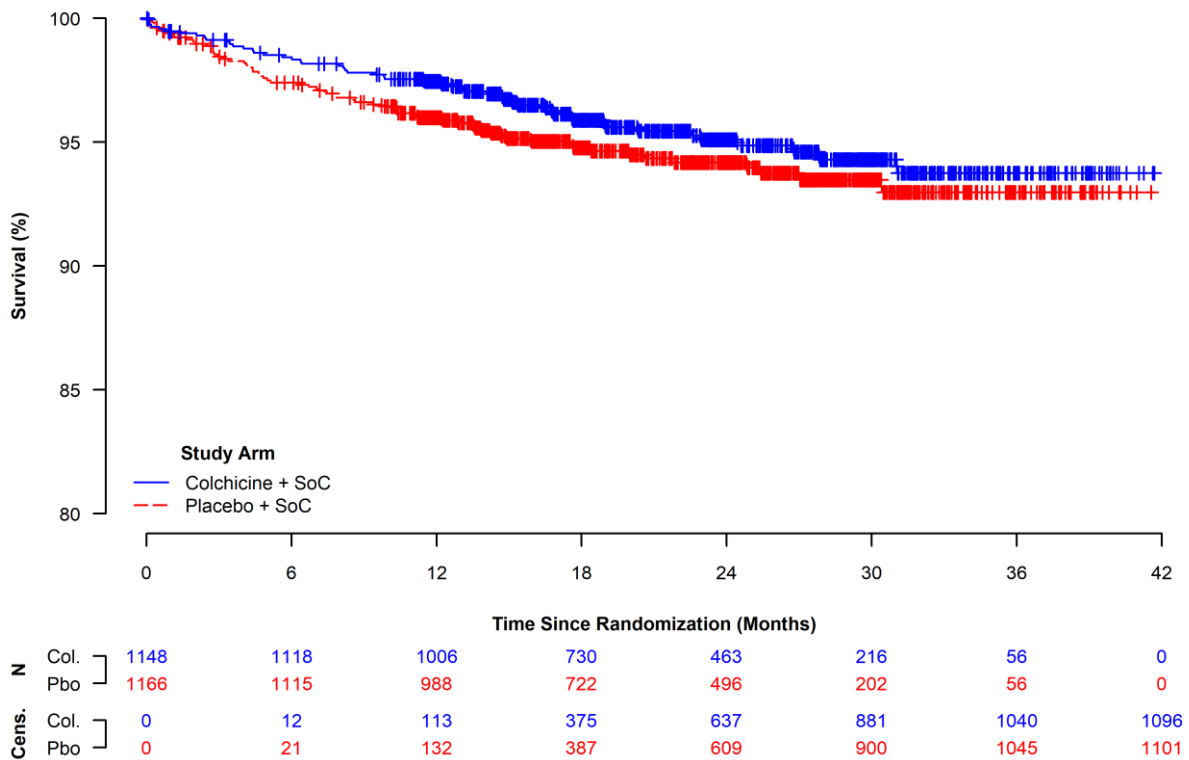
#### 4.4.2.1.2 Subgrouped by Age Group

**Table 63:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Age Group (ITT Population).

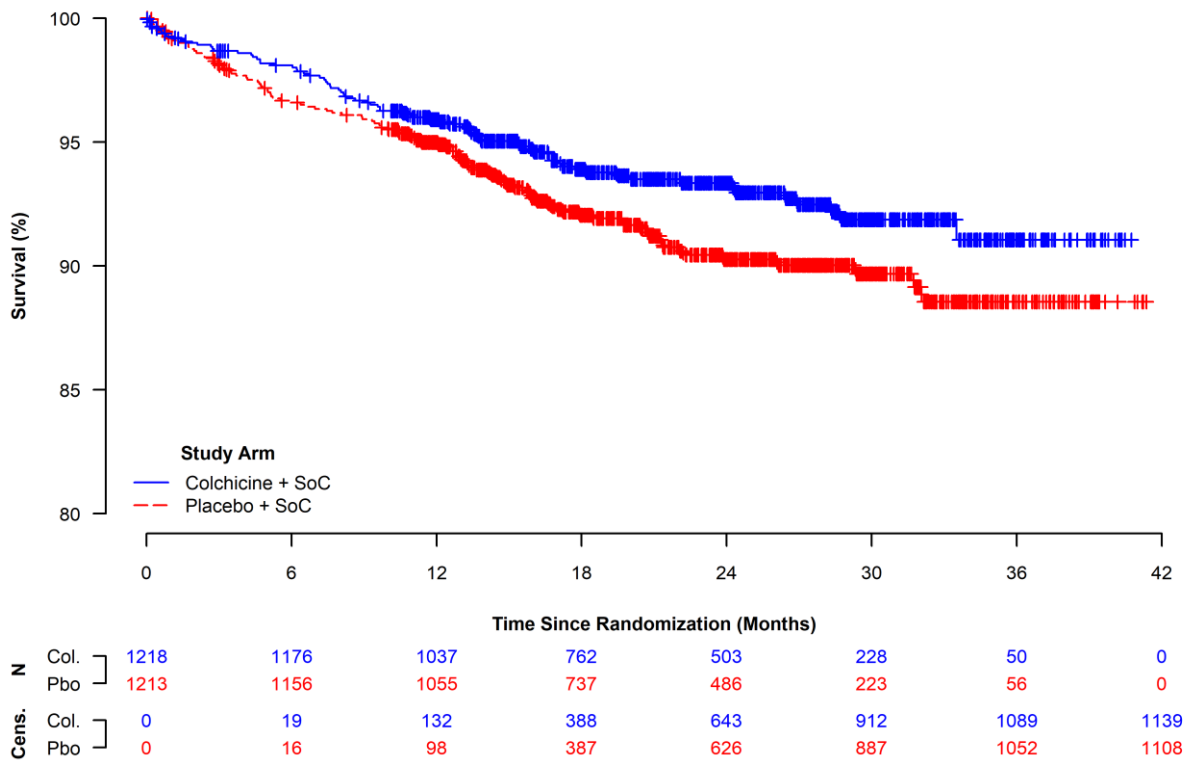
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Age</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7037</b>					
<b>&lt; 60 Years</b>	52/1,148 (4.5)	65/1,166 (5.6)	0.813 [0.569, 1.159] 0.2523	0.804 [0.553, 1.168] 0.2521	-1.045 [-2.829, 0.739] 0.2508
<b>≥ 60 Years</b>	79/1,218 (6.5)	105/1,213 (8.7)	0.749 [0.566, 0.992] 0.0440	0.732 [0.540, 0.991] 0.0438	-2.170 [-4.272, -0.069] 0.0430
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 64:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Age Group (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.7866</b>							
<b>&lt; 60 Years</b>	52/1,148 (4.5)	NE [NE, NE]	6.3 [4.3, 8.2]	65/1,166 (5.6)	NE [NE, NE]	7.0 [5.1, 8.9]	0.799 [0.555, 1.150] 0.2275
<b>≥ 60 Years</b>	79/1,218 (6.5)	NE [NE, NE]	9.0 [6.4, 11.4]	105/1,213 3 (8.7)	NE [NE, NE]	11.4 [8.9, 13.9]	0.748 [0.559, 1.002] 0.0514
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. SEs presented on the log-scale. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours colchicine. SEs presented on the log-scale. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 53:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Age 59 Years or Younger Subgroup (ITT Population).



**Figure 54:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Age 60 Years or Older Subgroup (ITT Population).

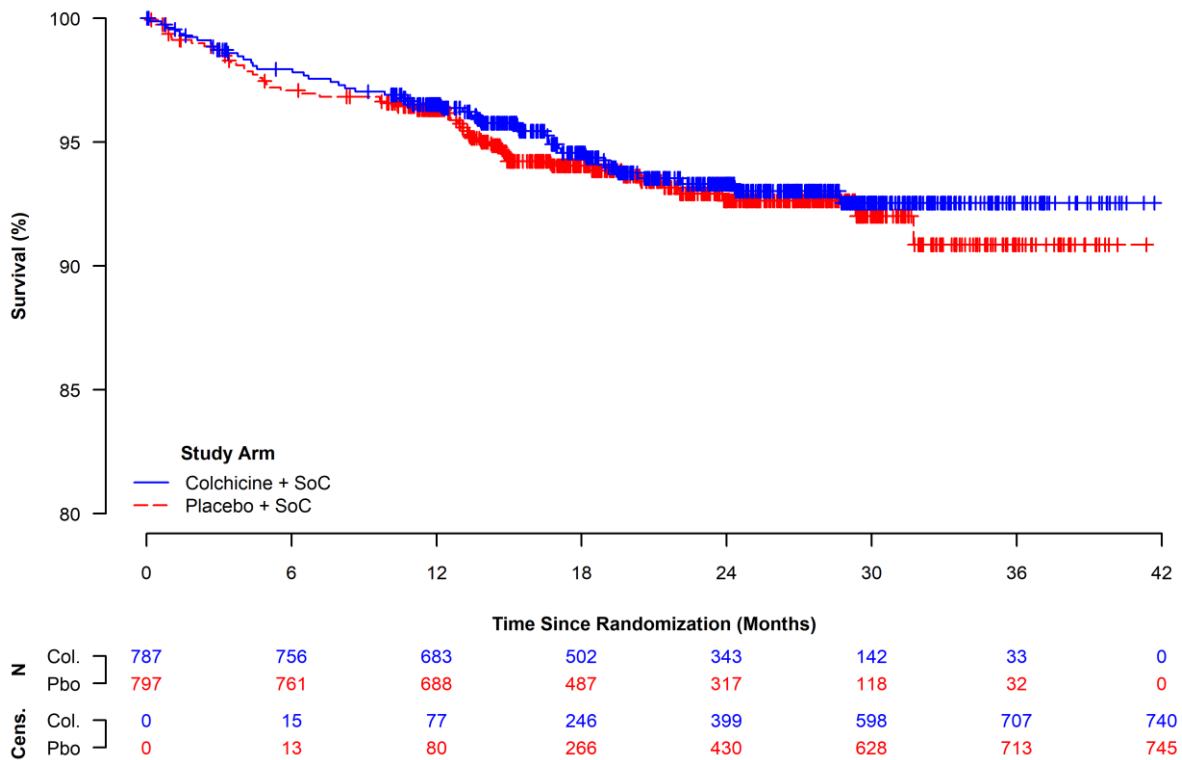
#### 4.4.2.1.3 Subgrouped by Smoking Status

**Table 65:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Smoking Status (ITT Population).

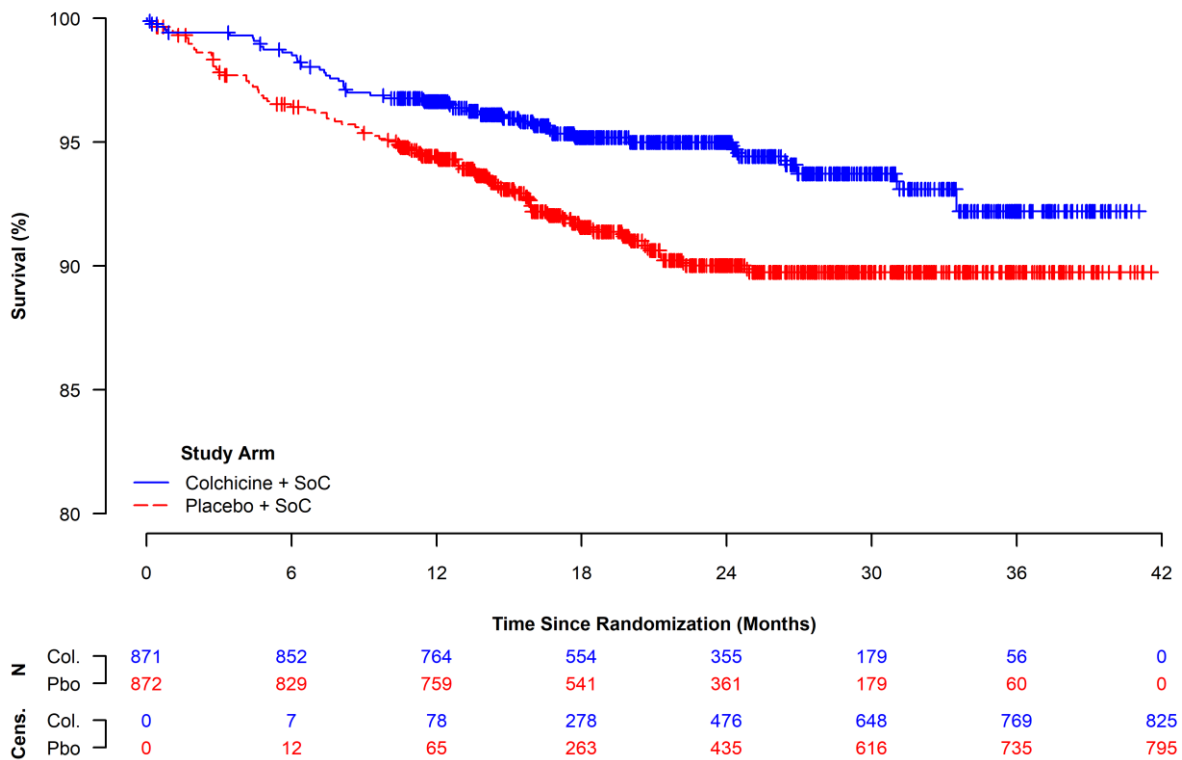
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,377)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Smoking Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1688</b>					
<b>Non</b>	47/787 (6.0)	52/797 (6.5)	0.915 [0.625, 1.341] 0.6499	0.910 [0.605, 1.368] 0.6498	-0.552 [-2.936, 1.831] 0.6496
<b>Ex</b>	46/871 (5.3)	77/872 (8.8)	0.598 [0.420, 0.851] 0.0043	0.576 [0.394, 0.840] 0.0042	-3.549 [-5.947, -1.150] 0.0037
<b>Current</b>	38/708 (5.4)	41/708 (5.8)	0.927 [0.604, 1.423] 0.7284	0.923 [0.586, 1.453] 0.7284	-0.424 [-2.815, 1.967] 0.7283
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 66:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Smoking Status (ITT Population).

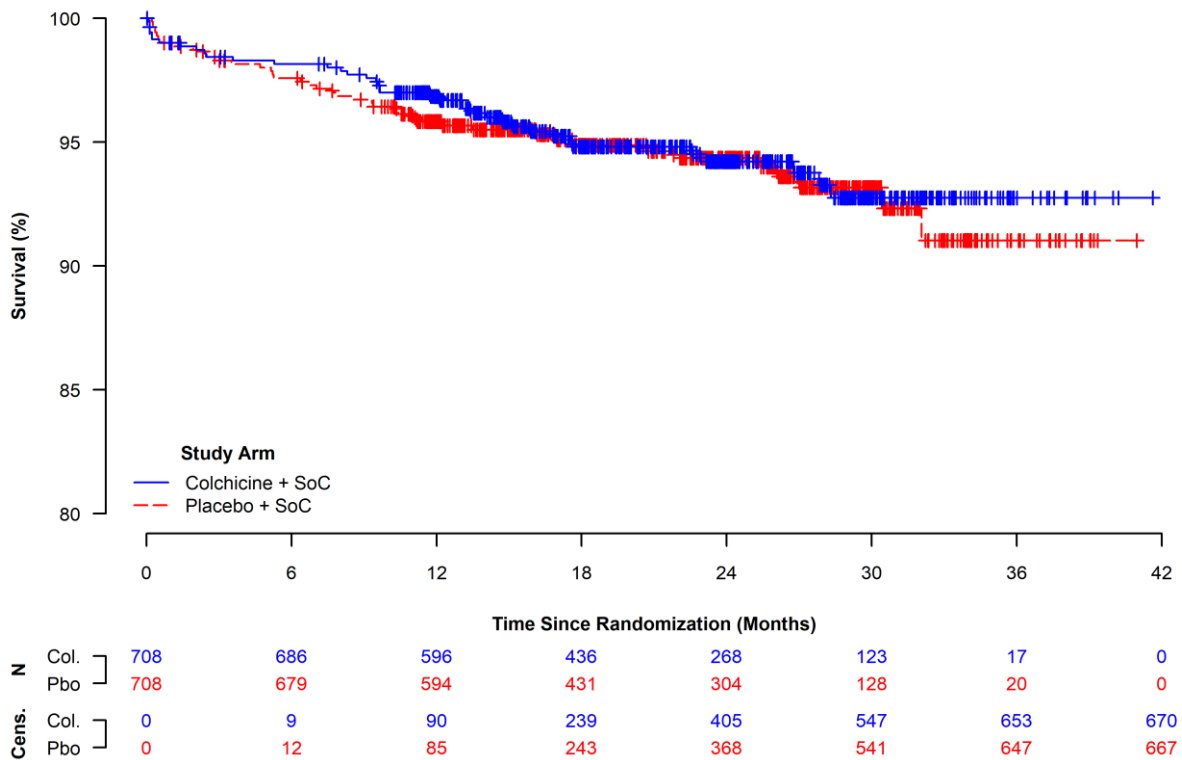
Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,377)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.1909</b>							
<b>Non</b>	47/787 (6.0)	NE [NE, NE]	7.5 [5.2, 9.6]	52/797 (6.5)	NE [NE, NE]	9.1 [5.8, 12.3]	0.901 [0.607, 1.336] 0.6028
<b>Ex</b>	46/871 (5.3)	NE [NE, NE]	7.8 [4.9, 10.6]	77/872 (8.8)	NE [NE, NE]	10.3 [8.0, 12.5]	0.590 [0.410, 0.851] 0.0047
<b>Current</b>	38/708 (5.4)	NE [NE, NE]	7.3 [4.7, 9.7]	41/708 (5.8)	NE [NE, NE]	9.0 [5.2, 12.6]	0.927 [0.596, 1.442] 0.7381
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 55:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Non-Smoker Subgroup (ITT Population).



**Figure 56:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Ex-Smoker Subgroup (ITT Population).



**Figure 57:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Current Smoker Subgroup (ITT Population).

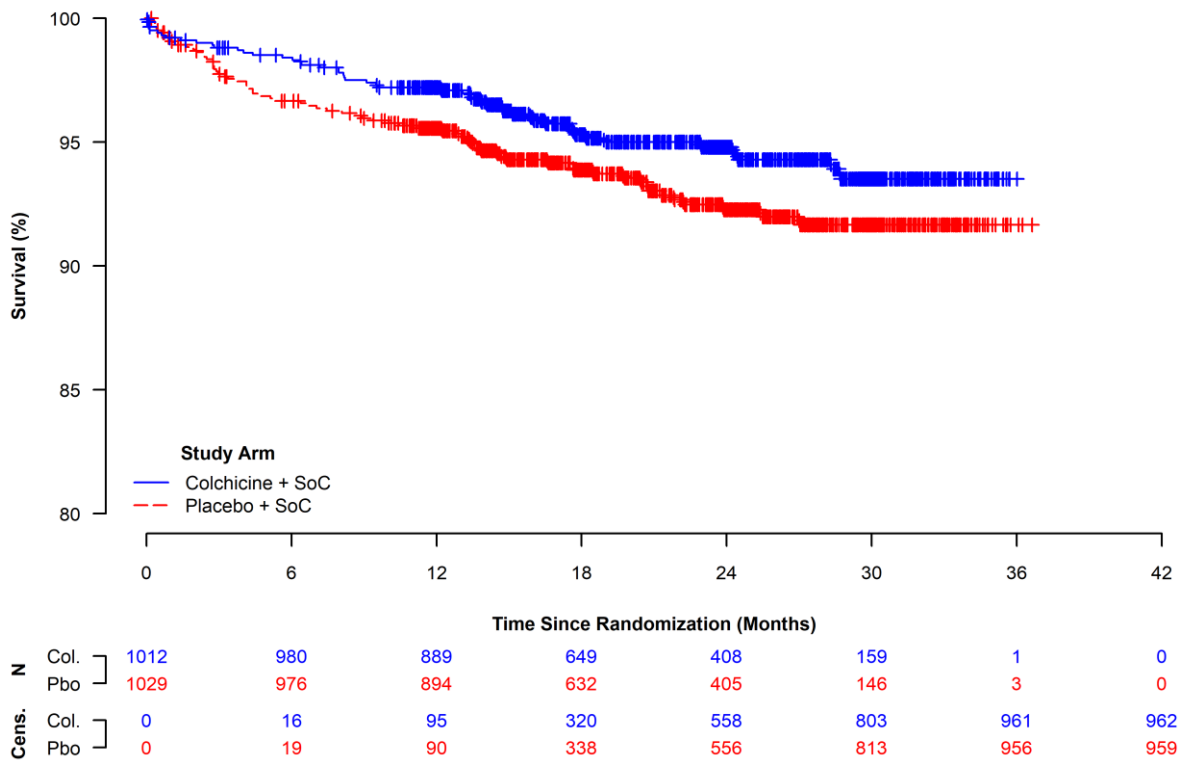
#### 4.4.2.1.4 Subgrouped by Region

**Table 67:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Region (ITT Population).

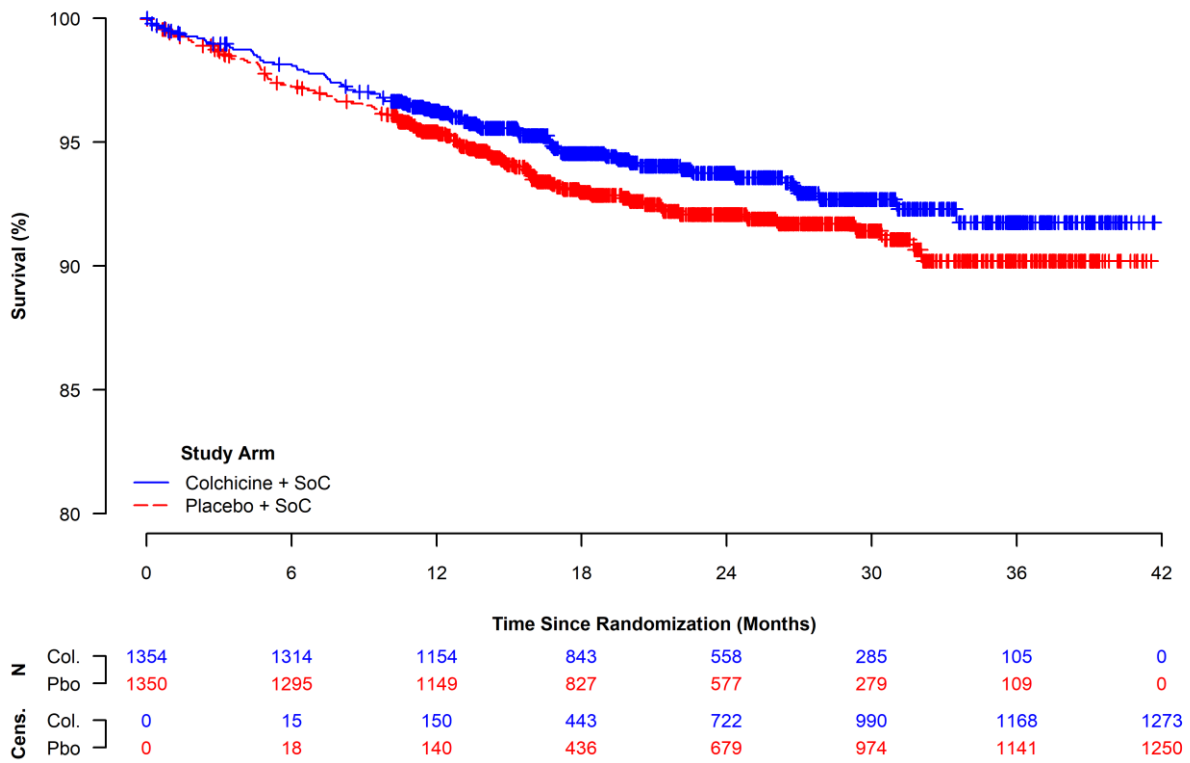
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>d</sup> = 0.6521</b>					
<b>Europe</b>	50/1,012 (4.9)	70/1,029 (6.8)	0.726 [0.511, 1.033] 0.0753	0.712 [0.490, 1.035] 0.0750	-1.862 [-3.899, 0.175] 0.0732
<b>Non-Europe</b>	81/1,354 (6.0)	100/1,350 (7.4)	0.808 [0.608, 1.072] 0.1391	0.795 [0.587, 1.077] 0.1389	-1.425 [-3.309, 0.458] 0.1381
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 68:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Region (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.6074</b>							
<b>Europe</b>	50/1,012 (4.9)	NE [NE, NE]	6.5 [4.5, 8.4]	70/1,029 (6.8)	NE [NE, NE]	8.3 [6.3, 10.3]	0.713 [0.496, 1.025] 0.0681
<b>Non-Europe</b>	81/1,354 (6.0)	NE [NE, NE]	8.2 [6.1, 10.3]	100/1,350 (7.4)	NE [NE, NE]	9.8 [7.6, 12.0]	0.805 [0.600, 1.079] 0.1462
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 58:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within European Countries (ITT Population).



**Figure 59:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within Non-European Countries (ITT Population).

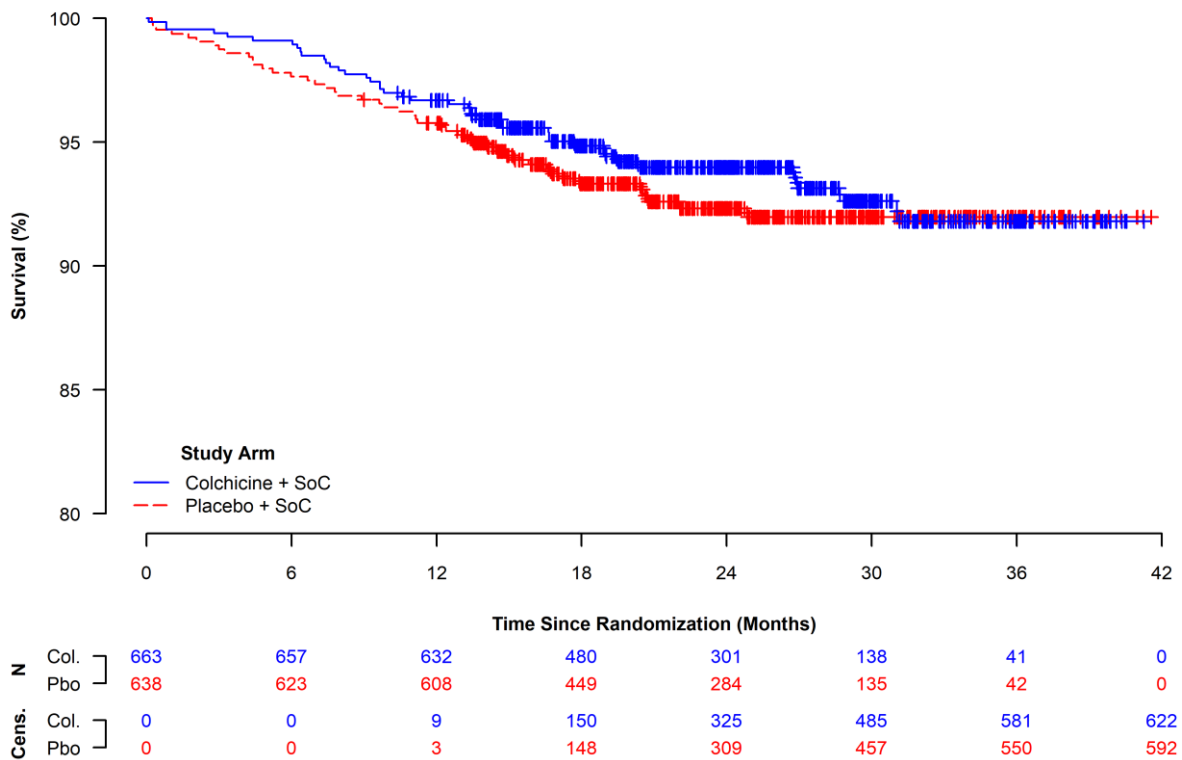
#### 4.4.2.1.5 Subgrouped by White Blood Cell Count

**Table 69:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by White Blood Cell Count (ITT Population).

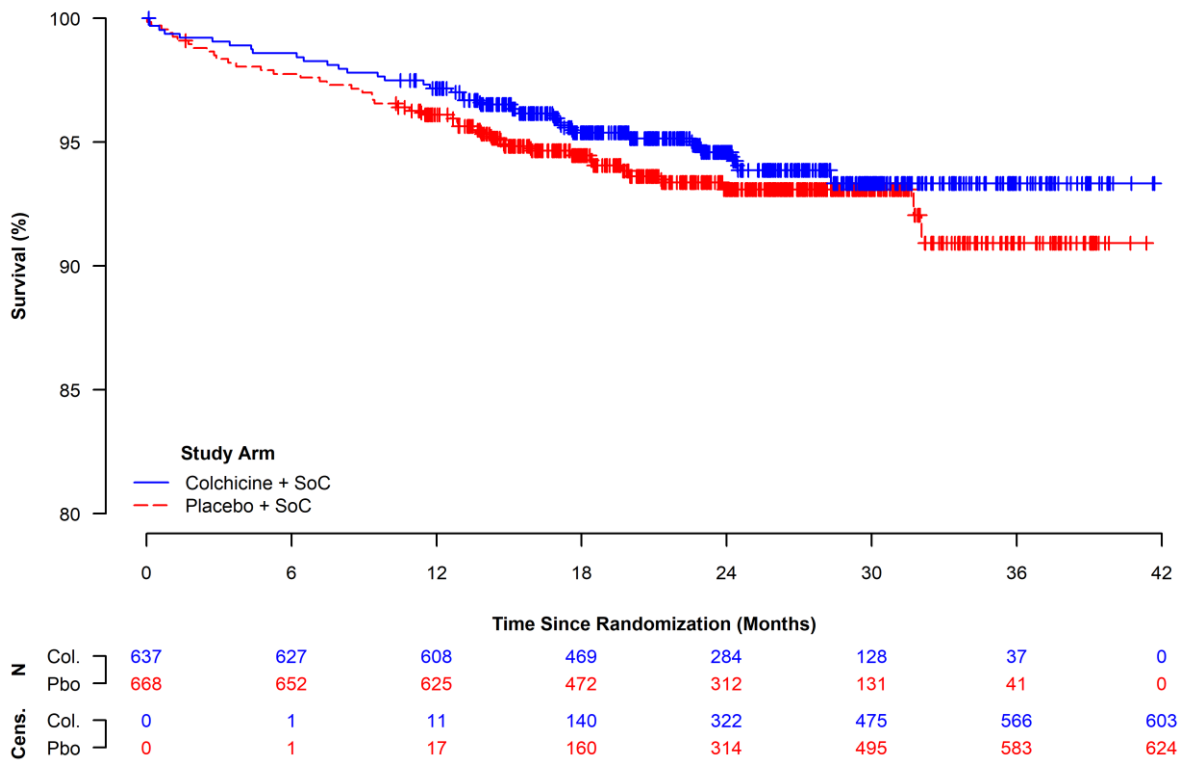
Subgroup	Colchicine + SoC (N = 1,300)	Placebo + SoC (N = 1,306)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8552</b>					
< 8.66 10 <sup>3</sup> /μL	41/663 (6.2)	46/638 (7.2)	0.858 [0.571, 1.288] 0.4594	0.848 [0.549, 1.312] 0.4593	-1.026 [-3.744, 1.692] 0.4594
≥ 8.66 10 <sup>3</sup> /μL	34/637 (5.3)	44/668 (6.6)	0.810 [0.525, 1.251] 0.3424	0.800 [0.504, 1.268] 0.3421	-1.249 [-3.816, 1.317] 0.3400
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 70:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by White Blood Cell Count (ITT Population).

Subgroup	Colchicine + SoC (N = 1,300)			Placebo + SoC (N = 1,306)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.8589</b>							
< 8.66 10 <sup>3</sup> /μL	41/663 (6.2)	NE [NE, NE]	8.2 [5.3, 11.0]	46/638 (7.2)	NE [NE, NE]	8.0 [5.7, 10.3]	0.847 [0.556, 1.291] 0.4407
≥ 8.66 10 <sup>3</sup> /μL	34/637 (5.3)	NE [NE, NE]	6.7 [4.3, 9.0]	44/668 (6.6)	NE [NE, NE]	9.1 [5.4, 12.6]	0.803 [0.513, 1.256] 0.3359
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 60:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Lower White Blood Cell Count Subgroup (ITT Population).



**Figure 61:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Upper White Blood Cell Count Subgroup (ITT Population).

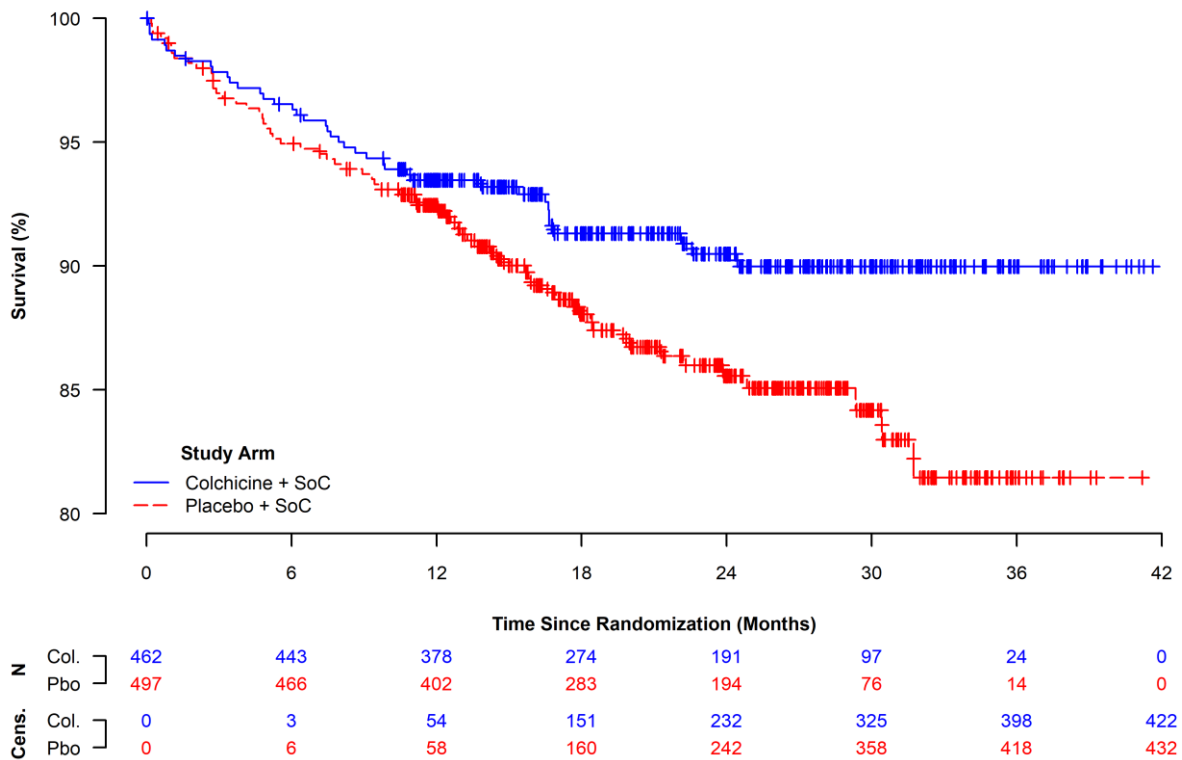
#### 4.4.2.1.6 Subgrouped by Diabetes Status

**Table 71:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Diabetes Status (ITT Population).

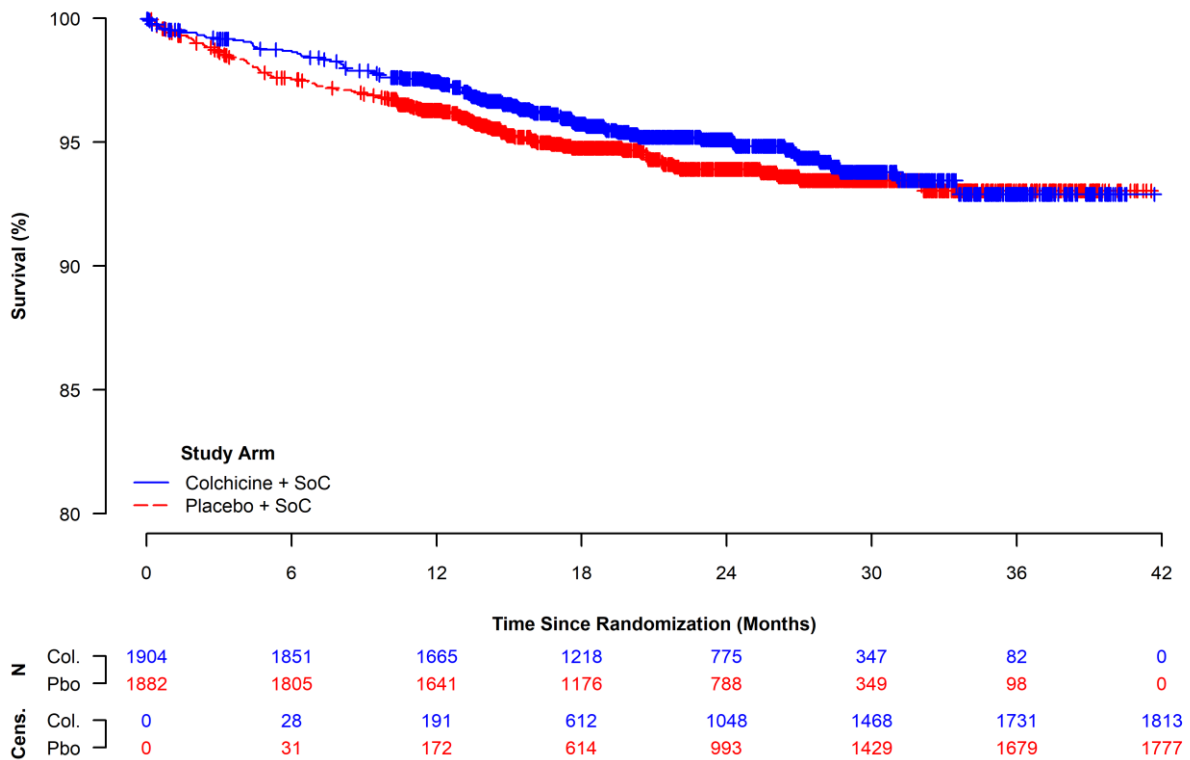
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2454</b>					
<b>Yes</b>	40/462 (8.7)	65/497 (13.1)	0.662 [0.456, 0.961] 0.0302	0.630 [0.416, 0.955] 0.0295	-4.420 [-8.340, -0.501] 0.0271
<b>No</b>	91/1,904 (4.8)	105/1,882 (5.6)	0.857 [0.652, 1.126] 0.2673	0.849 [0.637, 1.133] 0.2672	-0.800 [-2.212, 0.612] 0.2669
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 72:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Diabetes Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.2673</b>							
<b>Yes</b>	40/462 (8.7)	NE [NE, NE]	10.0 [6.9, 13.1]	65/497 (13.1)	NE [NE, NE]	18.6 [13.0, 23.7]	0.649 [0.437, 0.962] 0.0313
<b>No</b>	91/1,904 (4.8)	NE [NE, NE]	7.1 [5.2, 9.0]	105/1,882 (5.6)	NE [NE, NE]	7.0 [5.4, 8.5]	0.851 [0.643, 1.127] 0.2604
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 62:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Diabetic Subgroup (ITT Population).



**Figure 63:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Non-Diabetic Subgroup (ITT Population).

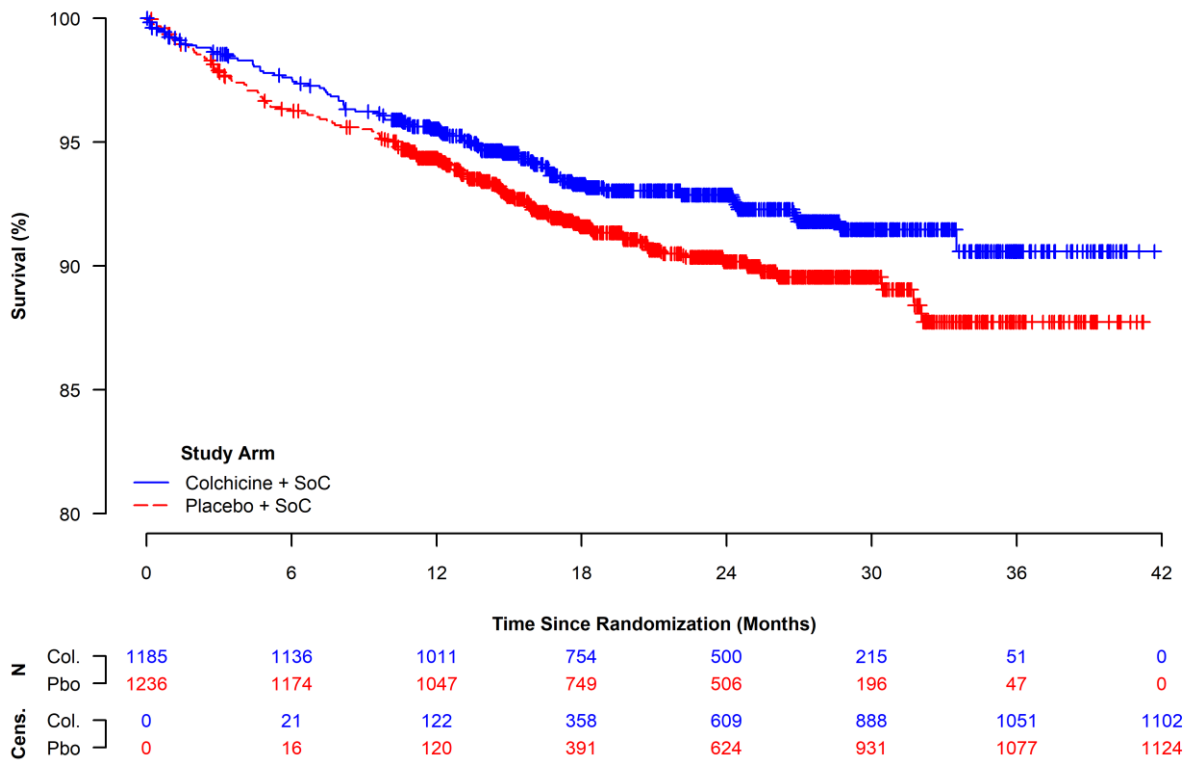
#### 4.4.2.1.7 Subgrouped by Hypertension Status

**Table 73:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Hypertension Status (ITT Population).

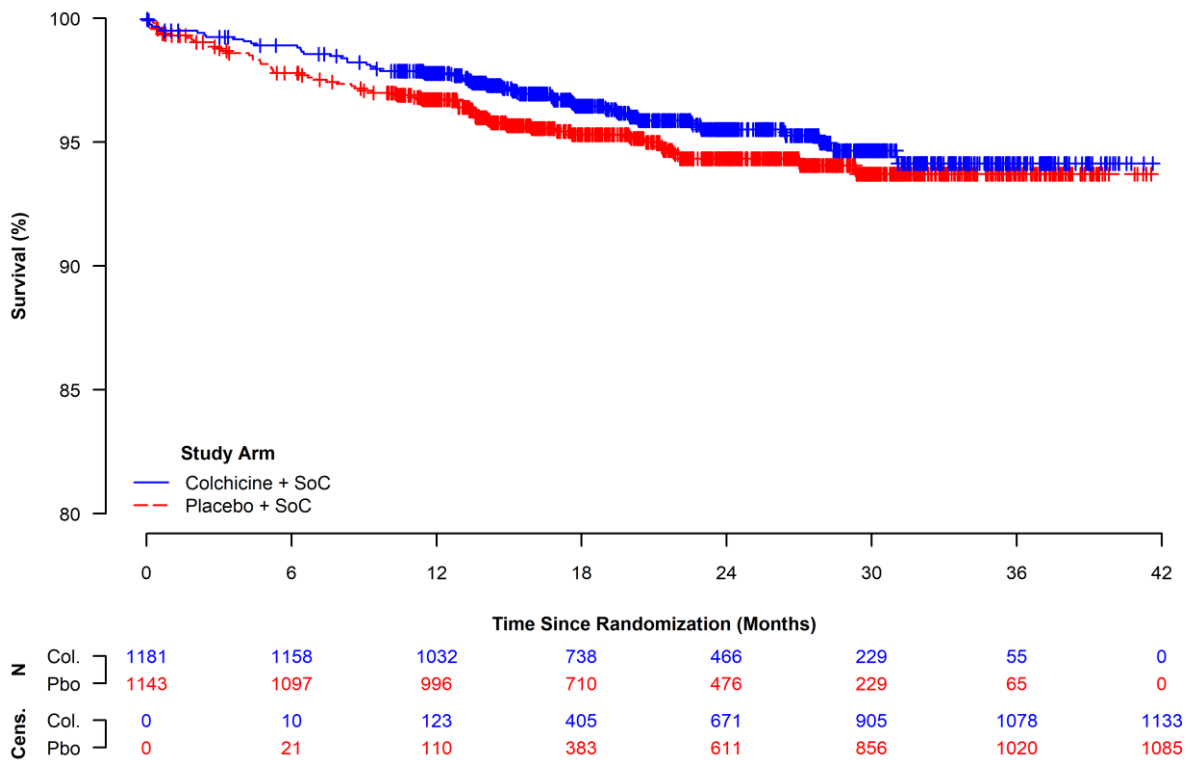
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8500</b>					
<b>Yes</b>	83/1,185 (7.0)	112/1,236 (9.1)	0.773 [0.589, 1.015] 0.0639	0.756 [0.562, 1.016] 0.0636	-2.057 [-4.219, 0.104] 0.0621
<b>No</b>	48/1,181 (4.1)	58/1,143 (5.1)	0.801 [0.551, 1.164] 0.2444	0.793 [0.536, 1.172] 0.2443	-1.010 [-2.709, 0.689] 0.2440
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 74:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Hypertension Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.8608</b>							
<b>Yes</b>	83/1,185 (7.0)	NE [NE, NE]	9.4 [6.8, 11.9]	112/1,236 (9.1)	NE [NE, NE]	12.3 [9.4, 15.0]	0.763 [0.574, 1.014] 0.0619
<b>No</b>	48/1,181 (4.1)	NE [NE, NE]	5.9 [3.9, 7.8]	58/1,143 (5.1)	NE [NE, NE]	6.3 [4.6, 8.0]	0.796 [0.543, 1.167] 0.2420
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 64:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Hypertensive Subgroup (ITT Population).



**Figure 65:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Normotensive Subgroup (ITT Population).

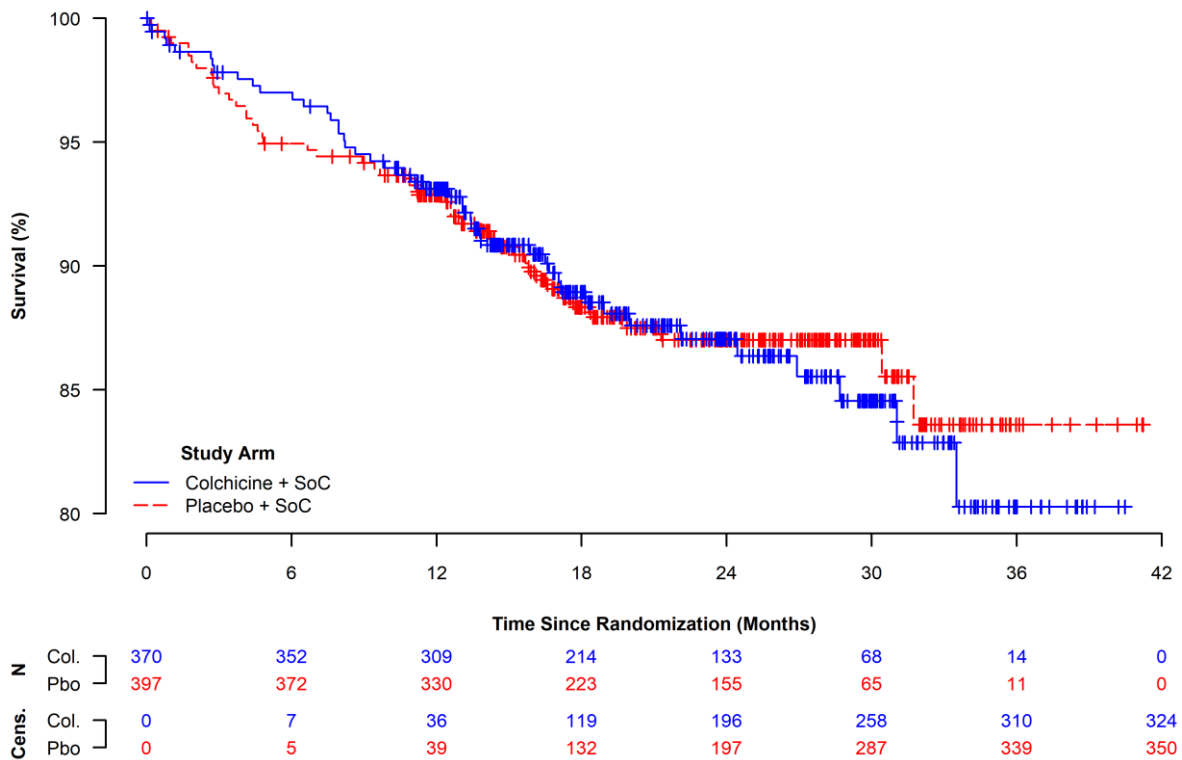
#### 4.4.2.1.8 Subgrouped by History of Myocardial Infarction

**Table 75:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by History of Myocardial Infarction (ITT Population).

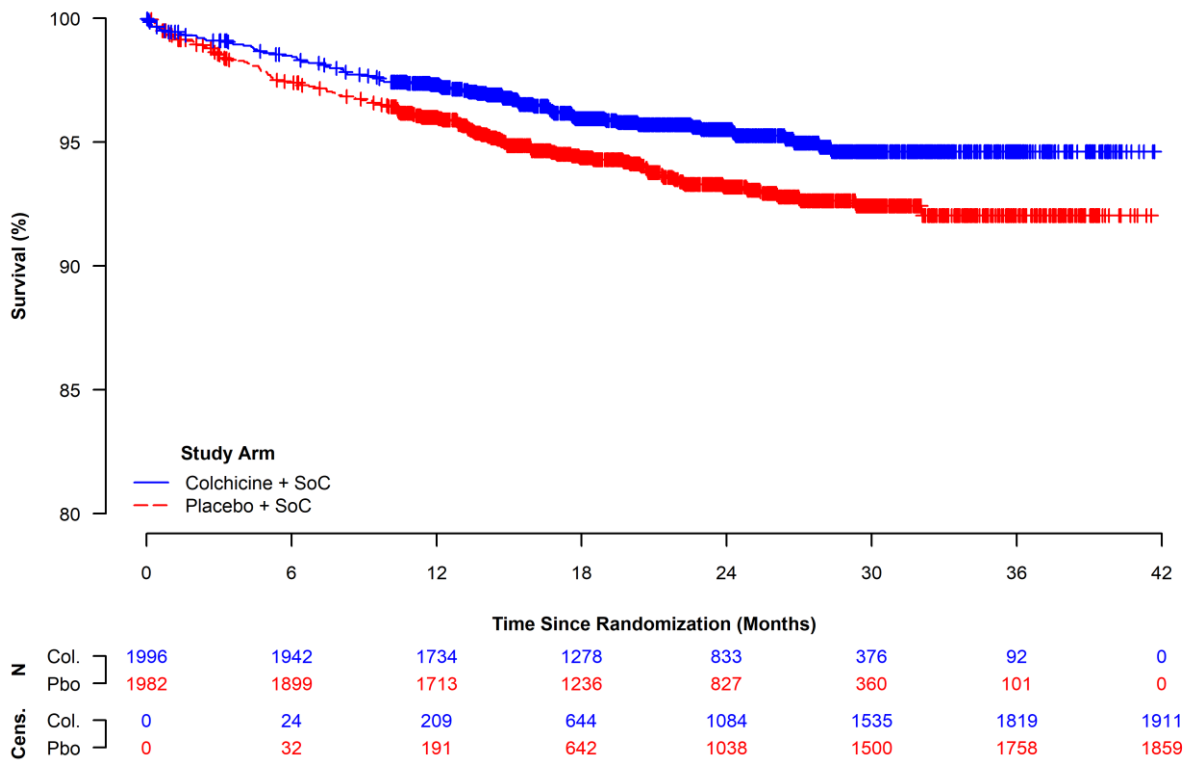
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of MI</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.0869</b>					
<b>Yes</b>	46/370 (12.4)	47/397 (11.8)	1.050 [0.717, 1.537] 0.8013	1.057 [0.685, 1.631] 0.8013	0.594 [-4.033, 5.220] 0.8014
<b>No</b>	85/1,996 (4.3)	123/1,982 (6.2)	0.686 [0.524, 0.898] 0.0061	0.672 [0.506, 0.893] 0.0061	-1.947 [-3.330, -0.564] 0.0058
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 76:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by History of Myocardial Infarction (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of MI</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.0810</b>							
<b>Yes</b>	46/370 (12.4)	NE [NE, NE]	19.7 [12.0, 26.8]	47/397 (11.8)	NE [NE, NE]	16.4 [10.4, 22.1]	1.048 [0.698, 1.573] 0.8227
<b>No</b>	85/1,996 (4.3)	NE [NE, NE]	5.4 [4.2, 6.6]	123/1,982 (6.2)	NE [NE, NE]	8.0 [6.4, 9.5]	0.678 [0.515, 0.895] 0.0060
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 66:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Subgroup With History of Myocardial Infarction (ITT Population).



**Figure 67:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Subgroup Without History of Myocardial Infarction (ITT Population).

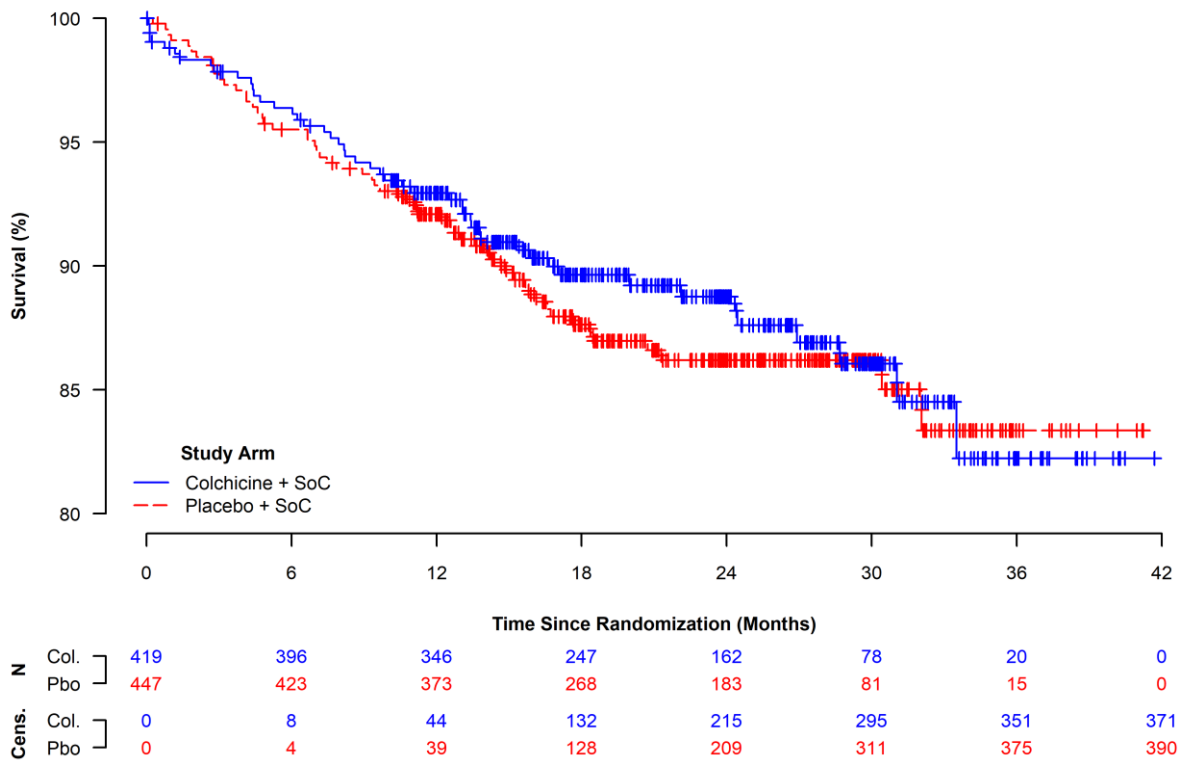
#### 4.4.2.1.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 77:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

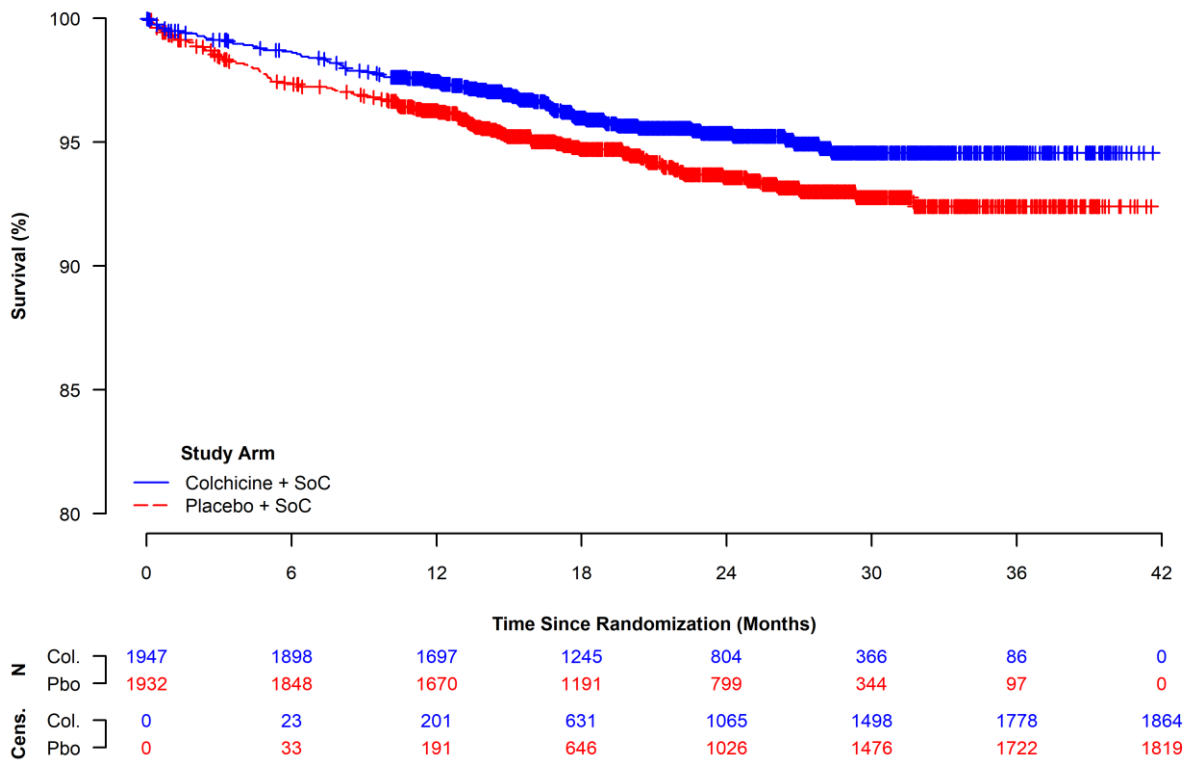
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4103</b>					
<b>Yes</b>	48/419 (11.5)	57/447 (12.8)	0.898 [0.627, 1.288] 0.5597	0.885 [0.588, 1.333] 0.5595	-1.296 [-5.639, 3.047] 0.5587
<b>No</b>	83/1,947 (4.3)	113/1,932 (5.8)	0.729 [0.553, 0.961] 0.0248	0.717 [0.536, 0.959] 0.0247	-1.586 [-2.964, -0.207] 0.0241
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 78:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.3269</b>							
<b>Yes</b>	48/419 (11.5)	NE [NE, NE]	17.8 [10.9, 24.1]	57/447 (12.8)	NE [NE, NE]	16.6 [11.3, 21.7]	0.911 [0.621, 1.338] 0.6357
<b>No</b>	83/1,947 (4.3)	NE [NE, NE]	5.4 [4.2, 6.7]	113/1,932 (5.8)	NE [NE, NE]	7.6 [6.0, 9.2]	0.718 [0.541, 0.954] 0.0221
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 68:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Subgroup With History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).



**Figure 69:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Subgroup Without History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

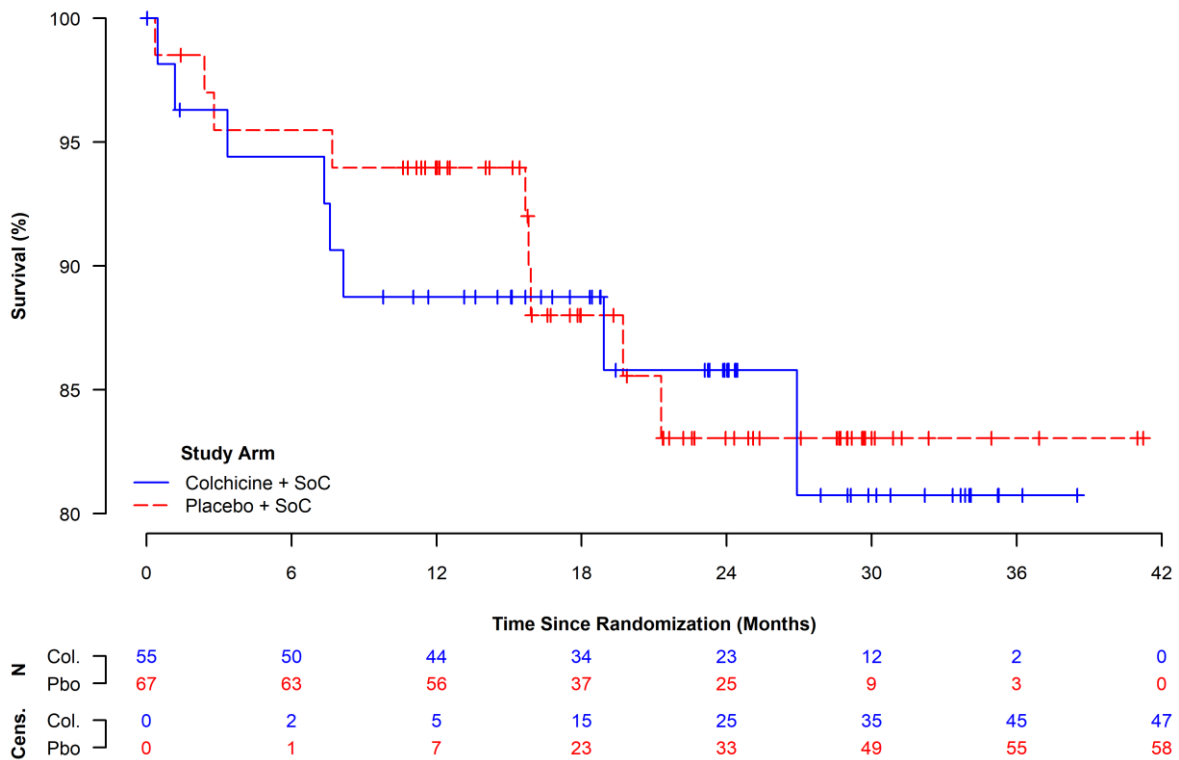
#### 4.4.2.1.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 79:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

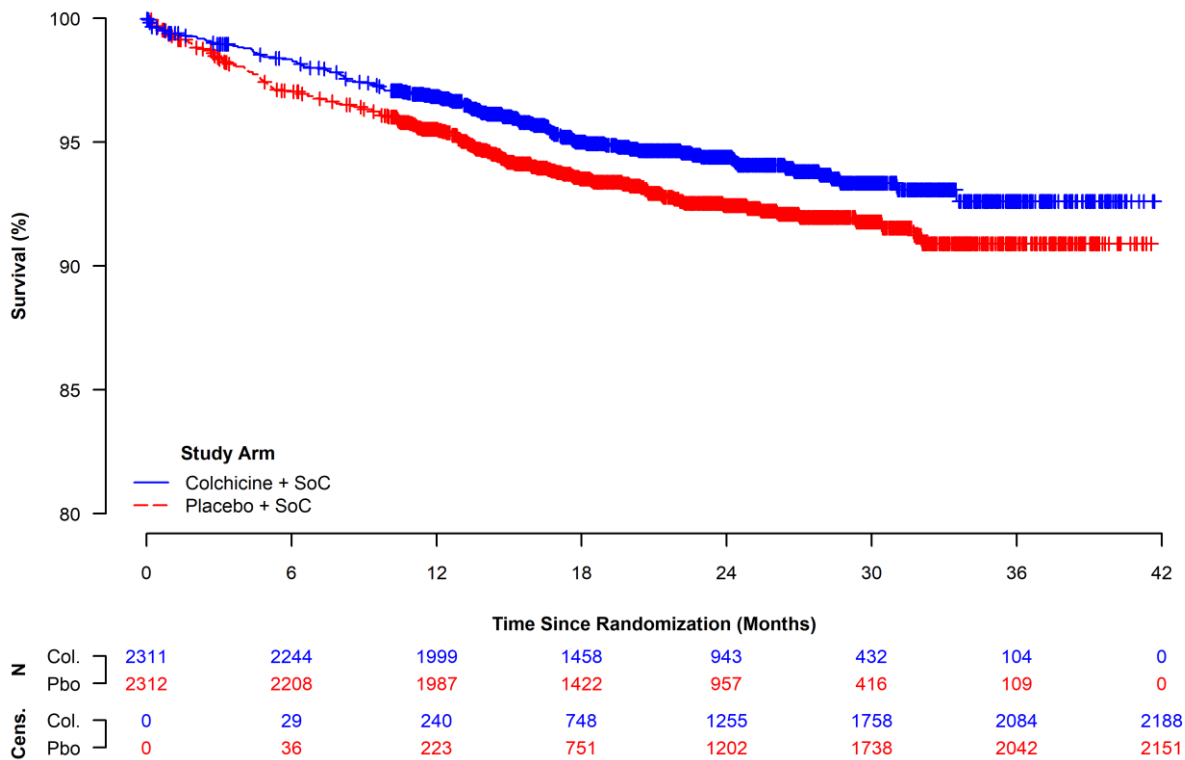
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4835</b>					
<b>Yes</b>	8/55 (14.5)	9/67 (13.4)	1.083 [0.448, 2.619] 0.8598	1.097 [0.393, 3.064] 0.8599	1.113 [-11.276, 13.502] 0.8603
<b>No</b>	123/2,311 (5.3)	161/2,312 (7.0)	0.764 [0.609, 0.960] 0.0206	0.751 [0.590, 0.957] 0.0205	-1.641 [-3.025, -0.258] 0.0201
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 80:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.4722</b>							
<b>Yes</b>	8/55 (14.5)	NE [NE, NE]	19.3 [4.6, 31.6]	9/67 (13.4)	NE [NE, NE]	17.0 [5.9, 26.7]	1.106 [0.427, 2.866] 0.8360
<b>No</b>	123/2,31 1 (5.3)	NE [NE, NE]	7.4 [5.8, 9.0]	161/2,31 2 (7.0)	NE [NE, NE]	9.1 [7.4, 10.7]	0.757 [0.598, 0.957] 0.0199
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 70:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Subgroup With History of Stroke or Transient Ischaemic Attack (ITT Population).



**Figure 71:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Subgroup Without History of Stroke or Transient Ischaemic Attack (ITT Population).

#### 4.4.2.2 Secondary Composite Outcome (Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke)

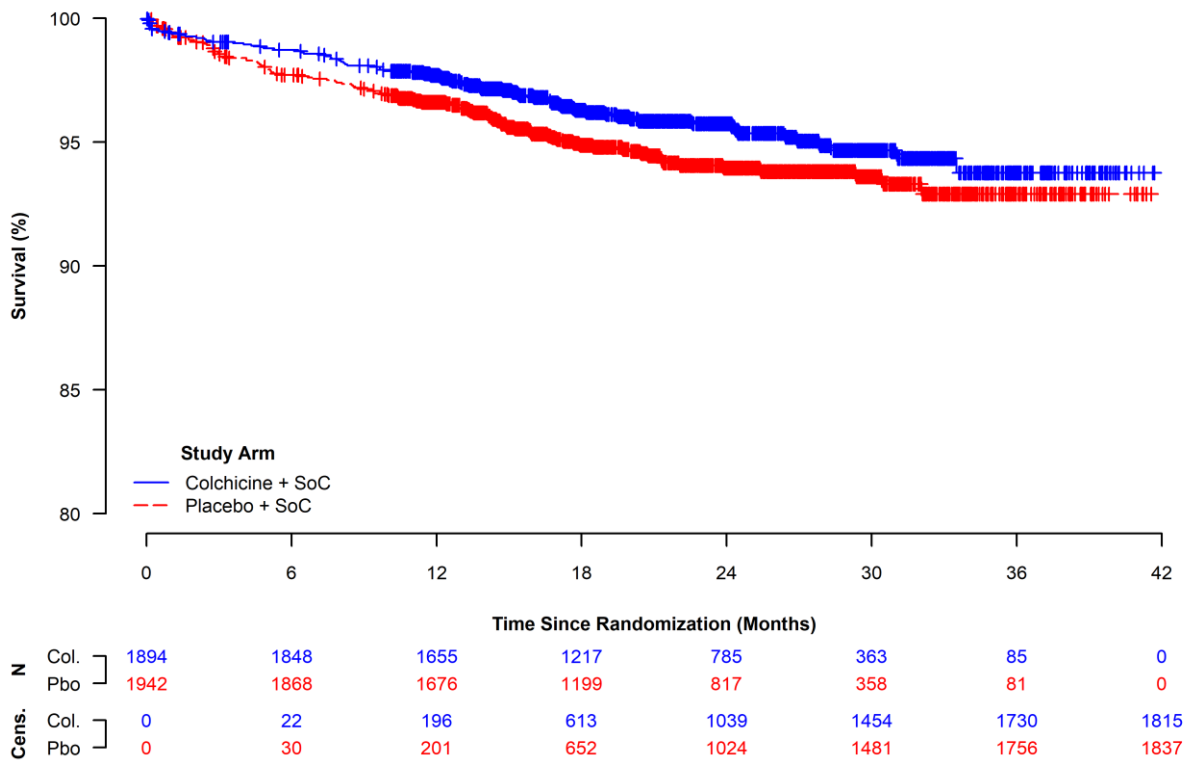
##### 4.4.2.2.1 Subgrouped by Sex

**Table 81:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by Sex (ITT Population).

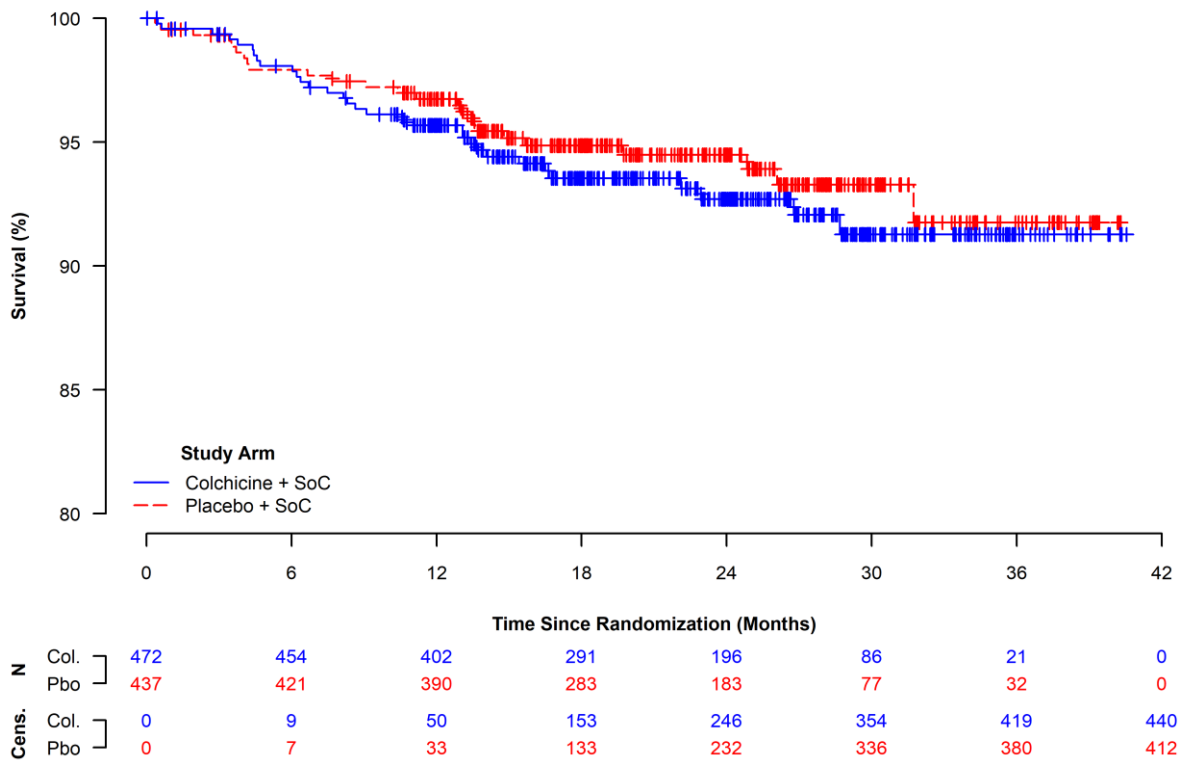
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Sex</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1484</b>					
<b>Male</b>	79/1,894 (4.2)	105/1,942 (5.4)	0.771 [0.580, 1.026] 0.0743	0.762 [0.565, 1.027] 0.0741	-1.236 [-2.586, 0.114] 0.0728
<b>Female</b>	32/472 (6.8)	25/437 (5.7)	1.185 [0.714, 1.967] 0.5113	1.199 [0.698, 2.057] 0.5111	1.059 [-2.085, 4.203] 0.5092
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 82:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by Sex (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Sex</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.1300</b>							
<b>Male</b>	79/1,894 (4.2)	NE [NE, NE]	6.2 [4.4, 8.0]	105/1,942 (5.4)	NE [NE, NE]	7.1 [5.5, 8.7]	0.762 [0.569, 1.020] 0.0681
<b>Female</b>	32/472 (6.8)	NE [NE, NE]	8.7 [5.5, 11.9]	25/437 (5.7)	NE [NE, NE]	8.2 [4.1, 12.2]	1.207 [0.715, 2.036] 0.4817
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 72:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Male Sex Subgroup (ITT Population).



**Figure 73:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Female Sex Subgroup (ITT Population).

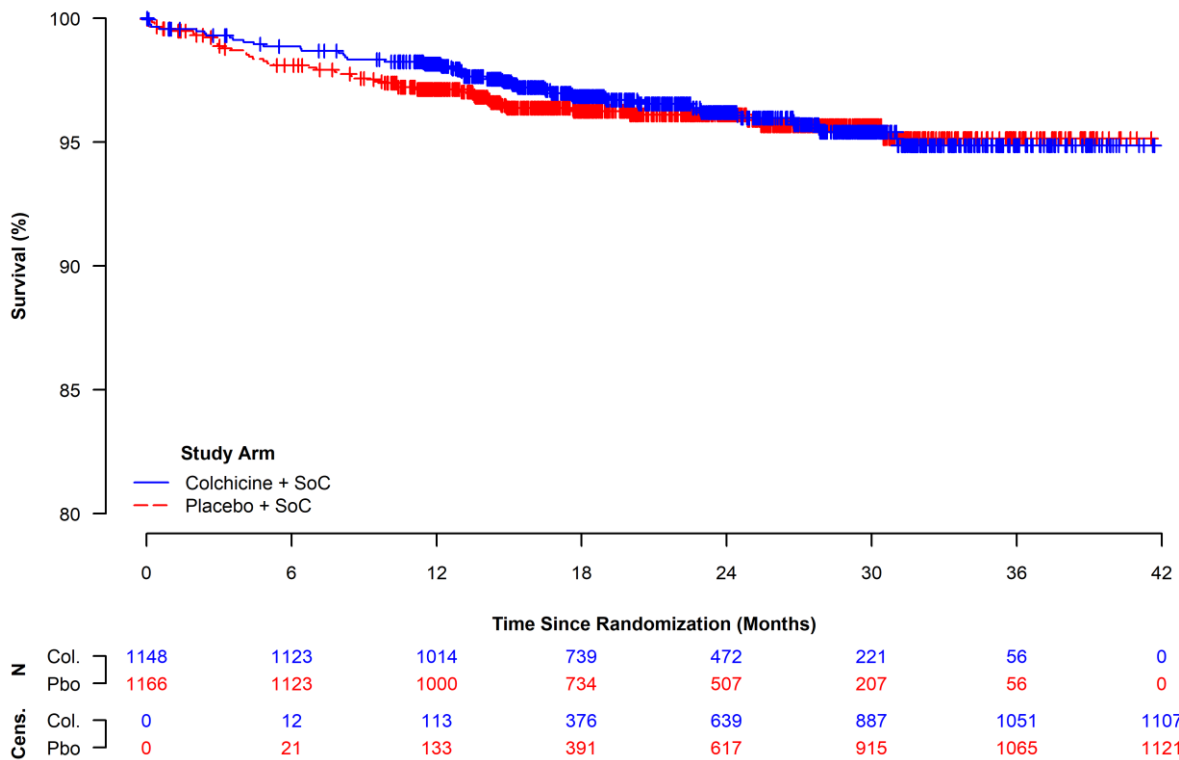
#### 4.4.2.2.2 Subgrouped by Age Group

**Table 83:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by Age Group (ITT Population).

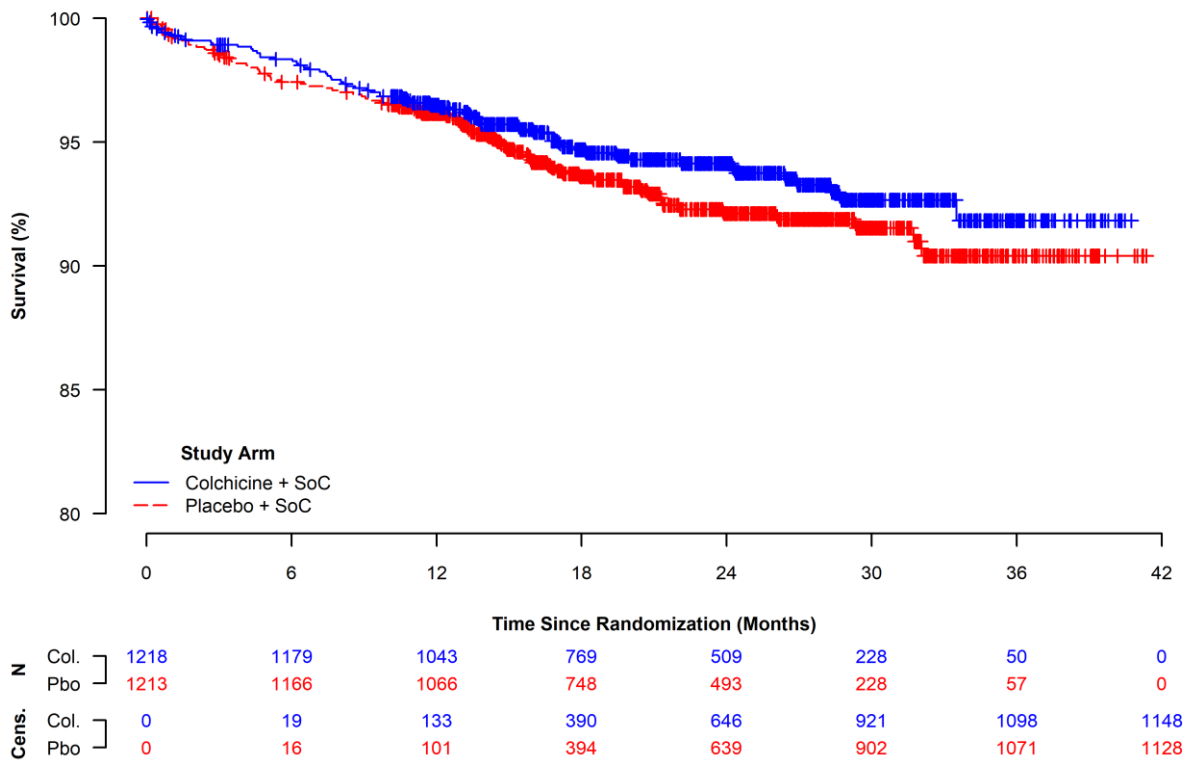
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Age</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.6347</b>					
<b>&lt; 60 Years</b>	41/1,148 (3.6)	45/1,166 (3.9)	0.925 [0.611, 1.402] 0.7144	0.923 [0.599, 1.420] 0.7144	-0.288 [-1.829, 1.253] 0.7142
<b>≥ 60 Years</b>	70/1,218 (5.7)	85/1,213 (7.0)	0.820 [0.604, 1.114] 0.2044	0.809 [0.584, 1.122] 0.2042	-1.260 [-3.202, 0.682] 0.2034
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 84:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by Age Group (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.7058</b>							
< 60 Years	41/1,148 (3.6)	NE [NE, NE]	5.1 [3.3, 7.0]	45/1,166 (3.9)	NE [NE, NE]	4.9 [3.2, 6.5]	0.912 [0.597, 1.392] 0.6686
≥ 60 Years	70/1,218 (5.7)	NE [NE, NE]	8.2 [5.7, 10.6]	85/1,213 (7.0)	NE [NE, NE]	9.6 [7.1, 12.0]	0.823 [0.599, 1.129] 0.2260
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 74:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Age 59 Years or Younger Subgroup (ITT Population).



**Figure 75:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Age 60 Years or Older Subgroup (ITT Population).

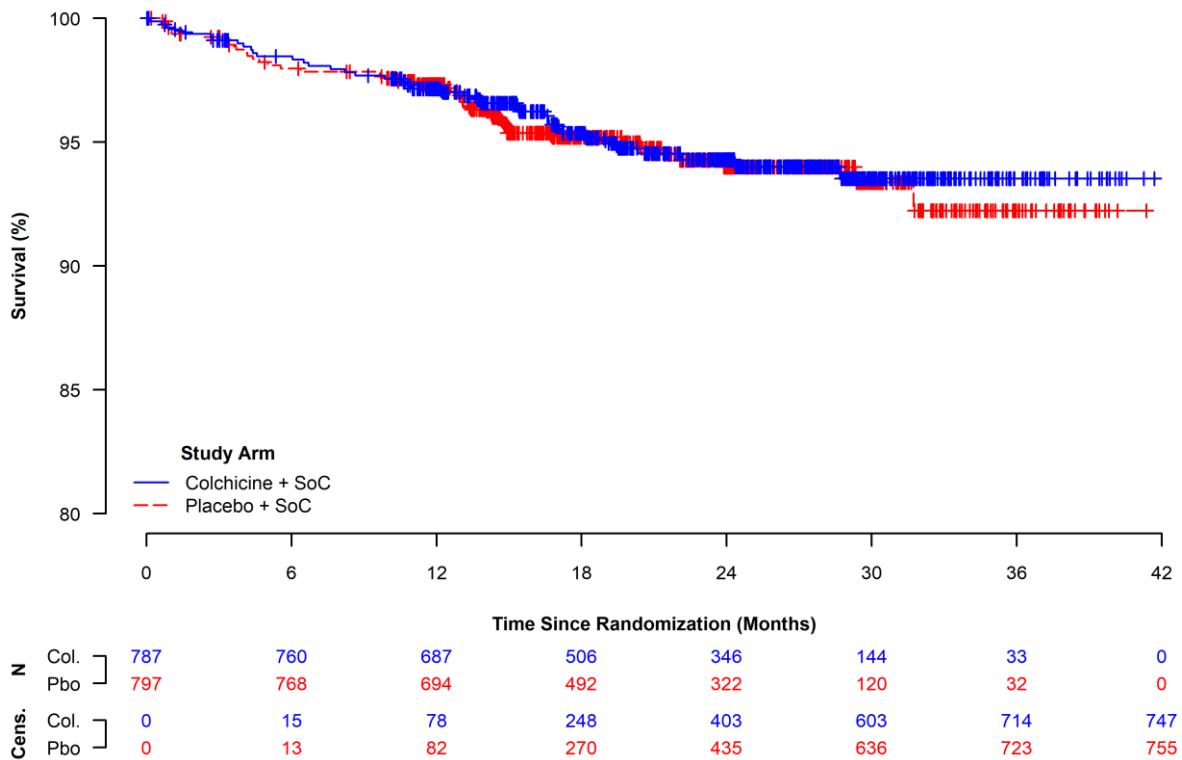
#### 4.4.2.2.3 Subgrouped by Smoking Status

**Table 85:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by Smoking Status (ITT Population).

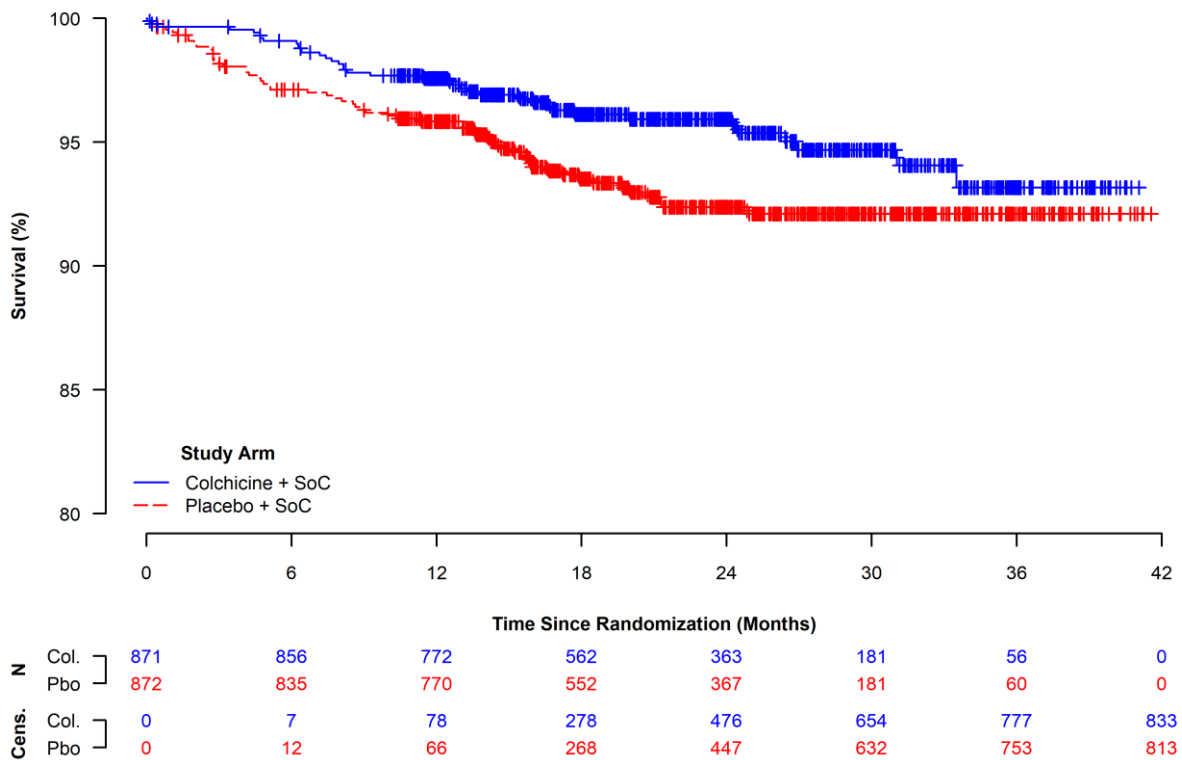
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,377)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Smoking Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1623</b>					
<b>Non</b>	40/787 (5.1)	42/797 (5.3)	0.964 [0.633, 1.470] 0.8665	0.963 [0.617, 1.502] 0.8665	-0.187 [-2.369, 1.995] 0.8665
<b>Ex</b>	38/871 (4.4)	59/872 (6.8)	0.645 [0.434, 0.959] 0.0302	0.629 [0.413, 0.956] 0.0299	-2.403 [-4.552, -0.254] 0.0284
<b>Current</b>	33/708 (4.7)	29/708 (4.1)	1.138 [0.699, 1.854] 0.6037	1.145 [0.687, 1.906] 0.6037	0.565 [-1.566, 2.696] 0.6034
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 86:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by Smoking Status (ITT Population).

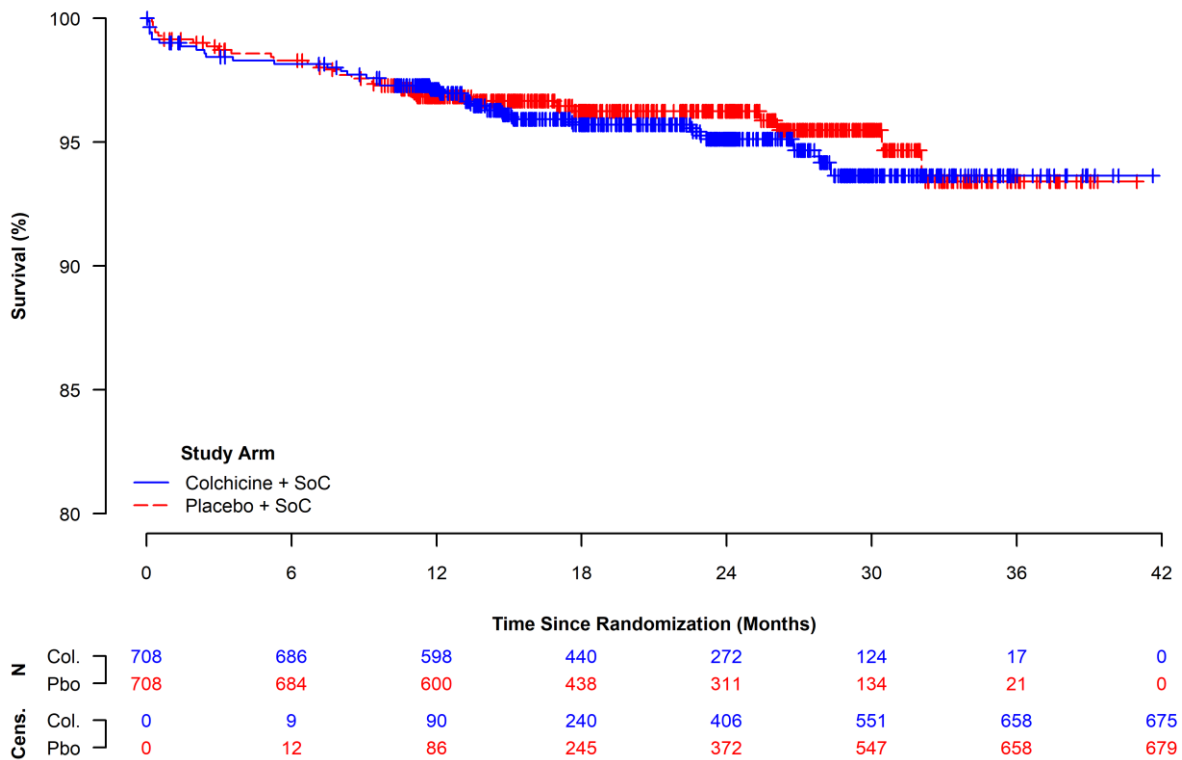
Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,377)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Smoking Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.1694</b>							
<b>Non</b>	40/787 (5.1)	NE [NE, NE]	6.5 [4.4, 8.5]	42/797 (5.3)	NE [NE, NE]	7.8 [4.6, 10.8]	0.949 [0.616, 1.464] 0.8144
<b>Ex</b>	38/871 (4.4)	NE [NE, NE]	6.8 [4.0, 9.6]	59/872 (6.8)	NE [NE, NE]	7.9 [5.9, 9.9]	0.638 [0.425, 0.959] 0.0308
<b>Current</b>	33/708 (4.7)	NE [NE, NE]	6.4 [3.9, 8.7]	29/708 (4.1)	NE [NE, NE]	6.6 [3.1, 9.9]	1.148 [0.697, 1.890] 0.5885
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 76:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Non-Smoker Subgroup (ITT Population).



**Figure 77:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Ex-Smoker Subgroup (ITT Population).



**Figure 78:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Current Smoker Subgroup (ITT Population).

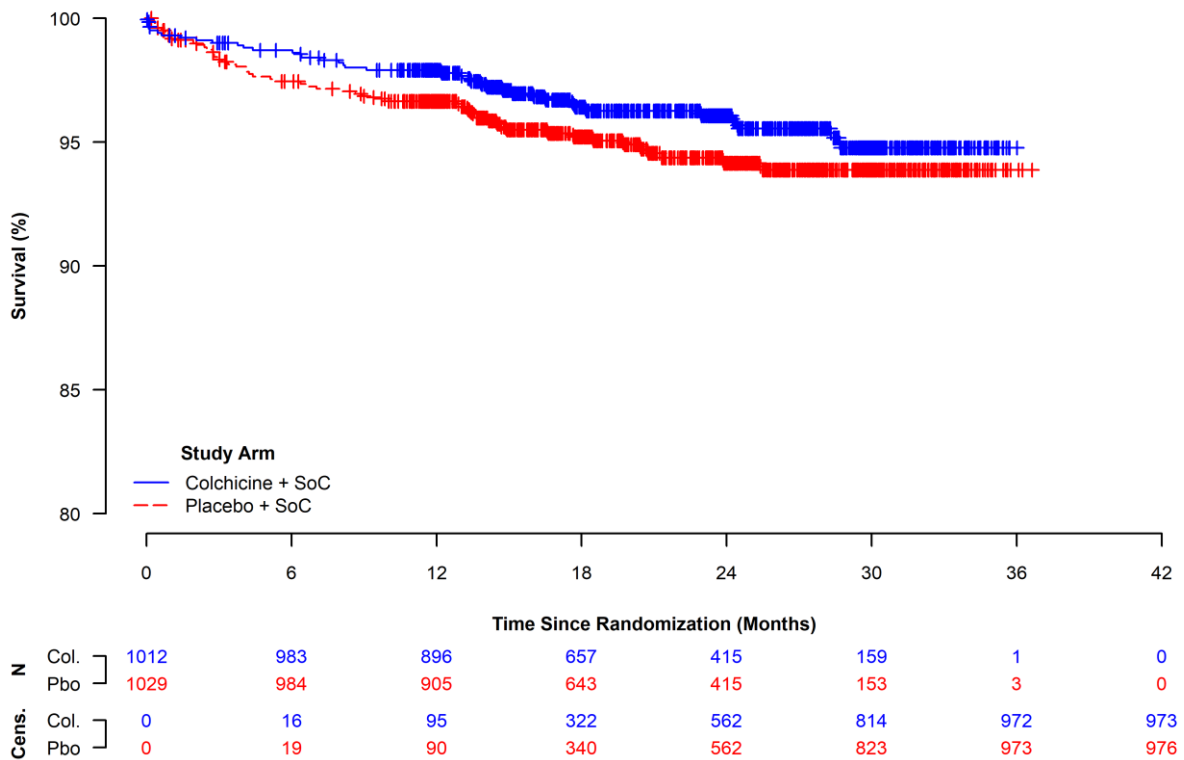
#### 4.4.2.2.4 Subgrouped by Region

**Table 87:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by Region (ITT Population).

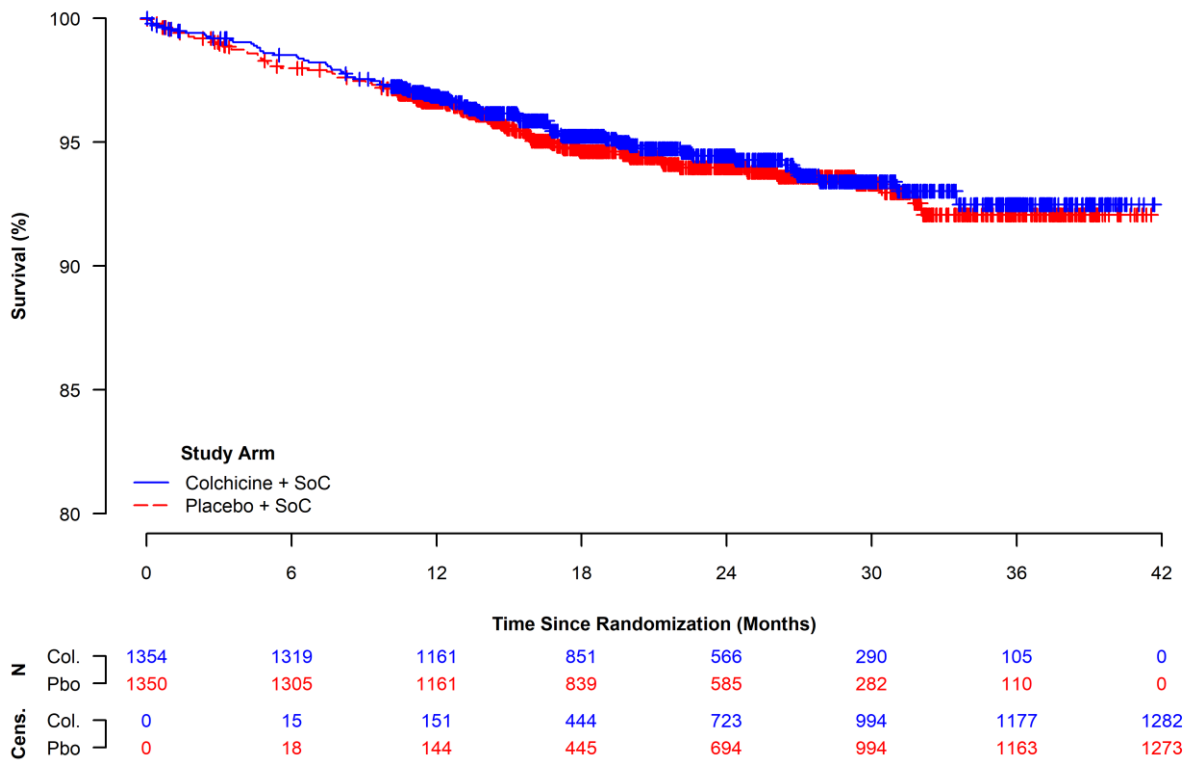
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>d</sup> = 0.4013</b>					
<b>Region</b>					
<b>Europe</b>	39/1,012 (3.9)	53/1,029 (5.2)	0.748 [0.499, 1.121] 0.1597	0.738 [0.484, 1.127] 0.1594	-1.297 [-3.094, 0.500] 0.1573
<b>Non-Europe</b>	72/1,354 (5.3)	77/1,350 (5.7)	0.932 [0.682, 1.274] 0.6600	0.929 [0.667, 1.292] 0.6600	-0.386 [-2.106, 1.334] 0.6600
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 88:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by Region (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.3787</b>							
<b>Europe</b>	39/1,012 (3.9)	NE [NE, NE]	5.2 [3.4, 7.0]	53/1,029 (5.2)	NE [NE, NE]	6.1 [4.4, 7.8]	0.738 [0.488, 1.116] 0.1498
<b>Non-Europe</b>	72/1,354 (5.3)	NE [NE, NE]	7.5 [5.4, 9.6]	77/1,350 (5.7)	NE [NE, NE]	7.9 [5.8, 10.0]	0.932 [0.676, 1.286] 0.6688
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 79:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within European Countries (ITT Population).



**Figure 80:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within Non-European Countries (ITT Population).

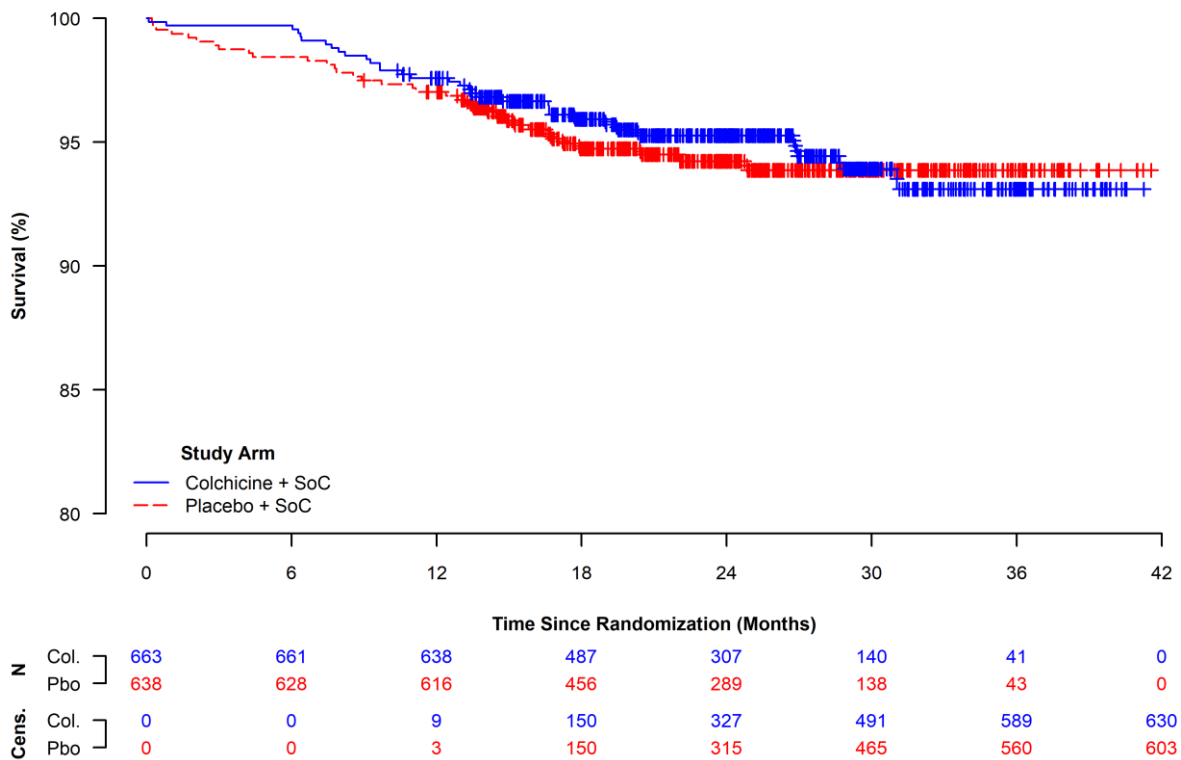
#### 4.4.2.2.5 Subgrouped by White Blood Cell Count

**Table 89:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by White Blood Cell Count (ITT Population).

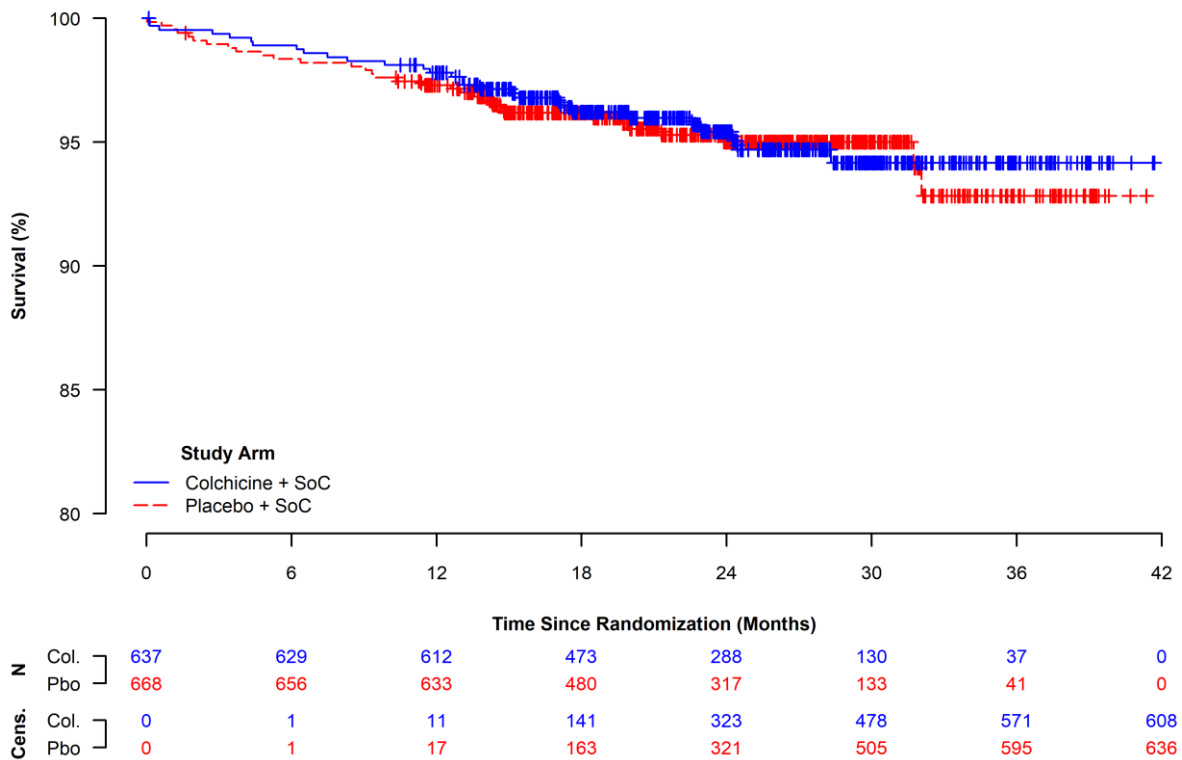
Subgroup	Colchicine + SoC (N = 1,300)	Placebo + SoC (N = 1,306)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8919</b>					
< 8.66 10 <sup>3</sup> /μL	33/663 (5.0)	35/638 (5.5)	0.907 [0.571, 1.442] 0.6805	0.902 [0.554, 1.471] 0.6805	-0.509 [-2.930, 1.913] 0.6806
≥ 8.66 10 <sup>3</sup> /μL	29/637 (4.6)	32/668 (4.8)	0.950 [0.582, 1.552] 0.8388	0.948 [0.567, 1.586] 0.8388	-0.238 [-2.528, 2.052] 0.8387
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 90:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by White Blood Cell Count (ITT Population).

Subgroup	Colchicine + SoC (N = 1,300)			Placebo + SoC (N = 1,306)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.8858</b>							
< 8.66 10 <sup>3</sup> /μL	33/663 (5.0)	NE [NE, NE]	6.9 [4.1, 9.6]	35/638 (5.5)	NE [NE, NE]	6.1 [4.1, 8.1]	0.898 [0.558, 1.444] 0.6561
≥ 8.66 10 <sup>3</sup> /μL	29/637 (4.6)	NE [NE, NE]	5.8 [3.6, 8.1]	32/668 (4.8)	NE [NE, NE]	7.2 [3.7, 10.6]	0.945 [0.572, 1.562] 0.8263
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 81:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Lower White Blood Cell Count Subgroup (ITT Population).



**Figure 82:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Upper White Blood Cell Count Subgroup (ITT Population).

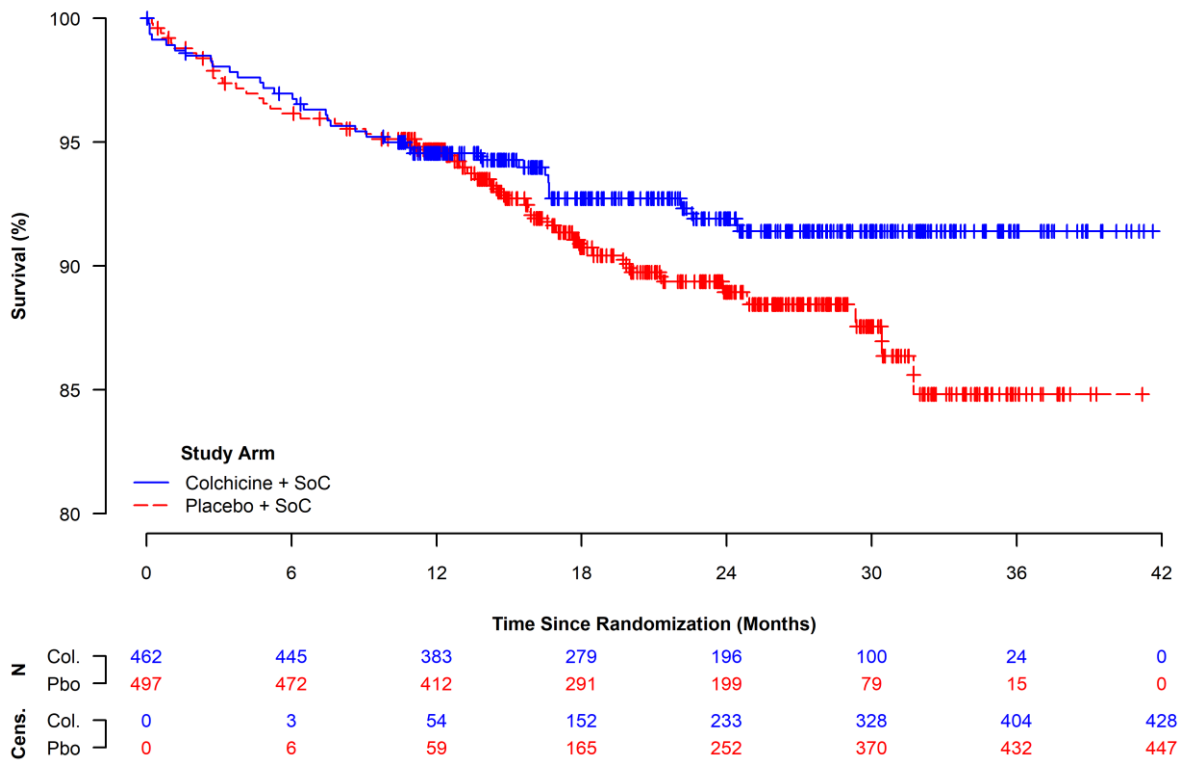
#### 4.4.2.2.6 Subgrouped by Diabetes Status

**Table 91:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by Diabetes Status (ITT Population).

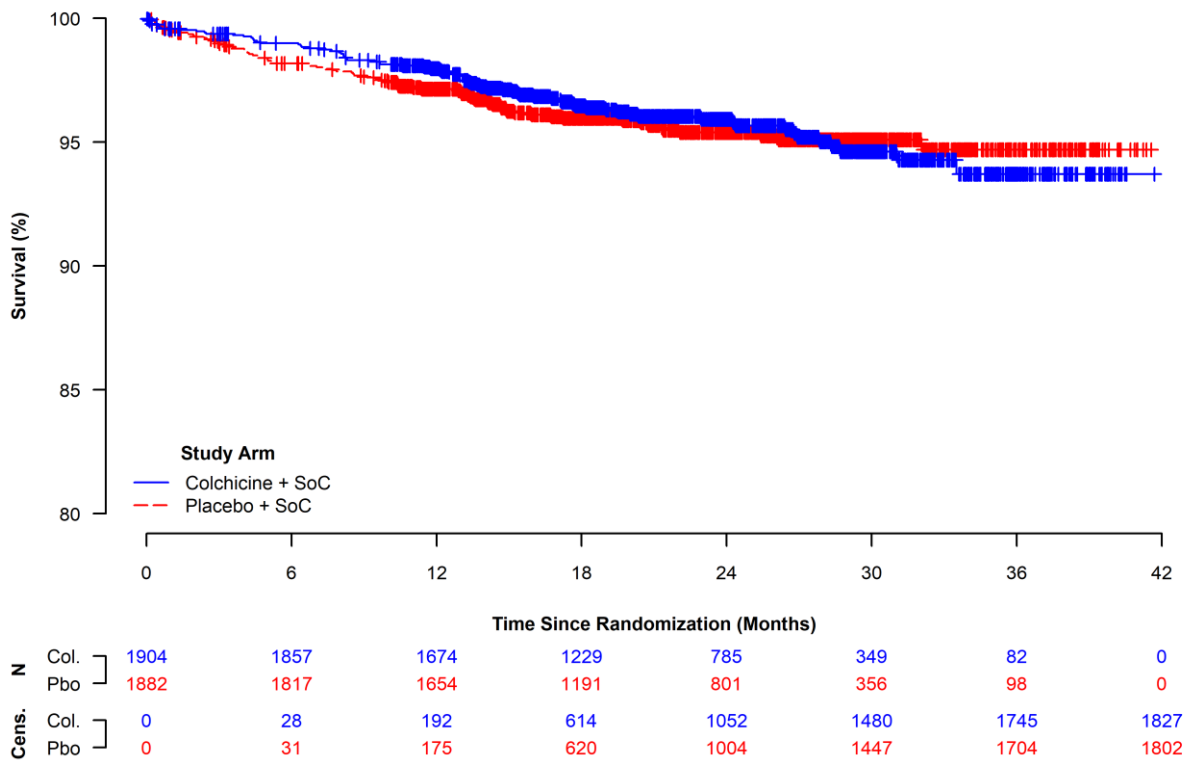
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.3052</b>					
<b>Yes</b>	34/462 (7.4)	50/497 (10.1)	0.732 [0.482, 1.110] 0.1416	0.710 [0.450, 1.120] 0.1408	-2.701 [-6.259, 0.857] 0.1368
<b>No</b>	77/1,904 (4.0)	80/1,882 (4.3)	0.951 [0.700, 1.292] 0.7498	0.949 [0.690, 1.307] 0.7498	-0.207 [-1.477, 1.064] 0.7498
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 92:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by Diabetes Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.3117</b>							
<b>Yes</b>	34/462 (7.4)	NE [NE, NE]	8.6 [5.7, 11.4]	50/497 (10.1)	NE [NE, NE]	15.2 [9.9, 20.2]	0.720 [0.466, 1.114] 0.1401
<b>No</b>	77/1,904 (4.0)	NE [NE, NE]	6.3 [4.4, 8.1]	80/1,882 (4.3)	NE [NE, NE]	5.3 [3.9, 6.7]	0.948 [0.693, 1.297] 0.7392
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 83:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Diabetic Subgroup (ITT Population).



**Figure 84:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Non-Diabetic Subgroup (ITT Population).

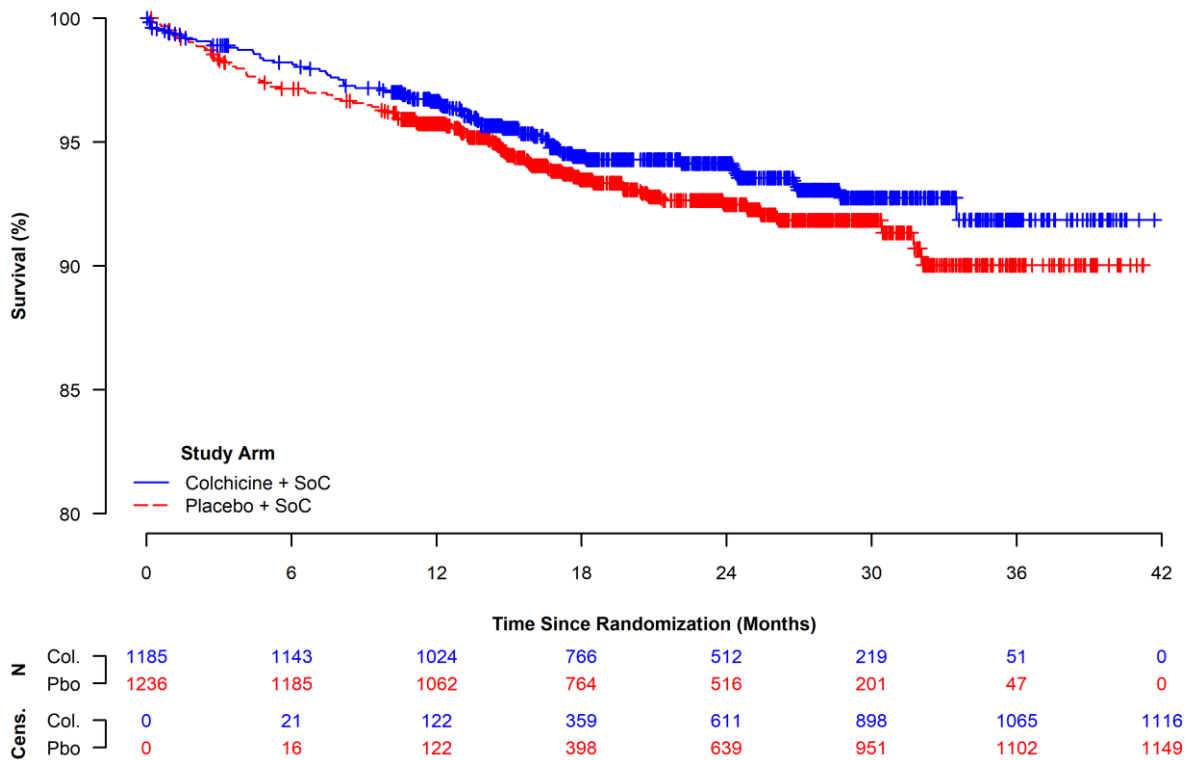
#### 4.4.2.2.7 Subgrouped by Hypertension Status

**Table 93:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by Hypertension Status (ITT Population).

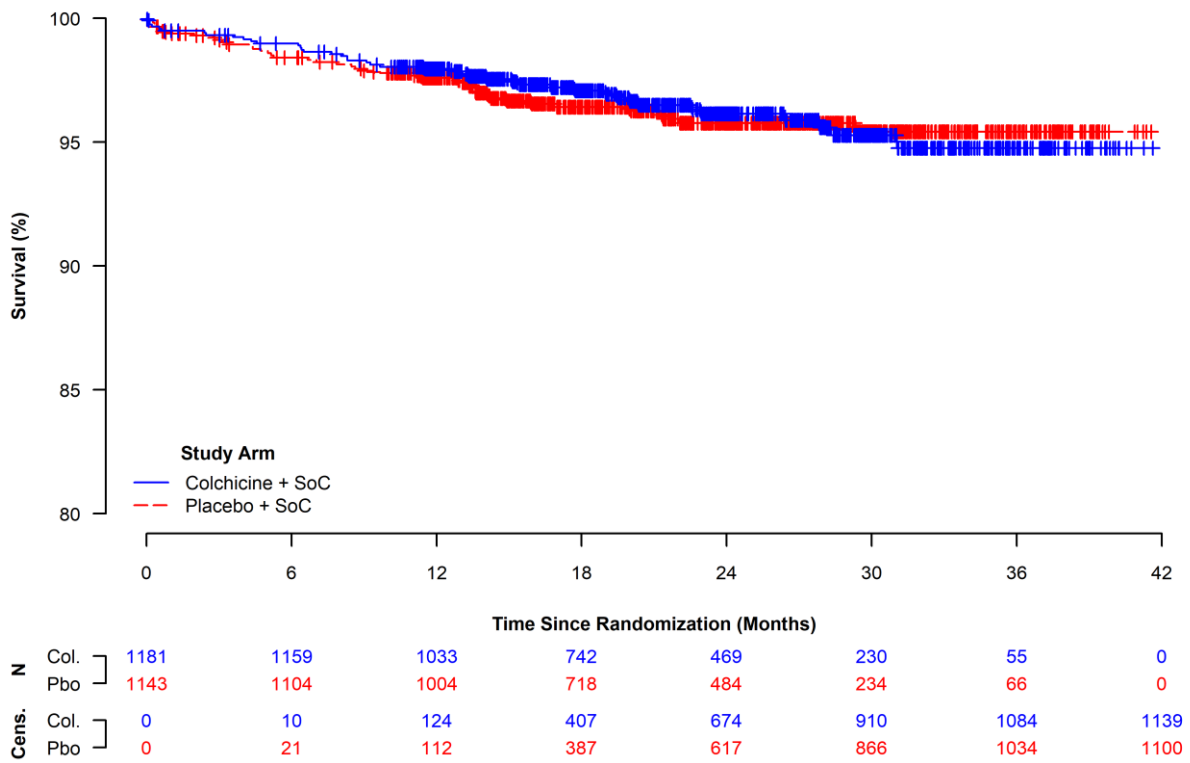
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>					
				<b>Interaction Test p-Value<sup>d</sup> = 0.6021</b>	
<b>Yes</b>	69/1,185 (5.8)	87/1,236 (7.0)	0.827 [0.609, 1.123] 0.2240	0.817 [0.589, 1.132] 0.2238	-1.216 [-3.168, 0.736] 0.2221
<b>No</b>	42/1,181 (3.6)	43/1,143 (3.8)	0.945 [0.623, 1.435] 0.7917	0.943 [0.612, 1.455] 0.7917	-0.206 [-1.733, 1.322] 0.7918
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 94:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by Hypertension Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.5883</b>							
<b>Yes</b>	69/1,185 (5.8)	NE [NE, NE]	8.1 [5.6, 10.6]	87/1,236 (7.0)	NE [NE, NE]	10.0 [7.3, 12.6]	0.817 [0.596, 1.121] 0.2098
<b>No</b>	42/1,181 (3.6)	NE [NE, NE]	5.2 [3.4, 7.1]	43/1,143 (3.8)	NE [NE, NE]	4.6 [3.1, 6.0]	0.945 [0.617, 1.445] 0.7925
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 85:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Hypertensive Subgroup (ITT Population).



**Figure 86:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Normotensive Subgroup (ITT Population).

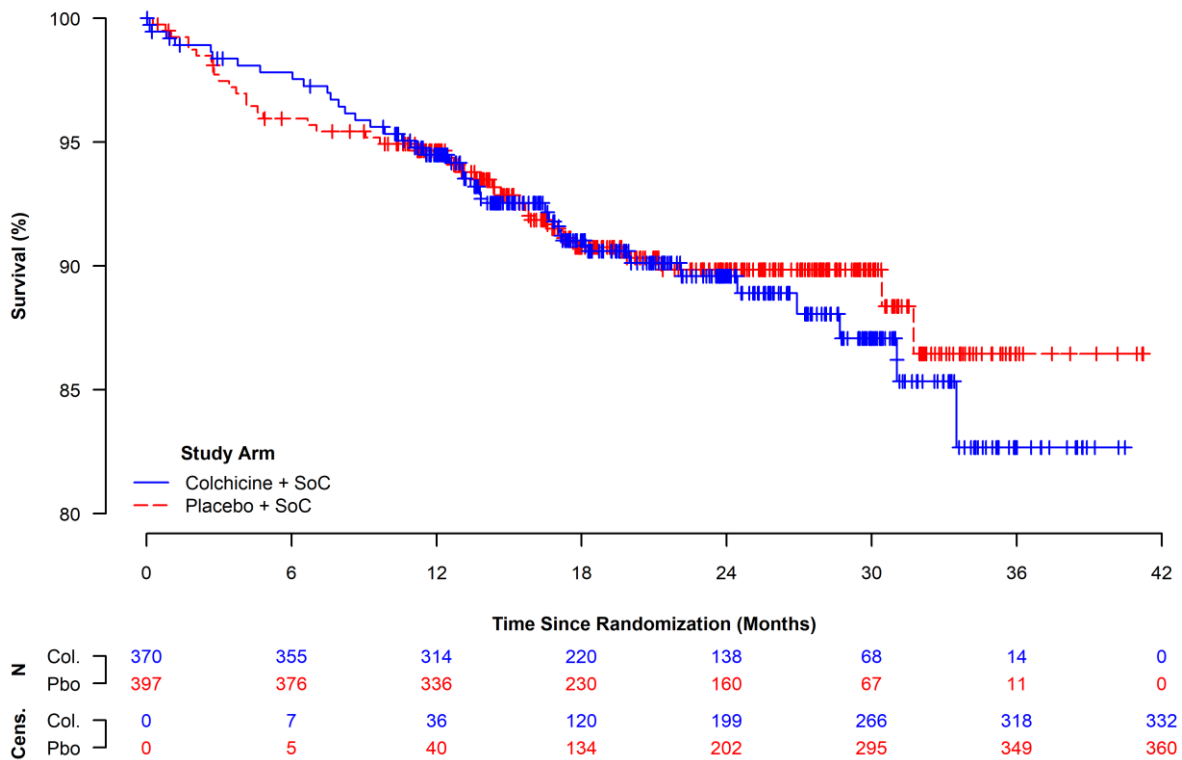
#### 4.4.2.2.8 Subgrouped by History of Myocardial Infarction

**Table 95:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by History of Myocardial Infarction (ITT Population).

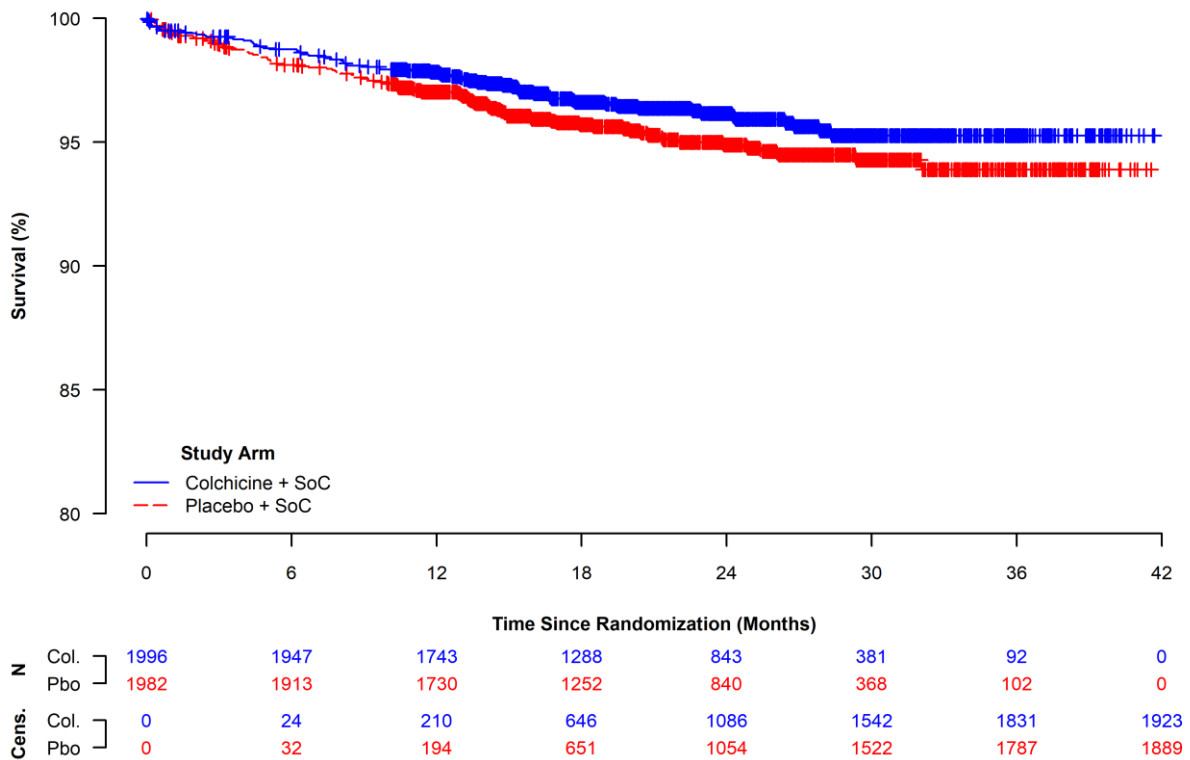
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of MI</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2063</b>					
<b>Yes</b>	38/370 (10.3)	37/397 (9.3)	1.102 [0.717, 1.694] 0.6580	1.114 [0.691, 1.794] 0.6580	0.950 [-3.262, 5.163] 0.6584
<b>No</b>	73/1,996 (3.7)	93/1,982 (4.7)	0.779 [0.577, 1.052] 0.1037	0.771 [0.564, 1.054] 0.1035	-1.035 [-2.278, 0.208] 0.1027
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 96:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by History of Myocardial Infarction (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of MI</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.2013</b>							
<b>Yes</b>	38/370 (10.3)	NE [NE, NE]	17.3 [9.6, 24.4]	37/397 (9.3)	NE [NE, NE]	13.5 [7.7, 19.0]	1.102 [0.701, 1.733] 0.6747
<b>No</b>	73/1,996 (3.7)	NE [NE, NE]	4.7 [3.6, 5.9]	93/1,982 (4.7)	NE [NE, NE]	6.1 [4.7, 7.5]	0.774 [0.569, 1.051] 0.1007
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 87:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Subgroup With History of Myocardial Infarction (ITT Population).



**Figure 88:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Subgroup Without History of Myocardial Infarction (ITT Population).

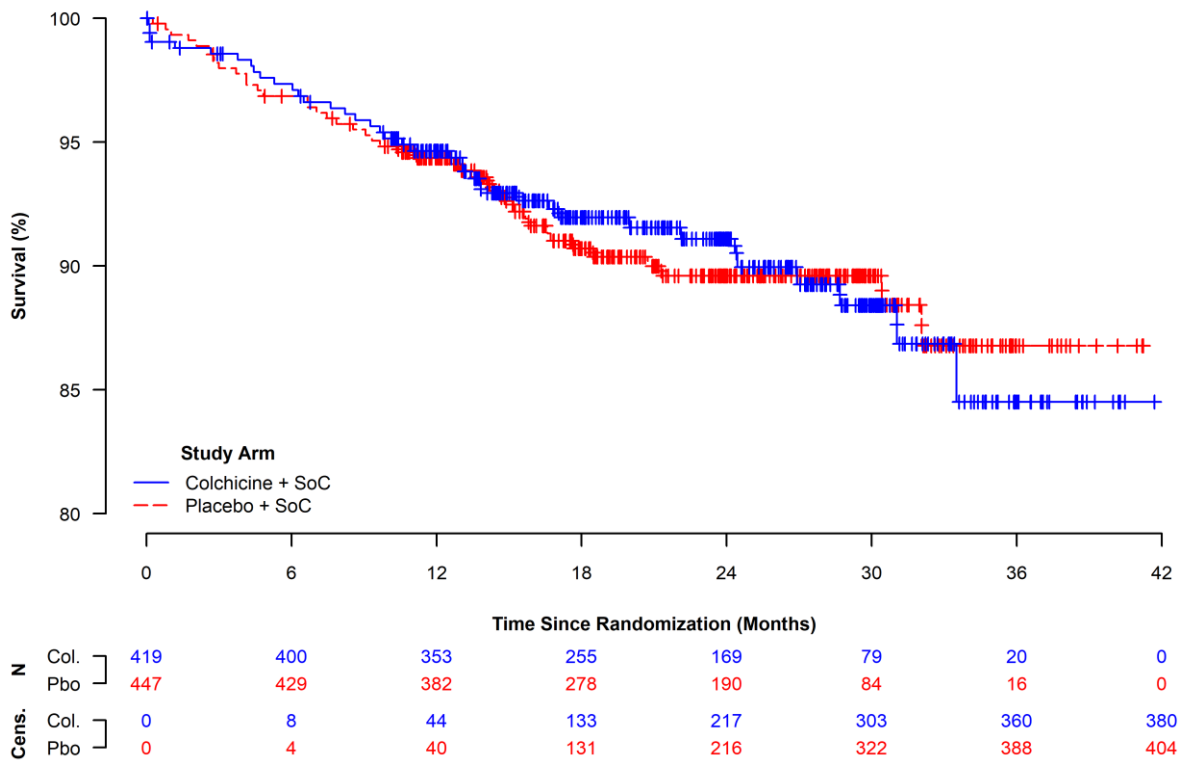
#### 4.4.2.2.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 97:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

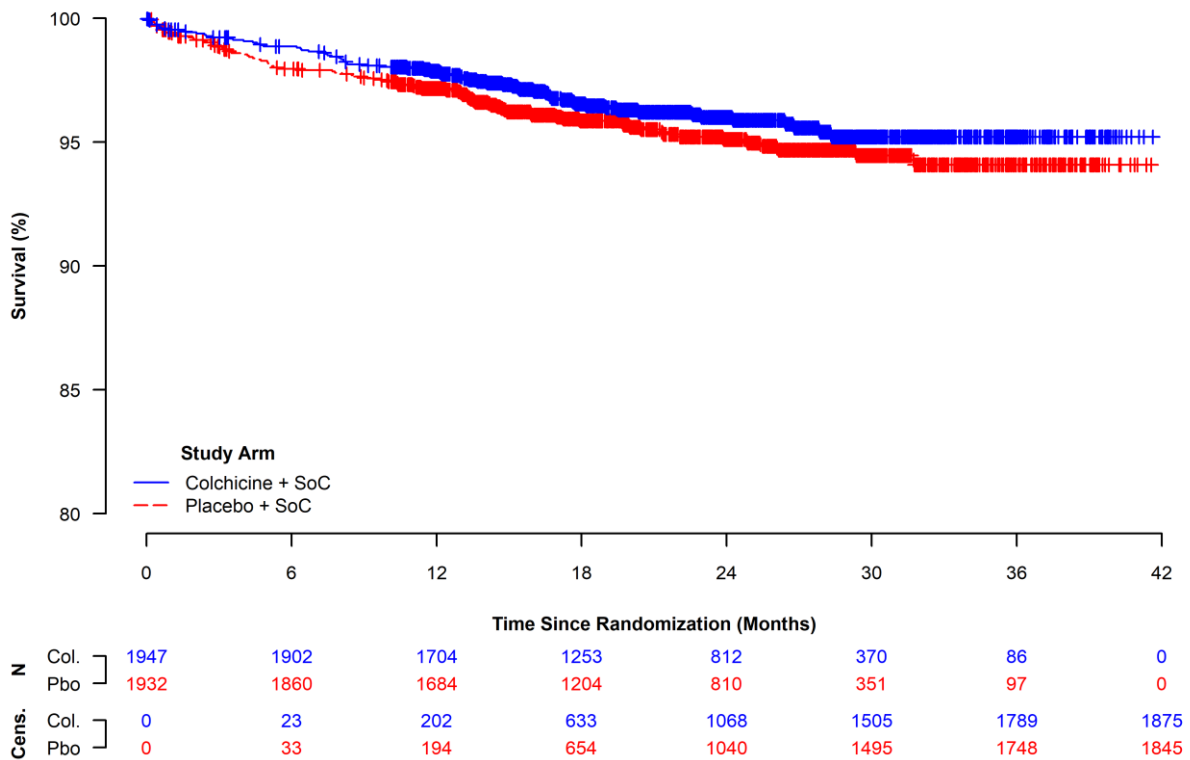
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.5515</b>					
<b>Yes</b>	39/419 (9.3)	43/447 (9.6)	0.968 [0.641, 1.461] 0.8756	0.964 [0.611, 1.521] 0.8755	-0.312 [-4.212, 3.588] 0.8755
<b>No</b>	72/1,947 (3.7)	87/1,932 (4.5)	0.821 [0.605, 1.115] 0.2069	0.814 [0.592, 1.120] 0.2067	-0.805 [-2.053, 0.443] 0.2061
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 98:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.4789</b>							
<b>Yes</b>	39/419 (9.3)	NE [NE, NE]	15.5 [8.7, 21.8]	43/447 (9.6)	NE [NE, NE]	13.2 [8.2, 18.0]	0.986 [0.639, 1.521] 0.9497
<b>No</b>	72/1,947 (3.7)	NE [NE, NE]	4.8 [3.6, 6.0]	87/1,932 (4.5)	NE [NE, NE]	5.9 [4.5, 7.3]	0.812 [0.594, 1.110] 0.1917
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 89:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Subgroup With History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).



**Figure 90:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Subgroup Without History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

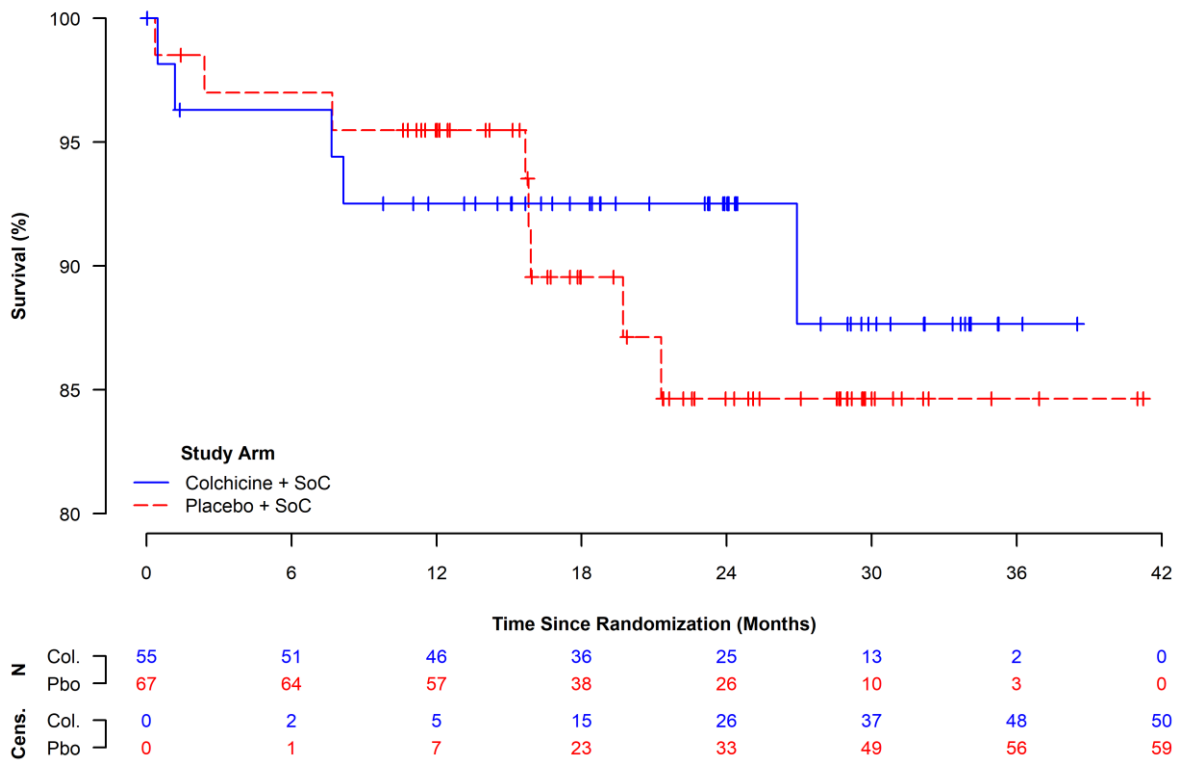
#### 4.4.2.2.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 99:** Proportion of Patients with Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

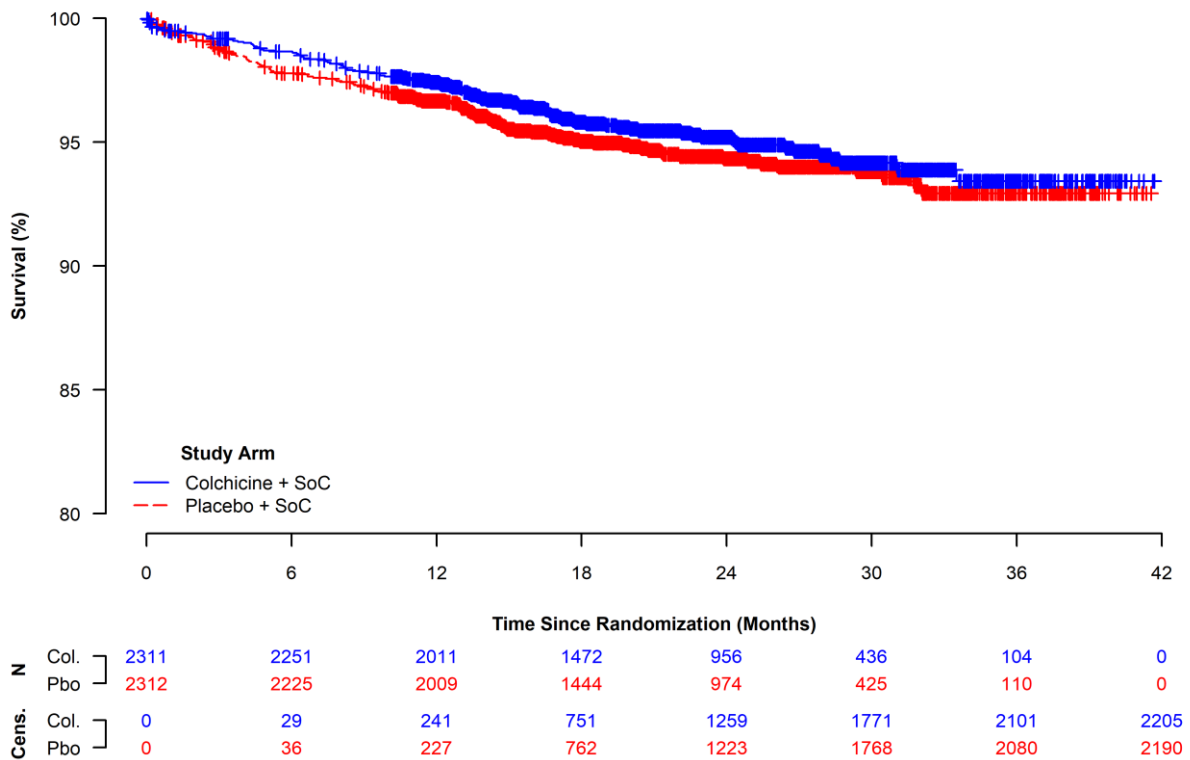
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7982</b>					
<b>Yes</b>	5/55 (9.1)	8/67 (11.9)	0.761 [0.264, 2.195] 0.6138	0.738 [0.227, 2.398] 0.6128	-2.849 [-13.713, 8.014] 0.6072
<b>No</b>	106/2,311 (4.6)	122/2,312 (5.3)	0.869 [0.674, 1.120] 0.2791	0.863 [0.661, 1.127] 0.2790	-0.690 [-1.938, 0.558] 0.2786
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 100:** Time to Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.7993</b>							
<b>Yes</b>	5/55 (9.1)	NE [NE, NE]	12.3 [0.1, 23.1]	8/67 (11.9)	NE [NE, NE]	15.4 [4.7, 24.8]	0.757 [0.248, 2.315] 0.6254
<b>No</b>	106/2,31 1 (4.6)	NE [NE, NE]	6.6 [5.0, 8.1]	122/2,31 2 (5.3)	NE [NE, NE]	7.1 [5.5, 8.6]	0.864 [0.666, 1.121] 0.2714
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 91:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Subgroup With History of Stroke or Transient Ischaemic Attack (ITT Population).



**Figure 92:** Kaplan-Meier Curves for Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, or Stroke, Within the Subgroup Without History of Stroke or Transient Ischaemic Attack (ITT Population).

### **4.4.2.3 Resuscitated Cardiac Arrest**

#### **4.4.2.3.1 Subgrouped by Sex**

The requirements for performing subgroup analyses were not met, i.e., at least one subgroup contained fewer than ten patients and/or, in the case of binary data and time-to-event analyses, no subgroup had at least ten events.

#### **4.4.2.3.2 Subgrouped by Age Group**

The requirements for performing subgroup analyses were not met, i.e., at least one subgroup contained fewer than ten patients and/or, in the case of binary data and time-to-event analyses, no subgroup had at least ten events.

#### **4.4.2.3.3 Subgrouped by Smoking Status**

The requirements for performing subgroup analyses were not met, i.e., at least one subgroup contained fewer than ten patients and/or, in the case of binary data and time-to-event analyses, no subgroup had at least ten events.

#### **4.4.2.3.4 Subgrouped by Region**

The requirements for performing subgroup analyses were not met, i.e., at least one subgroup contained fewer than ten patients and/or, in the case of binary data and time-to-event analyses, no subgroup had at least ten events.

#### **4.4.2.3.5 Subgrouped by White Blood Cell Count**

The requirements for performing subgroup analyses were not met, i.e., at least one subgroup contained fewer than ten patients and/or, in the case of binary data and time-to-event analyses, no subgroup had at least ten events.

#### **4.4.2.3.6 Subgrouped by Diabetes Status**

The requirements for performing subgroup analyses were not met, i.e., at least one subgroup contained fewer than ten patients and/or, in the case of binary data and time-to-event analyses, no subgroup had at least ten events.

#### **4.4.2.3.7 Subgrouped by Hypertension Status**

The requirements for performing subgroup analyses were not met, i.e., at least one subgroup contained fewer than ten patients and/or, in the case of binary data and time-to-event analyses, no subgroup had at least ten events.

#### **4.4.2.3.8 Subgrouped by History of Myocardial Infarction**

The requirements for performing subgroup analyses were not met, i.e., at least one subgroup contained fewer than ten patients and/or, in the case of binary data and time-to-event analyses, no subgroup had at least ten events.

#### **4.4.2.3.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft**

The requirements for performing subgroup analyses were not met, i.e., at least one subgroup contained fewer than ten patients and/or, in the case of binary data and time-to-event analyses, no subgroup had at least ten events.

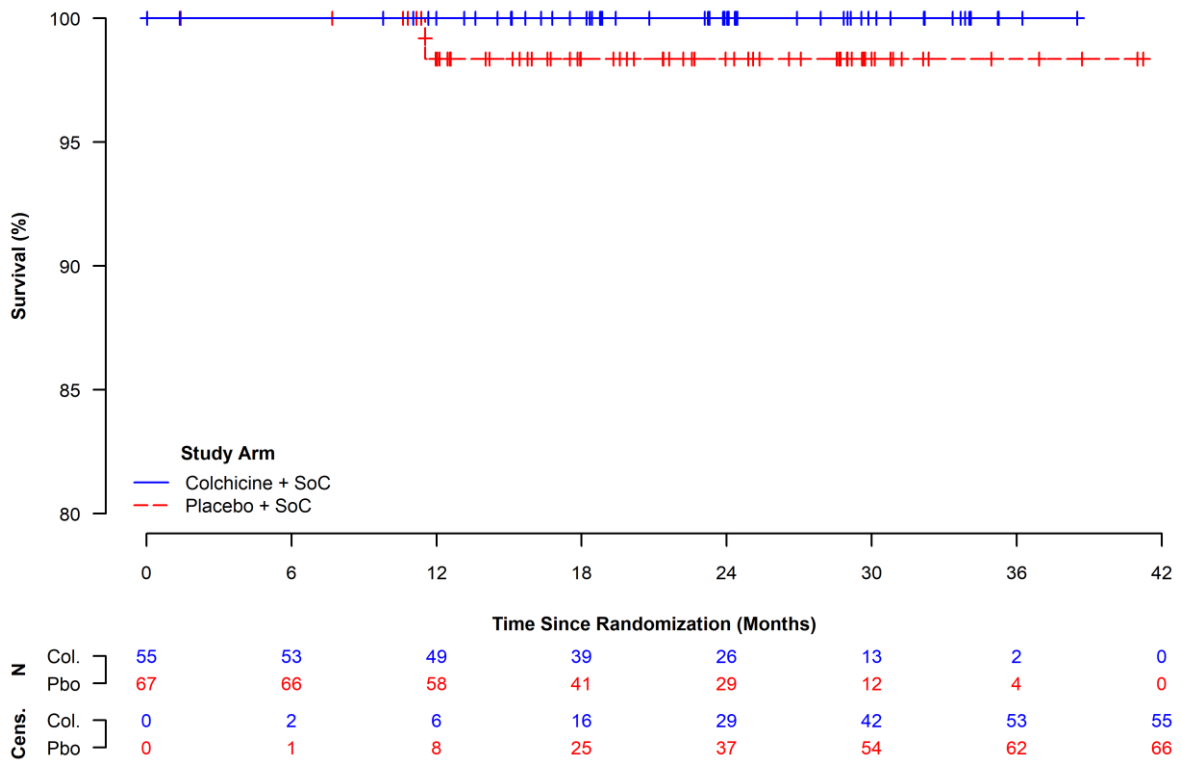
#### 4.4.2.3.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 101:** Proportion of Patients with Resuscitated Cardiac Arrest, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

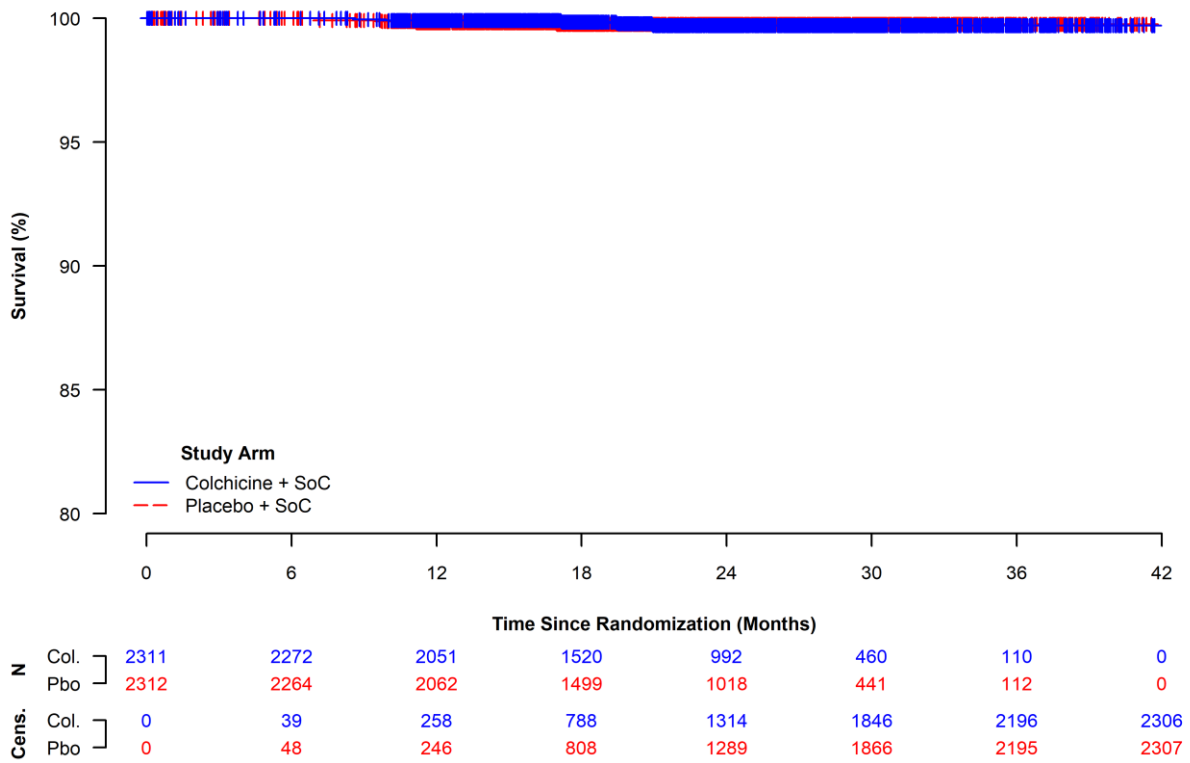
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2875</b>					
<b>Yes</b>	0/55 (0.0)	1/67 (1.5)	0.405 [0.017, 9.743] 0.5773	0.399 [0.016, 10.000] 0.5764	-1.313 [-5.586, 2.960] 0.5470
<b>No</b>	5/2,311 (0.2)	5/2,312 (0.2)	1.000 [0.307, 3.257] 0.9994	1.000 [0.306, 3.267] 0.9994	0.000 [-0.281, 0.281] 0.9994
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 102:** Time to Resuscitated Cardiac Arrest, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>							
<b>Interaction Test p-Value<sup>f</sup> = NE</b>							
<b>Yes</b>	0/55 (0.0)	NE [NE, NE]	0.0 [0.0, 0.0]	1/67 (1.5)	NE [NE, NE]	1.6 [0.0, 4.8]	NE [NE, NE] NE
<b>No</b>	5/2,311 (0.2)	NE [NE, NE]	0.3 [0.0, 0.6]	5/2,312 (0.2)	NE [NE, NE]	0.2 [0.0, 0.5]	0.995 [0.288, 3.435] 0.9931
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 93:** Kaplan-Meier Curves for Resuscitated Cardiac Arrest, Within the Subgroup With History of Stroke or Transient Ischaemic Attack (ITT Population).



**Figure 94:** Kaplan-Meier Curves for Resuscitated Cardiac Arrest, Within the Subgroup Without History of Stroke or Transient Ischaemic Attack (ITT Population).

#### 4.4.2.4 Acute Myocardial Infarction

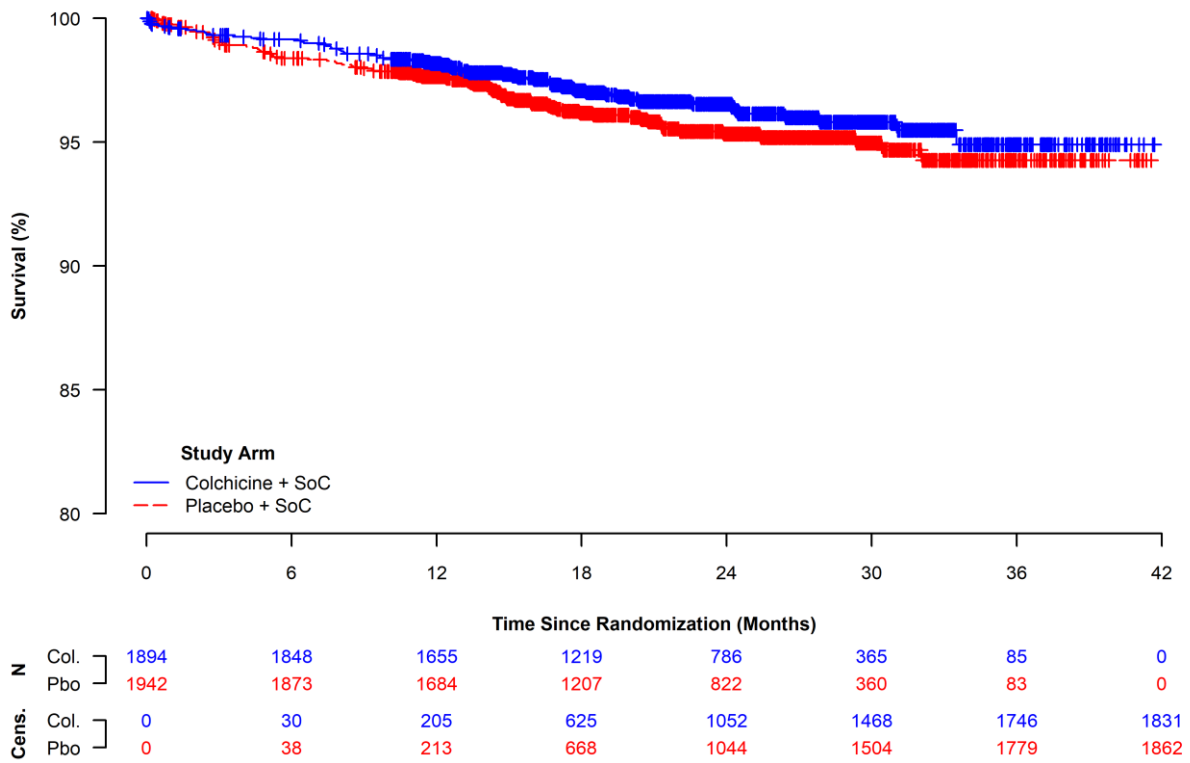
##### 4.4.2.4.1 Subgrouped by Sex

**Table 103:** Proportion of Patients with Acute Myocardial Infarction, Subgrouped by Sex (ITT Population).

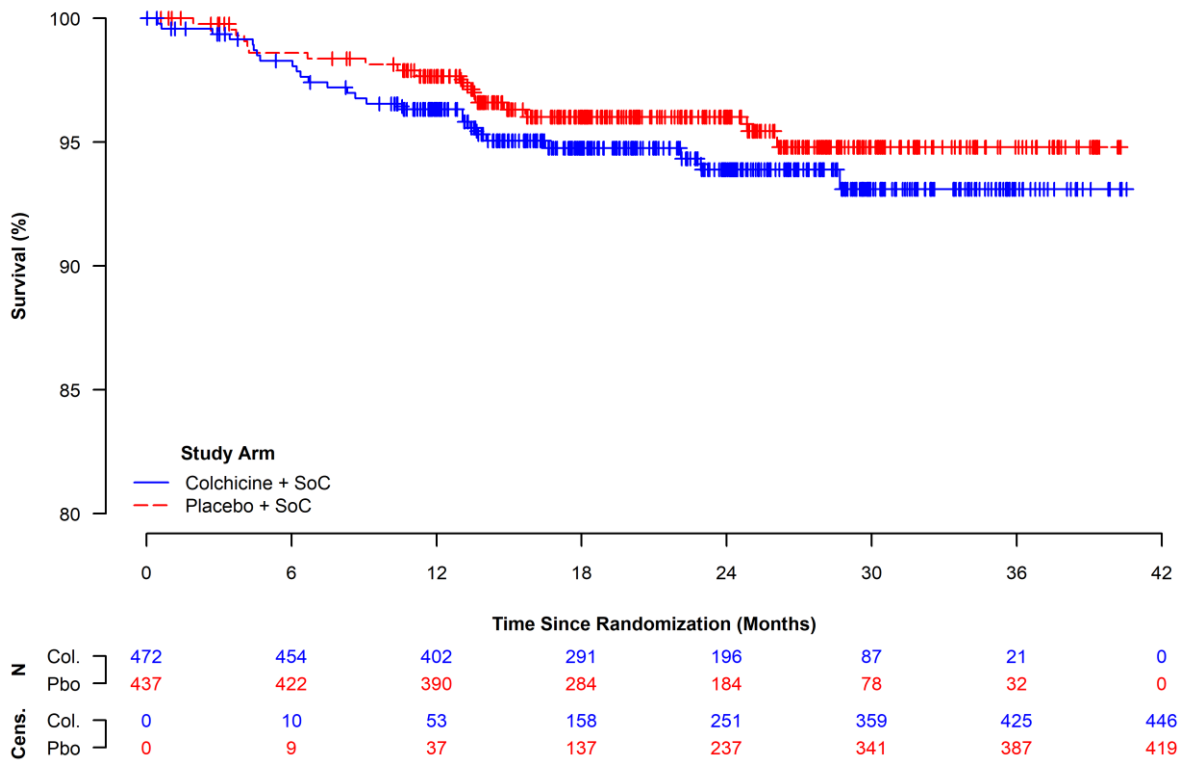
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Sex</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1379</b>					
<b>Male</b>	63/1,894 (3.3)	80/1,942 (4.1)	0.807 [0.584, 1.116] 0.1958	0.801 [0.572, 1.121] 0.1956	-0.793 [-1.990, 0.404] 0.1941
<b>Female</b>	26/472 (5.5)	18/437 (4.1)	1.337 [0.744, 2.405] 0.3315	1.357 [0.733, 2.511] 0.3311	1.389 [-1.387, 4.166] 0.3266
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 104:** Time to Acute Myocardial Infarction, Subgrouped by Sex (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Sex</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.1220</b>							
<b>Male</b>	63/1,894 (3.3)	NE [NE, NE]	5.1 [3.4, 6.8]	80/1,942 (4.1)	NE [NE, NE]	5.7 [4.2, 7.2]	0.800 [0.575, 1.113] 0.1846
<b>Female</b>	26/472 (5.5)	NE [NE, NE]	6.9 [4.0, 9.7]	18/437 (4.1)	NE [NE, NE]	5.2 [2.6, 7.7]	1.363 [0.747, 2.487] 0.3121
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 95:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Male Sex Subgroup (ITT Population).



**Figure 96:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Female Sex Subgroup (ITT Population).

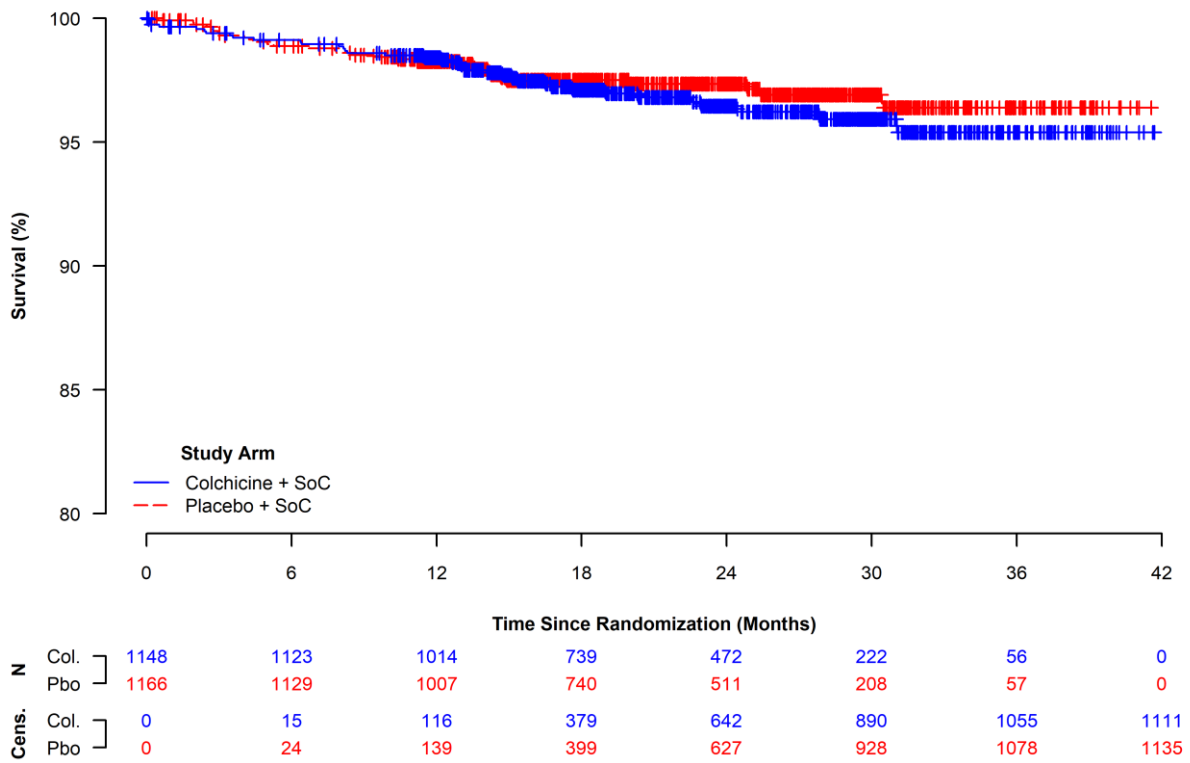
#### 4.4.2.4.2 Subgrouped by Age Group

**Table 105:** Proportion of Patients with Acute Myocardial Infarction, Subgrouped by Age Group (ITT Population).

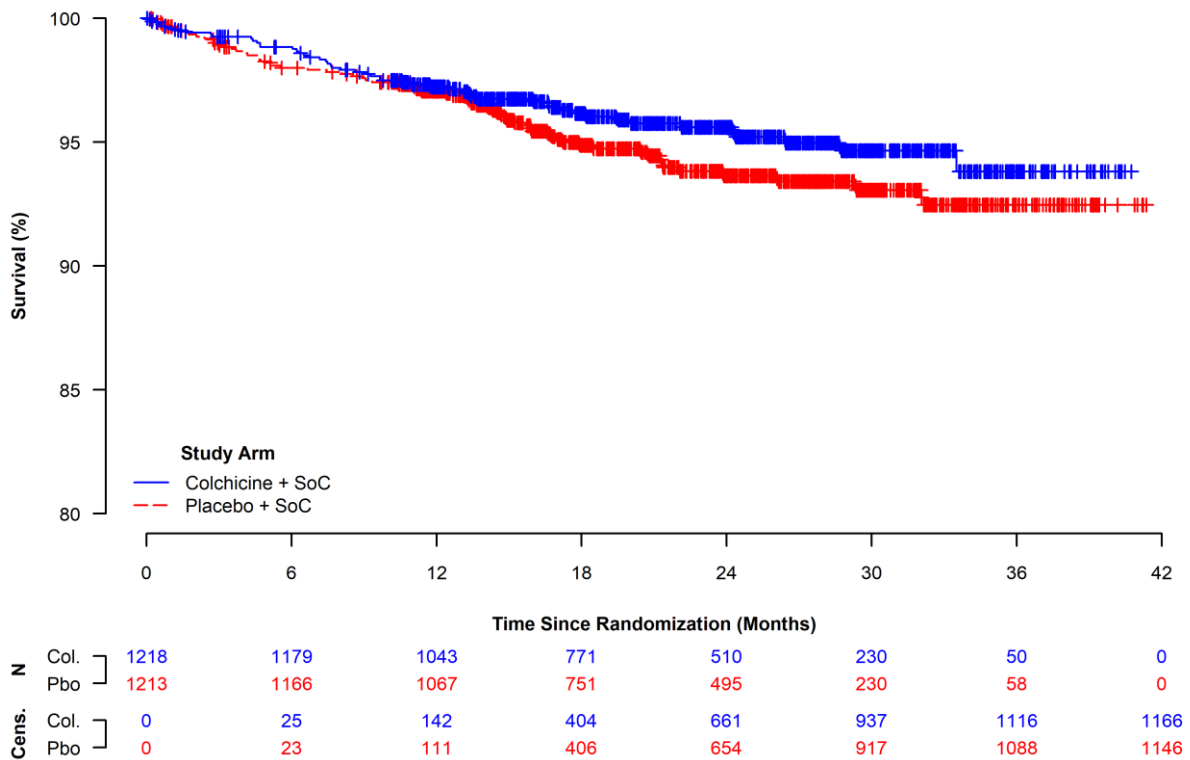
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Age</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1310</b>					
<b>&lt; 60 Years</b>	37/1,148 (3.2)	31/1,166 (2.7)	1.212 [0.758, 1.940] 0.4224	1.219 [0.751, 1.979] 0.4223	0.564 [-0.813, 1.941] 0.4219
<b>≥ 60 Years</b>	52/1,218 (4.3)	67/1,213 (5.5)	0.773 [0.543, 1.101] 0.1532	0.763 [0.526, 1.106] 0.1529	-1.254 [-2.969, 0.461] 0.1518
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 106:** Time to Acute Myocardial Infarction, Subgrouped by Age Group (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.1526</b>							
<b>&lt; 60 Years</b>	37/1,148 (3.2)	NE [NE, NE]	4.6 [2.8, 6.4]	31/1,166 (2.7)	NE [NE, NE]	3.6 [2.1, 5.1]	1.199 [0.744, 1.932] 0.4563
<b>≥ 60 Years</b>	52/1,218 (4.3)	NE [NE, NE]	6.2 [3.9, 8.4]	67/1,213 (5.5)	NE [NE, NE]	7.5 [5.4, 9.6]	0.775 [0.540, 1.113] 0.1679
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 97:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Age 59 Years or Younger Subgroup (ITT Population).



**Figure 98:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Age 60 Years or Older Subgroup (ITT Population).

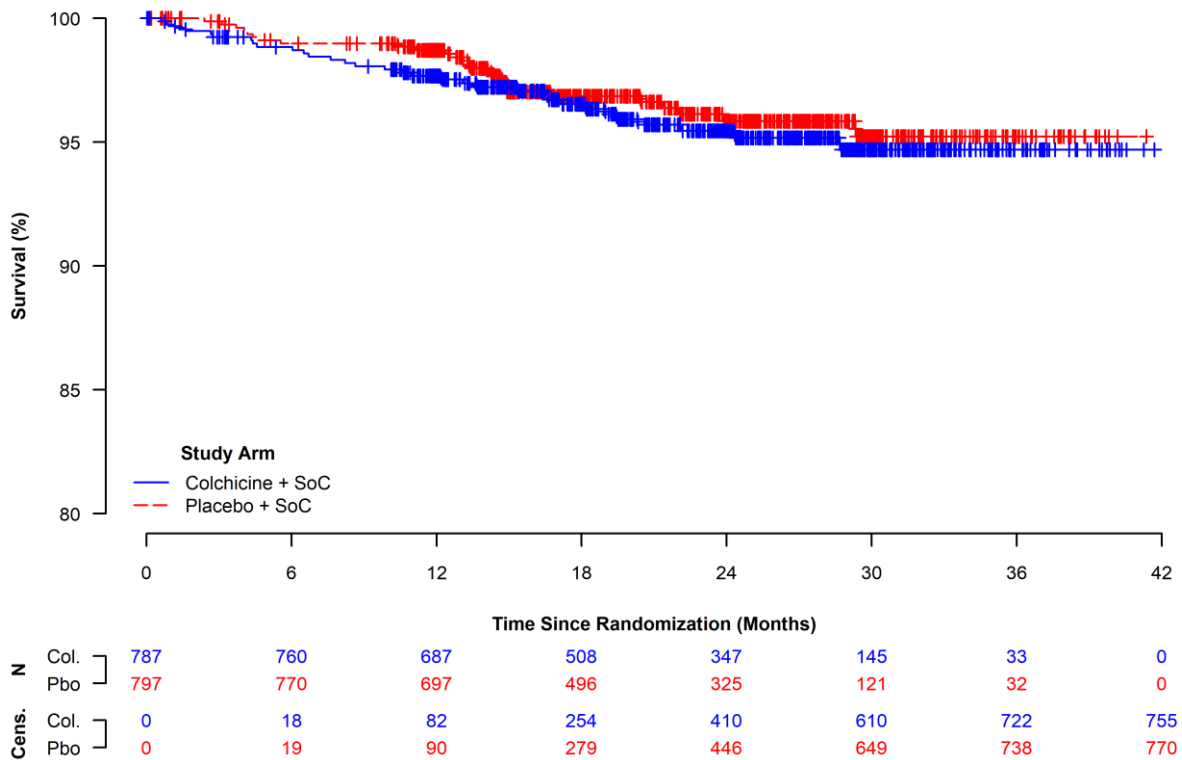
#### 4.4.2.4.3 Subgrouped by Smoking Status

**Table 107:** Proportion of Patients with Acute Myocardial Infarction, Subgrouped by Smoking Status (ITT Population).

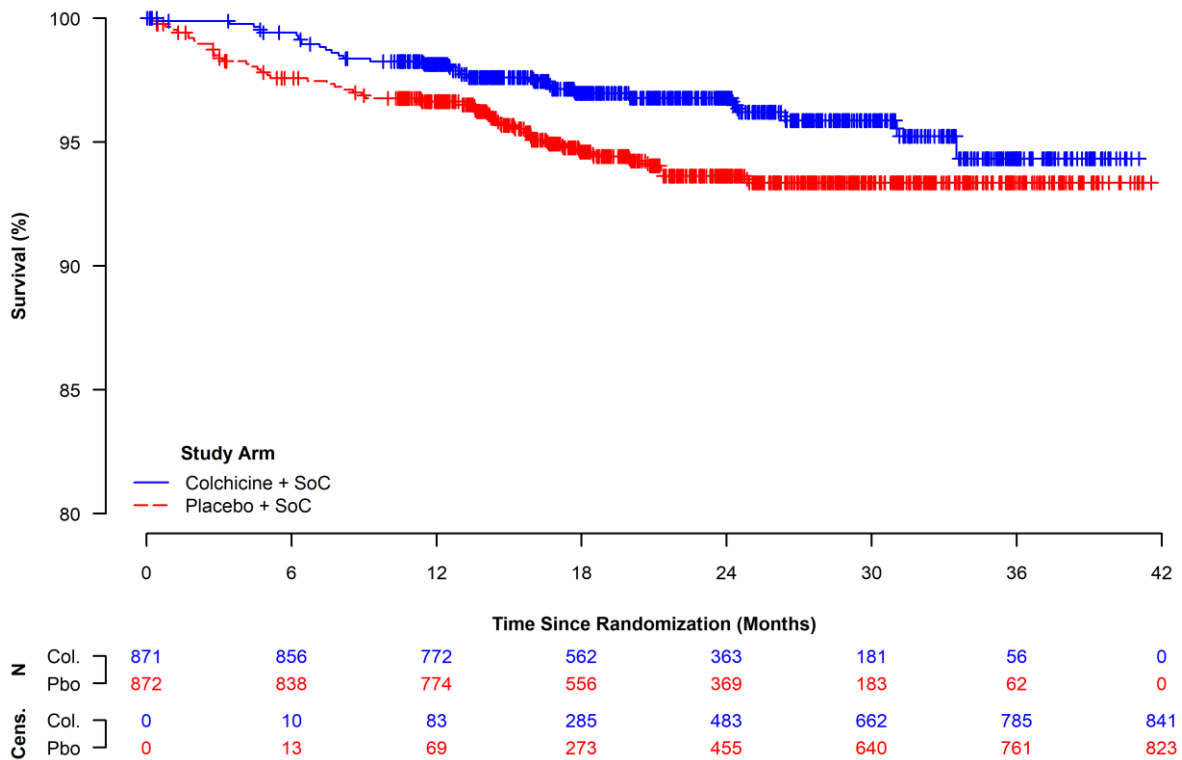
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,377)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Smoking Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.0660</b>					
<b>Non</b>	32/787 (4.1)	27/797 (3.4)	1.200 [0.726, 1.984] 0.4766	1.209 [0.717, 2.037] 0.4765	0.678 [-1.188, 2.544] 0.4761
<b>Ex</b>	30/871 (3.4)	49/872 (5.6)	0.613 [0.393, 0.956] 0.0309	0.599 [0.377, 0.953] 0.0306	-2.175 [-4.125, -0.225] 0.0288
<b>Current</b>	27/708 (3.8)	22/708 (3.1)	1.227 [0.706, 2.134] 0.4681	1.236 [0.697, 2.192] 0.4680	0.706 [-1.197, 2.610] 0.4672
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 108:** Time to Acute Myocardial Infarction, Subgrouped by Smoking Status (ITT Population).

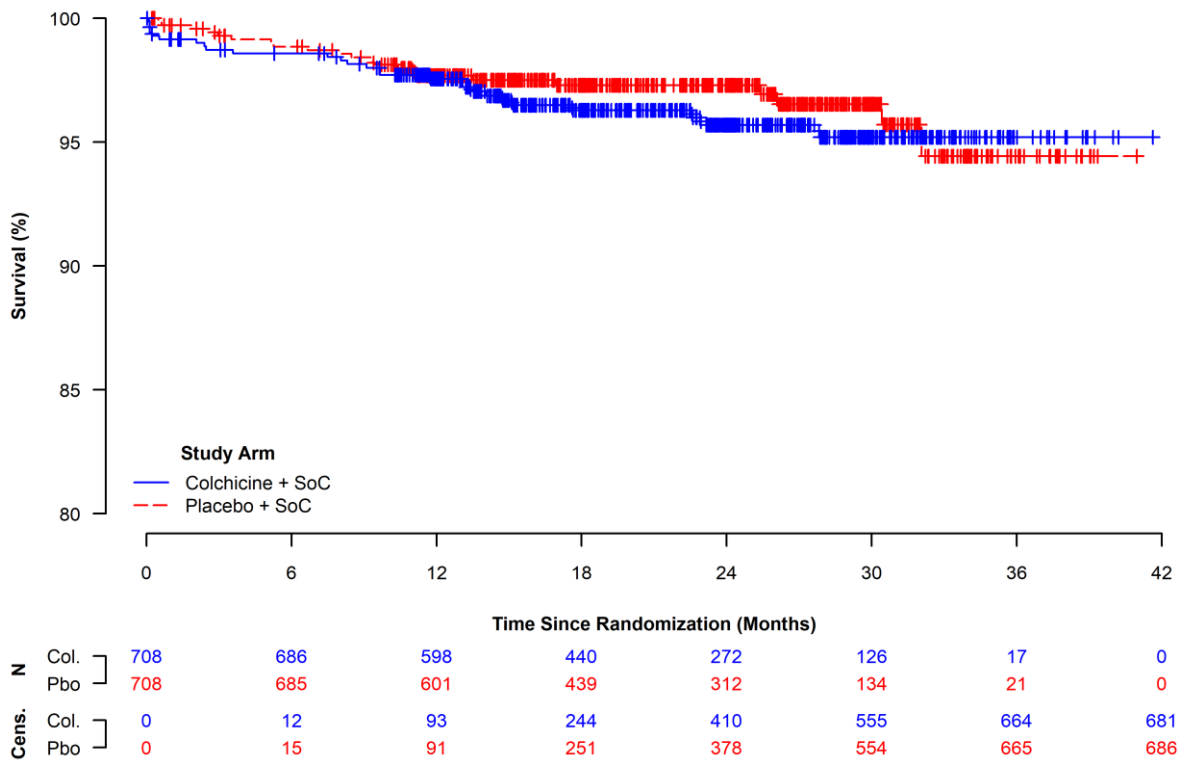
Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,377)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Smoking Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.0726</b>							
<b>Non</b>	32/787 (4.1)	NE [NE, NE]	5.3 [3.3, 7.2]	27/797 (3.4)	NE [NE, NE]	4.8 [2.7, 6.8]	1.184 [0.710, 1.977] 0.5175
<b>Ex</b>	30/871 (3.4)	NE [NE, NE]	5.7 [3.0, 8.3]	49/872 (5.6)	NE [NE, NE]	6.6 [4.8, 8.5]	0.609 [0.387, 0.960] 0.0326
<b>Current</b>	27/708 (3.8)	NE [NE, NE]	4.8 [2.9, 6.7]	22/708 (3.1)	NE [NE, NE]	5.6 [2.2, 8.9]	1.238 [0.705, 2.174] 0.4569
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 99:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Non-Smoker Subgroup (ITT Population).



**Figure 100:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Ex-Smoker Subgroup (ITT Population).



**Figure 101:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Current Smoker Subgroup (ITT Population).

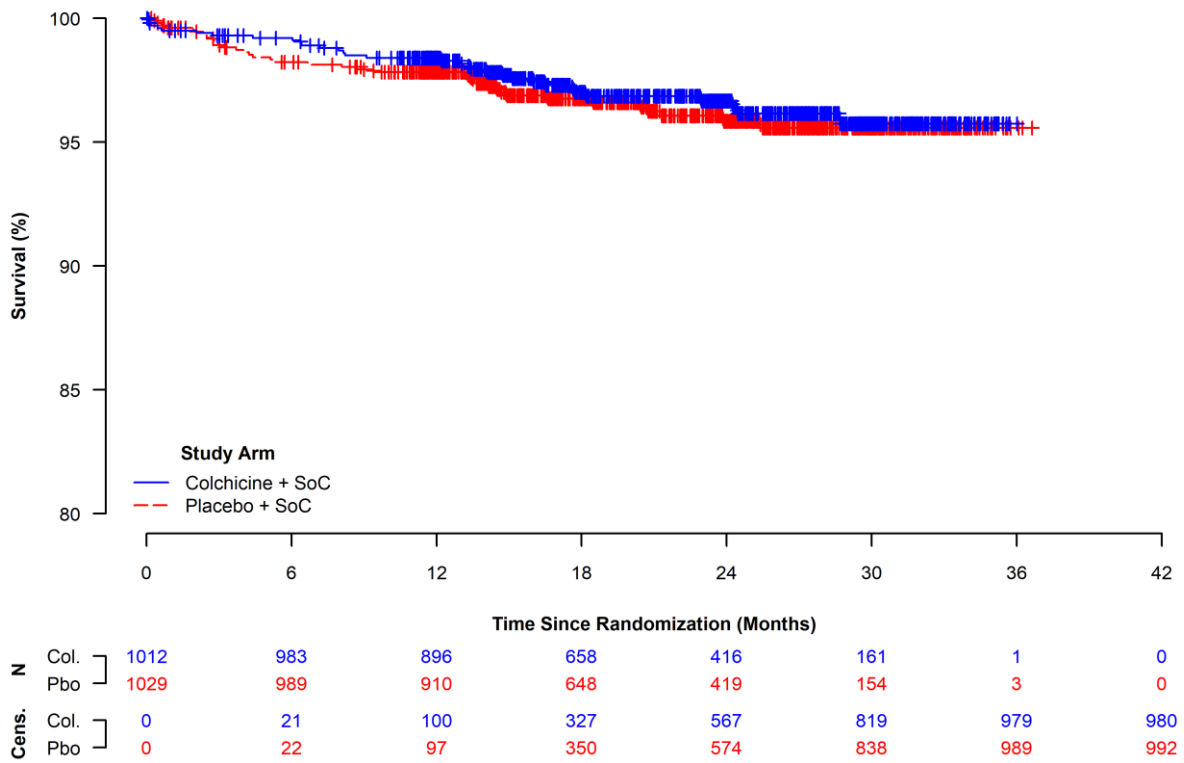
#### 4.4.2.4.4 Subgrouped by Region

**Table 109:** Proportion of Patients with Acute Myocardial Infarction, Subgrouped by Region (ITT Population).

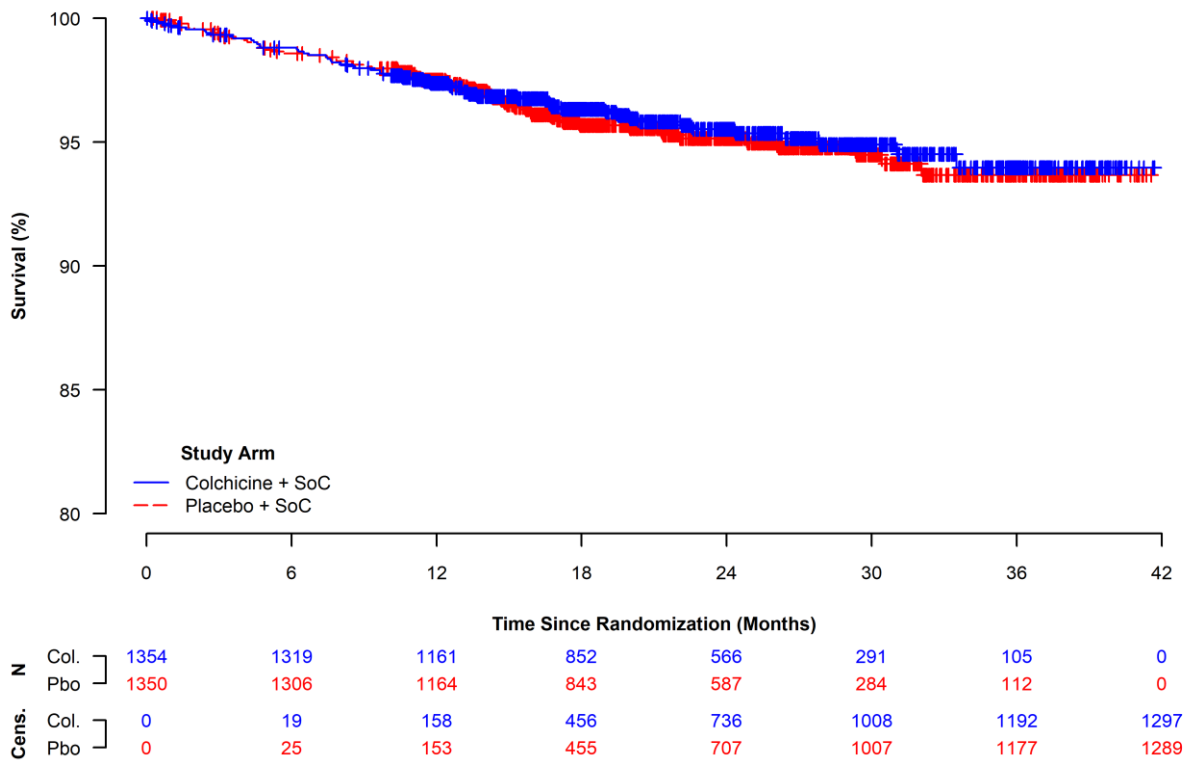
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Region</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8488</b>					
<b>Europe</b>	32/1,012 (3.2)	37/1,029 (3.6)	0.879 [0.552, 1.400] 0.5881	0.875 [0.541, 1.417] 0.5881	-0.434 [-2.001, 1.134] 0.5876
<b>Non-Europe</b>	57/1,354 (4.2)	61/1,350 (4.5)	0.932 [0.654, 1.326] 0.6944	0.929 [0.642, 1.343] 0.6944	-0.309 [-1.849, 1.231] 0.6943
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 110:** Time to Acute Myocardial Infarction, Subgrouped by Region (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.8159</b>							
<b>Europe</b>	32/1,012 (3.2)	NE [NE, NE]	4.3 [2.6, 5.8]	37/1,029 (3.6)	NE [NE, NE]	4.4 [2.9, 5.9]	0.871 [0.543, 1.398] 0.5674
<b>Non-Europe</b>	57/1,354 (4.2)	NE [NE, NE]	6.0 [4.1, 7.9]	61/1,350 (4.5)	NE [NE, NE]	6.3 [4.5, 8.2]	0.934 [0.651, 1.340] 0.7094
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 102:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within European Countries (ITT Population).



**Figure 103:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within Non-European Countries (ITT Population).

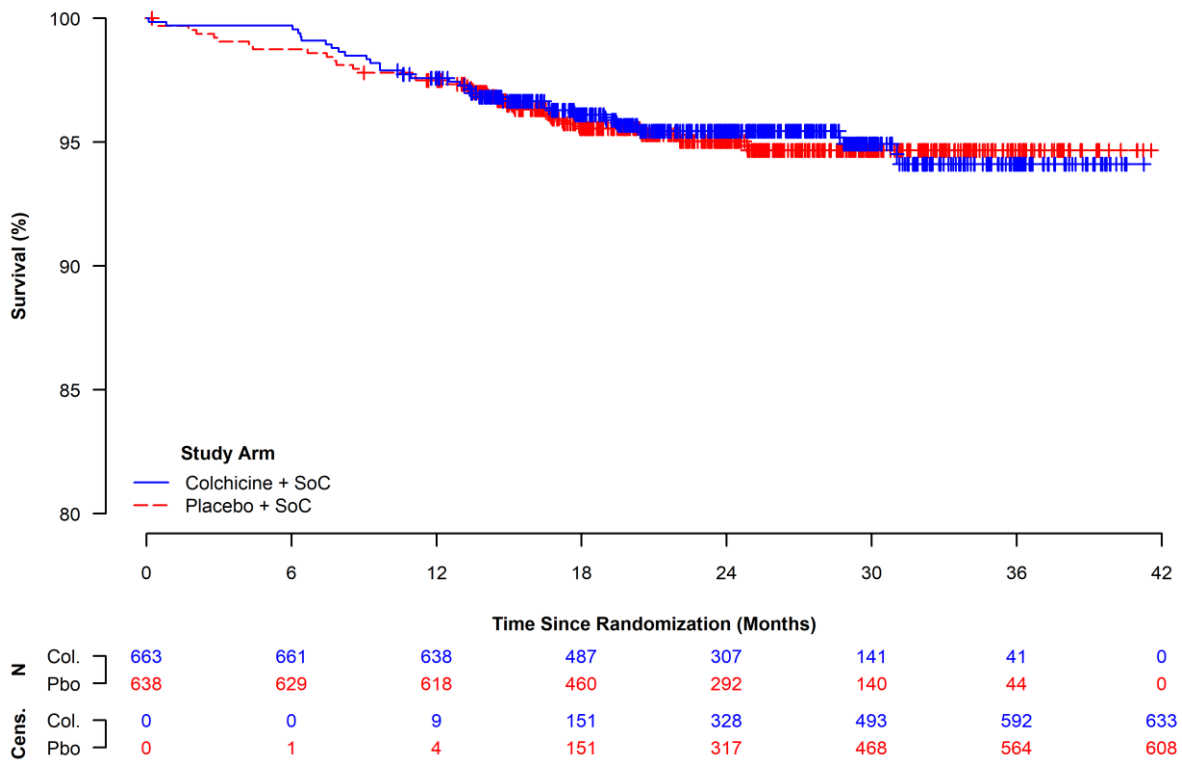
#### 4.4.2.4.5 Subgrouped by White Blood Cell Count

**Table 111:** Proportion of Patients with Acute Myocardial Infarction, Subgrouped by White Blood Cell Count (ITT Population).

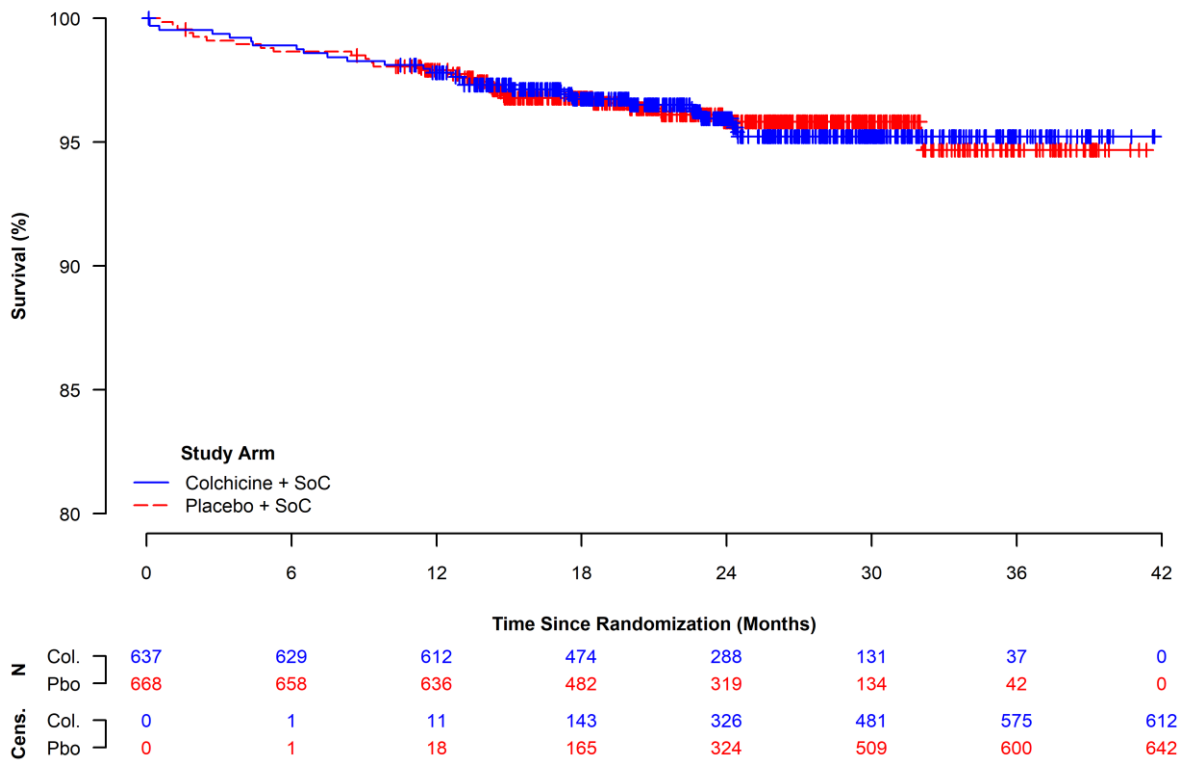
Subgroup	Colchicine + SoC (N = 1,300)	Placebo + SoC (N = 1,306)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.9000</b>					
< 8.66 10 <sup>3</sup> /μL	30/663 (4.5)	30/638 (4.7)	0.962 [0.587, 1.577] 0.8789	0.961 [0.572, 1.613] 0.8789	-0.177 [-2.458, 2.103] 0.8789
≥ 8.66 10 <sup>3</sup> /μL	25/637 (3.9)	26/668 (3.9)	1.008 [0.589, 1.727] 0.9759	1.009 [0.576, 1.766] 0.9759	0.032 [-2.071, 2.136] 0.9759
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 112:** Time to Acute Myocardial Infarction, Subgrouped by White Blood Cell Count (ITT Population).

Subgroup	Colchicine + SoC (N = 1,300)			Placebo + SoC (N = 1,306)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.8925</b>							
< 8.66 10 <sup>3</sup> /μL	30/663 (4.5)	NE [NE, NE]	5.9 [3.4, 8.4]	30/638 (4.7)	NE [NE, NE]	5.3 [3.4, 7.2]	0.956 [0.576, 1.585] 0.8611
≥ 8.66 10 <sup>3</sup> /μL	25/637 (3.9)	NE [NE, NE]	4.8 [2.8, 6.7]	26/668 (3.9)	NE [NE, NE]	5.3 [2.5, 8.0]	1.008 [0.582, 1.745] 0.9773
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 104:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Lower White Blood Cell Count Subgroup (ITT Population).



**Figure 105:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Upper White Blood Cell Count Subgroup (ITT Population).

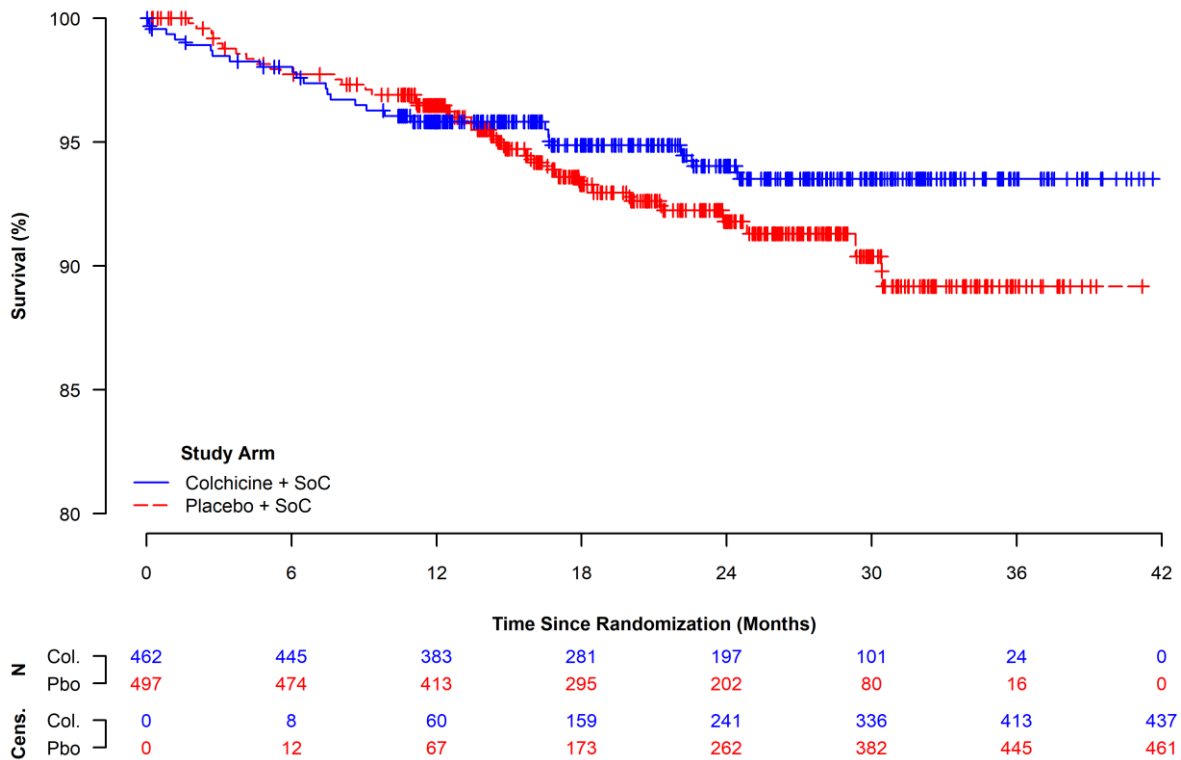
#### 4.4.2.4.6 Subgrouped by Diabetes Status

**Table 113:** Proportion of Patients with Acute Myocardial Infarction, Subgrouped by Diabetes Status (ITT Population).

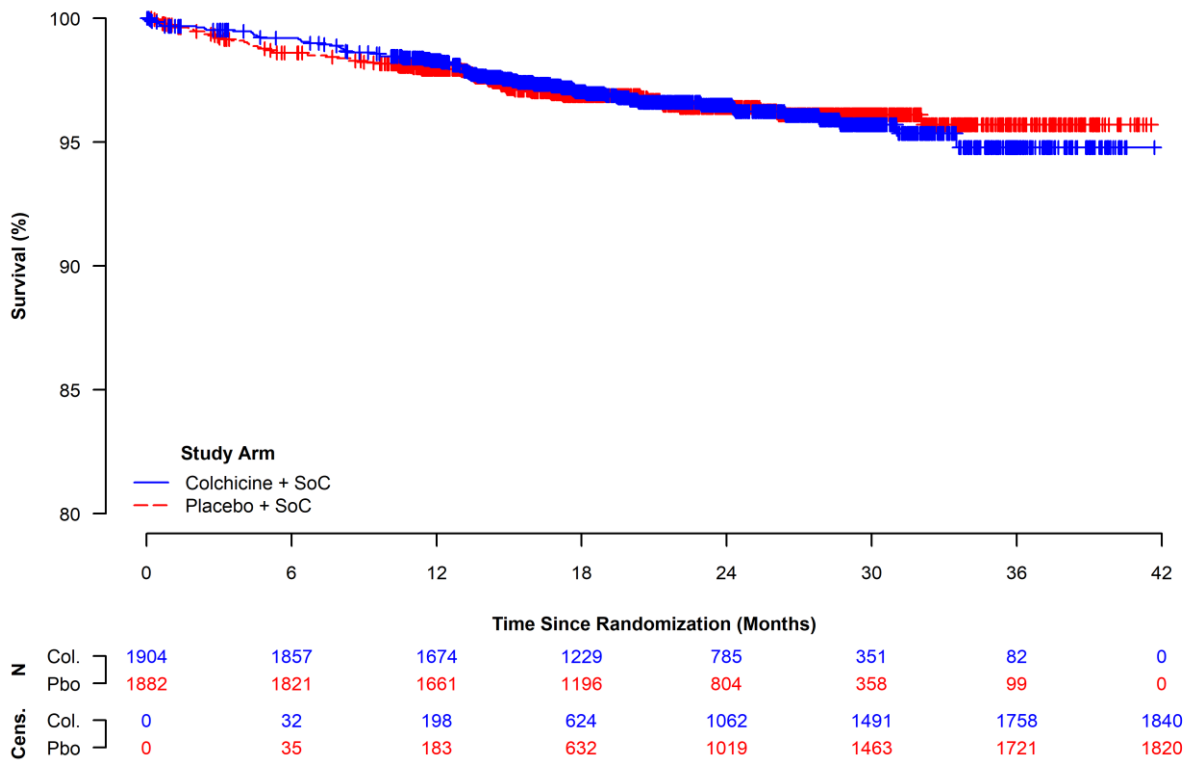
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.3040</b>					
<b>Yes</b>	25/462 (5.4)	36/497 (7.2)	0.747 [0.456, 1.225] 0.2475	0.733 [0.433, 1.241] 0.2469	-1.832 [-4.906, 1.242] 0.2427
<b>No</b>	64/1,904 (3.4)	62/1,882 (3.3)	1.020 [0.724, 1.438] 0.9085	1.021 [0.716, 1.457] 0.9085	0.067 [-1.076, 1.210] 0.9085
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 114:** Time to Acute Myocardial Infarction, Subgrouped by Diabetes Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.3018</b>							
<b>Yes</b>	25/462 (5.4)	NE [NE, NE]	6.5 [3.9, 9.0]	36/497 (7.2)	NE [NE, NE]	10.8 [6.6, 14.8]	0.738 [0.443, 1.230] 0.2443
<b>No</b>	64/1,904 (3.4)	NE [NE, NE]	5.2 [3.5, 6.9]	62/1,882 (3.3)	NE [NE, NE]	4.3 [3.0, 5.6]	1.020 [0.719, 1.447] 0.9107
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 106:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Diabetic Subgroup (ITT Population).



**Figure 107:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Non-Diabetic Subgroup (ITT Population).

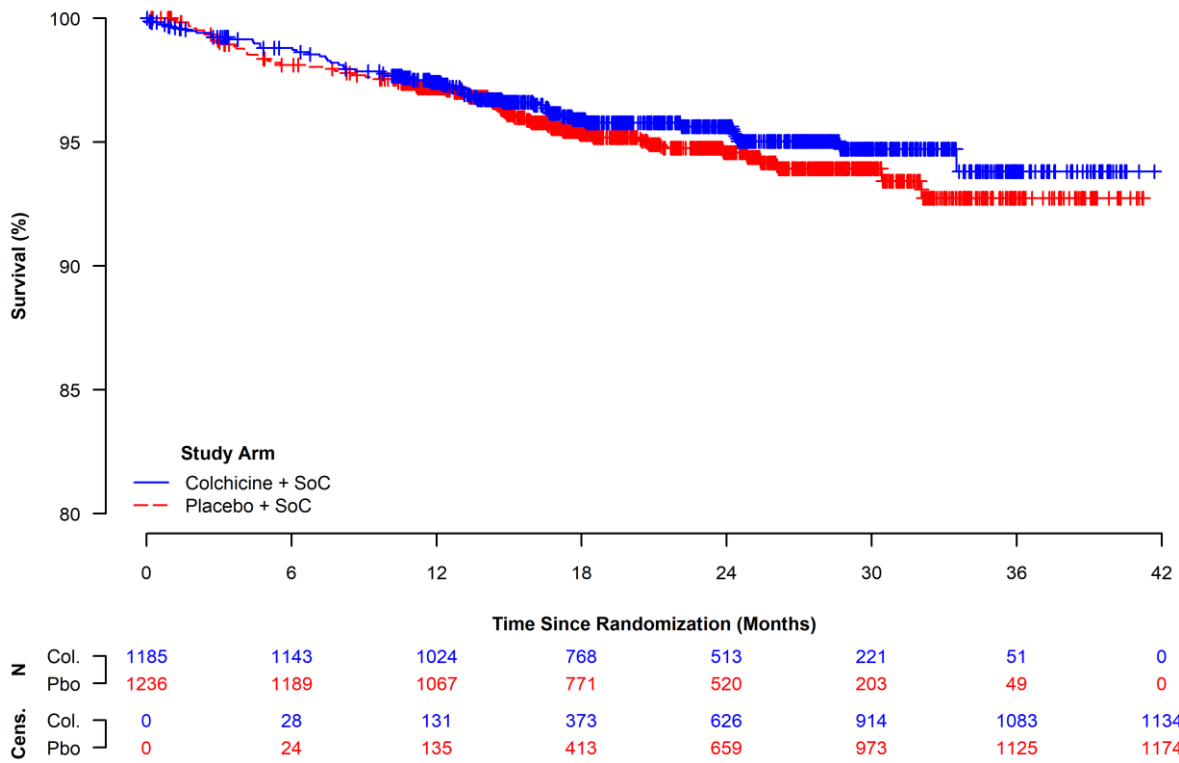
#### 4.4.2.4.7 Subgrouped by Hypertension Status

**Table 115:** Proportion of Patients with Acute Myocardial Infarction, Subgrouped by Hypertension Status (ITT Population).

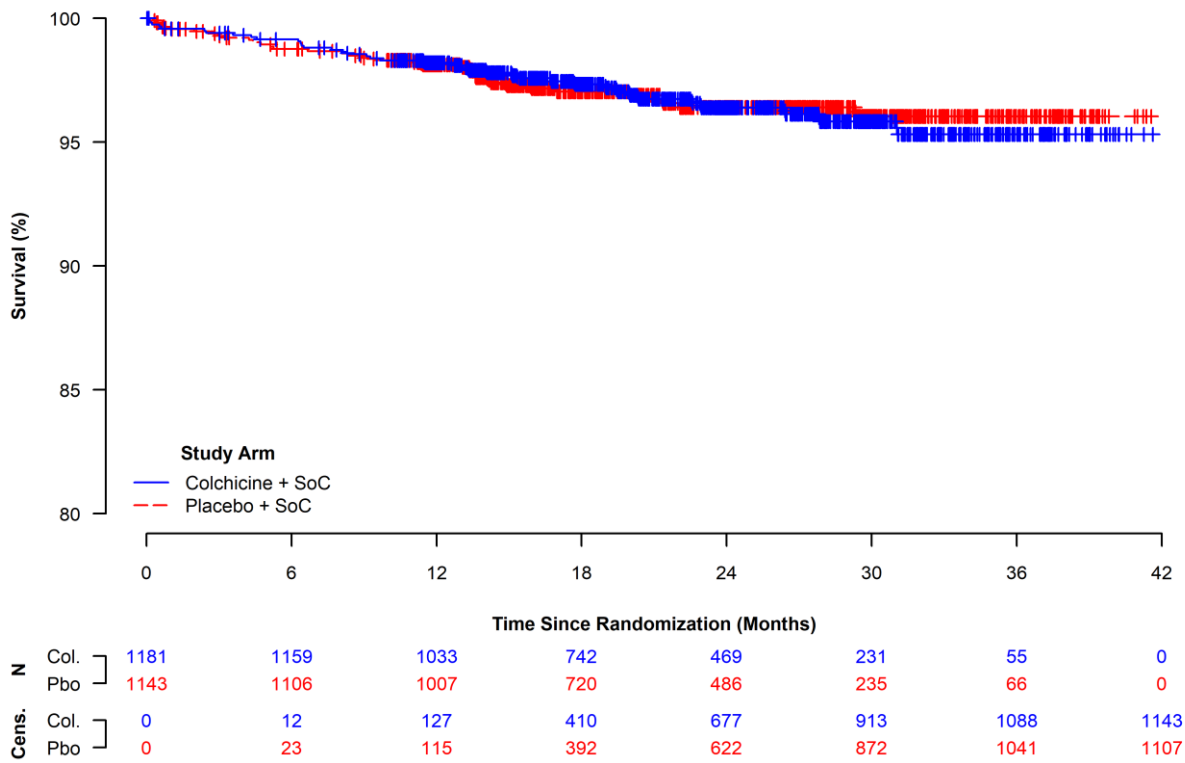
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.5496</b>					
<b>Yes</b>	51/1,185 (4.3)	62/1,236 (5.0)	0.858 [0.597, 1.232] 0.4067	0.852 [0.583, 1.245] 0.4066	-0.712 [-2.390, 0.966] 0.4054
<b>No</b>	38/1,181 (3.2)	36/1,143 (3.1)	1.022 [0.652, 1.600] 0.9256	1.022 [0.643, 1.625] 0.9256	0.068 [-1.360, 1.496] 0.9256
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 116:** Time to Acute Myocardial Infarction, Subgrouped by Hypertension Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.5325</b>							
<b>Yes</b>	51/1,185 (4.3)	NE [NE, NE]	6.2 [3.8, 8.5]	62/1,236 (5.0)	NE [NE, NE]	7.3 [5.0, 9.5]	0.850 [0.587, 1.231] 0.3900
<b>No</b>	38/1,181 (3.2)	NE [NE, NE]	4.7 [2.9, 6.4]	36/1,143 (3.1)	NE [NE, NE]	4.0 [2.6, 5.3]	1.024 [0.649, 1.615] 0.9188
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 108:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Hypertensive Subgroup (ITT Population).



**Figure 109:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Normotensive Subgroup (ITT Population).

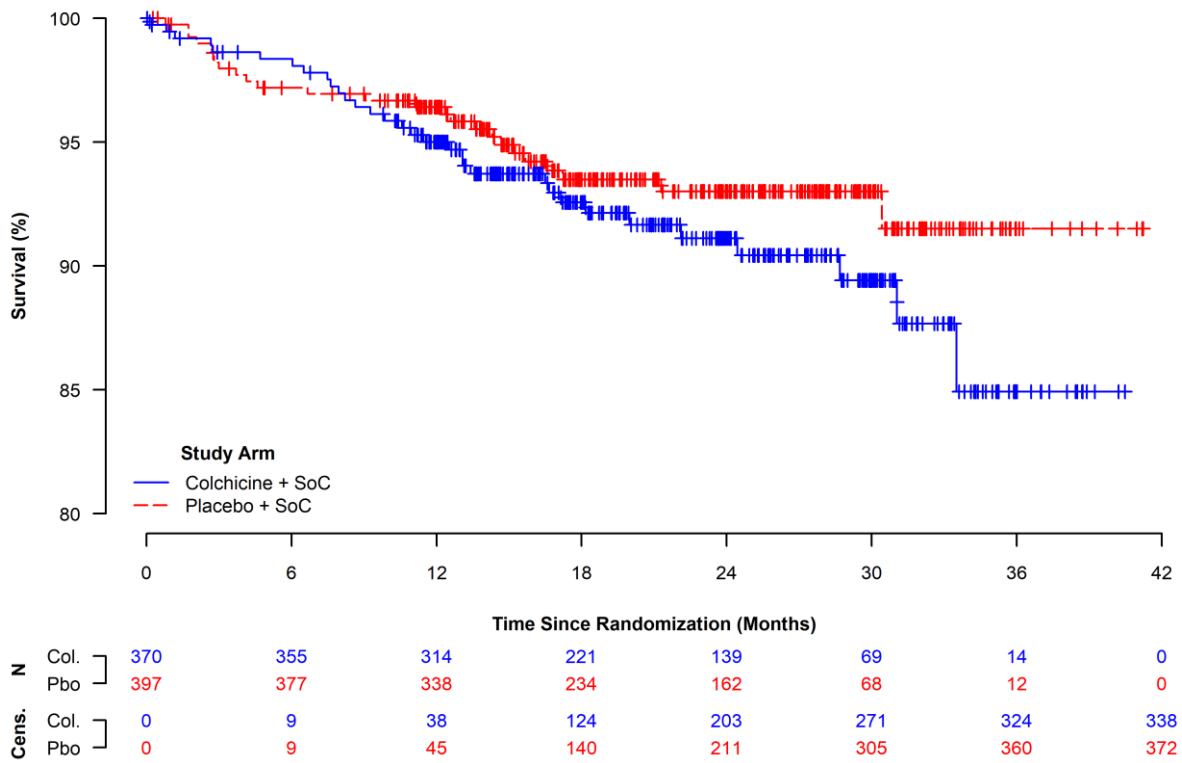
#### 4.4.2.4.8 Subgrouped by History of Myocardial Infarction

**Table 117:** Proportion of Patients with Acute Myocardial Infarction, Subgrouped by History of Myocardial Infarction (ITT Population).

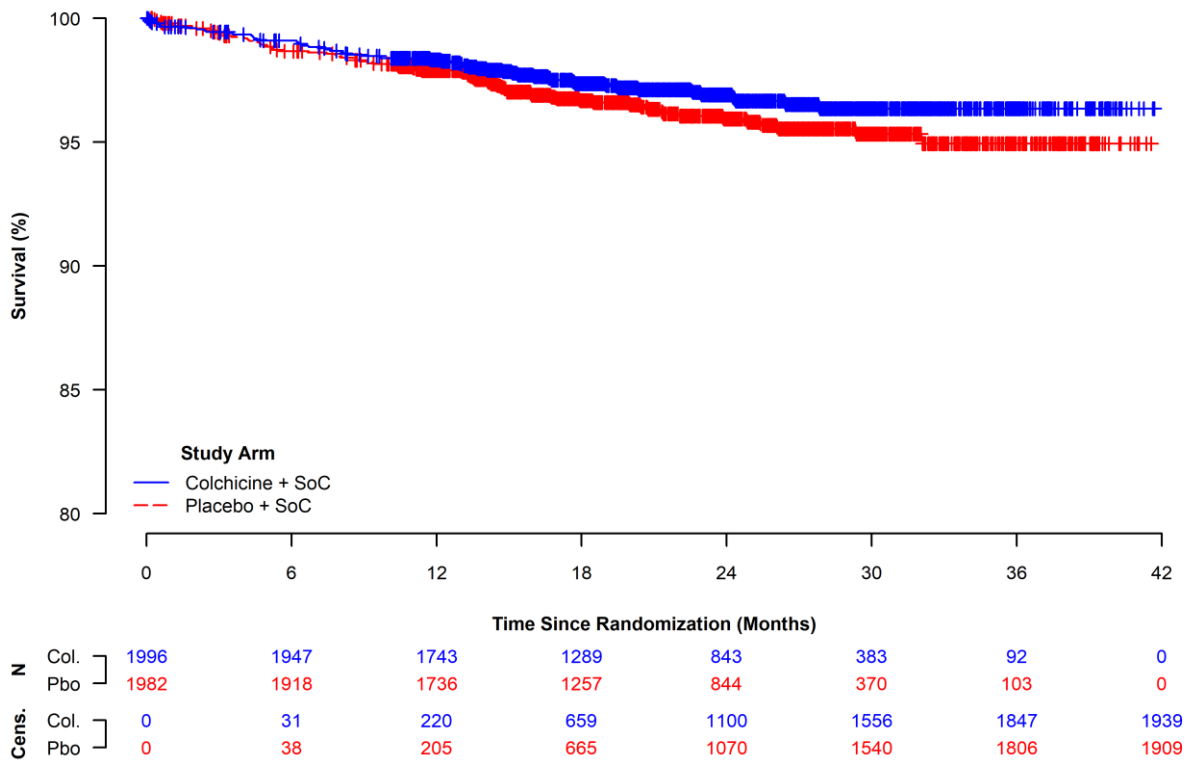
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of MI</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.0657</b>					
<b>Yes</b>	32/370 (8.6)	25/397 (6.3)	1.373 [0.830, 2.273] 0.2169	1.409 [0.818, 2.426] 0.2165	2.351 [-1.379, 6.081] 0.2166
<b>No</b>	57/1,996 (2.9)	73/1,982 (3.7)	0.775 [0.551, 1.090] 0.1434	0.769 [0.541, 1.093] 0.1433	-0.827 [-1.933, 0.278] 0.1423
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 118:** Time to Acute Myocardial Infarction, Subgrouped by History of Myocardial Infarction (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of MI</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.0669</b>							
<b>Yes</b>	32/370 (8.6)	NE [NE, NE]	15.1 [7.5, 22.0]	25/397 (6.3)	NE [NE, NE]	8.5 [4.4, 12.4]	1.378 [0.817, 2.326] 0.2293
<b>No</b>	57/1,996 (2.9)	NE [NE, NE]	3.7 [2.6, 4.7]	73/1,982 (3.7)	NE [NE, NE]	5.1 [3.7, 6.4]	0.772 [0.546, 1.091] 0.1423
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 110:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Subgroup With History of Myocardial Infarction (ITT Population).



**Figure 111:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Subgroup Without History of Myocardial Infarction (ITT Population).

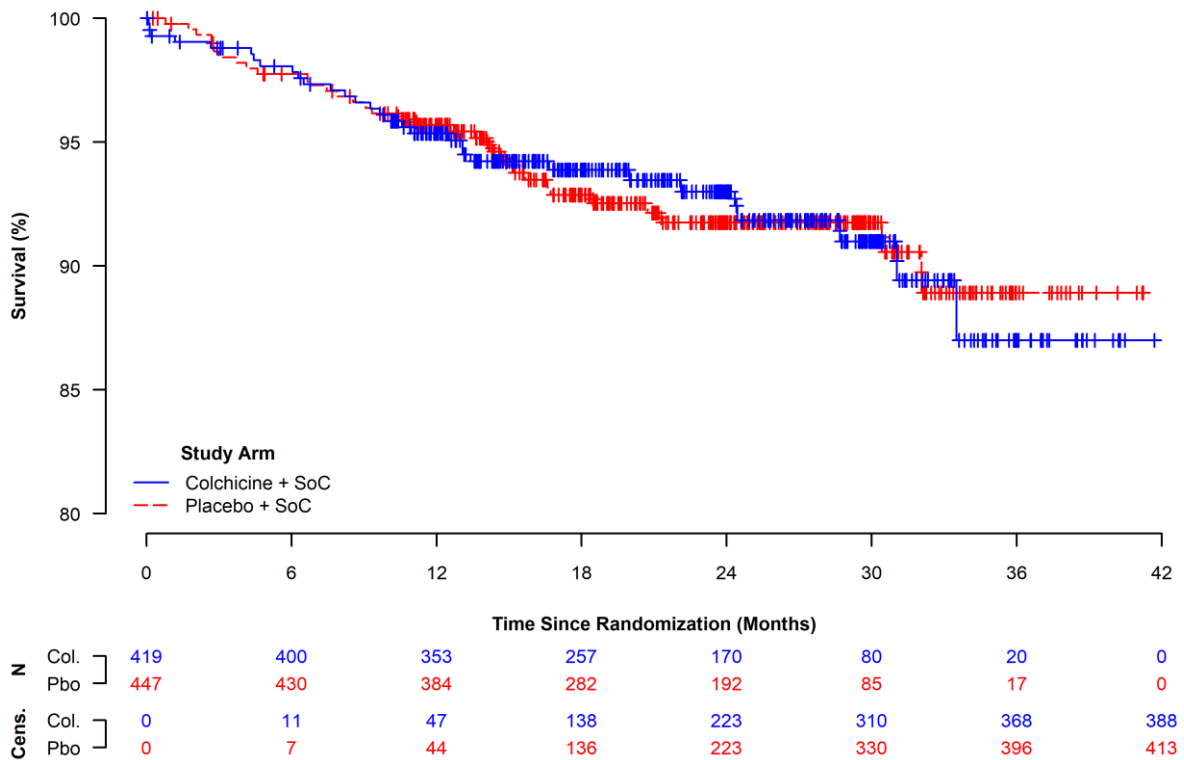
#### 4.4.2.4.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 119:** Proportion of Patients with Acute Myocardial Infarction, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

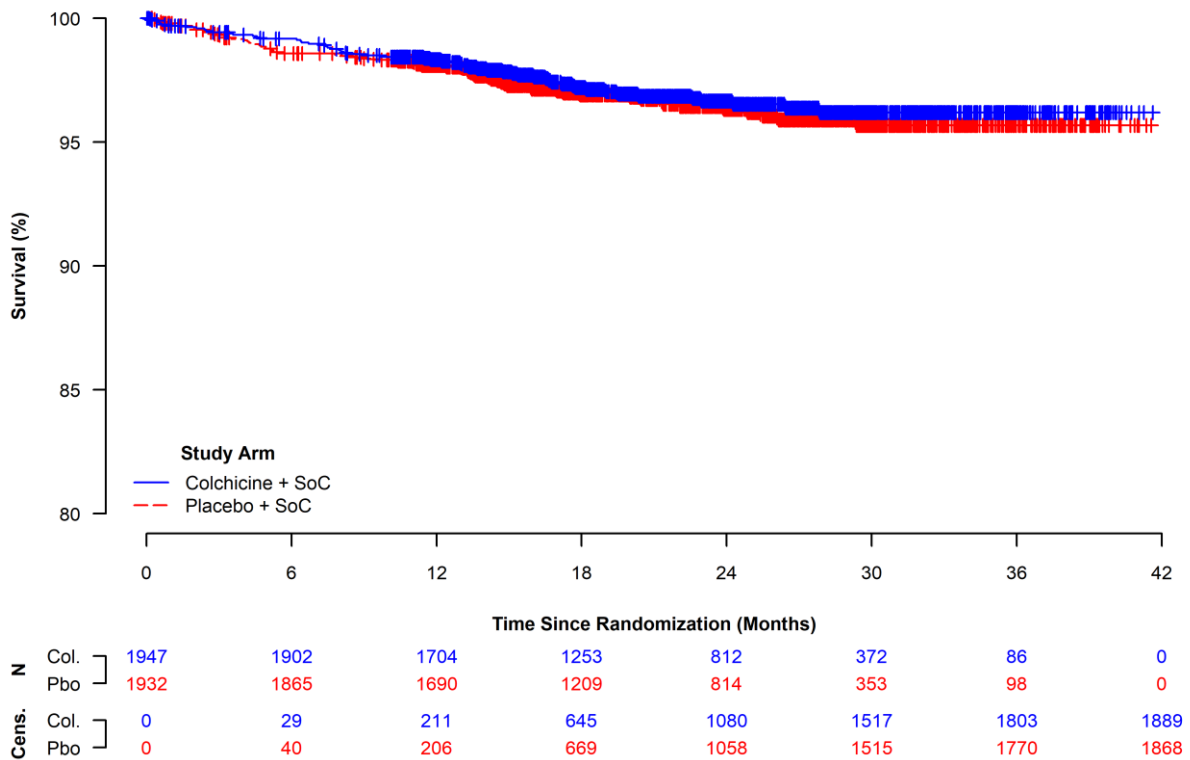
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8017</b>					
<b>Yes</b>	31/419 (7.4)	34/447 (7.6)	0.973 [0.609, 1.553] 0.9077	0.971 [0.585, 1.610] 0.9077	-0.208 [-3.718, 3.302] 0.9077
<b>No</b>	58/1,947 (3.0)	64/1,932 (3.3)	0.899 [0.634, 1.276] 0.5518	0.896 [0.625, 1.286] 0.5518	-0.334 [-1.432, 0.765] 0.5517
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 120:** Time to Acute Myocardial Infarction, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.7238</b>							
<b>Yes</b>	31/419 (7.4)	NE [NE, NE]	13.0 [6.3, 19.2]	34/447 (7.6)	NE [NE, NE]	11.1 [6.2, 15.7]	0.995 [0.612, 1.619] 0.9841
<b>No</b>	58/1,947 (3.0)	NE [NE, NE]	3.8 [2.8, 4.8]	64/1,932 (3.3)	NE [NE, NE]	4.3 [3.2, 5.5]	0.892 [0.625, 1.272] 0.5280
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 112:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Subgroup With History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).



**Figure 113:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Subgroup Without History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

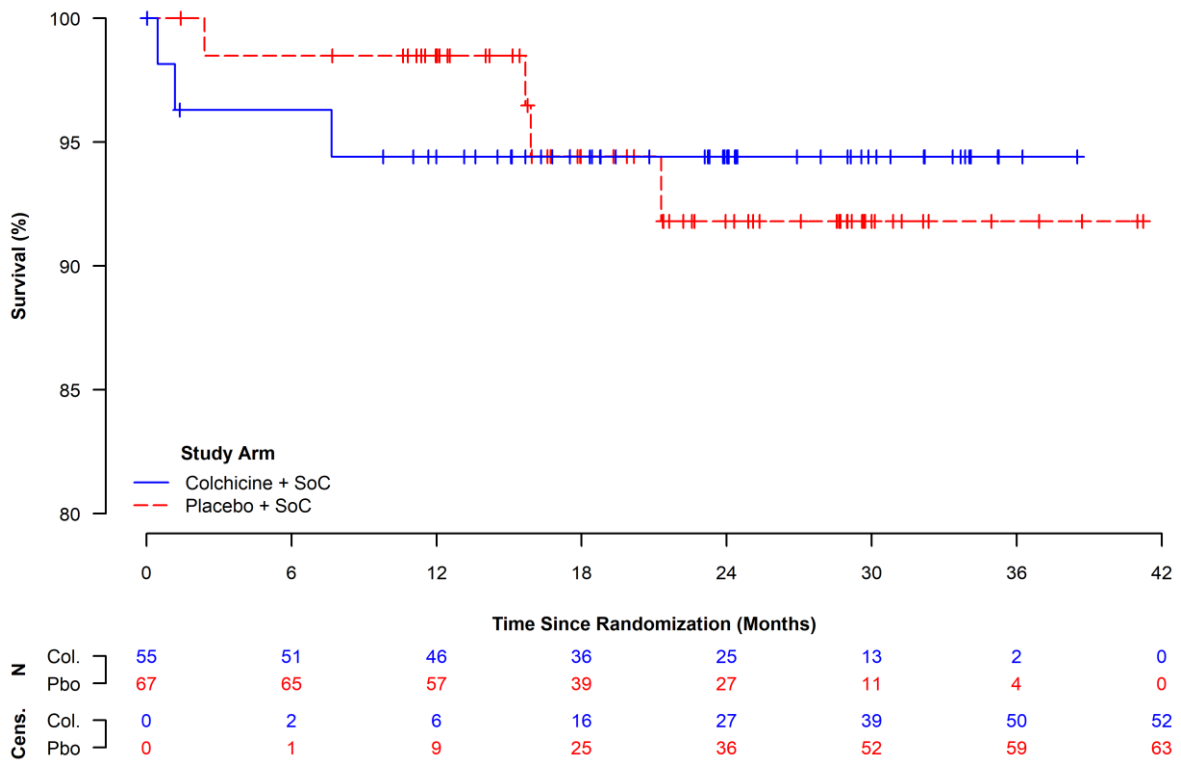
#### 4.4.2.4.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 121:** Proportion of Patients with Acute Myocardial Infarction, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

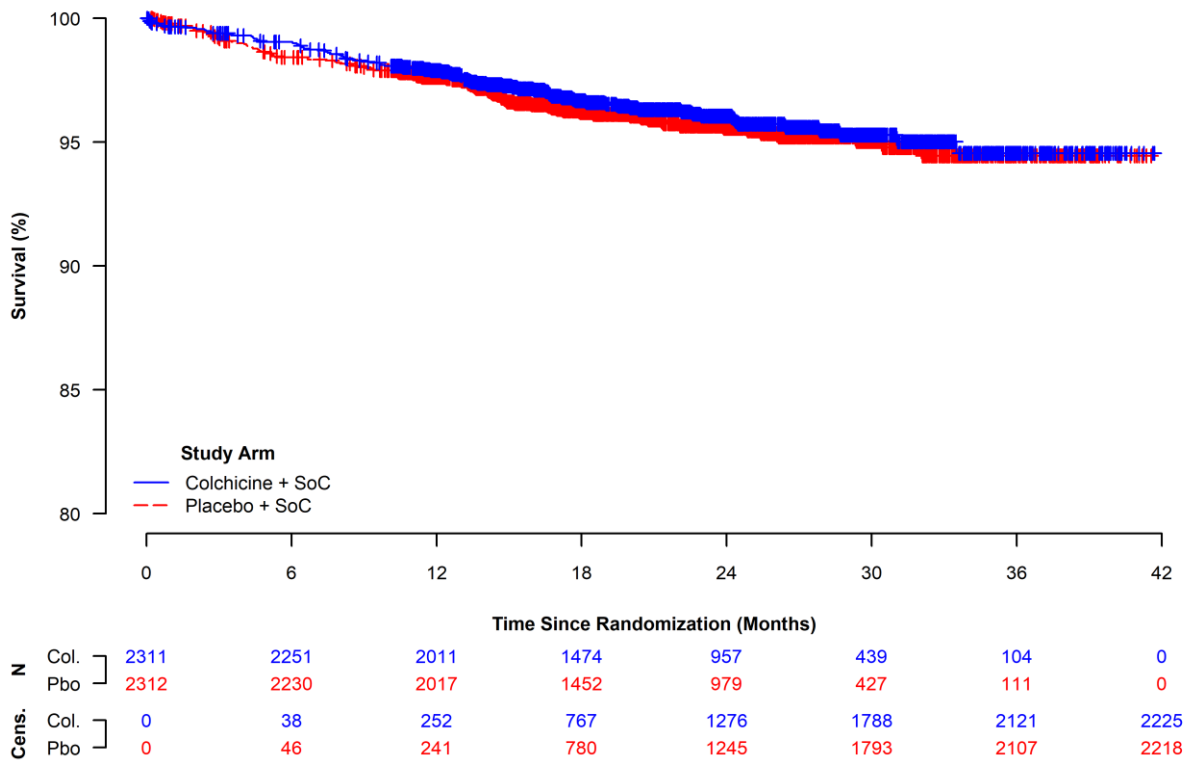
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.9963</b>					
<b>Yes</b>	3/55 (5.5)	4/67 (6.0)	0.914 [0.213, 3.910] 0.9031	0.909 [0.195, 4.244] 0.9031	-0.516 [-8.774, 7.743] 0.9026
<b>No</b>	86/2,311 (3.7)	94/2,312 (4.1)	0.915 [0.687, 1.219] 0.5451	0.912 [0.677, 1.229] 0.5451	-0.344 [-1.460, 0.771] 0.5450
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 122:** Time to Acute Myocardial Infarction, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.9918</b>							
<b>Yes</b>	3/55 (5.5)	NE [NE, NE]	5.6 [0.0, 11.5]	4/67 (6.0)	NE [NE, NE]	8.2 [0.0, 15.7]	0.925 [0.207, 4.136] 0.9193
<b>No</b>	86/2,311 (3.7)	NE [NE, NE]	5.4 [3.9, 6.9]	94/2,312 (4.1)	NE [NE, NE]	5.6 [4.2, 6.9]	0.913 [0.681, 1.223] 0.5395
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 114:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Subgroup With History of Stroke or Transient Ischaemic Attack (ITT Population).



**Figure 115:** Kaplan-Meier Curves for Acute Myocardial Infarction, Within the Subgroup Without History of Stroke or Transient Ischaemic Attack (ITT Population).

#### 4.4.2.5 Stroke

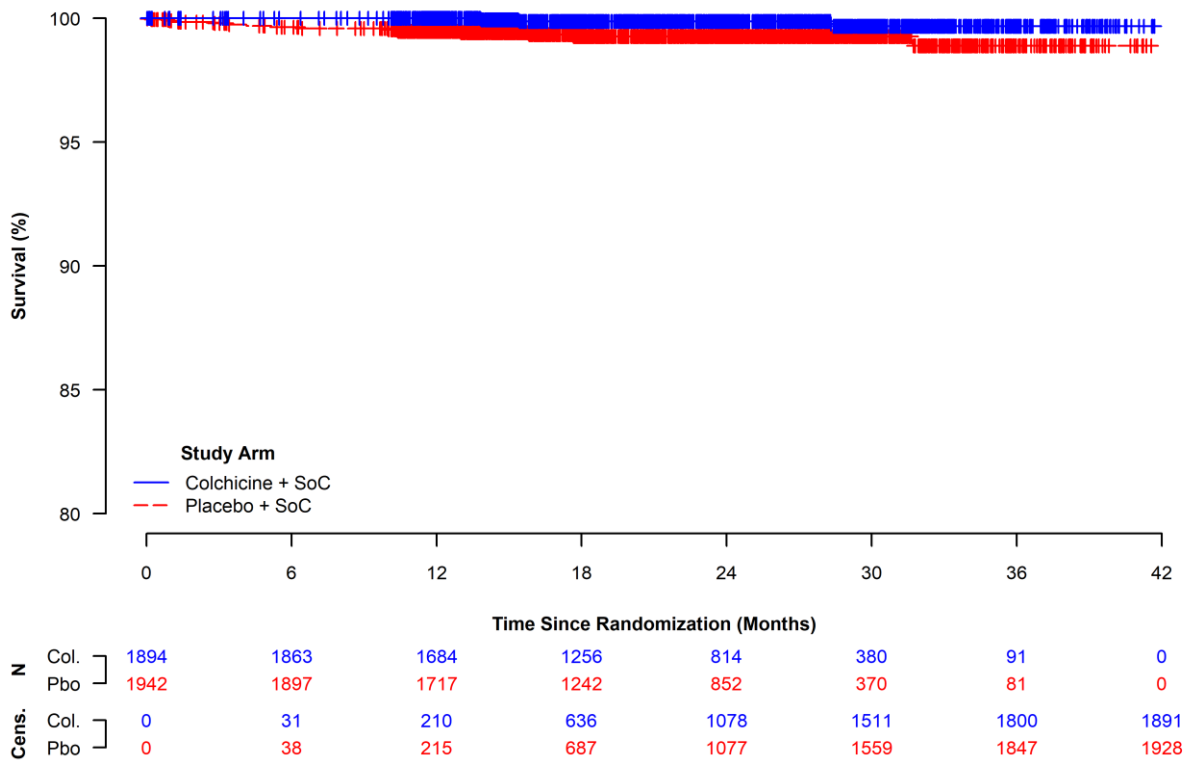
##### 4.4.2.5.1 Subgrouped by Sex

**Table 123:** Proportion of Patients with Stroke, Subgrouped by Sex (ITT Population).

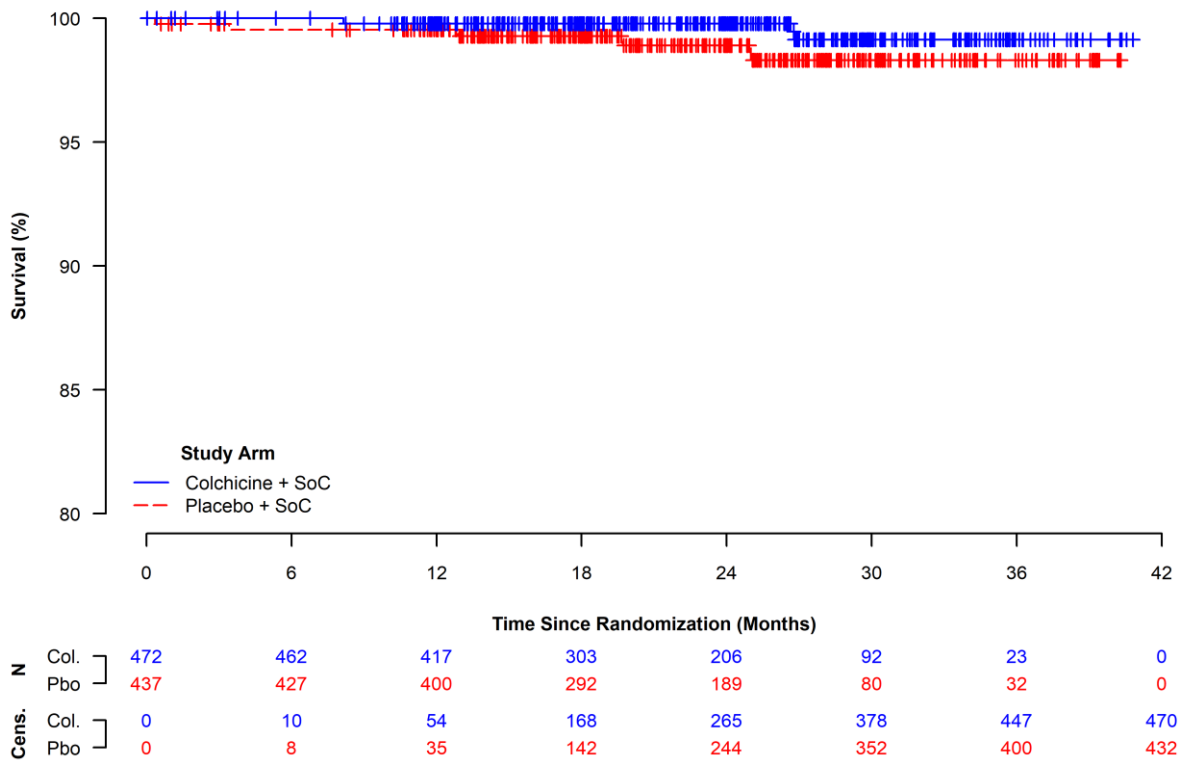
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Sex</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.6248</b>					
<b>Male</b>	3/1,894 (0.2)	14/1,942 (0.7)	0.220 [0.063, 0.763] 0.0171	0.218 [0.063, 0.761] 0.0170	-0.563 [-0.979, -0.146] 0.0082
<b>Female</b>	2/472 (0.4)	5/437 (1.1)	0.370 [0.072, 1.899] 0.2336	0.368 [0.071, 1.905] 0.2332	-0.720 [-1.877, 0.436] 0.2221
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 124:** Time to Stroke, Subgrouped by Sex (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Sex</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.6127</b>							
<b>Male</b>	3/1,894 (0.2)	NE [NE, NE]	0.3 [0.0, 0.7]	14/1,942 (0.7)	NE [NE, NE]	1.1 [0.3, 1.9]	0.217 [0.062, 0.756] 0.0164
<b>Female</b>	2/472 (0.4)	NE [NE, NE]	0.9 [0.0, 2.2]	5/437 (1.1)	NE [NE, NE]	1.7 [0.1, 3.3]	0.373 [0.072, 1.925] 0.2391
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 116:** Kaplan-Meier Curves for Stroke, Within the Male Sex Subgroup (ITT Population).



**Figure 117:** Kaplan-Meier Curves for Stroke, Within the Female Sex Subgroup (ITT Population).

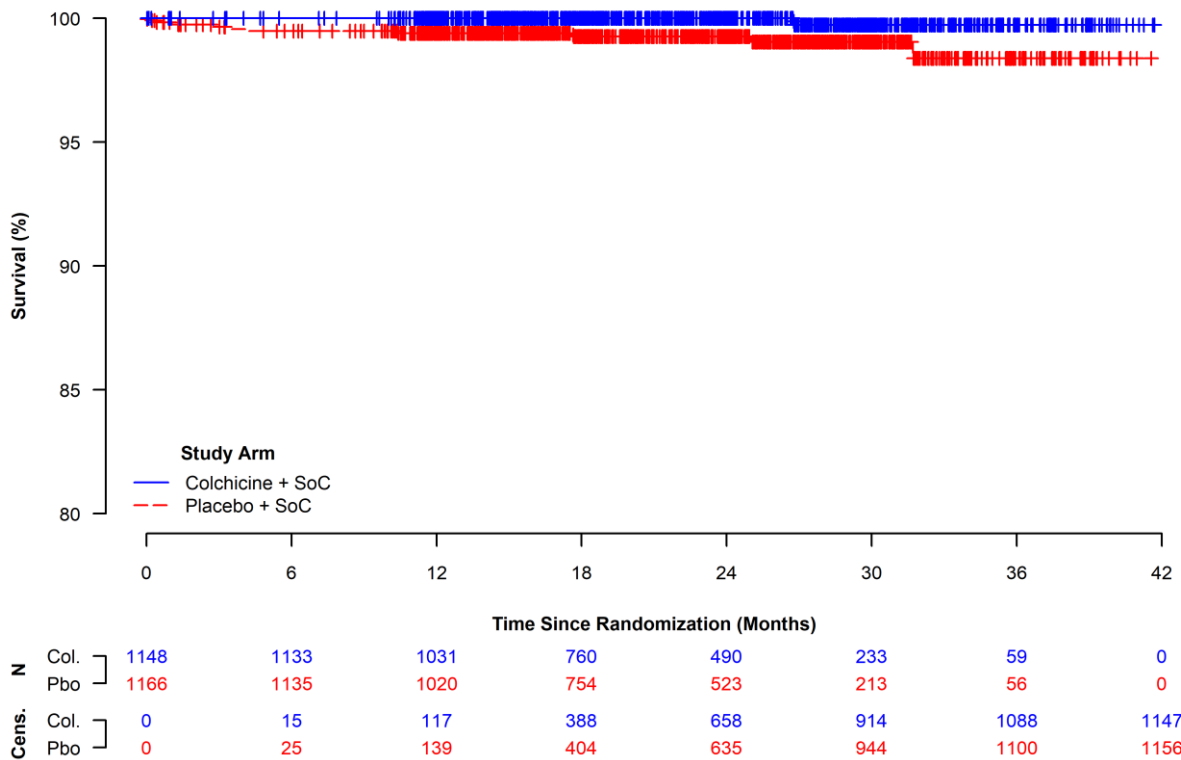
#### 4.4.2.5.2 Subgrouped by Age Group

**Table 125:** Proportion of Patients with Stroke, Subgrouped by Age Group (ITT Population).

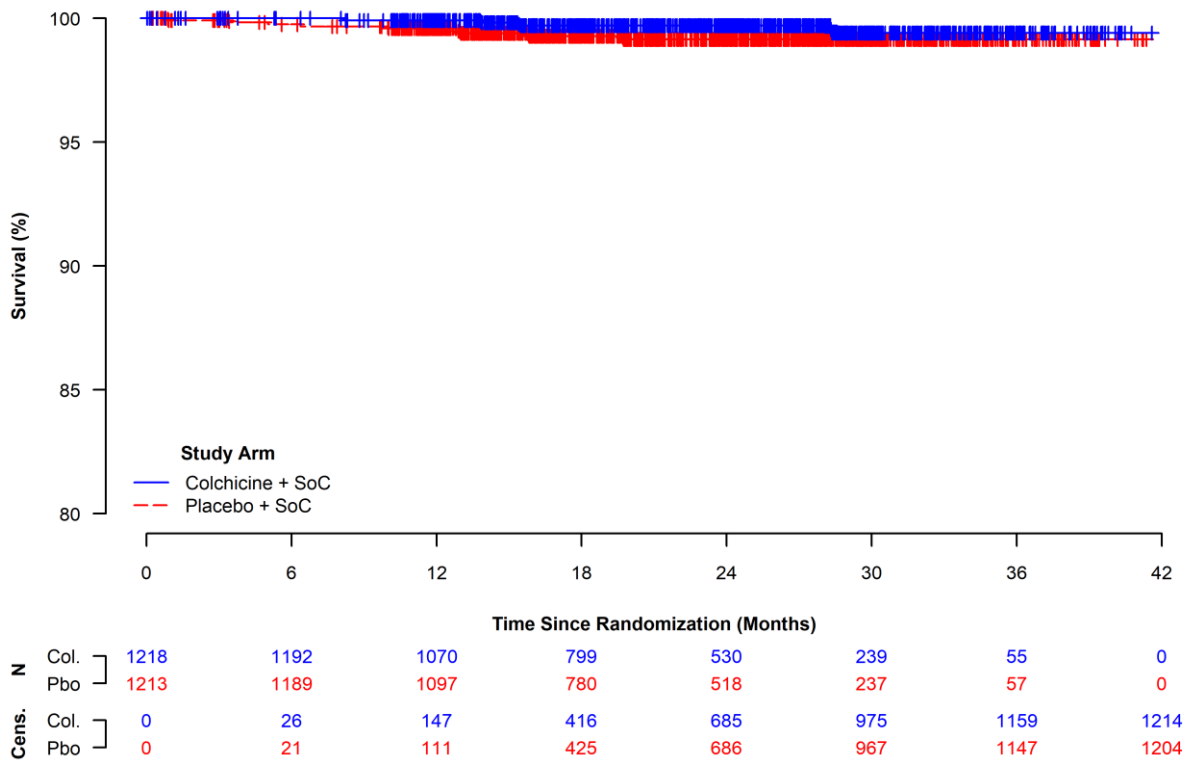
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Age</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1838</b>					
< 60 Years	1/1,148 (0.1)	10/1,166 (0.9)	0.102 [0.013, 0.792] 0.0291	0.101 [0.013, 0.789] 0.0288	-0.771 [-1.327, -0.214] 0.0066
≥ 60 Years	4/1,218 (0.3)	9/1,213 (0.7)	0.443 [0.137, 1.433] 0.1740	0.441 [0.135, 1.435] 0.1738	-0.414 [-0.994, 0.167] 0.1623
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 126:** Time to Stroke, Subgrouped by Age Group (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Age</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.1769</b>							
<b>&lt; 60 Years</b>	1/1,148 (0.1)	NE [NE, NE]	0.3 [0.0, 0.8]	10/1,166 (0.9)	NE [NE, NE]	1.6 [0.2, 3.1]	0.100 [0.013, 0.783] 0.0283
<b>≥ 60 Years</b>	4/1,218 (0.3)	NE [NE, NE]	0.6 [0.0, 1.3]	9/1,213 (0.7)	NE [NE, NE]	0.9 [0.3, 1.4]	0.445 [0.137, 1.447] 0.1784
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours colchicine. SEs presented on the log-scale. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 118:** Kaplan-Meier Curves for Stroke, Within the Age 59 Years or Younger Subgroup (ITT Population).



**Figure 119:** Kaplan-Meier Curves for Stroke, Within the Age 60 Years or Older Subgroup (ITT Population).

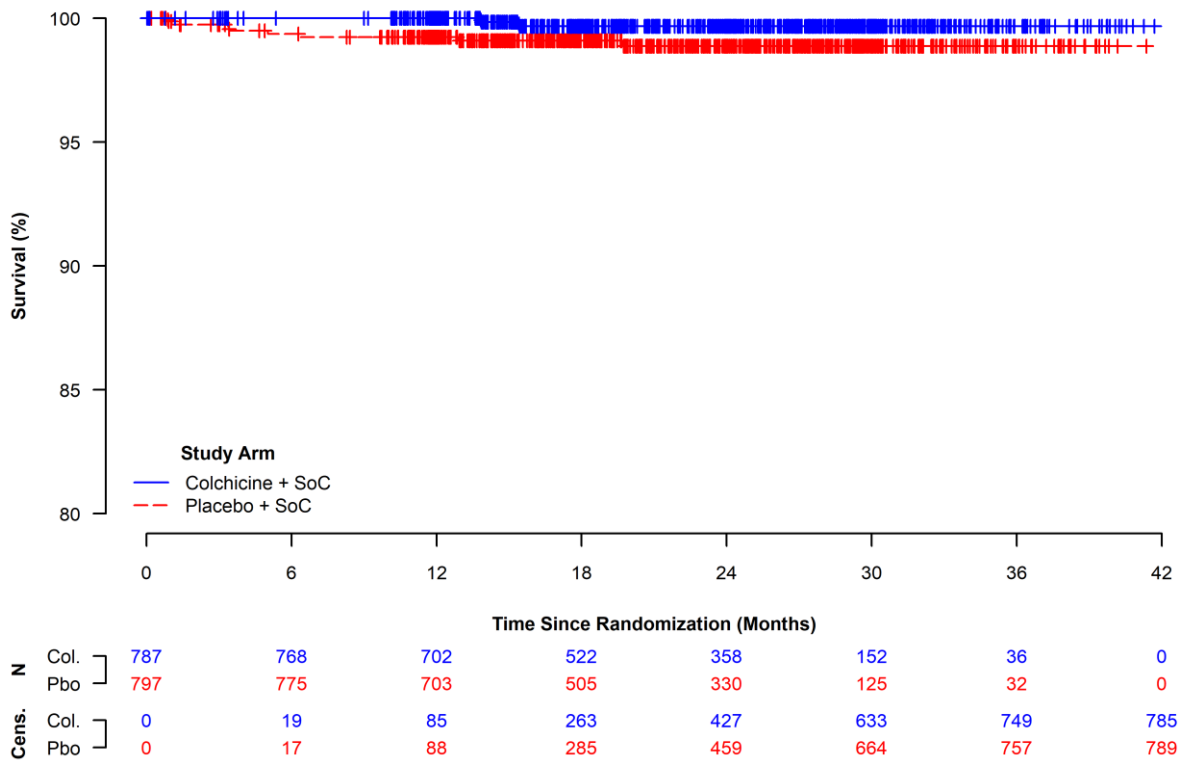
#### 4.4.2.5.3 Subgrouped by Smoking Status

**Table 127:** Proportion of Patients with Stroke, Subgrouped by Smoking Status (ITT Population).

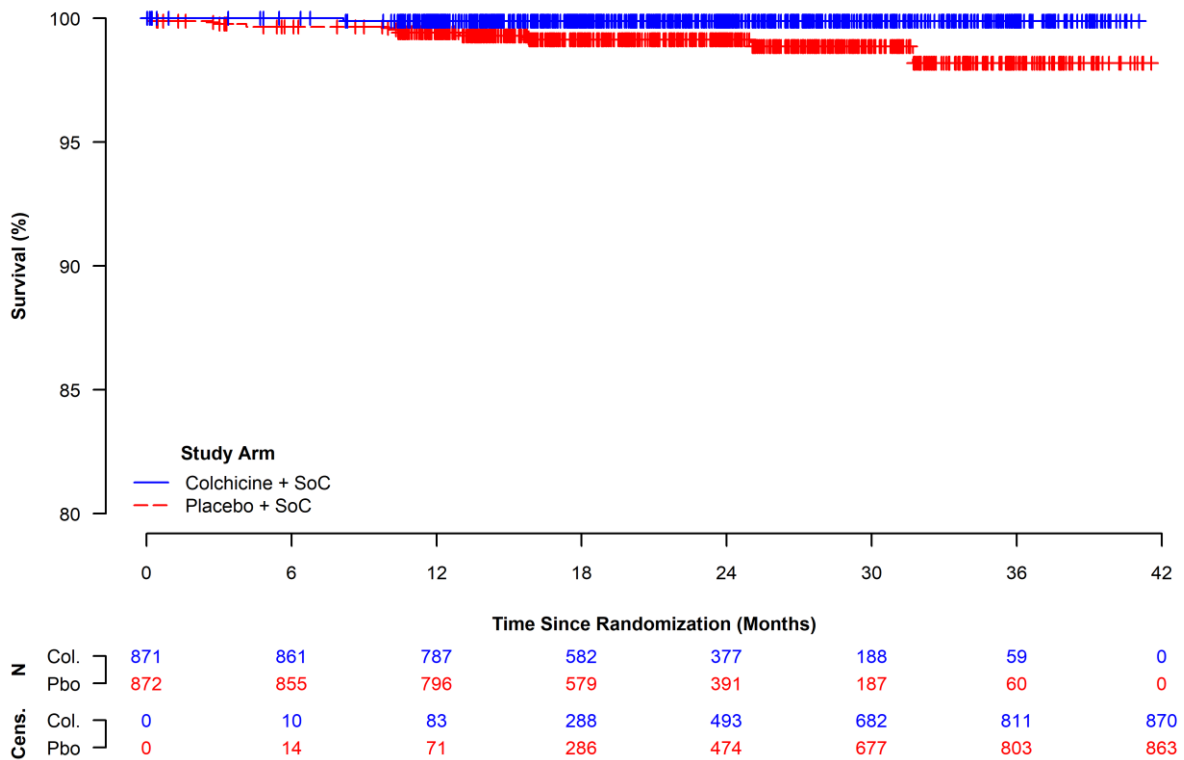
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,377)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Smoking Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2838</b>					
<b>Non</b>	2/787 (0.3)	8/797 (1.0)	0.253 [0.054, 1.188] 0.0817	0.251 [0.053, 1.187] 0.0812	-0.750 [-1.526, 0.027] 0.0584
<b>Ex</b>	1/871 (0.1)	9/872 (1.0)	0.111 [0.014, 0.876] 0.0370	0.110 [0.014, 0.872] 0.0366	-0.917 [-1.625, -0.210] 0.0110
<b>Current</b>	2/708 (0.3)	2/708 (0.3)	1.000 [0.141, 7.079] 1.0000	1.000 [0.140, 7.119] 1.0000	0.000 [-0.553, 0.553] 1.0000
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 128:** Time to Stroke, Subgrouped by Smoking Status (ITT Population).

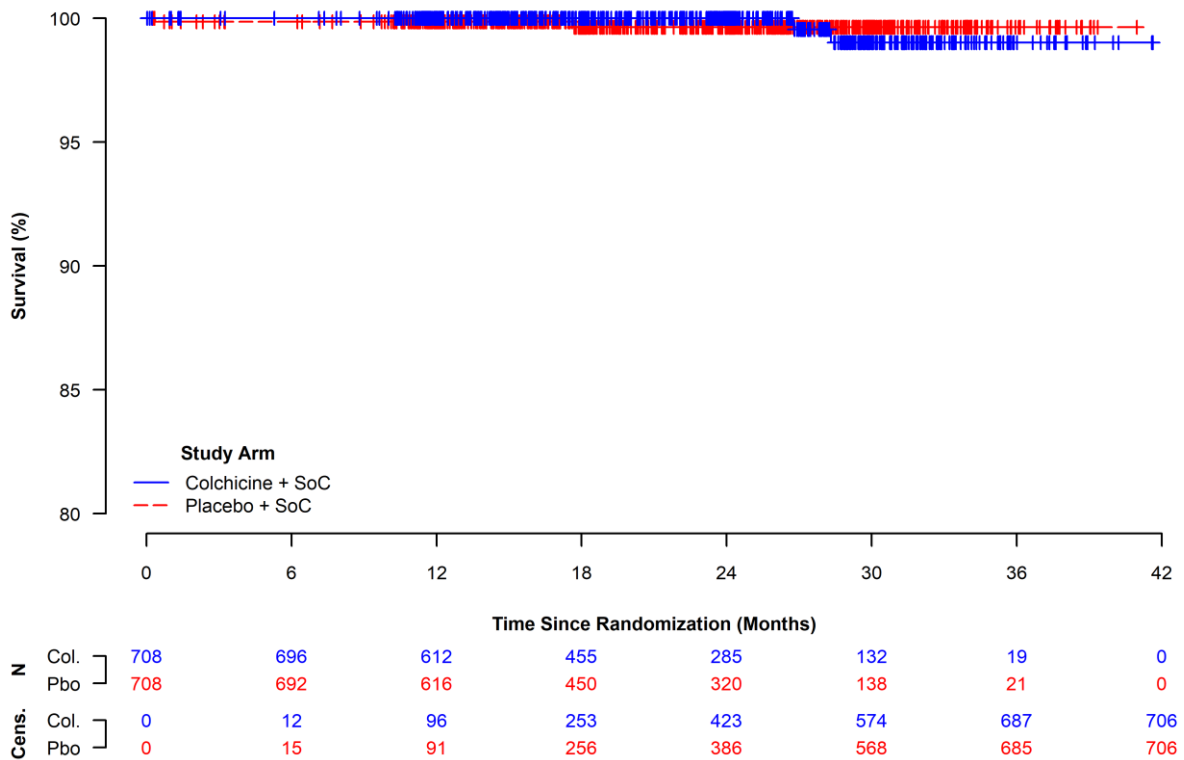
Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,377)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Smoking Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.2859</b>							
<b>Non</b>	2/787 (0.3)	NE [NE, NE]	0.3 [0.0, 0.8]	8/797 (1.0)	NE [NE, NE]	1.1 [0.3, 1.9]	0.251 [0.053, 1.182] 0.0804
<b>Ex</b>	1/871 (0.1)	NE [NE, NE]	0.1 [0.0, 0.3]	9/872 (1.0)	NE [NE, NE]	1.8 [0.3, 3.3]	0.112 [0.014, 0.886] 0.0380
<b>Current</b>	2/708 (0.3)	NE [NE, NE]	1.0 [0.0, 2.3]	2/708 (0.3)	NE [NE, NE]	0.4 [0.0, 0.9]	1.017 [0.143, 7.223] 0.9863
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 120:** Kaplan-Meier Curves for Stroke, Within the Non-Smoker Subgroup (ITT Population).



**Figure 121:** Kaplan-Meier Curves for Stroke, Within the Ex-Smoker Subgroup (ITT Population).



**Figure 122:** Kaplan-Meier Curves for Stroke, Within the Current Smoker Subgroup (ITT Population).

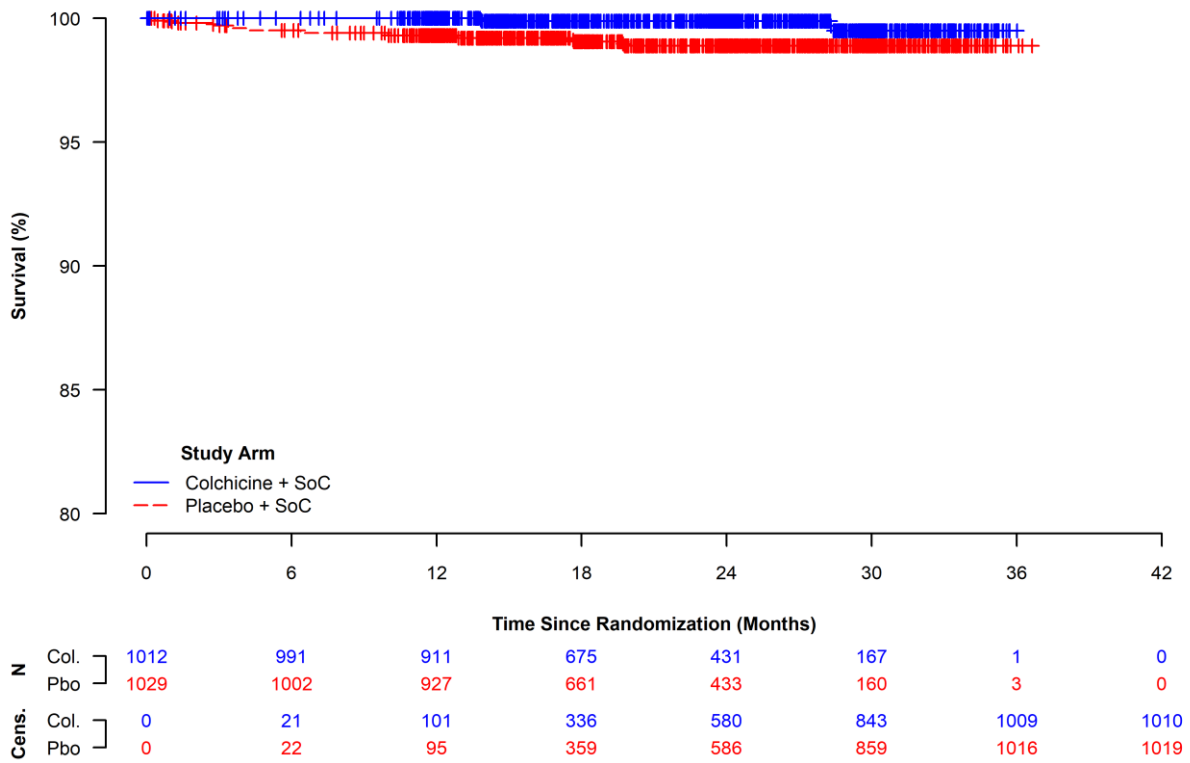
#### 4.4.2.5.4 Subgrouped by Region

**Table 129:** Proportion of Patients with Stroke, Subgrouped by Region (ITT Population).

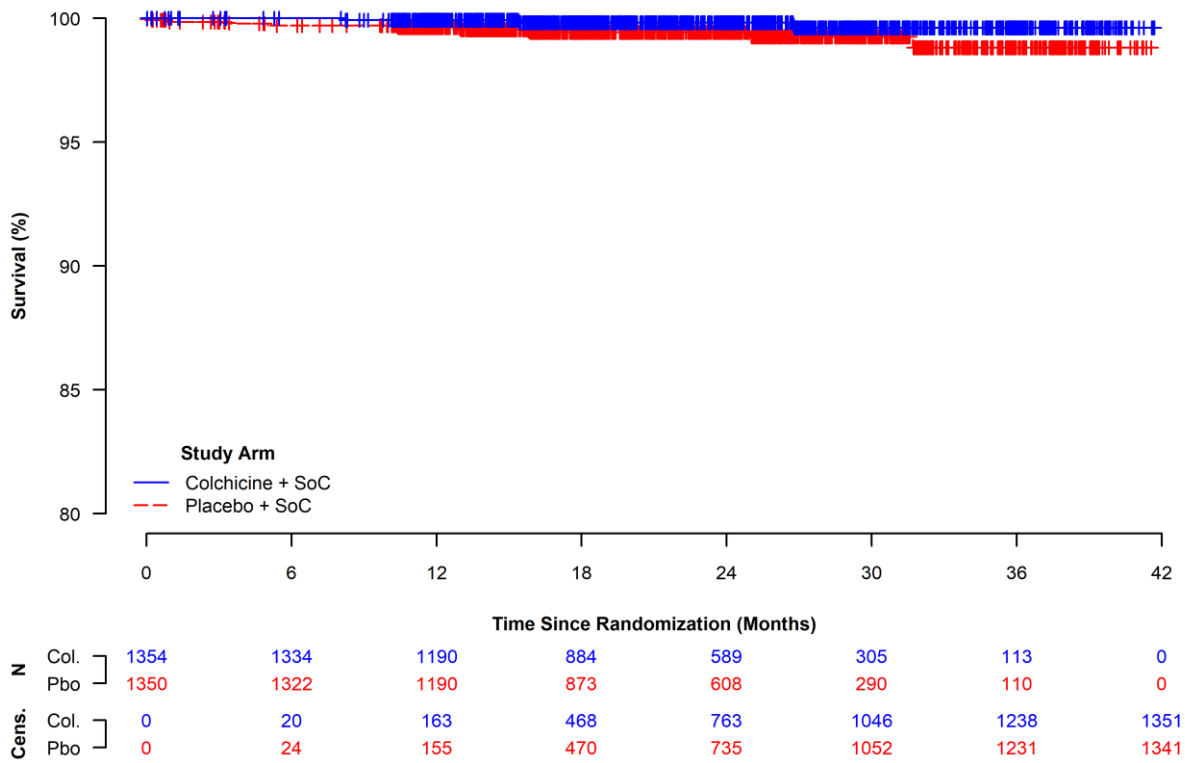
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Region</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.6263</b>					
<b>Europe</b>	2/1,012 (0.2)	10/1,029 (1.0)	0.203 [0.045, 0.926] 0.0394	0.202 [0.044, 0.923] 0.0391	-0.774 [-1.433, -0.115] 0.0213
<b>Non-Europe</b>	3/1,354 (0.2)	9/1,350 (0.7)	0.332 [0.090, 1.225] 0.0979	0.331 [0.089, 1.225] 0.0977	-0.445 [-0.946, 0.056] 0.0817
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 130:** Time to Stroke, Subgrouped by Region (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Region</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.6224</b>							
<b>Europe</b>	2/1,012 (0.2)	NE [NE, NE]	0.5 [0.0, 1.3]	10/1,029 (1.0)	NE [NE, NE]	1.1 [0.4, 1.8]	0.200 [0.044, 0.914] 0.0378
<b>Non-Europe</b>	3/1,354 (0.2)	NE [NE, NE]	0.4 [0.0, 0.9]	9/1,350 (0.7)	NE [NE, NE]	1.2 [0.2, 2.2]	0.332 [0.090, 1.225] 0.0979
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 123:** Kaplan-Meier Curves for Stroke, Within European Countries (ITT Population).



**Figure 124:** Kaplan-Meier Curves for Stroke, Within Non-European Countries (ITT Population).

#### **4.4.2.5.5 Subgrouped by White Blood Cell Count**

The requirements for performing subgroup analyses were not met, i.e., at least one subgroup contained fewer than ten patients and/or, in the case of binary data and time-to-event analyses, no subgroup had at least ten events.

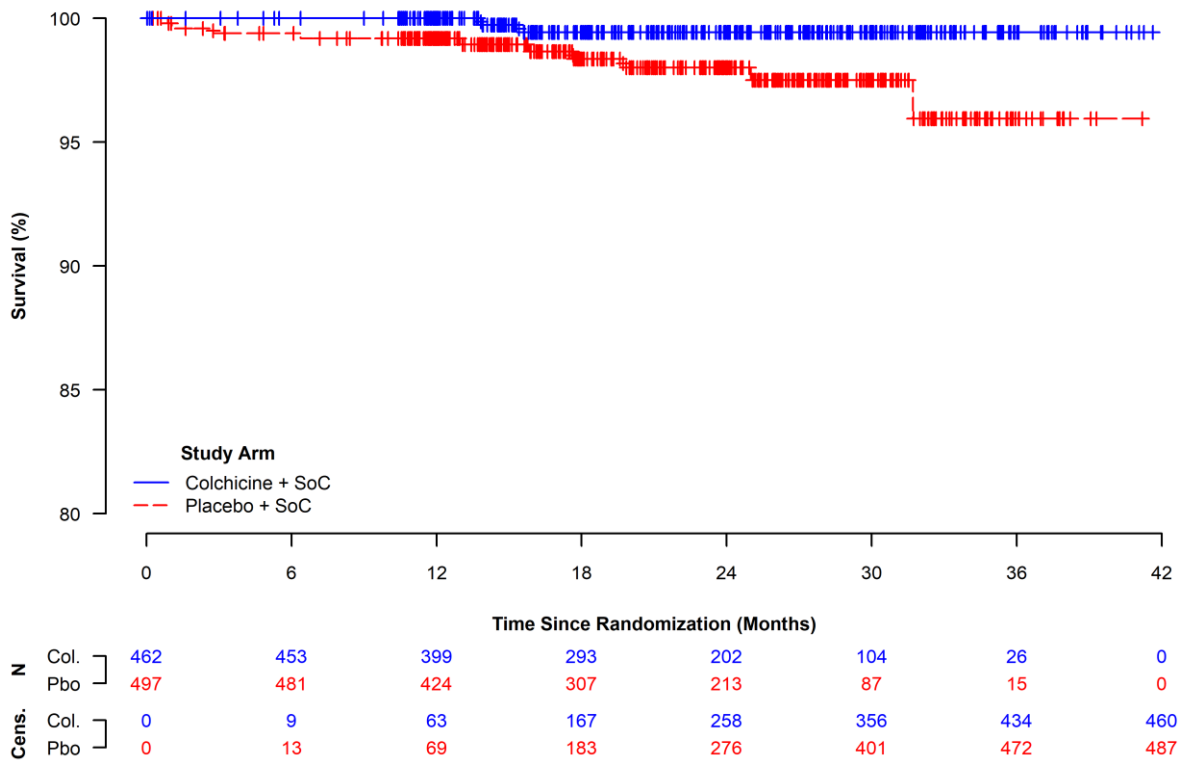
#### 4.4.2.5.6 Subgrouped by Diabetes Status

**Table 131:** Proportion of Patients with Stroke, Subgrouped by Diabetes Status (ITT Population).

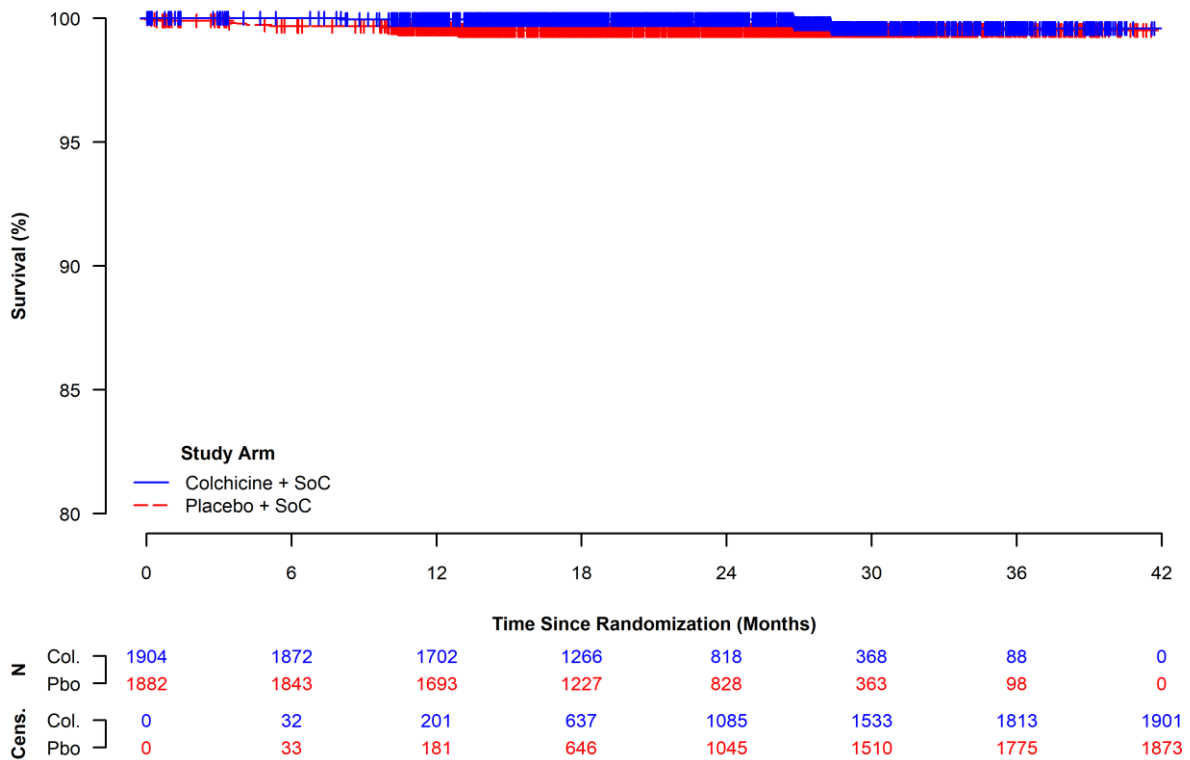
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.6660</b>					
<b>Yes</b>	2/462 (0.4)	10/497 (2.0)	0.215 [0.047, 0.977] 0.0465	0.212 [0.046, 0.972] 0.0458	-1.579 [-2.951, -0.207] 0.0241
<b>No</b>	3/1,904 (0.2)	9/1,882 (0.5)	0.329 [0.089, 1.215] 0.0954	0.328 [0.089, 1.215] 0.0953	-0.321 [-0.680, 0.038] 0.0800
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 132: Time to Stroke, Subgrouped by Diabetes Status (ITT Population).**

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.6600</b>							
<b>Yes</b>	2/462 (0.4)	NE [NE, NE]	0.6 [0.0, 1.4]	10/497 (2.0)	NE [NE, NE]	4.1 [0.5, 7.4]	0.211 [0.046, 0.962] 0.0445
<b>No</b>	3/1,904 (0.2)	NE [NE, NE]	0.4 [0.0, 0.9]	9/1,882 (0.5)	NE [NE, NE]	0.5 [0.2, 0.8]	0.329 [0.089, 1.214] 0.0950
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 125:** Kaplan-Meier Curves for Stroke, Within the Diabetic Subgroup (ITT Population).



**Figure 126:** Kaplan-Meier Curves for Stroke, Within the Non-Diabetic Subgroup (ITT Population).

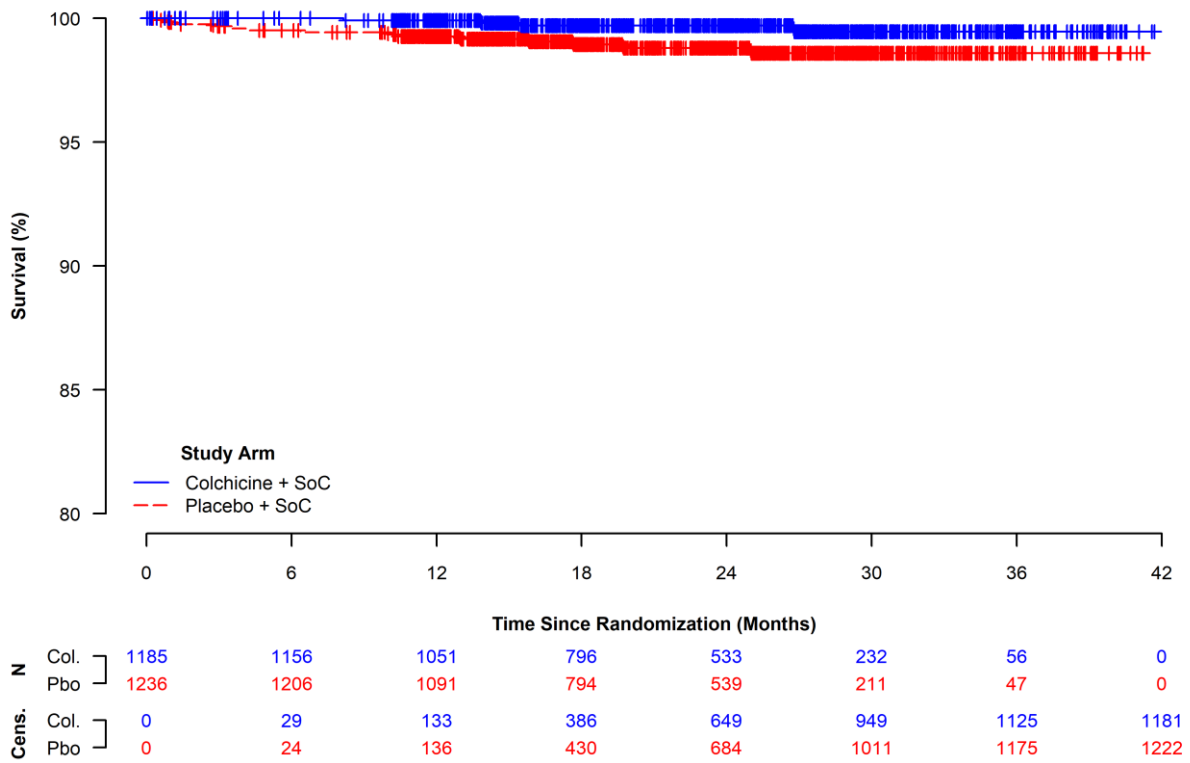
#### 4.4.2.5.7 Subgrouped by Hypertension Status

**Table 133:** Proportion of Patients with Stroke, Subgrouped by Hypertension Status (ITT Population).

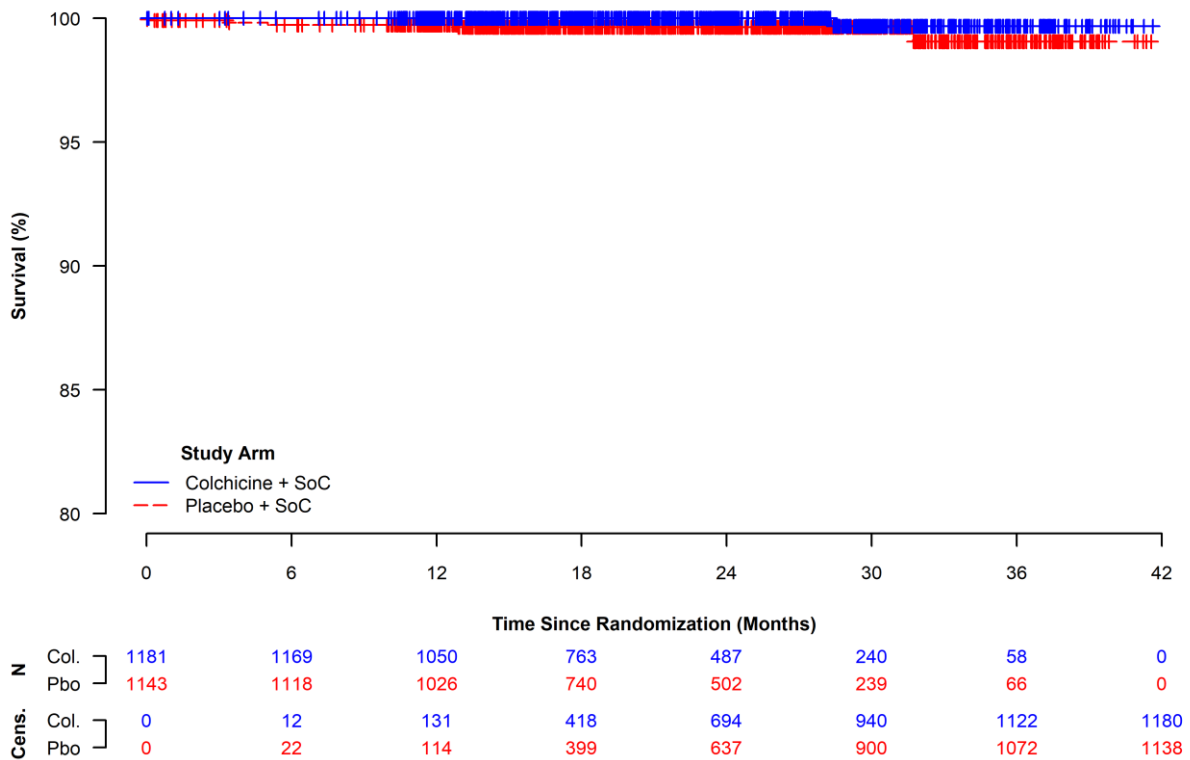
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7227</b>					
<b>Yes</b>	4/1,185 (0.3)	14/1,236 (1.1)	0.298 [0.098, 0.903] 0.0323	0.296 [0.097, 0.901] 0.0320	-0.795 [-1.471, -0.119] 0.0212
<b>No</b>	1/1,181 (0.1)	5/1,143 (0.4)	0.194 [0.023, 1.654] 0.1336	0.193 [0.022, 1.654] 0.1333	-0.353 [-0.770, 0.064] 0.0973
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 134:** Time to Stroke, Subgrouped by Hypertension Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.7326</b>							
<b>Yes</b>	4/1,185 (0.3)	NE [NE, NE]	0.5 [0.0, 1.1]	14/1,236 (1.1)	NE [NE, NE]	1.4 [0.6, 2.2]	0.295 [0.097, 0.896] 0.0313
<b>No</b>	1/1,181 (0.1)	NE [NE, NE]	0.3 [0.0, 0.9]	5/1,143 (0.4)	NE [NE, NE]	0.9 [0.0, 2.1]	0.195 [0.023, 1.670] 0.1357
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 127:** Kaplan-Meier Curves for Stroke, Within the Hypertensive Subgroup (ITT Population).



**Figure 128:** Kaplan-Meier Curves for Stroke, Within the Normotensive Subgroup (ITT Population).

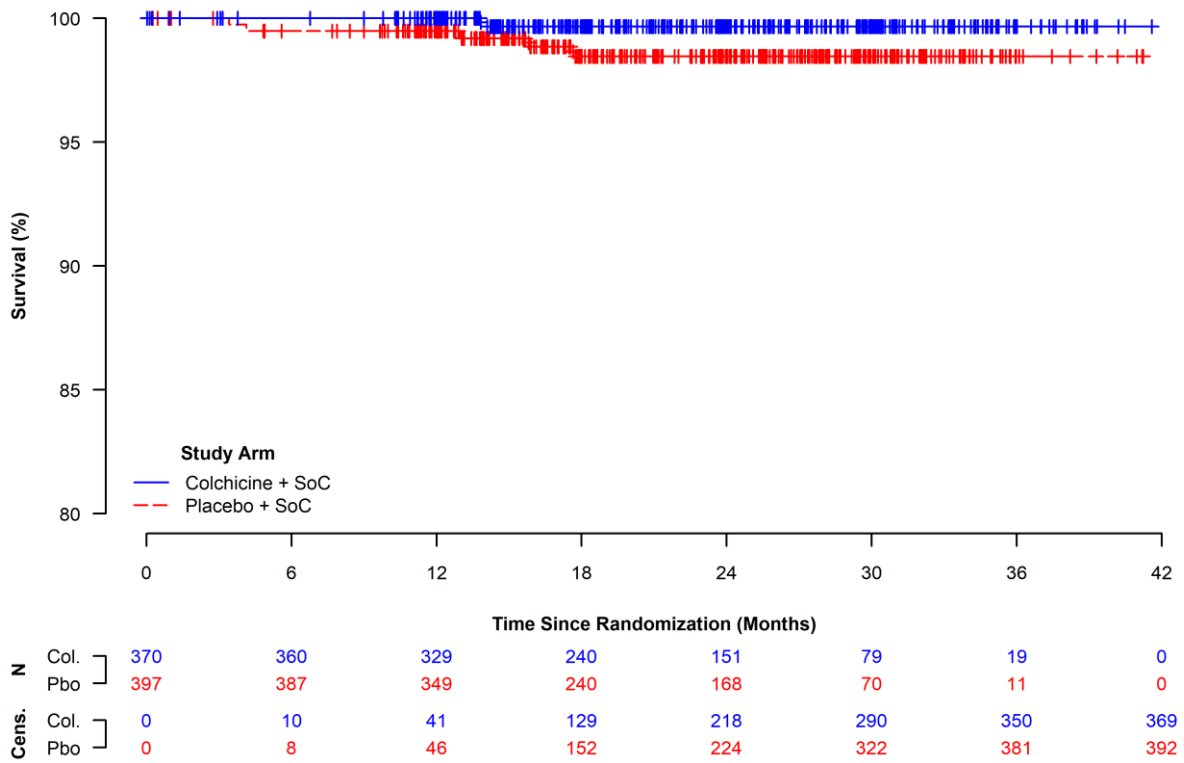
#### 4.4.2.5.8 Subgrouped by History of Myocardial Infarction

**Table 135:** Proportion of Patients with Stroke, Subgrouped by History of Myocardial Infarction (ITT Population).

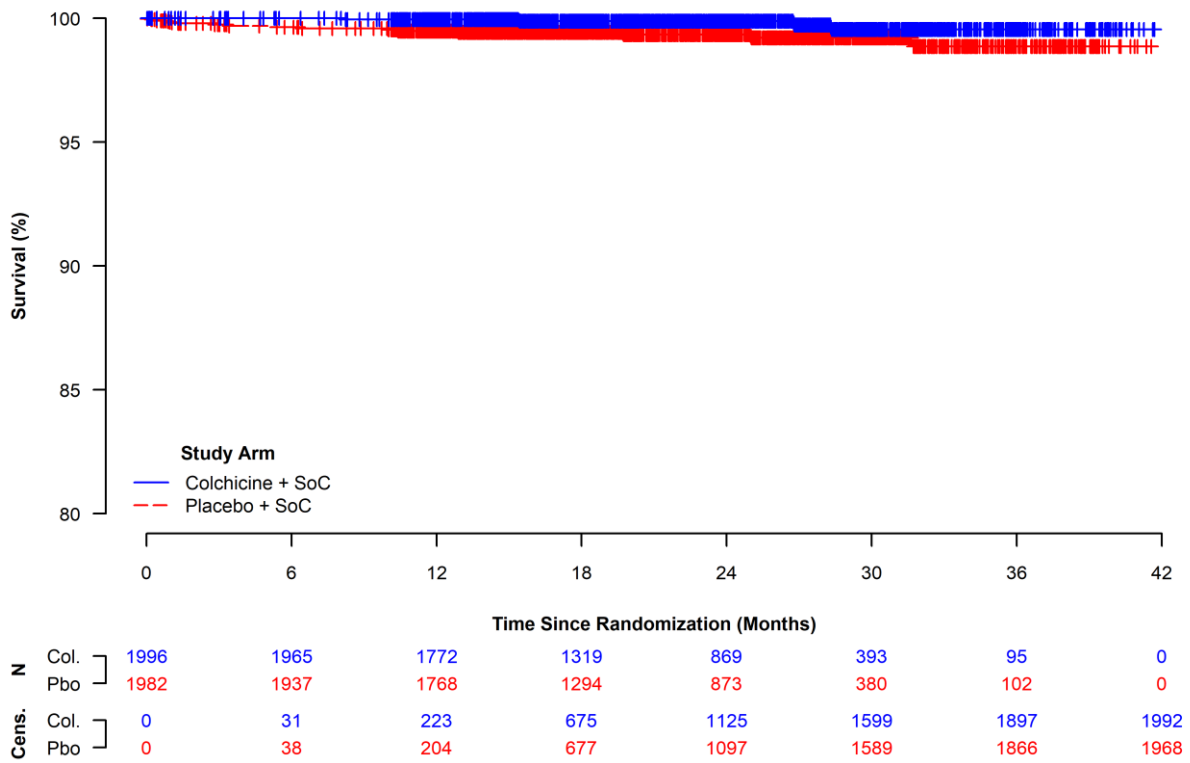
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of MI</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8151</b>					
<b>Yes</b>	1/370 (0.3)	5/397 (1.3)	0.215 [0.025, 1.828] 0.1591	0.212 [0.025, 1.827] 0.1583	-0.989 [-2.207, 0.229] 0.1114
<b>No</b>	4/1,996 (0.2)	14/1,982 (0.7)	0.284 [0.094, 0.860] 0.0260	0.282 [0.093, 0.859] 0.0259	-0.506 [-0.924, -0.088] 0.0176
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 136:** Time to Stroke, Subgrouped by History of Myocardial Infarction (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of MI</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.8096</b>							
<b>Yes</b>	1/370 (0.3)	NE [NE, NE]	0.3 [0.0, 1.0]	5/397 (1.3)	NE [NE, NE]	1.5 [0.2, 2.9]	0.213 [0.025, 1.821] 0.1577
<b>No</b>	4/1,996 (0.2)	NE [NE, NE]	0.5 [0.0, 1.0]	14/1,982 (0.7)	NE [NE, NE]	1.1 [0.3, 2.0]	0.283 [0.093, 0.859] 0.0259
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 129:** Kaplan-Meier Curves for Stroke, Within the Subgroup With History of Myocardial Infarction (ITT Population).



**Figure 130:** Kaplan-Meier Curves for Stroke, Within the Subgroup Without History of Myocardial Infarction (ITT Population).

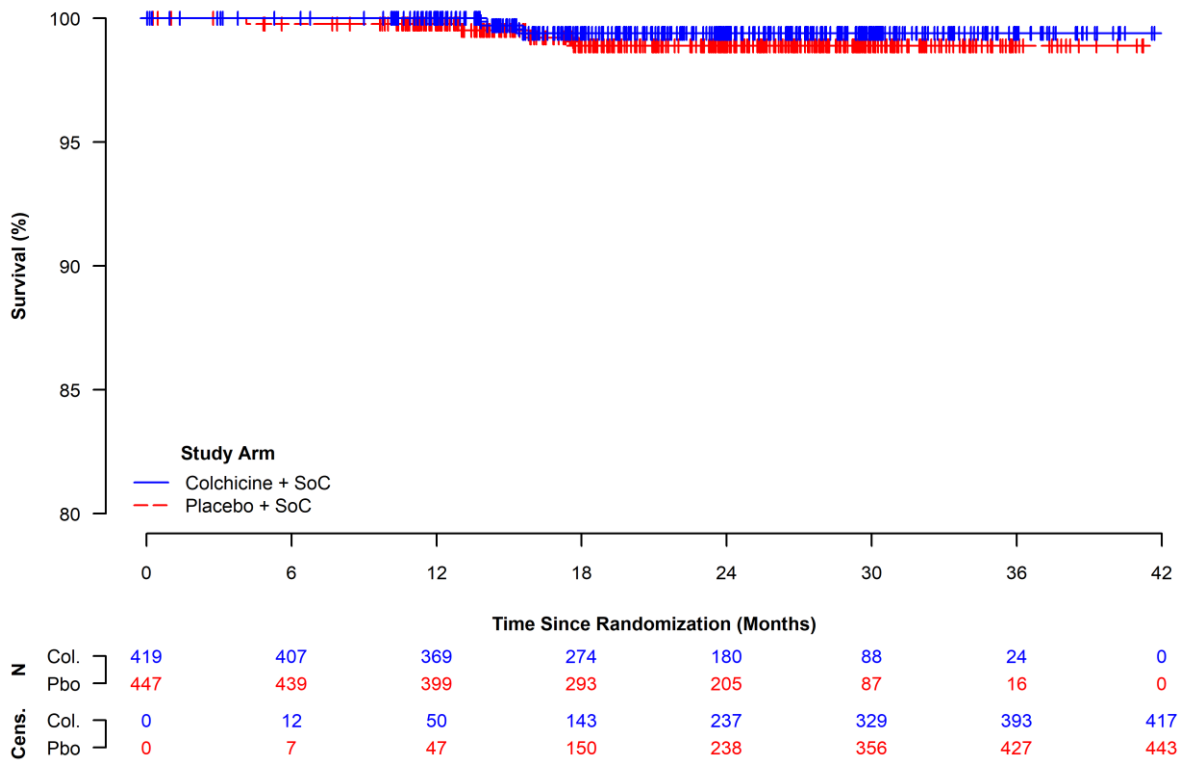
#### 4.4.2.5.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 137:** Proportion of Patients with Stroke, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

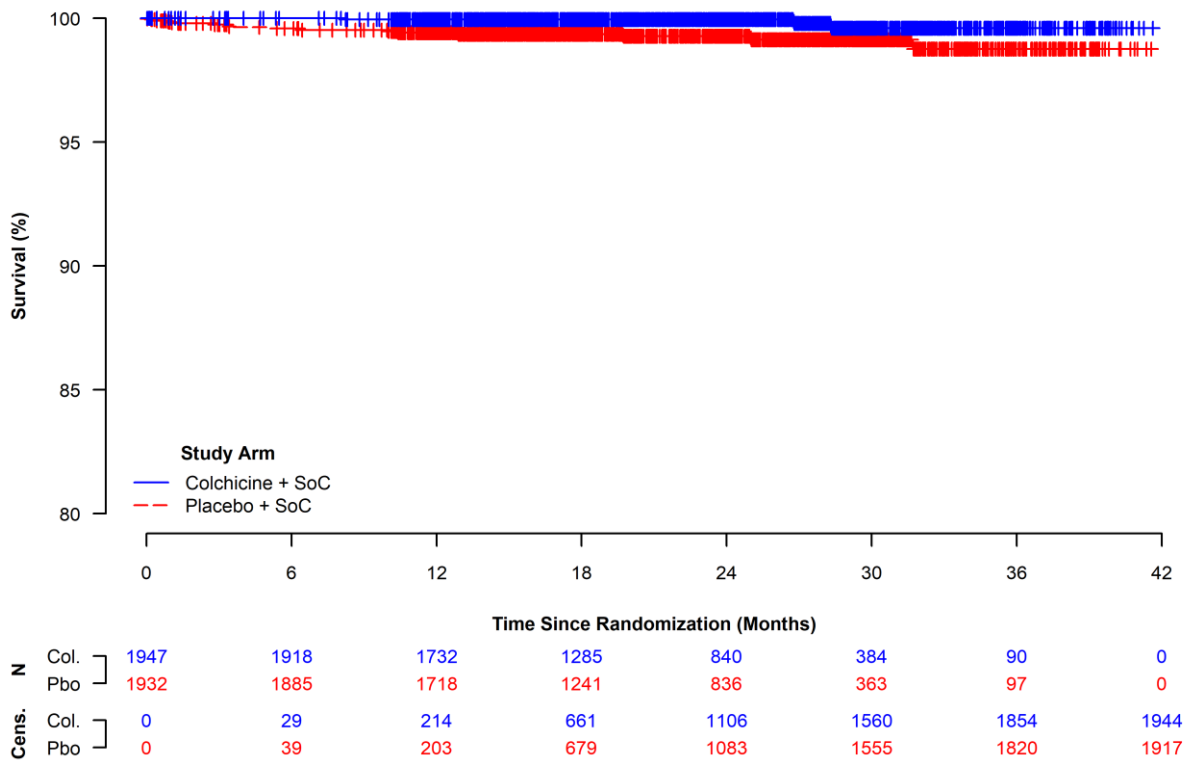
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.3660</b>					
<b>Yes</b>	2/419 (0.5)	4/447 (0.9)	0.533 [0.098, 2.897] 0.4667	0.531 [0.097, 2.915] 0.4664	-0.418 [-1.512, 0.677] 0.4546
<b>No</b>	3/1,947 (0.2)	15/1,932 (0.8)	0.198 [0.058, 0.684] 0.0105	0.197 [0.057, 0.682] 0.0104	-0.622 [-1.051, -0.194] 0.0044
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 138:** Time to Stroke, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.3544</b>							
<b>Yes</b>	2/419 (0.5)	NE [NE, NE]	0.6 [0.0, 1.5]	4/447 (0.9)	NE [NE, NE]	1.1 [0.0, 2.2]	0.543 [0.099, 2.965] 0.4809
<b>No</b>	3/1,947 (0.2)	NE [NE, NE]	0.4 [0.0, 0.9]	15/1,932 (0.8)	NE [NE, NE]	1.2 [0.4, 2.1]	0.196 [0.057, 0.679] 0.0101
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 131:** Kaplan-Meier Curves for Stroke, Within the Subgroup With History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).



**Figure 132:** Kaplan-Meier Curves for Stroke, Within the Subgroup Without History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

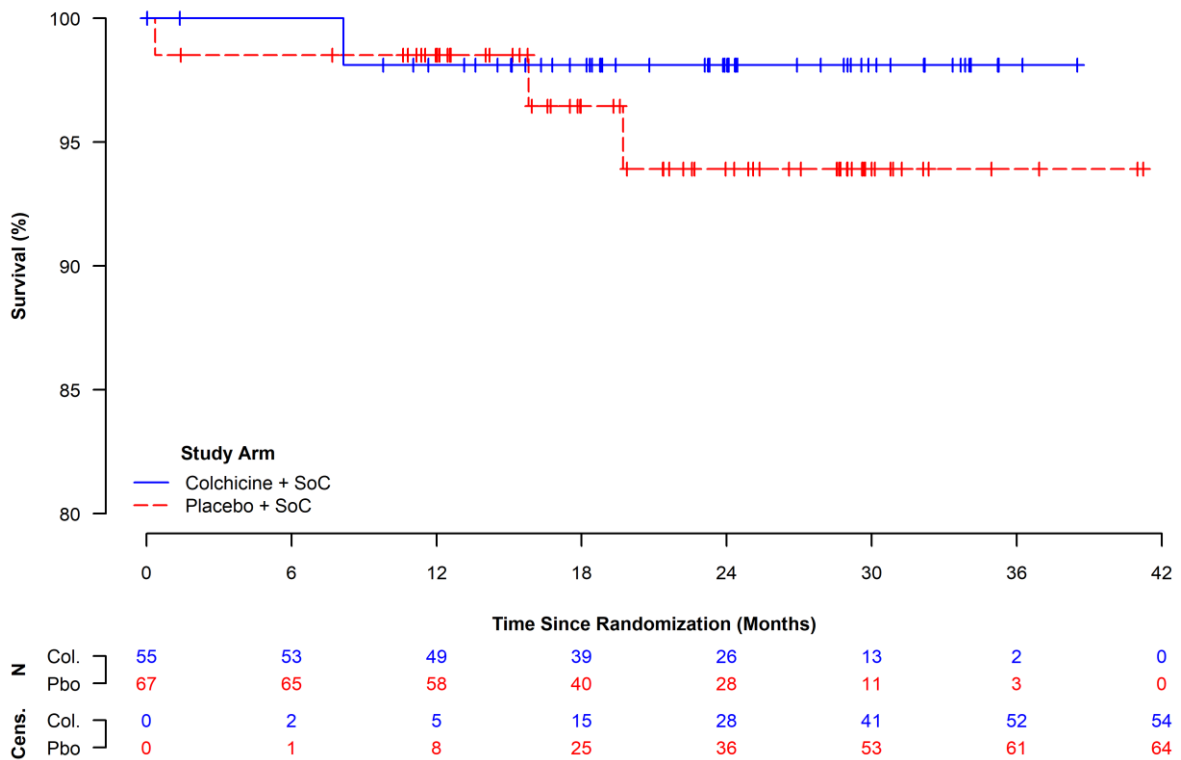
#### 4.4.2.5.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 139:** Proportion of Patients with Stroke, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

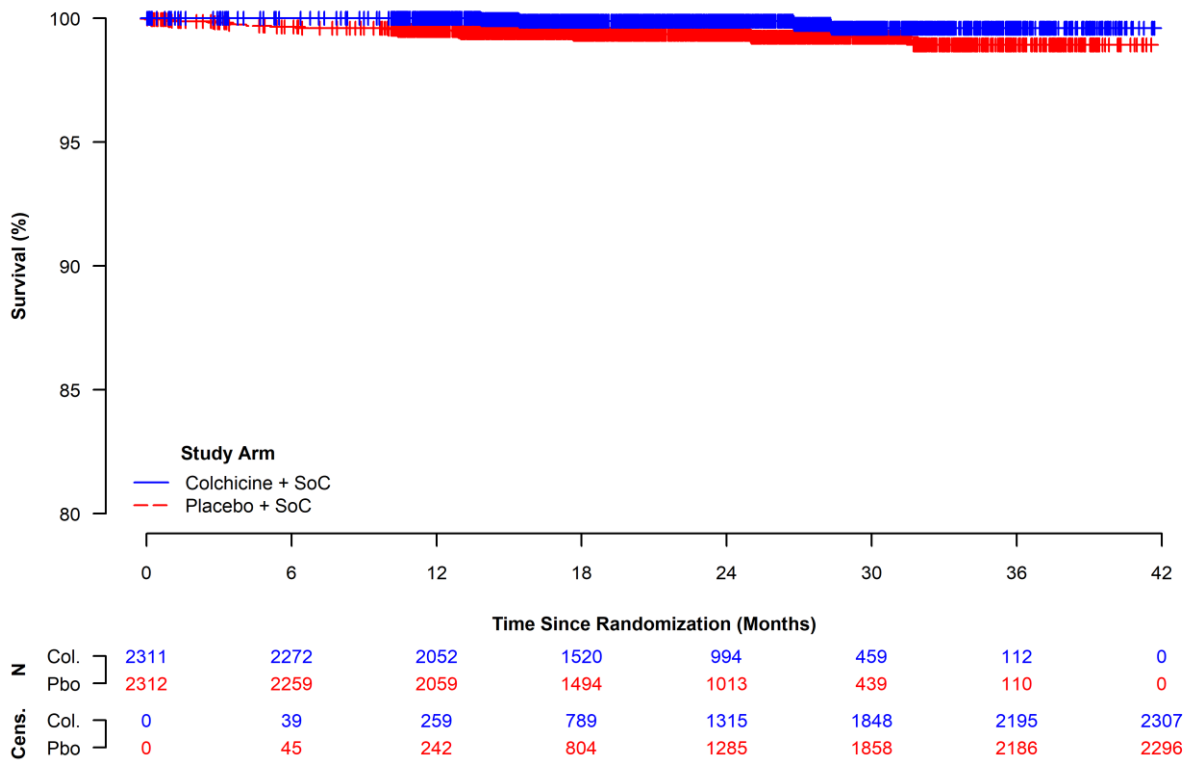
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7279</b>					
<b>Yes</b>	1/55 (1.8)	3/67 (4.5)	0.406 [0.043, 3.795] 0.4293	0.395 [0.040, 3.909] 0.4271	-2.659 [-8.741, 3.423] 0.3914
<b>No</b>	4/2,311 (0.2)	16/2,312 (0.7)	0.250 [0.084, 0.747] 0.0130	0.249 [0.083, 0.745] 0.0130	-0.519 [-0.897, -0.141] 0.0071
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 140:** Time to Stroke, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.7432</b>							
<b>Yes</b>	1/55 (1.8)	NE [NE, NE]	1.9 [0.0, 5.5]	3/67 (4.5)	NE [NE, NE]	6.1 [0.0, 12.7]	0.396 [0.041, 3.804] 0.4219
<b>No</b>	4/2,311 (0.2)	NE [NE, NE]	0.4 [0.0, 0.8]	16/2,312 (0.7)	NE [NE, NE]	1.1 [0.3, 1.8]	0.249 [0.083, 0.745] 0.0129
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 133:** Kaplan-Meier Curves for Stroke, Within the Subgroup With History of Stroke or Transient Ischaemic Attack (ITT Population).



**Figure 134:** Kaplan-Meier Curves for Stroke, Within the Subgroup Without History of Stroke or Transient Ischaemic Attack (ITT Population).

#### 4.4.2.6 Urgent Hospitalization for Angina Requiring Coronary Revascularization

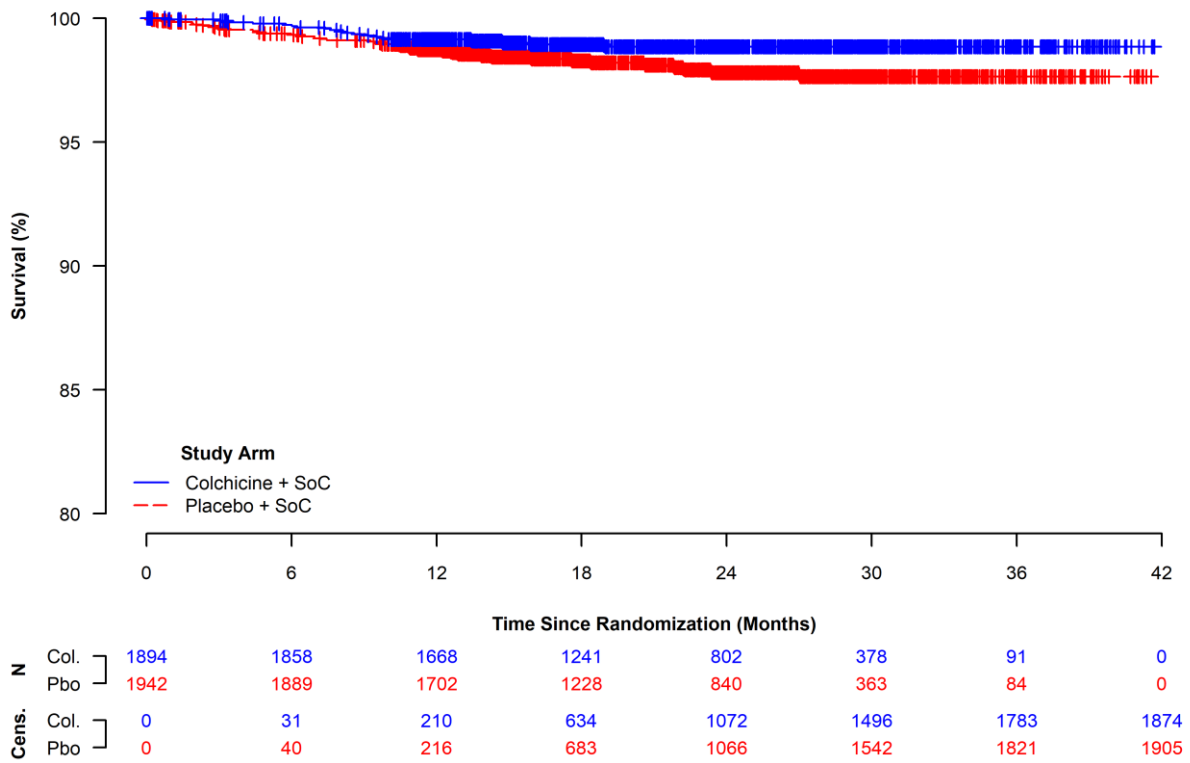
##### 4.4.2.6.1 Subgrouped by Sex

**Table 141:** Proportion of Patients with Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Sex (ITT Population).

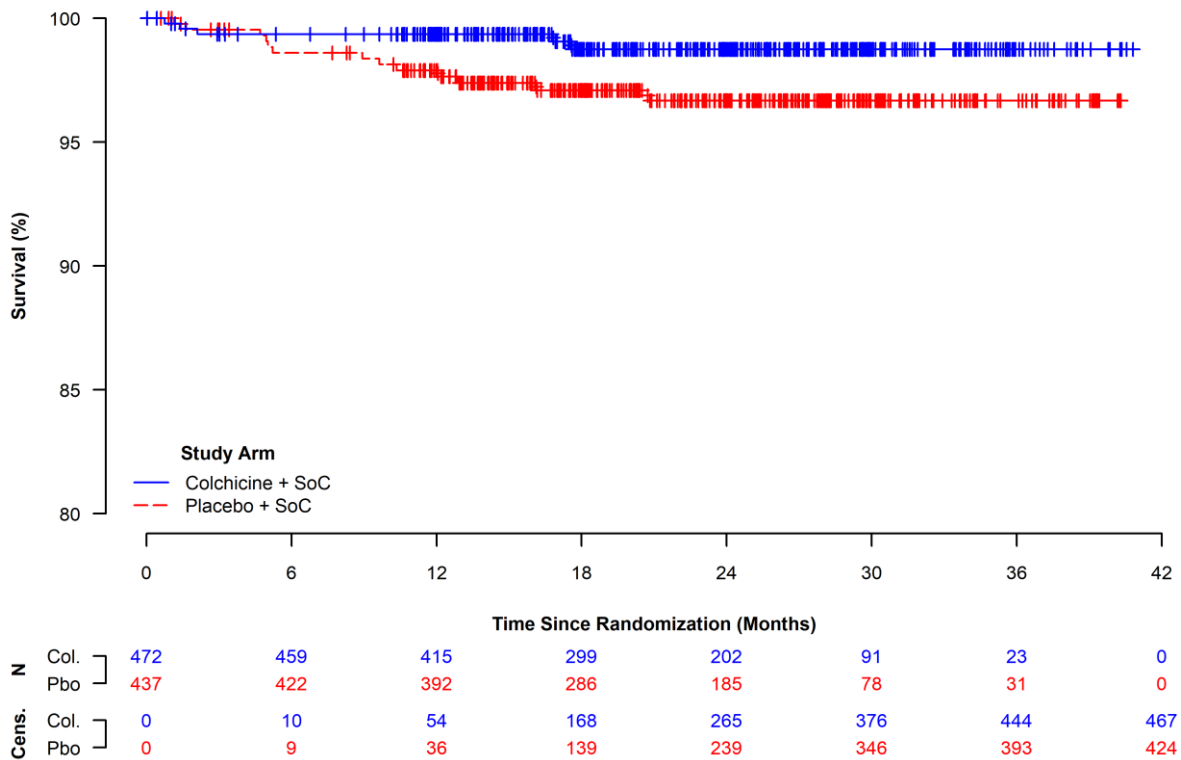
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>d</sup> = 0.4419</b>					
<b>Sex</b>					
<b>Male</b>	20/1,894 (1.1)	37/1,942 (1.9)	0.554 [0.323, 0.951] 0.0323	0.549 [0.318, 0.950] 0.0321	-0.849 [-1.612, -0.087] 0.0291
<b>Female</b>	5/472 (1.1)	13/437 (3.0)	0.356 [0.128, 0.991] 0.0479	0.349 [0.123, 0.988] 0.0473	-1.916 [-3.757, -0.074] 0.0415
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 142:** Time to Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Sex (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.4640</b>							
<b>Sex</b>							
<b>Male</b>	20/1,894 (1.1)	NE [NE, NE]	1.1 [0.6, 1.6]	37/1,942 (1.9)	NE [NE, NE]	2.4 [1.6, 3.1]	0.549 [0.319, 0.946] 0.0308
<b>Female</b>	5/472 (1.1)	NE [NE, NE]	1.3 [0.1, 2.4]	13/437 (3.0)	NE [NE, NE]	3.3 [1.5, 5.1]	0.359 [0.128, 1.006] 0.0513
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 135:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Male Sex Subgroup (ITT Population).



**Figure 136:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Female Sex Subgroup (ITT Population).

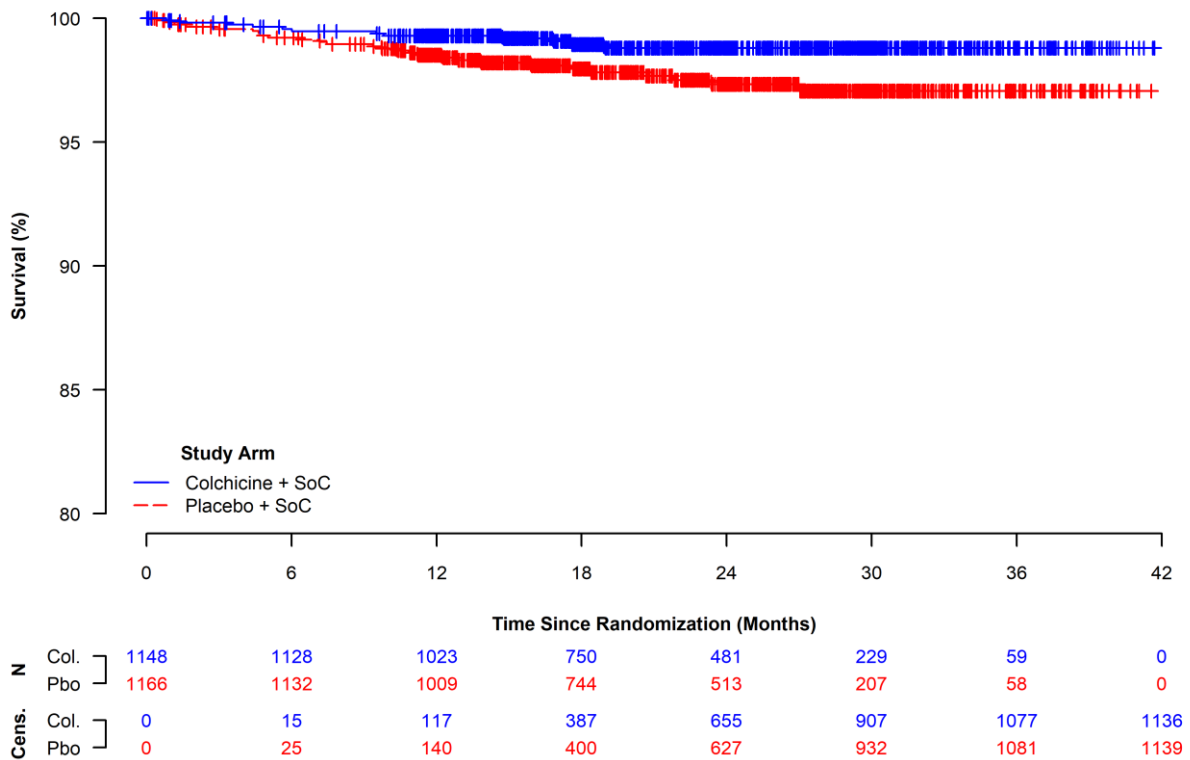
#### 4.4.2.6.2 Subgrouped by Age Group

**Table 143:** Proportion of Patients with Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Age Group (ITT Population).

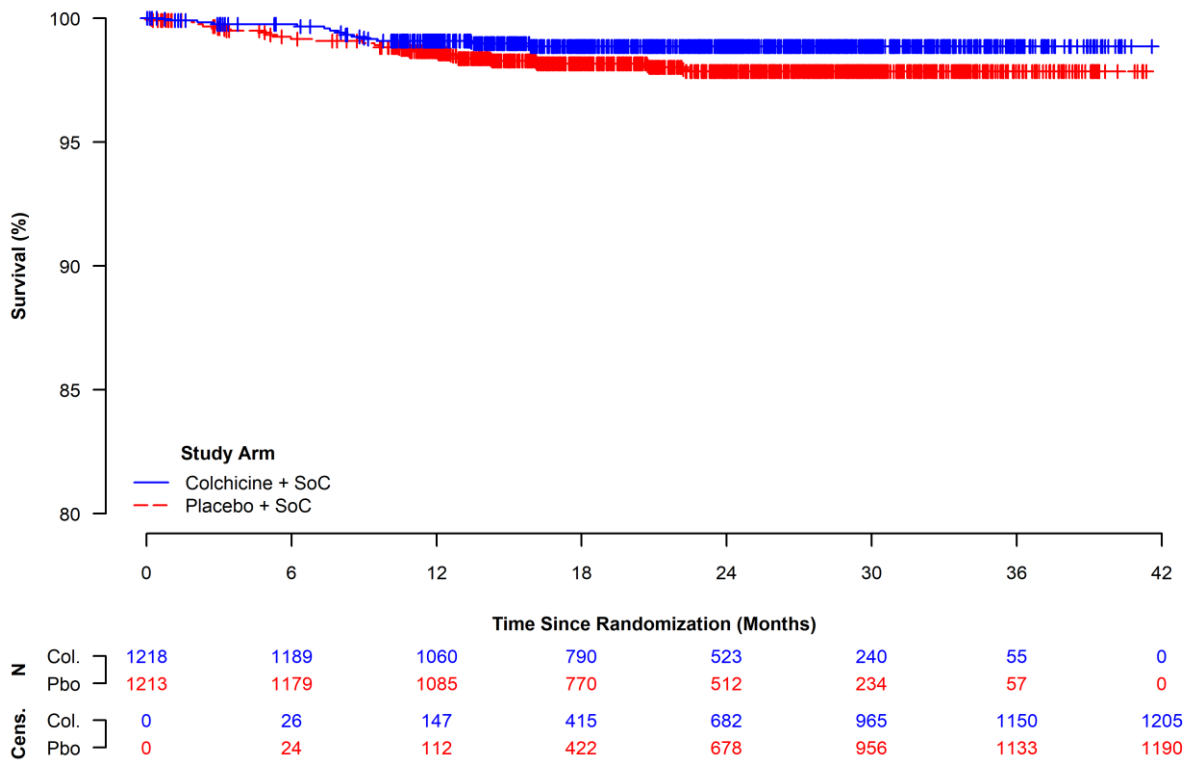
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Age</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.6484</b>					
<b>&lt; 60 Years</b>	12/1,148 (1.0)	27/1,166 (2.3)	0.451 [0.230, 0.887] 0.0209	0.446 [0.225, 0.884] 0.0207	-1.270 [-2.315, -0.226] 0.0172
<b>≥ 60 Years</b>	13/1,218 (1.1)	23/1,213 (1.9)	0.563 [0.286, 1.106] 0.0954	0.558 [0.281, 1.107] 0.0951	-0.829 [-1.789, 0.131] 0.0907
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 144:** Time to Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Age Group (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.6277</b>							
<b>&lt; 60 Years</b>	12/1,148 (1.0)	NE [NE, NE]	1.2 [0.5, 1.9]	27/1,166 (2.3)	NE [NE, NE]	2.9 [1.8, 4.1]	0.445 [0.225, 0.878] 0.0196
<b>≥ 60 Years</b>	13/1,218 (1.1)	NE [NE, NE]	1.1 [0.5, 1.7]	23/1,213 (1.9)	NE [NE, NE]	2.1 [1.3, 3.0]	0.565 [0.286, 1.114] 0.0994
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 137:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Age 59 Years or Younger Subgroup (ITT Population).



**Figure 138:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Age 60 Years or Older Subgroup (ITT Population).

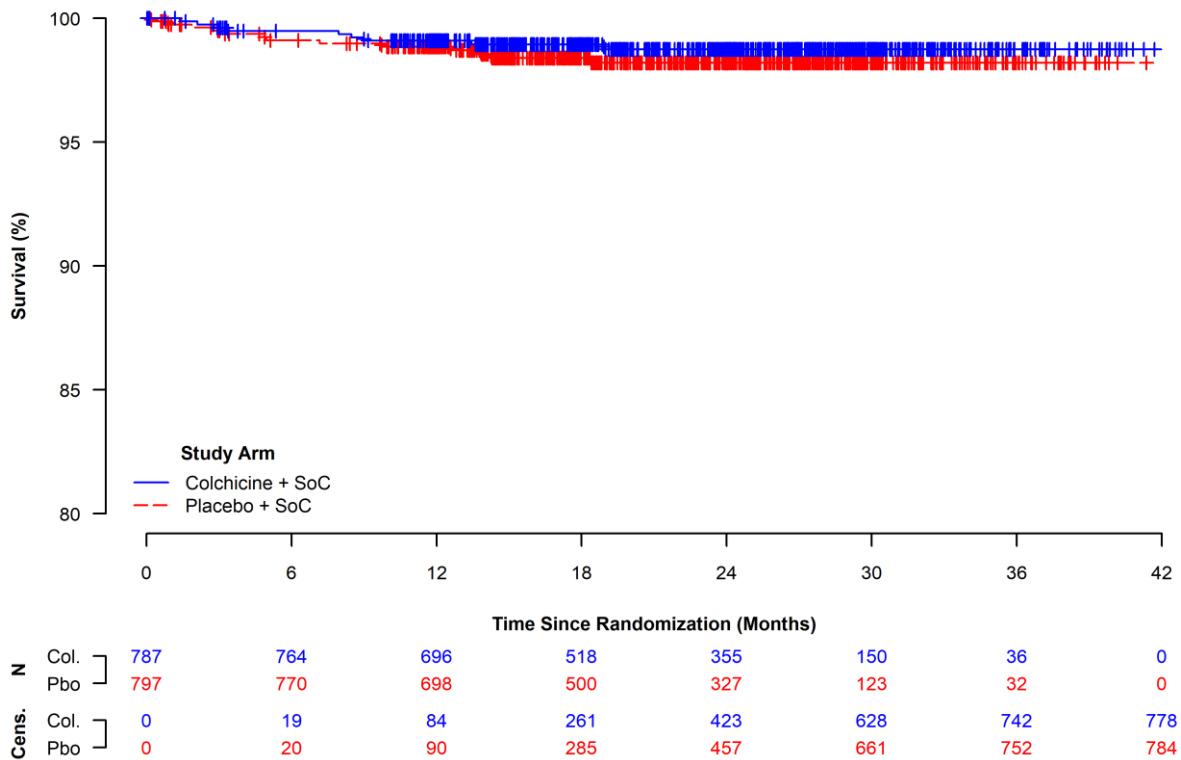
#### 4.4.2.6.3 Subgrouped by Smoking Status

**Table 145:** Proportion of Patients with Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Smoking Status (ITT Population).

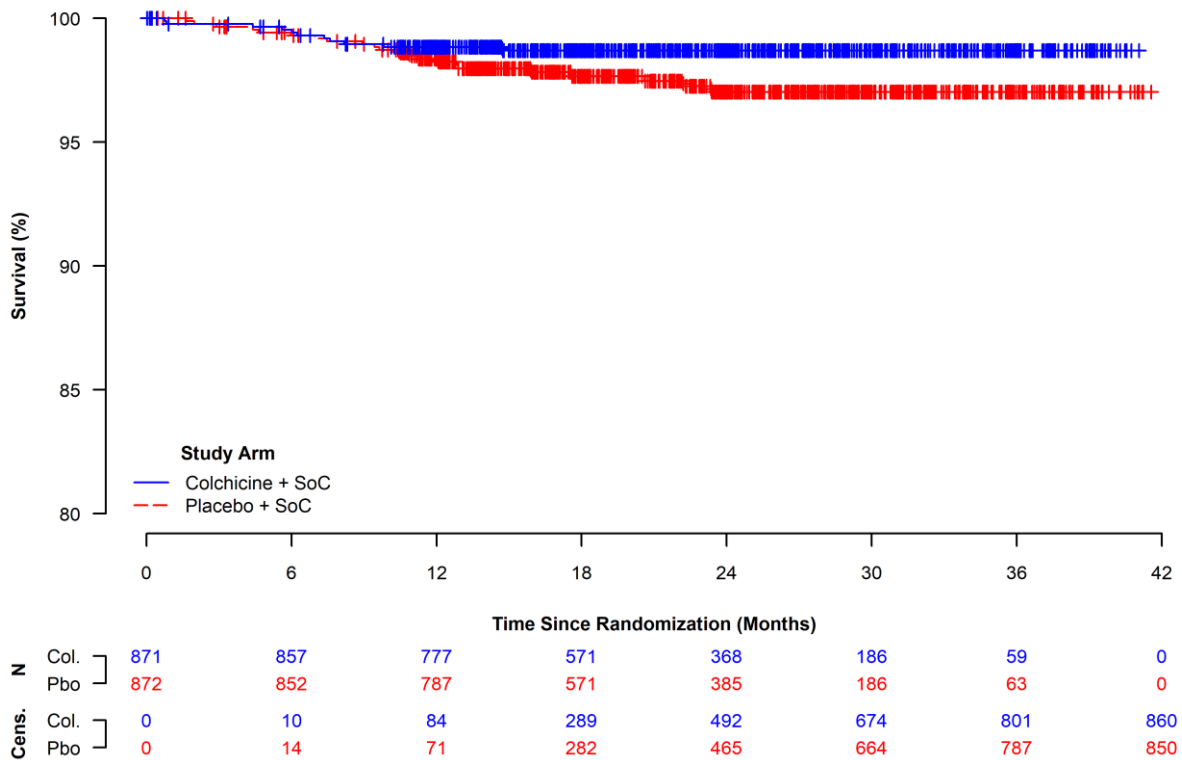
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,377)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Smoking Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.5311</b>					
<b>Non</b>	9/787 (1.1)	13/797 (1.6)	0.701 [0.301, 1.631] 0.4097	0.698 [0.297, 1.642] 0.4095	-0.488 [-1.639, 0.664] 0.4065
<b>Ex</b>	11/871 (1.3)	22/872 (2.5)	0.501 [0.244, 1.026] 0.0588	0.494 [0.238, 1.025] 0.0584	-1.260 [-2.538, 0.018] 0.0533
<b>Current</b>	5/708 (0.7)	15/708 (2.1)	0.333 [0.122, 0.912] 0.0325	0.329 [0.119, 0.909] 0.0321	-1.412 [-2.639, -0.185] 0.0241
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 146:** Time to Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Smoking Status (ITT Population).

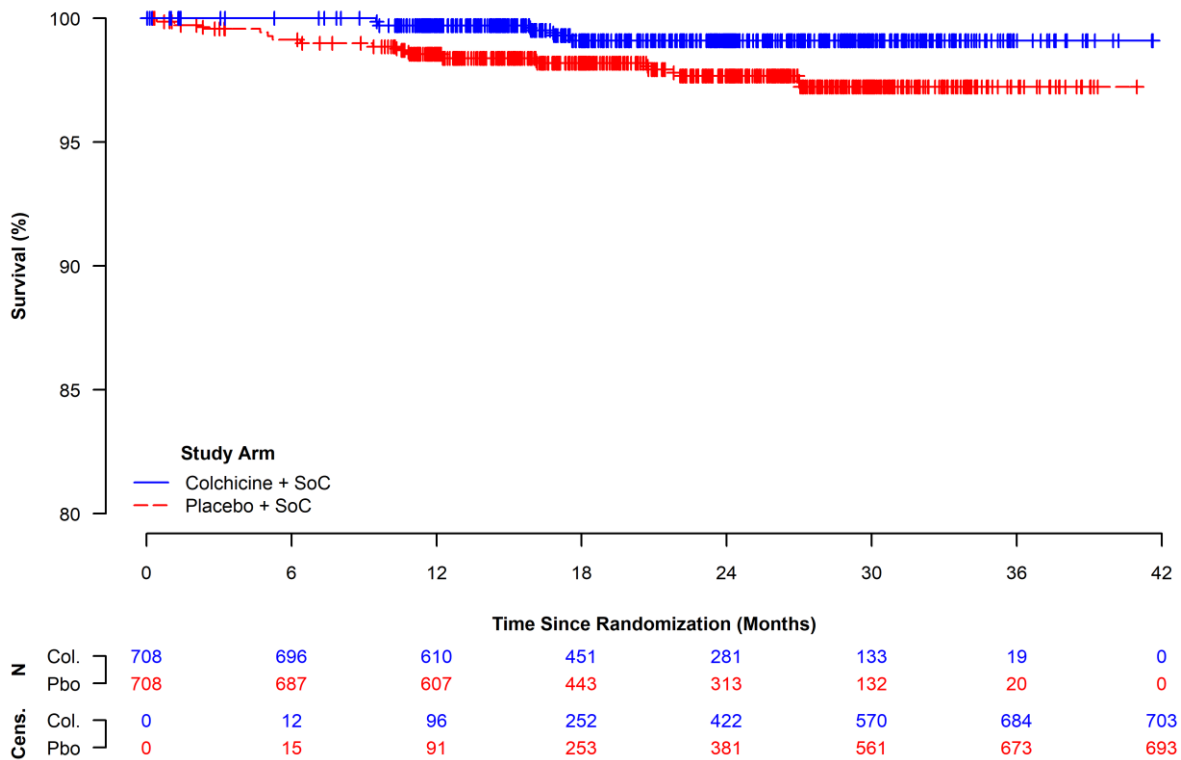
Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,377)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Smoking Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.5389</b>							
<b>Non</b>	9/787 (1.1)	NE [NE, NE]	1.3 [0.4, 2.1]	13/797 (1.6)	NE [NE, NE]	1.8 [0.8, 2.8]	0.695 [0.297, 1.625] 0.4010
<b>Ex</b>	11/871 (1.3)	NE [NE, NE]	1.3 [0.5, 2.1]	22/872 (2.5)	NE [NE, NE]	3.0 [1.7, 4.2]	0.501 [0.243, 1.033] 0.0612
<b>Current</b>	5/708 (0.7)	NE [NE, NE]	0.9 [0.1, 1.7]	15/708 (2.1)	NE [NE, NE]	2.8 [1.3, 4.3]	0.331 [0.120, 0.911] 0.0323
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 139:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Non-Smoker Subgroup (ITT Population).



**Figure 140:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Ex-Smoker Subgroup (ITT Population).



**Figure 141:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Current Smoker Subgroup (ITT Population).

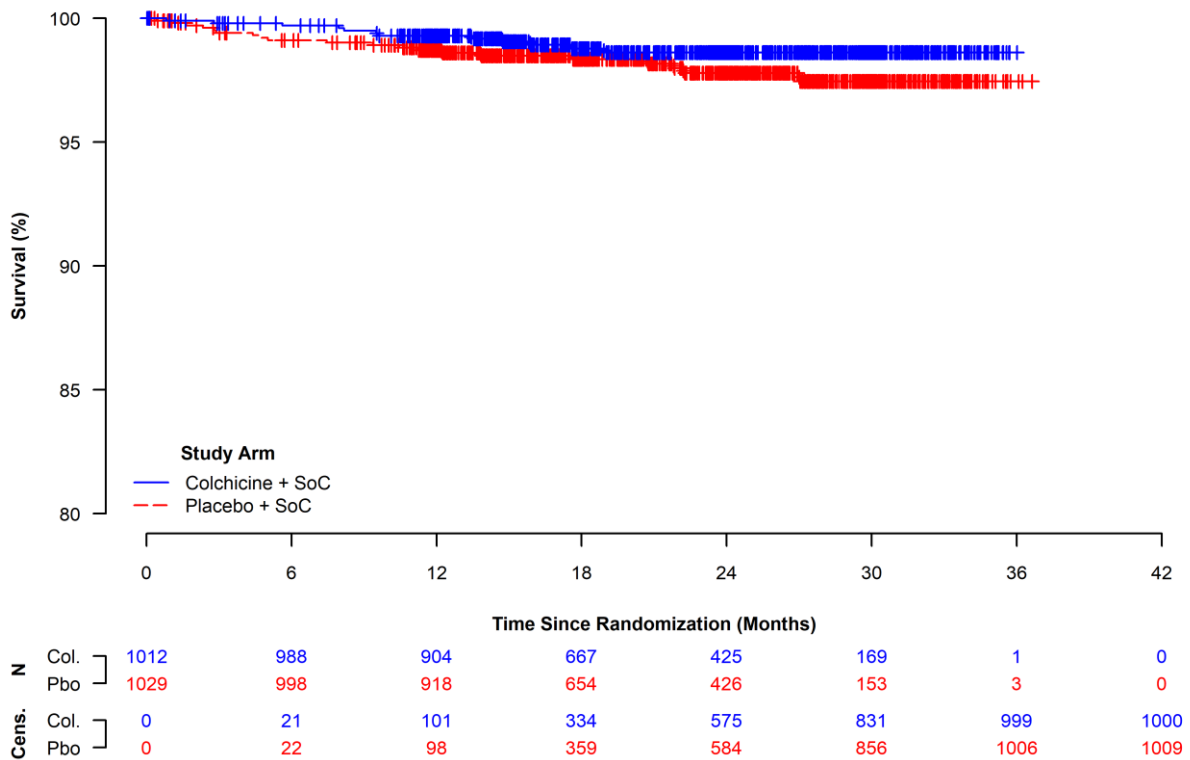
#### 4.4.2.6.4 Subgrouped by Region

**Table 147:** Proportion of Patients with Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Region (ITT Population).

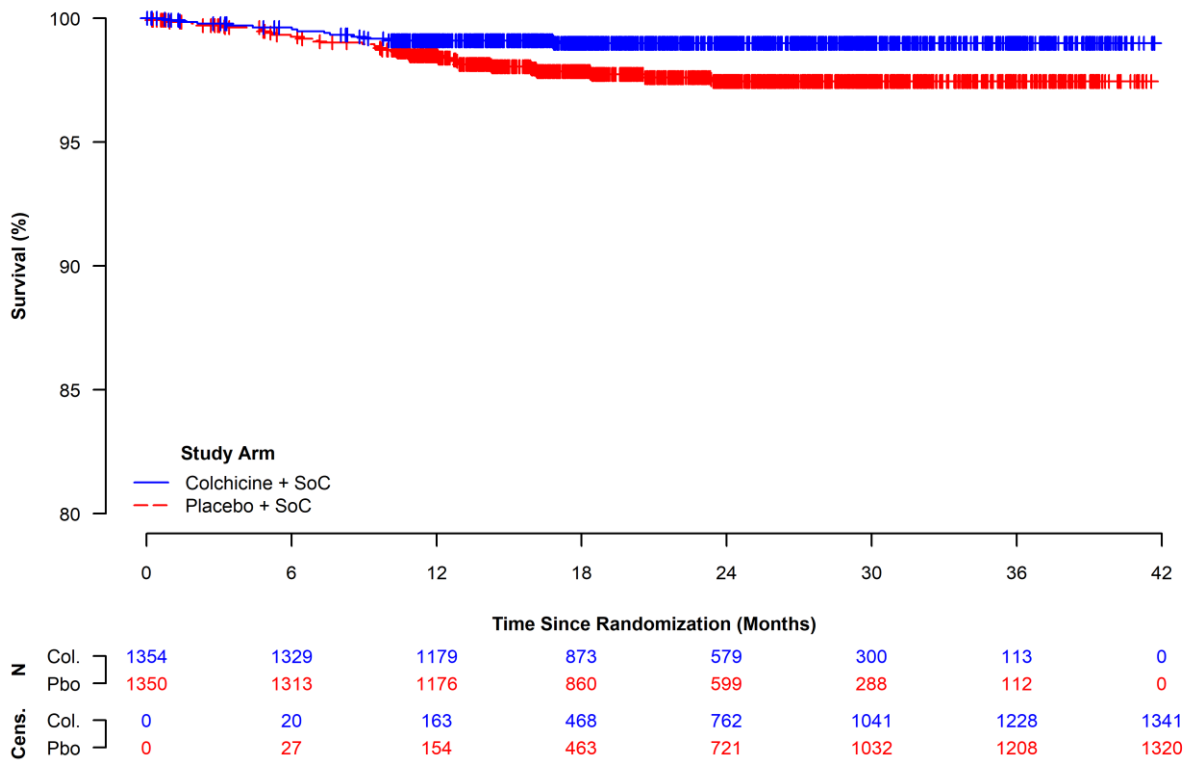
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Region</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4814</b>					
<b>Europe</b>	12/1,012 (1.2)	20/1,029 (1.9)	0.610 [0.300, 1.241] 0.1728	0.605 [0.294, 1.245] 0.1725	-0.758 [-1.833, 0.317] 0.1672
<b>Non-Europe</b>	13/1,354 (1.0)	30/1,350 (2.2)	0.432 [0.226, 0.825] 0.0109	0.427 [0.222, 0.821] 0.0108	-1.262 [-2.204, -0.320] 0.0087
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 148:** Time to Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Region (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.4931</b>							
<b>Europe</b>	12/1,012 (1.2)	NE [NE, NE]	1.4 [0.6, 2.2]	20/1,029 (1.9)	NE [NE, NE]	2.5 [1.3, 3.7]	0.603 [0.295, 1.234] 0.1666
<b>Non-Europe</b>	13/1,354 (1.0)	NE [NE, NE]	1.0 [0.5, 1.5]	30/1,350 (2.2)	NE [NE, NE]	2.6 [1.6, 3.5]	0.430 [0.224, 0.824] 0.0110
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 142:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within European Countries (ITT Population).



**Figure 143:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within Non-European Countries (ITT Population).

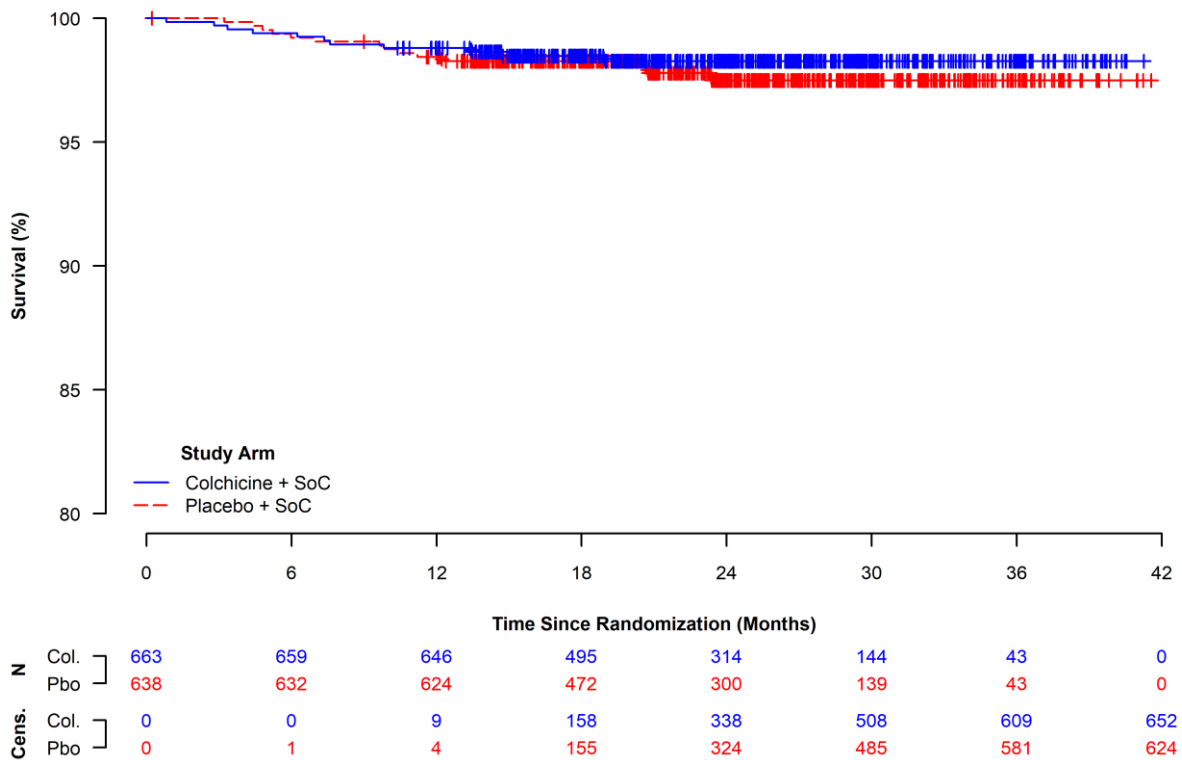
#### 4.4.2.6.5 Subgrouped by White Blood Cell Count

**Table 149:** Proportion of Patients with Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by White Blood Cell Count (ITT Population).

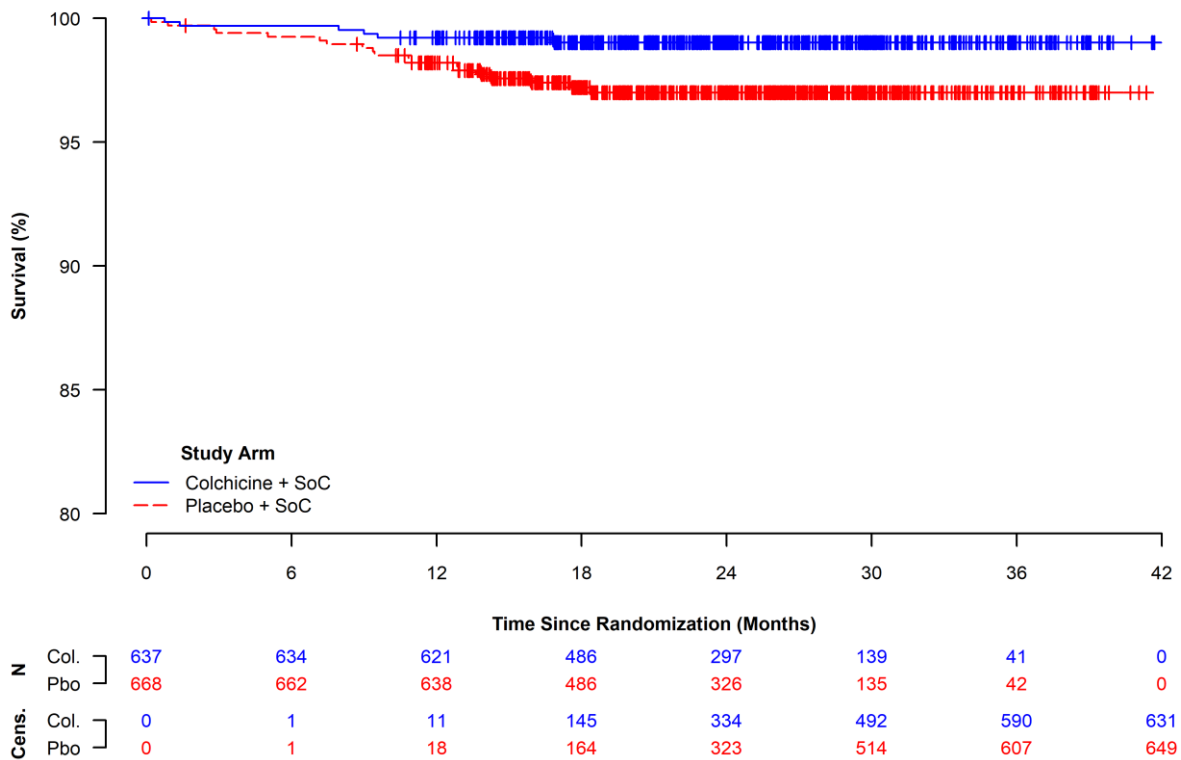
Subgroup	Colchicine + SoC (N = 1,300)	Placebo + SoC (N = 1,306)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1709</b>					
< 8.66 10 <sup>3</sup> /μL	11/663 (1.7)	14/638 (2.2)	0.756 [0.346, 1.653] 0.4835	0.752 [0.339, 1.669] 0.4835	-0.535 [-2.031, 0.961] 0.4831
≥ 8.66 10 <sup>3</sup> /μL	6/637 (0.9)	19/668 (2.8)	0.331 [0.133, 0.824] 0.0175	0.325 [0.129, 0.819] 0.0171	-1.902 [-3.369, -0.435] 0.0110
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 150:** Time to Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by White Blood Cell Count (ITT Population).

Subgroup	Colchicine + SoC (N = 1,300)			Placebo + SoC (N = 1,306)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.1719</b>							
< 8.66 10 <sup>3</sup> /μL	11/663 (1.7)	NE [NE, NE]	1.7 [0.7, 2.8]	14/638 (2.2)	NE [NE, NE]	2.5 [1.2, 3.8]	0.753 [0.342, 1.659] 0.4818
≥ 8.66 10 <sup>3</sup> /μL	6/637 (0.9)	NE [NE, NE]	1.0 [0.2, 1.8]	19/668 (2.8)	NE [NE, NE]	3.0 [1.7, 4.3]	0.328 [0.131, 0.821] 0.0172
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 144:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Lower White Blood Cell Count Subgroup (ITT Population).



**Figure 145:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Upper White Blood Cell Count Subgroup (ITT Population).

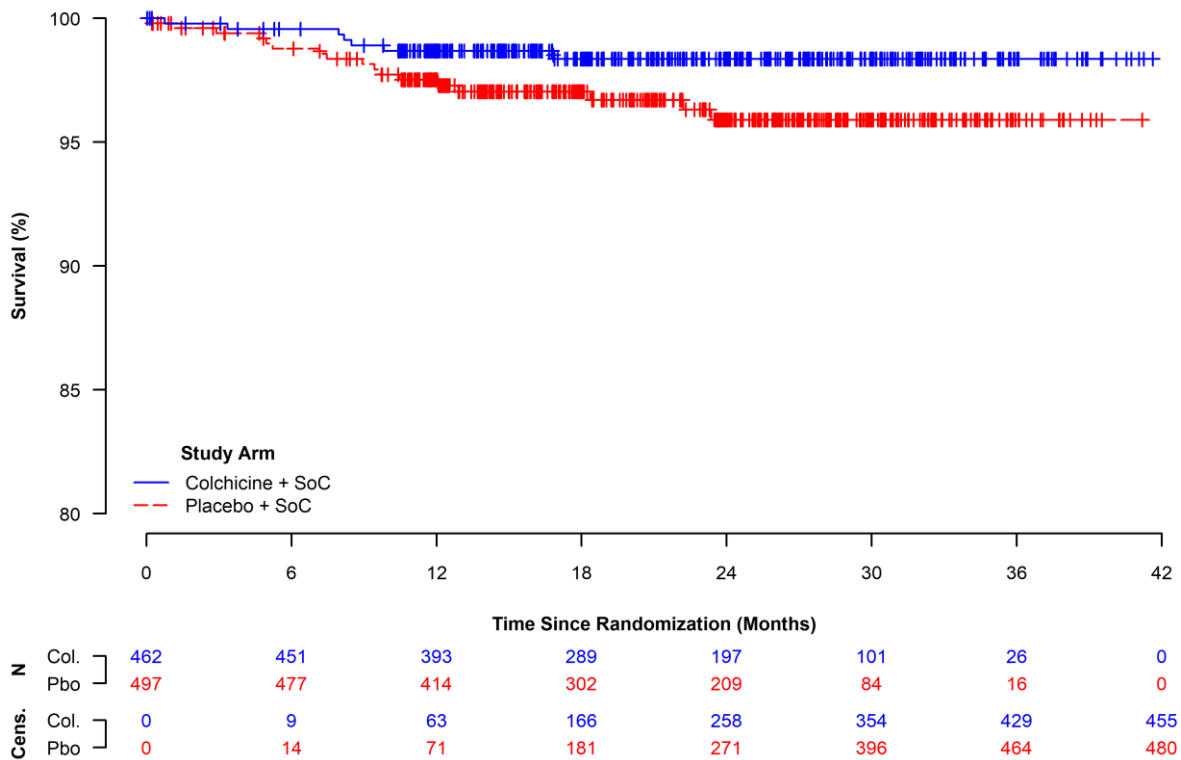
#### 4.4.2.6.6 Subgrouped by Diabetes Status

**Table 151:** Proportion of Patients with Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Diabetes Status (ITT Population).

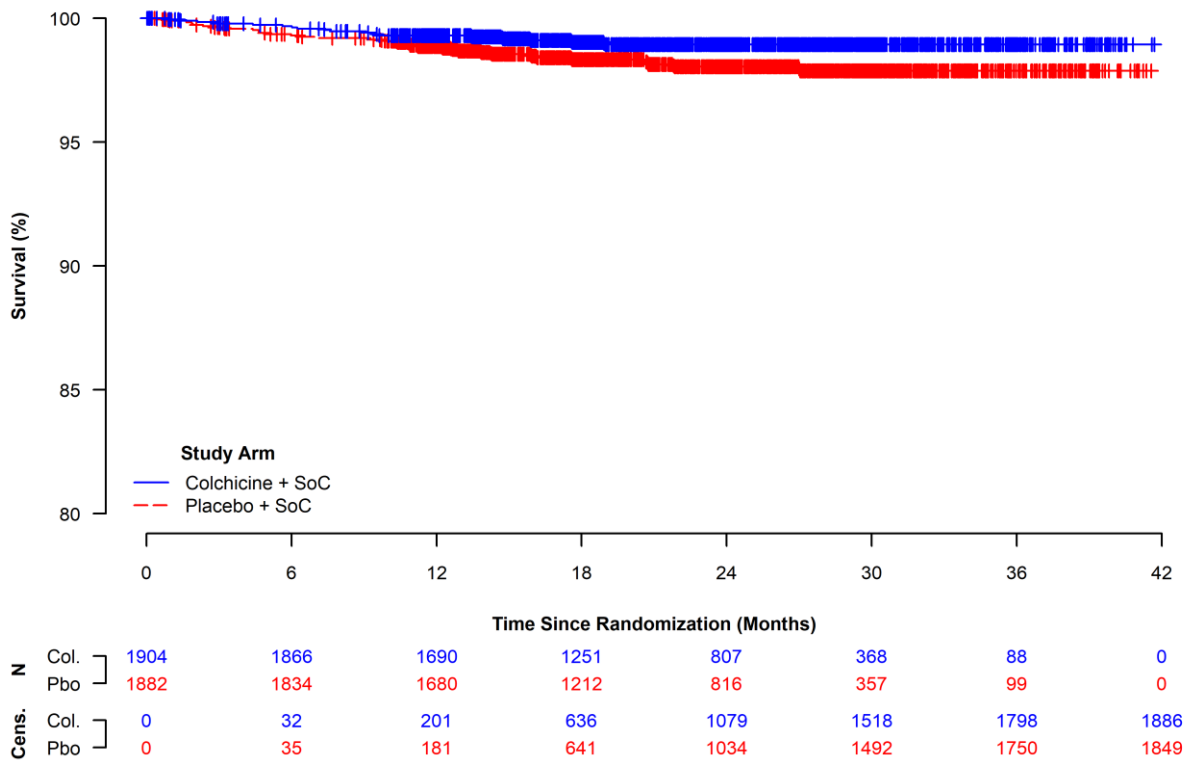
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.6993</b>					
<b>Yes</b>	7/462 (1.5)	17/497 (3.4)	0.443 [0.185, 1.058] 0.0669	0.434 [0.178, 1.057] 0.0662	-1.905 [-3.853, 0.042] 0.0552
<b>No</b>	18/1,904 (0.9)	33/1,882 (1.8)	0.539 [0.305, 0.954] 0.0339	0.535 [0.300, 0.953] 0.0338	-0.808 [-1.543, -0.073] 0.0312
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 152:** Time to Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Diabetes Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.6938</b>							
<b>Yes</b>	7/462 (1.5)	NE [NE, NE]	1.6 [0.4, 2.9]	17/497 (3.4)	NE [NE, NE]	4.1 [2.1, 6.1]	0.436 [0.181, 1.051] 0.0644
<b>No</b>	18/1,904 (0.9)	NE [NE, NE]	1.1 [0.6, 1.5]	33/1,882 (1.8)	NE [NE, NE]	2.1 [1.4, 2.9]	0.537 [0.303, 0.954] 0.0341
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 146:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Diabetic Subgroup (ITT Population).



**Figure 147:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Non-Diabetic Subgroup (ITT Population).

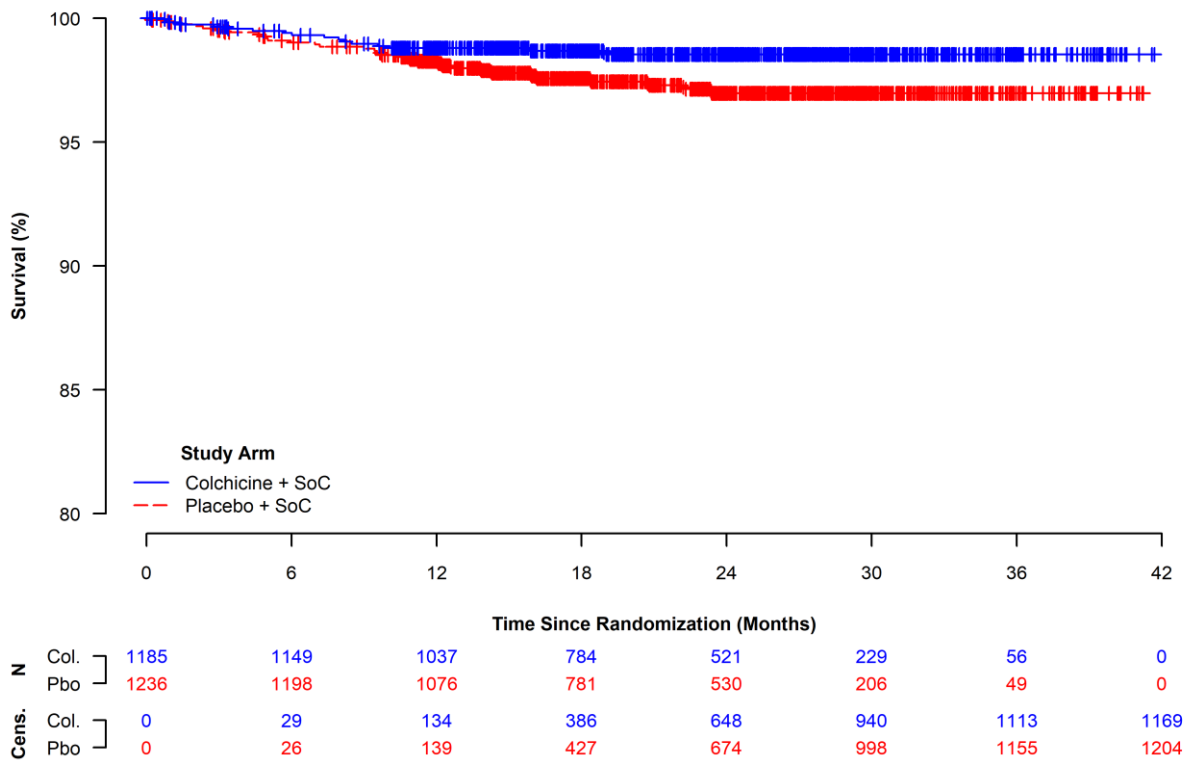
#### 4.4.2.6.7 Subgrouped by Hypertension Status

**Table 153:** Proportion of Patients with Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Hypertension Status (ITT Population).

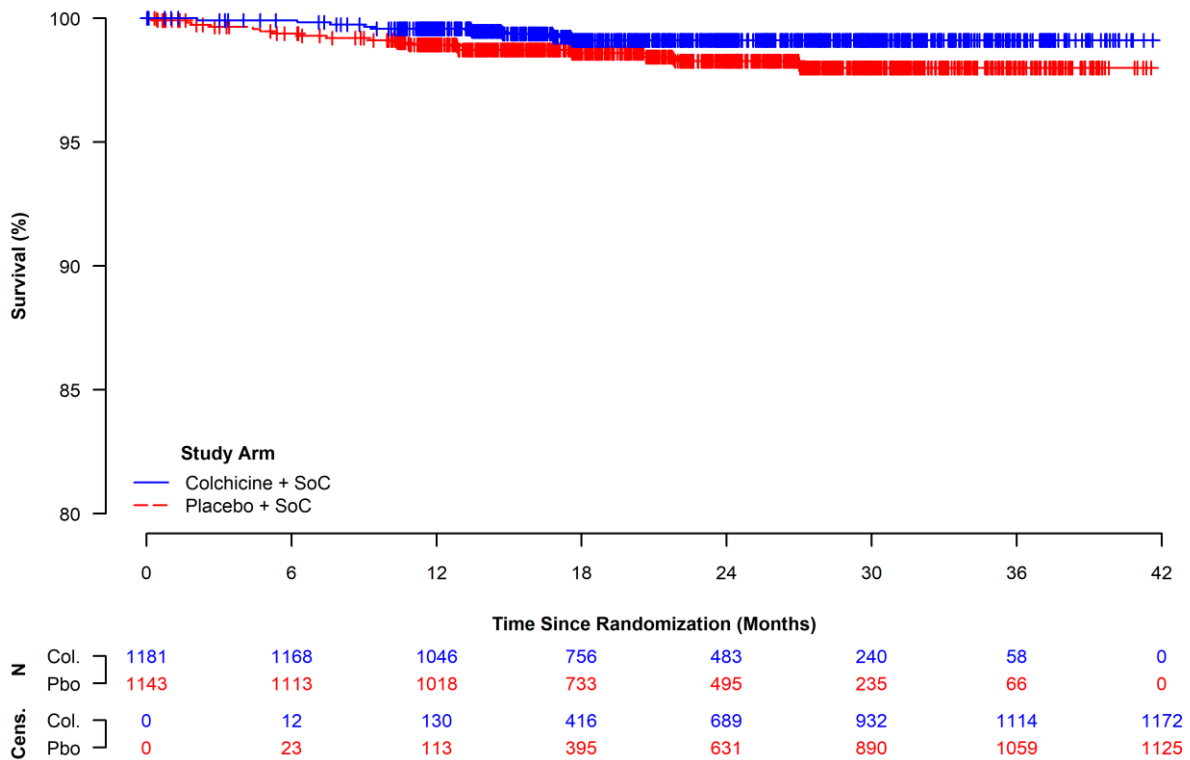
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8908</b>					
<b>Yes</b>	16/1,185 (1.4)	32/1,236 (2.6)	0.522 [0.288, 0.945] 0.0319	0.515 [0.281, 0.943] 0.0317	-1.239 [-2.341, -0.136] 0.0277
<b>No</b>	9/1,181 (0.8)	18/1,143 (1.6)	0.484 [0.218, 1.073] 0.0739	0.480 [0.215, 1.073] 0.0736	-0.813 [-1.688, 0.063] 0.0689
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 154:** Time to Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Hypertension Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.8837</b>							
<b>Yes</b>	16/1,185 (1.4)	NE [NE, NE]	1.5 [0.7, 2.2]	32/1,236 (2.6)	NE [NE, NE]	3.0 [2.0, 4.1]	0.519 [0.285, 0.946] 0.0322
<b>No</b>	9/1,181 (0.8)	NE [NE, NE]	0.9 [0.3, 1.5]	18/1,143 (1.6)	NE [NE, NE]	2.0 [1.0, 3.0]	0.482 [0.217, 1.073] 0.0738
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 148:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Hypertensive Subgroup (ITT Population).



**Figure 149:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Normotensive Subgroup (ITT Population).

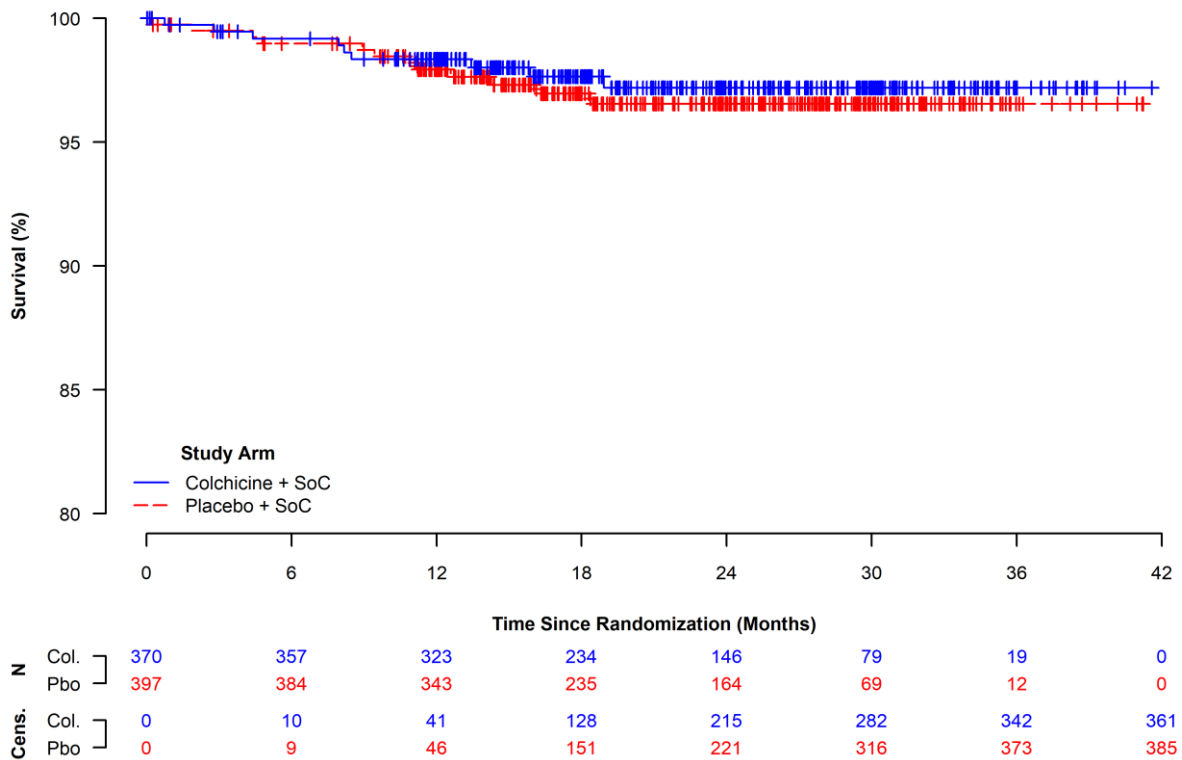
#### 4.4.2.6.8 Subgrouped by History of Myocardial Infarction

**Table 155:** Proportion of Patients with Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by History of Myocardial Infarction (ITT Population).

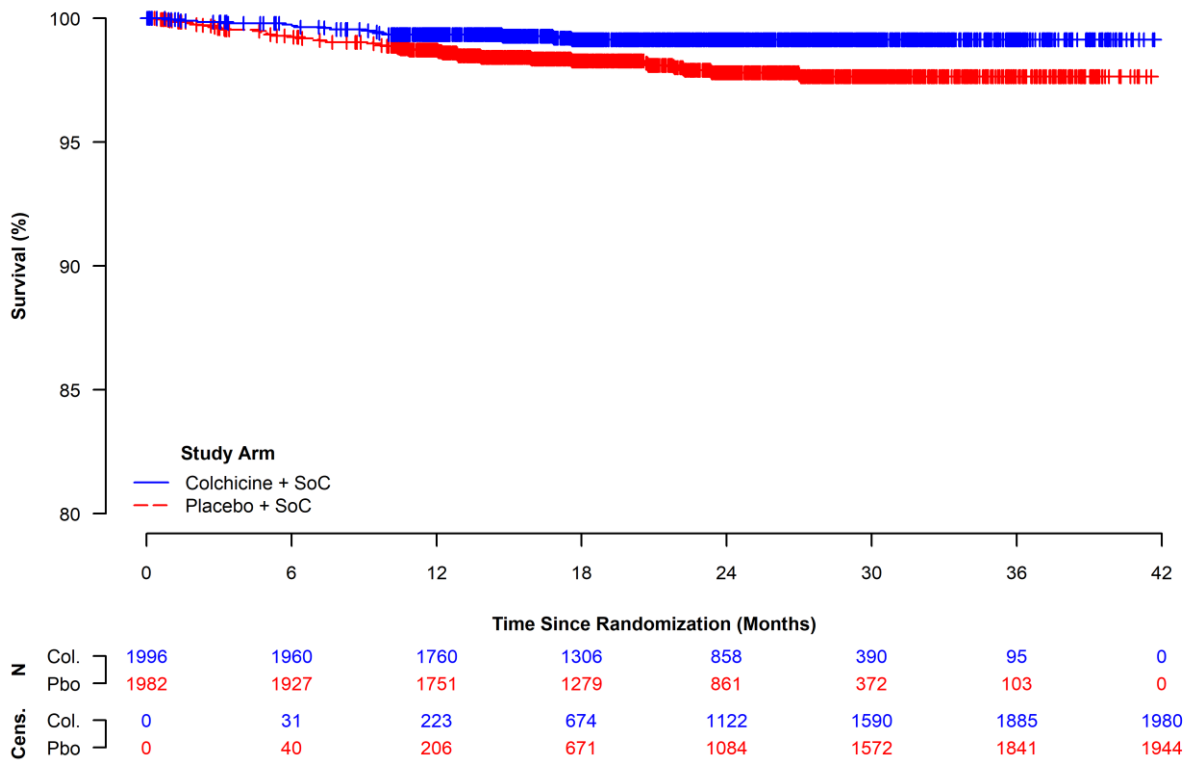
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of MI</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2229</b>					
<b>Yes</b>	9/370 (2.4)	12/397 (3.0)	0.805 [0.343, 1.888] 0.6175	0.800 [0.333, 1.921] 0.6174	-0.590 [-2.892, 1.712] 0.6153
<b>No</b>	16/1,996 (0.8)	38/1,982 (1.9)	0.418 [0.234, 0.747] 0.0033	0.413 [0.230, 0.744] 0.0032	-1.116 [-1.835, -0.396] 0.0024
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 156:** Time to Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by History of Myocardial Infarction (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of MI</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.2187</b>							
<b>Yes</b>	9/370 (2.4)	NE [NE, NE]	2.8 [0.9, 4.6]	12/397 (3.0)	NE [NE, NE]	3.5 [1.5, 5.4]	0.801 [0.338, 1.902] 0.6153
<b>No</b>	16/1,996 (0.8)	NE [NE, NE]	0.9 [0.4, 1.3]	38/1,982 (1.9)	NE [NE, NE]	2.4 [1.6, 3.1]	0.415 [0.232, 0.745] 0.0032
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 150:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Subgroup With History of Myocardial Infarction (ITT Population).



**Figure 151:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Subgroup Without History of Myocardial Infarction (ITT Population).

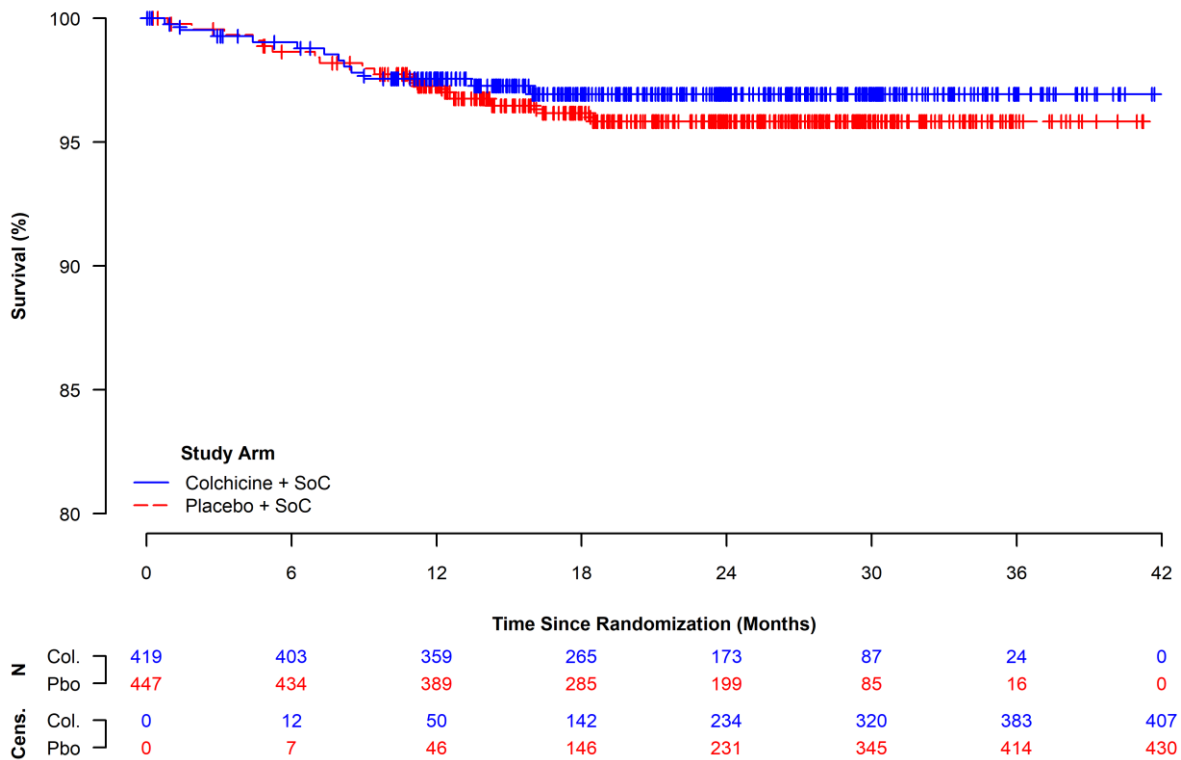
#### 4.4.2.6.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 157:** Proportion of Patients with Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

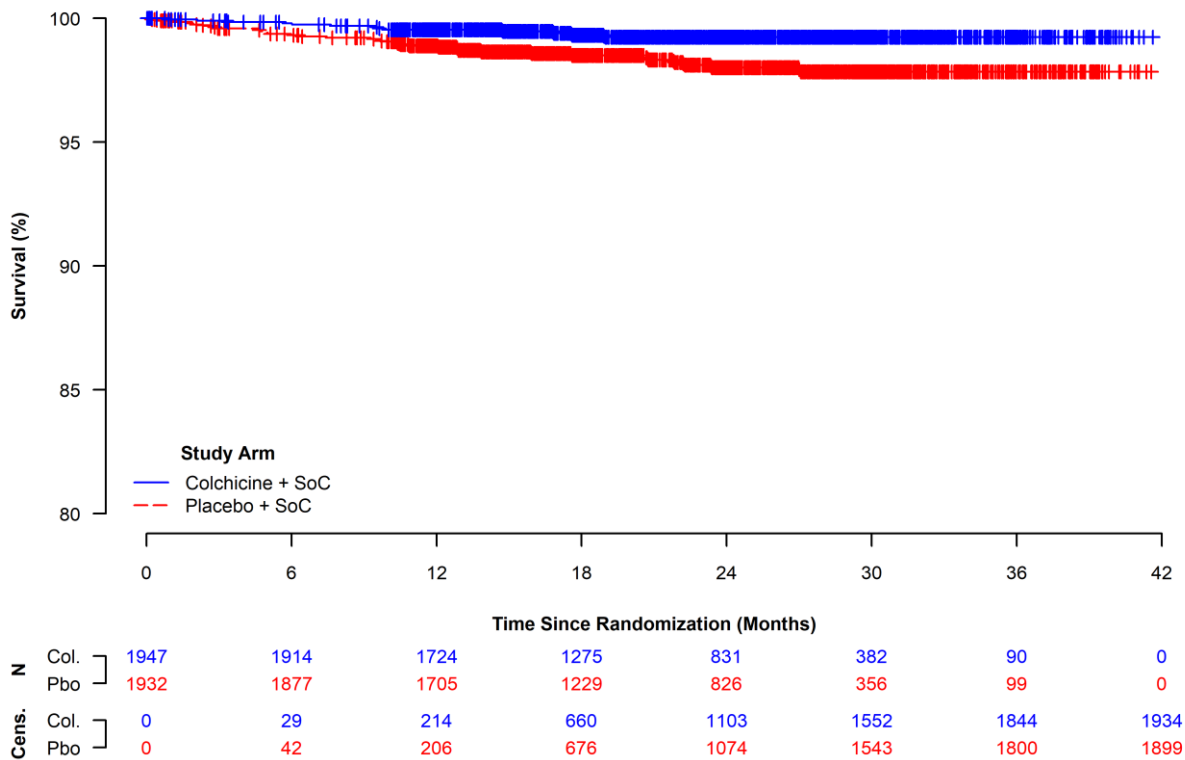
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1939</b>					
<b>Yes</b>	12/419 (2.9)	17/447 (3.8)	0.753 [0.364, 1.558] 0.4444	0.746 [0.352, 1.581] 0.4441	-0.939 [-3.326, 1.447] 0.4405
<b>No</b>	13/1,947 (0.7)	33/1,932 (1.7)	0.391 [0.206, 0.740] 0.0039	0.387 [0.203, 0.737] 0.0039	-1.040 [-1.722, -0.359] 0.0028
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 158:** Time to Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.1713</b>							
<b>Yes</b>	12/419 (2.9)	NE [NE, NE]	3.1 [1.3, 4.8]	17/447 (3.8)	NE [NE, NE]	4.2 [2.2, 6.1]	0.763 [0.365, 1.598] 0.4736
<b>No</b>	13/1,947 (0.7)	NE [NE, NE]	0.8 [0.3, 1.2]	33/1,932 (1.7)	NE [NE, NE]	2.2 [1.4, 2.9]	0.387 [0.203, 0.734] 0.0037
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 152:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Subgroup With History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).



**Figure 153:** Kaplan-Meier Curves for Urgent Hospitalization for Angina Requiring Coronary Revascularization, Within the Subgroup Without History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

#### **4.4.2.6.10 Subgrouped by History of Stroke or Transient Ischaemic Attack**

Due to a significant interaction term, the data is presented in Module 4A.

## 4.4.2.7 Recurrent Primary Composite Outcomes

### 4.4.2.7.1 Subgrouped by Sex

**Table 159:** Time to Recurrent Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Sex (ITT Population).

Subgroup	Event	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
		e <sup>a</sup>	e <sup>a</sup>	IRR <sup>b</sup> <sub>NB</sub> [95 %-CI] p-Value	HR <sup>c</sup> <sub>AG</sub> [95 %-CI] p-Value	HR <sup>d</sup> <sub>WLW</sub> [95 %-CI] p-Value
<b>Sex</b>						
<b>Interaction Test p-Value<sup>e</sup> = 0.3547</b>						
<b>Male</b>	Any or Average	113	178	0.612 [0.452; 0.828] 0.0015	0.646 [0.487; 0.857] 0.0025	0.704 [0.677; 0.733] 0.0033
<b>Female</b>		41	45	0.836 [0.498; 1.405] 0.4996	0.853 [0.529; 1.375] 0.5141	0.871 [0.648; 1.170] 0.4560
<b>Male</b>	First	.	.	.	.	0.703 [0.540; 0.914] 0.0086
<b>Female</b>		.	.	.	.	0.991 [0.624; 1.573] 0.9684
<b>Male</b>	Second	.	.	.	.	0.735 [0.456; 1.186] 0.2073
<b>Female</b>		.	.	.	.	0.687 [0.276; 1.709] 0.4195
<b>Male</b>	Third	.	.	.	.	0.664 [0.360; 1.223] 0.1885
<b>Female</b>		.	.	.	.	0.539 [0.158; 1.843] 0.3247
<sup>a</sup> Number of events in the study population. <sup>b</sup> Estimated using a negative binomial model with 95 %-CI estimated via the normal (Wald) approximation. An IRR < 1 favours colchicine. <sup>c</sup> Estimated using an Andersen-Gill model, with 95 %-CI estimated via the normal (Wald) approximation. A HR < 1 favours colchicine. <sup>d</sup> Estimated using marginal Wei-Lin-Weissfeld models, with 95 %-CI estimated via the normal (Wald) approximation. Average HR estimated as the inverse variance weighted mean of the HRs for the first, second and third event, on the log scale. A HR < 1 favours colchicine. <sup>e</sup> Interaction significance assessed via a likelihood ratio test comparing negative binomial model fits with and without the addition of a treatment x subgroup interaction term.						

#### 4.4.2.7.2 Subgrouped by Age Group

**Table 160:** Time to Recurrent Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Age Group (ITT Population).

Subgroup	Event	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
		e <sup>a</sup>	e <sup>a</sup>	IRR <sup>b</sup> <sub>NB</sub> [95 %-CI] p-Value	HR <sup>c</sup> <sub>AG</sub> [95 %-CI] p-Value	HR <sup>d</sup> <sub>WLW</sub> [95 %-CI] p-Value
<b>Age</b>						
<b>Interaction Test p-Value<sup>e</sup> = 0.7087</b>						
<b>&lt; 60 Years</b>	Any or Average	56	88	0.620 [0.414; 0.930] 0.0207	0.638 [0.435; 0.935] 0.0213	0.661 [0.396; 1.102] 0.2529
		<b>≥ 60 Years</b>	98	135	0.686 [0.487; 0.968] 0.0317	0.725 [0.530; 0.992] 0.0443
<b>&lt; 60 Years</b>	First	.	.	.	.	0.797 [0.554; 1.148] 0.2239
		<b>≥ 60 Years</b>	.	.	.	0.747 [0.558; 1.000] 0.0499
<b>&lt; 60 Years</b>	Second	.	.	.	.	0.332 [0.141; 0.782] 0.0116
		<b>≥ 60 Years</b>	.	.	.	0.999 [0.602; 1.657] 0.9961
<b>&lt; 60 Years</b>	Third	.	.	.	.	0.298 [0.082; 1.084] 0.0661
		<b>≥ 60 Years</b>	.	.	.	0.781 [0.421; 1.447] 0.4322
<sup>a</sup> Number of events in the study population. <sup>b</sup> Estimated using a negative binomial model with 95 %-CI estimated via the normal (Wald) approximation. An IRR < 1 favours colchicine. <sup>c</sup> Estimated using an Andersen-Gill model, with 95 %-CI estimated via the normal (Wald) approximation. A HR < 1 favours colchicine. <sup>d</sup> Estimated using marginal Wei-Lin-Weissfeld models, with 95 %-CI estimated via the normal (Wald) approximation. Average HR estimated as the inverse variance weighted mean of the HRs for the first, second and third event, on the log scale. A HR < 1 favours colchicine. <sup>e</sup> Interaction significance assessed via a likelihood ratio test comparing negative binomial model fits with and without the addition of a treatment x subgroup interaction term.						

#### 4.4.2.7.3 Subgrouped by Smoking Status

**Table 161:** Time to Recurrent Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Smoking Status (ITT Population).

Subgroup	Event	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,377)	Colchicine + SoC vs. Placebo + SoC		
		e <sup>a</sup>	e <sup>a</sup>	IRR <sup>b</sup> <sub>NB</sub> [95 %-CI] p-Value	HR <sup>c</sup> <sub>AG</sub> [95 %-CI] p-Value	HR <sup>d</sup> <sub>WLW</sub> [95 %-CI] p-Value
<b>Smoking Status</b>						
<b>Interaction Test p-Value<sup>e</sup> = 0.1883</b>						
<b>Non</b>		59	69	0.774 [0.476; 1.257] 0.2999	0.837 [0.551; 1.272] 0.4045	0.821 [0.637; 1.058] 0.2669
<b>Ex</b>	Any or Average	51	100	0.491 [0.328; 0.735] 0.0005	0.516 [0.353; 0.756] 0.0007	0.613 [0.569; 0.661] 0.0060
<b>Current</b>		44	54	0.815 [0.494; 1.344] 0.4225	0.821 [0.508; 1.326] 0.4195	0.848 [0.685; 1.050] 0.2699
<b>Non</b>		.	.	.	.	0.885 [0.597; 1.314] 0.5450
<b>Ex</b>	First	.	.	.	.	0.595 [0.413; 0.858] 0.0054
<b>Current</b>		.	.	.	.	0.932 [0.599; 1.449] 0.7535
<b>Non</b>		.	.	.	.	0.873 [0.454; 1.681] 0.6853
<b>Ex</b>	Second	.	.	.	.	0.637 [0.309; 1.312] 0.2209
<b>Current</b>		.	.	.	.	0.626 [0.259; 1.509] 0.2965

Subgroup	Event	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,377)	Colchicine + SoC vs. Placebo + SoC		
		e <sup>a</sup>	e <sup>a</sup>	IRR <sup>b</sup> <sub>NB</sub> [95 %-CI] p-Value	HR <sup>c</sup> <sub>AG</sub> [95 %-CI] p-Value	HR <sup>d</sup> <sub>WLW</sub> [95 %-CI] p-Value
<b>Smoking Status</b>						
<b>Non</b>		.	.	.	.	0.515 [0.218; 1.216] 0.1300
<b>Ex</b>	Third	.	.	.	.	0.706 [0.269; 1.854] 0.4793
<b>Current</b>		.	.	.	.	0.767 [0.266; 2.210] 0.6227
<sup>a</sup> Number of events in the study population. <sup>b</sup> Estimated using a negative binomial model with 95 %-CI estimated via the normal (Wald) approximation. An IRR < 1 favours colchicine. <sup>c</sup> Estimated using an Andersen-Gill model, with 95 %-CI estimated via the normal (Wald) approximation. A HR < 1 favours colchicine. <sup>d</sup> Estimated using marginal Wei-Lin-Weissfeld models, with 95 %-CI estimated via the normal (Wald) approximation. Average HR estimated as the inverse variance weighted mean of the HRs for the first, second and third event, on the log scale. A HR < 1 favours colchicine. <sup>e</sup> Interaction significance assessed via a likelihood ratio test comparing negative binomial model fits with and without the addition of a treatment x subgroup interaction term.						

#### 4.4.2.7.4 Subgrouped by Region

**Table 162:** Time to Recurrent Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Region (ITT Population).

Subgroup	Event	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
		e <sup>a</sup>	e <sup>a</sup>	IRR <sup>b</sup> <sub>NB</sub> [95 %-CI] p-Value	HR <sup>c</sup> <sub>AG</sub> [95 %-CI] p-Value	HR <sup>d</sup> <sub>WLW</sub> [95 %-CI] p-Value
<b>Region</b>						
<b>Interaction Test p-Value<sup>e</sup> = 0.6086</b>						
<b>Europe</b>	Any or Average	52	85	0.608 [0.412; 0.897] 0.0123	0.614 [0.422; 0.892] 0.0104	0.649 [0.511; 0.824] 0.0709
<b>Non-Europe</b>		102	138	0.687 [0.483; 0.977] 0.0365	0.738 [0.538; 1.012] 0.0596	0.797 [0.718; 0.885] 0.0516
<b>Europe</b>	First	.	.	.	.	0.707 [0.492; 1.017] 0.0613
<b>Non-Europe</b>		.	.	.	.	0.808 [0.603; 1.083] 0.1534
<b>Europe</b>	Second	.	.	.	.	0.433 [0.178; 1.052] 0.0645
<b>Non-Europe</b>		.	.	.	.	0.855 [0.525; 1.393] 0.5302
<b>Europe</b>	Third	.	.	.	.	0.550 [0.184; 1.643] 0.2845
<b>Non-Europe</b>		.	.	.	.	0.665 [0.353; 1.251] 0.2057
<sup>a</sup> Number of events in the study population. <sup>b</sup> Estimated using a negative binomial model with 95 %-CI estimated via the normal (Wald) approximation. An IRR < 1 favours colchicine. <sup>c</sup> Estimated using an Andersen-Gill model, with 95 %-CI estimated via the normal (Wald) approximation. A HR < 1 favours colchicine. <sup>d</sup> Estimated using marginal Wei-Lin-Weissfeld models, with 95 %-CI estimated via the normal (Wald) approximation. Average HR estimated as the inverse variance weighted mean of the HRs for the first, second and third event, on the log scale. A HR < 1 favours colchicine. <sup>e</sup> Interaction significance assessed via a likelihood ratio test comparing negative binomial model fits with and without the addition of a treatment x subgroup interaction term.						

#### 4.4.2.7.5 Subgrouped by White Blood Cell Count

**Table 163:** Time to Recurrent Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by White Blood Cell Count (ITT Population).

Subgroup	Event	Colchicine + SoC (N = 1,300)	Placebo + SoC (N = 1,306)	Colchicine + SoC vs. Placebo + SoC		
		e <sup>a</sup>	e <sup>a</sup>	IRR <sup>b</sup> <sub>NB</sub> [95 %-CI] p-Value	HR <sup>c</sup> <sub>AG</sub> [95 %-CI] p-Value	HR <sup>d</sup> <sub>WLW</sub> [95 %-CI] p-Value
<b>White Blood Cell Count</b>						
<b>Interaction Test p-Value<sup>e</sup> = 0.7727</b>						
< 8.66 10 <sup>3</sup> /μL	Any or Average	51	61	0.781 [0.489; 1.246]	0.801 [0.507; 1.263]	0.821 [0.675; 0.999]
				0.2993	0.3390	0.1880
≥ 8.66 10 <sup>3</sup> /μL	Average	42	61	0.704 [0.428; 1.160]	0.715 [0.442; 1.156]	0.748 [0.602; 0.930]
				0.1683	0.1710	0.1205
< 8.66 10 <sup>3</sup> /μL	First	.	.	.	.	0.848 [0.557; 1.292]
						0.4432
≥ 8.66 10 <sup>3</sup> /μL	First	.	.	.	.	0.800 [0.511; 1.252]
						0.3294
< 8.66 10 <sup>3</sup> /μL	Second	.	.	.	.	0.877 [0.372; 2.064]
						0.7632
≥ 8.66 10 <sup>3</sup> /μL	Second	.	.	.	.	0.720 [0.308; 1.683]
						0.4478
< 8.66 10 <sup>3</sup> /μL	Third	.	.	.	.	0.490 [0.123; 1.960]
						0.3133
≥ 8.66 10 <sup>3</sup> /μL	Third	.	.	.	.	0.446 [0.115; 1.726]
						0.2424

<sup>a</sup>Number of events in the study population.  
<sup>b</sup>Estimated using a negative binomial model with 95 %-CI estimated via the normal (Wald) approximation. An IRR < 1 favours colchicine.  
<sup>c</sup>Estimated using an Andersen-Gill model, with 95 %-CI estimated via the normal (Wald) approximation. A HR < 1 favours colchicine.  
<sup>d</sup>Estimated using marginal Wei-Lin-Weissfeld models, with 95 %-CI estimated via the normal (Wald) approximation. Average HR estimated as the inverse variance weighted mean of the HRs for the first, second and third event, on the log scale. A HR < 1 favours colchicine.  
<sup>e</sup>Interaction significance assessed via a likelihood ratio test comparing negative binomial model fits with and without the addition of a treatment x subgroup interaction term.

#### 4.4.2.7.6 Subgrouped by Diabetes Status

**Table 164:** Time to Recurrent Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Diabetes Status (ITT Population).

Subgroup	Event	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
		e <sup>a</sup>	e <sup>a</sup>	IRR <sup>b</sup> <sub>NB</sub> [95 %-CI] p-Value	HR <sup>c</sup> <sub>AG</sub> [95 %-CI] p-Value	HR <sup>d</sup> <sub>WLW</sub> [95 %-CI] p-Value
<b>Diabetes Status</b>						
<b>Interaction Test p-Value<sup>e</sup> = 0.2137</b>						
<b>Yes</b>	Any or Average	50	93	0.531 [0.325; 0.868] 0.0116	0.561 [0.372; 0.847] 0.0060	0.620 [0.487; 0.788] 0.0596
		<b>No</b>	104	130	0.767 [0.564; 1.043] 0.0912	0.792 [0.588; 1.068] 0.1260
<b>Yes</b>	First	.	.	.	.	0.631 [0.426; 0.937] 0.0223
		<b>No</b>	.	.	.	0.854 [0.645; 1.131] 0.2711
<b>Yes</b>	Second	.	.	.	.	0.741 [0.398; 1.379] 0.3443
		<b>No</b>	.	.	.	0.733 [0.411; 1.306] 0.2918
<b>Yes</b>	Third	.	.	.	.	0.418 [0.184; 0.949] 0.0372
		<b>No</b>	.	.	.	0.991 [0.460; 2.138] 0.9821
<sup>a</sup> Number of events in the study population. <sup>b</sup> Estimated using a negative binomial model with 95 %-CI estimated via the normal (Wald) approximation. An IRR < 1 favours colchicine. <sup>c</sup> Estimated using an Andersen-Gill model, with 95 %-CI estimated via the normal (Wald) approximation. A HR < 1 favours colchicine. <sup>d</sup> Estimated using marginal Wei-Lin-Weissfeld models, with 95 %-CI estimated via the normal (Wald) approximation. Average HR estimated as the inverse variance weighted mean of the HRs for the first, second and third event, on the log scale. A HR < 1 favours colchicine. <sup>e</sup> Interaction significance assessed via a likelihood ratio test comparing negative binomial model fits with and without the addition of a treatment x subgroup interaction term.						

#### 4.4.2.7.7 Subgrouped by Hypertension Status

**Table 165:** Time to Recurrent Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by Hypertension Status (ITT Population).

Subgroup	Event	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
		e <sup>a</sup>	e <sup>a</sup>	IRR <sup>b</sup> <sub>NB</sub> [95 %-CI] p-Value	HR <sup>c</sup> <sub>AG</sub> [95 %-CI] p-Value	HR <sup>d</sup> <sub>WLW</sub> [95 %-CI] p-Value
<b>Hypertension Status</b>						
<b>Interaction Test p-Value<sup>e</sup> = 0.3162</b>						
<b>Yes</b>	Any or Average	97	154	0.607 [0.434; 0.850] 0.0036	0.645 [0.478; 0.870] 0.0041	0.713 [0.629; 0.810] 0.0346
		<b>No</b>	57	69	0.798 [0.526; 1.209] 0.2868	0.807 [0.536; 1.216] 0.3058
<b>Yes</b>	First				.	.
		<b>No</b>	.	.	.	.
<b>Yes</b>	Second					
		<b>No</b>	.	.	.	.
<b>Yes</b>	Third					
		<b>No</b>	.	.	.	.

<sup>a</sup>Number of events in the study population.  
<sup>b</sup>Estimated using a negative binomial model with 95 %-CI estimated via the normal (Wald) approximation. An IRR < 1 favours colchicine.  
<sup>c</sup>Estimated using an Andersen-Gill model, with 95 %-CI estimated via the normal (Wald) approximation. A HR < 1 favours colchicine.  
<sup>d</sup>Estimated using marginal Wei-Lin-Weissfeld models, with 95 %-CI estimated via the normal (Wald) approximation. Average HR estimated as the inverse variance weighted mean of the HRs for the first, second and third event, on the log scale. A HR < 1 favours colchicine.  
<sup>e</sup>Interaction significance assessed via a likelihood ratio test comparing negative binomial model fits with and without the addition of a treatment x subgroup interaction term.

#### 4.4.2.7.8 Subgrouped by History of Myocardial Infarction

**Table 166:** Time to Recurrent Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by History of Myocardial Infarction (ITT Population).

Subgroup	Event	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
		e <sup>a</sup>	e <sup>a</sup>	IRR <sup>b</sup> <sub>NB</sub> [95 %-CI] p-Value	HR <sup>c</sup> <sub>AG</sub> [95 %-CI] p-Value	HR <sup>d</sup> <sub>WLW</sub> [95 %-CI] p-Value
<b>History of MI</b>						
<b>Interaction Test p-Value<sup>e</sup> = 0.3290</b>						
<b>Yes</b>	Any or Average	57	67	0.828 [0.517; 1.325] 0.4307	0.892 [0.584; 1.361] 0.5948	0.892 [0.644; 1.236] 0.5629
		<b>No</b>	97	156	0.602 [0.440; 0.822] 0.0014	0.617 [0.459; 0.829] 0.0014
<b>Yes</b>	First				.	.
		<b>No</b>	.	.	.	.
<b>Yes</b>	Second					
		<b>No</b>	.	.	.	.
<b>Yes</b>	Third					
		<b>No</b>	.	.	.	.

<sup>a</sup>Number of events in the study population.  
<sup>b</sup>Estimated using a negative binomial model with 95 %-CI estimated via the normal (Wald) approximation. An IRR < 1 favours colchicine.  
<sup>c</sup>Estimated using an Andersen-Gill model, with 95 %-CI estimated via the normal (Wald) approximation. A HR < 1 favours colchicine.  
<sup>d</sup>Estimated using marginal Wei-Lin-Weissfeld models, with 95 %-CI estimated via the normal (Wald) approximation. Average HR estimated as the inverse variance weighted mean of the HRs for the first, second and third event, on the log scale. A HR < 1 favours colchicine.  
<sup>e</sup>Interaction significance assessed via a likelihood ratio test comparing negative binomial model fits with and without the addition of a treatment x subgroup interaction term.

#### 4.4.2.7.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 167:** Time to Recurrent Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

Subgroup	Event	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
		e <sup>a</sup>	e <sup>a</sup>	IRR <sup>b</sup> <sub>NB</sub> [95 %-CI] p-Value	HR <sup>c</sup> <sub>AG</sub> [95 %-CI] p-Value	HR <sup>d</sup> <sub>WLW</sub> [95 %-CI] p-Value
<b>History of PCI or CABG</b>						
<b>Interaction Test p-Value<sup>e</sup> = 0.4268</b>						
<b>Yes</b>	Any or Average	59	78	0.792 [0.511; 1.227] 0.2964	0.819 [0.545; 1.231] 0.3367	0.893 [0.836; 0.954] 0.0782
		<b>No</b>	95	145	0.615 [0.445; 0.850] 0.0032	0.644 [0.477; 0.869] 0.0041
<b>Yes</b>	First	.	.	.	.	0.912 [0.621; 1.338] 0.6365
<b>No</b>		.	.	.	.	0.717 [0.540; 0.952] 0.0213
<b>Yes</b>	Second	.	.	.	.	0.900 [0.454; 1.787] 0.7642
<b>No</b>		.	.	.	.	0.655 [0.382; 1.123] 0.1236
<b>Yes</b>	Third	.	.	.	.	0.786 [0.316; 1.953] 0.6036
<b>No</b>		.	.	.	.	0.582 [0.293; 1.154] 0.1213
<sup>a</sup> Number of events in the study population. <sup>b</sup> Estimated using a negative binomial model with 95 %-CI estimated via the normal (Wald) approximation. An IRR < 1 favours colchicine. <sup>c</sup> Estimated using an Andersen-Gill model, with 95 %-CI estimated via the normal (Wald) approximation. A HR < 1 favours colchicine. <sup>d</sup> Estimated using marginal Wei-Lin-Weissfeld models, with 95 %-CI estimated via the normal (Wald) approximation. Average HR estimated as the inverse variance weighted mean of the HRs for the first, second and third event, on the log scale. A HR < 1 favours colchicine. <sup>e</sup> Interaction significance assessed via a likelihood ratio test comparing negative binomial model fits with and without the addition of a treatment x subgroup interaction term.						

#### 4.4.2.7.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 168:** Time to Recurrent Cardiovascular Death, Resuscitated Cardiac Arrest, Acute Myocardial Infarction, Stroke or Urgent Hospitalization for Angina Requiring Coronary Revascularization, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

Subgroup	Event	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC				
		e <sup>a</sup>	e <sup>a</sup>	IRR <sup>b</sup> <sub>NB</sub> [95 %-CI] p-Value	HR <sup>c</sup> <sub>AG</sub> [95 %-CI] p-Value	HR <sup>d</sup> <sub>WLW</sub> [95 %-CI] p-Value		
<b>History of Stroke or TIA</b>								
<b>Interaction Test p-Value<sup>e</sup> = 0.5298</b>								
<b>Yes</b>	Any or Average	10	11	1.044 [0.378; 2.887] 0.9335	1.042 [0.415; 2.617] 0.9305	1.013 [0.772; 1.329] 0.9334		
		<b>No</b>	144	212	0.648 [0.495; 0.849] 0.0017	0.677 [0.527; 0.871] 0.0024	0.732 [0.677; 0.791] 0.0157	
<b>Yes</b>	First							.
		<b>No</b>	.	.	.	.	.	
<b>Yes</b>	Second							.
		<b>No</b>	.	.	.	.	.	
<b>Yes</b>	Third							.
		<b>No</b>	.	.	.	.	.	

<sup>a</sup>Number of events in the study population.  
<sup>b</sup>Estimated using a negative binomial model with 95 %-CI estimated via the normal (Wald) approximation. An IRR < 1 favours colchicine.  
<sup>c</sup>Estimated using an Andersen-Gill model, with 95 %-CI estimated via the normal (Wald) approximation. A HR < 1 favours colchicine.  
<sup>d</sup>Estimated using marginal Wei-Lin-Weissfeld models, with 95 %-CI estimated via the normal (Wald) approximation. Average HR estimated as the inverse variance weighted mean of the HRs for the first, second and third event, on the log scale. A HR < 1 favours colchicine.  
<sup>e</sup>Interaction significance assessed via a likelihood ratio test comparing negative binomial model fits with and without the addition of a treatment x subgroup interaction term.

#### 4.4.2.8 Deep Vein Thrombosis or Pulmonary Embolus

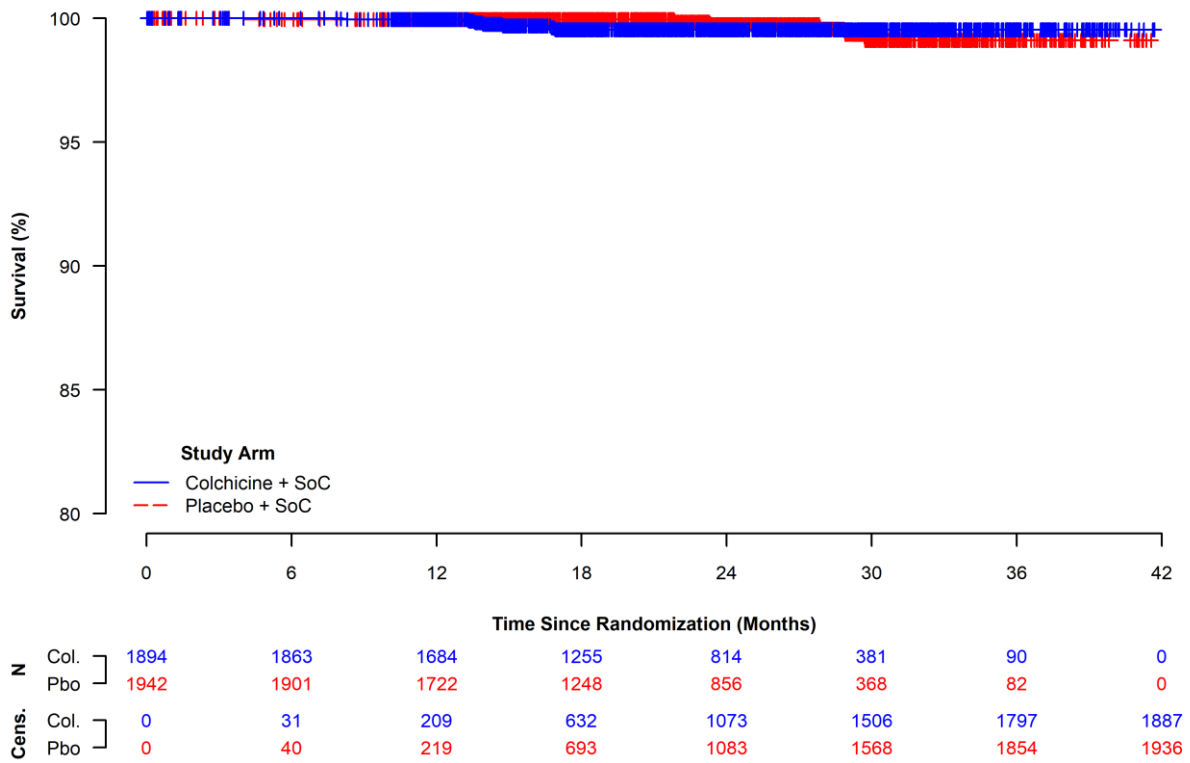
##### 4.4.2.8.1 Subgrouped by Sex

**Table 169:** Proportion of Patients with Deep Vein Thrombosis or Pulmonary Embolus, Subgrouped by Sex (ITT Population).

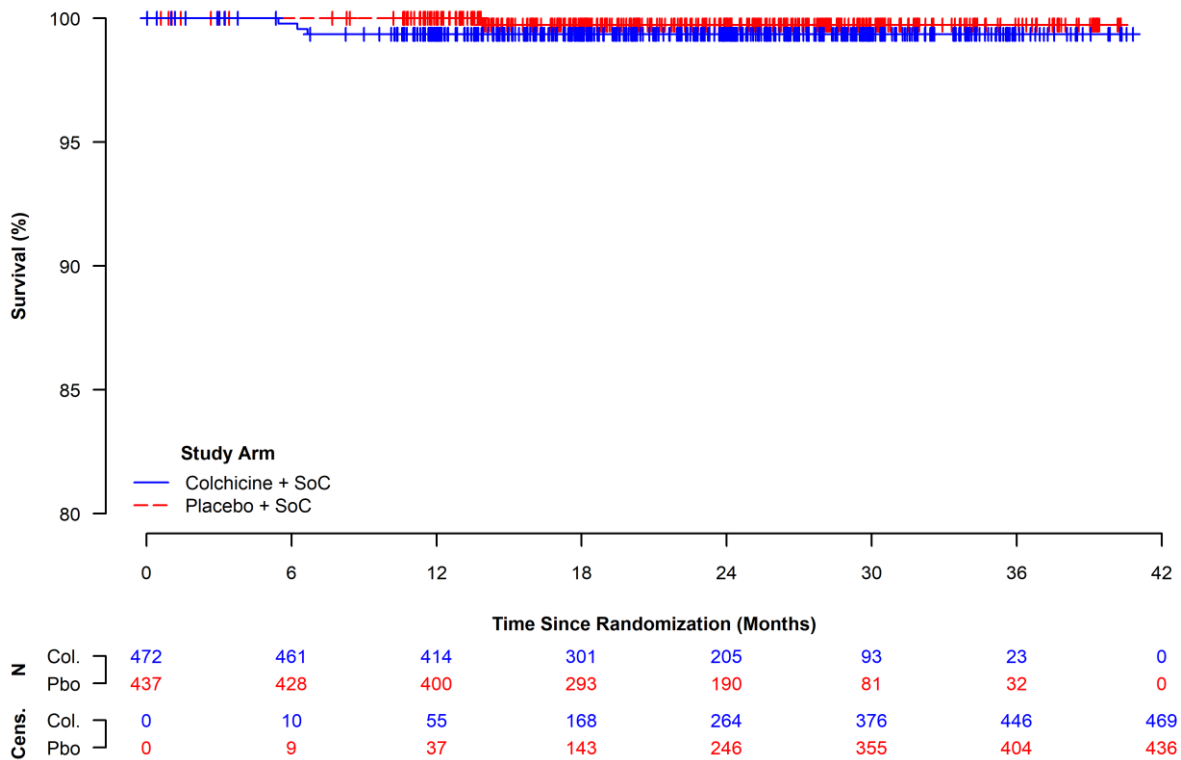
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Sex</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4934</b>					
<b>Male</b>	7/1,894 (0.4)	6/1,942 (0.3)	1.196 [0.403, 3.553] 0.7470	1.197 [0.402, 3.568] 0.7470	0.061 [-0.308, 0.429] 0.7469
<b>Female</b>	3/472 (0.6)	1/437 (0.2)	2.778 [0.290, 26.602] 0.3755	2.789 [0.289, 26.912] 0.3752	0.407 [-0.439, 1.252] 0.3457
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 170:** Time to Deep Vein Thrombosis or Pulmonary Embolus, Subgrouped by Sex (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.4799</b>							
<b>Male</b>	7/1,894 (0.4)	NE [NE, NE]	0.5 [0.1, 0.8]	6/1,942 (0.3)	NE [NE, NE]	0.9 [0.1, 1.7]	1.180 [0.396, 3.510] 0.7665
<b>Female</b>	3/472 (0.6)	NE [NE, NE]	0.6 [0.0, 1.4]	1/437 (0.2)	NE [NE, NE]	0.3 [0.0, 0.8]	2.815 [0.293, 27.065] 0.3701
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 154:** Kaplan-Meier Curves for Deep Vein Thrombosis or Pulmonary Embolus, Within the Male Sex Subgroup (ITT Population).



**Figure 155:** Kaplan-Meier Curves for Deep Vein Thrombosis or Pulmonary Embolus, Within the Female Sex Subgroup (ITT Population).

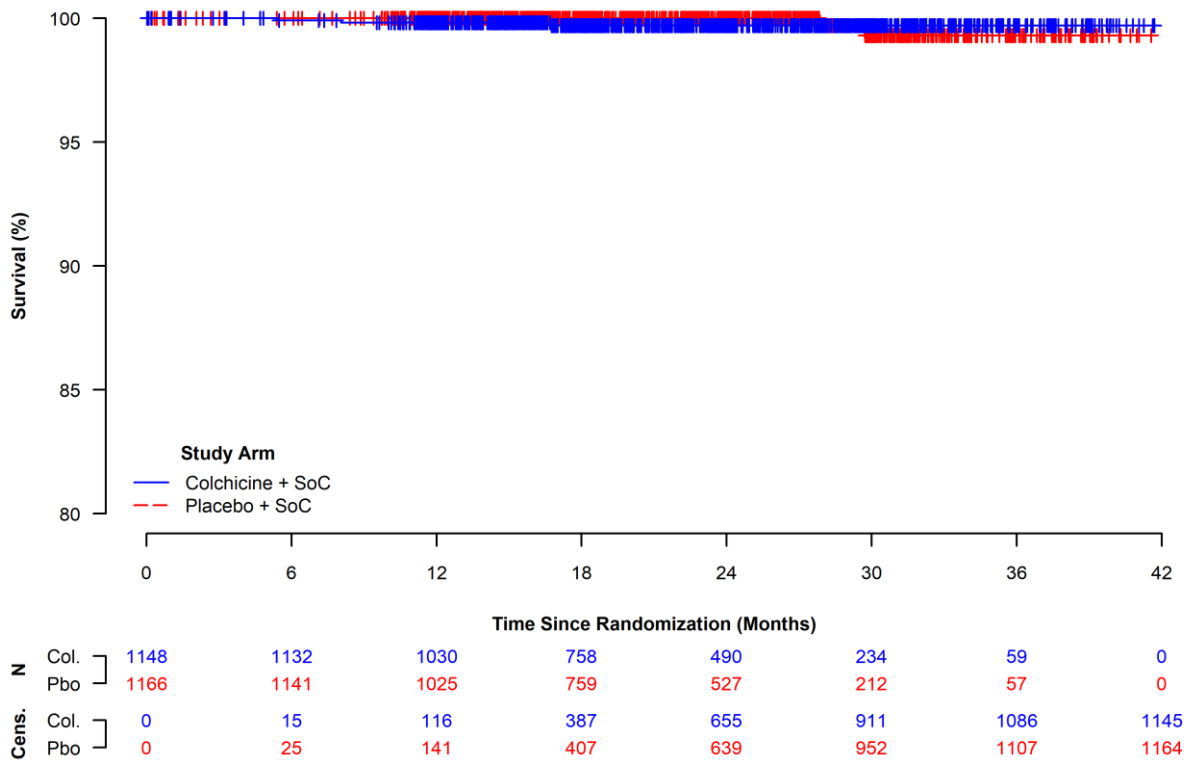
#### 4.4.2.8.2 Subgrouped by Age Group

**Table 171:** Proportion of Patients with Deep Vein Thrombosis or Pulmonary Embolus, Subgrouped by Age Group (ITT Population).

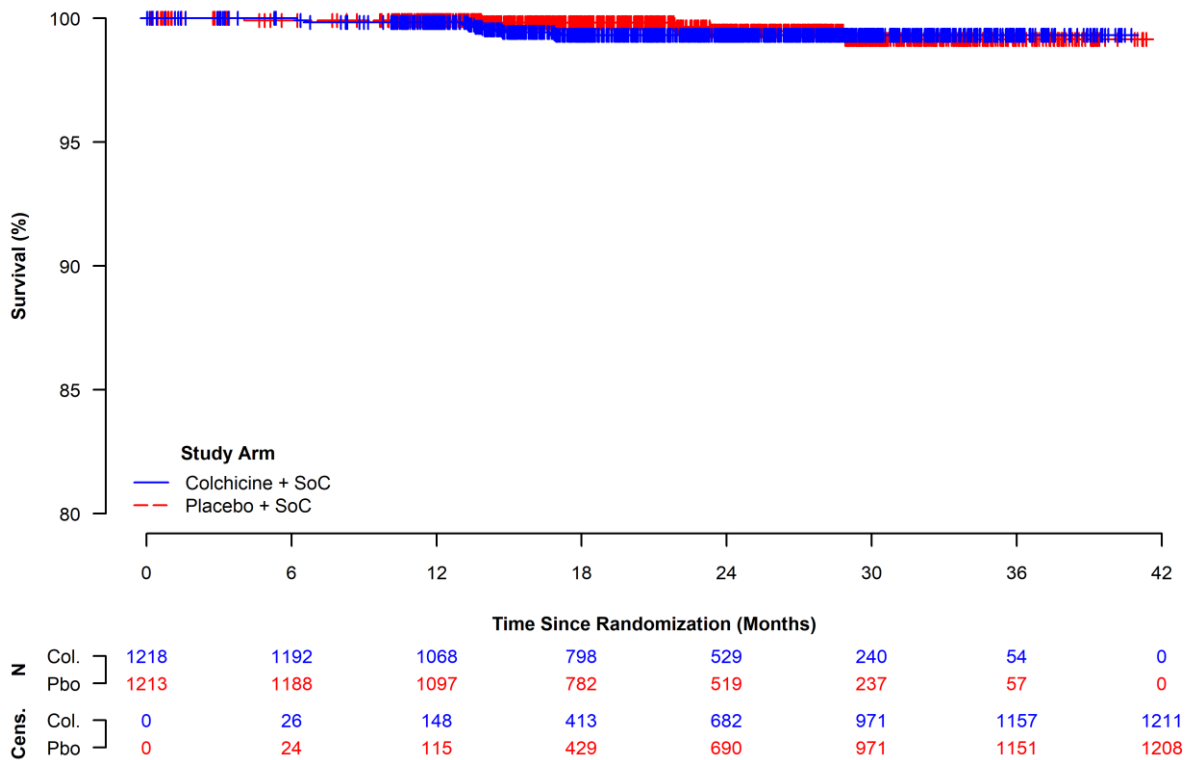
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Age</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.9354</b>					
< 60 Years	3/1,148 (0.3)	2/1,166 (0.2)	1.524 [0.255, 9.101] 0.6443	1.525 [0.254, 9.143] 0.6443	0.090 [-0.289, 0.469] 0.6424
≥ 60 Years	7/1,218 (0.6)	5/1,213 (0.4)	1.394 [0.444, 4.381] 0.5694	1.397 [0.442, 4.412] 0.5693	0.163 [-0.394, 0.719] 0.5674
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 172:** Time to Deep Vein Thrombosis or Pulmonary Embolus, Subgrouped by Age Group (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.9548</b>							
< 60 Years	3/1,148 (0.3)	NE [NE, NE]	0.3 [0.0, 0.6]	2/1,166 (0.2)	NE [NE, NE]	0.7 [0.0, 1.7]	1.484 [0.248, 8.880] 0.6656
≥ 60 Years	7/1,218 (0.6)	NE [NE, NE]	0.7 [0.2, 1.2]	5/1,213 (0.4)	NE [NE, NE]	0.8 [0.0, 1.7]	1.411 [0.448, 4.446] 0.5564
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 156:** Kaplan-Meier Curves for Deep Vein Thrombosis or Pulmonary Embolus, Within the Age 59 Years or Younger Subgroup (ITT Population).



**Figure 157:** Kaplan-Meier Curves for Deep Vein Thrombosis or Pulmonary Embolus, Within the Age 60 Years or Older Subgroup (ITT Population).

#### **4.4.2.8.3 Subgrouped by Smoking Status**

The requirements for performing subgroup analyses were not met, i.e., at least one subgroup contained fewer than ten patients and/or, in the case of binary data and time-to-event analyses, no subgroup had at least ten events.

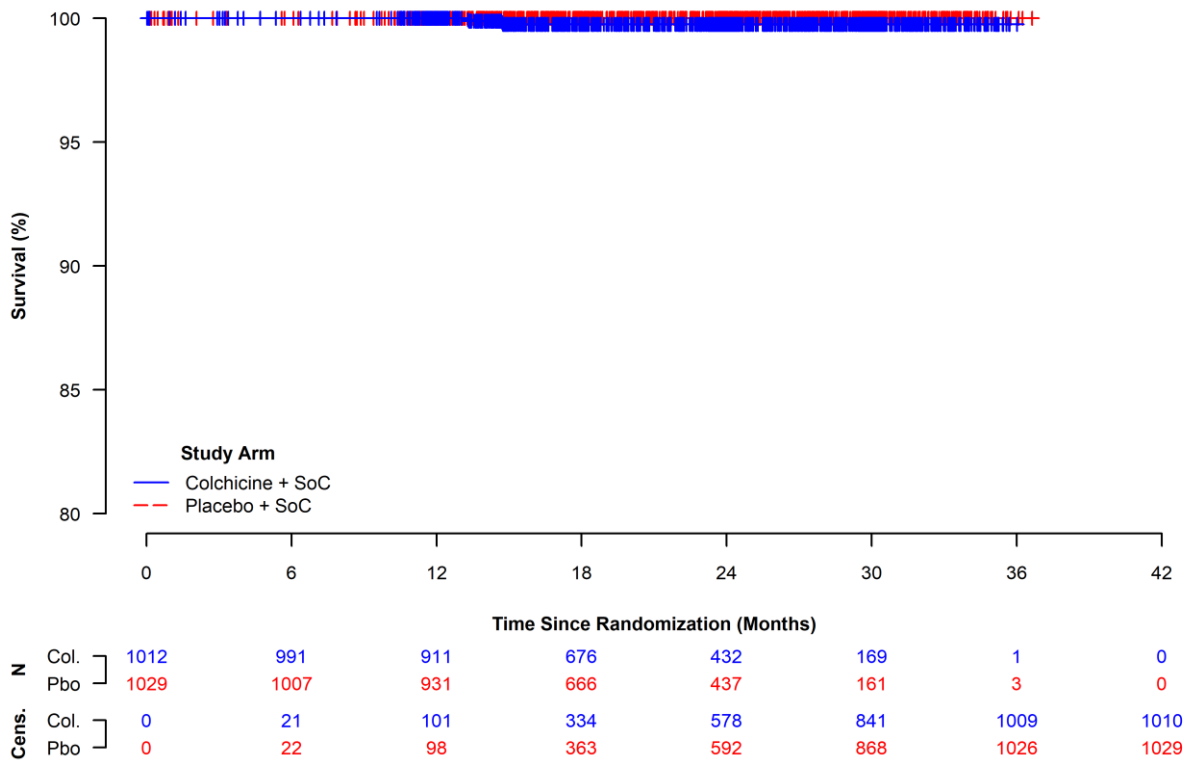
#### 4.4.2.8.4 Subgrouped by Region

**Table 173:** Proportion of Patients with Deep Vein Thrombosis or Pulmonary Embolus, Subgrouped by Region (ITT Population).

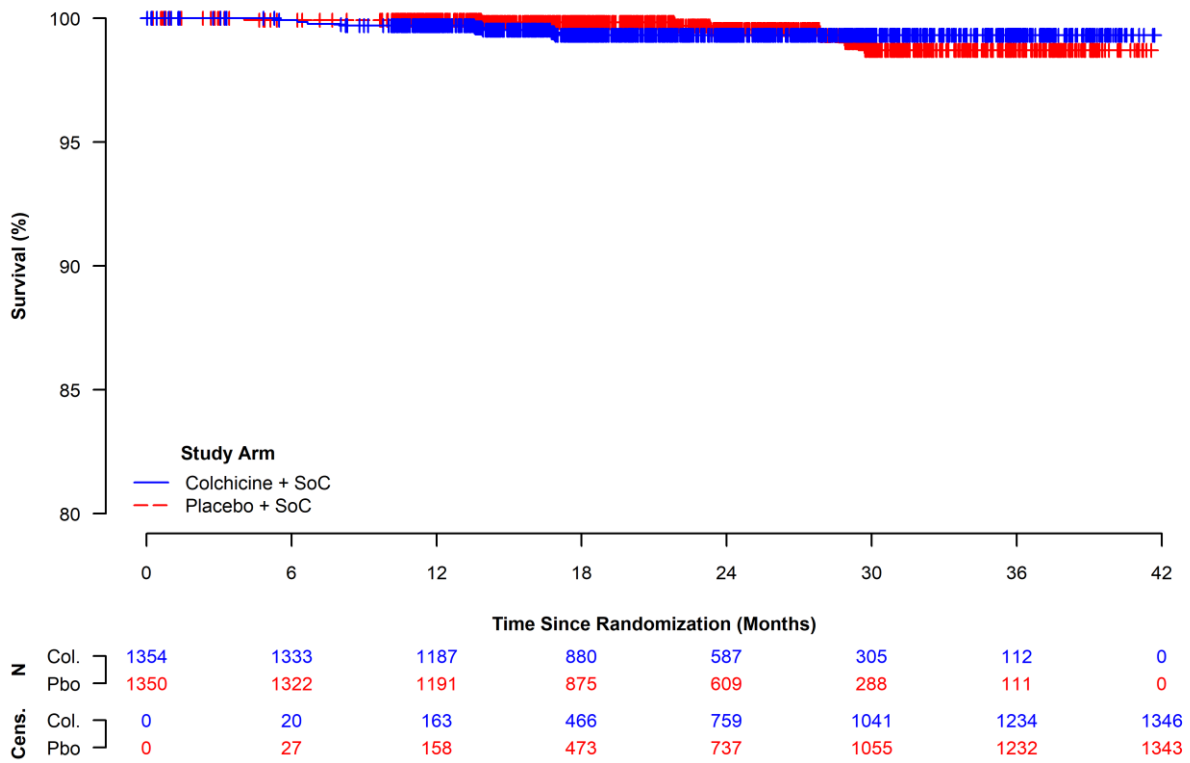
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Region</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1261</b>					
<b>Europe</b>	2/1,012 (0.2)	0/1,029 (0.0)	5.084 [0.244, 105.763] 0.2937	5.094 [0.244, 106.237] 0.2935	0.198 [-0.136, 0.532] 0.2445
<b>Non-Europe</b>	8/1,354 (0.6)	7/1,350 (0.5)	1.130 [0.425, 3.008] 0.8067	1.131 [0.422, 3.028] 0.8067	0.072 [-0.506, 0.650] 0.8066
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 174:** Time to Deep Vein Thrombosis or Pulmonary Embolus, Subgrouped by Region (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = NE</b>							
<b>Europe</b>	2/1,012 (0.2)	NE [NE, NE]	0.2 [0.0, 0.6]	0/1,029 (0.0)	NE [NE, NE]	0.0 [0.0, 0.0]	NE [NE, NE] NE
<b>Non-Europe</b>	8/1,354 (0.6)	NE [NE, NE]	0.7 [0.2, 1.2]	7/1,350 (0.5)	NE [NE, NE]	1.3 [0.2, 2.3]	1.142 [0.414, 3.150] 0.7974
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 158:** Kaplan-Meier Curves for Deep Vein Thrombosis or Pulmonary Embolus, Within European Countries (ITT Population).



**Figure 159:** Kaplan-Meier Curves for Deep Vein Thrombosis or Pulmonary Embolus, Within Non-European Countries (ITT Population).

#### **4.4.2.8.5 Subgrouped by White Blood Cell Count**

The requirements for performing subgroup analyses were not met, i.e., at least one subgroup contained fewer than ten patients and/or, in the case of binary data and time-to-event analyses, no subgroup had at least ten events.

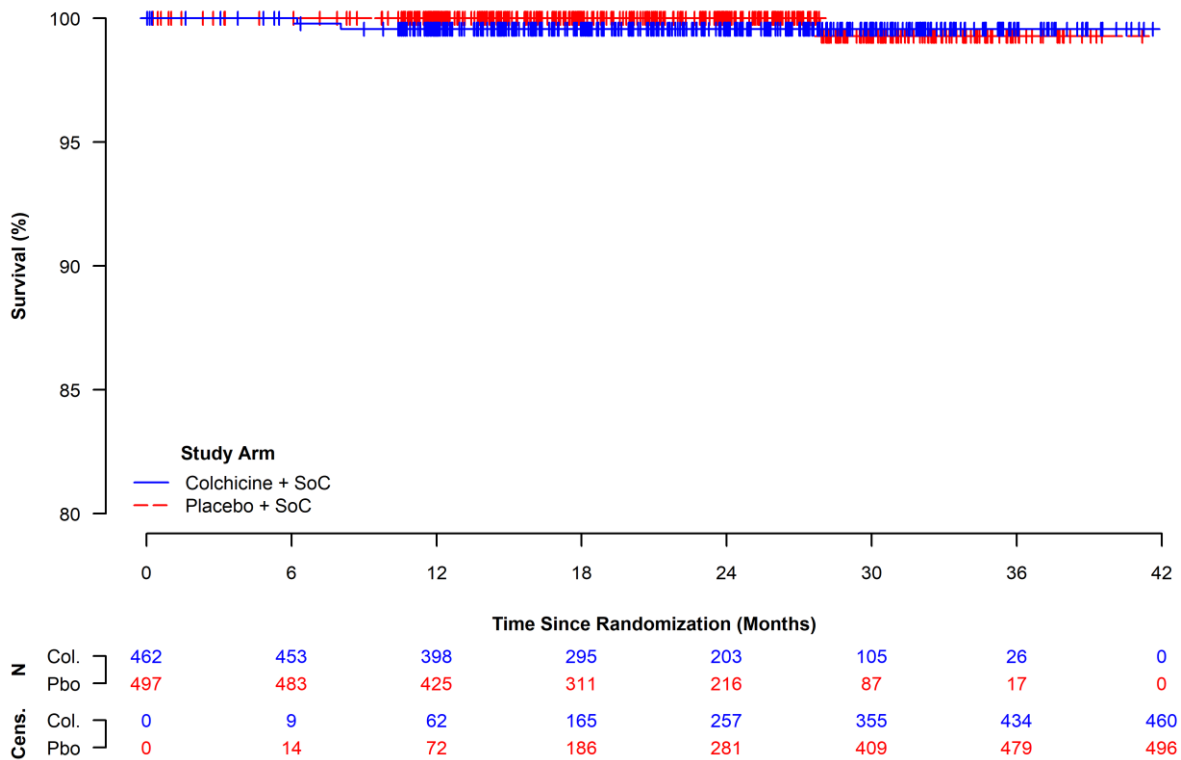
#### 4.4.2.8.6 Subgrouped by Diabetes Status

**Table 175:** Proportion of Patients with Deep Vein Thrombosis or Pulmonary Embolus, Subgrouped by Diabetes Status (ITT Population).

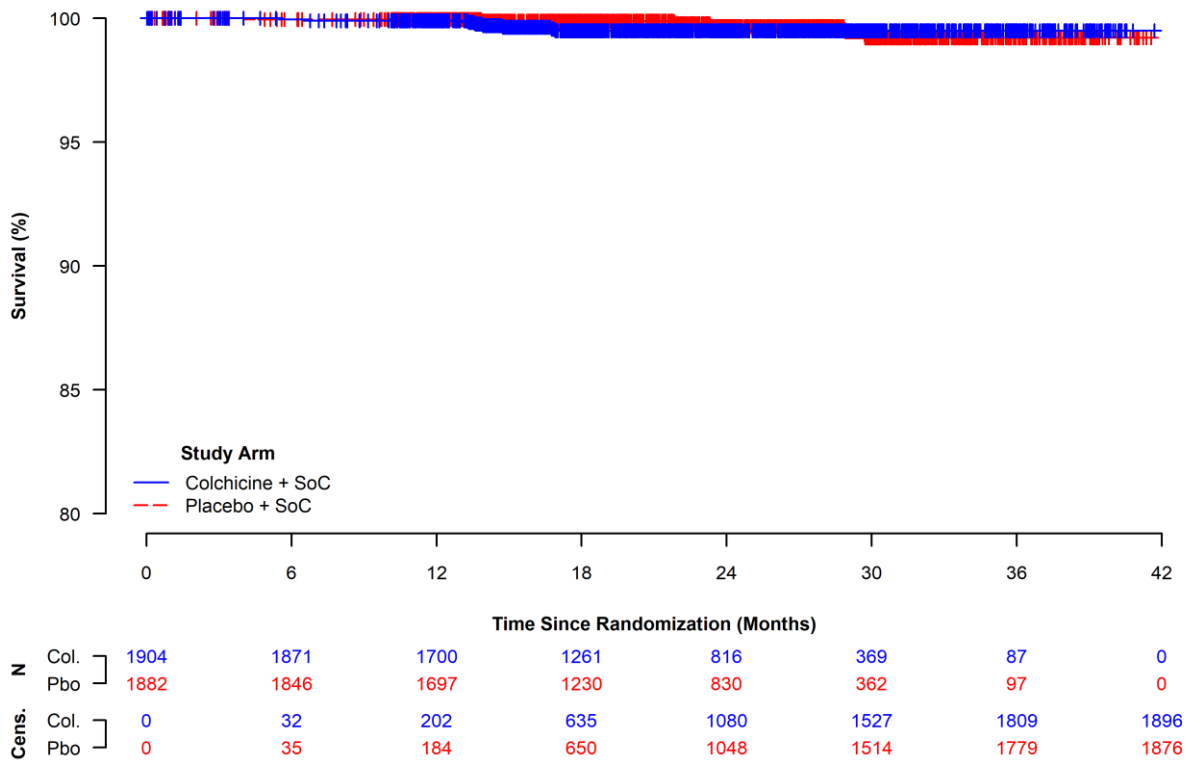
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7095</b>					
<b>Yes</b>	2/462 (0.4)	1/497 (0.2)	2.152 [0.196, 23.648] 0.5310	2.157 [0.195, 23.862] 0.5309	0.232 [-0.485, 0.948] 0.5263
<b>No</b>	8/1,904 (0.4)	6/1,882 (0.3)	1.318 [0.458, 3.791] 0.6086	1.319 [0.457, 3.810] 0.6086	0.101 [-0.285, 0.488] 0.6071
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 176:** Time to Deep Vein Thrombosis or Pulmonary Embolus, Subgrouped by Diabetes Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.7234</b>							
<b>Yes</b>	2/462 (0.4)	NE [NE, NE]	0.4 [0.0, 1.1]	1/497 (0.2)	NE [NE, NE]	0.7 [0.0, 2.1]	2.095 [0.190, 23.106] 0.5460
<b>No</b>	8/1,904 (0.4)	NE [NE, NE]	0.5 [0.2, 0.9]	6/1,882 (0.3)	NE [NE, NE]	0.8 [0.1, 1.5]	1.316 [0.457, 3.794] 0.6109
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 160:** Kaplan-Meier Curves for Deep Vein Thrombosis or Pulmonary Embolus, Within the Diabetic Subgroup (ITT Population).



**Figure 161:** Kaplan-Meier Curves for Deep Vein Thrombosis or Pulmonary Embolus, Within the Non-Diabetic Subgroup (ITT Population).

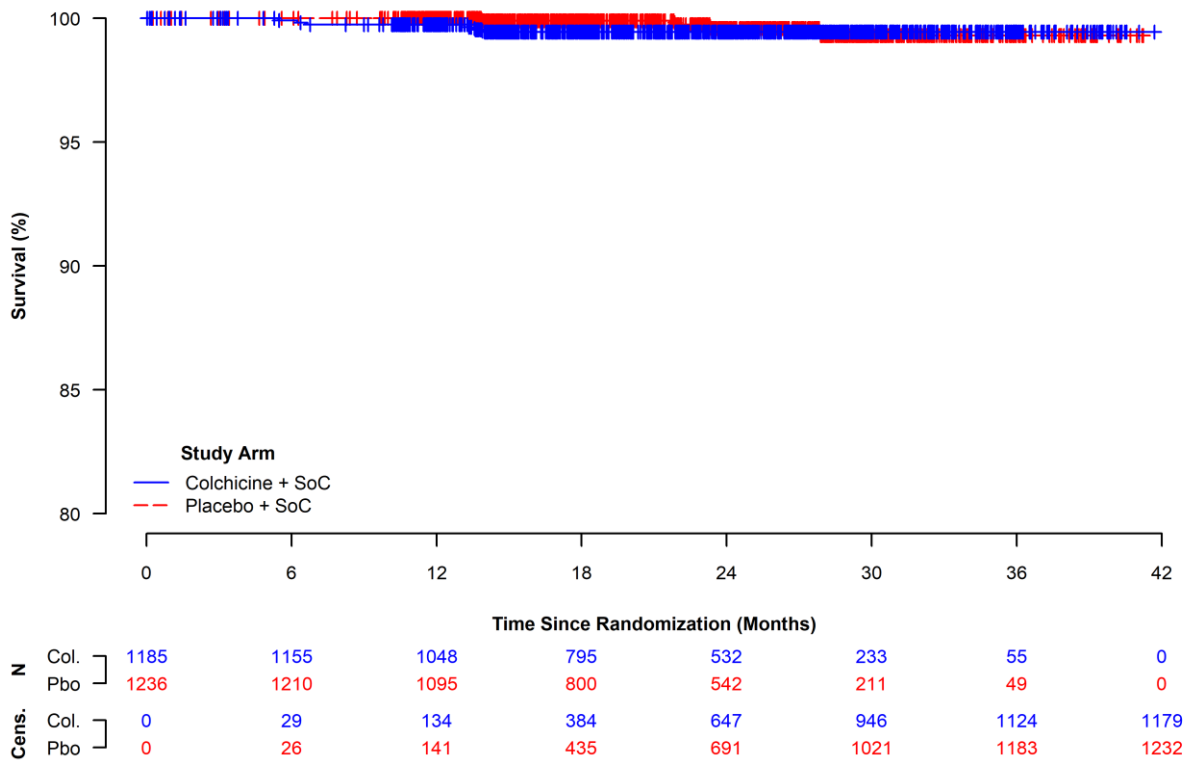
#### 4.4.2.8.7 Subgrouped by Hypertension Status

**Table 177:** Proportion of Patients with Deep Vein Thrombosis or Pulmonary Embolus, Subgrouped by Hypertension Status (ITT Population).

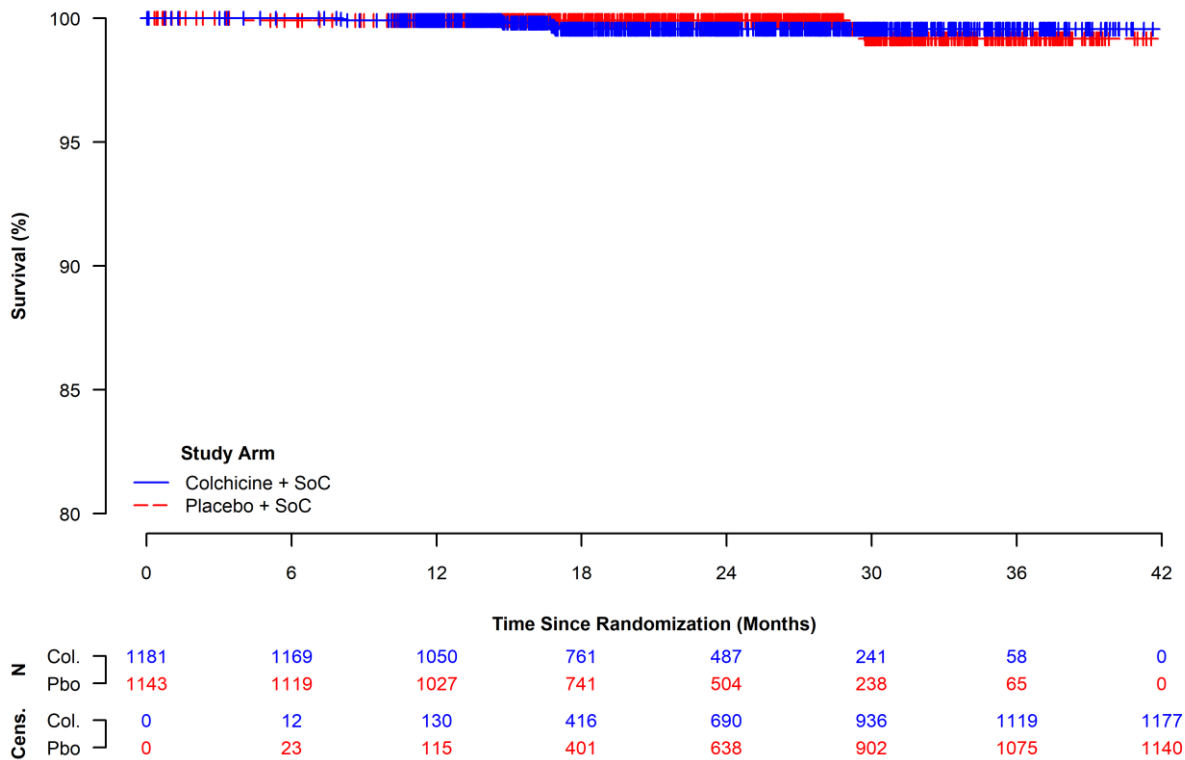
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8468</b>					
<b>Yes</b>	6/1,185 (0.5)	4/1,236 (0.3)	1.565 [0.443, 5.530] 0.4872	1.567 [0.441, 5.568] 0.4871	0.183 [-0.331, 0.696] 0.4855
<b>No</b>	4/1,181 (0.3)	3/1,143 (0.3)	1.290 [0.289, 5.753] 0.7381	1.291 [0.288, 5.783] 0.7381	0.076 [-0.368, 0.521] 0.7369
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 178:** Time to Deep Vein Thrombosis or Pulmonary Embolus, Subgrouped by Hypertension Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.8677</b>							
<b>Yes</b>	6/1,185 (0.5)	NE [NE, NE]	0.6 [0.1, 1.0]	4/1,236 (0.3)	NE [NE, NE]	0.7 [0.0, 1.4]	1.550 [0.437, 5.493] 0.4972
<b>No</b>	4/1,181 (0.3)	NE [NE, NE]	0.4 [0.0, 0.9]	3/1,143 (0.3)	NE [NE, NE]	0.8 [0.0, 1.8]	1.300 [0.291, 5.807] 0.7315
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 162:** Kaplan-Meier Curves for Deep Vein Thrombosis or Pulmonary Embolus, Within the Hypertensive Subgroup (ITT Population).



**Figure 163:** Kaplan-Meier Curves for Deep Vein Thrombosis or Pulmonary Embolus, Within the Normotensive Subgroup (ITT Population).

#### **4.4.2.8.8 Subgrouped by History of Myocardial Infarction**

The requirements for performing subgroup analyses were not met, i.e., at least one subgroup contained fewer than ten patients and/or, in the case of binary data and time-to-event analyses, no subgroup had at least ten events.

#### **4.4.2.8.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft**

The requirements for performing subgroup analyses were not met, i.e., at least one subgroup contained fewer than ten patients and/or, in the case of binary data and time-to-event analyses, no subgroup had at least ten events.

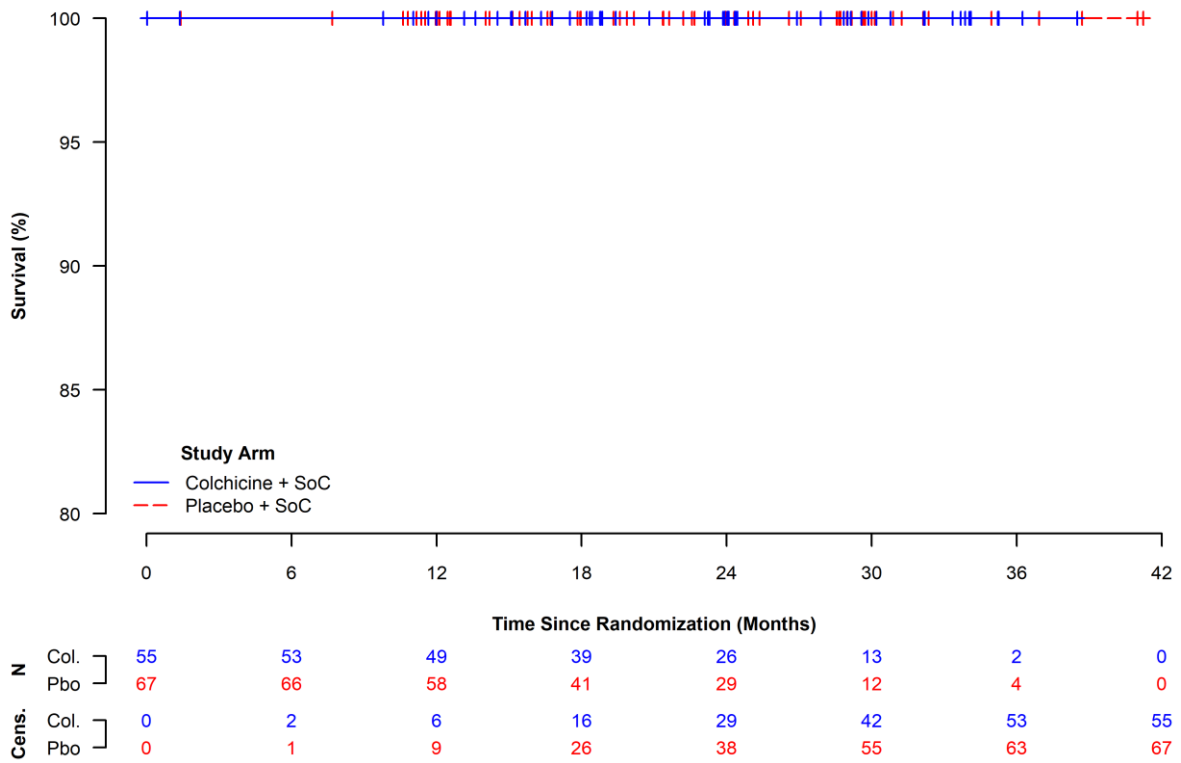
#### 4.4.2.8.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 179:** Proportion of Patients with Deep Vein Thrombosis or Pulmonary Embolus, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

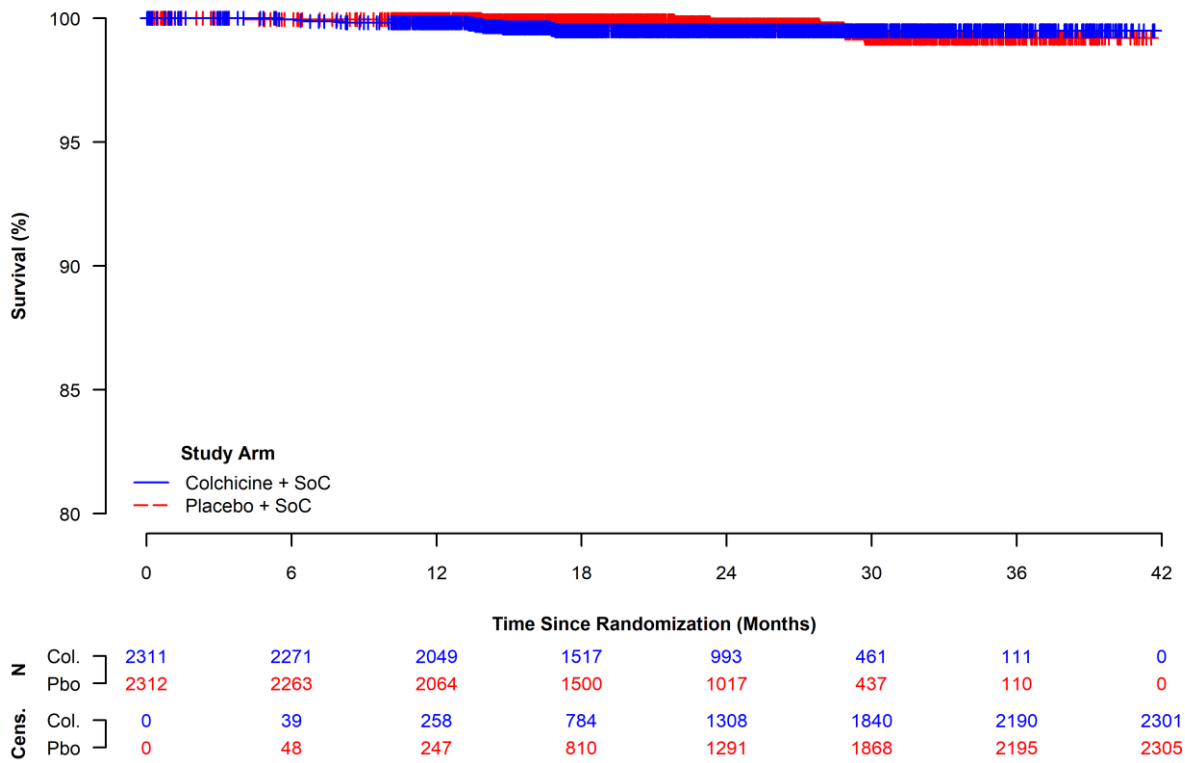
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>					
<b>Interaction Test p-Value<sup>d</sup> = 1.0000</b>					
<b>Yes</b>	0/55 (0.0)	0/67 (0.0)	1.214 [0.024, 60.225] 0.9223	1.216 [0.024, 62.285] 0.9224	0.158 [-3.035, 3.350] 0.9229
<b>No</b>	10/2,311 (0.4)	7/2,312 (0.3)	1.401 [0.550, 3.569] 0.4802	1.402 [0.548, 3.586] 0.4801	0.130 [-0.229, 0.489] 0.4781
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 180:** Time to Deep Vein Thrombosis or Pulmonary Embolus, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>							
<b>Interaction Test p-Value<sup>f</sup> = NE</b>							
<b>Yes</b>	0/55 (0.0)	NE [NE, NE]	0.0 [0.0, 0.0]	0/67 (0.0)	NE [NE, NE]	0.0 [0.0, 0.0]	NE [NE, NE] NE
<b>No</b>	10/2,311 (0.4)	NE [NE, NE]	0.5 [0.2, 0.8]	7/2,312 (0.3)	NE [NE, NE]	0.8 [0.1, 1.5]	1.422 [0.541, 3.735] 0.4753
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 164:** Kaplan-Meier Curves for Deep Vein Thrombosis or Pulmonary Embolus, Within the Subgroup With History of Stroke or Transient Ischaemic Attack (ITT Population).



**Figure 165:** Kaplan-Meier Curves for Deep Vein Thrombosis or Pulmonary Embolus, Within the Subgroup Without History of Stroke or Transient Ischaemic Attack (ITT Population).

#### 4.4.2.9 Atrial Fibrillation

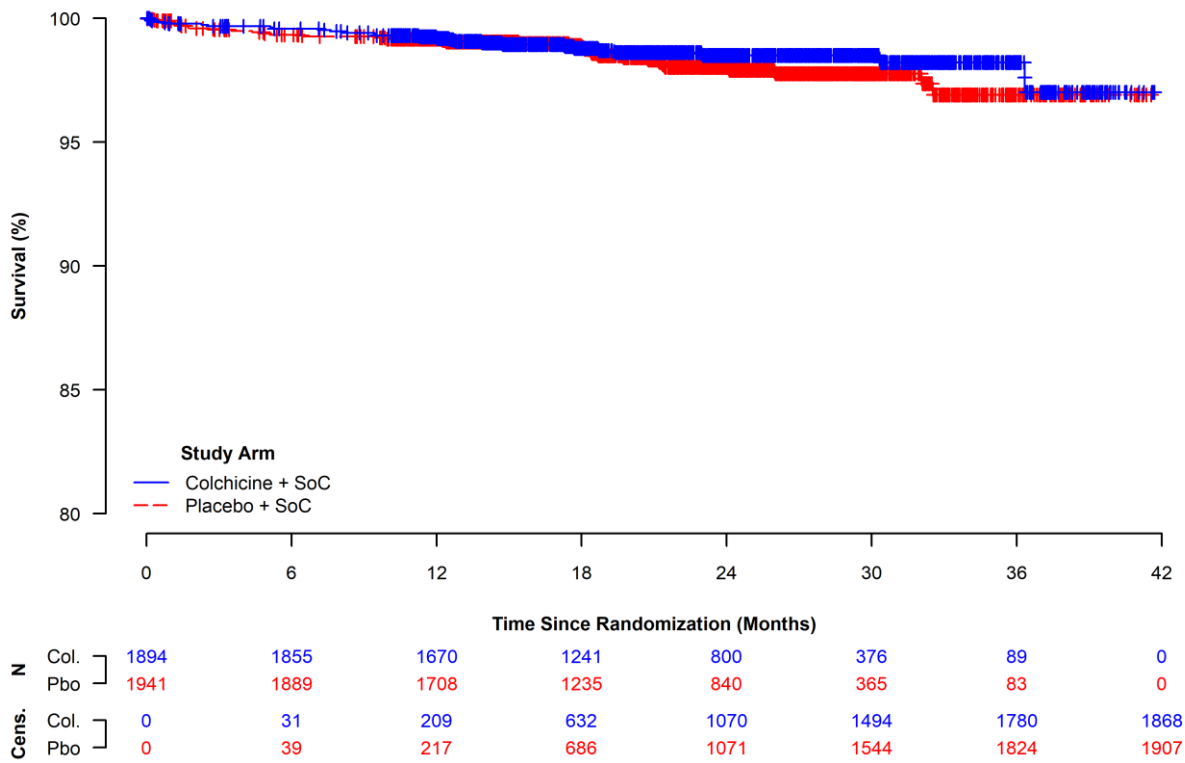
##### 4.4.2.9.1 Subgrouped by Sex

**Table 181:** Proportion of Patients with Atrial Fibrillation, Subgrouped by Sex (ITT Population).

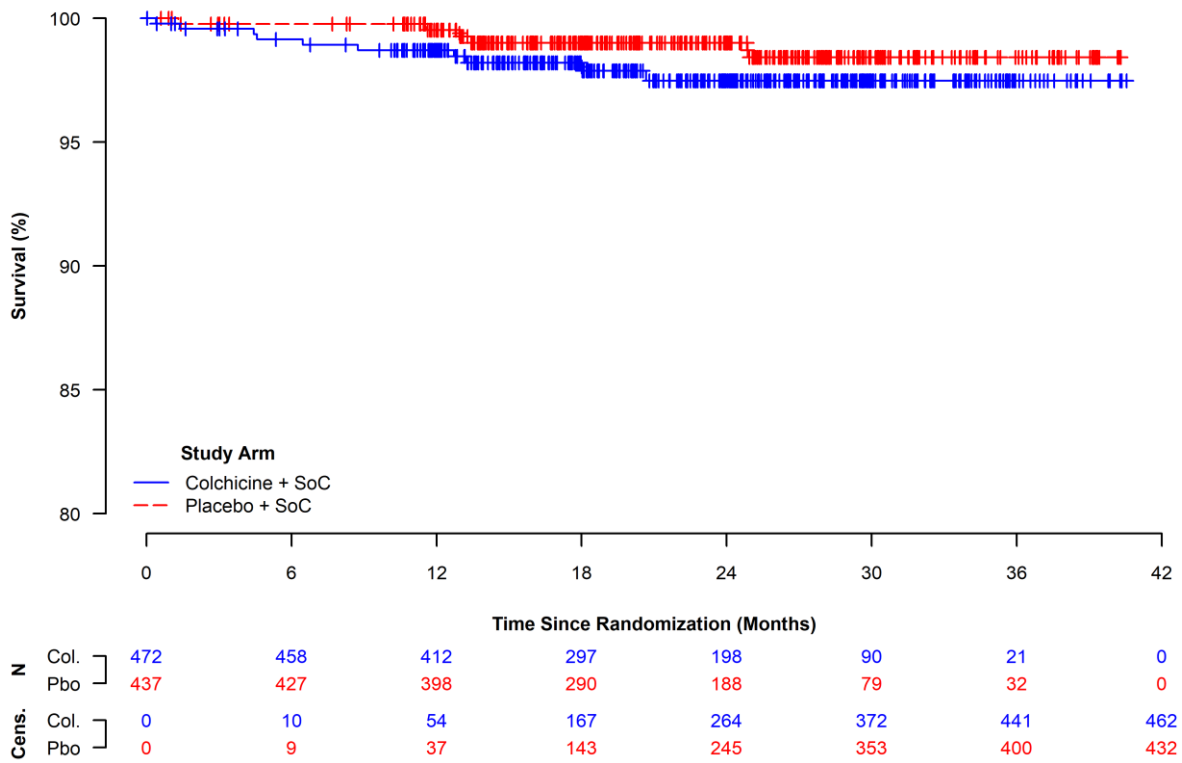
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,378)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Sex</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1430</b>					
<b>Male</b>	26/1,894 (1.4)	34/1,941 (1.8)	0.784 [0.472, 1.301] 0.3457	0.781 [0.467, 1.306] 0.3457	-0.379 [-1.163, 0.405] 0.3437
<b>Female</b>	10/472 (2.1)	5/437 (1.1)	1.852 [0.638, 5.375] 0.2571	1.870 [0.634, 5.515] 0.2566	0.974 [-0.663, 2.612] 0.2435
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 182:** Time to Atrial Fibrillation, Subgrouped by Sex (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,378)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Sex</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.1264</b>							
<b>Male</b>	26/1,894 (1.4)	NE [NE, NE]	3.0 [0.5, 5.5]	34/1,941 (1.8)	NE [NE, NE]	3.1 [1.7, 4.5]	0.776 [0.466, 1.293] 0.3301
<b>Female</b>	10/472 (2.1)	NE [NE, NE]	2.5 [0.9, 4.1]	5/437 (1.1)	NE [NE, NE]	1.6 [0.1, 3.1]	1.903 [0.650, 5.568] 0.2401
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 166:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Male Sex Subgroup (ITT Population).



**Figure 167:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Female Sex Subgroup (ITT Population).

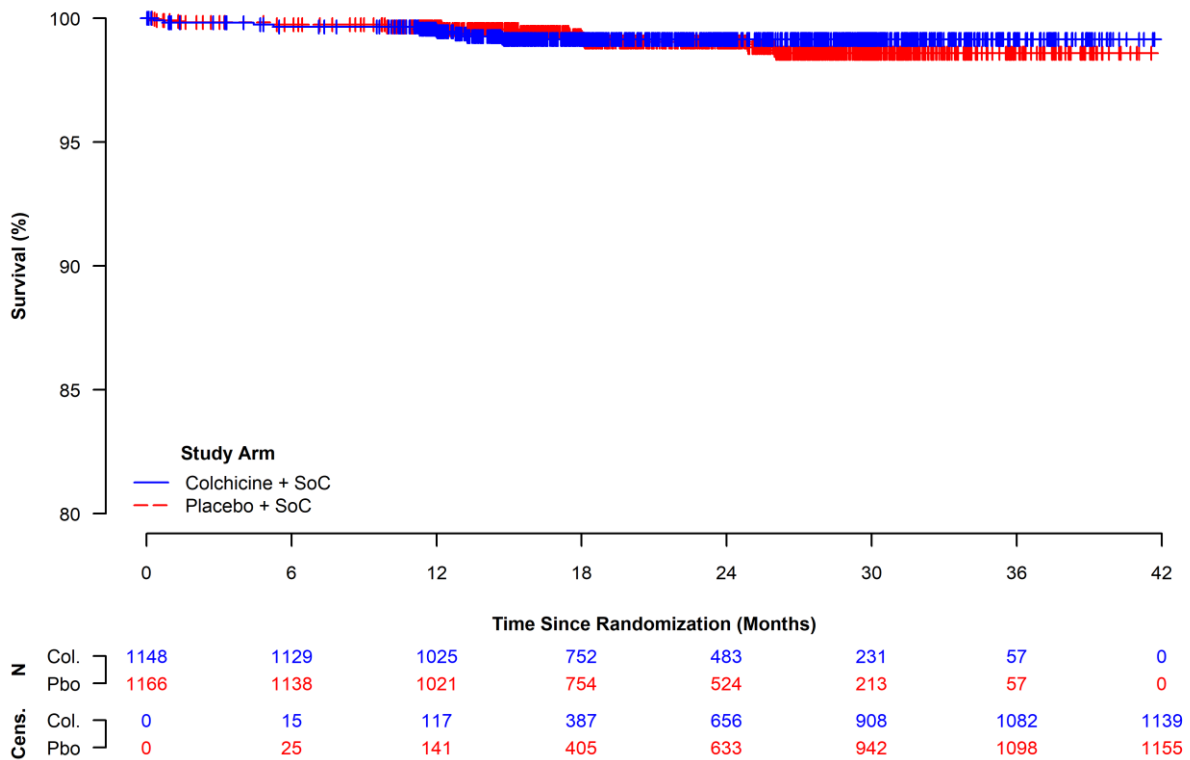
#### 4.4.2.9.2 Subgrouped by Age Group

**Table 183:** Proportion of Patients with Atrial Fibrillation, Subgrouped by Age Group (ITT Population).

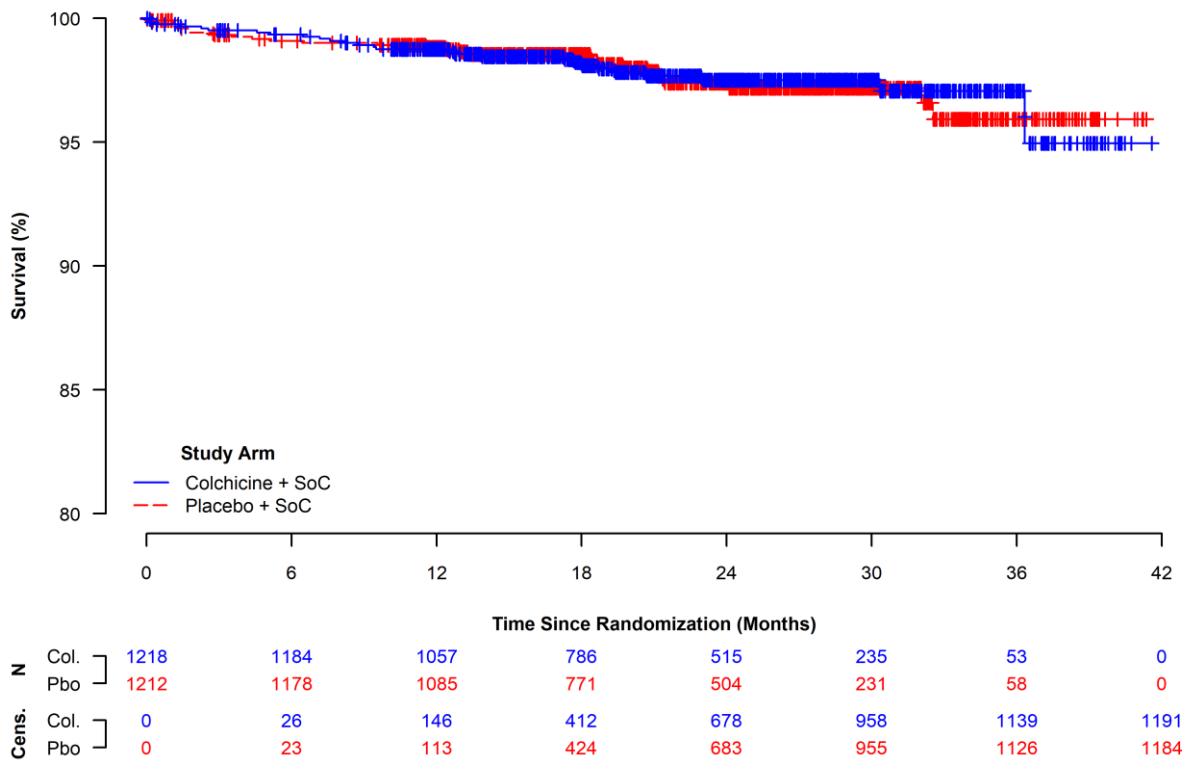
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,378)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Age</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7839</b>					
<b>&lt; 60 Years</b>	9/1,148 (0.8)	11/1,166 (0.9)	0.831 [0.346, 1.998] 0.6791	0.830 [0.343, 2.010] 0.6791	-0.159 [-0.913, 0.594] 0.6785
<b>≥ 60 Years</b>	27/1,218 (2.2)	28/1,212 (2.3)	0.960 [0.569, 1.618] 0.8769	0.959 [0.562, 1.636] 0.8769	-0.093 [-1.276, 1.089] 0.8769
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 184:** Time to Atrial Fibrillation, Subgrouped by Age Group (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,378)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Age</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.7649</b>							
<b>&lt; 60 Years</b>	9/1,148 (0.8)	NE [NE, NE]	0.9 [0.3, 1.4]	11/1,166 (0.9)	NE [NE, NE]	1.4 [0.5, 2.3]	0.825 [0.342, 1.992] 0.6692
<b>≥ 60 Years</b>	27/1,218 (2.2)	NE [NE, NE]	5.0 [0.7, 9.2]	28/1,212 (2.3)	NE [NE, NE]	4.1 [2.0, 6.1]	0.963 [0.568, 1.634] 0.8899
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 168:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Age 59 Years or Younger Subgroup (ITT Population).



**Figure 169:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Age 60 Years or Older Subgroup (ITT Population).

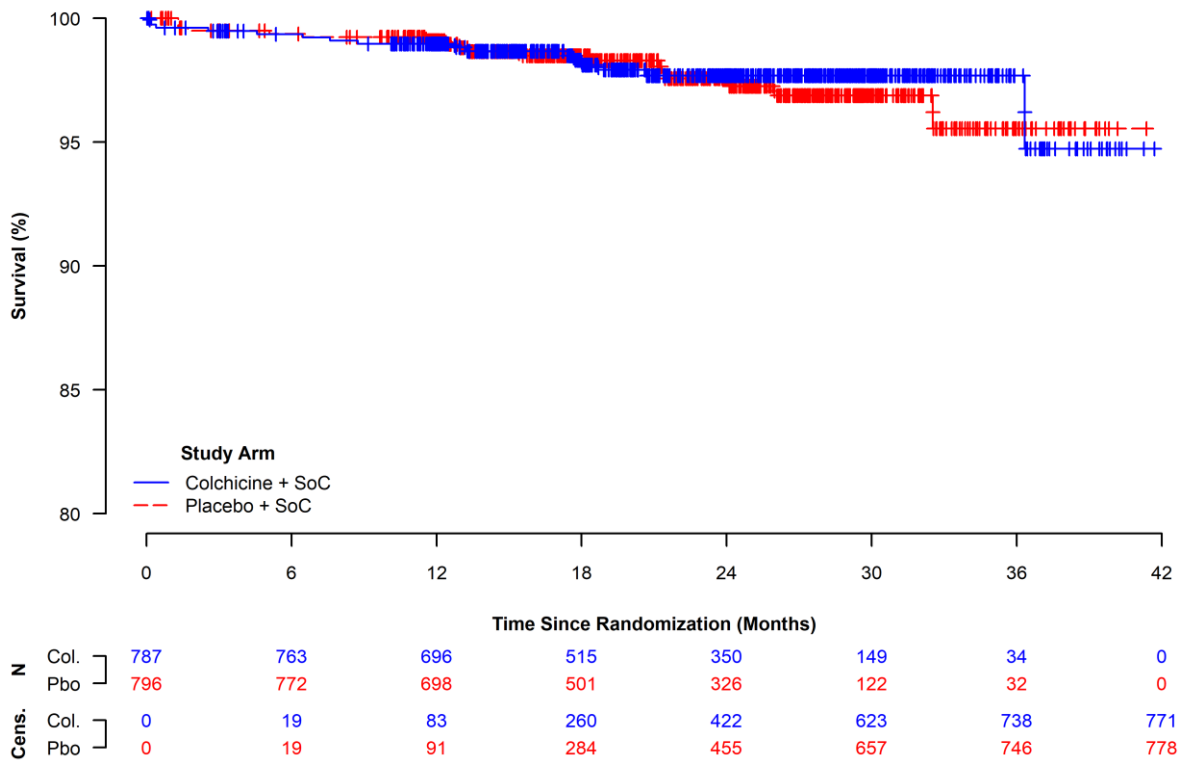
#### 4.4.2.9.3 Subgrouped by Smoking Status

**Table 185:** Proportion of Patients with Atrial Fibrillation, Subgrouped by Smoking Status (ITT Population).

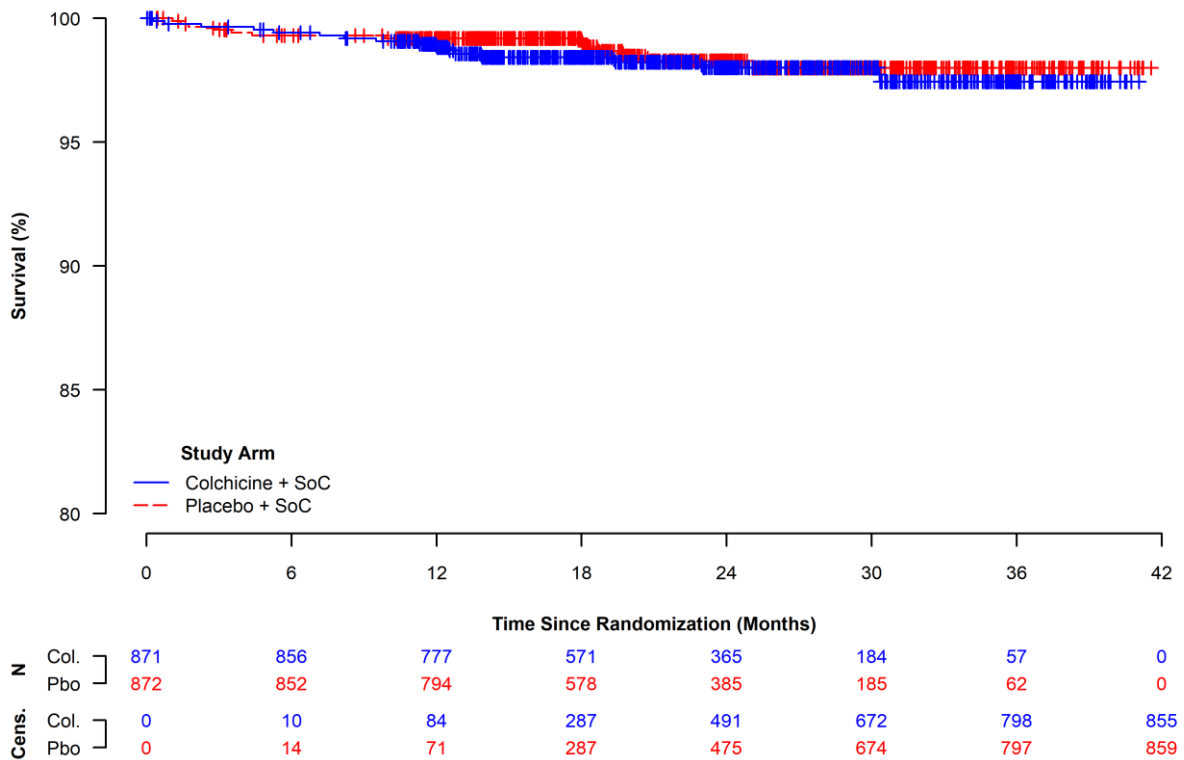
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,376)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Smoking Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4311</b>					
<b>Non</b>	16/787 (2.0)	18/796 (2.3)	0.899 [0.462, 1.750] 0.7542	0.897 [0.454, 1.772] 0.7542	-0.228 [-1.656, 1.200] 0.7540
<b>Ex</b>	16/871 (1.8)	13/872 (1.5)	1.232 [0.596, 2.546] 0.5729	1.237 [0.591, 2.586] 0.5728	0.346 [-0.855, 1.547] 0.5721
<b>Current</b>	4/708 (0.6)	8/708 (1.1)	0.500 [0.151, 1.653] 0.2559	0.497 [0.149, 1.659] 0.2556	-0.565 [-1.519, 0.389] 0.2460
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 186:** Time to Atrial Fibrillation, Subgrouped by Smoking Status (ITT Population).

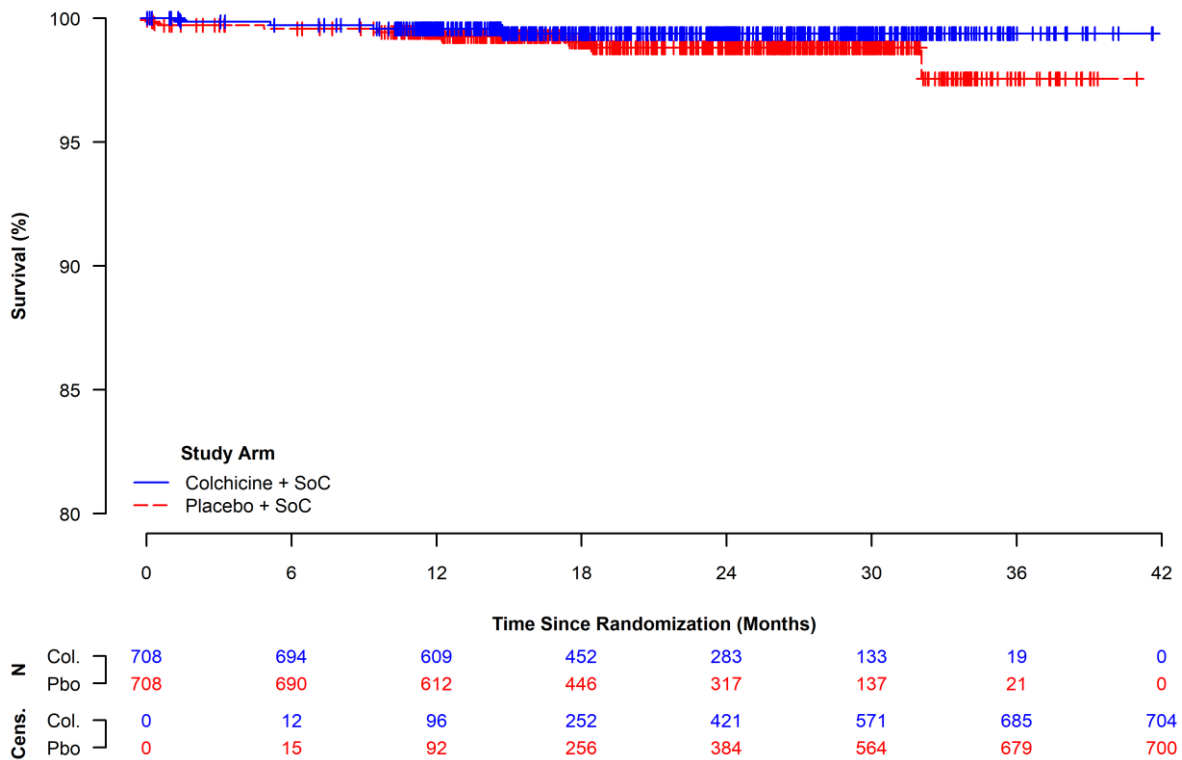
Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,376)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.4218</b>							
<b>Non</b>	16/787 (2.0)	NE [NE, NE]	5.3 [0.0, 10.9]	18/796 (2.3)	NE [NE, NE]	4.5 [1.4, 7.4]	0.877 [0.447, 1.720] 0.7022
<b>Ex</b>	16/871 (1.8)	NE [NE, NE]	2.6 [1.0, 4.1]	13/872 (1.5)	NE [NE, NE]	2.0 [0.9, 3.1]	1.244 [0.599, 2.587] 0.5581
<b>Current</b>	4/708 (0.6)	NE [NE, NE]	0.6 [0.0, 1.2]	8/708 (1.1)	NE [NE, NE]	2.5 [0.0, 5.0]	0.497 [0.150, 1.652] 0.2542
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 170:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Non-Smoker Subgroup (ITT Population).



**Figure 171:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Ex-Smoker Subgroup (ITT Population).



**Figure 172:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Current Smoker Subgroup (ITT Population).

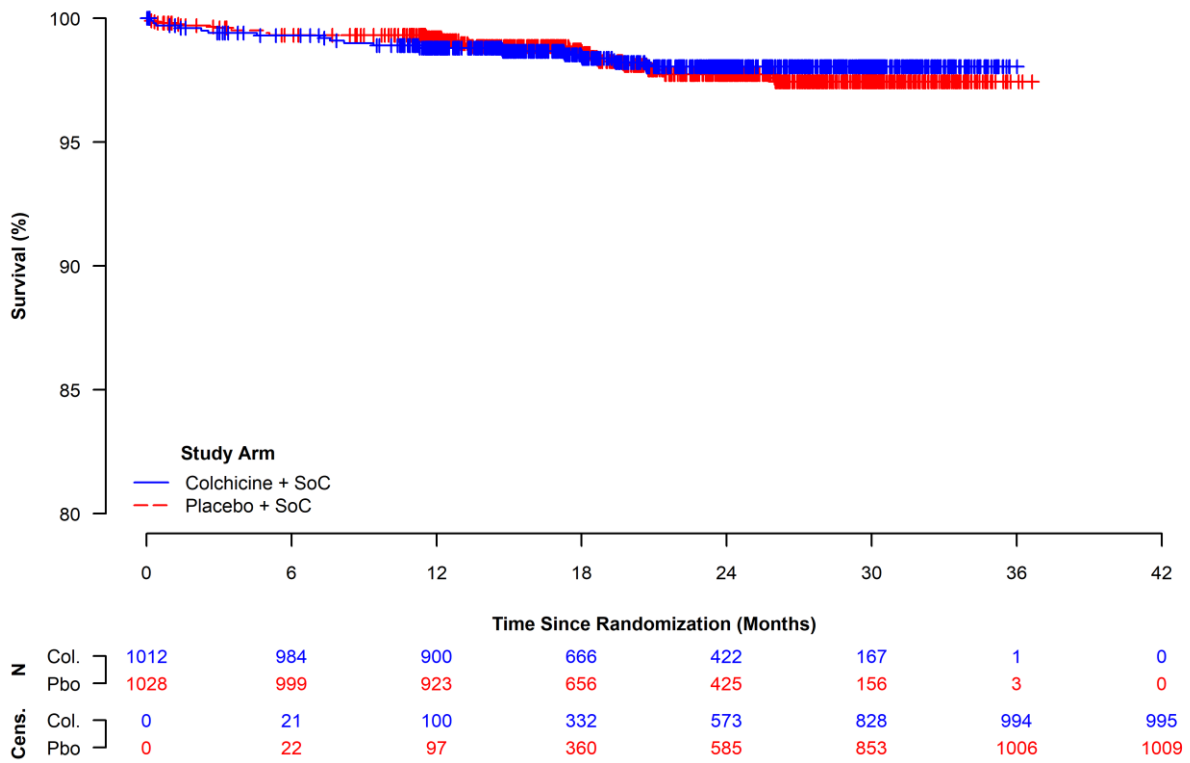
#### 4.4.2.9.4 Subgrouped by Region

**Table 187:** Proportion of Patients with Atrial Fibrillation, Subgrouped by Region (ITT Population).

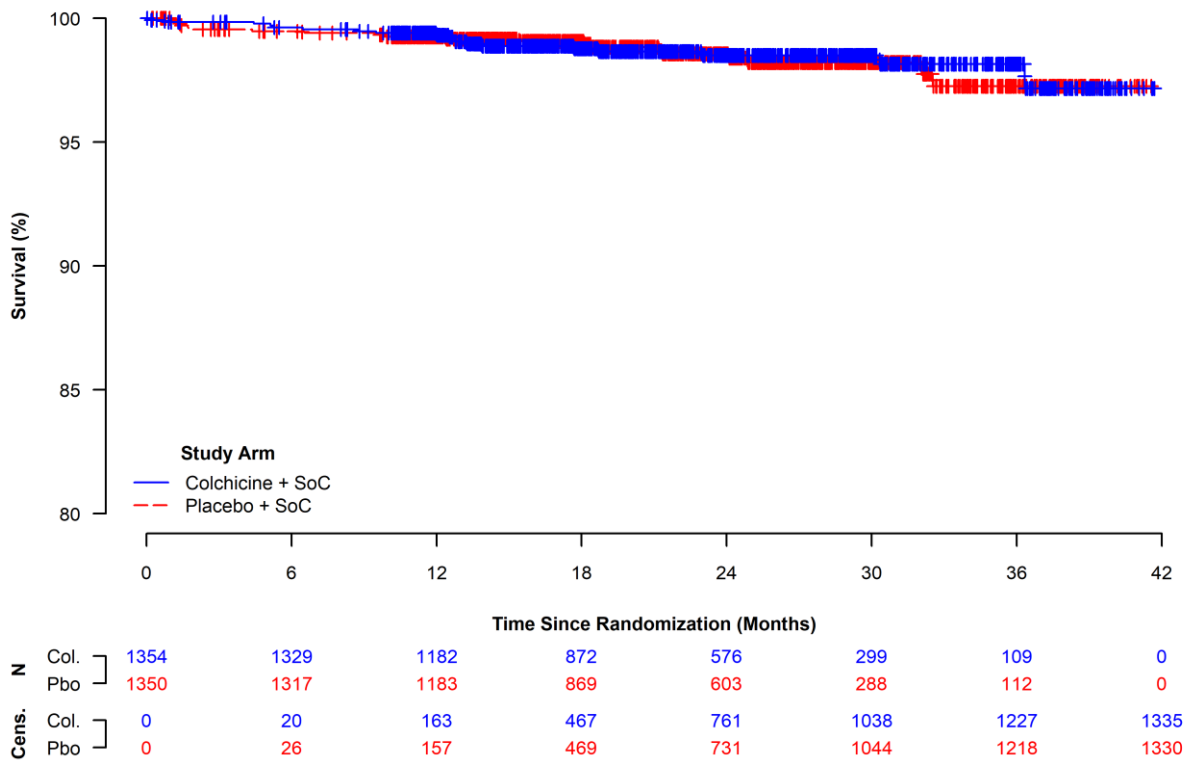
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,378)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Region</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.9279</b>					
<b>Europe</b>	17/1,012 (1.7)	19/1,028 (1.8)	0.909 [0.475, 1.738] 0.7728	0.907 [0.469, 1.756] 0.7728	-0.168 [-1.311, 0.974] 0.7726
<b>Non-Europe</b>	19/1,354 (1.4)	20/1,350 (1.5)	0.947 [0.508, 1.767] 0.8646	0.946 [0.503, 1.781] 0.8646	-0.078 [-0.977, 0.821] 0.8645
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 188:** Time to Atrial Fibrillation, Subgrouped by Region (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,378)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.9135</b>							
<b>Europe</b>	17/1,012 (1.7)	NE [NE, NE]	2.0 [1.0, 2.9]	19/1,028 (1.8)	NE [NE, NE]	2.6 [1.3, 3.8]	0.903 [0.469, 1.736] 0.7589
<b>Non-Europe</b>	19/1,354 (1.4)	NE [NE, NE]	2.8 [0.7, 5.0]	20/1,350 (1.5)	NE [NE, NE]	2.7 [1.2, 4.3]	0.950 [0.507, 1.781] 0.8736
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 173:** Kaplan-Meier Curves for Atrial Fibrillation, Within European Countries (ITT Population).



**Figure 174:** Kaplan-Meier Curves for Atrial Fibrillation, Within Non-European Countries (ITT Population).

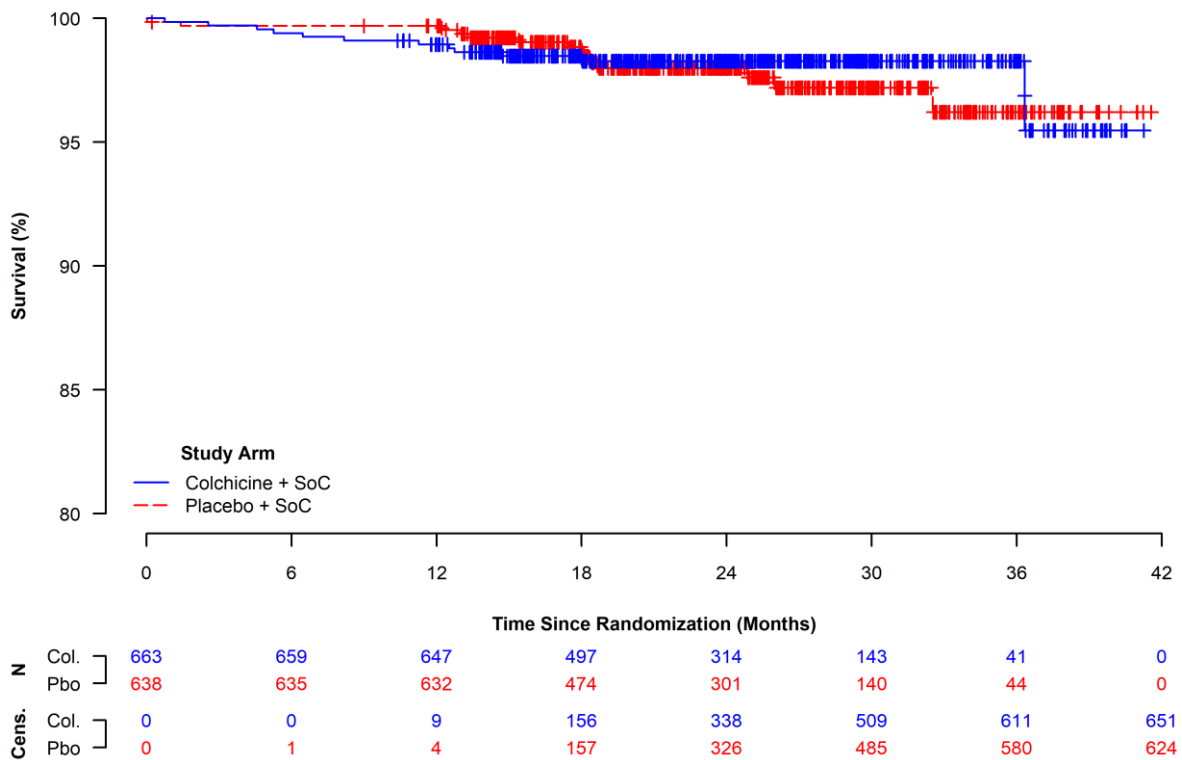
#### 4.4.2.9.5 Subgrouped by White Blood Cell Count

**Table 189:** Proportion of Patients with Atrial Fibrillation, Subgrouped by White Blood Cell Count (ITT Population).

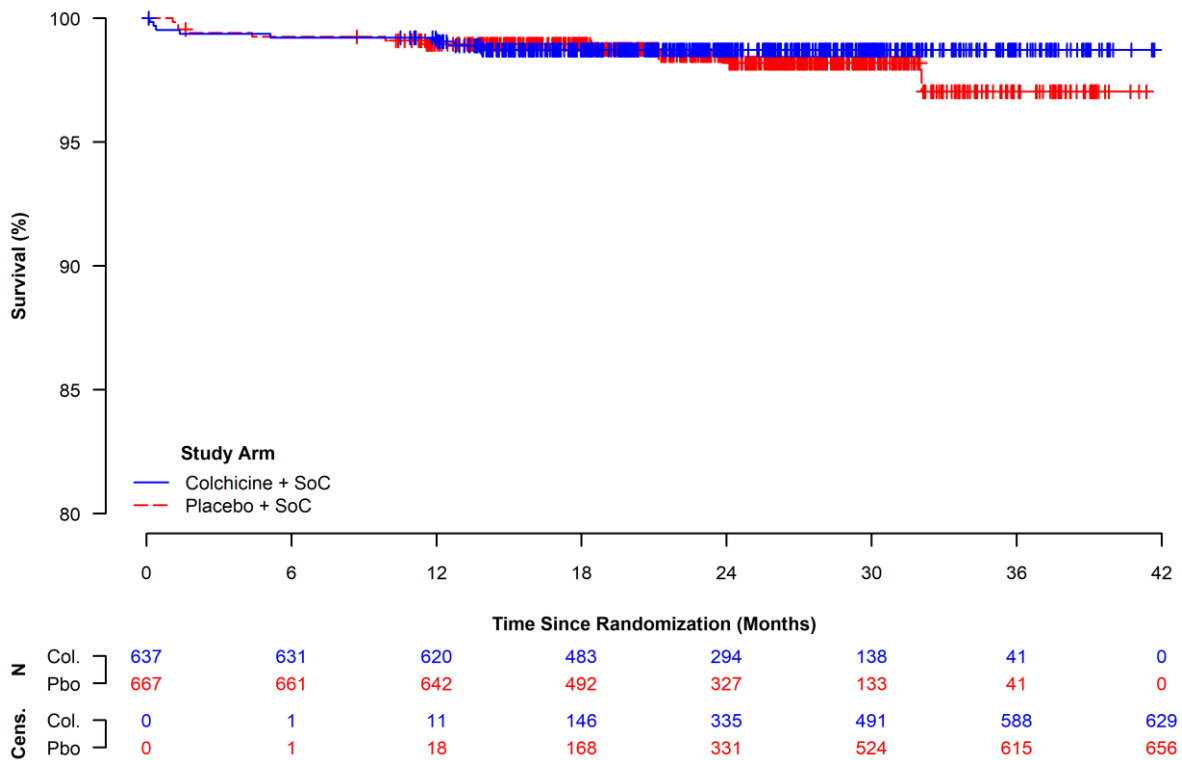
Subgroup	Colchicine + SoC (N = 1,300)	Placebo + SoC (N = 1,305)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8964</b>					
< 8.66 10 <sup>3</sup> /μL	12/663 (1.8)	14/638 (2.2)	0.825 [0.384, 1.770] 0.6210	0.822 [0.377, 1.790] 0.6209	-0.384 [-1.908, 1.139] 0.6210
≥ 8.66 10 <sup>3</sup> /μL	8/637 (1.3)	11/667 (1.6)	0.762 [0.308, 1.881] 0.5548	0.758 [0.303, 1.898] 0.5548	-0.393 [-1.690, 0.904] 0.5523
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 190:** Time to Atrial Fibrillation, Subgrouped by White Blood Cell Count (ITT Population).

Subgroup	Colchicine + SoC (N = 1,300)			Placebo + SoC (N = 1,305)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.8788</b>							
< 8.66 10 <sup>3</sup> /μL	12/663 (1.8)	NE [NE, NE]	4.5 [0.0, 9.9]	14/638 (2.2)	NE [NE, NE]	3.8 [1.3, 6.3]	0.830 [0.384, 1.795] 0.6358
≥ 8.66 10 <sup>3</sup> /μL	8/637 (1.3)	NE [NE, NE]	1.3 [0.4, 2.1]	11/667 (1.6)	NE [NE, NE]	3.0 [0.4, 5.5]	0.756 [0.304, 1.881] 0.5482
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 175:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Lower White Blood Cell Count Subgroup (ITT Population).



**Figure 176:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Upper White Blood Cell Count Subgroup (ITT Population).

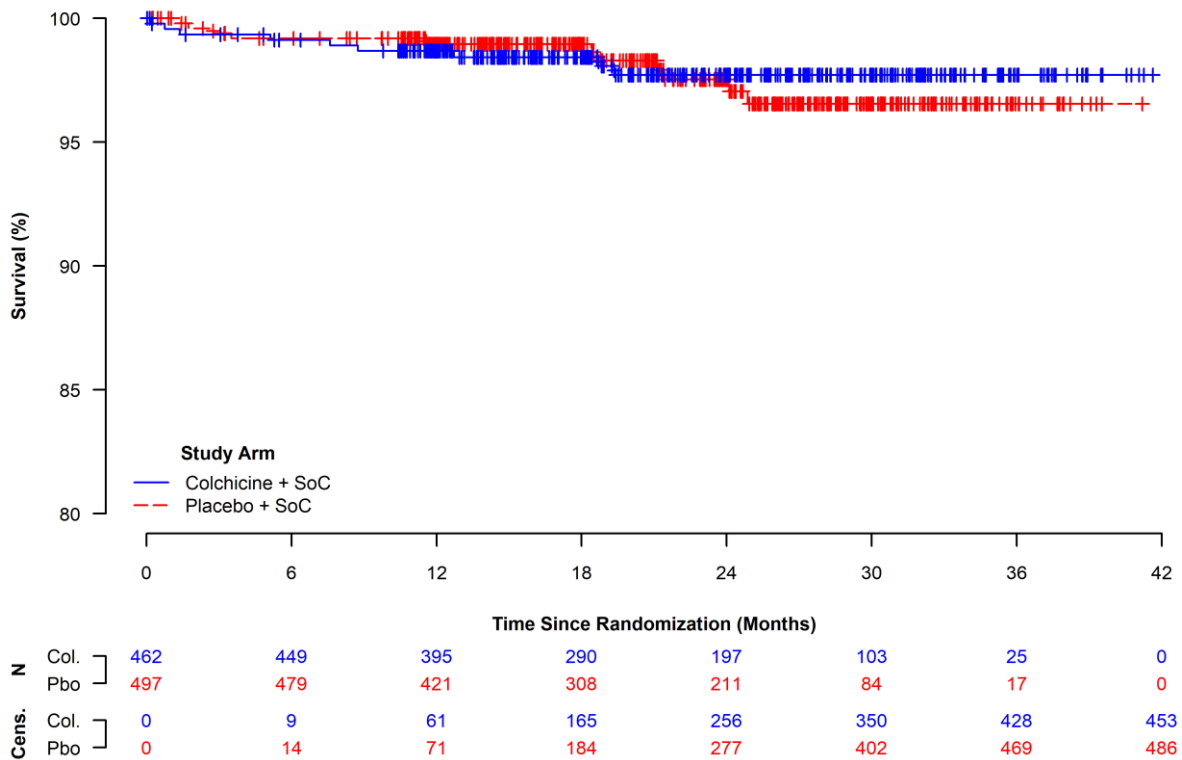
#### 4.4.2.9.6 Subgrouped by Diabetes Status

**Table 191:** Proportion of Patients with Atrial Fibrillation, Subgrouped by Diabetes Status (ITT Population).

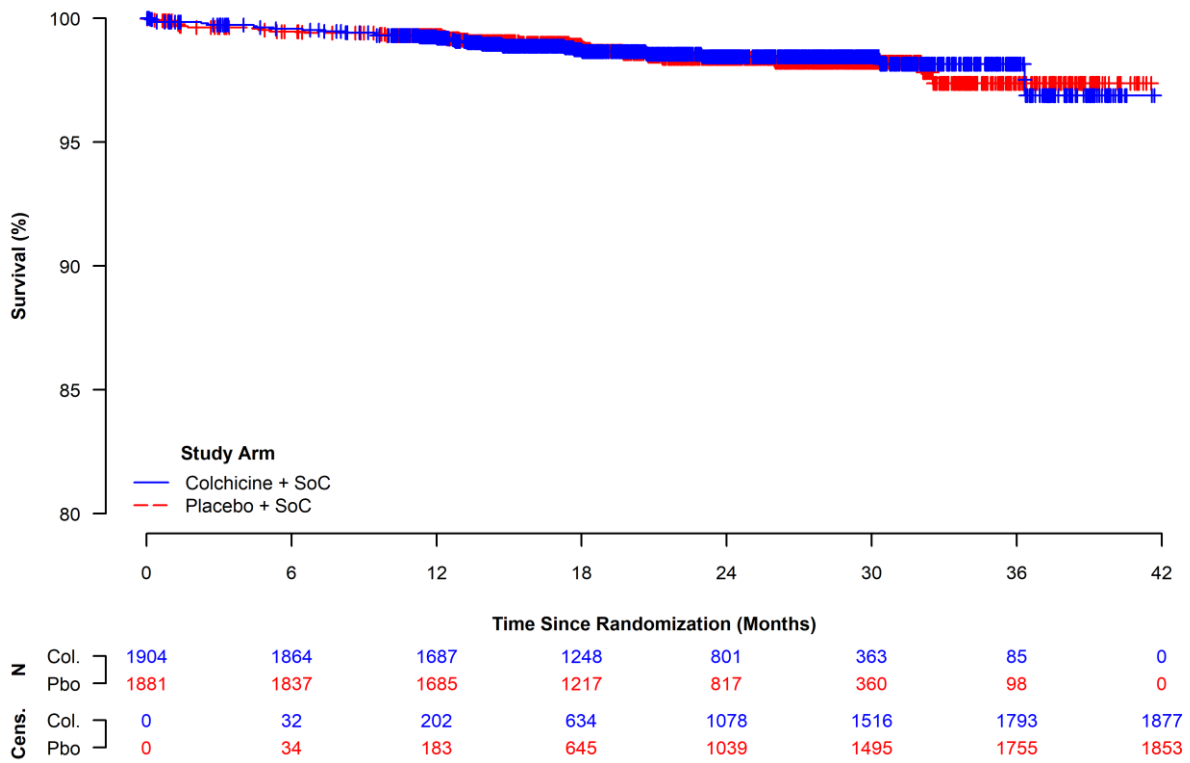
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,378)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8781</b>					
<b>Yes</b>	9/462 (1.9)	11/497 (2.2)	0.880 [0.368, 2.105] 0.7741	0.878 [0.360, 2.138] 0.7741	-0.265 [-2.071, 1.541] 0.7735
<b>No</b>	27/1,904 (1.4)	28/1,881 (1.5)	0.953 [0.564, 1.610] 0.8562	0.952 [0.559, 1.621] 0.8562	-0.071 [-0.833, 0.692] 0.8562
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 192: Time to Atrial Fibrillation, Subgrouped by Diabetes Status (ITT Population).**

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,378)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.8441</b>							
<b>Yes</b>	9/462 (1.9)	NE [NE, NE]	2.3 [0.8, 3.8]	11/497 (2.2)	NE [NE, NE]	3.5 [1.3, 5.6]	0.873 [0.362, 2.106] 0.7618
<b>No</b>	27/1,904 (1.4)	NE [NE, NE]	3.1 [0.5, 5.7]	28/1,881 (1.5)	NE [NE, NE]	2.6 [1.2, 4.0]	0.957 [0.564, 1.623] 0.8698
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 177:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Diabetic Subgroup (ITT Population).



**Figure 178:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Non-Diabetic Subgroup (ITT Population).

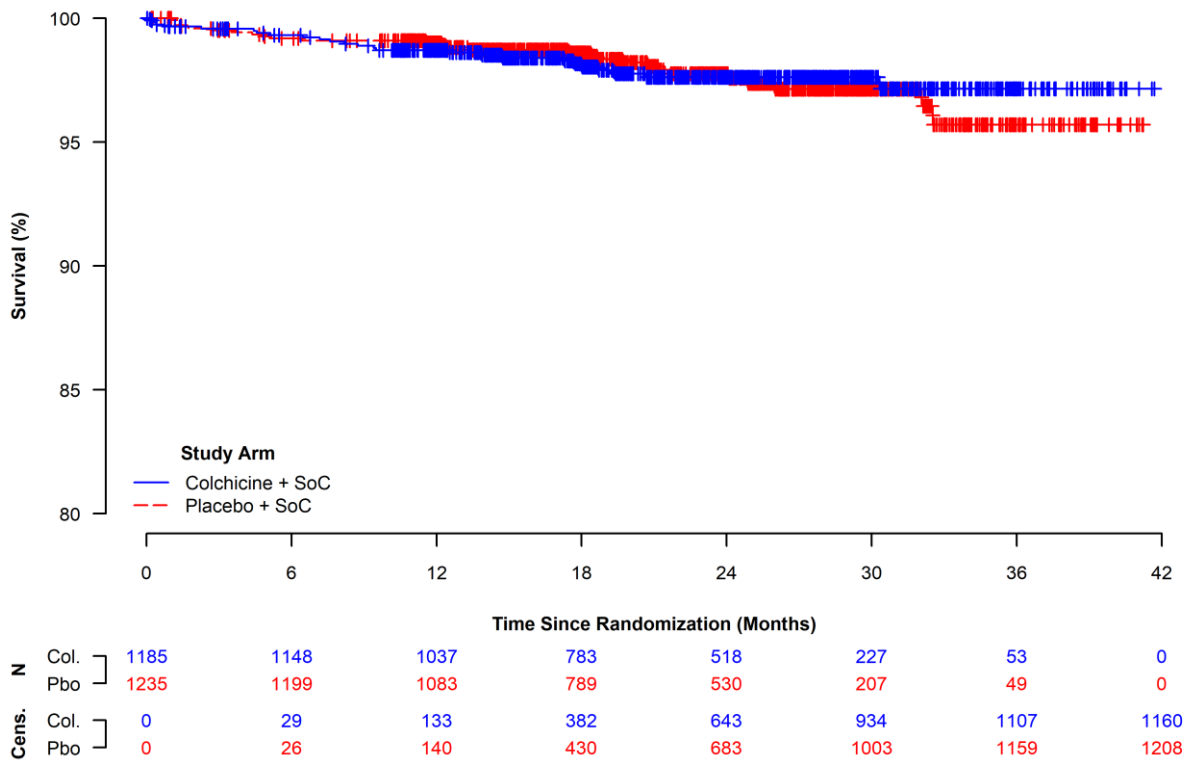
#### 4.4.2.9.7 Subgrouped by Hypertension Status

**Table 193:** Proportion of Patients with Atrial Fibrillation, Subgrouped by Hypertension Status (ITT Population).

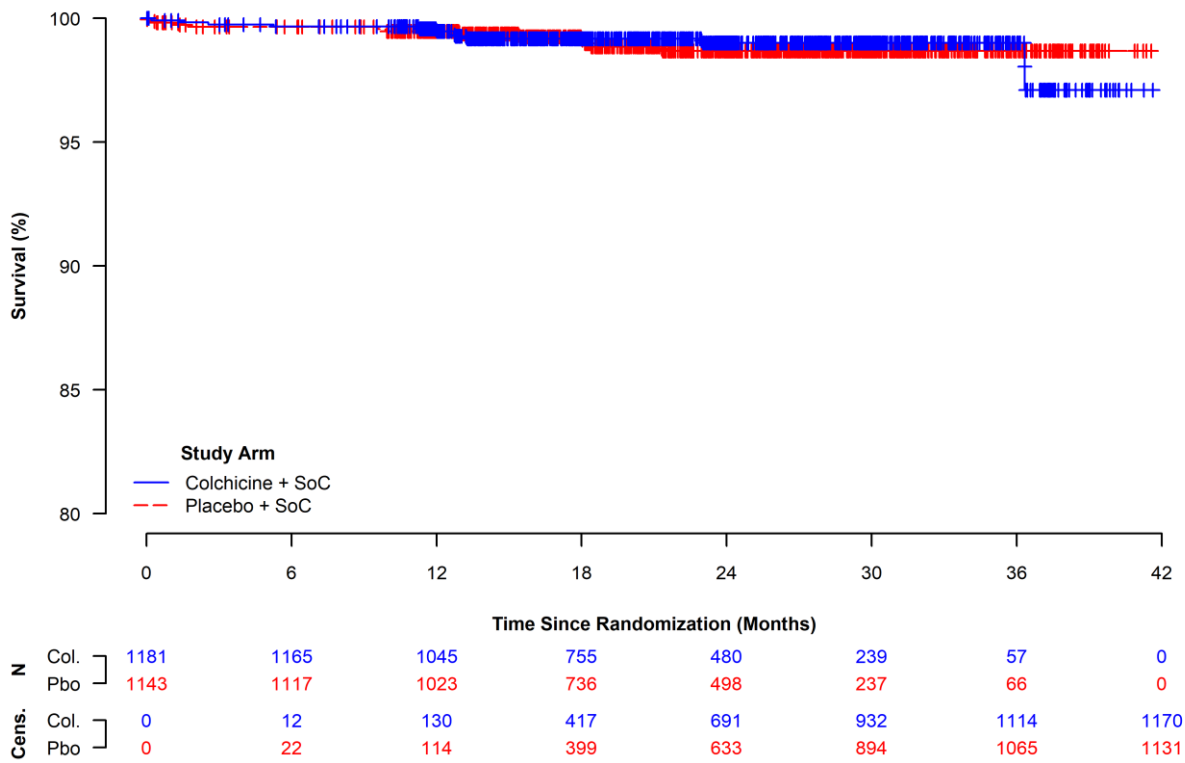
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,378)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8670</b>					
<b>Yes</b>	25/1,185 (2.1)	27/1,235 (2.2)	0.965 [0.563, 1.653] 0.8967	0.964 [0.556, 1.671] 0.8967	-0.077 [-1.232, 1.079] 0.8967
<b>No</b>	11/1,181 (0.9)	12/1,143 (1.0)	0.887 [0.393, 2.002] 0.7732	0.886 [0.389, 2.016] 0.7732	-0.118 [-0.924, 0.687] 0.7732
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 194:** Time to Atrial Fibrillation, Subgrouped by Hypertension Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,378)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.8997</b>							
<b>Yes</b>	25/1,185 (2.1)	NE [NE, NE]	2.8 [1.5, 4.1]	27/1,235 (2.2)	NE [NE, NE]	4.3 [2.0, 6.6]	0.955 [0.554, 1.645] 0.8683
<b>No</b>	11/1,181 (0.9)	NE [NE, NE]	2.9 [0.0, 6.6]	12/1,143 (1.0)	NE [NE, NE]	1.3 [0.6, 2.1]	0.898 [0.396, 2.035] 0.7961
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 179:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Hypertensive Subgroup (ITT Population).



**Figure 180:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Normotensive Subgroup (ITT Population).

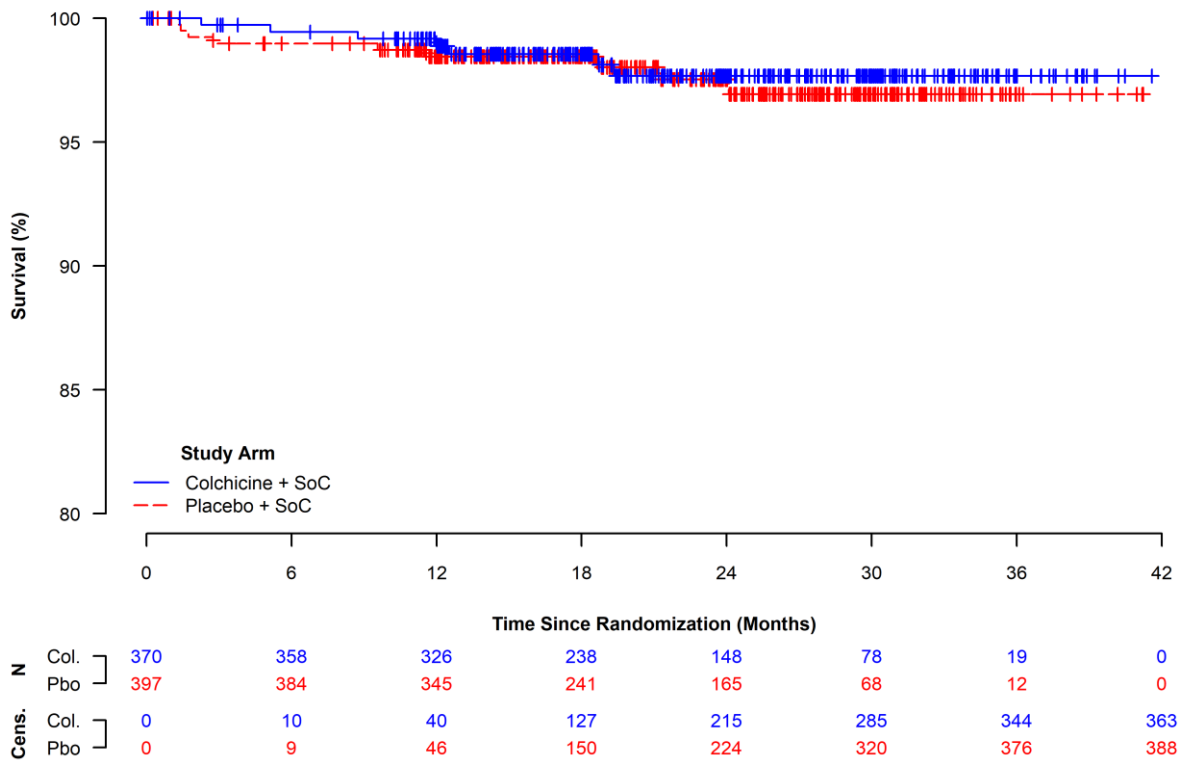
#### 4.4.2.9.8 Subgrouped by History of Myocardial Infarction

**Table 195:** Proportion of Patients with Atrial Fibrillation, Subgrouped by History of Myocardial Infarction (ITT Population).

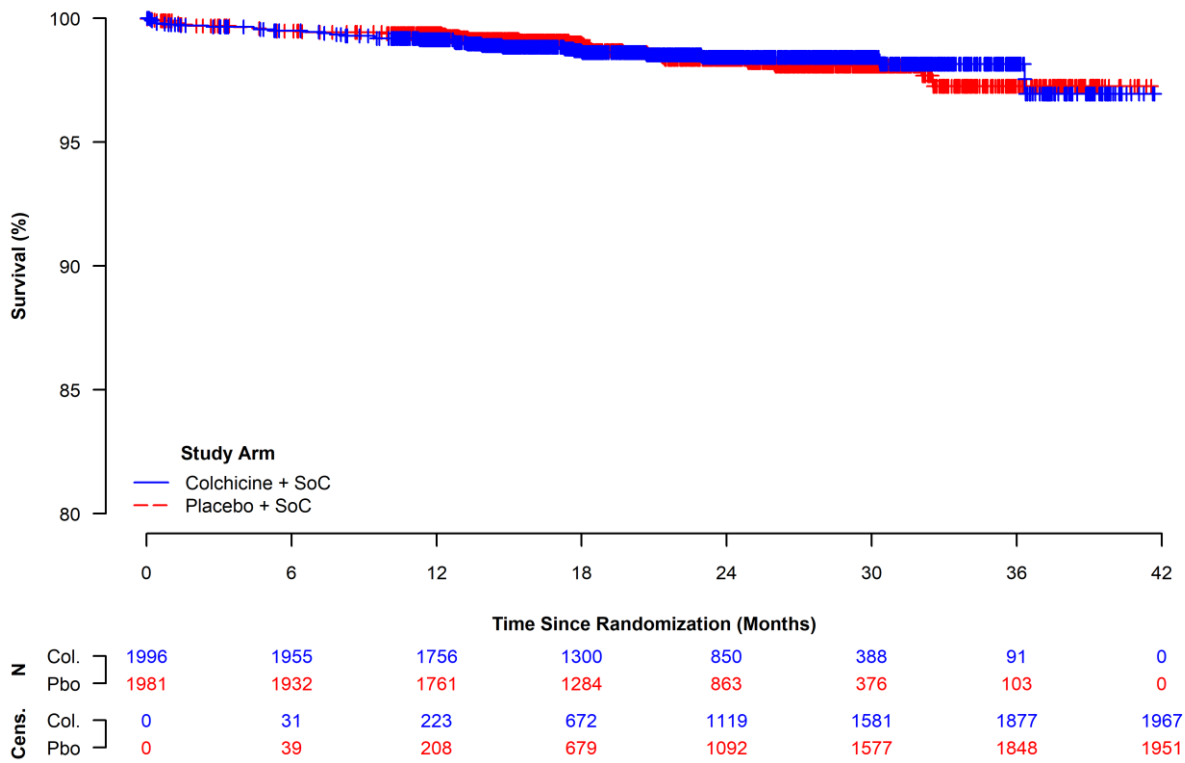
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,378)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of MI</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8030</b>					
<b>Yes</b>	7/370 (1.9)	9/397 (2.3)	0.835 [0.314, 2.218] 0.7168	0.831 [0.306, 2.255] 0.7168	-0.375 [-2.393, 1.643] 0.7156
<b>No</b>	29/1,996 (1.5)	30/1,981 (1.5)	0.959 [0.578, 1.592] 0.8726	0.959 [0.573, 1.603] 0.8726	-0.061 [-0.813, 0.690] 0.8726
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 196:** Time to Atrial Fibrillation, Subgrouped by History of Myocardial Infarction (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,378)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of MI</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.7649</b>							
<b>Yes</b>	7/370 (1.9)	NE [NE, NE]	2.3 [0.6, 4.1]	9/397 (2.3)	NE [NE, NE]	3.1 [0.9, 5.1]	0.823 [0.306, 2.210] 0.6989
<b>No</b>	29/1,996 (1.5)	NE [NE, NE]	3.1 [0.6, 5.5]	30/1,981 (1.5)	NE [NE, NE]	2.7 [1.4, 4.1]	0.964 [0.578, 1.605] 0.8868
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 181:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Subgroup With History of Myocardial Infarction (ITT Population).



**Figure 182:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Subgroup Without History of Myocardial Infarction (ITT Population).

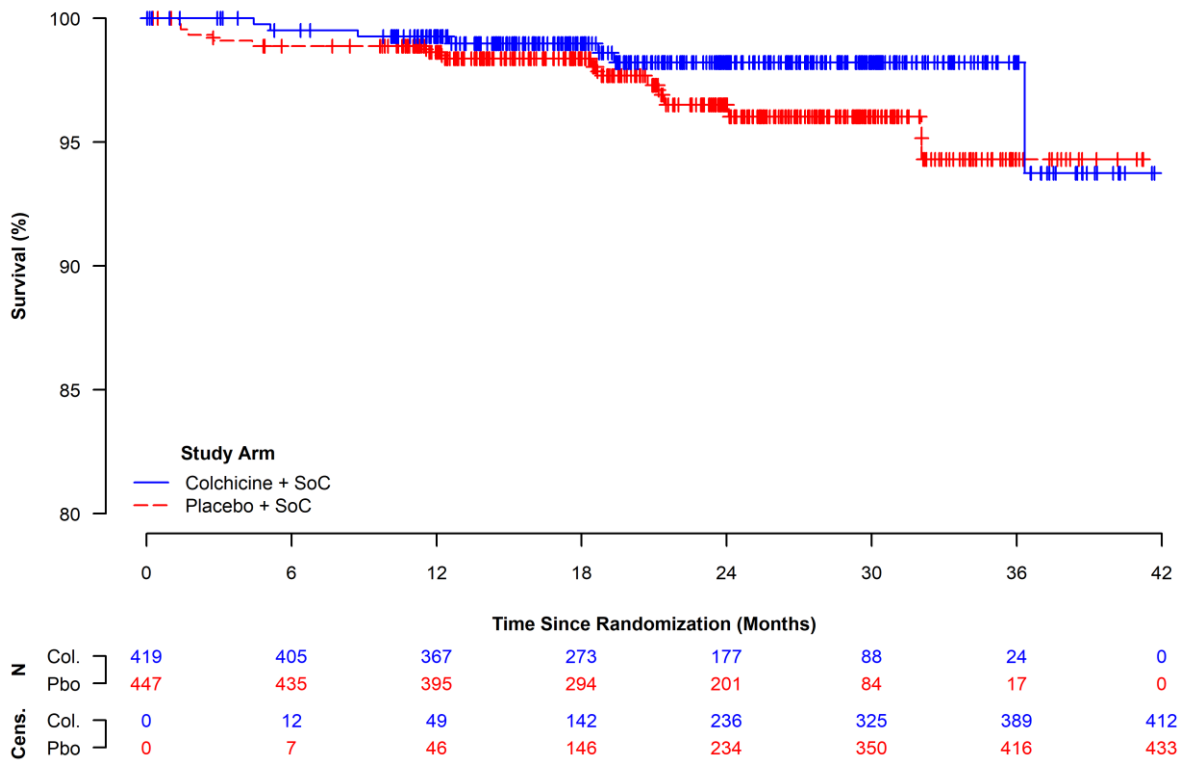
#### 4.4.2.9.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 197:** Proportion of Patients with Atrial Fibrillation, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

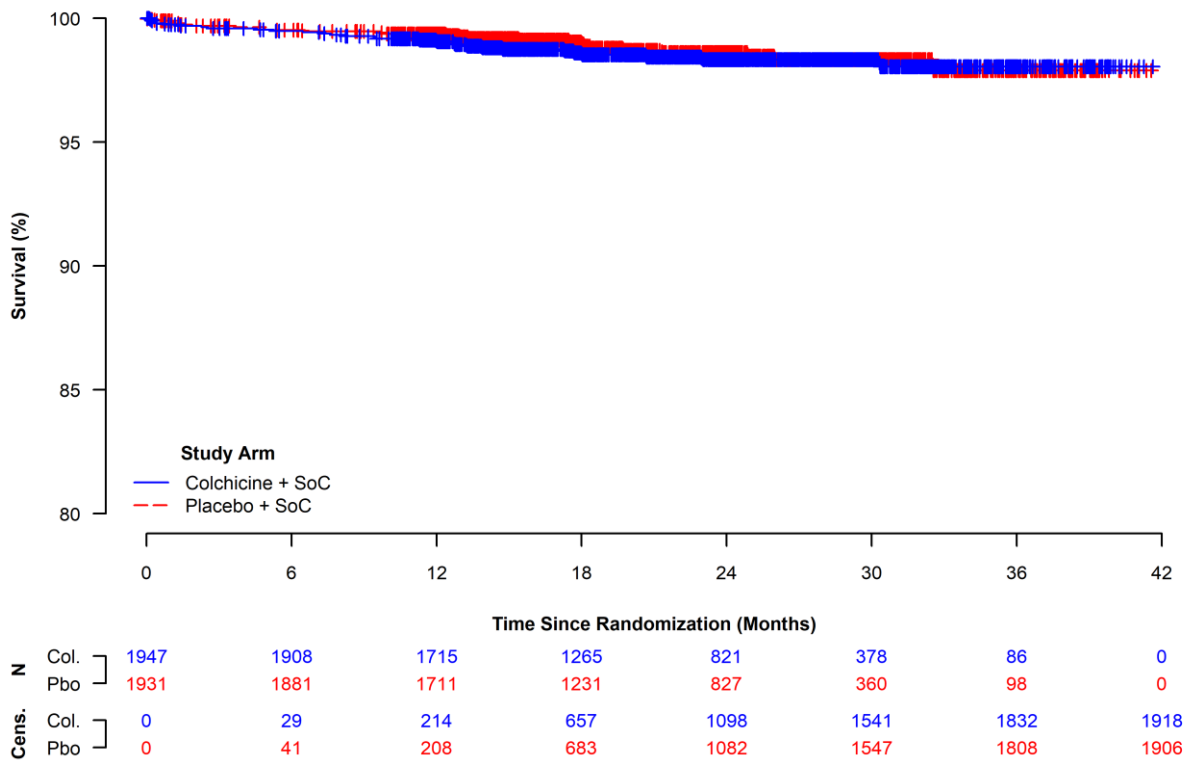
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,378)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1402</b>					
<b>Yes</b>	7/419 (1.7)	14/447 (3.1)	0.533 [0.217, 1.309] 0.1699	0.525 [0.210, 1.315] 0.1692	-1.461 [-3.489, 0.567] 0.1579
<b>No</b>	29/1,947 (1.5)	25/1,931 (1.3)	1.150 [0.676, 1.957] 0.6050	1.153 [0.673, 1.975] 0.6050	0.195 [-0.543, 0.932] 0.6046
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 198:** Time to Atrial Fibrillation, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,378)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.1477</b>							
<b>Yes</b>	7/419 (1.7)	NE [NE, NE]	6.3 [0.0, 14.5]	14/447 (3.1)	NE [NE, NE]	5.7 [1.6, 9.6]	0.527 [0.212, 1.307] 0.1670
<b>No</b>	29/1,947 (1.5)	NE [NE, NE]	2.0 [1.1, 2.8]	25/1,931 (1.3)	NE [NE, NE]	2.1 [1.0, 3.2]	1.147 [0.672, 1.958] 0.6162
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 183:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Subgroup With History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).



**Figure 184:** Kaplan-Meier Curves for Atrial Fibrillation, Within the Subgroup Without History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

#### **4.4.2.9.10 Subgrouped by History of Stroke or Transient Ischaemic Attack**

Due to a significant interaction term, the data is presented in Module 4A.

#### 4.4.2.10 Hospitalization for Heart Failure

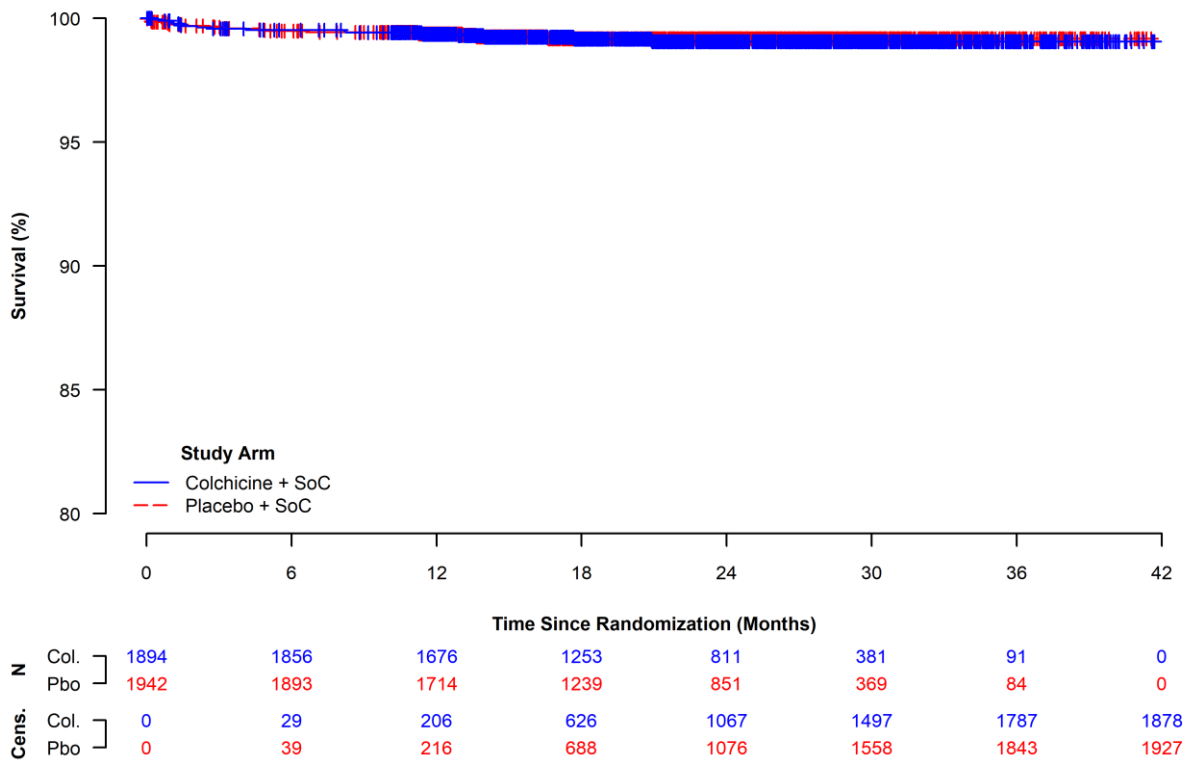
##### 4.4.2.10.1 Subgrouped by Sex

**Table 199:** Proportion of Patients with Hospitalization for Heart Failure, Subgrouped by Sex (ITT Population).

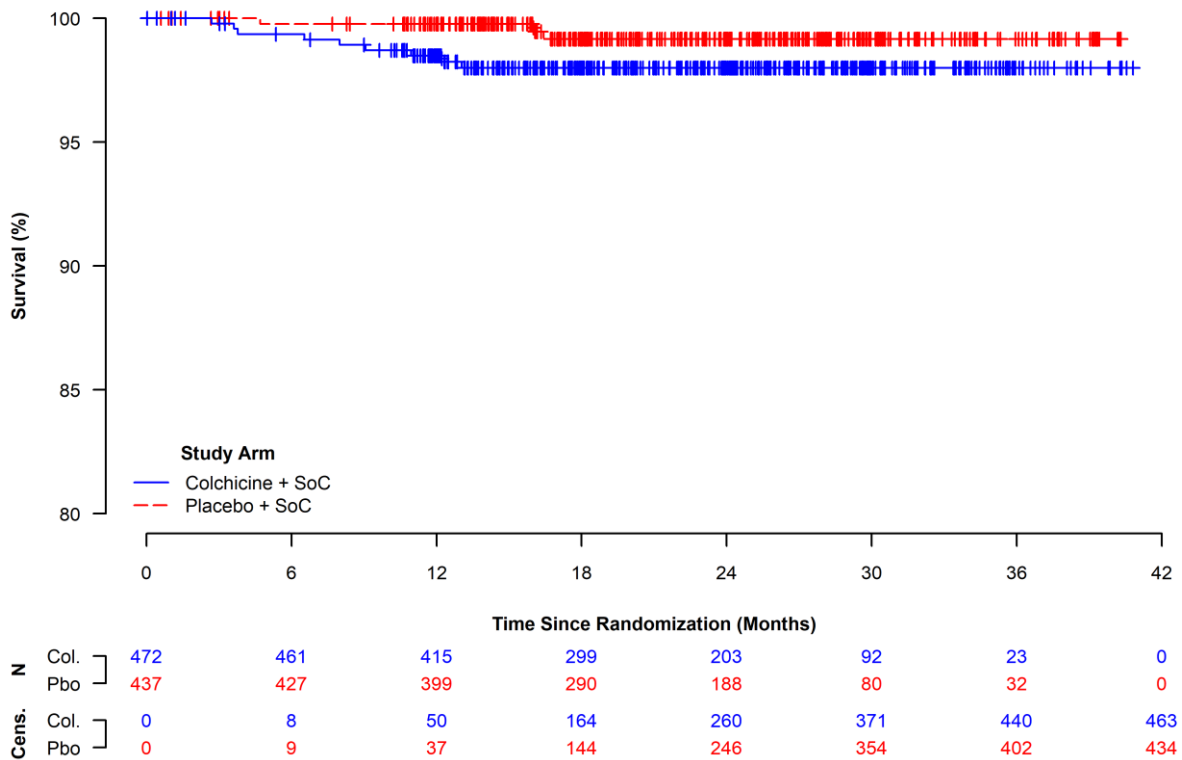
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Sex</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1976</b>					
<b>Male</b>	16/1,894 (0.8)	15/1,942 (0.8)	1.094 [0.542, 2.206] 0.8024	1.094 [0.540, 2.220] 0.8024	0.072 [-0.495, 0.639] 0.8025
<b>Female</b>	9/472 (1.9)	3/437 (0.7)	2.778 [0.757, 10.193] 0.1236	2.812 [0.756, 10.455] 0.1228	1.220 [-0.236, 2.677] 0.1006
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 200:** Time to Hospitalization for Heart Failure, Subgrouped by Sex (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Sex</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.1914</b>							
<b>Male</b>	16/1,894 (0.8)	NE [NE, NE]	0.9 [0.5, 1.4]	15/1,942 (0.8)	NE [NE, NE]	0.8 [0.4, 1.2]	1.088 [0.538, 2.200] 0.8147
<b>Female</b>	9/472 (1.9)	NE [NE, NE]	2.0 [0.7, 3.3]	3/437 (0.7)	NE [NE, NE]	0.8 [0.0, 1.8]	2.824 [0.764, 10.432] 0.1194
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 185:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Male Sex Subgroup (ITT Population).



**Figure 186:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Female Sex Subgroup (ITT Population).

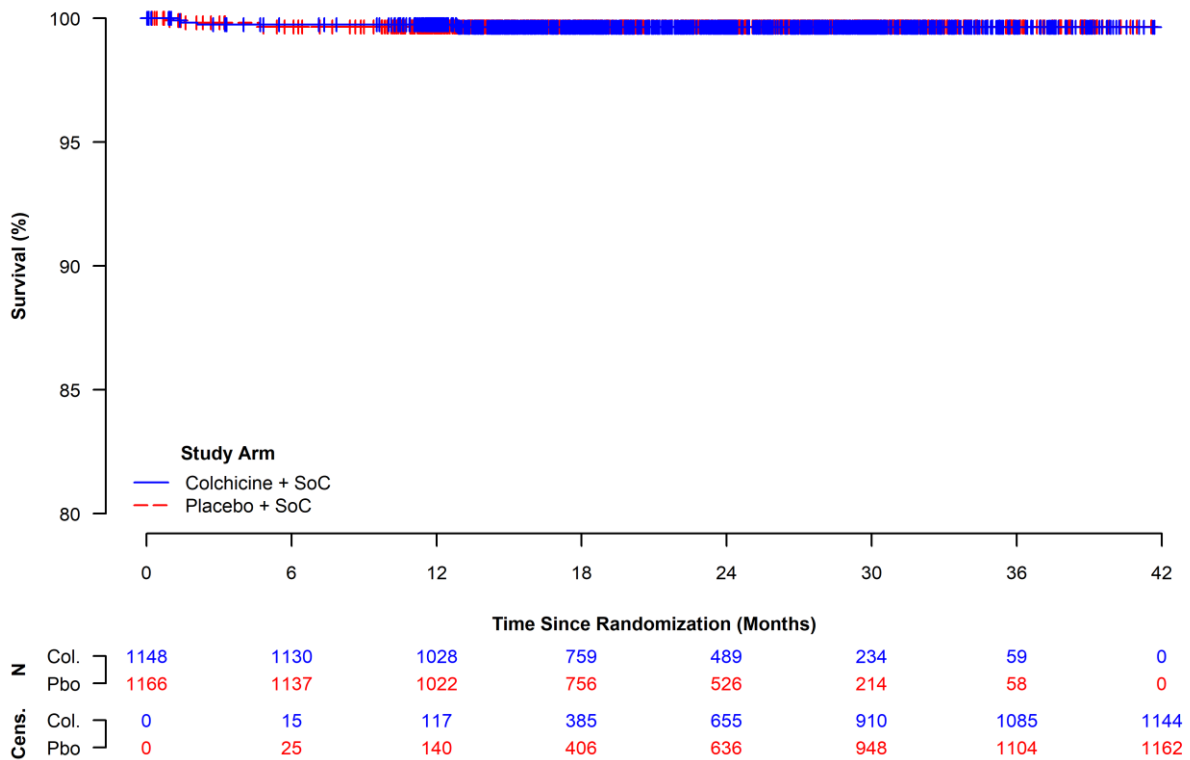
#### 4.4.2.10.2 Subgrouped by Age Group

**Table 201:** Proportion of Patients with Hospitalization for Heart Failure, Subgrouped by Age Group (ITT Population).

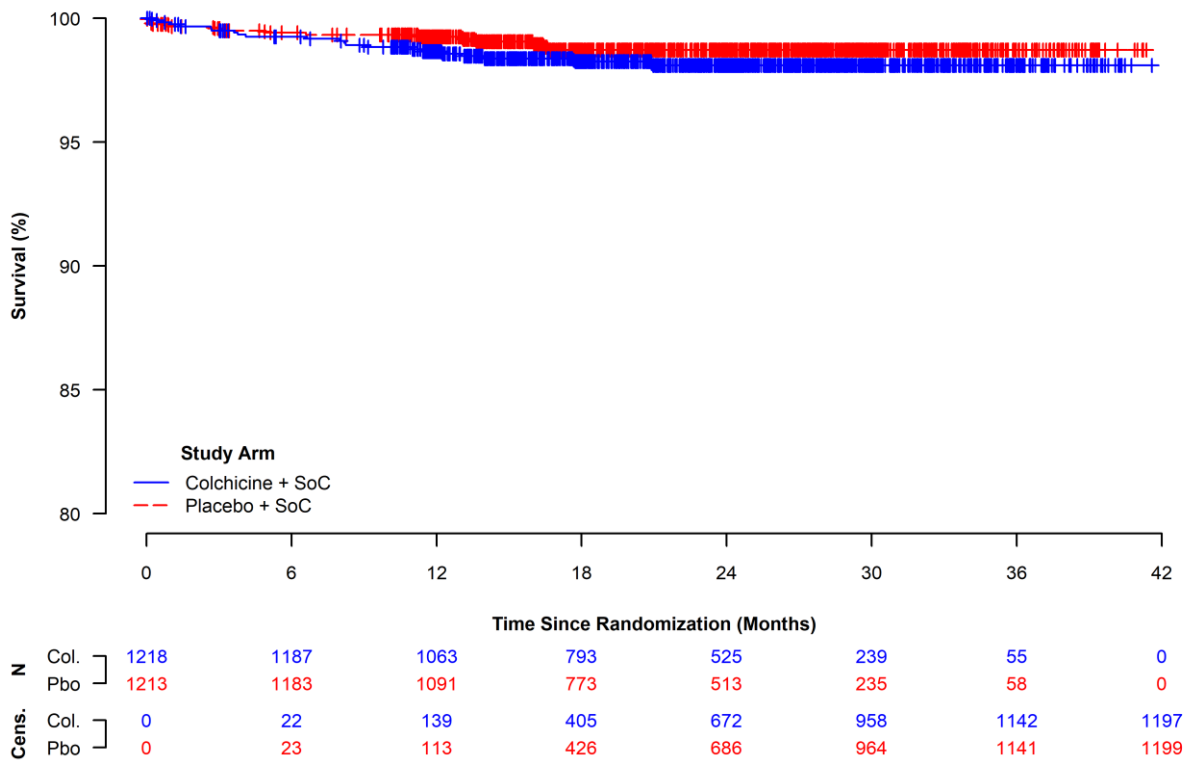
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Age</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.6201</b>					
< 60 Years	4/1,148 (0.3)	4/1,166 (0.3)	1.016 [0.255, 4.051] 0.9824	1.016 [0.253, 4.071] 0.9824	0.005 [-0.473, 0.484] 0.9824
≥ 60 Years	21/1,218 (1.7)	14/1,213 (1.2)	1.494 [0.763, 2.924] 0.2415	1.503 [0.760, 2.969] 0.2413	0.570 [-0.376, 1.516] 0.2378
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 202:** Time to Hospitalization for Heart Failure, Subgrouped by Age Group (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.6088</b>							
<b>&lt; 60 Years</b>	4/1,148 (0.3)	NE [NE, NE]	0.4 [0.0, 0.7]	4/1,166 (0.3)	NE [NE, NE]	0.3 [0.0, 0.7]	1.008 [0.252, 4.032] 0.9907
<b>≥ 60 Years</b>	21/1,218 (1.7)	NE [NE, NE]	1.9 [1.1, 2.7]	14/1,213 (1.2)	NE [NE, NE]	1.3 [0.6, 2.0]	1.504 [0.765, 2.958] 0.2367
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 187:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Age 59 Years or Younger Subgroup (ITT Population).



**Figure 188:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Age 60 Years or Older Subgroup (ITT Population).

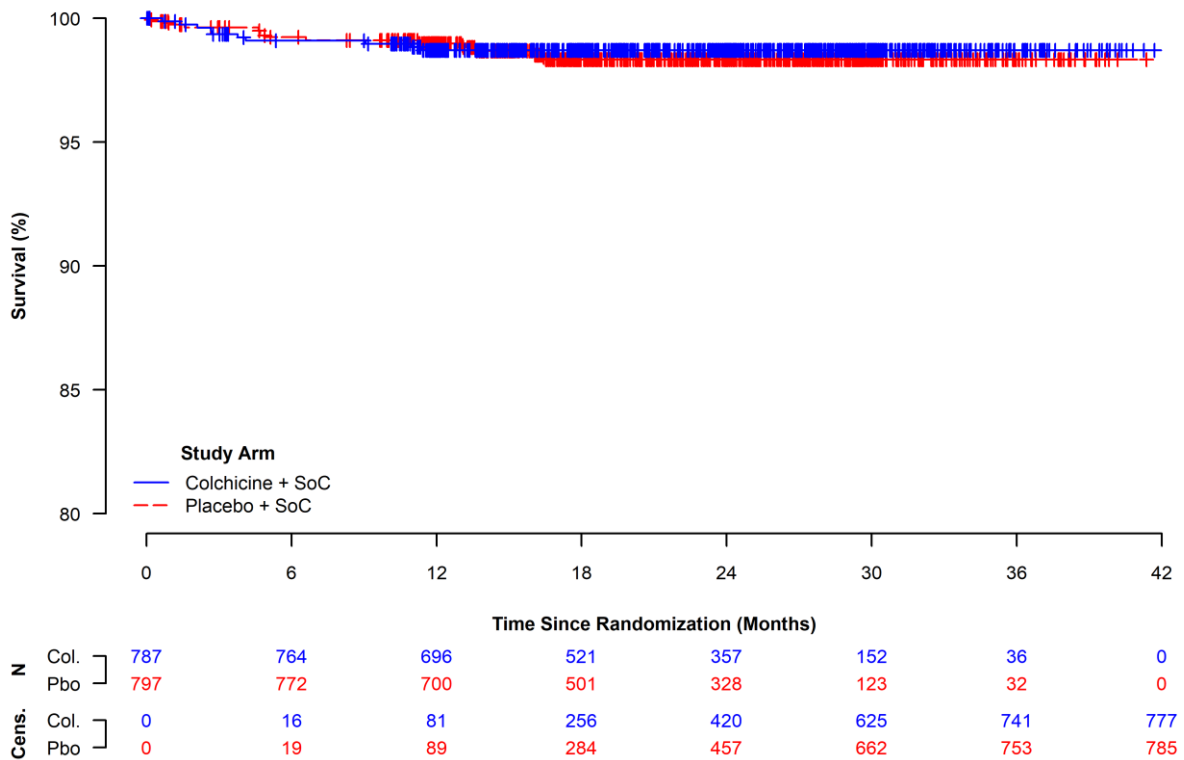
#### 4.4.2.10.3 Subgrouped by Smoking Status

**Table 203:** Proportion of Patients with Hospitalization for Heart Failure, Subgrouped by Smoking Status (ITT Population).

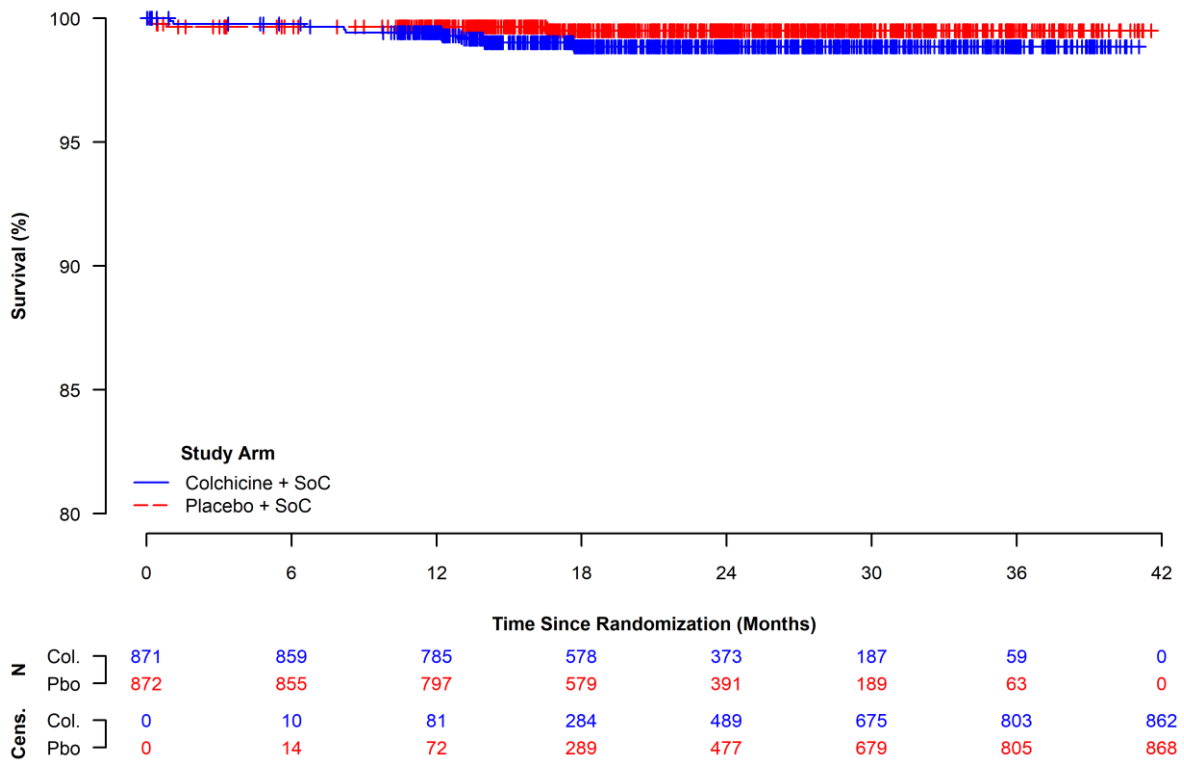
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,377)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Smoking Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2173</b>					
<b>Non</b>	10/787 (1.3)	12/797 (1.5)	0.844 [0.367, 1.942] 0.6898	0.842 [0.362, 1.960] 0.6898	-0.235 [-1.387, 0.917] 0.6893
<b>Ex</b>	9/871 (1.0)	4/872 (0.5)	2.253 [0.696, 7.287] 0.1752	2.266 [0.695, 7.385] 0.1749	0.575 [-0.233, 1.382] 0.1632
<b>Current</b>	6/708 (0.8)	2/708 (0.3)	3.000 [0.608, 14.813] 0.1775	3.017 [0.607, 14.999] 0.1771	0.565 [-0.215, 1.345] 0.1558
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 204:** Time to Hospitalization for Heart Failure, Subgrouped by Smoking Status (ITT Population).

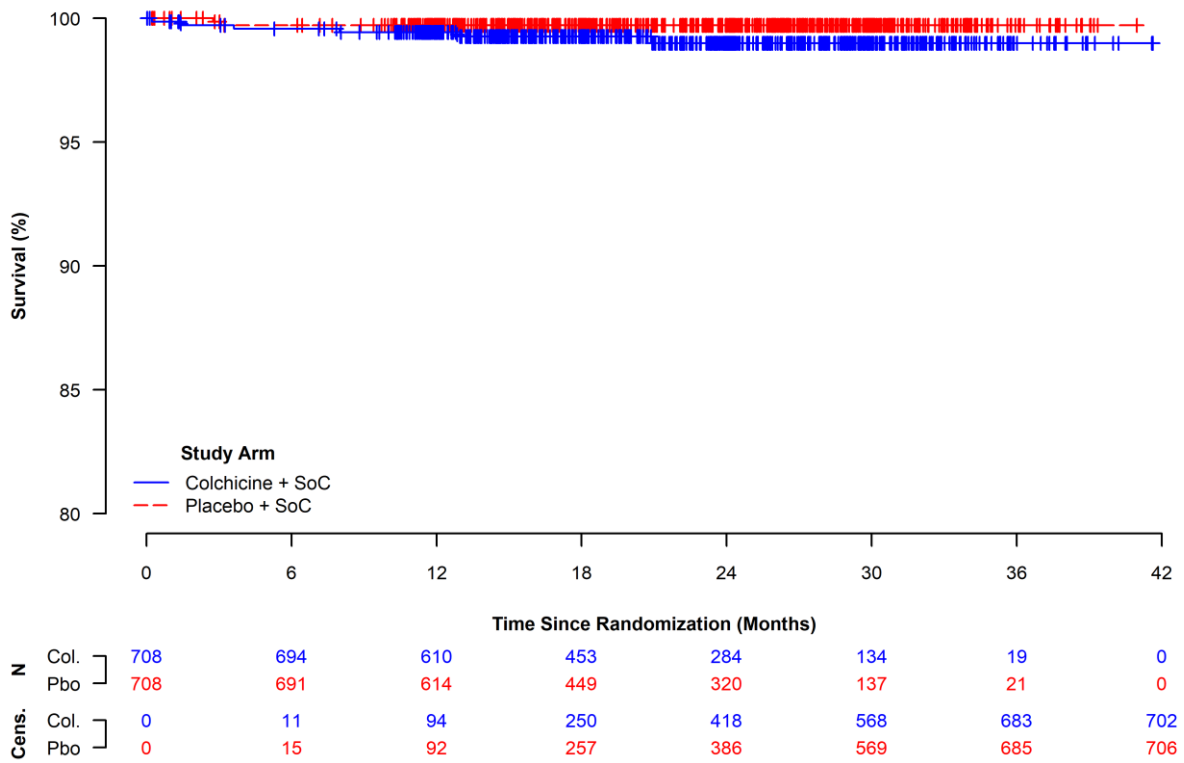
Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,377)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Smoking Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.2163</b>							
<b>Non</b>	10/787 (1.3)	NE [NE, NE]	1.3 [0.5, 2.1]	12/797 (1.5)	NE [NE, NE]	1.7 [0.7, 2.6]	0.842 [0.364, 1.948] 0.6871
<b>Ex</b>	9/871 (1.0)	NE [NE, NE]	1.1 [0.4, 1.9]	4/872 (0.5)	NE [NE, NE]	0.5 [0.0, 1.0]	2.257 [0.695, 7.330] 0.1755
<b>Current</b>	6/708 (0.8)	NE [NE, NE]	1.0 [0.2, 1.8]	2/708 (0.3)	NE [NE, NE]	0.3 [0.0, 0.7]	3.005 [0.606, 14.887] 0.1778
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 189:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Non-Smoker Subgroup (ITT Population).



**Figure 190:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Ex-Smoker Subgroup (ITT Population).



**Figure 191:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Current Smoker Subgroup (ITT Population).

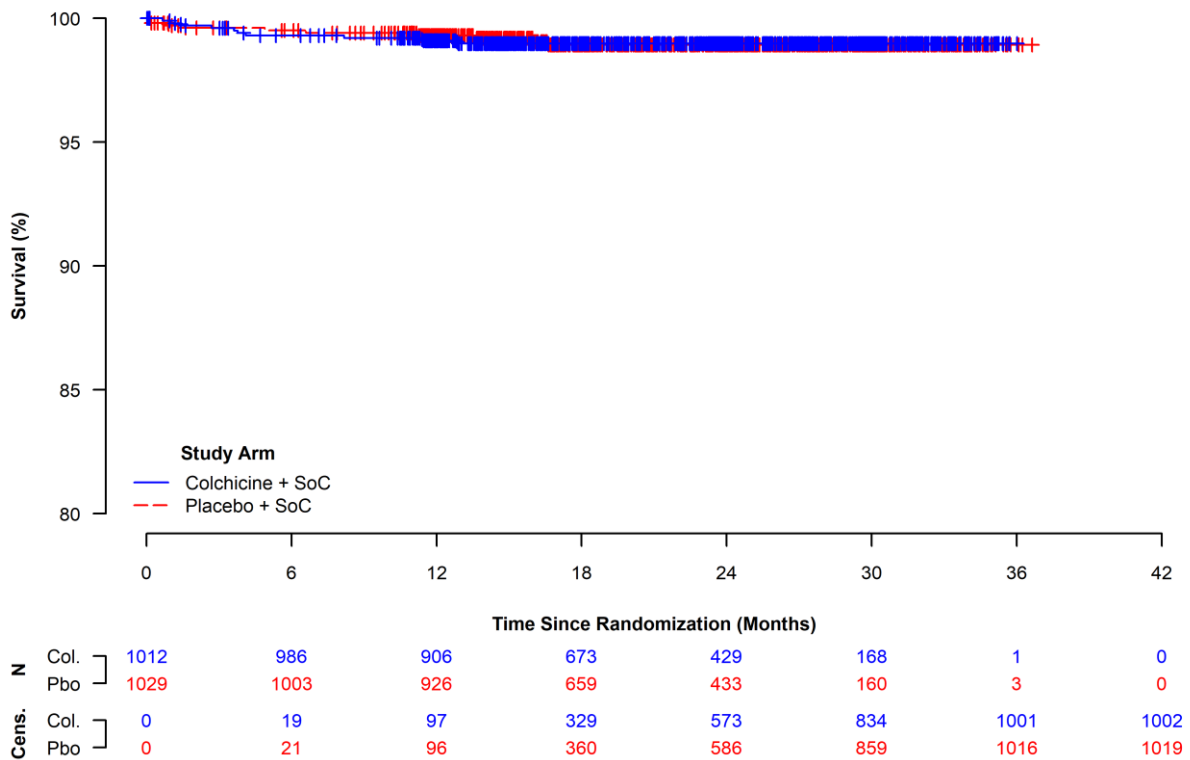
#### 4.4.2.10.4 Subgrouped by Region

**Table 205:** Proportion of Patients with Hospitalization for Heart Failure, Subgrouped by Region (ITT Population).

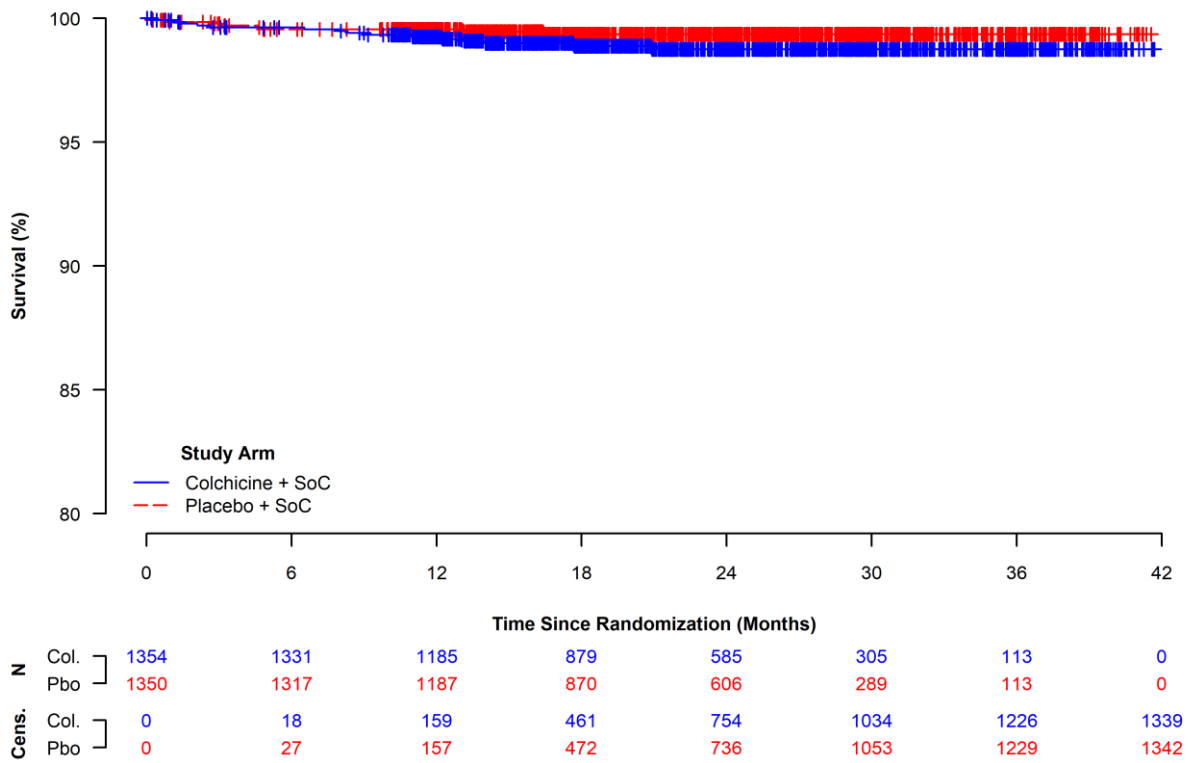
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Region</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.3261</b>					
<b>Europe</b>	10/1,012 (1.0)	10/1,029 (1.0)	1.017 [0.425, 2.432] 0.9701	1.017 [0.421, 2.454] 0.9701	0.016 [-0.838, 0.871] 0.9701
<b>Non-Europe</b>	15/1,354 (1.1)	8/1,350 (0.6)	1.869 [0.795, 4.395] 0.1514	1.879 [0.794, 4.447] 0.1512	0.515 [-0.176, 1.207] 0.1443
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 206:** Time to Hospitalization for Heart Failure, Subgrouped by Region (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.3258</b>							
<b>Region</b>							
<b>Europe</b>	10/1,012 (1.0)	NE [NE, NE]	1.0 [0.4, 1.6]	10/1,029 (1.0)	NE [NE, NE]	1.1 [0.4, 1.7]	1.014 [0.422, 2.437] 0.9749
<b>Non-Europe</b>	15/1,354 (1.1)	NE [NE, NE]	1.3 [0.6, 1.9]	8/1,350 (0.6)	NE [NE, NE]	0.6 [0.2, 1.1]	1.869 [0.792, 4.408] 0.1532
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 192:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within European Countries (ITT Population).



**Figure 193:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within Non-European Countries (ITT Population).

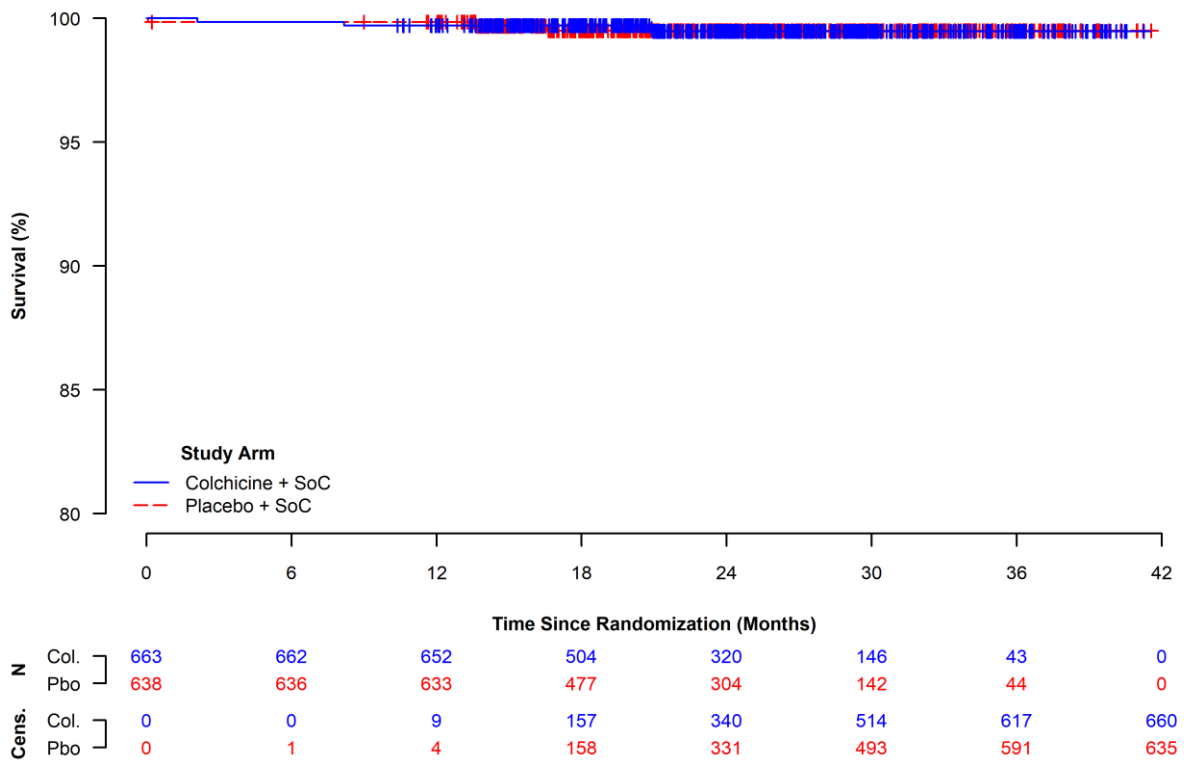
#### 4.4.2.10.5 Subgrouped by White Blood Cell Count

**Table 207:** Proportion of Patients with Hospitalization for Heart Failure, Subgrouped by White Blood Cell Count (ITT Population).

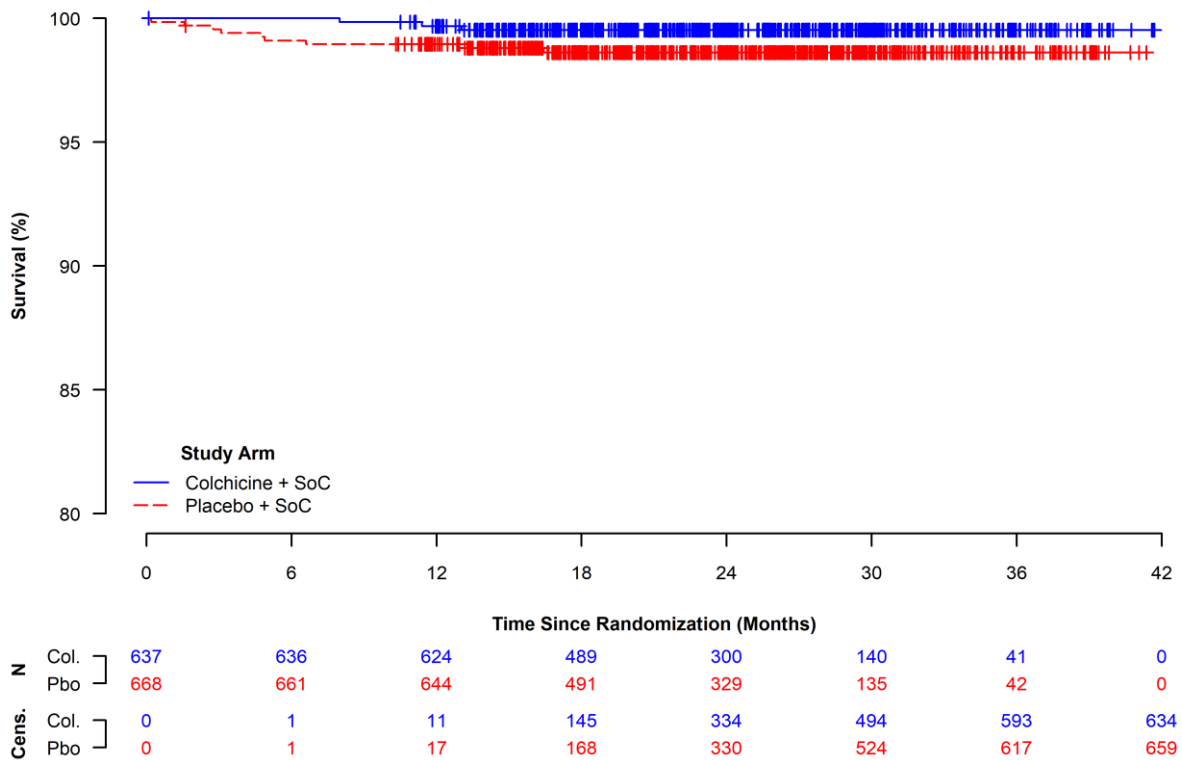
Subgroup	Colchicine + SoC (N = 1,300)	Placebo + SoC (N = 1,306)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.3307</b>					
< 8.66 10 <sup>3</sup> /μL	3/663 (0.5)	3/638 (0.5)	0.962 [0.195, 4.750] 0.9624	0.962 [0.193, 4.785] 0.9624	-0.018 [-0.754, 0.719] 0.9624
≥ 8.66 10 <sup>3</sup> /μL	3/637 (0.5)	9/668 (1.3)	0.350 [0.095, 1.285] 0.1136	0.346 [0.093, 1.286] 0.1131	-0.876 [-1.900, 0.147] 0.0932
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 208:** Time to Hospitalization for Heart Failure, Subgrouped by White Blood Cell Count (ITT Population).

Subgroup	Colchicine + SoC (N = 1,300)			Placebo + SoC (N = 1,306)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.3309</b>							
< 8.66 10 <sup>3</sup> /μL	3/663 (0.5)	NE [NE, NE]	0.5 [0.0, 1.2]	3/638 (0.5)	NE [NE, NE]	0.5 [0.0, 1.1]	0.956 [0.193, 4.736] 0.9559
≥ 8.66 10 <sup>3</sup> /μL	3/637 (0.5)	NE [NE, NE]	0.5 [0.0, 1.0]	9/668 (1.3)	NE [NE, NE]	1.4 [0.5, 2.3]	0.347 [0.094, 1.281] 0.1123
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 194:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Lower White Blood Cell Count Subgroup (ITT Population).



**Figure 195:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Upper White Blood Cell Count Subgroup (ITT Population).

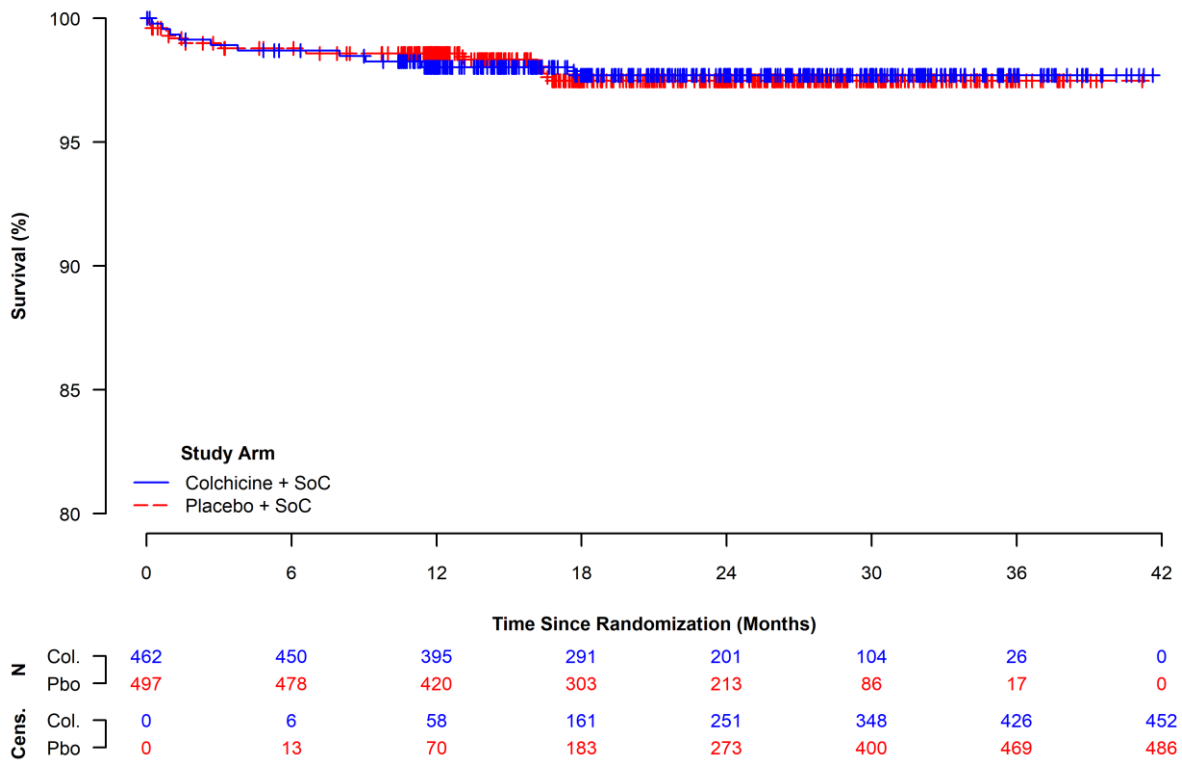
#### 4.4.2.10.6 Subgrouped by Diabetes Status

**Table 209:** Proportion of Patients with Hospitalization for Heart Failure, Subgrouped by Diabetes Status (ITT Population).

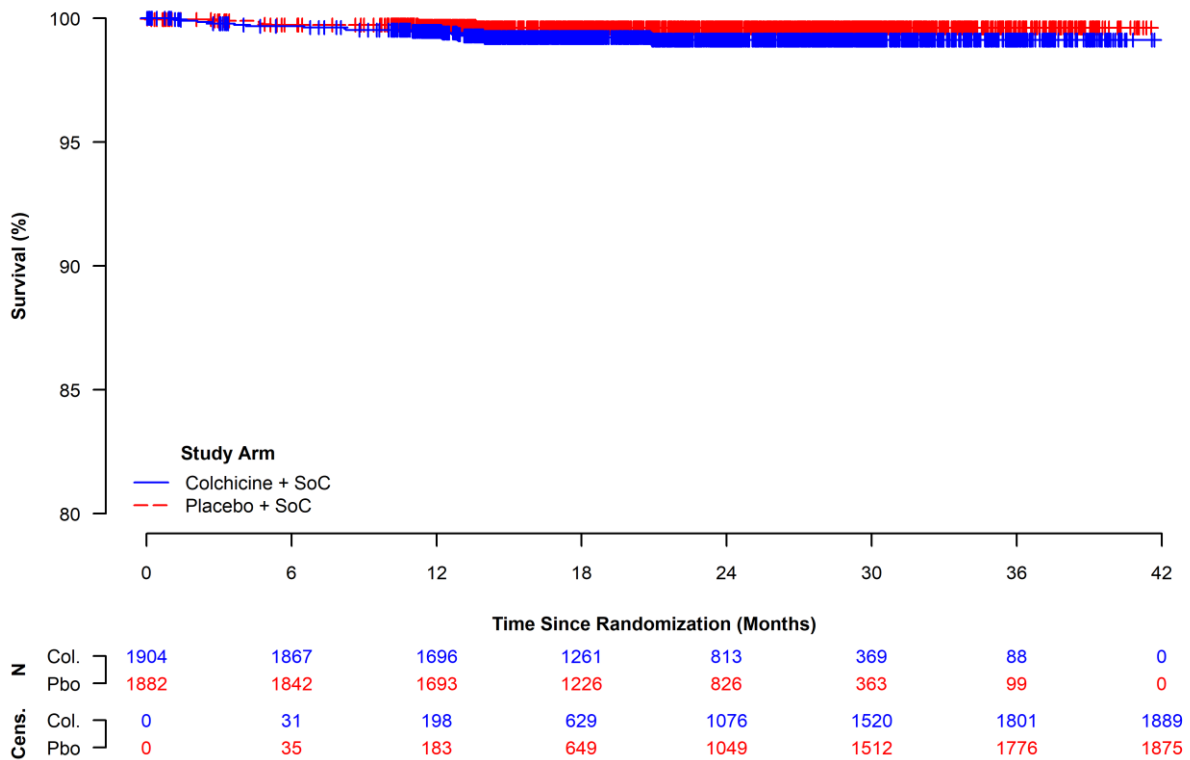
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2173</b>					
<b>Yes</b>	10/462 (2.2)	11/497 (2.2)	0.978 [0.419, 2.281] 0.9589	0.977 [0.411, 2.324] 0.9589	-0.049 [-1.902, 1.804] 0.9589
<b>No</b>	15/1,904 (0.8)	7/1,882 (0.4)	2.118 [0.866, 5.183] 0.1002	2.127 [0.865, 5.228] 0.1001	0.416 [-0.067, 0.899] 0.0915
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 210:** Time to Hospitalization for Heart Failure, Subgrouped by Diabetes Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.2115</b>							
<b>Yes</b>	10/462 (2.2)	NE [NE, NE]	2.3 [0.9, 3.7]	11/497 (2.2)	NE [NE, NE]	2.5 [1.0, 4.0]	0.973 [0.413, 2.292] 0.9505
<b>No</b>	15/1,904 (0.8)	NE [NE, NE]	0.9 [0.4, 1.3]	7/1,882 (0.4)	NE [NE, NE]	0.4 [0.1, 0.7]	2.120 [0.864, 5.200] 0.1007
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 196:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Diabetic Subgroup (ITT Population).



**Figure 197:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Non-Diabetic Subgroup (ITT Population).

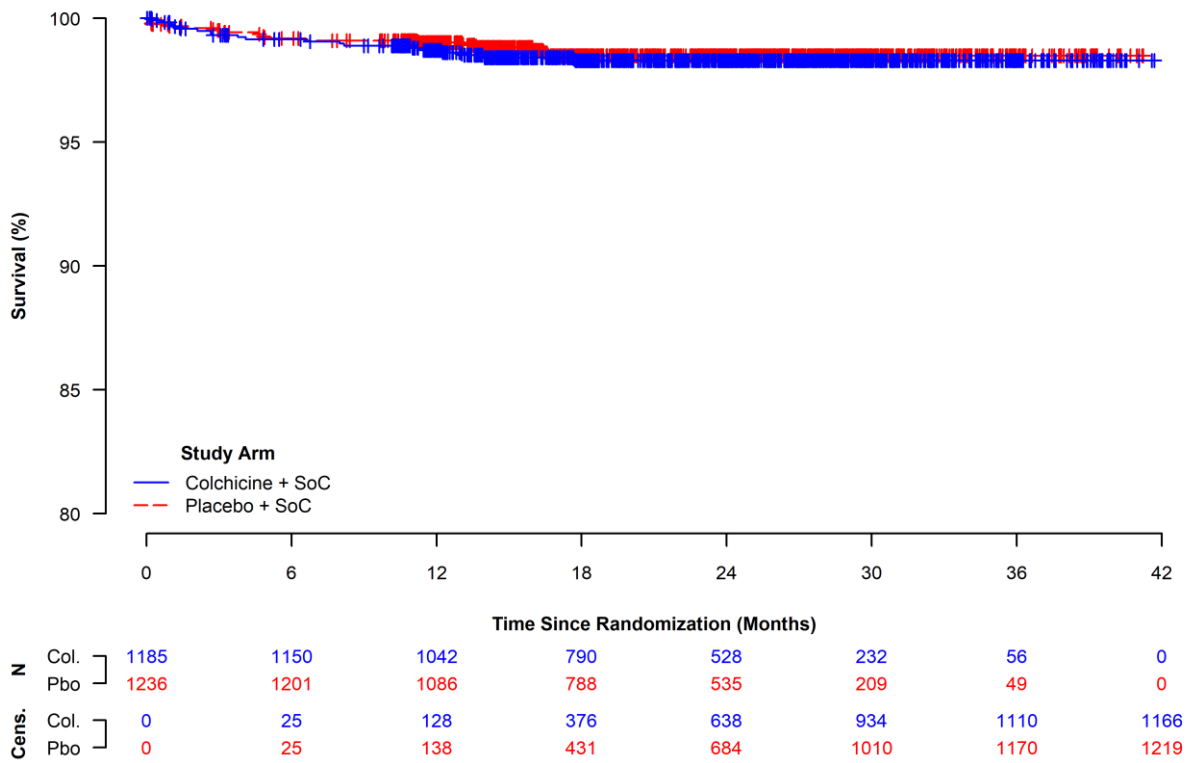
#### 4.4.2.10.7 Subgrouped by Hypertension Status

**Table 211:** Proportion of Patients with Hospitalization for Heart Failure, Subgrouped by Hypertension Status (ITT Population).

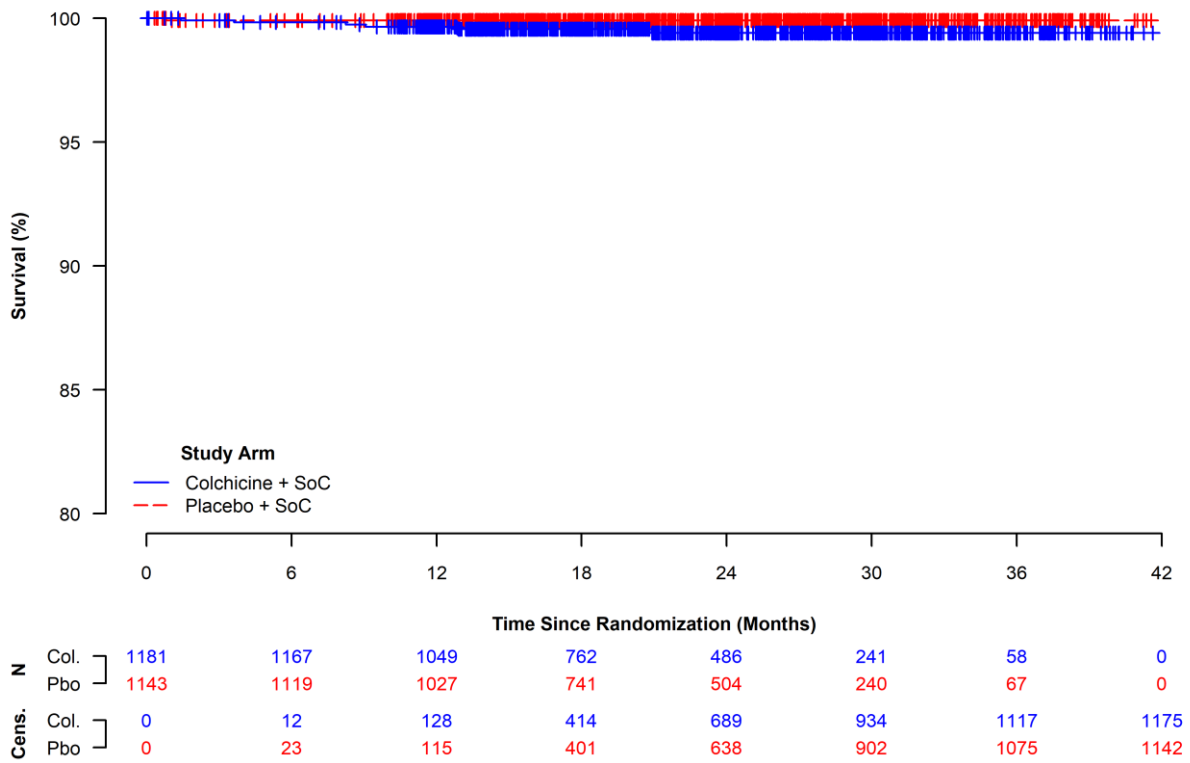
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1040</b>					
<b>Yes</b>	19/1,185 (1.6)	17/1,236 (1.4)	1.166 [0.609, 2.232] 0.6435	1.168 [0.604, 2.259] 0.6435	0.228 [-0.738, 1.194] 0.6437
<b>No</b>	6/1,181 (0.5)	1/1,143 (0.1)	5.807 [0.700, 48.158] 0.1031	5.831 [0.701, 48.513] 0.1028	0.421 [-0.020, 0.861] 0.0611
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 212:** Time to Hospitalization for Heart Failure, Subgrouped by Hypertension Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.1034</b>							
<b>Yes</b>	19/1,185 (1.6)	NE [NE, NE]	1.7 [0.9, 2.5]	17/1,236 (1.4)	NE [NE, NE]	1.5 [0.8, 2.2]	1.163 [0.604, 2.237] 0.6512
<b>No</b>	6/1,181 (0.5)	NE [NE, NE]	0.6 [0.1, 1.1]	1/1,143 (0.1)	NE [NE, NE]	0.1 [0.0, 0.3]	5.804 [0.699, 48.208] 0.1035
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 198:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Hypertensive Subgroup (ITT Population).



**Figure 199:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Normotensive Subgroup (ITT Population).

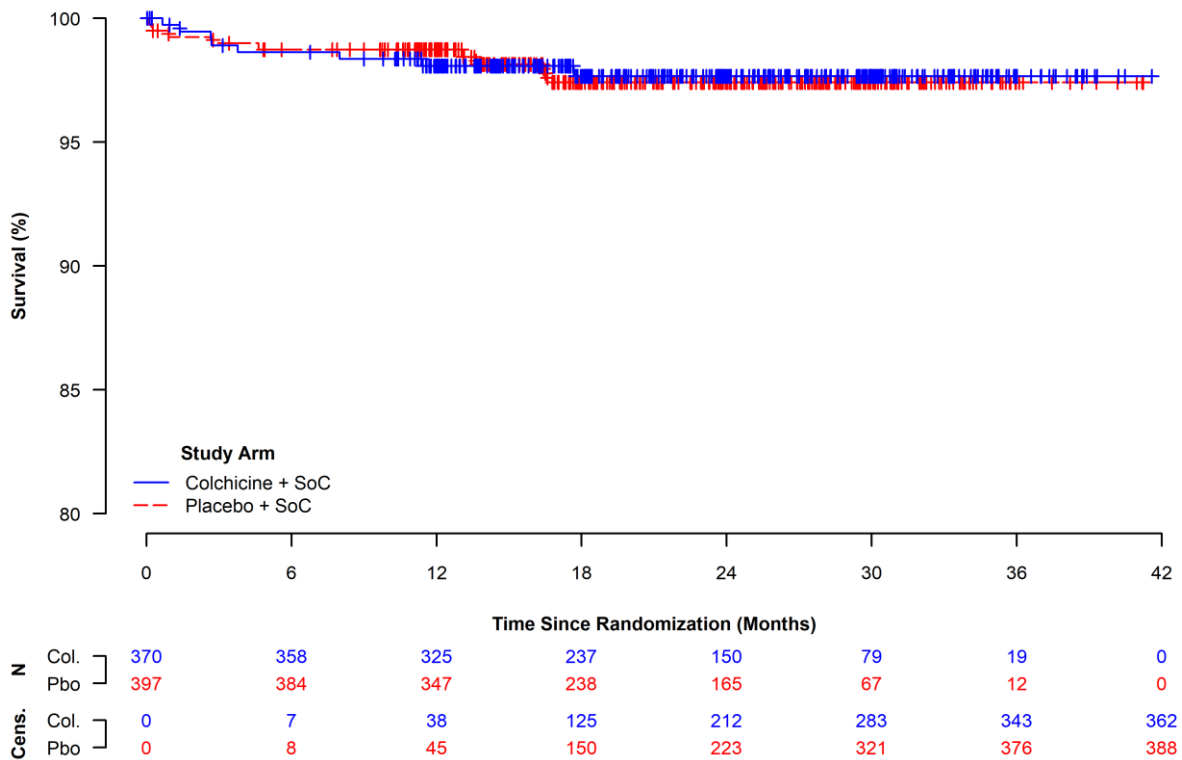
#### 4.4.2.10.8 Subgrouped by History of Myocardial Infarction

**Table 213:** Proportion of Patients with Hospitalization for Heart Failure, Subgrouped by History of Myocardial Infarction (ITT Population).

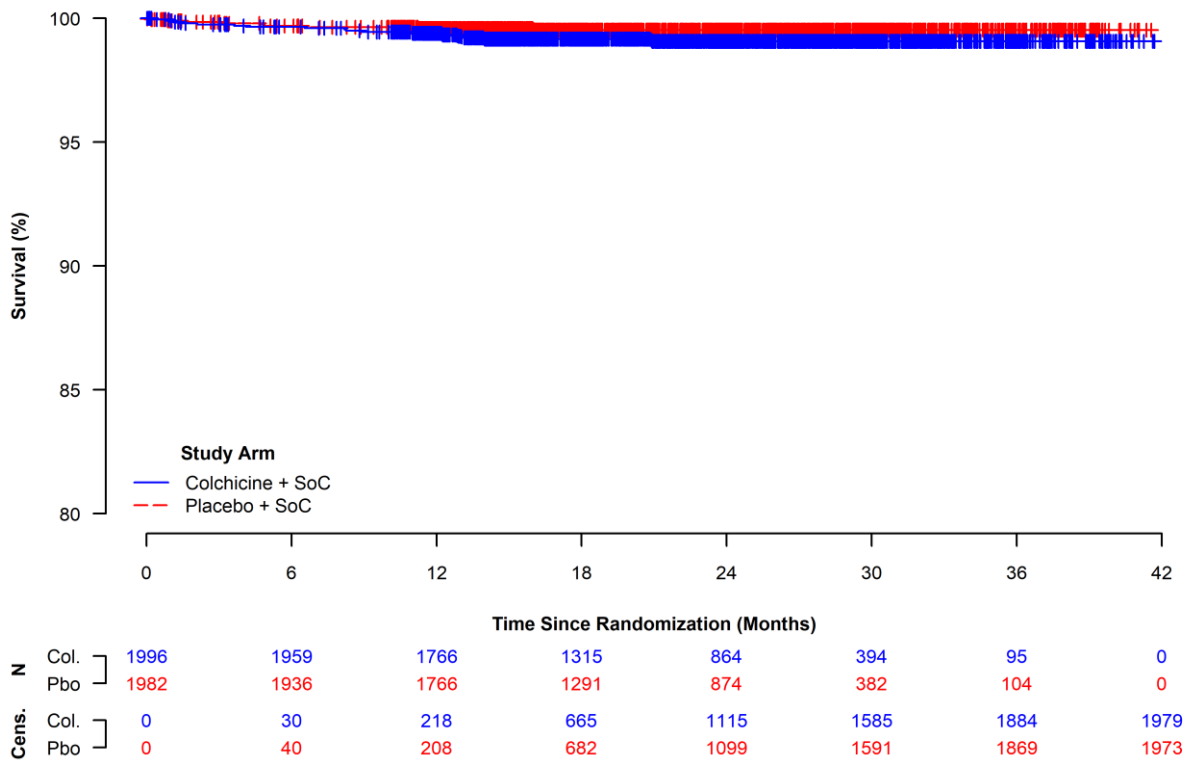
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of MI</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2860</b>					
<b>Yes</b>	8/370 (2.2)	9/397 (2.3)	0.954 [0.372, 2.446] 0.9215	0.953 [0.364, 2.496] 0.9215	-0.105 [-2.188, 1.978] 0.9214
<b>No</b>	17/1,996 (0.9)	9/1,982 (0.5)	1.876 [0.838, 4.198] 0.1260	1.883 [0.837, 4.235] 0.1258	0.398 [-0.103, 0.898] 0.1192
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 214:** Time to Hospitalization for Heart Failure, Subgrouped by History of Myocardial Infarction (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of MI</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.2858</b>							
<b>Yes</b>	8/370 (2.2)	NE [NE, NE]	2.3 [0.7, 3.9]	9/397 (2.3)	NE [NE, NE]	2.6 [0.9, 4.3]	0.950 [0.366, 2.461] 0.9152
<b>No</b>	17/1,996 (0.9)	NE [NE, NE]	0.9 [0.5, 1.4]	9/1,982 (0.5)	NE [NE, NE]	0.5 [0.2, 0.8]	1.871 [0.834, 4.198] 0.1285
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 200:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Subgroup With History of Myocardial Infarction (ITT Population).



**Figure 201:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Subgroup Without History of Myocardial Infarction (ITT Population).

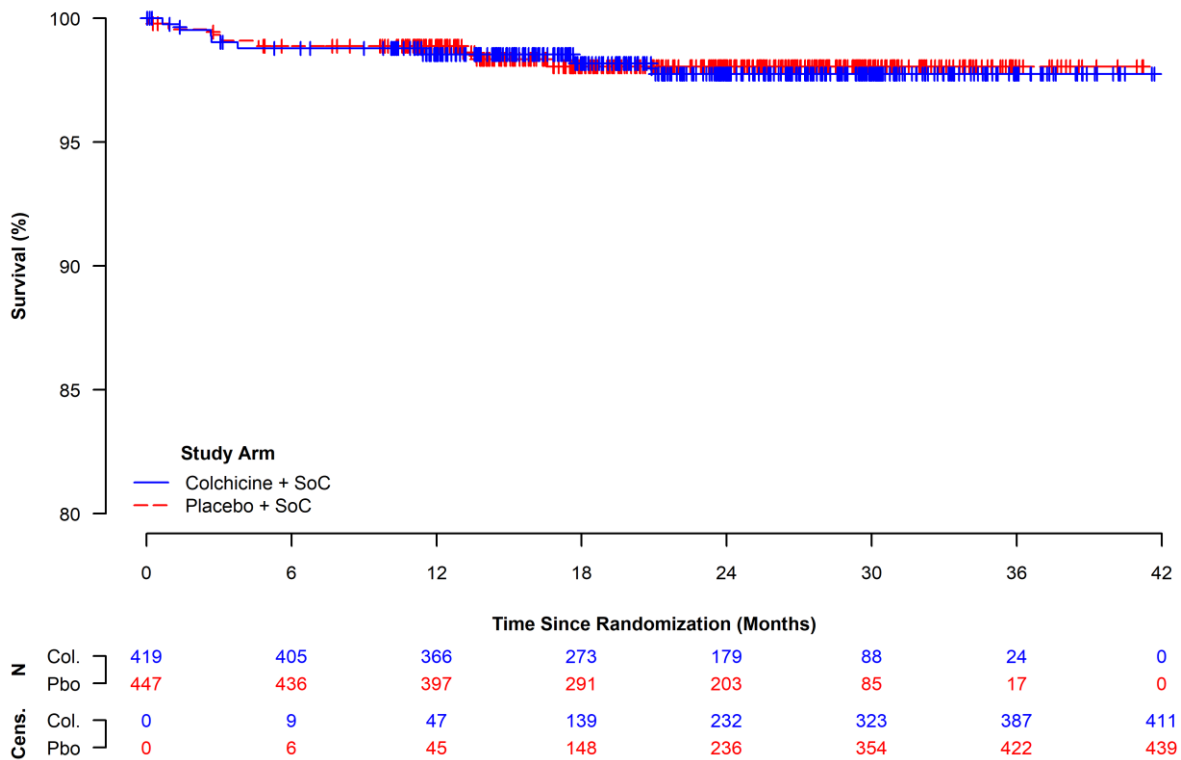
#### 4.4.2.10.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 215:** Proportion of Patients with Hospitalization for Heart Failure, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

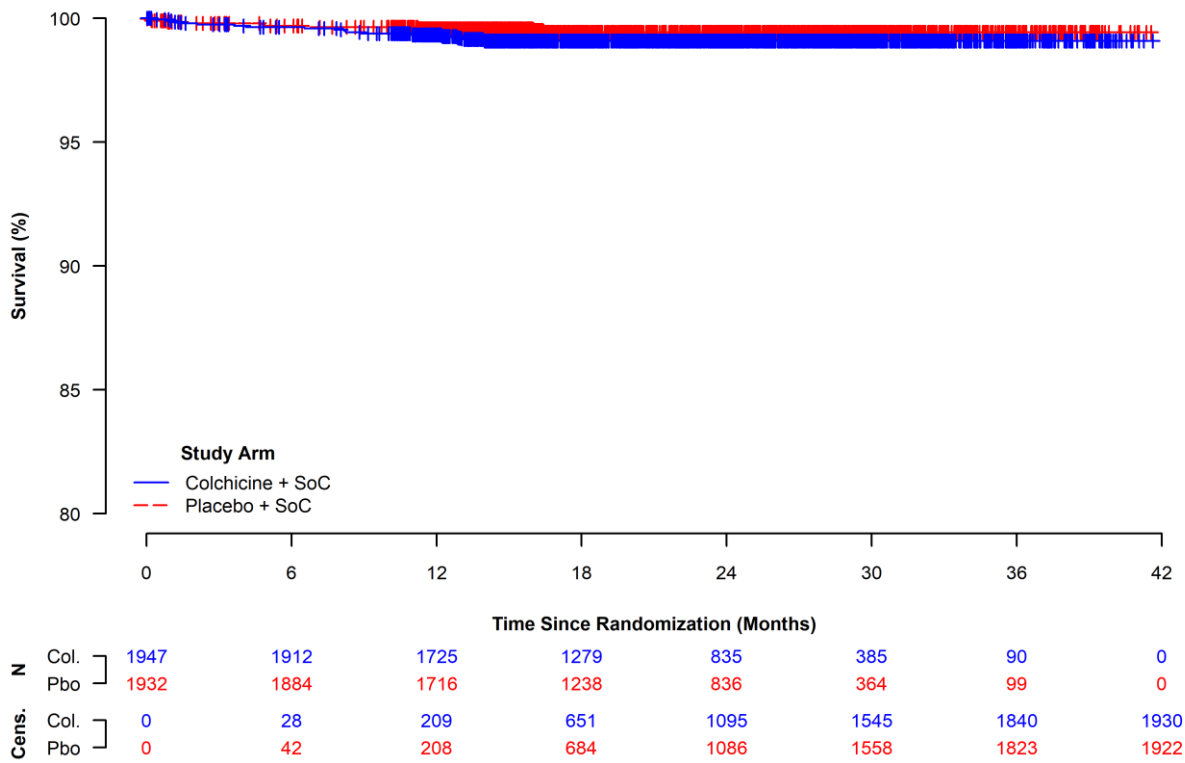
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4737</b>					
<b>Yes</b>	8/419 (1.9)	8/447 (1.8)	1.067 [0.404, 2.817] 0.8961	1.068 [0.397, 2.872] 0.8961	0.120 [-1.677, 1.916] 0.8962
<b>No</b>	17/1,947 (0.9)	10/1,932 (0.5)	1.687 [0.774, 3.675] 0.1881	1.693 [0.773, 3.707] 0.1879	0.356 [-0.167, 0.878] 0.1824
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 216:** Time to Hospitalization for Heart Failure, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.4871</b>							
<b>Yes</b>	8/419 (1.9)	NE [NE, NE]	2.2 [0.6, 3.8]	8/447 (1.8)	NE [NE, NE]	2.0 [0.6, 3.3]	1.078 [0.405, 2.872] 0.8805
<b>No</b>	17/1,947 (0.9)	NE [NE, NE]	0.9 [0.5, 1.4]	10/1,932 (0.5)	NE [NE, NE]	0.6 [0.2, 0.9]	1.679 [0.769, 3.667] 0.1934
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 202:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Subgroup With History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).



**Figure 203:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Subgroup Without History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

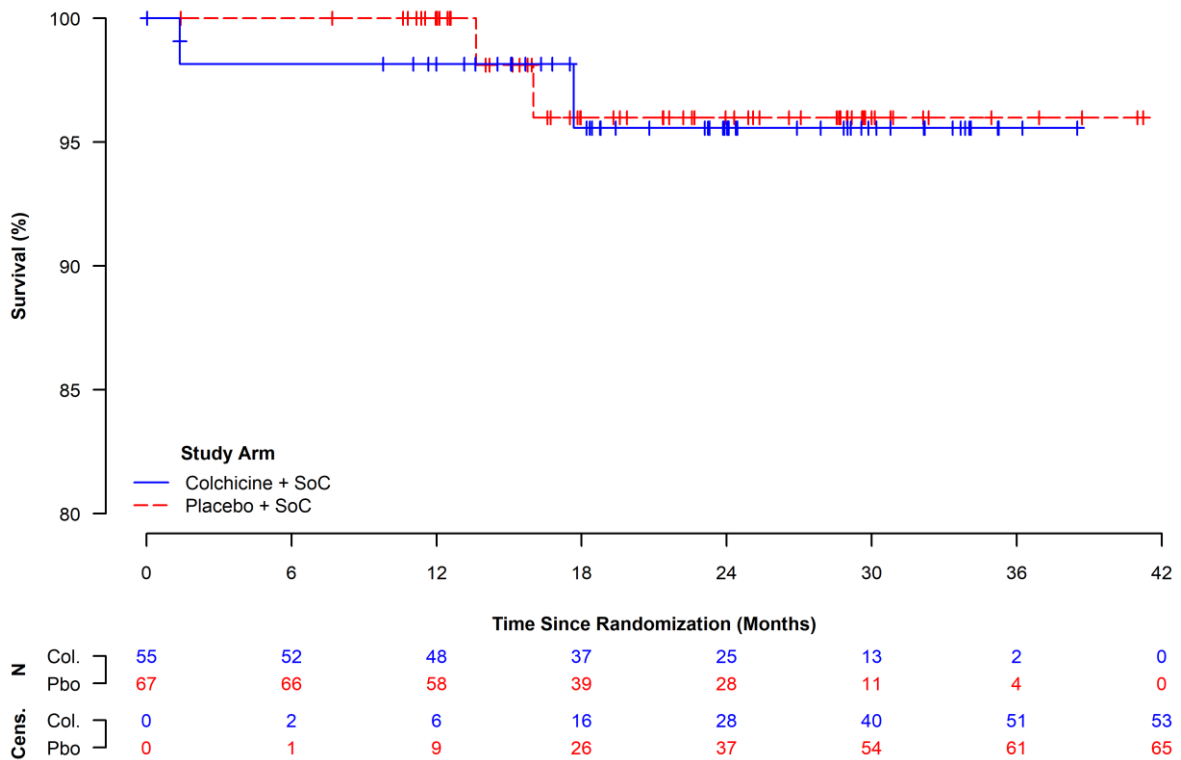
#### 4.4.2.10.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 217:** Proportion of Patients with Hospitalization for Heart Failure, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

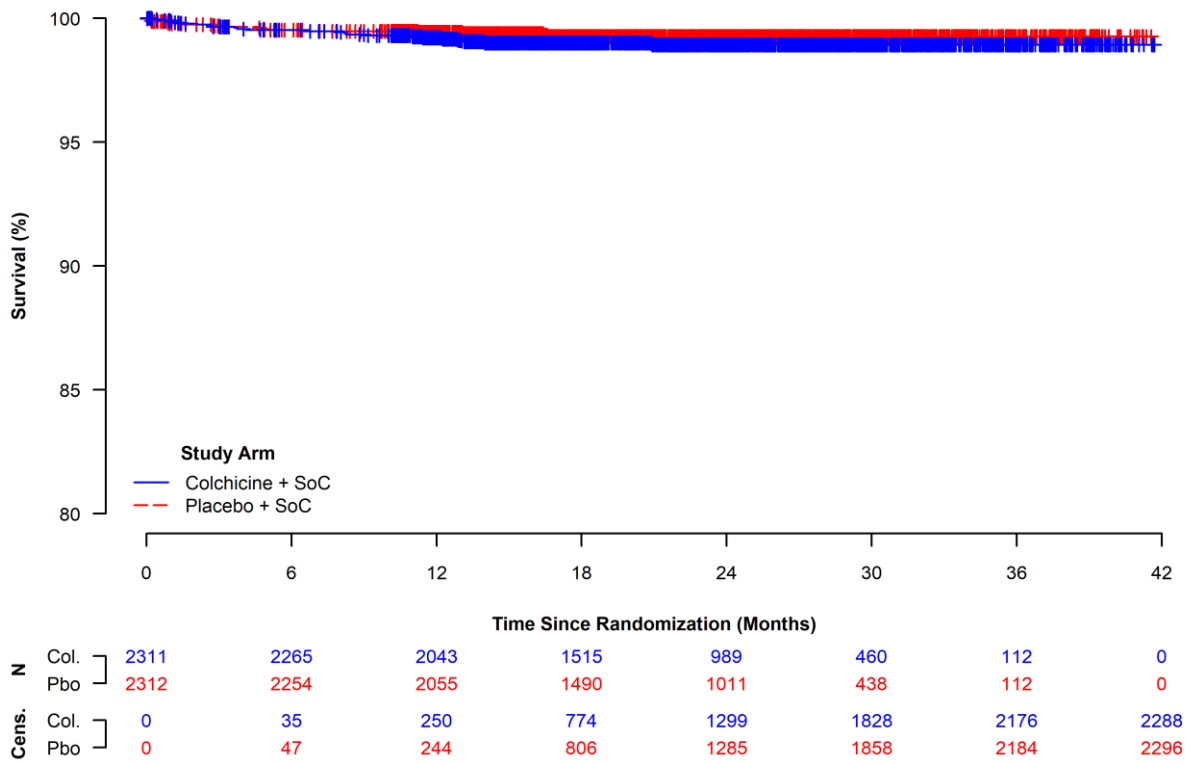
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,379)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8793</b>					
<b>Yes</b>	2/55 (3.6)	2/67 (3.0)	1.218 [0.177, 8.370] 0.8409	1.226 [0.167, 9.001] 0.8409	0.651 [-5.758, 7.061] 0.8421
<b>No</b>	23/2,311 (1.0)	16/2,312 (0.7)	1.438 [0.762, 2.715] 0.2624	1.443 [0.760, 2.738] 0.2623	0.303 [-0.224, 0.830] 0.2597
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 218:** Time to Hospitalization for Heart Failure, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,379)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.8768</b>							
<b>Yes</b>	2/55 (3.6)	NE [NE, NE]	4.4 [0.0, 10.3]	2/67 (3.0)	NE [NE, NE]	4.0 [0.0, 9.3]	1.147 [0.161, 8.147] 0.8910
<b>No</b>	23/2,311 (1.0)	NE [NE, NE]	1.1 [0.6, 1.5]	16/2,312 (0.7)	NE [NE, NE]	0.7 [0.4, 1.1]	1.435 [0.758, 2.716] 0.2673
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 204:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Subgroup With History of Stroke or Transient Ischaemic Attack (ITT Population).



**Figure 205:** Kaplan-Meier Curves for Hospitalization for Heart Failure, Within the Subgroup Without History of Stroke or Transient Ischaemic Attack (ITT Population).

#### 4.4.2.11 Coronary Revascularization

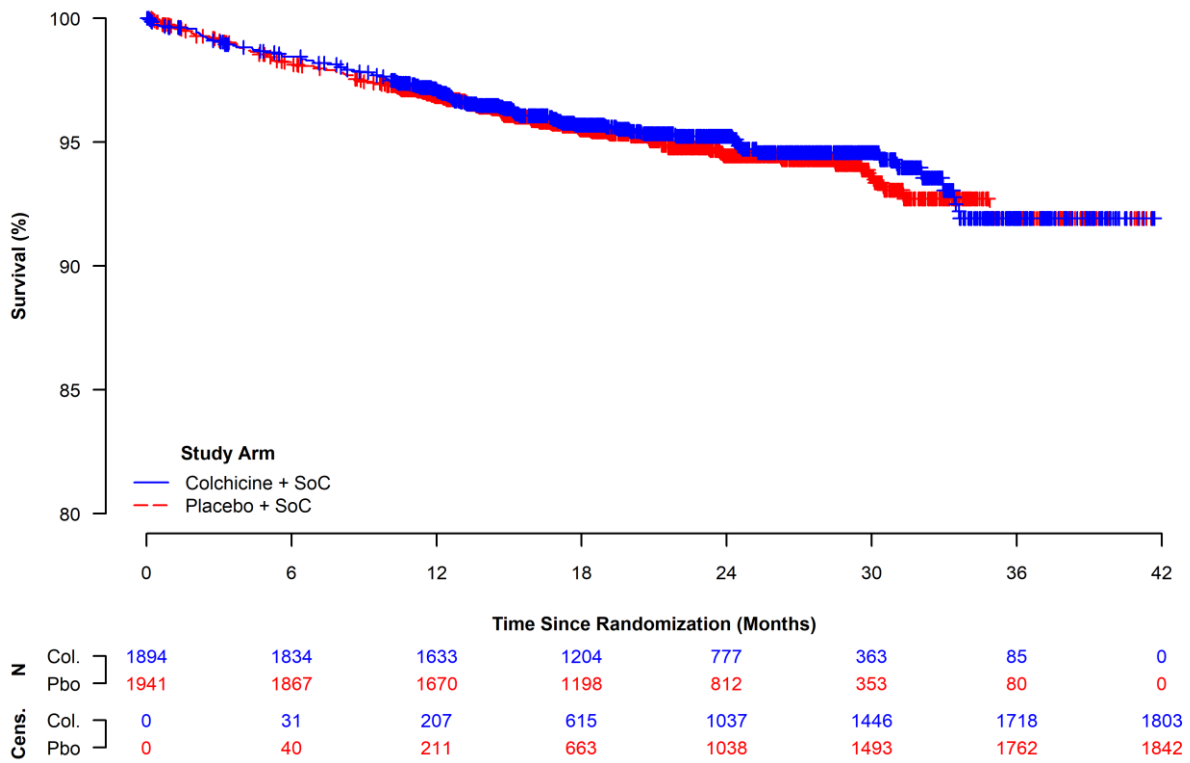
##### 4.4.2.11.1 Subgrouped by Sex

**Table 219:** Proportion of Patients with Coronary Revascularization, Subgrouped by Sex (ITT Population).

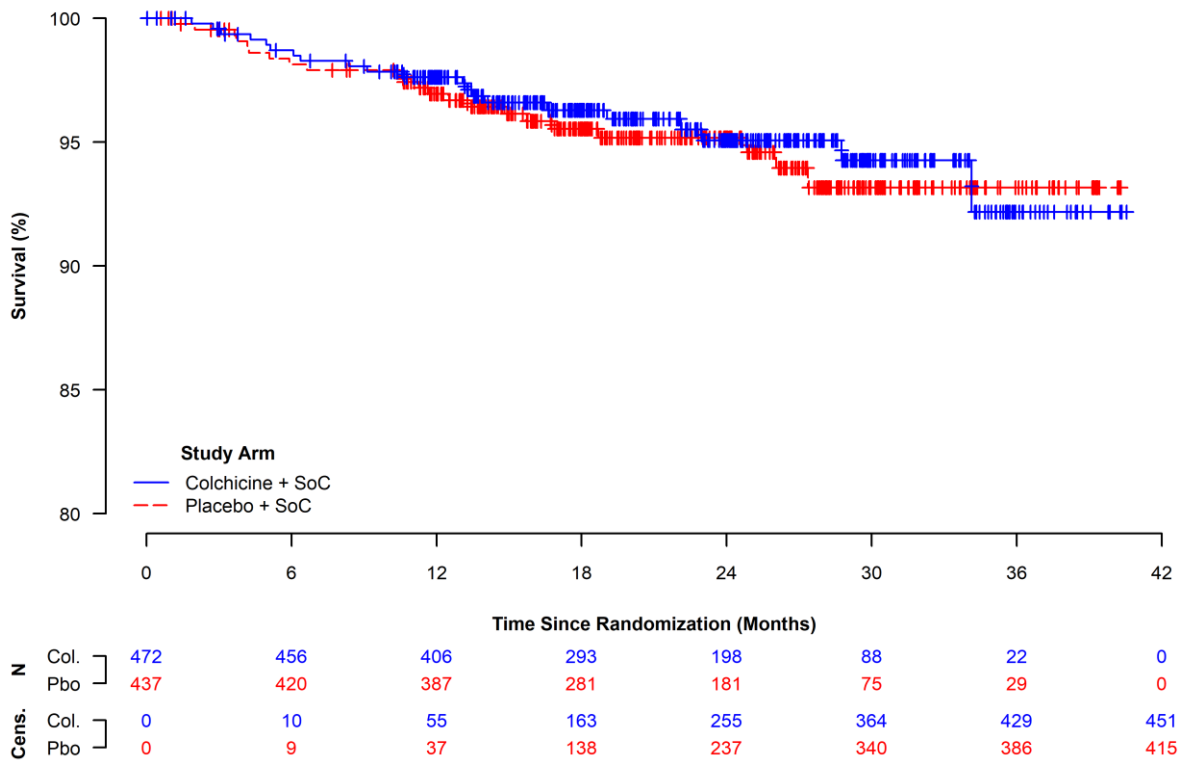
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,378)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Sex</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8469</b>					
<b>Male</b>	91/1,894 (4.8)	99/1,941 (5.1)	0.942 [0.714, 1.243] 0.6730	0.939 [0.701, 1.257] 0.6730	-0.296 [-1.669, 1.077] 0.6729
<b>Female</b>	21/472 (4.4)	22/437 (5.0)	0.884 [0.493, 1.584] 0.6782	0.878 [0.476, 1.621] 0.6782	-0.585 [-3.353, 2.183] 0.6786
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 220:** Time to Coronary Revascularization, Subgrouped by Sex (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,378)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Sex</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.8817</b>							
<b>Male</b>	91/1,894 (4.8)	NE [NE, NE]	8.1 [5.6, 10.5]	99/1,941 (5.1)	NE [NE, NE]	8.1 [5.7, 10.4]	0.935 [0.703, 1.243] 0.6439
<b>Female</b>	21/472 (4.4)	NE [NE, NE]	7.8 [2.8, 12.6]	22/437 (5.0)	NE [NE, NE]	6.8 [3.7, 9.9]	0.890 [0.489, 1.618] 0.7020
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 206:** Kaplan-Meier Curves for Coronary Revascularization, Within the Male Sex Subgroup (ITT Population).



**Figure 207:** Kaplan-Meier Curves for Coronary Revascularization, Within the Female Sex Subgroup (ITT Population).

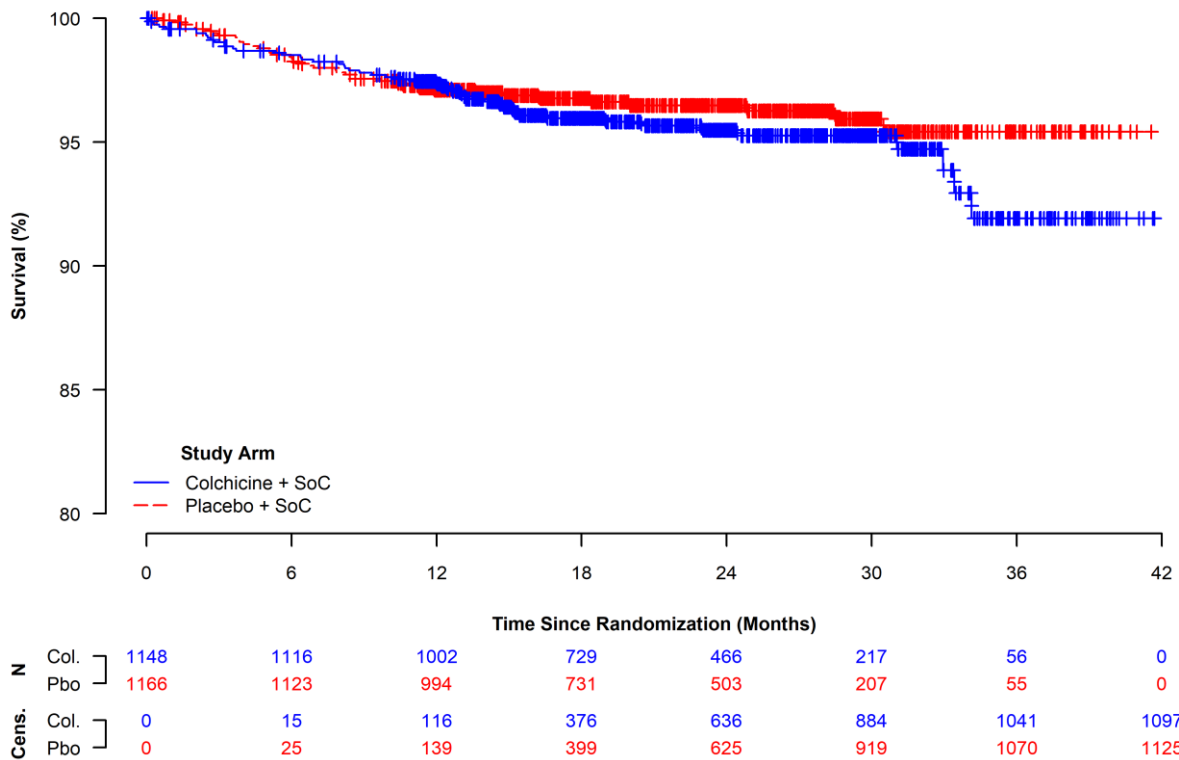
#### 4.4.2.11.2 Subgrouped by Age Group

**Table 221:** Proportion of Patients with Coronary Revascularization, Subgrouped by Age Group (ITT Population).

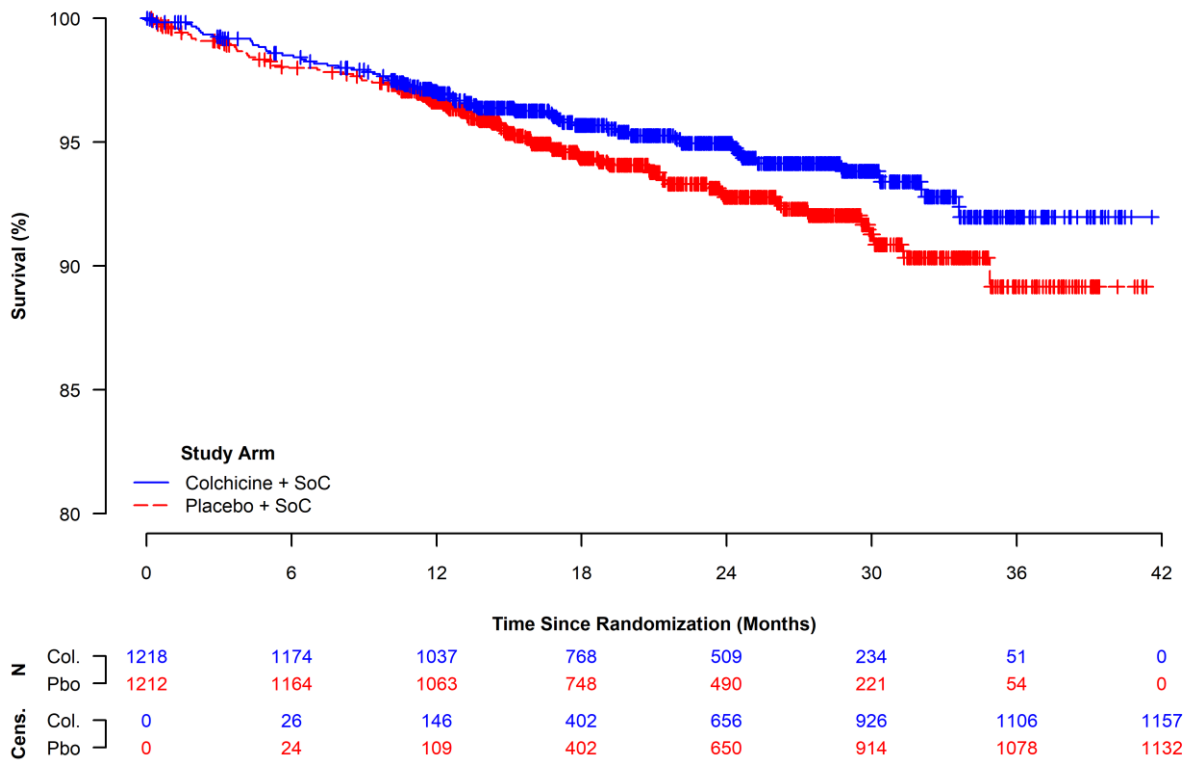
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,378)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Age</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.0515</b>					
< 60 Years	51/1,148 (4.4)	41/1,166 (3.5)	1.263 [0.844, 1.890] 0.2554	1.276 [0.839, 1.940] 0.2553	0.926 [-0.667, 2.519] 0.2545
≥ 60 Years	61/1,218 (5.0)	80/1,212 (6.6)	0.759 [0.549, 1.049] 0.0944	0.746 [0.529, 1.051] 0.0942	-1.592 [-3.451, 0.266] 0.0931
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 222:** Time to Coronary Revascularization, Subgrouped by Age Group (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,378)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.0649</b>							
<b>&lt; 60 Years</b>	51/1,148 (4.4)	NE [NE, NE]	8.1 [4.5, 11.6]	41/1,166 (3.5)	NE [NE, NE]	4.6 [2.9, 6.2]	1.247 [0.827, 1.882] 0.2919
<b>≥ 60 Years</b>	61/1,218 (5.0)	NE [NE, NE]	8.0 [5.3, 10.7]	80/1,212 (6.6)	NE [NE, NE]	10.8 [7.4, 14.1]	0.759 [0.544, 1.059] 0.1048
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 208:** Kaplan-Meier Curves for Coronary Revascularization, Within the Age 59 Years or Younger Subgroup (ITT Population).



**Figure 209:** Kaplan-Meier Curves for Coronary Revascularization, Within the Age 60 Years or Older Subgroup (ITT Population).

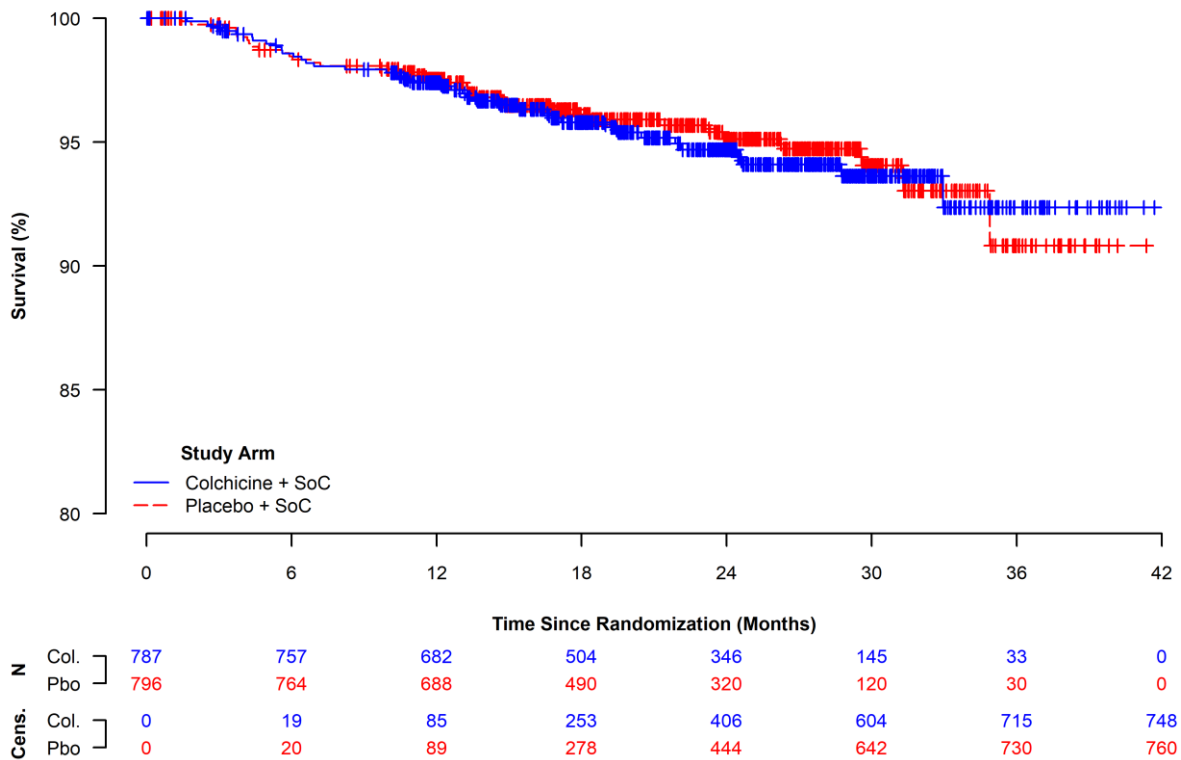
#### 4.4.2.11.3 Subgrouped by Smoking Status

**Table 223:** Proportion of Patients with Coronary Revascularization, Subgrouped by Smoking Status (ITT Population).

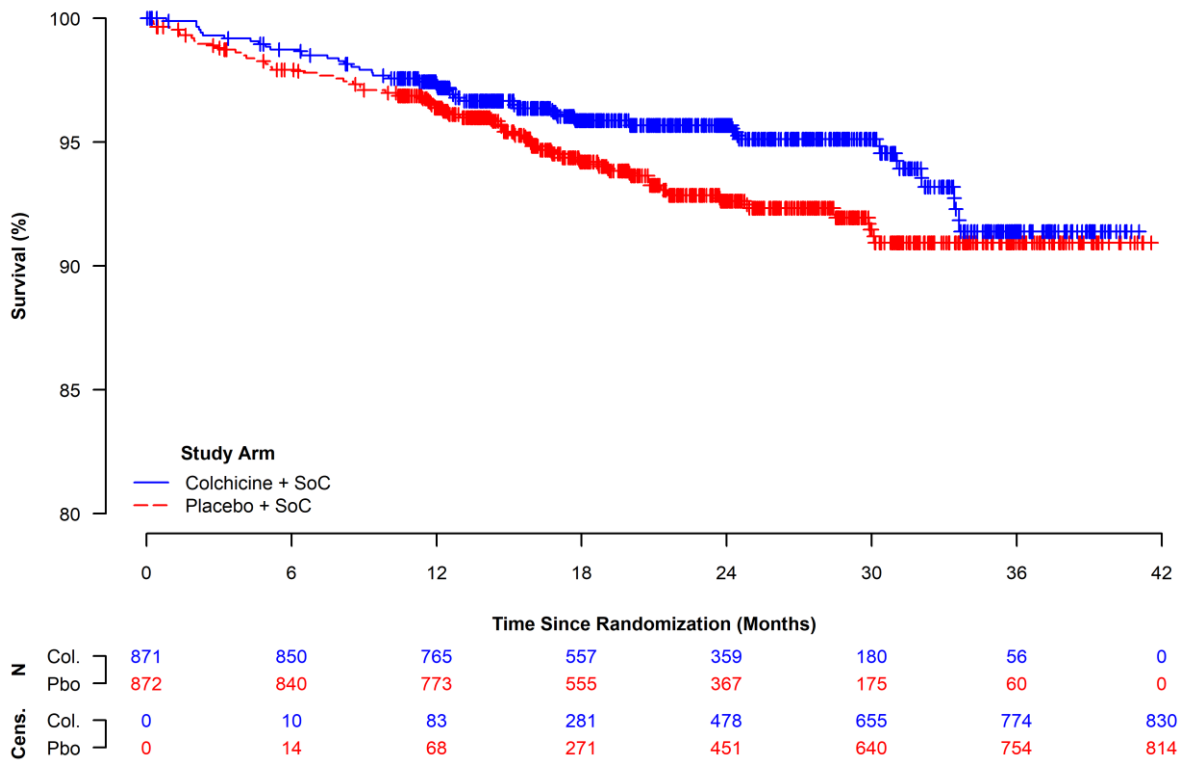
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,376)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Smoking Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1856</b>					
<b>Non</b>	39/787 (5.0)	36/796 (4.5)	1.096 [0.704, 1.705] 0.6853	1.101 [0.692, 1.751] 0.6853	0.433 [-1.661, 2.526] 0.6853
<b>Ex</b>	41/871 (4.7)	58/872 (6.7)	0.708 [0.480, 1.044] 0.0813	0.693 [0.459, 1.046] 0.0810	-1.944 [-4.115, 0.227] 0.0792
<b>Current</b>	32/708 (4.5)	27/708 (3.8)	1.185 [0.718, 1.957] 0.5067	1.194 [0.708, 2.015] 0.5066	0.706 [-1.375, 2.787] 0.5060
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 224:** Time to Coronary Revascularization, Subgrouped by Smoking Status (ITT Population).

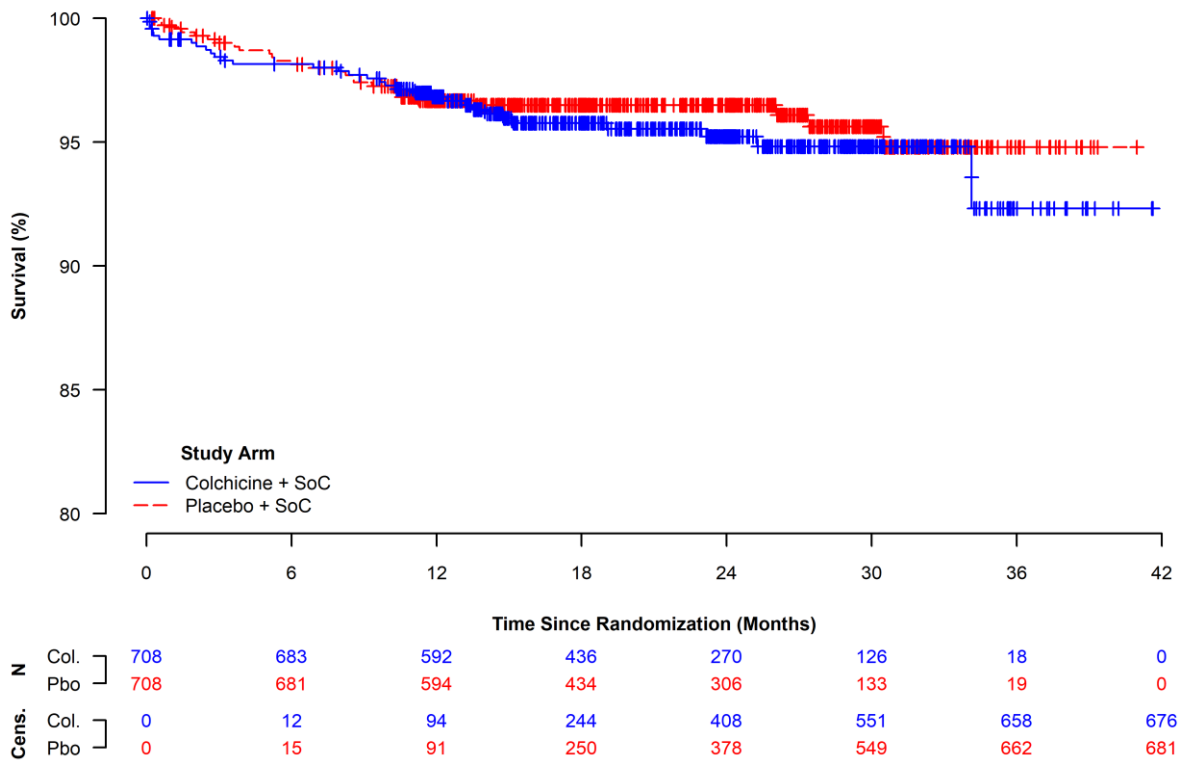
Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,376)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.2111</b>							
<b>Non</b>	39/787 (5.0)	NE [NE, NE]	7.6 [4.3, 10.8]	36/796 (4.5)	NE [NE, NE]	9.2 [3.8, 14.2]	1.068 [0.679, 1.680] 0.7765
<b>Ex</b>	41/871 (4.7)	NE [NE, NE]	8.6 [4.9, 12.2]	58/872 (6.7)	NE [NE, NE]	9.1 [6.5, 11.6]	0.708 [0.475, 1.057] 0.0910
<b>Current</b>	32/708 (4.5)	NE [NE, NE]	7.7 [2.4, 12.7]	27/708 (3.8)	NE [NE, NE]	5.2 [2.8, 7.6]	1.193 [0.715, 1.991] 0.5002
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 210:** Kaplan-Meier Curves for Coronary Revascularization, Within the Non-Smoker Subgroup (ITT Population).



**Figure 211:** Kaplan-Meier Curves for Coronary Revascularization, Within the Ex-Smoker Subgroup (ITT Population).



**Figure 212:** Kaplan-Meier Curves for Coronary Revascularization, Within the Current Smoker Subgroup (ITT Population).

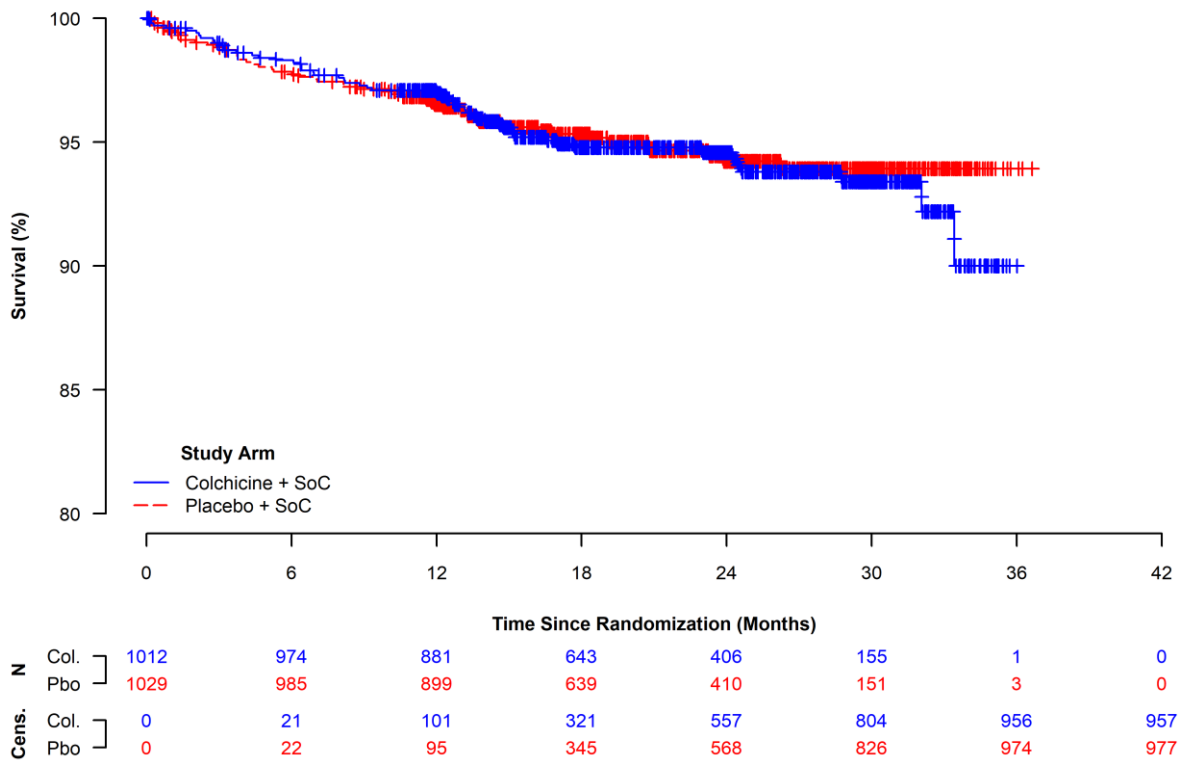
#### 4.4.2.11.4 Subgrouped by Region

**Table 225:** Proportion of Patients with Coronary Revascularization, Subgrouped by Region (ITT Population).

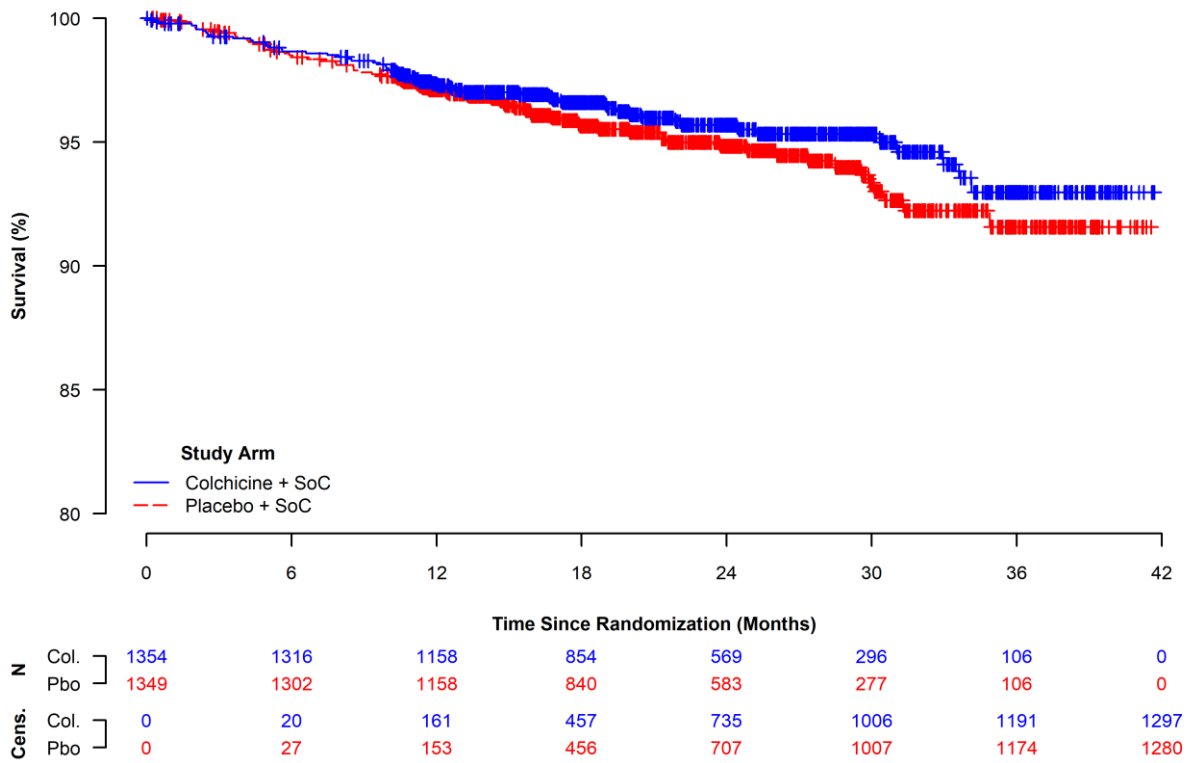
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,378)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Region</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2981</b>					
<b>Europe</b>	55/1,012 (5.4)	52/1,029 (5.1)	1.075 [0.744, 1.555] 0.6992	1.080 [0.731, 1.594] 0.6992	0.381 [-1.553, 2.316] 0.6992
<b>Non-Europe</b>	57/1,354 (4.2)	69/1,349 (5.1)	0.823 [0.584, 1.159] 0.2652	0.815 [0.569, 1.168] 0.2651	-0.905 [-2.495, 0.684] 0.2643
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 226:** Time to Coronary Revascularization, Subgrouped by Region (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,378)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.3154</b>							
<b>Europe</b>	55/1,012 (5.4)	NE [NE, NE]	10.0 [4.7, 15.0]	52/1,029 (5.1)	NE [NE, NE]	6.1 [4.4, 7.8]	1.070 [0.733, 1.564] 0.7251
<b>Non-Europe</b>	57/1,354 (4.2)	NE [NE, NE]	7.0 [4.6, 9.4]	69/1,349 (5.1)	NE [NE, NE]	8.4 [5.9, 10.9]	0.819 [0.577, 1.164] 0.2657
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 213:** Kaplan-Meier Curves for Coronary Revascularization, Within European Countries (ITT Population).



**Figure 214:** Kaplan-Meier Curves for Coronary Revascularization, Within Non-European Countries (ITT Population).

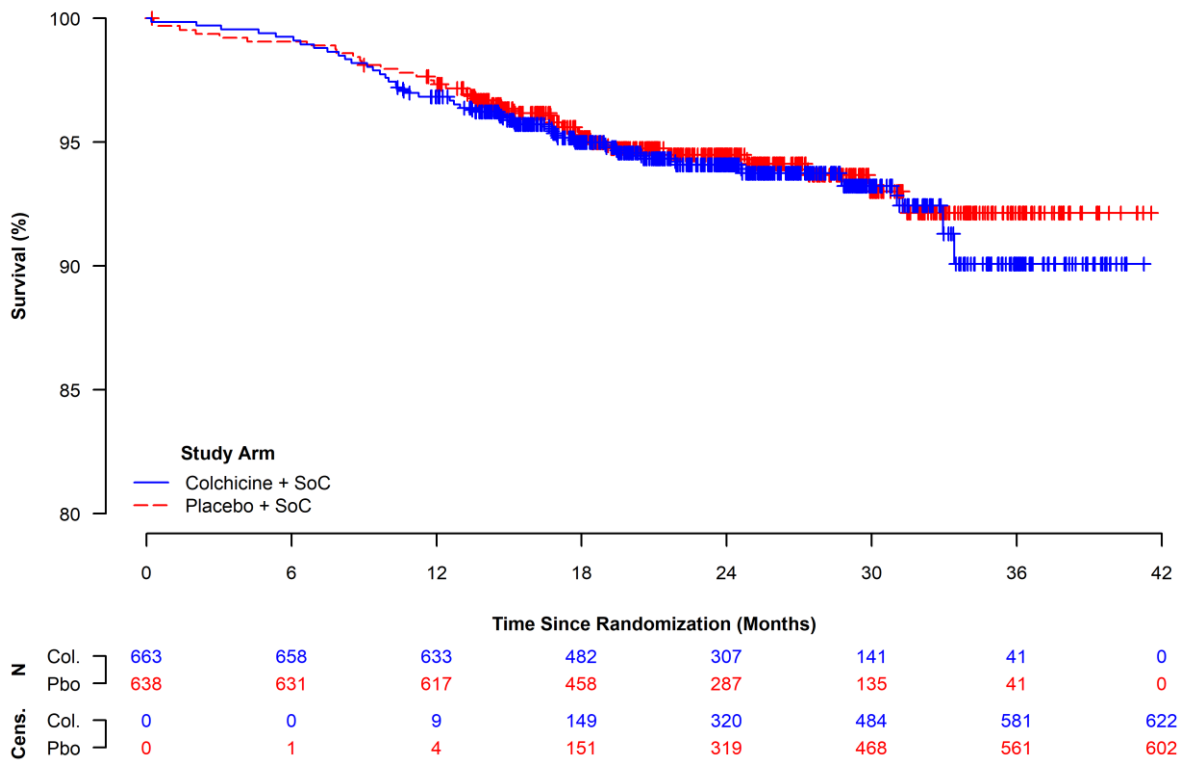
#### 4.4.2.11.5 Subgrouped by White Blood Cell Count

**Table 227:** Proportion of Patients with Coronary Revascularization, Subgrouped by White Blood Cell Count (ITT Population).

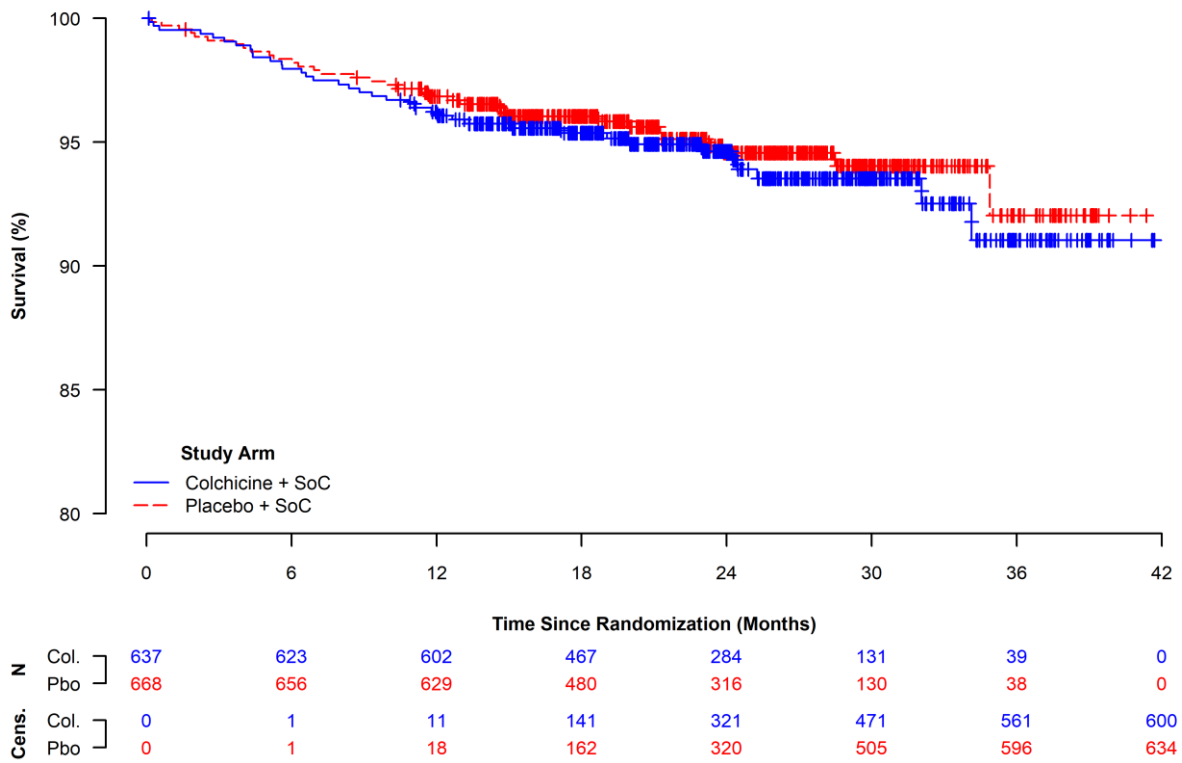
Subgroup	Colchicine + SoC (N = 1,300)	Placebo + SoC (N = 1,306)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.9008</b>					
< 8.66 10 <sup>3</sup> /μL	41/663 (6.2)	36/638 (5.6)	1.096 [0.710, 1.692] 0.6792	1.102 [0.695, 1.749] 0.6792	0.541 [-2.021, 3.104] 0.6788
≥ 8.66 10 <sup>3</sup> /μL	37/637 (5.8)	34/668 (5.1)	1.141 [0.726, 1.795] 0.5675	1.150 [0.712, 1.856] 0.5675	0.719 [-1.747, 3.184] 0.5678
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 228:** Time to Coronary Revascularization, Subgrouped by White Blood Cell Count (ITT Population).

Subgroup	Colchicine + SoC (N = 1,300)			Placebo + SoC (N = 1,306)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.9048</b>							
< 8.66 10 <sup>3</sup> /μL	41/663 (6.2)	NE [NE, NE]	9.9 [5.7, 14.0]	36/638 (5.6)	NE [NE, NE]	7.9 [4.8, 10.8]	1.095 [0.700, 1.713] 0.6910
≥ 8.66 10 <sup>3</sup> /μL	37/637 (5.8)	NE [NE, NE]	9.0 [4.8, 12.9]	34/668 (5.1)	NE [NE, NE]	8.0 [3.5, 12.3]	1.139 [0.715, 1.814] 0.5845
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 215:** Kaplan-Meier Curves for Coronary Revascularization, Within the Lower White Blood Cell Count Subgroup (ITT Population).



**Figure 216:** Kaplan-Meier Curves for Coronary Revascularization, Within the Upper White Blood Cell Count Subgroup (ITT Population).

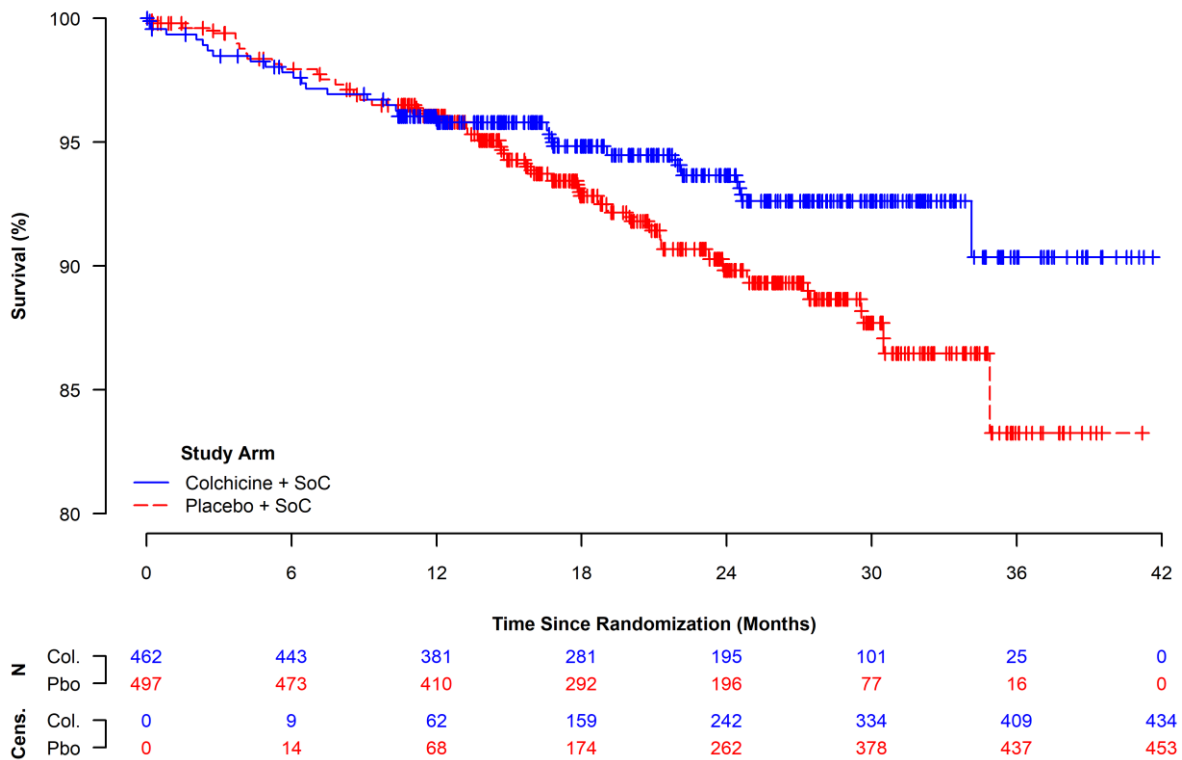
#### 4.4.2.11.6 Subgrouped by Diabetes Status

**Table 229:** Proportion of Patients with Coronary Revascularization, Subgrouped by Diabetes Status (ITT Population).

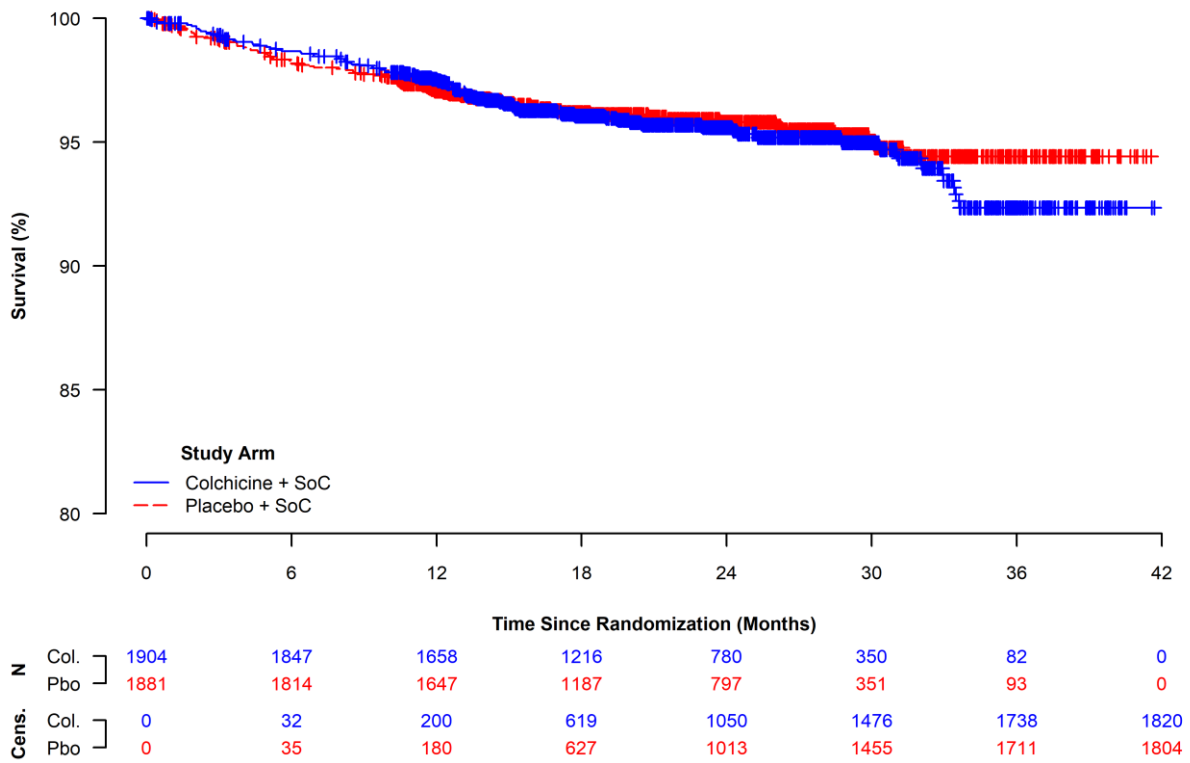
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,378)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1000</b>					
<b>Yes</b>	28/462 (6.1)	44/497 (8.9)	0.685 [0.434, 1.081] 0.1038	0.664 [0.406, 1.086] 0.1030	-2.793 [-6.105, 0.520] 0.0984
<b>No</b>	84/1,904 (4.4)	77/1,881 (4.1)	1.078 [0.796, 1.459] 0.6278	1.081 [0.788, 1.483] 0.6277	0.318 [-0.967, 1.604] 0.6276
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 230:** Time to Coronary Revascularization, Subgrouped by Diabetes Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,378)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Interaction Test p-Value<sup>f</sup> = 0.0930</b>							
<b>Yes</b>	28/462 (6.1)	NE [NE, NE]	9.6 [4.3, 14.7]	44/497 (8.9)	NE [NE, NE]	16.7 [8.8, 24.0]	0.665 [0.414, 1.068] 0.0917
<b>No</b>	84/1,904 (4.4)	NE [NE, NE]	7.7 [5.2, 10.0]	77/1,881 (4.1)	NE [NE, NE]	5.6 [4.1, 7.1]	1.079 [0.792, 1.469] 0.6317
Database lock: 28-08-2019							
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method. <sup>d</sup> Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE. <sup>e</sup> HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR < 1 favours Colchicine + SoC. <sup>f</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.							
Study: COLCOT							



**Figure 217:** Kaplan-Meier Curves for Coronary Revascularization, Within the Diabetic Subgroup (ITT Population).



**Figure 218:** Kaplan-Meier Curves for Coronary Revascularization, Within the Non-Diabetic Subgroup (ITT Population).

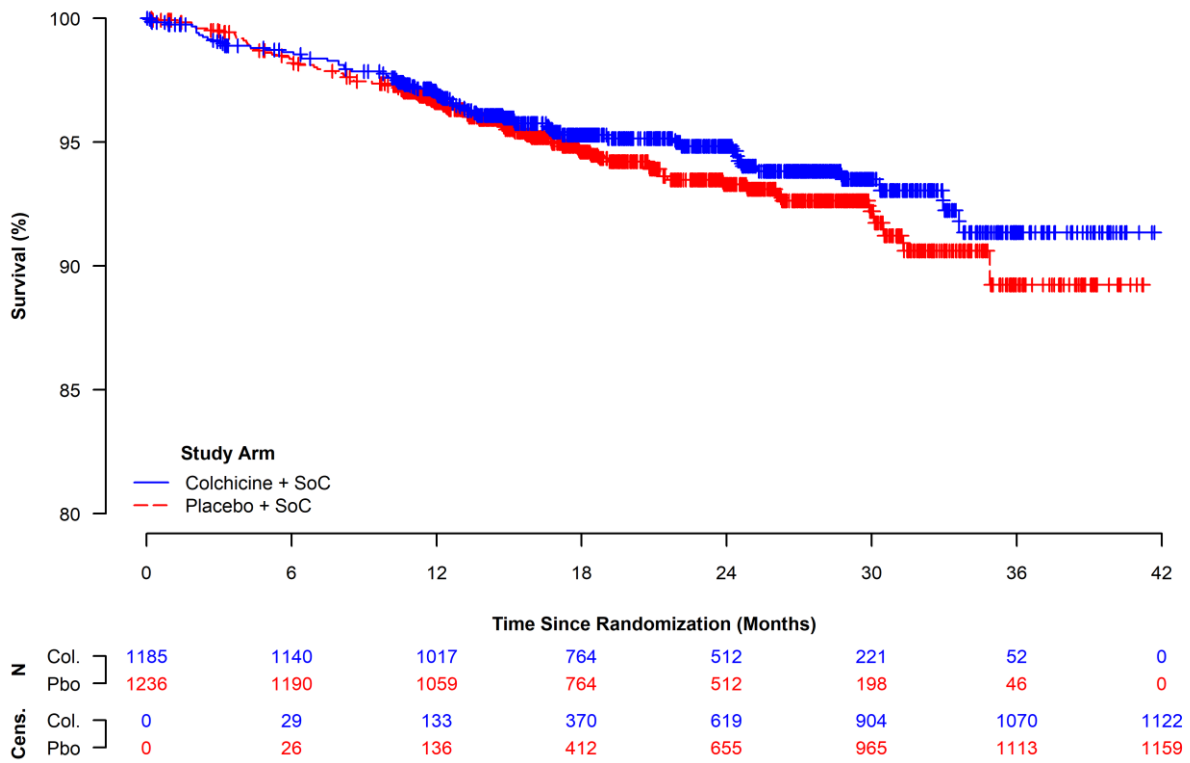
#### 4.4.2.11.7 Subgrouped by Hypertension Status

**Table 231:** Proportion of Patients with Coronary Revascularization, Subgrouped by Hypertension Status (ITT Population).

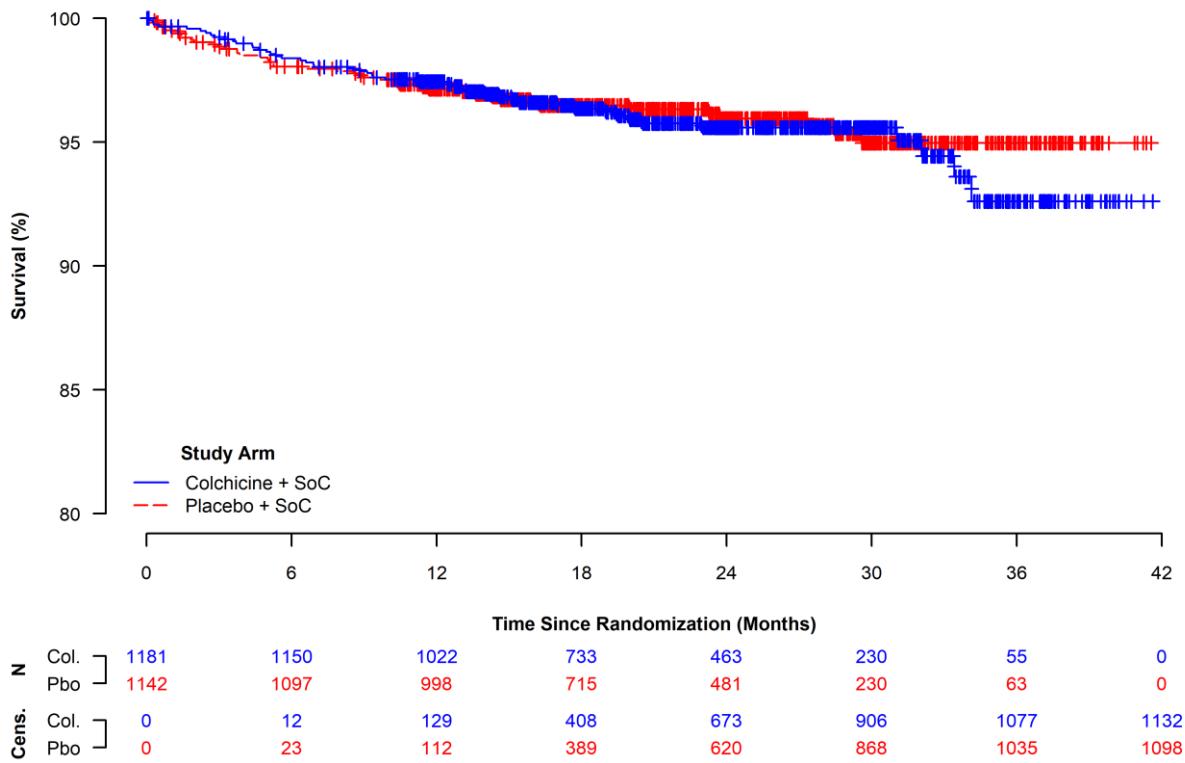
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,378)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.3715</b>					
<b>Yes</b>	63/1,185 (5.3)	77/1,236 (6.2)	0.853 [0.618, 1.179] 0.3365	0.845 [0.600, 1.191] 0.3363	-0.913 [-2.770, 0.943] 0.3350
<b>No</b>	49/1,181 (4.1)	44/1,142 (3.9)	1.077 [0.723, 1.605] 0.7159	1.080 [0.713, 1.637] 0.7159	0.296 [-1.297, 1.890] 0.7157
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 232:** Time to Coronary Revascularization, Subgrouped by Hypertension Status (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,378)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.3484</b>							
<b>Yes</b>	63/1,185 (5.3)	NE [NE, NE]	8.6 [5.6, 11.6]	77/1,236 (6.2)	NE [NE, NE]	10.8 [7.0, 14.4]	0.840 [0.602, 1.171] 0.3035
<b>No</b>	49/1,181 (4.1)	NE [NE, NE]	7.4 [4.1, 10.5]	44/1,142 (3.9)	NE [NE, NE]	5.0 [3.4, 6.7]	1.078 [0.718, 1.620] 0.7163
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 219:** Kaplan-Meier Curves for Coronary Revascularization, Within the Hypertensive Subgroup (ITT Population).



**Figure 220:** Kaplan-Meier Curves for Coronary Revascularization, Within the Normotensive Subgroup (ITT Population).

#### **4.4.2.11.8 Subgrouped by History of Myocardial Infarction**

Due to a significant interaction term, the data is presented in Module 4A.

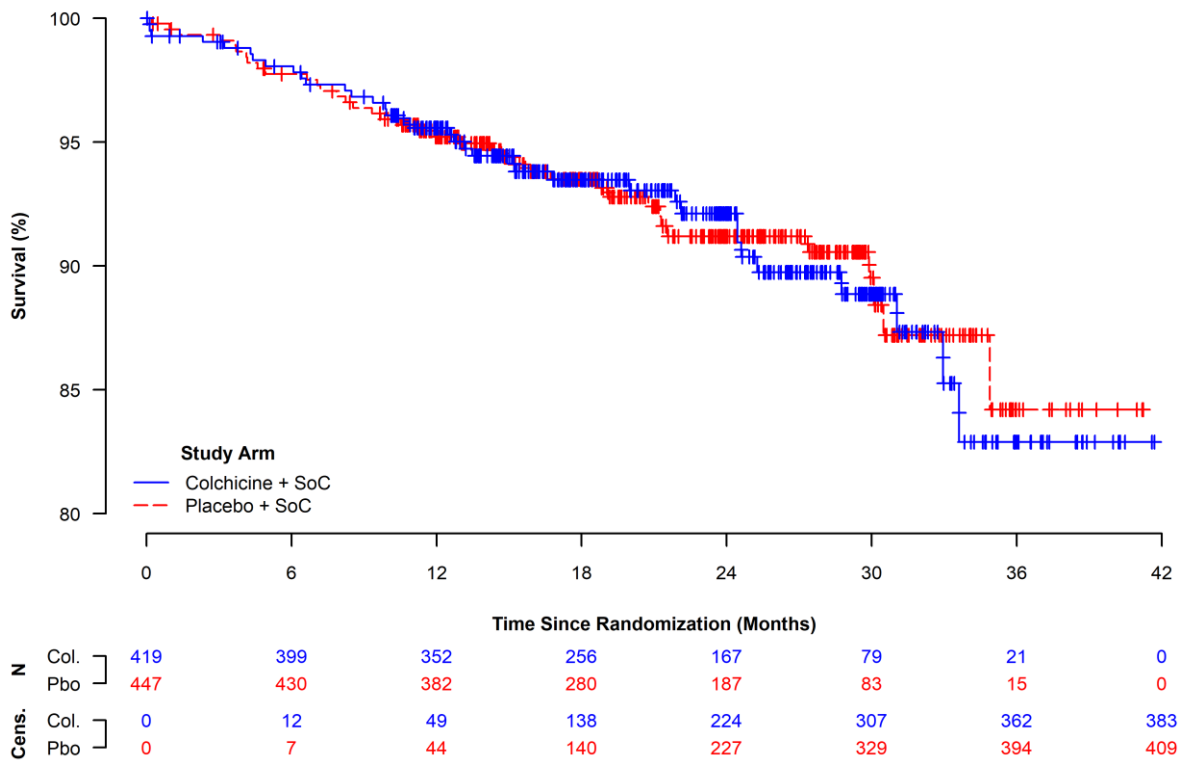
#### 4.4.2.11.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 233:** Proportion of Patients with Coronary Revascularization, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

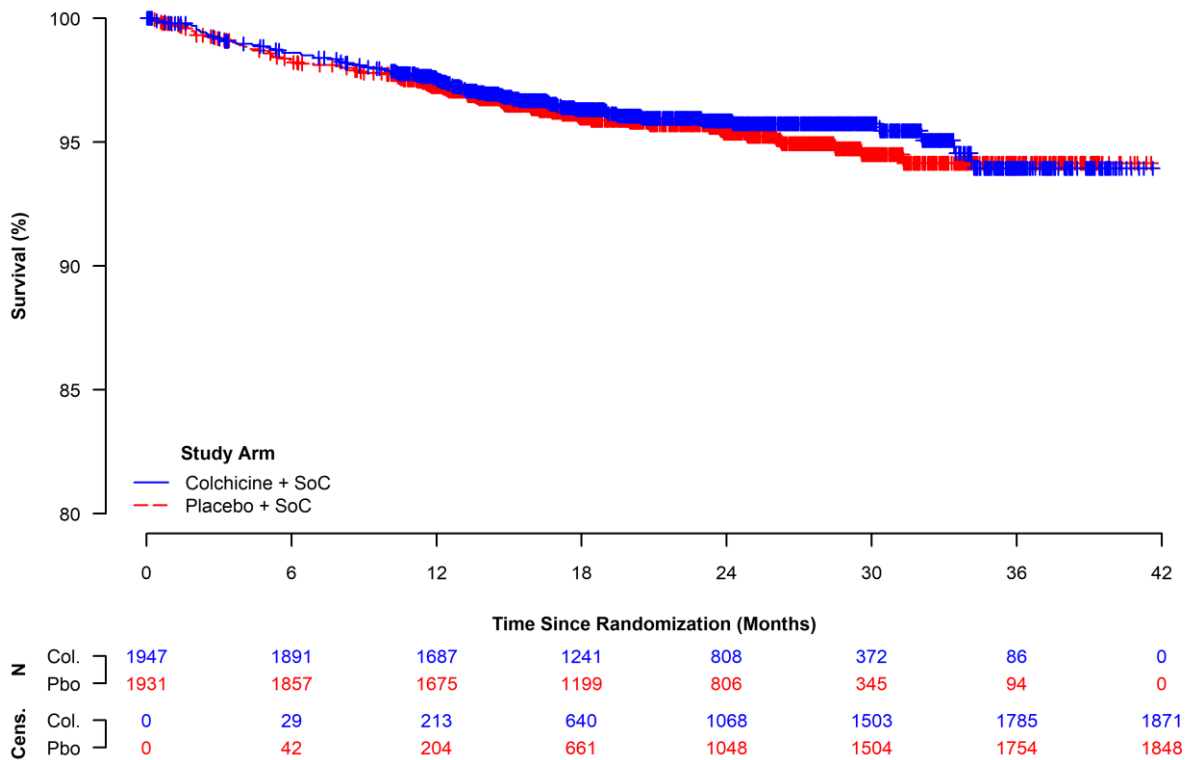
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,378)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7014</b>					
<b>Yes</b>	36/419 (8.6)	38/447 (8.5)	1.011 [0.654, 1.563] 0.9619	1.012 [0.628, 1.630] 0.9619	0.091 [-3.635, 3.817] 0.9619
<b>No</b>	76/1,947 (3.9)	83/1,931 (4.3)	0.908 [0.670, 1.232] 0.5354	0.904 [0.658, 1.243] 0.5354	-0.395 [-1.643, 0.854] 0.5353
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 234:** Time to Coronary Revascularization, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,378)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.6233</b>							
<b>Yes</b>	36/419 (8.6)	NE [NE, NE]	17.1 [9.1, 24.4]	38/447 (8.5)	NE [NE, NE]	15.8 [8.0, 22.9]	1.034 [0.656, 1.632] 0.8843
<b>No</b>	76/1,947 (3.9)	NE [NE, NE]	6.1 [4.0, 8.1]	83/1,931 (4.3)	NE [NE, NE]	5.9 [4.4, 7.3]	0.900 [0.659, 1.228] 0.5049
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 221:** Kaplan-Meier Curves for Coronary Revascularization, Within the Subgroup With History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).



**Figure 222:** Kaplan-Meier Curves for Coronary Revascularization, Within the Subgroup Without History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (ITT Population).

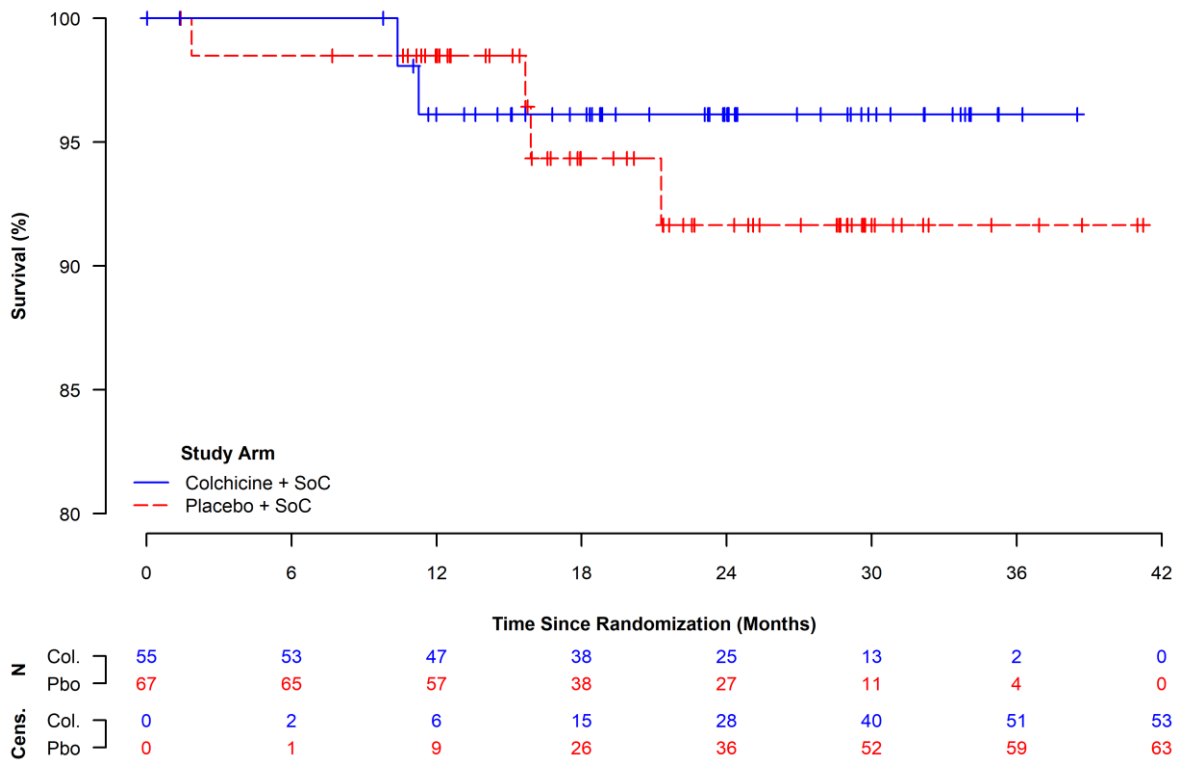
#### 4.4.2.11.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 235:** Proportion of Patients with Coronary Revascularization, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

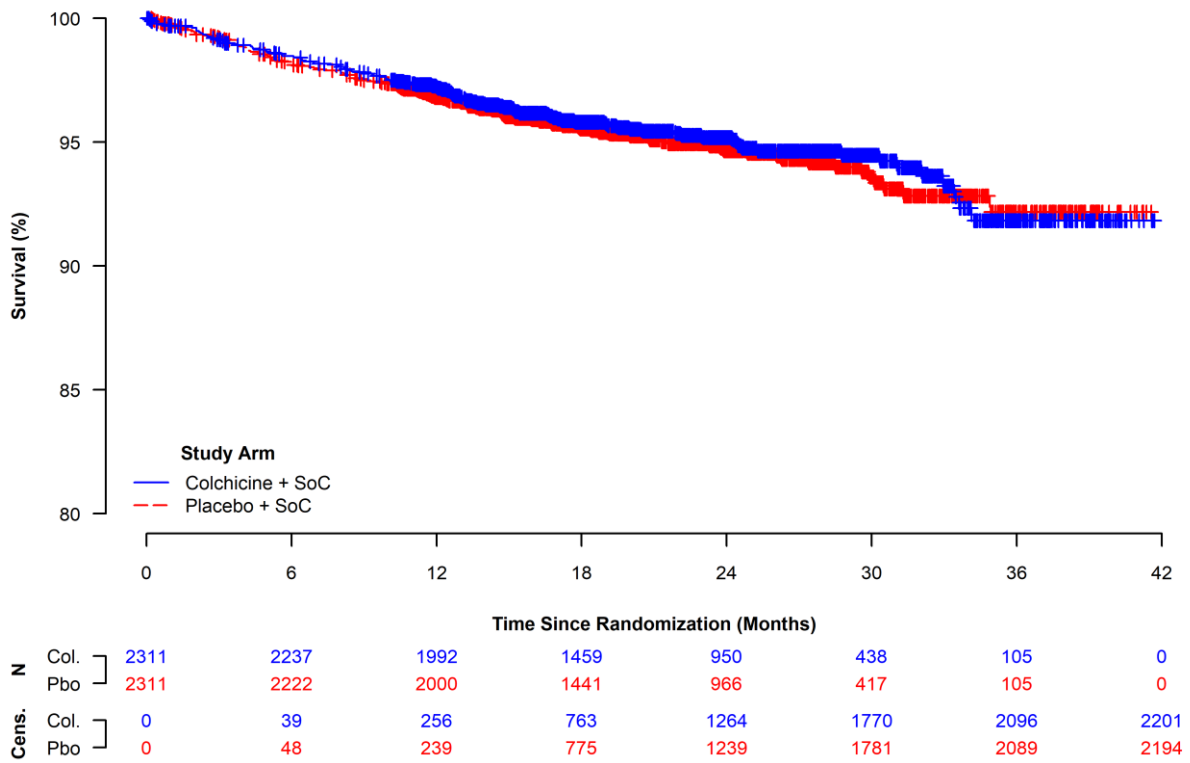
Subgroup	Colchicine + SoC (N = 2,366)	Placebo + SoC (N = 2,378)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.6046</b>					
<b>Yes</b>	2/55 (3.6)	4/67 (6.0)	0.609 [0.116, 3.202] 0.5582	0.594 [0.105, 3.373] 0.5570	-2.334 [-9.861, 5.194] 0.5434
<b>No</b>	110/2,311 (4.8)	117/2,311 (5.1)	0.940 [0.729, 1.212] 0.6338	0.937 [0.718, 1.224] 0.6338	-0.303 [-1.549, 0.943] 0.6337
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

**Table 236:** Time to Coronary Revascularization, Subgrouped by History of Stroke or Transient Ischaemic Attack (ITT Population).

Subgroup	Colchicine + SoC (N = 2,366)			Placebo + SoC (N = 2,378)			Colchicine + SoC vs. Placebo + SoC
	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	n <sup>a</sup> /N <sup>b</sup> (%)	Median Survival <sup>c</sup> [95 %-CI]	Cumulative Risk <sup>d</sup> [95 %-CI]	HR <sup>e</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>							
<b>Interaction Test p-Value<sup>f</sup> = 0.5745</b>							
<b>Yes</b>	2/55 (3.6)	NE [NE, NE]	3.9 [0.0, 9.0]	4/67 (6.0)	NE [NE, NE]	8.4 [0.0, 16.0]	0.593 [0.109, 3.240] 0.5468
<b>No</b>	110/2,31 1 (4.8)	NE [NE, NE]	8.2 [5.9, 10.4]	117/2,31 1 (5.1)	NE [NE, NE]	7.8 [5.8, 9.8]	0.937 [0.722, 1.215] 0.6226
Database lock: 28-08-2019							
<p><sup>a</sup>Number of patients with the event.  <sup>b</sup>Number of patients in the study population.  <sup>c</sup>Median time to event was estimated using the Kaplan-Meier method with the corresponding 95 %-CI estimated using the Brookmeyer-Crowley method.  <sup>d</sup>Cumulative risk at maximum follow-up was calculated from the complement of the Kaplan-Meier survival estimate, with the corresponding 95 %-CI estimated on the log-scale using the Greenwood estimate of the SE.  <sup>e</sup>HR, two-sided 95 %-CI, and p-value were calculated using the normal approximation. A HR &lt; 1 favours Colchicine + SoC.  <sup>f</sup>Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.</p>							
Study: COLCOT							



**Figure 223:** Kaplan-Meier Curves for Coronary Revascularization, Within the Subgroup With History of Stroke or Transient Ischaemic Attack (ITT Population).



**Figure 224:** Kaplan-Meier Curves for Coronary Revascularization, Within the Subgroup Without History of Stroke or Transient Ischaemic Attack (ITT Population).

### 4.4.3 Safety

#### 4.4.3.1 Treatment Emergent Adverse Events

##### 4.4.3.1.1 Treatment Emergent Adverse Events — Overall

##### 4.4.3.1.1.1 Subgrouped by Sex

**Table 237:** Proportion of Patients with Treatment Emergent Adverse Events, Subgrouped by Sex (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Sex</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1794</b>					
<b>Male</b>	751/1,867 (40.2)	815/1,917 (42.5)	0.946 [0.877, 1.021] 0.1531	0.910 [0.799, 1.036] 0.1529	-2.289 [-5.427, 0.848] 0.1527
<b>Female</b>	213/463 (46.0)	186/429 (43.4)	1.061 [0.917, 1.228] 0.4275	1.113 [0.855, 1.450] 0.4269	2.648 [-3.879, 9.175] 0.4266
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.1.2 Subgrouped by Age Group

**Table 238:** Proportion of Patients with Treatment Emergent Adverse Events, Subgrouped by Age Group (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Age</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.9042</b>					
<b>&lt; 60 Years</b>	435/1,133 (38.4)	458/1,149 (39.9)	0.963 [0.869, 1.067] 0.4729	0.940 [0.795, 1.112] 0.4728	-1.467 [-5.471, 2.537] 0.4727
<b>≥ 60 Years</b>	529/1,197 (44.2)	543/1,197 (45.4)	0.974 [0.891, 1.065] 0.5651	0.954 [0.812, 1.121] 0.5650	-1.170 [-5.153, 2.814] 0.5650
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.1.3 Subgrouped by Smoking Status

**Table 239:** Proportion of Patients with Treatment Emergent Adverse Events, Subgrouped by Smoking Status (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,344)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Smoking Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1367</b>					
<b>Non</b>	326/775 (42.1)	310/788 (39.3)	1.069 [0.949, 1.205] 0.2732	1.120 [0.915, 1.370] 0.2731	2.724 [-2.145, 7.594] 0.2728
<b>Ex</b>	377/860 (43.8)	412/867 (47.5)	0.922 [0.832, 1.023] 0.1249	0.862 [0.713, 1.042] 0.1246	-3.683 [-8.378, 1.012] 0.1242
<b>Current</b>	261/695 (37.6)	279/689 (40.5)	0.927 [0.813, 1.058] 0.2626	0.884 [0.712, 1.097] 0.2624	-2.940 [-8.077, 2.198] 0.2621
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.1.4 Subgrouped by Region

**Table 240:** Proportion of Patients with Treatment Emergent Adverse Events, Subgrouped by Region (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Region</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4545</b>					
<b>Europe</b>	462/988 (46.8)	473/1,011 (46.8)	0.999 [0.910, 1.097] 0.9913	0.999 [0.838, 1.191] 0.9913	-0.024 [-4.399, 4.351] 0.9913
<b>Non-Europe</b>	502/1,342 (37.4)	528/1,335 (39.6)	0.946 [0.859, 1.041] 0.2545	0.913 [0.782, 1.067] 0.2544	-2.144 [-5.829, 1.542] 0.2543
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.1.5 Subgrouped by White Blood Cell Count

**Table 241:** Proportion of Patients with Treatment Emergent Adverse Events, Subgrouped by White Blood Cell Count (Safety Population).

Subgroup	Colchicine + SoC (N = 1,293)	Placebo + SoC (N = 1,300)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2939</b>					
< 8.66 10 <sup>3</sup> /μL	289/660 (43.8)	301/634 (47.5)	0.922 [0.819, 1.039] 0.1831	0.862 [0.692, 1.073] 0.1831	-3.688 [-9.114, 1.737] 0.1827
≥ 8.66 10 <sup>3</sup> /μL	284/633 (44.9)	296/666 (44.4)	1.009 [0.894, 1.139] 0.8787	1.017 [0.817, 1.266] 0.8787	0.421 [-4.987, 5.830] 0.8787
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.1.6 Subgrouped by Diabetes Status

**Table 242:** Proportion of Patients with Treatment Emergent Adverse Events, Subgrouped by Diabetes Status (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.6201</b>					
<b>Yes</b>	195/451 (43.2)	212/492 (43.1)	1.003 [0.867, 1.162] 0.9635	1.006 [0.777, 1.302] 0.9635	0.148 [-6.181, 6.476] 0.9635
<b>No</b>	769/1,879 (40.9)	789/1,854 (42.6)	0.962 [0.891, 1.037] 0.3125	0.935 [0.821, 1.065] 0.3125	-1.631 [-4.794, 1.533] 0.3124
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.1.7 Subgrouped by Hypertension Status

**Table 243:** Proportion of Patients with Treatment Emergent Adverse Events, Subgrouped by Hypertension Status (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2657</b>					
<b>Yes</b>	518/1,163 (44.5)	539/1,220 (44.2)	1.008 [0.921, 1.103] 0.8598	1.015 [0.863, 1.193] 0.8598	0.360 [-3.631, 4.350] 0.8598
<b>No</b>	446/1,167 (38.2)	462/1,126 (41.0)	0.931 [0.842, 1.031] 0.1687	0.889 [0.752, 1.051] 0.1687	-2.813 [-6.816, 1.191] 0.1685
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.1.8 Subgrouped by History of Myocardial Infarction

**Table 244:** Proportion of Patients with Treatment Emergent Adverse Events, Subgrouped by History of Myocardial Infarction (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of MI</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4045</b>					
<b>Yes</b>	175/362 (48.3)	184/393 (46.8)	1.033 [0.889, 1.199] 0.6753	1.063 [0.799, 1.415] 0.6755	1.523 [-5.607, 8.653] 0.6754
<b>No</b>	789/1,968 (40.1)	817/1,953 (41.8)	0.958 [0.889, 1.033] 0.2676	0.931 [0.819, 1.057] 0.2675	-1.742 [-4.820, 1.336] 0.2674
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.1.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 245:** Proportion of Patients with Treatment Emergent Adverse Events, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7744</b>					
<b>Yes</b>	199/410 (48.5)	217/444 (48.9)	0.993 [0.865, 1.140] 0.9215	0.987 [0.754, 1.291] 0.9215	-0.337 [-7.047, 6.373] 0.9215
<b>No</b>	765/1,920 (39.8)	784/1,902 (41.2)	0.967 [0.895, 1.044] 0.3863	0.945 [0.830, 1.075] 0.3863	-1.376 [-4.489, 1.737] 0.3863
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.1.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 246:** Proportion of Patients with Treatment Emergent Adverse Events, Subgrouped by History of Stroke or Transient Ischaemic Attack (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7368</b>					
<b>Yes</b>	25/53 (47.2)	34/66 (51.5)	0.916 [0.633, 1.324] 0.6395	0.840 [0.407, 1.733] 0.6376	-4.345 [-22.401, 13.710] 0.6371
<b>No</b>	939/2,277 (41.2)	967/2,280 (42.4)	0.972 [0.908, 1.041] 0.4219	0.953 [0.847, 1.072] 0.4219	-1.174 [-4.038, 1.690] 0.4218
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.2 Serious Treatment Emergent Adverse Events — Overall

##### 4.4.3.1.2.1 Subgrouped by Sex

**Table 247:** Proportion of Patients with Serious Treatment Emergent Adverse Events, Subgrouped by Sex (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Sex</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8212</b>					
<b>Male</b>	304/1,867 (16.3)	325/1,917 (17.0)	0.960 [0.833, 1.108] 0.5796	0.953 [0.803, 1.131] 0.5795	-0.671 [-3.043, 1.701] 0.5794
<b>Female</b>	79/463 (17.1)	79/429 (18.4)	0.927 [0.698, 1.229] 0.5971	0.911 [0.646, 1.285] 0.5972	-1.352 [-6.372, 3.667] 0.5975
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.2.2 Subgrouped by Age Group

**Table 248:** Proportion of Patients with Serious Treatment Emergent Adverse Events, Subgrouped by Age Group (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Age</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8845</b>					
< 60 Years	154/1,133 (13.6)	166/1,149 (14.4)	0.941 [0.768, 1.153] 0.5565	0.932 [0.735, 1.180] 0.5564	-0.855 [-3.704, 1.993] 0.5563
≥ 60 Years	229/1,197 (19.1)	238/1,197 (19.9)	0.962 [0.818, 1.132] 0.6425	0.953 [0.779, 1.167] 0.6425	-0.752 [-3.926, 2.423] 0.6425
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.2.3 Subgrouped by Smoking Status

**Table 249:** Proportion of Patients with Serious Treatment Emergent Adverse Events, Subgrouped by Smoking Status (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,344)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Smoking Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2967</b>					
<b>Non</b>	131/775 (16.9)	124/788 (15.7)	1.074 [0.858, 1.345] 0.5325	1.089 [0.833, 1.425] 0.5324	1.167 [-2.497, 4.831] 0.5324
<b>Ex</b>	146/860 (17.0)	173/867 (20.0)	0.851 [0.697, 1.038] 0.1116	0.820 [0.643, 1.047] 0.1112	-2.977 [-6.634, 0.680] 0.1106
<b>Current</b>	106/695 (15.3)	107/689 (15.5)	0.982 [0.767, 1.257] 0.8861	0.979 [0.731, 1.311] 0.8861	-0.278 [-4.080, 3.524] 0.8861
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.2.4 Subgrouped by Region

**Table 250:** Proportion of Patients with Serious Treatment Emergent Adverse Events, Subgrouped by Region (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Region</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2198</b>					
<b>Europe</b>	190/988 (19.2)	187/1,011 (18.5)	1.040 [0.867, 1.247] 0.6748	1.049 [0.838, 1.313] 0.6748	0.734 [-2.696, 4.165] 0.6748
<b>Non-Europe</b>	193/1,342 (14.4)	217/1,335 (16.3)	0.885 [0.740, 1.058] 0.1789	0.865 [0.701, 1.068] 0.1787	-1.873 [-4.601, 0.855] 0.1784
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.2.5 Subgrouped by White Blood Cell Count

**Table 251:** Proportion of Patients with Serious Treatment Emergent Adverse Events, Subgrouped by White Blood Cell Count (Safety Population).

Subgroup	Colchicine + SoC (N = 1,293)	Placebo + SoC (N = 1,300)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4874</b>					
< 8.66 10 <sup>3</sup> /μL	125/660 (18.9)	129/634 (20.3)	0.931 [0.747, 1.160] 0.5240	0.915 [0.695, 1.203] 0.5240	-1.408 [-5.738, 2.923] 0.5241
≥ 8.66 10 <sup>3</sup> /μL	114/633 (18.0)	115/666 (17.3)	1.043 [0.824, 1.319] 0.7257	1.052 [0.791, 1.400] 0.7257	0.742 [-3.405, 4.890] 0.7258
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.2.6 Subgrouped by Diabetes Status

**Table 252:** Proportion of Patients with Serious Treatment Emergent Adverse Events, Subgrouped by Diabetes Status (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.3087</b>					
<b>Yes</b>	92/451 (20.4)	93/492 (18.9)	1.079 [0.833, 1.397] 0.5632	1.099 [0.797, 1.516] 0.5632	1.497 [-3.583, 6.576] 0.5636
<b>No</b>	291/1,879 (15.5)	311/1,854 (16.8)	0.923 [0.797, 1.069] 0.2850	0.909 [0.764, 1.083] 0.2850	-1.288 [-3.647, 1.072] 0.2849
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.2.7 Subgrouped by Hypertension Status

**Table 253:** Proportion of Patients with Serious Treatment Emergent Adverse Events, Subgrouped by Hypertension Status (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.2391</b>					
<b>Yes</b>	224/1,163 (19.3)	229/1,220 (18.8)	1.026 [0.869, 1.211] 0.7606	1.032 [0.841, 1.267] 0.7606	0.490 [-2.662, 3.642] 0.7606
<b>No</b>	159/1,167 (13.6)	175/1,126 (15.5)	0.877 [0.719, 1.069] 0.1937	0.857 [0.680, 1.081] 0.1936	-1.917 [-4.807, 0.973] 0.1936
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.2.8 Subgrouped by History of Myocardial Infarction

**Table 254:** Proportion of Patients with Serious Treatment Emergent Adverse Events, Subgrouped by History of Myocardial Infarction (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of MI</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7333</b>					
<b>Yes</b>	84/362 (23.2)	91/393 (23.2)	1.002 [0.773, 1.300] 0.9872	1.003 [0.715, 1.407] 0.9872	0.049 [-5.976, 6.074] 0.9872
<b>No</b>	299/1,968 (15.2)	313/1,953 (16.0)	0.948 [0.820, 1.097] 0.4722	0.939 [0.790, 1.115] 0.4722	-0.834 [-3.106, 1.439] 0.4721
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.2.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 255:** Proportion of Patients with Serious Treatment Emergent Adverse Events, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1921</b>					
<b>Yes</b>	89/410 (21.7)	115/444 (25.9)	0.838 [0.658, 1.068] 0.1525	0.793 [0.578, 1.089] 0.1514	-4.194 [-9.897, 1.510] 0.1496
<b>No</b>	294/1,920 (15.3)	289/1,902 (15.2)	1.008 [0.868, 1.170] 0.9192	1.009 [0.846, 1.204] 0.9192	0.118 [-2.162, 2.398] 0.9192
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.2.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 256:** Proportion of Patients with Serious Treatment Emergent Adverse Events, Subgrouped by History of Stroke or Transient Ischaemic Attack (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.3861</b>					
<b>Yes</b>	9/53 (17.0)	16/66 (24.2)	0.700 [0.337, 1.457] 0.3407	0.639 [0.257, 1.591] 0.3360	-7.261 [-21.721, 7.198] 0.3250
<b>No</b>	374/2,277 (16.4)	388/2,280 (17.0)	0.965 [0.848, 1.099] 0.5921	0.958 [0.820, 1.120] 0.5921	-0.592 [-2.759, 1.574] 0.5921
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

### 4.4.3.1.3 Severe Treatment Emergent Adverse Events — Overall

#### 4.4.3.1.3.1 Subgrouped by Sex

**Table 257:** Proportion of Patients with Severe Treatment Emergent Adverse Events, Subgrouped by Sex (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Sex</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.5626</b>					
<b>Male</b>	186/1,867 (10.0)	209/1,917 (10.9)	0.914 [0.758, 1.102] 0.3447	0.904 [0.734, 1.114] 0.3446	-0.940 [-2.887, 1.007] 0.3441
<b>Female</b>	62/463 (13.4)	56/429 (13.1)	1.026 [0.733, 1.436] 0.8819	1.030 [0.699, 1.518] 0.8819	0.337 [-4.111, 4.785] 0.8818
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.3.2 Subgrouped by Age Group

**Table 258:** Proportion of Patients with Severe Treatment Emergent Adverse Events, Subgrouped by Age Group (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Age</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4536</b>					
< 60 Years	99/1,133 (8.7)	115/1,149 (10.0)	0.873 [0.676, 1.128] 0.2983	0.861 [0.649, 1.142] 0.2981	-1.271 [-3.661, 1.120] 0.2975
≥ 60 Years	149/1,197 (12.4)	150/1,197 (12.5)	0.993 [0.804, 1.228] 0.9507	0.992 [0.779, 1.265] 0.9507	-0.084 [-2.732, 2.565] 0.9507
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.3.3 Subgrouped by Smoking Status

**Table 259:** Proportion of Patients with Severe Treatment Emergent Adverse Events, Subgrouped by Smoking Status (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,344)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Smoking Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1478</b>					
<b>Non</b>	86/775 (11.1)	76/788 (9.6)	1.151 [0.859, 1.541] 0.3468	1.169 [0.844, 1.620] 0.3467	1.452 [-1.571, 4.475] 0.3465
<b>Ex</b>	92/860 (10.7)	118/867 (13.6)	0.786 [0.609, 1.015] 0.0650	0.760 [0.569, 1.017] 0.0646	-2.912 [-5.991, 0.166] 0.0637
<b>Current</b>	70/695 (10.1)	71/689 (10.3)	0.977 [0.715, 1.336] 0.8861	0.975 [0.688, 1.381] 0.8861	-0.233 [-3.420, 2.955] 0.8861
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.3.4 Subgrouped by Region

**Table 260:** Proportion of Patients with Severe Treatment Emergent Adverse Events, Subgrouped by Region (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Region</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4126</b>					
<b>Europe</b>	105/988 (10.6)	123/1,011 (12.2)	0.874 [0.684, 1.116] 0.2798	0.858 [0.651, 1.132] 0.2796	-1.539 [-4.323, 1.246] 0.2788
<b>Non-Europe</b>	143/1,342 (10.7)	142/1,335 (10.6)	1.002 [0.804, 1.248] 0.9873	1.002 [0.784, 1.281] 0.9873	0.019 [-2.318, 2.356] 0.9873
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### **4.4.3.1.3.5 Subgrouped by White Blood Cell Count**

Due to a significant interaction term, the data is presented in Module 4A.

#### 4.4.3.1.3.6 Subgrouped by Diabetes Status

**Table 261:** Proportion of Patients with Severe Treatment Emergent Adverse Events, Subgrouped by Diabetes Status (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.5357</b>					
<b>Yes</b>	67/451 (14.9)	83/492 (16.9)	0.881 [0.655, 1.183] 0.3990	0.860 [0.605, 1.221] 0.3985	-2.014 [-6.675, 2.647] 0.3970
<b>No</b>	181/1,879 (9.6)	182/1,854 (9.8)	0.981 [0.807, 1.193] 0.8497	0.979 [0.789, 1.216] 0.8497	-0.184 [-2.085, 1.717] 0.8497
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.3.7 Subgrouped by Hypertension Status

**Table 262:** Proportion of Patients with Severe Treatment Emergent Adverse Events, Subgrouped by Hypertension Status (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.3004</b>					
<b>Yes</b>	139/1,163 (12.0)	165/1,220 (13.5)	0.884 [0.716, 1.091] 0.2505	0.868 [0.682, 1.105] 0.2503	-1.573 [-4.248, 1.103] 0.2493
<b>No</b>	109/1,167 (9.3)	100/1,126 (8.9)	1.052 [0.812, 1.362] 0.7026	1.057 [0.795, 1.405] 0.7025	0.459 [-1.896, 2.815] 0.7024
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.3.8 Subgrouped by History of Myocardial Infarction

**Table 263:** Proportion of Patients with Severe Treatment Emergent Adverse Events, Subgrouped by History of Myocardial Infarction (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of MI</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.9294</b>					
<b>Yes</b>	55/362 (15.2)	62/393 (15.8)	0.963 [0.690, 1.345] 0.8251	0.956 [0.644, 1.420] 0.8251	-0.583 [-5.746, 4.581] 0.8249
<b>No</b>	193/1,968 (9.8)	203/1,953 (10.4)	0.943 [0.783, 1.137] 0.5417	0.937 [0.761, 1.154] 0.5417	-0.587 [-2.474, 1.299] 0.5417
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.3.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 264:** Proportion of Patients with Severe Treatment Emergent Adverse Events, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.0532</b>					
<b>Yes</b>	57/410 (13.9)	84/444 (18.9)	0.735 [0.540, 1.000] 0.0502	0.692 [0.479, 0.999] 0.0493	-5.016 [-9.965, -0.068] 0.0469
<b>No</b>	191/1,920 (9.9)	181/1,902 (9.5)	1.045 [0.862, 1.268] 0.6527	1.050 [0.848, 1.301] 0.6527	0.432 [-1.448, 2.311] 0.6526
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.3.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 265:** Proportion of Patients with Severe Treatment Emergent Adverse Events, Subgrouped by History of Stroke or Transient Ischaemic Attack (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1377</b>					
<b>Yes</b>	5/53 (9.4)	13/66 (19.7)	0.479 [0.182, 1.258] 0.1353	0.425 [0.141, 1.279] 0.1280	-10.263 [-22.672, 2.146] 0.1050
<b>No</b>	243/2,277 (10.7)	252/2,280 (11.1)	0.966 [0.818, 1.140] 0.6797	0.961 [0.798, 1.159] 0.6797	-0.381 [-2.188, 1.426] 0.6796
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.4 Treatment Emergent Adverse Events Leading to Treatment Discontinuation — Overall

##### 4.4.3.1.4.1 Subgrouped by Sex

**Table 266:** Proportion of Patients with Treatment Emergent Adverse Events Leading to Treatment Discontinuation, Subgrouped by Sex (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Sex</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7402</b>					
<b>Male</b>	123/1,867 (6.6)	126/1,917 (6.6)	1.002 [0.788, 1.274] 0.9848	1.002 [0.775, 1.296] 0.9848	0.015 [-1.565, 1.595] 0.9848
<b>Female</b>	43/463 (9.3)	43/429 (10.0)	0.927 [0.620, 1.385] 0.7098	0.919 [0.589, 1.434] 0.7099	-0.736 [-4.617, 3.145] 0.7101
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.4.2 Subgrouped by Age Group

**Table 267:** Proportion of Patients with Treatment Emergent Adverse Events Leading to Treatment Discontinuation, Subgrouped by Age Group (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Age</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7854</b>					
<b>&lt; 60 Years</b>	60/1,133 (5.3)	64/1,149 (5.6)	0.951 [0.675, 1.339] 0.7725	0.948 [0.660, 1.362] 0.7725	-0.274 [-2.134, 1.585] 0.7725
<b>≥ 60 Years</b>	106/1,197 (8.9)	105/1,197 (8.8)	1.010 [0.780, 1.306] 0.9425	1.010 [0.762, 1.340] 0.9425	0.084 [-2.188, 2.355] 0.9425
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.4.3 Subgrouped by Smoking Status

**Table 268:** Proportion of Patients with Treatment Emergent Adverse Events Leading to Treatment Discontinuation, Subgrouped by Smoking Status (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,344)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Smoking Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.5723</b>					
<b>Non</b>	55/775 (7.1)	54/788 (6.9)	1.036 [0.721, 1.488] 0.8498	1.038 [0.703, 1.533] 0.8498	0.244 [-2.282, 2.770] 0.8498
<b>Ex</b>	61/860 (7.1)	71/867 (8.2)	0.866 [0.623, 1.203] 0.3918	0.856 [0.600, 1.222] 0.3917	-1.096 [-3.601, 1.409] 0.3911
<b>Current</b>	50/695 (7.2)	44/689 (6.4)	1.127 [0.762, 1.666] 0.5505	1.136 [0.747, 1.729] 0.5504	0.808 [-1.842, 3.458] 0.5500
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.4.4 Subgrouped by Region

**Table 269:** Proportion of Patients with Treatment Emergent Adverse Events Leading to Treatment Discontinuation, Subgrouped by Region (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Region</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.4775</b>					
<b>Europe</b>	84/988 (8.5)	93/1,011 (9.2)	0.924 [0.697, 1.225] 0.5836	0.917 [0.673, 1.249] 0.5836	-0.697 [-3.186, 1.793] 0.5833
<b>Non-Europe</b>	82/1,342 (6.1)	76/1,335 (5.7)	1.073 [0.793, 1.453] 0.6469	1.078 [0.782, 1.487] 0.6469	0.417 [-1.368, 2.203] 0.6468
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.4.5 Subgrouped by White Blood Cell Count

**Table 270:** Proportion of Patients with Treatment Emergent Adverse Events Leading to Treatment Discontinuation, Subgrouped by White Blood Cell Count (Safety Population).

Subgroup	Colchicine + SoC (N = 1,293)	Placebo + SoC (N = 1,300)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>White Blood Cell Count</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.1585</b>					
< 8.66 10 <sup>3</sup> /μL	39/660 (5.9)	46/634 (7.3)	0.814 [0.539, 1.230] 0.3294	0.803 [0.516, 1.248] 0.3292	-1.346 [-4.051, 1.358] 0.3291
≥ 8.66 10 <sup>3</sup> /μL	48/633 (7.6)	41/666 (6.2)	1.232 [0.824, 1.842] 0.3099	1.251 [0.812, 1.926] 0.3098	1.427 [-1.327, 4.181] 0.3099
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.4.6 Subgrouped by Diabetes Status

**Table 271:** Proportion of Patients with Treatment Emergent Adverse Events Leading to Treatment Discontinuation, Subgrouped by Diabetes Status (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Diabetes Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.3695</b>					
<b>Yes</b>	38/451 (8.4)	35/492 (7.1)	1.184 [0.762, 1.841] 0.4520	1.201 [0.745, 1.938] 0.4519	1.312 [-2.113, 4.737] 0.4528
<b>No</b>	128/1,879 (6.8)	134/1,854 (7.2)	0.943 [0.746, 1.191] 0.6194	0.938 [0.730, 1.206] 0.6193	-0.415 [-2.055, 1.224] 0.6194
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.4.7 Subgrouped by Hypertension Status

**Table 272:** Proportion of Patients with Treatment Emergent Adverse Events Leading to Treatment Discontinuation, Subgrouped by Hypertension Status (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>Hypertension Status</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.7277</b>					
<b>Yes</b>	87/1,163 (7.5)	89/1,220 (7.3)	1.025 [0.772, 1.363] 0.8625	1.027 [0.756, 1.397] 0.8625	0.186 [-1.916, 2.287] 0.8626
<b>No</b>	79/1,167 (6.8)	80/1,126 (7.1)	0.953 [0.706, 1.286] 0.7520	0.949 [0.688, 1.310] 0.7520	-0.335 [-2.416, 1.745] 0.7521
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### **4.4.3.1.4.8 Subgrouped by History of Myocardial Infarction**

Due to a significant interaction term, the data is presented in Module 4A.

#### 4.4.3.1.4.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 273:** Proportion of Patients with Treatment Emergent Adverse Events Leading to Treatment Discontinuation, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of PCI or CABG</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.0734</b>					
<b>Yes</b>	30/410 (7.3)	21/444 (4.7)	1.547 [0.900, 2.658] 0.1141	1.590 [0.895, 2.825] 0.1136	2.587 [-0.615, 5.789] 0.1133
<b>No</b>	136/1,920 (7.1)	148/1,902 (7.8)	0.910 [0.728, 1.139] 0.4109	0.903 [0.709, 1.151] 0.4109	-0.698 [-2.361, 0.965] 0.4108
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.1.4.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 274:** Proportion of Patients with Treatment Emergent Adverse Events Leading to Treatment Discontinuation, Subgrouped by History of Stroke or Transient Ischaemic Attack (Safety Population).

Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
	n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> [95 %-CI] p-Value	OR <sup>c</sup> [95 %-CI] p-Value	RD <sup>c</sup> [95 %-CI] p-Value
<b>History of Stroke or TIA</b>					
<b>Interaction Test p-Value<sup>d</sup> = 0.8874</b>					
<b>Yes</b>	6/53 (11.3)	7/66 (10.6)	1.067 [0.382, 2.986] 0.9011	1.076 [0.339, 3.418] 0.9012	0.715 [-10.597, 12.026] 0.9014
<b>No</b>	160/2,277 (7.0)	162/2,280 (7.1)	0.989 [0.801, 1.221] 0.9177	0.988 [0.788, 1.239] 0.9177	-0.078 [-1.567, 1.410] 0.9177
Database lock: 28-08-2019					
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.					
Study: COLCOT					

#### 4.4.3.2 Treatment Emergent Adverse Events — Stratified by MedDRA System Organ Class and Preferred Term

##### 4.4.3.2.1 Treatment Emergent Adverse Events — Occurring in $\geq 1\%$ of Participants in Either Study Arm

###### 4.4.3.2.1.1 Subgrouped by Sex

**Table 275:** Proportion of Patients with Treatment Emergent Adverse Events Occurring in  $\geq 1\%$  of Participants in Either Study Arm, Stratified by MedDRA System Organ Class and Preferred Term, Subgrouped by Sex (Safety Population).

Preferred Terms	Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
		n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> (SE) [95 %-CI] p-Value	OR <sup>c</sup> (SE) [95 %-CI] p-Value	RD <sup>c</sup> (SE) [95 %-CI] p-Value
<b>Sex</b>						
<b>Cardiac disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.6360</b>						
<b>Any PT meeting criteria</b>	<b>Male</b>	148/1,867 (7.9)	187/1,917 (9.8)	0.813 [0.661, 0.999] 0.0484	0.797 [0.636, 0.998] 0.0482	-1.828 [-3.635, -0.021] 0.0475
	<b>Female</b>	45/463 (9.7)	46/429 (10.7)	0.906 [0.614, 1.338] 0.6209	0.896 [0.581, 1.383] 0.6209	-1.003 [-4.985, 2.978] 0.6213
<b>Gastrointestinal disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.9337</b>						
<b>Nausea</b>	<b>Male</b>	30/1,867 (1.6)	17/1,917 (0.9)	1.812 [1.003, 3.274] 0.0489	1.825 [1.003, 3.321] 0.0488	0.720 [0.012, 1.428] 0.0463
	<b>Female</b>	13/463 (2.8)	7/429 (1.6)	1.721 [0.693, 4.272] 0.2421	1.742 [0.688, 4.407] 0.2415	1.176 [-0.748, 3.100] 0.2309
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.						
Study: COLCOT						

#### 4.4.3.2.1.2 Subgrouped by Age Group

**Table 276:** Proportion of Patients with Treatment Emergent Adverse Events Occurring in  $\geq 1\%$  of Participants in Either Study Arm, Stratified by MedDRA System Organ Class and Preferred Term, Subgrouped by Age Group (Safety Population).

Preferred Terms	Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
		n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> (SE) [95 %-CI] p-Value	OR <sup>c</sup> (SE) [95 %-CI] p-Value	RD <sup>c</sup> (SE) [95 %-CI] p-Value
<b>Age</b>						
<b>Cardiac disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.1662</b>						
<b>Any PT meeting criteria</b>	<b>&lt; 60 Years</b>	91/1,133 (8.0)	96/1,149 (8.4)	0.961 [0.730, 1.265] 0.7783	0.958 [0.710, 1.292] 0.7783	-0.323 [-2.574, 1.927] 0.7783
	<b><math>\geq 60</math> Years</b>	102/1,197 (8.5)	137/1,197 (11.4)	0.745 [0.584, 0.950] 0.0176	0.721 [0.550, 0.944] 0.0174	-2.924 [-5.323, -0.525] 0.0169
<b>Gastrointestinal disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.7698</b>						
<b>Nausea</b>	<b>&lt; 60 Years</b>	18/1,133 (1.6)	11/1,149 (1.0)	1.659 [0.787, 3.498] 0.1830	1.670 [0.785, 3.552] 0.1828	0.631 [-0.289, 1.552] 0.1788
	<b><math>\geq 60</math> Years</b>	25/1,197 (2.1)	13/1,197 (1.1)	1.923 [0.989, 3.741] 0.0541	1.943 [0.989, 3.816] 0.0538	1.003 [0.002, 2.003] 0.0495
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.						
Study: COLCOT						

#### 4.4.3.2.1.3 Subgrouped by Smoking Status

**Table 277:** Proportion of Patients with Treatment Emergent Adverse Events Occurring in  $\geq$  1% of Participants in Either Study Arm, Stratified by MedDRA System Organ Class and Preferred Term, Subgrouped by Smoking Status (Safety Population).

Preferred Terms	Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,344)	Colchicine + SoC vs. Placebo + SoC		
		n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> (SE) [95 %-CI] p-Value	OR <sup>c</sup> (SE) [95 %-CI] p-Value	RD <sup>c</sup> (SE) [95 %-CI] p-Value
<b>Smoking Status</b>						
<b>Cardiac disorders:</b> Due to a significant interaction term, the data is presented in Module 4A.						
<b>Gastrointestinal disorders</b>						
				<b>Interaction Test p-Value<sup>d</sup> = 0.0959</b>		
	<b>Non</b>	12/775 (1.5)	7/788 (0.9)	1.743 [0.690, 4.404] 0.2400	1.755 [0.687, 4.481] 0.2397	0.660 [-0.428, 1.749] 0.2346
<b>Nausea</b>	<b>Ex</b>	24/860 (2.8)	8/867 (0.9)	3.024 [1.366, 6.695] 0.0063	3.083 [1.377, 6.900] 0.0062	1.868 [0.596, 3.140] 0.0040
	<b>Current</b>	7/695 (1.0)	9/689 (1.3)	0.771 [0.289, 2.059] 0.6039	0.769 [0.285, 2.076] 0.6038	-0.299 [-1.426, 0.828] 0.6030
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.						
Study: COLCOT						

#### 4.4.3.2.1.4 Subgrouped by Region

**Table 278:** Proportion of Patients with Treatment Emergent Adverse Events Occurring in  $\geq$  1% of Participants in Either Study Arm, Stratified by MedDRA System Organ Class and Preferred Term, Subgrouped by Region (Safety Population).

Preferred Terms	Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
		n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> (SE) [95 %-CI] p-Value	OR <sup>c</sup> (SE) [95 %-CI] p-Value	RD <sup>c</sup> (SE) [95 %-CI] p-Value
<b>Region</b>						
<b>Cardiac disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.1791</b>						
<b>Any PT meeting criteria</b>	<b>Europe</b>	91/988 (9.2)	97/1,011 (9.6)	0.960 [0.731, 1.260] 0.7688	0.956 [0.708, 1.291] 0.7688	-0.384 [-2.943, 2.175] 0.7687
	<b>Non-Europe</b>	102/1,342 (7.6)	136/1,335 (10.2)	0.746 [0.584, 0.953] 0.0193	0.725 [0.554, 0.949] 0.0191	-2.587 [-4.741, -0.432] 0.0186
<b>Gastrointestinal disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.5271</b>						
<b>Nausea</b>	<b>Europe</b>	11/988 (1.1)	8/1,011 (0.8)	1.407 [0.568, 3.483] 0.4603	1.412 [0.565, 3.524] 0.4603	0.322 [-0.530, 1.174] 0.4589
	<b>Non-Europe</b>	32/1,342 (2.4)	16/1,335 (1.2)	1.990 [1.097, 3.608] 0.0235	2.014 [1.100, 3.688] 0.0233	1.186 [0.182, 2.190] 0.0205
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.						
Study: COLCOT						

#### 4.4.3.2.1.5 Subgrouped by White Blood Cell Count

**Table 279:** Proportion of Patients with Treatment Emergent Adverse Events Occurring in  $\geq 1\%$  of Participants in Either Study Arm, Stratified by MedDRA System Organ Class and Preferred Term, Subgrouped by White Blood Cell Count (Safety Population).

Preferred Terms	Subgroup	Colchicine + SoC (N = 1,293)	Placebo + SoC (N = 1,300)	Colchicine + SoC vs. Placebo + SoC		
		n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> (SE) [95 %-CI] p-Value	OR <sup>c</sup> (SE) [95 %-CI] p-Value	RD <sup>c</sup> (SE) [95 %-CI] p-Value
<b>White Blood Cell Count</b>						
<b>Cardiac disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.7936</b>						
<b>Any PT meeting criteria</b>	< 8.66 10 <sup>3</sup> /μL	67/660 (10.2)	68/634 (10.7)	0.946 [0.688, 1.303] 0.7356	0.940 [0.658, 1.343] 0.7356	-0.574 [-3.907, 2.759] 0.7357
	≥ 8.66 10 <sup>3</sup> /μL	54/633 (8.5)	64/666 (9.6)	0.888 [0.628, 1.254] 0.4993	0.877 [0.600, 1.282] 0.4991	-1.079 [-4.201, 2.043] 0.4982
<b>Gastrointestinal disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.6129</b>						
<b>Nausea</b>	< 8.66 10 <sup>3</sup> /μL	12/660 (1.8)	10/634 (1.6)	1.153 [0.502, 2.649] 0.7378	1.156 [0.496, 2.694] 0.7378	0.241 [-1.166, 1.648] 0.7372
	≥ 8.66 10 <sup>3</sup> /μL	12/633 (1.9)	8/666 (1.2)	1.578 [0.649, 3.835] 0.3139	1.589 [0.645, 3.914] 0.3137	0.695 [-0.652, 2.041] 0.3120
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.						
Study: COLCOT						

#### 4.4.3.2.1.6 Subgrouped by Diabetes Status

**Table 280:** Proportion of Patients with Treatment Emergent Adverse Events Occurring in  $\geq$  1% of Participants in Either Study Arm, Stratified by MedDRA System Organ Class and Preferred Term, Subgrouped by Diabetes Status (Safety Population).

Preferred Terms	Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
		n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> (SE) [95 %-CI] p-Value	OR <sup>c</sup> (SE) [95 %-CI] p-Value	RD <sup>c</sup> (SE) [95 %-CI] p-Value
<b>Diabetes Status</b>						
<b>Cardiac disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.6076</b>						
<b>Any PT meeting criteria</b>	<b>Yes</b>	56/451 (12.4)	67/492 (13.6)	0.912 [0.655, 1.270] 0.5847	0.899 [0.615, 1.316] 0.5845	-1.201 [-5.496, 3.094] 0.5836
	<b>No</b>	137/1,879 (7.3)	166/1,854 (9.0)	0.814 [0.656, 1.012] 0.0635	0.800 [0.632, 1.013] 0.0634	-1.663 [-3.415, 0.090] 0.0630
<b>Gastrointestinal disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.2175</b>						
<b>Nausea</b>	<b>Yes</b>	12/451 (2.7)	4/492 (0.8)	3.273 [1.063, 10.074] 0.0388	3.335 [1.068, 10.416] 0.0382	1.848 [0.164, 3.532] 0.0315
	<b>No</b>	31/1,879 (1.6)	20/1,854 (1.1)	1.529 [0.875, 2.673] 0.1359	1.538 [0.874, 2.709] 0.1358	0.571 [-0.172, 1.315] 0.1322
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.						
Study: COLCOT						

#### 4.4.3.2.1.7 Subgrouped by Hypertension Status

**Table 281:** Proportion of Patients with Treatment Emergent Adverse Events Occurring in  $\geq 1\%$  of Participants in Either Study Arm, Stratified by MedDRA System Organ Class and Preferred Term, Subgrouped by Hypertension Status (Safety Population).

Preferred Terms	Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
		n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> (SE) [95 %-CI] p-Value	OR <sup>c</sup> (SE) [95 %-CI] p-Value	RD <sup>c</sup> (SE) [95 %-CI] p-Value
<b>Hypertension Status</b>						
<b>Cardiac disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.9709</b>						
<b>Any PT meeting criteria</b>	<b>Yes</b>	118/1,163 (10.1)	147/1,220 (12.0)	0.842 [0.670, 1.058] 0.1404	0.824 [0.638, 1.066] 0.1401	-1.903 [-4.423, 0.617] 0.1388
	<b>No</b>	75/1,167 (6.4)	86/1,126 (7.6)	0.841 [0.624, 1.134] 0.2572	0.831 [0.602, 1.145] 0.2571	-1.211 [-3.305, 0.883] 0.2571
<b>Gastrointestinal disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.4411</b>						
<b>Nausea</b>	<b>Yes</b>	23/1,163 (2.0)	11/1,220 (0.9)	2.193 [1.074, 4.479] 0.0311	2.217 [1.076, 4.570] 0.0309	1.076 [0.116, 2.036] 0.0280
	<b>No</b>	20/1,167 (1.7)	13/1,126 (1.2)	1.484 [0.742, 2.970] 0.2642	1.493 [0.739, 3.016] 0.2640	0.559 [-0.412, 1.531] 0.2592
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.						
Study: COLCOT						

#### 4.4.3.2.1.8 Subgrouped by History of Myocardial Infarction

**Table 282:** Proportion of Patients with Treatment Emergent Adverse Events Occurring in  $\geq$  1% of Participants in Either Study Arm, Stratified by MedDRA System Organ Class and Preferred Term, Subgrouped by History of Myocardial Infarction (Safety Population).

Preferred Terms	Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
		n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> (SE) [95 %-CI] p-Value	OR <sup>c</sup> (SE) [95 %-CI] p-Value	RD <sup>c</sup> (SE) [95 %-CI] p-Value
<b>History of MI</b>						
<b>Cardiac disorders:</b> Due to a significant interaction term, the data is presented in Module 4A.						
<b>Gastrointestinal disorders</b>						
				<b>Interaction Test p-Value<sup>d</sup> = 0.5837</b>		
	<b>Yes</b>	7/362 (1.9)	3/393 (0.8)	2.533 [0.660, 9.722] 0.1756	2.563 [0.658, 9.989] 0.1749	1.170 [-0.489, 2.829] 0.1668
	<b>No</b>	36/1,968 (1.8)	21/1,953 (1.1)	1.701 [0.997, 2.903] 0.0514	1.714 [0.997, 2.947] 0.0512	0.754 [0.006, 1.502] 0.0482
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.						
Study: COLCOT						

#### 4.4.3.2.1.9 Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft

**Table 283:** Proportion of Patients with Treatment Emergent Adverse Events Occurring in  $\geq$  1% of Participants in Either Study Arm, Stratified by MedDRA System Organ Class and Preferred Term, Subgrouped by History of Percutaneous Coronary Intervention or Coronary Artery Bypass Graft (Safety Population).

Preferred Terms	Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
		n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> (SE) [95 %-CI] p-Value	OR <sup>c</sup> (SE) [95 %-CI] p-Value	RD <sup>c</sup> (SE) [95 %-CI] p-Value
<b>History of PCI or CABG</b>						
<b>Cardiac disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.5124</b>						
<b>Any PT meeting criteria</b>	<b>Yes</b>	56/410 (13.7)	65/444 (14.6)	0.933 [0.670, 1.299] 0.6814	0.922 [0.627, 1.356] 0.6813	-0.981 [-5.657, 3.694] 0.6809
	<b>No</b>	137/1,920 (7.1)	168/1,902 (8.8)	0.808 [0.651, 1.003] 0.0534	0.793 [0.627, 1.003] 0.0533	-1.697 [-3.416, 0.021] 0.0528
<b>Gastrointestinal disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.2235</b>						
<b>Nausea</b>	<b>Yes</b>	12/410 (2.9)	4/444 (0.9)	3.249 [1.056, 9.993] 0.0398	3.317 [1.061, 10.367] 0.0392	2.026 [0.173, 3.879] 0.0321
	<b>No</b>	31/1,920 (1.6)	20/1,902 (1.1)	1.535 [0.878, 2.684] 0.1324	1.544 [0.877, 2.719] 0.1322	0.563 [-0.164, 1.290] 0.1288
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.						
Study: COLCOT						

#### 4.4.3.2.1.10 Subgrouped by History of Stroke or Transient Ischaemic Attack

**Table 284:** Proportion of Patients with Treatment Emergent Adverse Events Occurring in  $\geq 1\%$  of Participants in Either Study Arm, Stratified by MedDRA System Organ Class and Preferred Term, Subgrouped by History of Stroke or Transient Ischaemic Attack (Safety Population).

Preferred Terms	Subgroup	Colchicine + SoC (N = 2,330)	Placebo + SoC (N = 2,346)	Colchicine + SoC vs. Placebo + SoC		
		n <sup>a</sup> /N <sup>b</sup> (%)	n <sup>a</sup> /N <sup>b</sup> (%)	RR <sup>c</sup> (SE) [95 %-CI] p-Value	OR <sup>c</sup> (SE) [95 %-CI] p-Value	RD <sup>c</sup> (SE) [95 %-CI] p-Value
<b>History of Stroke or TIA</b>						
<b>Cardiac disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.0959</b>						
<b>Any PT meeting criteria</b>	<b>Yes</b>	8/53 (15.1)	5/66 (7.6)	1.992 [0.692, 5.735] 0.2013	2.169 [0.665, 7.072] 0.1992	7.519 [-4.042, 19.079] 0.2024
	<b>No</b>	185/2,277 (8.1)	228/2,280 (10.0)	0.812 [0.675, 0.978] 0.0278	0.796 [0.649, 0.975] 0.0277	-1.875 [-3.541, -0.209] 0.0274
<b>Gastrointestinal disorders</b>						
<b>Interaction Test p-Value<sup>d</sup> = 0.7891</b>						
<b>Nausea</b>	<b>Yes</b>	1/53 (1.9)	1/66 (1.5)	1.245 [0.080, 19.443] 0.8757	1.250 [0.076, 20.467] 0.8757	0.372 [-4.330, 5.073] 0.8769
	<b>No</b>	42/2,277 (1.8)	23/2,280 (1.0)	1.828 [1.103, 3.030] 0.0192	1.844 [1.105, 3.076] 0.0191	0.836 [0.148, 1.524] 0.0173
Database lock: 28-08-2019						
<sup>a</sup> Number of patients with the event. <sup>b</sup> Number of patients in the study population. <sup>c</sup> OR, RR and RD two-sided 95 %-CI and p-value were calculated using the normal approximation. An OR or RR < 1 and an RD < 0 favour Colchicine + SoC. <sup>d</sup> Interaction significance assessed via a likelihood ratio test comparing model fits with and without the addition of a treatment x subgroup interaction term.						
Study: COLCOT						

#### **4.4.3.2.2 Serious Treatment Emergent Adverse Events — Occurring in $\geq 5\%$ of Participants in Either Study Arm**

No MedDRA preferred terms associated with serious treatment emergent adverse events met the 5% threshold. Hence, no subgroup analyses were possible for this outcome.

#### **4.4.3.2.3 Severe Treatment Emergent Adverse Events — Occurring in $\geq 5\%$ of Participants in Either Study Arm**

No MedDRA preferred terms associated with severe treatment emergent adverse events met the 5% threshold. Hence, no subgroup analyses were possible for this outcome.

#### **4.4.3.2.4 Treatment Emergent Adverse Events Leading to Treatment Discontinuation — Stratified by Reason for Discontinuation**

The reasons for treatment discontinuation from the study were not collected in the electronic case report form beyond attribution to an adverse event.