Indacaterolacetat / Glycopyrroniumbromid / Mometasonfuroat (Enerzair® Breezhaler®)

Novartis Pharma GmbH

Modul 4 A, Anhang 4-H-2

ARGON-Gesamtpopulation

CQVM149B2306 (ARGON)
AMNOG Analysis

Table of Contents

Tables

1. Patient Disposition and Baseline Characteristics

Table 1.1 Patient Disposition and Compliance (RAN, FAS)

	Treatment groups		
Disposition/Reason (RAN/SAF)	**IND/GLY/ MF 160 n (%)**	**SAL/FLU + TIO n (%)**	**Total n (%)**
Randomized (RAN)	**476 (100,0)**	**476 (100,0)**	**952 (100,0)**
Full Analysis Set (FAS)	**476 (100,0)**	**475 (99,8)**	**951 (99,9)**
Reasons for exclusion			
Subject was randomized but did not receive any study drug	0 (0,0)	1 (0,2)	1 (0,1)
Study Discontinuation (FAS)	**13 (2,7)**	**17 (3,6)**	**30 (3,2)**
Reasons for study discontinuation			
Subject/guardian decision	**7 (1,5)**	**9 (1,9)**	**16 (1,7)**
Physician decision	**2 (0,4)**	**4 (0,8)**	**6 (0,6)**
Adverse event	**2 (0,4)**	**2 (0,4)**	**4 (0,4)**
Benign neoplasm	1 (0,2)	0 (0,0)	1 (0,1)
Dermatitis atopic	0 (0,0)	1 (0,2)	1 (0,1)
Dysphonia	1 (0,2)	0 (0,0)	1 (0,1)
Haemorrhagic stroke	0 (0,0)	1 (0,2)	1 (0,1)
Lost to follow-up	**1 (0,2)**	**1 (0,2)**	**2 (0,2)**
Pregnancy	**1 (0,2)**	**0 (0,0)**	**1 (0,1)**
Protocol deviation	**0 (0,0)**	**1 (0,2)**	**1 (0,1)**
Selection criteria not met	0 (0,0)	1 (0,2)	1 (0,1)
Treatment Discontinuation (FAS)	**16 (3,4)**	**27 (5,7)**	**43 (4,5)**
Discontinued study directly afterwards	4 (0,8)	10 (2,1)	14 (1,5)
Continued in study for a while	9 (1,9)	7 (1,5)	16 (1,7)
Completed study	3 (0,6)	10 (2,1)	13 (1,4)
Primary reason for discontinuation from study treatment			
Subject/guardian decision	6 (1,3)	11 (2,3)	17 (1,8)
Physician decision	3 (0,6)	7 (1,5)	10 (1,1)
Adverse event	3 (0,6)	3 (0,6)	6 (0,6)
Technical problems	1 (0,2)	5 (1,1)	6 (0,6)
Lost to follow-up	1 (0,2)	1 (0,2)	2 (0,2)
Pregnancy	2 (0,4)	0 (0,0)	2 (0,2)

	Treatment groups		
Disposition/Reason (RAN/SAF)	**IND/GLY/ MF 160 n (%)**	**SAL/FLU + TIO n (%)**	**Total n (%)**
Percentages refer to the number of randomized patients. Analysis population: B2306 RAN total population			

Table 1.2 Demographic Patient Characteristics (FAS)

	Treatment Groups		
Demographic Patient Characteristics (FAS)	**IND/GLY/ MF 160 (N=476)**	**SAL/FLU + TIO (N=475)**	**Total (N=951)**
Age (years)			
Mean ± SD	52,7 ± 13,34	53,0 ± 13,09	52,9 ± 13,21
Median	53,0	54,0	54,0
Range	21 to 82	18 to 81	18 to 82
Age group (years), n (%)			
18-39 years	85 (17,9)	73 (15,4)	158 (16,6)
40-64 years	290 (60,9)	307 (64,6)	597 (62,8)
>64 years	101 (21,2)	95 (20,0)	196 (20,6)
Sex, n (%)			
Male	187 (39,3)	169 (35,6)	356 (37,4)
Female	289 (60,7)	306 (64,4)	595 (62,6)
Ethnicity, n (%)			
Hispanic or Latino	162 (34,0)	164 (34,5)	326 (34,3)
East Asian	2 (0,4)	1 (0,2)	3 (0,3)
Southeast Asian	30 (6,3)	31 (6,5)	61 (6,4)
South Asian	3 (0,6)	0 (0,0)	3 (0,3)
West Asian	9 (1,9)	11 (2,3)	20 (2,1)
Russian	86 (18,1)	86 (18,1)	172 (18,1)
Mixed Ethnicity	7 (1,5)	2 (0,4)	9 (0,9)
Not Reported	13 (2,7)	9 (1,9)	22 (2,3)
Unknown	8 (1,7)	3 (0,6)	11 (1,2)
Other	156 (32,8)	168 (35,4)	324 (34,1)
Weight (kg)			
Mean ± SD	79,6 ± 17,67	79,1 ± 16,55	79,4 ± 17,11
Median	78,0	78,0	78,0
Range	42,2 to 158,0	34,0 to 143,0	34,0 to 158,0
BMI (kg/m^2)			
Mean ± SD	29,0 ± 5,74	29,1 ± 5,61	29,0 ± 5,67
Median	28,6	28,5	28,6
Range	16,5 to 50,6	15,2 to 51,9	15,2 to 51,9
Analysis population: B2306 FAS total population			

Table 1.3 Asthma Related Patient Characteristics (FAS)

	Treatment Groups		
Asthma Patient Characteristics (FAS)	**IND/GLY/ MF 160 (N=476)**	**SAL/FLU + TIO (N=475)**	**Total (N=951)**
Duration of asthma (years)			
Mean ± SD	22,1 ± 16,27	20,2 ± 14,68	21,1 ± 15,52
Median	19,2	17,0	18,0
Range	0,5 to 73,4	0,6 to 73,4	0,5 to 73,4
Duration of asthma (years), n (%)			
< 1 year	9 (1,9)	7 (1,5)	16 (1,7)
1 - 5 years	70 (14,7)	57 (12,0)	127 (13,4)
>5 - 10 years	67 (14,1)	79 (16,6)	146 (15,4)
>10 - 15 years	51 (10,7)	71 (14,9)	122 (12,8)
>15 - 20 years	46 (9,7)	59 (12,4)	105 (11,0)
>20 years	233 (48,9)	202 (42,5)	435 (45,7)
Number of asthma exacerbations in the 12 months prior to study start that required treatment, n (%)			
1	375 (78,8)	383 (80,6)	758 (79,7)
2	74 (15,5)	73 (15,4)	147 (15,5)
3	20 (4,2)	18 (3,8)	38 (4,0)
≥ 4	7 (1,5)	1 (0,2)	8 (0,8)
Smoking history, n (%)			
Never smoked	354 (74,4)	363 (76,4)	717 (75,4)
Ex-smoker	112 (23,5)	102 (21,5)	214 (22,5)
Current smoker	10 (2,1)	10 (2,1)	20 (2,1)
Amount of tobacco consumed on average (in pack years)			
Mean ± SD	6,4 ± 4,22	5,9 ± 4,17	6,2 ± 4,20
Median	6,0	5,0	5,0
Range	0,1 to 16,0	0,3 to 19,0	0,1 to 19,0
Time since smoking stopped (years)			
Mean ± SD	16,1 ± 14,13	16,0 ± 12,12	16,1 ± 13,18
Median	13,0	13,3	13,1
Range	0,3 to 58,7	0,6 to 48,2	0,3 to 58,7

Asthma Patient Characteristics (FAS)	Treatment Groups IND/GLY/ MF 160 (N=476)	SAL/FLU + TIO (N=475)	Total (N=951)
Systolic blood pressure (mmHg)			
Mean ± SD	125,9 ± 12,25	125,2 ± 12,08	125,6 ± 12,17
Median	126,0	125,0	125,0
Range	80 to 197	94 to 169	80 to 197
Diastolic blood pressure (mmHg)			
Mean ± SD	77,8 ± 8,39	77,3 ± 8,36	77,6 ± 8,37
Median	80,0	79,0	79,0
Range	50 to 106	52 to 100	50 to 106
Pulse rate (beats per minute)			
Mean ± SD	72,5 ± 9,12	73,3 ± 8,98	72,9 ± 9,05
Median	72,0	72,0	72,0
Range	47 to 106	44 to 98	44 to 106
QTcF (ms)			
Mean ± SD	405,8 ± 19,13	403,9 ± 19,93	404,8 ± 19,55
Median	406,0	404,0	406,0
Range	355 to 460	348 to 460	348 to 460
AQLQ-S total score			
Mean ± SD	4,7 ± 0,86	4,7 ± 0,89	4,7 ± 0,87
Median	4,7	4,6	4,6
Range	2,2 to 6,9	1,6 to 6,9	1,6 to 6,9
Baseline AQLQ-S score, n (%)			
<0.5	0 (0,0)	0 (0,0)	0 (0,0)
0.5 - <1	0 (0,0)	0 (0,0)	0 (0,0)
1 - <1.5	0 (0,0)	0 (0,0)	0 (0,0)
1.5 - <2	0 (0,0)	1 (0,2)	1 (0,1)
≥ 2	474 (99,6)	465 (97,9)	939 (98,7)
missing	2 (0,4)	9 (1,9)	11 (1,2)
ACQ-5 total score			
Mean ± SD	2,5 ± 0,61	2,5 ± 0,61	2,5 ± 0,61
Median	2,4	2,4	2,4
Range	1,0 to 4,4	1,2 to 4,8	1,0 to 4,8
Baseline ACQ-5 score, n (%)			
<1.5	17 (3,6)	4 (0,8)	21 (2,2)
1.5 - <2	53 (11,1)	54 (11,4)	107 (11,3)

	Treatment Groups		
Asthma Patient Characteristics (FAS)	**IND/GLY/ MF 160 (N=476)**	**SAL/FLU + TIO (N=475)**	**Total (N=951)**
2 - <2.5	174 (36,6)	198 (41,7)	372 (39,1)
≥ 2.5	232 (48,7)	219 (46,1)	451 (47,4)
ACQ-7 total score			
Mean ± SD	2,6 ± 0,53	2,6 ± 0,53	2,6 ± 0,53
Median	2,6	2,6	2,6
Range	1,3 to 4,3	1,6 to 4,6	1,3 to 4,6
Baseline ACQ-7 score, n (%)			
<1.5	2 (0,4)	0 (0,0)	2 (0,2)
1.5 - <2	42 (8,8)	32 (6,7)	74 (7,8)
2 - <2.5	167 (35,1)	196 (41,3)	363 (38,2)
≥ 2.5	265 (55,7)	247 (52,0)	512 (53,8)
SGRQ total score			
Mean ± SD	39,7 ± 16,83	39,4 ± 17,98	39,6 ± 17,40
Median	39,8	39,2	39,5
Range	0,8 to 89,4	0,0 to 96,1	0,0 to 96,1
Baseline eosinophils count (cells/µL)			
Mean ± SD	356,6 ± 337,60	343,0 ± 315,00	349,8 ± 326,39
Median	260,0	250,0	260,0
Range	10 to 2970	0 to 3160	0 to 3160
Baseline eosinophils count (cells/µL), n (%)			
<300	270 (56,7)	278 (58,5)	548 (57,6)
≥ 300	201 (42,2)	193 (40,6)	394 (41,4)
missing	5 (1,1)	4 (0,8)	9 (0,9)
ICS component background theapy, n (%)			
Low-dose ICS/LABA	1 (0,2)	1 (0,2)	2 (0,2)
Mid-dose ICS/LABA	230 (48,3)	240 (50,5)	470 (49,4)
High-dose ICS/LABA	242 (50,8)	232 (48,8)	474 (49,8)
missing	3 (0,6)	2 (0,4)	5 (0,5)
FEV1 reversibility (%)			
Mean ± SD	28,5 ± 17,56	28,3 ± 17,89	28,4 ± 17,72
Median	23,0	23,0	23,0
Range	0 to 138	12 to 164	0 to 164
FEV1 reversibility (%), n (%)			
<40%	363 (76,3)	376 (79,2)	739 (77,7)

	Treatment Groups		
Asthma Patient Characteristics (FAS)	**IND/GLY/ MF 160 (N=476)**	**SAL/FLU + TIO (N=475)**	**Total (N=951)**
40% - <50%	44 (9,2)	30 (6,3)	74 (7,8)
50% - <60%	17 (3,6)	20 (4,2)	37 (3,9)
60% - <70%	9 (1,9)	11 (2,3)	20 (2,1)
70% - <80%	5 (1,1)	8 (1,7)	13 (1,4)
≥ 80%	11 (2,3)	10 (2,1)	21 (2,2)
missing	27 (5,7)	20 (4,2)	47 (4,9)
FEV1 predicted			
Mean ± SD	62,2 ± 14,01	63,3 ± 13,91	62,7 ± 13,97
Median	64,0	65,0	64,8
Range	20 to 98	23 to 101	20 to 101
FEV1 predicted (%), n (%)			
≤ 60%	198 (41,6)	174 (36,6)	372 (39,1)
>60%	274 (57,6)	294 (61,9)	568 (59,7)
missing	4 (0,8)	7 (1,5)	11 (1,2)
IgE level (IU/ml), n (%)			
≤ 75	157 (33,0)	143 (30,1)	300 (31,5)
>75 - ≤1500	272 (57,1)	291 (61,3)	563 (59,2)
>1500	33 (6,9)	27 (5,7)	60 (6,3)
missing	14 (2,9)	14 (2,9)	28 (2,9)
Concomitant asthma medication at baseline, n (%)			
ICS/LABA Fixcombination	2 (0,4)	0 (0,0)	2 (0,2)
LABA	0 (0,0)	0 (0,0)	0 (0,0)
LABA/LAMA	0 (0,0)	0 (0,0)	0 (0,0)
LAMA	0 (0,0)	0 (0,0)	0 (0,0)
LTRA	54 (11,3)	55 (11,6)	109 (11,5)
Mepolizumab	2 (0,4)	4 (0,8)	6 (0,6)
OCS	4 (0,8)	6 (1,3)	10 (1,1)
Omalizumab	8 (1,7)	9 (1,9)	17 (1,8)
Reslizumab	1 (0,2)	1 (0,2)	2 (0,2)
SABA	0 (0,0)	1 (0,2)	1 (0,1)
SAMA	0 (0,0)	0 (0,0)	0 (0,0)
Other	23 (4,8)	23 (4,8)	46 (4,8)

Analysis population: B2306 FAS total population

Table 1.4 Duration of Study Participation (FAS)

	Treatment Groups		
Duration of Study Participation (FAS)	**IND/GLY/ MF 160 (N=476)**	**SAL/FLU + TIO (N=475)**	**Total (N=951)**
Study participation			
Mean ± SD (in days)	194,5 ± 15,37	194,6 ± 17,66	194,5 ± 16,55
Median (in days)	196,0	196,0	196,0
Minimum, Maximum (in days)	59 to 225	50 to 238	50 to 238
Study participation on treatment			
Mean ± SD (in days)	166,9 ± 19,33	165,4 ± 23,25	166,2 ± 21,38
Median (in days)	169,0	169,0	169,0
Minimum, Maximum (in days)	1 to 190	16 to 203	1 to 203

Analysis population: B2306 FAS total population
Study participation was defined as the time from date of informed consent up to the end of follow-up epoch resp. treatment epoch

Table 1.5 Overview Subgroups (FAS)

	Treatment Groups		
Overview Subgroups (FAS)	**IND/GLY/ MF 160 (N=476)**	**SAL/FLU + TIO (N=475)**	**Total (N=951)**
Age			
18-39	85	73	158
40-64	290	307	597
>64	101	95	196
Gender			
male	187	169	356
female	289	306	595
Region			
Asia	124	131	255
Europe	166	169	335
Latin America	166	166	332
Others	20	9	29
History of asthma exacerbation in the 12 months prior to screening			
1	375	383	758
≥ 2	101	92	193
Patients' prior therapies for at least 1 month prior to visit 1			
mid dose ICS/LABA	230	240	470
high dose ICS/LABA	242	232	474

Analysis population: B2306 FAS total population

Table 1.6 OCS Use (FAS)

	Treatment Groups		
OCS Use (FAS)	**IND/GLY/ MF 160 (N=476)**	**SAL/FLU + TIO (N=475)**	**Total (N=951)**
OCS use at baseline			
At least one OCS			
n (%)	4 (0,8)	6 (1,3)	10 (1,1)
METHYLPREDNISOLONE			
n (%)	3 (0,6)	1 (0,2)	4 (0,4)
OCS dosage (mg/day)			
Mean ± SD	5,3 ± 2,31	4,0 ± N.E.	5,0 ± 2,00
Median	4,0	4,0	4,0
PREDNISONE			
n (%)	1 (0,2)	5 (1,1)	6 (0,6)
OCS dosage (mg/day)			
Mean ± SD	10,0 ± N.E.	9,0 ± 4,18	9,2 ± 3,76
Median	10,0	10,0	10,0
Escalation of OCS during study			
At least one OCS			
n (%)	1 (0,2)	2 (0,4)	3 (0,3)
METHYLPREDNISOLONE			
n (%)	1 (0,2)	0 (0,0)	1 (0,1)
OCS dosage (mg/day)			
Mean ± SD	27,6 ± N.E.		27,6 ± N.E.
Median	27,6		27,6
Duration of escalation (days)			
Mean ± SD	18,0 ± N.E.		18,0 ± N.E.
Median	18,0		18,0
PREDNISONE			
n (%)	0 (0,0)	2 (0,4)	2 (0,2)
OCS dosage (mg/day)			
Mean ± SD		23,5 ± 4,03	23,5 ± 4,03
Median		23,5	23,5
Duration of escalation (days)			
Mean ± SD		18,5 ± 4,95	18,5 ± 4,95
Median		18,5	18,5

	Treatment Groups		
OCS Use (FAS)	**IND/GLY/ MF 160 (N=476)**	**SAL/FLU + TIO (N=475)**	**Total (N=951)**
New onset of OCS during study			
At least one OCS			
n (%)	71 (14,9)	61 (12,8)	132 (13,9)
BETAMETHASONE			
n (%)	3 (0,6)	2 (0,4)	5 (0,5)
OCS dosage (mg/day)			
Mean ± SD	2,4 ± 0,00	2,4 ± 1,70	2,4 ± 0,85
Median	2,4	2,4	2,4
Duration of use (days)			
Mean ± SD	7,0 ± 0,00	11,0 ± 0,00	8,6 ± 2,19
Median	7,0	11,0	7,0
DEFLAZACORT			
n (%)	1 (0,2)	0 (0,0)	1 (0,1)
OCS dosage (mg/day)			
Mean ± SD	30,0 ± N.E.		30,0 ± N.E.
Median	30,0		30,0
Duration of use (days)			
Mean ± SD	9,0 ± N.E.		9,0 ± N.E.
Median	9,0		9,0
MEPREDNISONE			
n (%)	15 (3,2)	7 (1,5)	22 (2,3)
OCS dosage (mg/day)			
Mean ± SD	32,6 ± 10,75	30,3 ± 11,04	31,8 ± 10,63
Median	40,0	36,0	40,0
Duration of use (days)			
Mean ± SD	6,6 ± 2,13	9,1 ± 5,27	7,4 ± 3,53
Median	6,0	8,0	6,5
METHYLPREDNISOLONE			
n (%)	16 (3,4)	16 (3,4)	32 (3,4)
OCS dosage (mg/day)			
Mean ± SD	27,4 ± 10,91	20,5 ± 8,96	23,8 ± 10,38
Median	32,0	16,0	24,0

	Treatment Groups		
OCS Use (FAS)	**IND/GLY/ MF 160 (N=476)**	**SAL/FLU + TIO (N=475)**	**Total (N=951)**
Duration of use (days)			
Mean ± SD	10,1 ± 8,68	7,4 ± 2,94	8,7 ± 6,52
Median	6,0	7,0	6,0
PREDNISOLONE			
n (%)	20 (4,2)	15 (3,2)	35 (3,7)
OCS dosage (mg/day)			
Mean ± SD	30,0 ± 11,49	26,1 ± 15,80	28,3 ± 13,43
Median	30,6	20,0	28,6
Duration of use (days)			
Mean ± SD	7,4 ± 2,76	10,3 ± 9,46	8,6 ± 6,58
Median	7,5	8,0	8,0
PREDNISONE			
n (%)	20 (4,2)	21 (4,4)	41 (4,3)
OCS dosage (mg/day)			
Mean ± SD	30,3 ± 10,59	33,3 ± 14,83	31,8 ± 12,87
Median	30,0	40,0	30,0
Duration of use (days)			
Mean ± SD	6,2 ± 4,03	7,1 ± 3,66	6,7 ± 3,83
Median	5,0	6,0	6,0

An escalation is any daily dose higher than the baseline dose. For the duration of escalation all days with a so defined dose have been summed up, no matter if these days were consecutive or not.
A new onset of OCS is any post-baseline onset of OCS in patients who have no OCS use at baseline. For the duration of use all days of post-baseline OCS use have been summed up, no matter if these days were consecutive or not.
Medication data up to end of treatment phase have been included.
N.E.: not estimable
Analysis population: B2306 FAS total population

2. All-cause Mortality - Binary Analysis

Table 2.1 All-cause Mortality - Binary Analysis (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	476	475			
Death, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment
If it was not possible to fit the minimal model, the OR is not given.

Analysis population: B2306 FAS total population

3. ACQ-5 - Return Rate / Change from Baseline

Table 3.1 ACQ-5 - Return Rate (FAS)

	Treatment groups		
Patient Reported Outcome - Return Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Total N=951**
Return Rate*, n (%)			
Baseline Returns	474 (99,6)	467 (98,3)	941 (98,9)
Week 16 Returns	448 (94,1)	440 (92,6)	888 (93,4)
Week 24 Returns	460 (96,6)	447 (94,1)	907 (95,4)

* The return rate is the proportion of patients with non-missing data for the total score at given visit on the whole study population.

Analysis population: B2306 FAS total population

Table 3.2 ACQ-5 - Change from Baseline (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
ACQ-5 score			
N'	456	450	
Baseline Mean (SD)	2,53 (0,614)	2,54 (0,607)	
Week 16:			
Adjusted Mean Change (SE)	-1,19 (0,055)	-1,13 (0,056)	-0,06 [-0,176; 0,051] 0,278
Week 24:			
Adjusted Mean Change (SE)	-1,28 (0,056)	-1,18 (0,056)	-0,10 [-0,216; 0,016] 0,090

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 3.3 ACQ-5 - Change from Baseline by Age (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
ACQ-5 score			
Interaction Test	0,952		
Age = 18-39 years			
N'	79	71	
Baseline Mean (SD)	2,50 (0,554)	2,57 (0,629)	
Week 16:			
Adjusted Mean Change (SE)	-1,36 (0,105)	-1,24 (0,109)	-0,12 [-0,399; 0,156] 0,390
Week 24:			
Adjusted Mean Change (SE)	-1,38 (0,107)	-1,27 (0,113)	-0,11 [-0,402; 0,172] 0,432
Age = 40-64 years			
N'	278	290	
Baseline Mean (SD)	2,55 (0,628)	2,56 (0,613)	
Week 16:			
Adjusted Mean Change (SE)	-1,18 (0,063)	-1,13 (0,063)	-0,05 [-0,195; 0,091] 0,475
Week 24:			
Adjusted Mean Change (SE)	-1,29 (0,064)	-1,19 (0,064)	-0,10 [-0,245; 0,047] 0,184
Age = ≥65 years			
N'	99	89	
Baseline Mean (SD)	2,49 (0,622)	2,46 (0,572)	
Week 16:			
Adjusted Mean Change (SE)	-1,09 (0,096)	-1,04 (0,101)	-0,04 [-0,292; 0,205] 0,731

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 24:			
Adjusted Mean Change (SE)	-1,18 (0,098)	-1,09 (0,103)	-0,09 [-0,350; 0,160] 0,466

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + age + age * treatment + age * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 3.4 ACQ-5 - Change from Baseline by Gender (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
ACQ-5 score			
Interaction Test	0,452		
Gender = Male			
N'	181	166	
Baseline Mean (SD)	2,45 (0,597)	2,46 (0,570)	
Week 16:			
Adjusted Mean Change (SE)	-1,26 (0,073)	-1,14 (0,078)	-0,12 [-0,304; 0,062] 0,195
Week 24:			
Adjusted Mean Change (SE)	-1,33 (0,075)	-1,19 (0,079)	-0,14 [-0,326; 0,048] 0,144
Gender = Female			
N'	275	284	
Baseline Mean (SD)	2,58 (0,620)	2,59 (0,624)	
Week 16:			
Adjusted Mean Change (SE)	-1,14 (0,065)	-1,12 (0,063)	-0,02 [-0,167; 0,121] 0,749
Week 24:			
Adjusted Mean Change (SE)	-1,24 (0,066)	-1,17 (0,065)	-0,07 [-0,221; 0,074] 0,330

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + gender + gender * treatment + gender * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 3.5 ACQ-5 - Change from Baseline by Region (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
ACQ-5 score			
Interaction Test	0,248		
Region = Asia			
N'	117	126	
Baseline Mean (SD)	2,45 (0,614)	2,48 (0,604)	
Week 16:			
Adjusted Mean Change (SE)	-1,09 (0,082)	-1,04 (0,079)	-0,05 [-0,268; 0,177] 0,688
Week 24:			
Adjusted Mean Change (SE)	-1,12 (0,081)	-0,98 (0,079)	-0,14 [-0,360; 0,081] 0,216
Region = Europe			
N'	158	157	
Baseline Mean (SD)	2,45 (0,581)	2,48 (0,553)	
Week 16:			
Adjusted Mean Change (SE)	-1,14 (0,070)	-1,08 (0,070)	-0,06 [-0,254; 0,135] 0,549
Week 24:			
Adjusted Mean Change (SE)	-1,18 (0,070)	-1,11 (0,070)	-0,07 [-0,266; 0,120] 0,456
Region = Latin America			
N'	161	158	
Baseline Mean (SD)	2,67 (0,611)	2,62 (0,635)	
Week 16:			
Adjusted Mean Change (SE)	-1,29 (0,070)	-1,19 (0,070)	-0,10 [-0,289; 0,097] 0,330
Week 24:			
Adjusted Mean Change (SE)	-1,48 (0,069)	-1,36 (0,070)	-0,13 [-0,318; 0,067] 0,201

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Region = Others			
N'	20	9	
Baseline Mean (SD)	2,53 (0,718)	3,07 (0,748)	
Week 16:			
Adjusted Mean Change (SE)	-1,36 (0,196)	-1,92 (0,292)	0,56 [-0,134; 1,244] 0,114
Week 24:			
Adjusted Mean Change (SE)	-1,30 (0,196)	-1,86 (0,292)	0,56 [-0,133; 1,244] 0,114

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + region + region * treatment + region * treatment * visit, within-patient correlation: unstructured covariance matrix
Exceptional model(s): **ACQ-5 score**: treatment + visit + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + region + region * treatment + region * treatment * visit, within-patient correlation: compound symmetry covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 3.6 ACQ-5 - Change from Baseline by History of Asthma Exacerbation (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
ACQ-5 score			
Interaction Test	0,574		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	361	363	
Baseline Mean (SD)	2,51 (0,591)	2,50 (0,577)	
Week 16:			
Adjusted Mean Change (SE)	-1,24 (0,058)	-1,19 (0,059)	-0,04 [-0,168; 0,083] 0,508
Week 24:			
Adjusted Mean Change (SE)	-1,33 (0,059)	-1,23 (0,060)	-0,10 [-0,227; 0,030] 0,132
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	95	87	
Baseline Mean (SD)	2,59 (0,693)	2,73 (0,692)	
Week 16:			
Adjusted Mean Change (SE)	-1,04 (0,098)	-0,87 (0,102)	-0,17 [-0,421; 0,085] 0,194
Week 24:			
Adjusted Mean Change (SE)	-1,09 (0,100)	-0,97 (0,103)	-0,12 [-0,378; 0,136] 0,356

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + history of asthma exacerbation + history of asthma exacerbation * treatment + history of asthma exacerbation * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 3.7 ACQ-5 - Change from Baseline by Patients' Prior Therapies (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
ACQ-5 score			
Interaction Test	0,721		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	224	231	
Baseline Mean (SD)	2,47 (0,625)	2,56 (0,642)	
Week 16:			
Adjusted Mean Change (SE)	-1,25 (0,069)	-1,24 (0,068)	-0,01 [-0,169; 0,149] 0,904
Week 24:			
Adjusted Mean Change (SE)	-1,40 (0,070)	-1,20 (0,069)	-0,19 [-0,356; -0,029] 0,021 *
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	232	219	
Baseline Mean (SD)	2,59 (0,597)	2,52 (0,570)	
Week 16:			
Adjusted Mean Change (SE)	-1,14 (0,069)	-1,02 (0,070)	-0,12 [-0,281; 0,041] 0,143
Week 24:			
Adjusted Mean Change (SE)	-1,17 (0,069)	-1,16 (0,071)	-0,01 [-0,171; 0,158] 0,937

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + patients' prior therapies + patients' prior therapies * treatment + patients' prior therapies * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

4. ACQ-5 - Responder Analysis

Table 4.1a ACQ-5 - Responder Analysis (as observed) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	456	450			
ACQ-5 response (decrease of at least 0.5 points), n (%)	391 (85,7)	379 (84,2)	1,20 [0,91; 1,57] 0,189	1,04 [0,98; 1,11] 0,192	0,02 [-0,03; 0,06] 0,521

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction

Analysis population: B2306 FAS total population

Table 4.1b ACQ-5 - Responder Analysis (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	472	472			
ACQ-5 response (decrease of at least 0.5 points), n (%)	395 (83,7)	388 (82,2)	1,14 [0,89; 1,48] 0,299	1,04 [0,97; 1,11] 0,277	0,01 [-0,03; 0,06] 0,545

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction

Analysis population: B2306 FAS total population

Table 4.2a ACQ-5 - Responder Analysis by Age (as observed) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ACQ-5 response (decrease of at least 0.5 points)					
Interaction Test:	p=0,711				
Age = 18-39 years					
N'	79	71			
ACQ-5 response (decrease of at least 0.5 points), n (%)	72 (91,1)	63 (88,7)	1,56 [0,79; 3,08] 0,202	1,09 [0,97; 1,24] 0,158	0,02 [-0,07; 0,12] 0,625
Age = 40-64 years					
N'	278	290			
ACQ-5 response (decrease of at least 0.5 points), n (%)	236 (84,9)	245 (84,5)	1,13 [0,80; 1,59] 0,485	1,03 [0,95; 1,11] 0,510	0,00 [-0,06; 0,06] 0,892
Age = ≥65 years					
N'	99	89			
ACQ-5 response (decrease of at least 0.5 points), n (%)	83 (83,8)	71 (79,8)	1,18 [0,66; 2,12] 0,574	1,05 [0,90; 1,22] 0,560	0,04 [-0,07; 0,15] 0,471

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + age + age * treatment + age * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + age + age * treatment + age * treatment * visit

Analysis population: B2306 FAS total population

Table 4.2b ACQ-5 - Responder Analysis by Age (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ACQ-5 response (decrease of at least 0.5 points)					
Interaction Test:	p=0,951				
Age = 18-39 years					
N'	84	73			
ACQ-5 response (decrease of at least 0.5 points), n (%)	74 (88,1)	65 (89,0)	1,17 [0,61; 2,25] 0,634	1,04 [0,91; 1,19] 0,542	-0,01 [-0,11; 0,09] 0,852
Age = 40-64 years					
N'	288	305			
ACQ-5 response (decrease of at least 0.5 points), n (%)	238 (82,6)	250 (82,0)	1,10 [0,80; 1,52] 0,550	1,03 [0,94; 1,12] 0,546	0,01 [-0,05; 0,07] 0,830
Age = ≥65 years					
N'	100	94			
ACQ-5 response (decrease of at least 0.5 points), n (%)	83 (83,0)	73 (77,7)	1,22 [0,70; 2,13] 0,488	1,06 [0,90; 1,24] 0,473	0,05 [-0,06; 0,17] 0,349

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + age + age * treatment + age * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + age + age * treatment + age * treatment * visit

Analysis population: B2306 FAS total population

Table 4.3a ACQ-5 - Responder Analysis by Gender (as observed) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ACQ-5 response (decrease of at least 0.5 points)					
Interaction Test:	p=0,649				
Gender = Male					
N'	181	166			
ACQ-5 response (decrease of at least 0.5 points), n (%)	157 (86,7)	138 (83,1)	1,30 [0,84; 2,01] 0,241	1,06 [0,96; 1,17] 0,249	0,04 [-0,04; 0,11] 0,348
Gender = Female					
N'	275	284			
ACQ-5 response (decrease of at least 0.5 points), n (%)	234 (85,1)	241 (84,9)	1,14 [0,81; 1,61] 0,453	1,03 [0,95; 1,11] 0,470	0,00 [-0,06; 0,06] 0,939

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + gender + gender * treatment + gender * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + gender + gender * treatment + gender * treatment * visit

Analysis population: B2306 FAS total population

Table 4.3b ACQ-5 - Responder Analysis by Gender (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ACQ-5 response (decrease of at least 0.5 points)					
Interaction Test:	p=0,826				
Gender = Male					
N'	185	169			
ACQ-5 response (decrease of at least 0.5 points), n (%)	158 (85,4)	141 (83,4)	1,10 [0,72; 1,67] 0,662	1,02 [0,92; 1,13] 0,648	0,02 [-0,06; 0,10] 0,609
Gender = Female					
N'	287	303			
ACQ-5 response (decrease of at least 0.5 points), n (%)	237 (82,6)	247 (81,5)	1,16 [0,84; 1,61] 0,357	1,04 [0,96; 1,13] 0,344	0,01 [-0,05; 0,07] 0,737

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + gender + gender * treatment + gender * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + gender + gender * treatment + gender * treatment * visit

Analysis population: B2306 FAS total population

Table 4.4a ACQ-5 - Responder Analysis by Region (as observed) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ACQ-5 response (decrease of at least 0.5 points)					
Interaction Test:	N.E.				
Region = Asia					
N'	117	126			
ACQ-5 response (decrease of at least 0.5 points), n (%)	95 (81,2)	94 (74,6)	1,52 [0,93; 2,50] 0,096	1,13 [0,97; 1,31] 0,109	0,07 [-0,04; 0,17] 0,213
Region = Europe					
N'	158	157			
ACQ-5 response (decrease of at least 0.5 points), n (%)	132 (83,5)	129 (82,2)	1,05 [0,67; 1,64] 0,829	1,01 [0,90; 1,13] 0,824	0,01 [-0,07; 0,10] 0,745
Region = Latin America					
N'	161	158			
ACQ-5 response (decrease of at least 0.5 points), n (%)	147 (91,3)	147 (93,0)	1,13 [0,68; 1,87] 0,635	1,02 [0,94; 1,11] 0,576	-0,02 [-0,08; 0,04] 0,564
Region = Others					
N'	20	9			
ACQ-5 response (decrease of at least 0.5 points), n (%)	17 (85,0)	9 (100,0)	0,20 [0,02; 2,20] 0,187	0,89 [0,69; 1,15] 0,389	-0,15 [-0,31; 0,01] 0,060

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + region + region * treatment + region * treatment * visit
Exceptional model(s) for OR: ACQ-5 response (decrease of at least 0.5 points): logit(proportion) = treatment + baseline + visit [by region]

Applied model for RR: log(proportion) = treatment + baseline + visit + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + region + region * treatment + region * treatment * visit

Analysis population: B2306 FAS total population

Table 4.4b ACQ-5 - Responder Analysis by Region (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ACQ-5 response (decrease of at least 0.5 points)					
Interaction Test:	N.E.				
Region = Asia					
N'	123	131			
ACQ-5 response (decrease of at least 0.5 points), n (%)	96 (78,0)	96 (73,3)	1,34 [0,85; 2,12] 0,207	1,10 [0,95; 1,29] 0,211	0,05 [-0,06; 0,15] 0,375
Region = Europe					
N'	164	168			
ACQ-5 response (decrease of at least 0.5 points), n (%)	135 (82,3)	134 (79,8)	1,10 [0,72; 1,68] 0,663	1,03 [0,91; 1,16] 0,650	0,03 [-0,06; 0,11] 0,552
Region = Latin America					
N'	165	164			
ACQ-5 response (decrease of at least 0.5 points), n (%)	147 (89,1)	149 (90,9)	1,01 [0,63; 1,60] 0,981	1,01 [0,92; 1,10] 0,836	-0,02 [-0,08; 0,05] 0,594
Region = Others					
N'	20	9			
ACQ-5 response (decrease of at least 0.5 points), n (%)	17 (85,0)	9 (100,0)	0,20 [0,02; 2,20] 0,187	0,89 [0,69; 1,14] 0,349	-0,15 [-0,31; 0,01] 0,060

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + region + region * treatment + region * treatment * visit
Exceptional model(s) for OR: ACQ-5 response (decrease of at least 0.5 points): logit(proportion) = treatment + baseline + visit [by region]

Applied model for RR: log(proportion) = treatment + baseline + visit + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + region + region * treatment + region * treatment * visit

Analysis population: B2306 FAS total population

Table 4.5a ACQ-5 - Responder Analysis by History of Asthma Exacerbation (as observed) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ACQ-5 response (decrease of at least 0.5 points)					
Interaction Test:	p=0,914				
Asthma exacerbations in the 12 months prior to screening = 1					
N'	361	363			
ACQ-5 response (decrease of at least 0.5 points), n (%)	314 (87,0)	306 (84,3)	1,23 [0,90; 1,68] 0,188	1,05 [0,98; 1,12] 0,182	0,03 [-0,02; 0,08] 0,303
Asthma exacerbations in the 12 months prior to screening = ≥2					
N'	95	87			
ACQ-5 response (decrease of at least 0.5 points), n (%)	77 (81,1)	73 (83,9)	1,19 [0,69; 2,06] 0,533	1,03 [0,89; 1,20] 0,659	-0,03 [-0,14; 0,08] 0,612

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + history of asthma exacerbation + history of asthma exacerbation * treatment + history of asthma exacerbation * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + history of asthma exacerbation + history of asthma exacerbation * treatment + history of asthma exacerbation * treatment * visit

Analysis population: B2306 FAS total population

Table 4.5b ACQ-5 - Responder Analysis by History of Asthma Exacerbation (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ACQ-5 response (decrease of at least 0.5 points)					
Interaction Test:	p=0,696				
Asthma exacerbations in the 12 months prior to screening = 1					
N'	372	382			
ACQ-5 response (decrease of at least 0.5 points), n (%)	318 (85,5)	313 (81,9)	1,20 [0,89; 1,60] 0,231	1,05 [0,97; 1,12] 0,217	0,04 [-0,02; 0,09] 0,187
Asthma exacerbations in the 12 months prior to screening = ≥2					
N'	100	90			
ACQ-5 response (decrease of at least 0.5 points), n (%)	77 (77,0)	75 (83,3)	1,06 [0,63; 1,79] 0,818	1,01 [0,86; 1,18] 0,883	-0,06 [-0,18; 0,05] 0,271

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + history of asthma exacerbation + history of asthma exacerbation * treatment + history of asthma exacerbation * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + history of asthma exacerbation + history of asthma exacerbation * treatment + history of asthma exacerbation * treatment * visit

Analysis population: B2306 FAS total population

Table 4.6a ACQ-5 - Responder Analysis by Patients' Prior Therapies (as observed) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ACQ-5 response (decrease of at least 0.5 points)					
Interaction Test:	p=0,300				
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA					
N'	224	231			
ACQ-5 response (decrease of at least 0.5 points), n (%)	196 (87,5)	193 (83,5)	1,39 [0,94; 2,05] 0,096	1,07 [0,99; 1,17] 0,102	0,04 [-0,03; 0,10] 0,230
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA					
N'	232	219			
ACQ-5 response (decrease of at least 0.5 points), n (%)	195 (84,1)	186 (84,9)	1,04 [0,72; 1,52] 0,824	1,01 [0,92; 1,10] 0,829	-0,01 [-0,08; 0,06] 0,796

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + baseline-by-visit interaction + treatment-by-visit-interaction + patients' prior therapies + patients' prior therapies * treatment + patients' prior therapies * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + baseline-by-visit interaction + treatment-by-visit-interaction + patients' prior therapies + patients' prior therapies * treatment + patients' prior therapies * treatment * visit

Analysis population: B2306 FAS total population

Table 4.6b ACQ-5 - Responder Analysis by Patients' Prior Therapies (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
ACQ-5 response (decrease of at least 0.5 points)					
Interaction Test:	p=0,374				
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA					
N'	230	240			
ACQ-5 response (decrease of at least 0.5 points), n (%)	199 (86,5)	200 (83,3)	1,30 [0,89; 1,89] 0,171	1,06 [0,97; 1,16] 0,166	0,03 [-0,03; 0,10] 0,333
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA					
N'	242	232			
ACQ-5 response (decrease of at least 0.5 points), n (%)	196 (81,0)	188 (81,0)	1,03 [0,72; 1,46] 0,878	1,01 [0,92; 1,12] 0,837	-0,00 [-0,07; 0,07] 0,991

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + baseline-by-visit interaction + treatment-by-visit-interaction + patients' prior therapies + patients' prior therapies * treatment + patients' prior therapies * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + baseline-by-visit interaction + treatment-by-visit-interaction + patients' prior therapies + patients' prior therapies * treatment + patients' prior therapies * treatment * visit

Analysis population: B2306 FAS total population

5. AQLQ-S - Return Rate / Change from Baseline

Table 5.1 AQLQ-S - Return Rate (FAS)

	Treatment groups		
Patient Reported Outcome - Return Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Total N=951**
Return Rate*, n (%)			
Baseline Returns	474 (99,6)	466 (98,1)	940 (98,8)
Week 16 Returns	451 (94,7)	446 (93,9)	897 (94,3)
Week 24 Returns	462 (97,1)	455 (95,8)	917 (96,4)

* The return rate is the proportion of patients with non-missing data for the total score at given visit on the whole study population.

Analysis population: B2306 FAS total population

Table 5.2 AQLQ-S - Change from Baseline (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
N'	457	450	
Baseline Mean (SD)	4,68 (0,858)	4,68 (0,891)	
Week 16:			
Adjusted Mean Change (SE)	0,75 (0,052)	0,69 (0,053)	0,06 [-0,044; 0,167] 0,253
Week 24:			
Adjusted Mean Change (SE)	0,82 (0,053)	0,77 (0,054)	0,05 [-0,057; 0,161] 0,348
Symptoms score			
N'	457	450	
Baseline Mean (SD)	4,71 (0,873)	4,76 (0,859)	
Week 16:			
Adjusted Mean Change (SE)	0,83 (0,055)	0,72 (0,056)	0,11 [0,002; 0,224] 0,047 *
Week 24:			
Adjusted Mean Change (SE)	0,88 (0,056)	0,84 (0,056)	0,04 [-0,076; 0,153] 0,512
Activity limitation score			
N'	457	450	
Baseline Mean (SD)	4,63 (0,899)	4,61 (0,913)	
Week 16:			
Adjusted Mean Change (SE)	0,72 (0,055)	0,69 (0,056)	0,03 [-0,085; 0,140] 0,627
Week 24:			
Adjusted Mean Change (SE)	0,80 (0,055)	0,77 (0,056)	0,03 [-0,084; 0,142] 0,616
Emotional function score			
N'	457	450	
Baseline Mean (SD)	4,98 (1,228)	4,87 (1,326)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 16:			
Adjusted Mean Change (SE)	0,69 (0,066)	0,64 (0,066)	0,05 [-0,085; 0,179] 0,484
Week 24:			
Adjusted Mean Change (SE)	0,76 (0,068)	0,66 (0,069)	0,11 [-0,035; 0,248] 0,141
Environmental stimuli score			
N'	457	450	
Baseline Mean (SD)	4,40 (1,316)	4,43 (1,391)	
Week 16:			
Adjusted Mean Change (SE)	0,63 (0,075)	0,63 (0,075)	0,01 [-0,148; 0,158] 0,948
Week 24:			
Adjusted Mean Change (SE)	0,75 (0,076)	0,67 (0,076)	0,08 [-0,077; 0,235] 0,319

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 5.3 AQLQ-S - Change from Baseline by Age (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
Interaction Test	0,685		
Age = 18-39 years			
N'	80	72	
Baseline Mean (SD)	4,79 (0,931)	4,63 (0,926)	
Week 16:			
Adjusted Mean Change (SE)	0,94 (0,098)	0,81 (0,101)	0,13 [-0,129; 0,385] 0,329
Week 24:			
Adjusted Mean Change (SE)	0,97 (0,101)	0,85 (0,106)	0,12 [-0,143; 0,392] 0,360
Age = 40-64 years			
N'	278	290	
Baseline Mean (SD)	4,67 (0,864)	4,69 (0,924)	
Week 16:			
Adjusted Mean Change (SE)	0,71 (0,060)	0,69 (0,060)	0,03 [-0,107; 0,160] 0,694
Week 24:			
Adjusted Mean Change (SE)	0,79 (0,061)	0,77 (0,061)	0,02 [-0,119; 0,156] 0,788
Age = ≥65 years			
N'	99	88	
Baseline Mean (SD)	4,63 (0,775)	4,72 (0,750)	
Week 16:			
Adjusted Mean Change (SE)	0,70 (0,090)	0,59 (0,095)	0,11 [-0,127; 0,339] 0,371
Week 24:			
Adjusted Mean Change (SE)	0,77 (0,093)	0,68 (0,097)	0,09 [-0,148; 0,331] 0,454

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Symptoms score			
Interaction Test	0,623		
Age = 18-39 years			
N'	80	72	
Baseline Mean (SD)	4,79 (0,898)	4,71 (0,934)	
Week 16:			
Adjusted Mean Change (SE)	1,04 (0,103)	0,80 (0,107)	0,23 [-0,036; 0,506] 0,090
Week 24:			
Adjusted Mean Change (SE)	1,02 (0,106)	0,89 (0,111)	0,14 [-0,144; 0,420] 0,336
Age = 40-64 years			
N'	278	290	
Baseline Mean (SD)	4,69 (0,850)	4,77 (0,876)	
Week 16:			
Adjusted Mean Change (SE)	0,80 (0,063)	0,71 (0,063)	0,08 [-0,057; 0,224] 0,246
Week 24:			
Adjusted Mean Change (SE)	0,87 (0,064)	0,84 (0,064)	0,03 [-0,110; 0,179] 0,641
Age = ≥65 years			
N'	99	88	
Baseline Mean (SD)	4,67 (0,922)	4,75 (0,738)	
Week 16:			
Adjusted Mean Change (SE)	0,76 (0,095)	0,66 (0,100)	0,10 [-0,150; 0,341] 0,447
Week 24:			
Adjusted Mean Change (SE)	0,77 (0,097)	0,80 (0,102)	-0,03 [-0,283; 0,223] 0,815

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Activity limitation score			
Interaction Test	0,350		
Age = 18-39 years			
N'	80	72	
Baseline Mean (SD)	4,79 (0,991)	4,71 (0,934)	
Week 16:			
Adjusted Mean Change (SE)	0,92 (0,103)	0,85 (0,107)	0,07 [-0,205; 0,341] 0,626
Week 24:			
Adjusted Mean Change (SE)	1,00 (0,105)	0,91 (0,110)	0,10 [-0,183; 0,374] 0,502
Age = 40-64 years			
N'	278	290	
Baseline Mean (SD)	4,63 (0,915)	4,59 (0,950)	
Week 16:			
Adjusted Mean Change (SE)	0,67 (0,063)	0,69 (0,063)	-0,02 [-0,165; 0,118] 0,745
Week 24:			
Adjusted Mean Change (SE)	0,75 (0,063)	0,78 (0,064)	-0,03 [-0,178; 0,108] 0,635
Age = ≥65 years			
N'	99	88	
Baseline Mean (SD)	4,48 (0,749)	4,60 (0,763)	
Week 16:			
Adjusted Mean Change (SE)	0,70 (0,096)	0,56 (0,100)	0,14 [-0,105; 0,389] 0,260
Week 24:			
Adjusted Mean Change (SE)	0,79 (0,096)	0,62 (0,101)	0,16 [-0,088; 0,411] 0,205

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Emotional function score			
Interaction Test	0,486		
Age = 18-39 years			
N'	80	72	
Baseline Mean (SD)	5,02 (1,193)	4,50 (1,362)	
Week 16:			
Adjusted Mean Change (SE)	0,89 (0,122)	0,70 (0,127)	0,19 [-0,127; 0,516] 0,235
Week 24:			
Adjusted Mean Change (SE)	0,89 (0,130)	0,61 (0,137)	0,28 [-0,065; 0,632] 0,111
Age = 40-64 years			
N'	278	290	
Baseline Mean (SD)	4,99 (1,238)	4,92 (1,345)	
Week 16:			
Adjusted Mean Change (SE)	0,66 (0,075)	0,66 (0,075)	-0,00 [-0,167; 0,166] 0,997
Week 24:			
Adjusted Mean Change (SE)	0,75 (0,078)	0,68 (0,078)	0,06 [-0,117; 0,240] 0,500
Age = ≥65 years			
N'	99	88	
Baseline Mean (SD)	4,91 (1,238)	5,00 (1,186)	
Week 16:			
Adjusted Mean Change (SE)	0,59 (0,113)	0,52 (0,119)	0,07 [-0,220; 0,362] 0,632
Week 24:			
Adjusted Mean Change (SE)	0,72 (0,120)	0,61 (0,126)	0,10 [-0,207; 0,417] 0,509

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Environmental stimuli score			
Interaction Test	0,663		
Age = 18-39 years			
N'	80	72	
Baseline Mean (SD)	4,52 (1,362)	4,31 (1,374)	
Week 16:			
Adjusted Mean Change (SE)	0,74 (0,141)	0,83 (0,147)	-0,10 [-0,470; 0,274] 0,606
Week 24:			
Adjusted Mean Change (SE)	0,85 (0,144)	0,86 (0,151)	-0,01 [-0,394; 0,373] 0,956
Age = 40-64 years			
N'	278	290	
Baseline Mean (SD)	4,31 (1,317)	4,40 (1,414)	
Week 16:			
Adjusted Mean Change (SE)	0,61 (0,086)	0,60 (0,086)	0,01 [-0,185; 0,203] 0,927
Week 24:			
Adjusted Mean Change (SE)	0,72 (0,087)	0,67 (0,087)	0,05 [-0,147; 0,246] 0,621
Age = ≥65 years			
N'	99	88	
Baseline Mean (SD)	4,53 (1,269)	4,63 (1,323)	
Week 16:			
Adjusted Mean Change (SE)	0,60 (0,130)	0,53 (0,137)	0,07 [-0,268; 0,407] 0,686

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 24:			
Adjusted Mean Change (SE)	0,77 (0,132)	0,54 (0,139)	0,23 [-0,111; 0,576] 0,185

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + age + age * treatment + age * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 5.4 AQLQ-S - Change from Baseline by Gender (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
Interaction Test	0,345		
Gender = Male			
N'	181	165	
Baseline Mean (SD)	4,84 (0,826)	4,87 (0,850)	
Week 16:			
Adjusted Mean Change (SE)	0,79 (0,069)	0,69 (0,073)	0,10 [-0,070; 0,273] 0,245
Week 24:			
Adjusted Mean Change (SE)	0,88 (0,071)	0,75 (0,075)	0,13 [-0,046; 0,307] 0,147
Gender = Female			
N'	276	285	
Baseline Mean (SD)	4,58 (0,863)	4,57 (0,898)	
Week 16:			
Adjusted Mean Change (SE)	0,71 (0,062)	0,68 (0,060)	0,03 [-0,100; 0,169] 0,611
Week 24:			
Adjusted Mean Change (SE)	0,77 (0,063)	0,77 (0,062)	0,00 [-0,137; 0,140] 0,982
Symptoms score			
Interaction Test	0,396		
Gender = Male			
N'	181	165	
Baseline Mean (SD)	4,83 (0,839)	4,90 (0,823)	
Week 16:			
Adjusted Mean Change (SE)	0,90 (0,073)	0,72 (0,077)	0,18 [0,003; 0,364] 0,047 *

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 24:			
Adjusted Mean Change (SE)	0,93 (0,074)	0,85 (0,079)	0,08 [-0,108; 0,264] 0,411
Gender = Female			
N'	276	285	
Baseline Mean (SD)	4,62 (0,887)	4,67 (0,869)	
Week 16:			
Adjusted Mean Change (SE)	0,78 (0,065)	0,71 (0,063)	0,07 [-0,076; 0,208] 0,359
Week 24:			
Adjusted Mean Change (SE)	0,83 (0,066)	0,82 (0,065)	0,01 [-0,135; 0,157] 0,884
Activity limitation score			
Interaction Test	0,165		
Gender = Male			
N'	181	165	
Baseline Mean (SD)	4,79 (0,888)	4,81 (0,889)	
Week 16:			
Adjusted Mean Change (SE)	0,76 (0,073)	0,70 (0,078)	0,06 [-0,123; 0,241] 0,525
Week 24:			
Adjusted Mean Change (SE)	0,91 (0,073)	0,73 (0,078)	0,18 [-0,005; 0,362] 0,056
Gender = Female			
N'	276	285	
Baseline Mean (SD)	4,52 (0,892)	4,49 (0,908)	
Week 16:			
Adjusted Mean Change (SE)	0,68 (0,065)	0,68 (0,064)	0,01 [-0,137; 0,150] 0,930
Week 24:			
Adjusted Mean Change (SE)	0,72 (0,066)	0,78 (0,064)	-0,07 [-0,211; 0,077] 0,362

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Emotional function score			
Interaction Test	0,812		
Gender = Male			
N'	181	165	
Baseline Mean (SD)	5,13 (1,188)	5,13 (1,253)	
Week 16:			
Adjusted Mean Change (SE)	0,70 (0,086)	0,63 (0,092)	0,07 [-0,144; 0,285] 0,518
Week 24:			
Adjusted Mean Change (SE)	0,74 (0,091)	0,62 (0,097)	0,12 [-0,107; 0,352] 0,294
Gender = Female			
N'	276	285	
Baseline Mean (SD)	4,87 (1,244)	4,71 (1,345)	
Week 16:			
Adjusted Mean Change (SE)	0,68 (0,078)	0,64 (0,076)	0,03 [-0,135; 0,202] 0,699
Week 24:			
Adjusted Mean Change (SE)	0,78 (0,081)	0,68 (0,079)	0,10 [-0,082; 0,279] 0,285
Environmental stimuli score			
Interaction Test	0,674		
Gender = Male			
N'	181	165	
Baseline Mean (SD)	4,67 (1,243)	4,62 (1,358)	
Week 16:			
Adjusted Mean Change (SE)	0,66 (0,099)	0,66 (0,105)	0,00 [-0,245; 0,250] 0,986
Week 24:			
Adjusted Mean Change (SE)	0,81 (0,100)	0,66 (0,107)	0,15 [-0,098; 0,406] 0,232

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Gender = Female			
N'	276	285	
Baseline Mean (SD)	4,21 (1,333)	4,33 (1,402)	
Week 16:			
Adjusted Mean Change (SE)	0,60 (0,089)	0,60 (0,086)	0,00 [-0,191; 0,198] 0,969
Week 24:			
Adjusted Mean Change (SE)	0,70 (0,090)	0,67 (0,087)	0,03 [-0,168; 0,228] 0,766

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + gender + gender * treatment + gender * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 5.5 AQLQ-S - Change from Baseline by Region (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
Interaction Test	N.E.		
Region = Asia			
N'	118	125	
Baseline Mean (SD)	4,53 (0,820)	4,47 (0,925)	
Week 16:			
Adjusted Mean Change (SE)	0,73 (0,077)	0,66 (0,075)	0,07 [-0,140; 0,281] 0,510
Week 24:			
Adjusted Mean Change (SE)	0,79 (0,080)	0,68 (0,078)	0,11 [-0,115; 0,325] 0,349
Region = Europe			
N'	160	162	
Baseline Mean (SD)	4,92 (0,854)	4,97 (0,771)	
Week 16:			
Adjusted Mean Change (SE)	0,61 (0,054)	0,54 (0,054)	0,07 [-0,077; 0,223] 0,337
Week 24:			
Adjusted Mean Change (SE)	0,64 (0,062)	0,67 (0,061)	-0,02 [-0,193; 0,150] 0,809
Region = Latin America			
N'	159	154	
Baseline Mean (SD)	4,58 (0,829)	4,58 (0,903)	
Week 16:			
Adjusted Mean Change (SE)	0,94 (0,069)	0,87 (0,070)	0,07 [-0,128; 0,258] 0,507
Week 24:			
Adjusted Mean Change (SE)	1,02 (0,066)	0,95 (0,067)	0,07 [-0,111; 0,260] 0,430

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Region = Others			
N'	20	9	
Baseline Mean (SD)	4,49 (0,988)	4,22 (1,011)	
Week 16:			
Adjusted Mean Change (SE)	0,93 (0,258)	1,45 (0,385)	-0,52 [-1,454; 0,420] 0,272
Week 24:			
Adjusted Mean Change (SE)	1,31 (0,250)	1,57 (0,373)	-0,26 [-1,171; 0,645] 0,562
Symptoms score			
Interaction Test	0,451		
Region = Asia			
N'	118	125	
Baseline Mean (SD)	4,50 (0,854)	4,51 (0,872)	
Week 16:			
Adjusted Mean Change (SE)	0,73 (0,080)	0,61 (0,078)	0,12 [-0,096; 0,338] 0,275
Week 24:			
Adjusted Mean Change (SE)	0,80 (0,082)	0,70 (0,080)	0,09 [-0,130; 0,317] 0,412
Region = Europe			
N'	160	162	
Baseline Mean (SD)	4,89 (0,853)	4,97 (0,803)	
Week 16:			
Adjusted Mean Change (SE)	0,80 (0,068)	0,73 (0,068)	0,08 [-0,109; 0,266] 0,410
Week 24:			
Adjusted Mean Change (SE)	0,78 (0,070)	0,87 (0,070)	-0,09 [-0,283; 0,104] 0,365
Region = Latin America			
N'	159	154	
Baseline Mean (SD)	4,69 (0,861)	4,76 (0,849)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 16:			
Adjusted Mean Change (SE)	0,99 (0,068)	0,83 (0,069)	0,17 [-0,025; 0,356] 0,088
Week 24:			
Adjusted Mean Change (SE)	1,07 (0,070)	0,95 (0,071)	0,11 [-0,082; 0,311] 0,253
Region = Others			
N'	20	9	
Baseline Mean (SD)	4,51 (0,989)	4,45 (0,921)	
Week 16:			
Adjusted Mean Change (SE)	0,89 (0,191)	1,32 (0,285)	-0,43 [-1,102; 0,240] 0,208
Week 24:			
Adjusted Mean Change (SE)	1,19 (0,198)	1,31 (0,295)	-0,12 [-0,817; 0,576] 0,734
Activity limitation score			
Interaction Test	0,754		
Region = Asia			
N'	118	125	
Baseline Mean (SD)	4,53 (0,851)	4,43 (0,931)	
Week 16:			
Adjusted Mean Change (SE)	0,64 (0,080)	0,60 (0,078)	0,04 [-0,176; 0,261] 0,701
Week 24:			
Adjusted Mean Change (SE)	0,67 (0,080)	0,58 (0,078)	0,09 [-0,129; 0,309] 0,422
Region = Europe			
N'	160	162	
Baseline Mean (SD)	4,84 (0,926)	4,84 (0,827)	
Week 16:			
Adjusted Mean Change (SE)	0,72 (0,068)	0,66 (0,068)	0,06 [-0,125; 0,253] 0,507

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 24:			
Adjusted Mean Change (SE)	0,80 (0,069)	0,77 (0,068)	0,02 [-0,165; 0,215] 0,796
Region = Latin America			
N'	159	154	
Baseline Mean (SD)	4,49 (0,840)	4,54 (0,938)	
Week 16:			
Adjusted Mean Change (SE)	0,80 (0,069)	0,80 (0,069)	-0,01 [-0,197; 0,186] 0,955
Week 24:			
Adjusted Mean Change (SE)	0,88 (0,069)	0,91 (0,070)	-0,03 [-0,223; 0,163] 0,758
Region = Others			
N'	20	9	
Baseline Mean (SD)	4,56 (1,144)	4,22 (0,988)	
Week 16:			
Adjusted Mean Change (SE)	0,79 (0,192)	1,12 (0,286)	-0,33 [-1,005; 0,345] 0,338
Week 24:			
Adjusted Mean Change (SE)	1,18 (0,194)	1,35 (0,290)	-0,16 [-0,848; 0,519] 0,637
Emotional function score			
Interaction Test	N.E.		
Region = Asia			
N'	118	125	
Baseline Mean (SD)	4,82 (1,222)	4,69 (1,414)	
Week 16:			
Adjusted Mean Change (SE)	0,60 (0,106)	0,56 (0,103)	0,03 [-0,257; 0,324] 0,820
Week 24:			
Adjusted Mean Change (SE)	0,69 (0,109)	0,50 (0,106)	0,19 [-0,107; 0,491] 0,207

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Region = Europe			
N'	160	162	
Baseline Mean (SD)	5,38 (1,184)	5,40 (1,063)	
Week 16:			
Adjusted Mean Change (SE)	0,49 (0,063)	0,46 (0,063)	0,02 [-0,152; 0,198] 0,798
Week 24:			
Adjusted Mean Change (SE)	0,53 (0,073)	0,51 (0,073)	0,02 [-0,185; 0,220] 0,863
Region = Latin America			
N'	159	154	
Baseline Mean (SD)	4,76 (1,198)	4,48 (1,320)	
Week 16:			
Adjusted Mean Change (SE)	1,01 (0,086)	0,88 (0,087)	0,13 [-0,115; 0,367] 0,306
Week 24:			
Adjusted Mean Change (SE)	1,07 (0,092)	0,93 (0,093)	0,15 [-0,111; 0,405] 0,263
Region = Others			
N'	20	9	
Baseline Mean (SD)	4,42 (1,034)	4,18 (1,398)	
Week 16:			
Adjusted Mean Change (SE)	0,92 (0,269)	1,52 (0,399)	-0,60 [-1,574; 0,371] 0,219
Week 24:			
Adjusted Mean Change (SE)	1,25 (0,298)	1,71 (0,441)	-0,46 [-1,535; 0,615] 0,393
Environmental stimuli score			
Interaction Test	0,788		
Region = Asia			
N'	118	125	
Baseline Mean (SD)	4,27 (1,203)	4,21 (1,480)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 16:			
Adjusted Mean Change (SE)	0,51 (0,108)	0,53 (0,106)	-0,02 [-0,313; 0,279] 0,913
Week 24:			
Adjusted Mean Change (SE)	0,56 (0,110)	0,53 (0,107)	0,03 [-0,273; 0,327] 0,860
Region = Europe			
N'	160	162	
Baseline Mean (SD)	4,64 (1,380)	4,79 (1,194)	
Week 16:			
Adjusted Mean Change (SE)	0,70 (0,092)	0,60 (0,093)	0,10 [-0,159; 0,352] 0,461
Week 24:			
Adjusted Mean Change (SE)	0,78 (0,094)	0,81 (0,094)	-0,03 [-0,285; 0,235] 0,850
Region = Latin America			
N'	159	154	
Baseline Mean (SD)	4,26 (1,329)	4,29 (1,429)	
Week 16:			
Adjusted Mean Change (SE)	0,77 (0,093)	0,82 (0,094)	-0,06 [-0,316; 0,203] 0,669
Week 24:			
Adjusted Mean Change (SE)	0,93 (0,095)	0,72 (0,096)	0,21 [-0,059; 0,469] 0,127
Region = Others			
N'	20	9	
Baseline Mean (SD)	4,29 (1,133)	3,53 (1,513)	
Week 16:			
Adjusted Mean Change (SE)	0,76 (0,260)	1,23 (0,388)	-0,46 [-1,379; 0,450] 0,319

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 24:			
Adjusted Mean Change (SE)	1,30 (0,266)	1,57 (0,397)	-0,27 [-1,206; 0,667] 0,573

N': Number of patients in the analysis
CI: Confidence Interval
N.E.: not estimable
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + region + region * treatment + region * treatment * visit, within-patient correlation: unstructured covariance matrix
Exceptional model(s): **Total score**: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region], **Emotional function score**: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region]
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 5.6 AQLQ-S - Change from Baseline by History of Asthma Exacerbation (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
Interaction Test	0,949		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	364	364	
Baseline Mean (SD)	4,69 (0,821)	4,76 (0,911)	
Week 16:			
Adjusted Mean Change (SE)	0,80 (0,055)	0,73 (0,056)	0,07 [-0,049; 0,185] 0,256
Week 24:			
Adjusted Mean Change (SE)	0,85 (0,056)	0,81 (0,057)	0,05 [-0,073; 0,169] 0,440
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	93	86	
Baseline Mean (SD)	4,64 (0,994)	4,36 (0,720)	
Week 16:			
Adjusted Mean Change (SE)	0,55 (0,093)	0,49 (0,097)	0,05 [-0,184; 0,293] 0,654
Week 24:			
Adjusted Mean Change (SE)	0,69 (0,095)	0,61 (0,098)	0,08 [-0,168; 0,322] 0,536
Symptoms score			
Interaction Test	0,941		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	364	364	
Baseline Mean (SD)	4,71 (0,836)	4,83 (0,862)	
Week 16:			
Adjusted Mean Change (SE)	0,88 (0,058)	0,77 (0,059)	0,12 [-0,008; 0,240] 0,066

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 24:			
Adjusted Mean Change (SE)	0,92 (0,059)	0,88 (0,060)	0,04 [-0,092; 0,163] 0,583
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	93	86	
Baseline Mean (SD)	4,70 (1,008)	4,44 (0,771)	
Week 16:			
Adjusted Mean Change (SE)	0,63 (0,098)	0,51 (0,102)	0,12 [-0,136; 0,367] 0,369
Week 24:			
Adjusted Mean Change (SE)	0,71 (0,100)	0,65 (0,103)	0,06 [-0,201; 0,314] 0,668
Activity limitation score			
Interaction Test	0,840		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	364	364	
Baseline Mean (SD)	4,64 (0,858)	4,69 (0,930)	
Week 16:			
Adjusted Mean Change (SE)	0,78 (0,058)	0,74 (0,059)	0,04 [-0,082; 0,167] 0,506
Week 24:			
Adjusted Mean Change (SE)	0,83 (0,059)	0,80 (0,059)	0,03 [-0,095; 0,157] 0,631
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	93	86	
Baseline Mean (SD)	4,58 (1,049)	4,27 (0,746)	
Week 16:			
Adjusted Mean Change (SE)	0,49 (0,098)	0,49 (0,103)	-0,01 [-0,262; 0,246] 0,950
Week 24:			
Adjusted Mean Change (SE)	0,66 (0,099)	0,64 (0,102)	0,03 [-0,227; 0,284] 0,827

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Emotional function score			
Interaction Test	0,766		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	364	364	
Baseline Mean (SD)	5,04 (1,196)	4,96 (1,353)	
Week 16:			
Adjusted Mean Change (SE)	0,73 (0,069)	0,69 (0,070)	0,04 [-0,105; 0,188] 0,580
Week 24:			
Adjusted Mean Change (SE)	0,79 (0,072)	0,69 (0,073)	0,10 [-0,057; 0,258] 0,209
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	93	86	
Baseline Mean (SD)	4,72 (1,321)	4,47 (1,130)	
Week 16:			
Adjusted Mean Change (SE)	0,52 (0,116)	0,43 (0,121)	0,10 [-0,202; 0,394] 0,529
Week 24:			
Adjusted Mean Change (SE)	0,65 (0,123)	0,51 (0,127)	0,14 [-0,177; 0,458] 0,385
Environmental stimuli score			
Interaction Test	0,522		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	364	364	
Baseline Mean (SD)	4,37 (1,303)	4,48 (1,426)	
Week 16:			
Adjusted Mean Change (SE)	0,67 (0,079)	0,67 (0,080)	0,00 [-0,168; 0,171] 0,986
Week 24:			
Adjusted Mean Change (SE)	0,76 (0,080)	0,72 (0,081)	0,04 [-0,132; 0,216] 0,638

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	93	86	
Baseline Mean (SD)	4,50 (1,367)	4,22 (1,217)	
Week 16:			
Adjusted Mean Change (SE)	0,49 (0,133)	0,45 (0,139)	0,03 [-0,311; 0,380] 0,844
Week 24:			
Adjusted Mean Change (SE)	0,72 (0,136)	0,48 (0,140)	0,24 [-0,115; 0,586] 0,188

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + history of asthma exacerbation + history of asthma exacerbation * treatment + history of asthma exacerbation * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 5.7 AQLQ-S - Change from Baseline by Patients' Prior Therapies (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
Interaction Test	0,882		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	226	235	
Baseline Mean (SD)	4,68 (0,862)	4,66 (0,902)	
Week 16:			
Adjusted Mean Change (SE)	0,78 (0,065)	0,75 (0,064)	0,03 [-0,118; 0,178] 0,691
Week 24:			
Adjusted Mean Change (SE)	0,89 (0,066)	0,79 (0,066)	0,10 [-0,052; 0,254] 0,197
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	231	215	
Baseline Mean (SD)	4,69 (0,855)	4,71 (0,881)	
Week 16:			
Adjusted Mean Change (SE)	0,71 (0,065)	0,62 (0,067)	0,10 [-0,054; 0,248] 0,207
Week 24:			
Adjusted Mean Change (SE)	0,75 (0,066)	0,74 (0,068)	0,00 [-0,151; 0,159] 0,963
Symptoms score			
Interaction Test	0,606		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	226	235	
Baseline Mean (SD)	4,71 (0,887)	4,73 (0,879)	
Week 16:			
Adjusted Mean Change (SE)	0,88 (0,068)	0,79 (0,067)	0,09 [-0,070; 0,242] 0,278

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 24:			
Adjusted Mean Change (SE)	0,98 (0,070)	0,86 (0,069)	0,12 [-0,038; 0,283] 0,136
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	231	215	
Baseline Mean (SD)	4,70 (0,861)	4,79 (0,837)	
Week 16:			
Adjusted Mean Change (SE)	0,79 (0,068)	0,64 (0,070)	0,15 [-0,014; 0,305] 0,074
Week 24:			
Adjusted Mean Change (SE)	0,77 (0,069)	0,82 (0,071)	-0,04 [-0,208; 0,118] 0,589
Activity limitation score			
Interaction Test	0,794		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	226	235	
Baseline Mean (SD)	4,65 (0,899)	4,61 (0,910)	
Week 16:			
Adjusted Mean Change (SE)	0,74 (0,068)	0,75 (0,068)	-0,01 [-0,166; 0,149] 0,916
Week 24:			
Adjusted Mean Change (SE)	0,88 (0,069)	0,78 (0,068)	0,09 [-0,065; 0,254] 0,245
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	231	215	
Baseline Mean (SD)	4,60 (0,900)	4,61 (0,918)	
Week 16:			
Adjusted Mean Change (SE)	0,70 (0,069)	0,63 (0,071)	0,07 [-0,093; 0,229] 0,406
Week 24:			
Adjusted Mean Change (SE)	0,72 (0,069)	0,76 (0,071)	-0,04 [-0,198; 0,125] 0,657

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Emotional function score			
Interaction Test	0,565		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	226	235	
Baseline Mean (SD)	4,93 (1,286)	4,82 (1,343)	
Week 16:			
Adjusted Mean Change (SE)	0,71 (0,081)	0,72 (0,080)	-0,00 [-0,188; 0,182] 0,975
Week 24:			
Adjusted Mean Change (SE)	0,79 (0,085)	0,71 (0,085)	0,09 [-0,114; 0,284] 0,400
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	231	215	
Baseline Mean (SD)	5,02 (1,169)	4,92 (1,308)	
Week 16:			
Adjusted Mean Change (SE)	0,66 (0,081)	0,56 (0,084)	0,10 [-0,089; 0,289] 0,299
Week 24:			
Adjusted Mean Change (SE)	0,73 (0,085)	0,60 (0,088)	0,13 [-0,074; 0,330] 0,214
Environmental stimuli score			
Interaction Test	0,907		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	226	235	
Baseline Mean (SD)	4,33 (1,355)	4,36 (1,419)	
Week 16:			
Adjusted Mean Change (SE)	0,66 (0,093)	0,66 (0,092)	0,00 [-0,213; 0,214] 0,999
Week 24:			
Adjusted Mean Change (SE)	0,76 (0,094)	0,70 (0,093)	0,07 [-0,152; 0,286] 0,549

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	231	215	
Baseline Mean (SD)	4,46 (1,276)	4,52 (1,359)	
Week 16:			
Adjusted Mean Change (SE)	0,60 (0,093)	0,59 (0,096)	0,01 [-0,209; 0,229] 0,928
Week 24:			
Adjusted Mean Change (SE)	0,74 (0,094)	0,65 (0,097)	0,09 [-0,132; 0,312] 0,427

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + patients' prior therapies + patients' prior therapies * treatment + patients' prior therapies * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

6. AQLQ-S - Responder Analysis

Table 6.1a AQLQ-S - Responder Analysis (as observed) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	457	450			
AQLQ-S response, n (%)	335 (73,3)	304 (67,6)	1,33 [1,04; 1,70] 0,025 *	1,11 [1,02; 1,21] 0,022 *	0,06 [-0,00; 0,12] 0,057

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction

Analysis population: B2306 FAS total population

Table 6.1b AQLQ-S - Responder Analysis (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	470	464			
AQLQ-S response, n (%)	337 (71,7)	308 (66,4)	1,27 [1,00; 1,62] 0,048 *	1,10 [1,00; 1,21] 0,041 *	0,05 [-0,01; 0,11] 0,078

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction

Analysis population: B2306 FAS total population

Table 6.2a AQLQ-S - Responder Analysis by Age (as observed) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test:	p=0,637				
Age = 18-39 years					
N'	80	72			
AQLQ-S response, n (%)	65 (81,3)	53 (73,6)	1,37 [0,77; 2,45] 0,285	1,11 [0,92; 1,33] 0,284	0,08 [-0,06; 0,21] 0,260
Age = 40-64 years					
N'	278	290			
AQLQ-S response, n (%)	199 (71,6)	199 (68,6)	1,22 [0,89; 1,67] 0,209	1,08 [0,96; 1,21] 0,187	0,03 [-0,05; 0,10] 0,440
Age = ≥65 years					
N'	99	88			
AQLQ-S response, n (%)	71 (71,7)	52 (59,1)	1,66 [0,95; 2,88] 0,073	1,24 [0,98; 1,57] 0,069	0,13 [-0,01; 0,26] 0,068

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + age + age * treatment + age * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + age + age * treatment + age * treatment * visit

Analysis population: B2306 FAS total population

Table 6.2b AQLQ-S - Responder Analysis by Age (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test:	p=0,371				
Age = 18-39 years					
N'	84	72			
AQLQ-S response, n (%)	66 (78,6)	53 (73,6)	1,17 [0,66; 2,08] 0,601	1,05 [0,87; 1,28] 0,588	0,05 [-0,08; 0,18] 0,469
Age = 40-64 years					
N'	286	300			
AQLQ-S response, n (%)	199 (69,6)	202 (67,3)	1,16 [0,85; 1,56] 0,346	1,06 [0,95; 1,19] 0,313	0,02 [-0,05; 0,10] 0,558
Age = ≥65 years					
N'	100	92			
AQLQ-S response, n (%)	72 (72,0)	53 (57,6)	1,78 [1,04; 3,05] 0,035 *	1,29 [1,02; 1,63] 0,032 *	0,14 [0,01; 0,28] 0,035 *

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + age + age * treatment + age * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + age + age * treatment + age * treatment * visit

Analysis population: B2306 FAS total population

Table 6.3a AQLQ-S - Responder Analysis by Gender (as observed) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test:	p=0,210				
Gender = Male					
N'	181	165			
AQLQ-S response, n (%)	131 (72,4)	106 (64,2)	1,62 [1,08; 2,42] 0,019 *	1,20 [1,03; 1,40] 0,017 *	0,08 [-0,02; 0,18] 0,104
Gender = Female					
N'	276	285			
AQLQ-S response, n (%)	204 (73,9)	198 (69,5)	1,17 [0,85; 1,60] 0,330	1,06 [0,95; 1,18] 0,327	0,04 [-0,03; 0,12] 0,242

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + gender + gender * treatment + gender * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + gender + gender * treatment + gender * treatment * visit

Analysis population: B2306 FAS total population

Table 6.3b AQLQ-S - Responder Analysis by Gender (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test:	p=0,239				
Gender = Male					
N'	184	166			
AQLQ-S response, n (%)	132 (71,7)	106 (63,9)	1,52 [1,03; 2,24] 0,033 *	1,19 [1,02; 1,38] 0,028 *	0,08 [-0,02; 0,18] 0,114
Gender = Female					
N'	286	298			
AQLQ-S response, n (%)	205 (71,7)	202 (67,8)	1,13 [0,84; 1,54] 0,419	1,05 [0,94; 1,18] 0,410	0,04 [-0,04; 0,11] 0,305

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + gender + gender * treatment + gender * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + gender + gender * treatment + gender * treatment * visit

Analysis population: B2306 FAS total population

Table 6.4a AQLQ-S - Responder Analysis by Region (as observed) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test:	p=0,305				
Region = Asia					
N'	118	125			
AQLQ-S response, n (%)	81 (68,6)	79 (63,2)	1,73 [1,08; 2,77] 0,022 *	1,25 [1,04; 1,50] 0,020 *	0,05 [-0,06; 0,17] 0,370
Region = Europe					
N'	160	162			
AQLQ-S response, n (%)	107 (66,9)	104 (64,2)	1,05 [0,69; 1,60] 0,819	1,02 [0,86; 1,21] 0,843	0,03 [-0,08; 0,13] 0,613
Region = Latin America					
N'	159	154			
AQLQ-S response, n (%)	130 (81,8)	113 (73,4)	1,46 [0,96; 2,22] 0,077	1,13 [0,99; 1,28] 0,064	0,08 [-0,01; 0,18] 0,074
Region = Others					
N'	20	9			
AQLQ-S response, n (%)	17 (85,0)	8 (88,9)	0,46 [0,06; 3,58] 0,455	0,87 [0,56; 1,37] 0,556	-0,04 [-0,30; 0,22] 0,768

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + region + region * treatment + region * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + region + region * treatment + region * treatment * visit

Analysis population: B2306 FAS total population

Table 6.4b AQLQ-S - Responder Analysis by Region (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test:	p=0,549				
Region = Asia					
N'	123	129			
AQLQ-S response, n (%)	81 (65,9)	81 (62,8)	1,51 [0,96; 2,37] 0,078	1,20 [0,99; 1,45] 0,065	0,03 [-0,09; 0,15] 0,612
Region = Europe					
N'	164	168			
AQLQ-S response, n (%)	108 (65,9)	105 (62,5)	1,10 [0,73; 1,65] 0,660	1,04 [0,87; 1,24] 0,666	0,03 [-0,07; 0,14] 0,524
Region = Latin America					
N'	163	158			
AQLQ-S response, n (%)	131 (80,4)	114 (72,2)	1,36 [0,91; 2,04] 0,136	1,11 [0,97; 1,27] 0,117	0,08 [-0,01; 0,17] 0,083
Region = Others					
N'	20	9			
AQLQ-S response, n (%)	17 (85,0)	8 (88,9)	0,46 [0,06; 3,49] 0,451	0,87 [0,56; 1,36] 0,552	-0,04 [-0,30; 0,22] 0,768

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + region + region * treatment + region * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + region + region * treatment + region * treatment * visit

Analysis population: B2306 FAS total population

Table 6.5a AQLQ-S - Responder Analysis by History of Asthma Exacerbation (as observed) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test:	p=0,173				
Asthma exacerbations in the 12 months prior to screening = 1					
N'	364	364			
AQLQ-S response, n (%)	276 (75,8)	243 (66,8)	1,45 [1,10; 1,91] 0,009 *	1,15 [1,04; 1,27] 0,005 *	0,09 [0,03; 0,16] 0,007 *
Asthma exacerbations in the 12 months prior to screening = ≥2					
N'	93	86			
AQLQ-S response, n (%)	59 (63,4)	61 (70,9)	0,94 [0,54; 1,64] 0,837	0,95 [0,77; 1,18] 0,664	-0,07 [-0,21; 0,06] 0,284

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + history of asthma exacerbation + history of asthma exacerbation * treatment + history of asthma exacerbation * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + history of asthma exacerbation + history of asthma exacerbation * treatment + history of asthma exacerbation * treatment * visit

Analysis population: B2306 FAS total population

Table 6.5b AQLQ-S - Responder Analysis by History of Asthma Exacerbation (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test:	p=0,170				
Asthma exacerbations in the 12 months prior to screening = 1					
N'	372	376			
AQLQ-S response, n (%)	277 (74,5)	246 (65,4)	1,39 [1,06; 1,82] 0,016 *	1,14 [1,03; 1,26] 0,010 *	0,09 [0,02; 0,16] 0,007 *
Asthma exacerbations in the 12 months prior to screening = ≥2					
N'	98	88			
AQLQ-S response, n (%)	60 (61,2)	62 (70,5)	0,92 [0,54; 1,56] 0,745	0,95 [0,76; 1,18] 0,617	-0,09 [-0,23; 0,04] 0,182

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + history of asthma exacerbation + history of asthma exacerbation * treatment + history of asthma exacerbation * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + background ICS/LABA + baseline-by-visit interaction + treatment-by-visit-interaction + history of asthma exacerbation + history of asthma exacerbation * treatment + history of asthma exacerbation * treatment * visit

Analysis population: B2306 FAS total population

Table 6.6a AQLQ-S - Responder Analysis by Patients' Prior Therapies (as observed) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test:	p=0,850				
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA					
N'	226	235			
AQLQ-S response, n (%)	172 (76,1)	164 (69,8)	1,36 [0,96; 1,94] 0,084	1,11 [0,99; 1,25] 0,084	0,06 [-0,02; 0,14] 0,126
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA					
N'	231	215			
AQLQ-S response, n (%)	163 (70,6)	140 (65,1)	1,30 [0,92; 1,84] 0,137	1,11 [0,97; 1,27] 0,114	0,05 [-0,03; 0,14] 0,218

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + baseline-by-visit interaction + treatment-by-visit-interaction + patients' prior therapies + patients' prior therapies * treatment + patients' prior therapies * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + baseline-by-visit interaction + treatment-by-visit-interaction + patients' prior therapies + patients' prior therapies * treatment + patients' prior therapies * treatment * visit

Analysis population: B2306 FAS total population

Table 6.6b AQLQ-S - Responder Analysis by Patients' Prior Therapies (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test:	p=0,791				
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA					
N'	230	240			
AQLQ-S response, n (%)	173 (75,2)	167 (69,6)	1,32 [0,94; 1,86] 0,109	1,10 [0,98; 1,25] 0,104	0,06 [-0,02; 0,14] 0,171
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA					
N'	240	224			
AQLQ-S response, n (%)	164 (68,3)	141 (62,9)	1,24 [0,89; 1,73] 0,211	1,10 [0,96; 1,27] 0,178	0,05 [-0,03; 0,14] 0,222

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + visit + region + baseline-by-visit interaction + treatment-by-visit-interaction + patients' prior therapies + patients' prior therapies * treatment + patients' prior therapies * treatment * visit
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: log(proportion) = treatment + baseline + visit + region + baseline-by-visit interaction + treatment-by-visit-interaction + patients' prior therapies + patients' prior therapies * treatment + patients' prior therapies * treatment * visit

Analysis population: B2306 FAS total population

7. SGRQ - Return Rate / Change from Baseline

Table 7.1 SGRQ - Return Rate (FAS)

	Treatment groups		
Patient Reported Outcome - Return Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Total N=951**
Return Rate*, n (%)			
Baseline Returns	474 (99,6)	464 (97,7)	938 (98,6)
Week 24 Returns	458 (96,2)	446 (93,9)	904 (95,1)

* The return rate is the proportion of patients with non-missing data for the total score at given visit on the whole study population.

Analysis population: B2306 FAS total population

Table 7.2a SGRQ - Change from Baseline (as observed) (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
N'	452	436	
Baseline Mean (SD)	39,56 (16,809)	39,43 (18,018)	
Week 24:			
Adjusted Mean Change (SE)	-14,44 (1,052)	-12,35 (1,067)	-2,09 [-4,132; -0,044] 0,045 *
Symptoms score			
N'	452	436	
Baseline Mean (SD)	52,21 (19,416)	51,50 (19,621)	
Week 24:			
Adjusted Mean Change (SE)	-18,46 (1,380)	-17,35 (1,399)	-1,11 [-3,796; 1,586] 0,421
Activity score			
N'	452	436	
Baseline Mean (SD)	52,77 (21,233)	51,94 (21,618)	
Week 24:			
Adjusted Mean Change (SE)	-15,31 (1,407)	-13,30 (1,426)	-2,00 [-4,747; 0,737] 0,152
Impacts score			
N'	452	436	
Baseline Mean (SD)	28,23 (18,372)	28,63 (20,258)	
Week 24:			
Adjusted Mean Change (SE)	-12,25 (1,054)	-9,82 (1,070)	-2,43 [-4,475; -0,387] 0,020 *

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + region + background ICS/LABA + baseline value
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 7.2b SGRQ - Change from Baseline (LOCF) (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
N'	470	462	
Baseline Mean (SD)	39,80 (16,822)	39,44 (18,017)	
Week 24:			
Adjusted Mean Change (SE)	-13,75 (1,039)	-11,43 (1,042)	-2,32 [-4,340; -0,299] 0,024 *
Symptoms score			
N'	470	462	
Baseline Mean (SD)	52,44 (19,419)	51,66 (19,545)	
Week 24:			
Adjusted Mean Change (SE)	-17,85 (1,361)	-16,39 (1,366)	-1,46 [-4,118; 1,198] 0,282
Activity score			
N'	470	462	
Baseline Mean (SD)	52,89 (21,241)	51,89 (21,658)	
Week 24:			
Adjusted Mean Change (SE)	-14,55 (1,370)	-12,26 (1,375)	-2,29 [-4,966; 0,382] 0,093
Impacts score			
N'	470	462	
Baseline Mean (SD)	28,52 (18,405)	28,65 (20,262)	
Week 24:			
Adjusted Mean Change (SE)	-11,60 (1,044)	-9,05 (1,049)	-2,55 [-4,575; -0,519] 0,014 *

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + region + background ICS/LABA + baseline value
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.
Imputation method: LOCF

Analysis population: B2306 FAS total population

Table 7.3a SGRQ - Change from Baseline by Age (as observed) (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
Interaction Test	0,714		
Age = 18-39 years			
N'	79	67	
Baseline Mean (SD)	32,36 (17,754)	35,67 (17,355)	
Week 24:			
Adjusted Mean Change (SE)	-16,57 (1,917)	-16,46 (2,036)	-0,11 [-5,160; 4,936] 0,965
Age = 40-64 years			
N'	274	284	
Baseline Mean (SD)	40,74 (16,568)	39,18 (18,707)	
Week 24:			
Adjusted Mean Change (SE)	-14,23 (1,186)	-11,79 (1,193)	-2,44 [-5,011; 0,136] 0,063
Age = ≥65 years			
N'	99	85	
Baseline Mean (SD)	42,05 (15,259)	43,20 (15,479)	
Week 24:			
Adjusted Mean Change (SE)	-13,06 (1,764)	-10,68 (1,873)	-2,38 [-6,876; 2,114] 0,299
Symptoms score			
Interaction Test	0,356		
Age = 18-39 years			
N'	79	67	
Baseline Mean (SD)	47,29 (21,197)	49,86 (19,965)	
Week 24:			
Adjusted Mean Change (SE)	-19,27 (2,528)	-21,52 (2,684)	2,25 [-4,406; 8,902] 0,508

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Age = 40-64 years			
N'	274	284	
Baseline Mean (SD)	53,68 (18,319)	51,00 (19,883)	
Week 24:			
Adjusted Mean Change (SE)	-19,40 (1,558)	-16,79 (1,568)	-2,61 [-6,006; 0,785] 0,132
Age = ≥65 years			
N'	99	85	
Baseline Mean (SD)	52,06 (20,413)	54,47 (18,349)	
Week 24:			
Adjusted Mean Change (SE)	-14,71 (2,314)	-15,37 (2,458)	0,66 [-5,267; 6,588] 0,827
Activity score			
Interaction Test	0,492		
Age = 18-39 years			
N'	79	67	
Baseline Mean (SD)	41,38 (22,386)	45,86 (20,346)	
Week 24:			
Adjusted Mean Change (SE)	-20,76 (2,560)	-22,61 (2,713)	1,84 [-4,878; 8,568] 0,590
Age = 40-64 years			
N'	274	284	
Baseline Mean (SD)	54,00 (20,784)	51,27 (22,325)	
Week 24:			
Adjusted Mean Change (SE)	-14,54 (1,575)	-11,82 (1,584)	-2,73 [-6,155; 0,701] 0,119
Age = ≥65 years			
N'	99	85	
Baseline Mean (SD)	58,43 (18,200)	58,96 (18,302)	
Week 24:			
Adjusted Mean Change (SE)	-12,68 (2,350)	-10,57 (2,493)	-2,11 [-8,092; 3,878] 0,490

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Impacts score			
Interaction Test	0,881		
Age = 18-39 years			
N'	79	67	
Baseline Mean (SD)	22,86 (18,222)	25,55 (20,333)	
Week 24:			
Adjusted Mean Change (SE)	-13,47 (1,923)	-11,21 (2,044)	-2,27 [-7,330; 2,799] 0,380
Age = 40-64 years			
N'	274	284	
Baseline Mean (SD)	29,26 (18,603)	28,71 (20,926)	
Week 24:			
Adjusted Mean Change (SE)	-11,97 (1,192)	-9,85 (1,201)	-2,12 [-4,700; 0,464] 0,108
Age = ≥65 years			
N'	99	85	
Baseline Mean (SD)	29,65 (17,227)	30,80 (17,682)	
Week 24:			
Adjusted Mean Change (SE)	-12,09 (1,770)	-8,65 (1,879)	-3,44 [-7,954; 1,067] 0,134

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + region + background ICS/LABA + baseline value + age + age * treatment
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 7.3b SGRQ - Change from Baseline by Age (LOCF) (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
Interaction Test	0,761		
Age = 18-39 years			
N'	84	72	
Baseline Mean (SD)	33,29 (17,989)	36,86 (18,099)	
Week 24:			
Adjusted Mean Change (SE)	-15,31 (1,880)	-14,66 (1,986)	-0,65 [-5,595; 4,300] 0,797
Age = 40-64 years			
N'	286	299	
Baseline Mean (SD)	40,91 (16,599)	39,22 (18,521)	
Week 24:			
Adjusted Mean Change (SE)	-13,57 (1,173)	-11,11 (1,168)	-2,46 [-5,010; 0,083] 0,058
Age = ≥65 years			
N'	100	91	
Baseline Mean (SD)	42,13 (15,200)	42,21 (15,978)	
Week 24:			
Adjusted Mean Change (SE)	-12,69 (1,768)	-9,66 (1,833)	-3,02 [-7,485; 1,436] 0,184
Symptoms score			
Interaction Test	0,500		
Age = 18-39 years			
N'	84	72	
Baseline Mean (SD)	48,03 (21,068)	50,26 (19,753)	
Week 24:			
Adjusted Mean Change (SE)	-18,15 (2,476)	-19,89 (2,616)	1,74 [-4,773; 8,256] 0,600

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Age = 40-64 years			
N'	286	299	
Baseline Mean (SD)	53,80 (18,418)	51,45 (19,639)	
Week 24:			
Adjusted Mean Change (SE)	-18,71 (1,540)	-16,15 (1,535)	-2,56 [-5,912; 0,799] 0,135
Age = ≥65 years			
N'	100	91	
Baseline Mean (SD)	52,24 (20,392)	53,46 (19,155)	
Week 24:			
Adjusted Mean Change (SE)	-14,62 (2,318)	-13,84 (2,406)	-0,78 [-6,658; 5,093] 0,794
Activity score			
Interaction Test	0,602		
Age = 18-39 years			
N'	84	72	
Baseline Mean (SD)	42,60 (22,696)	46,76 (20,340)	
Week 24:			
Adjusted Mean Change (SE)	-19,26 (2,477)	-20,16 (2,612)	0,90 [-5,603; 7,407] 0,786
Age = 40-64 years			
N'	286	299	
Baseline Mean (SD)	53,95 (20,853)	51,33 (22,353)	
Week 24:			
Adjusted Mean Change (SE)	-13,83 (1,539)	-11,00 (1,532)	-2,83 [-6,183; 0,515] 0,097
Age = ≥65 years			
N'	100	91	
Baseline Mean (SD)	58,52 (18,129)	57,79 (19,094)	
Week 24:			
Adjusted Mean Change (SE)	-12,14 (2,325)	-9,72 (2,409)	-2,42 [-8,289; 3,441] 0,418

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Impacts score			
Interaction Test	0,785		
Age = 18-39 years			
N'	84	72	
Baseline Mean (SD)	23,63 (18,401)	27,16 (21,843)	
Week 24:			
Adjusted Mean Change (SE)	-12,26 (1,891)	-9,68 (2,000)	-2,58 [-7,563; 2,394] 0,309
Age = 40-64 years			
N'	286	299	
Baseline Mean (SD)	29,56 (18,658)	28,63 (20,615)	
Week 24:			
Adjusted Mean Change (SE)	-11,37 (1,182)	-9,29 (1,179)	-2,08 [-4,644; 0,480] 0,111
Age = ≥65 years			
N'	100	91	
Baseline Mean (SD)	29,68 (17,143)	29,91 (17,776)	
Week 24:			
Adjusted Mean Change (SE)	-11,74 (1,778)	-7,83 (1,844)	-3,91 [-8,403; 0,576] 0,087

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + region + background ICS/LABA + baseline value + age + age * treatment
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.
Imputation method: LOCF

Analysis population: B2306 FAS total population

Table 7.4a SGRQ - Change from Baseline by Gender (as observed) (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
Interaction Test	0,874		
Gender = Male			
N'	180	163	
Baseline Mean (SD)	36,46 (17,203)	35,58 (17,020)	
Week 24:			
Adjusted Mean Change (SE)	-14,85 (1,351)	-12,99 (1,446)	-1,86 [-5,155; 1,444] 0,270
Gender = Female			
N'	272	273	
Baseline Mean (SD)	41,61 (16,252)	41,72 (18,235)	
Week 24:			
Adjusted Mean Change (SE)	-14,10 (1,242)	-11,90 (1,213)	-2,20 [-4,810; 0,416] 0,099
Symptoms score			
Interaction Test	0,728		
Gender = Male			
N'	180	163	
Baseline Mean (SD)	50,28 (19,892)	50,13 (21,281)	
Week 24:			
Adjusted Mean Change (SE)	-18,97 (1,779)	-17,27 (1,904)	-1,70 [-6,043; 2,645] 0,443
Gender = Female			
N'	272	273	
Baseline Mean (SD)	53,49 (19,023)	52,32 (18,551)	
Week 24:			
Adjusted Mean Change (SE)	-18,07 (1,624)	-17,35 (1,584)	-0,72 [-4,156; 2,726] 0,684

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Activity score			
Interaction Test	0,522		
Gender = Male			
N'	180	163	
Baseline Mean (SD)	47,64 (21,593)	46,01 (20,658)	
Week 24:			
Adjusted Mean Change (SE)	-16,71 (1,806)	-15,93 (1,935)	-0,78 [-5,190; 3,632] 0,729
Gender = Female			
N'	272	273	
Baseline Mean (SD)	56,15 (20,331)	55,48 (21,439)	
Week 24:			
Adjusted Mean Change (SE)	-14,17 (1,657)	-11,55 (1,616)	-2,62 [-6,111; 0,874] 0,142
Impacts score			
Interaction Test	0,930		
Gender = Male			
N'	180	163	
Baseline Mean (SD)	25,98 (18,338)	25,24 (18,409)	
Week 24:			
Adjusted Mean Change (SE)	-12,34 (1,353)	-9,80 (1,447)	-2,55 [-5,846; 0,754] 0,130
Gender = Female			
N'	272	273	
Baseline Mean (SD)	29,71 (18,275)	30,66 (21,057)	
Week 24:			
Adjusted Mean Change (SE)	-12,18 (1,243)	-9,82 (1,217)	-2,36 [-4,970; 0,257] 0,077

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + region + background ICS/LABA + baseline value + gender + gender * treatment
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 7.4b SGRQ - Change from Baseline by Gender (LOCF) (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
Interaction Test	0,640		
Gender = Male			
N'	184	166	
Baseline Mean (SD)	36,53 (17,149)	35,39 (16,952)	
Week 24:			
Adjusted Mean Change (SE)	-14,44 (1,346)	-12,80 (1,441)	-1,64 [-4,943; 1,668] 0,331
Gender = Female			
N'	286	296	
Baseline Mean (SD)	41,91 (16,291)	41,72 (18,223)	
Week 24:			
Adjusted Mean Change (SE)	-13,24 (1,220)	-10,60 (1,175)	-2,64 [-5,197; -0,077] 0,043 *
Symptoms score			
Interaction Test	0,977		
Gender = Male			
N'	184	166	
Baseline Mean (SD)	50,44 (19,890)	49,92 (21,200)	
Week 24:			
Adjusted Mean Change (SE)	-18,83 (1,772)	-17,38 (1,897)	-1,45 [-5,803; 2,897] 0,512
Gender = Female			
N'	286	296	
Baseline Mean (SD)	53,72 (19,034)	52,63 (18,519)	
Week 24:			
Adjusted Mean Change (SE)	-17,15 (1,594)	-15,78 (1,534)	-1,37 [-4,743; 1,996] 0,424

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Activity score			
Interaction Test	0,314		
Gender = Male			
N'	184	166	
Baseline Mean (SD)	47,70 (21,430)	45,85 (20,603)	
Week 24:			
Adjusted Mean Change (SE)	-16,12 (1,776)	-15,75 (1,903)	-0,37 [-4,728; 3,988] 0,868
Gender = Female			
N'	286	296	
Baseline Mean (SD)	56,23 (20,469)	55,28 (21,531)	
Week 24:			
Adjusted Mean Change (SE)	-13,38 (1,604)	-10,18 (1,543)	-3,20 [-6,577; 0,172] 0,063
Impacts score			
Interaction Test	0,924		
Gender = Male			
N'	184	166	
Baseline Mean (SD)	26,01 (18,321)	25,03 (18,315)	
Week 24:			
Adjusted Mean Change (SE)	-12,00 (1,354)	-9,61 (1,448)	-2,39 [-5,715; 0,926] 0,157
Gender = Female			
N'	286	296	
Baseline Mean (SD)	30,14 (18,309)	30,69 (21,034)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 24:			
Adjusted Mean Change (SE)	-11,31 (1,226)	-8,71 (1,182)	-2,60 [-5,169; -0,027] 0,048 *

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + region + background ICS/LABA + baseline value + gender + gender * treatment
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.
Imputation method: LOCF

Analysis population: B2306 FAS total population

Table 7.5a SGRQ - Change from Baseline by Region (as observed) (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
Interaction Test	0,910		
Region = Asia			
N'	116	122	
Baseline Mean (SD)	45,37 (16,863)	47,44 (19,378)	
Week 24:			
Adjusted Mean Change (SE)	-9,04 (1,467)	-8,22 (1,436)	-0,82 [-4,813; 3,178] 0,688
Region = Europe			
N'	157	155	
Baseline Mean (SD)	38,70 (16,483)	35,79 (16,619)	
Week 24:			
Adjusted Mean Change (SE)	-12,09 (1,253)	-9,46 (1,265)	-2,63 [-6,125; 0,856] 0,139
Region = Latin America			
N'	159	150	
Baseline Mean (SD)	35,96 (15,411)	36,82 (15,783)	
Week 24:			
Adjusted Mean Change (SE)	-16,23 (1,253)	-14,19 (1,284)	-2,04 [-5,548; 1,470] 0,254
Region = Others			
N'	20	9	
Baseline Mean (SD)	41,35 (21,352)	36,82 (25,401)	
Week 24:			
Adjusted Mean Change (SE)	-18,47 (3,521)	-14,73 (5,245)	-3,74 [-16,104; 8,627] 0,553

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Symptoms score			
Interaction Test	0,153		
Region = Asia			
N'	116	122	
Baseline Mean (SD)	56,63 (19,148)	57,00 (18,741)	
Week 24:			
Adjusted Mean Change (SE)	-14,72 (1,908)	-16,12 (1,860)	1,39 [-3,818; 6,604] 0,600
Region = Europe			
N'	157	155	
Baseline Mean (SD)	51,76 (19,193)	49,60 (19,083)	
Week 24:			
Adjusted Mean Change (SE)	-15,32 (1,635)	-16,72 (1,648)	1,40 [-3,150; 5,953] 0,546
Region = Latin America			
N'	159	150	
Baseline Mean (SD)	50,10 (18,212)	49,45 (19,938)	
Week 24:			
Adjusted Mean Change (SE)	-26,31 (1,632)	-21,10 (1,676)	-5,20 [-9,779; -0,623] 0,026 *
Region = Others			
N'	20	9	
Baseline Mean (SD)	46,86 (27,526)	44,14 (23,151)	
Week 24:			
Adjusted Mean Change (SE)	-27,21 (4,596)	-29,47 (6,846)	2,26 [-13,871; 18,390] 0,783
Activity score			
Interaction Test	0,691		
Region = Asia			
N'	116	122	
Baseline Mean (SD)	58,73 (18,456)	58,63 (22,357)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 24:			
Adjusted Mean Change (SE)	-9,30 (1,947)	-7,42 (1,898)	-1,89 [-7,191; 3,418] 0,485
Region = Europe			
N'	157	155	
Baseline Mean (SD)	51,61 (21,261)	48,47 (20,302)	
Week 24:			
Adjusted Mean Change (SE)	-13,45 (1,664)	-10,82 (1,678)	-2,63 [-7,262; 2,007] 0,266
Region = Latin America			
N'	159	150	
Baseline Mean (SD)	48,93 (21,188)	50,37 (20,666)	
Week 24:			
Adjusted Mean Change (SE)	-16,96 (1,662)	-16,80 (1,704)	-0,16 [-4,818; 4,502] 0,947
Region = Others			
N'	20	9	
Baseline Mean (SD)	57,73 (28,590)	47,27 (31,256)	
Week 24:			
Adjusted Mean Change (SE)	-24,80 (4,678)	-15,22 (6,966)	-9,58 [-26,008; 6,848] 0,253
Impacts score			
Interaction Test	0,875		
Region = Asia			
N'	116	122	
Baseline Mean (SD)	34,24 (20,451)	38,06 (23,277)	
Week 24:			
Adjusted Mean Change (SE)	-6,63 (1,471)	-5,50 (1,445)	-1,13 [-5,142; 2,884] 0,581
Region = Europe			
N'	157	155	
Baseline Mean (SD)	27,39 (17,514)	24,45 (17,956)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 24:			
Adjusted Mean Change (SE)	-10,46 (1,258)	-7,08 (1,269)	-3,38 [-6,885; 0,121] 0,058
Region = Latin America			
N'	159	150	
Baseline Mean (SD)	24,42 (16,203)	25,30 (16,751)	
Week 24:			
Adjusted Mean Change (SE)	-13,40 (1,258)	-10,97 (1,289)	-2,42 [-5,947; 1,097] 0,177
Region = Others			
N'	20	9	
Baseline Mean (SD)	30,10 (20,661)	28,54 (27,988)	
Week 24:			
Adjusted Mean Change (SE)	-12,40 (3,534)	-10,31 (5,264)	-2,09 [-14,504; 10,316] 0,741

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + background ICS/LABA + baseline value + region + region * treatment
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 7.5b SGRQ - Change from Baseline by Region (LOCF) (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
Interaction Test	0,890		
Region = Asia			
N'	123	129	
Baseline Mean (SD)	45,49 (16,939)	47,46 (19,487)	
Week 24:			
Adjusted Mean Change (SE)	-8,70 (1,435)	-7,81 (1,407)	-0,89 [-4,801; 3,025] 0,656
Region = Europe			
N'	164	167	
Baseline Mean (SD)	38,85 (16,540)	36,02 (16,446)	
Week 24:			
Adjusted Mean Change (SE)	-11,71 (1,236)	-8,93 (1,228)	-2,79 [-6,201; 0,630] 0,110
Region = Latin America			
N'	163	157	
Baseline Mean (SD)	36,29 (15,369)	36,64 (15,900)	
Week 24:			
Adjusted Mean Change (SE)	-15,82 (1,248)	-13,42 (1,266)	-2,40 [-5,879; 1,071] 0,175
Region = Others			
N'	20	9	
Baseline Mean (SD)	41,35 (21,352)	36,82 (25,401)	
Week 24:			
Adjusted Mean Change (SE)	-18,46 (3,548)	-14,56 (5,285)	-3,91 [-16,370; 8,554] 0,539

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Symptoms score			
Interaction Test	0,112		
Region = Asia			
N'	123	129	
Baseline Mean (SD)	56,16 (19,051)	57,03 (18,347)	
Week 24:			
Adjusted Mean Change (SE)	-14,26 (1,869)	-15,73 (1,826)	1,47 [-3,638; 6,587] 0,572
Region = Europe			
N'	164	167	
Baseline Mean (SD)	52,25 (19,433)	50,11 (19,008)	
Week 24:			
Adjusted Mean Change (SE)	-14,88 (1,615)	-15,78 (1,602)	0,90 [-3,563; 5,360] 0,693
Region = Latin America			
N'	163	157	
Baseline Mean (SD)	50,50 (18,203)	49,32 (20,139)	
Week 24:			
Adjusted Mean Change (SE)	-25,86 (1,628)	-20,06 (1,654)	-5,79 [-10,335; -1,252] 0,012 *
Region = Others			
N'	20	9	
Baseline Mean (SD)	46,86 (27,526)	44,14 (23,151)	
Week 24:			
Adjusted Mean Change (SE)	-26,89 (4,639)	-28,99 (6,911)	2,10 [-14,184; 18,383] 0,800
Activity score			
Interaction Test	0,707		
Region = Asia			
N'	123	129	
Baseline Mean (SD)	58,70 (18,702)	58,45 (22,171)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 24:			
Adjusted Mean Change (SE)	-9,09 (1,885)	-6,84 (1,840)	-2,24 [-7,386; 2,898] 0,392
Region = Europe			
N'	164	167	
Baseline Mean (SD)	51,56 (21,372)	48,89 (20,391)	
Week 24:			
Adjusted Mean Change (SE)	-12,94 (1,624)	-10,19 (1,612)	-2,75 [-7,239; 1,737] 0,229
Region = Latin America			
N'	163	157	
Baseline Mean (SD)	49,25 (21,064)	49,96 (20,977)	
Week 24:			
Adjusted Mean Change (SE)	-16,44 (1,638)	-15,93 (1,661)	-0,51 [-5,080; 4,056] 0,826
Region = Others			
N'	20	9	
Baseline Mean (SD)	57,73 (28,590)	47,27 (31,256)	
Week 24:			
Adjusted Mean Change (SE)	-24,83 (4,666)	-15,03 (6,948)	-9,79 [-26,181; 6,593] 0,241
Impacts score			
Interaction Test	0,844		
Region = Asia			
N'	123	129	
Baseline Mean (SD)	34,61 (20,582)	38,22 (23,635)	
Week 24:			
Adjusted Mean Change (SE)	-6,26 (1,442)	-5,22 (1,418)	-1,03 [-4,971; 2,903] 0,607
Region = Europe			
N'	164	167	
Baseline Mean (SD)	27,54 (17,446)	24,49 (17,538)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 24:			
Adjusted Mean Change (SE)	-10,17 (1,243)	-6,75 (1,235)	-3,42 [-6,855; 0,014] 0,051
Region = Latin America			
N'	163	157	
Baseline Mean (SD)	24,73 (16,169)	25,23 (16,773)	
Week 24:			
Adjusted Mean Change (SE)	-13,06 (1,255)	-10,37 (1,273)	-2,69 [-6,186; 0,804] 0,131
Region = Others			
N'	20	9	
Baseline Mean (SD)	30,10 (20,661)	28,54 (27,988)	
Week 24:			
Adjusted Mean Change (SE)	-12,47 (3,568)	-10,28 (5,315)	-2,19 [-14,720; 10,342] 0,732

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + background ICS/LABA + baseline value + region + region * treatment
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.
Imputation method: LOCF

Analysis population: B2306 FAS total population

Table 7.6a SGRQ - Change from Baseline by History of Asthma Exacerbation (as observed) (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
Interaction Test	0,762		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	359	351	
Baseline Mean (SD)	39,41 (17,060)	37,98 (17,864)	
Week 24:			
Adjusted Mean Change (SE)	-14,81 (1,104)	-12,57 (1,122)	-2,25 [-4,526; 0,031] 0,053
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	93	85	
Baseline Mean (SD)	40,16 (15,881)	45,41 (17,503)	
Week 24:			
Adjusted Mean Change (SE)	-13,55 (1,817)	-12,09 (1,881)	-1,46 [-6,026; 3,105] 0,530
Symptoms score			
Interaction Test	0,287		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	359	351	
Baseline Mean (SD)	52,69 (19,574)	49,94 (19,633)	
Week 24:			
Adjusted Mean Change (SE)	-18,54 (1,447)	-18,16 (1,473)	-0,37 [-3,371; 2,624] 0,807
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	93	85	
Baseline Mean (SD)	50,35 (18,779)	57,95 (18,313)	
Week 24:			
Adjusted Mean Change (SE)	-19,24 (2,381)	-15,21 (2,457)	-4,03 [-10,035; 1,980] 0,189

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Activity score			
Interaction Test	0,500		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	359	351	
Baseline Mean (SD)	52,54 (21,704)	50,58 (21,311)	
Week 24:			
Adjusted Mean Change (SE)	-16,28 (1,479)	-13,78 (1,504)	-2,49 [-5,553; 0,565] 0,110
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	93	85	
Baseline Mean (SD)	53,64 (19,391)	57,55 (22,097)	
Week 24:			
Adjusted Mean Change (SE)	-11,83 (2,436)	-11,70 (2,510)	-0,14 [-6,260; 5,987] 0,965
Impacts score			
Interaction Test	0,978		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	359	351	
Baseline Mean (SD)	27,91 (18,516)	27,18 (19,887)	
Week 24:			
Adjusted Mean Change (SE)	-12,39 (1,107)	-9,95 (1,125)	-2,44 [-4,722; -0,163] 0,036 *
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	93	85	
Baseline Mean (SD)	29,44 (17,849)	34,62 (20,788)	
Week 24:			
Adjusted Mean Change (SE)	-12,35 (1,821)	-9,98 (1,885)	-2,37 [-6,937; 2,199] 0,309

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + region + background ICS/LABA + baseline value + history of asthma exacerbation + history of asthma exacerbation * treatment
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 7.6b SGRQ - Change from Baseline by History of Asthma Exacerbation (LOCF) (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
Interaction Test	0,473		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	374	
Baseline Mean (SD)	39,56 (17,054)	38,01 (17,924)	
Week 24:			
Adjusted Mean Change (SE)	-14,19 (1,091)	-11,49 (1,094)	-2,70 [-4,949; -0,446] 0,019 *
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	98	88	
Baseline Mean (SD)	40,75 (15,959)	45,53 (17,217)	
Week 24:			
Adjusted Mean Change (SE)	-12,55 (1,791)	-11,70 (1,867)	-0,84 [-5,371; 3,681] 0,714
Symptoms score			
Interaction Test	0,461		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	374	
Baseline Mean (SD)	52,80 (19,593)	50,14 (19,566)	
Week 24:			
Adjusted Mean Change (SE)	-18,00 (1,430)	-17,03 (1,436)	-0,97 [-3,934; 1,986] 0,519
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	98	88	
Baseline Mean (SD)	51,07 (18,777)	58,10 (18,197)	
Week 24:			
Adjusted Mean Change (SE)	-18,17 (2,346)	-14,69 (2,438)	-3,47 [-9,425; 2,477] 0,252

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Activity score			
Interaction Test	0,301		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	374	
Baseline Mean (SD)	52,48 (21,640)	50,55 (21,432)	
Week 24:			
Adjusted Mean Change (SE)	-15,60 (1,442)	-12,56 (1,447)	-3,04 [-6,018; -0,057] 0,046 *
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	98	88	
Baseline Mean (SD)	54,45 (19,681)	57,58 (21,812)	
Week 24:			
Adjusted Mean Change (SE)	-10,68 (2,368)	-11,18 (2,457)	0,49 [-5,493; 6,480] 0,872
Impacts score			
Interaction Test	0,681		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	374	
Baseline Mean (SD)	28,17 (18,582)	27,22 (19,960)	
Week 24:			
Adjusted Mean Change (SE)	-11,79 (1,098)	-9,04 (1,101)	-2,76 [-5,016; -0,494] 0,017 *
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	98	88	
Baseline Mean (SD)	29,86 (17,746)	34,77 (20,510)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 24:			
Adjusted Mean Change (SE)	-11,44 (1,802)	-9,75 (1,878)	-1,69 [-6,237; 2,855] 0,466

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + region + background ICS/LABA + baseline value + history of asthma exacerbation + history of asthma exacerbation * treatment
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.
Imputation method: LOCF

Analysis population: B2306 FAS total population

Table 7.7a SGRQ - Change from Baseline by Patients' Prior Therapies (as observed) (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
Interaction Test	0,672		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	224	225	
Baseline Mean (SD)	39,26 (17,548)	40,29 (18,688)	
Week 24:			
Adjusted Mean Change (SE)	-16,22 (1,281)	-13,69 (1,283)	-2,53 [-5,407; 0,344] 0,084
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	228	211	
Baseline Mean (SD)	39,86 (16,084)	38,51 (17,271)	
Week 24:			
Adjusted Mean Change (SE)	-12,65 (1,288)	-11,01 (1,325)	-1,65 [-4,559; 1,262] 0,267
Symptoms score			
Interaction Test	0,253		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	224	225	
Baseline Mean (SD)	52,93 (20,223)	51,56 (18,534)	
Week 24:			
Adjusted Mean Change (SE)	-21,12 (1,683)	-18,44 (1,682)	-2,68 [-6,458; 1,107] 0,165
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	228	211	
Baseline Mean (SD)	51,50 (18,606)	51,44 (20,761)	
Week 24:			
Adjusted Mean Change (SE)	-15,80 (1,687)	-16,27 (1,739)	0,46 [-3,364; 4,291] 0,812

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Activity score			
Interaction Test	0,896		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	224	225	
Baseline Mean (SD)	51,42 (21,971)	53,00 (21,913)	
Week 24:			
Adjusted Mean Change (SE)	-17,75 (1,715)	-15,56 (1,717)	-2,19 [-6,048; 1,668] 0,266
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	228	211	
Baseline Mean (SD)	54,09 (20,443)	50,81 (21,293)	
Week 24:			
Adjusted Mean Change (SE)	-12,86 (1,725)	-11,04 (1,774)	-1,82 [-5,732; 2,083] 0,360
Impacts score			
Interaction Test	0,753		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	224	225	
Baseline Mean (SD)	28,22 (19,022)	29,65 (21,096)	
Week 24:			
Adjusted Mean Change (SE)	-13,42 (1,283)	-10,66 (1,286)	-2,76 [-5,634; 0,119] 0,060
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	228	211	
Baseline Mean (SD)	28,24 (17,751)	27,55 (19,314)	
Week 24:			
Adjusted Mean Change (SE)	-11,09 (1,289)	-8,99 (1,327)	-2,10 [-5,012; 0,809] 0,157

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + region + baseline value + patients' prior therapies + patients' prior therapies * treatment
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 7.7b SGRQ - Change from Baseline by Patients' Prior Therapies (LOCF) (FAS)

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Total score			
Interaction Test	0,646		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	238	
Baseline Mean (SD)	39,08 (17,537)	40,04 (18,861)	
Week 24:			
Adjusted Mean Change (SE)	-15,93 (1,272)	-13,13 (1,261)	-2,80 [-5,656; 0,049] 0,054
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	240	224	
Baseline Mean (SD)	40,50 (16,113)	38,81 (17,094)	
Week 24:			
Adjusted Mean Change (SE)	-11,58 (1,269)	-9,73 (1,292)	-1,86 [-4,722; 1,012] 0,205
Symptoms score			
Interaction Test	0,296		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	238	
Baseline Mean (SD)	52,71 (20,140)	51,35 (18,676)	
Week 24:			
Adjusted Mean Change (SE)	-21,01 (1,670)	-18,11 (1,653)	-2,89 [-6,644; 0,856] 0,130
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	240	224	
Baseline Mean (SD)	52,18 (18,740)	51,98 (20,466)	
Week 24:			
Adjusted Mean Change (SE)	-14,72 (1,660)	-14,66 (1,695)	-0,06 [-3,826; 3,709] 0,976

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Activity score			
Interaction Test	0,823		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	238	
Baseline Mean (SD)	51,21 (22,009)	52,60 (21,909)	
Week 24:			
Adjusted Mean Change (SE)	-17,35 (1,681)	-14,75 (1,665)	-2,61 [-6,381; 1,169] 0,176
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	240	224	
Baseline Mean (SD)	54,51 (20,394)	51,14 (21,412)	
Week 24:			
Adjusted Mean Change (SE)	-11,75 (1,676)	-9,75 (1,707)	-1,99 [-5,790; 1,802] 0,303
Impacts score			
Interaction Test	0,706		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	238	
Baseline Mean (SD)	28,06 (18,948)	29,48 (21,364)	
Week 24:			
Adjusted Mean Change (SE)	-13,21 (1,278)	-10,27 (1,269)	-2,94 [-5,807; -0,079] 0,044 *
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	240	224	
Baseline Mean (SD)	28,97 (17,897)	27,77 (19,030)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**
Week 24:			
Adjusted Mean Change (SE)	-10,00 (1,275)	-7,84 (1,299)	-2,16 [-5,039; 0,716] 0,141

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + region + baseline value + patients' prior therapies + patients' prior therapies * treatment
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.
Imputation method: LOCF

Analysis population: B2306 FAS total population

8. SGRQ - Responder Analysis

Table 8.1 SGRQ - Responder Analysis (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	470	462			
SGRQ Response, n (%)	326 (69,4)	291 (63,0)	1,34 [1,01; 1,77] 0,042 *	1,10 [1,00; 1,21] 0,040 *	0,06 [0,00; 0,12] 0,039 *

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + region + background ICS/LABA
If it was not possible to fit the minimal model, the OR is not given.

Analysis population: B2306 FAS total population

Table 8.2 SGRQ - Responder Analysis by Age (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test:	p=0,108				
Age = 18-39 years					
N'	84	72			
SGRQ Response, n (%)	55 (65,5)	53 (73,6)	0,76 [0,37; 1,55] 0,445	0,89 [0,72; 1,10] 0,270	-0,08 [-0,23; 0,06] 0,268
Age = 40-64 years					
N'	286	299			
SGRQ Response, n (%)	206 (72,0)	180 (60,2)	1,67 [1,16; 2,38] 0,005 *	1,20 [1,06; 1,35] 0,003 *	0,12 [0,04; 0,19] 0,002 *
Age = ≥65 years					
N'	100	91			
SGRQ Response, n (%)	65 (65,0)	58 (63,7)	1,06 [0,57; 1,94] 0,861	1,02 [0,83; 1,26] 0,856	0,01 [-0,12; 0,15] 0,855

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + region + background ICS/LABA + age + age * treatment
If it was not possible to fit the minimal model, the OR is not given.

Analysis population: B2306 FAS total population

Table 8.3 SGRQ - Responder Analysis by Gender (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test:	p=0,348				
Gender = Male					
N'	184	166			
SGRQ Response, n (%)	130 (70,7)	112 (67,5)	1,11 [0,69; 1,77] 0,667	1,05 [0,91; 1,21] 0,521	0,03 [-0,07; 0,13] 0,520
Gender = Female					
N'	286	296			
SGRQ Response, n (%)	196 (68,5)	179 (60,5)	1,47 [1,03; 2,09] 0,033 *	1,13 [1,00; 1,28] 0,043 *	0,08 [0,00; 0,16] 0,041 *

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + region + background ICS/LABA + gender + gender * treatment
If it was not possible to fit the minimal model, the OR is not given.

Analysis population: B2306 FAS total population

Table 8.4 SGRQ - Responder Analysis by Region (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test:	p=0,967				
Region = Asia					
N'	123	129			
SGRQ Response, n (%)	77 (62,6)	76 (58,9)	1,23 [0,73; 2,07] 0,445	1,06 [0,87; 1,30] 0,549	0,04 [-0,08; 0,16] 0,549
Region = Europe					
N'	164	167			
SGRQ Response, n (%)	109 (66,5)	97 (58,1)	1,34 [0,85; 2,12] 0,210	1,14 [0,97; 1,35] 0,117	0,08 [-0,02; 0,19] 0,114
Region = Latin America					
N'	163	157			
SGRQ Response, n (%)	124 (76,1)	112 (71,3)	1,36 [0,82; 2,27] 0,237	1,07 [0,94; 1,22] 0,337	0,05 [-0,05; 0,14] 0,336
Region = Others					
N'	20	9			
SGRQ Response, n (%)	16 (80,0)	6 (66,7)	1,93 [0,31; 12,01] 0,479	1,20 [0,72; 2,00] 0,485	0,13 [-0,22; 0,49] 0,461

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + background ICS/LABA + region + region * treatment
If it was not possible to fit the minimal model, the OR is not given.

Analysis population: B2306 FAS total population

Table 8.5 SGRQ - Responder Analysis by History of Asthma Exacerbation (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test:	p=0,137				
Asthma exacerbations in the 12 months prior to screening = 1					
N'	372	374			
SGRQ Response, n (%)	259 (69,6)	225 (60,2)	1,48 [1,08; 2,02] 0,014 *	1,16 [1,04; 1,29] 0,007 *	0,09 [0,03; 0,16] 0,007 *
Asthma exacerbations in the 12 months prior to screening = ≥2					
N'	98	88			
SGRQ Response, n (%)	67 (68,4)	66 (75,0)	0,85 [0,44; 1,65] 0,625	0,91 [0,76; 1,09] 0,315	-0,07 [-0,20; 0,06] 0,314

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + region + background ICS/LABA + history of asthma exacerbation + history of asthma exacerbation * treatment
If it was not possible to fit the minimal model, the OR is not given.

Analysis population: B2306 FAS total population

Table 8.6 SGRQ - Responder Analysis by Patients' Prior Therapies (LOCF) (FAS)

	Treatment groups		Comparison		
Binary Efficacy Outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Interaction Test:	p=0,887				
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA					
N'	230	238			
SGRQ Response, n (%)	168 (73,0)	162 (68,1)	1,31 [0,87; 1,97] 0,197	1,07 [0,95; 1,21] 0,238	0,05 [-0,03; 0,13] 0,237
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA					
N'	240	224			
SGRQ Response, n (%)	158 (65,8)	129 (57,6)	1,36 [0,93; 2,01] 0,115	1,14 [0,99; 1,32] 0,070	0,08 [-0,01; 0,17] 0,067

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + baseline + region + patients' prior therapies + patients' prior therapies * treatment
If it was not possible to fit the minimal model, the OR is not given.

Analysis population: B2306 FAS total population

9. E-Diary - Symptoms

Table 9.1 Symptoms - Documentation Rate (FAS)

		Treatment groups		
Outcome - Documentation Rate (FAS)		**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Total N=951**
No symptoms on rising - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	428 (89,9)	422 (88,8)	850 (89,4)
	50%-<70%	35 (7,4)	37 (7,8)	72 (7,6)
	<50%	13 (2,7)	16 (3,4)	29 (3,0)
Baseline to Week 8	70%-100%	421 (88,4)	427 (89,9)	848 (89,2)
	50%-<70%	33 (6,9)	28 (5,9)	61 (6,4)
	<50%	22 (4,6)	20 (4,2)	42 (4,4)
Week 9 to Week 16	70%-100%	400 (84,0)	409 (86,1)	809 (85,1)
	50%-<70%	48 (10,1)	33 (6,9)	81 (8,5)
	<50%	28 (5,9)	33 (6,9)	61 (6,4)
Week 17 to Week 24	70%-100%	391 (82,1)	407 (85,7)	798 (83,9)
	50%-<70%	47 (9,9)	17 (3,6)	64 (6,7)
	<50%	38 (8,0)	51 (10,7)	89 (9,4)
Baseline to Week 24	70%-100%	413 (86,8)	407 (85,7)	820 (86,2)
	50%-<70%	36 (7,6)	33 (6,9)	69 (7,3)
	<50%	27 (5,7)	35 (7,4)	62 (6,5)
No day-time symptoms - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	431 (90,5)	420 (88,4)	851 (89,5)
	50%-<70%	34 (7,1)	41 (8,6)	75 (7,9)
	<50%	11 (2,3)	14 (2,9)	25 (2,6)
Baseline to Week 8	70%-100%	419 (88,0)	420 (88,4)	839 (88,2)
	50%-<70%	38 (8,0)	32 (6,7)	70 (7,4)
	<50%	19 (4,0)	23 (4,8)	42 (4,4)
Week 9 to Week 16	70%-100%	412 (86,6)	408 (85,9)	820 (86,2)
	50%-<70%	35 (7,4)	27 (5,7)	62 (6,5)
	<50%	29 (6,1)	40 (8,4)	69 (7,3)
Week 17 to Week 24	70%-100%	394 (82,8)	384 (80,8)	778 (81,8)
	50%-<70%	40 (8,4)	41 (8,6)	81 (8,5)
	<50%	42 (8,8)	50 (10,5)	92 (9,7)

		Treatment groups		
Outcome - Documentation Rate (FAS)		**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Total N=951**
Baseline to Week 24	70%-100%	410 (86,1)	403 (84,8)	813 (85,5)
	50%-<70%	38 (8,0)	35 (7,4)	73 (7,7)
	<50%	28 (5,9)	37 (7,8)	65 (6,8)
No night-time awakenings - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	428 (89,9)	422 (88,8)	850 (89,4)
	50%-<70%	35 (7,4)	37 (7,8)	72 (7,6)
	<50%	13 (2,7)	16 (3,4)	29 (3,0)
Baseline to Week 8	70%-100%	421 (88,4)	427 (89,9)	848 (89,2)
	50%-<70%	33 (6,9)	28 (5,9)	61 (6,4)
	<50%	22 (4,6)	20 (4,2)	42 (4,4)
Week 9 to Week 16	70%-100%	400 (84,0)	409 (86,1)	809 (85,1)
	50%-<70%	48 (10,1)	33 (6,9)	81 (8,5)
	<50%	28 (5,9)	33 (6,9)	61 (6,4)
Week 17 to Week 24	70%-100%	391 (82,1)	407 (85,7)	798 (83,9)
	50%-<70%	47 (9,9)	17 (3,6)	64 (6,7)
	<50%	38 (8,0)	51 (10,7)	89 (9,4)
Baseline to Week 24	70%-100%	413 (86,8)	407 (85,7)	820 (86,2)
	50%-<70%	36 (7,6)	33 (6,9)	69 (7,3)
	<50%	27 (5,7)	35 (7,4)	62 (6,5)
Days with no asthma symptoms - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	393 (82,6)	384 (80,8)	777 (81,7)
	50%-<70%	52 (10,9)	51 (10,7)	103 (10,8)
	<50%	31 (6,5)	40 (8,4)	71 (7,5)
Baseline to Week 8	70%-100%	365 (76,7)	379 (79,8)	744 (78,2)
	50%-<70%	63 (13,2)	52 (10,9)	115 (12,1)
	<50%	48 (10,1)	44 (9,3)	92 (9,7)
Week 9 to Week 16	70%-100%	340 (71,4)	353 (74,3)	693 (72,9)
	50%-<70%	71 (14,9)	59 (12,4)	130 (13,7)
	<50%	65 (13,7)	63 (13,3)	128 (13,5)
Week 17 to Week 24	70%-100%	324 (68,1)	335 (70,5)	659 (69,3)
	50%-<70%	73 (15,3)	61 (12,8)	134 (14,1)
	<50%	79 (16,6)	79 (16,6)	158 (16,6)

		Treatment groups		
Outcome - Documentation Rate (FAS)		**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Total N=951**
Baseline to Week 24	70%-100%	340 (71,4)	350 (73,7)	690 (72,6)
	50%-<70%	82 (17,2)	64 (13,5)	146 (15,4)
	<50%	54 (11,3)	61 (12,8)	115 (12,1)
Mean total daily symptom score - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	393 (82,6)	384 (80,8)	777 (81,7)
	50%-<70%	52 (10,9)	51 (10,7)	103 (10,8)
	<50%	31 (6,5)	40 (8,4)	71 (7,5)
Baseline to Week 8	70%-100%	365 (76,7)	379 (79,8)	744 (78,2)
	50%-<70%	63 (13,2)	52 (10,9)	115 (12,1)
	<50%	48 (10,1)	44 (9,3)	92 (9,7)
Week 9 to Week 16	70%-100%	340 (71,4)	353 (74,3)	693 (72,9)
	50%-<70%	71 (14,9)	59 (12,4)	130 (13,7)
	<50%	65 (13,7)	63 (13,3)	128 (13,5)
Week 17 to Week 24	70%-100%	324 (68,1)	335 (70,5)	659 (69,3)
	50%-<70%	73 (15,3)	61 (12,8)	134 (14,1)
	<50%	79 (16,6)	79 (16,6)	158 (16,6)
Baseline to Week 24	70%-100%	340 (71,4)	350 (73,7)	690 (72,6)
	50%-<70%	82 (17,2)	64 (13,5)	146 (15,4)
	<50%	54 (11,3)	61 (12,8)	115 (12,1)
Mean day-time symptom score - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	431 (90,5)	420 (88,4)	851 (89,5)
	50%-<70%	34 (7,1)	41 (8,6)	75 (7,9)
	<50%	11 (2,3)	14 (2,9)	25 (2,6)
Baseline to Week 8	70%-100%	419 (88,0)	420 (88,4)	839 (88,2)
	50%-<70%	38 (8,0)	32 (6,7)	70 (7,4)
	<50%	19 (4,0)	23 (4,8)	42 (4,4)
Week 9 to Week 16	70%-100%	412 (86,6)	408 (85,9)	820 (86,2)
	50%-<70%	35 (7,4)	27 (5,7)	62 (6,5)
	<50%	29 (6,1)	40 (8,4)	69 (7,3)
Week 17 to Week 24	70%-100%	394 (82,8)	384 (80,8)	778 (81,8)
	50%-<70%	40 (8,4)	41 (8,6)	81 (8,5)
	<50%	42 (8,8)	50 (10,5)	92 (9,7)

		Treatment groups		
Outcome - Documentation Rate (FAS)		**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Total N=951**
Baseline to Week 24	70%-100%	410 (86,1)	403 (84,8)	813 (85,5)
	50%-<70%	38 (8,0)	35 (7,4)	73 (7,7)
	<50%	28 (5,9)	37 (7,8)	65 (6,8)
Mean night-time symptom score - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	428 (89,9)	422 (88,8)	850 (89,4)
	50%-<70%	35 (7,4)	37 (7,8)	72 (7,6)
	<50%	13 (2,7)	16 (3,4)	29 (3,0)
Baseline to Week 8	70%-100%	421 (88,4)	427 (89,9)	848 (89,2)
	50%-<70%	33 (6,9)	28 (5,9)	61 (6,4)
	<50%	22 (4,6)	20 (4,2)	42 (4,4)
Week 9 to Week 16	70%-100%	400 (84,0)	409 (86,1)	809 (85,1)
	50%-<70%	48 (10,1)	33 (6,9)	81 (8,5)
	<50%	28 (5,9)	33 (6,9)	61 (6,4)
Week 17 to Week 24	70%-100%	391 (82,1)	407 (85,7)	798 (83,9)
	50%-<70%	47 (9,9)	17 (3,6)	64 (6,7)
	<50%	38 (8,0)	51 (10,7)	89 (9,4)
Baseline to Week 24	70%-100%	413 (86,8)	407 (85,7)	820 (86,2)
	50%-<70%	36 (7,6)	33 (6,9)	69 (7,3)
	<50%	27 (5,7)	35 (7,4)	62 (6,5)
How did you sleep last night? - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	428 (89,9)	422 (88,8)	850 (89,4)
	50%-<70%	35 (7,4)	37 (7,8)	72 (7,6)
	<50%	13 (2,7)	16 (3,4)	29 (3,0)
Baseline to Week 8	70%-100%	421 (88,4)	427 (89,9)	848 (89,2)
	50%-<70%	33 (6,9)	28 (5,9)	61 (6,4)
	<50%	22 (4,6)	20 (4,2)	42 (4,4)
Week 9 to Week 16	70%-100%	400 (84,0)	409 (86,1)	809 (85,1)
	50%-<70%	48 (10,1)	33 (6,9)	81 (8,5)
	<50%	28 (5,9)	33 (6,9)	61 (6,4)
Week 17 to Week 24	70%-100%	391 (82,1)	407 (85,7)	798 (83,9)
	50%-<70%	47 (9,9)	17 (3,6)	64 (6,7)
	<50%	38 (8,0)	51 (10,7)	89 (9,4)

		Treatment groups		
Outcome - Documentation Rate (FAS)		**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Total N=951**
Baseline to Week 24	70%-100%	413 (86,8)	407 (85,7)	820 (86,2)
	50%-<70%	36 (7,6)	33 (6,9)	69 (7,3)
	<50%	27 (5,7)	35 (7,4)	62 (6,5)
Did you have asthma symptoms upon awakening in the morning? - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	428 (89,9)	422 (88,8)	850 (89,4)
	50%-<70%	35 (7,4)	37 (7,8)	72 (7,6)
	<50%	13 (2,7)	16 (3,4)	29 (3,0)
Baseline to Week 8	70%-100%	421 (88,4)	427 (89,9)	848 (89,2)
	50%-<70%	33 (6,9)	28 (5,9)	61 (6,4)
	<50%	22 (4,6)	20 (4,2)	42 (4,4)
Week 9 to Week 16	70%-100%	400 (84,0)	409 (86,1)	809 (85,1)
	50%-<70%	48 (10,1)	33 (6,9)	81 (8,5)
	<50%	28 (5,9)	33 (6,9)	61 (6,4)
Week 17 to Week 24	70%-100%	391 (82,1)	407 (85,7)	798 (83,9)
	50%-<70%	47 (9,9)	17 (3,6)	64 (6,7)
	<50%	38 (8,0)	51 (10,7)	89 (9,4)
Baseline to Week 24	70%-100%	413 (86,8)	407 (85,7)	820 (86,2)
	50%-<70%	36 (7,6)	33 (6,9)	69 (7,3)
	<50%	27 (5,7)	35 (7,4)	62 (6,5)
Did your respiratory symptoms stop you from performing your usual daily activities? - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	431 (90,5)	420 (88,4)	851 (89,5)
	50%-<70%	34 (7,1)	41 (8,6)	75 (7,9)
	<50%	11 (2,3)	14 (2,9)	25 (2,6)
Baseline to Week 8	70%-100%	419 (88,0)	420 (88,4)	839 (88,2)
	50%-<70%	38 (8,0)	32 (6,7)	70 (7,4)
	<50%	19 (4,0)	23 (4,8)	42 (4,4)
Week 9 to Week 16	70%-100%	412 (86,6)	408 (85,9)	820 (86,2)
	50%-<70%	35 (7,4)	27 (5,7)	62 (6,5)
	<50%	29 (6,1)	40 (8,4)	69 (7,3)
Week 17 to Week 24	70%-100%	394 (82,8)	384 (80,8)	778 (81,8)
	50%-<70%	40 (8,4)	41 (8,6)	81 (8,5)
	<50%	42 (8,8)	50 (10,5)	92 (9,7)

		Treatment groups		
Outcome - Documentation Rate (FAS)		**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Total N=951**
Baseline to Week 24	70%-100%	410 (86,1)	403 (84,8)	813 (85,5)
	50%-<70%	38 (8,0)	35 (7,4)	73 (7,7)
	<50%	28 (5,9)	37 (7,8)	65 (6,8)
How severe was your shortness of breath today? - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	431 (90,5)	420 (88,4)	851 (89,5)
	50%-<70%	34 (7,1)	41 (8,6)	75 (7,9)
	<50%	11 (2,3)	14 (2,9)	25 (2,6)
Baseline to Week 8	70%-100%	419 (88,0)	420 (88,4)	839 (88,2)
	50%-<70%	38 (8,0)	32 (6,7)	70 (7,4)
	<50%	19 (4,0)	23 (4,8)	42 (4,4)
Week 9 to Week 16	70%-100%	412 (86,6)	408 (85,9)	820 (86,2)
	50%-<70%	35 (7,4)	27 (5,7)	62 (6,5)
	<50%	29 (6,1)	40 (8,4)	69 (7,3)
Week 17 to Week 24	70%-100%	394 (82,8)	384 (80,8)	778 (81,8)
	50%-<70%	40 (8,4)	41 (8,6)	81 (8,5)
	<50%	42 (8,8)	50 (10,5)	92 (9,7)
Baseline to Week 24	70%-100%	410 (86,1)	403 (84,8)	813 (85,5)
	50%-<70%	38 (8,0)	35 (7,4)	73 (7,7)
	<50%	28 (5,9)	37 (7,8)	65 (6,8)
How was your wheeze during the past 12 hours? - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	431 (90,5)	420 (88,4)	851 (89,5)
	50%-<70%	34 (7,1)	41 (8,6)	75 (7,9)
	<50%	11 (2,3)	14 (2,9)	25 (2,6)
Baseline to Week 8	70%-100%	419 (88,0)	420 (88,4)	839 (88,2)
	50%-<70%	38 (8,0)	32 (6,7)	70 (7,4)
	<50%	19 (4,0)	23 (4,8)	42 (4,4)
Week 9 to Week 16	70%-100%	412 (86,6)	408 (85,9)	820 (86,2)
	50%-<70%	35 (7,4)	27 (5,7)	62 (6,5)
	<50%	29 (6,1)	40 (8,4)	69 (7,3)
Week 17 to Week 24	70%-100%	394 (82,8)	384 (80,8)	778 (81,8)
	50%-<70%	40 (8,4)	41 (8,6)	81 (8,5)
	<50%	42 (8,8)	50 (10,5)	92 (9,7)

		Treatment groups		
Outcome - Documentation Rate (FAS)		**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Total N=951**
Baseline to Week 24	70%-100%	410 (86,1)	403 (84,8)	813 (85,5)
	50%-<70%	38 (8,0)	35 (7,4)	73 (7,7)
	<50%	28 (5,9)	37 (7,8)	65 (6,8)
How was your cough during the past 12 hours? - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	431 (90,5)	420 (88,4)	851 (89,5)
	50%-<70%	34 (7,1)	41 (8,6)	75 (7,9)
	<50%	11 (2,3)	14 (2,9)	25 (2,6)
Baseline to Week 8	70%-100%	419 (88,0)	420 (88,4)	839 (88,2)
	50%-<70%	38 (8,0)	32 (6,7)	70 (7,4)
	<50%	19 (4,0)	23 (4,8)	42 (4,4)
Week 9 to Week 16	70%-100%	412 (86,6)	408 (85,9)	820 (86,2)
	50%-<70%	35 (7,4)	27 (5,7)	62 (6,5)
	<50%	29 (6,1)	40 (8,4)	69 (7,3)
Week 17 to Week 24	70%-100%	394 (82,8)	384 (80,8)	778 (81,8)
	50%-<70%	40 (8,4)	41 (8,6)	81 (8,5)
	<50%	42 (8,8)	50 (10,5)	92 (9,7)
Baseline to Week 24	70%-100%	410 (86,1)	403 (84,8)	813 (85,5)
	50%-<70%	38 (8,0)	35 (7,4)	73 (7,7)
	<50%	28 (5,9)	37 (7,8)	65 (6,8)
Did you have chest tightness during the past 12 hours? - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	431 (90,5)	420 (88,4)	851 (89,5)
	50%-<70%	34 (7,1)	41 (8,6)	75 (7,9)
	<50%	11 (2,3)	14 (2,9)	25 (2,6)
Baseline to Week 8	70%-100%	419 (88,0)	420 (88,4)	839 (88,2)
	50%-<70%	38 (8,0)	32 (6,7)	70 (7,4)
	<50%	19 (4,0)	23 (4,8)	42 (4,4)
Week 9 to Week 16	70%-100%	412 (86,6)	408 (85,9)	820 (86,2)
	50%-<70%	35 (7,4)	27 (5,7)	62 (6,5)
	<50%	29 (6,1)	40 (8,4)	69 (7,3)
Week 17 to Week 24	70%-100%	394 (82,8)	384 (80,8)	778 (81,8)
	50%-<70%	40 (8,4)	41 (8,6)	81 (8,5)
	<50%	42 (8,8)	50 (10,5)	92 (9,7)

		Treatment groups		
Outcome - Documentation Rate (FAS)		**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Total N=951**
Baseline to Week 24	70%-100%	410 (86,1)	403 (84,8)	813 (85,5)
	50%-<70%	38 (8,0)	35 (7,4)	73 (7,7)
	<50%	28 (5,9)	37 (7,8)	65 (6,8)

* For each time period and patient the documentation rate is calculated as the number of documented days divided by the number of days of the whole time period.

Analysis population: B2306 FAS total population

Table 9.2 Symptoms - Change from Baseline (FAS)

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Percentage of mornings with no symptoms on rising				
N'	452	451		
Baseline Mean (SD)	36,13 (38,316)	39,17 (38,382)		
Week 8:				
Adjusted Mean Change (SE)	9,88 (1,826)	7,10 (1,822)	2,79 [-0,813; 6,384] 0,129	0,073 [-0,059; 0,205]
Week 16:				
Adjusted Mean Change (SE)	16,85 (2,018)	12,76 (2,016)	4,09 [-0,229; 8,402] 0,063	0,096 [-0,035; 0,227]
Week 24:				
Adjusted Mean Change (SE)	18,95 (2,082)	15,24 (2,083)	3,72 [-0,830; 8,264] 0,109	0,085 [-0,047; 0,218]
Percentage of days with no day-time symptoms				
N'	455	451		
Baseline Mean (SD)	17,71 (30,217)	16,97 (30,552)		
Week 8:				
Adjusted Mean Change (SE)	9,44 (1,626)	7,71 (1,640)	1,72 [-1,483; 4,933] 0,292	0,050 [-0,082; 0,182]
Week 16:				
Adjusted Mean Change (SE)	18,80 (1,897)	13,92 (1,911)	4,88 [0,682; 9,081] 0,023 *	0,121 [-0,010; 0,252]
Week 24:				
Adjusted Mean Change (SE)	20,54 (1,990)	17,00 (2,005)	3,54 [-0,984; 8,062] 0,125	0,084 [-0,048; 0,216]
Percentage of days with no night-time awakenings				
N'	452	451		
Baseline Mean (SD)	58,78 (38,755)	62,29 (38,126)		
Week 8:				
Adjusted Mean Change (SE)	10,49 (1,641)	9,19 (1,636)	1,30 [-1,942; 4,535] 0,432	0,038 [-0,094; 0,170]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 16:				
Adjusted Mean Change (SE)	15,39 (1,751)	13,54 (1,748)	1,85 [-1,800; 5,505] 0,320	0,050 [-0,081; 0,181]
Week 24:				
Adjusted Mean Change (SE)	16,58 (1,798)	15,85 (1,799)	0,74 [-3,094; 4,568] 0,706	0,020 [-0,113; 0,152]
Percentage of days with no asthma symptoms				
N'	434	423		
Baseline Mean (SD)	15,21 (29,229)	15,55 (29,976)		
Week 8:				
Adjusted Mean Change (SE)	9,35 (1,665)	6,93 (1,684)	2,42 [-0,852; 5,697] 0,147	0,072 [-0,066; 0,209]
Week 16:				
Adjusted Mean Change (SE)	18,75 (1,939)	13,81 (1,964)	4,94 [0,650; 9,234] 0,024 *	0,123 [-0,012; 0,258]
Week 24:				
Adjusted Mean Change (SE)	20,93 (2,040)	16,07 (2,068)	4,86 [0,214; 9,506] 0,040 *	0,116 [-0,020; 0,252]
Mean total daily symptom score				
N'	434	423		
Baseline Mean (SD)	2,26 (1,580)	2,11 (1,505)		
Week 8:				
Adjusted Mean Change (SE)	-0,47 (0,063)	-0,45 (0,064)	-0,02 [-0,149; 0,100] 0,699	-0,019 [-0,156; 0,118]
Week 16:				
Adjusted Mean Change (SE)	-0,73 (0,067)	-0,66 (0,068)	-0,07 [-0,213; 0,069] 0,317	-0,051 [-0,186; 0,083]
Week 24:				
Adjusted Mean Change (SE)	-0,80 (0,069)	-0,73 (0,070)	-0,08 [-0,222; 0,071] 0,314	-0,053 [-0,189; 0,083]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Mean day-time symptom score				
N'	455	451		
Baseline Mean (SD)	0,88 (0,591)	0,86 (0,563)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,024)	-0,17 (0,024)	0,01 [-0,036; 0,058] 0,654	0,021 [-0,111; 0,153]
Week 16:				
Adjusted Mean Change (SE)	-0,27 (0,026)	-0,25 (0,026)	-0,03 [-0,079; 0,029] 0,356	-0,046 [-0,177; 0,084]
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,027)	-0,27 (0,027)	-0,02 [-0,075; 0,040] 0,543	-0,032 [-0,164; 0,100]
Mean night-time symptom score				
N'	452	451		
Baseline Mean (SD)	0,69 (0,536)	0,64 (0,508)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,021)	-0,15 (0,021)	-0,02 [-0,058; 0,024] 0,409	-0,040 [-0,172; 0,092]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,022)	-0,22 (0,022)	-0,02 [-0,064; 0,026] 0,411	-0,041 [-0,172; 0,090]
Week 24:				
Adjusted Mean Change (SE)	-0,26 (0,022)	-0,24 (0,022)	-0,02 [-0,066; 0,028] 0,427	-0,041 [-0,173; 0,092]
Mean of: How did you sleep last night?				
N'	452	451		
Baseline Mean (SD)	0,53 (0,557)	0,48 (0,528)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,020)	-0,15 (0,020)	-0,01 [-0,052; 0,027] 0,533	-0,030 [-0,162; 0,102]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,021)	-0,22 (0,021)	-0,01 [-0,055; 0,031] 0,587	-0,027 [-0,158; 0,104]
Week 24:				
Adjusted Mean Change (SE)	-0,24 (0,021)	-0,24 (0,021)	-0,00 [-0,044; 0,043] 0,987	-0,001 [-0,133; 0,131]
Mean of: Did you have asthma symptoms upon awakening in the morning?				
N'	452	451		
Baseline Mean (SD)	0,85 (0,621)	0,80 (0,598)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,026)	-0,14 (0,026)	-0,02 [-0,072; 0,030] 0,427	-0,038 [-0,170; 0,094]
Week 16:				
Adjusted Mean Change (SE)	-0,25 (0,028)	-0,22 (0,028)	-0,03 [-0,084; 0,032] 0,383	-0,044 [-0,175; 0,087]
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,029)	-0,24 (0,029)	-0,04 [-0,100; 0,024] 0,228	-0,063 [-0,195; 0,069]
Mean of: Did your respiratory symptoms stop you from performing your usual daily activities?				
N'	455	451		
Baseline Mean (SD)	0,89 (0,684)	0,88 (0,670)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,027)	-0,18 (0,027)	0,02 [-0,031; 0,075] 0,421	0,038 [-0,094; 0,170]
Week 16:				
Adjusted Mean Change (SE)	-0,27 (0,029)	-0,26 (0,029)	-0,01 [-0,071; 0,052] 0,758	-0,016 [-0,146; 0,115]
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,030)	-0,29 (0,030)	0,00 [-0,063; 0,066] 0,966	0,002 [-0,130; 0,134]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Mean of: How severe was your shortness of breath today?				
N'	455	451		
Baseline Mean (SD)	1,03 (0,653)	1,01 (0,641)		
Week 8:				
Adjusted Mean Change (SE)	-0,22 (0,027)	-0,21 (0,028)	-0,00 [-0,055; 0,053] 0,965	-0,002 [-0,134; 0,130]
Week 16:				
Adjusted Mean Change (SE)	-0,35 (0,030)	-0,31 (0,030)	-0,04 [-0,104; 0,021] 0,190	-0,066 [-0,197; 0,065]
Week 24:				
Adjusted Mean Change (SE)	-0,38 (0,031)	-0,33 (0,031)	-0,05 [-0,113; 0,019] 0,162	-0,073 [-0,205; 0,059]
Mean of: How was your wheeze during the past 12 hours?				
N'	455	451		
Baseline Mean (SD)	0,90 (0,669)	0,85 (0,632)		
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,027)	-0,21 (0,028)	0,03 [-0,026; 0,082] 0,313	0,048 [-0,084; 0,180]
Week 16:				
Adjusted Mean Change (SE)	-0,29 (0,029)	-0,28 (0,030)	-0,02 [-0,081; 0,043] 0,550	-0,030 [-0,161; 0,101]
Week 24:				
Adjusted Mean Change (SE)	-0,31 (0,030)	-0,30 (0,031)	-0,01 [-0,075; 0,056] 0,778	-0,015 [-0,147; 0,117]
Mean of: How was your cough during the past 12 hours?				
N'	455	451		
Baseline Mean (SD)	0,93 (0,680)	0,90 (0,656)		
Week 8:				
Adjusted Mean Change (SE)	-0,14 (0,029)	-0,13 (0,029)	-0,01 [-0,067; 0,048] 0,749	-0,015 [-0,147; 0,117]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 16:				
Adjusted Mean Change (SE)	-0,26 (0,031)	-0,23 (0,032)	-0,03 [-0,098; 0,035] 0,351	-0,047 [-0,178; 0,083]
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,033)	-0,26 (0,033)	-0,02 [-0,090; 0,051] 0,592	-0,028 [-0,160; 0,104]
Did you have chest tightness during the past 12 hours?				
N'	455	451		
Baseline Mean (SD)	0,67 (0,640)	0,66 (0,638)		
Week 8:				
Adjusted Mean Change (SE)	-0,08 (0,026)	-0,10 (0,026)	0,02 [-0,031; 0,071] 0,443	0,037 [-0,095; 0,168]
Week 16:				
Adjusted Mean Change (SE)	-0,17 (0,028)	-0,15 (0,028)	-0,02 [-0,077; 0,038] 0,510	-0,033 [-0,164; 0,098]
Week 24:				
Adjusted Mean Change (SE)	-0,18 (0,029)	-0,18 (0,029)	-0,01 [-0,070; 0,052] 0,782	-0,014 [-0,146; 0,118]

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 9.3 Symptoms - Change from Baseline by Age (FAS)

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Percentage of mornings with no symptoms on rising				
Interaction Test	0,450			
Age = 18-39 years				
N'	81	70		
Baseline Mean (SD)	42,32 (36,942)	46,14 (39,293)		
Week 8:				
Adjusted Mean Change (SE)	17,22 (3,374)	8,44 (3,528)	8,78 [-0,084; 17,650] 0,052	0,302 [-0,029; 0,634]
Week 16:				
Adjusted Mean Change (SE)	23,23 (3,909)	14,29 (4,134)	8,94 [-1,612; 19,492] 0,097	0,256 [-0,065; 0,577]
Week 24:				
Adjusted Mean Change (SE)	25,34 (4,103)	16,14 (4,343)	9,20 [-1,942; 20,338] 0,106	0,255 [-0,071; 0,582]
Age = 40-64 years				
N'	271	291		
Baseline Mean (SD)	34,58 (39,520)	38,43 (38,442)		
Week 8:				
Adjusted Mean Change (SE)	9,32 (2,077)	7,68 (2,054)	1,64 [-2,917; 6,197] 0,480	0,048 [-0,119; 0,215]
Week 16:				
Adjusted Mean Change (SE)	16,95 (2,355)	13,50 (2,317)	3,44 [-2,027; 8,910] 0,217	0,088 [-0,078; 0,255]
Week 24:				
Adjusted Mean Change (SE)	19,19 (2,445)	15,80 (2,410)	3,40 [-2,368; 9,163] 0,248	0,085 [-0,083; 0,252]
Age = ≥65 years				
N'	100	90		
Baseline Mean (SD)	35,31 (35,879)	36,11 (37,242)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	5,34 (3,075)	3,90 (3,208)	1,45 [-6,374; 9,270] 0,716	0,047 [-0,238; 0,333]
Week 16:				
Adjusted Mean Change (SE)	11,12 (3,589)	8,89 (3,748)	2,23 [-7,191; 11,656] 0,642	0,063 [-0,225; 0,351]
Week 24:				
Adjusted Mean Change (SE)	12,86 (3,753)	12,46 (3,930)	0,40 [-9,542; 10,337] 0,938	0,011 [-0,279; 0,300]
Percentage of days with no day-time symptoms				
Interaction Test	0,044 *			
Age = 18-39 years				
N'	78	71		
Baseline Mean (SD)	21,88 (29,600)	26,51 (35,704)		
Week 8:				
Adjusted Mean Change (SE)	19,15 (3,028)	8,60 (3,114)	10,55 [2,659; 18,443] 0,009 *	0,408 [0,075; 0,740]
Week 16:				
Adjusted Mean Change (SE)	30,05 (3,812)	14,20 (3,964)	15,85 [5,566; 26,140] 0,003 *	0,474 [0,147; 0,801]
Week 24:				
Adjusted Mean Change (SE)	31,62 (4,100)	16,76 (4,256)	14,86 [3,734; 25,985] 0,009 *	0,421 [0,089; 0,752]
Age = 40-64 years				
N'	277	291		
Baseline Mean (SD)	17,93 (30,788)	16,33 (29,586)		
Week 8:				
Adjusted Mean Change (SE)	7,84 (1,828)	8,51 (1,837)	-0,67 [-4,691; 3,351] 0,744	-0,022 [-0,189; 0,145]
Week 16:				
Adjusted Mean Change (SE)	17,33 (2,209)	15,87 (2,198)	1,45 [-3,809; 6,715] 0,588	0,039 [-0,126; 0,204]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	20,02 (2,341)	18,64 (2,328)	1,38 [-4,296; 7,065] 0,633	0,036 [-0,131; 0,202]
Age = ≥65 years				
N'	100	89		
Baseline Mean (SD)	13,83 (28,879)	11,44 (27,725)		
Week 8:				
Adjusted Mean Change (SE)	6,73 (2,730)	4,77 (2,870)	1,95 [-5,007; 8,913] 0,582	0,072 [-0,215; 0,359]
Week 16:				
Adjusted Mean Change (SE)	14,51 (3,430)	7,70 (3,612)	6,81 [-2,333; 15,944] 0,144	0,200 [-0,088; 0,488]
Week 24:				
Adjusted Mean Change (SE)	13,75 (3,662)	12,24 (3,862)	1,51 [-8,341; 11,357] 0,764	0,042 [-0,246; 0,330]
Percentage of days with no night-time awakenings				
Interaction Test	0,174			
Age = 18-39 years				
N'	81	70		
Baseline Mean (SD)	67,68 (35,509)	73,34 (35,593)		
Week 8:				
Adjusted Mean Change (SE)	17,38 (3,026)	10,88 (3,168)	6,50 [-1,458; 14,462] 0,109	0,249 [-0,081; 0,580]
Week 16:				
Adjusted Mean Change (SE)	20,44 (3,332)	15,33 (3,520)	5,11 [-3,823; 14,041] 0,262	0,172 [-0,149; 0,492]
Week 24:				
Adjusted Mean Change (SE)	19,09 (3,482)	15,11 (3,681)	3,98 [-5,413; 13,367] 0,406	0,130 [-0,195; 0,456]
Age = 40-64 years				
N'	271	291		
Baseline Mean (SD)	57,48 (38,874)	59,63 (37,533)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	10,85 (1,864)	9,05 (1,844)	1,79 [-2,296; 5,885] 0,390	0,058 [-0,109; 0,225]
Week 16:				
Adjusted Mean Change (SE)	16,16 (2,026)	13,51 (1,998)	2,66 [-1,969; 7,283] 0,260	0,079 [-0,087; 0,246]
Week 24:				
Adjusted Mean Change (SE)	17,89 (2,094)	15,63 (2,069)	2,26 [-2,595; 7,117] 0,361	0,066 [-0,102; 0,233]
Age = ≥65 years				
N'	100	90		
Baseline Mean (SD)	55,07 (40,231)	62,30 (40,720)		
Week 8:				
Adjusted Mean Change (SE)	3,65 (2,765)	7,93 (2,879)	-4,27 [-11,307; 2,758] 0,233	-0,156 [-0,442; 0,130]
Week 16:				
Adjusted Mean Change (SE)	8,76 (3,068)	11,81 (3,196)	-3,06 [-11,036; 4,924] 0,453	-0,101 [-0,389; 0,187]
Week 24:				
Adjusted Mean Change (SE)	10,55 (3,194)	16,73 (3,337)	-6,19 [-14,566; 2,195] 0,148	-0,198 [-0,488; 0,093]
Percentage of days with no asthma symptoms				
Interaction Test	0,062			
Age = 18-39 years				
N'	74	64		
Baseline Mean (SD)	19,14 (28,742)	24,03 (34,097)		
Week 8:				
Adjusted Mean Change (SE)	18,65 (3,120)	7,80 (3,242)	10,85 [2,639; 19,062] 0,010 *	0,432 [0,077; 0,787]
Week 16:				
Adjusted Mean Change (SE)	29,30 (3,897)	14,78 (4,141)	14,52 [3,863; 25,182] 0,008 *	0,437 [0,097; 0,777]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	32,80 (4,195)	16,33 (4,477)	16,47 [4,889; 28,043] 0,005 *	0,470 [0,121; 0,818]
Age = 40-64 years				
N'	263	275		
Baseline Mean (SD)	15,94 (30,891)	15,08 (29,320)		
Week 8:				
Adjusted Mean Change (SE)	7,66 (1,877)	7,70 (1,887)	-0,04 [-4,153; 4,077] 0,986	-0,001 [-0,175; 0,172]
Week 16:				
Adjusted Mean Change (SE)	17,32 (2,263)	15,75 (2,258)	1,56 [-3,819; 6,949] 0,569	0,042 [-0,127; 0,212]
Week 24:				
Adjusted Mean Change (SE)	20,19 (2,404)	17,84 (2,395)	2,34 [-3,483; 8,172] 0,430	0,060 [-0,111; 0,232]
Age = ≥65 years				
N'	97	84		
Baseline Mean (SD)	10,23 (24,134)	10,62 (27,705)		
Week 8:				
Adjusted Mean Change (SE)	7,08 (2,768)	3,80 (2,935)	3,29 [-3,761; 10,331] 0,361	0,122 [-0,172; 0,415]
Week 16:				
Adjusted Mean Change (SE)	14,68 (3,480)	6,82 (3,708)	7,86 [-1,443; 17,155] 0,098	0,231 [-0,063; 0,526]
Week 24:				
Adjusted Mean Change (SE)	14,07 (3,723)	10,19 (3,975)	3,87 [-6,180; 13,926] 0,450	0,107 [-0,188; 0,402]
Mean total daily symptom score				
Interaction Test	0,251			
Age = 18-39 years				
N'	74	64		
Baseline Mean (SD)	1,87 (1,467)	1,68 (1,458)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,73 (0,119)	-0,45 (0,123)	-0,27 [-0,587; 0,038] 0,085	-0,287 [-0,640; 0,066]
Week 16:				
Adjusted Mean Change (SE)	-0,89 (0,130)	-0,70 (0,138)	-0,19 [-0,543; 0,158] 0,282	-0,174 [-0,510; 0,163]
Week 24:				
Adjusted Mean Change (SE)	-0,96 (0,136)	-0,75 (0,144)	-0,20 [-0,572; 0,162] 0,274	-0,181 [-0,526; 0,163]
Age = 40-64 years				
N'	263	275		
Baseline Mean (SD)	2,31 (1,618)	2,14 (1,500)		
Week 8:				
Adjusted Mean Change (SE)	-0,50 (0,072)	-0,47 (0,072)	-0,03 [-0,182; 0,132] 0,752	-0,022 [-0,196; 0,151]
Week 16:				
Adjusted Mean Change (SE)	-0,81 (0,078)	-0,69 (0,078)	-0,12 [-0,292; 0,062] 0,202	-0,091 [-0,261; 0,079]
Week 24:				
Adjusted Mean Change (SE)	-0,87 (0,080)	-0,75 (0,080)	-0,12 [-0,302; 0,068] 0,216	-0,090 [-0,262; 0,081]
Age = ≥65 years				
N'	97	84		
Baseline Mean (SD)	2,44 (1,527)	2,31 (1,514)		
Week 8:				
Adjusted Mean Change (SE)	-0,19 (0,106)	-0,33 (0,112)	0,14 [-0,126; 0,412] 0,297	0,139 [-0,154; 0,432]
Week 16:				
Adjusted Mean Change (SE)	-0,36 (0,117)	-0,48 (0,124)	0,12 [-0,188; 0,423] 0,451	0,103 [-0,191; 0,397]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,47 (0,121)	-0,59 (0,129)	0,12 [-0,200; 0,438] 0,466	0,101 [-0,194; 0,396]
Mean day-time symptom score				
Interaction Test	0,172			
Age = 18-39 years				
N'	78	71		
Baseline Mean (SD)	0,73 (0,529)	0,69 (0,549)		
Week 8:				
Adjusted Mean Change (SE)	-0,26 (0,045)	-0,16 (0,046)	-0,10 [-0,213; 0,019] 0,100	-0,255 [-0,586; 0,075]
Week 16:				
Adjusted Mean Change (SE)	-0,34 (0,050)	-0,24 (0,052)	-0,10 [-0,228; 0,037] 0,156	-0,220 [-0,543; 0,104]
Week 24:				
Adjusted Mean Change (SE)	-0,35 (0,053)	-0,26 (0,055)	-0,09 [-0,232; 0,051] 0,211	-0,198 [-0,527; 0,131]
Age = 40-64 years				
N'	277	291		
Baseline Mean (SD)	0,89 (0,601)	0,87 (0,562)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,027)	-0,18 (0,027)	0,02 [-0,043; 0,076] 0,587	0,036 [-0,130; 0,203]
Week 16:				
Adjusted Mean Change (SE)	-0,31 (0,030)	-0,27 (0,029)	-0,04 [-0,106; 0,029] 0,266	-0,078 [-0,243; 0,088]
Week 24:				
Adjusted Mean Change (SE)	-0,32 (0,031)	-0,30 (0,031)	-0,03 [-0,101; 0,043] 0,429	-0,057 [-0,223; 0,110]
Age = ≥65 years				
N'	100	89		
Baseline Mean (SD)	0,98 (0,591)	0,94 (0,557)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,04 (0,040)	-0,11 (0,042)	0,07 [-0,033; 0,172] 0,183	0,174 [-0,113; 0,461]
Week 16:				
Adjusted Mean Change (SE)	-0,11 (0,045)	-0,17 (0,047)	0,05 [-0,063; 0,172] 0,365	0,122 [-0,166; 0,409]
Week 24:				
Adjusted Mean Change (SE)	-0,14 (0,048)	-0,20 (0,050)	0,06 [-0,066; 0,184] 0,356	0,126 [-0,163; 0,414]
Mean night-time symptom score				
Interaction Test	0,223			
Age = 18-39 years				
N'	81	70		
Baseline Mean (SD)	0,58 (0,498)	0,50 (0,473)		
Week 8:				
Adjusted Mean Change (SE)	-0,25 (0,041)	-0,15 (0,043)	-0,10 [-0,208; 0,010] 0,074	-0,280 [-0,611; 0,051]
Week 16:				
Adjusted Mean Change (SE)	-0,31 (0,041)	-0,25 (0,043)	-0,06 [-0,168; 0,048] 0,273	-0,166 [-0,487; 0,154]
Week 24:				
Adjusted Mean Change (SE)	-0,32 (0,041)	-0,25 (0,043)	-0,07 [-0,177; 0,040] 0,216	-0,191 [-0,517; 0,135]
Age = 40-64 years				
N'	271	291		
Baseline Mean (SD)	0,71 (0,545)	0,65 (0,507)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,025)	-0,16 (0,025)	-0,01 [-0,068; 0,044] 0,669	-0,029 [-0,197; 0,138]
Week 16:				
Adjusted Mean Change (SE)	-0,26 (0,025)	-0,23 (0,025)	-0,03 [-0,086; 0,026] 0,289	-0,073 [-0,239; 0,094]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,025)	-0,25 (0,025)	-0,03 [-0,087; 0,025] 0,278	-0,075 [-0,243; 0,092]
Age = ≥65 years				
N'	100	90		
Baseline Mean (SD)	0,72 (0,533)	0,69 (0,526)		
Week 8:				
Adjusted Mean Change (SE)	-0,08 (0,037)	-0,11 (0,039)	0,03 [-0,068; 0,125] 0,560	0,077 [-0,209; 0,363]
Week 16:				
Adjusted Mean Change (SE)	-0,13 (0,038)	-0,18 (0,039)	0,05 [-0,051; 0,142] 0,357	0,122 [-0,166; 0,411]
Week 24:				
Adjusted Mean Change (SE)	-0,17 (0,038)	-0,22 (0,039)	0,05 [-0,045; 0,148] 0,293	0,141 [-0,149; 0,431]
Mean of: How did you sleep last night?				
Interaction Test	0,087			
Age = 18-39 years				
N'	81	70		
Baseline Mean (SD)	0,42 (0,537)	0,33 (0,456)		
Week 8:				
Adjusted Mean Change (SE)	-0,26 (0,037)	-0,18 (0,039)	-0,08 [-0,178; 0,017] 0,104	-0,253 [-0,584; 0,077]
Week 16:				
Adjusted Mean Change (SE)	-0,30 (0,039)	-0,25 (0,041)	-0,05 [-0,156; 0,053] 0,333	-0,148 [-0,468; 0,173]
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,040)	-0,25 (0,042)	-0,04 [-0,149; 0,064] 0,432	-0,122 [-0,448; 0,203]
Age = 40-64 years				
N'	271	291		
Baseline Mean (SD)	0,55 (0,557)	0,51 (0,524)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,023)	-0,15 (0,022)	-0,02 [-0,071; 0,030] 0,423	-0,055 [-0,222; 0,112]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,024)	-0,21 (0,024)	-0,03 [-0,083; 0,026] 0,300	-0,072 [-0,239; 0,094]
Week 24:				
Adjusted Mean Change (SE)	-0,26 (0,024)	-0,24 (0,024)	-0,02 [-0,075; 0,035] 0,481	-0,050 [-0,217; 0,118]
Age = ≥65 years				
N'	100	90		
Baseline Mean (SD)	0,57 (0,566)	0,49 (0,577)		
Week 8:				
Adjusted Mean Change (SE)	-0,07 (0,034)	-0,13 (0,035)	0,06 [-0,023; 0,149] 0,149	0,189 [-0,097; 0,475]
Week 16:				
Adjusted Mean Change (SE)	-0,12 (0,036)	-0,19 (0,038)	0,07 [-0,025; 0,162] 0,151	0,193 [-0,096; 0,481]
Week 24:				
Adjusted Mean Change (SE)	-0,15 (0,037)	-0,24 (0,038)	0,09 [-0,006; 0,184] 0,067	0,248 [-0,043; 0,538]
Mean of: Did you have asthma symptoms upon awakening in the morning?				
Interaction Test	0,502			
Age = 18-39 years				
N'	81	70		
Baseline Mean (SD)	0,74 (0,581)	0,68 (0,567)		
Week 8:				
Adjusted Mean Change (SE)	-0,24 (0,048)	-0,13 (0,050)	-0,11 [-0,235; 0,016] 0,089	-0,265 [-0,596; 0,066]
Week 16:				
Adjusted Mean Change (SE)	-0,31 (0,053)	-0,24 (0,056)	-0,06 [-0,205; 0,080] 0,388	-0,132 [-0,453; 0,188]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,34 (0,056)	-0,25 (0,059)	-0,09 [-0,241; 0,063] 0,249	-0,181 [-0,507; 0,145]
Age = 40-64 years				
N'	271	291		
Baseline Mean (SD)	0,88 (0,633)	0,79 (0,592)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,029)	-0,15 (0,029)	-0,01 [-0,071; 0,058] 0,847	-0,013 [-0,180; 0,154]
Week 16:				
Adjusted Mean Change (SE)	-0,27 (0,032)	-0,23 (0,032)	-0,04 [-0,111; 0,037] 0,329	-0,069 [-0,235; 0,098]
Week 24:				
Adjusted Mean Change (SE)	-0,30 (0,034)	-0,25 (0,033)	-0,05 [-0,126; 0,031] 0,236	-0,086 [-0,253; 0,082]
Age = ≥65 years				
N'	100	90		
Baseline Mean (SD)	0,87 (0,614)	0,89 (0,631)		
Week 8:				
Adjusted Mean Change (SE)	-0,07 (0,044)	-0,08 (0,045)	0,00 [-0,109; 0,112] 0,980	0,003 [-0,282; 0,289]
Week 16:				
Adjusted Mean Change (SE)	-0,13 (0,049)	-0,16 (0,051)	0,03 [-0,099; 0,155] 0,665	0,058 [-0,230; 0,346]
Week 24:				
Adjusted Mean Change (SE)	-0,17 (0,051)	-0,19 (0,054)	0,02 [-0,111; 0,160] 0,727	0,048 [-0,242; 0,337]
Mean of: Did your respiratory symptoms stop you from performing your usual daily activities?				
Interaction Test	0,796			
Age = 18-39 years				
N'	78	71		
Baseline Mean (SD)	0,71 (0,582)	0,66 (0,613)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,23 (0,051)	-0,18 (0,052)	-0,05 [-0,184; 0,079] 0,437	-0,121 [-0,450; 0,209]
Week 16:				
Adjusted Mean Change (SE)	-0,31 (0,057)	-0,28 (0,059)	-0,03 [-0,183; 0,119] 0,679	-0,064 [-0,387; 0,259]
Week 24:				
Adjusted Mean Change (SE)	-0,32 (0,060)	-0,31 (0,062)	-0,01 [-0,167; 0,154] 0,936	-0,013 [-0,341; 0,315]
Age = 40-64 years				
N'	277	291		
Baseline Mean (SD)	0,90 (0,709)	0,88 (0,670)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,031)	-0,20 (0,031)	0,03 [-0,041; 0,094] 0,440	0,052 [-0,115; 0,218]
Week 16:				
Adjusted Mean Change (SE)	-0,31 (0,034)	-0,29 (0,034)	-0,02 [-0,095; 0,060] 0,660	-0,031 [-0,196; 0,134]
Week 24:				
Adjusted Mean Change (SE)	-0,33 (0,035)	-0,31 (0,035)	-0,01 [-0,092; 0,071] 0,802	-0,018 [-0,185; 0,149]
Age = ≥65 years				
N'	100	89		
Baseline Mean (SD)	1,02 (0,662)	1,03 (0,673)		
Week 8:				
Adjusted Mean Change (SE)	-0,06 (0,046)	-0,12 (0,048)	0,06 [-0,060; 0,173] 0,340	0,125 [-0,162; 0,411]
Week 16:				
Adjusted Mean Change (SE)	-0,13 (0,051)	-0,15 (0,054)	0,01 [-0,120; 0,148] 0,839	0,027 [-0,260; 0,315]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,16 (0,054)	-0,19 (0,057)	0,03 [-0,113; 0,171] 0,692	0,054 [-0,234; 0,342]
Mean of: How severe was your shortness of breath today?				
Interaction Test	0,130			
Age = 18-39 years				
N'	78	71		
Baseline Mean (SD)	0,88 (0,540)	0,78 (0,599)		
Week 8:				
Adjusted Mean Change (SE)	-0,34 (0,051)	-0,20 (0,053)	-0,15 [-0,283; -0,015] 0,030 *	-0,338 [-0,669; -0,006]
Week 16:				
Adjusted Mean Change (SE)	-0,45 (0,058)	-0,31 (0,060)	-0,15 [-0,299; 0,008] 0,063	-0,288 [-0,612; 0,037]
Week 24:				
Adjusted Mean Change (SE)	-0,46 (0,061)	-0,31 (0,063)	-0,15 [-0,309; 0,018] 0,082	-0,276 [-0,606; 0,053]
Age = 40-64 years				
N'	277	291		
Baseline Mean (SD)	1,03 (0,681)	1,01 (0,635)		
Week 8:				
Adjusted Mean Change (SE)	-0,21 (0,031)	-0,23 (0,031)	0,02 [-0,052; 0,085] 0,634	0,032 [-0,135; 0,199]
Week 16:				
Adjusted Mean Change (SE)	-0,38 (0,034)	-0,33 (0,034)	-0,05 [-0,129; 0,028] 0,208	-0,088 [-0,253; 0,077]
Week 24:				
Adjusted Mean Change (SE)	-0,41 (0,036)	-0,36 (0,036)	-0,05 [-0,135; 0,032] 0,229	-0,086 [-0,253; 0,080]
Age = ≥65 years				
N'	100	89		
Baseline Mean (SD)	1,15 (0,637)	1,17 (0,646)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,12 (0,046)	-0,17 (0,049)	0,06 [-0,062; 0,174] 0,355	0,121 [-0,166; 0,408]
Week 16:				
Adjusted Mean Change (SE)	-0,19 (0,052)	-0,24 (0,055)	0,05 [-0,082; 0,190] 0,436	0,105 [-0,183; 0,392]
Week 24:				
Adjusted Mean Change (SE)	-0,24 (0,055)	-0,27 (0,058)	0,03 [-0,115; 0,175] 0,687	0,055 [-0,233; 0,343]
Mean of: How was your wheeze during the past 12 hours?				
Interaction Test	0,262			
Age = 18-39 years				
N'	78	71		
Baseline Mean (SD)	0,67 (0,589)	0,70 (0,580)		
Week 8:				
Adjusted Mean Change (SE)	-0,29 (0,051)	-0,19 (0,053)	-0,10 [-0,234; 0,034] 0,144	-0,227 [-0,557; 0,103]
Week 16:				
Adjusted Mean Change (SE)	-0,36 (0,057)	-0,28 (0,059)	-0,08 [-0,231; 0,072] 0,305	-0,159 [-0,482; 0,165]
Week 24:				
Adjusted Mean Change (SE)	-0,39 (0,061)	-0,30 (0,063)	-0,09 [-0,251; 0,072] 0,275	-0,173 [-0,501; 0,156]
Age = 40-64 years				
N'	277	291		
Baseline Mean (SD)	0,93 (0,679)	0,87 (0,635)		
Week 8:				
Adjusted Mean Change (SE)	-0,19 (0,031)	-0,23 (0,031)	0,04 [-0,025; 0,112] 0,209	0,085 [-0,082; 0,251]
Week 16:				
Adjusted Mean Change (SE)	-0,33 (0,034)	-0,30 (0,034)	-0,03 [-0,111; 0,044] 0,401	-0,058 [-0,223; 0,107]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,35 (0,035)	-0,33 (0,035)	-0,02 [-0,102; 0,063] 0,643	-0,033 [-0,200; 0,133]
Age = ≥65 years				
N'	100	89		
Baseline Mean (SD)	0,98 (0,667)	0,89 (0,655)		
Week 8:				
Adjusted Mean Change (SE)	-0,07 (0,046)	-0,14 (0,049)	0,07 [-0,048; 0,188] 0,244	0,153 [-0,134; 0,440]
Week 16:				
Adjusted Mean Change (SE)	-0,13 (0,052)	-0,18 (0,054)	0,06 [-0,078; 0,192] 0,411	0,110 [-0,177; 0,398]
Week 24:				
Adjusted Mean Change (SE)	-0,15 (0,054)	-0,22 (0,057)	0,07 [-0,074; 0,213] 0,341	0,129 [-0,159; 0,418]
Mean of: How was your cough during the past 12 hours?				
Interaction Test	0,168			
Age = 18-39 years				
N'	78	71		
Baseline Mean (SD)	0,78 (0,700)	0,76 (0,655)		
Week 8:				
Adjusted Mean Change (SE)	-0,26 (0,054)	-0,13 (0,056)	-0,14 [-0,277; 0,007] 0,062	-0,291 [-0,622; 0,040]
Week 16:				
Adjusted Mean Change (SE)	-0,36 (0,061)	-0,23 (0,064)	-0,13 [-0,291; 0,035] 0,125	-0,238 [-0,562; 0,086]
Week 24:				
Adjusted Mean Change (SE)	-0,38 (0,065)	-0,27 (0,067)	-0,11 [-0,286; 0,061] 0,202	-0,203 [-0,531; 0,126]
Age = 40-64 years				
N'	277	291		
Baseline Mean (SD)	0,93 (0,672)	0,93 (0,655)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,033)	-0,15 (0,033)	-0,01 [-0,081; 0,064] 0,824	-0,015 [-0,182; 0,152]
Week 16:				
Adjusted Mean Change (SE)	-0,29 (0,036)	-0,25 (0,036)	-0,04 [-0,123; 0,044] 0,353	-0,065 [-0,230; 0,100]
Week 24:				
Adjusted Mean Change (SE)	-0,31 (0,038)	-0,28 (0,038)	-0,03 [-0,115; 0,063] 0,563	-0,042 [-0,208; 0,125]
Age = ≥65 years				
N'	100	89		
Baseline Mean (SD)	1,02 (0,671)	0,90 (0,652)		
Week 8:				
Adjusted Mean Change (SE)	-0,00 (0,049)	-0,08 (0,051)	0,08 [-0,050; 0,201] 0,238	0,155 [-0,132; 0,442]
Week 16:				
Adjusted Mean Change (SE)	-0,10 (0,055)	-0,16 (0,058)	0,05 [-0,091; 0,199] 0,465	0,099 [-0,189; 0,386]
Week 24:				
Adjusted Mean Change (SE)	-0,11 (0,058)	-0,17 (0,061)	0,06 [-0,093; 0,214] 0,441	0,105 [-0,183; 0,393]
Did you have chest tightness during the past 12 hours?				
Interaction Test	0,058			
Age = 18-39 years				
N'	78	71		
Baseline Mean (SD)	0,58 (0,604)	0,53 (0,627)		
Week 8:				
Adjusted Mean Change (SE)	-0,15 (0,049)	-0,10 (0,050)	-0,05 [-0,179; 0,074] 0,414	-0,127 [-0,457; 0,203]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,054)	-0,13 (0,055)	-0,10 [-0,239; 0,045] 0,182	-0,207 [-0,530; 0,117]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,24 (0,056)	-0,14 (0,058)	-0,10 [-0,251; 0,050] 0,190	-0,207 [-0,536; 0,121]
Age = 40-64 years				
N'	277	291		
Baseline Mean (SD)	0,67 (0,640)	0,67 (0,625)		
Week 8:				
Adjusted Mean Change (SE)	-0,10 (0,029)	-0,11 (0,029)	0,01 [-0,057; 0,072] 0,824	0,015 [-0,152; 0,182]
Week 16:				
Adjusted Mean Change (SE)	-0,21 (0,032)	-0,16 (0,032)	-0,05 [-0,120; 0,025] 0,202	-0,089 [-0,254; 0,077]
Week 24:				
Adjusted Mean Change (SE)	-0,22 (0,033)	-0,19 (0,033)	-0,03 [-0,111; 0,043] 0,388	-0,061 [-0,228; 0,105]
Age = ≥65 years				
N'	100	89		
Baseline Mean (SD)	0,74 (0,667)	0,73 (0,680)		
Week 8:				
Adjusted Mean Change (SE)	0,05 (0,044)	-0,06 (0,046)	0,11 [-0,006; 0,218] 0,063	0,243 [-0,044; 0,531]
Week 16:				
Adjusted Mean Change (SE)	0,01 (0,048)	-0,10 (0,051)	0,11 [-0,016; 0,236] 0,087	0,229 [-0,059; 0,518]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,02 (0,051)	-0,15 (0,053)	0,13 [-0,008; 0,259] 0,065	0,251 [-0,038; 0,540]

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + age + age * treatment + age * treatment * visit, within-patient correlation: unstructured covariance matrix
Exceptional model(s): **Mean night-time symptom score**: treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + age + age * treatment + age * treatment * visit, within-patient correlation: compound symmetry covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 9.4 Symptoms - Change from Baseline by Gender (FAS)

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Percentage of mornings with no symptoms on rising				
Interaction Test	0,155			
Gender = Male				
N'	179	162		
Baseline Mean (SD)	35,64 (39,139)	33,94 (37,527)		
Week 8:				
Adjusted Mean Change (SE)	8,07 (2,381)	8,83 (2,550)	-0,76 [-6,625; 5,109] 0,800	-0,024 [-0,239; 0,191]
Week 16:				
Adjusted Mean Change (SE)	14,25 (2,748)	14,24 (2,923)	0,01 [-7,025; 7,041] 0,998	0,000 [-0,214; 0,214]
Week 24:				
Adjusted Mean Change (SE)	17,23 (2,867)	16,65 (3,047)	0,57 [-6,837; 7,981] 0,880	0,015 [-0,200; 0,230]
Gender = Female				
N'	273	289		
Baseline Mean (SD)	36,45 (37,836)	42,10 (38,608)		
Week 8:				
Adjusted Mean Change (SE)	11,31 (2,148)	6,35 (2,047)	4,96 [0,392; 9,536] 0,033 *	0,143 [-0,025; 0,311]
Week 16:				
Adjusted Mean Change (SE)	18,78 (2,413)	12,15 (2,315)	6,63 [1,152; 12,112] 0,018 *	0,168 [0,002; 0,335]
Week 24:				
Adjusted Mean Change (SE)	20,32 (2,501)	14,66 (2,408)	5,66 [-0,118; 11,436] 0,055	0,140 [-0,028; 0,308]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Percentage of days with no day-time symptoms				
Interaction Test	0,822			
Gender = Male				
N'	180	160		
Baseline Mean (SD)	18,01 (30,473)	16,11 (29,942)		
Week 8:				
Adjusted Mean Change (SE)	8,24 (2,115)	5,91 (2,290)	2,33 [-2,920; 7,574] 0,384	0,082 [-0,133; 0,297]
Week 16:				
Adjusted Mean Change (SE)	15,59 (2,625)	10,12 (2,813)	5,47 [-1,397; 12,331] 0,118	0,155 [-0,059; 0,369]
Week 24:				
Adjusted Mean Change (SE)	18,52 (2,797)	14,06 (2,991)	4,46 [-2,937; 11,853] 0,237	0,119 [-0,096; 0,334]
Gender = Female				
N'	275	291		
Baseline Mean (SD)	17,51 (30,102)	17,44 (30,923)		
Week 8:				
Adjusted Mean Change (SE)	10,16 (1,914)	8,66 (1,839)	1,50 [-2,563; 5,567] 0,469	0,048 [-0,119; 0,216]
Week 16:				
Adjusted Mean Change (SE)	20,85 (2,285)	15,97 (2,205)	4,88 [-0,433; 10,189] 0,072	0,130 [-0,036; 0,295]
Week 24:				
Adjusted Mean Change (SE)	21,80 (2,415)	18,56 (2,336)	3,24 [-2,491; 8,969] 0,268	0,082 [-0,085; 0,250]
Percentage of days with no night-time awakenings				
Interaction Test	0,620			
Gender = Male				
N'	179	162		
Baseline Mean (SD)	58,76 (38,870)	65,13 (38,213)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	10,69 (2,141)	9,71 (2,288)	0,98 [-4,305; 6,265] 0,716	0,034 [-0,181; 0,249]
Week 16:				
Adjusted Mean Change (SE)	15,71 (2,350)	13,42 (2,500)	2,29 [-3,660; 8,246] 0,450	0,073 [-0,141; 0,287]
Week 24:				
Adjusted Mean Change (SE)	17,45 (2,437)	13,58 (2,591)	3,88 [-2,354; 10,108] 0,222	0,120 [-0,096; 0,335]
Gender = Female				
N'	273	289		
Baseline Mean (SD)	58,79 (38,751)	60,70 (38,051)		
Week 8:				
Adjusted Mean Change (SE)	10,39 (1,931)	8,94 (1,840)	1,46 [-2,653; 5,568] 0,487	0,047 [-0,121; 0,214]
Week 16:				
Adjusted Mean Change (SE)	15,22 (2,081)	13,65 (1,993)	1,58 [-3,053; 6,207] 0,504	0,046 [-0,120; 0,213]
Week 24:				
Adjusted Mean Change (SE)	16,06 (2,145)	17,18 (2,062)	-1,12 [-5,968; 3,731] 0,651	-0,032 [-0,200; 0,136]
Percentage of days with no asthma symptoms				
Interaction Test	0,576			
Gender = Male				
N'	170	151		
Baseline Mean (SD)	15,55 (29,833)	14,94 (30,000)		
Week 8:				
Adjusted Mean Change (SE)	8,31 (2,162)	4,59 (2,352)	3,72 [-1,635; 9,079] 0,173	0,133 [-0,091; 0,357]
Week 16:				
Adjusted Mean Change (SE)	15,57 (2,685)	9,35 (2,890)	6,22 [-0,804; 13,239] 0,083	0,178 [-0,044; 0,399]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	19,11 (2,873)	12,20 (3,086)	6,91 [-0,691; 14,513] 0,075	0,185 [-0,037; 0,408]
Gender = Female				
N'	264	272		
Baseline Mean (SD)	14,99 (28,888)	15,88 (30,013)		
Week 8:				
Adjusted Mean Change (SE)	9,90 (1,956)	8,14 (1,881)	1,76 [-2,391; 5,904] 0,406	0,058 [-0,117; 0,232]
Week 16:				
Adjusted Mean Change (SE)	20,70 (2,326)	16,18 (2,261)	4,52 [-0,894; 9,936] 0,102	0,121 [-0,049; 0,291]
Week 24:				
Adjusted Mean Change (SE)	22,00 (2,467)	18,12 (2,406)	3,87 [-2,004; 9,746] 0,196	0,099 [-0,074; 0,271]
Mean total daily symptom score				
Interaction Test	0,822			
Gender = Male				
N'	170	151		
Baseline Mean (SD)	2,20 (1,534)	2,02 (1,390)		
Week 8:				
Adjusted Mean Change (SE)	-0,43 (0,082)	-0,46 (0,089)	0,03 [-0,175; 0,234] 0,778	0,028 [-0,196; 0,251]
Week 16:				
Adjusted Mean Change (SE)	-0,65 (0,091)	-0,61 (0,098)	-0,03 [-0,264; 0,198] 0,778	-0,028 [-0,249; 0,193]
Week 24:				
Adjusted Mean Change (SE)	-0,78 (0,094)	-0,66 (0,101)	-0,12 [-0,357; 0,124] 0,340	-0,096 [-0,318; 0,126]
Gender = Female				
N'	264	272		
Baseline Mean (SD)	2,30 (1,611)	2,16 (1,566)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,51 (0,074)	-0,45 (0,072)	-0,06 [-0,216; 0,100] 0,472	-0,050 [-0,224; 0,124]
Week 16:				
Adjusted Mean Change (SE)	-0,79 (0,080)	-0,68 (0,078)	-0,10 [-0,279; 0,077] 0,266	-0,079 [-0,248; 0,091]
Week 24:				
Adjusted Mean Change (SE)	-0,82 (0,082)	-0,77 (0,080)	-0,05 [-0,240; 0,131] 0,566	-0,042 [-0,214; 0,131]
Mean day-time symptom score				
Interaction Test	0,954			
Gender = Male				
N'	180	160		
Baseline Mean (SD)	0,86 (0,594)	0,80 (0,512)		
Week 8:				
Adjusted Mean Change (SE)	-0,15 (0,031)	-0,17 (0,034)	0,02 [-0,060; 0,094] 0,670	0,040 [-0,175; 0,255]
Week 16:				
Adjusted Mean Change (SE)	-0,25 (0,035)	-0,24 (0,037)	-0,01 [-0,101; 0,075] 0,772	-0,028 [-0,242; 0,186]
Week 24:				
Adjusted Mean Change (SE)	-0,30 (0,036)	-0,26 (0,039)	-0,04 [-0,137; 0,051] 0,367	-0,089 [-0,304; 0,126]
Gender = Female				
N'	275	291		
Baseline Mean (SD)	0,90 (0,591)	0,89 (0,587)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,028)	-0,17 (0,027)	0,01 [-0,053; 0,067] 0,817	0,015 [-0,152; 0,183]
Week 16:				
Adjusted Mean Change (SE)	-0,29 (0,031)	-0,25 (0,030)	-0,03 [-0,103; 0,034] 0,321	-0,069 [-0,234; 0,097]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,032)	-0,28 (0,031)	-0,00 [-0,076; 0,070] 0,938	-0,006 [-0,173; 0,162]
Mean night-time symptom score				
Interaction Test	0,441			
Gender = Male				
N'	179	162		
Baseline Mean (SD)	0,68 (0,508)	0,62 (0,471)		
Week 8:				
Adjusted Mean Change (SE)	-0,14 (0,027)	-0,16 (0,029)	0,01 [-0,055; 0,077] 0,747	0,031 [-0,185; 0,246]
Week 16:				
Adjusted Mean Change (SE)	-0,21 (0,029)	-0,22 (0,031)	0,01 [-0,063; 0,084] 0,781	0,027 [-0,187; 0,241]
Week 24:				
Adjusted Mean Change (SE)	-0,25 (0,030)	-0,23 (0,032)	-0,02 [-0,092; 0,060] 0,684	-0,040 [-0,255; 0,175]
Gender = Female				
N'	273	289		
Baseline Mean (SD)	0,70 (0,554)	0,65 (0,529)		
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,024)	-0,14 (0,023)	-0,03 [-0,086; 0,017] 0,184	-0,089 [-0,257; 0,078]
Week 16:				
Adjusted Mean Change (SE)	-0,26 (0,026)	-0,22 (0,025)	-0,04 [-0,095; 0,019] 0,189	-0,091 [-0,257; 0,075]
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,026)	-0,25 (0,025)	-0,02 [-0,082; 0,037] 0,460	-0,052 [-0,220; 0,116]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Mean of: How did you sleep last night?				
Interaction Test	0,848			
Gender = Male				
N'	179	162		
Baseline Mean (SD)	0,51 (0,517)	0,42 (0,494)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,026)	-0,16 (0,028)	-0,00 [-0,065; 0,064] 0,988	-0,001 [-0,216; 0,214]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,028)	-0,22 (0,030)	-0,01 [-0,083; 0,057] 0,715	-0,035 [-0,249; 0,179]
Week 24:				
Adjusted Mean Change (SE)	-0,25 (0,028)	-0,22 (0,030)	-0,03 [-0,098; 0,044] 0,455	-0,072 [-0,288; 0,143]
Gender = Female				
N'	273	289		
Baseline Mean (SD)	0,55 (0,582)	0,51 (0,544)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,024)	-0,15 (0,022)	-0,02 [-0,071; 0,030] 0,432	-0,053 [-0,221; 0,114]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,025)	-0,22 (0,024)	-0,01 [-0,066; 0,043] 0,681	-0,028 [-0,195; 0,138]
Week 24:				
Adjusted Mean Change (SE)	-0,24 (0,025)	-0,26 (0,024)	0,01 [-0,040; 0,070] 0,594	0,037 [-0,131; 0,205]
Mean of: Did you have asthma symptoms upon awakening in the morning?				
Interaction Test	0,139			
Gender = Male				
N'	179	162		
Baseline Mean (SD)	0,84 (0,623)	0,82 (0,557)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,12 (0,034)	-0,15 (0,036)	0,03 [-0,055; 0,111] 0,514	0,062 [-0,154; 0,277]
Week 16:				
Adjusted Mean Change (SE)	-0,19 (0,037)	-0,23 (0,040)	0,04 [-0,056; 0,134] 0,419	0,078 [-0,136; 0,292]
Week 24:				
Adjusted Mean Change (SE)	-0,24 (0,039)	-0,24 (0,042)	0,00 [-0,100; 0,102] 0,988	0,002 [-0,214; 0,217]
Gender = Female				
N'	273	289		
Baseline Mean (SD)	0,86 (0,621)	0,78 (0,621)		
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,030)	-0,13 (0,029)	-0,05 [-0,116; 0,014] 0,123	-0,104 [-0,271; 0,064]
Week 16:				
Adjusted Mean Change (SE)	-0,29 (0,033)	-0,22 (0,032)	-0,07 [-0,142; 0,006] 0,072	-0,126 [-0,292; 0,041]
Week 24:				
Adjusted Mean Change (SE)	-0,30 (0,034)	-0,24 (0,033)	-0,06 [-0,142; 0,015] 0,114	-0,114 [-0,282; 0,054]
Mean of: Did your respiratory symptoms stop you from performing your usual daily activities?				
Interaction Test	0,817			
Gender = Male				
N'	180	160		
Baseline Mean (SD)	0,88 (0,699)	0,81 (0,631)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,035)	-0,19 (0,038)	0,02 [-0,070; 0,105] 0,692	0,037 [-0,178; 0,252]
Week 16:				
Adjusted Mean Change (SE)	-0,26 (0,039)	-0,26 (0,042)	0,00 [-0,096; 0,106] 0,924	0,009 [-0,204; 0,223]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,31 (0,041)	-0,28 (0,044)	-0,03 [-0,140; 0,073] 0,538	-0,061 [-0,276; 0,154]
Gender = Female				
N'	275	291		
Baseline Mean (SD)	0,90 (0,674)	0,91 (0,688)		
Week 8:				
Adjusted Mean Change (SE)	-0,15 (0,032)	-0,17 (0,031)	0,03 [-0,041; 0,094] 0,448	0,050 [-0,117; 0,218]
Week 16:				
Adjusted Mean Change (SE)	-0,28 (0,035)	-0,26 (0,034)	-0,02 [-0,097; 0,059] 0,634	-0,033 [-0,198; 0,132]
Week 24:				
Adjusted Mean Change (SE)	-0,27 (0,036)	-0,30 (0,035)	0,02 [-0,059; 0,106] 0,579	0,040 [-0,128; 0,207]
Mean of: How severe was your shortness of breath today?				
Interaction Test	0,926			
Gender = Male				
N'	180	160		
Baseline Mean (SD)	1,02 (0,654)	0,95 (0,577)		
Week 8:				
Adjusted Mean Change (SE)	-0,21 (0,036)	-0,22 (0,039)	0,01 [-0,081; 0,096] 0,870	0,015 [-0,200; 0,230]
Week 16:				
Adjusted Mean Change (SE)	-0,33 (0,040)	-0,31 (0,043)	-0,02 [-0,127; 0,077] 0,634	-0,046 [-0,260; 0,167]
Week 24:				
Adjusted Mean Change (SE)	-0,39 (0,042)	-0,31 (0,045)	-0,08 [-0,192; 0,025] 0,129	-0,150 [-0,365; 0,066]
Gender = Female				
N'	275	291		
Baseline Mean (SD)	1,04 (0,654)	1,04 (0,673)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,22 (0,032)	-0,21 (0,031)	-0,01 [-0,075; 0,062] 0,855	-0,012 [-0,179; 0,155]
Week 16:				
Adjusted Mean Change (SE)	-0,36 (0,035)	-0,31 (0,034)	-0,05 [-0,132; 0,026] 0,190	-0,091 [-0,256; 0,075]
Week 24:				
Adjusted Mean Change (SE)	-0,37 (0,037)	-0,35 (0,036)	-0,03 [-0,109; 0,059] 0,554	-0,042 [-0,210; 0,125]
Mean of: How was your wheeze during the past 12 hours?				
Interaction Test	0,434			
Gender = Male				
N'	180	160		
Baseline Mean (SD)	0,87 (0,658)	0,77 (0,586)		
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,036)	-0,18 (0,039)	-0,00 [-0,090; 0,088] 0,977	-0,003 [-0,218; 0,212]
Week 16:				
Adjusted Mean Change (SE)	-0,27 (0,040)	-0,25 (0,043)	-0,02 [-0,123; 0,079] 0,669	-0,041 [-0,255; 0,172]
Week 24:				
Adjusted Mean Change (SE)	-0,32 (0,042)	-0,26 (0,045)	-0,07 [-0,175; 0,039] 0,214	-0,122 [-0,337; 0,093]
Gender = Female				
N'	275	291		
Baseline Mean (SD)	0,92 (0,676)	0,88 (0,654)		
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,032)	-0,22 (0,031)	0,04 [-0,024; 0,113] 0,205	0,084 [-0,083; 0,252]
Week 16:				
Adjusted Mean Change (SE)	-0,31 (0,035)	-0,29 (0,034)	-0,02 [-0,098; 0,058] 0,618	-0,034 [-0,200; 0,131]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,31 (0,037)	-0,33 (0,035)	0,02 [-0,059; 0,107] 0,568	0,041 [-0,127; 0,208]
Mean of: How was your cough during the past 12 hours?				
Interaction Test	0,615			
Gender = Male				
N'	180	160		
Baseline Mean (SD)	0,87 (0,663)	0,88 (0,609)		
Week 8:				
Adjusted Mean Change (SE)	-0,12 (0,038)	-0,14 (0,041)	0,02 [-0,071; 0,118] 0,624	0,046 [-0,169; 0,261]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,042)	-0,22 (0,046)	-0,02 [-0,125; 0,093] 0,769	-0,028 [-0,242; 0,185]
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,045)	-0,27 (0,048)	-0,01 [-0,126; 0,105] 0,863	-0,017 [-0,232; 0,198]
Gender = Female				
N'	275	291		
Baseline Mean (SD)	0,96 (0,689)	0,91 (0,681)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,034)	-0,13 (0,033)	-0,03 [-0,103; 0,043] 0,421	-0,054 [-0,221; 0,113]
Week 16:				
Adjusted Mean Change (SE)	-0,29 (0,038)	-0,24 (0,036)	-0,04 [-0,127; 0,041] 0,314	-0,070 [-0,235; 0,096]
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,039)	-0,26 (0,038)	-0,02 [-0,114; 0,065] 0,585	-0,039 [-0,206; 0,128]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Did you have chest tightness during the past 12 hours?				
Interaction Test	0,721			
Gender = Male				
N'	180	160		
Baseline Mean (SD)	0,67 (0,630)	0,58 (0,582)		
Week 8:				
Adjusted Mean Change (SE)	-0,07 (0,034)	-0,11 (0,037)	0,04 [-0,042; 0,126] 0,328	0,092 [-0,123; 0,307]
Week 16:				
Adjusted Mean Change (SE)	-0,15 (0,037)	-0,15 (0,040)	0,00 [-0,094; 0,096] 0,985	0,002 [-0,212; 0,215]
Week 24:				
Adjusted Mean Change (SE)	-0,18 (0,039)	-0,17 (0,042)	-0,01 [-0,114; 0,086] 0,789	-0,026 [-0,241; 0,189]
Gender = Female				
N'	275	291		
Baseline Mean (SD)	0,67 (0,648)	0,70 (0,663)		
Week 8:				
Adjusted Mean Change (SE)	-0,09 (0,031)	-0,10 (0,029)	0,01 [-0,058; 0,072] 0,830	0,014 [-0,153; 0,182]
Week 16:				
Adjusted Mean Change (SE)	-0,18 (0,033)	-0,15 (0,032)	-0,03 [-0,106; 0,041] 0,381	-0,060 [-0,226; 0,105]
Week 24:				
Adjusted Mean Change (SE)	-0,19 (0,034)	-0,18 (0,033)	-0,01 [-0,083; 0,072] 0,886	-0,010 [-0,177; 0,157]

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + gender + gender * treatment + gender * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 9.5 Symptoms - Change from Baseline by Region (FAS)

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Percentage of mornings with no symptoms on rising				
Interaction Test	N.E.			
Region = Asia				
N'	117	126		
Baseline Mean (SD)	23,13 (33,104)	30,52 (36,141)		
Week 8:				
Adjusted Mean Change (SE)	14,50 (2,646)	10,71 (2,542)	3,79 [-3,441; 11,012] 0,304	0,134 [-0,121; 0,389]
Week 16:				
Adjusted Mean Change (SE)	23,59 (3,198)	13,25 (3,072)	10,34 [1,608; 19,073] 0,020 *	0,302 [0,047; 0,557]
Week 24:				
Adjusted Mean Change (SE)	24,51 (3,382)	18,12 (3,255)	6,39 [-2,856; 15,629] 0,175	0,177 [-0,078; 0,432]
Region = Europe				
N'	157	164		
Baseline Mean (SD)	29,20 (35,952)	37,48 (37,633)		
Week 8:				
Adjusted Mean Change (SE)	10,22 (2,241)	8,28 (2,182)	1,95 [-4,212; 8,104] 0,535	0,070 [-0,150; 0,290]
Week 16:				
Adjusted Mean Change (SE)	16,50 (2,669)	15,16 (2,611)	1,35 [-6,003; 8,699] 0,719	0,040 [-0,179; 0,260]
Week 24:				
Adjusted Mean Change (SE)	18,14 (2,811)	17,49 (2,758)	0,65 [-7,108; 8,401] 0,870	0,019 [-0,204; 0,241]
Region = Latin America				
N'	158	152		
Baseline Mean (SD)	50,33 (39,568)	47,48 (39,655)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	8,84 (2,070)	7,08 (2,109)	1,76 [-4,050; 7,565] 0,552	0,069 [-0,158; 0,296]
Week 16:				
Adjusted Mean Change (SE)	15,72 (2,489)	13,58 (2,531)	2,14 [-4,831; 9,121] 0,546	0,069 [-0,155; 0,293]
Week 24:				
Adjusted Mean Change (SE)	19,62 (2,630)	14,46 (2,680)	5,16 [-2,216; 12,544] 0,170	0,159 [-0,068; 0,385]
Region = Others				
N'	20	9		
Baseline Mean (SD)	54,37 (33,854)	50,52 (35,009)		
Week 8:				
Adjusted Mean Change (SE)	20,30 (6,589)	10,44 (9,846)	9,86 [-13,998; 33,722] 0,409	0,334 [-0,457; 1,126]
Week 16:				
Adjusted Mean Change (SE)	22,25 (7,318)	22,65 (10,936)	-0,41 [-26,909; 26,096] 0,975	-0,012 [-0,799; 0,774]
Week 24:				
Adjusted Mean Change (SE)	20,35 (7,790)	22,55 (11,640)	-2,20 [-30,411; 26,005] 0,876	-0,063 [-0,850; 0,724]
Percentage of days with no day-time symptoms				
Interaction Test	N.E.			
Region = Asia				
N'	118	121		
Baseline Mean (SD)	11,35 (27,197)	10,45 (23,855)		
Week 8:				
Adjusted Mean Change (SE)	8,71 (2,348)	10,15 (2,311)	-1,45 [-7,926; 5,031] 0,661	-0,057 [-0,313; 0,198]
Week 16:				
Adjusted Mean Change (SE)	19,21 (3,068)	16,27 (3,024)	2,93 [-5,538; 11,404] 0,496	0,089 [-0,167; 0,344]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	19,56 (3,219)	18,56 (3,168)	1,00 [-7,881; 9,884] 0,825	0,029 [-0,228; 0,286]
Region = Europe				
N'	157	164		
Baseline Mean (SD)	13,14 (25,803)	10,80 (24,008)		
Week 8:				
Adjusted Mean Change (SE)	8,94 (1,705)	9,43 (1,668)	-0,49 [-5,183; 4,194] 0,836	-0,023 [-0,242; 0,196]
Week 16:				
Adjusted Mean Change (SE)	15,52 (2,350)	14,38 (2,299)	1,15 [-5,317; 7,609] 0,728	0,039 [-0,180; 0,258]
Week 24:				
Adjusted Mean Change (SE)	17,58 (2,644)	19,23 (2,598)	-1,65 [-8,940; 5,635] 0,656	-0,050 [-0,272; 0,171]
Region = Latin America				
N'	160	157		
Baseline Mean (SD)	25,61 (34,069)	27,92 (37,274)		
Week 8:				
Adjusted Mean Change (SE)	11,58 (2,049)	8,42 (2,078)	3,17 [-2,568; 8,903] 0,278	0,125 [-0,101; 0,352]
Week 16:				
Adjusted Mean Change (SE)	22,73 (2,635)	16,18 (2,663)	6,55 [-0,814; 13,909] 0,081	0,197 [-0,024; 0,419]
Week 24:				
Adjusted Mean Change (SE)	25,57 (2,822)	18,33 (2,850)	7,24 [-0,643; 15,119] 0,072	0,205 [-0,018; 0,429]
Region = Others				
N'	20	9		
Baseline Mean (SD)	27,89 (32,011)	25,87 (35,560)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	34,33 (6,870)	12,42 (10,371)	21,91 [-3,179; 46,996] 0,085	0,722 [-0,120; 1,563]
Week 16:				
Adjusted Mean Change (SE)	44,76 (7,869)	20,72 (11,738)	24,05 [-4,462; 52,557] 0,096	0,683 [-0,123; 1,489]
Week 24:				
Adjusted Mean Change (SE)	42,95 (7,871)	19,62 (11,741)	23,32 [-5,194; 51,843] 0,106	0,662 [-0,143; 1,467]
Percentage of days with no night-time awakenings				
Interaction Test	0,864			
Region = Asia				
N'	117	126		
Baseline Mean (SD)	48,97 (38,687)	51,83 (39,590)		
Week 8:				
Adjusted Mean Change (SE)	11,81 (2,553)	11,37 (2,454)	0,43 [-6,486; 7,352] 0,902	0,016 [-0,239; 0,271]
Week 16:				
Adjusted Mean Change (SE)	19,59 (2,552)	14,59 (2,454)	5,00 [-1,911; 11,918] 0,156	0,183 [-0,071; 0,437]
Week 24:				
Adjusted Mean Change (SE)	20,61 (2,552)	19,92 (2,460)	0,69 [-6,236; 7,608] 0,846	0,025 [-0,230; 0,280]
Region = Europe				
N'	157	164		
Baseline Mean (SD)	56,97 (39,102)	63,32 (37,412)		
Week 8:				
Adjusted Mean Change (SE)	12,28 (2,192)	10,71 (2,138)	1,57 [-4,442; 7,576] 0,609	0,057 [-0,163; 0,277]
Week 16:				
Adjusted Mean Change (SE)	14,46 (2,186)	16,06 (2,142)	-1,60 [-7,605; 4,408] 0,602	-0,058 [-0,278; 0,161]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	15,41 (2,190)	16,99 (2,154)	-1,58 [-7,604; 4,449] 0,608	-0,058 [-0,281; 0,164]
Region = Latin America				
N'	158	152		
Baseline Mean (SD)	65,39 (37,777)	70,45 (35,883)		
Week 8:				
Adjusted Mean Change (SE)	10,91 (2,200)	9,09 (2,242)	1,81 [-4,333; 7,960] 0,563	0,067 [-0,160; 0,294]
Week 16:				
Adjusted Mean Change (SE)	16,66 (2,195)	13,70 (2,231)	2,96 [-3,164; 9,085] 0,343	0,108 [-0,116; 0,332]
Week 24:				
Adjusted Mean Change (SE)	18,19 (2,196)	14,83 (2,240)	3,36 [-2,774; 9,503] 0,283	0,124 [-0,103; 0,350]
Region = Others				
N'	20	9		
Baseline Mean (SD)	78,08 (28,142)	52,09 (36,416)		
Week 8:				
Adjusted Mean Change (SE)	13,27 (6,147)	14,73 (9,144)	-1,46 [-23,036; 20,121] 0,895	-0,053 [-0,840; 0,734]
Week 16:				
Adjusted Mean Change (SE)	16,98 (6,147)	16,85 (9,144)	0,12 [-21,456; 21,700] 0,991	0,004 [-0,782; 0,791]
Week 24:				
Adjusted Mean Change (SE)	18,68 (6,147)	19,84 (9,144)	-1,16 [-22,740; 20,417] 0,916	-0,042 [-0,829; 0,745]
Percentage of days with no asthma symptoms				
Interaction Test	N.E.			
Region = Asia				
N'	113	114		
Baseline Mean (SD)	10,16 (27,156)	10,07 (24,536)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	9,05 (2,351)	8,53 (2,315)	0,53 [-5,961; 7,017] 0,873	0,022 [-0,245; 0,288]
Week 16:				
Adjusted Mean Change (SE)	18,40 (3,045)	14,56 (3,026)	3,84 [-4,600; 12,288] 0,371	0,120 [-0,143; 0,382]
Week 24:				
Adjusted Mean Change (SE)	19,08 (3,234)	16,23 (3,208)	2,85 [-6,112; 11,805] 0,532	0,084 [-0,180; 0,348]
Region = Europe				
N'	154	160		
Baseline Mean (SD)	11,70 (25,637)	9,72 (23,129)		
Week 8:				
Adjusted Mean Change (SE)	8,40 (1,683)	8,77 (1,647)	-0,37 [-5,001; 4,259] 0,875	-0,018 [-0,241; 0,205]
Week 16:				
Adjusted Mean Change (SE)	15,42 (2,353)	14,56 (2,312)	0,86 [-5,627; 7,342] 0,795	0,029 [-0,193; 0,251]
Week 24:				
Adjusted Mean Change (SE)	17,43 (2,646)	18,32 (2,611)	-0,89 [-8,196; 6,418] 0,811	-0,027 [-0,252; 0,197]
Region = Latin America				
N'	147	140		
Baseline Mean (SD)	21,59 (32,904)	26,37 (37,352)		
Week 8:				
Adjusted Mean Change (SE)	12,71 (2,175)	9,26 (2,227)	3,45 [-2,671; 9,577] 0,268	0,136 [-0,105; 0,377]
Week 16:				
Adjusted Mean Change (SE)	24,39 (2,761)	18,02 (2,828)	6,37 [-1,408; 14,139] 0,108	0,191 [-0,042; 0,424]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	28,03 (2,976)	19,41 (3,051)	8,62 [0,241; 17,006] 0,044 *	0,243 [0,007; 0,479]
Region = Others				
N'	20	9		
Baseline Mean (SD)	23,96 (29,388)	20,15 (29,064)		
Week 8:				
Adjusted Mean Change (SE)	32,85 (7,589)	7,66 (11,885)	25,19 [-3,238; 53,610] 0,081	0,799 [-0,152; 1,750]
Week 16:				
Adjusted Mean Change (SE)	43,66 (8,216)	23,81 (12,283)	19,85 [-9,913; 49,618] 0,186	0,540 [-0,259; 1,339]
Week 24:				
Adjusted Mean Change (SE)	44,77 (8,135)	22,20 (12,161)	22,57 [-6,907; 52,042] 0,130	0,620 [-0,183; 1,423]
Mean total daily symptom score				
Interaction Test	0,996			
Region = Asia				
N'	113	114		
Baseline Mean (SD)	2,80 (1,617)	2,57 (1,583)		
Week 8:				
Adjusted Mean Change (SE)	-0,44 (0,098)	-0,49 (0,097)	0,05 [-0,218; 0,319] 0,712	0,050 [-0,217; 0,316]
Week 16:				
Adjusted Mean Change (SE)	-0,75 (0,098)	-0,57 (0,097)	-0,17 [-0,439; 0,096] 0,208	-0,167 [-0,430; 0,095]
Week 24:				
Adjusted Mean Change (SE)	-0,75 (0,098)	-0,72 (0,097)	-0,03 [-0,300; 0,237] 0,818	-0,031 [-0,295; 0,233]
Region = Europe				
N'	154	160		
Baseline Mean (SD)	2,38 (1,444)	2,09 (1,258)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,52 (0,083)	-0,48 (0,081)	-0,05 [-0,273; 0,183] 0,698	-0,044 [-0,267; 0,179]
Week 16:				
Adjusted Mean Change (SE)	-0,71 (0,083)	-0,69 (0,081)	-0,01 [-0,241; 0,214] 0,908	-0,013 [-0,235; 0,209]
Week 24:				
Adjusted Mean Change (SE)	-0,76 (0,083)	-0,73 (0,082)	-0,03 [-0,261; 0,195] 0,776	-0,033 [-0,258; 0,192]
Region = Latin America				
N'	147	140		
Baseline Mean (SD)	1,82 (1,574)	1,76 (1,621)		
Week 8:				
Adjusted Mean Change (SE)	-0,55 (0,086)	-0,52 (0,088)	-0,02 [-0,261; 0,219] 0,862	-0,021 [-0,262; 0,220]
Week 16:				
Adjusted Mean Change (SE)	-0,85 (0,085)	-0,82 (0,087)	-0,03 [-0,264; 0,212] 0,832	-0,025 [-0,258; 0,208]
Week 24:				
Adjusted Mean Change (SE)	-0,99 (0,085)	-0,87 (0,087)	-0,13 [-0,364; 0,113] 0,303	-0,123 [-0,358; 0,112]
Region = Others				
N'	20	9		
Baseline Mean (SD)	1,54 (1,322)	2,02 (1,337)		
Week 8:				
Adjusted Mean Change (SE)	-0,89 (0,233)	-0,65 (0,362)	-0,24 [-1,082; 0,603] 0,577	-0,248 [-1,174; 0,679]
Week 16:				
Adjusted Mean Change (SE)	-1,04 (0,230)	-0,97 (0,342)	-0,07 [-0,877; 0,738] 0,866	-0,067 [-0,854; 0,719]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-1,09 (0,230)	-1,07 (0,342)	-0,02 [-0,826; 0,789] 0,965	-0,018 [-0,805; 0,769]
Mean day-time symptom score				
Interaction Test	N.E.			
Region = Asia				
N'	118	121		
Baseline Mean (SD)	1,08 (0,628)	1,01 (0,581)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,036)	-0,24 (0,036)	0,07 [-0,026; 0,175] 0,144	0,191 [-0,065; 0,447]
Week 16:				
Adjusted Mean Change (SE)	-0,33 (0,042)	-0,29 (0,041)	-0,03 [-0,148; 0,084] 0,590	-0,070 [-0,326; 0,185]
Week 24:				
Adjusted Mean Change (SE)	-0,33 (0,044)	-0,35 (0,043)	0,02 [-0,105; 0,138] 0,784	0,036 [-0,221; 0,293]
Region = Europe				
N'	157	164		
Baseline Mean (SD)	0,92 (0,523)	0,90 (0,483)		
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,026)	-0,19 (0,026)	0,01 [-0,065; 0,079] 0,841	0,022 [-0,196; 0,241]
Week 16:				
Adjusted Mean Change (SE)	-0,27 (0,031)	-0,27 (0,030)	0,00 [-0,084; 0,087] 0,969	0,004 [-0,215; 0,223]
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,034)	-0,30 (0,034)	0,01 [-0,081; 0,108] 0,778	0,032 [-0,190; 0,254]
Region = Latin America				
N'	160	157		
Baseline Mean (SD)	0,73 (0,596)	0,71 (0,596)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,029)	-0,15 (0,029)	-0,01 [-0,092; 0,068] 0,761	-0,035 [-0,262; 0,191]
Week 16:				
Adjusted Mean Change (SE)	-0,27 (0,032)	-0,24 (0,032)	-0,03 [-0,116; 0,062] 0,552	-0,067 [-0,289; 0,154]
Week 24:				
Adjusted Mean Change (SE)	-0,31 (0,033)	-0,26 (0,034)	-0,06 [-0,150; 0,037] 0,237	-0,135 [-0,358; 0,089]
Region = Others				
N'	20	9		
Baseline Mean (SD)	0,66 (0,450)	0,76 (0,471)		
Week 8:				
Adjusted Mean Change (SE)	-0,34 (0,088)	-0,24 (0,133)	-0,11 [-0,430; 0,213] 0,499	-0,280 [-1,103; 0,544]
Week 16:				
Adjusted Mean Change (SE)	-0,44 (0,097)	-0,28 (0,144)	-0,16 [-0,513; 0,189] 0,357	-0,375 [-1,167; 0,418]
Week 24:				
Adjusted Mean Change (SE)	-0,41 (0,094)	-0,26 (0,141)	-0,16 [-0,500; 0,187] 0,362	-0,371 [-1,163; 0,422]
Mean night-time symptom score				
Interaction Test	N.E.			
Region = Asia				
N'	117	126		
Baseline Mean (SD)	0,86 (0,528)	0,81 (0,546)		
Week 8:				
Adjusted Mean Change (SE)	-0,23 (0,031)	-0,23 (0,030)	-0,00 [-0,089; 0,083] 0,952	-0,008 [-0,263; 0,247]
Week 16:				
Adjusted Mean Change (SE)	-0,34 (0,035)	-0,28 (0,034)	-0,06 [-0,155; 0,037] 0,227	-0,157 [-0,411; 0,097]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,37 (0,036)	-0,35 (0,035)	-0,02 [-0,119; 0,080] 0,700	-0,050 [-0,305; 0,205]
Region = Europe				
N'	157	164		
Baseline Mean (SD)	0,74 (0,499)	0,60 (0,433)		
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,023)	-0,14 (0,022)	-0,03 [-0,097; 0,030] 0,305	-0,116 [-0,336; 0,104]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,026)	-0,22 (0,026)	-0,01 [-0,077; 0,067] 0,883	-0,016 [-0,236; 0,203]
Week 24:				
Adjusted Mean Change (SE)	-0,24 (0,028)	-0,23 (0,027)	-0,01 [-0,090; 0,064] 0,738	-0,038 [-0,260; 0,184]
Region = Latin America				
N'	158	152		
Baseline Mean (SD)	0,55 (0,540)	0,53 (0,524)		
Week 8:				
Adjusted Mean Change (SE)	-0,13 (0,025)	-0,13 (0,025)	-0,01 [-0,075; 0,064] 0,883	-0,017 [-0,244; 0,210]
Week 16:				
Adjusted Mean Change (SE)	-0,21 (0,027)	-0,21 (0,027)	-0,00 [-0,077; 0,073] 0,955	-0,007 [-0,231; 0,218]
Week 24:				
Adjusted Mean Change (SE)	-0,24 (0,028)	-0,22 (0,028)	-0,03 [-0,106; 0,049] 0,473	-0,083 [-0,309; 0,143]
Region = Others				
N'	20	9		
Baseline Mean (SD)	0,46 (0,487)	0,68 (0,452)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,20 (0,070)	-0,22 (0,107)	0,02 [-0,241; 0,277] 0,889	0,057 [-0,730; 0,844]
Week 16:				
Adjusted Mean Change (SE)	-0,22 (0,074)	-0,30 (0,113)	0,07 [-0,201; 0,346] 0,595	0,218 [-0,571; 1,006]
Week 24:				
Adjusted Mean Change (SE)	-0,23 (0,074)	-0,33 (0,112)	0,10 [-0,170; 0,374] 0,452	0,308 [-0,483; 1,098]
Mean of: How did you sleep last night?				
Interaction Test	0,997			
Region = Asia				
N'	117	126		
Baseline Mean (SD)	0,65 (0,562)	0,63 (0,584)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,028)	-0,18 (0,027)	0,01 [-0,067; 0,086] 0,808	0,031 [-0,223; 0,286]
Week 16:				
Adjusted Mean Change (SE)	-0,26 (0,031)	-0,22 (0,029)	-0,04 [-0,123; 0,043] 0,340	-0,123 [-0,377; 0,131]
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,031)	-0,29 (0,030)	0,00 [-0,080; 0,089] 0,913	0,014 [-0,241; 0,269]
Region = Europe				
N'	157	164		
Baseline Mean (SD)	0,54 (0,545)	0,44 (0,460)		
Week 8:				
Adjusted Mean Change (SE)	-0,20 (0,024)	-0,17 (0,024)	-0,03 [-0,097; 0,037] 0,377	-0,099 [-0,319; 0,121]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,026)	-0,24 (0,026)	0,01 [-0,064; 0,080] 0,835	0,023 [-0,196; 0,243]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,24 (0,027)	-0,25 (0,026)	0,01 [-0,066; 0,081] 0,839	0,023 [-0,199; 0,245]
Region = Latin America				
N'	158	152		
Baseline Mean (SD)	0,46 (0,562)	0,39 (0,521)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,024)	-0,16 (0,025)	-0,01 [-0,080; 0,056] 0,738	-0,039 [-0,266; 0,188]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,026)	-0,22 (0,027)	-0,01 [-0,082; 0,065] 0,814	-0,027 [-0,251; 0,197]
Week 24:				
Adjusted Mean Change (SE)	-0,25 (0,027)	-0,24 (0,027)	-0,02 [-0,090; 0,059] 0,682	-0,047 [-0,273; 0,179]
Region = Others				
N'	20	9		
Baseline Mean (SD)	0,31 (0,453)	0,71 (0,526)		
Week 8:				
Adjusted Mean Change (SE)	-0,20 (0,068)	-0,22 (0,101)	0,02 [-0,217; 0,261] 0,858	0,072 [-0,715; 0,858]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,074)	-0,22 (0,110)	-0,02 [-0,279; 0,239] 0,879	-0,061 [-0,848; 0,726]
Week 24:				
Adjusted Mean Change (SE)	-0,26 (0,075)	-0,31 (0,111)	0,04 [-0,222; 0,303] 0,763	0,121 [-0,667; 0,908]
Mean of: Did you have asthma symptoms upon awakening in the morning?				
Interaction Test	N.E.			
Region = Asia				
N'	117	126		
Baseline Mean (SD)	1,06 (0,607)	0,98 (0,637)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,22 (0,039)	-0,20 (0,037)	-0,02 [-0,126; 0,085] 0,706	-0,049 [-0,304; 0,206]
Week 16:				
Adjusted Mean Change (SE)	-0,34 (0,044)	-0,26 (0,042)	-0,09 [-0,206; 0,032] 0,152	-0,186 [-0,440; 0,069]
Week 24:				
Adjusted Mean Change (SE)	-0,36 (0,047)	-0,31 (0,045)	-0,05 [-0,181; 0,073] 0,405	-0,108 [-0,363; 0,147]
Region = Europe				
N'	157	164		
Baseline Mean (SD)	0,94 (0,587)	0,77 (0,534)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,031)	-0,13 (0,030)	-0,04 [-0,124; 0,047] 0,371	-0,101 [-0,321; 0,119]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,037)	-0,22 (0,036)	-0,02 [-0,125; 0,078] 0,654	-0,050 [-0,270; 0,169]
Week 24:				
Adjusted Mean Change (SE)	-0,27 (0,039)	-0,23 (0,038)	-0,04 [-0,149; 0,065] 0,442	-0,088 [-0,310; 0,135]
Region = Latin America				
N'	158	152		
Baseline Mean (SD)	0,64 (0,598)	0,68 (0,605)		
Week 8:				
Adjusted Mean Change (SE)	-0,13 (0,029)	-0,14 (0,030)	0,01 [-0,076; 0,087] 0,895	0,015 [-0,212; 0,242]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,032)	-0,24 (0,033)	0,01 [-0,082; 0,099] 0,859	0,020 [-0,204; 0,244]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,035)	-0,24 (0,035)	-0,04 [-0,132; 0,062] 0,480	-0,082 [-0,308; 0,145]
Region = Others				
N'	20	9		
Baseline Mean (SD)	0,61 (0,570)	0,66 (0,472)		
Week 8:				
Adjusted Mean Change (SE)	-0,26 (0,095)	-0,24 (0,142)	-0,02 [-0,364; 0,325] 0,909	-0,046 [-0,833; 0,741]
Week 16:				
Adjusted Mean Change (SE)	-0,27 (0,103)	-0,39 (0,153)	0,11 [-0,257; 0,486] 0,537	0,250 [-0,540; 1,039]
Week 24:				
Adjusted Mean Change (SE)	-0,26 (0,106)	-0,37 (0,159)	0,11 [-0,275; 0,496] 0,566	0,232 [-0,557; 1,021]
Mean of: Did your respiratory symptoms stop you from performing your usual daily activities?				
Interaction Test	0,996			
Region = Asia				
N'	118	121		
Baseline Mean (SD)	1,14 (0,667)	1,06 (0,673)		
Week 8:				
Adjusted Mean Change (SE)	-0,13 (0,038)	-0,19 (0,037)	0,06 [-0,048; 0,159] 0,289	0,138 [-0,119; 0,394]
Week 16:				
Adjusted Mean Change (SE)	-0,28 (0,044)	-0,24 (0,043)	-0,05 [-0,166; 0,073] 0,446	-0,099 [-0,354; 0,157]
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,046)	-0,28 (0,046)	0,00 [-0,124; 0,130] 0,961	0,006 [-0,250; 0,263]
Region = Europe				
N'	157	164		
Baseline Mean (SD)	0,98 (0,626)	0,97 (0,597)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,032)	-0,17 (0,032)	-0,00 [-0,094; 0,085] 0,921	-0,011 [-0,230; 0,208]
Week 16:				
Adjusted Mean Change (SE)	-0,25 (0,038)	-0,26 (0,037)	0,01 [-0,092; 0,115] 0,826	0,025 [-0,194; 0,243]
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,040)	-0,30 (0,039)	0,02 [-0,093; 0,126] 0,768	0,033 [-0,189; 0,255]
Region = Latin America				
N'	160	157		
Baseline Mean (SD)	0,67 (0,685)	0,65 (0,683)		
Week 8:				
Adjusted Mean Change (SE)	-0,19 (0,033)	-0,22 (0,033)	0,03 [-0,057; 0,124] 0,473	0,082 [-0,144; 0,309]
Week 16:				
Adjusted Mean Change (SE)	-0,32 (0,038)	-0,32 (0,038)	0,00 [-0,100; 0,108] 0,939	0,009 [-0,213; 0,230]
Week 24:				
Adjusted Mean Change (SE)	-0,35 (0,040)	-0,34 (0,040)	-0,01 [-0,123; 0,097] 0,814	-0,027 [-0,250; 0,196]
Region = Others				
N'	20	9		
Baseline Mean (SD)	0,55 (0,526)	0,66 (0,536)		
Week 8:				
Adjusted Mean Change (SE)	-0,32 (0,091)	-0,39 (0,138)	0,07 [-0,254; 0,394] 0,673	0,173 [-0,648; 0,994]
Week 16:				
Adjusted Mean Change (SE)	-0,40 (0,106)	-0,43 (0,157)	0,02 [-0,346; 0,396] 0,896	0,052 [-0,734; 0,839]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,36 (0,112)	-0,41 (0,166)	0,06 [-0,337; 0,447] 0,783	0,110 [-0,677; 0,898]
Mean of: How severe was your shortness of breath today?				
Interaction Test	0,657			
Region = Asia				
N'	118	121		
Baseline Mean (SD)	1,25 (0,654)	1,19 (0,660)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,039)	-0,23 (0,038)	0,07 [-0,036; 0,175] 0,199	0,167 [-0,090; 0,423]
Week 16:				
Adjusted Mean Change (SE)	-0,33 (0,045)	-0,29 (0,044)	-0,04 [-0,160; 0,084] 0,543	-0,079 [-0,334; 0,176]
Week 24:				
Adjusted Mean Change (SE)	-0,32 (0,047)	-0,33 (0,046)	0,01 [-0,124; 0,135] 0,930	0,011 [-0,245; 0,268]
Region = Europe				
N'	157	164		
Baseline Mean (SD)	1,09 (0,591)	1,06 (0,563)		
Week 8:				
Adjusted Mean Change (SE)	-0,24 (0,033)	-0,23 (0,032)	-0,01 [-0,103; 0,079] 0,797	-0,029 [-0,248; 0,190]
Week 16:				
Adjusted Mean Change (SE)	-0,35 (0,038)	-0,33 (0,037)	-0,03 [-0,130; 0,079] 0,633	-0,053 [-0,272; 0,166]
Week 24:				
Adjusted Mean Change (SE)	-0,39 (0,041)	-0,34 (0,040)	-0,05 [-0,158; 0,065] 0,417	-0,092 [-0,314; 0,130]
Region = Latin America				
N'	160	157		
Baseline Mean (SD)	0,84 (0,666)	0,83 (0,666)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,26 (0,033)	-0,24 (0,034)	-0,02 [-0,111; 0,074] 0,697	-0,045 [-0,271; 0,182]
Week 16:				
Adjusted Mean Change (SE)	-0,40 (0,038)	-0,36 (0,038)	-0,04 [-0,143; 0,068] 0,489	-0,078 [-0,299; 0,144]
Week 24:				
Adjusted Mean Change (SE)	-0,46 (0,041)	-0,39 (0,041)	-0,07 [-0,180; 0,044] 0,235	-0,134 [-0,358; 0,089]
Region = Others				
N'	20	9		
Baseline Mean (SD)	0,77 (0,518)	0,79 (0,536)		
Week 8:				
Adjusted Mean Change (SE)	-0,45 (0,093)	-0,28 (0,141)	-0,17 [-0,502; 0,159] 0,309	-0,417 [-1,244; 0,410]
Week 16:				
Adjusted Mean Change (SE)	-0,55 (0,107)	-0,33 (0,160)	-0,22 [-0,598; 0,156] 0,250	-0,461 [-1,257; 0,335]
Week 24:				
Adjusted Mean Change (SE)	-0,52 (0,114)	-0,29 (0,169)	-0,23 [-0,627; 0,172] 0,264	-0,448 [-1,243; 0,347]
Mean of: How was your wheeze during the past 12 hours?				
Interaction Test	N.E.			
Region = Asia				
N'	118	121		
Baseline Mean (SD)	1,05 (0,731)	0,94 (0,659)		
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,042)	-0,29 (0,041)	0,11 [-0,004; 0,228] 0,059	0,247 [-0,010; 0,504]
Week 16:				
Adjusted Mean Change (SE)	-0,34 (0,047)	-0,33 (0,047)	-0,01 [-0,136; 0,126] 0,939	-0,010 [-0,265; 0,245]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,35 (0,050)	-0,39 (0,049)	0,04 [-0,096; 0,181] 0,545	0,079 [-0,178; 0,336]
Region = Europe				
N'	157	164		
Baseline Mean (SD)	0,91 (0,605)	0,83 (0,560)		
Week 8:				
Adjusted Mean Change (SE)	-0,21 (0,030)	-0,25 (0,029)	0,03 [-0,051; 0,115] 0,454	0,084 [-0,135; 0,303]
Week 16:				
Adjusted Mean Change (SE)	-0,30 (0,036)	-0,32 (0,035)	0,02 [-0,077; 0,119] 0,671	0,047 [-0,171; 0,266]
Week 24:				
Adjusted Mean Change (SE)	-0,32 (0,039)	-0,33 (0,038)	0,01 [-0,098; 0,116] 0,869	0,019 [-0,203; 0,241]
Region = Latin America				
N'	160	157		
Baseline Mean (SD)	0,80 (0,674)	0,78 (0,676)		
Week 8:				
Adjusted Mean Change (SE)	-0,22 (0,033)	-0,20 (0,034)	-0,01 [-0,105; 0,082] 0,807	-0,028 [-0,255; 0,198]
Week 16:				
Adjusted Mean Change (SE)	-0,32 (0,037)	-0,28 (0,038)	-0,04 [-0,144; 0,064] 0,449	-0,086 [-0,307; 0,136]
Week 24:				
Adjusted Mean Change (SE)	-0,35 (0,039)	-0,31 (0,039)	-0,04 [-0,146; 0,070] 0,492	-0,078 [-0,301; 0,145]
Region = Others				
N'	20	9		
Baseline Mean (SD)	0,69 (0,567)	0,97 (0,661)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,42 (0,093)	-0,22 (0,141)	-0,19 [-0,536; 0,149] 0,261	-0,472 [-1,302; 0,357]
Week 16:				
Adjusted Mean Change (SE)	-0,56 (0,102)	-0,27 (0,154)	-0,29 [-0,665; 0,086] 0,127	-0,631 [-1,435; 0,172]
Week 24:				
Adjusted Mean Change (SE)	-0,56 (0,099)	-0,24 (0,148)	-0,32 [-0,683; 0,042] 0,081	-0,724 [-1,533; 0,084]
Mean of: How was your cough during the past 12 hours?				
Interaction Test	N.E.			
Region = Asia				
N'	118	121		
Baseline Mean (SD)	1,10 (0,693)	0,99 (0,656)		
Week 8:				
Adjusted Mean Change (SE)	-0,14 (0,043)	-0,22 (0,042)	0,08 [-0,039; 0,199] 0,188	0,172 [-0,084; 0,429]
Week 16:				
Adjusted Mean Change (SE)	-0,29 (0,050)	-0,29 (0,049)	-0,00 [-0,138; 0,136] 0,988	-0,002 [-0,257; 0,253]
Week 24:				
Adjusted Mean Change (SE)	-0,31 (0,053)	-0,35 (0,052)	0,05 [-0,097; 0,194] 0,510	0,086 [-0,171; 0,343]
Region = Europe				
N'	157	164		
Baseline Mean (SD)	0,96 (0,628)	0,98 (0,592)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,032)	-0,16 (0,032)	0,00 [-0,088; 0,091] 0,973	0,004 [-0,215; 0,223]
Week 16:				
Adjusted Mean Change (SE)	-0,25 (0,039)	-0,24 (0,038)	-0,02 [-0,126; 0,088] 0,728	-0,039 [-0,258; 0,180]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,24 (0,043)	-0,29 (0,042)	0,05 [-0,064; 0,171] 0,373	0,101 [-0,121; 0,323]
Region = Latin America				
N'	160	157		
Baseline Mean (SD)	0,80 (0,702)	0,75 (0,699)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,036)	-0,10 (0,037)	-0,06 [-0,158; 0,043] 0,264	-0,129 [-0,356; 0,097]
Week 16:				
Adjusted Mean Change (SE)	-0,28 (0,040)	-0,25 (0,041)	-0,03 [-0,142; 0,084] 0,611	-0,057 [-0,279; 0,164]
Week 24:				
Adjusted Mean Change (SE)	-0,34 (0,042)	-0,23 (0,042)	-0,11 [-0,223; 0,011] 0,076	-0,202 [-0,426; 0,021]
Region = Others				
N'	20	9		
Baseline Mean (SD)	0,68 (0,570)	0,85 (0,633)		
Week 8:				
Adjusted Mean Change (SE)	-0,36 (0,092)	-0,14 (0,142)	-0,22 [-0,555; 0,125] 0,209	-0,524 [-1,356; 0,307]
Week 16:				
Adjusted Mean Change (SE)	-0,47 (0,102)	-0,15 (0,153)	-0,32 [-0,687; 0,053] 0,091	-0,695 [-1,501; 0,112]
Week 24:				
Adjusted Mean Change (SE)	-0,45 (0,098)	-0,16 (0,148)	-0,29 [-0,647; 0,065] 0,107	-0,663 [-1,468; 0,142]
Did you have chest tightness during the past 12 hours?				
Interaction Test	0,765			
Region = Asia				
N'	118	121		
Baseline Mean (SD)	0,88 (0,732)	0,87 (0,720)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,03 (0,036)	-0,11 (0,036)	0,08 [-0,023; 0,176] 0,132	0,196 [-0,061; 0,452]
Week 16:				
Adjusted Mean Change (SE)	-0,14 (0,041)	-0,10 (0,041)	-0,04 [-0,149; 0,076] 0,521	-0,083 [-0,338; 0,172]
Week 24:				
Adjusted Mean Change (SE)	-0,13 (0,043)	-0,15 (0,043)	0,02 [-0,103; 0,135] 0,790	0,035 [-0,222; 0,292]
Region = Europe				
N'	157	164		
Baseline Mean (SD)	0,65 (0,576)	0,64 (0,580)		
Week 8:				
Adjusted Mean Change (SE)	-0,11 (0,031)	-0,13 (0,031)	0,02 [-0,062; 0,109] 0,590	0,060 [-0,159; 0,279]
Week 16:				
Adjusted Mean Change (SE)	-0,17 (0,035)	-0,20 (0,035)	0,02 [-0,072; 0,122] 0,615	0,056 [-0,163; 0,275]
Week 24:				
Adjusted Mean Change (SE)	-0,19 (0,037)	-0,23 (0,037)	0,04 [-0,064; 0,141] 0,460	0,084 [-0,138; 0,306]
Region = Latin America				
N'	160	157		
Baseline Mean (SD)	0,55 (0,611)	0,51 (0,596)		
Week 8:				
Adjusted Mean Change (SE)	-0,13 (0,031)	-0,13 (0,032)	-0,01 [-0,094; 0,080] 0,880	-0,017 [-0,244; 0,209]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,035)	-0,19 (0,036)	-0,03 [-0,131; 0,065] 0,506	-0,075 [-0,296; 0,146]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,27 (0,037)	-0,21 (0,037)	-0,06 [-0,162; 0,044] 0,260	-0,128 [-0,351; 0,096]
Region = Others				
N'	20	9		
Baseline Mean (SD)	0,63 (0,502)	0,55 (0,440)		
Week 8:				
Adjusted Mean Change (SE)	-0,31 (0,088)	-0,27 (0,133)	-0,05 [-0,361; 0,264] 0,761	-0,125 [-0,945; 0,696]
Week 16:				
Adjusted Mean Change (SE)	-0,40 (0,099)	-0,35 (0,148)	-0,05 [-0,402; 0,296] 0,765	-0,120 [-0,907; 0,667]
Week 24:				
Adjusted Mean Change (SE)	-0,37 (0,104)	-0,31 (0,155)	-0,06 [-0,428; 0,306] 0,744	-0,131 [-0,918; 0,657]

N': Number of patients in the analysis
CI: Confidence Interval
N.E.: not estimable
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + region + region * treatment + region * treatment * visit, within-patient correlation: unstructured covariance matrix
Exceptional model(s): **Percentage of mornings with no symptoms on rising**: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region], **Percentage of days with no day-time symptoms**: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region], **Percentage of days with no night-time awakenings**: treatment + visit + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + region + region * treatment + region * treatment * visit, within-patient correlation: compound symmetry covariance matrix, **Percentage of days with no asthma symptoms**: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region], **Mean total daily symptom score**: treatment + visit + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + region + region * treatment + region * treatment * visit, within-patient correlation: compound symmetry covariance matrix, **Mean day-time symptom score**: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region], **Mean night-time symptom score**: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region], **Mean of: Did you have asthma symptoms upon awakening in the morning?**: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region], **Mean of: How was your wheeze during the past 12 hours?**: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region], **Mean of: How was your cough during the past 12 hours?**: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region]
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 9.6 Symptoms - Change from Baseline by History of Asthma Exacerbation (FAS)

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Percentage of mornings with no symptoms on rising				
Interaction Test	0,484			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	357	366		
Baseline Mean (SD)	35,64 (38,577)	40,32 (38,729)		
Week 8:				
Adjusted Mean Change (SE)	10,72 (2,183)	7,85 (2,174)	2,87 [-1,792; 7,534] 0,227	0,070 [-0,077; 0,218]
Week 16:				
Adjusted Mean Change (SE)	17,50 (2,180)	14,01 (2,177)	3,49 [-1,165; 8,145] 0,142	0,085 [-0,062; 0,231]
Week 24:				
Adjusted Mean Change (SE)	19,11 (2,181)	16,86 (2,182)	2,25 [-2,419; 6,916] 0,345	0,055 [-0,093; 0,203]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	95	85		
Baseline Mean (SD)	37,95 (37,466)	34,18 (36,655)		
Week 8:				
Adjusted Mean Change (SE)	7,87 (3,645)	5,12 (3,788)	2,75 [-6,621; 12,121] 0,565	0,079 [-0,218; 0,376]
Week 16:				
Adjusted Mean Change (SE)	15,51 (3,647)	8,90 (3,777)	6,60 [-2,754; 15,959] 0,167	0,189 [-0,107; 0,485]
Week 24:				
Adjusted Mean Change (SE)	19,62 (3,651)	9,96 (3,782)	9,66 [0,288; 19,033] 0,043 *	0,278 [-0,020; 0,576]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Percentage of days with no day-time symptoms				
Interaction Test	0,348			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	359	365		
Baseline Mean (SD)	17,82 (30,783)	17,16 (30,447)		
Week 8:				
Adjusted Mean Change (SE)	9,47 (1,720)	8,21 (1,734)	1,25 [-2,336; 4,839] 0,494	0,039 [-0,109; 0,186]
Week 16:				
Adjusted Mean Change (SE)	18,70 (2,040)	14,52 (2,046)	4,18 [-0,514; 8,877] 0,081	0,108 [-0,038; 0,254]
Week 24:				
Adjusted Mean Change (SE)	20,32 (2,149)	18,22 (2,155)	2,11 [-2,946; 7,162] 0,413	0,052 [-0,095; 0,200]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	96	86		
Baseline Mean (SD)	17,27 (28,146)	16,14 (31,159)		
Week 8:				
Adjusted Mean Change (SE)	9,79 (2,828)	6,13 (2,937)	3,66 [-3,512; 10,839] 0,317	0,135 [-0,160; 0,430]
Week 16:				
Adjusted Mean Change (SE)	19,63 (3,543)	11,91 (3,699)	7,72 [-1,686; 17,120] 0,108	0,225 [-0,069; 0,520]
Week 24:				
Adjusted Mean Change (SE)	21,80 (3,775)	12,34 (3,949)	9,46 [-0,652; 19,576] 0,067	0,261 [-0,036; 0,557]
Percentage of days with no night-time awakenings				
Interaction Test	0,186			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	357	366		
Baseline Mean (SD)	59,24 (38,915)	64,72 (37,376)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	10,58 (1,733)	10,18 (1,726)	0,40 [-3,218; 4,012] 0,829	0,012 [-0,135; 0,160]
Week 16:				
Adjusted Mean Change (SE)	15,23 (1,863)	14,69 (1,857)	0,55 [-3,533; 4,628] 0,792	0,016 [-0,131; 0,162]
Week 24:				
Adjusted Mean Change (SE)	16,42 (1,920)	16,79 (1,917)	-0,37 [-4,657; 3,911] 0,864	-0,010 [-0,158; 0,137]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	95	85		
Baseline Mean (SD)	57,04 (38,300)	51,82 (39,756)		
Week 8:				
Adjusted Mean Change (SE)	10,44 (2,864)	5,38 (2,973)	5,05 [-2,212; 12,318] 0,173	0,185 [-0,112; 0,483]
Week 16:				
Adjusted Mean Change (SE)	16,27 (3,162)	9,04 (3,284)	7,22 [-0,972; 15,418] 0,084	0,238 [-0,058; 0,534]
Week 24:				
Adjusted Mean Change (SE)	17,49 (3,293)	12,21 (3,422)	5,28 [-3,323; 13,879] 0,229	0,168 [-0,129; 0,465]
Percentage of days with no asthma symptoms				
Interaction Test	0,365			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	342	343		
Baseline Mean (SD)	15,59 (30,241)	15,90 (30,101)		
Week 8:				
Adjusted Mean Change (SE)	9,43 (1,761)	7,39 (1,781)	2,04 [-1,622; 5,694] 0,275	0,063 [-0,090; 0,217]
Week 16:				
Adjusted Mean Change (SE)	18,61 (2,086)	14,41 (2,105)	4,20 [-0,595; 9,001] 0,086	0,109 [-0,042; 0,259]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	20,69 (2,203)	17,28 (2,225)	3,41 [-1,782; 8,600] 0,198	0,084 [-0,067; 0,236]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	92	80		
Baseline Mean (SD)	13,81 (25,214)	14,04 (29,577)		
Week 8:				
Adjusted Mean Change (SE)	9,63 (2,889)	5,62 (3,024)	4,01 [-3,358; 11,373] 0,286	0,152 [-0,160; 0,463]
Week 16:				
Adjusted Mean Change (SE)	19,83 (3,603)	11,93 (3,799)	7,90 [-1,705; 17,511] 0,107	0,232 [-0,071; 0,534]
Week 24:				
Adjusted Mean Change (SE)	22,41 (3,866)	11,53 (4,085)	10,89 [0,470; 21,307] 0,041 *	0,303 [-0,006; 0,611]
Mean total daily symptom score				
Interaction Test	0,340			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	342	343		
Baseline Mean (SD)	2,26 (1,558)	2,04 (1,484)		
Week 8:				
Adjusted Mean Change (SE)	-0,49 (0,067)	-0,48 (0,068)	-0,01 [-0,148; 0,131] 0,907	-0,007 [-0,160; 0,146]
Week 16:				
Adjusted Mean Change (SE)	-0,73 (0,072)	-0,69 (0,073)	-0,04 [-0,195; 0,120] 0,643	-0,028 [-0,178; 0,123]
Week 24:				
Adjusted Mean Change (SE)	-0,80 (0,074)	-0,77 (0,075)	-0,03 [-0,197; 0,131] 0,689	-0,025 [-0,176; 0,127]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	92	80		
Baseline Mean (SD)	2,26 (1,671)	2,39 (1,570)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,45 (0,110)	-0,35 (0,115)	-0,09 [-0,373; 0,187] 0,514	-0,093 [-0,404; 0,218]
Week 16:				
Adjusted Mean Change (SE)	-0,74 (0,121)	-0,53 (0,127)	-0,21 [-0,528; 0,101] 0,184	-0,187 [-0,489; 0,115]
Week 24:				
Adjusted Mean Change (SE)	-0,83 (0,125)	-0,59 (0,132)	-0,25 [-0,575; 0,083] 0,143	-0,211 [-0,519; 0,096]
Mean day-time symptom score				
Interaction Test	0,423			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	359	365		
Baseline Mean (SD)	0,89 (0,591)	0,84 (0,557)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,025)	-0,18 (0,025)	0,01 [-0,038; 0,067] 0,587	0,031 [-0,117; 0,178]
Week 16:				
Adjusted Mean Change (SE)	-0,27 (0,027)	-0,26 (0,028)	-0,01 [-0,074; 0,047] 0,659	-0,026 [-0,172; 0,120]
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,029)	-0,29 (0,029)	-0,00 [-0,068; 0,060] 0,899	-0,008 [-0,155; 0,140]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	96	86		
Baseline Mean (SD)	0,86 (0,597)	0,92 (0,588)		
Week 8:				
Adjusted Mean Change (SE)	-0,14 (0,041)	-0,13 (0,043)	-0,01 [-0,113; 0,097] 0,887	-0,019 [-0,314; 0,275]
Week 16:				
Adjusted Mean Change (SE)	-0,28 (0,046)	-0,20 (0,048)	-0,07 [-0,195; 0,046] 0,228	-0,166 [-0,460; 0,128]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,30 (0,049)	-0,23 (0,051)	-0,07 [-0,202; 0,055] 0,263	-0,156 [-0,452; 0,139]
Mean night-time symptom score				
Interaction Test	0,227			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	357	366		
Baseline Mean (SD)	0,68 (0,524)	0,61 (0,500)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,022)	-0,16 (0,022)	-0,01 [-0,056; 0,035] 0,647	-0,026 [-0,173; 0,121]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,023)	-0,23 (0,023)	-0,01 [-0,056; 0,045] 0,837	-0,012 [-0,159; 0,134]
Week 24:				
Adjusted Mean Change (SE)	-0,26 (0,024)	-0,26 (0,024)	-0,00 [-0,054; 0,050] 0,939	-0,005 [-0,152; 0,143]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	95	85		
Baseline Mean (SD)	0,72 (0,579)	0,75 (0,531)		
Week 8:				
Adjusted Mean Change (SE)	-0,15 (0,036)	-0,10 (0,037)	-0,05 [-0,137; 0,046] 0,327	-0,133 [-0,430; 0,164]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,039)	-0,16 (0,040)	-0,08 [-0,177; 0,025] 0,141	-0,202 [-0,498; 0,093]
Week 24:				
Adjusted Mean Change (SE)	-0,27 (0,040)	-0,19 (0,042)	-0,09 [-0,193; 0,017] 0,099	-0,230 [-0,528; 0,068]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Mean of: How did you sleep last night?				
Interaction Test	0,145			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	357	366		
Baseline Mean (SD)	0,52 (0,548)	0,45 (0,518)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,021)	-0,17 (0,021)	-0,00 [-0,047; 0,041] 0,899	-0,007 [-0,155; 0,140]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,022)	-0,23 (0,022)	0,01 [-0,042; 0,054] 0,805	0,014 [-0,132; 0,161]
Week 24:				
Adjusted Mean Change (SE)	-0,24 (0,022)	-0,26 (0,022)	0,01 [-0,034; 0,063] 0,565	0,034 [-0,114; 0,182]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	95	85		
Baseline Mean (SD)	0,58 (0,590)	0,61 (0,554)		
Week 8:				
Adjusted Mean Change (SE)	-0,15 (0,035)	-0,10 (0,036)	-0,05 [-0,144; 0,034] 0,227	-0,164 [-0,462; 0,133]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,037)	-0,15 (0,039)	-0,09 [-0,182; 0,010] 0,078	-0,242 [-0,538; 0,054]
Week 24:				
Adjusted Mean Change (SE)	-0,25 (0,038)	-0,19 (0,039)	-0,06 [-0,159; 0,036] 0,219	-0,170 [-0,467; 0,127]
Mean of: Did you have asthma symptoms upon awakening in the morning?				
Interaction Test	0,424			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	357	366		
Baseline Mean (SD)	0,85 (0,608)	0,77 (0,592)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,027)	-0,14 (0,027)	-0,02 [-0,074; 0,040] 0,548	-0,034 [-0,181; 0,114]
Week 16:				
Adjusted Mean Change (SE)	-0,25 (0,030)	-0,23 (0,030)	-0,02 [-0,082; 0,048] 0,616	-0,030 [-0,176; 0,117]
Week 24:				
Adjusted Mean Change (SE)	-0,27 (0,031)	-0,25 (0,031)	-0,02 [-0,088; 0,050] 0,587	-0,033 [-0,181; 0,115]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	95	85		
Baseline Mean (SD)	0,86 (0,671)	0,89 (0,618)		
Week 8:				
Adjusted Mean Change (SE)	-0,14 (0,045)	-0,10 (0,047)	-0,04 [-0,150; 0,079] 0,538	-0,084 [-0,381; 0,213]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,050)	-0,17 (0,052)	-0,07 [-0,196; 0,065] 0,326	-0,136 [-0,431; 0,159]
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,053)	-0,18 (0,055)	-0,12 [-0,255; 0,023] 0,103	-0,229 [-0,527; 0,069]
Mean of: Did your respiratory symptoms stop you from performing your usual daily activities?				
Interaction Test	0,455			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	359	365		
Baseline Mean (SD)	0,91 (0,670)	0,86 (0,661)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,029)	-0,20 (0,029)	0,03 [-0,031; 0,088] 0,345	0,053 [-0,094; 0,201]
Week 16:				
Adjusted Mean Change (SE)	-0,28 (0,031)	-0,28 (0,031)	0,01 [-0,063; 0,074] 0,872	0,010 [-0,136; 0,156]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,032)	-0,30 (0,032)	0,01 [-0,063; 0,082] 0,791	0,016 [-0,131; 0,164]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	96	86		
Baseline Mean (SD)	0,85 (0,733)	0,94 (0,706)		
Week 8:				
Adjusted Mean Change (SE)	-0,13 (0,047)	-0,12 (0,049)	-0,01 [-0,129; 0,108] 0,862	-0,023 [-0,318; 0,271]
Week 16:				
Adjusted Mean Change (SE)	-0,27 (0,053)	-0,20 (0,055)	-0,07 [-0,212; 0,063] 0,290	-0,146 [-0,440; 0,148]
Week 24:				
Adjusted Mean Change (SE)	-0,30 (0,055)	-0,26 (0,058)	-0,03 [-0,178; 0,113] 0,664	-0,061 [-0,356; 0,235]
Mean of: How severe was your shortness of breath today?				
Interaction Test	0,558			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	359	365		
Baseline Mean (SD)	1,03 (0,654)	0,99 (0,635)		
Week 8:				
Adjusted Mean Change (SE)	-0,23 (0,029)	-0,23 (0,029)	-0,00 [-0,062; 0,059] 0,962	-0,003 [-0,150; 0,145]
Week 16:				
Adjusted Mean Change (SE)	-0,35 (0,032)	-0,33 (0,032)	-0,03 [-0,098; 0,041] 0,426	-0,047 [-0,193; 0,099]
Week 24:				
Adjusted Mean Change (SE)	-0,38 (0,033)	-0,35 (0,033)	-0,04 [-0,111; 0,037] 0,323	-0,060 [-0,208; 0,087]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	96	86		
Baseline Mean (SD)	1,02 (0,654)	1,07 (0,665)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,048)	-0,17 (0,050)	-0,00 [-0,126; 0,116] 0,938	-0,010 [-0,305; 0,284]
Week 16:				
Adjusted Mean Change (SE)	-0,33 (0,054)	-0,23 (0,056)	-0,10 [-0,240; 0,039] 0,159	-0,194 [-0,488; 0,100]
Week 24:				
Adjusted Mean Change (SE)	-0,37 (0,056)	-0,28 (0,059)	-0,09 [-0,238; 0,058] 0,235	-0,166 [-0,462; 0,130]
Mean of: How was your wheeze during the past 12 hours?				
Interaction Test	0,855			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	359	365		
Baseline Mean (SD)	0,89 (0,666)	0,82 (0,624)		
Week 8:				
Adjusted Mean Change (SE)	-0,19 (0,029)	-0,21 (0,029)	0,02 [-0,039; 0,083] 0,478	0,040 [-0,107; 0,188]
Week 16:				
Adjusted Mean Change (SE)	-0,29 (0,031)	-0,28 (0,032)	-0,01 [-0,080; 0,058] 0,758	-0,018 [-0,164; 0,128]
Week 24:				
Adjusted Mean Change (SE)	-0,31 (0,033)	-0,31 (0,033)	-0,00 [-0,076; 0,070] 0,934	-0,005 [-0,153; 0,143]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	96	86		
Baseline Mean (SD)	0,92 (0,684)	0,96 (0,656)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,048)	-0,22 (0,050)	0,05 [-0,070; 0,172] 0,411	0,111 [-0,184; 0,405]
Week 16:				
Adjusted Mean Change (SE)	-0,32 (0,053)	-0,27 (0,055)	-0,05 [-0,187; 0,089] 0,487	-0,095 [-0,389; 0,198]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,33 (0,056)	-0,30 (0,058)	-0,03 [-0,180; 0,113] 0,656	-0,062 [-0,357; 0,233]
Mean of: How was your cough during the past 12 hours?				
Interaction Test	0,259			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	359	365		
Baseline Mean (SD)	0,94 (0,690)	0,89 (0,651)		
Week 8:				
Adjusted Mean Change (SE)	-0,14 (0,031)	-0,14 (0,031)	0,00 [-0,064; 0,064] 0,999	0,000 [-0,147; 0,148]
Week 16:				
Adjusted Mean Change (SE)	-0,26 (0,034)	-0,24 (0,034)	-0,02 [-0,095; 0,054] 0,584	-0,032 [-0,178; 0,114]
Week 24:				
Adjusted Mean Change (SE)	-0,27 (0,035)	-0,29 (0,035)	0,01 [-0,068; 0,090] 0,781	0,017 [-0,131; 0,165]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	96	86		
Baseline Mean (SD)	0,86 (0,638)	0,96 (0,678)		
Week 8:				
Adjusted Mean Change (SE)	-0,14 (0,051)	-0,10 (0,053)	-0,05 [-0,177; 0,080] 0,460	-0,100 [-0,394; 0,195]
Week 16:				
Adjusted Mean Change (SE)	-0,27 (0,057)	-0,20 (0,059)	-0,08 [-0,225; 0,073] 0,318	-0,138 [-0,432; 0,156]
Week 24:				
Adjusted Mean Change (SE)	-0,32 (0,060)	-0,18 (0,062)	-0,14 [-0,301; 0,014] 0,075	-0,249 [-0,546; 0,047]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Did you have chest tightness during the past 12 hours?				
Interaction Test	0,255			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	359	365		
Baseline Mean (SD)	0,68 (0,640)	0,65 (0,638)		
Week 8:				
Adjusted Mean Change (SE)	-0,09 (0,027)	-0,12 (0,028)	0,03 [-0,026; 0,089] 0,280	0,061 [-0,087; 0,209]
Week 16:				
Adjusted Mean Change (SE)	-0,17 (0,030)	-0,16 (0,030)	-0,00 [-0,069; 0,060] 0,896	-0,008 [-0,154; 0,138]
Week 24:				
Adjusted Mean Change (SE)	-0,18 (0,031)	-0,19 (0,031)	0,01 [-0,059; 0,077] 0,793	0,016 [-0,132; 0,163]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	96	86		
Baseline Mean (SD)	0,65 (0,644)	0,68 (0,642)		
Week 8:				
Adjusted Mean Change (SE)	-0,06 (0,045)	-0,03 (0,047)	-0,03 [-0,146; 0,083] 0,595	-0,072 [-0,366; 0,223]
Week 16:				
Adjusted Mean Change (SE)	-0,17 (0,050)	-0,09 (0,052)	-0,08 [-0,212; 0,047] 0,211	-0,172 [-0,466; 0,122]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,19 (0,052)	-0,11 (0,054)	-0,08 [-0,218; 0,054] 0,239	-0,164 [-0,459; 0,132]

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + history of asthma exacerbation + history of asthma exacerbation * treatment + history of asthma exacerbation * treatment * visit, within-patient correlation: unstructured covariance matrix
Exceptional model(s): **Percentage of mornings with no symptoms on rising**: treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + history of asthma exacerbation + history of asthma exacerbation * treatment + history of asthma exacerbation * treatment * visit, within-patient correlation: compound symmetry covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 9.7 Symptoms - Change from Baseline by Patients' Prior Therapies (FAS)

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Percentage of mornings with no symptoms on rising				
Interaction Test	0,736			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	221	232		
Baseline Mean (SD)	36,58 (38,192)	36,07 (37,607)		
Week 8:				
Adjusted Mean Change (SE)	11,00 (2,254)	8,25 (2,220)	2,75 [-2,331; 7,834] 0,288	0,083 [-0,104; 0,269]
Week 16:				
Adjusted Mean Change (SE)	17,57 (2,565)	14,08 (2,521)	3,49 [-2,598; 9,577] 0,261	0,091 [-0,093; 0,276]
Week 24:				
Adjusted Mean Change (SE)	19,13 (2,666)	16,75 (2,624)	2,38 [-4,034; 8,791] 0,467	0,060 [-0,126; 0,247]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	231	219		
Baseline Mean (SD)	35,69 (38,513)	42,44 (39,005)		
Week 8:				
Adjusted Mean Change (SE)	8,77 (2,238)	5,93 (2,263)	2,84 [-2,266; 7,945] 0,275	0,085 [-0,102; 0,272]
Week 16:				
Adjusted Mean Change (SE)	16,11 (2,540)	11,41 (2,583)	4,71 [-1,422; 10,836] 0,132	0,123 [-0,063; 0,310]
Week 24:				
Adjusted Mean Change (SE)	18,75 (2,640)	13,68 (2,692)	5,07 [-1,391; 11,532] 0,124	0,129 [-0,059; 0,317]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Percentage of days with no day-time symptoms				
Interaction Test	0,946			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	222	233		
Baseline Mean (SD)	18,84 (31,383)	15,72 (29,422)		
Week 8:				
Adjusted Mean Change (SE)	9,59 (2,007)	8,55 (1,995)	1,04 [-3,491; 5,572] 0,652	0,035 [-0,151; 0,221]
Week 16:				
Adjusted Mean Change (SE)	19,79 (2,446)	14,44 (2,415)	5,35 [-0,580; 11,282] 0,077	0,146 [-0,038; 0,330]
Week 24:				
Adjusted Mean Change (SE)	21,32 (2,591)	17,19 (2,559)	4,13 [-2,253; 10,514] 0,205	0,107 [-0,078; 0,293]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	233	218		
Baseline Mean (SD)	16,63 (29,089)	18,30 (31,729)		
Week 8:				
Adjusted Mean Change (SE)	9,27 (1,992)	6,86 (2,033)	2,41 [-2,146; 6,959] 0,300	0,081 [-0,106; 0,268]
Week 16:				
Adjusted Mean Change (SE)	17,84 (2,416)	13,42 (2,476)	4,42 [-1,544; 10,386] 0,146	0,121 [-0,065; 0,307]
Week 24:				
Adjusted Mean Change (SE)	19,77 (2,560)	16,85 (2,626)	2,92 [-3,502; 9,349] 0,372	0,076 [-0,111; 0,264]
Percentage of days with no night-time awakenings				
Interaction Test	0,496			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	221	232		
Baseline Mean (SD)	60,46 (37,154)	57,90 (38,217)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	11,75 (2,025)	10,78 (1,996)	0,96 [-3,611; 5,534] 0,680	0,032 [-0,154; 0,219]
Week 16:				
Adjusted Mean Change (SE)	17,58 (2,203)	14,22 (2,168)	3,35 [-1,796; 8,506] 0,202	0,102 [-0,083; 0,287]
Week 24:				
Adjusted Mean Change (SE)	19,13 (2,279)	16,06 (2,247)	3,07 [-2,333; 8,470] 0,265	0,091 [-0,095; 0,278]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	231	219		
Baseline Mean (SD)	57,17 (40,241)	66,94 (37,560)		
Week 8:				
Adjusted Mean Change (SE)	9,23 (2,013)	7,56 (2,033)	1,67 [-2,925; 6,273] 0,475	0,056 [-0,131; 0,243]
Week 16:				
Adjusted Mean Change (SE)	13,23 (2,186)	12,89 (2,218)	0,35 [-4,844; 5,538] 0,896	0,011 [-0,176; 0,197]
Week 24:				
Adjusted Mean Change (SE)	14,08 (2,261)	15,70 (2,301)	-1,62 [-7,066; 3,830] 0,560	-0,048 [-0,236; 0,140]
Percentage of days with no asthma symptoms				
Interaction Test	0,491			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	215	221		
Baseline Mean (SD)	16,43 (31,027)	13,91 (28,016)		
Week 8:				
Adjusted Mean Change (SE)	9,34 (2,046)	8,65 (2,045)	0,69 [-3,909; 5,286] 0,769	0,023 [-0,170; 0,216]
Week 16:				
Adjusted Mean Change (SE)	19,09 (2,484)	15,26 (2,477)	3,83 [-2,195; 9,852] 0,213	0,105 [-0,084; 0,294]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	20,90 (2,640)	17,15 (2,634)	3,74 [-2,774; 10,258] 0,260	0,097 [-0,093; 0,288]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	219	202		
Baseline Mean (SD)	14,01 (27,368)	17,34 (31,958)		
Week 8:				
Adjusted Mean Change (SE)	9,37 (2,039)	5,17 (2,082)	4,20 [-0,475; 8,870] 0,078	0,144 [-0,052; 0,339]
Week 16:				
Adjusted Mean Change (SE)	18,42 (2,475)	12,33 (2,546)	6,09 [-0,049; 12,220] 0,052	0,168 [-0,024; 0,360]
Week 24:				
Adjusted Mean Change (SE)	20,98 (2,634)	15,00 (2,715)	5,98 [-0,670; 12,622] 0,078	0,157 [-0,038; 0,351]
Mean total daily symptom score				
Interaction Test	0,307			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	215	221		
Baseline Mean (SD)	2,16 (1,471)	2,26 (1,523)		
Week 8:				
Adjusted Mean Change (SE)	-0,51 (0,078)	-0,55 (0,078)	0,04 [-0,130; 0,219] 0,618	0,040 [-0,153; 0,233]
Week 16:				
Adjusted Mean Change (SE)	-0,75 (0,084)	-0,74 (0,084)	-0,01 [-0,206; 0,189] 0,931	-0,007 [-0,196; 0,182]
Week 24:				
Adjusted Mean Change (SE)	-0,80 (0,087)	-0,79 (0,087)	-0,01 [-0,216; 0,196] 0,923	-0,008 [-0,198; 0,182]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	219	202		
Baseline Mean (SD)	2,36 (1,678)	1,94 (1,472)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,44 (0,078)	-0,34 (0,079)	-0,10 [-0,277; 0,079] 0,275	-0,089 [-0,285; 0,106]
Week 16:				
Adjusted Mean Change (SE)	-0,71 (0,084)	-0,57 (0,086)	-0,14 [-0,341; 0,062] 0,176	-0,113 [-0,305; 0,079]
Week 24:				
Adjusted Mean Change (SE)	-0,81 (0,087)	-0,67 (0,089)	-0,14 [-0,353; 0,068] 0,184	-0,113 [-0,308; 0,081]
Mean day-time symptom score				
Interaction Test	0,515			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	222	233		
Baseline Mean (SD)	0,85 (0,576)	0,89 (0,573)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,029)	-0,20 (0,029)	0,03 [-0,038; 0,095] 0,403	0,065 [-0,121; 0,251]
Week 16:				
Adjusted Mean Change (SE)	-0,28 (0,032)	-0,28 (0,032)	-0,01 [-0,083; 0,069] 0,856	-0,015 [-0,199; 0,170]
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,034)	-0,29 (0,034)	-0,01 [-0,087; 0,076] 0,894	-0,011 [-0,197; 0,175]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	233	218		
Baseline Mean (SD)	0,92 (0,605)	0,82 (0,551)		
Week 8:				
Adjusted Mean Change (SE)	-0,15 (0,029)	-0,14 (0,030)	-0,01 [-0,075; 0,059] 0,809	-0,019 [-0,206; 0,168]
Week 16:				
Adjusted Mean Change (SE)	-0,26 (0,032)	-0,22 (0,033)	-0,05 [-0,122; 0,032] 0,248	-0,093 [-0,279; 0,093]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,034)	-0,26 (0,034)	-0,03 [-0,112; 0,052] 0,473	-0,059 [-0,247; 0,128]
Mean night-time symptom score				
Interaction Test	0,492			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	221	232		
Baseline Mean (SD)	0,65 (0,479)	0,70 (0,514)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,025)	-0,18 (0,025)	0,00 [-0,055; 0,060] 0,924	0,007 [-0,179; 0,194]
Week 16:				
Adjusted Mean Change (SE)	-0,25 (0,027)	-0,24 (0,027)	-0,01 [-0,070; 0,057] 0,843	-0,016 [-0,201; 0,169]
Week 24:				
Adjusted Mean Change (SE)	-0,27 (0,028)	-0,26 (0,028)	-0,01 [-0,074; 0,058] 0,811	-0,019 [-0,206; 0,167]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	231	219		
Baseline Mean (SD)	0,73 (0,584)	0,58 (0,496)		
Week 8:				
Adjusted Mean Change (SE)	-0,15 (0,025)	-0,12 (0,025)	-0,04 [-0,096; 0,020] 0,198	-0,101 [-0,288; 0,086]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,027)	-0,20 (0,027)	-0,03 [-0,096; 0,032] 0,333	-0,078 [-0,264; 0,109]
Week 24:				
Adjusted Mean Change (SE)	-0,26 (0,028)	-0,23 (0,028)	-0,03 [-0,096; 0,037] 0,385	-0,071 [-0,259; 0,117]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Mean of: How did you sleep last night?				
Interaction Test	0,924			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	221	232		
Baseline Mean (SD)	0,48 (0,472)	0,54 (0,532)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,025)	-0,17 (0,024)	0,00 [-0,056; 0,056] 1,000	0,000 [-0,187; 0,187]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,026)	-0,22 (0,026)	-0,02 [-0,079; 0,042] 0,554	-0,047 [-0,232; 0,138]
Week 24:				
Adjusted Mean Change (SE)	-0,26 (0,026)	-0,25 (0,026)	-0,01 [-0,074; 0,049] 0,694	-0,032 [-0,218; 0,155]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	231	219		
Baseline Mean (SD)	0,58 (0,624)	0,41 (0,517)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,025)	-0,13 (0,025)	-0,03 [-0,082; 0,031] 0,371	-0,070 [-0,257; 0,117]
Week 16:				
Adjusted Mean Change (SE)	-0,21 (0,026)	-0,21 (0,026)	-0,01 [-0,066; 0,056] 0,866	-0,014 [-0,200; 0,173]
Week 24:				
Adjusted Mean Change (SE)	-0,23 (0,026)	-0,24 (0,027)	0,01 [-0,050; 0,074] 0,706	0,031 [-0,157; 0,218]
Mean of: Did you have asthma symptoms upon awakening in the morning?				
Interaction Test	0,325			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	221	232		
Baseline Mean (SD)	0,82 (0,588)	0,85 (0,598)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,032)	-0,17 (0,031)	0,00 [-0,070; 0,074] 0,963	0,004 [-0,183; 0,190]
Week 16:				
Adjusted Mean Change (SE)	-0,25 (0,035)	-0,25 (0,034)	0,00 [-0,081; 0,083] 0,977	0,002 [-0,183; 0,187]
Week 24:				
Adjusted Mean Change (SE)	-0,27 (0,037)	-0,26 (0,036)	-0,01 [-0,095; 0,079] 0,858	-0,015 [-0,201; 0,172]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	231	219		
Baseline Mean (SD)	0,88 (0,651)	0,74 (0,595)		
Week 8:				
Adjusted Mean Change (SE)	-0,14 (0,032)	-0,09 (0,032)	-0,04 [-0,117; 0,028] 0,229	-0,094 [-0,281; 0,093]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,035)	-0,18 (0,035)	-0,05 [-0,137; 0,029] 0,202	-0,103 [-0,290; 0,083]
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,036)	-0,21 (0,037)	-0,07 [-0,156; 0,020] 0,131	-0,125 [-0,313; 0,063]
Mean of: Did your respiratory symptoms stop you from performing your usual daily activities?				
Interaction Test	0,559			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	222	233		
Baseline Mean (SD)	0,85 (0,664)	0,90 (0,671)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,033)	-0,21 (0,033)	0,03 [-0,040; 0,110] 0,366	0,070 [-0,116; 0,256]
Week 16:				
Adjusted Mean Change (SE)	-0,29 (0,037)	-0,30 (0,037)	0,01 [-0,077; 0,097] 0,820	0,018 [-0,166; 0,202]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,038)	-0,31 (0,038)	0,02 [-0,074; 0,109] 0,701	0,031 [-0,154; 0,217]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	233	218		
Baseline Mean (SD)	0,94 (0,700)	0,85 (0,669)		
Week 8:				
Adjusted Mean Change (SE)	-0,15 (0,033)	-0,15 (0,034)	0,01 [-0,068; 0,083] 0,836	0,016 [-0,171; 0,203]
Week 16:				
Adjusted Mean Change (SE)	-0,26 (0,037)	-0,23 (0,037)	-0,03 [-0,118; 0,056] 0,485	-0,056 [-0,242; 0,130]
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,038)	-0,27 (0,039)	-0,02 [-0,107; 0,077] 0,746	-0,027 [-0,214; 0,161]
Mean of: How severe was your shortness of breath today?				
Interaction Test	0,527			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	222	233		
Baseline Mean (SD)	0,99 (0,633)	1,04 (0,647)		
Week 8:				
Adjusted Mean Change (SE)	-0,23 (0,034)	-0,25 (0,034)	0,01 [-0,063; 0,090] 0,729	0,027 [-0,159; 0,213]
Week 16:				
Adjusted Mean Change (SE)	-0,36 (0,037)	-0,34 (0,037)	-0,02 [-0,105; 0,071] 0,702	-0,031 [-0,215; 0,153]
Week 24:				
Adjusted Mean Change (SE)	-0,38 (0,039)	-0,35 (0,039)	-0,03 [-0,126; 0,061] 0,490	-0,057 [-0,242; 0,129]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	233	218		
Baseline Mean (SD)	1,07 (0,671)	0,97 (0,634)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,20 (0,034)	-0,18 (0,034)	-0,02 [-0,095; 0,059] 0,649	-0,035 [-0,222; 0,152]
Week 16:				
Adjusted Mean Change (SE)	-0,34 (0,037)	-0,27 (0,038)	-0,07 [-0,156; 0,021] 0,133	-0,121 [-0,307; 0,065]
Week 24:				
Adjusted Mean Change (SE)	-0,38 (0,039)	-0,32 (0,040)	-0,06 [-0,156; 0,033] 0,200	-0,106 [-0,294; 0,082]
Mean of: How was your wheeze during the past 12 hours?				
Interaction Test	0,283			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	222	233		
Baseline Mean (SD)	0,85 (0,651)	0,89 (0,633)		
Week 8:				
Adjusted Mean Change (SE)	-0,20 (0,034)	-0,26 (0,034)	0,06 [-0,013; 0,140] 0,103	0,127 [-0,060; 0,313]
Week 16:				
Adjusted Mean Change (SE)	-0,30 (0,037)	-0,32 (0,037)	0,01 [-0,073; 0,102] 0,744	0,026 [-0,158; 0,210]
Week 24:				
Adjusted Mean Change (SE)	-0,32 (0,039)	-0,33 (0,038)	0,01 [-0,080; 0,105] 0,787	0,022 [-0,164; 0,208]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	233	218		
Baseline Mean (SD)	0,94 (0,684)	0,79 (0,628)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,034)	-0,16 (0,034)	-0,01 [-0,087; 0,067] 0,802	-0,020 [-0,207; 0,167]
Week 16:				
Adjusted Mean Change (SE)	-0,29 (0,037)	-0,23 (0,038)	-0,05 [-0,141; 0,034] 0,233	-0,096 [-0,282; 0,090]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,31 (0,038)	-0,28 (0,039)	-0,03 [-0,125; 0,062] 0,509	-0,055 [-0,242; 0,133]
Mean of: How was your cough during the past 12 hours?				
Interaction Test	0,960			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	222	233		
Baseline Mean (SD)	0,91 (0,699)	0,92 (0,667)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,036)	-0,15 (0,036)	-0,00 [-0,084; 0,079] 0,953	-0,005 [-0,191; 0,182]
Week 16:				
Adjusted Mean Change (SE)	-0,29 (0,040)	-0,25 (0,039)	-0,04 [-0,136; 0,052] 0,377	-0,071 [-0,255; 0,113]
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,042)	-0,27 (0,041)	-0,02 [-0,120; 0,079] 0,684	-0,033 [-0,219; 0,152]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	233	218		
Baseline Mean (SD)	0,93 (0,661)	0,88 (0,645)		
Week 8:				
Adjusted Mean Change (SE)	-0,13 (0,036)	-0,11 (0,036)	-0,02 [-0,099; 0,065] 0,684	-0,032 [-0,219; 0,155]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,039)	-0,21 (0,040)	-0,02 [-0,117; 0,072] 0,646	-0,037 [-0,223; 0,149]
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,041)	-0,26 (0,042)	-0,02 [-0,117; 0,083] 0,738	-0,028 [-0,215; 0,160]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Did you have chest tightness during the past 12 hours?				
Interaction Test	0,760			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	222	233		
Baseline Mean (SD)	0,63 (0,606)	0,70 (0,658)		
Week 8:				
Adjusted Mean Change (SE)	-0,09 (0,032)	-0,12 (0,032)	0,03 [-0,043; 0,102] 0,417	0,063 [-0,123; 0,249]
Week 16:				
Adjusted Mean Change (SE)	-0,17 (0,035)	-0,16 (0,035)	-0,00 [-0,086; 0,077] 0,911	-0,009 [-0,193; 0,175]
Week 24:				
Adjusted Mean Change (SE)	-0,18 (0,036)	-0,17 (0,036)	-0,01 [-0,095; 0,077] 0,831	-0,017 [-0,203; 0,168]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	233	218		
Baseline Mean (SD)	0,71 (0,669)	0,61 (0,613)		
Week 8:				
Adjusted Mean Change (SE)	-0,07 (0,032)	-0,08 (0,033)	0,01 [-0,064; 0,082] 0,814	0,018 [-0,169; 0,205]
Week 16:				
Adjusted Mean Change (SE)	-0,17 (0,035)	-0,13 (0,035)	-0,04 [-0,117; 0,047] 0,399	-0,068 [-0,253; 0,118]
Week 24:				
Adjusted Mean Change (SE)	-0,19 (0,036)	-0,18 (0,037)	-0,01 [-0,094; 0,079] 0,868	-0,014 [-0,201; 0,174]

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + patients' prior therapies + patients' prior therapies * treatment + patients' prior therapies * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

10. E-Diary - Rescue Medication

Table 10.1 Rescue Medication - Documentation Rate (FAS)

		Treatment groups		
Outcome - Documentation Rate (FAS)		**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Total N=951**
Rescue medication during the night - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	428 (89,9)	422 (88,8)	850 (89,4)
	50%-<70%	35 (7,4)	37 (7,8)	72 (7,6)
	<50%	13 (2,7)	16 (3,4)	29 (3,0)
Baseline to Week 8	70%-100%	421 (88,4)	427 (89,9)	848 (89,2)
	50%-<70%	33 (6,9)	28 (5,9)	61 (6,4)
	<50%	22 (4,6)	20 (4,2)	42 (4,4)
Week 9 to Week 16	70%-100%	400 (84,0)	409 (86,1)	809 (85,1)
	50%-<70%	48 (10,1)	33 (6,9)	81 (8,5)
	<50%	28 (5,9)	33 (6,9)	61 (6,4)
Week 17 to Week 24	70%-100%	391 (82,1)	407 (85,7)	798 (83,9)
	50%-<70%	47 (9,9)	17 (3,6)	64 (6,7)
	<50%	38 (8,0)	51 (10,7)	89 (9,4)
Baseline to Week 24	70%-100%	413 (86,8)	407 (85,7)	820 (86,2)
	50%-<70%	36 (7,6)	33 (6,9)	69 (7,3)
	<50%	27 (5,7)	35 (7,4)	62 (6,5)
Rescue medication during the day - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	431 (90,5)	420 (88,4)	851 (89,5)
	50%-<70%	34 (7,1)	41 (8,6)	75 (7,9)
	<50%	11 (2,3)	14 (2,9)	25 (2,6)
Baseline to Week 8	70%-100%	419 (88,0)	420 (88,4)	839 (88,2)
	50%-<70%	38 (8,0)	32 (6,7)	70 (7,4)
	<50%	19 (4,0)	23 (4,8)	42 (4,4)
Week 9 to Week 16	70%-100%	412 (86,6)	408 (85,9)	820 (86,2)
	50%-<70%	35 (7,4)	27 (5,7)	62 (6,5)
	<50%	29 (6,1)	40 (8,4)	69 (7,3)
Week 17 to Week 24	70%-100%	394 (82,8)	384 (80,8)	778 (81,8)
	50%-<70%	40 (8,4)	41 (8,6)	81 (8,5)
	<50%	42 (8,8)	50 (10,5)	92 (9,7)

		Treatment groups		
Outcome - Documentation Rate (FAS)		**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Total N=951**
Baseline to Week 24	70%-100%	410 (86,1)	403 (84,8)	813 (85,5)
	50%-<70%	38 (8,0)	35 (7,4)	73 (7,7)
	<50%	28 (5,9)	37 (7,8)	65 (6,8)
Rescue medication free days - Documentation rate in standardized days*, n (%)				
Baseline	70%-100%	421 (88,4)	416 (87,6)	837 (88,0)
	50%-<70%	38 (8,0)	38 (8,0)	76 (8,0)
	<50%	17 (3,6)	21 (4,4)	38 (4,0)
Baseline to Week 8	70%-100%	401 (84,2)	408 (85,9)	809 (85,1)
	50%-<70%	44 (9,2)	45 (9,5)	89 (9,4)
	<50%	31 (6,5)	22 (4,6)	53 (5,6)
Week 9 to Week 16	70%-100%	373 (78,4)	387 (81,5)	760 (79,9)
	50%-<70%	55 (11,6)	37 (7,8)	92 (9,7)
	<50%	48 (10,1)	51 (10,7)	99 (10,4)
Week 17 to Week 24	70%-100%	352 (73,9)	371 (78,1)	723 (76,0)
	50%-<70%	60 (12,6)	45 (9,5)	105 (11,0)
	<50%	64 (13,4)	59 (12,4)	123 (12,9)
Baseline to Week 24	70%-100%	376 (79,0)	388 (81,7)	764 (80,3)
	50%-<70%	59 (12,4)	43 (9,1)	102 (10,7)
	<50%	41 (8,6)	44 (9,3)	85 (8,9)

* For each time period and patient the documentation rate is calculated as the number of documented days divided by the number of days of the whole time period.

Analysis population: B2306 FAS total population

Table 10.2 Rescue Medication - Change from Baseline (FAS)

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Daily number of puffs of rescue medication during the night				
N'	452	451		
Baseline Mean (SD)	0,69 (0,939)	0,67 (0,877)		
Week 8:				
Adjusted Mean Change (SE)	-0,25 (0,035)	-0,17 (0,035)	-0,08 [-0,144; -0,007] 0,031 *	-0,104 [-0,236; 0,028]
Week 16:				
Adjusted Mean Change (SE)	-0,30 (0,037)	-0,26 (0,037)	-0,04 [-0,119; 0,035] 0,287	-0,054 [-0,185; 0,077]
Week 24:				
Adjusted Mean Change (SE)	-0,34 (0,038)	-0,27 (0,038)	-0,06 [-0,144; 0,017] 0,124	-0,080 [-0,212; 0,053]
Daily number of puffs of rescue medication during the day				
N'	455	451		
Baseline Mean (SD)	1,05 (1,272)	1,04 (1,123)		
Week 8:				
Adjusted Mean Change (SE)	-0,30 (0,044)	-0,25 (0,045)	-0,06 [-0,147; 0,029] 0,188	-0,063 [-0,195; 0,069]
Week 16:				
Adjusted Mean Change (SE)	-0,43 (0,048)	-0,35 (0,048)	-0,08 [-0,183; 0,020] 0,115	-0,080 [-0,210; 0,051]
Week 24:				
Adjusted Mean Change (SE)	-0,46 (0,049)	-0,40 (0,050)	-0,06 [-0,170; 0,044] 0,249	-0,060 [-0,192; 0,072]
Percentage of rescue medication free days				
N'	447	443		
Baseline Mean (SD)	42,01 (40,325)	41,36 (41,003)		
Week 8:				
Adjusted Mean Change (SE)	11,71 (1,826)	11,38 (1,823)	0,32 [-3,336; 3,983] 0,862	0,009 [-0,125; 0,142]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 16:				
Adjusted Mean Change (SE)	19,30 (1,985)	17,55 (1,988)	1,75 [-2,507; 6,007] 0,420	0,042 [-0,090; 0,174]
Week 24:				
Adjusted Mean Change (SE)	21,60 (2,026)	20,29 (2,031)	1,32 [-3,087; 5,721] 0,558	0,031 [-0,102; 0,165]

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 10.3 Rescue Medication - Change from Baseline by Age (FAS)

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Daily number of puffs of rescue medication during the night				
Interaction Test	0,307			
Age = 18-39 years				
N'	81	70		
Baseline Mean (SD)	0,69 (1,200)	0,61 (0,925)		
Week 8:				
Adjusted Mean Change (SE)	-0,32 (0,064)	-0,19 (0,067)	-0,14 [-0,309; 0,030] 0,106	-0,252 [-0,583; 0,079]
Week 16:				
Adjusted Mean Change (SE)	-0,34 (0,071)	-0,33 (0,075)	-0,02 [-0,208; 0,171] 0,849	-0,029 [-0,349; 0,291]
Week 24:				
Adjusted Mean Change (SE)	-0,38 (0,073)	-0,34 (0,078)	-0,04 [-0,238; 0,158] 0,691	-0,062 [-0,388; 0,263]
Age = 40-64 years				
N'	271	291		
Baseline Mean (SD)	0,70 (0,871)	0,68 (0,877)		
Week 8:				
Adjusted Mean Change (SE)	-0,25 (0,039)	-0,16 (0,039)	-0,09 [-0,177; -0,003] 0,042 *	-0,138 [-0,306; 0,029]
Week 16:				
Adjusted Mean Change (SE)	-0,32 (0,043)	-0,24 (0,042)	-0,08 [-0,180; 0,016] 0,102	-0,115 [-0,282; 0,051]
Week 24:				
Adjusted Mean Change (SE)	-0,35 (0,044)	-0,24 (0,044)	-0,11 [-0,210; -0,005] 0,040 *	-0,148 [-0,315; 0,020]
Age = ≥65 years				
N'	100	90		
Baseline Mean (SD)	0,69 (0,884)	0,67 (0,848)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,19 (0,059)	-0,21 (0,061)	0,02 [-0,128; 0,171] 0,774	0,038 [-0,248; 0,323]
Week 16:				
Adjusted Mean Change (SE)	-0,22 (0,065)	-0,29 (0,068)	0,06 [-0,108; 0,230] 0,477	0,096 [-0,192; 0,384]
Week 24:				
Adjusted Mean Change (SE)	-0,26 (0,067)	-0,32 (0,070)	0,05 [-0,122; 0,231] 0,547	0,082 [-0,207; 0,372]
Daily number of puffs of rescue medication during the day				
Interaction Test	0,966			
Age = 18-39 years				
N'	78	71		
Baseline Mean (SD)	0,92 (1,323)	0,91 (1,085)		
Week 8:				
Adjusted Mean Change (SE)	-0,38 (0,084)	-0,25 (0,086)	-0,13 [-0,343; 0,093] 0,260	-0,175 [-0,505; 0,155]
Week 16:				
Adjusted Mean Change (SE)	-0,47 (0,094)	-0,40 (0,097)	-0,07 [-0,319; 0,181] 0,591	-0,083 [-0,406; 0,239]
Week 24:				
Adjusted Mean Change (SE)	-0,54 (0,099)	-0,48 (0,102)	-0,06 [-0,321; 0,208] 0,675	-0,067 [-0,395; 0,262]
Age = 40-64 years				
N'	277	291		
Baseline Mean (SD)	1,09 (1,289)	1,05 (1,103)		
Week 8:				
Adjusted Mean Change (SE)	-0,31 (0,050)	-0,27 (0,051)	-0,04 [-0,151; 0,070] 0,474	-0,048 [-0,215; 0,118]
Week 16:				
Adjusted Mean Change (SE)	-0,44 (0,055)	-0,37 (0,055)	-0,08 [-0,205; 0,051] 0,236	-0,083 [-0,248; 0,082]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,47 (0,058)	-0,41 (0,058)	-0,06 [-0,198; 0,072] 0,359	-0,066 [-0,233; 0,101]
Age = ≥65 years				
N'	100	89		
Baseline Mean (SD)	1,04 (1,186)	1,13 (1,219)		
Week 8:				
Adjusted Mean Change (SE)	-0,23 (0,075)	-0,15 (0,079)	-0,07 [-0,265; 0,119] 0,457	-0,097 [-0,384; 0,189]
Week 16:				
Adjusted Mean Change (SE)	-0,35 (0,085)	-0,24 (0,089)	-0,11 [-0,336; 0,109] 0,317	-0,135 [-0,423; 0,152]
Week 24:				
Adjusted Mean Change (SE)	-0,36 (0,089)	-0,28 (0,093)	-0,08 [-0,310; 0,158] 0,523	-0,087 [-0,375; 0,201]
Percentage of rescue medication free days				
Interaction Test	0,848			
Age = 18-39 years				
N'	78	67		
Baseline Mean (SD)	50,95 (41,145)	47,20 (39,784)		
Week 8:				
Adjusted Mean Change (SE)	15,83 (3,483)	12,87 (3,625)	2,96 [-6,241; 12,158] 0,528	0,102 [-0,237; 0,441]
Week 16:				
Adjusted Mean Change (SE)	21,46 (3,909)	21,04 (4,138)	0,43 [-10,148; 11,006] 0,937	0,013 [-0,314; 0,339]
Week 24:				
Adjusted Mean Change (SE)	25,12 (4,039)	23,56 (4,277)	1,56 [-9,415; 12,527] 0,781	0,045 [-0,290; 0,380]
Age = 40-64 years				
N'	271	288		
Baseline Mean (SD)	39,87 (40,620)	40,34 (40,647)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	10,60 (2,084)	12,11 (2,063)	-1,51 [-6,125; 3,113] 0,523	-0,044 [-0,212; 0,124]
Week 16:				
Adjusted Mean Change (SE)	19,52 (2,313)	18,05 (2,287)	1,47 [-3,913; 6,847] 0,593	0,038 [-0,128; 0,205]
Week 24:				
Adjusted Mean Change (SE)	21,93 (2,370)	20,78 (2,344)	1,14 [-4,422; 6,707] 0,687	0,029 [-0,139; 0,198]
Age = ≥65 years				
N'	98	88		
Baseline Mean (SD)	40,83 (38,231)	40,24 (43,121)		
Week 8:				
Adjusted Mean Change (SE)	11,60 (3,119)	7,84 (3,256)	3,76 [-4,236; 11,754] 0,357	0,123 [-0,167; 0,413]
Week 16:				
Adjusted Mean Change (SE)	16,99 (3,552)	13,24 (3,714)	3,75 [-5,593; 13,095] 0,431	0,108 [-0,183; 0,399]
Week 24:				
Adjusted Mean Change (SE)	17,99 (3,649)	16,16 (3,817)	1,82 [-7,819; 11,465] 0,711	0,051 [-0,239; 0,341]

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + age + age * treatment + age * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 10.4 Rescue Medication - Change from Baseline by Gender (FAS)

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Daily number of puffs of rescue medication during the night				
Interaction Test	0,342			
Gender = Male				
N'	179	162		
Baseline Mean (SD)	0,74 (0,991)	0,65 (0,863)		
Week 8:				
Adjusted Mean Change (SE)	-0,20 (0,045)	-0,21 (0,048)	0,01 [-0,105; 0,119] 0,904	0,011 [-0,204; 0,227]
Week 16:				
Adjusted Mean Change (SE)	-0,29 (0,050)	-0,30 (0,053)	0,01 [-0,120; 0,132] 0,930	0,009 [-0,205; 0,222]
Week 24:				
Adjusted Mean Change (SE)	-0,35 (0,051)	-0,29 (0,055)	-0,06 [-0,193; 0,070] 0,359	-0,090 [-0,305; 0,125]
Gender = Female				
N'	273	289		
Baseline Mean (SD)	0,66 (0,904)	0,67 (0,886)		
Week 8:				
Adjusted Mean Change (SE)	-0,28 (0,041)	-0,16 (0,039)	-0,13 [-0,214; -0,040] 0,004 *	-0,192 [-0,360; -0,025]
Week 16:				
Adjusted Mean Change (SE)	-0,31 (0,044)	-0,24 (0,042)	-0,07 [-0,168; 0,028] 0,160	-0,098 [-0,264; 0,068]
Week 24:				
Adjusted Mean Change (SE)	-0,33 (0,045)	-0,27 (0,044)	-0,06 [-0,166; 0,039] 0,225	-0,087 [-0,255; 0,081]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Daily number of puffs of rescue medication during the day				
Interaction Test	0,787			
Gender = Male				
N'	180	160		
Baseline Mean (SD)	1,17 (1,494)	1,00 (1,096)		
Week 8:				
Adjusted Mean Change (SE)	-0,28 (0,058)	-0,27 (0,063)	-0,01 [-0,153; 0,134] 0,894	-0,013 [-0,228; 0,202]
Week 16:				
Adjusted Mean Change (SE)	-0,42 (0,065)	-0,36 (0,070)	-0,06 [-0,226; 0,106] 0,477	-0,069 [-0,283; 0,145]
Week 24:				
Adjusted Mean Change (SE)	-0,49 (0,068)	-0,41 (0,073)	-0,08 [-0,258; 0,092] 0,352	-0,092 [-0,307; 0,123]
Gender = Female				
N'	275	291		
Baseline Mean (SD)	0,97 (1,100)	1,07 (1,139)		
Week 8:				
Adjusted Mean Change (SE)	-0,32 (0,052)	-0,23 (0,050)	-0,09 [-0,201; 0,022] 0,116	-0,105 [-0,272; 0,062]
Week 16:				
Adjusted Mean Change (SE)	-0,43 (0,057)	-0,34 (0,055)	-0,09 [-0,222; 0,034] 0,151	-0,100 [-0,265; 0,066]
Week 24:				
Adjusted Mean Change (SE)	-0,44 (0,059)	-0,39 (0,057)	-0,05 [-0,184; 0,087] 0,483	-0,050 [-0,217; 0,117]
Percentage of rescue medication free days				
Interaction Test	0,865			
Gender = Male				
N'	177	159		
Baseline Mean (SD)	41,83 (41,304)	43,45 (42,618)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	10,54 (2,401)	12,06 (2,568)	-1,52 [-7,491; 4,451] 0,618	-0,048 [-0,265; 0,169]
Week 16:				
Adjusted Mean Change (SE)	19,40 (2,707)	18,60 (2,885)	0,80 [-6,144; 7,754] 0,820	0,022 [-0,193; 0,237]
Week 24:				
Adjusted Mean Change (SE)	23,78 (2,781)	21,02 (2,962)	2,76 [-4,425; 9,937] 0,452	0,075 [-0,142; 0,292]
Gender = Female				
N'	270	284		
Baseline Mean (SD)	42,14 (39,747)	40,19 (40,099)		
Week 8:				
Adjusted Mean Change (SE)	12,55 (2,158)	11,06 (2,058)	1,49 [-3,159; 6,142] 0,529	0,043 [-0,126; 0,213]
Week 16:				
Adjusted Mean Change (SE)	19,30 (2,376)	17,02 (2,286)	2,28 [-3,122; 7,686] 0,408	0,059 [-0,108; 0,226]
Week 24:				
Adjusted Mean Change (SE)	20,24 (2,431)	19,94 (2,343)	0,30 [-5,286; 5,894] 0,915	0,008 [-0,162; 0,177]

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + gender + gender * treatment + gender * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 10.5 Rescue Medication - Change from Baseline by Region (FAS)

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Daily number of puffs of rescue medication during the night				
Interaction Test	N.E.			
Region = Asia				
N'	117	126		
Baseline Mean (SD)	0,65 (0,867)	0,72 (0,929)		
Week 8:				
Adjusted Mean Change (SE)	-0,31 (0,049)	-0,16 (0,048)	-0,15 [-0,281; -0,011] 0,034 *	-0,277 [-0,533; -0,021]
Week 16:				
Adjusted Mean Change (SE)	-0,39 (0,053)	-0,21 (0,051)	-0,18 [-0,322; -0,032] 0,017 *	-0,312 [-0,567; -0,057]
Week 24:				
Adjusted Mean Change (SE)	-0,45 (0,054)	-0,27 (0,053)	-0,18 [-0,325; -0,027] 0,021 *	-0,302 [-0,558; -0,046]
Region = Europe				
N'	157	164		
Baseline Mean (SD)	0,59 (0,799)	0,54 (0,763)		
Week 8:				
Adjusted Mean Change (SE)	-0,23 (0,038)	-0,22 (0,037)	-0,01 [-0,118; 0,093] 0,818	-0,026 [-0,246; 0,194]
Week 16:				
Adjusted Mean Change (SE)	-0,27 (0,042)	-0,31 (0,041)	0,05 [-0,069; 0,162] 0,431	0,088 [-0,131; 0,308]
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,044)	-0,31 (0,044)	0,03 [-0,095; 0,150] 0,662	0,050 [-0,173; 0,272]
Region = Latin America				
N'	158	152		
Baseline Mean (SD)	0,82 (1,096)	0,76 (0,947)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,21 (0,045)	-0,13 (0,046)	-0,08 [-0,209; 0,042] 0,190	-0,152 [-0,379; 0,075]
Week 16:				
Adjusted Mean Change (SE)	-0,28 (0,053)	-0,23 (0,054)	-0,04 [-0,192; 0,104] 0,558	-0,067 [-0,291; 0,157]
Week 24:				
Adjusted Mean Change (SE)	-0,31 (0,055)	-0,23 (0,056)	-0,09 [-0,242; 0,067] 0,267	-0,128 [-0,354; 0,098]
Region = Others				
N'	20	9		
Baseline Mean (SD)	0,74 (0,970)	0,64 (0,658)		
Week 8:				
Adjusted Mean Change (SE)	-0,27 (0,110)	-0,09 (0,164)	-0,18 [-0,576; 0,220] 0,373	-0,361 [-1,154; 0,431]
Week 16:				
Adjusted Mean Change (SE)	-0,28 (0,121)	-0,42 (0,180)	0,14 [-0,301; 0,572] 0,536	0,250 [-0,539; 1,040]
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,118)	-0,33 (0,176)	0,05 [-0,374; 0,477] 0,809	0,098 [-0,689; 0,885]
Daily number of puffs of rescue medication during the day				
Interaction Test	0,575			
Region = Asia				
N'	118	121		
Baseline Mean (SD)	1,09 (1,344)	1,10 (1,217)		
Week 8:				
Adjusted Mean Change (SE)	-0,25 (0,070)	-0,18 (0,069)	-0,08 [-0,268; 0,118] 0,446	-0,099 [-0,355; 0,157]
Week 16:				
Adjusted Mean Change (SE)	-0,46 (0,070)	-0,23 (0,069)	-0,23 [-0,421; -0,035] 0,020 *	-0,302 [-0,559; -0,045]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	-0,50 (0,070)	-0,28 (0,069)	-0,22 [-0,415; -0,029] 0,024 *	-0,295 [-0,553; -0,037]
Region = Europe				
N'	157	164		
Baseline Mean (SD)	0,97 (1,196)	1,00 (1,102)		
Week 8:				
Adjusted Mean Change (SE)	-0,30 (0,061)	-0,27 (0,059)	-0,03 [-0,193; 0,139] 0,752	-0,035 [-0,254; 0,184]
Week 16:				
Adjusted Mean Change (SE)	-0,43 (0,061)	-0,38 (0,059)	-0,05 [-0,218; 0,114] 0,541	-0,068 [-0,287; 0,151]
Week 24:				
Adjusted Mean Change (SE)	-0,42 (0,061)	-0,45 (0,060)	0,03 [-0,134; 0,199] 0,701	0,044 [-0,178; 0,265]
Region = Latin America				
N'	160	157		
Baseline Mean (SD)	1,09 (1,333)	1,05 (1,094)		
Week 8:				
Adjusted Mean Change (SE)	-0,27 (0,061)	-0,20 (0,061)	-0,07 [-0,238; 0,099] 0,420	-0,093 [-0,320; 0,133]
Week 16:				
Adjusted Mean Change (SE)	-0,33 (0,060)	-0,33 (0,061)	-0,00 [-0,170; 0,165] 0,977	-0,003 [-0,225; 0,218]
Week 24:				
Adjusted Mean Change (SE)	-0,40 (0,060)	-0,36 (0,061)	-0,04 [-0,207; 0,128] 0,644	-0,052 [-0,276; 0,171]
Region = Others				
N'	20	9		
Baseline Mean (SD)	1,08 (0,934)	0,81 (0,736)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	-0,44 (0,170)	-0,20 (0,258)	-0,24 [-0,846; 0,363] 0,433	-0,322 [-1,146; 0,503]
Week 16:				
Adjusted Mean Change (SE)	-0,53 (0,170)	-0,59 (0,253)	0,06 [-0,537; 0,657] 0,843	0,079 [-0,708; 0,866]
Week 24:				
Adjusted Mean Change (SE)	-0,53 (0,170)	-0,58 (0,253)	0,05 [-0,548; 0,646] 0,871	0,065 [-0,722; 0,852]
Percentage of rescue medication free days				
Interaction Test	0,496			
Region = Asia				
N'	115	121		
Baseline Mean (SD)	36,36 (40,404)	37,11 (40,494)		
Week 8:				
Adjusted Mean Change (SE)	9,52 (2,612)	13,17 (2,519)	-3,65 [-10,753; 3,457] 0,314	-0,133 [-0,393; 0,127]
Week 16:				
Adjusted Mean Change (SE)	24,15 (3,023)	16,17 (2,940)	7,98 [-0,281; 16,236] 0,058	0,248 [-0,010; 0,506]
Week 24:				
Adjusted Mean Change (SE)	26,12 (3,126)	18,74 (3,042)	7,38 [-1,168; 15,919] 0,091	0,223 [-0,036; 0,482]
Region = Europe				
N'	154	162		
Baseline Mean (SD)	46,73 (41,294)	45,41 (40,940)		
Week 8:				
Adjusted Mean Change (SE)	14,89 (2,233)	14,77 (2,174)	0,12 [-5,989; 6,231] 0,969	0,004 [-0,217; 0,226]
Week 16:				
Adjusted Mean Change (SE)	19,83 (2,600)	22,98 (2,535)	-3,14 [-10,264; 3,974] 0,386	-0,098 [-0,319; 0,123]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	21,56 (2,687)	27,26 (2,628)	-5,70 [-13,067; 1,672] 0,130	-0,173 [-0,397; 0,051]
Region = Latin America				
N'	158	151		
Baseline Mean (SD)	41,48 (40,013)	39,98 (41,416)		
Week 8:				
Adjusted Mean Change (SE)	12,98 (2,235)	10,61 (2,266)	2,37 [-3,864; 8,611] 0,456	0,087 [-0,142; 0,315]
Week 16:				
Adjusted Mean Change (SE)	18,50 (2,577)	16,63 (2,626)	1,87 [-5,346; 9,080] 0,612	0,058 [-0,166; 0,282]
Week 24:				
Adjusted Mean Change (SE)	22,18 (2,668)	18,10 (2,718)	4,08 [-3,389; 11,547] 0,284	0,124 [-0,103; 0,351]
Region = Others				
N'	20	9		
Baseline Mean (SD)	42,40 (32,222)	48,78 (41,181)		
Week 8:				
Adjusted Mean Change (SE)	23,34 (6,262)	16,89 (9,473)	6,46 [-15,773; 28,690] 0,569	0,238 [-0,591; 1,066]
Week 16:				
Adjusted Mean Change (SE)	28,28 (7,222)	31,60 (10,761)	-3,33 [-28,710; 22,058] 0,797	-0,103 [-0,890; 0,684]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	26,43 (7,453)	30,63 (11,106)	-4,20 [-30,401; 21,998] 0,753	-0,126 [-0,913; 0,661]

N': Number of patients in the analysis
CI: Confidence Interval
N.E.: not estimable
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + region + region * treatment + region * treatment * visit, within-patient correlation: unstructured covariance matrix
Exceptional model(s): **Daily number of puffs of rescue medication during the night**: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region], **Daily number of puffs of rescue medication during the day**: treatment + visit + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + region + region * treatment + region * treatment * visit, within-patient correlation: compound symmetry covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 10.6 Rescue Medication - Change from Baseline by History of Asthma Exacerbation (FAS)

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Daily number of puffs of rescue medication during the night				
Interaction Test	0,134			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	357	366		
Baseline Mean (SD)	0,65 (0,938)	0,64 (0,859)		
Week 8:				
Adjusted Mean Change (SE)	-0,27 (0,037)	-0,17 (0,036)	-0,10 [-0,175; -0,022] 0,012 *	-0,143 [-0,291; 0,004]
Week 16:				
Adjusted Mean Change (SE)	-0,34 (0,039)	-0,26 (0,039)	-0,07 [-0,157; 0,015] 0,108	-0,095 [-0,242; 0,051]
Week 24:				
Adjusted Mean Change (SE)	-0,37 (0,040)	-0,28 (0,040)	-0,10 [-0,186; -0,006] 0,036 *	-0,127 [-0,275; 0,021]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	95	85		
Baseline Mean (SD)	0,85 (0,931)	0,77 (0,949)		
Week 8:				
Adjusted Mean Change (SE)	-0,15 (0,060)	-0,16 (0,063)	0,01 [-0,143; 0,165] 0,889	0,019 [-0,278; 0,316]
Week 16:				
Adjusted Mean Change (SE)	-0,18 (0,067)	-0,24 (0,069)	0,07 [-0,107; 0,240] 0,453	0,104 [-0,191; 0,399]
Week 24:				
Adjusted Mean Change (SE)	-0,19 (0,069)	-0,25 (0,072)	0,06 [-0,120; 0,242] 0,511	0,092 [-0,205; 0,389]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Daily number of puffs of rescue medication during the day				
Interaction Test	0,083			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	359	365		
Baseline Mean (SD)	1,02 (1,299)	1,02 (1,115)		
Week 8:				
Adjusted Mean Change (SE)	-0,33 (0,047)	-0,25 (0,047)	-0,08 [-0,178; 0,018] 0,110	-0,090 [-0,238; 0,057]
Week 16:				
Adjusted Mean Change (SE)	-0,47 (0,051)	-0,35 (0,051)	-0,13 [-0,240; -0,014] 0,028 *	-0,130 [-0,277; 0,016]
Week 24:				
Adjusted Mean Change (SE)	-0,50 (0,053)	-0,38 (0,053)	-0,12 [-0,241; -0,002] 0,046 *	-0,122 [-0,269; 0,026]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	96	86		
Baseline Mean (SD)	1,15 (1,168)	1,12 (1,162)		
Week 8:				
Adjusted Mean Change (SE)	-0,22 (0,077)	-0,24 (0,080)	0,02 [-0,176; 0,217] 0,837	0,028 [-0,267; 0,322]
Week 16:				
Adjusted Mean Change (SE)	-0,26 (0,087)	-0,35 (0,090)	0,09 [-0,135; 0,318] 0,428	0,109 [-0,184; 0,403]
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,091)	-0,45 (0,095)	0,17 [-0,073; 0,405] 0,174	0,190 [-0,106; 0,486]
Percentage of rescue medication free days				
Interaction Test	0,181			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	351	358		
Baseline Mean (SD)	43,23 (40,301)	42,60 (41,779)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	12,36 (1,938)	11,54 (1,930)	0,83 [-3,268; 4,922] 0,692	0,023 [-0,126; 0,172]
Week 16:				
Adjusted Mean Change (SE)	21,10 (2,127)	17,58 (2,121)	3,52 [-1,237; 8,286] 0,147	0,088 [-0,059; 0,236]
Week 24:				
Adjusted Mean Change (SE)	23,10 (2,174)	20,01 (2,171)	3,09 [-1,833; 8,018] 0,218	0,077 [-0,073; 0,226]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	96	85		
Baseline Mean (SD)	37,58 (40,310)	36,15 (37,337)		
Week 8:				
Adjusted Mean Change (SE)	9,59 (3,195)	11,07 (3,308)	-1,48 [-9,637; 6,669] 0,721	-0,049 [-0,346; 0,249]
Week 16:				
Adjusted Mean Change (SE)	12,95 (3,603)	17,78 (3,766)	-4,82 [-14,283; 4,642] 0,318	-0,139 [-0,434; 0,156]
Week 24:				
Adjusted Mean Change (SE)	16,36 (3,714)	21,80 (3,876)	-5,44 [-15,231; 4,350] 0,276	-0,154 [-0,452; 0,144]

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + history of asthma exacerbation + history of asthma exacerbation * treatment + history of asthma exacerbation * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 10.7 Rescue Medication - Change from Baseline by Patients' Prior Therapies (FAS)

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Daily number of puffs of rescue medication during the night				
Interaction Test	0,108			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	221	232		
Baseline Mean (SD)	0,58 (0,773)	0,71 (0,912)		
Week 8:				
Adjusted Mean Change (SE)	-0,30 (0,043)	-0,17 (0,042)	-0,13 [-0,226; -0,032] 0,009 *	-0,205 [-0,392; -0,018]
Week 16:				
Adjusted Mean Change (SE)	-0,35 (0,047)	-0,24 (0,046)	-0,12 [-0,226; -0,008] 0,036 *	-0,169 [-0,354; 0,017]
Week 24:				
Adjusted Mean Change (SE)	-0,36 (0,048)	-0,26 (0,047)	-0,11 [-0,220; 0,008] 0,068	-0,150 [-0,336; 0,037]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	231	219		
Baseline Mean (SD)	0,80 (1,064)	0,62 (0,838)		
Week 8:				
Adjusted Mean Change (SE)	-0,19 (0,042)	-0,17 (0,043)	-0,02 [-0,119; 0,075] 0,656	-0,035 [-0,222; 0,152]
Week 16:				
Adjusted Mean Change (SE)	-0,25 (0,046)	-0,29 (0,047)	0,03 [-0,075; 0,144] 0,535	0,050 [-0,136; 0,237]
Week 24:				
Adjusted Mean Change (SE)	-0,31 (0,048)	-0,29 (0,049)	-0,02 [-0,133; 0,096] 0,753	-0,026 [-0,214; 0,162]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Daily number of puffs of rescue medication during the day				
Interaction Test	0,094			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	222	233		
Baseline Mean (SD)	0,90 (1,149)	1,03 (1,103)		
Week 8:				
Adjusted Mean Change (SE)	-0,36 (0,055)	-0,22 (0,054)	-0,14 [-0,268; -0,020] 0,022 *	-0,177 [-0,364; 0,009]
Week 16:				
Adjusted Mean Change (SE)	-0,48 (0,061)	-0,31 (0,060)	-0,17 [-0,308; -0,023] 0,023 *	-0,182 [-0,366; 0,003]
Week 24:				
Adjusted Mean Change (SE)	-0,49 (0,063)	-0,36 (0,062)	-0,13 [-0,278; 0,023] 0,098	-0,136 [-0,322; 0,050]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	233	218		
Baseline Mean (SD)	1,20 (1,366)	1,06 (1,147)		
Week 8:				
Adjusted Mean Change (SE)	-0,25 (0,054)	-0,27 (0,055)	0,03 [-0,098; 0,151] 0,680	0,032 [-0,155; 0,219]
Week 16:				
Adjusted Mean Change (SE)	-0,38 (0,060)	-0,39 (0,061)	0,00 [-0,140; 0,147] 0,963	0,004 [-0,182; 0,189]
Week 24:				
Adjusted Mean Change (SE)	-0,43 (0,062)	-0,43 (0,064)	0,00 [-0,149; 0,155] 0,969	0,003 [-0,184; 0,191]
Percentage of rescue medication free days				
Interaction Test	0,105			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	219	232		
Baseline Mean (SD)	45,24 (41,045)	42,15 (40,992)		

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	14,97 (2,268)	10,91 (2,214)	4,06 [-1,081; 9,199] 0,122	0,123 [-0,065; 0,310]
Week 16:				
Adjusted Mean Change (SE)	22,62 (2,524)	17,34 (2,468)	5,28 [-0,702; 11,253] 0,084	0,141 [-0,044; 0,327]
Week 24:				
Adjusted Mean Change (SE)	24,04 (2,588)	20,78 (2,533)	3,26 [-2,926; 9,443] 0,302	0,086 [-0,101; 0,273]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	228	211		
Baseline Mean (SD)	38,91 (39,462)	40,49 (41,094)		
Week 8:				
Adjusted Mean Change (SE)	8,52 (2,244)	12,07 (2,291)	-3,55 [-8,758; 1,652] 0,181	-0,107 [-0,297; 0,083]
Week 16:				
Adjusted Mean Change (SE)	16,06 (2,497)	17,95 (2,566)	-1,90 [-7,961; 4,169] 0,540	-0,051 [-0,239; 0,137]
Week 24:				
Adjusted Mean Change (SE)	19,22 (2,565)	19,91 (2,638)	-0,69 [-6,977; 5,594] 0,829	-0,018 [-0,209; 0,172]

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + patients' prior therapies + patients' prior therapies * treatment + patients' prior therapies * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

11. Exacerbations - Time-to-event Analysis

Table 11.1 Exacerbations - Time-to-event Analysis (FAS)

	Treatment groups		Comparison
Time-to-first outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
Asthma exacerbation			
N'	472	472	
Number of patients with at least one event, n (%)	115 (24,4)	127 (26,9)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	75,02 [70,97; 79,08]	72,70 [68,64; 76,75]	0,89 [0,69; 1,14] 0,356
Severe asthma exacerbation			
N'	472	472	
Number of patients with at least one event, n (%)	64 (13,6)	60 (12,7)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	85,92 [82,61; 89,23]	87,08 [84,03; 90,14]	1,06 [0,74; 1,51] 0,751
SCS use due to asthma exacerbation (for at least three consecutive days)			
N'	472	472	
Number of patients with at least one event, n (%)	68 (14,4)	64 (13,6)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	85,07 [81,69; 88,45]	86,20 [83,06; 89,34]	1,07 [0,76; 1,50] 0,717
ER visit and/or hospitalization due to asthma exacerbation			
N'	472	472	
Number of patients with at least one event, n (%)	8 (1,7)	5 (1,1)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	98,29 [97,12; 99,47]	98,93 [97,99; 99,86]	1,57 [0,51; 4,80] 0,429

	Treatment groups		Comparison
Time-to-first outcome (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
ER visit due to asthma exacerbation			
N'	472	472	
Number of patients with at least one event, n (%)	6 (1,3)	3 (0,6)	
Median (in weeks)	-	-	
% of outcome-free patients+	98,72 [97,70; 99,74]	99,36 [98,63; 100,00]	1,94 [0,49; 7,78] 0,347
Hospitalization due to asthma exacerbation			
N'	472	472	
Number of patients with at least one event, n (%)	3 (0,6)	2 (0,4)	
Median (in weeks)	-	-	
% of outcome-free patients+	99,36 [98,63; 100,00]	99,57 [98,98; 100,00]	1,50 [0,25; 8,96] 0,659

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: $p < 0,05$
+ K-M estimate (%) of outcome-free patients

Applied model for HR: log(hazard ratio) = treatment + region + background ICS/LABA + history of asthma exacerbation
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: B2306 FAS total population

Table 11.2 Exacerbations - Time-to-event Analysis by Age (FAS)

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
Asthma exacerbation			
Interaction Test:	p=0,401		
Age = 18-39 years			
N'	84	73	
Number of patients with at least one event, n (%)	17 (20,2)	11 (15,1)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	79,66 [71,03; 88,29]	84,89 [76,66; 93,12]	1,28 [0,60; 2,75] 0,518
Age = 40-64 years			
N'	288	305	
Number of patients with at least one event, n (%)	69 (24,0)	81 (26,6)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	75,07 [69,71; 80,42]	73,03 [68,00; 78,05]	0,92 [0,66; 1,26] 0,588
Age = ≥65 years			
N'	100	94	
Number of patients with at least one event, n (%)	29 (29,0)	35 (37,2)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	70,78 [61,83; 79,73]	62,00 [52,05; 71,94]	0,70 [0,43; 1,15] 0,157
Severe asthma exacerbation			
Interaction Test:	p=0,044 *		
Age = 18-39 years			
N'	84	73	
Number of patients with at least one event, n (%)	10 (11,9)	6 (8,2)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	88,02 [81,05; 94,99]	91,78 [85,48; 98,08]	1,50 [0,54; 4,13] 0,434

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
Age = 40-64 years			
N'	288	305	
Number of patients with at least one event, n (%)	43 (14,9)	35 (11,5)	
Median (in weeks)	-	-	
% of outcome-free patients+	84,19 [79,60; 88,79]	88,31 [84,67; 91,95]	1,34 [0,86; 2,10] 0,197
Age = ≥65 years			
N'	100	94	
Number of patients with at least one event, n (%)	11 (11,0)	19 (20,2)	
Median (in weeks)	-	-	
% of outcome-free patients+	88,94 [82,77; 95,10]	79,42 [71,16; 87,68]	0,46 [0,22; 0,98] 0,043 *
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,131		
Age = 18-39 years			
N'	84	73	
Number of patients with at least one event, n (%)	12 (14,3)	7 (9,6)	
Median (in weeks)	-	-	
% of outcome-free patients+	85,63 [78,11; 93,16]	90,39 [83,62; 97,16]	1,56 [0,62; 3,98] 0,347
Age = 40-64 years			
N'	288	305	
Number of patients with at least one event, n (%)	42 (14,6)	37 (12,1)	
Median (in weeks)	-	-	
% of outcome-free patients+	84,56 [80,01; 89,11]	87,63 [83,90; 91,36]	1,24 [0,80; 1,93] 0,345

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
Age = ≥65 years			
N'	100	94	
Number of patients with at least one event, n (%)	14 (14,0)	20 (21,3)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	85,91 [79,07; 92,75]	78,25 [69,81; 86,70]	0,58 [0,29; 1,16] 0,122
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,613		
Age = 18-39 years			
N'	84	73	
Number of patients with at least one event, n (%)	2 (2,4)	2 (2,7)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	97,60 [94,32; 100,00]	97,26 [93,52; 100,00]	0,88 [0,12; 6,26] 0,899
Age = 40-64 years			
N'	288	305	
Number of patients with at least one event, n (%)	5 (1,7)	2 (0,7)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	98,25 [96,73; 99,77]	99,33 [98,41; 100,00]	2,71 [0,53; 13,96] 0,234
Age = ≥65 years			
N'	100	94	
Number of patients with at least one event, n (%)	1 (1,0)	1 (1,1)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	99,00 [97,05; 100,00]	98,92 [96,83; 100,00]	0,80 [0,05; 12,80] 0,874

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
ER visit due to asthma exacerbation			
Interaction Test:	p=0,609		
Age = 18-39 years			
N'	84	73	
Number of patients with at least one event, n (%)	1 (1,2)	1 (1,4)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	98,81 [96,49; 100,00]	98,63 [95,96; 100,00]	0,92 [0,06; 14,67] 0,951
Age = 40-64 years			
N'	288	305	
Number of patients with at least one event, n (%)	5 (1,7)	1 (0,3)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	98,25 [96,73; 99,77]	99,67 [99,01; 100,00]	5,45 [0,64; 46,63] 0,122
Age = ≥65 years			
N'	100	94	
Number of patients with at least one event, n (%)	0 (0,0)	1 (1,1)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	100,00 [100,00; 100,00]	98,92 [96,83; 100,00]	0,00 [0,00; -] 0,994
Hospitalization due to asthma exacerbation			
Interaction Test:	p=0,982		
Age = 18-39 years			
N'	84	73	
Number of patients with at least one event, n (%)	1 (1,2)	1 (1,4)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	98,80 [96,45; 100,00]	98,63 [95,96; 100,00]	0,74 [0,05; 11,99] 0,834

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
Age = 40-64 years			
N'	288	305	
Number of patients with at least one event, n (%)	1 (0,3)	1 (0,3)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	99,64 [98,94; 100,00]	99,67 [99,01; 100,00]	1,08 [0,07; 17,33] 0,955
Age = ≥65 years			
N'	100	94	
Number of patients with at least one event, n (%)	1 (1,0)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	99,00 [97,05; 100,00]	100,00 [100,00; 100,00]	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: $p < 0,05$
[+] K-M estimate (%) of outcome-free patients

Applied model for HR: log(hazard ratio) = treatment + region + background ICS/LABA + history of asthma exacerbation + age + age * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: B2306 FAS total population

Table 11.3 Exacerbations - Time-to-event Analysis by Gender (FAS)

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
Asthma exacerbation			
Interaction Test:	p=0,529		
Gender = Male			
N'	185	169	
Number of patients with at least one event, n (%)	45 (24,3)	42 (24,9)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	75,43 [69,19; 81,67]	75,07 [68,54; 81,61]	0,99 [0,65; 1,51] 0,967
Gender = Female			
N'	287	303	
Number of patients with at least one event, n (%)	70 (24,4)	85 (28,1)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	74,66 [69,25; 80,06]	71,35 [66,20; 76,50]	0,84 [0,61; 1,15] 0,269
Severe asthma exacerbation			
Interaction Test:	p=0,544		
Gender = Male			
N'	185	169	
Number of patients with at least one event, n (%)	26 (14,1)	20 (11,8)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	85,80 [80,74; 90,86]	88,13 [83,25; 93,02]	1,22 [0,68; 2,19] 0,500
Gender = Female			
N'	287	303	
Number of patients with at least one event, n (%)	38 (13,2)	40 (13,2)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	85,85 [81,35; 90,34]	86,49 [82,59; 90,39]	0,97 [0,62; 1,52] 0,907

Time-to-first outcome by subgroup (FAS)	Treatment groups: IND/GLY/ MF 160 N=476	Treatment groups: SAL/FLU + TIO N=475	Comparison: HR [95% CI] p-value
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,567		
Gender = Male			
N'	185	169	
Number of patients with at least one event, n (%)	26 (14,1)	20 (11,8)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	85,81 [80,75; 90,86]	88,13 [83,24; 93,01]	1,23 [0,68; 2,20] 0,494
Gender = Female			
N'	287	303	
Number of patients with at least one event, n (%)	42 (14,6)	44 (14,5)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	84,46 [79,85; 89,08]	85,10 [81,03; 89,16]	0,99 [0,65; 1,52] 0,974
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,705		
Gender = Male			
N'	185	169	
Number of patients with at least one event, n (%)	1 (0,5)	1 (0,6)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	99,46 [98,40; 100,00]	99,41 [98,25; 100,00]	0,96 [0,06; 15,43] 0,980
Gender = Female			
N'	287	303	
Number of patients with at least one event, n (%)	7 (2,4)	4 (1,3)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	97,54 [95,74; 99,34]	98,65 [97,34; 99,96]	1,73 [0,51; 5,93] 0,380

Time-to-first outcome by subgroup (FAS)	Treatment groups: IND/GLY/ MF 160 N=476	Treatment groups: SAL/FLU + TIO N=475	Comparison: HR [95% CI] p-value
ER visit due to asthma exacerbation			
Interaction Test:	p=0,994		
Gender = Male			
N'	185	169	
Number of patients with at least one event, n (%)	1 (0,5)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	99,46 [98,40; 100,00]	100,00 [100,00; 100,00]	-
Gender = Female			
N'	287	303	
Number of patients with at least one event, n (%)	5 (1,7)	3 (1,0)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	98,24 [96,71; 99,77]	98,99 [97,86; 100,00]	1,64 [0,39; 6,85] 0,500
Hospitalization due to asthma exacerbation			
Interaction Test:	p=0,993		
Gender = Male			
N'	185	169	
Number of patients with at least one event, n (%)	0 (0,0)	1 (0,6)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	100,00 [100,00; 100,00]	99,41 [98,25; 100,00]	0,00 [0,00; -] 0,993

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
Gender = Female			
N'	287	303	
Number of patients with at least one event, n (%)	3 (1,0)	1 (0,3)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	98,94 [97,74; 100,00]	99,66 [99,00; 100,00]	3,02 [0,31; 29,02] 0,339

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: $p < 0,05$
[+] K-M estimate (%) of outcome-free patients

Applied model for HR: log(hazard ratio) = treatment + region + background ICS/LABA + history of asthma exacerbation + gender + gender * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: B2306 FAS total population

Table 11.4 Exacerbations - Time-to-event Analysis by Region (FAS)

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
Asthma exacerbation			
Interaction Test:	p=0,872		
Region = Asia			
N'	123	131	
Number of patients with at least one event, n (%)	41 (33,3)	46 (35,1)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	65,25 [56,24; 74,26]	64,51 [56,26; 72,76]	0,95 [0,62; 1,45] 0,820
Region = Europe			
N'	164	168	
Number of patients with at least one event, n (%)	39 (23,8)	41 (24,4)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	76,01 [69,44; 82,58]	75,38 [68,83; 81,93]	0,99 [0,64; 1,53] 0,947
Region = Latin America			
N'	165	164	
Number of patients with at least one event, n (%)	31 (18,8)	38 (23,2)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	81,02 [75,00; 87,04]	76,28 [69,69; 82,87]	0,76 [0,47; 1,22] 0,262
Region = Others			
N'	20	9	
Number of patients with at least one event, n (%)	4 (20,0)	2 (22,2)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	80,00 [62,47; 97,53]	77,78 [50,62; 100,00]	0,86 [0,16; 4,68] 0,858

Time-to-first outcome by subgroup (FAS)	Treatment groups: IND/GLY/ MF 160 N=476	Treatment groups: SAL/FLU + TIO N=475	Comparison: HR [95% CI] p-value
Severe asthma exacerbation			
Interaction Test:	p=0,463		
Region = Asia			
N'	123	131	
Number of patients with at least one event, n (%)	19 (15,4)	12 (9,2)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	83,38 [76,19; 90,56]	90,75 [85,76; 95,74]	1,76 [0,85; 3,62] 0,127
Region = Europe			
N'	164	168	
Number of patients with at least one event, n (%)	19 (11,6)	20 (11,9)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	88,31 [83,36; 93,25]	87,99 [83,05; 92,93]	0,98 [0,52; 1,83] 0,945
Region = Latin America			
N'	165	164	
Number of patients with at least one event, n (%)	24 (14,5)	27 (16,5)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	85,30 [79,87; 90,73]	83,11 [77,30; 88,92]	0,85 [0,49; 1,47] 0,562
Region = Others			
N'	20	9	
Number of patients with at least one event, n (%)	2 (10,0)	1 (11,1)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	90,00 [76,85; 100,00]	88,89 [68,36; 100,00]	0,91 [0,08; 10,00] 0,936

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,573		
Region = Asia			
N'	123	131	
Number of patients with at least one event, n (%)	19 (15,4)	13 (9,9)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	83,38 [76,19; 90,56]	89,93 [84,74; 95,12]	1,63 [0,80; 3,30] 0,176
Region = Europe			
N'	164	168	
Number of patients with at least one event, n (%)	20 (12,2)	23 (13,7)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	87,70 [82,65; 92,75]	86,16 [80,91; 91,41]	0,90 [0,49; 1,64] 0,726
Region = Latin America			
N'	165	164	
Number of patients with at least one event, n (%)	26 (15,8)	27 (16,5)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	84,08 [78,46; 89,69]	83,11 [77,29; 88,92]	0,93 [0,54; 1,60] 0,795
Region = Others			
N'	20	9	
Number of patients with at least one event, n (%)	3 (15,0)	1 (11,1)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	85,00 [69,35; 100,00]	88,89 [68,36; 100,00]	1,41 [0,15; 13,59] 0,765

Time-to-first outcome by subgroup (FAS)	Treatment groups: IND/GLY/ MF 160 N=476	Treatment groups: SAL/FLU + TIO N=475	Comparison: HR [95% CI] p-value
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,978		
Region = Asia			
N'	123	131	
Number of patients with at least one event, n (%)	2 (1,6)	1 (0,8)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	98,36 [96,11; 100,00]	99,22 [97,71; 100,00]	2,17 [0,20; 23,94] 0,527
Region = Europe			
N'	164	168	
Number of patients with at least one event, n (%)	1 (0,6)	1 (0,6)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	99,37 [98,14; 100,00]	99,40 [98,24; 100,00]	1,02 [0,06; 16,23] 0,992
Region = Latin America			
N'	165	164	
Number of patients with at least one event, n (%)	4 (2,4)	3 (1,8)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	97,56 [95,21; 99,92]	98,13 [96,04; 100,00]	1,25 [0,28; 5,60] 0,769
Region = Others			
N'	20	9	
Number of patients with at least one event, n (%)	1 (5,0)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	95,00 [85,45; 100,00]	100,00 [100,00; 100,00]	-

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
ER visit due to asthma exacerbation			
Interaction Test:	p=1,000		
Region = Asia			
N'	123	131	
Number of patients with at least one event, n (%)	0 (0,0)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]	1,02 [0,00; -] 1,000
Region = Europe			
N'	164	168	
Number of patients with at least one event, n (%)	1 (0,6)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	99,37 [98,14; 100,00]	100,00 [100,00; 100,00]	-
Region = Latin America			
N'	165	164	
Number of patients with at least one event, n (%)	4 (2,4)	3 (1,8)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	97,56 [95,21; 99,92]	98,13 [96,04; 100,00]	1,23 [0,28; 5,51] 0,785
Region = Others			
N'	20	9	
Number of patients with at least one event, n (%)	1 (5,0)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	95,00 [85,45; 100,00]	100,00 [100,00; 100,00]	-

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
Hospitalization due to asthma exacerbation			
Interaction Test:	p=0,984		
Region = Asia			
N'	123	131	
Number of patients with at least one event, n (%)	2 (1,6)	1 (0,8)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	98,36 [96,11; 100,00]	99,22 [97,71; 100,00]	2,16 [0,20; 23,79] 0,530
Region = Europe			
N'	164	168	
Number of patients with at least one event, n (%)	1 (0,6)	1 (0,6)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	99,37 [98,14; 100,00]	99,40 [98,24; 100,00]	1,02 [0,06; 16,25] 0,991
Region = Latin America			
N'	165	164	
Number of patients with at least one event, n (%)	0 (0,0)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]	0,97 [0,00; -] 1,000

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
Region = Others			
N'	20	9	
Number of patients with at least one event, n (%)	0 (0,0)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	100,00 [100,00; 100,00]	100,00 [100,00; 100,00]	0,97 [0,00; -] 1,000

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: $p < 0,05$
[+] K-M estimate (%) of outcome-free patients

Applied model for HR: log(hazard ratio) = treatment + background ICS/LABA + history of asthma exacerbation + region + region * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: B2306 FAS total population

Table 11.5 Exacerbations - Time-to-event Analysis by History of Asthma Exacerbation (FAS)

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
Asthma exacerbation			
Interaction Test:	p=0,885		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	382	
Number of patients with at least one event, n (%)	82 (22,0)	94 (24,6)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	77,26 [72,77; 81,74]	75,02 [70,65; 79,40]	0,87 [0,65; 1,17] 0,359
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	100	90	
Number of patients with at least one event, n (%)	33 (33,0)	33 (36,7)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	66,64 [57,33; 75,94]	62,87 [52,80; 72,93]	0,91 [0,56; 1,47] 0,694
Severe asthma exacerbation			
Interaction Test:	p=0,794		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	382	
Number of patients with at least one event, n (%)	41 (11,0)	39 (10,2)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	88,36 [84,84; 91,88]	89,63 [86,54; 92,71]	1,08 [0,69; 1,67] 0,743

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	100	90	
Number of patients with at least one event, n (%)	23 (23,0)	21 (23,3)	
Median (in weeks)	-	-	
% of outcome-free patients+	76,76 [68,43; 85,08]	76,37 [67,52; 85,21]	0,98 [0,54; 1,76] 0,934
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,648		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	382	
Number of patients with at least one event, n (%)	44 (11,8)	41 (10,7)	
Median (in weeks)	-	-	
% of outcome-free patients+	87,55 [83,93; 91,16]	89,08 [85,92; 92,23]	1,11 [0,72; 1,70] 0,637
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	100	90	
Number of patients with at least one event, n (%)	24 (24,0)	23 (25,6)	
Median (in weeks)	-	-	
% of outcome-free patients+	75,73 [67,28; 84,19]	74,07 [64,94; 83,20]	0,94 [0,53; 1,66] 0,827
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,992		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	382	
Number of patients with at least one event, n (%)	3 (0,8)	5 (1,3)	
Median (in weeks)	-	-	
% of outcome-free patients+	99,19 [98,28; 100,00]	98,68 [97,52; 99,83]	0,61 [0,15; 2,55] 0,496

Time-to-first outcome by subgroup (FAS)	Treatment groups: IND/GLY/ MF 160 N=476	Treatment groups: SAL/FLU + TIO N=475	Comparison: HR [95% CI] p-value
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	100	90	
Number of patients with at least one event, n (%)	5 (5,0)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients+	94,88 [90,51; 99,25]	100,00 [100,00; 100,00]	-
ER visit due to asthma exacerbation			
Interaction Test:	p=0,996		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	382	
Number of patients with at least one event, n (%)	2 (0,5)	3 (0,8)	
Median (in weeks)	-	-	
% of outcome-free patients+	99,46 [98,72; 100,00]	99,20 [98,31; 100,00]	0,67 [0,11; 4,01] 0,661
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	100	90	
Number of patients with at least one event, n (%)	4 (4,0)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients+	95,91 [91,99; 99,84]	100,00 [100,00; 100,00]	-
Hospitalization due to asthma exacerbation			
Interaction Test:	p=0,996		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	382	
Number of patients with at least one event, n (%)	1 (0,3)	2 (0,5)	
Median (in weeks)	-	-	
% of outcome-free patients+	99,73 [99,21; 100,00]	99,47 [98,74; 100,00]	0,51 [0,05; 5,65] 0,585

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	100	90	
Number of patients with at least one event, n (%)	2 (2,0)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	97,92 [95,06; 100,00]	100,00 [100,00; 100,00]	-

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: $p < 0,05$
[+] K-M estimate (%) of outcome-free patients

Applied model for HR: log(hazard ratio) = treatment + region + background ICS/LABA + history of asthma exacerbation + history of asthma exacerbation * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: B2306 FAS total population

Table 11.6 Exacerbations - Time-to-event Analysis by Patients' Prior Therapies (FAS)

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**HR [95% CI] p-value**
Asthma exacerbation			
Interaction Test:	p=0,020 *		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	240	
Number of patients with at least one event, n (%)	44 (19,1)	67 (27,9)	
Median (in weeks)	-	-	
% of outcome-free patients+	80,74 [75,62; 85,86]	71,78 [66,05; 77,51]	0,64 [0,44; 0,93] 0,020 *
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	242	232	
Number of patients with at least one event, n (%)	71 (29,3)	60 (25,9)	
Median (in weeks)	-	-	
% of outcome-free patients+	69,49 [63,26; 75,72]	73,64 [67,91; 79,37]	1,17 [0,83; 1,65] 0,368
Severe asthma exacerbation			
Interaction Test:	p=0,026 *		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	240	
Number of patients with at least one event, n (%)	21 (9,1)	32 (13,3)	
Median (in weeks)	-	-	
% of outcome-free patients+	90,79 [87,04; 94,55]	86,49 [82,13; 90,84]	0,66 [0,38; 1,15] 0,140
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	242	232	
Number of patients with at least one event, n (%)	43 (17,8)	28 (12,1)	
Median (in weeks)	-	-	
% of outcome-free patients+	81,17 [75,76; 86,57]	87,70 [83,43; 91,97]	1,51 [0,94; 2,43] 0,091

Time-to-first outcome by subgroup (FAS)	Treatment groups: IND/GLY/ MF 160 N=476	Treatment groups: SAL/FLU + TIO N=475	Comparison: HR [95% CI] p-value
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,107		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	240	
Number of patients with at least one event, n (%)	25 (10,9)	33 (13,8)	
Median (in weeks)	-	-	
% of outcome-free patients+	89,05 [85,00; 93,10]	86,05 [81,63; 90,47]	0,77 [0,46; 1,30] 0,332
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	242	232	
Number of patients with at least one event, n (%)	43 (17,8)	31 (13,4)	
Median (in weeks)	-	-	
% of outcome-free patients+	81,17 [75,76; 86,58]	86,35 [81,88; 90,82]	1,37 [0,86; 2,17] 0,182
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,619		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	240	
Number of patients with at least one event, n (%)	2 (0,9)	2 (0,8)	
Median (in weeks)	-	-	
% of outcome-free patients+	99,13 [97,93; 100,00]	99,16 [98,00; 100,00]	1,04 [0,15; 7,38] 0,969
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	242	232	
Number of patients with at least one event, n (%)	6 (2,5)	3 (1,3)	
Median (in weeks)	-	-	
% of outcome-free patients+	97,49 [95,51; 99,47]	98,69 [97,21; 100,00]	1,91 [0,48; 7,65] 0,359

Time-to-first outcome by subgroup (FAS)	Treatment groups: IND/GLY/ MF 160 N=476	Treatment groups: SAL/FLU + TIO N=475	Comparison: HR [95% CI] p-value
ER visit due to asthma exacerbation			
Interaction Test:	p=0,610		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	240	
Number of patients with at least one event, n (%)	1 (0,4)	1 (0,4)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	99,57 [98,71; 100,00]	99,58 [98,76; 100,00]	1,03 [0,06; 16,51] 0,982
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	242	232	
Number of patients with at least one event, n (%)	5 (2,1)	2 (0,9)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	97,91 [96,10; 99,72]	99,12 [97,91; 100,00]	2,39 [0,46; 12,30] 0,298
Hospitalization due to asthma exacerbation			
Interaction Test:	p=0,750		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	240	
Number of patients with at least one event, n (%)	1 (0,4)	1 (0,4)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	99,57 [98,71; 100,00]	99,58 [98,76; 100,00]	1,05 [0,07; 16,81] 0,972

Time-to-first outcome by subgroup (FAS)	Treatment groups: IND/GLY/MF 160 N=476	Treatment groups: SAL/FLU + TIO N=475	Comparison: HR [95% CI] p-value
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	242	232	
Number of patients with at least one event, n (%)	2 (0,8)	1 (0,4)	
Median (in weeks)	-	-	
% of outcome-free patients[+]	99,15 [97,98; 100,00]	99,57 [98,71; 100,00]	1,91 [0,17; 21,06] 0,597

N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
*: $p < 0,05$
[+] K-M estimate (%) of outcome-free patients

Applied model for HR: log(hazard ratio) = treatment + region + history of asthma exacerbation + patients' prior therapies + patients' prior therapies * treatment
If it was not possible to fit the minimal model, the HR is not given.

Analysis population: B2306 FAS total population

12. Exacerbations - Annualized Exacerbation Rate

Table 12.1 Exacerbations - Annualized Exacerbation Rate (FAS)

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
Asthma exacerbation			
N'	472	472	
Number of patients with outcome	115	127	
Number of outcomes	160	200	
Annualized Rate [95% CI]	0,71 [0,59; 0,87]	0,89 [0,74; 1,07]	0,80 [0,62; 1,05] 0,103
Severe asthma exacerbation			
N'	472	472	
Number of patients with outcome	64	60	
Number of outcomes	81	73	
Annualized Rate [95% CI]	0,37 [0,29; 0,48]	0,35 [0,27; 0,45]	1,09 [0,75; 1,57] 0,659
SCS use due to asthma exacerbation (for at least three consecutive days)			
N'	472	472	
Number of patients with outcome	68	64	
Number of outcomes	84	75	
Annualized Rate [95% CI]	0,39 [0,30; 0,49]	0,35 [0,27; 0,45]	1,12 [0,79; 1,58] 0,539
ER visit and/or hospitalization due to asthma exacerbation			
N'	472	472	
Number of patients with outcome	6	3	
Number of outcomes	8	3	
Annualized Rate [95% CI]	0,03 [0,01; 0,07]	0,01 [0,00; 0,04]	2,51 [0,62; 10,13] 0,197

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
ER visit due to asthma exacerbation			
N'	472	472	
Number of patients with outcome	6	3	
Number of outcomes	8	3	
Annualized Rate [95% CI]	0,03 [0,01; 0,07]	0,01 [0,00; 0,04]	2,51 [0,62; 10,13] 0,197
Hospitalization due to asthma exacerbation			
N'	472	472	
Number of patients with outcome	3	2	
Number of outcomes	3	2	
Annualized Rate [95% CI]	0,01 [0,00; 0,04]	0,01 [0,00; 0,04]	1,48 [0,25; 8,86] 0,668

N': Number of patients in the analysis
CI: Confidence Interval
RR: Rate Ratio
*: $p < 0,05$

Annualized Rate and Rate Ratio are calculated based on negative binomial regression model.
Applied model for Annualized Rate/Rate Ratio: Number of events = treatment + region + background ICS/LABA + history of asthma exacerbation, offset variable: log(exposure in years)
Exceptional model(s) for Annualized Rate/Rate Ratio: Number of events = treatment + background ICS/LABA + history of asthma exacerbation (for Severe asthma exacerbation), treatment + background ICS/LABA + history of asthma exacerbation (for ER visit and/or hospitalization due to asthma exacerbation), treatment + background ICS/LABA + history of asthma exacerbation (for ER visit due to asthma exacerbation), treatment + background ICS/LABA + history of asthma exacerbation (for Hospitalization due to asthma exacerbation), offset variable: log(exposure in years)
If it was not possible to fit the minimal model, the Annualized Rate and Rate Ratio are not given.

Analysis population: B2306 FAS total population

Table 12.2 Exacerbations - Annualized Exacerbation Rate by Age (FAS)

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
Asthma exacerbation			
Interaction Test:	p=0,447		
Age = 18-39 years			
N'	84	73	
Number of patients with outcome	17	11	
Number of outcomes	20	16	
Annualized Rate [95% CI]	0,54 [0,32; 0,90]	0,52 [0,29; 0,92]	1,04 [0,48; 2,23] 0,926
Age = 40-64 years			
N'	288	305	
Number of patients with outcome	69	81	
Number of outcomes	101	127	
Annualized Rate [95% CI]	0,75 [0,59; 0,96]	0,87 [0,69; 1,09]	0,87 [0,62; 1,21] 0,395
Age = ≥65 years			
N'	100	94	
Number of patients with outcome	29	35	
Number of outcomes	39	57	
Annualized Rate [95% CI]	0,75 [0,50; 1,12]	1,23 [0,85; 1,77]	0,61 [0,36; 1,05] 0,073
Severe asthma exacerbation			
Interaction Test:	p=0,092		
Age = 18-39 years			
N'	84	73	
Number of patients with outcome	10	6	
Number of outcomes	12	8	
Annualized Rate [95% CI]	0,28 [0,15; 0,54]	0,22 [0,10; 0,48]	1,27 [0,47; 3,42] 0,641

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
Age = 40-64 years			
N'	288	305	
Number of patients with outcome	43	35	
Number of outcomes	55	42	
Annualized Rate [95% CI]	0,43 [0,31; 0,58]	0,30 [0,21; 0,42]	1,42 [0,90; 2,26] 0,132
Age = ≥65 years			
N'	100	94	
Number of patients with outcome	11	19	
Number of outcomes	14	23	
Annualized Rate [95% CI]	0,29 [0,16; 0,52]	0,55 [0,33; 0,90]	0,53 [0,24; 1,14] 0,103
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,196		
Age = 18-39 years			
N'	84	73	
Number of patients with outcome	12	7	
Number of outcomes	12	9	
Annualized Rate [95% CI]	0,29 [0,16; 0,54]	0,25 [0,12; 0,51]	1,17 [0,46; 2,99] 0,748
Age = 40-64 years			
N'	288	305	
Number of patients with outcome	42	37	
Number of outcomes	54	42	
Annualized Rate [95% CI]	0,42 [0,31; 0,57]	0,30 [0,22; 0,42]	1,39 [0,89; 2,18] 0,147
Age = ≥65 years			
N'	100	94	
Number of patients with outcome	14	20	
Number of outcomes	18	24	
Annualized Rate [95% CI]	0,38 [0,23; 0,63]	0,58 [0,36; 0,93]	0,65 [0,32; 1,30] 0,226

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,897		
Age = 18-39 years			
N'	84	73	
Number of patients with outcome	1	1	
Number of outcomes	3	1	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	2,56 [0,24; 27,87] 0,440
Age = 40-64 years			
N'	288	305	
Number of patients with outcome	5	1	
Number of outcomes	5	1	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	5,54 [0,62; 49,77] 0,127
Age = ≥65 years			
N'	100	94	
Number of patients with outcome	0	1	
Number of outcomes	0	1	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	0,00 [0,00; -] 0,994
ER visit due to asthma exacerbation			
Interaction Test:	p=0,897		
Age = 18-39 years			
N'	84	73	
Number of patients with outcome	1	1	
Number of outcomes	3	1	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	2,56 [0,24; 27,87] 0,440

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
Age = 40-64 years			
N'	288	305	
Number of patients with outcome	5	1	
Number of outcomes	5	1	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	5,54 [0,62; 49,77] 0,127
Age = ≥65 years			
N'	100	94	
Number of patients with outcome	0	1	
Number of outcomes	0	1	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	0,00 [0,00; -] 0,994
Hospitalization due to asthma exacerbation			
Interaction Test:	p=0,995		
Age = 18-39 years			
N'	84	73	
Number of patients with outcome	1	1	
Number of outcomes	1	1	
Annualized Rate [95% CI]	0,03 [0,00; 0,19]	0,03 [0,00; 0,21]	0,88 [0,05; 14,02] 0,926
Age = 40-64 years			
N'	288	305	
Number of patients with outcome	1	1	
Number of outcomes	1	1	
Annualized Rate [95% CI]	0,01 [0,00; 0,05]	0,01 [0,00; 0,05]	1,06 [0,07; 16,88] 0,969

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
Age = ≥65 years			
N'	100	94	
Number of patients with outcome	1	0	
Number of outcomes	1	0	
Annualized Rate [95% CI]	0,02 [0,00; 0,15]	0,00 [0,00; -]	-

N': Number of patients in the analysis
CI: Confidence Interval
RR: Rate Ratio
*: $p < 0,05$

Annualized Rate and Rate Ratio are calculated based on negative binomial regression model.
Applied model for Annualized Rate/Rate Ratio: Number of events = treatment + region + background ICS/LABA + history of asthma exacerbation + age + age * treatment, offset variable: log(exposure in years)
Exceptional model(s) for Annualized Rate/Rate Ratio: Number of events = treatment + history of asthma exacerbation + age + age * treatment (for Hospitalization due to asthma exacerbation), offset variable: log(exposure in years)
If it was not possible to fit the minimal model, the Annualized Rate and Rate Ratio are not given.

Analysis population: B2306 FAS total population

Table 12.3 Exacerbations - Annualized Exacerbation Rate by Gender (FAS)

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
Asthma exacerbation			
Interaction Test:	p=0,927		
Gender = Male			
N'	185	169	
Number of patients with outcome	45	42	
Number of outcomes	57	67	
Annualized Rate [95% CI]	0,67 [0,48; 0,92]	0,81 [0,60; 1,11]	0,82 [0,53; 1,27] 0,375
Gender = Female			
N'	287	303	
Number of patients with outcome	70	85	
Number of outcomes	103	133	
Annualized Rate [95% CI]	0,74 [0,58; 0,95]	0,93 [0,74; 1,16]	0,80 [0,57; 1,11] 0,179
Severe asthma exacerbation			
Interaction Test:	p=0,426		
Gender = Male			
N'	185	169	
Number of patients with outcome	26	20	
Number of outcomes	32	22	
Annualized Rate [95% CI]	0,38 [0,25; 0,57]	0,28 [0,18; 0,45]	1,35 [0,73; 2,51] 0,340
Gender = Female			
N'	287	303	
Number of patients with outcome	38	40	
Number of outcomes	49	51	
Annualized Rate [95% CI]	0,36 [0,26; 0,50]	0,37 [0,27; 0,50]	0,99 [0,63; 1,56] 0,963

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,384		
Gender = Male			
N'	185	169	
Number of patients with outcome	26	20	
Number of outcomes	33	22	
Annualized Rate [95% CI]	0,39 [0,27; 0,57]	0,28 [0,18; 0,44]	1,39 [0,76; 2,53] 0,280
Gender = Female			
N'	287	303	
Number of patients with outcome	42	44	
Number of outcomes	51	53	
Annualized Rate [95% CI]	0,39 [0,28; 0,53]	0,38 [0,28; 0,52]	1,00 [0,65; 1,54] 0,996
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,992		
Gender = Male			
N'	185	169	
Number of patients with outcome	1	0	
Number of outcomes	1	0	
Annualized Rate [95% CI]	-	0,00 [0,00; -]	-
Gender = Female			
N'	287	303	
Number of patients with outcome	5	3	
Number of outcomes	7	3	
Annualized Rate [95% CI]	-	-	2,25 [0,53; 9,50] 0,270

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
ER visit due to asthma exacerbation			
Interaction Test:	p=0,992		
Gender = Male			
N'	185	169	
Number of patients with outcome	1	0	
Number of outcomes	1	0	
Annualized Rate [95% CI]	-	0,00 [0,00; -]	-
Gender = Female			
N'	287	303	
Number of patients with outcome	5	3	
Number of outcomes	7	3	
Annualized Rate [95% CI]	-	-	2,25 [0,53; 9,50] 0,270
Hospitalization due to asthma exacerbation			
Interaction Test:	p=0,953		
Gender = Male			
N'	185	169	
Number of patients with outcome	0	1	
Number of outcomes	0	1	
Annualized Rate [95% CI]	-	0,01 [0,00; 0,09]	-
Gender = Female			
N'	287	303	
Number of patients with outcome	3	1	
Number of outcomes	3	1	
Annualized Rate [95% CI]	0,02 [0,01; 0,07]	0,01 [0,00; 0,05]	3,09 [0,32; 29,75] 0,328

N': Number of patients in the analysis
CI: Confidence Interval
RR: Rate Ratio
*: $p < 0,05$

Annualized Rate and Rate Ratio are calculated based on negative binomial regression model.
Applied model for Annualized Rate/Rate Ratio: Number of events = treatment + region + background ICS/LABA + history of asthma exacerbation + gender + gender * treatment, offset variable: log(exposure in years)
Exceptional model(s) for Annualized Rate/Rate Ratio: Number of events = treatment + background ICS/LABA + history of asthma exacerbation + gender + gender * treatment (for Hospitalization due to asthma exacerbation), offset variable: log(exposure in years)
If it was not possible to fit the minimal model, the Annualized Rate and Rate Ratio are not given.

Analysis population: B2306 FAS total population

Table 12.4 Exacerbations - Annualized Exacerbation Rate by Region (FAS)

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
Asthma exacerbation			
Interaction Test:	p=0,411		
Region = Asia			
N'	123	131	
Number of patients with outcome	41	46	
Number of outcomes	60	84	
Annualized Rate [95% CI]	1,09 [0,78; 1,52]	1,42 [1,05; 1,92]	0,77 [0,49; 1,21] 0,254
Region = Europe			
N'	164	168	
Number of patients with outcome	39	41	
Number of outcomes	53	48	
Annualized Rate [95% CI]	0,72 [0,52; 1,01]	0,65 [0,47; 0,92]	1,10 [0,69; 1,78] 0,682
Region = Latin America			
N'	165	164	
Number of patients with outcome	31	38	
Number of outcomes	42	65	
Annualized Rate [95% CI]	0,55 [0,38; 0,78]	0,88 [0,64; 1,19]	0,62 [0,39; 1,00] 0,050
Region = Others			
N'	20	9	
Number of patients with outcome	4	2	
Number of outcomes	5	3	
Annualized Rate [95% CI]	0,55 [0,20; 1,55]	0,75 [0,19; 3,02]	0,74 [0,13; 4,15] 0,730

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
Severe asthma exacerbation			
Interaction Test:	p=0,332		
Region = Asia			
N'	123	131	
Number of patients with outcome	19	12	
Number of outcomes	22	12	
Annualized Rate [95% CI]	0,41 [0,25; 0,66]	0,20 [0,11; 0,37]	2,01 [0,92; 4,40] 0,080
Region = Europe			
N'	164	168	
Number of patients with outcome	19	20	
Number of outcomes	24	23	
Annualized Rate [95% CI]	0,33 [0,21; 0,51]	0,31 [0,20; 0,50]	1,04 [0,55; 1,99] 0,904
Region = Latin America			
N'	165	164	
Number of patients with outcome	24	27	
Number of outcomes	32	36	
Annualized Rate [95% CI]	0,41 [0,27; 0,61]	0,48 [0,33; 0,71]	0,84 [0,48; 1,48] 0,548
Region = Others			
N'	20	9	
Number of patients with outcome	2	1	
Number of outcomes	3	2	
Annualized Rate [95% CI]	0,34 [0,10; 1,24]	0,52 [0,10; 2,72]	0,66 [0,08; 5,34] 0,698

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,483		
Region = Asia			
N'	123	131	
Number of patients with outcome	19	13	
Number of outcomes	22	13	
Annualized Rate [95% CI]	0,40 [0,25; 0,64]	0,22 [0,12; 0,39]	1,84 [0,87; 3,90] 0,109
Region = Europe			
N'	164	168	
Number of patients with outcome	20	23	
Number of outcomes	25	25	
Annualized Rate [95% CI]	0,34 [0,22; 0,53]	0,34 [0,22; 0,52]	1,02 [0,55; 1,87] 0,962
Region = Latin America			
N'	165	164	
Number of patients with outcome	26	27	
Number of outcomes	33	35	
Annualized Rate [95% CI]	0,43 [0,29; 0,63]	0,47 [0,32; 0,69]	0,90 [0,52; 1,56] 0,713
Region = Others			
N'	20	9	
Number of patients with outcome	3	1	
Number of outcomes	4	2	
Annualized Rate [95% CI]	0,45 [0,15; 1,38]	0,51 [0,10; 2,51]	0,89 [0,13; 6,19] 0,905
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	N.E.		
Region = Asia			
N'	123	131	
Number of patients with outcome	0	0	
Number of outcomes	0	0	
Annualized Rate [95% CI]	-	-	-

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
Region = Europe			
N'	164	168	
Number of patients with outcome	1	0	
Number of outcomes	1	0	
Annualized Rate [95% CI]	-	-	-
Region = Latin America			
N'	165	164	
Number of patients with outcome	4	3	
Number of outcomes	6	3	
Annualized Rate [95% CI]	0,08 [0,04; 0,18]	0,04 [0,01; 0,12]	1,97 [0,49; 7,89] 0,337
Region = Others			
N'	20	9	
Number of patients with outcome	1	0	
Number of outcomes	1	0	
Annualized Rate [95% CI]	0,11 [0,02; 0,76]	0,00 [0,00; -]	-
ER visit due to asthma exacerbation			
Interaction Test:	N.E.		
Region = Asia			
N'	123	131	
Number of patients with outcome	0	0	
Number of outcomes	0	0	
Annualized Rate [95% CI]	-	-	-
Region = Europe			
N'	164	168	
Number of patients with outcome	1	0	
Number of outcomes	1	0	
Annualized Rate [95% CI]	-	-	-
Region = Latin America			
N'	165	164	
Number of patients with outcome	4	3	
Number of outcomes	6	3	
Annualized Rate [95% CI]	0,08 [0,04; 0,18]	0,04 [0,01; 0,12]	1,97 [0,49; 7,89] 0,337

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
Region = Others			
N'	20	9	
Number of patients with outcome	1	0	
Number of outcomes	1	0	
Annualized Rate [95% CI]	0,11 [0,02; 0,76]	0,00 [0,00; -]	-
Hospitalization due to asthma exacerbation			
Interaction Test:	N.E.		
Region = Asia			
N'	123	131	
Number of patients with outcome	2	1	
Number of outcomes	2	1	
Annualized Rate [95% CI]	0,04 [0,01; 0,14]	0,02 [0,00; 0,12]	2,13 [0,19; 23,50] 0,537
Region = Europe			
N'	164	168	
Number of patients with outcome	1	1	
Number of outcomes	1	1	
Annualized Rate [95% CI]	0,01 [0,00; 0,10]	0,01 [0,00; 0,09]	1,01 [0,06; 16,11] 0,996
Region = Latin America			
N'	165	164	
Number of patients with outcome	0	0	
Number of outcomes	0	0	
Annualized Rate [95% CI]	-	-	-

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
Region = Others			
N'	20	9	
Number of patients with outcome	0	0	
Number of outcomes	0	0	
Annualized Rate [95% CI]	-	-	-

N': Number of patients in the analysis
CI: Confidence Interval
RR: Rate Ratio
*: $p < 0,05$

Annualized Rate and Rate Ratio are calculated based on negative binomial regression model.
Applied model for Annualized Rate/Rate Ratio: Number of events = treatment + background ICS/LABA + history of asthma exacerbation + region + region * treatment, offset variable: log(exposure in years)
Exceptional model(s) for Annualized Rate/Rate Ratio: Number of events = treatment + history of asthma exacerbation [by region] (for ER visit and/or hospitalization due to asthma exacerbation), treatment + history of asthma exacerbation [by region] (for ER visit due to asthma exacerbation), treatment + history of asthma exacerbation [by region] (for Hospitalization due to asthma exacerbation), offset variable: log(exposure in years)
If it was not possible to fit the minimal model, the Annualized Rate and Rate Ratio are not given.

Analysis population: B2306 FAS total population

Table 12.5 Exacerbations - Annualized Exacerbation Rate by History of Asthma Exacerbation (FAS)

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
Asthma exacerbation			
Interaction Test:	p=0,451		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	382	
Number of patients with outcome	82	94	
Number of outcomes	114	156	
Annualized Rate [95% CI]	0,62 [0,49; 0,78]	0,83 [0,67; 1,02]	0,75 [0,55; 1,01] 0,058
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	100	90	
Number of patients with outcome	33	33	
Number of outcomes	46	44	
Annualized Rate [95% CI]	1,09 [0,74; 1,59]	1,14 [0,77; 1,70]	0,95 [0,55; 1,64] 0,853
Severe asthma exacerbation			
Interaction Test:	p=0,916		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	382	
Number of patients with outcome	41	39	
Number of outcomes	50	47	
Annualized Rate [95% CI]	0,30 [0,22; 0,41]	0,27 [0,20; 0,37]	1,09 [0,70; 1,70] 0,696
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	100	90	
Number of patients with outcome	23	21	
Number of outcomes	31	26	
Annualized Rate [95% CI]	0,64 [0,41; 1,00]	0,61 [0,38; 0,99]	1,05 [0,55; 1,99] 0,889

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,642		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	382	
Number of patients with outcome	44	41	
Number of outcomes	53	47	
Annualized Rate [95% CI]	0,32 [0,24; 0,42]	0,27 [0,20; 0,37]	1,16 [0,76; 1,78] 0,487
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	100	90	
Number of patients with outcome	24	23	
Number of outcomes	31	28	
Annualized Rate [95% CI]	0,66 [0,43; 1,01]	0,68 [0,43; 1,06]	0,98 [0,53; 1,78] 0,937
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,992		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	382	
Number of patients with outcome	2	3	
Number of outcomes	4	3	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	1,29 [0,27; 6,23] 0,754
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	100	90	
Number of patients with outcome	4	0	
Number of outcomes	4	0	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	-

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
ER visit due to asthma exacerbation			
Interaction Test:	p=0,992		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	382	
Number of patients with outcome	2	3	
Number of outcomes	4	3	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	1,29 [0,27; 6,23] 0,754
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	100	90	
Number of patients with outcome	4	0	
Number of outcomes	4	0	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	-
Hospitalization due to asthma exacerbation			
Interaction Test:	p=0,955		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	372	382	
Number of patients with outcome	1	2	
Number of outcomes	1	2	
Annualized Rate [95% CI]	-	-	0,51 [0,05; 5,60] 0,580
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	100	90	
Number of patients with outcome	2	0	
Number of outcomes	2	0	
Annualized Rate [95% CI]	-	-	-

N': Number of patients in the analysis
CI: Confidence Interval
RR: Rate Ratio
*: $p < 0,05$

Annualized Rate and Rate Ratio are calculated based on negative binomial regression model.
Applied model for Annualized Rate/Rate Ratio: Number of events = treatment + region + background ICS/LABA + history of asthma exacerbation + history of asthma exacerbation * treatment, offset variable: log(exposure in years)
If it was not possible to fit the minimal model, the Annualized Rate and Rate Ratio are not given.

Analysis population: B2306 FAS total population

Table 12.6 Exacerbations - Annualized Exacerbation Rate by Patients' Prior Therapies (FAS)

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
Asthma exacerbation			
Interaction Test:	p=0,009 *		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	240	
Number of patients with outcome	44	67	
Number of outcomes	59	114	
Annualized Rate [95% CI]	0,52 [0,38; 0,71]	0,95 [0,74; 1,22]	0,55 [0,37; 0,81] 0,002 *
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	242	232	
Number of patients with outcome	71	60	
Number of outcomes	101	86	
Annualized Rate [95% CI]	0,90 [0,70; 1,16]	0,81 [0,62; 1,06]	1,11 [0,77; 1,61] 0,563
Severe asthma exacerbation			
Interaction Test:	p=0,071		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	240	
Number of patients with outcome	21	32	
Number of outcomes	25	36	
Annualized Rate [95% CI]	0,24 [0,16; 0,37]	0,33 [0,23; 0,48]	0,73 [0,41; 1,29] 0,278
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	242	232	
Number of patients with outcome	43	28	
Number of outcomes	56	37	
Annualized Rate [95% CI]	0,49 [0,36; 0,68]	0,34 [0,23; 0,49]	1,45 [0,89; 2,36] 0,131

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,140		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	240	
Number of patients with outcome	25	33	
Number of outcomes	29	37	
Annualized Rate [95% CI]	0,28 [0,19; 0,42]	0,34 [0,24; 0,49]	0,82 [0,48; 1,39] 0,461
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	242	232	
Number of patients with outcome	43	31	
Number of outcomes	55	38	
Annualized Rate [95% CI]	0,49 [0,36; 0,67]	0,35 [0,25; 0,50]	1,40 [0,87; 2,23] 0,163
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,484		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	240	
Number of patients with outcome	1	1	
Number of outcomes	1	1	
Annualized Rate [95% CI]	0,01 [0,00; 0,07]	0,01 [0,00; 0,07]	1,02 [0,06; 17,22] 0,987
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	242	232	
Number of patients with outcome	5	2	
Number of outcomes	7	2	
Annualized Rate [95% CI]	0,06 [0,03; 0,15]	0,02 [0,00; 0,08]	3,30 [0,63; 17,33] 0,158

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
ER visit due to asthma exacerbation			
Interaction Test:	p=0,484		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	240	
Number of patients with outcome	1	1	
Number of outcomes	1	1	
Annualized Rate [95% CI]	0,01 [0,00; 0,07]	0,01 [0,00; 0,07]	1,02 [0,06; 17,22] 0,987
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	242	232	
Number of patients with outcome	5	2	
Number of outcomes	7	2	
Annualized Rate [95% CI]	0,06 [0,03; 0,15]	0,02 [0,00; 0,08]	3,30 [0,63; 17,33] 0,158
Hospitalization due to asthma exacerbation			
Interaction Test:	p=0,748		
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA			
N'	230	240	
Number of patients with outcome	1	1	
Number of outcomes	1	1	
Annualized Rate [95% CI]	0,01 [0,00; 0,07]	0,01 [0,00; 0,06]	1,04 [0,06; 16,60] 0,979

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**RR [95% CI] p-value**
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA			
N'	242	232	
Number of patients with outcome	2	1	
Number of outcomes	2	1	
Annualized Rate [95% CI]	0,02 [0,00; 0,07]	0,01 [0,00; 0,07]	1,89 [0,17; 20,87] 0,603

N': Number of patients in the analysis
CI: Confidence Interval
RR: Rate Ratio
*: $p < 0,05$

Annualized Rate and Rate Ratio are calculated based on negative binomial regression model.
Applied model for Annualized Rate/Rate Ratio: Number of events = treatment + region + history of asthma exacerbation + patients' prior therapies + patients' prior therapies * treatment, offset variable: log(exposure in years)
Exceptional model(s) for Annualized Rate/Rate Ratio: Number of events = treatment + history of asthma exacerbation + patients' prior therapies + patients' prior therapies * treatment (for ER visit and/or hospitalization due to asthma exacerbation), treatment + history of asthma exacerbation + patients' prior therapies + patients' prior therapies * treatment (for ER visit due to asthma exacerbation), treatment + history of asthma exacerbation + patients' prior therapies + patients' prior therapies * treatment (for Hospitalization due to asthma exacerbation), offset variable: log(exposure in years)
If it was not possible to fit the minimal model, the Annualized Rate and Rate Ratio are not given.

Analysis population: B2306 FAS total population

13. Adverse Events - Binary Analysis (SAF)

Table 13.1 Adverse Events - Binary Analysis (SAF)

	Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	476	475			
Any AE, n (%)	250 (52,5)	246 (51,8)	1,03 [0,80; 1,33] 0,821	1,01 [0,90; 1,15] 0,821	0,01 [-0,06; 0,07] 0,821
Any AE, disease specific events excluded, n (%)	225 (47,3)	219 (46,1)	1,05 [0,81; 1,35] 0,719	1,03 [0,90; 1,17] 0,719	0,01 [-0,05; 0,08] 0,719
Any SAE, n (%)	18 (3,8)	19 (4,0)	0,94 [0,49; 1,82] 0,862	0,95 [0,50; 1,78] 0,862	-0,00 [-0,03; 0,02] 0,862

	Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, disease specific events excluded, n (%)	16 (3,4)	17 (3,6)	0,94 [0,47; 1,88] 0,854	0,94 [0,48; 1,84] 0,855	-0,00 [-0,03; 0,02] 0,855
Any severe AE, n (%)	74 (15,5)	71 (14,9)	1,05 [0,74; 1,49] 0,797	1,04 [0,77; 1,40] 0,797	0,01 [-0,04; 0,05] 0,797
Any severe AE, disease specific events excluded, n (%)	24 (5,0)	21 (4,4)	1,15 [0,63; 2,09] 0,652	1,14 [0,64; 2,02] 0,652	0,01 [-0,02; 0,03] 0,652
Any AE leading to study drug discontinuation, n (%)	3 (0,6)	3 (0,6)	1,00 [0,20; 4,97] 0,998	1,00 [0,20; 4,92] 0,998	-0,00 [-0,01; 0,01] 0,998
Any AE leading to study discontinuation, n (%)	2 (0,4)	2 (0,4)	1,00 [0,14; 7,11] 0,998	1,00 [0,14; 7,05] 0,998	-0,00 [-0,01; 0,01] 0,998

CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment
If it was not possible to fit the minimal model, the OR is not given.

Analysis population: B2306 SAF total population

Table 13.2 Adverse Events - Binary Analysis by Age (SAF)

	Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	476	475			
N' Age = 18-39 years	85	73			
N' Age = 40-64 years	290	307			
N' Age = ≥65 years	101	95			
Any AE					
Interaction Test:	p=0,091				
Age = 18-39 years	40 (47,1)	24 (32,9)	1,81 [0,95; 3,47] 0,071	1,43 [0,96; 2,13] 0,077	0,14 [-0,01; 0,29] 0,066
Age = 40-64 years	153 (52,8)	160 (52,1)	1,03 [0,74; 1,41] 0,875	1,01 [0,87; 1,18] 0,875	0,01 [-0,07; 0,09] 0,875
Age = ≥65 years	57 (56,4)	62 (65,3)	0,69 [0,39; 1,23] 0,207	0,86 [0,69; 1,08] 0,207	-0,09 [-0,22; 0,05] 0,204
Any AE, disease specific events excluded					
Interaction Test:	p=0,149				
Age = 18-39 years	38 (44,7)	23 (31,5)	1,76 [0,91; 3,38] 0,091	1,42 [0,94; 2,14] 0,097	0,13 [-0,02; 0,28] 0,085
Age = 40-64 years	138 (47,6)	143 (46,6)	1,04 [0,75; 1,44] 0,806	1,02 [0,86; 1,21] 0,805	0,01 [-0,07; 0,09] 0,806
Age = ≥65 years	49 (48,5)	53 (55,8)	0,75 [0,43; 1,31] 0,309	0,87 [0,66; 1,14] 0,309	-0,07 [-0,21; 0,07] 0,307
Any SAE					
Interaction Test:	p=0,718				
Age = 18-39 years	6 (7,1)	4 (5,5)	1,31 [0,36; 4,83] 0,685	1,29 [0,38; 4,39] 0,686	0,02 [-0,06; 0,09] 0,682
Age = 40-64 years	8 (2,8)	9 (2,9)	0,94 [0,36; 2,47] 0,899	0,94 [0,37; 2,41] 0,899	-0,00 [-0,03; 0,02] 0,899
Age = ≥65 years	4 (4,0)	6 (6,3)	0,61 [0,17; 2,24] 0,458	0,63 [0,18; 2,15] 0,458	-0,02 [-0,09; 0,04] 0,456

	Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, disease specific events excluded					
Interaction Test:	p=0,413				
Age = 18-39 years	6 (7,1)	3 (4,1)	1,77 [0,43; 7,35] 0,431	1,72 [0,45; 6,63] 0,432	0,03 [-0,04; 0,10] 0,415
Age = 40-64 years	7 (2,4)	8 (2,6)	0,92 [0,33; 2,58] 0,881	0,93 [0,34; 2,52] 0,881	-0,00 [-0,03; 0,02] 0,881
Age = ≥65 years	3 (3,0)	6 (6,3)	0,45 [0,11; 1,87] 0,274	0,47 [0,12; 1,83] 0,276	-0,03 [-0,09; 0,03] 0,267
Any severe AE					
Interaction Test:	p=0,016 *				
Age = 18-39 years	13 (15,3)	7 (9,6)	1,70 [0,64; 4,53] 0,286	1,59 [0,67; 3,78] 0,290	0,06 [-0,05; 0,16] 0,273
Age = 40-64 years	48 (16,6)	39 (12,7)	1,36 [0,86; 2,15] 0,184	1,30 [0,88; 1,93] 0,185	0,04 [-0,02; 0,10] 0,184
Age = ≥65 years	13 (12,9)	25 (26,3)	0,41 [0,20; 0,87] 0,019 *	0,49 [0,27; 0,90] 0,021 *	-0,13 [-0,24; -0,02] 0,017 *
Any severe AE, disease specific events excluded					
Interaction Test:	p=0,559				
Age = 18-39 years	6 (7,1)	4 (5,5)	1,31 [0,36; 4,83] 0,685	1,29 [0,38; 4,39] 0,686	0,02 [-0,06; 0,09] 0,682
Age = 40-64 years	15 (5,2)	12 (3,9)	1,34 [0,62; 2,92] 0,459	1,32 [0,63; 2,78] 0,459	0,01 [-0,02; 0,05] 0,459
Age = ≥65 years	3 (3,0)	5 (5,3)	0,55 [0,13; 2,37] 0,424	0,56 [0,14; 2,30] 0,424	-0,02 [-0,08; 0,03] 0,421

CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + age + age * treatment
If it was not possible to fit the minimal model, the OR is not given.

Analysis population: B2306 SAF total population

Table 13.3 Adverse Events - Binary Analysis by Gender (SAF)

	Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	476	475			
N' Gender = Male	187	169			
N' Gender = Female	289	306			
Any AE					
Interaction Test:	p=0,430				
Gender = Male	88 (47,1)	72 (42,6)	1,20 [0,79; 1,82] 0,399	1,10 [0,88; 1,39] 0,400	0,04 [-0,06; 0,15] 0,398
Gender = Female	162 (56,1)	174 (56,9)	0,97 [0,70; 1,34] 0,843	0,99 [0,86; 1,14] 0,843	-0,01 [-0,09; 0,07] 0,843
Any AE, disease specific events excluded					
Interaction Test:	p=0,664				
Gender = Male	76 (40,6)	63 (37,3)	1,15 [0,75; 1,77] 0,516	1,09 [0,84; 1,42] 0,517	0,03 [-0,07; 0,13] 0,515
Gender = Female	149 (51,6)	156 (51,0)	1,02 [0,74; 1,41] 0,888	1,01 [0,86; 1,18] 0,888	0,01 [-0,07; 0,09] 0,888
Any SAE					
Interaction Test:	p=0,208				
Gender = Male	3 (1,6)	6 (3,6)	0,44 [0,11; 1,80] 0,255	0,45 [0,11; 1,78] 0,256	-0,02 [-0,05; 0,01] 0,251
Gender = Female	15 (5,2)	13 (4,2)	1,23 [0,58; 2,64] 0,588	1,22 [0,59; 2,52] 0,588	0,01 [-0,02; 0,04] 0,589
Any SAE, disease specific events excluded					
Interaction Test:	p=0,362				
Gender = Male	3 (1,6)	5 (3,0)	0,53 [0,13; 2,27] 0,396	0,54 [0,13; 2,23] 0,397	-0,01 [-0,04; 0,02] 0,396
Gender = Female	13 (4,5)	12 (3,9)	1,15 [0,52; 2,57] 0,726	1,15 [0,53; 2,47] 0,726	0,01 [-0,03; 0,04] 0,726

	Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE					
Interaction Test:	p=0,544				
Gender = Male	30 (16,0)	23 (13,6)	1,21 [0,67; 2,18] 0,520	1,18 [0,71; 1,95] 0,521	0,02 [-0,05; 0,10] 0,518
Gender = Female	44 (15,2)	48 (15,7)	0,97 [0,62; 1,51] 0,876	0,97 [0,67; 1,41] 0,876	-0,00 [-0,06; 0,05] 0,876
Any severe AE, disease specific events excluded					
Interaction Test:	p=0,381				
Gender = Male	6 (3,2)	7 (4,1)	0,77 [0,25; 2,33] 0,640	0,77 [0,27; 2,26] 0,640	-0,01 [-0,05; 0,03] 0,641
Gender = Female	18 (6,2)	14 (4,6)	1,39 [0,68; 2,84] 0,373	1,36 [0,69; 2,69] 0,374	0,02 [-0,02; 0,05] 0,373

CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + gender + gender * treatment
If it was not possible to fit the minimal model, the OR is not given.

Analysis population: B2306 SAF total population

Table 13.4 Adverse Events - Binary Analysis by Region (SAF)

	Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	476	475			
N' Region = Asia	124	131			
N' Region = Europe	166	169			
N' Region = Latin America	166	166			
N' Region = Others	20	9			
Any AE					
Interaction Test:	p=0,940				
Region = Asia	84 (67,7)	86 (65,6)	1,10 [0,65; 1,85] 0,723	1,03 [0,87; 1,23] 0,723	0,02 [-0,09; 0,14] 0,723
Region = Europe	83 (50,0)	80 (47,3)	1,11 [0,72; 1,71] 0,626	1,06 [0,85; 1,32] 0,626	0,03 [-0,08; 0,13] 0,626
Region = Latin America	73 (44,0)	75 (45,2)	0,95 [0,62; 1,47] 0,825	0,97 [0,77; 1,24] 0,825	-0,01 [-0,12; 0,09] 0,825
Region = Others	10 (50,0)	5 (55,6)	0,80 [0,16; 3,88] 0,782	0,90 [0,43; 1,87] 0,777	-0,06 [-0,45; 0,34] 0,781
Any AE, disease specific events excluded					
Interaction Test:	p=0,888				
Region = Asia	75 (60,5)	82 (62,6)	0,91 [0,55; 1,52] 0,729	0,97 [0,80; 1,17] 0,729	-0,02 [-0,14; 0,10] 0,729
Region = Europe	74 (44,6)	69 (40,8)	1,17 [0,76; 1,80] 0,488	1,09 [0,85; 1,40] 0,488	0,04 [-0,07; 0,14] 0,488
Region = Latin America	66 (39,8)	63 (38,0)	1,08 [0,69; 1,68] 0,736	1,05 [0,80; 1,37] 0,736	0,02 [-0,09; 0,12] 0,735
Region = Others	10 (50,0)	5 (55,6)	0,80 [0,16; 3,88] 0,782	0,90 [0,43; 1,87] 0,777	-0,06 [-0,45; 0,34] 0,781

	Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE					
Interaction Test:	N.E.				
Region = Asia	4 (3,2)	9 (6,9)	-	0,47 [0,15; 1,49] 0,198	-0,04 [-0,09; 0,02] 0,180
Region = Europe	9 (5,4)	8 (4,7)	-	1,15 [0,45; 2,90] 0,774	0,01 [-0,04; 0,05] 0,774
Region = Latin America	5 (3,0)	2 (1,2)	-	2,50 [0,49; 12,70] 0,269	0,02 [-0,01; 0,05] 0,251
Region = Others	0 (0,0)	0 (0,0)	-	-	-
Any SAE, disease specific events excluded					
Interaction Test:	N.E.				
Region = Asia	3 (2,4)	8 (6,1)	-	0,40 [0,11; 1,46] 0,164	-0,04 [-0,09; 0,01] 0,141
Region = Europe	8 (4,8)	7 (4,1)	-	1,16 [0,43; 3,14] 0,765	0,01 [-0,04; 0,05] 0,765
Region = Latin America	5 (3,0)	2 (1,2)	-	2,50 [0,49; 12,70] 0,269	0,02 [-0,01; 0,05] 0,251
Region = Others	0 (0,0)	0 (0,0)	-	-	-
Any severe AE					
Interaction Test:	p=0,902				
Region = Asia	19 (15,3)	16 (12,2)	1,30 [0,64; 2,66] 0,472	1,25 [0,68; 2,33] 0,472	0,03 [-0,05; 0,12] 0,472
Region = Europe	26 (15,7)	25 (14,8)	1,07 [0,59; 1,94] 0,825	1,06 [0,64; 1,76] 0,825	0,01 [-0,07; 0,09] 0,825
Region = Latin America	27 (16,3)	29 (17,5)	0,92 [0,52; 1,63] 0,769	0,93 [0,58; 1,50] 0,770	-0,01 [-0,09; 0,07] 0,769
Region = Others	2 (10,0)	1 (11,1)	0,89 [0,07; 11,28] 0,928	0,90 [0,09; 8,69] 0,927	-0,01 [-0,25; 0,23] 0,929

	Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, disease specific events excluded					
Interaction Test:	N.E.				
Region = Asia	8 (6,5)	6 (4,6)	-	1,41 [0,50; 3,94] 0,514	0,02 [-0,04; 0,07] 0,513
Region = Europe	8 (4,8)	7 (4,1)	-	1,16 [0,43; 3,14] 0,765	0,01 [-0,04; 0,05] 0,765
Region = Latin America	7 (4,2)	8 (4,8)	-	0,88 [0,32; 2,36] 0,792	-0,01 [-0,05; 0,04] 0,792
Region = Others	1 (5,0)	0 (0,0)	-	1,43 [0,06; 32,05] 0,822	0,05 [-0,05; 0,15] 0,305

CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + region + region * treatment
If it was not possible to fit the minimal model, the OR is not given.

Analysis population: B2306 SAF total population

Table 13.5 Adverse Events - Binary Analysis by History of Asthma Exacerbation (SAF)

	Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	476	475			
N' Asthma exacerbations in the 12 months prior to screening = 1	375	383			
N' Asthma exacerbations in the 12 months prior to screening = ≥2	101	92			
Any AE					
Interaction Test:	p=0,866				
Asthma exacerbations in the 12 months prior to screening = 1	188 (50,1)	189 (49,3)	1,03 [0,78; 1,37] 0,829	1,02 [0,88; 1,17] 0,829	0,01 [-0,06; 0,08] 0,829
Asthma exacerbations in the 12 months prior to screening = ≥2	62 (61,4)	57 (62,0)	0,98 [0,55; 1,75] 0,935	0,99 [0,79; 1,24] 0,935	-0,01 [-0,14; 0,13] 0,935
Any AE, disease specific events excluded					
Interaction Test:	p=0,751				
Asthma exacerbations in the 12 months prior to screening = 1	169 (45,1)	167 (43,6)	1,06 [0,80; 1,41] 0,685	1,03 [0,88; 1,21] 0,685	0,01 [-0,06; 0,09] 0,685
Asthma exacerbations in the 12 months prior to screening = ≥2	56 (55,4)	52 (56,5)	0,96 [0,54; 1,69] 0,880	0,98 [0,76; 1,26] 0,880	-0,01 [-0,15; 0,13] 0,880
Any SAE					
Interaction Test:	p=0,018 *				
Asthma exacerbations in the 12 months prior to screening = 1	9 (2,4)	17 (4,4)	0,53 [0,23; 1,20] 0,129	0,54 [0,24; 1,20] 0,130	-0,02 [-0,05; 0,01] 0,121
Asthma exacerbations in the 12 months prior to screening = ≥2	9 (8,9)	2 (2,2)	4,40 [0,93; 20,94] 0,063	4,10 [0,91; 18,48] 0,066	0,07 [0,00; 0,13] 0,036 *
Any SAE, disease specific events excluded					
Interaction Test:	p=0,031 *				
Asthma exacerbations in the 12 months prior to screening = 1	8 (2,1)	15 (3,9)	0,53 [0,22; 1,28] 0,159	0,54 [0,23; 1,27] 0,159	-0,02 [-0,04; 0,01] 0,151

	Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Asthma exacerbations in the 12 months prior to screening = ≥2	8 (7,9)	2 (2,2)	3,87 [0,80; 18,73] 0,092	3,64 [0,79; 16,72] 0,096	0,06 [-0,00; 0,12] 0,063
Any severe AE					
Interaction Test:	p=0,521				
Asthma exacerbations in the 12 months prior to screening = 1	47 (12,5)	50 (13,1)	0,95 [0,62; 1,46] 0,830	0,96 [0,66; 1,39] 0,830	-0,01 [-0,05; 0,04] 0,830
Asthma exacerbations in the 12 months prior to screening = ≥2	27 (26,7)	21 (22,8)	1,23 [0,64; 2,38] 0,531	1,17 [0,71; 1,92] 0,532	0,04 [-0,08; 0,16] 0,529
Any severe AE, disease specific events excluded					
Interaction Test:	p=0,005 *				
Asthma exacerbations in the 12 months prior to screening = 1	11 (2,9)	19 (5,0)	0,58 [0,27; 1,23] 0,157	0,59 [0,29; 1,23] 0,158	-0,02 [-0,05; 0,01] 0,151
Asthma exacerbations in the 12 months prior to screening = ≥2	13 (12,9)	2 (2,2)	6,65 [1,46; 30,32] 0,014 *	5,92 [1,37; 25,54] 0,017 *	0,11 [0,04; 0,18] 0,003 *

CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + history of asthma exacerbation + history of asthma exacerbation * treatment
If it was not possible to fit the minimal model, the OR is not given.

Analysis population: B2306 SAF total population

Table 13.6 Adverse Events - Binary Analysis by Patients' Prior Therapies (SAF)

	Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	472	472			
N' Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA	230	240			
N' Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA	242	232			
Any AE					
Interaction Test:	p=0,062				
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA	108 (47,0)	125 (52,1)	0,81 [0,57; 1,17] 0,267	0,90 [0,75; 1,08] 0,268	-0,05 [-0,14; 0,04] 0,266
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA	141 (58,3)	119 (51,3)	1,33 [0,92; 1,91] 0,128	1,14 [0,96; 1,34] 0,129	0,07 [-0,02; 0,16] 0,127
Any AE, disease specific events excluded					
Interaction Test:	p=0,140				
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA	98 (42,6)	111 (46,3)	0,86 [0,60; 1,24] 0,427	0,92 [0,75; 1,13] 0,428	-0,04 [-0,13; 0,05] 0,427
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA	126 (52,1)	107 (46,1)	1,27 [0,88; 1,82] 0,196	1,13 [0,94; 1,36] 0,197	0,06 [-0,03; 0,15] 0,195
Any SAE					
Interaction Test:	p=0,781				
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA	8 (3,5)	8 (3,3)	1,05 [0,39; 2,83] 0,931	1,04 [0,40; 2,73] 0,931	0,00 [-0,03; 0,03] 0,931
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA	10 (4,1)	11 (4,7)	0,87 [0,36; 2,08] 0,747	0,87 [0,38; 2,01] 0,748	-0,01 [-0,04; 0,03] 0,748

	Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, disease specific events excluded					
Interaction Test:	p=0,783				
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA	7 (3,0)	7 (2,9)	1,04 [0,36; 3,03] 0,936	1,04 [0,37; 2,93] 0,936	0,00 [-0,03; 0,03] 0,936
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA	9 (3,7)	10 (4,3)	0,86 [0,34; 2,15] 0,743	0,86 [0,36; 2,09] 0,743	-0,01 [-0,04; 0,03] 0,743
Any severe AE					
Interaction Test:	p=0,031 *				
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA	25 (10,9)	37 (15,4)	0,67 [0,39; 1,15] 0,147	0,71 [0,44; 1,13] 0,149	-0,05 [-0,11; 0,02] 0,143
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA	48 (19,8)	33 (14,2)	1,49 [0,92; 2,42] 0,106	1,39 [0,93; 2,09] 0,108	0,06 [-0,01; 0,12] 0,103
Any severe AE, disease specific events excluded					
Interaction Test:	p=0,340				
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA	11 (4,8)	13 (5,4)	0,88 [0,38; 2,00] 0,755	0,88 [0,40; 1,93] 0,755	-0,01 [-0,05; 0,03] 0,755
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA	13 (5,4)	8 (3,4)	1,59 [0,65; 3,91] 0,313	1,56 [0,66; 3,69] 0,314	0,02 [-0,02; 0,06] 0,306

CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + patients' prior therapies + patients' prior therapies * treatment
If it was not possible to fit the minimal model, the OR is not given.

Analysis population: B2306 SAF total population

14. Any AE by SOC and PT - Binary Analysis (SAF)

Table 14.1 Any AE by SOC, PT and Severity - Binary Analysis (SAF)

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	476	475			
Any adverse event, n (%)**	250 (52,5)	246 (51,8)	1,03 [0,80; 1,33] 0,821	1,01 [0,90; 1,15] 0,821	0,01 [-0,06; 0,07] 0,821
Mild, n (%)	157 (33,0)	168 (35,4)	0,90 [0,69; 1,18] 0,438	0,93 [0,78; 1,11] 0,438	-0,02 [-0,08; 0,04] 0,438
Moderate, n (%)	120 (25,2)	136 (28,6)	0,84 [0,63; 1,12] 0,235	0,88 [0,71; 1,09] 0,235	-0,03 [-0,09; 0,02] 0,234
Severe, n (%)	74 (15,5)	71 (14,9)	1,05 [0,74; 1,49] 0,797	1,04 [0,77; 1,40] 0,797	0,01 [-0,04; 0,05] 0,797
Infections and infestations, n (%)	146 (30,7)	143 (30,1)	1,03 [0,78; 1,35] 0,850	1,02 [0,84; 1,23] 0,849	0,01 [-0,05; 0,06] 0,849
Mild, n (%)	89 (18,7)	82 (17,3)	1,10 [0,79; 1,53] 0,565	1,08 [0,83; 1,42] 0,565	0,01 [-0,03; 0,06] 0,565
Moderate, n (%)	60 (12,6)	75 (15,8)	0,77 [0,53; 1,11] 0,160	0,80 [0,58; 1,09] 0,161	-0,03 [-0,08; 0,01] 0,159
Severe, n (%)	16 (3,4)	11 (2,3)	1,47 [0,67; 3,19] 0,335	1,45 [0,68; 3,09] 0,335	0,01 [-0,01; 0,03] 0,331
Nasopharyngitis, n (%)	34 (7,1)	43 (9,1)	0,77 [0,48; 1,24] 0,281	0,79 [0,51; 1,21] 0,282	-0,02 [-0,05; 0,02] 0,280
Mild, n (%)	24 (5,0)	27 (5,7)	0,88 [0,50; 1,55] 0,660	0,89 [0,52; 1,51] 0,660	-0,01 [-0,04; 0,02] 0,660
Moderate, n (%)	10 (2,1)	20 (4,2)	0,49 [0,23; 1,05] 0,068	0,50 [0,24; 1,05] 0,069	-0,02 [-0,04; 0,00] 0,062
Severe, n (%)	1 (0,2)	2 (0,4)	0,50 [0,04; 5,51] 0,570	0,50 [0,05; 5,48] 0,570	-0,00 [-0,01; 0,01] 0,562

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Bronchitis, n (%)	22 (4,6)	21 (4,4)	1,05 [0,57; 1,93] 0,882	1,05 [0,58; 1,88] 0,882	0,00 [-0,02; 0,03] 0,882
Mild, n (%)	7 (1,5)	8 (1,7)	0,87 [0,31; 2,42] 0,792	0,87 [0,32; 2,39] 0,792	-0,00 [-0,02; 0,01] 0,792
Moderate, n (%)	15 (3,2)	14 (2,9)	1,07 [0,51; 2,25] 0,855	1,07 [0,52; 2,19] 0,855	0,00 [-0,02; 0,02] 0,855
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Pharyngitis, n (%)	17 (3,6)	11 (2,3)	1,56 [0,72; 3,37] 0,256	1,54 [0,73; 3,26] 0,256	0,01 [-0,01; 0,03] 0,252
Mild, n (%)	14 (2,9)	8 (1,7)	1,77 [0,74; 4,26] 0,203	1,75 [0,74; 4,12] 0,204	0,01 [-0,01; 0,03] 0,197
Moderate, n (%)	3 (0,6)	3 (0,6)	1,00 [0,20; 4,97] 0,998	1,00 [0,20; 4,92] 0,998	-0,00 [-0,01; 0,01] 0,998
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Viral upper respiratory tract infection, n (%)	11 (2,3)	10 (2,1)	1,10 [0,46; 2,62] 0,829	1,10 [0,47; 2,56] 0,829	0,00 [-0,02; 0,02] 0,829
Mild, n (%)	5 (1,1)	6 (1,3)	0,83 [0,25; 2,74] 0,759	0,83 [0,26; 2,71] 0,759	-0,00 [-0,02; 0,01] 0,759
Moderate, n (%)	6 (1,3)	3 (0,6)	2,01 [0,50; 8,08] 0,326	2,00 [0,50; 7,93] 0,326	0,01 [-0,01; 0,02] 0,316
Severe, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Upper respiratory tract infection, n (%)	10 (2,1)	9 (1,9)	1,11 [0,45; 2,76] 0,821	1,11 [0,45; 2,70] 0,820	0,00 [-0,02; 0,02] 0,820
Mild, n (%)	6 (1,3)	4 (0,8)	1,50 [0,42; 5,36] 0,530	1,50 [0,43; 5,27] 0,530	0,00 [-0,01; 0,02] 0,527
Moderate, n (%)	4 (0,8)	5 (1,1)	0,80 [0,21; 2,99] 0,736	0,80 [0,22; 2,95] 0,736	-0,00 [-0,01; 0,01] 0,735
Severe, n (%)	2 (0,4)	0 (0,0)	-	4,99 [0,24; 103,65] 0,299	0,00 [-0,00; 0,01] 0,156

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Respiratory, thoracic and mediastinal disorders, n (%)	139 (29,2)	149 (31,4)	0,90 [0,68; 1,19] 0,467	0,93 [0,77; 1,13] 0,467	-0,02 [-0,08; 0,04] 0,467
Mild, n (%)	52 (10,9)	68 (14,3)	0,73 [0,50; 1,08] 0,116	0,76 [0,54; 1,07] 0,117	-0,03 [-0,08; 0,01] 0,115
Moderate, n (%)	40 (8,4)	44 (9,3)	0,90 [0,57; 1,41] 0,640	0,91 [0,60; 1,37] 0,641	-0,01 [-0,04; 0,03] 0,640
Severe, n (%)	65 (13,7)	61 (12,8)	1,07 [0,74; 1,56] 0,711	1,06 [0,77; 1,47] 0,712	0,01 [-0,03; 0,05] 0,711
Asthma, n (%)	116 (24,4)	128 (26,9)	0,87 [0,65; 1,17] 0,363	0,90 [0,73; 1,12] 0,363	-0,03 [-0,08; 0,03] 0,363
Mild, n (%)	34 (7,1)	47 (9,9)	0,70 [0,44; 1,11] 0,130	0,72 [0,47; 1,10] 0,131	-0,03 [-0,06; 0,01] 0,128
Moderate, n (%)	26 (5,5)	39 (8,2)	0,65 [0,39; 1,08] 0,095	0,67 [0,41; 1,07] 0,096	-0,03 [-0,06; 0,00] 0,093
Severe, n (%)	65 (13,7)	61 (12,8)	1,07 [0,74; 1,56] 0,711	1,06 [0,77; 1,47] 0,712	0,01 [-0,03; 0,05] 0,711
Gastrointestinal disorders, n (%)	26 (5,5)	25 (5,3)	1,04 [0,59; 1,83] 0,892	1,04 [0,61; 1,77] 0,892	0,00 [-0,03; 0,03] 0,892
Mild, n (%)	15 (3,2)	16 (3,4)	0,93 [0,46; 1,91] 0,850	0,94 [0,47; 1,87] 0,850	-0,00 [-0,02; 0,02] 0,850
Moderate, n (%)	10 (2,1)	13 (2,7)	0,76 [0,33; 1,76] 0,524	0,77 [0,34; 1,73] 0,525	-0,01 [-0,03; 0,01] 0,523
Severe, n (%)	1 (0,2)	1 (0,2)	1,00 [0,06; 16,00] 0,999	1,00 [0,06; 15,91] 0,999	-0,00 [-0,01; 0,01] 0,999

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Nervous system disorders, n (%)	21 (4,4)	27 (5,7)	0,77 [0,43; 1,37] 0,371	0,78 [0,45; 1,35] 0,372	-0,01 [-0,04; 0,02] 0,370
Mild, n (%)	16 (3,4)	17 (3,6)	0,94 [0,47; 1,88] 0,855	0,94 [0,48; 1,84] 0,855	-0,00 [-0,03; 0,02] 0,855
Moderate, n (%)	5 (1,1)	8 (1,7)	0,62 [0,20; 1,91] 0,404	0,62 [0,21; 1,89] 0,405	-0,01 [-0,02; 0,01] 0,400
Severe, n (%)	0 (0,0)	2 (0,4)	-	0,20 [0,01; 4,15] 0,298	-0,00 [-0,01; 0,00] 0,156
Headache, n (%)	15 (3,2)	9 (1,9)	1,68 [0,73; 3,89] 0,222	1,66 [0,74; 3,76] 0,222	0,01 [-0,01; 0,03] 0,216
Mild, n (%)	11 (2,3)	5 (1,1)	2,22 [0,77; 6,45] 0,141	2,20 [0,77; 6,27] 0,142	0,01 [-0,00; 0,03] 0,131
Moderate, n (%)	4 (0,8)	4 (0,8)	1,00 [0,25; 4,01] 0,998	1,00 [0,25; 3,97] 0,998	-0,00 [-0,01; 0,01] 0,998
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Musculoskeletal and connective tissue disorders, n (%)	16 (3,4)	12 (2,5)	1,34 [0,63; 2,87] 0,448	1,33 [0,64; 2,78] 0,448	0,01 [-0,01; 0,03] 0,446
Mild, n (%)	10 (2,1)	5 (1,1)	2,02 [0,68; 5,95] 0,203	2,00 [0,69; 5,80] 0,204	0,01 [-0,01; 0,03] 0,194
Moderate, n (%)	6 (1,3)	8 (1,7)	0,75 [0,26; 2,16] 0,589	0,75 [0,26; 2,14] 0,589	-0,00 [-0,02; 0,01] 0,587
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
General disorders and administration site conditions, n (%)	13 (2,7)	8 (1,7)	1,64 [0,67; 3,99] 0,277	1,62 [0,68; 3,88] 0,277	0,01 [-0,01; 0,03] 0,272
Mild, n (%)	11 (2,3)	5 (1,1)	2,22 [0,77; 6,45] 0,141	2,20 [0,77; 6,27] 0,142	0,01 [-0,00; 0,03] 0,131
Moderate, n (%)	1 (0,2)	3 (0,6)	0,33 [0,03; 3,19] 0,339	0,33 [0,03; 3,19] 0,340	-0,00 [-0,01; 0,00] 0,315
Severe, n (%)	1 (0,2)	0 (0,0)	-	2,99 [0,12; 73,30] 0,502	0,00 [-0,00; 0,01] 0,317
Injury, poisoning and procedural complications, n (%)	12 (2,5)	14 (2,9)	0,85 [0,39; 1,86] 0,687	0,86 [0,40; 1,83] 0,687	-0,00 [-0,02; 0,02] 0,687
Mild, n (%)	4 (0,8)	9 (1,9)	0,44 [0,13; 1,43] 0,173	0,44 [0,14; 1,43] 0,174	-0,01 [-0,03; 0,00] 0,161
Moderate, n (%)	6 (1,3)	5 (1,1)	1,20 [0,36; 3,96] 0,765	1,20 [0,37; 3,90] 0,765	0,00 [-0,01; 0,02] 0,764
Severe, n (%)	2 (0,4)	1 (0,2)	2,00 [0,18; 22,13] 0,572	2,00 [0,18; 21,94] 0,572	0,00 [-0,01; 0,01] 0,564

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment

SOCs are sorted by descending frequencies in the IND/GLY/MF 160 treatment group. PTs are sorted by descending frequencies in the IND/GLY/MF 160 treatment group within their SOC.

A patient with multiple AEs with the same SOC/PT is counted only once for that SOC/PT. A patient with multiple AEs is counted only once in the 'any adverse event' row.

Analysis population: B2306 SAF total population

Table 14.2 Any AE by SOC and PT - Binary Analysis by Age (SAF)

There are no data meeting the display criteria for this table.

Table 14.3 Any AE by SOC and PT - Binary Analysis by Gender (SAF)

There are no data meeting the display criteria for this table.

Table 14.4 Any AE by SOC and PT - Binary Analysis by Region (SAF)

There are no data meeting the display criteria for this table.

Table 14.5 Any AE by SOC and PT - Binary Analysis by History of Asthma Exacerbation (SAF)

There are no data meeting the display criteria for this table.

Table 14.6 Any AE by SOC and PT - Binary Analysis by Patients' Prior Therapies (SAF)

There are no data meeting the display criteria for this table.

Table 14.7 Any severe AE by SOC and PT - Binary Analysis by Age (SAF)

There are no data meeting the display criteria for this table.

Table 14.8 Any severe AE by SOC and PT - Binary Analysis by Gender (SAF)

There are no data meeting the display criteria for this table.

Table 14.9 Any severe AE by SOC and PT - Binary Analysis by Region (SAF)

There are no data meeting the display criteria for this table.

Table 14.10 Any severe AE by SOC and PT - Binary Analysis by History of Asthma Exacerbation (SAF)

There are no data meeting the display criteria for this table.

Table 14.11 Any severe AE by SOC and PT - Binary Analysis by Patients' Prior Therapies (SAF)

There are no data meeting the display criteria for this table.

15. Any SAE by SOC and PT - Binary Analysis (SAF)

Table 15.1 Any SAE by SOC and PT - Binary Analysis (SAF)

There are no data meeting the display criteria for this table.

Table 15.2 Any SAE by SOC and PT - Binary Analysis by Age (SAF)

There are no data meeting the display criteria for this table.

Table 15.3 Any SAE by SOC and PT - Binary Analysis by Gender (SAF)

There are no data meeting the display criteria for this table.

Table 15.4 Any SAE by SOC and PT - Binary Analysis by Region (SAF)

There are no data meeting the display criteria for this table.

Table 15.5 Any SAE by SOC and PT - Binary Analysis by History of Asthma Exacerbation (SAF)

There are no data meeting the display criteria for this table.

Table 15.6 Any SAE by SOC and PT - Binary Analysis by Patients' Prior Therapies (SAF)

There are no data meeting the display criteria for this table.

16. Any AE leading to Study Discontinuation by SOC and PT - Binary Analysis

Table 16.1 Any AE leading to Study Discontinuation by SOC and PT - Binary Analysis (SAF)

	Treatment groups	
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**
N'	476	475
Infections and infestations, n (%)	0 (0,0)	0 (0,0)
Laryngitis, n (%)	0 (0,0)	0 (0,0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps), n (%)	1 (0,2)	0 (0,0)
Benign neoplasm, n (%)	1 (0,2)	0 (0,0)
Nervous system disorders, n (%)	0 (0,0)	1 (0,2)
Haemorrhagic stroke, n (%)	0 (0,0)	1 (0,2)
Tension headache, n (%)	0 (0,0)	0 (0,0)
Respiratory, thoracic and mediastinal disorders, n (%)	1 (0,2)	0 (0,0)
Dysphonia, n (%)	1 (0,2)	0 (0,0)
Oropharyngeal discomfort, n (%)	0 (0,0)	0 (0,0)
Skin and subcutaneous tissue disorders, n (%)	0 (0,0)	1 (0,2)
Dermatitis atopic, n (%)	0 (0,0)	1 (0,2)
Pruritus, n (%)	0 (0,0)	0 (0,0)

N': Number of patients in the analysis
SOCs are sorted alphabetically. PTs are sorted alphabetically within their SOC.

A patient with multiple AEs with the same SOC/PT is counted only once for that SOC/PT.

Analysis population: B2306 SAF total population

17. Any AE leading to Study Drug Discontinuation by SOC and PT - Binary Analysis

Table 17.1 Any AE leading to Study Drug Discontinuation by SOC and PT - Binary Analysis (SAF)

	Treatment groups	
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**
N'	476	475
Gastrointestinal disorders, n (%)	0 (0,0)	0 (0,0)
Dry mouth, n (%)	0 (0,0)	0 (0,0)
General disorders and administration site conditions, n (%)	0 (0,0)	0 (0,0)
Hyperpyrexia, n (%)	0 (0,0)	0 (0,0)
Infections and infestations, n (%)	0 (0,0)	0 (0,0)
Laryngitis, n (%)	0 (0,0)	0 (0,0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps), n (%)	1 (0,2)	0 (0,0)
Benign neoplasm, n (%)	1 (0,2)	0 (0,0)
Nervous system disorders, n (%)	1 (0,2)	1 (0,2)
Burning sensation, n (%)	1 (0,2)	0 (0,0)
Haemorrhagic stroke, n (%)	0 (0,0)	1 (0,2)
Headache, n (%)	1 (0,2)	0 (0,0)
Tension headache, n (%)	0 (0,0)	0 (0,0)
Respiratory, thoracic and mediastinal disorders, n (%)	1 (0,2)	1 (0,2)
Dysphonia, n (%)	1 (0,2)	0 (0,0)
Larynx irritation, n (%)	0 (0,0)	1 (0,2)
Oropharyngeal discomfort, n (%)	0 (0,0)	0 (0,0)
Skin and subcutaneous tissue disorders, n (%)	0 (0,0)	1 (0,2)
Dermatitis atopic, n (%)	0 (0,0)	1 (0,2)
Pruritus, n (%)	0 (0,0)	0 (0,0)

N': Number of patients in the analysis
SOCs are sorted alphabetically. PTs are sorted alphabetically within their SOC.

A patient with multiple AEs with the same SOC/PT is counted only once for that SOC/PT.

Analysis population: B2306 SAF total population

18. AESI - Binary Analysis (SAF)

Table 18.1 AESI by Severity - Binary Analysis (SAF)

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	476	475			
Bladder obstruction-Urinary retention, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Mild, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Moderate, n (%)	0 (0,0)	0 (0,0)	-	-	-
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-
Bone fracture, n (%)	3 (0,6)	3 (0,6)	1,00 [0,20; 4,97] 0,998	1,00 [0,20; 4,92] 0,998	-0,00 [-0,01; 0,01] 0,998
Mild, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Moderate, n (%)	3 (0,6)	1 (0,2)	-	2,99 [0,31; 28,68] 0,342	0,00 [-0,00; 0,01] 0,317
Severe, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Serious, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
CCV events: Cardiac arrhythmia terms (incl brady- and tachyarrhythmias): Conduction abnormalities, n (%)	1 (0,2)	1 (0,2)	1,00 [0,06; 16,00] 0,999	1,00 [0,06; 15,91] 0,999	-0,00 [-0,01; 0,01] 0,999
Mild, n (%)	1 (0,2)	1 (0,2)	-	1,00 [0,06; 15,91] 0,999	-0,00 [-0,01; 0,01] 0,999
Moderate, n (%)	0 (0,0)	0 (0,0)	-	-	-
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
CCV events: Cardiac arrhythmia terms (incl brady- and tachyarrhythmias): Tachyarrhythmias, n (%)	3 (0,6)	2 (0,4)	1,50 [0,25; 9,02] 0,658	1,50 [0,25; 8,92] 0,658	0,00 [-0,01; 0,01] 0,655
Mild, n (%)	2 (0,4)	2 (0,4)	1,00 [0,14; 7,11] 0,998	1,00 [0,14; 7,05] 0,998	-0,00 [-0,01; 0,01] 0,998
Moderate, n (%)	1 (0,2)	0 (0,0)	-	2,99 [0,12; 73,30] 0,502	0,00 [-0,00; 0,01] 0,317
Severe, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Serious, n (%)	1 (0,2)	1 (0,2)	-	1,00 [0,06; 15,91] 0,999	-0,00 [-0,01; 0,01] 0,999
CCV events: Cardiac failure, n (%)	1 (0,2)	1 (0,2)	-	1,00 [0,06; 15,91] 0,999	-0,00 [-0,01; 0,01] 0,999
Mild, n (%)	1 (0,2)	0 (0,0)	-	2,99 [0,12; 73,30] 0,502	0,00 [-0,00; 0,01] 0,317
Moderate, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-
CCV events: Cerebrovascular events, n (%)	0 (0,0)	2 (0,4)	-	0,20 [0,01; 4,15] 0,298	-0,00 [-0,01; 0,00] 0,156
Mild, n (%)	0 (0,0)	0 (0,0)	-	-	-
Moderate, n (%)	0 (0,0)	0 (0,0)	-	-	-
Severe, n (%)	0 (0,0)	2 (0,4)	-	0,20 [0,01; 4,15] 0,298	-0,00 [-0,01; 0,00] 0,156
Serious, n (%)	0 (0,0)	2 (0,4)	-	0,20 [0,01; 4,15] 0,298	-0,00 [-0,01; 0,00] 0,156

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
CCV events: Ischaemic heart disease, n (%)	2 (0,4)	1 (0,2)	-	2,00 [0,18; 21,94] 0,572	0,00 [-0,01; 0,01] 0,564
Mild, n (%)	0 (0,0)	0 (0,0)	-	-	-
Moderate, n (%)	2 (0,4)	0 (0,0)	-	4,99 [0,24; 103,65] 0,299	0,00 [-0,00; 0,01] 0,156
Severe, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-
CCV events: Myocardial infarction, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Mild, n (%)	0 (0,0)	0 (0,0)	-	-	-
Moderate, n (%)	0 (0,0)	0 (0,0)	-	-	-
Severe, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Serious, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Cataracts, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Mild, n (%)	0 (0,0)	0 (0,0)	-	-	-
Moderate, n (%)	0 (0,0)	0 (0,0)	-	-	-
Severe, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-
Diabetes mellitus/hyperglycaemia, n (%)	2 (0,4)	4 (0,8)	0,50 [0,09; 2,73] 0,421	0,50 [0,09; 2,71] 0,421	-0,00 [-0,01; 0,01] 0,411
Mild, n (%)	1 (0,2)	3 (0,6)	0,33 [0,03; 3,20] 0,339	0,33 [0,03; 3,19] 0,340	-0,00 [-0,01; 0,00] 0,315
Moderate, n (%)	1 (0,2)	1 (0,2)	1,00 [0,06; 16,00] 0,999	1,00 [0,06; 15,91] 0,999	-0,00 [-0,01; 0,01] 0,999
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Hypersensitivity, n (%)	119 (25,0)	140 (29,5)	0,80 [0,60; 1,06] 0,122	0,85 [0,69; 1,05] 0,122	-0,04 [-0,10; 0,01] 0,121
Mild, n (%)	35 (7,4)	54 (11,4)	0,62 [0,40; 0,97] 0,035 *	0,65 [0,43; 0,97] 0,035 *	-0,04 [-0,08; -0,00] 0,033 *
Moderate, n (%)	30 (6,3)	44 (9,3)	0,66 [0,41; 1,07] 0,090	0,68 [0,44; 1,06] 0,091	-0,03 [-0,06; 0,00] 0,088
Severe, n (%)	65 (13,7)	61 (12,8)	1,07 [0,74; 1,56] 0,711	1,06 [0,77; 1,47] 0,712	0,01 [-0,03; 0,05] 0,711
Serious, n (%)	3 (0,6)	2 (0,4)	1,50 [0,25; 9,02] 0,658	1,50 [0,25; 8,92] 0,658	0,00 [-0,01; 0,01] 0,655
Immunosuppression, n (%)	36 (7,6)	35 (7,4)	1,03 [0,63; 1,67] 0,909	1,03 [0,66; 1,61] 0,909	0,00 [-0,03; 0,04] 0,909
Mild, n (%)	12 (2,5)	11 (2,3)	1,09 [0,48; 2,50] 0,837	1,09 [0,49; 2,44] 0,837	0,00 [-0,02; 0,02] 0,837
Moderate, n (%)	20 (4,2)	19 (4,0)	1,05 [0,55; 2,00] 0,875	1,05 [0,57; 1,94] 0,875	0,00 [-0,02; 0,03] 0,875
Severe, n (%)	8 (1,7)	6 (1,3)	1,34 [0,46; 3,88] 0,594	1,33 [0,47; 3,81] 0,594	0,00 [-0,01; 0,02] 0,593
Serious, n (%)	5 (1,1)	0 (0,0)	-	10,98 [0,61; 197,96] 0,104	0,01 [0,00; 0,02] 0,025 *
Intubation hospitalization and death due to asthma related events, n (%)	3 (0,6)	2 (0,4)	1,50 [0,25; 9,02] 0,658	1,50 [0,25; 8,92] 0,658	0,00 [-0,01; 0,01] 0,655
Mild, n (%)	0 (0,0)	0 (0,0)	-	-	-
Moderate, n (%)	0 (0,0)	0 (0,0)	-	-	-
Severe, n (%)	3 (0,6)	2 (0,4)	1,50 [0,25; 9,02] 0,658	1,50 [0,25; 8,92] 0,658	0,00 [-0,01; 0,01] 0,655
Serious, n (%)	3 (0,6)	2 (0,4)	1,50 [0,25; 9,02] 0,658	1,50 [0,25; 8,92] 0,658	0,00 [-0,01; 0,01] 0,655

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Liver toxicity, n (%)	2 (0,4)	3 (0,6)	0,66 [0,11; 3,99] 0,654	0,67 [0,11; 3,96] 0,654	-0,00 [-0,01; 0,01] 0,652
Mild, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Moderate, n (%)	2 (0,4)	2 (0,4)	1,00 [0,14; 7,11] 0,998	1,00 [0,14; 7,05] 0,998	-0,00 [-0,01; 0,01] 0,998
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-
Medication error: Device interchangeability or Swallowing of capsules, n (%)	0 (0,0)	2 (0,4)	-	0,20 [0,01; 4,15] 0,298	-0,00 [-0,01; 0,00] 0,156
Mild, n (%)	0 (0,0)	2 (0,4)	-	0,20 [0,01; 4,15] 0,298	-0,00 [-0,01; 0,00] 0,156
Moderate, n (%)	0 (0,0)	0 (0,0)	-	-	-
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-
Reduced bone mineral density, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Mild, n (%)	0 (0,0)	0 (0,0)	-	-	-
Moderate, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-
Adjudicated serious cardiovascular and cerebrovascular (CCV) events: MACE, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317
Mild, n (%)	-	-	-	-	-
Moderate, n (%)	-	-	-	-	-
Severe, n (%)	-	-	-	-	-
Serious, n (%)	0 (0,0)	1 (0,2)	-	0,33 [0,01; 8,14] 0,500	-0,00 [-0,01; 0,00] 0,317

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Adjudicated serious cardiovascular and cerebrovascular (CCV) events: Non-MACE, n (%)	3 (0,6)	3 (0,6)	1,00 [0,20; 4,97] 0,998	1,00 [0,20; 4,92] 0,998	-0,00 [-0,01; 0,01] 0,998
Mild, n (%)	-	-	-	-	-
Moderate, n (%)	-	-	-	-	-
Severe, n (%)	-	-	-	-	-
Serious, n (%)	3 (0,6)	3 (0,6)	1,00 [0,20; 4,97] 0,998	1,00 [0,20; 4,92] 0,998	-0,00 [-0,01; 0,01] 0,998
Adjudicated new onset of atrial fibrillation/ flutter: New onset, n (%)	0 (0,0)	0 (0,0)	-	-	-
Mild, n (%)	-	-	-	-	-
Moderate, n (%)	-	-	-	-	-
Severe, n (%)	-	-	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-
Adjudicated new onset of atrial fibrillation/ flutter: Recurrent/persistent, n (%)	0 (0,0)	0 (0,0)	-	-	-
Mild, n (%)	-	-	-	-	-
Moderate, n (%)	-	-	-	-	-
Severe, n (%)	-	-	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-
Adjudicated new onset of atrial fibrillation/ flutter: Unknown, n (%)	0 (0,0)	0 (0,0)	-	-	-
Mild, n (%)	-	-	-	-	-
Moderate, n (%)	-	-	-	-	-
Severe, n (%)	-	-	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Composite endpoint of serious asthma outcomes: Asthma-related hospitalization, n (%)	2 (0,4)	1 (0,2)	2,00 [0,18; 22,12] 0,572	2,00 [0,18; 21,94] 0,572	0,00 [-0,01; 0,01] 0,564
Mild, n (%)	-	-	-	-	-
Moderate, n (%)	-	-	-	-	-
Severe, n (%)	-	-	-	-	-
Serious, n (%)	2 (0,4)	1 (0,2)	2,00 [0,18; 22,12] 0,572	2,00 [0,18; 21,94] 0,572	0,00 [-0,01; 0,01] 0,564
Composite endpoint of serious asthma outcomes: Asthma-related intubation, n (%)	0 (0,0)	0 (0,0)	-	-	-
Mild, n (%)	-	-	-	-	-
Moderate, n (%)	-	-	-	-	-
Severe, n (%)	-	-	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-
Composite endpoint of serious asthma outcomes: Asthma-related death, n (%)	0 (0,0)	0 (0,0)	-	-	-
Mild, n (%)	-	-	-	-	-
Moderate, n (%)	-	-	-	-	-
Severe, n (%)	-	-	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment

For adjudicated data severity was not collected.

Adjudicated data is sorted as listed in the SAP. Other events are sorted alphabetically.

A patient with multiple events in the same AESI category is counted only once for that AESI category.

Analysis population: B2306 SAF total population

Table 18.2 AESI - Binary Analysis by Age (SAF)

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	476	475			
N' Age = 18-39 years	85	73			
N' Age = 40-64 years	290	307			
N' Age = ≥65 years	101	95			
Hypersensitivity					
Interaction test:	p=0,317				
Age = 18-39 years	18 (21,2)	12 (16,4)	1,37 [0,61; 3,07] 0,450	1,29 [0,67; 2,49] 0,452	0,05 [-0,07; 0,17] 0,445
Age = 40-64 years	72 (24,8)	91 (29,6)	0,78 [0,55; 1,13] 0,187	0,84 [0,64; 1,09] 0,189	-0,05 [-0,12; 0,02] 0,186
Age = ≥65 years	29 (28,7)	37 (38,9)	0,63 [0,35; 1,15] 0,131	0,74 [0,50; 1,10] 0,133	-0,10 [-0,23; 0,03] 0,128
Immunosuppression					
Interaction test:	p=0,362				
Age = 18-39 years	9 (10,6)	5 (6,8)	1,61 [0,51; 5,04] 0,413	1,55 [0,54; 4,41] 0,415	0,04 [-0,05; 0,12] 0,402
Age = 40-64 years	20 (6,9)	19 (6,2)	1,12 [0,59; 2,15] 0,727	1,11 [0,61; 2,04] 0,727	0,01 [-0,03; 0,05] 0,727
Age = ≥65 years	7 (6,9)	11 (11,6)	0,57 [0,21; 1,53] 0,265	0,60 [0,24; 1,48] 0,267	-0,05 [-0,13; 0,03] 0,262

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: p < 0,05

Applied model for OR: logit(proportion) = treatment + age + treatment * age

For adjudicated data severity was not collected.

Adjudicated data is sorted as listed in the SAP. Other events are sorted alphabetically.

Analysis population: B2306 SAF total population

Table 18.3 AESI - Binary Analysis by Gender (SAF)

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	476	475			
N' Gender = Male	187	169			
N' Gender = Female	289	306			
Hypersensitivity					
Interaction test:	p=0,459				
Gender = Male	46 (24,6)	44 (26,0)	0,93 [0,57; 1,50] 0,756	0,94 [0,66; 1,35] 0,755	-0,01 [-0,10; 0,08] 0,756
Gender = Female	73 (25,3)	96 (31,4)	0,74 [0,52; 1,06] 0,099	0,81 [0,62; 1,04] 0,100	-0,06 [-0,13; 0,01] 0,097
Immunosuppression					
Interaction test:	p=0,681				
Gender = Male	12 (6,4)	9 (5,3)	1,22 [0,50; 2,97] 0,663	1,20 [0,52; 2,79] 0,663	0,01 [-0,04; 0,06] 0,661
Gender = Female	24 (8,3)	26 (8,5)	0,98 [0,55; 1,74] 0,933	0,98 [0,57; 1,66] 0,933	-0,00 [-0,05; 0,04] 0,933

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + gender + treatment * gender

For adjudicated data severity was not collected.

Adjudicated data is sorted as listed in the SAP. Other events are sorted alphabetically.

Analysis population: B2306 SAF total population

Table 18.4 AESI - Binary Analysis by Region (SAF)

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	476	475			
N' Region = Asia	124	131			
N' Region = Europe	166	169			
N' Region = Latin America	166	166			
N' Region = Others	20	9			
Hypersensitivity					
Interaction test:	p=0,925				
Region = Asia	41 (33,1)	51 (38,9)	0,77 [0,46; 1,29] 0,330	0,85 [0,61; 1,18] 0,332	-0,06 [-0,18; 0,06] 0,328
Region = Europe	40 (24,1)	44 (26,0)	0,90 [0,55; 1,48] 0,682	0,93 [0,64; 1,34] 0,682	-0,02 [-0,11; 0,07] 0,682
Region = Latin America	32 (19,3)	42 (25,3)	0,71 [0,42; 1,19] 0,188	0,76 [0,51; 1,14] 0,190	-0,06 [-0,15; 0,03] 0,186
Region = Others	6 (30,0)	3 (33,3)	0,86 [0,16; 4,62] 0,858	0,90 [0,29; 2,82] 0,856	-0,03 [-0,40; 0,33] 0,859
Immunosuppression					
Interaction test:	N.E.				
Region = Asia	8 (6,5)	4 (3,1)	-	2,11 [0,65; 6,84] 0,212	0,03 [-0,02; 0,09] 0,203
Region = Europe	18 (10,8)	17 (10,1)	-	1,08 [0,58; 2,02] 0,815	0,01 [-0,06; 0,07] 0,815
Region = Latin America	8 (4,8)	13 (7,8)	-	0,62 [0,26; 1,45] 0,265	-0,03 [-0,08; 0,02] 0,259

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Region = Others	2 (10,0)	1 (11,1)	-	0,90 [0,09; 8,69] 0,927	-0,01 [-0,25; 0,23] 0,929

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
N.E.: not estimable
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + region + treatment * region

For adjudicated data severity was not collected.

Adjudicated data is sorted as listed in the SAP. Other events are sorted alphabetically.

Analysis population: B2306 SAF total population

Table 18.5 AESI - Binary Analysis by History of Asthma Exacerbation (SAF)

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=476)	**SAL/FLU + TIO (N=475)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	476	475			
N' Asthma exacerbations in the 12 months prior to screening = 1	375	383			
N' Asthma exacerbations in the 12 months prior to screening = ≥2	101	92			
Hypersensitivity					
Interaction test:	p=0,741				
Asthma exacerbations in the 12 months prior to screening = 1	85 (22,7)	102 (26,6)	0,81 [0,58; 1,12] 0,206	0,85 [0,66; 1,09] 0,207	-0,04 [-0,10; 0,02] 0,205
Asthma exacerbations in the 12 months prior to screening = ≥2	34 (33,7)	38 (41,3)	0,72 [0,40; 1,29] 0,273	0,82 [0,56; 1,18] 0,274	-0,08 [-0,21; 0,06] 0,272
Immunosuppression					
Interaction test:	p=0,610				
Asthma exacerbations in the 12 months prior to screening = 1	24 (6,4)	26 (6,8)	0,94 [0,53; 1,67] 0,829	0,94 [0,55; 1,61] 0,829	-0,00 [-0,04; 0,03] 0,829
Asthma exacerbations in the 12 months prior to screening = ≥2	12 (11,9)	9 (9,8)	1,24 [0,50; 3,10] 0,641	1,21 [0,54; 2,75] 0,641	0,02 [-0,07; 0,11] 0,639

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + history of asthma exacerbation + treatment * history of asthma exacerbation

For adjudicated data severity was not collected.

Adjudicated data is sorted as listed in the SAP. Other events are sorted alphabetically.

Analysis population: B2306 SAF total population

Table 18.6 AESI - Binary Analysis by Patients' Prior Therapies (SAF)

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=472)	**SAL/FLU + TIO (N=472)**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
N'	472	472			
N' Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA	230	240			
N' Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA	242	232			
Hypersensitivity					
Interaction test:	p=0,025 *				
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA	46 (20,0)	74 (30,8)	0,56 [0,37; 0,86] 0,007 *	0,65 [0,47; 0,89] 0,008 *	-0,11 [-0,19; -0,03] 0,006 *
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA	72 (29,8)	65 (28,0)	1,09 [0,73; 1,62] 0,677	1,06 [0,80; 1,41] 0,677	0,02 [-0,06; 0,10] 0,677
Immunosuppression					
Interaction test:	p=0,412				
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA	17 (7,4)	14 (5,8)	1,29 [0,62; 2,68] 0,498	1,27 [0,64; 2,51] 0,497	0,02 [-0,03; 0,06] 0,497
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA	19 (7,9)	21 (9,1)	0,86 [0,45; 1,64] 0,638	0,87 [0,48; 1,57] 0,639	-0,01 [-0,06; 0,04] 0,639

N': Number of patients in the analysis
CI: Confidence Interval
OR: Odds Ratio
RR: Relative Risk
RD: Risk Difference
*: $p < 0,05$

Applied model for OR: logit(proportion) = treatment + patients' prior therapies + treatment * patients' prior therapies

For adjudicated data severity was not collected.

Adjudicated data is sorted as listed in the SAP. Other events are sorted alphabetically.

Analysis population: B2306 SAF total population

19. Trough FEV1 - Change from Baseline

Table 19.1 Trough FEV1 - Change from Baseline (FAS)

	Treatment groups		Comparison	
Outcome - Change from Baseline (FAS)	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Trough FEV1				
N'	440	430		
Baseline Mean (SD)	1,86 (0,642)	1,86 (0,660)		
Week 8:				
Adjusted Mean Change (SE)	0,29 (0,024)	0,23 (0,024)	0,06 [0,009; 0,108] 0,020 *	0,124 [-0,018; 0,265]
Week 16:				
Adjusted Mean Change (SE)	0,30 (0,024)	0,24 (0,024)	0,06 [0,008; 0,105] 0,024 *	0,120 [-0,021; 0,262]
Week 24:				
Adjusted Mean Change (SE)	0,32 (0,024)	0,23 (0,025)	0,09 [0,036; 0,139] 0,001 *	0,182 [0,040; 0,324]

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 19.2 Trough FEV1 - Change from Baseline by Age (FAS)

	Treatment groups		Comparison	
Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Trough FEV1				
Interaction Test	0,763			
Age = 18-39 years				
N'	82	64		
Baseline Mean (SD)	2,42 (0,664)	2,38 (0,745)		
Week 8:				
Adjusted Mean Change (SE)	0,40 (0,045)	0,39 (0,049)	0,00 [-0,118; 0,123] 0,963	0,008 [-0,335; 0,350]
Week 16:				
Adjusted Mean Change (SE)	0,44 (0,045)	0,38 (0,049)	0,07 [-0,052; 0,187] 0,270	0,183 [-0,170; 0,535]
Week 24:				
Adjusted Mean Change (SE)	0,45 (0,047)	0,43 (0,051)	0,02 [-0,108; 0,143] 0,785	0,045 [-0,308; 0,399]
Age = 40-64 years				
N'	265	278		
Baseline Mean (SD)	1,83 (0,568)	1,87 (0,597)		
Week 8:				
Adjusted Mean Change (SE)	0,28 (0,027)	0,21 (0,027)	0,06 [0,001; 0,125] 0,047 *	0,148 [-0,031; 0,326]
Week 16:				
Adjusted Mean Change (SE)	0,28 (0,027)	0,24 (0,027)	0,04 [-0,023; 0,100] 0,217	0,091 [-0,087; 0,270]
Week 24:				
Adjusted Mean Change (SE)	0,30 (0,028)	0,20 (0,028)	0,09 [0,030; 0,158] 0,004 *	0,216 [0,037; 0,395]
Age = ≥65 years				
N'	93	88		
Baseline Mean (SD)	1,46 (0,458)	1,44 (0,489)		

	Treatment groups		Comparison	
Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	0,20 (0,043)	0,13 (0,045)	0,07 [-0,040; 0,178] 0,213	0,179 [-0,138; 0,496]
Week 16:				
Adjusted Mean Change (SE)	0,20 (0,043)	0,12 (0,044)	0,09 [-0,021; 0,193] 0,114	0,224 [-0,090; 0,537]
Week 24:				
Adjusted Mean Change (SE)	0,22 (0,044)	0,12 (0,046)	0,10 [-0,011; 0,211] 0,077	0,251 [-0,062; 0,564]

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + age + age * treatment + age * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 19.3 Trough FEV1 - Change from Baseline by Gender (FAS)

	Treatment groups		Comparison	
Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Trough FEV1				
Interaction Test	0,833			
Gender = Male				
N'	171	158		
Baseline Mean (SD)	2,21 (0,699)	2,29 (0,723)		
Week 8:				
Adjusted Mean Change (SE)	0,34 (0,032)	0,33 (0,035)	0,02 [-0,065; 0,096] 0,714	0,037 [-0,193; 0,268]
Week 16:				
Adjusted Mean Change (SE)	0,36 (0,032)	0,29 (0,034)	0,07 [-0,013; 0,146] 0,100	0,167 [-0,063; 0,396]
Week 24:				
Adjusted Mean Change (SE)	0,40 (0,033)	0,30 (0,035)	0,09 [0,011; 0,176] 0,027 *	0,226 [-0,003; 0,455]
Gender = Female				
N'	269	272		
Baseline Mean (SD)	1,64 (0,489)	1,61 (0,466)		
Week 8:				
Adjusted Mean Change (SE)	0,25 (0,029)	0,17 (0,028)	0,08 [0,018; 0,143] 0,012 *	0,182 [0,002; 0,361]
Week 16:				
Adjusted Mean Change (SE)	0,25 (0,029)	0,21 (0,028)	0,05 [-0,015; 0,109] 0,138	0,107 [-0,073; 0,288]

	Treatment groups		Comparison	
Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	0,25 (0,030)	0,17 (0,029)	0,08 [0,014; 0,143] 0,018 *	0,174 [-0,007; 0,355]

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + gender + gender * treatment + gender * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 19.4 Trough FEV1 - Change from Baseline by Region (FAS)

	Treatment groups		Comparison	
Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Trough FEV1				
Interaction Test	N.E.			
Region = Asia				
N'	118	122		
Baseline Mean (SD)	1,64 (0,551)	1,67 (0,608)		
Week 8:				
Adjusted Mean Change (SE)	0,27 (0,028)	0,23 (0,028)	0,04 [-0,036; 0,118] 0,296	0,144 [-0,126; 0,413]
Week 16:				
Adjusted Mean Change (SE)	0,28 (0,029)	0,23 (0,028)	0,05 [-0,029; 0,129] 0,214	0,174 [-0,100; 0,448]
Week 24:				
Adjusted Mean Change (SE)	0,32 (0,030)	0,21 (0,029)	0,11 [0,027; 0,190] 0,009 *	0,360 [0,089; 0,632]
Region = Europe				
N'	149	153		
Baseline Mean (SD)	2,08 (0,647)	2,05 (0,655)		
Week 8:				
Adjusted Mean Change (SE)	0,24 (0,025)	0,20 (0,025)	0,04 [-0,027; 0,110] 0,232	0,147 [-0,094; 0,387]
Week 16:				
Adjusted Mean Change (SE)	0,25 (0,025)	0,22 (0,025)	0,03 [-0,041; 0,097] 0,428	0,096 [-0,141; 0,332]
Week 24:				
Adjusted Mean Change (SE)	0,26 (0,027)	0,20 (0,027)	0,06 [-0,012; 0,139] 0,100	0,202 [-0,039; 0,443]
Region = Latin America				
N'	153	147		
Baseline Mean (SD)	1,82 (0,655)	1,82 (0,652)		

	Treatment groups		Comparison	
Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 8:				
Adjusted Mean Change (SE)	0,43 (0,038)	0,32 (0,039)	0,11 [0,004; 0,220] 0,043 *	0,248 [0,008; 0,488]
Week 16:				
Adjusted Mean Change (SE)	0,42 (0,037)	0,33 (0,038)	0,09 [-0,014; 0,196] 0,090	0,211 [-0,033; 0,455]
Week 24:				
Adjusted Mean Change (SE)	0,41 (0,039)	0,32 (0,039)	0,09 [-0,019; 0,197] 0,106	0,200 [-0,043; 0,443]
Region = Others				
N'	20	8		
Baseline Mean (SD)	1,80 (0,513)	1,89 (0,814)		
Week 8:				
Adjusted Mean Change (SE)	0,18 (0,085)	0,44 (0,127)	-0,26 [-0,569; 0,049] 0,096	-0,770 [-1,686; 0,145]
Week 16:				
Adjusted Mean Change (SE)	0,31 (0,082)	0,36 (0,126)	-0,05 [-0,350; 0,256] 0,757	-0,133 [-0,966; 0,701]
Week 24:				
Adjusted Mean Change (SE)	0,35 (0,079)	0,30 (0,121)	0,05 [-0,241; 0,341] 0,732	0,147 [-0,687; 0,981]

N': Number of patients in the analysis
CI: Confidence Interval
N.E.: not estimable
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + region + region * treatment + region * treatment * visit, within-patient correlation: unstructured covariance matrix
Exceptional model(s): **Trough FEV1**: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region]
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 19.5 Trough FEV1 - Change from Baseline by History of Asthma Exacerbation (FAS)

	Treatment groups		Comparison	
Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Trough FEV1				
Interaction Test	0,382			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	350	349		
Baseline Mean (SD)	1,90 (0,632)	1,90 (0,662)		
Week 8:				
Adjusted Mean Change (SE)	0,31 (0,025)	0,23 (0,026)	0,07 [0,016; 0,126] 0,012 *	0,157 [0,000; 0,314]
Week 16:				
Adjusted Mean Change (SE)	0,31 (0,025)	0,25 (0,026)	0,06 [0,009; 0,118] 0,022 *	0,142 [-0,015; 0,299]
Week 24:				
Adjusted Mean Change (SE)	0,33 (0,026)	0,23 (0,026)	0,10 [0,043; 0,157] 0,001 *	0,219 [0,060; 0,377]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	90	81		
Baseline Mean (SD)	1,71 (0,659)	1,67 (0,618)		
Week 8:				
Adjusted Mean Change (SE)	0,23 (0,044)	0,22 (0,046)	0,01 [-0,103; 0,124] 0,856	0,028 [-0,300; 0,355]
Week 16:				
Adjusted Mean Change (SE)	0,25 (0,044)	0,22 (0,045)	0,03 [-0,081; 0,143] 0,587	0,083 [-0,247; 0,414]

	Treatment groups		Comparison	
Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	0,25 (0,045)	0,21 (0,046)	0,04 [-0,078; 0,154] 0,522	0,096 [-0,225; 0,417]

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + background ICS/LABA + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + history of asthma exacerbation + history of asthma exacerbation * treatment + history of asthma exacerbation * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

Analysis population: B2306 FAS total population

Table 19.6 Trough FEV1 - Change from Baseline by Patients' Prior Therapies (FAS)

	Treatment groups		Comparison	
Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Trough FEV1				
Interaction Test	0,414			
Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA				
N'	221	222		
Baseline Mean (SD)	1,92 (0,606)	1,88 (0,663)		
Week 8:				
Adjusted Mean Change (SE)	0,36 (0,030)	0,28 (0,030)	0,08 [0,009; 0,149] 0,026 *	0,190 [-0,009; 0,389]
Week 16:				
Adjusted Mean Change (SE)	0,36 (0,029)	0,29 (0,030)	0,07 [-0,000; 0,137] 0,051	0,165 [-0,033; 0,364]
Week 24:				
Adjusted Mean Change (SE)	0,39 (0,030)	0,28 (0,030)	0,11 [0,041; 0,184] 0,002 *	0,264 [0,066; 0,463]
Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA				
N'	219	208		
Baseline Mean (SD)	1,80 (0,671)	1,84 (0,657)		
Week 8:				
Adjusted Mean Change (SE)	0,22 (0,030)	0,19 (0,031)	0,04 [-0,032; 0,109] 0,289	0,091 [-0,110; 0,292]
Week 16:				
Adjusted Mean Change (SE)	0,24 (0,030)	0,19 (0,030)	0,04 [-0,025; 0,115] 0,209	0,108 [-0,094; 0,311]

	Treatment groups		Comparison	
Outcome - Change from Baseline (FAS) by Subgroup	**IND/GLY/ MF 160 N=476**	**SAL/FLU + TIO N=475**	**Mean Difference [95% CI] p-value**	**Hedges' G [95% CI]**
Week 24:				
Adjusted Mean Change (SE)	0,24 (0,031)	0,18 (0,031)	0,06 [-0,012; 0,135] 0,100	0,145 [-0,059; 0,348]

N': Number of patients in the analysis
CI: Confidence Interval
*: $p < 0,05$

Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + region + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + patients' prior therapies + patients' prior therapies * treatment + patients' prior therapies * treatment * visit, within-patient correlation: unstructured covariance matrix
If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.

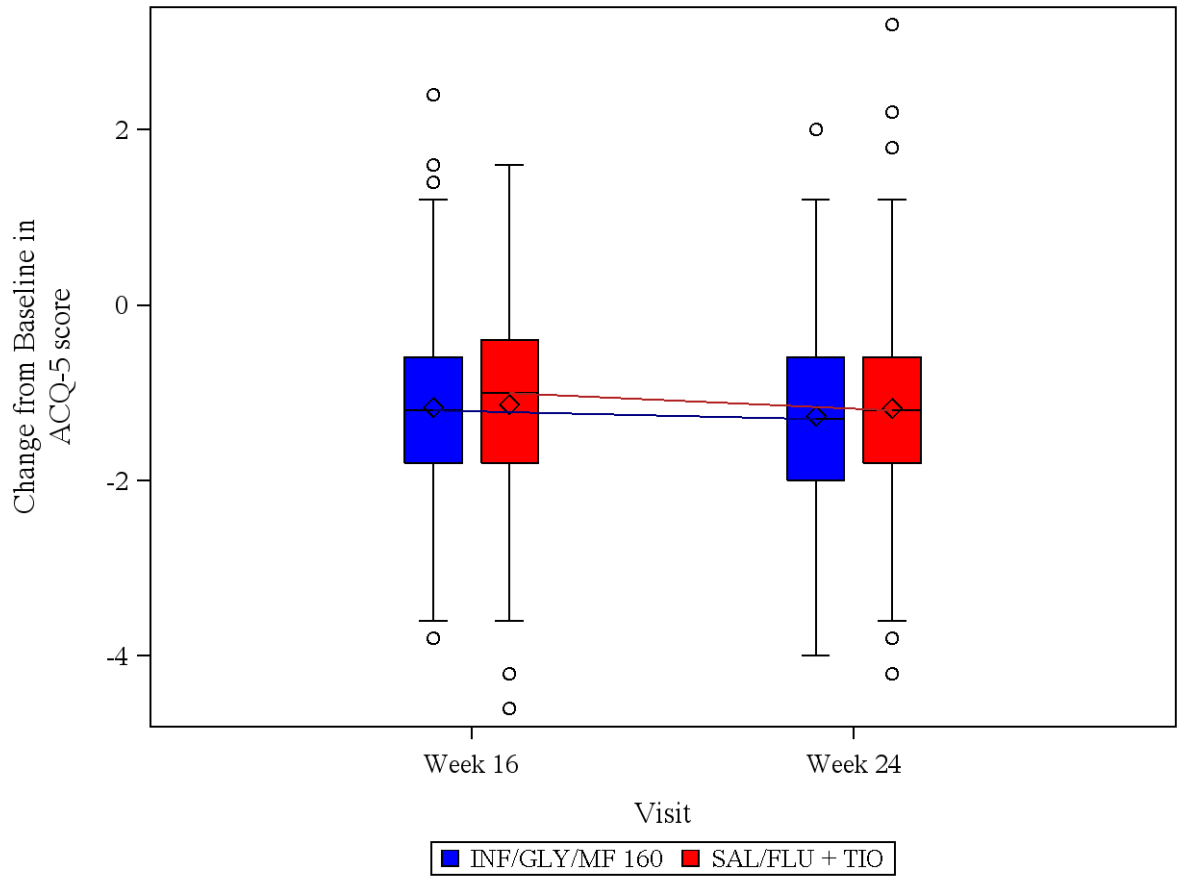
Analysis population: B2306 FAS total population

Figures

3. Boxplot: ACQ-5 - Change from Baseline (FAS)

3.1 Boxplot: ACQ-5 - Change from Baseline (FAS)

Figure 3.1 ACQ-5 - Change from Baseline (FAS)



3.2 Boxplot: ACQ-5 - Change from Baseline by Age (FAS)

Figure 3.2.1 ACQ-5 - Change from Baseline by Age (FAS), Age = 18-39 years

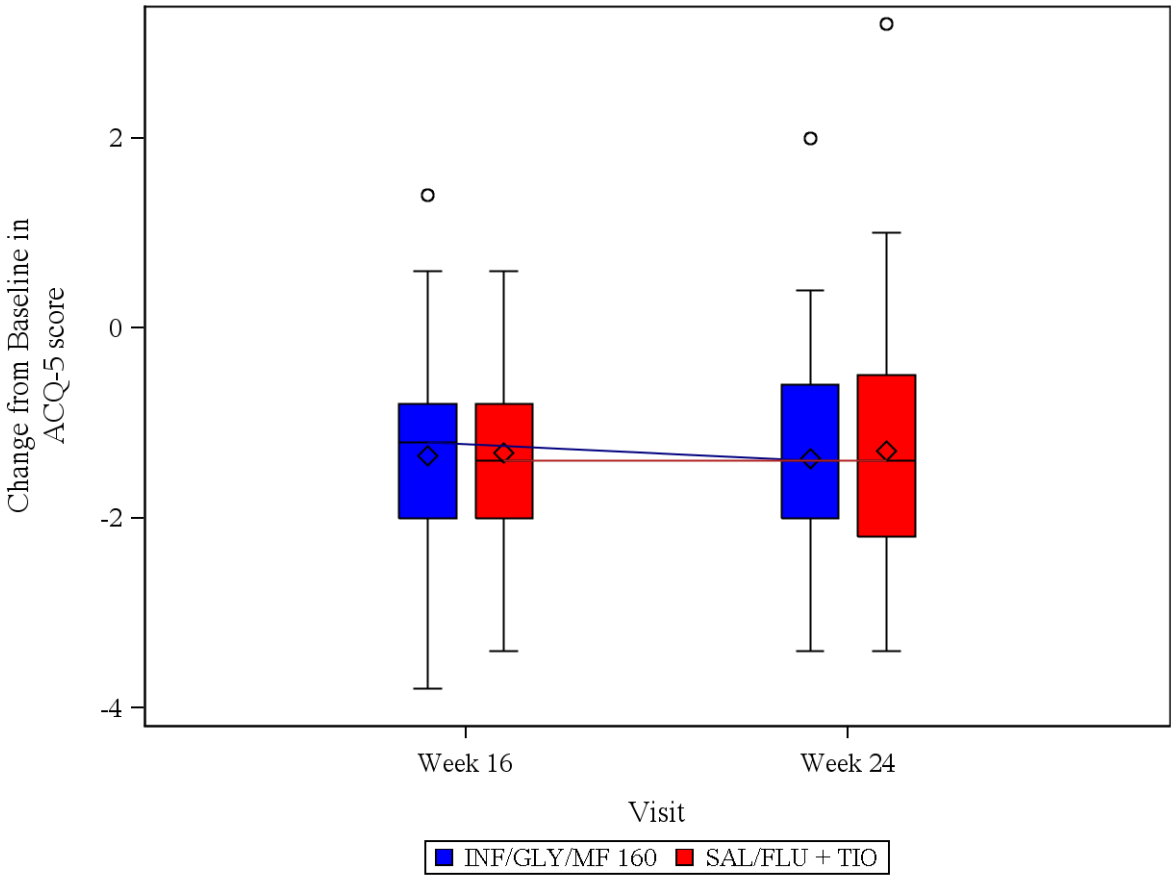


Figure 3.2.2 ACQ-5 - Change from Baseline by Age (FAS), Age = 40-64 years

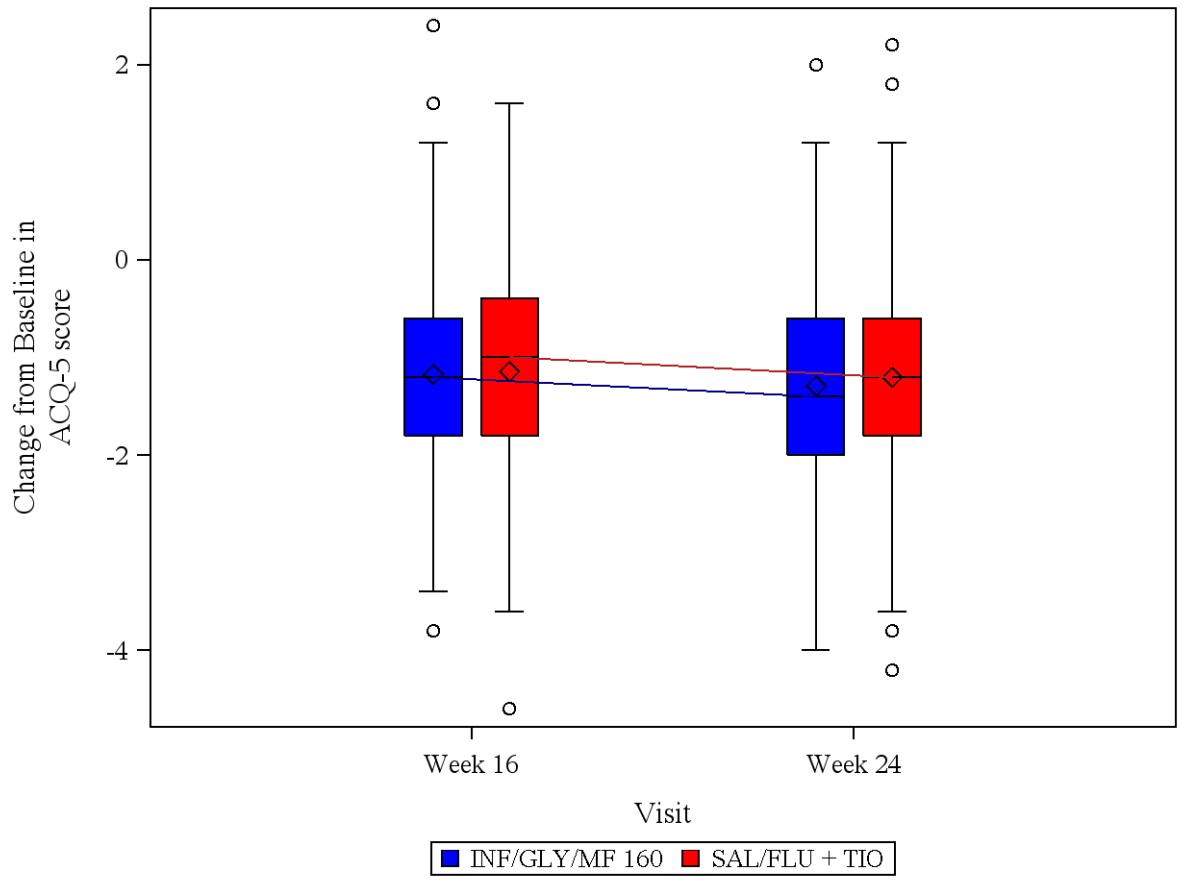
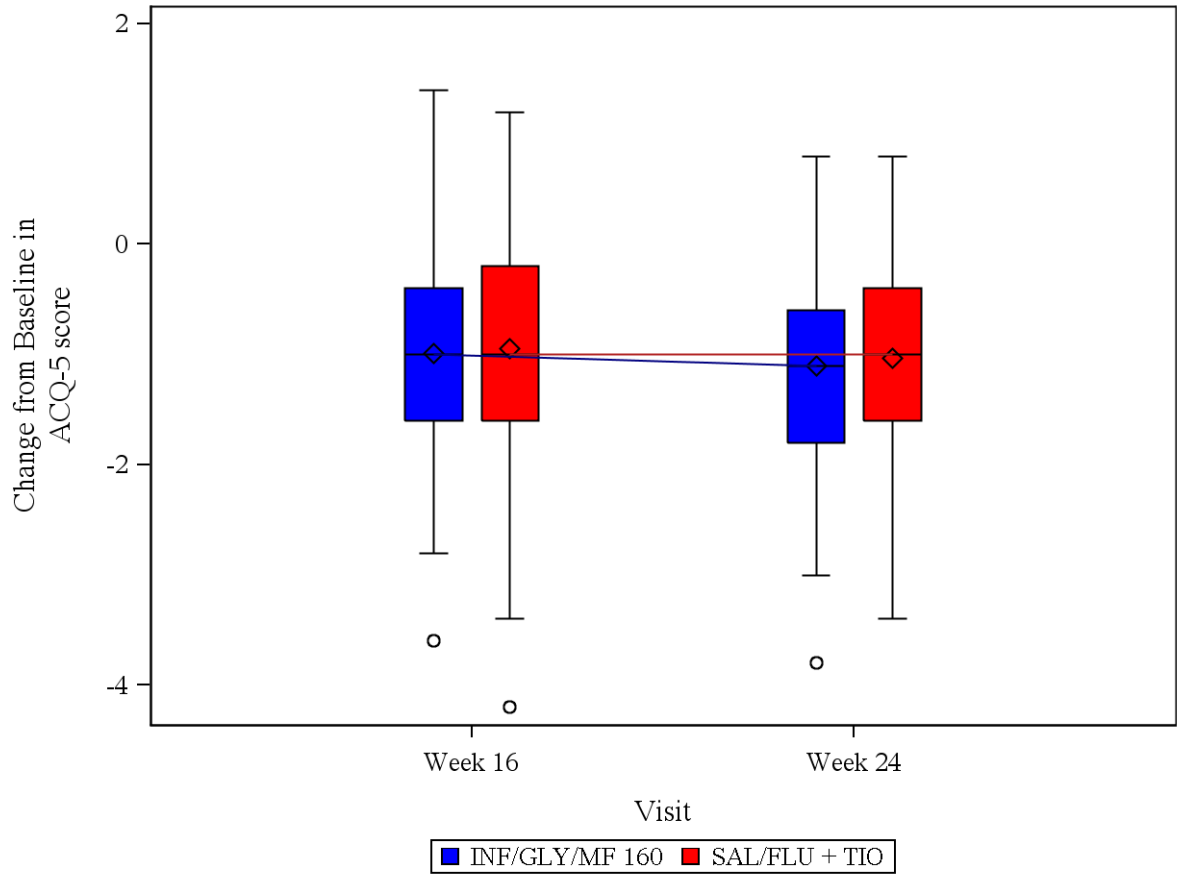


Figure 3.2.3 ACQ-5 - Change from Baseline by Age (FAS), Age = ≥65 years



3.3 Boxplot: ACQ-5 - Change from Baseline by Gender (FAS)

Figure 3.3.1 ACQ-5 - Change from Baseline by Gender (FAS), Gender = Male

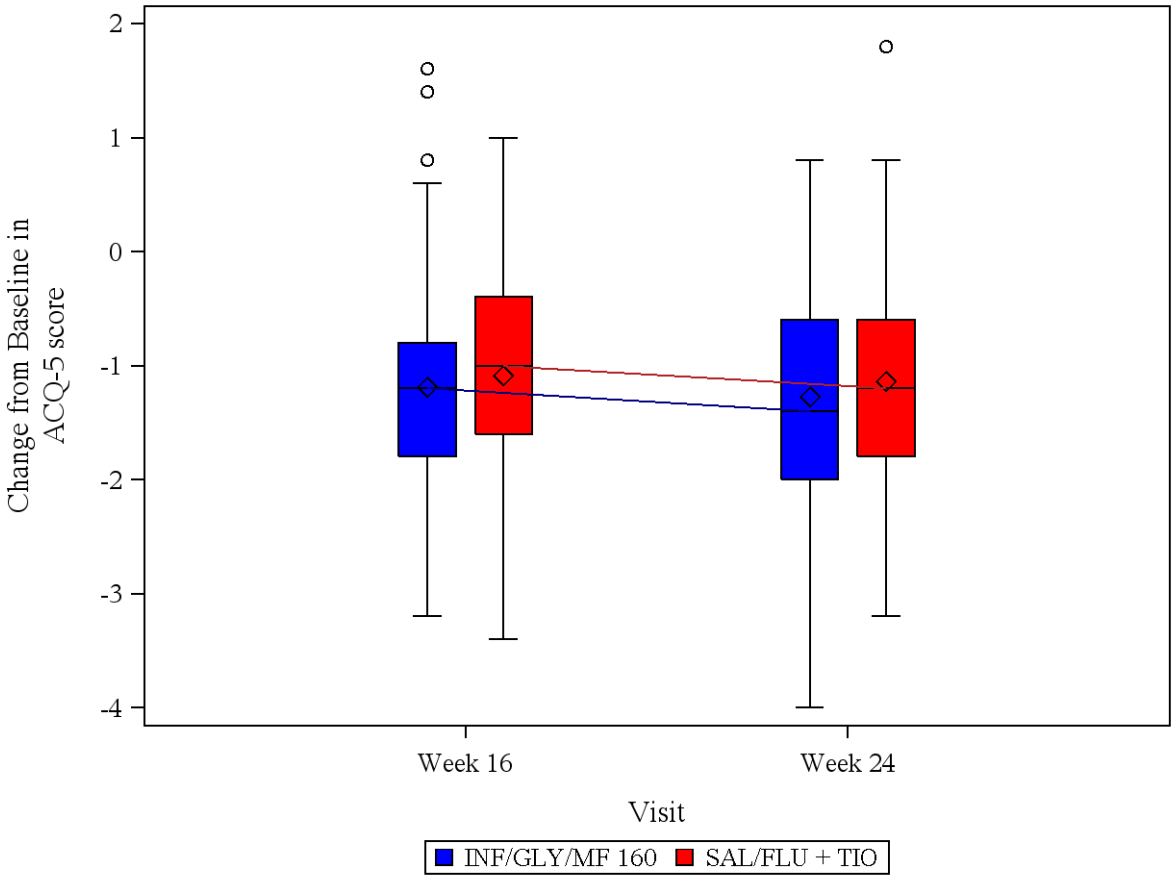
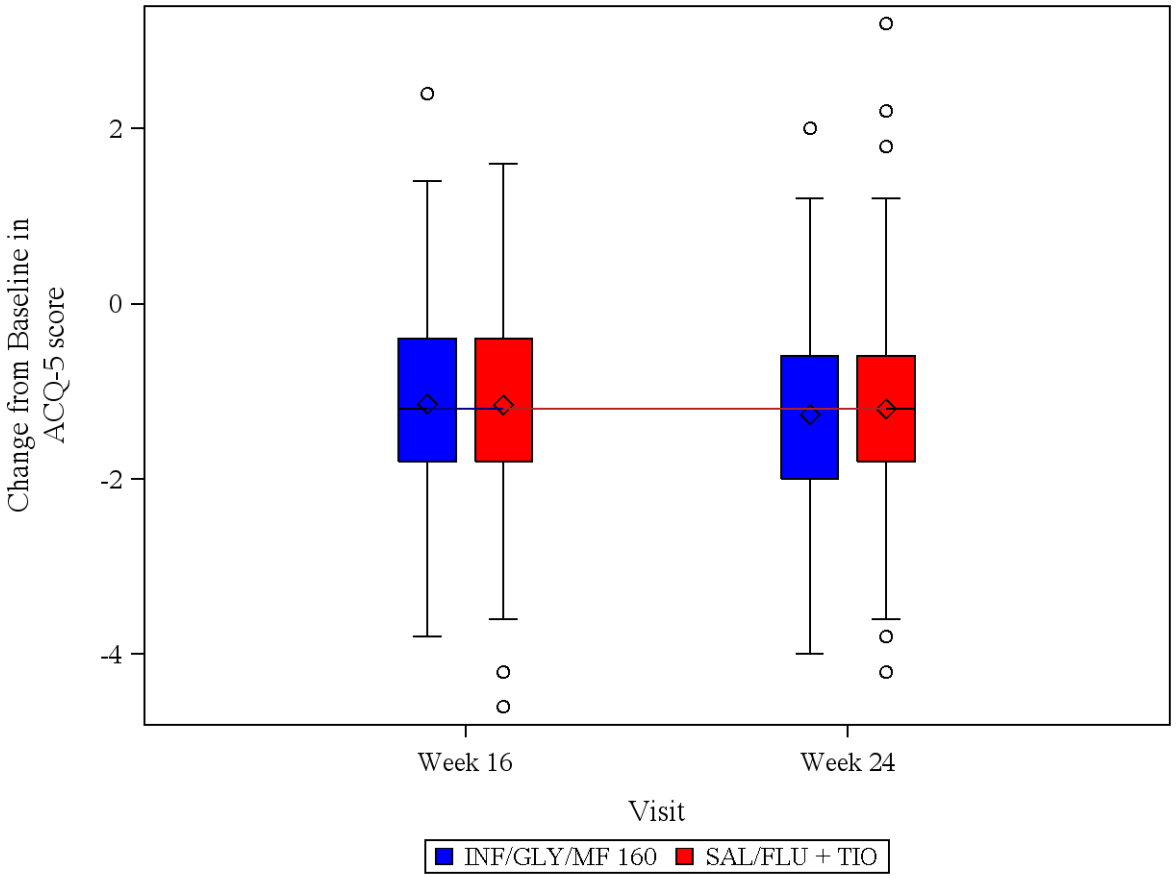


Figure 3.3.2 ACQ-5 - Change from Baseline by Gender (FAS), Gender = Female



3.4 Boxplot: ACQ-5 - Change from Baseline by Region (FAS)

Figure 3.4.1 ACQ-5 - Change from Baseline by Region (FAS), Region = Asia

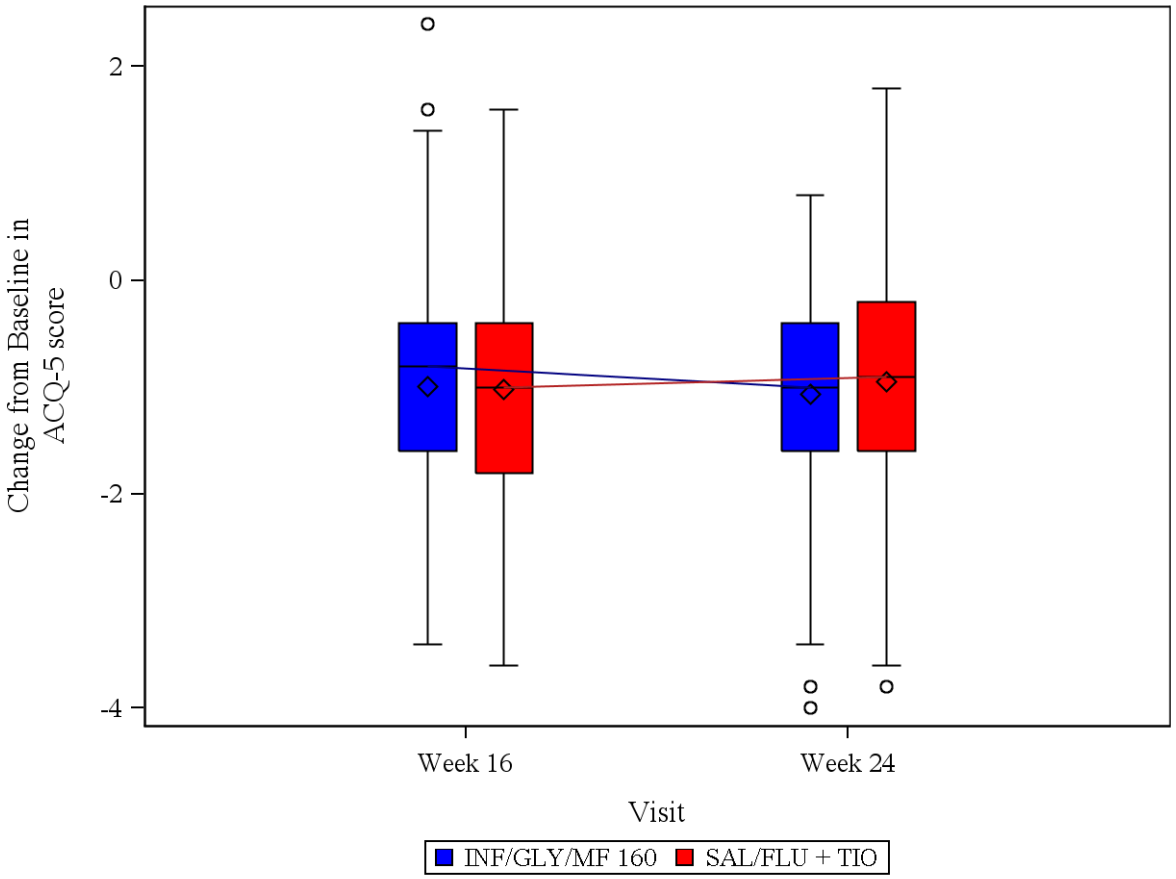


Figure 3.4.2 ACQ-5 - Change from Baseline by Region (FAS), Region = Europe

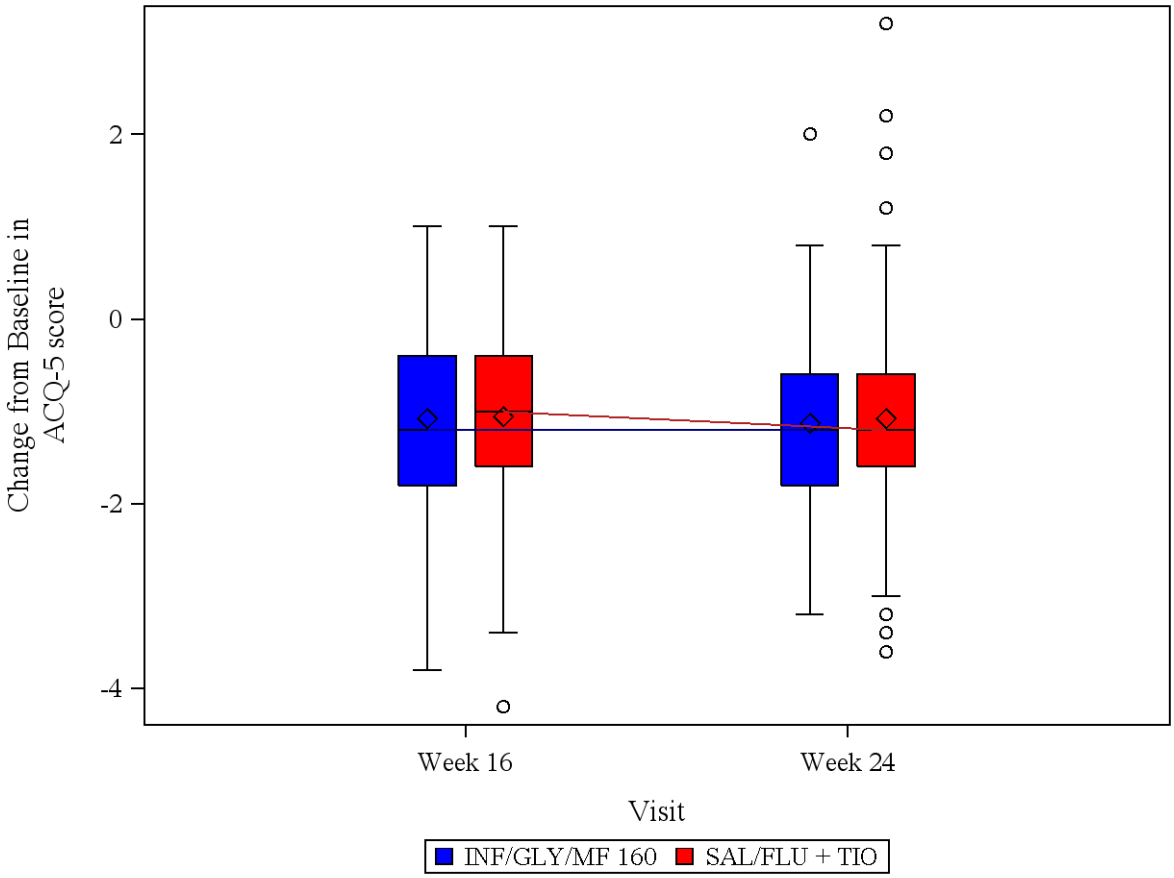


Figure 3.4.3 ACQ-5 - Change from Baseline by Region (FAS), Region = Latin America

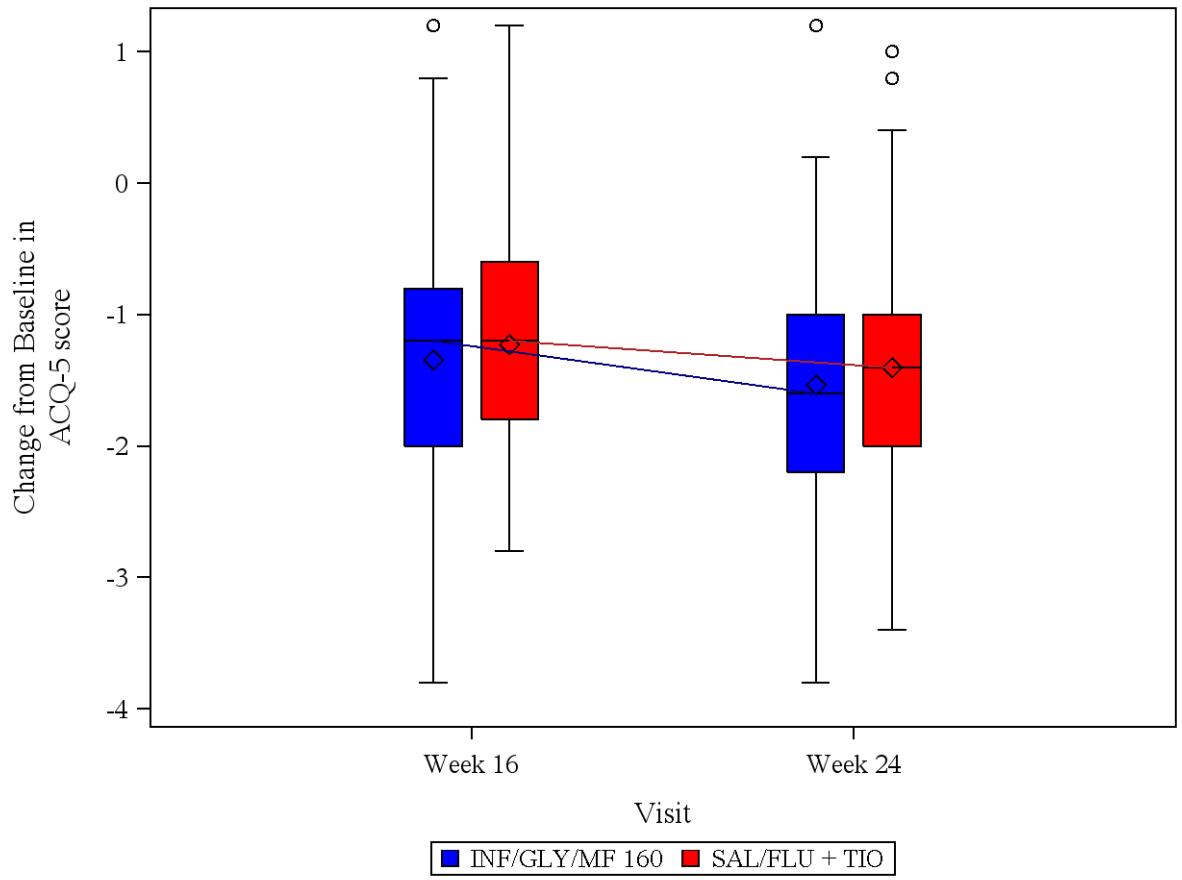
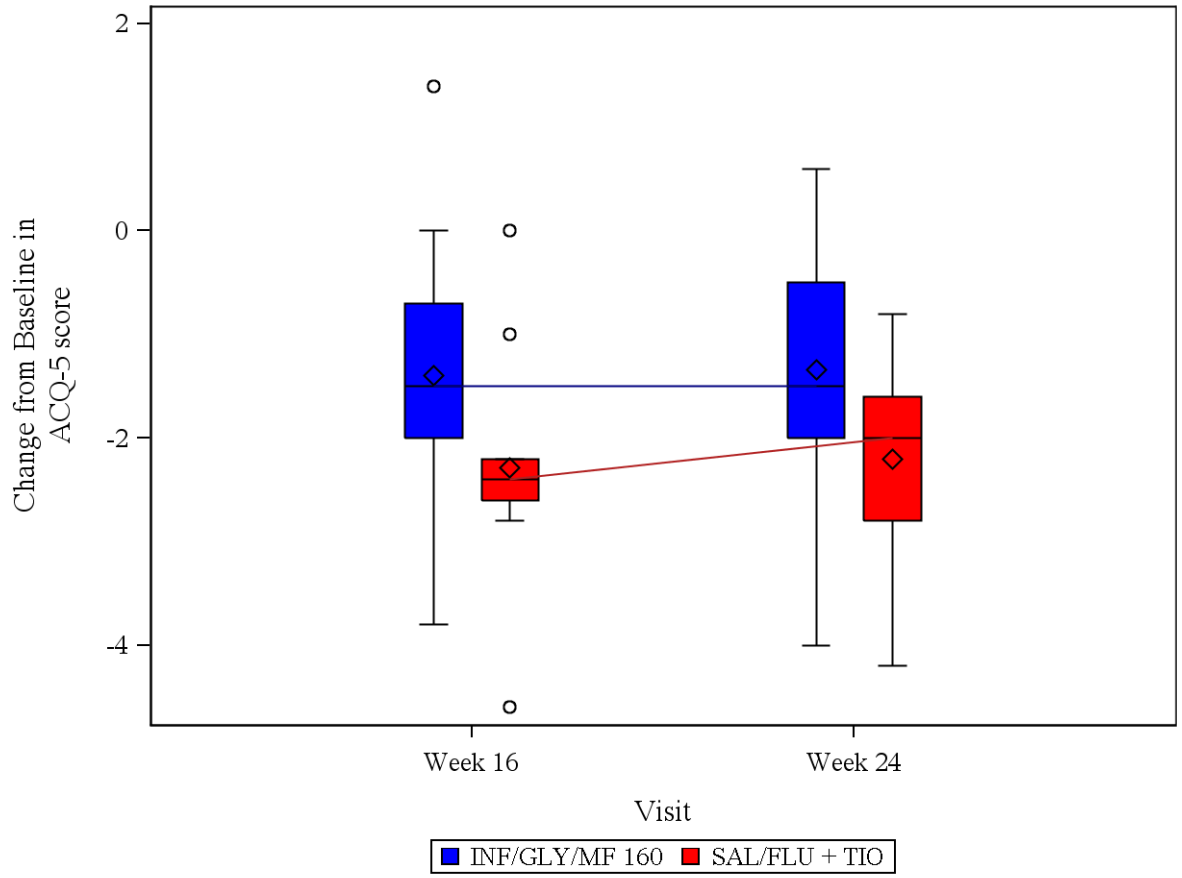


Figure 3.4.4 ACQ-5 - Change from Baseline by Region (FAS), Region = Others



3.5 Boxplot: ACQ-5 - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 3.5.1 ACQ-5 - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

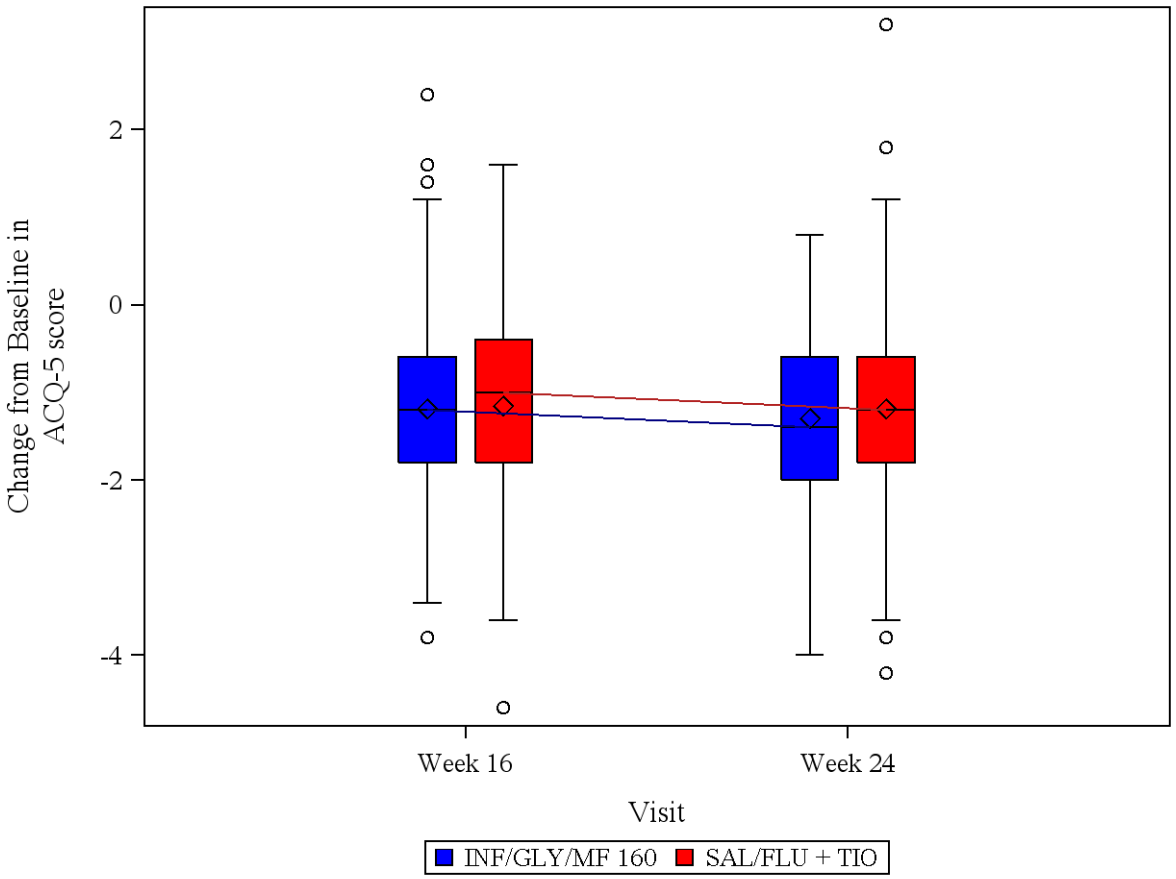
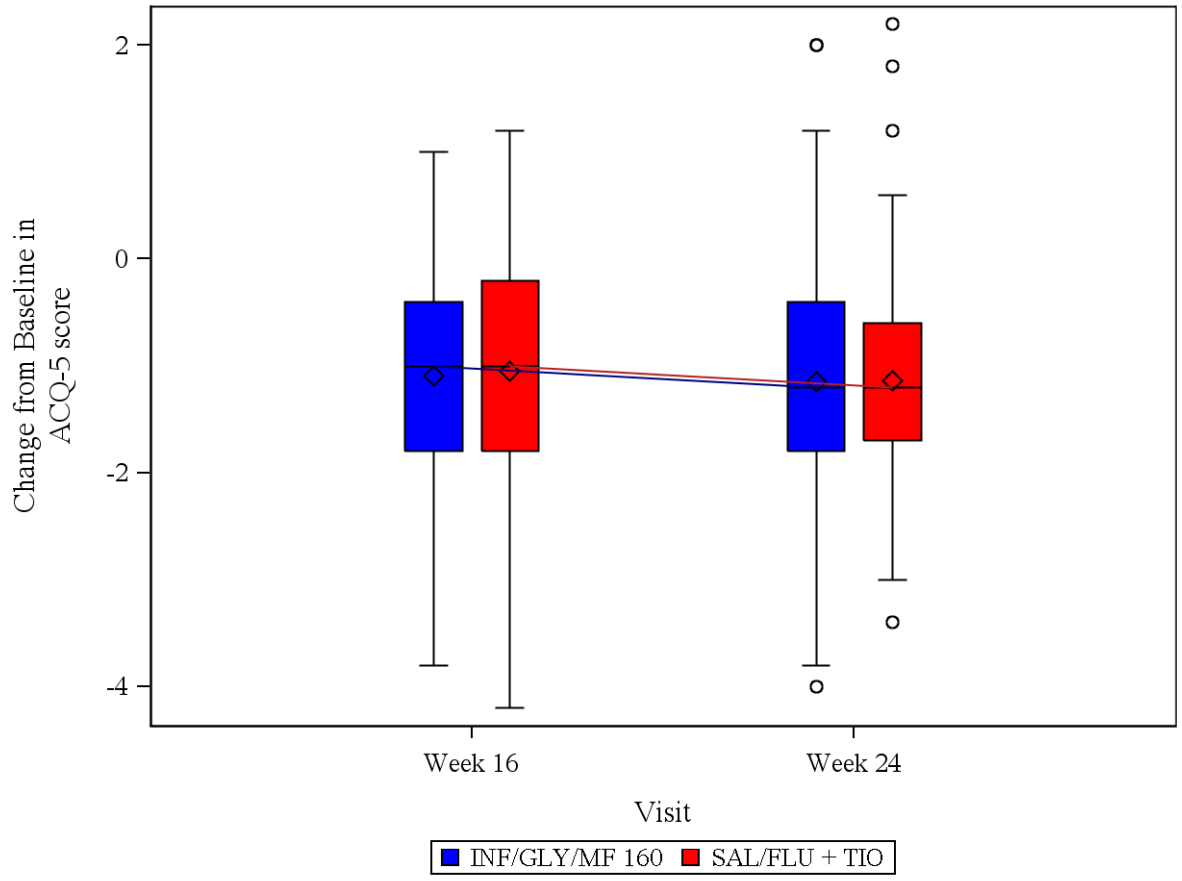


Figure 3.5.2 ACQ-5 - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



3.6 Boxplot: ACQ-5 - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 3.6.1 ACQ-5 - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

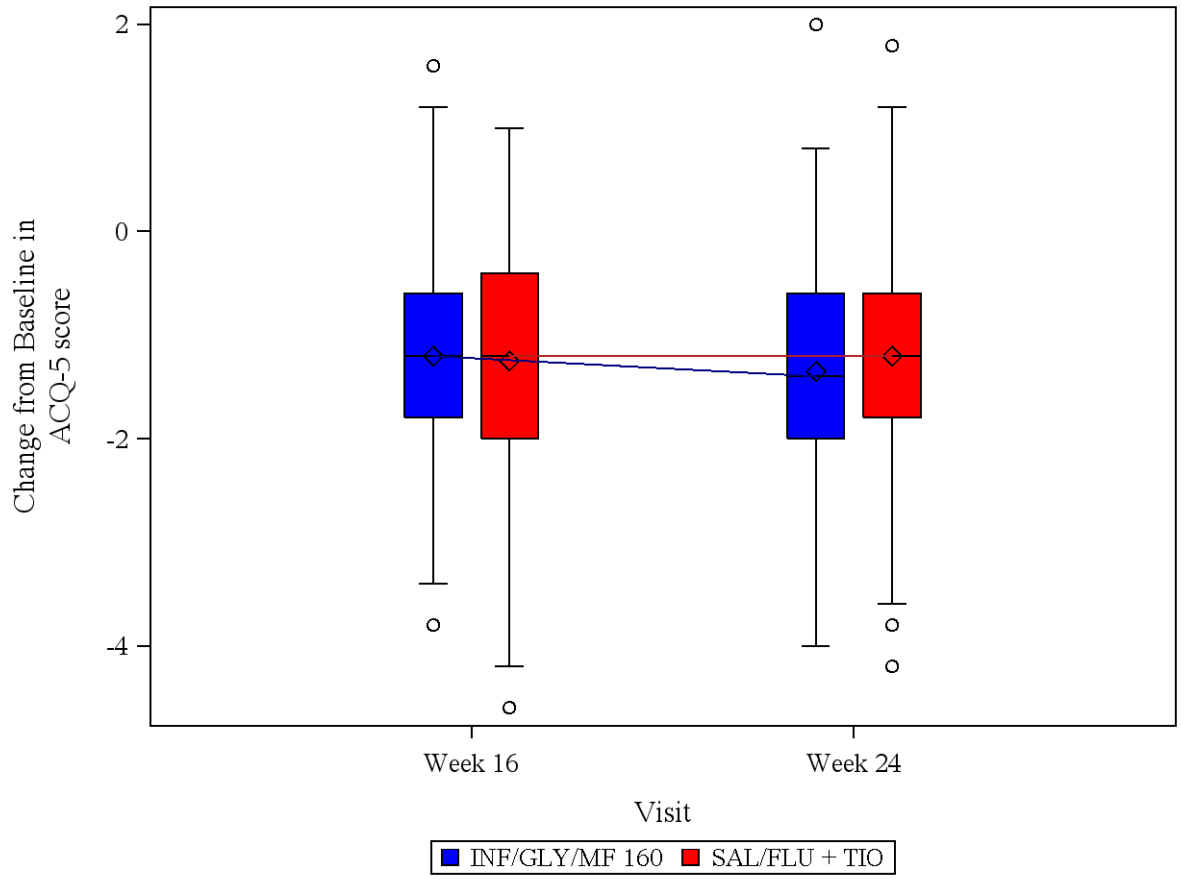
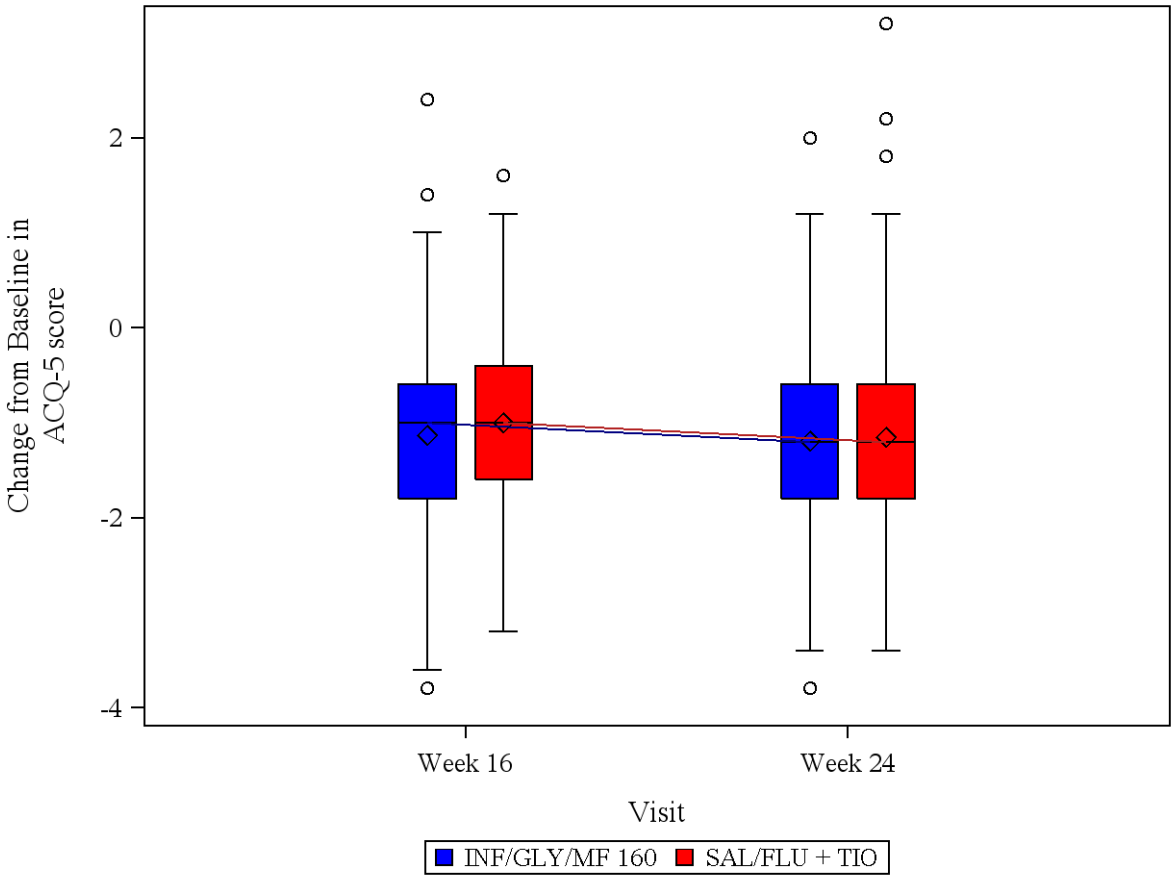


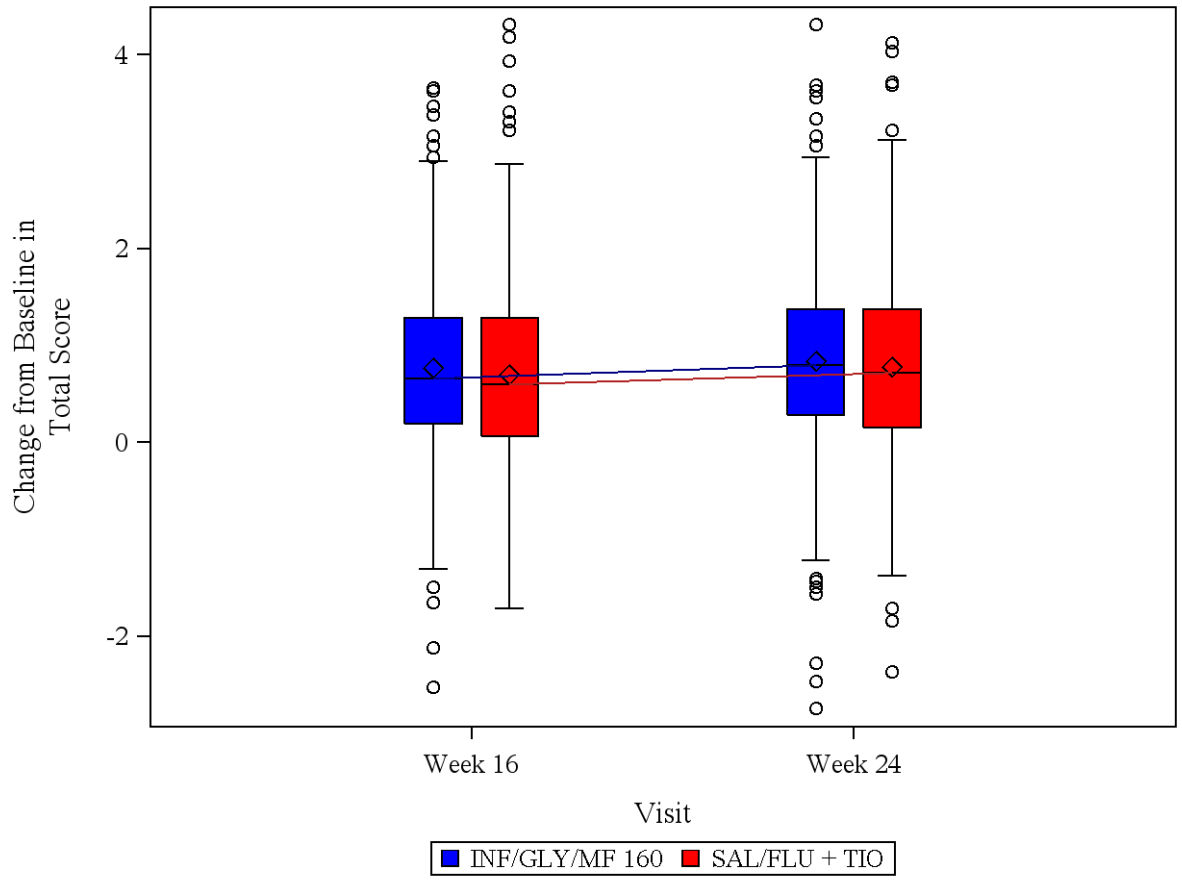
Figure 3.6.2 ACQ-5 - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



5. Boxplot: AQLQ-S - Change from Baseline (FAS)

5.1 Boxplot: AQLQ-S (Total Score) - Change from Baseline (FAS)

Figure 5.1 AQLQ-S (Total Score) - Change from Baseline (FAS)



5.2 Boxplot: AQLQ-S (Total Score) - Change from Baseline by Age (FAS)

Figure 5.2.1 AQLQ-S (Total Score) - Change from Baseline by Age (FAS), Age = 18-39 years

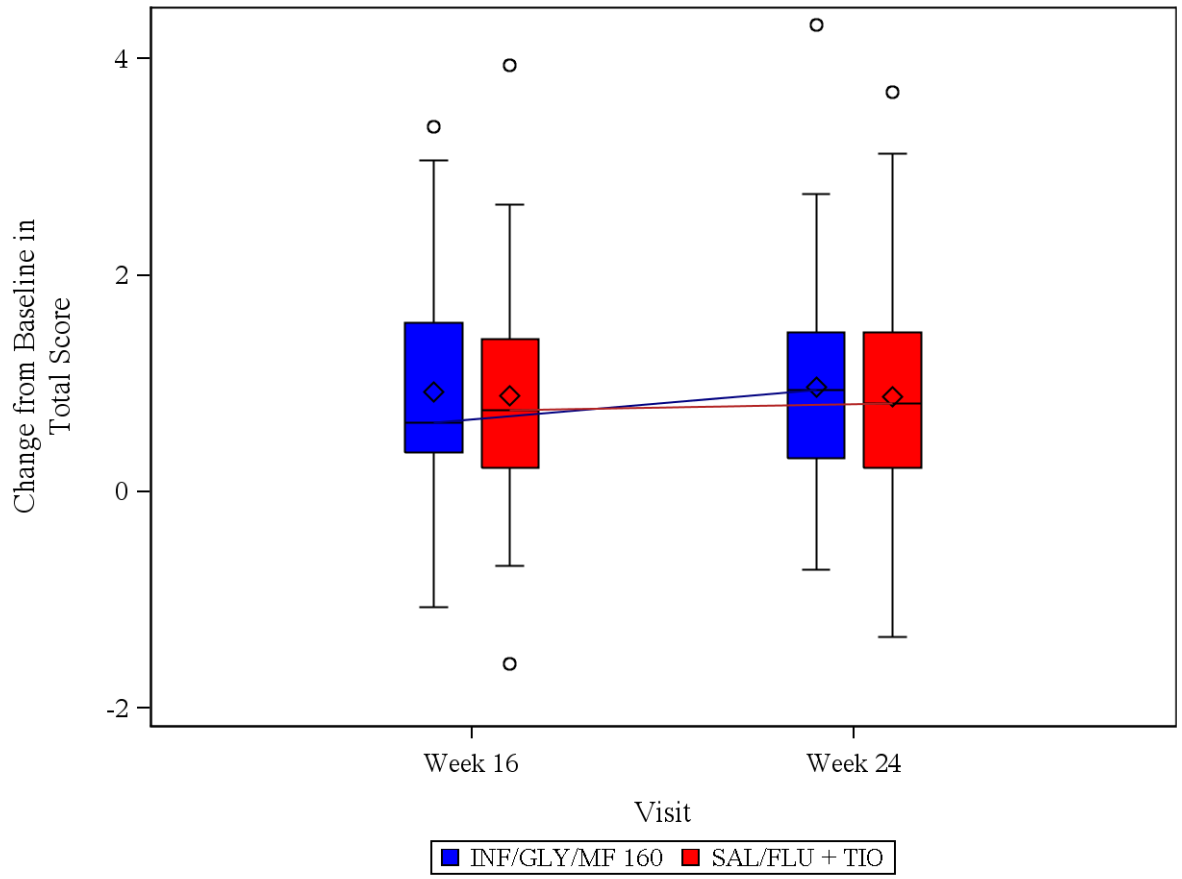


Figure 5.2.2 AQLQ-S (Total Score) - Change from Baseline by Age (FAS), Age = 40-64 years

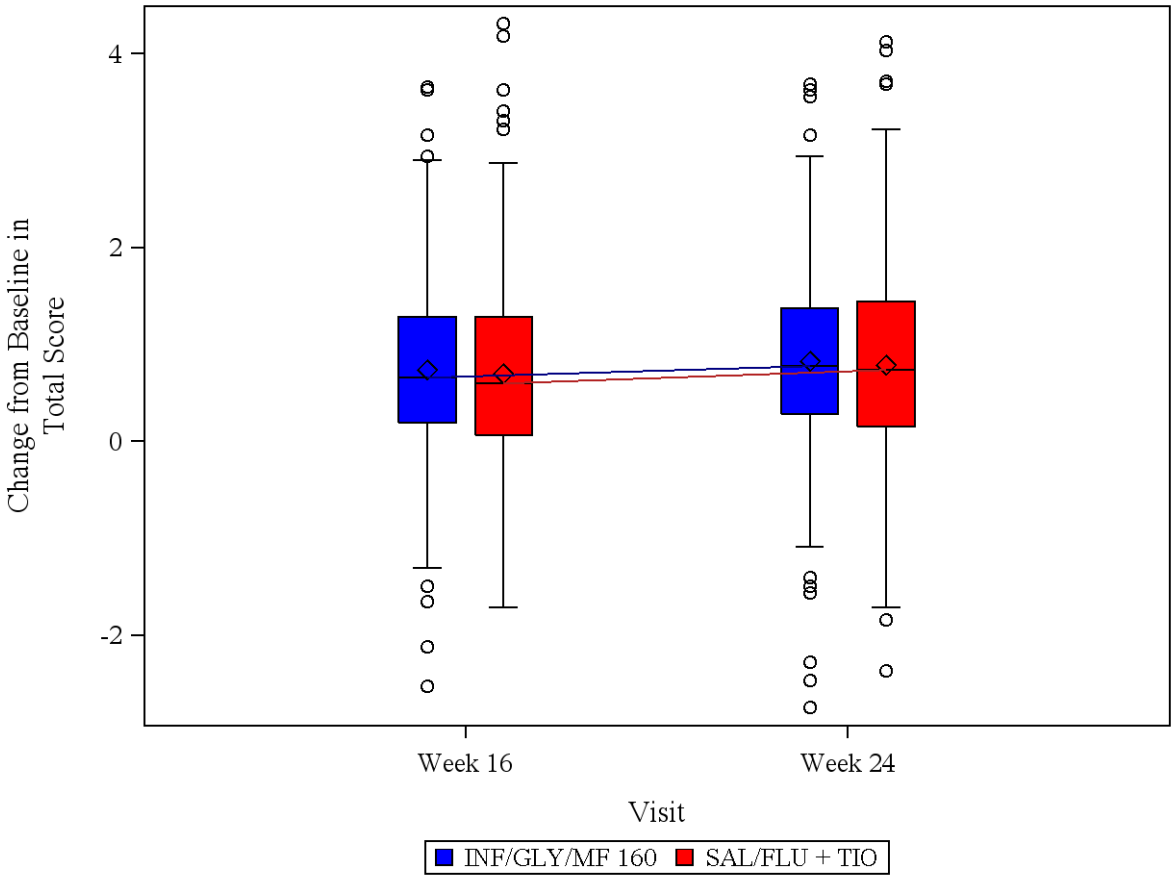
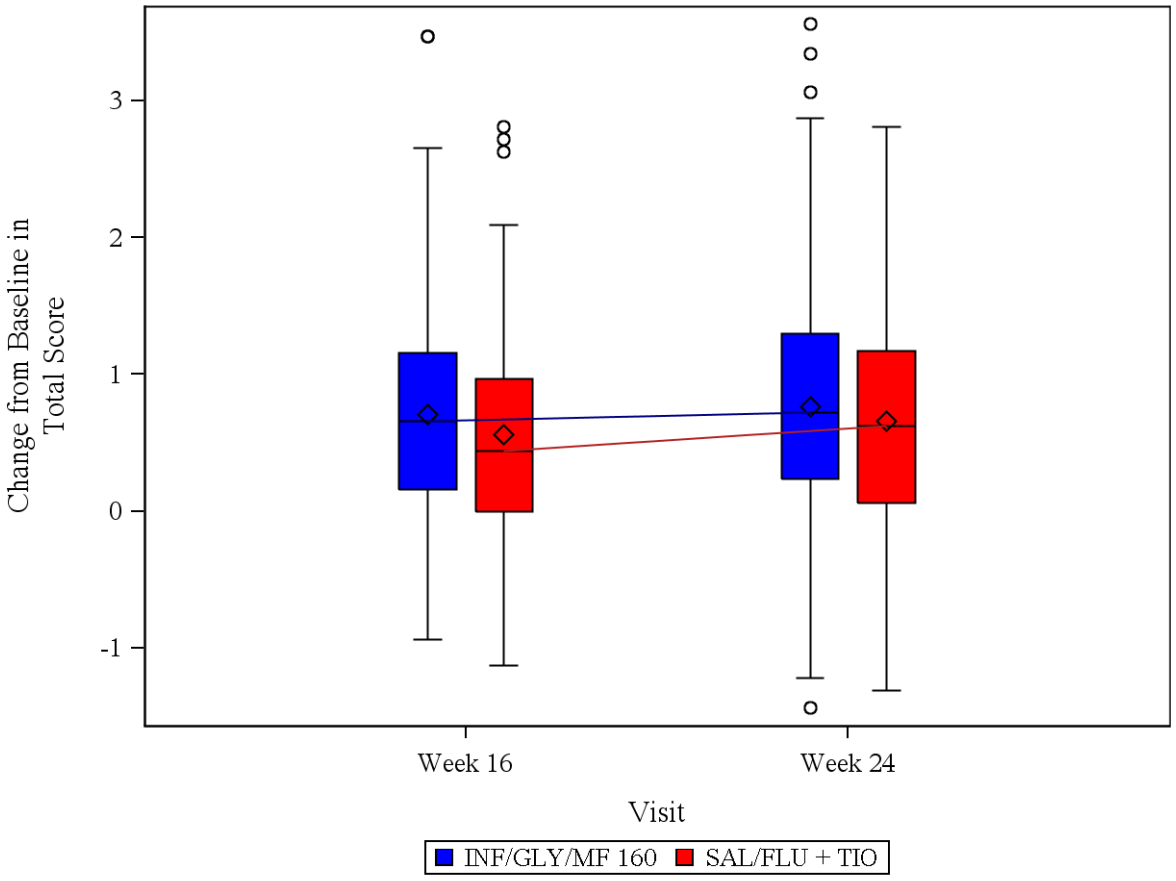


Figure 5.2.3 AQLQ-S (Total Score) - Change from Baseline by Age (FAS), Age = ≥65 years



5.3 Boxplot: AQLQ-S (Total Score) - Change from Baseline by Gender (FAS)

Figure 5.3.1 AQLQ-S (Total Score) - Change from Baseline by Gender (FAS), Gender = Male

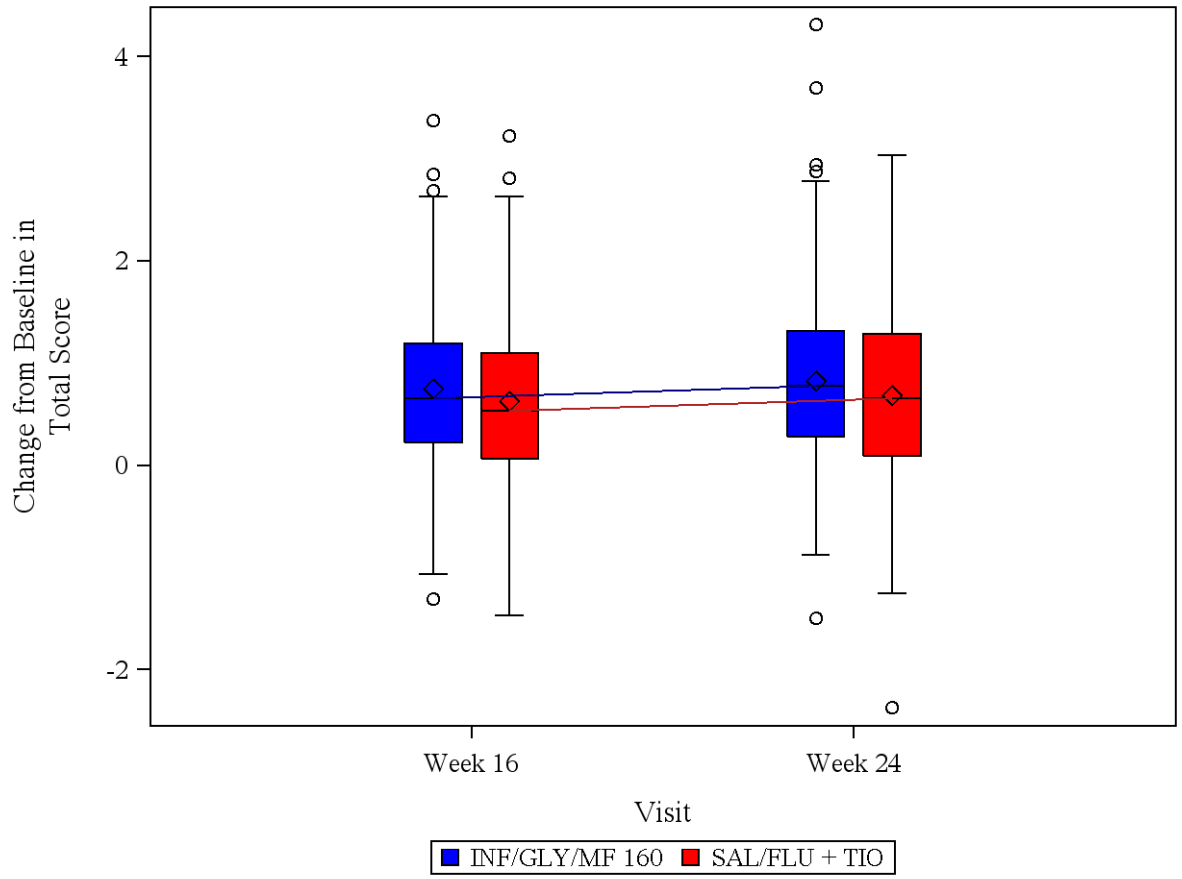
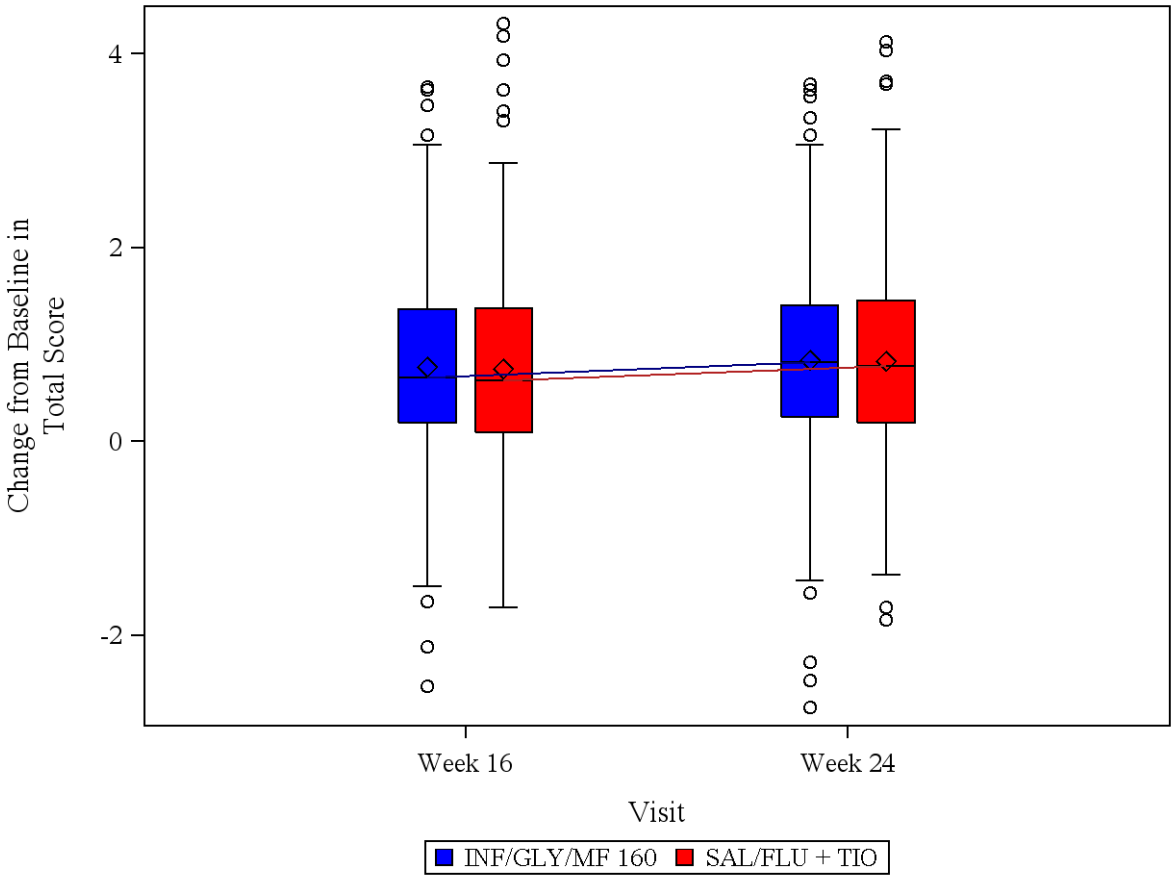


Figure 5.3.2 AQLQ-S (Total Score) - Change from Baseline by Gender (FAS), Gender = Female



5.4 Boxplot: AQLQ-S (Total Score) - Change from Baseline by Region (FAS)

Figure 5.4.1 AQLQ-S (Total Score) - Change from Baseline by Region (FAS), Region = Asia

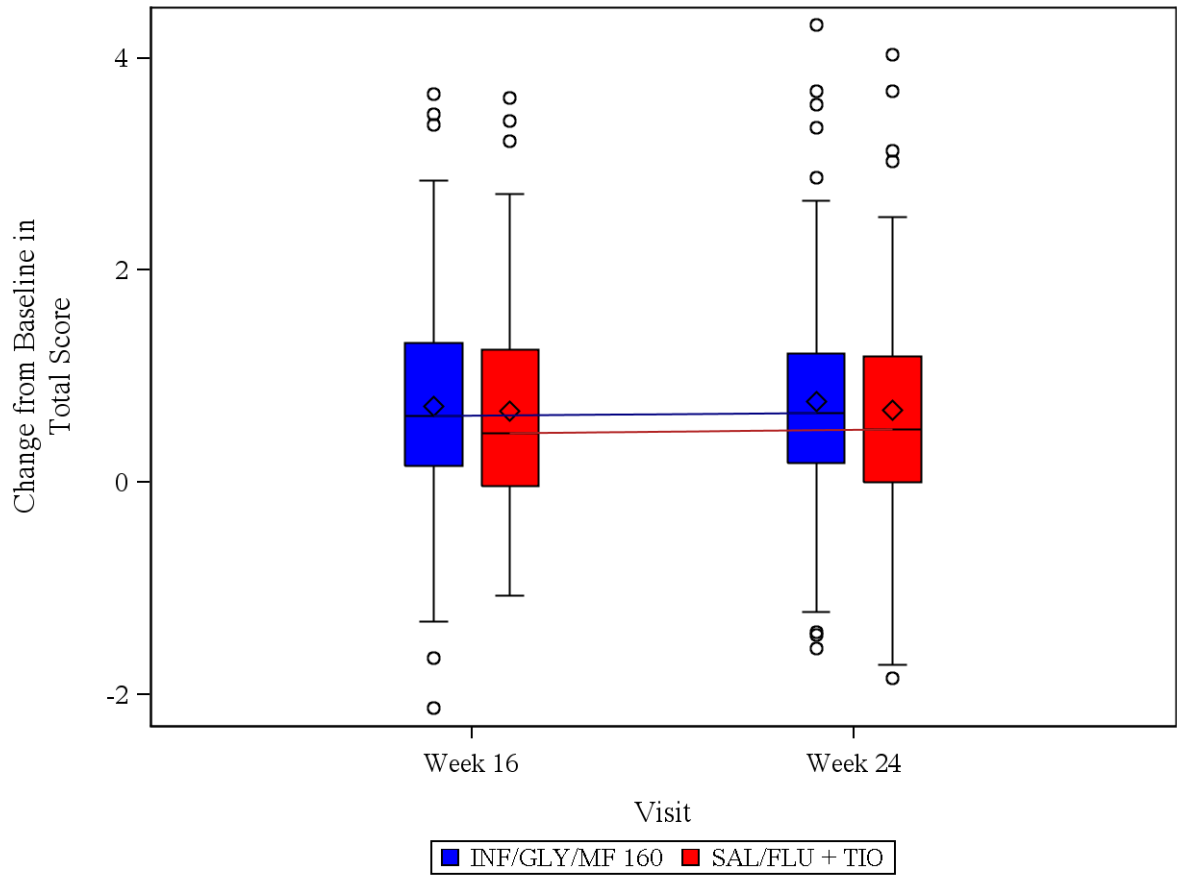


Figure 5.4.2 AQLQ-S (Total Score) - Change from Baseline by Region (FAS), Region = Europe

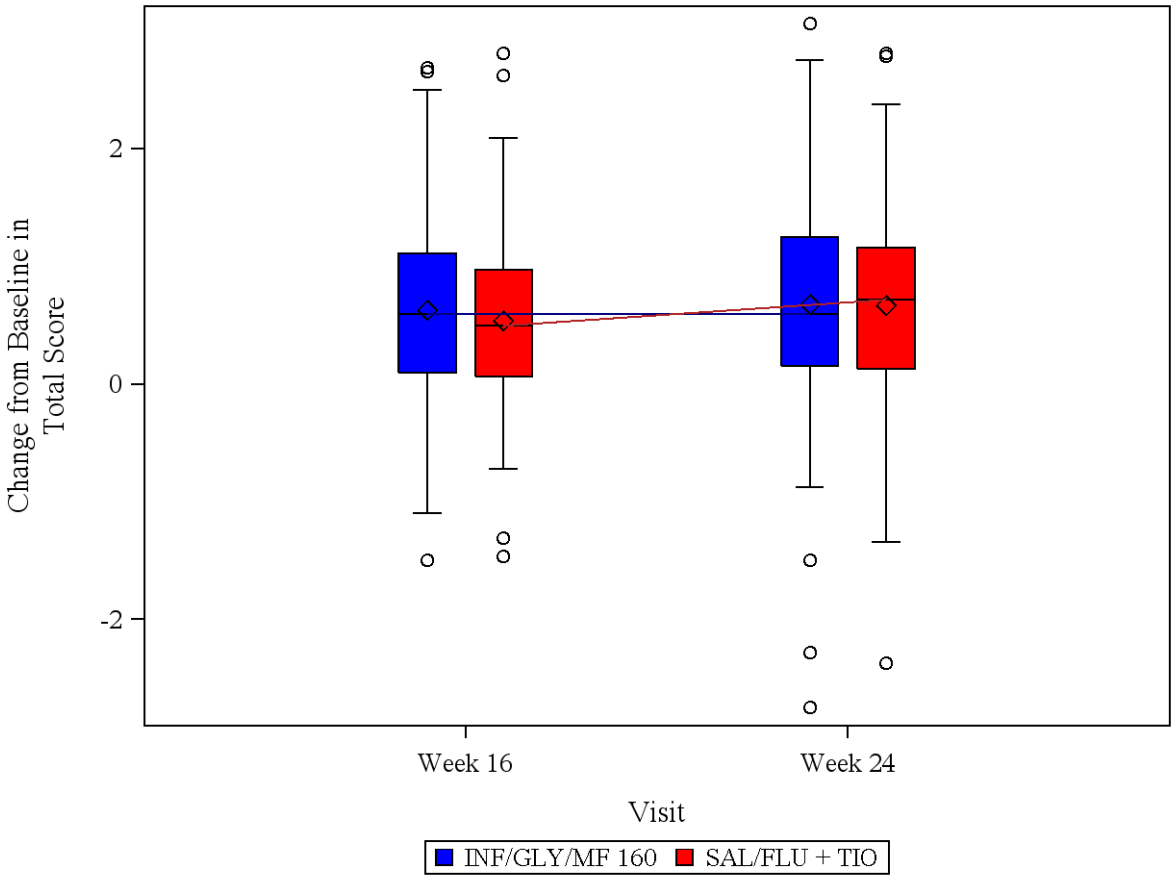


Figure 5.4.3 AQLQ-S (Total Score) - Change from Baseline by Region (FAS), Region = Latin America

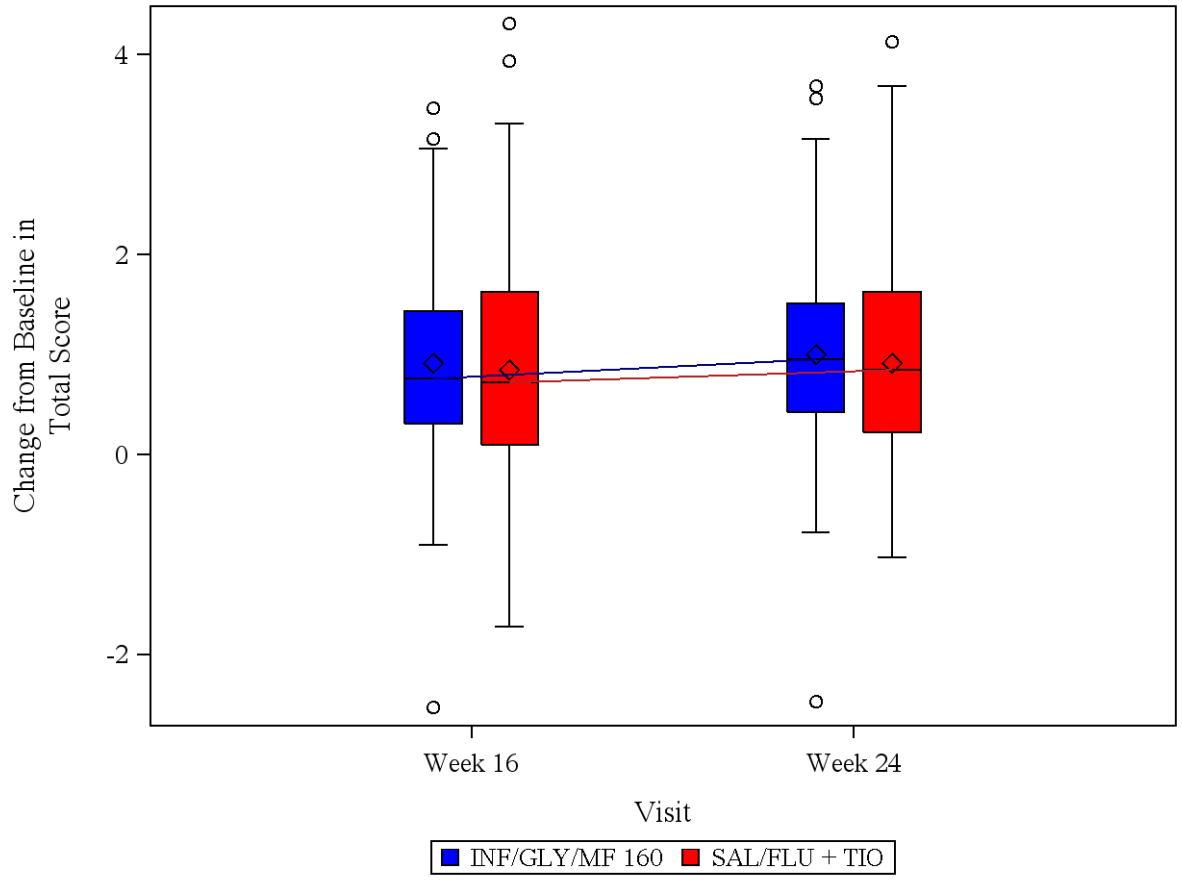
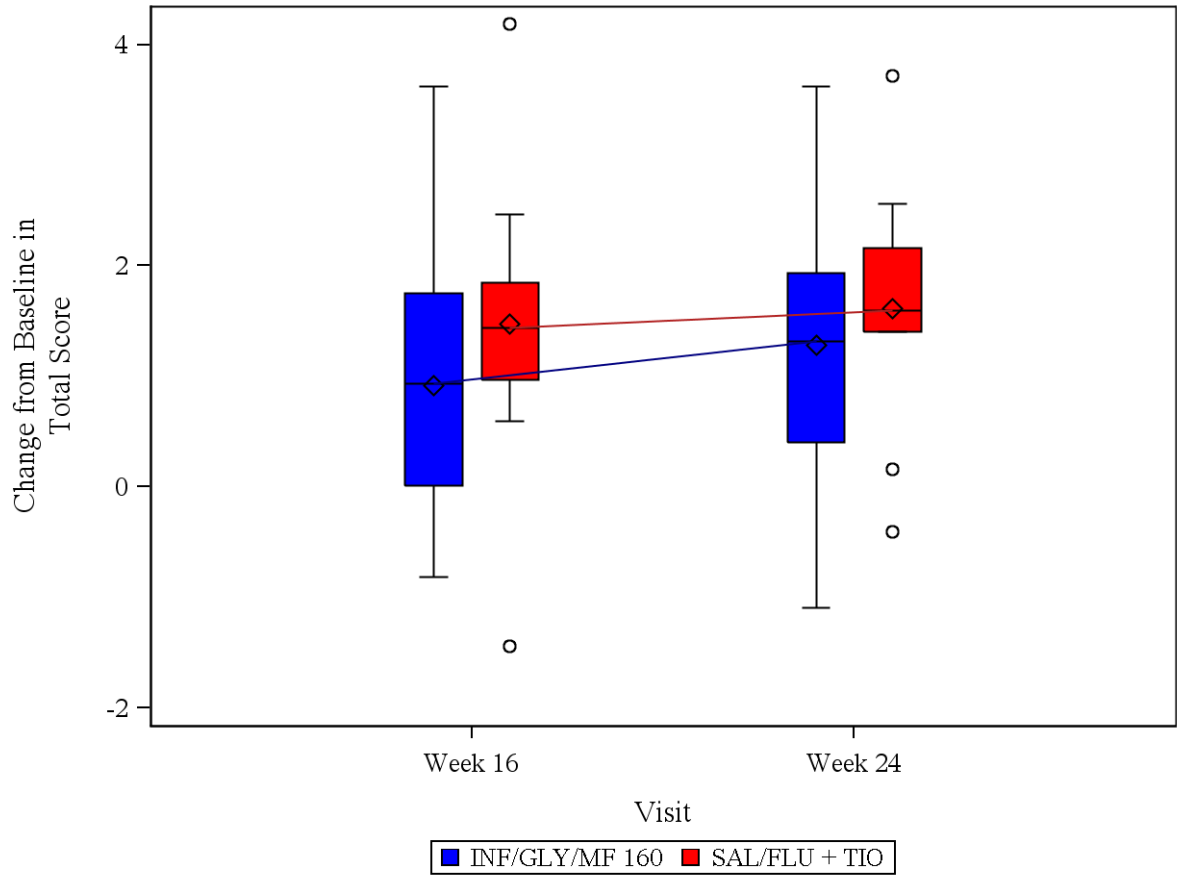


Figure 5.4.4 AQLQ-S (Total Score) - Change from Baseline by Region (FAS), Region = Others



5.5 Boxplot: AQLQ-S (Total Score) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 5.5.1 AQLQ-S (Total Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

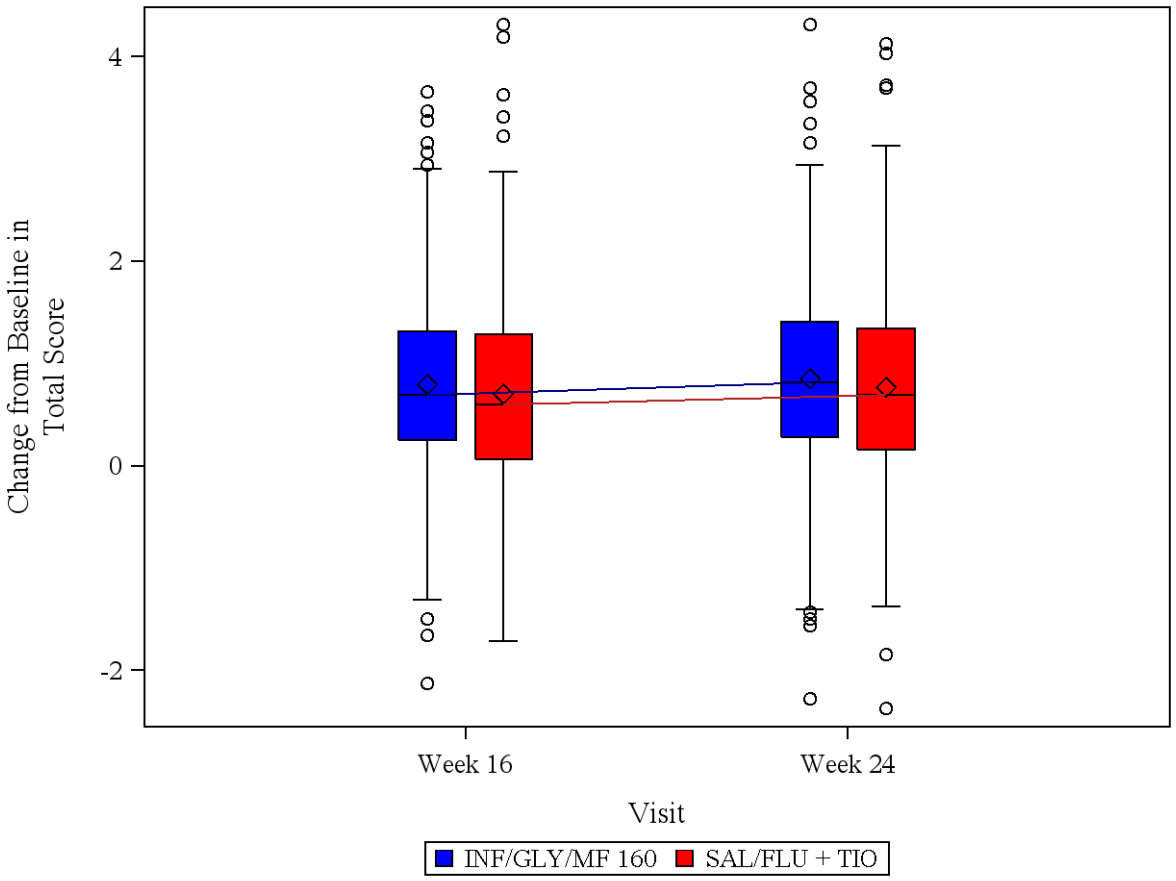
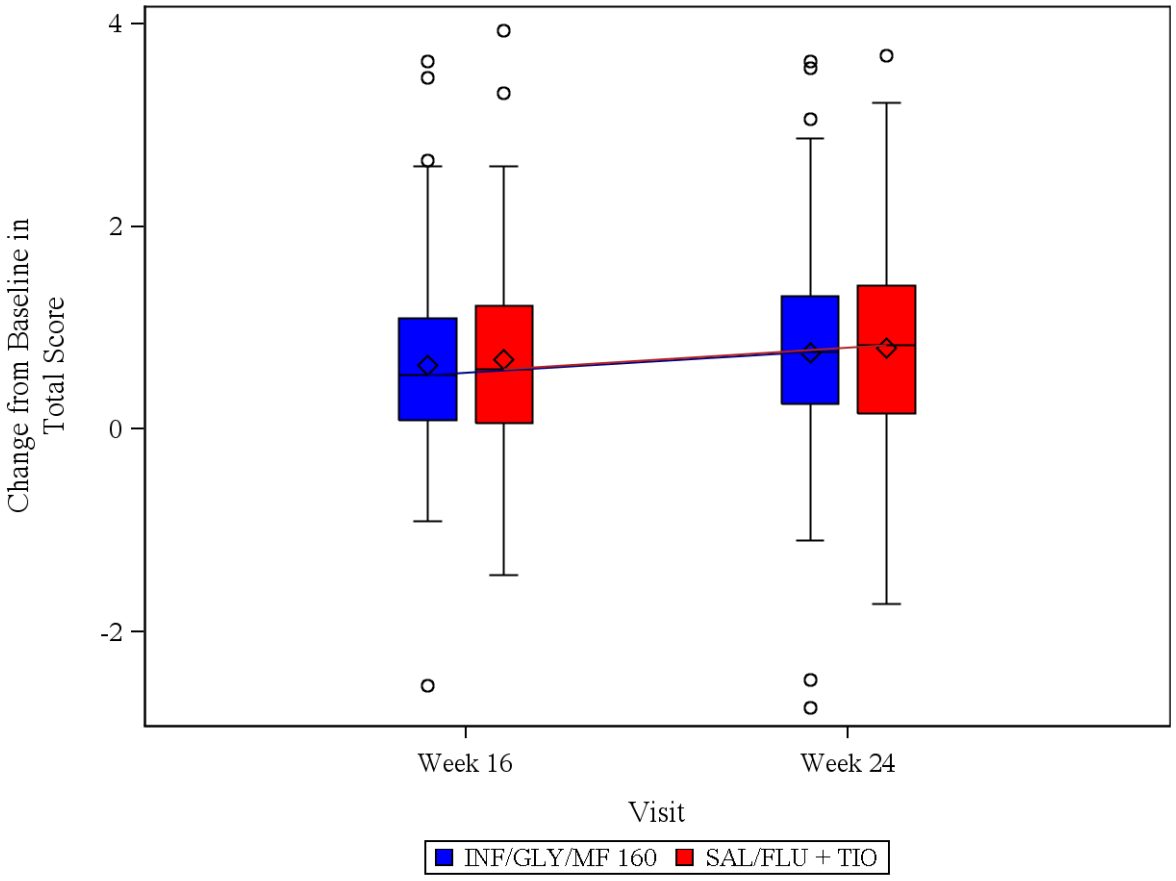


Figure 5.5.2 AQLQ-S (Total Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



5.6 Boxplot: AQLQ-S (Total Score) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 5.6.1 AQLQ-S (Total Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

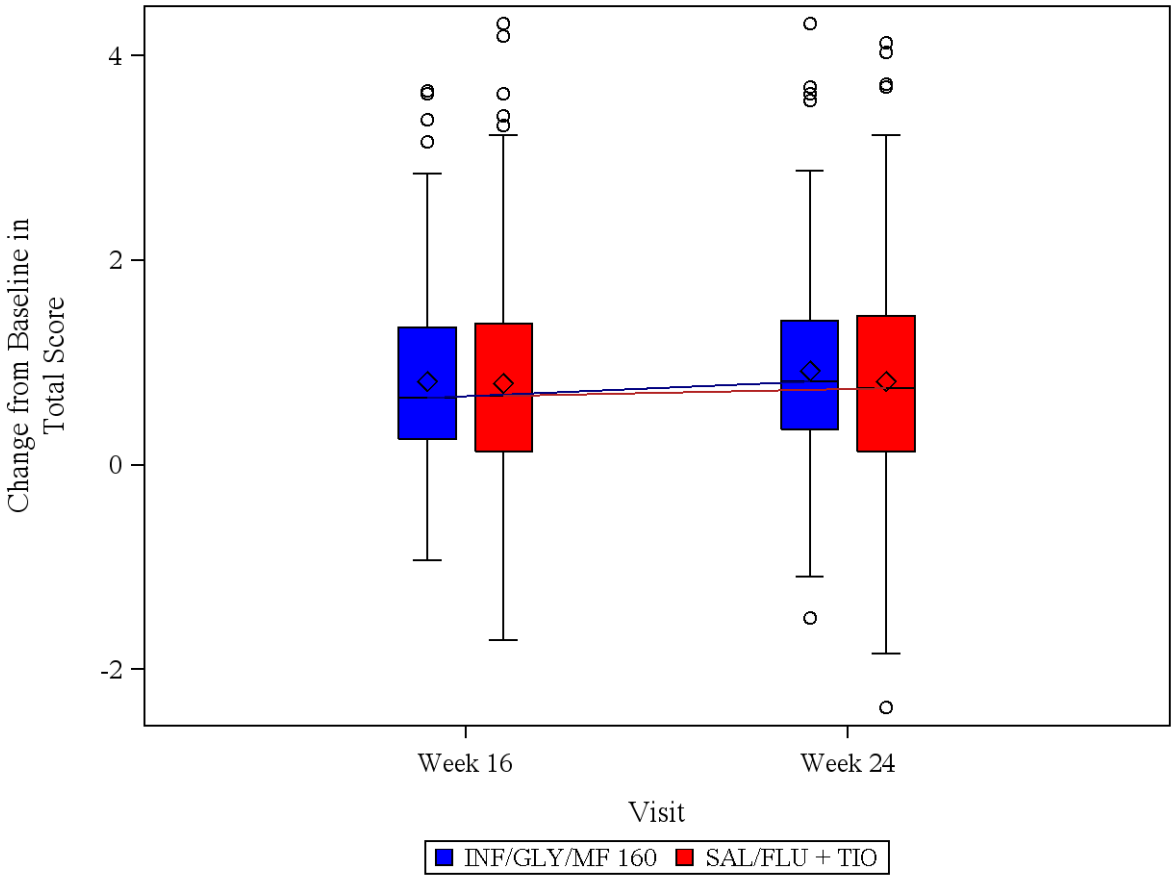
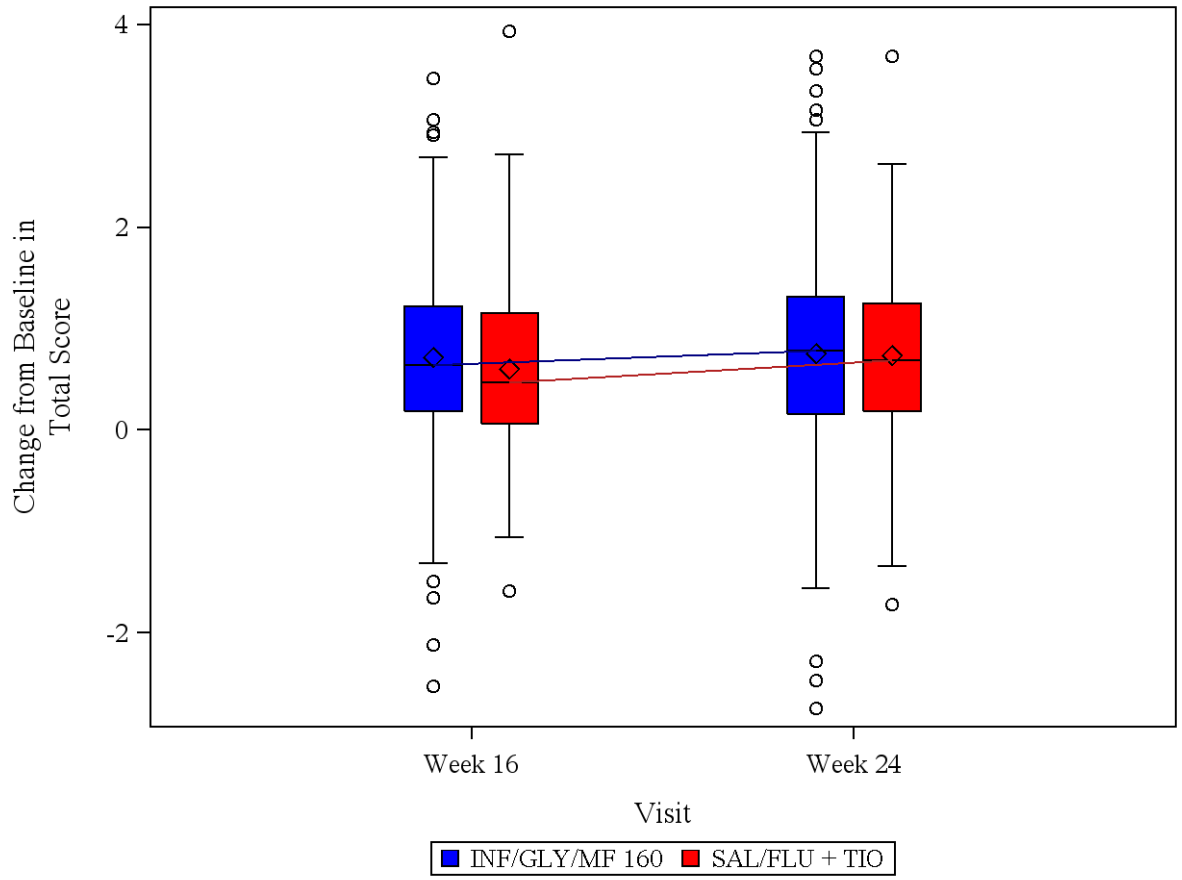
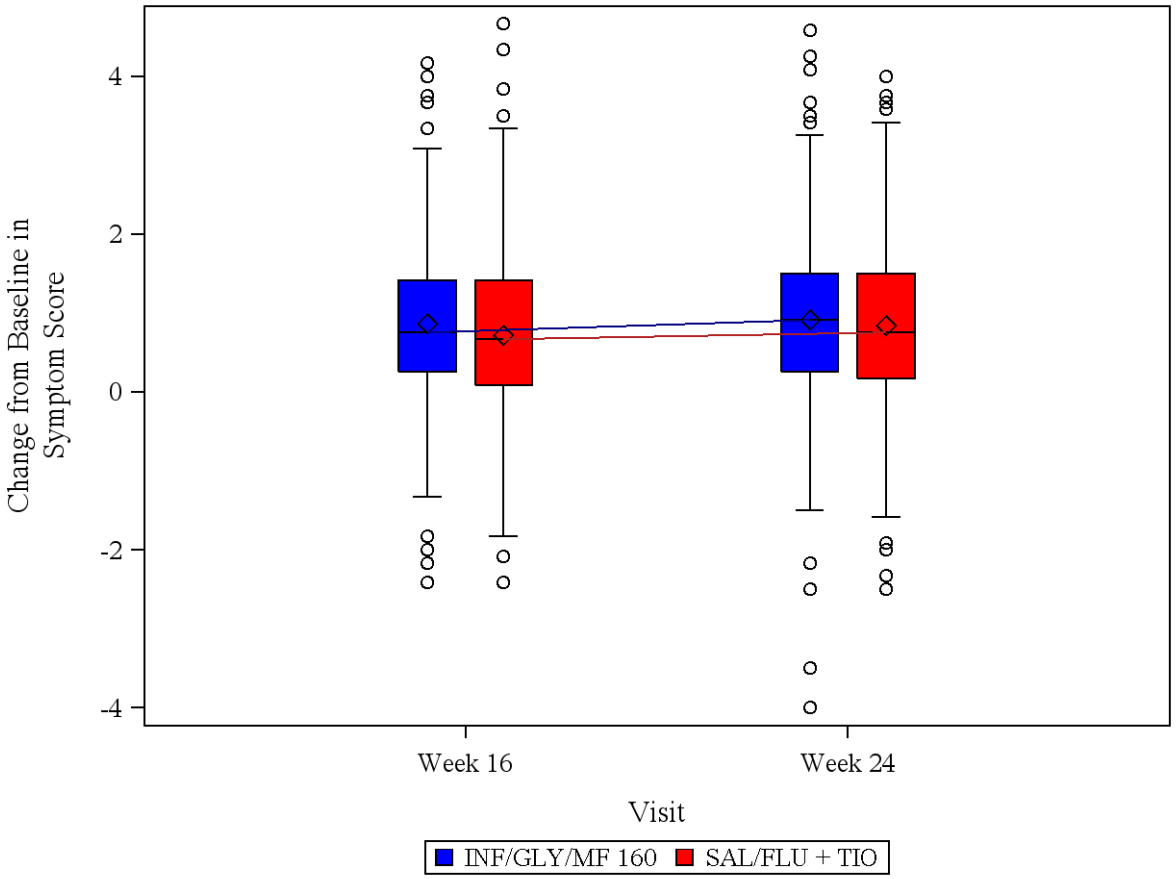


Figure 5.6.2 AQLQ-S (Total Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



5.7 Boxplot: AQLQ-S (Symptom Score) - Change from Baseline (FAS)

Figure 5.7 AQLQ-S (Symptom Score) - Change from Baseline (FAS)



5.8 Boxplot: AQLQ-S (Symptom Score) - Change from Baseline by Age (FAS)

Figure 5.8.1 AQLQ-S (Symptom Score) - Change from Baseline by Age (FAS), Age = 18-39 years

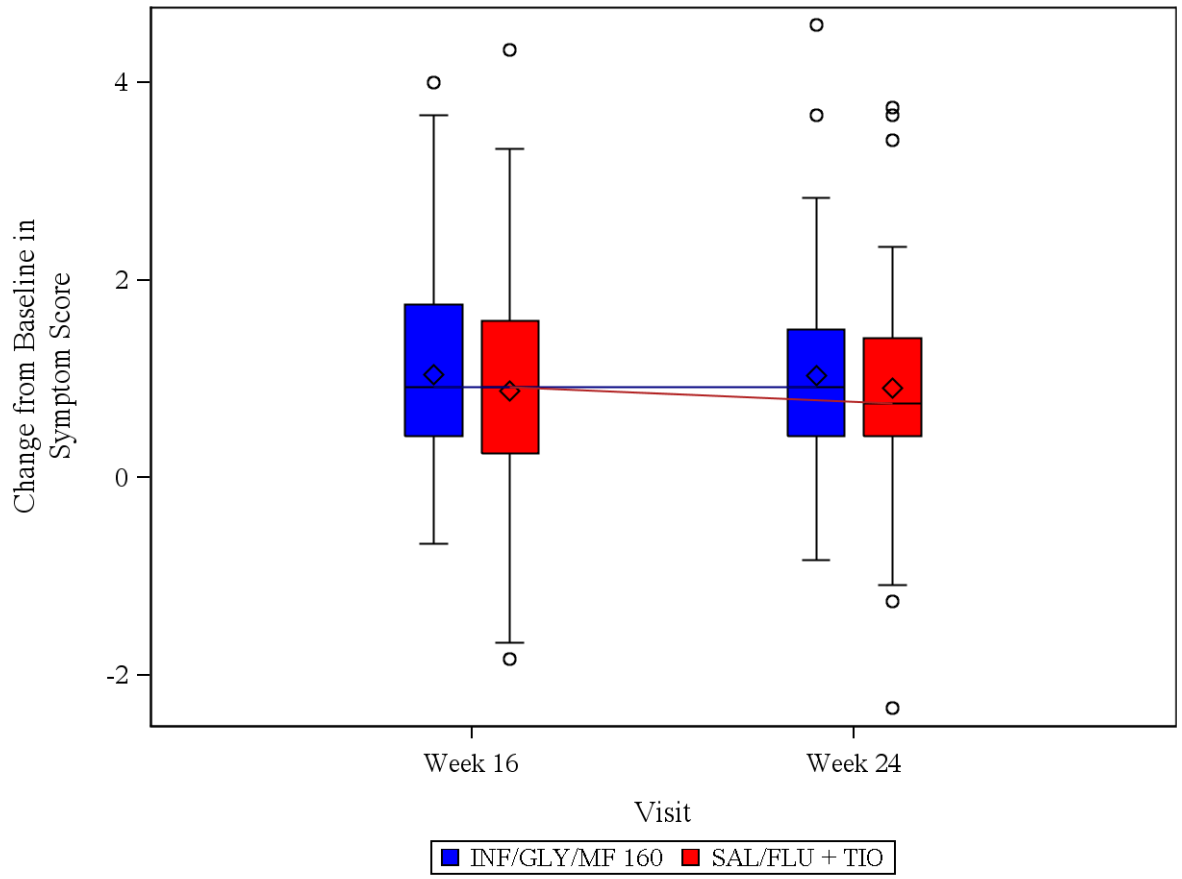


Figure 5.8.2 AQLQ-S (Symptom Score) - Change from Baseline by Age (FAS), Age = 40-64 years

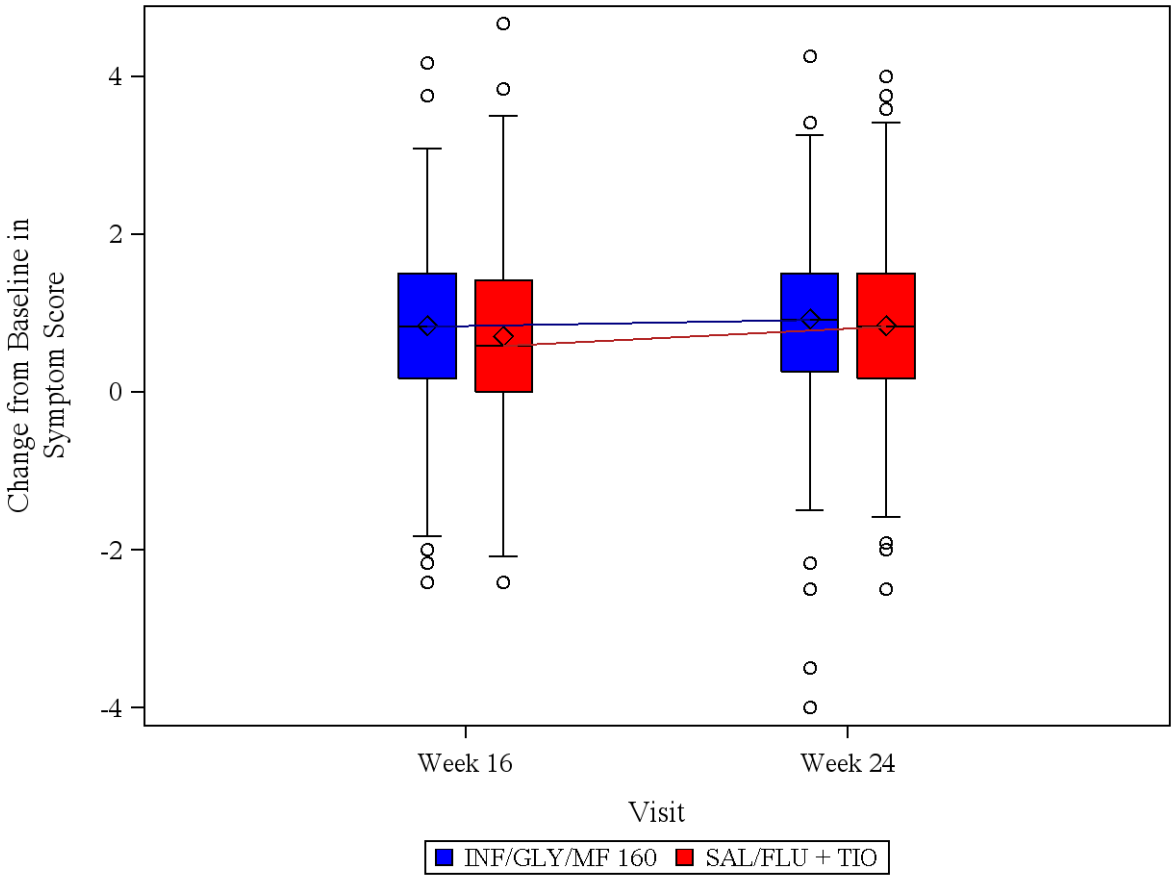
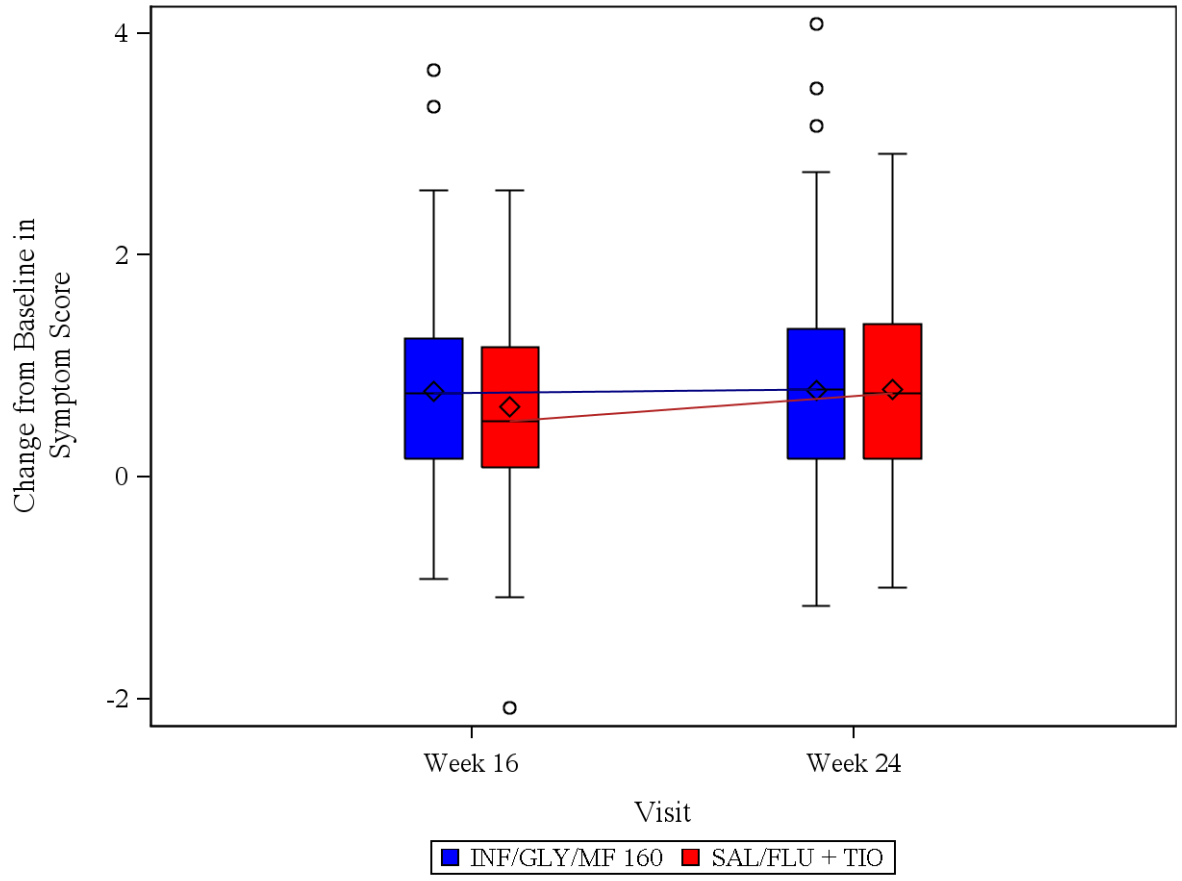


Figure 5.8.3 AQLQ-S (Symptom Score) - Change from Baseline by Age (FAS), Age = ≥65 years



5.9 Boxplot: AQLQ-S (Symptom Score) - Change from Baseline by Gender (FAS)

Figure 5.9.1 AQLQ-S (Symptom Score) - Change from Baseline by Gender (FAS), Gender = Male

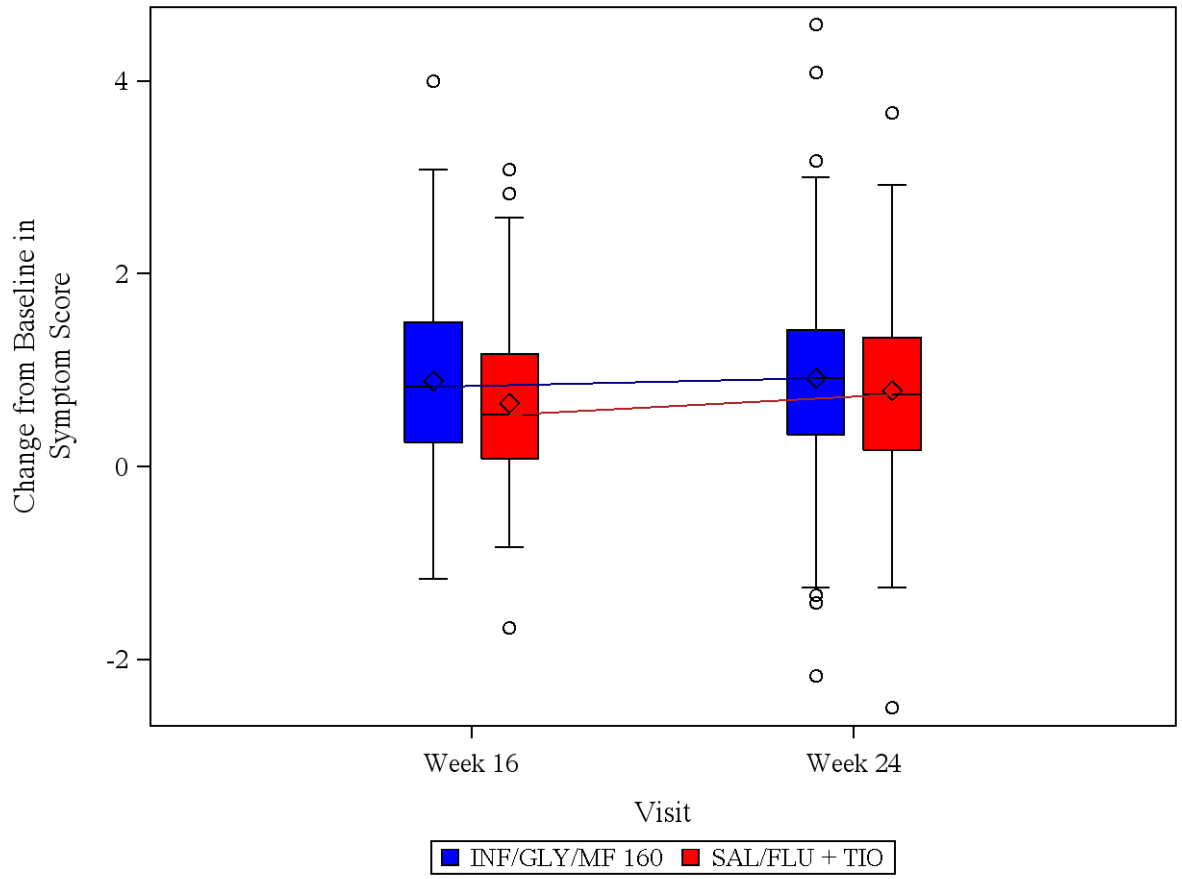
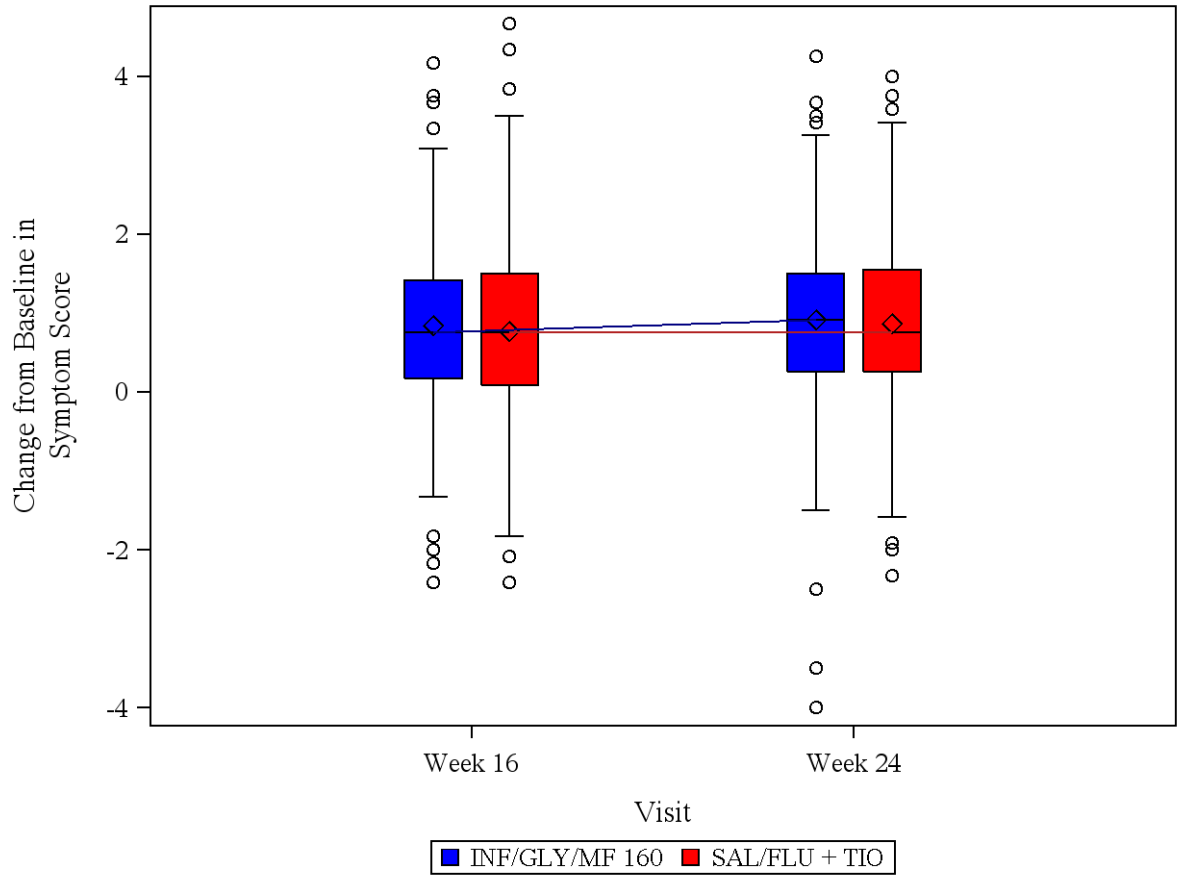


Figure 5.9.2 AQLQ-S (Symptom Score) - Change from Baseline by Gender (FAS), Gender = Female



5.10 Boxplot: AQLQ-S (Symptom Score) - Change from Baseline by Region (FAS)

Figure 5.10.1 AQLQ-S (Symptom Score) - Change from Baseline by Region (FAS), Region = Asia

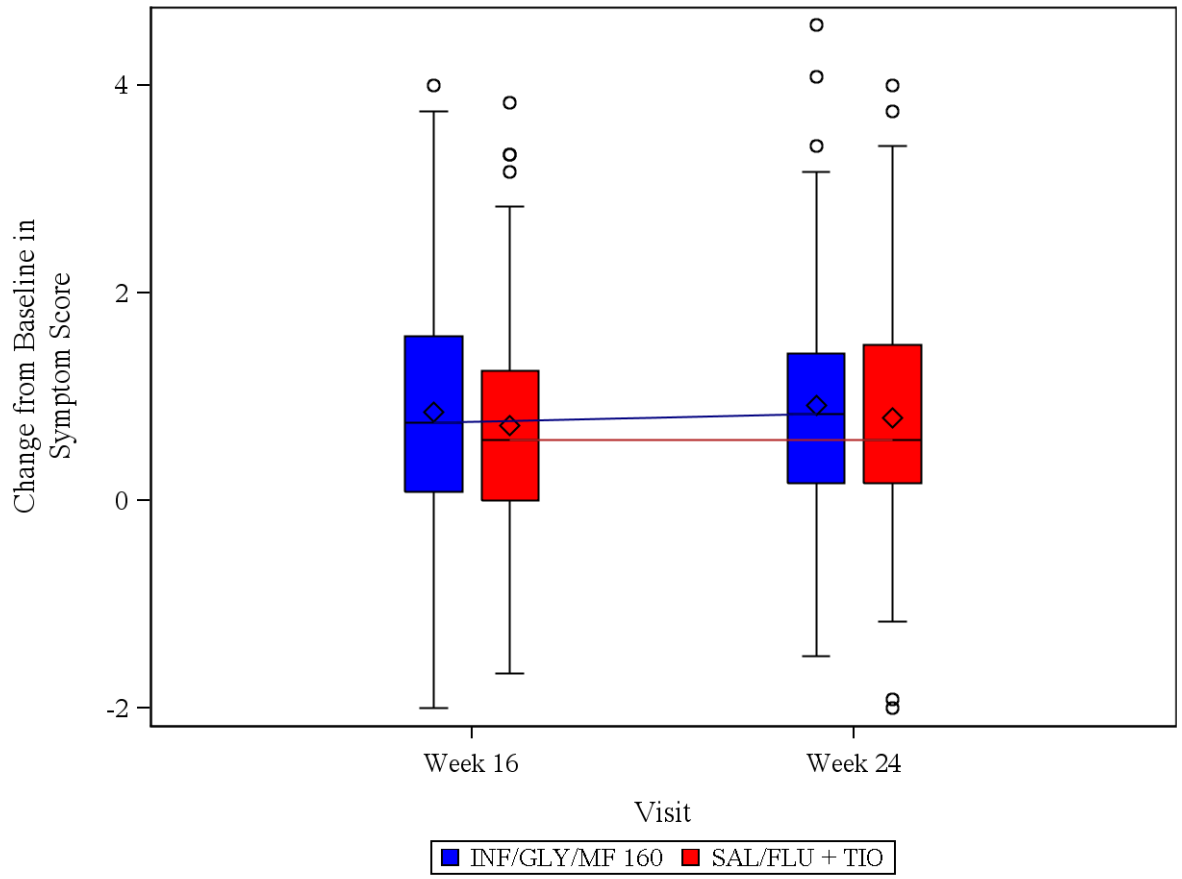


Figure 5.10.2 AQLQ-S (Symptom Score) - Change from Baseline by Region (FAS), Region = Europe

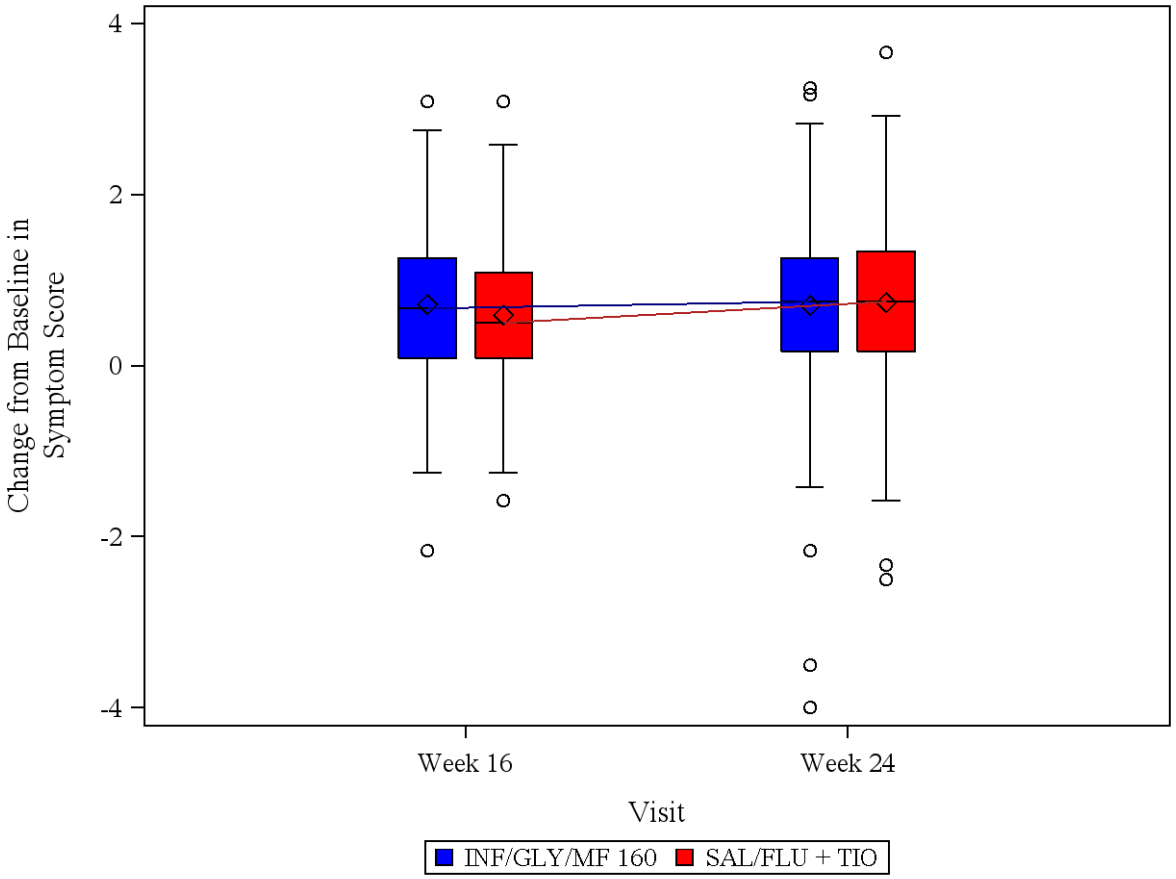


Figure 5.10.3 AQLQ-S (Symptom Score) - Change from Baseline by Region (FAS), Region = Latin America

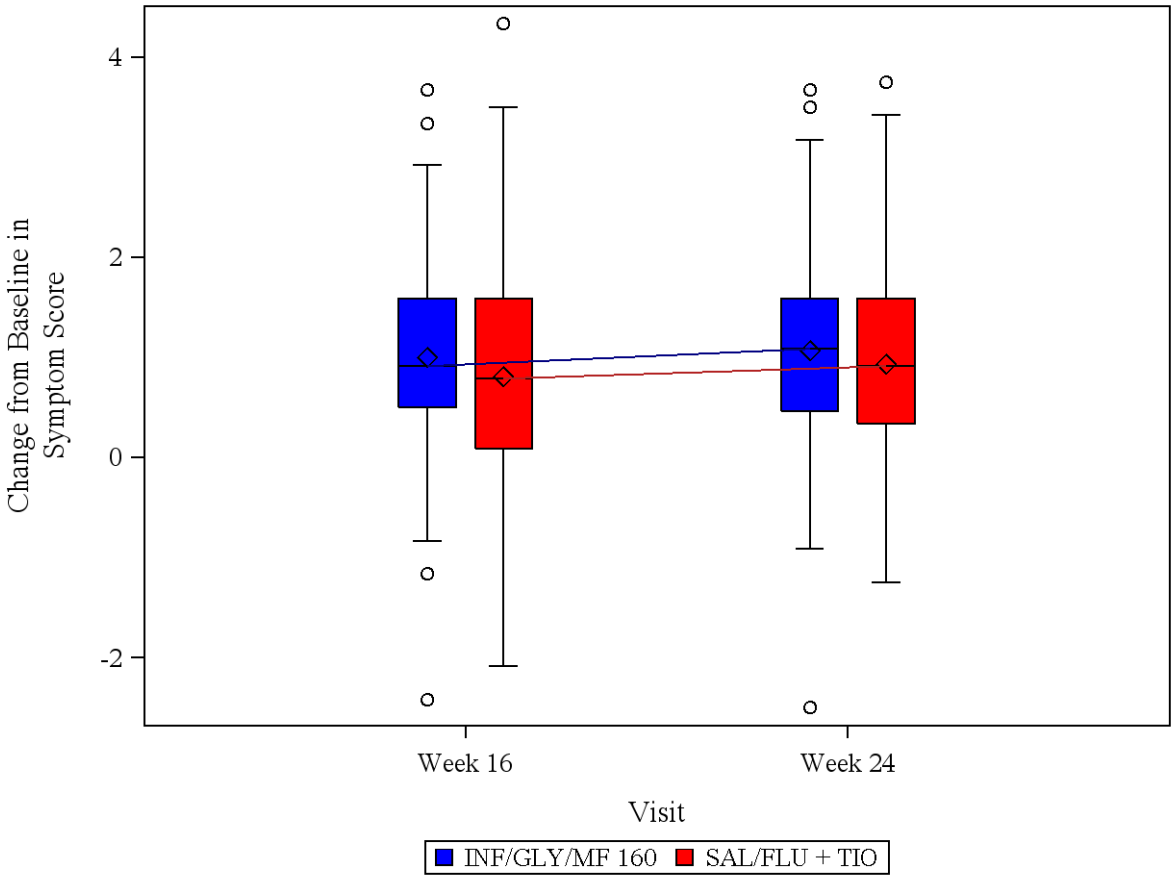
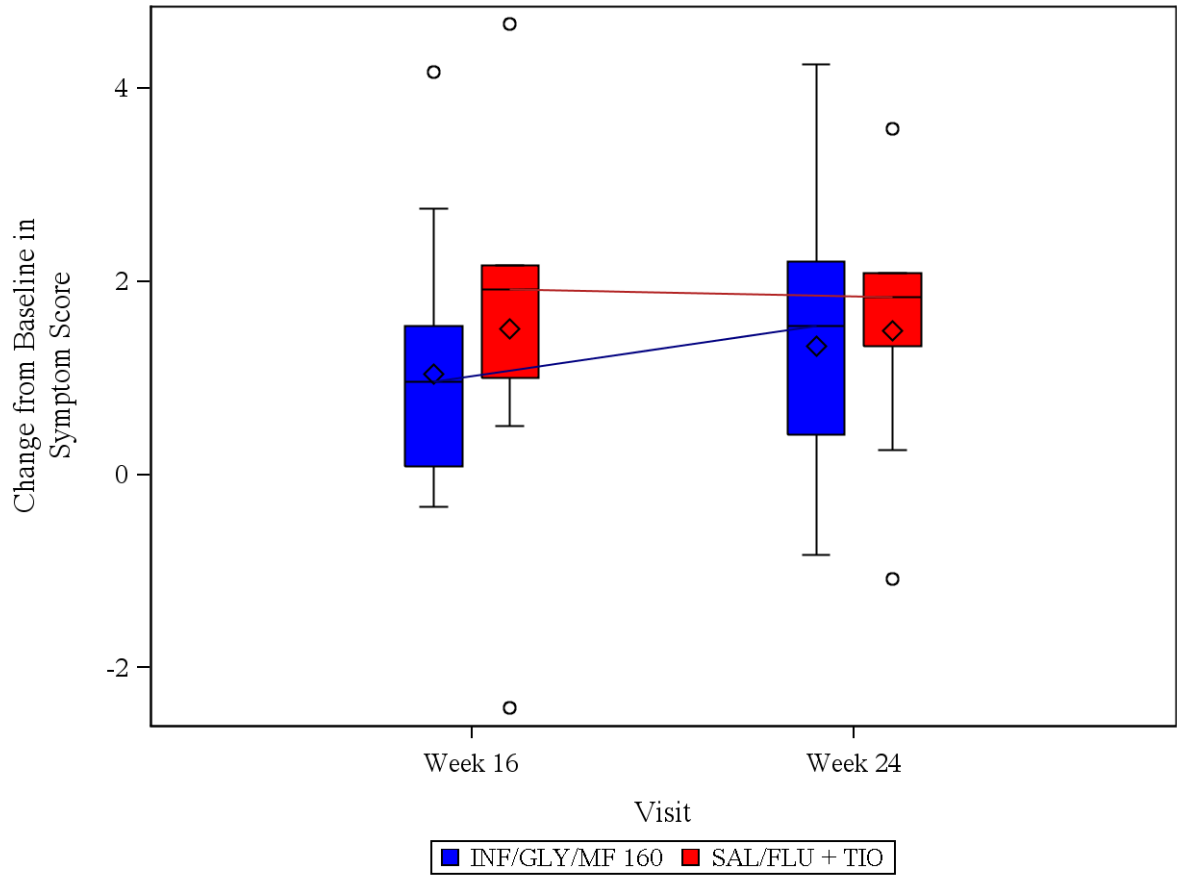


Figure 5.10.4 AQLQ-S (Symptom Score) - Change from Baseline by Region (FAS), Region = Others



5.11 Boxplot: AQLQ-S (Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 5.11.1 AQLQ-S (Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

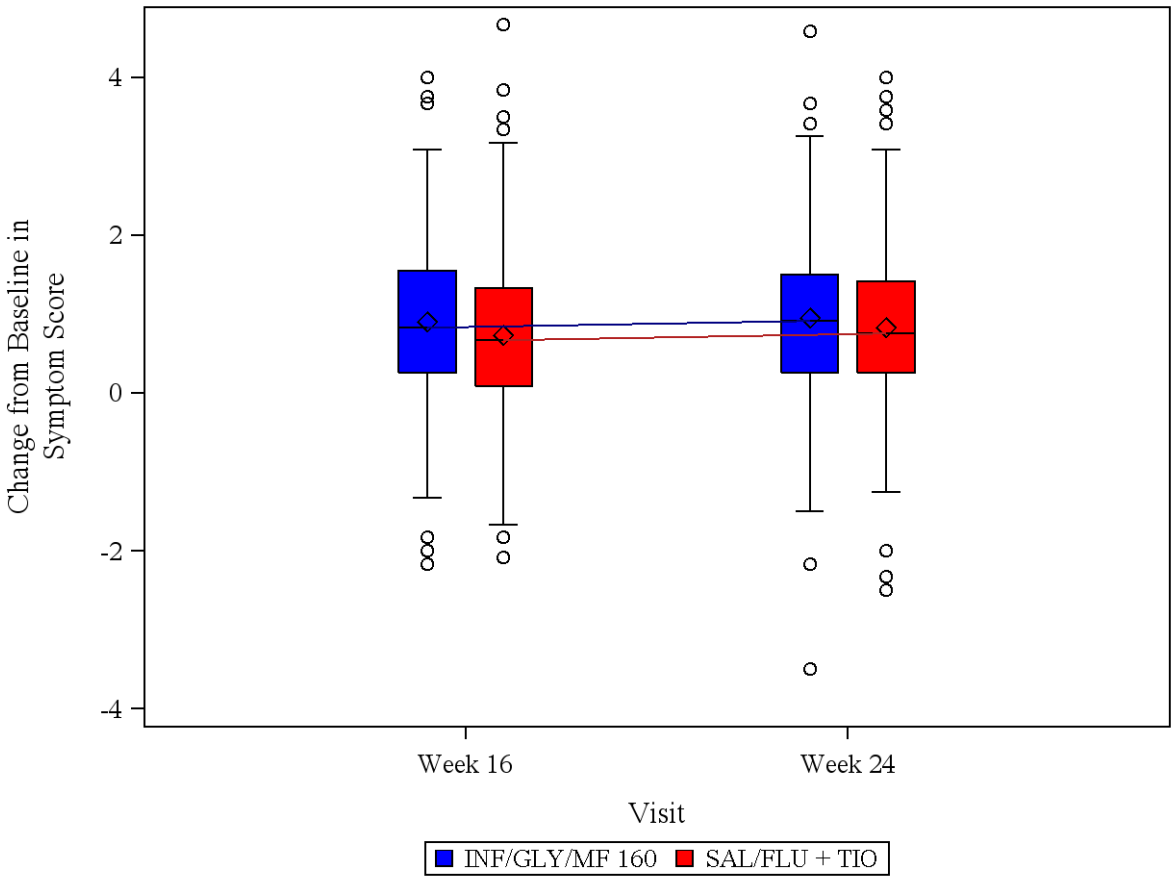
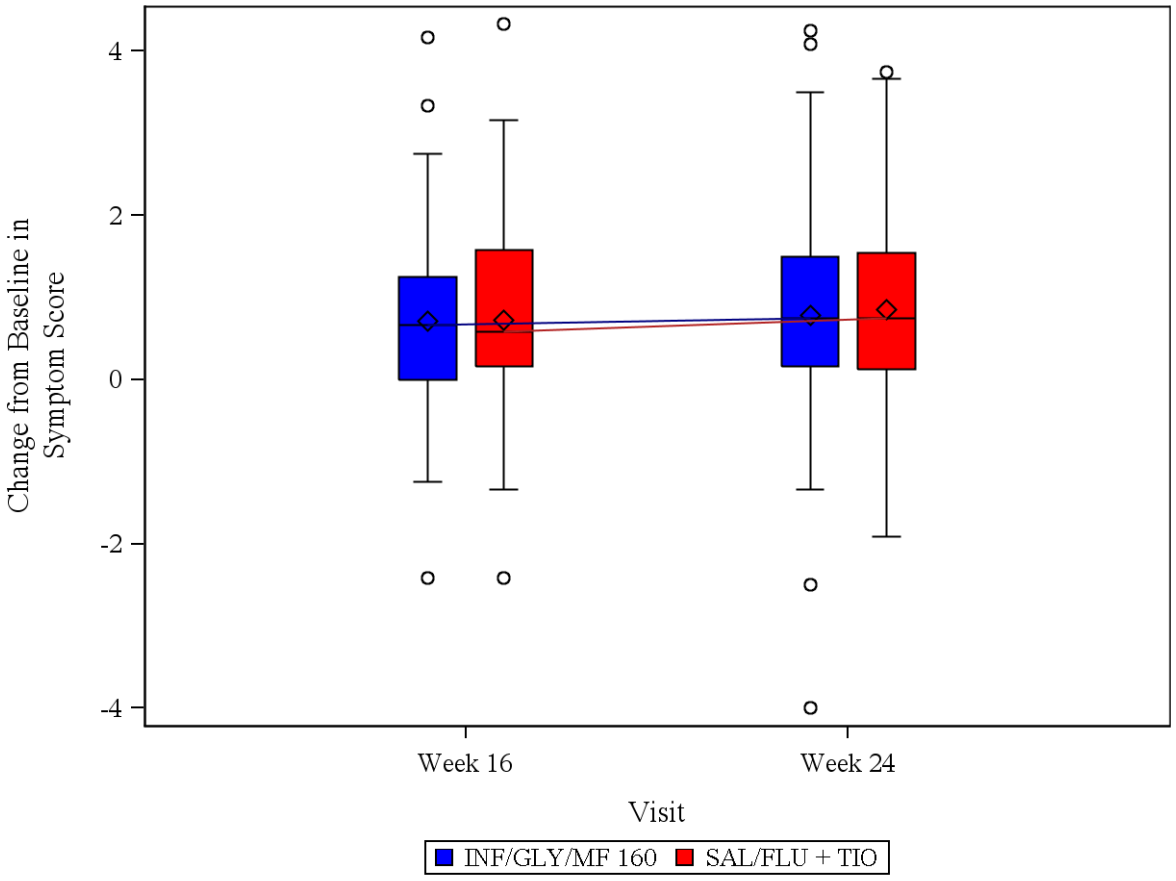


Figure 5.11.2 AQLQ-S (Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



5.12 Boxplot: AQLQ-S (Symptom Score) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 5.12.1 AQLQ-S (Symptom Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

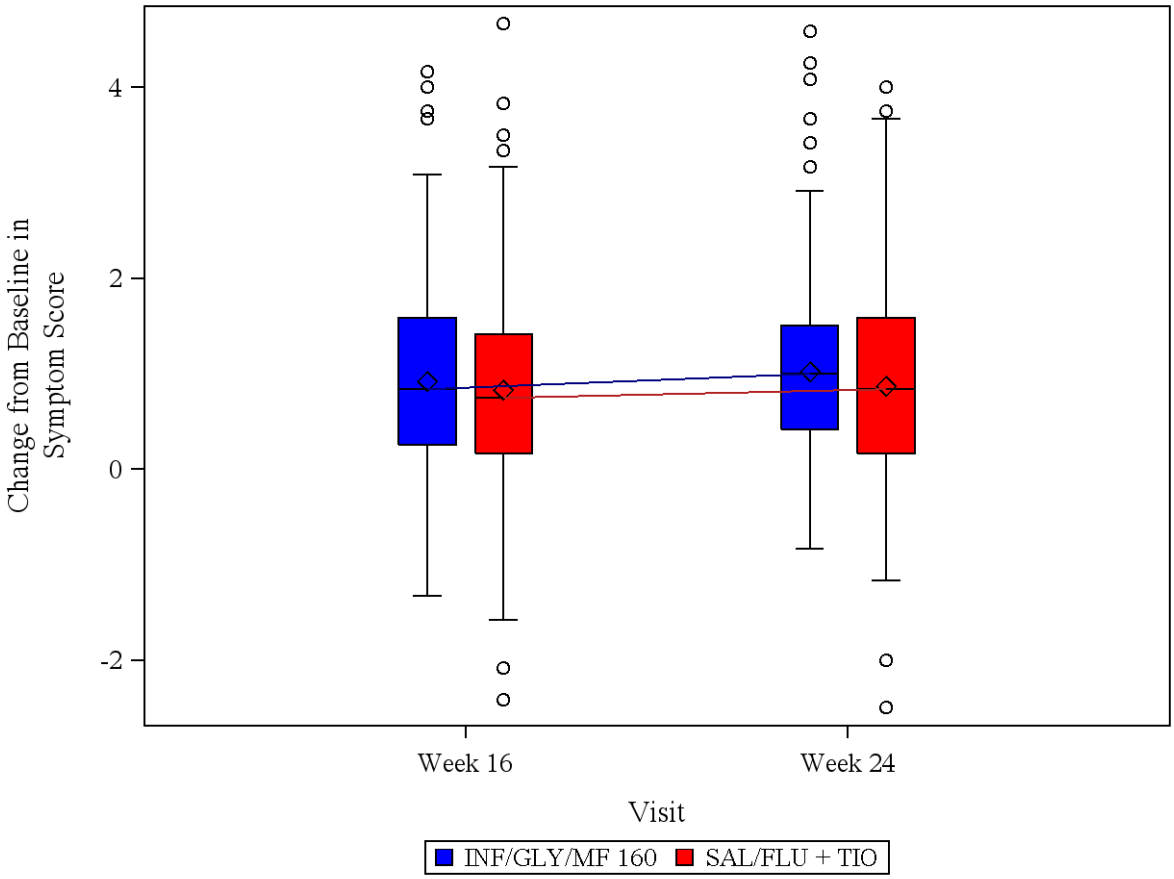
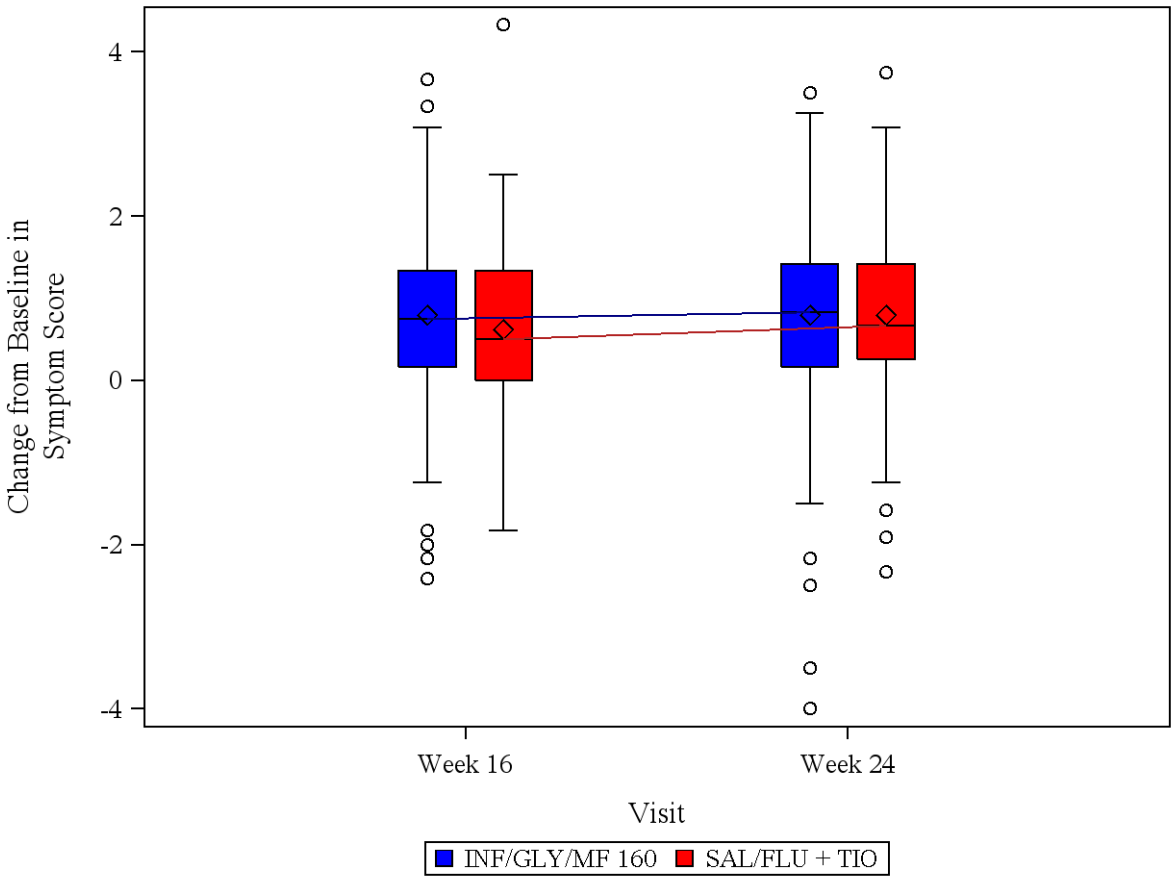
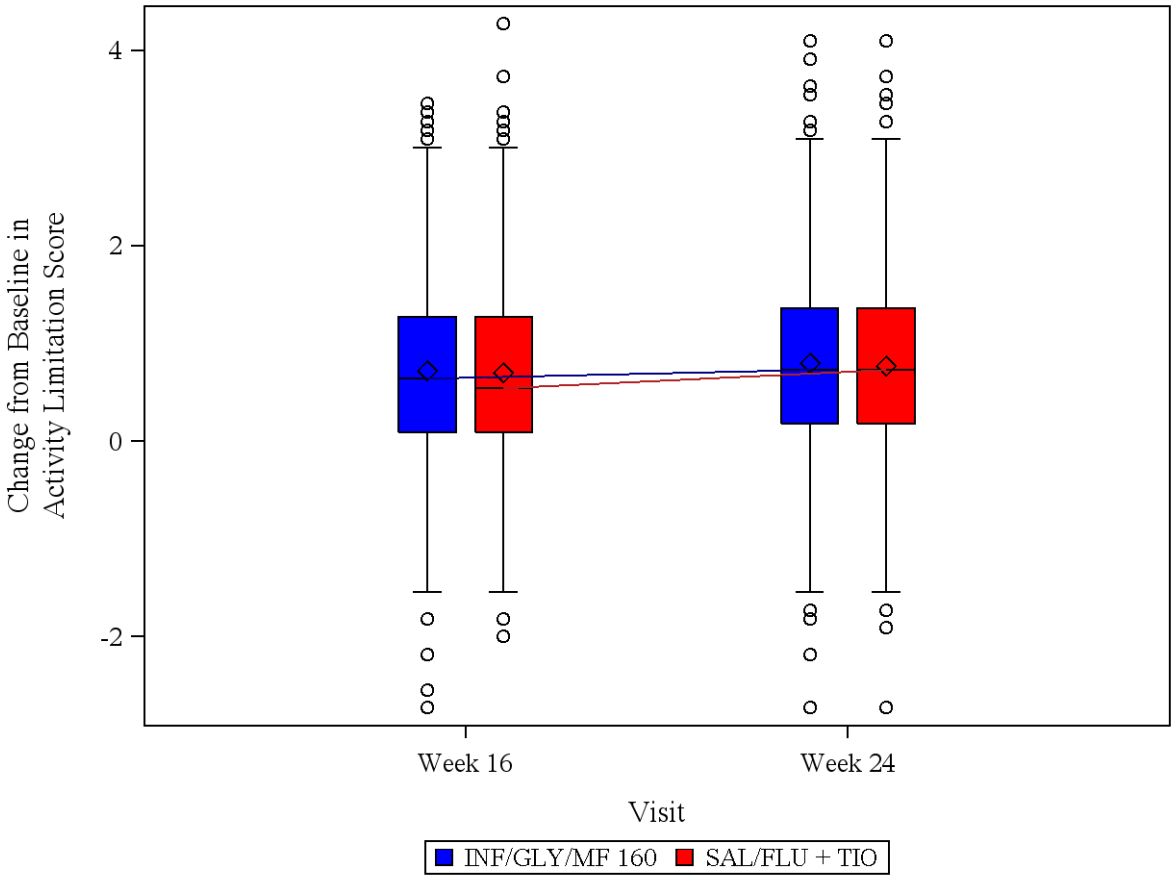


Figure 5.12.2 AQLQ-S (Symptom Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



5.13 Boxplot: AQLQ-S (Activity Limitation Score) - Change from Baseline (FAS)

Figure 5.13 AQLQ-S (Activity Limitation Score) - Change from Baseline (FAS)



5.14 Boxplot: AQLQ-S (Activity Limitation Score) - Change from Baseline by Age (FAS)

Figure 5.14.1 AQLQ-S (Activity Limitation Score) - Change from Baseline by Age (FAS), Age = 18-39 years

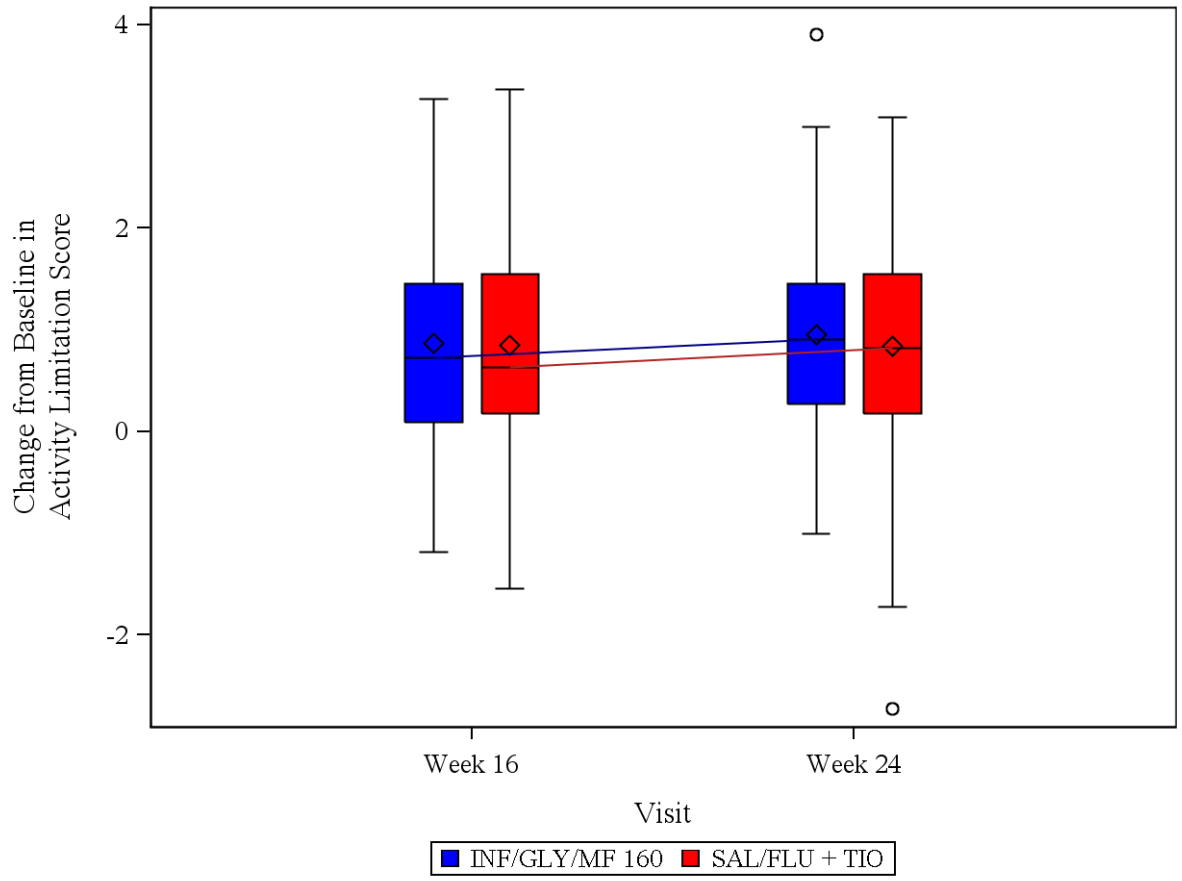


Figure 5.14.2 AQLQ-S (Activity Limitation Score) - Change from Baseline by Age (FAS), Age = 40-64 years

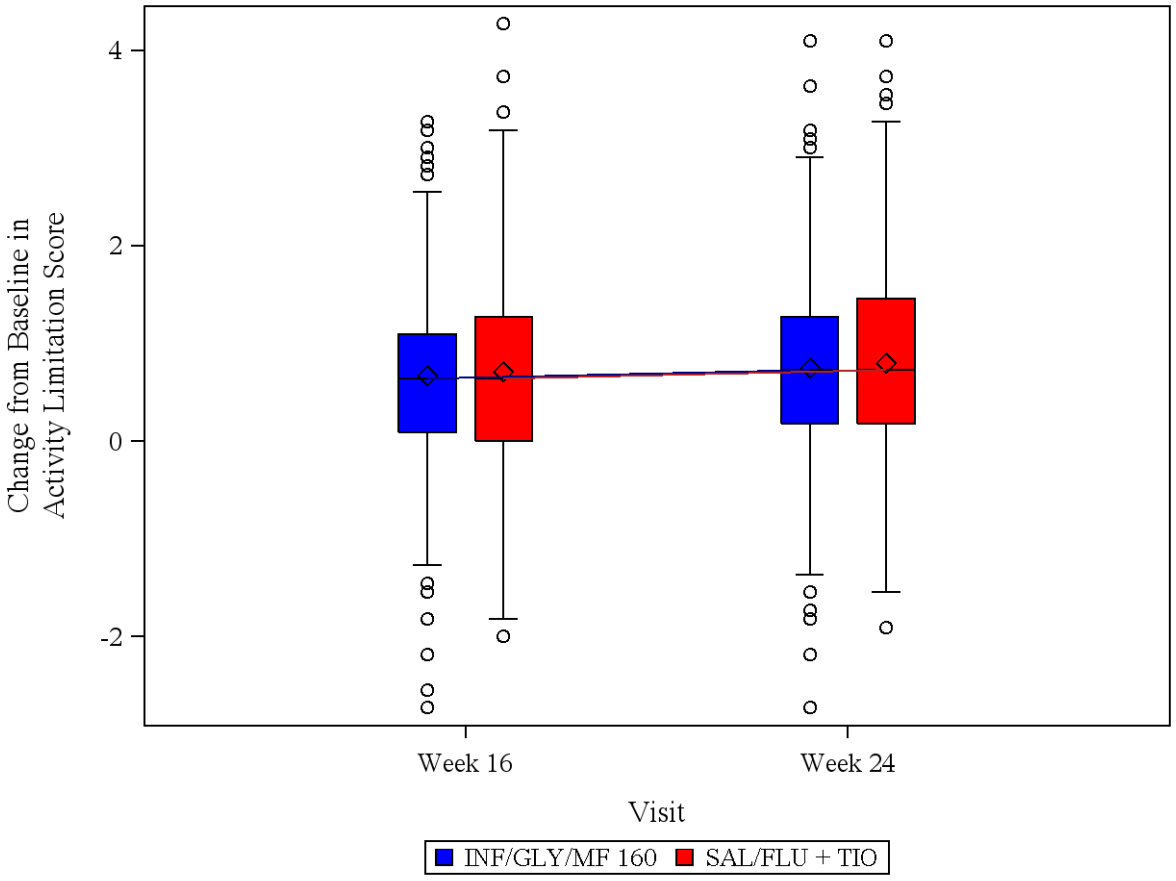
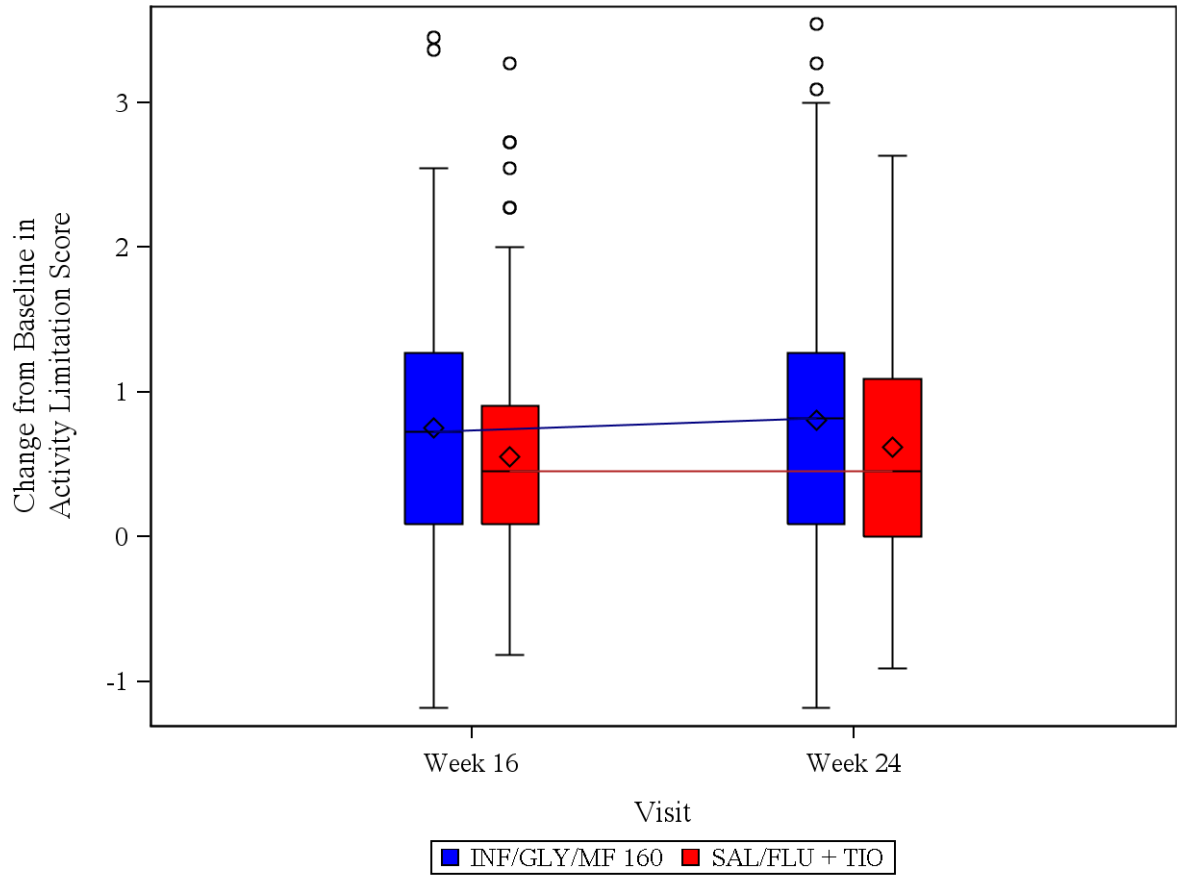


Figure 5.14.3 AQLQ-S (Activity Limitation Score) - Change from Baseline by Age (FAS), Age = ≥65 years



5.15 Boxplot: AQLQ-S (Activity Limitation Score) - Change from Baseline by Gender (FAS)

Figure 5.15.1 AQLQ-S (Activity Limitation Score) - Change from Baseline by Gender (FAS), Gender = Male

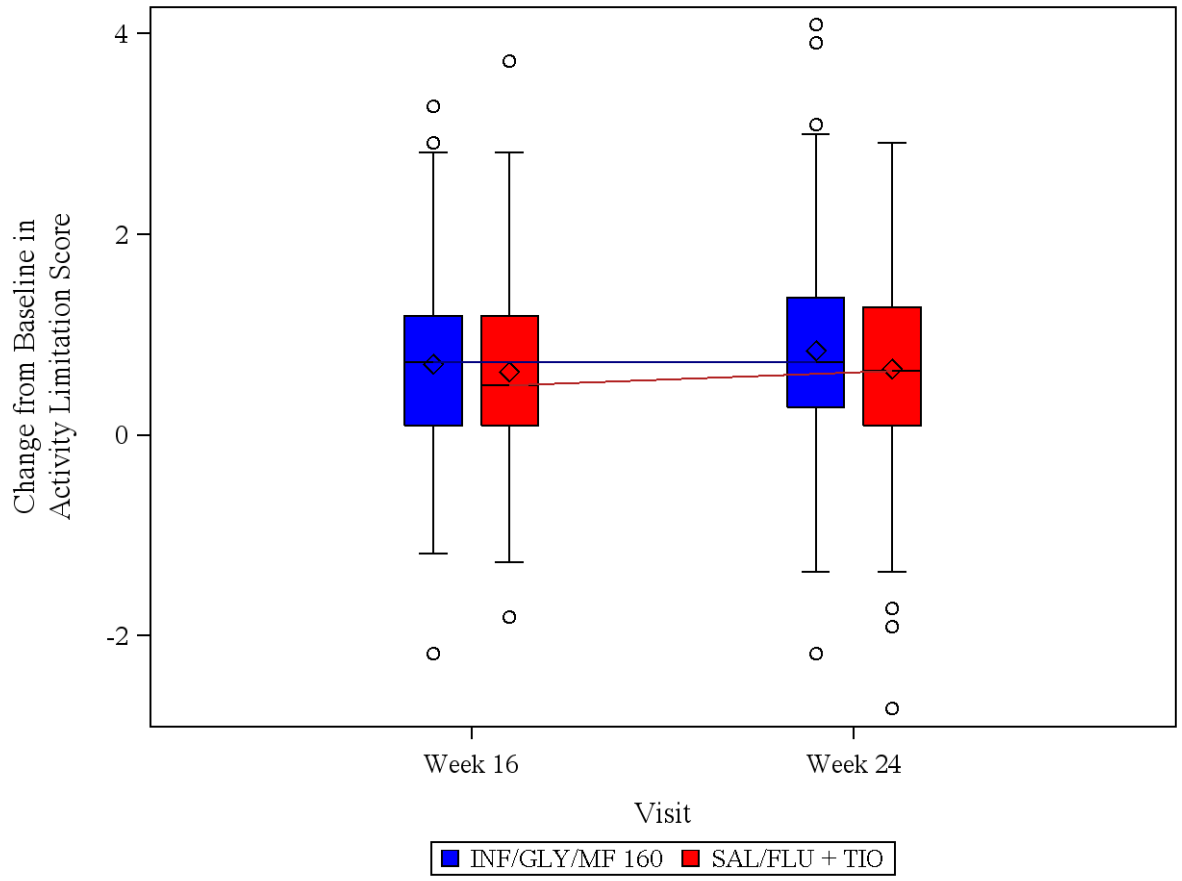
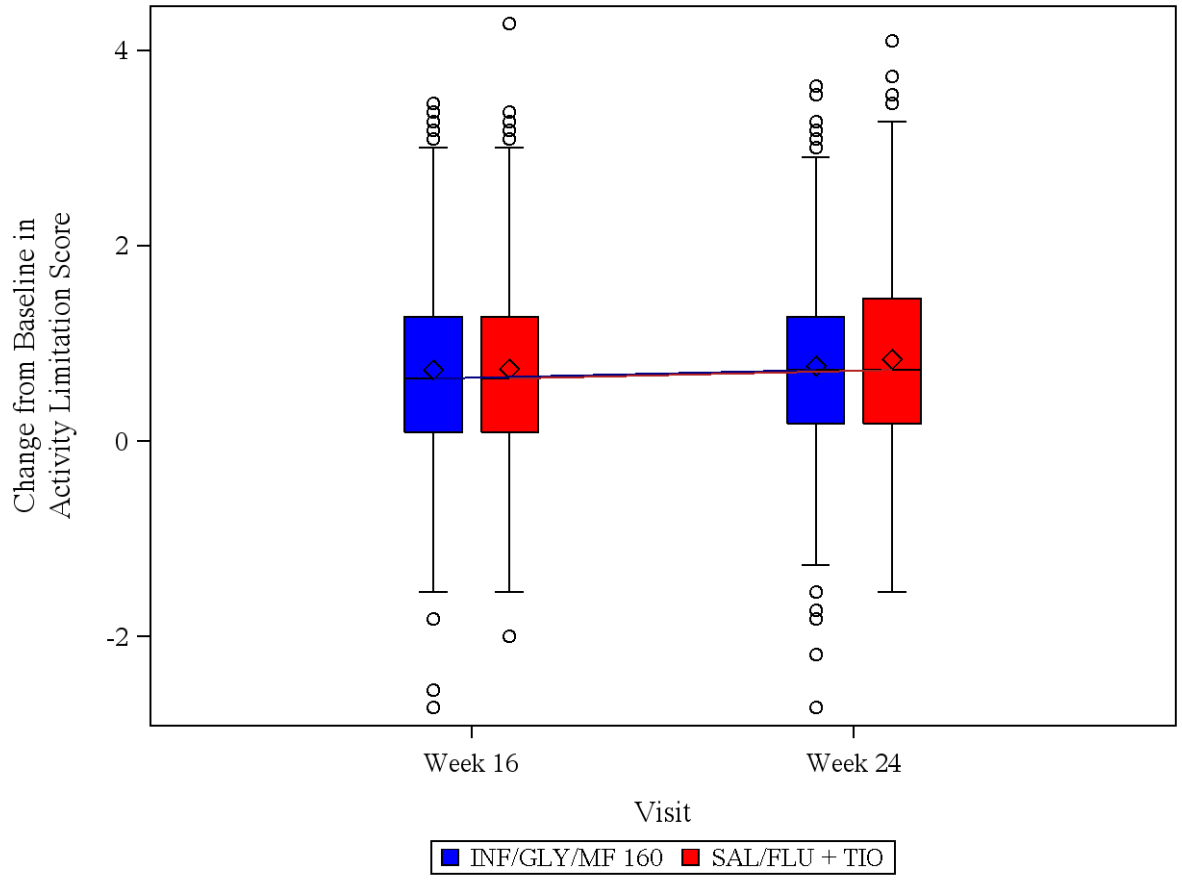


Figure 5.15.2 AQLQ-S (Activity Limitation Score) - Change from Baseline by Gender (FAS), Gender = Female



5.16 Boxplot: AQLQ-S (Activity Limitation Score) - Change from Baseline by Region (FAS)

Figure 5.16.1 AQLQ-S (Activity Limitation Score) - Change from Baseline by Region (FAS), Region = Asia

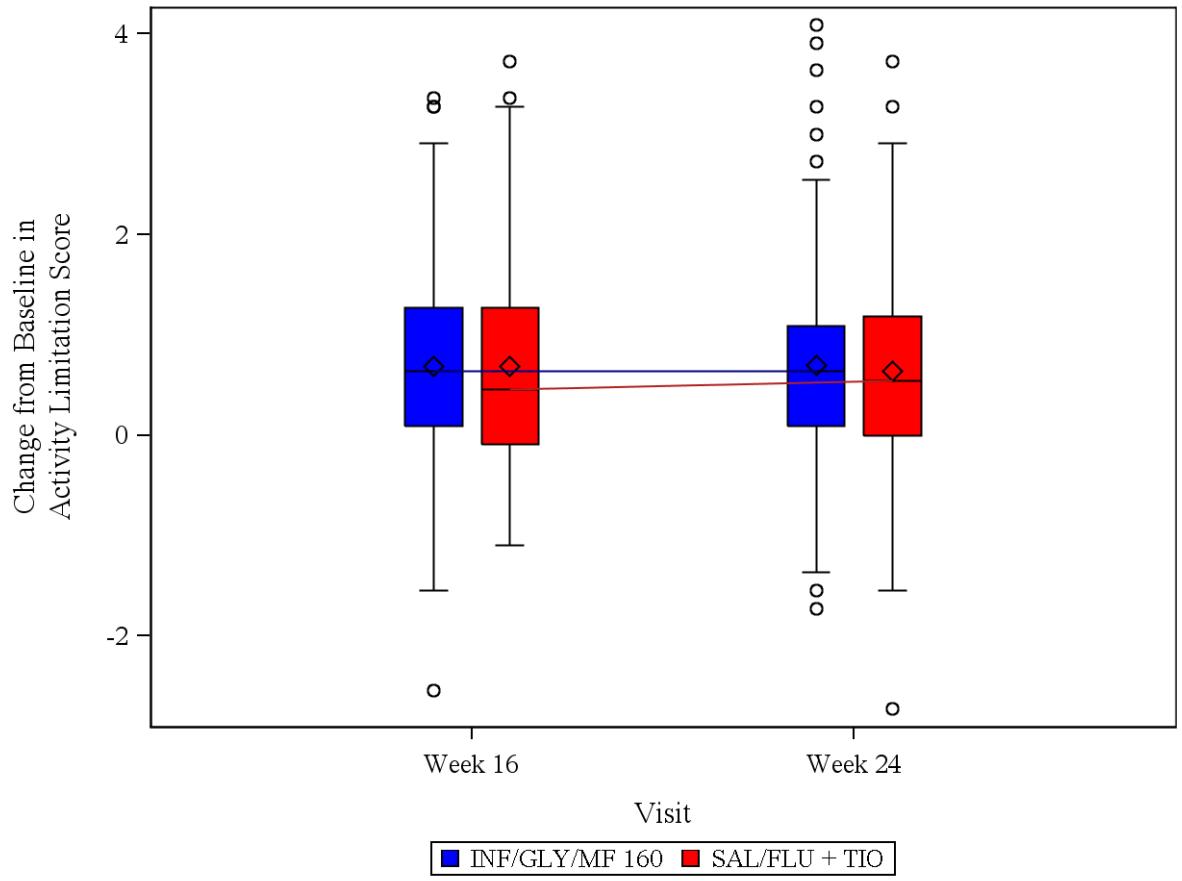


Figure 5.16.2 AQLQ-S (Activity Limitation Score) - Change from Baseline by Region (FAS), Region = Europe

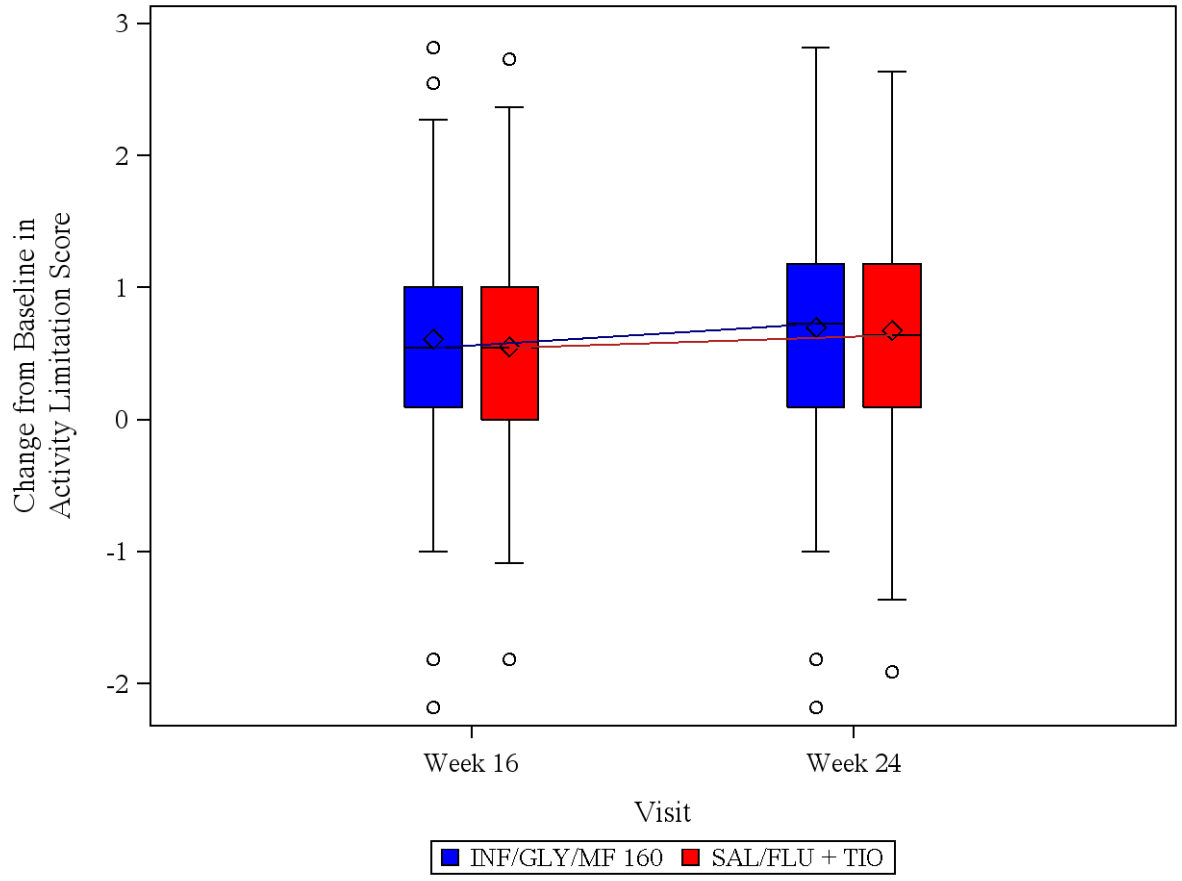


Figure 5.16.3 AQLQ-S (Activity Limitation Score) - Change from Baseline by Region (FAS), Region = Latin America

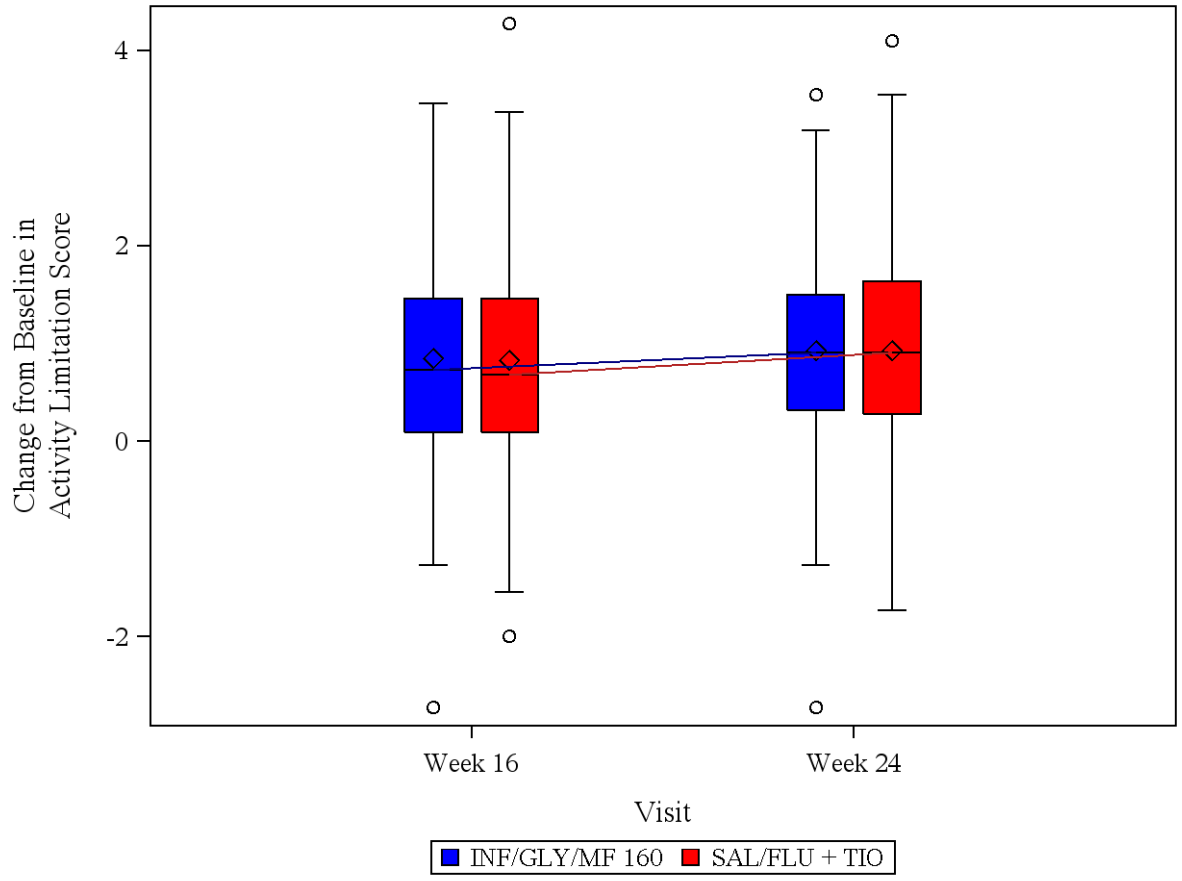
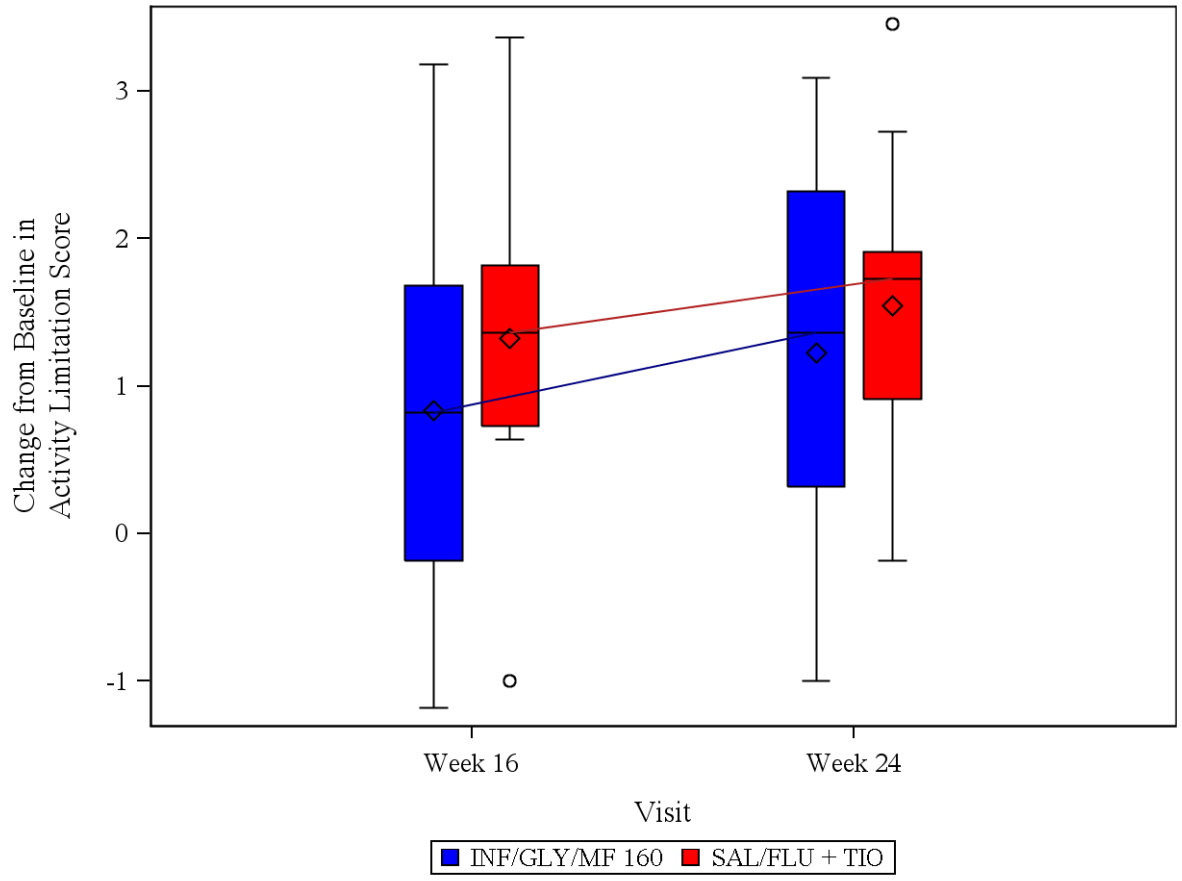


Figure 5.16.4 AQLQ-S (Activity Limitation Score) - Change from Baseline by Region (FAS), Region = Others



5.17 Boxplot: AQLQ-S (Activity Limitation Score) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 5.17.1 AQLQ-S (Activity Limitation Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

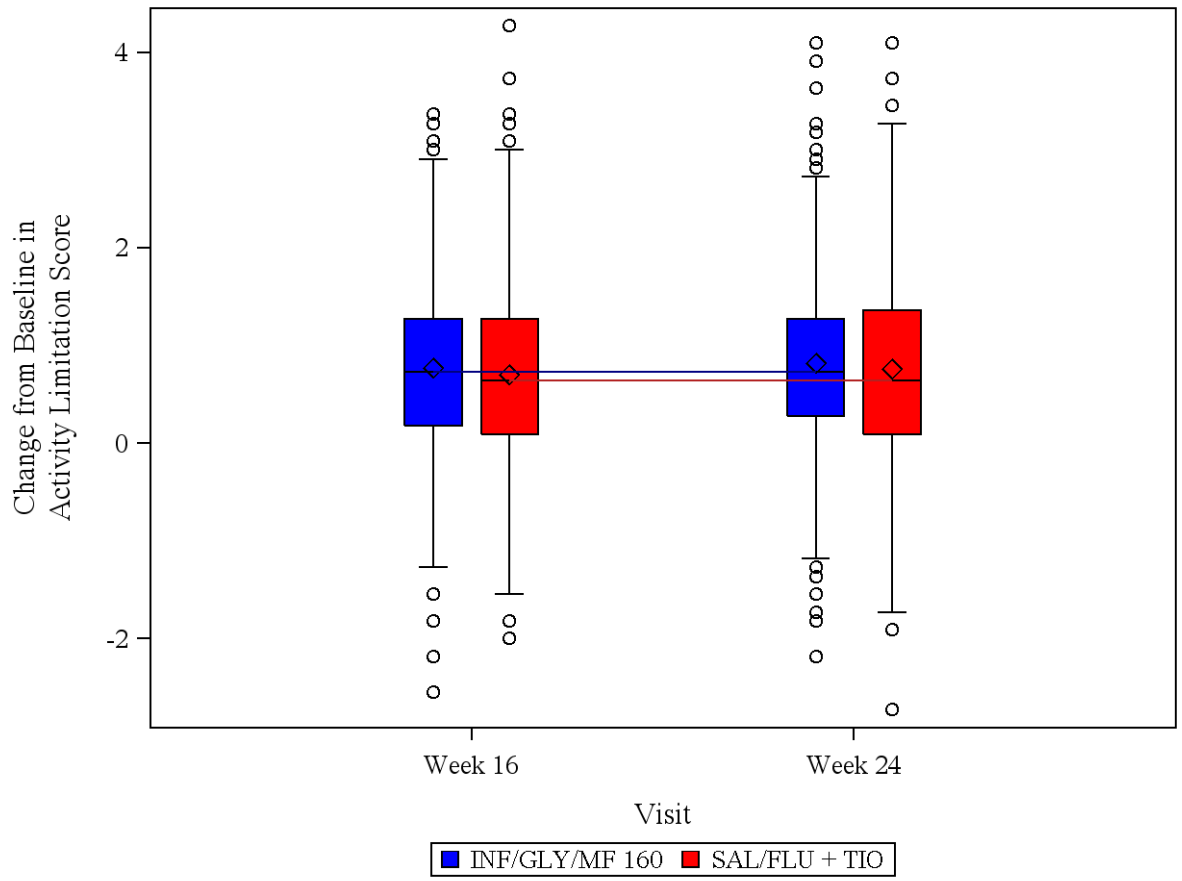
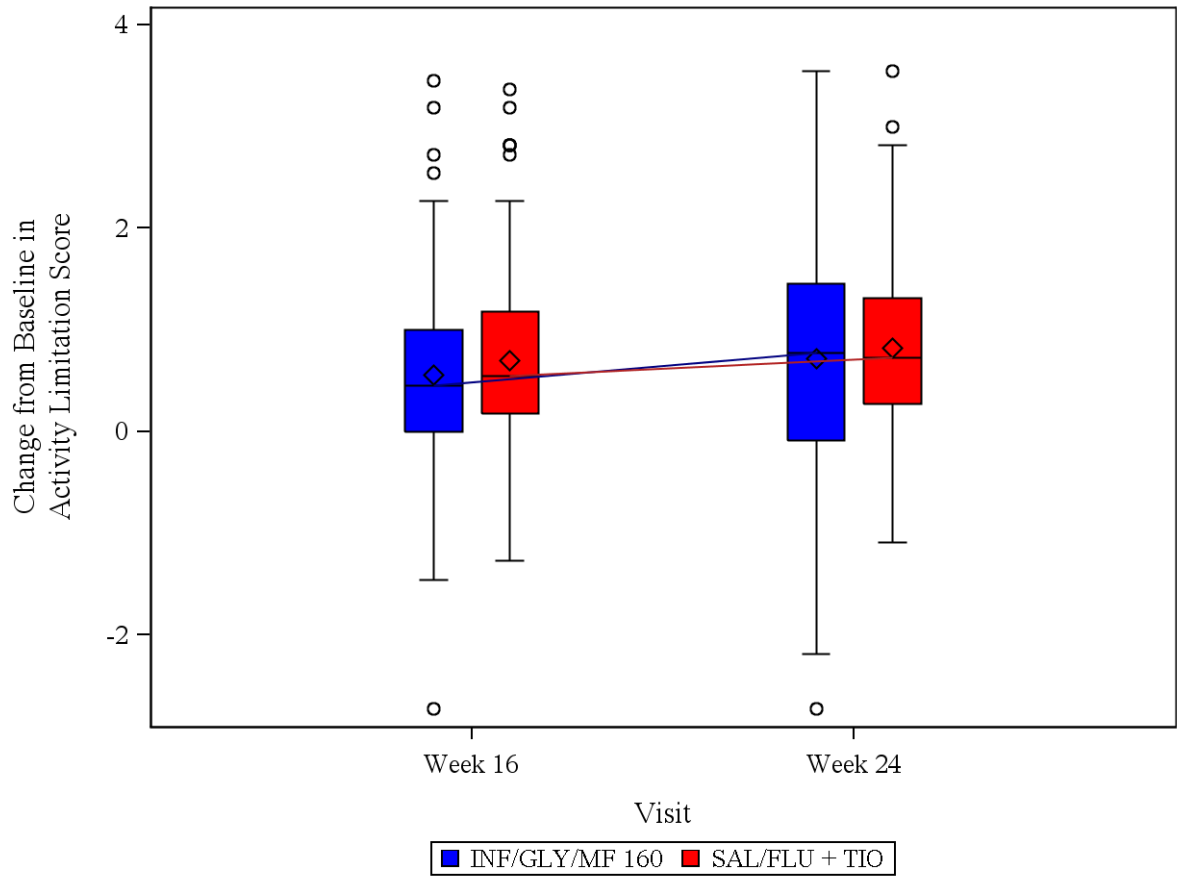


Figure 5.17.2 AQLQ-S (Activity Limitation Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



5.18 Boxplot: AQLQ-S (Activity Limitation Score) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 5.18.1 AQLQ-S (Activity Limitation Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

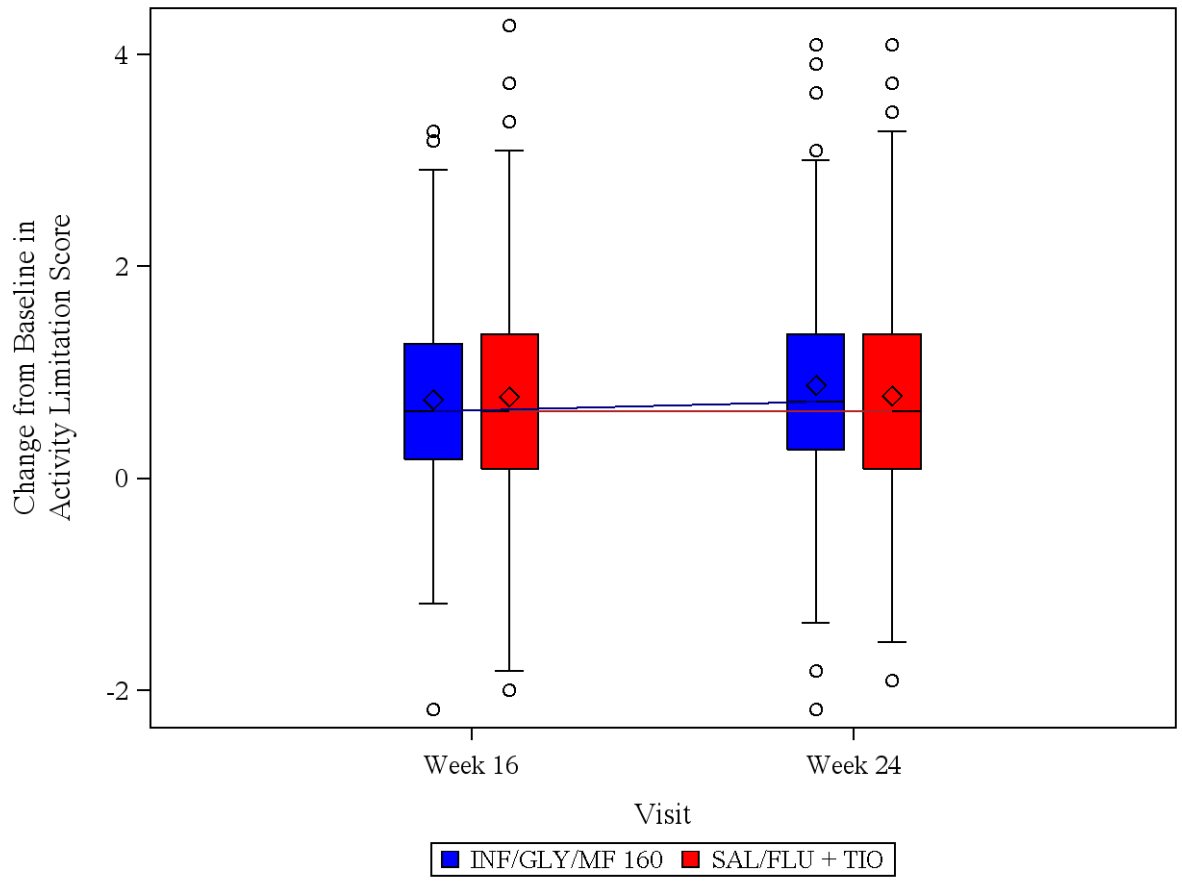
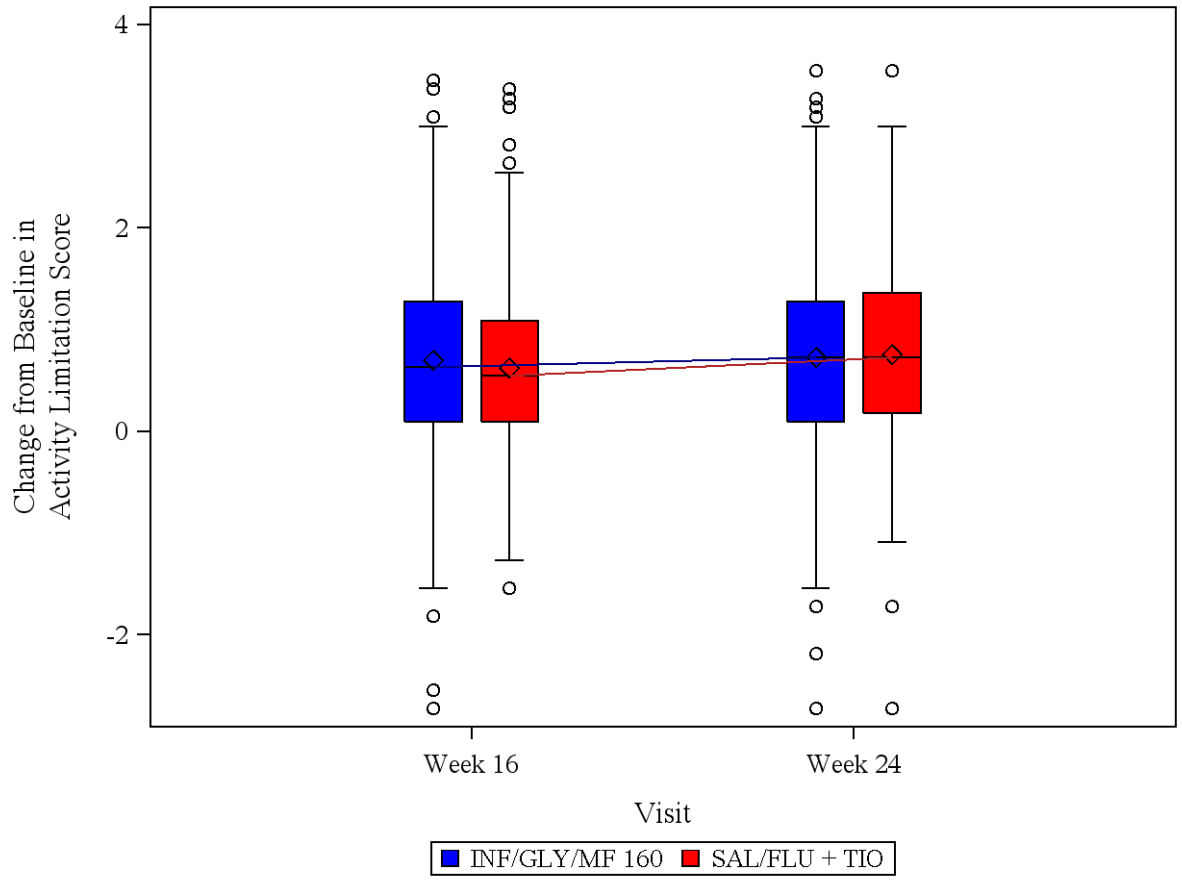
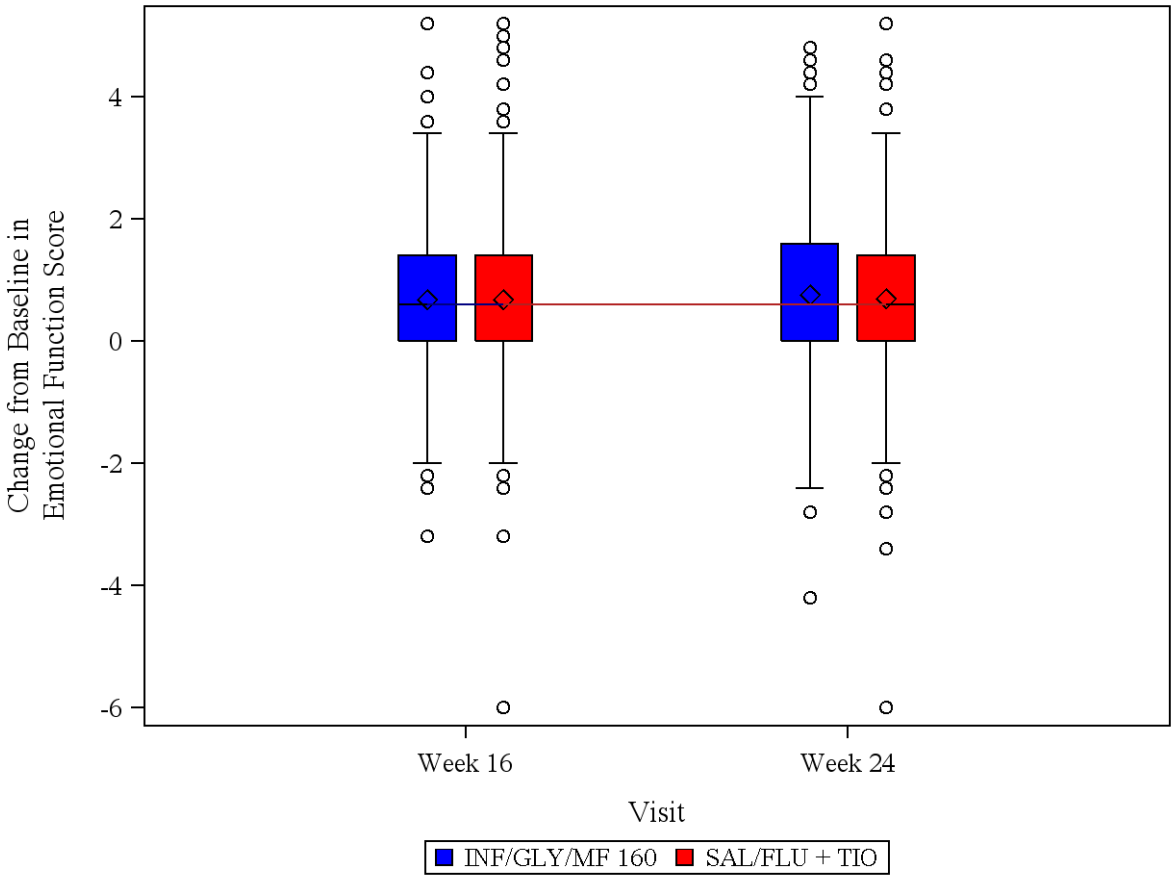


Figure 5.18.2 AQLQ-S (Activity Limitation Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



5.19 Boxplot: AQLQ-S (Emotional Function Score) - Change from Baseline (FAS)

Figure 5.19 AQLQ-S (Emotional Function Score) - Change from Baseline (FAS)



5.20 Boxplot: AQLQ-S (Emotional Function Score) - Change from Baseline by Age (FAS)

Figure 5.20.1 AQLQ-S (Emotional Function Score) - Change from Baseline by Age (FAS), Age = 18-39 years

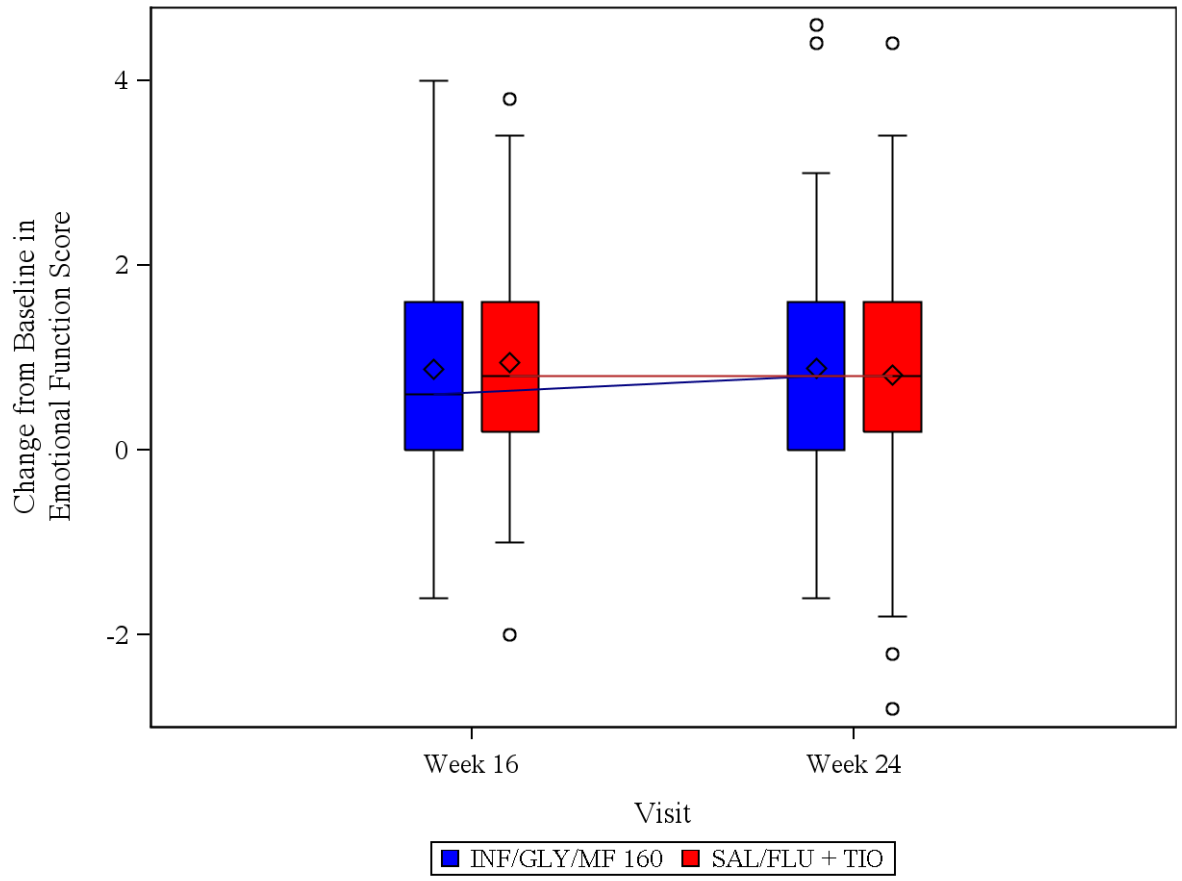


Figure 5.20.2 AQLQ-S (Emotional Function Score) - Change from Baseline by Age (FAS), Age = 40-64 years

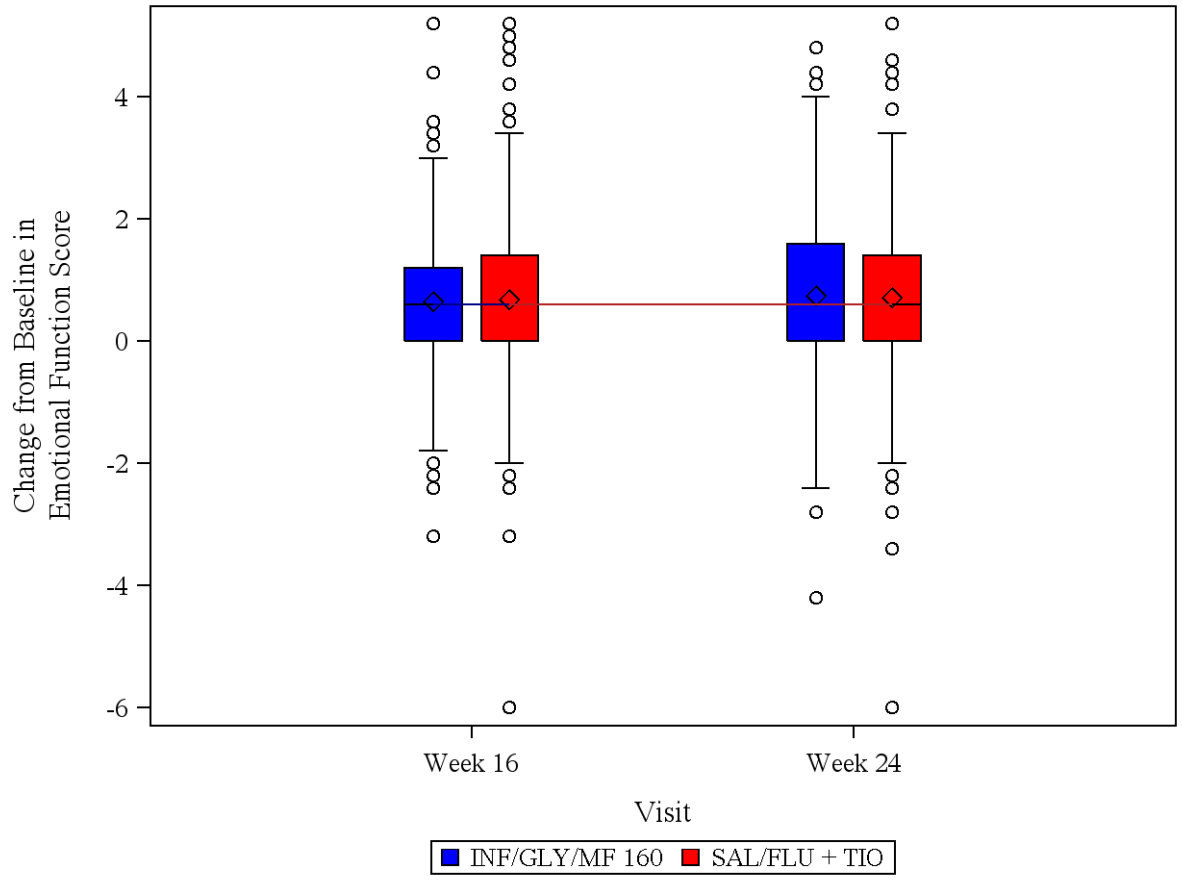
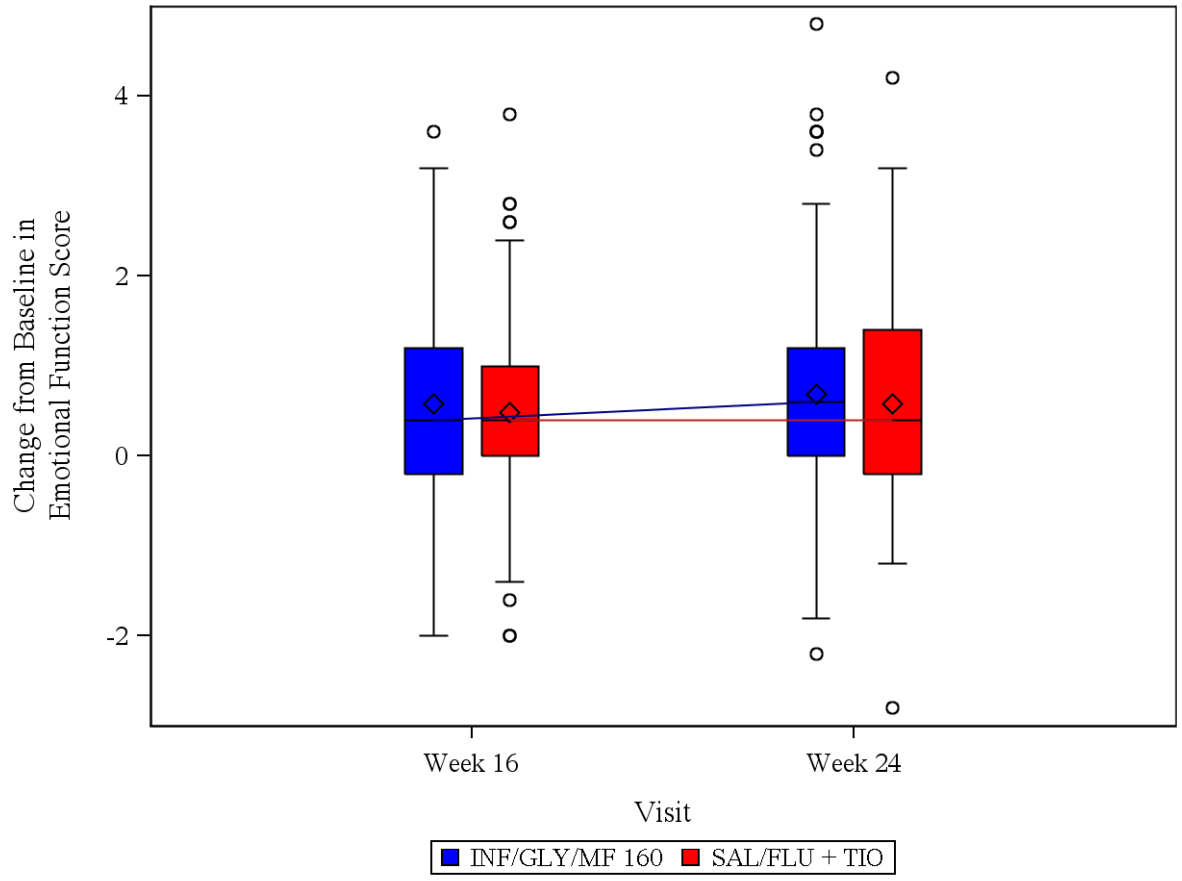


Figure 5.20.3 AQLQ-S (Emotional Function Score) - Change from Baseline by Age (FAS), Age = ≥65 years



5.21 Boxplot: AQLQ-S (Emotional Function Score) - Change from Baseline by Gender (FAS)

Figure 5.21.1 AQLQ-S (Emotional Function Score) - Change from Baseline by Gender (FAS), Gender = Male

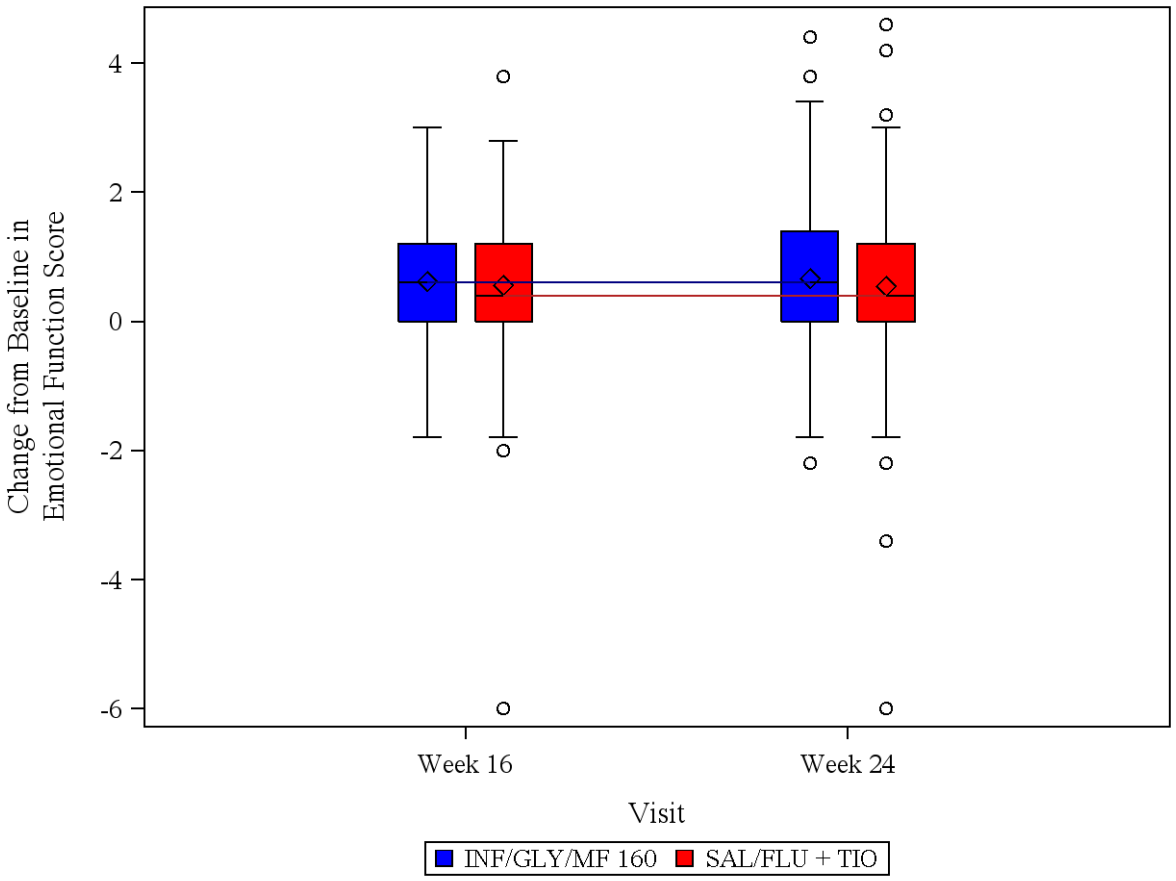
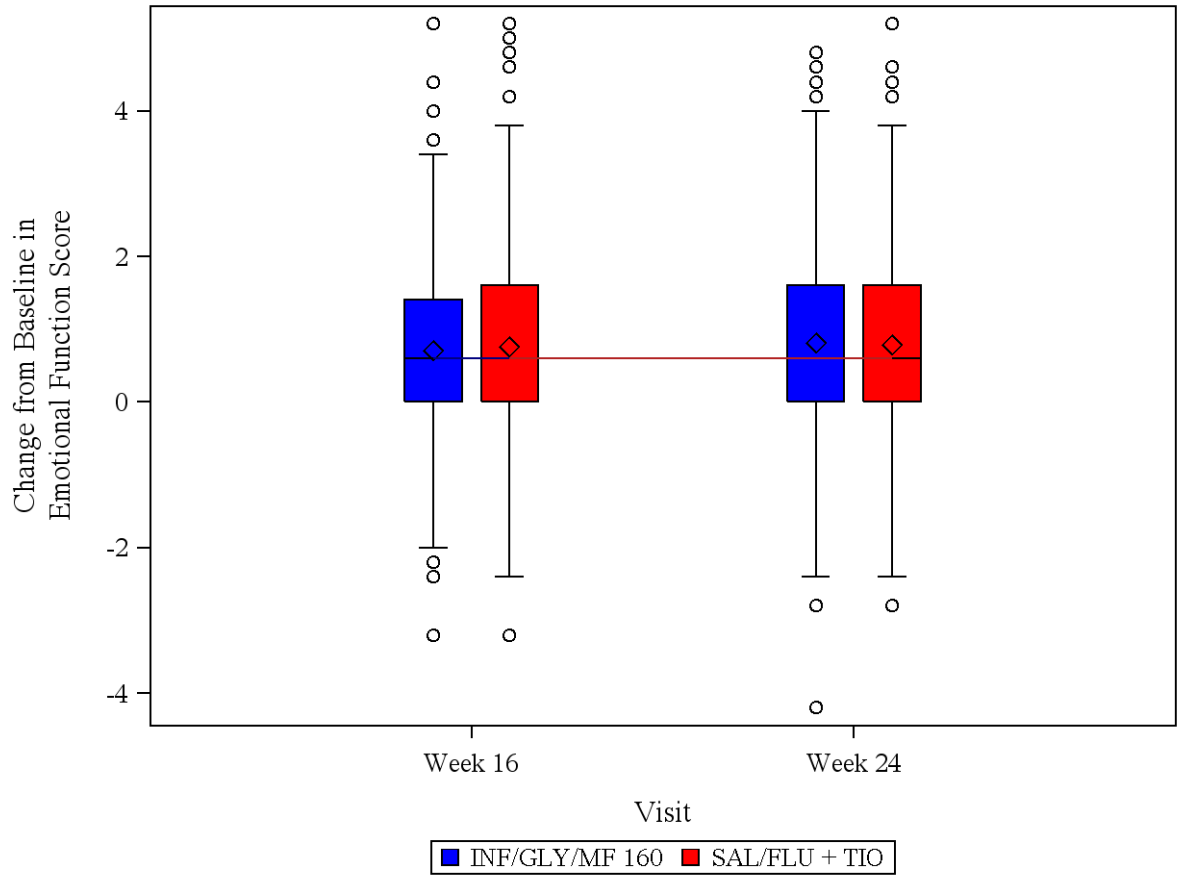


Figure 5.21.2 AQLQ-S (Emotional Function Score) - Change from Baseline by Gender (FAS), Gender = Female



5.22 Boxplot: AQLQ-S (Emotional Function Score) - Change from Baseline by Region (FAS)

Figure 5.22.1 AQLQ-S (Emotional Function Score) - Change from Baseline by Region (FAS), Region = Asia

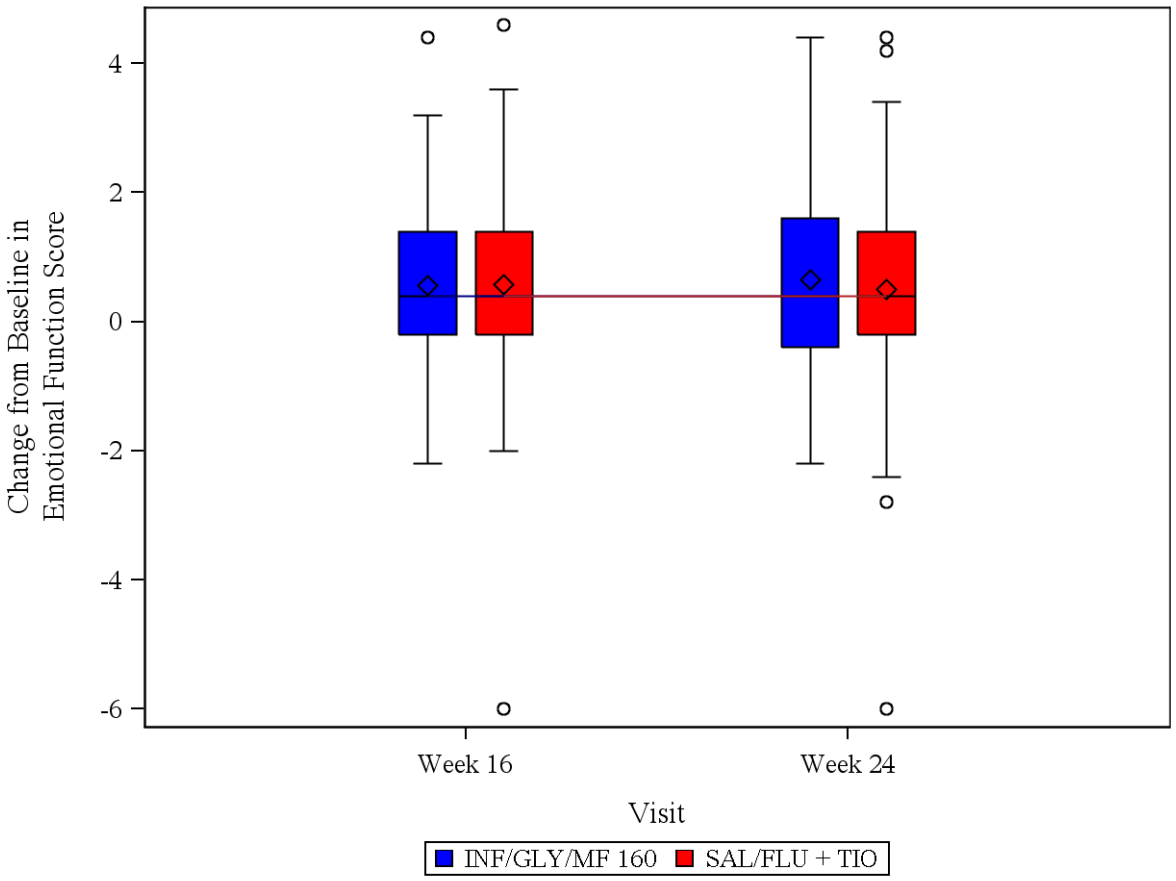


Figure 5.22.2 AQLQ-S (Emotional Function Score) - Change from Baseline by Region (FAS), Region = Europe

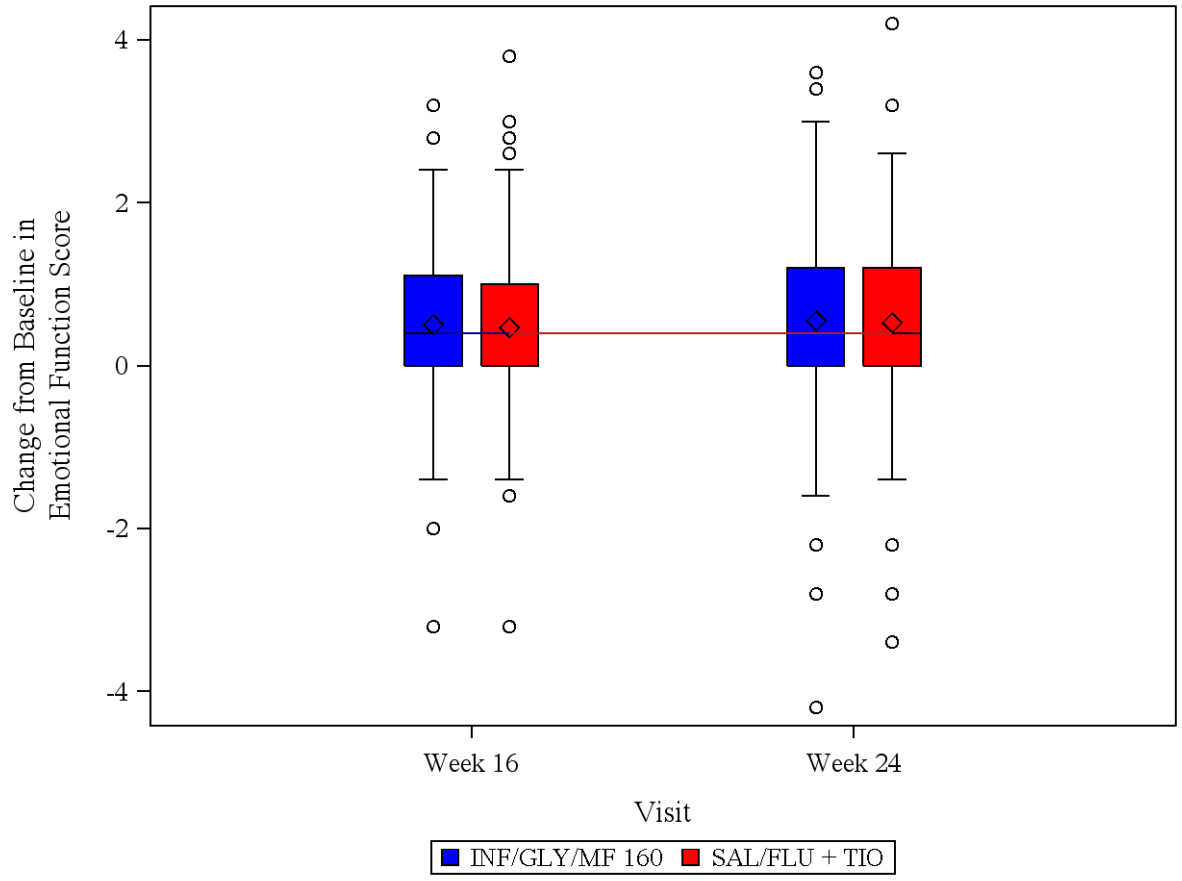


Figure 5.22.3 AQLQ-S (Emotional Function Score) - Change from Baseline by Region (FAS), Region = Latin America

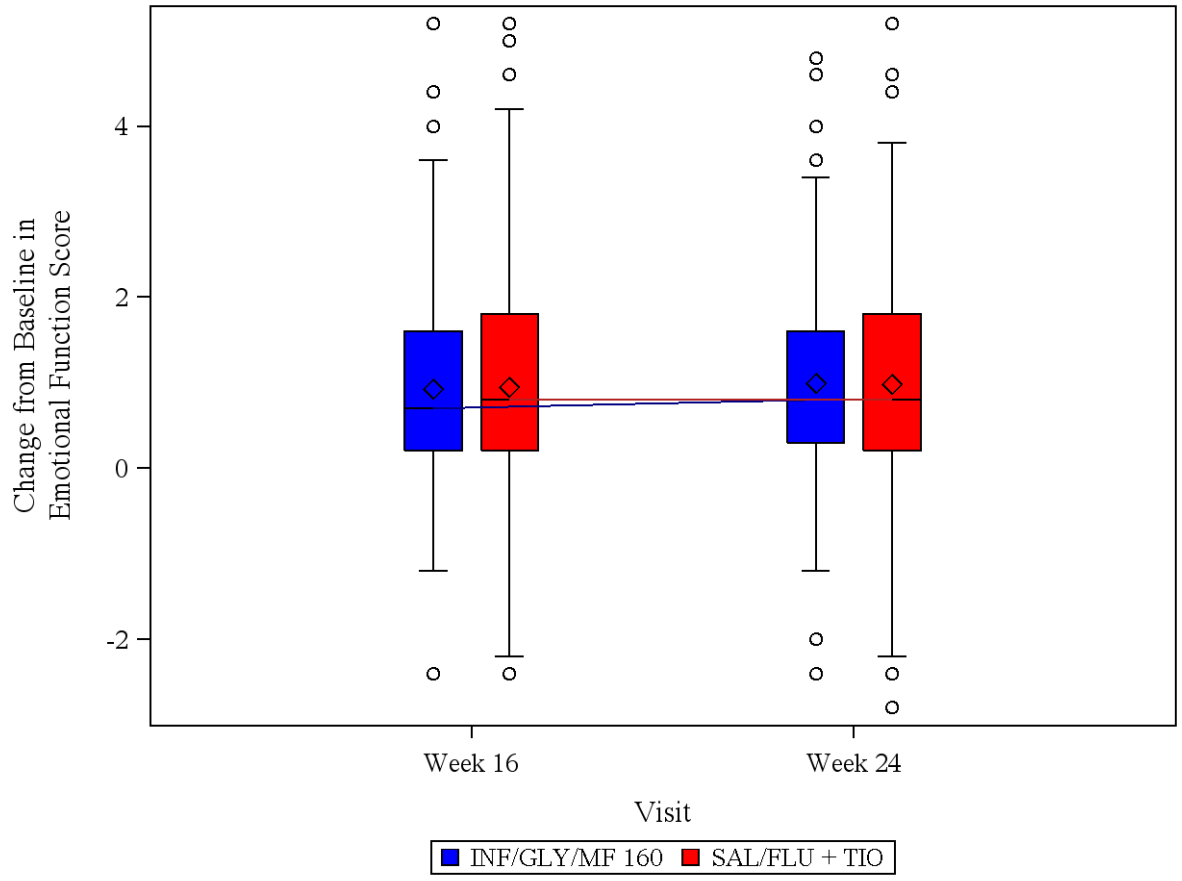
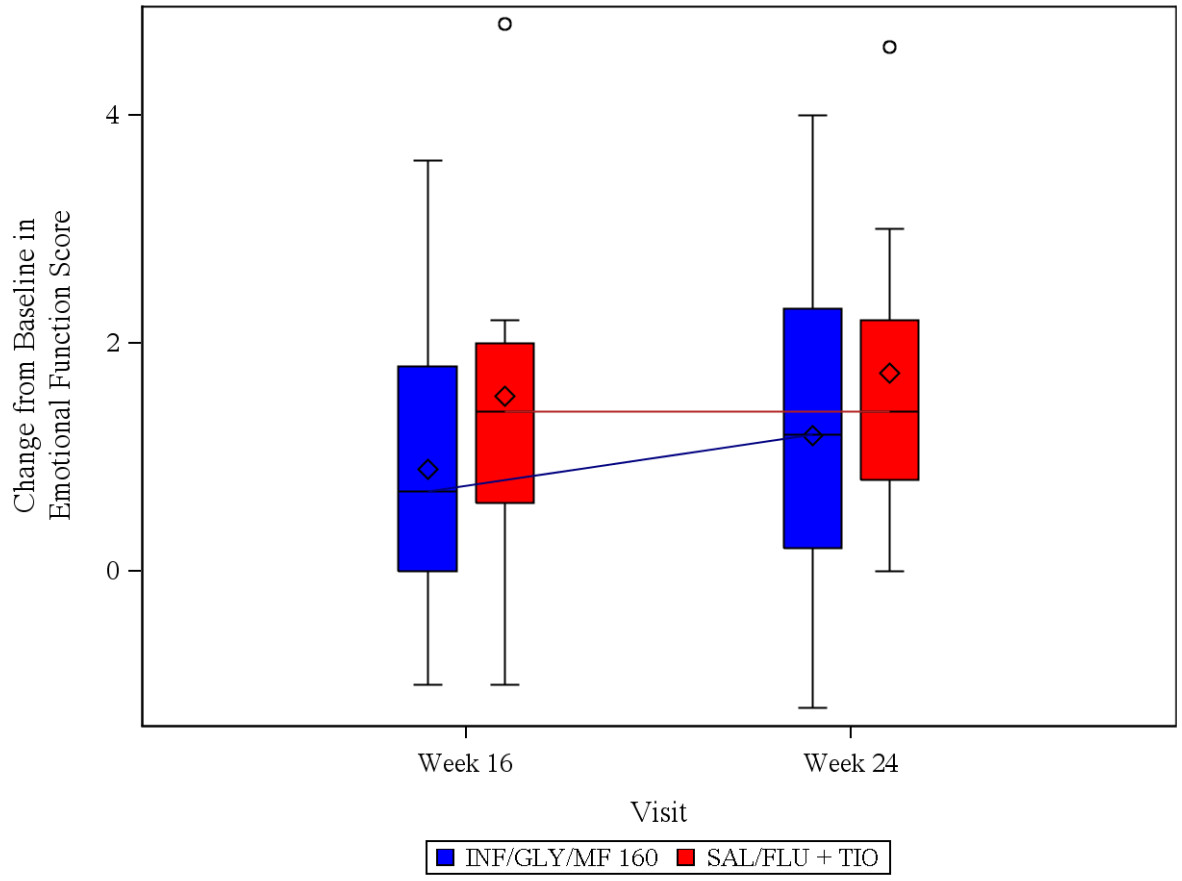


Figure 5.22.4 AQLQ-S (Emotional Function Score) - Change from Baseline by Region (FAS), Region = Others



5.23 Boxplot: AQLQ-S (Emotional Function Score) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 5.23.1 AQLQ-S (Emotional Function Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

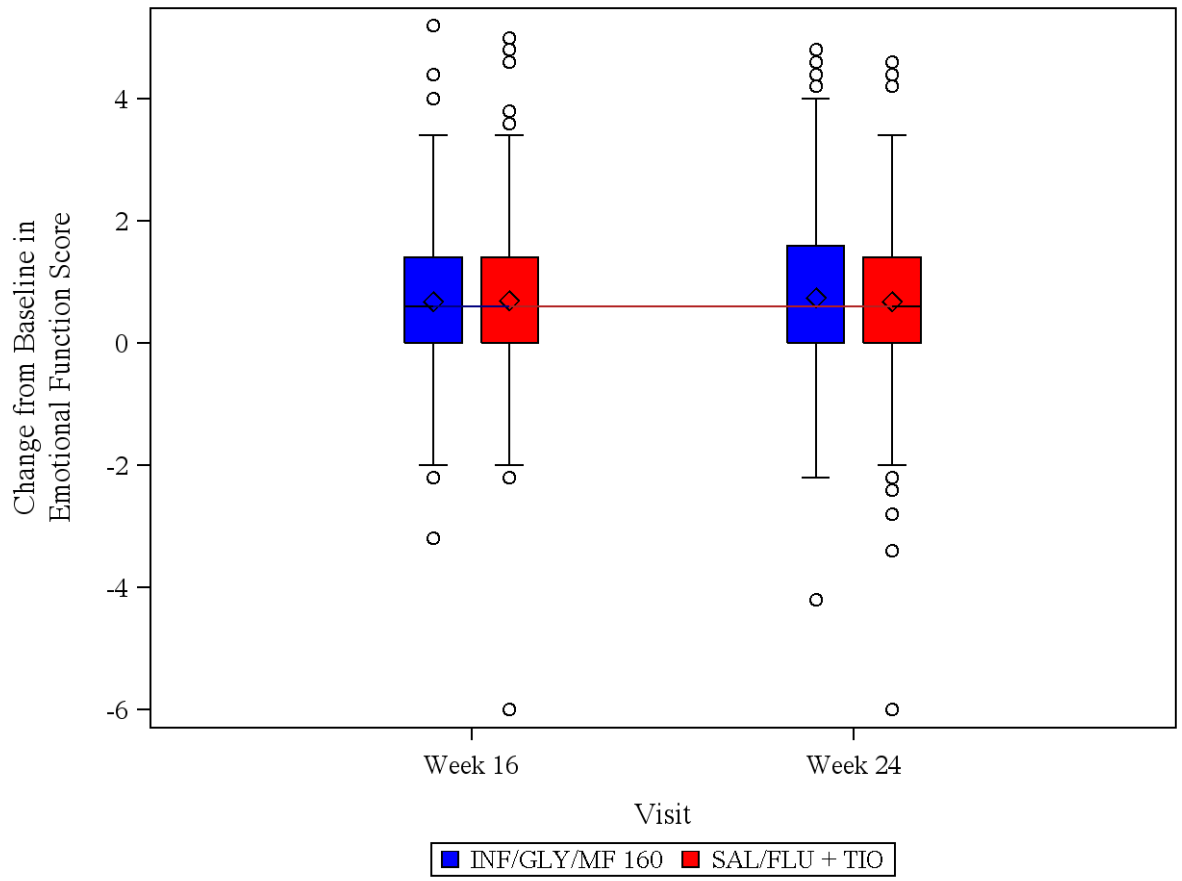
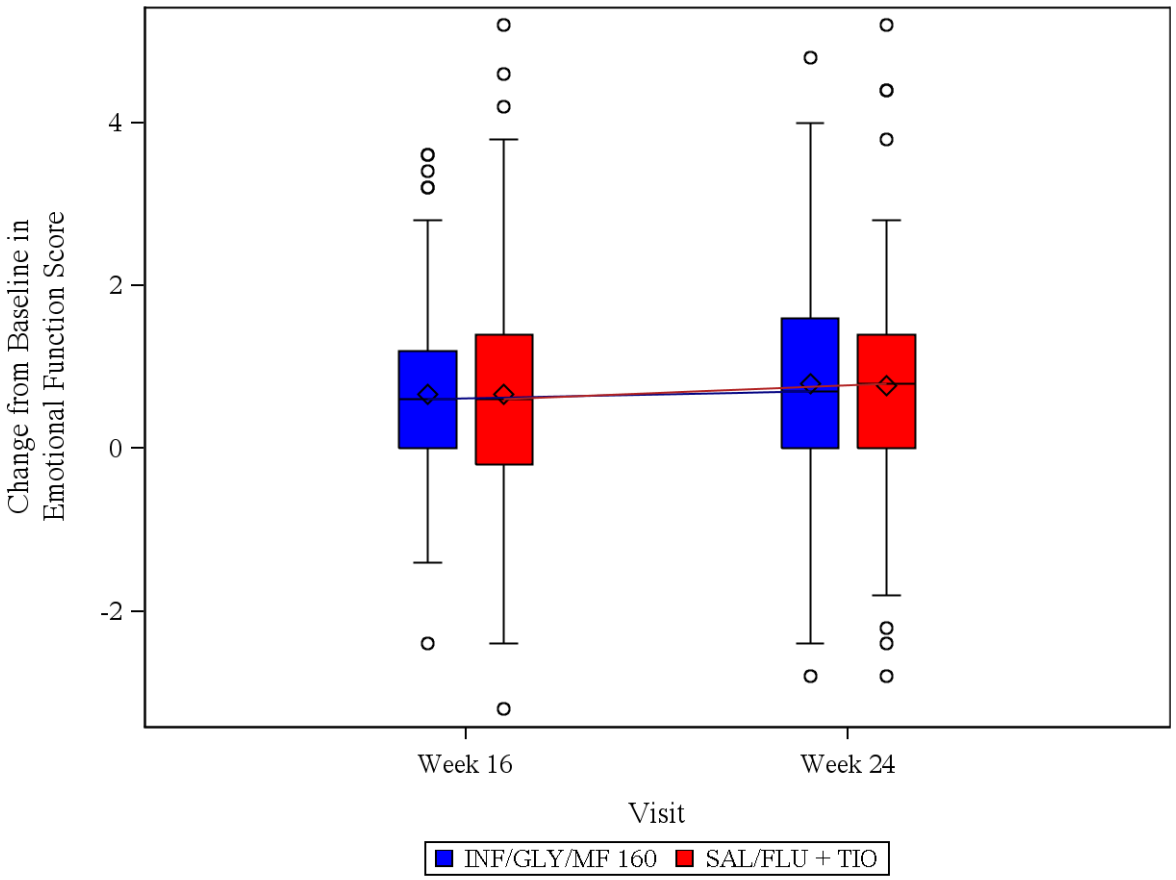


Figure 5.23.2 AQLQ-S (Emotional Function Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



5.24 Boxplot: AQLQ-S (Emotional Function Score) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 5.24.1 AQLQ-S (Emotional Function Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

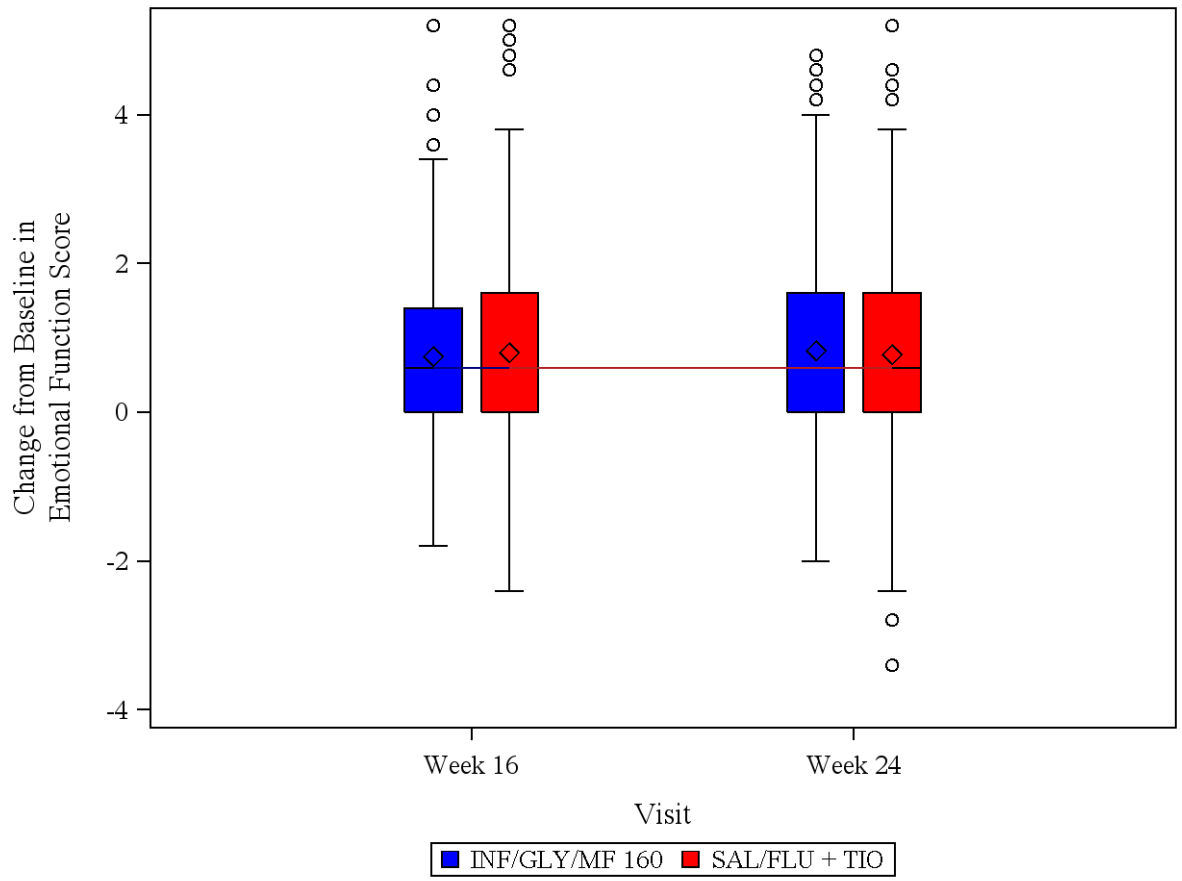
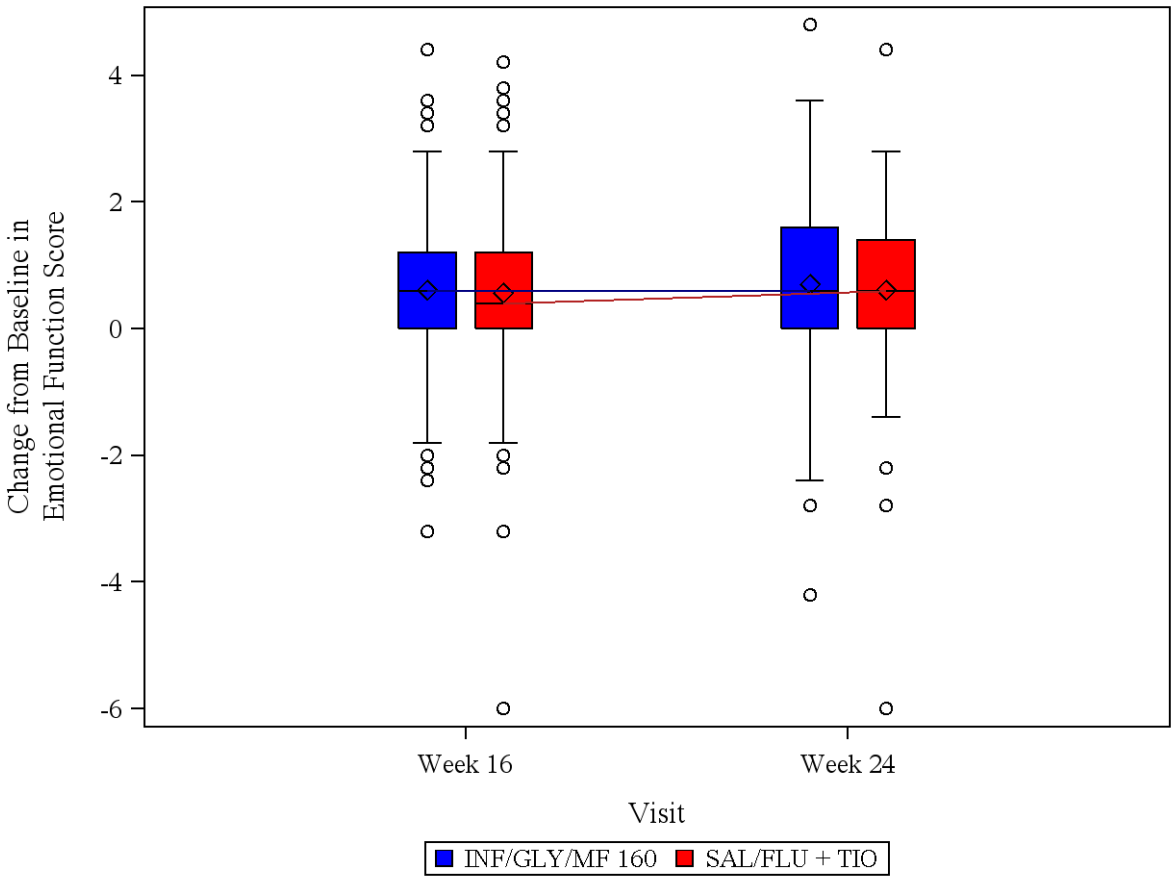
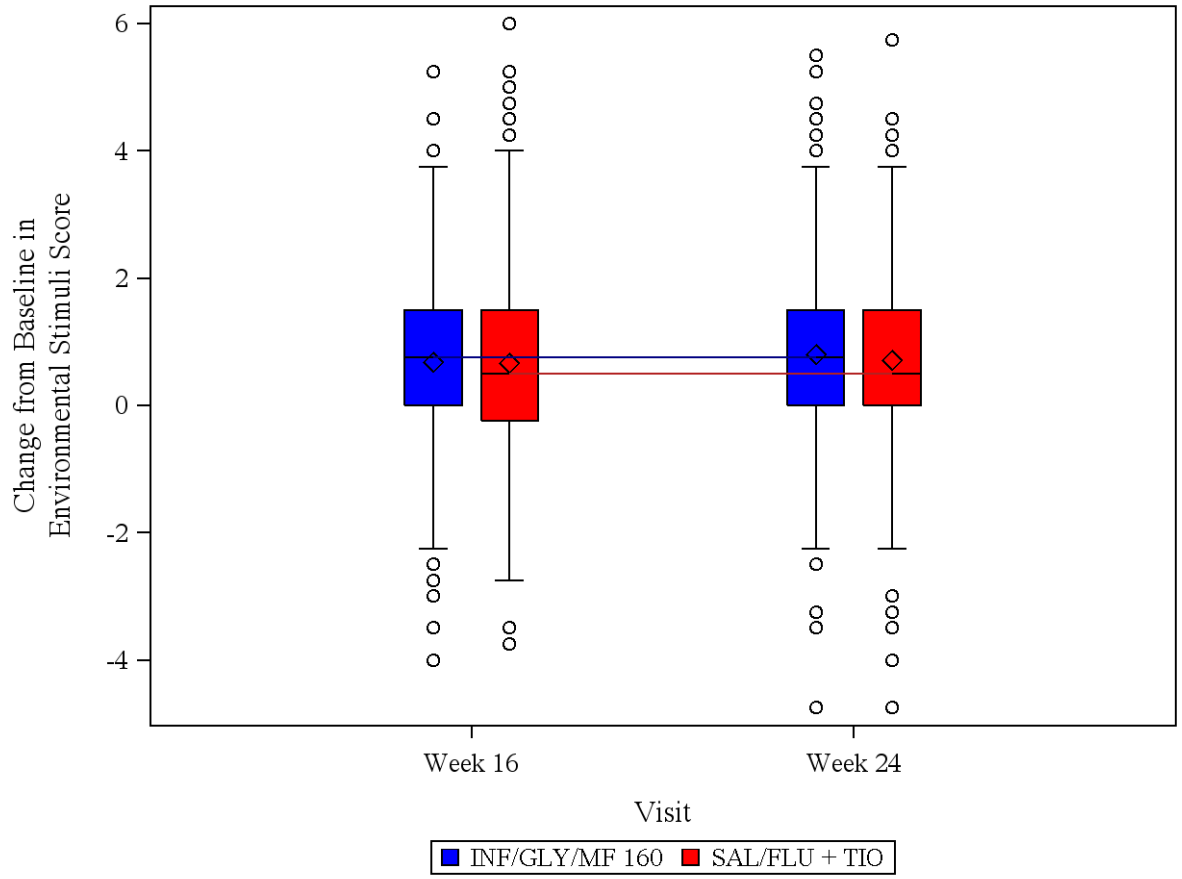


Figure 5.24.2 AQLQ-S (Emotional Function Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



5.25 Boxplot: AQLQ-S (Environmental Stimuli Score) - Change from Baseline (FAS)

Figure 5.25 AQLQ-S (Environmental Stimuli Score) - Change from Baseline (FAS)



5.26 Boxplot: AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Age (FAS)

Figure 5.26.1 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Age (FAS), Age = 18-39 years

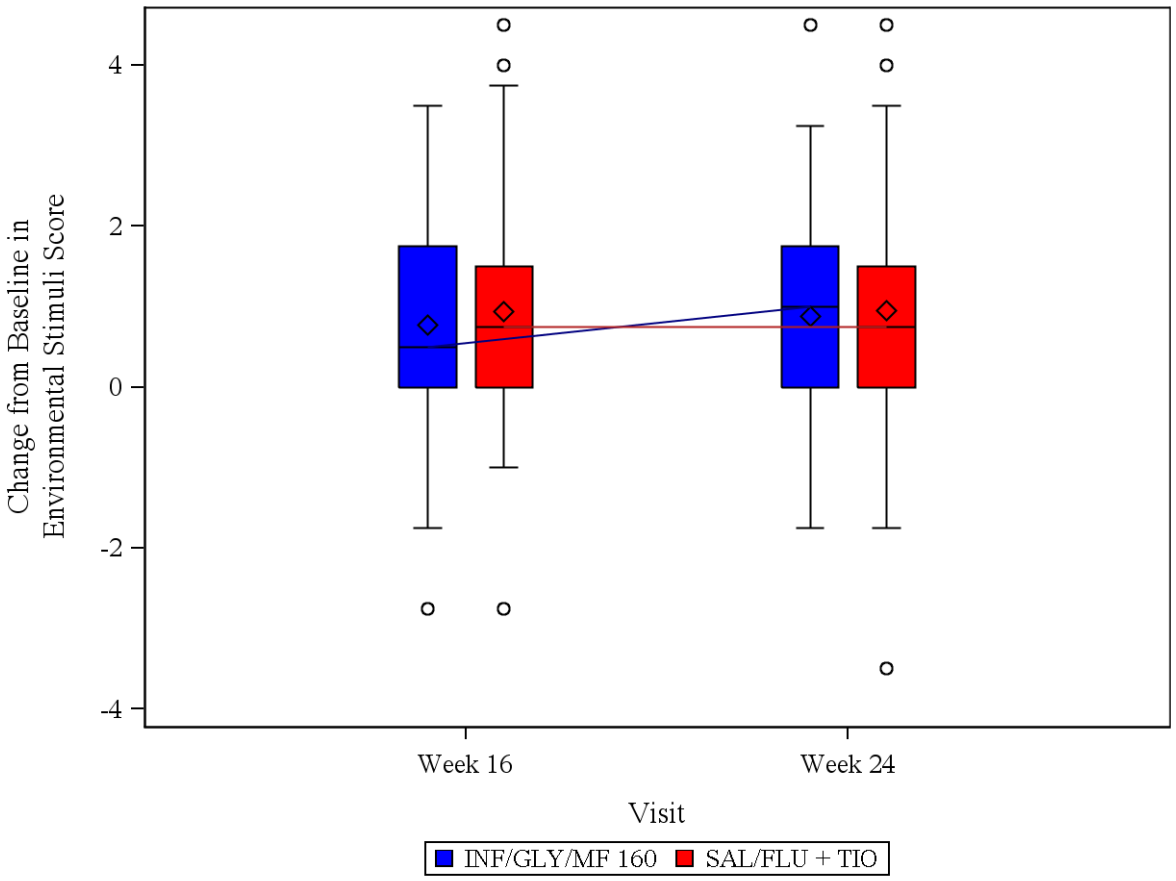


Figure 5.26.2 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Age (FAS), Age = 40-64 years

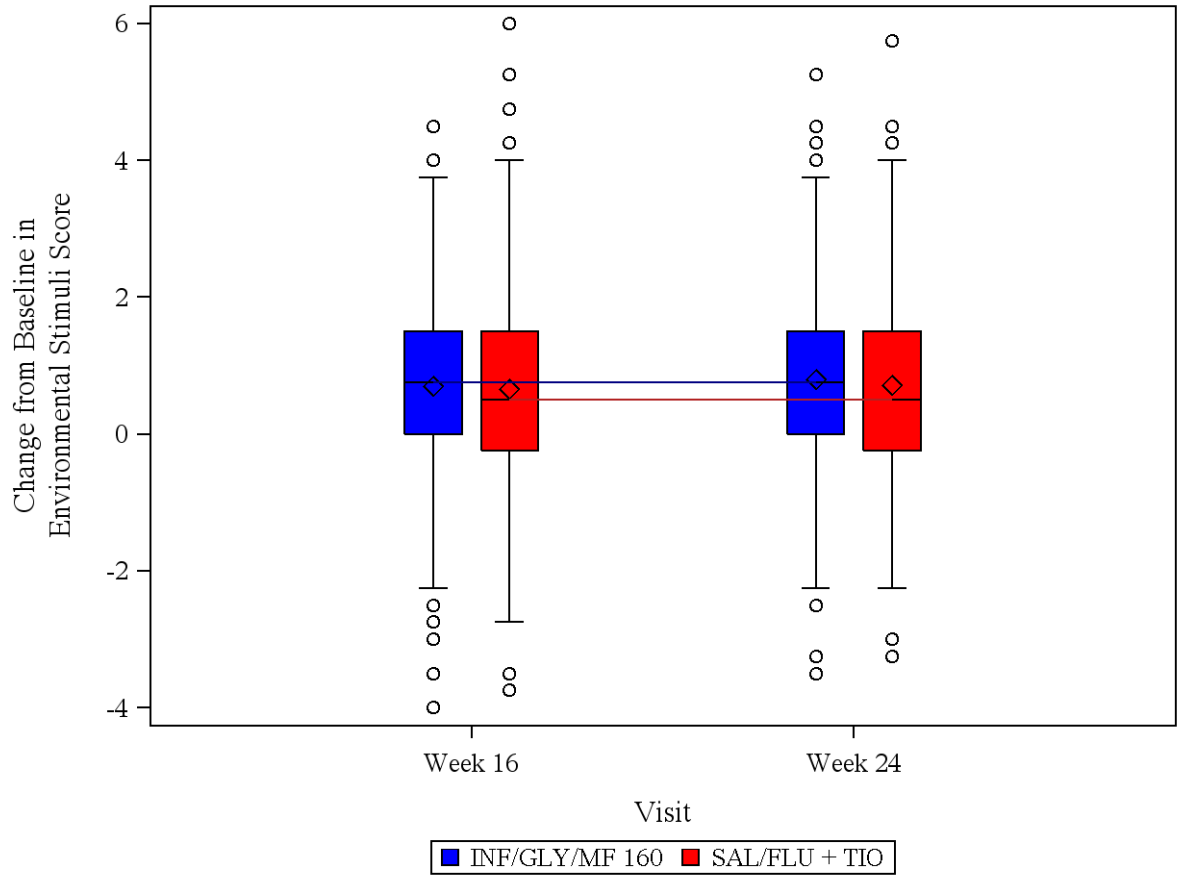
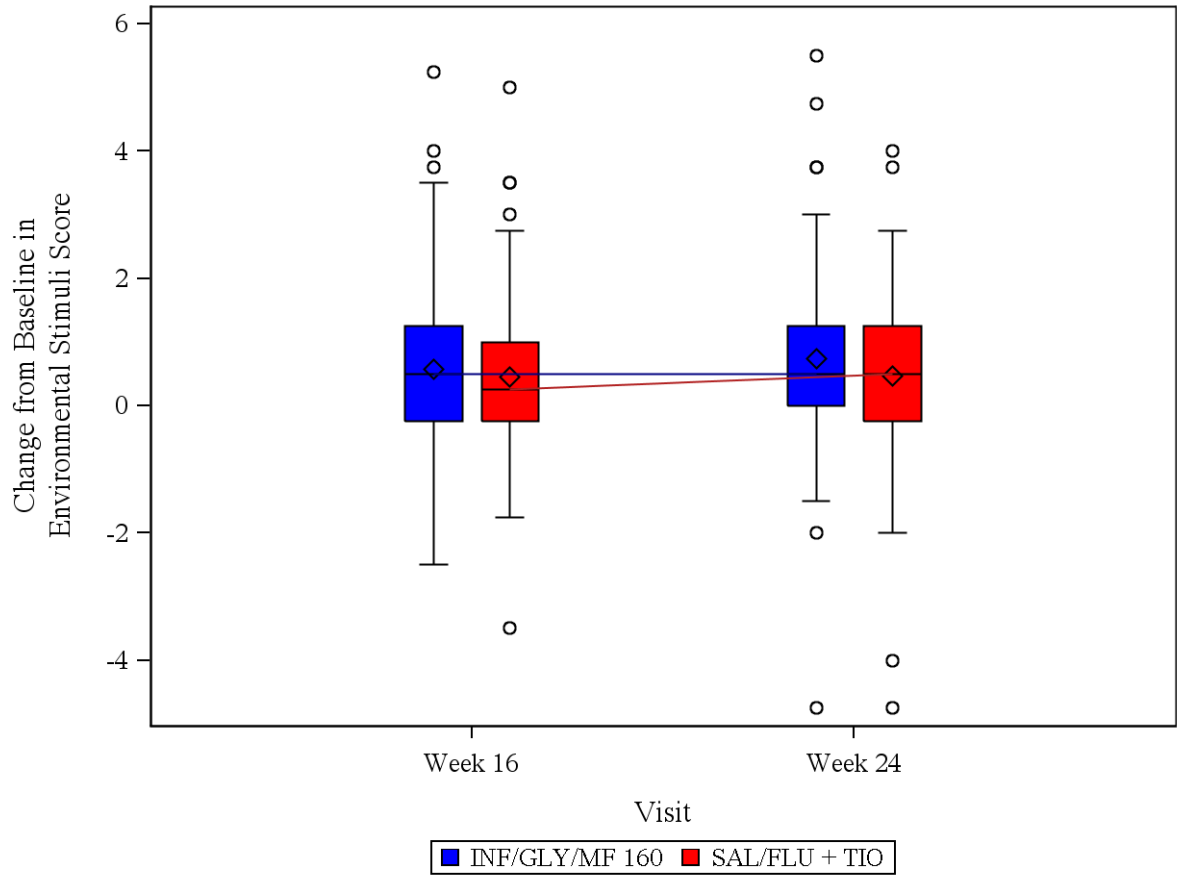


Figure 5.26.3 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Age (FAS), Age = ≥65 years



5.27 Boxplot: AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Gender (FAS)

Figure 5.27.1 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Gender (FAS), Gender = Male

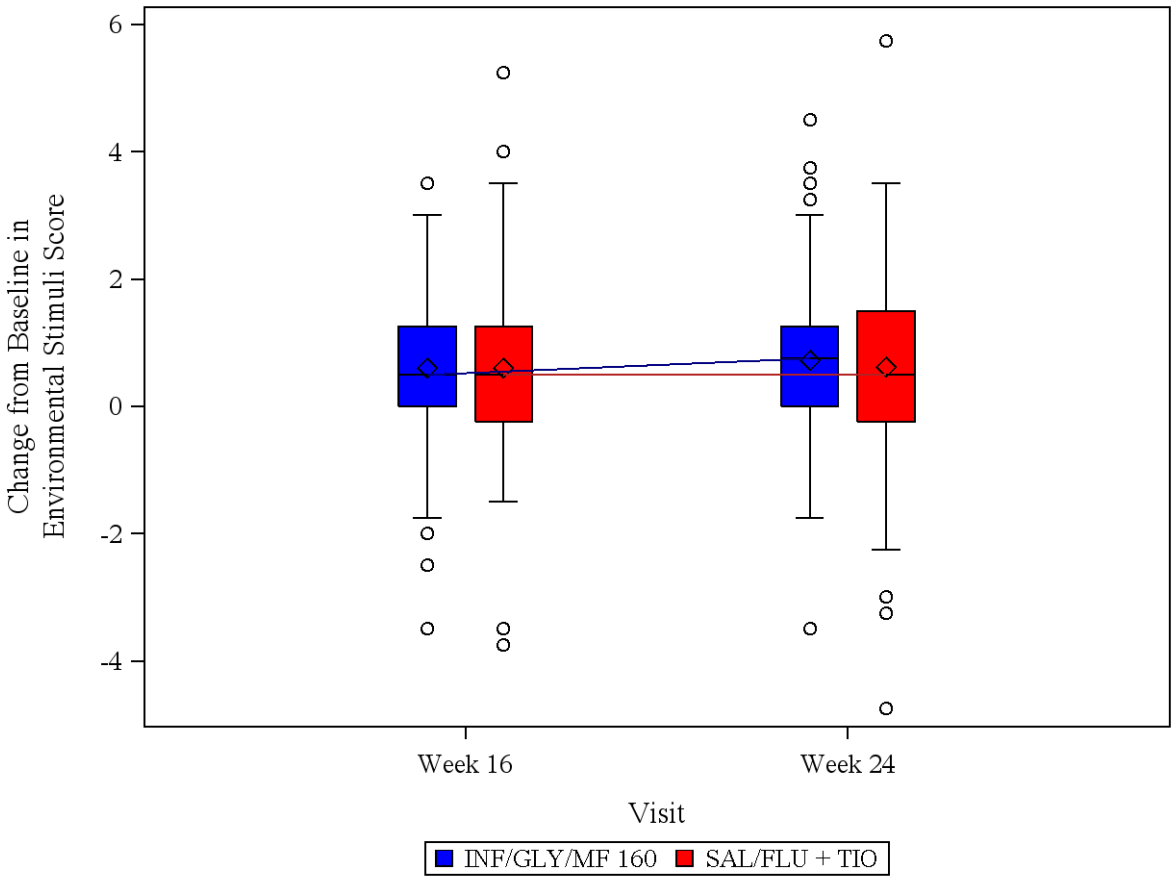
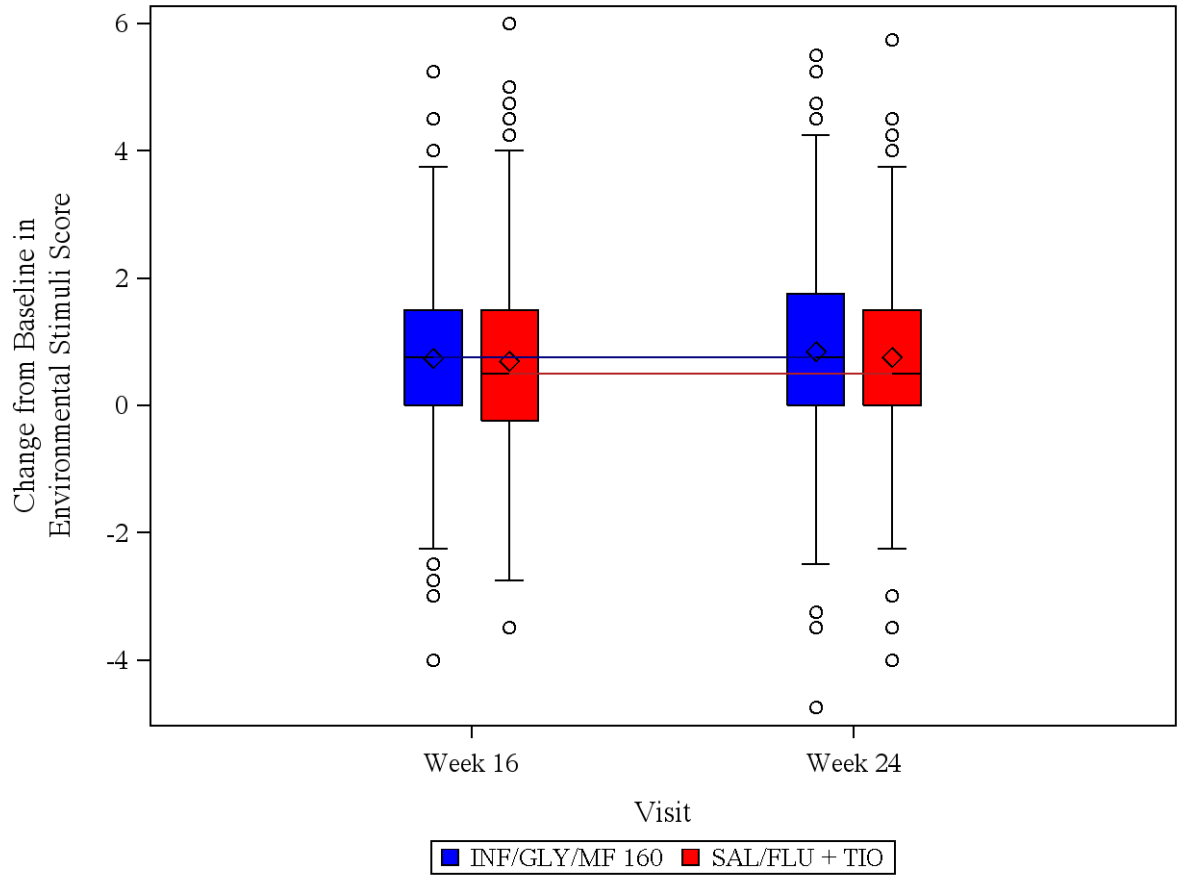


Figure 5.27.2 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Gender (FAS), Gender = Female



5.28 Boxplot: AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Region (FAS)

Figure 5.28.1 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Region (FAS), Region = Asia

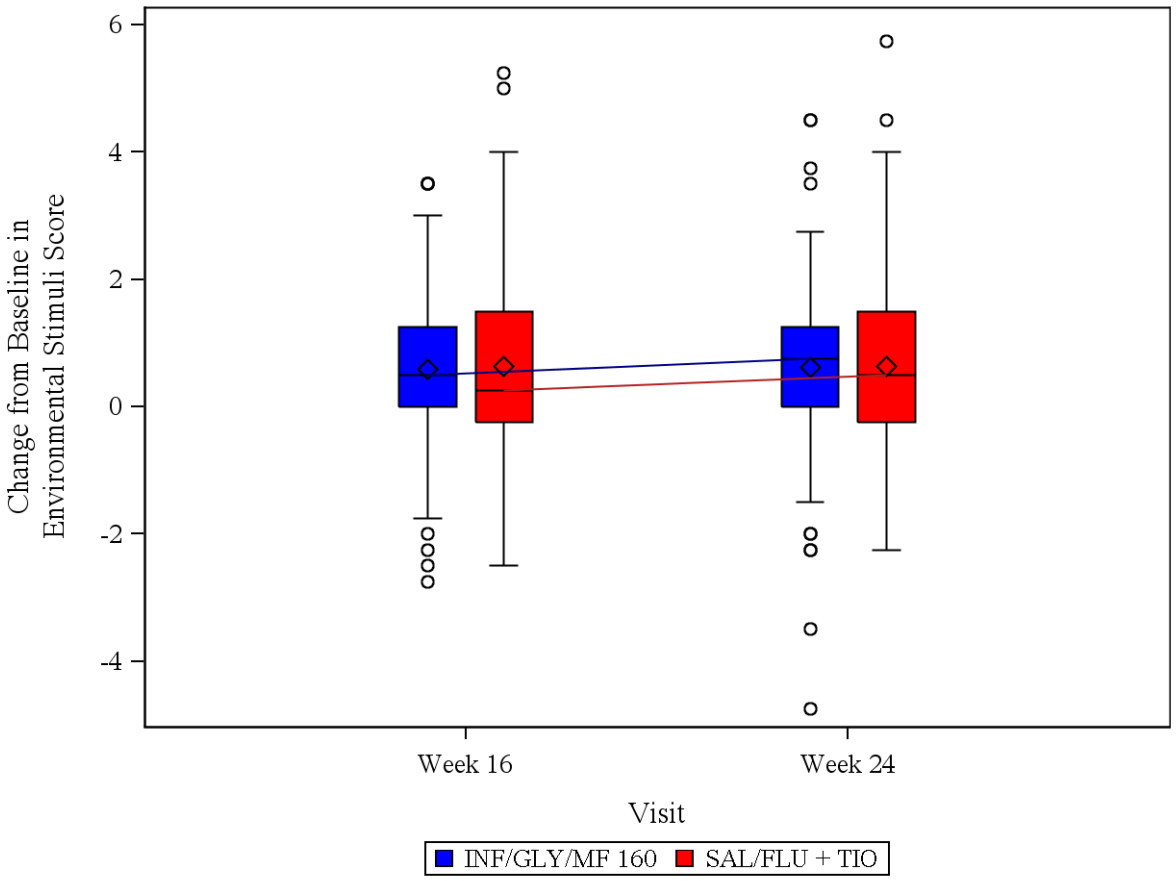


Figure 5.28.2 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Region (FAS), Region = Europe

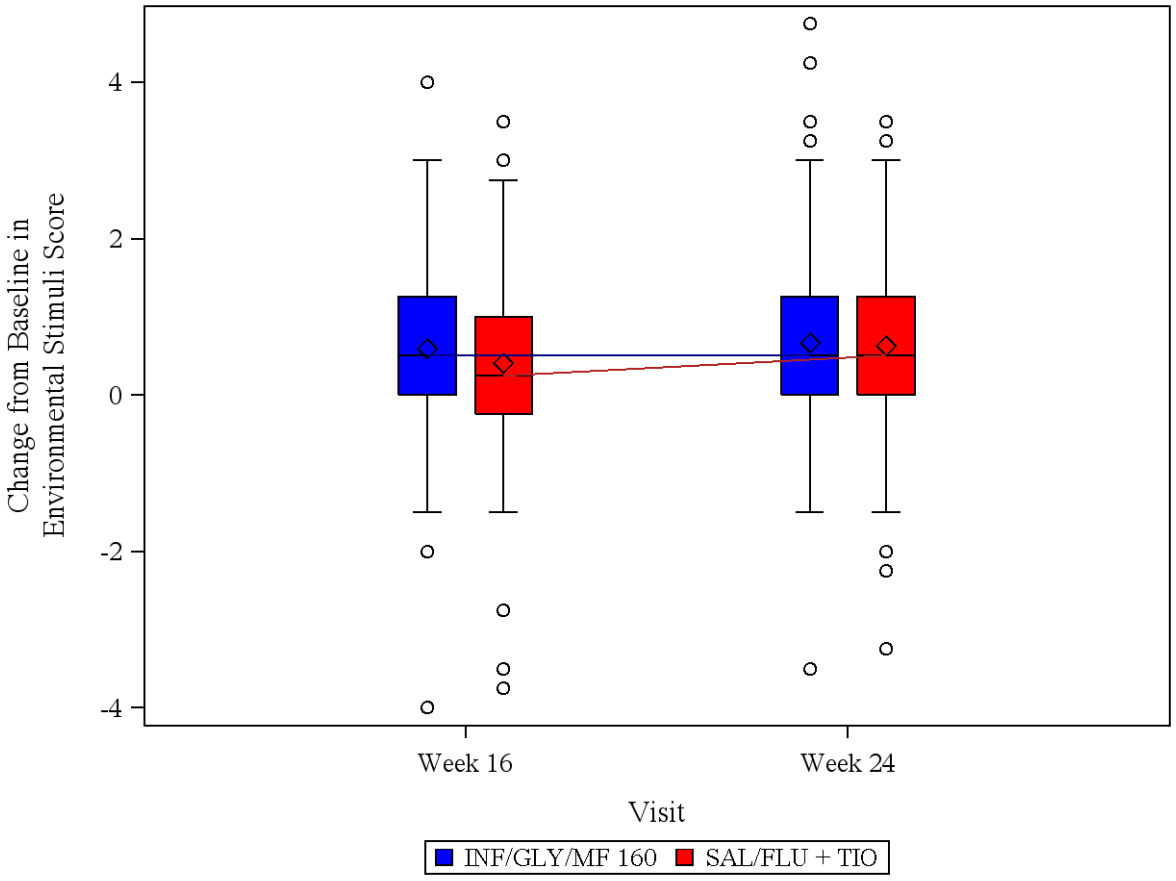


Figure 5.28.3 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Region (FAS), Region = Latin America

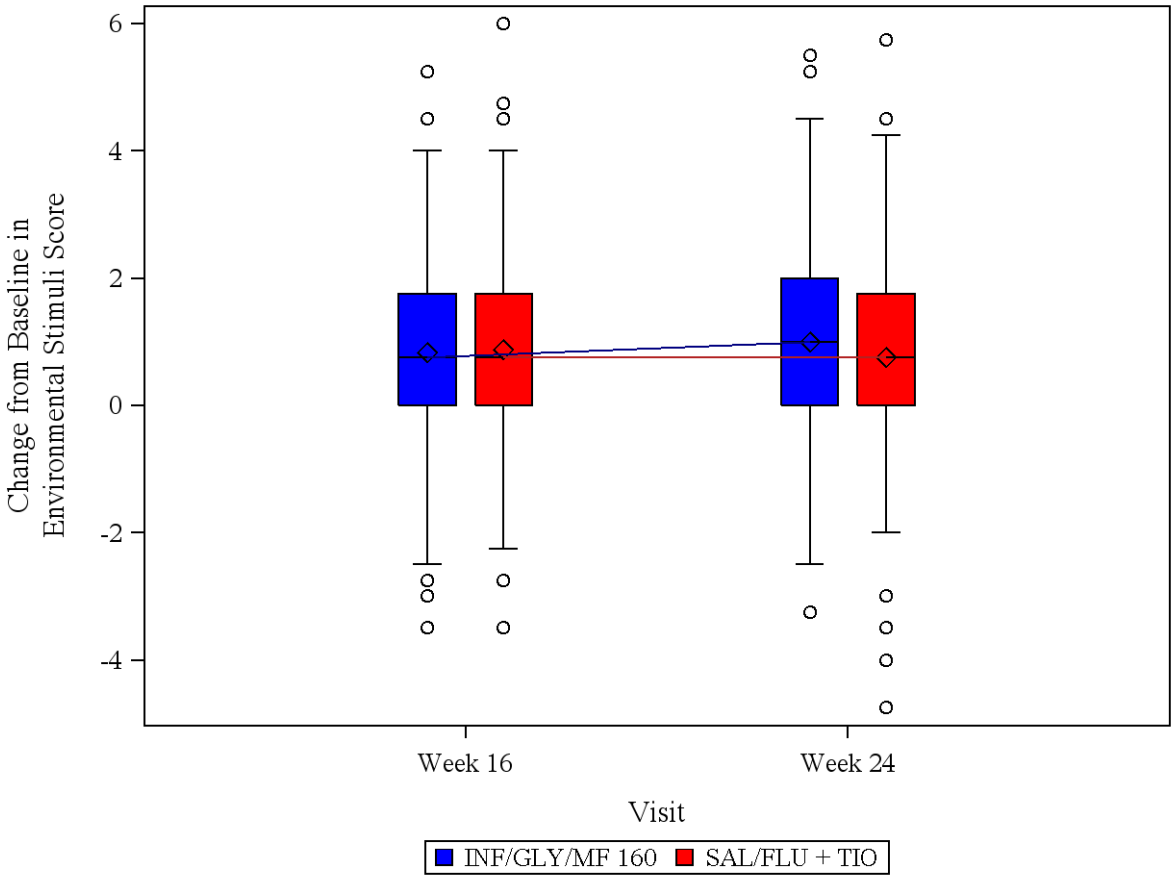
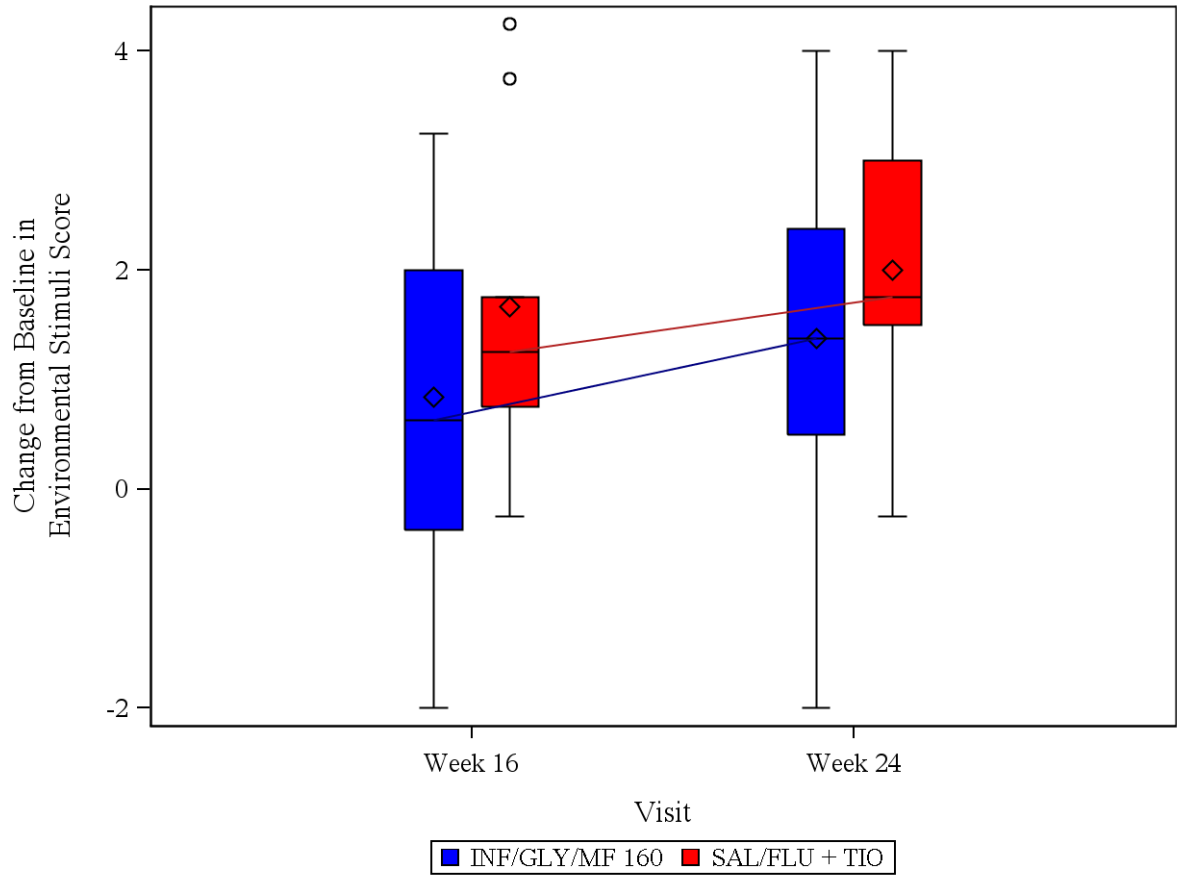


Figure 5.28.4 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Region (FAS), Region = Others



5.29 Boxplot: AQLQ-S (Environmental Stimuli Score) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 5.29.1 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

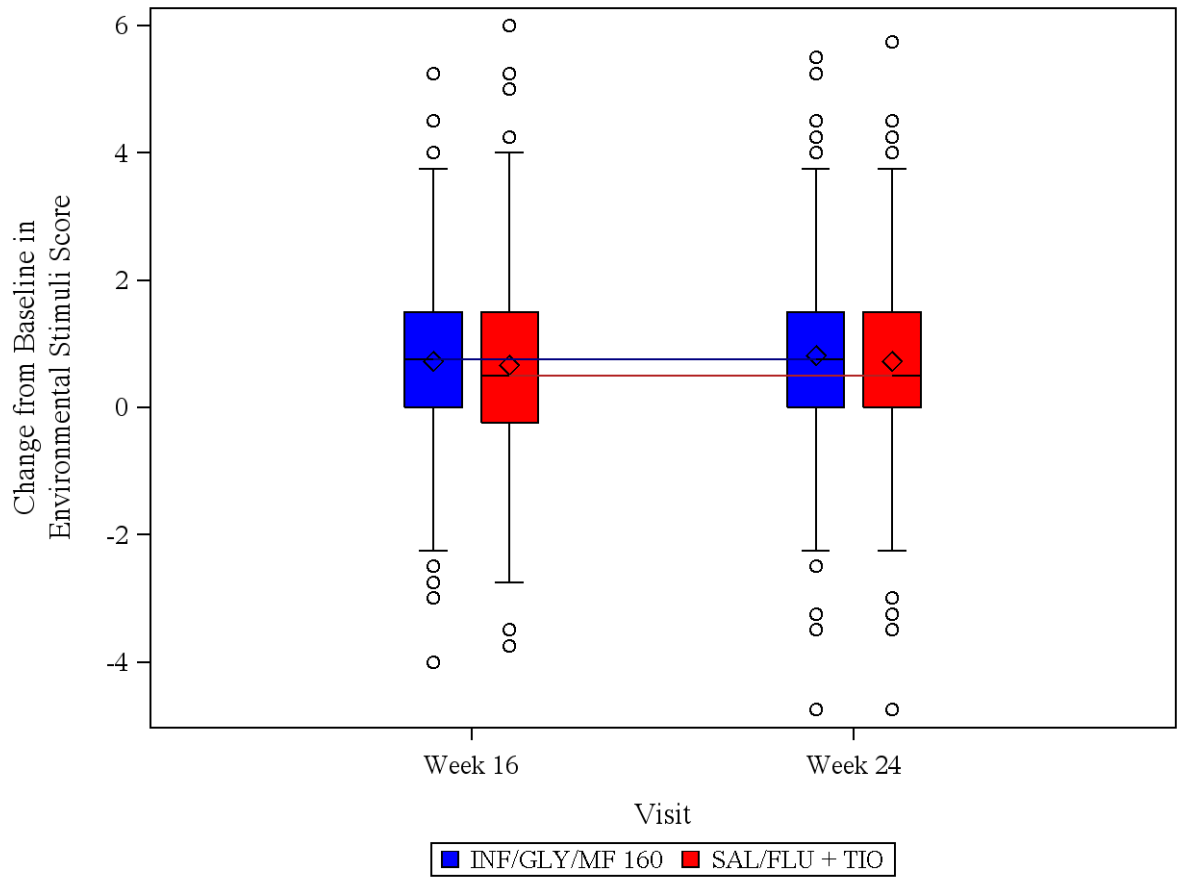
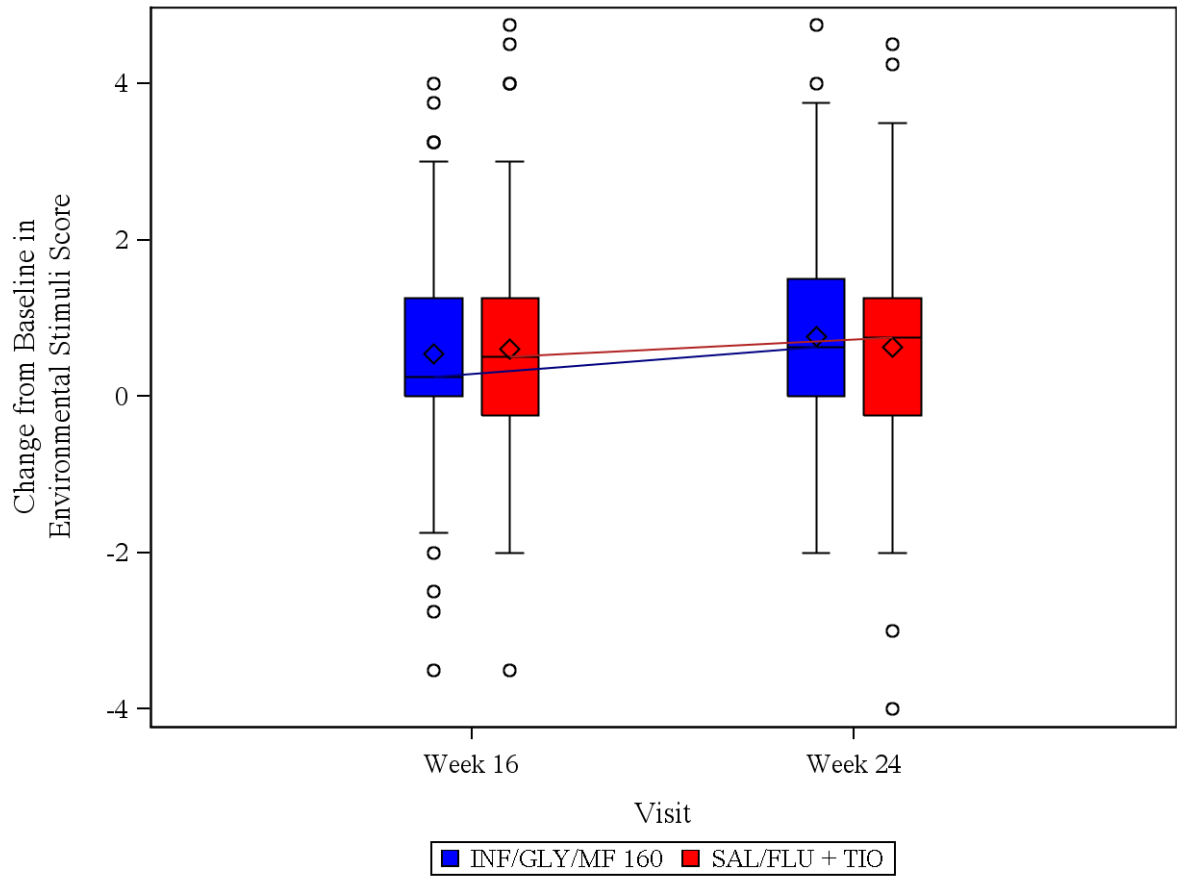


Figure 5.29.2 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



5.30 Boxplot: AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 5.30.1 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

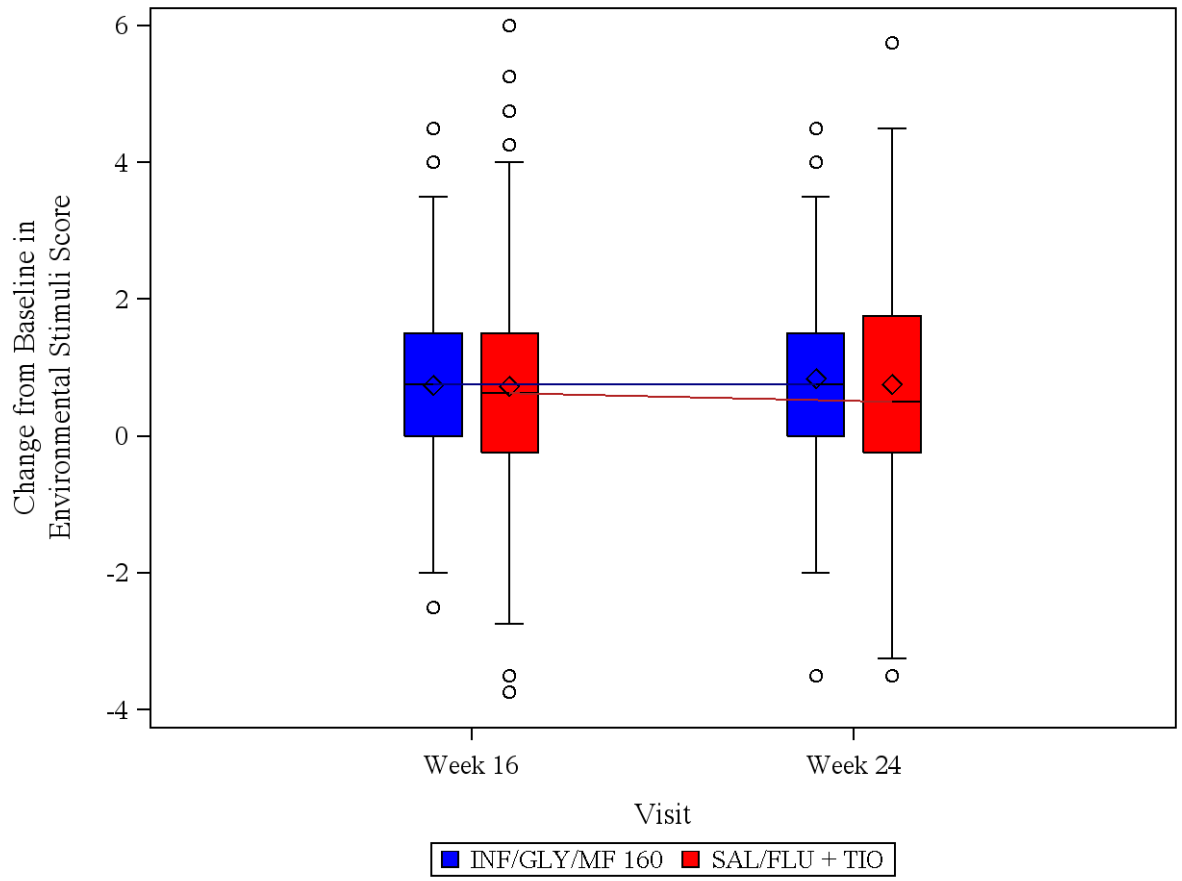
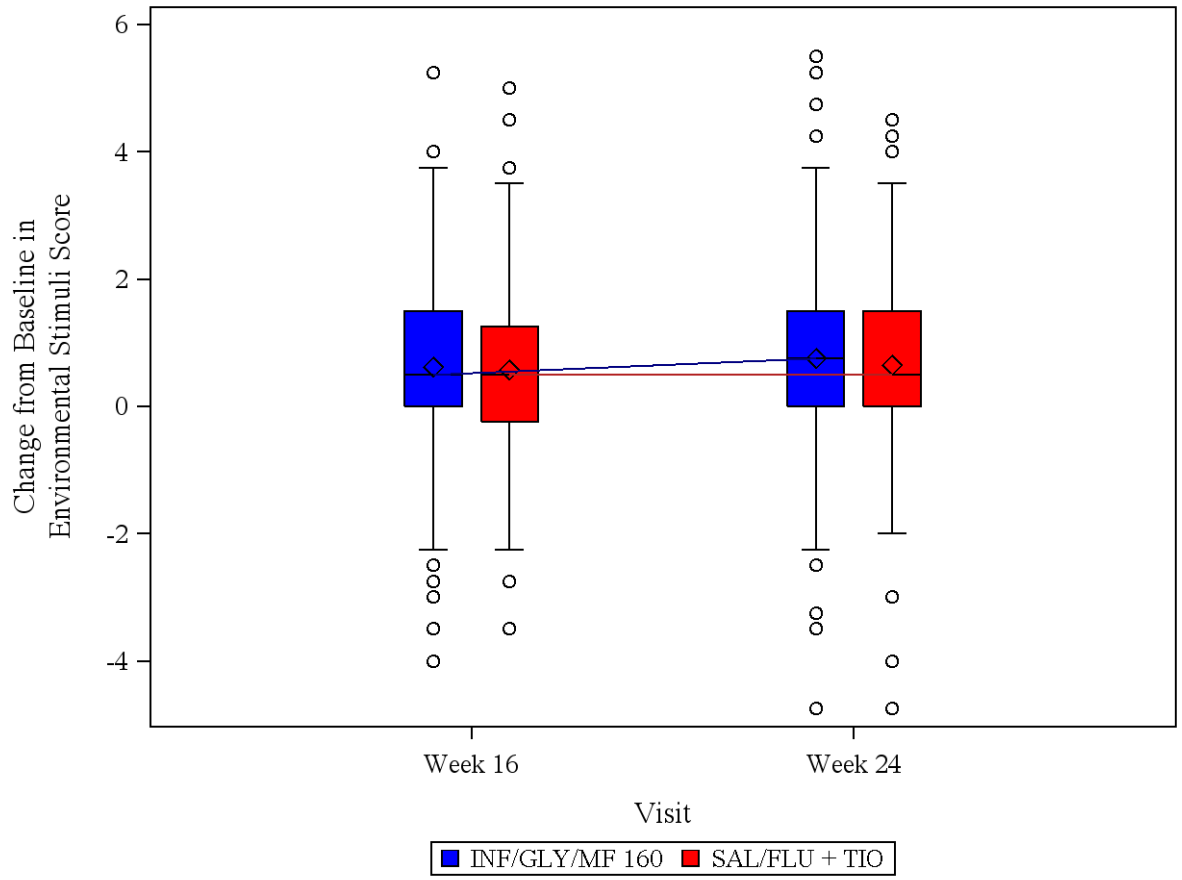


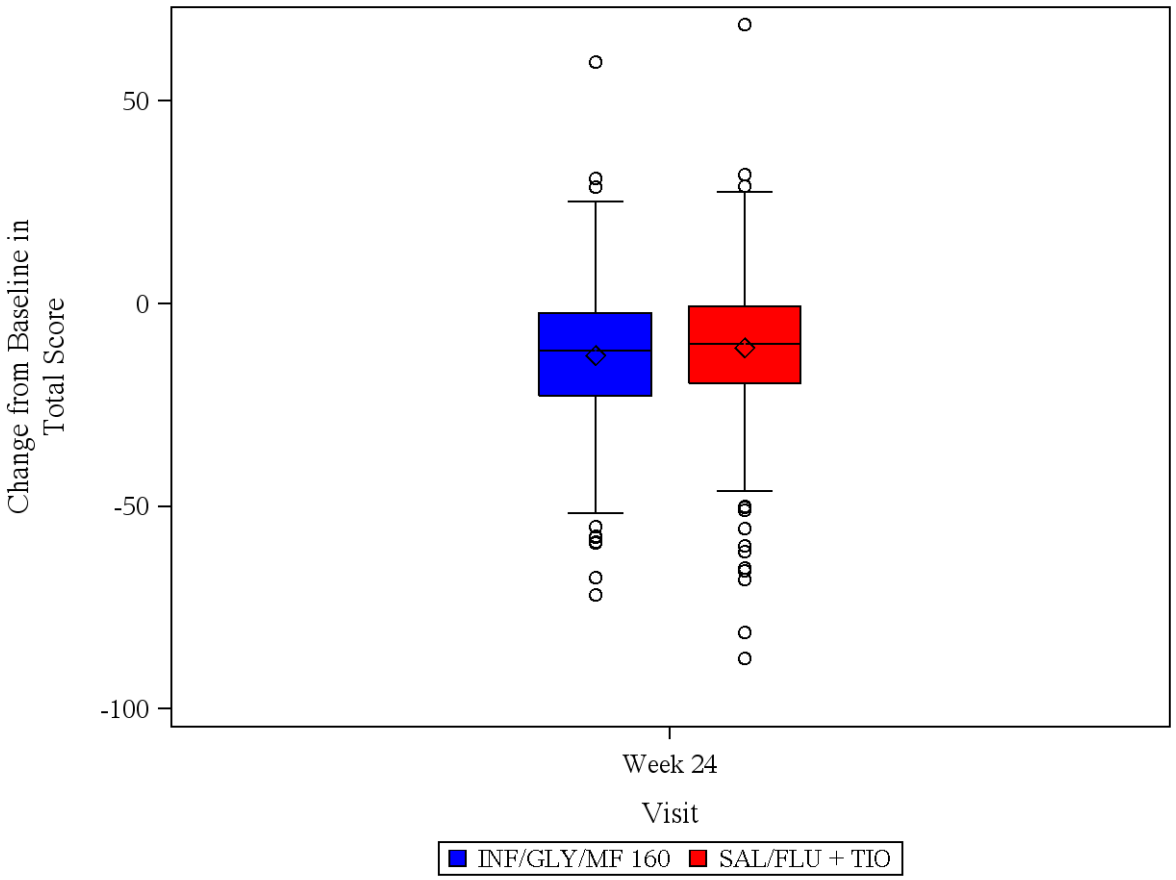
Figure 5.30.2 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



7. Boxplot: SGRQ - Change from Baseline (FAS)

7.1 Boxplot: SGRQ (Total Score) - Change from Baseline (FAS)

Figure 7.1 SGRQ (Total Score) - Change from Baseline (FAS)



7.2 Boxplot: SGRQ (Total Score) - Change from Baseline by Age (FAS)

Figure 7.2.1 SGRQ (Total Score) - Change from Baseline by Age (FAS), Age = 18-39 years

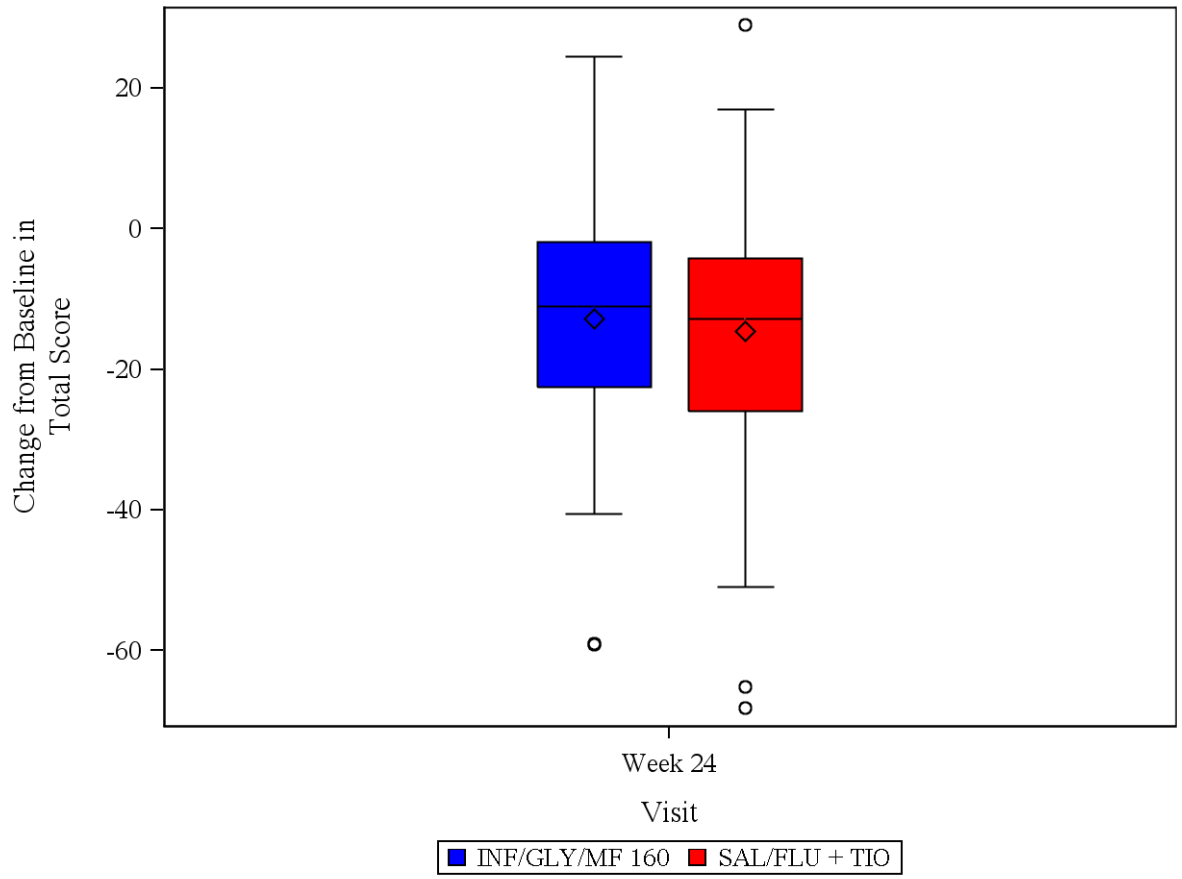


Figure 7.2.2 SGRQ (Total Score) - Change from Baseline by Age (FAS), Age = 40-64 years

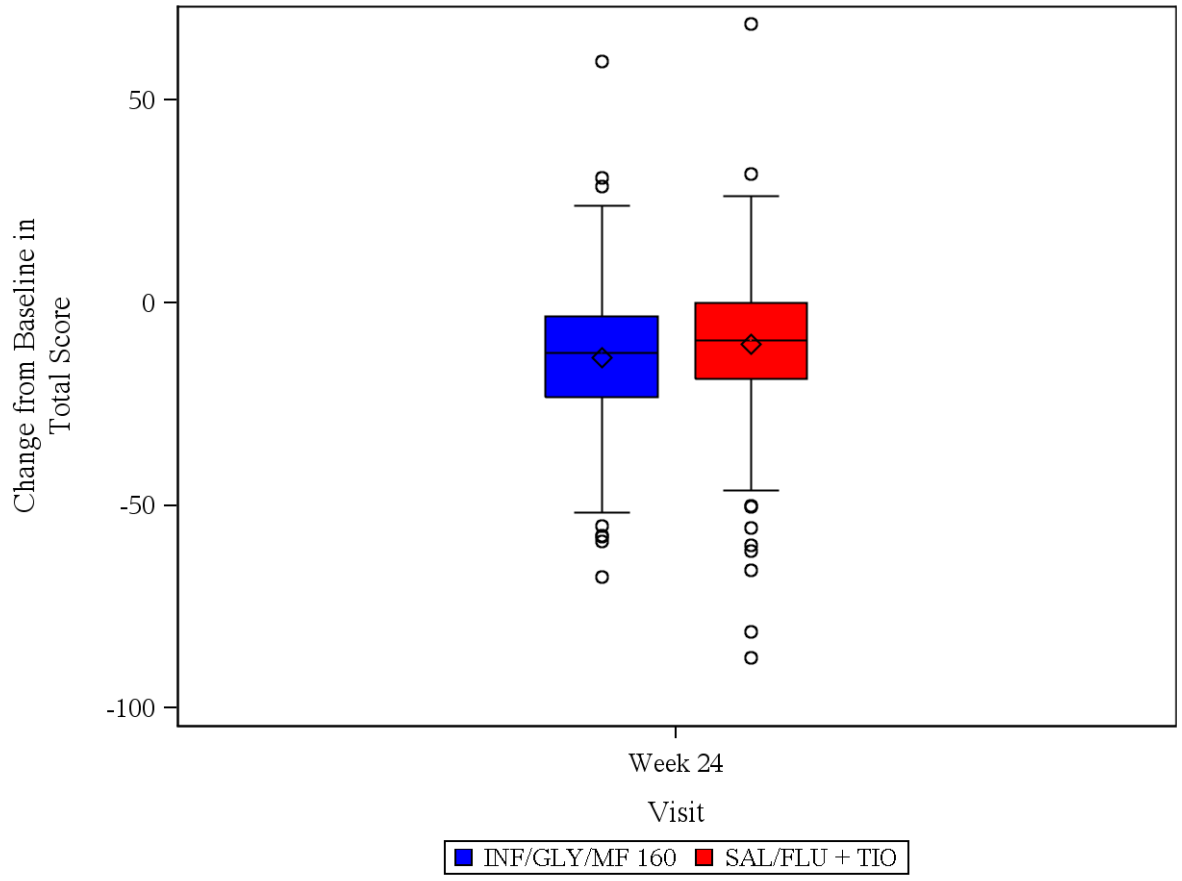
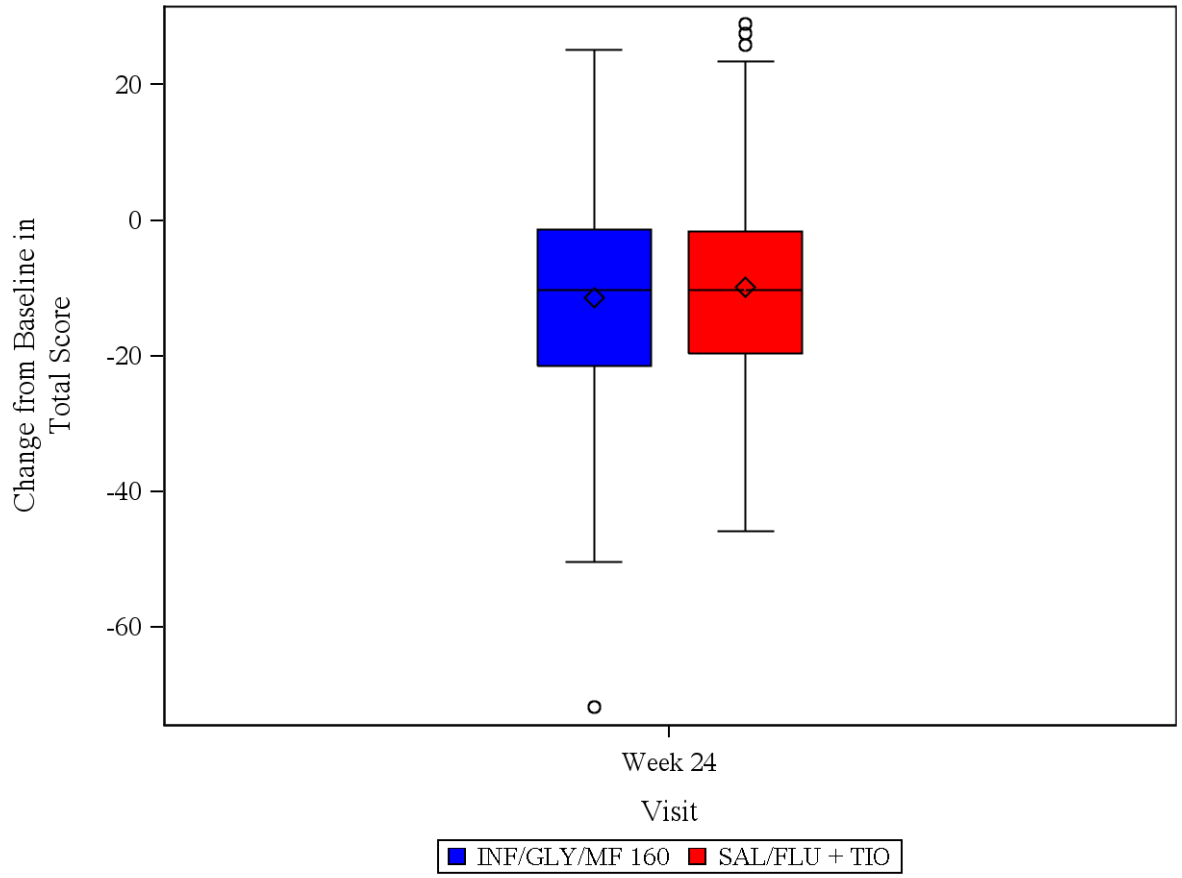


Figure 7.2.3 SGRQ (Total Score) - Change from Baseline by Age (FAS), Age = ≥65 years



7.3 Boxplot: SGRQ (Total Score) - Change from Baseline by Gender (FAS)

Figure 7.3.1 SGRQ (Total Score) - Change from Baseline by Gender (FAS), Gender = Male

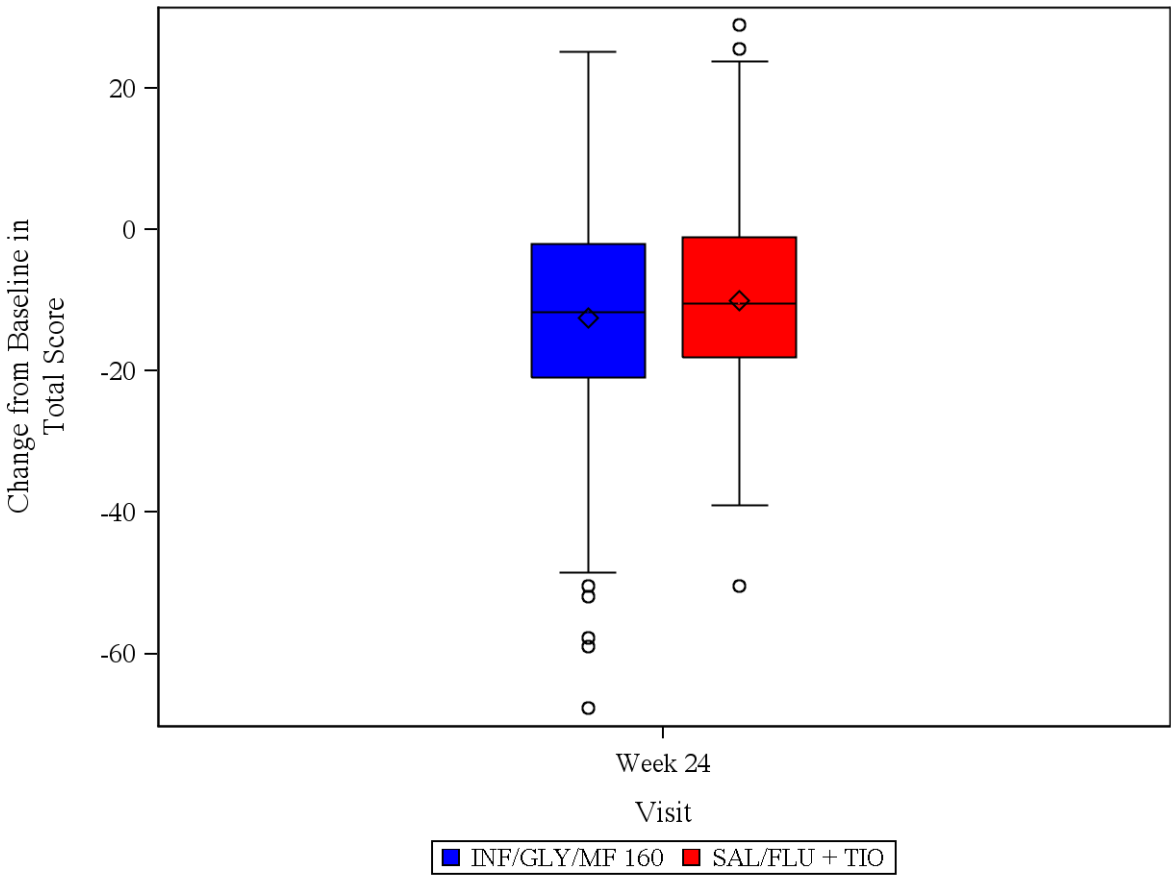
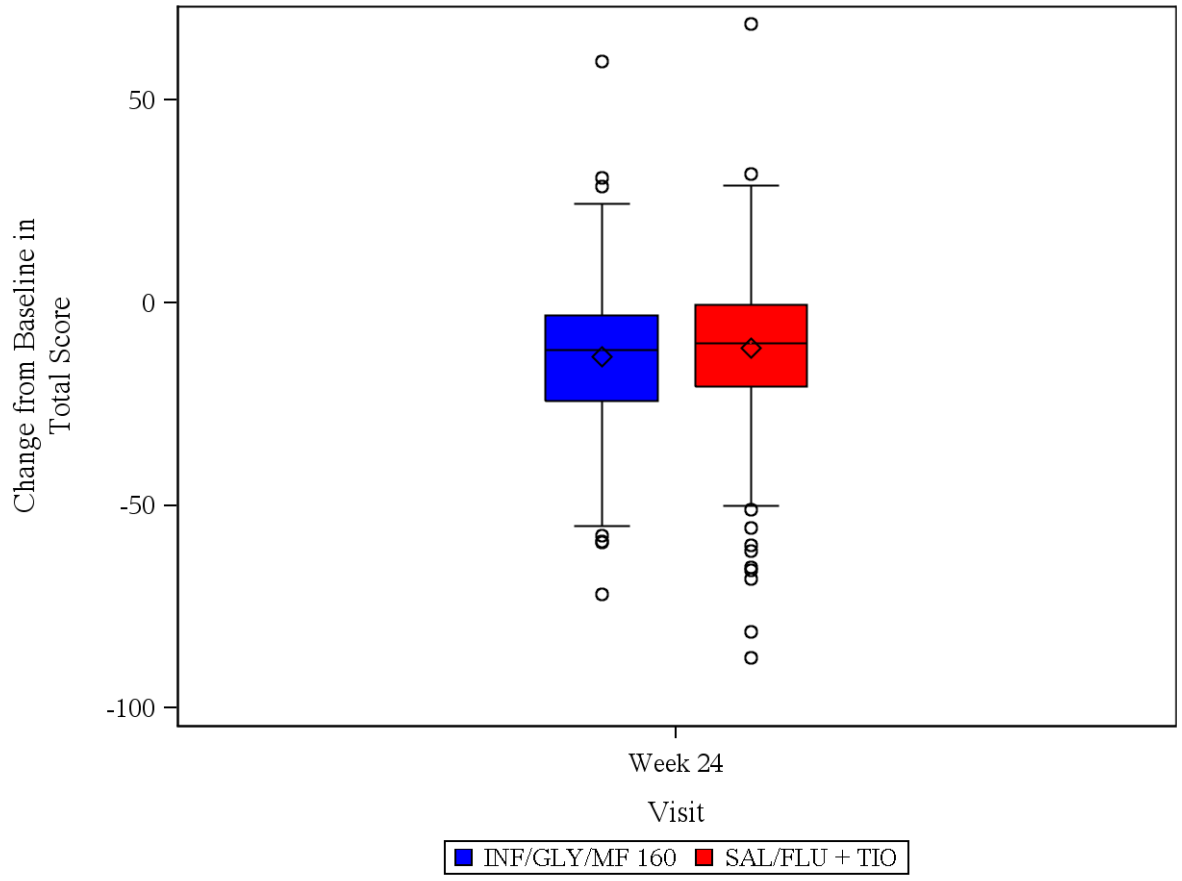


Figure 7.3.2 SGRQ (Total Score) - Change from Baseline by Gender (FAS), Gender = Female



7.4 Boxplot: SGRQ (Total Score) - Change from Baseline by Region (FAS)

Figure 7.4.1 SGRQ (Total Score) - Change from Baseline by Region (FAS), Region = Asia

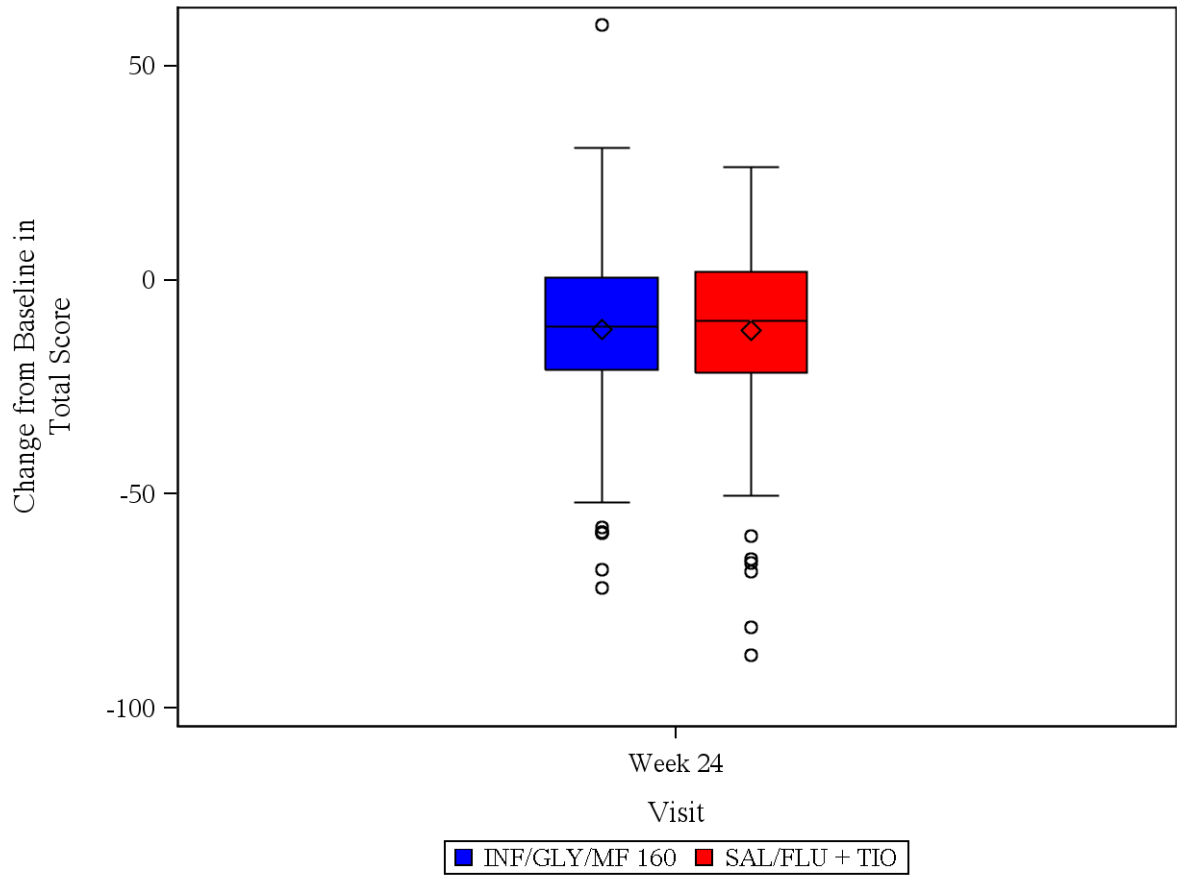


Figure 7.4.2 SGRQ (Total Score) - Change from Baseline by Region (FAS), Region = Europe

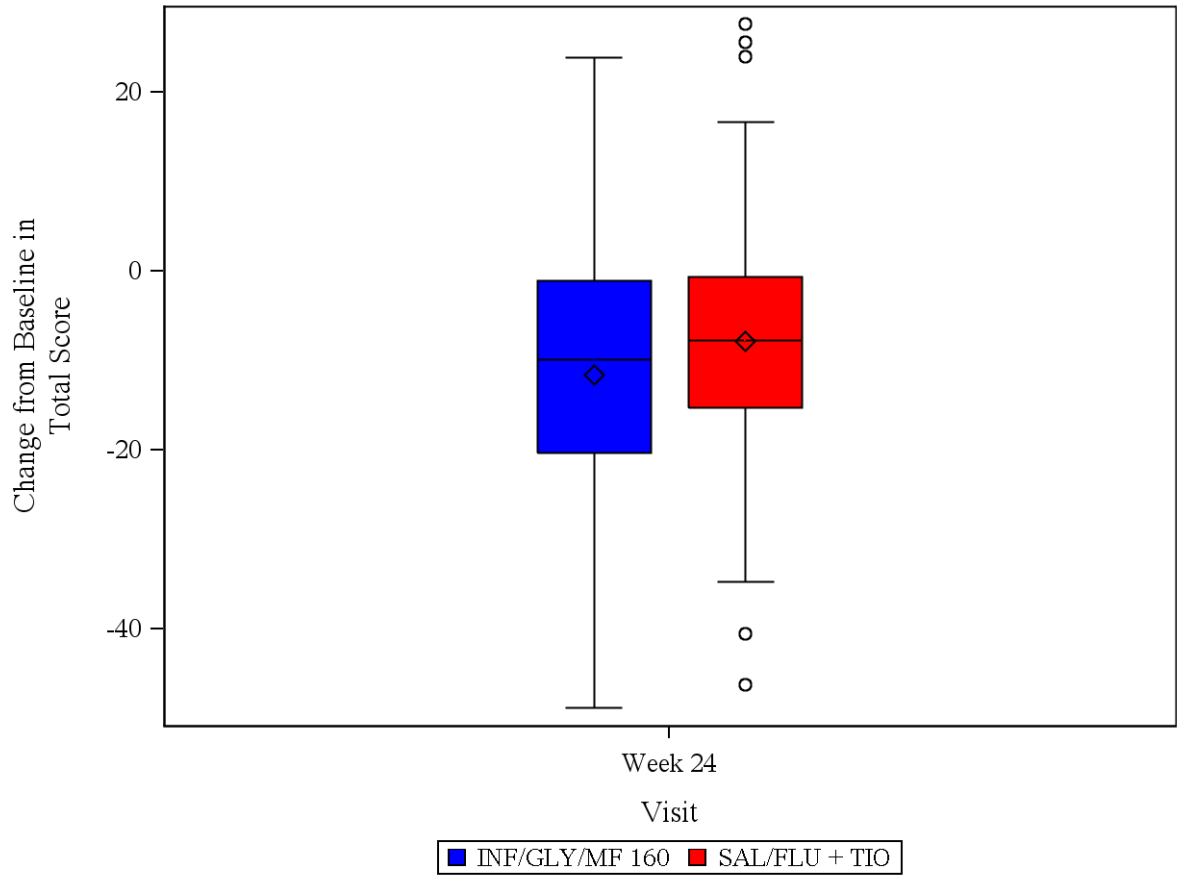


Figure 7.4.3 SGRQ (Total Score) - Change from Baseline by Region (FAS), Region = Latin America

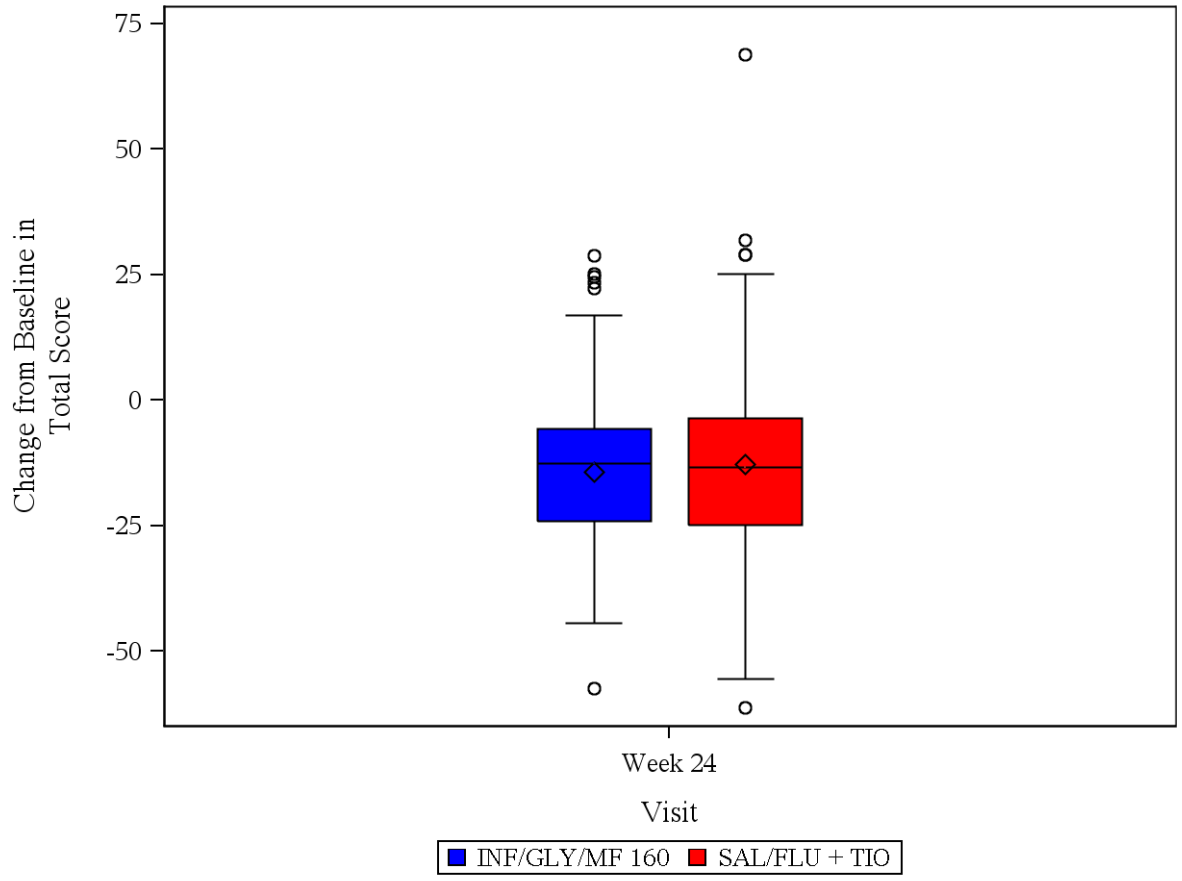
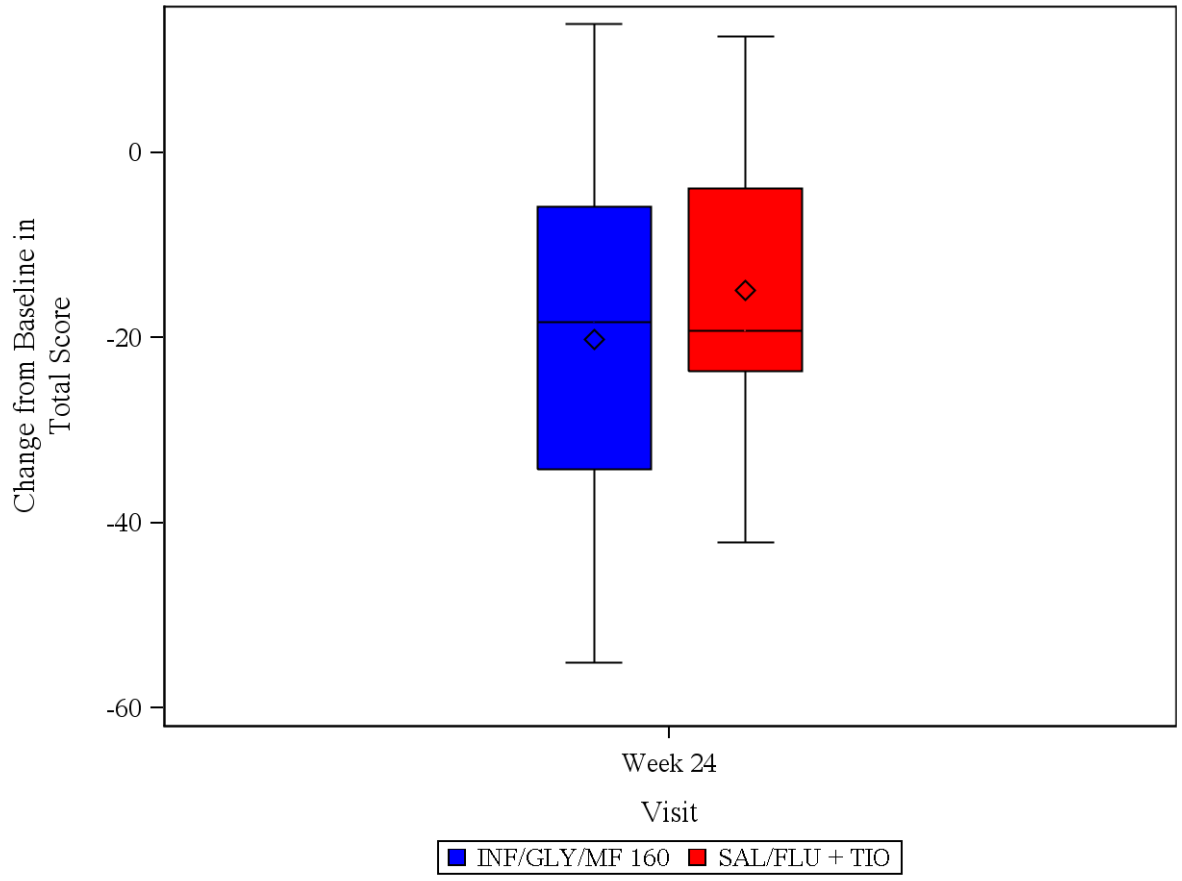


Figure 7.4.4 SGRQ (Total Score) - Change from Baseline by Region (FAS), Region = Others



7.5 Boxplot: SGRQ (Total Score) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 7.5.1 SGRQ (Total Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

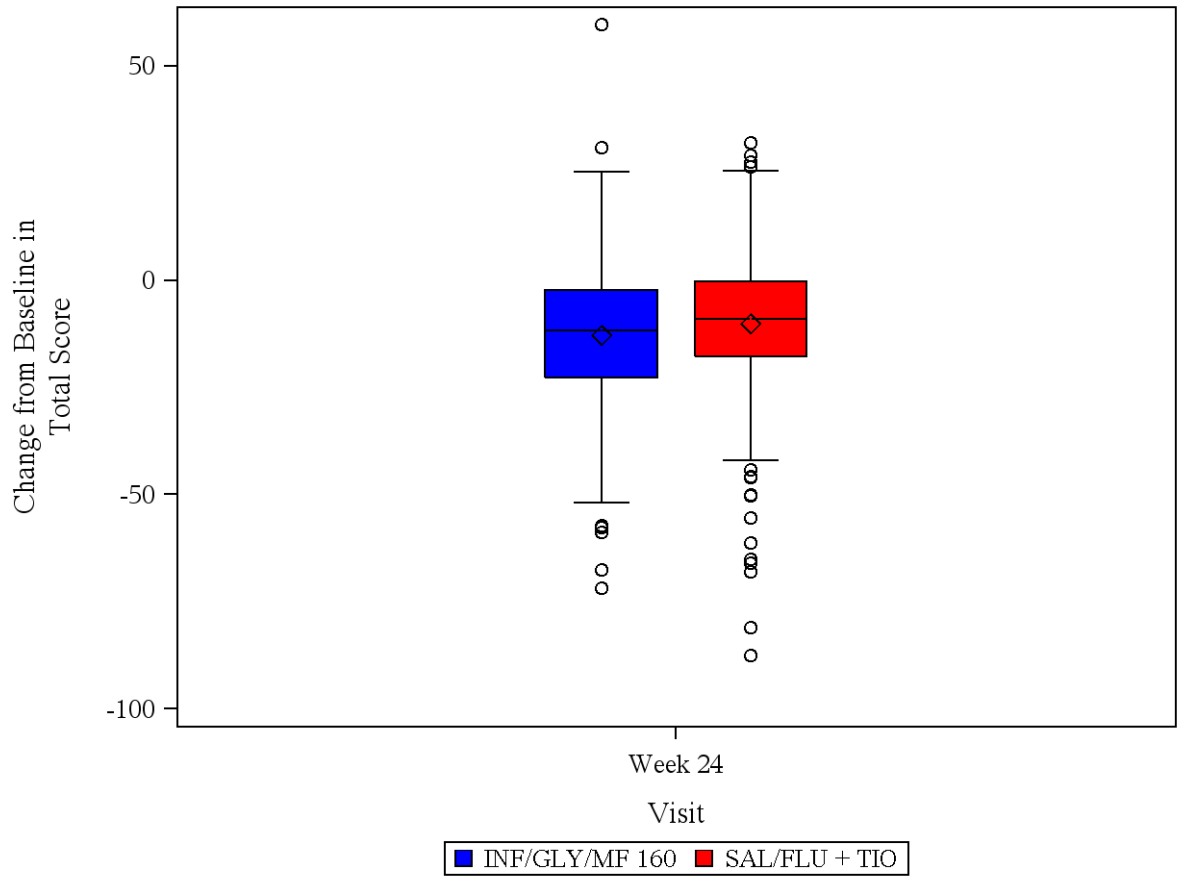
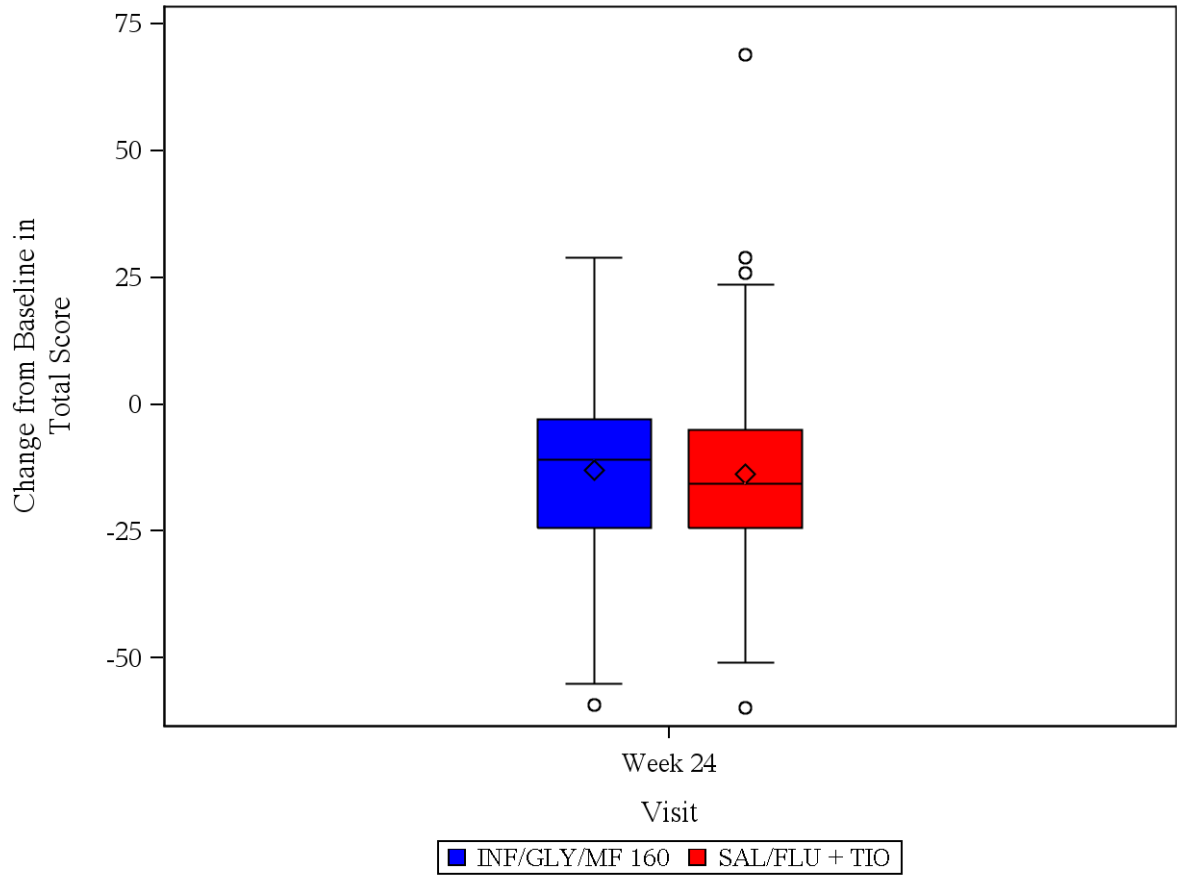


Figure 7.5.2 SGRQ (Total Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



7.6 Boxplot: SGRQ (Total Score) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 7.6.1 SGRQ (Total Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

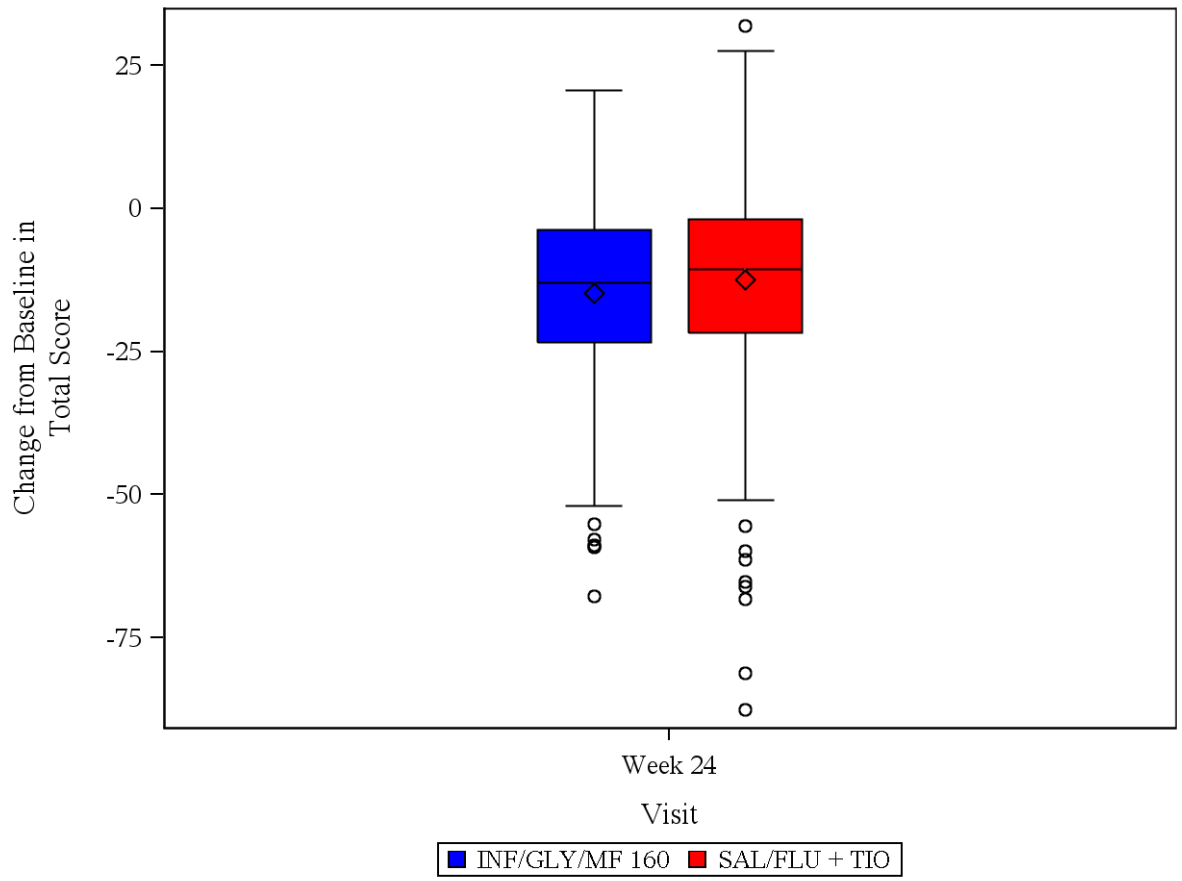
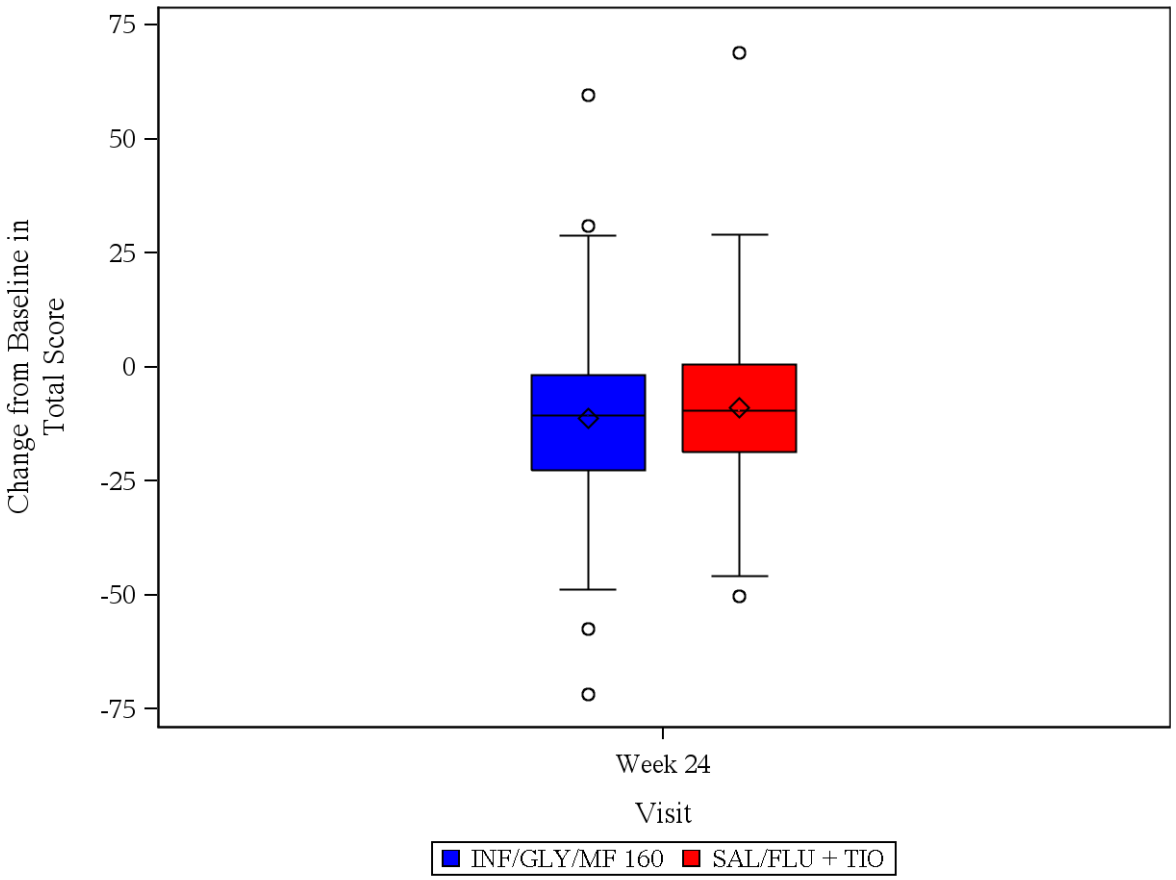
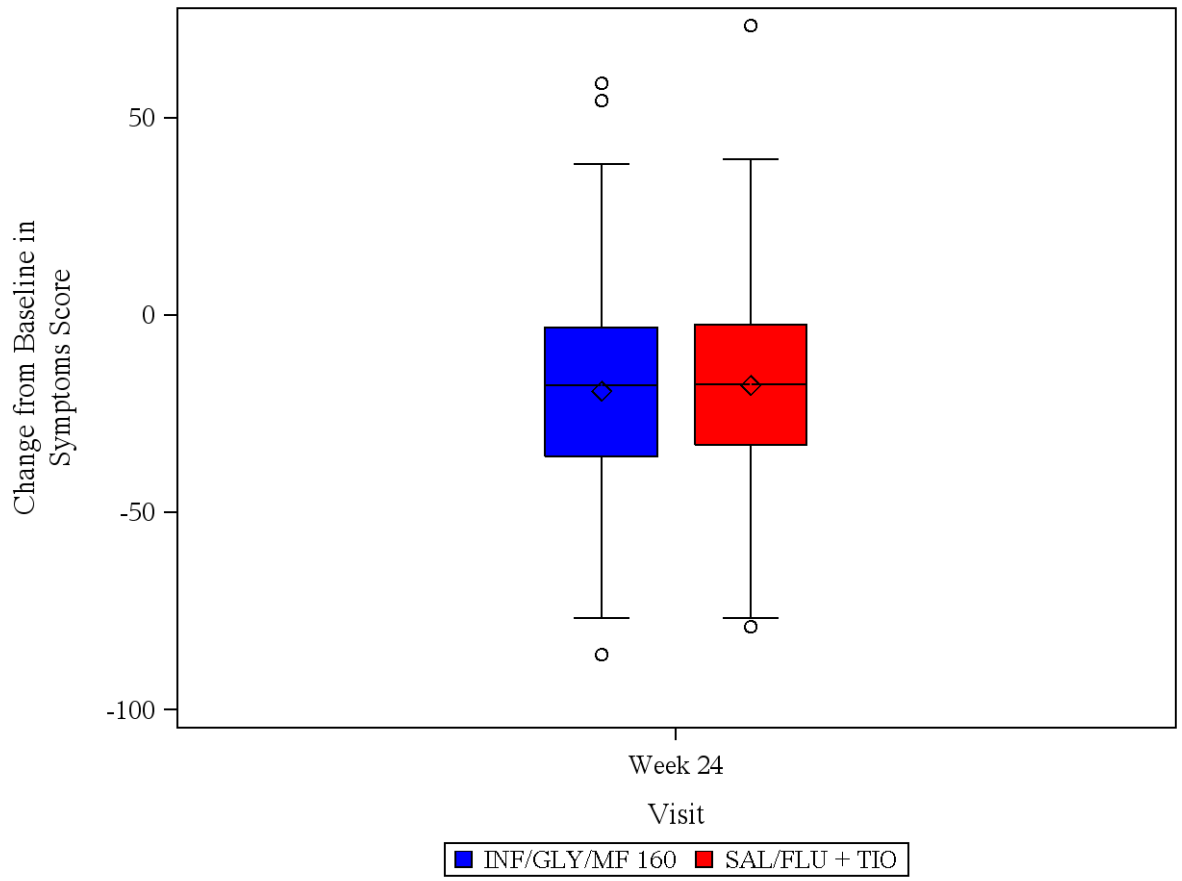


Figure 7.6.2 SGRQ (Total Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



7.7 Boxplot: SGRQ (Symptoms Score) - Change from Baseline (FAS)

Figure 7.7 SGRQ (Symptoms Score) - Change from Baseline (FAS)



7.8 Boxplot: SGRQ (Symptoms Score) - Change from Baseline by Age (FAS)

Figure 7.8.1 SGRQ (Symptoms Score) - Change from Baseline by Age (FAS), Age = 18-39 years

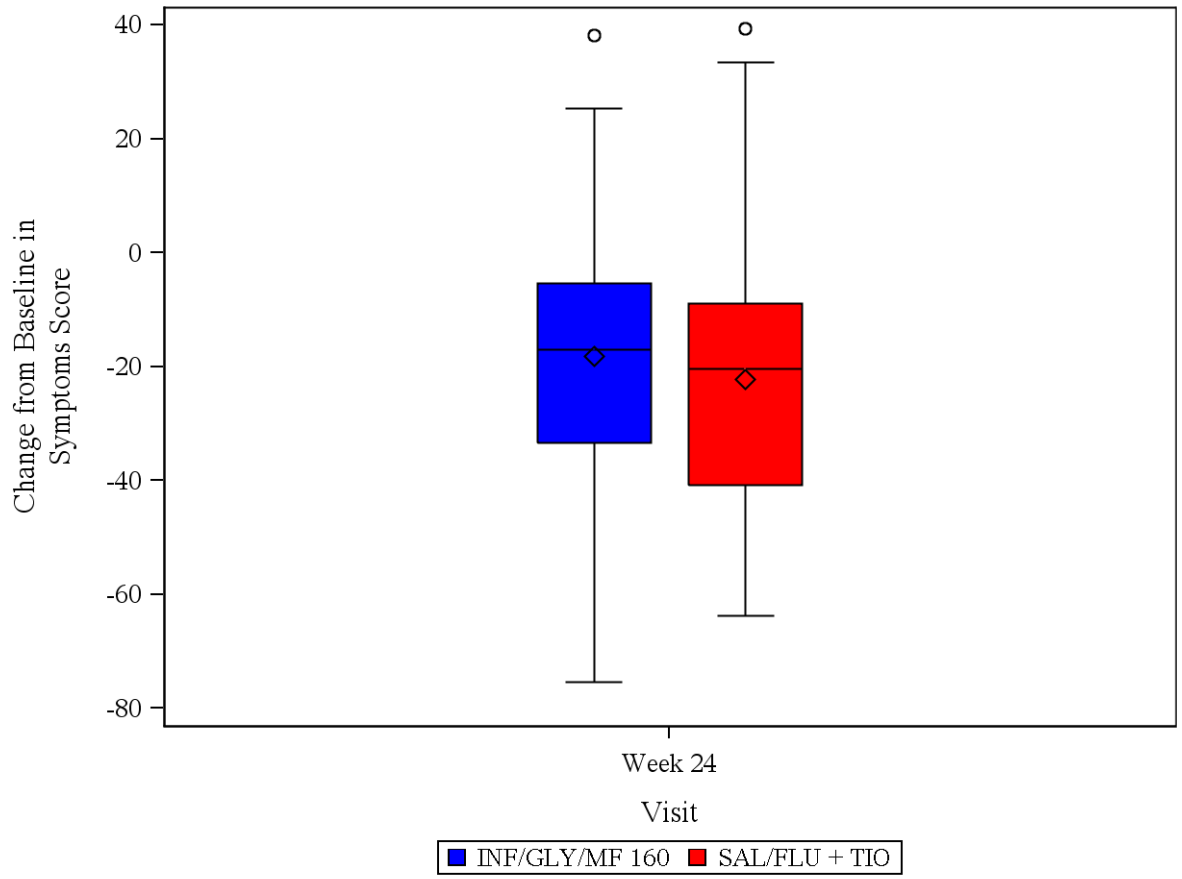


Figure 7.8.2 SGRQ (Symptoms Score) - Change from Baseline by Age (FAS), Age = 40-64 years

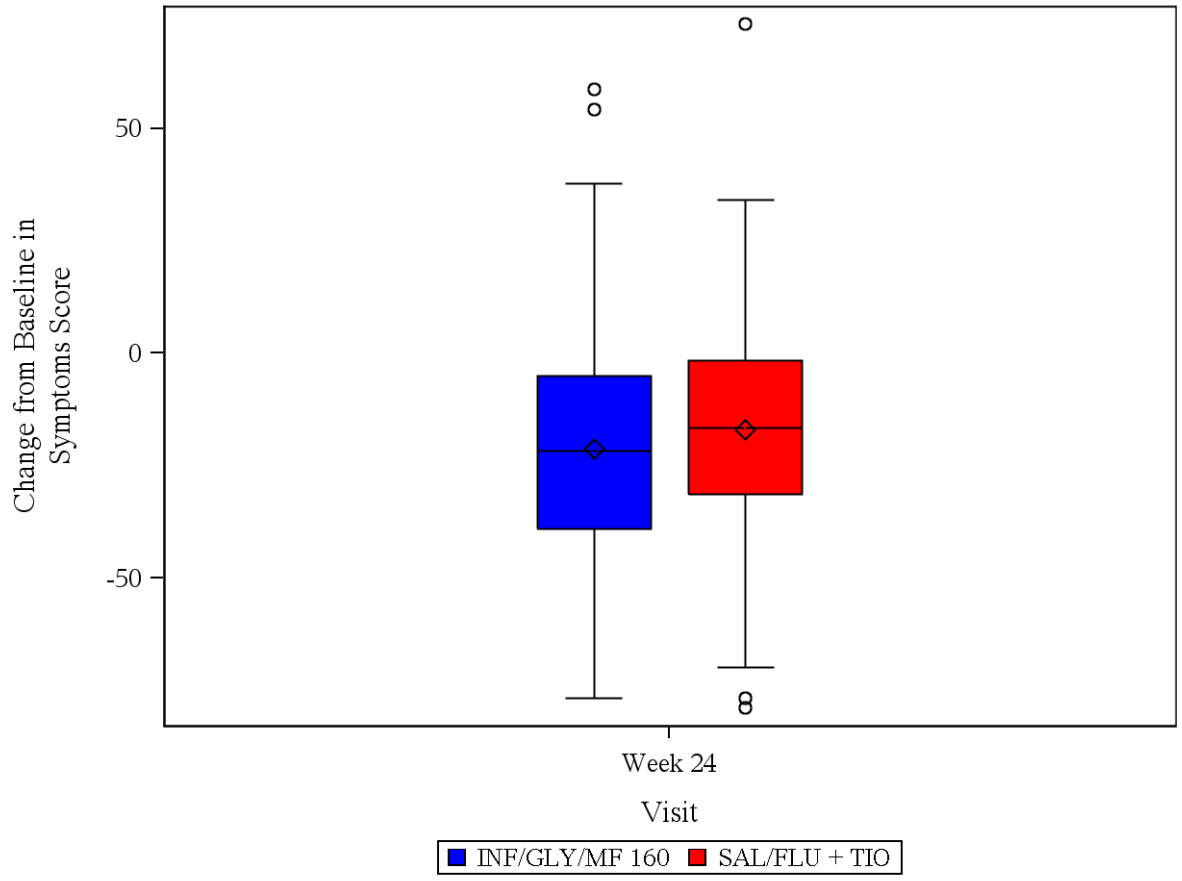
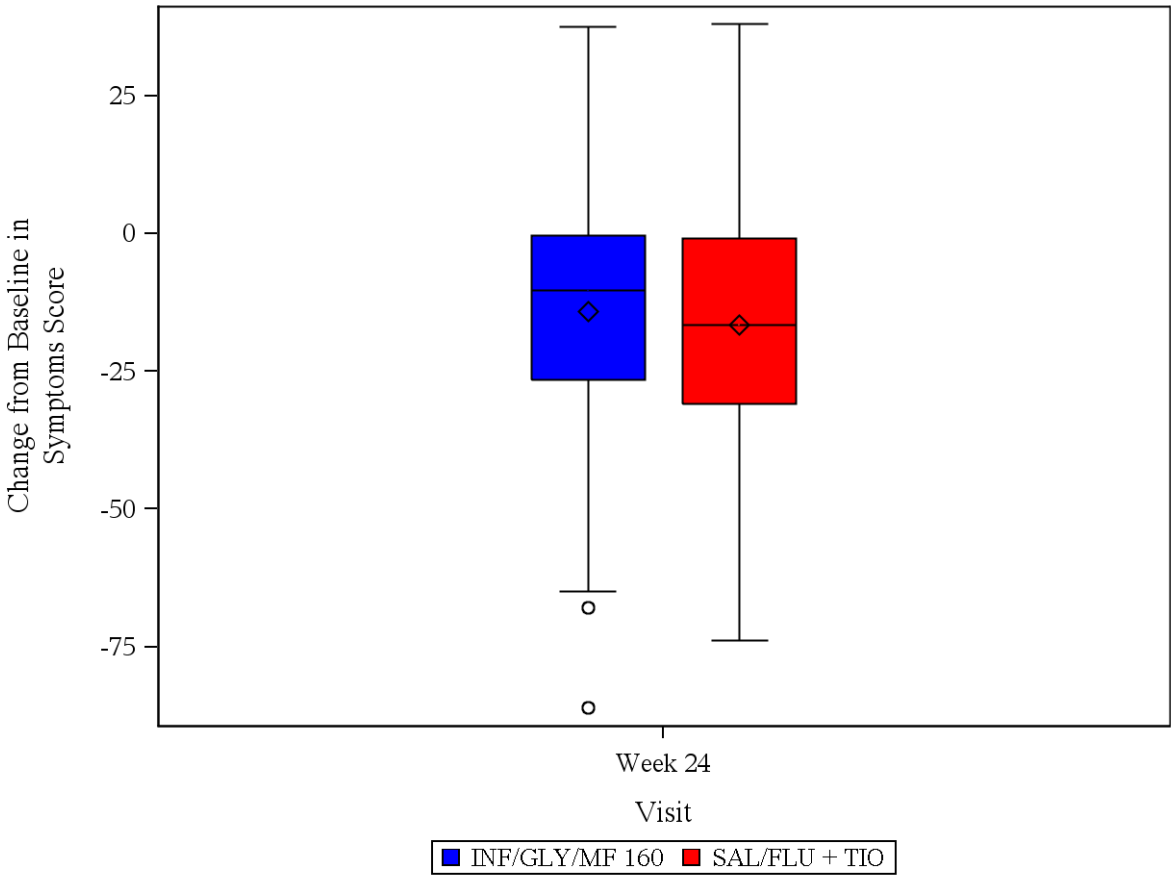


Figure 7.8.3 SGRQ (Symptoms Score) - Change from Baseline by Age (FAS), Age = ≥65 years



7.9 Boxplot: SGRQ (Symptoms Score) - Change from Baseline by Gender (FAS)

Figure 7.9.1 SGRQ (Symptoms Score) - Change from Baseline by Gender (FAS), Gender = Male

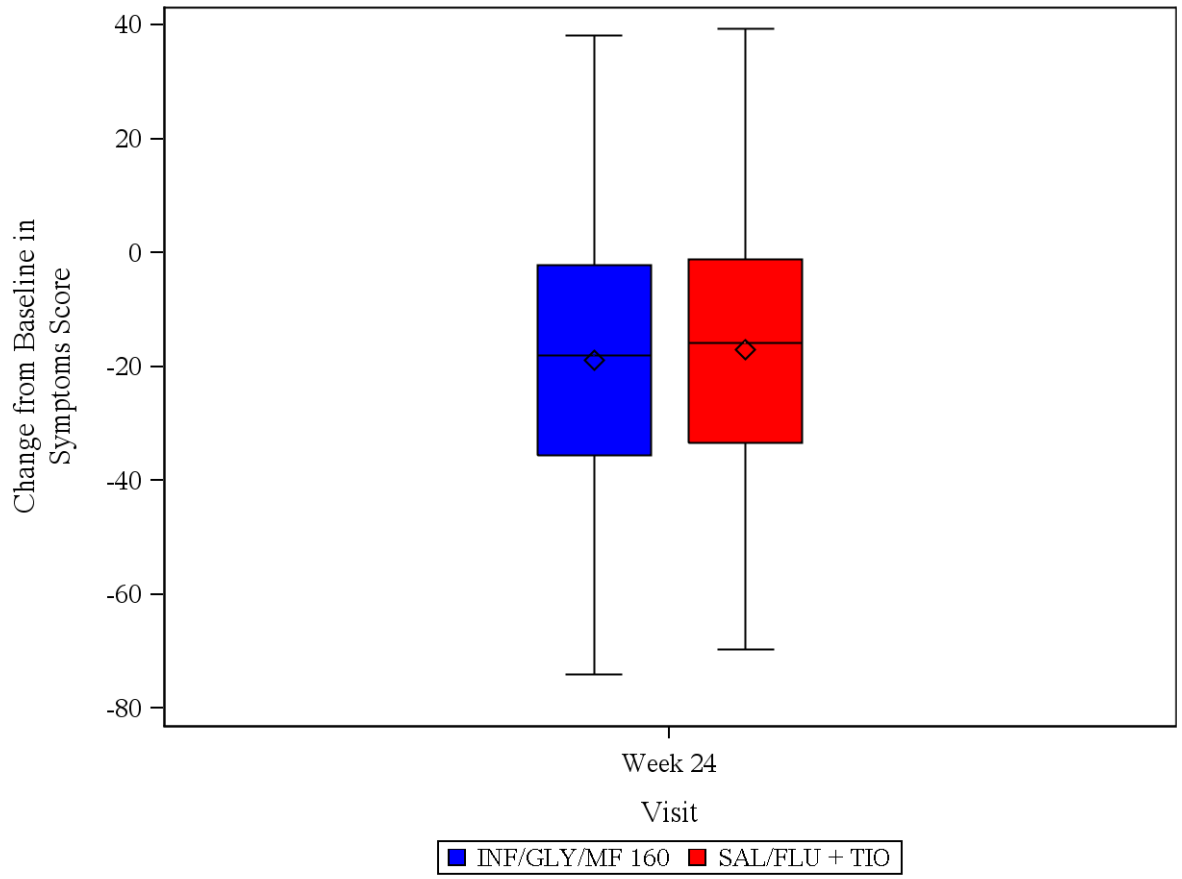
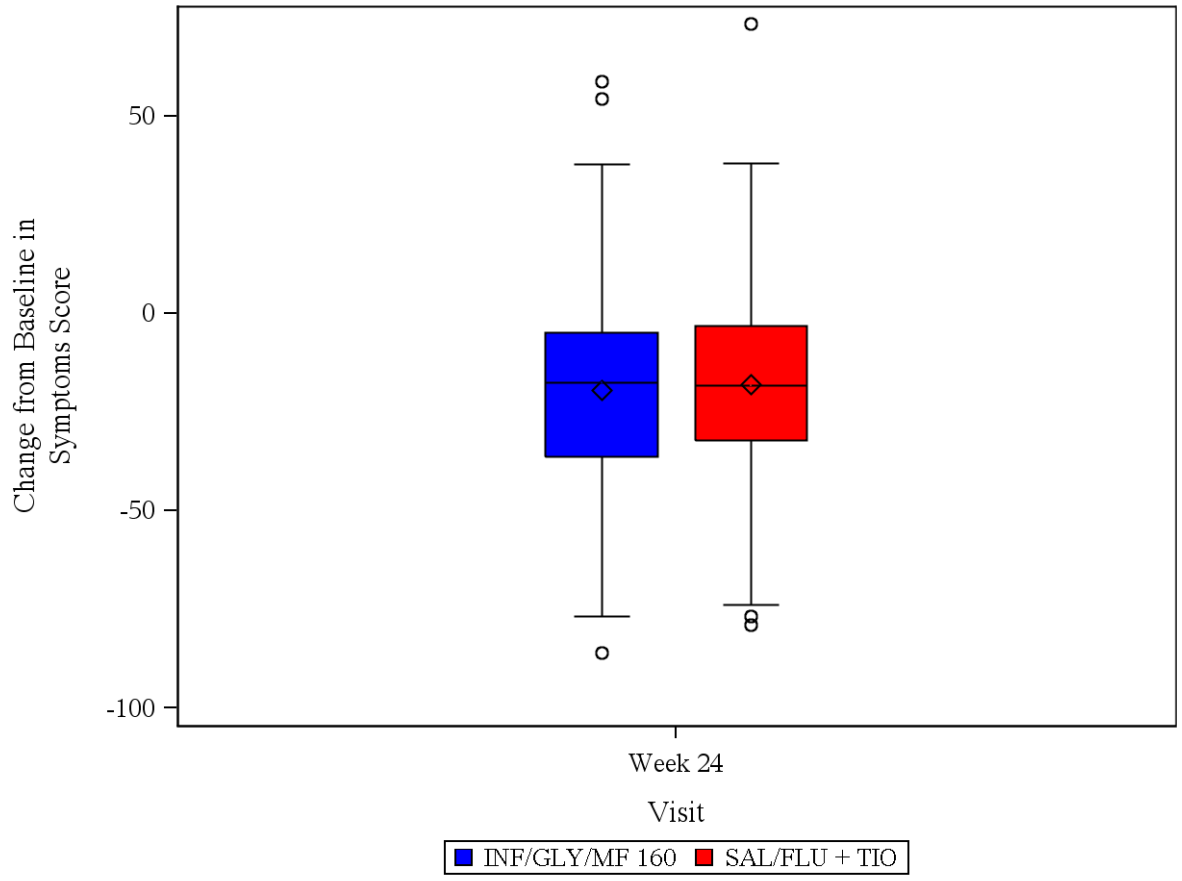


Figure 7.9.2 SGRQ (Symptoms Score) - Change from Baseline by Gender (FAS), Gender = Female



7.10 Boxplot: SGRQ (Symptoms Score) - Change from Baseline by Region (FAS)

Figure 7.10.1 SGRQ (Symptoms Score) - Change from Baseline by Region (FAS), Region = Asia

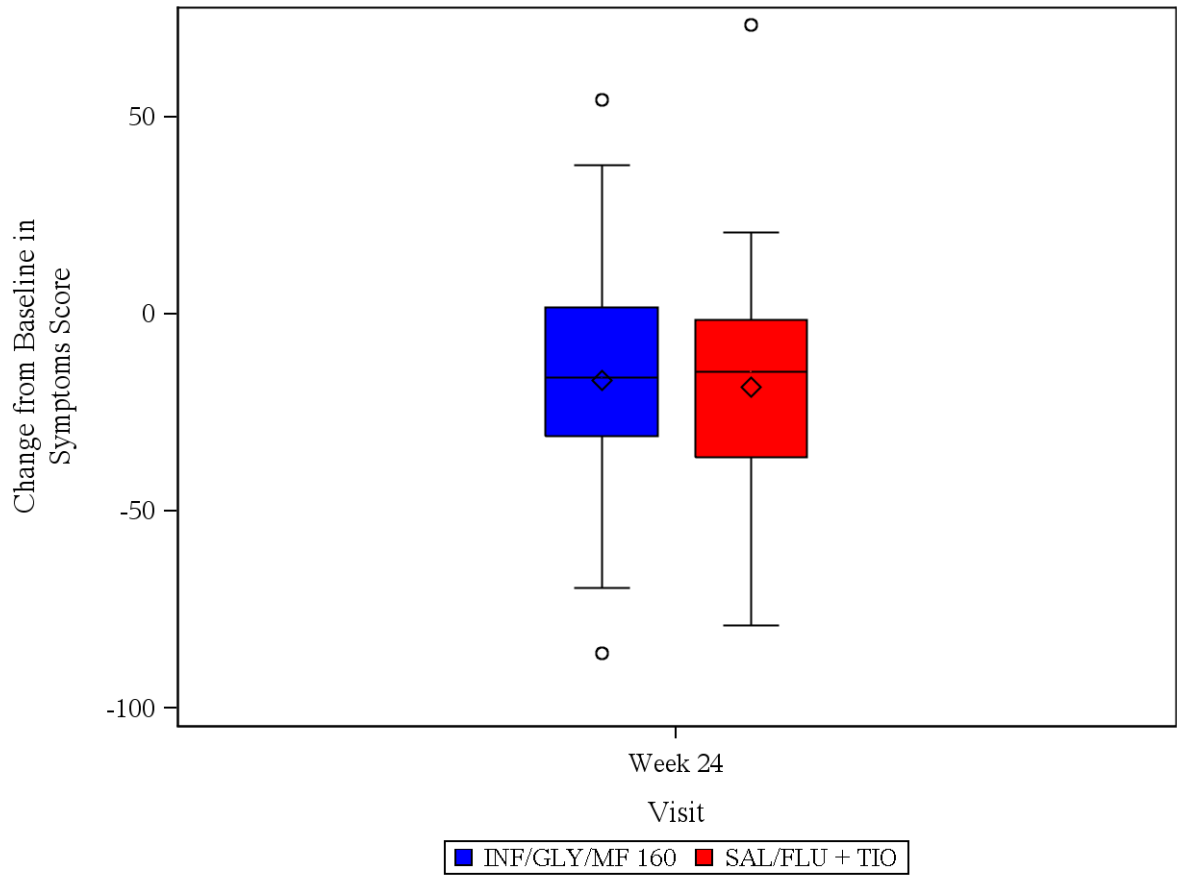


Figure 7.10.2 SGRQ (Symptoms Score) - Change from Baseline by Region (FAS), Region = Europe

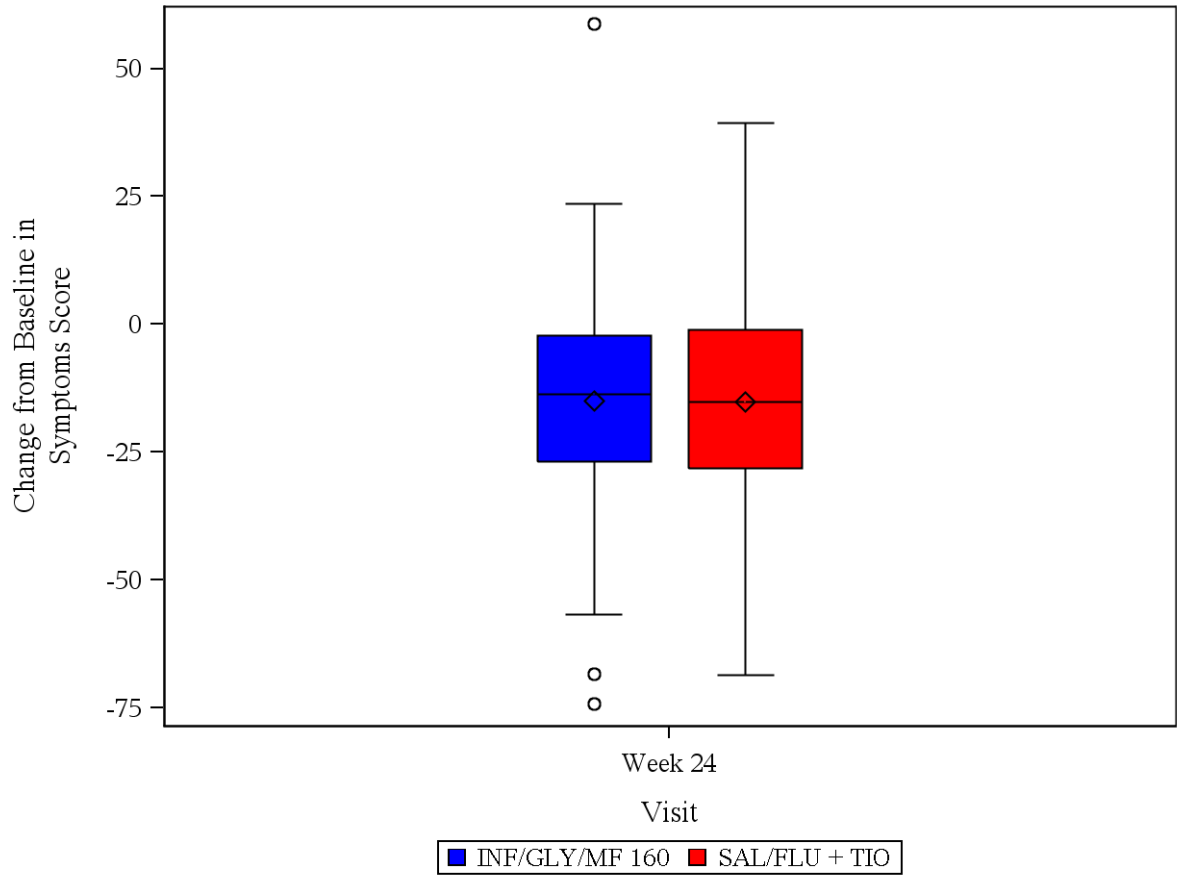


Figure 7.10.3 SGRQ (Symptoms Score) - Change from Baseline by Region (FAS), Region = Latin America

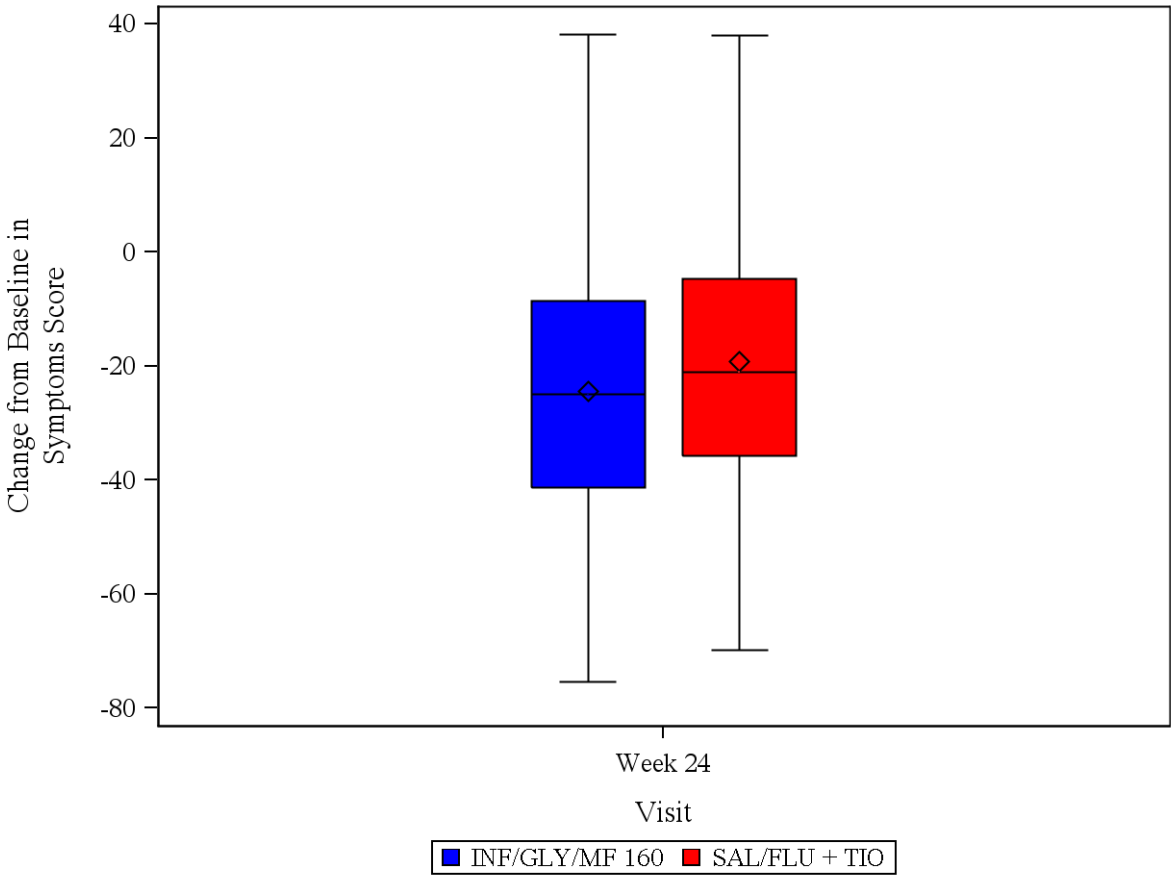
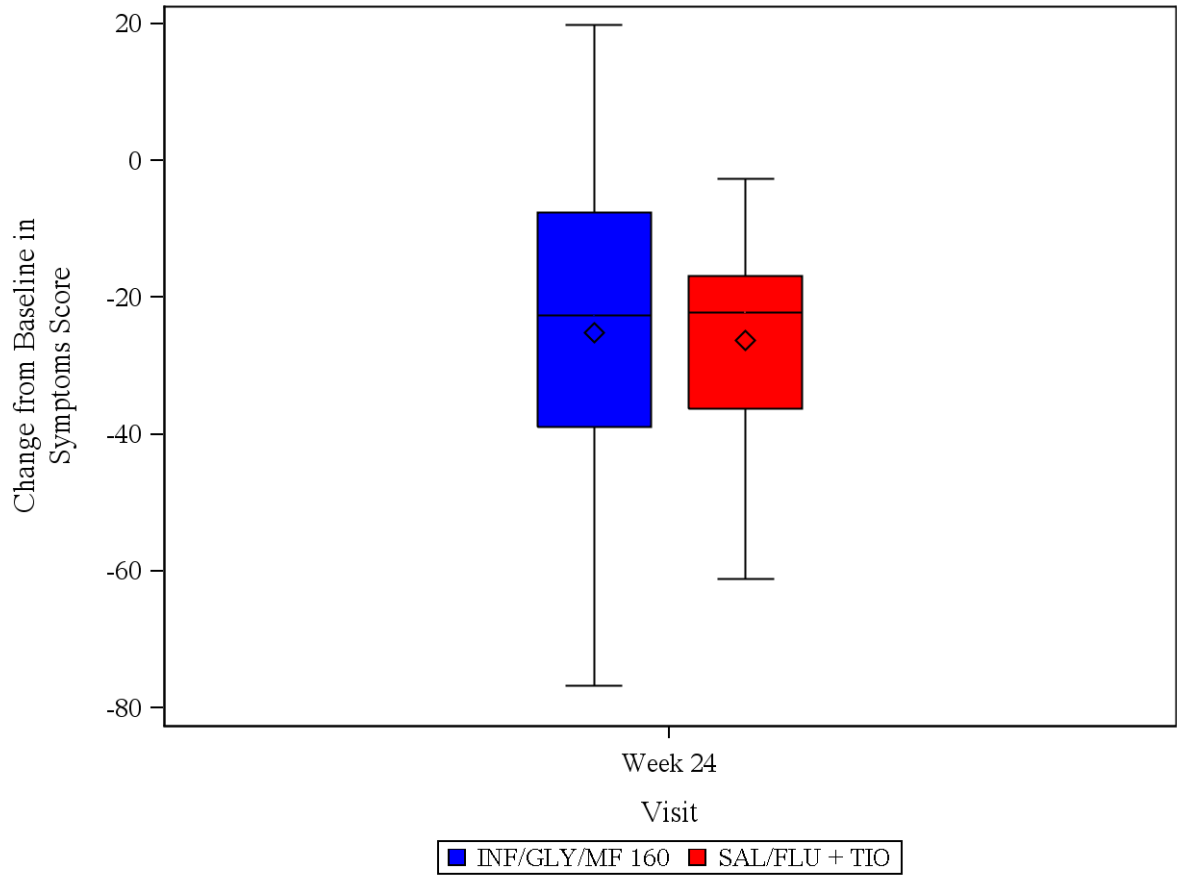


Figure 7.10.4 SGRQ (Symptoms Score) - Change from Baseline by Region (FAS), Region = Others



7.11 Boxplot: SGRQ (Symptoms Score) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 7.11.1 SGRQ (Symptoms Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

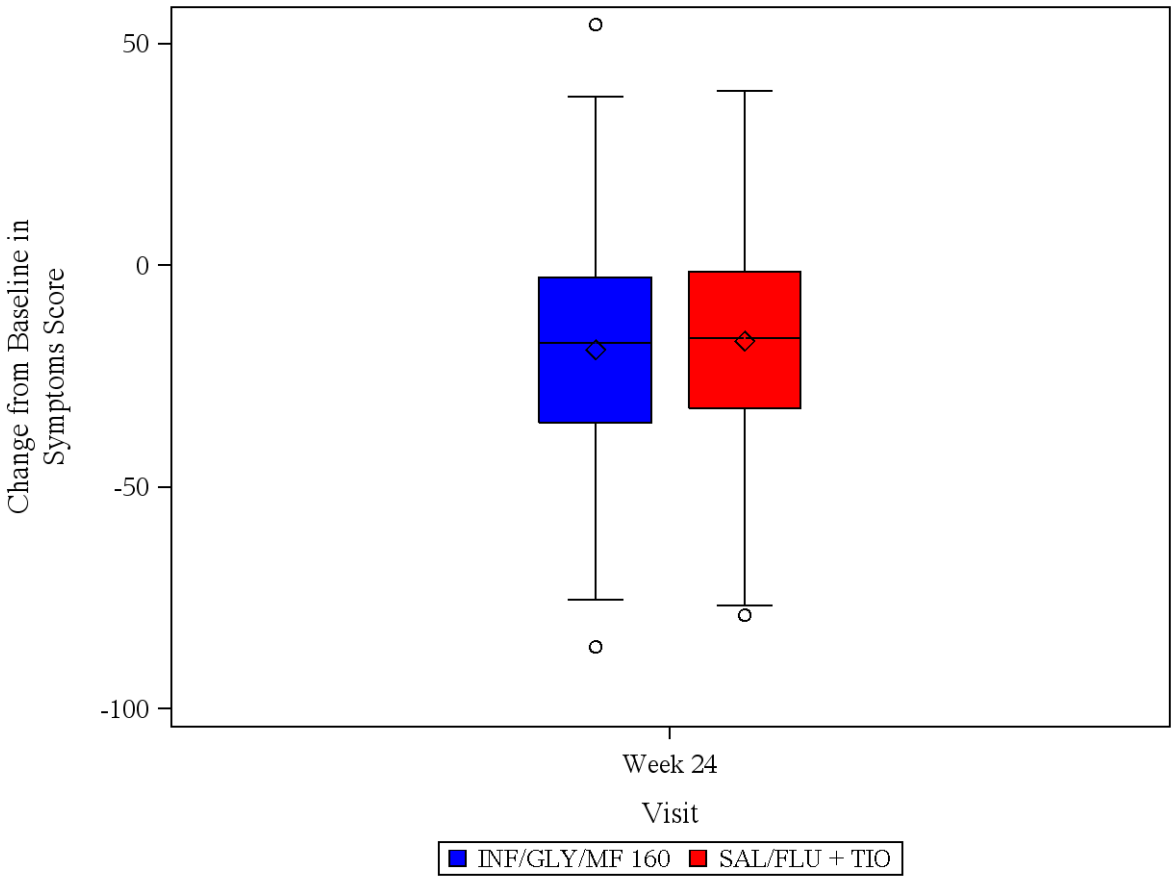
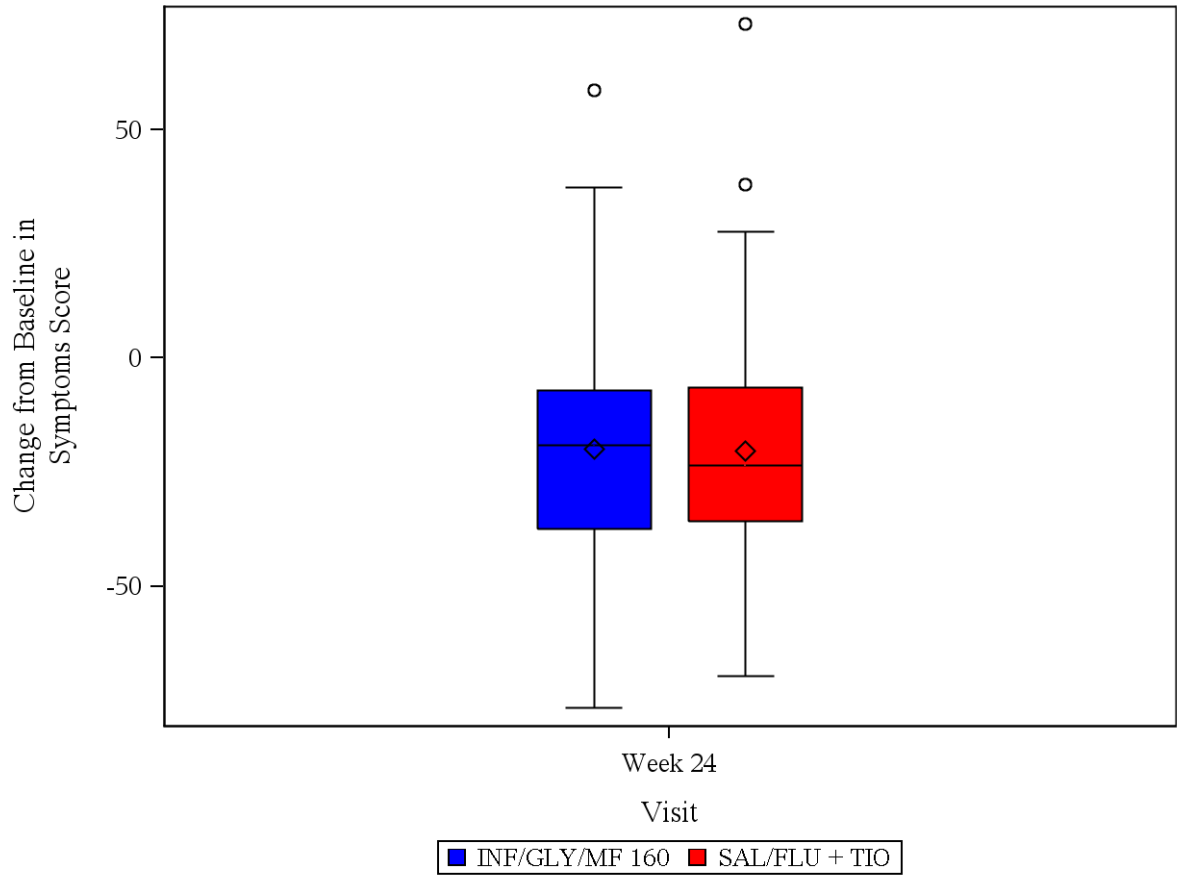


Figure 7.11.2 SGRQ (Symptoms Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



7.12 Boxplot: SGRQ (Symptoms Score) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 7.12.1 SGRQ (Symptoms Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

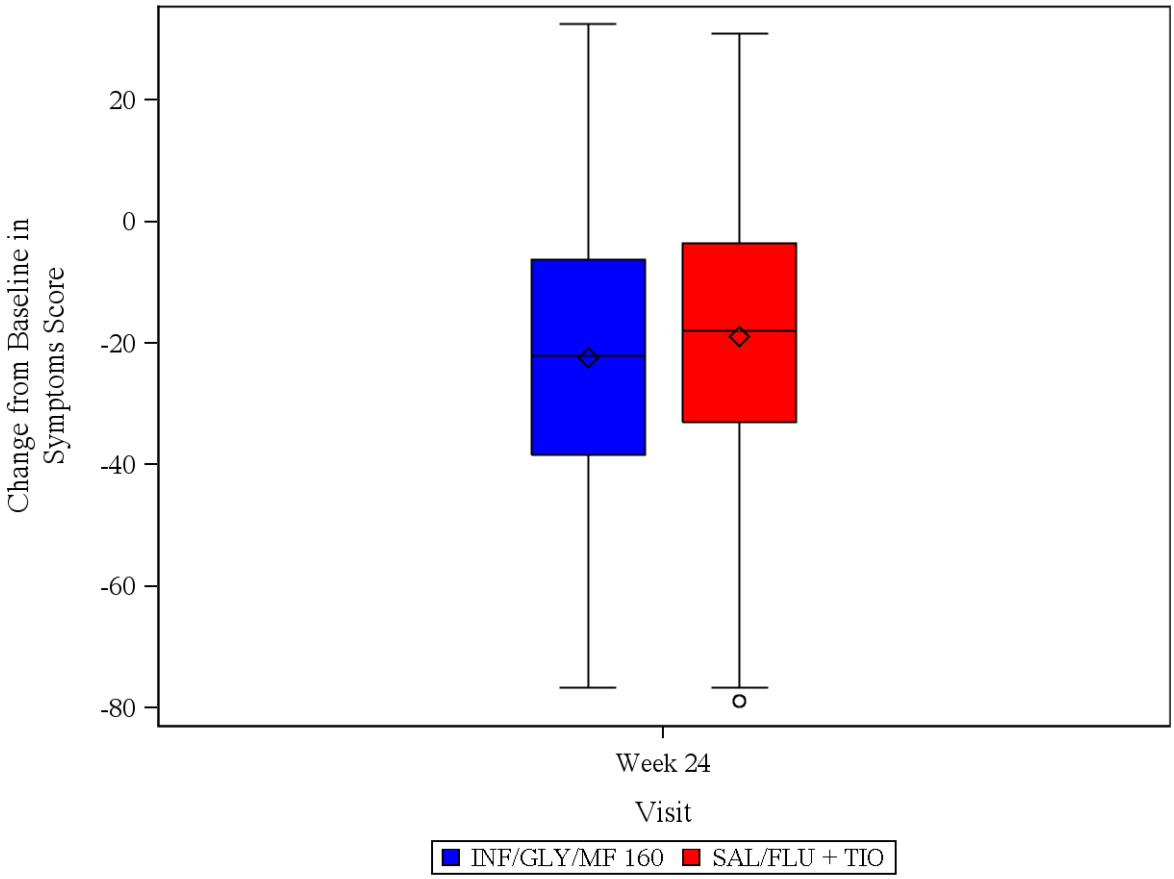
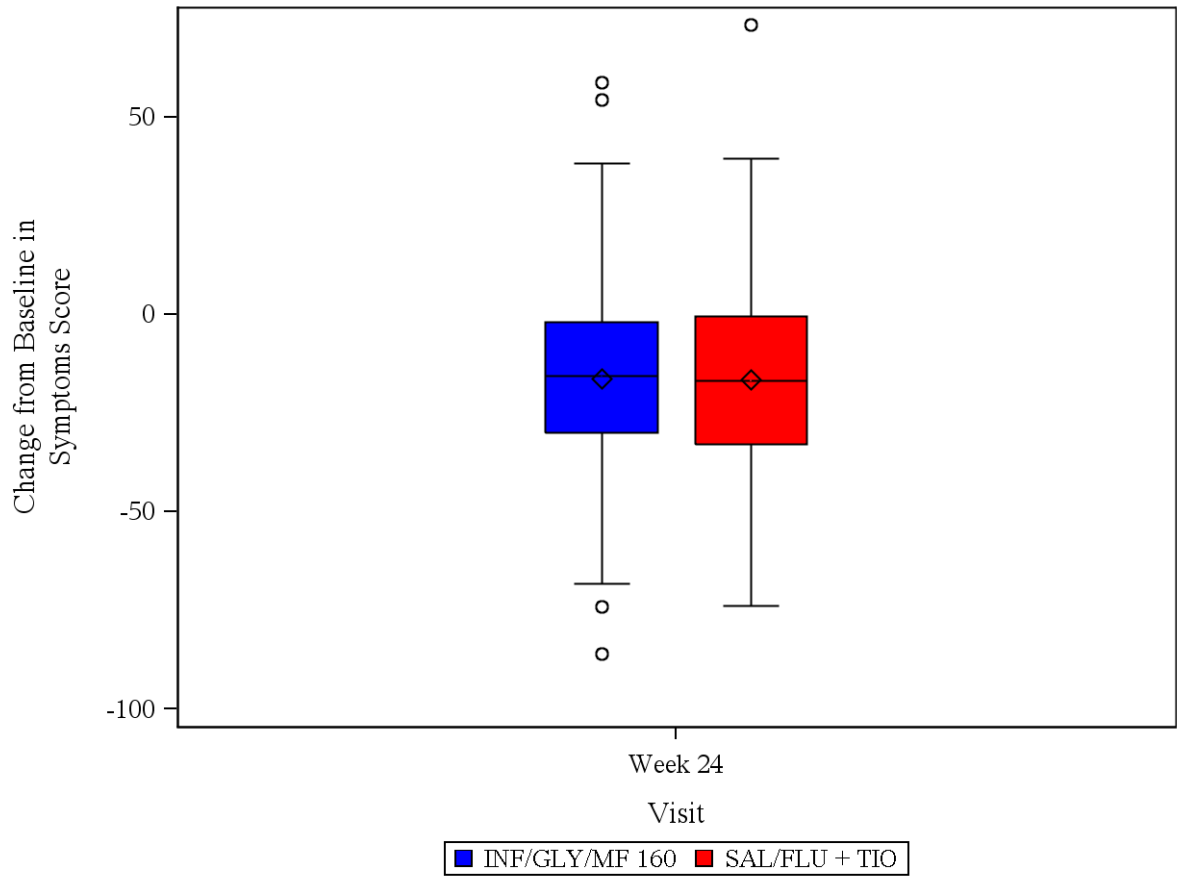
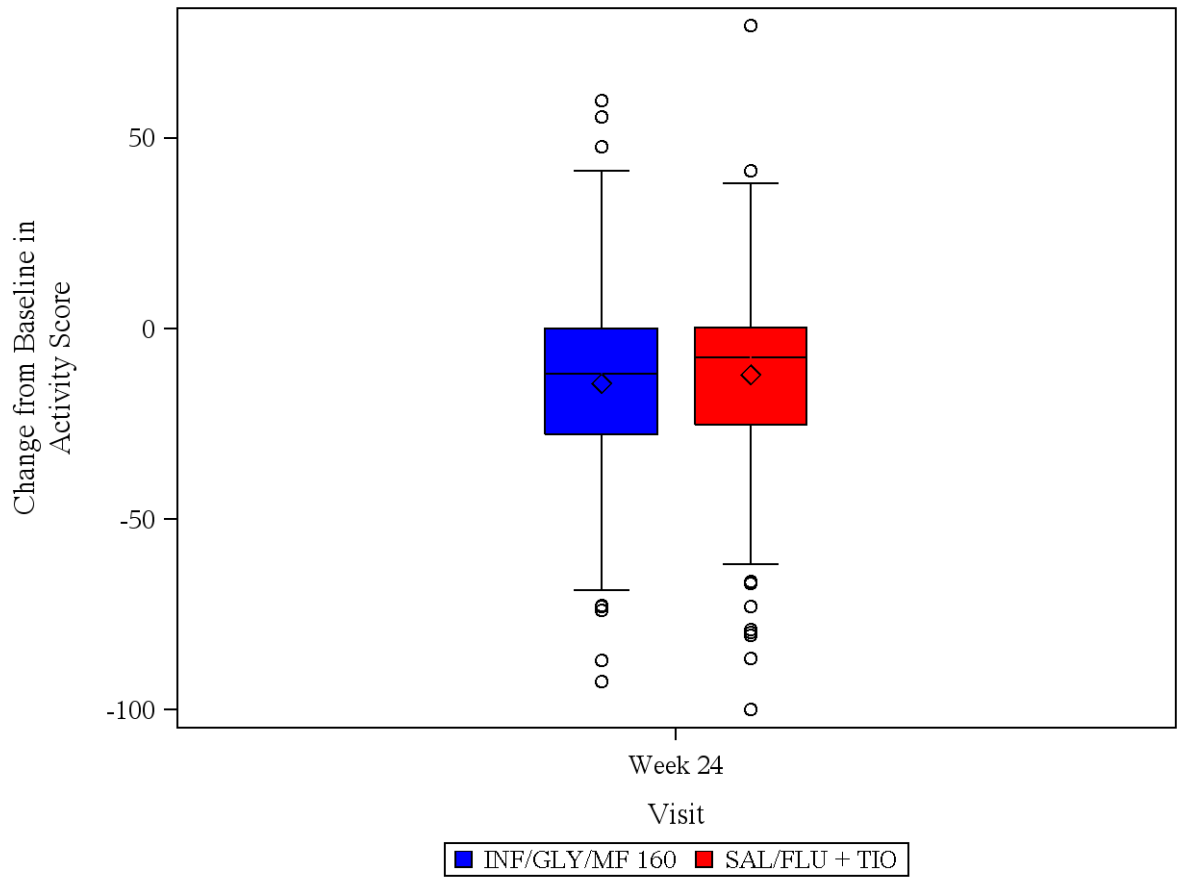


Figure 7.12.2 SGRQ (Symptoms Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



7.13 Boxplot: SGRQ (Activity Score) - Change from Baseline (FAS)

Figure 7.13 SGRQ (Activity Score) - Change from Baseline (FAS)



7.14 Boxplot: SGRQ (Activity Score) - Change from Baseline by Age (FAS)

Figure 7.14.1 SGRQ (Activity Score) - Change from Baseline by Age (FAS), Age = 18-39 years

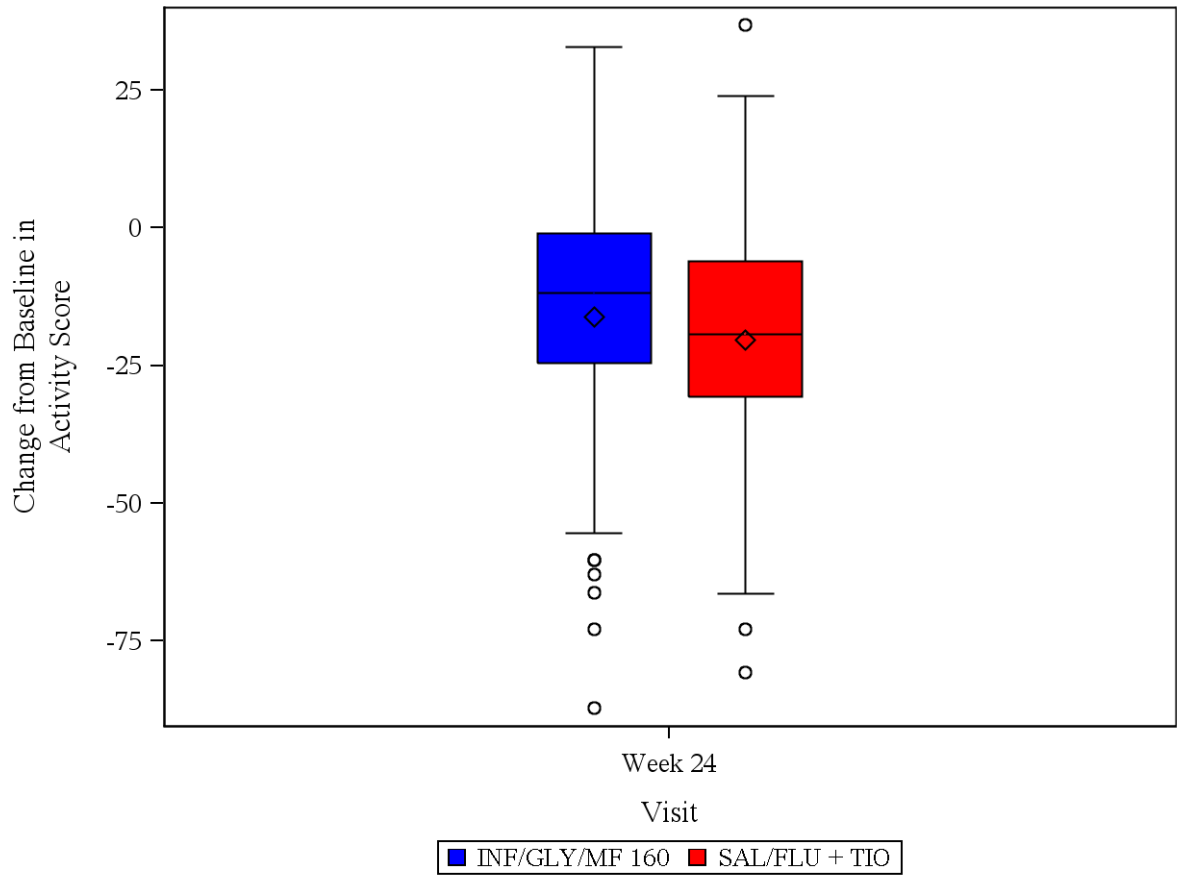


Figure 7.14.2 SGRQ (Activity Score) - Change from Baseline by Age (FAS), Age = 40-64 years

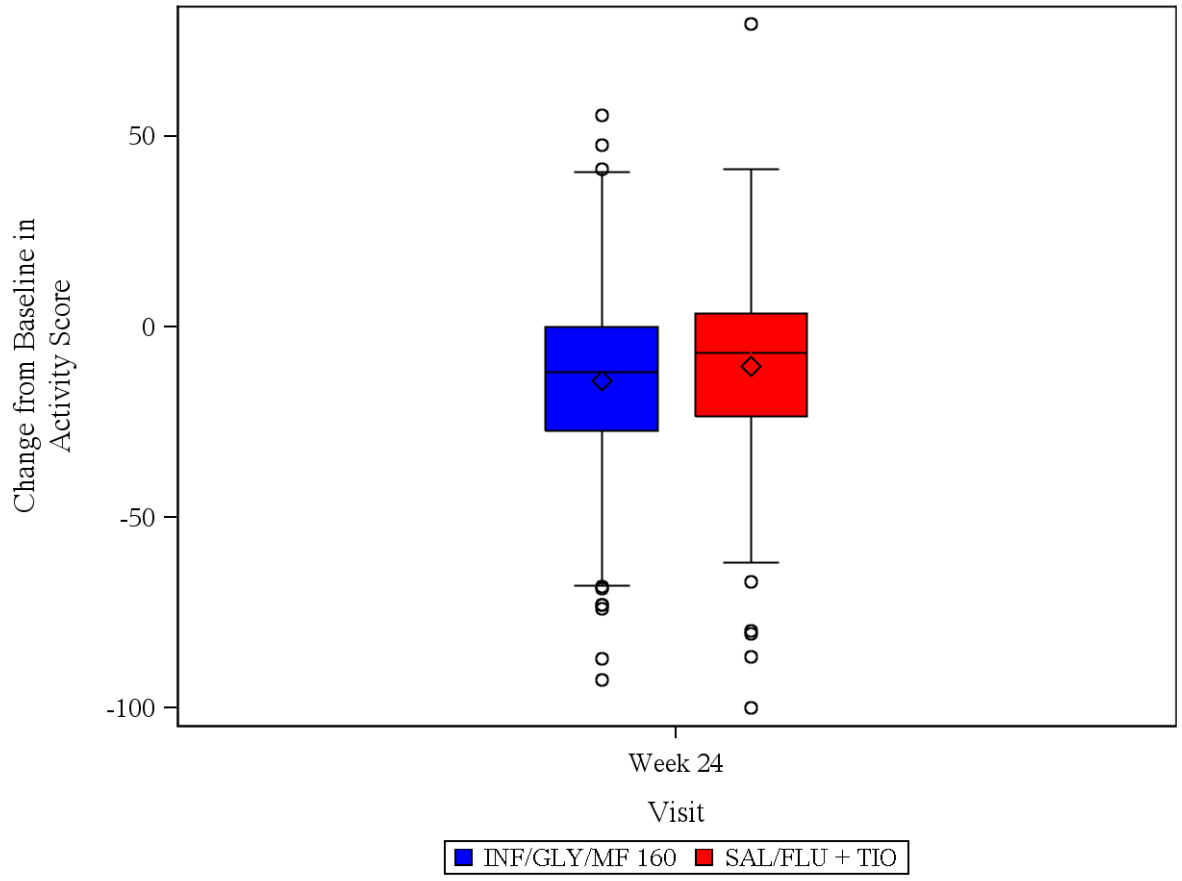
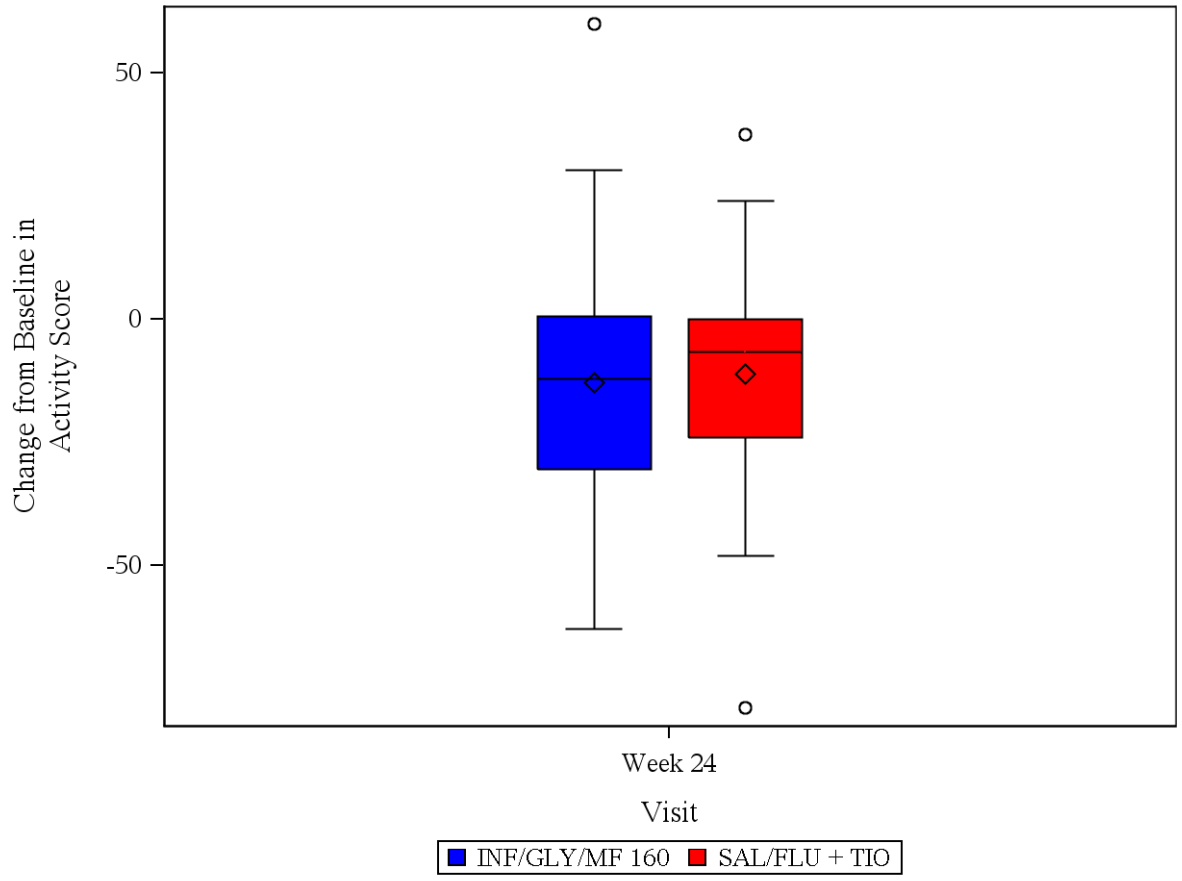


Figure 7.14.3 SGRQ (Activity Score) - Change from Baseline by Age (FAS), Age = ≥65 years



7.15 Boxplot: SGRQ (Activity Score) - Change from Baseline by Gender (FAS)

Figure 7.15.1 SGRQ (Activity Score) - Change from Baseline by Gender (FAS), Gender = Male

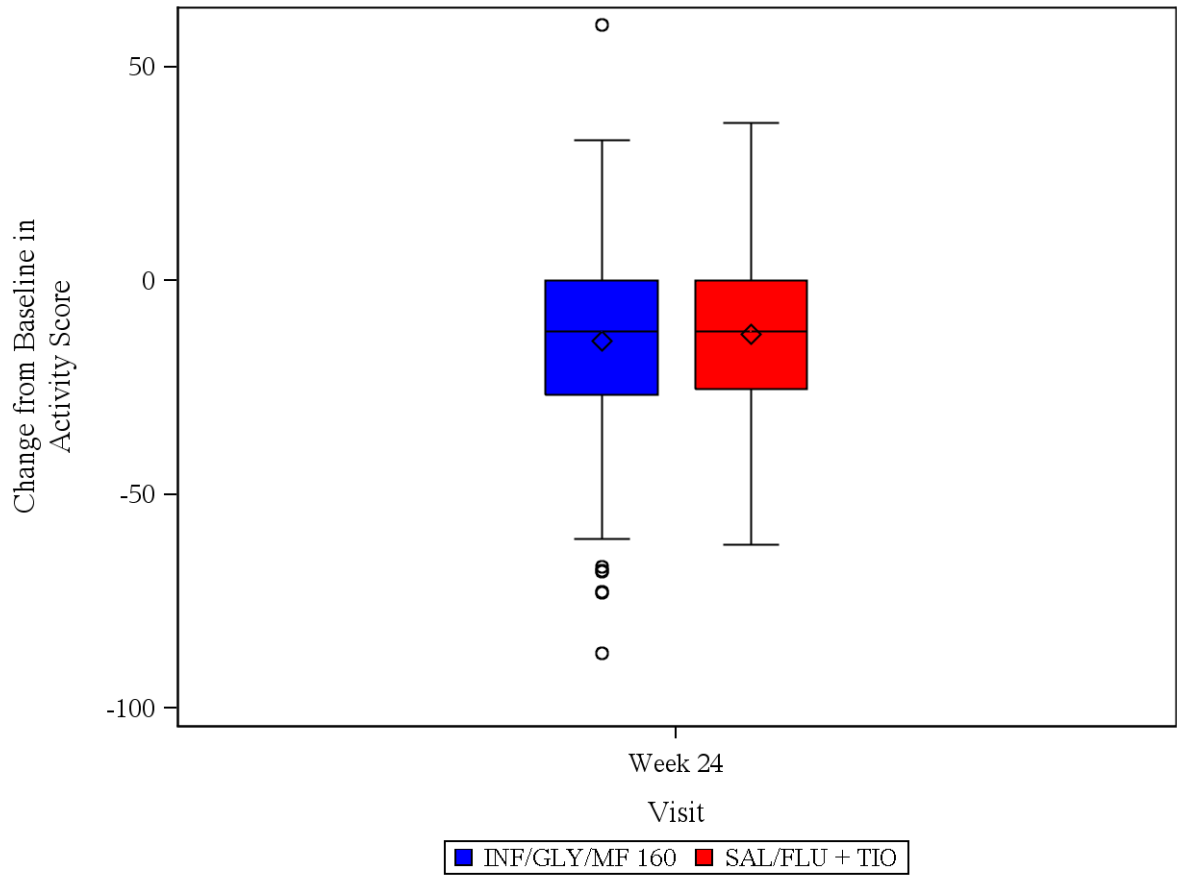
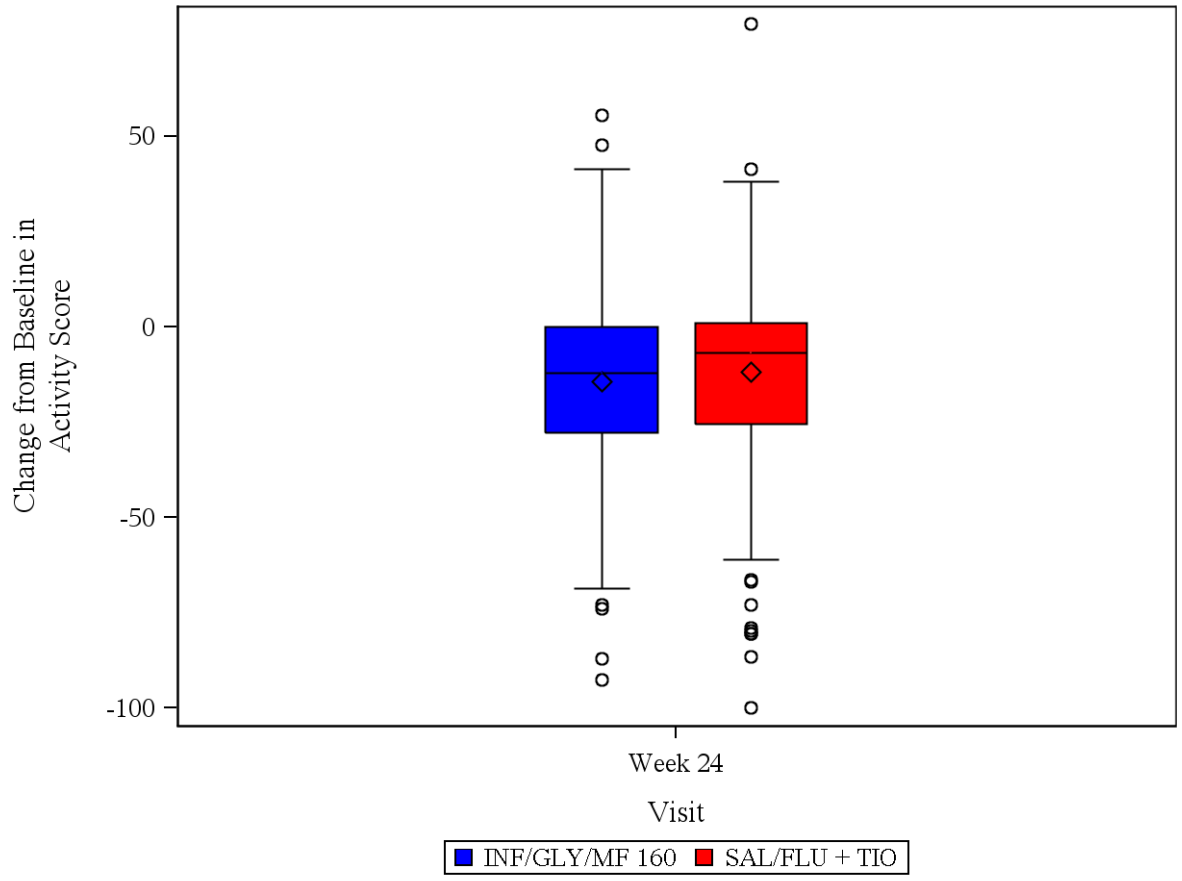


Figure 7.15.2 SGRQ (Activity Score) - Change from Baseline by Gender (FAS), Gender = Female



7.16 Boxplot: SGRQ (Activity Score) - Change from Baseline by Region (FAS)

Figure 7.16.1 SGRQ (Activity Score) - Change from Baseline by Region (FAS), Region = Asia

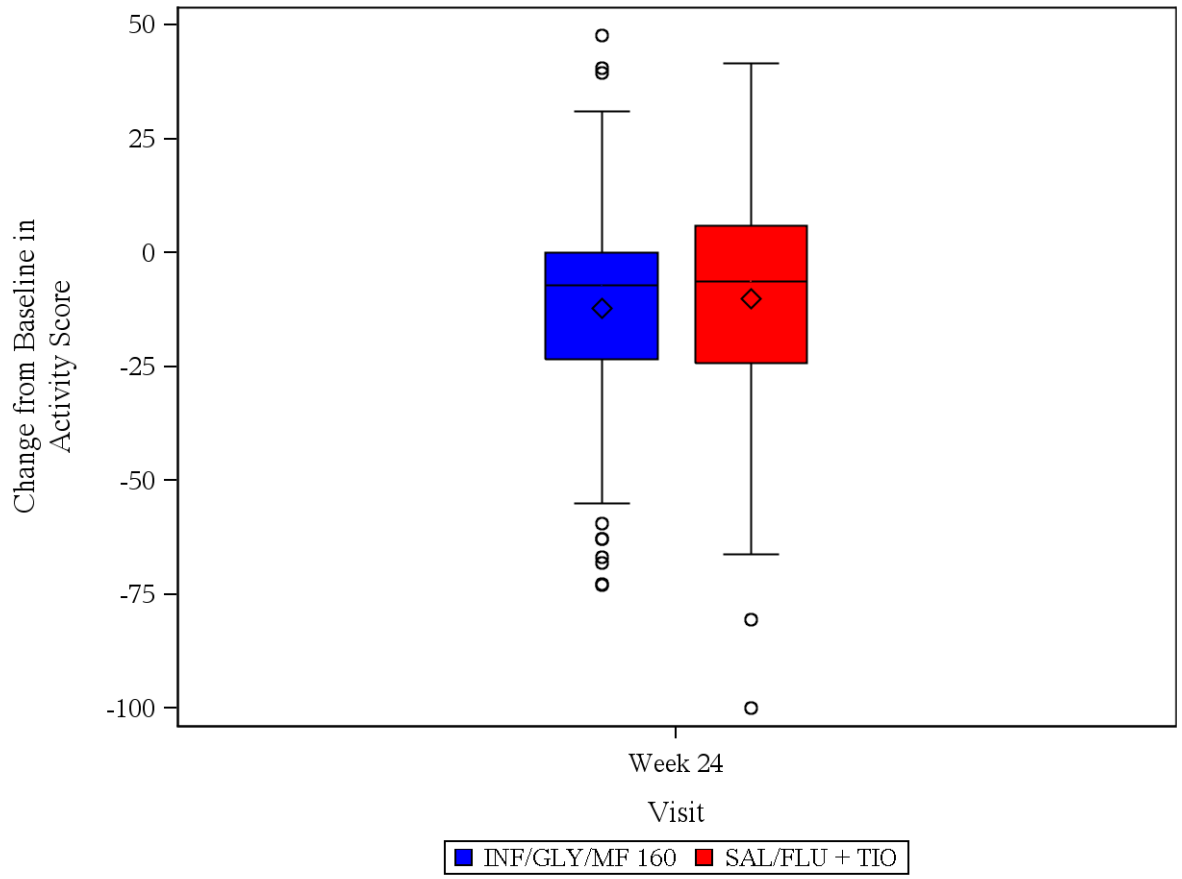


Figure 7.16.2 SGRQ (Activity Score) - Change from Baseline by Region (FAS), Region = Europe

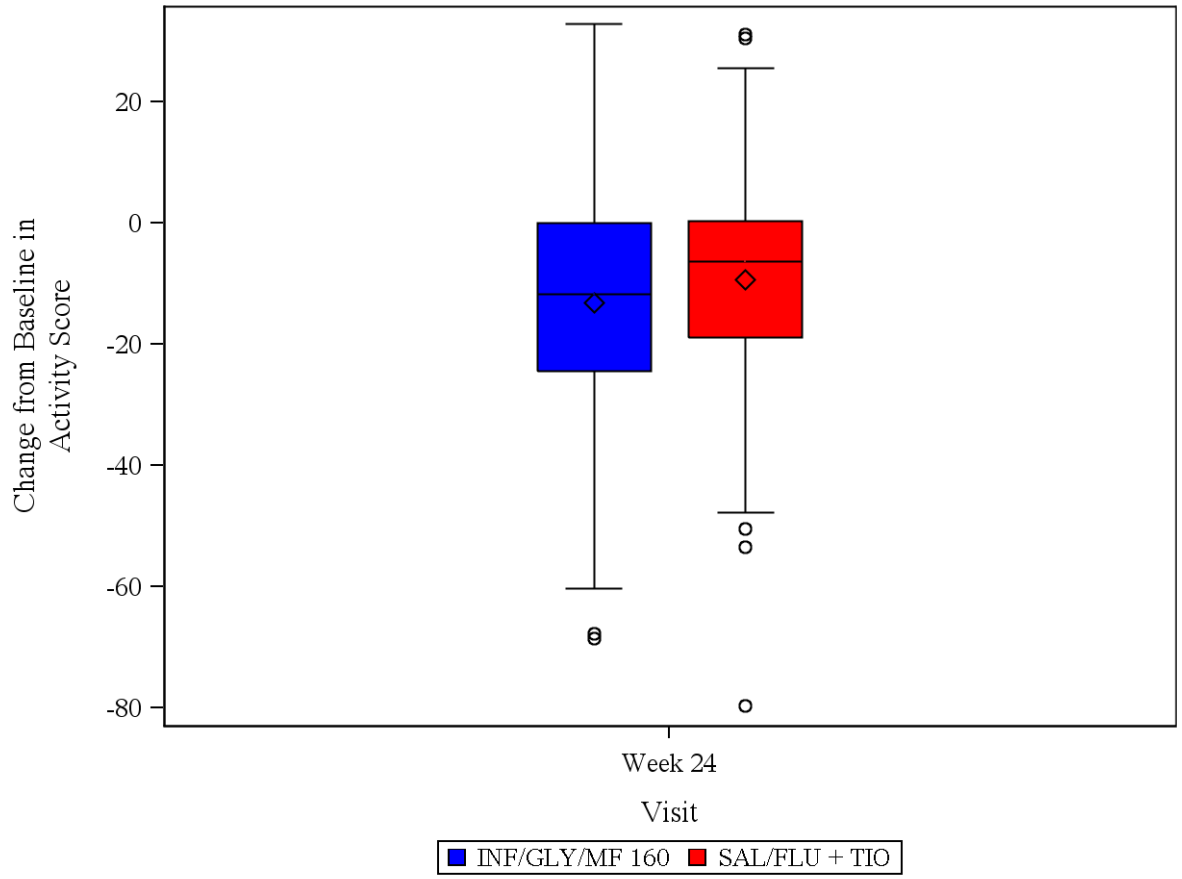


Figure 7.16.3 SGRQ (Activity Score) - Change from Baseline by Region (FAS), Region = Latin America

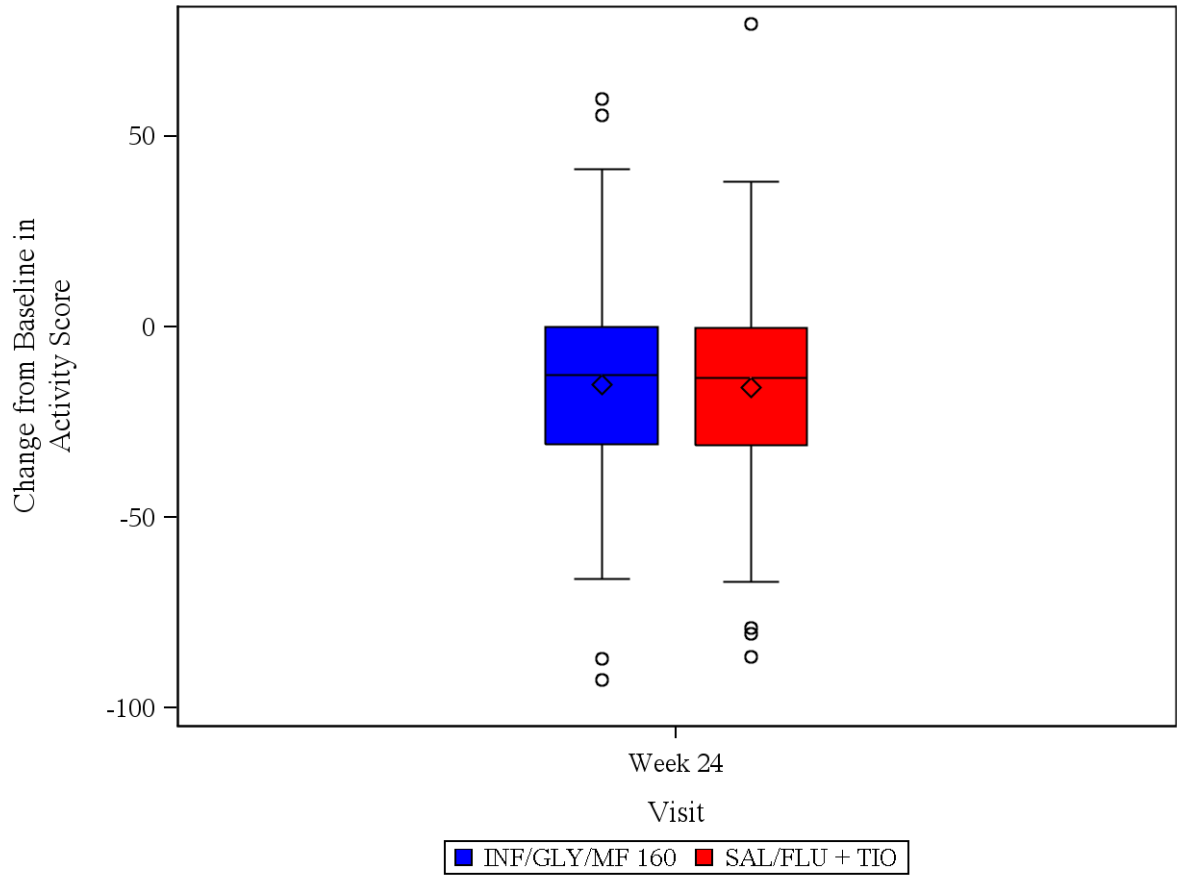
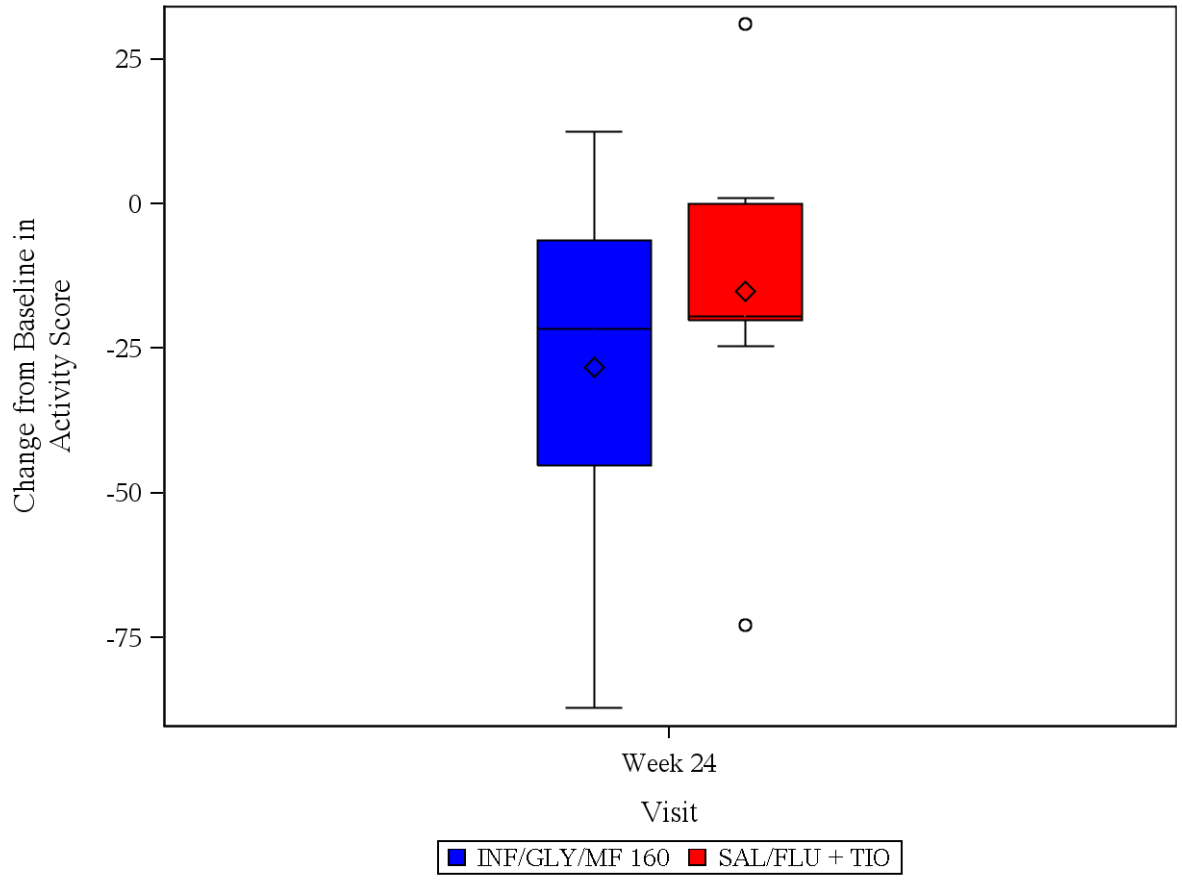


Figure 7.16.4 SGRQ (Activity Score) - Change from Baseline by Region (FAS), Region = Others



7.17 Boxplot: SGRQ (Activity Score) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 7.17.1 SGRQ (Activity Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

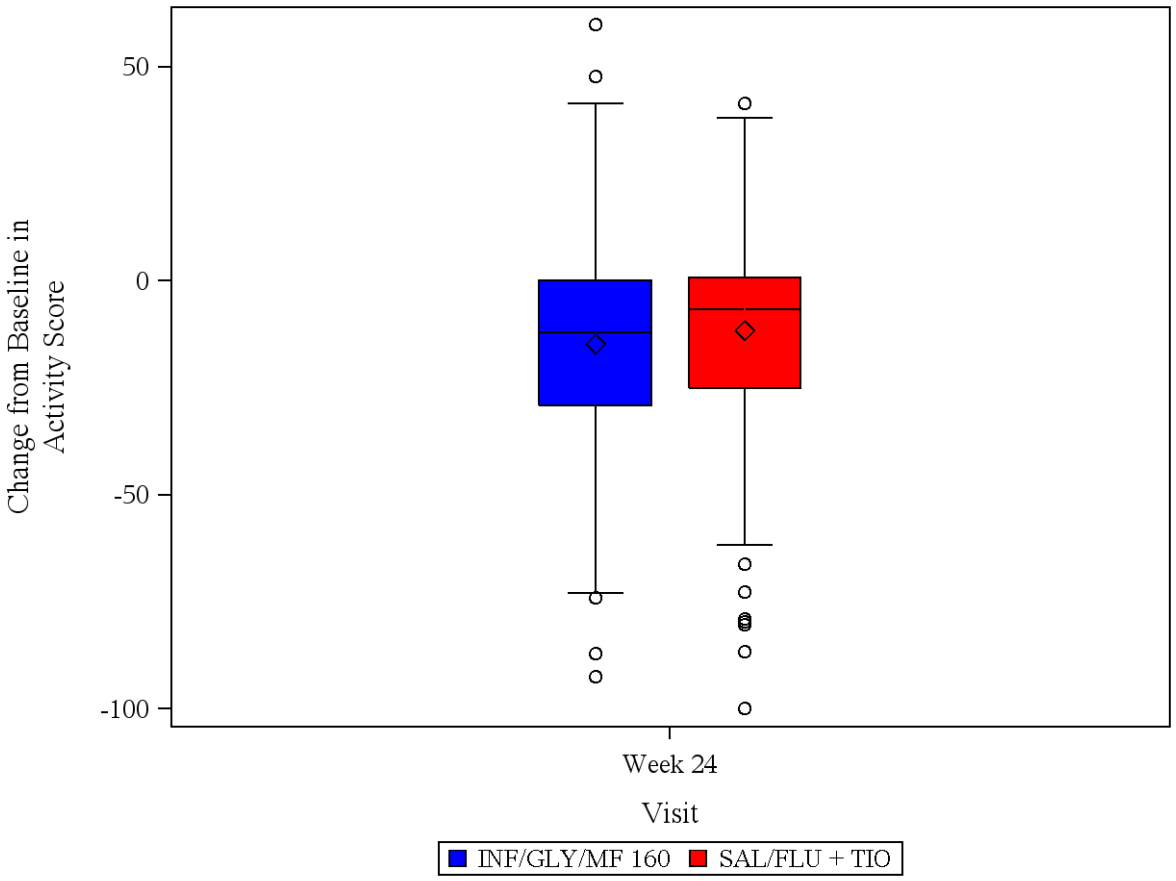
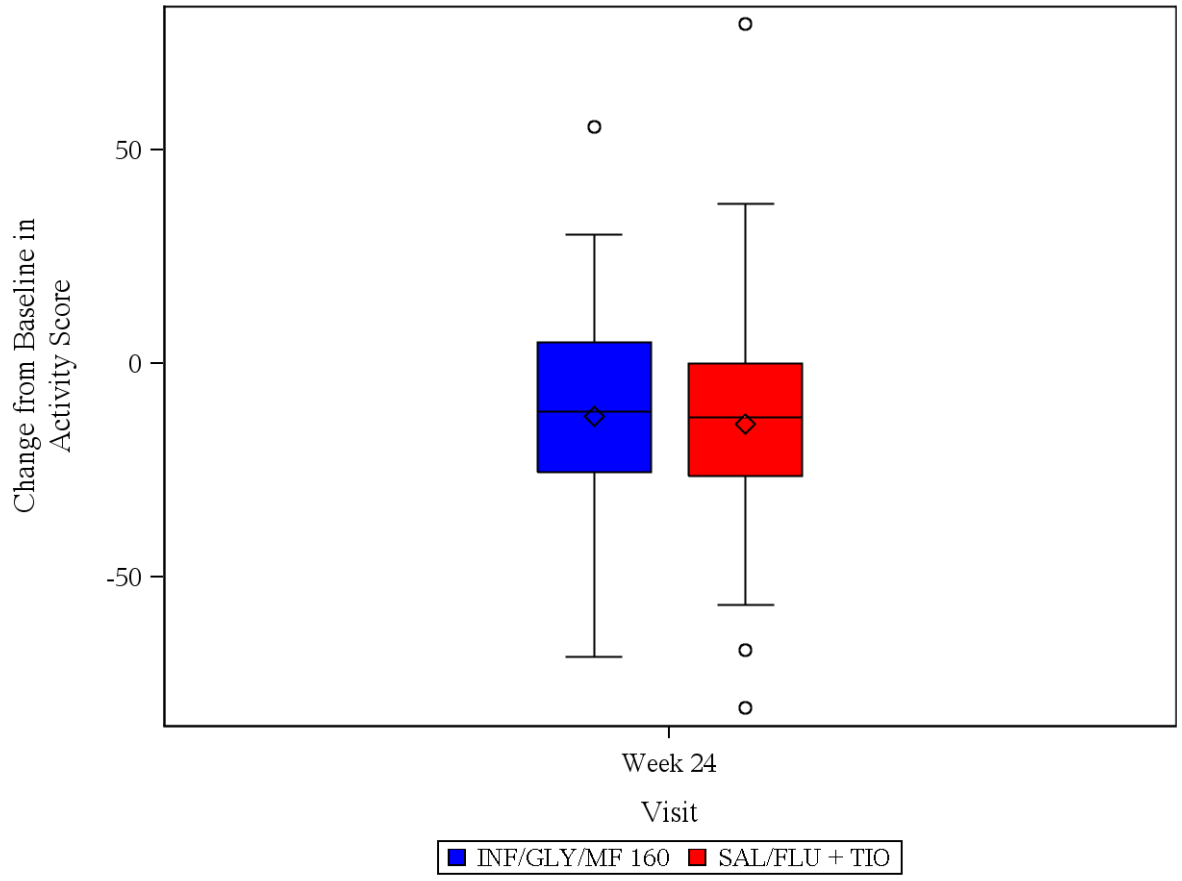


Figure 7.17.2 SGRQ (Activity Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



7.18 Boxplot: SGRQ (Activity Score) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 7.18.1 SGRQ (Activity Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

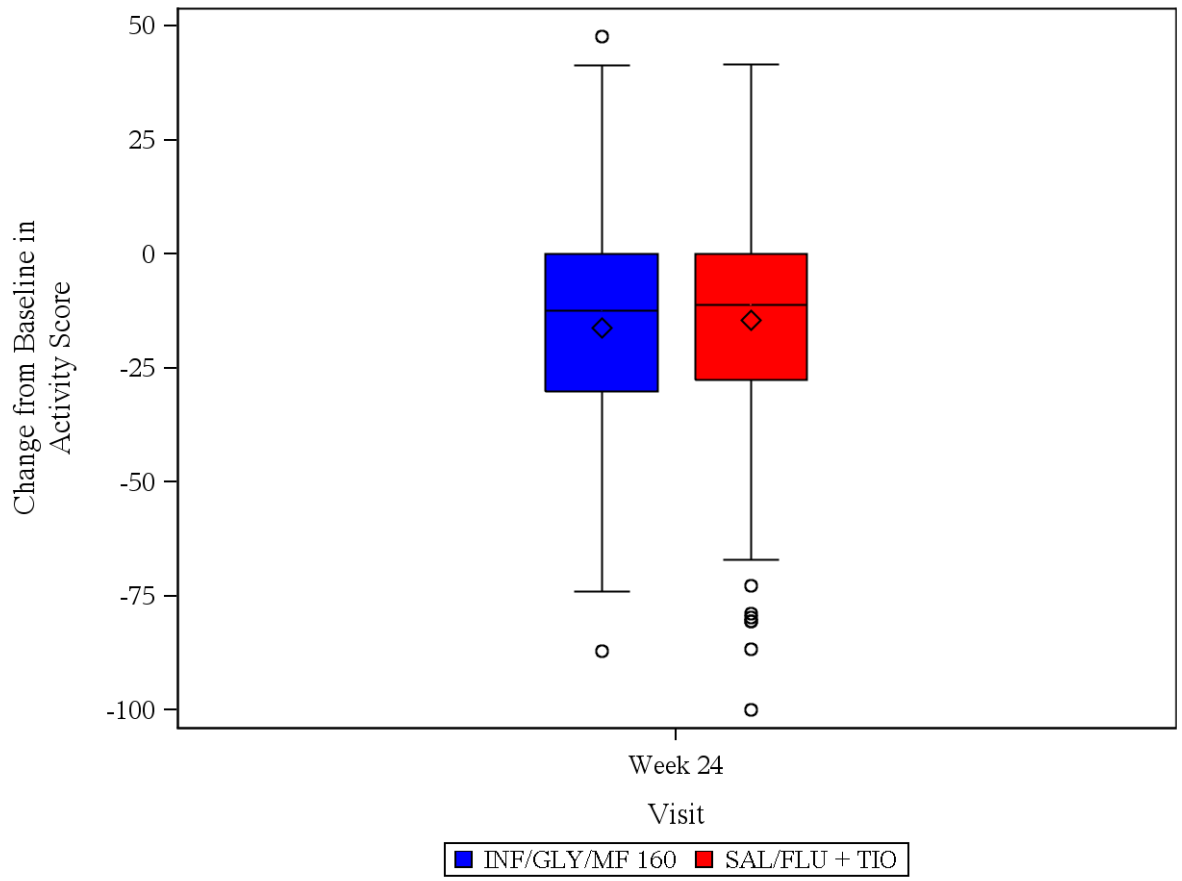
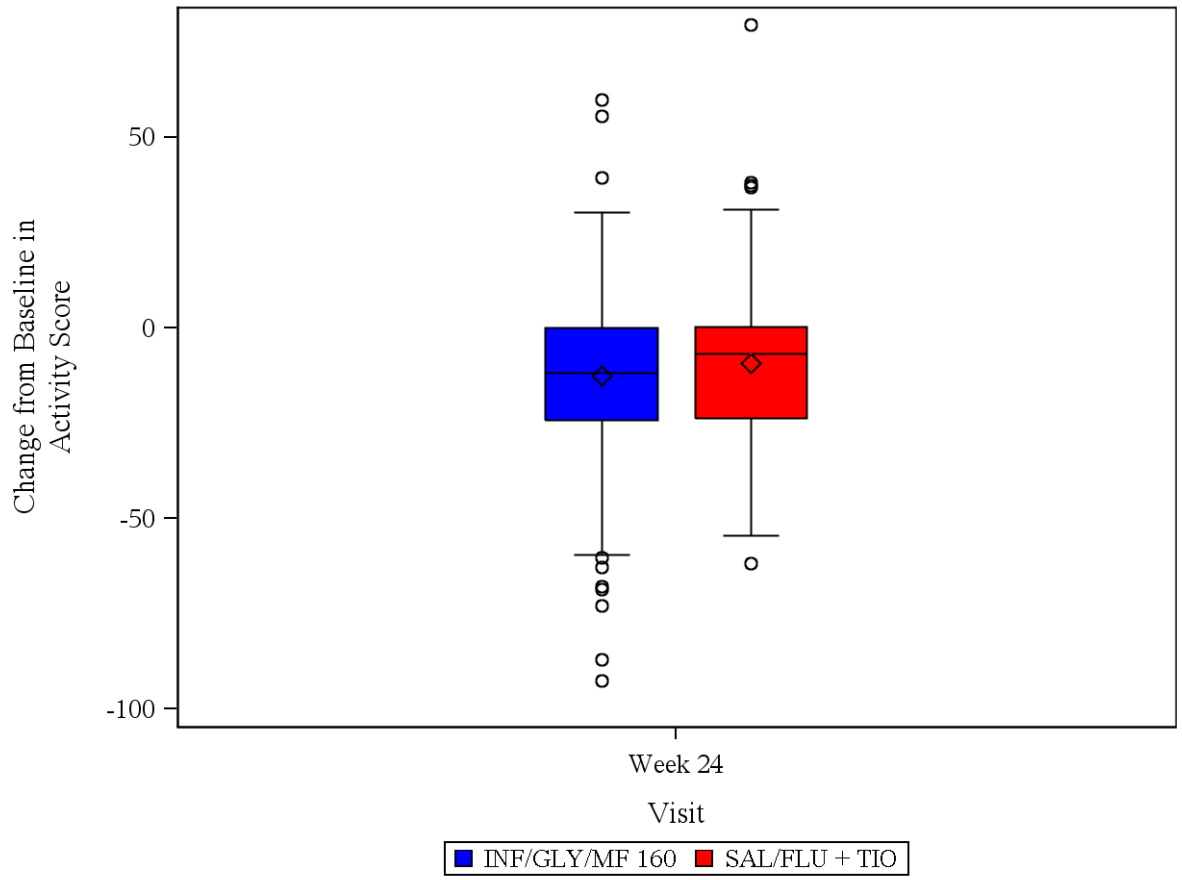
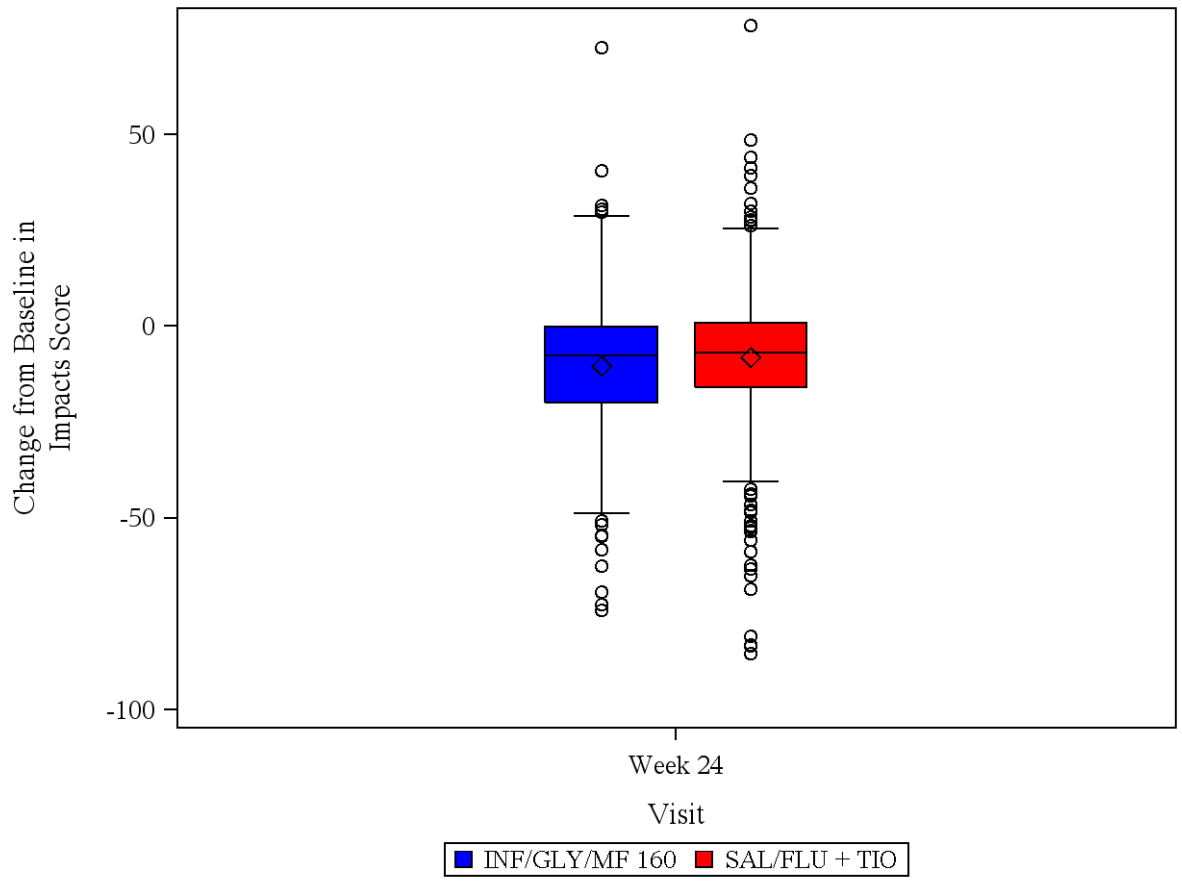


Figure 7.18.2 SGRQ (Activity Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



7.19 Boxplot: SGRQ (Impacts Score) - Change from Baseline (FAS)

Figure 7.19 SGRQ (Impacts Score) - Change from Baseline (FAS)



7.20 Boxplot: SGRQ (Impacts Score) - Change from Baseline by Age (FAS)

Figure 7.20.1 SGRQ (Impacts Score) - Change from Baseline by Age (FAS), Age = 18-39 years

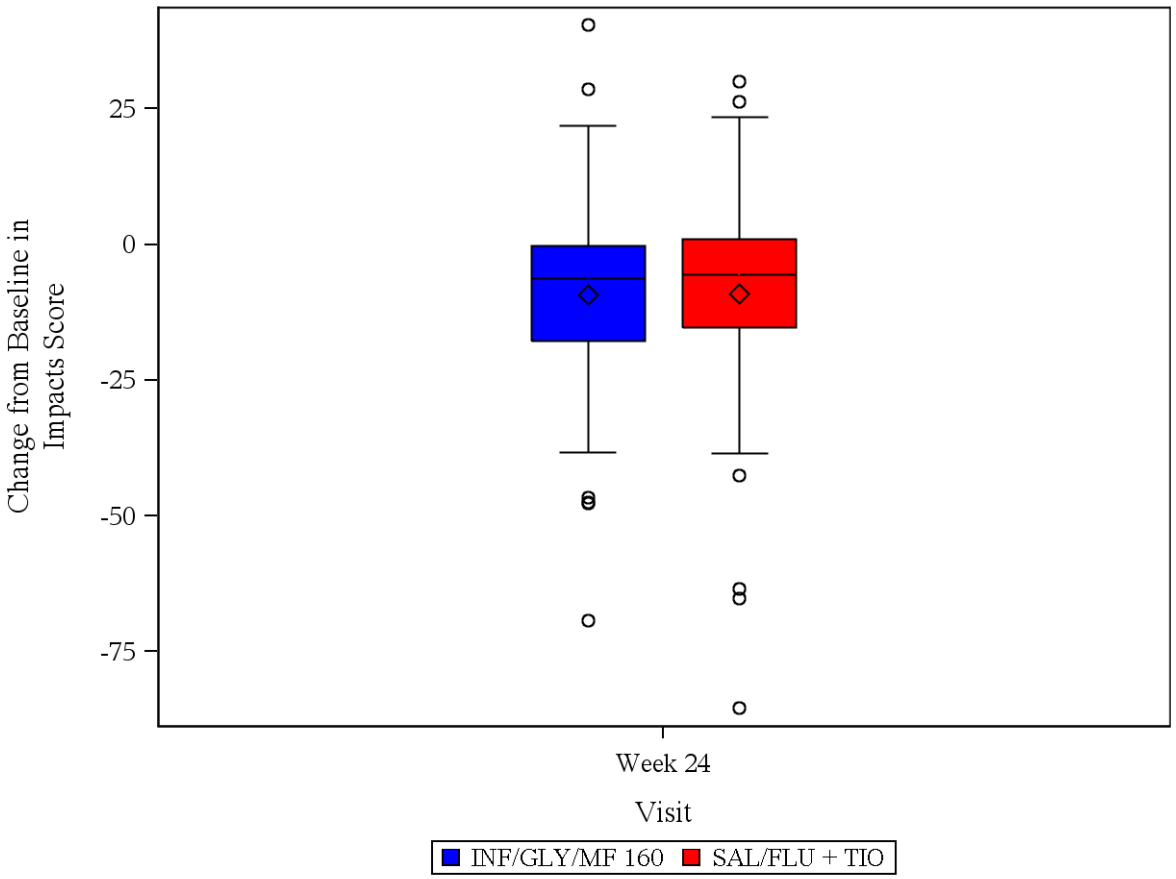


Figure 7.20.2 SGRQ (Impacts Score) - Change from Baseline by Age (FAS), Age = 40-64 years

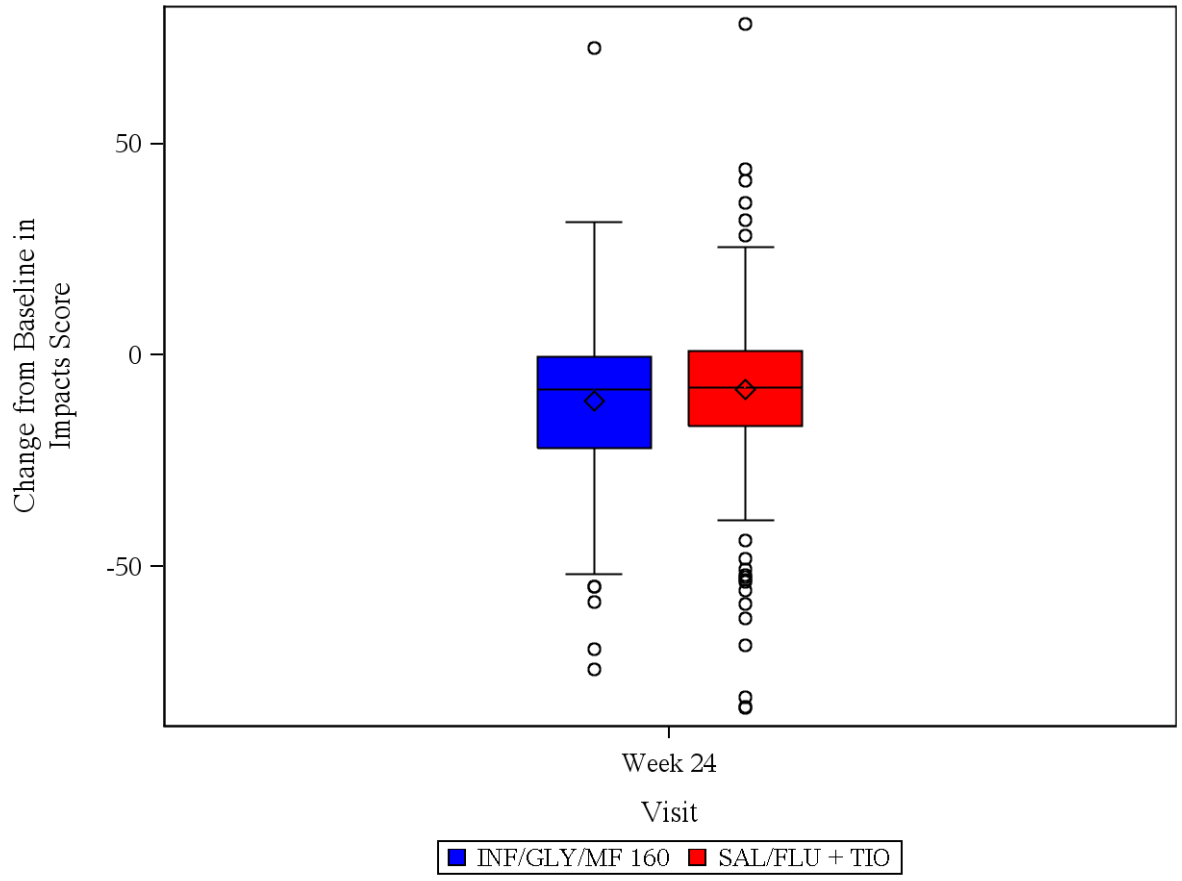
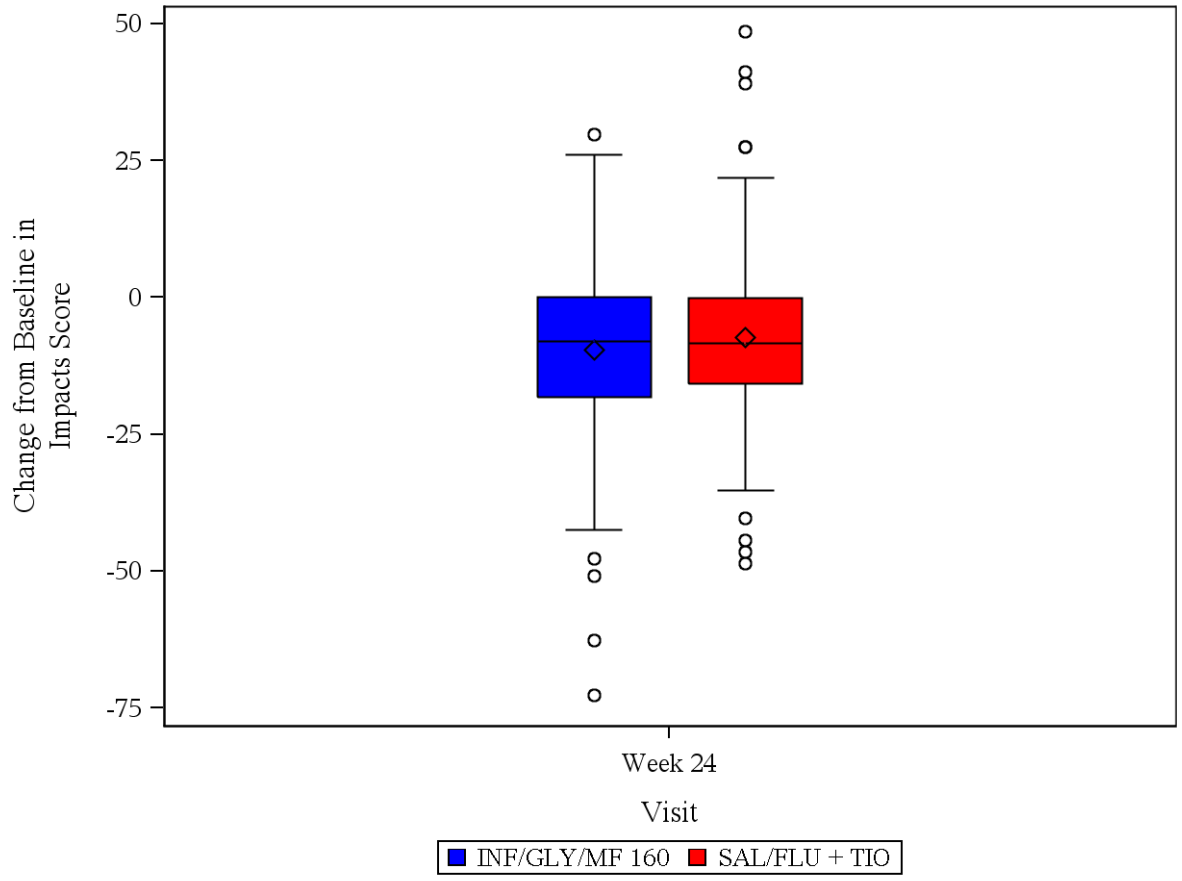


Figure 7.20.3 SGRQ (Impacts Score) - Change from Baseline by Age (FAS), Age = ≥65 years



7.21 Boxplot: SGRQ (Impacts Score) - Change from Baseline by Gender (FAS)

Figure 7.21.1 SGRQ (Impacts Score) - Change from Baseline by Gender (FAS), Gender = Male

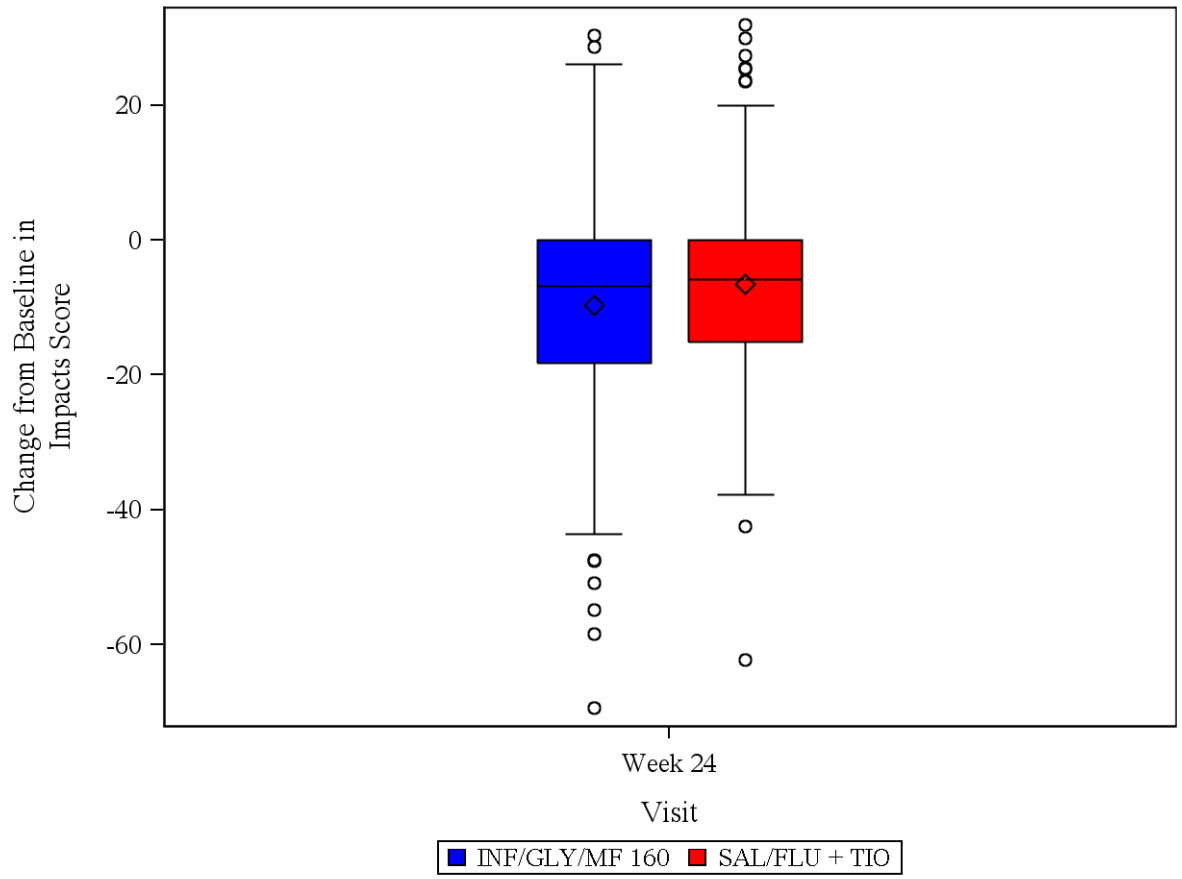
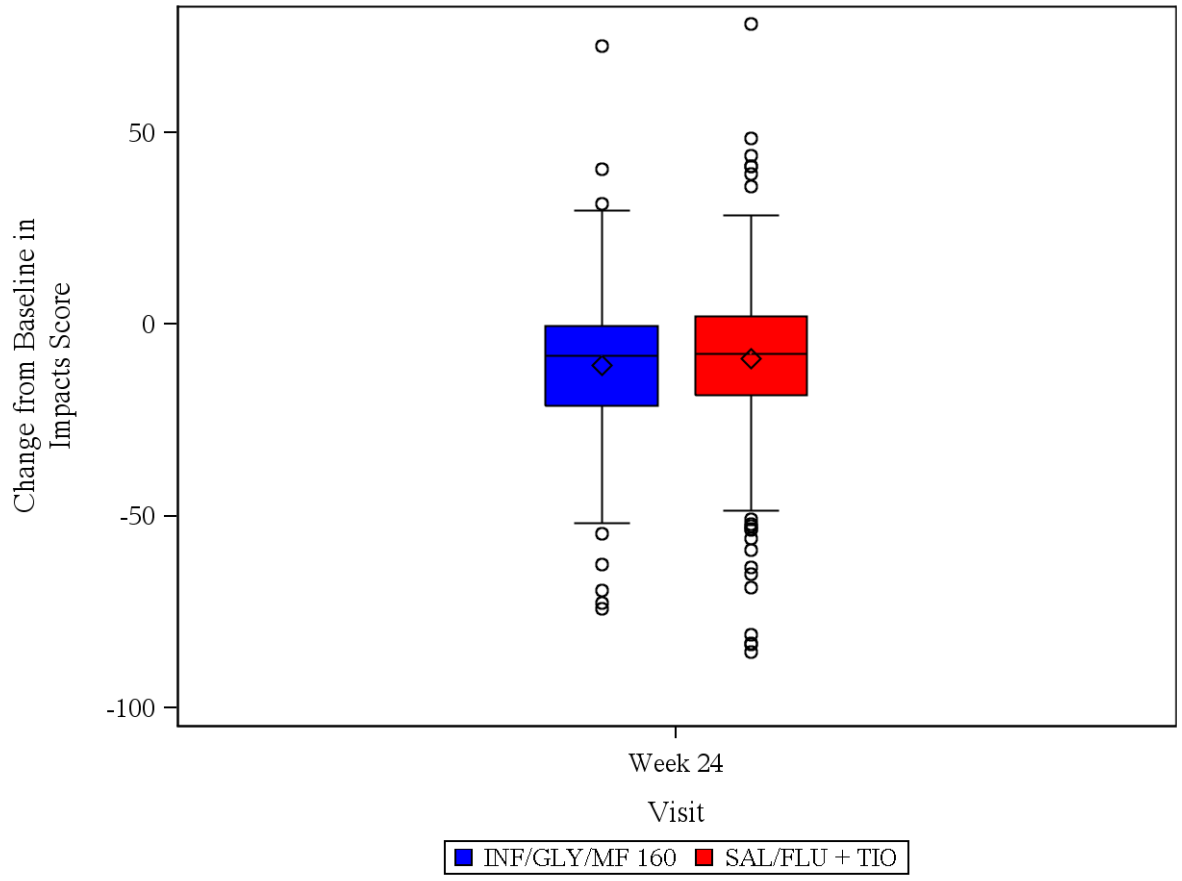


Figure 7.21.2 SGRQ (Impacts Score) - Change from Baseline by Gender (FAS), Gender = Female



7.22 Boxplot: SGRQ (Impacts Score) - Change from Baseline by Region (FAS)

Figure 7.22.1 SGRQ (Impacts Score) - Change from Baseline by Region (FAS), Region = Asia

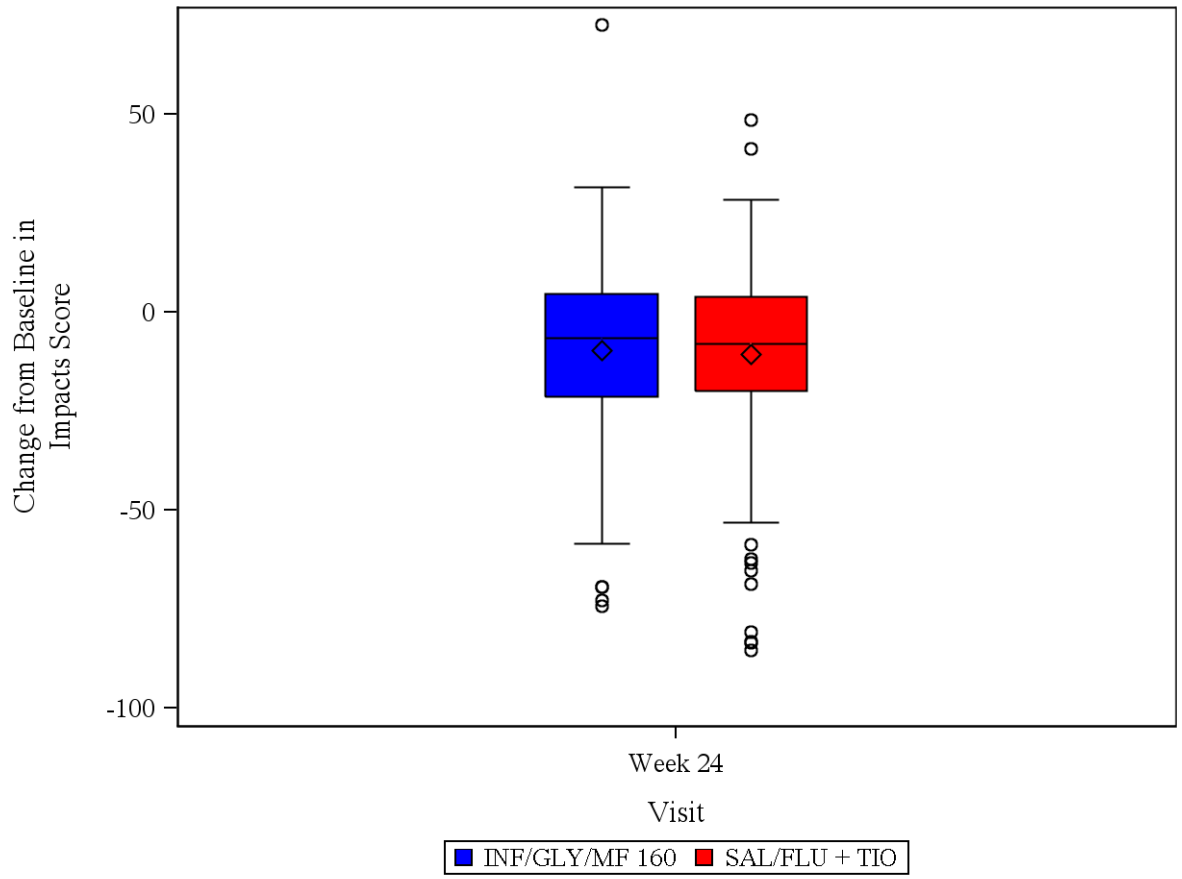


Figure 7.22.2 SGRQ (Impacts Score) - Change from Baseline by Region (FAS), Region = Europe

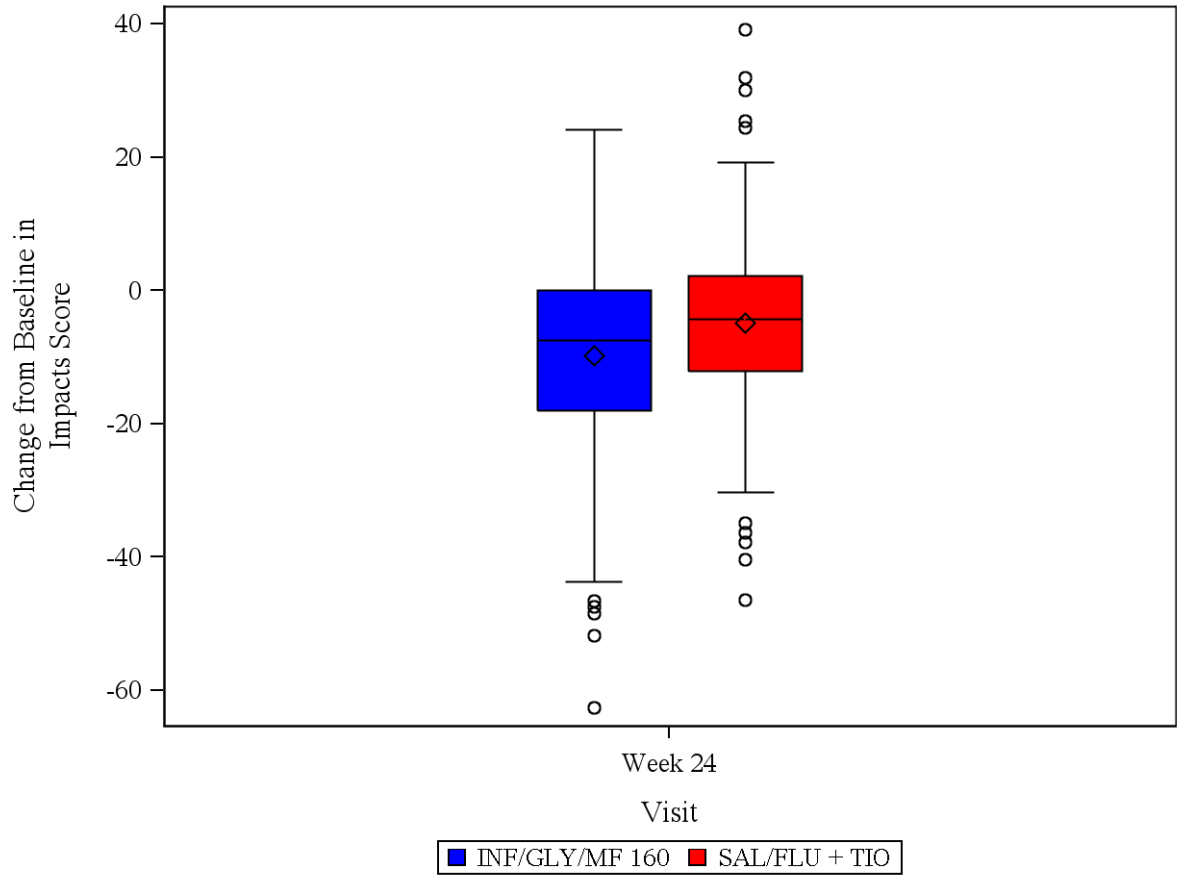


Figure 7.22.3 SGRQ (Impacts Score) - Change from Baseline by Region (FAS), Region = Latin America

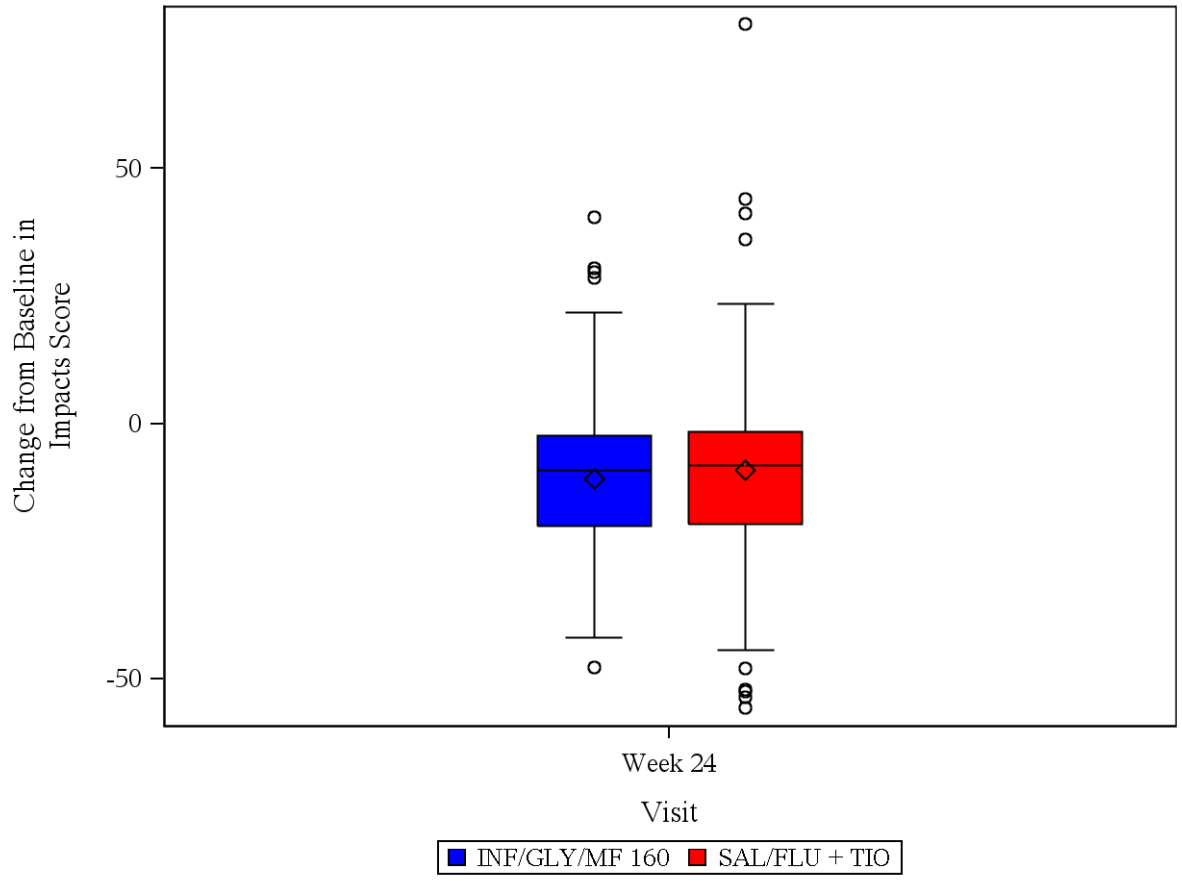
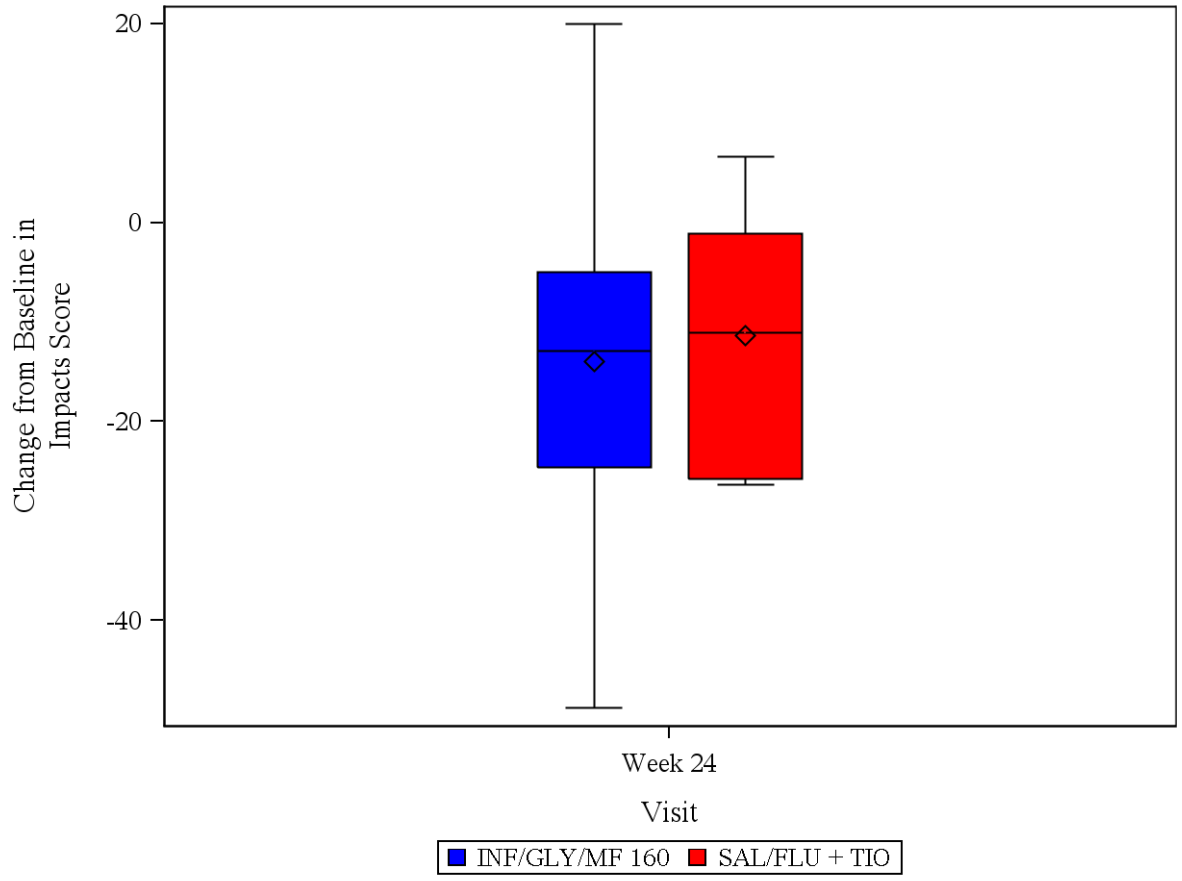


Figure 7.22.4 SGRQ (Impacts Score) - Change from Baseline by Region (FAS), Region = Others



7.23 Boxplot: SGRQ (Impacts Score) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 7.23.1 SGRQ (Impacts Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

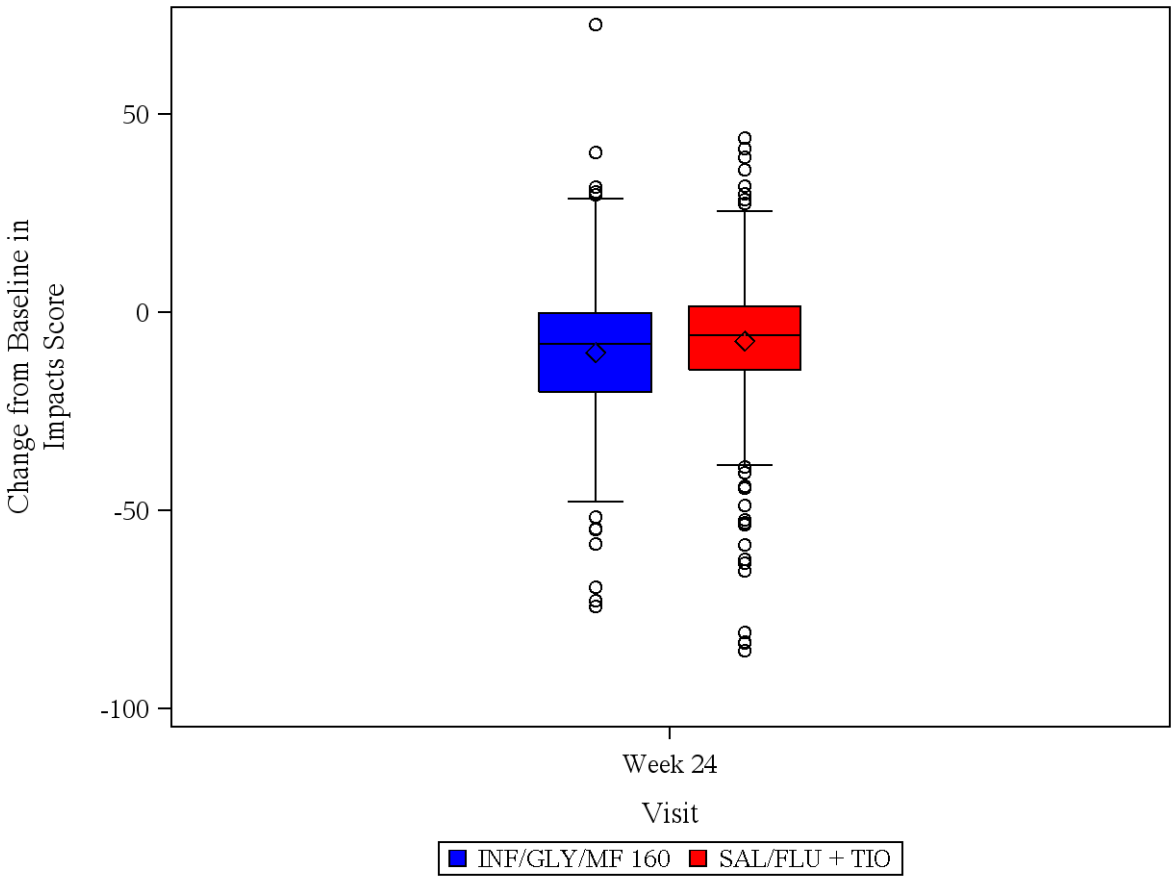
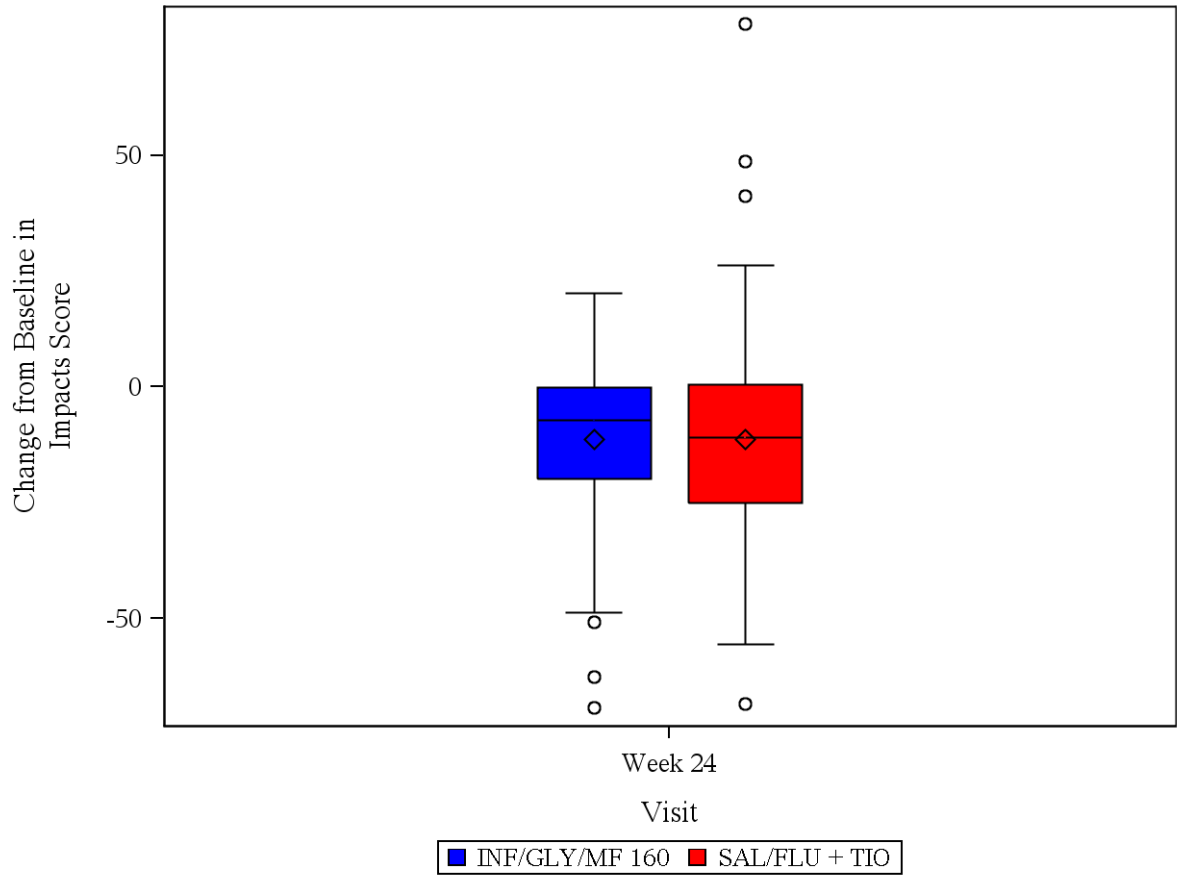


Figure 7.23.2 SGRQ (Impacts Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



7.24 Boxplot: SGRQ (Impacts Score) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 7.24.1 SGRQ (Impacts Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

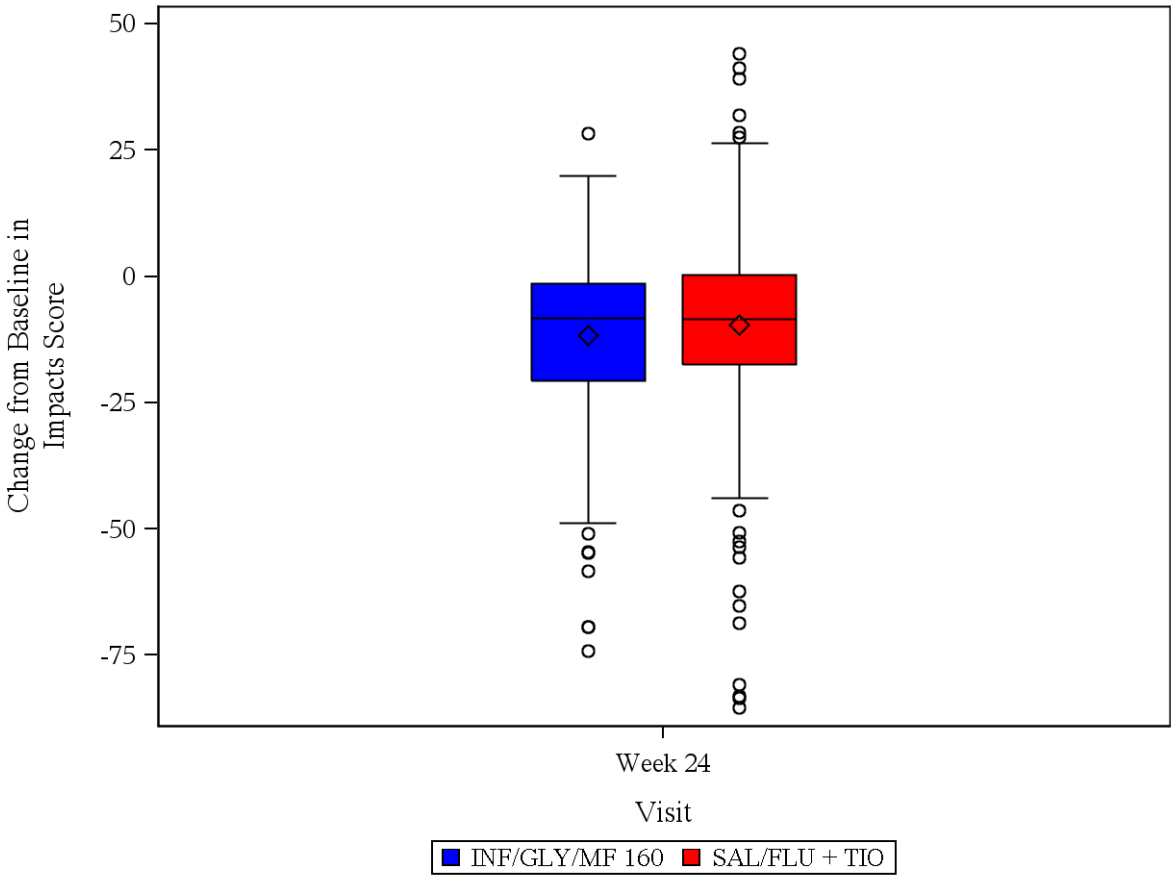
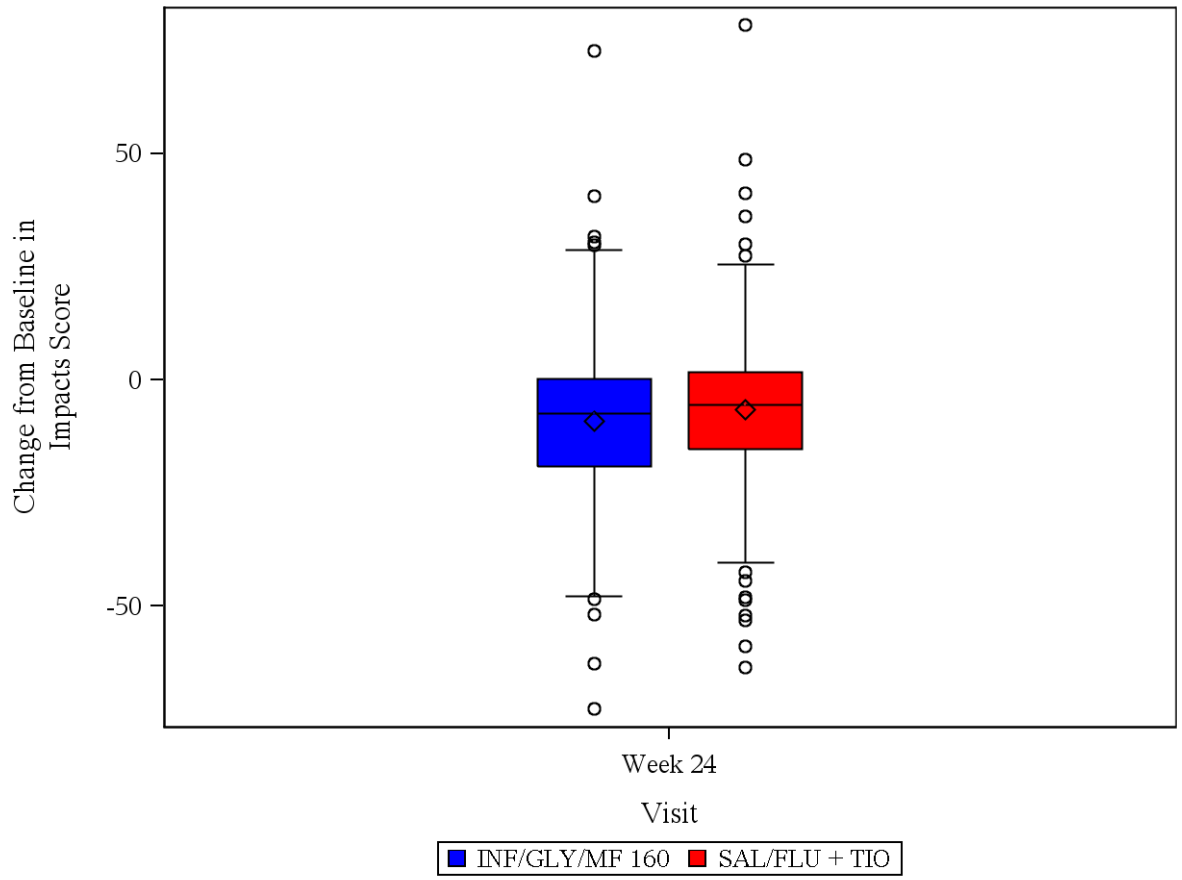


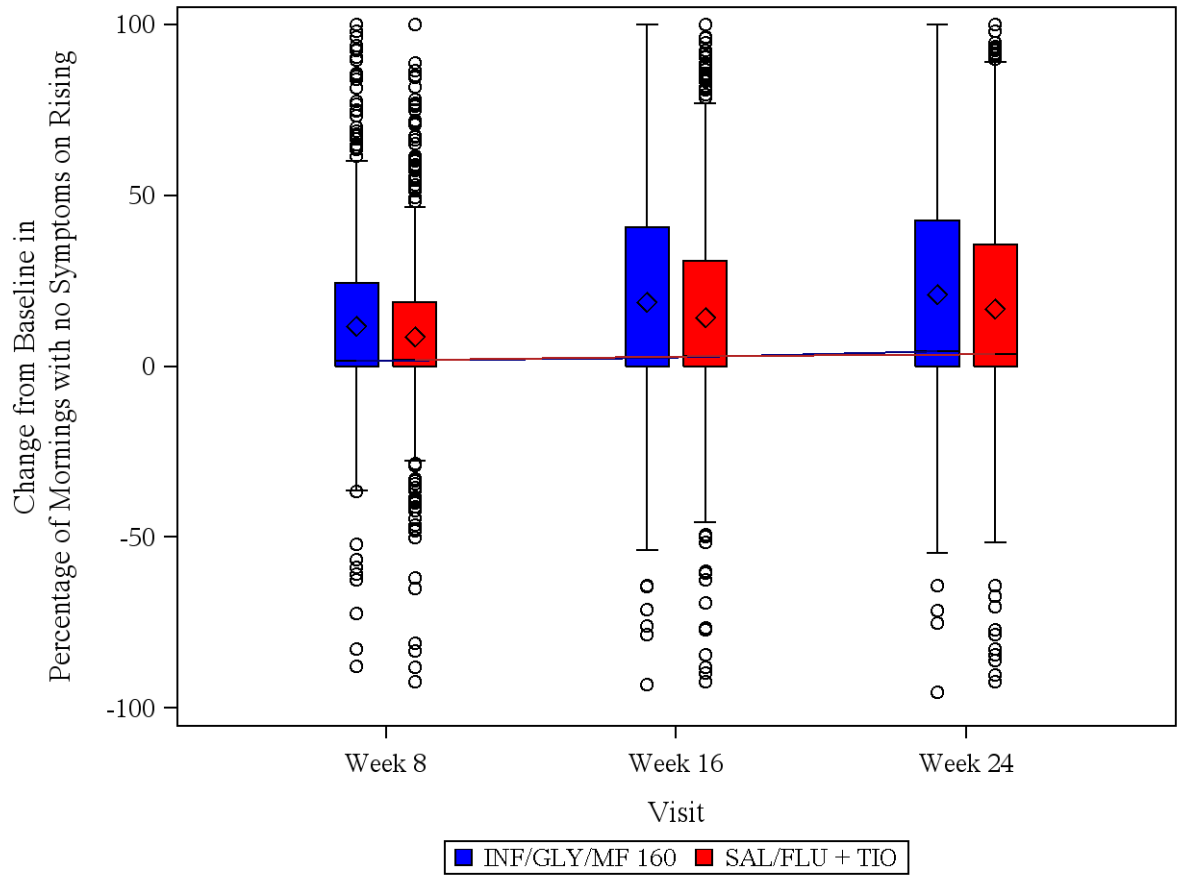
Figure 7.24.2 SGRQ (Impacts Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



9. Boxplot: Symptoms - Change from Baseline (FAS)

9.1 Boxplot: Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline (FAS)

Figure 9.1 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline (FAS)



9.2 Boxplot: Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Age (FAS)

Figure 9.2.1 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Age (FAS), Age = 18-39 years

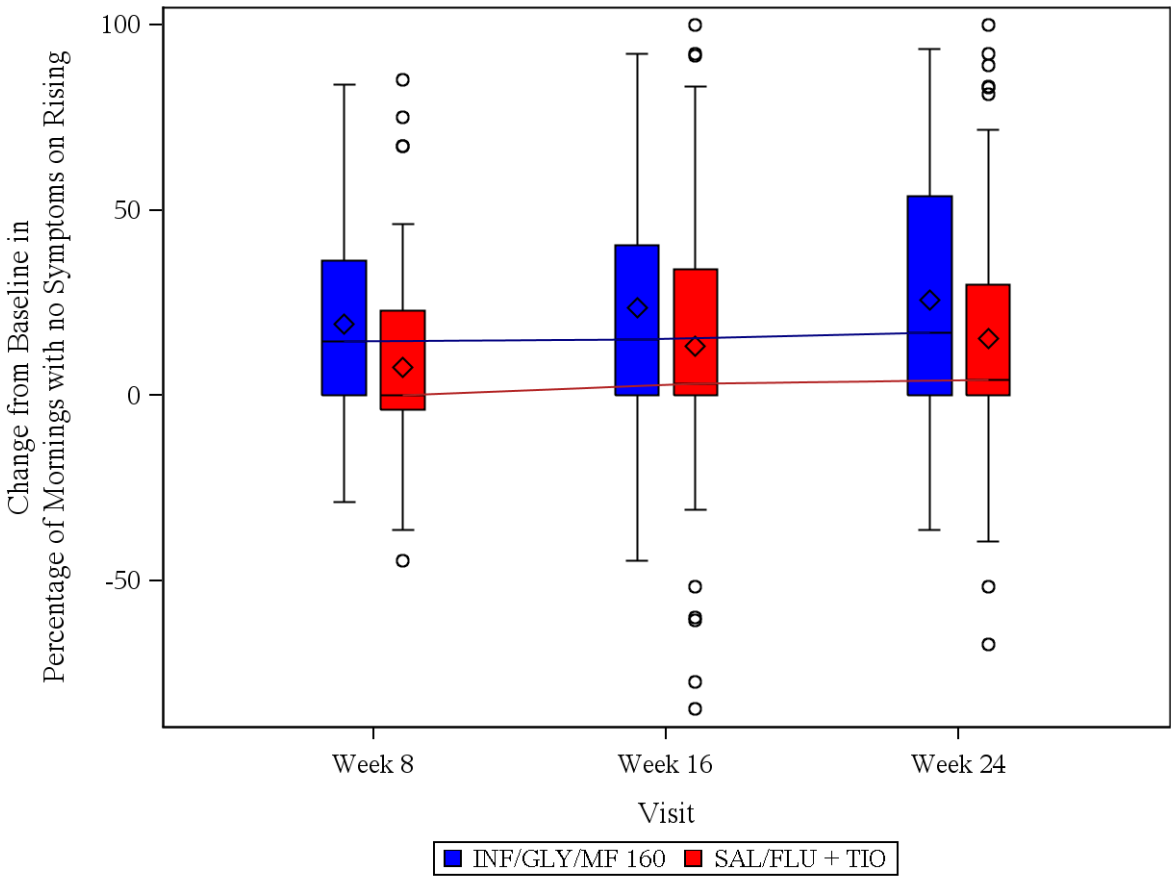


Figure 9.2.2 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Age (FAS), Age = 40-64 years

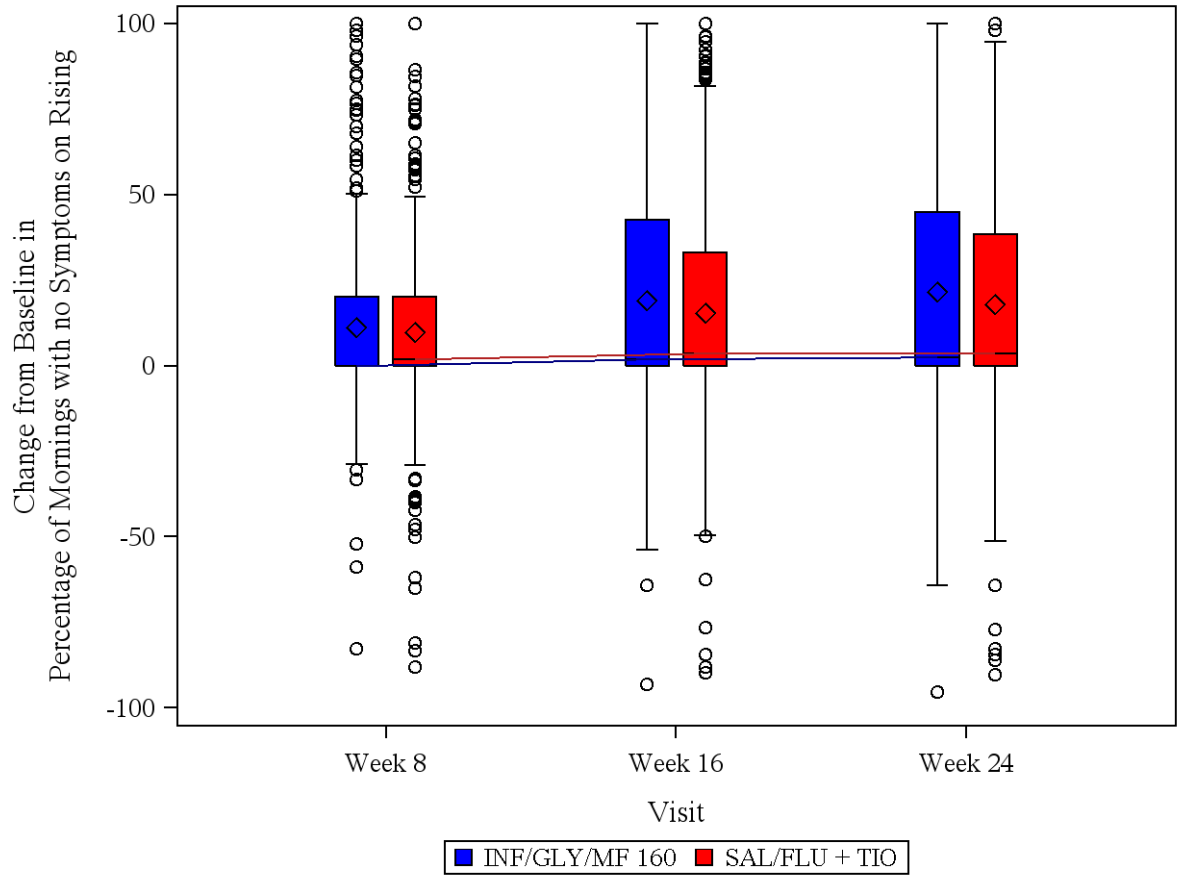
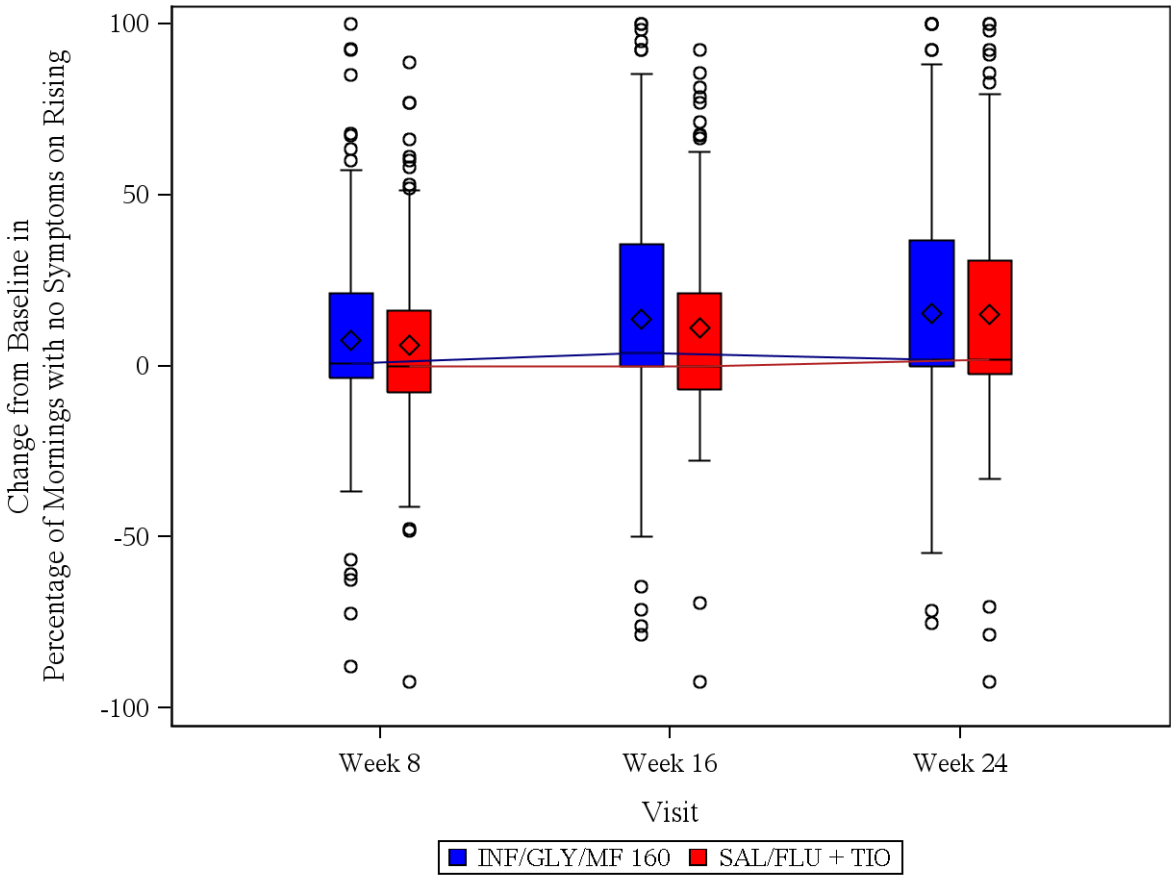


Figure 9.2.3 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Age (FAS), Age = ≥65 years



9.3 Boxplot: Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Gender (FAS)

Figure 9.3.1 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Gender (FAS), Gender = Male

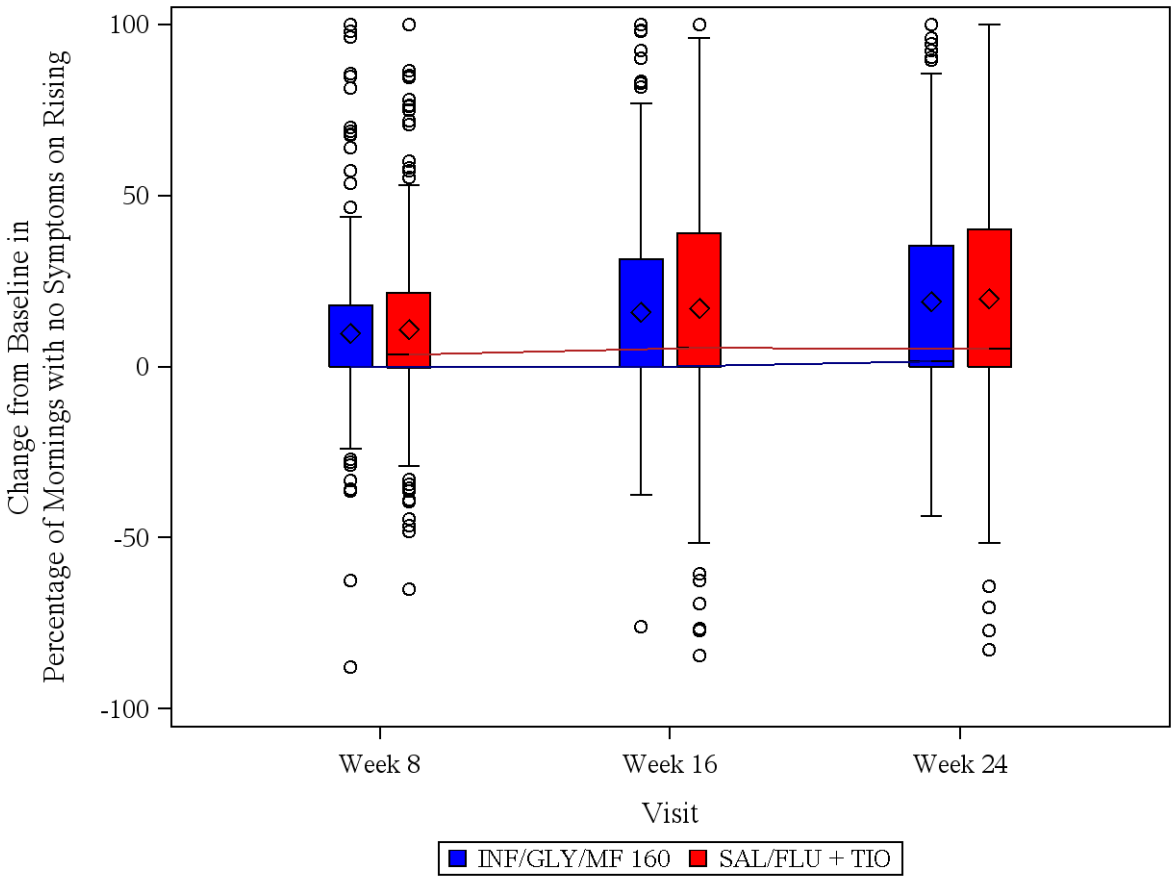
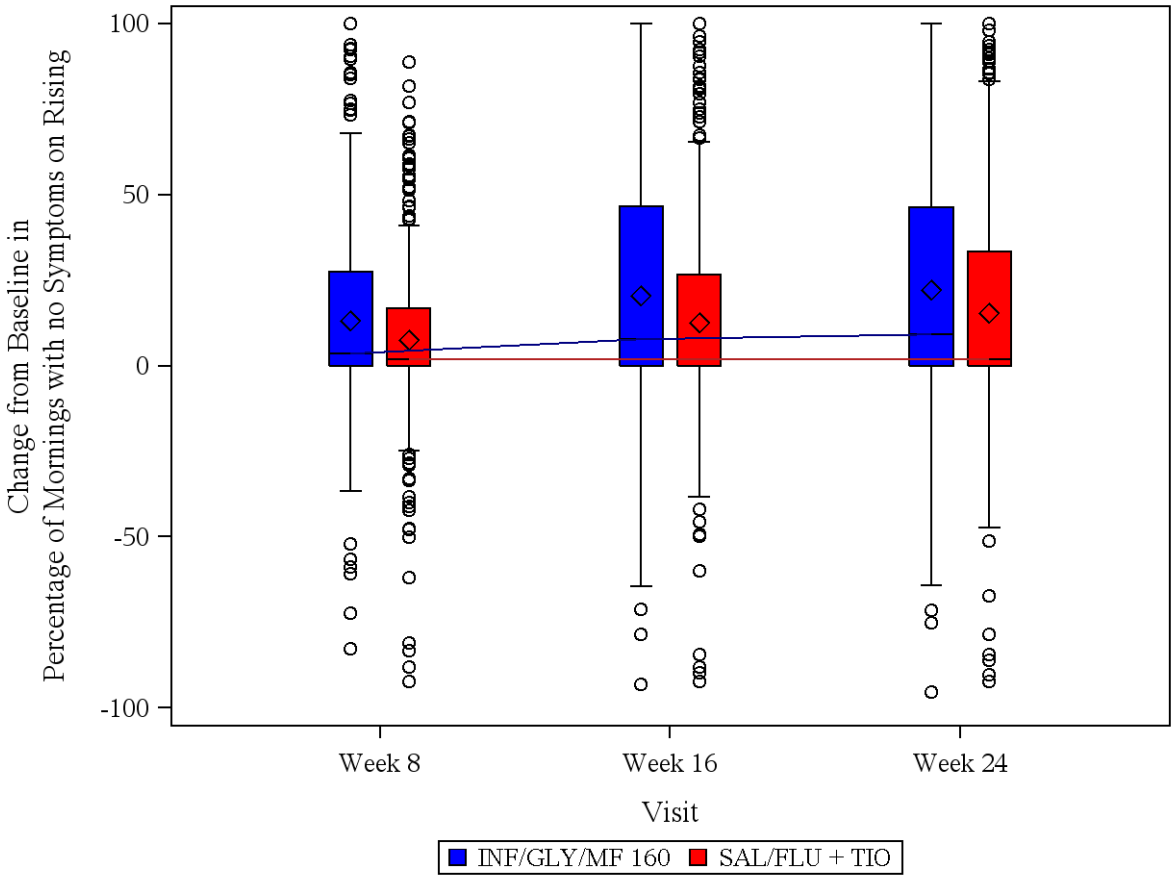


Figure 9.3.2 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Gender (FAS), Gender = Female



9.4 Boxplot: Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Region (FAS)

Figure 9.4.1 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Region (FAS), Region = Asia

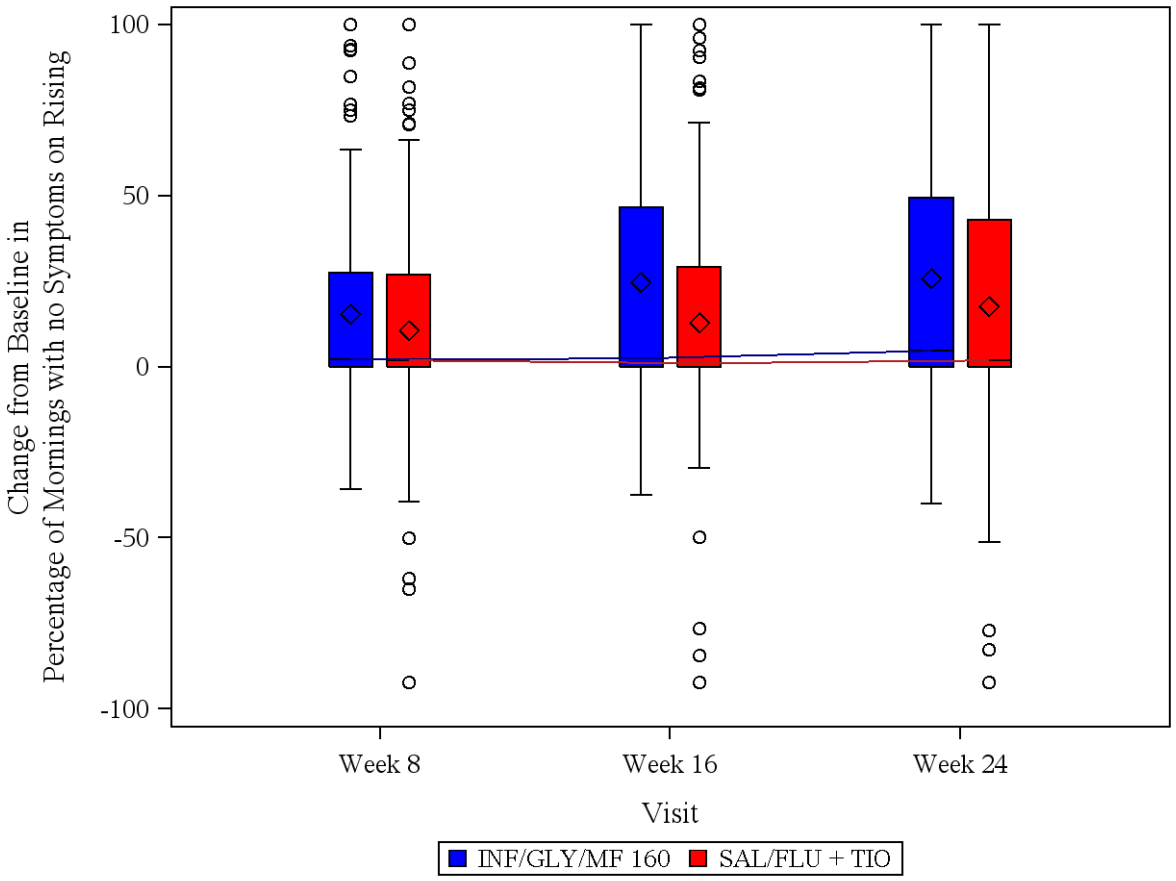


Figure 9.4.2 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Region (FAS), Region = Europe

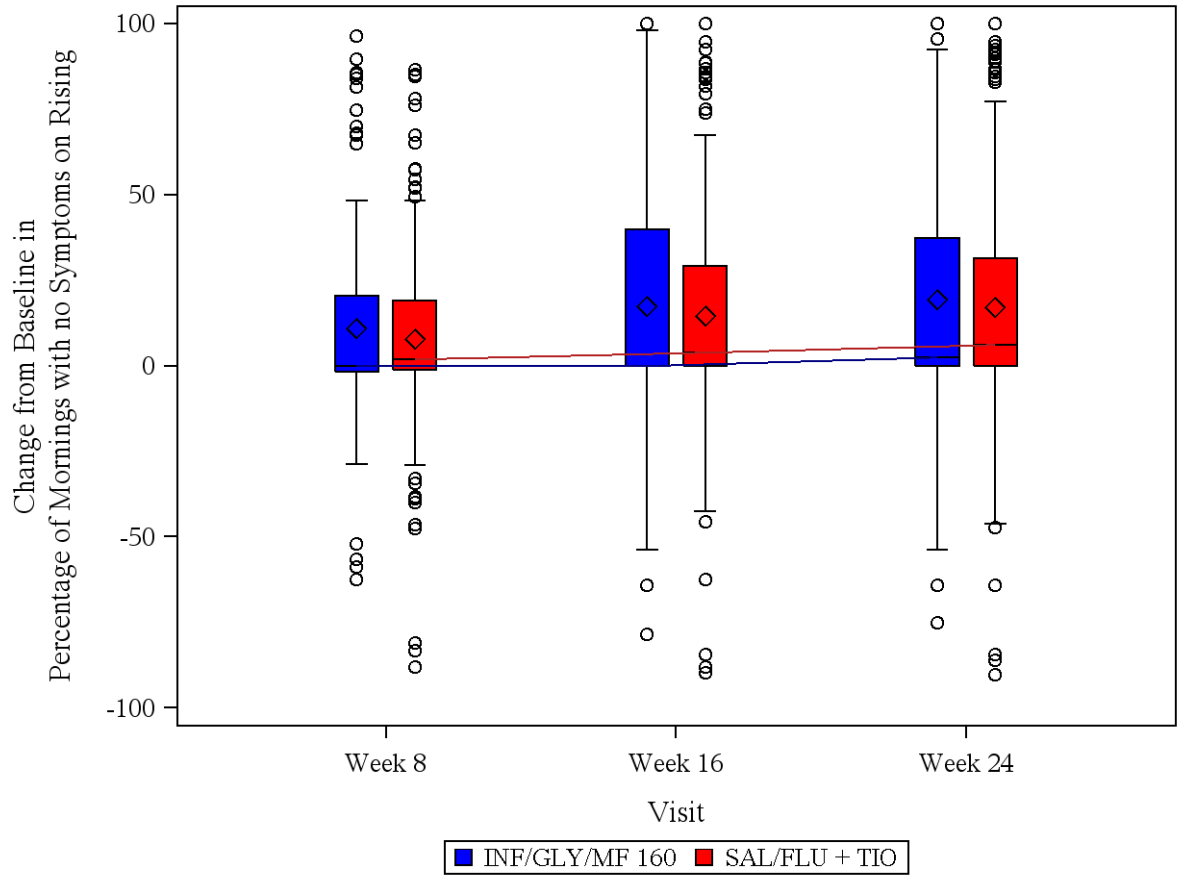


Figure 9.4.3 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Region (FAS), Region = Latin America

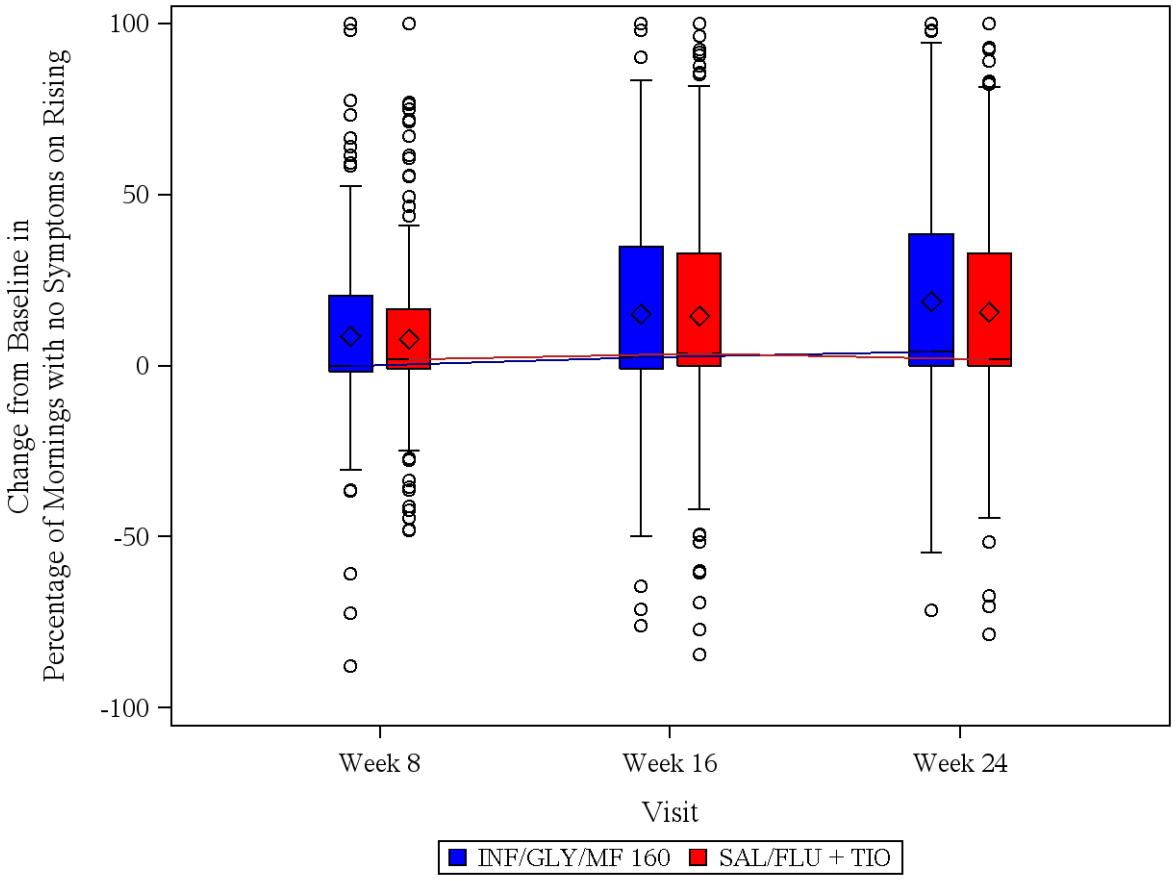
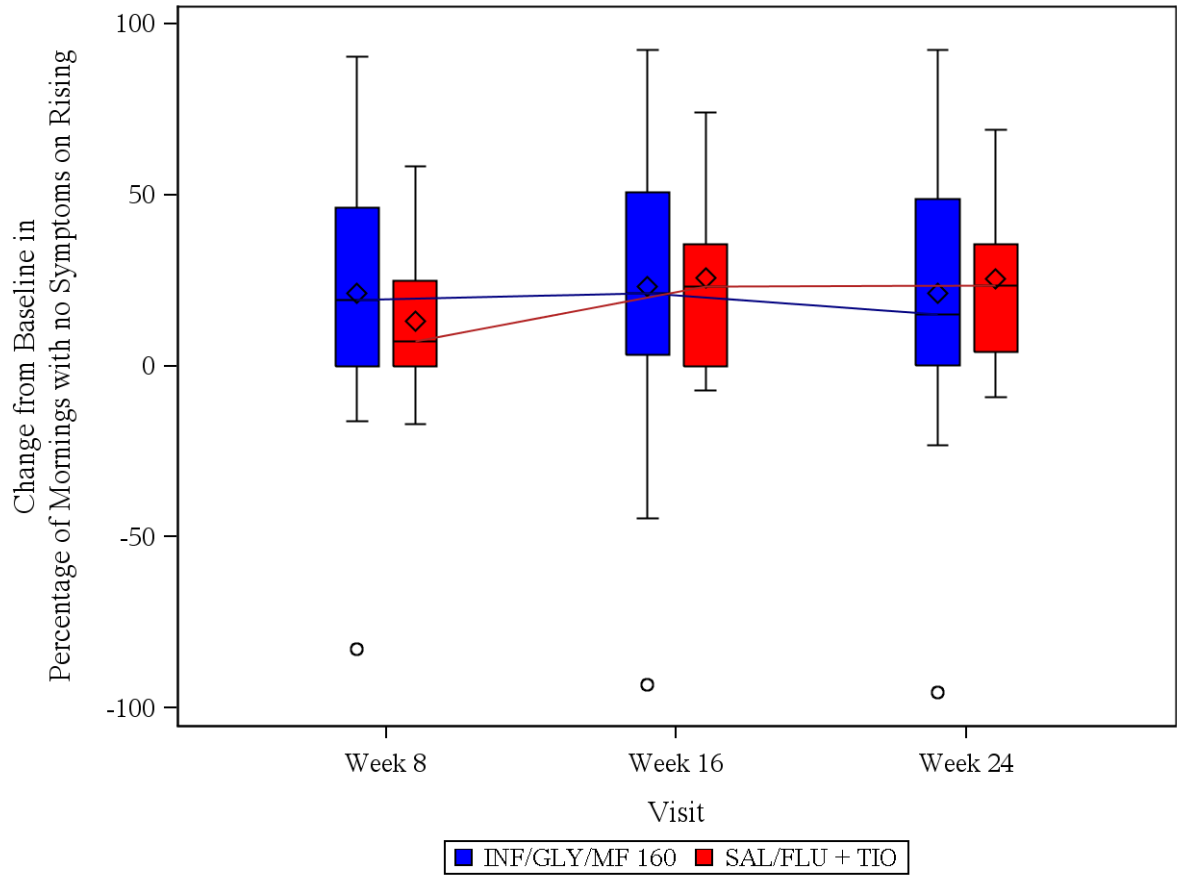


Figure 9.4.4 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Region (FAS), Region = Others



9.5 Boxplot: Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 9.5.1 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

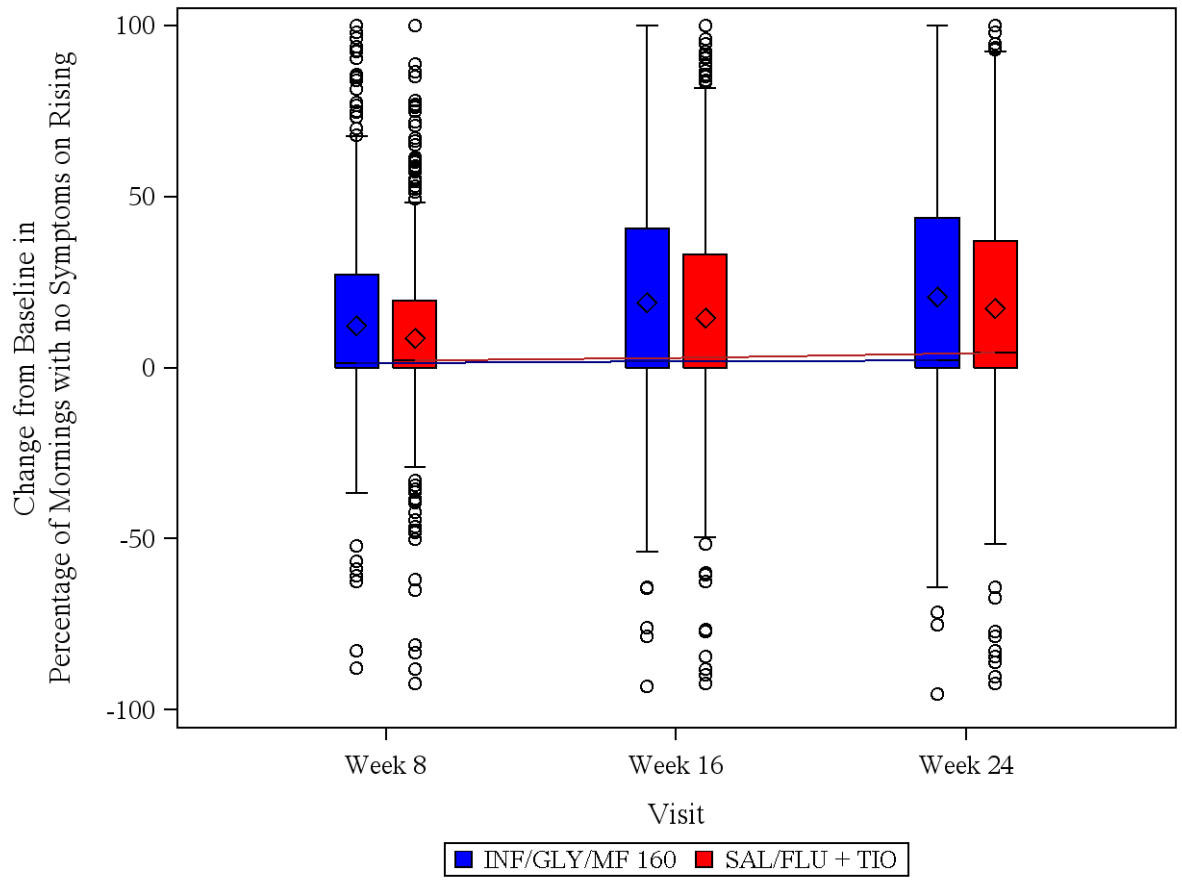
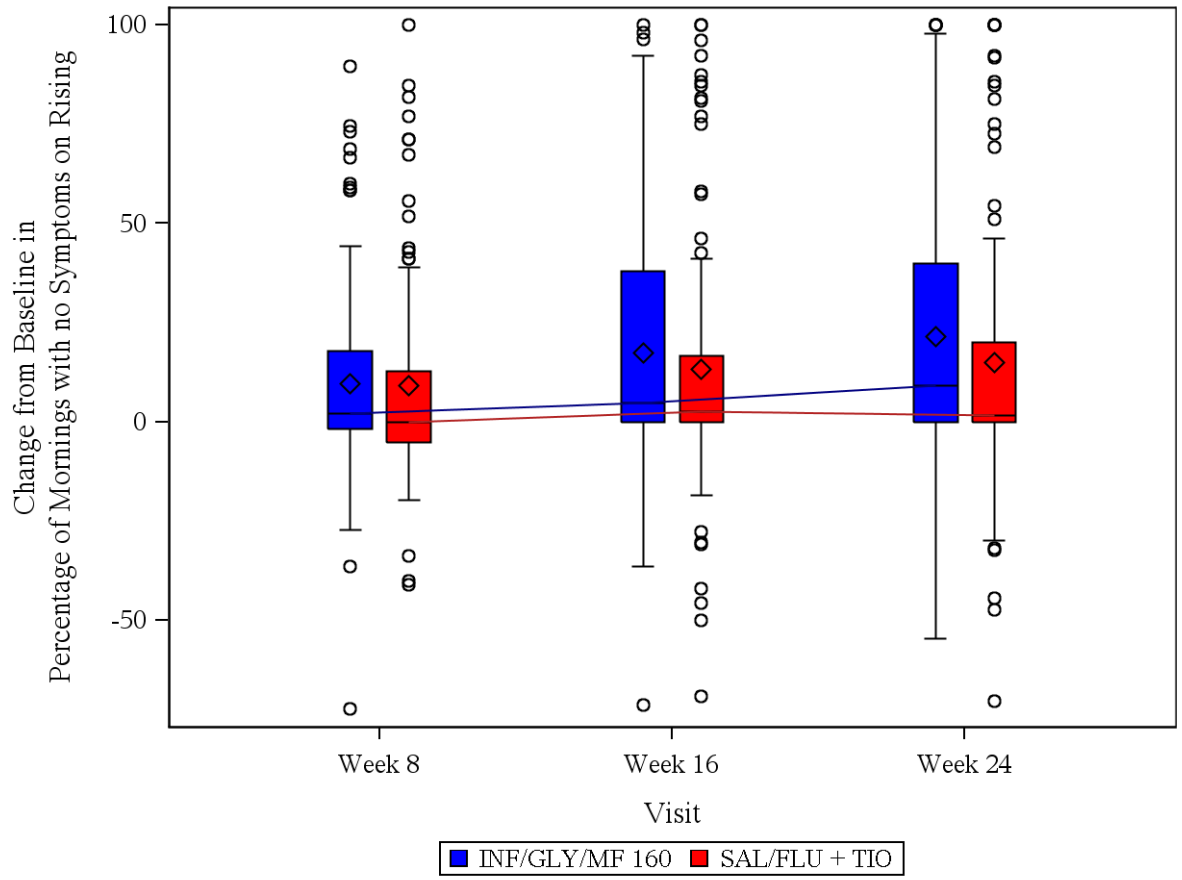


Figure 9.5.2 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.6 Boxplot: Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 9.6.1 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

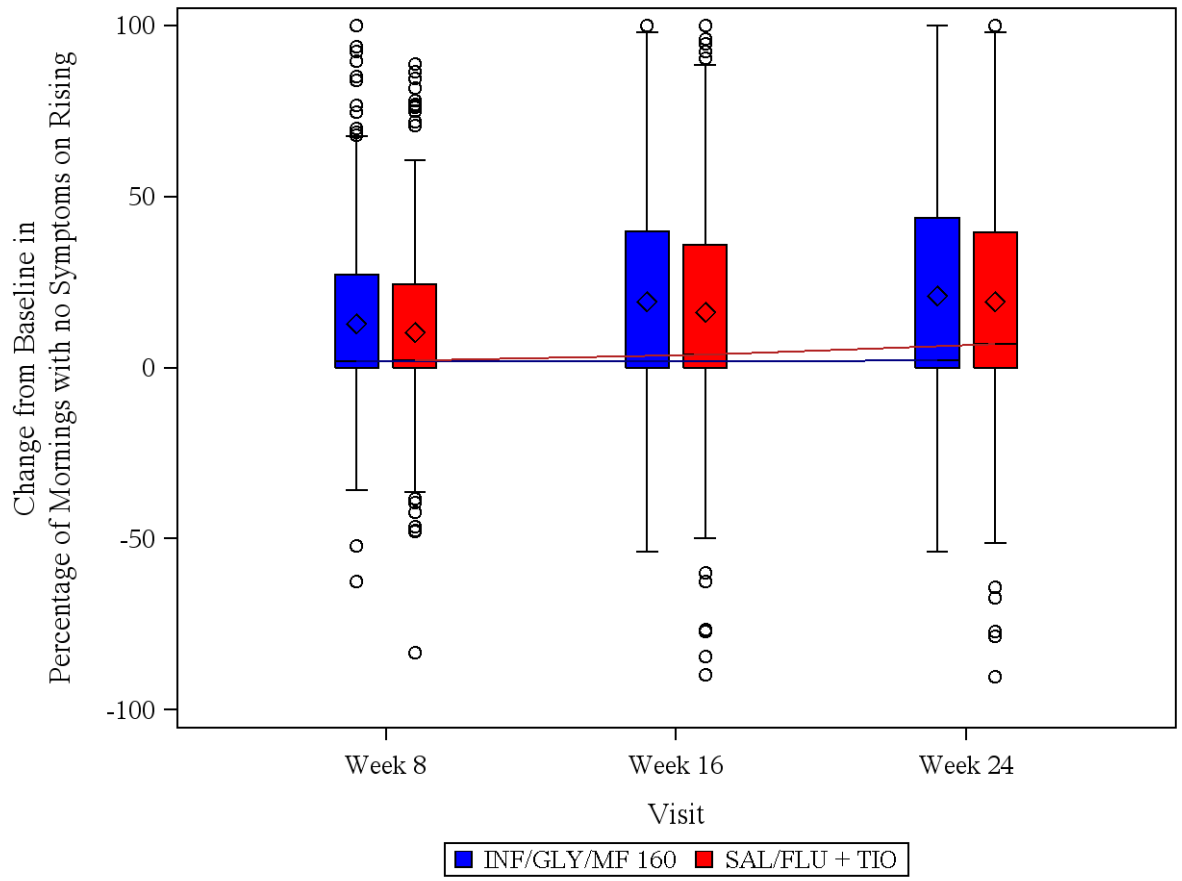
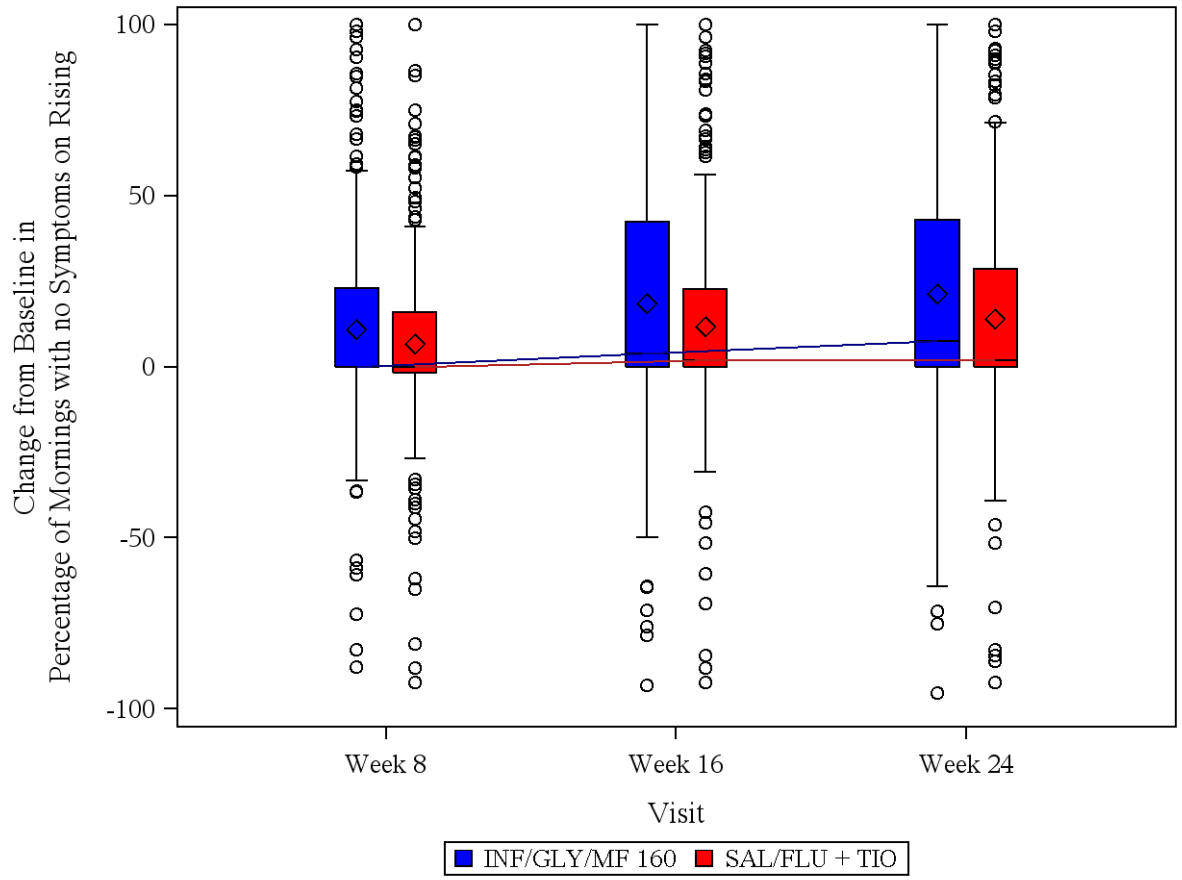
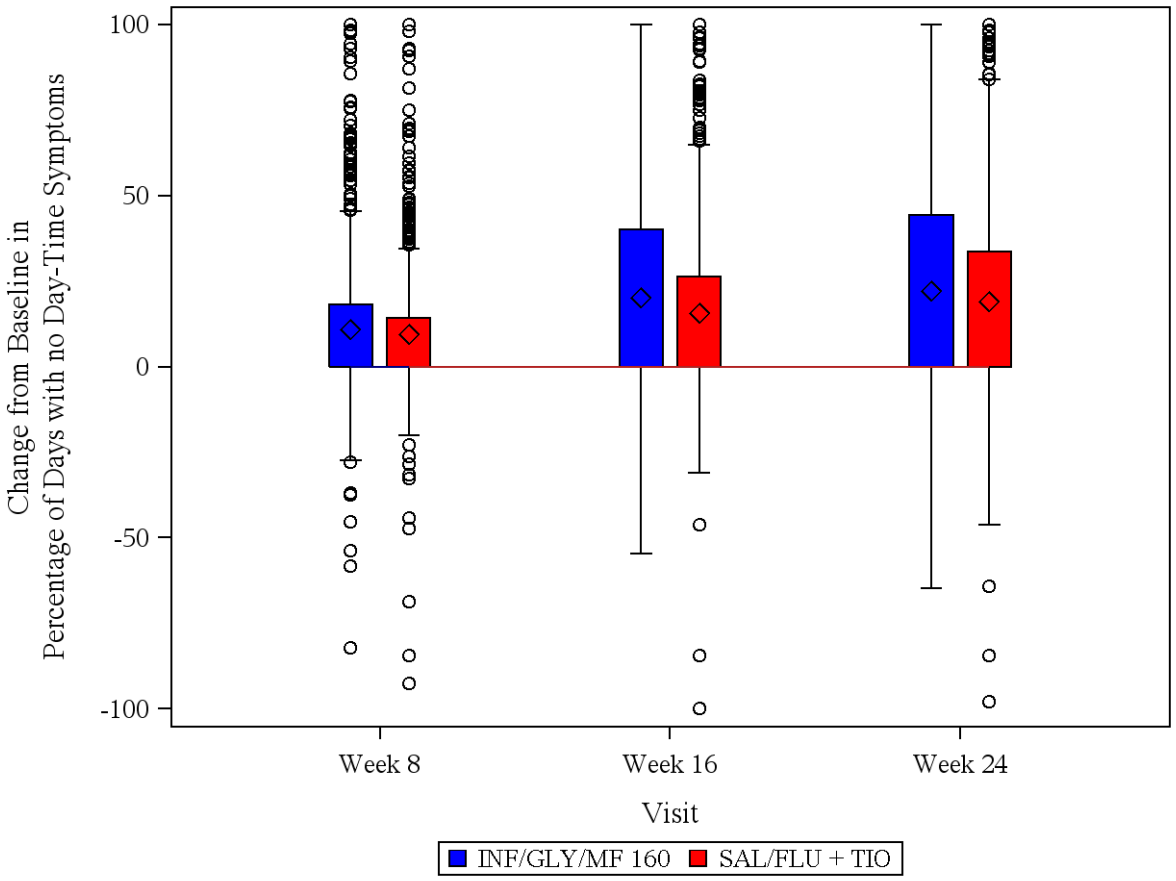


Figure 9.6.2 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



9.7 Boxplot: Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline (FAS)

Figure 9.7 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline (FAS)



9.8 Boxplot: Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Age (FAS)

Figure 9.8.1 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Age (FAS), Age = 18-39 years

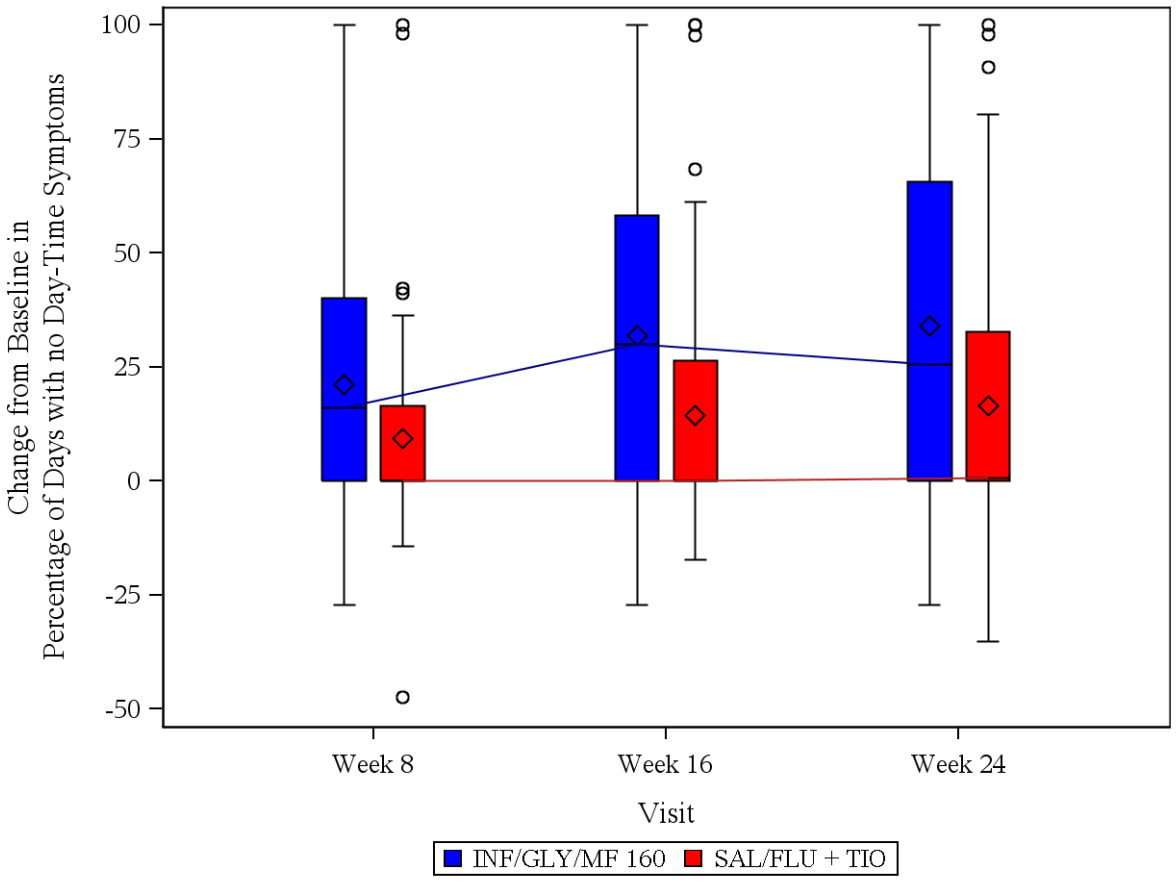


Figure 9.8.2 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Age (FAS), Age = 40-64 years

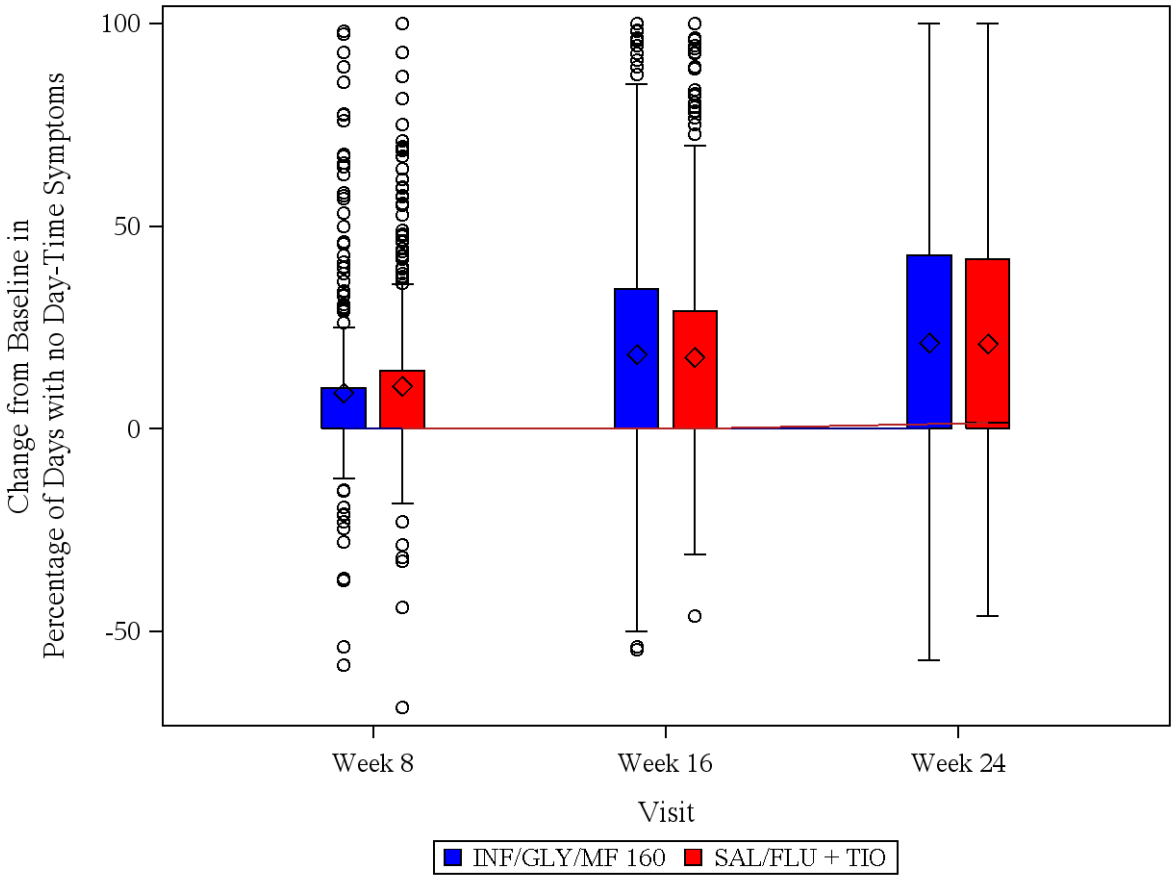
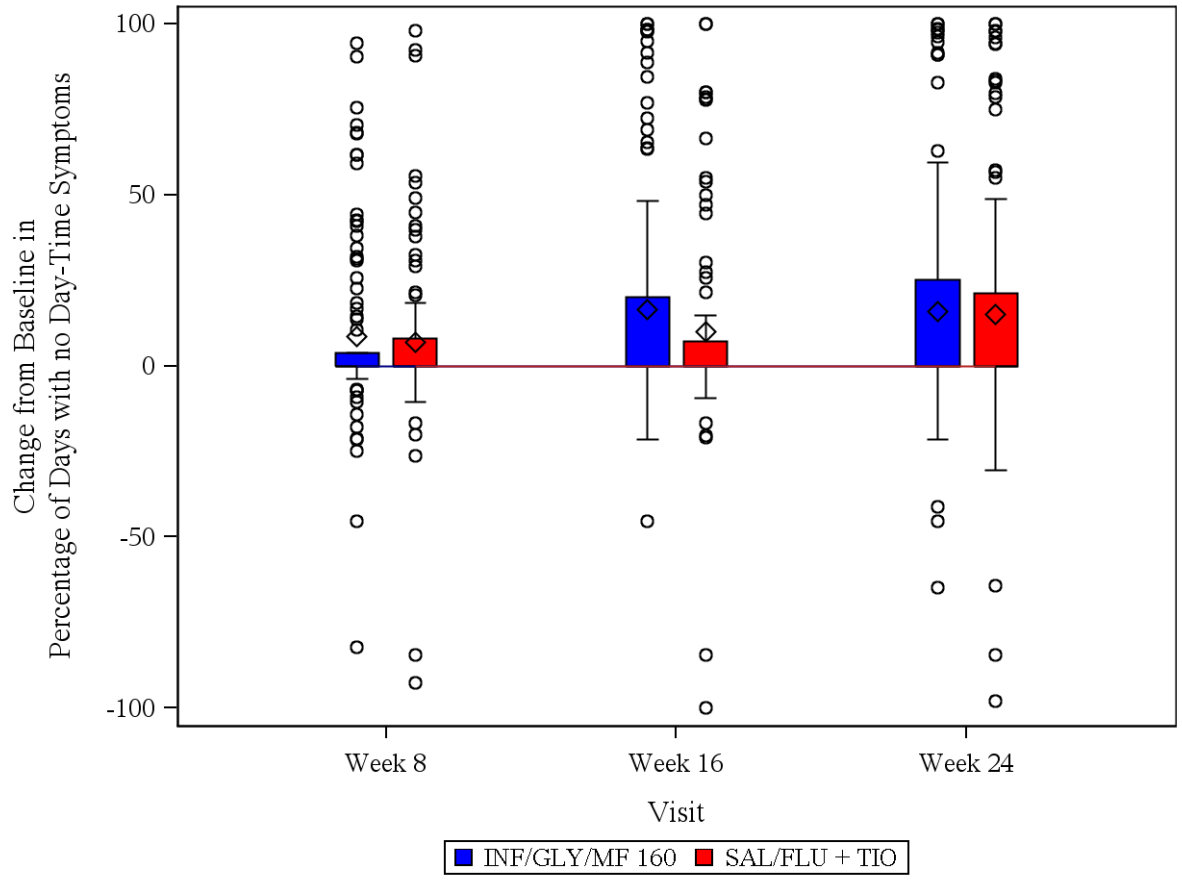


Figure 9.8.3 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Age (FAS), Age = ≥65 years



9.9 Boxplot: Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Gender (FAS)

Figure 9.9.1 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Gender (FAS), Gender = Male

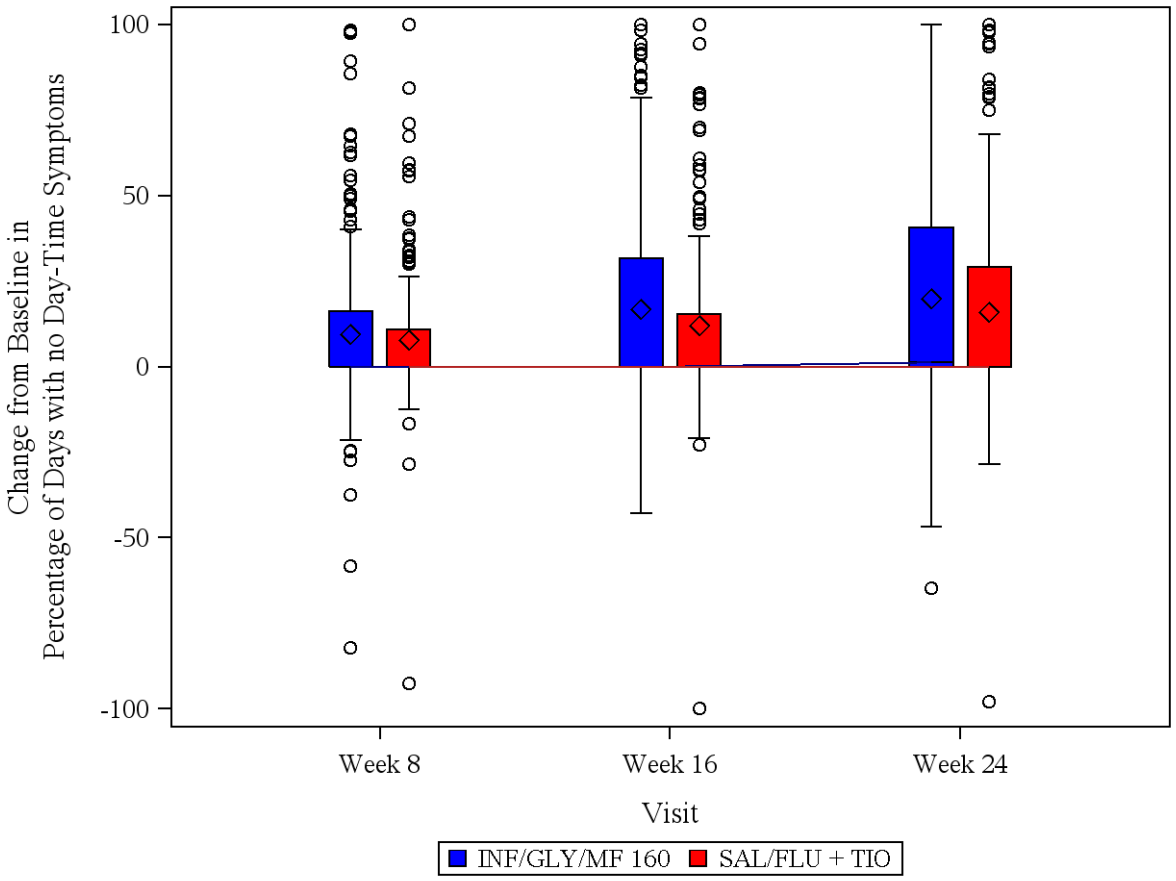
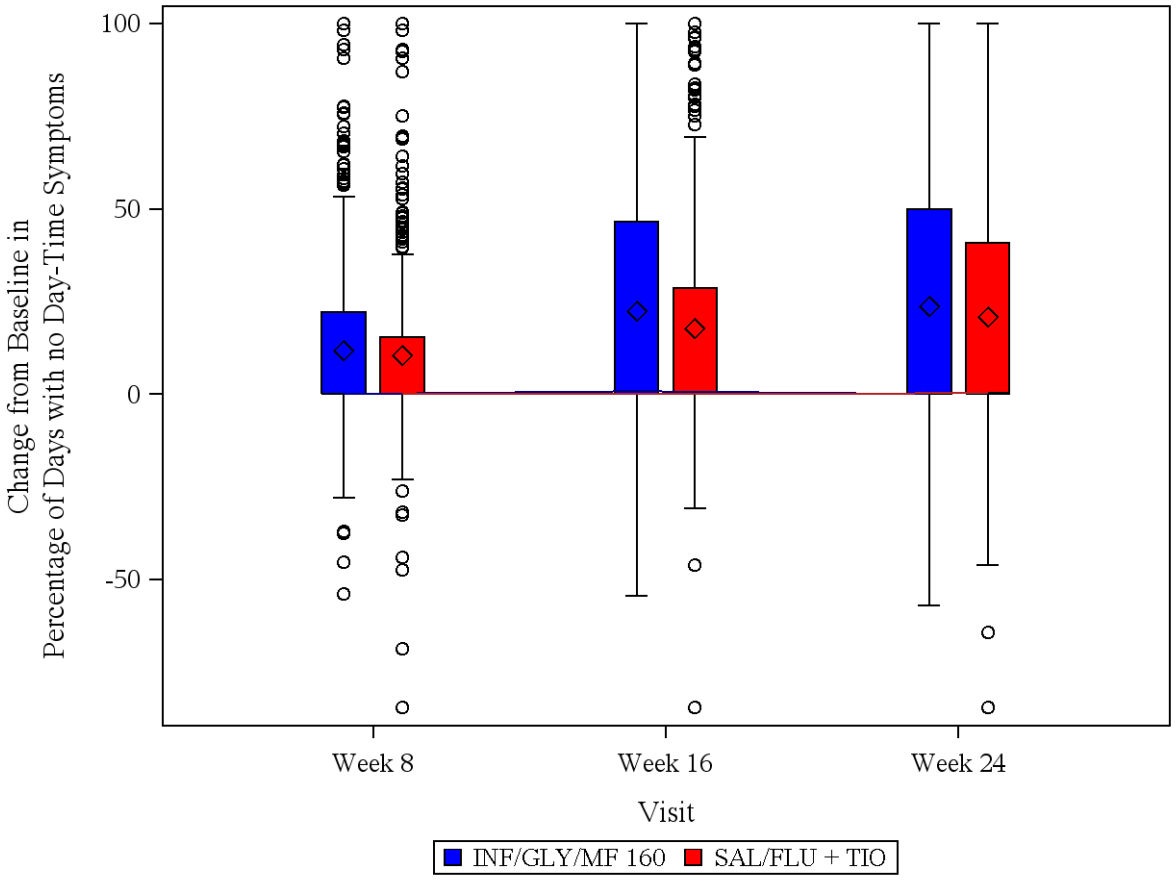


Figure 9.9.2 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Gender (FAS), Gender = Female



9.10 Boxplot: Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Region (FAS)

Figure 9.10.1 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Region (FAS), Region = Asia

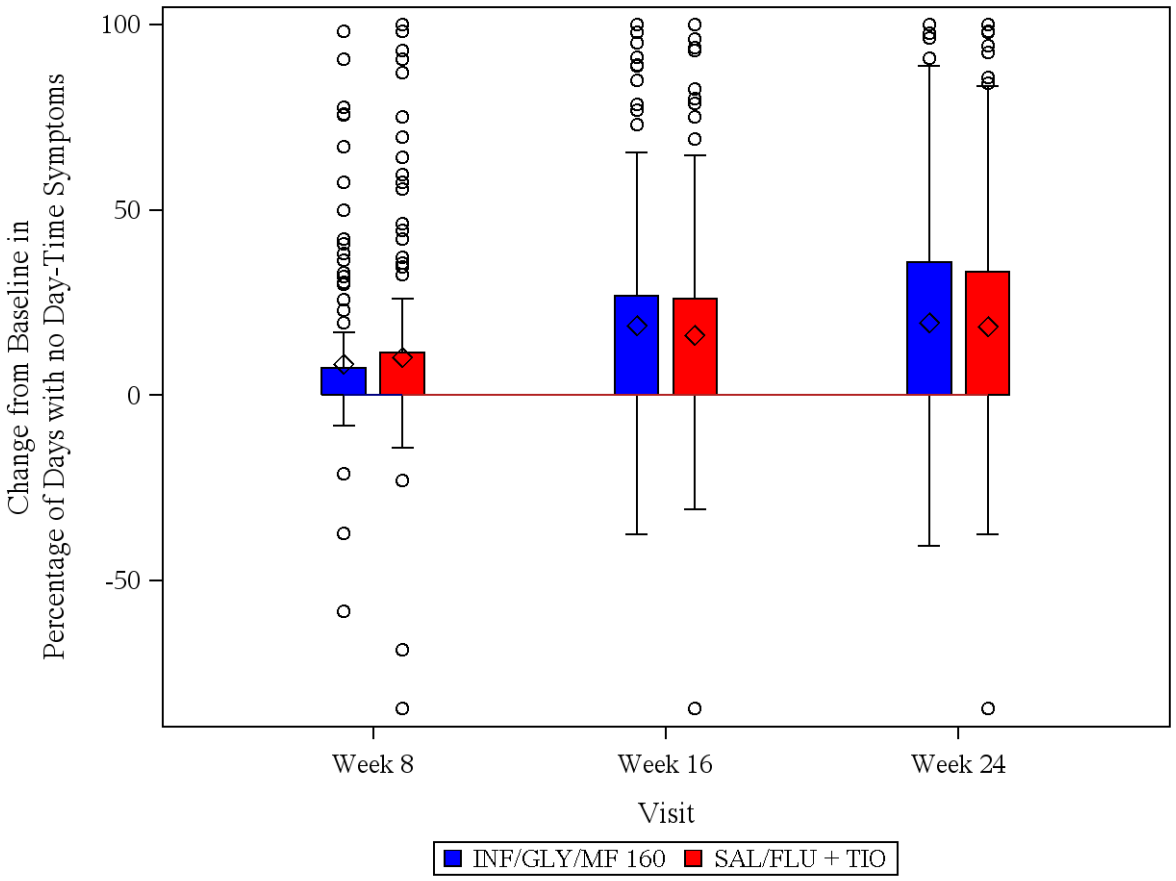


Figure 9.10.2 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Region (FAS), Region = Europe

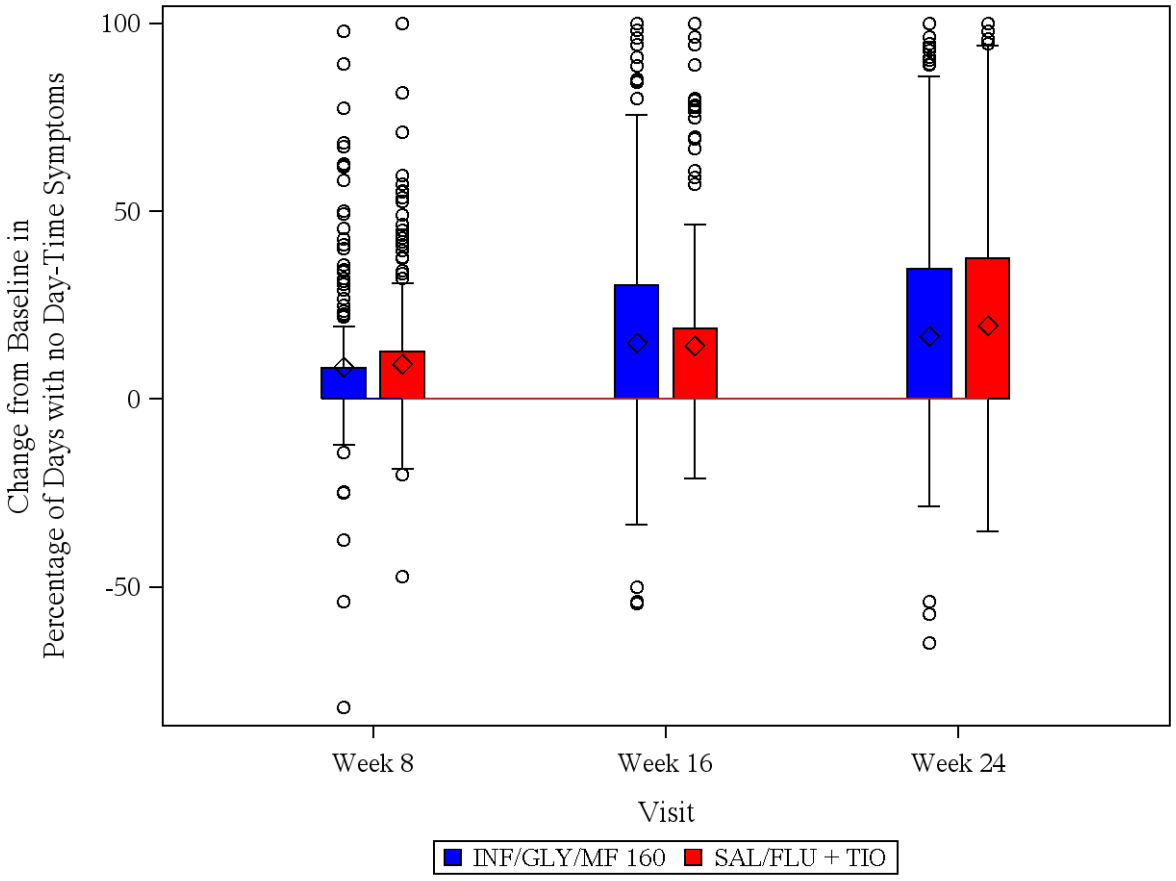


Figure 9.10.3 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Region (FAS), Region = Latin America

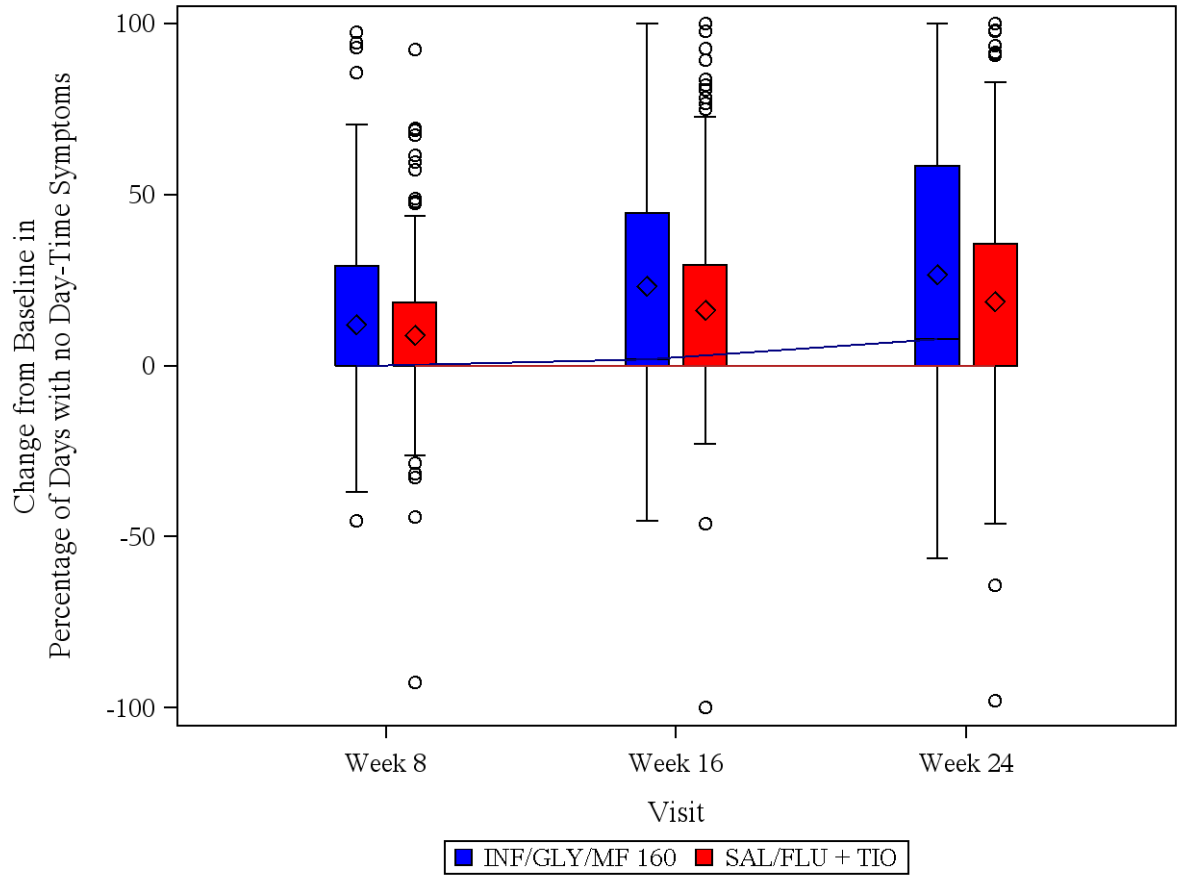
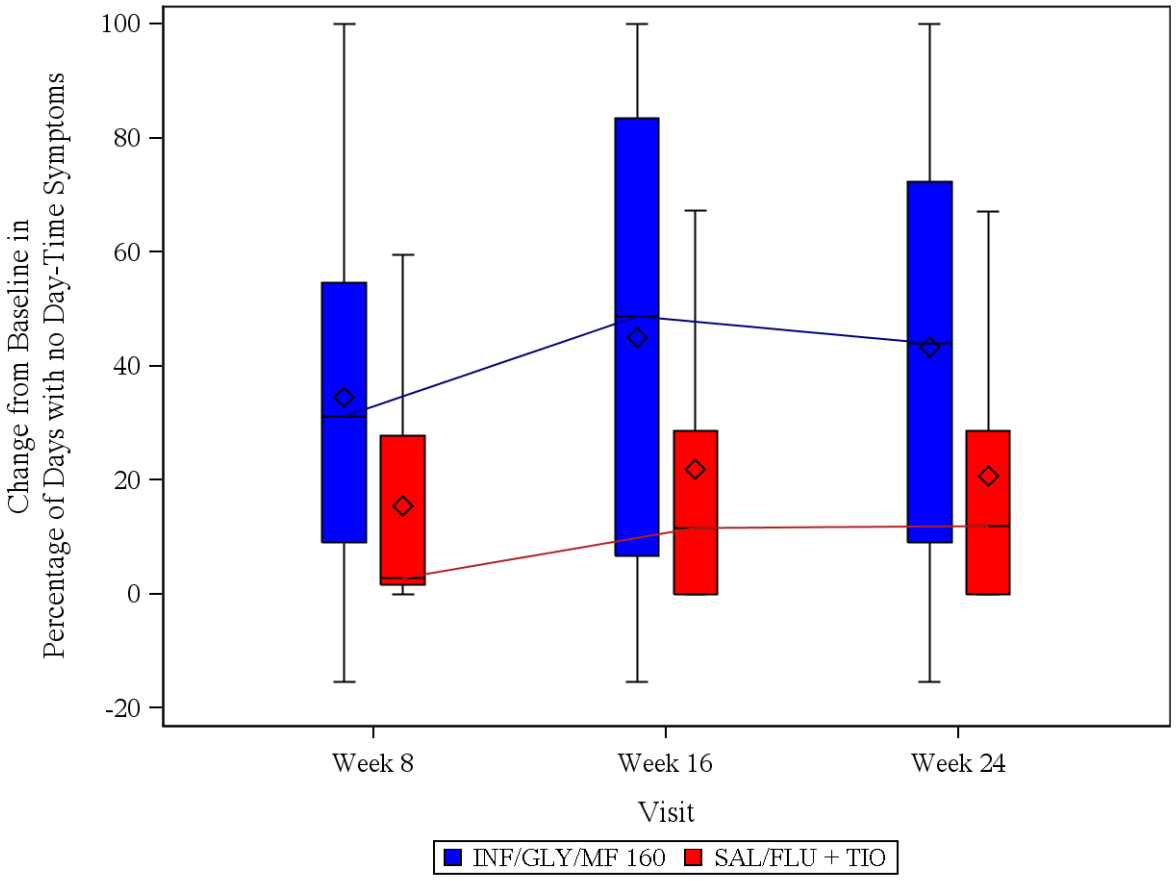


Figure 9.10.4 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Region (FAS), Region = Others



9.11 Boxplot: Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 9.11.1 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

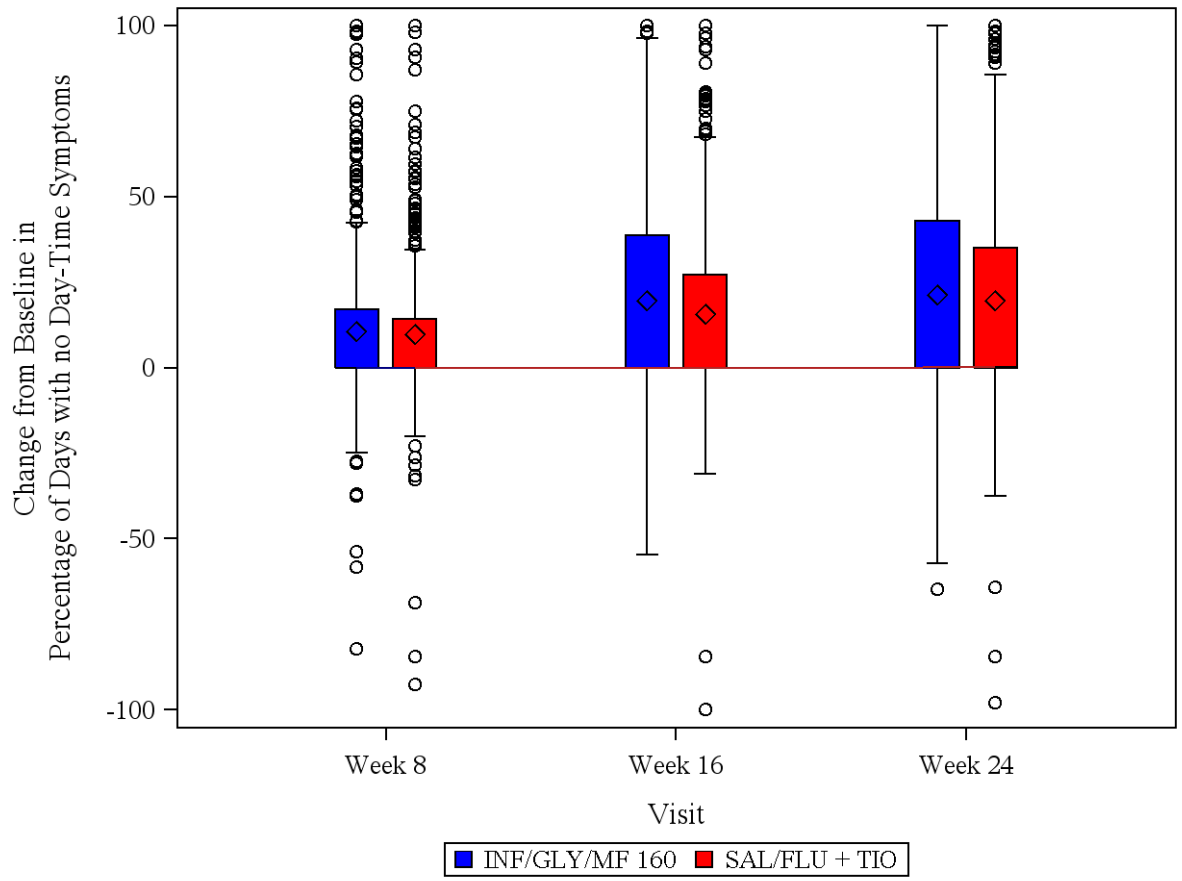
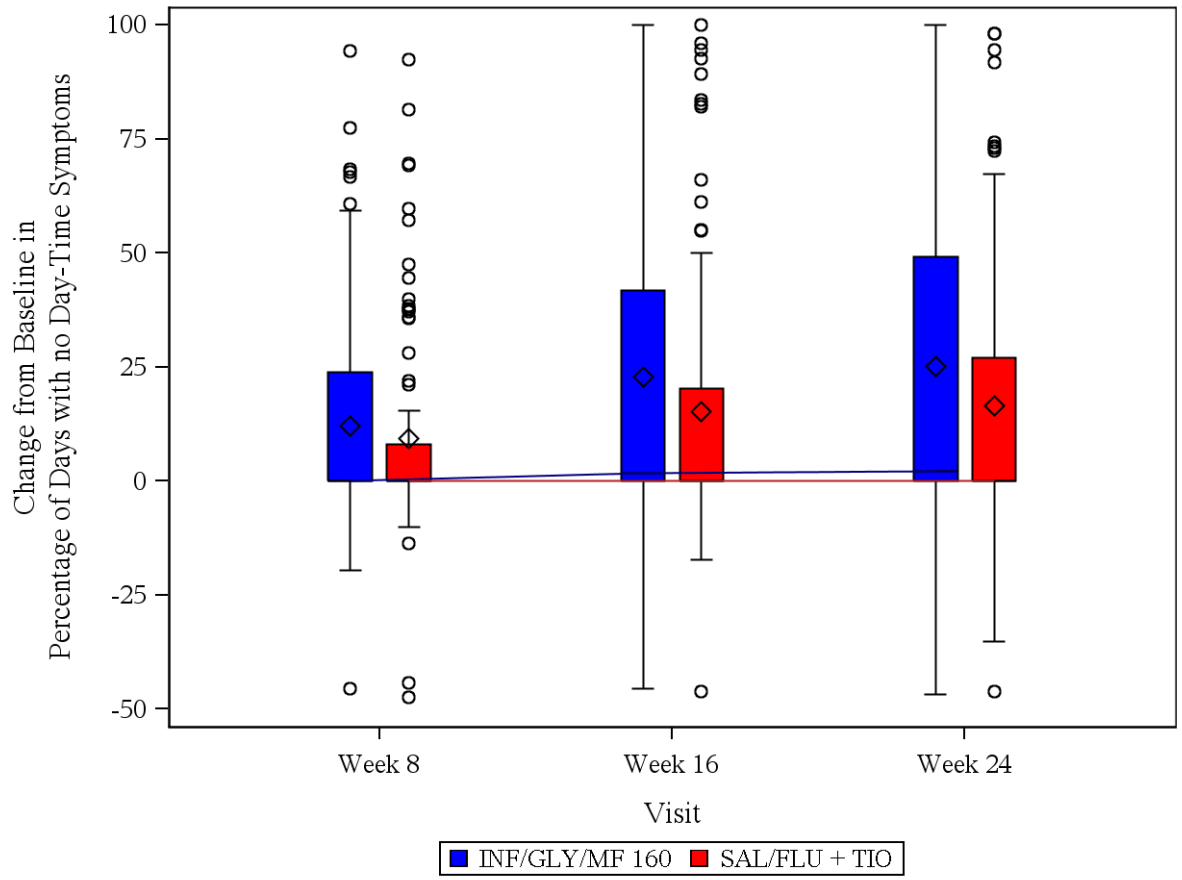


Figure 9.11.2 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.12 Boxplot: Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 9.12.1 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

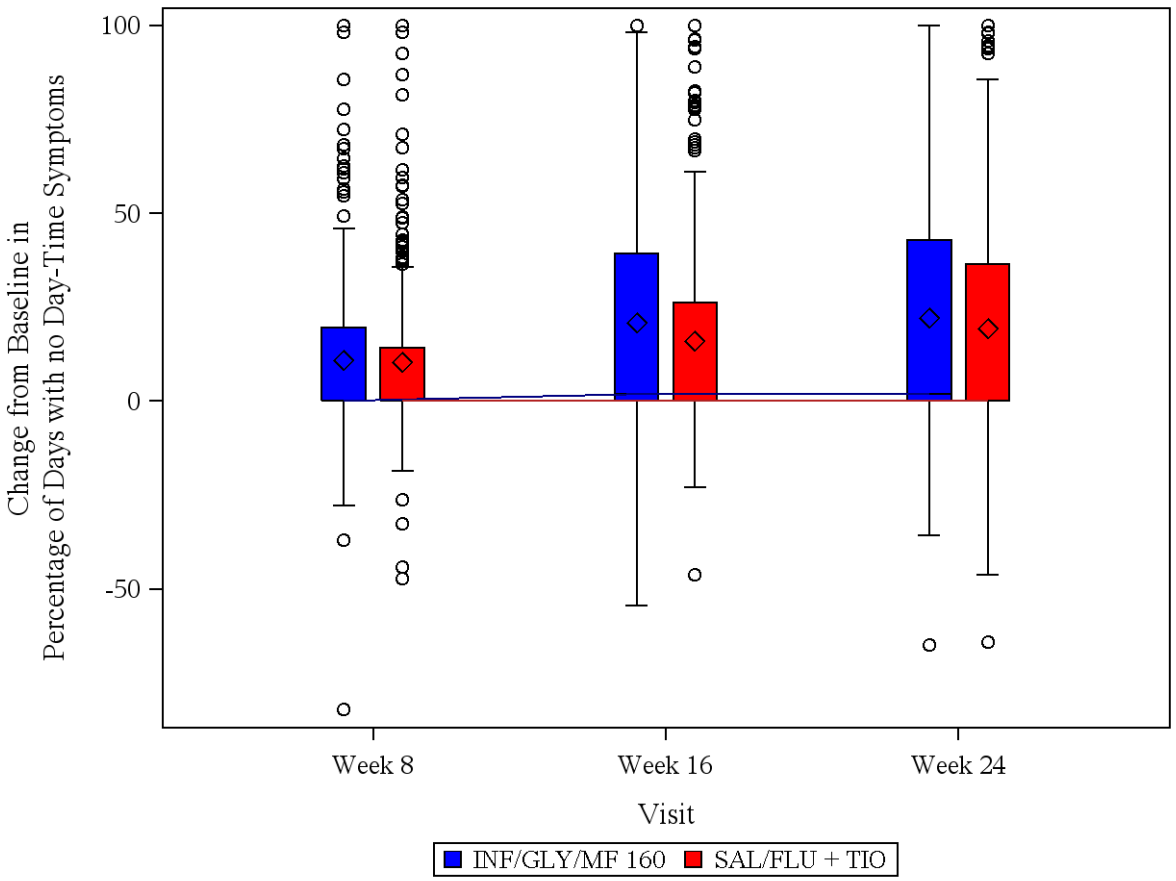
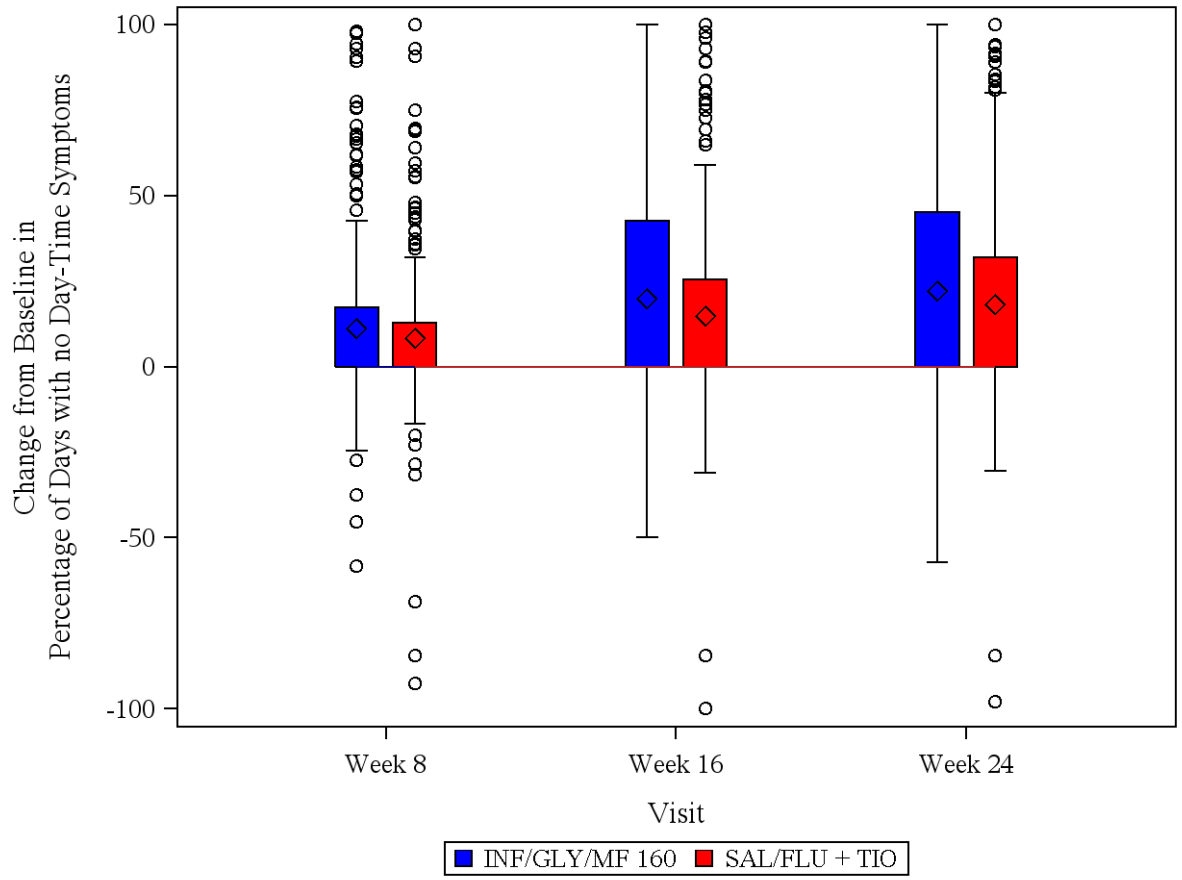
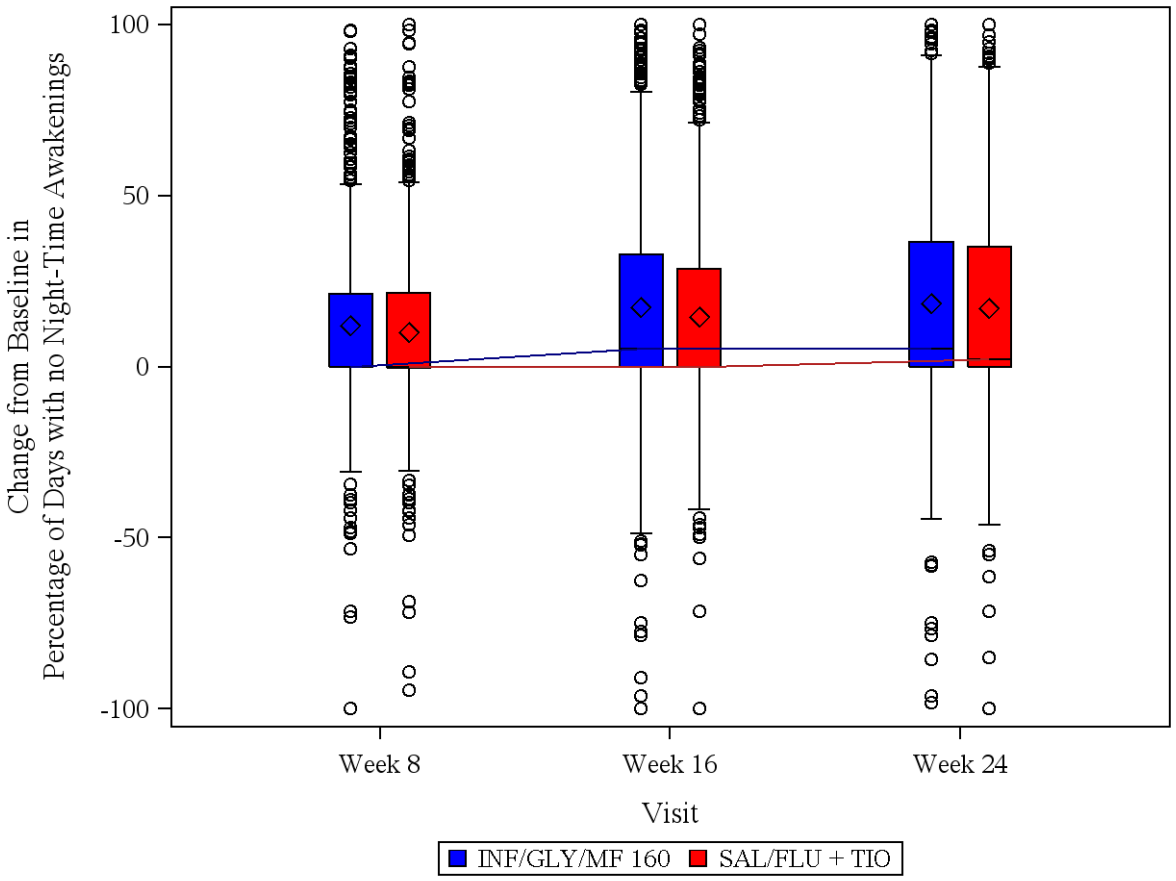


Figure 9.12.2 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



9.13 Boxplot: Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline (FAS)

Figure 9.13 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline (FAS)



9.14 Boxplot: Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Age (FAS)

Figure 9.14.1 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Age (FAS), Age = 18-39 years

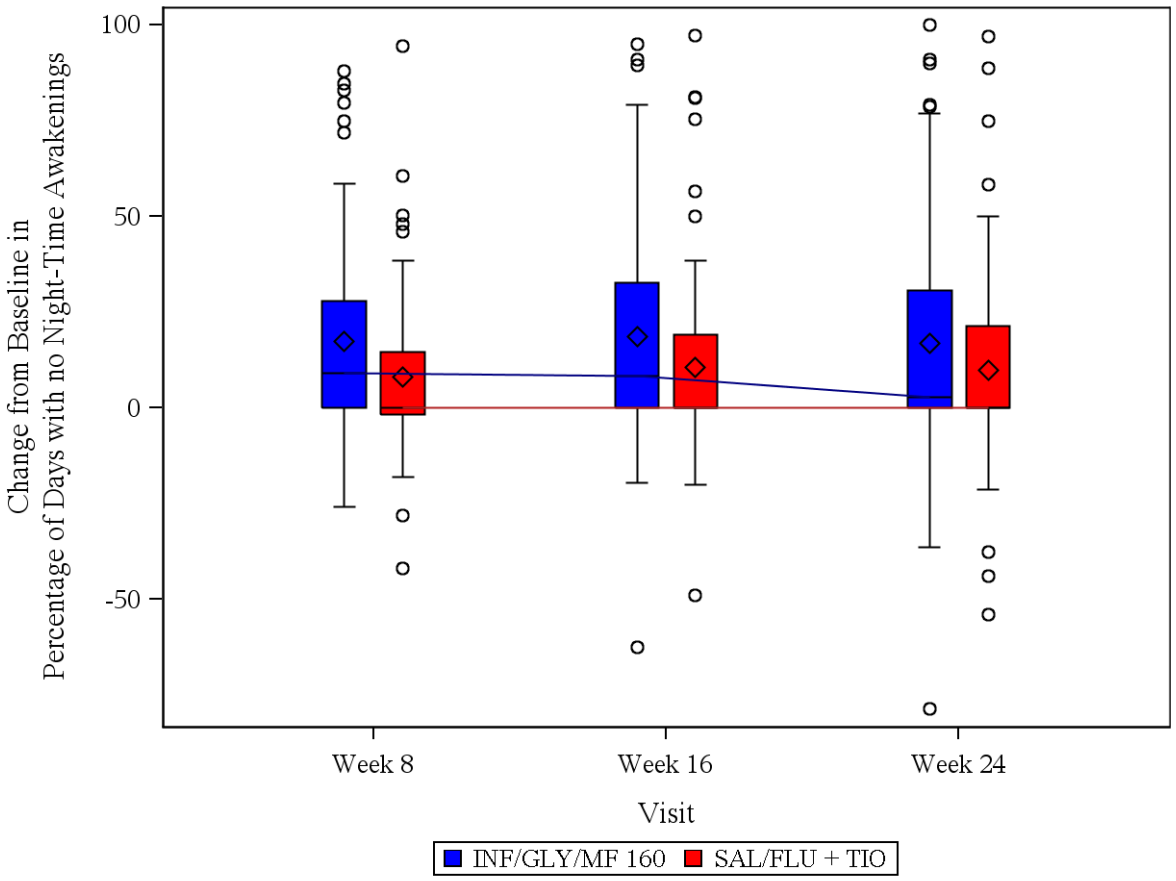


Figure 9.14.2 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Age (FAS), Age = 40-64 years

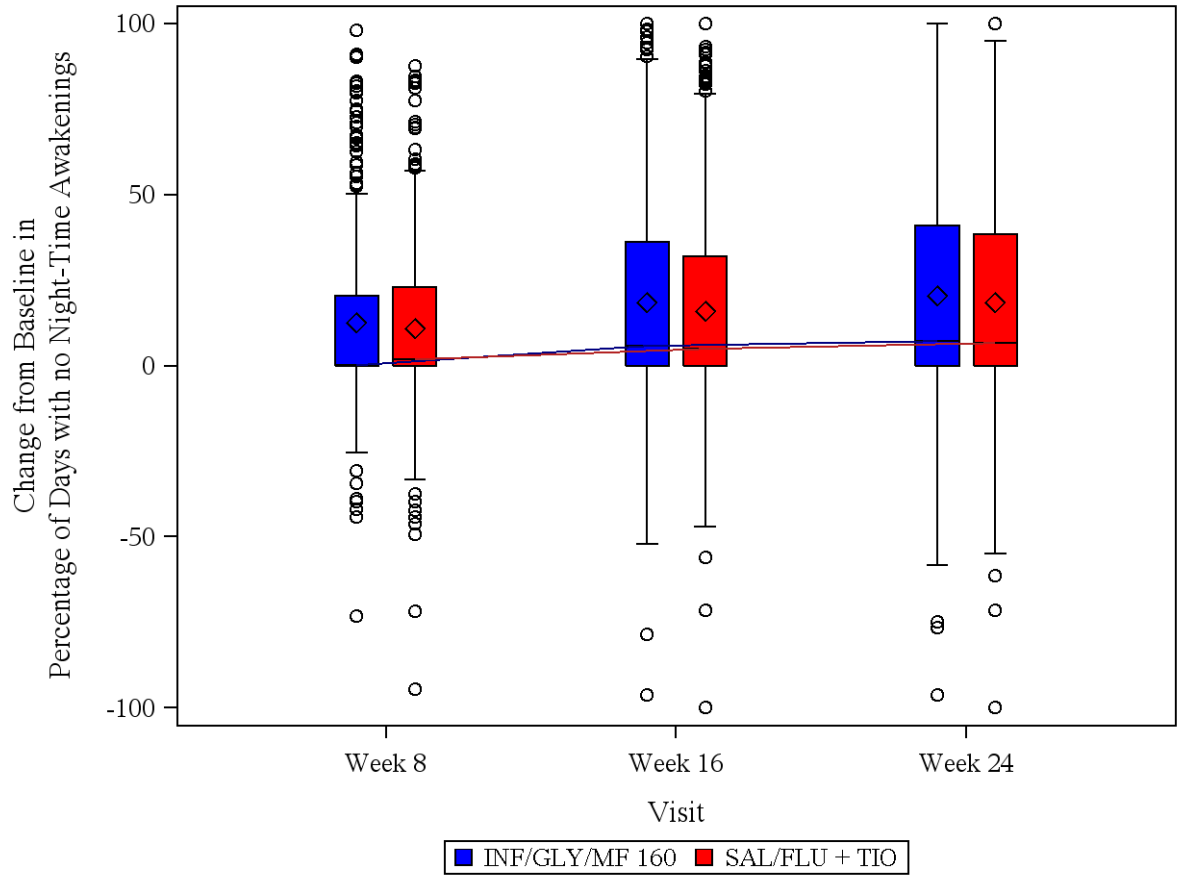
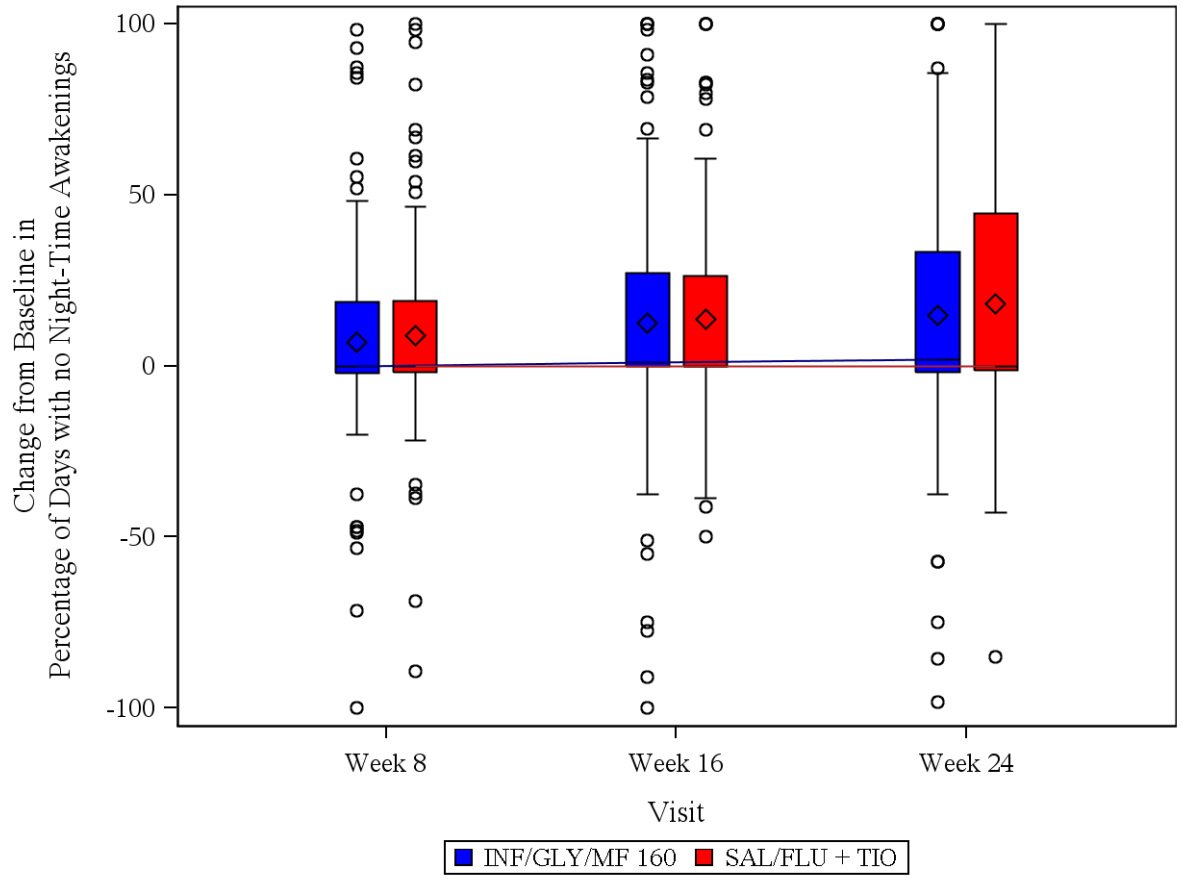


Figure 9.14.3 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Age (FAS), Age = ≥65 years



9.15 Boxplot: Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Gender (FAS)

Figure 9.15.1 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Gender (FAS), Gender = Male

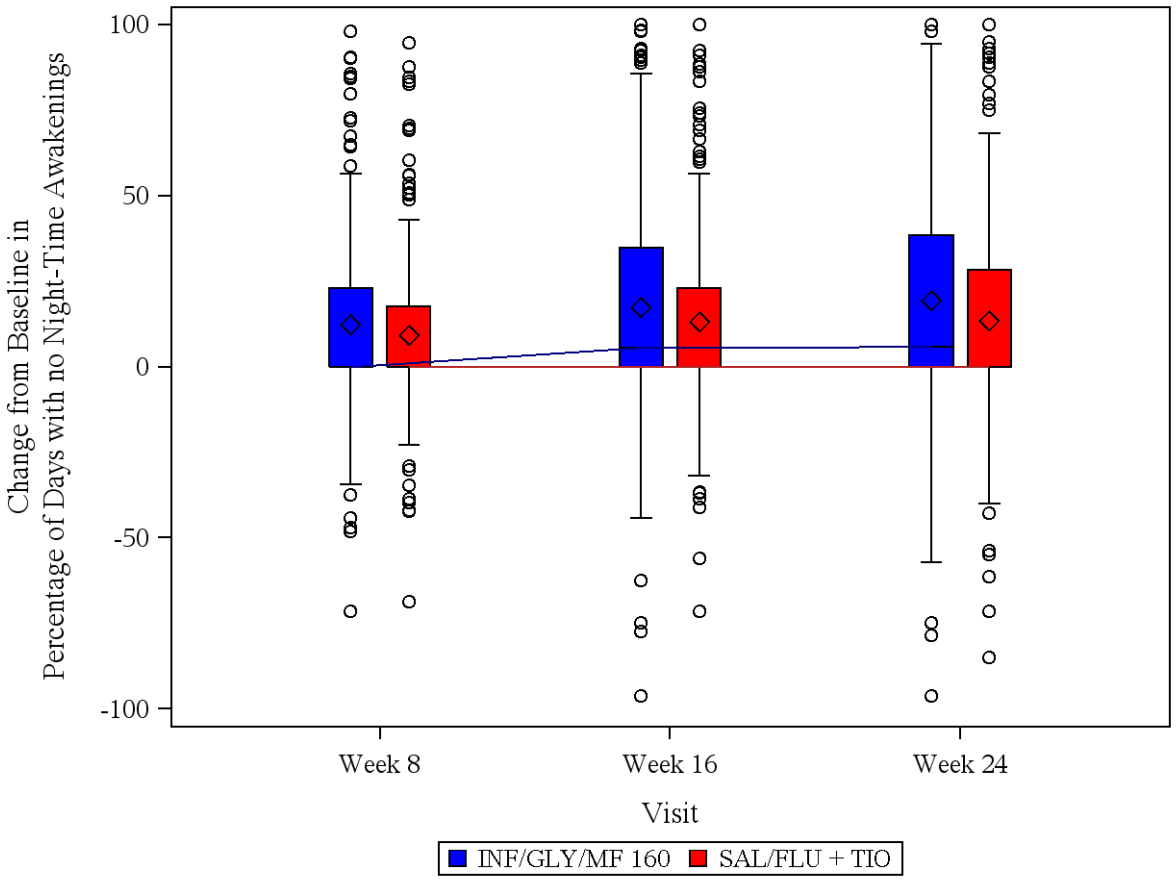
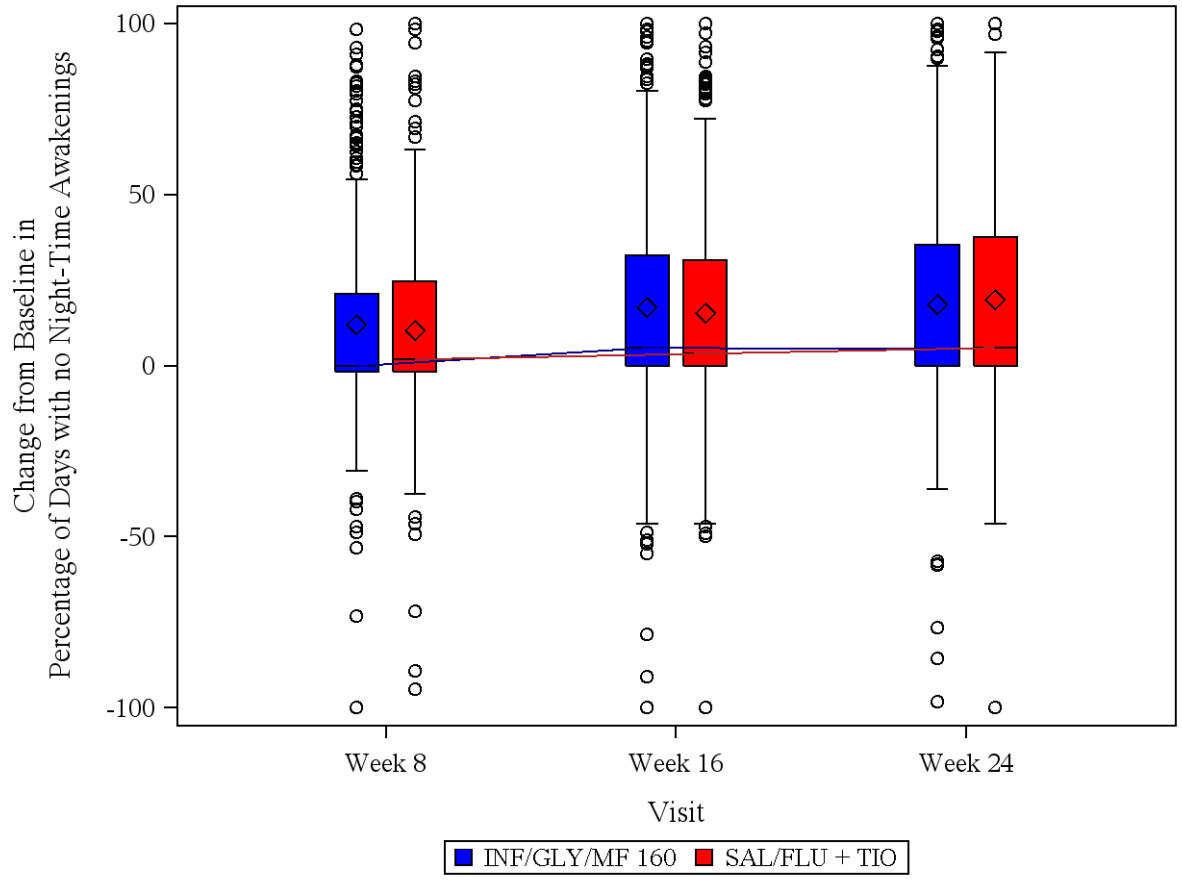


Figure 9.15.2 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Gender (FAS), Gender = Female



9.16 Boxplot: Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Region (FAS)

Figure 9.16.1 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Region (FAS), Region = Asia

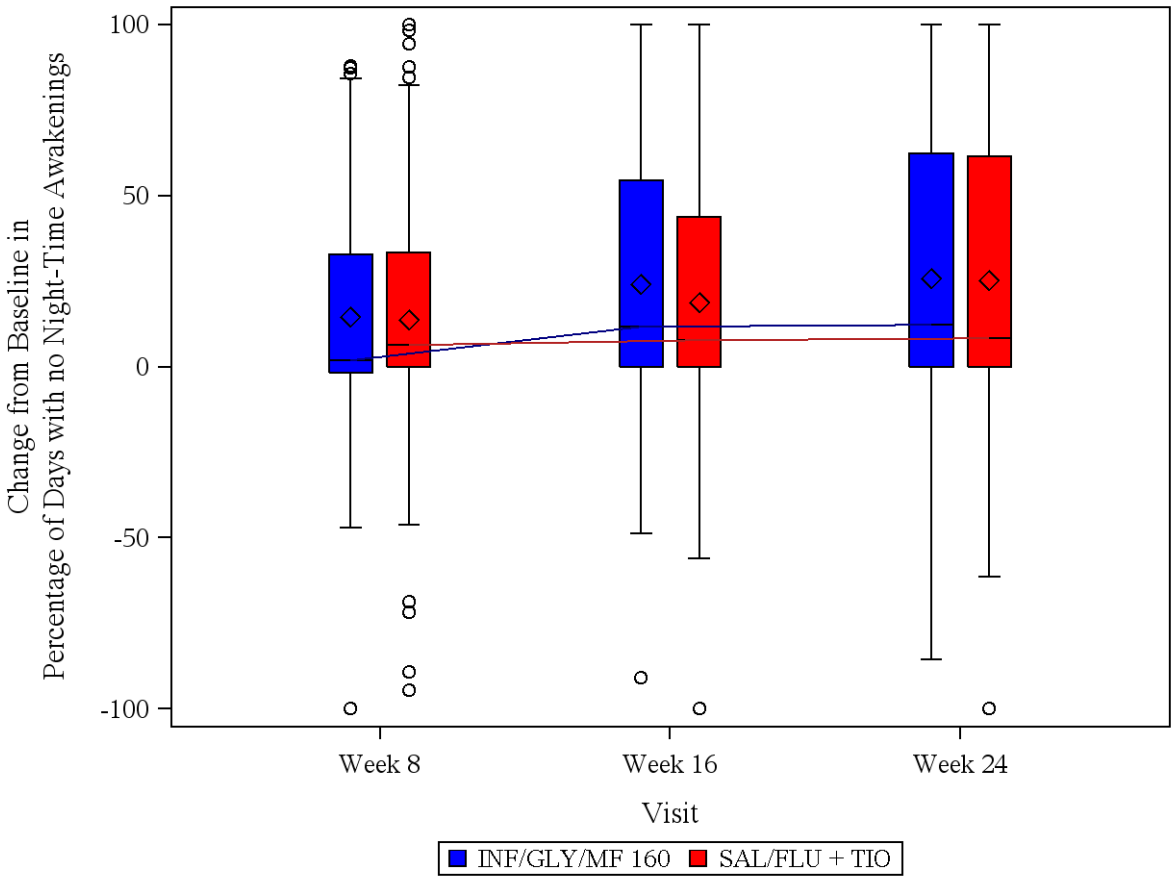


Figure 9.16.2 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Region (FAS), Region = Europe

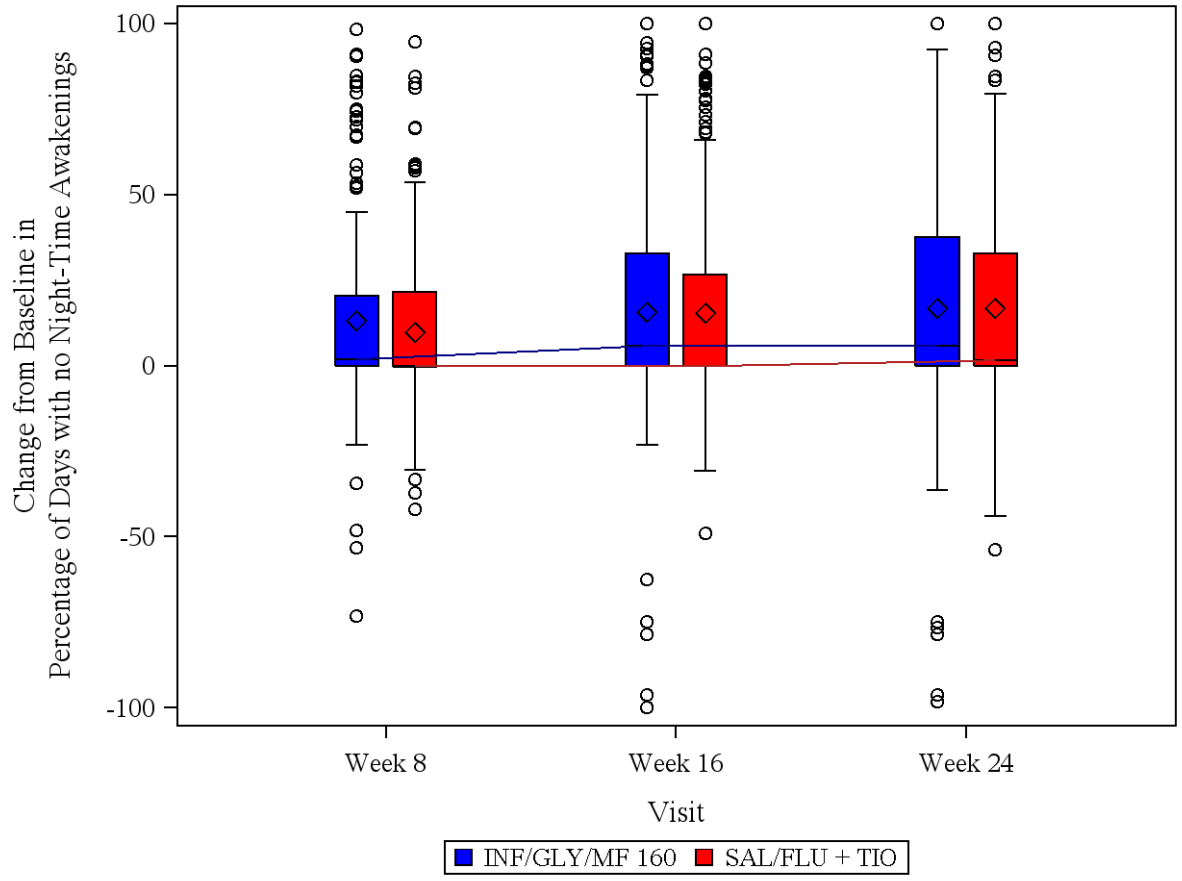


Figure 9.16.3 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Region (FAS), Region = Latin America

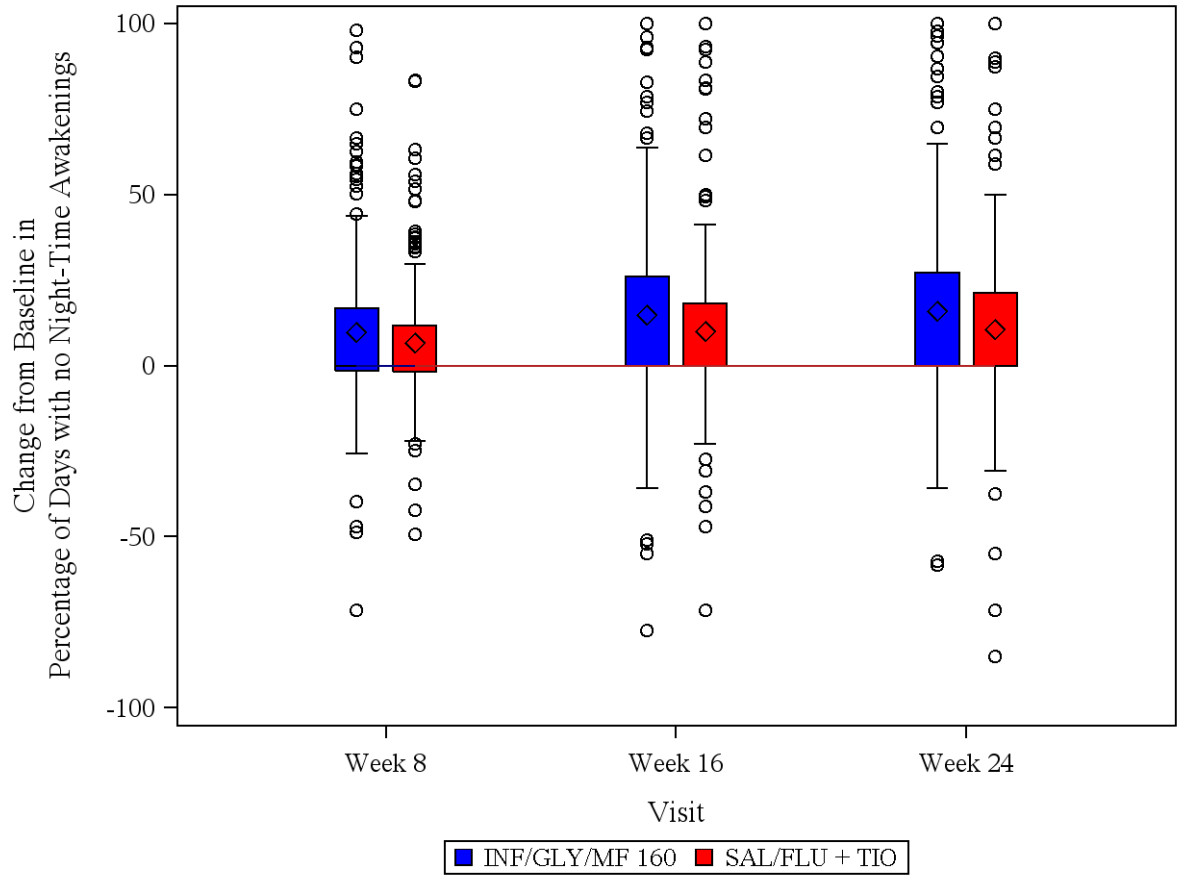
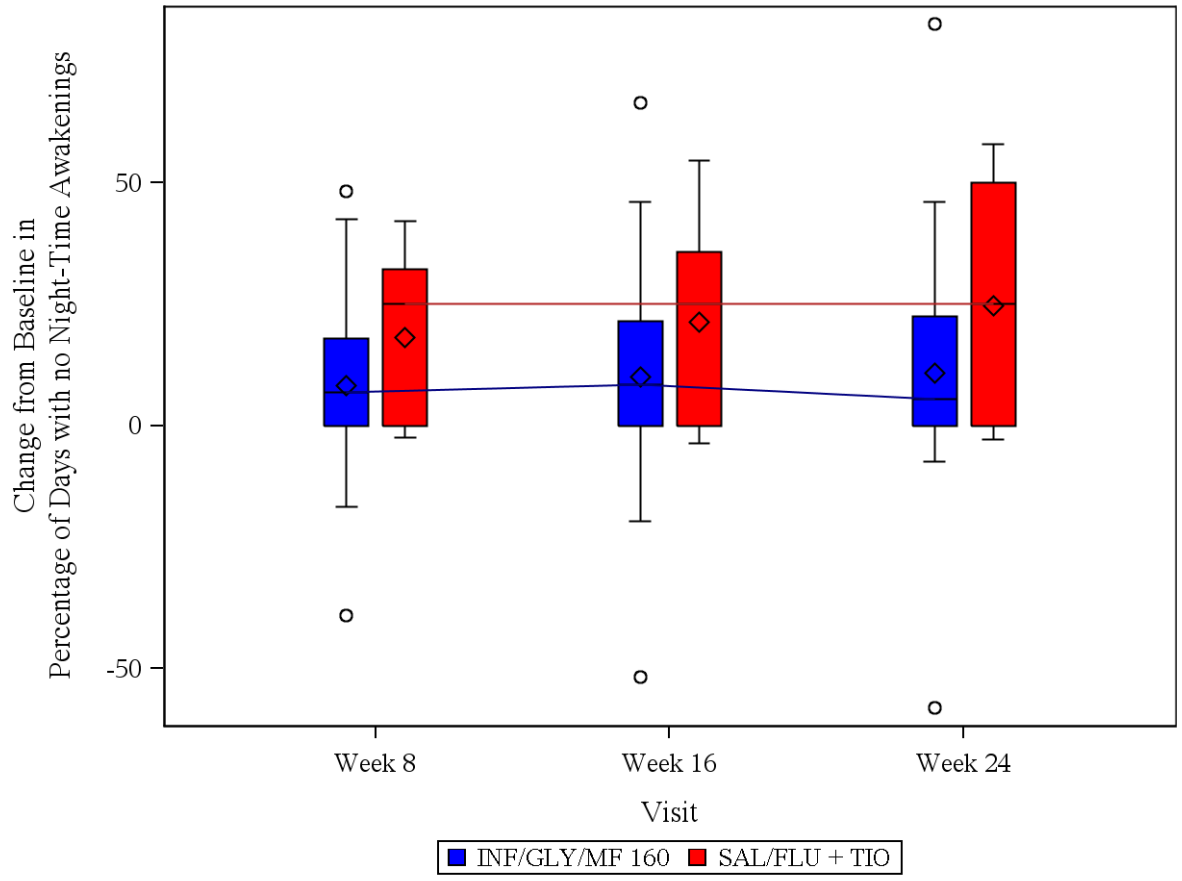


Figure 9.16.4 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Region (FAS), Region = Others



9.17 Boxplot: Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 9.17.1 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

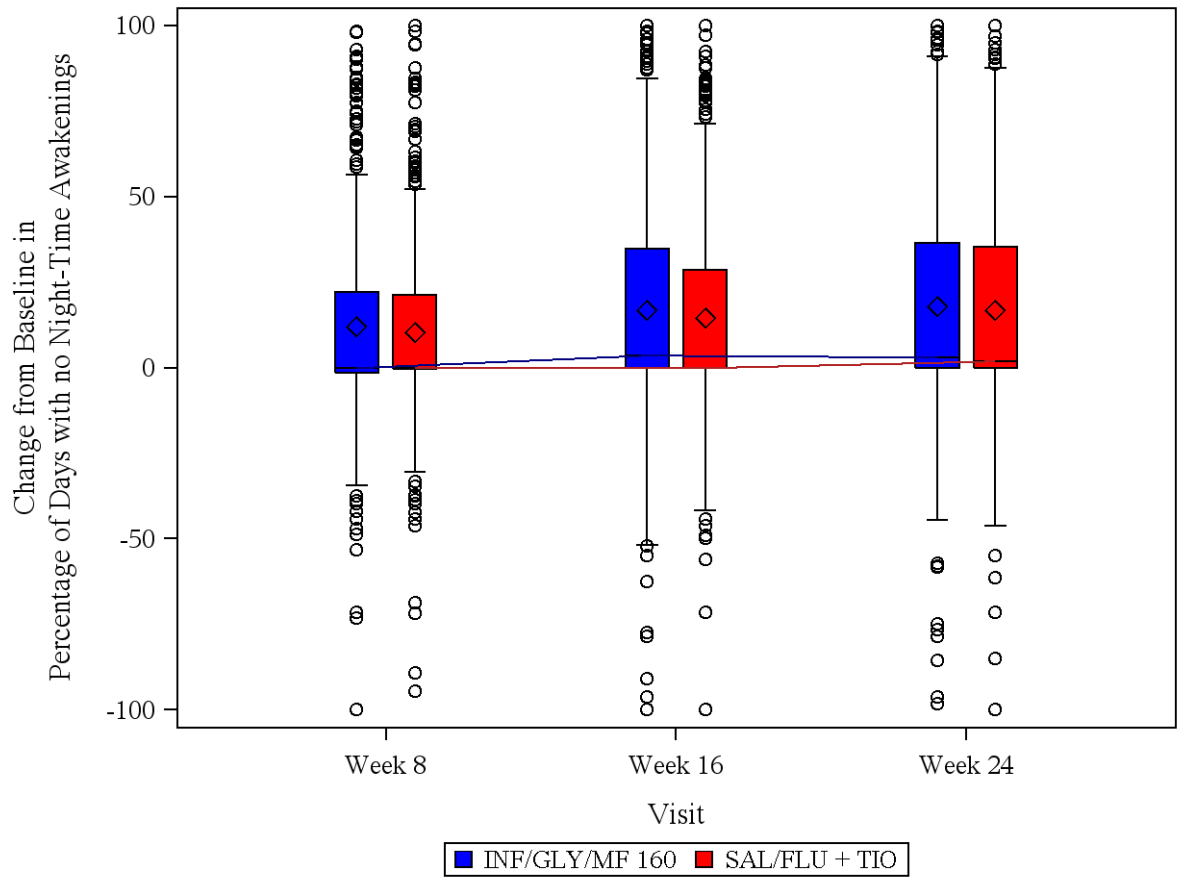
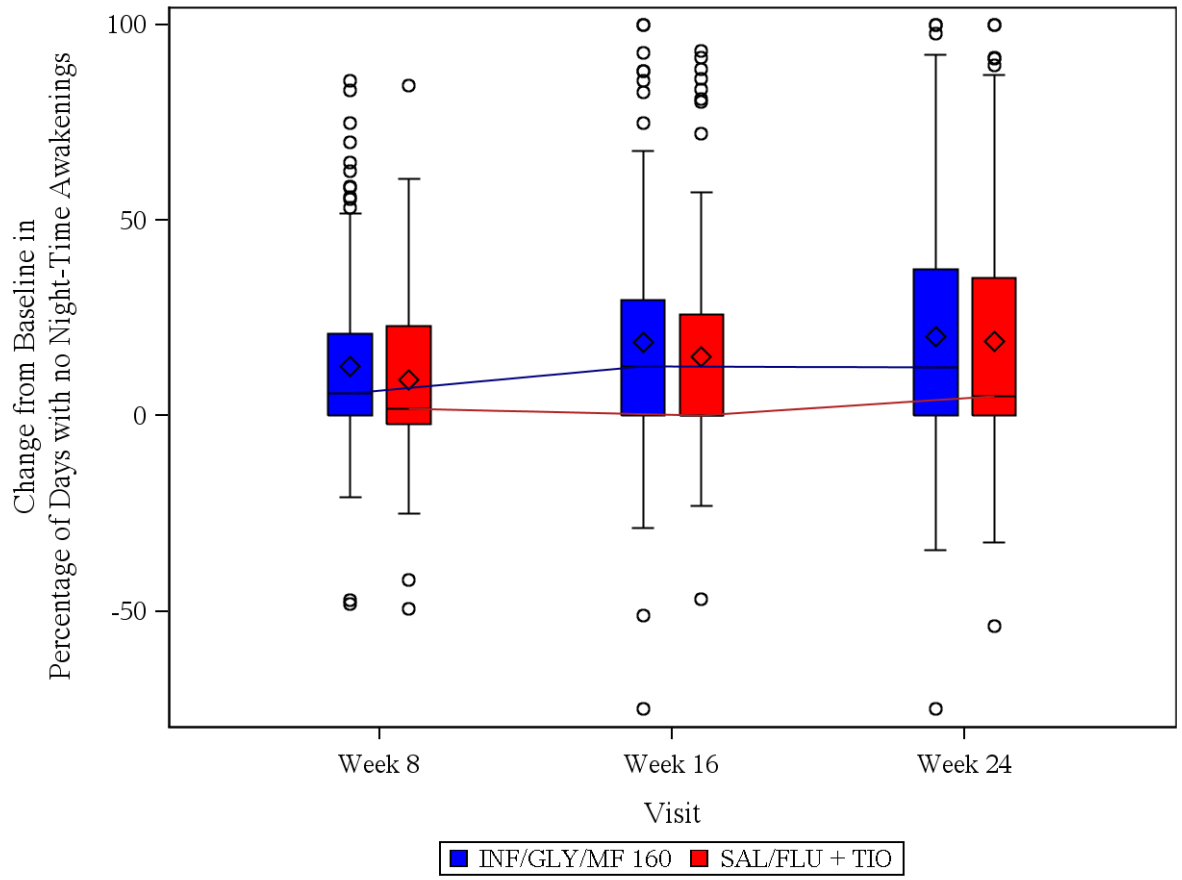


Figure 9.17.2 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.18 Boxplot: Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 9.18.1 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

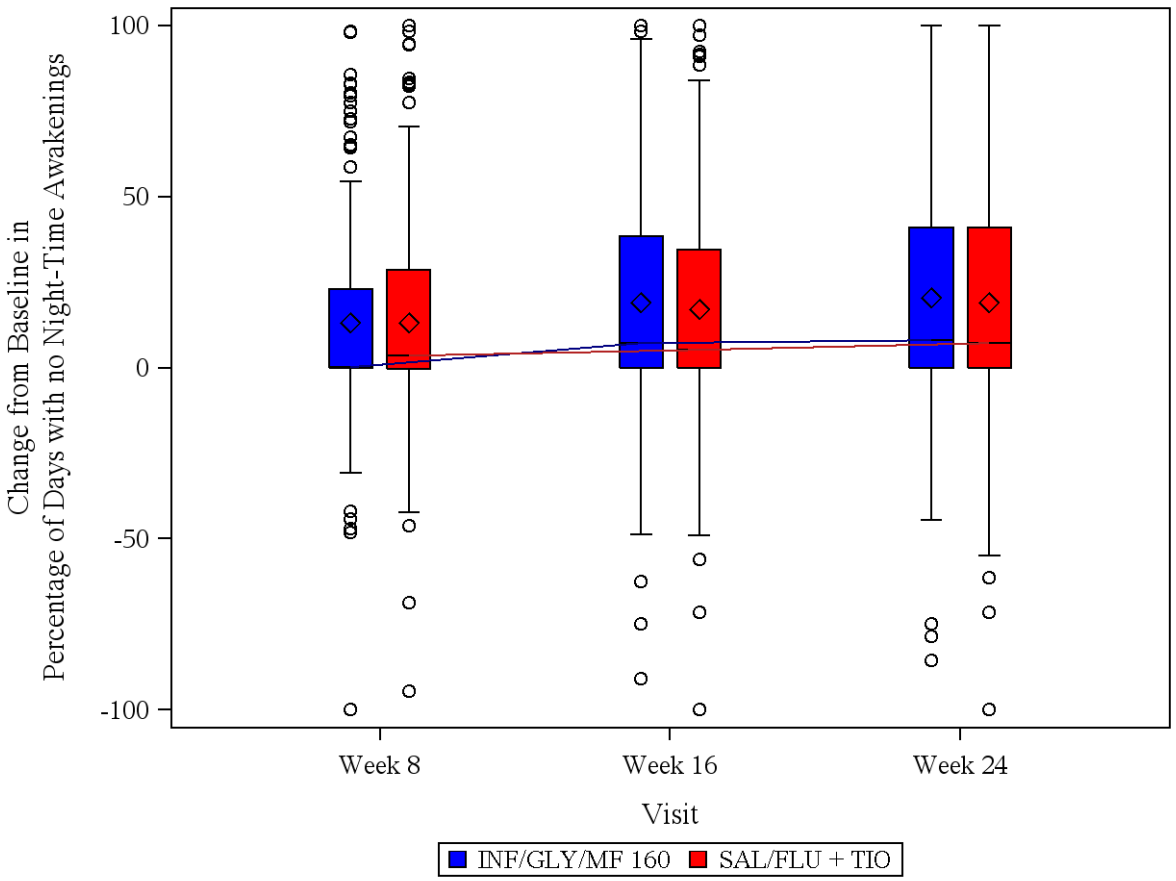
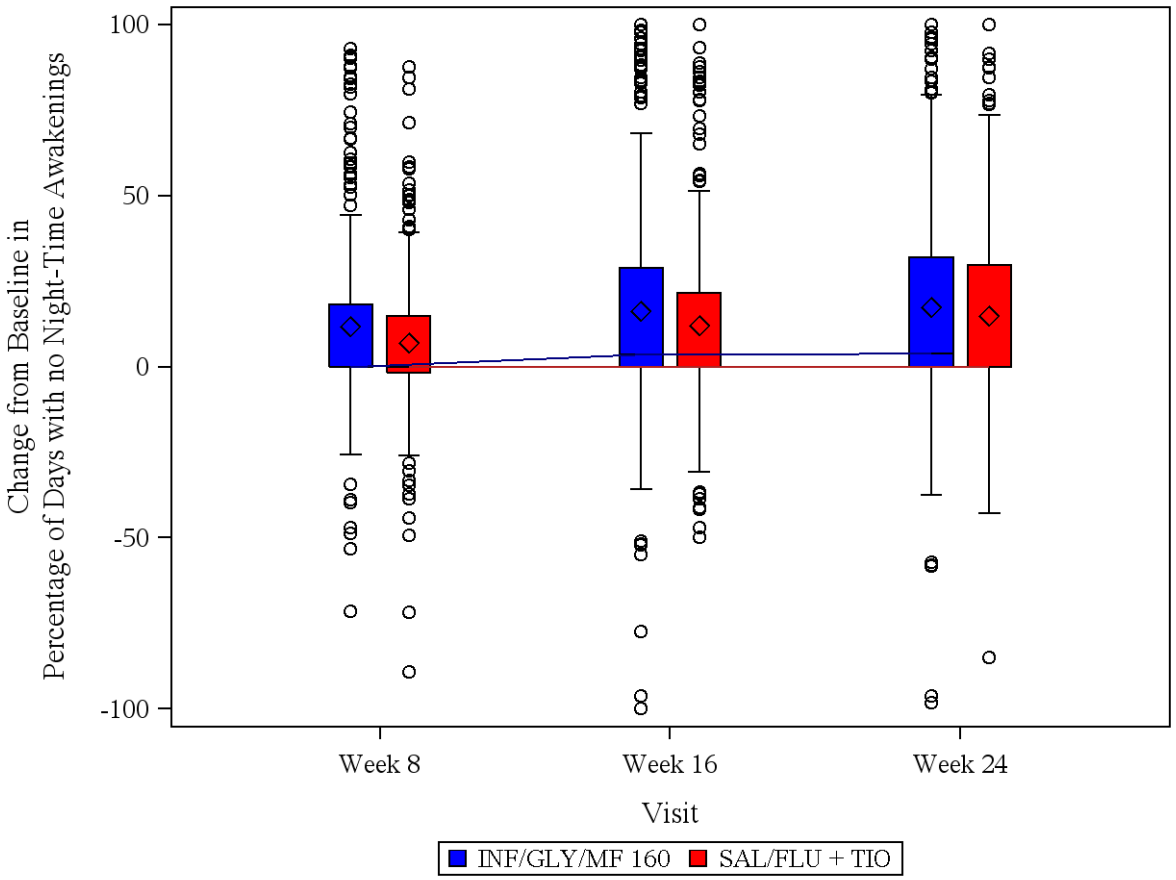
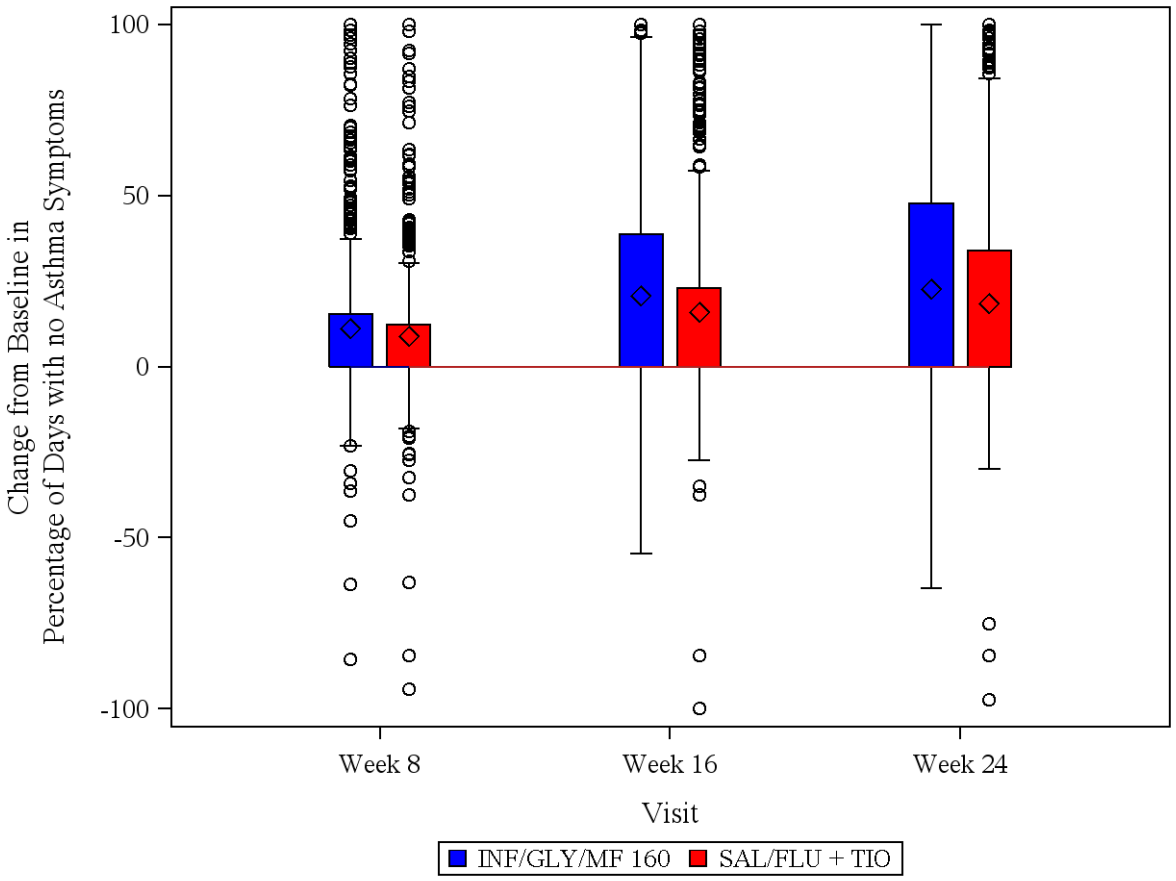


Figure 9.18.2 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



9.19 Boxplot: Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline (FAS)

Figure 9.19 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline (FAS)



9.20 Boxplot: Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Age (FAS)

Figure 9.20.1 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Age (FAS), Age = 18-39 years

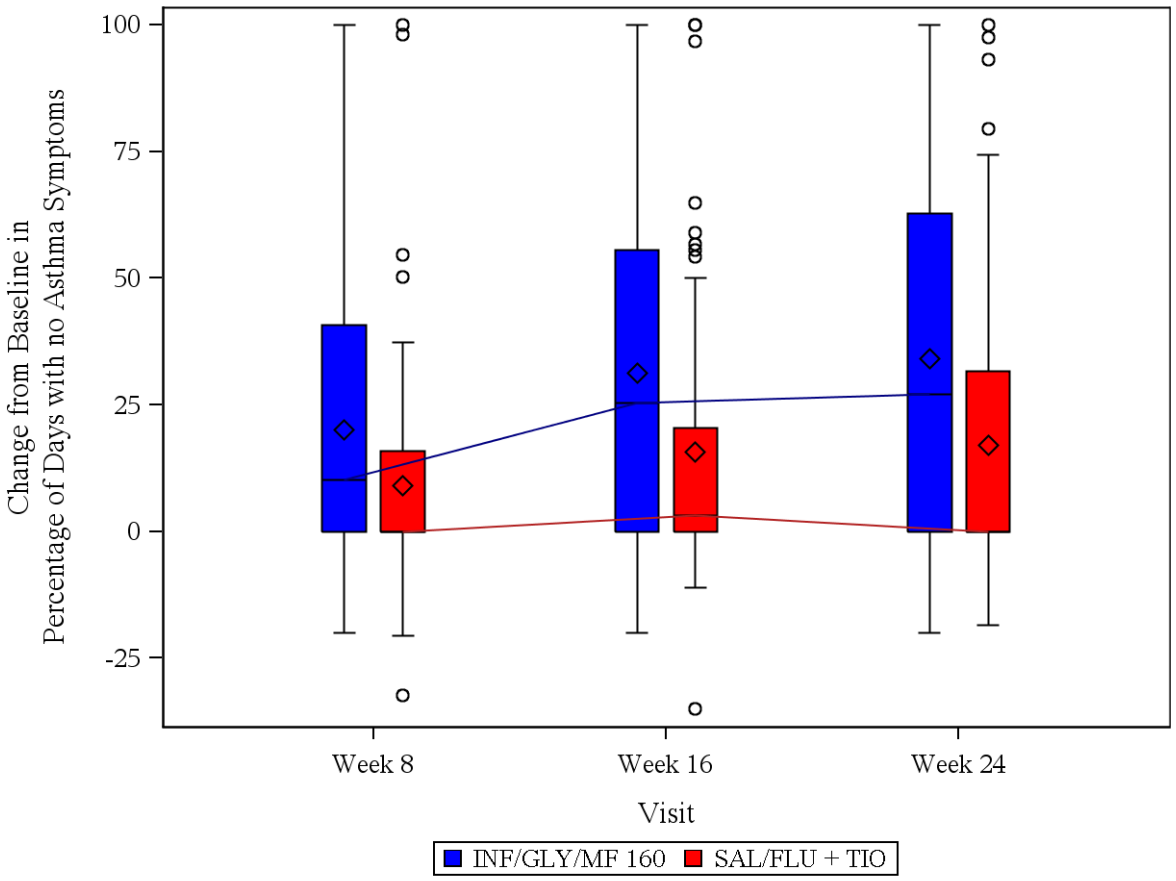


Figure 9.20.2 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Age (FAS), Age = 40-64 years

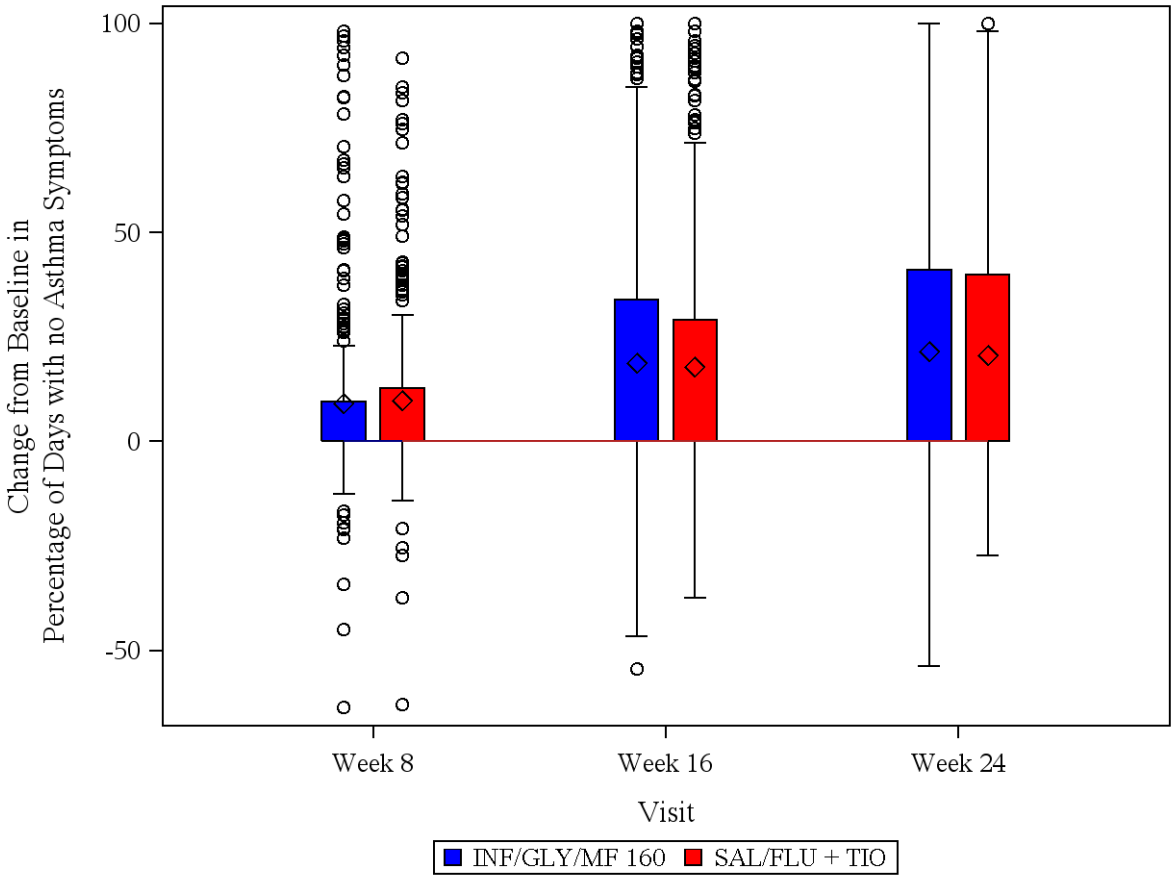
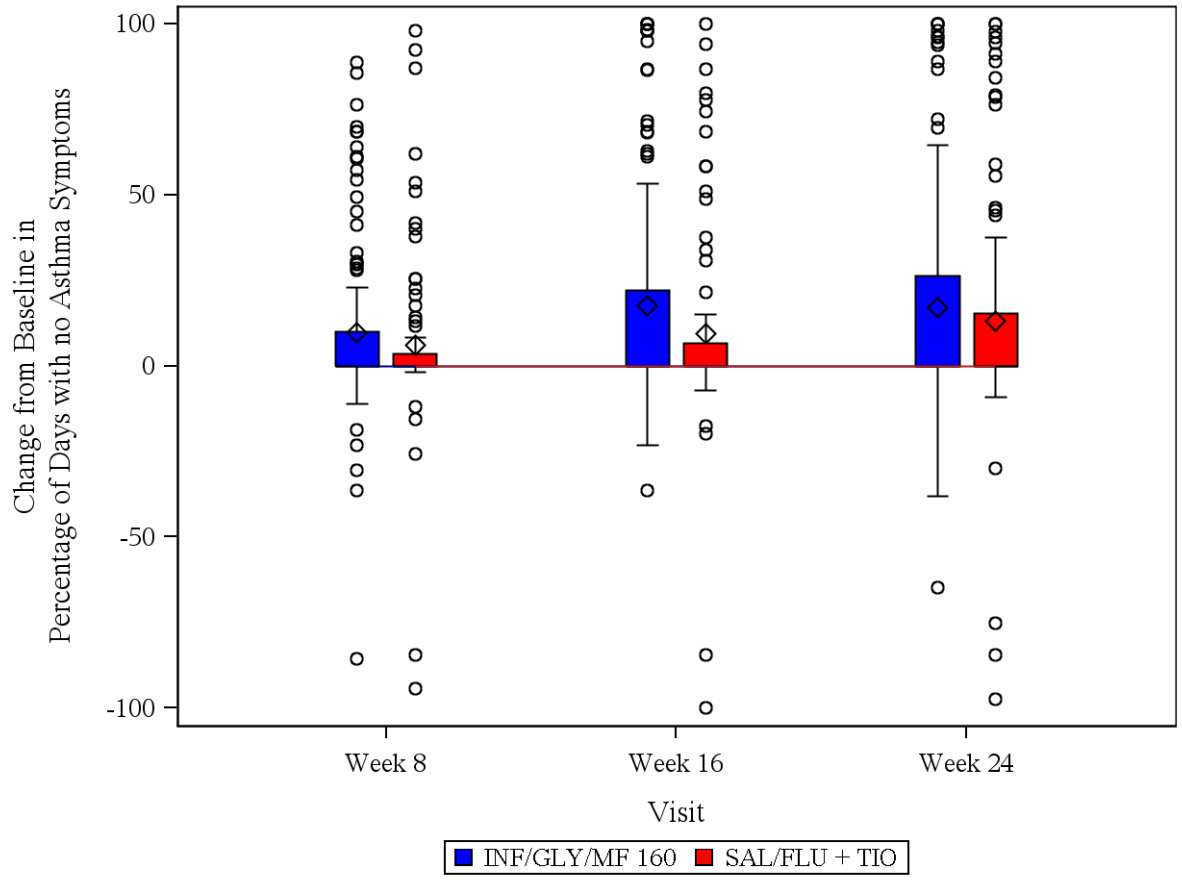


Figure 9.20.3 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Age (FAS), Age = ≥65 years



9.21 Boxplot: Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Gender (FAS)

Figure 9.21.1 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Gender (FAS), Gender = Male

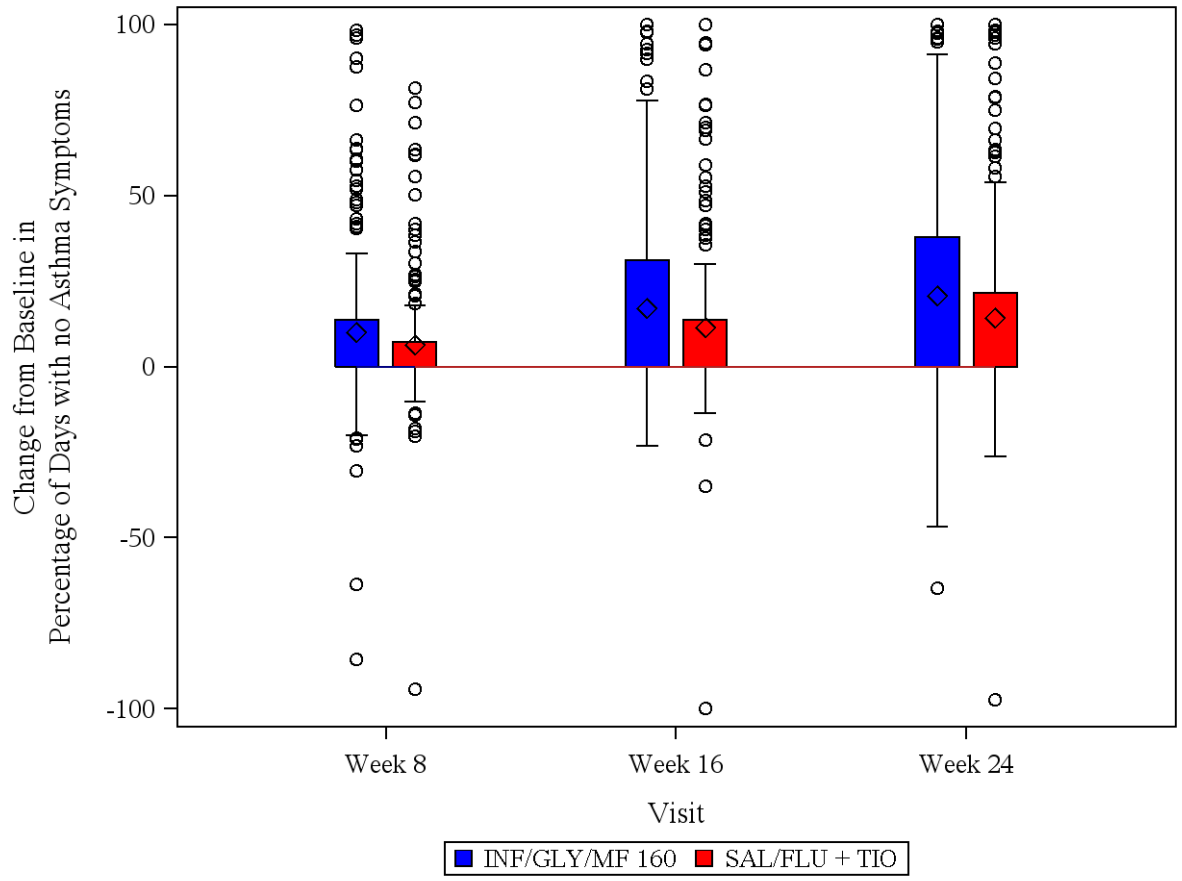
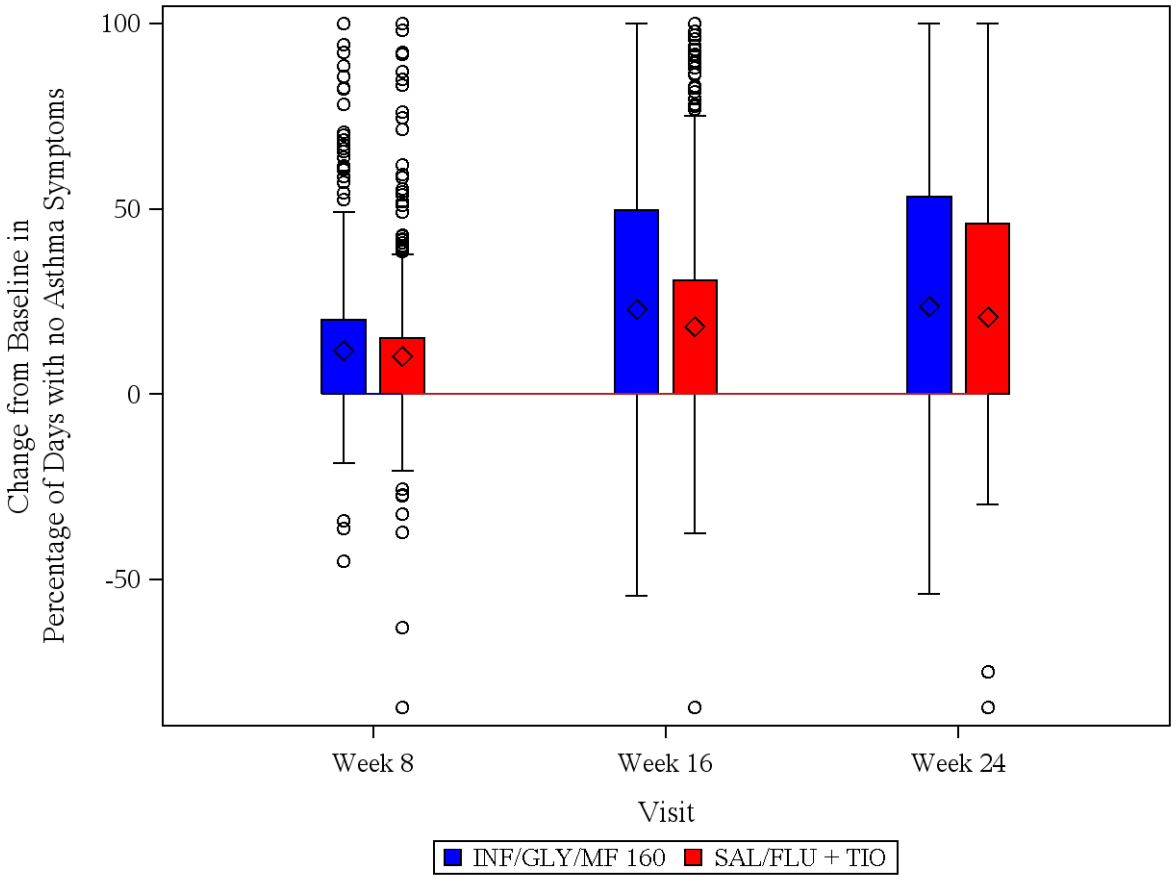


Figure 9.21.2 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Gender (FAS), Gender = Female



9.22 Boxplot: Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Region (FAS)

Figure 9.22.1 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Region (FAS), Region = Asia

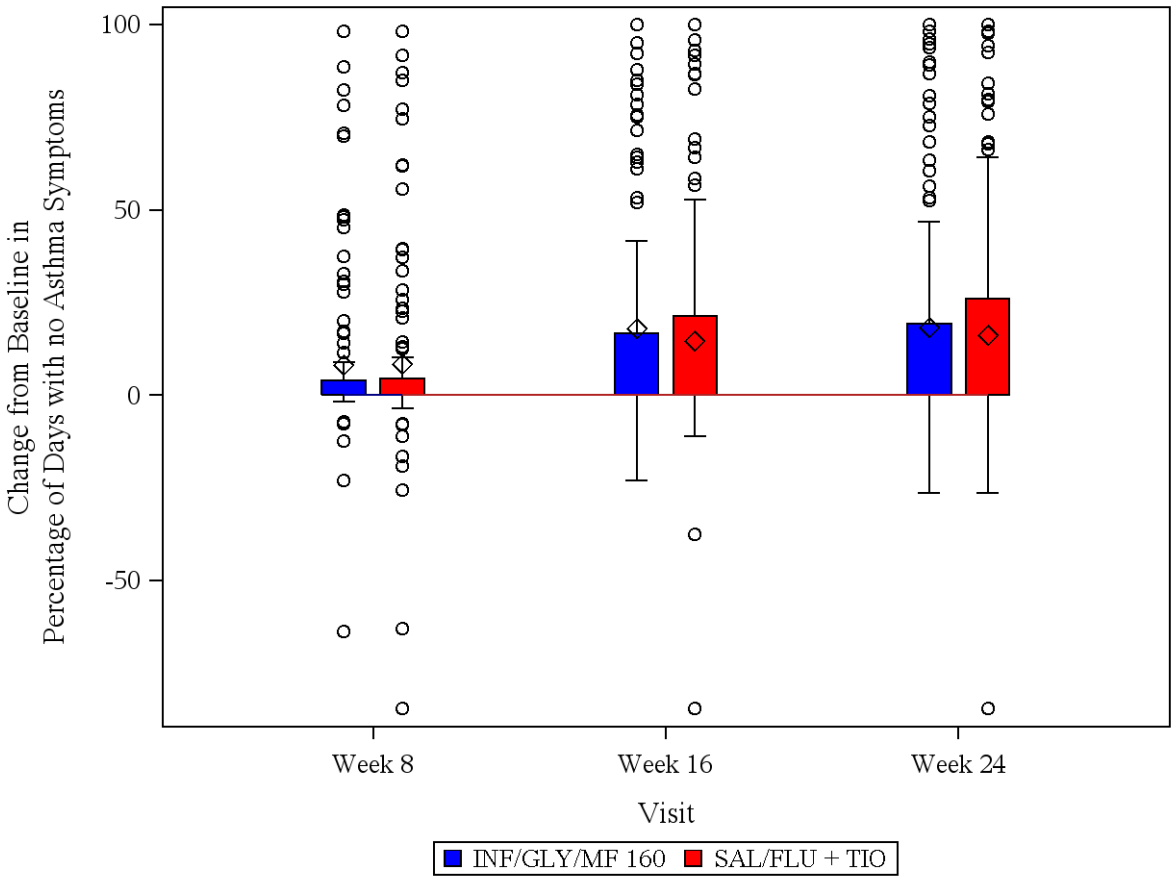


Figure 9.22.2 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Region (FAS), Region = Europe

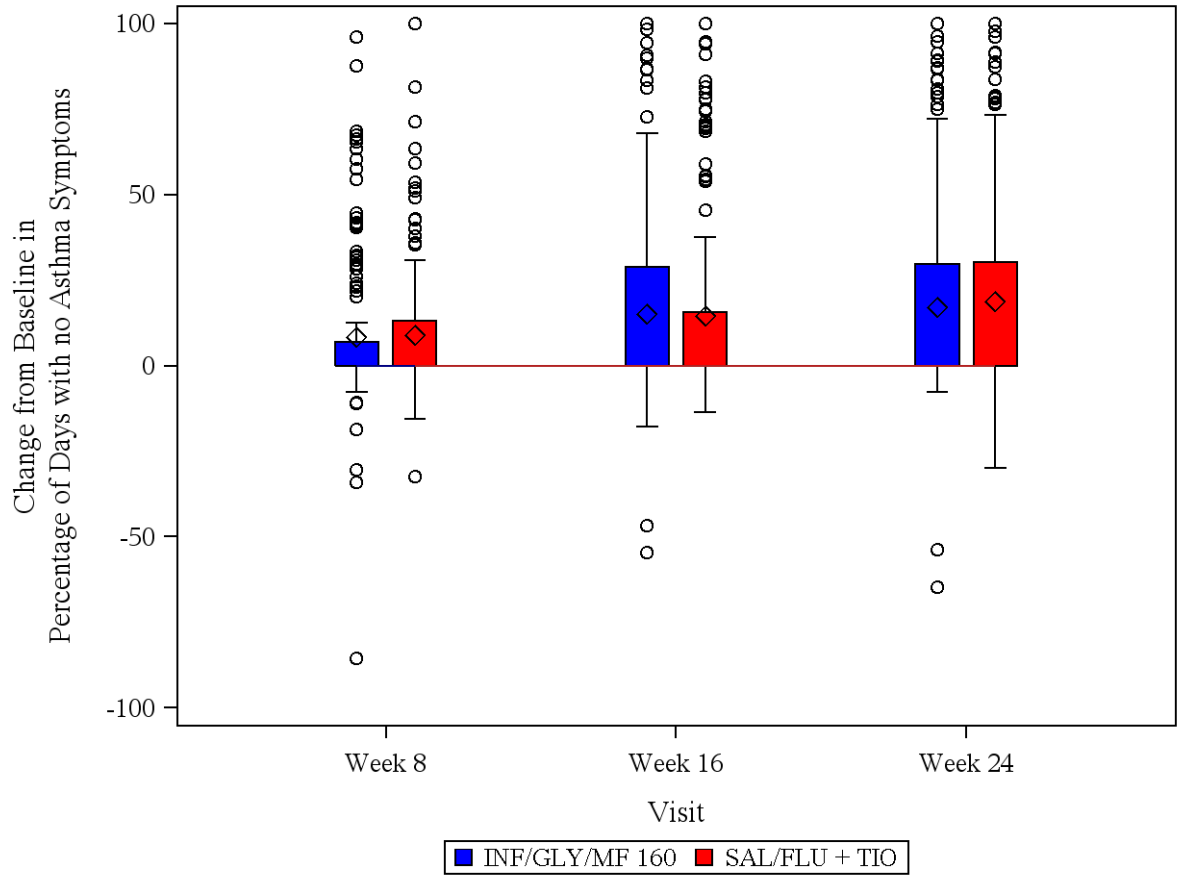


Figure 9.22.3 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Region (FAS), Region = Latin America

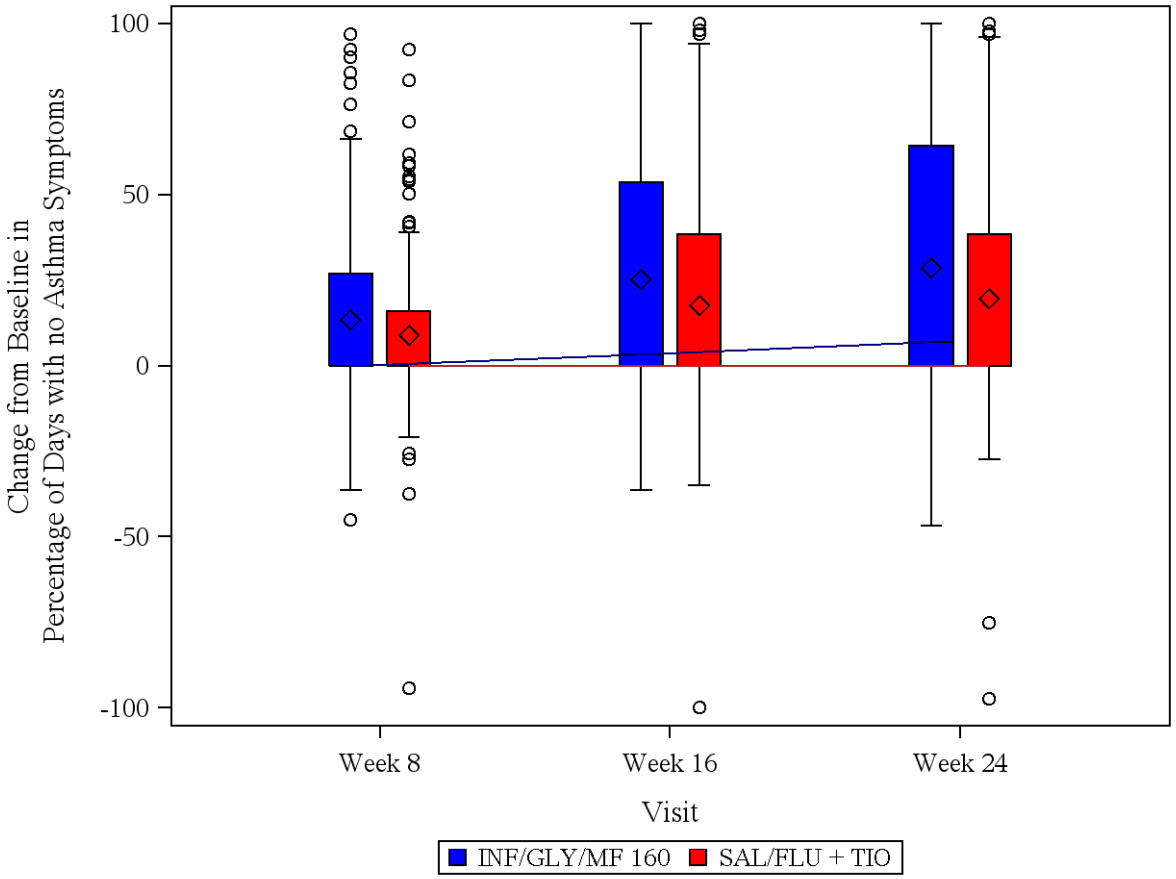
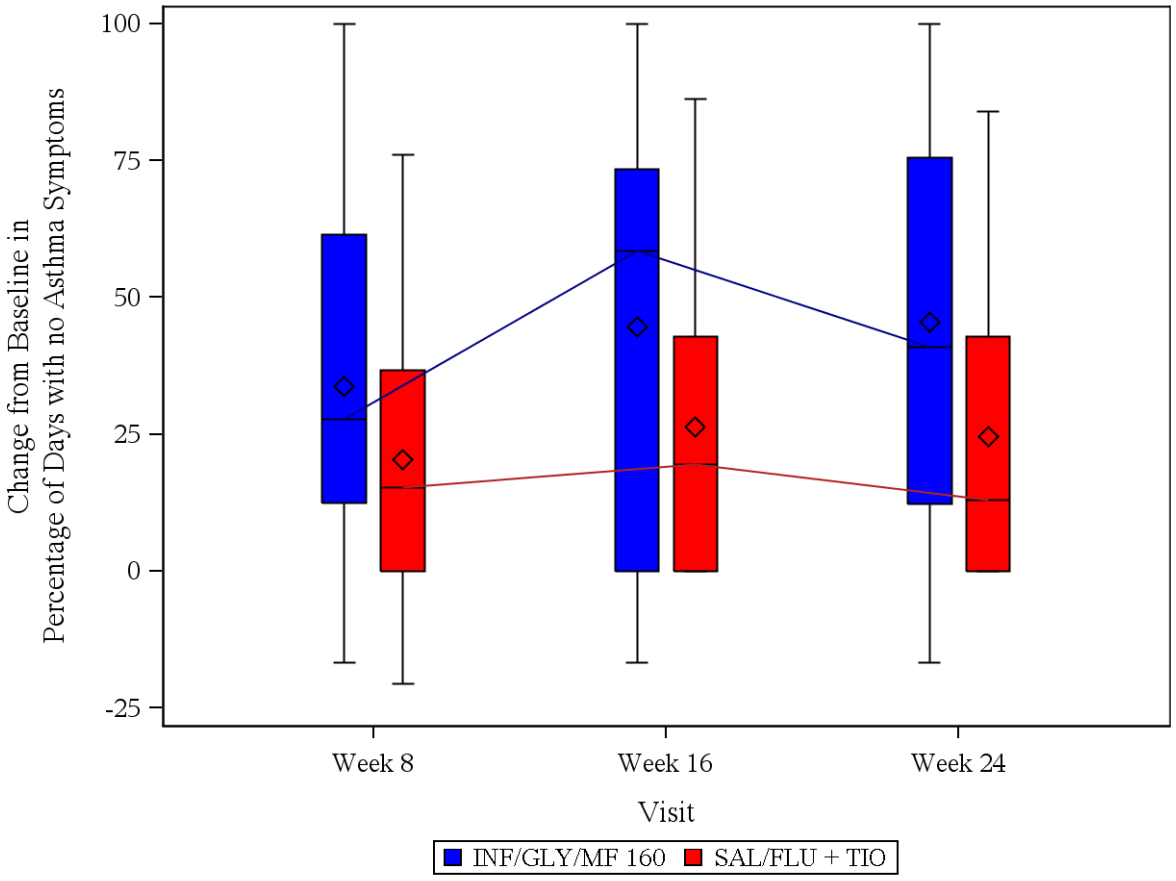


Figure 9.22.4 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Region (FAS), Region = Others



9.23 Boxplot: Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 9.23.1 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

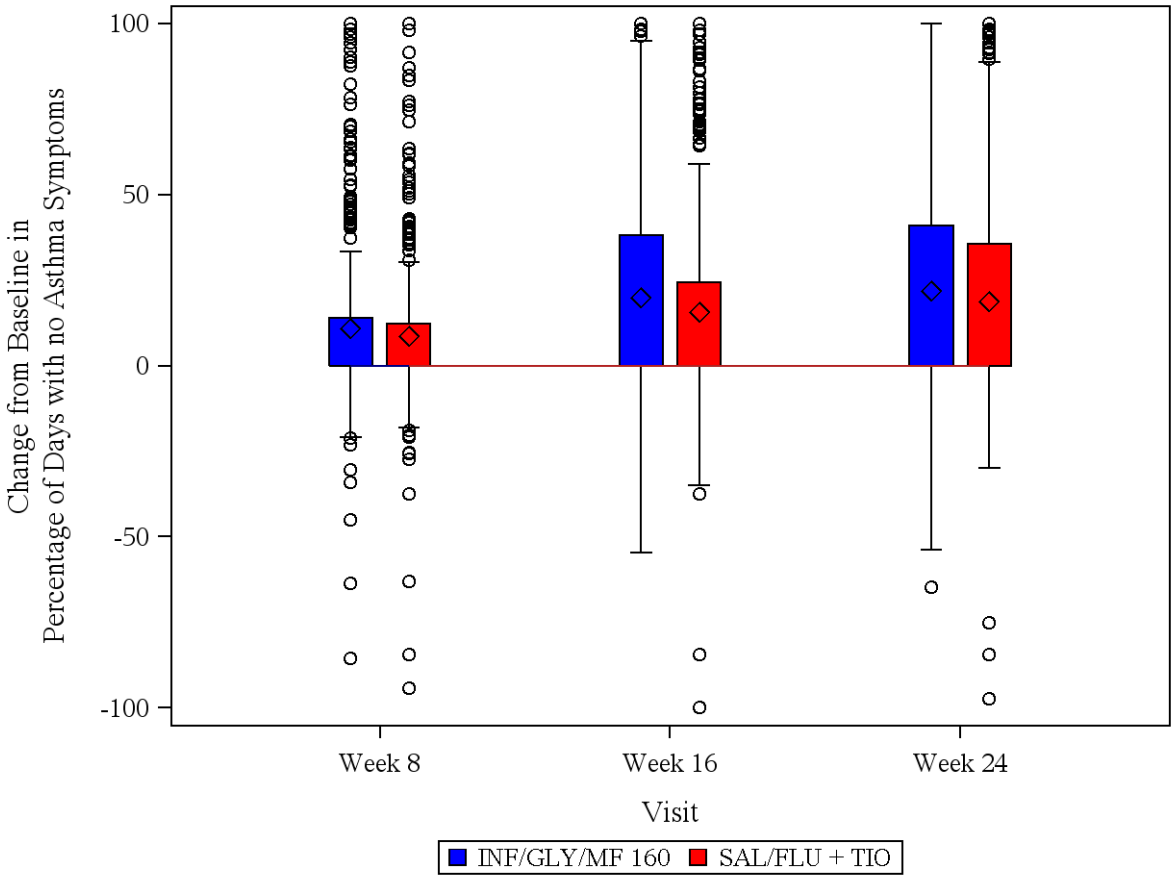
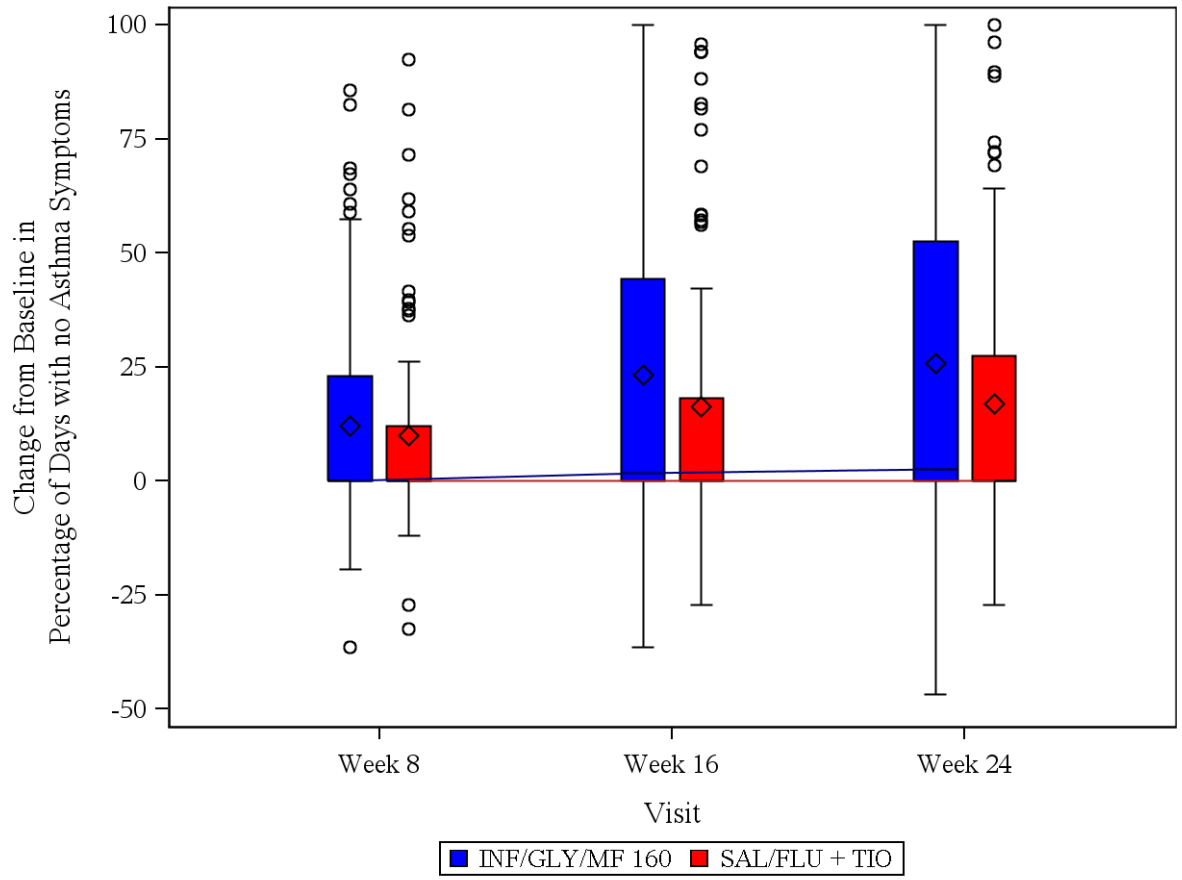


Figure 9.23.2 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.24 Boxplot: Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 9.24.1 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

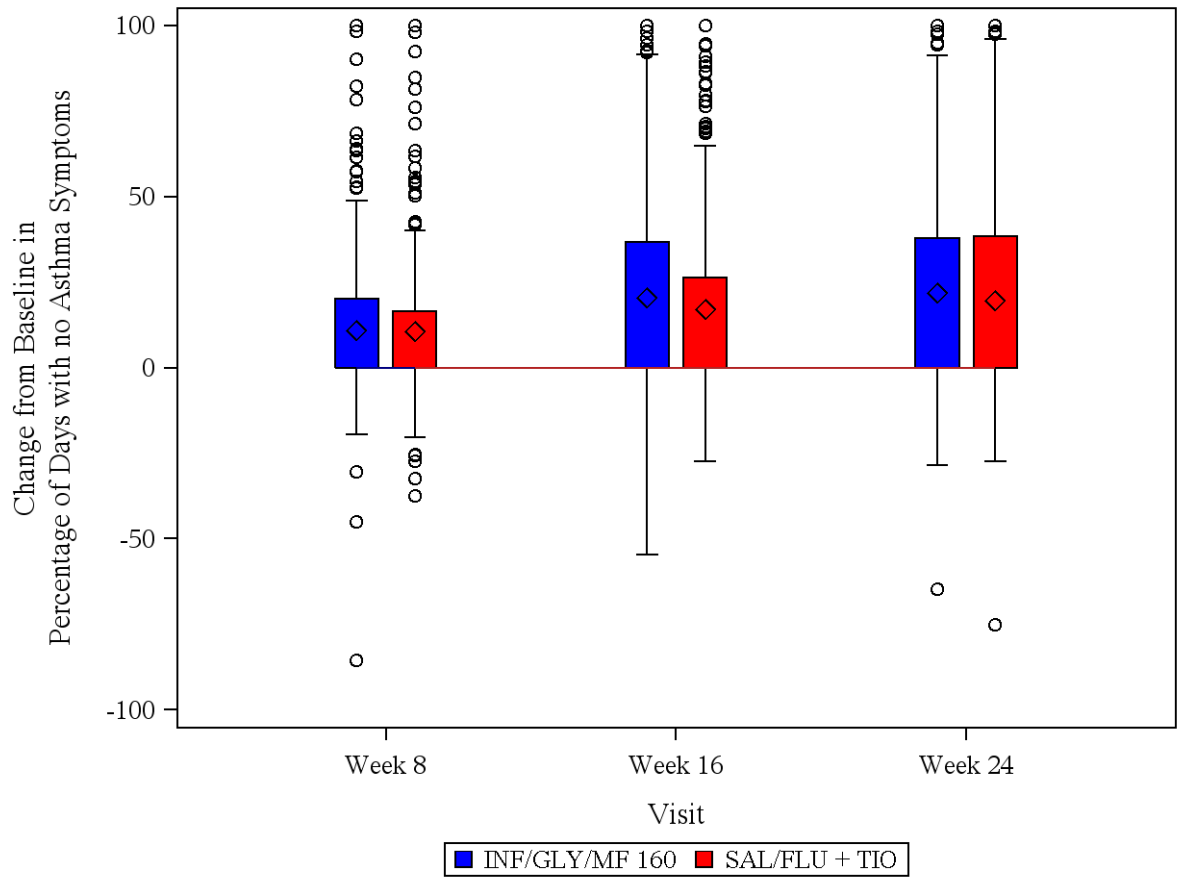
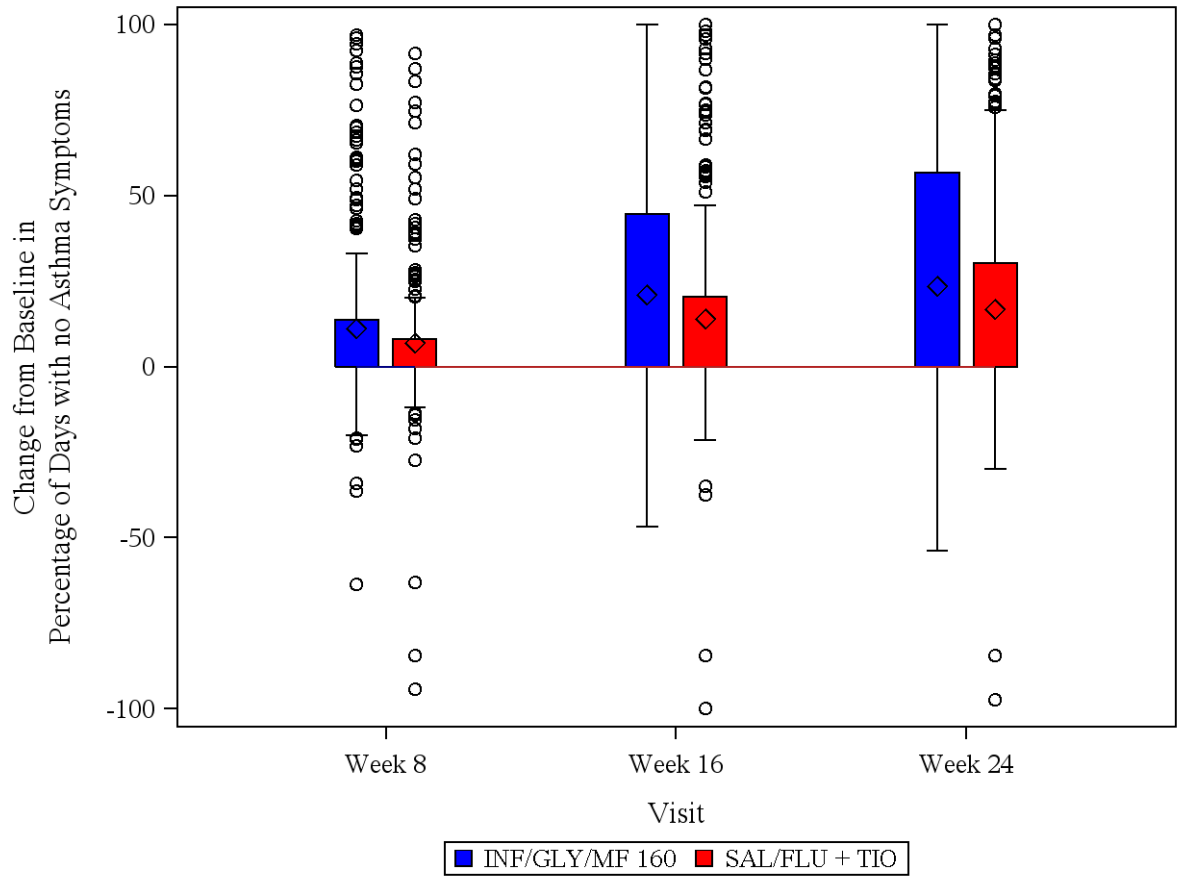
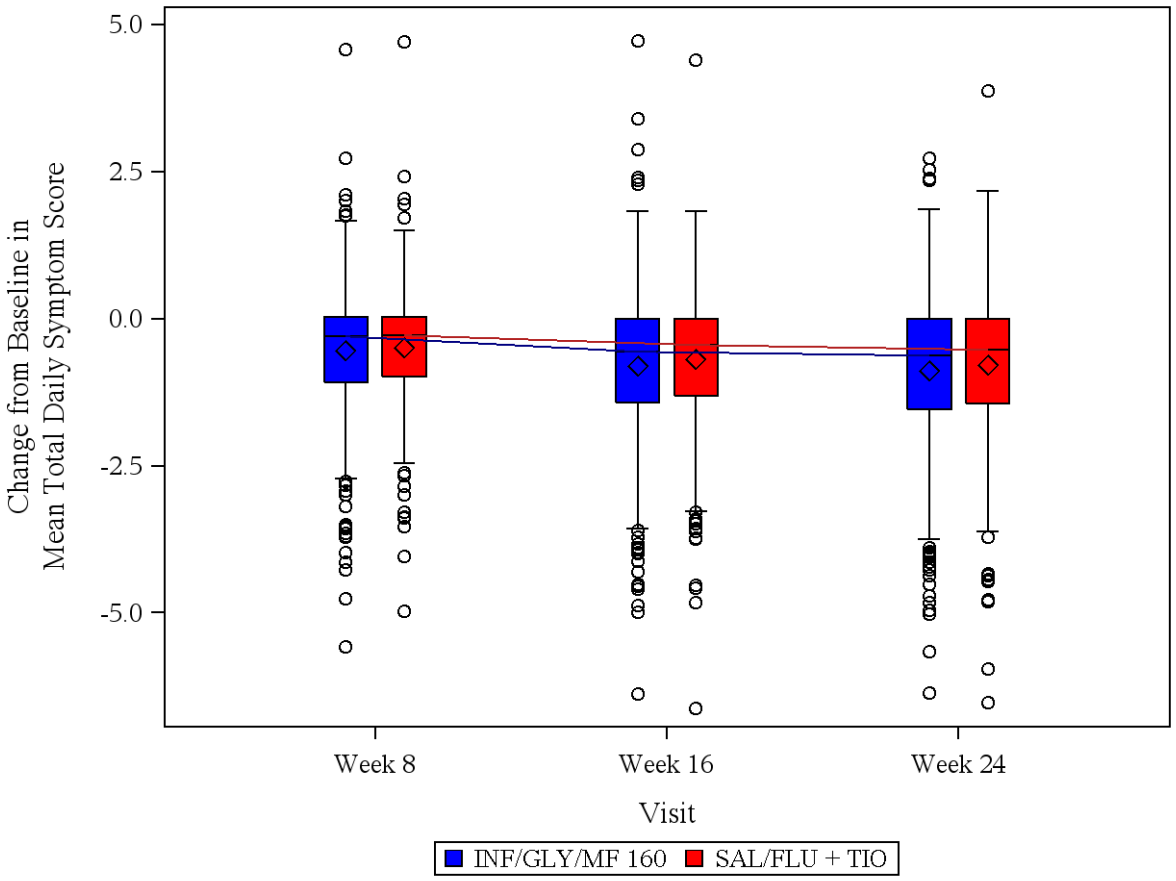


Figure 9.24.2 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



9.25 Boxplot: Symptoms (Mean Total Daily Symptom Score) - Change from Baseline (FAS)

Figure 9.25 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline (FAS)



9.26 Boxplot: Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Age (FAS)

Figure 9.26.1 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Age (FAS), Age = 18-39 years

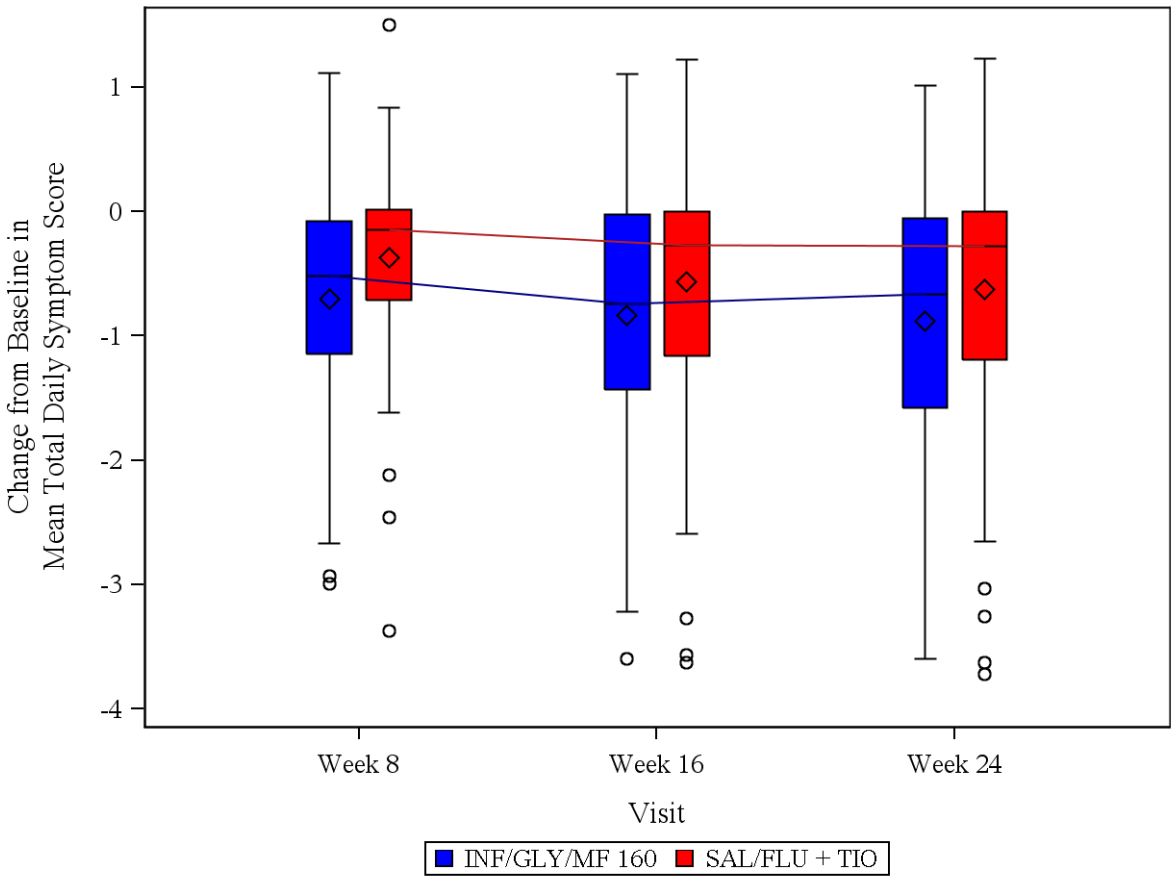


Figure 9.26.2 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Age (FAS), Age = 40-64 years

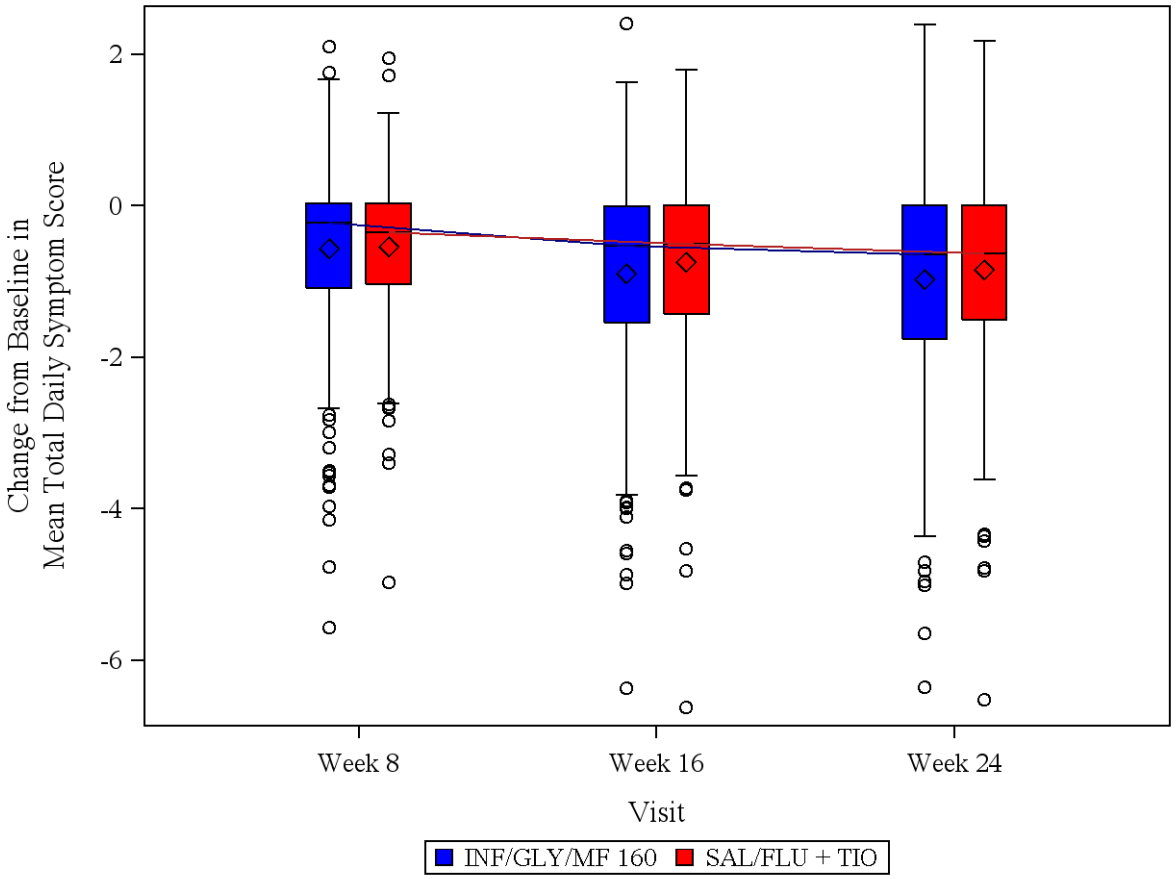
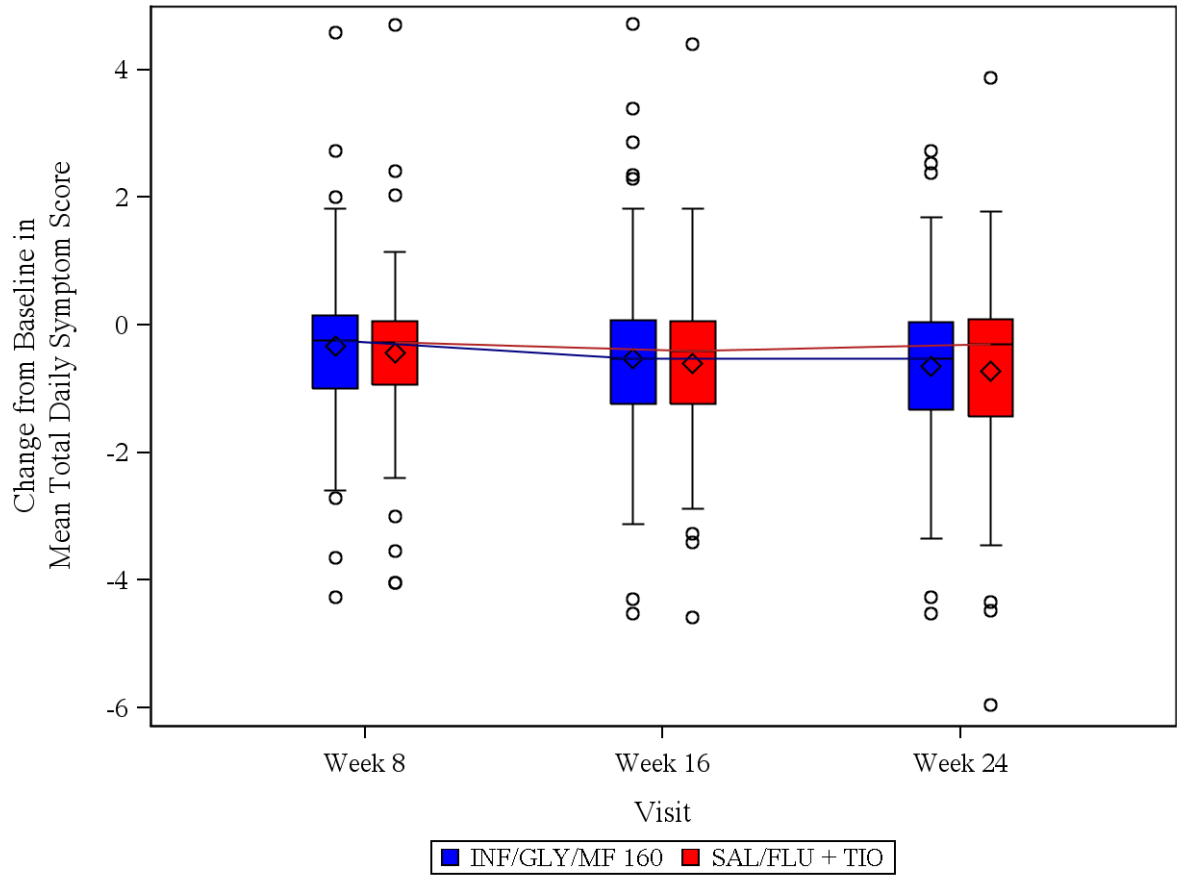


Figure 9.26.3 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Age (FAS), Age = ≥65 years



9.27 Boxplot: Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Gender (FAS)

Figure 9.27.1 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Gender (FAS), Gender = Male

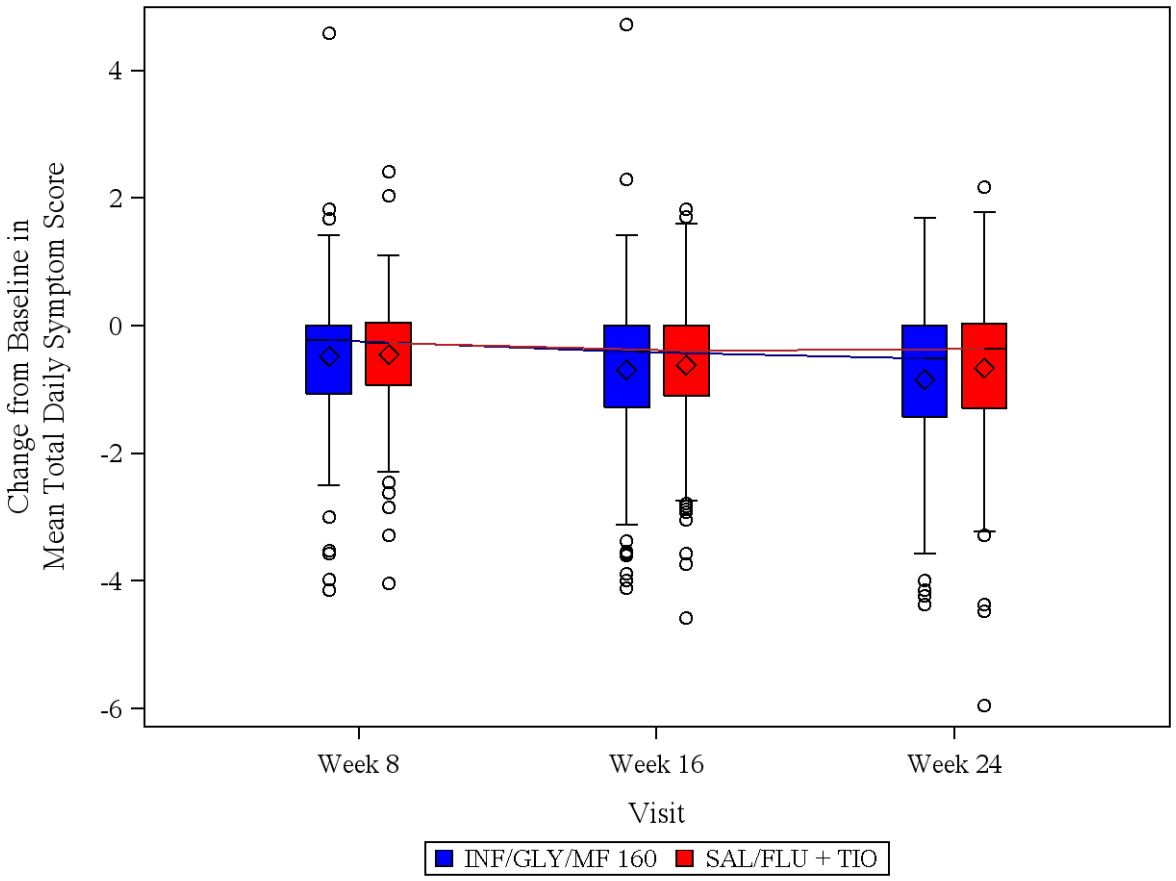
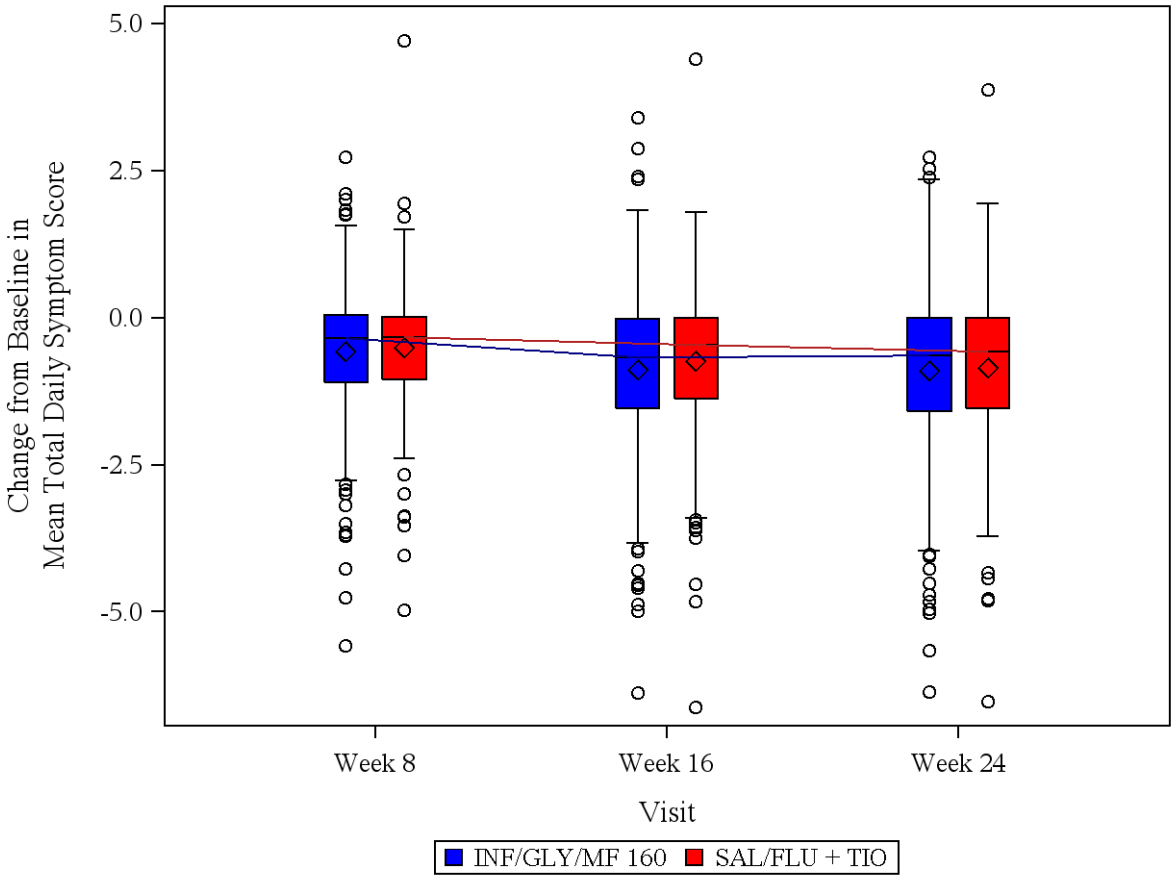


Figure 9.27.2 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Gender (FAS), Gender = Female



9.28 Boxplot: Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Region (FAS)

Figure 9.28.1 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Region (FAS), Region = Asia

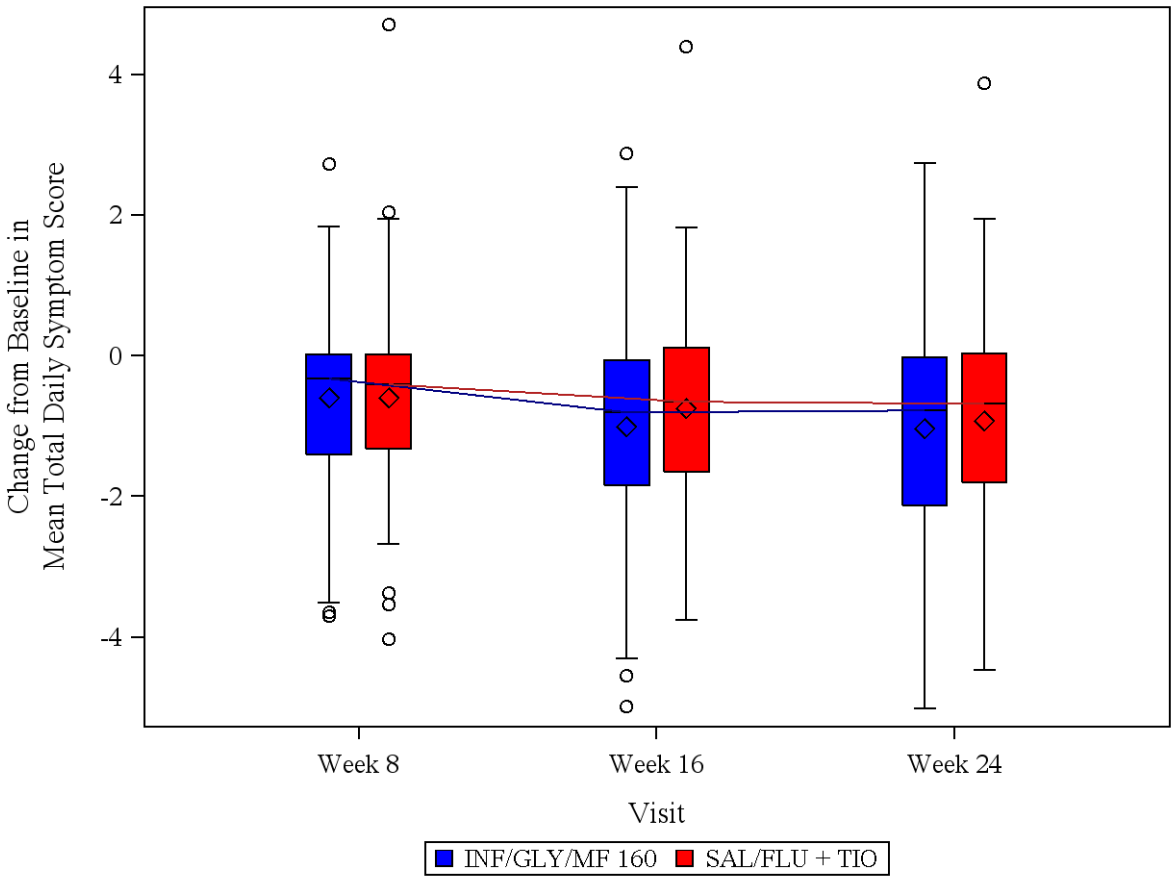


Figure 9.28.2 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Region (FAS), Region = Europe

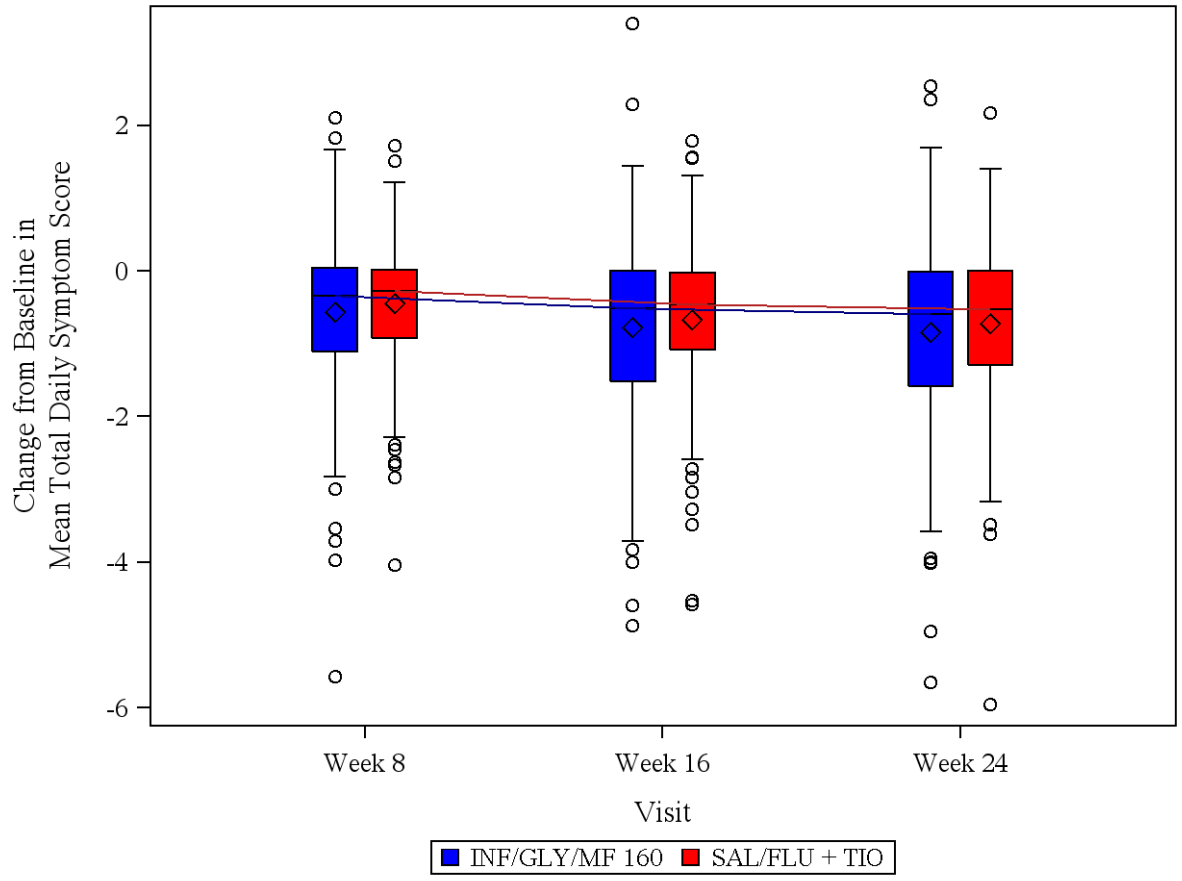


Figure 9.28.3 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Region (FAS), Region = Latin America

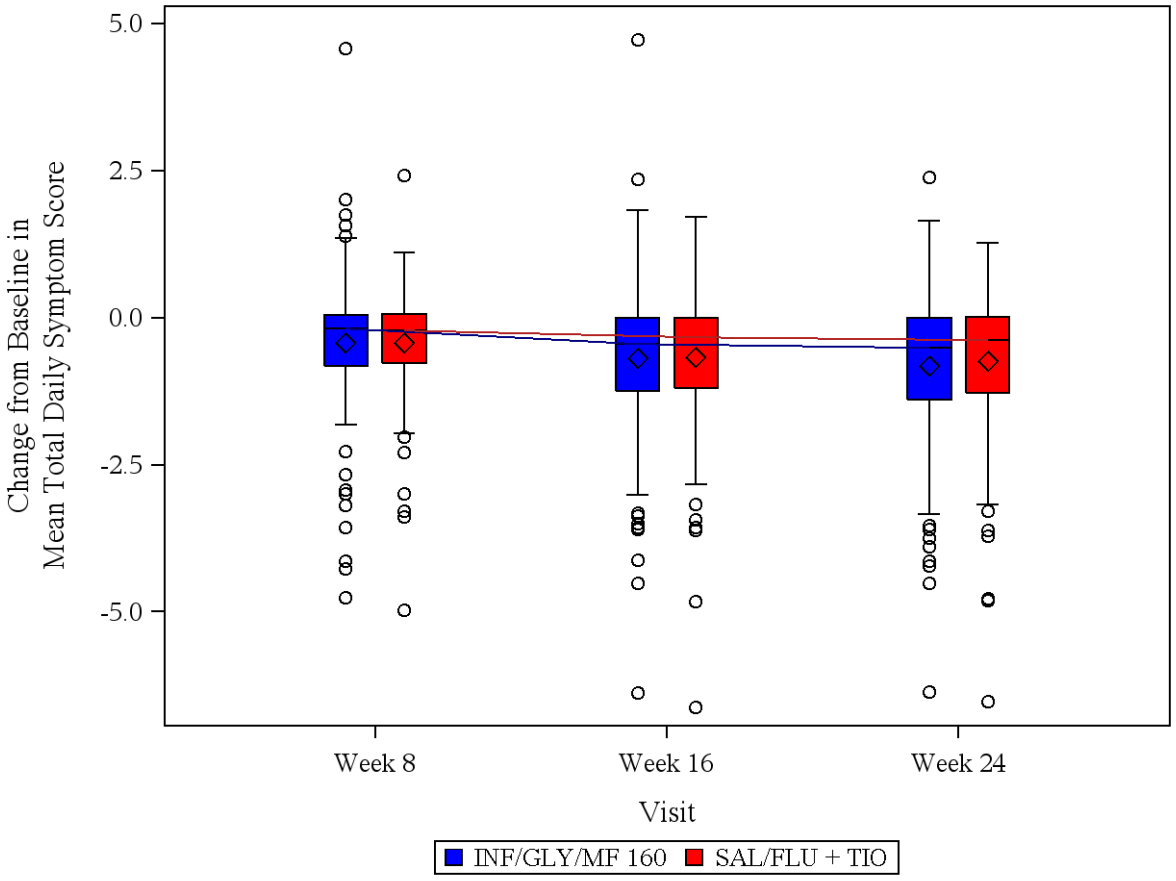
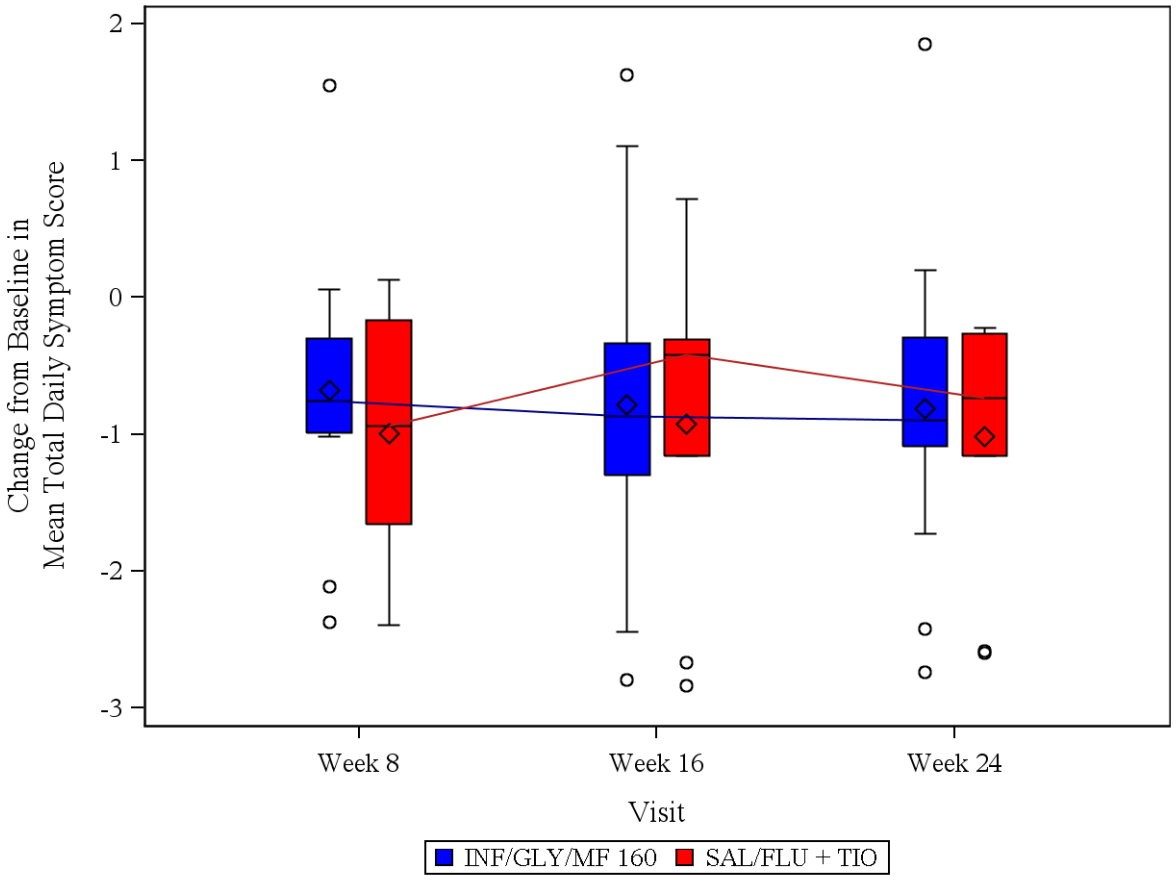


Figure 9.28.4 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Region (FAS), Region = Others



9.29 Boxplot: Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 9.29.1 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

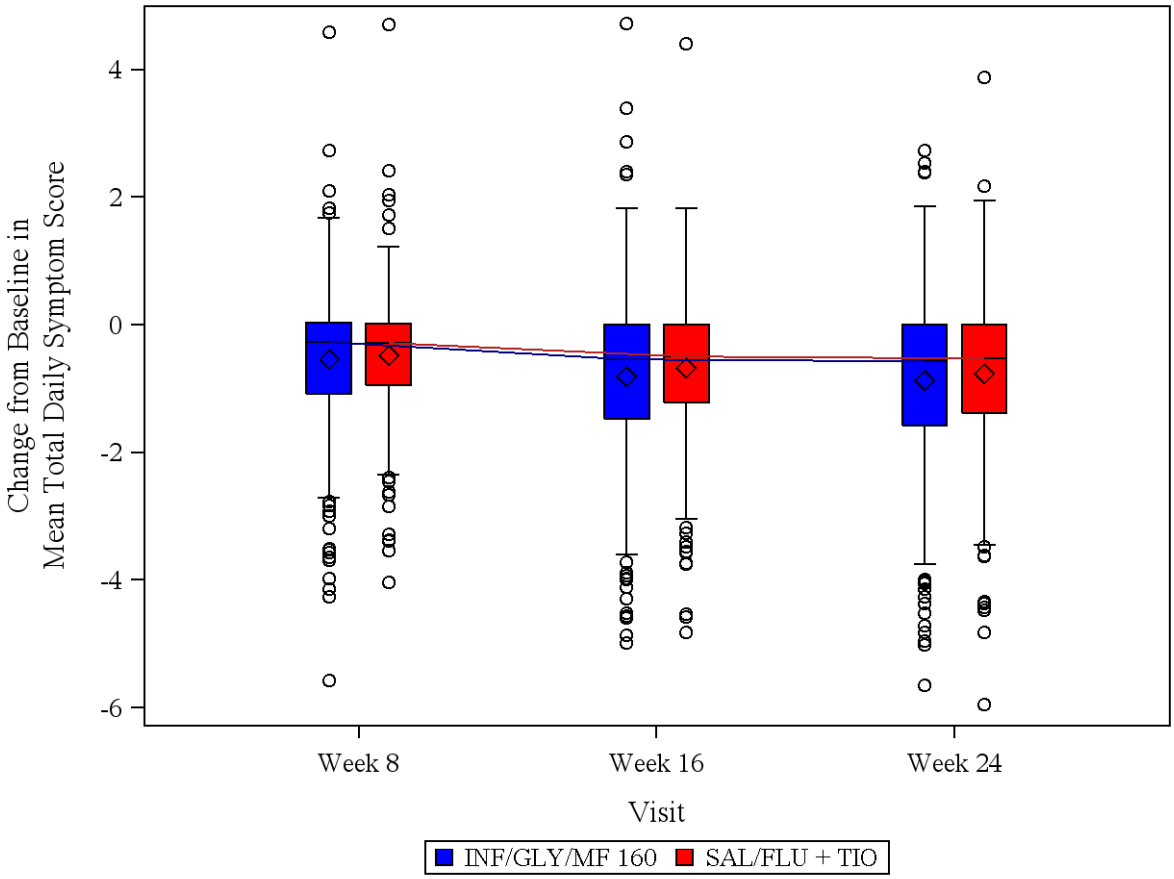
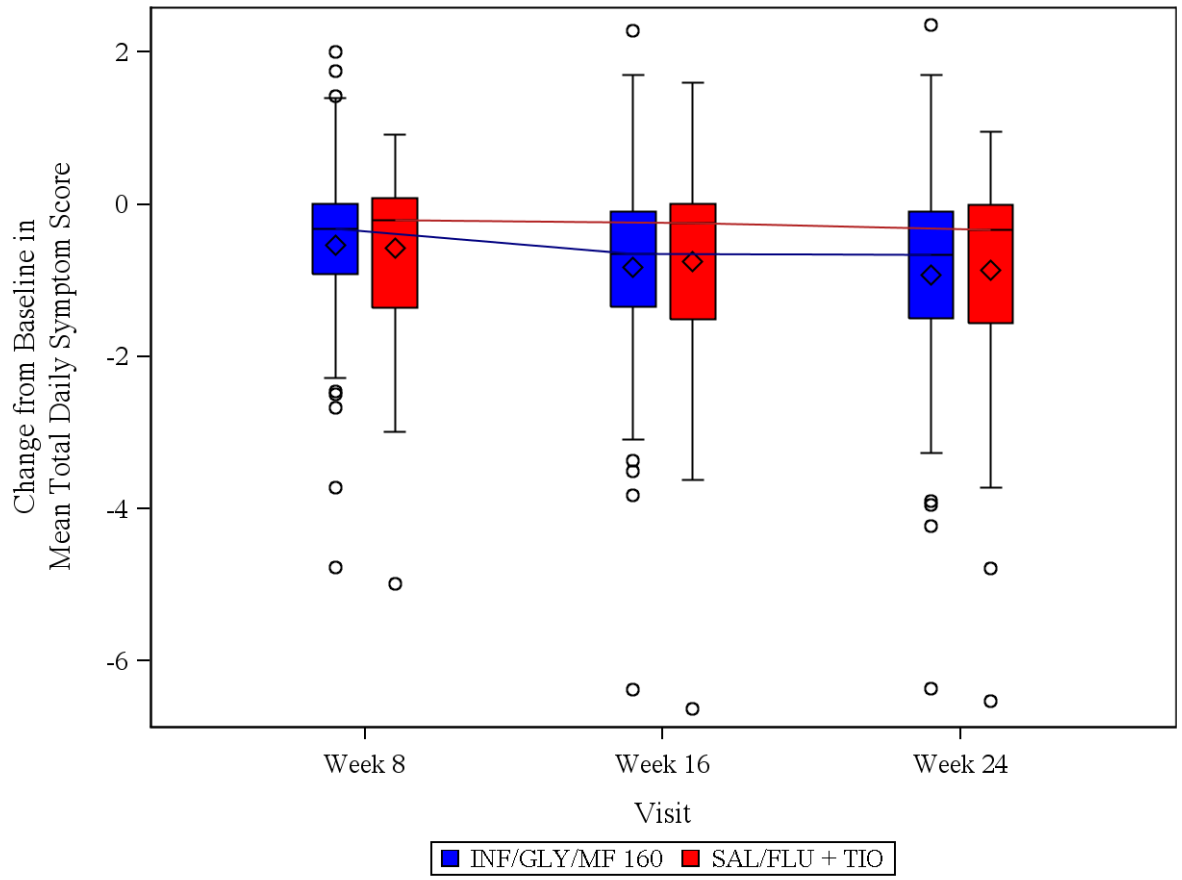


Figure 9.29.2 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.30 Boxplot: Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 9.30.1 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

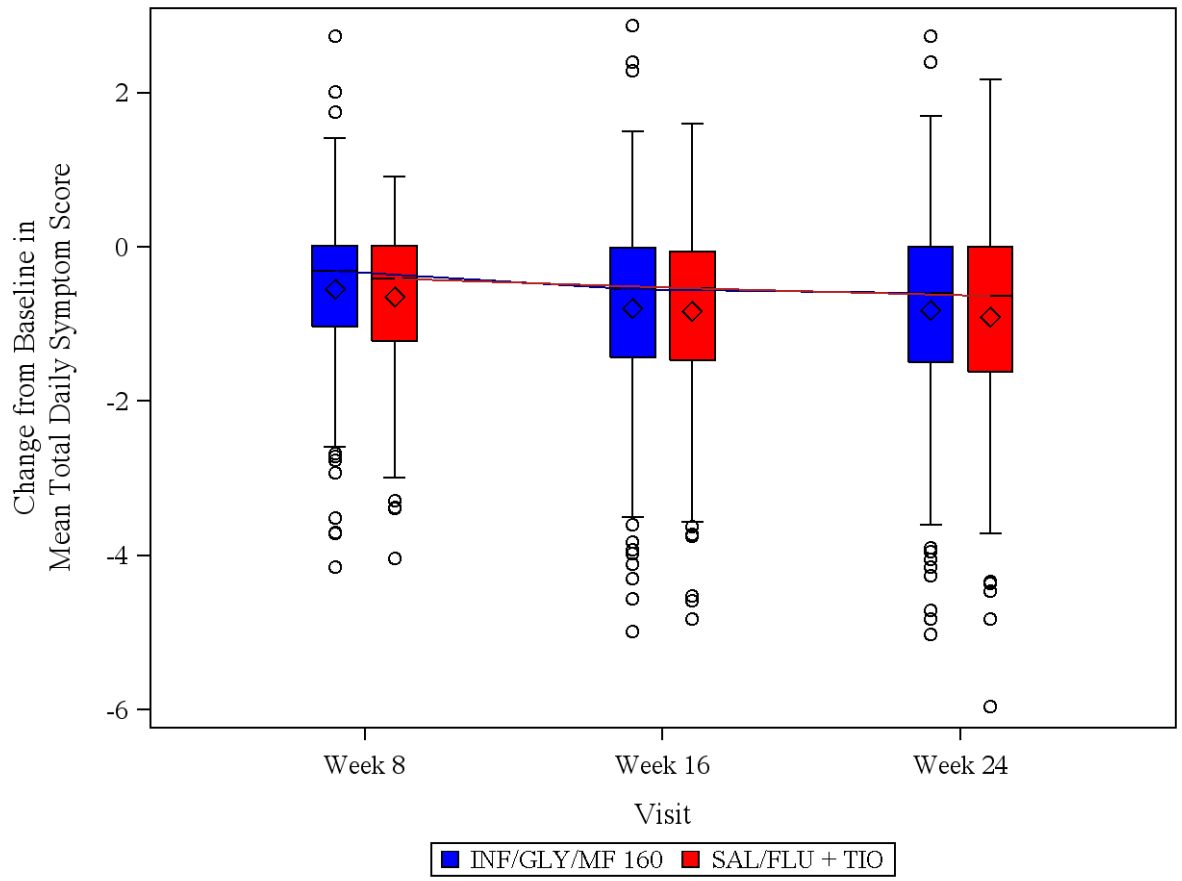
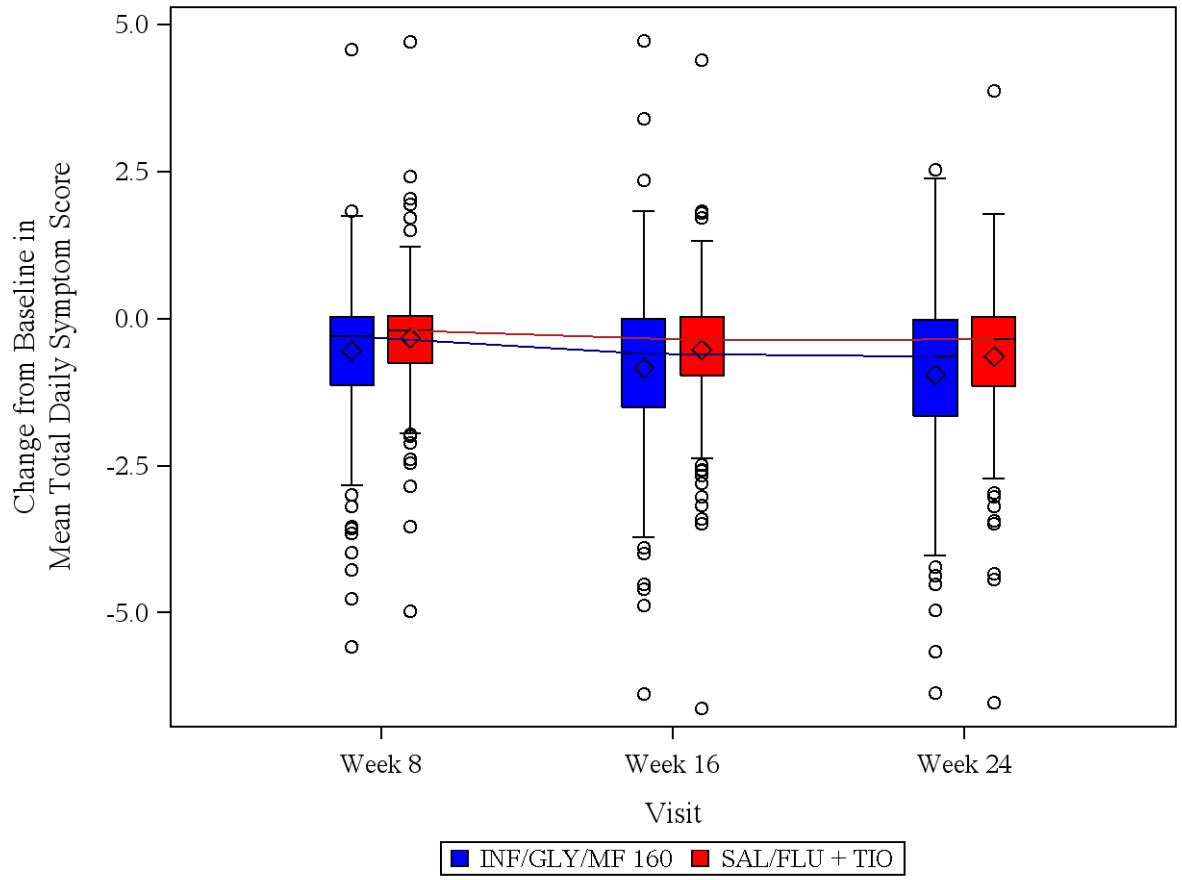
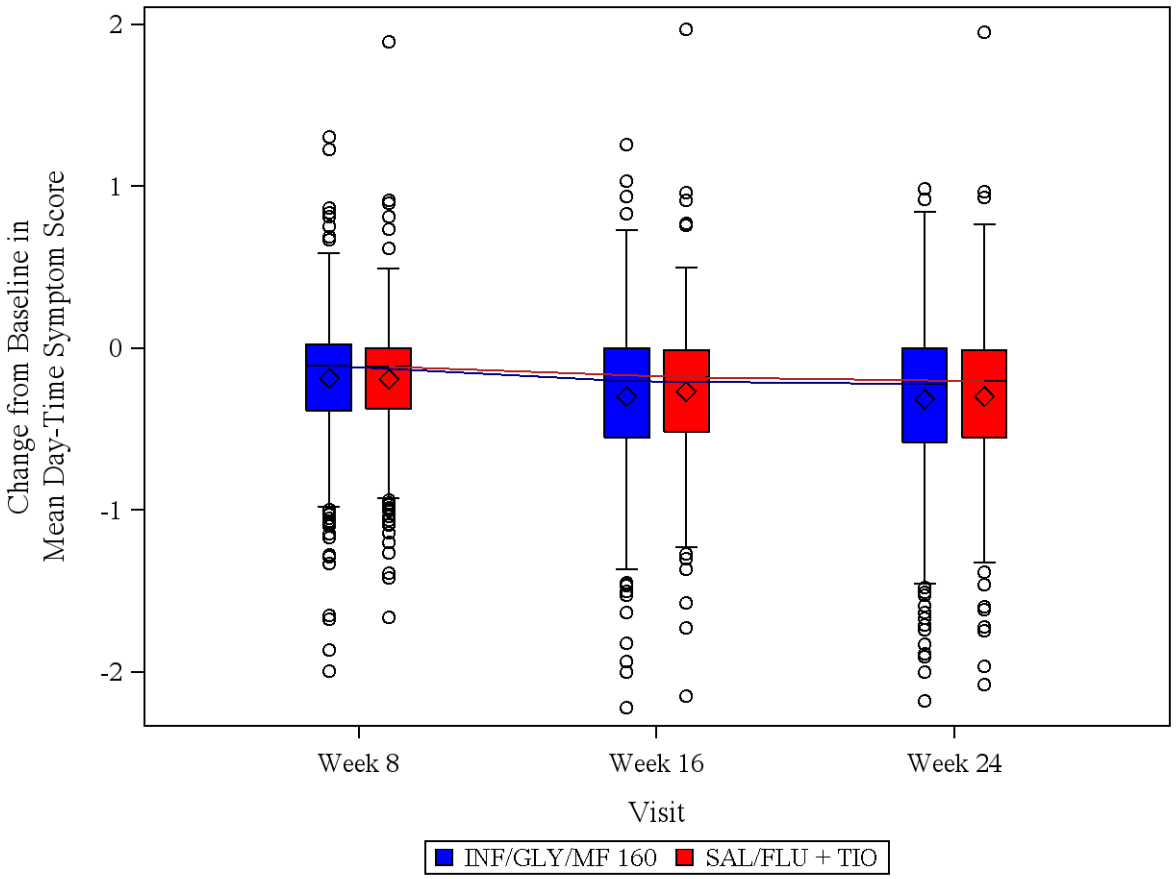


Figure 9.30.2 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



9.31 Boxplot: Symptoms (Mean Day-Time Symptom Score) - Change from Baseline (FAS)

Figure 9.31 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline (FAS)



9.32 Boxplot: Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Age (FAS)

Figure 9.32.1 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Age (FAS), Age = 18-39 years

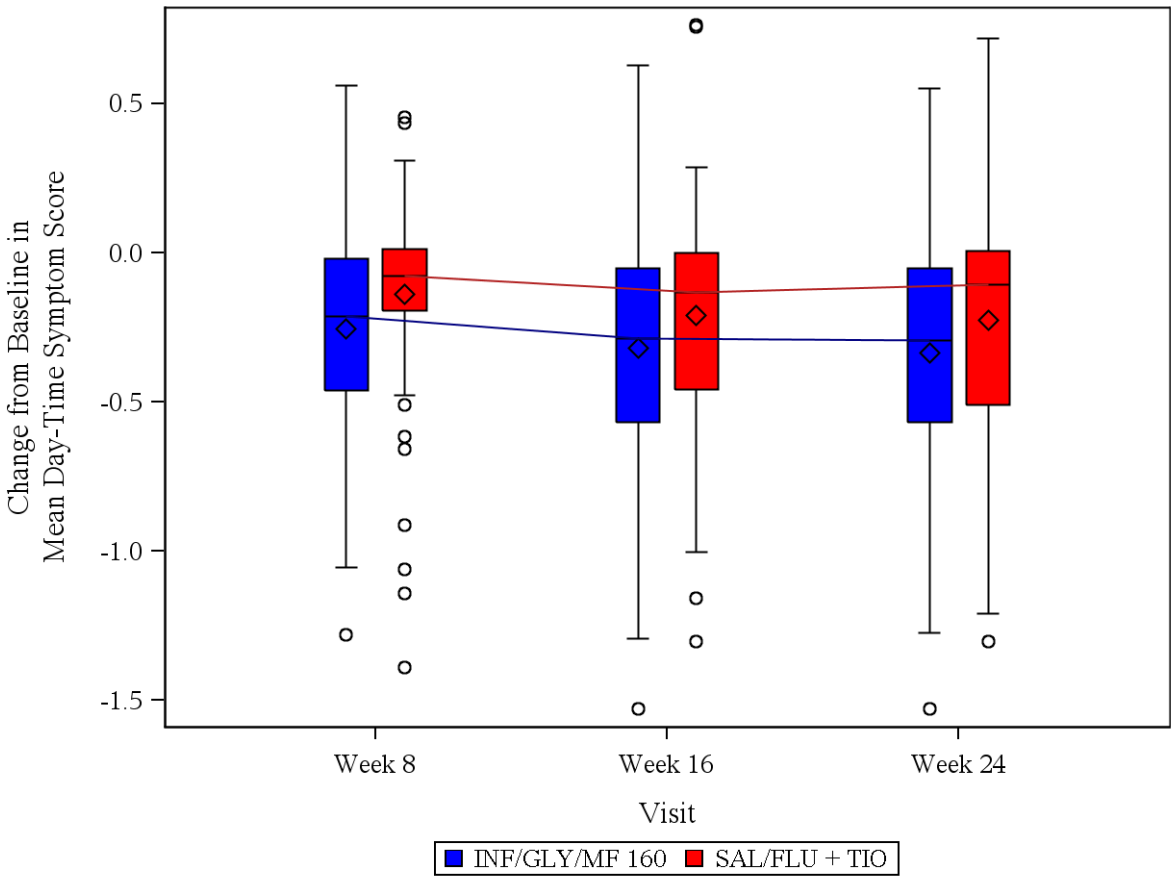


Figure 9.32.2 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Age (FAS), Age = 40-64 years

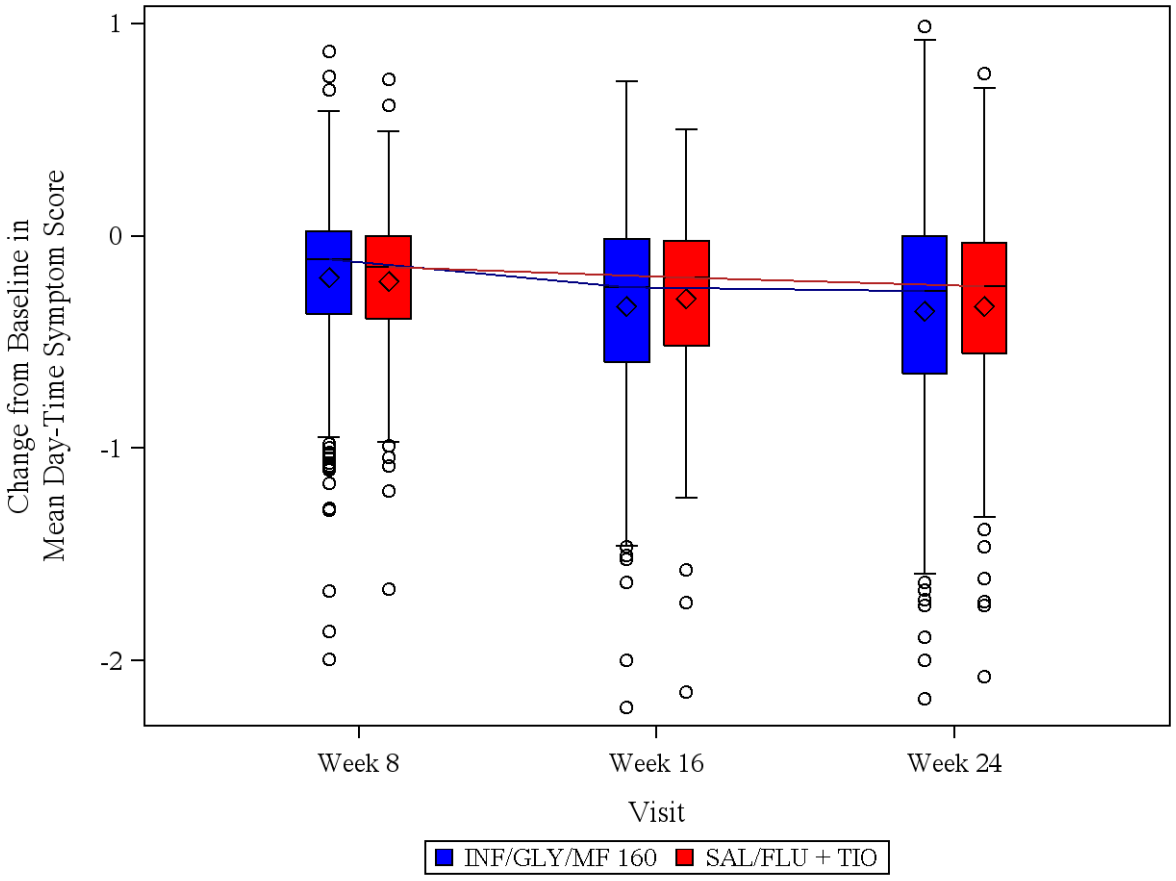
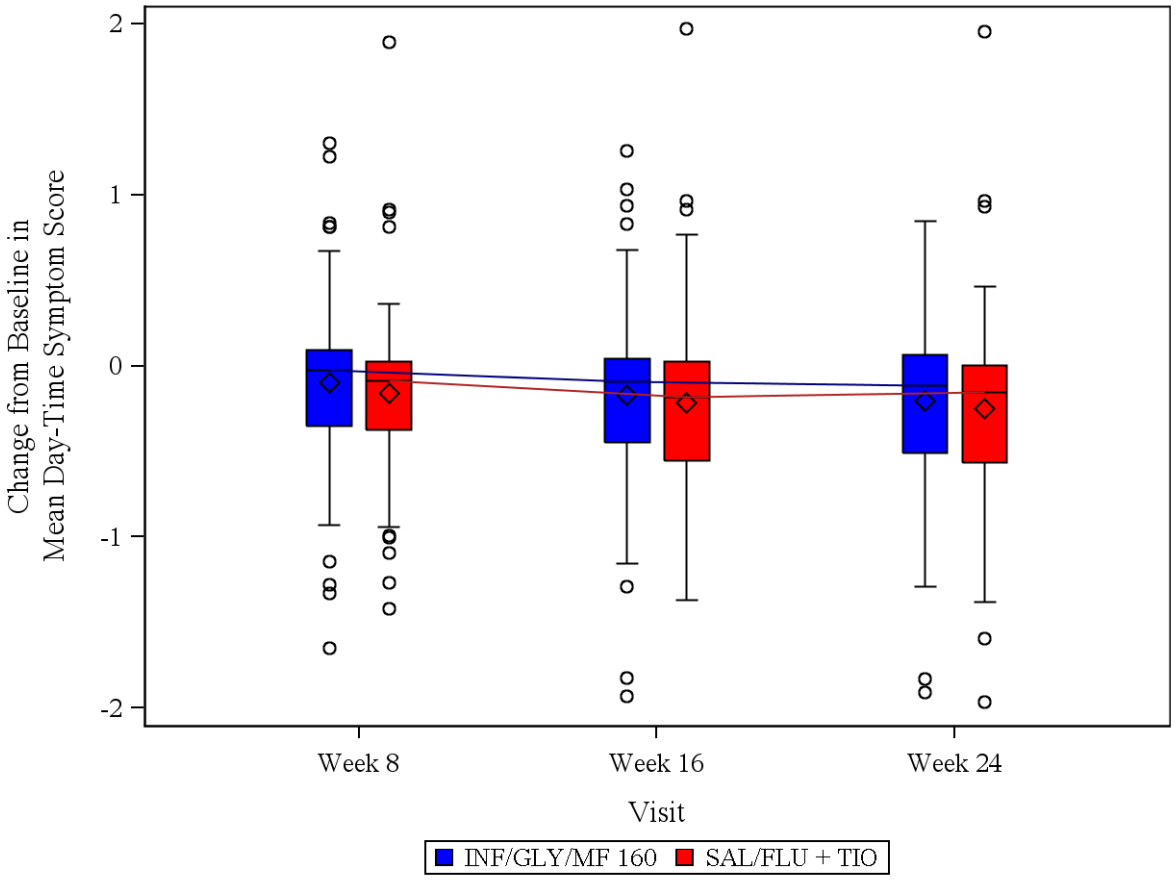


Figure 9.32.3 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Age (FAS), Age = ≥65 years



9.33 Boxplot: Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Gender (FAS)

Figure 9.33.1 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Gender (FAS), Gender = Male

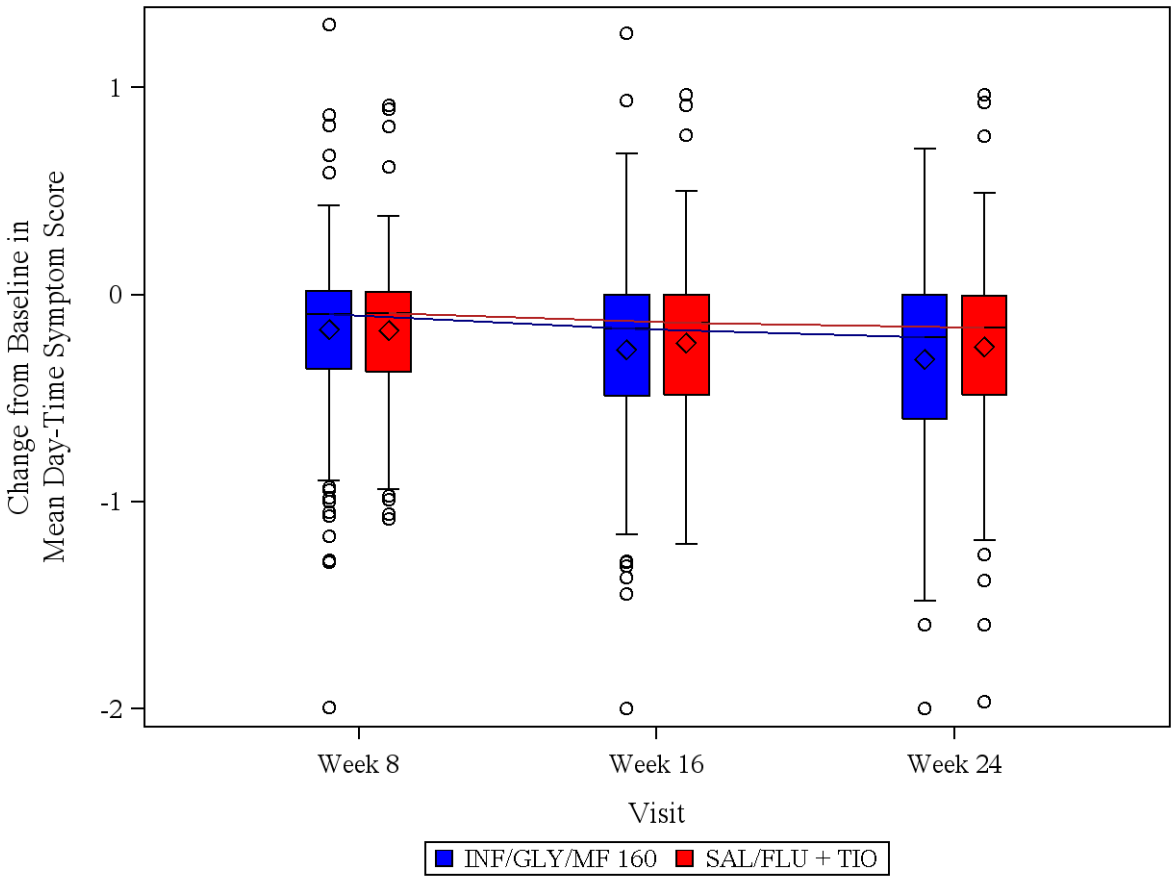
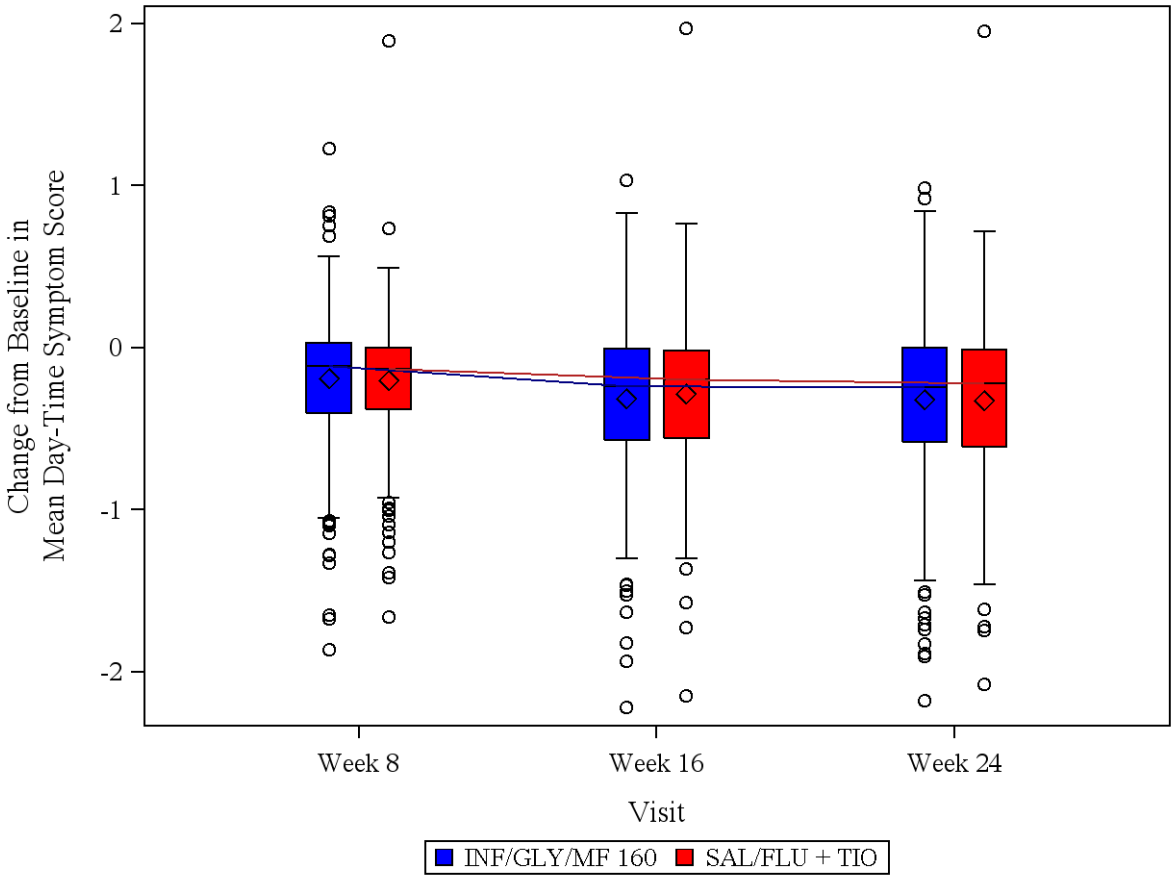


Figure 9.33.2 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Gender (FAS), Gender = Female



9.34 Boxplot: Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Region (FAS)

Figure 9.34.1 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Region (FAS), Region = Asia

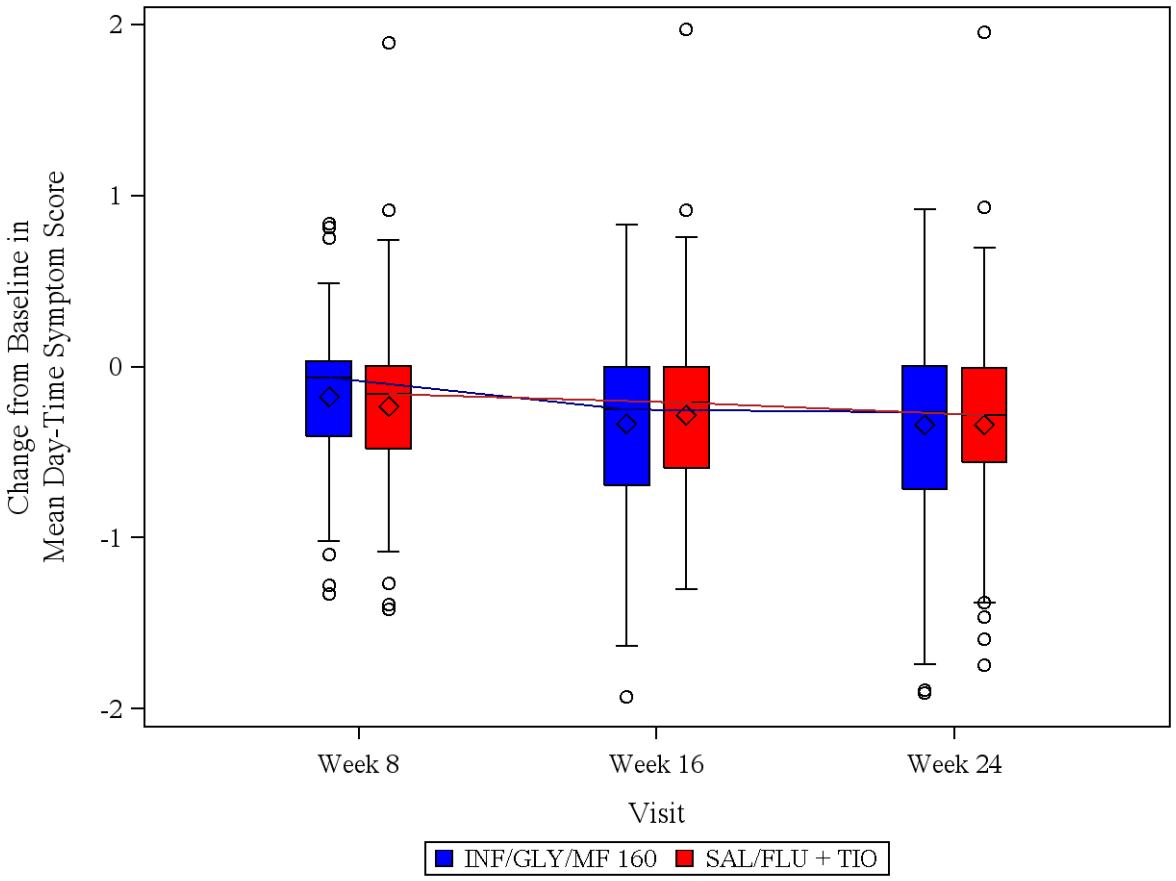


Figure 9.34.2 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Region (FAS), Region = Europe

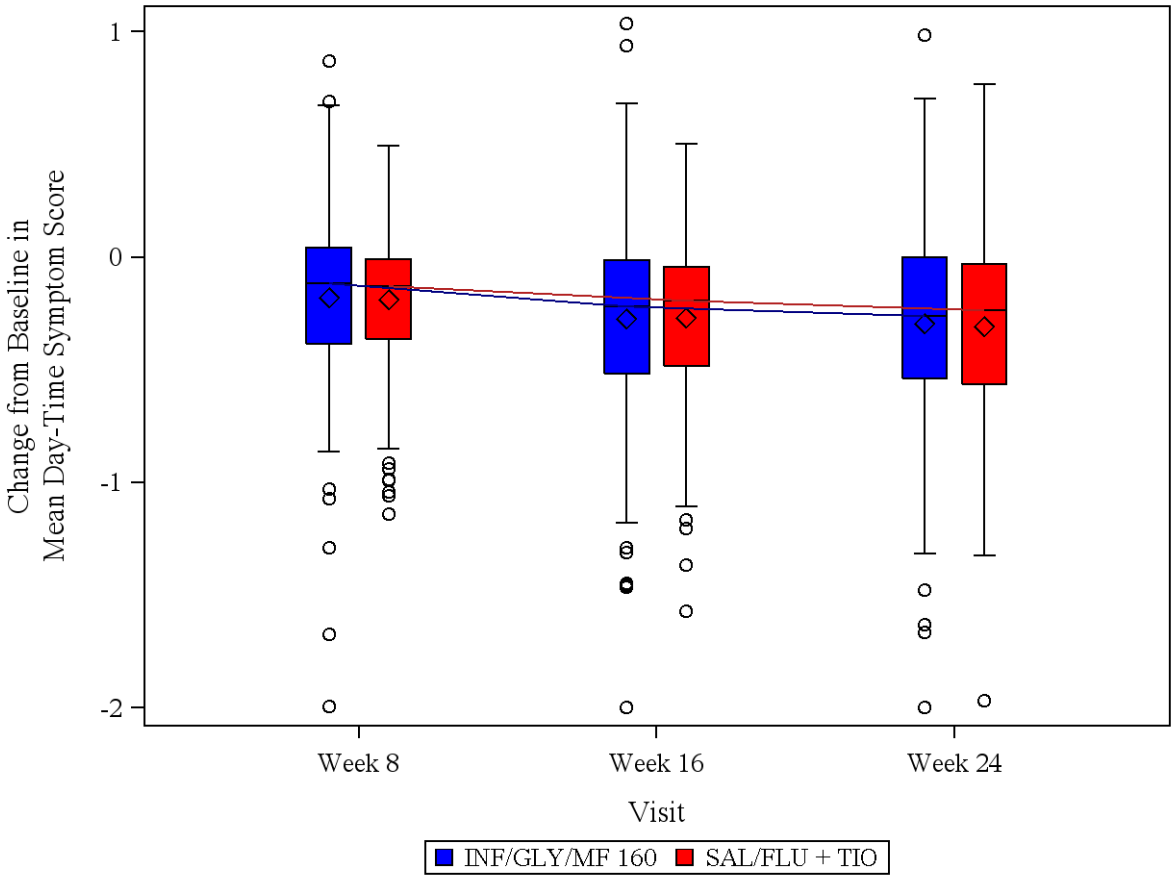


Figure 9.34.3 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Region (FAS), Region = Latin America

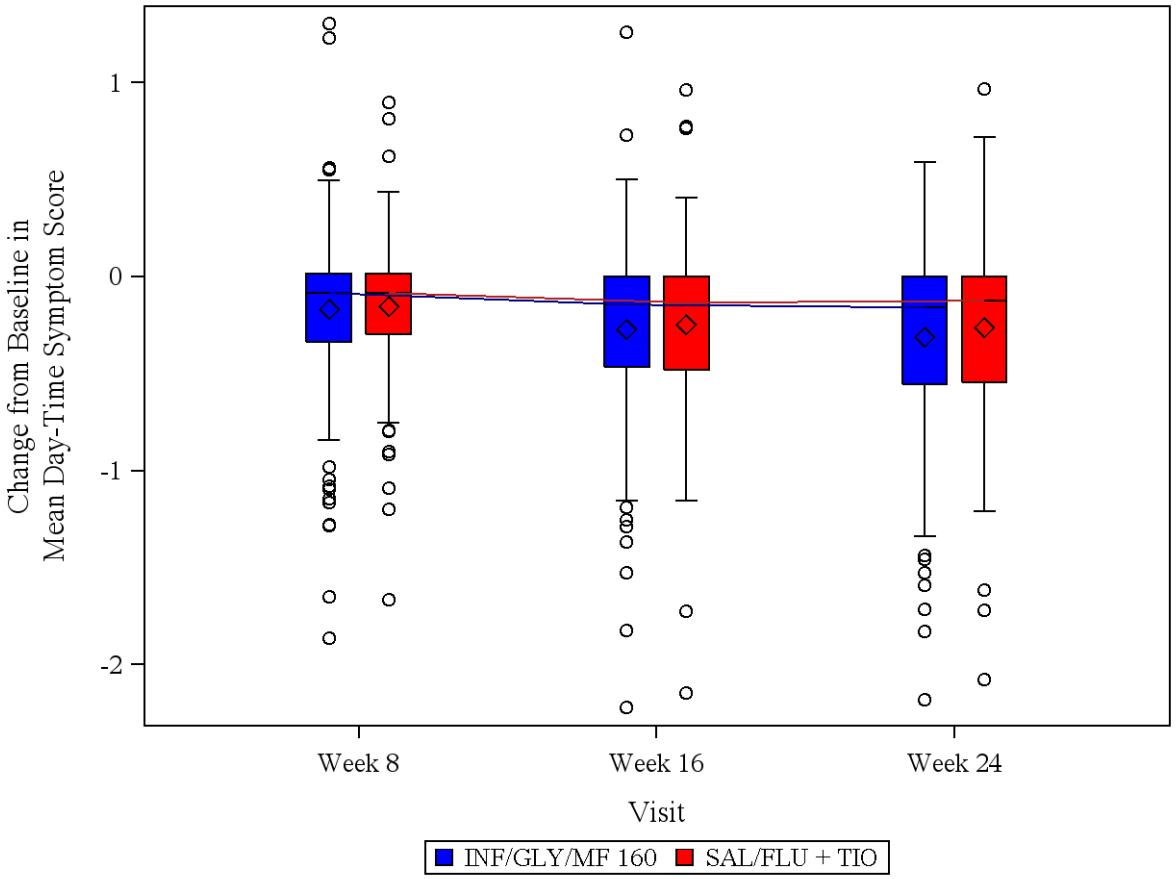
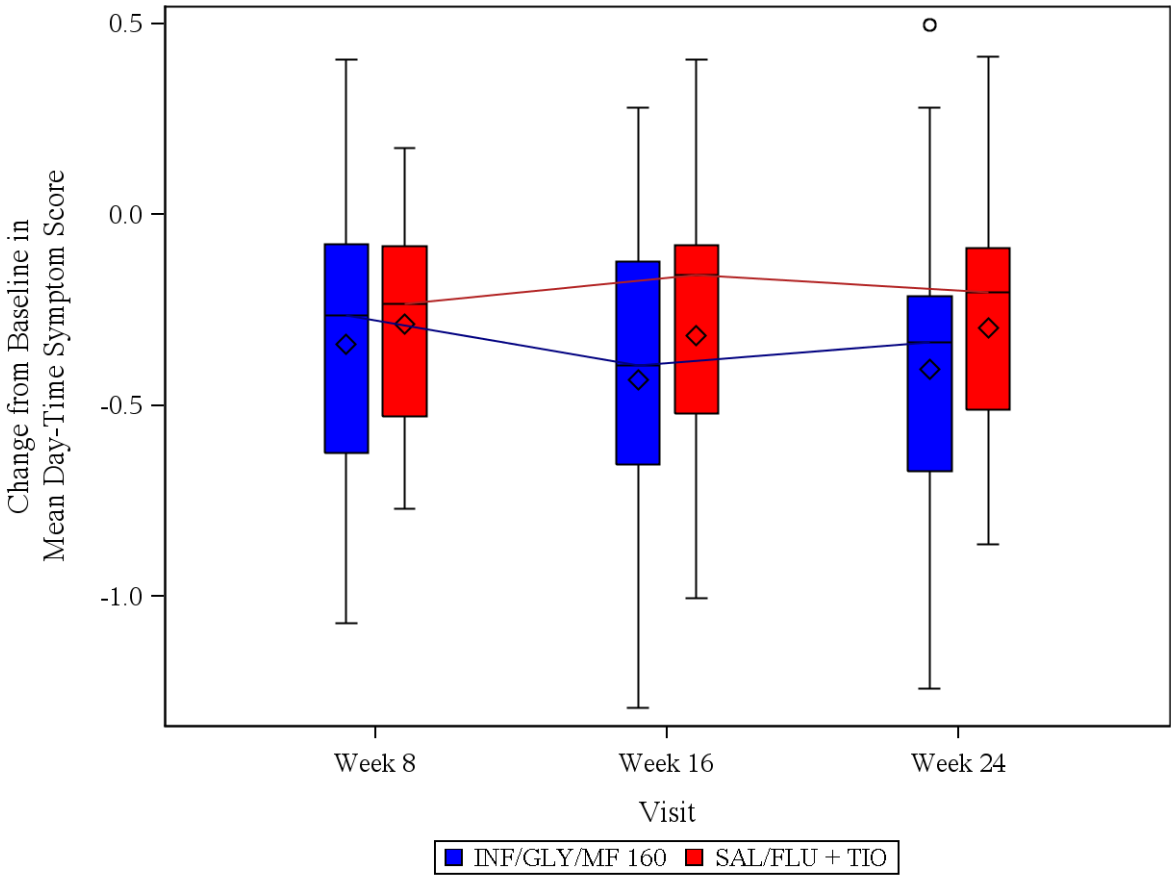


Figure 9.34.4 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Region (FAS), Region = Others



9.35 Boxplot: Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 9.35.1 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

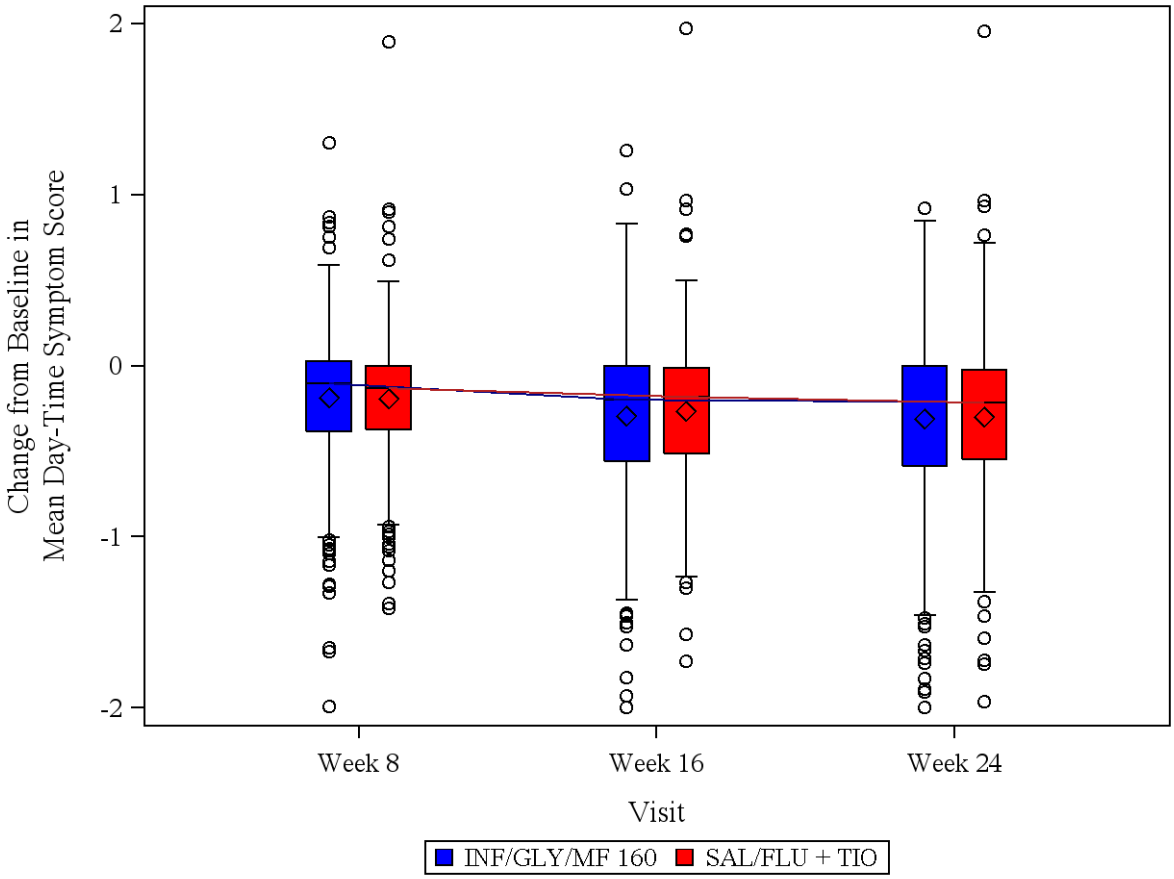
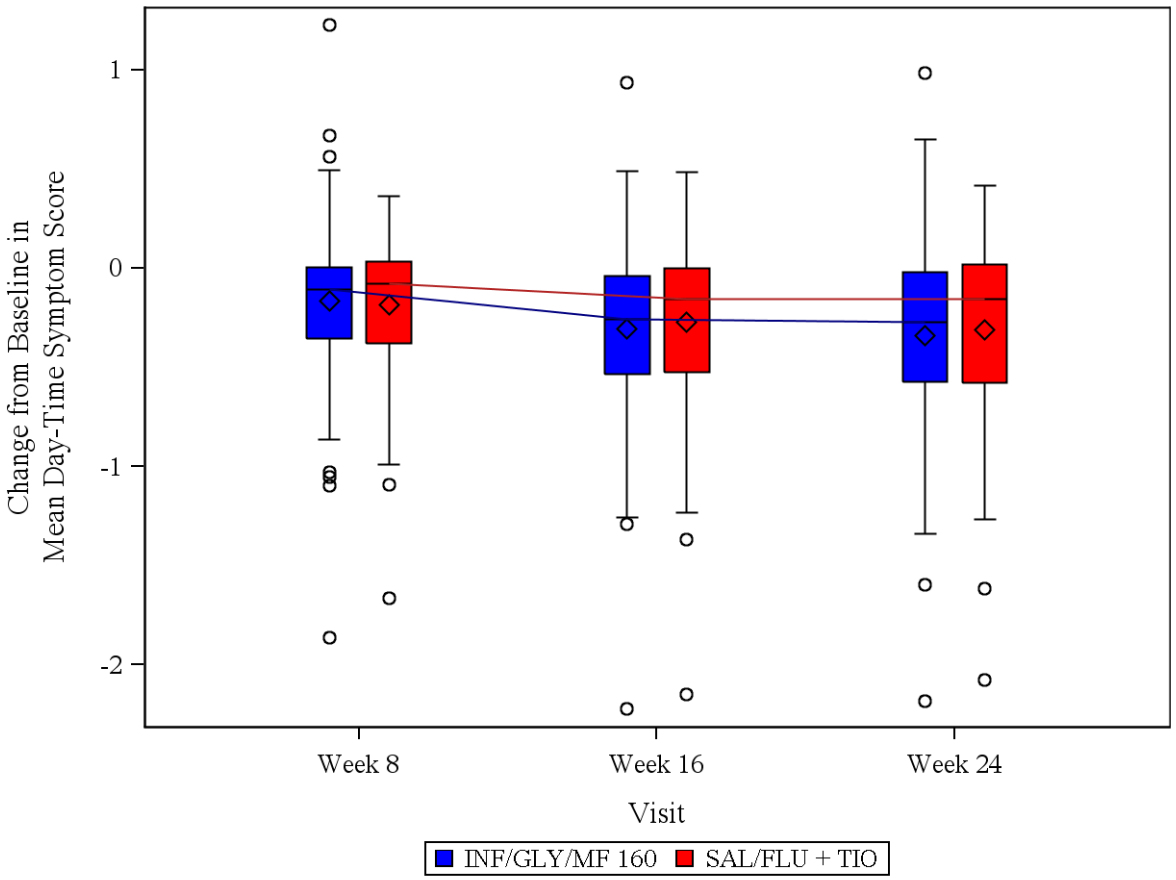


Figure 9.35.2 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.36 Boxplot: Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 9.36.1 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

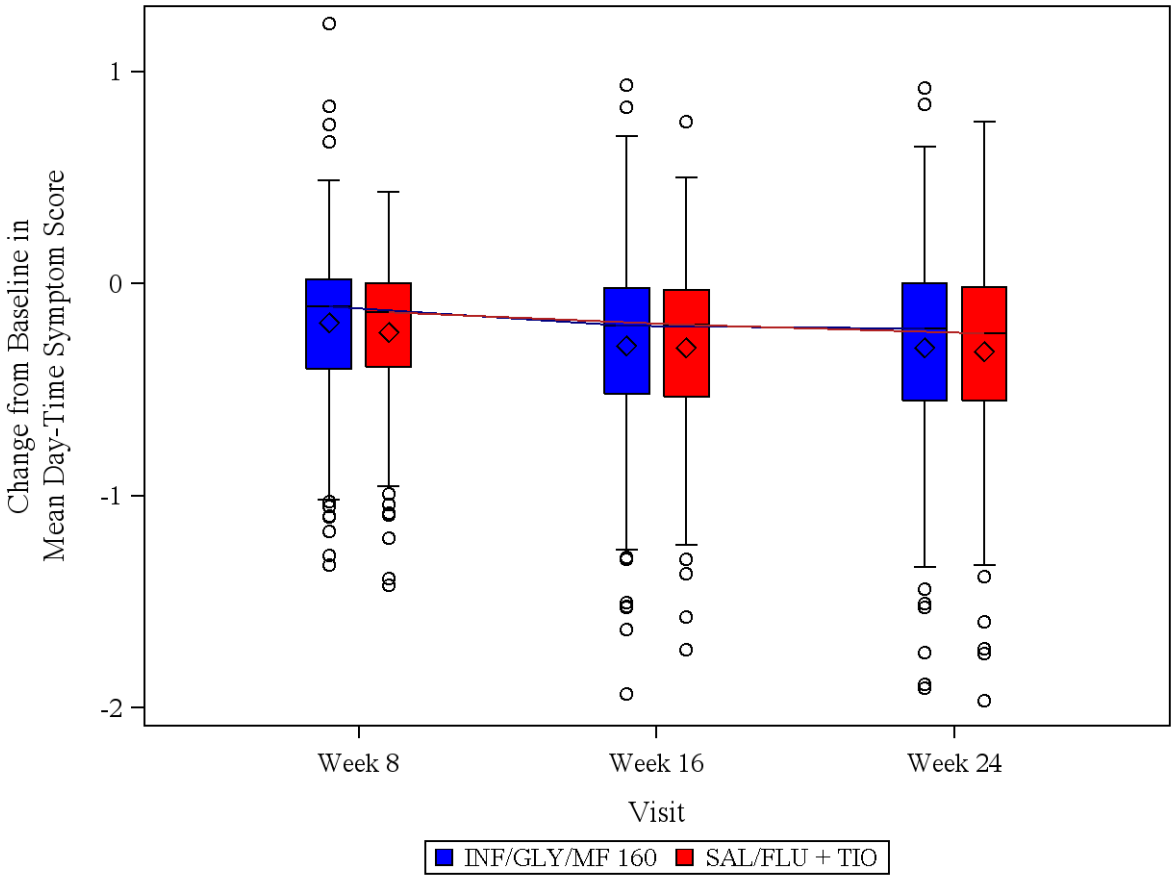
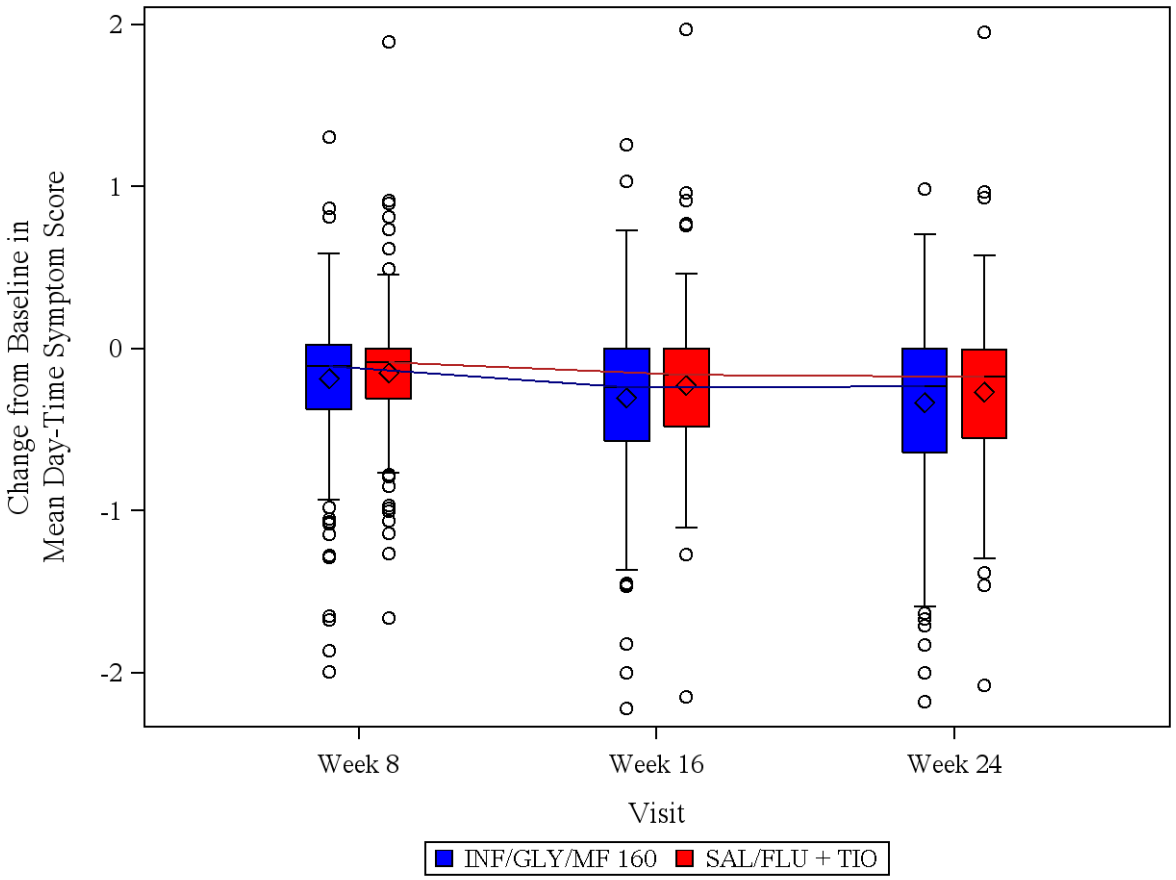
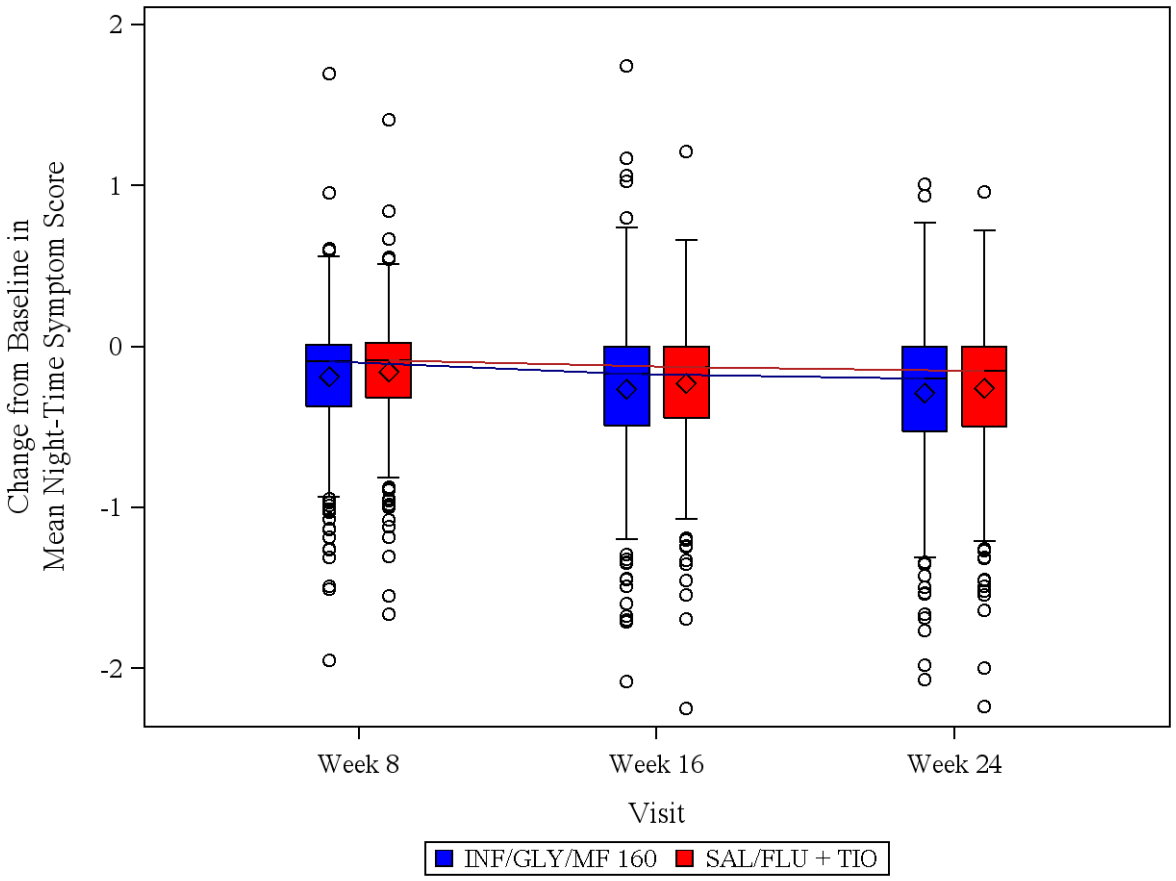


Figure 9.36.2 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



9.37 Boxplot: Symptoms (Mean Night-Time Symptom Score) - Change from Baseline (FAS)

Figure 9.37 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline (FAS)



9.38 Boxplot: Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Age (FAS)

Figure 9.38.1 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Age (FAS), Age = 18-39 years

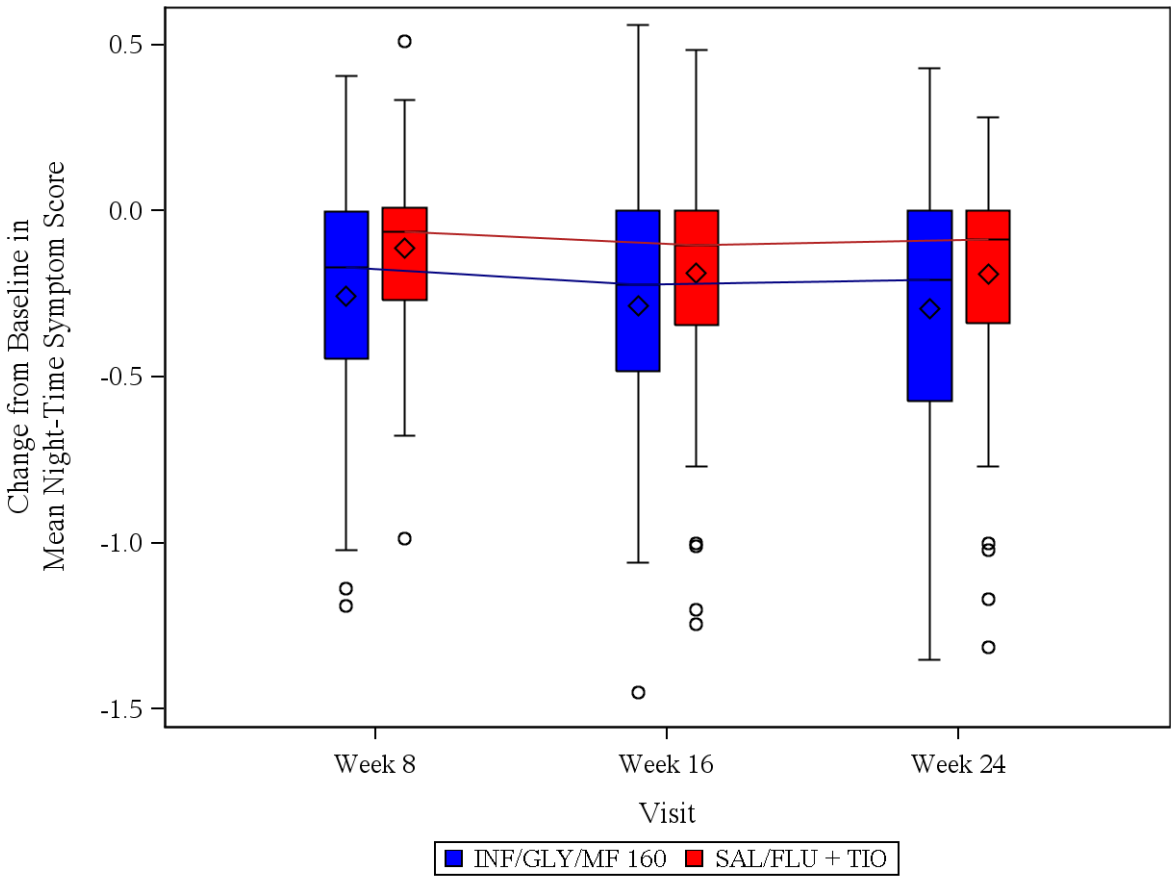


Figure 9.38.2 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Age (FAS), Age = 40-64 years

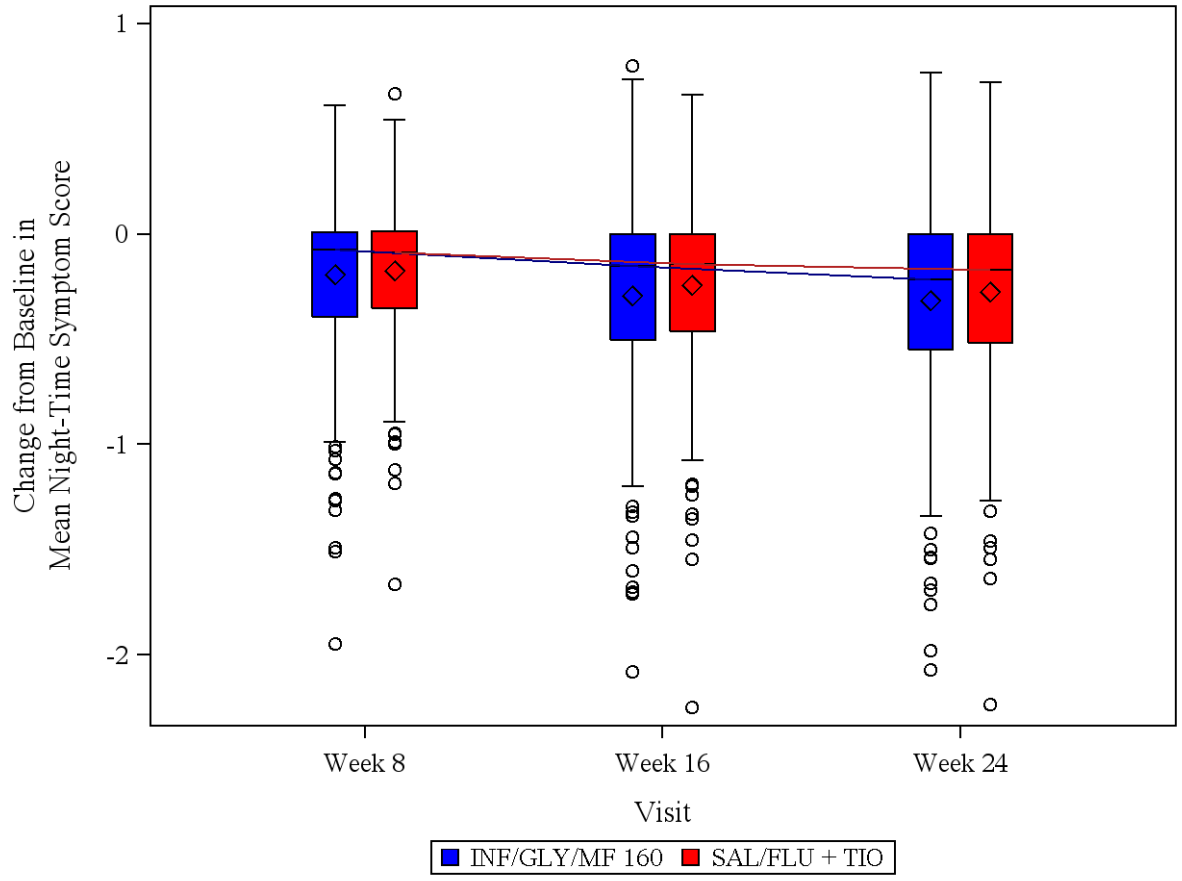
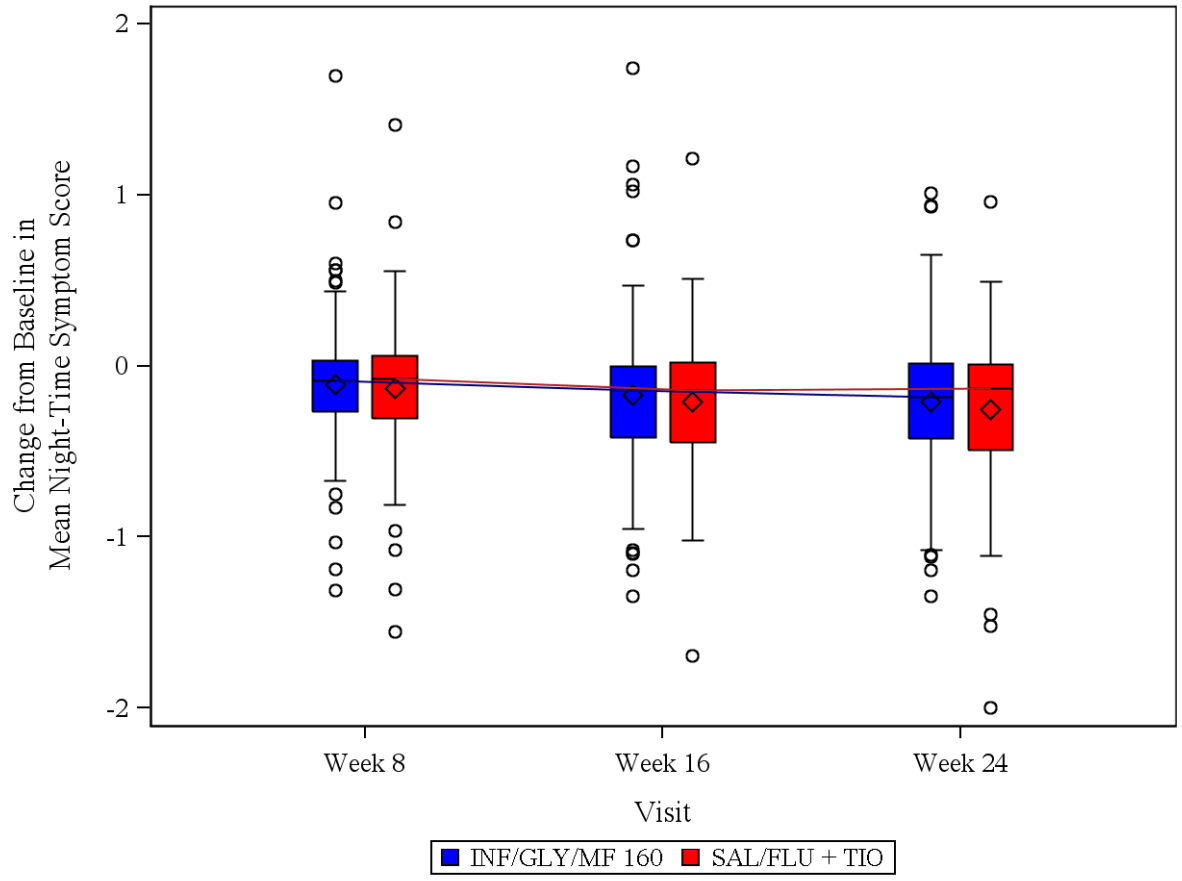


Figure 9.38.3 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Age (FAS), Age = ≥65 years



9.39 Boxplot: Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Gender (FAS)

Figure 9.39.1 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Gender (FAS), Gender = Male

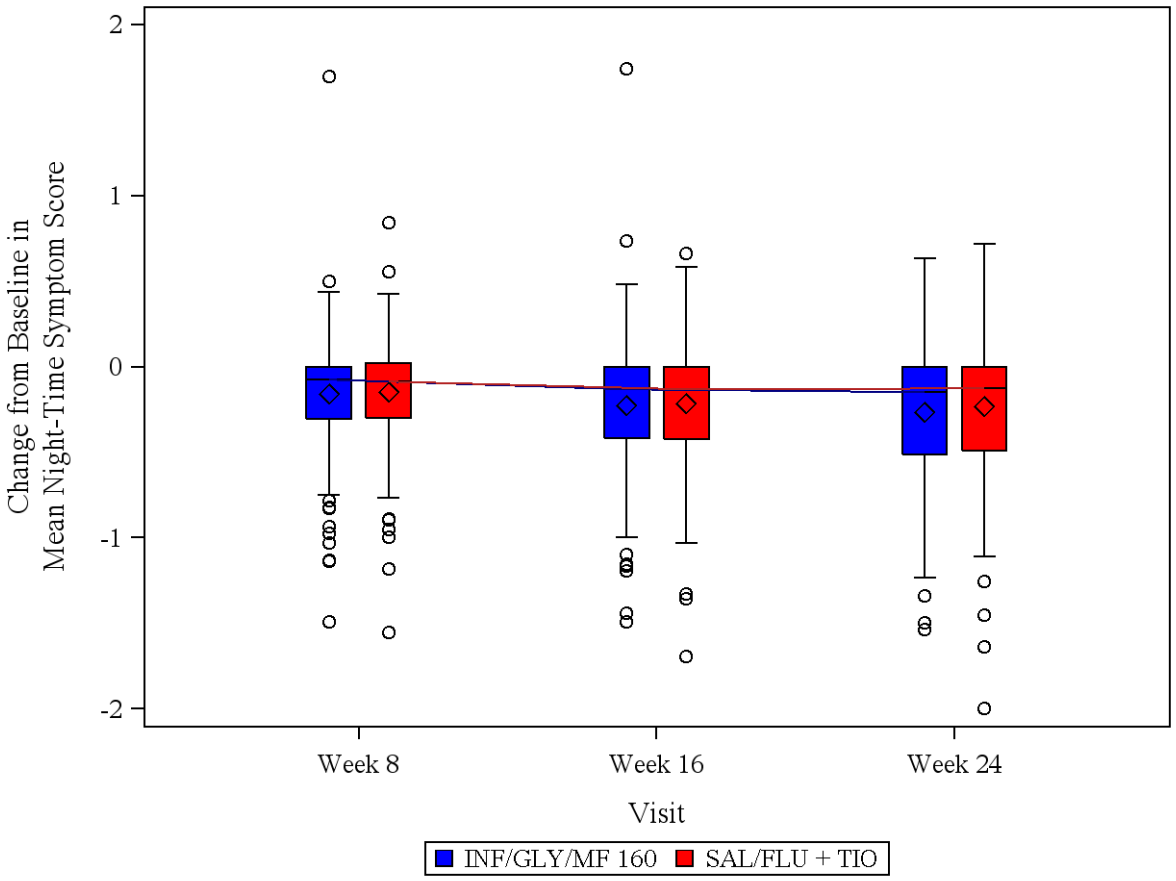
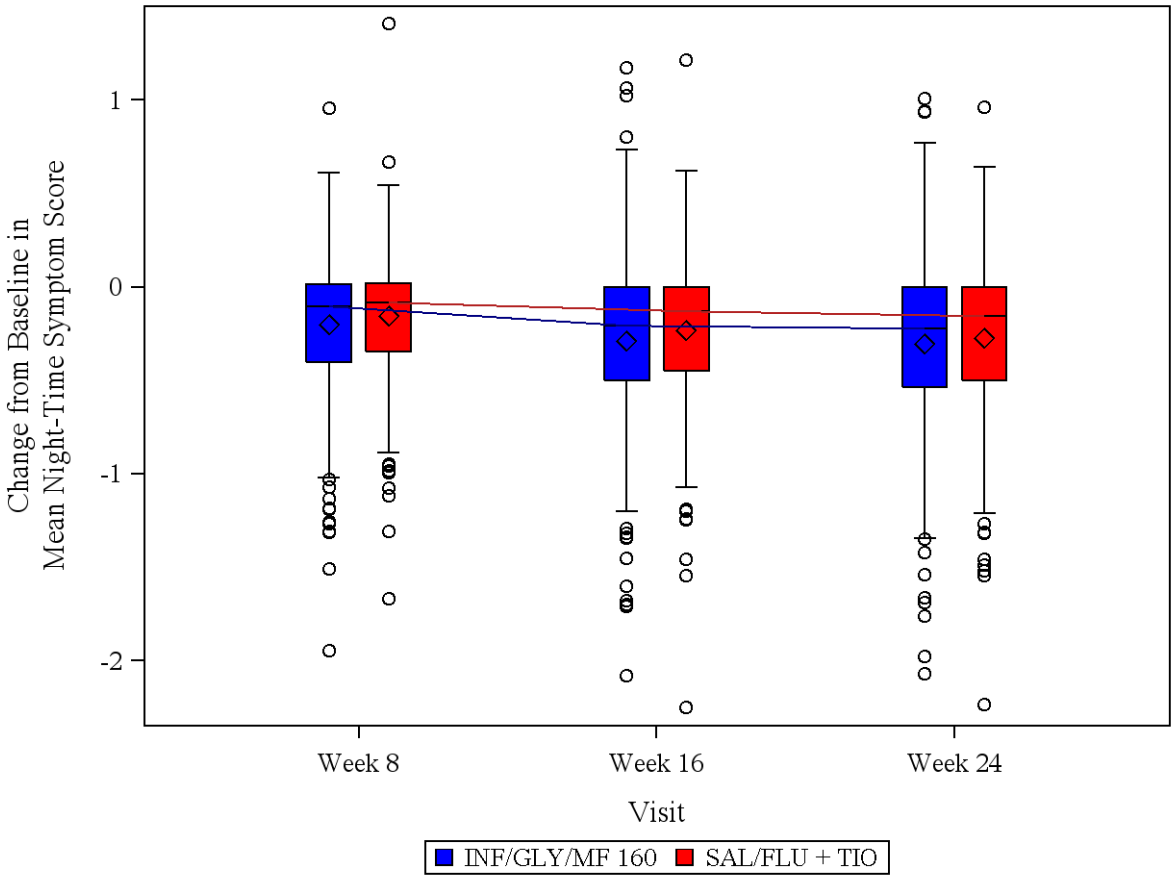


Figure 9.39.2 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Gender (FAS), Gender = Female



9.40 Boxplot: Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Region (FAS)

Figure 9.40.1 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Region (FAS), Region = Asia

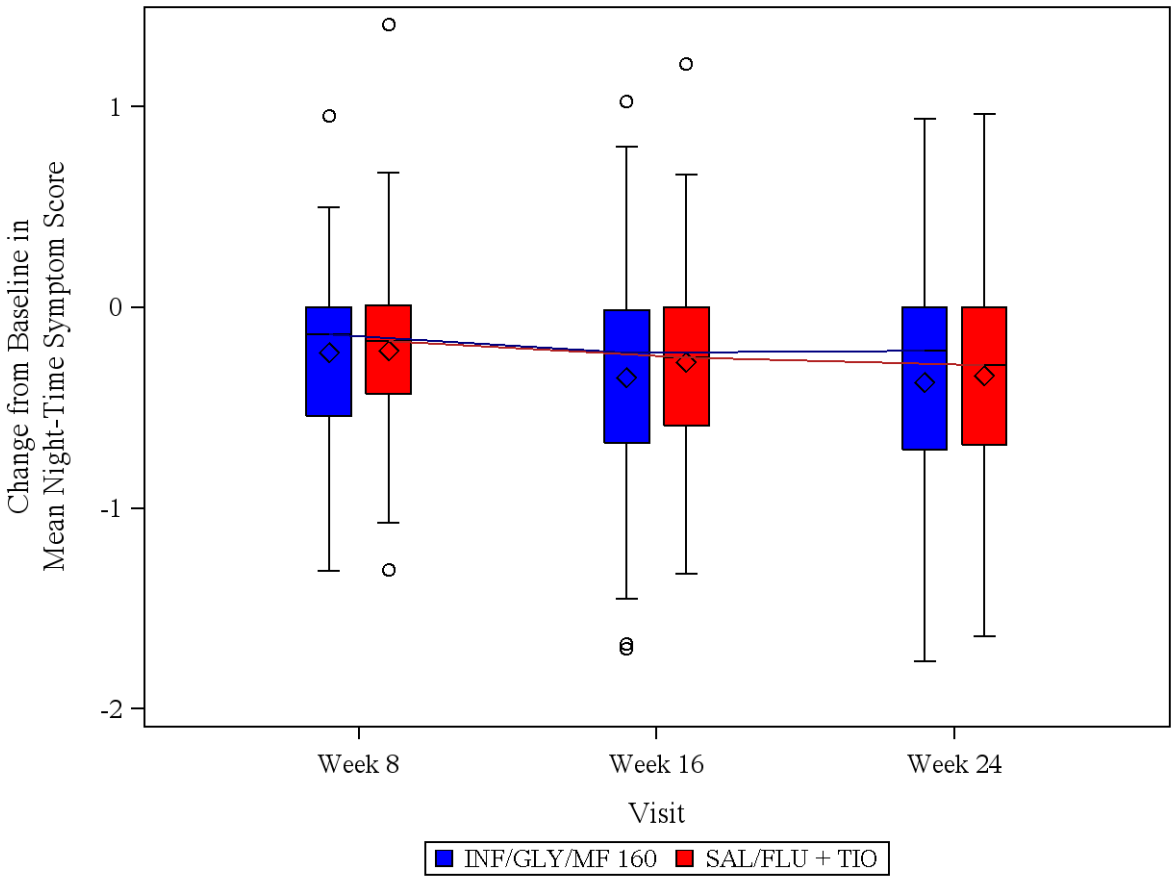


Figure 9.40.2 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Region (FAS), Region = Europe

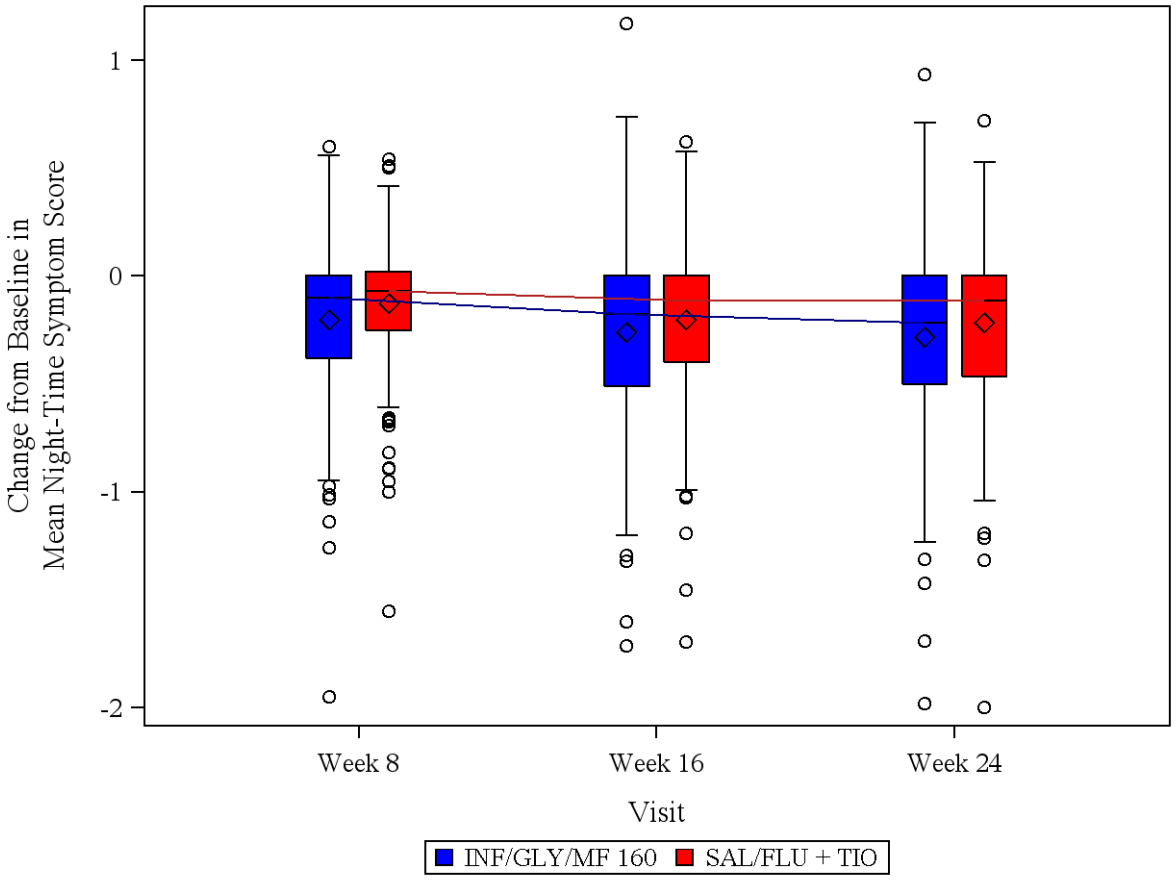


Figure 9.40.3 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Region (FAS), Region = Latin America

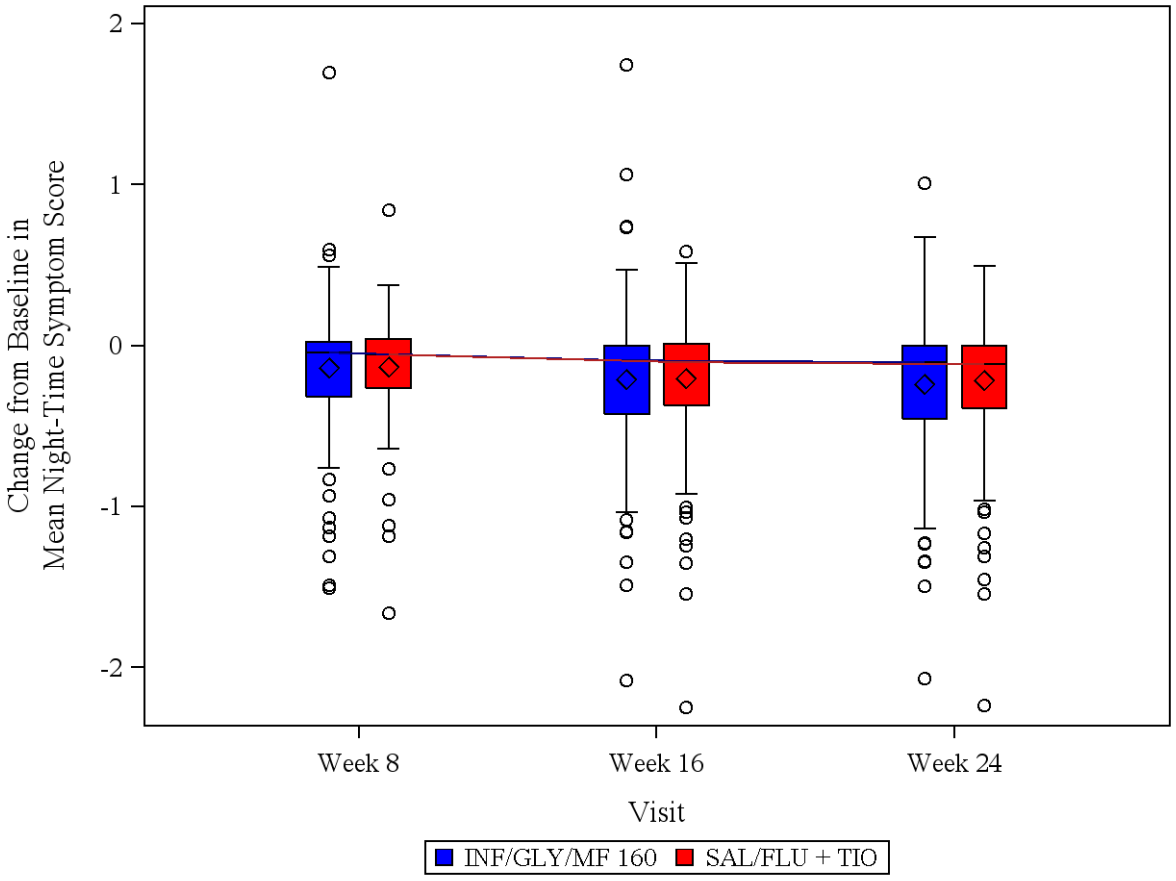
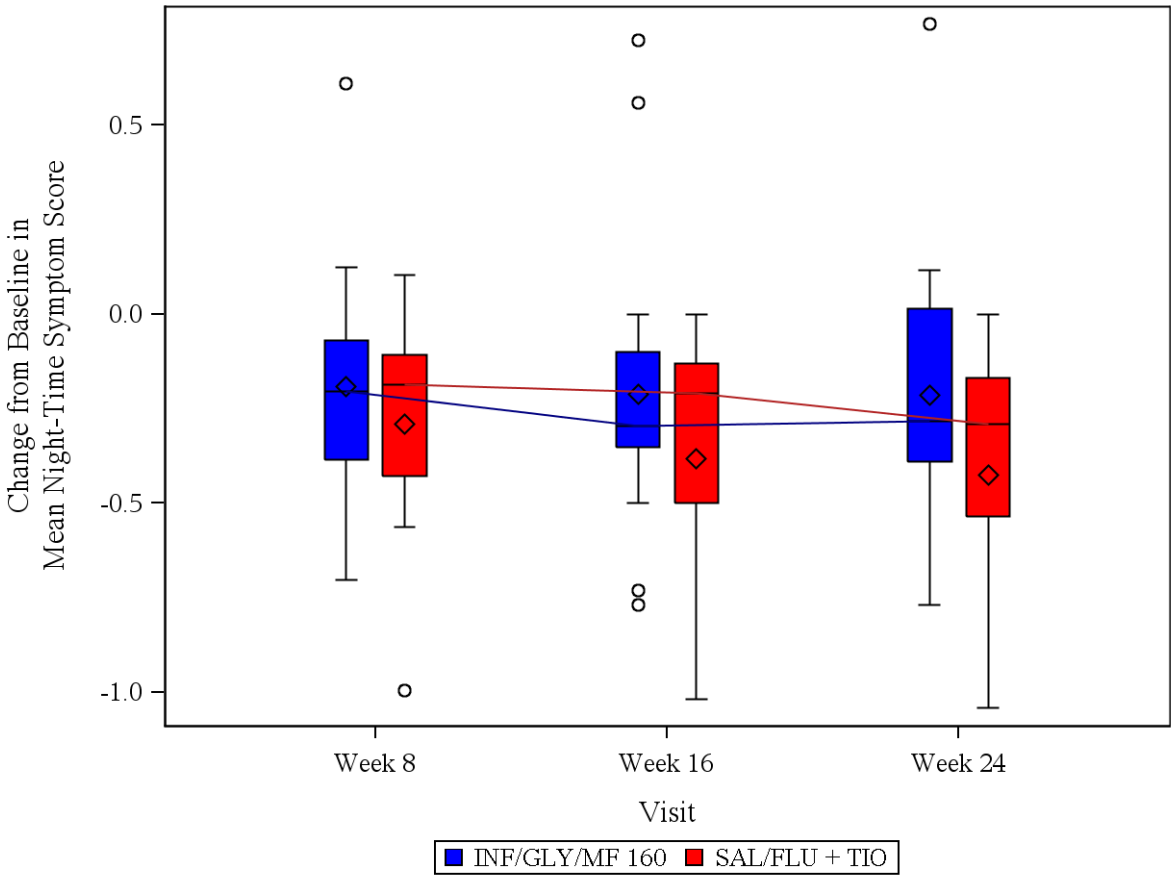


Figure 9.40.4 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Region (FAS), Region = Others



9.41 Boxplot: Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 9.41.1 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

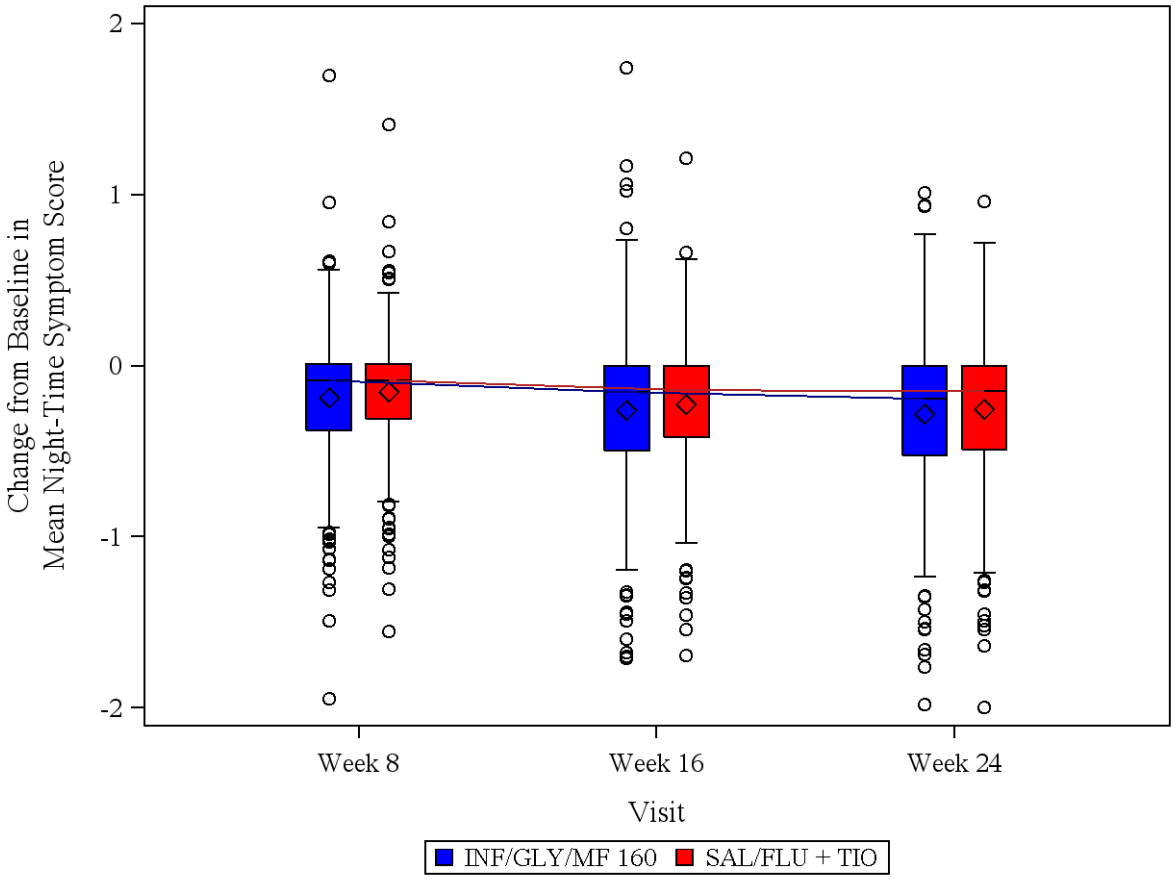
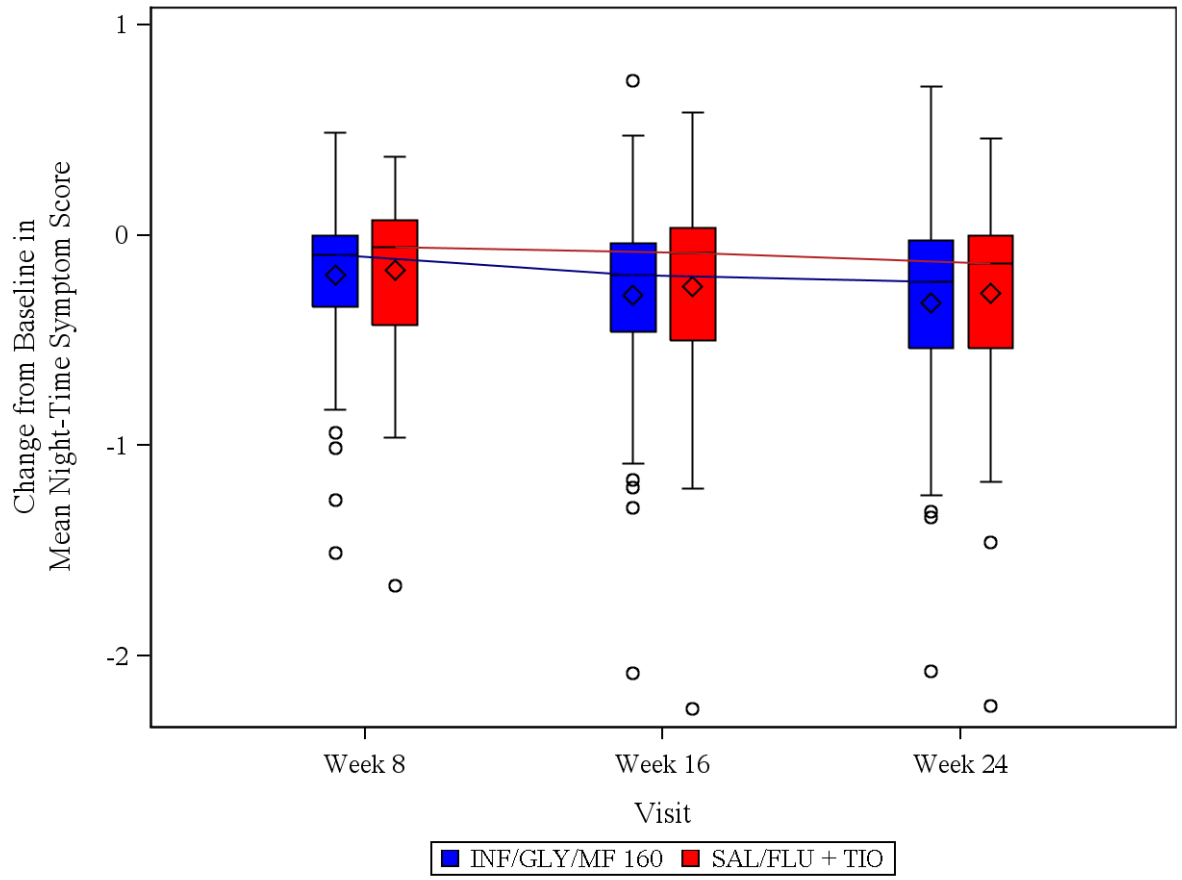


Figure 9.41.2 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.42 Boxplot: Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 9.42.1 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

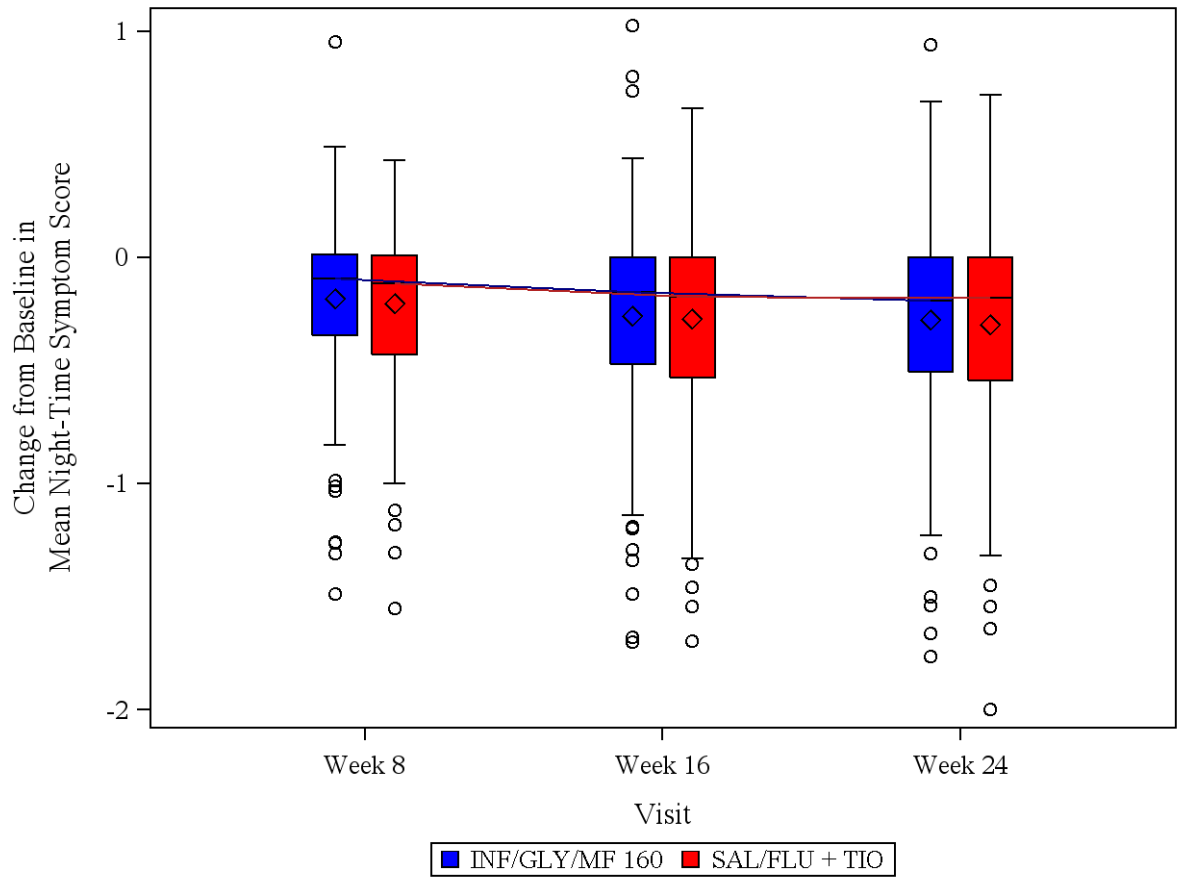
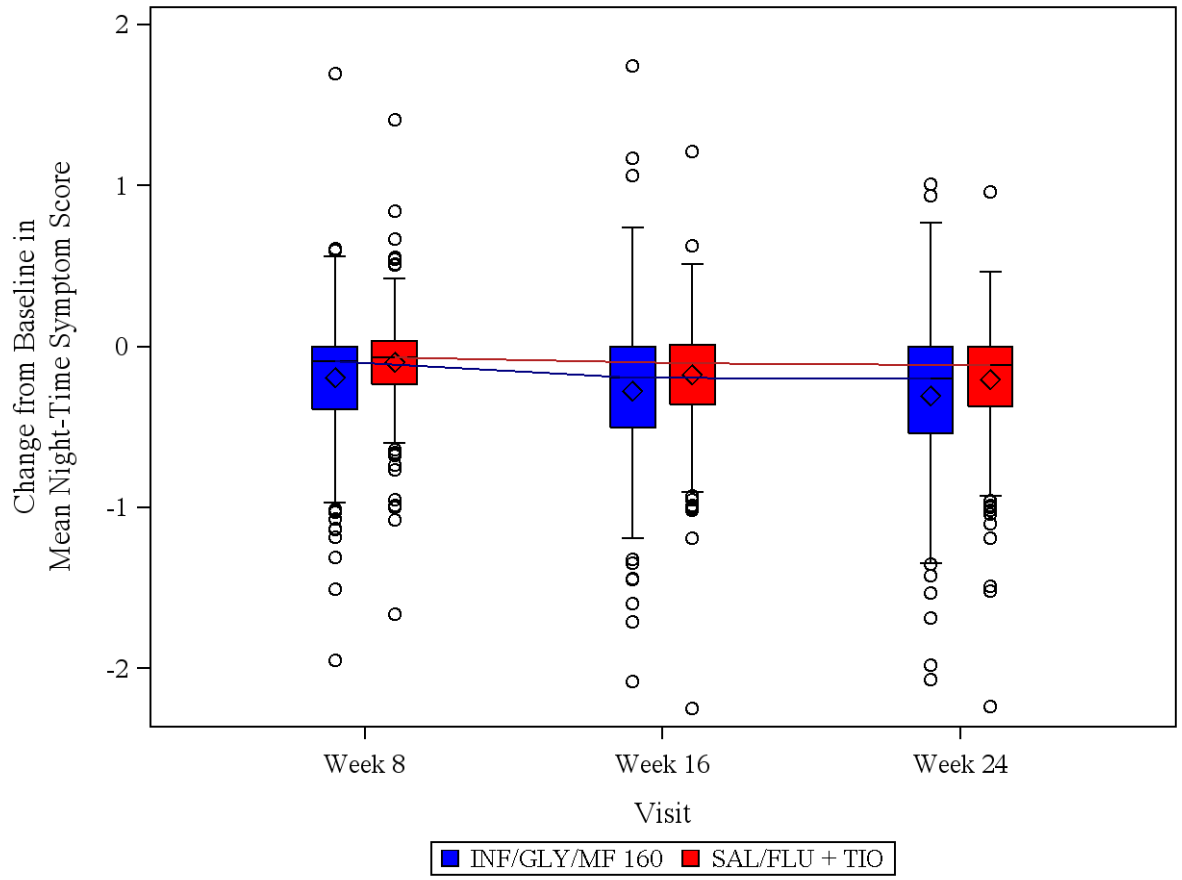
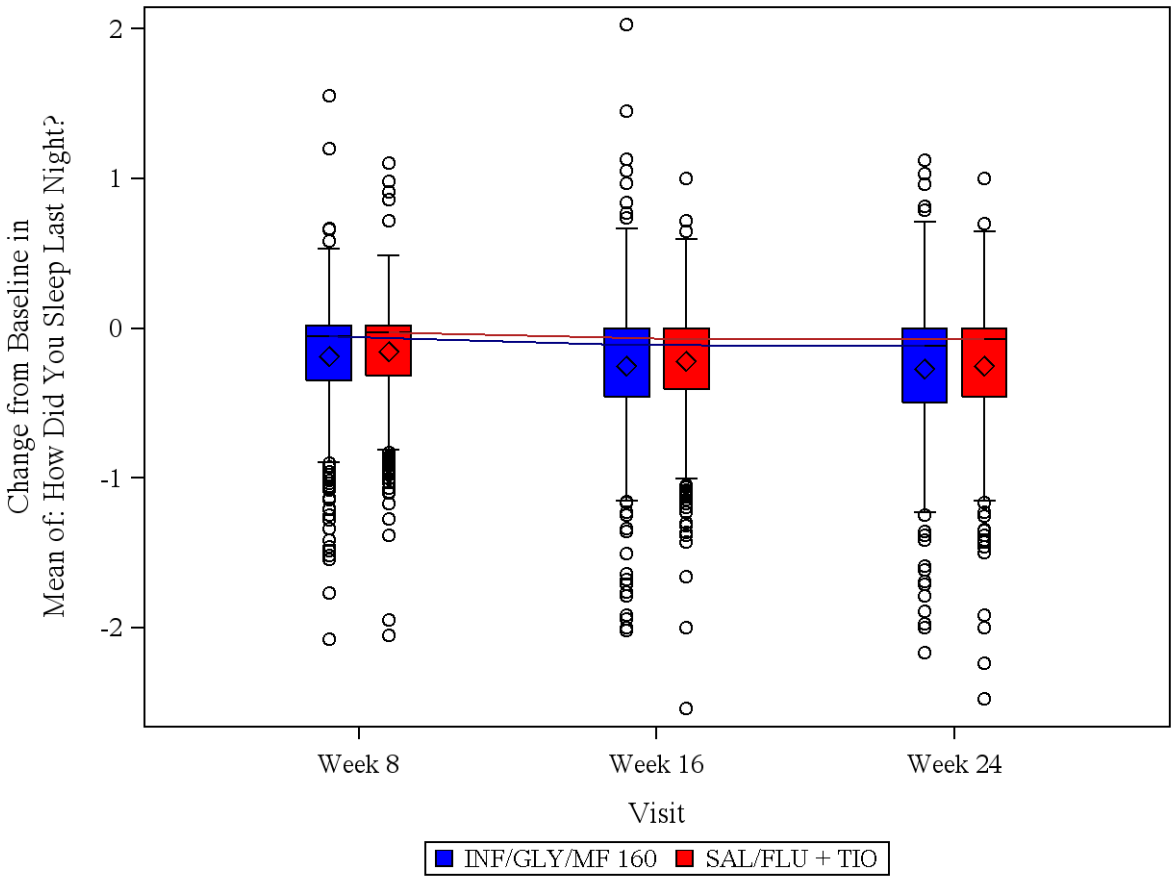


Figure 9.42.2 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



9.43 Boxplot: Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline (FAS)

Figure 9.43 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline (FAS)



9.44 Boxplot: Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Age (FAS)

Figure 9.44.1 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Age (FAS), Age = 18-39 years

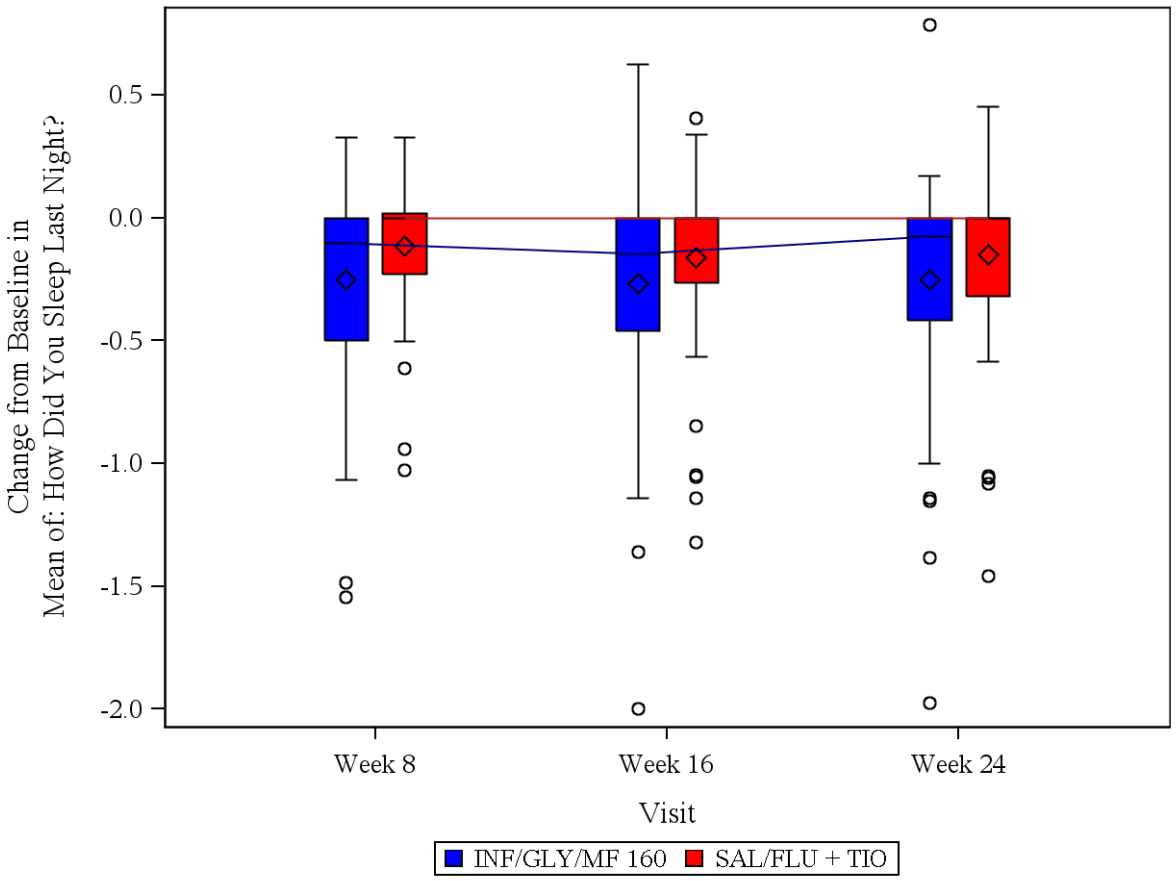


Figure 9.44.2 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Age (FAS), Age = 40-64 years

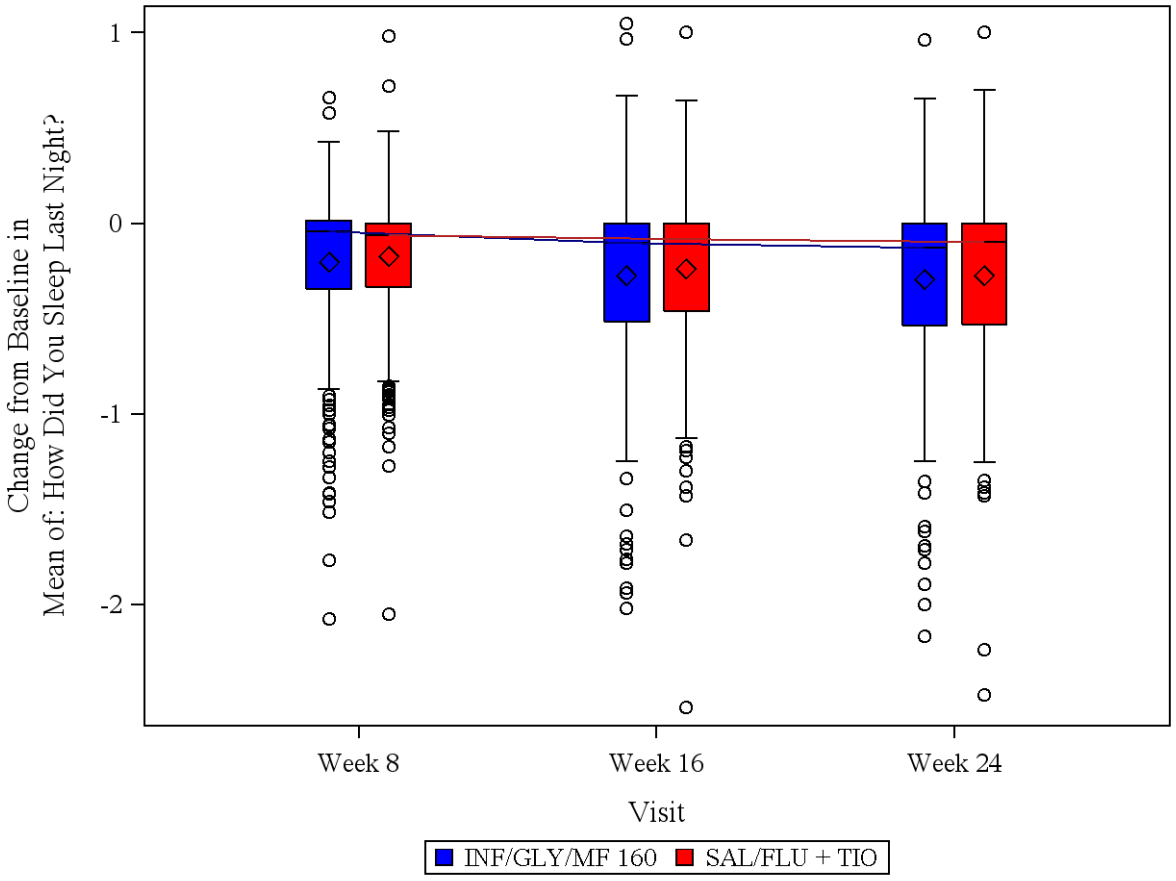
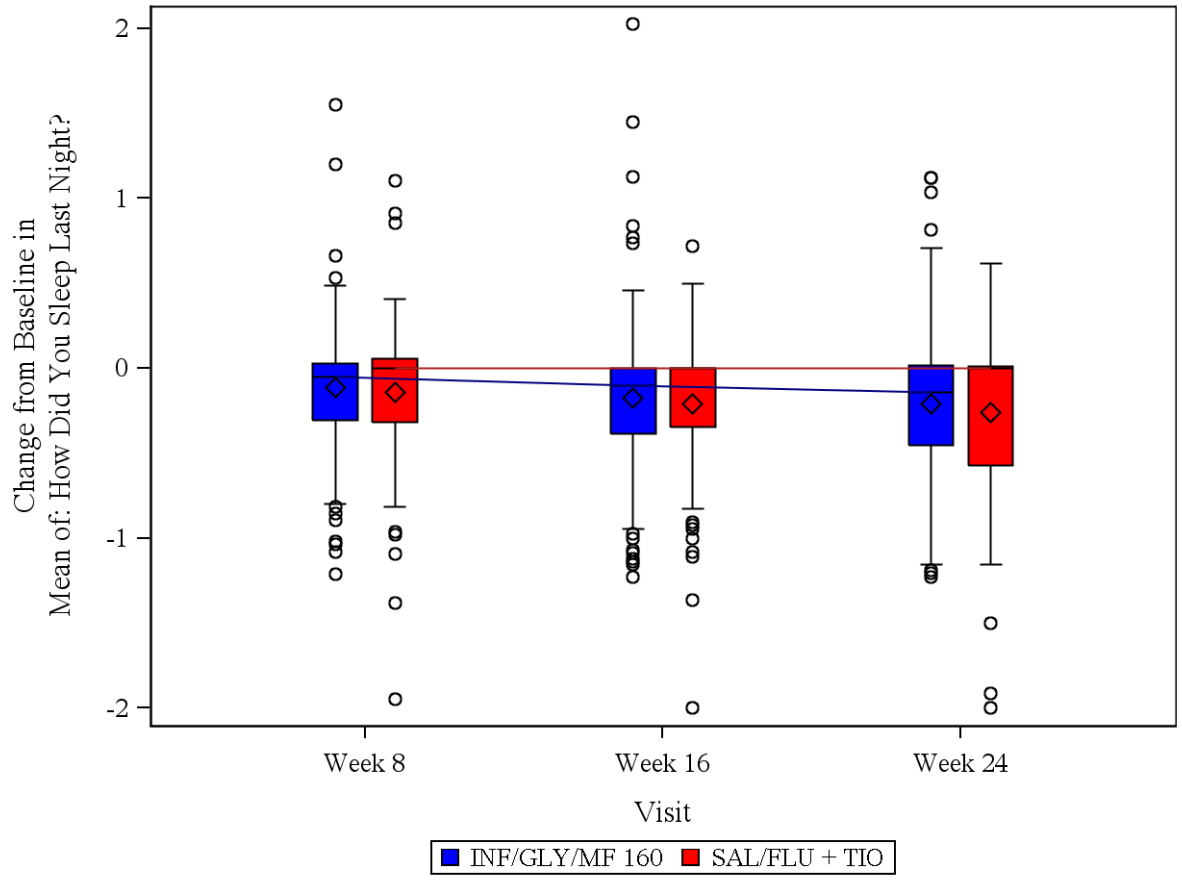


Figure 9.44.3 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Age (FAS), Age = ≥65 years



9.45 Boxplot: Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Gender (FAS)

Figure 9.45.1 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Gender (FAS), Gender = Male

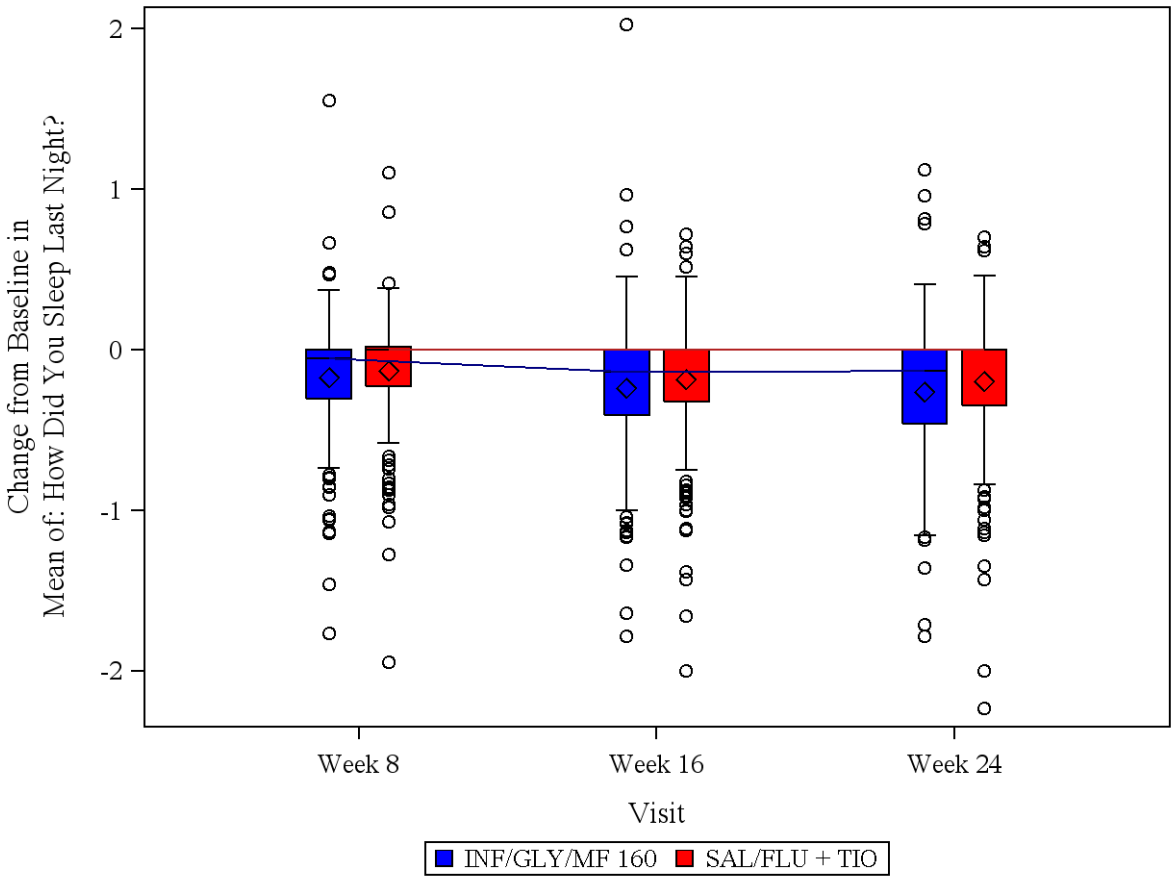
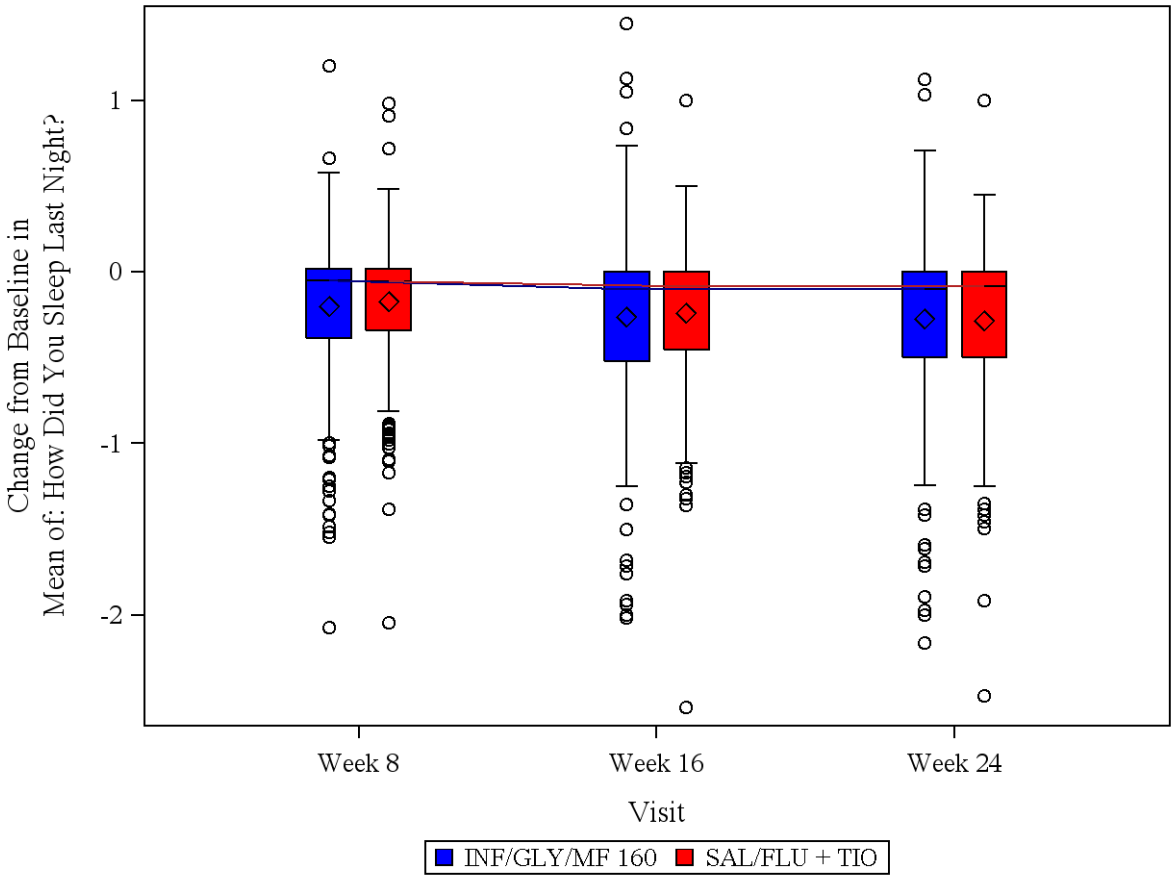


Figure 9.45.2 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Gender (FAS), Gender = Female



9.46 Boxplot: Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Region (FAS)

Figure 9.46.1 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Region (FAS), Region = Asia

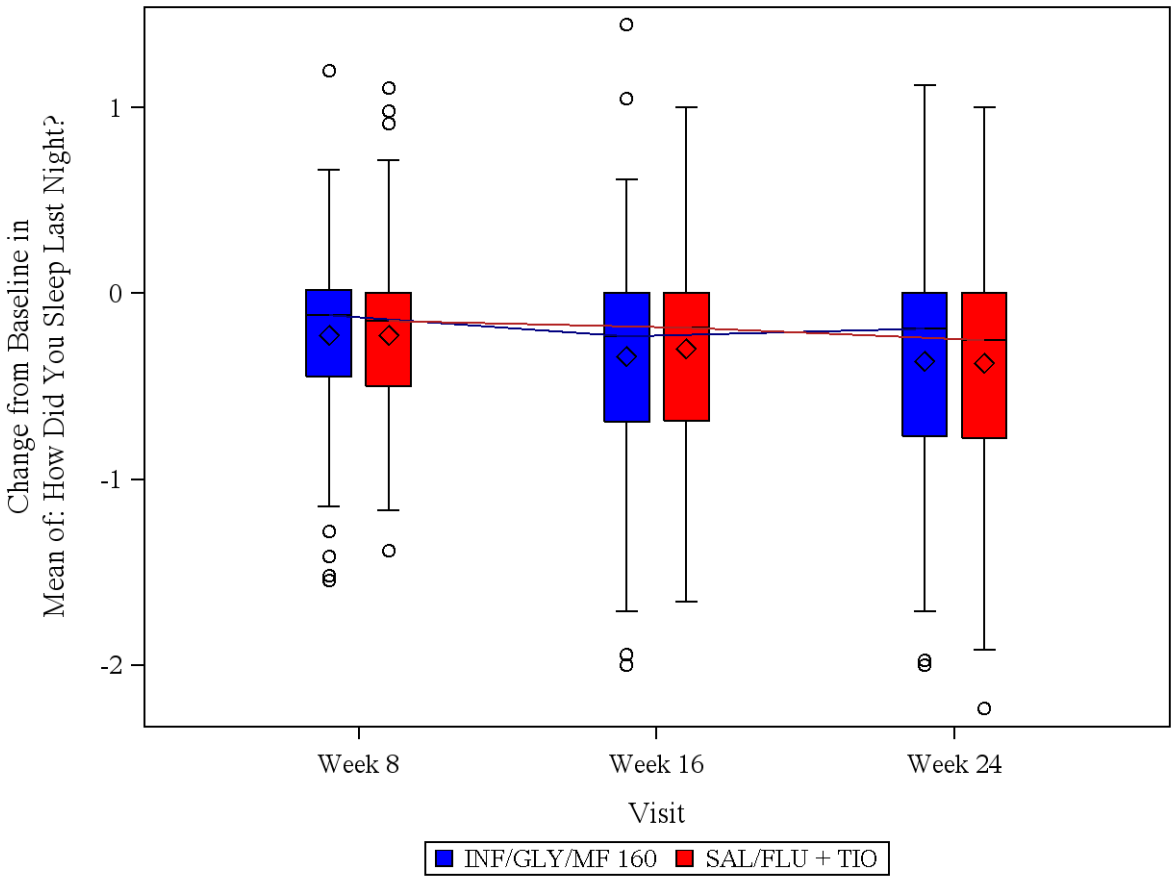


Figure 9.46.2 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Region (FAS), Region = Europe

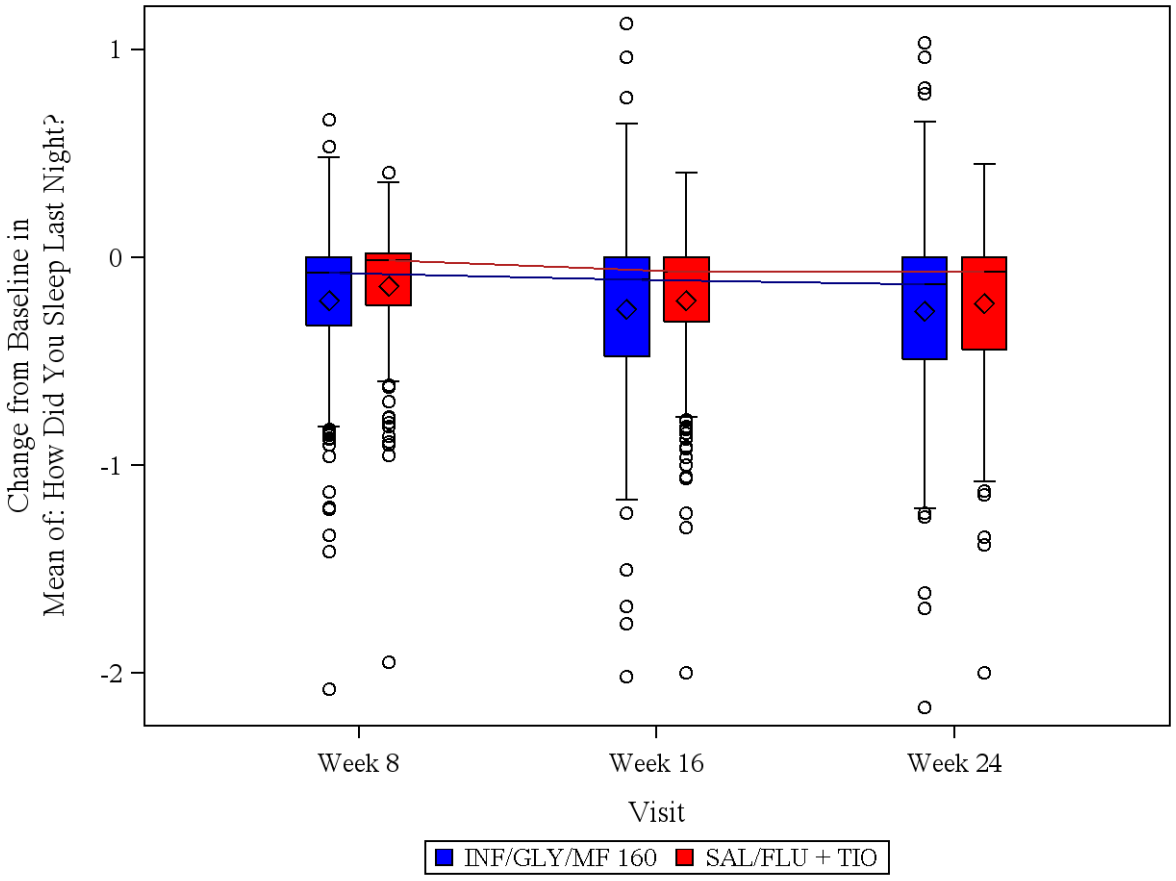


Figure 9.46.3 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Region (FAS), Region = Latin America

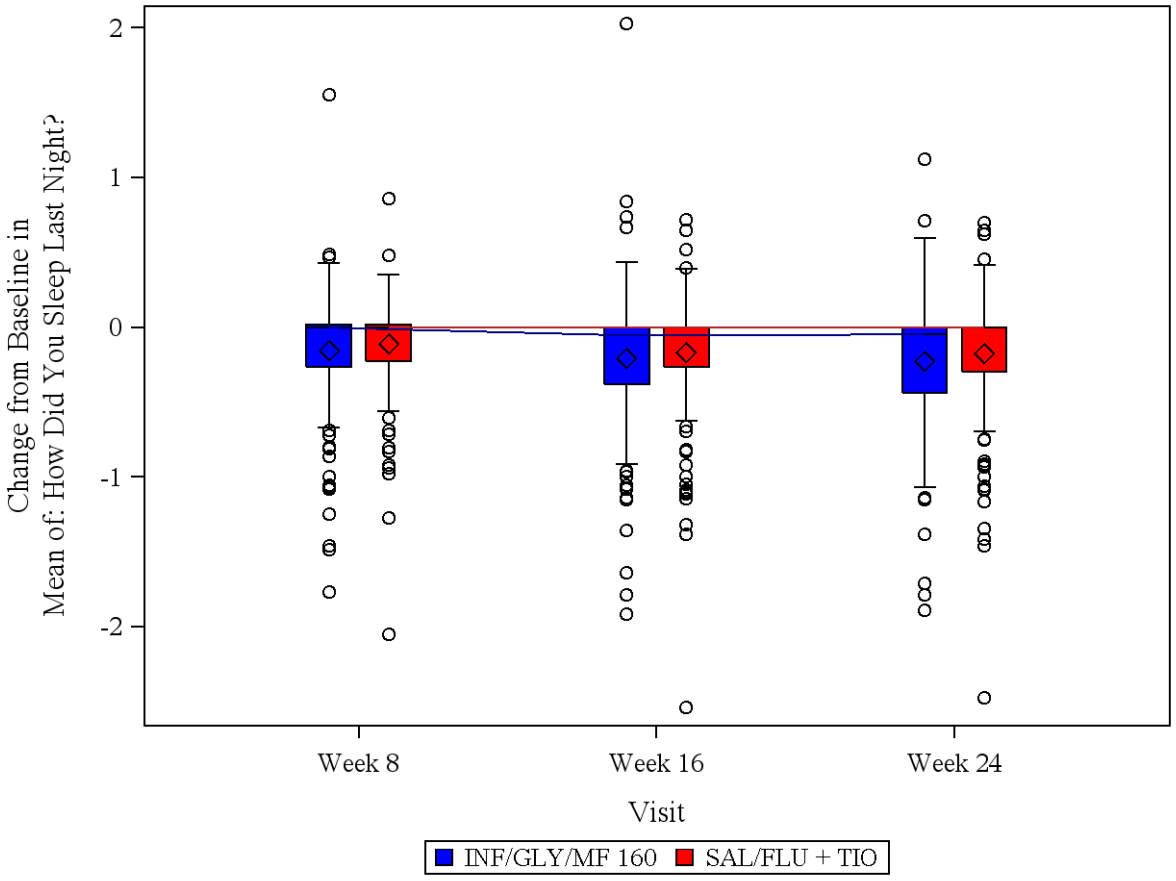
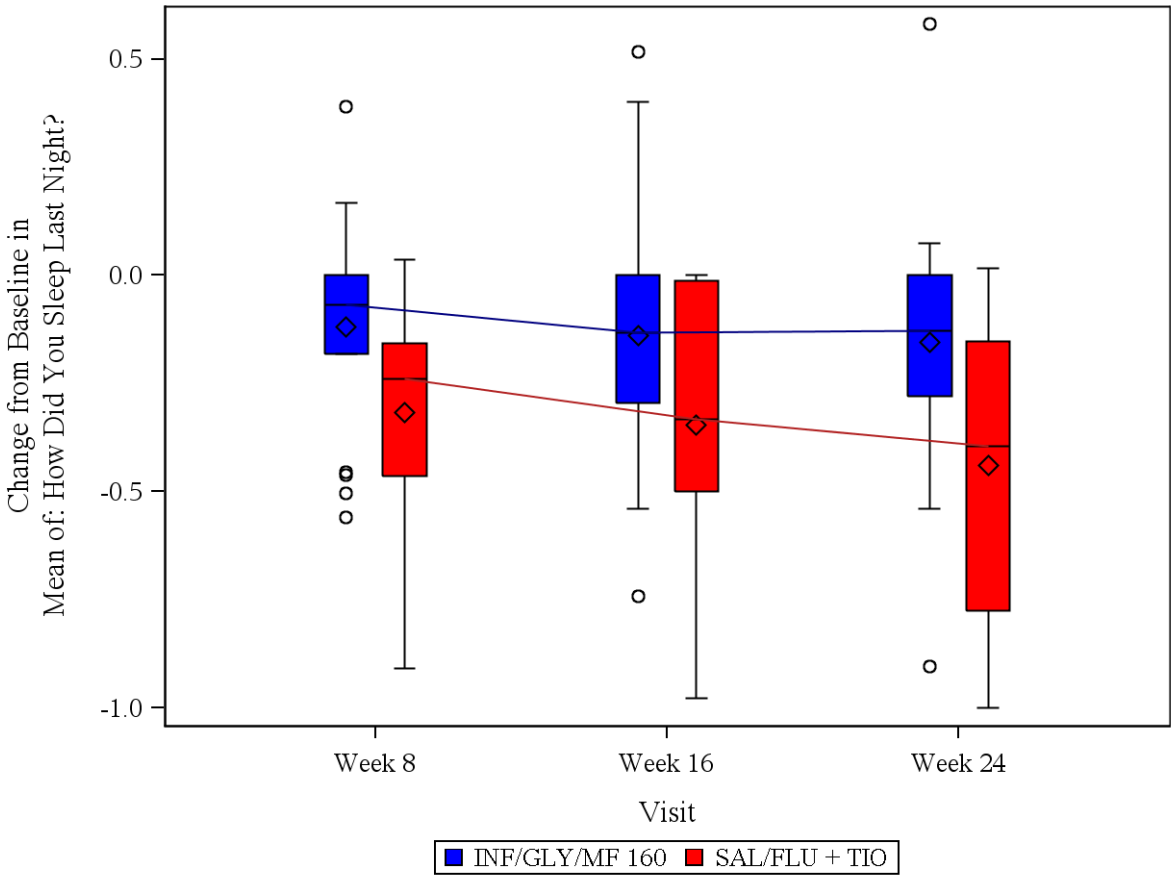


Figure 9.46.4 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Region (FAS), Region = Others



9.47 Boxplot: Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 9.47.1 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

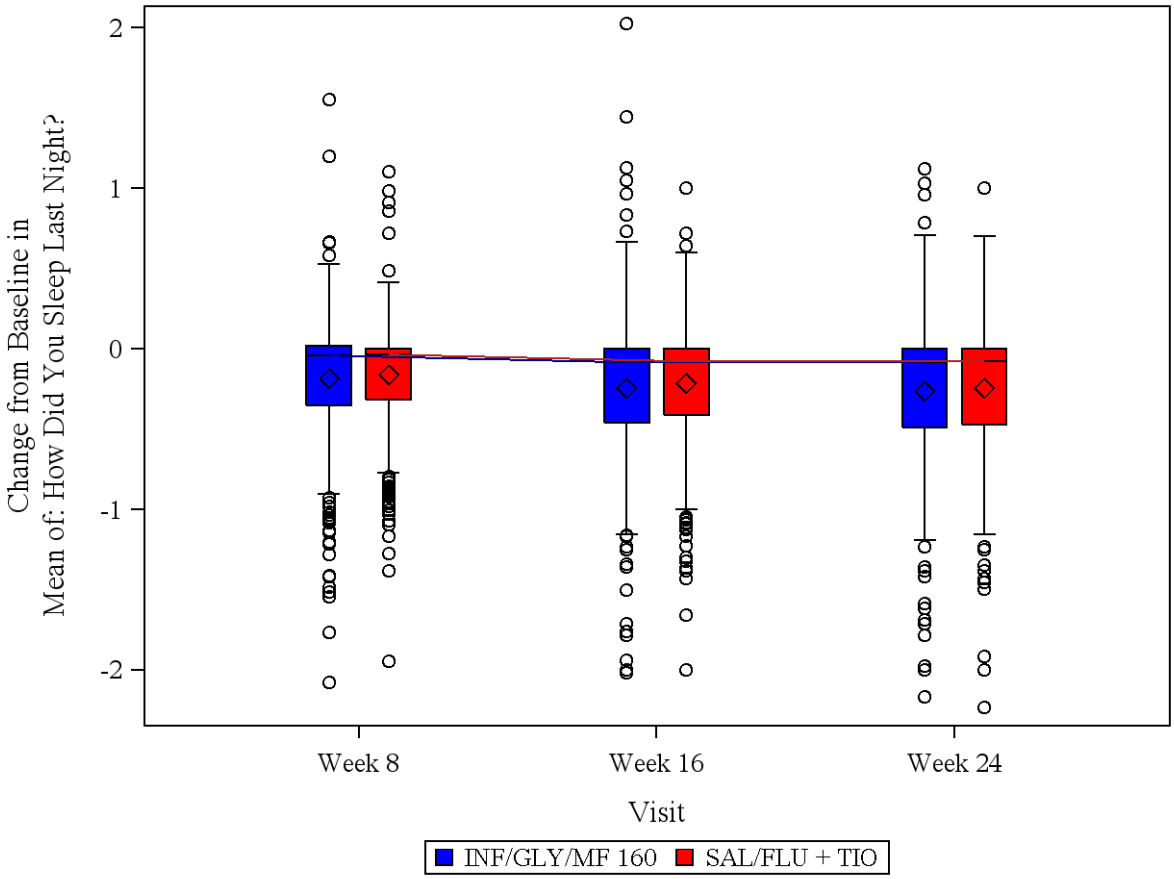
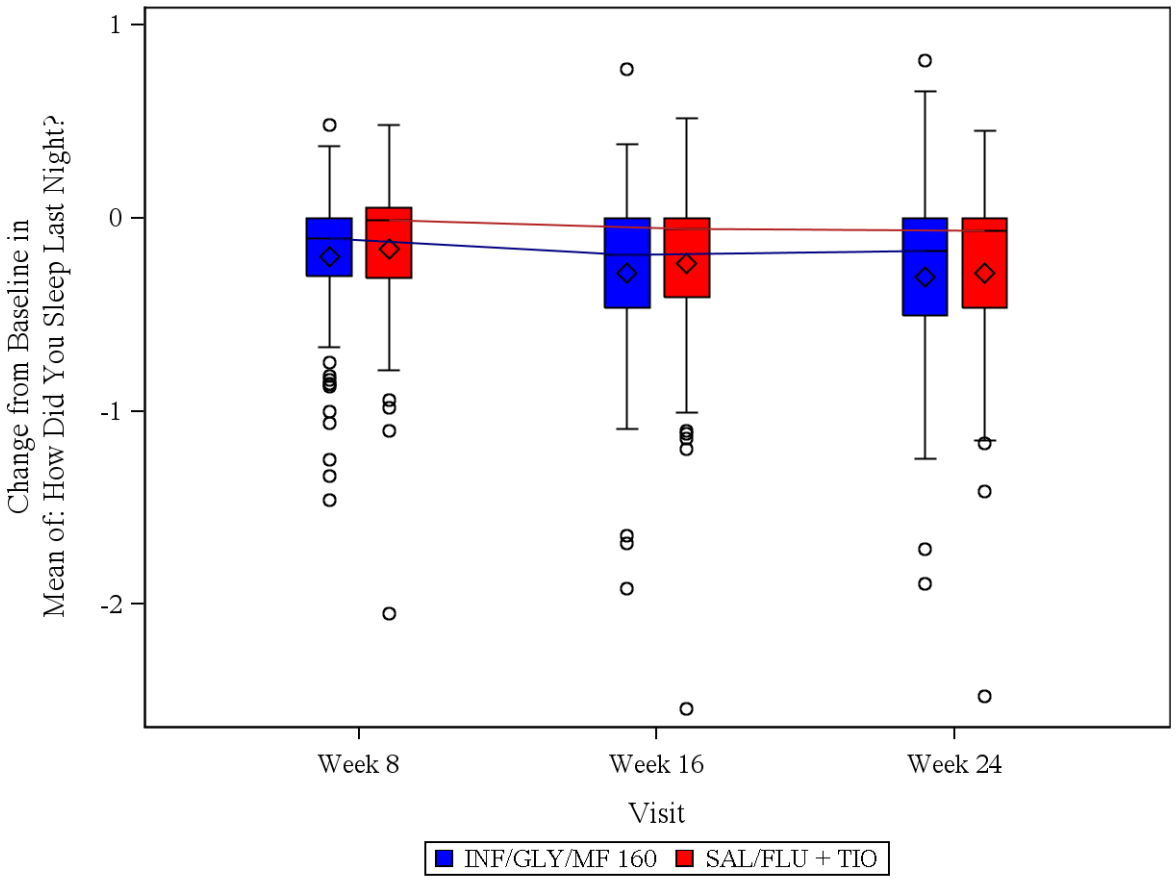


Figure 9.47.2 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.48 Boxplot: Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 9.48.1 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

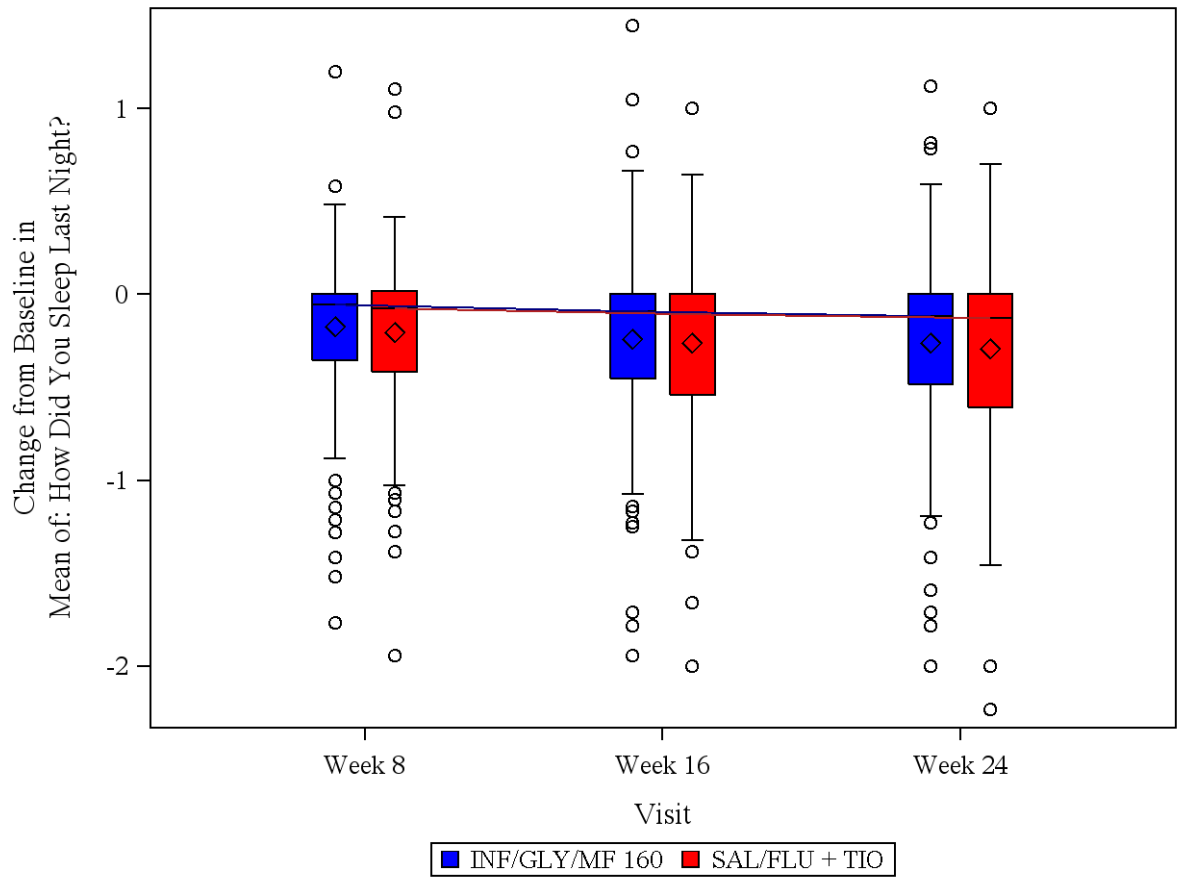
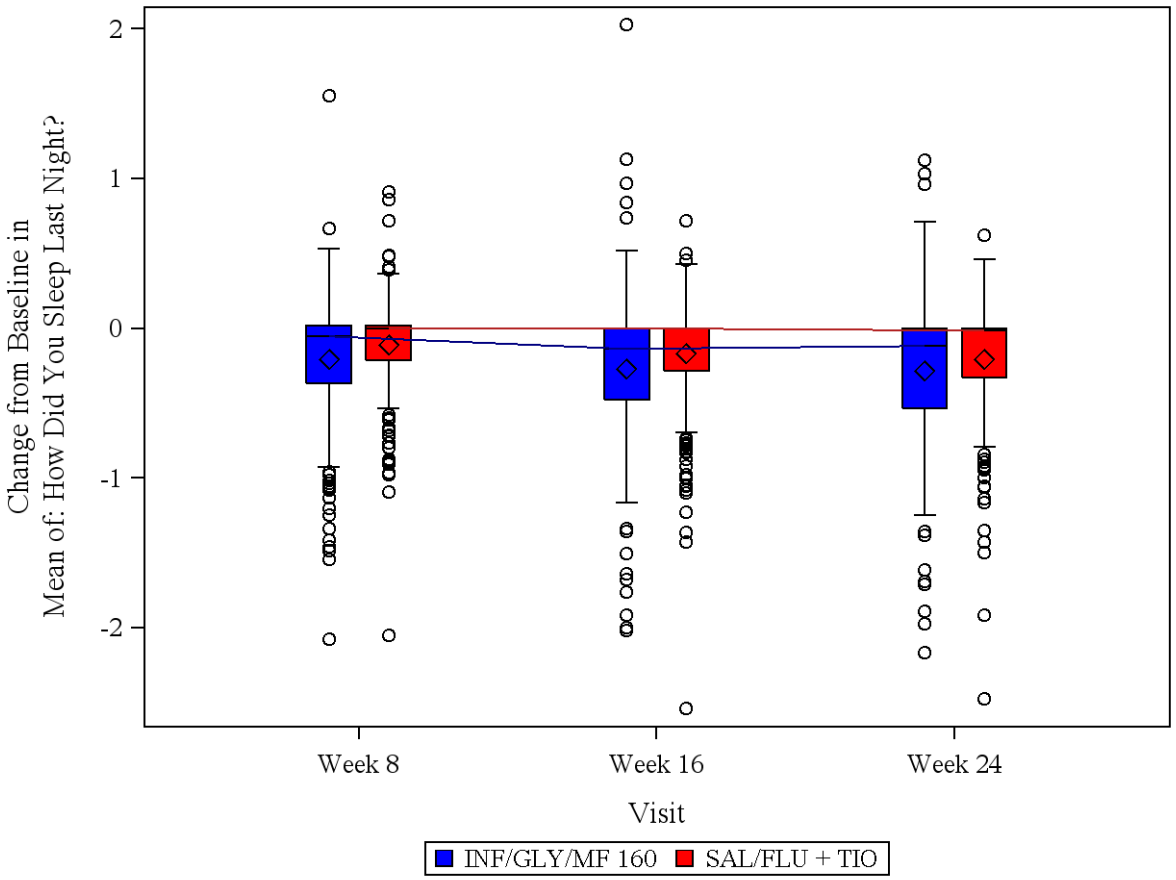
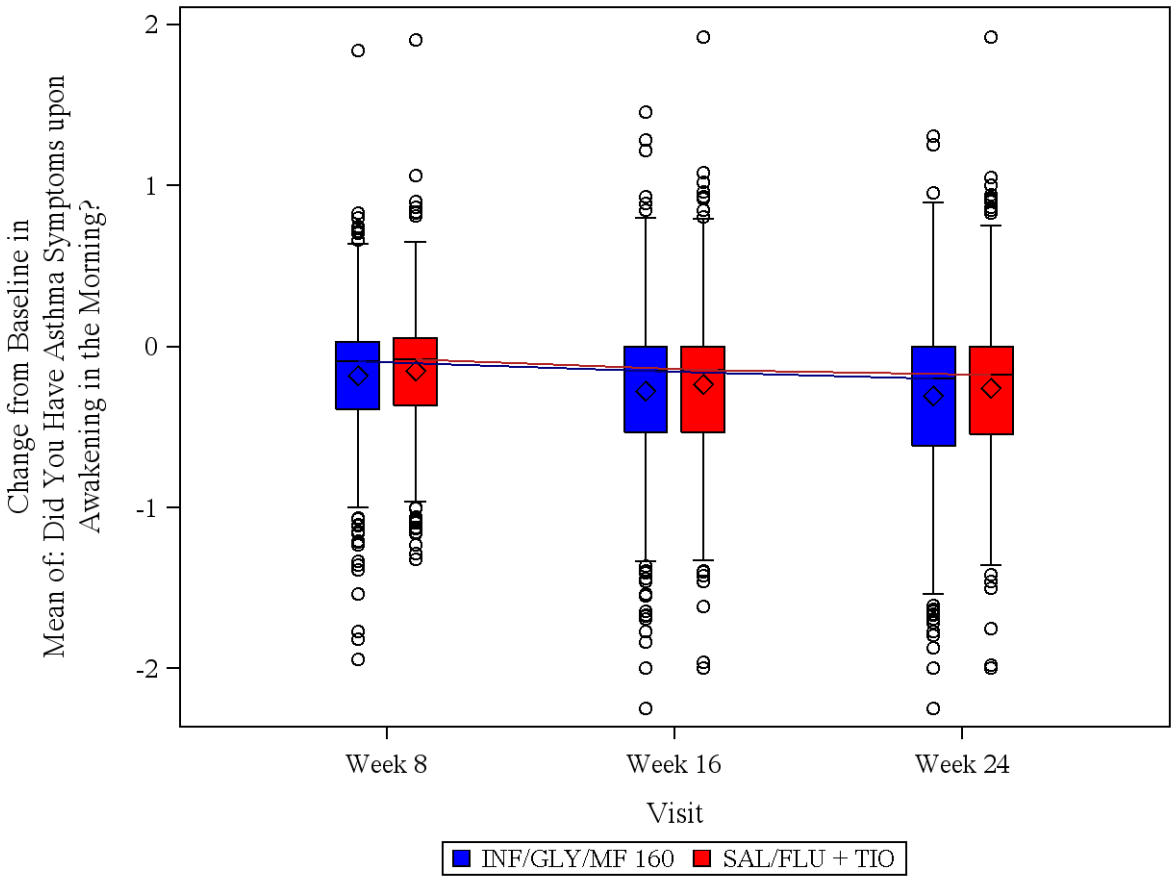


Figure 9.48.2 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



9.49 Boxplot: Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline (FAS)

Figure 9.49 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline (FAS)



9.50 Boxplot: Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Age (FAS)

Figure 9.50.1 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Age (FAS), Age = 18-39 years

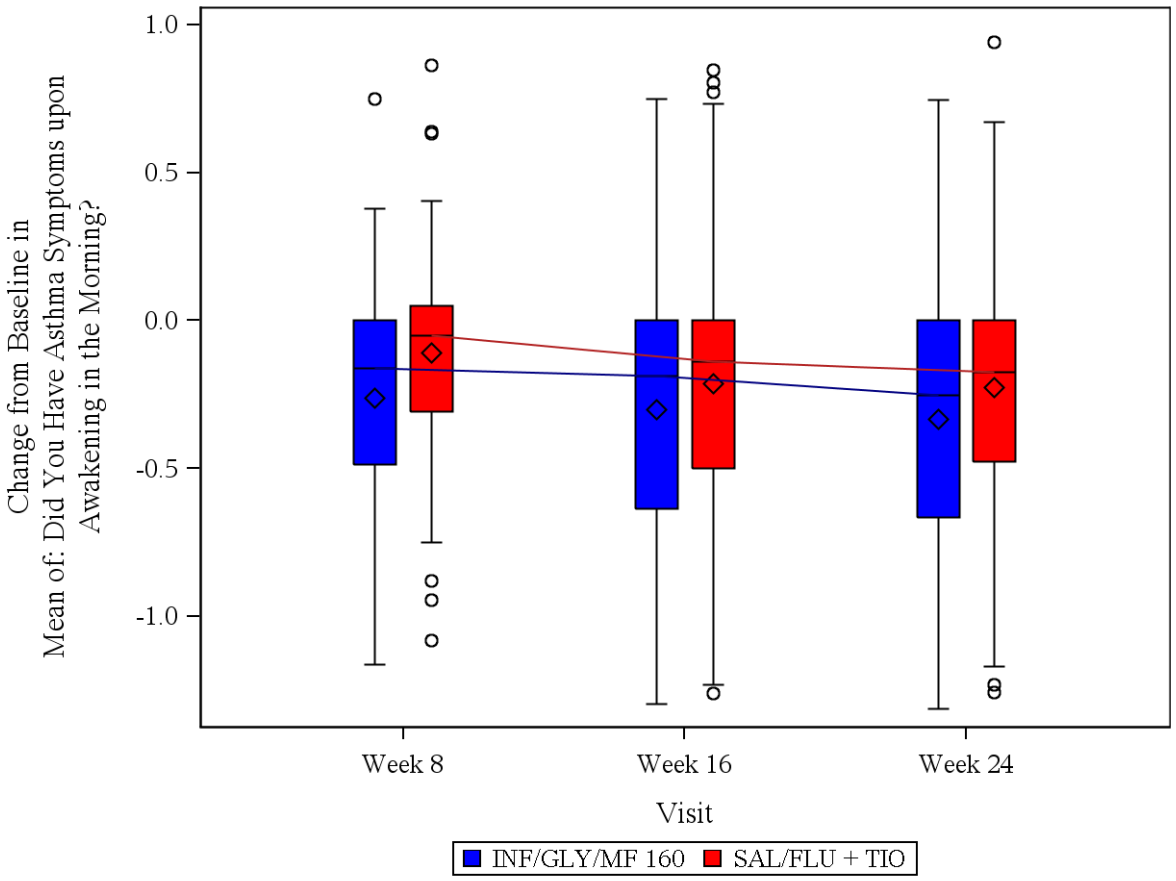


Figure 9.50.2 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Age (FAS), Age = 40-64 years

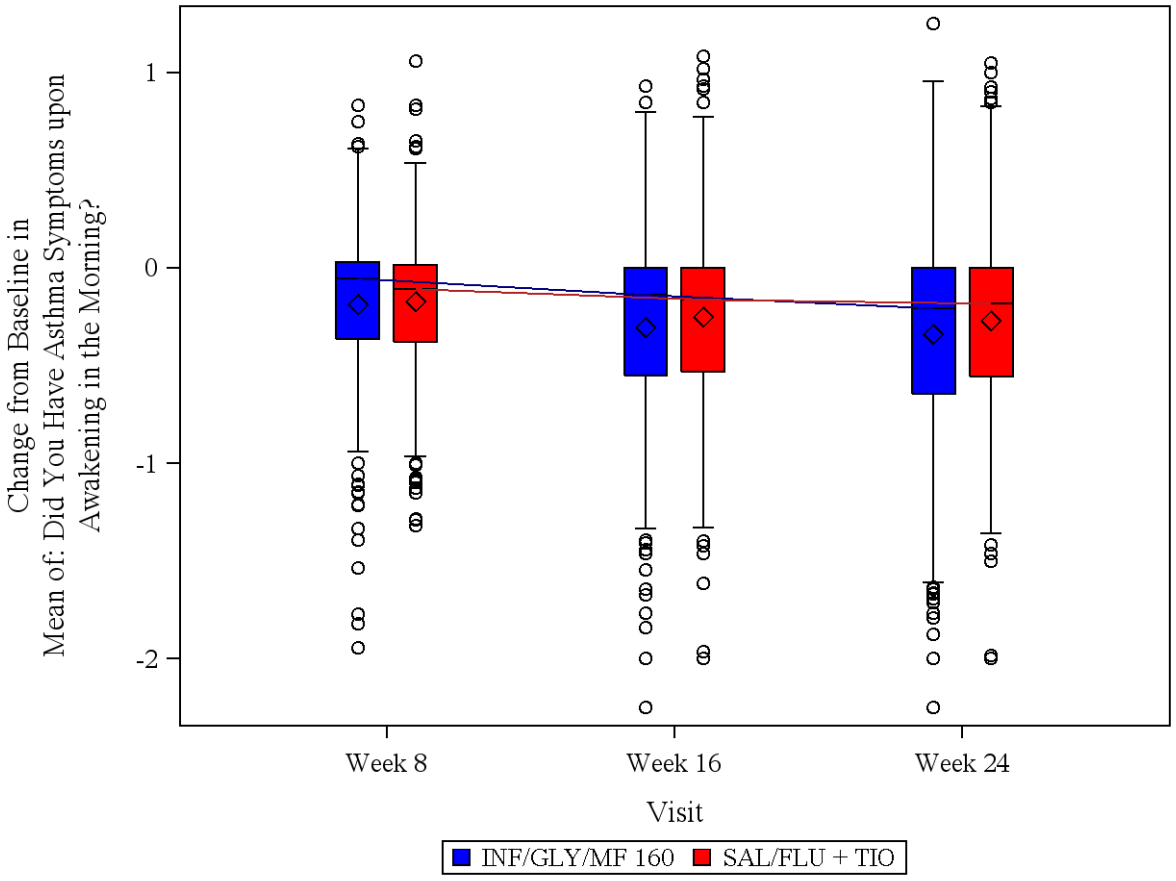
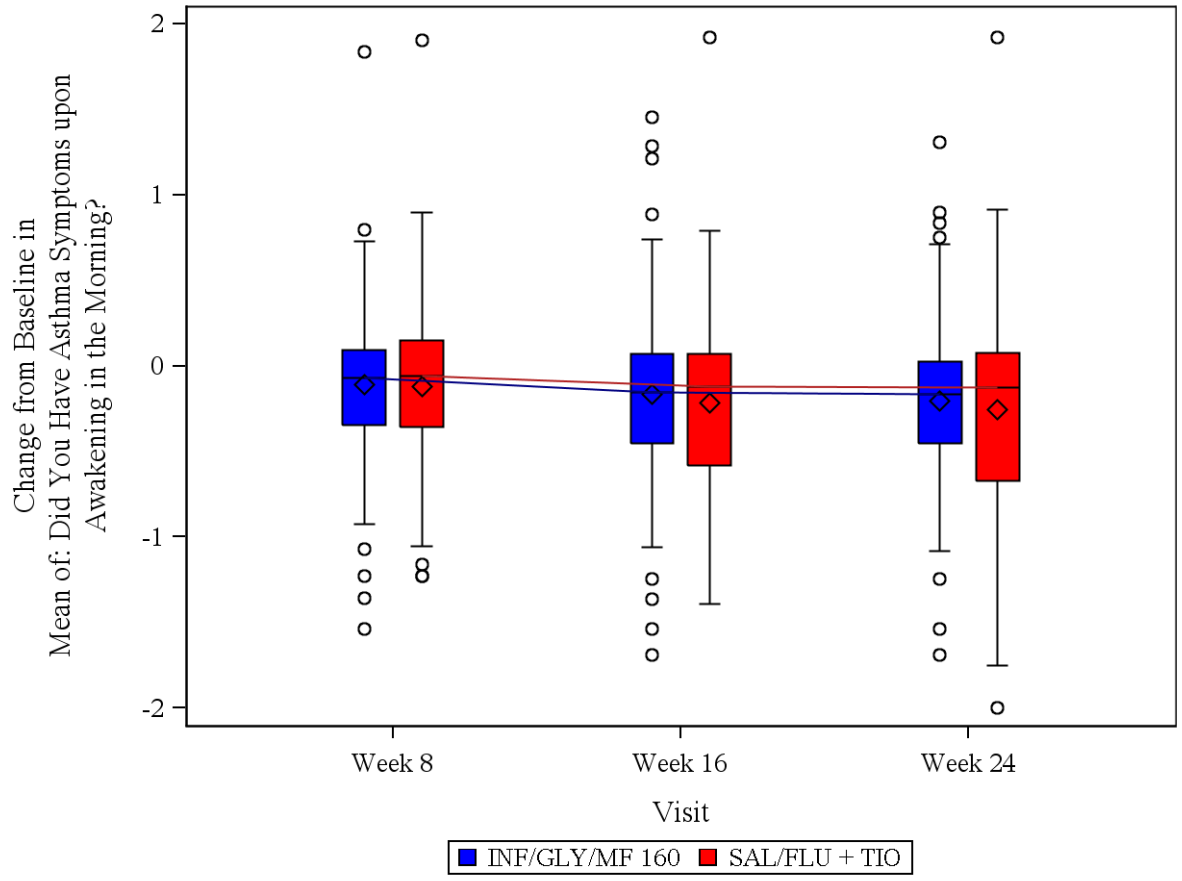


Figure 9.50.3 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Age (FAS), Age = ≥65 years



9.51 Boxplot: Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Gender (FAS)

Figure 9.51.1 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Gender (FAS), Gender = Male

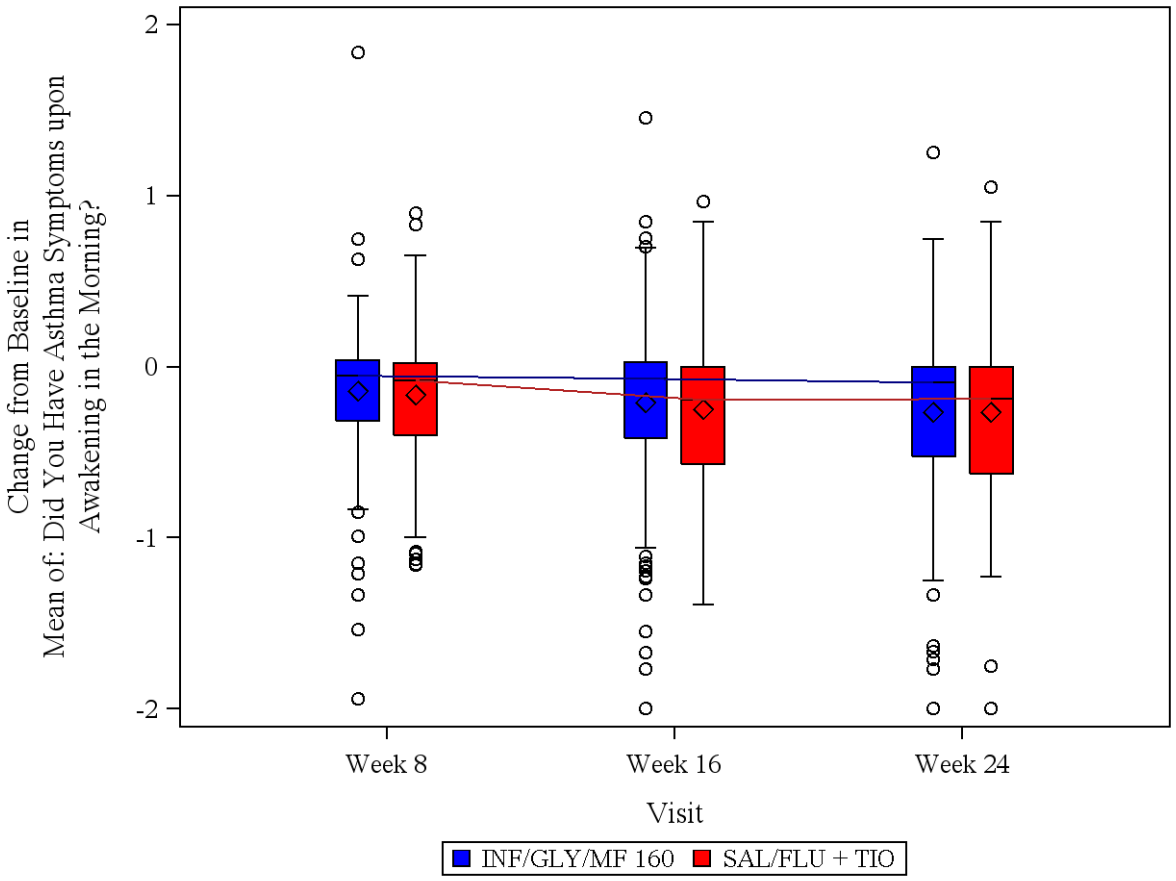
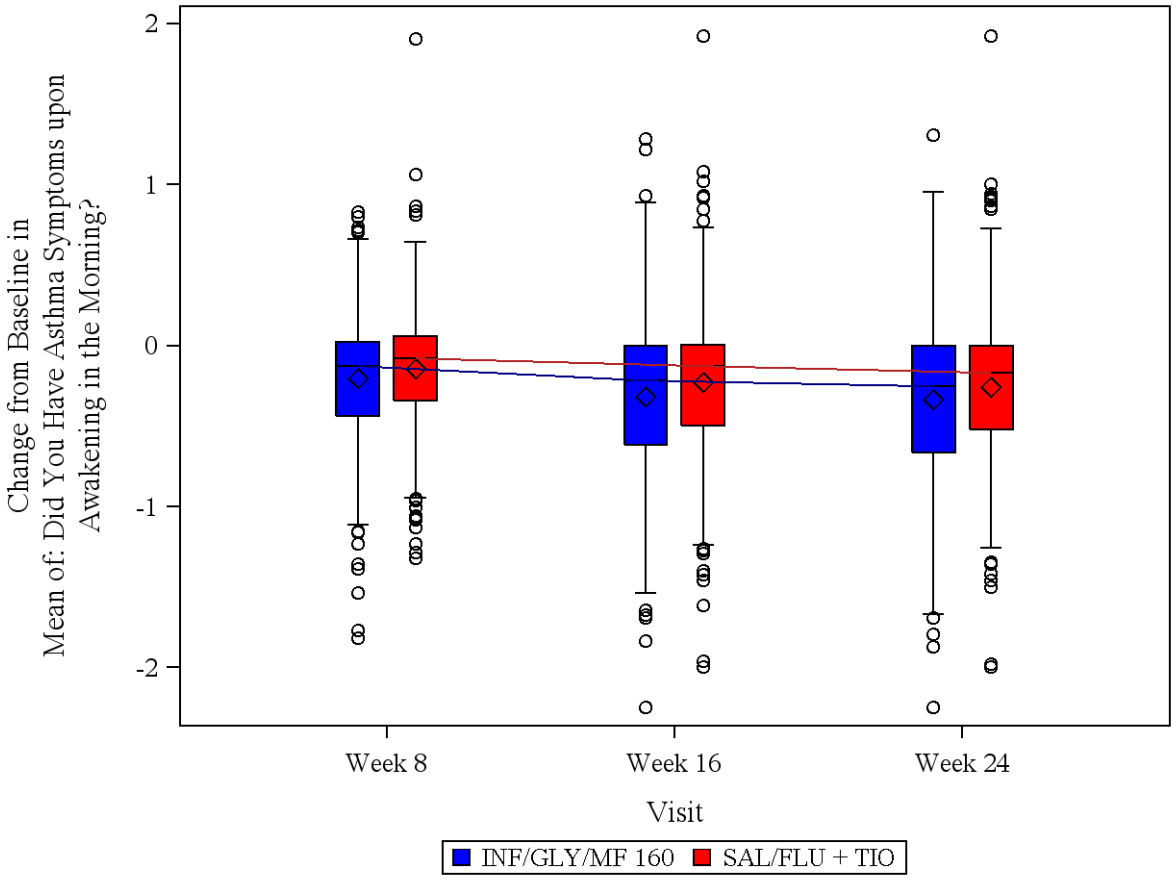


Figure 9.51.2 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Gender (FAS), Gender = Female



9.52 Boxplot: Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Region (FAS)

Figure 9.52.1 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Region (FAS), Region = Asia

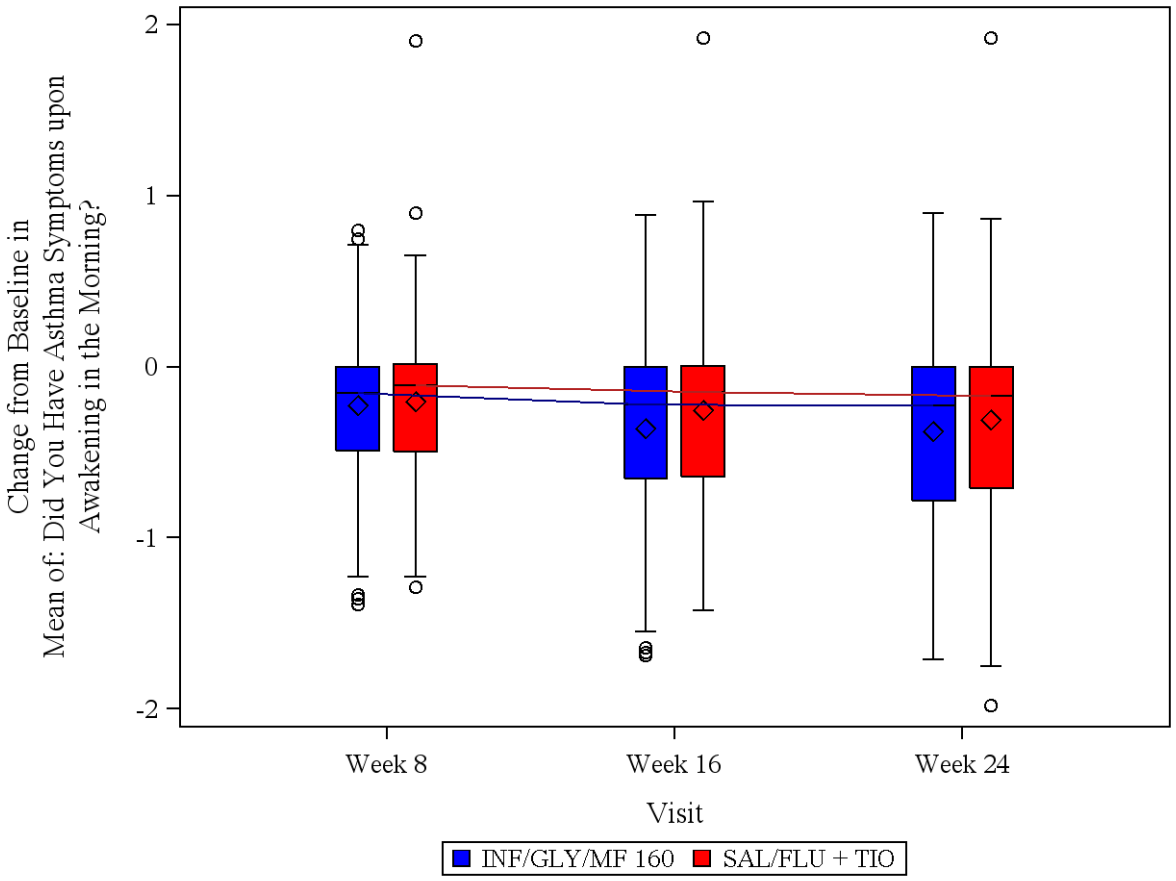


Figure 9.52.2 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Region (FAS), Region = Europe

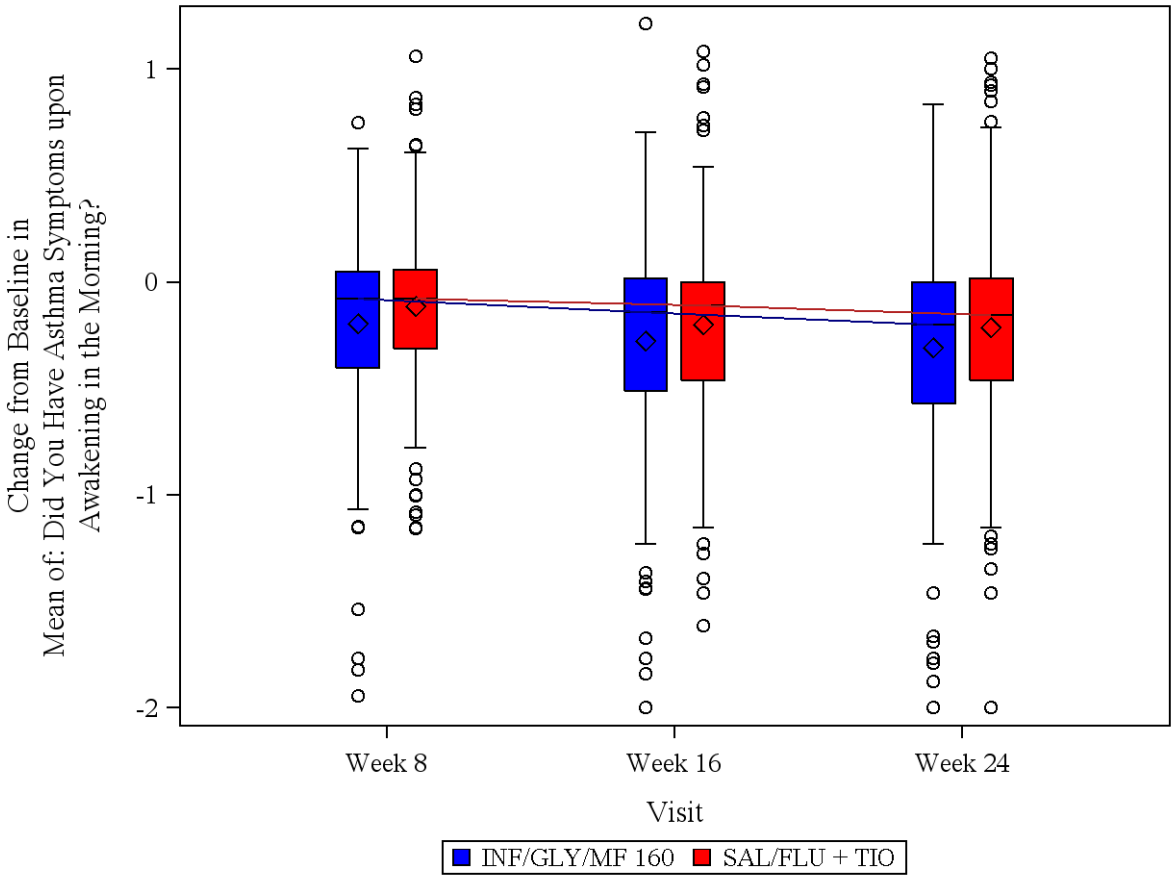


Figure 9.52.3 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Region (FAS), Region = Latin America

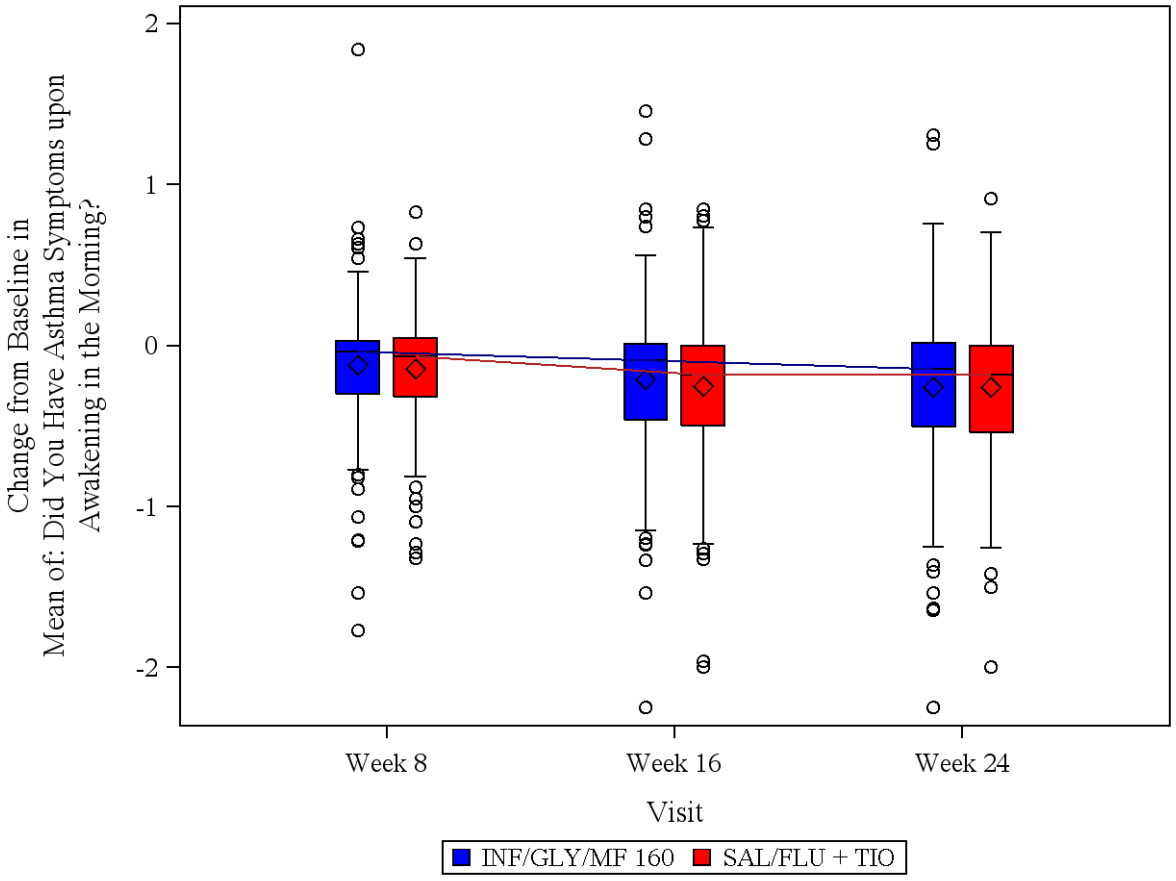
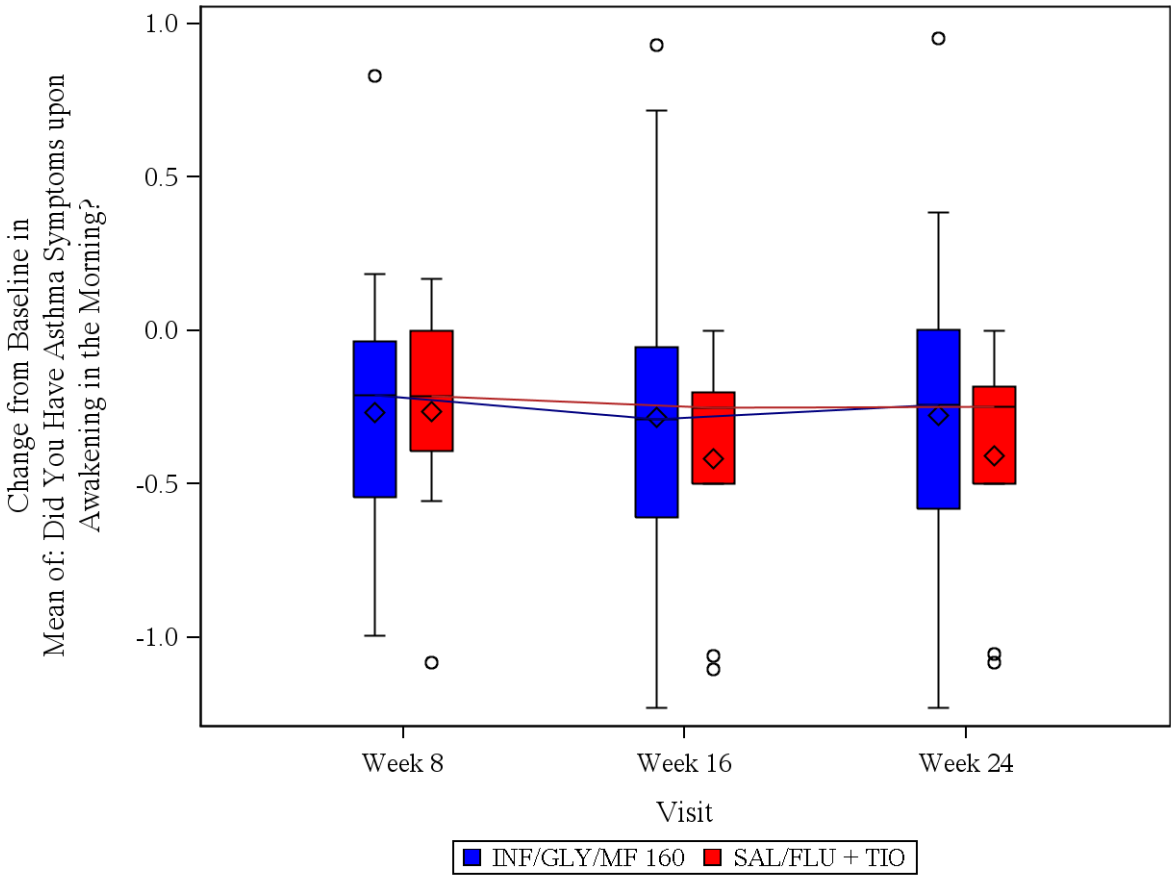


Figure 9.52.4 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Region (FAS), Region = Others



9.53 Boxplot: Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 9.53.1 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

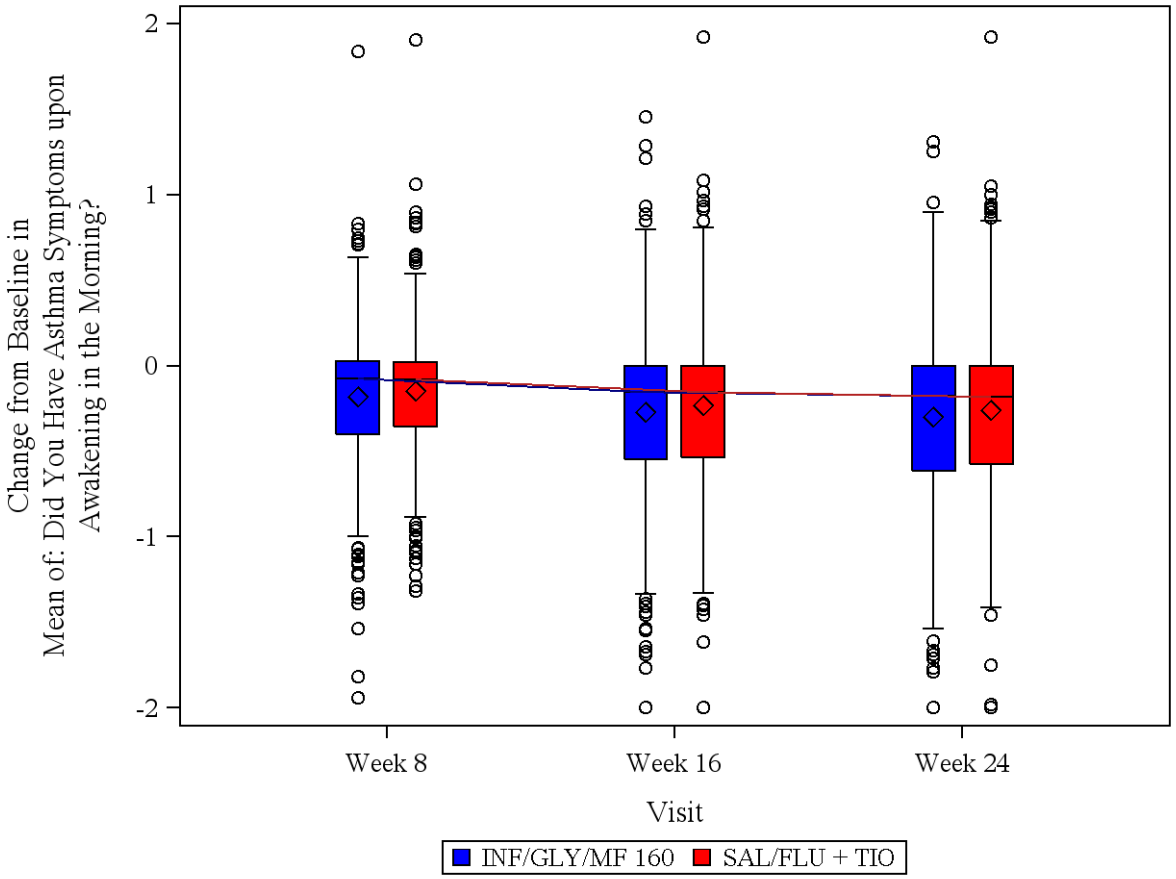
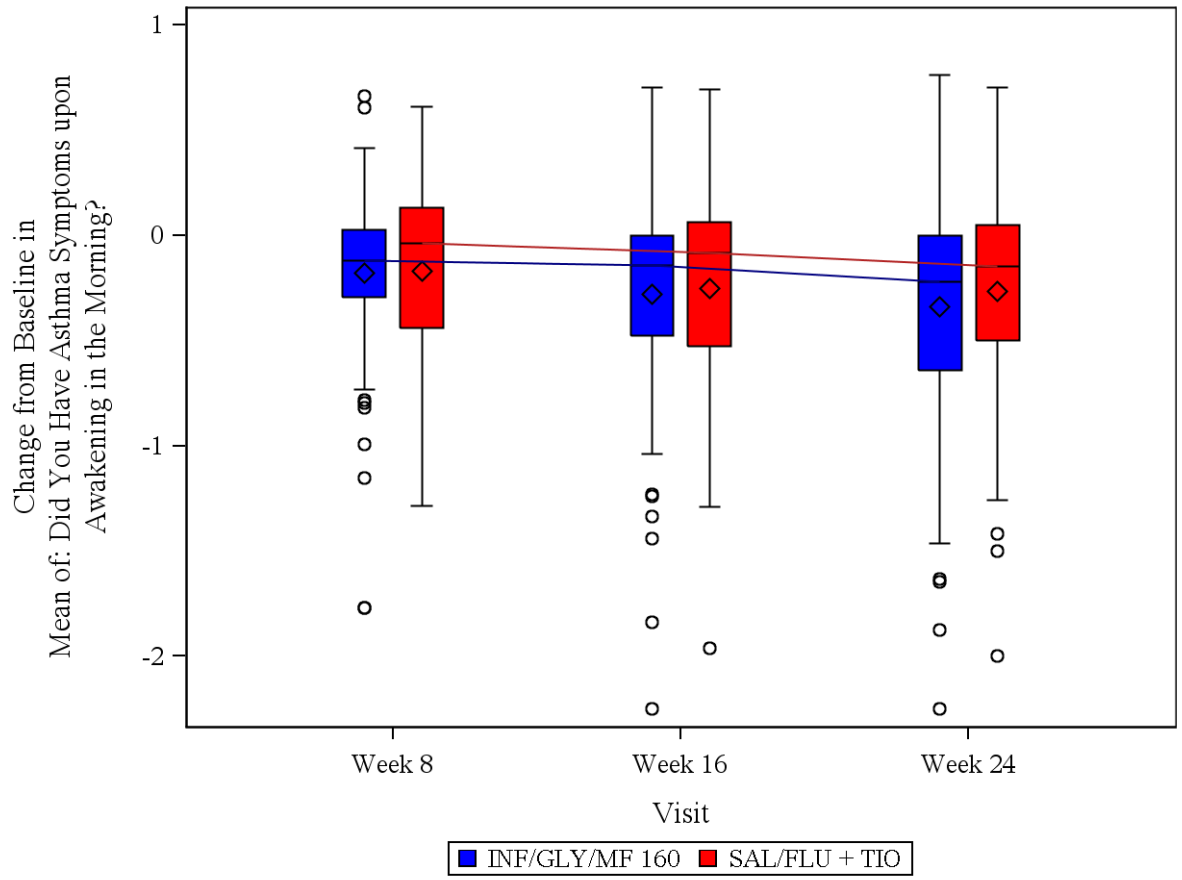


Figure 9.53.2 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.54 Boxplot: Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 9.54.1 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

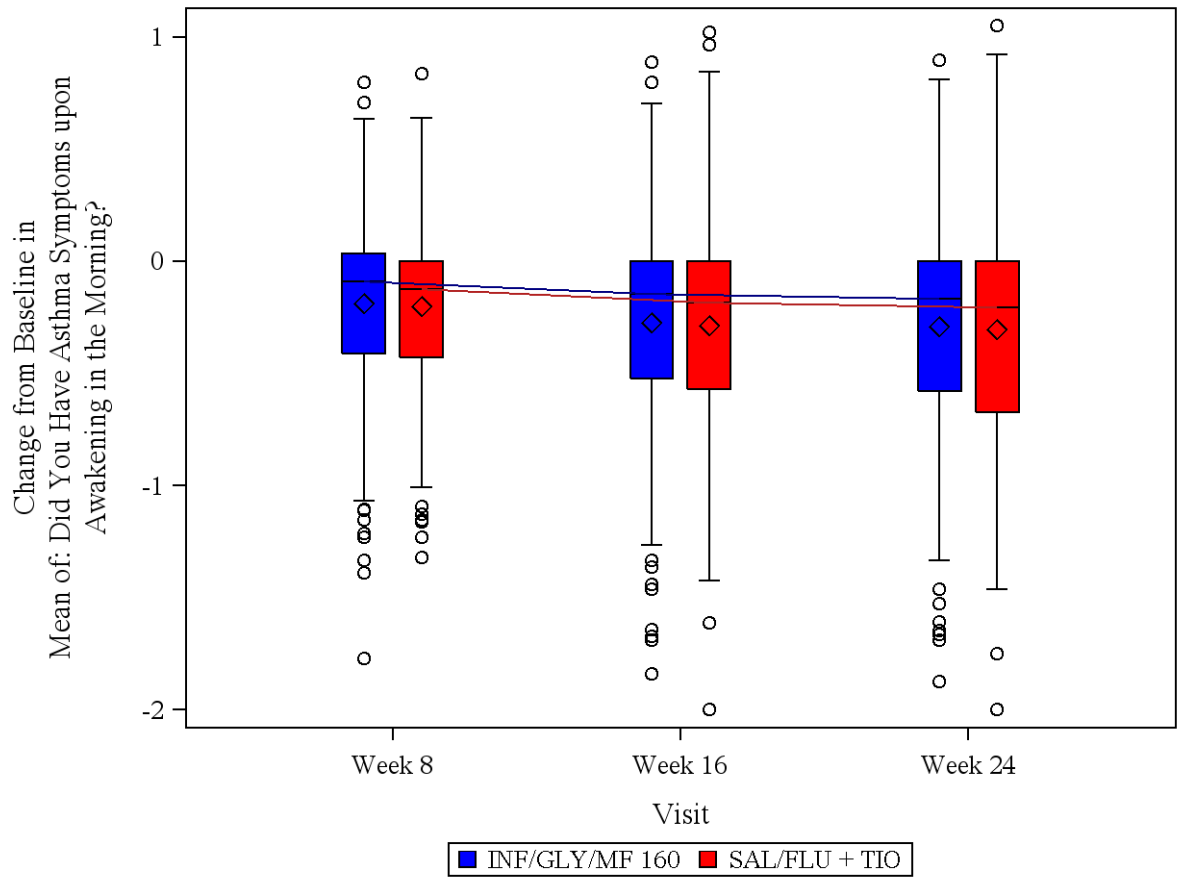
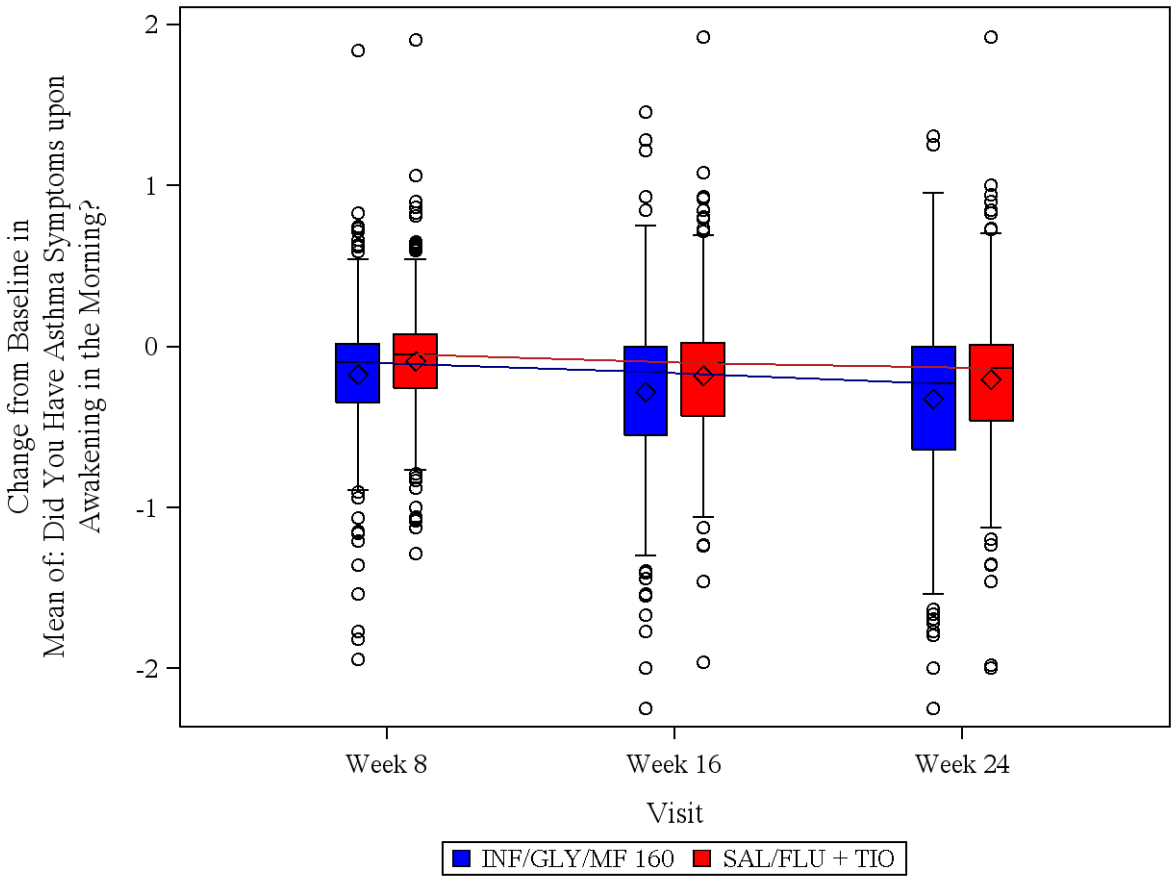
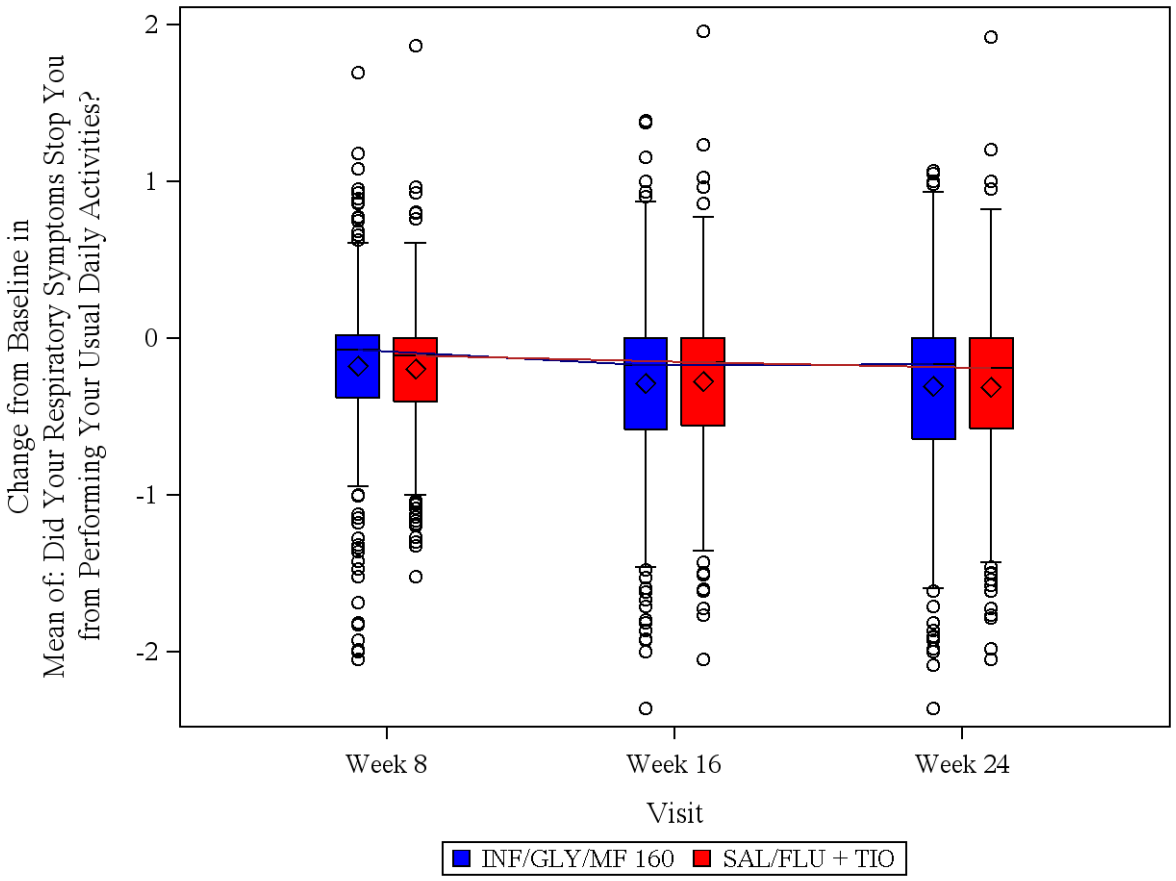


Figure 9.54.2 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



9.55 Boxplot: Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline (FAS)

Figure 9.55 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline (FAS)



9.56 Boxplot: Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Age (FAS)

Figure 9.56.1 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Age (FAS), Age = 18-39 years

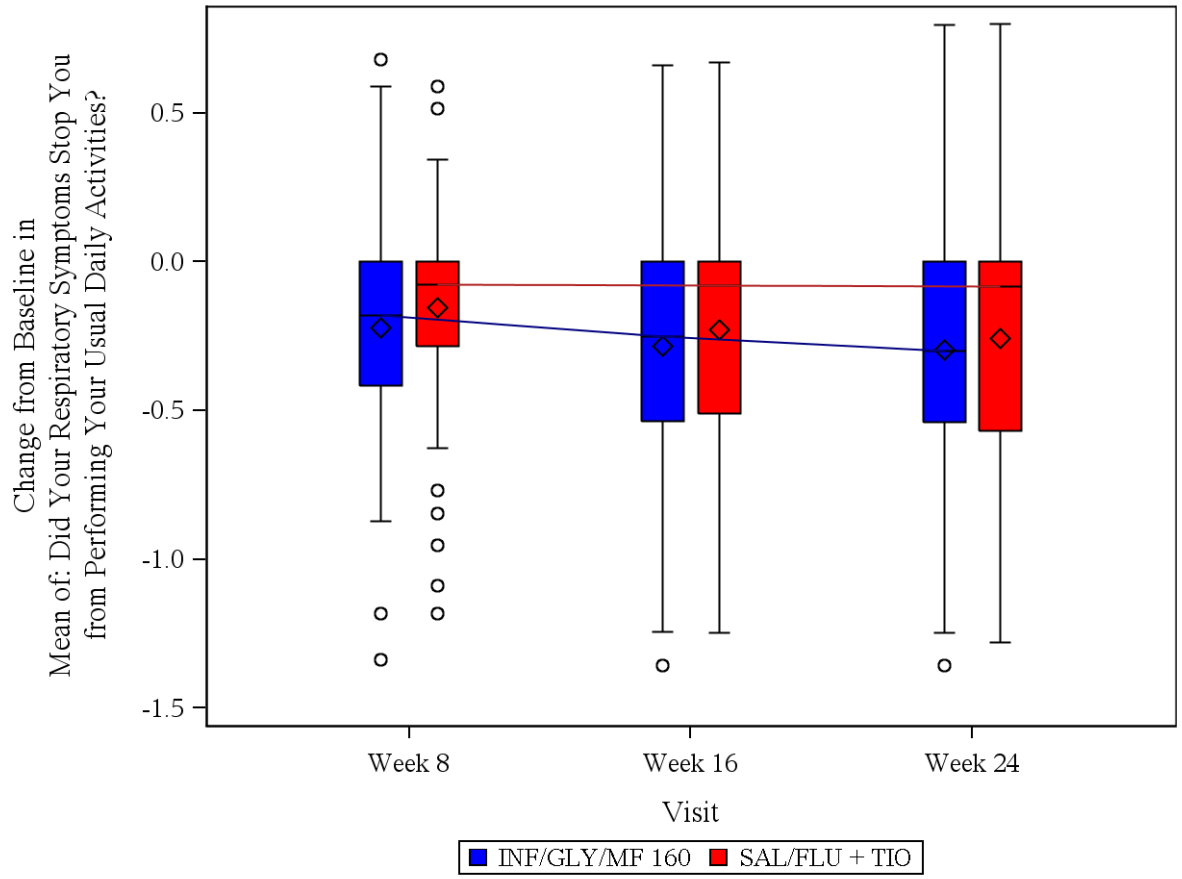


Figure 9.56.2 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Age (FAS), Age = 40-64 years

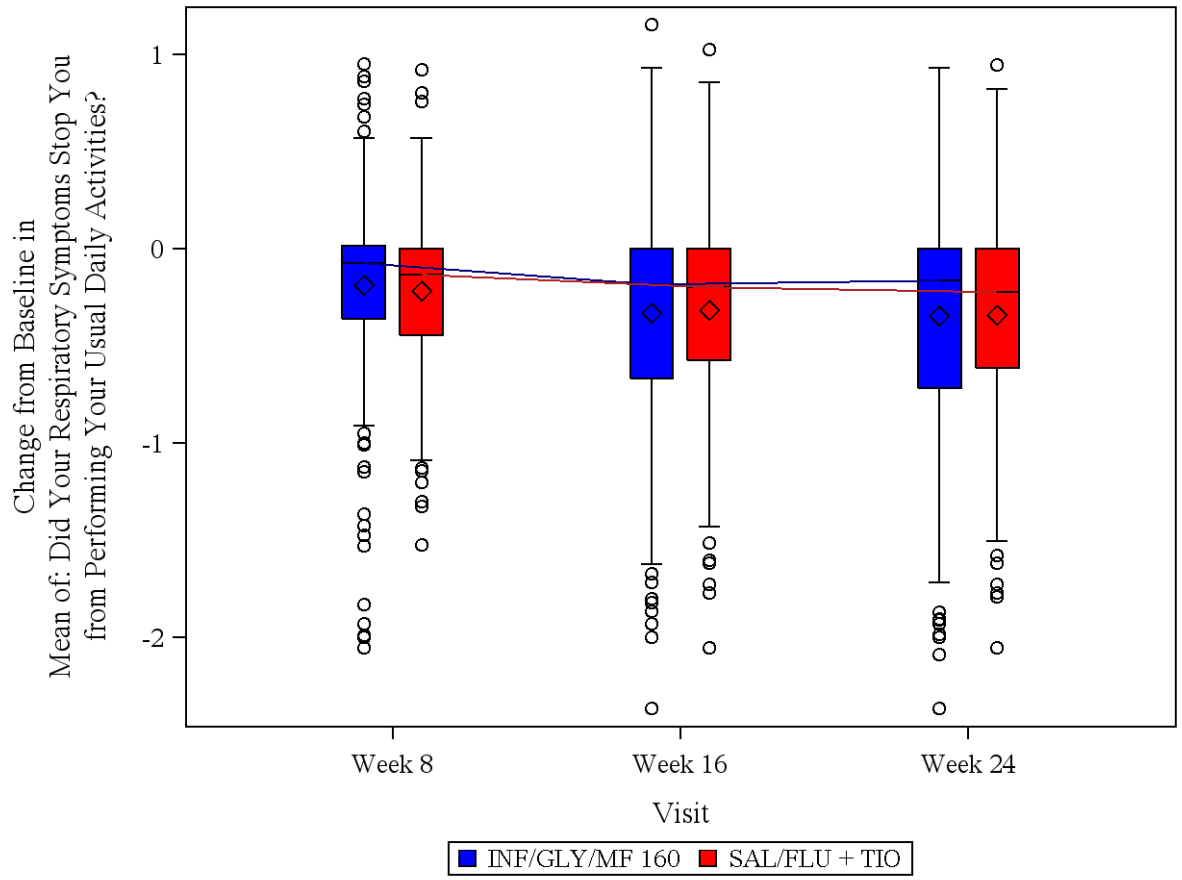
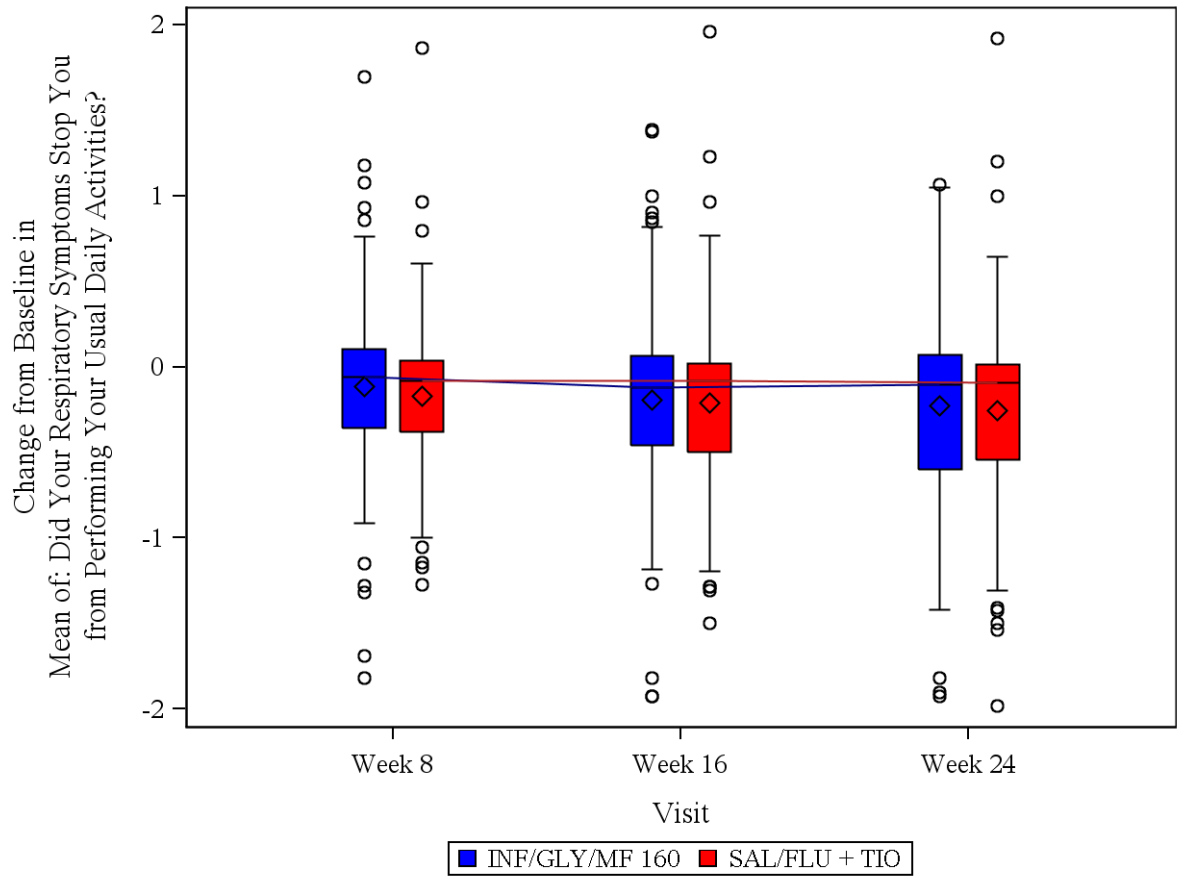


Figure 9.56.3 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Age (FAS), Age = ≥65 years



9.57 Boxplot: Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Gender (FAS)

Figure 9.57.1 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Gender (FAS), Gender = Male

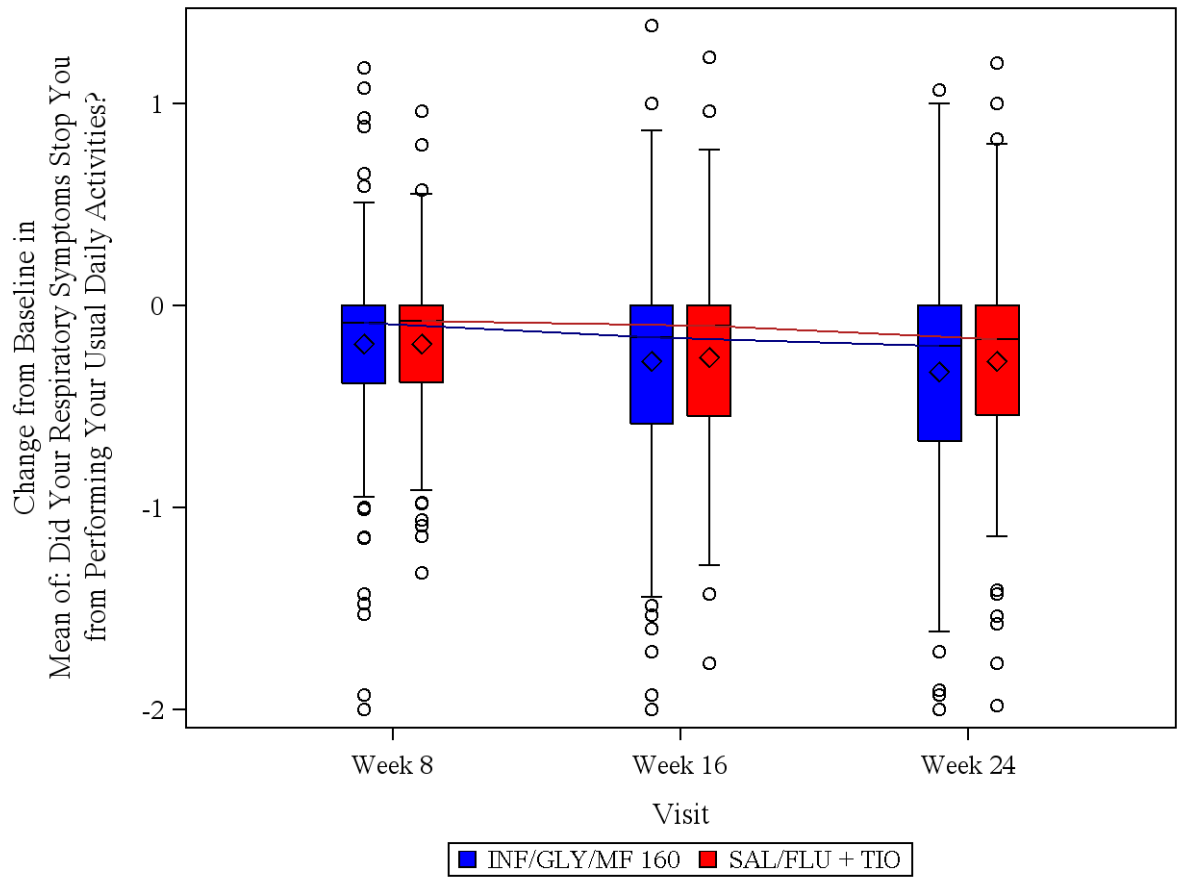
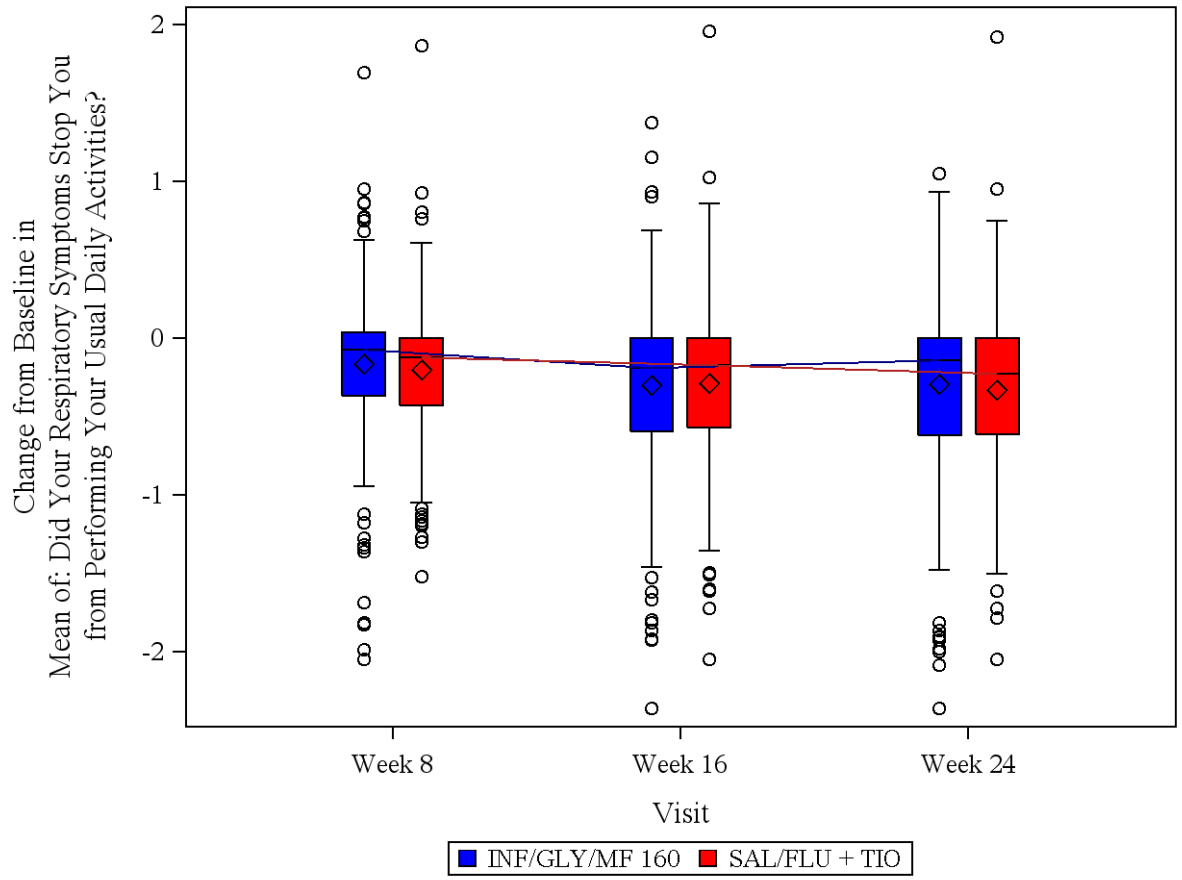


Figure 9.57.2 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Gender (FAS), Gender = Female



9.58 Boxplot: Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Region (FAS)

Figure 9.58.1 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Region (FAS), Region = Asia

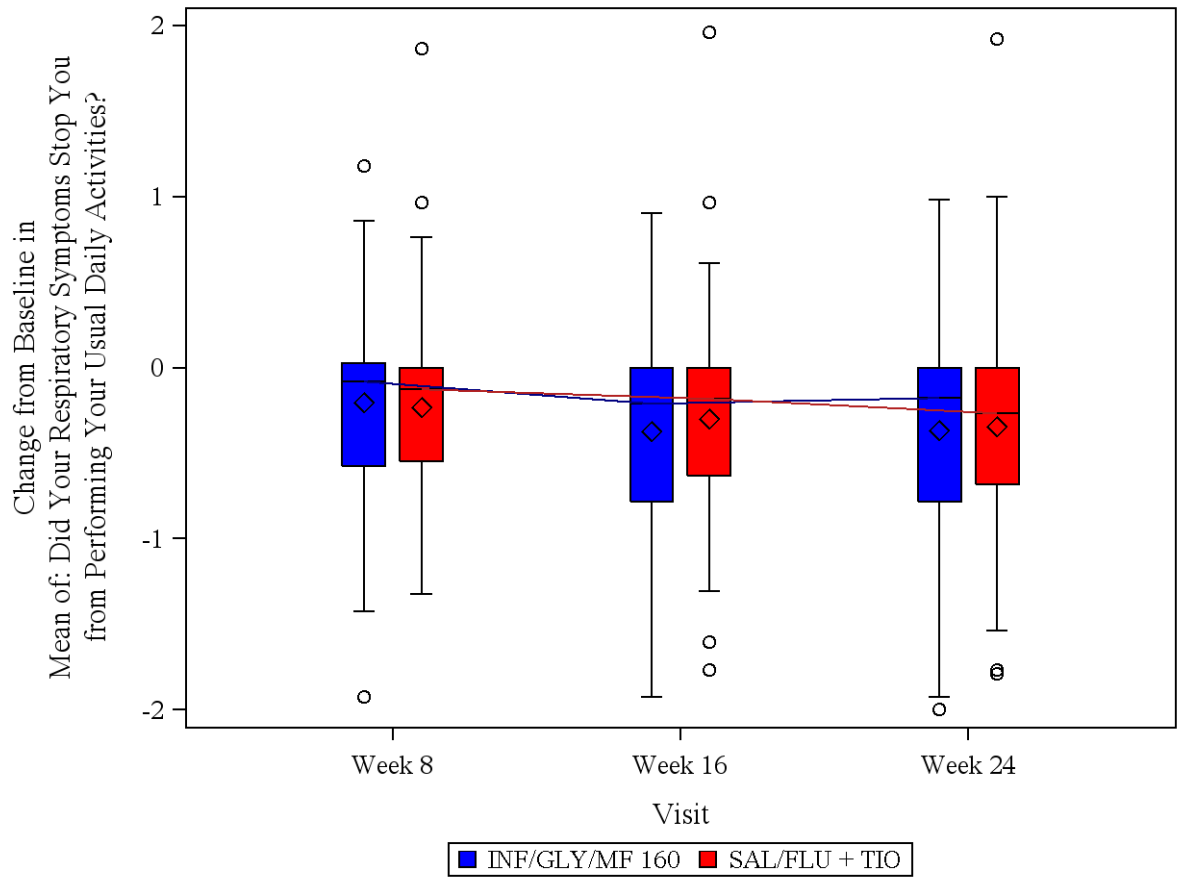


Figure 9.58.2 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Region (FAS), Region = Europe

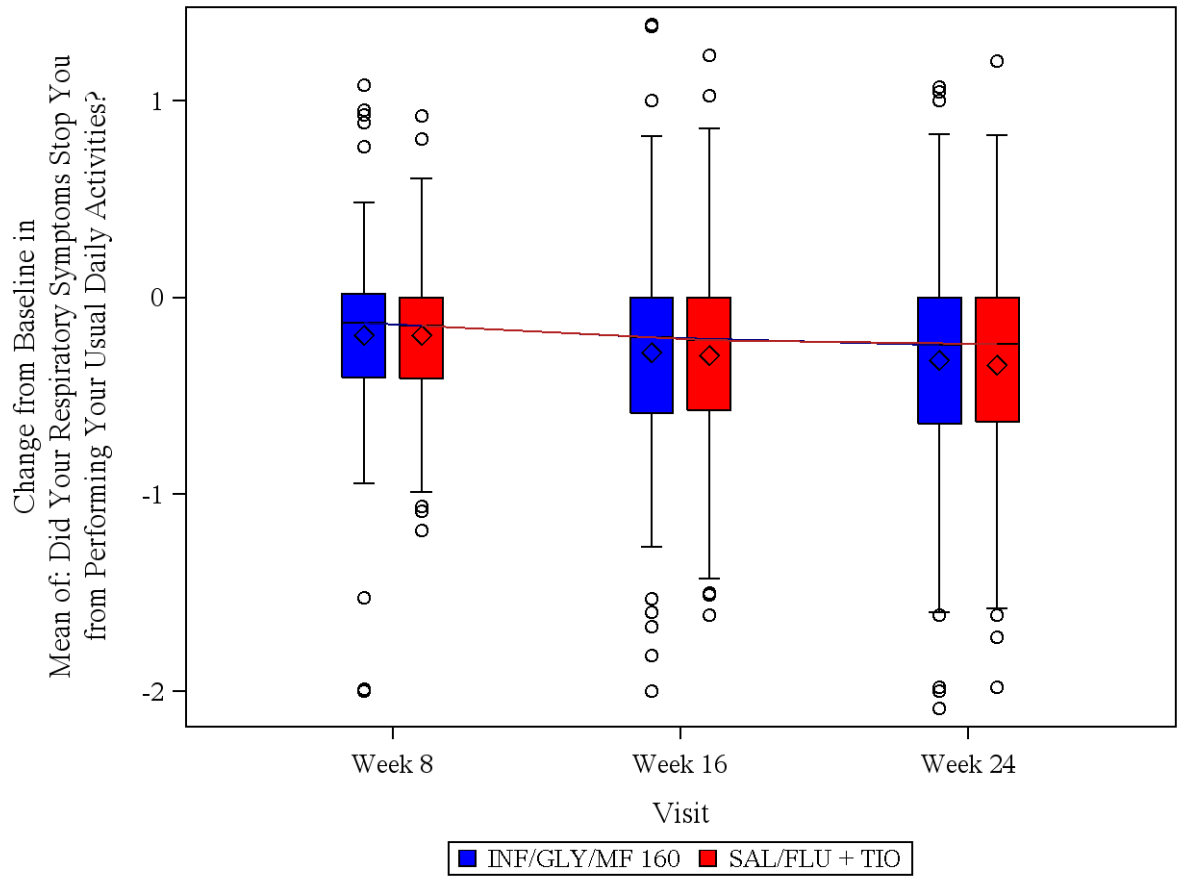


Figure 9.58.3 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Region (FAS), Region = Latin America

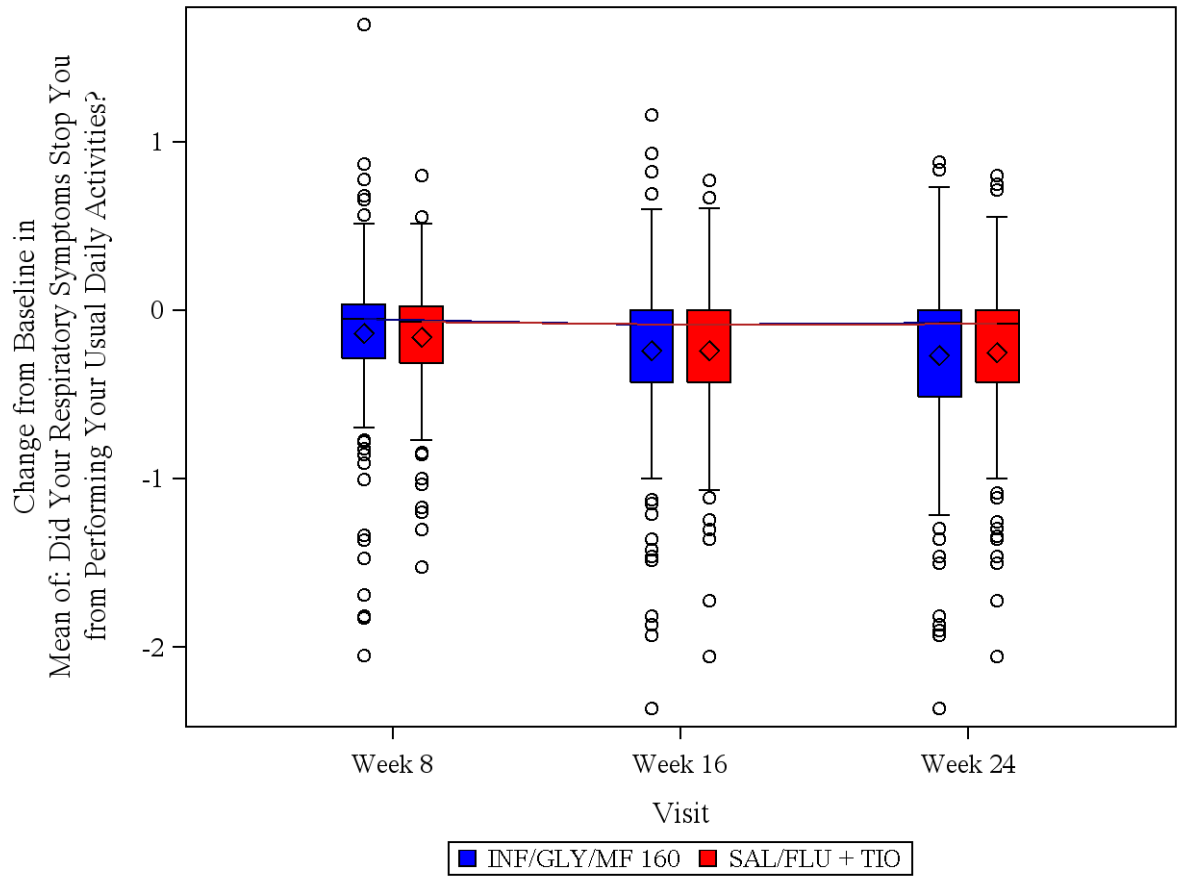
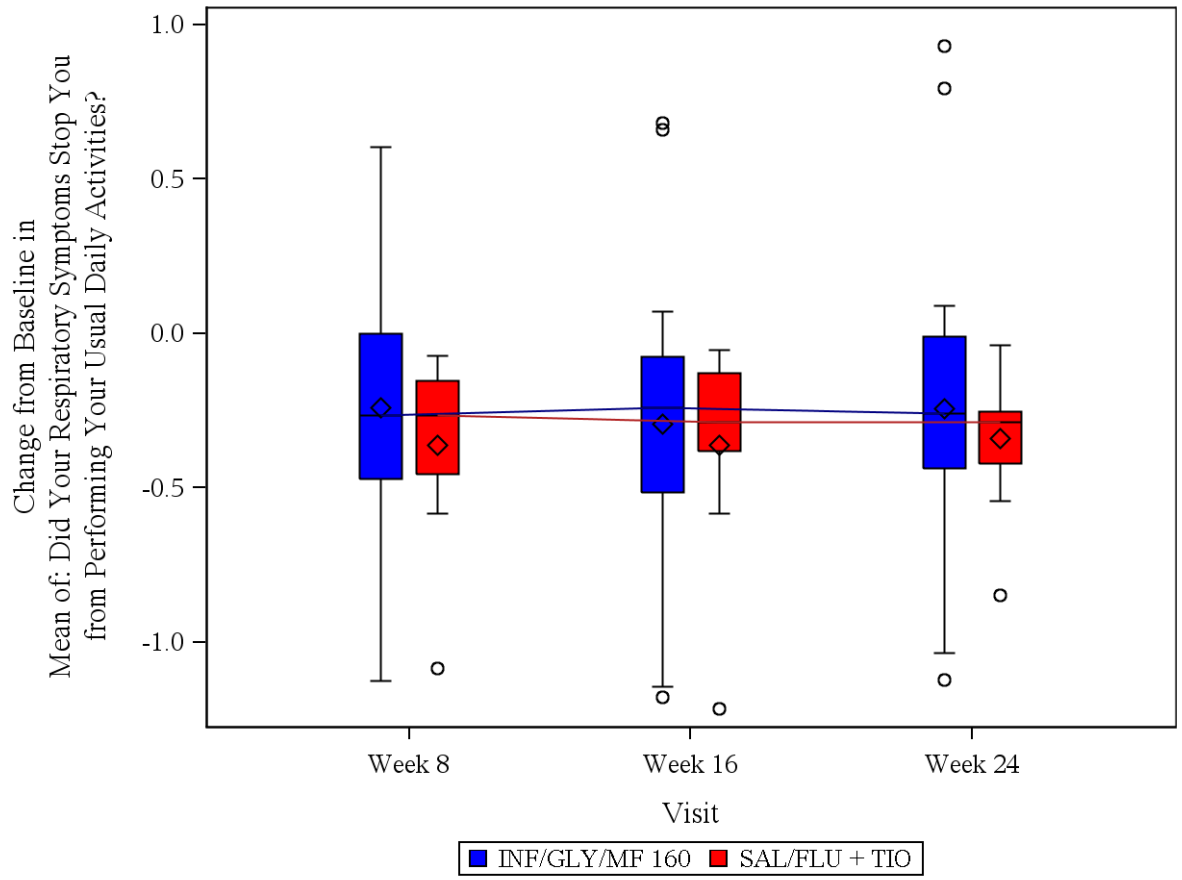


Figure 9.58.4 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Region (FAS), Region = Others



9.59 Boxplot: Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 9.59.1 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

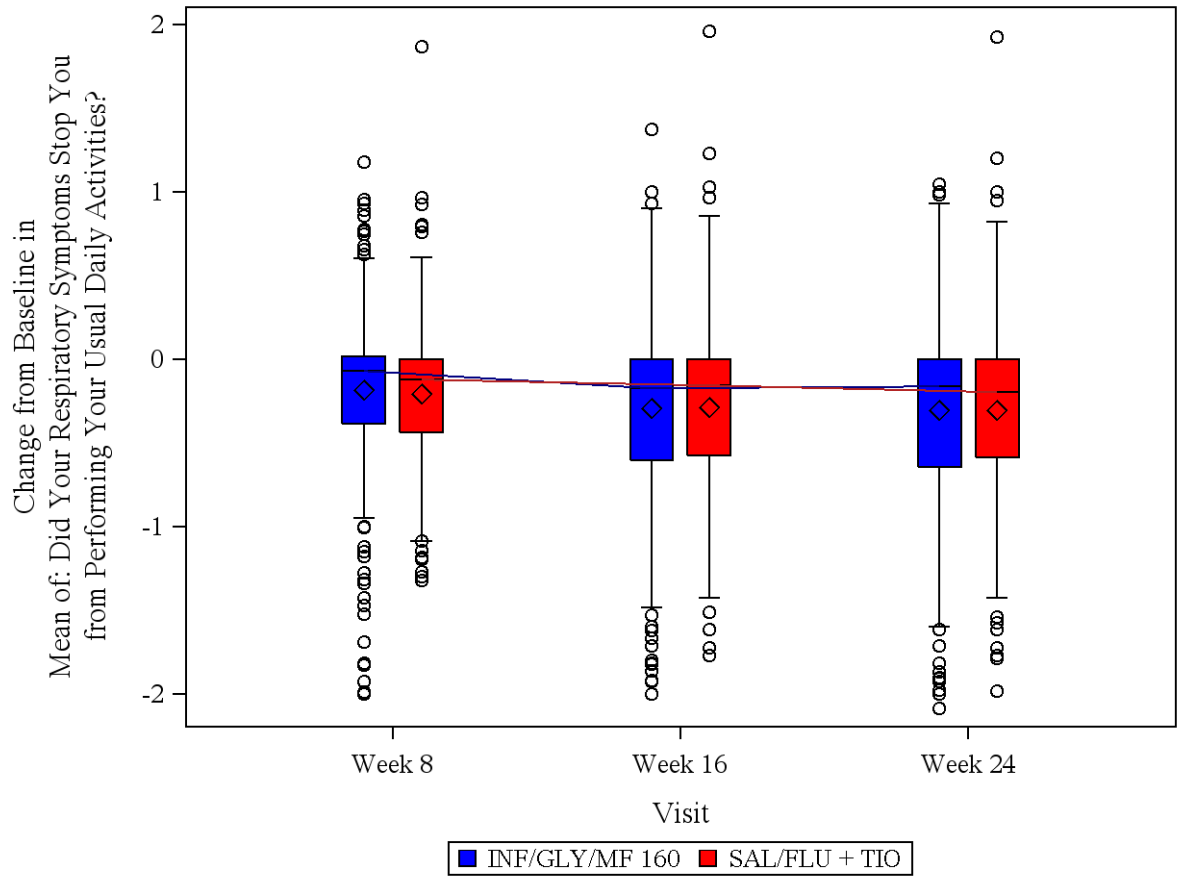
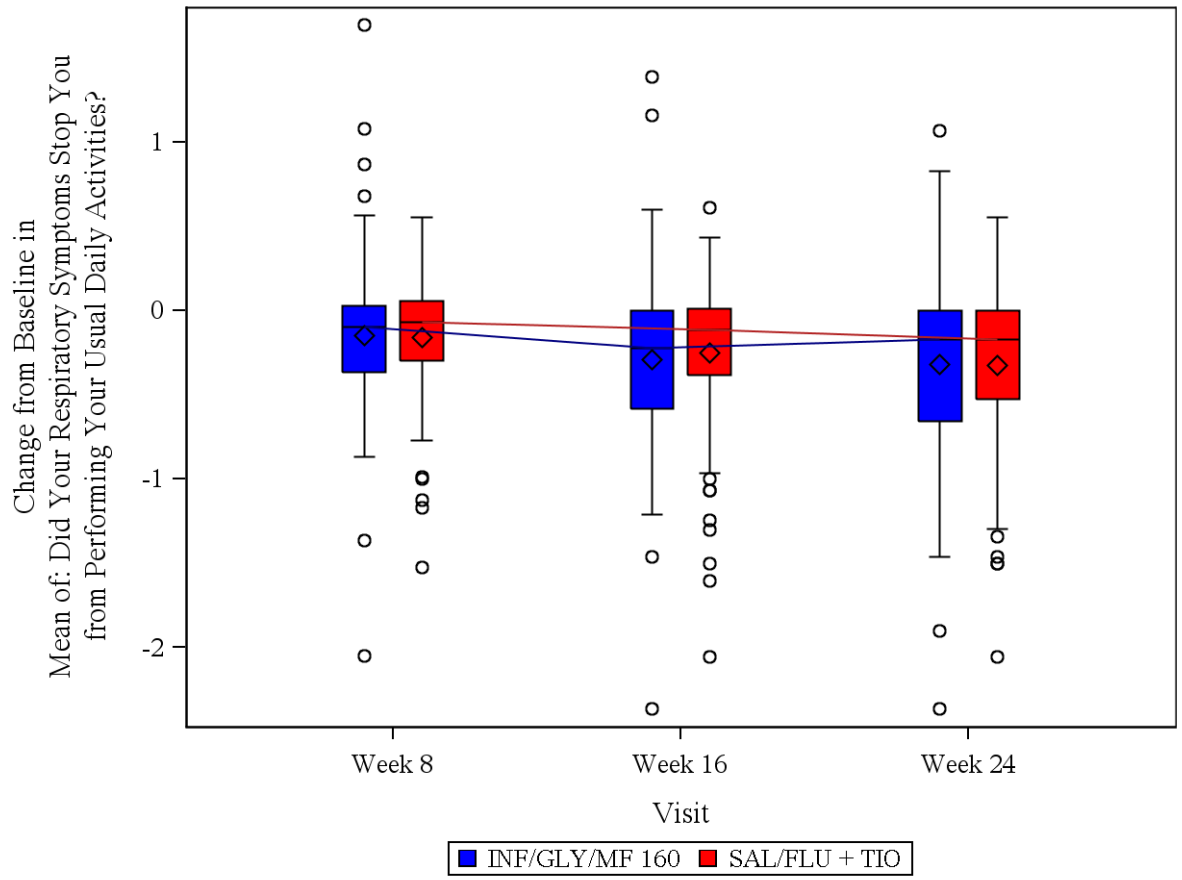


Figure 9.59.2 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.60 Boxplot: Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 9.60.1 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

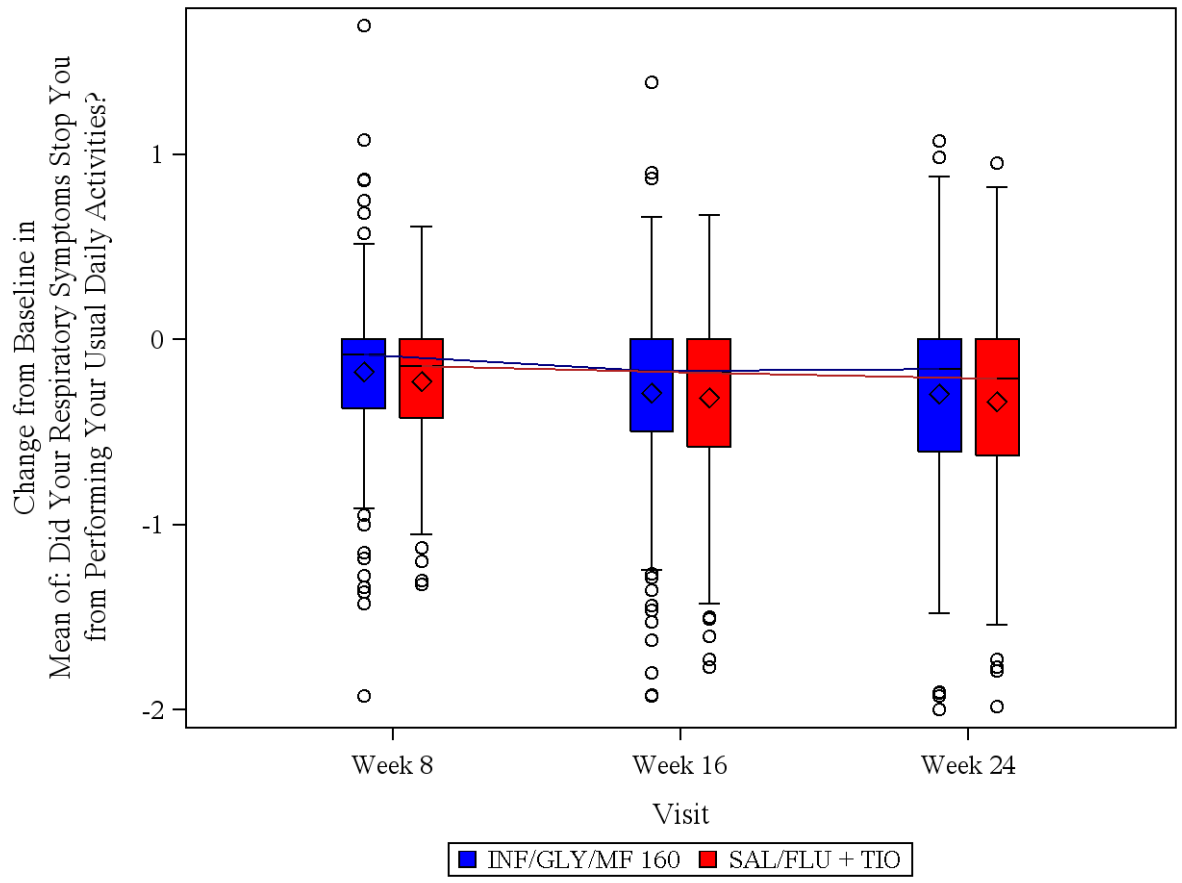
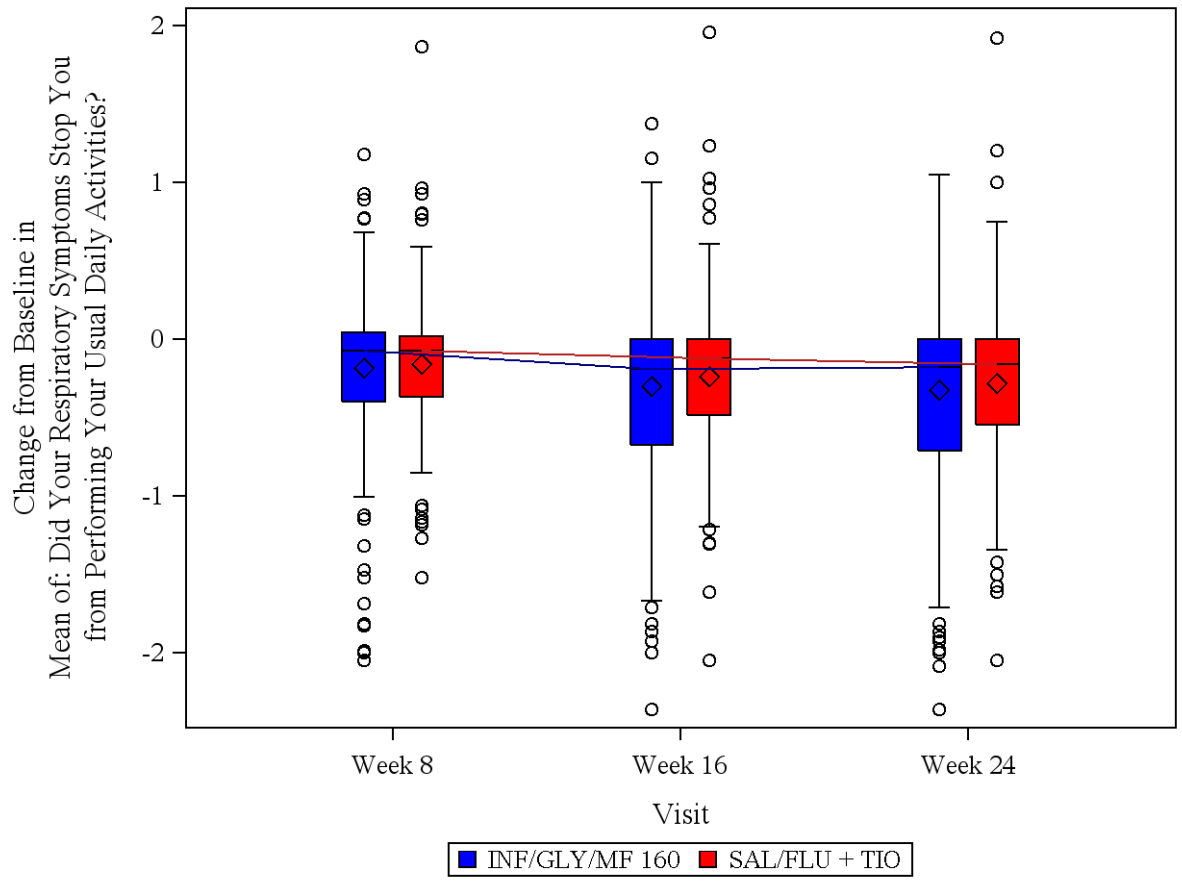
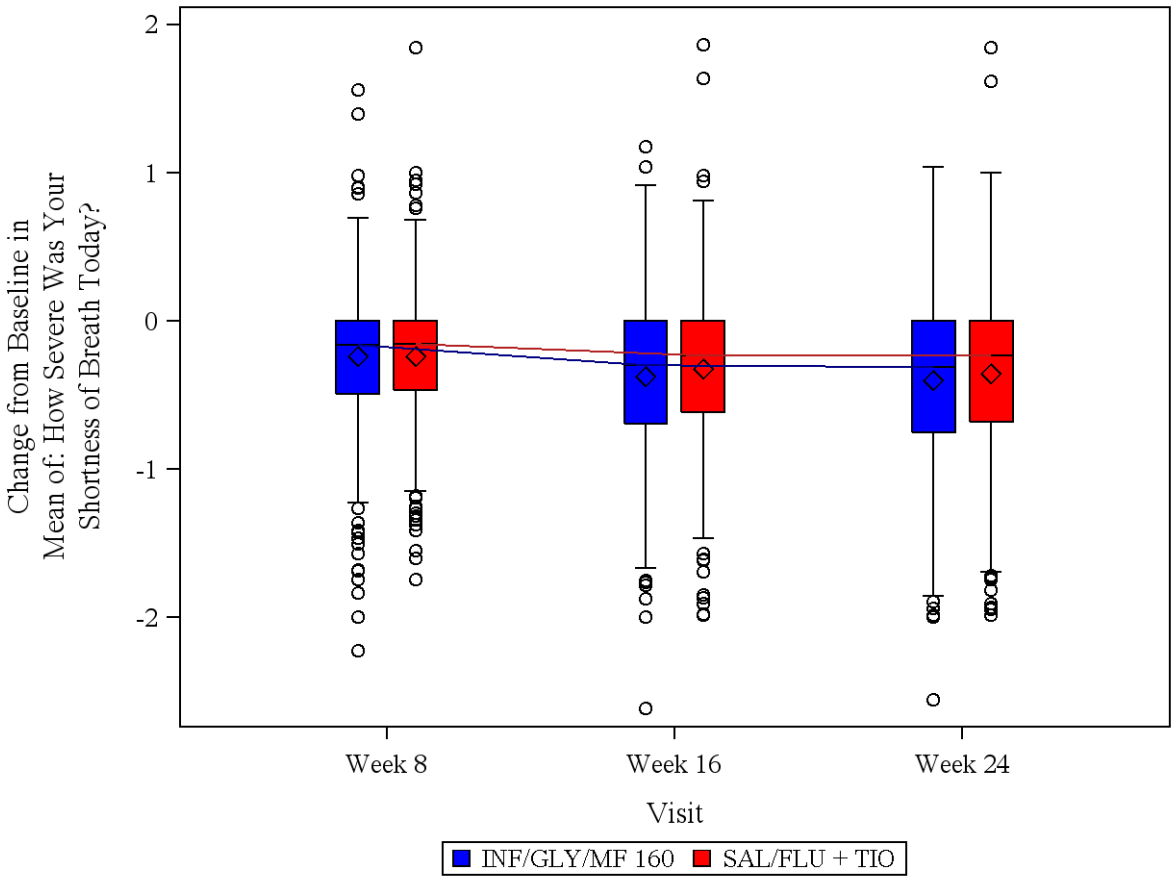


Figure 9.60.2 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



9.61 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline (FAS)

Figure 9.61 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline (FAS)



9.62 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Age (FAS)

Figure 9.62.1 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Age (FAS), Age = 18-39 years

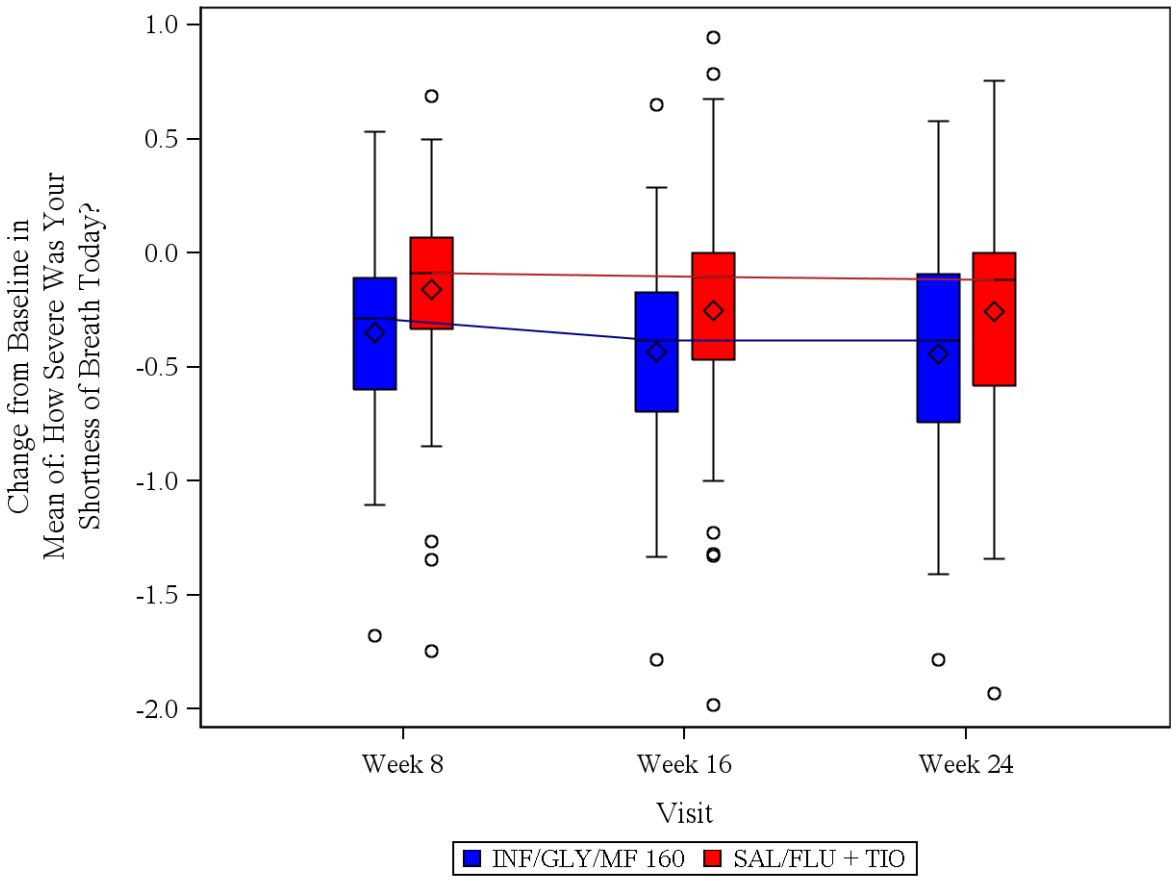


Figure 9.62.2 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Age (FAS), Age = 40-64 years

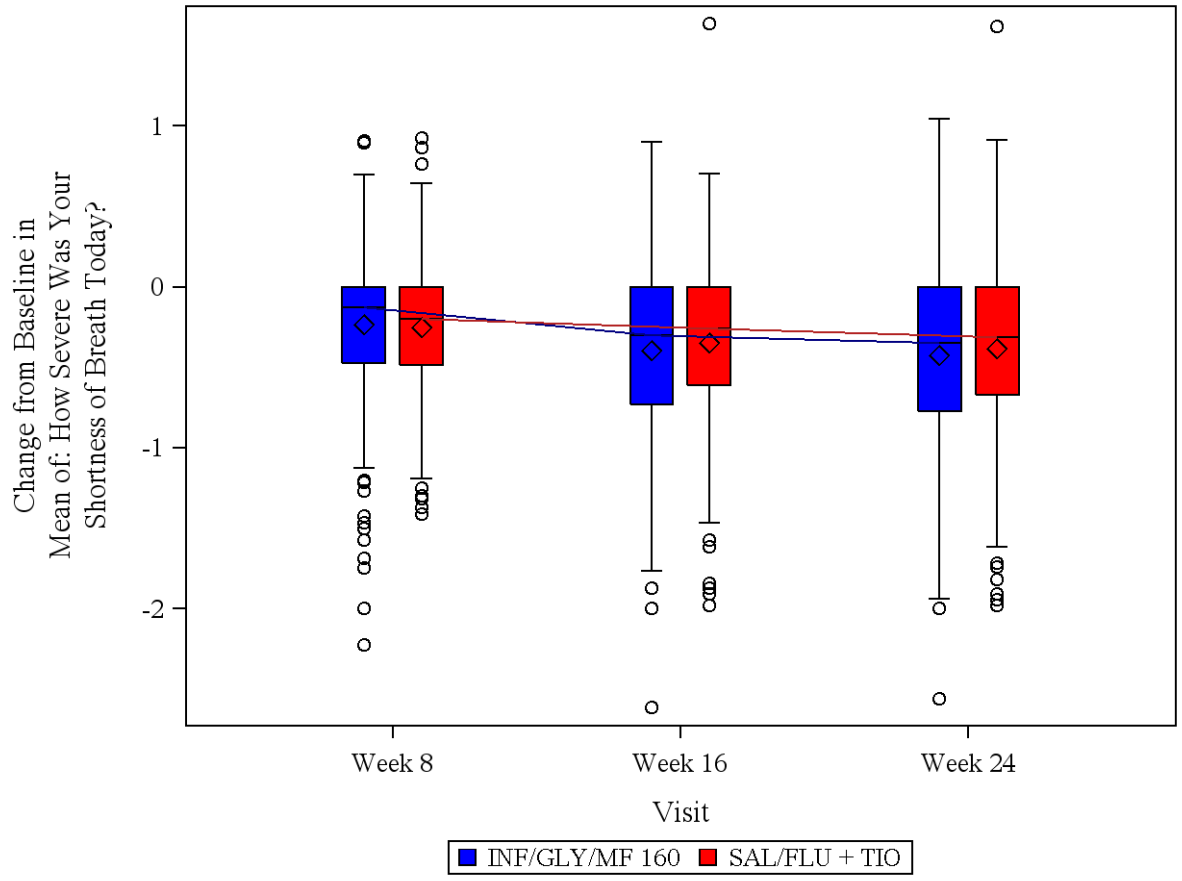
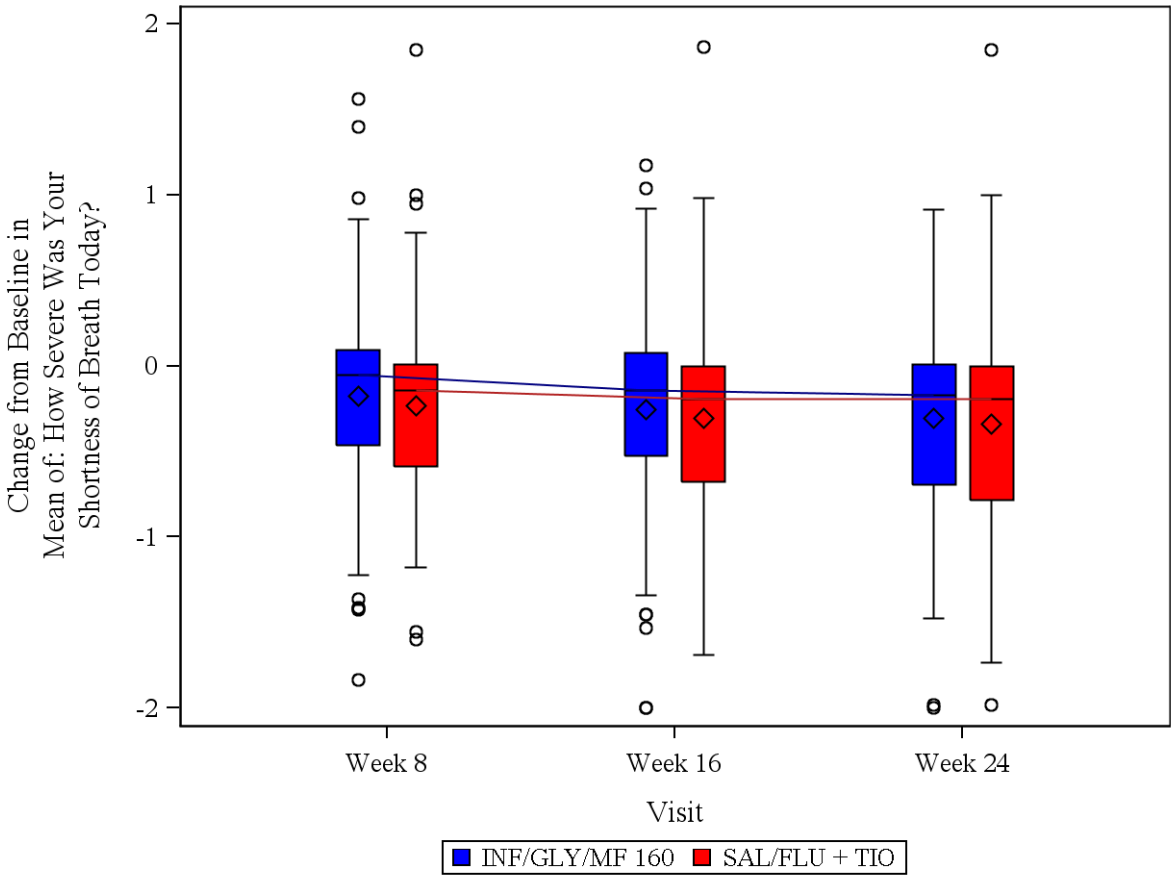


Figure 9.62.3 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Age (FAS), Age = ≥65 years



9.63 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Gender (FAS)

Figure 9.63.1 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Gender (FAS), Gender = Male

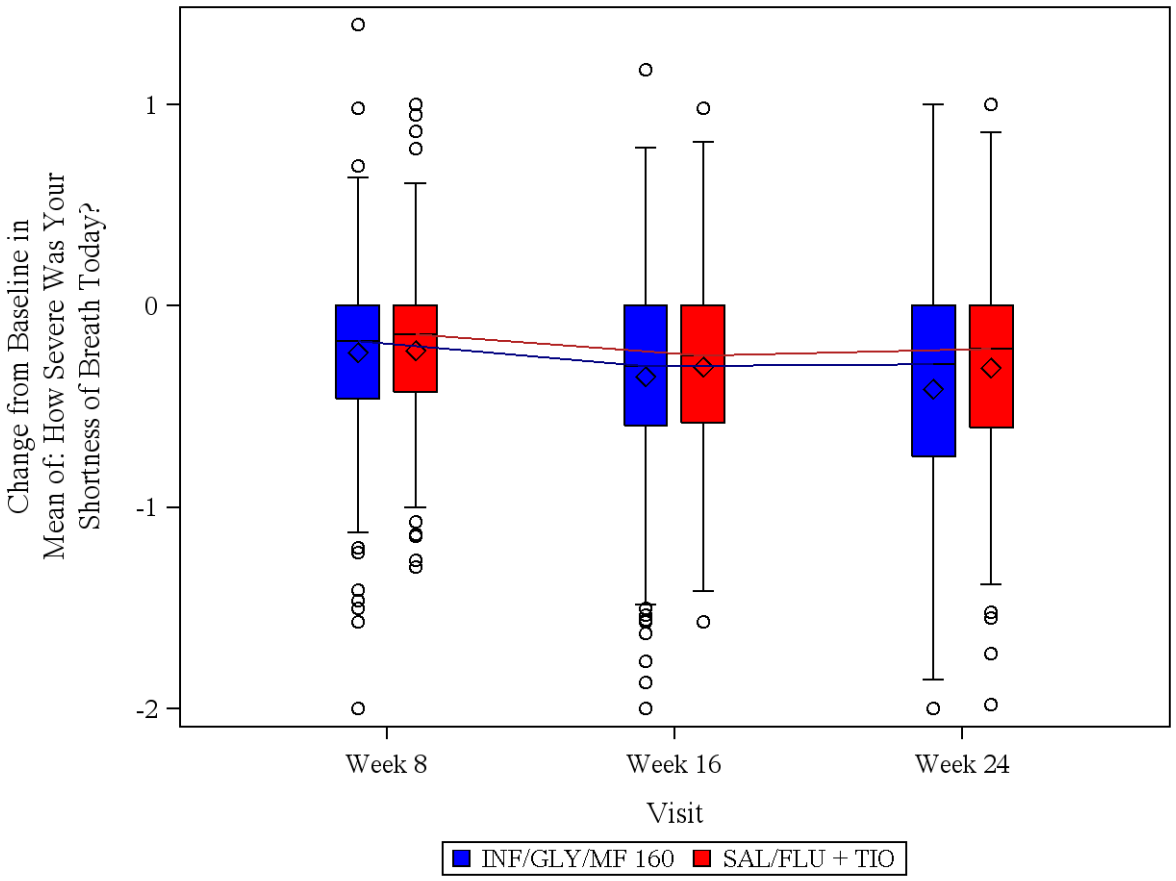
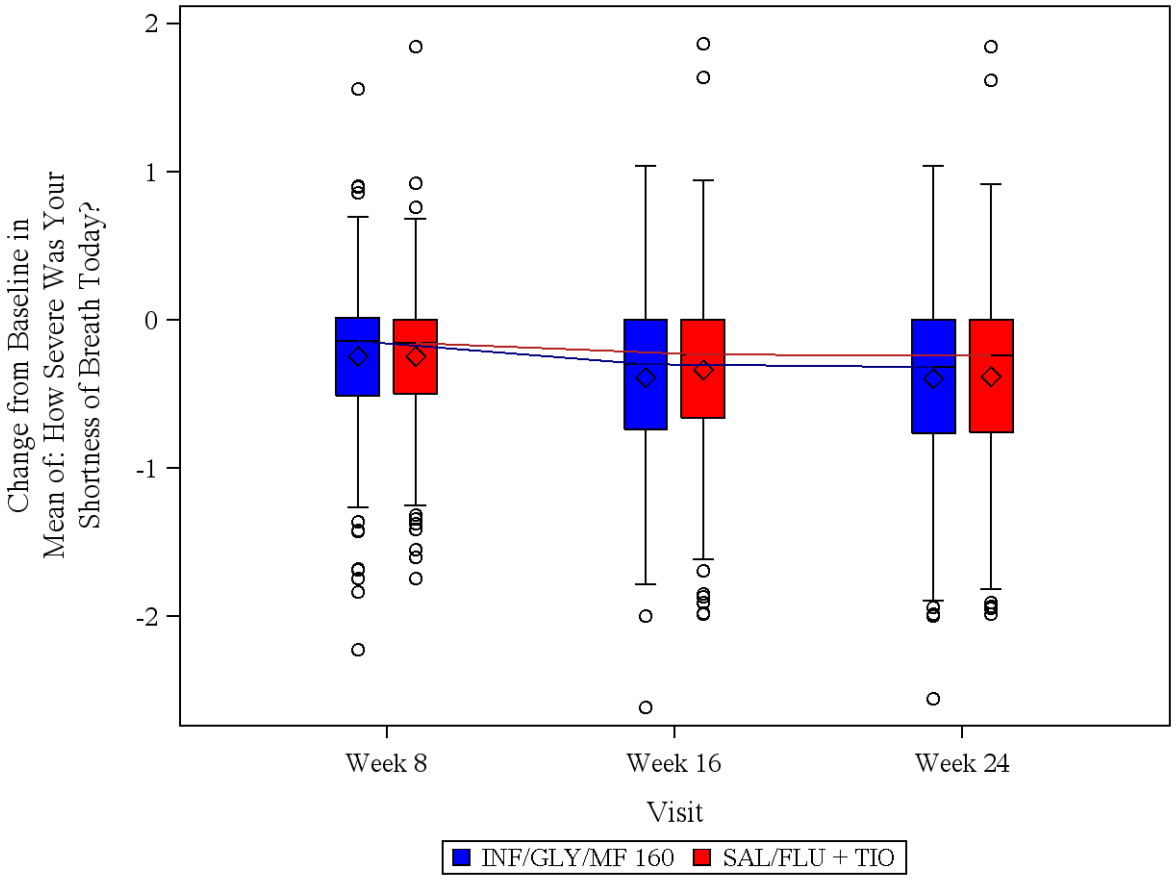


Figure 9.63.2 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Gender (FAS), Gender = Female



9.64 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Region (FAS)

Figure 9.64.1 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Region (FAS), Region = Asia

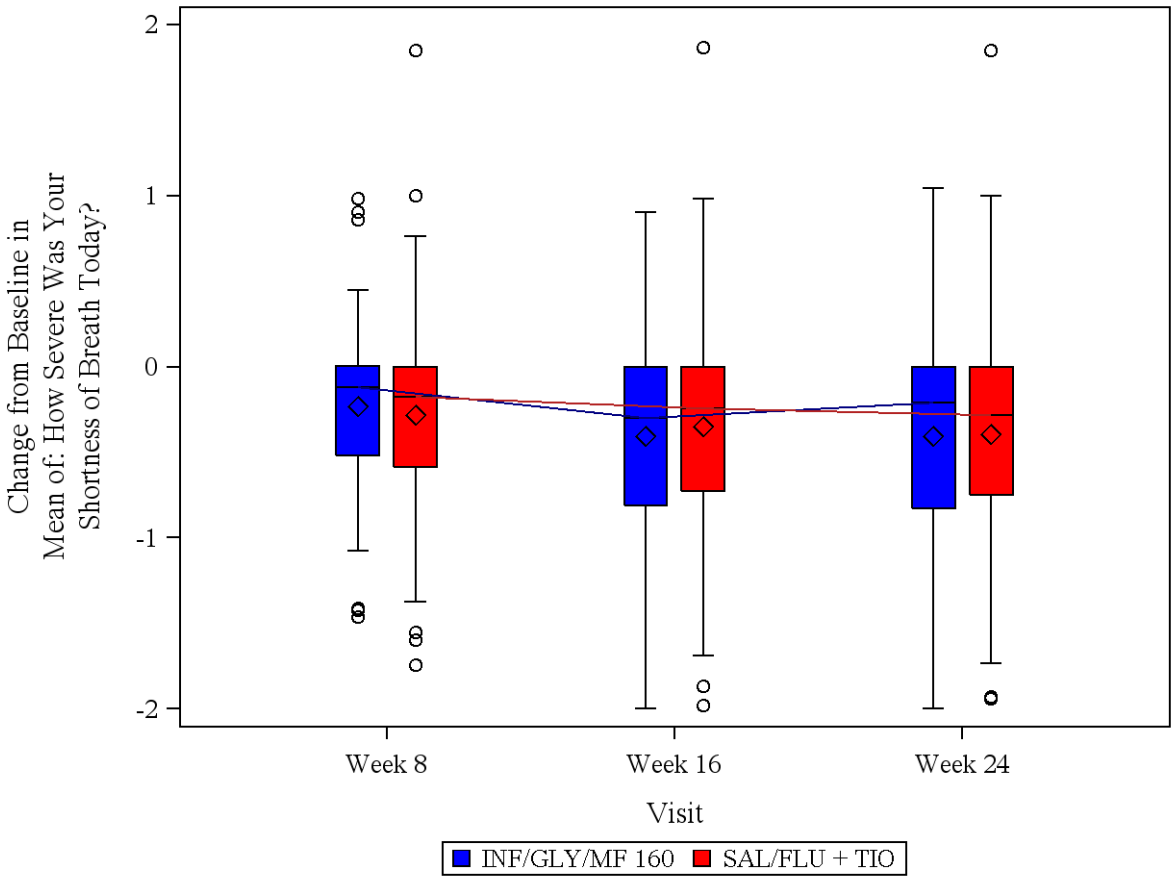


Figure 9.64.2 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Region (FAS), Region = Europe

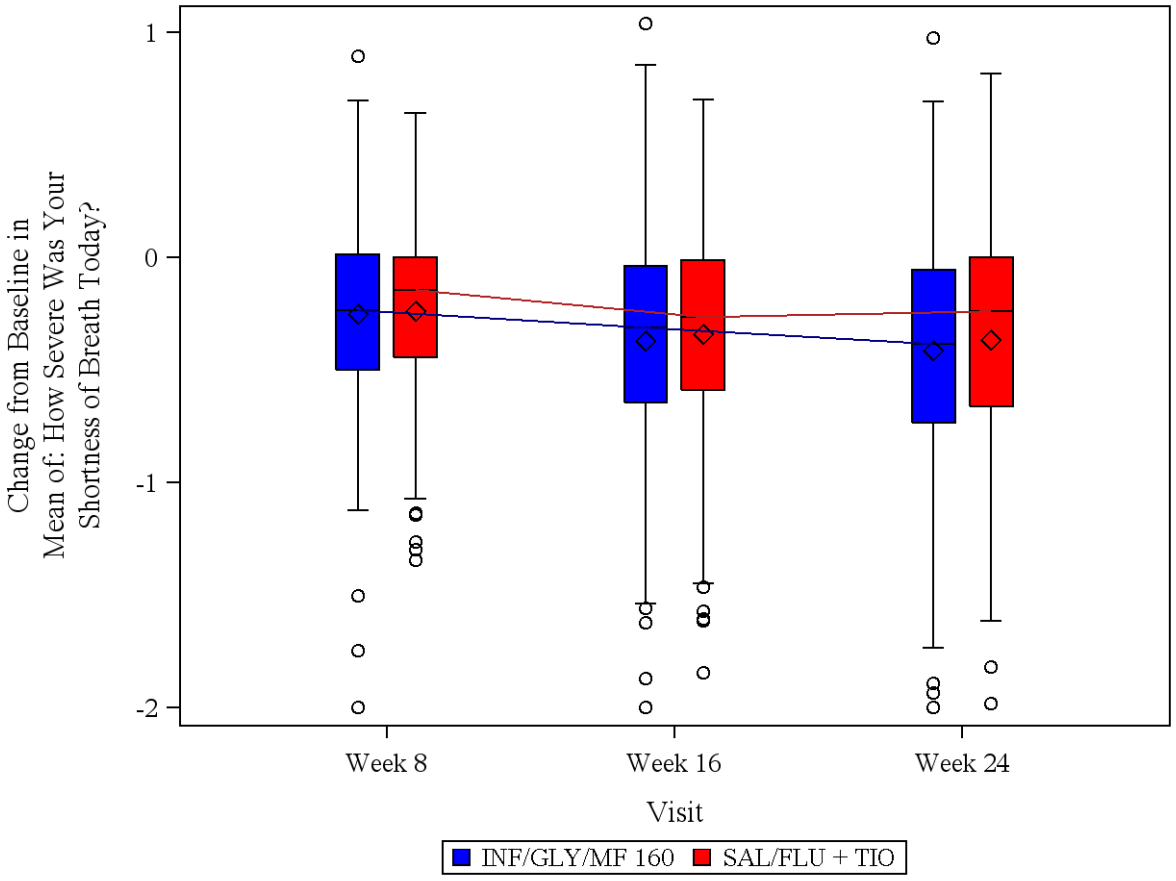


Figure 9.64.3 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Region (FAS), Region = Latin America

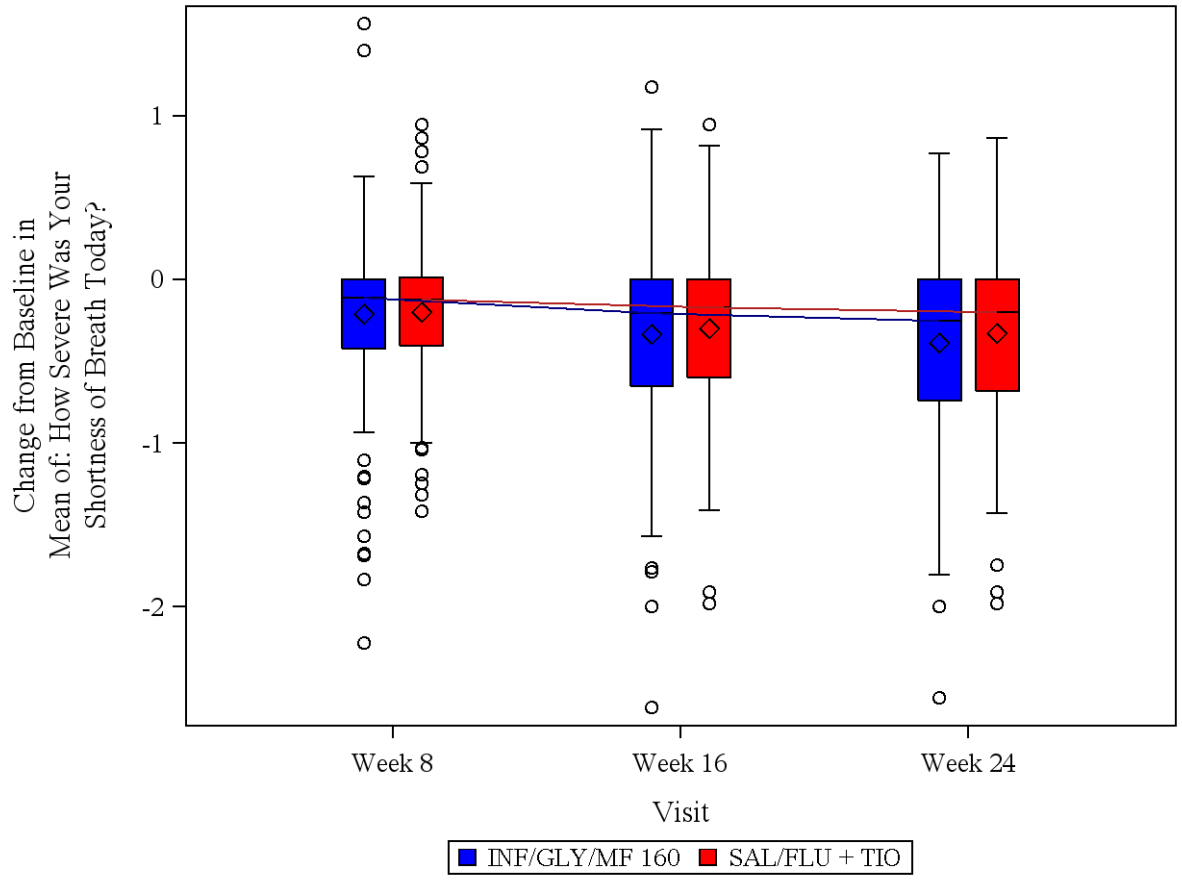
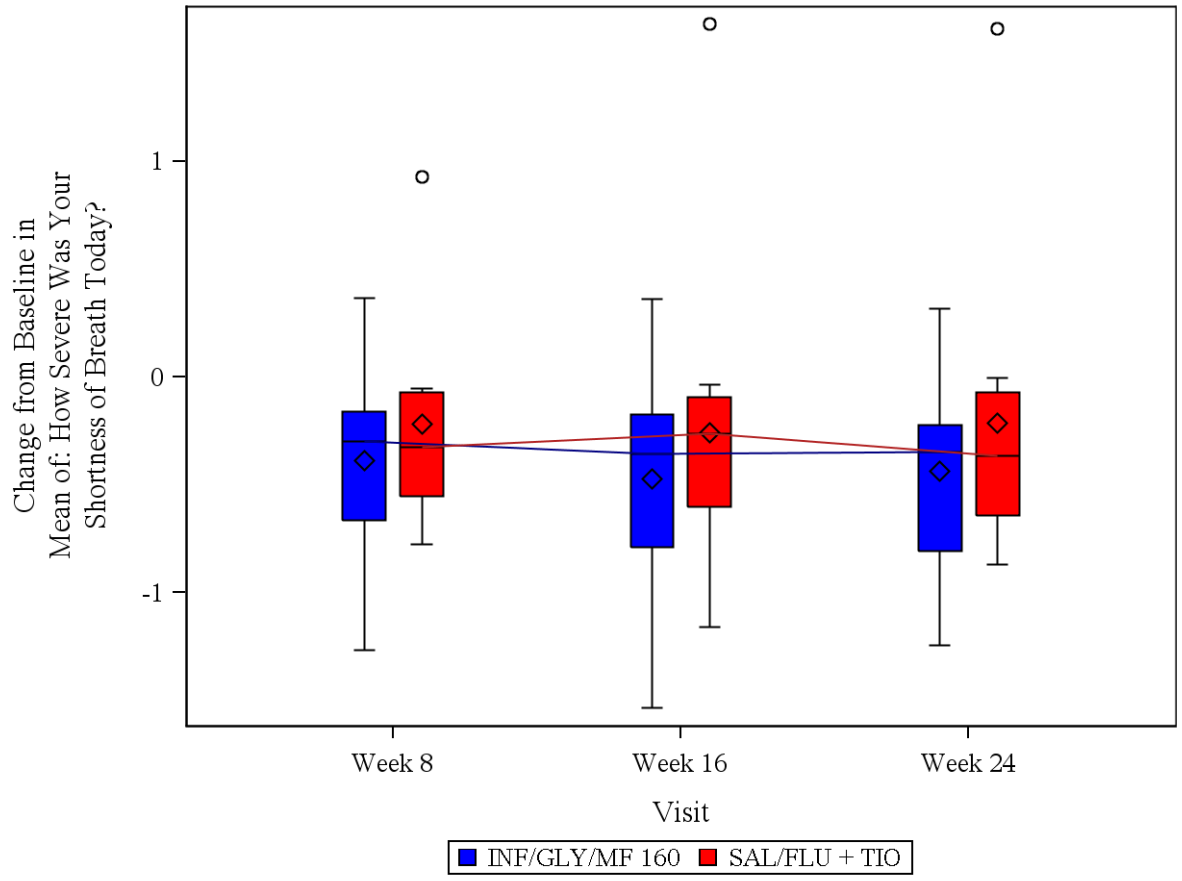


Figure 9.64.4 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Region (FAS), Region = Others



9.65 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 9.65.1 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

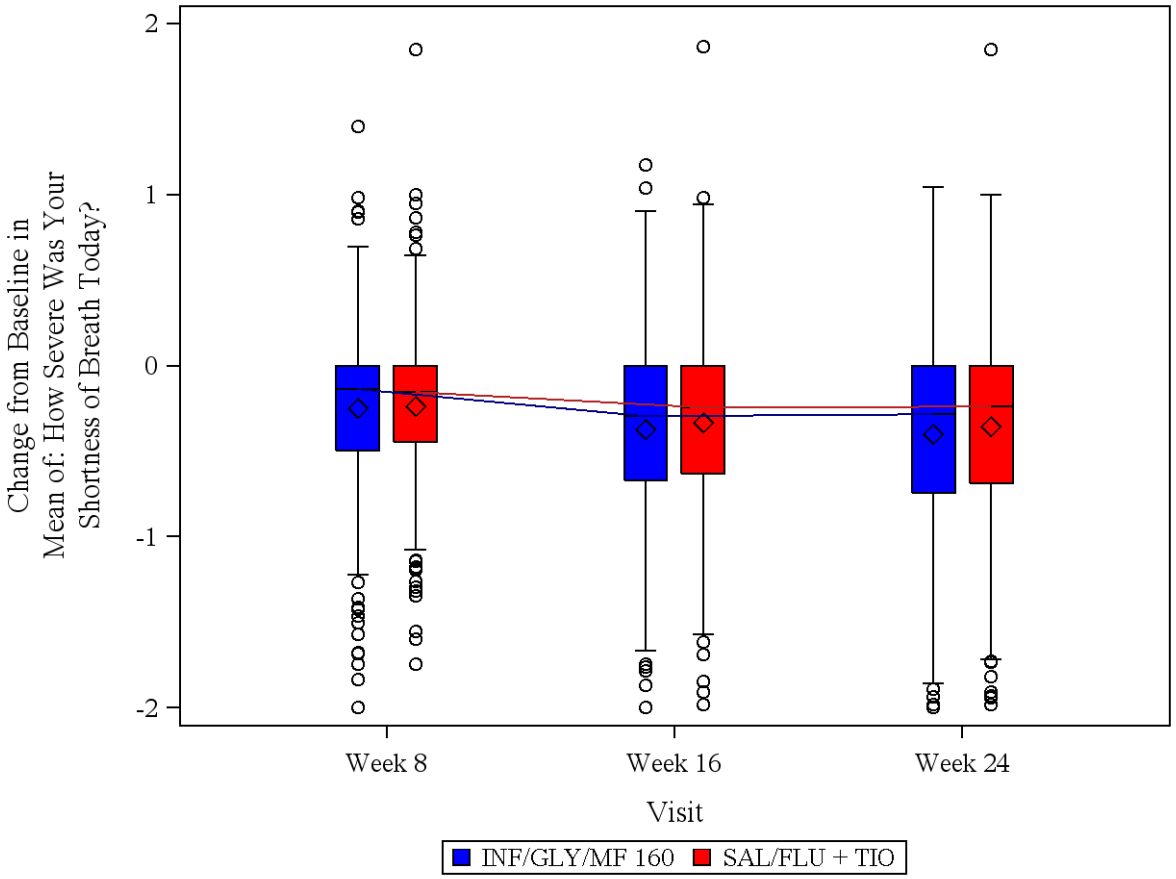
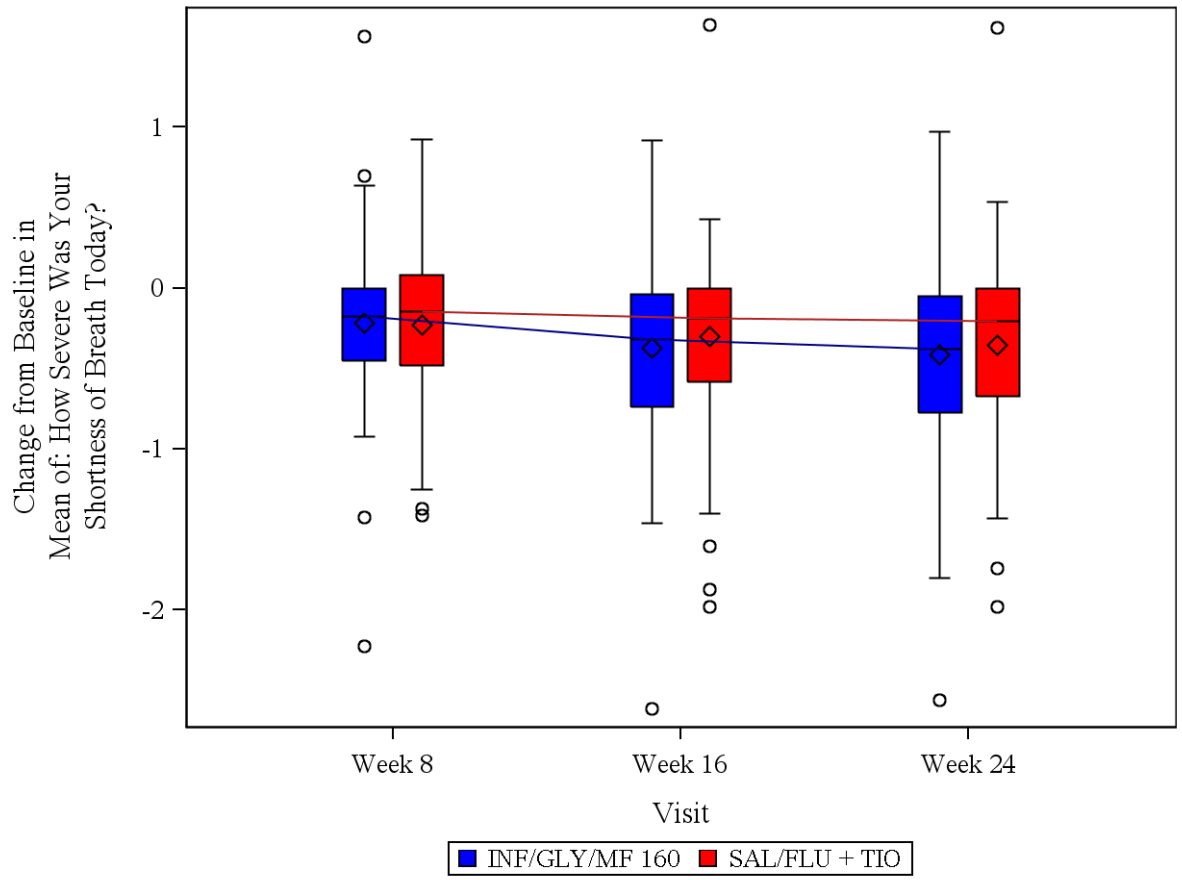


Figure 9.65.2 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.66 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 9.66.1 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

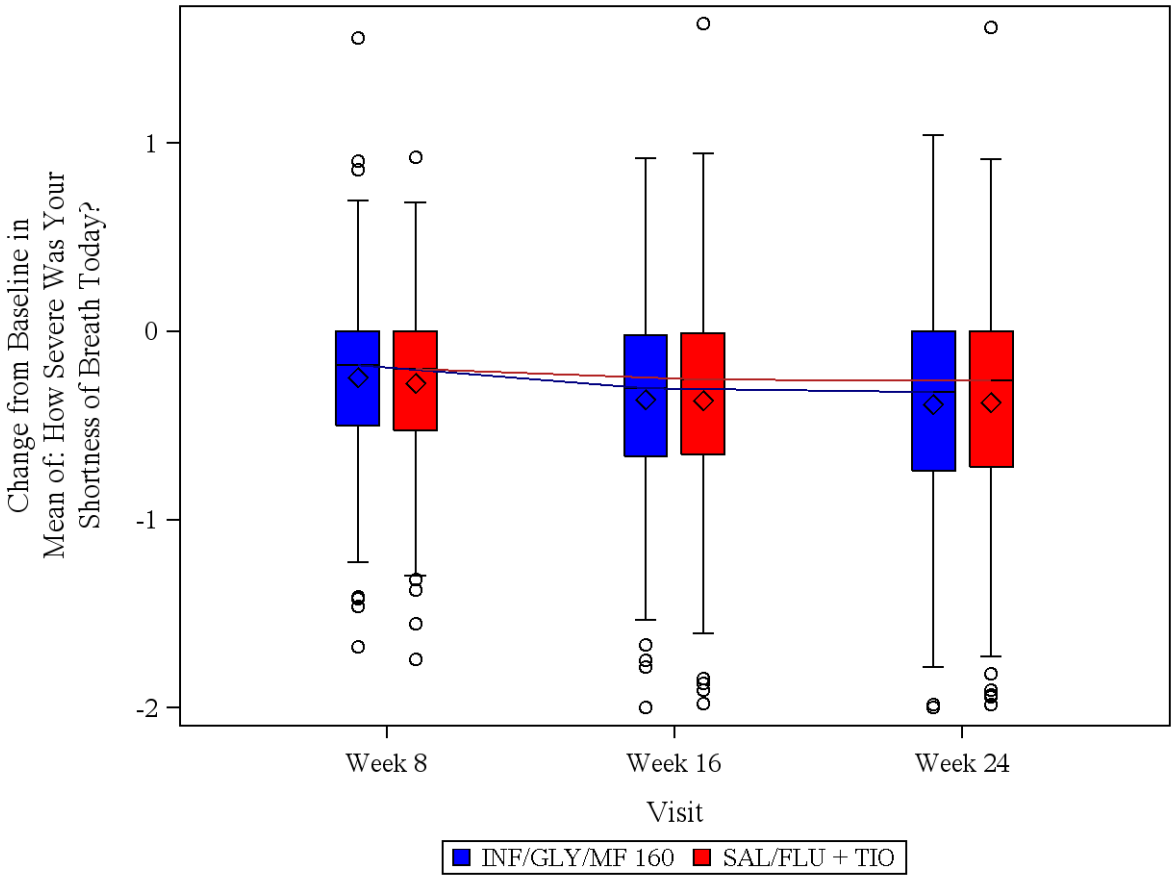
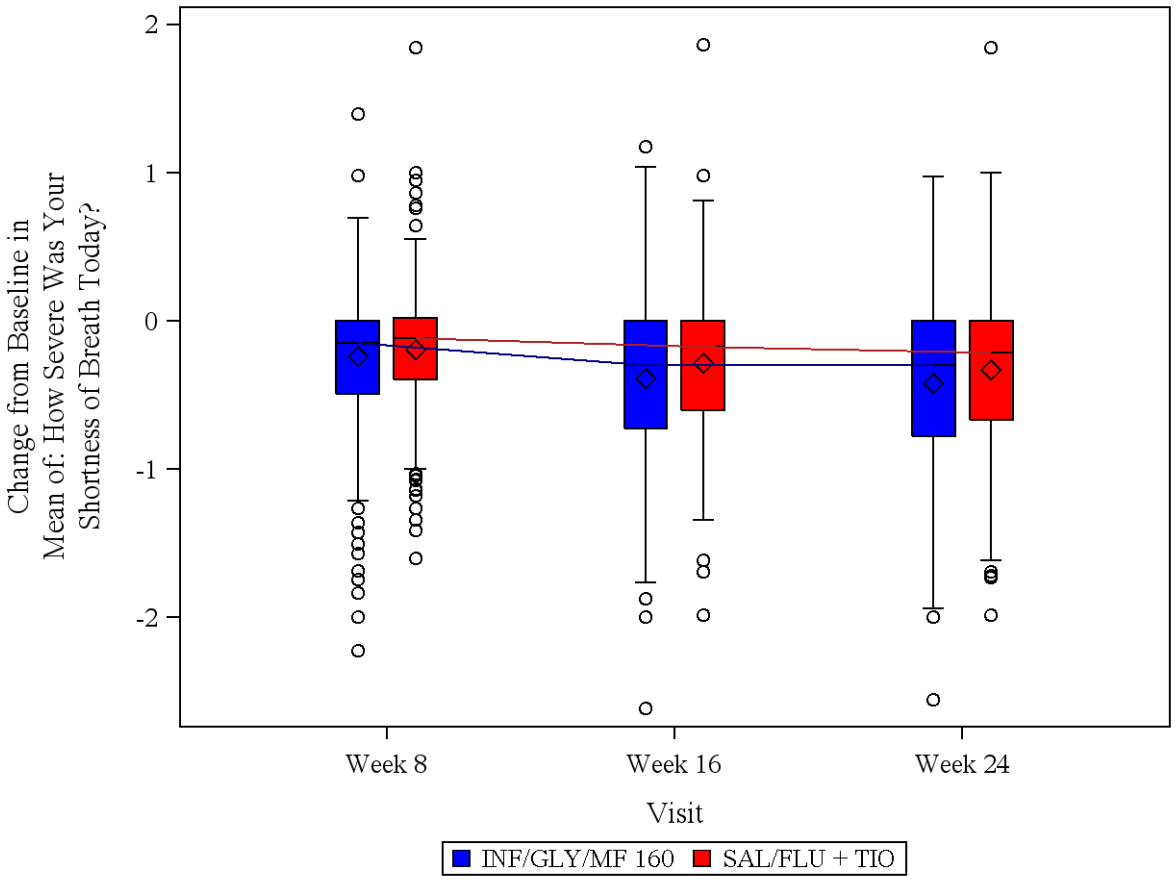
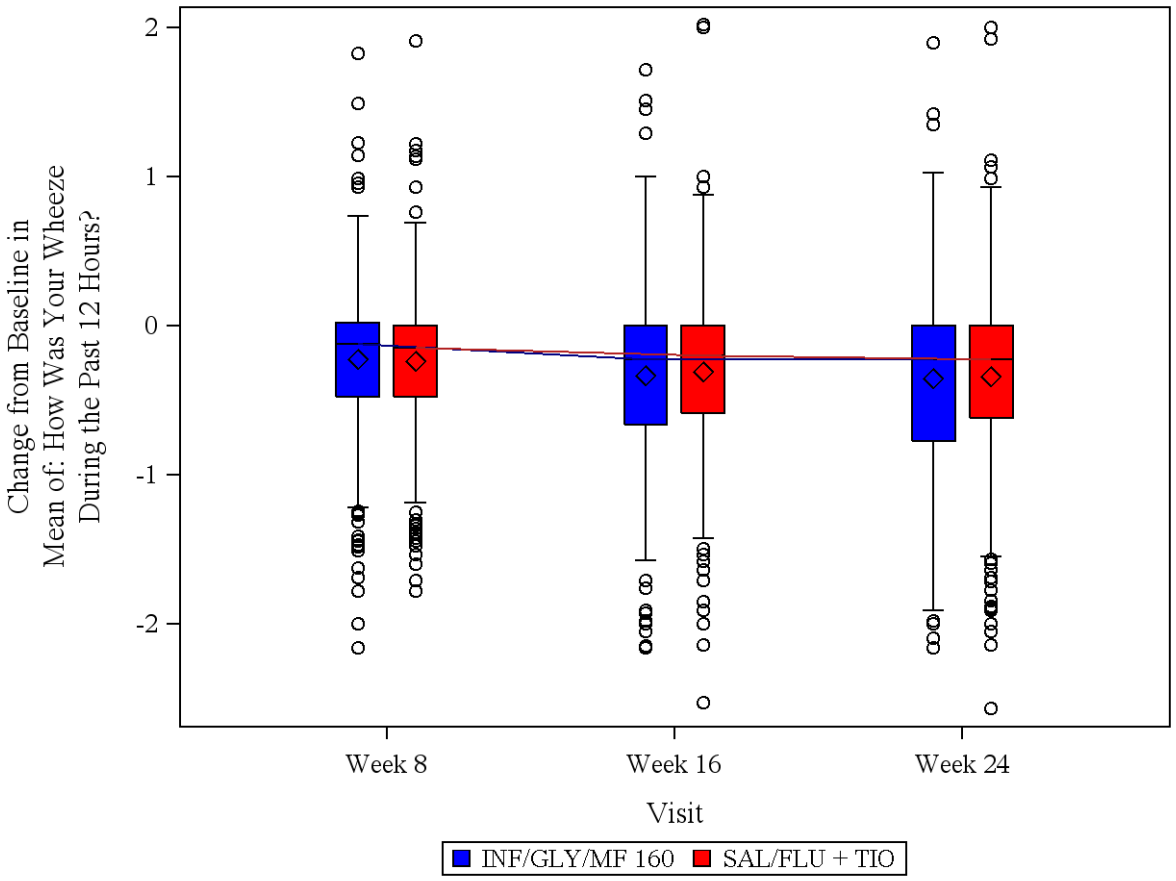


Figure 9.66.2 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



9.67 Boxplot: Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline (FAS)

Figure 9.67 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline (FAS)



9.68 Boxplot: Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Age (FAS)

Figure 9.68.1 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Age (FAS), Age = 18-39 years

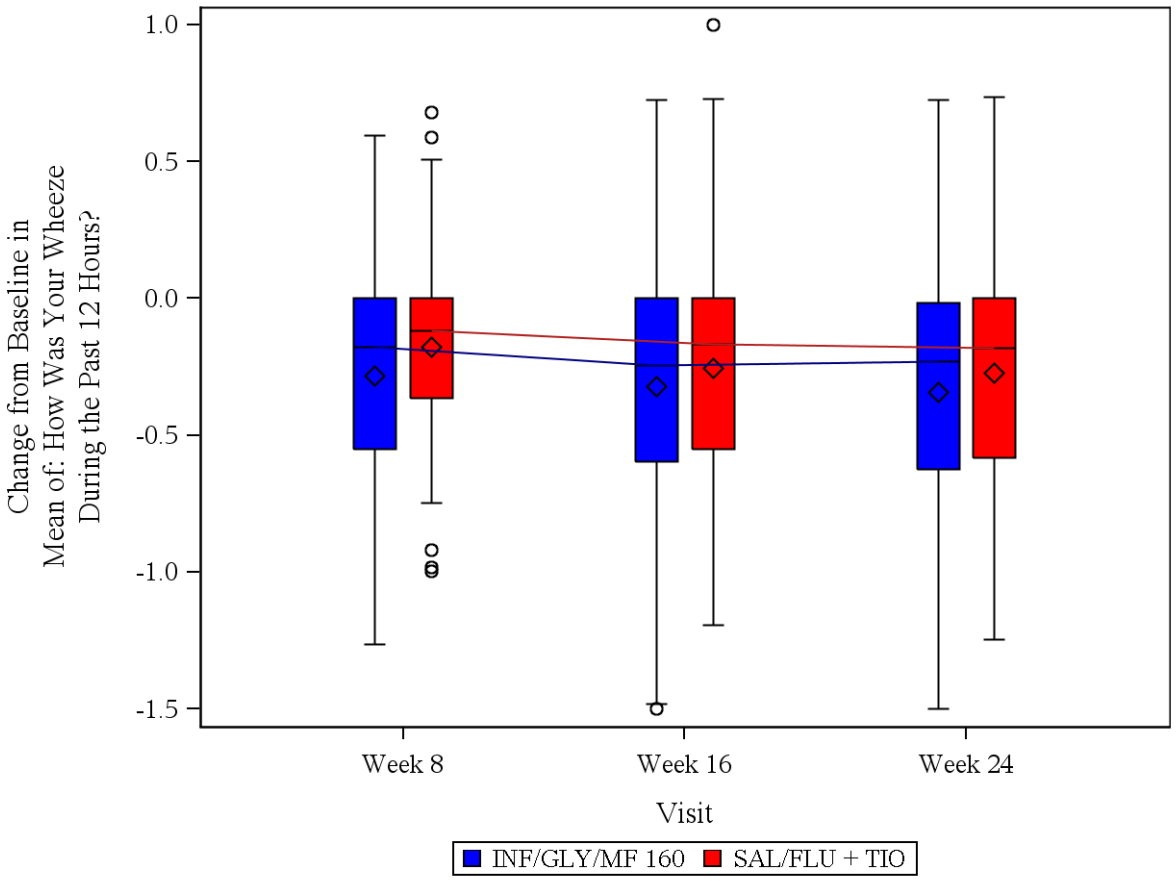


Figure 9.68.2 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Age (FAS), Age = 40-64 years

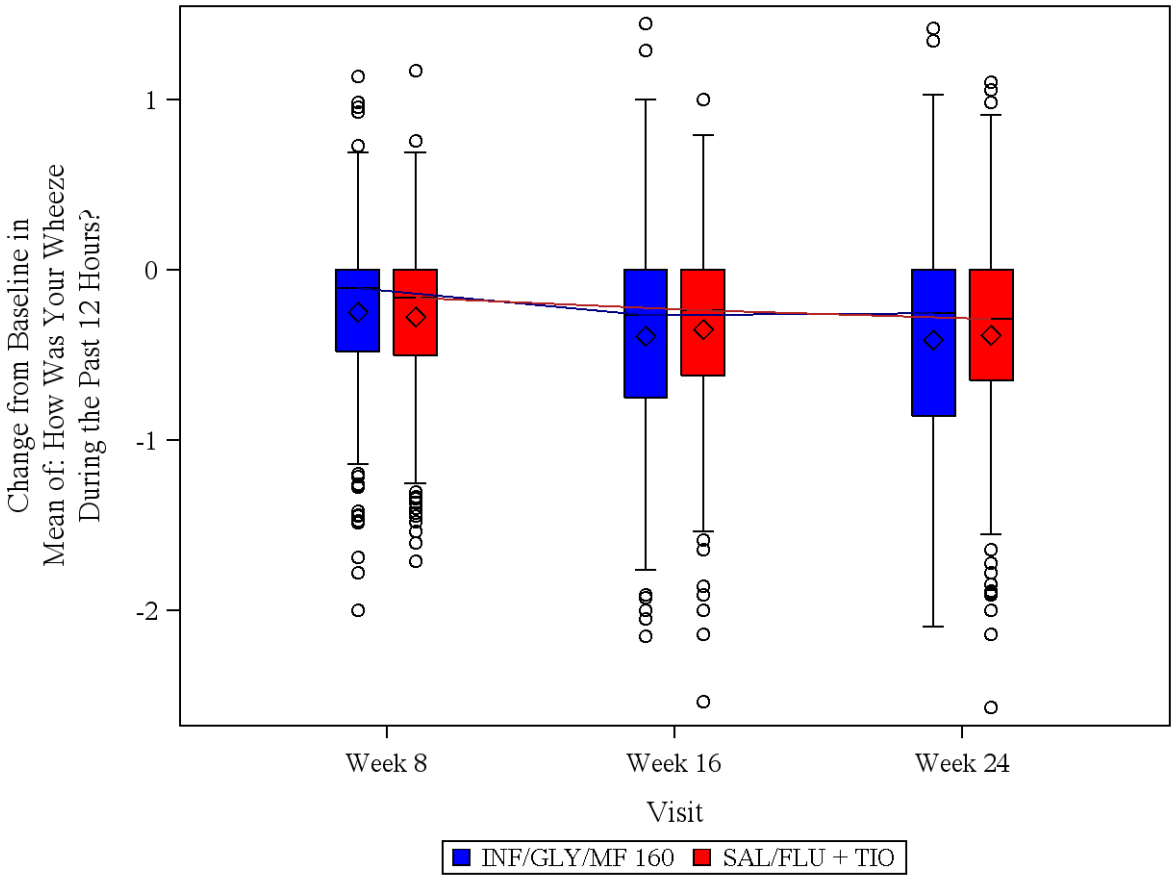
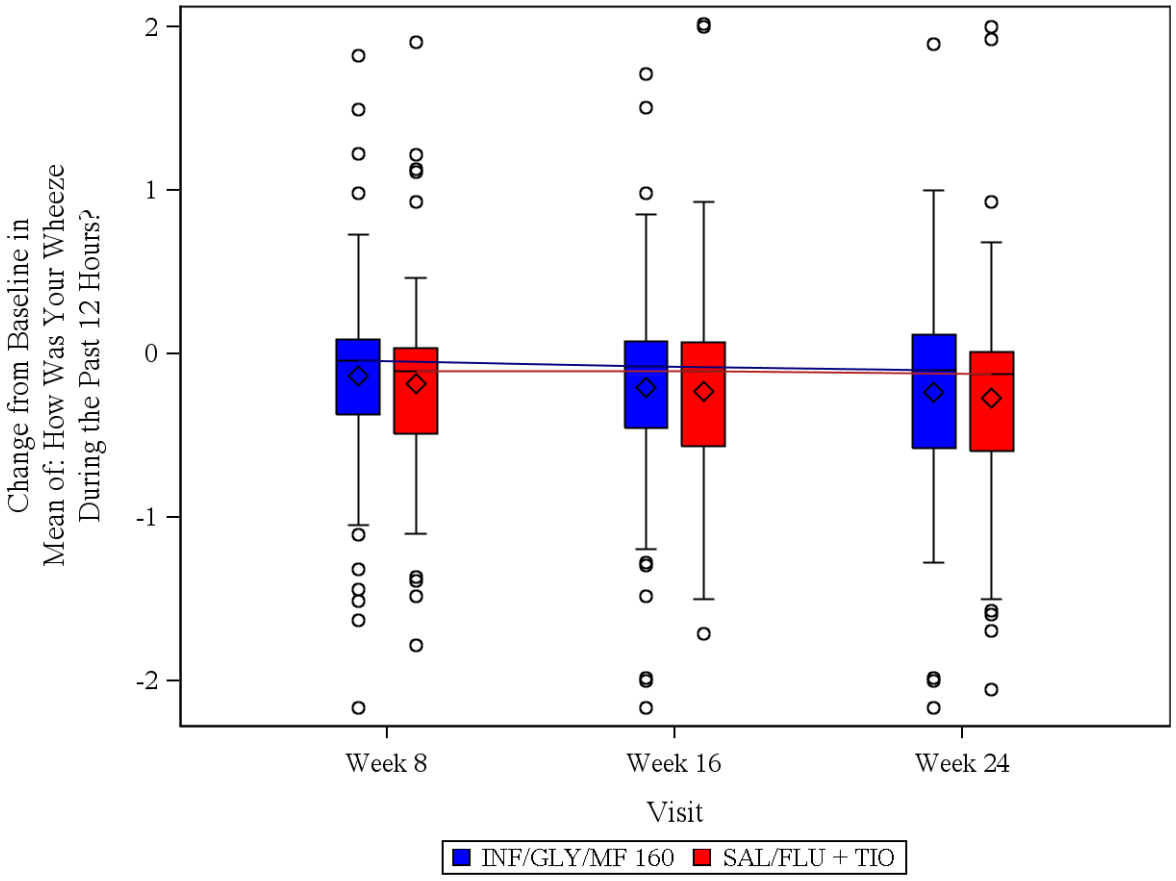


Figure 9.68.3 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Age (FAS), Age = ≥65 years



9.69 Boxplot: Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Gender (FAS)

Figure 9.69.1 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Gender (FAS), Gender = Male

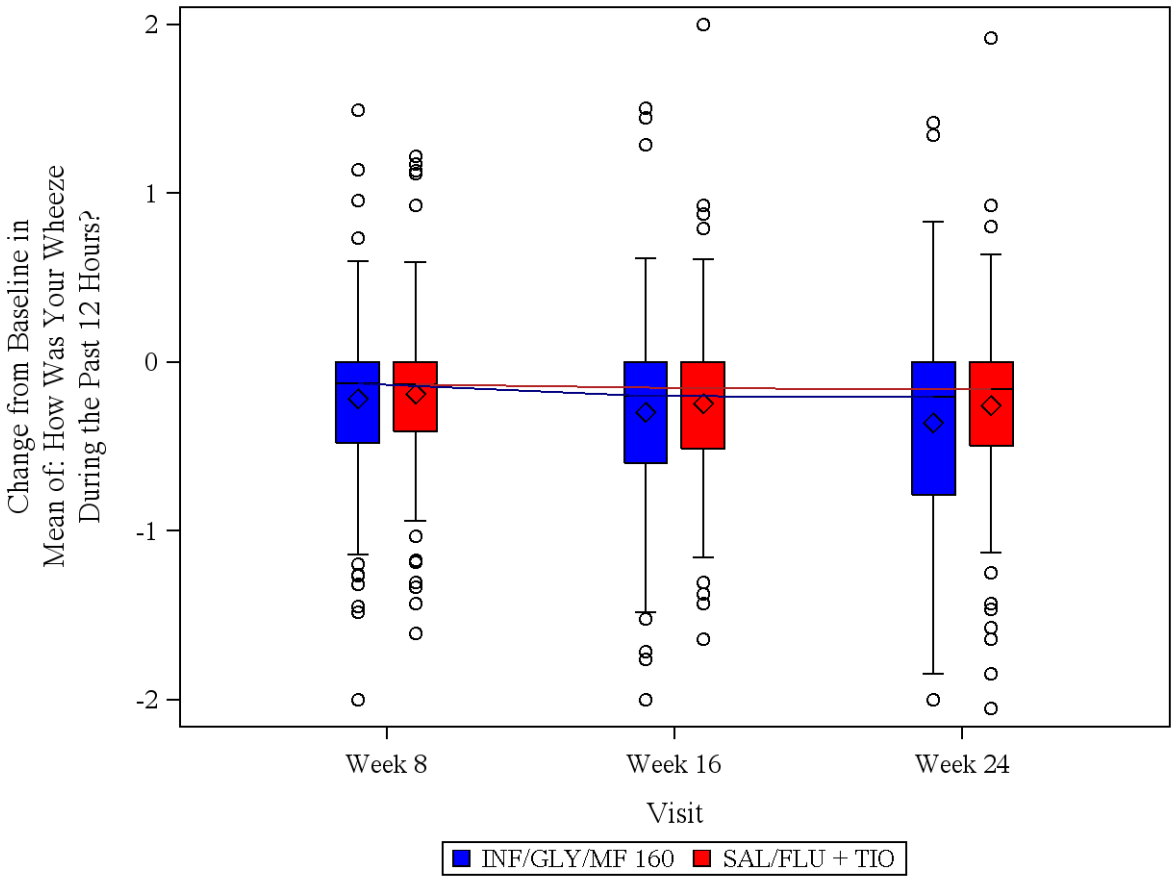
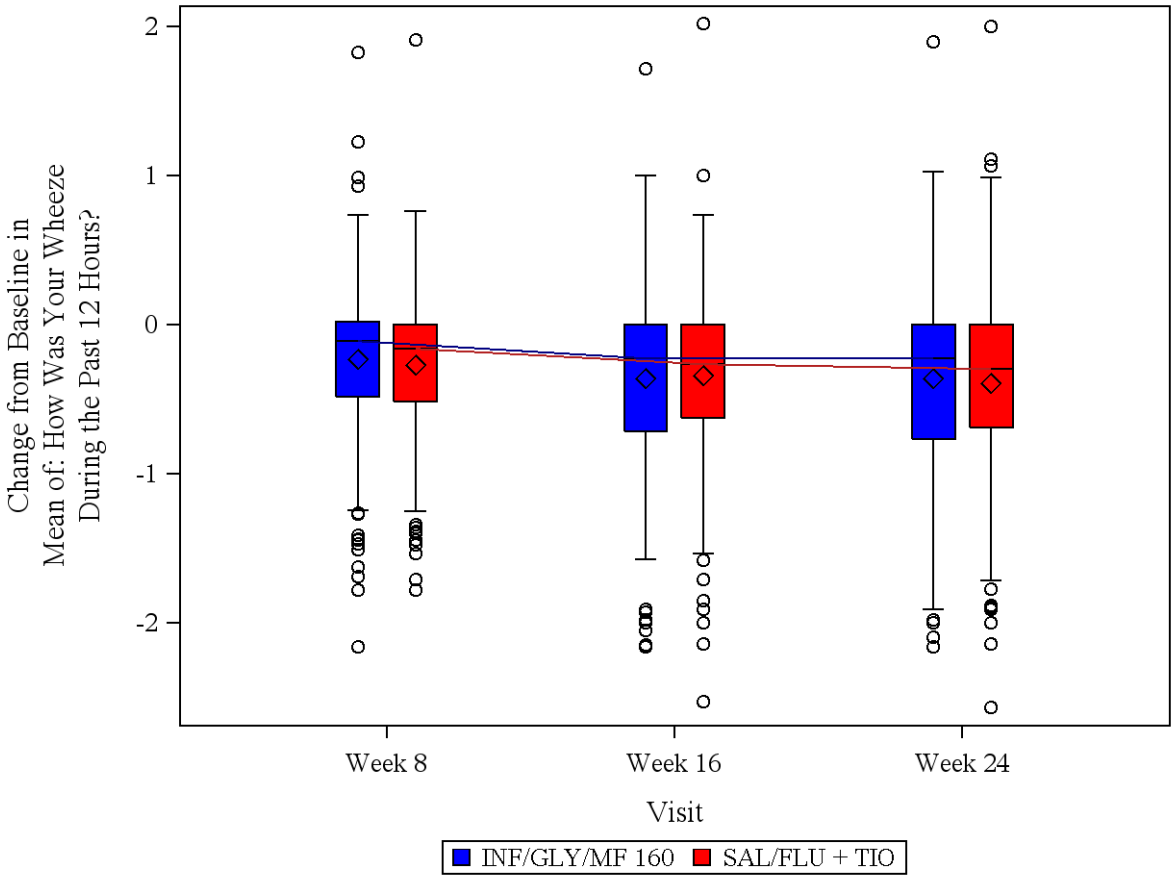


Figure 9.69.2 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Gender (FAS), Gender = Female



9.70 Boxplot: Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Region (FAS)

Figure 9.70.1 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Asia

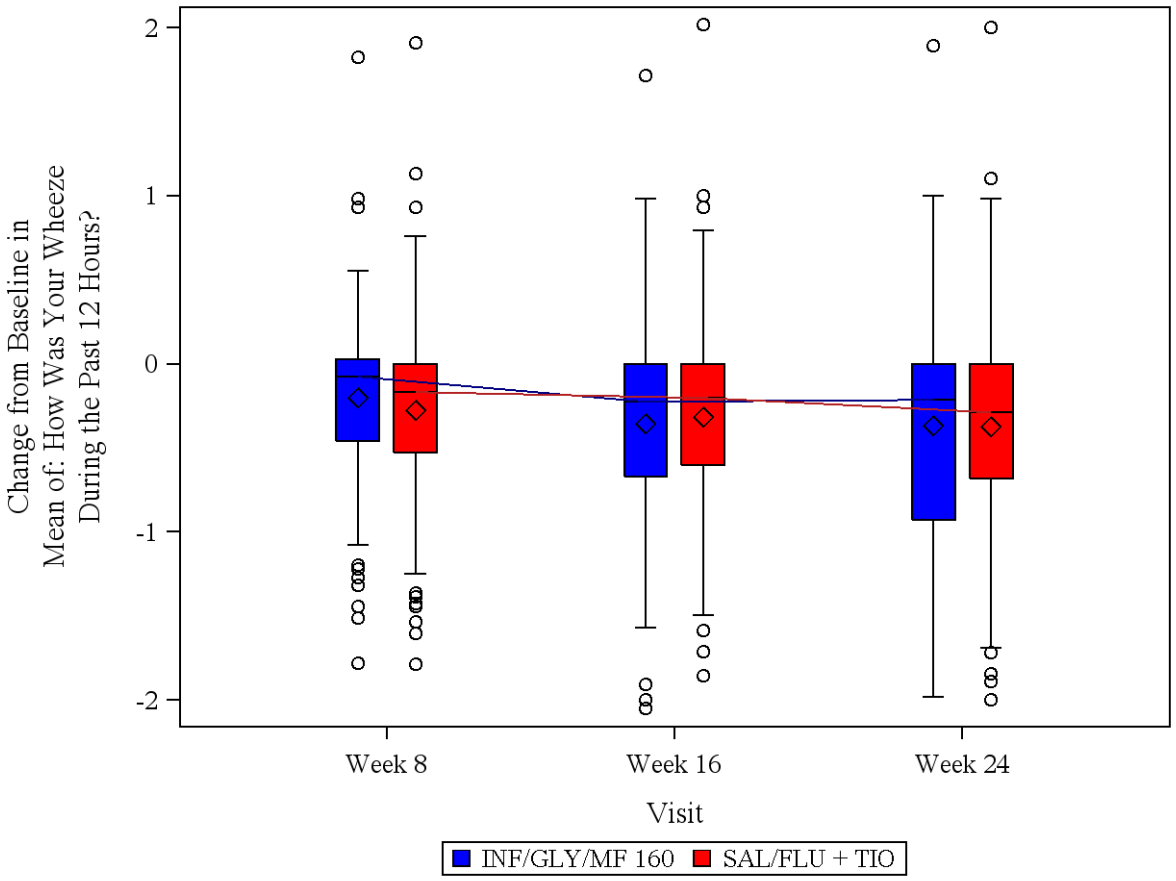


Figure 9.70.2 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Europe

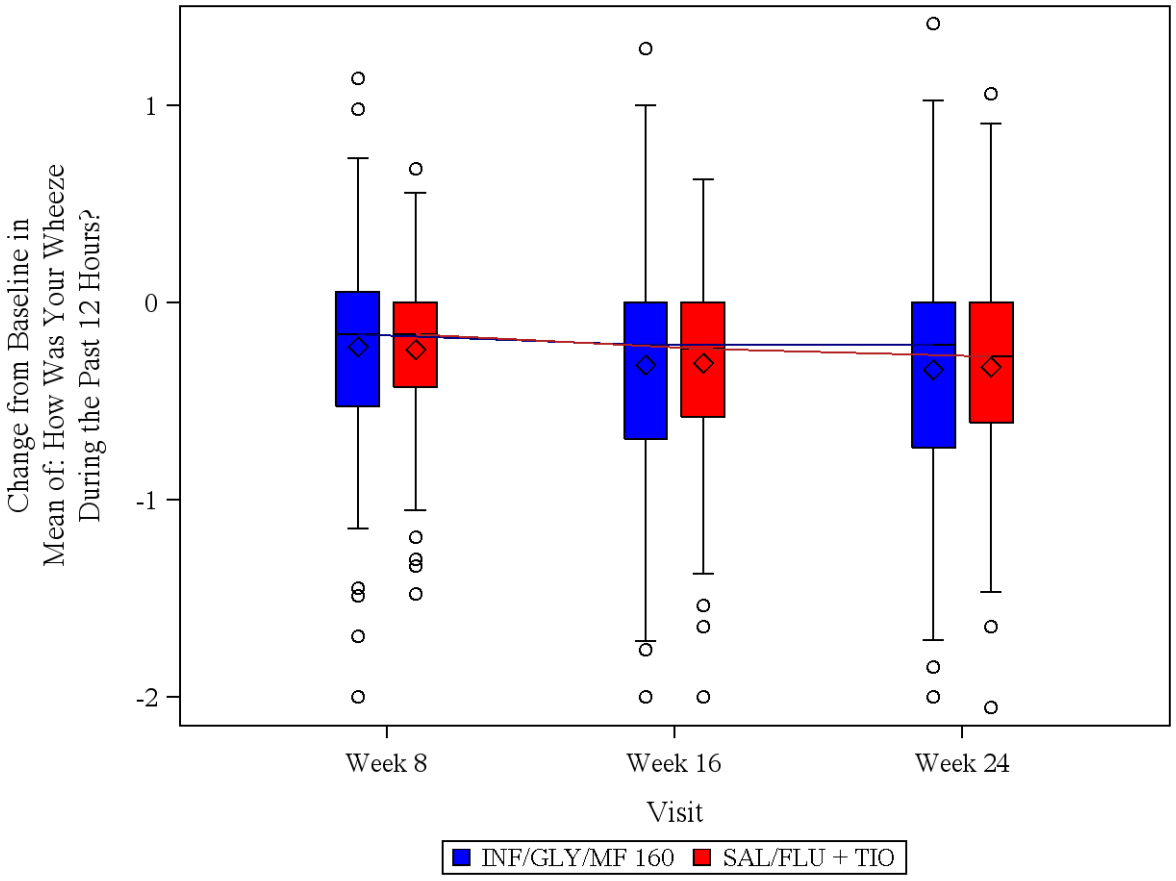


Figure 9.70.3 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Latin America

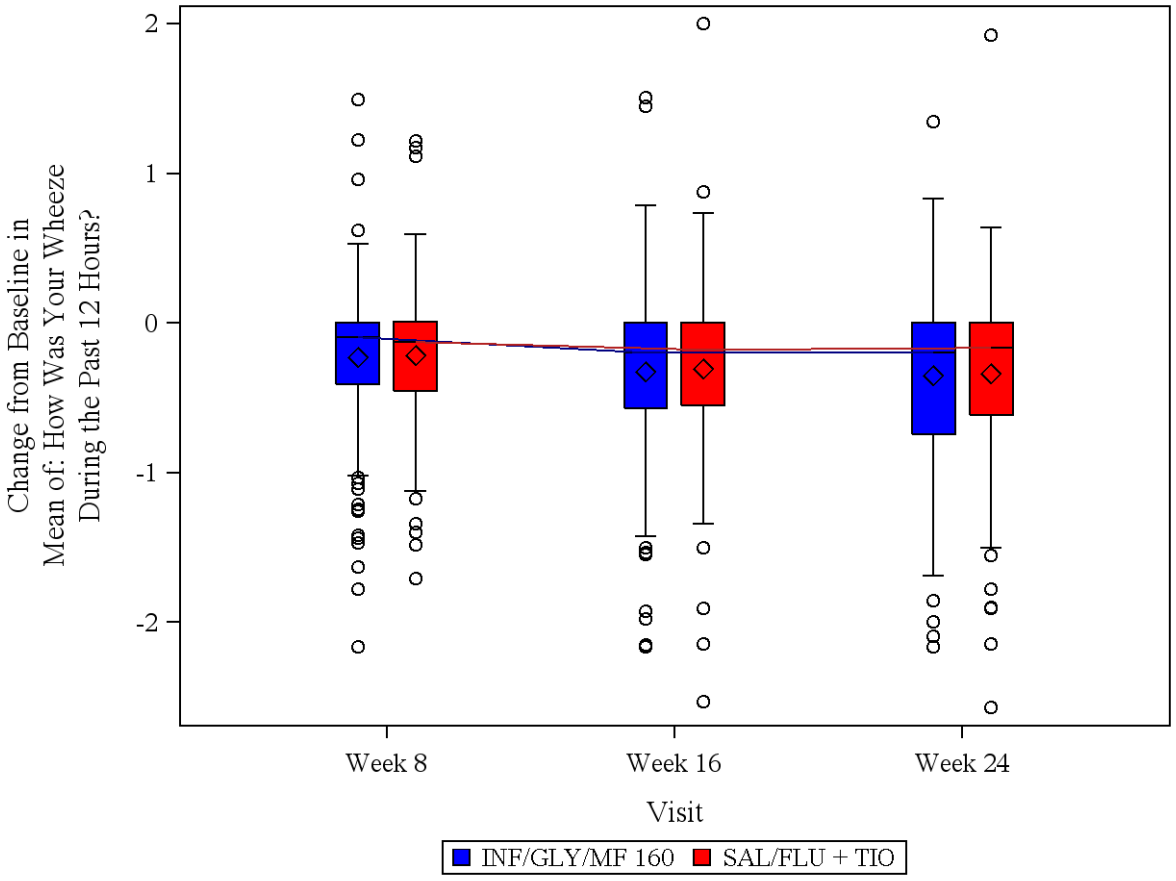
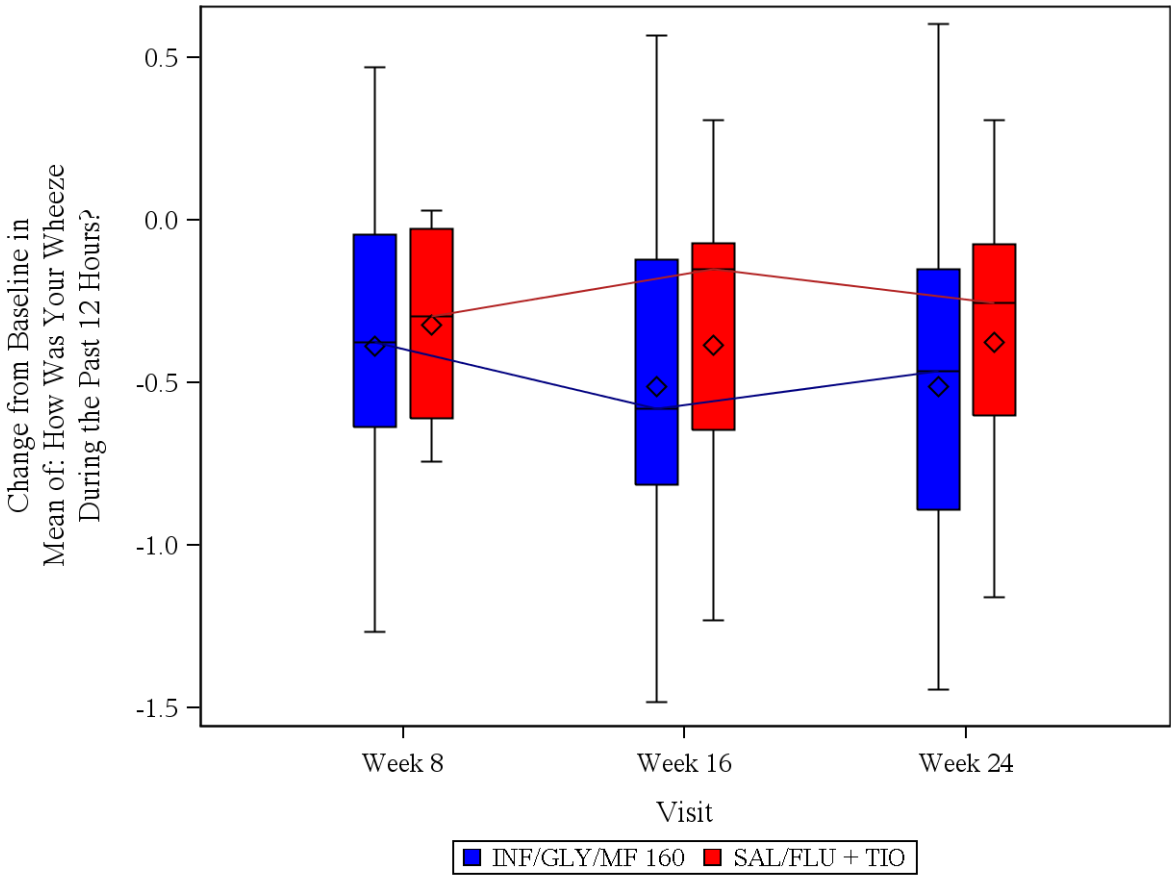


Figure 9.70.4 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Others



9.71 Boxplot: Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 9.71.1 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

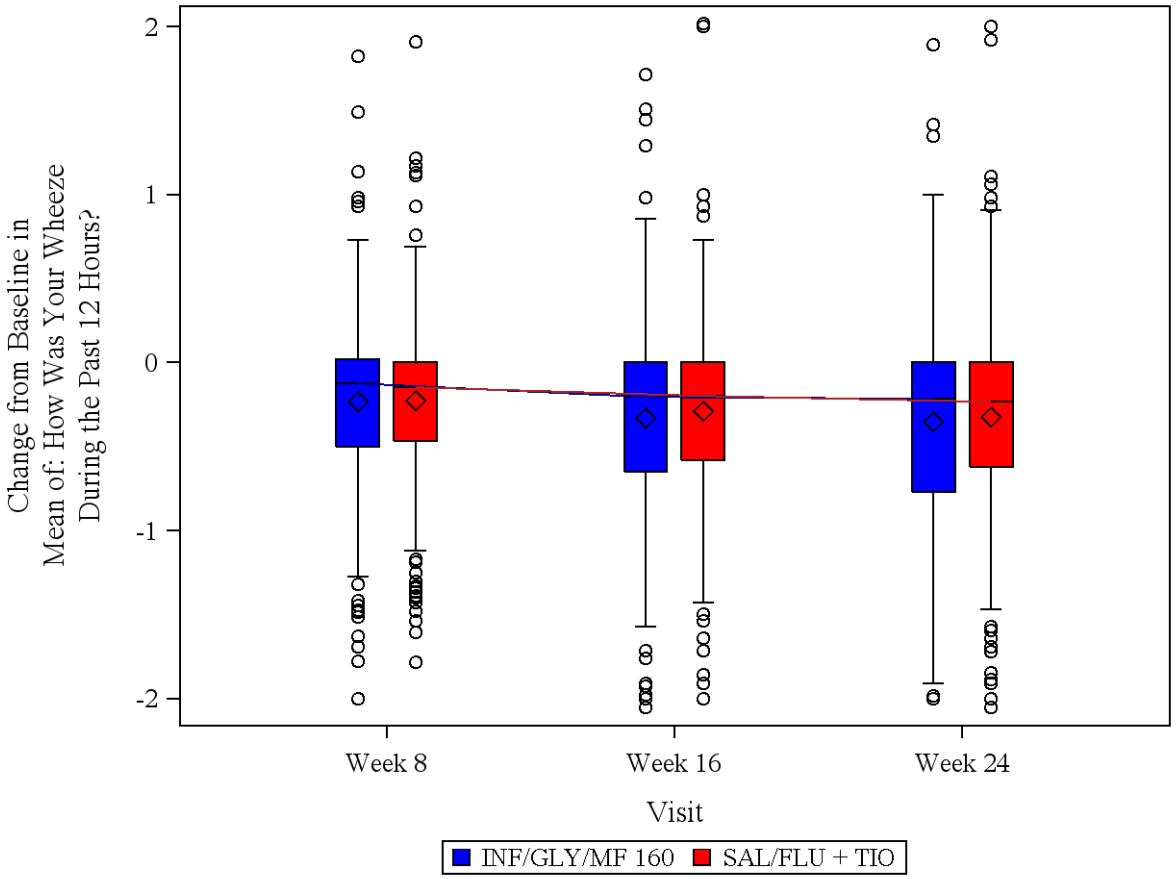
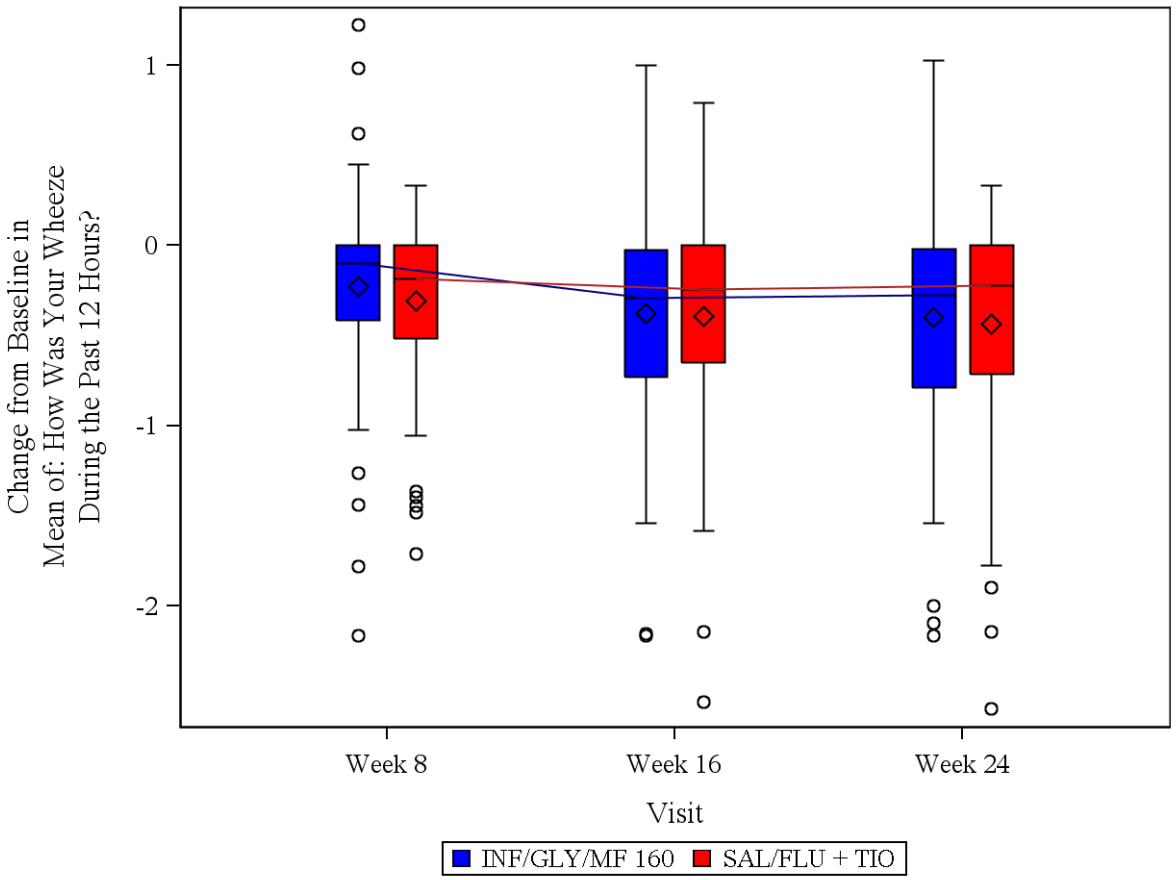


Figure 9.71.2 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.72 Boxplot: Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 9.72.1 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

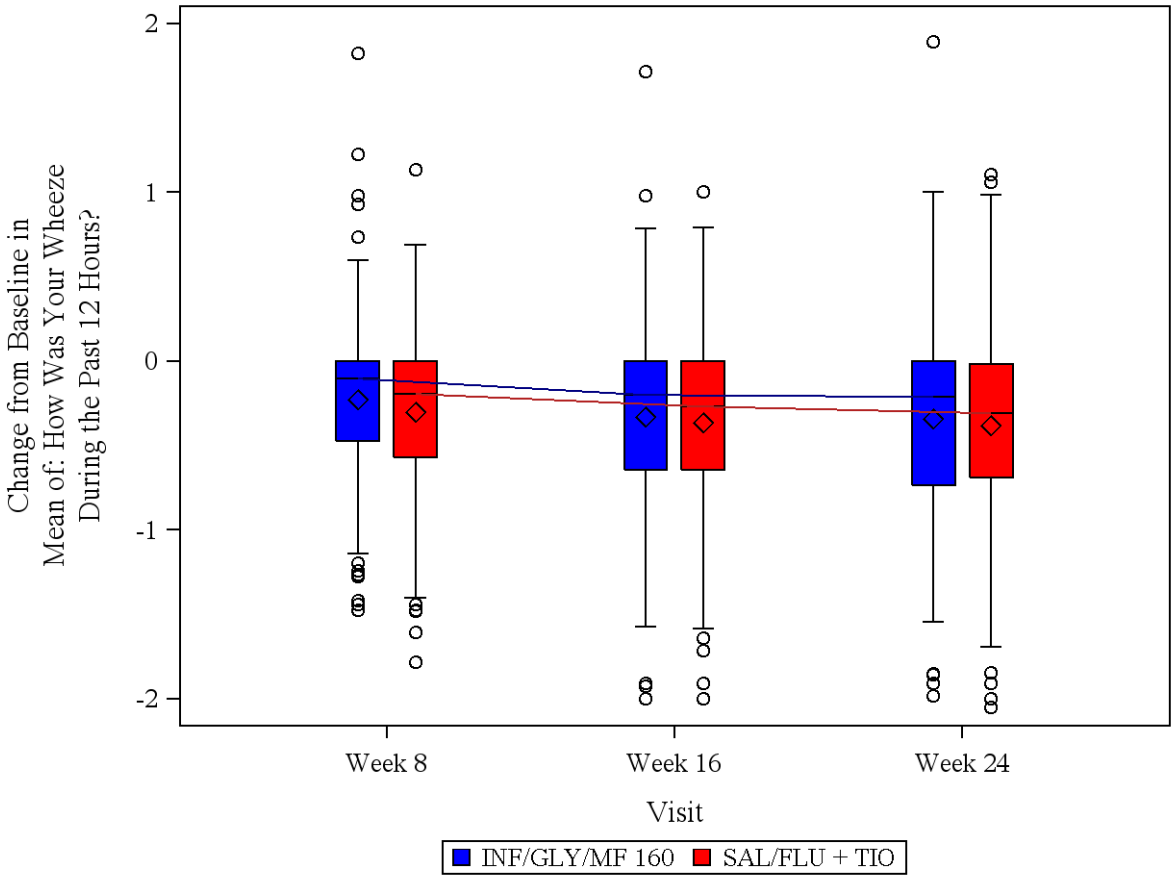
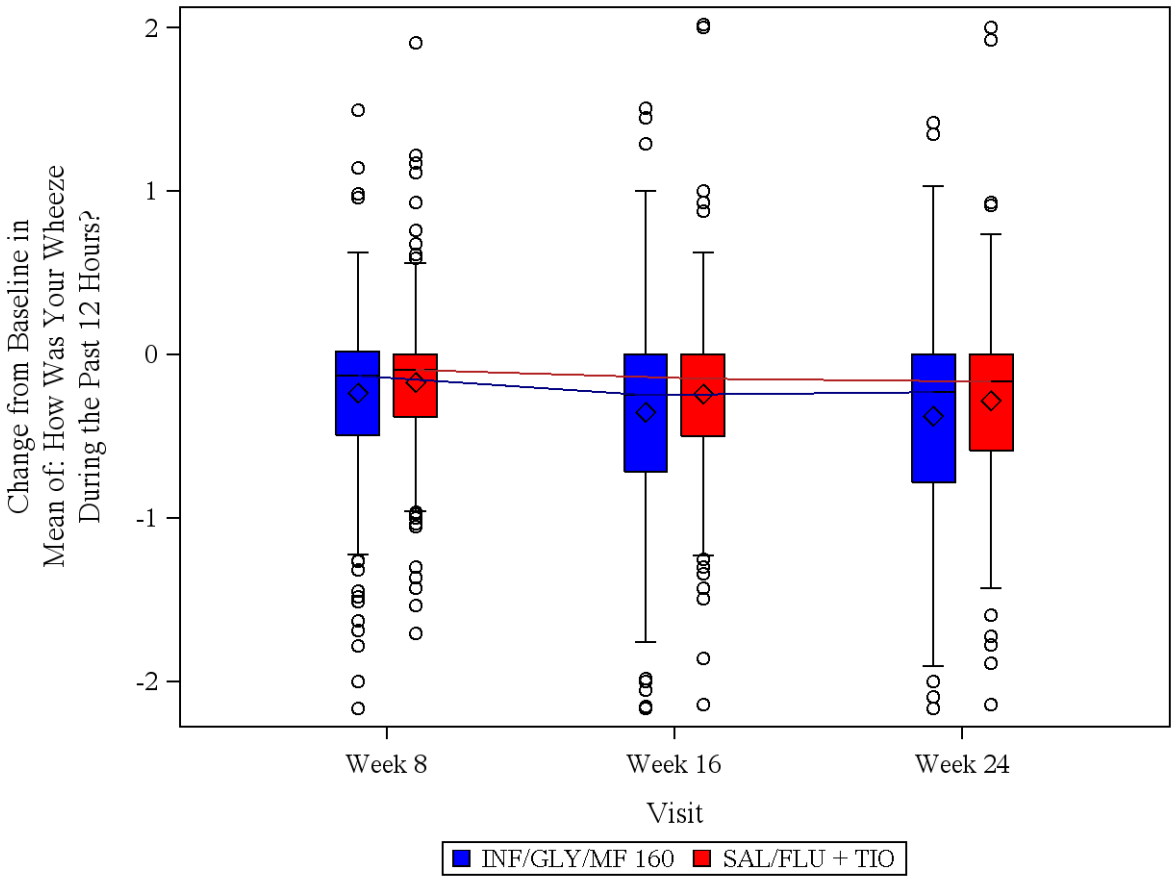
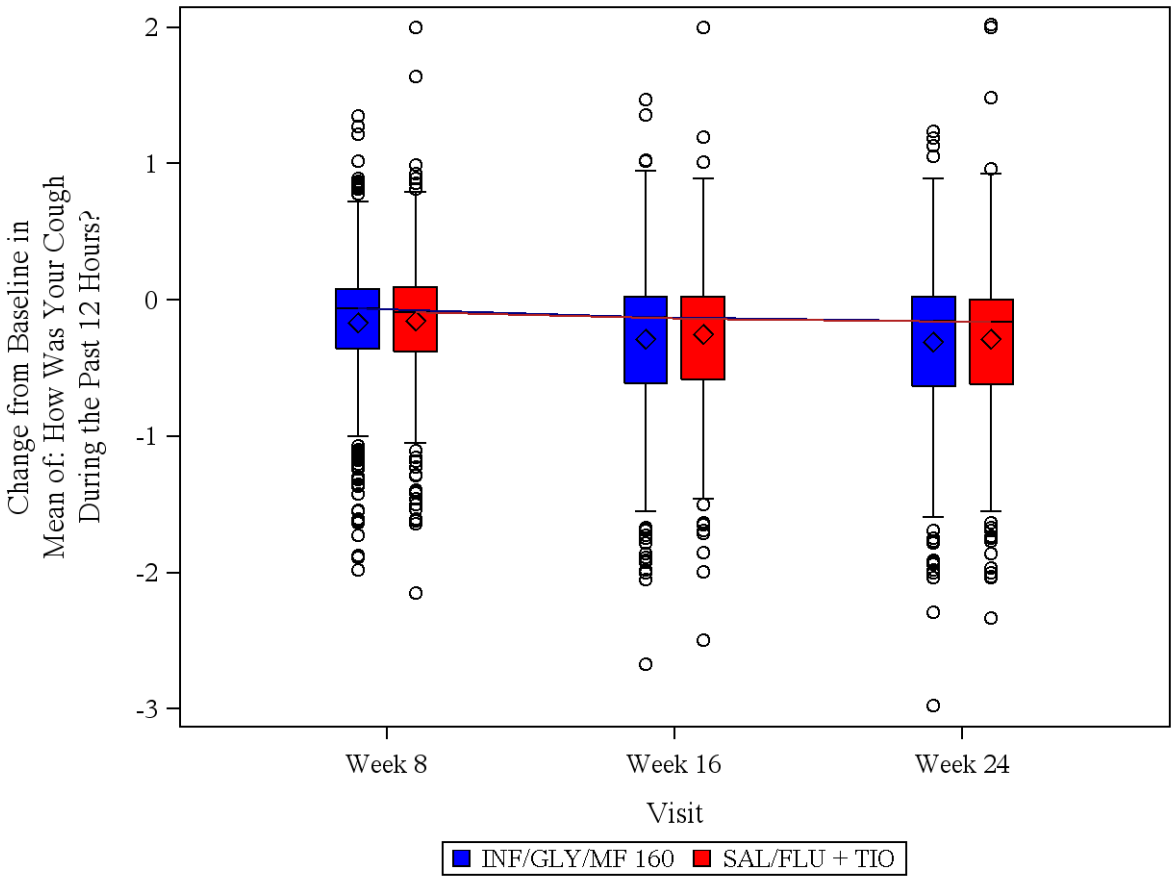


Figure 9.72.2 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



9.73 Boxplot: Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline (FAS)

Figure 9.73 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline (FAS)



9.74 Boxplot: Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Age (FAS)

Figure 9.74.1 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Age (FAS), Age = 18-39 years

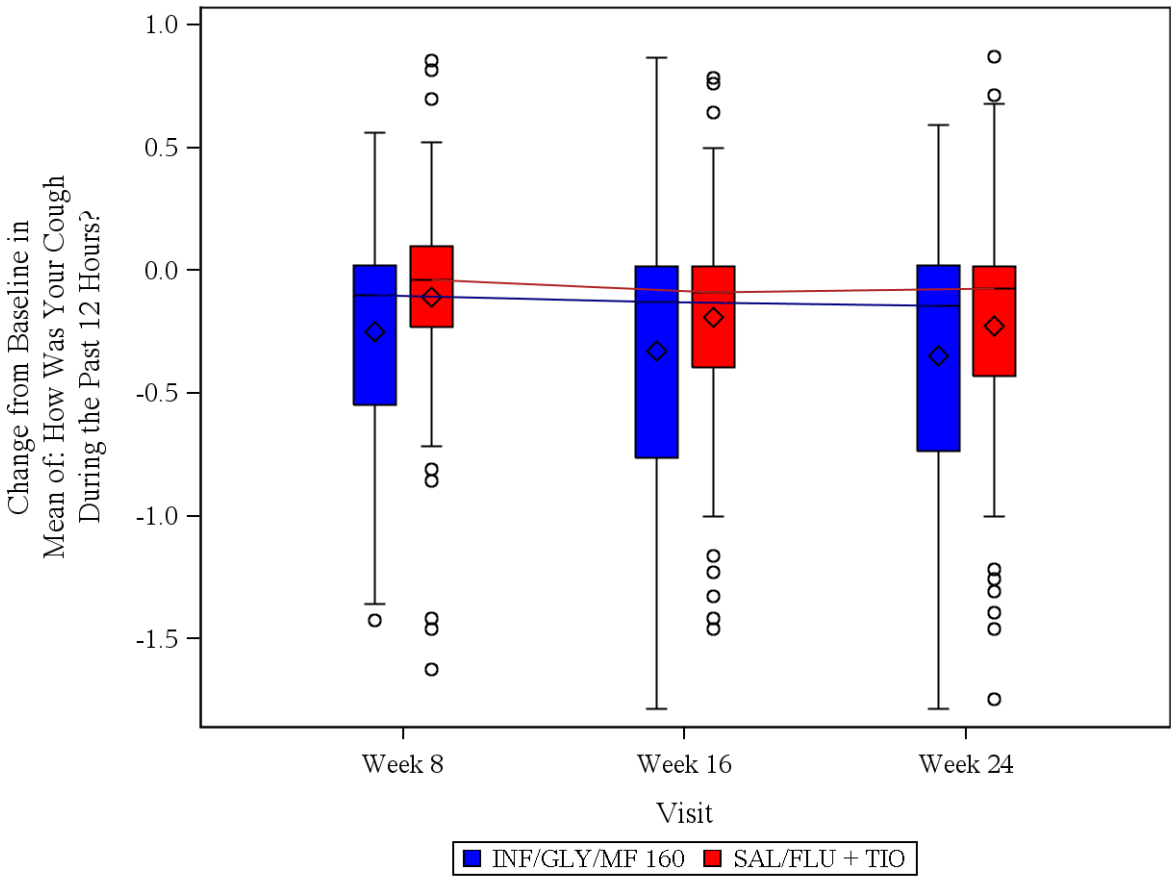


Figure 9.74.2 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Age (FAS), Age = 40-64 years

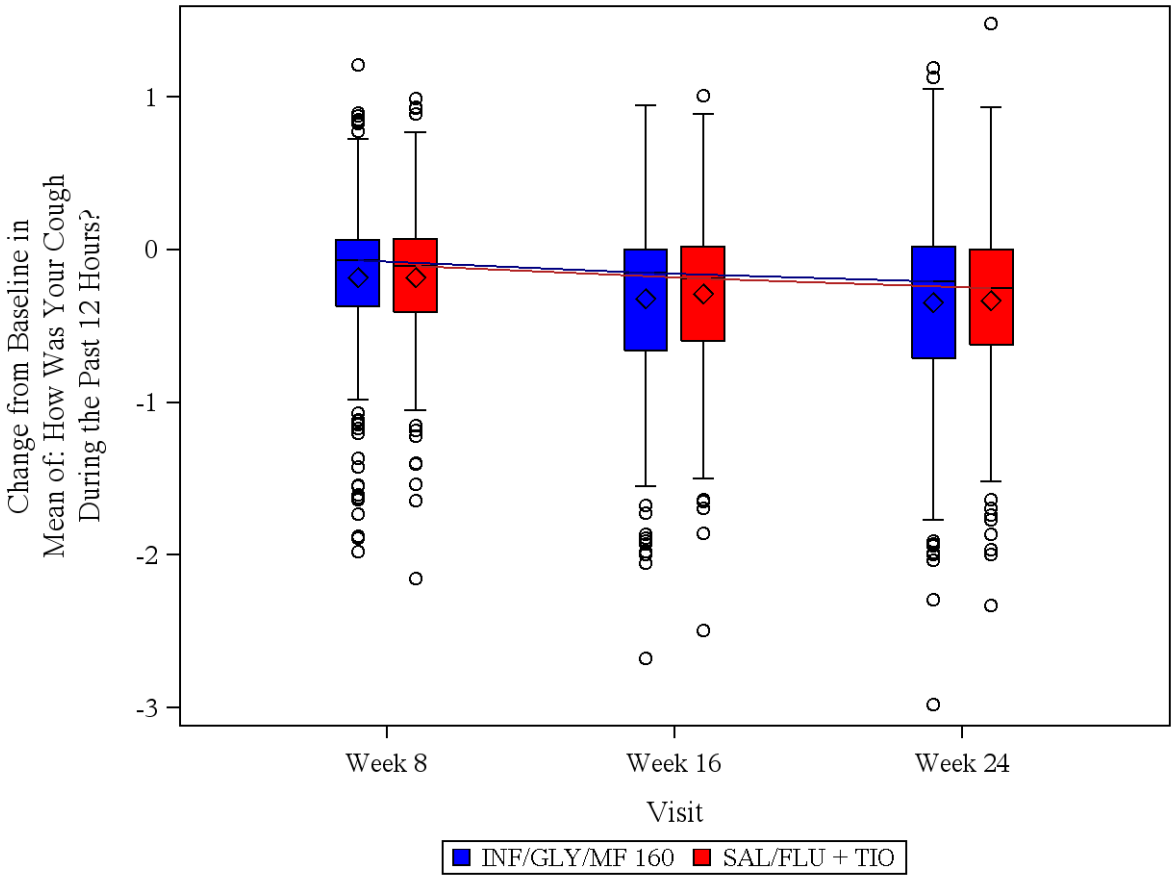
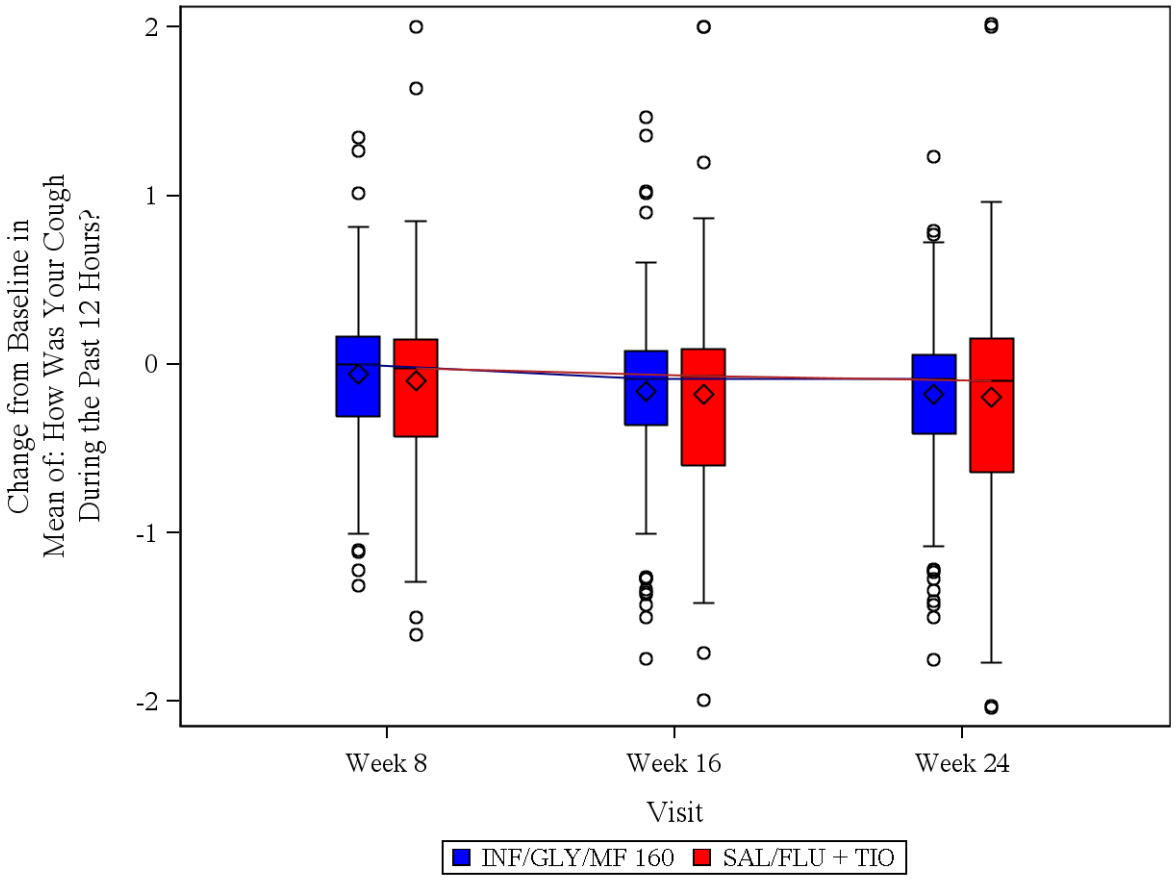


Figure 9.74.3 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Age (FAS), Age = ≥65 years



9.75 Boxplot: Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Gender (FAS)

Figure 9.75.1 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Gender (FAS), Gender = Male

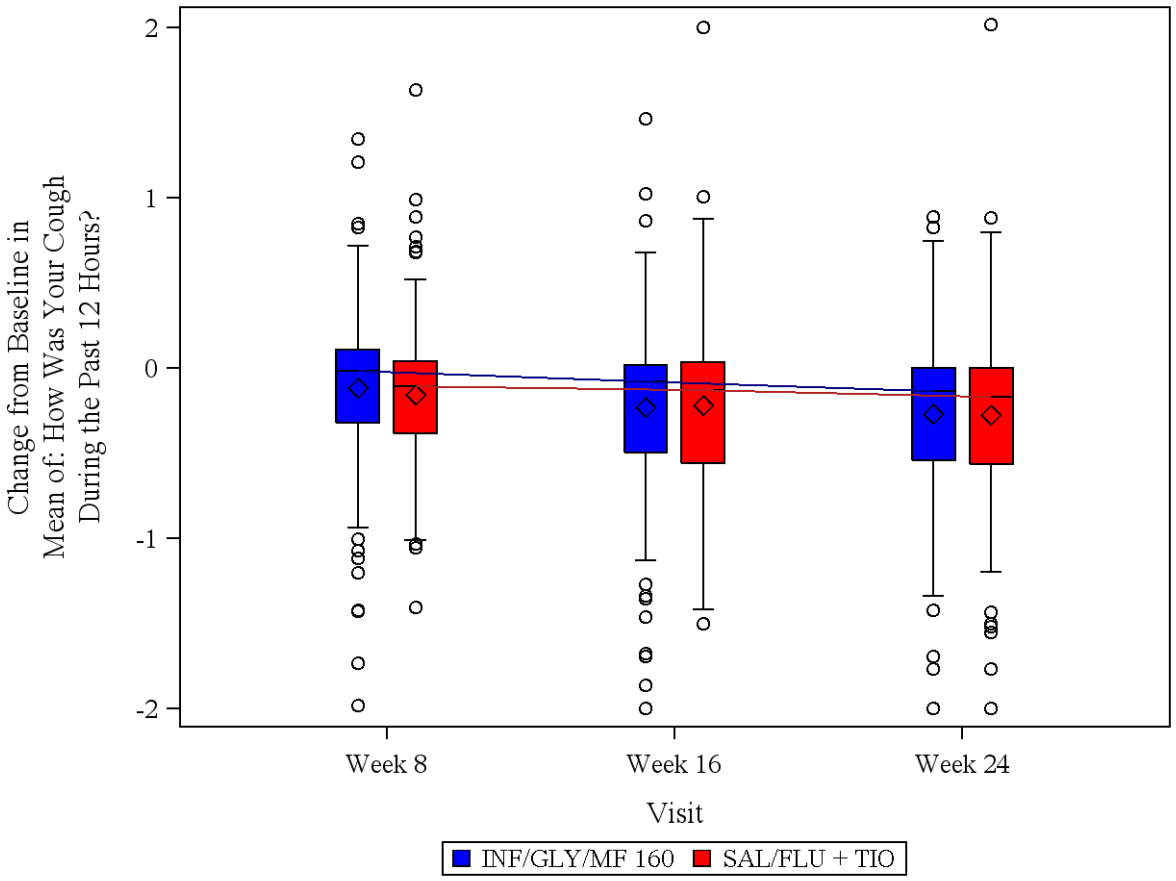
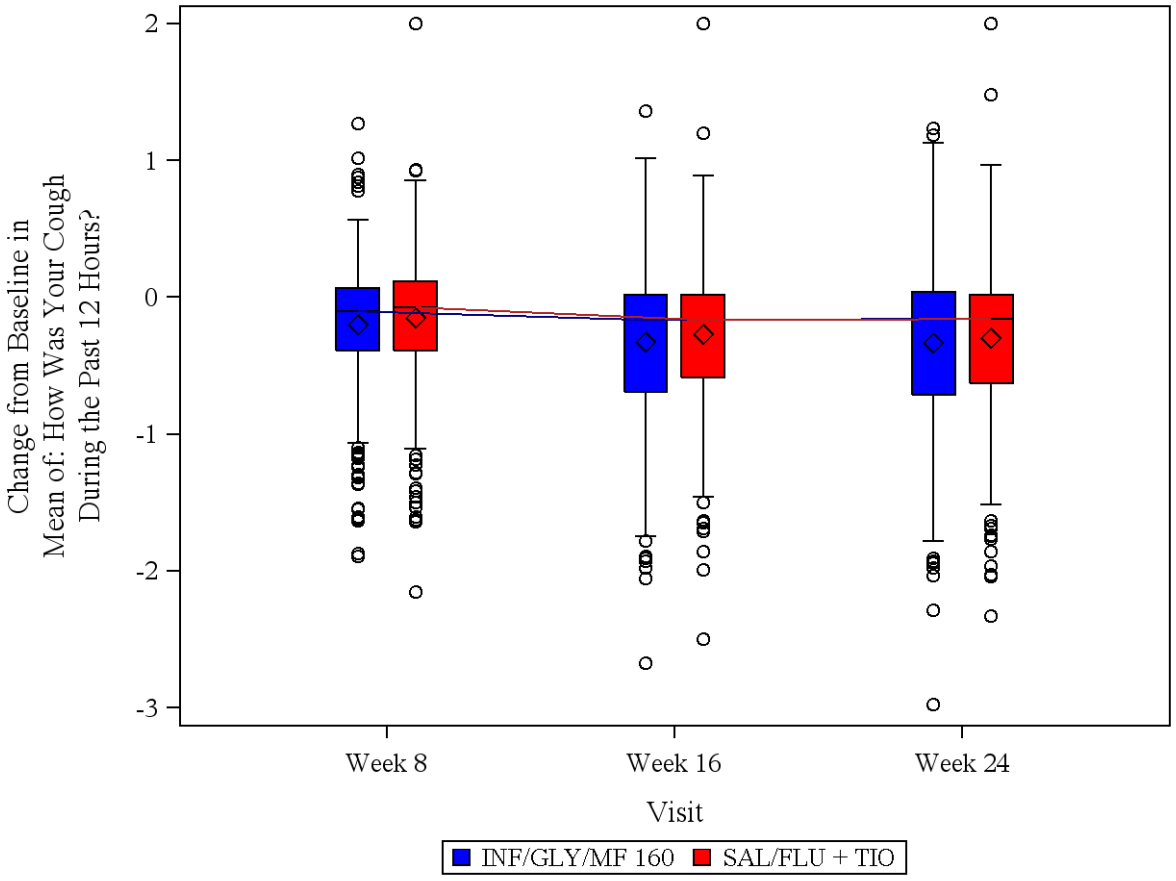


Figure 9.75.2 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Gender (FAS), Gender = Female



9.76 Boxplot: Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Region (FAS)

Figure 9.76.1 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Asia

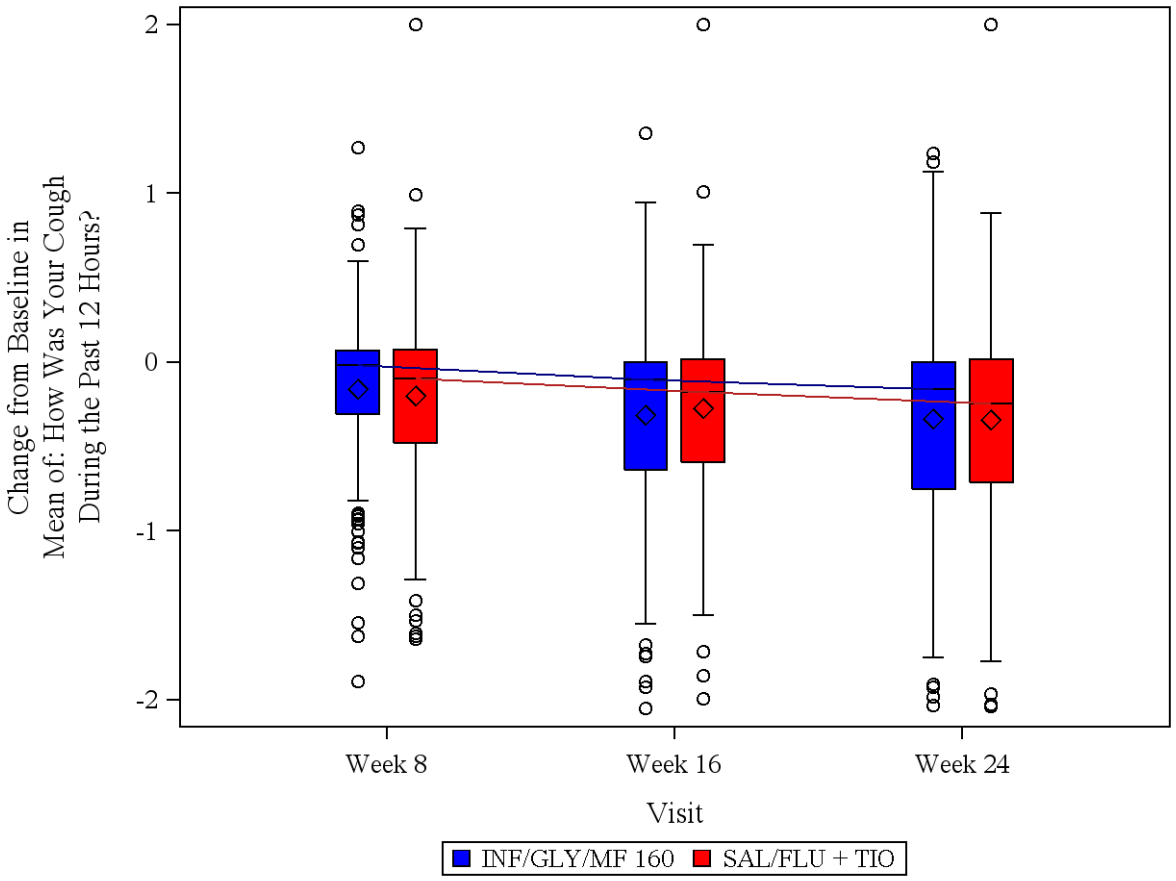


Figure 9.76.2 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Europe

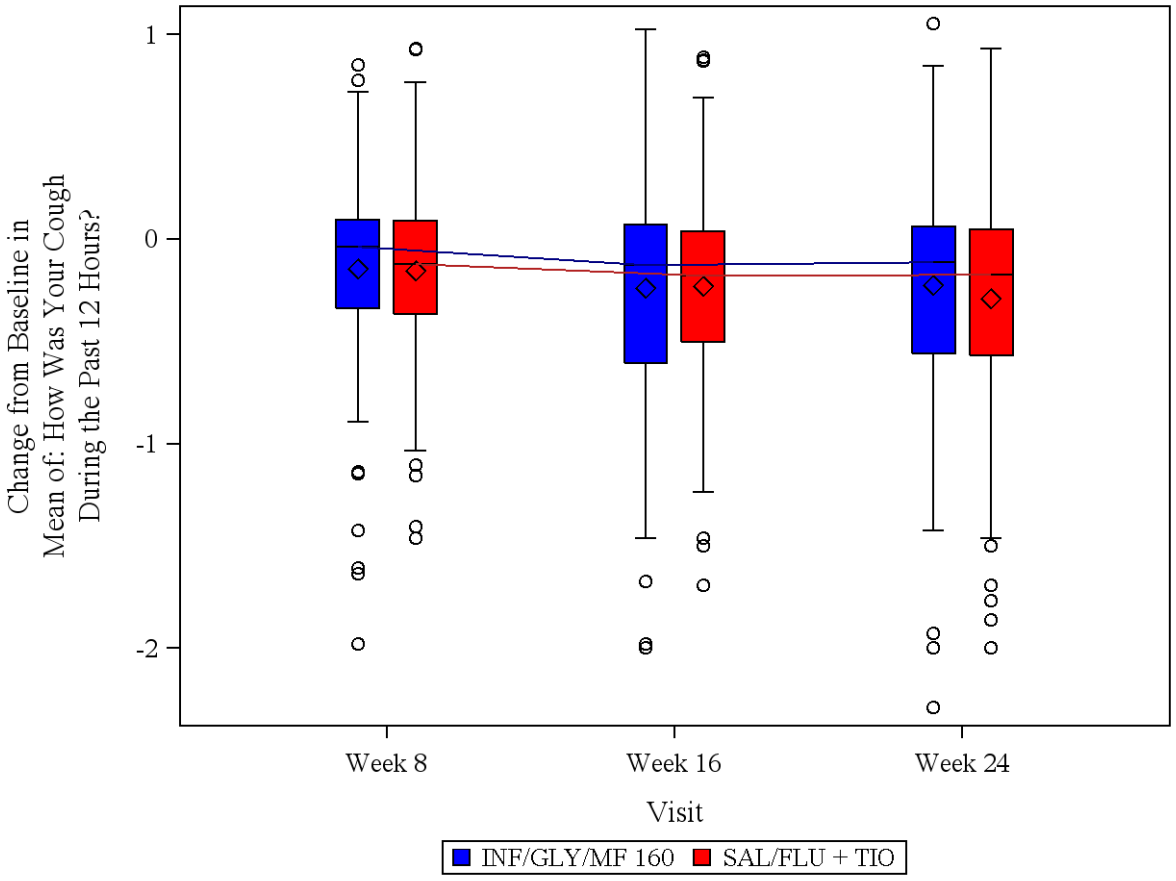


Figure 9.76.3 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Latin America

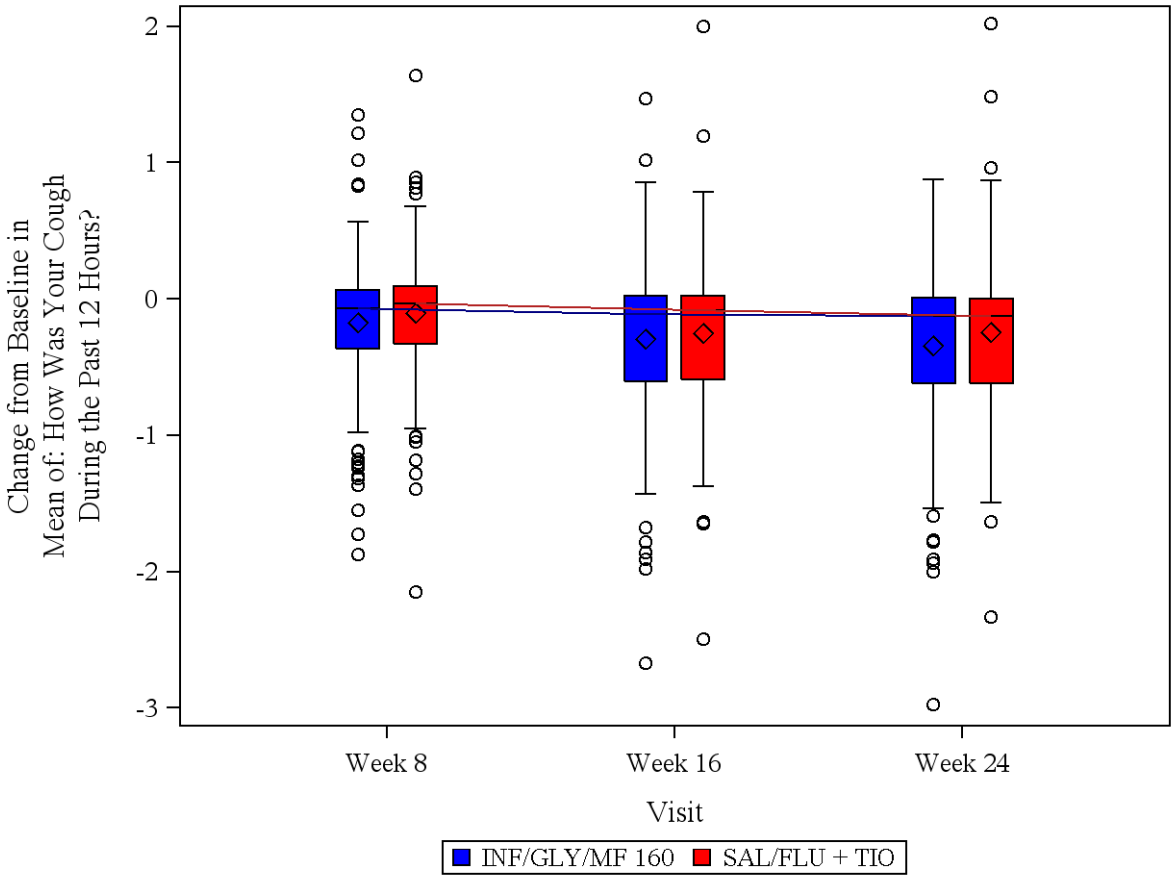
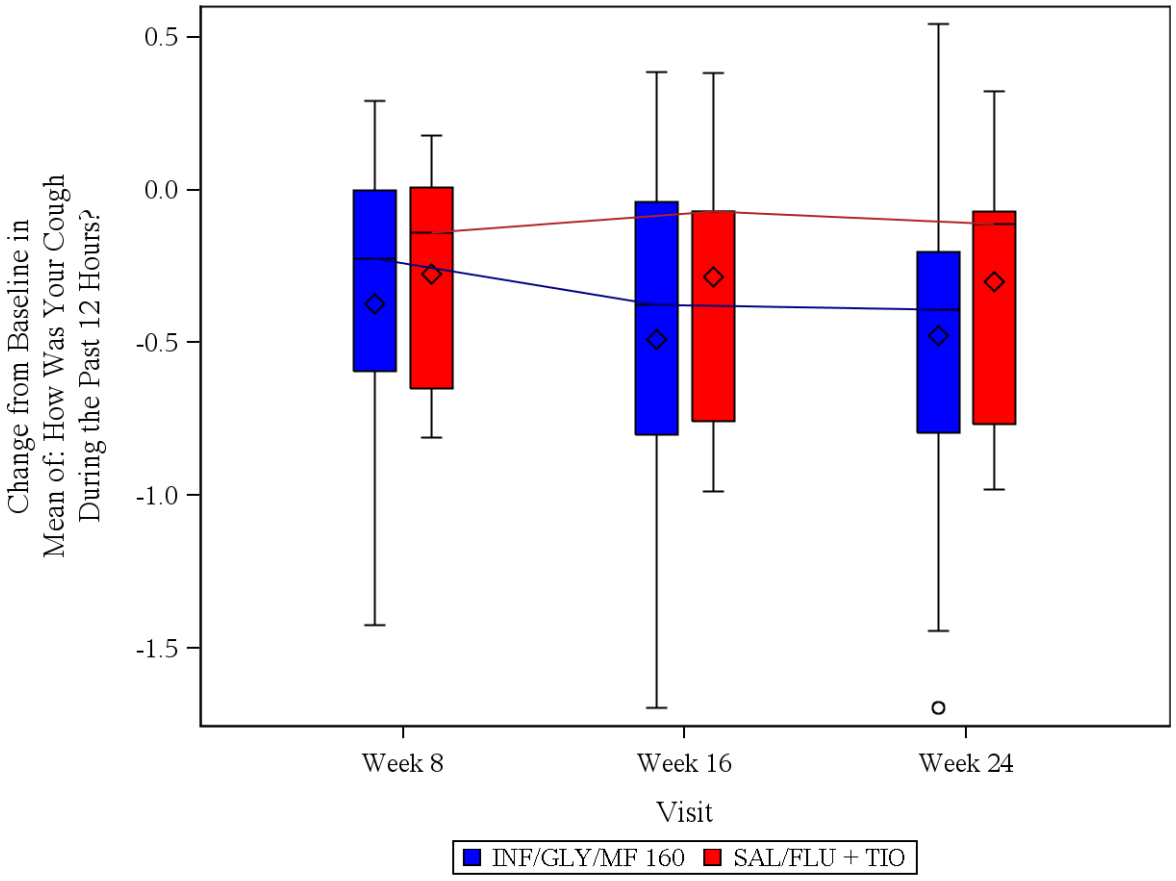


Figure 9.76.4 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Others



9.77 Boxplot: Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 9.77.1 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

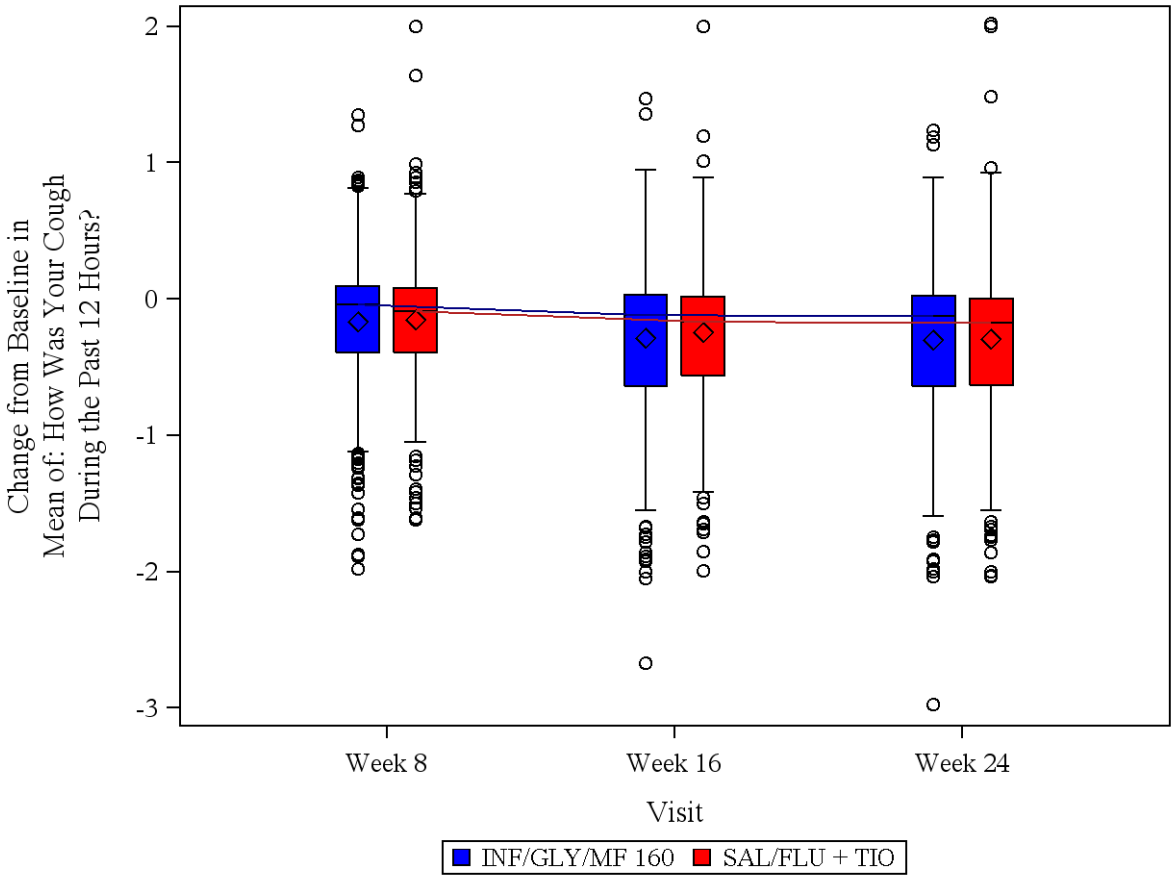
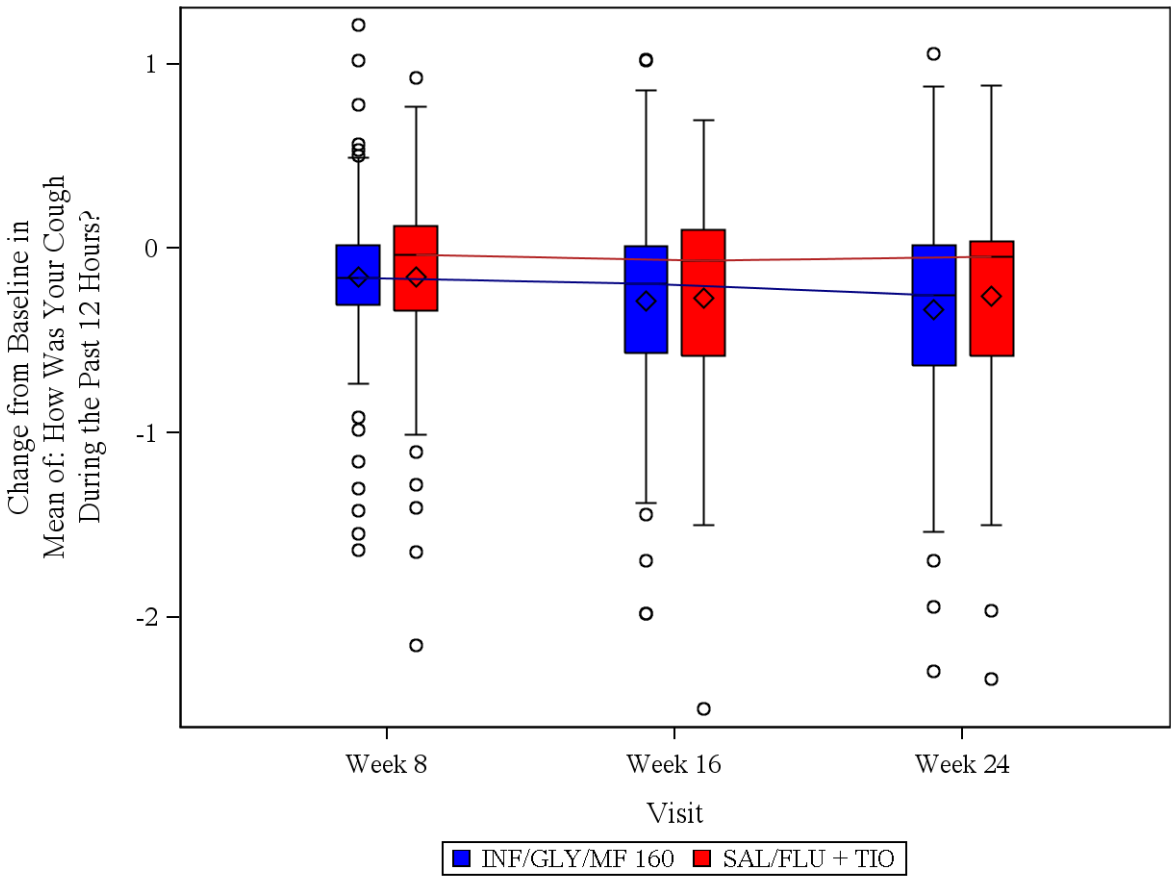


Figure 9.77.2 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.78 Boxplot: Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 9.78.1 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

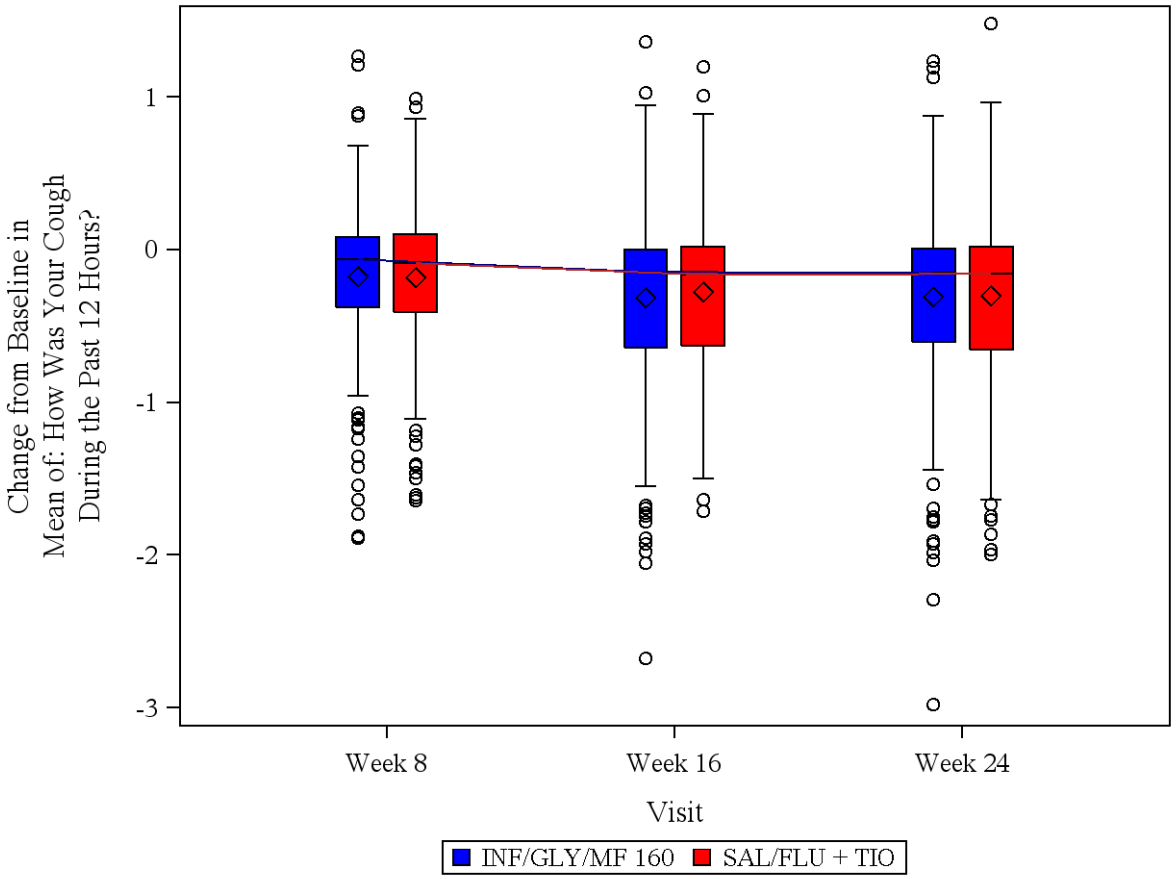
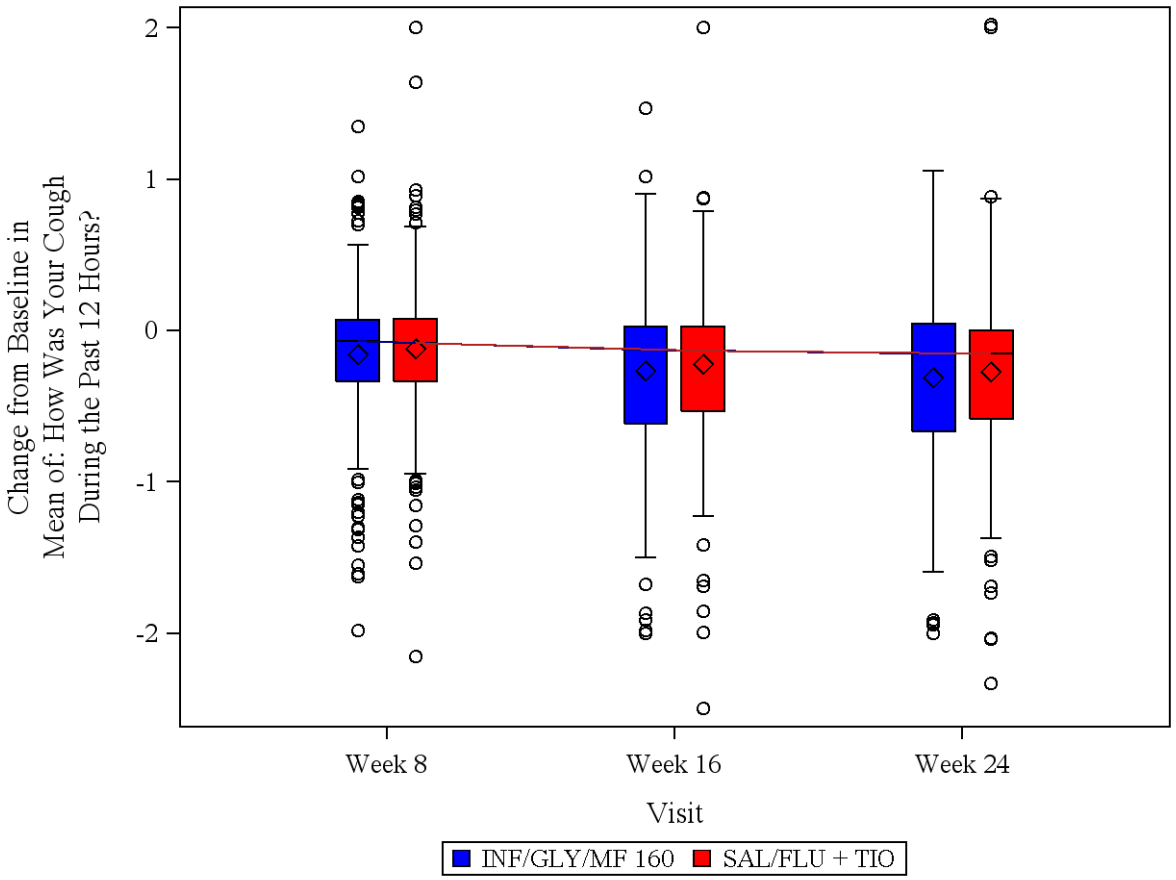
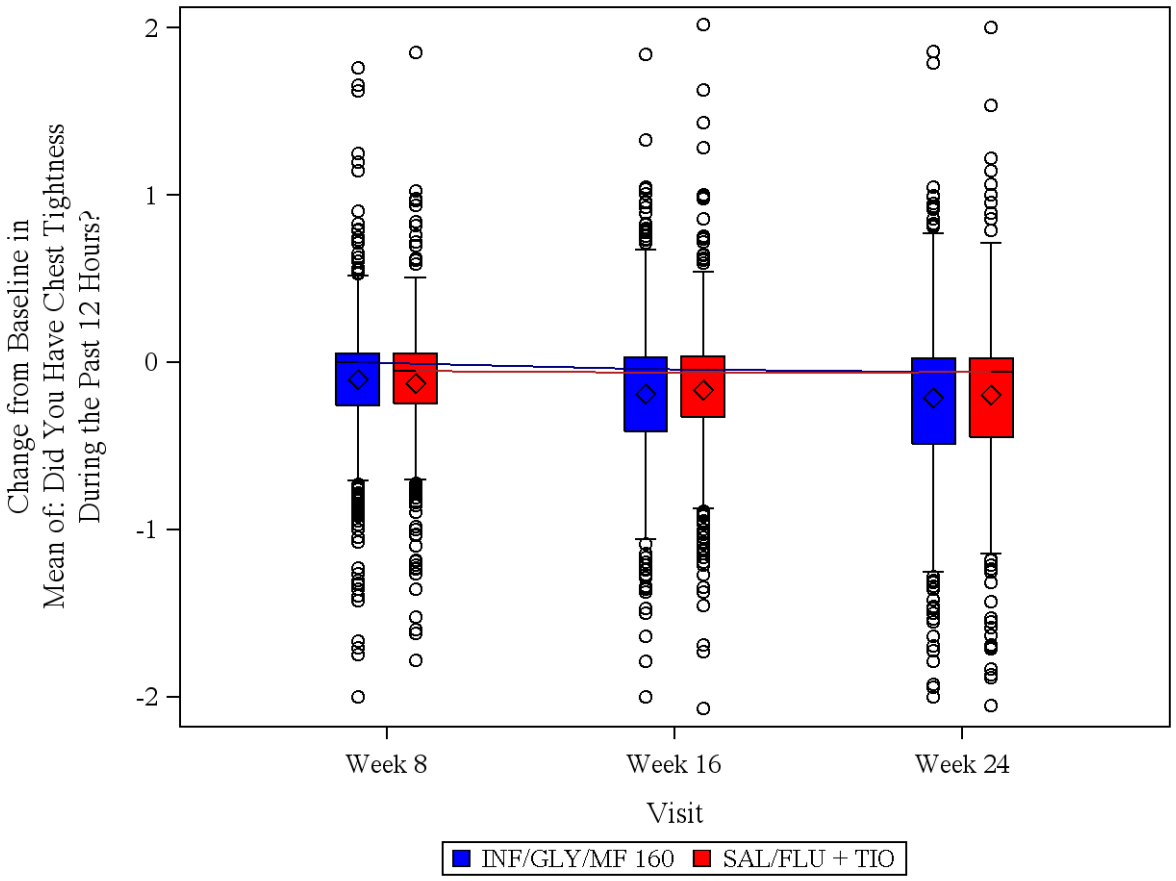


Figure 9.78.2 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



9.79 Boxplot: Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline (FAS)

Figure 9.79 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline (FAS)



9.80 Boxplot: Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Age (FAS)

Figure 9.80.1 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Age (FAS), Age = 18-39 years

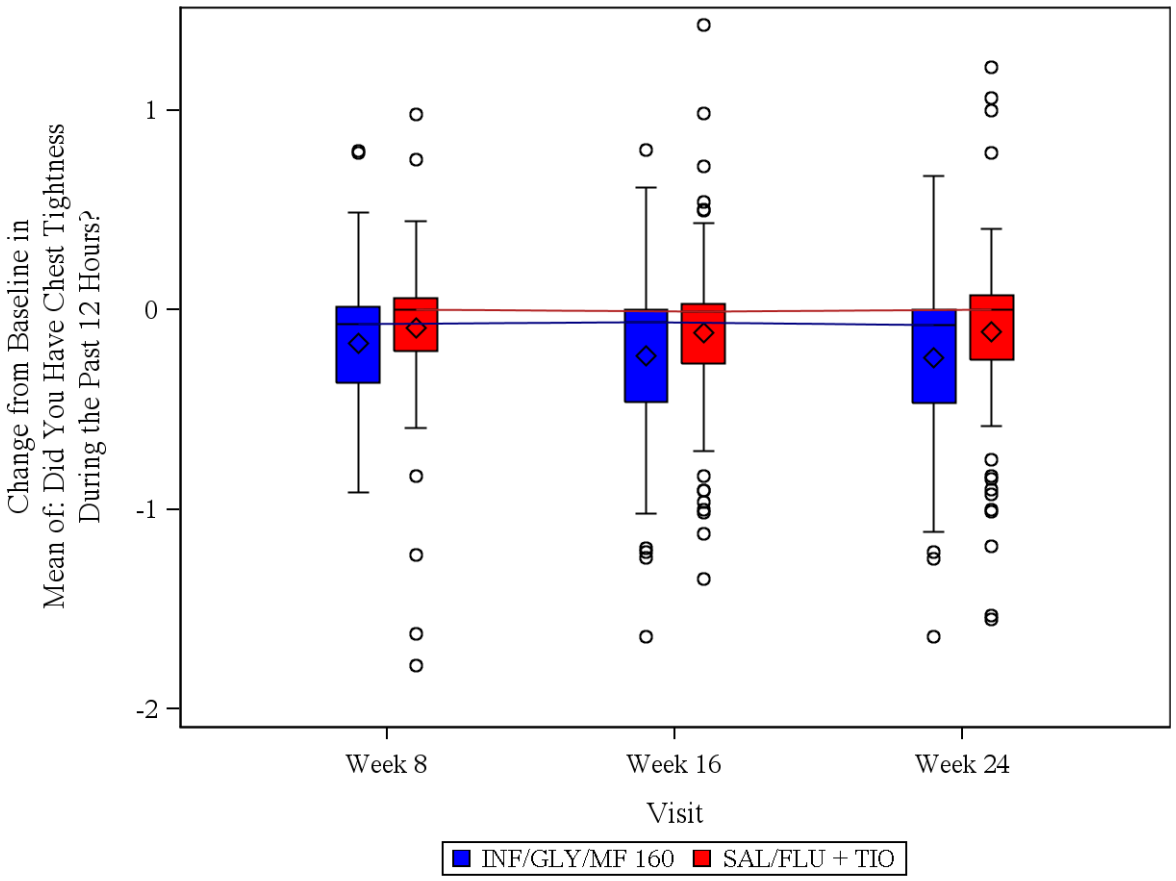


Figure 9.80.2 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Age (FAS), Age = 40-64 years

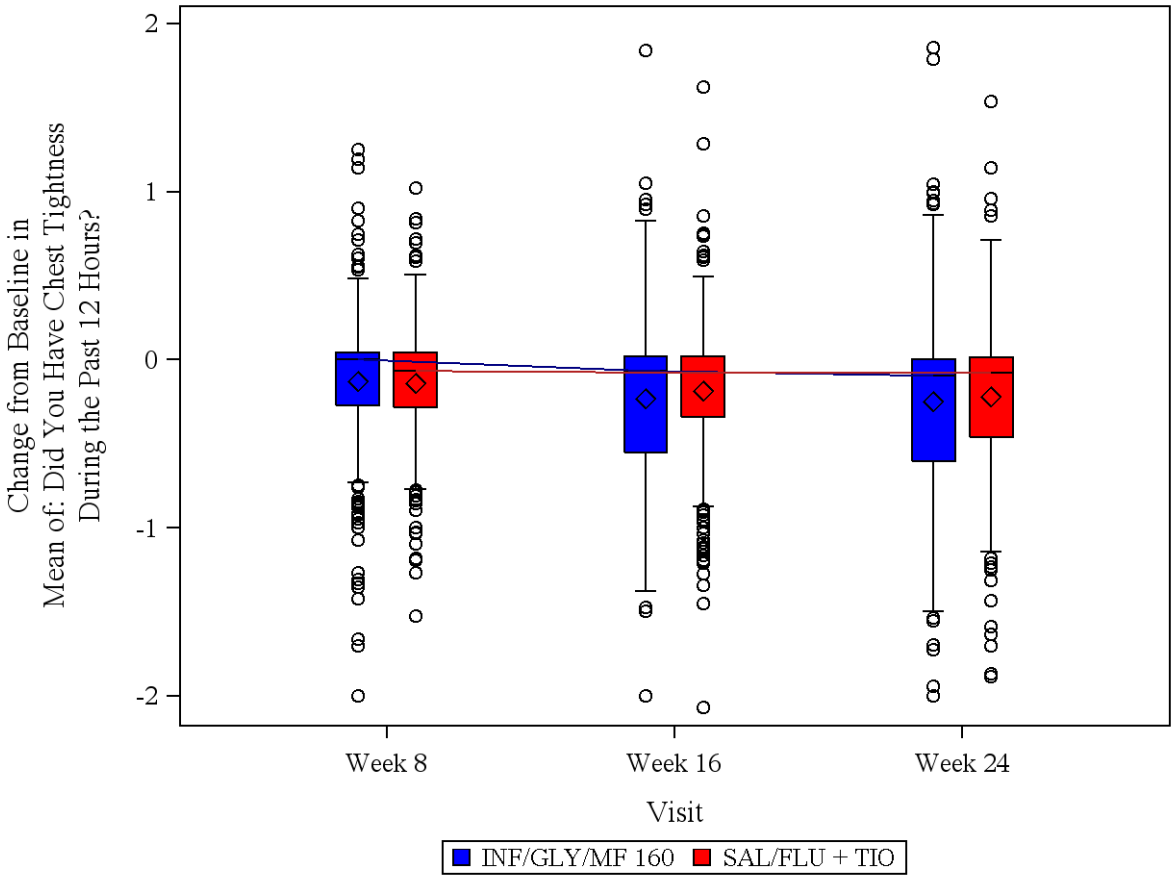
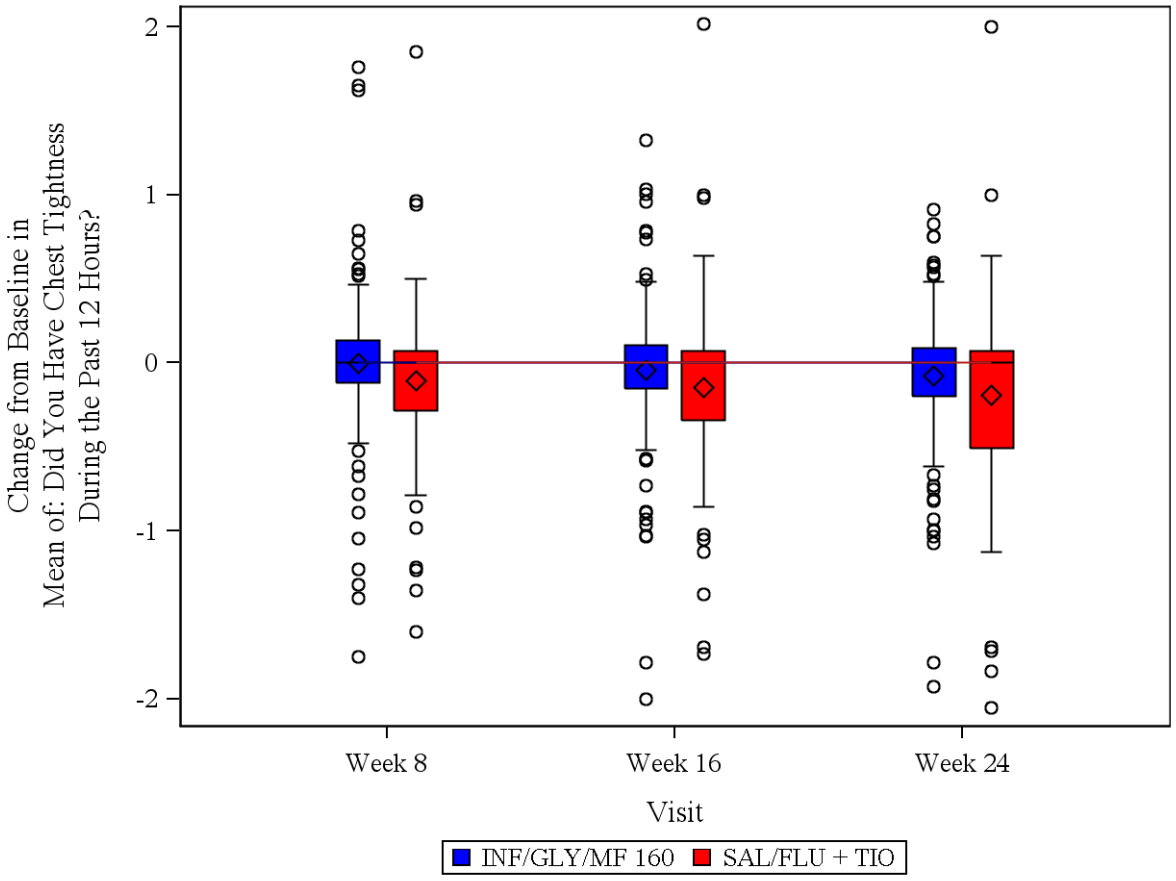


Figure 9.80.3 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Age (FAS), Age = ≥65 years



9.81 Boxplot: Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Gender (FAS)

Figure 9.81.1 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Gender (FAS), Gender = Male

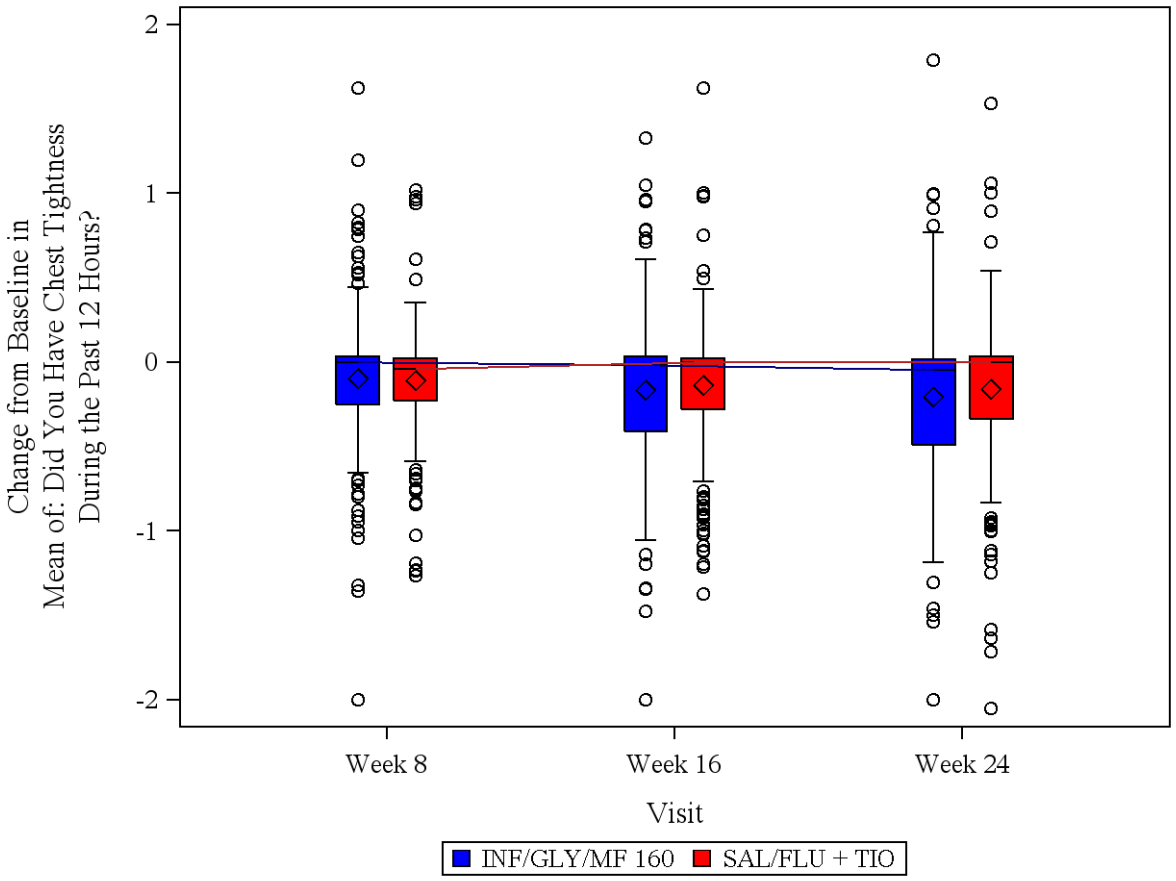
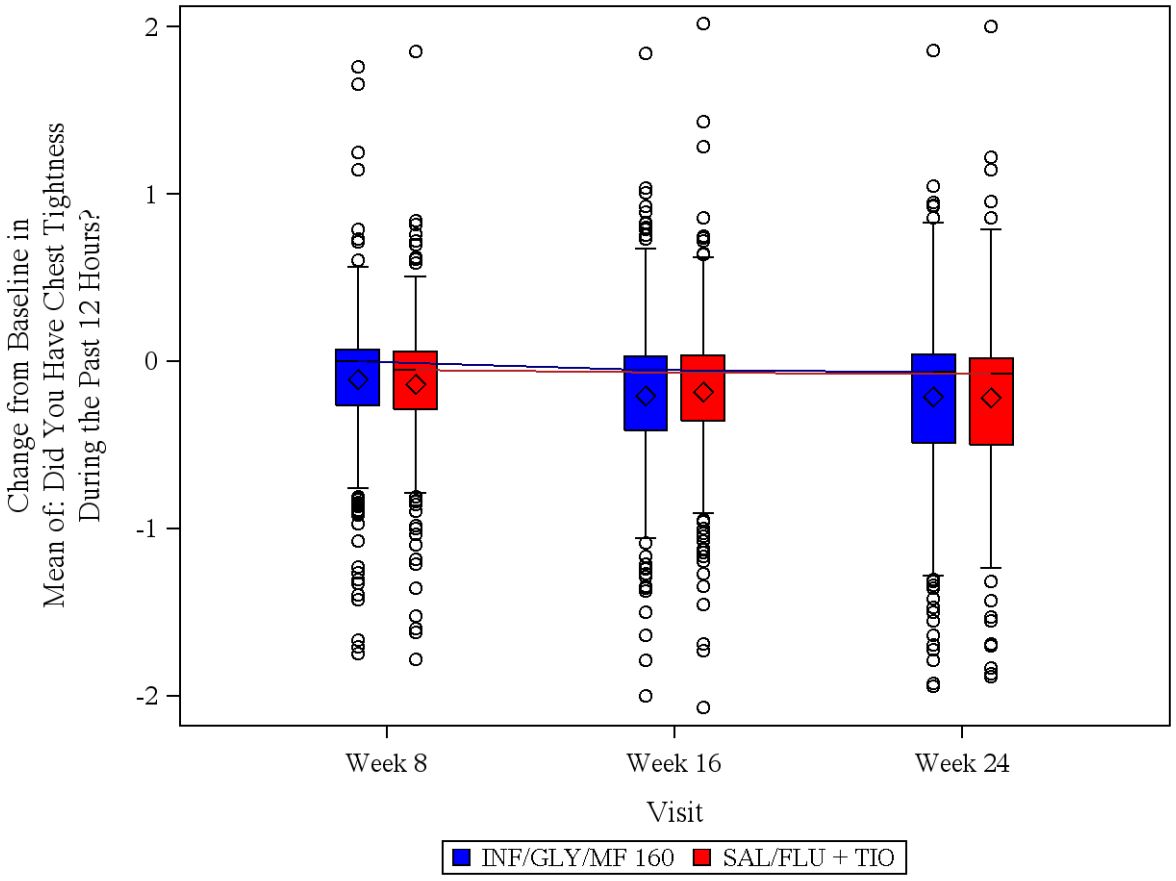


Figure 9.81.2 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Gender (FAS), Gender = Female



9.82 Boxplot: Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Region (FAS)

Figure 9.82.1 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Asia

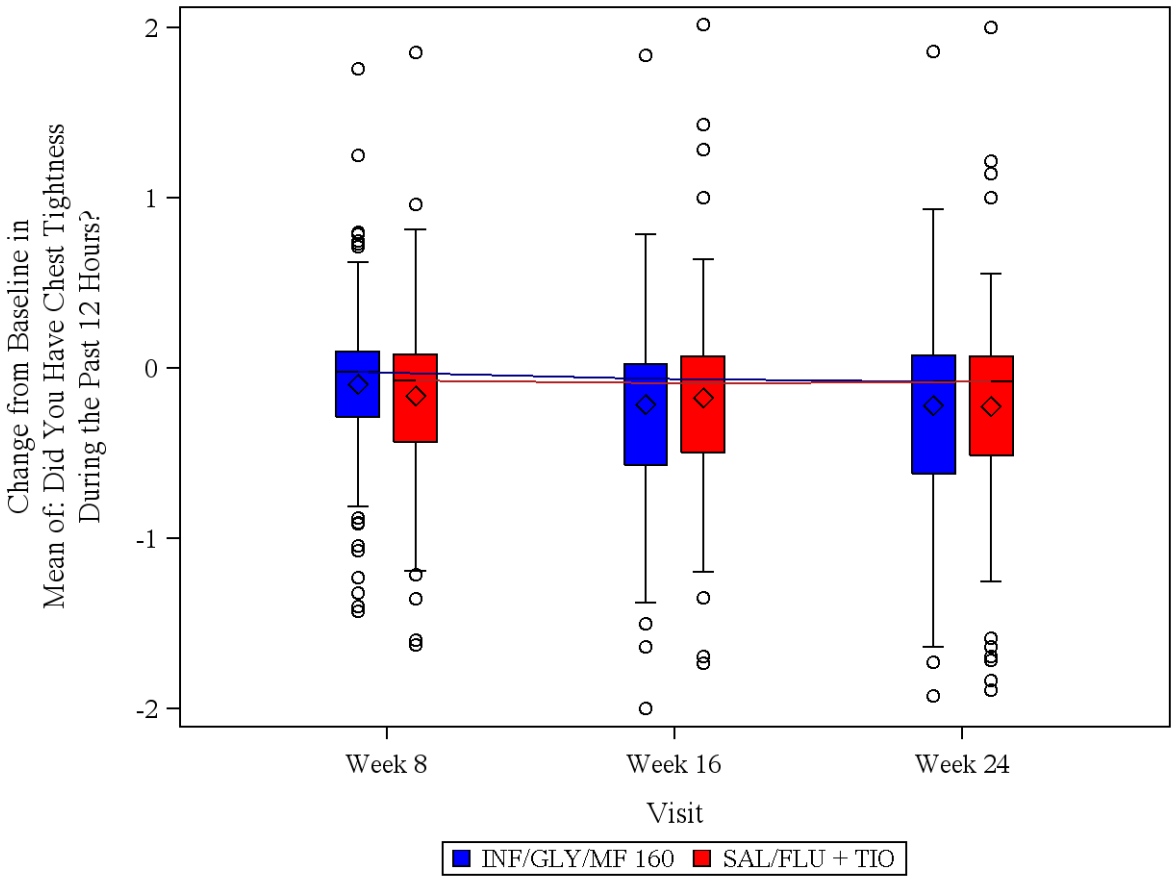


Figure 9.82.2 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Europe

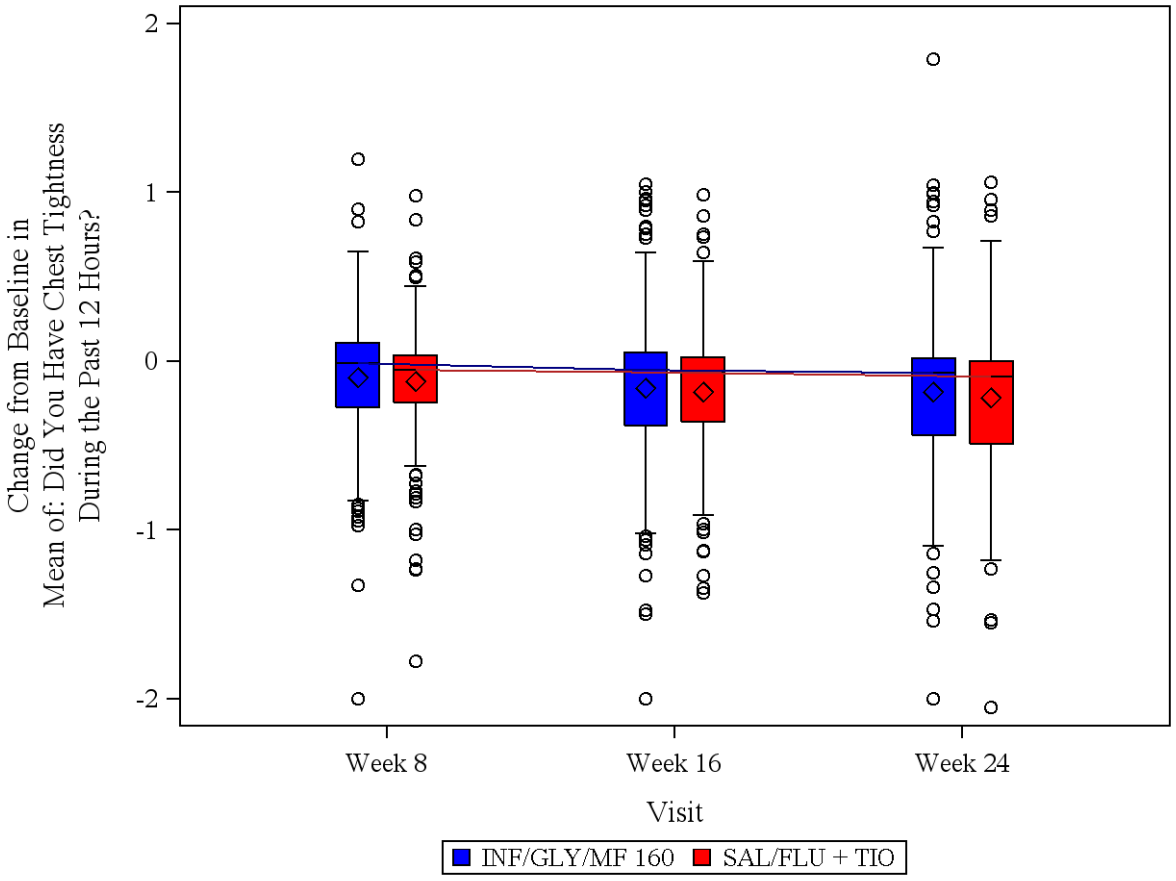


Figure 9.82.3 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Latin America

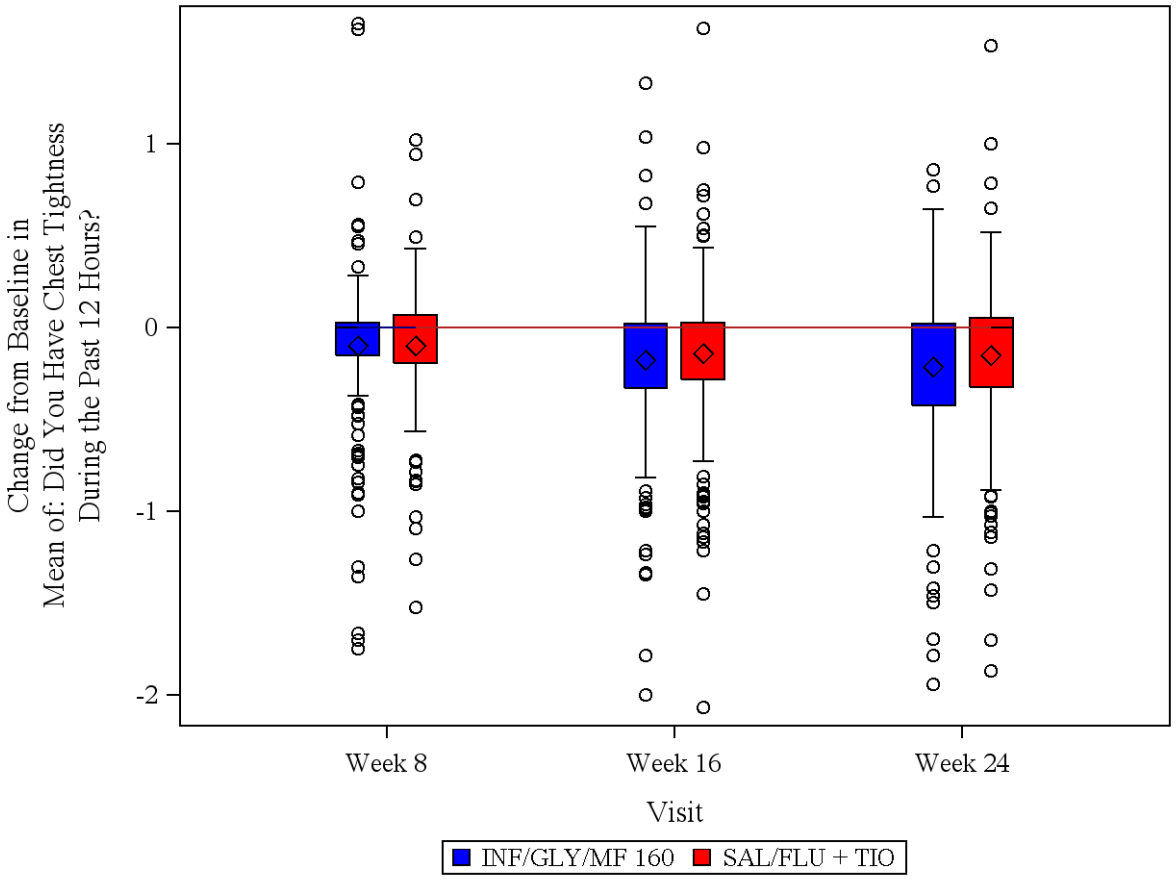
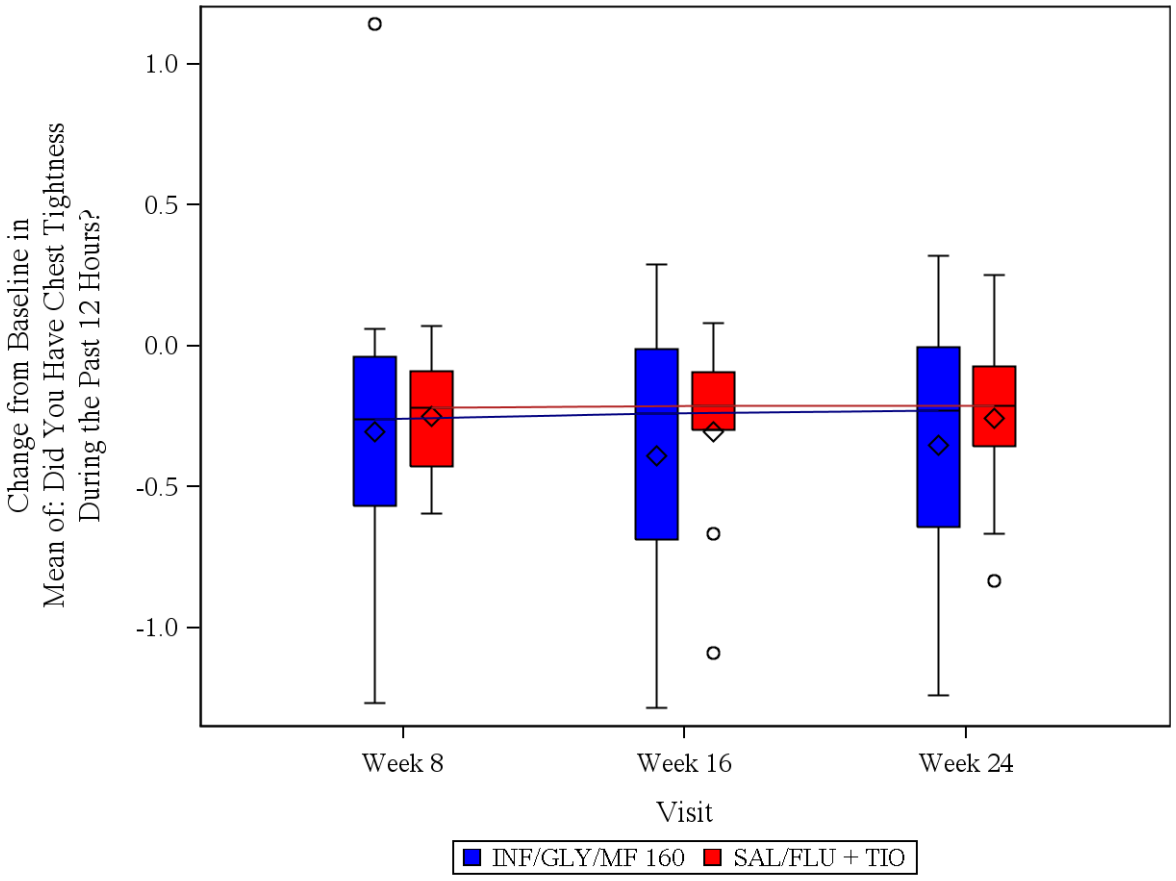


Figure 9.82.4 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Others



9.83 Boxplot: Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 9.83.1 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

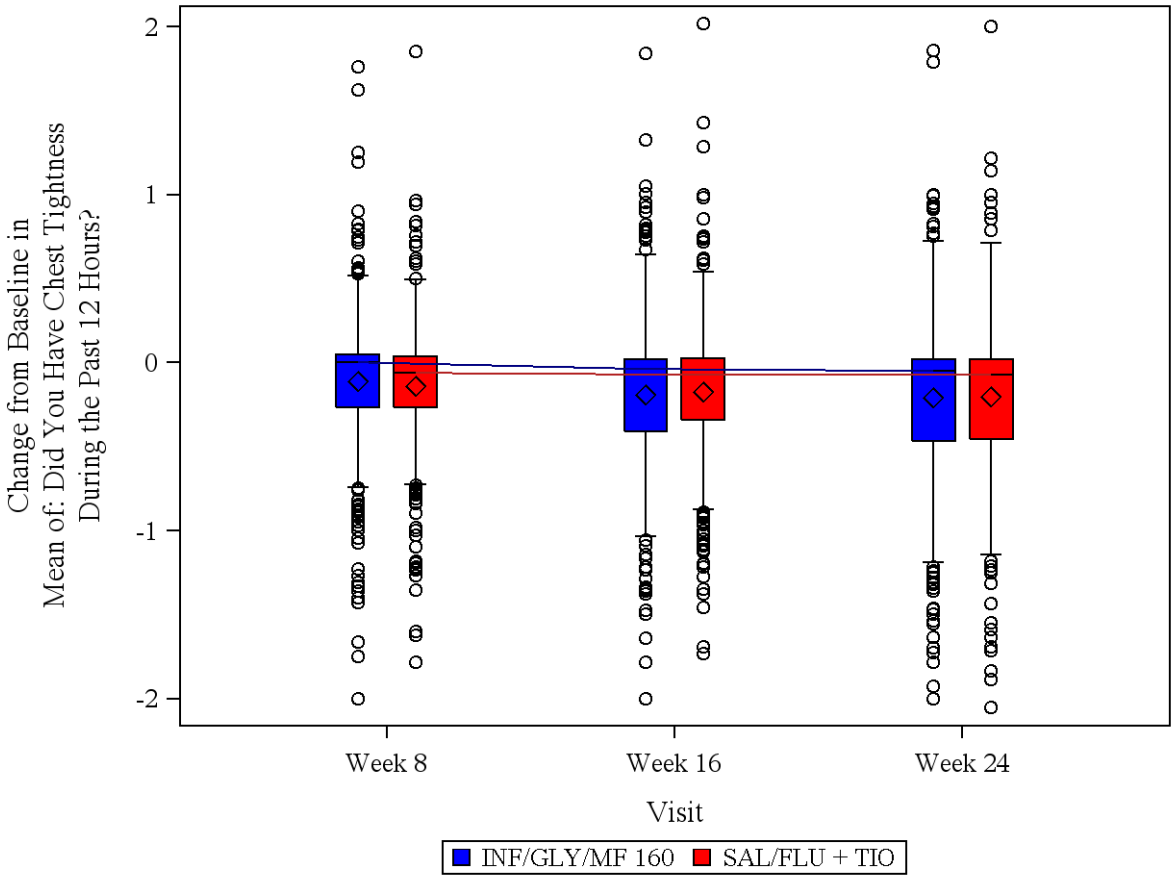
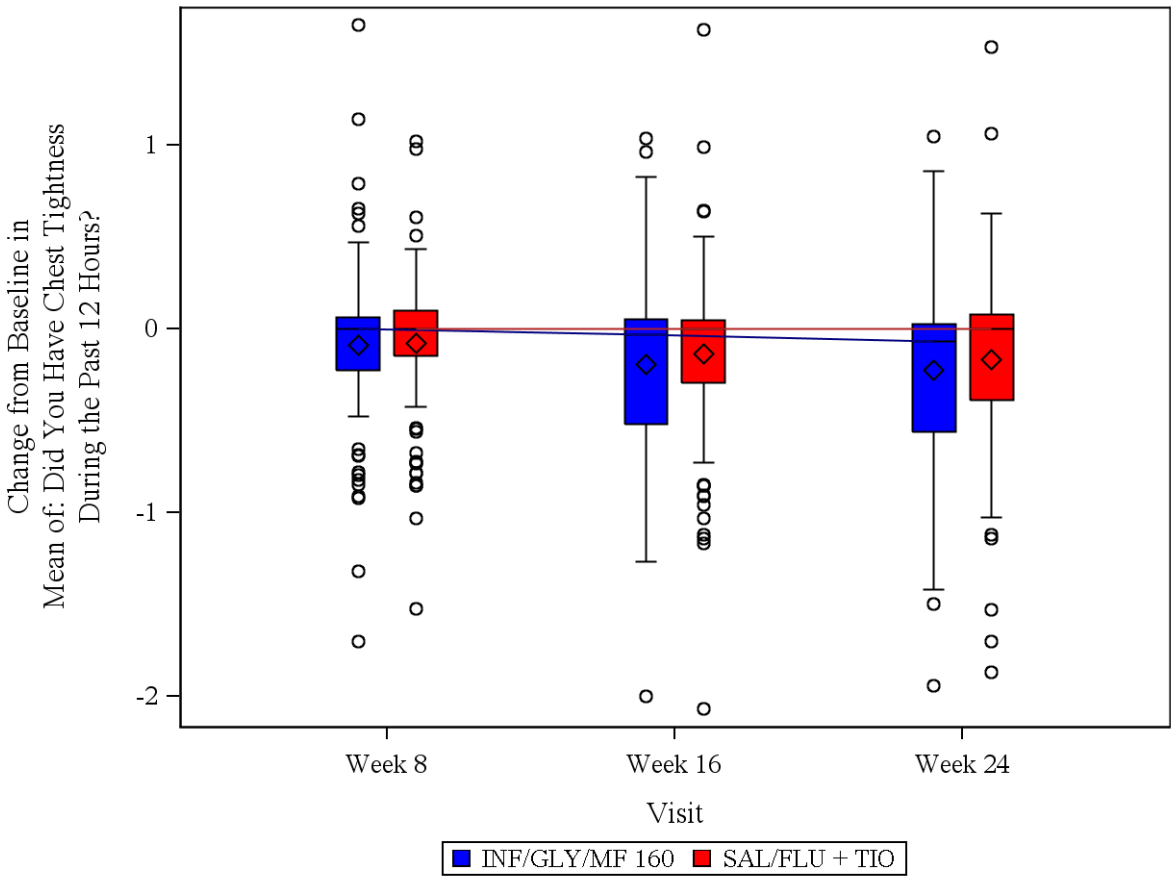


Figure 9.83.2 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.84 Boxplot: Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 9.84.1 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

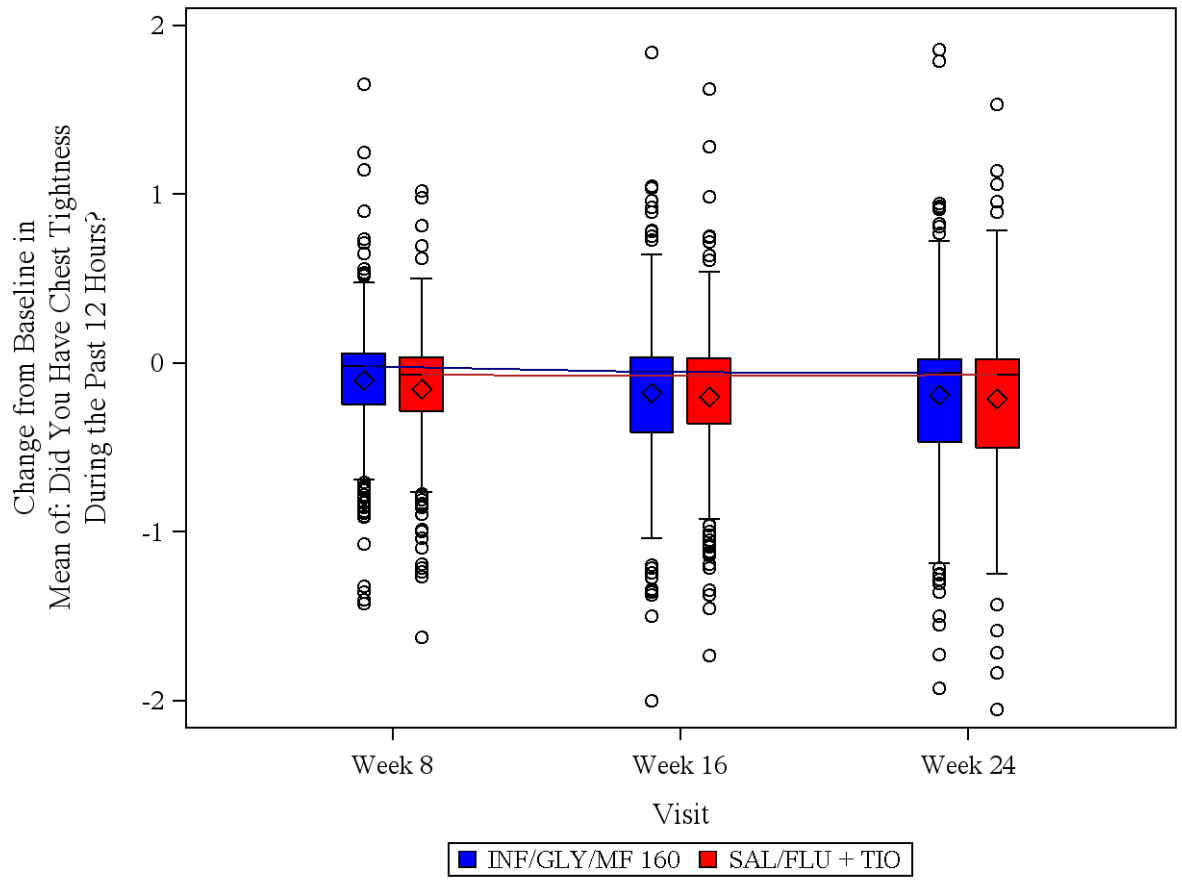
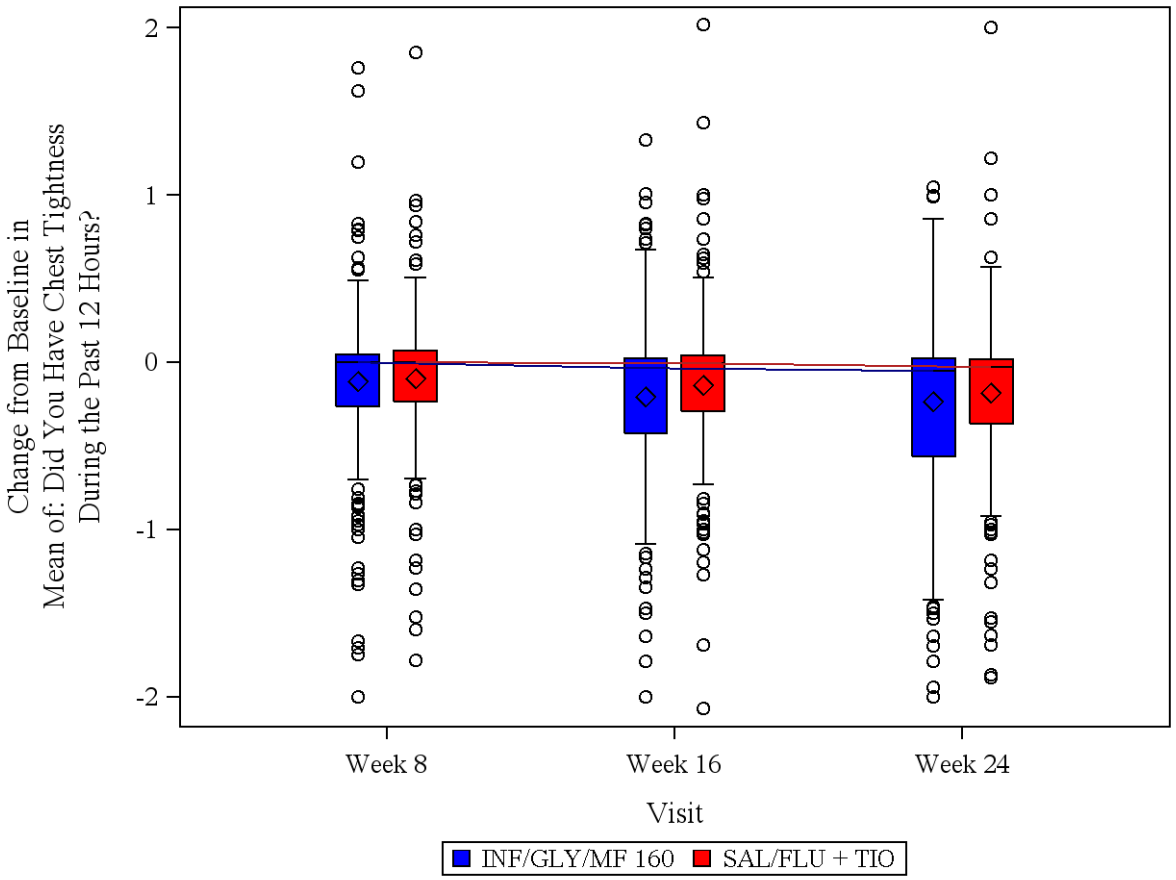


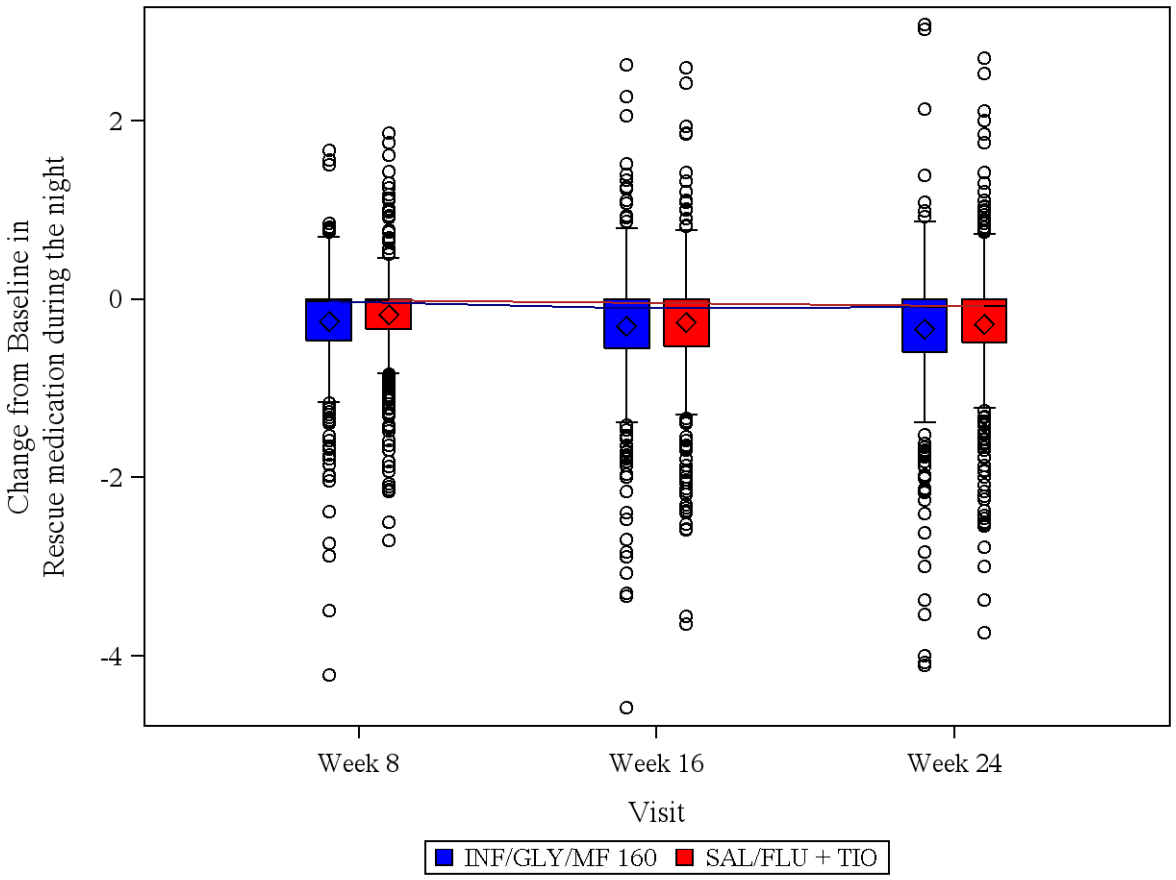
Figure 9.84.2 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



10. Boxplot: Rescue Medication Change from Baseline (FAS)

10.1 Boxplot: Rescue Medication (Rescue medication during the night) - Change from Baseline (FAS)

Figure 5.1 Rescue Medication (Rescue medication during the night) - Change from Baseline (FAS)



10.2 Boxplot: Rescue Medication (Rescue medication during the night) - Change from Baseline by Age (FAS)

Figure 5.2.1 Rescue Medication (Rescue medication during the night) - Change from Baseline by Age (FAS), Age = 18-39 years

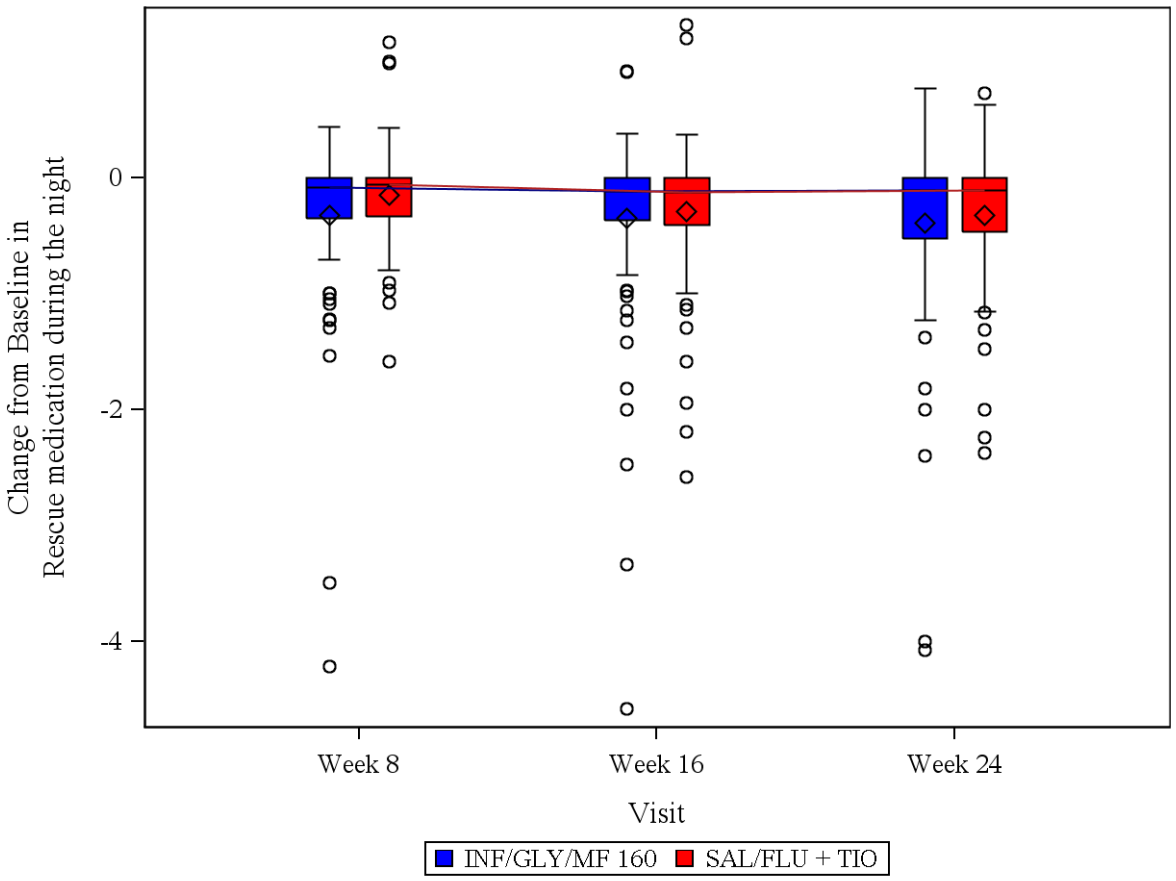


Figure 5.2.2 Rescue Medication (Rescue medication during the night) - Change from Baseline by Age (FAS), Age = 40-64 years

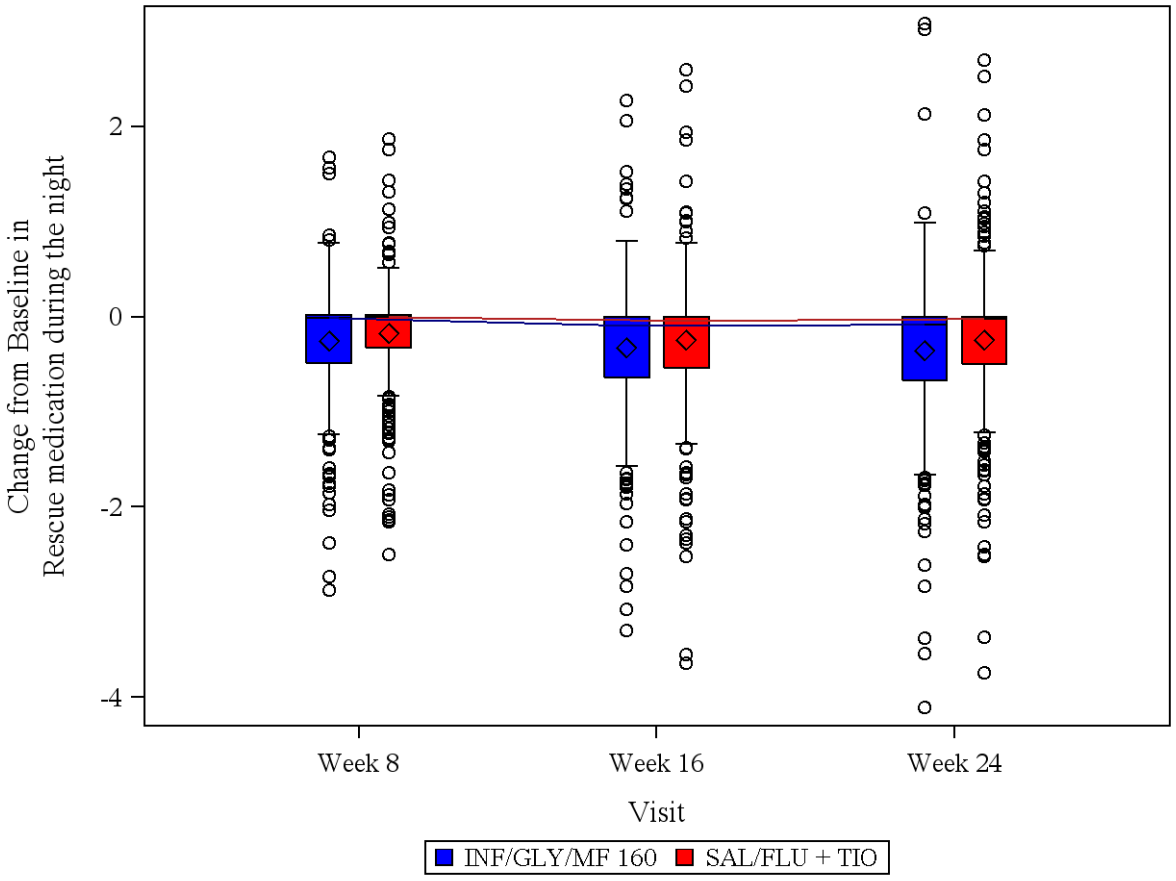
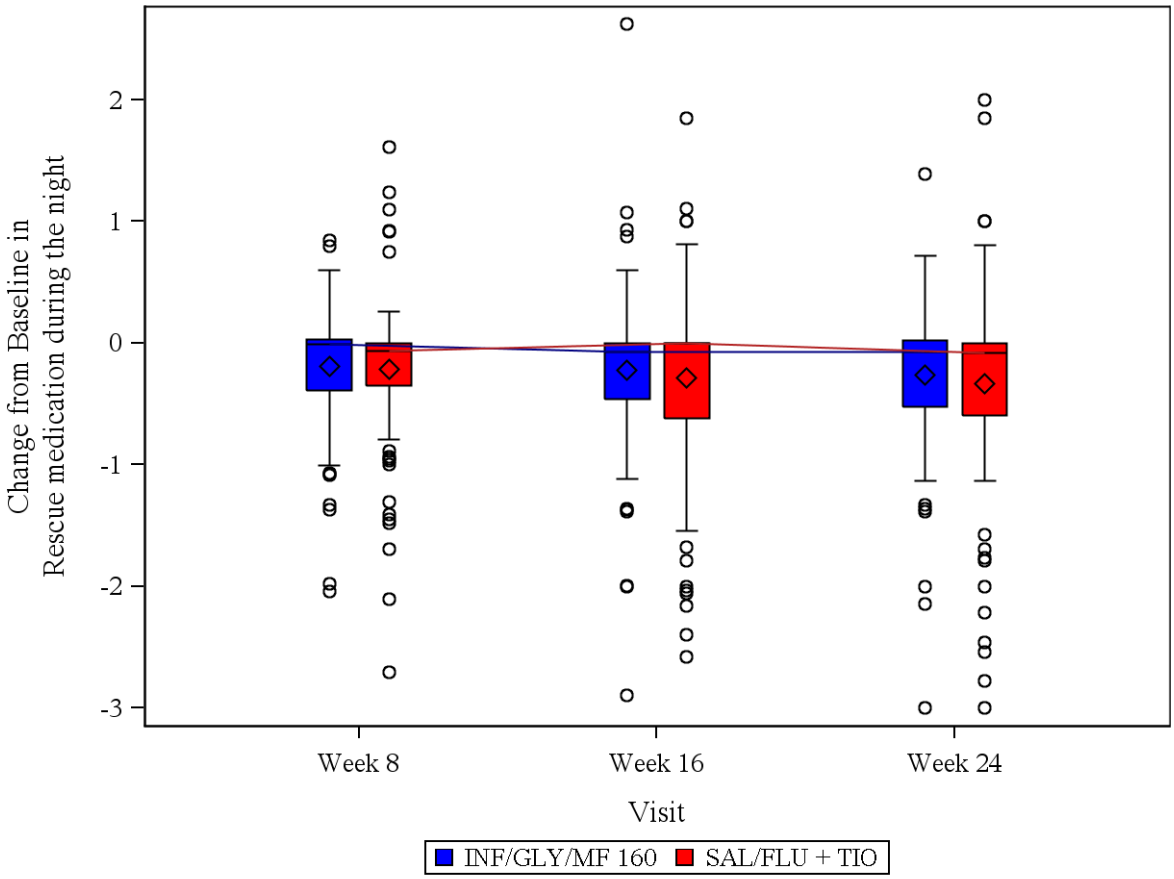


Figure 5.2.3 Rescue Medication (Rescue medication during the night) - Change from Baseline by Age (FAS), Age = ≥65 years



10.3 Boxplot: Rescue Medication (Rescue medication during the night) - Change from Baseline by Gender (FAS)

Figure 5.3.1 Rescue Medication (Rescue medication during the night) - Change from Baseline by Gender (FAS), Gender = Male

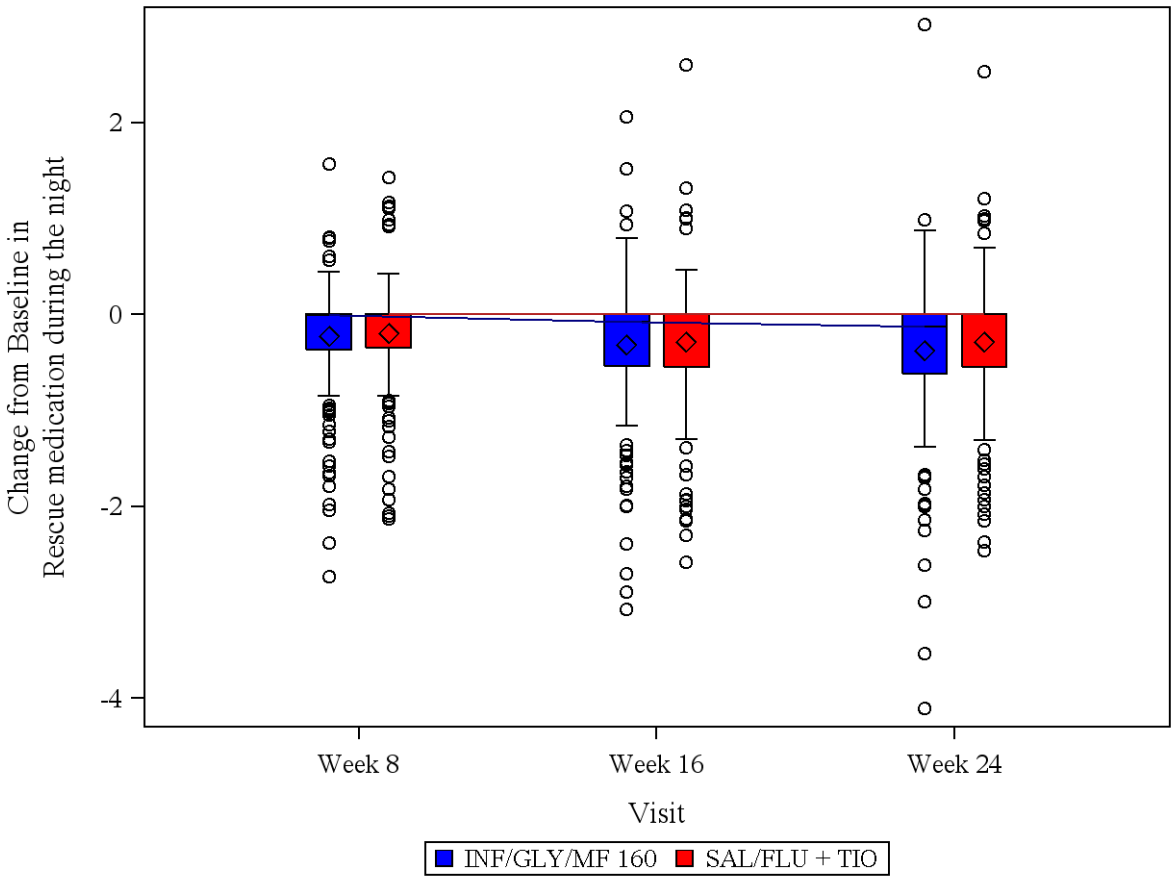
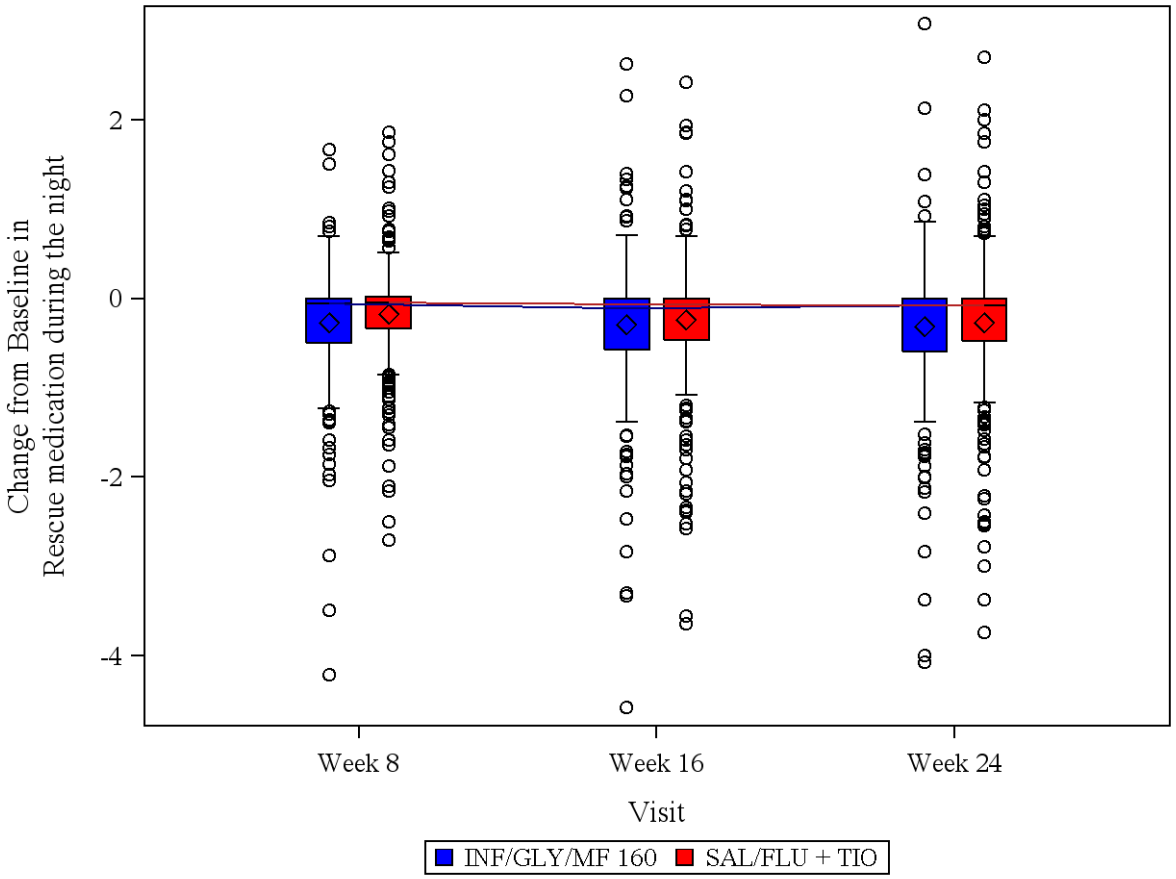


Figure 5.3.2 Rescue Medication (Rescue medication during the night) - Change from Baseline by Gender (FAS), Gender = Female



10.4 Boxplot: Rescue Medication (Rescue medication during the night) - Change from Baseline by Region (FAS)

Figure 5.4.1 Rescue Medication (Rescue medication during the night) - Change from Baseline by Region (FAS), Region = Asia

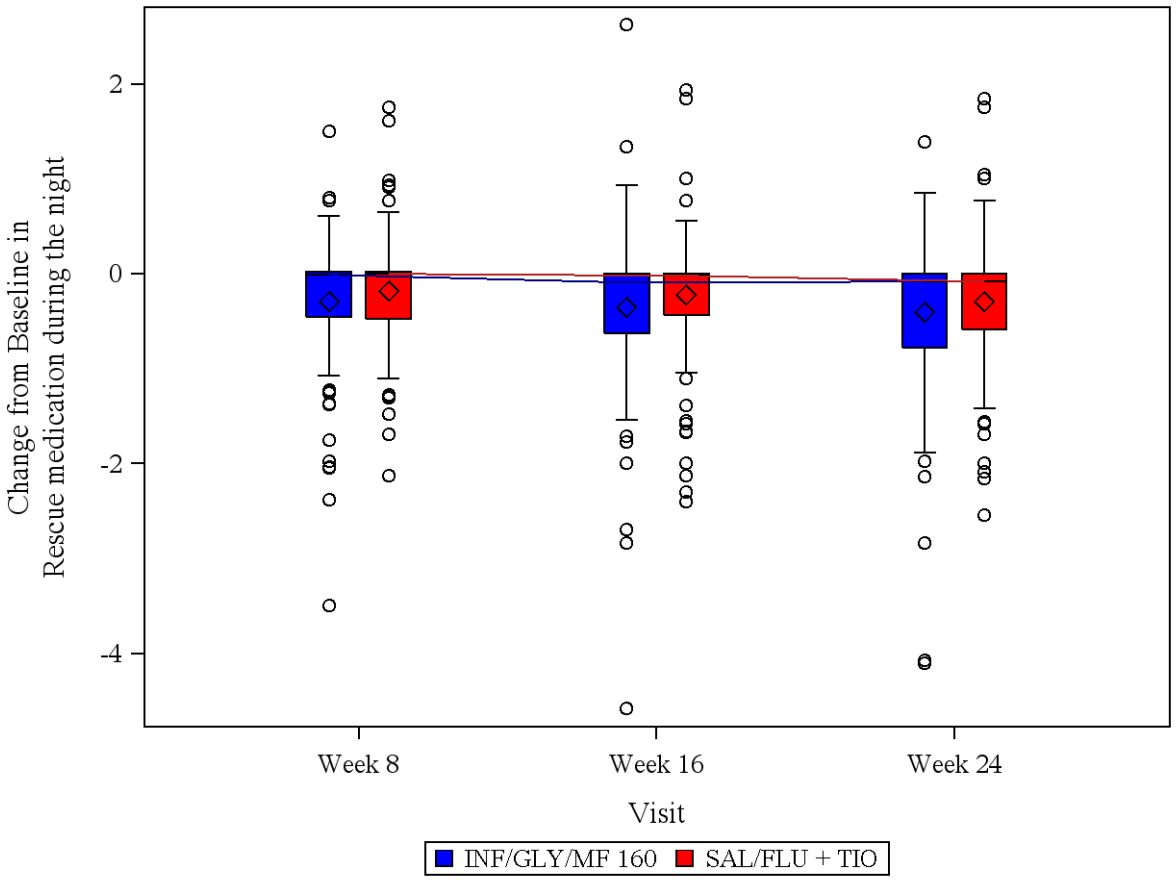


Figure 5.4.2 Rescue Medication (Rescue medication during the night) - Change from Baseline by Region (FAS), Region = Europe

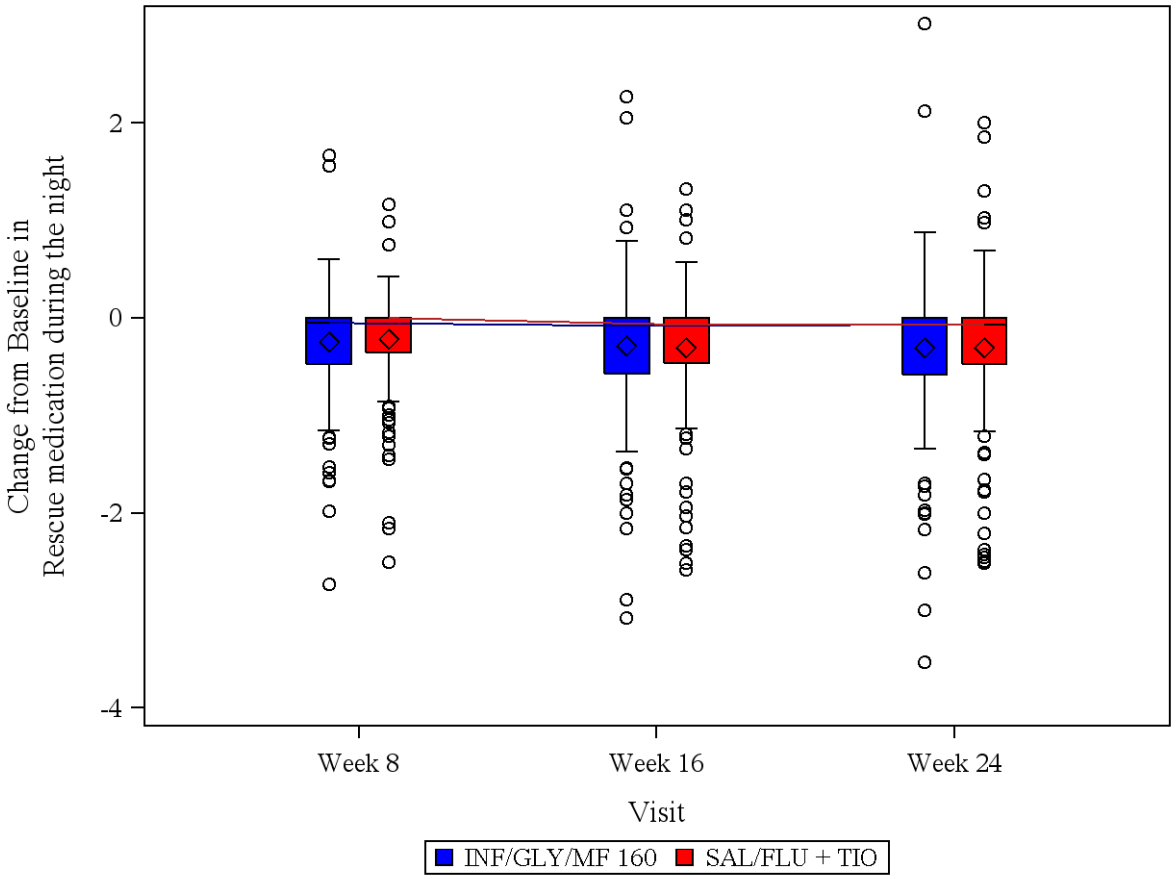


Figure 5.4.3 Rescue Medication (Rescue medication during the night) - Change from Baseline by Region (FAS), Region = Latin America

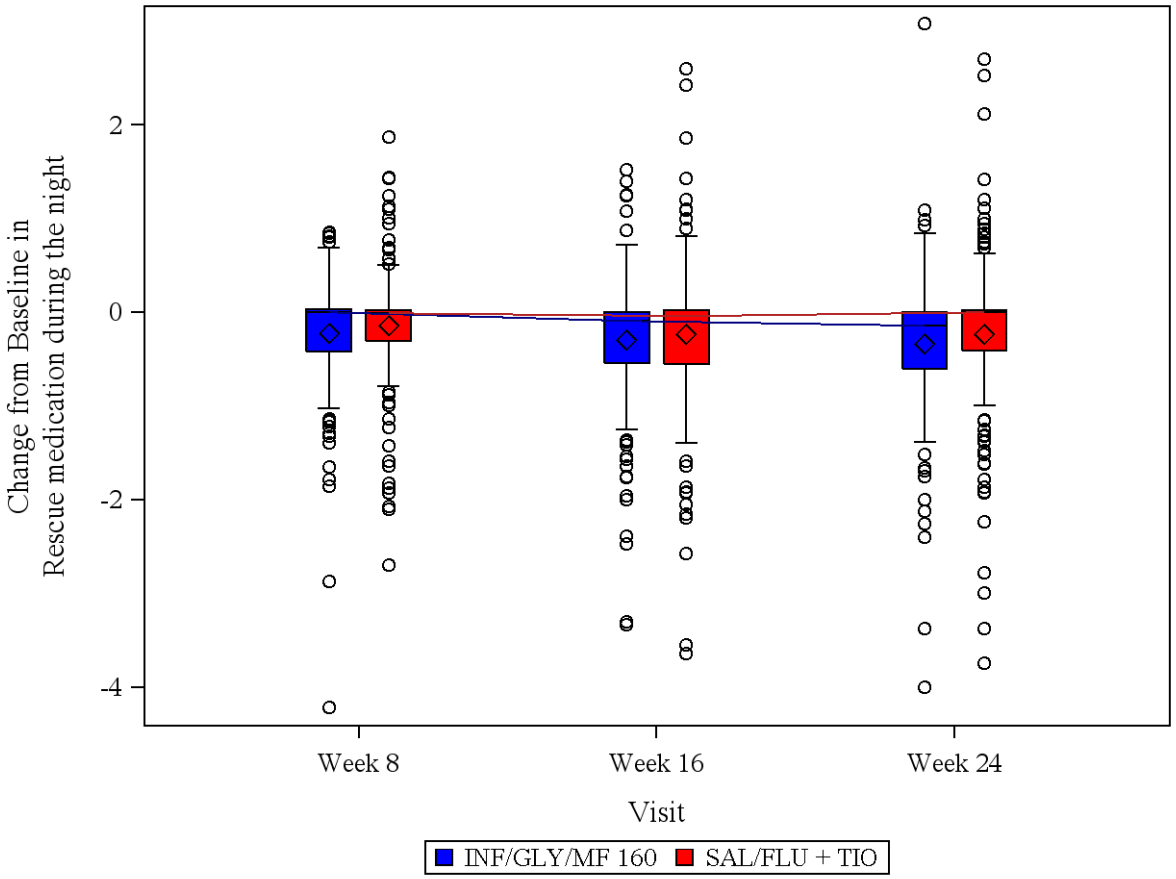
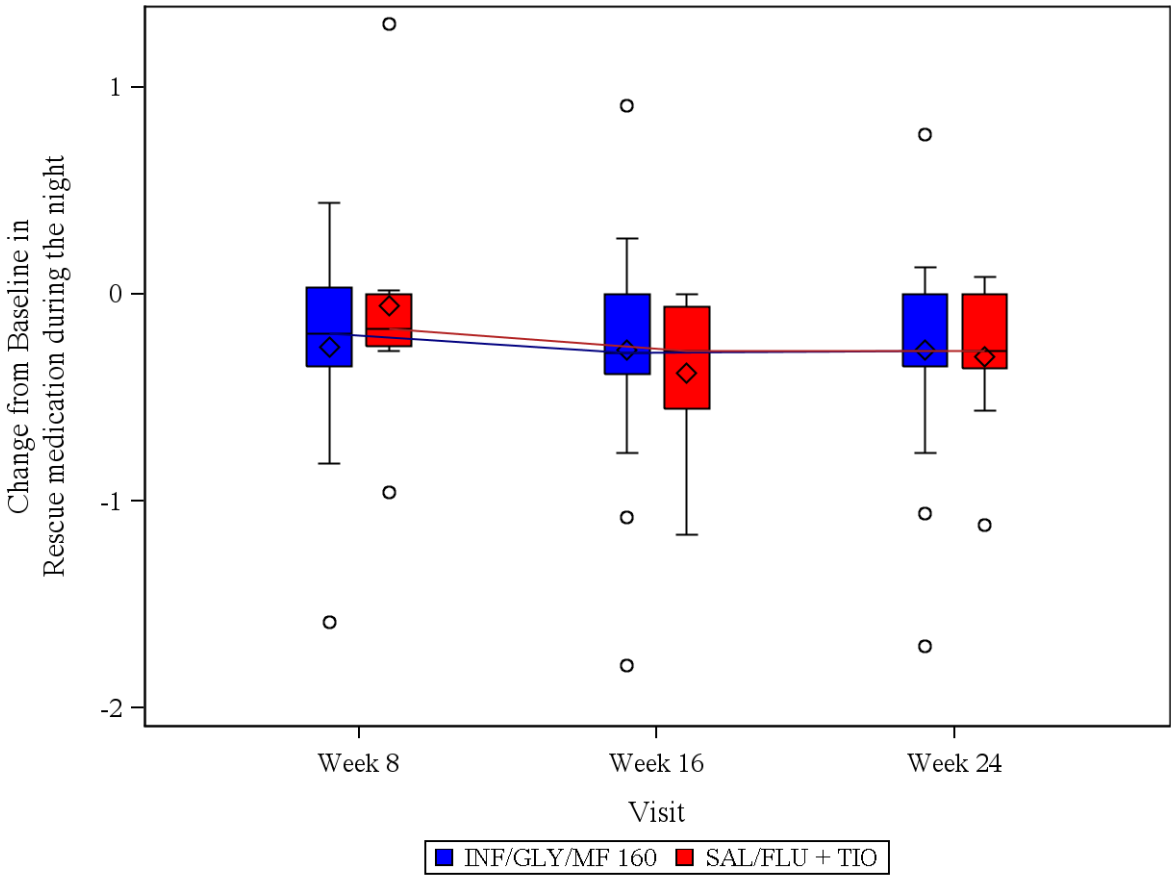


Figure 5.4.4 Rescue Medication (Rescue medication during the night) - Change from Baseline by Region (FAS), Region = Others



10.5 Boxplot: Rescue Medication (Rescue medication during the night) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 5.5.1 Rescue Medication (Rescue medication during the night) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

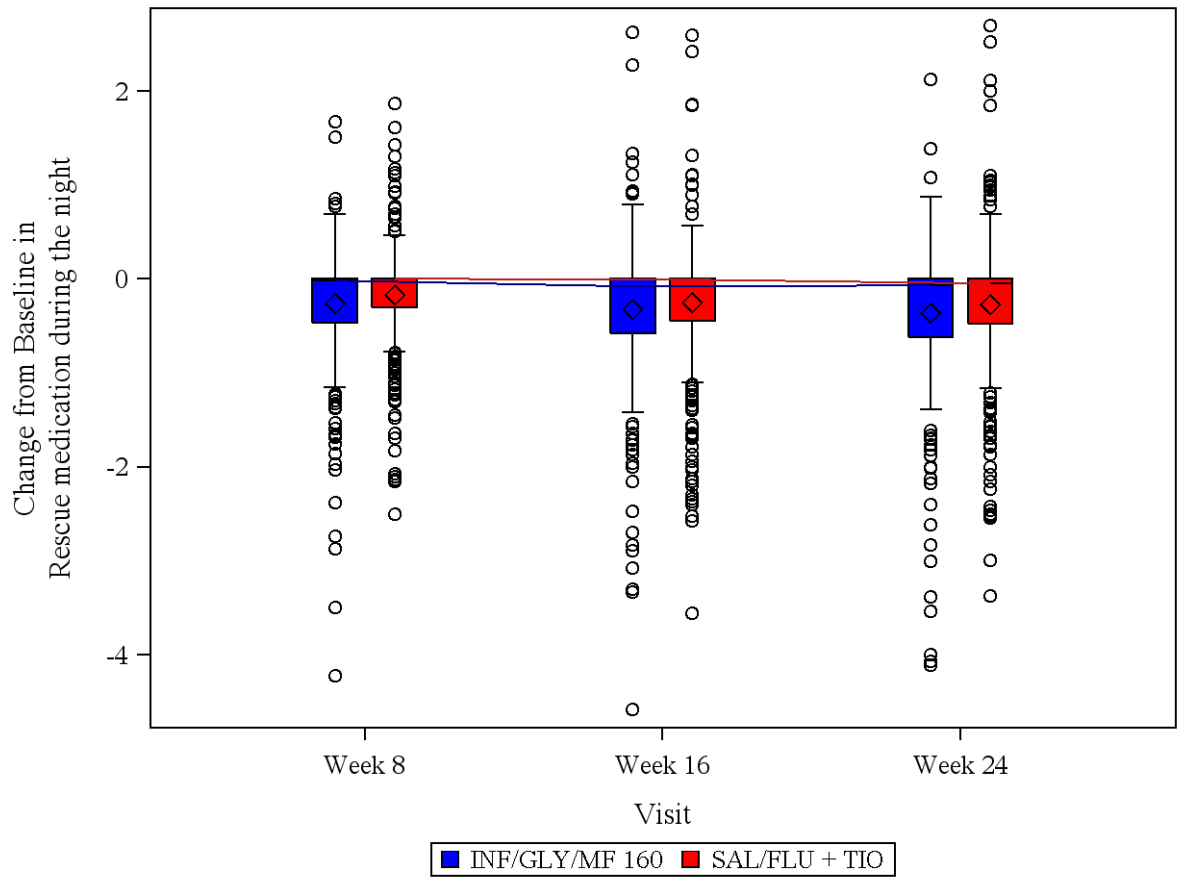
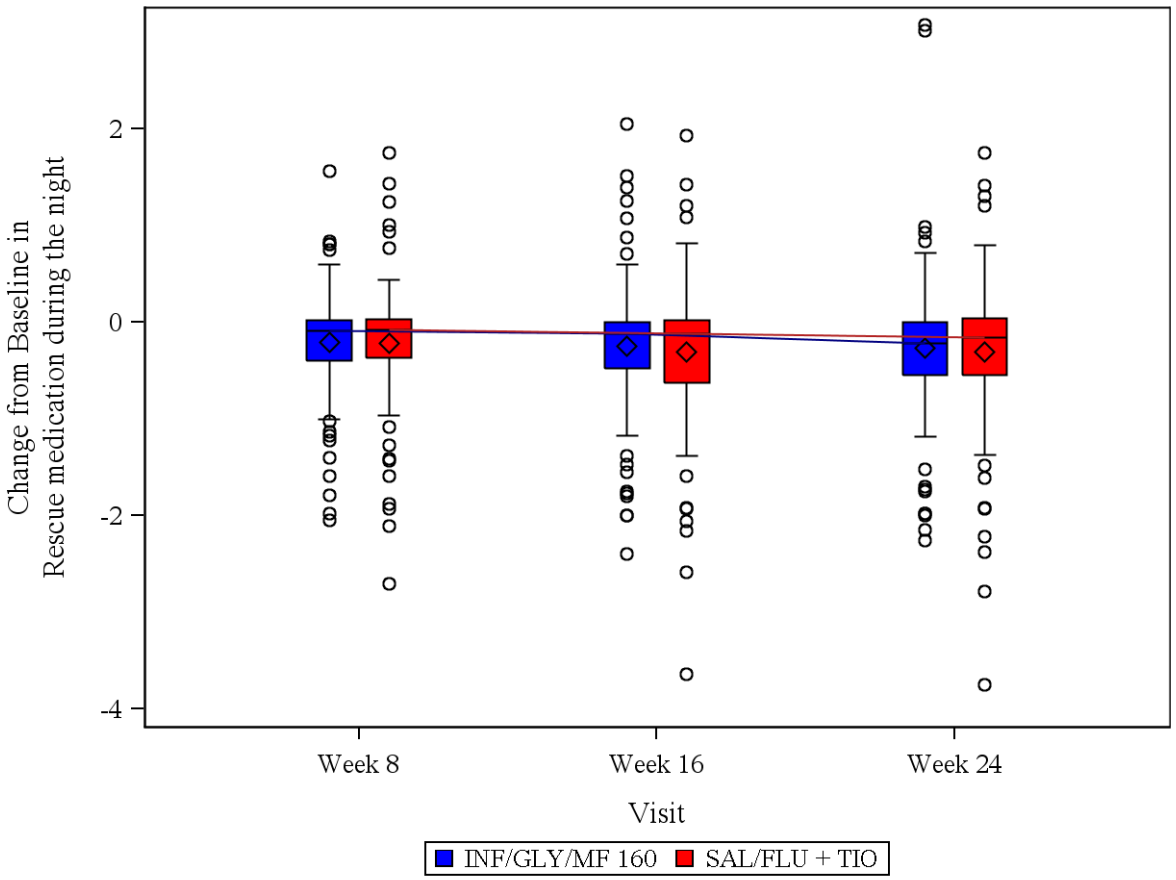


Figure 5.5.2 Rescue Medication (Rescue medication during the night) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



10.6 Boxplot: Rescue Medication (Rescue medication during the night) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 5.6.1 Rescue Medication (Rescue medication during the night) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

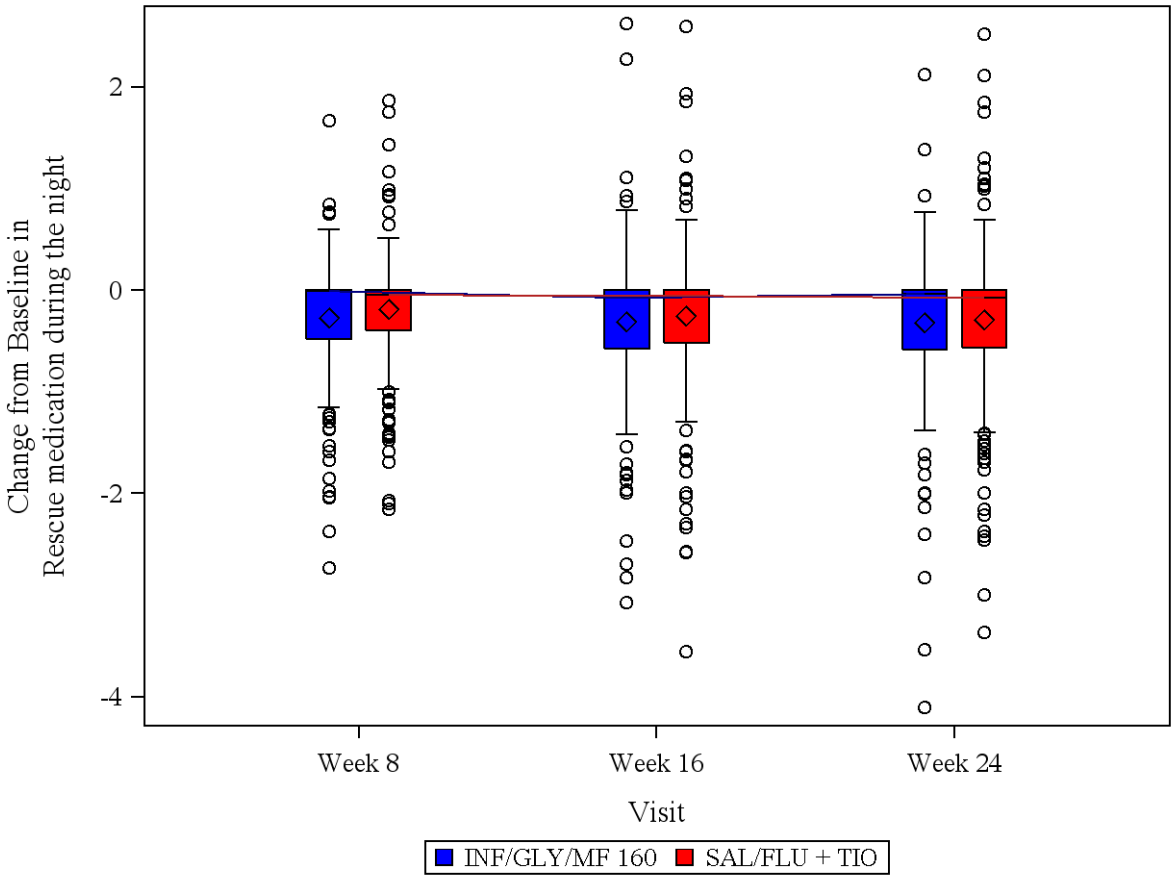
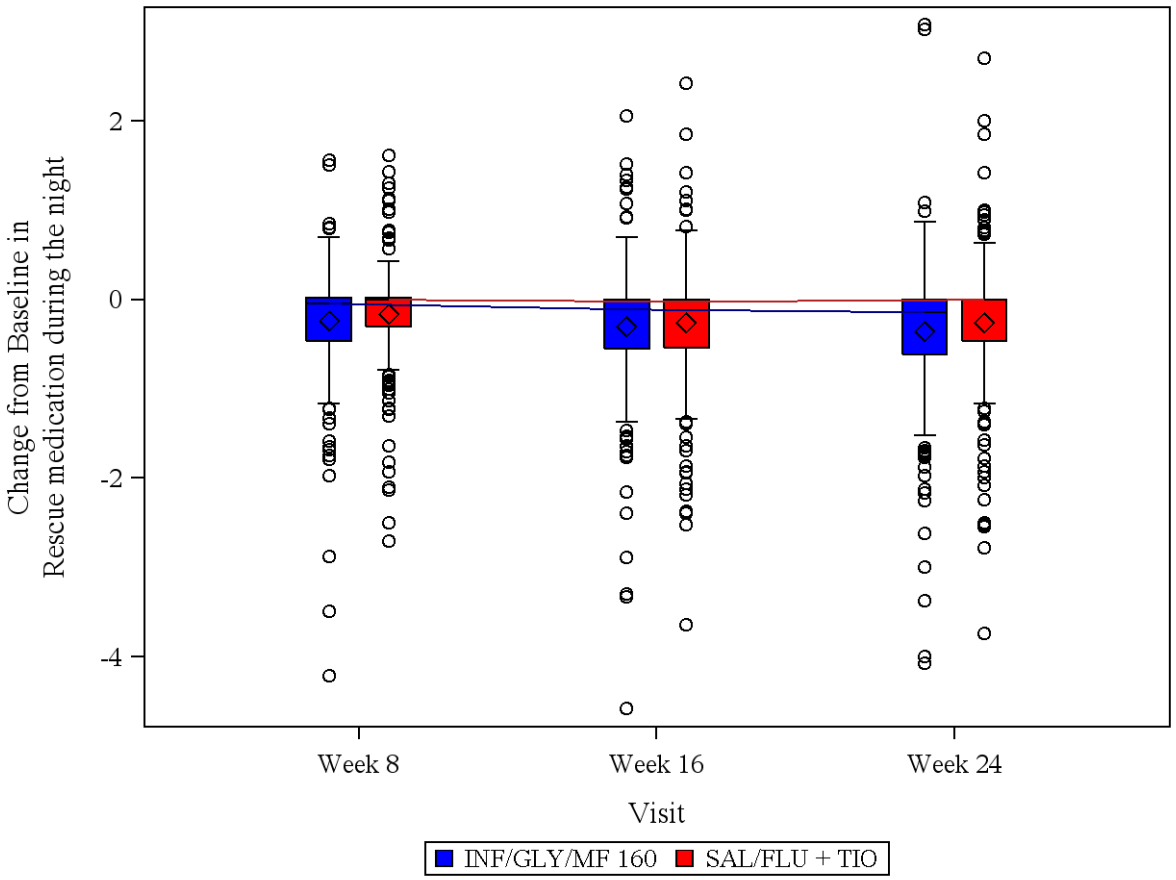
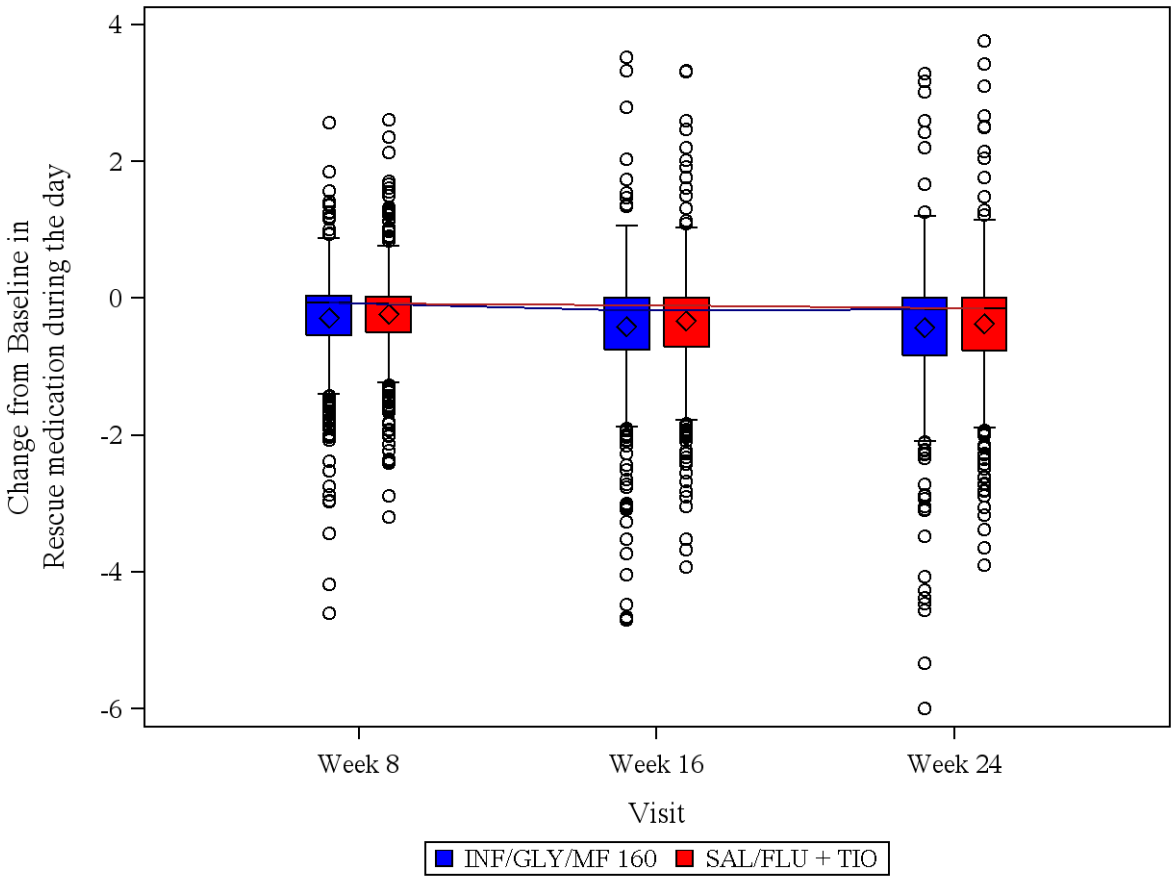


Figure 5.6.2 Rescue Medication (Rescue medication during the night) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



10.7 Boxplot: Rescue Medication (Rescue medication during the day) - Change from Baseline (FAS)

Figure 5.7 Rescue Medication (Rescue medication during the day) - Change from Baseline (FAS)



10.8 Boxplot: Rescue Medication (Rescue medication during the day) - Change from Baseline by Age (FAS)

Figure 5.8.1 Rescue Medication (Rescue medication during the day) - Change from Baseline by Age (FAS), Age = 18-39 years

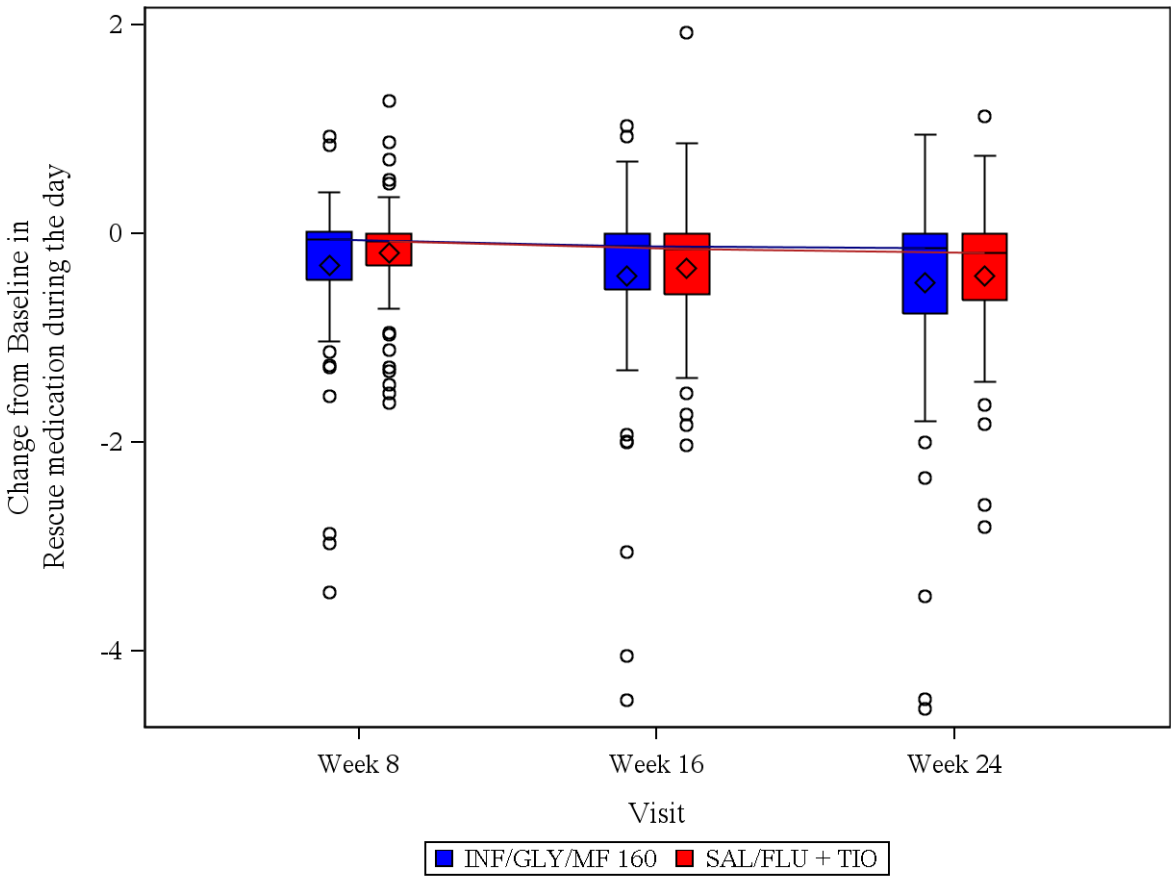


Figure 5.8.2 Rescue Medication (Rescue medication during the day) - Change from Baseline by Age (FAS), Age = 40-64 years

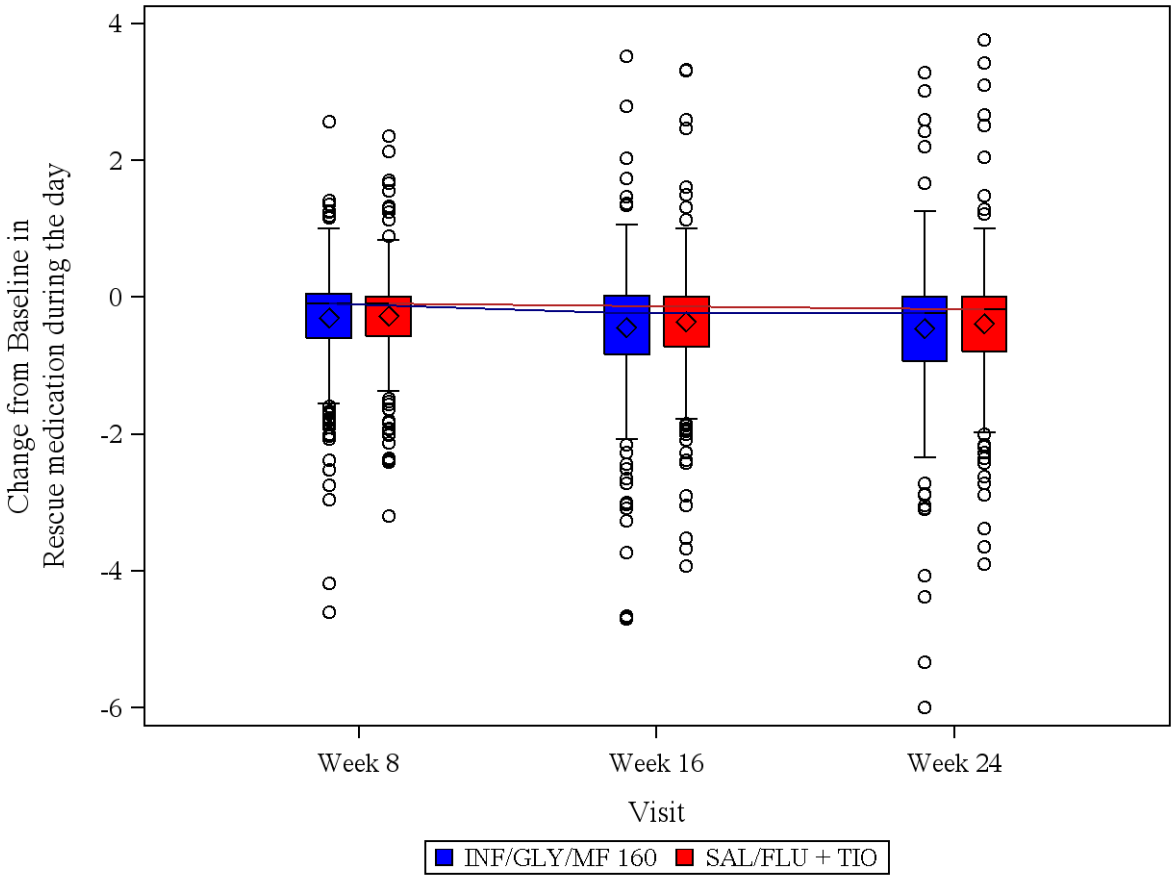
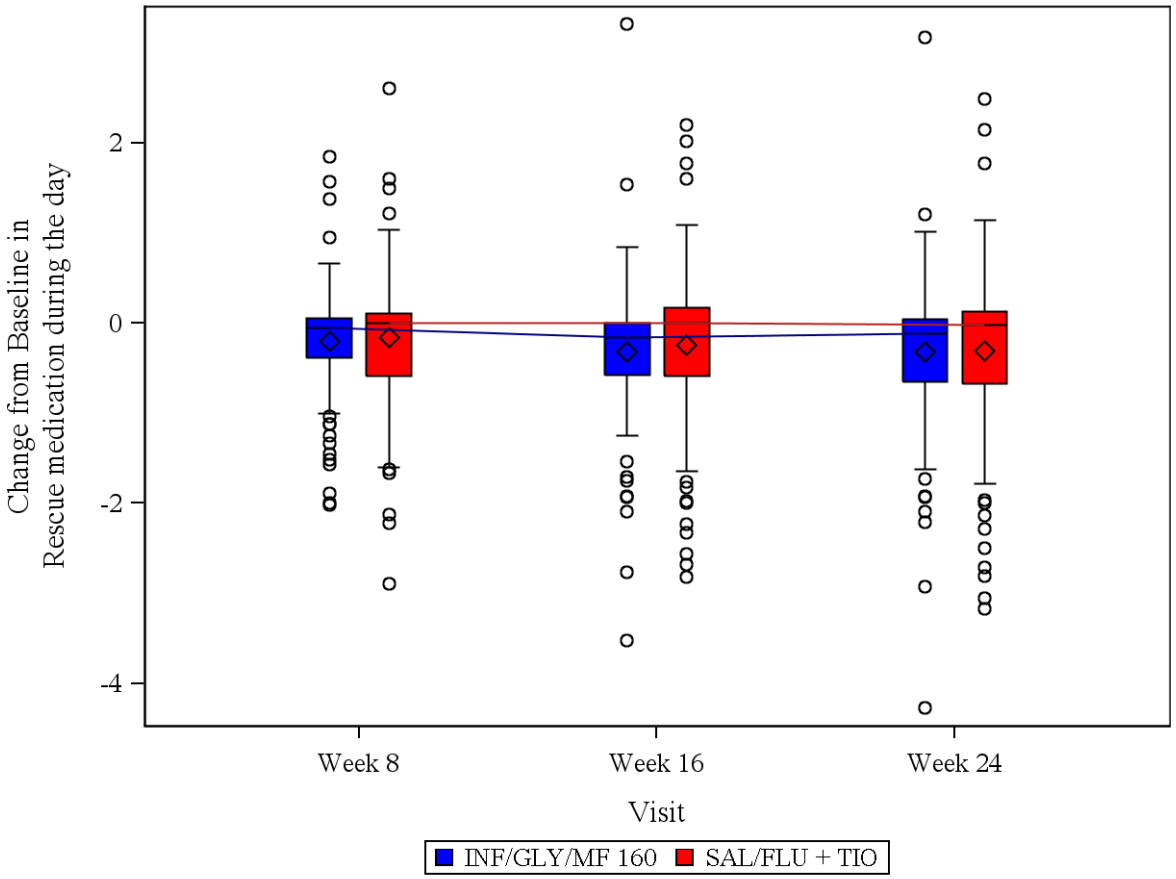


Figure 5.8.3 Rescue Medication (Rescue medication during the day) - Change from Baseline by Age (FAS), Age = ≥65 years



10.9 Boxplot: Rescue Medication (Rescue medication during the day) - Change from Baseline by Gender (FAS)

Figure 5.9.1 Rescue Medication (Rescue medication during the day) - Change from Baseline by Gender (FAS), Gender = Male

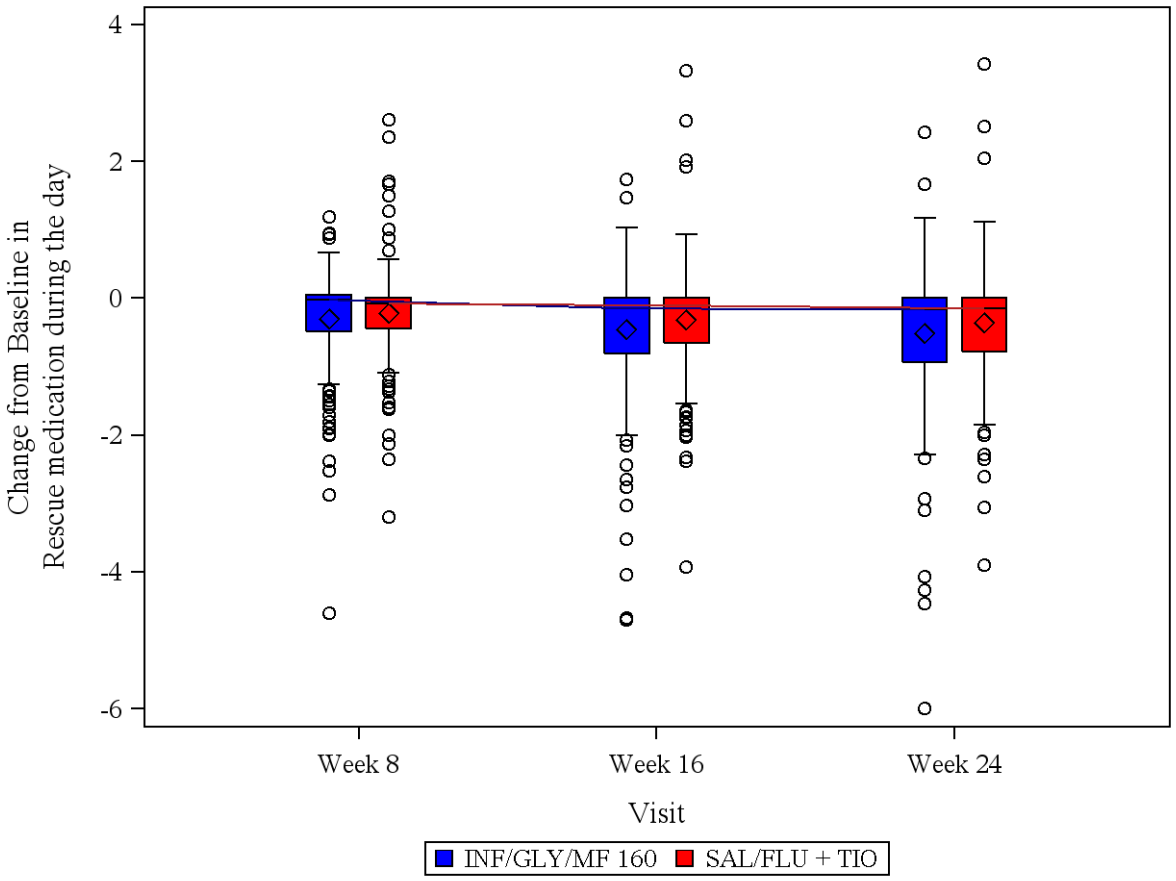
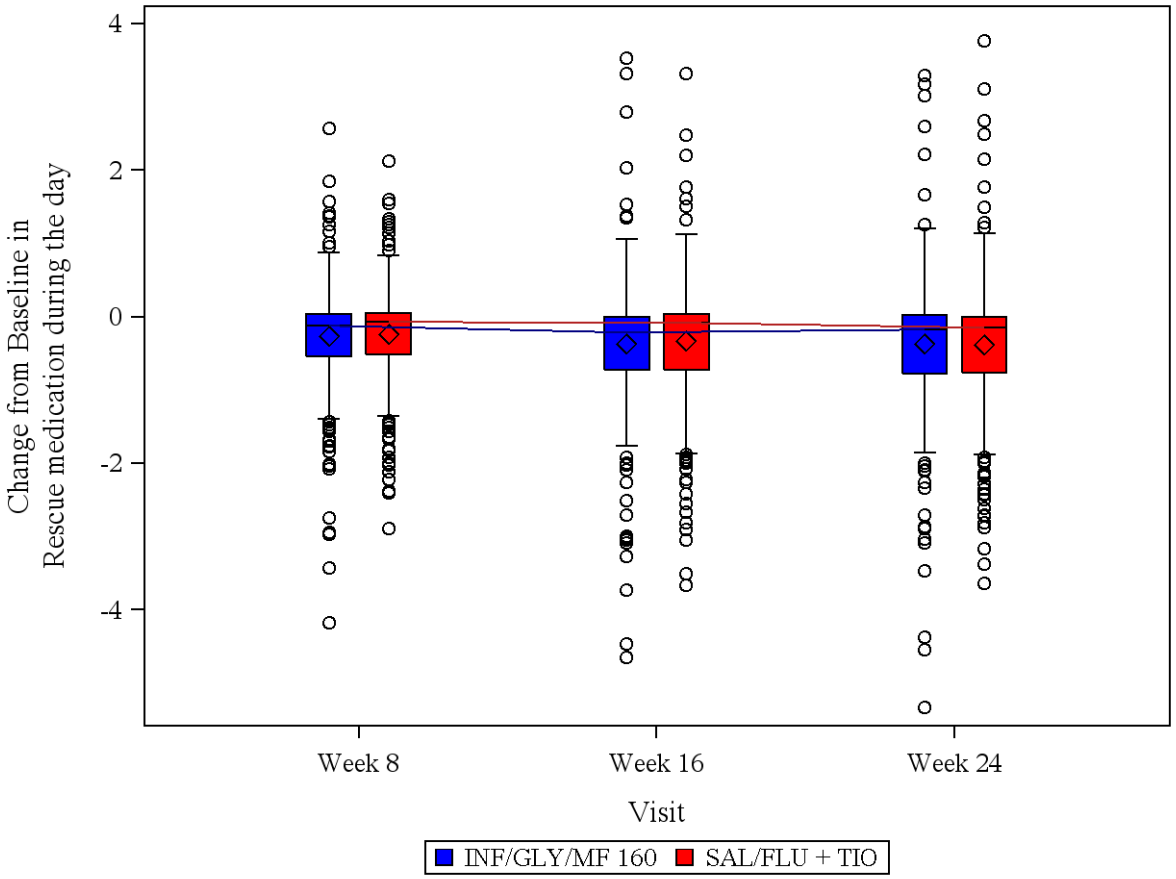


Figure 5.9.2 Rescue Medication (Rescue medication during the day) - Change from Baseline by Gender (FAS), Gender = Female



10.10 Boxplot: Rescue Medication (Rescue medication during the day) - Change from Baseline by Region (FAS)

Figure 5.10.1 Rescue Medication (Rescue medication during the day) - Change from Baseline by Region (FAS), Region = Asia

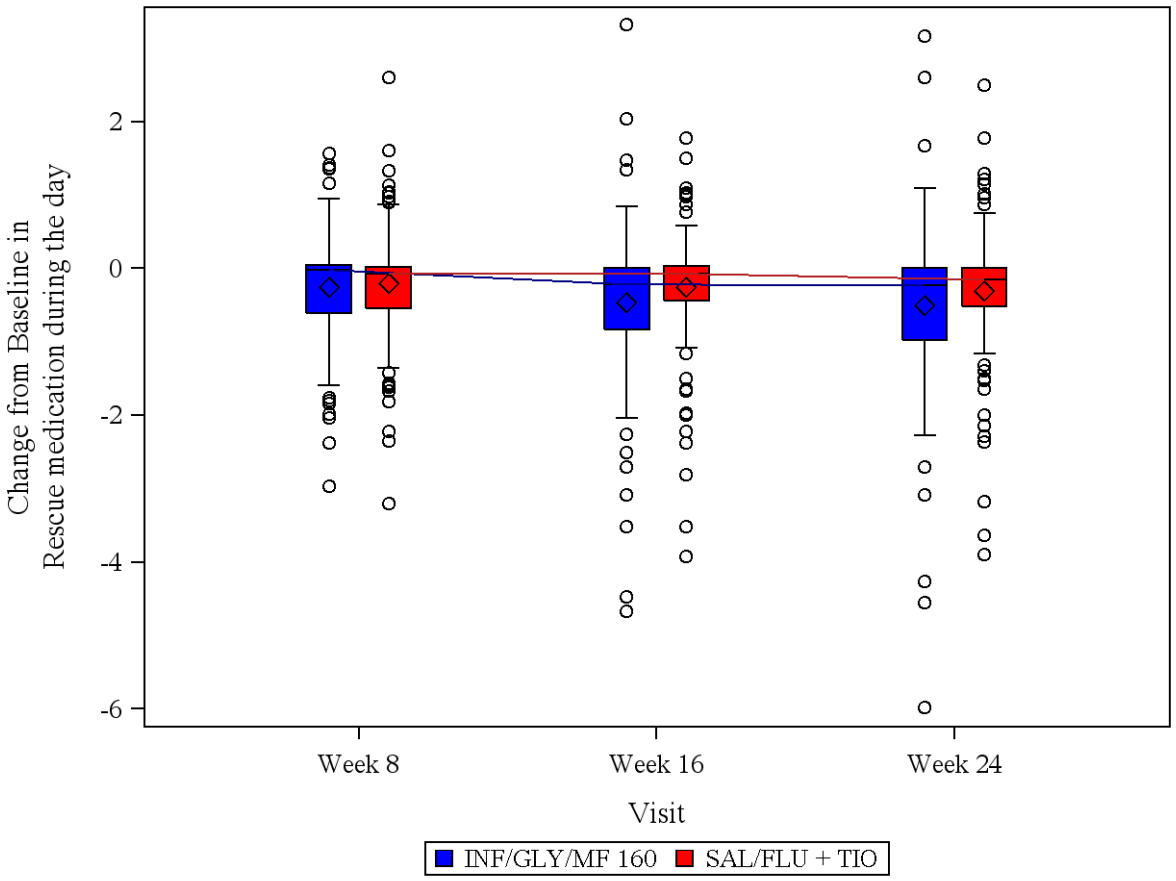


Figure 5.10.2 Rescue Medication (Rescue medication during the day) - Change from Baseline by Region (FAS), Region = Europe

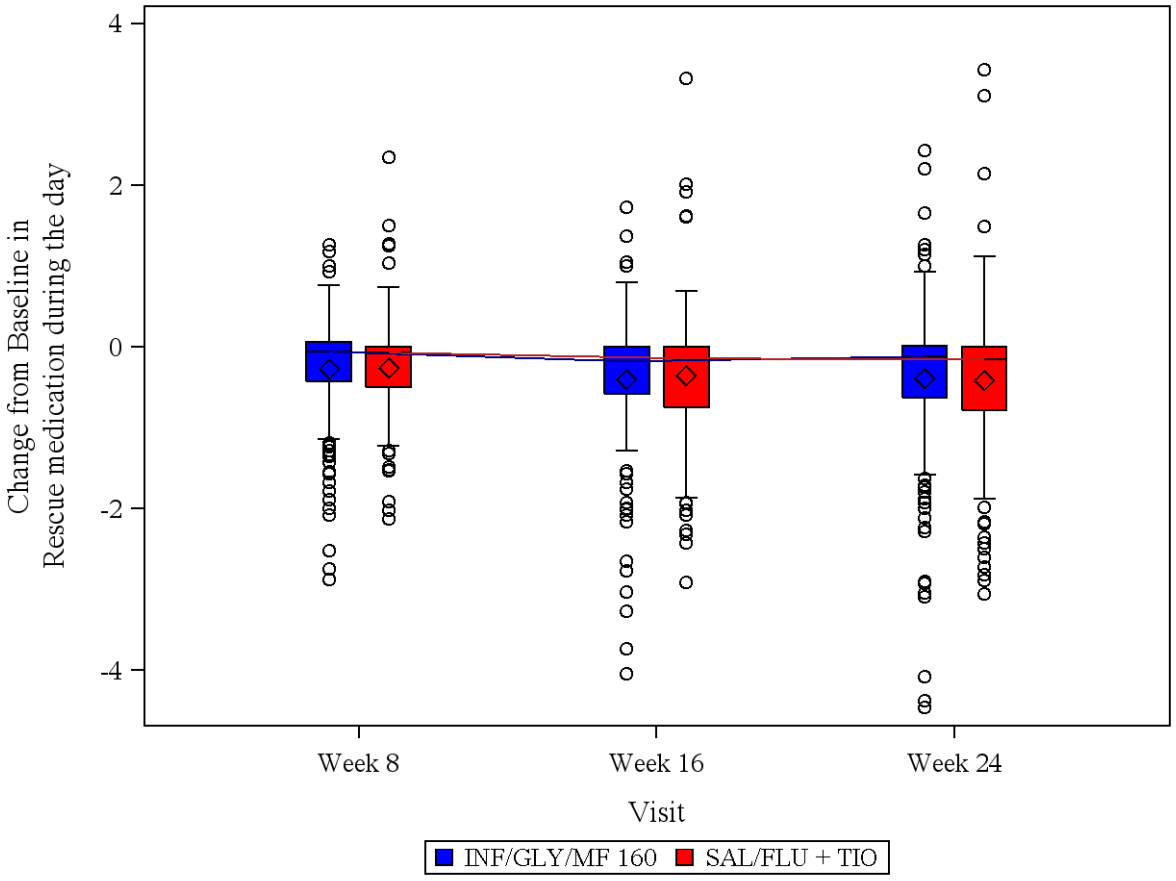


Figure 5.10.3 Rescue Medication (Rescue medication during the day) - Change from Baseline by Region (FAS), Region = Latin America

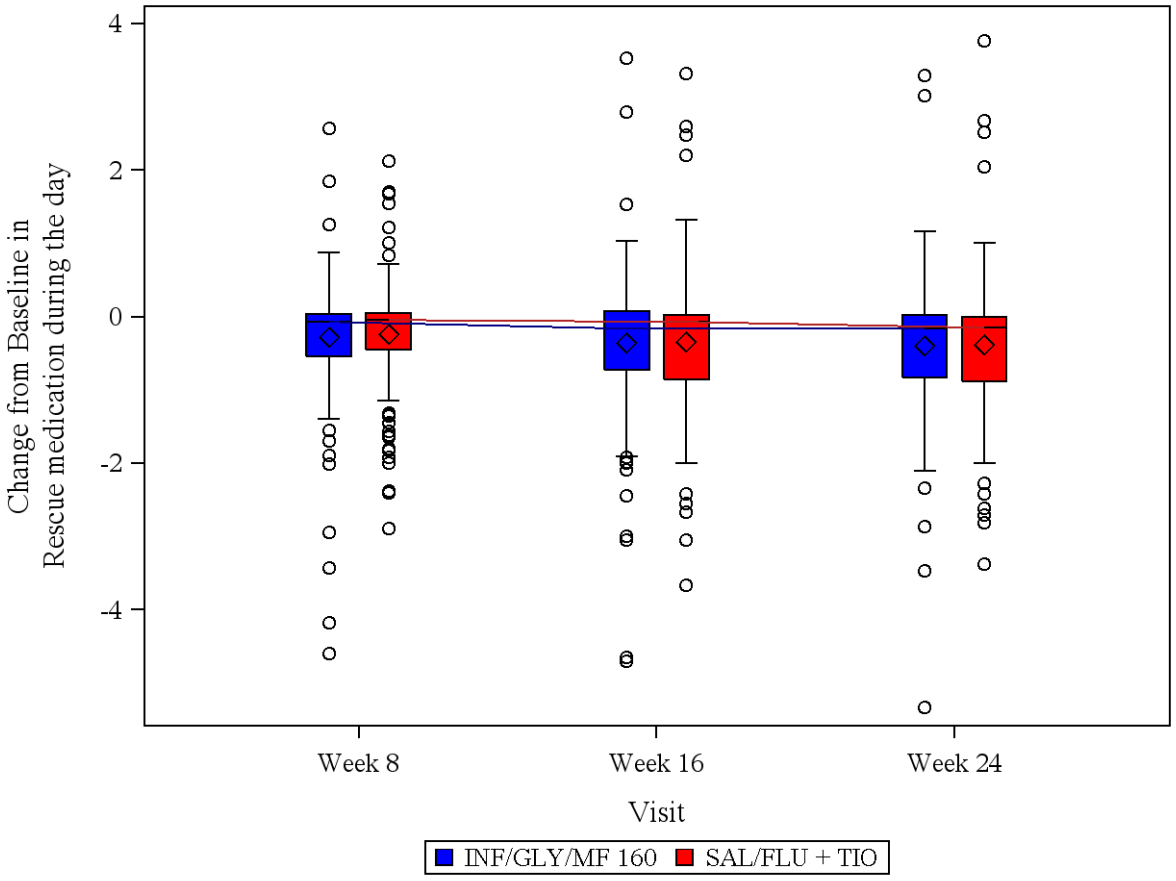
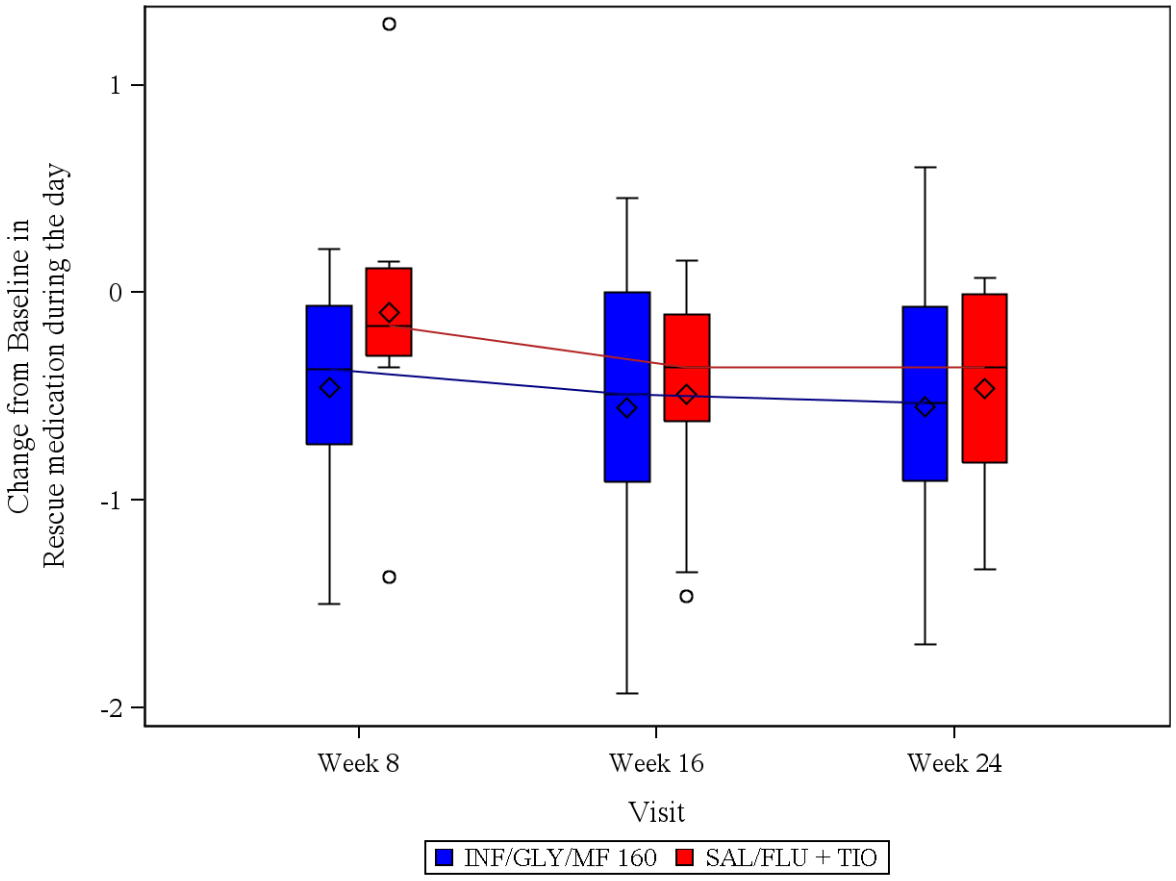


Figure 5.10.4 Rescue Medication (Rescue medication during the day) - Change from Baseline by Region (FAS), Region = Others



10.11 Boxplot: Rescue Medication (Rescue medication during the day) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 5.11.1 Rescue Medication (Rescue medication during the day) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

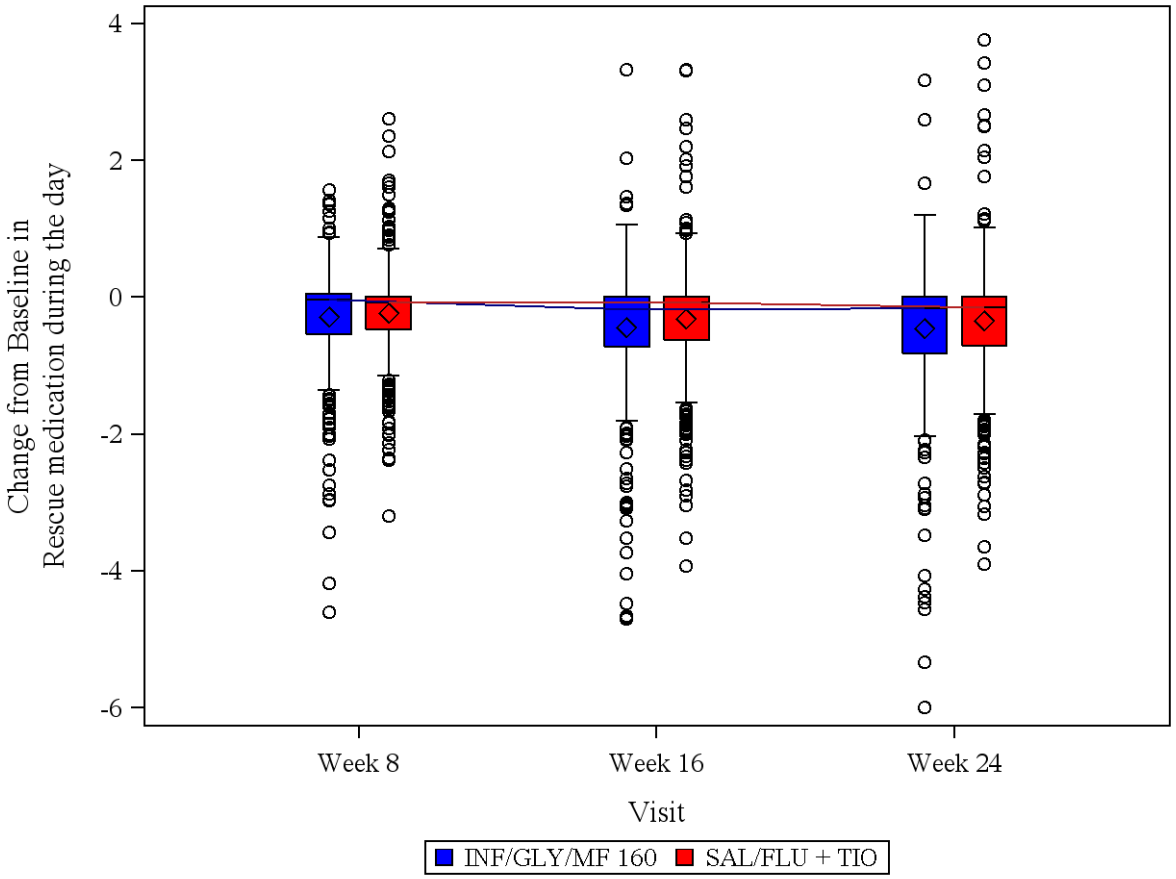
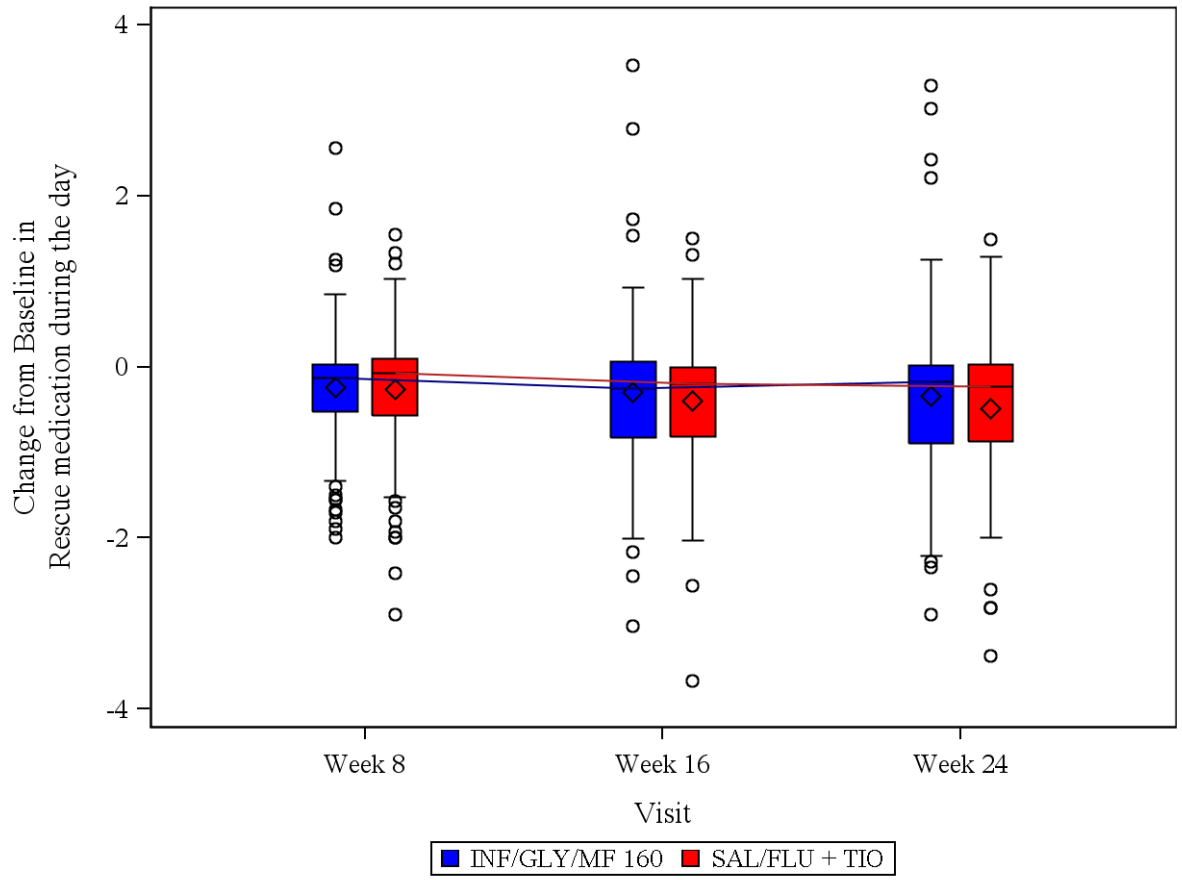


Figure 5.11.2 Rescue Medication (Rescue medication during the day) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



10.12 Boxplot: Rescue Medication (Rescue medication during the day) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 5.12.1 Rescue Medication (Rescue medication during the day) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

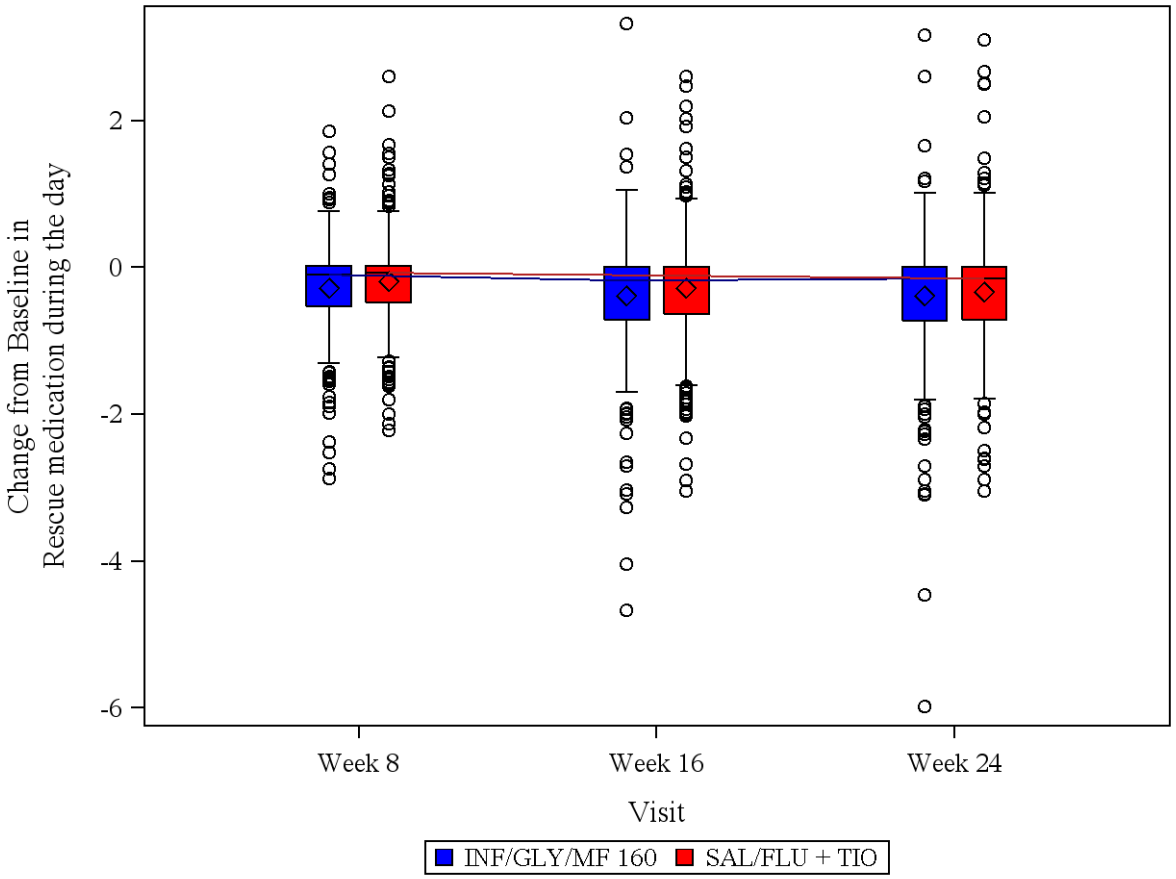
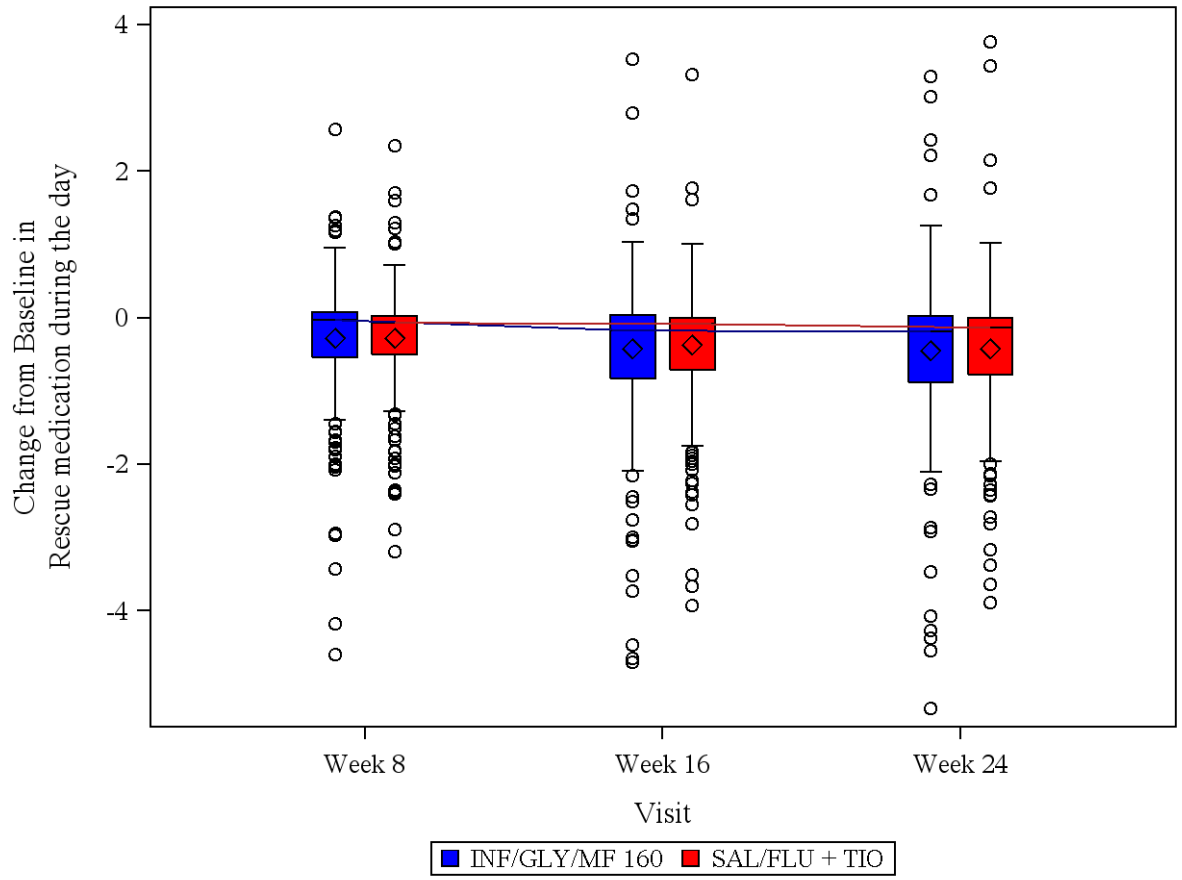
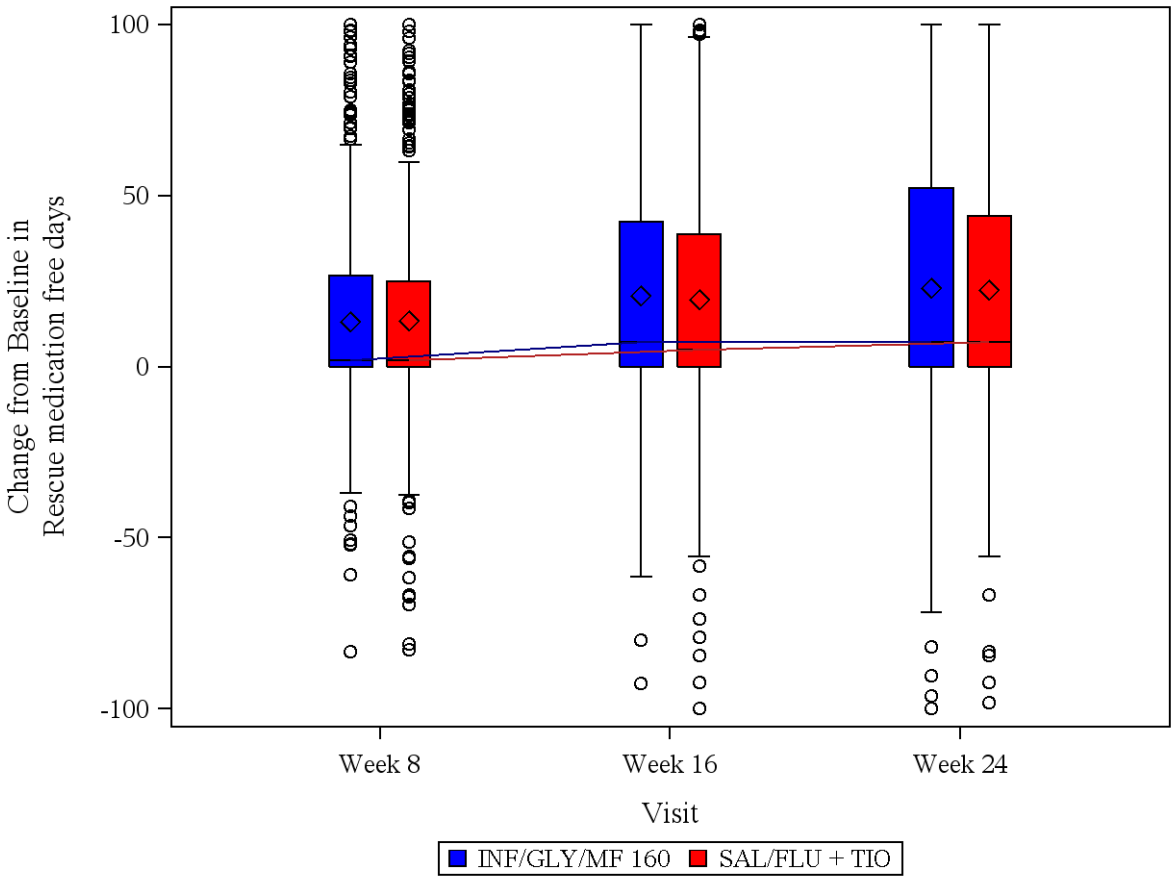


Figure 5.12.2 Rescue Medication (Rescue medication during the day) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



10.13 Boxplot: Rescue Medication (Rescue medication free days) - Change from Baseline (FAS)

Figure 5.13 Rescue Medication (Rescue medication free days) - Change from Baseline (FAS)



10.14 Boxplot: Rescue Medication (Rescue medication free days) - Change from Baseline by Age (FAS)

Figure 5.14.1 Rescue Medication (Rescue medication free days) - Change from Baseline by Age (FAS), Age = 18-39 years

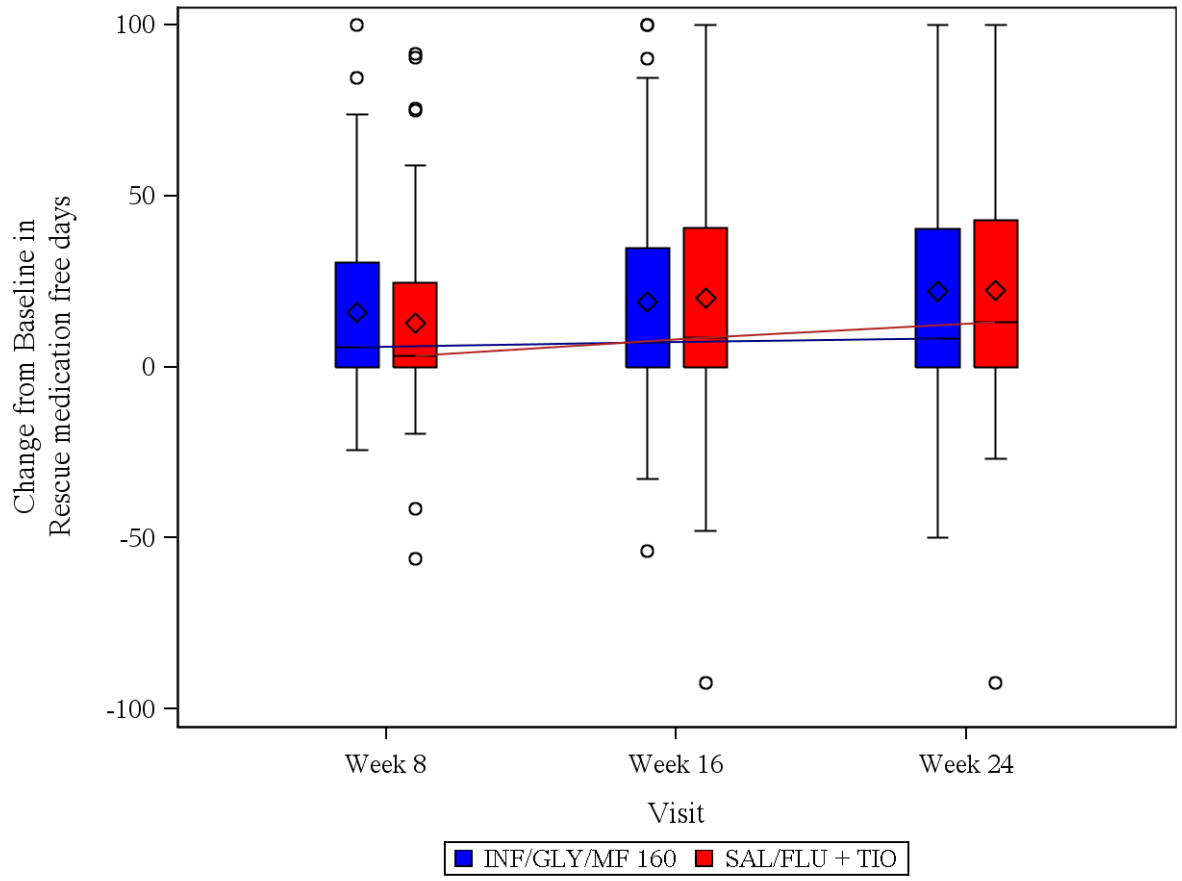


Figure 5.14.2 Rescue Medication (Rescue medication free days) - Change from Baseline by Age (FAS), Age = 40-64 years

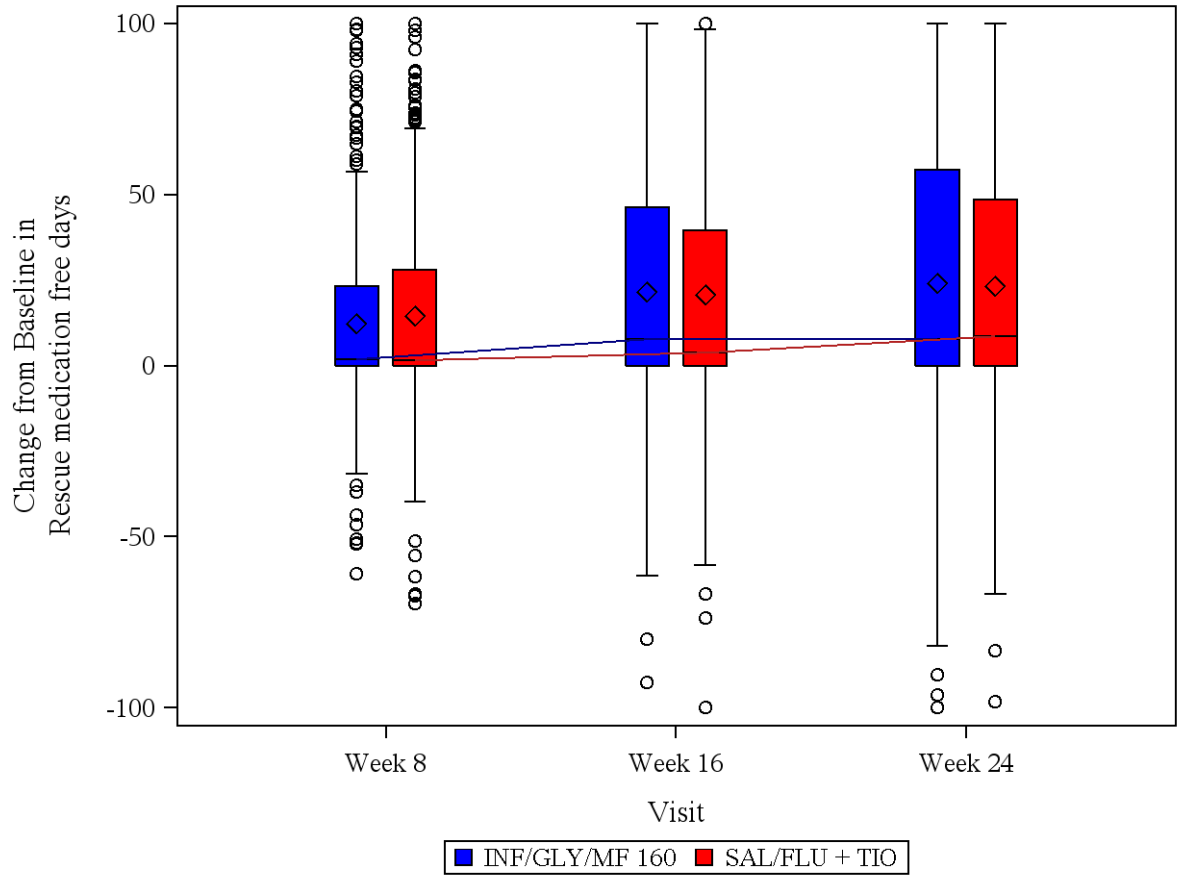
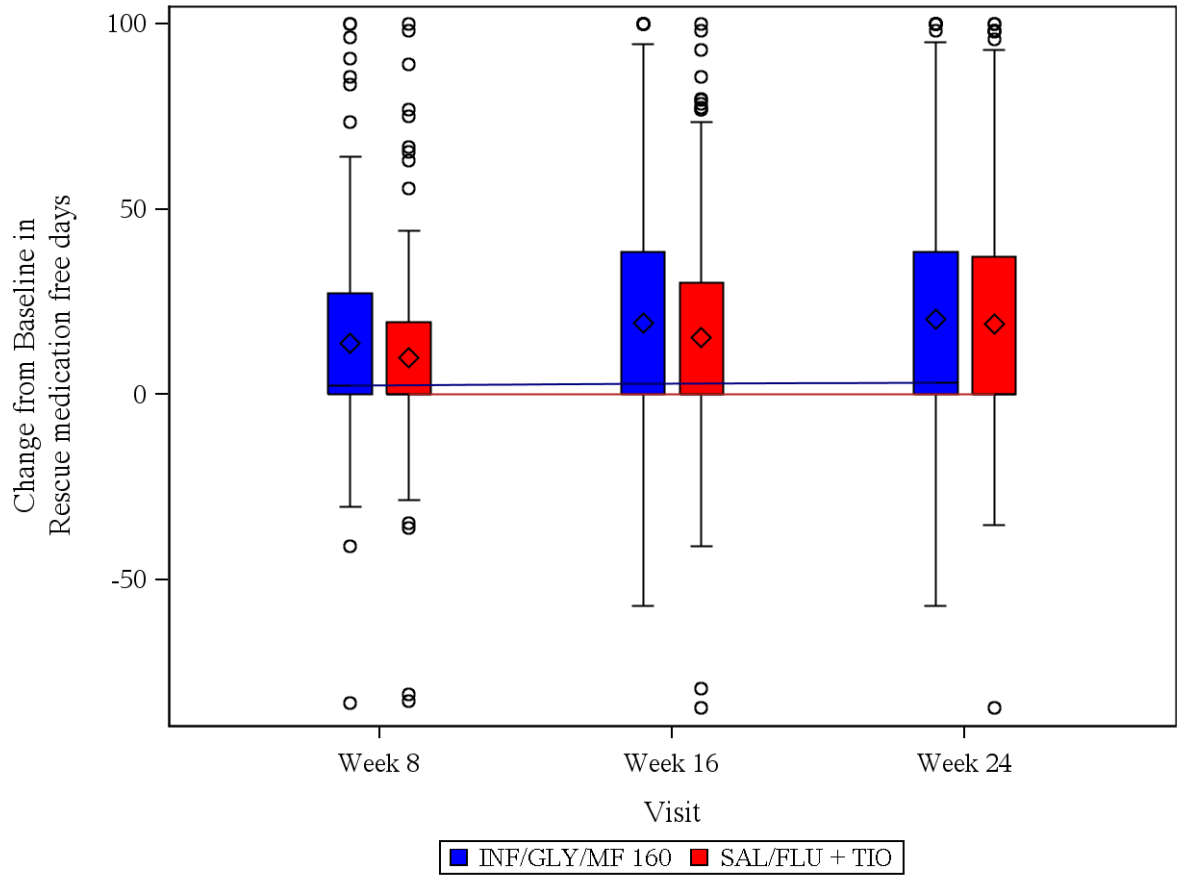


Figure 5.14.3 Rescue Medication (Rescue medication free days) - Change from Baseline by Age (FAS), Age = ≥65 years



10.15 Boxplot: Rescue Medication (Rescue medication free days) - Change from Baseline by Gender (FAS)

Figure 5.15.1 Rescue Medication (Rescue medication free days) - Change from Baseline by Gender (FAS), Gender = Male

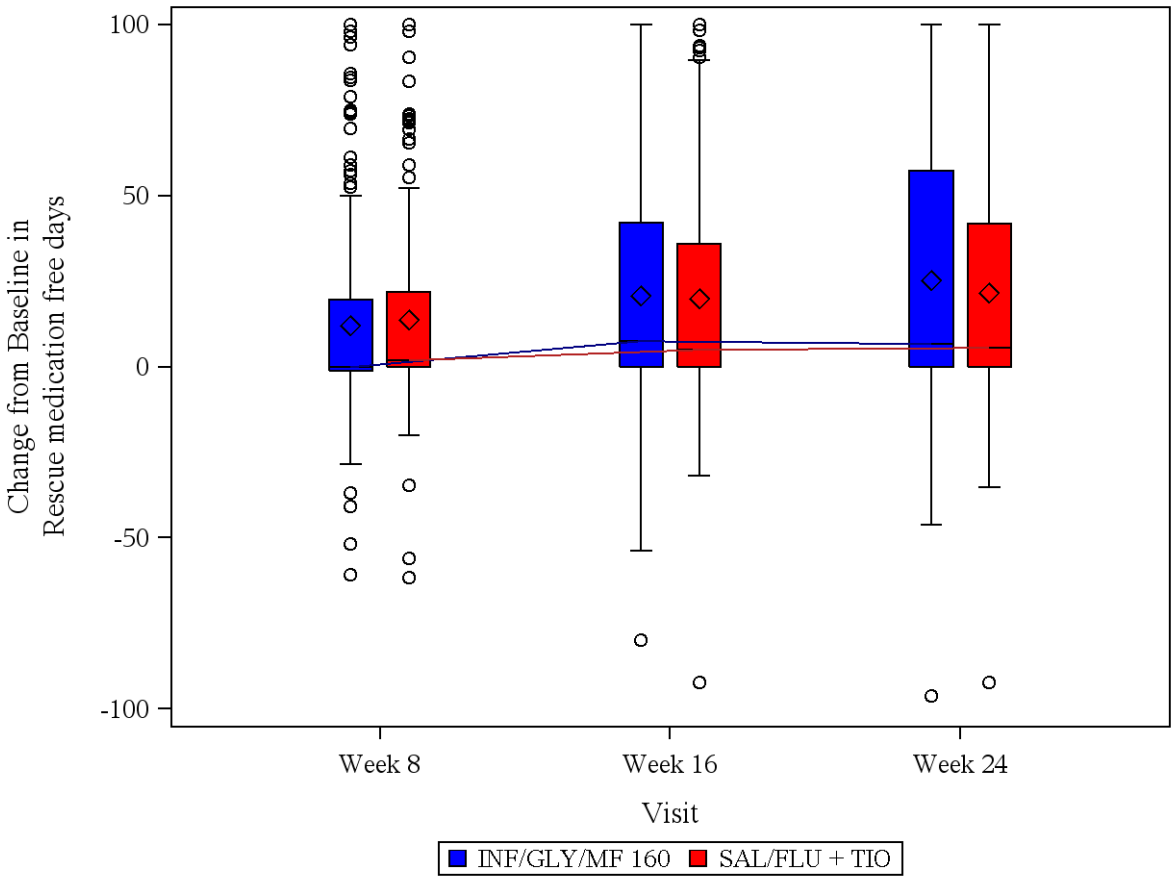
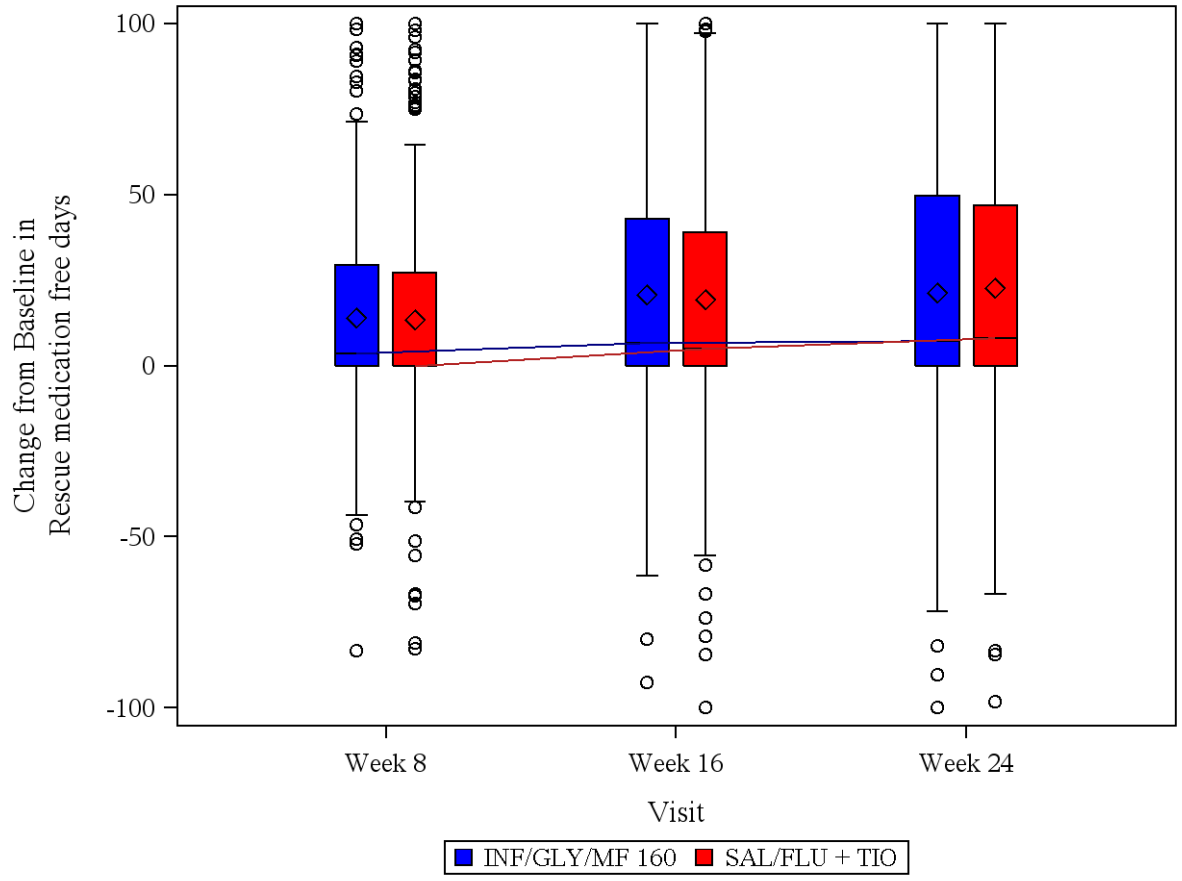


Figure 5.15.2 Rescue Medication (Rescue medication free days) - Change from Baseline by Gender (FAS), Gender = Female



10.16 Boxplot: Rescue Medication (Rescue medication free days) - Change from Baseline by Region (FAS)

Figure 5.16.1 Rescue Medication (Rescue medication free days) - Change from Baseline by Region (FAS), Region = Asia

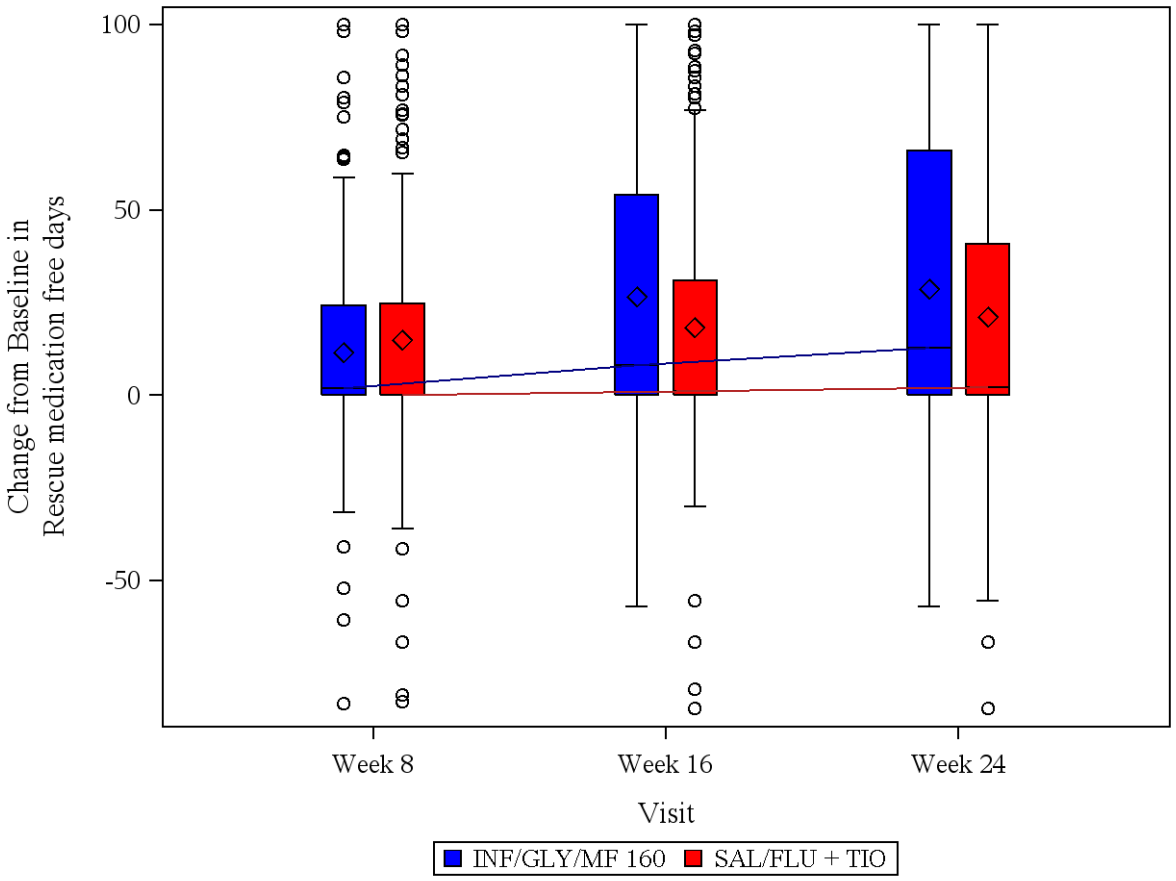


Figure 5.16.2 Rescue Medication (Rescue medication free days) - Change from Baseline by Region (FAS), Region = Europe

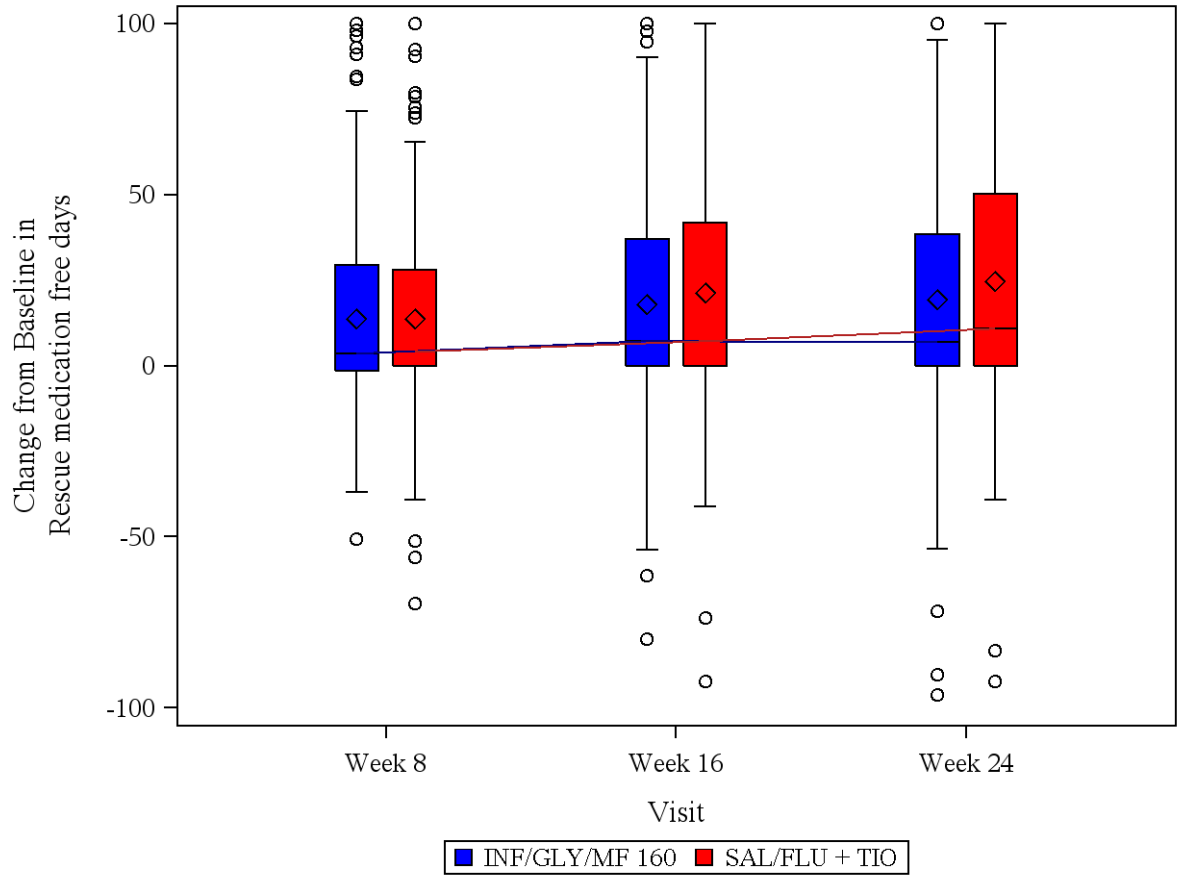


Figure 5.16.3 Rescue Medication (Rescue medication free days) - Change from Baseline by Region (FAS), Region = Latin America

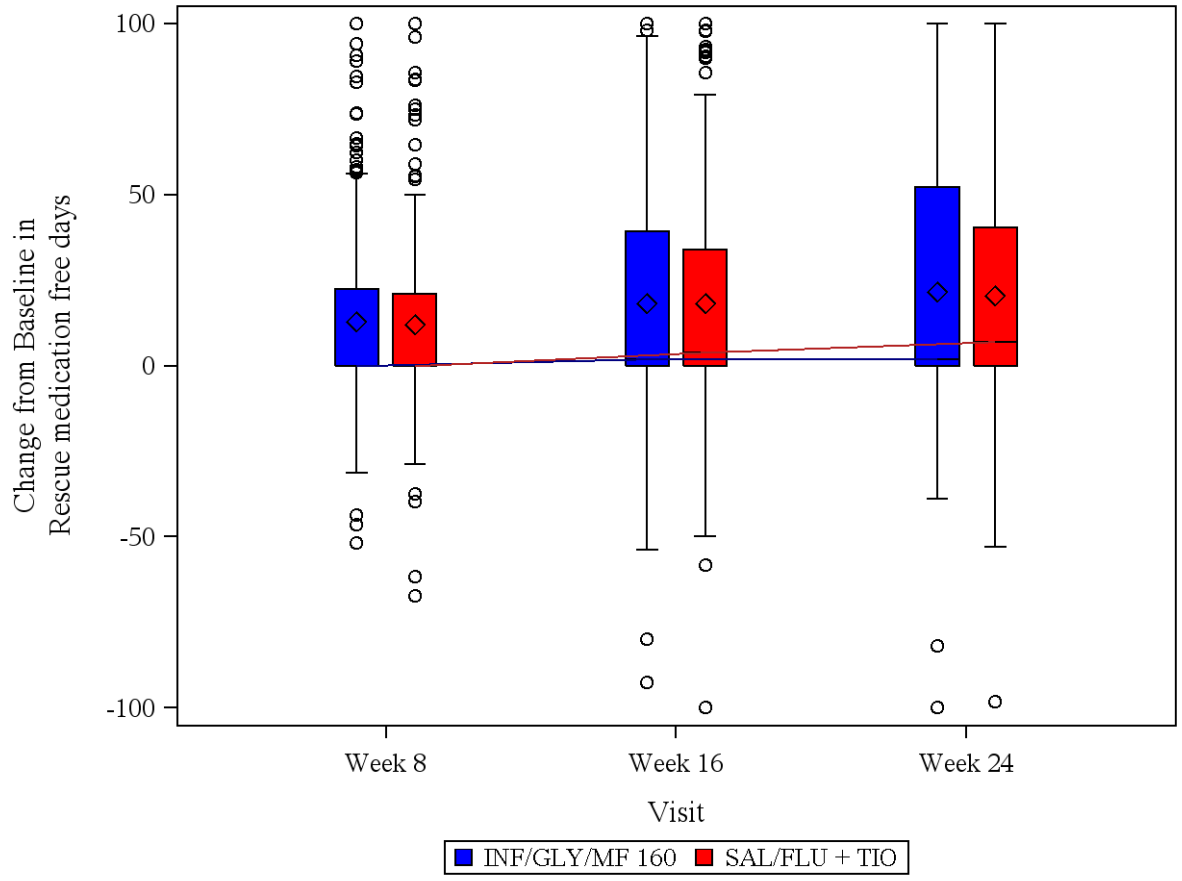
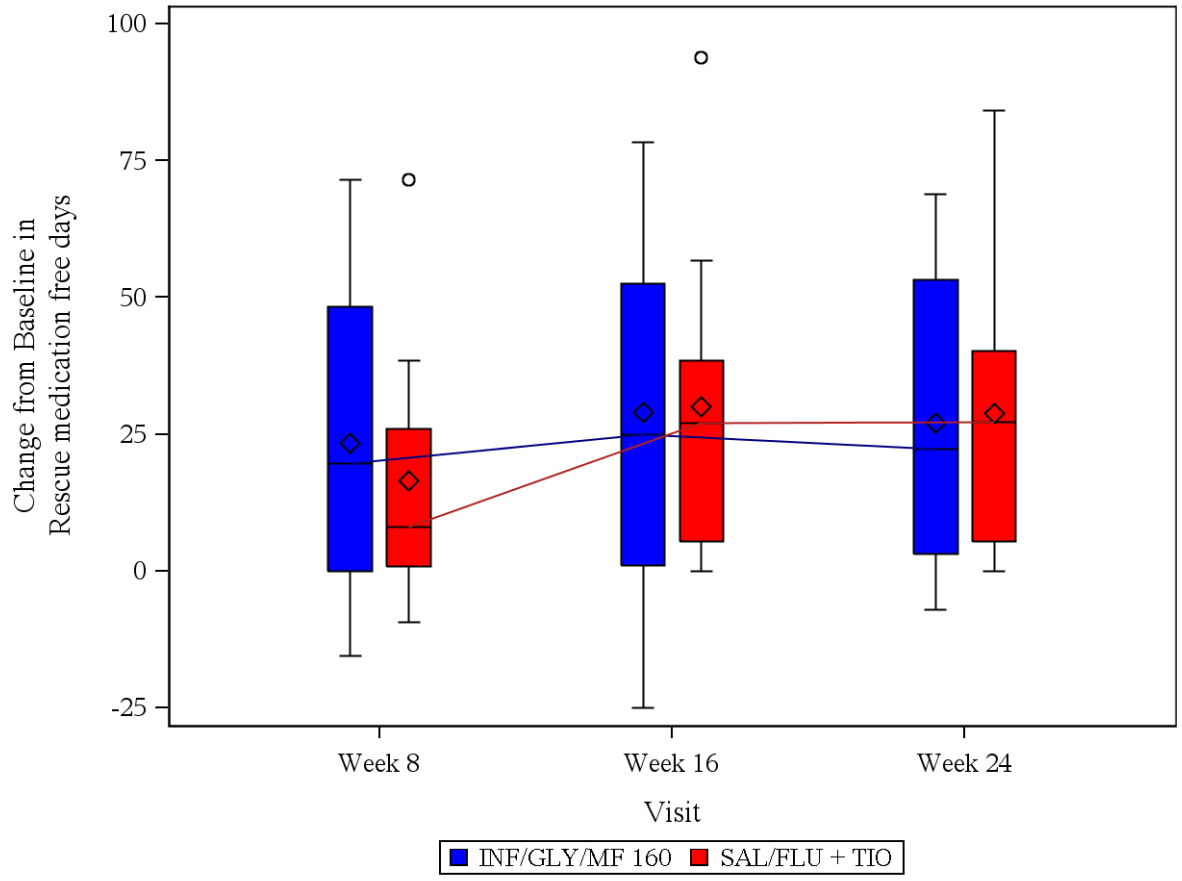


Figure 5.16.4 Rescue Medication (Rescue medication free days) - Change from Baseline by Region (FAS), Region = Others



10.17 Boxplot: Rescue Medication (Rescue medication free days) - Change from Baseline by History of Asthma Exacerbation (FAS)

Figure 5.17.1 Rescue Medication (Rescue medication free days) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1

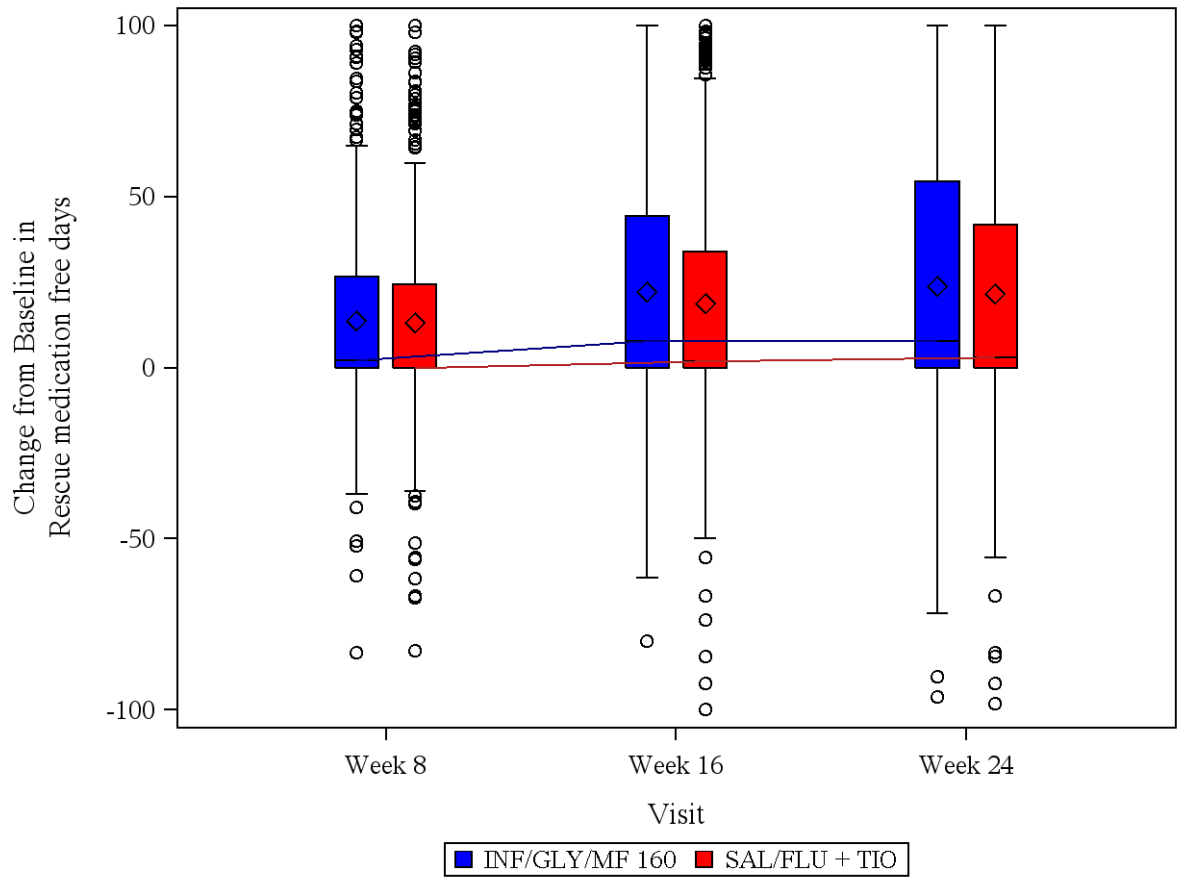
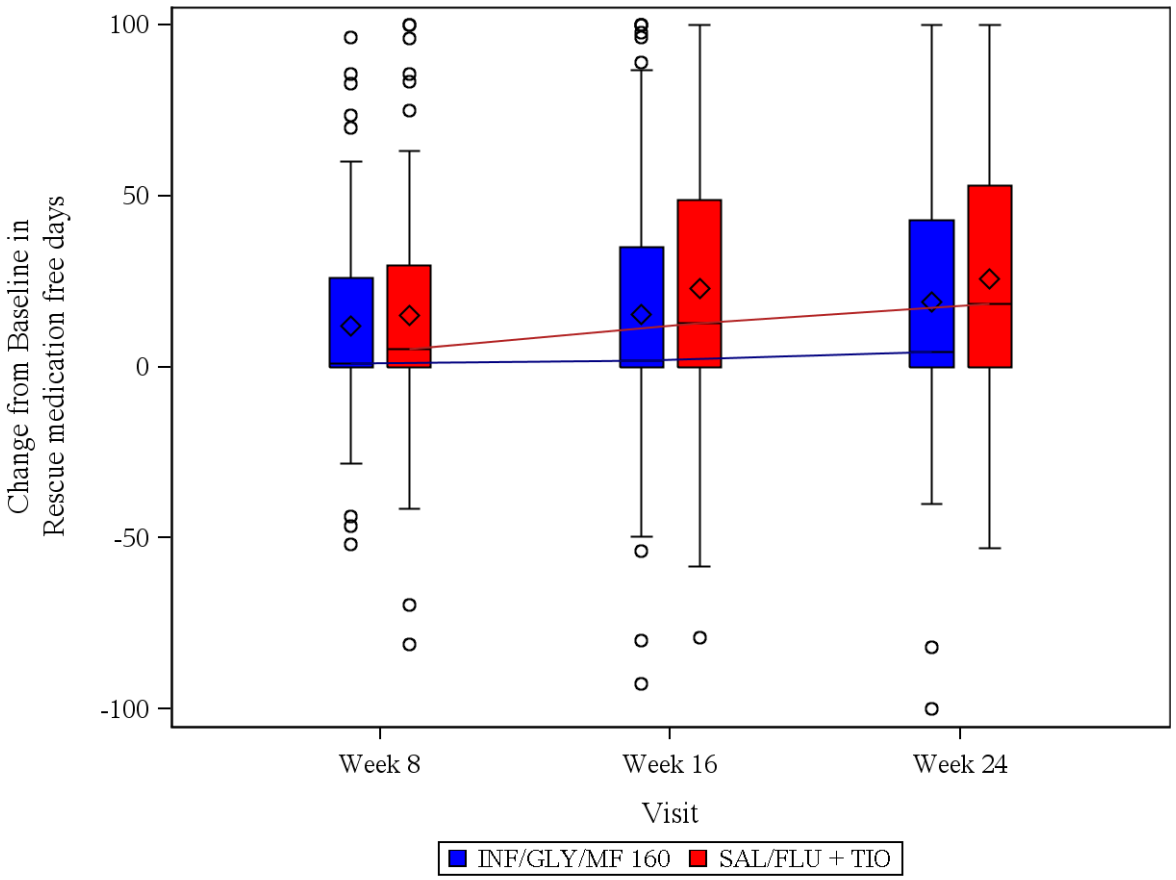


Figure 5.17.2 Rescue Medication (Rescue medication free days) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



10.18 Boxplot: Rescue Medication (Rescue medication free days) - Change from Baseline by Patients' Prior Therapies (FAS)

Figure 5.18.1 Rescue Medication (Rescue medication free days) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA

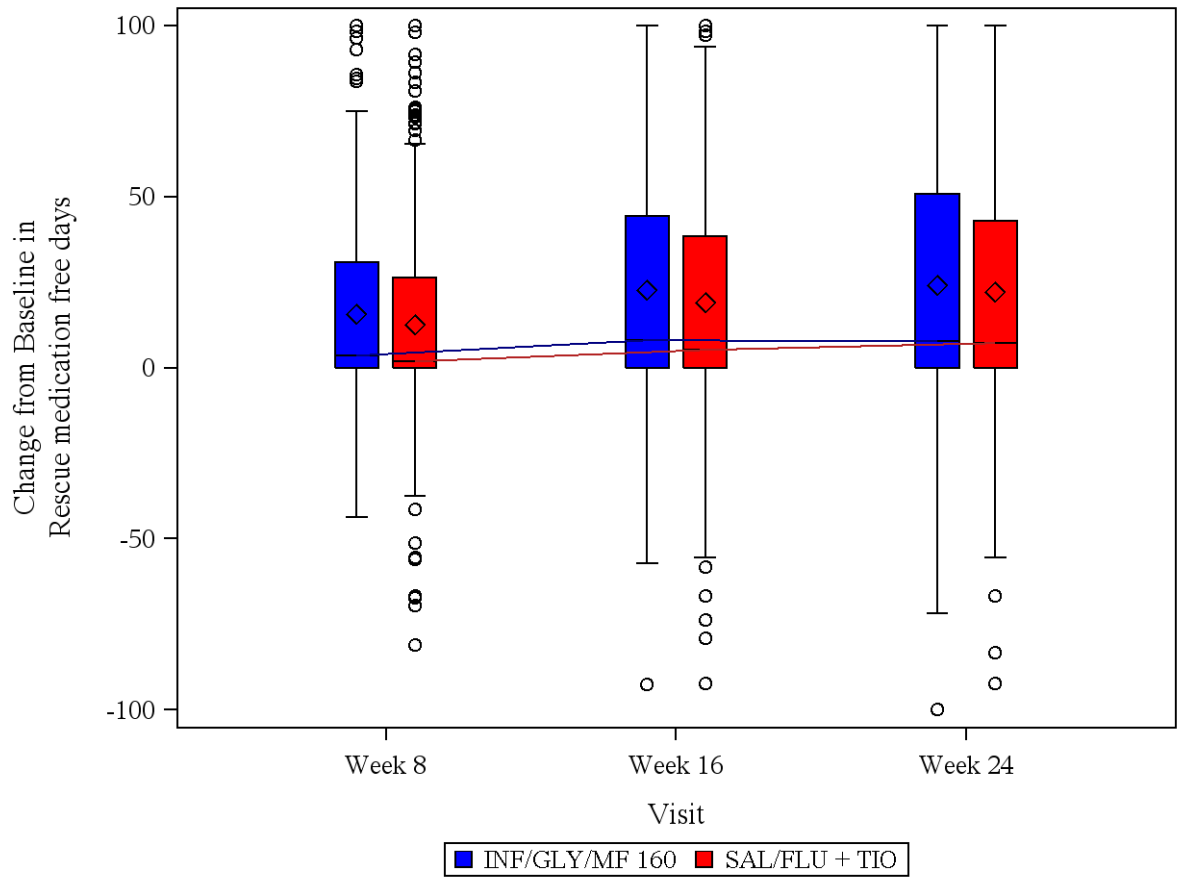
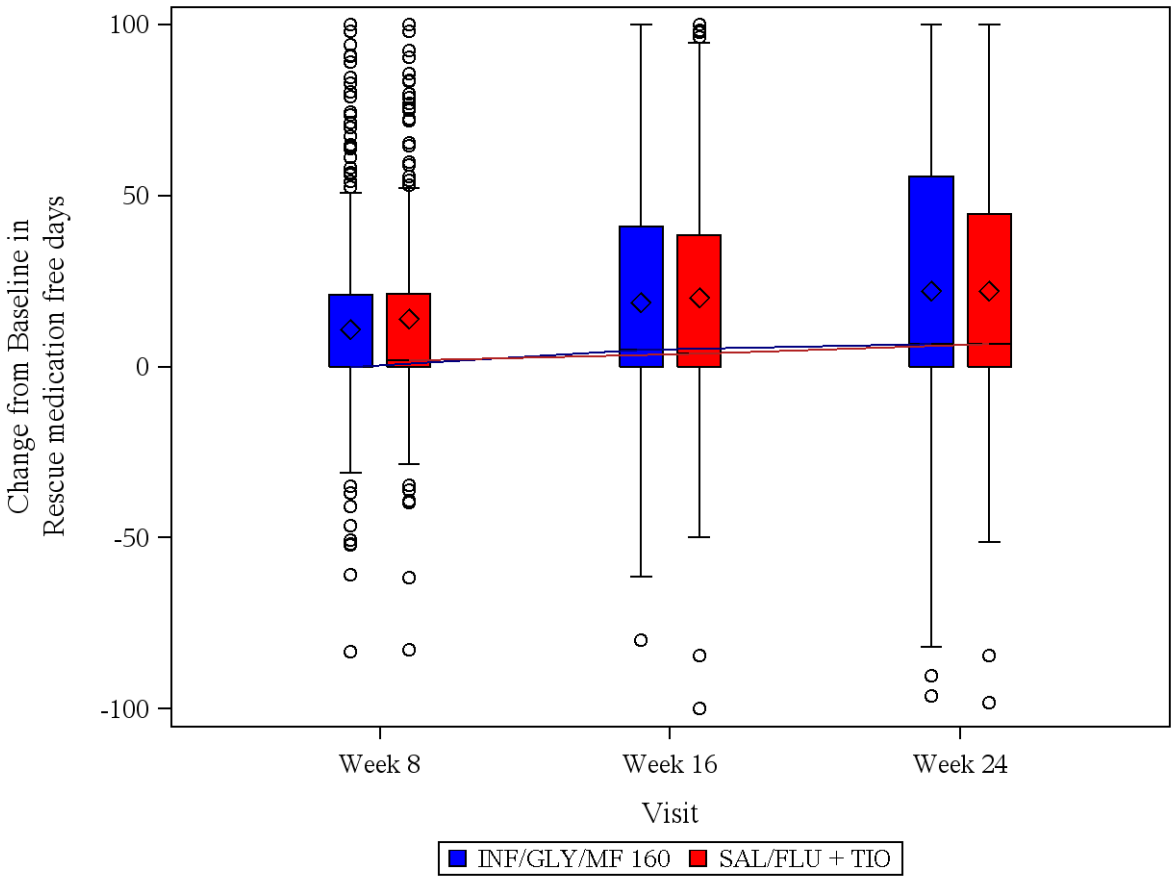


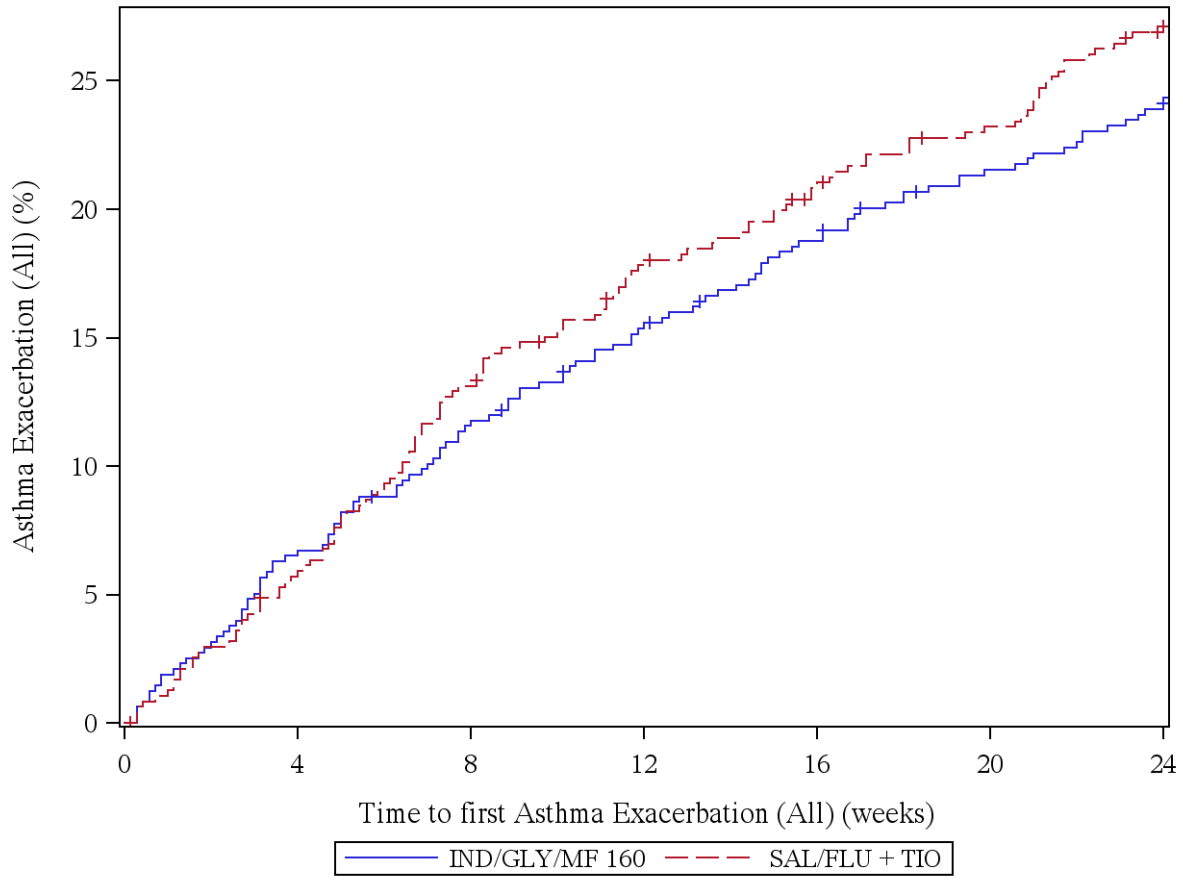
Figure 5.18.2 Rescue Medication (Rescue medication free days) - Change from Baseline by Patients' Prior Therapies (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



11. Kaplan-Meier-Plot: Asthma exacerbations (FAS)

11.1 Kaplan-Meier-Plot: Asthma Exacerbation (All) (FAS)

Figure 11.1 Asthma Exacerbation (All) (FAS)

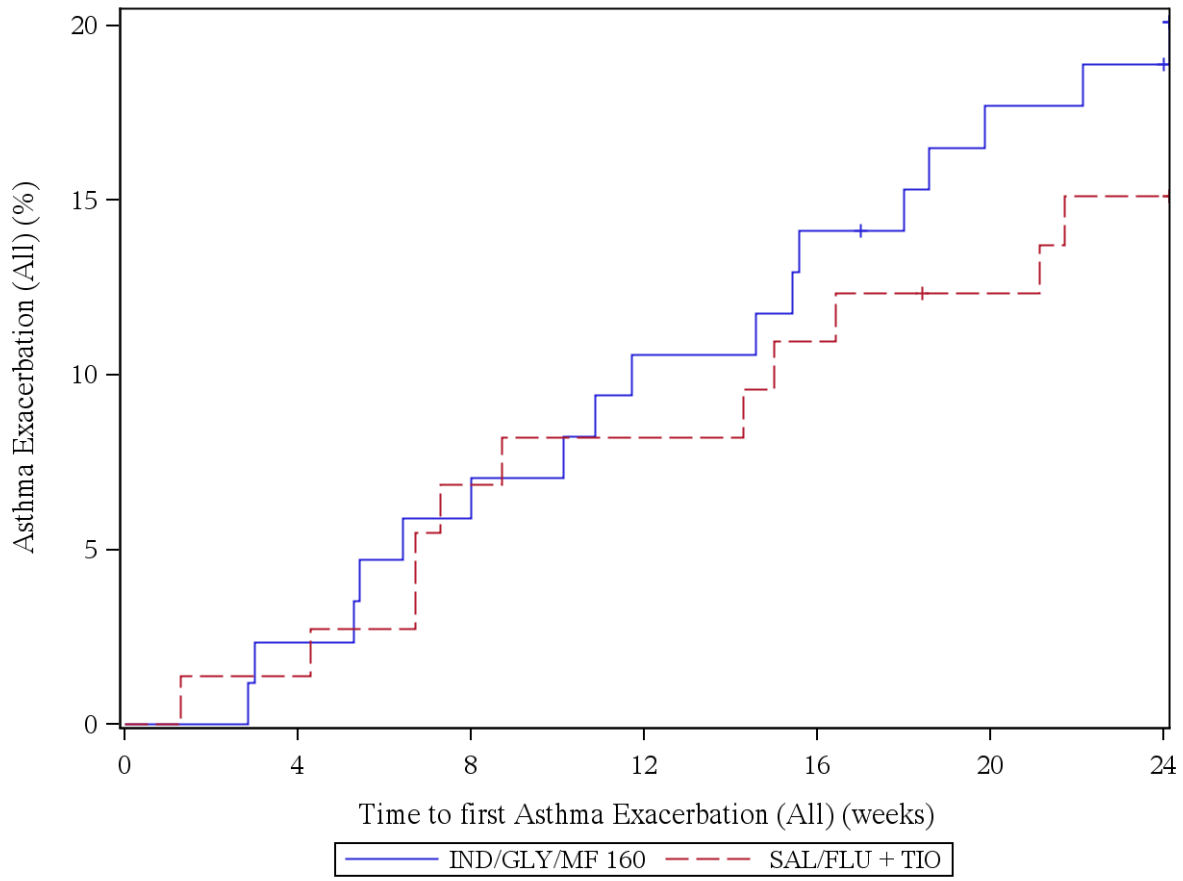


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 476/475, Week 8: 419/410, Week 16: 382/366, Week 24: 351/332

Analysis population: B2306 FAS total population

11.2 Kaplan-Meier-Plot: Asthma Exacerbation (All) by Age (FAS)

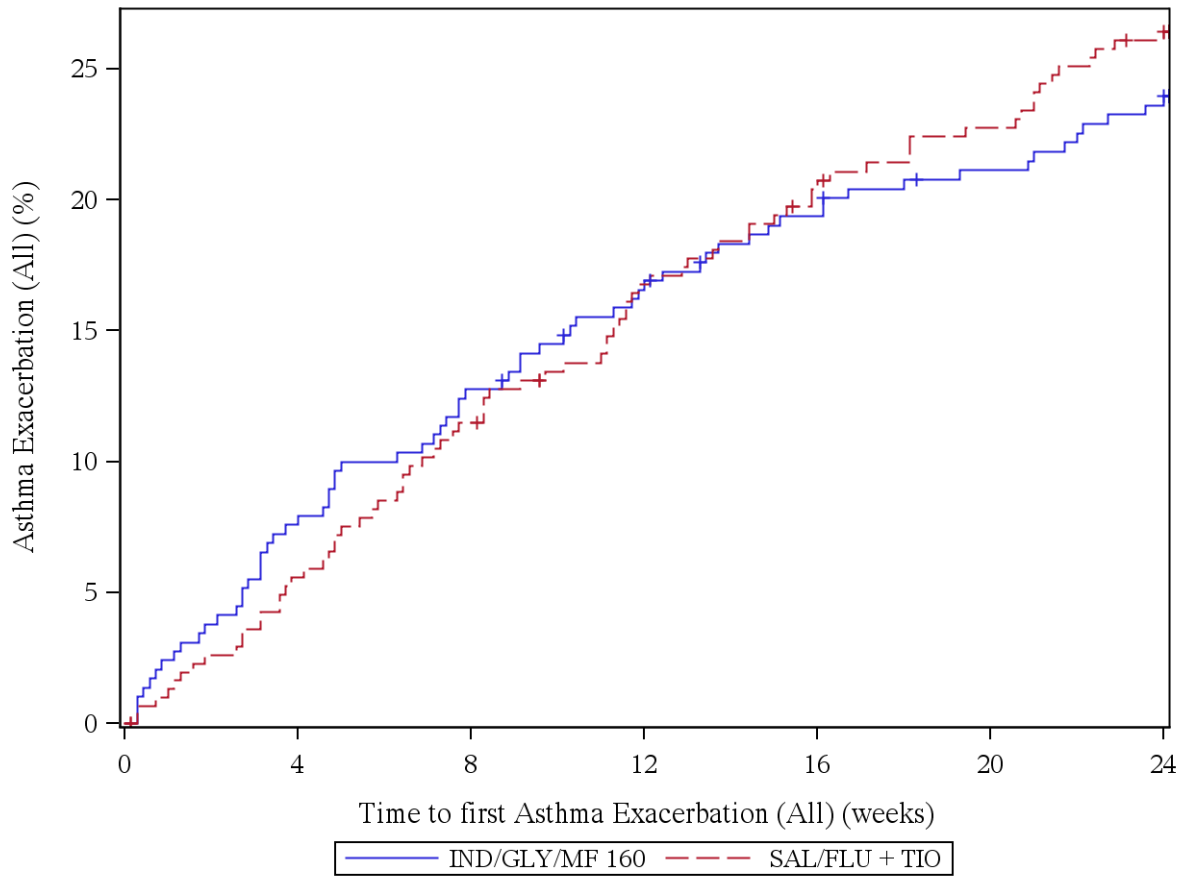
Figure 11.2.1 Asthma Exacerbation (All) (FAS), Age = 18-39 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 85/73, Week 8: 79/68, Week 16: 73/65, Week 24: 67/61

Analysis population: B2306 FAS total population

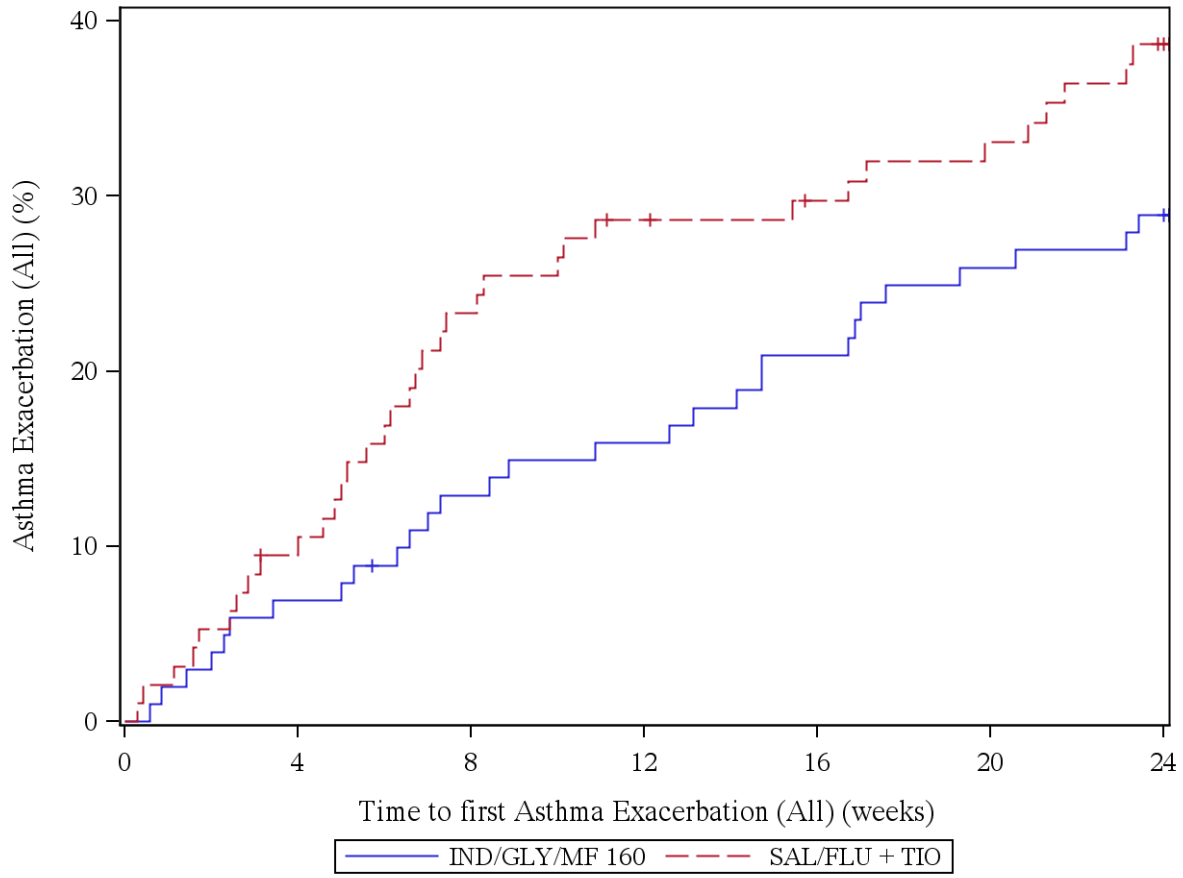
Figure 11.2.2 Asthma Exacerbation (All) (FAS), Age = 40-64 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 290/307, Week 8: 253/270, Week 16: 230/238, Week 24: 214/218

Analysis population: B2306 FAS total population

Figure 11.2.3 Asthma Exacerbation (All) (FAS), Age = ≥65 years

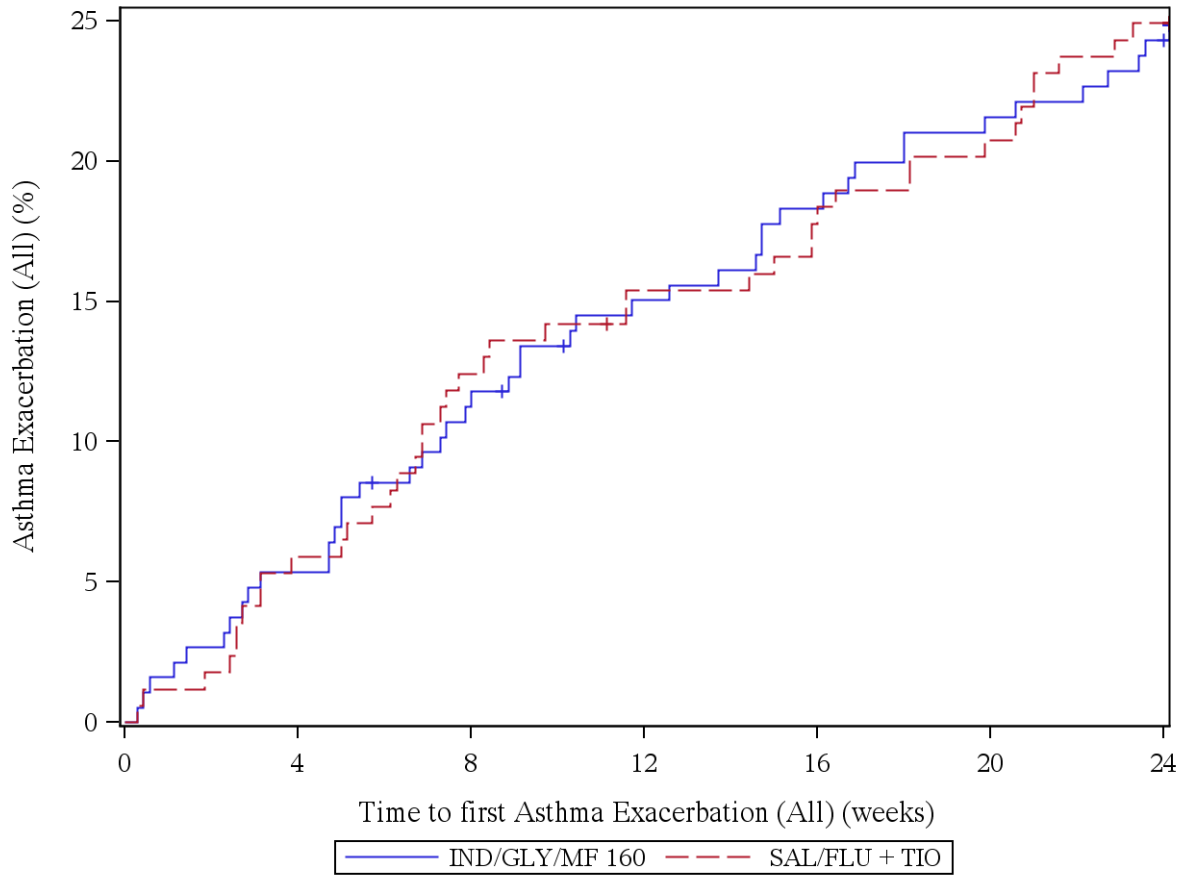


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 101/95, Week 8: 87/72, Week 16: 79/63, Week 24: 70/53

Analysis population: B2306 FAS total population

11.3 Kaplan-Meier-Plot: Asthma Exacerbation (All) by Gender (FAS)

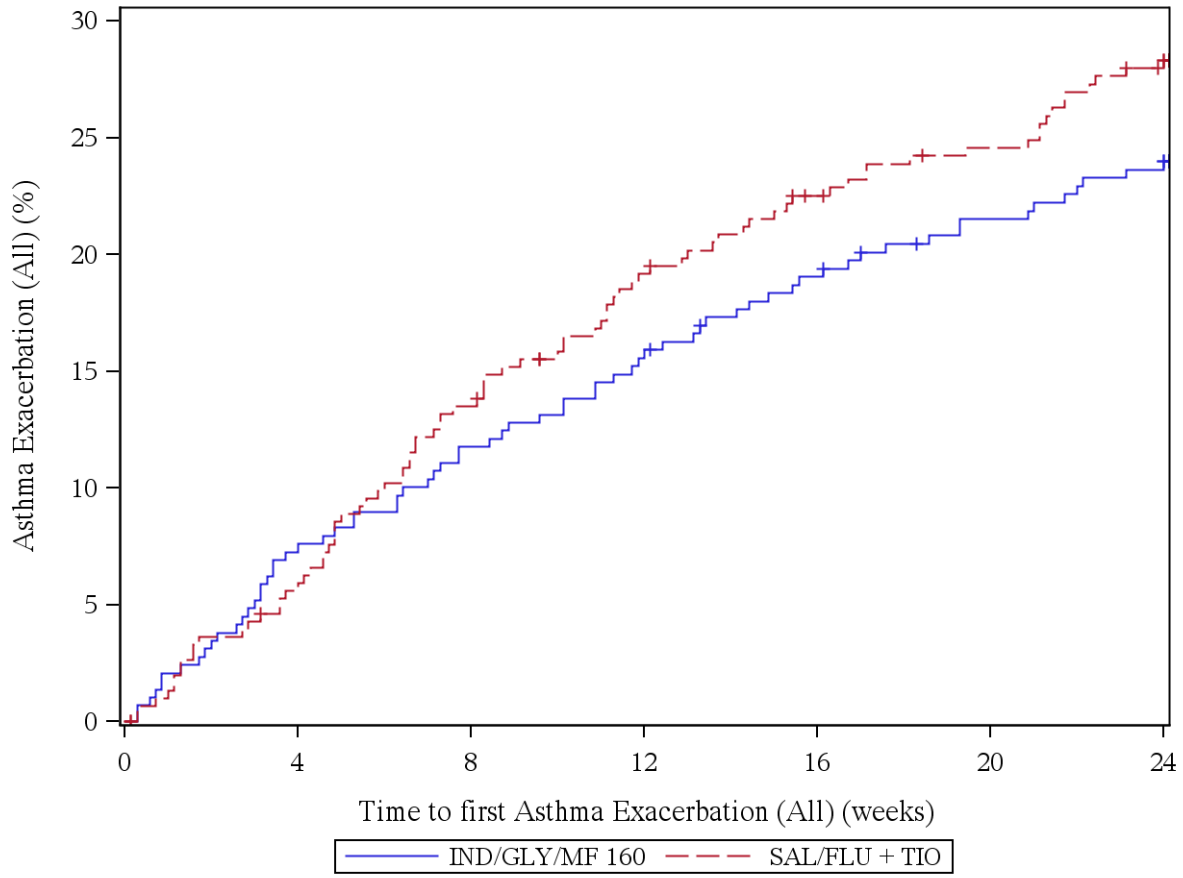
Figure 11.3.1 Asthma Exacerbation (All) (FAS), Gender = Male



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 187/169, Week 8: 164/148, Week 16: 150/137, Week 24: 138/126

Analysis population: B2306 FAS total population

Figure 11.3.2 Asthma Exacerbation (All) (FAS), Gender = Female

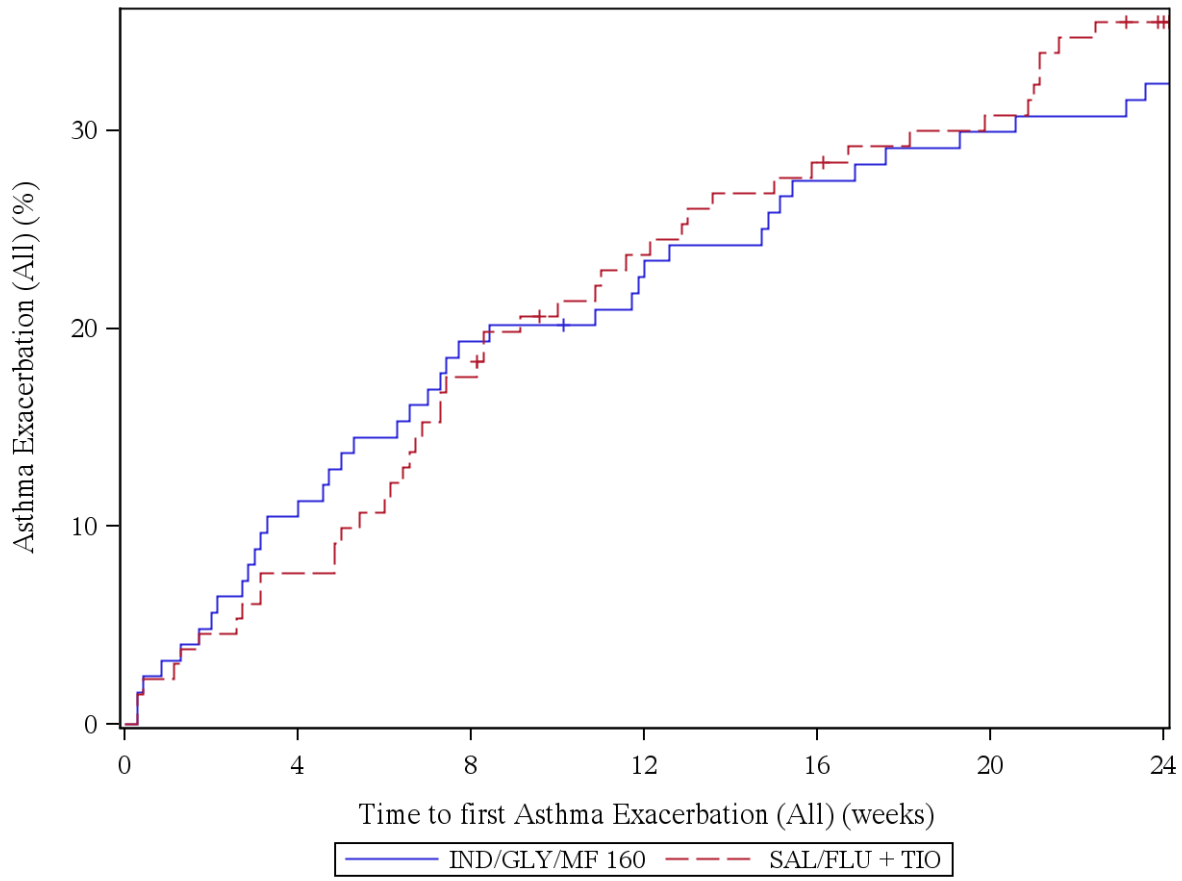


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 289/306, Week 8: 255/262, Week 16: 232/229, Week 24: 213/206

Analysis population: B2306 FAS total population

11.4 Kaplan-Meier-Plot: Asthma Exacerbation (All) by Region (FAS)

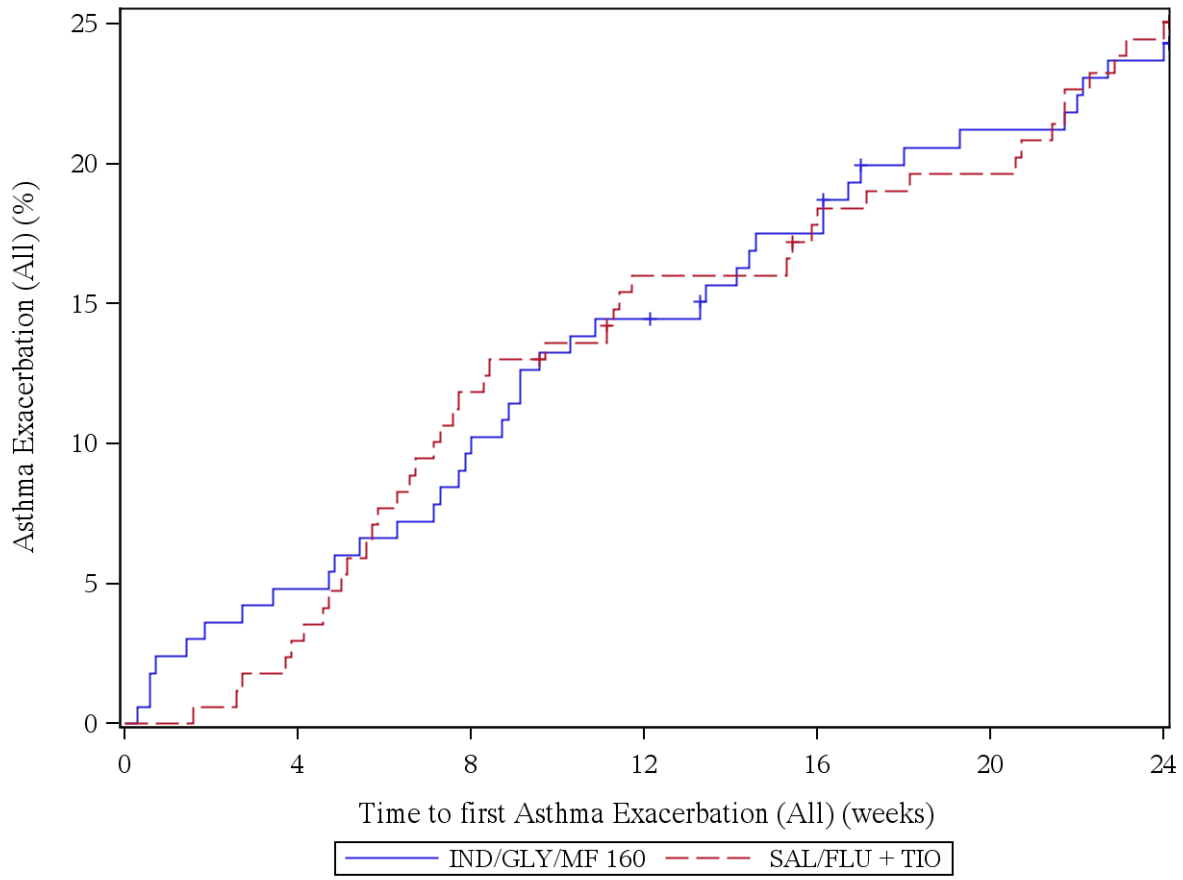
Figure 11.4.1 Asthma Exacerbation (All) (FAS), Region = Asia



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 124/131, Week 8: 100/108, Week 16: 89/92, Week 24: 83/79

Analysis population: B2306 FAS total population

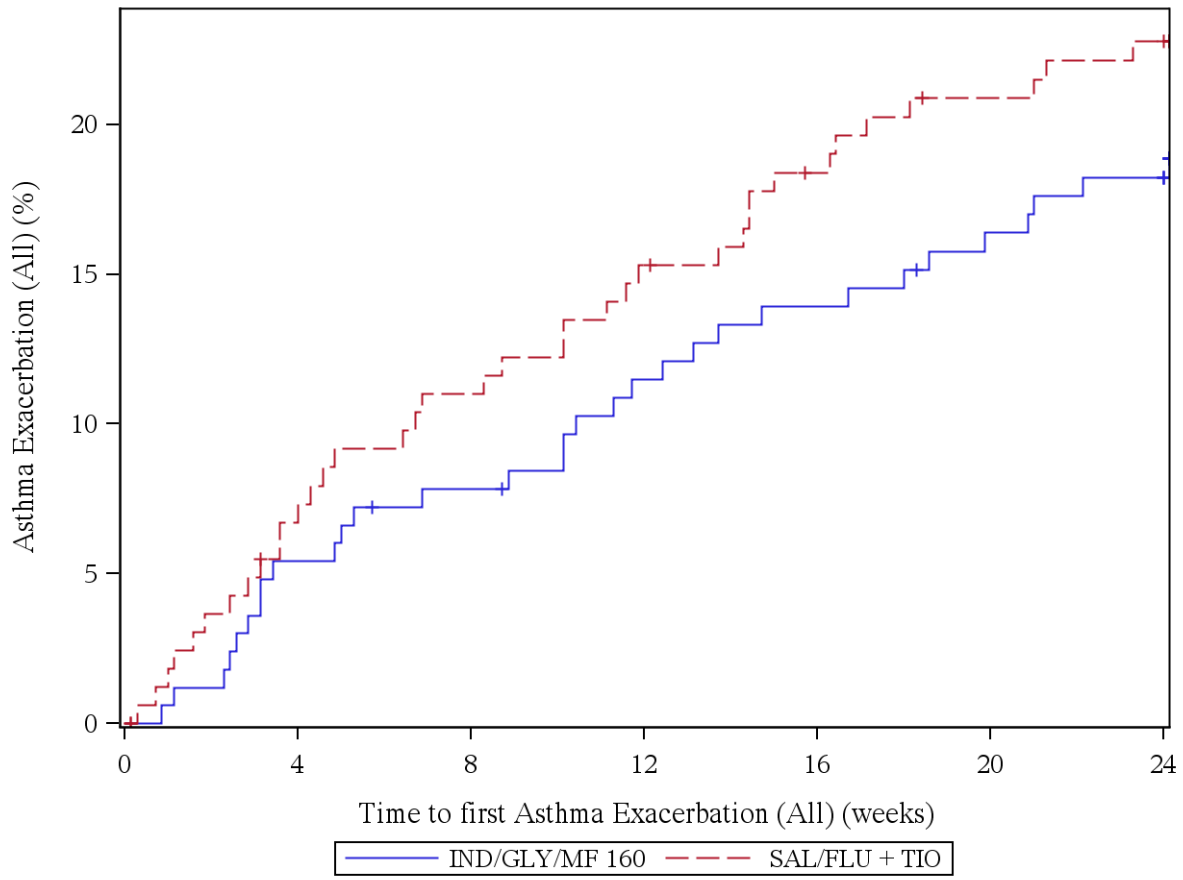
Figure 11.4.2 Asthma Exacerbation (All) (FAS), Region = Europe



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 166/169, Week 8: 149/149, Week 16: 135/135, Week 24: 122/124

Analysis population: B2306 FAS total population

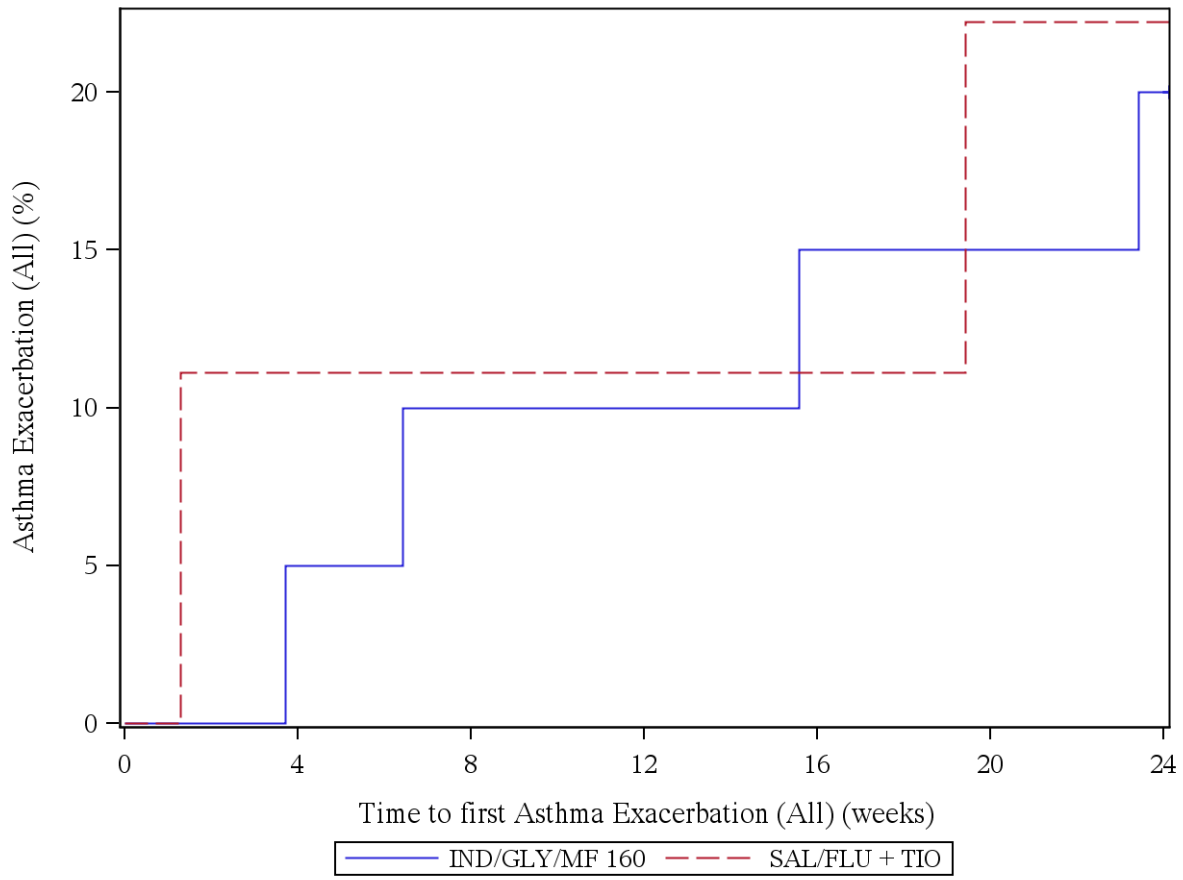
Figure 11.4.3 Asthma Exacerbation (All) (FAS), Region = Latin America



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 166/166, Week 8: 152/145, Week 16: 141/131, Week 24: 130/122

Analysis population: B2306 FAS total population

Figure 11.4.4 Asthma Exacerbation (All) (FAS), Region = Others

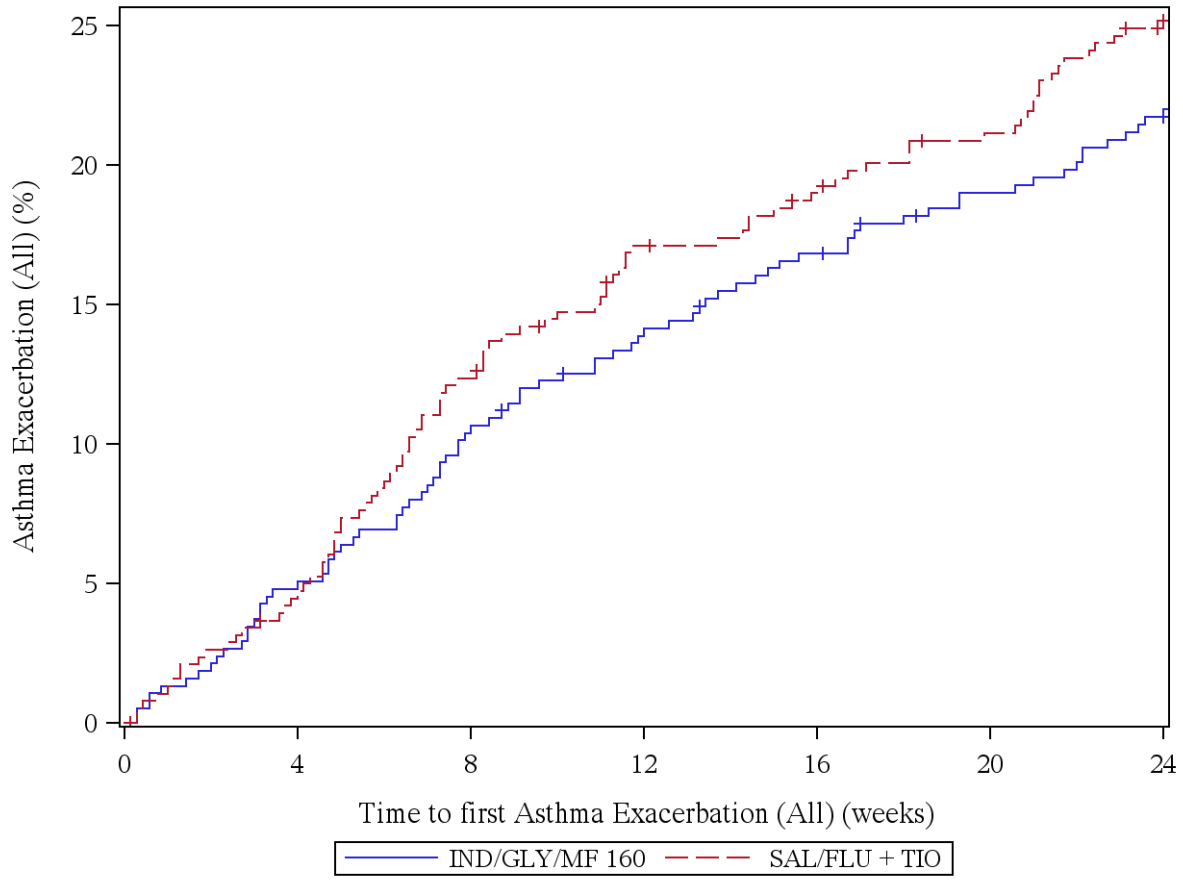


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 20/9, Week 8: 18/8, Week 16: 17/8, Week 24: 16/7

Analysis population: B2306 FAS total population

11.5 Kaplan-Meier-Plot: Asthma Exacerbation (All) by History of Asthma Exacerbation (FAS)

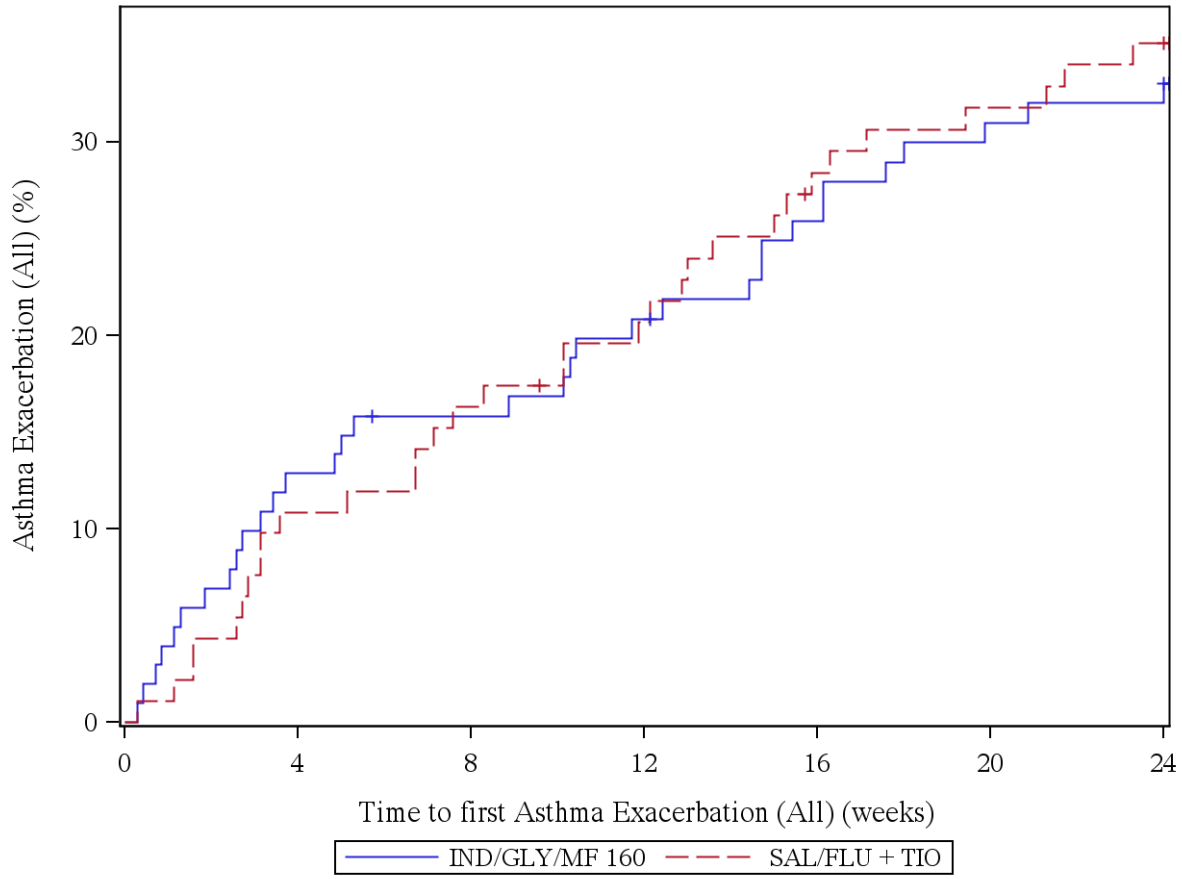
Figure 11.5.1 Asthma Exacerbation (All) (FAS), Asthma exacerbations in the 12 months prior to screening = 1



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 375/383, Week 8: 335/333, Week 16: 309/302, Week 24: 286/275

Analysis population: B2306 FAS total population

Figure 11.5.2 Asthma Exacerbation (All) (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2

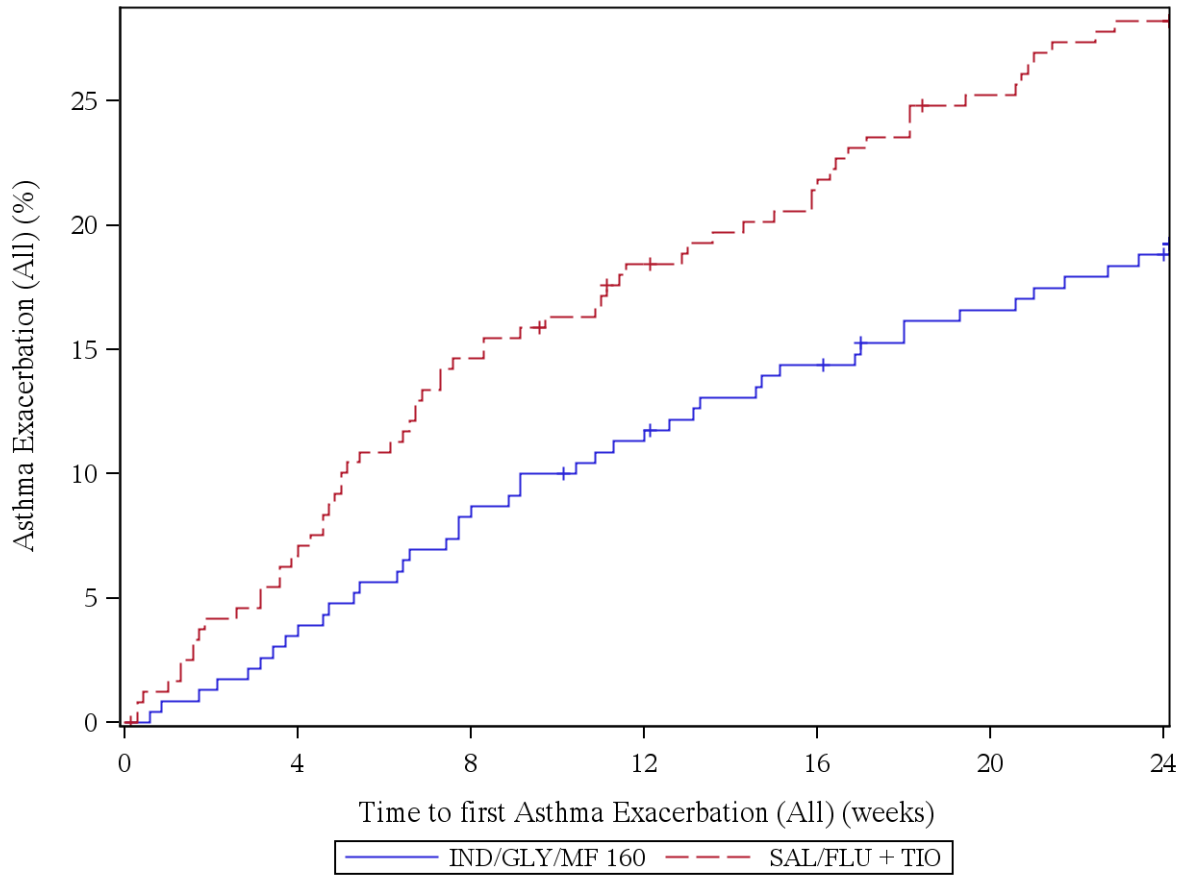


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 101/92, Week 8: 84/77, Week 16: 73/64, Week 24: 65/57

Analysis population: B2306 FAS total population

11.6 Kaplan-Meier-Plot: Asthma Exacerbation (All) by Patients' Prior Therapies (FAS)

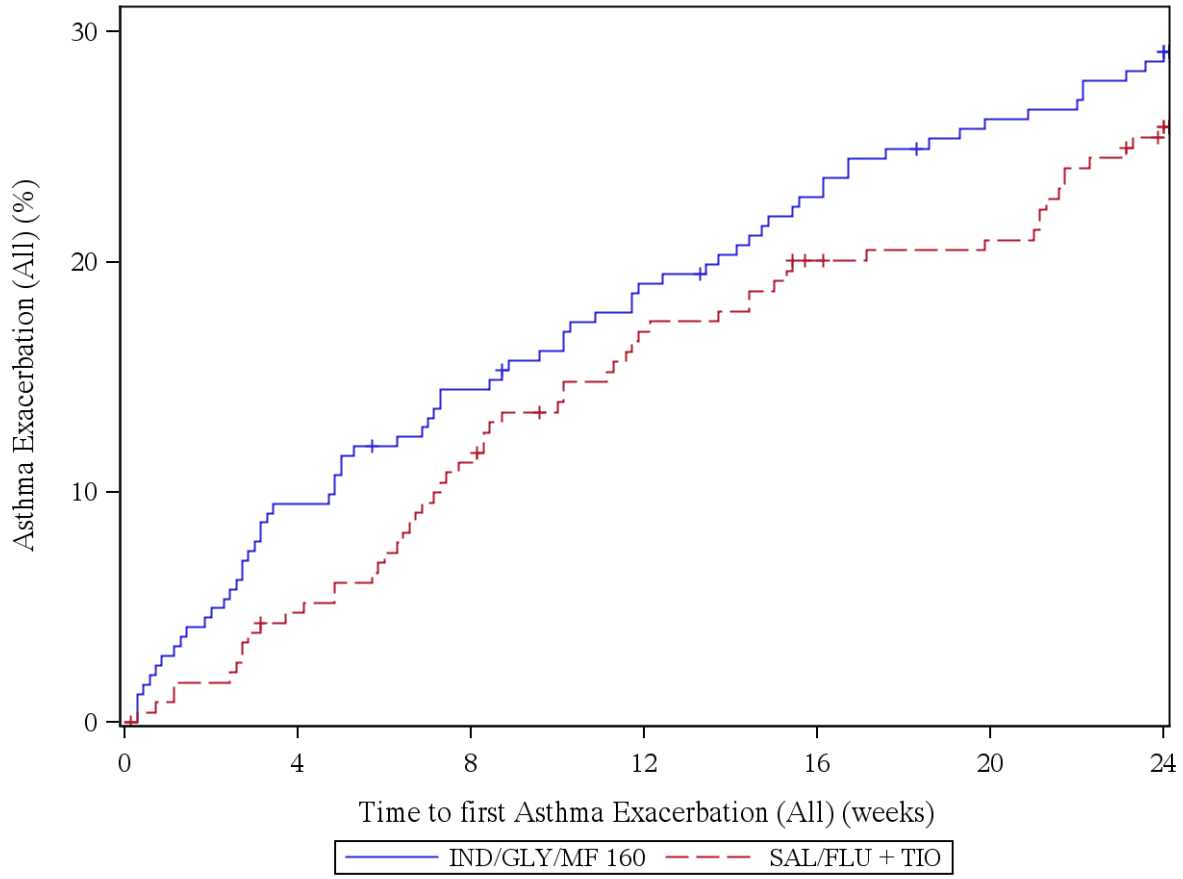
Figure 11.6.1 Asthma Exacerbation (All) (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 230/240, Week 8: 210/204, Week 16: 195/184, Week 24: 182/168

Analysis population: B2306 FAS total population

Figure 11.6.2 Asthma Exacerbation (All) (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA

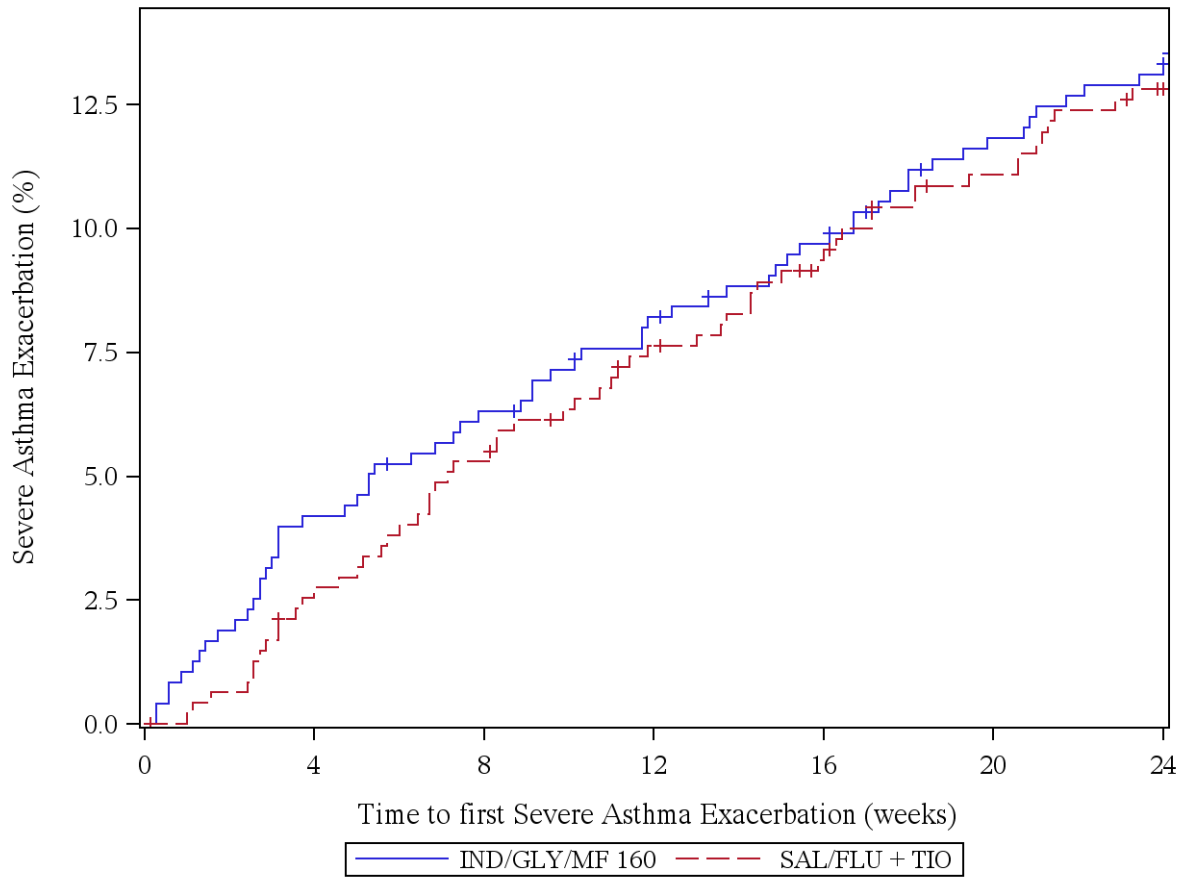


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 242/232, Week 8: 206/204, Week 16: 184/180, Week 24: 166/162

Analysis population: B2306 FAS total population

11.7 Kaplan-Meier-Plot: Severe Asthma Exacerbation (FAS)

Figure 11.7 Severe Asthma Exacerbation (FAS)

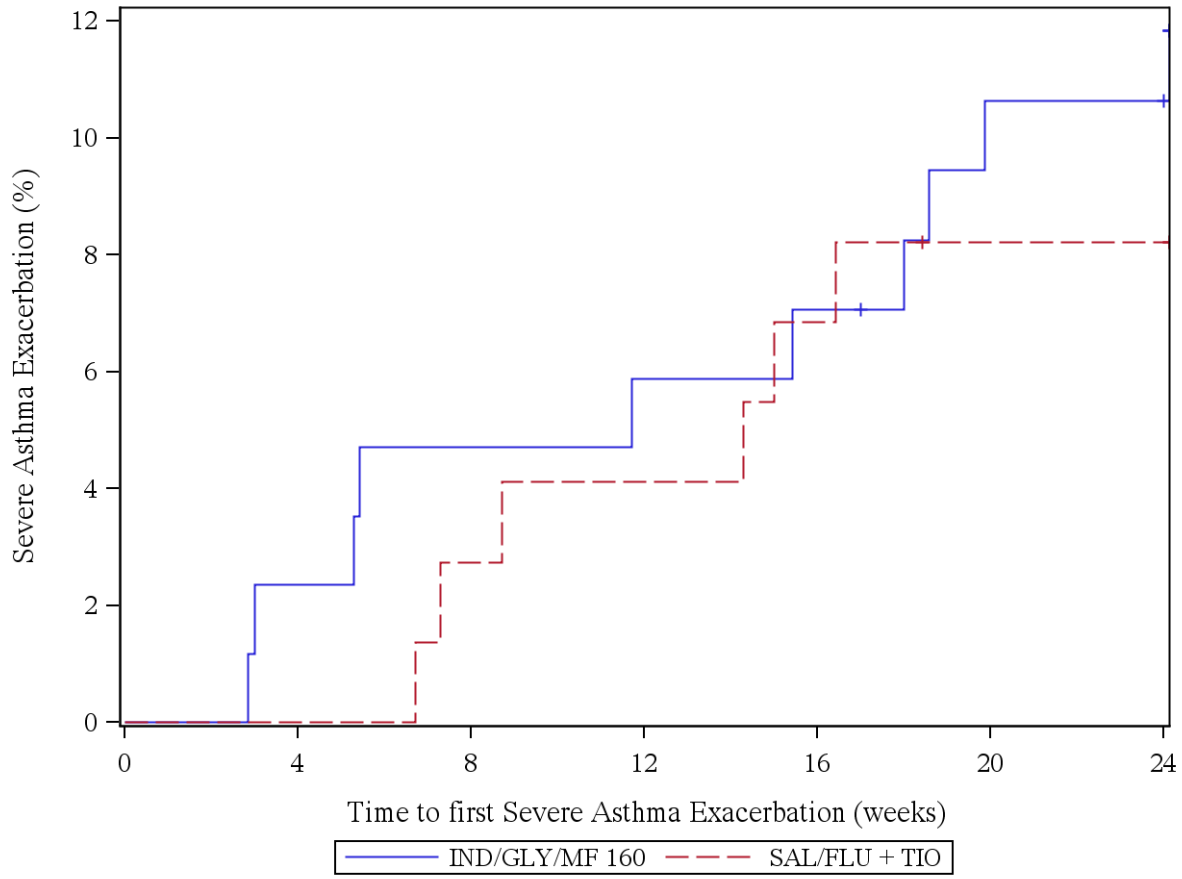


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 476/475, Week 8: 445/447, Week 16: 425/420, Week 24: 402/398

Analysis population: B2306 FAS total population

11.8 Kaplan-Meier-Plot: Severe Asthma Exacerbation by Age (FAS)

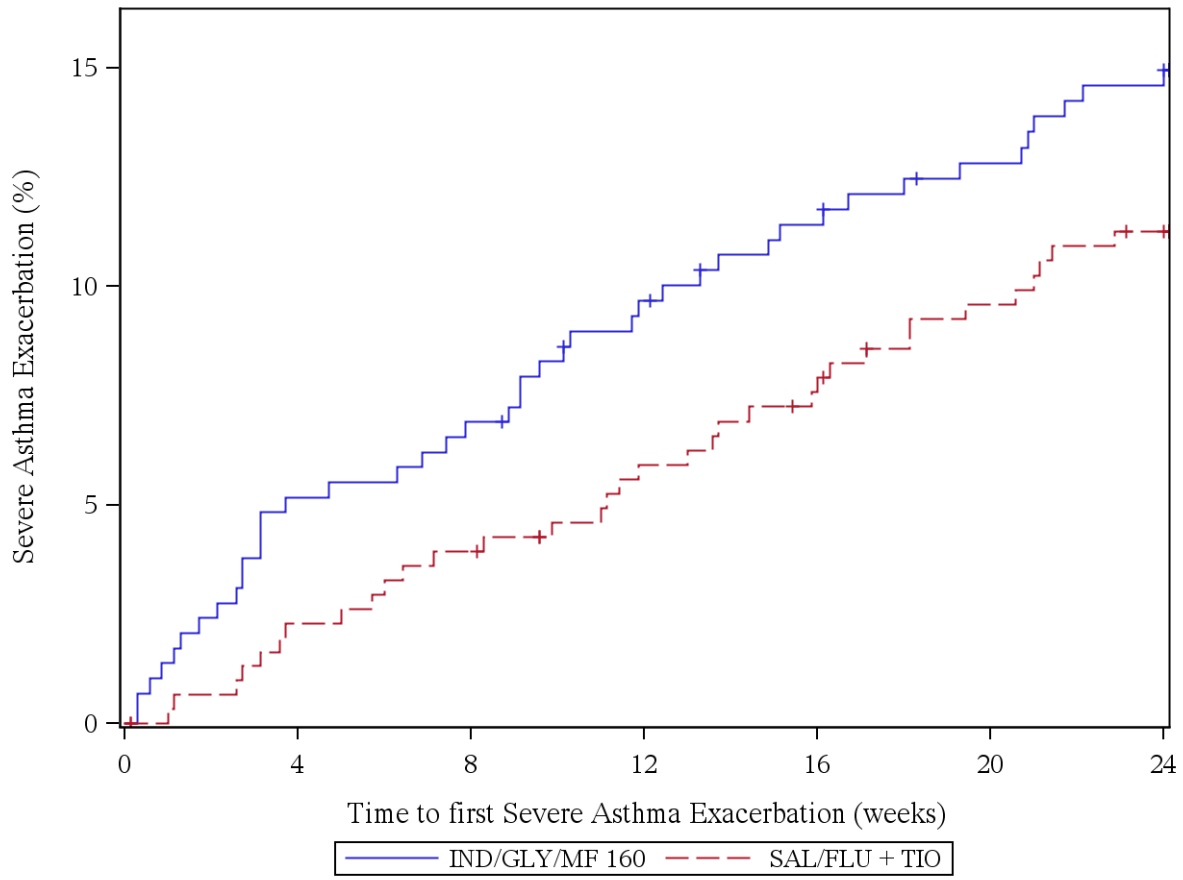
Figure 11.8.1 Severe Asthma Exacerbation (FAS), Age = 18-39 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 85/73, Week 8: 81/71, Week 16: 79/68, Week 24: 74/66

Analysis population: B2306 FAS total population

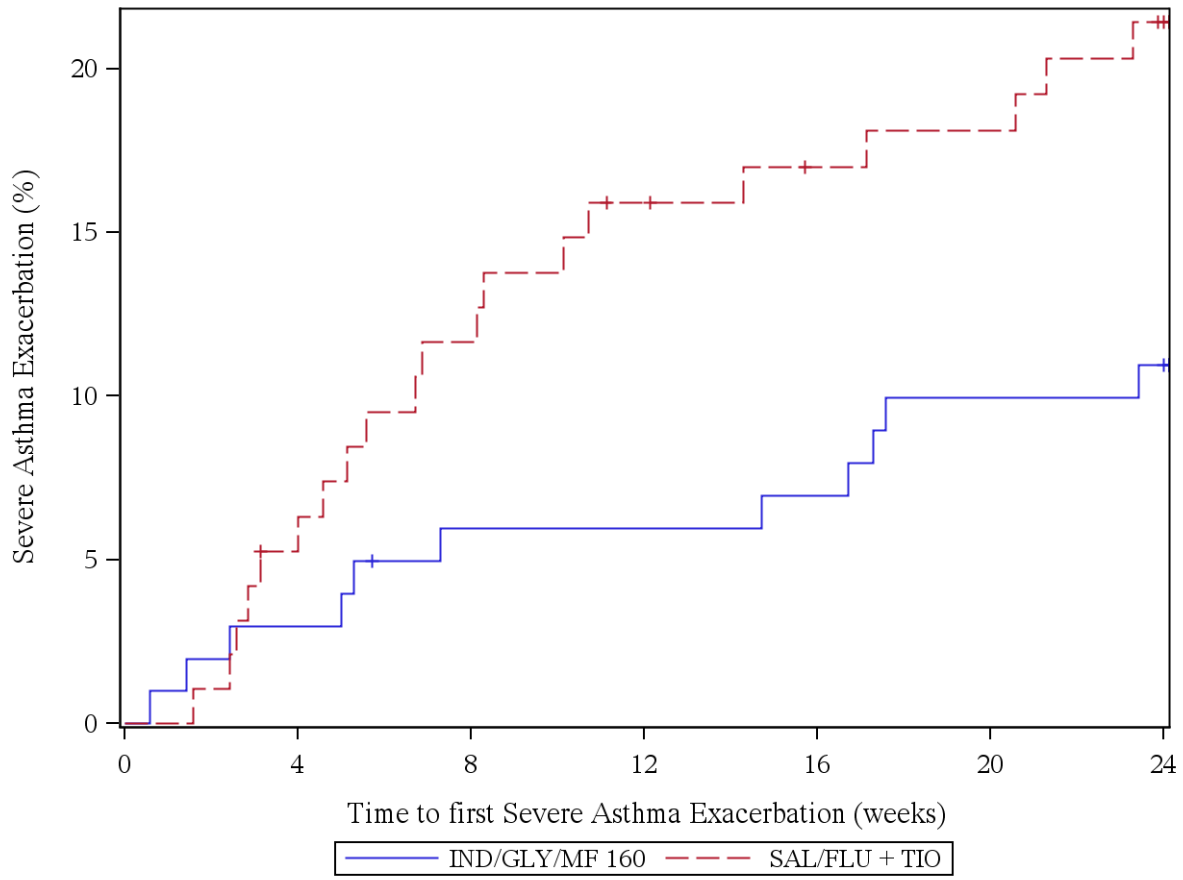
Figure 11.8.2 Severe Asthma Exacerbation (FAS), Age = 40-64 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 290/307, Week 8: 270/293, Week 16: 253/277, Week 24: 240/263

Analysis population: B2306 FAS total population

Figure 11.8.3 Severe Asthma Exacerbation (FAS), Age = ≥65 years

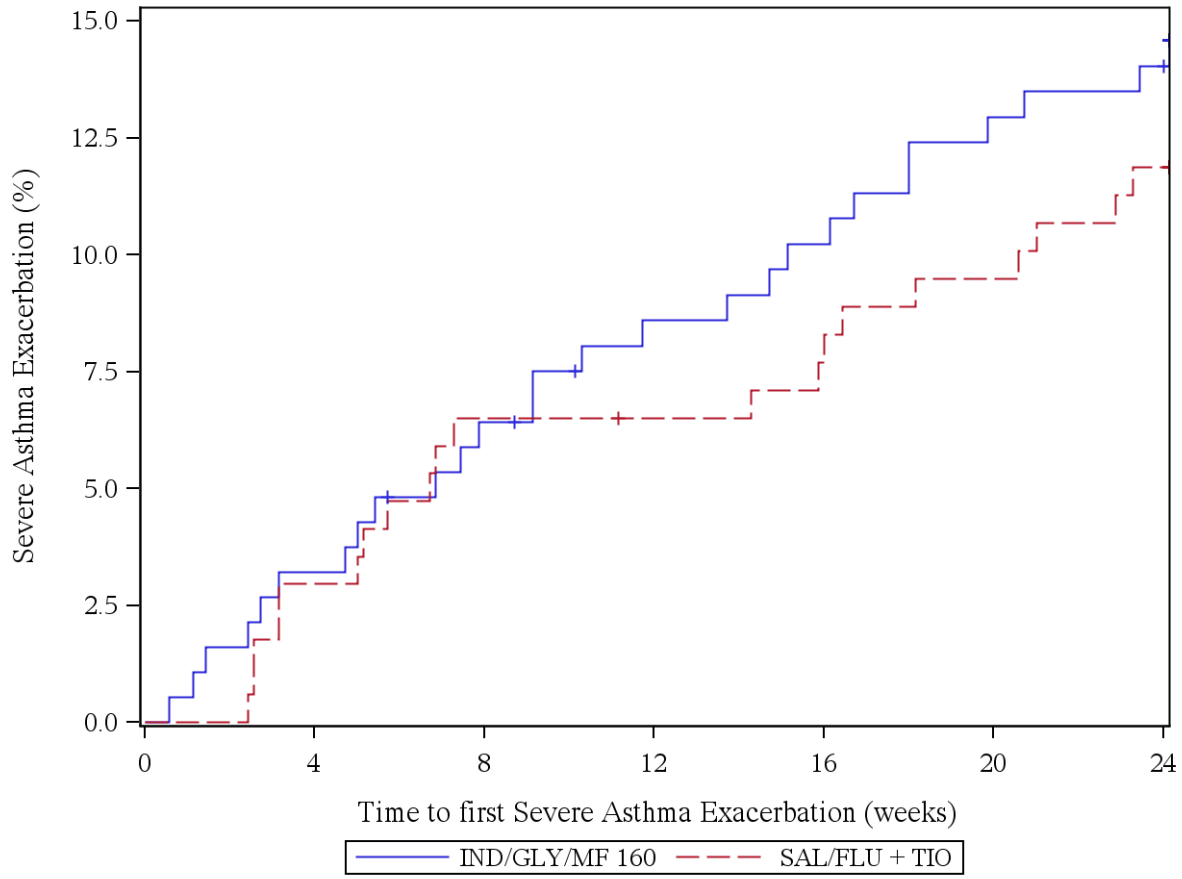


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 101/95, Week 8: 94/83, Week 16: 93/75, Week 24: 88/69

Analysis population: B2306 FAS total population

11.9 Kaplan-Meier-Plot: Severe Asthma Exacerbation by Gender (FAS)

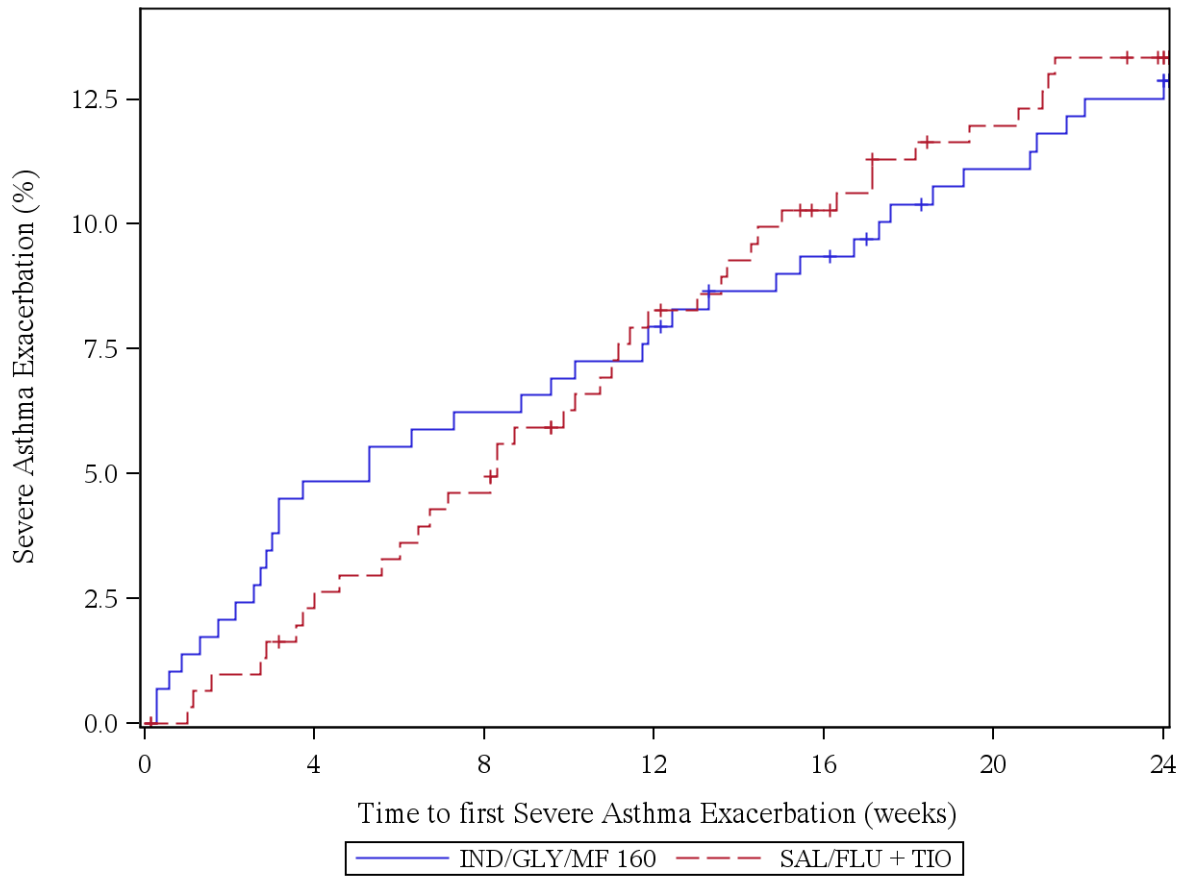
Figure 11.9.1 Severe Asthma Exacerbation (FAS), Gender = Male



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 187/169, Week 8: 174/158, Week 16: 165/154, Week 24: 157/148

Analysis population: B2306 FAS total population

Figure 11.9.2 Severe Asthma Exacerbation (FAS), Gender = Female

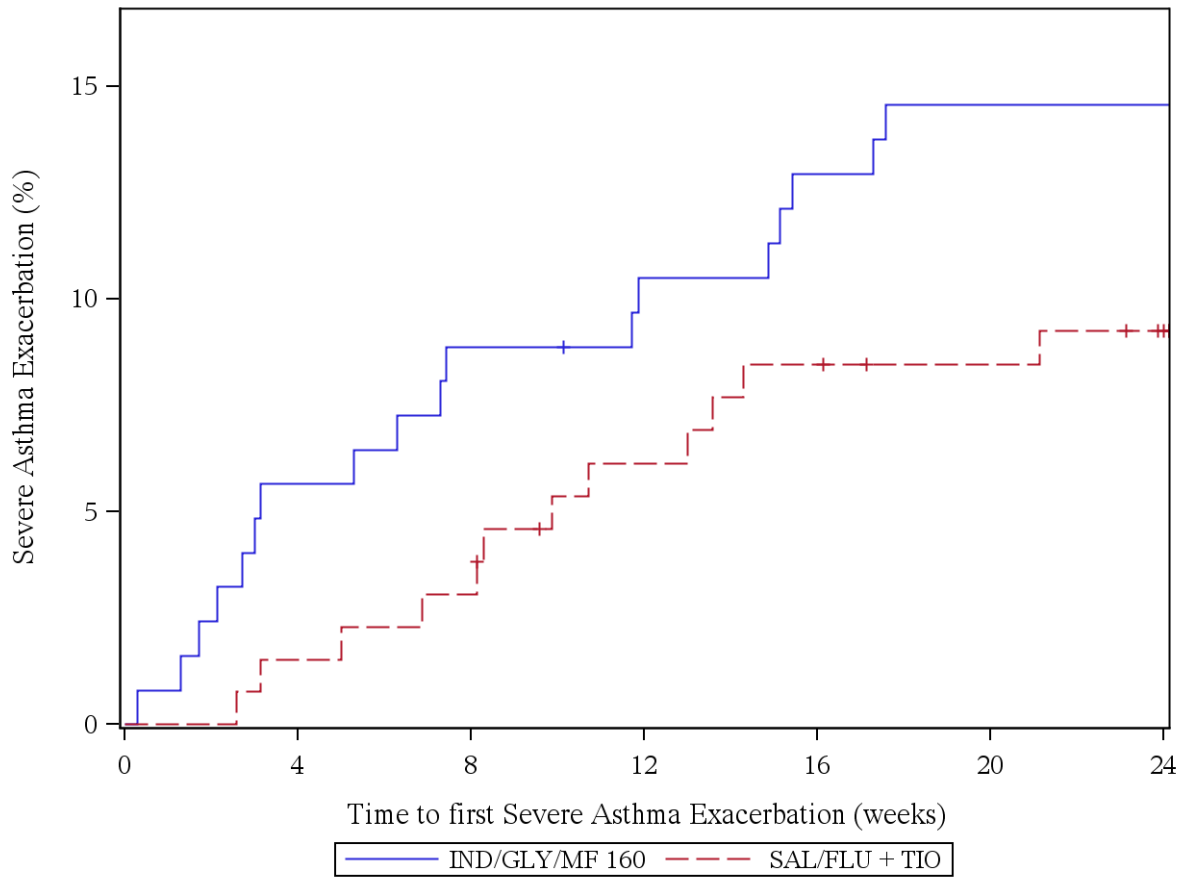


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 289/306, Week 8: 271/289, Week 16: 260/266, Week 24: 245/250

Analysis population: B2306 FAS total population

11.10 Kaplan-Meier-Plot: Severe Asthma Exacerbation by Region (FAS)

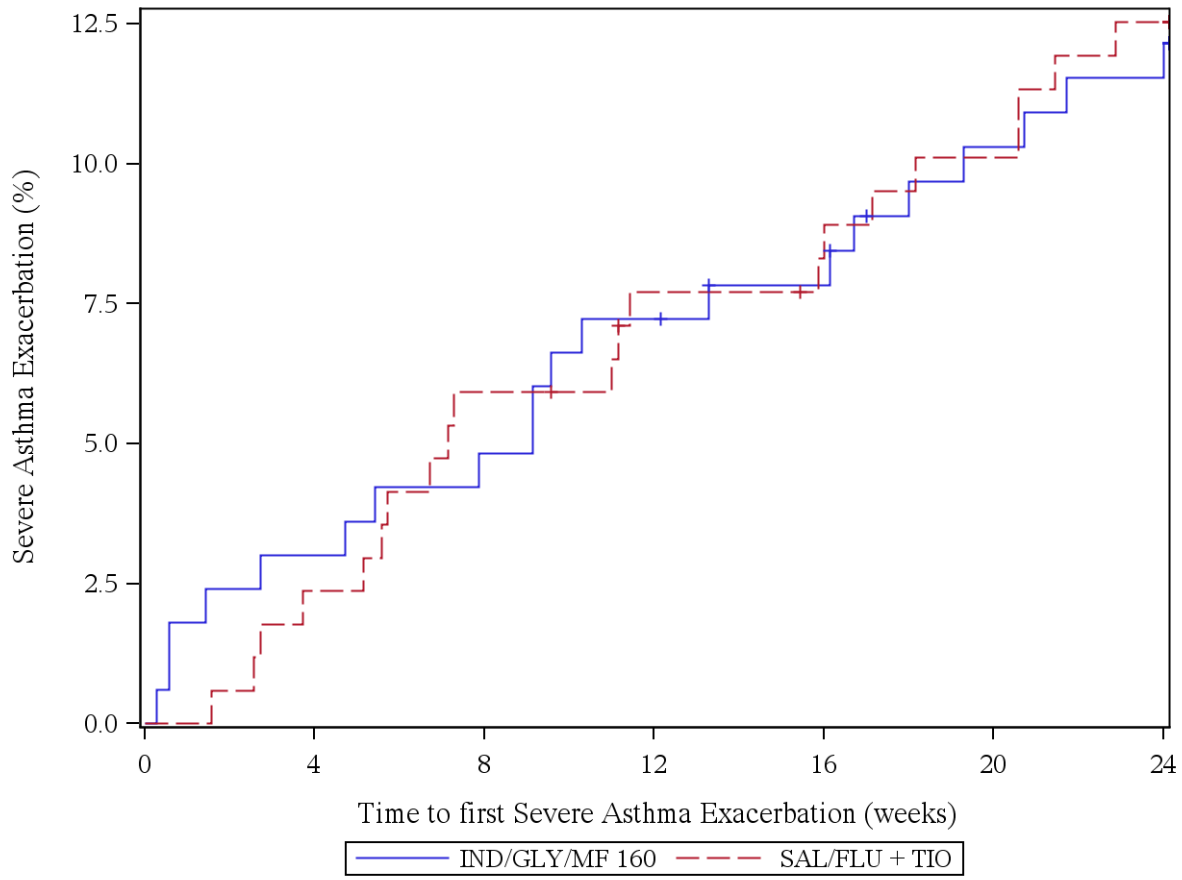
Figure 11.10.1 Severe Asthma Exacerbation (FAS), Region = Asia



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 124/131, Week 8: 113/127, Week 16: 107/118, Week 24: 105/112

Analysis population: B2306 FAS total population

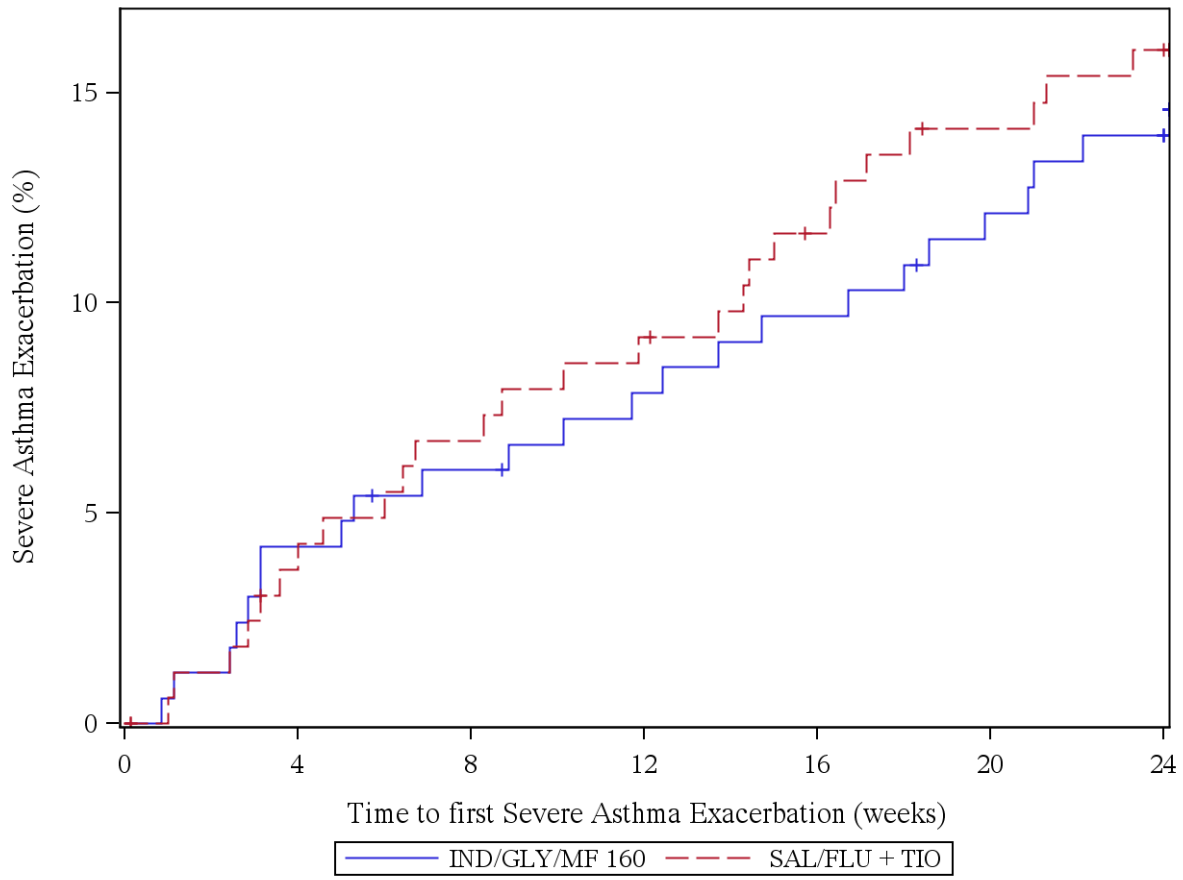
Figure 11.10.2 Severe Asthma Exacerbation (FAS), Region = Europe



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 166/169, Week 8: 158/159, Week 16: 151/151, Week 24: 142/145

Analysis population: B2306 FAS total population

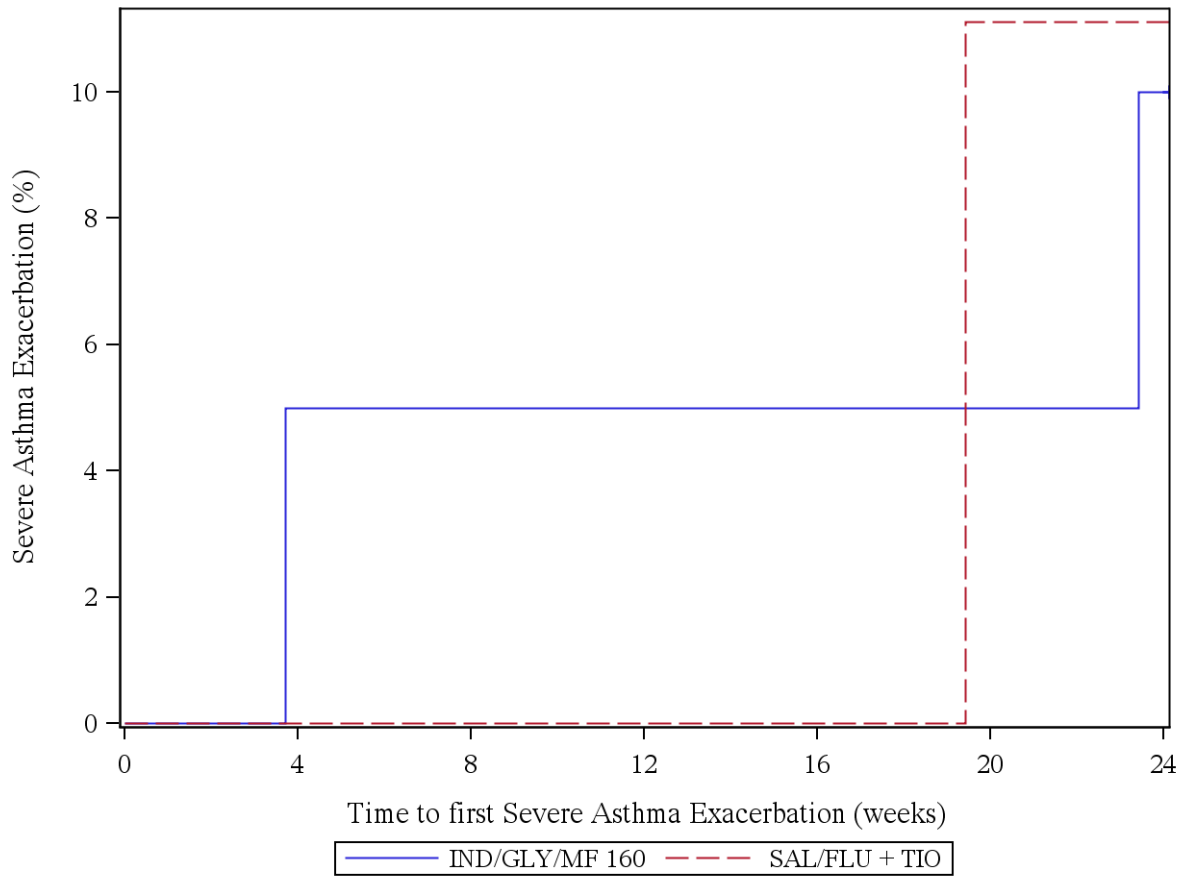
Figure 11.10.3 Severe Asthma Exacerbation (FAS), Region = Latin America



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 166/166, Week 8: 155/152, Week 16: 148/142, Week 24: 137/133

Analysis population: B2306 FAS total population

Figure 11.10.4 Severe Asthma Exacerbation (FAS), Region = Others

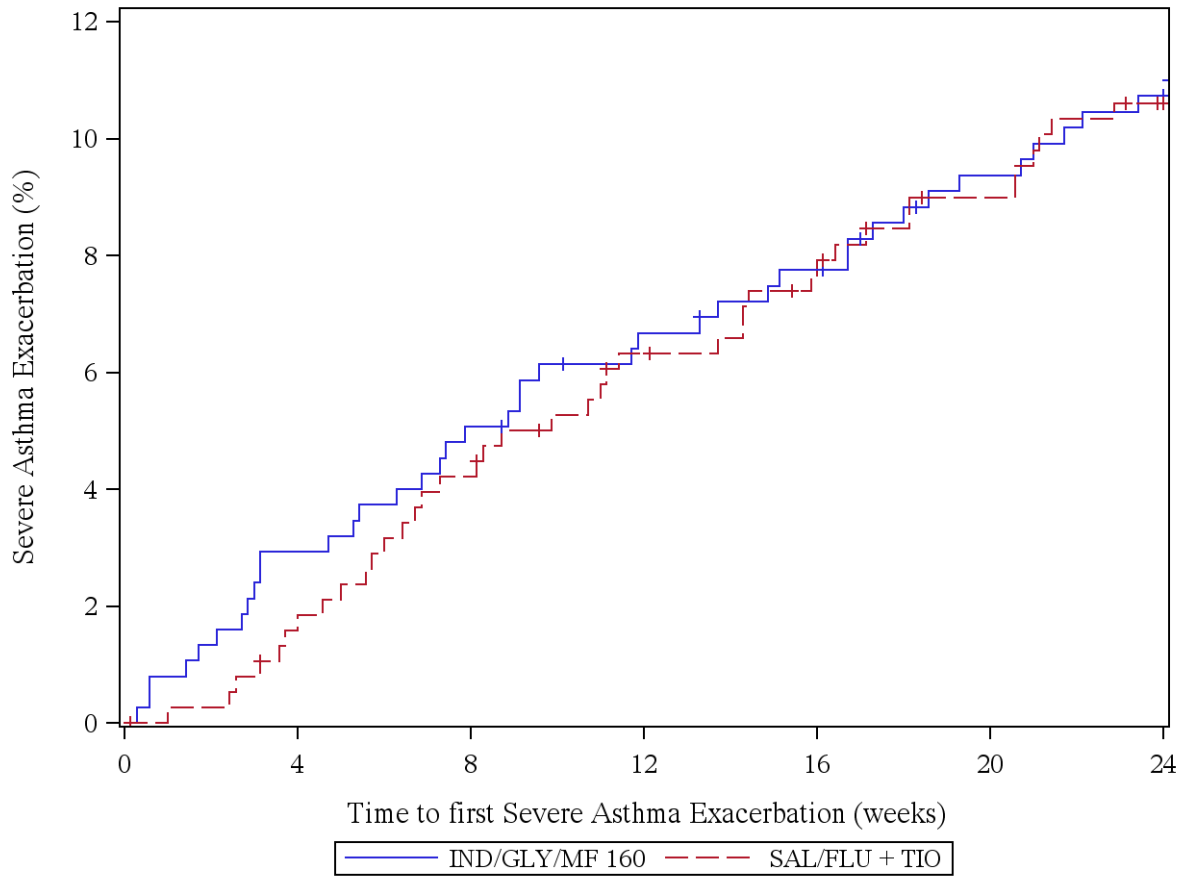


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 20/9, Week 8: 19/9, Week 16: 19/9, Week 24: 18/8

Analysis population: B2306 FAS total population

11.11 Kaplan-Meier-Plot: Severe Asthma Exacerbation by History of Asthma Exacerbation (FAS)

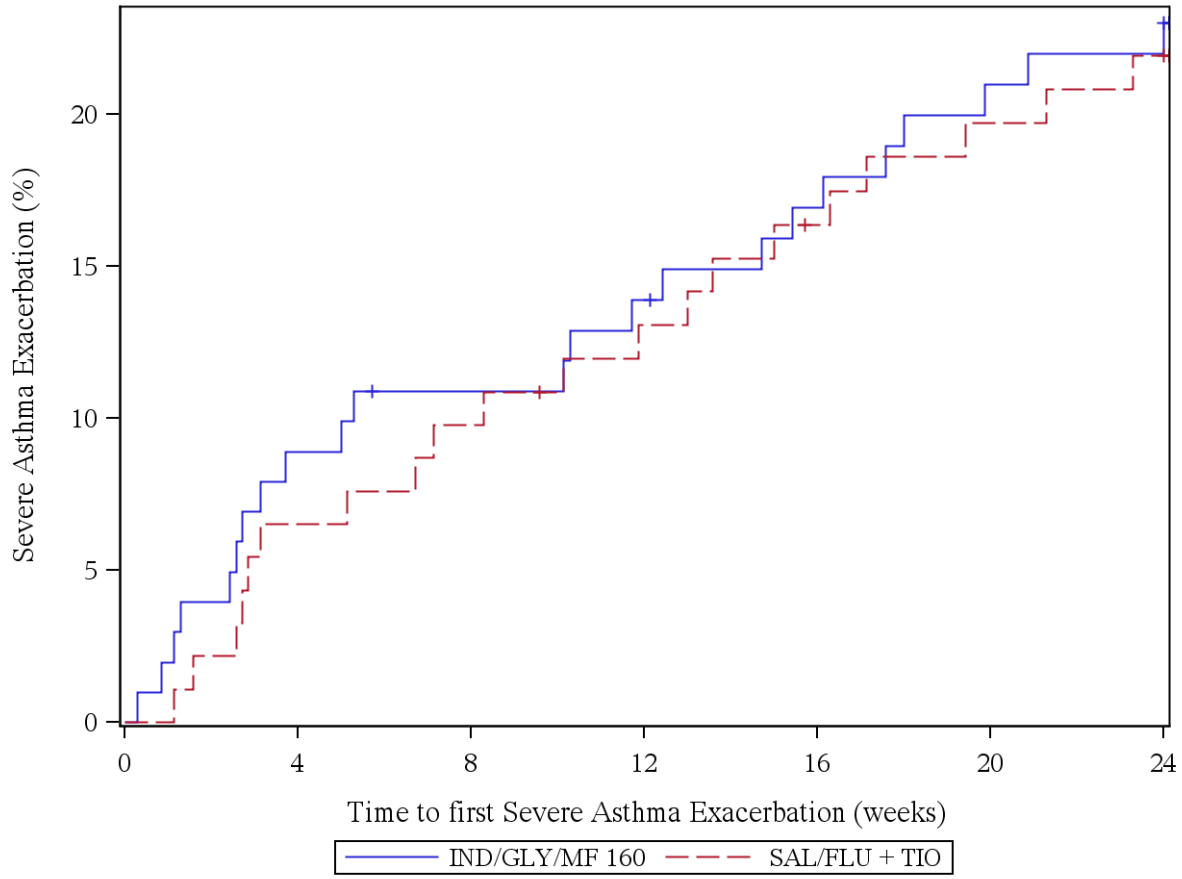
Figure 11.11.1 Severe Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 375/383, Week 8: 356/364, Week 16: 343/345, Week 24: 327/329

Analysis population: B2306 FAS total population

Figure 11.11.2 Severe Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2

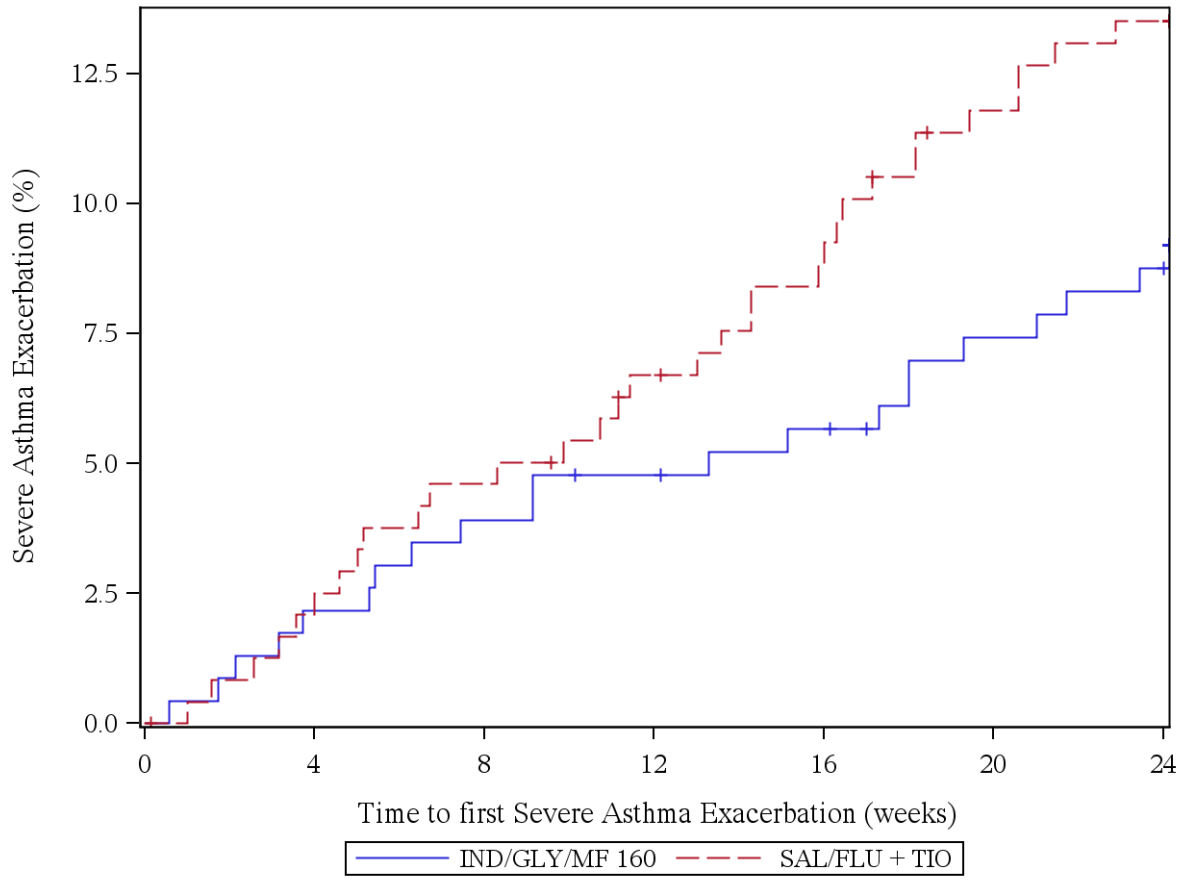


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 101/92, Week 8: 89/83, Week 16: 82/75, Week 24: 75/69

Analysis population: B2306 FAS total population

11.12 Kaplan-Meier-Plot: Severe Asthma Exacerbation by Patients' Prior Therapies (FAS)

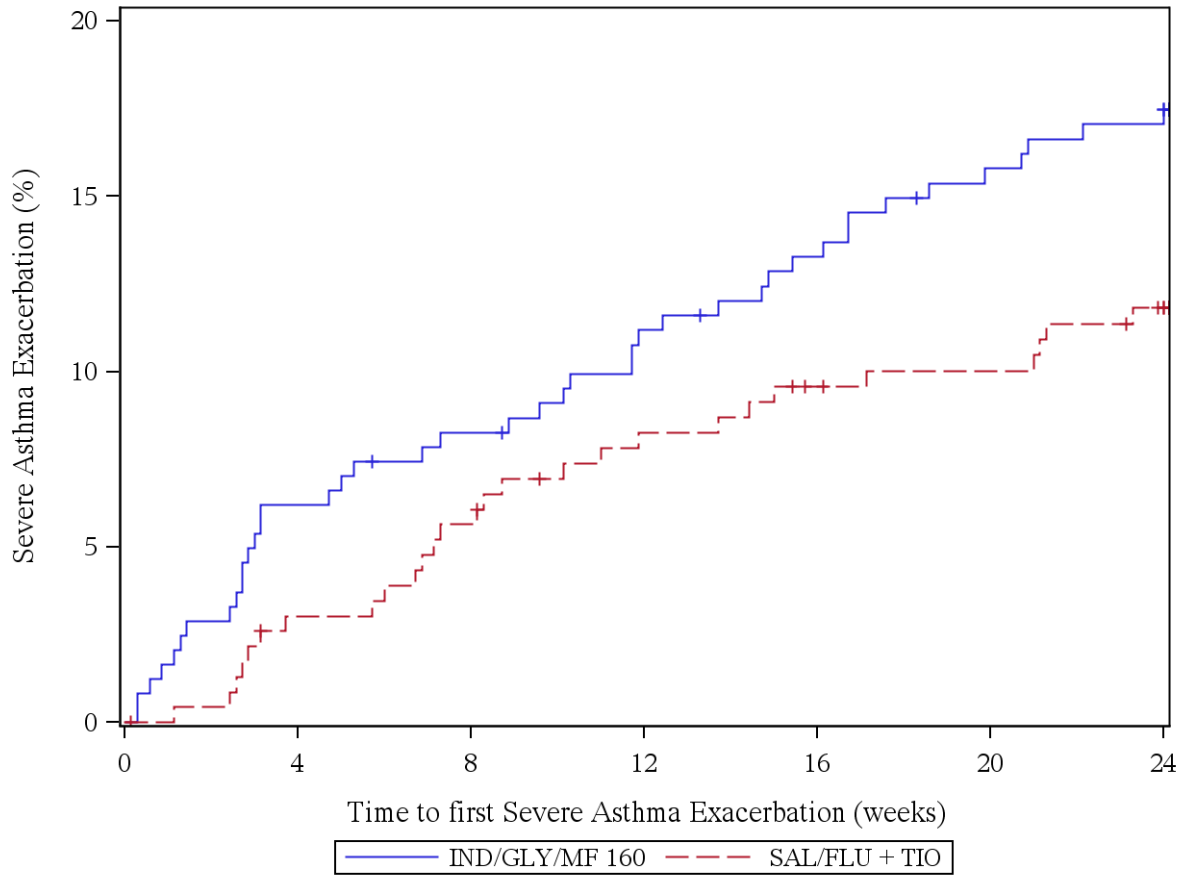
Figure 11.12.1 Severe Asthma Exacerbation (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 230/240, Week 8: 221/228, Week 16: 215/214, Week 24: 205/202

Analysis population: B2306 FAS total population

Figure 11.12.2 Severe Asthma Exacerbation (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA

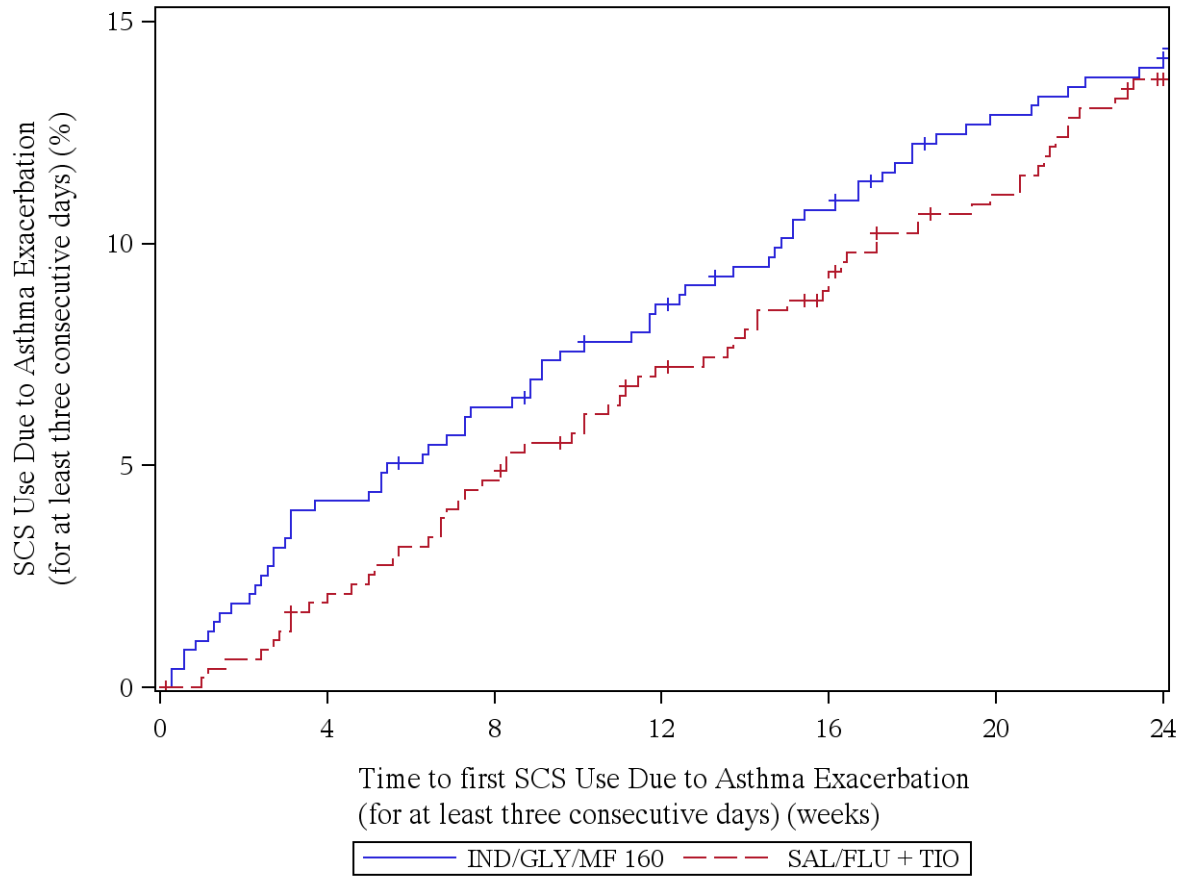


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 242/232, Week 8: 221/217, Week 16: 207/204, Week 24: 194/194

Analysis population: B2306 FAS total population

11.13 Kaplan-Meier-Plot: SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS)

Figure 11.13 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS)

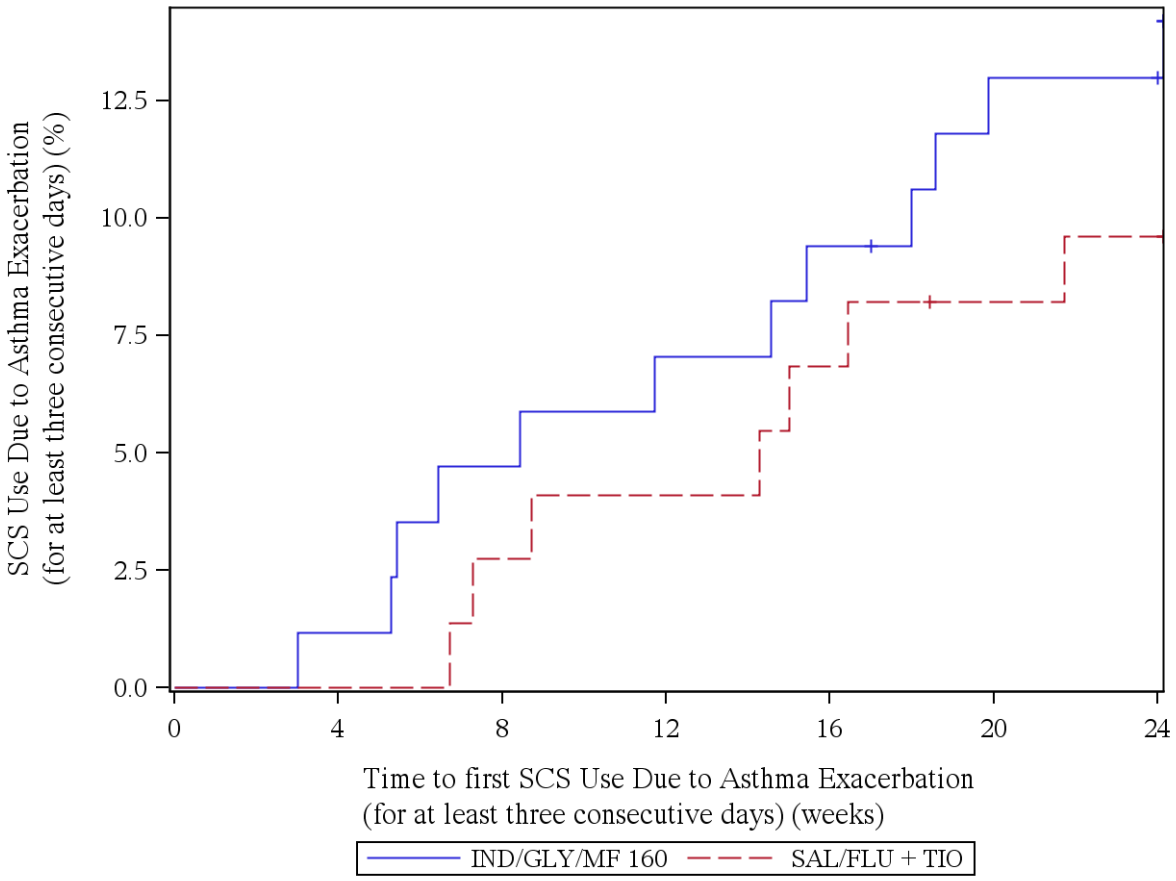


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 476/475, Week 8: 445/450, Week 16: 420/421, Week 24: 398/394

Analysis population: B2306 FAS total population

11.14 Kaplan-Meier-Plot: SCS Use Due to Asthma Exacerbation (for at least three consecutive days) by Age (FAS)

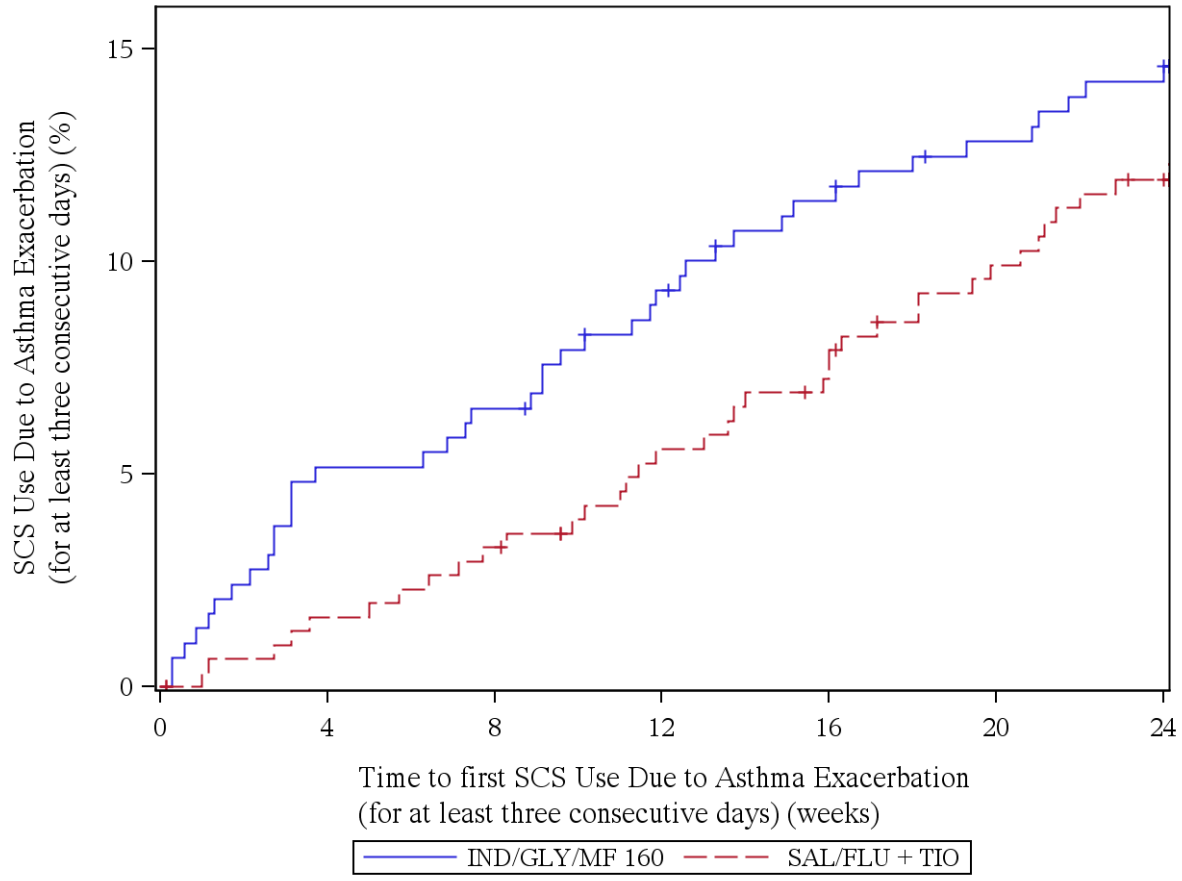
Figure 11.14.1 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Age = 18-39 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 85/73, Week 8: 81/71, Week 16: 77/68, Week 24: 72/65

Analysis population: B2306 FAS total population

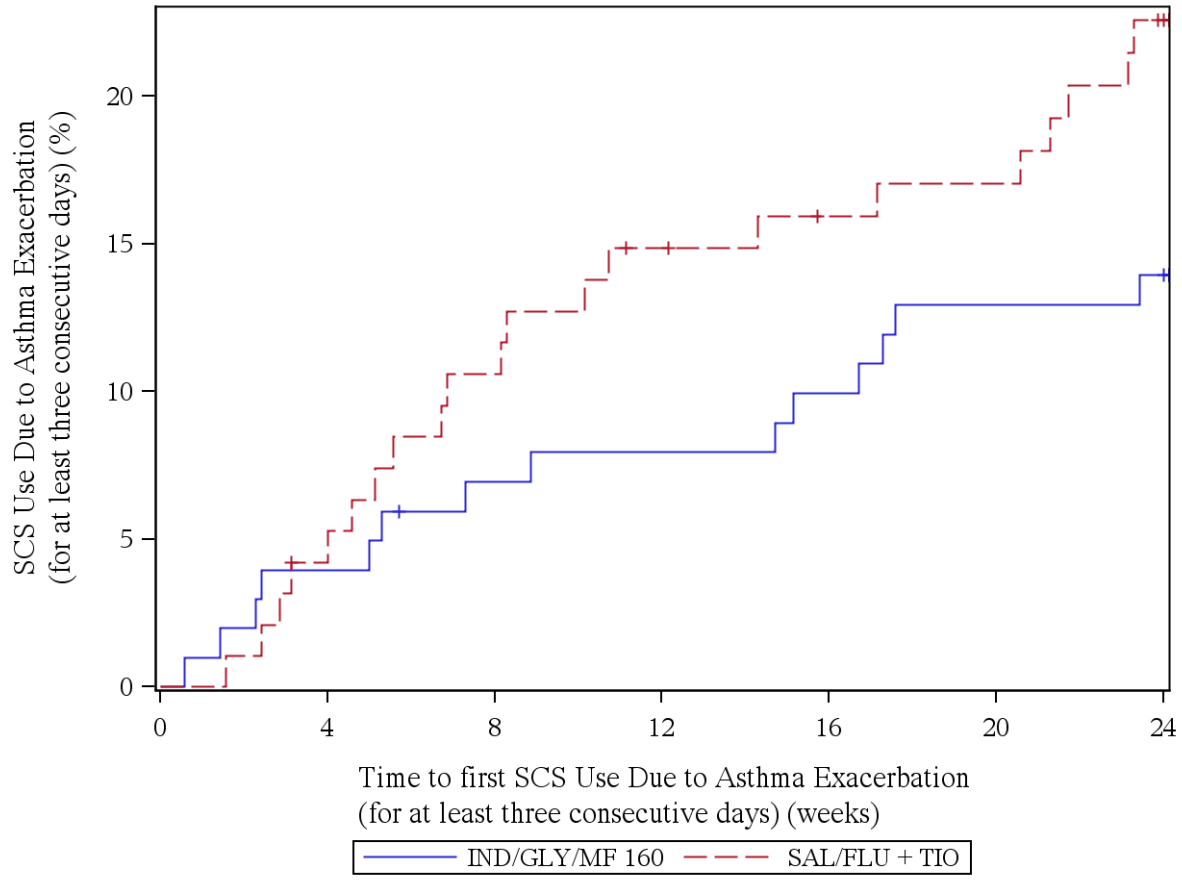
Figure 11.14.2 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Age = 40-64 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 290/307, Week 8: 271/295, Week 16: 253/277, Week 24: 241/261

Analysis population: B2306 FAS total population

Figure 11.14.3 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Age = ≥65 years

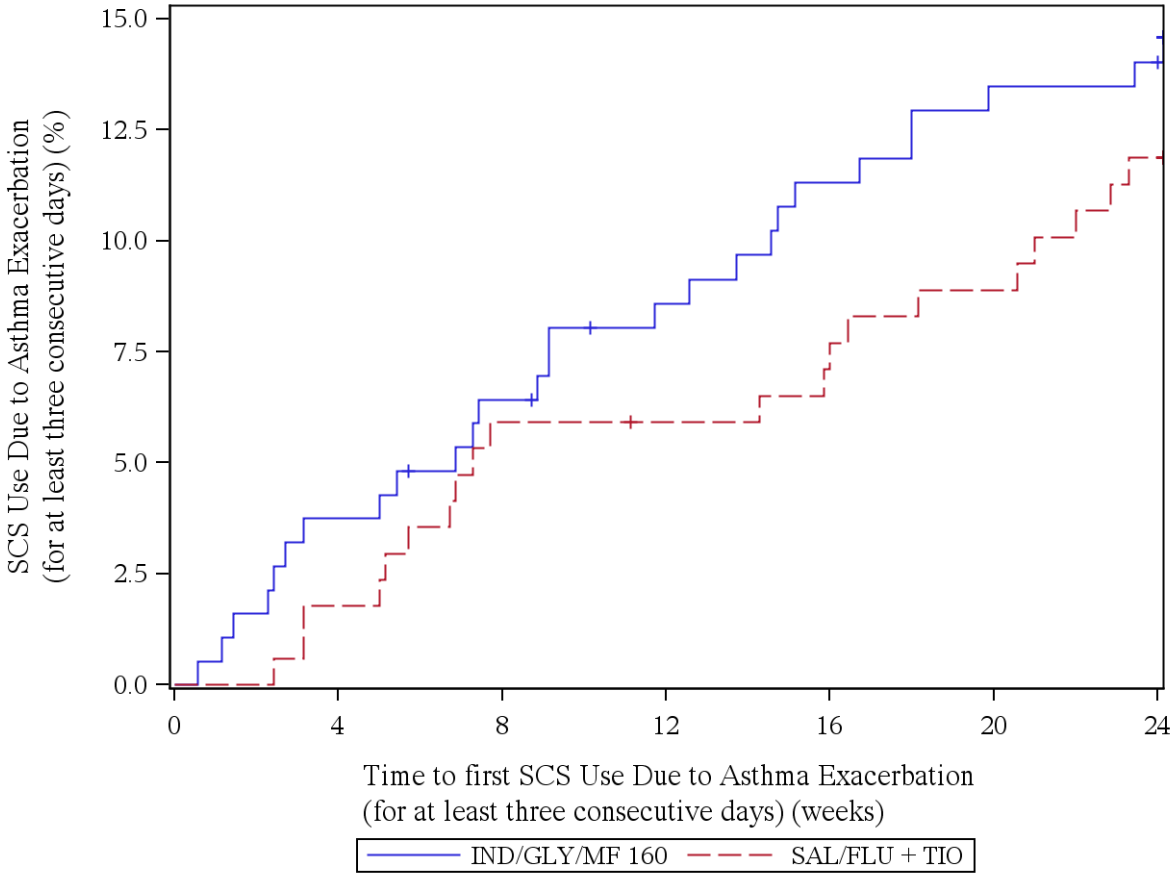


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 101/95, Week 8: 93/84, Week 16: 90/76, Week 24: 85/68

Analysis population: B2306 FAS total population

11.15 Kaplan-Meier-Plot: SCS Use Due to Asthma Exacerbation (for at least three consecutive days) by Gender (FAS)

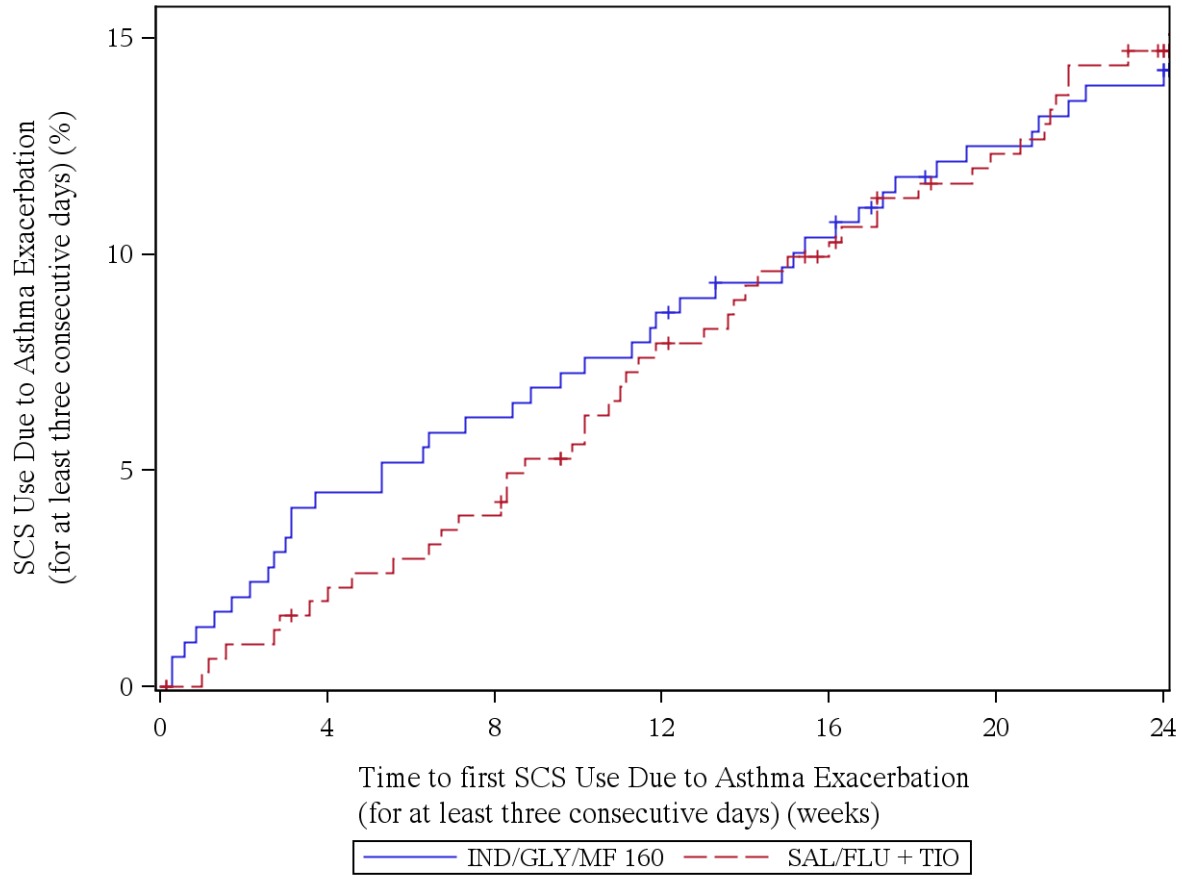
Figure 11.15.1 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Gender = Male



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 187/169, Week 8: 174/159, Week 16: 163/155, Week 24: 157/148

Analysis population: B2306 FAS total population

Figure 11.15.2 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Gender = Female

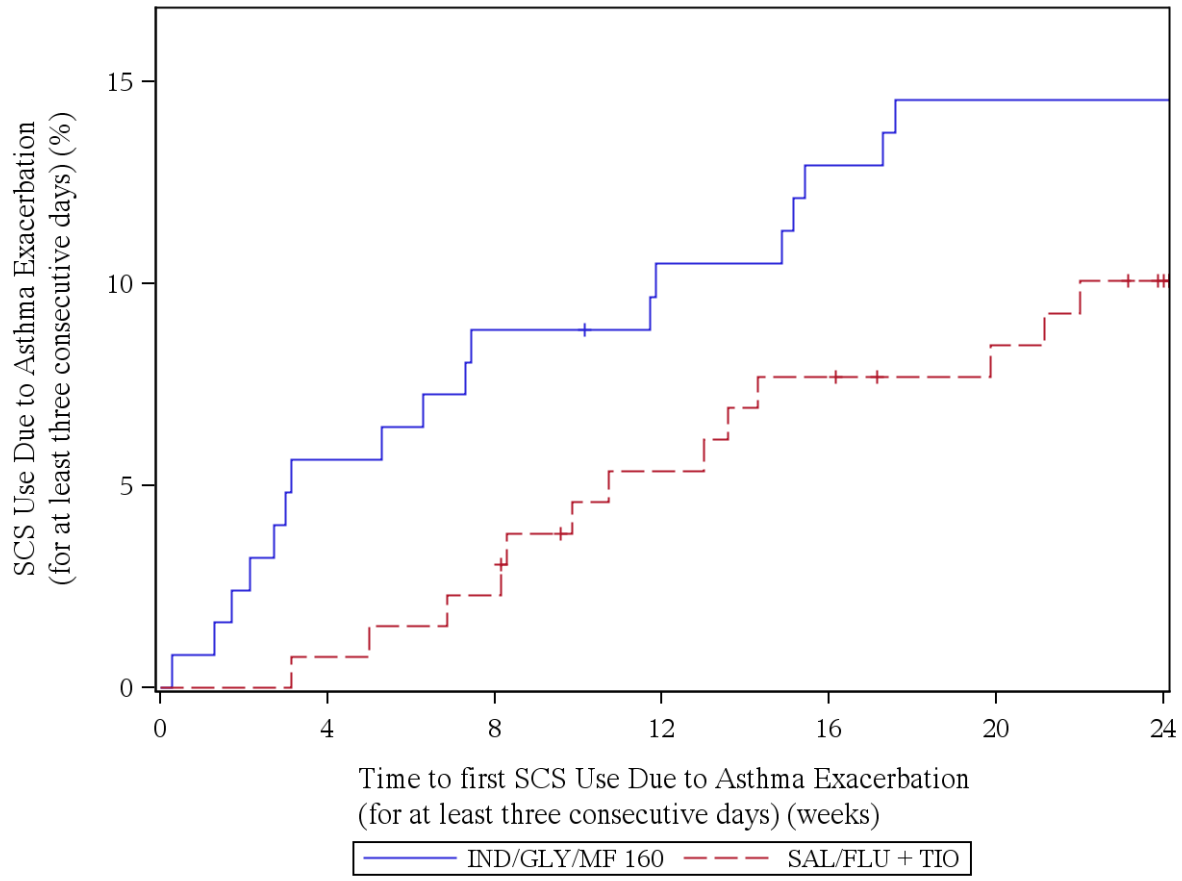


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 289/306, Week 8: 271/291, Week 16: 257/266, Week 24: 241/246

Analysis population: B2306 FAS total population

11.16 Kaplan-Meier-Plot: SCS Use Due to Asthma Exacerbation (for at least three consecutive days) by Region (FAS)

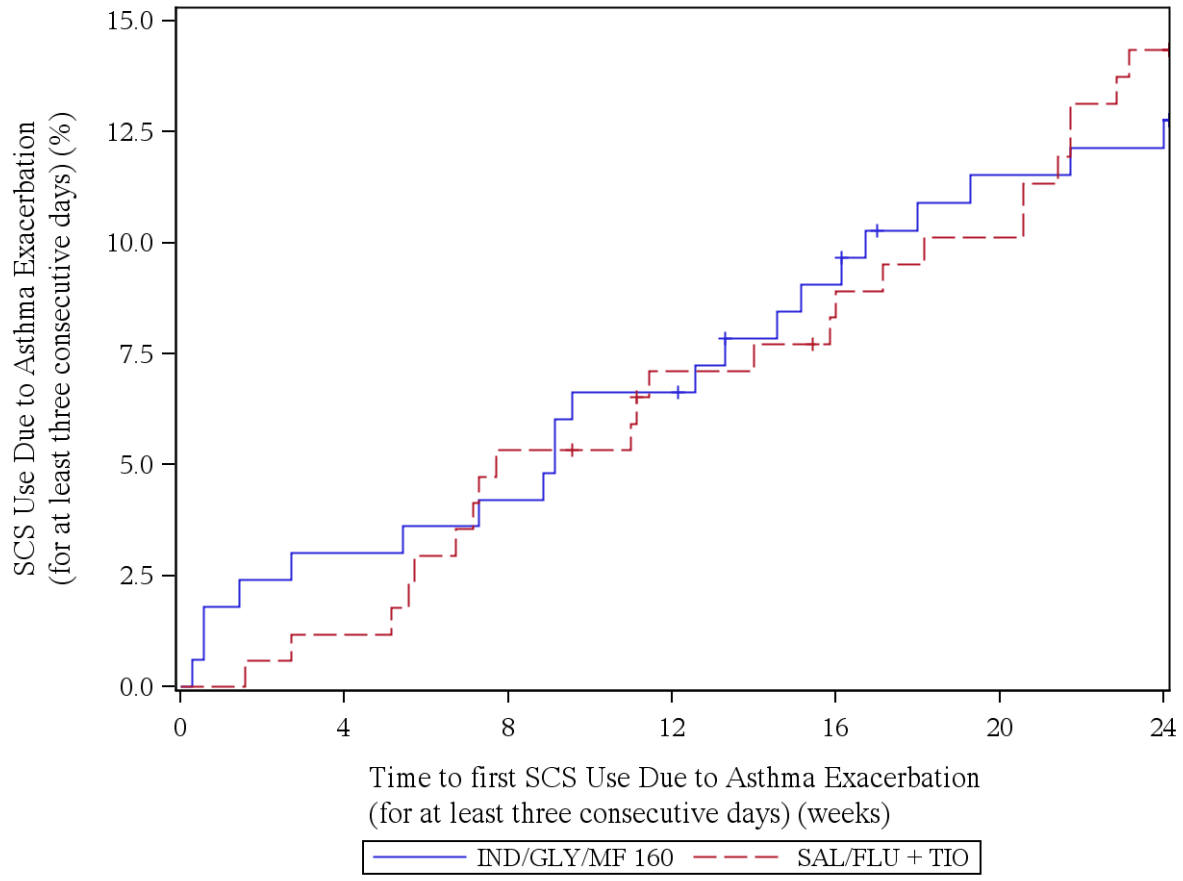
Figure 11.16.1 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Region = Asia



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 124/131, Week 8: 113/128, Week 16: 107/119, Week 24: 105/111

Analysis population: B2306 FAS total population

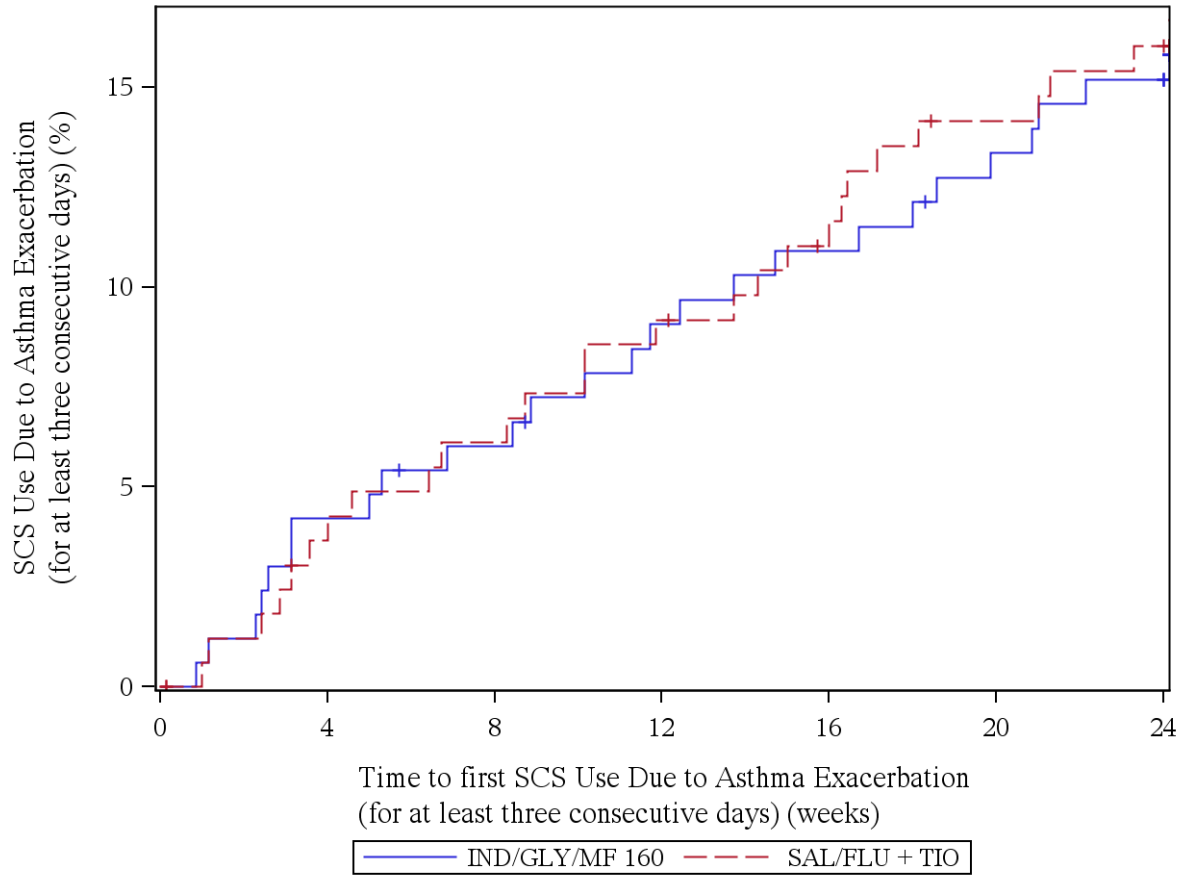
Figure 11.16.2 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Region = Europe



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 166/169, Week 8: 159/160, Week 16: 149/151, Week 24: 141/142

Analysis population: B2306 FAS total population

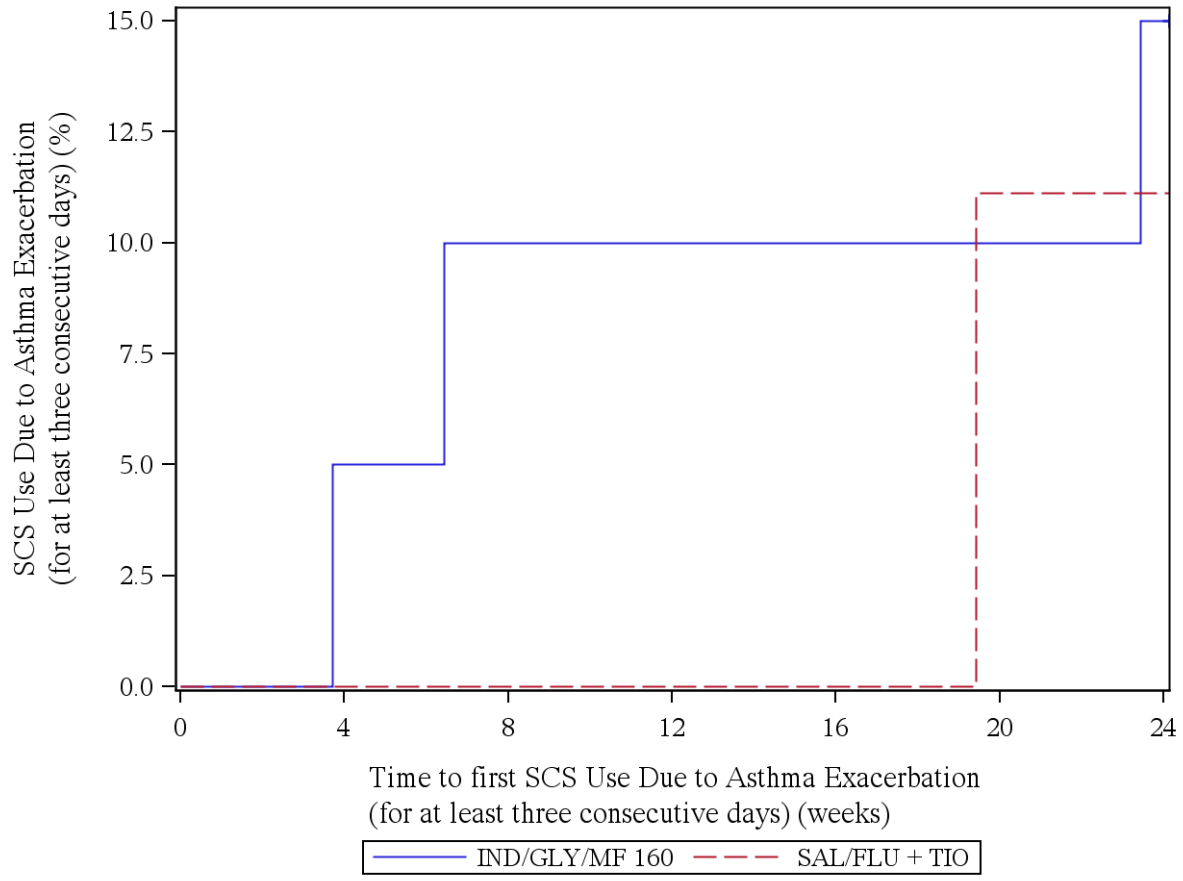
Figure 11.16.3 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Region = Latin America



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 166/166, Week 8: 155/153, Week 16: 146/142, Week 24: 135/133

Analysis population: B2306 FAS total population

Figure 11.16.4 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Region = Others

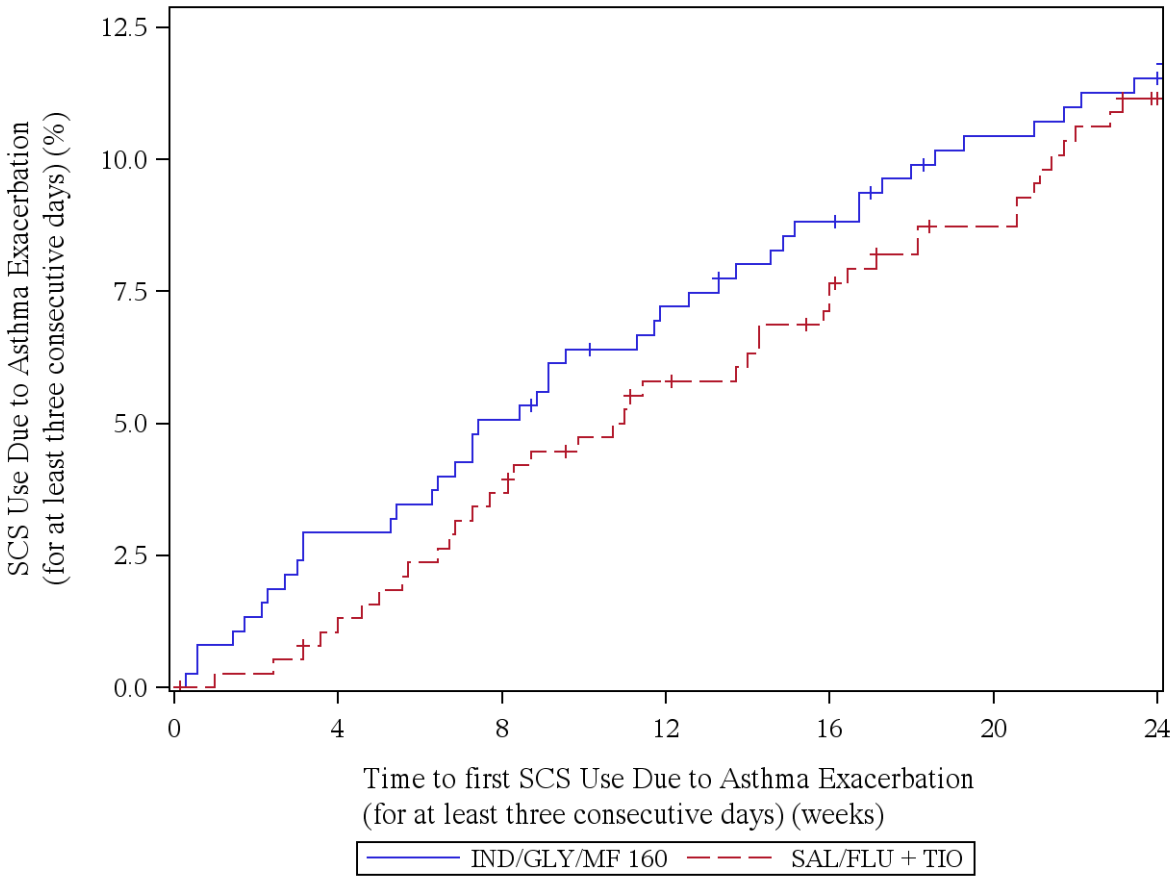


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 20/9, Week 8: 18/9, Week 16: 18/9, Week 24: 17/8

Analysis population: B2306 FAS total population

11.17 Kaplan-Meier-Plot: SCS Use Due to Asthma Exacerbation (for at least three consecutive days) by History of Asthma Exacerbation (FAS)

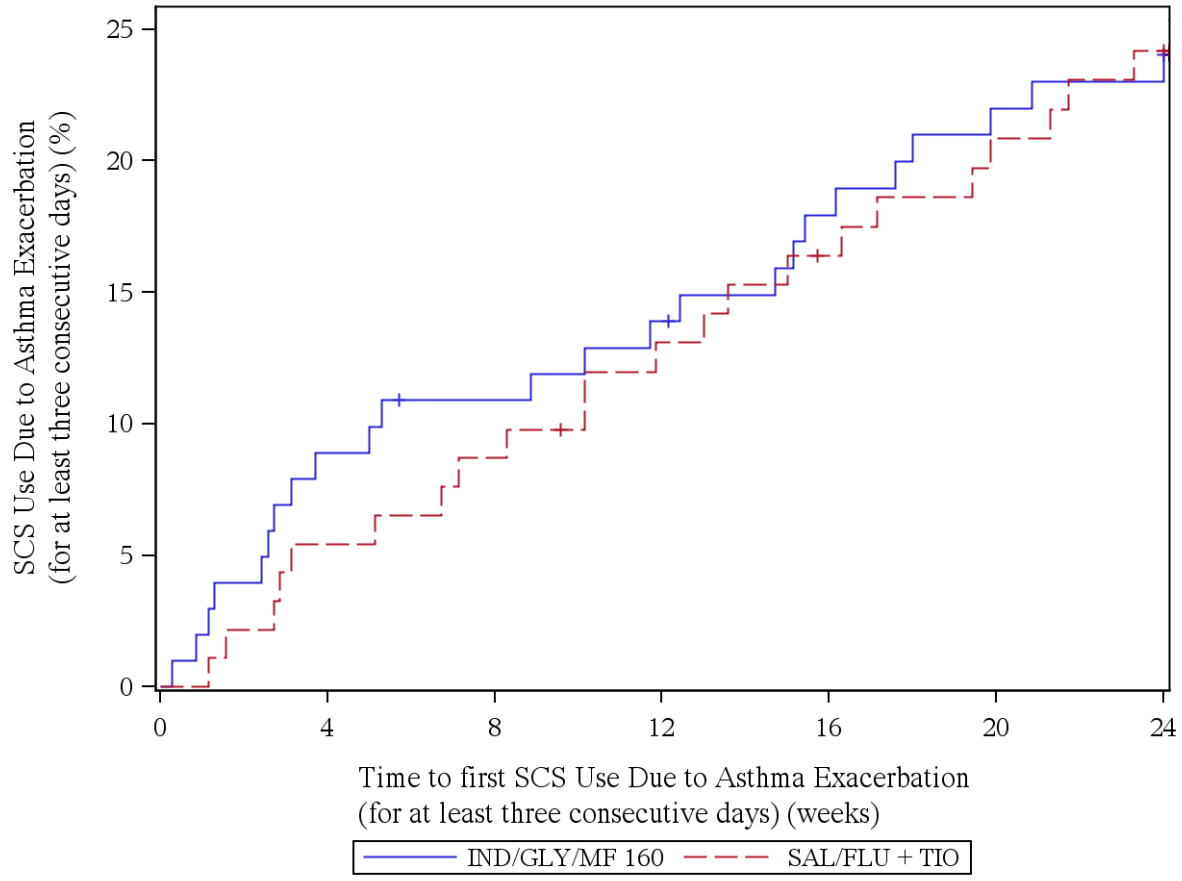
Figure 11.17.1 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Asthma exacerbations in the 12 months prior to screening = 1



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 375/383, Week 8: 356/366, Week 16: 339/346, Week 24: 324/327

Analysis population: B2306 FAS total population

Figure 11.17.2 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2

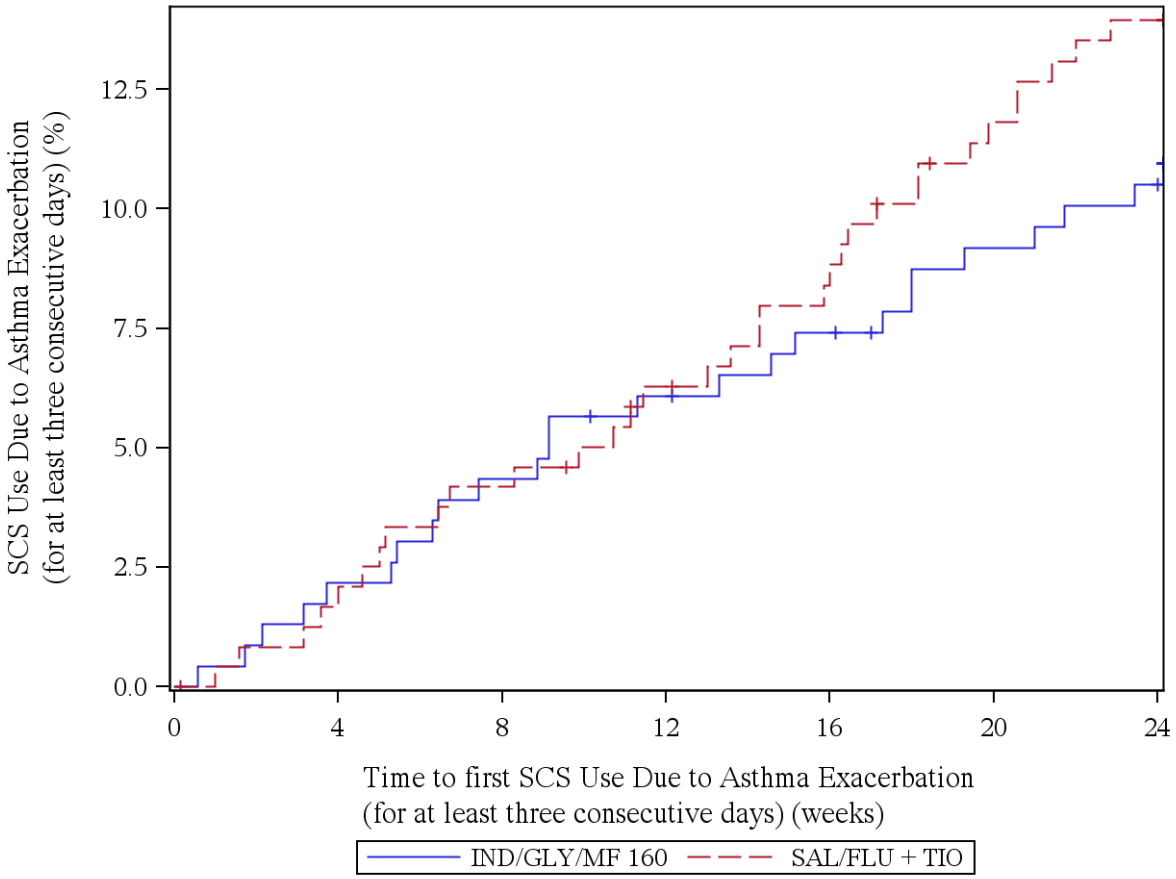


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 101/92, Week 8: 89/84, Week 16: 81/75, Week 24: 74/67

Analysis population: B2306 FAS total population

11.18 Kaplan-Meier-Plot: SCS Use Due to Asthma Exacerbation (for at least three consecutive days) by Patients' Prior Therapies (FAS)

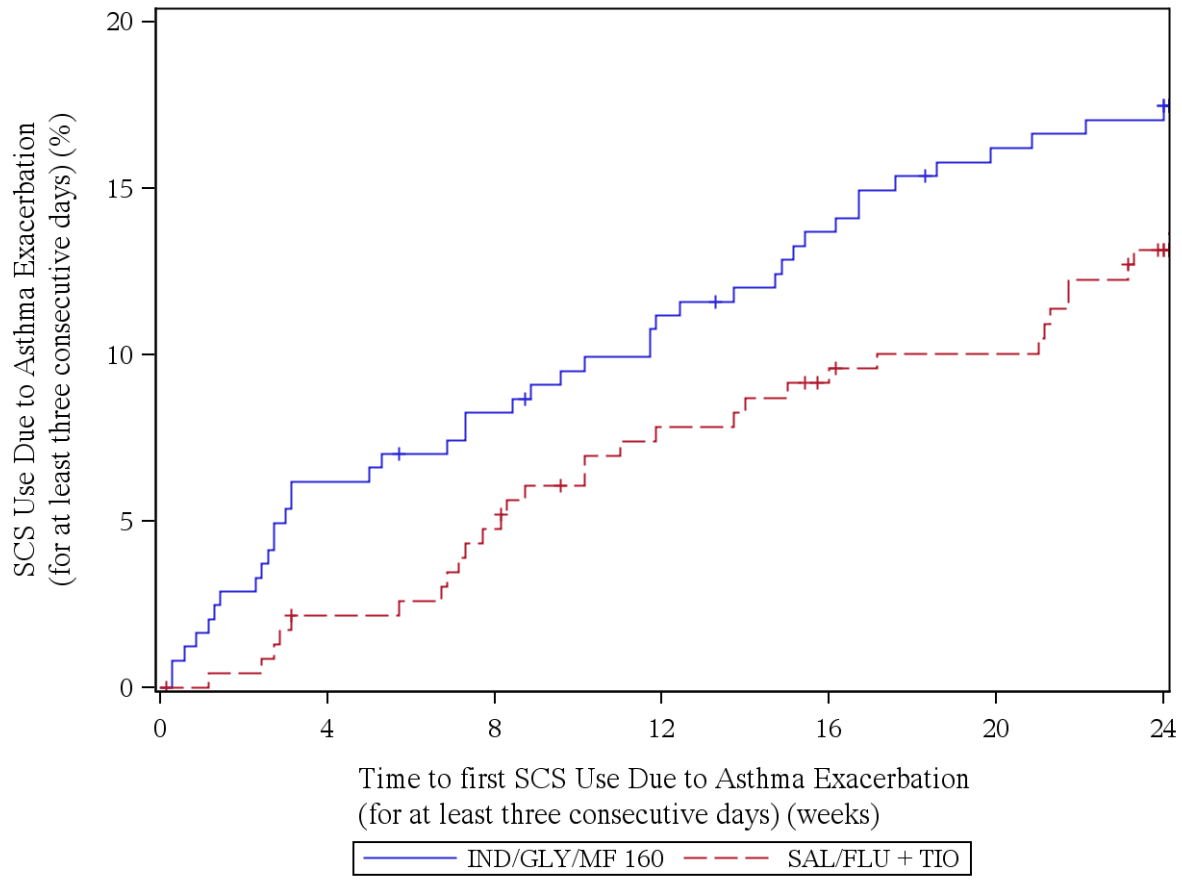
Figure 11.18.1 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 230/240, Week 8: 220/229, Week 16: 211/215, Week 24: 201/201

Analysis population: B2306 FAS total population

Figure 11.18.2 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA

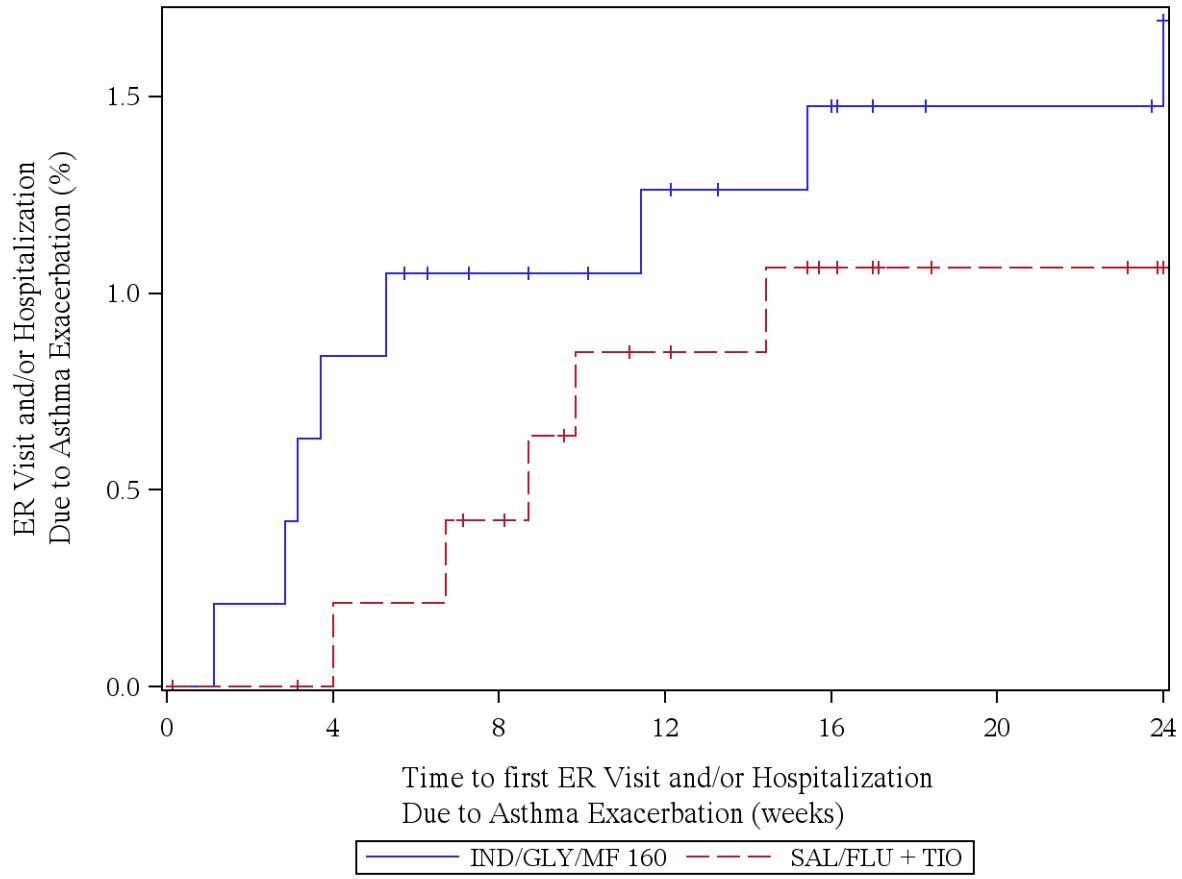


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 242/232, Week 8: 221/219, Week 16: 206/204, Week 24: 194/191

Analysis population: B2306 FAS total population

11.19 Kaplan-Meier-Plot: ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS)

Figure 11.19 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS)

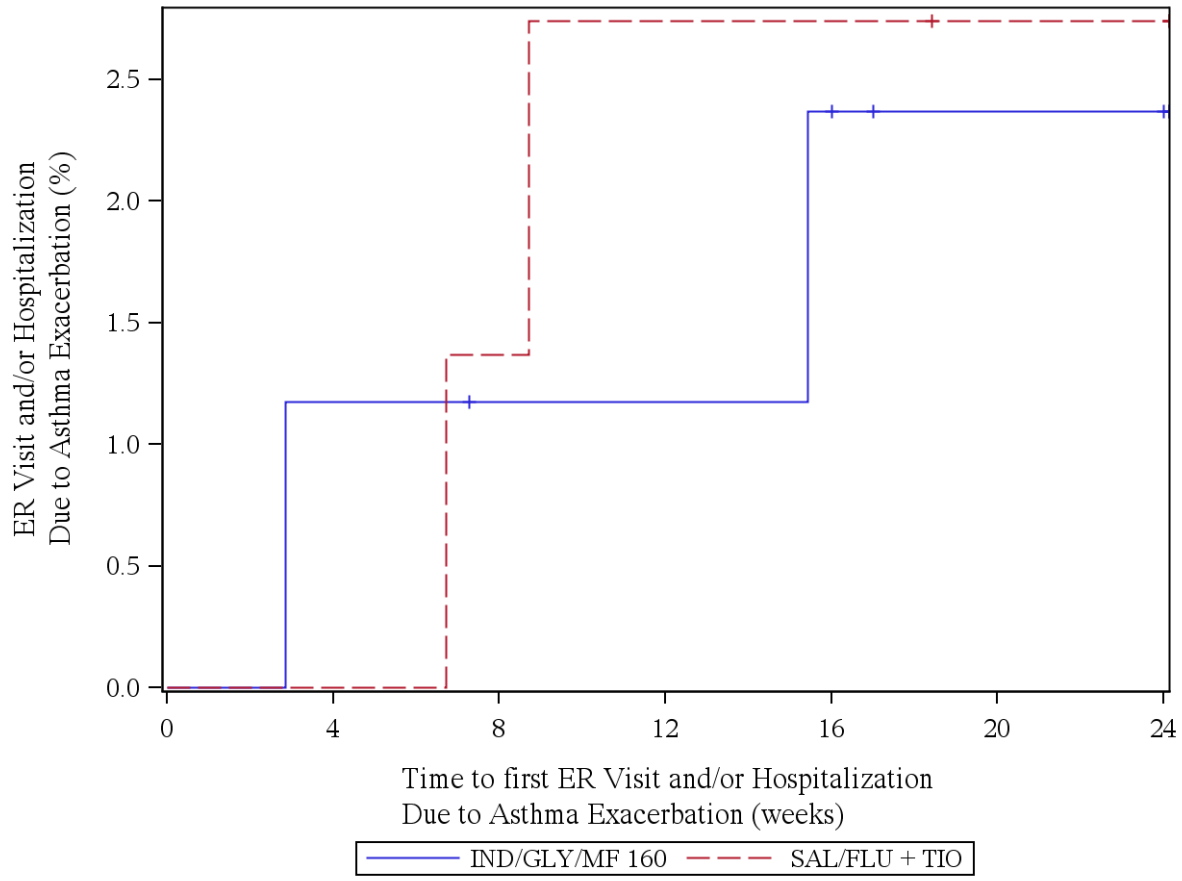


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 476/475, Week 8: 468/469, Week 16: 461/459, Week 24: 451/451

Analysis population: B2306 FAS total population

11.20 Kaplan-Meier-Plot: ER Visit and/or Hospitalization Due to Asthma Exacerbation by Age (FAS)

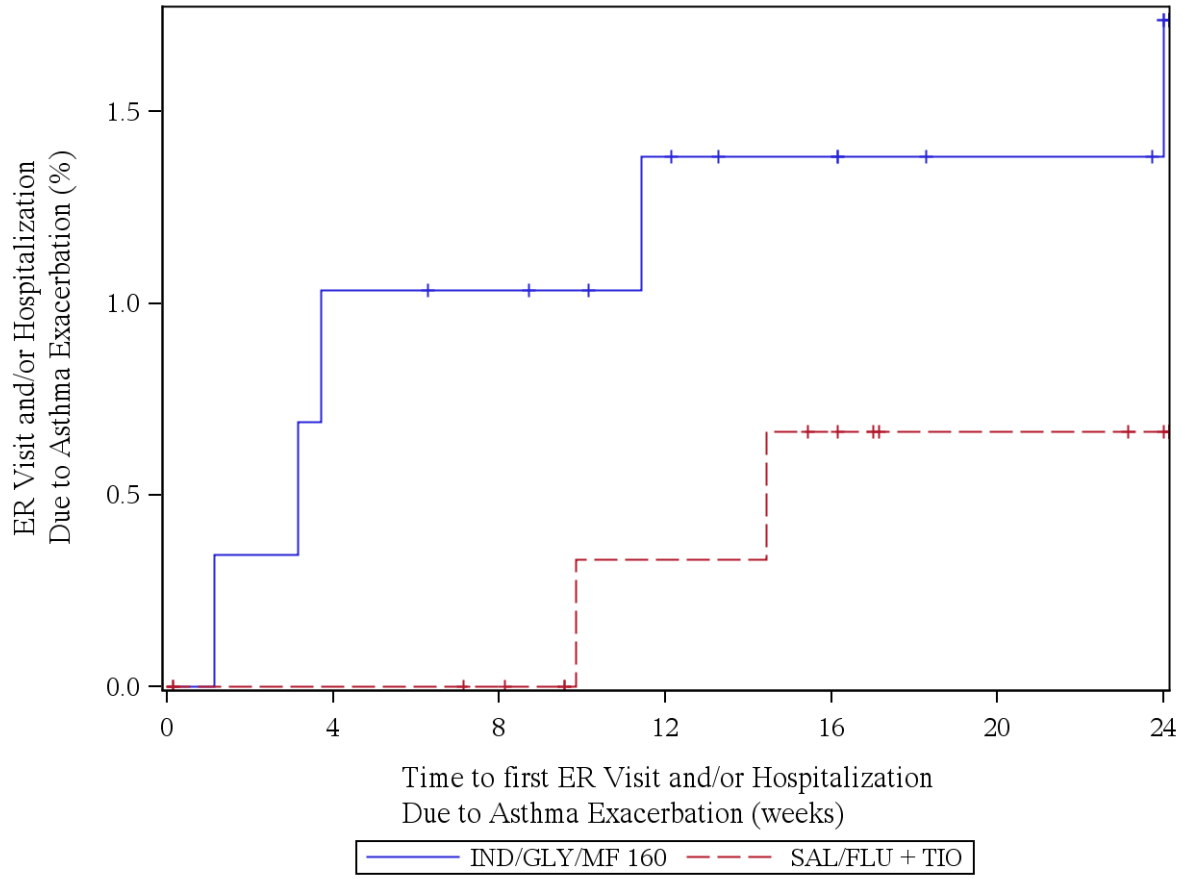
Figure 11.20.1 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Age = 18-39 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 85/73, Week 8: 83/72, Week 16: 81/71, Week 24: 79/70

Analysis population: B2306 FAS total population

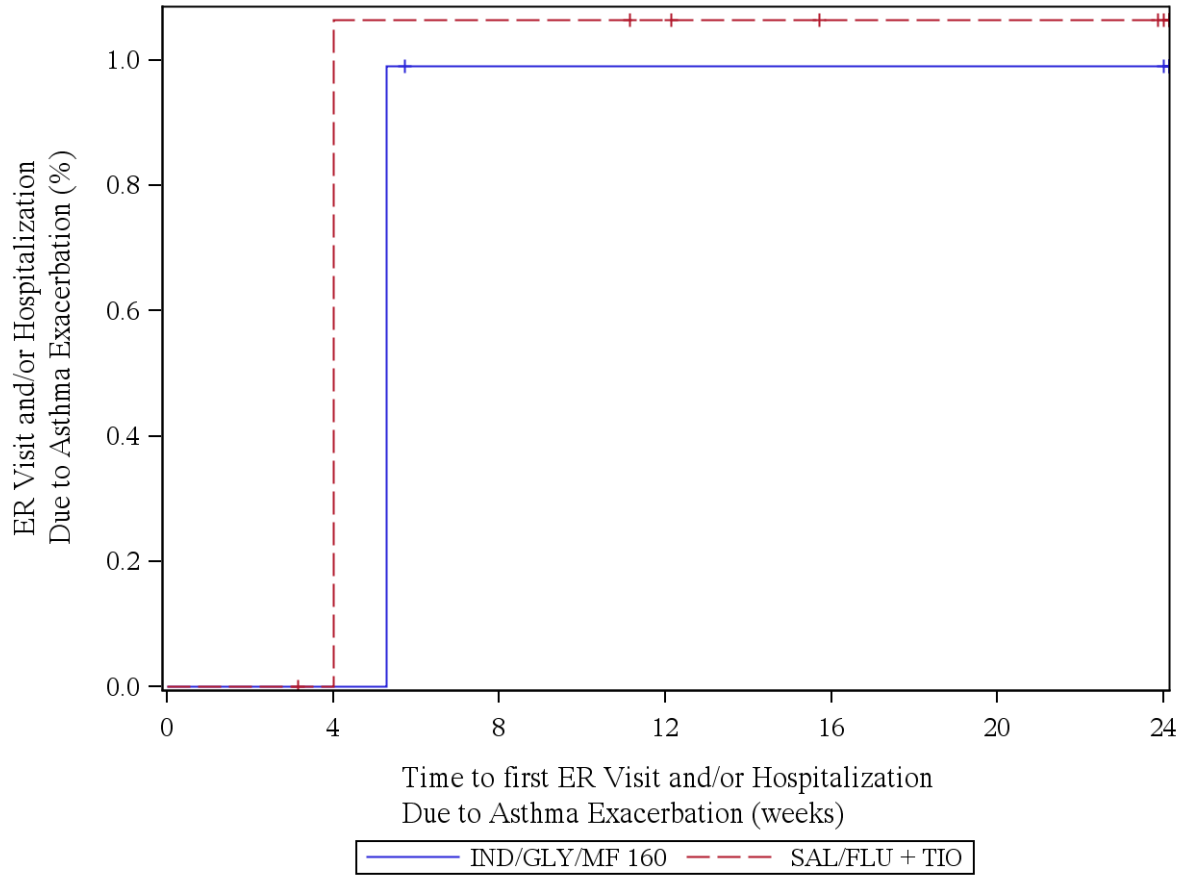
Figure 11.20.2 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Age = 40-64 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 290/307, Week 8: 286/304, Week 16: 281/298, Week 24: 274/293

Analysis population: B2306 FAS total population

Figure 11.20.3 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Age = ≥65 years

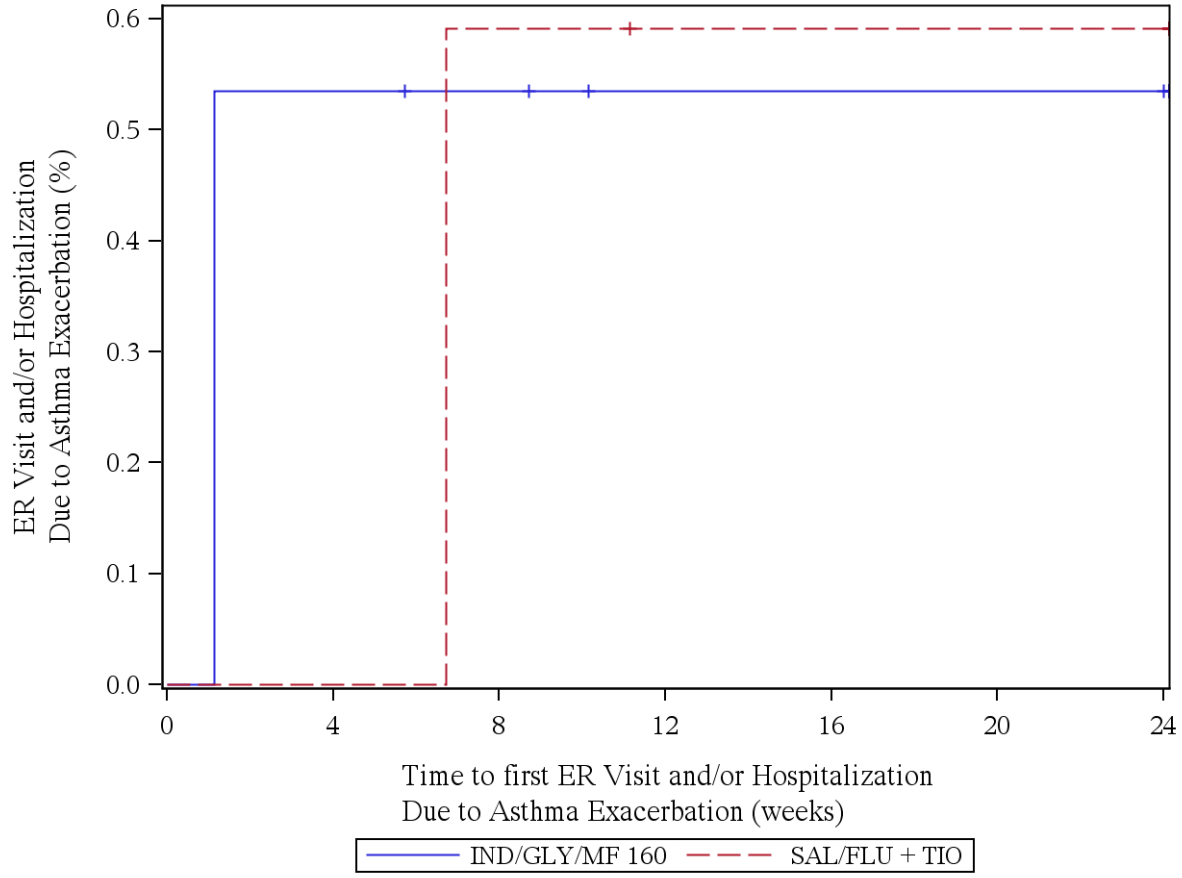


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 101/95, Week 8: 99/93, Week 16: 99/90, Week 24: 98/88

Analysis population: B2306 FAS total population

11.21 Kaplan-Meier-Plot: ER Visit and/or Hospitalization Due to Asthma Exacerbation by Gender (FAS)

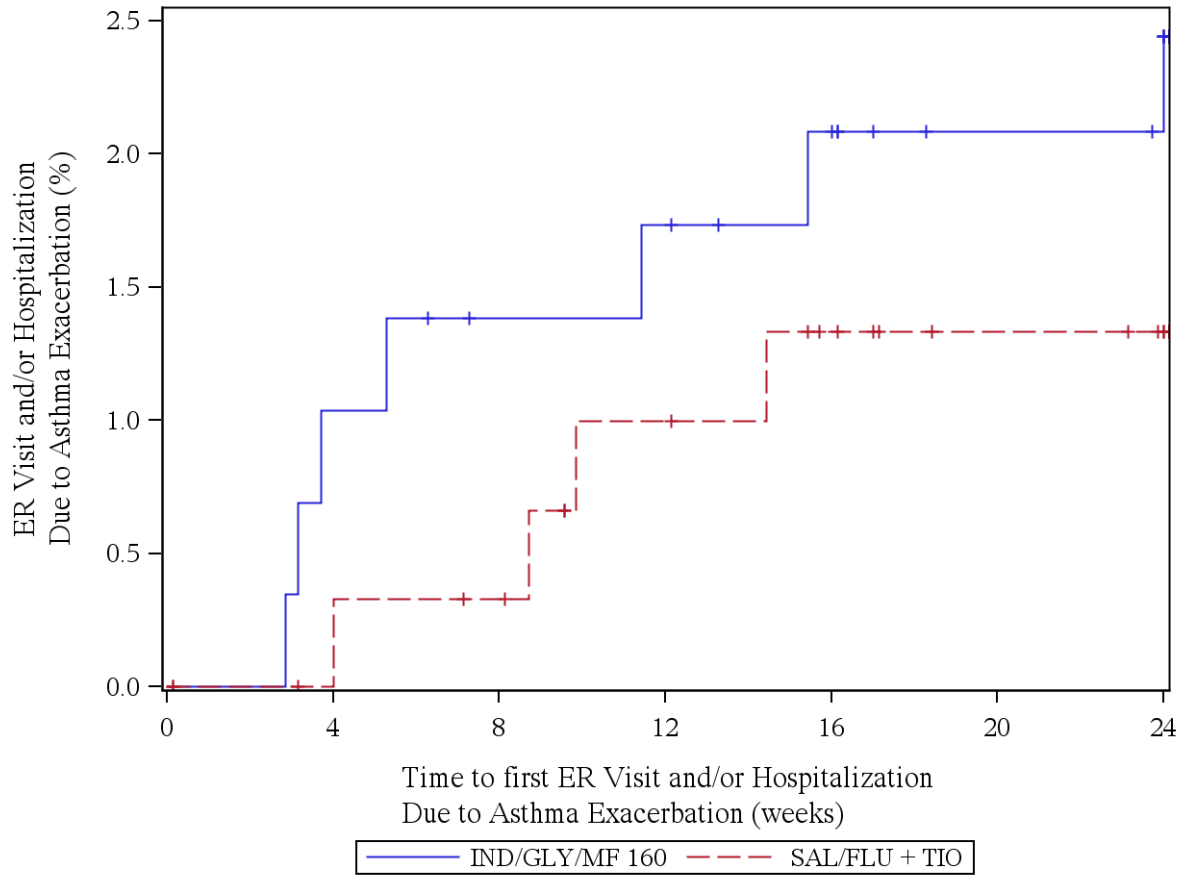
Figure 11.21.1 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Gender = Male



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 187/169, Week 8: 185/168, Week 16: 183/167, Week 24: 182/167

Analysis population: B2306 FAS total population

Figure 11.21.2 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Gender = Female

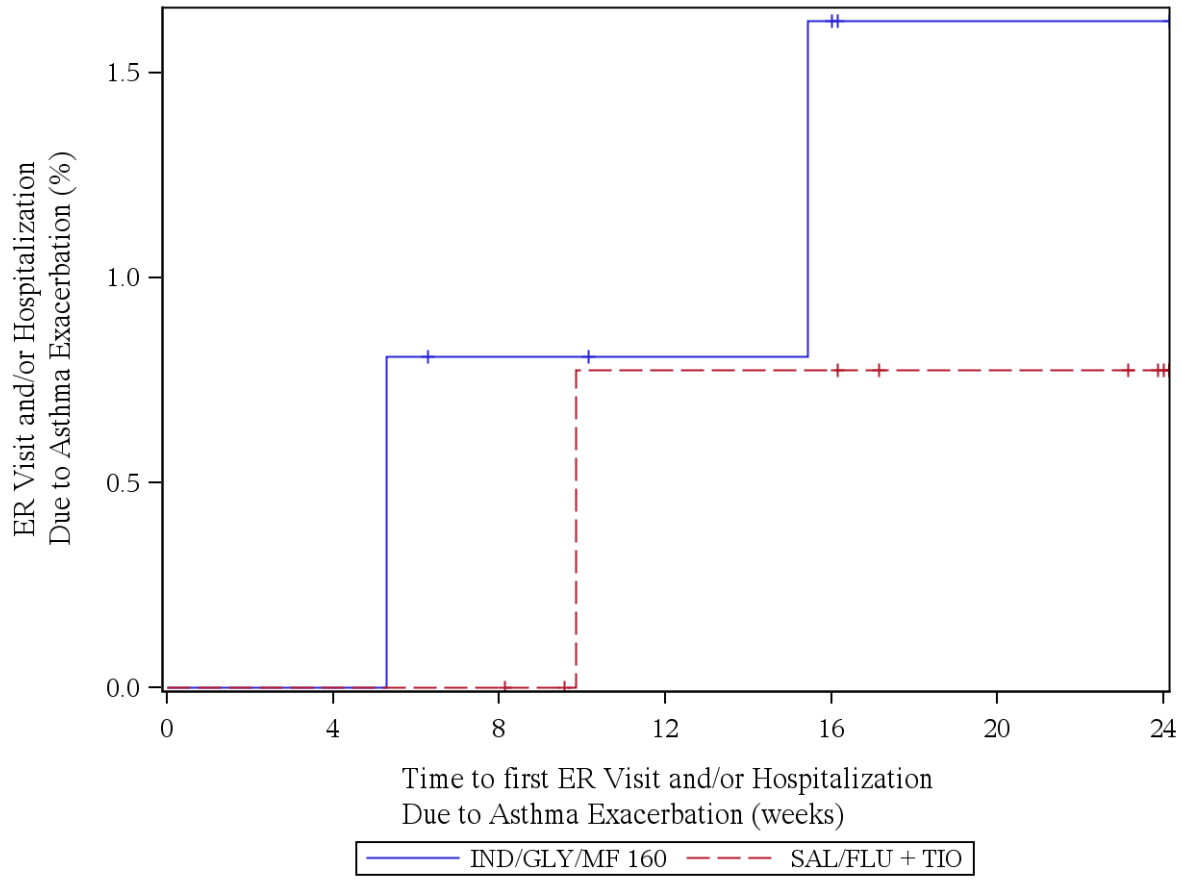


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 289/306, Week 8: 283/301, Week 16: 278/292, Week 24: 269/284

Analysis population: B2306 FAS total population

11.22 Kaplan-Meier-Plot: ER Visit and/or Hospitalization Due to Asthma Exacerbation by Region (FAS)

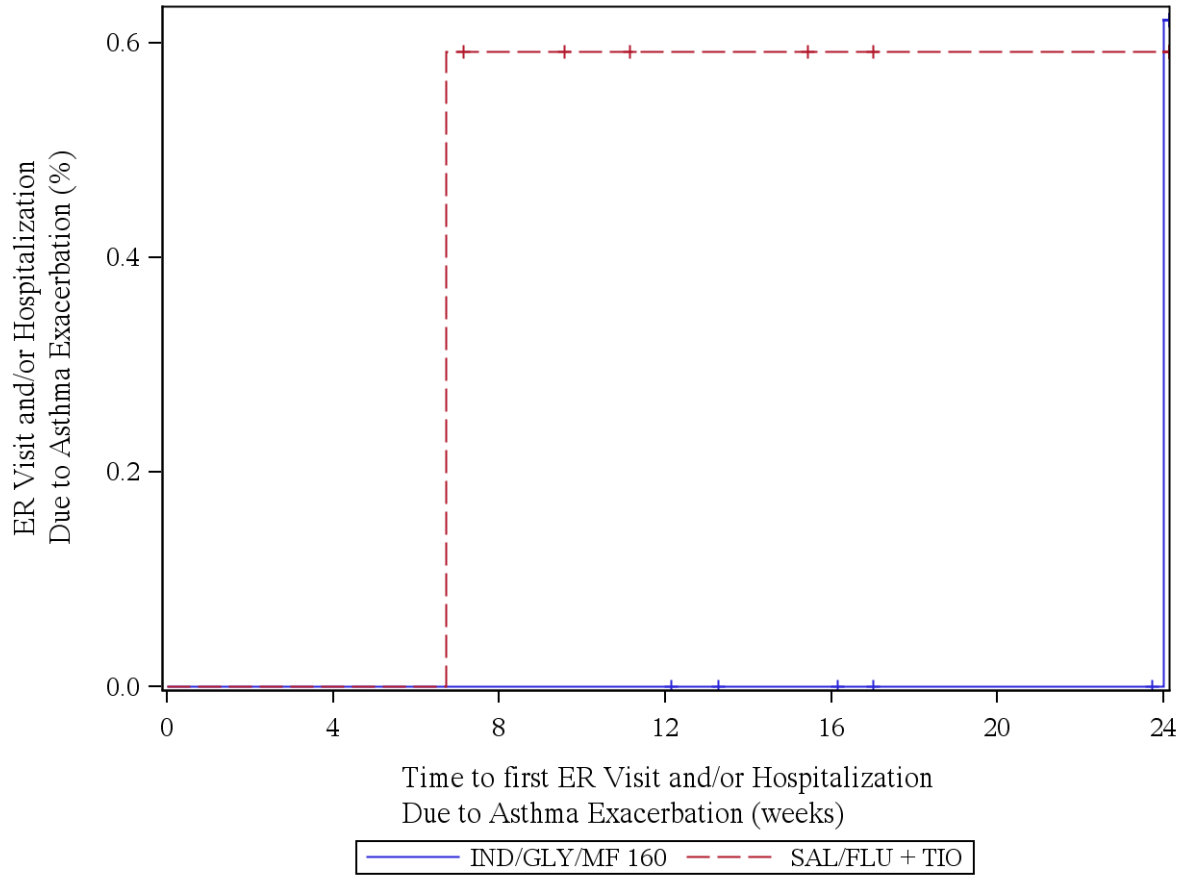
Figure 11.22.1 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Region = Asia



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 124/131, Week 8: 122/131, Week 16: 119/128, Week 24: 118/123

Analysis population: B2306 FAS total population

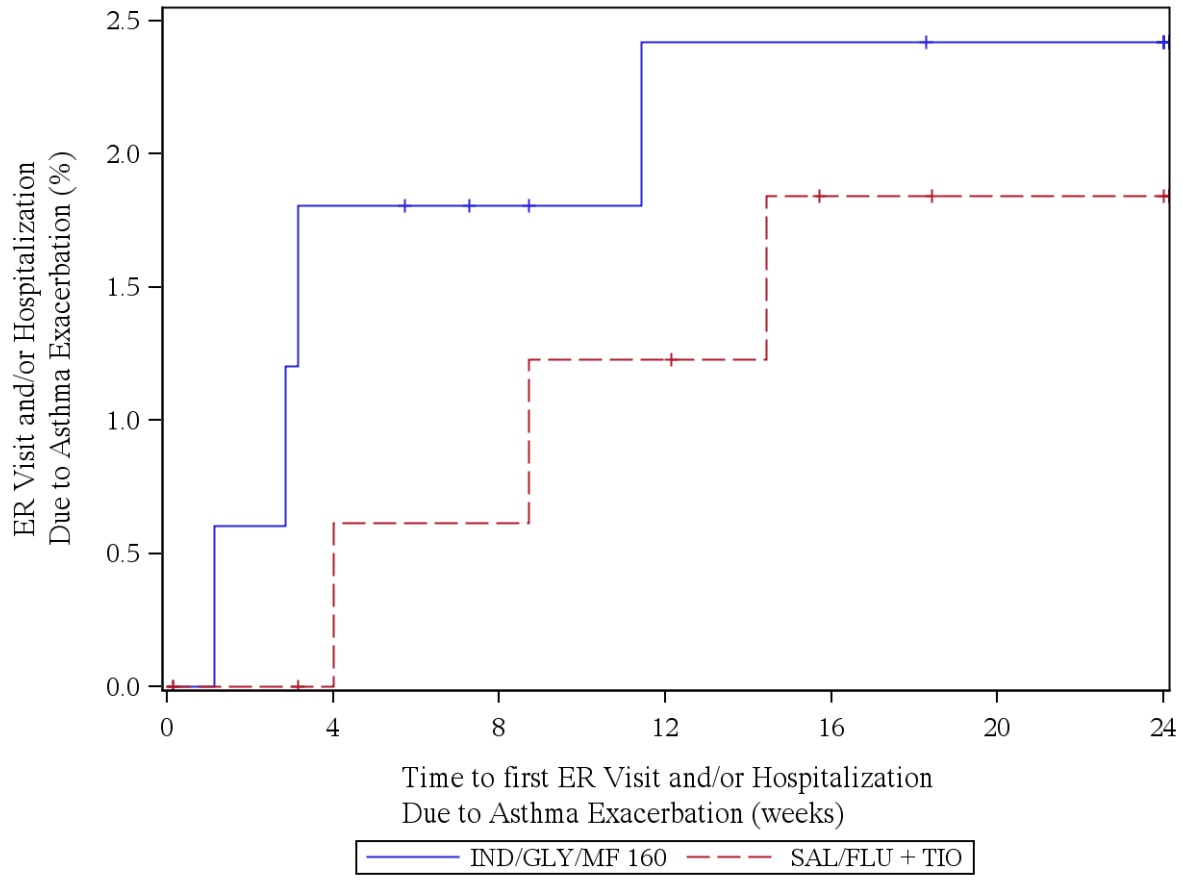
Figure 11.22.2 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Region = Europe



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 166/169, Week 8: 166/167, Week 16: 164/164, Week 24: 160/163

Analysis population: B2306 FAS total population

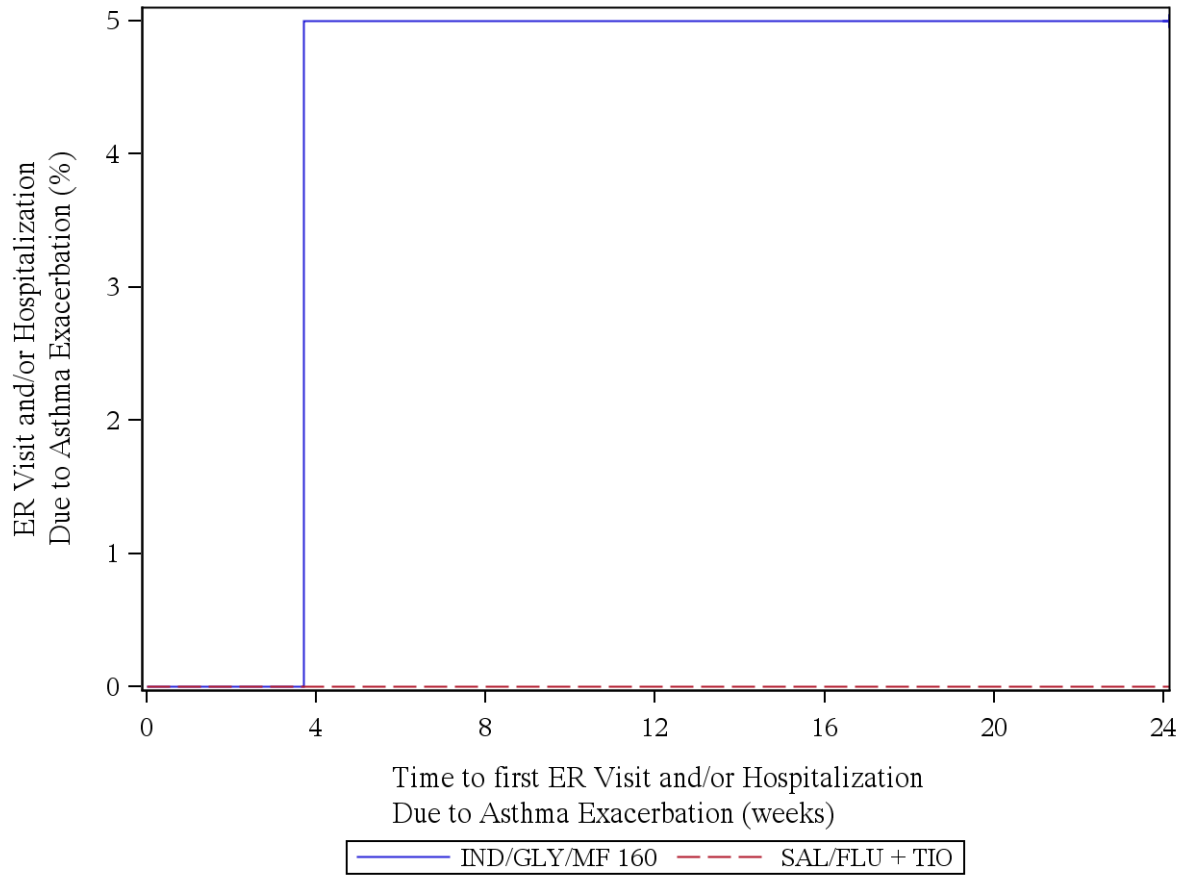
Figure 11.22.3 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Region = Latin America



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 166/166, Week 8: 161/162, Week 16: 159/158, Week 24: 154/156

Analysis population: B2306 FAS total population

Figure 11.22.4 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Region = Others

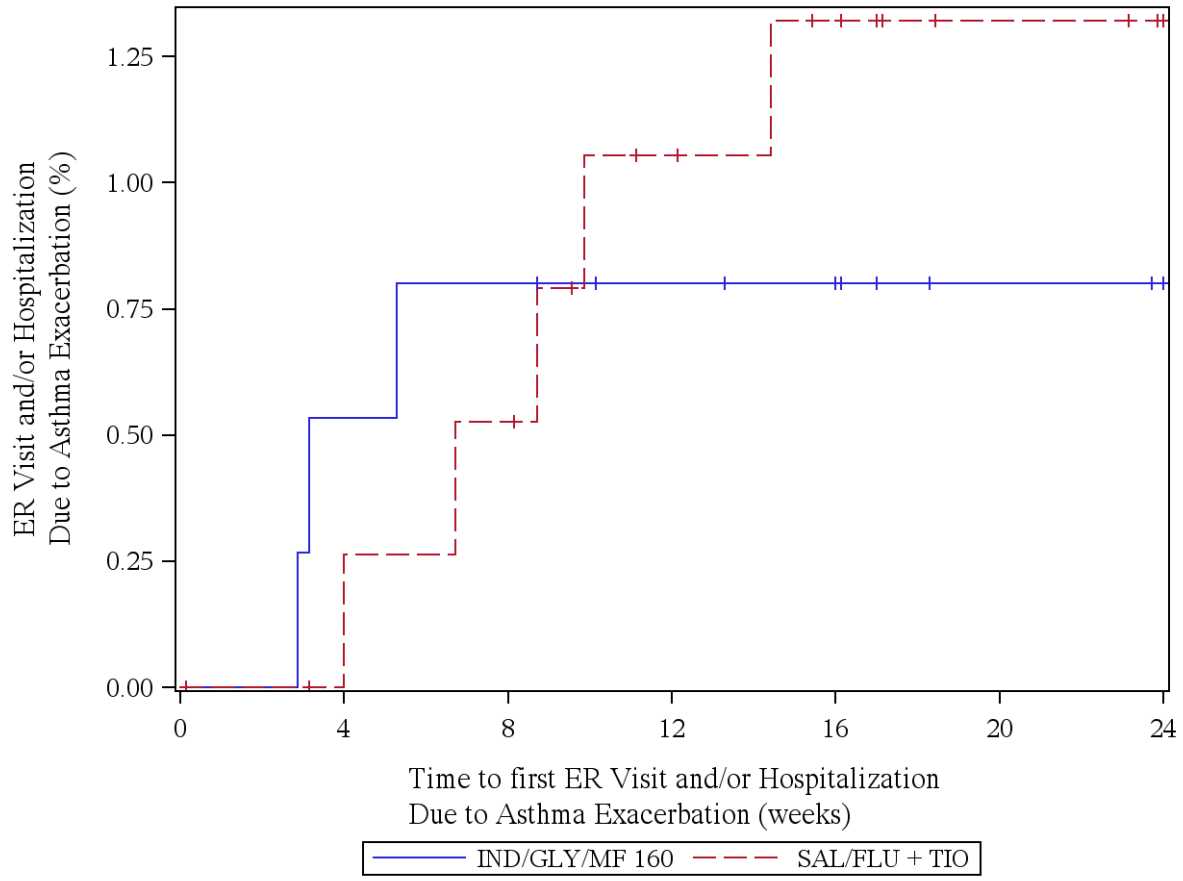


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 20/9, Week 8: 19/9, Week 16: 19/9, Week 24: 19/9

Analysis population: B2306 FAS total population

11.23 Kaplan-Meier-Plot: ER Visit and/or Hospitalization Due to Asthma Exacerbation by History of Asthma Exacerbation (FAS)

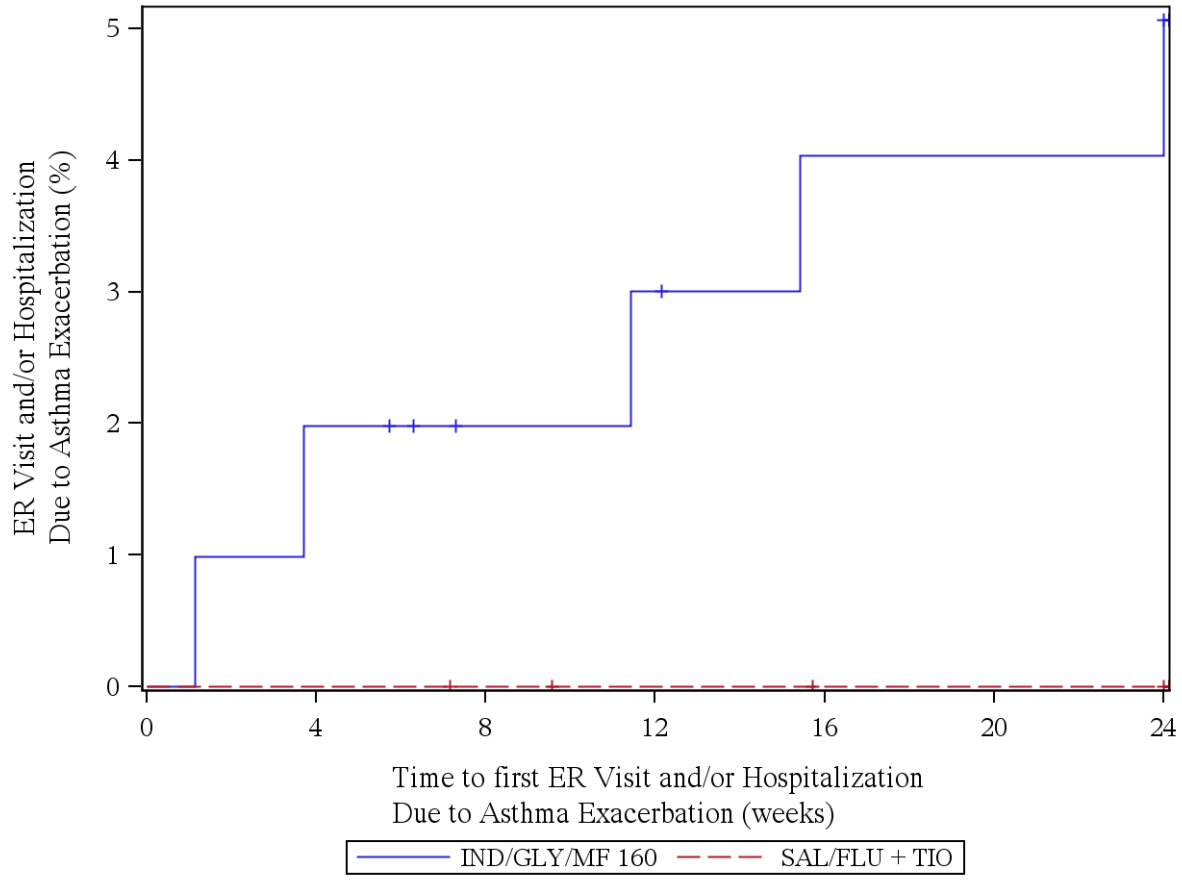
Figure 11.23.1 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 375/383, Week 8: 372/378, Week 16: 368/370, Week 24: 360/363

Analysis population: B2306 FAS total population

Figure 11.23.2 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2

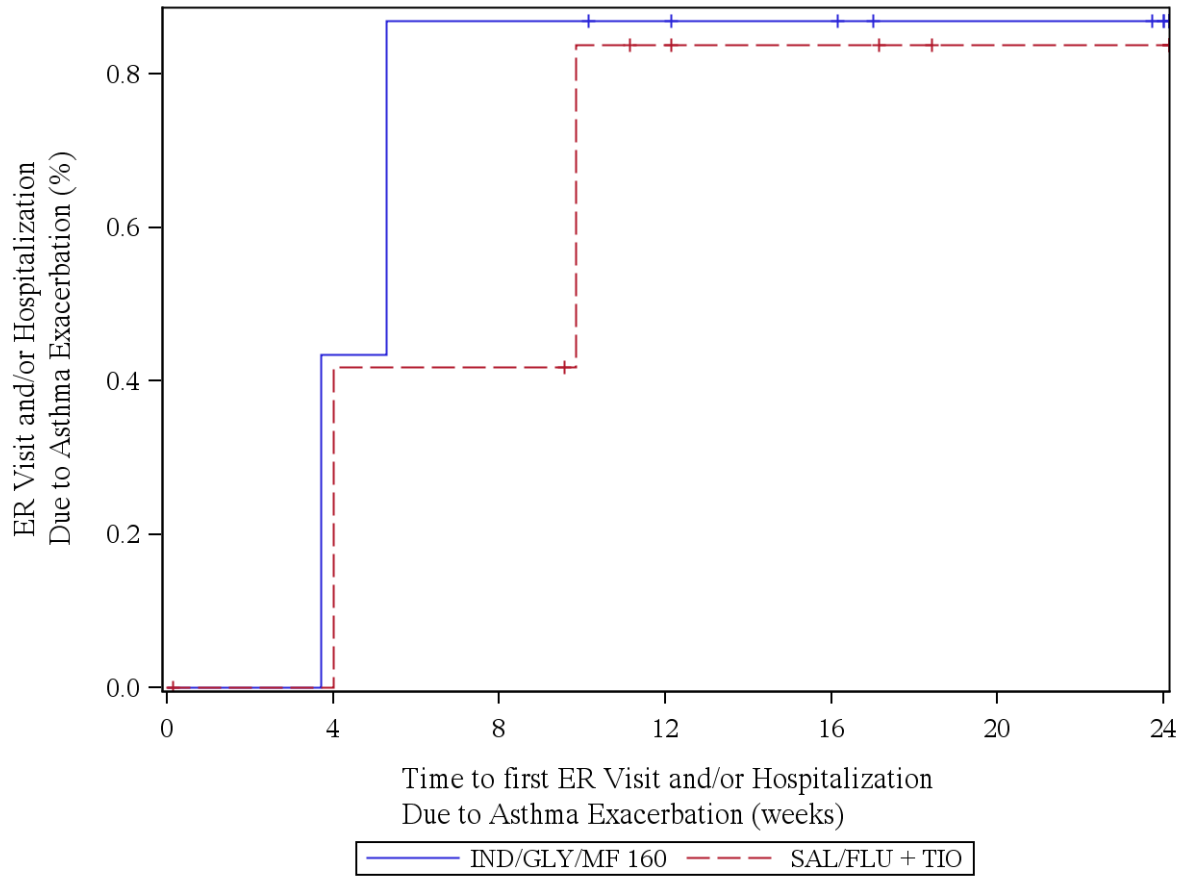


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 101/92, Week 8: 96/91, Week 16: 93/89, Week 24: 91/88

Analysis population: B2306 FAS total population

11.24 Kaplan-Meier-Plot: ER Visit and/or Hospitalization Due to Asthma Exacerbation by Patients' Prior Therapies (FAS)

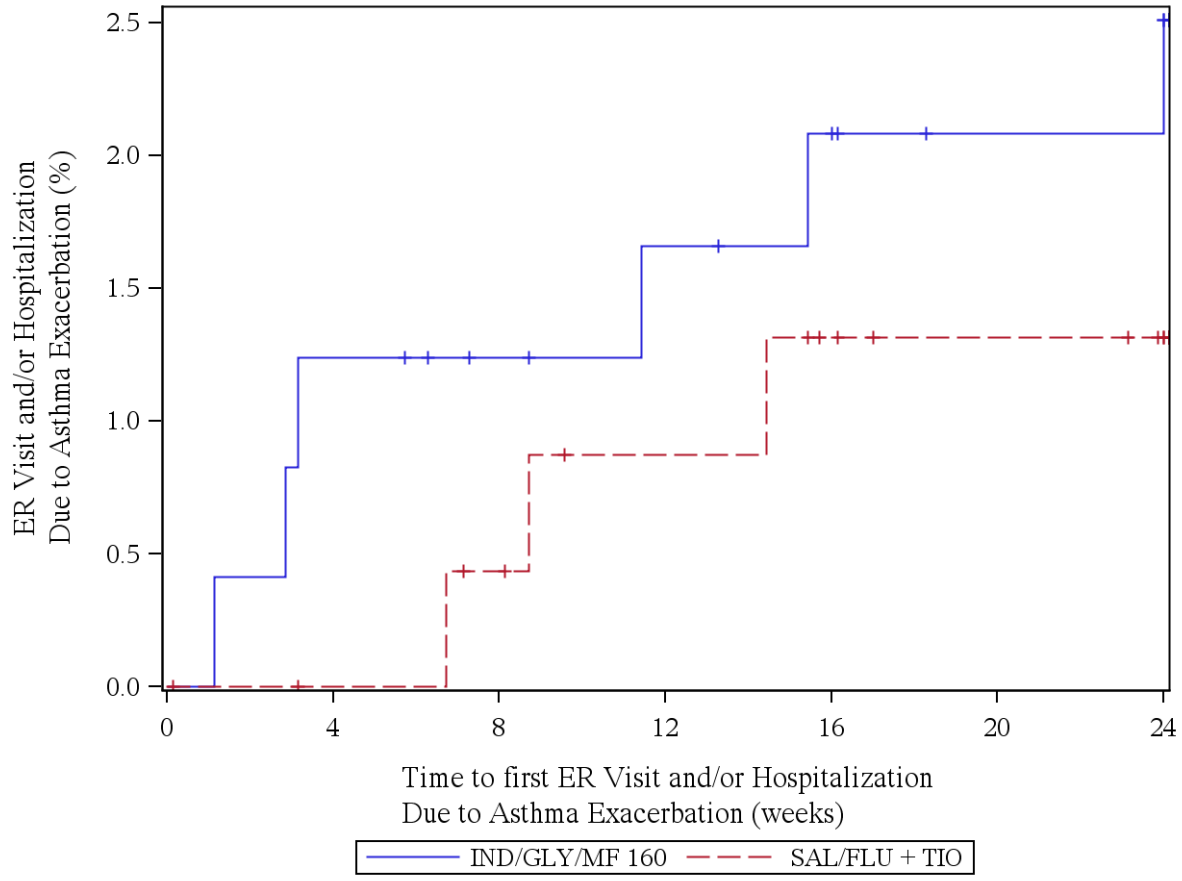
Figure 11.24.1 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 230/240, Week 8: 228/238, Week 16: 226/234, Week 24: 221/232

Analysis population: B2306 FAS total population

Figure 11.24.2 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA

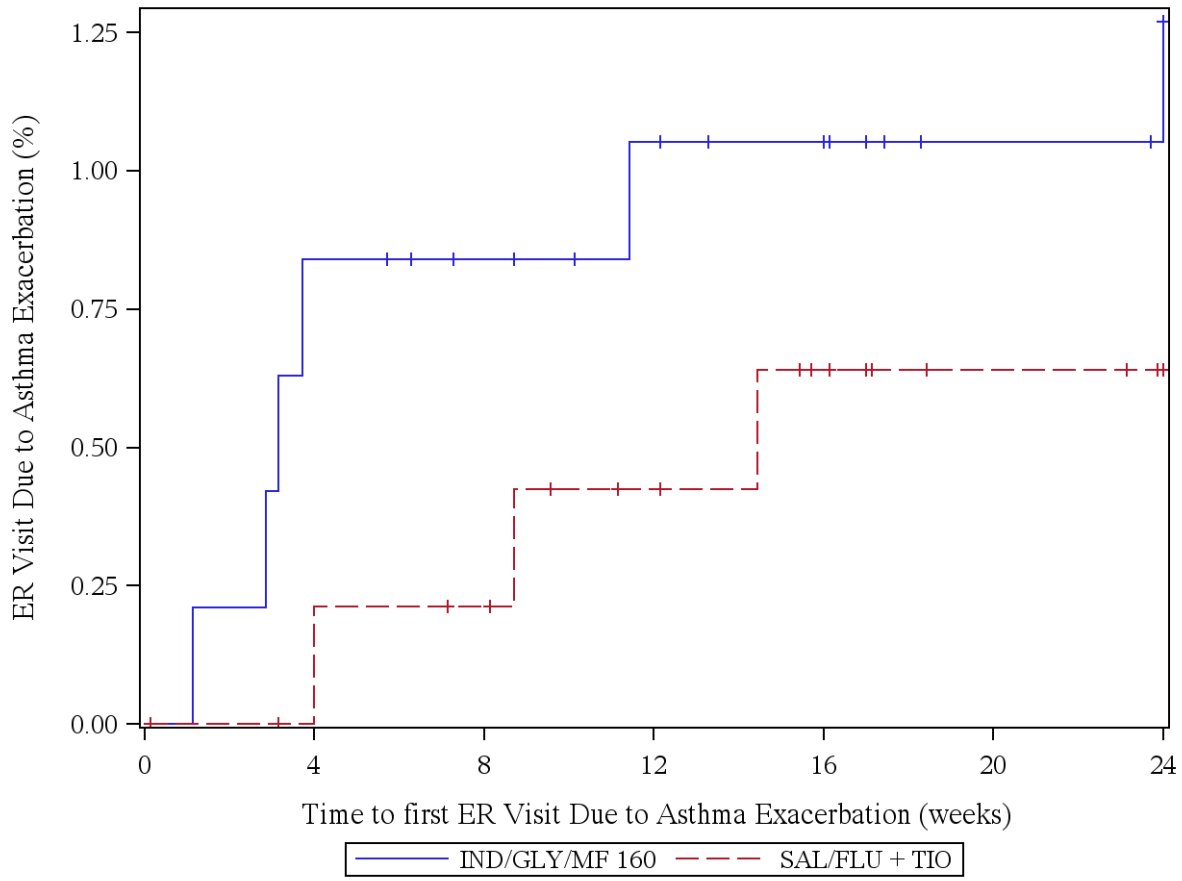


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 242/232, Week 8: 236/228, Week 16: 231/222, Week 24: 226/216

Analysis population: B2306 FAS total population

11.25 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation (FAS)

Figure 11.25 ER Visit Due to Asthma Exacerbation (FAS)

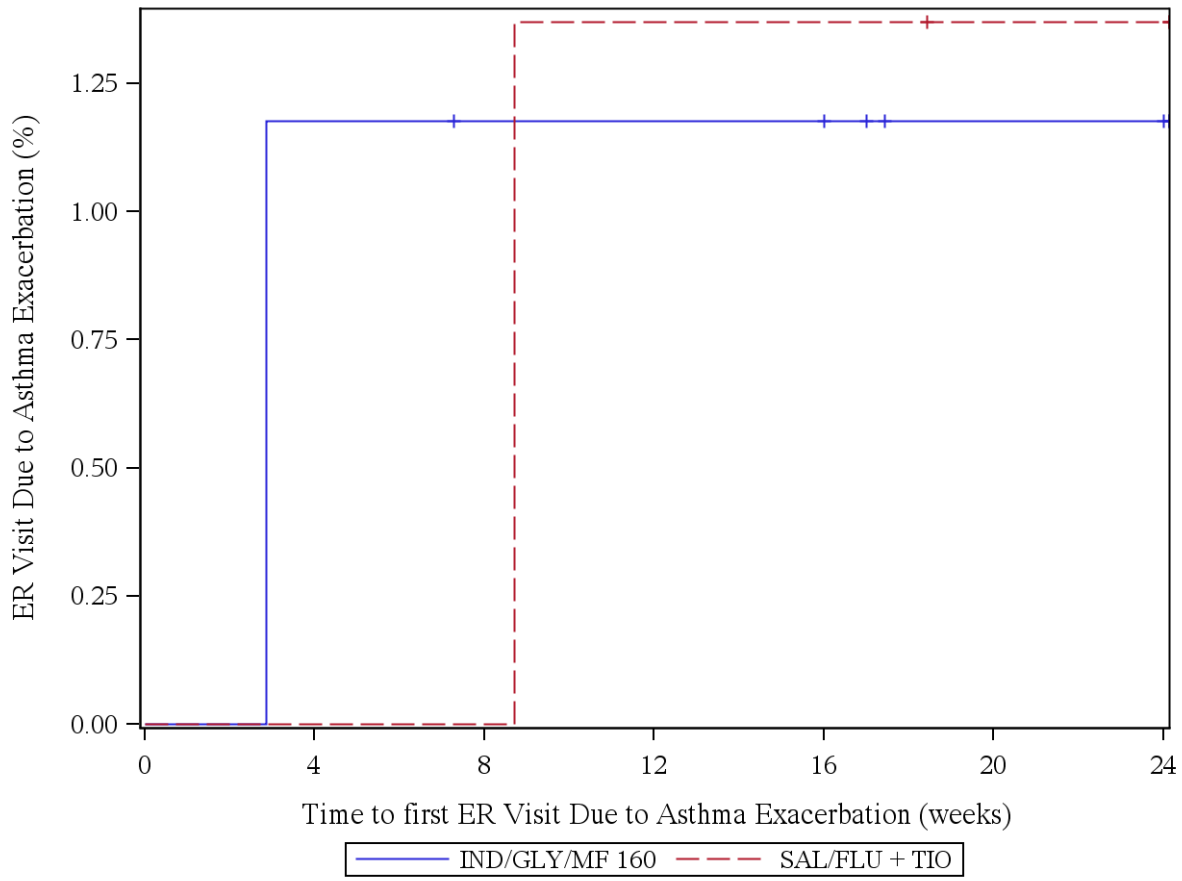


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 476/475, Week 8: 469/470, Week 16: 463/461, Week 24: 452/453

Analysis population: B2306 FAS total population

11.26 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation by Age (FAS)

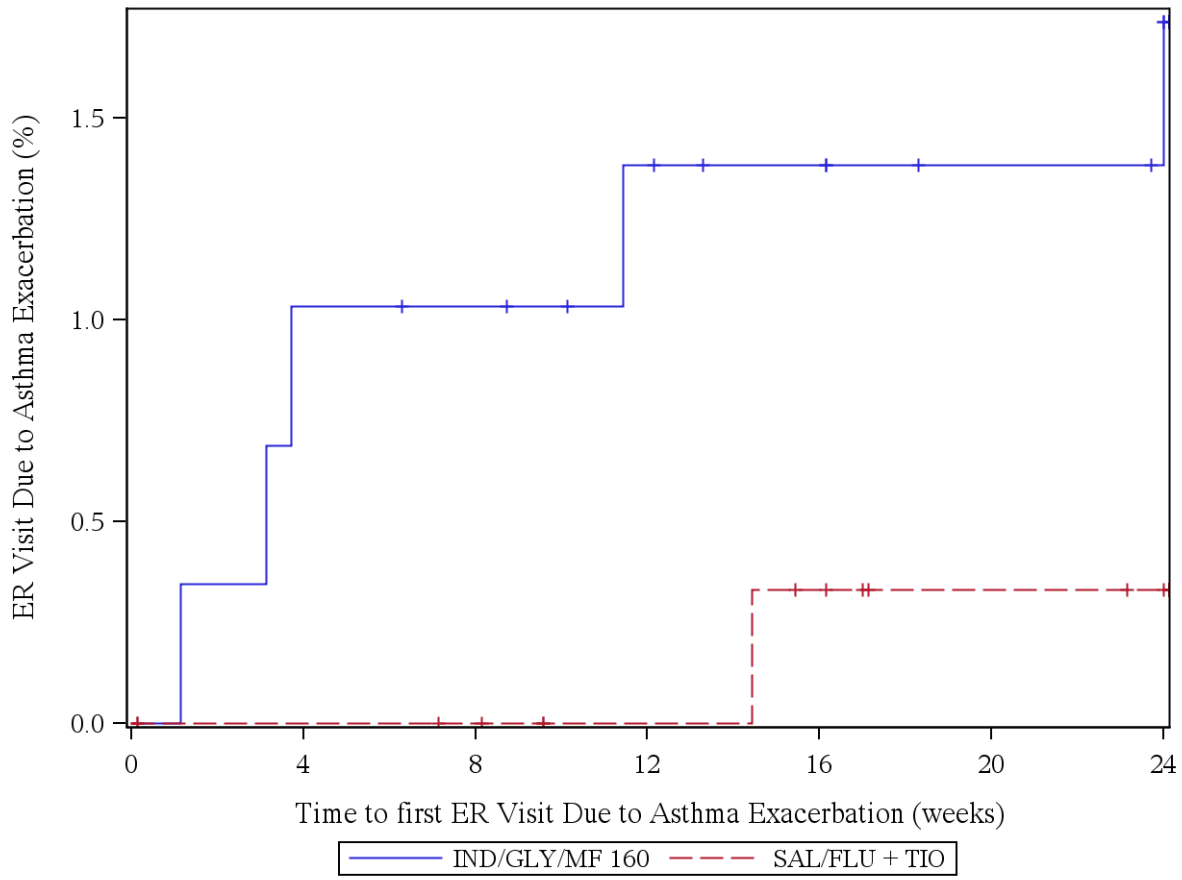
Figure 11.26.1 ER Visit Due to Asthma Exacerbation (FAS), Age = 18-39 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 85/73, Week 8: 83/73, Week 16: 82/72, Week 24: 79/71

Analysis population: B2306 FAS total population

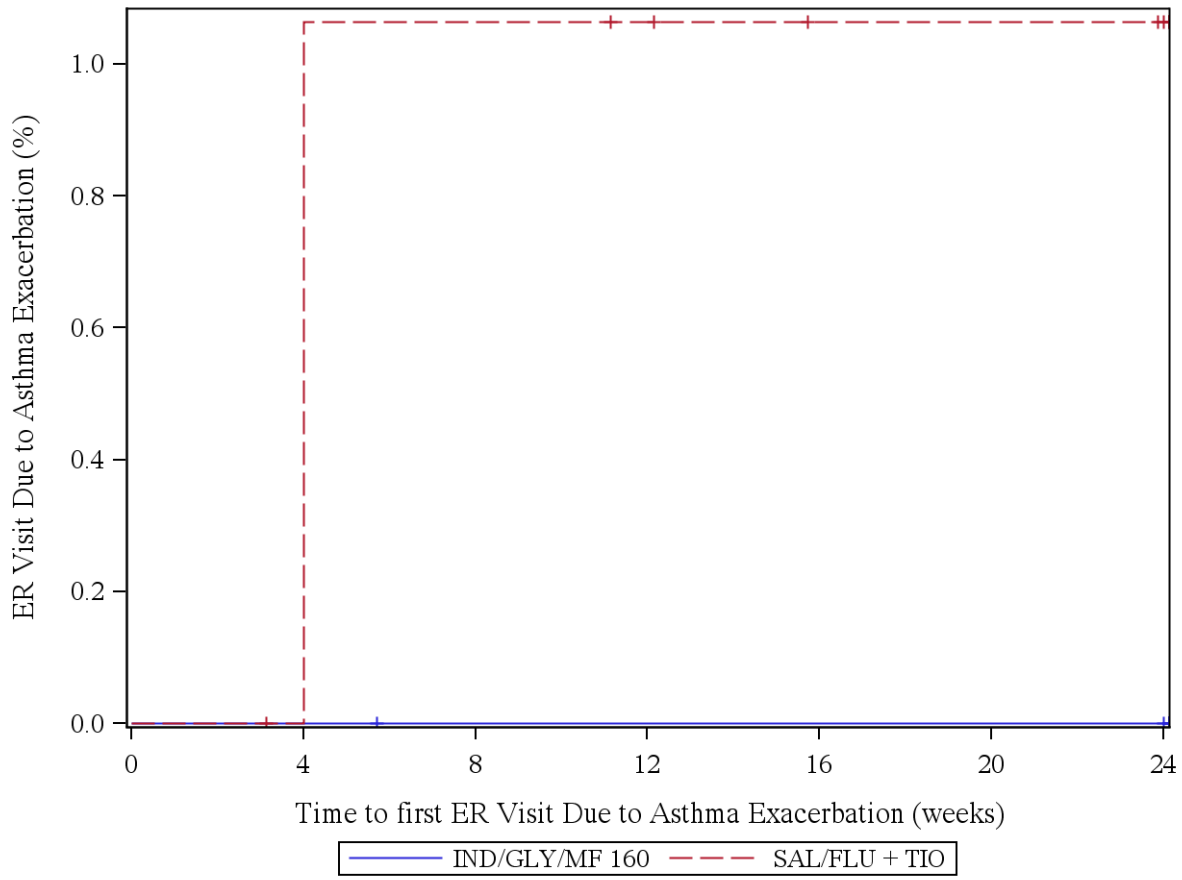
Figure 11.26.2 ER Visit Due to Asthma Exacerbation (FAS), Age = 40-64 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 290/307, Week 8: 286/304, Week 16: 281/299, Week 24: 274/294

Analysis population: B2306 FAS total population

Figure 11.26.3 ER Visit Due to Asthma Exacerbation (FAS), Age = ≥65 years

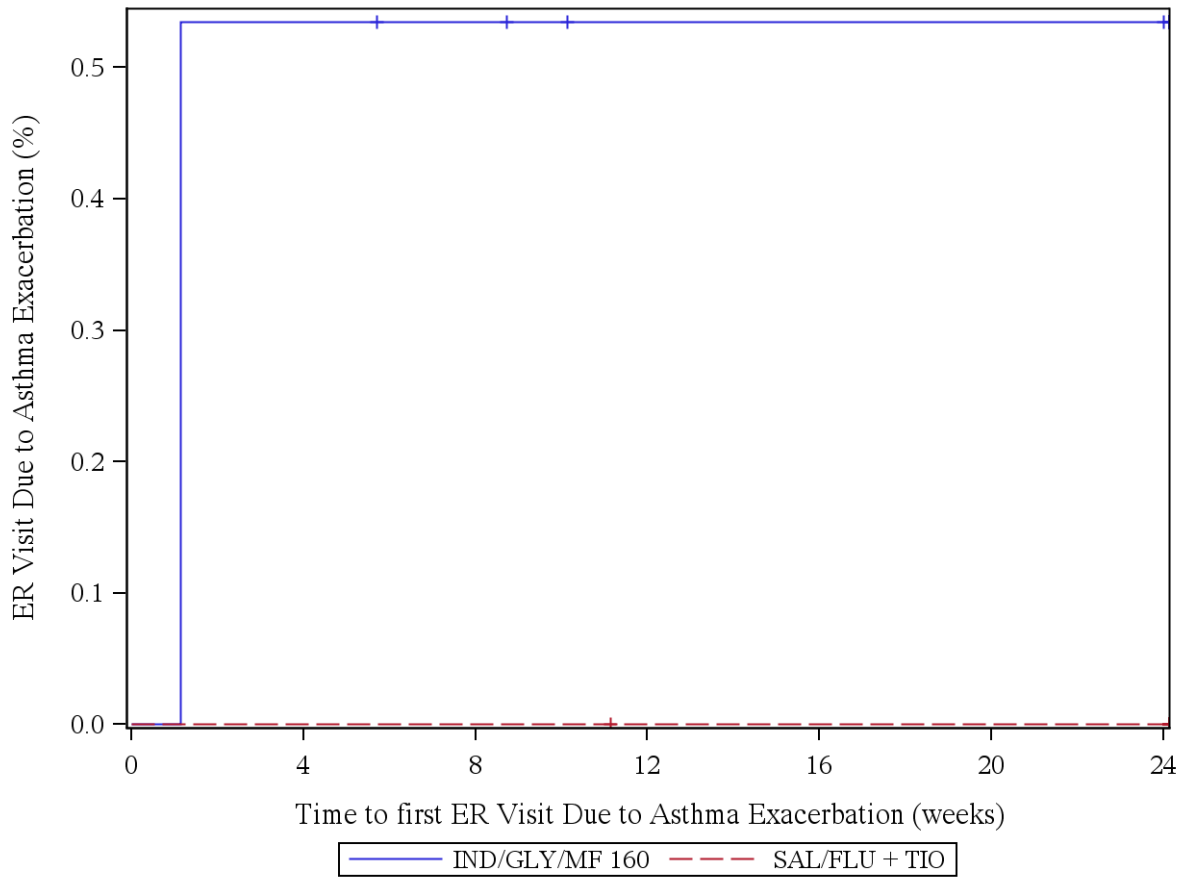


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 101/95, Week 8: 100/93, Week 16: 100/90, Week 24: 99/88

Analysis population: B2306 FAS total population

11.27 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation by Gender (FAS)

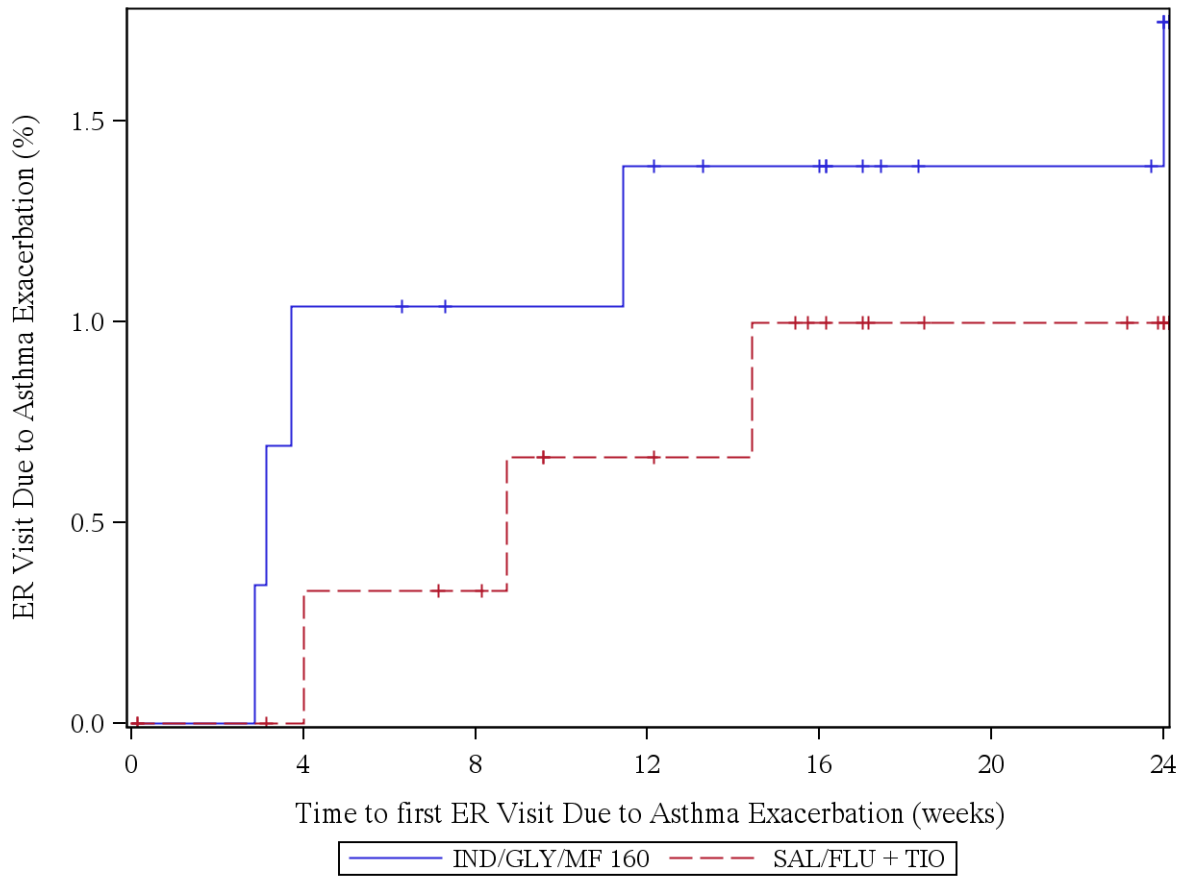
Figure 11.27.1 ER Visit Due to Asthma Exacerbation (FAS), Gender = Male



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 187/169, Week 8: 185/169, Week 16: 183/168, Week 24: 182/168

Analysis population: B2306 FAS total population

Figure 11.27.2 ER Visit Due to Asthma Exacerbation (FAS), Gender = Female

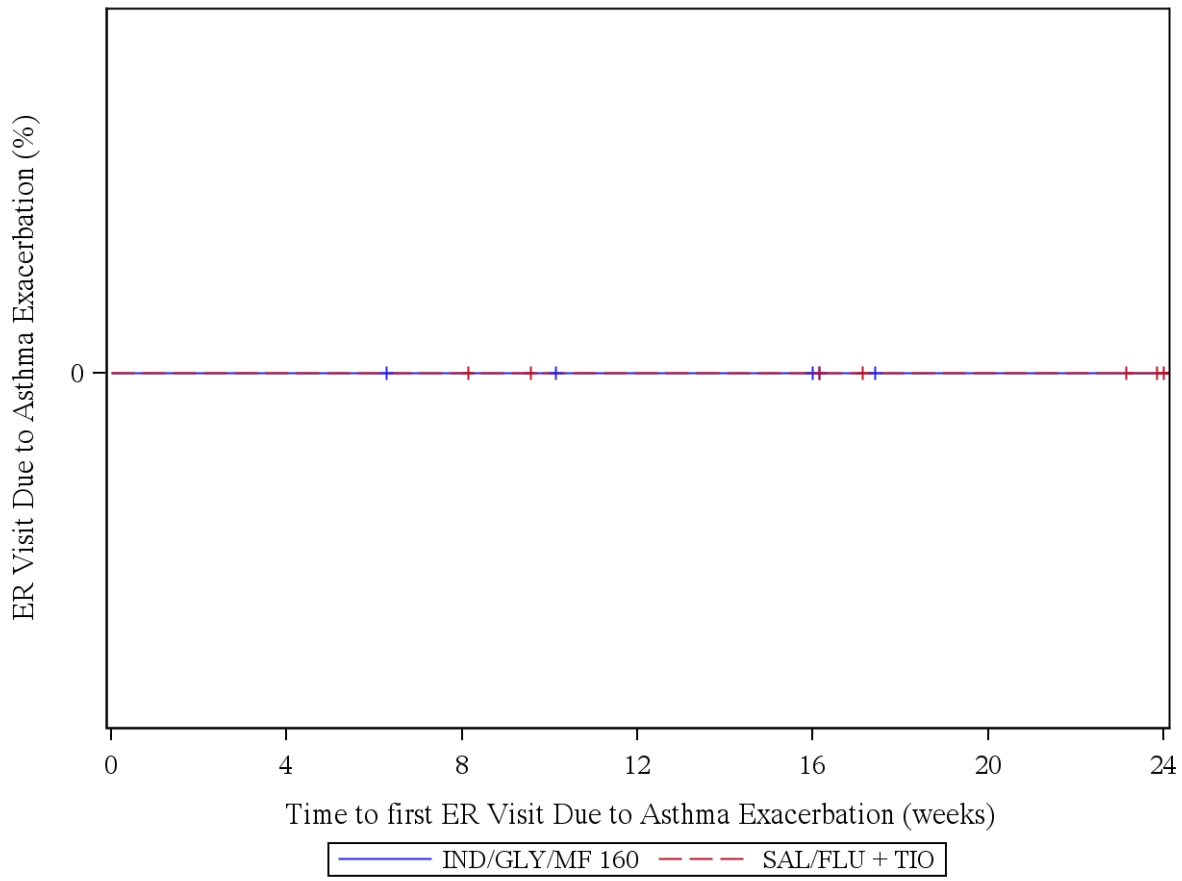


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 289/306, Week 8: 284/301, Week 16: 280/293, Week 24: 270/285

Analysis population: B2306 FAS total population

11.28 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation by Region (FAS)

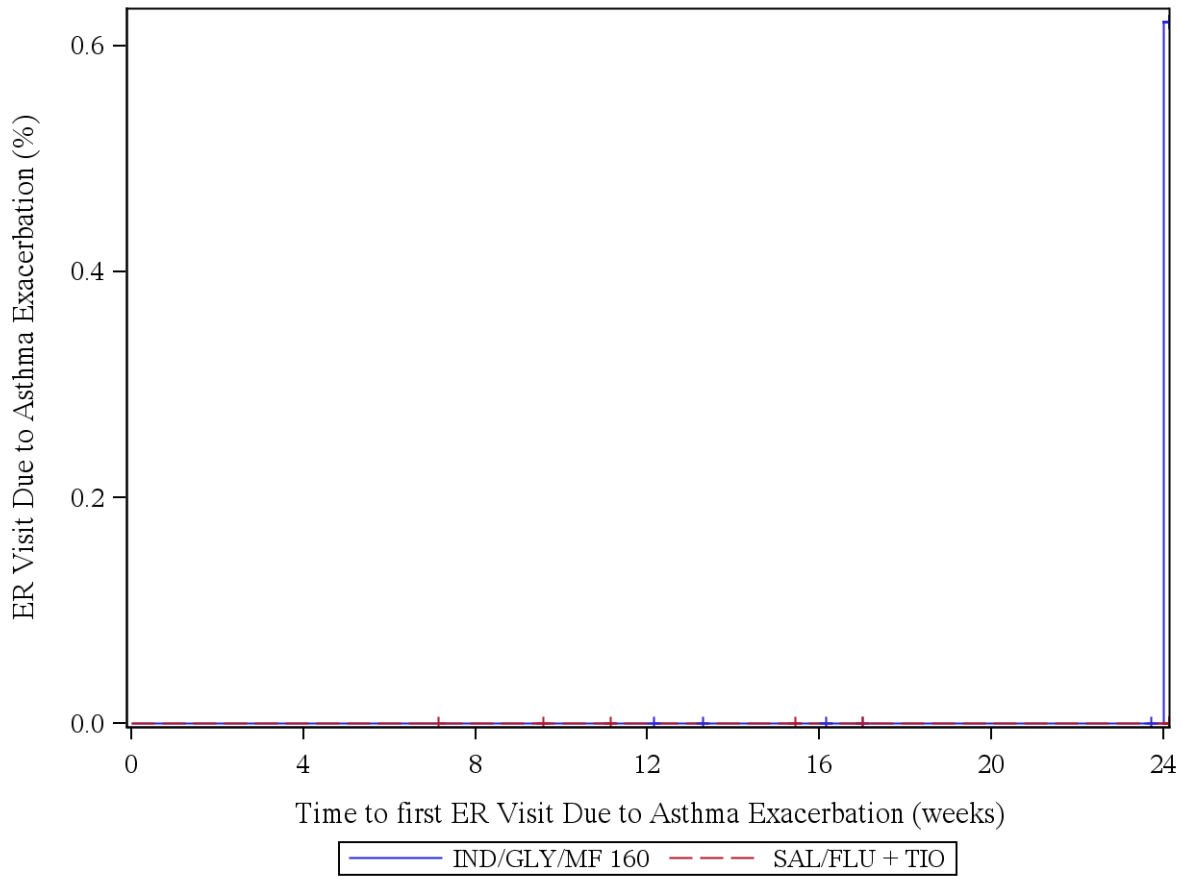
Figure 11.28.1 ER Visit Due to Asthma Exacerbation (FAS), Region = Asia



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 124/131, Week 8: 123/131, Week 16: 121/129, Week 24: 119/124

Analysis population: B2306 FAS total population

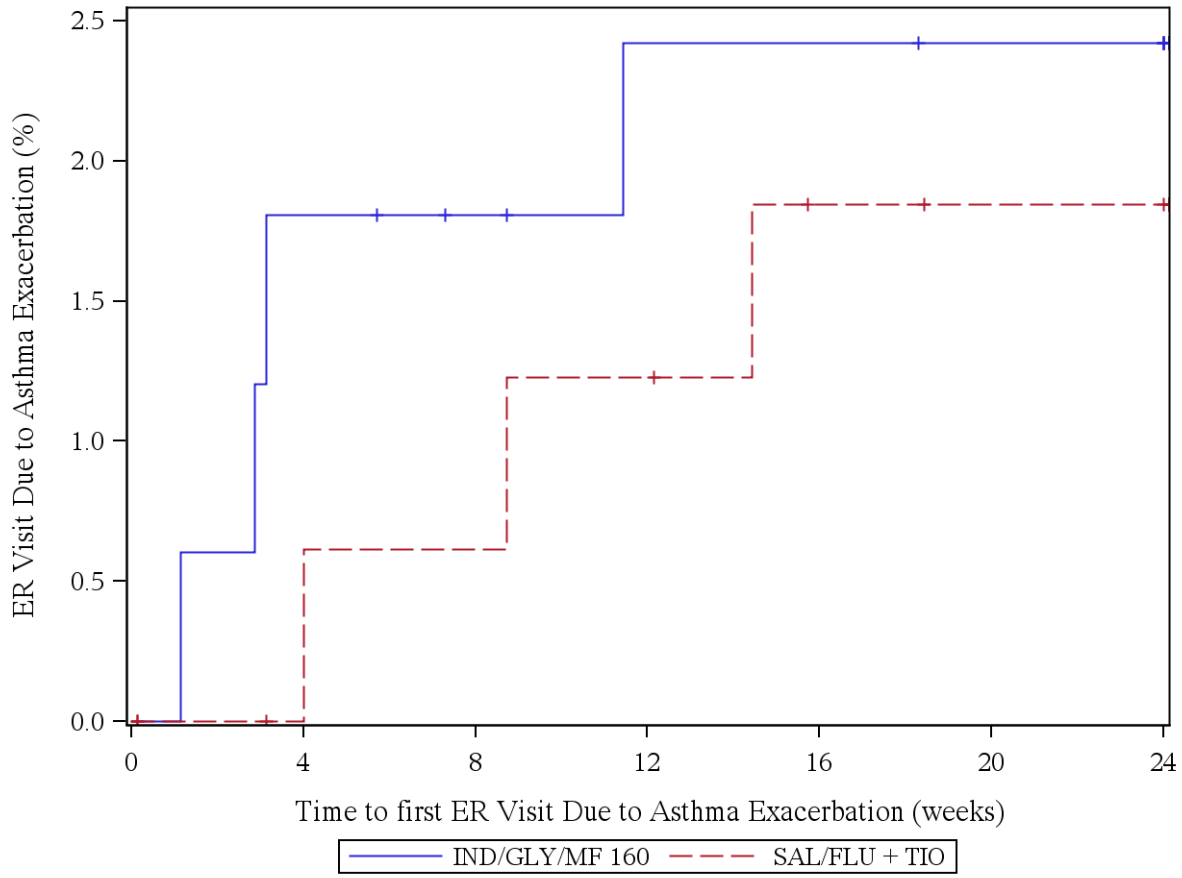
Figure 11.28.2 ER Visit Due to Asthma Exacerbation (FAS), Region = Europe



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 166/169, Week 8: 166/168, Week 16: 164/165, Week 24: 160/164

Analysis population: B2306 FAS total population

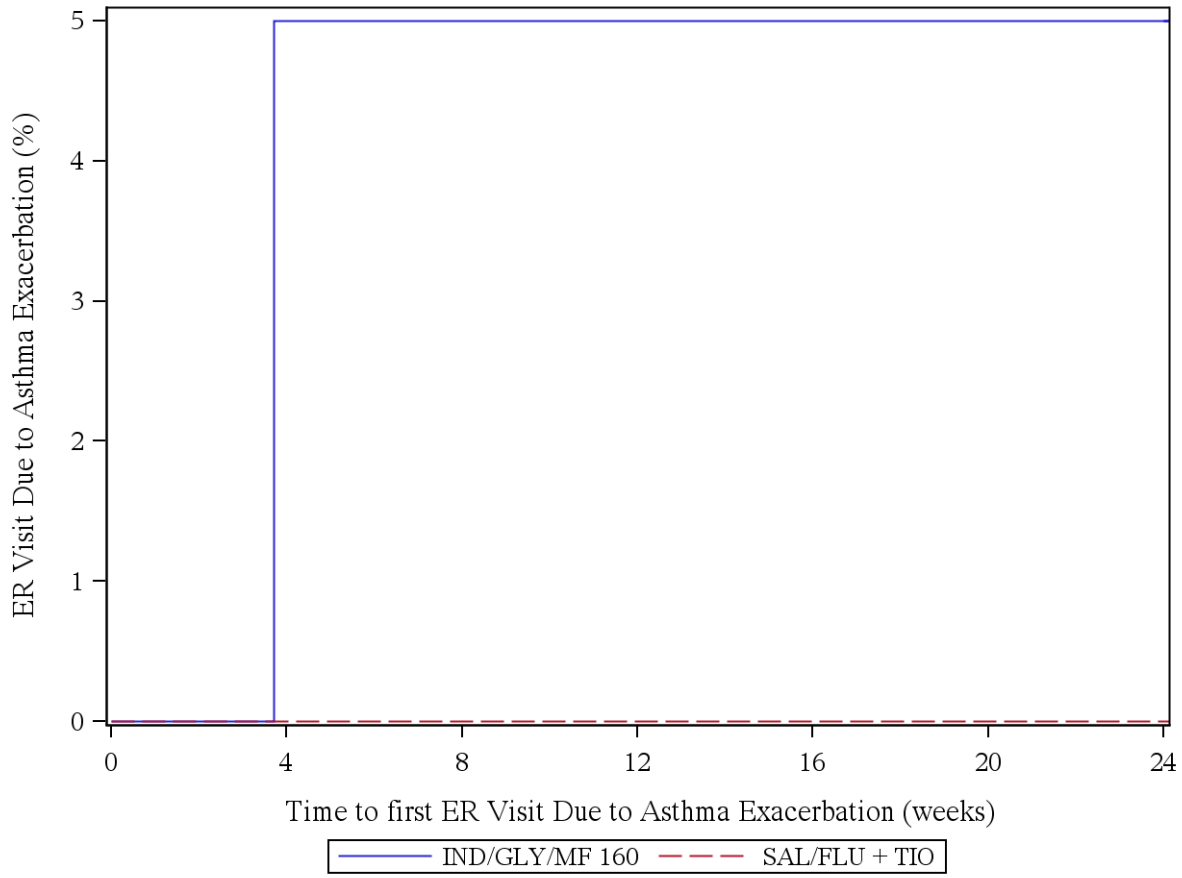
Figure 11.28.3 ER Visit Due to Asthma Exacerbation (FAS), Region = Latin America



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 166/166, Week 8: 161/162, Week 16: 159/158, Week 24: 154/156

Analysis population: B2306 FAS total population

Figure 11.28.4 ER Visit Due to Asthma Exacerbation (FAS), Region = Others

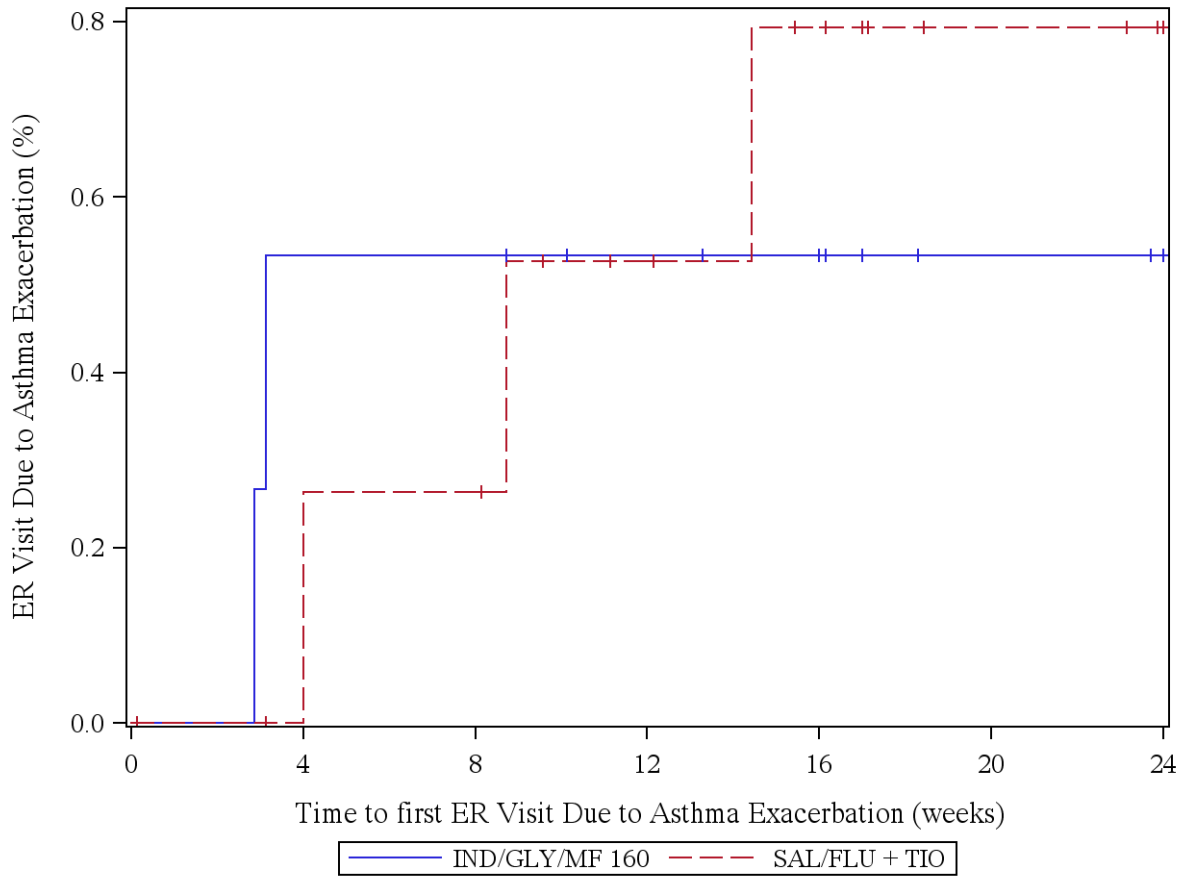


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 20/9, Week 8: 19/9, Week 16: 19/9, Week 24: 19/9

Analysis population: B2306 FAS total population

11.29 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation by History of Asthma Exacerbation (FAS)

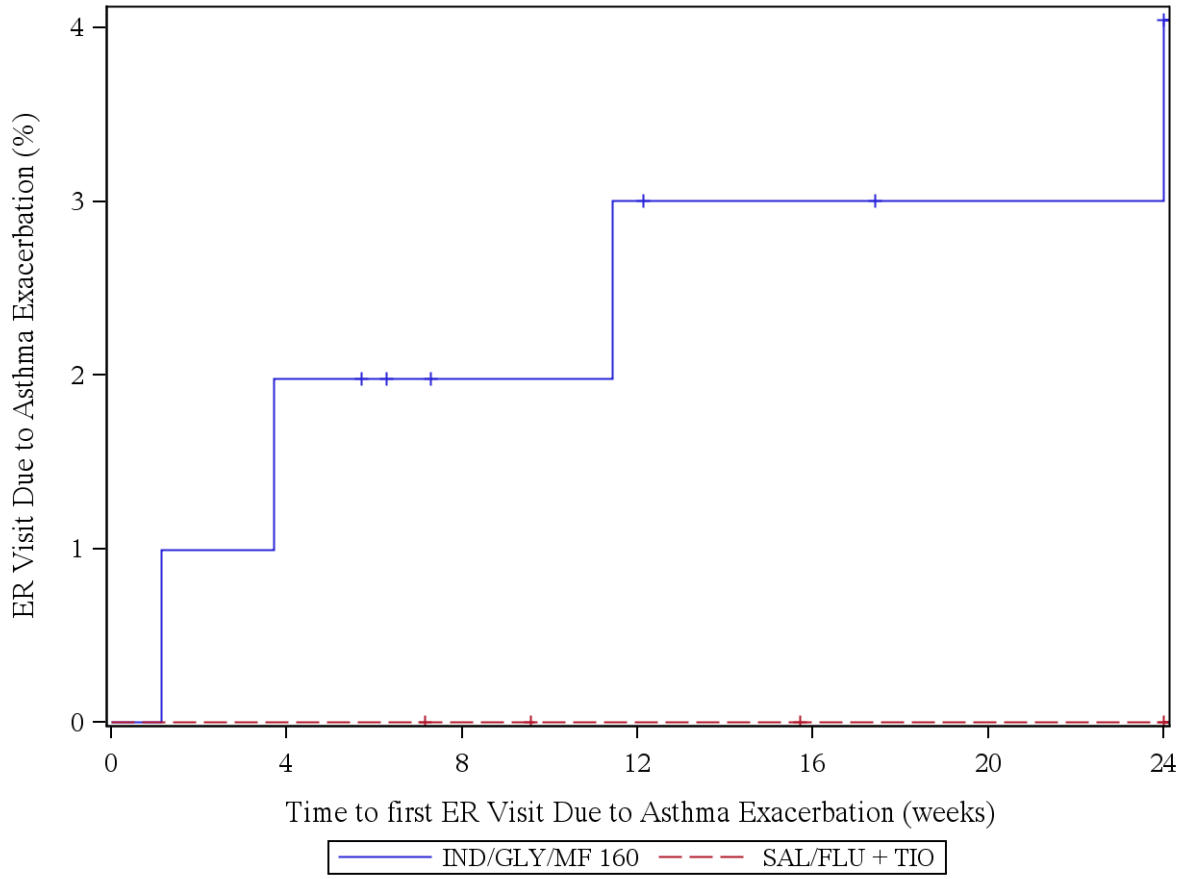
Figure 11.29.1 ER Visit Due to Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 375/383, Week 8: 373/379, Week 16: 369/372, Week 24: 361/365

Analysis population: B2306 FAS total population

Figure 11.29.2 ER Visit Due to Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2

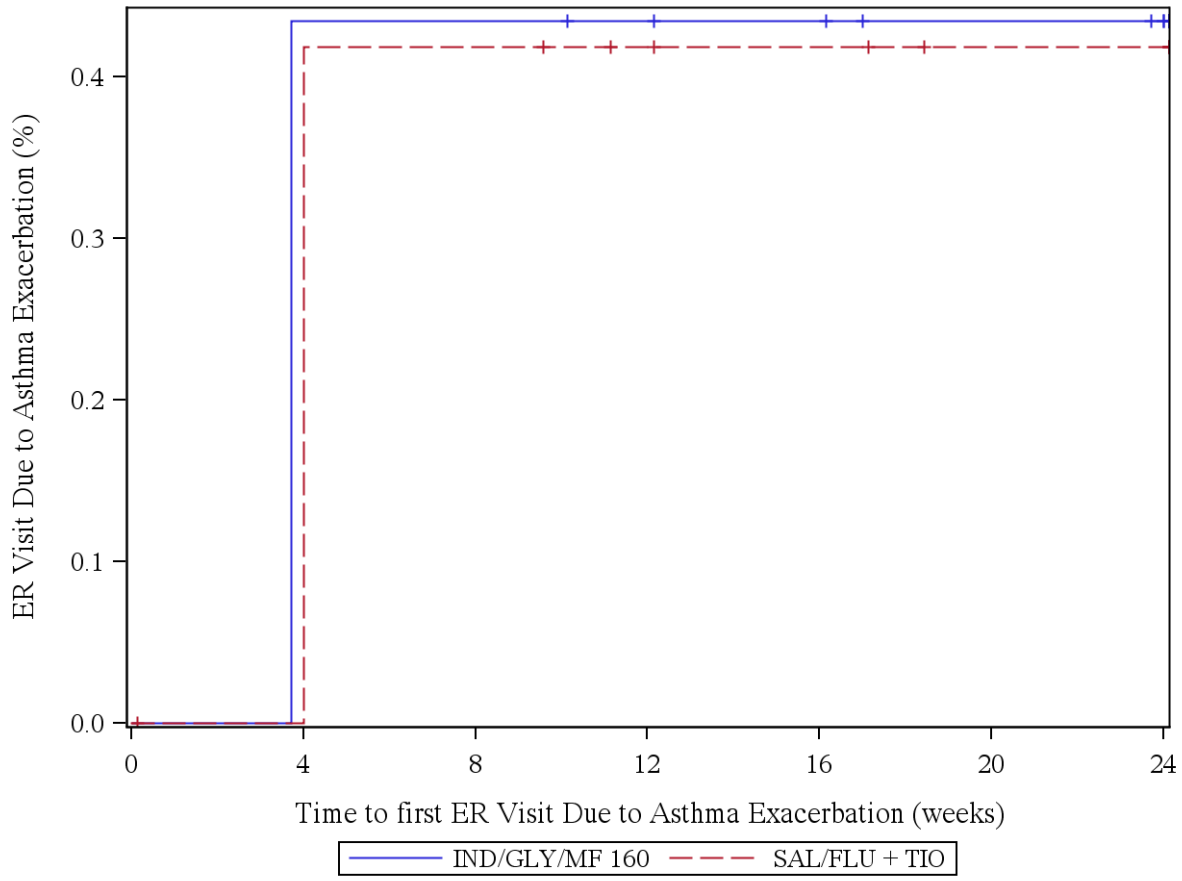


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 101/92, Week 8: 96/91, Week 16: 94/89, Week 24: 91/88

Analysis population: B2306 FAS total population

11.30 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation by Patients' Prior Therapies (FAS)

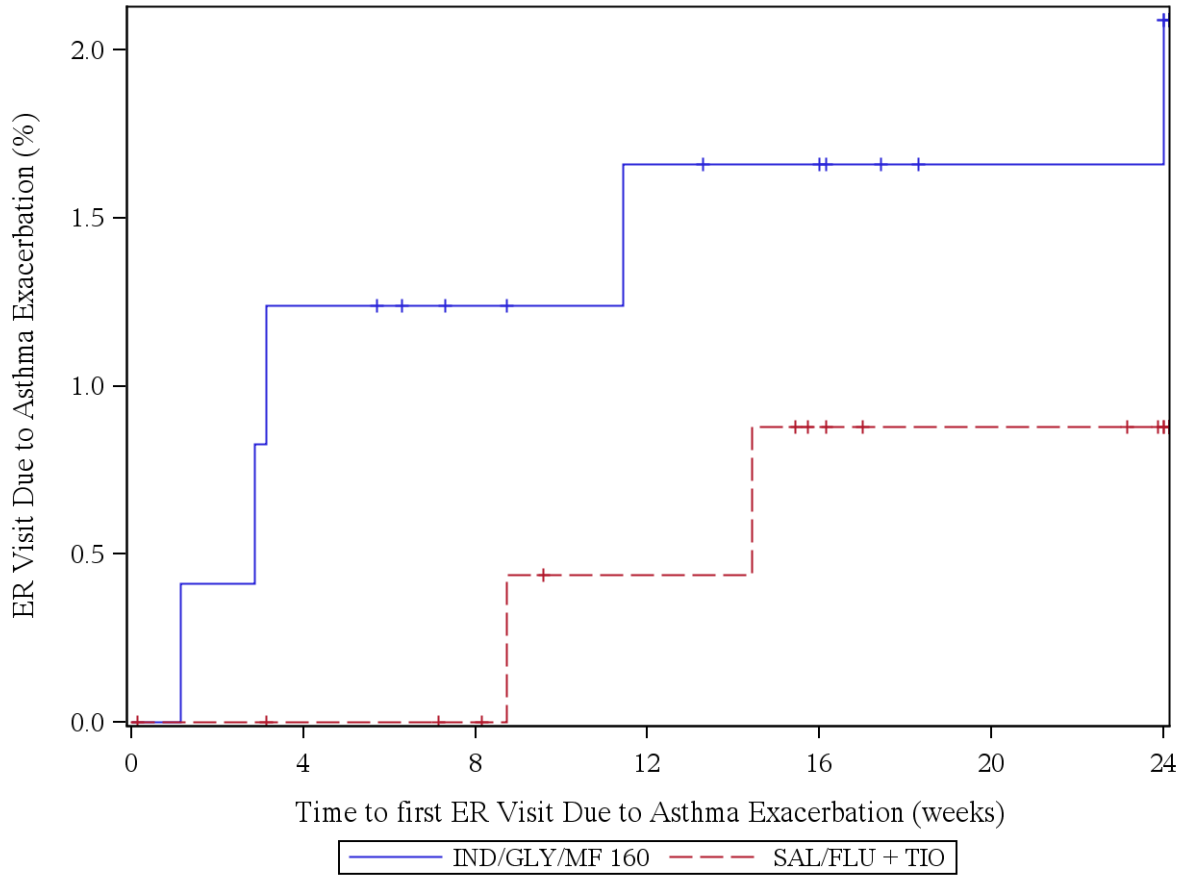
Figure 11.30.1 ER Visit Due to Asthma Exacerbation (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 230/240, Week 8: 229/238, Week 16: 227/235, Week 24: 222/233

Analysis population: B2306 FAS total population

Figure 11.30.2 ER Visit Due to Asthma Exacerbation (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA

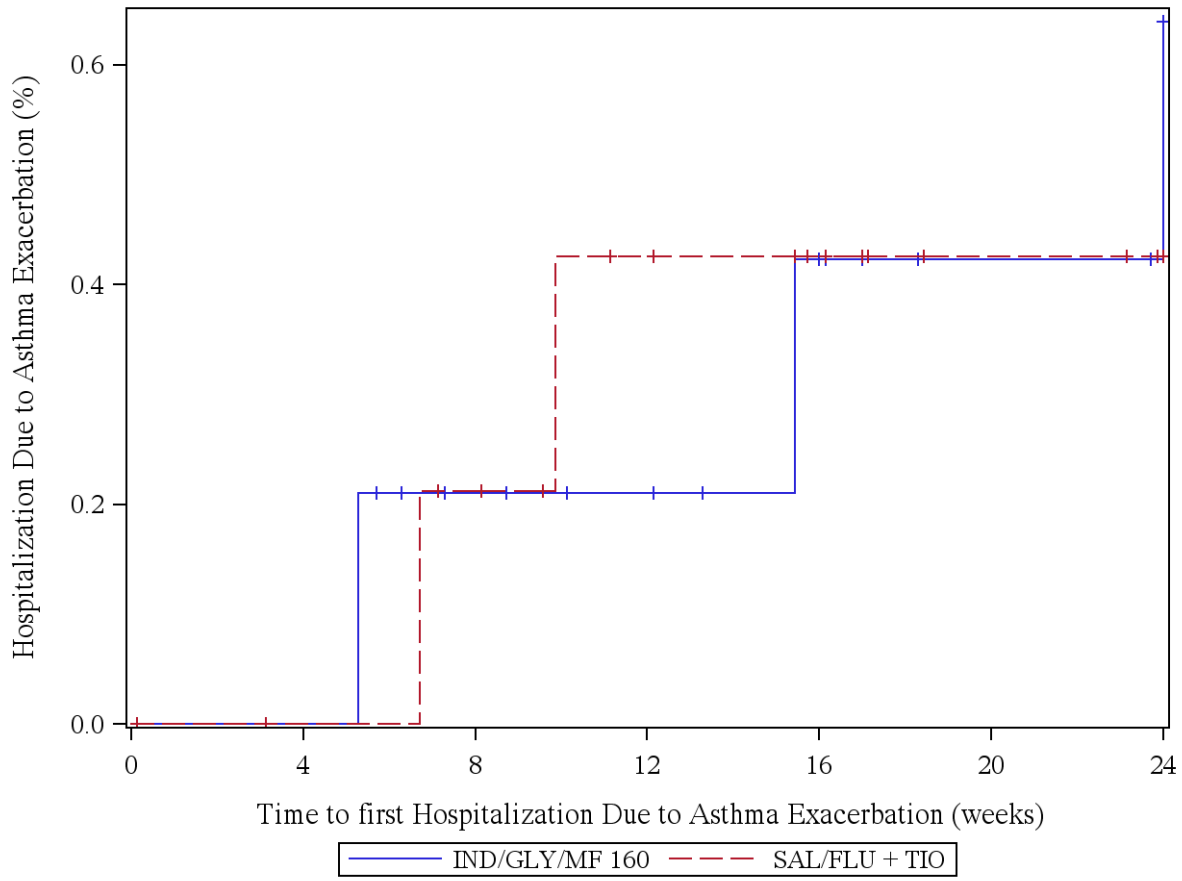


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 242/232, Week 8: 236/229, Week 16: 232/223, Week 24: 226/217

Analysis population: B2306 FAS total population

11.31 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation (FAS)

Figure 11.31 Hospitalization Due to Asthma Exacerbation (FAS)

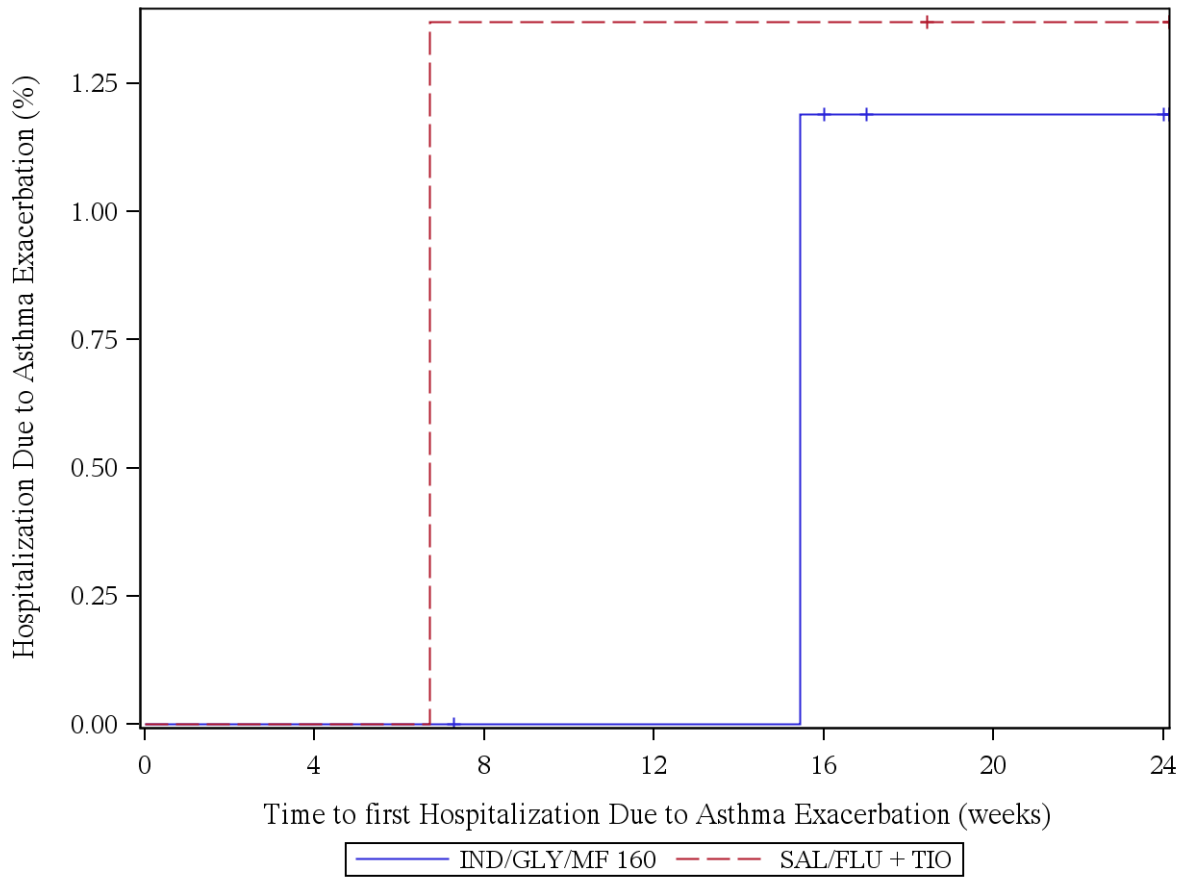


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 476/475, Week 8: 472/470, Week 16: 466/462, Week 24: 456/454

Analysis population: B2306 FAS total population

11.32 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation by Age (FAS)

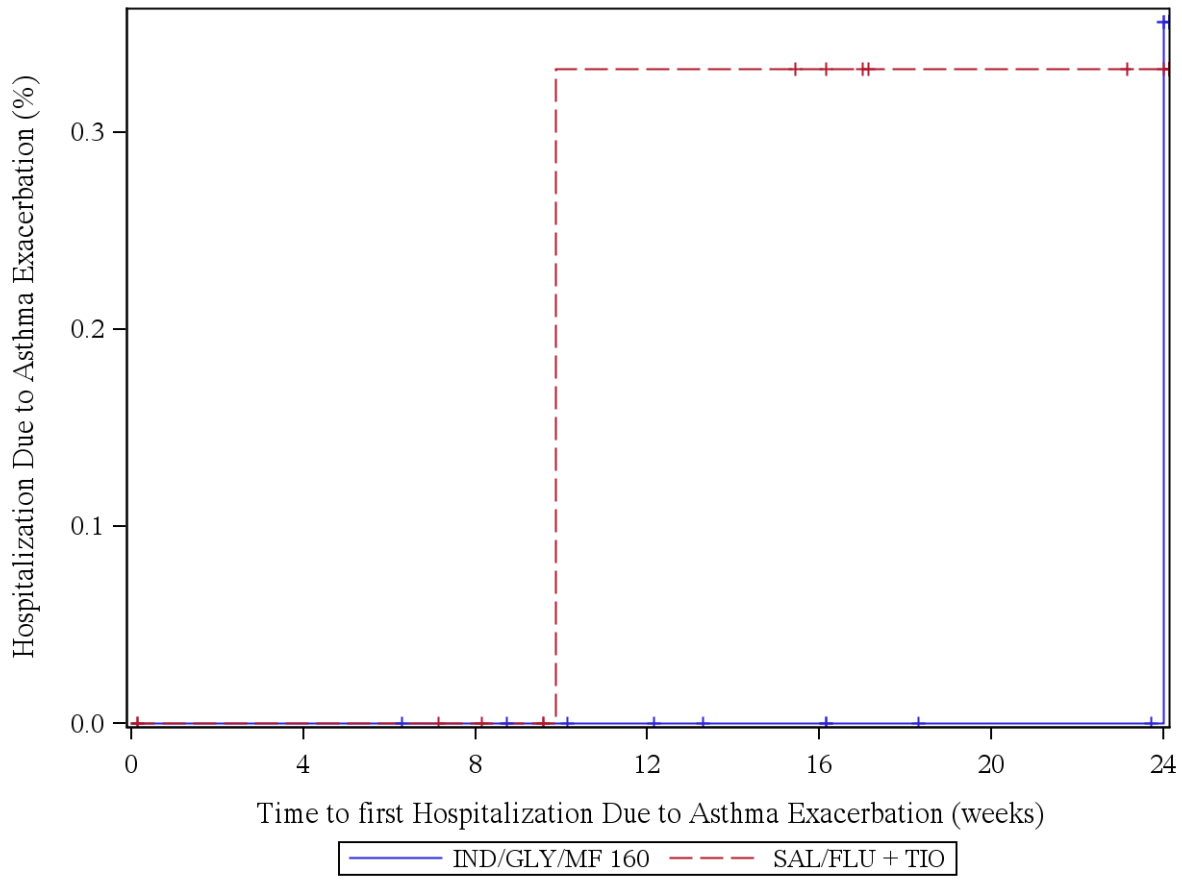
Figure 11.32.1 Hospitalization Due to Asthma Exacerbation (FAS), Age = 18-39 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 85/73, Week 8: 84/72, Week 16: 82/72, Week 24: 80/71

Analysis population: B2306 FAS total population

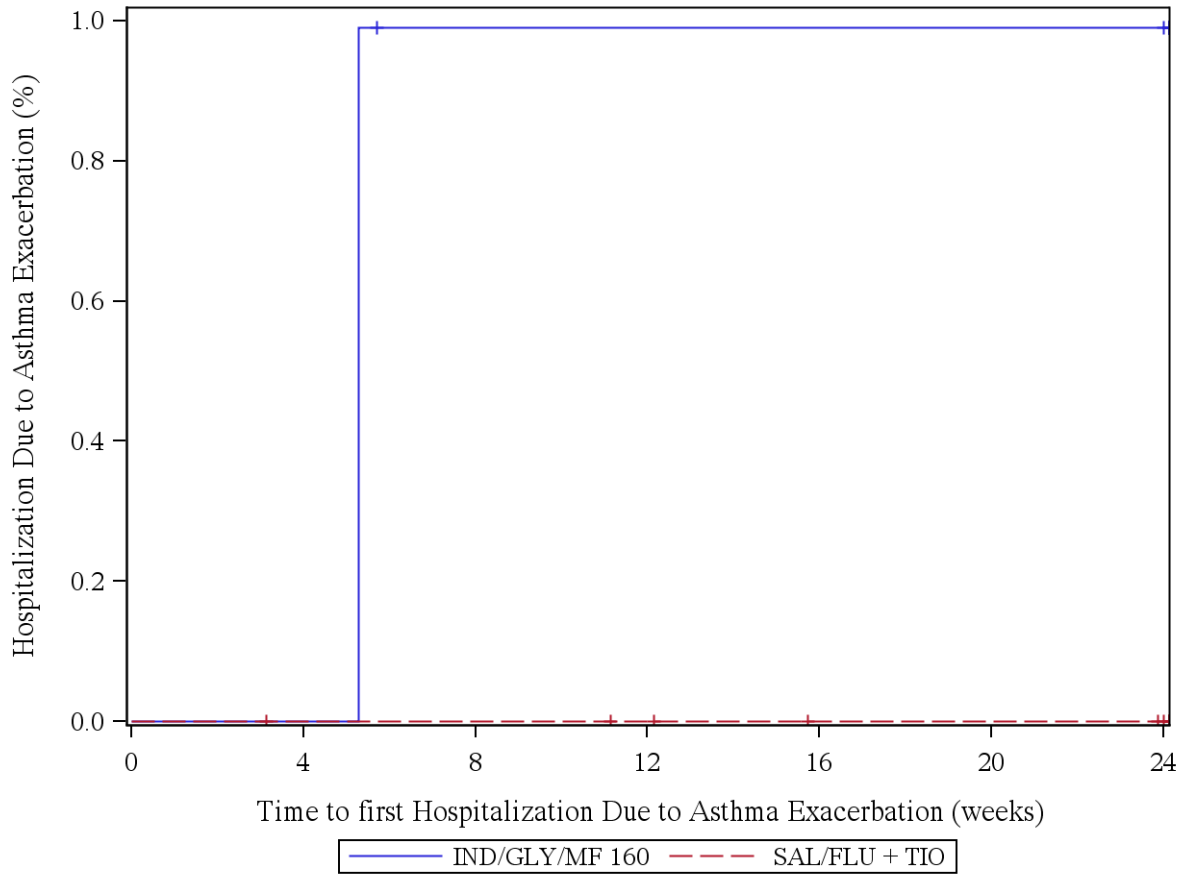
Figure 11.32.2 Hospitalization Due to Asthma Exacerbation (FAS), Age = 40-64 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 290/307, Week 8: 289/304, Week 16: 285/299, Week 24: 278/294

Analysis population: B2306 FAS total population

Figure 11.32.3 Hospitalization Due to Asthma Exacerbation (FAS), Age = ≥65 years

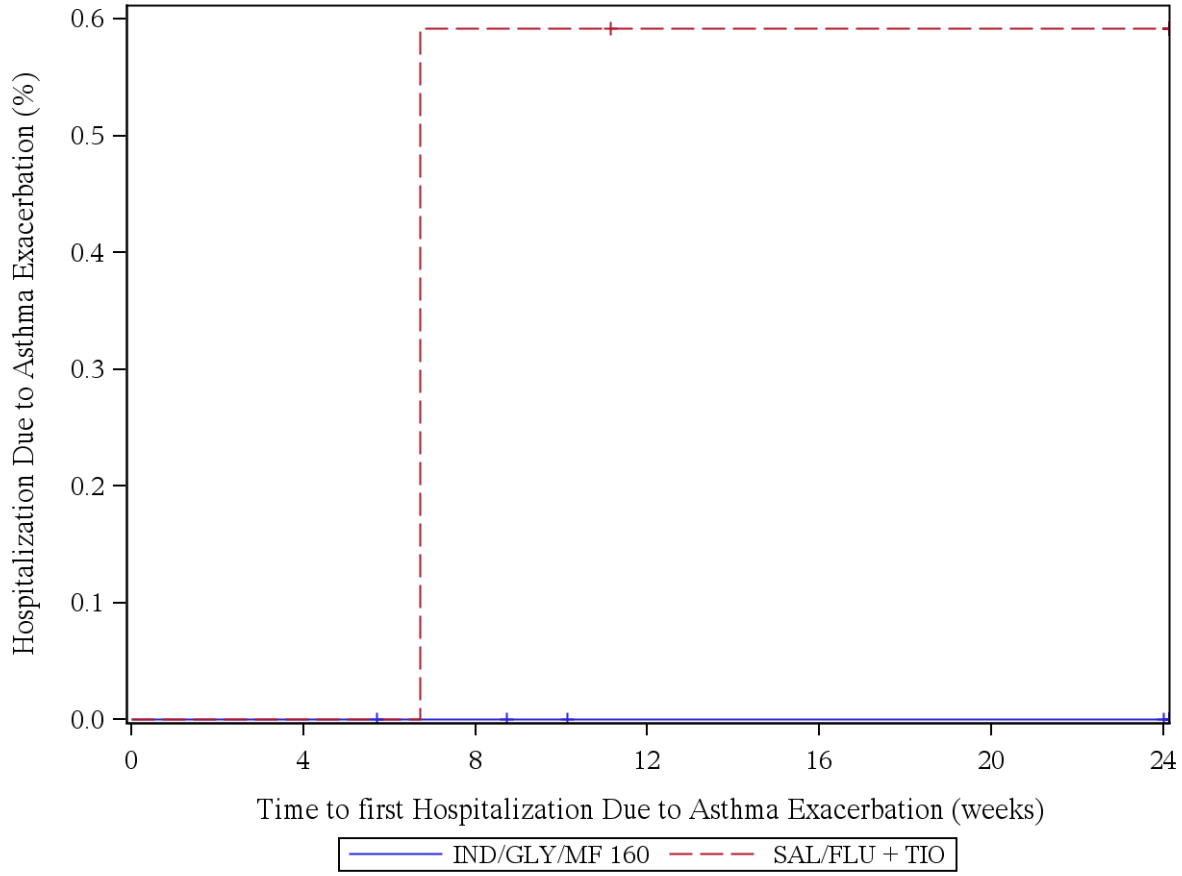


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 101/95, Week 8: 99/94, Week 16: 99/91, Week 24: 98/89

Analysis population: B2306 FAS total population

11.33 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation by Gender (FAS)

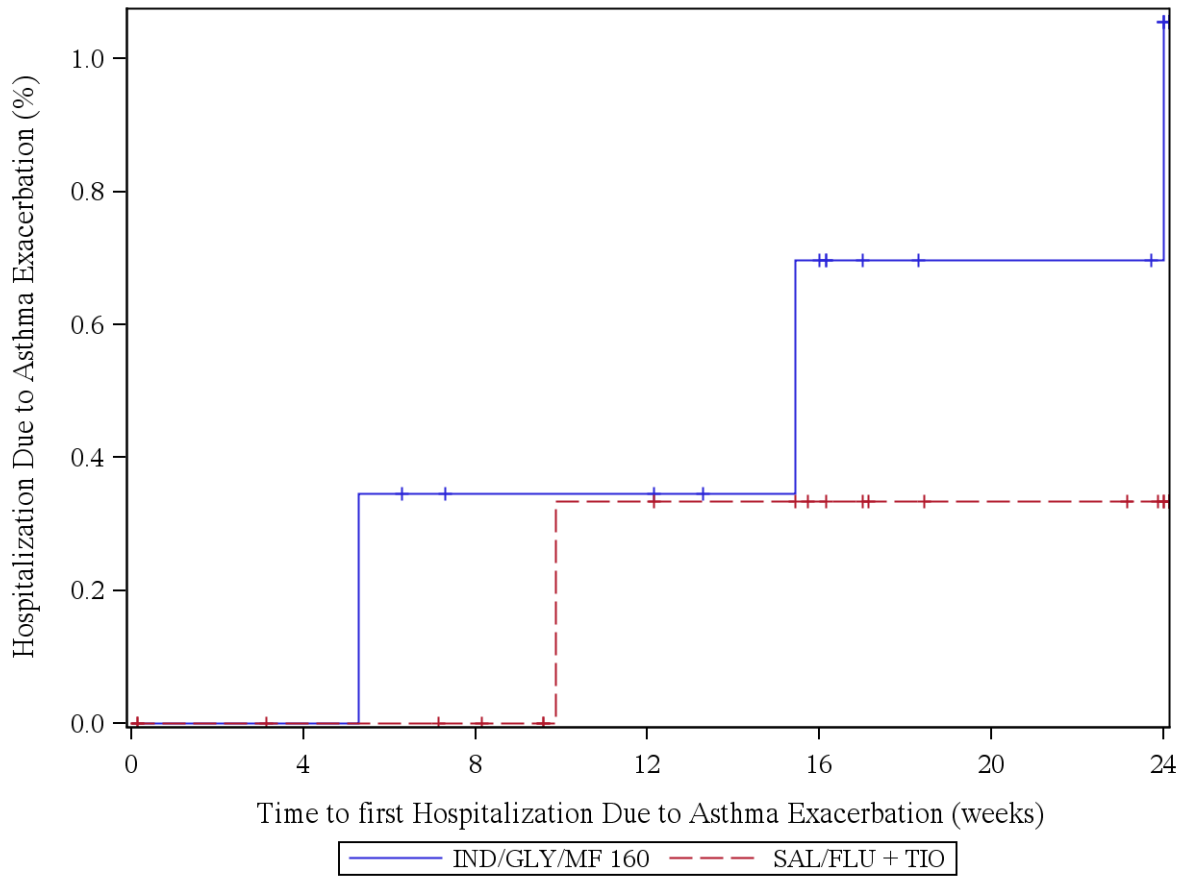
Figure 11.33.1 Hospitalization Due to Asthma Exacerbation (FAS), Gender = Male



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 187/169, Week 8: 186/168, Week 16: 184/167, Week 24: 183/167

Analysis population: B2306 FAS total population

Figure 11.33.2 Hospitalization Due to Asthma Exacerbation (FAS), Gender = Female

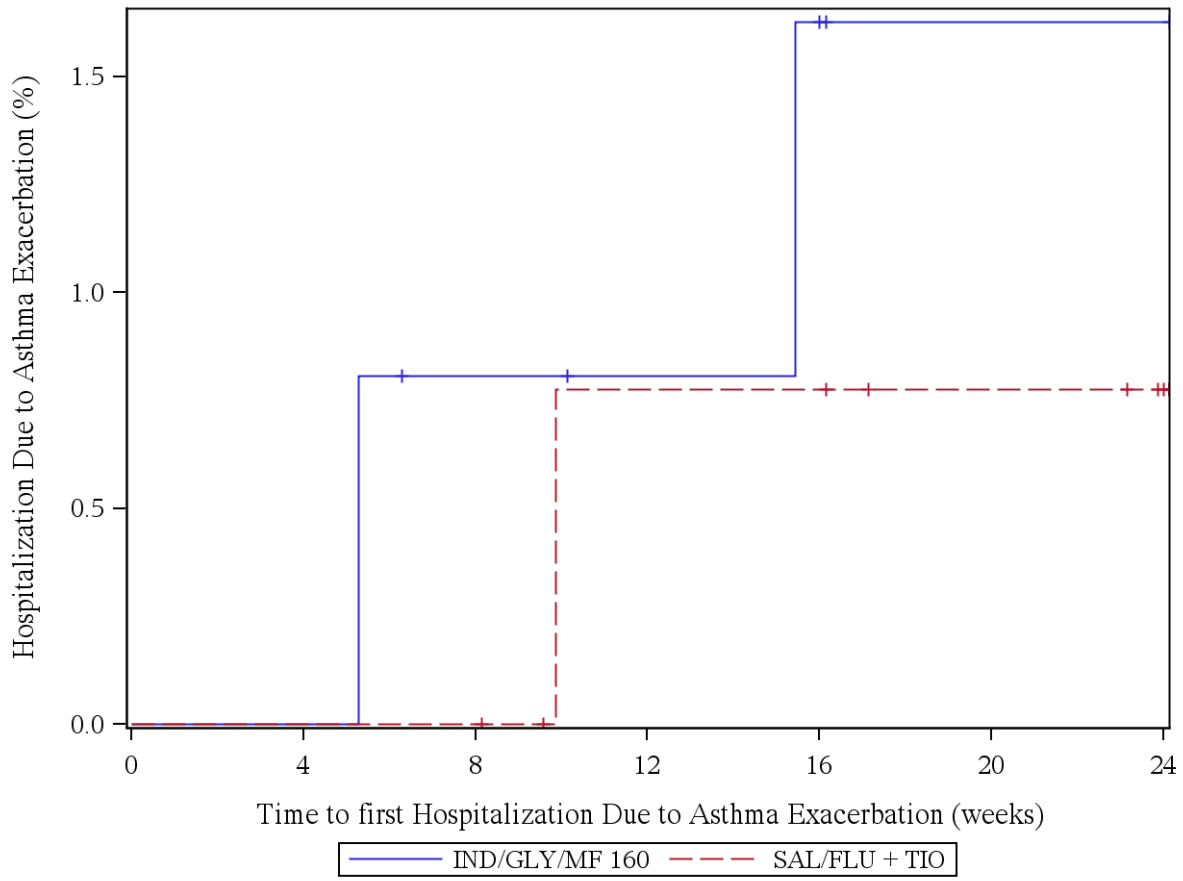


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 289/306, Week 8: 286/302, Week 16: 282/295, Week 24: 273/287

Analysis population: B2306 FAS total population

11.34 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation by Region (FAS)

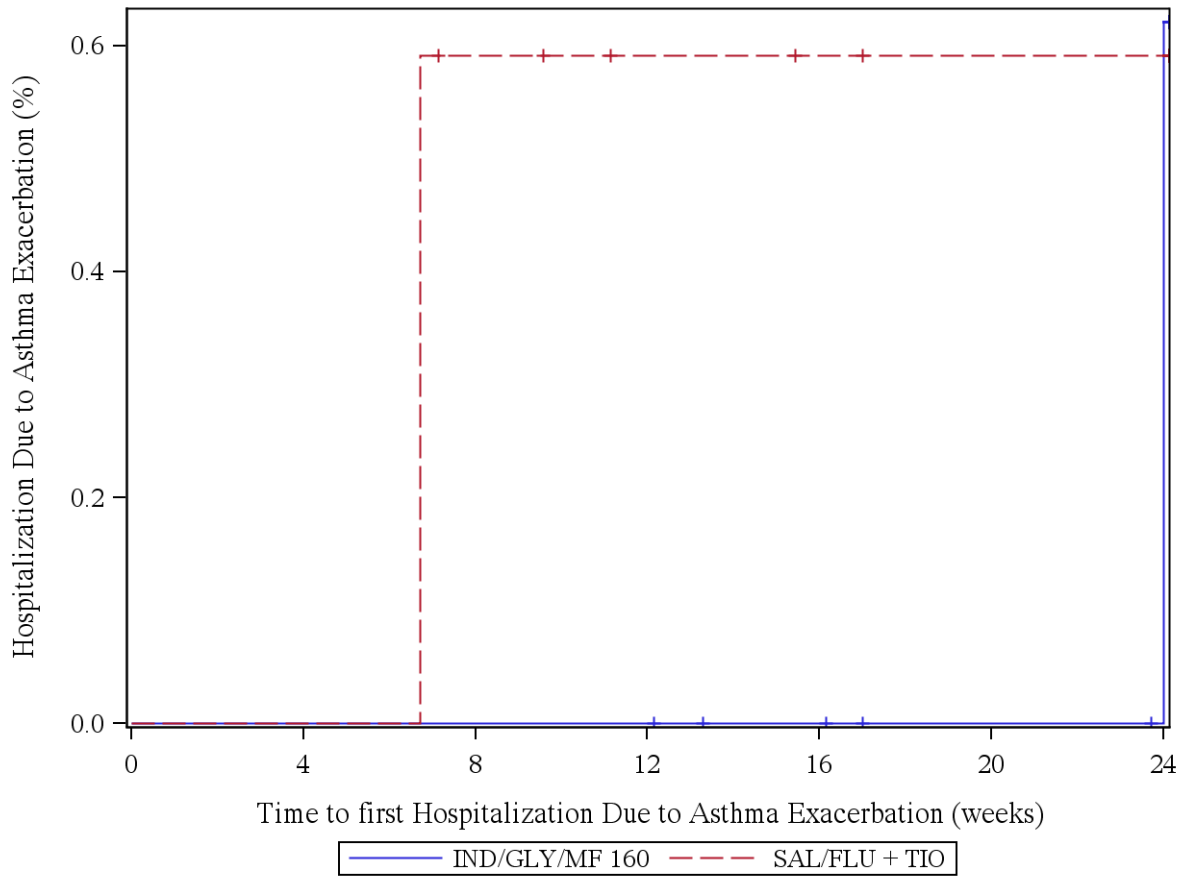
Figure 11.34.1 Hospitalization Due to Asthma Exacerbation (FAS), Region = Asia



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 124/131, Week 8: 122/131, Week 16: 119/128, Week 24: 118/123

Analysis population: B2306 FAS total population

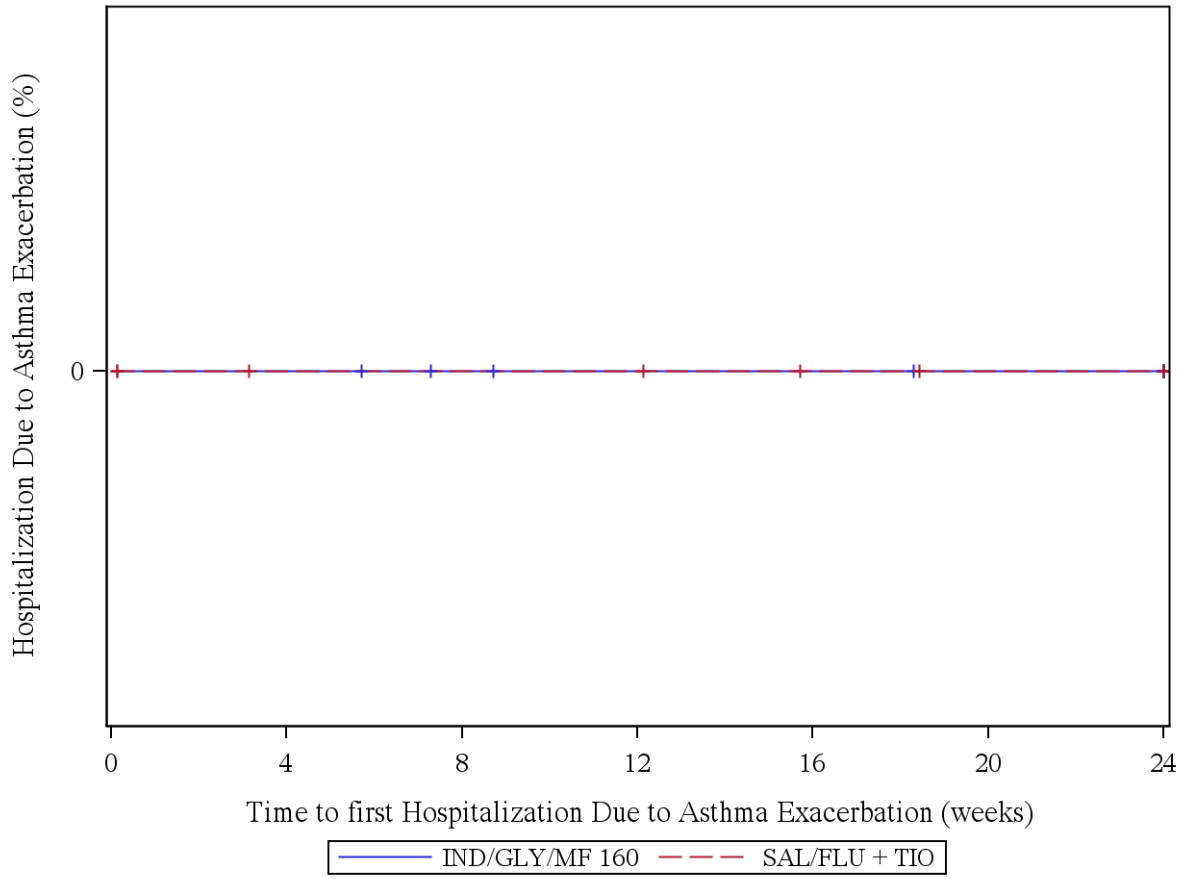
Figure 11.34.2 Hospitalization Due to Asthma Exacerbation (FAS), Region = Europe



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 166/169, Week 8: 166/167, Week 16: 164/164, Week 24: 160/163

Analysis population: B2306 FAS total population

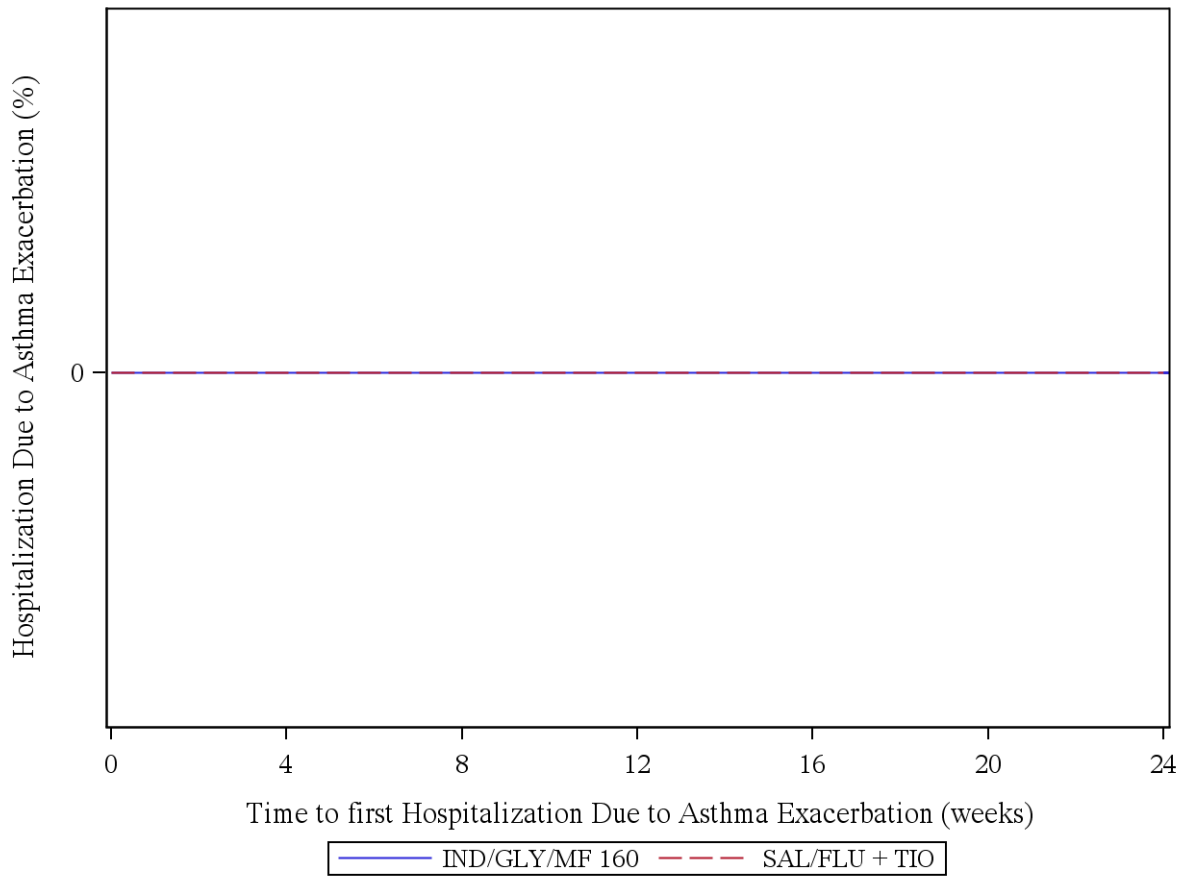
Figure 11.34.3 Hospitalization Due to Asthma Exacerbation (FAS), Region = Latin America



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 166/166, Week 8: 164/163, Week 16: 163/161, Week 24: 158/159

Analysis population: B2306 FAS total population

Figure 11.34.4 Hospitalization Due to Asthma Exacerbation (FAS), Region = Others

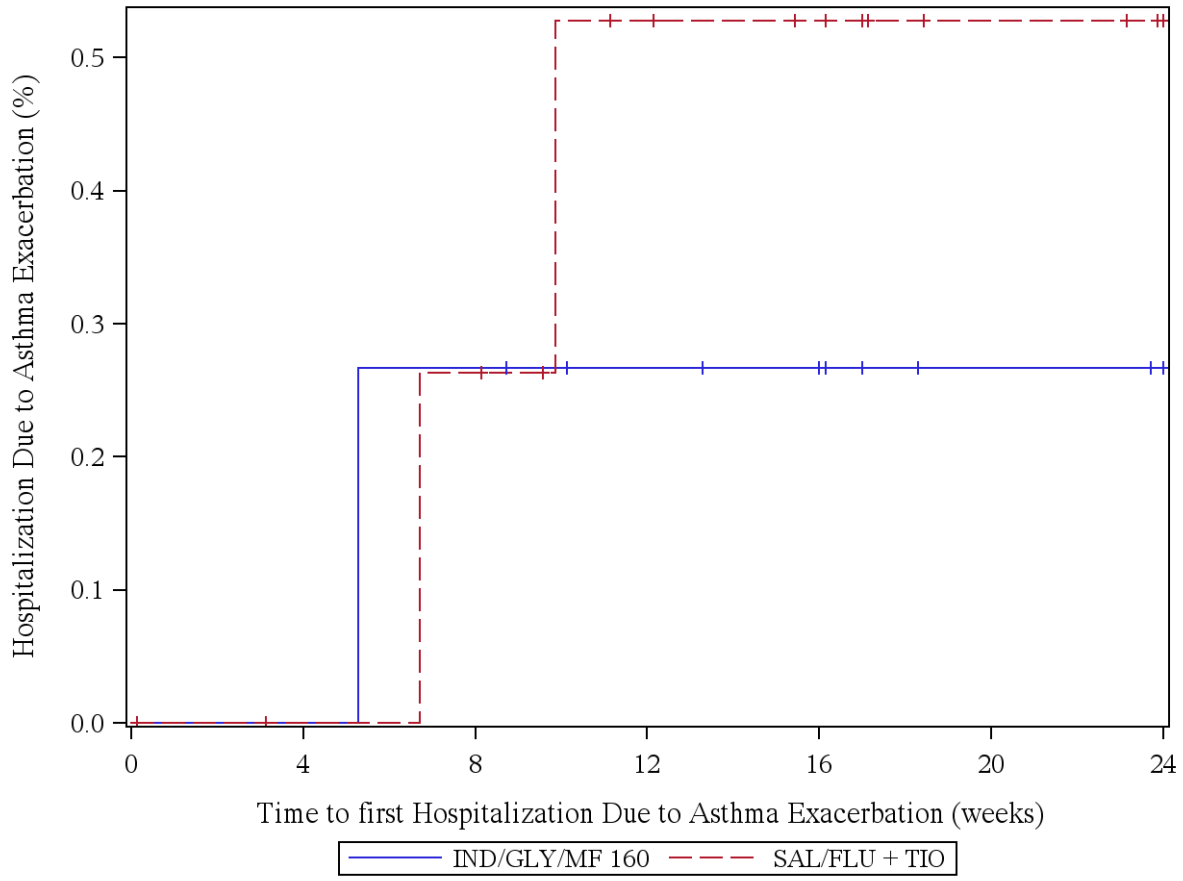


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 20/9, Week 8: 20/9, Week 16: 20/9, Week 24: 20/9

Analysis population: B2306 FAS total population

11.35 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation by History of Asthma Exacerbation (FAS)

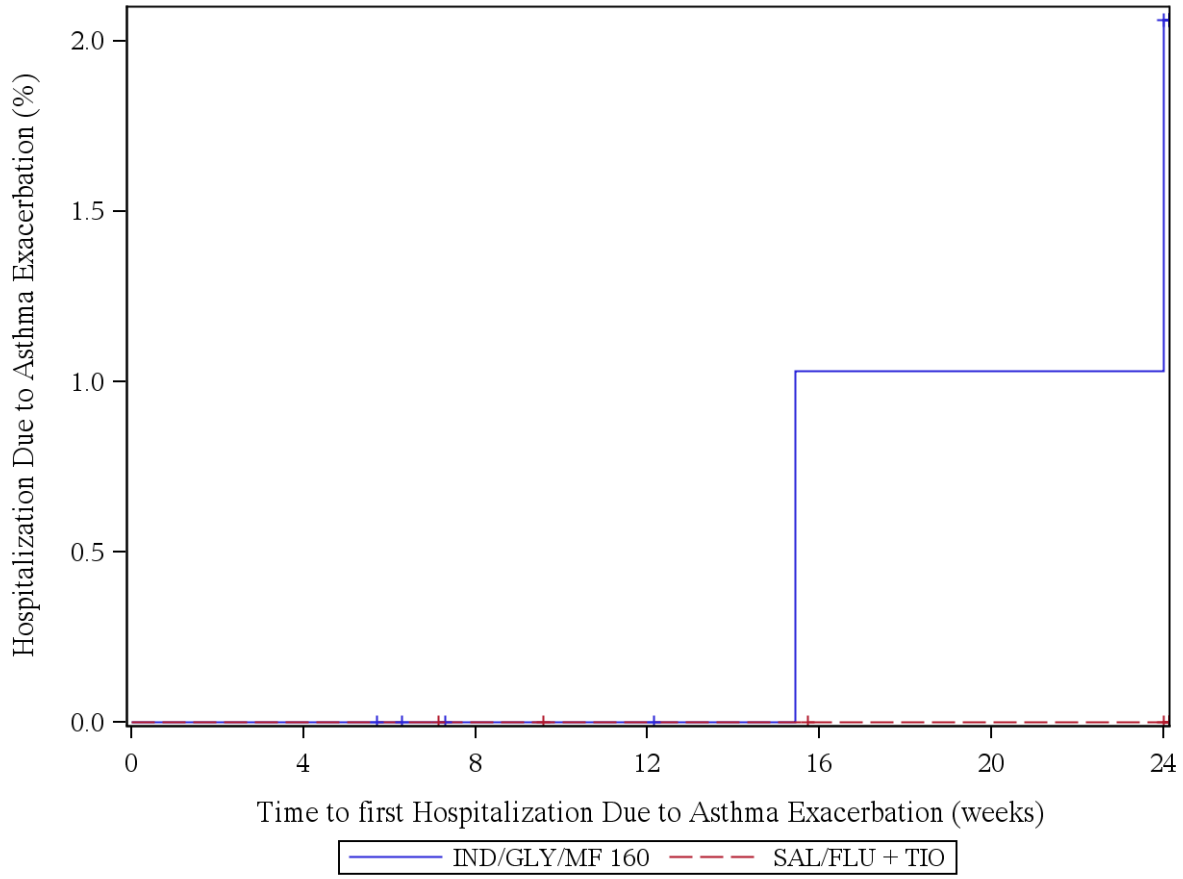
Figure 11.35.1 Hospitalization Due to Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 375/383, Week 8: 374/379, Week 16: 370/373, Week 24: 362/366

Analysis population: B2306 FAS total population

Figure 11.35.2 Hospitalization Due to Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2

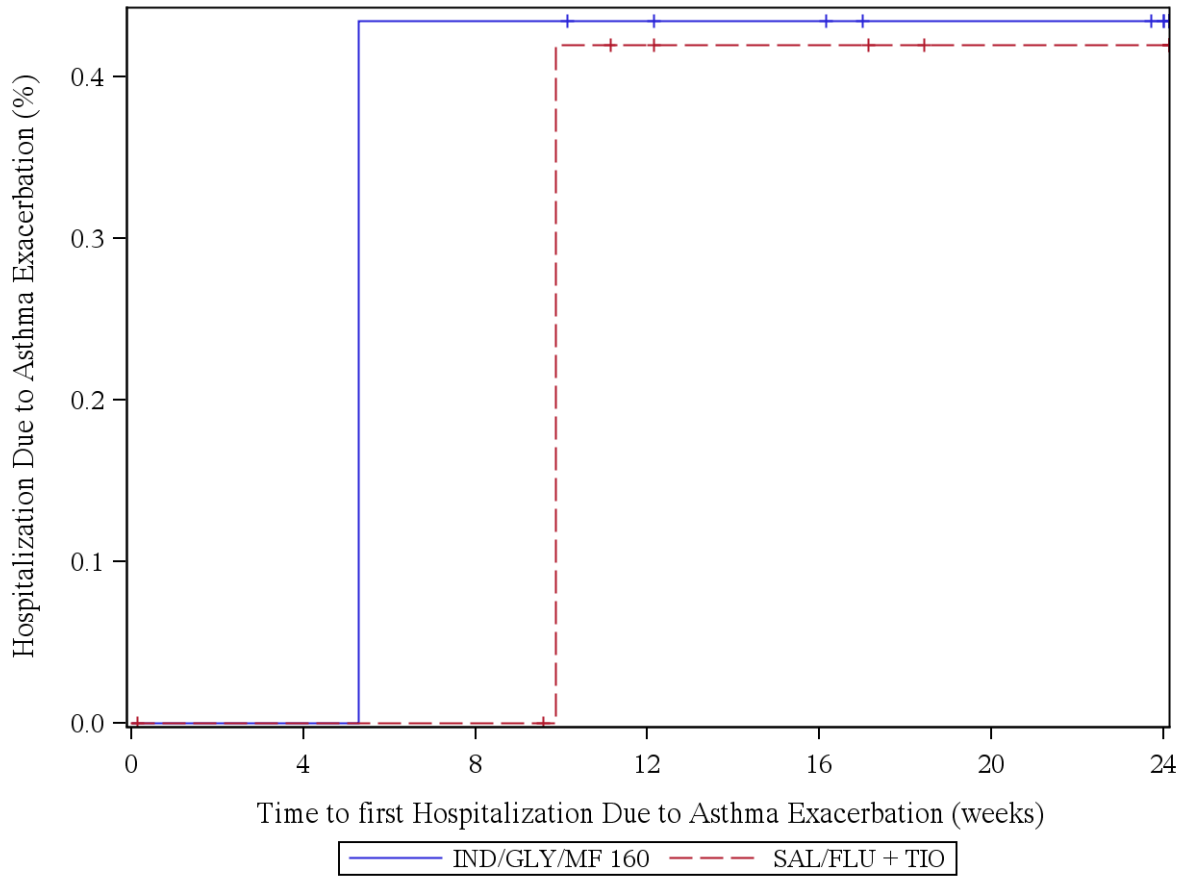


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 101/92, Week 8: 98/91, Week 16: 96/89, Week 24: 94/88

Analysis population: B2306 FAS total population

11.36 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation by Patients' Prior Therapies (FAS)

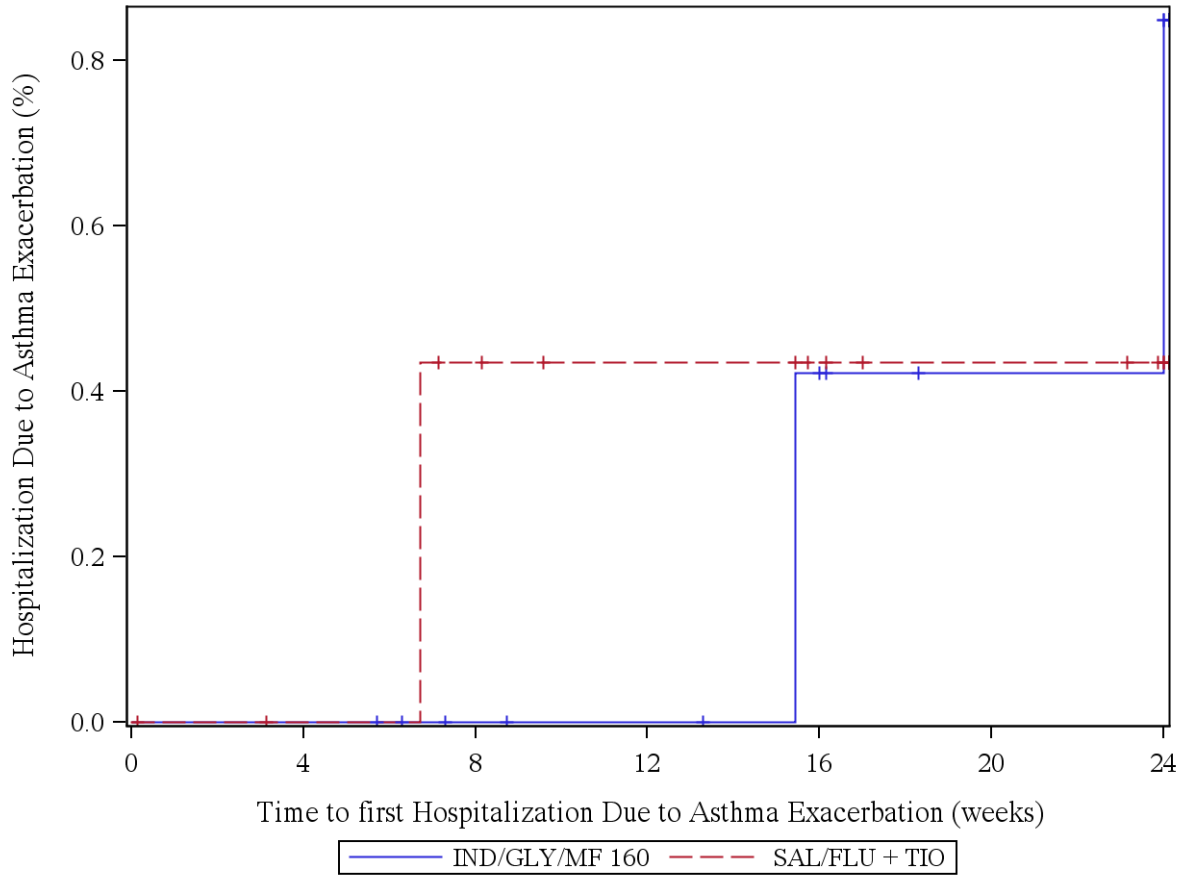
Figure 11.36.1 Hospitalization Due to Asthma Exacerbation (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = Mid dose ICS/LABA



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 230/240, Week 8: 229/239, Week 16: 227/235, Week 24: 222/233

Analysis population: B2306 FAS total population

Figure 11.36.2 Hospitalization Due to Asthma Exacerbation (FAS), Patients' prior therapies for at least 1 month prior to visit 1 = High dose ICS/LABA



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 242/232, Week 8: 239/228, Week 16: 235/224, Week 24: 230/218

Analysis population: B2306 FAS total population