

Table S1 Independent Ethics Committees

Bulgaria	Poland
Ethics Committee for Multicentre Trials (ECMT), 5, Sveta Nedelya Square, 1000 Sofia	Okręgowa Izba Lekarska, Ul. Świetojańska 7, 15-082 Białystok
MHAT Plovdiv, 234, Bulgaria Blvd., 4003 Plovdiv	Komisja Bioetyczna przy Wielkopolskiej Izbie Lekarskiej, Ul. Nowowiejskiego 5, 61-734 Poznań
MHAT Aleksandrowska, 1, Georgi Sofiiski St., 1431 Sofia	Komisja Bioetyki Uniwersytetu Medycznego w Łodzi, Al. Kościuszki 4, 90-419 Łódź
District Dispensary for Pulmonary and Phthisiatric Diseases - Ruse, 1, Aleya Lilia St., 7000 Ruse	Komisja Bioetyczna Lubelskiej Izby Lekarskiej, ul. Chmielna 4, 20-079 Lublin
MHAT "Sveti Georgi", 15 A Vasil Aprilov St., 4002 Plovdiv,	Komisja Bioetyczna przy Okręgowej Izbie Lekarskiej w Łodzi, ul. Czerwona 3, 90-005 Łódź
MHAT "Dr. Georgi Stranski", 8 A Georgi Kochev Str., 5800 Pleven	Komisja Bioetyczna przy Okręgowej Izbie Lekarskiej w Gdańsku, ul. Śniadeckich 33, 80-204 Gdańsk
Czech Republic	Okręgowa Izba Lekarska, ul. Krupnicza 11 A, 31-123 Kraków
Etická komise FN Brno, Jihlavská 20, 625 00 Brno	Komisja Bioetyczna przy Dolnośląskiej Izbie Lekarskiej, ul. Matejki 6, 50-333 Wrocław
Etická komise, FN na Bulovce, Budínova 2, 180 00 Praha 8	Romania
Etická komise, IKEM a FTNSP, Vídeňská 800, 140 59 Praha 4	Comisia Nationala de Etica pentru Studiul Clinic al Medicamentului (National Ethics Commission for Clinical Study of Medicine), 48 Av. Sanatescu Street, district 1, 011478, Bucharest
Hungary	Russia
Arany János u. 6-8., Budapest, 1051 - H	3, Rakhmanovsky per., Moscow, 127994
Szent István lakótelep 7., Szigetvar, 2673 - H	1, Ostrovityanova str., Moscow, 117997
Szentpéteri kapu 72-76., Miskolc, 3526 - H	25, Mytninskaya str., Saint-Petersburg, 191144
Nagyerdei krt. 98. , Debrecen, 4032 - H	14, Avangardnaya str., Saint-Petersburg, 198205
Korányi fasor 8-10., Szeged, 6701 - H	112, Bolshaya Kazachya, Saratov, 410012
Semmelweis u. 1., Gyula, 5700 - H	2, Litovskaya str., Moscow, 194100
Dr. Monszpart L. u. 1., Kiskunhalas, 6400 - H	2, Taldomskaya str., Moscow, 125412
Bartók Béla út 2-26., Debrecen, 4043 - H	20., bld.1, Delegatskaya, str., Moscow, 127473
Vasvári P. u. 2-4. , Győr, 9024 - H	Ukraine
Üllői út 93. , Budapest, 1091 - H	73 Lugova Str., 95003 Simferopol
Kórház utca 1., Veszprem, 8200 - H	70 Lenina Ave., 69063 Zaporizhzhia
India	5 Muranova Str., 61093 Kharkiv
Institutional Ethics Committee, Sterling Hospital, 8th Floor, sterling Hospital Road, Memnagar, Ahmedabad - 380052, Gujarat	10 N.Amosova Str., 03680 Kyiv
Sir Ganga Ram Hospital Ethics Committee, Room No 1496, IV Floor, Old Building , Sir Ganga Ram Hospital, Old Rajinder Nagar, New Delhi-110060	337-A Klochkivska Str., 61051 Kharkiv
Ethics Committee, Inamdar Multispeciality Hospital, Hospital Building, S.No. 15, Fatima Nagar, Pune-411040, Maharashtra	3 Academic Vorobyev Str., 65031 Odesa
Institutional Ethics Committee, CMC Ludhiana, Brown Road, Punjab – 141 008	8 Mayborody Str., 04050 Kyiv
MidcityIndependent Ethics Committee, 3rd Floor, 799, Omnagar, Opp. Tajshree Building, Mirchi Bazaar, SakkardaraChowk, Umred Road, Nagpur-440009	77 Titova Str., 95034 Simferopol

Table S2 Change in Morning and Evening FEV₁ (Litres) and Peak Flow Measurements (Litres/Minute) from Baseline over the 12 Week Treatment Period, Full Analysis Population

Analysis Visit		Fluticasone/formoterol (N=167)	Fluticasone (N=171)	Fluticasone/salmeterol (N=168)
Change in diary morning FEV₁ from Baseline				
Overall	n	163	165	162
	LS Mean* (95% CI)	0.06 (0.02, 0.10)	0.01 (-0.03, 0.05)	0.02 (-0.02, 0.06)
	Difference† (95% CI of Difference)		0.06 (0.00, 0.11)	0.05 (-0.01, 0.10)
	P-Value‡		0.036	0.086
Change in diary evening FEV₁ from Baseline				
Overall	n	163	169	164
	LS Mean* (95% CI)	0.05 (0.01, 0.08)	0.01 (-0.02, 0.05)	-0.00 (-0.04, 0.03)
	Difference† (95% CI of Difference)		0.03 (-0.02, 0.08)	0.05 (-0.00, 0.10)
	P-Value‡		0.203	0.060
Change in Morning Peak Flow Measurements				
Overall	n	167	169	166
	LS Mean* (95% CI)	16.49 (11.50, 21.48)	9.00 (4.03, 13.97)	12.67 (7.68, 17.67)
	Difference† (95% CI of Difference)		7.49 (1.24, 13.75)	3.82 (-2.48, 10.12)
	P-Value‡		0.019	0.234
Change in Evening Peak Flow Measurements				
Overall	n	167	170	166
	LS Mean* (95% CI)	14.22 (9.53, 18.91)	7.68 (3.03, 12.34)	11.92 (7.19, 16.64)
	Difference† (95% CI of Difference)		6.54 (0.37, 12.71)	2.31 (-3.91, 8.52)
	P-Value‡		0.038	0.466
Change in Peak Flow from pre-dose baseline to pre-dose at Week 12				
Overall	n	166	167	165
	LS Mean* (95% CI)	27.94 (21.20, 34.69)	20.39 (13.66, 27.12)	27.30 (20.51, 34.09)
	Difference† (95% CI of Difference)		7.56 (1.07, 14.04)	0.65 (-5.87, 7.17)
	P-Value‡		0.022	0.845
Change in Peak Flow Measurements from pre-dose baseline to 2-hours post-dose at Week 12				
Overall	n	165	165	165
	LS Mean* (95% CI)	43.59 (36.35, 50.83)	29.77 (22.54, 36.99)	41.33 (34.05, 48.61)
	Difference† (95% CI of Difference)		13.83 (7.06, 20.59)	2.26 (-4.53, 9.05)
	P-Value‡		<0.001	0.513

N: Number of patients in population. n: Number of patients with data available. CI: Confidence Interval. FEV₁: forced expiratory volume in the 1st second.

Note: Daily morning peak flow measurement was calculated from the patient's diary for the 7 days prior to the visit.

*Least square mean from a repeated measures ANCOVA with fixed terms for treatment, age group, PEF_R at baseline, visit and treatment by visit interaction, and centre as a random effect. † Difference: LS Mean Flutiform - LS Mean Fluticasone/Seretide. ‡P-value of the pairwise treatment comparisons (based on the null hypothesis that there is no difference in treatment means).

Table S3 Change in PAQLQ Overall Score from Baseline to Week 12 of ≥ 0.5 Units, Stratified by Age Group, Full Analysis Population

	Fluticasone/formoterol	Fluticasone	Fluticasone/salmeterol
Age Group = 5 to 6 years			
N	27	31	24
Yes*	17 (63.0)	20 (64.5)	15 (62.5)
No	7 (25.9)	8 (25.8)	7 (29.2)
Missing	3 (11.1)	3 (9.7)	2 (8.3)
Odds Ratio**		1.51	3.16
95% CI**		(0.24, 9.75)	(0.40, 24.66)
Age Group = 7 to <12 years			
N	140	140	144
Yes*	83 (59.3)	84 (60.0)	89 (61.8)
No	51 (36.4)	43 (30.7)	46 (31.9)
Missing	6 (4.3)	13 (9.3)	9 (6.3)
Odds Ratio**		0.98	0.87
95% CI**		(0.52, 1.82)	(0.47, 1.59)
Overall			
N	167	171	168
Yes*	100 (59.9)	104 (60.8)	104 (61.9)
No	58 (34.7)	51 (29.8)	53 (31.5)
Missing	9 (5.4)	16 (9.4)	11 (6.5)
Odds Ratio**		1.02	0.96
95% CI**		(0.57, 1.84)	(0.54, 1.71)

PAQLQ-IA: Paediatric Asthma Quality of Life Questionnaire - Interviewer Administered. N: Number of patients in population. n: Number of patients with data available. %: Percentage based on N. CI: Confidence Interval.

* Patients with a change in PAQLQ overall score from baseline to week 12 of ≥ 0.5 units.

** Logistic regression estimates with fixed terms for treatment, age (years) and PAQLQ score at baseline, and centre as a random effect.

Table S4 Reduction in ACQ-IA Overall Score from Baseline to Week 12 of ≥ 0.5 Units, Stratified by Age Group, Full Analysis Population

	Fluticasone/formoterol (N=167)	Fluticasone (N=171)	Fluticasone/salmeterol (N=168)
Age group = 5			
N	12	11	6
Yes*	10 (83.3)	7 (63.6)	5 (83.3)
No	2 (16.7)	2 (18.2)	-
Missing	-	2 (18.2)	1 (16.7)
Odds Ratio**		NC	NC
95% CI**		NC	NC
Age group = 6 – 10 years			
N	126	129	126
Yes*	92 (73.0)	102 (79.1)	98 (77.8)
No	26 (20.6)	17 (13.2)	21 (16.7)
Missing	8 (6.3)	10 (7.8)	7 (5.6)
Odds Ratio**		0.75	0.85
95% CI**		(0.36, 1.56)	(0.42, 1.72)
Age group = 11 years			
N	29	31	36
Yes*	20 (69.0)	21 (67.7)	24 (66.7)
No	7 (24.1)	7 (22.6)	7 (19.4)
Missing	2 (6.9)	3 (9.7)	5 (13.9)
Odds Ratio**		0.75	0.59
95% CI**		(0.19, 2.93)	(0.15, 2.26)
Overall			
Yes*	122 (73.1)	130 (76.0)	127 (75.6)
No	35 (21.0)	26 (15.2)	28 (16.7)
Missing	10 (6.0)	15 (8.8)	13 (7.7)
Odds Ratio**		0.79	0.81
95% CI**		(0.42, 1.48)	(0.44, 1.50)

ACQ-IA: Asthma Control Questionnaire - Interviewer administered. N: Number of patients in population. n: Number of patients with data available. %: Percentage based on N. CI: Confidence Interval.

NC = Not calculable.

* Patients with a reduction in ACQ-IA overall score from baseline to week 12 of ≥ 0.5 units.

** Logistic regression estimates with fixed terms for treatment, age (years) and ACQ-IA score at baseline, and centre as a random effect.