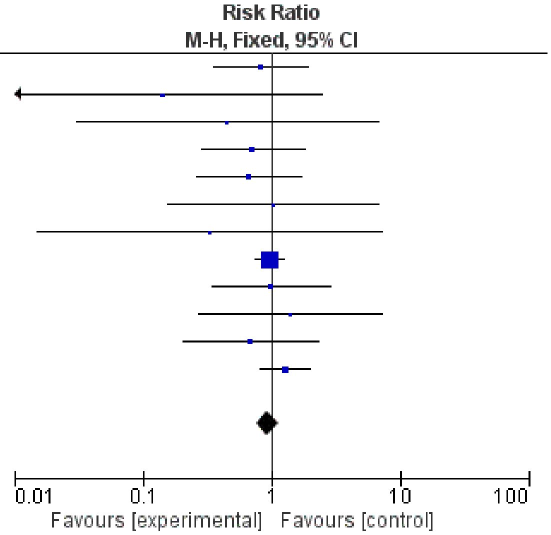
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Assmus 2014	9	101	11	103	8.0%	0.83 [0.36, 1.93]
Chullikana 2015	0	10	3	10	2.6%	0.14 [0.01, 2.45]
Grajek 2010	1	31	1	14	1.0%	0.45 [0.03, 6.71]
Hare 2009	8	39	6	21	5.8%	0.72 [0.29, 1.79]
Huikuri 2008	6	40	9	40	6.6%	0.67 [0.26, 1.70]
Janssens 2006	2	33	2	34	1.5%	1.03 [0.15, 6.89]
Laguna 2018	0	10	1	10	1.1%	0.33 [0.02, 7.32]
Mathur A 2020	57	161	78	214	49.4%	0.97 [0.74, 1.28]
Piepoli MF 2010	5	19	5	19	3.7%	1.00 [0.35, 2.90]
Quyyumi 2011	3	16	2	15	1.5%	1.41 [0.27, 7.28]
Roman 2015	4	59	6	61	4.4%	0.69 [0.20, 2.32]
Roncalli 2011	26	52	19	49	14.4%	1.29 [0.83, 2.01]
Total (95% CI)		**571**		**590**	**100.0%**	**0.93 [0.76, 1.14]**
Total events	121		143			

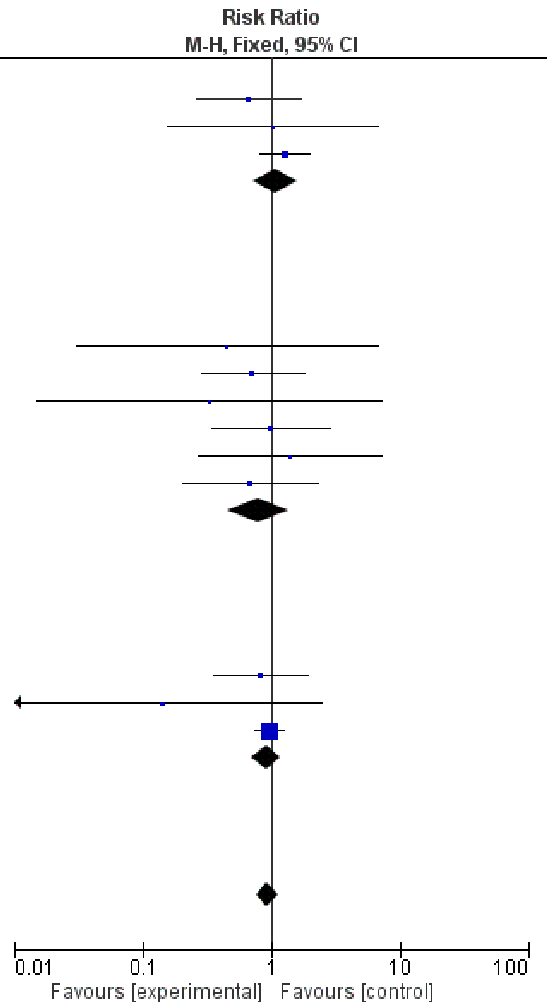
Heterogeneity: Chi² = 5.87, df = 11 (P = 0.88); I² = 0%

Test for overall effect: Z = 0.66 (P = 0.51)



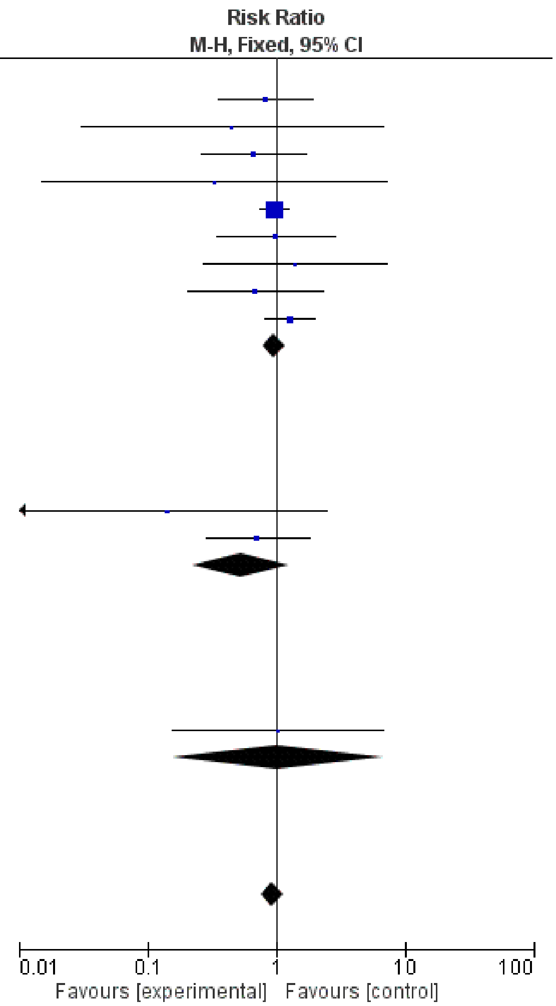
Supplementary Fig. 2A. This Forest plot summarizes the overall incidence of serious adverse events reported in the stem cell therapy group in comparison with thecontrol.

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.26.1 time of assessment upto 6 months						
Huikuri 2008	6	40	9	40	6.6%	0.67 [0.26, 1.70]
Janssens 2006	2	33	2	34	1.5%	1.03 [0.15, 6.89]
Roncalli 2011	26	52	19	49	14.4%	1.29 [0.83, 2.01]
Subtotal (95% CI)		**125**		**123**	**22.5%**	**1.09 [0.73, 1.62]**
Total events	34		30			
Heterogeneity: Chi² = 1.62, df = 2 (P = 0.45); I² = 0%						
Test for overall effect: Z = 0.42 (P = 0.67)						
1.26.2 time of assessment upto 12 months						
Grajek 2010	1	31	1	14	1.0%	0.45 [0.03, 6.71]
Hare 2009	8	39	6	21	5.8%	0.72 [0.29, 1.79]
Laguna 2018	0	10	1	10	1.1%	0.33 [0.02, 7.32]
Piepoli MF 2010	5	19	5	19	3.7%	1.00 [0.35, 2.90]
Quyyumi 2011	3	16	2	15	1.5%	1.41 [0.27, 7.28]
Roman 2015	4	59	6	61	4.4%	0.69 [0.20, 2.32]
Subtotal (95% CI)		**174**		**140**	**17.4%**	**0.79 [0.46, 1.36]**
Total events	21		21			
Heterogeneity: Chi² = 1.22, df = 5 (P = 0.94); I² = 0%						
Test for overall effect: Z = 0.85 (P = 0.40)						
1.26.3 time of assessment more than 12 months						
Assmus 2014	9	101	11	103	8.0%	0.83 [0.36, 1.93]
Chullikana 2015	0	10	3	10	2.6%	0.14 [0.01, 2.45]
Mathur A 2020	57	161	78	214	49.4%	0.97 [0.74, 1.28]
Subtotal (95% CI)		**272**		**327**	**60.0%**	**0.92 [0.71, 1.19]**
Total events	66		92			
Heterogeneity: Chi² = 1.86, df = 2 (P = 0.39); I² = 0%						
Test for overall effect: Z = 0.65 (P = 0.52)						
Total (95% CI)		**571**		**590**	**100.0%**	**0.93 [0.76, 1.14]**
Total events	121		143			
Heterogeneity: Chi² = 5.87, df = 11 (P = 0.88); I² = 0%						
Test for overall effect: Z = 0.66 (P = 0.51)						
Test for subgroup differences: Chi² = 0.96, df = 2 (P = 0.62), I² = 0%						



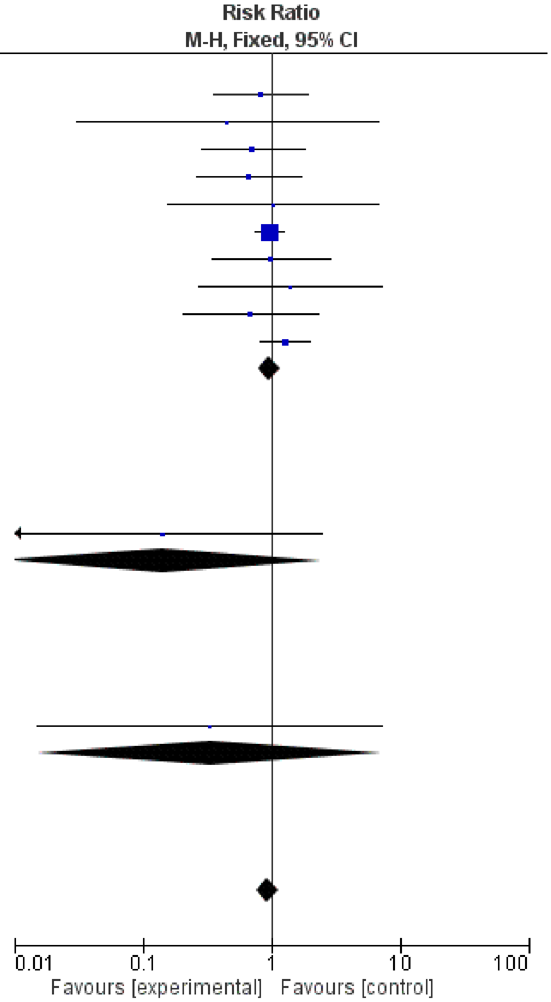
Supplementary Fig. 2B. This forest plot displays a subgroup analysis of serious adverse events incidence based on the time of assessment.

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.27.1 Mononuclear						
Assmus 2014	9	101	11	103	8.0%	0.83 [0.36, 1.93]
Grajek 2010	1	31	1	14	1.0%	0.45 [0.03, 6.71]
Huikuri 2008	6	40	9	40	6.6%	0.67 [0.26, 1.70]
Laguna 2018	0	10	1	10	1.1%	0.33 [0.02, 7.32]
Mathur A 2020	57	161	78	214	49.4%	0.97 [0.74, 1.28]
Piepoli MF 2010	5	19	5	19	3.7%	1.00 [0.35, 2.90]
Quyyumi 2011	3	16	2	15	1.5%	1.41 [0.27, 7.28]
Roman 2015	4	59	6	61	4.4%	0.69 [0.20, 2.32]
Roncalli 2011	26	52	19	49	14.4%	1.29 [0.83, 2.01]
Subtotal (95% CI)		**489**		**525**	**90.2%**	**0.97 [0.79, 1.19]**
Total events	111		132			
Heterogeneity: Chi² = 3.59, df = 8 (P = 0.89); I² = 0%						
Test for overall effect: Z = 0.30 (P = 0.77)						
1.27.2 Mesenchymal						
Chullikana 2015	0	10	3	10	2.6%	0.14 [0.01, 2.45]
Hare 2009	8	39	6	21	5.8%	0.72 [0.29, 1.79]
Subtotal (95% CI)		**49**		**31**	**8.3%**	**0.54 [0.23, 1.27]**
Total events	8		9			
Heterogeneity: Chi² = 1.21, df = 1 (P = 0.27); I² = 18%						
Test for overall effect: Z = 1.41 (P = 0.16)						
1.27.3 Both						
Janssens 2006	2	33	2	34	1.5%	1.03 [0.15, 6.89]
Subtotal (95% CI)		**33**		**34**	**1.5%**	**1.03 [0.15, 6.89]**
Total events	2		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.03 (P = 0.98)						
Total (95% CI)		**571**		**590**	**100.0%**	**0.93 [0.76, 1.14]**
Total events	121		143			
Heterogeneity: Chi² = 5.87, df = 11 (P = 0.88); I² = 0%						
Test for overall effect: Z = 0.66 (P = 0.51)						
Test for subgroup differences: Chi² = 1.69, df = 2 (P = 0.43), I² = 0%						



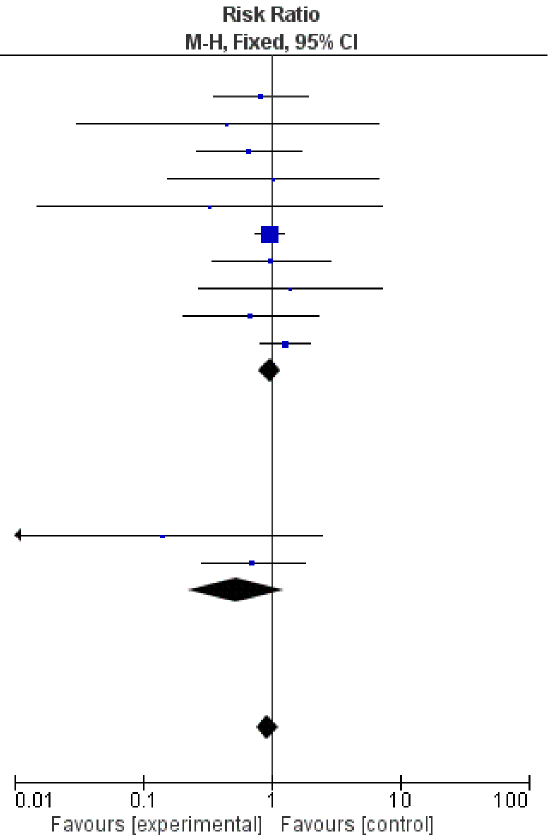
Supplementary Fig. 2C. This forest plot displays a subgroup analysis of serious adverse events incidence based on the type of cells administered.

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.28.1 Intracoronary						
Assmus 2014	9	101	11	103	8.0%	0.83 [0.36, 1.93]
Grajek 2010	1	31	1	14	1.0%	0.45 [0.03, 6.71]
Hare 2009	8	39	6	21	5.8%	0.72 [0.29, 1.79]
Huikuri 2008	6	40	9	40	6.6%	0.67 [0.26, 1.70]
Janssens 2006	2	33	2	34	1.5%	1.03 [0.15, 6.89]
Mathur A 2020	57	161	78	214	49.4%	0.97 [0.74, 1.28]
Piepoli MF 2010	5	19	5	19	3.7%	1.00 [0.35, 2.90]
Quyyumi 2011	3	16	2	15	1.5%	1.41 [0.27, 7.28]
Roman 2015	4	59	6	61	4.4%	0.69 [0.20, 2.32]
Roncalli 2011	26	52	19	49	14.4%	1.29 [0.83, 2.01]
Subtotal (95% CI)		**551**		**570**	**96.3%**	**0.96 [0.79, 1.18]**
Total events	121		139			
Heterogeneity: Chi² = 3.57, df = 9 (P = 0.94); I² = 0%						
Test for overall effect: Z = 0.37 (P = 0.71)						
1.28.2 anticubital vein of forearm						
Chullikana 2015	0	10	3	10	2.6%	0.14 [0.01, 2.45]
Subtotal (95% CI)		**10**		**10**	**2.6%**	**0.14 [0.01, 2.45]**
Total events	0		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.34 (P = 0.18)						
1.28.3 direct intramyocardia						
Laguna 2018	0	10	1	10	1.1%	0.33 [0.02, 7.32]
Subtotal (95% CI)		**10**		**10**	**1.1%**	**0.33 [0.02, 7.32]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.70 (P = 0.49)						
Total (95% CI)		**571**		**590**	**100.0%**	**0.93 [0.76, 1.14]**
Total events	121		143			
Heterogeneity: Chi² = 5.87, df = 11 (P = 0.88); I² = 0%						
Test for overall effect: Z = 0.66 (P = 0.51)						
Test for subgroup differences: Chi² = 2.16, df = 2 (P = 0.34), I² = 7.5%						



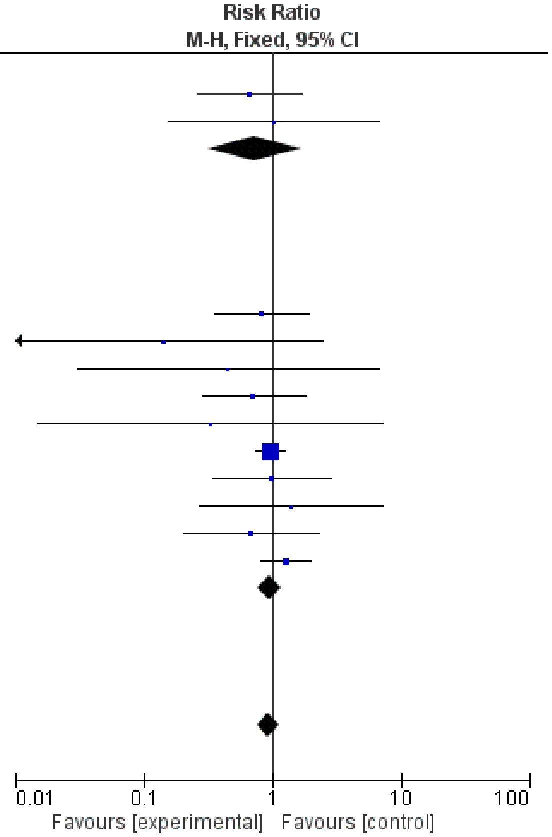
Supplementary Fig. 2D. This forest plot displays a subgroup analysis of serious adverse eventsincidence based on route of administration.

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.29.1 Autologous						
Assmus 2014	9	101	11	103	8.0%	0.83 [0.36, 1.93]
Grajek 2010	1	31	1	14	1.0%	0.45 [0.03, 6.71]
Huikuri 2008	6	40	9	40	6.6%	0.67 [0.26, 1.70]
Janssens 2006	2	33	2	34	1.5%	1.03 [0.15, 6.89]
Laguna 2018	0	10	1	10	1.1%	0.33 [0.02, 7.32]
Mathur A 2020	57	161	78	214	49.4%	0.97 [0.74, 1.28]
Piepoli MF 2010	5	19	5	19	3.7%	1.00 [0.35, 2.90]
Quyyumi 2011	3	16	2	15	1.5%	1.41 [0.27, 7.28]
Roman 2015	4	59	6	61	4.4%	0.69 [0.20, 2.32]
Roncalli 2011	26	52	19	49	14.4%	1.29 [0.83, 2.01]
Subtotal (95% CI)		**522**		**559**	**91.7%**	**0.97 [0.79, 1.19]**
Total events	113		134			
Heterogeneity: Chi² = 3.59, df = 9 (P = 0.94); I² = 0%						
Test for overall effect: Z = 0.29 (P = 0.77)						
1.29.2 Allogeneic						
Chullikana 2015	0	10	3	10	2.6%	0.14 [0.01, 2.45]
Hare 2009	8	39	6	21	5.8%	0.72 [0.29, 1.79]
Subtotal (95% CI)		**49**		**31**	**8.3%**	**0.54 [0.23, 1.27]**
Total events	8		9			
Heterogeneity: Chi² = 1.21, df = 1 (P = 0.27); I² = 18%						
Test for overall effect: Z = 1.41 (P = 0.16)						
Total (95% CI)		**571**		**590**	**100.0%**	**0.93 [0.76, 1.14]**
Total events	121		143			
Heterogeneity: Chi² = 5.87, df = 11 (P = 0.88); I² = 0%						
Test for overall effect: Z = 0.66 (P = 0.51)						
Test for subgroup differences: Chi² = 1.69, df = 1 (P = 0.19), I² = 40.8%						



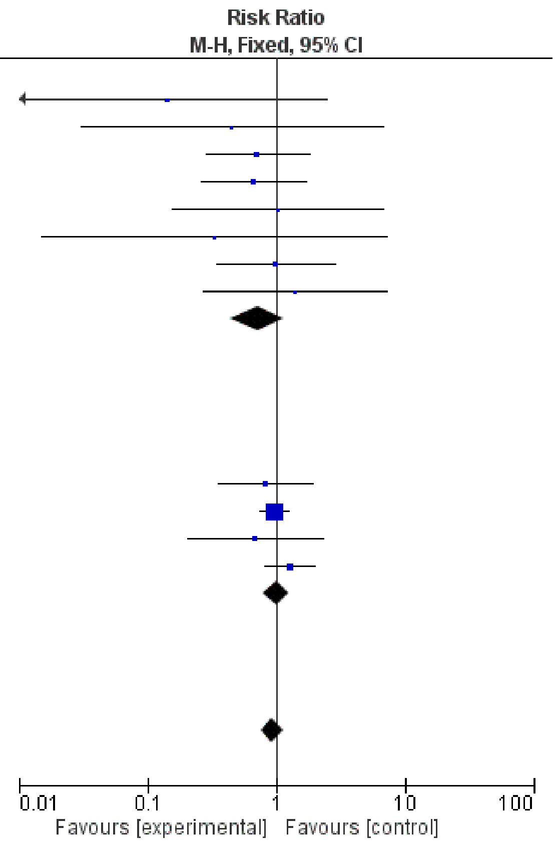
Supplementary Fig. 2E. This forest plot displays a subgroup analysis of serious adverse eventsincidencebased on autologous and allogeneic stem cell therapy.

	Intervention		Control			Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**
1.30.1 Administration < 24 hours						
Huikuri 2008	6	40	9	40	6.6%	0.67 [0.26, 1.70]
Janssens 2006	2	33	2	34	1.5%	1.03 [0.15, 6.89]
Subtotal (95% CI)		**73**		**74**	**8.1%**	**0.73 [0.32, 1.69]**
Total events	8		11			
Heterogeneity: Chi² = 0.16, df = 1 (P = 0.69); I² = 0%						
Test for overall effect: Z = 0.73 (P = 0.46)						
1.30.2 Administration 1 - 21 days						
Assmus 2014	9	101	11	103	8.0%	0.83 [0.36, 1.93]
Chullikana 2015	0	10	3	10	2.6%	0.14 [0.01, 2.45]
Grajek 2010	1	31	1	14	1.0%	0.45 [0.03, 6.71]
Hare 2009	8	39	6	21	5.8%	0.72 [0.29, 1.79]
Laguna 2018	0	10	1	10	1.1%	0.33 [0.02, 7.32]
Mathur A 2020	57	161	78	214	49.4%	0.97 [0.74, 1.28]
Piepoli MF 2010	5	19	5	19	3.7%	1.00 [0.35, 2.90]
Quyyumi 2011	3	16	2	15	1.5%	1.41 [0.27, 7.28]
Roman 2015	4	59	6	61	4.4%	0.69 [0.20, 2.32]
Roncalli 2011	26	52	19	49	14.4%	1.29 [0.83, 2.01]
Subtotal (95% CI)		**498**		**516**	**91.9%**	**0.95 [0.77, 1.17]**
Total events	113		132			
Heterogeneity: Chi² = 5.21, df = 9 (P = 0.82); I² = 0%						
Test for overall effect: Z = 0.47 (P = 0.64)						
Total (95% CI)		**571**		**590**	**100.0%**	**0.93 [0.76, 1.14]**
Total events	121		143			
Heterogeneity: Chi² = 5.87, df = 11 (P = 0.88); I² = 0%						
Test for overall effect: Z = 0.66 (P = 0.51)						
Test for subgroup differences: Chi² = 0.36, df = 1 (P = 0.55), I² = 0%						



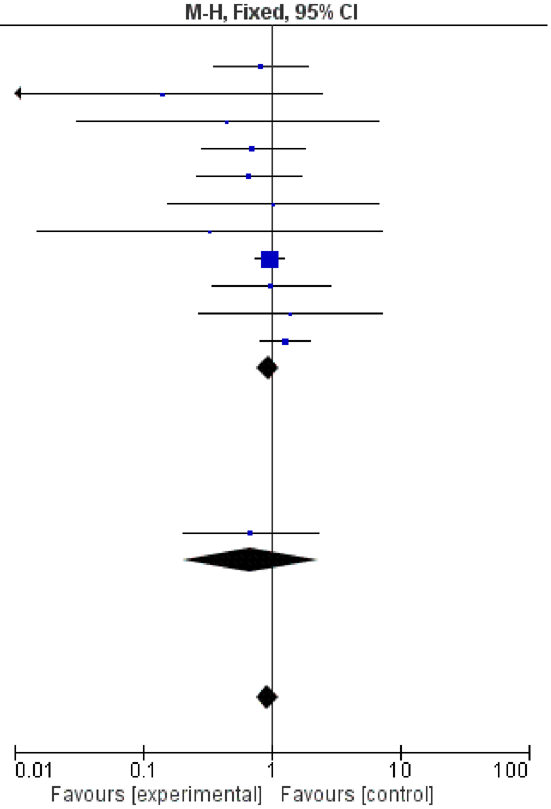
Supplementary Fig. 2F This forest plot displays a subgroup analysis of serious adverse eventsincidence based on the administration time of cells.

	Intervention		Control			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
1.47.1 < 100						
Chullikana 2015	0	10	3	10	2.6%	0.14 [0.01, 2.45]
Grajek 2010	1	31	1	14	1.0%	0.45 [0.03, 6.71]
Hare 2009	8	39	6	21	5.8%	0.72 [0.29, 1.79]
Huikuri 2008	6	40	9	40	6.6%	0.67 [0.26, 1.70]
Janssens 2006	2	33	2	34	1.5%	1.03 [0.15, 6.89]
Laguna 2018	0	10	1	10	1.1%	0.33 [0.02, 7.32]
Piepoli MF 2010	5	19	5	19	3.7%	1.00 [0.35, 2.90]
Quyyumi 2011	3	16	2	15	1.5%	1.41 [0.27, 7.28]
Subtotal (95% CI)		**198**		**163**	**23.8%**	**0.72 [0.45, 1.16]**
Total events	25		29			
Heterogeneity: Chi² = 2.76, df = 7 (P = 0.91); I² = 0%						
Test for overall effect: Z = 1.35 (P = 0.18)						
1.47.2 ≥ 100						
Assmus 2014	9	101	11	103	8.0%	0.83 [0.36, 1.93]
Mathur A 2020	57	161	78	214	49.4%	0.97 [0.74, 1.28]
Roman 2015	4	59	6	61	4.4%	0.69 [0.20, 2.32]
Roncalli 2011	26	52	19	49	14.4%	1.29 [0.83, 2.01]
Subtotal (95% CI)		**373**		**427**	**76.2%**	**1.00 [0.80, 1.25]**
Total events	96		114			
Heterogeneity: Chi² = 1.84, df = 3 (P = 0.61); I² = 0%						
Test for overall effect: Z = 0.01 (P = 0.99)						
Total (95% CI)		**571**		**590**	**100.0%**	**0.93 [0.76, 1.14]**
Total events	121		143			
Heterogeneity: Chi² = 5.87, df = 11 (P = 0.88); I² = 0%						
Test for overall effect: Z = 0.66 (P = 0.51)						
Test for subgroup differences: Chi² = 1.52, df = 1 (P = 0.22), I² = 34.0%						



Supplementary Fig. 2G This forest plot displays a subgroup analysis of serious adverse events incidence based on sample size

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
1.55.1 < 500 million							
Assmus 2014	9	101	11	103	8.0%	0.83 [0.36, 1.93]	
Chullikana 2015	0	10	3	10	2.6%	0.14 [0.01, 2.45]	
Grajek 2010	1	31	1	14	1.0%	0.45 [0.03, 6.71]	
Hare 2009	8	39	6	21	5.8%	0.72 [0.29, 1.79]	
Huikuri 2008	6	40	9	40	6.6%	0.67 [0.26, 1.70]	
Janssens 2006	2	33	2	34	1.5%	1.03 [0.15, 6.89]	
Laguna 2018	0	10	1	10	1.1%	0.33 [0.02, 7.32]	
Mathur A 2020	57	161	78	214	49.4%	0.97 [0.74, 1.28]	
Piepoli MF 2010	5	19	5	19	3.7%	1.00 [0.35, 2.90]	
Quyyumi 2011	3	16	2	15	1.5%	1.41 [0.27, 7.28]	
Roncalli 2011	26	52	19	49	14.4%	1.29 [0.83, 2.01]	
Subtotal (95% CI)		**512**		**529**	**95.6%**	**0.95 [0.77, 1.16]**	
Total events	117		137				
Heterogeneity: Chi² = 5.54, df = 10 (P = 0.85); I² = 0%							
Test for overall effect: Z = 0.54 (P = 0.59)							
1.55.2 > 500 million							
Roman 2015	4	59	6	61	4.4%	0.69 [0.20, 2.32]	
Subtotal (95% CI)		**59**		**61**	**4.4%**	**0.69 [0.20, 2.32]**	
Total events	4		6				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.60 (P = 0.55)							
Total (95% CI)		**571**		**590**	**100.0%**	**0.93 [0.76, 1.14]**	
Total events	121		143				
Heterogeneity: Chi² = 5.87, df = 11 (P = 0.88); I² = 0%							
Test for overall effect: Z = 0.66 (P = 0.51)							
Test for subgroup differences: Chi² = 0.25, df = 1 (P = 0.62), I² = 0%							



Supplementary Fig. 2H This forest plot displays a subgroup analysis of serious adverse events incidence based ondose administered