

Table S1. Data structure of included outcomes.

Study, year	No. of patients†	Duration of treatment (weeks)	FEV1 (reported as mean with SE)			SGRQ (reported as mean with SE)			SGRQ Responder (reported as no. events/ no. patients)		
			3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months
Buhl 2015[19]	5162	52	No	Yes	No	No	No*	No	No	Yes	No
Celli 2014 [20]	1489	24	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No
Decramer 2014a [21]	843	24	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No
Decramer 2014b [21]	869	24	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No
D'Urzo 2014[22]	1669	24	No	Yes	No	No	Yes	No	No	Yes	No
Maleki-Yazdi 2014[22]	905	24	No	Yes	No	Yes	Yes	No	No	Yes	No
Singh 2014[24]	1729	24	No	Yes	No	No	Yes	No	No	Yes	No
ZuWallack 2014[26]	2267	12	Yes	No	No	Yes	No	No	Yes	No	No
Donohue 2013 [29]	1532	24	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No
Donohue 2014 [31]	562	52	Yes	Yes	Yes	No	No	No	No	No	No
DB2114417 2012 [32]	641	12	Yes	No	No	No	No	No	No	No	No
DB2114418 2012 [33]	554	12	Yes	No	No	No	No	No	No	No	No
Vincken 2014 [25]	447	12	No	No	No	No	No	No	No	No	No
Bateman 2013 [27]	2135	26	No	Yes	No	Yes	Yes	No	No	Yes	No
Dahl 2013 [28]	338	52	No	No	Yes	No	No	No	No	No	No
Wedzicha 2013 [30]	2205	64	Yes	Yes	Yes	Yes	Yes	Yes	Yes [¶]	Yes [¶]	Yes [¶]
Novartis A1301 2012 [35]	158	52	Yes	Yes	Yes	No	No	No	No	No	No
Mahler 2012a [34]	1131	12	Yes	No	No	No	No	No	No	No	No
Mahler 2012b [34]	1142	12	Yes	No	No	No	No	No	No	No	No
Tashkin 2009 [36]	243	12	Yes	No	No	No*	No	No	No	No	No
Vogelmeier 2008 [37]	847	24	No	No	No	No	No	No	No	No	No
Aaron 2007 [38]	304	52	No	No	No*	No	No	No*	No	No	No

† Number of patients included in this study. *Insufficient data. [¶] Figure only. FEV1= forced expiratory volume in 1 second; No. =number; SE= standard error; SGRQ= St. George's Respiratory Questionnaire.

			TDI (reported as mean with SE)			TDI Responder (reported as no. events/ no. patients)			Exacerbations (at trial follow-up)		
Study, year	No. of patients [†]	Duration of treatment (weeks)	3 months	6 months	12 months	3 months	6 months	12 months	No. events/person years at risk	HR for first event (with SE)	No. patients with ≥ 1 event(s)/total no. of patients
Buhl 2015[19]	5162	52	No	Yes	No	No	No	No	No	No	Yes
Celli 2014 [20]	1489	24	Yes	Yes	No	Yes	Yes	No	No	Yes*	Yes
Decramer 2014a [21]	843	24	Yes	Yes	No	Yes	Yes	No	No	Yes*	Yes
Decramer 2014b [21]	869	24	Yes	Yes	No	Yes	Yes	No	No	Yes*	Yes
D'Urzo 2014[22]	1669	24	No	Yes	No	No	Yes	No	Yes	Yes*	No
Maleki-Yazdi 2014[22]	905	24	No	No	No	No	No	No	No	Yes	Yes
Singh 2014[24]	1729	24	No	Yes	No	No	Yes	No	Yes	Yes*	Yes
ZuWallack 2014[26]	2267	12	No	No	No	No	No	No	No	No	Yes
Donohue 2013 [29]	1532	24	Yes	Yes	No	Yes	Yes	No	No	Yes*	Yes
Donohue 2014 [31]	562	52	No	No	No	No	No	No	No	No	Yes
DB2114417 2012 [32]	641	12	No	No	No	No	No	No	No	No	Yes [¶]
DB2114418 2012 [33]	554	12	No	No	No	No	No	No	No	No	Yes [¶]
Vincken 2014 [25]	447	12	Yes	No	No	No	No	No	No	No	Yes
Bateman 2013 [27]	2135	26	Yes	Yes	No	No	Yes	No	Yes	Yes*	Yes
Dahl 2013 [28]	338	52	No	No	No	No	No	No	No	No	Yes
Wedzicha 2013 [30]	2205	64	No	No	No	No	No	No	Yes	Yes [¶]	Yes
Novartis A1301 2012 [35]	158	52	No	No	No	No	No	No	No	No	No
Mahler 2012a [34]	1131	12	No	No	No	No	No	No	No	No	Yes
Mahler 2012b [34]	1142	12	No	No	No	No	No	No	No	No	Yes
Tashkin 2009 [36]	243	12	No*	No	No	No	No	No	No	No	Yes
Vogelmeier 2008 [37]	847	24	No	No	No	No	No	No	No	No	Yes
Aaron 2007 [38]	304	52	No	No	Yes	No	No	No	Yes	Yes	Yes

[†] Number of patients included in this study. *Insufficient data. [¶]Data available for severe exacerbation only. HR= hazard ratio; No. =number; SE= standard error; TDI= Transitional Dyspnea Index.

			Cardiac SAE			total SAE		
Study, year	No. of patients†	Duration of treatment (weeks)	No. events/person years at risk	HR for first event (with SE)	No. events/no. of patients	No. events/person years at risk	HR for first event (with SE)	No. events/no. of patients
Buhl 2015[19]	5162	52	No	No	Yes	No	No	Yes
Celli 2014 [20]	1489	24	No	No	Yes	No	No	Yes
Decramer 2014a [21]	843	24	No	No	Yes	No	No	Yes
Decramer 2014b [21]	869	24	No	No	Yes	No	No	Yes
D'Urzo 2014[22]	1669	24	No	No	Yes	No	No	Yes
Maleki-Yazdi 2014[22]	905	24	No	No	Yes	No	No	Yes
Singh 2014[24]	1729	24	No	No	Yes	No	No	Yes
ZuWallack 2014[26]	2267	12	No	No	Yes	No	No	Yes
Donohue 2013 [29]	1532	24	No	No	Yes	No	No	Yes
Donohue 2014 [31]	562	52	No	No	Yes	No	No	Yes
DB2114417 2012 [32]	641	12	No	No	Yes	No	No	Yes
DB2114418 2012 [33]	554	12	No	No	No	No	No	Yes
Vincken 2014 [25]	447	12	No	No	Yes	No	No	Yes
Bateman 2013 [27]	2135	26	No	No	Yes	No	No	Yes
Dahl 2013 [28]	338	52	No	No	Yes	No	No	Yes
Wedzicha 2013 [30]	2205	64	No	No	Yes	No	No	Yes
Novartis A1301 2012 [35]	158	52	No	No	No	No	No	Yes
Mahler 2012a [34]	1131	12	No	No	Yes	No	No	Yes
Mahler 2012b [34]	1142	12	No	No	Yes	No	No	Yes
Tashkin 2009 [36]	243	12	No	No	No	No	No	Yes
Vogelmeier 2008 [37]	847	24	No	No	Yes	No	No	Yes
Aaron 2007 [38]	304	52	No	No	No	No	No	Yes

† Number of patients included in this study. HR= hazard ratio; No.= number; SAE= severe adverse event; SE= standard error

Study, year	No. of patients†	Duration of treatment (weeks)	Mortality			Dropouts due to AE		
			No. events/person years at risk	HR for first event (with SE)	No. events/number of patients	No. events/person years at risk	HR for first event (with SE)	No. events/number of patients
Buhl 2015[19]	5162	52	No	No	Yes	No	No	Yes
Celli 2014 [20]	1489	24	No	No	Yes	No	No	Yes
Decramer 2014a [21]	843	24	No	No	Yes	No	No	Yes
Decramer 2014b [21]	869	24	No	No	Yes	No	No	Yes
D'Urzo 2014[22]	1669	24	No	No	Yes	No	No	Yes
Maleki-Yazdi 2014[22]	905	24	No	No	Yes	No	No	Yes
Singh 2014[24]	1729	24	No	No	No	No	No	Yes
ZuWallack 2014[26]	2267	12	No	No	Yes	No	No	Yes
Donohue 2013 [29]	1532	24	No	No	Yes	No	No	Yes
Donohue 2014 [31]	562	52	No	No	Yes	No	No	Yes
DB2114417 2012 [32]	641	12	No	No	Yes	No	No	Yes
DB2114418 2012 [33]	554	12	No	No	No	No	No	Yes
Vincken 2014 [25]	447	12	No	No	Yes [¶]	No	No	Yes
Bateman 2013 [27]	2135	26	No	No	Yes	No	No	Yes
Dahl 2013 [28]	338	52	No	Yes	Yes	No	No	Yes
Wedzicha 2013 [30]	2205	64	No	No	Yes	No	No	Yes
Novartis A1301 2012 [35]	158	52	No	No	Yes	No	No	Yes
Mahler 2012a [34]	1131	12	No	No	Yes	No	No	Yes
Mahler 2012b [34]	1142	12	No	No	Yes	No	No	Yes
Tashkin 2009 [36]	243	12	No	No	Yes [¶]	No	No	No
Vogelmeier 2008 [37]	847	24	No	No	Yes	No	No	No
Aaron 2007 [38]	304	52	No	No	Yes	No	No	Yes

† Number of patients included in this study. [¶] No fatal events. HR= hazard ratio; AE= adverse event; No.= number; SE= standard error