

**Indacaterolacetat / Glycopyrroniumbromid / Mometasonfuroat
(Enerzair® Breezhaler®)**

Novartis Pharma GmbH

Modul 4 A, Anhang 4-H-1

Bewertungsrelevante Population
(ARGON-Teilpopulation, die mit einer hochdosierten ICS/LABA-
Therapie nicht ausreichend kontrolliert ist)

CQVM149B2306 (ARGON)
AMNOG Analysis

Table of Contents

Tables	12
 1. Patient Disposition and Baseline Characteristics	12
Table 1.1 Patient Disposition and Compliance (RAN, FAS)	12
Table 1.2 Demographic Patient Characteristics (FAS)	13
Table 1.3 Asthma Related Patient Characteristics (FAS).....	15
Table 1.4 Duration of Study Participation (FAS).....	19
Table 1.5 Overview Subgroups (FAS).....	20
Table 1.6 OCS Use (FAS)	21
 2. All-cause Mortality - Binary Analysis	24
Table 2.1 All-cause Mortality - Binary Analysis (FAS)	24
 3. ACQ-5 - Return Rate / Change from Baseline	25
Table 3.1 ACQ-5 - Return Rate (FAS)	25
Table 3.2 ACQ-5 - Change from Baseline (FAS).....	26
Table 3.3 ACQ-5 - Change from Baseline by Age (FAS).....	27
Table 3.4 ACQ-5 - Change from Baseline by Gender (FAS).....	29
Table 3.5 ACQ-5 - Change from Baseline by Region (FAS).....	30
Table 3.6 ACQ-5 - Change from Baseline by History of Asthma Exacerbation (FAS).....	32
 4. ACQ-5 - Responder Analysis	33
Table 4.1a ACQ-5 - Responder Analysis (as observed) (FAS)	33
Table 4.1b ACQ-5 - Responder Analysis (LOCF) (FAS)	34
Table 4.2a ACQ-5 - Responder Analysis by Age (as observed) (FAS)	35
Table 4.2b ACQ-5 - Responder Analysis by Age (LOCF) (FAS)	36
Table 4.3a ACQ-5 - Responder Analysis by Gender (as observed) (FAS)	37
Table 4.3b ACQ-5 - Responder Analysis by Gender (LOCF) (FAS)	38
Table 4.4a ACQ-5 - Responder Analysis by Region (as observed) (FAS)	39
Table 4.4b ACQ-5 - Responder Analysis by Region (LOCF) (FAS).....	40
Table 4.5a ACQ-5 - Responder Analysis by History of Asthma Exacerbation (as observed) (FAS) ...	41
Table 4.5b ACQ-5 - Responder Analysis by History of Asthma Exacerbation (LOCF) (FAS).....	42
 5. AQLQ-S - Return Rate / Change from Baseline	43
Table 5.1 AQLQ-S - Return Rate (FAS)	43
Table 5.2 AQLQ-S - Change from Baseline (FAS).....	44
Table 5.3 AQLQ-S - Change from Baseline by Age (FAS)	46
Table 5.4 AQLQ-S - Change from Baseline by Gender (FAS).....	52
Table 5.5 AQLQ-S - Change from Baseline by Region (FAS).....	56
Table 5.6 AQLQ-S - Change from Baseline by History of Asthma Exacerbation (FAS).....	63
 6. AQLQ-S - Responder Analysis	67
Table 6.1a AQLQ-S - Responder Analysis (as observed) (FAS)	67
Table 6.1b AQLQ-S - Responder Analysis (LOCF) (FAS).....	68
Table 6.2a AQLQ-S - Responder Analysis by Age (as observed) (FAS)	69

Table 6.2b AQLQ-S - Responder Analysis by Age (LOCF) (FAS)	70
Table 6.3a AQLQ-S - Responder Analysis by Gender (as observed) (FAS)	71
Table 6.3b AQLQ-S - Responder Analysis by Gender (LOCF) (FAS)	72
Table 6.4a AQLQ-S - Responder Analysis by Region (as observed) (FAS)	73
Table 6.4b AQLQ-S - Responder Analysis by Region (LOCF) (FAS)	74
Table 6.5a AQLQ-S - Responder Analysis by History of Asthma Exacerbation (as observed) (FAS) 75	
Table 6.5b AQLQ-S - Responder Analysis by History of Asthma Exacerbation (LOCF) (FAS)	76
7. SGRQ - Return Rate / Change from Baseline	77
Table 7.1 SGRQ - Return Rate (FAS)	77
Table 7.2a SGRQ - Change from Baseline (as observed) (FAS)	78
Table 7.2b SGRQ - Change from Baseline (LOCF) (FAS)	79
Table 7.3a SGRQ - Change from Baseline by Age (as observed) (FAS)	81
Table 7.3b SGRQ - Change from Baseline by Age (LOCF) (FAS)	84
Table 7.4a SGRQ - Change from Baseline by Gender (as observed) (FAS)	87
Table 7.4b SGRQ - Change from Baseline by Gender (LOCF) (FAS)	90
Table 7.5a SGRQ - Change from Baseline by Region (as observed) (FAS)	93
Table 7.5b SGRQ - Change from Baseline by Region (LOCF) (FAS)	97
Table 7.6a SGRQ - Change from Baseline by History of Asthma Exacerbation (as observed) (FAS)	101
Table 7.6b SGRQ - Change from Baseline by History of Asthma Exacerbation (LOCF) (FAS)	104
8. SGRQ - Responder Analysis	107
Table 8.1 SGRQ - Responder Analysis (LOCF) (FAS)	107
Table 8.2 SGRQ - Responder Analysis by Age (LOCF) (FAS)	108
Table 8.3 SGRQ - Responder Analysis by Gender (LOCF) (FAS)	109
Table 8.4 SGRQ - Responder Analysis by Region (LOCF) (FAS)	110
Table 8.5 SGRQ - Responder Analysis by History of Asthma Exacerbation (LOCF) (FAS)	111
9. E-Diary - Symptoms	112
Table 9.1 Symptoms - Documentation Rate (FAS)	112
Table 9.2 Symptoms - Change from Baseline (FAS)	120
Table 9.3 Symptoms - Change from Baseline by Age (FAS)	126
Table 9.4 Symptoms - Change from Baseline by Gender (FAS)	144
Table 9.5 Symptoms - Change from Baseline by Region (FAS)	157
Table 9.6 Symptoms - Change from Baseline by History of Asthma Exacerbation (FAS)	181
10. E-Diary - Rescue Medication	194
Table 10.1 Rescue Medication - Documentation Rate (FAS)	194
Table 10.2 Rescue Medication - Change from Baseline (FAS)	196
Table 10.3 Rescue Medication - Change from Baseline by Age (FAS)	198
Table 10.4 Rescue Medication - Change from Baseline by Gender (FAS)	202
Table 10.5 Rescue Medication - Change from Baseline by Region (FAS)	205
Table 10.6 Rescue Medication - Change from Baseline by History of Asthma Exacerbation (FAS)	211
11. Exacerbations - Time-to-event Analysis	214

Table 11.1 Exacerbations - Time-to-event Analysis (FAS)	214
Table 11.2 Exacerbations - Time-to-event Analysis by Age (FAS)	216
Table 11.3 Exacerbations - Time-to-event Analysis by Gender (FAS)	221
Table 11.4 Exacerbations - Time-to-event Analysis by Region (FAS)	225
Table 11.5 Exacerbations - Time-to-event Analysis by History of Asthma Exacerbation (FAS).....	232
12. Exacerbations - Annualized Exacerbation Rate	236
Table 12.1 Exacerbations - Annualized Exacerbation Rate (FAS)	236
Table 12.2 Exacerbations - Annualized Exacerbation Rate by Age (FAS)	238
Table 12.3 Exacerbations - Annualized Exacerbation Rate by Gender (FAS)	243
Table 12.4 Exacerbations - Annualized Exacerbation Rate by Region (FAS)	246
Table 12.5 Exacerbations - Annualized Exacerbation Rate by History of Asthma Exacerbation (FAS)	251
13. Adverse Events - Binary Analysis (SAF).....	254
Table 13.1 Adverse Events - Binary Analysis (SAF)	254
Table 13.2 Adverse Events - Binary Analysis by Age (SAF)	255
Table 13.3 Adverse Events - Binary Analysis by Gender (SAF)	257
Table 13.4 Adverse Events - Binary Analysis by Region (SAF).....	259
Table 13.5 Adverse Events - Binary Analysis by History of Asthma Exacerbation (SAF)	261
14. Any AE by SOC and PT - Binary Analysis (SAF).....	263
Table 14.1 Any AE by SOC, PT and Severity - Binary Analysis (SAF)	263
Table 14.2 Any AE by SOC and PT - Binary Analysis by Age (SAF)	267
Table 14.3 Any AE by SOC and PT - Binary Analysis by Gender (SAF)	268
Table 14.4 Any AE by SOC and PT - Binary Analysis by Region (SAF)	269
Table 14.5 Any AE by SOC and PT - Binary Analysis by History of Asthma Exacerbation (SAF)	270
Table 14.7 Any severe AE by SOC and PT - Binary Analysis by Age (SAF).....	271
Table 14.8 Any severe AE by SOC and PT - Binary Analysis by Gender (SAF).....	272
Table 14.9 Any severe AE by SOC and PT - Binary Analysis by Region (SAF)	273
Table 14.10 Any severe AE by SOC and PT - Binary Analysis by History of Asthma Exacerbation (SAF)	274
15. Any SAE by SOC and PT - Binary Analysis (SAF).....	275
Table 15.1 Any SAE by SOC and PT - Binary Analysis (SAF)	275
Table 15.2 Any SAE by SOC and PT - Binary Analysis by Age (SAF)	276
Table 15.3 Any SAE by SOC and PT - Binary Analysis by Gender (SAF)	277
Table 15.4 Any SAE by SOC and PT - Binary Analysis by Region (SAF).....	278
Table 15.5 Any SAE by SOC and PT - Binary Analysis by History of Asthma Exacerbation (SAF)	279
16. Any AE leading to Study Discontinuation by SOC and PT - Binary Analysis	280
Table 16.1 Any AE leading to Study Discontinuation by SOC and PT - Binary Analysis (SAF).....	280
17. Any AE leading to Study Drug Discontinuation by SOC and PT - Binary Analysis.....	281
Table 17.1 Any AE leading to Study Drug Discontinuation by SOC and PT - Binary Analysis (SAF)	281
18. AESI - Binary Analysis (SAF).....	282

Table 18.1 AESI by Severity - Binary Analysis (SAF)	282
Table 18.2 AESI - Binary Analysis by Age (SAF)	288
Table 18.3 AESI - Binary Analysis by Gender (SAF)	289
Table 18.4 AESI - Binary Analysis by Region (SAF)	290
Table 18.5 AESI - Binary Analysis by History of Asthma Exacerbation (SAF)	292
19. Trough FEV1 - Change from Baseline	293
Table 19.1 Trough FEV1 - Change from Baseline (FAS)	293
Table 19.2 Trough FEV1 - Change from Baseline by Age (FAS)	294
Table 19.3 Trough FEV1 - Change from Baseline by Gender (FAS)	296
Table 19.4 Trough FEV1 - Change from Baseline by Region (FAS)	298
Table 19.5 Trough FEV1 - Change from Baseline by History of Asthma Exacerbation (FAS)	300
Figures.....	302
3. Boxplot: ACQ-5 - Change from Baseline (FAS).....	302
3.1 Boxplot: ACQ-5 - Change from Baseline (FAS)	302
3.2 Boxplot: ACQ-5 - Change from Baseline by Age (FAS)	303
3.3 Boxplot: ACQ-5 - Change from Baseline by Gender (FAS)	306
3.4 Boxplot: ACQ-5 - Change from Baseline by Region (FAS)	308
3.5 Boxplot: ACQ-5 - Change from Baseline by History of Asthma Exacerbation (FAS).....	312
5. Boxplot: AQLQ-S - Change from Baseline (FAS).....	314
5.1 Boxplot: AQLQ-S (Total Score) - Change from Baseline (FAS).....	314
5.2 Boxplot: AQLQ-S (Total Score) - Change from Baseline by Age (FAS)	315
5.3 Boxplot: AQLQ-S (Total Score) - Change from Baseline by Gender (FAS)	318
5.4 Boxplot: AQLQ-S (Total Score) - Change from Baseline by Region (FAS).....	320
5.5 Boxplot: AQLQ-S (Total Score) - Change from Baseline by History of Asthma Exacerbation (FAS)	324
5.7 Boxplot: AQLQ-S (Symptom Score) - Change from Baseline (FAS)	326
5.8 Boxplot: AQLQ-S (Symptom Score) - Change from Baseline by Age (FAS)	327
5.9 Boxplot: AQLQ-S (Symptom Score) - Change from Baseline by Gender (FAS)	330
5.10 Boxplot: AQLQ-S (Symptom Score) - Change from Baseline by Region (FAS)	332
5.11 Boxplot: AQLQ-S (Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS)	336
5.13 Boxplot: AQLQ-S (Activity Limitation Score) - Change from Baseline (FAS)	338
5.14 Boxplot: AQLQ-S (Activity Limitation Score) - Change from Baseline by Age (FAS)	339
5.15 Boxplot: AQLQ-S (Activity Limitation Score) - Change from Baseline by Gender (FAS)	342
5.16 Boxplot: AQLQ-S (Activity Limitation Score) - Change from Baseline by Region (FAS)	344
5.17 Boxplot: AQLQ-S (Activity Limitation Score) - Change from Baseline by History of Asthma Exacerbation (FAS)	348
5.19 Boxplot: AQLQ-S (Emotional Function Score) - Change from Baseline (FAS)	350
5.20 Boxplot: AQLQ-S (Emotional Function Score) - Change from Baseline by Age (FAS)	351
5.21 Boxplot: AQLQ-S (Emotional Function Score) - Change from Baseline by Gender (FAS)	354
5.22 Boxplot: AQLQ-S (Emotional Function Score) - Change from Baseline by Region (FAS)	356

5.23 Boxplot: AQLQ-S (Emotional Function Score) - Change from Baseline by History of Asthma Exacerbation (FAS).....	360
5.25 Boxplot: AQLQ-S (Environmental Stimuli Score) - Change from Baseline (FAS).....	362
5.26 Boxplot: AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Age (FAS)	363
5.27 Boxplot: AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Gender (FAS)..	366
5.28 Boxplot: AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Region (FAS)...	368
5.29 Boxplot: AQLQ-S (Environmental Stimuli Score) - Change from Baseline by History of Asthma Exacerbation (FAS).....	372
7. Boxplot: SGRQ - Change from Baseline (FAS).....	374
7.1 Boxplot: SGRQ (Total Score) - Change from Baseline (FAS).....	374
7.2 Boxplot: SGRQ (Total Score) - Change from Baseline by Age (FAS).....	375
7.3 Boxplot: SGRQ (Total Score) - Change from Baseline by Gender (FAS).....	378
7.4 Boxplot: SGRQ (Total Score) - Change from Baseline by Region (FAS).....	380
7.5 Boxplot: SGRQ (Total Score) - Change from Baseline by History of Asthma Exacerbation (FAS)	384
7.7 Boxplot: SGRQ (Symptoms Score) - Change from Baseline (FAS).....	386
7.8 Boxplot: SGRQ (Symptoms Score) - Change from Baseline by Age (FAS)	387
7.9 Boxplot: SGRQ (Symptoms Score) - Change from Baseline by Gender (FAS)	390
7.10 Boxplot: SGRQ (Symptoms Score) - Change from Baseline by Region (FAS).....	392
7.11 Boxplot: SGRQ (Symptoms Score) - Change from Baseline by History of Asthma Exacerbation (FAS)	396
7.13 Boxplot: SGRQ (Activity Score) - Change from Baseline (FAS)	398
7.14 Boxplot: SGRQ (Activity Score) - Change from Baseline by Age (FAS)	399
7.15 Boxplot: SGRQ (Activity Score) - Change from Baseline by Gender (FAS)	402
7.16 Boxplot: SGRQ (Activity Score) - Change from Baseline by Region (FAS)	404
7.17 Boxplot: SGRQ (Activity Score) - Change from Baseline by History of Asthma Exacerbation (FAS)	408
7.19 Boxplot: SGRQ (Impacts Score) - Change from Baseline (FAS)	410
7.20 Boxplot: SGRQ (Impacts Score) - Change from Baseline by Age (FAS)	411
7.21 Boxplot: SGRQ (Impacts Score) - Change from Baseline by Gender (FAS)	414
7.22 Boxplot: SGRQ (Impacts Score) - Change from Baseline by Region (FAS)	416
7.23 Boxplot: SGRQ (Impacts Score) - Change from Baseline by History of Asthma Exacerbation (FAS)	420
9. Boxplot: Symptoms - Change from Baseline (FAS)	422
9.1 Boxplot: Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline (FAS)	422
9.2 Boxplot: Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Age (FAS)	423
9.3 Boxplot: Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Gender (FAS)	426
9.4 Boxplot: Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Region (FAS)	428
9.5 Boxplot: Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by History of Asthma Exacerbation (FAS)	432

9.7 Boxplot: Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline (FAS)	434
9.8 Boxplot: Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Age (FAS).....	435
9.9 Boxplot: Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Gender (FAS).....	438
9.10 Boxplot: Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Region (FAS)	440
9.11 Boxplot: Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by History of Asthma Exacerbation (FAS)	444
9.13 Boxplot: Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline (FAS)	446
9.14 Boxplot: Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Age (FAS)	447
9.15 Boxplot: Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Gender (FAS)	450
9.16 Boxplot: Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Region (FAS)	452
9.17 Boxplot: Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by History of Asthma Exacerbation (FAS)	456
9.19 Boxplot: Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline (FAS)	458
9.20 Boxplot: Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Age (FAS).....	459
9.21 Boxplot: Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Gender (FAS).....	462
9.22 Boxplot: Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Region (FAS)	464
9.23 Boxplot: Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by History of Asthma Exacerbation (FAS)	468
9.25 Boxplot: Symptoms (Mean Total Daily Symptom Score) - Change from Baseline (FAS)	470
9.26 Boxplot: Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Age (FAS)	471
9.27 Boxplot: Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Gender (FAS)	474
9.28 Boxplot: Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Region (FAS)	476
9.29 Boxplot: Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS)	480
9.31 Boxplot: Symptoms (Mean Day-Time Symptom Score) - Change from Baseline (FAS)	482
9.32 Boxplot: Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Age (FAS)	483
9.33 Boxplot: Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Gender (FAS)	486
9.34 Boxplot: Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Region (FAS)	488
9.35 Boxplot: Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS)	492

9.37 Boxplot: Symptoms (Mean Night-Time Symptom Score) - Change from Baseline (FAS)	494
9.38 Boxplot: Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Age (FAS)	495
9.39 Boxplot: Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Gender (FAS)	498
9.40 Boxplot: Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Region (FAS)	500
9.41 Boxplot: Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS)	504
9.43 Boxplot: Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline (FAS)	506
9.44 Boxplot: Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Age (FAS)	507
9.45 Boxplot: Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Gender (FAS)	510
9.46 Boxplot: Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Region (FAS)	512
9.47 Boxplot: Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by History of Asthma Exacerbation (FAS)	516
9.49 Boxplot: Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline (FAS)	518
9.50 Boxplot: Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Age (FAS)	519
9.51 Boxplot: Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Gender (FAS)	522
9.52 Boxplot: Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Region (FAS)	524
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)	528
9.55 Boxplot: Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline (FAS)	530
9.56 Boxplot: Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Age (FAS)	531
9.57 Boxplot: Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Gender (FAS)	534
9.58 Boxplot: Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Region (FAS)	536
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) ..	540
9.61 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline (FAS)	542
9.62 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Age (FAS)	543
9.63 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Gender (FAS)	546
9.64 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by Region (FAS)	548

9.65 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline by History of Asthma Exacerbation (FAS).....	552
9.67 Boxplot: Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline (FAS).....	554
9.68 Boxplot: Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Age (FAS).....	555
9.69 Boxplot: Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Gender (FAS)	558
9.70 Boxplot: Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Region (FAS)	560
9.71 Boxplot: Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by History of Asthma Exacerbation (FAS).....	564
9.73 Boxplot: Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline (FAS)	566
9.74 Boxplot: Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Age (FAS)	567
9.75 Boxplot: Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Gender (FAS)	570
9.76 Boxplot: Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Region (FAS)	572
9.77 Boxplot: Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by History of Asthma Exacerbation (FAS)	576
9.79 Boxplot: Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline (FAS).....	578
9.80 Boxplot: Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Age (FAS)	579
9.81 Boxplot: Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Gender (FAS)	582
9.82 Boxplot: Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Region (FAS)	584
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).....	588
10. Boxplot: Rescue Medication Change from Baseline (FAS)	590
10.1 Boxplot: Rescue Medication (Rescue medication during the night) - Change from Baseline (FAS)	590
10.2 Boxplot: Rescue Medication (Rescue medication during the night) - Change from Baseline by Age (FAS).....	591
10.3 Boxplot: Rescue Medication (Rescue medication during the night) - Change from Baseline by Gender (FAS).....	594
10.4 Boxplot: Rescue Medication (Rescue medication during the night) - Change from Baseline by Region (FAS)	596
10.5 Boxplot: Rescue Medication (Rescue medication during the night) - Change from Baseline by History of Asthma Exacerbation (FAS)	600
10.7 Boxplot: Rescue Medication (Rescue medication during the day) - Change from Baseline (FAS)	602
10.8 Boxplot: Rescue Medication (Rescue medication during the day) - Change from Baseline by Age (FAS)	603

10.9 Boxplot: Rescue Medication (Rescue medication during the day) - Change from Baseline by Gender (FAS).....	606
10.10 Boxplot: Rescue Medication (Rescue medication during the day) - Change from Baseline by Region (FAS)	608
10.11 Boxplot: Rescue Medication (Rescue medication during the day) - Change from Baseline by History of Asthma Exacerbation (FAS)	612
10.13 Boxplot: Rescue Medication (Rescue medication free days) - Change from Baseline (FAS) ...	614
10.14 Boxplot: Rescue Medication (Rescue medication free days) - Change from Baseline by Age (FAS)	615
10.15 Boxplot: Rescue Medication (Rescue medication free days) - Change from Baseline by Gender (FAS)	618
10.16 Boxplot: Rescue Medication (Rescue medication free days) - Change from Baseline by Region (FAS)	620
10.17 Boxplot: Rescue Medication (Rescue medication free days) - Change from Baseline by History of Asthma Exacerbation (FAS)	624
11. Kaplan-Meier-Plot: Asthma exacerbations (FAS)	626
11.1 Kaplan-Meier-Plot: Asthma Exacerbation (All) (FAS)	626
11.2 Kaplan-Meier-Plot: Asthma Exacerbation (All) by Age (FAS)	627
11.3 Kaplan-Meier-Plot: Asthma Exacerbation (All) by Gender (FAS)	630
11.4 Kaplan-Meier-Plot: Asthma Exacerbation (All) by Region (FAS)	632
11.5 Kaplan-Meier-Plot: Asthma Exacerbation (All) by History of Asthma Exacerbation (FAS)	636
11.7 Kaplan-Meier-Plot: Severe Asthma Exacerbation (FAS).....	638
11.8 Kaplan-Meier-Plot: Severe Asthma Exacerbation by Age (FAS)	639
11.9 Kaplan-Meier-Plot: Severe Asthma Exacerbation by Gender (FAS).....	642
11.10 Kaplan-Meier-Plot: Severe Asthma Exacerbation by Region (FAS).....	644
11.11 Kaplan-Meier-Plot: Severe Asthma Exacerbation by History of Asthma Exacerbation (FAS)648	
11.13 Kaplan-Meier-Plot: SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS)	650
11.14 Kaplan-Meier-Plot: SCS Use Due to Asthma Exacerbation (for at least three consecutive days) by Age (FAS).....	651
11.15 Kaplan-Meier-Plot: SCS Use Due to Asthma Exacerbation (for at least three consecutive days) by Gender (FAS)	654
11.16 Kaplan-Meier-Plot: SCS Use Due to Asthma Exacerbation (for at least three consecutive days) by Region (FAS)	656
11.17 Kaplan-Meier-Plot: SCS Use Due to Asthma Exacerbation (for at least three consecutive days) by History of Asthma Exacerbation (FAS)	660
11.19 Kaplan-Meier-Plot: ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS)	662
11.20 Kaplan-Meier-Plot: ER Visit and/or Hospitalization Due to Asthma Exacerbation by Age (FAS)	663
11.21 Kaplan-Meier-Plot: ER Visit and/or Hospitalization Due to Asthma Exacerbation by Gender (FAS)	666
11.22 Kaplan-Meier-Plot: ER Visit and/or Hospitalization Due to Asthma Exacerbation by Region (FAS)	668
11.23 Kaplan-Meier-Plot: ER Visit and/or Hospitalization Due to Asthma Exacerbation by History of Asthma Exacerbation (FAS)	672

11.25 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation (FAS)	674
11.26 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation by Age (FAS).....	675
11.27 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation by Gender (FAS)	678
11.28 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation by Region (FAS)	680
11.29 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation by History of Asthma Exacerbation (FAS)	684
11.31 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation (FAS).....	686
11.32 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation by Age (FAS)	687
11.33 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation by Gender (FAS)	690
11.34 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation by Region (FAS)	692
11.35 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation by History of Asthma Exacerbation (FAS).....	696

Tables

1. Patient Disposition and Baseline Characteristics

Table 1.1 Patient Disposition and Compliance (RAN, FAS)

Disposition/Reason (RAN/SAF)	Treatment groups		
	IND/GLY/ MF 160 n (%)	SAL/FLU + TIO n (%)	Total n (%)
Randomized (RAN)	242 (100,0)	232 (100,0)	474 (100,0)
Full Analysis Set (FAS)	242 (100,0)	232 (100,0)	474 (100,0)
Study Discontinuation (FAS)	9 (3,7)	10 (4,3)	19 (4,0)
<u>Reasons for study discontinuation</u>			
Subject/guardian decision	5 (2,1)	4 (1,7)	9 (1,9)
Physician decision	2 (0,8)	3 (1,3)	5 (1,1)
Adverse event	1 (0,4)	2 (0,9)	3 (0,6)
Benign neoplasm	1 (0,4)	0 (0,0)	1 (0,2)
Dermatitis atopic	0 (0,0)	1 (0,4)	1 (0,2)
Haemorrhagic stroke	0 (0,0)	1 (0,4)	1 (0,2)
Lost to follow-up	1 (0,4)	1 (0,4)	2 (0,4)
Treatment Discontinuation (FAS)	11 (4,5)	14 (6,0)	25 (5,3)
Discontinued study directly afterwards	4 (1,7)	6 (2,6)	10 (2,1)
Continued in study for a while	5 (2,1)	4 (1,7)	9 (1,9)
Completed study	2 (0,8)	4 (1,7)	6 (1,3)
<u>Primary reason for discontinuation from study treatment</u>			
Subject/guardian decision	5 (2,1)	5 (2,2)	10 (2,1)
Physician decision	3 (1,2)	5 (2,2)	8 (1,7)
Adverse event	1 (0,4)	3 (1,3)	4 (0,8)
Lost to follow-up	1 (0,4)	1 (0,4)	2 (0,4)
Technical problems	1 (0,4)	0 (0,0)	1 (0,2)
Percentages refer to the number of randomized patients.			
Analysis population: B2306 RAN subpopulation "high-dose ICS/LABA"			

Table 1.2 Demographic Patient Characteristics (FAS)

Treatment Groups			
Demographic Patient Characteristics (FAS)	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	Total (N=474)
Age (years)			
Mean ± SD	53,4 ± 13,11	53,6 ± 12,61	53,5 ± 12,85
Median	53,0	55,0	54,0
Range	21 to 82	18 to 78	18 to 82
Age group (years), n (%)			
18-39 years	40 (16,5)	33 (14,2)	73 (15,4)
40-64 years	144 (59,5)	150 (64,7)	294 (62,0)
>64 years	58 (24,0)	49 (21,1)	107 (22,6)
Sex, n (%)			
Male	88 (36,4)	81 (34,9)	169 (35,7)
Female	154 (63,6)	151 (65,1)	305 (64,3)
Ethnicity, n (%)			
Hispanic or Latino	103 (42,6)	88 (37,9)	191 (40,3)
East Asian	1 (0,4)	0 (0,0)	1 (0,2)
Southeast Asian	9 (3,7)	10 (4,3)	19 (4,0)
South Asian	1 (0,4)	0 (0,0)	1 (0,2)
West Asian	6 (2,5)	5 (2,2)	11 (2,3)
Russian	33 (13,6)	32 (13,8)	65 (13,7)
Mixed Ethnicity	2 (0,8)	0 (0,0)	2 (0,4)
Not Reported	7 (2,9)	6 (2,6)	13 (2,7)
Unknown	2 (0,8)	2 (0,9)	4 (0,8)
Other	78 (32,2)	89 (38,4)	167 (35,2)
Weight (kg)			
Mean ± SD	80,4 ± 17,74	80,2 ± 16,70	80,3 ± 17,22
Median	78,9	78,5	78,7
Range	45,0 to 158,0	34,0 to 139,0	34,0 to 158,0
BMI (kg/m²)			
Mean ± SD	29,4 ± 5,88	29,6 ± 5,65	29,5 ± 5,76
Median	28,6	29,3	28,9
Range	17,2 to 50,6	15,3 to 46,1	15,3 to 50,6
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"			

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CQVM149B2306

Table 1.3 Asthma Related Patient Characteristics (FAS)

Treatment Groups			
Asthma Patient Characteristics (FAS)	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	Total (N=474)
Duration of asthma (years)			
Mean ± SD	24,0 ± 16,91	21,3 ± 15,52	22,7 ± 16,28
Median	21,5	17,5	18,9
Range	0,5 to 73,4	0,6 to 73,4	0,5 to 73,4
Duration of asthma (years), n (%)			
< 1 year	4 (1,7)	2 (0,9)	6 (1,3)
1 - 5 years	32 (13,2)	31 (13,4)	63 (13,3)
>5 - 10 years	28 (11,6)	33 (14,2)	61 (12,9)
>10 - 15 years	31 (12,8)	33 (14,2)	64 (13,5)
>15 - 20 years	23 (9,5)	30 (12,9)	53 (11,2)
>20 years	124 (51,2)	103 (44,4)	227 (47,9)
Number of asthma exacerbations in the 12 months prior to study start that required treatment, n (%)			
1	176 (72,7)	184 (79,3)	360 (75,9)
2	50 (20,7)	39 (16,8)	89 (18,8)
3	14 (5,8)	9 (3,9)	23 (4,9)
≥ 4	2 (0,8)	0 (0,0)	2 (0,4)
Smoking history, n (%)			
Never smoked	178 (73,6)	174 (75,0)	352 (74,3)
Ex-smoker	62 (25,6)	54 (23,3)	116 (24,5)
Current smoker	2 (0,8)	4 (1,7)	6 (1,3)
Amount of tobacco consumed on average (in pack years)			
Mean ± SD	6,3 ± 4,13	5,6 ± 3,66	6,0 ± 3,91
Median	5,1	5,0	5,0
Range	0,1 to 15,7	0,4 to 15,0	0,1 to 15,7
Time since smoking stopped (years)			
Mean ± SD	16,4 ± 14,05	16,8 ± 12,49	16,6 ± 13,29
Median	13,1	13,4	13,3
Range	0,3 to 56,9	0,8 to 43,0	0,3 to 56,9

Treatment Groups			
Asthma Patient Characteristics (FAS)	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	Total (N=474)
Systolic blood pressure (mmHg)			
Mean ± SD	126,4 ± 11,23	125,0 ± 10,99	125,7 ± 11,12
Median	126,0	125,0	125,0
Range	93 to 180	95 to 161	93 to 180
Diastolic blood pressure (mmHg)			
Mean ± SD	78,4 ± 7,87	77,5 ± 8,40	78,0 ± 8,14
Median	80,0	80,0	80,0
Range	55 to 100	52 to 100	52 to 100
Pulse rate (beats per minute)			
Mean ± SD	73,2 ± 9,03	73,0 ± 8,93	73,1 ± 8,97
Median	72,5	72,0	72,0
Range	51 to 106	44 to 98	44 to 106
QTcF (ms)			
Mean ± SD	405,8 ± 18,96	404,5 ± 19,53	405,1 ± 19,23
Median	406,0	404,0	406,0
Range	358 to 460	349 to 460	349 to 460
AQLQ-S total score			
Mean ± SD	4,6 ± 0,87	4,7 ± 0,87	4,7 ± 0,87
Median	4,6	4,6	4,6
Range	2,2 to 6,6	2,1 to 6,9	2,1 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)	0 (0,0)	0 (0,0)
≥ 2	240 (99,2)	224 (96,6)	464 (97,9)
missing	2 (0,8)	8 (3,4)	10 (2,1)
ACQ-5 total score			
Mean ± SD	2,6 ± 0,60	2,5 ± 0,58	2,6 ± 0,59
Median	2,6	2,4	2,6
Range	1,0 to 4,4	1,4 to 4,6	1,0 to 4,6
Baseline ACQ-5 score, n (%)			
<1,5	6 (2,5)	3 (1,3)	9 (1,9)
1,5 - <2	26 (10,7)	24 (10,3)	50 (10,5)

Treatment Groups			
Asthma Patient Characteristics (FAS)	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	Total (N=474)
2 - <2,5	80 (33,1)	97 (41,8)	177 (37,3)
≥ 2,5	130 (53,7)	108 (46,6)	238 (50,2)
ACQ-7 total score			
Mean ± SD	2,7 ± 0,53	2,6 ± 0,52	2,7 ± 0,53
Median	2,7	2,6	2,6
Range	1,3 to 4,3	1,6 to 4,1	1,3 to 4,3
Baseline ACQ-7 score, n (%)			
<1,5	1 (0,4)	0 (0,0)	1 (0,2)
1,5 - <2	13 (5,4)	12 (5,2)	25 (5,3)
2 - <2,5	83 (34,3)	102 (44,0)	185 (39,0)
≥ 2,5	145 (59,9)	118 (50,9)	263 (55,5)
SGRQ total score			
Mean ± SD	40,5 ± 16,11	38,8 ± 17,09	39,7 ± 16,60
Median	40,7	39,0	40,0
Range	8,1 to 77,9	4,6 to 77,9	4,6 to 77,9
Baseline eosinophils count (cells/µL)			
Mean ± SD	357,4 ± 341,69	327,1 ± 321,86	342,6 ± 332,11
Median	260,0	240,0	250,0
Range	10 to 2190	10 to 3160	10 to 3160
Baseline eosinophils count (cells/µL), n (%)			
<300	141 (58,3)	140 (60,3)	281 (59,3)
≥ 300	98 (40,5)	90 (38,8)	188 (39,7)
missing	3 (1,2)	2 (0,9)	5 (1,1)
ICS component background therapy, n (%)			
Low-dose ICS/LABA	0 (0,0)	0 (0,0)	0 (0,0)
Mid-dose ICS/LABA	0 (0,0)	0 (0,0)	0 (0,0)
High-dose ICS/LABA	242 (100,0)	232 (100,0)	474 (100,0)
FEV1 reversibility (%)			
Mean ± SD	29,1 ± 17,10	27,5 ± 15,89	28,3 ± 16,51
Median	23,0	24,0	23,0
Range	12 to 116	12 to 118	12 to 118
FEV1 reversibility (%), n (%)			
<40%	187 (77,3)	189 (81,5)	376 (79,3)
40% - <50%	23 (9,5)	15 (6,5)	38 (8,0)

Treatment Groups			
Asthma Patient Characteristics (FAS)	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	Total (N=474)
50% - <60%	8 (3,3)	7 (3,0)	15 (3,2)
60% - <70%	4 (1,7)	3 (1,3)	7 (1,5)
70% - <80%	2 (0,8)	2 (0,9)	4 (0,8)
≥ 80%	6 (2,5)	5 (2,2)	11 (2,3)
missing	12 (5,0)	11 (4,7)	23 (4,9)
FEV1 predicted			
Mean ± SD	60,4 ± 14,90	62,9 ± 13,30	61,6 ± 14,18
Median	61,5	64,0	63,0
Range	20 to 98	24,5 to 85	20 to 98
FEV1 predicted (%), n (%)			
≤ 60%	114 (47,1)	89 (38,4)	203 (42,8)
>60%	124 (51,2)	137 (59,1)	261 (55,1)
missing	4 (1,7)	6 (2,6)	10 (2,1)
IgE level (IU/ml), n (%)			
≤ 75	74 (30,6)	69 (29,7)	143 (30,2)
>75 - ≤1500	145 (59,9)	143 (61,6)	288 (60,8)
>1500	15 (6,2)	14 (6,0)	29 (6,1)
missing	8 (3,3)	6 (2,6)	14 (3,0)
Concomitant asthma medication at baseline, n (%)			
ICS/LABA Fixcombination	1 (0,4)	0 (0,0)	1 (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	31 (12,8)	29 (12,5)	60 (12,7)
Mepolizumab	1 (0,4)	3 (1,3)	4 (0,8)
OCS	4 (1,7)	5 (2,2)	9 (1,9)
Omalizumab	7 (2,9)	7 (3,0)	14 (3,0)
Reslizumab	0 (0,0)	0 (0,0)	0 (0,0)
SABA	0 (0,0)	0 (0,0)	0 (0,0)
SAMA	0 (0,0)	0 (0,0)	0 (0,0)
Other	12 (5,0)	14 (6,0)	26 (5,5)
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"			

Table 1.4 Duration of Study Participation (FAS)

Treatment Groups			
Duration of Study Participation (FAS)	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	Total (N=474)
Study participation			
Mean ± SD (in days)	193,3 ± 17,53	193,0 ± 19,04	193,2 ± 18,27
Median (in days)	195,0	196,0	195,0
Minimum, Maximum (in days)	59 to 225	50 to 227	50 to 227
Study participation on treatment			
Mean ± SD (in days)	166,0 ± 20,09	163,8 ± 26,29	164,9 ± 23,33
Median (in days)	169,0	169,0	169,0
Minimum, Maximum (in days)	6 to 186	16 to 194	6 to 194
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA" 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=242)	SAL/FLU + TIO (N=232)	Total (N=474)
Age			
18-39	40	33	73
40-64	144	150	294
>64	58	49	107
Gender			
male	88	81	169
female	154	151	305
Region			
Asia	53	59	112
Europe	81	83	164
Latin America	104	89	193
Others	4	1	5
History of asthma exacerbation in the 12 months prior to screening			
1	176	184	360
≥ 2	66	48	114
Patients' prior therapies for at least 1 month prior to visit 1			
high dose ICS/LABA	242	232	474
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"			

Table 1.6 OCS Use (FAS)

Treatment Groups			
OCS Use (FAS)	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	Total (N=474)
OCS use at baseline			
At least one OCS			
n (%)	4 (1,7)	5 (2,2)	9 (1,9)
METHYLPREDNISOLONE			
n (%)	3 (1,2)	1 (0,4)	4 (0,8)
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 (0,4)	4 (1,7)	5 (1,1)
OCS dosage (mg/day)			
Mean ± SD	10,0 ± N.E.	8,8 ± 4,79	9,0 ± 4,18
Median	10,0	7,5	10,0
Escalation of OCS during study			
At least one OCS			
n (%)	1 (0,4)	2 (0,9)	3 (0,6)
METHYLPREDNISOLONE			
n (%)	1 (0,4)	0 (0,0)	1 (0,2)
OCS dosage (mg/day)			
Mean ± SD	27,6 ± N.E.	27,6 ± N.E.	27,6 ± N.E.
Median	27,6	27,6	27,6
Duration of escalation (days)			
Mean ± SD	18,0 ± N.E.	18,0 ± N.E.	18,0 ± N.E.
Median	18,0	18,0	18,0
PREDNISONE			
n (%)	0 (0,0)	2 (0,9)	2 (0,4)
OCS dosage (mg/day)			
Mean ± SD	23,5 ± 4,03	23,5 ± 4,03	23,5 ± 4,03
Median	23,5	23,5	23,5
Duration of escalation (days)			
Mean ± SD	18,5 ± 4,95	18,5 ± 4,95	18,5 ± 4,95
Median	18,5	18,5	18,5

OCS Use (FAS)	Treatment Groups		
	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	Total (N=474)
New onset of OCS during study			
At least one OCS			
n (%)	46 (19,0)	28 (12,1)	74 (15,6)
BETAMETHASONE			
n (%)	3 (1,2)	1 (0,4)	4 (0,8)
OCS dosage (mg/day)			
Mean ± SD	2,4 ± 0,00	1,2 ± N.E.	2,1 ± 0,60
Median	2,4	1,2	2,4
Duration of use (days)			
Mean ± SD	7,0 ± 0,00	11,0 ± N.E.	8,0 ± 2,00
Median	7,0	11,0	7,0
MEPREDNISONE			
n (%)	12 (5,0)	5 (2,2)	17 (3,6)
OCS dosage (mg/day)			
Mean ± SD	33,9 ± 10,88	27,2 ± 11,80	31,8 ± 11,24
Median	40,0	20,0	40,0
Duration of use (days)			
Mean ± SD	6,9 ± 2,27	7,2 ± 2,68	7,0 ± 2,32
Median	7,0	6,0	7,0
METHYLPREDNISOLONE			
n (%)	10 (4,1)	4 (1,7)	14 (3,0)
OCS dosage (mg/day)			
Mean ± SD	28,6 ± 11,22	24,0 ± 11,31	27,2 ± 10,99
Median	32,0	20,0	29,2
Duration of use (days)			
Mean ± SD	11,2 ± 10,38	6,5 ± 3,42	9,9 ± 9,06
Median	5,5	6,0	5,5
PREDNISOLONE			
n (%)	10 (4,1)	7 (3,0)	17 (3,6)
OCS dosage (mg/day)			
Mean ± SD	31,0 ± 13,04	22,0 ± 14,42	27,3 ± 13,94
Median	29,3	20,0	25,0

OCS Use (FAS)	Treatment Groups		
	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	Total (N=474)
	Duration of use (days)		
Mean ± SD	8,3 ± 2,45	13,9 ± 12,02	10,6 ± 8,09
Median	9,0	11,0	10,0
PREDNISONE			
n (%)	14 (5,8)	11 (4,7)	25 (5,3)
OCS dosage (mg/day)			
Mean ± SD	28,0 ± 11,64	27,2 ± 15,96	27,7 ± 13,40
Median	28,7	20,0	25,0
Duration of use (days)			
Mean ± SD	6,9 ± 4,49	8,6 ± 4,13	7,6 ± 4,34
Median	5,0	7,0	7,0
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 subpopulation "high-dose ICS/LABA"			

2. All-cause Mortality - Binary Analysis

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	242	232			
Death, n (%)	0 (0,0)	1 (0,4)	-	0,32 [0,01; 7,81] 0,484	-0,00 [-0,01; 0,00] 0,316

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 subpopulation "high-dose ICS/LABA"

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

Table 3.1 ACQ-5 - Return Rate (FAS)

Patient Reported Outcome - Return Rate (FAS)	Treatment groups		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Total N=474
Return Rate*, n (%)			
Baseline Returns	240 (99,2)	225 (97,0)	465 (98,1)
Week 16 Returns	223 (92,1)	210 (90,5)	433 (91,4)
Week 24 Returns	232 (95,9)	216 (93,1)	448 (94,5)

* 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 subpopulation "high-dose ICS/LABA"

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

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
ACQ-5 score			
N'	232	219	
Baseline Mean (SD)	2,59 (0,597)	2,52 (0,570)	
Week 16:			
Adjusted Mean Change (SE)	-1,22 (0,084)	-1,09 (0,086)	-0,12 [-0,288; 0,039] 0,136
Week 24:			
Adjusted Mean Change (SE)	-1,25 (0,083)	-1,24 (0,086)	-0,01 [-0,171; 0,156] 0,926
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, 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 subpopulation "high-dose ICS/LABA"			

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
ACQ-5 score			
Interaction Test	0,846		
Age = 18-39 years			
N'	37	32	
Baseline Mean (SD)	2,65 (0,623)	2,49 (0,592)	
Week 16:			
Adjusted Mean Change (SE)	-1,36 (0,157)	-1,15 (0,166)	-0,22 [-0,631; 0,197] 0,304
Week 24:			
Adjusted Mean Change (SE)	-1,27 (0,158)	-1,42 (0,167)	0,15 [-0,267; 0,569] 0,479
Age = 40-64 years			
N'	138	140	
Baseline Mean (SD)	2,58 (0,600)	2,56 (0,582)	
Week 16:			
Adjusted Mean Change (SE)	-1,22 (0,095)	-1,14 (0,097)	-0,09 [-0,298; 0,120] 0,401
Week 24:			
Adjusted Mean Change (SE)	-1,28 (0,094)	-1,27 (0,097)	-0,01 [-0,221; 0,195] 0,903
Age = ≥65 years			
N'	57	47	
Baseline Mean (SD)	2,57 (0,583)	2,43 (0,516)	
Week 16:			
Adjusted Mean Change (SE)	-1,09 (0,134)	-0,91 (0,144)	-0,17 [-0,513; 0,172] 0,329

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:			
Adjusted Mean Change (SE)	-1,14 (0,133)	-1,01 (0,145)	-0,13 [-0,472; 0,215] 0,463
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 + 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 subpopulation "high-dose ICS/LABA"			

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
ACQ-5 score			
Interaction Test	0,996		
Gender = Male			
N'	85	81	
Baseline Mean (SD)	2,52 (0,526)	2,40 (0,530)	
Week 16:			
Adjusted Mean Change (SE)	-1,28 (0,112)	-1,13 (0,118)	-0,15 [-0,421; 0,120] 0,275
Week 24:			
Adjusted Mean Change (SE)	-1,27 (0,111)	-1,28 (0,117)	0,02 [-0,253; 0,287] 0,901
Gender = Female			
N'	147	138	
Baseline Mean (SD)	2,63 (0,633)	2,59 (0,583)	
Week 16:			
Adjusted Mean Change (SE)	-1,18 (0,096)	-1,07 (0,097)	-0,11 [-0,315; 0,097] 0,299
Week 24:			
Adjusted Mean Change (SE)	-1,24 (0,096)	-1,21 (0,097)	-0,02 [-0,229; 0,184] 0,830
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 + 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 subpopulation "high-dose ICS/LABA"			

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
ACQ-5 score			
Interaction Test	0,717		
Region = Asia			
N'	49	55	
Baseline Mean (SD)	2,42 (0,573)	2,36 (0,499)	
Week 16:			
Adjusted Mean Change (SE)	-1,08 (0,129)	-0,99 (0,122)	-0,09 [-0,438; 0,255] 0,605
Week 24:			
Adjusted Mean Change (SE)	-1,00 (0,126)	-0,99 (0,121)	-0,02 [-0,356; 0,326] 0,931
Region = Europe			
N'	79	77	
Baseline Mean (SD)	2,54 (0,580)	2,48 (0,493)	
Week 16:			
Adjusted Mean Change (SE)	-1,05 (0,099)	-1,00 (0,102)	-0,05 [-0,327; 0,230] 0,734
Week 24:			
Adjusted Mean Change (SE)	-1,05 (0,099)	-1,05 (0,100)	0,00 [-0,276; 0,277] 0,995
Region = Latin America			
N'	100	86	
Baseline Mean (SD)	2,72 (0,593)	2,66 (0,645)	
Week 16:			
Adjusted Mean Change (SE)	-1,27 (0,090)	-1,06 (0,096)	-0,21 [-0,468; 0,046] 0,107
Week 24:			
Adjusted Mean Change (SE)	-1,39 (0,088)	-1,39 (0,095)	0,00 [-0,252; 0,257] 0,987

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Region = Others			
N'	4	1	
Baseline Mean (SD)	2,50 (0,825)	3,20 (-)	
Week 16:			
Adjusted Mean Change (SE)	-1,03 (0,440)	-2,08 (0,880)	1,05 [-0,883; 2,980] 0,287
Week 24:			
Adjusted Mean Change (SE)	-0,98 (0,440)	-1,70 (0,880)	0,71 [-1,220; 2,643] 0,470
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 + 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 + 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 subpopulation "high-dose ICS/LABA"			

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
ACQ-5 score			
Interaction Test	0,308		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	170	173	
Baseline Mean (SD)	2,57 (0,586)	2,45 (0,524)	
Week 16:			
Adjusted Mean Change (SE)	-1,28 (0,089)	-1,17 (0,090)	-0,10 [-0,291; 0,083] 0,277
Week 24:			
Adjusted Mean Change (SE)	-1,30 (0,088)	-1,32 (0,090)	0,02 [-0,168; 0,204] 0,851
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	62	46	
Baseline Mean (SD)	2,65 (0,627)	2,81 (0,649)	
Week 16:			
Adjusted Mean Change (SE)	-1,00 (0,129)	-0,73 (0,147)	-0,27 [-0,609; 0,062] 0,110
Week 24:			
Adjusted Mean Change (SE)	-1,04 (0,130)	-0,87 (0,147)	-0,17 [-0,506; 0,166] 0,320
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 + 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 subpopulation "high-dose ICS/LABA"			

4. ACQ-5 - Responder Analysis

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	232	219			
ACQ-5 response (decrease of at least 0.5 points), n (%)	195 (84,1)	186 (84,9)	1,04 [0,71; 1,51] 0,836	1,01 [0,92; 1,10] 0,837	-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: $\text{logit}(\text{proportion}) = \text{treatment} + \text{baseline} + \text{visit} + \text{region} + \text{baseline-by-visit interaction} + \text{treatment-by-visit-interaction}$
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: $\text{log}(\text{proportion}) = \text{treatment} + \text{baseline} + \text{visit} + \text{region} + \text{baseline-by-visit interaction} + \text{treatment-by-visit-interaction}$

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

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

Binary Efficacy Outcome (FAS)	Treatment groups			Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value	
	N'	242	232			
ACQ-5 response (decrease of at least 0.5 points), n (%)	196 (81,0)	188 (81,0)	1,04 [0,73; 1,47] 0,840	1,01 [0,92; 1,12] 0,804	-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: $\text{logit}(\text{proportion}) = \text{treatment} + \text{baseline} + \text{visit} + \text{region} + \text{baseline-by-visit interaction} + \text{treatment-by-visit interaction}$
 If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: $\text{log}(\text{proportion}) = \text{treatment} + \text{baseline} + \text{visit} + \text{region} + \text{baseline-by-visit interaction} + \text{treatment-by-visit interaction}$

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	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=0,846				
Age = 18-39 years					
N'	37	32			
ACQ-5 response (decrease of at least 0.5 points), n (%)	33 (89,2)	29 (90,6)	1,36 [0,49; 3,74] 0,551	1,04 [0,85; 1,28] 0,671	-0,01 [-0,16; 0,13] 0,843
Age = 40-64 years					
N'	138	140			
ACQ-5 response (decrease of at least 0.5 points), n (%)	117 (84,8)	120 (85,7)	1,05 [0,65; 1,71] 0,839	1,01 [0,91; 1,13] 0,838	-0,01 [-0,09; 0,07] 0,827
Age = ≥65 years					
N'	57	47			
ACQ-5 response (decrease of at least 0.5 points), n (%)	45 (78,9)	37 (78,7)	0,93 [0,43; 2,02] 0,863	0,99 [0,79; 1,24] 0,909	0,00 [-0,16; 0,16] 0,978
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 + 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 + baseline-by-visit interaction + treatment-by-visit-interaction + age + age * treatment + age * treatment * visit					
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"					

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	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=0,886				
Age = 18-39 years					
N'	40	33			
ACQ-5 response (decrease of at least 0.5 points), n (%)	33 (82,5)	30 (90,9)	0,89 [0,35; 2,24] 0,802	0,96 [0,77; 1,20] 0,719	-0,08 [-0,24; 0,07] 0,282
Age = 40-64 years					
N'	144	150			
ACQ-5 response (decrease of at least 0.5 points), n (%)	118 (81,9)	121 (80,7)	1,12 [0,72; 1,74] 0,630	1,03 [0,91; 1,17] 0,602	0,01 [-0,08; 0,10] 0,779
Age = ≥65 years					
N'	58	49			
ACQ-5 response (decrease of at least 0.5 points), n (%)	45 (77,6)	37 (75,5)	0,97 [0,47; 2,01] 0,933	0,99 [0,78; 1,26] 0,961	0,02 [-0,14; 0,18] 0,801
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 + 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 + baseline-by-visit interaction + treatment-by-visit-interaction + age + age * treatment + age * treatment * visit					
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"					

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	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=0,870				
Gender = Male					
N'	85	81			
ACQ-5 response (decrease of at least 0.5 points), n (%)	71 (83,5)	67 (82,7)	1,09 [0,58; 2,05] 0,794	1,02 [0,87; 1,20] 0,774	0,01 [-0,11; 0,12] 0,889
Gender = Female					
N'	147	138			
ACQ-5 response (decrease of at least 0.5 points), n (%)	124 (84,4)	119 (86,2)	1,02 [0,64; 1,63] 0,940	1,00 [0,90; 1,12] 0,981	-0,02 [-0,10; 0,06] 0,654
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 + 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 + baseline-by-visit interaction + treatment-by-visit-interaction + gender + gender * treatment + gender * treatment * visit					
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"					

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	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=0,789				
Gender = Male					
N'	88	81			
ACQ-5 response (decrease of at least 0.5 points), n (%)	72 (81,8)	67 (82,7)	0,97 [0,53; 1,77] 0,921	1,00 [0,84; 1,17] 0,955	-0,01 [-0,12; 0,11] 0,879
Gender = Female					
N'	154	151			
ACQ-5 response (decrease of at least 0.5 points), n (%)	124 (80,5)	121 (80,1)	1,07 [0,70; 1,66] 0,747	1,02 [0,90; 1,16] 0,744	0,00 [-0,09; 0,09] 0,932
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 + 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 + baseline-by-visit interaction + treatment-by-visit-interaction + gender + gender * treatment + gender * treatment * visit					
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"					

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	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'	49	55			
ACQ-5 response (decrease of at least 0.5 points), n (%)	42 (85,7)	40 (72,7)	1,48 [0,71; 3,09] 0,298	1,12 [0,90; 1,41] 0,303	0,13 [-0,02; 0,28] 0,096
Region = Europe					
N'	79	77			
ACQ-5 response (decrease of at least 0.5 points), n (%)	61 (77,2)	65 (84,4)	0,71 [0,38; 1,30] 0,266	0,90 [0,76; 1,07] 0,255	-0,07 [-0,19; 0,05] 0,251
Region = Latin America					
N'	100	86			
ACQ-5 response (decrease of at least 0.5 points), n (%)	89 (89,0)	80 (93,0)	1,22 [0,65; 2,31] 0,537	1,04 [0,93; 1,16] 0,530	-0,04 [-0,12; 0,04] 0,334
Region = Others					
N'	4	1			
ACQ-5 response (decrease of at least 0.5 points), n (%)	3 (75,0)	1 (100,0)	-	0,83 [0,49; 1,38] 0,463	-0,25 [-0,67; 0,17] 0,248
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: $\text{logit}(\text{proportion}) = \text{treatment} + \text{baseline} + \text{visit} + \text{baseline-by-visit interaction} + \text{treatment-by-visit-interaction} + \text{region} + \text{region} * \text{treatment} + \text{region} * \text{treatment} * \text{visit}$ Exceptional model(s) for OR: ACQ-5 response (decrease of at least 0.5 points): $\text{logit}(\text{proportion}) = \text{treatment} + \text{baseline} + \text{visit} [\text{by region}]$					
Applied model for RR: $\text{log}(\text{proportion}) = \text{treatment} + \text{baseline} + \text{visit} + \text{baseline-by-visit interaction} + \text{treatment-by-visit-interaction} + \text{region} + \text{region} * \text{treatment} + \text{region} * \text{treatment} * \text{visit}$					
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"					

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

Binary Efficacy Outcome (FAS)	Treatment groups			Comparison								
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	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'	53	59										
ACQ-5 response (decrease of at least 0.5 points), n (%)	42 (79,2)	41 (69,5)	1,24 [0,65; 2,39] 0,515	1,08 [0,85; 1,39] 0,530	0,10 [-0,06; 0,26] 0,233							
Region = Europe												
N'	81	83										
ACQ-5 response (decrease of at least 0.5 points), n (%)	62 (76,5)	65 (78,3)	0,92 [0,52; 1,66] 0,793	0,97 [0,81; 1,17] 0,780	-0,02 [-0,15; 0,11] 0,786							
Region = Latin America												
N'	104	89										
ACQ-5 response (decrease of at least 0.5 points), n (%)	89 (85,6)	81 (91,0)	1,00 [0,56; 1,78] 0,993	1,00 [0,88; 1,14] 0,995	-0,05 [-0,14; 0,04] 0,236							
Region = Others												
N'	4	1										
ACQ-5 response (decrease of at least 0.5 points), n (%)	3 (75,0)	1 (100,0)	-	0,80 [0,47; 1,36] 0,412	-0,25 [-0,67; 0,17] 0,248							
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: $\text{logit}(\text{proportion}) = \text{treatment} + \text{baseline} + \text{visit} + \text{baseline-by-visit interaction} + \text{treatment-by-visit-interaction} + \text{region} + \text{region} * \text{treatment} + \text{region} * \text{treatment} * \text{visit}$ Exceptional model(s) for OR: ACQ-5 response (decrease of at least 0.5 points): $\text{logit}(\text{proportion}) = \text{treatment} + \text{baseline} + \text{visit} [\text{by region}]$												
Applied model for RR: $\text{log}(\text{proportion}) = \text{treatment} + \text{baseline} + \text{visit} + \text{baseline-by-visit interaction} + \text{treatment-by-visit-interaction} + \text{region} + \text{region} * \text{treatment} + \text{region} * \text{treatment} * \text{visit}$												
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"												

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	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=0,674			
Asthma exacerbations in the 12 months prior to screening = 1					
N'	170	173			
ACQ-5 response (decrease of at least 0.5 points), n (%)	147 (86,5)	149 (86,1)	1,07 [0,68; 1,69] 0,762	1,01 [0,92; 1,11] 0,858	0,00 [-0,07; 0,08] 0,926
Asthma exacerbations in the 12 months prior to screening = ≥2					
N'	62	46			
ACQ-5 response (decrease of at least 0.5 points), n (%)	48 (77,4)	37 (80,4)	1,28 [0,64; 2,54] 0,483	1,06 [0,86; 1,31] 0,575	-0,03 [-0,18; 0,12] 0,703
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 + 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 + 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 subpopulation "high-dose ICS/LABA"					

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=242	SAL/FLU + TIO N=232	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=0,854				
Asthma exacerbations in the 12 months prior to screening = 1						
N'	176	184				
ACQ-5 response (decrease of at least 0.5 points), n (%)	148 (84,1)	150 (81,5)	1,12 [0,74; 1,69] 0,598	1,03 [0,92; 1,15] 0,619	0,03 [-0,05; 0,10] 0,518	
Asthma exacerbations in the 12 months prior to screening = ≥2						
N'	66	48				
ACQ-5 response (decrease of at least 0.5 points), n (%)	48 (72,7)	38 (79,2)	1,04 [0,54; 2,00] 0,906	1,01 [0,80; 1,27] 0,927	-0,06 [-0,22; 0,09] 0,422	
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 + 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 + 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 subpopulation "high-dose ICS/LABA"						

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=242	SAL/FLU + TIO N=232	Total N=474
Return Rate*, n (%)			
Baseline Returns	240 (99,2)	224 (96,6)	464 (97,9)
Week 16 Returns	224 (92,6)	213 (91,8)	437 (92,2)
Week 24 Returns	233 (96,3)	220 (94,8)	453 (95,6)

* 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 subpopulation "high-dose ICS/LABA"

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

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Total score			
N'	231	215	
Baseline Mean (SD)	4,69 (0,855)	4,71 (0,881)	
Week 16:			
Adjusted Mean Change (SE)	0,71 (0,077)	0,61 (0,079)	0,10 [-0,053; 0,247] 0,204
Week 24:			
Adjusted Mean Change (SE)	0,74 (0,078)	0,74 (0,080)	0,00 [-0,150; 0,158] 0,957
Symptoms score			
N'	231	215	
Baseline Mean (SD)	4,70 (0,861)	4,79 (0,837)	
Week 16:			
Adjusted Mean Change (SE)	0,77 (0,082)	0,63 (0,084)	0,14 [-0,017; 0,302] 0,079
Week 24:			
Adjusted Mean Change (SE)	0,76 (0,083)	0,80 (0,085)	-0,05 [-0,211; 0,119] 0,584
Activity limitation score			
N'	231	215	
Baseline Mean (SD)	4,60 (0,900)	4,61 (0,918)	
Week 16:			
Adjusted Mean Change (SE)	0,72 (0,081)	0,65 (0,083)	0,07 [-0,089; 0,226] 0,395
Week 24:			
Adjusted Mean Change (SE)	0,75 (0,081)	0,78 (0,083)	-0,04 [-0,197; 0,124] 0,659
Emotional function score			
N'	231	215	
Baseline Mean (SD)	5,02 (1,169)	4,92 (1,308)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 16:			
Adjusted Mean Change (SE)	0,67 (0,100)	0,57 (0,103)	0,10 [-0,095; 0,293] 0,317
Week 24:			
Adjusted Mean Change (SE)	0,74 (0,102)	0,61 (0,105)	0,12 [-0,080; 0,327] 0,233
Environmental stimuli score			
N'	231	215	
Baseline Mean (SD)	4,46 (1,276)	4,52 (1,359)	
Week 16:			
Adjusted Mean Change (SE)	0,52 (0,113)	0,51 (0,115)	0,01 [-0,210; 0,231] 0,927
Week 24:			
Adjusted Mean Change (SE)	0,66 (0,113)	0,57 (0,116)	0,09 [-0,133; 0,315] 0,426
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, 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 subpopulation "high-dose ICS/LABA"			

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Total score			
Interaction Test	0,375		
Age = 18-39 years			
N'	37	32	
Baseline Mean (SD)	4,59 (0,872)	4,75 (1,109)	
Week 16:			
Adjusted Mean Change (SE)	0,90 (0,144)	0,59 (0,152)	0,31 [-0,064; 0,691] 0,103
Week 24:			
Adjusted Mean Change (SE)	0,87 (0,149)	0,71 (0,157)	0,16 [-0,232; 0,555] 0,421
Age = 40-64 years			
N'	137	138	
Baseline Mean (SD)	4,74 (0,868)	4,69 (0,890)	
Week 16:			
Adjusted Mean Change (SE)	0,68 (0,088)	0,66 (0,089)	0,02 [-0,172; 0,210] 0,846
Week 24:			
Adjusted Mean Change (SE)	0,74 (0,089)	0,80 (0,091)	-0,06 [-0,255; 0,138] 0,557
Age = ≥65 years			
N'	57	45	
Baseline Mean (SD)	4,63 (0,820)	4,74 (0,664)	
Week 16:			
Adjusted Mean Change (SE)	0,66 (0,122)	0,50 (0,133)	0,17 [-0,148; 0,481] 0,298
Week 24:			
Adjusted Mean Change (SE)	0,67 (0,125)	0,58 (0,137)	0,09 [-0,234; 0,416] 0,583

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Symptoms score			
Interaction Test	0,314		
Age = 18-39 years			
N'	37	32	
Baseline Mean (SD)	4,59 (0,838)	4,79 (1,064)	
Week 16:			
Adjusted Mean Change (SE)	0,99 (0,153)	0,50 (0,161)	0,50 [0,096; 0,899] 0,015 *
Week 24:			
Adjusted Mean Change (SE)	0,85 (0,159)	0,74 (0,168)	0,11 [-0,312; 0,530] 0,611
Age = 40-64 years			
N'	137	138	
Baseline Mean (SD)	4,73 (0,852)	4,77 (0,843)	
Week 16:			
Adjusted Mean Change (SE)	0,74 (0,093)	0,69 (0,095)	0,05 [-0,157; 0,250] 0,656
Week 24:			
Adjusted Mean Change (SE)	0,78 (0,095)	0,86 (0,097)	-0,08 [-0,293; 0,127] 0,437
Age = ≥65 years			
N'	57	45	
Baseline Mean (SD)	4,72 (0,907)	4,84 (0,631)	
Week 16:			
Adjusted Mean Change (SE)	0,71 (0,130)	0,54 (0,141)	0,17 [-0,165; 0,503] 0,322
Week 24:			
Adjusted Mean Change (SE)	0,66 (0,134)	0,68 (0,146)	-0,02 [-0,371; 0,325] 0,897

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Activity limitation score			
Interaction Test	0,243		
Age = 18-39 years			
N'	37	32	
Baseline Mean (SD)	4,58 (0,947)	4,89 (1,096)	
Week 16:			
Adjusted Mean Change (SE)	0,94 (0,151)	0,72 (0,159)	0,22 [-0,177; 0,618] 0,276
Week 24:			
Adjusted Mean Change (SE)	0,94 (0,155)	0,78 (0,164)	0,16 [-0,252; 0,568] 0,450
Age = 40-64 years			
N'	137	138	
Baseline Mean (SD)	4,68 (0,921)	4,56 (0,929)	
Week 16:			
Adjusted Mean Change (SE)	0,67 (0,092)	0,69 (0,094)	-0,02 [-0,225; 0,178] 0,820
Week 24:			
Adjusted Mean Change (SE)	0,73 (0,092)	0,86 (0,094)	-0,13 [-0,338; 0,072] 0,202
Age = ≥65 years			
N'	57	45	
Baseline Mean (SD)	4,41 (0,796)	4,56 (0,703)	
Week 16:			
Adjusted Mean Change (SE)	0,73 (0,128)	0,51 (0,139)	0,21 [-0,117; 0,544] 0,205
Week 24:			
Adjusted Mean Change (SE)	0,70 (0,131)	0,58 (0,142)	0,12 [-0,219; 0,458] 0,488

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Emotional function score			
Interaction Test	0,523		
Age = 18-39 years			
N'	37	32	
Baseline Mean (SD)	4,68 (1,087)	4,48 (1,652)	
Week 16:			
Adjusted Mean Change (SE)	0,88 (0,187)	0,52 (0,197)	0,35 [-0,136; 0,843] 0,157
Week 24:			
Adjusted Mean Change (SE)	0,86 (0,196)	0,49 (0,207)	0,36 [-0,155; 0,883] 0,169
Age = 40-64 years			
N'	137	138	
Baseline Mean (SD)	5,12 (1,192)	4,97 (1,266)	
Week 16:			
Adjusted Mean Change (SE)	0,67 (0,114)	0,60 (0,116)	0,07 [-0,179; 0,318] 0,582
Week 24:			
Adjusted Mean Change (SE)	0,75 (0,117)	0,66 (0,119)	0,09 [-0,172; 0,347] 0,510
Age = ≥65 years			
N'	57	45	
Baseline Mean (SD)	5,01 (1,141)	5,07 (1,110)	
Week 16:			
Adjusted Mean Change (SE)	0,53 (0,159)	0,51 (0,173)	0,02 [-0,390; 0,426] 0,931
Week 24:			
Adjusted Mean Change (SE)	0,64 (0,165)	0,56 (0,180)	0,08 [-0,350; 0,508] 0,716

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Environmental stimuli score			
Interaction Test	0,481		
Age = 18-39 years			
N'	37	32	
Baseline Mean (SD)	4,49 (1,300)	4,55 (1,445)	
Week 16:			
Adjusted Mean Change (SE)	0,54 (0,212)	0,60 (0,223)	-0,06 [-0,616; 0,499] 0,836
Week 24:			
Adjusted Mean Change (SE)	0,75 (0,217)	0,71 (0,229)	0,03 [-0,540; 0,607] 0,909
Age = 40-64 years			
N'	137	138	
Baseline Mean (SD)	4,45 (1,303)	4,49 (1,376)	
Week 16:			
Adjusted Mean Change (SE)	0,51 (0,129)	0,55 (0,131)	-0,04 [-0,323; 0,243] 0,780
Week 24:			
Adjusted Mean Change (SE)	0,62 (0,129)	0,61 (0,132)	0,01 [-0,275; 0,298] 0,938
Age = ≥65 years			
N'	57	45	
Baseline Mean (SD)	4,46 (1,216)	4,57 (1,268)	
Week 16:			
Adjusted Mean Change (SE)	0,54 (0,180)	0,34 (0,196)	0,21 [-0,257; 0,673] 0,379

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:			
Adjusted Mean Change (SE)	0,72 (0,182)	0,37 (0,199)	0,35 [-0,121; 0,827] 0,145
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 + 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 subpopulation "high-dose ICS/LABA"			

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Total score			
Interaction Test	0,448		
Gender = Male			
N'	85	78	
Baseline Mean (SD)	4,85 (0,803)	5,03 (0,806)	
Week 16:			
Adjusted Mean Change (SE)	0,73 (0,102)	0,59 (0,109)	0,14 [-0,111; 0,387] 0,277
Week 24:			
Adjusted Mean Change (SE)	0,78 (0,104)	0,68 (0,111)	0,11 [-0,150; 0,361] 0,418
Gender = Female			
N'	146	137	
Baseline Mean (SD)	4,59 (0,873)	4,53 (0,874)	
Week 16:			
Adjusted Mean Change (SE)	0,69 (0,089)	0,62 (0,089)	0,07 [-0,115; 0,262] 0,446
Week 24:			
Adjusted Mean Change (SE)	0,71 (0,090)	0,77 (0,090)	-0,05 [-0,247; 0,140] 0,585
Symptoms score			
Interaction Test	0,564		
Gender = Male			
N'	85	78	
Baseline Mean (SD)	4,84 (0,789)	5,05 (0,776)	
Week 16:			
Adjusted Mean Change (SE)	0,81 (0,109)	0,61 (0,116)	0,21 [-0,059; 0,471] 0,127

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:			
Adjusted Mean Change (SE)	0,78 (0,111)	0,78 (0,119)	0,01 [-0,268; 0,279] 0,970
Gender = Female			
N'	146	137	
Baseline Mean (SD)	4,62 (0,894)	4,64 (0,837)	
Week 16:			
Adjusted Mean Change (SE)	0,74 (0,094)	0,64 (0,095)	0,11 [-0,094; 0,307] 0,298
Week 24:			
Adjusted Mean Change (SE)	0,74 (0,096)	0,82 (0,096)	-0,07 [-0,281; 0,132] 0,479
Activity limitation score			
Interaction Test	0,452		
Gender = Male			
N'	85	78	
Baseline Mean (SD)	4,77 (0,877)	4,96 (0,885)	
Week 16:			
Adjusted Mean Change (SE)	0,72 (0,107)	0,66 (0,114)	0,07 [-0,197; 0,327] 0,626
Week 24:			
Adjusted Mean Change (SE)	0,84 (0,108)	0,73 (0,116)	0,11 [-0,154; 0,379] 0,406
Gender = Female			
N'	146	137	
Baseline Mean (SD)	4,50 (0,900)	4,41 (0,880)	
Week 16:			
Adjusted Mean Change (SE)	0,72 (0,093)	0,65 (0,094)	0,07 [-0,129; 0,269] 0,488
Week 24:			
Adjusted Mean Change (SE)	0,69 (0,094)	0,81 (0,094)	-0,12 [-0,324; 0,080] 0,235

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Emotional function score			
Interaction Test	0,654		
Gender = Male			
N'	85	78	
Baseline Mean (SD)	5,11 (1,126)	5,26 (1,203)	
Week 16:			
Adjusted Mean Change (SE)	0,66 (0,133)	0,50 (0,141)	0,16 [-0,164; 0,480] 0,336
Week 24:			
Adjusted Mean Change (SE)	0,68 (0,136)	0,50 (0,146)	0,17 [-0,163; 0,511] 0,310
Gender = Female			
N'	146	137	
Baseline Mean (SD)	4,97 (1,194)	4,72 (1,328)	
Week 16:			
Adjusted Mean Change (SE)	0,67 (0,116)	0,60 (0,116)	0,07 [-0,179; 0,310] 0,599
Week 24:			
Adjusted Mean Change (SE)	0,77 (0,118)	0,68 (0,119)	0,09 [-0,161; 0,350] 0,468
Environmental stimuli score			
Interaction Test	0,341		
Gender = Male			
N'	85	78	
Baseline Mean (SD)	4,77 (1,192)	4,87 (1,238)	
Week 16:			
Adjusted Mean Change (SE)	0,60 (0,150)	0,52 (0,159)	0,08 [-0,285; 0,447] 0,663
Week 24:			
Adjusted Mean Change (SE)	0,77 (0,151)	0,50 (0,161)	0,27 [-0,098; 0,647] 0,148

Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	
Gender = Female			
N'	146	137	
Baseline Mean (SD)	4,28 (1,293)	4,31 (1,387)	
Week 16:			
Adjusted Mean Change (SE)	0,47 (0,130)	0,50 (0,131)	-0,03 [-0,309; 0,246] 0,824
Week 24:			
Adjusted Mean Change (SE)	0,59 (0,131)	0,60 (0,131)	-0,02 [-0,297; 0,267] 0,916
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 + 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 subpopulation "high-dose ICS/LABA"			

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Total score			
Interaction Test			N.E.
Region = Asia			
N'	49	54	
Baseline Mean (SD)	4,73 (0,828)	4,59 (0,823)	
Week 16:			
Adjusted Mean Change (SE)	0,57 (0,117)	0,61 (0,112)	-0,04 [-0,356; 0,285] 0,829
Week 24:			
Adjusted Mean Change (SE)	0,52 (0,120)	0,66 (0,114)	-0,13 [-0,461; 0,192] 0,418
Region = Europe			
N'	80	79	
Baseline Mean (SD)	4,79 (0,878)	4,96 (0,826)	
Week 16:			
Adjusted Mean Change (SE)	0,65 (0,074)	0,52 (0,075)	0,13 [-0,083; 0,335] 0,237
Week 24:			
Adjusted Mean Change (SE)	0,65 (0,087)	0,65 (0,088)	0,00 [-0,244; 0,245] 0,999
Region = Latin America			
N'	98	81	
Baseline Mean (SD)	4,58 (0,839)	4,56 (0,929)	
Week 16:			
Adjusted Mean Change (SE)	0,92 (0,090)	0,75 (0,097)	0,17 [-0,095; 0,425] 0,212
Week 24:			
Adjusted Mean Change (SE)	1,01 (0,088)	0,93 (0,097)	0,08 [-0,176; 0,337] 0,537

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Region = Others			
N'	4	1	
Baseline Mean (SD)	4,75 (1,185)	4,06 (-)	
Week 16:			
Adjusted Mean Change (SE)	0,76 (0,644)	1,36 (1,156)	-0,60 [-3,735; 2,544] 0,668
Week 24:			
Adjusted Mean Change (SE)	0,91 (0,350)	1,44 (0,628)	-0,53 [-2,237; 1,177] 0,487
Symptoms score			
Interaction Test	0,487		
Region = Asia			
N'	49	54	
Baseline Mean (SD)	4,72 (0,814)	4,64 (0,706)	
Week 16:			
Adjusted Mean Change (SE)	0,59 (0,126)	0,59 (0,121)	0,00 [-0,338; 0,348] 0,977
Week 24:			
Adjusted Mean Change (SE)	0,56 (0,124)	0,74 (0,118)	-0,18 [-0,513; 0,160] 0,304
Region = Europe			
N'	80	79	
Baseline Mean (SD)	4,75 (0,879)	4,99 (0,841)	
Week 16:			
Adjusted Mean Change (SE)	0,77 (0,098)	0,66 (0,100)	0,12 [-0,156; 0,390] 0,399
Week 24:			
Adjusted Mean Change (SE)	0,69 (0,097)	0,80 (0,098)	-0,11 [-0,377; 0,165] 0,445
Region = Latin America			
N'	98	81	
Baseline Mean (SD)	4,64 (0,877)	4,69 (0,889)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 16:			
Adjusted Mean Change (SE)	0,94 (0,089)	0,71 (0,097)	0,24 [-0,023; 0,494] 0,074
Week 24:			
Adjusted Mean Change (SE)	1,00 (0,088)	0,95 (0,097)	0,05 [-0,203; 0,309] 0,682
Region = Others			
N'	4	1	
Baseline Mean (SD)	5,04 (0,798)	4,33 (-)	
Week 16:			
Adjusted Mean Change (SE)	0,82 (0,435)	1,97 (0,869)	-1,15 [-3,059; 0,754] 0,236
Week 24:			
Adjusted Mean Change (SE)	0,82 (0,435)	1,31 (0,869)	-0,49 [-2,392; 1,421] 0,617
Activity limitation score			
Interaction Test	N.E.		
Region = Asia			
N'	49	54	
Baseline Mean (SD)	4,66 (0,901)	4,55 (0,880)	
Week 16:			
Adjusted Mean Change (SE)	0,58 (0,120)	0,66 (0,114)	-0,09 [-0,415; 0,240] 0,599
Week 24:			
Adjusted Mean Change (SE)	0,50 (0,129)	0,69 (0,123)	-0,19 [-0,545; 0,159] 0,281
Region = Europe			
N'	80	79	
Baseline Mean (SD)	4,68 (0,933)	4,80 (0,875)	
Week 16:			
Adjusted Mean Change (SE)	0,68 (0,079)	0,52 (0,081)	0,16 [-0,062; 0,384] 0,156

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:			
Adjusted Mean Change (SE)	0,68 (0,087)	0,64 (0,087)	0,04 [-0,205; 0,281] 0,760
Region = Latin America			
N'	98	81	
Baseline Mean (SD)	4,50 (0,849)	4,48 (0,959)	
Week 16:			
Adjusted Mean Change (SE)	0,86 (0,094)	0,77 (0,102)	0,09 [-0,186; 0,359] 0,533
Week 24:			
Adjusted Mean Change (SE)	0,96 (0,092)	0,97 (0,101)	-0,02 [-0,285; 0,253] 0,908
Region = Others			
N'	4	1	
Baseline Mean (SD)	4,70 (1,500)	3,36 (-)	
Week 16:			
Adjusted Mean Change (SE)	0,86 (0,629)	0,42 (1,223)	0,45 [-2,901; 3,792] 0,762
Week 24:			
Adjusted Mean Change (SE)	0,91 (0,323)	1,29 (0,628)	-0,38 [-2,100; 1,340] 0,617
Emotional function score			
Interaction Test	N.E.		
Region = Asia			
N'	49	54	
Baseline Mean (SD)	5,15 (1,110)	4,83 (1,377)	
Week 16:			
Adjusted Mean Change (SE)	0,44 (0,178)	0,36 (0,169)	0,08 [-0,408; 0,562] 0,755
Week 24:			
Adjusted Mean Change (SE)	0,47 (0,171)	0,24 (0,162)	0,24 [-0,229; 0,703] 0,316

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Region = Europe			
N'	80	79	
Baseline Mean (SD)	5,27 (1,178)	5,39 (1,096)	
Week 16:			
Adjusted Mean Change (SE)	0,48 (0,090)	0,46 (0,092)	0,01 [-0,240; 0,267] 0,916
Week 24:			
Adjusted Mean Change (SE)	0,56 (0,108)	0,52 (0,108)	0,04 [-0,264; 0,338] 0,810
Region = Latin America			
N'	98	81	
Baseline Mean (SD)	4,77 (1,152)	4,52 (1,326)	
Week 16:			
Adjusted Mean Change (SE)	0,97 (0,112)	0,76 (0,122)	0,21 [-0,116; 0,538] 0,205
Week 24:			
Adjusted Mean Change (SE)	1,06 (0,115)	0,93 (0,126)	0,13 [-0,203; 0,470] 0,436
Region = Others			
N'	4	1	
Baseline Mean (SD)	4,65 (1,170)	4,80 (-)	
Week 16:			
Adjusted Mean Change (SE)	0,26 (0,530)	1,35 (0,991)	-1,09 [-3,604; 1,421] 0,338
Week 24:			
Adjusted Mean Change (SE)	-0,03 (0,577)	0,94 (1,079)	-0,97 [-3,710; 1,760] 0,427
Environmental stimuli score			
Interaction Test	N.E.		
Region = Asia			
N'	49	54	
Baseline Mean (SD)	4,42 (1,237)	4,29 (1,490)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 16:			
Adjusted Mean Change (SE)	0,48 (0,163)	0,71 (0,156)	-0,23 [-0,671; 0,220] 0,318
Week 24:			
Adjusted Mean Change (SE)	0,38 (0,173)	0,74 (0,164)	-0,36 [-0,836; 0,106] 0,128
Region = Europe			
N'	80	79	
Baseline Mean (SD)	4,58 (1,335)	4,80 (1,234)	
Week 16:			
Adjusted Mean Change (SE)	0,61 (0,104)	0,54 (0,105)	0,08 [-0,213; 0,370] 0,596
Week 24:			
Adjusted Mean Change (SE)	0,77 (0,106)	0,66 (0,106)	0,11 [-0,188; 0,403] 0,475
Region = Latin America			
N'	98	81	
Baseline Mean (SD)	4,39 (1,244)	4,40 (1,362)	
Week 16:			
Adjusted Mean Change (SE)	0,78 (0,141)	0,67 (0,153)	0,11 [-0,300; 0,518] 0,599
Week 24:			
Adjusted Mean Change (SE)	1,01 (0,141)	0,67 (0,155)	0,33 [-0,076; 0,745] 0,110
Region = Others			
N'	4	1	
Baseline Mean (SD)	4,13 (1,652)	4,25 (-)	
Week 16:			
Adjusted Mean Change (SE)	0,61 (0,688)	0,98 (1,366)	-0,38 [-3,963; 3,211] 0,811

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:			
Adjusted Mean Change (SE)	1,32 (0,489)	1,86 (0,970)	-0,54 [-3,085; 2,012] 0,634
N: Number of patients in the analysis CI: Confidence Interval N.E.: not estimable *: p < 0,05			
<p>Applied model for Adjusted Mean Change and Mean Difference: Change from baseline = treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + region + region * treatment + region * treatment * visit, within-patient correlation: unstructured covariance matrix</p> <p>Exceptional model(s): Total score: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region], Symptoms score: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + region + region * treatment + region * treatment * visit, within-patient correlation: compound symmetry covariance matrix, Activity limitation 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], Environmental stimuli score: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region]</p> <p>If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.</p>			
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"			

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Total score			
Interaction Test	0,856		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	171	170	
Baseline Mean (SD)	4,69 (0,824)	4,82 (0,891)	
Week 16:			
Adjusted Mean Change (SE)	0,76 (0,082)	0,67 (0,083)	0,10 [-0,073; 0,269] 0,260
Week 24:			
Adjusted Mean Change (SE)	0,79 (0,083)	0,78 (0,084)	0,01 [-0,163; 0,188] 0,889
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	60	45	
Baseline Mean (SD)	4,68 (0,946)	4,30 (0,716)	
Week 16:			
Adjusted Mean Change (SE)	0,52 (0,120)	0,37 (0,136)	0,15 [-0,161; 0,461] 0,344
Week 24:			
Adjusted Mean Change (SE)	0,57 (0,124)	0,55 (0,139)	0,02 [-0,299; 0,342] 0,895
Symptoms score			
Interaction Test	0,779		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	171	170	
Baseline Mean (SD)	4,68 (0,841)	4,90 (0,832)	
Week 16:			
Adjusted Mean Change (SE)	0,83 (0,087)	0,68 (0,089)	0,15 [-0,036; 0,329] 0,116

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:			
Adjusted Mean Change (SE)	0,82 (0,088)	0,86 (0,090)	-0,05 [-0,234; 0,142] 0,631
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	60	45	
Baseline Mean (SD)	4,76 (0,921)	4,37 (0,728)	
Week 16:			
Adjusted Mean Change (SE)	0,57 (0,128)	0,39 (0,145)	0,19 [-0,144; 0,520] 0,266
Week 24:			
Adjusted Mean Change (SE)	0,55 (0,132)	0,54 (0,148)	0,01 [-0,331; 0,354] 0,946
Activity limitation score			
Interaction Test	0,900		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	171	170	
Baseline Mean (SD)	4,60 (0,845)	4,73 (0,924)	
Week 16:			
Adjusted Mean Change (SE)	0,80 (0,086)	0,71 (0,087)	0,08 [-0,096; 0,263] 0,363
Week 24:			
Adjusted Mean Change (SE)	0,79 (0,087)	0,81 (0,088)	-0,02 [-0,199; 0,168] 0,866
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	60	45	
Baseline Mean (SD)	4,60 (1,047)	4,14 (0,727)	
Week 16:			
Adjusted Mean Change (SE)	0,49 (0,126)	0,40 (0,143)	0,09 [-0,238; 0,417] 0,591
Week 24:			
Adjusted Mean Change (SE)	0,59 (0,129)	0,65 (0,146)	-0,07 [-0,402; 0,270] 0,700

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Emotional function score			
Interaction Test	0,878		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	171	170	
Baseline Mean (SD)	5,09 (1,163)	5,02 (1,339)	
Week 16:			
Adjusted Mean Change (SE)	0,71 (0,107)	0,63 (0,108)	0,08 [-0,139; 0,305] 0,463
Week 24:			
Adjusted Mean Change (SE)	0,81 (0,109)	0,66 (0,110)	0,15 [-0,079; 0,382] 0,197
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	60	45	
Baseline Mean (SD)	4,84 (1,176)	4,56 (1,121)	
Week 16:			
Adjusted Mean Change (SE)	0,51 (0,157)	0,30 (0,177)	0,21 [-0,192; 0,614] 0,305
Week 24:			
Adjusted Mean Change (SE)	0,51 (0,162)	0,42 (0,182)	0,09 [-0,330; 0,511] 0,674
Environmental stimuli score			
Interaction Test	0,427		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	171	170	
Baseline Mean (SD)	4,45 (1,286)	4,59 (1,415)	
Week 16:			
Adjusted Mean Change (SE)	0,54 (0,120)	0,57 (0,122)	-0,03 [-0,279; 0,224] 0,830
Week 24:			
Adjusted Mean Change (SE)	0,67 (0,121)	0,62 (0,123)	0,05 [-0,208; 0,306] 0,705

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	60	45	
Baseline Mean (SD)	4,49 (1,260)	4,24 (1,091)	
Week 16:			
Adjusted Mean Change (SE)	0,49 (0,176)	0,33 (0,200)	0,16 [-0,294; 0,620] 0,485
Week 24:			
Adjusted Mean Change (SE)	0,68 (0,180)	0,44 (0,203)	0,24 [-0,227; 0,710] 0,311
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 + 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 subpopulation "high-dose ICS/LABA"			

6. AQLQ-S - Responder Analysis

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	231	215			
AQLQ-S response, n (%)	163 (70,6)	140 (65,1)	1,30 [0,91; 1,86] 0,143	1,11 [0,97; 1,27] 0,113	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: $\text{logit}(\text{proportion}) = \text{treatment} + \text{baseline} + \text{visit} + \text{region} + \text{baseline-by-visit interaction} + \text{treatment-by-visit-interaction}$
If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: $\text{log}(\text{proportion}) = \text{treatment} + \text{baseline} + \text{visit} + \text{region} + \text{baseline-by-visit interaction} + \text{treatment-by-visit-interaction}$

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

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

Binary Efficacy Outcome (FAS)	Treatment groups			Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value	
	N'	240	224			
AQLQ-S response, n (%)	164 (68,3)	141 (62,9)	1,24 [0,88; 1,75] 0,214	1,10 [0,96; 1,27] 0,182	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: $\text{logit}(\text{proportion}) = \text{treatment} + \text{baseline} + \text{visit} + \text{region} + \text{baseline-by-visit interaction} + \text{treatment-by-visit interaction}$
 If it was not possible to fit the minimal model, the OR is not given.

Applied model for RR: $\text{log}(\text{proportion}) = \text{treatment} + \text{baseline} + \text{visit} + \text{region} + \text{baseline-by-visit interaction} + \text{treatment-by-visit interaction}$

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
	Interaction Test: p=0,471				
Age = 18-39 years					
N'	37	32			
AQLQ-S response, n (%)	30 (81,1)	20 (62,5)	1,84 [0,74; 4,59] 0,190	1,28 [0,92; 1,77] 0,139	0,19 [-0,02; 0,40] 0,083
Age = 40-64 years					
N'	137	138			
AQLQ-S response, n (%)	95 (69,3)	96 (69,6)	1,11 [0,71; 1,73] 0,658	1,04 [0,89; 1,22] 0,610	-0,00 [-0,11; 0,11] 0,968
Age = ≥65 years					
N'	57	45			
AQLQ-S response, n (%)	38 (66,7)	24 (53,3)	1,69 [0,78; 3,68] 0,186	1,29 [0,90; 1,85] 0,172	0,13 [-0,06; 0,32] 0,170
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 + 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 + baseline-by-visit interaction + treatment-by-visit-interaction + age + age * treatment + age * treatment * visit					
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"					

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
	Interaction Test: p=0,383				
Age = 18-39 years					
N'	40	32			
AQLQ-S response, n (%)	30 (75,0)	20 (62,5)	1,35 [0,55; 3,32] 0,513	1,15 [0,81; 1,63] 0,434	0,13 [-0,09; 0,34] 0,254
Age = 40-64 years					
N'	142	145			
AQLQ-S response, n (%)	95 (66,9)	97 (66,9)	1,05 [0,68; 1,60] 0,832	1,02 [0,86; 1,21] 0,792	0,00 [-0,11; 0,11] 0,999
Age = ≥65 years					
N'	58	47			
AQLQ-S response, n (%)	39 (67,2)	24 (51,1)	1,91 [0,90; 4,05] 0,090	1,38 [0,95; 1,99] 0,087	0,16 [-0,03; 0,35] 0,090
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 + 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 + baseline-by-visit interaction + treatment-by-visit-interaction + age + age * treatment + age * treatment * visit					
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"					

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
	Interaction Test: p=0,331				
Gender = Male					
N'	85	78			
AQLQ-S response, n (%)	58 (68,2)	40 (51,3)	1,65 [0,90; 3,02] 0,107	1,26 [0,96; 1,66] 0,097	0,17 [0,02; 0,32] 0,025 *
Gender = Female					
N'	146	137			
AQLQ-S response, n (%)	105 (71,9)	100 (73,0)	1,13 [0,73; 1,76] 0,575	1,05 [0,91; 1,23] 0,502	-0,01 [-0,11; 0,09] 0,840
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 + 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 + baseline-by-visit interaction + treatment-by-visit-interaction + gender + gender * treatment + gender * treatment * visit					
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"					

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
	Interaction Test: p=0,318				
Gender = Male					
N'	87	78			
AQLQ-S response, n (%)	59 (67,8)	40 (51,3)	1,57 [0,88; 2,82] 0,129	1,24 [0,94; 1,64] 0,120	0,17 [0,02; 0,31] 0,029*
Gender = Female					
N'	153	146			
AQLQ-S response, n (%)	105 (68,6)	101 (69,2)	1,09 [0,71; 1,66] 0,696	1,04 [0,88; 1,22] 0,641	-0,01 [-0,11; 0,10] 0,918
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 + 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 + baseline-by-visit interaction + treatment-by-visit-interaction + gender + gender * treatment + gender * treatment * visit					
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"					

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
	N.E.				
Interaction Test:	N.E.				
Region = Asia					
N'	49	54			
AQLQ-S response, n (%)	30 (61,2)	35 (64,8)	1,26 [0,58; 2,71] 0,558	1,08 [0,79; 1,46] 0,643	-0,04 [-0,22; 0,15] 0,706
Region = Europe					
N'	80	79			
AQLQ-S response, n (%)	54 (67,5)	48 (60,8)	1,27 [0,70; 2,29] 0,434	1,10 [0,86; 1,40] 0,454	0,07 [-0,08; 0,22] 0,374
Region = Latin America					
N'	98	81			
AQLQ-S response, n (%)	77 (78,6)	56 (69,1)	1,46 [0,83; 2,56] 0,191	1,15 [0,95; 1,39] 0,149	0,09 [-0,03; 0,22] 0,153
Region = Others					
N'	4	1			
AQLQ-S response, n (%)	2 (50,0)	1 (100,0)	-	0,42 [0,16; 1,13] 0,085	-0,50 [-0,99; -0,01] 0,046 *
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 [by region] If it was not possible to fit the minimal model, the OR is not given.					
Applied model for RR: log(proportion) = treatment + baseline + visit + baseline-by-visit interaction + treatment-by-visit-interaction + region + region * treatment + region * treatment * visit					
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"					

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
	N.E.				
Interaction Test:	N.E.				
Region = Asia					
N'	53	57			
AQLQ-S response, n (%)	30 (56,6)	36 (63,2)	0,96 [0,47; 1,98] 0,916	0,98 [0,70; 1,37] 0,908	-0,07 [-0,25; 0,12] 0,483
Region = Europe					
N'	81	83			
AQLQ-S response, n (%)	54 (66,7)	48 (57,8)	1,40 [0,79; 2,49] 0,247	1,15 [0,89; 1,49] 0,278	0,09 [-0,06; 0,24] 0,241
Region = Latin America					
N'	102	83			
AQLQ-S response, n (%)	78 (76,5)	56 (67,5)	1,33 [0,77; 2,28] 0,302	1,12 [0,92; 1,37] 0,246	0,09 [-0,04; 0,22] 0,175
Region = Others					
N'	4	1			
AQLQ-S response, n (%)	2 (50,0)	1 (100,0)	-	0,42 [0,15; 1,13] 0,086	-0,50 [-0,99; -0,01] 0,046 *
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 [by region] If it was not possible to fit the minimal model, the OR is not given.					
Applied model for RR: log(proportion) = treatment + baseline + visit + baseline-by-visit interaction + treatment-by-visit-interaction + region + region * treatment + region * treatment * visit					
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"					

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
	Interaction Test: p=0,309				
Asthma exacerbations in the 12 months prior to screening = 1					
N'	171	170			
AQLQ-S response, n (%)	128 (74,9)	108 (63,5)	1,48 [0,98; 2,24] 0,062	1,17 [1,00; 1,36] 0,044 *	0,11 [0,02; 0,21] 0,023 *
Asthma exacerbations in the 12 months prior to screening = ≥2					
N'	60	45			
AQLQ-S response, n (%)	35 (58,3)	32 (71,1)	0,96 [0,47; 1,97] 0,922	0,96 [0,73; 1,28] 0,796	-0,13 [-0,31; 0,05] 0,169
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 + 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 + 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 subpopulation "high-dose ICS/LABA"					

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
	Interaction Test: p=0,256				
Asthma exacerbations in the 12 months prior to screening = 1					
N'	176	178			
AQLQ-S response, n (%)	128 (72,7)	109 (61,2)	1,42 [0,95; 2,11] 0,084	1,16 [0,99; 1,36] 0,066	0,11 [0,02; 0,21] 0,021 *
Asthma exacerbations in the 12 months prior to screening = ≥2					
N'	64	46			
AQLQ-S response, n (%)	36 (56,3)	32 (69,6)	0,89 [0,45; 1,78] 0,751	0,94 [0,70; 1,26] 0,692	-0,13 [-0,31; 0,05] 0,147
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 + 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 + 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 subpopulation "high-dose ICS/LABA"					

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=242	SAL/FLU + TIO N=232	Total N=474
Return Rate*, n (%)			
Baseline Returns	240 (99,2)	224 (96,6)	464 (97,9)
Week 24 Returns	230 (95,0)	216 (93,1)	446 (94,1)

* 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 subpopulation "high-dose ICS/LABA"

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

Patient Reported Outcome - Change from Baseline (FAS)	Treatment groups		Comparison
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	
Total score			
N'	228	211	
Baseline Mean (SD)	39,86 (16,084)	38,51 (17,271)	
Week 24:			
Adjusted Mean Change (SE)	-11,85 (1,635)	-10,19 (1,675)	-1,66 [-4,639; 1,311] 0,273
Symptoms score			
N'	228	211	
Baseline Mean (SD)	51,50 (18,606)	51,44 (20,761)	
Week 24:			
Adjusted Mean Change (SE)	-16,78 (2,165)	-17,25 (2,221)	0,48 [-3,462; 4,413] 0,813
Activity score			
N'	228	211	
Baseline Mean (SD)	54,09 (20,443)	50,81 (21,293)	
Week 24:			
Adjusted Mean Change (SE)	-11,54 (2,129)	-9,60 (2,186)	-1,94 [-5,821; 1,947] 0,328
Impacts score			
N'	228	211	
Baseline Mean (SD)	28,24 (17,751)	27,55 (19,314)	
Week 24:			
Adjusted Mean Change (SE)	-10,49 (1,671)	-8,37 (1,712)	-2,12 [-5,157; 0,912] 0,170
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 If it was not possible to fit the minimal model, the Adjusted Mean Change and Mean Difference are not given.			
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"			

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

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Total score			
N'	240	224	
Baseline Mean (SD)	40,50 (16,113)	38,81 (17,094)	
Week 24:			
Adjusted Mean Change (SE)	-10,29 (1,541)	-8,40 (1,566)	-1,89 [-4,814; 1,033] 0,205
Symptoms score			
N'	240	224	
Baseline Mean (SD)	52,18 (18,740)	51,98 (20,466)	
Week 24:			
Adjusted Mean Change (SE)	-14,87 (2,057)	-14,82 (2,095)	-0,05 [-3,955; 3,851] 0,979
Activity score			
N'	240	224	
Baseline Mean (SD)	54,51 (20,394)	51,14 (21,412)	
Week 24:			
Adjusted Mean Change (SE)	-10,29 (1,970)	-8,16 (2,008)	-2,13 [-5,878; 1,618] 0,265
Impacts score			
N'	240	224	
Baseline Mean (SD)	28,97 (17,897)	27,77 (19,030)	
Week 24:			
Adjusted Mean Change (SE)	-8,73 (1,579)	-6,54 (1,605)	-2,20 [-5,185; 0,790] 0,149
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 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 subpopulation "high-dose ICS/LABA"			

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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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Total score			
Interaction Test	0,800		
Age = 18-39 years			
N'	37	31	
Baseline Mean (SD)	34,62 (16,814)	35,63 (18,711)	
Week 24:			
Adjusted Mean Change (SE)	-12,63 (2,940)	-11,29 (3,124)	-1,33 [-8,949; 6,279] 0,731
Age = 40-64 years			
N'	134	136	
Baseline Mean (SD)	40,50 (15,604)	37,63 (17,243)	
Week 24:			
Adjusted Mean Change (SE)	-12,20 (1,830)	-9,80 (1,878)	-2,40 [-6,205; 1,415] 0,218
Age = ≥65 years			
N'	57	44	
Baseline Mean (SD)	41,75 (16,308)	43,24 (15,739)	
Week 24:			
Adjusted Mean Change (SE)	-10,54 (2,503)	-10,62 (2,733)	0,08 [-6,197; 6,363] 0,979
Symptoms score			
Interaction Test	0,502		
Age = 18-39 years			
N'	37	31	
Baseline Mean (SD)	50,16 (20,229)	50,03 (21,488)	
Week 24:			
Adjusted Mean Change (SE)	-14,83 (3,888)	-20,49 (4,134)	5,65 [-4,415; 15,721] 0,271

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Age = 40-64 years			
N'	134	136	
Baseline Mean (SD)	52,62 (17,014)	50,83 (21,528)	
Week 24:			
Adjusted Mean Change (SE)	-18,25 (2,418)	-17,17 (2,488)	-1,08 [-6,115; 3,953] 0,673
Age = ≥65 years			
N'	57	44	
Baseline Mean (SD)	49,75 (21,106)	54,32 (17,797)	
Week 24:			
Adjusted Mean Change (SE)	-13,96 (3,311)	-14,47 (3,605)	0,51 [-7,803; 8,824] 0,904
Activity score			
Interaction Test	0,733		
Age = 18-39 years			
N'	37	31	
Baseline Mean (SD)	43,03 (19,941)	43,47 (20,706)	
Week 24:			
Adjusted Mean Change (SE)	-16,19 (3,838)	-13,45 (4,076)	-2,75 [-12,638; 7,143] 0,586
Age = 40-64 years			
N'	134	136	
Baseline Mean (SD)	55,18 (20,746)	49,99 (21,190)	
Week 24:			
Adjusted Mean Change (SE)	-11,79 (2,375)	-9,05 (2,444)	-2,73 [-7,694; 2,224] 0,279
Age = ≥65 years			
N'	57	44	
Baseline Mean (SD)	58,72 (17,630)	58,53 (20,089)	
Week 24:			
Adjusted Mean Change (SE)	-8,10 (3,253)	-9,09 (3,547)	0,99 [-7,167; 9,147] 0,812

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Impacts score			
Interaction Test	0,905		
Age = 18-39 years			
N'	37	31	
Baseline Mean (SD)	25,09 (18,157)	26,75 (22,187)	
Week 24:			
Adjusted Mean Change (SE)	-9,95 (2,997)	-7,38 (3,185)	-2,57 [-10,335; 5,200] 0,516
Age = 40-64 years			
N'	134	136	
Baseline Mean (SD)	28,54 (17,241)	26,56 (19,030)	
Week 24:			
Adjusted Mean Change (SE)	-10,55 (1,869)	-8,11 (1,917)	-2,44 [-6,322; 1,445] 0,218
Age = ≥65 years			
N'	57	44	
Baseline Mean (SD)	29,56 (18,731)	31,16 (18,016)	
Week 24:			
Adjusted Mean Change (SE)	-10,87 (2,555)	-10,06 (2,790)	-0,81 [-7,213; 5,600] 0,805
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 + 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 subpopulation "high-dose ICS/LABA"			

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Total score			
Interaction Test	0,736		
Age = 18-39 years			
N'	40	32	
Baseline Mean (SD)	36,33 (17,596)	36,05 (18,561)	
Week 24:			
Adjusted Mean Change (SE)	-9,88 (2,823)	-9,92 (3,065)	0,04 [-7,447; 7,537] 0,991
Age = 40-64 years			
N'	142	145	
Baseline Mean (SD)	41,10 (15,565)	38,04 (17,167)	
Week 24:			
Adjusted Mean Change (SE)	-10,76 (1,739)	-7,98 (1,760)	-2,78 [-6,516; 0,948] 0,143
Age = ≥65 years			
N'	58	47	
Baseline Mean (SD)	41,88 (16,197)	43,08 (15,362)	
Week 24:			
Adjusted Mean Change (SE)	-9,47 (2,447)	-8,75 (2,641)	-0,73 [-6,926; 5,475] 0,818
Symptoms score			
Interaction Test	0,298		
Age = 18-39 years			
N'	40	32	
Baseline Mean (SD)	51,27 (20,344)	49,85 (21,164)	
Week 24:			
Adjusted Mean Change (SE)	-11,49 (3,765)	-18,60 (4,090)	7,10 [-2,887; 17,094] 0,163

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Age = 40-64 years			
N'	142	145	
Baseline Mean (SD)	53,28 (17,254)	51,57 (21,256)	
Week 24:			
Adjusted Mean Change (SE)	-16,40 (2,316)	-14,82 (2,349)	-1,58 [-6,548; 3,392] 0,533
Age = ≥65 years			
N'	58	47	
Baseline Mean (SD)	50,10 (21,096)	54,72 (17,404)	
Week 24:			
Adjusted Mean Change (SE)	-12,80 (3,262)	-11,48 (3,514)	-1,32 [-9,596; 6,957] 0,754
Activity score			
Interaction Test	0,658		
Age = 18-39 years			
N'	40	32	
Baseline Mean (SD)	45,28 (21,218)	43,58 (20,380)	
Week 24:			
Adjusted Mean Change (SE)	-13,47 (3,618)	-12,30 (3,931)	-1,17 [-10,738; 8,396] 0,810
Age = 40-64 years			
N'	142	145	
Baseline Mean (SD)	55,33 (20,588)	50,53 (21,582)	
Week 24:			
Adjusted Mean Change (SE)	-10,73 (2,218)	-7,42 (2,251)	-3,31 [-8,077; 1,464] 0,174
Age = ≥65 years			
N'	58	47	
Baseline Mean (SD)	58,86 (17,510)	58,16 (19,828)	
Week 24:			
Adjusted Mean Change (SE)	-7,24 (3,125)	-8,14 (3,369)	0,90 [-7,013; 8,821] 0,823

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Impacts score			
Interaction Test	0,934		
Age = 18-39 years			
N'	40	32	
Baseline Mean (SD)	26,65 (18,752)	27,52 (22,264)	
Week 24:			
Adjusted Mean Change (SE)	-7,21 (2,885)	-5,98 (3,132)	-1,23 [-8,885; 6,428] 0,753
Age = 40-64 years			
N'	142	145	
Baseline Mean (SD)	29,37 (17,447)	26,80 (18,728)	
Week 24:			
Adjusted Mean Change (SE)	-8,92 (1,780)	-6,30 (1,800)	-2,62 [-6,427; 1,195] 0,178
Age = ≥65 years			
N'	58	47	
Baseline Mean (SD)	29,62 (18,571)	30,94 (17,616)	
Week 24:			
Adjusted Mean Change (SE)	-9,62 (2,502)	-7,96 (2,701)	-1,66 [-7,994; 4,680] 0,608
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 + 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 subpopulation "high-dose ICS/LABA"			

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Total score			
Interaction Test	0,408		
Gender = Male			
N'	84	78	
Baseline Mean (SD)	35,52 (16,190)	34,04 (16,450)	
Week 24:			
Adjusted Mean Change (SE)	-11,05 (2,077)	-11,03 (2,222)	-0,01 [-4,929; 4,900] 0,995
Gender = Female			
N'	144	133	
Baseline Mean (SD)	42,39 (15,525)	41,13 (17,262)	
Week 24:			
Adjusted Mean Change (SE)	-12,44 (1,882)	-9,81 (1,875)	-2,63 [-6,381; 1,127] 0,170
Symptoms score			
Interaction Test	0,724		
Gender = Male			
N'	84	78	
Baseline Mean (SD)	48,63 (17,558)	48,99 (22,654)	
Week 24:			
Adjusted Mean Change (SE)	-14,83 (2,755)	-16,24 (2,943)	1,41 [-5,093; 7,911] 0,671
Gender = Female			
N'	144	133	
Baseline Mean (SD)	53,18 (19,051)	52,88 (19,512)	
Week 24:			
Adjusted Mean Change (SE)	-18,13 (2,478)	-18,07 (2,475)	-0,06 [-5,029; 4,902] 0,980

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Activity score			
Interaction Test	0,066		
Gender = Male			
N'	84	78	
Baseline Mean (SD)	48,04 (21,710)	43,75 (19,560)	
Week 24:			
Adjusted Mean Change (SE)	-11,16 (2,699)	-14,03 (2,900)	2,87 [-3,511; 9,258] 0,377
Gender = Female			
N'	144	133	
Baseline Mean (SD)	57,62 (18,861)	54,95 (21,247)	
Week 24:			
Adjusted Mean Change (SE)	-11,84 (2,437)	-7,17 (2,428)	-4,67 [-9,541; 0,206] 0,060
Impacts score			
Interaction Test	0,957		
Gender = Male			
N'	84	78	
Baseline Mean (SD)	24,55 (16,973)	23,99 (18,291)	
Week 24:			
Adjusted Mean Change (SE)	-10,20 (2,119)	-7,97 (2,265)	-2,23 [-7,249; 2,784] 0,382
Gender = Female			
N'	144	133	
Baseline Mean (SD)	30,39 (17,899)	29,64 (19,658)	
Week 24:			
Adjusted Mean Change (SE)	-10,70 (1,924)	-8,64 (1,918)	-2,06 [-5,890; 1,773] 0,292
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 + 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 subpopulation "high-dose ICS/LABA"			

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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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Total score			
Interaction Test	0,331		
Gender = Male			
N'	87	78	
Baseline Mean (SD)	35,92 (16,086)	34,04 (16,450)	
Week 24:			
Adjusted Mean Change (SE)	-9,92 (2,019)	-10,01 (2,176)	0,09 [-4,831; 5,007] 0,972
Gender = Female			
N'	153	146	
Baseline Mean (SD)	43,10 (15,589)	41,36 (16,937)	
Week 24:			
Adjusted Mean Change (SE)	-10,54 (1,773)	-7,59 (1,744)	-2,95 [-6,597; 0,700] 0,113
Symptoms score			
Interaction Test	0,613		
Gender = Male			
N'	87	78	
Baseline Mean (SD)	49,29 (17,645)	48,99 (22,654)	
Week 24:			
Adjusted Mean Change (SE)	-13,82 (2,705)	-15,12 (2,911)	1,30 [-5,275; 7,877] 0,698
Gender = Female			
N'	153	146	
Baseline Mean (SD)	53,82 (19,198)	53,58 (19,085)	
Week 24:			
Adjusted Mean Change (SE)	-15,57 (2,356)	-14,75 (2,327)	-0,81 [-5,689; 4,061] 0,743

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Activity score			
Interaction Test	0,043 *		
Gender = Male			
N'	87	78	
Baseline Mean (SD)	48,27 (21,446)	43,75 (19,560)	
Week 24:			
Adjusted Mean Change (SE)	-10,15 (2,576)	-13,34 (2,788)	3,18 [-3,088; 9,453] 0,319
Gender = Female			
N'	153	146	
Baseline Mean (SD)	58,06 (18,941)	55,08 (21,374)	
Week 24:			
Adjusted Mean Change (SE)	-10,43 (2,250)	-5,55 (2,217)	-4,87 [-9,520; -0,225] 0,040 *
Impacts score			
Interaction Test	0,959		
Gender = Male			
N'	87	78	
Baseline Mean (SD)	24,95 (16,922)	23,99 (18,291)	
Week 24:			
Adjusted Mean Change (SE)	-8,89 (2,065)	-6,81 (2,223)	-2,08 [-7,117; 2,949] 0,417
Gender = Female			
N'	153	146	
Baseline Mean (SD)	31,26 (18,087)	29,79 (19,169)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:			
Adjusted Mean Change (SE)	-8,62 (1,818)	-6,37 (1,789)	-2,25 [-5,983; 1,484] 0,237
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 + 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 subpopulation "high-dose ICS/LABA"			

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Total score			
Interaction Test	0,194		
Region = Asia			
N'	48	53	
Baseline Mean (SD)	43,82 (15,164)	45,53 (16,709)	
Week 24:			
Adjusted Mean Change (SE)	-3,09 (2,276)	-7,55 (2,172)	4,46 [-1,705; 10,615] 0,156
Region = Europe			
N'	78	77	
Baseline Mean (SD)	42,59 (16,344)	36,22 (17,332)	
Week 24:			
Adjusted Mean Change (SE)	-12,31 (1,785)	-8,19 (1,799)	-4,11 [-9,100; 0,874] 0,106
Region = Latin America			
N'	98	80	
Baseline Mean (SD)	35,82 (15,462)	35,73 (16,314)	
Week 24:			
Adjusted Mean Change (SE)	-14,29 (1,598)	-12,12 (1,767)	-2,17 [-6,827; 2,488] 0,361
Region = Others			
N'	4	1	
Baseline Mean (SD)	37,90 (20,101)	63,69 (-)	
Week 24:			
Adjusted Mean Change (SE)	-17,44 (7,871)	-17,98 (15,766)	0,53 [-34,075; 35,144] 0,976

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Symptoms score			
Interaction Test	0,392		
Region = Asia			
N'	48	53	
Baseline Mean (SD)	53,91 (20,367)	55,55 (18,580)	
Week 24:			
Adjusted Mean Change (SE)	-9,91 (3,030)	-15,21 (2,885)	5,31 [-2,910; 13,520] 0,205
Region = Europe			
N'	78	77	
Baseline Mean (SD)	52,63 (17,713)	50,91 (20,960)	
Week 24:			
Adjusted Mean Change (SE)	-13,57 (2,377)	-14,94 (2,394)	1,37 [-5,256; 7,991] 0,685
Region = Latin America			
N'	98	80	
Baseline Mean (SD)	49,71 (17,865)	49,04 (21,801)	
Week 24:			
Adjusted Mean Change (SE)	-23,99 (2,126)	-21,70 (2,354)	-2,28 [-8,493; 3,931] 0,471
Region = Others			
N'	4	1	
Baseline Mean (SD)	44,68 (32,114)	67,38 (-)	
Week 24:			
Adjusted Mean Change (SE)	-17,89 (10,503)	-40,63 (21,001)	22,74 [-23,388; 68,866] 0,333
Activity score			
Interaction Test	0,287		
Region = Asia			
N'	48	53	
Baseline Mean (SD)	57,67 (17,182)	55,74 (21,257)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:			
Adjusted Mean Change (SE)	-3,51 (2,976)	-8,32 (2,829)	4,82 [-3,237; 12,870] 0,241
Region = Europe			
N'	78	77	
Baseline Mean (SD)	56,85 (20,734)	47,56 (20,512)	
Week 24:			
Adjusted Mean Change (SE)	-13,65 (2,335)	-9,07 (2,354)	-4,58 [-11,111; 1,948] 0,169
Region = Latin America			
N'	98	80	
Baseline Mean (SD)	50,44 (21,103)	50,15 (21,308)	
Week 24:			
Adjusted Mean Change (SE)	-14,66 (2,081)	-12,34 (2,303)	-2,32 [-8,405; 3,774] 0,455
Region = Others			
N'	4	1	
Baseline Mean (SD)	46,85 (25,589)	92,51 (-)	
Week 24:			
Adjusted Mean Change (SE)	-23,45 (10,293)	-6,07 (20,636)	-17,38 [-62,694; 27,932] 0,452
Impacts score			
Interaction Test	0,210		
Region = Asia			
N'	48	53	
Baseline Mean (SD)	32,74 (18,836)	36,59 (20,476)	
Week 24:			
Adjusted Mean Change (SE)	-0,54 (2,323)	-4,27 (2,224)	3,73 [-2,558; 10,025] 0,244
Region = Europe			
N'	78	77	
Baseline Mean (SD)	31,40 (17,754)	25,29 (18,474)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:			
Adjusted Mean Change (SE)	-11,04 (1,822)	-6,08 (1,835)	-4,95 [-10,037; 0,132] 0,056
Region = Latin America			
N'	98	80	
Baseline Mean (SD)	23,42 (16,308)	23,50 (17,508)	
Week 24:			
Adjusted Mean Change (SE)	-11,89 (1,633)	-9,71 (1,805)	-2,19 [-6,940; 2,567] 0,367
Region = Others			
N'	4	1	
Baseline Mean (SD)	30,44 (15,788)	46,08 (-)	
Week 24:			
Adjusted Mean Change (SE)	-14,36 (8,033)	-17,25 (16,078)	2,89 [-32,395; 38,182] 0,872
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 + 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 subpopulation "high-dose ICS/LABA"			

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Total score			
Interaction Test	0,093		
Region = Asia			
N'	53	57	
Baseline Mean (SD)	45,02 (15,345)	45,26 (16,586)	
Week 24:			
Adjusted Mean Change (SE)	-2,13 (2,183)	-6,95 (2,107)	4,82 [-1,122; 10,754] 0,112
Region = Europe			
N'	81	83	
Baseline Mean (SD)	42,87 (16,334)	36,96 (17,214)	
Week 24:			
Adjusted Mean Change (SE)	-12,17 (1,763)	-7,20 (1,744)	-4,97 [-9,850; -0,093] 0,046 *
Region = Latin America			
N'	102	83	
Baseline Mean (SD)	36,36 (15,393)	35,94 (16,190)	
Week 24:			
Adjusted Mean Change (SE)	-13,61 (1,576)	-11,33 (1,747)	-2,28 [-6,880; 2,321] 0,331
Region = Others			
N'	4	1	
Baseline Mean (SD)	37,90 (20,101)	63,69 (-)	
Week 24:			
Adjusted Mean Change (SE)	-17,52 (7,925)	-18,95 (15,872)	1,42 [-33,418; 36,264] 0,936

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Symptoms score			
Interaction Test	0,330		
Region = Asia			
N'	53	57	
Baseline Mean (SD)	53,79 (19,913)	55,66 (18,081)	
Week 24:			
Adjusted Mean Change (SE)	-8,76 (2,931)	-14,27 (2,827)	5,51 [-2,485; 13,506] 0,176
Region = Europe			
N'	81	83	
Baseline Mean (SD)	53,77 (18,389)	52,02 (20,857)	
Week 24:			
Adjusted Mean Change (SE)	-13,26 (2,371)	-13,17 (2,343)	-0,09 [-6,631; 6,458] 0,979
Region = Latin America			
N'	102	83	
Baseline Mean (SD)	50,37 (17,874)	49,23 (21,466)	
Week 24:			
Adjusted Mean Change (SE)	-23,10 (2,117)	-20,56 (2,350)	-2,54 [-8,737; 3,650] 0,420
Region = Others			
N'	4	1	
Baseline Mean (SD)	44,68 (32,114)	67,38 (-)	
Week 24:			
Adjusted Mean Change (SE)	-17,70 (10,675)	-41,67 (21,343)	23,98 [-22,895; 70,849] 0,316
Activity score			
Interaction Test	0,221		
Region = Asia			
N'	53	57	
Baseline Mean (SD)	58,34 (17,976)	55,47 (21,026)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:			
Adjusted Mean Change (SE)	-2,72 (2,808)	-7,36 (2,703)	4,64 [-3,002; 12,287] 0,233
Region = Europe			
N'	81	83	
Baseline Mean (SD)	56,92 (20,565)	48,87 (21,036)	
Week 24:			
Adjusted Mean Change (SE)	-13,38 (2,271)	-8,00 (2,244)	-5,38 [-11,661; 0,902] 0,093
Region = Latin America			
N'	102	83	
Baseline Mean (SD)	50,90 (20,870)	49,92 (21,487)	
Week 24:			
Adjusted Mean Change (SE)	-13,87 (2,021)	-11,77 (2,242)	-2,10 [-8,018; 3,823] 0,487
Region = Others			
N'	4	1	
Baseline Mean (SD)	46,85 (25,589)	92,51 (-)	
Week 24:			
Adjusted Mean Change (SE)	-23,39 (10,201)	-7,03 (20,448)	-16,36 [-61,253; 28,539] 0,475
Impacts score			
Interaction Test	0,083		
Region = Asia			
N'	53	57	
Baseline Mean (SD)	34,64 (19,147)	36,23 (20,267)	
Week 24:			
Adjusted Mean Change (SE)	0,57 (2,230)	-4,05 (2,156)	4,63 [-1,438; 10,690] 0,135
Region = Europe			
N'	81	83	
Baseline Mean (SD)	31,52 (17,739)	25,57 (18,021)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:			
Adjusted Mean Change (SE)	-10,98 (1,800)	-5,39 (1,780)	-5,60 [-10,577; -0,621] 0,028 *
Region = Latin America			
N'	102	83	
Baseline Mean (SD)	23,95 (16,277)	23,94 (17,491)	
Week 24:			
Adjusted Mean Change (SE)	-11,31 (1,612)	-8,89 (1,785)	-2,42 [-7,117; 2,277] 0,312
Region = Others			
N'	4	1	
Baseline Mean (SD)	30,44 (15,788)	46,08 (-)	
Week 24:			
Adjusted Mean Change (SE)	-14,63 (8,092)	-18,08 (16,193)	3,44 [-32,095; 38,983] 0,849
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 + 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 subpopulation "high-dose ICS/LABA"			

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Total score			
Interaction Test	0,924		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	168	167	
Baseline Mean (SD)	40,60 (16,601)	37,39 (17,132)	
Week 24:			
Adjusted Mean Change (SE)	-12,51 (1,725)	-10,83 (1,753)	-1,68 [-5,082; 1,716] 0,331
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	60	44	
Baseline Mean (SD)	37,79 (14,468)	42,75 (17,332)	
Week 24:			
Adjusted Mean Change (SE)	-10,54 (2,467)	-8,51 (2,784)	-2,03 [-8,204; 4,147] 0,519
Symptoms score			
Interaction Test	0,267		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	168	167	
Baseline Mean (SD)	52,28 (18,601)	50,45 (21,028)	
Week 24:			
Adjusted Mean Change (SE)	-16,87 (2,283)	-18,49 (2,328)	1,62 [-2,875; 6,119] 0,479
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	60	44	
Baseline Mean (SD)	49,34 (18,607)	55,21 (19,487)	
Week 24:			
Adjusted Mean Change (SE)	-17,34 (3,275)	-13,67 (3,680)	-3,67 [-11,857; 4,513] 0,379

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Activity score			
Interaction Test	0,391		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	168	167	
Baseline Mean (SD)	54,77 (21,289)	49,59 (20,346)	
Week 24:			
Adjusted Mean Change (SE)	-12,88 (2,250)	-9,84 (2,295)	-3,04 [-7,490; 1,405] 0,180
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	60	44	
Baseline Mean (SD)	52,18 (17,887)	55,46 (24,255)	
Week 24:			
Adjusted Mean Change (SE)	-7,78 (3,224)	-8,77 (3,629)	0,99 [-7,070; 9,046] 0,810
Impacts score			
Interaction Test	0,501		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	168	167	
Baseline Mean (SD)	28,98 (18,258)	26,48 (18,950)	
Week 24:			
Adjusted Mean Change (SE)	-10,81 (1,763)	-9,19 (1,789)	-1,62 [-5,084; 1,843] 0,358
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	60	44	
Baseline Mean (SD)	26,15 (16,212)	31,61 (20,353)	
Week 24:			
Adjusted Mean Change (SE)	-10,27 (2,518)	-6,18 (2,845)	-4,09 [-10,390; 2,211] 0,203
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 + 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 subpopulation "high-dose ICS/LABA"			

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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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Total score			
Interaction Test	0,735		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	176	178	
Baseline Mean (SD)	41,06 (16,518)	37,71 (16,985)	
Week 24:			
Adjusted Mean Change (SE)	-11,06 (1,637)	-8,77 (1,642)	-2,29 [-5,633; 1,052] 0,179
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	64	46	
Baseline Mean (SD)	38,94 (14,954)	43,09 (17,021)	
Week 24:			
Adjusted Mean Change (SE)	-8,42 (2,369)	-7,33 (2,706)	-1,09 [-7,166; 4,987] 0,725
Symptoms score			
Interaction Test	0,494		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	176	178	
Baseline Mean (SD)	52,80 (18,730)	51,08 (20,683)	
Week 24:			
Adjusted Mean Change (SE)	-15,16 (2,184)	-15,75 (2,199)	0,59 [-3,871; 5,046] 0,796
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	64	46	
Baseline Mean (SD)	50,46 (18,809)	55,48 (19,424)	
Week 24:			
Adjusted Mean Change (SE)	-14,64 (3,168)	-11,99 (3,606)	-2,65 [-10,769; 5,476] 0,523

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Activity score			
Interaction Test	0,228		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	176	178	
Baseline Mean (SD)	54,77 (21,063)	49,97 (20,633)	
Week 24:			
Adjusted Mean Change (SE)	-11,80 (2,094)	-8,19 (2,110)	-3,60 [-7,893; 0,684] 0,099
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	64	46	
Baseline Mean (SD)	53,79 (18,567)	55,67 (23,894)	
Week 24:			
Adjusted Mean Change (SE)	-5,92 (3,036)	-7,78 (3,460)	1,87 [-5,915; 9,648] 0,638
Impacts score			
Interaction Test	0,778		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	176	178	
Baseline Mean (SD)	29,68 (18,391)	26,67 (18,640)	
Week 24:			
Adjusted Mean Change (SE)	-9,13 (1,678)	-7,09 (1,681)	-2,05 [-5,462; 1,368] 0,240
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	64	46	
Baseline Mean (SD)	27,03 (16,443)	32,04 (20,113)	

	Treatment groups		Comparison
Patient Reported Outcome - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:			
Adjusted Mean Change (SE)	-8,02 (2,424)	-4,95 (2,773)	-3,07 [-9,283; 3,149] 0,333
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 + 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 subpopulation "high-dose ICS/LABA"			

8. SGRQ - Responder Analysis

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
	N'	240	224		
SGRQ Response, n (%)	158 (65,8)	129 (57,6)	1,36 [0,93; 2,01] 0,117	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
If it was not possible to fit the minimal model, the OR is not given.

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
	Interaction Test: p=0,035 *				
Age = 18-39 years					
N'	40	32			
SGRQ Response, n (%)	25 (62,5)	21 (65,6)	0,82 [0,30; 2,25] 0,698	0,95 [0,67; 1,35] 0,783	-0,03 [-0,25; 0,19] 0,783
Age = 40-64 years					
N'	142	145			
SGRQ Response, n (%)	99 (69,7)	76 (52,4)	2,02 [1,23; 3,33] 0,006 *	1,33 [1,10; 1,61] 0,003 *	0,17 [0,06; 0,28] 0,002 *
Age = ≥65 years					
N'	58	47			
SGRQ Response, n (%)	34 (58,6)	32 (68,1)	0,63 [0,28; 1,45] 0,279	0,86 [0,64; 1,15] 0,315	-0,09 [-0,28; 0,09] 0,313
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 + age + age * treatment If it was not possible to fit the minimal model, the OR is not given.					
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"					

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
Interaction Test:	p=0,523				
Gender = Male					
N'	87	78			
SGRQ Response, n (%)	56 (64,4)	47 (60,3)	1,14 [0,60; 2,19] 0,685	1,07 [0,84; 1,36] 0,588	0,04 [-0,11; 0,19] 0,586
Gender = Female					
N'	153	146			
SGRQ Response, n (%)	102 (66,7)	82 (56,2)	1,49 [0,92; 2,42] 0,107	1,19 [0,99; 1,42] 0,065	0,11 [-0,00; 0,21] 0,061
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 + gender * treatment If it was not possible to fit the minimal model, the OR is not given.					
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"					

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
Interaction Test:	N.E.				
Region = Asia					
N'	53	57			
SGRQ Response, n (%)	25 (47,2)	30 (52,6)	0,80 [0,38; 1,72] 0,573	0,90 [0,61; 1,31] 0,569	-0,05 [-0,24; 0,13] 0,566
Region = Europe					
N'	81	83			
SGRQ Response, n (%)	57 (70,4)	42 (50,6)	2,14 [1,12; 4,11] 0,022 *	1,39 [1,08; 1,80] 0,011 *	0,20 [0,05; 0,34] 0,008 *
Region = Latin America					
N'	102	83			
SGRQ Response, n (%)	73 (71,6)	56 (67,5)	1,20 [0,62; 2,33] 0,583	1,06 [0,87; 1,29] 0,549	0,04 [-0,09; 0,17] 0,547
Region = Others					
N'	4	1			
SGRQ Response, n (%)	3 (75,0)	1 (100,0)	-	0,93 [0,35; 2,50] 0,891	-0,25 [-0,67; 0,17] 0,248
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 [by region] If it was not possible to fit the minimal model, the OR is not given.					
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"					

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

Binary Efficacy Outcome (FAS)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
Interaction Test:	p=0,442				
Asthma exacerbations in the 12 months prior to screening = 1					
N'	176	178			
SGRQ Response, n (%)	117 (66,5)	98 (55,1)	1,49 [0,95; 2,31] 0,079	1,21 [1,02; 1,43] 0,029 *	0,11 [0,01; 0,22] 0,027 *
Asthma exacerbations in the 12 months prior to screening = ≥2					
N'	64	46			
SGRQ Response, n (%)	41 (64,1)	31 (67,4)	1,03 [0,45; 2,34] 0,944	0,95 [0,72; 1,25] 0,715	-0,03 [-0,21; 0,15] 0,716
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 + history of asthma exacerbation * treatment If it was not possible to fit the minimal model, the OR is not given.					
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"					

9. E-Diary - Symptoms

Table 9.1 Symptoms - Documentation Rate (FAS)

Treatment groups				
Outcome - Documentation Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Total N=474	
No symptoms on rising - Documentation rate in standardized days*, n (%)				
Baseline	70%-100% 50%-<70% <50%	217 (89,7) 18 (7,4) 7 (2,9)	205 (88,4) 19 (8,2) 8 (3,4)	422 (89,0) 37 (7,8) 15 (3,2)
Baseline to Week 8	70%-100% 50%-<70% <50%	210 (86,8) 19 (7,9) 13 (5,4)	207 (89,2) 12 (5,2) 13 (5,6)	417 (88,0) 31 (6,5) 26 (5,5)
Week 9 to Week 16	70%-100% 50%-<70% <50%	198 (81,8) 24 (9,9) 20 (8,3)	200 (86,2) 14 (6,0) 18 (7,8)	398 (84,0) 38 (8,0) 38 (8,0)
Week 17 to Week 24	70%-100% 50%-<70% <50%	192 (79,3) 24 (9,9) 26 (10,7)	192 (82,8) 11 (4,7) 29 (12,5)	384 (81,0) 35 (7,4) 55 (11,6)
Baseline to Week 24	70%-100% 50%-<70% <50%	204 (84,3) 20 (8,3) 18 (7,4)	196 (84,5) 16 (6,9) 20 (8,6)	400 (84,4) 36 (7,6) 38 (8,0)
No day-time symptoms - Documentation rate in standardized days*, n (%)				
Baseline	70%-100% 50%-<70% <50%	214 (88,4) 22 (9,1) 6 (2,5)	208 (89,7) 15 (6,5) 9 (3,9)	422 (89,0) 37 (7,8) 15 (3,2)
Baseline to Week 8	70%-100% 50%-<70% <50%	207 (85,5) 24 (9,9) 11 (4,5)	200 (86,2) 18 (7,8) 14 (6,0)	407 (85,9) 42 (8,9) 25 (5,3)
Week 9 to Week 16	70%-100% 50%-<70% <50%	202 (83,5) 21 (8,7) 19 (7,9)	195 (84,1) 16 (6,9) 21 (9,1)	397 (83,8) 37 (7,8) 40 (8,4)
Week 17 to Week 24	70%-100% 50%-<70% <50%	197 (81,4) 18 (7,4) 27 (11,2)	173 (74,6) 28 (12,1) 31 (13,4)	370 (78,1) 46 (9,7) 58 (12,2)

Treatment groups				
Outcome - Documentation Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Total	N=474
Baseline to Week 24	70%-100% 50%-<70% <50%	201 (83,1) 23 (9,5) 18 (7,4)	191 (82,3) 20 (8,6) 21 (9,1)	392 (82,7) 43 (9,1) 39 (8,2)
No night-time awakenings - Documentation rate in standardized days*, n (%)				
Baseline	70%-100% 50%-<70% <50%	217 (89,7) 18 (7,4) 7 (2,9)	205 (88,4) 19 (8,2) 8 (3,4)	422 (89,0) 37 (7,8) 15 (3,2)
Baseline to Week 8	70%-100% 50%-<70% <50%	210 (86,8) 19 (7,9) 13 (5,4)	207 (89,2) 12 (5,2) 13 (5,6)	417 (88,0) 31 (6,5) 26 (5,5)
Week 9 to Week 16	70%-100% 50%-<70% <50%	198 (81,8) 24 (9,9) 20 (8,3)	200 (86,2) 14 (6,0) 18 (7,8)	398 (84,0) 38 (8,0) 38 (8,0)
Week 17 to Week 24	70%-100% 50%-<70% <50%	192 (79,3) 24 (9,9) 26 (10,7)	192 (82,8) 11 (4,7) 29 (12,5)	384 (81,0) 35 (7,4) 55 (11,6)
Baseline to Week 24	70%-100% 50%-<70% <50%	204 (84,3) 20 (8,3) 18 (7,4)	196 (84,5) 16 (6,9) 20 (8,6)	400 (84,4) 36 (7,6) 38 (8,0)
Days with no asthma symptoms - Documentation rate in standardized days*, n (%)				
Baseline	70%-100% 50%-<70% <50%	196 (81,0) 27 (11,2) 19 (7,9)	184 (79,3) 26 (11,2) 22 (9,5)	380 (80,2) 53 (11,2) 41 (8,6)
Baseline to Week 8	70%-100% 50%-<70% <50%	180 (74,4) 35 (14,5) 27 (11,2)	179 (77,2) 29 (12,5) 24 (10,3)	359 (75,7) 64 (13,5) 51 (10,8)
Week 9 to Week 16	70%-100% 50%-<70% <50%	170 (70,2) 28 (11,6) 44 (18,2)	169 (72,8) 32 (13,8) 31 (13,4)	339 (71,5) 60 (12,7) 75 (15,8)
Week 17 to Week 24	70%-100% 50%-<70% <50%	159 (65,7) 35 (14,5) 48 (19,8)	151 (65,1) 35 (15,1) 46 (19,8)	310 (65,4) 70 (14,8) 94 (19,8)

Treatment groups				
Outcome - Documentation Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Total	N=474
Baseline to Week 24	70%-100% 50%-<70% <50%	163 (67,4) 44 (18,2) 35 (14,5)	165 (71,1) 35 (15,1) 32 (13,8)	328 (69,2) 79 (16,7) 67 (14,1)
Mean total daily symptom score - Documentation rate in standardized days*, n (%)				
Baseline	70%-100% 50%-<70% <50%	196 (81,0) 27 (11,2) 19 (7,9)	184 (79,3) 26 (11,2) 22 (9,5)	380 (80,2) 53 (11,2) 41 (8,6)
Baseline to Week 8	70%-100% 50%-<70% <50%	180 (74,4) 35 (14,5) 27 (11,2)	179 (77,2) 29 (12,5) 24 (10,3)	359 (75,7) 64 (13,5) 51 (10,8)
Week 9 to Week 16	70%-100% 50%-<70% <50%	170 (70,2) 28 (11,6) 44 (18,2)	169 (72,8) 32 (13,8) 31 (13,4)	339 (71,5) 60 (12,7) 75 (15,8)
Week 17 to Week 24	70%-100% 50%-<70% <50%	159 (65,7) 35 (14,5) 48 (19,8)	151 (65,1) 35 (15,1) 46 (19,8)	310 (65,4) 70 (14,8) 94 (19,8)
Baseline to Week 24	70%-100% 50%-<70% <50%	163 (67,4) 44 (18,2) 35 (14,5)	165 (71,1) 35 (15,1) 32 (13,8)	328 (69,2) 79 (16,7) 67 (14,1)
Mean day-time symptom score - Documentation rate in standardized days*, n (%)				
Baseline	70%-100% 50%-<70% <50%	214 (88,4) 22 (9,1) 6 (2,5)	208 (89,7) 15 (6,5) 9 (3,9)	422 (89,0) 37 (7,8) 15 (3,2)
Baseline to Week 8	70%-100% 50%-<70% <50%	207 (85,5) 24 (9,9) 11 (4,5)	200 (86,2) 18 (7,8) 14 (6,0)	407 (85,9) 42 (8,9) 25 (5,3)
Week 9 to Week 16	70%-100% 50%-<70% <50%	202 (83,5) 21 (8,7) 19 (7,9)	195 (84,1) 16 (6,9) 21 (9,1)	397 (83,8) 37 (7,8) 40 (8,4)
Week 17 to Week 24	70%-100% 50%-<70% <50%	197 (81,4) 18 (7,4) 27 (11,2)	173 (74,6) 28 (12,1) 31 (13,4)	370 (78,1) 46 (9,7) 58 (12,2)

Treatment groups				
Outcome - Documentation Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Total	N=474
Baseline to Week 24	70%-100% 50%-<70% <50%	201 (83,1) 23 (9,5) 18 (7,4)	191 (82,3) 20 (8,6) 21 (9,1)	392 (82,7) 43 (9,1) 39 (8,2)
Mean night-time symptom score - Documentation rate in standardized days*, n (%)				
Baseline	70%-100% 50%-<70% <50%	217 (89,7) 18 (7,4) 7 (2,9)	205 (88,4) 19 (8,2) 8 (3,4)	422 (89,0) 37 (7,8) 15 (3,2)
Baseline to Week 8	70%-100% 50%-<70% <50%	210 (86,8) 19 (7,9) 13 (5,4)	207 (89,2) 12 (5,2) 13 (5,6)	417 (88,0) 31 (6,5) 26 (5,5)
Week 9 to Week 16	70%-100% 50%-<70% <50%	198 (81,8) 24 (9,9) 20 (8,3)	200 (86,2) 14 (6,0) 18 (7,8)	398 (84,0) 38 (8,0) 38 (8,0)
Week 17 to Week 24	70%-100% 50%-<70% <50%	192 (79,3) 24 (9,9) 26 (10,7)	192 (82,8) 11 (4,7) 29 (12,5)	384 (81,0) 35 (7,4) 55 (11,6)
Baseline to Week 24	70%-100% 50%-<70% <50%	204 (84,3) 20 (8,3) 18 (7,4)	196 (84,5) 16 (6,9) 20 (8,6)	400 (84,4) 36 (7,6) 38 (8,0)
How did you sleep last night? - Documentation rate in standardized days*, n (%)				
Baseline	70%-100% 50%-<70% <50%	217 (89,7) 18 (7,4) 7 (2,9)	205 (88,4) 19 (8,2) 8 (3,4)	422 (89,0) 37 (7,8) 15 (3,2)
Baseline to Week 8	70%-100% 50%-<70% <50%	210 (86,8) 19 (7,9) 13 (5,4)	207 (89,2) 12 (5,2) 13 (5,6)	417 (88,0) 31 (6,5) 26 (5,5)
Week 9 to Week 16	70%-100% 50%-<70% <50%	198 (81,8) 24 (9,9) 20 (8,3)	200 (86,2) 14 (6,0) 18 (7,8)	398 (84,0) 38 (8,0) 38 (8,0)
Week 17 to Week 24	70%-100% 50%-<70% <50%	192 (79,3) 24 (9,9) 26 (10,7)	192 (82,8) 11 (4,7) 29 (12,5)	384 (81,0) 35 (7,4) 55 (11,6)

Treatment groups				
Outcome - Documentation Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Total N=474	
Baseline to Week 24	70%-100% 50%-<70% <50%	204 (84,3) 20 (8,3) 18 (7,4)	196 (84,5) 16 (6,9) 20 (8,6)	400 (84,4) 36 (7,6) 38 (8,0)
Did you have asthma symptoms upon awakening in the morning? - Documentation rate in standardized days*, n (%)				
Baseline	70%-100% 50%-<70% <50%	217 (89,7) 18 (7,4) 7 (2,9)	205 (88,4) 19 (8,2) 8 (3,4)	422 (89,0) 37 (7,8) 15 (3,2)
Baseline to Week 8	70%-100% 50%-<70% <50%	210 (86,8) 19 (7,9) 13 (5,4)	207 (89,2) 12 (5,2) 13 (5,6)	417 (88,0) 31 (6,5) 26 (5,5)
Week 9 to Week 16	70%-100% 50%-<70% <50%	198 (81,8) 24 (9,9) 20 (8,3)	200 (86,2) 14 (6,0) 18 (7,8)	398 (84,0) 38 (8,0) 38 (8,0)
Week 17 to Week 24	70%-100% 50%-<70% <50%	192 (79,3) 24 (9,9) 26 (10,7)	192 (82,8) 11 (4,7) 29 (12,5)	384 (81,0) 35 (7,4) 55 (11,6)
Baseline to Week 24	70%-100% 50%-<70% <50%	204 (84,3) 20 (8,3) 18 (7,4)	196 (84,5) 16 (6,9) 20 (8,6)	400 (84,4) 36 (7,6) 38 (8,0)
Did your respiratory symptoms stop you from performing your usual daily activities? - Documentation rate in standardized days*, n (%)				
Baseline	70%-100% 50%-<70% <50%	214 (88,4) 22 (9,1) 6 (2,5)	208 (89,7) 15 (6,5) 9 (3,9)	422 (89,0) 37 (7,8) 15 (3,2)
Baseline to Week 8	70%-100% 50%-<70% <50%	207 (85,5) 24 (9,9) 11 (4,5)	200 (86,2) 18 (7,8) 14 (6,0)	407 (85,9) 42 (8,9) 25 (5,3)
Week 9 to Week 16	70%-100% 50%-<70% <50%	202 (83,5) 21 (8,7) 19 (7,9)	195 (84,1) 16 (6,9) 21 (9,1)	397 (83,8) 37 (7,8) 40 (8,4)
Week 17 to Week 24	70%-100% 50%-<70% <50%	197 (81,4) 18 (7,4) 27 (11,2)	173 (74,6) 28 (12,1) 31 (13,4)	370 (78,1) 46 (9,7) 58 (12,2)

Treatment groups				
Outcome - Documentation Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Total	N=474
Baseline to Week 24	70%-100% 50%-<70% <50%	201 (83,1) 23 (9,5) 18 (7,4)	191 (82,3) 20 (8,6) 21 (9,1)	392 (82,7) 43 (9,1) 39 (8,2)
How severe was your shortness of breath today? - Documentation rate in standardized days*, n (%)				
Baseline	70%-100% 50%-<70% <50%	214 (88,4) 22 (9,1) 6 (2,5)	208 (89,7) 15 (6,5) 9 (3,9)	422 (89,0) 37 (7,8) 15 (3,2)
Baseline to Week 8	70%-100% 50%-<70% <50%	207 (85,5) 24 (9,9) 11 (4,5)	200 (86,2) 18 (7,8) 14 (6,0)	407 (85,9) 42 (8,9) 25 (5,3)
Week 9 to Week 16	70%-100% 50%-<70% <50%	202 (83,5) 21 (8,7) 19 (7,9)	195 (84,1) 16 (6,9) 21 (9,1)	397 (83,8) 37 (7,8) 40 (8,4)
Week 17 to Week 24	70%-100% 50%-<70% <50%	197 (81,4) 18 (7,4) 27 (11,2)	173 (74,6) 28 (12,1) 31 (13,4)	370 (78,1) 46 (9,7) 58 (12,2)
Baseline to Week 24	70%-100% 50%-<70% <50%	201 (83,1) 23 (9,5) 18 (7,4)	191 (82,3) 20 (8,6) 21 (9,1)	392 (82,7) 43 (9,1) 39 (8,2)
How was your wheeze during the past 12 hours? - Documentation rate in standardized days*, n (%)				
Baseline	70%-100% 50%-<70% <50%	214 (88,4) 22 (9,1) 6 (2,5)	208 (89,7) 15 (6,5) 9 (3,9)	422 (89,0) 37 (7,8) 15 (3,2)
Baseline to Week 8	70%-100% 50%-<70% <50%	207 (85,5) 24 (9,9) 11 (4,5)	200 (86,2) 18 (7,8) 14 (6,0)	407 (85,9) 42 (8,9) 25 (5,3)
Week 9 to Week 16	70%-100% 50%-<70% <50%	202 (83,5) 21 (8,7) 19 (7,9)	195 (84,1) 16 (6,9) 21 (9,1)	397 (83,8) 37 (7,8) 40 (8,4)
Week 17 to Week 24	70%-100% 50%-<70% <50%	197 (81,4) 18 (7,4) 27 (11,2)	173 (74,6) 28 (12,1) 31 (13,4)	370 (78,1) 46 (9,7) 58 (12,2)

Treatment groups				
Outcome - Documentation Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Total	N=474
Baseline to Week 24	70%-100% 50%-<70% <50%	201 (83,1) 23 (9,5) 18 (7,4)	191 (82,3) 20 (8,6) 21 (9,1)	392 (82,7) 43 (9,1) 39 (8,2)
How was your cough during the past 12 hours? - Documentation rate in standardized days*, n (%)				
Baseline	70%-100% 50%-<70% <50%	214 (88,4) 22 (9,1) 6 (2,5)	208 (89,7) 15 (6,5) 9 (3,9)	422 (89,0) 37 (7,8) 15 (3,2)
Baseline to Week 8	70%-100% 50%-<70% <50%	207 (85,5) 24 (9,9) 11 (4,5)	200 (86,2) 18 (7,8) 14 (6,0)	407 (85,9) 42 (8,9) 25 (5,3)
Week 9 to Week 16	70%-100% 50%-<70% <50%	202 (83,5) 21 (8,7) 19 (7,9)	195 (84,1) 16 (6,9) 21 (9,1)	397 (83,8) 37 (7,8) 40 (8,4)
Week 17 to Week 24	70%-100% 50%-<70% <50%	197 (81,4) 18 (7,4) 27 (11,2)	173 (74,6) 28 (12,1) 31 (13,4)	370 (78,1) 46 (9,7) 58 (12,2)
Baseline to Week 24	70%-100% 50%-<70% <50%	201 (83,1) 23 (9,5) 18 (7,4)	191 (82,3) 20 (8,6) 21 (9,1)	392 (82,7) 43 (9,1) 39 (8,2)
Did you have chest tightness during the past 12 hours? - Documentation rate in standardized days*, n (%)				
Baseline	70%-100% 50%-<70% <50%	214 (88,4) 22 (9,1) 6 (2,5)	208 (89,7) 15 (6,5) 9 (3,9)	422 (89,0) 37 (7,8) 15 (3,2)
Baseline to Week 8	70%-100% 50%-<70% <50%	207 (85,5) 24 (9,9) 11 (4,5)	200 (86,2) 18 (7,8) 14 (6,0)	407 (85,9) 42 (8,9) 25 (5,3)
Week 9 to Week 16	70%-100% 50%-<70% <50%	202 (83,5) 21 (8,7) 19 (7,9)	195 (84,1) 16 (6,9) 21 (9,1)	397 (83,8) 37 (7,8) 40 (8,4)
Week 17 to Week 24	70%-100% 50%-<70% <50%	197 (81,4) 18 (7,4) 27 (11,2)	173 (74,6) 28 (12,1) 31 (13,4)	370 (78,1) 46 (9,7) 58 (12,2)

Outcome - Documentation Rate (FAS)	Treatment groups		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Total N=474
Baseline to Week 24	70%-100%	201 (83,1)	191 (82,3)
	50%-<70%	23 (9,5)	20 (8,6)
	<50%	18 (7,4)	21 (9,1)
			392 (82,7)
			43 (9,1)
			39 (8,2)

* 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 subpopulation "high-dose ICS/LABA"

Table 9.2 Symptoms - Change from Baseline (FAS)

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Percentage of mornings with no symptoms on rising					
N'		231	219		
Baseline Mean (SD)		35,69 (38,513)	42,44 (39,005)		
Week 8:					
Adjusted Mean Change (SE)		10,27 (2,681)	7,64 (2,702)	2,63 [-2,599; 7,851] 0,324	0,066 [-0,121; 0,253]
Week 16:					
Adjusted Mean Change (SE)		17,59 (2,924)	13,04 (2,961)	4,55 [-1,628; 10,724] 0,149	0,104 [-0,083; 0,290]
Week 24:					
Adjusted Mean Change (SE)		20,19 (3,021)	15,29 (3,067)	4,90 [-1,645; 11,442] 0,142	0,109 [-0,079; 0,297]
Percentage of days with no day-time symptoms					
N'		233	218		
Baseline Mean (SD)		16,63 (29,089)	18,30 (31,729)		
Week 8:					
Adjusted Mean Change (SE)		10,09 (2,529)	7,81 (2,576)	2,28 [-2,531; 7,095] 0,352	0,060 [-0,127; 0,247]
Week 16:					
Adjusted Mean Change (SE)		18,65 (2,862)	14,35 (2,924)	4,31 [-1,809; 10,421] 0,167	0,100 [-0,086; 0,286]
Week 24:					
Adjusted Mean Change (SE)		20,55 (2,985)	17,76 (3,053)	2,79 [-3,781; 9,354] 0,405	0,062 [-0,125; 0,250]
Percentage of days with no night-time awakenings					
N'		231	219		
Baseline Mean (SD)		57,17 (40,241)	66,94 (37,560)		
Week 8:					
Adjusted Mean Change (SE)		10,53 (2,294)	8,77 (2,307)	1,75 [-2,750; 6,258] 0,445	0,051 [-0,136; 0,238]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 16:					
Adjusted Mean Change (SE)	14,40 (2,463)	13,90 (2,488)	0,49 [-4,672; 5,660] 0,851	0,013 [-0,173; 0,200]	
Week 24:					
Adjusted Mean Change (SE)	15,21 (2,523)	16,64 (2,556)	-1,43 [-6,824; 3,972] 0,604	-0,038 [-0,226; 0,150]	
Percentage of days with no asthma symptoms					
N'	219	202			
Baseline Mean (SD)	14,01 (27,368)	17,34 (31,958)			
Week 8:					
Adjusted Mean Change (SE)	10,04 (2,474)	5,98 (2,524)	4,06 [-0,765; 8,876] 0,099	0,114 [-0,081; 0,310]	
Week 16:					
Adjusted Mean Change (SE)	19,07 (2,848)	13,15 (2,921)	5,92 [-0,334; 12,180] 0,063	0,142 [-0,050; 0,334]	
Week 24:					
Adjusted Mean Change (SE)	21,59 (2,994)	15,82 (3,077)	5,78 [-1,005; 12,561] 0,095	0,133 [-0,061; 0,328]	
Mean total daily symptom score					
N'	219	202			
Baseline Mean (SD)	2,36 (1,678)	1,94 (1,472)			
Week 8:					
Adjusted Mean Change (SE)	-0,48 (0,097)	-0,40 (0,099)	-0,08 [-0,272; 0,108] 0,398	-0,059 [-0,254; 0,136]	
Week 16:					
Adjusted Mean Change (SE)	-0,75 (0,102)	-0,62 (0,104)	-0,13 [-0,336; 0,085] 0,243	-0,084 [-0,276; 0,108]	
Week 24:					
Adjusted Mean Change (SE)	-0,85 (0,103)	-0,72 (0,106)	-0,13 [-0,342; 0,090] 0,251	-0,085 [-0,279; 0,110]	

E-Diary - Change from Baseline (FAS)	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Mean day-time symptom score				
N'	233	218		
Baseline Mean (SD)	0,92 (0,605)	0,82 (0,551)		
Week 8:				
Adjusted Mean Change (SE)	-0,15 (0,038)	-0,15 (0,038)	-0,00 [-0,074; 0,070] 0,958	-0,003 [-0,190; 0,184]
Week 16:				
Adjusted Mean Change (SE)	-0,27 (0,040)	-0,23 (0,041)	-0,04 [-0,121; 0,041] 0,337	-0,066 [-0,252; 0,120]
Week 24:				
Adjusted Mean Change (SE)	-0,30 (0,041)	-0,28 (0,042)	-0,02 [-0,108; 0,061] 0,583	-0,039 [-0,226; 0,149]
Mean night-time symptom score				
N'	231	219		
Baseline Mean (SD)	0,73 (0,584)	0,58 (0,496)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,031)	-0,13 (0,031)	-0,03 [-0,095; 0,027] 0,272	-0,074 [-0,261; 0,113]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,032)	-0,21 (0,033)	-0,03 [-0,096; 0,037] 0,381	-0,061 [-0,248; 0,125]
Week 24:				
Adjusted Mean Change (SE)	-0,27 (0,033)	-0,24 (0,033)	-0,03 [-0,096; 0,041] 0,428	-0,057 [-0,245; 0,131]
Mean of: How did you sleep last night?				
N'	231	219		
Baseline Mean (SD)	0,58 (0,624)	0,41 (0,517)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,029)	-0,15 (0,029)	-0,03 [-0,082; 0,031] 0,374	-0,060 [-0,247; 0,127]

E-Diary - Change from Baseline (FAS)	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 16:				
Adjusted Mean Change (SE)	-0,22 (0,030)	-0,22 (0,030)	-0,01 [-0,068; 0,055] 0,830	-0,015 [-0,201; 0,171]
Week 24:				
Adjusted Mean Change (SE)	-0,24 (0,030)	-0,25 (0,030)	0,01 [-0,053; 0,071] 0,780	0,020 [-0,168; 0,208]
Mean of: Did you have asthma symptoms upon awakening in the morning?				
N'	231	219		
Baseline Mean (SD)	0,88 (0,651)	0,74 (0,595)		
Week 8:				
Adjusted Mean Change (SE)	-0,15 (0,040)	-0,11 (0,040)	-0,04 [-0,117; 0,038] 0,318	-0,067 [-0,254; 0,120]
Week 16:				
Adjusted Mean Change (SE)	-0,25 (0,042)	-0,20 (0,042)	-0,05 [-0,135; 0,037] 0,266	-0,078 [-0,265; 0,108]
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,043)	-0,23 (0,044)	-0,06 [-0,153; 0,029] 0,180	-0,097 [-0,285; 0,091]
Mean of: Did your respiratory symptoms stop you from performing your usual daily activities?				
N'	233	218		
Baseline Mean (SD)	0,94 (0,700)	0,85 (0,669)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,042)	-0,17 (0,043)	0,01 [-0,067; 0,095] 0,738	0,022 [-0,165; 0,209]
Week 16:				
Adjusted Mean Change (SE)	-0,28 (0,045)	-0,25 (0,046)	-0,03 [-0,119; 0,067] 0,581	-0,038 [-0,224; 0,148]
Week 24:				
Adjusted Mean Change (SE)	-0,30 (0,046)	-0,29 (0,047)	-0,01 [-0,105; 0,086] 0,842	-0,014 [-0,202; 0,174]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Mean of: How severe was your shortness of breath today?					
N'	233	218			
Baseline Mean (SD)	1,07 (0,671)	0,97 (0,634)			
Week 8:					
Adjusted Mean Change (SE)	-0,21 (0,042)	-0,20 (0,043)	-0,01 [-0,092; 0,070] 0,786	-0,018	[-0,205; 0,169]
Week 16:					
Adjusted Mean Change (SE)	-0,36 (0,045)	-0,30 (0,046)	-0,06 [-0,153; 0,031] 0,193	-0,090	[-0,275; 0,096]
Week 24:					
Adjusted Mean Change (SE)	-0,40 (0,046)	-0,34 (0,047)	-0,05 [-0,150; 0,042] 0,269	-0,078	[-0,266; 0,109]
Mean of: How was your wheeze during the past 12 hours?					
N'	233	218			
Baseline Mean (SD)	0,94 (0,684)	0,79 (0,628)			
Week 8:					
Adjusted Mean Change (SE)	-0,17 (0,042)	-0,17 (0,043)	-0,00 [-0,085; 0,077] 0,924	-0,006	[-0,193; 0,181]
Week 16:					
Adjusted Mean Change (SE)	-0,29 (0,045)	-0,24 (0,046)	-0,05 [-0,139; 0,044] 0,309	-0,070	[-0,255; 0,116]
Week 24:					
Adjusted Mean Change (SE)	-0,31 (0,046)	-0,29 (0,047)	-0,02 [-0,121; 0,071] 0,611	-0,036	[-0,224; 0,152]
Mean of: How was your cough during the past 12 hours?					
N'	233	218			
Baseline Mean (SD)	0,93 (0,661)	0,88 (0,645)			
Week 8:					
Adjusted Mean Change (SE)	-0,14 (0,044)	-0,13 (0,045)	-0,02 [-0,100; 0,068] 0,704	-0,025	[-0,212; 0,162]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 16:					
Adjusted Mean Change (SE)	-0,25 (0,047)	-0,23 (0,048)	-0,02 [-0,118; 0,074] 0,655	-0,031 [-0,217; 0,155]	
Week 24:					
Adjusted Mean Change (SE)	-0,29 (0,048)	-0,27 (0,049)	-0,02 [-0,116; 0,083] 0,744	-0,023 [-0,211; 0,164]	
Did you have chest tightness during the past 12 hours?					
N'	233	218			
Baseline Mean (SD)	0,71 (0,669)	0,61 (0,613)			
Week 8:					
Adjusted Mean Change (SE)	-0,08 (0,040)	-0,09 (0,041)	0,01 [-0,064; 0,090] 0,743	0,021 [-0,166; 0,208]	
Week 16:					
Adjusted Mean Change (SE)	-0,17 (0,042)	-0,14 (0,043)	-0,03 [-0,116; 0,054] 0,474	-0,049 [-0,234; 0,137]	
Week 24:					
Adjusted Mean Change (SE)	-0,19 (0,043)	-0,19 (0,044)	-0,00 [-0,091; 0,086] 0,959	-0,004 [-0,191; 0,184]	
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, 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 subpopulation "high-dose ICS/LABA"					

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Percentage of mornings with no symptoms on rising					
Interaction Test	0,556				
Age = 18-39 years					
N'	38	30			
Baseline Mean (SD)	42,23 (36,098)	42,99 (39,872)			
Week 8:					
Adjusted Mean Change (SE)	14,37 (5,079)	15,41 (5,465)	-1,04 [-14,619; 12,546] 0,881		-0,035 [-0,534; 0,464]
Week 16:					
Adjusted Mean Change (SE)	18,22 (5,748)	20,28 (6,327)	-2,07 [-17,922; 13,788] 0,798		-0,059 [-0,538; 0,420]
Week 24:					
Adjusted Mean Change (SE)	20,97 (6,038)	20,72 (6,646)	0,25 [-16,499; 16,996] 0,977		0,007 [-0,475; 0,488]
Age = 40-64 years					
N'	135	142			
Baseline Mean (SD)	32,46 (39,494)	43,01 (39,376)			
Week 8:					
Adjusted Mean Change (SE)	11,32 (3,031)	8,83 (3,021)	2,49 [-4,132; 9,114] 0,460		0,070 [-0,167; 0,308]
Week 16:					
Adjusted Mean Change (SE)	19,39 (3,395)	14,80 (3,373)	4,59 [-3,254; 12,433] 0,251		0,116 [-0,121; 0,354]
Week 24:					
Adjusted Mean Change (SE)	22,29 (3,531)	17,88 (3,516)	4,40 [-3,900; 12,705] 0,298		0,108 [-0,132; 0,348]
Age = ≥65 years					
N'	58	47			
Baseline Mean (SD)	38,93 (37,532)	40,38 (38,074)			

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 8:					
Adjusted Mean Change (SE)	5,06 (4,213)	-1,31 (4,554)	6,37 [-4,392; 17,130] 0,246	0,201 [-0,185; 0,587]	
Week 16:					
Adjusted Mean Change (SE)	12,61 (4,835)	2,66 (5,252)	9,95 [-2,853; 22,752] 0,128	0,277 [-0,115; 0,669]	
Week 24:					
Adjusted Mean Change (SE)	14,43 (5,064)	3,66 (5,506)	10,77 [-2,767; 24,302] 0,119	0,286 [-0,106; 0,678]	
Percentage of days with no day-time symptoms					
Interaction Test	0,065				
Age = 18-39 years					
N'	37	31			
Baseline Mean (SD)	21,24 (26,200)	24,24 (35,438)			
Week 8:					
Adjusted Mean Change (SE)	18,21 (4,697)	7,56 (4,995)	10,65 [-1,704; 23,010] 0,091	0,386 [-0,106; 0,878]	
Week 16:					
Adjusted Mean Change (SE)	26,19 (5,747)	10,49 (6,212)	15,71 [-0,020; 31,430] 0,050	0,455 [-0,033; 0,942]	
Week 24:					
Adjusted Mean Change (SE)	27,40 (6,143)	14,64 (6,634)	12,76 [-4,163; 29,677] 0,139	0,351 [-0,140; 0,842]	
Age = 40-64 years					
N'	138	141			
Baseline Mean (SD)	15,49 (28,997)	18,26 (30,958)			
Week 8:					
Adjusted Mean Change (SE)	8,87 (2,814)	10,90 (2,855)	-2,03 [-8,092; 4,024] 0,510	-0,062 [-0,299; 0,176]	
Week 16:					
Adjusted Mean Change (SE)	17,42 (3,307)	18,81 (3,330)	-1,39 [-9,112; 6,327] 0,723	-0,036 [-0,271; 0,200]	

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	20,62 (3,485)	22,21 (3,508)	-1,59 [-9,892; 6,714] 0,707	-0,039 [-0,278; 0,200]	
Age = ≥65 years					
N'	58	46			
Baseline Mean (SD)	16,40 (31,186)	14,41 (31,557)			
Week 8:					
Adjusted Mean Change (SE)	9,23 (3,919)	0,11 (4,273)	9,12 [-0,864; 19,096] 0,073	0,311 [-0,081; 0,702]	
Week 16:					
Adjusted Mean Change (SE)	18,13 (4,759)	4,81 (5,223)	13,32 [0,572; 26,063] 0,041 *	0,375 [-0,020; 0,769]	
Week 24:					
Adjusted Mean Change (SE)	17,40 (5,047)	7,85 (5,536)	9,55 [-4,095; 23,203] 0,170	0,252 [-0,138; 0,642]	
Percentage of days with no night-time awakenings					
Interaction Test	0,882				
Age = 18-39 years					
N'	38	30			
Baseline Mean (SD)	66,31 (36,454)	78,31 (34,472)			
Week 8:					
Adjusted Mean Change (SE)	16,79 (4,331)	11,40 (4,678)	5,40 [-6,226; 17,020] 0,362	0,216 [-0,285; 0,716]	
Week 16:					
Adjusted Mean Change (SE)	17,31 (4,788)	13,52 (5,283)	3,80 [-9,403; 16,994] 0,573	0,130 [-0,349; 0,609]	
Week 24:					
Adjusted Mean Change (SE)	13,87 (4,976)	15,53 (5,485)	-1,67 [-15,437; 12,107] 0,812	-0,055 [-0,537; 0,426]	
Age = 40-64 years					
N'	135	142			
Baseline Mean (SD)	56,92 (40,340)	64,53 (37,681)			

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 8:					
Adjusted Mean Change (SE)	12,16 (2,582)	10,31 (2,568)	1,85 [-3,806; 7,500] 0,521	0,061 [-0,176; 0,299]	
Week 16:					
Adjusted Mean Change (SE)	17,12 (2,837)	16,64 (2,815)	0,48 [-6,024; 6,992] 0,884	0,015 [-0,223; 0,252]	
Week 24:					
Adjusted Mean Change (SE)	19,00 (2,923)	18,68 (2,912)	0,32 [-6,489; 7,126] 0,927	0,009 [-0,230; 0,249]	
Age = ≥65 years					
N'	58	47			
Baseline Mean (SD)	51,73 (41,953)	66,97 (38,496)			
Week 8:					
Adjusted Mean Change (SE)	2,63 (3,603)	2,43 (3,885)	0,20 [-9,033; 9,435] 0,966	0,007 [-0,377; 0,392]	
Week 16:					
Adjusted Mean Change (SE)	5,88 (4,043)	5,83 (4,376)	0,05 [-10,625; 10,722] 0,993	0,002 [-0,388; 0,392]	
Week 24:					
Adjusted Mean Change (SE)	7,01 (4,192)	11,03 (4,540)	-4,02 [-15,168; 7,133] 0,480	-0,129 [-0,520; 0,261]	
Percentage of days with no asthma symptoms					
Interaction Test	0,058				
Age = 18-39 years					
N'	35	28			
Baseline Mean (SD)	19,19 (24,941)	23,54 (36,437)			
Week 8:					
Adjusted Mean Change (SE)	18,90 (4,736)	4,77 (5,073)	14,13 [1,498; 26,756] 0,028 *	0,550 [0,011; 1,089]	
Week 16:					
Adjusted Mean Change (SE)	26,15 (5,815)	7,56 (6,397)	18,60 [2,424; 34,767] 0,024 *	0,544 [0,038; 1,050]	

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	29,24 (6,267)	9,89 (6,896)	19,35 [1,804; 36,905] 0,031 *	0,539 [0,021; 1,056]	
Age = 40-64 years					
N'		129	130		
Baseline Mean (SD)		13,77 (29,050)	17,17 (31,034)		
Week 8:					
Adjusted Mean Change (SE)	8,48 (2,774)	8,93 (2,822)	-0,46 [-6,544; 5,631] 0,883	-0,015 [-0,263; 0,233]	
Week 16:					
Adjusted Mean Change (SE)	17,83 (3,328)	17,61 (3,364)	0,22 [-7,713; 8,156] 0,956	0,006 [-0,239; 0,250]	
Week 24:					
Adjusted Mean Change (SE)	21,18 (3,536)	20,03 (3,574)	1,15 [-7,453; 9,756] 0,793	0,029 [-0,219; 0,277]	
Age = ≥65 years					
N'		55	44		
Baseline Mean (SD)		11,28 (24,630)	13,93 (31,843)		
Week 8:					
Adjusted Mean Change (SE)	9,69 (3,875)	-0,34 (4,188)	10,04 [0,173; 19,901] 0,046 *	0,356 [-0,045; 0,758]	
Week 16:					
Adjusted Mean Change (SE)	18,74 (4,803)	5,09 (5,246)	13,65 [0,739; 26,565] 0,038 *	0,389 [-0,013; 0,791]	
Week 24:					
Adjusted Mean Change (SE)	19,01 (5,133)	8,68 (5,614)	10,33 [-3,628; 24,287] 0,147	0,275 [-0,124; 0,675]	
Mean total daily symptom score					
Interaction Test	0,998				
Age = 18-39 years					
N'		35	28		
Baseline Mean (SD)		1,97 (1,693)	1,71 (1,439)		

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	-0,64 (0,184)	-0,44 (0,198)	-0,20 [-0,692; 0,293] 0,428	-0,199 [-0,730; 0,332]
Week 16:				
Adjusted Mean Change (SE)	-0,70 (0,197)	-0,61 (0,215)	-0,09 [-0,631; 0,443] 0,731	-0,082 [-0,579; 0,416]
Week 24:				
Adjusted Mean Change (SE)	-0,79 (0,202)	-0,73 (0,220)	-0,06 [-0,614; 0,489] 0,823	-0,054 [-0,563; 0,454]
Age = 40-64 years				
N'	129	130		
Baseline Mean (SD)	2,40 (1,666)	1,95 (1,490)		
Week 8:				
Adjusted Mean Change (SE)	-0,58 (0,108)	-0,50 (0,110)	-0,08 [-0,316; 0,163] 0,530	-0,063 [-0,311; 0,185]
Week 16:				
Adjusted Mean Change (SE)	-0,91 (0,116)	-0,75 (0,117)	-0,16 [-0,424; 0,105] 0,237	-0,121 [-0,365; 0,124]
Week 24:				
Adjusted Mean Change (SE)	-1,01 (0,118)	-0,84 (0,120)	-0,17 [-0,439; 0,104] 0,225	-0,127 [-0,375; 0,122]
Age = ≥65 years				
N'	55	44		
Baseline Mean (SD)	2,52 (1,687)	2,07 (1,454)		
Week 8:				
Adjusted Mean Change (SE)	-0,14 (0,151)	-0,05 (0,164)	-0,09 [-0,481; 0,293] 0,635	-0,085 [-0,483; 0,313]
Week 16:				
Adjusted Mean Change (SE)	-0,36 (0,164)	-0,22 (0,178)	-0,14 [-0,570; 0,289] 0,520	-0,118 [-0,516; 0,281]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	-0,47 (0,167)	-0,33 (0,182)	-0,14 [-0,579; 0,299] 0,532	-0,115 [-0,513; 0,284]	
Mean day-time symptom score					
Interaction Test	0,978				
Age = 18-39 years					
N'	37	31			
Baseline Mean (SD)	0,74 (0,547)	0,74 (0,535)			
Week 8:					
Adjusted Mean Change (SE)	-0,20 (0,070)	-0,14 (0,074)	-0,06 [-0,241; 0,125] 0,535	-0,141 [-0,630; 0,347]	
Week 16:					
Adjusted Mean Change (SE)	-0,26 (0,077)	-0,20 (0,083)	-0,06 [-0,263; 0,150] 0,589	-0,123 [-0,605; 0,359]	
Week 24:					
Adjusted Mean Change (SE)	-0,29 (0,080)	-0,26 (0,086)	-0,03 [-0,242; 0,188] 0,807	-0,057 [-0,545; 0,431]	
Age = 40-64 years					
N'	138	141			
Baseline Mean (SD)	0,93 (0,602)	0,81 (0,562)			
Week 8:					
Adjusted Mean Change (SE)	-0,19 (0,042)	-0,20 (0,042)	0,00 [-0,086; 0,095] 0,920	0,009 [-0,228; 0,247]	
Week 16:					
Adjusted Mean Change (SE)	-0,33 (0,045)	-0,29 (0,046)	-0,05 [-0,147; 0,056] 0,383	-0,085 [-0,320; 0,151]	
Week 24:					
Adjusted Mean Change (SE)	-0,37 (0,046)	-0,33 (0,047)	-0,03 [-0,141; 0,071] 0,521	-0,064 [-0,303; 0,175]	
Age = ≥65 years					
N'	58	46			
Baseline Mean (SD)	1,00 (0,635)	0,91 (0,528)			

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	-0,02 (0,058)	-0,01 (0,063)	-0,01 [-0,162; 0,135] 0,861	-0,030 [-0,420; 0,359]
Week 16:				
Adjusted Mean Change (SE)	-0,12 (0,064)	-0,06 (0,070)	-0,05 [-0,222; 0,114] 0,527	-0,113 [-0,504; 0,278]
Week 24:				
Adjusted Mean Change (SE)	-0,14 (0,066)	-0,10 (0,072)	-0,03 [-0,207; 0,141] 0,708	-0,067 [-0,456; 0,322]
Mean night-time symptom score				
Interaction Test	0,986			
Age = 18-39 years				
N'	38	30		
Baseline Mean (SD)	0,63 (0,584)	0,48 (0,465)		
Week 8:				
Adjusted Mean Change (SE)	-0,23 (0,058)	-0,17 (0,063)	-0,06 [-0,220; 0,093] 0,425	-0,189 [-0,689; 0,311]
Week 16:				
Adjusted Mean Change (SE)	-0,26 (0,061)	-0,26 (0,067)	-0,01 [-0,174; 0,161] 0,939	-0,017 [-0,496; 0,461]
Week 24:				
Adjusted Mean Change (SE)	-0,27 (0,063)	-0,27 (0,069)	-0,00 [-0,174; 0,172] 0,992	-0,002 [-0,484; 0,479]
Age = 40-64 years				
N'	135	142		
Baseline Mean (SD)	0,75 (0,577)	0,58 (0,493)		
Week 8:				
Adjusted Mean Change (SE)	-0,19 (0,035)	-0,16 (0,035)	-0,03 [-0,105; 0,048] 0,460	-0,071 [-0,308; 0,166]
Week 16:				
Adjusted Mean Change (SE)	-0,28 (0,037)	-0,24 (0,037)	-0,04 [-0,124; 0,042] 0,330	-0,096 [-0,334; 0,141]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	-0,31 (0,037)	-0,27 (0,037)	-0,04 [-0,127; 0,044] 0,339	-0,096 [-0,337; 0,144]	
Age = ≥65 years					
N'	58	47			
Baseline Mean (SD)	0,75 (0,602)	0,62 (0,526)			
Week 8:					
Adjusted Mean Change (SE)	-0,06 (0,048)	-0,01 (0,052)	-0,05 [-0,174; 0,075] 0,433	-0,136 [-0,521; 0,249]	
Week 16:					
Adjusted Mean Change (SE)	-0,12 (0,052)	-0,08 (0,056)	-0,04 [-0,172; 0,099] 0,597	-0,095 [-0,485; 0,295]	
Week 24:					
Adjusted Mean Change (SE)	-0,15 (0,053)	-0,12 (0,058)	-0,03 [-0,172; 0,108] 0,651	-0,082 [-0,472; 0,309]	
Mean of: How did you sleep last night?					
Interaction Test	0,569				
Age = 18-39 years					
N'	38	30			
Baseline Mean (SD)	0,48 (0,655)	0,27 (0,477)			
Week 8:					
Adjusted Mean Change (SE)	-0,27 (0,054)	-0,17 (0,058)	-0,10 [-0,244; 0,047] 0,183	-0,316 [-0,818; 0,186]	
Week 16:					
Adjusted Mean Change (SE)	-0,29 (0,057)	-0,23 (0,062)	-0,05 [-0,208; 0,103] 0,505	-0,153 [-0,632; 0,327]	
Week 24:					
Adjusted Mean Change (SE)	-0,25 (0,057)	-0,25 (0,063)	-0,00 [-0,160; 0,155] 0,977	-0,007 [-0,488; 0,475]	
Age = 40-64 years					
N'	135	142			
Baseline Mean (SD)	0,58 (0,612)	0,43 (0,489)			

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 8:					
Adjusted Mean Change (SE)	-0,20 (0,032)	-0,17 (0,032)	-0,03 [-0,099; 0,042] 0,428	-0,076 [-0,314; 0,161]	
Week 16:					
Adjusted Mean Change (SE)	-0,27 (0,034)	-0,25 (0,034)	-0,02 [-0,097; 0,057] 0,605	-0,051 [-0,289; 0,186]	
Week 24:					
Adjusted Mean Change (SE)	-0,29 (0,034)	-0,27 (0,034)	-0,02 [-0,094; 0,062] 0,682	-0,041 [-0,281; 0,199]	
Age = ≥65 years					
N'	58	47			
Baseline Mean (SD)	0,65 (0,633)	0,45 (0,610)			
Week 8:					
Adjusted Mean Change (SE)	-0,05 (0,045)	-0,06 (0,048)	0,01 [-0,101; 0,130] 0,805	0,043 [-0,342; 0,428]	
Week 16:					
Adjusted Mean Change (SE)	-0,08 (0,048)	-0,12 (0,052)	0,04 [-0,085; 0,166] 0,527	0,114 [-0,277; 0,504]	
Week 24:					
Adjusted Mean Change (SE)	-0,11 (0,049)	-0,17 (0,052)	0,06 [-0,065; 0,189] 0,341	0,171 [-0,219; 0,562]	
Mean of: Did you have asthma symptoms upon awakening in the morning?					
Interaction Test	0,661				
Age = 18-39 years					
N'	38	30			
Baseline Mean (SD)	0,79 (0,647)	0,69 (0,546)			
Week 8:					
Adjusted Mean Change (SE)	-0,19 (0,075)	-0,17 (0,081)	-0,02 [-0,222; 0,179] 0,834	-0,050 [-0,549; 0,449]	
Week 16:					
Adjusted Mean Change (SE)	-0,23 (0,080)	-0,28 (0,088)	0,05 [-0,171; 0,270] 0,660	0,101 [-0,378; 0,580]	

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	-0,28 (0,084)	-0,29 (0,093)	0,01 [-0,224; 0,241] 0,941	0,017 [-0,464; 0,499]	
Age = 40-64 years					
N'	135	142			
Baseline Mean (SD)	0,91 (0,648)	0,73 (0,599)			
Week 8:					
Adjusted Mean Change (SE)	-0,18 (0,045)	-0,15 (0,044)	-0,03 [-0,127; 0,069] 0,562	-0,056 [-0,293; 0,182]	
Week 16:					
Adjusted Mean Change (SE)	-0,30 (0,048)	-0,23 (0,048)	-0,06 [-0,172; 0,046] 0,257	-0,113 [-0,350; 0,125]	
Week 24:					
Adjusted Mean Change (SE)	-0,34 (0,050)	-0,27 (0,050)	-0,07 [-0,185; 0,046] 0,236	-0,121 [-0,361; 0,119]	
Age = ≥65 years					
N'	58	47			
Baseline Mean (SD)	0,85 (0,662)	0,80 (0,619)			
Week 8:					
Adjusted Mean Change (SE)	-0,06 (0,062)	0,05 (0,067)	-0,10 [-0,263; 0,054] 0,195	-0,224 [-0,610; 0,161]	
Week 16:					
Adjusted Mean Change (SE)	-0,14 (0,068)	-0,04 (0,074)	-0,10 [-0,281; 0,075] 0,255	-0,205 [-0,596; 0,186]	
Week 24:					
Adjusted Mean Change (SE)	-0,18 (0,071)	-0,07 (0,077)	-0,12 [-0,306; 0,070] 0,219	-0,224 [-0,615; 0,168]	
Mean of: Did your respiratory symptoms stop you from performing your usual daily activities?					
Interaction Test	0,767				
Age = 18-39 years					
N'	37	31			
Baseline Mean (SD)	0,78 (0,628)	0,73 (0,650)			

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,079)	-0,19 (0,084)	0,03 [-0,183; 0,234] 0,811	0,055 [-0,433; 0,542]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,088)	-0,26 (0,095)	0,04 [-0,202; 0,273] 0,769	0,067 [-0,414; 0,549]
Week 24:				
Adjusted Mean Change (SE)	-0,25 (0,091)	-0,36 (0,098)	0,10 [-0,141; 0,350] 0,403	0,195 [-0,294; 0,684]
Age = 40-64 years				
N'	138	141		
Baseline Mean (SD)	0,96 (0,721)	0,82 (0,671)		
Week 8:				
Adjusted Mean Change (SE)	-0,20 (0,047)	-0,21 (0,048)	0,01 [-0,090; 0,115] 0,814	0,022 [-0,216; 0,260]
Week 16:				
Adjusted Mean Change (SE)	-0,33 (0,052)	-0,30 (0,052)	-0,03 [-0,151; 0,083] 0,571	-0,055 [-0,291; 0,181]
Week 24:				
Adjusted Mean Change (SE)	-0,37 (0,053)	-0,33 (0,053)	-0,04 [-0,161; 0,081] 0,518	-0,065 [-0,304; 0,174]
Age = ≥65 years				
N'	58	46		
Baseline Mean (SD)	0,98 (0,692)	1,02 (0,656)		
Week 8:				
Adjusted Mean Change (SE)	-0,05 (0,066)	-0,04 (0,072)	-0,02 [-0,186; 0,151] 0,839	-0,035 [-0,425; 0,354]
Week 16:				
Adjusted Mean Change (SE)	-0,16 (0,074)	-0,08 (0,080)	-0,08 [-0,275; 0,110] 0,401	-0,150 [-0,542; 0,241]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	-0,16 (0,075)	-0,12 (0,082)	-0,04 [-0,238; 0,158] 0,692	-0,071 [-0,460; 0,318]	
Mean of: How severe was your shortness of breath today?					
Interaction Test	0,854				
Age = 18-39 years					
N'	37	31			
Baseline Mean (SD)	0,93 (0,530)	0,87 (0,569)			
Week 8:					
Adjusted Mean Change (SE)	-0,30 (0,079)	-0,18 (0,084)	-0,13 [-0,335; 0,083] 0,236	-0,270 [-0,760; 0,220]	
Week 16:					
Adjusted Mean Change (SE)	-0,41 (0,088)	-0,28 (0,094)	-0,12 [-0,357; 0,114] 0,312	-0,231 [-0,714; 0,252]	
Week 24:					
Adjusted Mean Change (SE)	-0,41 (0,091)	-0,34 (0,098)	-0,07 [-0,318; 0,175] 0,571	-0,132 [-0,621; 0,356]	
Age = 40-64 years					
N'	138	141			
Baseline Mean (SD)	1,09 (0,698)	0,94 (0,635)			
Week 8:					
Adjusted Mean Change (SE)	-0,24 (0,047)	-0,25 (0,048)	0,01 [-0,093; 0,112] 0,860	0,016 [-0,221; 0,254]	
Week 16:					
Adjusted Mean Change (SE)	-0,41 (0,051)	-0,35 (0,052)	-0,06 [-0,179; 0,053] 0,289	-0,103 [-0,339; 0,133]	
Week 24:					
Adjusted Mean Change (SE)	-0,46 (0,053)	-0,40 (0,054)	-0,06 [-0,183; 0,059] 0,313	-0,101 [-0,340; 0,138]	
Age = ≥65 years					
N'	58	46			
Baseline Mean (SD)	1,13 (0,683)	1,15 (0,652)			

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	-0,10 (0,066)	-0,08 (0,072)	-0,02 [-0,184; 0,153] 0,854	-0,032 [-0,421; 0,357]
Week 16:				
Adjusted Mean Change (SE)	-0,19 (0,073)	-0,14 (0,080)	-0,05 [-0,244; 0,138] 0,588	-0,097 [-0,488; 0,294]
Week 24:				
Adjusted Mean Change (SE)	-0,23 (0,075)	-0,18 (0,082)	-0,06 [-0,257; 0,141] 0,566	-0,103 [-0,492; 0,286]
Mean of: How was your wheeze during the past 12 hours?				
Interaction Test	0,569			
Age = 18-39 years				
N'	37	31		
Baseline Mean (SD)	0,68 (0,649)	0,73 (0,554)		
Week 8:				
Adjusted Mean Change (SE)	-0,22 (0,079)	-0,12 (0,084)	-0,10 [-0,310; 0,106] 0,335	-0,220 [-0,709; 0,269]
Week 16:				
Adjusted Mean Change (SE)	-0,28 (0,086)	-0,21 (0,093)	-0,07 [-0,298; 0,166] 0,577	-0,127 [-0,609; 0,355]
Week 24:				
Adjusted Mean Change (SE)	-0,33 (0,090)	-0,25 (0,097)	-0,09 [-0,329; 0,159] 0,494	-0,160 [-0,648; 0,329]
Age = 40-64 years				
N'	138	141		
Baseline Mean (SD)	0,96 (0,675)	0,79 (0,632)		
Week 8:				
Adjusted Mean Change (SE)	-0,21 (0,047)	-0,24 (0,048)	0,03 [-0,069; 0,136] 0,519	0,060 [-0,177; 0,298]
Week 16:				
Adjusted Mean Change (SE)	-0,35 (0,051)	-0,32 (0,051)	-0,03 [-0,144; 0,085] 0,614	-0,049 [-0,285; 0,187]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	-0,37 (0,052)	-0,37 (0,053)	-0,01 [-0,125; 0,115] 0,932	-0,009 [-0,248; 0,230]	
Age = ≥65 years					
N'	58	46			
Baseline Mean (SD)	1,08 (0,693)	0,83 (0,671)			
Week 8:					
Adjusted Mean Change (SE)	-0,06 (0,066)	0,02 (0,072)	-0,08 [-0,245; 0,092] 0,373	-0,155 [-0,545; 0,235]	
Week 16:					
Adjusted Mean Change (SE)	-0,15 (0,072)	-0,02 (0,079)	-0,13 [-0,319; 0,059] 0,177	-0,242 [-0,634; 0,150]	
Week 24:					
Adjusted Mean Change (SE)	-0,15 (0,075)	-0,06 (0,082)	-0,09 [-0,284; 0,111] 0,393	-0,154 [-0,543; 0,235]	
Mean of: How was your cough during the past 12 hours?					
Interaction Test	0,782				
Age = 18-39 years					
N'	37	31			
Baseline Mean (SD)	0,75 (0,679)	0,74 (0,594)			
Week 8:					
Adjusted Mean Change (SE)	-0,24 (0,082)	-0,12 (0,087)	-0,11 [-0,330; 0,101] 0,297	-0,239 [-0,728; 0,251]	
Week 16:					
Adjusted Mean Change (SE)	-0,26 (0,091)	-0,17 (0,099)	-0,10 [-0,346; 0,149] 0,433	-0,180 [-0,662; 0,303]	
Week 24:					
Adjusted Mean Change (SE)	-0,33 (0,095)	-0,24 (0,102)	-0,09 [-0,345; 0,169] 0,501	-0,157 [-0,646; 0,331]	
Age = 40-64 years					
N'	138	141			
Baseline Mean (SD)	0,94 (0,629)	0,91 (0,665)			

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,049)	-0,17 (0,050)	-0,01 [-0,118; 0,094] 0,822	-0,021 [-0,259; 0,217]
Week 16:				
Adjusted Mean Change (SE)	-0,30 (0,053)	-0,29 (0,054)	-0,02 [-0,139; 0,104] 0,779	-0,027 [-0,263; 0,208]
Week 24:				
Adjusted Mean Change (SE)	-0,34 (0,055)	-0,33 (0,055)	-0,02 [-0,143; 0,109] 0,795	-0,026 [-0,265; 0,213]
Age = ≥65 years				
N'	58	46		
Baseline Mean (SD)	1,04 (0,711)	0,87 (0,613)		
Week 8:				
Adjusted Mean Change (SE)	0,04 (0,068)	0,04 (0,074)	-0,00 [-0,175; 0,174] 0,998	-0,000 [-0,390; 0,389]
Week 16:				
Adjusted Mean Change (SE)	-0,09 (0,076)	-0,07 (0,083)	-0,03 [-0,226; 0,175] 0,802	-0,045 [-0,436; 0,346]
Week 24:				
Adjusted Mean Change (SE)	-0,12 (0,078)	-0,10 (0,085)	-0,01 [-0,219; 0,196] 0,913	-0,020 [-0,408; 0,369]
Did you have chest tightness during the past 12 hours?				
Interaction Test	0,635			
Age = 18-39 years				
N'	37	31		
Baseline Mean (SD)	0,58 (0,657)	0,62 (0,677)		
Week 8:				
Adjusted Mean Change (SE)	-0,06 (0,075)	-0,09 (0,080)	0,03 [-0,171; 0,226] 0,784	0,063 [-0,425; 0,550]
Week 16:				
Adjusted Mean Change (SE)	-0,13 (0,081)	-0,10 (0,087)	-0,04 [-0,252; 0,182] 0,751	-0,072 [-0,554; 0,409]

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 24:				
Adjusted Mean Change (SE)	-0,14 (0,084)	-0,14 (0,090)	0,00 [-0,225; 0,227] 0,994	0,002 [-0,486; 0,489]
Age = 40-64 years				
N'	138	141		
Baseline Mean (SD)	0,73 (0,662)	0,59 (0,588)		
Week 8:				
Adjusted Mean Change (SE)	-0,13 (0,045)	-0,12 (0,046)	-0,02 [-0,115; 0,080] 0,718	-0,034 [-0,272; 0,204]
Week 16:				
Adjusted Mean Change (SE)	-0,25 (0,048)	-0,18 (0,048)	-0,07 [-0,179; 0,034] 0,183	-0,128 [-0,364; 0,108]
Week 24:				
Adjusted Mean Change (SE)	-0,27 (0,049)	-0,23 (0,050)	-0,04 [-0,151; 0,072] 0,489	-0,068 [-0,307; 0,171]
Age = ≥65 years				
N'	58	46		
Baseline Mean (SD)	0,77 (0,695)	0,66 (0,655)		
Week 8:				
Adjusted Mean Change (SE)	0,07 (0,063)	0,02 (0,069)	0,06 [-0,105; 0,216] 0,495	0,118 [-0,271; 0,508]
Week 16:				
Adjusted Mean Change (SE)	0,03 (0,068)	-0,01 (0,074)	0,04 [-0,137; 0,214] 0,666	0,077 [-0,314; 0,468]

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 24:				
Adjusted Mean Change (SE)	-0,00 (0,070)	-0,05 (0,076)	0,05 [-0,132; 0,234] 0,585	0,098 [-0,291; 0,486]
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 + 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 subpopulation "high-dose ICS/LABA"				

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Percentage of mornings with no symptoms on rising					
Interaction Test	0,553				
Gender = Male					
N'	86	78			
Baseline Mean (SD)	31,75 (38,299)	38,60 (38,914)			
Week 8:					
Adjusted Mean Change (SE)	7,07 (3,535)	8,62 (3,783)	-1,55 [-10,220; 7,123] 0,726	-0,047	
Week 16:					
Adjusted Mean Change (SE)	14,64 (4,028)	13,33 (4,276)	1,31 [-8,923; 11,550] 0,801	0,035	
Week 24:					
Adjusted Mean Change (SE)	18,97 (4,216)	13,34 (4,467)	5,64 [-5,189; 16,465] 0,307	0,145	
Gender = Female					
N'	145	141			
Baseline Mean (SD)	38,03 (38,581)	44,57 (39,030)			
Week 8:					
Adjusted Mean Change (SE)	12,45 (3,097)	7,39 (3,020)	5,05 [-1,502; 11,609] 0,131	0,140	
Week 16:					
Adjusted Mean Change (SE)	19,62 (3,427)	13,18 (3,382)	6,44 [-1,316; 14,192] 0,103	0,159	
Week 24:					
Adjusted Mean Change (SE)	21,20 (3,558)	16,73 (3,530)	4,47 [-3,749; 12,686] 0,286	0,107	

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Percentage of days with no day-time symptoms					
Interaction Test	0,998				
Gender = Male					
N'	86	75			
Baseline Mean (SD)	15,27 (27,508)	18,10 (31,838)			
Week 8:					
Adjusted Mean Change (SE)	5,92 (3,277)	4,88 (3,564)	1,04 [-6,989; 9,068] 0,799	0,034 [-0,277; 0,345]	
Week 16:					
Adjusted Mean Change (SE)	12,39 (3,951)	9,12 (4,266)	3,26 [-6,954; 13,483] 0,531	0,089 [-0,222; 0,400]	
Week 24:					
Adjusted Mean Change (SE)	16,68 (4,192)	11,13 (4,514)	5,55 [-5,426; 16,519] 0,321	0,143 [-0,169; 0,455]	
Gender = Female					
N'	147	143			
Baseline Mean (SD)	17,43 (30,039)	18,40 (31,783)			
Week 8:					
Adjusted Mean Change (SE)	12,64 (2,894)	9,45 (2,846)	3,19 [-2,794; 9,183] 0,295	0,094 [-0,140; 0,328]	
Week 16:					
Adjusted Mean Change (SE)	22,42 (3,343)	17,21 (3,316)	5,21 [-2,388; 12,809] 0,179	0,131 [-0,101; 0,363]	
Week 24:					
Adjusted Mean Change (SE)	22,90 (3,514)	21,41 (3,496)	1,49 [-6,689; 9,676] 0,720	0,036 [-0,199; 0,271]	
Percentage of days with no night-time awakenings					
Interaction Test	0,297				
Gender = Male					
N'	86	78			
Baseline Mean (SD)	56,30 (40,786)	71,76 (37,778)			

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	10,19 (3,033)	9,52 (3,250)	0,67 [-6,820; 8,167] 0,860	0,024 [-0,286; 0,334]
Week 16:				
Adjusted Mean Change (SE)	15,77 (3,368)	11,94 (3,585)	3,83 [-4,731; 12,388] 0,380	0,123 [-0,186; 0,431]
Week 24:				
Adjusted Mean Change (SE)	18,31 (3,471)	12,11 (3,689)	6,19 [-2,692; 15,079] 0,172	0,193 [-0,117; 0,503]
Gender = Female				
N'	145	141		
Baseline Mean (SD)	57,68 (40,048)	64,27 (37,305)		
Week 8:				
Adjusted Mean Change (SE)	10,78 (2,654)	8,42 (2,581)	2,36 [-3,279; 8,006] 0,411	0,076 [-0,158; 0,311]
Week 16:				
Adjusted Mean Change (SE)	13,68 (2,878)	15,06 (2,829)	-1,38 [-7,840; 5,075] 0,674	-0,041 [-0,275; 0,193]
Week 24:				
Adjusted Mean Change (SE)	13,49 (2,950)	19,26 (2,915)	-5,76 [-12,481; 0,956] 0,093	-0,167 [-0,404; 0,069]
Percentage of days with no asthma symptoms				
Interaction Test	0,575			
Gender = Male				
N'	81	72		
Baseline Mean (SD)	12,13 (24,977)	17,33 (32,535)		
Week 8:				
Adjusted Mean Change (SE)	6,73 (3,220)	2,24 (3,495)	4,50 [-3,458; 12,448] 0,267	0,156 [-0,167; 0,478]
Week 16:				
Adjusted Mean Change (SE)	14,06 (3,973)	6,63 (4,262)	7,43 [-2,912; 17,781] 0,159	0,207 [-0,112; 0,527]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	18,67 (4,257)	8,31 (4,554)	10,36 [-0,863; 21,584] 0,070	0,272 [-0,050; 0,594]	
Gender = Female					
N'	138	130			
Baseline Mean (SD)	15,12 (28,709)	17,35 (31,761)			
Week 8:					
Adjusted Mean Change (SE)	11,94 (2,848)	8,04 (2,805)	3,91 [-2,112; 9,923] 0,203	0,123 [-0,124; 0,369]	
Week 16:					
Adjusted Mean Change (SE)	21,97 (3,345)	16,75 (3,349)	5,22 [-2,582; 13,022] 0,189	0,135 [-0,106; 0,376]	
Week 24:					
Adjusted Mean Change (SE)	23,26 (3,545)	19,98 (3,565)	3,28 [-5,205; 11,762] 0,448	0,081 [-0,163; 0,326]	
Mean total daily symptom score					
Interaction Test	0,815				
Gender = Male					
N'	81	72			
Baseline Mean (SD)	2,42 (1,599)	1,76 (1,314)			
Week 8:					
Adjusted Mean Change (SE)	-0,35 (0,127)	-0,37 (0,138)	0,02 [-0,295; 0,336] 0,899	0,018 [-0,304; 0,340]	
Week 16:					
Adjusted Mean Change (SE)	-0,65 (0,138)	-0,51 (0,149)	-0,15 [-0,497; 0,203] 0,410	-0,118 [-0,437; 0,201]	
Week 24:					
Adjusted Mean Change (SE)	-0,84 (0,140)	-0,53 (0,151)	-0,31 [-0,665; 0,050] 0,092	-0,244 [-0,566; 0,077]	
Gender = Female					
N'	138	130			
Baseline Mean (SD)	2,33 (1,727)	2,04 (1,548)			

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	-0,57 (0,112)	-0,43 (0,110)	-0,15 [-0,383; 0,093] 0,231	-0,116 [-0,362; 0,130]
Week 16:				
Adjusted Mean Change (SE)	-0,81 (0,119)	-0,69 (0,118)	-0,12 [-0,381; 0,145] 0,379	-0,086 [-0,327; 0,154]
Week 24:				
Adjusted Mean Change (SE)	-0,86 (0,120)	-0,83 (0,120)	-0,03 [-0,296; 0,242] 0,844	-0,020 [-0,264; 0,225]
Mean day-time symptom score				
Interaction Test	0,690			
Gender = Male				
N'	86	75		
Baseline Mean (SD)	0,94 (0,602)	0,74 (0,502)		
Week 8:				
Adjusted Mean Change (SE)	-0,11 (0,049)	-0,13 (0,053)	0,03 [-0,094; 0,146] 0,672	0,057 [-0,254; 0,368]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,054)	-0,19 (0,058)	-0,05 [-0,188; 0,085] 0,459	-0,103 [-0,413; 0,208]
Week 24:				
Adjusted Mean Change (SE)	-0,31 (0,055)	-0,21 (0,060)	-0,11 [-0,247; 0,036] 0,144	-0,205 [-0,517; 0,107]
Gender = Female				
N'	147	143		
Baseline Mean (SD)	0,91 (0,609)	0,86 (0,573)		
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,043)	-0,16 (0,042)	-0,02 [-0,109; 0,069] 0,660	-0,039 [-0,274; 0,195]
Week 16:				
Adjusted Mean Change (SE)	-0,29 (0,046)	-0,25 (0,046)	-0,04 [-0,137; 0,065] 0,487	-0,065 [-0,297; 0,167]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	-0,29 (0,047)	-0,32 (0,047)	0,02 [-0,085; 0,125] 0,703	0,037 [-0,199; 0,272]	
Mean night-time symptom score					
Interaction Test	0,600				
Gender = Male					
N'	86	78			
Baseline Mean (SD)	0,74 (0,546)	0,53 (0,448)			
Week 8:					
Adjusted Mean Change (SE)	-0,12 (0,041)	-0,15 (0,044)	0,03 [-0,074; 0,128] 0,603	0,071 [-0,240; 0,381]	
Week 16:					
Adjusted Mean Change (SE)	-0,20 (0,043)	-0,20 (0,046)	-0,01 [-0,114; 0,104] 0,928	-0,012 [-0,321; 0,296]	
Week 24:					
Adjusted Mean Change (SE)	-0,25 (0,044)	-0,20 (0,047)	-0,05 [-0,163; 0,062] 0,381	-0,122 [-0,431; 0,188]	
Gender = Female					
N'	145	141			
Baseline Mean (SD)	0,72 (0,606)	0,60 (0,521)			
Week 8:					
Adjusted Mean Change (SE)	-0,20 (0,036)	-0,13 (0,035)	-0,07 [-0,145; 0,007] 0,073	-0,167 [-0,401; 0,068]	
Week 16:					
Adjusted Mean Change (SE)	-0,27 (0,037)	-0,22 (0,037)	-0,04 [-0,127; 0,038] 0,288	-0,102 [-0,336; 0,132]	
Week 24:					
Adjusted Mean Change (SE)	-0,28 (0,038)	-0,27 (0,038)	-0,02 [-0,101; 0,069] 0,718	-0,035 [-0,272; 0,201]	

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Mean of: How did you sleep last night?					
Interaction Test	0,882				
Gender = Male					
N'	86	78			
Baseline Mean (SD)	0,57 (0,587)	0,33 (0,447)			
Week 8:					
Adjusted Mean Change (SE)	-0,14 (0,038)	-0,16 (0,041)	0,02 [-0,073; 0,115]	0,060 0,661	[-0,250; 0,370]
Week 16:					
Adjusted Mean Change (SE)	-0,22 (0,040)	-0,20 (0,043)	-0,02 [-0,120; 0,083]	-0,049 0,723	[-0,357; 0,259]
Week 24:					
Adjusted Mean Change (SE)	-0,26 (0,040)	-0,21 (0,043)	-0,04 [-0,147; 0,057]	-0,119 0,391	[-0,429; 0,190]
Gender = Female					
N'	145	141			
Baseline Mean (SD)	0,59 (0,647)	0,46 (0,548)			
Week 8:					
Adjusted Mean Change (SE)	-0,19 (0,033)	-0,14 (0,032)	-0,05 [-0,124; 0,018]	-0,136 0,145	[-0,371; 0,098]
Week 16:					
Adjusted Mean Change (SE)	-0,23 (0,035)	-0,23 (0,034)	-0,00 [-0,078; 0,075]	-0,003 0,976	[-0,237; 0,231]
Week 24:					
Adjusted Mean Change (SE)	-0,23 (0,035)	-0,27 (0,034)	0,04 [-0,039; 0,116]	0,095 0,329	[-0,142; 0,331]
Mean of: Did you have asthma symptoms upon awakening in the morning?					
Interaction Test	0,349				
Gender = Male					
N'	86	78			
Baseline Mean (SD)	0,92 (0,649)	0,74 (0,556)			

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	-0,09 (0,052)	-0,13 (0,056)	0,04 [-0,091; 0,165] 0,570	0,077 [-0,233; 0,387]
Week 16:				
Adjusted Mean Change (SE)	-0,18 (0,057)	-0,19 (0,060)	0,01 [-0,129; 0,157] 0,849	0,026 [-0,282; 0,335]
Week 24:				
Adjusted Mean Change (SE)	-0,25 (0,059)	-0,19 (0,063)	-0,05 [-0,203; 0,098] 0,495	-0,096 [-0,405; 0,214]
Gender = Female				
N'	145	141		
Baseline Mean (SD)	0,85 (0,653)	0,74 (0,617)		
Week 8:				
Adjusted Mean Change (SE)	-0,19 (0,046)	-0,11 (0,044)	-0,08 [-0,181; 0,013] 0,089	-0,157 [-0,392; 0,077]
Week 16:				
Adjusted Mean Change (SE)	-0,30 (0,049)	-0,21 (0,048)	-0,09 [-0,194; 0,022] 0,119	-0,150 [-0,384; 0,084]
Week 24:				
Adjusted Mean Change (SE)	-0,32 (0,050)	-0,26 (0,050)	-0,07 [-0,183; 0,046] 0,240	-0,116 [-0,353; 0,120]
Mean of: Did your respiratory symptoms stop you from performing your usual daily activities?				
Interaction Test	0,876			
Gender = Male				
N'	86	75		
Baseline Mean (SD)	0,99 (0,711)	0,75 (0,648)		
Week 8:				
Adjusted Mean Change (SE)	-0,13 (0,055)	-0,17 (0,060)	0,05 [-0,089; 0,183] 0,495	0,092 [-0,219; 0,403]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,061)	-0,22 (0,067)	-0,02 [-0,176; 0,136] 0,801	-0,035 [-0,346; 0,275]

	Treatment groups		Comparison	
	E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:				
Adjusted Mean Change (SE)	-0,32 (0,063)	-0,24 (0,068)	-0,08 [-0,240; 0,082] 0,335	-0,136 [-0,447; 0,176]
Gender = Female				
N'	147	143		
Baseline Mean (SD)	0,91 (0,695)	0,90 (0,676)		
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,049)	-0,18 (0,048)	-0,01 [-0,107; 0,095] 0,905	-0,011 [-0,245; 0,224]
Week 16:				
Adjusted Mean Change (SE)	-0,30 (0,053)	-0,27 (0,052)	-0,03 [-0,147; 0,084] 0,594	-0,050 [-0,282; 0,182]
Week 24:				
Adjusted Mean Change (SE)	-0,30 (0,054)	-0,33 (0,053)	0,03 [-0,091; 0,148] 0,641	0,045 [-0,190; 0,280]
Mean of: How severe was your shortness of breath today?				
Interaction Test	0,560			
Gender = Male				
N'	86	75		
Baseline Mean (SD)	1,11 (0,677)	0,89 (0,562)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,055)	-0,18 (0,061)	0,02 [-0,121; 0,151] 0,827	0,029 [-0,281; 0,340]
Week 16:				
Adjusted Mean Change (SE)	-0,33 (0,061)	-0,25 (0,066)	-0,08 [-0,232; 0,078] 0,328	-0,136 [-0,447; 0,175]
Week 24:				
Adjusted Mean Change (SE)	-0,42 (0,063)	-0,25 (0,068)	-0,17 [-0,331; -0,009] 0,039 *	-0,291 [-0,604; 0,022]
Gender = Female				
N'	147	143		
Baseline Mean (SD)	1,05 (0,668)	1,02 (0,666)		

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	-0,25 (0,049)	-0,22 (0,048)	-0,03 [-0,130; 0,072] 0,576	-0,050 [-0,285; 0,184]
Week 16:				
Adjusted Mean Change (SE)	-0,38 (0,053)	-0,32 (0,052)	-0,05 [-0,170; 0,060] 0,349	-0,088 [-0,320; 0,144]
Week 24:				
Adjusted Mean Change (SE)	-0,38 (0,054)	-0,39 (0,053)	0,01 [-0,111; 0,129] 0,882	0,014 [-0,221; 0,250]
Mean of: How was your wheeze during the past 12 hours?				
Interaction Test	0,252			
Gender = Male				
N'	86	75		
Baseline Mean (SD)	0,94 (0,657)	0,70 (0,557)		
Week 8:				
Adjusted Mean Change (SE)	-0,14 (0,055)	-0,11 (0,060)	-0,02 [-0,161; 0,112] 0,722	-0,048 [-0,359; 0,263]
Week 16:				
Adjusted Mean Change (SE)	-0,26 (0,060)	-0,17 (0,066)	-0,09 [-0,245; 0,062] 0,241	-0,163 [-0,474; 0,148]
Week 24:				
Adjusted Mean Change (SE)	-0,34 (0,063)	-0,17 (0,068)	-0,16 [-0,324; -0,005] 0,044 *	-0,283 [-0,596; 0,029]
Gender = Female				
N'	147	143		
Baseline Mean (SD)	0,94 (0,702)	0,84 (0,659)		
Week 8:				
Adjusted Mean Change (SE)	-0,20 (0,049)	-0,20 (0,048)	0,00 [-0,098; 0,105] 0,942	0,007 [-0,228; 0,241]
Week 16:				
Adjusted Mean Change (SE)	-0,31 (0,052)	-0,28 (0,052)	-0,03 [-0,141; 0,086] 0,638	-0,044 [-0,276; 0,188]

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 24:				
Adjusted Mean Change (SE)	-0,30 (0,054)	-0,35 (0,053)	0,05 [-0,069; 0,168] 0,413	0,079 [-0,157; 0,314]
Mean of: How was your cough during the past 12 hours?				
Interaction Test	0,785			
Gender = Male				
N'	86	75		
Baseline Mean (SD)	0,92 (0,642)	0,85 (0,569)		
Week 8:				
Adjusted Mean Change (SE)	-0,08 (0,057)	-0,12 (0,062)	0,05 [-0,095; 0,187] 0,522	0,086 [-0,225; 0,397]
Week 16:				
Adjusted Mean Change (SE)	-0,20 (0,064)	-0,18 (0,069)	-0,02 [-0,177; 0,146] 0,847	-0,027 [-0,337; 0,284]
Week 24:				
Adjusted Mean Change (SE)	-0,26 (0,065)	-0,22 (0,071)	-0,04 [-0,209; 0,126] 0,627	-0,068 [-0,380; 0,243]
Gender = Female				
N'	147	143		
Baseline Mean (SD)	0,94 (0,674)	0,89 (0,683)		
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,051)	-0,13 (0,050)	-0,05 [-0,159; 0,051] 0,313	-0,091 [-0,325; 0,143]
Week 16:				
Adjusted Mean Change (SE)	-0,28 (0,055)	-0,25 (0,054)	-0,03 [-0,148; 0,092] 0,645	-0,043 [-0,275; 0,189]
Week 24:				
Adjusted Mean Change (SE)	-0,31 (0,056)	-0,30 (0,055)	-0,00 [-0,130; 0,120] 0,939	-0,007 [-0,243; 0,228]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Did you have chest tightness during the past 12 hours?					
Interaction Test	0,921				
Gender = Male					
N'	86	75			
Baseline Mean (SD)	0,75 (0,638)	0,51 (0,543)			
Week 8:					
Adjusted Mean Change (SE)	-0,04 (0,053)	-0,09 (0,057)	0,05 [-0,079; 0,180] 0,445	0,103 [-0,208; 0,414]	
Week 16:					
Adjusted Mean Change (SE)	-0,16 (0,057)	-0,13 (0,062)	-0,03 [-0,177; 0,109] 0,639	-0,065 [-0,375; 0,246]	
Week 24:					
Adjusted Mean Change (SE)	-0,22 (0,058)	-0,16 (0,063)	-0,05 [-0,203; 0,094] 0,474	-0,100 [-0,412; 0,211]	
Gender = Female					
N'	147	143			
Baseline Mean (SD)	0,69 (0,688)	0,67 (0,643)			
Week 8:					
Adjusted Mean Change (SE)	-0,10 (0,046)	-0,09 (0,046)	-0,01 [-0,106; 0,086] 0,839	-0,018 [-0,253; 0,216]	
Week 16:					
Adjusted Mean Change (SE)	-0,18 (0,049)	-0,15 (0,048)	-0,03 [-0,136; 0,076] 0,577	-0,052 [-0,283; 0,180]	
Week 24:					
Adjusted Mean Change (SE)	-0,18 (0,050)	-0,20 (0,050)	0,03 [-0,083; 0,137] 0,632	0,046 [-0,190; 0,281]	
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 + 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 subpopulation "high-dose ICS/LABA"					

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CQVM149B2306

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Percentage of mornings with no symptoms on rising					
Interaction Test	0,143				
Region = Asia					
N'	49	56			
Baseline Mean (SD)	26,86 (36,178)	35,39 (37,743)			
Week 8:					
Adjusted Mean Change (SE)	15,67 (4,639)	5,97 (4,311)	9,70 [-2,717; 22,119] 0,126	0,304 [-0,087; 0,696]	
Week 16:					
Adjusted Mean Change (SE)	24,88 (4,628)	8,43 (4,328)	16,45 [4,024; 28,871] 0,010 *	0,515 [0,120; 0,910]	
Week 24:					
Adjusted Mean Change (SE)	26,22 (4,628)	13,94 (4,352)	12,28 [-0,170; 24,740] 0,053	0,387 [-0,009; 0,783]	
Region = Europe					
N'	78	82			
Baseline Mean (SD)	27,16 (36,145)	38,00 (38,816)			
Week 8:					
Adjusted Mean Change (SE)	7,22 (3,669)	4,81 (3,553)	2,41 [-7,611; 12,432] 0,637	0,075 [-0,236; 0,386]	
Week 16:					
Adjusted Mean Change (SE)	14,85 (3,662)	10,17 (3,560)	4,68 [-5,344; 14,701] 0,360	0,145 [-0,166; 0,457]	
Week 24:					
Adjusted Mean Change (SE)	16,64 (3,668)	11,75 (3,573)	4,89 [-5,160; 14,939] 0,340	0,153 [-0,161; 0,467]	
Region = Latin America					
N'	100	80			
Baseline Mean (SD)	45,52 (38,915)	51,95 (38,917)			

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 8:					
Adjusted Mean Change (SE)	9,85 (3,239)	9,99 (3,643)	-0,14 [-9,665; 9,389] 0,977	-0,004 [-0,303; 0,295]	
Week 16:					
Adjusted Mean Change (SE)	16,37 (3,236)	17,89 (3,631)	-1,52 [-11,030; 7,982] 0,753	-0,047 [-0,344; 0,249]	
Week 24:					
Adjusted Mean Change (SE)	19,99 (3,242)	18,71 (3,637)	1,28 [-8,243; 10,800] 0,792	0,040 [-0,258; 0,338]	
Region = Others					
N'	4	1			
Baseline Mean (SD)	64,58 (42,026)	41,67 (-)			
Week 8:					
Adjusted Mean Change (SE)	7,99 (16,108)	59,01 (32,170)	-51,02 [-121,630; 19,588] 0,156	-1,584 [-3,985; 0,817]	
Week 16:					
Adjusted Mean Change (SE)	6,55 (16,108)	56,94 (32,170)	-50,39 [-120,999; 20,218] 0,162	-1,564 [-3,960; 0,832]	
Week 24:					
Adjusted Mean Change (SE)	17,87 (16,108)	59,35 (32,170)	-41,48 [-112,085; 29,132] 0,249	-1,287 [-3,620; 1,045]	
Percentage of days with no day-time symptoms					
Interaction Test	0,573				
Region = Asia					
N'	50	53			
Baseline Mean (SD)	13,13 (29,069)	12,96 (27,402)			
Week 8:					
Adjusted Mean Change (SE)	7,18 (4,515)	11,19 (4,370)	-4,02 [-16,337; 8,305] 0,523	-0,127 [-0,515; 0,262]	
Week 16:					
Adjusted Mean Change (SE)	17,63 (4,514)	18,26 (4,385)	-0,63 [-12,972; 11,712] 0,920	-0,020 [-0,410; 0,370]	

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	18,31 (4,545)	21,10 (4,397)	-2,79 [-15,186; 9,616] 0,659	-0,089 [-0,486; 0,307]	
Region = Europe					
N'	79	80			
Baseline Mean (SD)	11,42 (25,129)	9,03 (21,385)			
Week 8:					
Adjusted Mean Change (SE)	10,16 (3,585)	5,86 (3,571)	4,30 [-5,598; 14,195] 0,394	0,135 [-0,176; 0,446]	
Week 16:					
Adjusted Mean Change (SE)	16,88 (3,585)	9,56 (3,571)	7,32 [-2,578; 17,216] 0,147	0,229 [-0,082; 0,541]	
Week 24:					
Adjusted Mean Change (SE)	18,98 (3,591)	12,82 (3,590)	6,16 [-3,769; 16,096] 0,224	0,195 [-0,121; 0,511]	
Region = Latin America					
N'	100	84			
Baseline Mean (SD)	22,17 (31,458)	30,71 (38,279)			
Week 8:					
Adjusted Mean Change (SE)	12,65 (3,203)	9,47 (3,554)	3,18 [-6,165; 12,522] 0,505	0,101 [-0,198; 0,400]	
Week 16:					
Adjusted Mean Change (SE)	22,01 (3,191)	18,34 (3,529)	3,67 [-5,618; 12,960] 0,438	0,115 [-0,178; 0,408]	
Week 24:					
Adjusted Mean Change (SE)	24,24 (3,201)	22,66 (3,528)	1,57 [-7,725; 10,874] 0,740	0,050 [-0,244; 0,344]	
Region = Others					
N'	4	1			
Baseline Mean (SD)	25,00 (22,970)	0,00 (-)			

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 8:					
Adjusted Mean Change (SE)	38,59 (15,895)	-0,67 (31,792)	39,26 [-30,514; 109,039] 0,270	1,235 [-1,086; 3,556]	
Week 16:					
Adjusted Mean Change (SE)	37,80 (15,895)	22,13 (31,792)	15,67 [-54,108; 85,445] 0,660	0,493 [-1,720; 2,705]	
Week 24:					
Adjusted Mean Change (SE)	46,89 (15,895)	7,39 (31,792)	39,49 [-30,285; 109,268] 0,267	1,242 [-1,080; 3,565]	
Percentage of days with no night-time awakenings					
Interaction Test	0,569				
Region = Asia					
N'	49	56			
Baseline Mean (SD)	53,91 (41,099)	59,63 (39,198)			
Week 8:					
Adjusted Mean Change (SE)	13,48 (3,874)	8,11 (3,606)	5,37 [-5,014; 15,752] 0,310	0,201 [-0,189; 0,592]	
Week 16:					
Adjusted Mean Change (SE)	18,45 (3,865)	13,22 (3,621)	5,22 [-5,164; 15,614] 0,324	0,196 [-0,194; 0,586]	
Week 24:					
Adjusted Mean Change (SE)	19,26 (3,865)	19,63 (3,642)	-0,37 [-10,786; 10,046] 0,944	-0,014 [-0,406; 0,378]	
Region = Europe					
N'	78	82			
Baseline Mean (SD)	51,23 (39,959)	62,86 (39,384)			
Week 8:					
Adjusted Mean Change (SE)	12,10 (3,068)	8,12 (2,972)	3,98 [-4,409; 12,364] 0,352	0,148 [-0,164; 0,459]	
Week 16:					
Adjusted Mean Change (SE)	13,58 (3,062)	13,17 (2,979)	0,41 [-7,975; 8,796] 0,923	0,015 [-0,296; 0,326]	

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	13,88 (3,067)	14,34 (2,990)	-0,46 [-8,867; 7,950] 0,915	-0,017 [-0,331; 0,297]	
Region = Latin America					
N'	100	80			
Baseline Mean (SD)	62,47 (40,068)	76,45 (32,901)			
Week 8:					
Adjusted Mean Change (SE)	6,89 (2,703)	8,24 (3,050)	-1,36 [-9,357; 6,640] 0,739	-0,051 [-0,350; 0,248]	
Week 16:					
Adjusted Mean Change (SE)	12,54 (2,701)	13,83 (3,040)	-1,30 [-9,277; 6,683] 0,750	-0,048 [-0,345; 0,248]	
Week 24:					
Adjusted Mean Change (SE)	13,55 (2,705)	15,54 (3,045)	-1,98 [-9,977; 6,010] 0,626	-0,074 [-0,372; 0,224]	
Region = Others					
N'	4	1			
Baseline Mean (SD)	80,29 (20,495)	50,00 (-)			
Week 8:					
Adjusted Mean Change (SE)	9,24 (13,465)	37,07 (26,914)	-27,84 [-86,915; 31,239] 0,355	-1,034 [-3,317; 1,249]	
Week 16:					
Adjusted Mean Change (SE)	6,94 (13,465)	42,61 (26,914)	-35,67 [-94,748; 23,405] 0,236	-1,325 [-3,665; 1,015]	
Week 24:					
Adjusted Mean Change (SE)	12,30 (13,465)	44,29 (26,914)	-31,99 [-91,069; 27,084] 0,288	-1,188 [-3,500; 1,124]	
Percentage of days with no asthma symptoms					
Interaction Test	0,837				
Region = Asia					
N'	47	49			
Baseline Mean (SD)	12,33 (29,090)	12,37 (28,868)			

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	8,57 (4,649)	8,95 (4,505)	-0,39 [-13,088; 12,314] 0,952	-0,013 [-0,424; 0,399]
Week 16:				
Adjusted Mean Change (SE)	17,94 (4,604)	15,78 (4,509)	2,16 [-10,481; 14,805] 0,737	0,069 [-0,335; 0,474]
Week 24:				
Adjusted Mean Change (SE)	19,78 (4,619)	17,29 (4,523)	2,49 [-10,194; 15,175] 0,700	0,080 [-0,329; 0,489]
Region = Europe				
N'	77	78		
Baseline Mean (SD)	10,57 (24,678)	8,96 (21,498)		
Week 8:				
Adjusted Mean Change (SE)	9,16 (3,595)	4,85 (3,578)	4,31 [-5,620; 14,243] 0,394	0,137 [-0,180; 0,455]
Week 16:				
Adjusted Mean Change (SE)	15,68 (3,588)	9,50 (3,570)	6,18 [-3,733; 16,088] 0,222	0,196 [-0,120; 0,512]
Week 24:				
Adjusted Mean Change (SE)	18,65 (3,595)	12,44 (3,592)	6,21 [-3,742; 16,160] 0,221	0,199 [-0,121; 0,519]
Region = Latin America				
N'	91	74		
Baseline Mean (SD)	17,48 (28,755)	29,71 (39,063)		
Week 8:				
Adjusted Mean Change (SE)	14,59 (3,337)	8,91 (3,740)	5,68 [-4,136; 15,497] 0,256	0,184 [-0,134; 0,502]
Week 16:				
Adjusted Mean Change (SE)	25,46 (3,303)	18,62 (3,708)	6,85 [-2,877; 16,568] 0,167	0,217 [-0,092; 0,525]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	27,50 (3,321)	22,25 (3,727)	5,25 [-4,527; 15,018] 0,292	0,168 [-0,145; 0,481]	
Region = Others					
N'	4	1			
Baseline Mean (SD)	21,21 (20,885)	0,00 (-)			
Week 8:					
Adjusted Mean Change (SE)	29,71 (15,715)	-0,60 (31,434)	30,31 [-38,683; 99,299] 0,389	0,964 [-1,307; 3,236]	
Week 16:					
Adjusted Mean Change (SE)	33,08 (15,715)	24,31 (31,434)	8,78 [-60,213; 77,768] 0,803	0,279 [-1,919; 2,477]	
Week 24:					
Adjusted Mean Change (SE)	49,43 (15,715)	8,71 (31,434)	40,72 [-28,270; 109,711] 0,247	1,296 [-1,038; 3,629]	
Mean total daily symptom score					
Interaction Test	N.E.				
Region = Asia					
N'	47	49			
Baseline Mean (SD)	2,70 (1,767)	2,21 (1,568)			
Week 8:					
Adjusted Mean Change (SE)	-0,57 (0,148)	-0,36 (0,144)	-0,22 [-0,626; 0,194] 0,299	-0,220 [-0,632; 0,193]	
Week 16:					
Adjusted Mean Change (SE)	-0,94 (0,167)	-0,57 (0,164)	-0,37 [-0,833; 0,094] 0,118	-0,326 [-0,733; 0,081]	
Week 24:					
Adjusted Mean Change (SE)	-0,96 (0,167)	-0,76 (0,164)	-0,20 [-0,660; 0,268] 0,404	-0,175 [-0,585; 0,235]	
Region = Europe					
N'	77	78			
Baseline Mean (SD)	2,59 (1,562)	2,11 (1,291)			

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	-0,58 (0,105)	-0,40 (0,105)	-0,17 [-0,466; 0,123] 0,253	-0,186 [-0,504; 0,131]
Week 16:				
Adjusted Mean Change (SE)	-0,83 (0,119)	-0,58 (0,119)	-0,24 [-0,577; 0,088] 0,149	-0,234 [-0,550; 0,082]
Week 24:				
Adjusted Mean Change (SE)	-0,90 (0,128)	-0,63 (0,127)	-0,27 [-0,630; 0,084] 0,133	-0,247 [-0,567; 0,074]
Region = Latin America				
N'	91	74		
Baseline Mean (SD)	2,05 (1,691)	1,56 (1,532)		
Week 8:				
Adjusted Mean Change (SE)	-0,35 (0,108)	-0,41 (0,119)	0,06 [-0,255; 0,378] 0,701	0,062 [-0,255; 0,380]
Week 16:				
Adjusted Mean Change (SE)	-0,59 (0,115)	-0,69 (0,127)	0,10 [-0,241; 0,439] 0,566	0,091 [-0,217; 0,398]
Week 24:				
Adjusted Mean Change (SE)	-0,74 (0,117)	-0,78 (0,129)	0,05 [-0,296; 0,390] 0,788	0,043 [-0,269; 0,355]
Region = Others				
N'	4	1		
Baseline Mean (SD)	1,15 (1,011)	3,03 (-)		
Week 8:				
Adjusted Mean Change (SE)	-1,08 (0,496)	-1,37 (0,949)	0,29 [-2,363; 2,952] 0,801	0,297 [-1,902; 2,496]
Week 16:				
Adjusted Mean Change (SE)	-1,03 (0,476)	-1,58 (0,910)	0,55 [-1,997; 3,102] 0,624	0,581 [-1,640; 2,802]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	-1,17 (0,517)	-1,62 (0,989)	0,45 [-2,320; 3,219] 0,713	0,435 [-1,773; 2,643]	
Mean day-time symptom score					
Interaction Test	0,856				
Region = Asia					
N'	50	53			
Baseline Mean (SD)	1,05 (0,652)	0,87 (0,555)			
Week 8:					
Adjusted Mean Change (SE)	-0,11 (0,061)	-0,15 (0,059)	0,03 [-0,133; 0,199] 0,693	0,078 [-0,310; 0,467]	
Week 16:					
Adjusted Mean Change (SE)	-0,26 (0,061)	-0,21 (0,059)	-0,05 [-0,214; 0,118] 0,569	-0,114 [-0,504; 0,277]	
Week 24:					
Adjusted Mean Change (SE)	-0,27 (0,061)	-0,28 (0,059)	0,02 [-0,151; 0,182] 0,856	0,037 [-0,360; 0,433]	
Region = Europe					
N'	79	80			
Baseline Mean (SD)	0,99 (0,537)	0,95 (0,493)			
Week 8:					
Adjusted Mean Change (SE)	-0,16 (0,048)	-0,13 (0,048)	-0,03 [-0,162; 0,105] 0,674	-0,067 [-0,378; 0,244]	
Week 16:					
Adjusted Mean Change (SE)	-0,27 (0,048)	-0,19 (0,048)	-0,08 [-0,210; 0,056] 0,256	-0,180 [-0,492; 0,131]	
Week 24:					
Adjusted Mean Change (SE)	-0,28 (0,048)	-0,23 (0,048)	-0,05 [-0,183; 0,084] 0,467	-0,117 [-0,432; 0,198]	
Region = Latin America					
N'	100	84			
Baseline Mean (SD)	0,82 (0,624)	0,66 (0,569)			

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 8:					
Adjusted Mean Change (SE)	-0,20 (0,043)	-0,21 (0,047)	0,01 [-0,117; 0,134] 0,892	0,021 [-0,278; 0,319]	
Week 16:					
Adjusted Mean Change (SE)	-0,31 (0,043)	-0,31 (0,047)	-0,00 [-0,125; 0,125] 0,999	-0,000 [-0,293; 0,293]	
Week 24:					
Adjusted Mean Change (SE)	-0,36 (0,043)	-0,35 (0,047)	-0,02 [-0,140; 0,110] 0,811	-0,036 [-0,330; 0,258]	
Region = Others					
N'	4	1			
Baseline Mean (SD)	0,61 (0,392)	1,31 (-)			
Week 8:					
Adjusted Mean Change (SE)	-0,44 (0,214)	-0,63 (0,427)	0,19 [-0,748; 1,128] 0,691	0,444 [-1,764; 2,653]	
Week 16:					
Adjusted Mean Change (SE)	-0,47 (0,214)	-0,84 (0,427)	0,37 [-0,566; 1,311] 0,436	0,871 [-1,385; 3,128]	
Week 24:					
Adjusted Mean Change (SE)	-0,47 (0,214)	-0,68 (0,427)	0,21 [-0,729; 1,148] 0,661	0,491 [-1,721; 2,703]	
Mean night-time symptom score					
Interaction Test	0,097				
Region = Asia					
N'	49	56			
Baseline Mean (SD)	0,82 (0,593)	0,71 (0,546)			
Week 8:					
Adjusted Mean Change (SE)	-0,18 (0,050)	-0,12 (0,046)	-0,07 [-0,200; 0,068] 0,334	-0,192 [-0,582; 0,198]	
Week 16:					
Adjusted Mean Change (SE)	-0,29 (0,050)	-0,17 (0,047)	-0,12 [-0,252; 0,016] 0,084	-0,343 [-0,735; 0,048]	

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	-0,30 (0,050)	-0,24 (0,047)	-0,07 [-0,199; 0,069] 0,342	-0,190 [-0,583; 0,203]	
Region = Europe					
N'	78	82			
Baseline Mean (SD)	0,83 (0,551)	0,60 (0,436)			
Week 8:					
Adjusted Mean Change (SE)	-0,18 (0,040)	-0,09 (0,038)	-0,09 [-0,197; 0,020] 0,109	-0,255 [-0,568; 0,057]	
Week 16:					
Adjusted Mean Change (SE)	-0,23 (0,040)	-0,17 (0,038)	-0,06 [-0,172; 0,045] 0,251	-0,183 [-0,494; 0,129]	
Week 24:					
Adjusted Mean Change (SE)	-0,25 (0,040)	-0,18 (0,039)	-0,07 [-0,175; 0,043] 0,233	-0,192 [-0,506; 0,123]	
Region = Latin America					
N'	100	80			
Baseline Mean (SD)	0,62 (0,591)	0,46 (0,497)			
Week 8:					
Adjusted Mean Change (SE)	-0,14 (0,035)	-0,16 (0,039)	0,02 [-0,085; 0,121] 0,727	0,053 [-0,246; 0,352]	
Week 16:					
Adjusted Mean Change (SE)	-0,23 (0,035)	-0,27 (0,039)	0,04 [-0,062; 0,143] 0,436	0,118 [-0,179; 0,414]	
Week 24:					
Adjusted Mean Change (SE)	-0,27 (0,035)	-0,29 (0,039)	0,02 [-0,081; 0,124] 0,682	0,062 [-0,236; 0,361]	
Region = Others					
N'	4	1			
Baseline Mean (SD)	0,29 (0,329)	1,04 (-)			

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,174)	-0,85 (0,347)	0,69 [-0,071; 1,453] 0,075	1,990 [-0,525; 4,504]
Week 16:				
Adjusted Mean Change (SE)	-0,11 (0,174)	-0,83 (0,347)	0,72 [-0,041; 1,482] 0,064	2,075 [-0,466; 4,616]
Week 24:				
Adjusted Mean Change (SE)	-0,25 (0,174)	-0,84 (0,347)	0,59 [-0,170; 1,354] 0,128	1,705 [-0,728; 4,138]
Mean of: How did you sleep last night?				
Interaction Test	N.E.			
Region = Asia				
N'	49	56		
Baseline Mean (SD)	0,63 (0,651)	0,52 (0,597)		
Week 8:				
Adjusted Mean Change (SE)	-0,23 (0,046)	-0,18 (0,043)	-0,06 [-0,184; 0,067] 0,356	-0,184 [-0,574; 0,206]
Week 16:				
Adjusted Mean Change (SE)	-0,33 (0,049)	-0,25 (0,046)	-0,09 [-0,217; 0,047] 0,205	-0,253 [-0,643; 0,138]
Week 24:				
Adjusted Mean Change (SE)	-0,34 (0,050)	-0,32 (0,047)	-0,02 [-0,156; 0,115] 0,765	-0,060 [-0,452; 0,332]
Region = Europe				
N'	78	82		
Baseline Mean (SD)	0,66 (0,618)	0,43 (0,462)		
Week 8:				
Adjusted Mean Change (SE)	-0,23 (0,031)	-0,14 (0,030)	-0,08 [-0,170; 0,003] 0,058	-0,305 [-0,618; 0,008]
Week 16:				
Adjusted Mean Change (SE)	-0,26 (0,035)	-0,22 (0,034)	-0,04 [-0,136; 0,055] 0,407	-0,133 [-0,444; 0,178]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	-0,26 (0,037)	-0,23 (0,036)	-0,03 [-0,130; 0,074] 0,590	-0,087 [-0,401; 0,227]	
Region = Latin America					
N'	100	80			
Baseline Mean (SD)	0,51 (0,621)	0,31 (0,498)			
Week 8:					
Adjusted Mean Change (SE)	-0,08 (0,032)	-0,12 (0,035)	0,04 [-0,058; 0,130] 0,449	0,116 [-0,183; 0,416]	
Week 16:					
Adjusted Mean Change (SE)	-0,13 (0,034)	-0,19 (0,038)	0,06 [-0,046; 0,158] 0,278	0,165 [-0,132; 0,462]	
Week 24:					
Adjusted Mean Change (SE)	-0,16 (0,033)	-0,21 (0,037)	0,05 [-0,050; 0,148] 0,329	0,150 [-0,149; 0,448]	
Region = Others					
N'	4	1			
Baseline Mean (SD)	0,22 (0,239)	1,00 (-)			
Week 8:					
Adjusted Mean Change (SE)	-0,31 (0,089)	-0,32 (0,183)	0,01 [-0,502; 0,517] 0,973	0,042 [-2,149; 2,234]	
Week 16:					
Adjusted Mean Change (SE)	-0,22 (0,098)	-0,37 (0,202)	0,15 [-0,410; 0,716] 0,541	0,777 [-1,466; 3,021]	
Week 24:					
Adjusted Mean Change (SE)	-0,30 (0,100)	-0,43 (0,206)	0,13 [-0,444; 0,705] 0,607	0,652 [-1,577; 2,880]	
Mean of: Did you have asthma symptoms upon awakening in the morning?					
Interaction Test	N.E.				
Region = Asia					
N'	49	56			
Baseline Mean (SD)	1,02 (0,651)	0,89 (0,652)			

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	-0,22 (0,061)	-0,13 (0,057)	-0,09 [-0,252; 0,077] 0,297	-0,208 [-0,598; 0,182]
Week 16:				
Adjusted Mean Change (SE)	-0,36 (0,068)	-0,20 (0,063)	-0,16 [-0,348; 0,018] 0,077	-0,354 [-0,746; 0,038]
Week 24:				
Adjusted Mean Change (SE)	-0,38 (0,072)	-0,26 (0,068)	-0,12 [-0,320; 0,071] 0,210	-0,253 [-0,646; 0,141]
Region = Europe				
N'	78	82		
Baseline Mean (SD)	1,00 (0,628)	0,76 (0,552)		
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,047)	-0,08 (0,046)	-0,10 [-0,230; 0,032] 0,139	-0,237 [-0,549; 0,075]
Week 16:				
Adjusted Mean Change (SE)	-0,27 (0,056)	-0,16 (0,055)	-0,11 [-0,267; 0,042] 0,152	-0,230 [-0,542; 0,082]
Week 24:				
Adjusted Mean Change (SE)	-0,30 (0,059)	-0,18 (0,058)	-0,12 [-0,286; 0,040] 0,139	-0,240 [-0,555; 0,075]
Region = Latin America				
N'	100	80		
Baseline Mean (SD)	0,73 (0,641)	0,60 (0,574)		
Week 8:				
Adjusted Mean Change (SE)	-0,11 (0,041)	-0,14 (0,046)	0,03 [-0,093; 0,148] 0,656	0,068 [-0,231; 0,367]
Week 16:				
Adjusted Mean Change (SE)	-0,20 (0,042)	-0,25 (0,047)	0,05 [-0,071; 0,180] 0,393	0,129 [-0,167; 0,426]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	-0,25 (0,045)	-0,27 (0,051)	0,02 [-0,117; 0,150] 0,807	0,037 [-0,261; 0,335]	
Region = Others					
N'	4	1			
Baseline Mean (SD)	0,35 (0,420)	1,08 (-)			
Week 8:					
Adjusted Mean Change (SE)	-0,24 (0,242)	-0,78 (0,461)	0,54 [-0,744; 1,827] 0,352	1,121 [-1,178; 3,420]	
Week 16:					
Adjusted Mean Change (SE)	-0,20 (0,246)	-0,70 (0,469)	0,50 [-0,810; 1,802] 0,399	1,010 [-1,269; 3,289]	
Week 24:					
Adjusted Mean Change (SE)	-0,31 (0,261)	-0,77 (0,498)	0,45 [-0,934; 1,841] 0,465	0,869 [-1,388; 3,125]	
Mean of: Did your respiratory symptoms stop you from performing your usual daily activities?					
Interaction Test	N.E.				
Region = Asia					
N'	50	53			
Baseline Mean (SD)	1,07 (0,693)	0,91 (0,676)			
Week 8:					
Adjusted Mean Change (SE)	-0,14 (0,065)	-0,19 (0,063)	0,05 [-0,131; 0,228] 0,593	0,106 [-0,282; 0,495]	
Week 16:					
Adjusted Mean Change (SE)	-0,29 (0,077)	-0,27 (0,075)	-0,02 [-0,231; 0,195] 0,867	-0,034 [-0,424; 0,357]	
Week 24:					
Adjusted Mean Change (SE)	-0,30 (0,078)	-0,33 (0,075)	0,03 [-0,185; 0,244] 0,786	0,055 [-0,341; 0,451]	
Region = Europe					
N'	79	80			
Baseline Mean (SD)	1,07 (0,628)	1,04 (0,609)			

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	-0,20 (0,050)	-0,16 (0,049)	-0,04 [-0,180; 0,095] 0,545	-0,096 [-0,407; 0,215]
Week 16:				
Adjusted Mean Change (SE)	-0,31 (0,058)	-0,23 (0,058)	-0,09 [-0,248; 0,076] 0,299	-0,165 [-0,476; 0,146]
Week 24:				
Adjusted Mean Change (SE)	-0,34 (0,062)	-0,29 (0,061)	-0,06 [-0,226; 0,116] 0,526	-0,102 [-0,417; 0,213]
Region = Latin America				
N'	100	84		
Baseline Mean (SD)	0,78 (0,736)	0,62 (0,655)		
Week 8:				
Adjusted Mean Change (SE)	-0,14 (0,042)	-0,19 (0,046)	0,06 [-0,067; 0,177] 0,375	0,136 [-0,163; 0,435]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,045)	-0,28 (0,050)	0,03 [-0,099; 0,166] 0,622	0,074 [-0,219; 0,367]
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,047)	-0,30 (0,051)	0,03 [-0,112; 0,162] 0,716	0,055 [-0,239; 0,349]
Region = Others				
N'	4	1		
Baseline Mean (SD)	0,61 (0,495)	1,67 (-)		
Week 8:				
Adjusted Mean Change (SE)	-0,53 (0,161)	-0,14 (0,378)	-0,40 [-1,415; 0,625] 0,390	-1,225 [-3,544; 1,094]
Week 16:				
Adjusted Mean Change (SE)	-0,52 (0,239)	-0,33 (0,560)	-0,18 [-1,693; 1,328] 0,783	-0,382 [-2,586; 1,822]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	-0,50 (0,253)	-0,05 (0,592)	-0,45 [-2,049; 1,147] 0,526	-0,893 [-3,153; 1,367]	
Mean of: How severe was your shortness of breath today?					
Interaction Test	0,773				
Region = Asia					
N'	50	53			
Baseline Mean (SD)	1,23 (0,678)	1,03 (0,671)			
Week 8:					
Adjusted Mean Change (SE)	-0,17 (0,069)	-0,21 (0,067)	0,04 [-0,148; 0,230] 0,673	0,084 [-0,305; 0,472]	
Week 16:					
Adjusted Mean Change (SE)	-0,35 (0,069)	-0,27 (0,067)	-0,08 [-0,269; 0,110] 0,409	-0,164 [-0,555; 0,227]	
Week 24:					
Adjusted Mean Change (SE)	-0,34 (0,070)	-0,34 (0,067)	-0,00 [-0,194; 0,187] 0,971	-0,007 [-0,404; 0,389]	
Region = Europe					
N'	79	80			
Baseline Mean (SD)	1,17 (0,600)	1,13 (0,582)			
Week 8:					
Adjusted Mean Change (SE)	-0,21 (0,055)	-0,16 (0,054)	-0,06 [-0,207; 0,096] 0,470	-0,115 [-0,426; 0,197]	
Week 16:					
Adjusted Mean Change (SE)	-0,35 (0,055)	-0,24 (0,054)	-0,12 [-0,270; 0,033] 0,125	-0,243 [-0,555; 0,069]	
Week 24:					
Adjusted Mean Change (SE)	-0,38 (0,055)	-0,26 (0,055)	-0,12 [-0,268; 0,037] 0,137	-0,239 [-0,555; 0,077]	
Region = Latin America					
N'	100	84			
Baseline Mean (SD)	0,93 (0,704)	0,79 (0,617)			

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 8:					
Adjusted Mean Change (SE)	-0,25 (0,049)	-0,26 (0,054)	0,01 [-0,136; 0,150] 0,926	0,014 [-0,285; 0,313]	
Week 16:					
Adjusted Mean Change (SE)	-0,39 (0,049)	-0,39 (0,054)	0,00 [-0,141; 0,143] 0,994	0,001 [-0,291; 0,294]	
Week 24:					
Adjusted Mean Change (SE)	-0,46 (0,049)	-0,44 (0,054)	-0,02 [-0,157; 0,127] 0,833	-0,031 [-0,326; 0,263]	
Region = Others					
N'	4	1			
Baseline Mean (SD)	0,78 (0,419)	1,67 (-)			
Week 8:					
Adjusted Mean Change (SE)	-0,49 (0,244)	-0,57 (0,487)	0,08 [-0,990; 1,149] 0,884	0,164 [-2,030; 2,357]	
Week 16:					
Adjusted Mean Change (SE)	-0,56 (0,244)	-0,91 (0,487)	0,35 [-0,721; 1,418] 0,523	0,715 [-1,521; 2,950]	
Week 24:					
Adjusted Mean Change (SE)	-0,60 (0,244)	-0,60 (0,487)	-0,01 [-1,079; 1,060] 0,987	-0,019 [-2,210; 2,173]	
Mean of: How was your wheeze during the past 12 hours?					
Interaction Test	N.E.				
Region = Asia					
N'	50	53			
Baseline Mean (SD)	1,06 (0,775)	0,78 (0,658)			
Week 8:					
Adjusted Mean Change (SE)	-0,18 (0,065)	-0,18 (0,062)	0,00 [-0,175; 0,182] 0,967	0,008 [-0,380; 0,397]	
Week 16:					
Adjusted Mean Change (SE)	-0,35 (0,073)	-0,25 (0,071)	-0,10 [-0,297; 0,105] 0,348	-0,189 [-0,580; 0,203]	

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	-0,38 (0,075)	-0,34 (0,073)	-0,04 [-0,245; 0,171] 0,728	-0,071 [-0,467; 0,326]	
Region = Europe					
N'	79	80			
Baseline Mean (SD)	0,99 (0,618)	0,85 (0,564)			
Week 8:					
Adjusted Mean Change (SE)	-0,23 (0,047)	-0,21 (0,047)	-0,03 [-0,157; 0,106] 0,705	-0,060 [-0,371; 0,251]	
Week 16:					
Adjusted Mean Change (SE)	-0,36 (0,053)	-0,28 (0,053)	-0,08 [-0,232; 0,063] 0,261	-0,179 [-0,491; 0,132]	
Week 24:					
Adjusted Mean Change (SE)	-0,36 (0,057)	-0,29 (0,057)	-0,07 [-0,231; 0,087] 0,374	-0,143 [-0,459; 0,172]	
Region = Latin America					
N'	100	84			
Baseline Mean (SD)	0,86 (0,683)	0,73 (0,663)			
Week 8:					
Adjusted Mean Change (SE)	-0,17 (0,045)	-0,18 (0,049)	0,01 [-0,124; 0,136] 0,931	0,013 [-0,286; 0,312]	
Week 16:					
Adjusted Mean Change (SE)	-0,25 (0,050)	-0,25 (0,054)	0,00 [-0,145; 0,146] 0,990	0,002 [-0,291; 0,294]	
Week 24:					
Adjusted Mean Change (SE)	-0,29 (0,052)	-0,30 (0,057)	0,01 [-0,142; 0,161] 0,902	0,018 [-0,276; 0,312]	
Region = Others					
N'	4	1			
Baseline Mean (SD)	0,57 (0,602)	1,78 (-)			

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	-0,64 (0,276)	-0,13 (0,543)	-0,51 [-2,078; 1,066] 0,471	-0,918 [-3,181; 1,346]
Week 16:				
Adjusted Mean Change (SE)	-0,74 (0,244)	-0,63 (0,480)	-0,11 [-1,500; 1,279] 0,856	-0,226 [-2,422; 1,969]
Week 24:				
Adjusted Mean Change (SE)	-0,69 (0,257)	-0,48 (0,507)	-0,21 [-1,676; 1,259] 0,747	-0,405 [-2,611; 1,800]
Mean of: How was your cough during the past 12 hours?				
Interaction Test	N.E.			
Region = Asia				
N'	50	53		
Baseline Mean (SD)	1,05 (0,723)	0,92 (0,647)		
Week 8:				
Adjusted Mean Change (SE)	-0,12 (0,065)	-0,14 (0,063)	0,02 [-0,162; 0,195] 0,858	0,036 [-0,353; 0,424]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,074)	-0,25 (0,072)	0,01 [-0,198; 0,212] 0,946	0,014 [-0,377; 0,404]
Week 24:				
Adjusted Mean Change (SE)	-0,26 (0,079)	-0,34 (0,076)	0,08 [-0,135; 0,299] 0,454	0,152 [-0,245; 0,549]
Region = Europe				
N'	79	80		
Baseline Mean (SD)	0,95 (0,641)	1,04 (0,582)		
Week 8:				
Adjusted Mean Change (SE)	-0,16 (0,049)	-0,13 (0,048)	-0,03 [-0,160; 0,109] 0,710	-0,059 [-0,370; 0,252]
Week 16:				
Adjusted Mean Change (SE)	-0,26 (0,057)	-0,20 (0,057)	-0,06 [-0,220; 0,098] 0,448	-0,121 [-0,432; 0,191]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	-0,26 (0,060)	-0,24 (0,060)	-0,02 [-0,192; 0,144] 0,777	-0,046 [-0,361; 0,269]	
Region = Latin America					
N'	100	84			
Baseline Mean (SD)	0,88 (0,647)	0,69 (0,663)			
Week 8:					
Adjusted Mean Change (SE)	-0,13 (0,048)	-0,12 (0,052)	-0,01 [-0,150; 0,131] 0,889	-0,021 [-0,320; 0,278]	
Week 16:					
Adjusted Mean Change (SE)	-0,24 (0,054)	-0,26 (0,059)	0,02 [-0,139; 0,175] 0,822	0,034 [-0,259; 0,326]	
Week 24:					
Adjusted Mean Change (SE)	-0,31 (0,054)	-0,28 (0,059)	-0,04 [-0,196; 0,122] 0,647	-0,069 [-0,363; 0,225]	
Region = Others					
N'	4	1			
Baseline Mean (SD)	0,36 (0,187)	0,78 (-)			
Week 8:					
Adjusted Mean Change (SE)	-0,36 (0,139)	-0,54 (0,261)	0,18 [-0,540; 0,891] 0,580	0,630 [-1,596; 2,856]	
Week 16:					
Adjusted Mean Change (SE)	-0,35 (0,123)	-0,59 (0,230)	0,24 [-0,389; 0,871] 0,395	0,983 [-1,291; 3,258]	
Week 24:					
Adjusted Mean Change (SE)	-0,34 (0,152)	-0,63 (0,285)	0,30 [-0,486; 1,079] 0,400	0,972 [-1,301; 3,245]	
Did you have chest tightness during the past 12 hours?					
Interaction Test	N.E.				
Region = Asia					
N'	50	53			
Baseline Mean (SD)	0,83 (0,762)	0,70 (0,685)			

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	-0,08 (0,064)	-0,10 (0,062)	0,02 [-0,152; 0,200] 0,788	0,054 [-0,335; 0,442]
Week 16:				
Adjusted Mean Change (SE)	-0,20 (0,070)	-0,12 (0,068)	-0,08 [-0,270; 0,115] 0,427	-0,159 [-0,550; 0,232]
Week 24:				
Adjusted Mean Change (SE)	-0,19 (0,069)	-0,19 (0,068)	0,00 [-0,190; 0,193] 0,985	0,004 [-0,392; 0,400]
Region = Europe				
N'	79	80		
Baseline Mean (SD)	0,75 (0,622)	0,68 (0,601)		
Week 8:				
Adjusted Mean Change (SE)	-0,12 (0,046)	-0,12 (0,046)	0,00 [-0,125; 0,130] 0,969	0,006 [-0,305; 0,317]
Week 16:				
Adjusted Mean Change (SE)	-0,22 (0,050)	-0,18 (0,050)	-0,04 [-0,180; 0,099] 0,569	-0,091 [-0,402; 0,220]
Week 24:				
Adjusted Mean Change (SE)	-0,23 (0,053)	-0,23 (0,053)	-0,01 [-0,154; 0,140] 0,926	-0,015 [-0,330; 0,300]
Region = Latin America				
N'	100	84		
Baseline Mean (SD)	0,63 (0,660)	0,49 (0,568)		
Week 8:				
Adjusted Mean Change (SE)	-0,08 (0,040)	-0,11 (0,044)	0,03 [-0,089; 0,145] 0,633	0,073 [-0,226; 0,372]
Week 16:				
Adjusted Mean Change (SE)	-0,15 (0,045)	-0,17 (0,049)	0,01 [-0,119; 0,144] 0,850	0,028 [-0,264; 0,321]

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 24:				
Adjusted Mean Change (SE)	-0,19 (0,048)	-0,20 (0,052)	0,01 [-0,127; 0,150] 0,873	0,024 [-0,270; 0,318]
Region = Others				
N'	4	1		
Baseline Mean (SD)	0,74 (0,500)	0,67 (-)		
Week 8:				
Adjusted Mean Change (SE)	-0,67 (0,309)	-0,83 (0,586)	0,16 [-1,332; 1,649] 0,809	0,257 [-1,940; 2,454]
Week 16:				
Adjusted Mean Change (SE)	-0,67 (0,257)	-0,91 (0,488)	0,25 [-0,994; 1,486] 0,654	0,479 [-1,733; 2,690]
Week 24:				
Adjusted Mean Change (SE)	-0,62 (0,296)	-0,86 (0,562)	0,24 [-1,192; 1,666] 0,706	0,401 [-1,804; 2,607]
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 + 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 + region + region * treatment + region * treatment * visit, within-patient correlation: compound symmetry covariance matrix, Percentage of days with no day-time symptoms: treatment + visit + 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 night-time awakenings: treatment + visit + 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 + region + region * treatment + region * treatment * visit, within-patient correlation: compound symmetry covariance matrix, Mean total daily symptom score: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region], Mean day-time symptom score: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + region + region * treatment + region * treatment * visit, within-patient correlation: compound symmetry covariance matrix, Mean night-time symptom score: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + region + region * treatment + region * treatment * visit, within-patient correlation: compound symmetry covariance matrix, Mean of: How did you sleep last night?: 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: Did your respiratory symptoms stop you from performing your usual daily activities?: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction [by region], Mean of: How severe was your shortness of breath today?: treatment + visit + baseline value + baseline-by-visit interaction + treatment-by-visit interaction + region + region * treatment + region * treatment * visit, within-patient correlation: compound symmetry covariance matrix, 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 + treatment-by-visit interaction [by region], Did you have chest tightness 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 subpopulation "high-dose ICS/LABA"				

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AMNOG Dossier Subpopulation high-dose ICS/LABA

IND/GLY/MF
CQVM149B2306

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Percentage of mornings with no symptoms on rising					
Interaction Test	0,762				
Asthma exacerbations in the 12 months prior to screening = 1					
N'	169	175			
Baseline Mean (SD)	35,77 (39,045)	42,79 (38,943)			
Week 8:					
Adjusted Mean Change (SE)	11,42 (2,869)	7,64 (2,848)	3,78 [-2,195; 9,753] 0,215	0,102	[0,112; 0,315]
Week 16:					
Adjusted Mean Change (SE)	19,22 (3,174)	13,62 (3,155)	5,60 [-1,461; 12,659] 0,120	0,136	[-0,077; 0,349]
Week 24:					
Adjusted Mean Change (SE)	21,22 (3,295)	16,36 (3,282)	4,86 [-2,620; 12,341] 0,203	0,114	[-0,100; 0,329]
Asthma exacerbations in the 12 months prior to screening = ≥2					
N'	62	44			
Baseline Mean (SD)	35,50 (37,335)	41,06 (39,671)			
Week 8:					
Adjusted Mean Change (SE)	6,69 (4,215)	7,24 (4,823)	-0,55 [-11,488; 10,393] 0,922	-0,017	[-0,411; 0,377]
Week 16:					
Adjusted Mean Change (SE)	12,66 (4,782)	10,31 (5,489)	2,35 [-10,533; 15,225] 0,721	0,064	[-0,325; 0,453]
Week 24:					
Adjusted Mean Change (SE)	16,96 (5,014)	10,67 (5,761)	6,29 [-7,369; 19,939] 0,366	0,165	[-0,229; 0,558]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Percentage of days with no day-time symptoms				
Interaction Test	0,928			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	170	172		
Baseline Mean (SD)	16,69 (29,262)	18,03 (31,148)		
Week 8:				
Adjusted Mean Change (SE)	10,59 (2,699)	8,45 (2,717)	2,14 [-3,389; 7,674] 0,447	0,061 [-0,153; 0,276]
Week 16:				
Adjusted Mean Change (SE)	20,28 (3,119)	15,11 (3,129)	5,17 [-1,851; 12,184] 0,149	0,127 [-0,086; 0,340]
Week 24:				
Adjusted Mean Change (SE)	22,00 (3,273)	18,84 (3,281)	3,17 [-4,370; 10,703] 0,410	0,075 [-0,140; 0,290]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	63	46		
Baseline Mean (SD)	16,47 (28,848)	19,30 (34,153)		
Week 8:				
Adjusted Mean Change (SE)	8,87 (3,913)	5,64 (4,434)	3,23 [-6,715; 13,176] 0,524	0,107 [-0,280; 0,493]
Week 16:				
Adjusted Mean Change (SE)	14,36 (4,687)	11,70 (5,362)	2,66 [-9,969; 15,290] 0,679	0,073 [-0,313; 0,460]
Week 24:				
Adjusted Mean Change (SE)	16,72 (4,963)	13,92 (5,690)	2,80 [-10,755; 16,356] 0,685	0,073 [-0,315; 0,461]
Percentage of days with no night-time awakenings				
Interaction Test	0,873			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	169	175		
Baseline Mean (SD)	57,57 (40,260)	69,80 (36,153)		

	Treatment groups		Comparison	
	E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 8:				
Adjusted Mean Change (SE)	11,00 (2,459)	8,67 (2,439)	2,32 [-2,839; 7,487] 0,377	0,073 [-0,140; 0,286]
Week 16:				
Adjusted Mean Change (SE)	14,65 (2,672)	13,86 (2,656)	0,80 [-5,131; 6,721] 0,792	0,023 [-0,190; 0,236]
Week 24:				
Adjusted Mean Change (SE)	14,80 (2,744)	16,50 (2,736)	-1,70 [-7,886; 4,484] 0,589	-0,048 [-0,263; 0,166]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	62	44		
Baseline Mean (SD)	56,07 (40,496)	55,55 (41,197)		
Week 8:				
Adjusted Mean Change (SE)	9,44 (3,620)	9,46 (4,149)	-0,01 [-9,424; 9,399] 0,998	-0,000 [-0,395; 0,394]
Week 16:				
Adjusted Mean Change (SE)	13,92 (4,016)	14,38 (4,611)	-0,46 [-11,218; 10,308] 0,934	-0,015 [-0,404; 0,374]
Week 24:				
Adjusted Mean Change (SE)	16,60 (4,161)	17,45 (4,778)	-0,84 [-12,086; 10,400] 0,883	-0,027 [-0,420; 0,366]
Percentage of days with no asthma symptoms				
Interaction Test	0,797			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	160	162		
Baseline Mean (SD)	14,54 (28,221)	16,96 (31,212)		
Week 8:				
Adjusted Mean Change (SE)	10,52 (2,647)	6,30 (2,662)	4,23 [-1,282; 9,735] 0,132	0,128 [-0,095; 0,351]
Week 16:				
Adjusted Mean Change (SE)	20,34 (3,118)	13,48 (3,129)	6,85 [-0,303; 14,004] 0,061	0,173 [-0,046; 0,393]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	22,91 (3,297)	16,51 (3,308)	6,40 [-1,343; 14,153] 0,105	0,155 [-0,067; 0,376]	
Asthma exacerbations in the 12 months prior to screening = ≥2					
N'	59	40			
Baseline Mean (SD)	12,58 (25,082)	18,88 (35,201)			
Week 8:					
Adjusted Mean Change (SE)	9,19 (3,891)	5,35 (4,516)	3,84 [-6,324; 14,009] 0,458	0,135 [-0,279; 0,549]	
Week 16:					
Adjusted Mean Change (SE)	16,06 (4,739)	12,43 (5,579)	3,62 [-9,530; 16,775] 0,589	0,101 [-0,302; 0,504]	
Week 24:					
Adjusted Mean Change (SE)	18,43 (5,080)	13,65 (5,993)	4,78 [-9,513; 19,078] 0,511	0,128 [-0,286; 0,542]	
Mean total daily symptom score					
Interaction Test	0,659				
Asthma exacerbations in the 12 months prior to screening = 1					
N'	160	162			
Baseline Mean (SD)	2,37 (1,645)	1,87 (1,432)			
Week 8:					
Adjusted Mean Change (SE)	-0,51 (0,103)	-0,40 (0,104)	-0,12 [-0,334; 0,102] 0,296	-0,090 [-0,312; 0,133]	
Week 16:					
Adjusted Mean Change (SE)	-0,78 (0,110)	-0,63 (0,111)	-0,15 [-0,396; 0,086] 0,208	-0,111 [-0,330; 0,109]	
Week 24:					
Adjusted Mean Change (SE)	-0,86 (0,112)	-0,72 (0,113)	-0,14 [-0,388; 0,105] 0,261	-0,101 [-0,322; 0,121]	
Asthma exacerbations in the 12 months prior to screening = ≥2					
N'	59	40			
Baseline Mean (SD)	2,35 (1,777)	2,21 (1,613)			

	Treatment groups		Comparison	
	E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 8:				
Adjusted Mean Change (SE)	-0,42 (0,152)	-0,44 (0,177)	0,02 [-0,374; 0,422] 0,907	0,021 [-0,392; 0,435]
Week 16:				
Adjusted Mean Change (SE)	-0,68 (0,164)	-0,64 (0,191)	-0,04 [-0,481; 0,399] 0,855	-0,033 [-0,436; 0,370]
Week 24:				
Adjusted Mean Change (SE)	-0,82 (0,167)	-0,74 (0,196)	-0,08 [-0,534; 0,370] 0,721	-0,067 [-0,481; 0,346]
Mean day-time symptom score				
Interaction Test	0,894			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	170	172		
Baseline Mean (SD)	0,93 (0,600)	0,80 (0,538)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,040)	-0,16 (0,040)	-0,01 [-0,089; 0,076] 0,871	-0,013 [-0,228; 0,201]
Week 16:				
Adjusted Mean Change (SE)	-0,28 (0,043)	-0,24 (0,043)	-0,04 [-0,138; 0,049] 0,349	-0,079 [-0,292; 0,134]
Week 24:				
Adjusted Mean Change (SE)	-0,31 (0,044)	-0,28 (0,045)	-0,03 [-0,125; 0,069] 0,570	-0,049 [-0,264; 0,166]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	63	46		
Baseline Mean (SD)	0,89 (0,622)	0,91 (0,598)		
Week 8:				
Adjusted Mean Change (SE)	-0,12 (0,058)	-0,13 (0,066)	0,00 [-0,143; 0,152] 0,953	0,010 [-0,377; 0,396]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,064)	-0,20 (0,072)	-0,03 [-0,202; 0,132] 0,681	-0,071 [-0,457; 0,315]

	Treatment groups		Comparison	
	E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,066)	-0,27 (0,075)	-0,01 [-0,187; 0,161] 0,884	-0,026 [-0,413; 0,362]
Mean night-time symptom score				
Interaction Test	0,842			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	169	175		
Baseline Mean (SD)	0,72 (0,569)	0,55 (0,476)		
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,033)	-0,13 (0,033)	-0,04 [-0,114; 0,025] 0,211	-0,103 [-0,317; 0,110]
Week 16:				
Adjusted Mean Change (SE)	-0,25 (0,035)	-0,21 (0,035)	-0,03 [-0,110; 0,041] 0,370	-0,077 [-0,290; 0,136]
Week 24:				
Adjusted Mean Change (SE)	-0,27 (0,035)	-0,24 (0,035)	-0,02 [-0,102; 0,054] 0,542	-0,053 [-0,268; 0,162]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	62	44		
Baseline Mean (SD)	0,76 (0,624)	0,68 (0,564)		
Week 8:				
Adjusted Mean Change (SE)	-0,14 (0,049)	-0,14 (0,056)	-0,00 [-0,130; 0,124] 0,960	-0,009 [-0,403; 0,386]
Week 16:				
Adjusted Mean Change (SE)	-0,22 (0,052)	-0,21 (0,059)	-0,02 [-0,154; 0,121] 0,816	-0,041 [-0,430; 0,348]
Week 24:				
Adjusted Mean Change (SE)	-0,27 (0,053)	-0,23 (0,061)	-0,04 [-0,181; 0,102] 0,586	-0,097 [-0,491; 0,296]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Mean of: How did you sleep last night?				
Interaction Test	0,876			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	169	175		
Baseline Mean (SD)	0,57 (0,614)	0,38 (0,498)		
Week 8:				
Adjusted Mean Change (SE)	-0,18 (0,031)	-0,15 (0,030)	-0,03 [-0,093; 0,037] 0,398	-0,070 [-0,284; 0,143]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,032)	-0,22 (0,032)	-0,01 [-0,075; 0,065] 0,886	-0,012 [-0,225; 0,201]
Week 24:				
Adjusted Mean Change (SE)	-0,23 (0,032)	-0,25 (0,032)	0,02 [-0,053; 0,088] 0,624	0,042 [-0,172; 0,257]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	62	44		
Baseline Mean (SD)	0,62 (0,655)	0,55 (0,568)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,045)	-0,15 (0,052)	-0,02 [-0,138; 0,098] 0,744	-0,057 [-0,451; 0,337]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,048)	-0,22 (0,055)	-0,01 [-0,138; 0,116] 0,866	-0,030 [-0,419; 0,359]
Week 24:				
Adjusted Mean Change (SE)	-0,26 (0,048)	-0,25 (0,055)	-0,02 [-0,145; 0,112] 0,800	-0,045 [-0,438; 0,348]
Mean of: Did you have asthma symptoms upon awakening in the morning?				
Interaction Test	0,709			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	169	175		
Baseline Mean (SD)	0,87 (0,633)	0,72 (0,581)		

	Treatment groups		Comparison	
	E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,042)	-0,11 (0,042)	-0,06 [-0,145; 0,031] 0,206	-0,104 [-0,317; 0,109]
Week 16:				
Adjusted Mean Change (SE)	-0,27 (0,045)	-0,21 (0,045)	-0,06 [-0,158; 0,039] 0,235	-0,102 [-0,315; 0,111]
Week 24:				
Adjusted Mean Change (SE)	-0,30 (0,047)	-0,24 (0,047)	-0,06 [-0,168; 0,041] 0,231	-0,106 [-0,320; 0,109]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	62	44		
Baseline Mean (SD)	0,90 (0,701)	0,81 (0,650)		
Week 8:				
Adjusted Mean Change (SE)	-0,11 (0,062)	-0,12 (0,071)	0,01 [-0,148; 0,175] 0,869	0,029 [-0,366; 0,423]
Week 16:				
Adjusted Mean Change (SE)	-0,21 (0,068)	-0,19 (0,077)	-0,02 [-0,202; 0,157] 0,807	-0,043 [-0,432; 0,346]
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,071)	-0,21 (0,081)	-0,06 [-0,253; 0,126] 0,512	-0,118 [-0,512; 0,275]
Mean of: Did your respiratory symptoms stop you from performing your usual daily activities?				
Interaction Test	0,942			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	170	172		
Baseline Mean (SD)	0,96 (0,678)	0,82 (0,653)		
Week 8:				
Adjusted Mean Change (SE)	-0,17 (0,045)	-0,19 (0,046)	0,02 [-0,076; 0,111] 0,712	0,030 [-0,185; 0,244]
Week 16:				
Adjusted Mean Change (SE)	-0,28 (0,049)	-0,26 (0,049)	-0,02 [-0,130; 0,083] 0,664	-0,037 [-0,249; 0,176]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	-0,30 (0,050)	-0,29 (0,050)	-0,01 [-0,124; 0,096] 0,803	-0,022 [-0,237; 0,193]	
Asthma exacerbations in the 12 months prior to screening = ≥2					
N'	63	46			
Baseline Mean (SD)	0,89 (0,762)	0,97 (0,717)			
Week 8:					
Adjusted Mean Change (SE)	-0,14 (0,066)	-0,13 (0,074)	-0,01 [-0,175; 0,159] 0,923	-0,016 [-0,403; 0,370]	
Week 16:					
Adjusted Mean Change (SE)	-0,26 (0,073)	-0,21 (0,083)	-0,04 [-0,234; 0,149] 0,663	-0,075 [-0,462; 0,311]	
Week 24:					
Adjusted Mean Change (SE)	-0,30 (0,074)	-0,31 (0,085)	0,01 [-0,190; 0,206] 0,936	0,014 [-0,374; 0,402]	
Mean of: How severe was your shortness of breath today?					
Interaction Test	0,673				
Asthma exacerbations in the 12 months prior to screening = 1					
N'	170	172			
Baseline Mean (SD)	1,08 (0,666)	0,96 (0,627)			
Week 8:					
Adjusted Mean Change (SE)	-0,24 (0,045)	-0,21 (0,046)	-0,02 [-0,116; 0,070] 0,629	-0,039 [-0,254; 0,175]	
Week 16:					
Adjusted Mean Change (SE)	-0,38 (0,049)	-0,31 (0,049)	-0,07 [-0,178; 0,034] 0,181	-0,113 [-0,326; 0,100]	
Week 24:					
Adjusted Mean Change (SE)	-0,41 (0,050)	-0,34 (0,051)	-0,07 [-0,184; 0,037] 0,192	-0,113 [-0,328; 0,102]	
Asthma exacerbations in the 12 months prior to screening = ≥2					
N'	63	46			
Baseline Mean (SD)	1,04 (0,688)	1,03 (0,665)			

	Treatment groups		Comparison	
	E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 8:				
Adjusted Mean Change (SE)	-0,15 (0,066)	-0,16 (0,074)	0,01 [-0,159; 0,176] 0,923	0,016 [-0,370; 0,403]
Week 16:				
Adjusted Mean Change (SE)	-0,29 (0,072)	-0,24 (0,082)	-0,05 [-0,236; 0,144] 0,634	-0,082 [-0,469; 0,304]
Week 24:				
Adjusted Mean Change (SE)	-0,33 (0,075)	-0,33 (0,085)	-0,00 [-0,201; 0,196] 0,980	-0,004 [-0,392; 0,383]
Mean of: How was your wheeze during the past 12 hours?				
Interaction Test	0,594			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	170	172		
Baseline Mean (SD)	0,95 (0,676)	0,75 (0,610)		
Week 8:				
Adjusted Mean Change (SE)	-0,19 (0,045)	-0,17 (0,046)	-0,02 [-0,116; 0,071] 0,640	-0,038 [-0,252; 0,177]
Week 16:				
Adjusted Mean Change (SE)	-0,30 (0,049)	-0,24 (0,049)	-0,06 [-0,163; 0,047] 0,278	-0,091 [-0,304; 0,121]
Week 24:				
Adjusted Mean Change (SE)	-0,32 (0,050)	-0,28 (0,050)	-0,04 [-0,147; 0,074] 0,515	-0,057 [-0,272; 0,159]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	63	46		
Baseline Mean (SD)	0,93 (0,711)	0,93 (0,682)		
Week 8:				
Adjusted Mean Change (SE)	-0,14 (0,066)	-0,19 (0,075)	0,05 [-0,116; 0,219] 0,544	0,102 [-0,285; 0,488]
Week 16:				
Adjusted Mean Change (SE)	-0,26 (0,072)	-0,25 (0,082)	-0,02 [-0,206; 0,170] 0,850	-0,033 [-0,419; 0,354]

	Treatment groups		Comparison	
	E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:				
Adjusted Mean Change (SE)	-0,29 (0,074)	-0,31 (0,085)	0,01 [-0,187; 0,208]	0,019 [-0,369; 0,406] 0,915
Mean of: How was your cough during the past 12 hours?				
Interaction Test	0,567			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	170	172		
Baseline Mean (SD)	0,95 (0,669)	0,87 (0,629)		
Week 8:				
Adjusted Mean Change (SE)	-0,14 (0,047)	-0,13 (0,047)	-0,01 [-0,108; 0,086]	-0,018 [-0,233; 0,196] 0,820
Week 16:				
Adjusted Mean Change (SE)	-0,26 (0,051)	-0,24 (0,051)	-0,02 [-0,126; 0,095]	-0,023 [-0,236; 0,189] 0,785
Week 24:				
Adjusted Mean Change (SE)	-0,28 (0,052)	-0,29 (0,052)	0,01 [-0,104; 0,125]	0,016 [-0,199; 0,231] 0,857
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	63	46		
Baseline Mean (SD)	0,89 (0,644)	0,88 (0,708)		
Week 8:				
Adjusted Mean Change (SE)	-0,14 (0,068)	-0,10 (0,077)	-0,04 [-0,209; 0,138]	-0,067 [-0,453; 0,319] 0,690
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,075)	-0,18 (0,086)	-0,05 [-0,252; 0,146]	-0,091 [-0,477; 0,296] 0,602
Week 24:				
Adjusted Mean Change (SE)	-0,32 (0,077)	-0,21 (0,088)	-0,11 [-0,313; 0,099]	-0,179 [-0,568; 0,209] 0,308

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Did you have chest tightness during the past 12 hours?				
Interaction Test	0,849			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	170	172		
Baseline Mean (SD)	0,72 (0,666)	0,59 (0,613)		
Week 8:				
Adjusted Mean Change (SE)	-0,09 (0,043)	-0,10 (0,043)	0,01 [-0,078; 0,099] 0,822	0,018 [-0,196; 0,233]
Week 16:				
Adjusted Mean Change (SE)	-0,19 (0,046)	-0,15 (0,046)	-0,04 [-0,137; 0,058] 0,427	-0,066 [-0,279; 0,146]
Week 24:				
Adjusted Mean Change (SE)	-0,20 (0,047)	-0,19 (0,047)	-0,01 [-0,114; 0,089] 0,807	-0,021 [-0,236; 0,194]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	63	46		
Baseline Mean (SD)	0,69 (0,683)	0,71 (0,612)		
Week 8:				
Adjusted Mean Change (SE)	-0,03 (0,062)	-0,04 (0,071)	0,01 [-0,152; 0,166] 0,930	0,015 [-0,372; 0,401]
Week 16:				
Adjusted Mean Change (SE)	-0,12 (0,067)	-0,10 (0,076)	-0,02 [-0,192; 0,158] 0,847	-0,033 [-0,420; 0,353]
Week 24:				
Adjusted Mean Change (SE)	-0,15 (0,069)	-0,17 (0,079)	0,02 [-0,160; 0,204] 0,811	0,042 [-0,346; 0,429]
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 + 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 subpopulation "high-dose ICS/LABA"				

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10. E-Diary - Rescue Medication

Table 10.1 Rescue Medication - Documentation Rate (FAS)

Treatment groups			
Outcome - Documentation Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Total N=474
Rescue medication during the night - Documentation rate in standardized days*, n (%)			
Baseline	70%-100%	217 (89,7)	205 (88,4)
	50%-<70%	18 (7,4)	19 (8,2)
	<50%	7 (2,9)	8 (3,4)
Baseline to Week 8	70%-100%	210 (86,8)	207 (89,2)
	50%-<70%	19 (7,9)	12 (5,2)
	<50%	13 (5,4)	13 (5,6)
Week 9 to Week 16	70%-100%	198 (81,8)	200 (86,2)
	50%-<70%	24 (9,9)	14 (6,0)
	<50%	20 (8,3)	18 (7,8)
Week 17 to Week 24	70%-100%	192 (79,3)	192 (82,8)
	50%-<70%	24 (9,9)	11 (4,7)
	<50%	26 (10,7)	29 (12,5)
Baseline to Week 24	70%-100%	204 (84,3)	196 (84,5)
	50%-<70%	20 (8,3)	16 (6,9)
	<50%	18 (7,4)	20 (8,6)
Rescue medication during the day - Documentation rate in standardized days*, n (%)			
Baseline	70%-100%	214 (88,4)	208 (89,7)
	50%-<70%	22 (9,1)	15 (6,5)
	<50%	6 (2,5)	9 (3,9)
Baseline to Week 8	70%-100%	207 (85,5)	200 (86,2)
	50%-<70%	24 (9,9)	18 (7,8)
	<50%	11 (4,5)	14 (6,0)
Week 9 to Week 16	70%-100%	202 (83,5)	195 (84,1)
	50%-<70%	21 (8,7)	16 (6,9)
	<50%	19 (7,9)	21 (9,1)
Week 17 to Week 24	70%-100%	197 (81,4)	173 (74,6)
	50%-<70%	18 (7,4)	28 (12,1)
	<50%	27 (11,2)	31 (13,4)

Treatment groups				
Outcome - Documentation Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Total N=474	
Baseline to Week 24	70%-100% 50%-<70% <50%	201 (83,1) 23 (9,5) 18 (7,4)	191 (82,3) 20 (8,6) 21 (9,1)	392 (82,7) 43 (9,1) 39 (8,2)
Rescue medication free days - Documentation rate in standardized days*, n (%)				
Baseline	70%-100% 50%-<70% <50%	213 (88,0) 20 (8,3) 9 (3,7)	203 (87,5) 15 (6,5) 14 (6,0)	416 (87,8) 35 (7,4) 23 (4,9)
Baseline to Week 8	70%-100% 50%-<70% <50%	201 (83,1) 23 (9,5) 18 (7,4)	190 (81,9) 27 (11,6) 15 (6,5)	391 (82,5) 50 (10,5) 33 (7,0)
Week 9 to Week 16	70%-100% 50%-<70% <50%	185 (76,4) 24 (9,9) 33 (13,6)	185 (79,7) 20 (8,6) 27 (11,6)	370 (78,1) 44 (9,3) 60 (12,7)
Week 17 to Week 24	70%-100% 50%-<70% <50%	175 (72,3) 26 (10,7) 41 (16,9)	171 (73,7) 25 (10,8) 36 (15,5)	346 (73,0) 51 (10,8) 77 (16,2)
Baseline to Week 24	70%-100% 50%-<70% <50%	182 (75,2) 34 (14,0) 26 (10,7)	182 (78,4) 25 (10,8) 25 (10,8)	364 (76,8) 59 (12,4) 51 (10,8)

* 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 subpopulation "high-dose ICS/LABA"

Table 10.2 Rescue Medication - Change from Baseline (FAS)

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Daily number of puffs of rescue medication during the night					
N'	231	219			
Baseline Mean (SD)	0,80 (1,064)	0,62 (0,838)			
Week 8:					
Adjusted Mean Change (SE)	-0,23 (0,052)	-0,20 (0,052)	-0,03 [-0,129; 0,076] 0,612	-0,034	[-0,221; 0,153]
Week 16:					
Adjusted Mean Change (SE)	-0,29 (0,055)	-0,32 (0,055)	0,03 [-0,080; 0,146] 0,567	0,040	[-0,146; 0,227]
Week 24:					
Adjusted Mean Change (SE)	-0,34 (0,056)	-0,32 (0,057)	-0,02 [-0,137; 0,099] 0,752	-0,023	[-0,211; 0,165]
Daily number of puffs of rescue medication during the day					
N'	233	218			
Baseline Mean (SD)	1,20 (1,366)	1,06 (1,147)			
Week 8:					
Adjusted Mean Change (SE)	-0,29 (0,070)	-0,32 (0,071)	0,03 [-0,104; 0,164] 0,662	0,029	[-0,158; 0,216]
Week 16:					
Adjusted Mean Change (SE)	-0,44 (0,074)	-0,44 (0,076)	0,01 [-0,145; 0,158] 0,930	0,006	[-0,180; 0,192]
Week 24:					
Adjusted Mean Change (SE)	-0,49 (0,076)	-0,49 (0,077)	0,01 [-0,151; 0,164] 0,935	0,006	[-0,182; 0,193]
Percentage of rescue medication free days					
N'	228	211			
Baseline Mean (SD)	38,91 (39,462)	40,49 (41,094)			
Week 8:					
Adjusted Mean Change (SE)	9,37 (2,663)	12,94 (2,713)	-3,58 [-8,788; 1,637] 0,178	-0,091	[-0,281; 0,099]

E-Diary - Change from Baseline (FAS)	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 16:				
Adjusted Mean Change (SE)	17,10 (2,902)	19,03 (2,973)	-1,93 [-8,085; 4,222] 0,538	-0,045 [-0,233; 0,144]
Week 24:				
Adjusted Mean Change (SE)	20,33 (2,958)	21,06 (3,031)	-0,73 [-7,092; 5,623] 0,821	-0,017 [-0,208; 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, 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 subpopulation "high-dose ICS/LABA"				

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Daily number of puffs of rescue medication during the night					
Interaction Test	0,995				
Age = 18-39 years					
N'	38	30			
Baseline Mean (SD)	0,74 (1,530)	0,65 (1,039)			
Week 8:					
Adjusted Mean Change (SE)	-0,28 (0,100)	-0,20 (0,107)	-0,08 [-0,345; 0,190] 0,569	-0,135 [-0,634; 0,365]	
Week 16:					
Adjusted Mean Change (SE)	-0,29 (0,107)	-0,36 (0,117)	0,06 [-0,228; 0,356] 0,666	0,099 [-0,380; 0,578]	
Week 24:					
Adjusted Mean Change (SE)	-0,36 (0,110)	-0,37 (0,121)	0,01 [-0,294; 0,311] 0,958	0,012 [-0,469; 0,494]	
Age = 40-64 years					
N'	135	142			
Baseline Mean (SD)	0,82 (0,923)	0,62 (0,803)			
Week 8:					
Adjusted Mean Change (SE)	-0,25 (0,059)	-0,22 (0,059)	-0,03 [-0,161; 0,099] 0,636	-0,046 [-0,283; 0,192]	
Week 16:					
Adjusted Mean Change (SE)	-0,31 (0,063)	-0,34 (0,063)	0,03 [-0,113; 0,176] 0,666	0,043 [-0,194; 0,280]	
Week 24:					
Adjusted Mean Change (SE)	-0,37 (0,065)	-0,34 (0,065)	-0,02 [-0,170; 0,129] 0,790	-0,027 [-0,267; 0,213]	
Age = ≥65 years					
N'	58	47			
Baseline Mean (SD)	0,81 (1,022)	0,58 (0,817)			

	Treatment groups		Comparison	
	E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 8:				
Adjusted Mean Change (SE)	-0,13 (0,082)	-0,13 (0,089)	-0,00 [-0,213; 0,210] 0,989	-0,002 [-0,387; 0,382]
Week 16:				
Adjusted Mean Change (SE)	-0,23 (0,090)	-0,23 (0,098)	-0,00 [-0,237; 0,236] 0,995	-0,001 [-0,391; 0,389]
Week 24:				
Adjusted Mean Change (SE)	-0,27 (0,093)	-0,22 (0,100)	-0,05 [-0,294; 0,195] 0,691	-0,072 [-0,462; 0,318]
Daily number of puffs of rescue medication during the day				
Interaction Test	0,519			
Age = 18-39 years				
N'	37	31		
Baseline Mean (SD)	0,95 (1,579)	1,20 (1,235)		
Week 8:				
Adjusted Mean Change (SE)	-0,31 (0,131)	-0,28 (0,139)	-0,03 [-0,374; 0,318] 0,873	-0,036 [-0,524; 0,451]
Week 16:				
Adjusted Mean Change (SE)	-0,44 (0,145)	-0,39 (0,156)	-0,05 [-0,439; 0,344] 0,812	-0,055 [-0,536; 0,427]
Week 24:				
Adjusted Mean Change (SE)	-0,55 (0,150)	-0,50 (0,161)	-0,06 [-0,465; 0,349] 0,780	-0,065 [-0,553; 0,422]
Age = 40-64 years				
N'	138	141		
Baseline Mean (SD)	1,27 (1,308)	1,05 (1,120)		
Week 8:				
Adjusted Mean Change (SE)	-0,32 (0,078)	-0,39 (0,079)	0,07 [-0,100; 0,240] 0,418	0,076 [-0,162; 0,314]
Week 16:				
Adjusted Mean Change (SE)	-0,44 (0,085)	-0,51 (0,086)	0,07 [-0,124; 0,261] 0,483	0,068 [-0,167; 0,304]

		Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Week 24:					
Adjusted Mean Change (SE)	-0,50 (0,087)	-0,56 (0,088)	0,06 [-0,139; 0,261] 0,550	0,060 [-0,179; 0,299]	
Age = ≥65 years					
N'	58	46			
Baseline Mean (SD)	1,18 (1,361)	0,98 (1,184)			
Week 8:					
Adjusted Mean Change (SE)	-0,21 (0,109)	-0,13 (0,119)	-0,08 [-0,359; 0,199] 0,576	-0,097 [-0,487; 0,292]	
Week 16:					
Adjusted Mean Change (SE)	-0,42 (0,121)	-0,26 (0,132)	-0,15 [-0,472; 0,162] 0,338	-0,172 [-0,563; 0,220]	
Week 24:					
Adjusted Mean Change (SE)	-0,42 (0,124)	-0,29 (0,136)	-0,13 [-0,457; 0,200] 0,441	-0,138 [-0,527; 0,251]	
Percentage of rescue medication free days					
Interaction Test	0,299				
Age = 18-39 years					
N'	37	28			
Baseline Mean (SD)	54,79 (40,831)	38,52 (38,476)			
Week 8:					
Adjusted Mean Change (SE)	9,71 (5,171)	16,12 (5,531)	-6,41 [-20,242; 7,421] 0,363	-0,221 [-0,733; 0,292]	
Week 16:					
Adjusted Mean Change (SE)	16,60 (5,783)	19,20 (6,453)	-2,60 [-18,719; 13,512] 0,751	-0,075 [-0,566; 0,416]	
Week 24:					
Adjusted Mean Change (SE)	23,07 (5,967)	21,20 (6,654)	1,87 [-14,806; 18,554] 0,825	0,054 [-0,449; 0,556]	
Age = 40-64 years					
N'	135	137			
Baseline Mean (SD)	34,21 (38,191)	38,98 (40,985)			

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	9,88 (2,996)	15,59 (3,041)	-5,72 [-12,299; 0,863] 0,088	-0,164 [-0,403; 0,076]
Week 16:				
Adjusted Mean Change (SE)	17,40 (3,358)	22,23 (3,393)	-4,83 [-12,624; 2,967] 0,224	-0,123 [-0,362; 0,116]
Week 24:				
Adjusted Mean Change (SE)	21,12 (3,439)	24,28 (3,477)	-3,17 [-11,232; 4,899] 0,441	-0,080 [-0,324; 0,163]
Age = ≥65 years				
N'	56	46		
Baseline Mean (SD)	39,77 (39,467)	46,18 (43,282)		
Week 8:				
Adjusted Mean Change (SE)	8,30 (4,235)	3,35 (4,574)	4,95 [-5,875; 15,776] 0,370	0,159 [-0,235; 0,554]
Week 16:				
Adjusted Mean Change (SE)	17,04 (4,848)	9,70 (5,250)	7,34 [-5,474; 20,152] 0,261	0,206 [-0,189; 0,601]
Week 24:				
Adjusted Mean Change (SE)	17,05 (4,970)	11,77 (5,370)	5,28 [-7,897; 18,463] 0,432	0,144 [-0,248; 0,536]
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 + 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 subpopulation "high-dose ICS/LABA"				

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Daily number of puffs of rescue medication during the night					
Interaction Test	0,241				
Gender = Male					
N'	86	78			
Baseline Mean (SD)	0,94 (1,059)	0,53 (0,821)			
Week 8:					
Adjusted Mean Change (SE)	-0,12 (0,069)	-0,24 (0,074)	0,12 [-0,046; 0,293] 0,154	0,195 [-0,116; 0,506]	
Week 16:					
Adjusted Mean Change (SE)	-0,24 (0,074)	-0,34 (0,079)	0,11 [-0,081; 0,296] 0,263	0,156 [-0,153; 0,464]	
Week 24:					
Adjusted Mean Change (SE)	-0,33 (0,077)	-0,33 (0,082)	-0,00 [-0,196; 0,195] 0,997	-0,001 [-0,310; 0,309]	
Gender = Female					
N'	145	141			
Baseline Mean (SD)	0,73 (1,063)	0,66 (0,846)			
Week 8:					
Adjusted Mean Change (SE)	-0,30 (0,060)	-0,19 (0,058)	-0,11 [-0,241; 0,015] 0,083	-0,161 [-0,396; 0,073]	
Week 16:					
Adjusted Mean Change (SE)	-0,33 (0,064)	-0,32 (0,063)	-0,01 [-0,152; 0,131] 0,882	-0,014 [-0,248; 0,220]	
Week 24:					
Adjusted Mean Change (SE)	-0,36 (0,065)	-0,33 (0,065)	-0,03 [-0,178; 0,117] 0,687	-0,040 [-0,276; 0,197]	

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Daily number of puffs of rescue medication during the day				
Interaction Test	0,621			
Gender = Male				
N'	86	75		
Baseline Mean (SD)	1,44 (1,516)	1,03 (1,175)		
Week 8:				
Adjusted Mean Change (SE)	-0,20 (0,091)	-0,33 (0,099)	0,13 [-0,097; 0,352] 0,266	0,150 [-0,161; 0,461]
Week 16:				
Adjusted Mean Change (SE)	-0,37 (0,100)	-0,43 (0,109)	0,06 [-0,198; 0,312] 0,662	0,061 [-0,250; 0,371]
Week 24:				
Adjusted Mean Change (SE)	-0,46 (0,103)	-0,46 (0,112)	-0,01 [-0,270; 0,259] 0,967	-0,006 [-0,317; 0,306]
Gender = Female				
N'	147	143		
Baseline Mean (SD)	1,06 (1,255)	1,07 (1,136)		
Week 8:				
Adjusted Mean Change (SE)	-0,35 (0,080)	-0,32 (0,079)	-0,03 [-0,195; 0,140] 0,748	-0,029 [-0,263; 0,205]
Week 16:				
Adjusted Mean Change (SE)	-0,48 (0,086)	-0,46 (0,085)	-0,02 [-0,212; 0,166] 0,809	-0,023 [-0,254; 0,209]
Week 24:				
Adjusted Mean Change (SE)	-0,51 (0,088)	-0,52 (0,088)	0,01 [-0,184; 0,209] 0,902	0,012 [-0,223; 0,247]
Percentage of rescue medication free days				
Interaction Test	0,724			
Gender = Male				
N'	86	74		
Baseline Mean (SD)	33,49 (38,618)	44,10 (41,926)		

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	5,19 (3,484)	12,33 (3,804)	-7,14 [-15,806; 1,530] 0,106	-0,222 [-0,536; 0,093]
Week 16:				
Adjusted Mean Change (SE)	14,18 (3,969)	18,76 (4,316)	-4,57 [-14,824; 5,675] 0,381	-0,124 [-0,436; 0,188]
Week 24:				
Adjusted Mean Change (SE)	21,53 (4,077)	19,74 (4,428)	1,79 [-8,804; 12,376] 0,741	0,048 [-0,268; 0,364]
Gender = Female				
N'	142	137		
Baseline Mean (SD)	42,20 (39,739)	38,53 (40,658)		
Week 8:				
Adjusted Mean Change (SE)	12,17 (3,093)	13,51 (3,030)	-1,34 [-7,885; 5,210] 0,688	-0,038 [-0,276; 0,201]
Week 16:				
Adjusted Mean Change (SE)	19,11 (3,418)	19,41 (3,387)	-0,30 [-8,029; 7,427] 0,939	-0,008 [-0,244; 0,228]
Week 24:				
Adjusted Mean Change (SE)	19,84 (3,493)	22,02 (3,467)	-2,17 [-10,165; 5,815] 0,593	-0,054 [-0,294; 0,186]
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 + 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 subpopulation "high-dose ICS/LABA"				

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=242	SAL/FLU + TIO N=232	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'	49	56			
Baseline Mean (SD)	0,63 (0,908)	0,50 (0,678)			
Week 8:					
Adjusted Mean Change (SE)	-0,22 (0,064)	-0,18 (0,060)	-0,04 [-0,214; 0,132] 0,642	-0,093 [-0,482; 0,297]	
Week 16:					
Adjusted Mean Change (SE)	-0,33 (0,070)	-0,25 (0,066)	-0,08 [-0,270; 0,112] 0,413	-0,163 [-0,552; 0,227]	
Week 24:					
Adjusted Mean Change (SE)	-0,39 (0,068)	-0,25 (0,064)	-0,14 [-0,328; 0,042] 0,129	-0,306 [-0,701; 0,089]	
Region = Europe					
N'	78	82			
Baseline Mean (SD)	0,67 (0,870)	0,56 (0,818)			
Week 8:					
Adjusted Mean Change (SE)	-0,21 (0,061)	-0,20 (0,059)	-0,01 [-0,181; 0,154] 0,872	-0,026 [-0,337; 0,285]	
Week 16:					
Adjusted Mean Change (SE)	-0,27 (0,066)	-0,33 (0,065)	0,06 [-0,119; 0,246] 0,494	0,109 [-0,203; 0,420]	
Week 24:					
Adjusted Mean Change (SE)	-0,30 (0,068)	-0,35 (0,067)	0,05 [-0,139; 0,238] 0,607	0,083 [-0,231; 0,397]	
Region = Latin America					
N'	100	80			
Baseline Mean (SD)	1,01 (1,247)	0,75 (0,947)			

	Treatment groups		Comparison	
	E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 8:				
Adjusted Mean Change (SE)	-0,19 (0,060)	-0,17 (0,066)	-0,02 [-0,201; 0,151] 0,783	-0,042 [-0,341; 0,257]
Week 16:				
Adjusted Mean Change (SE)	-0,24 (0,069)	-0,29 (0,077)	0,04 [-0,160; 0,246] 0,679	0,063 [-0,234; 0,359]
Week 24:				
Adjusted Mean Change (SE)	-0,30 (0,074)	-0,28 (0,082)	-0,02 [-0,241; 0,194] 0,831	-0,032 [-0,331; 0,266]
Region = Others				
N'	4	1		
Baseline Mean (SD)	0,48 (0,582)	1,17 (-)		
Week 8:				
Adjusted Mean Change (SE)	-0,22 (0,257)	1,51 (0,492)	-1,73 [-3,079; -0,386] 0,019 *	-3,367 [-6,393; -0,341]
Week 16:				
Adjusted Mean Change (SE)	-0,38 (0,236)	-0,55 (0,451)	0,17 [-1,061; 1,408] 0,749	0,368 [-1,835; 2,571]
Week 24:				
Adjusted Mean Change (SE)	-0,53 (0,165)	-0,10 (0,315)	-0,44 [-1,300; 0,426] 0,270	-1,325 [-3,665; 1,015]
Daily number of puffs of rescue medication during the day				
Interaction Test	0,616			
Region = Asia				
N'	50	53		
Baseline Mean (SD)	1,11 (1,221)	0,97 (1,134)		
Week 8:				
Adjusted Mean Change (SE)	-0,22 (0,113)	-0,31 (0,110)	0,09 [-0,221; 0,398] 0,574	0,111 [-0,277; 0,500]
Week 16:				
Adjusted Mean Change (SE)	-0,55 (0,113)	-0,45 (0,110)	-0,10 [-0,408; 0,211] 0,533	-0,124 [-0,515; 0,267]

	Treatment groups		Comparison	
	E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 24:				
Adjusted Mean Change (SE)	-0,59 (0,114)	-0,48 (0,110)	-0,11 [-0,422; 0,201] 0,485	-0,141 [-0,538; 0,256]
Region = Europe				
N'	79	80		
Baseline Mean (SD)	1,10 (1,261)	1,11 (1,209)		
Week 8:				
Adjusted Mean Change (SE)	-0,28 (0,090)	-0,23 (0,089)	-0,04 [-0,291; 0,205] 0,735	-0,054 [-0,365; 0,257]
Week 16:				
Adjusted Mean Change (SE)	-0,43 (0,090)	-0,32 (0,089)	-0,11 [-0,358; 0,139] 0,386	-0,137 [-0,449; 0,174]
Week 24:				
Adjusted Mean Change (SE)	-0,43 (0,090)	-0,40 (0,090)	-0,03 [-0,276; 0,222] 0,832	-0,034 [-0,349; 0,281]
Region = Latin America				
N'	100	84		
Baseline Mean (SD)	1,32 (1,534)	1,06 (1,108)		
Week 8:				
Adjusted Mean Change (SE)	-0,24 (0,080)	-0,32 (0,088)	0,08 [-0,156; 0,313] 0,510	0,100 [-0,199; 0,399]
Week 16:				
Adjusted Mean Change (SE)	-0,29 (0,080)	-0,44 (0,087)	0,16 [-0,076; 0,389] 0,187	0,197 [-0,096; 0,491]
Week 24:				
Adjusted Mean Change (SE)	-0,38 (0,080)	-0,49 (0,087)	0,11 [-0,125; 0,341] 0,364	0,136 [-0,158; 0,431]
Region = Others				
N'	4	1		
Baseline Mean (SD)	1,15 (0,440)	1,78 (-)		

	Treatment groups		Comparison	
	E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value
Week 8:				
Adjusted Mean Change (SE)	-0,39 (0,399)	1,54 (0,798)	-1,92 [-3,675; -0,175] 0,031 *	-2,414 [-5,067; 0,240]
Week 16:				
Adjusted Mean Change (SE)	-0,61 (0,399)	-1,03 (0,798)	0,41 [-1,336; 2,165] 0,642	0,520 [-1,695; 2,735]
Week 24:				
Adjusted Mean Change (SE)	-0,82 (0,399)	-0,73 (0,798)	-0,09 [-1,840; 1,661] 0,920	-0,112 [-2,305; 2,080]
Percentage of rescue medication free days				
Interaction Test	N.E.			
Region = Asia				
N'	48	51		
Baseline Mean (SD)	37,88 (40,959)	42,33 (42,085)		
Week 8:				
Adjusted Mean Change (SE)	5,09 (4,322)	14,24 (4,115)	-9,16 [-20,959; 2,647] 0,127	-0,314 [-0,717; 0,090]
Week 16:				
Adjusted Mean Change (SE)	24,75 (5,068)	19,80 (4,917)	4,95 [-9,010; 18,911] 0,484	0,142 [-0,256; 0,541]
Week 24:				
Adjusted Mean Change (SE)	25,02 (5,072)	20,29 (4,929)	4,73 [-9,251; 18,714] 0,505	0,138 [-0,267; 0,543]
Region = Europe				
N'	77	79		
Baseline Mean (SD)	42,44 (39,980)	43,13 (41,422)		
Week 8:				
Adjusted Mean Change (SE)	11,99 (2,959)	14,23 (2,921)	-2,25 [-10,438; 5,946] 0,590	-0,087 [-0,403; 0,229]
Week 16:				
Adjusted Mean Change (SE)	16,23 (3,434)	20,49 (3,390)	-4,25 [-13,761; 5,253] 0,379	-0,141 [-0,455; 0,173]

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 24:				
Adjusted Mean Change (SE)	19,09 (3,642)	24,44 (3,610)	-5,35 [-15,451; 4,754] 0,298	-0,169 [-0,488; 0,149]
Region = Latin America				
N'	99	80		
Baseline Mean (SD)	36,80 (39,081)	37,21 (40,413)		
Week 8:				
Adjusted Mean Change (SE)	11,12 (2,867)	13,90 (3,175)	-2,78 [-11,198; 5,636] 0,516	-0,100 [-0,400; 0,201]
Week 16:				
Adjusted Mean Change (SE)	16,34 (3,414)	19,39 (3,795)	-3,05 [-13,095; 6,995] 0,550	-0,090 [-0,387; 0,206]
Week 24:				
Adjusted Mean Change (SE)	21,19 (3,540)	20,71 (3,920)	0,48 [-9,915; 10,873] 0,928	0,014 [-0,286; 0,314]
Region = Others				
N'	4	1		
Baseline Mean (SD)	35,85 (25,808)	0,00 (-)		
Week 8:				
Adjusted Mean Change (SE)	26,56 (14,757)	-5,20 (28,941)	31,77 [-48,245; 111,775] 0,379	1,076 [-1,214; 3,367]
Week 16:				
Adjusted Mean Change (SE)	29,39 (18,436)	41,28 (36,157)	-11,88 [-111,842; 88,075] 0,787	-0,322 [-2,523; 1,878]

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 24:				
Adjusted Mean Change (SE)	29,79 (17,634)	36,12 (34,584)	-6,33 [-101,938; 89,283] 0,880	-0,179 [-2,374; 2,015]
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 + 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 + 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 rescue medication free days: 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 subpopulation "high-dose ICS/LABA"				

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

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Daily number of puffs of rescue medication during the night				
Interaction Test	0,097			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	169	175		
Baseline Mean (SD)	0,75 (1,073)	0,59 (0,782)		
Week 8:				
Adjusted Mean Change (SE)	-0,26 (0,055)	-0,19 (0,055)	-0,07 [-0,188; 0,045] 0,231	-0,099 [-0,312; 0,114]
Week 16:				
Adjusted Mean Change (SE)	-0,34 (0,059)	-0,32 (0,059)	-0,02 [-0,153; 0,106] 0,722	-0,031 [-0,243; 0,182]
Week 24:				
Adjusted Mean Change (SE)	-0,41 (0,060)	-0,33 (0,060)	-0,08 [-0,214; 0,054] 0,243	-0,102 [-0,317; 0,112]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	62	44		
Baseline Mean (SD)	0,94 (1,035)	0,70 (1,035)		
Week 8:				
Adjusted Mean Change (SE)	-0,12 (0,082)	-0,23 (0,094)	0,11 [-0,106; 0,322] 0,322	0,173 [-0,222; 0,568]
Week 16:				
Adjusted Mean Change (SE)	-0,13 (0,088)	-0,32 (0,101)	0,19 [-0,045; 0,427] 0,112	0,282 [-0,109; 0,673]
Week 24:				
Adjusted Mean Change (SE)	-0,15 (0,091)	-0,30 (0,104)	0,15 [-0,098; 0,391] 0,240	0,212 [-0,182; 0,606]

	Treatment groups		Comparison	
E-Diary - Change from Baseline (FAS) by Subgroup	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Daily number of puffs of rescue medication during the day				
Interaction Test	0,020 *			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	170	172		
Baseline Mean (SD)	1,19 (1,394)	1,05 (1,137)		
Week 8:				
Adjusted Mean Change (SE)	-0,34 (0,074)	-0,30 (0,075)	-0,03 [-0,185; 0,122] 0,684	-0,033 [-0,248; 0,182]
Week 16:				
Adjusted Mean Change (SE)	-0,52 (0,080)	-0,43 (0,080)	-0,10 [-0,271; 0,075] 0,266	-0,094 [-0,307; 0,119]
Week 24:				
Adjusted Mean Change (SE)	-0,58 (0,082)	-0,46 (0,082)	-0,12 [-0,303; 0,057] 0,180	-0,116 [-0,332; 0,099]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	63	46		
Baseline Mean (SD)	1,21 (1,299)	1,10 (1,194)		
Week 8:				
Adjusted Mean Change (SE)	-0,15 (0,108)	-0,36 (0,123)	0,21 [-0,068; 0,483] 0,140	0,249 [-0,139; 0,637]
Week 16:				
Adjusted Mean Change (SE)	-0,17 (0,118)	-0,47 (0,135)	0,30 [-0,010; 0,613] 0,058	0,329 [-0,060; 0,718]
Week 24:				
Adjusted Mean Change (SE)	-0,21 (0,122)	-0,60 (0,139)	0,39 [0,065; 0,712] 0,019 *	0,415 [0,023; 0,806]
Percentage of rescue medication free days				
Interaction Test	0,052			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	165	167		
Baseline Mean (SD)	38,97 (38,905)	42,63 (41,755)		

E-Diary - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	10,27 (2,855)	12,09 (2,869)	-1,82 [-7,810; 4,163] 0,550	-0,050 [-0,267; 0,167]
Week 16:				
Adjusted Mean Change (SE)	20,12 (3,155)	17,91 (3,173)	2,21 [-4,844; 9,269] 0,538	0,054 [-0,161; 0,270]
Week 24:				
Adjusted Mean Change (SE)	23,09 (3,223)	20,13 (3,244)	2,96 [-4,333; 10,256] 0,426	0,072 [-0,146; 0,291]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	63	44		
Baseline Mean (SD)	38,77 (41,204)	32,34 (37,828)		
Week 8:				
Adjusted Mean Change (SE)	7,04 (4,161)	16,11 (4,785)	-9,07 [-19,888; 1,746] 0,100	-0,287 [-0,685; 0,110]
Week 16:				
Adjusted Mean Change (SE)	9,05 (4,679)	23,20 (5,433)	-14,15 [-26,804; -1,492] 0,029 *	-0,389 [-0,782; 0,003]
Week 24:				
Adjusted Mean Change (SE)	12,98 (4,820)	24,51 (5,584)	-11,53 [-24,629; 1,572] 0,084	-0,314 [-0,712; 0,084]
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 + 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 subpopulation "high-dose ICS/LABA"				

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=242	SAL/FLU + TIO N=232	HR [95% CI] p-value
Asthma exacerbation			
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] 0,372
Severe asthma exacerbation			
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]	1,50 [0,93; 2,42] 0,094
SCS use due to asthma exacerbation (for at least three consecutive days)			
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] 0,184
ER visit and/or hospitalization due to asthma exacerbation			
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; 7,64] 0,360

Time-to-first outcome (FAS)	Treatment groups		Comparison
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	
ER visit due to asthma exacerbation			
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; 12,29] 0,299
Hospitalization due to asthma exacerbation			
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; 21,04] 0,598
<p>N': Number of patients in the analysis CI: Confidence Interval HR: Hazard Ratio [*]: p < 0,05 ⁺ K-M estimate (%) of outcome-free patients</p> <p>Applied model for HR: log(hazard ratio) = treatment + region + history of asthma exacerbation If it was not possible to fit the minimal model, the HR is not given.</p> <p>Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"</p>			

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

Time-to-first outcome by subgroup (FAS)	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	HR [95% CI] p-value	
Asthma exacerbation				
Interaction Test:	p=0,228			
Age = 18-39 years				
N'	40	33		
Number of patients with at least one event, n (%)	11 (27,5)	6 (18,2)		
Median (in weeks)	-	-		
% of outcome-free patients ⁺	72,50 [58,66; 86,34]	81,82 [68,66; 94,98]	1,59 [0,59; 4,31] 0,360	
Age = 40-64 years				
N'	144	150		
Number of patients with at least one event, n (%)	43 (29,9)	35 (23,3)		
Median (in weeks)	-	-		
% of outcome-free patients ⁺	68,09 [59,40; 76,78]	76,17 [69,26; 83,07]	1,35 [0,87; 2,12] 0,183	
Age = ≥65 years				
N'	58	49		
Number of patients with at least one event, n (%)	17 (29,3)	19 (38,8)		
Median (in weeks)	-	-		
% of outcome-free patients ⁺	70,34 [58,51; 82,18]	60,24 [46,33; 74,16]	0,71 [0,37; 1,38] 0,313	
Severe asthma exacerbation				
Interaction Test:	p=0,145			
Age = 18-39 years				
N'	40	33		
Number of patients with at least one event, n (%)	7 (17,5)	4 (12,1)		
Median (in weeks)	-	-		
% of outcome-free patients ⁺	82,50 [70,72; 94,28]	87,88 [76,74; 99,01]	1,50 [0,44; 5,13] 0,518	

Time-to-first outcome by subgroup (FAS)	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	HR [95% CI] p-value	
Age = 40-64 years				
N'	144	150		
Number of patients with at least one event, n (%)	28 (19,4)	15 (10,0)		
Median (in weeks)	-	-		
% of outcome-free patients ⁺	78,72 [70,96; 86,47]	89,75 [84,83; 94,67]	2,08 [1,11; 3,89] 0,022 *	
Age = ≥65 years				
N'	58	49		
Number of patients with at least one event, n (%)	8 (13,8)	9 (18,4)		
Median (in weeks)	-	-		
% of outcome-free patients ⁺	86,08 [77,12; 95,03]	81,26 [70,21; 92,31]	0,66 [0,25; 1,71] 0,394	
SCS use due to asthma exacerbation (for at least three consecutive days)				
Interaction Test:	p=0,187			
Age = 18-39 years				
N'	40	33		
Number of patients with at least one event, n (%)	7 (17,5)	5 (15,2)		
Median (in weeks)	-	-		
% of outcome-free patients ⁺	82,50 [70,72; 94,28]	84,85 [72,62; 97,08]	1,20 [0,38; 3,78] 0,757	
Age = 40-64 years				
N'	144	150		
Number of patients with at least one event, n (%)	26 (18,1)	15 (10,0)		
Median (in weeks)	-	-		
% of outcome-free patients ⁺	80,16 [72,58; 87,73]	89,73 [84,80; 94,66]	1,92 [1,01; 3,62] 0,045 *	

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	HR [95% CI] p-value
Age = ≥65 years			
N'	58	49	
Number of patients with at least one event, n (%)	10 (17,2)	11 (22,4)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	82,59 [72,78; 92,40]	76,98 [65,03; 88,93]	0,71 [0,30; 1,67] 0,432
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,535		
Age = 18-39 years			
N'	40	33	
Number of patients with at least one event, n (%)	2 (5,0)	2 (6,1)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	94,93 [88,09; 100,00]	93,94 [85,80; 100,00]	0,82 [0,12; 5,82] 0,841
Age = 40-64 years			
N'	144	150	
Number of patients with at least one event, n (%)	4 (2,8)	1 (0,7)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	97,19 [94,47; 99,91]	99,32 [97,98; 100,00]	4,38 [0,49; 39,23] 0,186
Age = ≥65 years			
N'	58	49	
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]	0,87 [0,00; -] 1,000

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	HR [95% CI] p-value
ER visit due to asthma exacerbation			
Interaction Test:	p=0,649		
Age = 18-39 years			
N'	40	33	
Number of patients with at least one event, n (%)	1 (2,5)	1 (3,0)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	97,50 [92,66; 100,00]	96,97 [91,12; 100,00]	0,83 [0,05; 13,24] 0,894
Age = 40-64 years			
N'	144	150	
Number of patients with at least one event, n (%)	4 (2,8)	1 (0,7)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	97,19 [94,47; 99,91]	99,32 [97,98; 100,00]	4,43 [0,50; 39,66] 0,183
Age = ≥65 years			
N'	58	49	
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]	0,79 [0,00; -] 1,000
Hospitalization due to asthma exacerbation			
Interaction Test:	p=1,000		
Age = 18-39 years			
N'	40	33	
Number of patients with at least one event, n (%)	1 (2,5)	1 (3,0)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	97,44 [92,48; 100,00]	96,97 [91,12; 100,00]	0,84 [0,05; 13,47] 0,900

Time-to-first outcome by subgroup (FAS)	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	HR [95% CI] p-value	
Age = 40-64 years				
N'	144	150		
Number of patients with at least one event, n (%)	1 (0,7)	0 (0,0)		
Median (in weeks)	-	-		
% of outcome-free patients ⁺	99,28 [97,88; 100,00]	100,00 [100,00; 100,00]		-
Age = ≥65 years				
N'	58	49		
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	
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 + age + age * treatment If it was not possible to fit the minimal model, the HR is not given.				
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"				

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=242	SAL/FLU + TIO N=232	HR [95% CI] p-value
Asthma exacerbation			
Interaction Test:	p=0,972		
Gender = Male			
N'	88	81	
Number of patients with at least one event, n (%)	23 (26,1)	19 (23,5)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	73,55 [64,27; 82,83]	76,54 [67,32; 85,77]	1,18 [0,64; 2,17] 0,592
Gender = Female			
N'	154	151	
Number of patients with at least one event, n (%)	48 (31,2)	41 (27,2)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	67,19 [58,97; 75,40]	71,99 [64,69; 79,28]	1,17 [0,77; 1,77] 0,473
Severe asthma exacerbation			
Interaction Test:	p=0,622		
Gender = Male			
N'	88	81	
Number of patients with at least one event, n (%)	16 (18,2)	9 (11,1)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	81,57 [73,41; 89,73]	88,89 [82,04; 95,73]	1,77 [0,78; 4,01] 0,170
Gender = Female			
N'	154	151	
Number of patients with at least one event, n (%)	27 (17,5)	19 (12,6)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	80,87 [73,71; 88,03]	87,03 [81,58; 92,48]	1,38 [0,76; 2,47] 0,288

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	HR [95% CI] p-value
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,739		
Gender = Male			
N'	88	81	
Number of patients with at least one event, n (%)	14 (15,9)	9 (11,1)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	83,92 [76,19; 91,64]	88,89 [82,04; 95,73]	1,54 [0,67; 3,56] 0,314
Gender = Female			
N'	154	151	
Number of patients with at least one event, n (%)	29 (18,8)	22 (14,6)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	79,60 [72,34; 86,86]	84,91 [79,09; 90,73]	1,30 [0,74; 2,26] 0,359
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,607		
Gender = Male			
N'	88	81	
Number of patients with at least one event, n (%)	1 (1,1)	1 (1,2)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	98,86 [96,65; 100,00]	98,77 [96,36; 100,00]	1,00 [0,06; 15,99] 1,000
Gender = Female			
N'	154	151	
Number of patients with at least one event, n (%)	5 (3,2)	2 (1,3)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	96,70 [93,86; 99,55]	98,63 [96,76; 100,00]	2,33 [0,45; 12,01] 0,312

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	HR [95% CI] p-value
ER visit due to asthma exacerbation			
Interaction Test:	p=0,995		
Gender = Male			
N'	88	81	
Number of patients with at least one event, n (%)	1 (1,1)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	98,86 [96,65; 100,00]	100,00 [100,00; 100,00]	-
Gender = Female			
N'	154	151	
Number of patients with at least one event, n (%)	4 (2,6)	2 (1,3)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	97,36 [94,81; 99,91]	98,63 [96,76; 100,00]	1,85 [0,34; 10,12] 0,476
Hospitalization due to asthma exacerbation			
Interaction Test:	p=0,995		
Gender = Male			
N'	88	81	
Number of patients with at least one event, n (%)	0 (0,0)	1 (1,2)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	100,00 [100,00; 100,00]	98,77 [96,36; 100,00]	0,00 [0,00; -] 0,997

Time-to-first outcome by subgroup (FAS)	Treatment groups		Comparison
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	
Gender = Female			
N ^a	154	151	
Number of patients with at least one event, n (%)	2 (1,3)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients ^b	98,66 [96,82; 100,00]	100,00 [100,00; 100,00]	-
N ^a : Number of patients in the analysis CI: Confidence Interval HR: Hazard Ratio ^a : p < 0,05 ^b K-M estimate (%) of outcome-free patients			
Applied model for HR: log(hazard ratio) = treatment + region + 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 subpopulation "high-dose ICS/LABA"			

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

Time-to-first outcome by subgroup (FAS)	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	HR [95% CI] p-value	
Asthma exacerbation				
Interaction Test:	p=0,793			
Region = Asia				
N'	53	59		
Number of patients with at least one event, n (%)	21 (39,6)	17 (28,8)		
Median (in weeks)	-	-		
% of outcome-free patients ⁺	57,82 [43,07; 72,56]	70,58 [58,79; 82,36]	1,43 [0,75; 2,71] 0,275	
Region = Europe				
N'	81	83		
Number of patients with at least one event, n (%)	25 (30,9)	21 (25,3)		
Median (in weeks)	-	-		
% of outcome-free patients ⁺	68,96 [58,85; 79,07]	74,61 [65,22; 83,99]	1,30 [0,72; 2,31] 0,382	
Region = Latin America				
N'	104	89		
Number of patients with at least one event, n (%)	24 (23,1)	22 (24,7)		
Median (in weeks)	-	-		
% of outcome-free patients ⁺	76,61 [68,41; 84,81]	74,62 [65,45; 83,80]	0,94 [0,53; 1,68] 0,833	
Region = Others				
N'	4	1		
Number of patients with at least one event, n (%)	1 (25,0)	0 (0,0)		
Median (in weeks)	-	-		
% of outcome-free patients ⁺	75,00 [32,57; 100,00]	100,00 [100,00; 100,00]	50027,29 [0,00; -] 0,980	

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	HR [95% CI] p-value
Severe asthma exacerbation			
Interaction Test:	p=0,430		
Region = Asia			
N'	53	59	
Number of patients with at least one event, n (%)	11 (20,8)	4 (6,8)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	76,36 [62,92; 89,80]	93,12 [86,62; 99,63]	3,21 [1,02; 10,09] 0,046 *
Region = Europe			
N'	81	83	
Number of patients with at least one event, n (%)	11 (13,6)	7 (8,4)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	86,35 [78,86; 93,85]	91,57 [85,59; 97,54]	1,64 [0,64; 4,24] 0,304
Region = Latin America			
N'	104	89	
Number of patients with at least one event, n (%)	21 (20,2)	17 (19,1)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	79,52 [71,70; 87,34]	80,36 [71,97; 88,74]	1,08 [0,57; 2,04] 0,822
Region = Others			
N'	4	1	
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]	1,00 [0,00; -] 1,000

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	HR [95% CI] p-value
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,243		
Region = Asia			
N'	53	59	
Number of patients with at least one event, n (%)	11 (20,8)	3 (5,1)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	76,36 [62,92; 89,80]	94,82 [89,11; 100,00]	4,36 [1,22; 15,63] 0,024 *
Region = Europe			
N'	81	83	
Number of patients with at least one event, n (%)	10 (12,3)	11 (13,3)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	87,59 [80,39; 94,79]	86,70 [79,38; 94,02]	0,94 [0,40; 2,21] 0,883
Region = Latin America			
N'	104	89	
Number of patients with at least one event, n (%)	22 (21,2)	17 (19,1)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	78,55 [70,60; 86,50]	80,34 [71,96; 88,73]	1,14 [0,61; 2,15] 0,683
Region = Others			
N'	4	1	
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]	1,00 [0,00; -] 1,000

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	HR [95% CI] p-value
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,991		
Region = Asia			
N'	53	59	
Number of patients with at least one event, n (%)	1 (1,9)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	98,08 [94,34; 100,00]	100,00 [100,00; 100,00]	-
Region = Europe			
N'	81	83	
Number of patients with at least one event, n (%)	1 (1,2)	1 (1,2)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	98,75 [96,32; 100,00]	98,80 [96,45; 100,00]	1,01 [0,06; 16,18] 0,993
Region = Latin America			
N'	104	89	
Number of patients with at least one event, n (%)	4 (3,8)	2 (2,2)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	96,12 [92,40; 99,85]	97,70 [94,55; 100,00]	1,73 [0,32; 9,47] 0,525
Region = Others			
N'	4	1	
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]	1,00 [0,00; -] 1,000

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	HR [95% CI] p-value
ER visit due to asthma exacerbation			
Interaction Test:	p=1,000		
Region = Asia			
N'	53	59	
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]	0,86 [0,00; -] 1,000
Region = Europe			
N'	81	83	
Number of patients with at least one event, n (%)	1 (1,2)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	98,75 [96,32; 100,00]	100,00 [100,00; 100,00]	-
Region = Latin America			
N'	104	89	
Number of patients with at least one event, n (%)	4 (3,8)	2 (2,2)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	96,12 [92,40; 99,85]	97,70 [94,55; 100,00]	1,73 [0,32; 9,46] 0,526
Region = Others			
N'	4	1	
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]	1,03 [0,00; -] 1,000

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	HR [95% CI] p-value
Hospitalization due to asthma exacerbation			
Interaction Test:	p=1,000		
Region = Asia			
N'	53	59	
Number of patients with at least one event, n (%)	1 (1,9)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	98,08 [94,34; 100,00]	100,00 [100,00; 100,00]	-
Region = Europe			
N'	81	83	
Number of patients with at least one event, n (%)	1 (1,2)	1 (1,2)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	98,75 [96,32; 100,00]	98,80 [96,45; 100,00]	1,01 [0,06; 16,14] 0,995
Region = Latin America			
N'	104	89	
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]	1,00 [0,00; -] 1,000
Region = Others			
N'	4	1	
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]	1,00 [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 + 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 subpopulation "high-dose ICS/LABA"			

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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=242	SAL/FLU + TIO N=232	HR [95% CI] p-value
Asthma exacerbation			
Interaction Test:	p=0,907		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	176	184	
Number of patients with at least one event, n (%)	44 (25,0)	42 (22,8)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	73,52 [66,31; 80,74]	76,72 [70,55; 82,89]	1,11 [0,72; 1,69] 0,640
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	66	48	
Number of patients with at least one event, n (%)	27 (40,9)	18 (37,5)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	58,70 [46,75; 70,65]	61,96 [48,07; 75,85]	1,16 [0,64; 2,10] 0,635
Severe asthma exacerbation			
Interaction Test:	p=0,369		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	176	184	
Number of patients with at least one event, n (%)	23 (13,1)	14 (7,6)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	85,57 [79,55; 91,58]	92,26 [88,37; 96,16]	1,73 [0,89; 3,37] 0,104

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	HR [95% CI] p-value
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	66	48	
Number of patients with at least one event, n (%)	20 (30,3)	14 (29,2)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	69,40 [58,22; 80,58]	70,40 [57,35; 83,45]	1,12 [0,56; 2,22] 0,747
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,378		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	176	184	
Number of patients with at least one event, n (%)	23 (13,1)	16 (8,7)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	85,54 [79,48; 91,59]	91,13 [86,98; 95,28]	1,54 [0,81; 2,91] 0,187
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	66	48	
Number of patients with at least one event, n (%)	20 (30,3)	15 (31,3)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	69,40 [58,22; 80,58]	68,25 [54,94; 81,57]	1,01 [0,52; 1,98] 0,970
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,993		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	176	184	
Number of patients with at least one event, n (%)	2 (1,1)	3 (1,6)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	98,86 [97,30; 100,00]	98,34 [96,48; 100,00]	0,67 [0,11; 4,00] 0,659

	Treatment groups		Comparison
Time-to-first outcome by subgroup (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	HR [95% CI] p-value
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	66	48	
Number of patients with at least one event, n (%)	4 (6,1)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	93,72 [87,76; 99,68]	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'	176	184	
Number of patients with at least one event, n (%)	2 (1,1)	2 (1,1)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	98,86 [97,30; 100,00]	98,89 [97,36; 100,00]	0,99 [0,14; 7,04] 0,994
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	66	48	
Number of patients with at least one event, n (%)	3 (4,5)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	95,28 [90,07; 100,00]	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'	176	184	
Number of patients with at least one event, n (%)	0 (0,0)	1 (0,5)	
Median (in weeks)	-	-	
% of outcome-free patients ⁺	100,00 [100,00; 100,00]	99,45 [98,38; 100,00]	0,00 [0,00; -] 0,996

Time-to-first outcome by subgroup (FAS)	Treatment groups		HR [95% CI] p-value
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	
Asthma exacerbations in the 12 months prior to screening = ≥2			
N [†]	66	48	
Number of patients with at least one event, n (%)	2 (3,0)	0 (0,0)	
Median (in weeks)	-	-	
% of outcome-free patients [‡]	96,83 [92,50; 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 + 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 subpopulation "high-dose ICS/LABA"

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=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
Asthma exacerbation				
N'		242	232	
Number of patients with outcome		71	60	
Number of outcomes		101	86	
Annualized Rate [95% CI]		0,92 [0,72; 1,17]	0,82 [0,64; 1,06]	1,12 [0,79; 1,59] 0,531
Severe asthma exacerbation				
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]	1,46 [0,91; 2,35] 0,121
SCS use due to asthma exacerbation (for at least three consecutive days)				
N'		242	232	
Number of patients with outcome		43	31	
Number of outcomes		55	38	
Annualized Rate [95% CI]		0,49 [0,36; 0,66]	0,35 [0,25; 0,50]	1,40 [0,88; 2,22] 0,156
ER visit and/or hospitalization due to asthma exacerbation				
N'		242	232	
Number of patients with outcome		5	2	
Number of outcomes		7	2	
Annualized Rate [95% CI]		-	-	-
ER visit due to asthma exacerbation				
N'		242	232	
Number of patients with outcome		5	2	
Number of outcomes		7	2	
Annualized Rate [95% CI]		-	-	-

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
Hospitalization due to asthma exacerbation			
N'	242	232	
Number of patients with outcome	2	1	
Number of outcomes	2	1	
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 + history of asthma exacerbation, offset variable: log(exposure in years) Exceptional model(s) for Annualized Rate/Rate Ratio: Number of events = treatment + history of asthma exacerbation (for ER visit and/or hospitalization due to asthma exacerbation), treatment + history of asthma exacerbation (for ER visit due to asthma exacerbation), treatment + 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 subpopulation "high-dose ICS/LABA"			

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

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
Asthma exacerbation			
Interaction Test:	p=0,297		
Age = 18-39 years			
N'	40	33	
Number of patients with outcome	11	6	
Number of outcomes	13	10	
Annualized Rate [95% CI]	0,72 [0,38; 1,36]	0,68 [0,33; 1,41]	1,05 [0,40; 2,76] 0,918
Age = 40-64 years			
N'	144	150	
Number of patients with outcome	43	35	
Number of outcomes	65	50	
Annualized Rate [95% CI]	1,02 [0,75; 1,38]	0,74 [0,53; 1,03]	1,37 [0,88; 2,15] 0,163
Age = ≥65 years			
N'	58	49	
Number of patients with outcome	17	19	
Number of outcomes	23	26	
Annualized Rate [95% CI]	0,83 [0,51; 1,37]	1,17 [0,71; 1,91]	0,71 [0,36; 1,43] 0,343
Severe asthma exacerbation			
Interaction Test:	p=0,192		
Age = 18-39 years			
N'	40	33	
Number of patients with outcome	7	4	
Number of outcomes	9	6	
Annualized Rate [95% CI]	0,43 [0,20; 0,93]	0,39 [0,16; 0,98]	1,10 [0,34; 3,62] 0,872

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
Age = 40-64 years			
N'	144	150	
Number of patients with outcome	28	15	
Number of outcomes	36	19	
Annualized Rate [95% CI]	0,55 [0,37; 0,82]	0,27 [0,16; 0,44]	2,08 [1,11; 3,90] 0,023 *
Age = ≥65 years			
N'	58	49	
Number of patients with outcome	8	9	
Number of outcomes	11	12	
Annualized Rate [95% CI]	0,39 [0,20; 0,77]	0,52 [0,27; 1,02]	0,75 [0,29; 1,95] 0,558
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,105		
Age = 18-39 years			
N'	40	33	
Number of patients with outcome	7	5	
Number of outcomes	7	7	
Annualized Rate [95% CI]	0,35 [0,15; 0,78]	0,44 [0,19; 1,00]	0,80 [0,25; 2,54] 0,700
Age = 40-64 years			
N'	144	150	
Number of patients with outcome	26	15	
Number of outcomes	34	17	
Annualized Rate [95% CI]	0,52 [0,35; 0,76]	0,24 [0,14; 0,40]	2,18 [1,16; 4,10] 0,016 *
Age = ≥65 years			
N'	58	49	
Number of patients with outcome	10	11	
Number of outcomes	14	14	
Annualized Rate [95% CI]	0,50 [0,28; 0,90]	0,63 [0,34; 1,16]	0,79 [0,34; 1,84] 0,587

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,927		
Age = 18-39 years			
N'	40	33	
Number of patients with outcome	1	1	
Number of outcomes	3	1	
Annualized Rate [95% CI]	-	-	2,32 [0,20; 27,34] 0,505
Age = 40-64 years			
N'	144	150	
Number of patients with outcome	4	1	
Number of outcomes	4	1	
Annualized Rate [95% CI]	-	-	4,50 [0,47; 43,04] 0,191
Age = ≥65 years			
N'	58	49	
Number of patients with outcome	0	0	
Number of outcomes	0	0	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	0,70 [0,00; -] 1,000
ER visit due to asthma exacerbation			
Interaction Test:	p=0,927		
Age = 18-39 years			
N'	40	33	
Number of patients with outcome	1	1	
Number of outcomes	3	1	
Annualized Rate [95% CI]	-	-	2,32 [0,20; 27,34] 0,505

Annualized Outcome Rate (FAS)	Treatment groups		Comparison
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
Age = 40-64 years			
N'	144	150	
Number of patients with outcome	4	1	
Number of outcomes	4	1	
Annualized Rate [95% CI]	-	-	4,50 [0,47; 43,04] 0,191
Age = ≥65 years			
N'	58	49	
Number of patients with outcome	0	0	
Number of outcomes	0	0	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	0,70 [0,00; -] 1,000
Hospitalization due to asthma exacerbation			
Interaction Test:	N.E.		
Age = 18-39 years			
N'	40	33	
Number of patients with outcome	1	1	
Number of outcomes	1	1	
Annualized Rate [95% CI]	-	-	-
Age = 40-64 years			
N'	144	150	
Number of patients with outcome	1	0	
Number of outcomes	1	0	
Annualized Rate [95% CI]	-	-	-

Annualized Outcome Rate (FAS)	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	RR [95% CI] p-value	
Age = ≥65 years				
N ^a	58	49		
Number of patients with outcome	0	0		
Number of outcomes	0	0		
Annualized Rate [95% CI]	-	-		-
N ^a : 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 + 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 [by age] (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 subpopulation "high-dose ICS/LABA"				

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

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
Asthma exacerbation			
Interaction Test:	p=0,828		
Gender = Male			
N'	88	81	
Number of patients with outcome	23	19	
Number of outcomes	32	30	
Annualized Rate [95% CI]	0,82 [0,54; 1,25]	0,78 [0,51; 1,20]	1,06 [0,58; 1,93] 0,855
Gender = Female			
N'	154	151	
Number of patients with outcome	48	41	
Number of outcomes	69	56	
Annualized Rate [95% CI]	0,97 [0,73; 1,31]	0,85 [0,62; 1,17]	1,15 [0,75; 1,77] 0,532
Severe asthma exacerbation			
Interaction Test:	p=0,292		
Gender = Male			
N'	88	81	
Number of patients with outcome	16	9	
Number of outcomes	21	10	
Annualized Rate [95% CI]	0,53 [0,32; 0,88]	0,25 [0,13; 0,50]	2,12 [0,91; 4,94] 0,083
Gender = Female			
N'	154	151	
Number of patients with outcome	27	19	
Number of outcomes	35	27	
Annualized Rate [95% CI]	0,47 [0,32; 0,70]	0,39 [0,25; 0,60]	1,22 [0,68; 2,18] 0,505

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,319		
Gender = Male			
N'	88	81	
Number of patients with outcome	14	9	
Number of outcomes	20	10	
Annualized Rate [95% CI]	0,50 [0,30; 0,83]	0,25 [0,13; 0,49]	1,98 [0,86; 4,56] 0,108
Gender = Female			
N'	154	151	
Number of patients with outcome	29	22	
Number of outcomes	35	28	
Annualized Rate [95% CI]	0,48 [0,33; 0,70]	0,40 [0,27; 0,61]	1,19 [0,68; 2,08] 0,543
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,986		
Gender = Male			
N'	88	81	
Number of patients with outcome	1	0	
Number of outcomes	1	0	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	-
Gender = Female			
N'	154	151	
Number of patients with outcome	4	2	
Number of outcomes	6	2	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	2,79 [0,50; 15,52] 0,240

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
ER visit due to asthma exacerbation			
Interaction Test:	p=0,986		
Gender = Male			
N'	88	81	
Number of patients with outcome	1	0	
Number of outcomes	1	0	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	-
Gender = Female			
N'	154	151	
Number of patients with outcome	4	2	
Number of outcomes	6	2	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	2,79 [0,50; 15,52] 0,240
Hospitalization due to asthma exacerbation			
Interaction Test:	N.E.		
Gender = Male			
N'	88	81	
Number of patients with outcome	0	1	
Number of outcomes	0	1	
Annualized Rate [95% CI]	-	-	-
Gender = Female			
N'	154	151	
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 + 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 + history of asthma exacerbation [by gender] (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 subpopulation "high-dose ICS/LABA"			

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

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
Asthma exacerbation			
Interaction Test:	p=0,140		
Region = Asia			
N'	53	59	
Number of patients with outcome	21	17	
Number of outcomes	30	23	
Annualized Rate [95% CI]	1,30 [0,82; 2,06]	0,87 [0,53; 1,42]	1,49 [0,76; 2,93] 0,244
Region = Europe			
N'	81	83	
Number of patients with outcome	25	21	
Number of outcomes	36	24	
Annualized Rate [95% CI]	1,00 [0,67; 1,50]	0,66 [0,42; 1,06]	1,51 [0,82; 2,79] 0,188
Region = Latin America			
N'	104	89	
Number of patients with outcome	24	22	
Number of outcomes	34	39	
Annualized Rate [95% CI]	0,72 [0,49; 1,07]	0,99 [0,67; 1,45]	0,73 [0,42; 1,27] 0,262
Region = Others			
N'	4	1	
Number of patients with outcome	1	0	
Number of outcomes	1	0	
Annualized Rate [95% CI]	0,55 [0,06; 5,03]	0,00 [0,00; 0,00]	-

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
Severe asthma exacerbation			
Interaction Test:	N.E.		
Region = Asia			
N'	53	59	
Number of patients with outcome	11	4	
Number of outcomes	13	4	
Annualized Rate [95% CI]	-	-	-
Region = Europe			
N'	81	83	
Number of patients with outcome	11	7	
Number of outcomes	14	9	
Annualized Rate [95% CI]	0,39 [0,21; 0,73]	0,25 [0,12; 0,52]	1,58 [0,60; 4,12] 0,354
Region = Latin America			
N'	104	89	
Number of patients with outcome	21	17	
Number of outcomes	29	24	
Annualized Rate [95% CI]	0,61 [0,40; 0,94]	0,61 [0,38; 0,98]	1,01 [0,53; 1,90] 0,986
Region = Others			
N'	4	1	
Number of patients with outcome	0	0	
Number of outcomes	0	0	
Annualized Rate [95% CI]	-	-	-
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	N.E.		
Region = Asia			
N'	53	59	
Number of patients with outcome	11	3	
Number of outcomes	13	3	
Annualized Rate [95% CI]	0,57 [0,30; 1,09]	0,11 [0,04; 0,37]	5,05 [1,32; 19,29] 0,018 *

Annualized Outcome Rate (FAS)	Treatment groups		Comparison
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
Region = Europe			
N'	81	83	
Number of patients with outcome	10	11	
Number of outcomes	13	12	
Annualized Rate [95% CI]	0,36 [0,20; 0,64]	0,33 [0,18; 0,59]	1,10 [0,48; 2,53] 0,817
Region = Latin America			
N'	104	89	
Number of patients with outcome	22	17	
Number of outcomes	29	23	
Annualized Rate [95% CI]	0,61 [0,40; 0,94]	0,58 [0,36; 0,94]	1,05 [0,55; 1,99] 0,881
Region = Others			
N'	4	1	
Number of patients with outcome	0	0	
Number of outcomes	0	0	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	0,66 [0,00; -] 1,000
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	N.E.		
Region = Asia			
N'	53	59	
Number of patients with outcome	0	0	
Number of outcomes	0	0	
Annualized Rate [95% CI]	-	-	-
Region = Europe			
N'	81	83	
Number of patients with outcome	1	0	
Number of outcomes	1	0	
Annualized Rate [95% CI]	-	-	-

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
Region = Latin America			
N'	104	89	
Number of patients with outcome	4	2	
Number of outcomes	6	2	
Annualized Rate [95% CI]	0,13 [0,05; 0,30]	0,05 [0,01; 0,21]	2,54 [0,47; 13,72] 0,279
Region = Others			
N'	4	1	
Number of patients with outcome	0	0	
Number of outcomes	0	0	
Annualized Rate [95% CI]	-	-	-
ER visit due to asthma exacerbation			
Interaction Test:	N.E.		
Region = Asia			
N'	53	59	
Number of patients with outcome	0	0	
Number of outcomes	0	0	
Annualized Rate [95% CI]	-	-	-
Region = Europe			
N'	81	83	
Number of patients with outcome	1	0	
Number of outcomes	1	0	
Annualized Rate [95% CI]	-	-	-
Region = Latin America			
N'	104	89	
Number of patients with outcome	4	2	
Number of outcomes	6	2	
Annualized Rate [95% CI]	0,13 [0,05; 0,30]	0,05 [0,01; 0,21]	2,54 [0,47; 13,72] 0,279
Region = Others			
N'	4	1	
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=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
Hospitalization due to asthma exacerbation			
Interaction Test:	N.E.		
Region = Asia			
N'	53	59	
Number of patients with outcome	1	0	
Number of outcomes	1	0	
Annualized Rate [95% CI]	-	-	-
Region = Europe			
N'	81	83	
Number of patients with outcome	1	1	
Number of outcomes	1	1	
Annualized Rate [95% CI]	-	-	-
Region = Latin America			
N'	104	89	
Number of patients with outcome	0	0	
Number of outcomes	0	0	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	0,58 [0,00; -] 1,000
Region = Others			
N'	4	1	
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 + 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 Severe asthma exacerbation), treatment + history of asthma exacerbation [by region] (for SCS use due to asthma exacerbation (for at least three consecutive days)), 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 subpopulation "high-dose ICS/LABA"			

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=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
Asthma exacerbation			
Interaction Test:	p=0,724		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	176	184	
Number of patients with outcome	44	42	
Number of outcomes	62	63	
Annualized Rate [95% CI]	0,76 [0,56; 1,02]	0,74 [0,55; 1,00]	1,02 [0,68; 1,55] 0,917
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	66	48	
Number of patients with outcome	27	18	
Number of outcomes	39	23	
Annualized Rate [95% CI]	1,34 [0,89; 2,02]	1,14 [0,68; 1,92]	1,17 [0,61; 2,25] 0,628
Severe asthma exacerbation			
Interaction Test:	p=0,513		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	176	184	
Number of patients with outcome	23	14	
Number of outcomes	29	19	
Annualized Rate [95% CI]	0,37 [0,25; 0,55]	0,23 [0,14; 0,38]	1,58 [0,84; 2,94] 0,153
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	66	48	
Number of patients with outcome	20	14	
Number of outcomes	27	18	
Annualized Rate [95% CI]	0,83 [0,52; 1,34]	0,73 [0,41; 1,31]	1,14 [0,55; 2,37] 0,720

	Treatment groups		Comparison
Annualized Outcome Rate (FAS)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
SCS use due to asthma exacerbation (for at least three consecutive days)			
Interaction Test:	p=0,336		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	176	184	
Number of patients with outcome	23	16	
Number of outcomes	29	19	
Annualized Rate [95% CI]	0,37 [0,25; 0,54]	0,23 [0,14; 0,37]	1,60 [0,87; 2,95] 0,133
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	66	48	
Number of patients with outcome	20	15	
Number of outcomes	26	19	
Annualized Rate [95% CI]	0,82 [0,52; 1,30]	0,81 [0,47; 1,39]	1,02 [0,51; 2,03] 0,963
ER visit and/or hospitalization due to asthma exacerbation			
Interaction Test:	p=0,996		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	176	184	
Number of patients with outcome	2	2	
Number of outcomes	4	2	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	1,95 [0,32; 11,93] 0,469
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	66	48	
Number of patients with outcome	3	0	
Number of outcomes	3	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=242	SAL/FLU + TIO N=232	RR [95% CI] p-value
ER visit due to asthma exacerbation			
Interaction Test:	p=0,996		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	176	184	
Number of patients with outcome	2	2	
Number of outcomes	4	2	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	1,95 [0,32; 11,93] 0,469
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	66	48	
Number of patients with outcome	3	0	
Number of outcomes	3	0	
Annualized Rate [95% CI]	0,00 [0,00; -]	0,00 [0,00; -]	-
Hospitalization due to asthma exacerbation			
Interaction Test:	p=0,969		
Asthma exacerbations in the 12 months prior to screening = 1			
N'	176	184	
Number of patients with outcome	0	1	
Number of outcomes	0	1	
Annualized Rate [95% CI]	0,00 [0,00; -]	-	0,00 [0,00; -] 0,979
Asthma exacerbations in the 12 months prior to screening = ≥2			
N'	66	48	
Number of patients with outcome	2	0	
Number of outcomes	2	0	
Annualized Rate [95% CI]	-	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 + 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 subpopulation "high-dose ICS/LABA"			

13. Adverse Events - Binary Analysis (SAF)

Table 13.1 Adverse Events - Binary Analysis (SAF)

Adverse Events - Binary Analysis (SAF)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	242	232			
Any AE, n (%)	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, n (%)	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, n (%)	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
Any SAE, disease specific events excluded, n (%)	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, n (%)	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, n (%)	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
Any AE leading to study drug discontinuation, n (%)	1 (0,4)	3 (1,3)	0,32 [0,03; 3,07] 0,321	0,32 [0,03; 3,05] 0,322	-0,01 [-0,03; 0,01] 0,300
Any AE leading to study discontinuation, n (%)	1 (0,4)	2 (0,9)	0,48 [0,04; 5,30] 0,547	0,48 [0,04; 5,25] 0,547	-0,00 [-0,02; 0,01] 0,541

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 subpopulation "high-dose ICS/LABA"

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

		Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value	
N'	242	232				
N' Age = 18-39 years	40	33				
N' Age = 40-64 years	144	150				
N' Age = ≥65 years	58	49				
Any AE						
Interaction Test:	p=0,410					
Age = 18-39 years	24 (60,0)	16 (48,5)	1,59 [0,63; 4,04] 0,326	1,24 [0,80; 1,91] 0,335	0,12 [-0,11; 0,34] 0,323	
Age = 40-64 years	83 (57,6)	72 (48,0)	1,47 [0,93; 2,34] 0,098	1,20 [0,97; 1,49] 0,099	0,10 [-0,02; 0,21] 0,096	
Age = ≥65 years	34 (58,6)	31 (63,3)	0,82 [0,38; 1,80] 0,624	0,93 [0,68; 1,26] 0,623	-0,05 [-0,23; 0,14] 0,623	
Any AE, disease specific events excluded						
Interaction Test:	p=0,322					
Age = 18-39 years	22 (55,0)	15 (45,5)	1,47 [0,58; 3,70] 0,418	1,21 [0,76; 1,93] 0,424	0,10 [-0,13; 0,32] 0,415	
Age = 40-64 years	75 (52,1)	64 (42,7)	1,46 [0,92; 2,31] 0,106	1,22 [0,96; 1,56] 0,107	0,09 [-0,02; 0,21] 0,104	
Age = ≥65 years	29 (50,0)	28 (57,1)	0,75 [0,35; 1,61] 0,461	0,88 [0,61; 1,25] 0,459	-0,07 [-0,26; 0,12] 0,459	
Any SAE						
Interaction Test:	N.E.					
Age = 18-39 years	3 (7,5)	4 (12,1)	-	0,62 [0,15; 2,57] 0,509	-0,05 [-0,18; 0,09] 0,512	
Age = 40-64 years	5 (3,5)	5 (3,3)	-	1,04 [0,31; 3,52] 0,948	0,00 [-0,04; 0,04] 0,948	
Age = ≥65 years	2 (3,4)	2 (4,1)	-	0,84 [0,12; 5,78] 0,864	-0,01 [-0,08; 0,07] 0,864	

		Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value	
Any severe AE						
Interaction Test:	p=0,124					
Age = 18-39 years	8 (20,0)	5 (15,2)	1,40 [0,41; 4,78] 0,591	1,32 [0,48; 3,65] 0,593	0,05 [-0,13; 0,22] 0,585	
Age = 40-64 years	31 (21,5)	17 (11,3)	2,15 [1,13; 4,08] 0,020 *	1,90 [1,10; 3,28] 0,021 *	0,10 [0,02; 0,19] 0,018 *	
Age = ≥65 years	9 (15,5)	11 (22,4)	0,63 [0,24; 1,69] 0,362	0,69 [0,31; 1,53] 0,362	-0,07 [-0,22; 0,08] 0,363	
Any severe AE, disease specific events excluded						
Interaction Test:	p=0,795					
Age = 18-39 years	4 (10,0)	2 (6,1)	1,72 [0,30; 10,05] 0,545	1,65 [0,32; 8,45] 0,548	0,04 [-0,08; 0,16] 0,532	
Age = 40-64 years	7 (4,9)	4 (2,7)	1,86 [0,53; 6,51] 0,329	1,82 [0,55; 6,09] 0,330	0,02 [-0,02; 0,07] 0,324	
Age = ≥65 years	2 (3,4)	2 (4,1)	0,84 [0,11; 6,19] 0,864	0,84 [0,12; 5,78] 0,864	-0,01 [-0,08; 0,07] 0,864	
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 + age + age * treatment If it was not possible to fit the minimal model, the OR is not given.						
Analysis population: B2306 SAF subpopulation "high-dose ICS/LABA"						

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

		Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value	
N'	242	232				
N' Gender = Male	88	81				
N' Gender = Female	154	151				
Any AE						
Interaction Test:	p=0,916					
Gender = Male	45 (51,1)	35 (43,2)	1,38 [0,75; 2,52] 0,303	1,18 [0,86; 1,63] 0,306	0,08 [-0,07; 0,23] 0,301	
Gender = Female	96 (62,3)	84 (55,6)	1,32 [0,84; 2,09] 0,234	1,12 [0,93; 1,35] 0,235	0,07 [-0,04; 0,18] 0,233	
Any AE, disease specific events excluded						
Interaction Test:	p=0,996					
Gender = Male	39 (44,3)	31 (38,3)	1,28 [0,69; 2,37] 0,426	1,16 [0,81; 1,66] 0,428	0,06 [-0,09; 0,21] 0,424	
Gender = Female	87 (56,5)	76 (50,3)	1,28 [0,82; 2,01] 0,281	1,12 [0,91; 1,39] 0,282	0,06 [-0,05; 0,17] 0,280	
Any SAE						
Interaction Test:	p=0,649					
Gender = Male	2 (2,3)	3 (3,7)	0,60 [0,10; 3,71] 0,587	0,61 [0,11; 3,58] 0,587	-0,01 [-0,07; 0,04] 0,587	
Gender = Female	8 (5,2)	8 (5,3)	0,98 [0,36; 2,68] 0,968	0,98 [0,38; 2,55] 0,968	-0,00 [-0,05; 0,05] 0,968	
Any SAE, disease specific events excluded						
Interaction Test:	p=0,947					
Gender = Male	2 (2,3)	2 (2,5)	0,92 [0,13; 6,68] 0,933	0,92 [0,13; 6,38] 0,933	-0,00 [-0,05; 0,04] 0,933	
Gender = Female	7 (4,5)	8 (5,3)	0,85 [0,30; 2,41] 0,761	0,86 [0,32; 2,31] 0,761	-0,01 [-0,06; 0,04] 0,761	

		Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value	
Any severe AE						
Interaction Test:		p=0,716				
Gender = Male	17 (19,3)	10 (12,3)	1,70 [0,73; 3,97] 0,220	1,56 [0,76; 3,22] 0,223	0,07 [-0,04; 0,18] 0,211	
Gender = Female	31 (20,1)	23 (15,2)	1,40 [0,77; 2,54] 0,264	1,32 [0,81; 2,16] 0,265	0,05 [-0,04; 0,13] 0,261	
Any severe AE, disease specific events excluded						
Interaction Test:		p=0,224				
Gender = Male	2 (2,3)	3 (3,7)	0,60 [0,10; 3,71] 0,587	0,61 [0,11; 3,58] 0,587	-0,01 [-0,07; 0,04] 0,587	
Gender = Female	11 (7,1)	5 (3,3)	2,25 [0,76; 6,63] 0,143	2,16 [0,77; 6,06] 0,145	0,04 [-0,01; 0,09] 0,131	
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 subpopulation "high-dose ICS/LABA"						

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

Adverse Events - Binary Analysis (SAF)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	242	232			
N' Region = Asia	53	59			
N' Region = Europe	81	83			
N' Region = Latin America	104	89			
N' Region = Others	4	1			
Any AE					
Interaction Test:	N.E.				
Region = Asia	42 (79,2)	34 (57,6)	-	1,38 [1,06; 1,78] 0,016 *	0,22 [0,05; 0,38] 0,011 *
Region = Europe	45 (55,6)	39 (47,0)	-	1,18 [0,88; 1,60] 0,274	0,09 [-0,07; 0,24] 0,271
Region = Latin America	51 (49,0)	45 (50,6)	-	0,97 [0,73; 1,29] 0,833	-0,02 [-0,16; 0,13] 0,833
Region = Others	3 (75,0)	1 (100,0)	-	0,93 [0,35; 2,50] 0,891	-0,25 [-0,67; 0,17] 0,248
Any AE, disease specific events excluded					
Interaction Test:	N.E.				
Region = Asia	38 (71,7)	34 (57,6)	-	1,24 [0,94; 1,64] 0,122	0,14 [-0,03; 0,32] 0,115
Region = Europe	38 (46,9)	35 (42,2)	-	1,11 [0,79; 1,57] 0,541	0,05 [-0,10; 0,20] 0,541
Region = Latin America	47 (45,2)	37 (41,6)	-	1,09 [0,79; 1,50] 0,614	0,04 [-0,10; 0,18] 0,613
Region = Others	3 (75,0)	1 (100,0)	-	0,93 [0,35; 2,50] 0,891	-0,25 [-0,67; 0,17] 0,248

	Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
Any severe AE					
Interaction Test:	N.E.				
Region = Asia	11 (20,8)	5 (8,5)	-	2,45 [0,91; 6,59] 0,076	0,12 [-0,01; 0,25] 0,065
Region = Europe	13 (16,0)	9 (10,8)	-	1,48 [0,67; 3,27] 0,332	0,05 [-0,05; 0,16] 0,328
Region = Latin America	24 (23,1)	19 (21,3)	-	1,08 [0,64; 1,84] 0,774	0,02 [-0,10; 0,13] 0,773
Region = Others	0 (0,0)	0 (0,0)	-	-	-
Any severe AE, disease specific events excluded					
Interaction Test:	N.E.				
Region = Asia	4 (7,5)	1 (1,7)	-	4,45 [0,51; 38,60] 0,175	0,06 [-0,02; 0,14] 0,143
Region = Europe	2 (2,5)	3 (3,6)	-	0,68 [0,12; 3,98] 0,672	-0,01 [-0,06; 0,04] 0,669
Region = Latin America	7 (6,7)	4 (4,5)	-	1,50 [0,45; 4,95] 0,508	0,02 [-0,04; 0,09] 0,497
Region = Others	0 (0,0)	0 (0,0)	-	-	-
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 subpopulation "high-dose ICS/LABA"					

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

Adverse Events - Binary Analysis (SAF)	Treatment groups		Comparison		
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	242	232			
N' Asthma exacerbations in the 12 months prior to screening = 1	176	184			
N' Asthma exacerbations in the 12 months prior to screening = ≥2	66	48			
Any AE					
Interaction Test:	p=0,621				
Asthma exacerbations in the 12 months prior to screening = 1	96 (54,5)	91 (49,5)	1,23 [0,81; 1,86] 0,334	1,10 [0,90; 1,35] 0,334	0,05 [-0,05; 0,15] 0,333
Asthma exacerbations in the 12 months prior to screening = ≥2	45 (68,2)	28 (58,3)	1,53 [0,71; 3,32] 0,281	1,17 [0,87; 1,56] 0,292	0,10 [-0,08; 0,28] 0,281
Any AE, disease specific events excluded					
Interaction Test:	p=0,723				
Asthma exacerbations in the 12 months prior to screening = 1	85 (48,3)	81 (44,0)	1,19 [0,78; 1,80] 0,416	1,10 [0,88; 1,37] 0,416	0,04 [-0,06; 0,15] 0,416
Asthma exacerbations in the 12 months prior to screening = ≥2	41 (62,1)	26 (54,2)	1,39 [0,65; 2,95] 0,395	1,15 [0,83; 1,58] 0,403	0,08 [-0,10; 0,26] 0,395
Any SAE					
Interaction Test:	p=0,022 *				
Asthma exacerbations in the 12 months prior to screening = 1	3 (1,7)	10 (5,4)	0,30 [0,08; 1,12] 0,072	0,31 [0,09; 1,12] 0,074	-0,04 [-0,08; 0,00] 0,054
Asthma exacerbations in the 12 months prior to screening = ≥2	7 (10,6)	1 (2,1)	5,58 [0,66; 46,93] 0,114	5,09 [0,65; 40,02] 0,122	0,09 [0,00; 0,17] 0,048 *
Any SAE, disease specific events excluded					
Interaction Test:	p=0,041 *				
Asthma exacerbations in the 12 months prior to screening = 1	3 (1,7)	9 (4,9)	0,34 [0,09; 1,27] 0,107	0,35 [0,10; 1,27] 0,109	-0,03 [-0,07; 0,00] 0,088

		Treatment groups		Comparison		
Adverse Events - Binary Analysis (SAF)	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	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	6 (9,1)	1 (2,1)	4,70 [0,55; 40,40] 0,159	4,36 [0,54; 35,07] 0,166	0,07 [-0,01; 0,15] 0,087	
Any severe AE						
Interaction Test:	p=0,846					
Asthma exacerbations in the 12 months prior to screening = 1	25 (14,2)	19 (10,3)	1,44 [0,76; 2,72] 0,263	1,38 [0,79; 2,41] 0,264	0,04 [-0,03; 0,11] 0,262	
Asthma exacerbations in the 12 months prior to screening = ≥2	23 (34,8)	14 (29,2)	1,30 [0,58; 2,90] 0,523	1,19 [0,69; 2,07] 0,526	0,06 [-0,12; 0,23] 0,519	
Any severe AE, disease specific events excluded						
Interaction Test:	p=0,021 *					
Asthma exacerbations in the 12 months prior to screening = 1	3 (1,7)	7 (3,8)	0,44 [0,11; 1,72] 0,238	0,45 [0,12; 1,71] 0,239	-0,02 [-0,05; 0,01] 0,221	
Asthma exacerbations in the 12 months prior to screening = ≥2	10 (15,2)	1 (2,1)	8,39 [1,04; 67,99] 0,046 *	7,27 [0,96; 54,92] 0,054	0,13 [0,04; 0,23] 0,007 *	
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 subpopulation "high-dose ICS/LABA"						

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=242)	SAL/FLU + TIO (N=232)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	242	232			
Any adverse event**, n (%)	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
Mild, n (%)	86 (35,5)	77 (33,2)	1,11 [0,76; 1,62] 0,591	1,07 [0,83; 1,37] 0,591	0,02 [-0,06; 0,11] 0,590
Moderate, n (%)	70 (28,9)	74 (31,9)	0,87 [0,59; 1,29] 0,482	0,91 [0,69; 1,19] 0,482	-0,03 [-0,11; 0,05] 0,482
Severe, n (%)	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
Respiratory, thoracic and mediastinal disorders, n (%)	83 (34,3)	68 (29,3)	1,26 [0,85; 1,86] 0,244	1,17 [0,90; 1,53] 0,246	0,05 [-0,03; 0,13] 0,243
Mild, n (%)	29 (12,0)	26 (11,2)	1,08 [0,61; 1,89] 0,792	1,07 [0,65; 1,76] 0,792	0,01 [-0,05; 0,07] 0,792
Moderate, n (%)	23 (9,5)	23 (9,9)	0,95 [0,52; 1,75] 0,880	0,96 [0,55; 1,66] 0,880	-0,00 [-0,06; 0,05] 0,880
Severe, n (%)	43 (17,8)	28 (12,1)	1,57 [0,94; 2,63] 0,084	1,47 [0,95; 2,29] 0,085	0,06 [-0,01; 0,12] 0,080
Asthma, n (%)	71 (29,3)	60 (25,9)	1,19 [0,79; 1,78] 0,398	1,13 [0,85; 1,52] 0,398	0,03 [-0,05; 0,12] 0,397
Mild, n (%)	18 (7,4)	17 (7,3)	1,02 [0,51; 2,02] 0,963	1,02 [0,54; 1,92] 0,963	0,00 [-0,05; 0,05] 0,963
Moderate, n (%)	14 (5,8)	20 (8,6)	0,65 [0,32; 1,32] 0,235	0,67 [0,35; 1,30] 0,235	-0,03 [-0,07; 0,02] 0,233
Severe, n (%)	43 (17,8)	28 (12,1)	1,57 [0,94; 2,63] 0,084	1,47 [0,95; 2,29] 0,085	0,06 [-0,01; 0,12] 0,080

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
Infections and infestations, n (%)	78 (32,2)	74 (31,9)	1,02 [0,69; 1,49] 0,938	1,01 [0,78; 1,31] 0,938	0,00 [-0,08; 0,09] 0,938
Mild, n (%)	46 (19,0)	42 (18,1)	1,06 [0,67; 1,69] 0,800	1,05 [0,72; 1,53] 0,800	0,01 [-0,06; 0,08] 0,800
Moderate, n (%)	34 (14,0)	40 (17,2)	0,78 [0,48; 1,29] 0,339	0,81 [0,54; 1,24] 0,340	-0,03 [-0,10; 0,03] 0,339
Severe, n (%)	9 (3,7)	4 (1,7)	2,20 [0,67; 7,25] 0,194	2,16 [0,67; 6,91] 0,196	0,02 [-0,01; 0,05] 0,180
Nasopharyngitis, n (%)	19 (7,9)	19 (8,2)	0,96 [0,49; 1,85] 0,892	0,96 [0,52; 1,76] 0,892	-0,00 [-0,05; 0,05] 0,892
Mild, n (%)	12 (5,0)	10 (4,3)	1,16 [0,49; 2,74] 0,738	1,15 [0,51; 2,61] 0,738	0,01 [-0,03; 0,04] 0,737
Moderate, n (%)	7 (2,9)	11 (4,7)	0,60 [0,23; 1,57] 0,297	0,61 [0,24; 1,55] 0,298	-0,02 [-0,05; 0,02] 0,294
Severe, n (%)	1 (0,4)	1 (0,4)	-	0,96 [0,06; 15,24] 0,976	-0,00 [-0,01; 0,01] 0,976
Bronchitis, n (%)	11 (4,5)	16 (6,9)	0,64 [0,29; 1,42] 0,273	0,66 [0,31; 1,39] 0,274	-0,02 [-0,07; 0,02] 0,271
Mild, n (%)	3 (1,2)	7 (3,0)	0,40 [0,10; 1,58] 0,192	0,41 [0,11; 1,57] 0,193	-0,02 [-0,04; 0,01] 0,181
Moderate, n (%)	8 (3,3)	10 (4,3)	0,76 [0,29; 1,96] 0,568	0,77 [0,31; 1,91] 0,569	-0,01 [-0,04; 0,02] 0,568
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Pharyngitis, n (%)	10 (4,1)	6 (2,6)	1,62 [0,58; 4,54] 0,356	1,60 [0,59; 4,33] 0,356	0,02 [-0,02; 0,05] 0,349
Mild, n (%)	9 (3,7)	5 (2,2)	1,75 [0,58; 5,31] 0,321	1,73 [0,59; 5,07] 0,321	0,02 [-0,01; 0,05] 0,312
Moderate, n (%)	1 (0,4)	1 (0,4)	0,96 [0,06; 15,41] 0,976	0,96 [0,06; 15,24] 0,976	-0,00 [-0,01; 0,01] 0,976
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
Gastrointestinal disorders, n (%)	16 (6,6)	14 (6,0)	1,10 [0,53; 2,31] 0,797	1,10 [0,55; 2,19] 0,797	0,01 [-0,04; 0,05] 0,796
Mild, n (%)	10 (4,1)	8 (3,4)	1,21 [0,47; 3,11] 0,697	1,20 [0,48; 2,98] 0,697	0,01 [-0,03; 0,04] 0,696
Moderate, n (%)	6 (2,5)	9 (3,9)	0,63 [0,22; 1,80] 0,388	0,64 [0,23; 1,77] 0,388	-0,01 [-0,05; 0,02] 0,386
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Musculoskeletal and connective tissue disorders, n (%)	14 (5,8)	7 (3,0)	1,97 [0,78; 4,98] 0,150	1,92 [0,79; 4,67] 0,151	0,03 [-0,01; 0,06] 0,140
Mild, n (%)	9 (3,7)	3 (1,3)	2,95 [0,79; 11,03] 0,108	2,88 [0,79; 10,49] 0,110	0,02 [-0,00; 0,05] 0,089
Moderate, n (%)	5 (2,1)	5 (2,2)	0,96 [0,27; 3,35] 0,946	0,96 [0,28; 3,27] 0,946	-0,00 [-0,03; 0,03] 0,946
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Nervous system disorders, n (%)	13 (5,4)	16 (6,9)	0,77 [0,36; 1,63] 0,490	0,78 [0,38; 1,58] 0,490	-0,02 [-0,06; 0,03] 0,490
Mild, n (%)	11 (4,5)	9 (3,9)	1,18 [0,48; 2,90] 0,719	1,17 [0,49; 2,78] 0,719	0,01 [-0,03; 0,04] 0,718
Moderate, n (%)	2 (0,8)	5 (2,2)	0,38 [0,07; 1,97] 0,248	0,38 [0,08; 1,96] 0,249	-0,01 [-0,04; 0,01] 0,234
Severe, n (%)	0 (0,0)	2 (0,9)	-	0,19 [0,01; 3,97] 0,286	-0,01 [-0,02; 0,00] 0,156

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
Injury, poisoning and procedural complications, n (%)	10 (4,1)	6 (2,6)	1,62 [0,58; 4,54] 0,356	1,60 [0,59; 4,33] 0,356	0,02 [-0,02; 0,05] 0,349
Mild, n (%)	4 (1,7)	5 (2,2)	0,76 [0,20; 2,88] 0,690	0,77 [0,21; 2,82] 0,690	-0,01 [-0,03; 0,02] 0,690
Moderate, n (%)	4 (1,7)	2 (0,9)	1,93 [0,35; 10,65] 0,449	1,92 [0,35; 10,37] 0,450	0,01 [-0,01; 0,03] 0,438
Severe, n (%)	2 (0,8)	0 (0,0)	-	4,79 [0,23; 99,33] 0,311	0,01 [-0,00; 0,02] 0,156

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 subpopulation "high-dose ICS/LABA"

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.
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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.
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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.
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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.
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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=242)	SAL/FLU + TIO (N=232)
N'	242	232
Neoplasms benign, malignant and unspecified (incl cysts and polyps), n (%)	1 (0,4)	0 (0,0)
Benign neoplasm, n (%)	1 (0,4)	0 (0,0)
Nervous system disorders, n (%)	0 (0,0)	1 (0,4)
Haemorrhagic stroke, n (%)	0 (0,0)	1 (0,4)
Tension headache, n (%)	0 (0,0)	0 (0,0)
Respiratory, thoracic and mediastinal disorders, n (%)	0 (0,0)	0 (0,0)
Oropharyngeal discomfort, n (%)	0 (0,0)	0 (0,0)
Skin and subcutaneous tissue disorders, n (%)	0 (0,0)	1 (0,4)
Dermatitis atopic, n (%)	0 (0,0)	1 (0,4)
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 subpopulation "high-dose ICS/LABA"

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=242)	SAL/FLU + TIO (N=232)
N'	242	232
Gastrointestinal disorders, n (%)	0 (0,0)	0 (0,0)
Dry mouth, n (%)	0 (0,0)	0 (0,0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps), n (%)	1 (0,4)	0 (0,0)
Benign neoplasm, n (%)	1 (0,4)	0 (0,0)
Nervous system disorders, n (%)	0 (0,0)	1 (0,4)
Haemorrhagic stroke, n (%)	0 (0,0)	1 (0,4)
Tension headache, n (%)	0 (0,0)	0 (0,0)
Respiratory, thoracic and mediastinal disorders, n (%)	0 (0,0)	1 (0,4)
Larynx irritation, n (%)	0 (0,0)	1 (0,4)
Oropharyngeal discomfort, n (%)	0 (0,0)	0 (0,0)
Skin and subcutaneous tissue disorders, n (%)	0 (0,0)	1 (0,4)
Dermatitis atopic, n (%)	0 (0,0)	1 (0,4)
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 subpopulation "high-dose ICS/LABA"

18. AESI - Binary Analysis (SAF)

Table 18.1 AESI by Severity - Binary Analysis (SAF)

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	242	232			
Bone fracture, n (%)	2 (0,8)	2 (0,9)	0,96 [0,13; 6,86] 0,966	0,96 [0,14; 6,75] 0,966	-0,00 [-0,02; 0,02] 0,966
Mild, n (%)	0 (0,0)	1 (0,4)	-	0,32 [0,01; 7,81] 0,484	-0,00 [-0,01; 0,00] 0,316
Moderate, n (%)	2 (0,8)	1 (0,4)	-	1,92 [0,18; 21,00] 0,594	0,00 [-0,01; 0,02] 0,585
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-
CCV events: Cardiac arrhythmia terms (incl brady- and tachyarrhythmias): Conduction abnormalities, n (%)	1 (0,4)	0 (0,0)	-	2,88 [0,12; 70,26] 0,517	0,00 [-0,00; 0,01] 0,316
Mild, n (%)	1 (0,4)	0 (0,0)	-	2,88 [0,12; 70,26] 0,517	0,00 [-0,00; 0,01] 0,316
Moderate, n (%)	0 (0,0)	0 (0,0)	-	-	-
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-
CCV events: Cardiac arrhythmia terms (incl brady- and tachyarrhythmias): Tachyarrhythmias, n (%)	2 (0,8)	1 (0,4)	-	1,92 [0,18; 21,00] 0,594	0,00 [-0,01; 0,02] 0,585
Mild, n (%)	2 (0,8)	1 (0,4)	-	1,92 [0,18; 21,00] 0,594	0,00 [-0,01; 0,02] 0,585
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=242)	SAL/FLU + TIO (N=232)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
CCV events: Cardiac failure, n (%)	0 (0,0)	1 (0,4)	-	0,32 [0,01; 7,81] 0,484	-0,00 [-0,01; 0,00] 0,316
Mild, n (%)	0 (0,0)	0 (0,0)	-	-	-
Moderate, n (%)	0 (0,0)	1 (0,4)	-	0,32 [0,01; 7,81] 0,484	-0,00 [-0,01; 0,00] 0,316
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 (0,9)	-	0,19 [0,01; 3,97] 0,286	-0,01 [-0,02; 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 (0,9)	-	0,19 [0,01; 3,97] 0,286	-0,01 [-0,02; 0,00] 0,156
Serious, n (%)	0 (0,0)	2 (0,9)	-	0,19 [0,01; 3,97] 0,286	-0,01 [-0,02; 0,00] 0,156
CCV events: Ischaemic heart disease, n (%)	2 (0,8)	0 (0,0)	-	4,79 [0,23; 99,33] 0,311	0,01 [-0,00; 0,02] 0,156
Mild, n (%)	0 (0,0)	0 (0,0)	-	-	-
Moderate, n (%)	2 (0,8)	0 (0,0)	-	4,79 [0,23; 99,33] 0,311	0,01 [-0,00; 0,02] 0,156
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-
Diabetes mellitus/hyperglycaemia, n (%)	1 (0,4)	2 (0,9)	0,48 [0,04; 5,30] 0,547	0,48 [0,04; 5,25] 0,547	-0,00 [-0,02; 0,01] 0,541
Mild, n (%)	1 (0,4)	1 (0,4)	0,96 [0,06; 15,41] 0,976	0,96 [0,06; 15,24] 0,976	-0,00 [-0,01; 0,01] 0,976
Moderate, n (%)	0 (0,0)	1 (0,4)	-	0,32 [0,01; 7,81] 0,484	-0,00 [-0,01; 0,00] 0,316
Severe, n (%)	0 (0,0)	0 (0,0)	-	-	-
Serious, n (%)	0 (0,0)	0 (0,0)	-	-	-

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
Hypersensitivity, n (%)	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
Mild, n (%)	19 (7,9)	18 (7,8)	1,01 [0,52; 1,98] 0,970	1,01 [0,54; 1,88] 0,970	0,00 [-0,05; 0,05] 0,970
Moderate, n (%)	16 (6,6)	24 (10,3)	0,61 [0,32; 1,19] 0,147	0,64 [0,35; 1,17] 0,148	-0,04 [-0,09; 0,01] 0,145
Severe, n (%)	43 (17,8)	28 (12,1)	1,57 [0,94; 2,63] 0,084	1,47 [0,95; 2,29] 0,085	0,06 [-0,01; 0,12] 0,080
Serious, n (%)	2 (0,8)	1 (0,4)	1,92 [0,17; 21,37] 0,594	1,92 [0,18; 21,00] 0,594	0,00 [-0,01; 0,02] 0,585
Immunosuppression, n (%)	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
Mild, n (%)	6 (2,5)	9 (3,9)	0,63 [0,22; 1,80] 0,388	0,64 [0,23; 1,77] 0,388	-0,01 [-0,05; 0,02] 0,386
Moderate, n (%)	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
Severe, n (%)	6 (2,5)	2 (0,9)	2,92 [0,58; 14,64] 0,192	2,88 [0,59; 14,11] 0,193	0,02 [-0,01; 0,04] 0,167
Serious, n (%)	4 (1,7)	0 (0,0)	-	8,63 [0,47; 159,40] 0,147	0,02 [0,00; 0,03] 0,044 *
Intubation hospitalization and death due to asthma related events, n (%)	2 (0,8)	1 (0,4)	1,92 [0,17; 21,37] 0,594	1,92 [0,18; 21,00] 0,594	0,00 [-0,01; 0,02] 0,585
Mild, n (%)	0 (0,0)	0 (0,0)	-	-	-
Moderate, n (%)	0 (0,0)	0 (0,0)	-	-	-
Severe, n (%)	2 (0,8)	1 (0,4)	1,92 [0,17; 21,37] 0,594	1,92 [0,18; 21,00] 0,594	0,00 [-0,01; 0,02] 0,585
Serious, n (%)	2 (0,8)	1 (0,4)	1,92 [0,17; 21,37] 0,594	1,92 [0,18; 21,00] 0,594	0,00 [-0,01; 0,02] 0,585

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
Liver toxicity, n (%)	1 (0,4)	2 (0,9)	0,48 [0,04; 5,30] 0,547	0,48 [0,04; 5,25] 0,547	-0,00 [-0,02; 0,01] 0,541
Mild, n (%)	0 (0,0)	1 (0,4)	-	0,32 [0,01; 7,81] 0,484	-0,00 [-0,01; 0,00] 0,316
Moderate, n (%)	1 (0,4)	1 (0,4)	-	0,96 [0,06; 15,24] 0,976	-0,00 [-0,01; 0,01] 0,976
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)	1 (0,4)	-	0,32 [0,01; 7,81] 0,484	-0,00 [-0,01; 0,00] 0,316
Mild, n (%)	0 (0,0)	1 (0,4)	-	0,32 [0,01; 7,81] 0,484	-0,00 [-0,01; 0,00] 0,316
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 (0,4)	-	0,32 [0,01; 7,81] 0,484	-0,00 [-0,01; 0,00] 0,316
Mild, n (%)	0 (0,0)	0 (0,0)	-	-	-
Moderate, n (%)	0 (0,0)	1 (0,4)	-	0,32 [0,01; 7,81] 0,484	-0,00 [-0,01; 0,00] 0,316
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)	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=242)	SAL/FLU + TIO (N=232)	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 (%)	1 (0,4)	3 (1,3)	-	0,32 [0,03; 3,05] 0,322	-0,01 [-0,03; 0,01] 0,300
Mild, n (%)	-	-	-	-	-
Moderate, n (%)	-	-	-	-	-
Severe, n (%)	-	-	-	-	-
Serious, n (%)	1 (0,4)	3 (1,3)	-	0,32 [0,03; 3,05] 0,322	-0,01 [-0,03; 0,01] 0,300
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=242)	SAL/FLU + TIO (N=232)	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 (%)	1 (0,4)	1 (0,4)	0,96 [0,06; 15,41] 0,976	0,96 [0,06; 15,24] 0,976	-0,00 [-0,01; 0,01] 0,976
Mild, n (%)	-	-	-	-	-
Moderate, n (%)	-	-	-	-	-
Severe, n (%)	-	-	-	-	-
Serious, n (%)	1 (0,4)	1 (0,4)	0,96 [0,06; 15,41] 0,976	0,96 [0,06; 15,24] 0,976	-0,00 [-0,01; 0,01] 0,976
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 subpopulation "high-dose ICS/LABA"					

Table 18.2 AESI - Binary Analysis by Age (SAF)

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	242	232			
N' Age = 18-39 years	40	33			
N' Age = 40-64 years	144	150			
N' Age = \geq 65 years	58	49			
Hypersensitivity					
Interaction test:	p=0,361				
Age = 18-39 years	11 (27,5)	7 (21,2)	1,41 [0,48; 4,17] 0,537	1,30 [0,57; 2,97] 0,539	0,06 [-0,13; 0,26] 0,530
Age = 40-64 years	44 (30,6)	39 (26,0)	1,25 [0,75; 2,08] 0,386	1,18 [0,82; 1,69] 0,386	0,05 [-0,06; 0,15] 0,386
Age = \geq 65 years	17 (29,3)	19 (38,8)	0,65 [0,29; 1,47] 0,303	0,76 [0,44; 1,29] 0,303	-0,09 [-0,27; 0,09] 0,302
Immunosuppression					
Interaction test:	p=0,252				
Age = 18-39 years	6 (15,0)	3 (9,1)	1,76 [0,41; 7,68] 0,449	1,65 [0,45; 6,10] 0,453	0,06 [-0,09; 0,21] 0,433
Age = 40-64 years	10 (6,9)	11 (7,3)	0,94 [0,39; 2,29] 0,897	0,95 [0,41; 2,16] 0,897	-0,00 [-0,06; 0,05] 0,897
Age = \geq 65 years	3 (5,2)	7 (14,3)	0,33 [0,08; 1,34] 0,121	0,36 [0,10; 1,33] 0,125	-0,09 [-0,20; 0,02] 0,115
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 subpopulation "high-dose ICS/LABA"					

Table 18.3 AESI - Binary Analysis by Gender (SAF)

Treatment groups		Comparison			
	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	242	232			
N' Gender = Male	88	81			
N' Gender = Female	154	151			
Hypersensitivity					
Interaction test:	p=0,853				
Gender = Male	23 (26,1)	19 (23,5)	1,15 [0,57; 2,33] 0,688	1,11 [0,66; 1,89] 0,688	0,03 [-0,10; 0,16] 0,687
Gender = Female	49 (31,8)	46 (30,5)	1,07 [0,66; 1,73] 0,798	1,04 [0,75; 1,46] 0,798	0,01 [-0,09; 0,12] 0,798
Immunosuppression					
Interaction test:	p=0,801				
Gender = Male	5 (5,7)	6 (7,4)	0,75 [0,22; 2,57] 0,651	0,77 [0,24; 2,42] 0,651	-0,02 [-0,09; 0,06] 0,651
Gender = Female	14 (9,1)	15 (9,9)	0,91 [0,42; 1,95] 0,802	0,92 [0,46; 1,83] 0,802	-0,01 [-0,07; 0,06] 0,802
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 subpopulation "high-dose ICS/LABA"					

Table 18.4 AESI - Binary Analysis by Region (SAF)

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	242	232			
N' Region = Asia	53	59			
N' Region = Europe	81	83			
N' Region = Latin America	104	89			
N' Region = Others	4	1			
Hypersensitivity					
Interaction test:	N.E.				
Region = Asia	21 (39,6)	19 (32,2)	-	1,23 [0,75; 2,02] 0,414	0,07 [-0,10; 0,25] 0,413
Region = Europe	25 (30,9)	22 (26,5)	-	1,16 [0,72; 1,89] 0,538	0,04 [-0,09; 0,18] 0,537
Region = Latin America	25 (24,0)	24 (27,0)	-	0,89 [0,55; 1,45] 0,641	-0,03 [-0,15; 0,09] 0,642
Region = Others	1 (25,0)	0 (0,0)	-	1,20 [0,08; 18,75] 0,897	0,25 [-0,17; 0,67] 0,248
Immunosuppression					
Interaction test:	N.E.				
Region = Asia	3 (5,7)	3 (5,1)	-	1,11 [0,23; 5,28] 0,893	0,01 [-0,08; 0,09] 0,893
Region = Europe	7 (8,6)	12 (14,5)	-	0,60 [0,25; 1,44] 0,252	-0,06 [-0,16; 0,04] 0,241
Region = Latin America	8 (7,7)	6 (6,7)	-	1,14 [0,41; 3,16] 0,800	0,01 [-0,06; 0,08] 0,799

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
Region = Others	1 (25,0)	0 (0,0)	-	1,20 [0,08; 18,75] 0,897	0,25 [-0,17; 0,67] 0,248

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 subpopulation "high-dose ICS/LABA"

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

	Treatment groups		Comparison		
	IND/GLY/ MF 160 (N=242)	SAL/FLU + TIO (N=232)	OR [95% CI] p-value	RR [95% CI] p-value	RD [95% CI] p-value
N'	242	232			
N' Asthma exacerbations in the 12 months prior to screening = 1	176	184			
N' Asthma exacerbations in the 12 months prior to screening = ≥2	66	48			
Hypersensitivity					
Interaction test:	p=0,843				
Asthma exacerbations in the 12 months prior to screening = 1	45 (25,6)	45 (24,5)	1,06 [0,66; 1,71] 0,808	1,05 [0,73; 1,50] 0,808	0,01 [-0,08; 0,10] 0,808
Asthma exacerbations in the 12 months prior to screening = ≥2	27 (40,9)	20 (41,7)	0,97 [0,46; 2,06] 0,935	0,98 [0,63; 1,53] 0,935	-0,01 [-0,19; 0,18] 0,935
Immunosuppression					
Interaction test:	p=0,498				
Asthma exacerbations in the 12 months prior to screening = 1	9 (5,1)	14 (7,6)	0,65 [0,28; 1,55] 0,336	0,67 [0,30; 1,51] 0,337	-0,02 [-0,08; 0,03] 0,331
Asthma exacerbations in the 12 months prior to screening = ≥2	10 (15,2)	7 (14,6)	1,05 [0,37; 2,98] 0,933	1,04 [0,43; 2,53] 0,933	0,01 [-0,13; 0,14] 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 + 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 subpopulation "high-dose ICS/LABA"					

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Trough FEV1					
N'	219	208			
Baseline Mean (SD)	1,80 (0,671)	1,84 (0,657)			
Week 8:					
Adjusted Mean Change (SE)	0,24 (0,034)	0,20 (0,035)	0,04 [-0,031; 0,107] 0,279	0,080 [-0,121; 0,281]	
Week 16:					
Adjusted Mean Change (SE)	0,25 (0,035)	0,21 (0,035)	0,04 [-0,025; 0,114] 0,207	0,094 [-0,109; 0,296]	
Week 24:					
Adjusted Mean Change (SE)	0,25 (0,035)	0,19 (0,036)	0,06 [-0,011; 0,133] 0,097	0,126 [-0,077; 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 + 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 subpopulation "high-dose ICS/LABA"					

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Trough FEV1					
Interaction Test	0,257				
Age = 18-39 years					
N'	39	28			
Baseline Mean (SD)	2,47 (0,782)	2,57 (0,749)			
Week 8:					
Adjusted Mean Change (SE)	0,32 (0,065)	0,43 (0,073)	-0,11 [-0,288; 0,062] 0,205	-0,301 [-0,814; 0,213]	
Week 16:					
Adjusted Mean Change (SE)	0,41 (0,066)	0,44 (0,074)	-0,02 [-0,200; 0,152] 0,791	-0,063 [-0,577; 0,451]	
Week 24:					
Adjusted Mean Change (SE)	0,40 (0,068)	0,50 (0,075)	-0,10 [-0,284; 0,079] 0,269	-0,271 [-0,799; 0,257]	
Age = 40-64 years					
N'	127	136			
Baseline Mean (SD)	1,74 (0,557)	1,81 (0,563)			
Week 8:					
Adjusted Mean Change (SE)	0,24 (0,039)	0,16 (0,039)	0,08 [-0,007; 0,168] 0,070	0,189 [-0,067; 0,444]	
Week 16:					
Adjusted Mean Change (SE)	0,23 (0,039)	0,19 (0,039)	0,04 [-0,046; 0,130] 0,346	0,099 [-0,158; 0,356]	
Week 24:					
Adjusted Mean Change (SE)	0,25 (0,040)	0,15 (0,040)	0,10 [0,009; 0,189] 0,031 *	0,229 [-0,029; 0,488]	
Age = ≥65 years					
N'	53	44			
Baseline Mean (SD)	1,45 (0,464)	1,45 (0,476)			

Outcome - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	0,11 (0,057)	0,11 (0,062)	-0,01 [-0,151; 0,139] 0,937	-0,015 [-0,445; 0,415]
Week 16:				
Adjusted Mean Change (SE)	0,15 (0,058)	0,08 (0,062)	0,07 [-0,075; 0,216] 0,342	0,184 [-0,249; 0,616]
Week 24:				
Adjusted Mean Change (SE)	0,12 (0,058)	0,08 (0,064)	0,04 [-0,111; 0,188] 0,616	0,097 [-0,337; 0,531]
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 + 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 subpopulation "high-dose ICS/LABA"				

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

	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Trough FEV1				
Interaction Test	0,074			
Gender = Male				
N'	77	76		
Baseline Mean (SD)	2,20 (0,769)	2,29 (0,729)		
Week 8:				
Adjusted Mean Change (SE)	0,25 (0,047)	0,32 (0,050)	-0,07 [-0,184; 0,047] 0,244	-0,174 [-0,515; 0,166]
Week 16:				
Adjusted Mean Change (SE)	0,26 (0,047)	0,27 (0,050)	-0,01 [-0,124; 0,109] 0,900	-0,019 [-0,355; 0,318]
Week 24:				
Adjusted Mean Change (SE)	0,28 (0,048)	0,29 (0,051)	-0,02 [-0,138; 0,102] 0,766	-0,044 [-0,381; 0,292]
Gender = Female				
N'	142	132		
Baseline Mean (SD)	1,58 (0,491)	1,58 (0,438)		
Week 8:				
Adjusted Mean Change (SE)	0,23 (0,041)	0,13 (0,041)	0,10 [0,011; 0,183] 0,027 *	0,214 [-0,035; 0,464]
Week 16:				
Adjusted Mean Change (SE)	0,24 (0,041)	0,17 (0,041)	0,07 [-0,013; 0,161] 0,096	0,165 [-0,089; 0,419]

Outcome - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 24:				
Adjusted Mean Change (SE)	0,24 (0,042)	0,13 (0,042)	0,11 [0,016; 0,196] 0,021 *	0,233 [-0,023; 0,489]
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 + 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 subpopulation "high-dose ICS/LABA"				

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=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]	
Trough FEV1					
Interaction Test					
Region = Asia					
N'	49	54			
Baseline Mean (SD)	1,62 (0,565)	1,74 (0,605)			
Week 8:					
Adjusted Mean Change (SE)	0,15 (0,040)	0,19 (0,038)	-0,04 [-0,153; 0,065] 0,431	-0,165 [-0,575; 0,244]	
Week 16:					
Adjusted Mean Change (SE)	0,16 (0,041)	0,20 (0,039)	-0,04 [-0,156; 0,069] 0,444	-0,162 [-0,577; 0,253]	
Week 24:					
Adjusted Mean Change (SE)	0,19 (0,040)	0,17 (0,038)	0,03 [-0,081; 0,138] 0,604	0,110 [-0,305; 0,524]	
Region = Europe					
N'	71	73			
Baseline Mean (SD)	2,00 (0,691)	1,95 (0,670)			
Week 8:					
Adjusted Mean Change (SE)	0,18 (0,031)	0,18 (0,032)	0,01 [-0,080; 0,095] 0,866	0,030 [-0,314; 0,374]	
Week 16:					
Adjusted Mean Change (SE)	0,19 (0,033)	0,19 (0,033)	0,01 [-0,085; 0,099] 0,877	0,027 [-0,318; 0,373]	
Week 24:					
Adjusted Mean Change (SE)	0,19 (0,036)	0,17 (0,035)	0,02 [-0,074; 0,124] 0,619	0,089 [-0,263; 0,442]	
Region = Latin America					
N'	95	80			
Baseline Mean (SD)	1,74 (0,675)	1,81 (0,669)			

Outcome - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 8:				
Adjusted Mean Change (SE)	0,37 (0,048)	0,26 (0,052)	0,11 [-0,030; 0,249] 0,123	0,249 [-0,067; 0,564]
Week 16:				
Adjusted Mean Change (SE)	0,37 (0,047)	0,27 (0,051)	0,10 [-0,035; 0,241] 0,143	0,239 [-0,081; 0,559]
Week 24:				
Adjusted Mean Change (SE)	0,36 (0,049)	0,28 (0,053)	0,09 [-0,054; 0,230] 0,225	0,197 [-0,121; 0,516]
Region = Others				
N'	4	1		
Baseline Mean (SD)	1,79 (0,774)	0,85 (-)		
Week 8:				
Adjusted Mean Change (SE)	0,04 (0,169)			-
Week 16:				
Adjusted Mean Change (SE)	0,44 (0,185)	0,01 (0,315)	0,43 [-0,618; 1,476] 0,307	1,335 [-1,110; 3,780]
Week 24:				
Adjusted Mean Change (SE)	0,38 (0,074)	-0,10 (0,171)	0,48 [-0,013; 0,969] 0,054	3,230 [0,262; 6,198]
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 + 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 subpopulation "high-dose ICS/LABA"				

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

	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Trough FEV1				
Interaction Test	0,490			
Asthma exacerbations in the 12 months prior to screening = 1				
N'	161	166		
Baseline Mean (SD)	1,84 (0,676)	1,90 (0,665)		
Week 8:				
Adjusted Mean Change (SE)	0,24 (0,037)	0,20 (0,037)	0,04 [-0,037; 0,121] 0,298	0,093 [-0,135; 0,322]
Week 16:				
Adjusted Mean Change (SE)	0,25 (0,037)	0,22 (0,037)	0,02 [-0,054; 0,104] 0,537	0,056 [-0,173; 0,285]
Week 24:				
Adjusted Mean Change (SE)	0,25 (0,038)	0,21 (0,038)	0,04 [-0,041; 0,124] 0,318	0,093 [-0,139; 0,324]
Asthma exacerbations in the 12 months prior to screening = ≥2				
N'	58	42		
Baseline Mean (SD)	1,68 (0,649)	1,59 (0,570)		
Week 8:				
Adjusted Mean Change (SE)	0,21 (0,056)	0,19 (0,064)	0,03 [-0,118; 0,174] 0,709	0,071 [-0,355; 0,497]
Week 16:				
Adjusted Mean Change (SE)	0,28 (0,056)	0,16 (0,064)	0,12 [-0,029; 0,264] 0,117	0,306 [-0,131; 0,744]

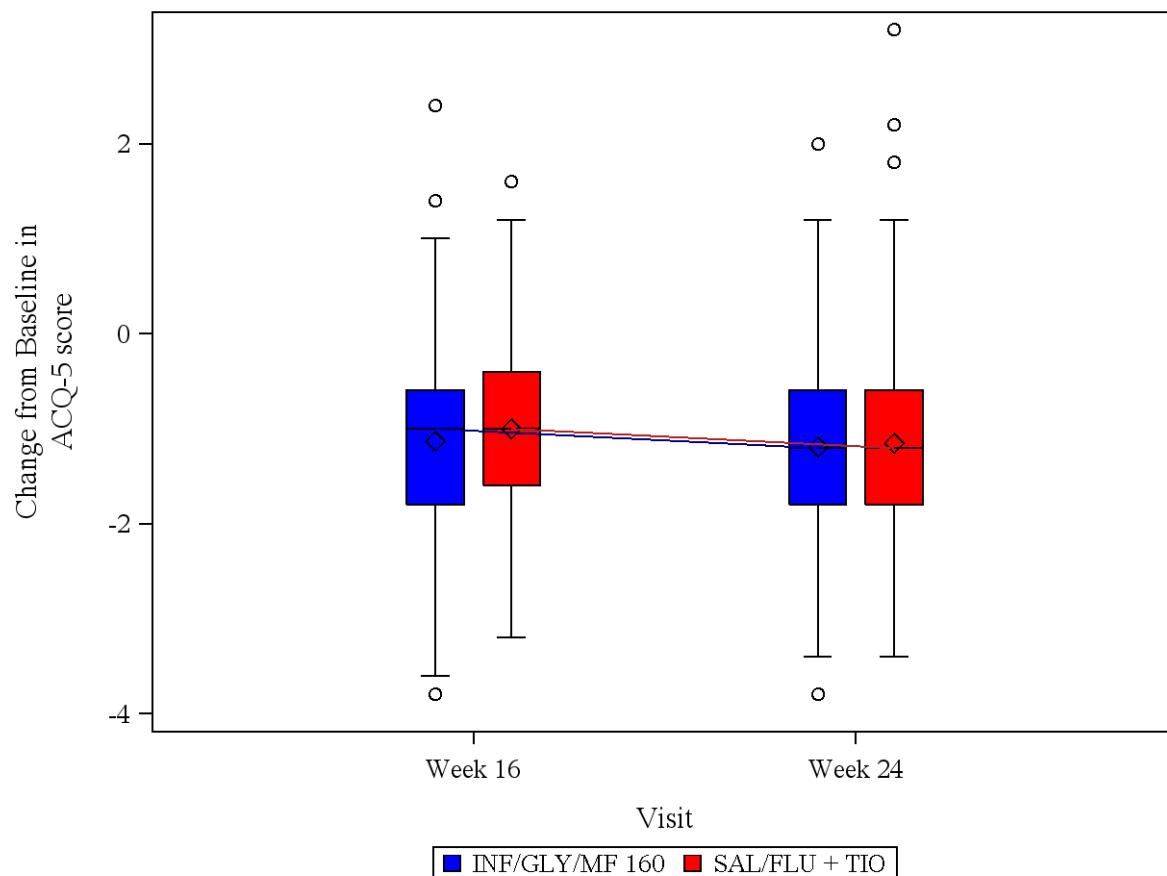
Outcome - Change from Baseline (FAS) by Subgroup	Treatment groups		Comparison	
	IND/GLY/ MF 160 N=242	SAL/FLU + TIO N=232	Mean Difference [95% CI] p-value	Hedges' G [95% CI]
Week 24:				
Adjusted Mean Change (SE)	0,27 (0,058)	0,14 (0,065)	0,13 [-0,023; 0,279] 0,097	0,319 [-0,110; 0,747]
N': Number of 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 + 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 subpopulation "high-dose ICS/LABA"				

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

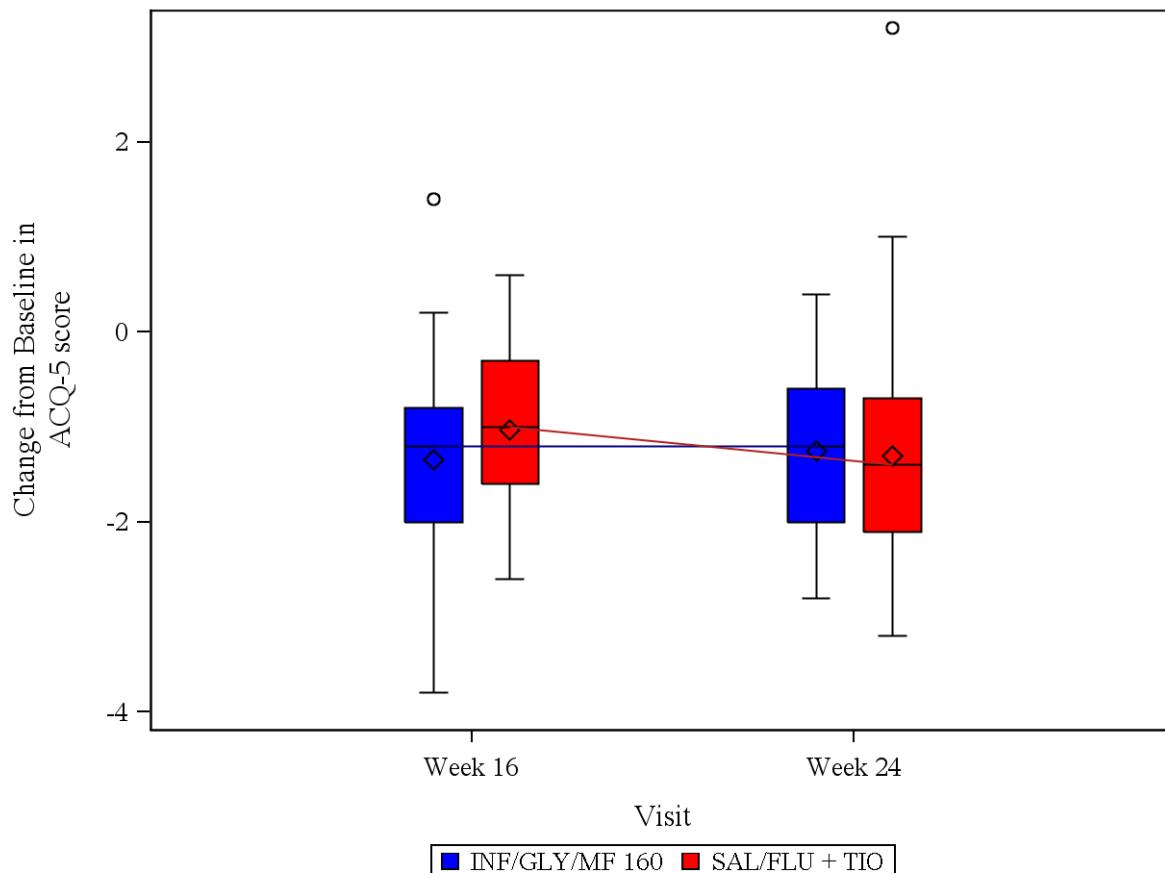


Figure 3.2.2 ACQ-5 - Change from Baseline by Age (FAS), Age = 40-64 years

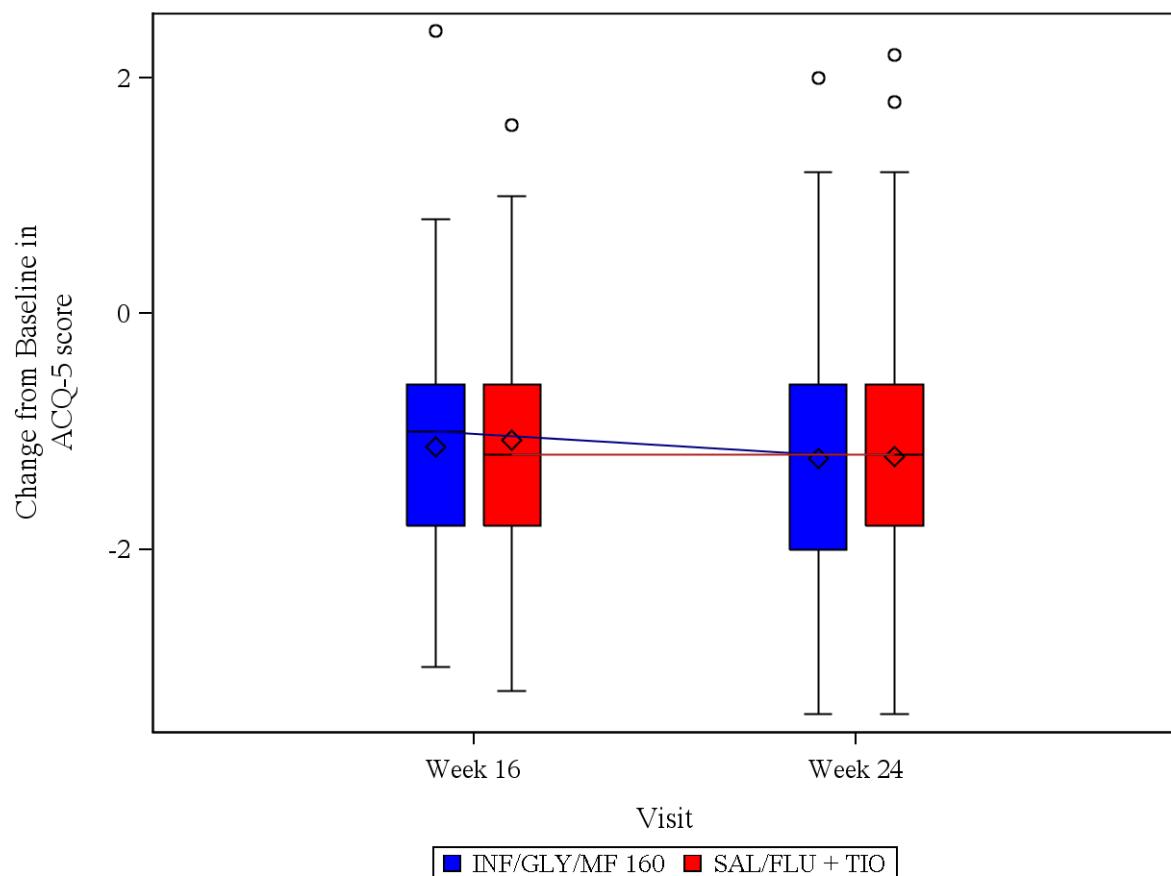
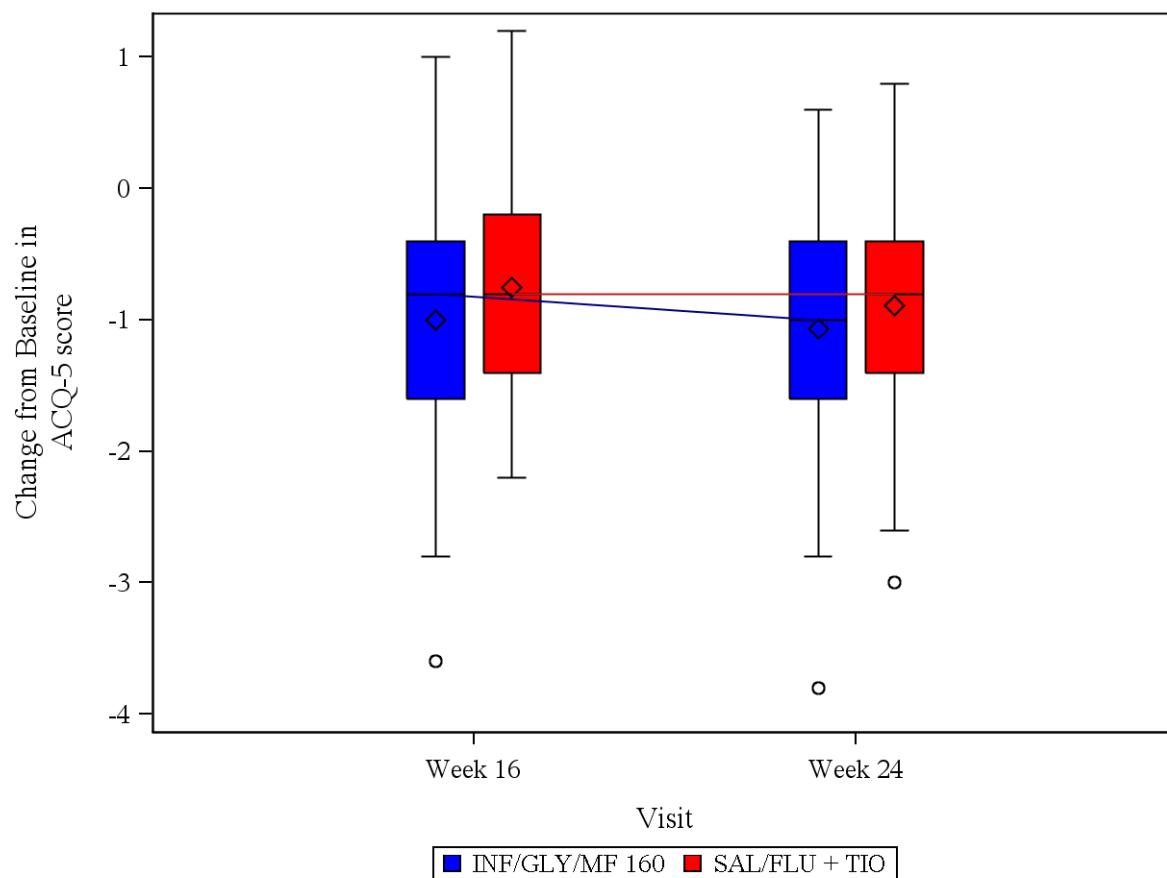


Figure 3.2.3 ACQ-5 - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

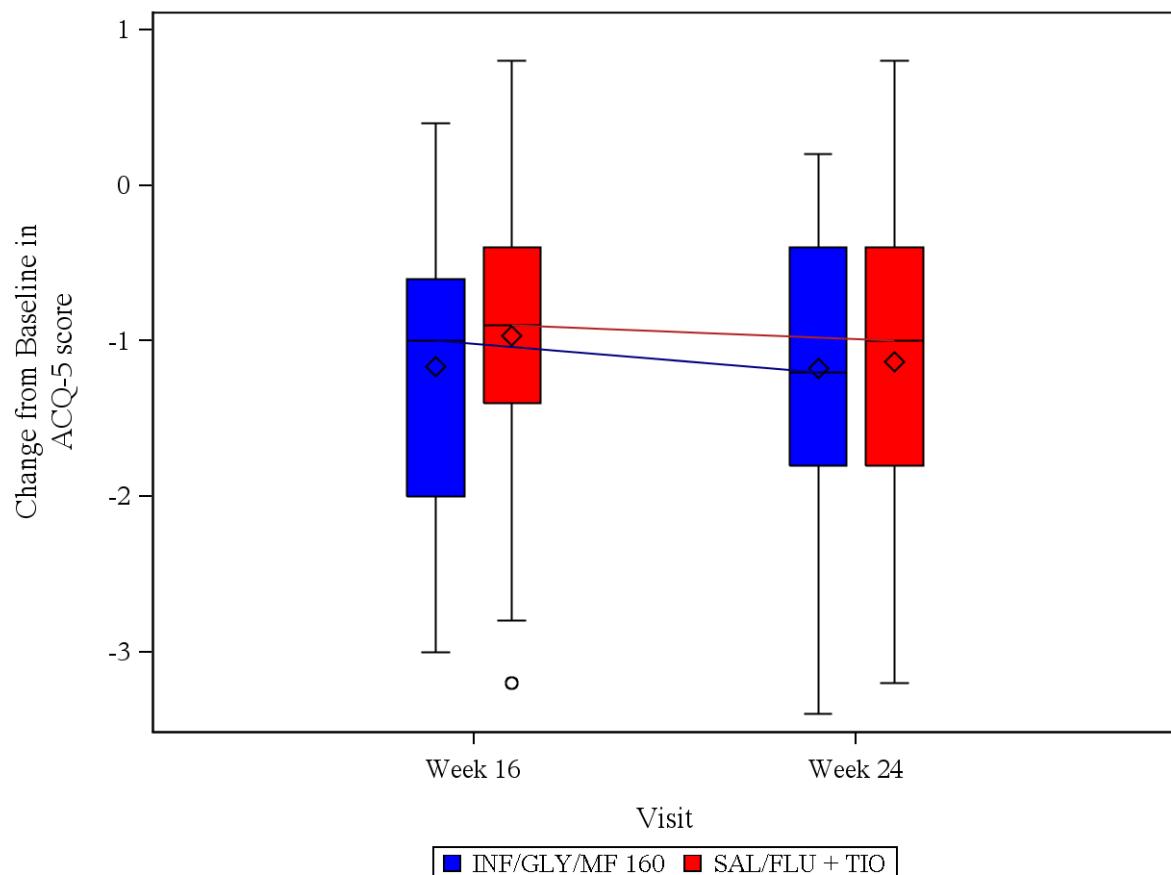
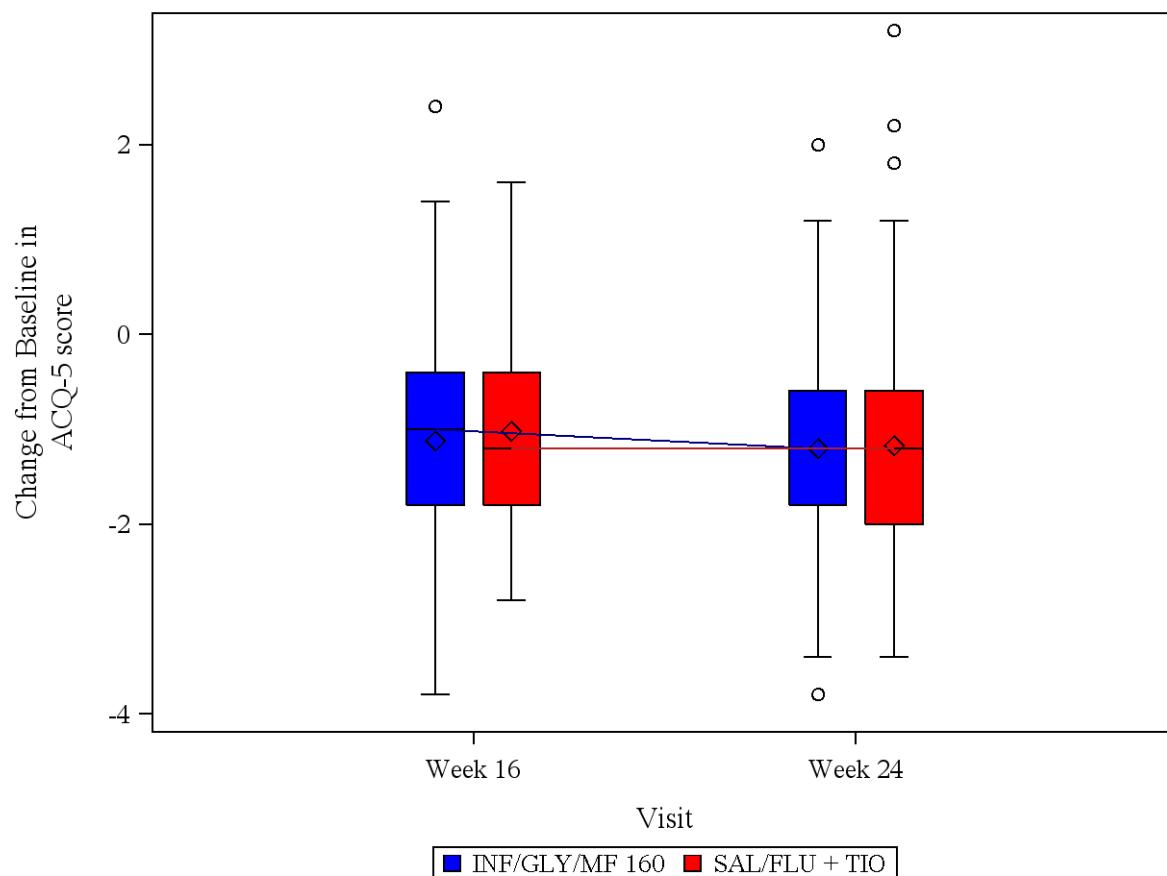


Figure 3.3.2 ACQ-5 - Change from Baseline by Gender (FAS), Gender = Female



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

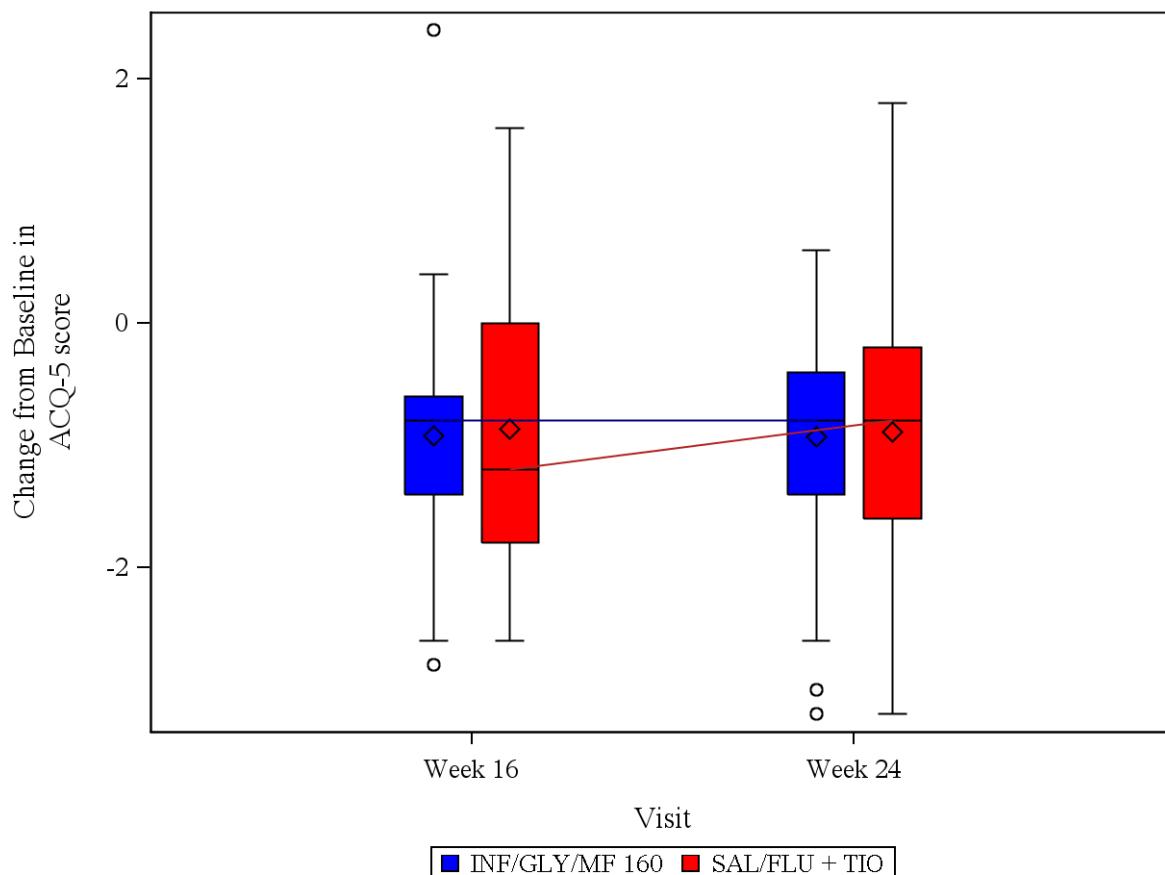


Figure 3.4.2 ACQ-5 - Change from Baseline by Region (FAS), Region = Europe

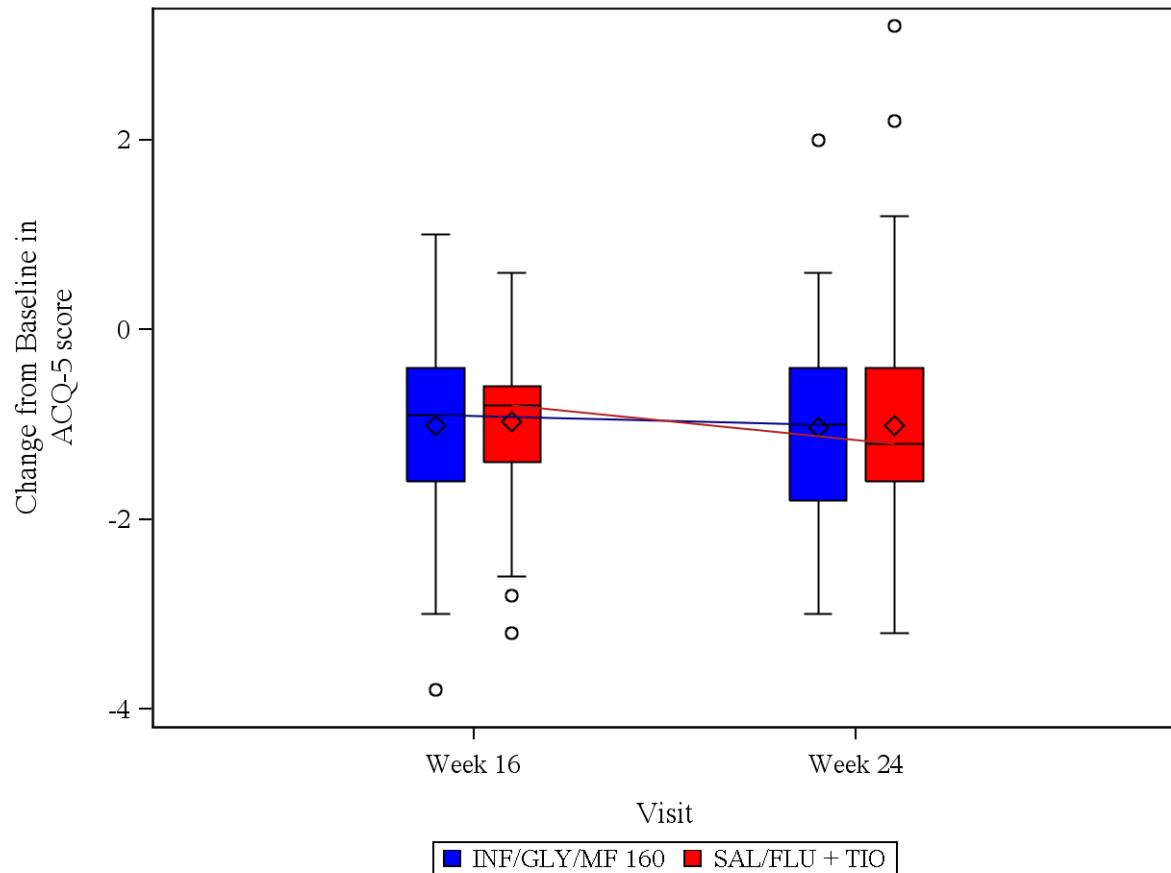


Figure 3.4.3 ACQ-5 - Change from Baseline by Region (FAS), Region = Latin America

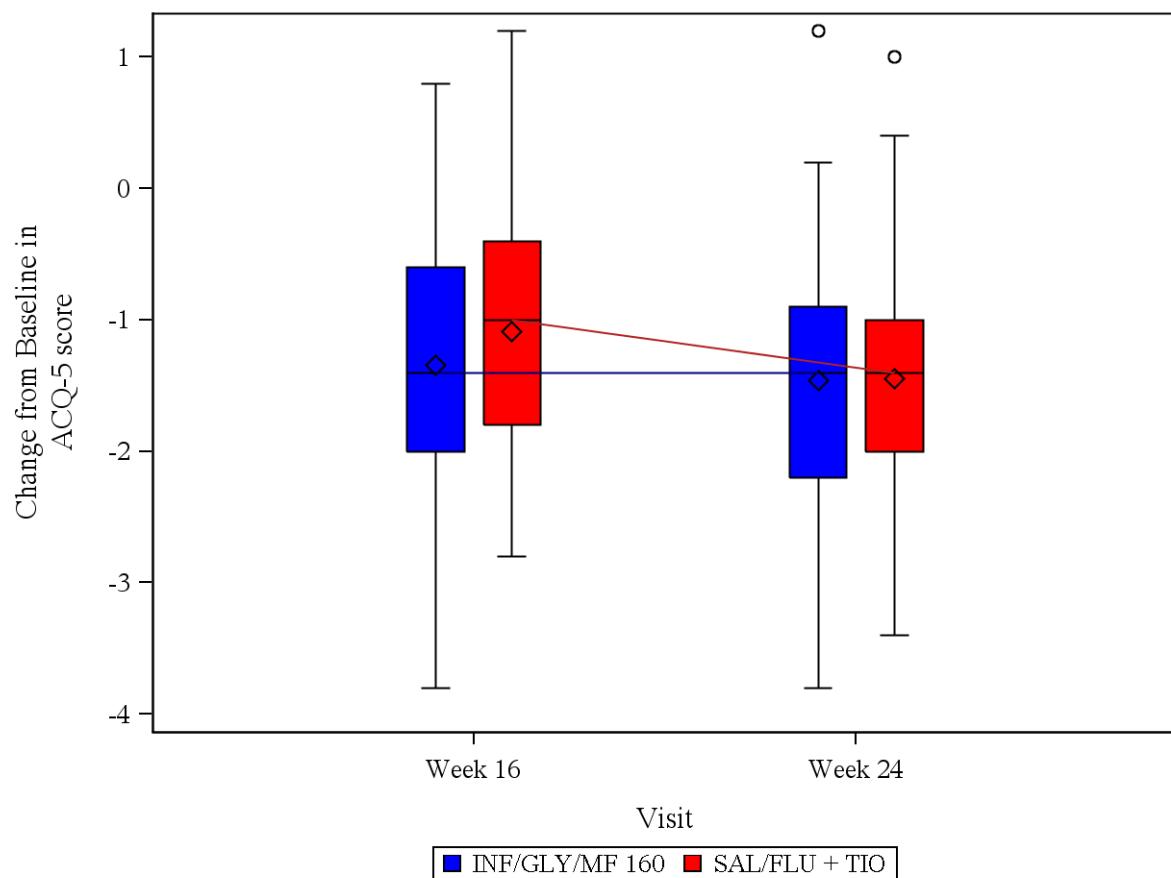
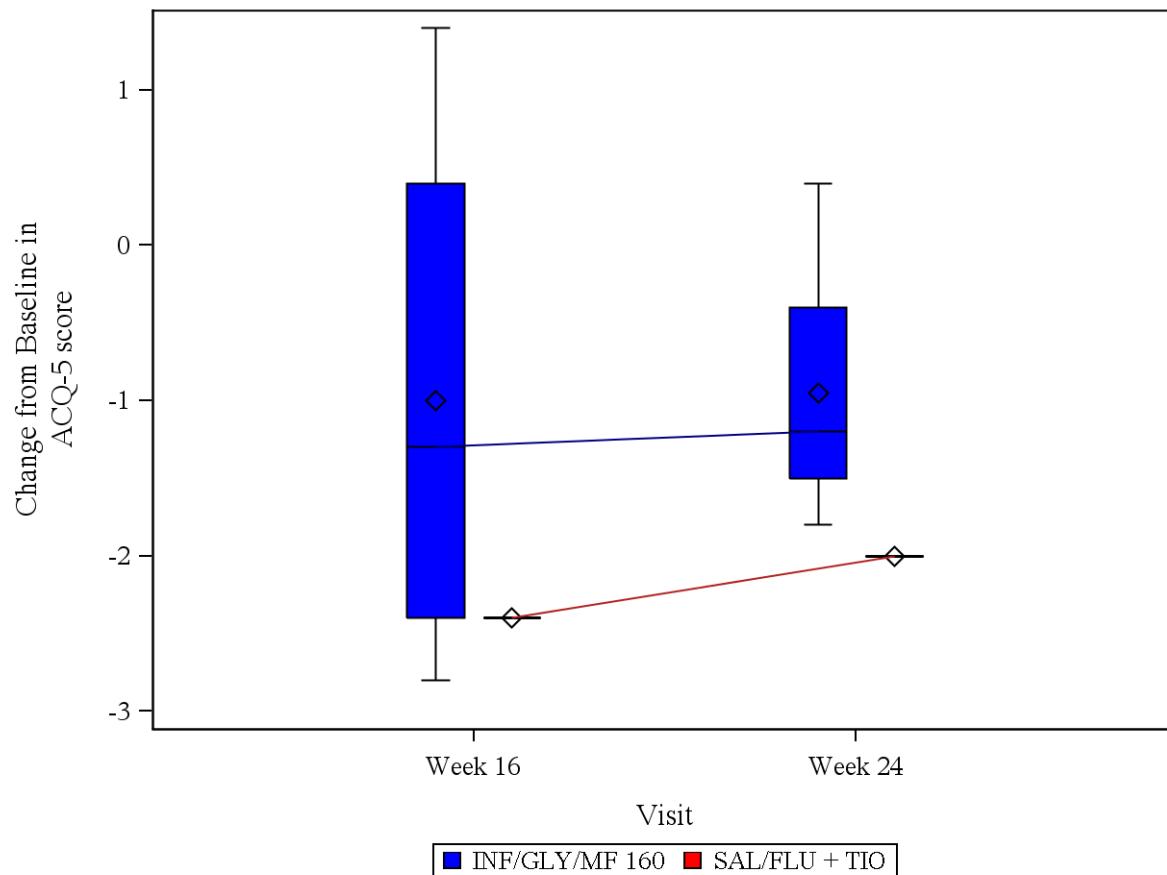
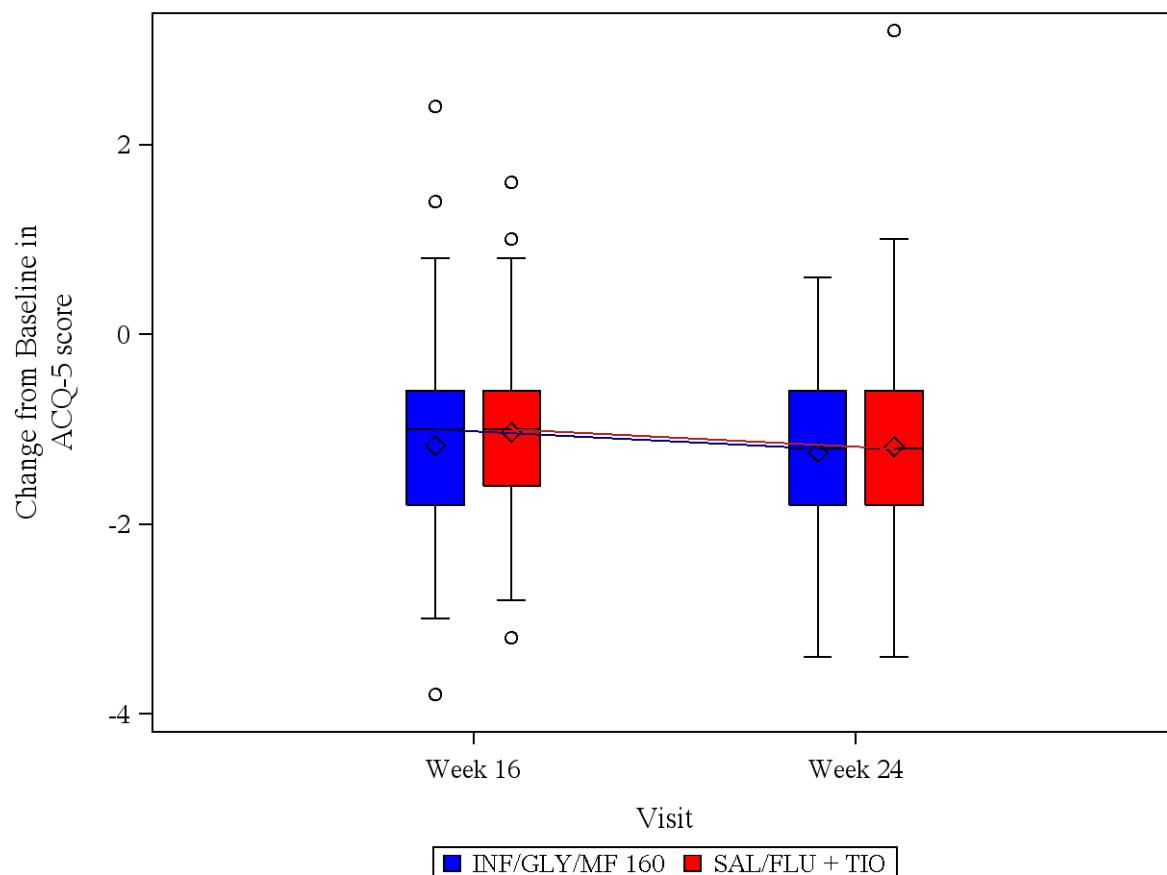


Figure 3.4.4 ACQ-5 - Change from Baseline by Region (FAS), Region = Others

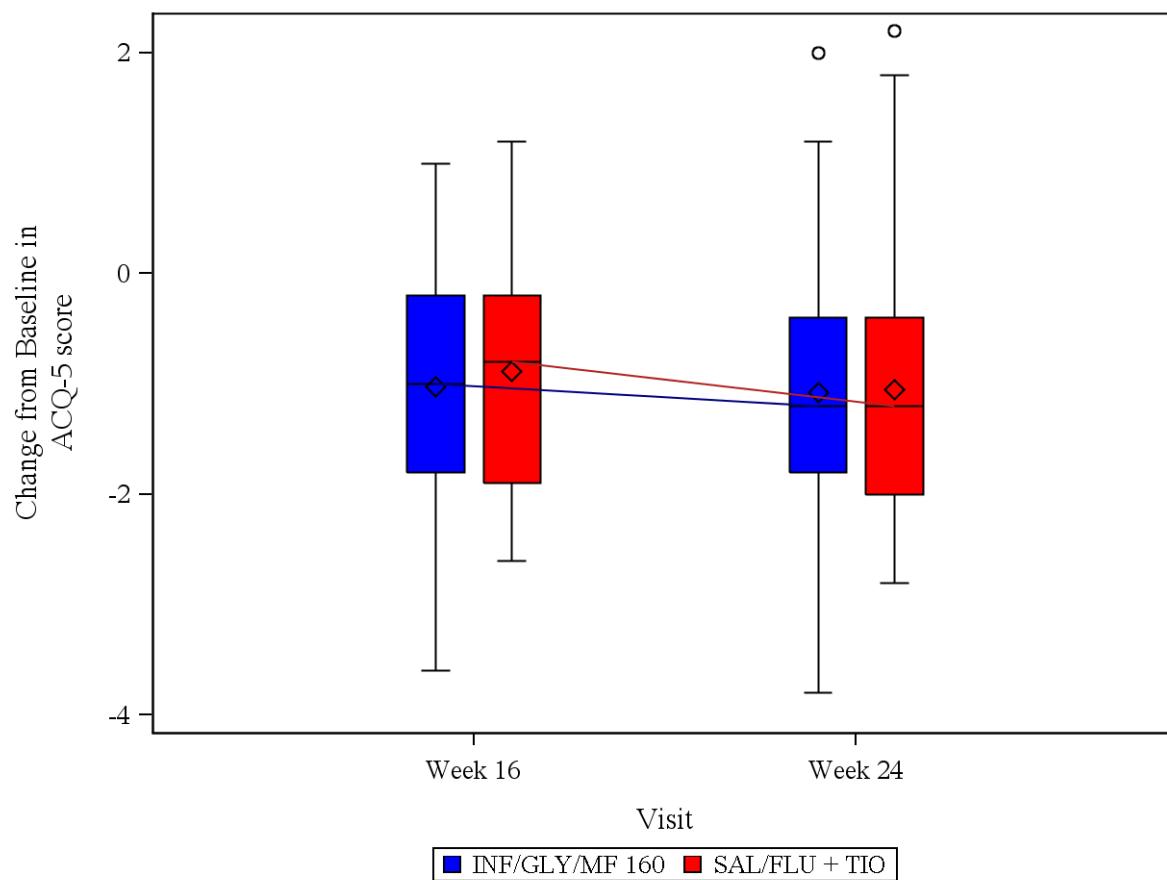


3.5 Boxplot: ACQ-5 - Change from Baseline by History of Asthma Exacerbation (FAS)

**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**



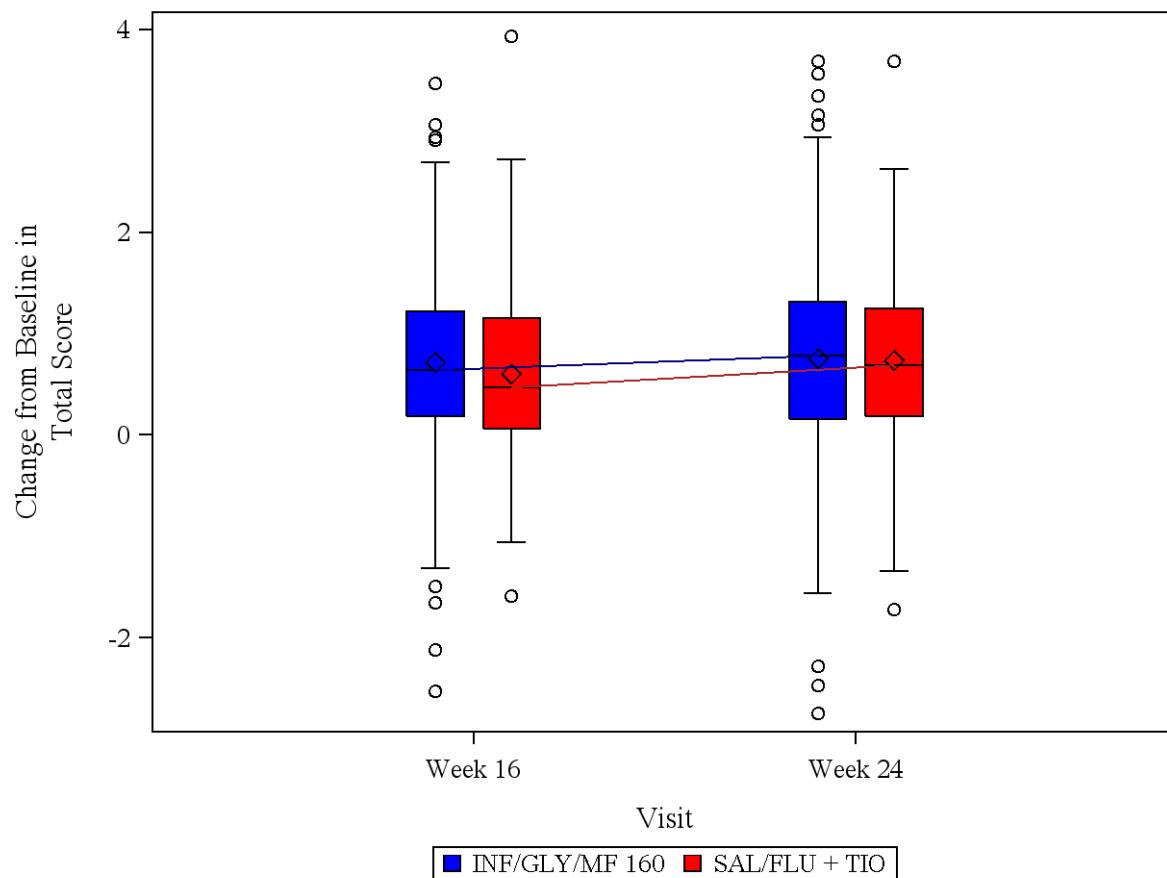
**Figure 3.5.2 ACQ-5 - Change from Baseline by History of Asthma Exacerbation (FAS),
Asthma exacerbations in the 12 months prior to screening = ≥ 2**



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

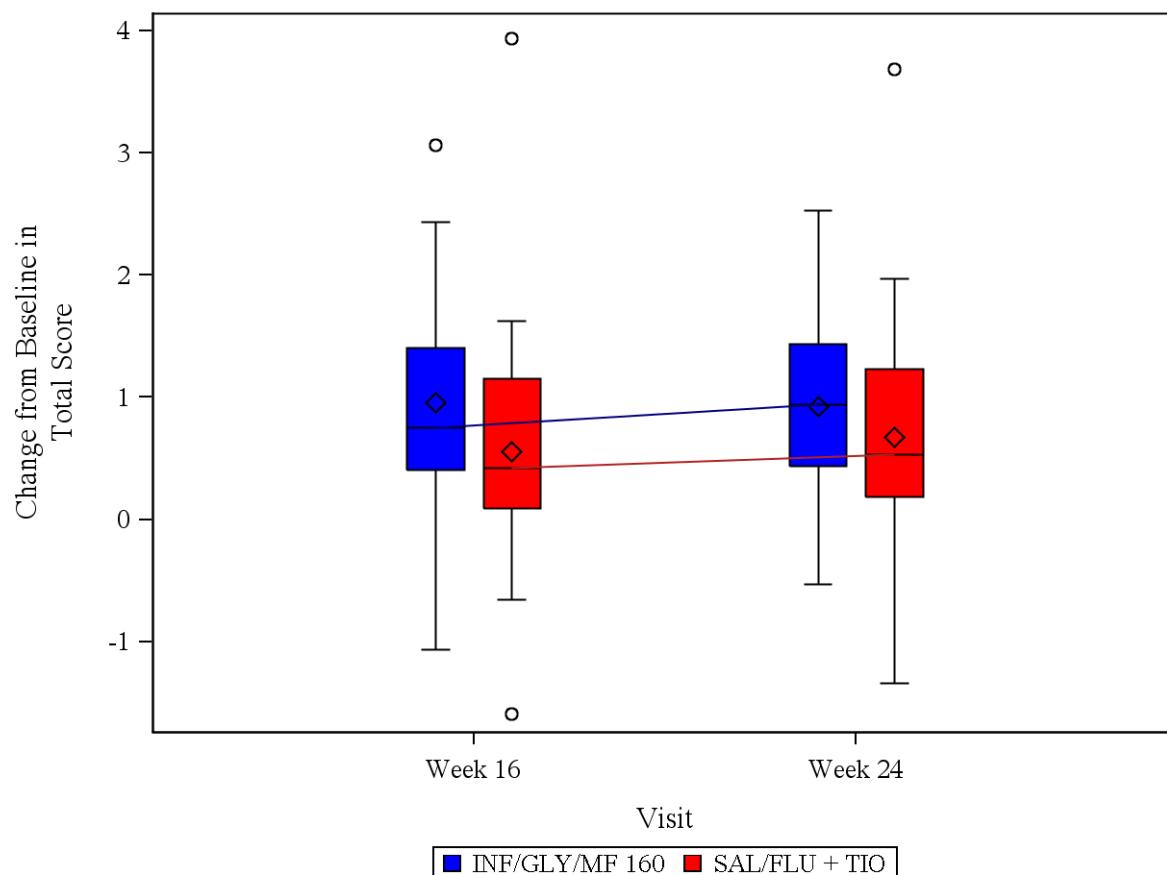


Figure 5.2.2 AQLQ-S (Total Score) - Change from Baseline by Age (FAS), Age = 40-64 years

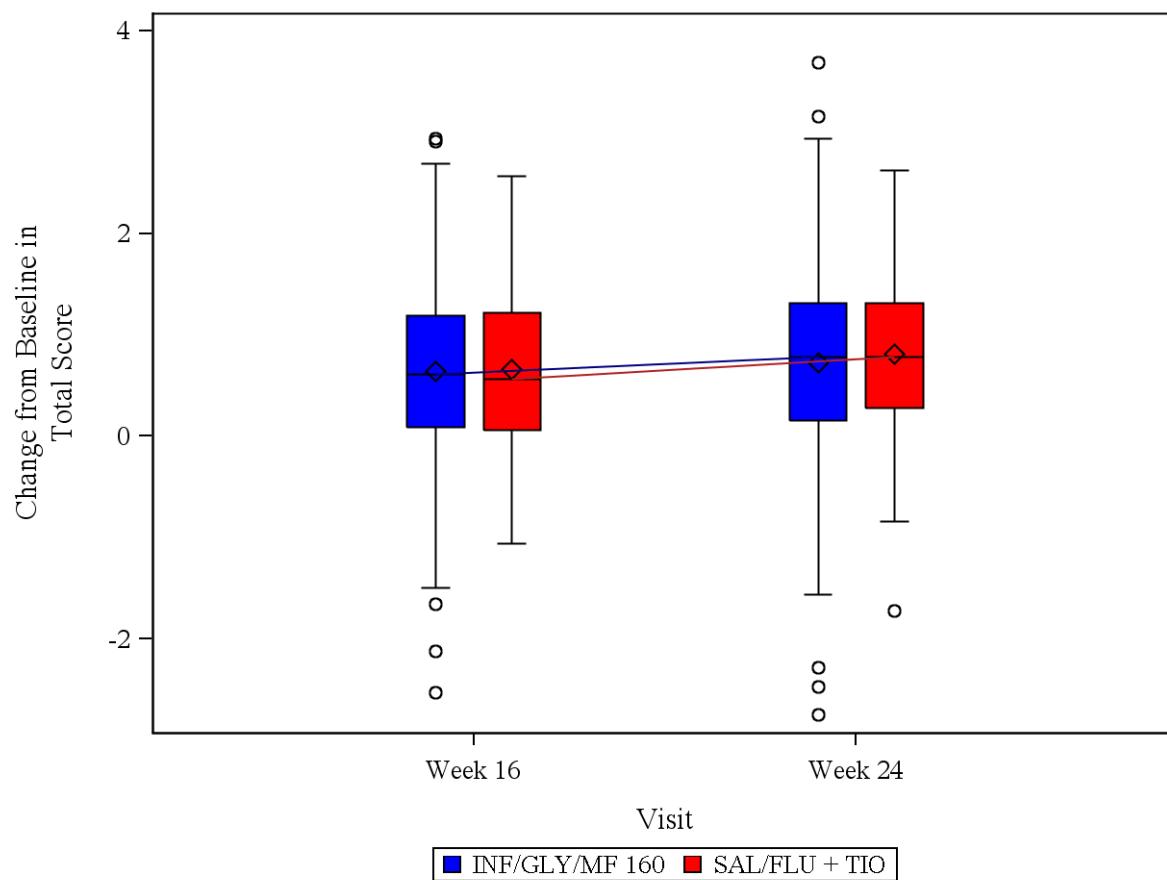
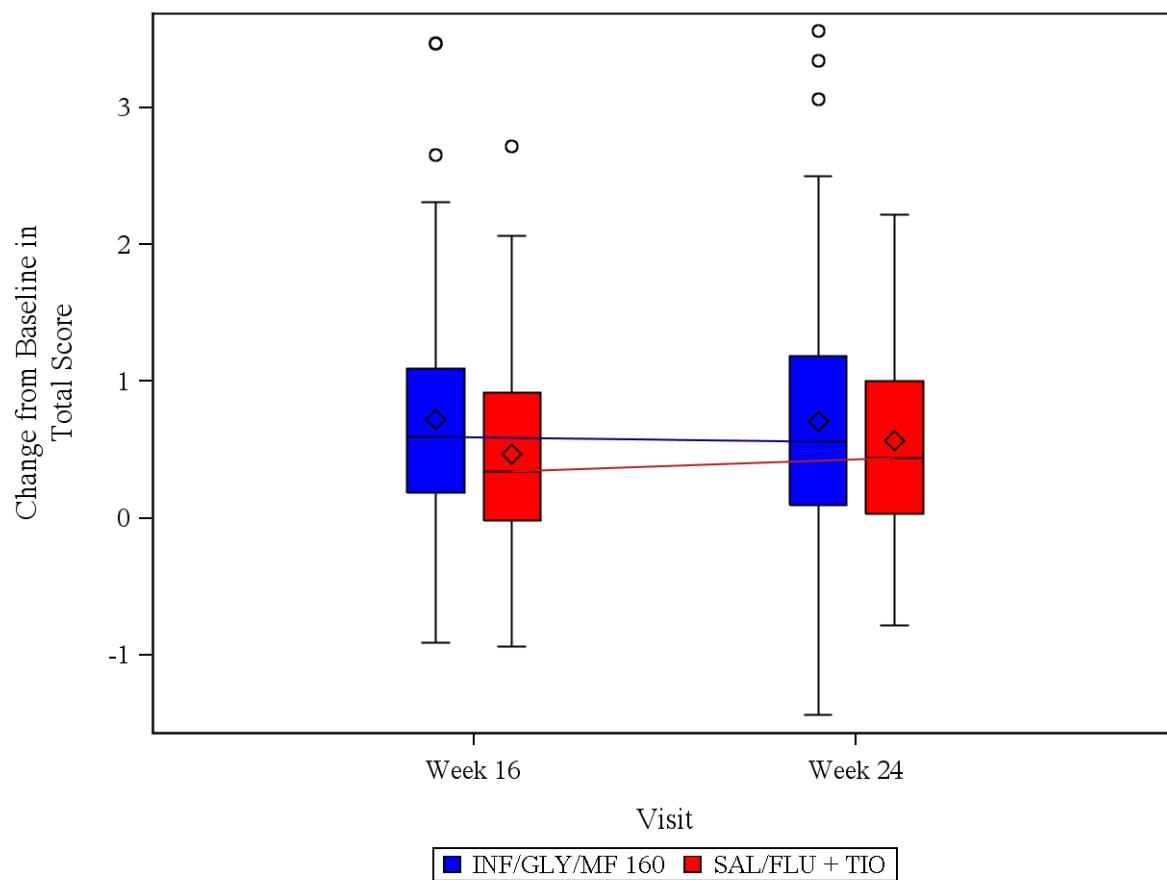


Figure 5.2.3 AQLQ-S (Total Score) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

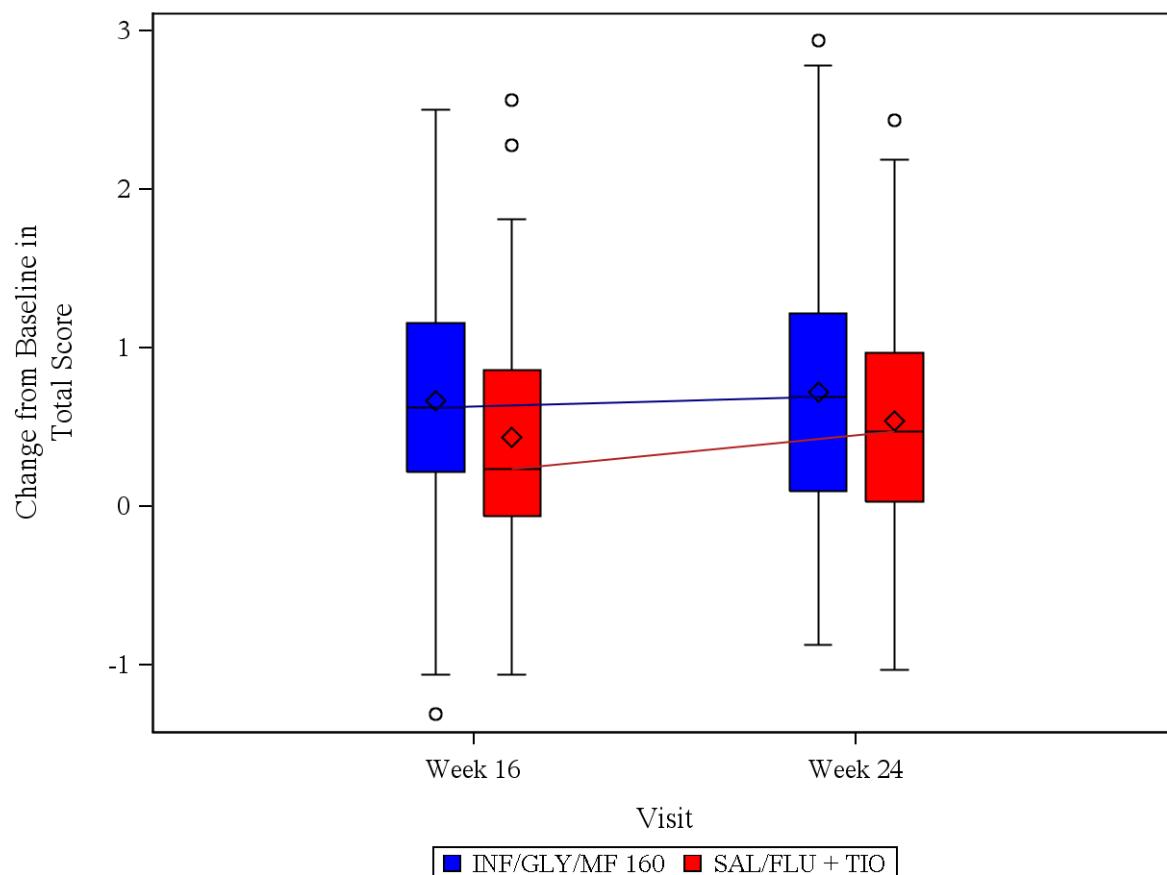
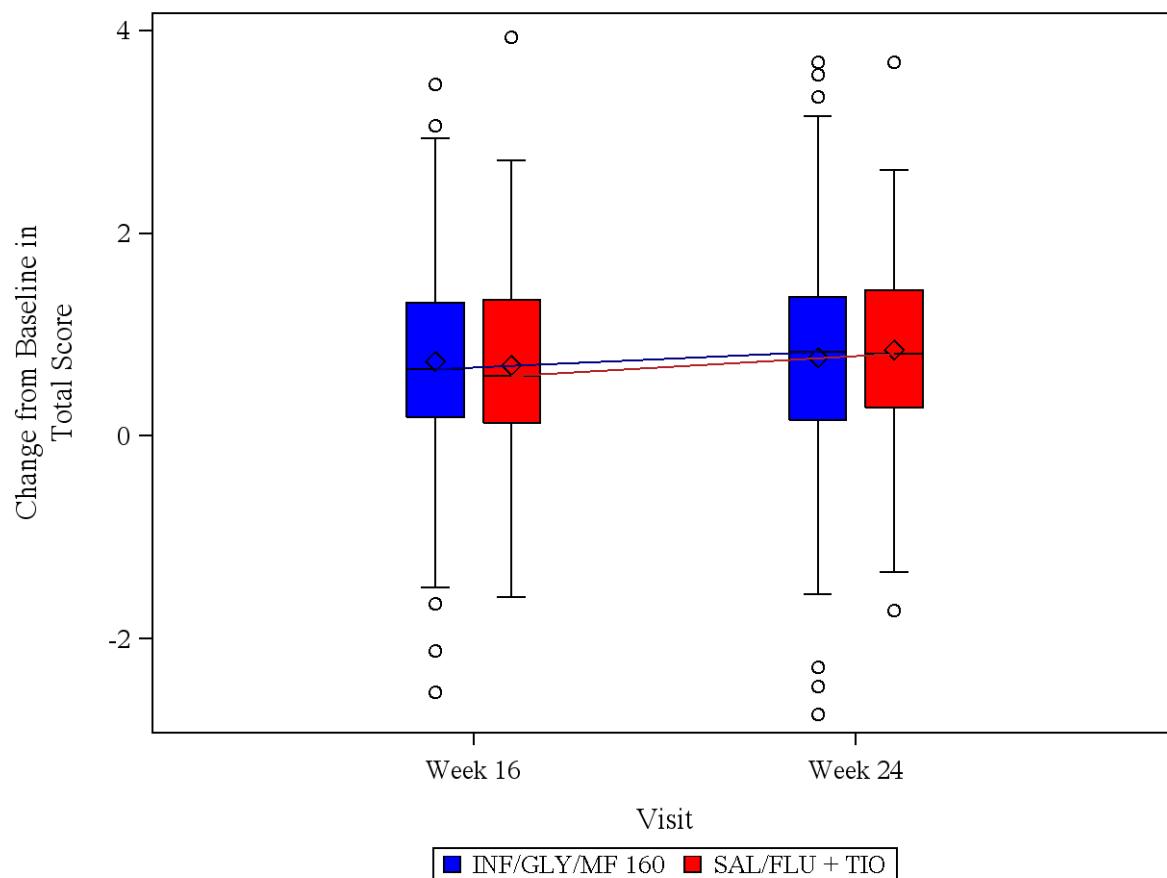


Figure 5.3.2 AQLQ-S (Total Score) - Change from Baseline by Gender (FAS), Gender = Female



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

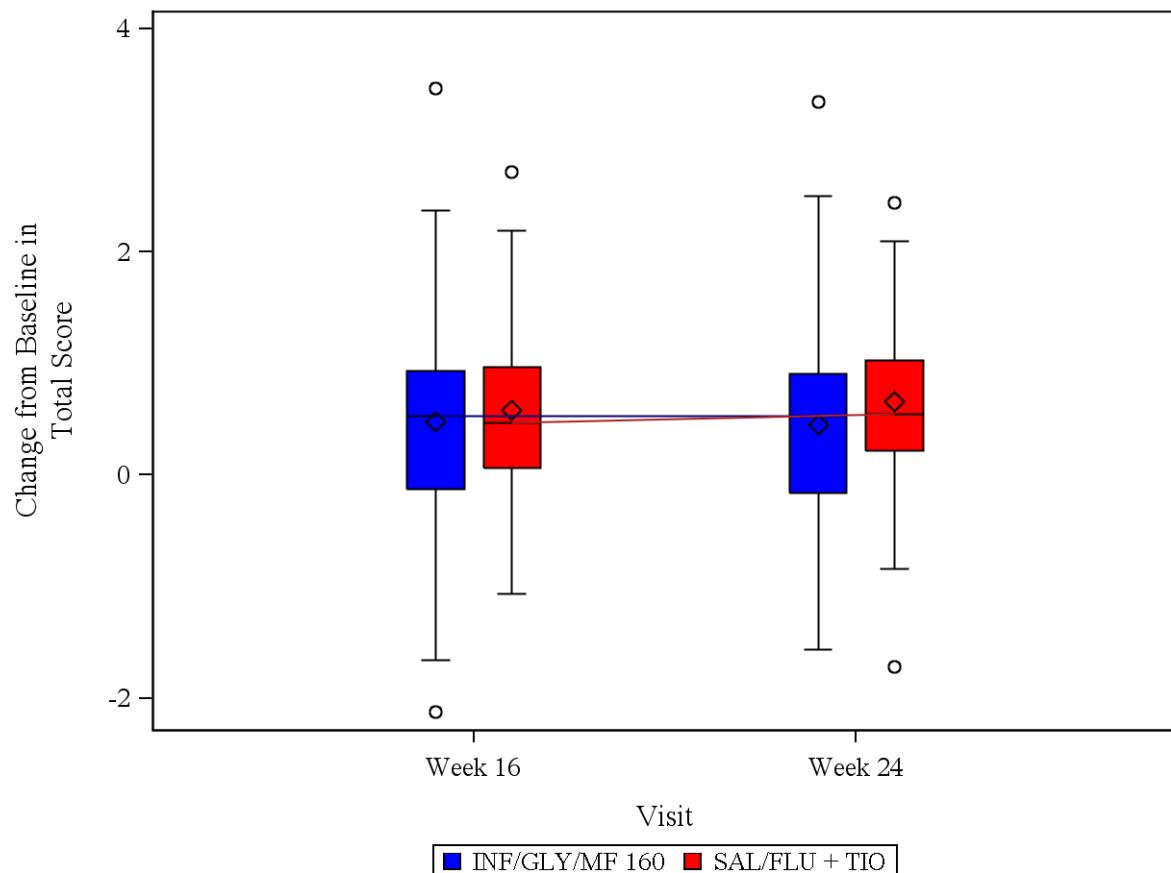


Figure 5.4.2 AQLQ-S (Total Score) - Change from Baseline by Region (FAS), Region = Europe

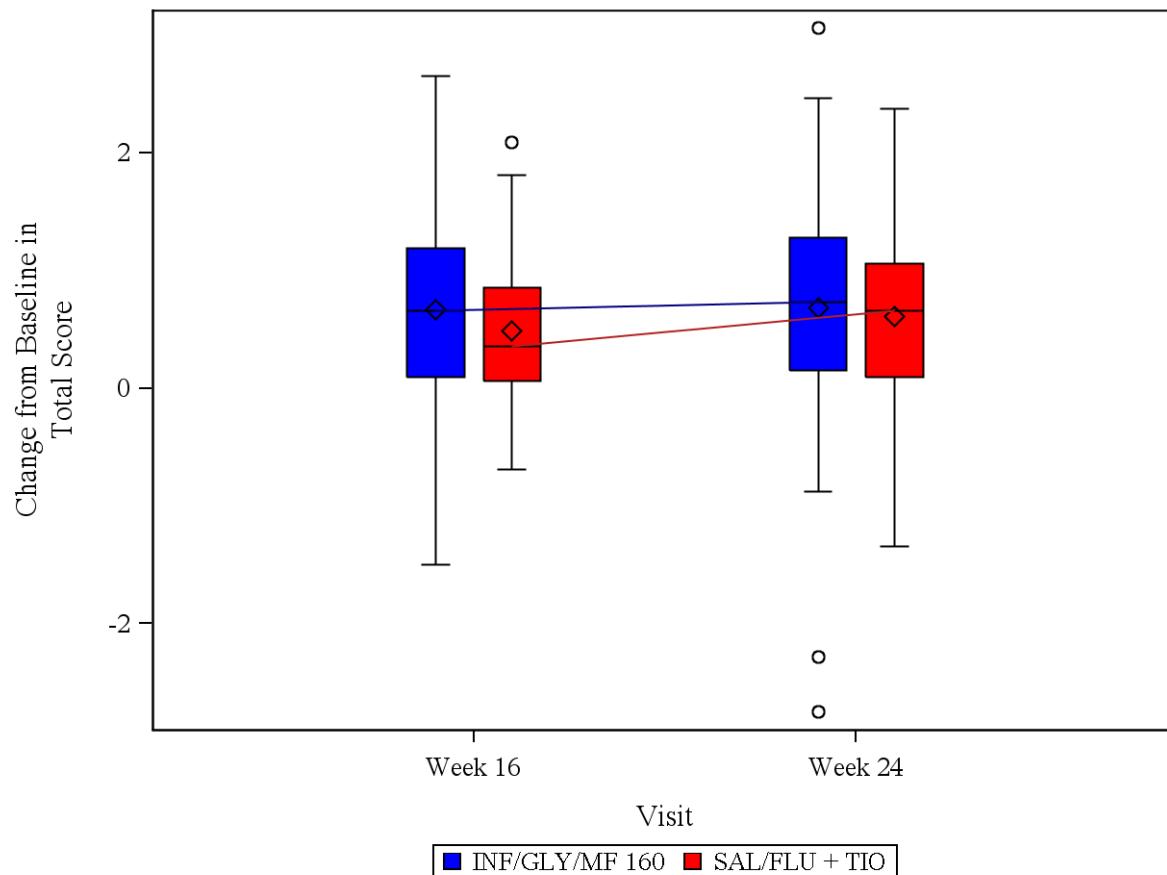


Figure 5.4.3 AQLQ-S (Total Score) - Change from Baseline by Region (FAS), Region = Latin America

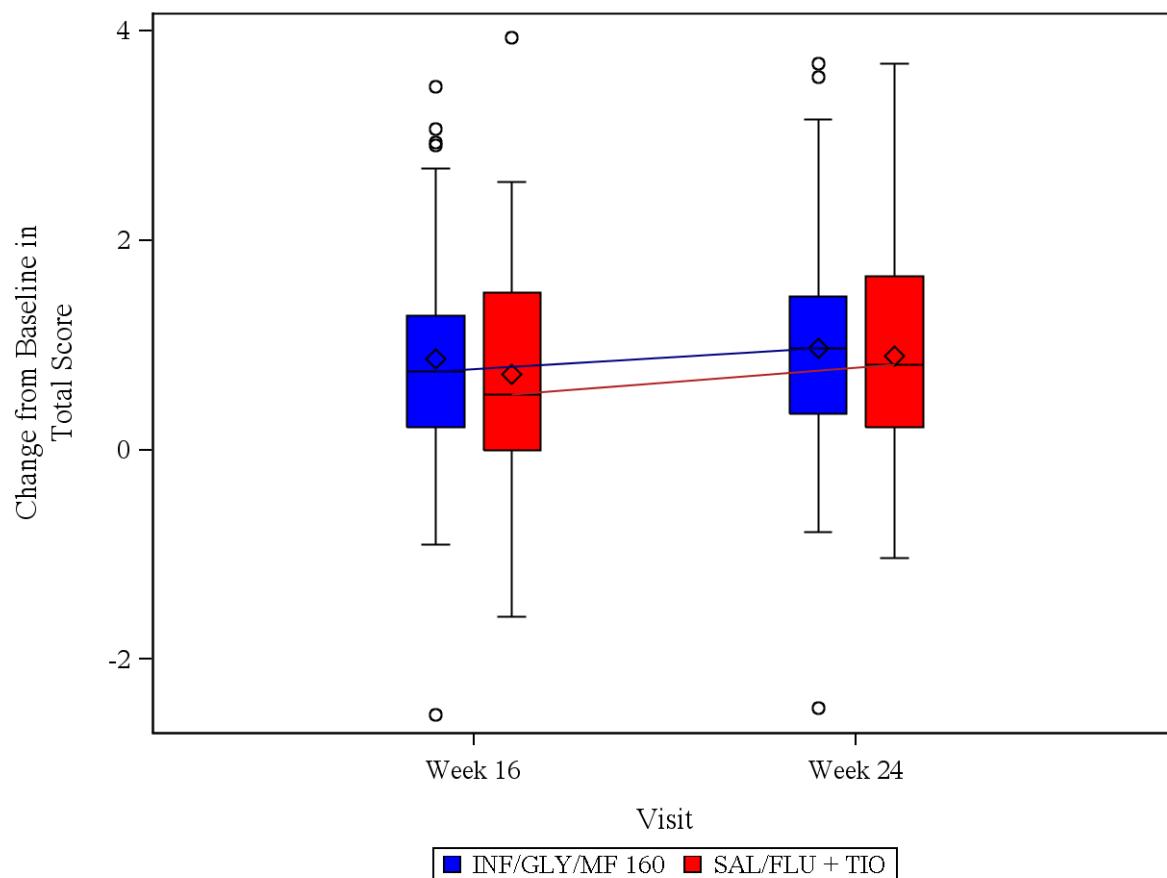
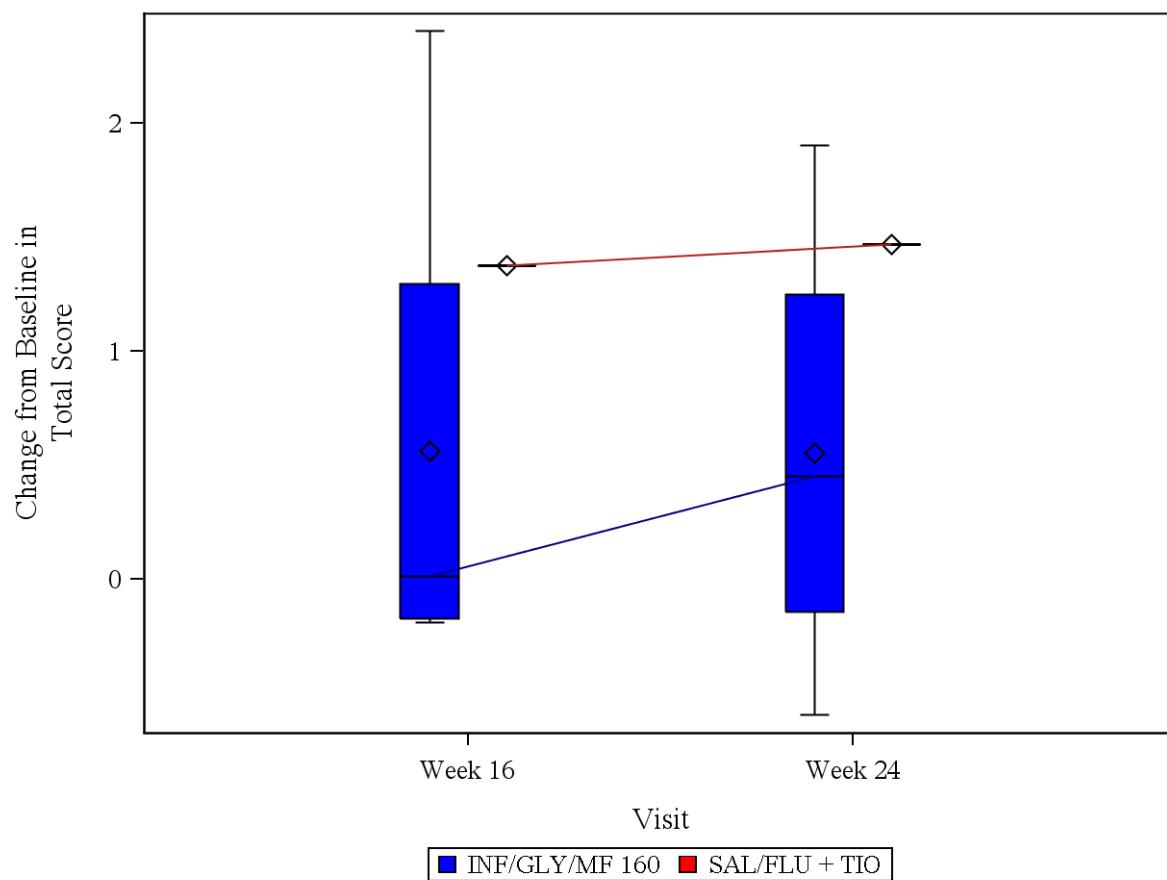


Figure 5.4.4 AQLQ-S (Total Score) - Change from Baseline by Region (FAS), Region = Others



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

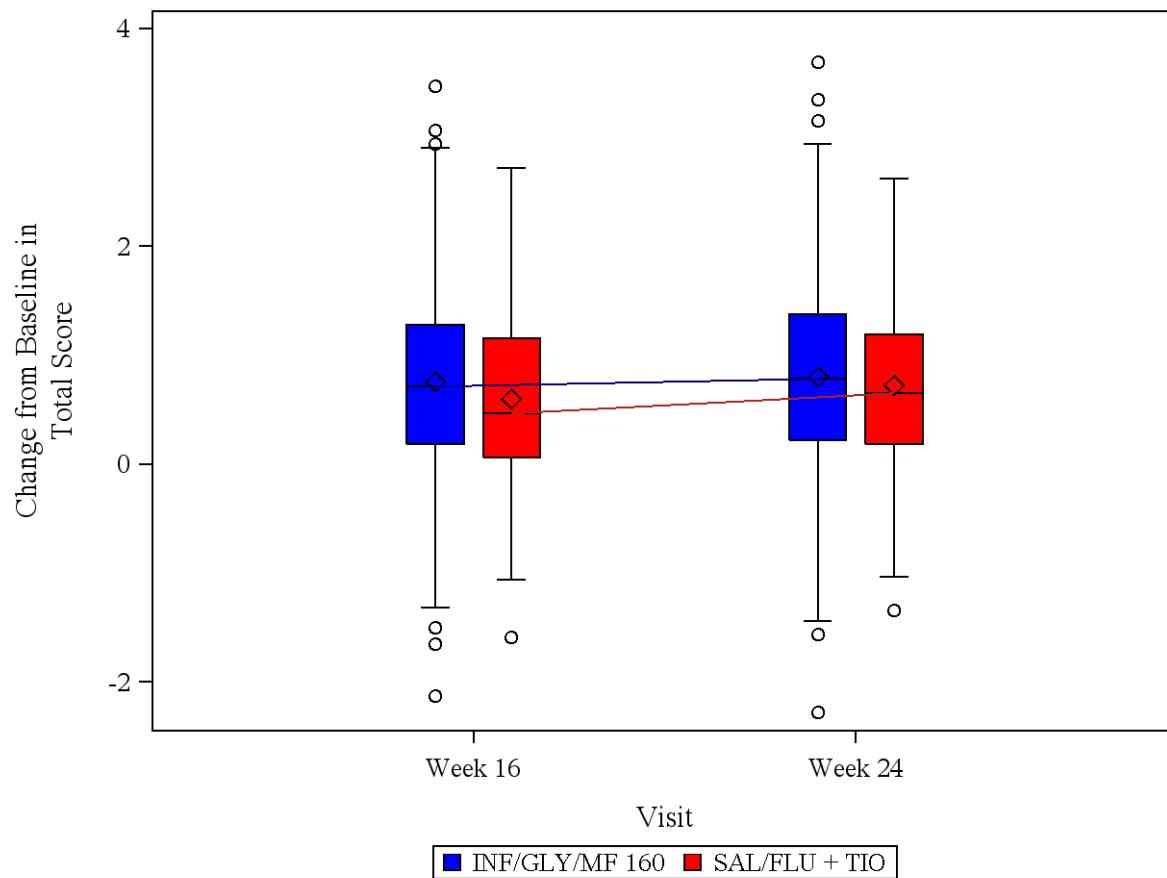
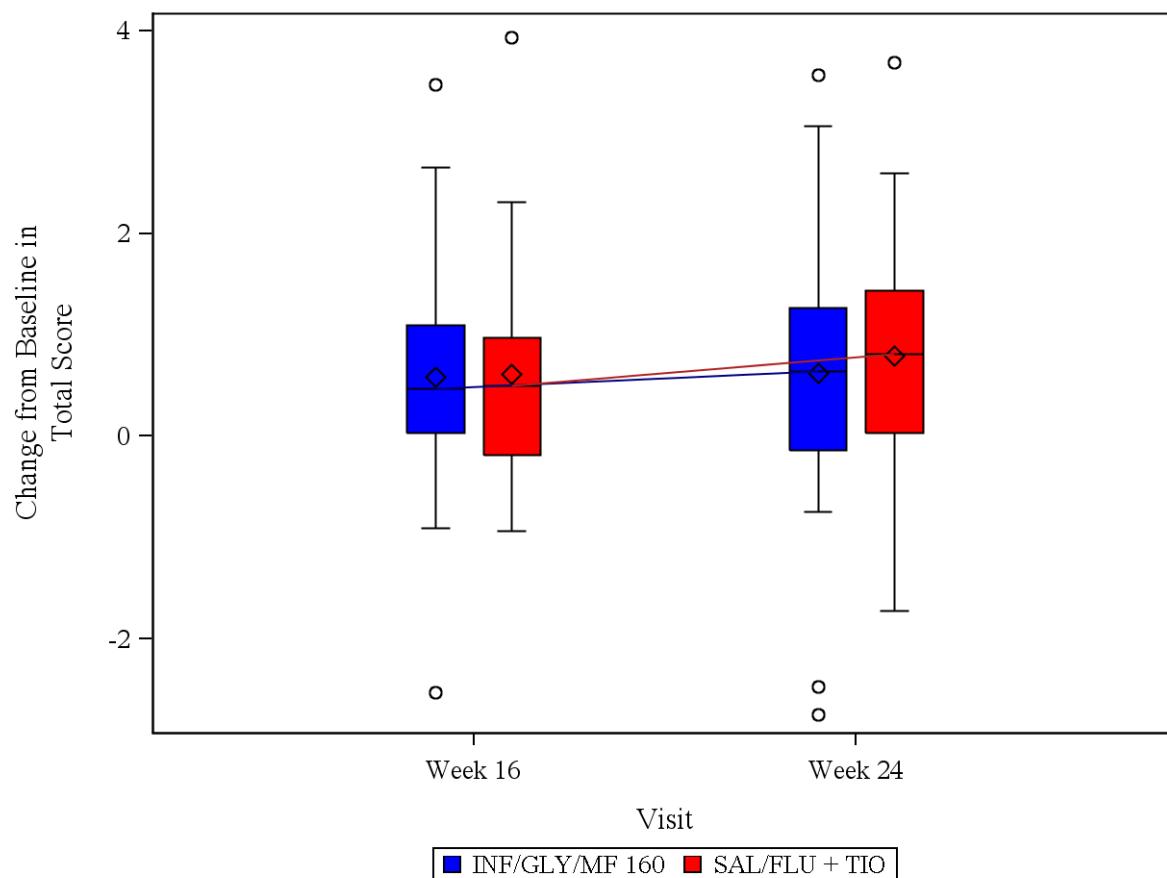
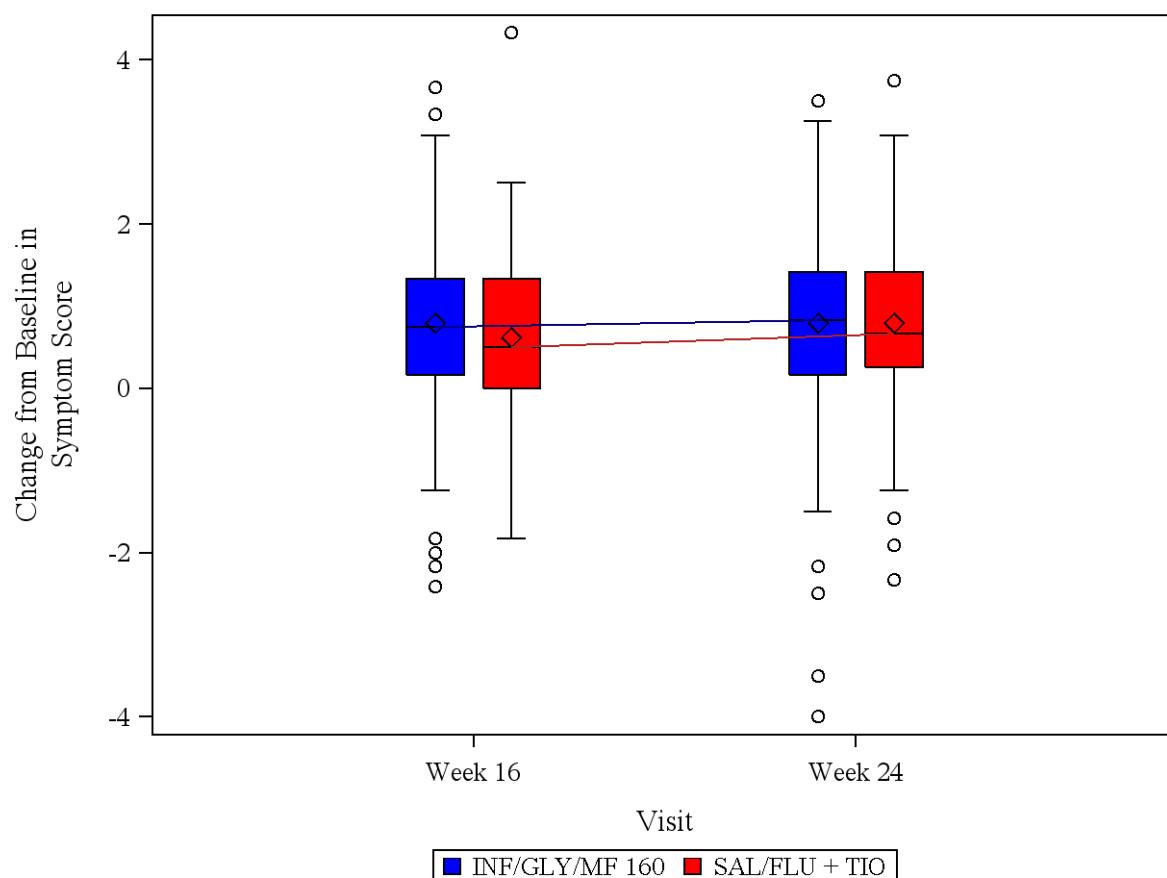


Figure 5.5.2 AQLQ-S (Total Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



5.7 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

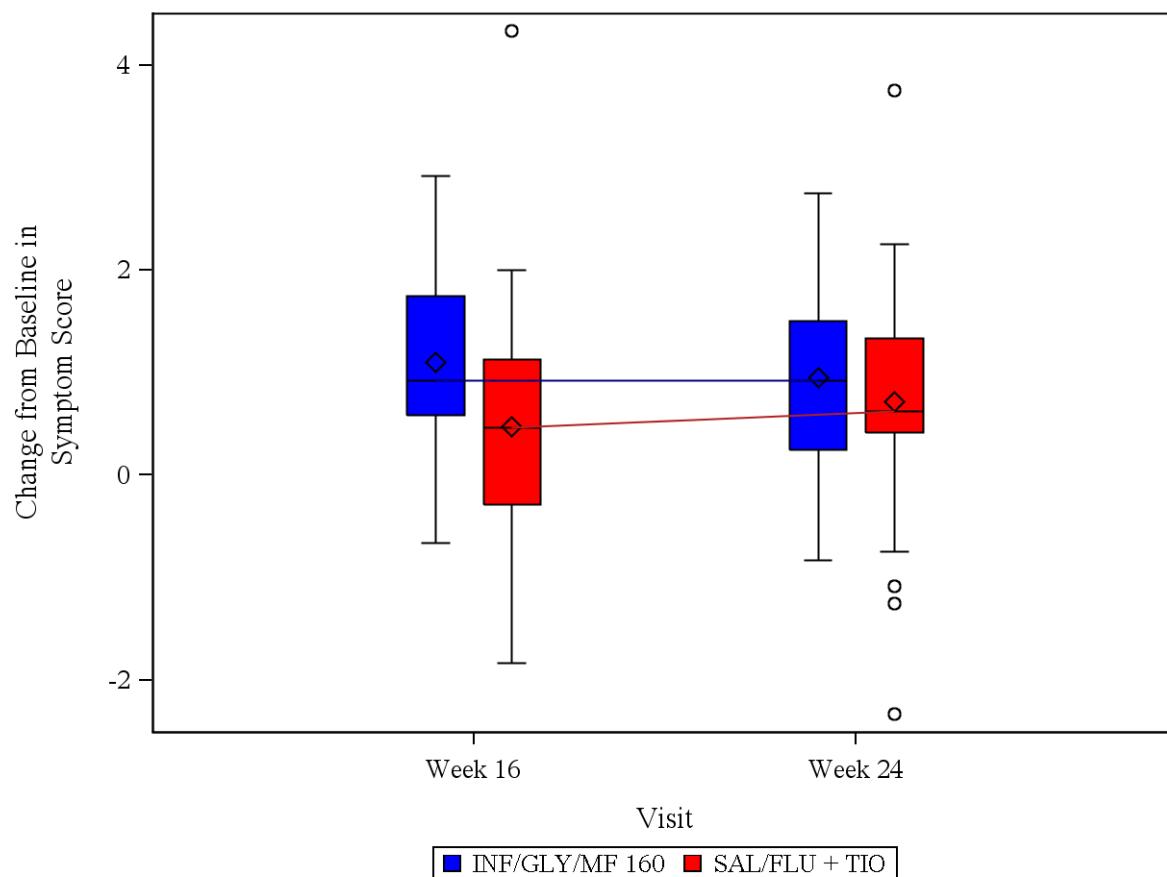


Figure 5.8.2 AQLQ-S (Symptom Score) - Change from Baseline by Age (FAS), Age = 40-64 years

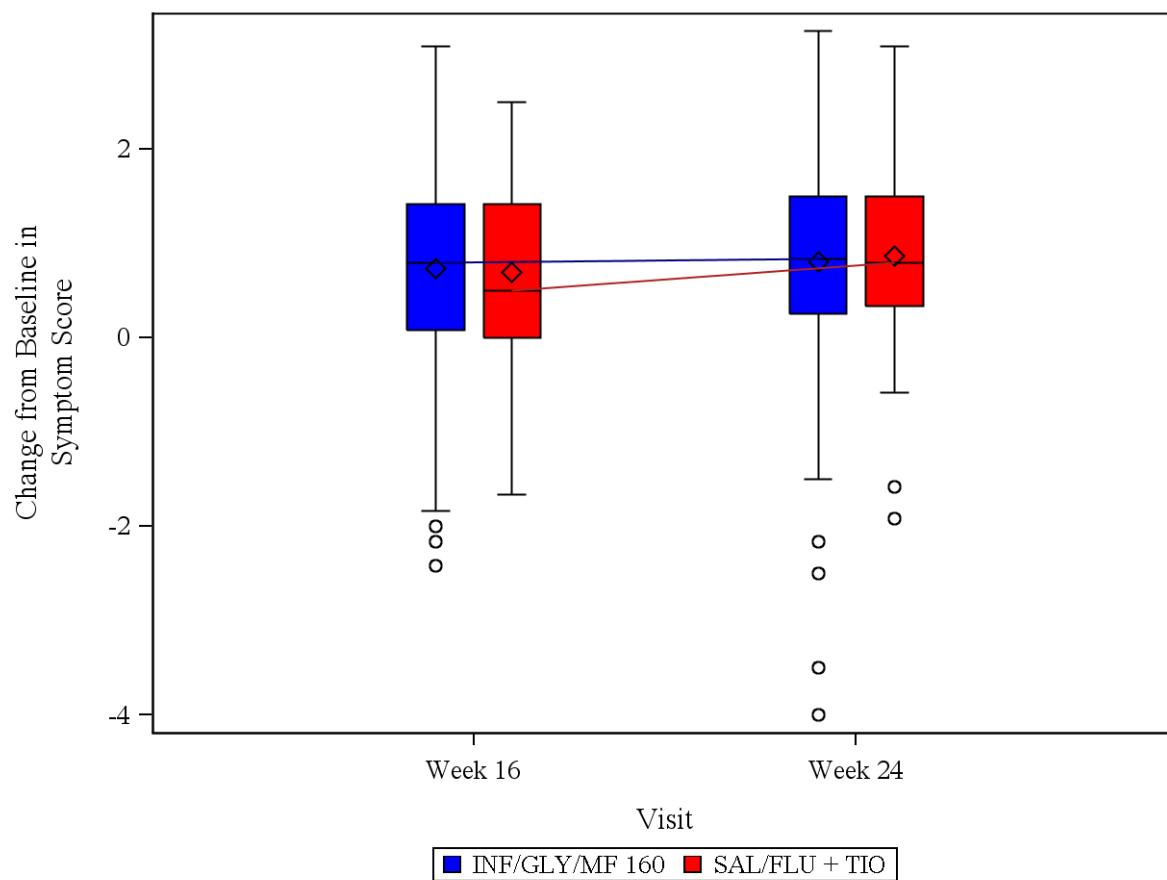
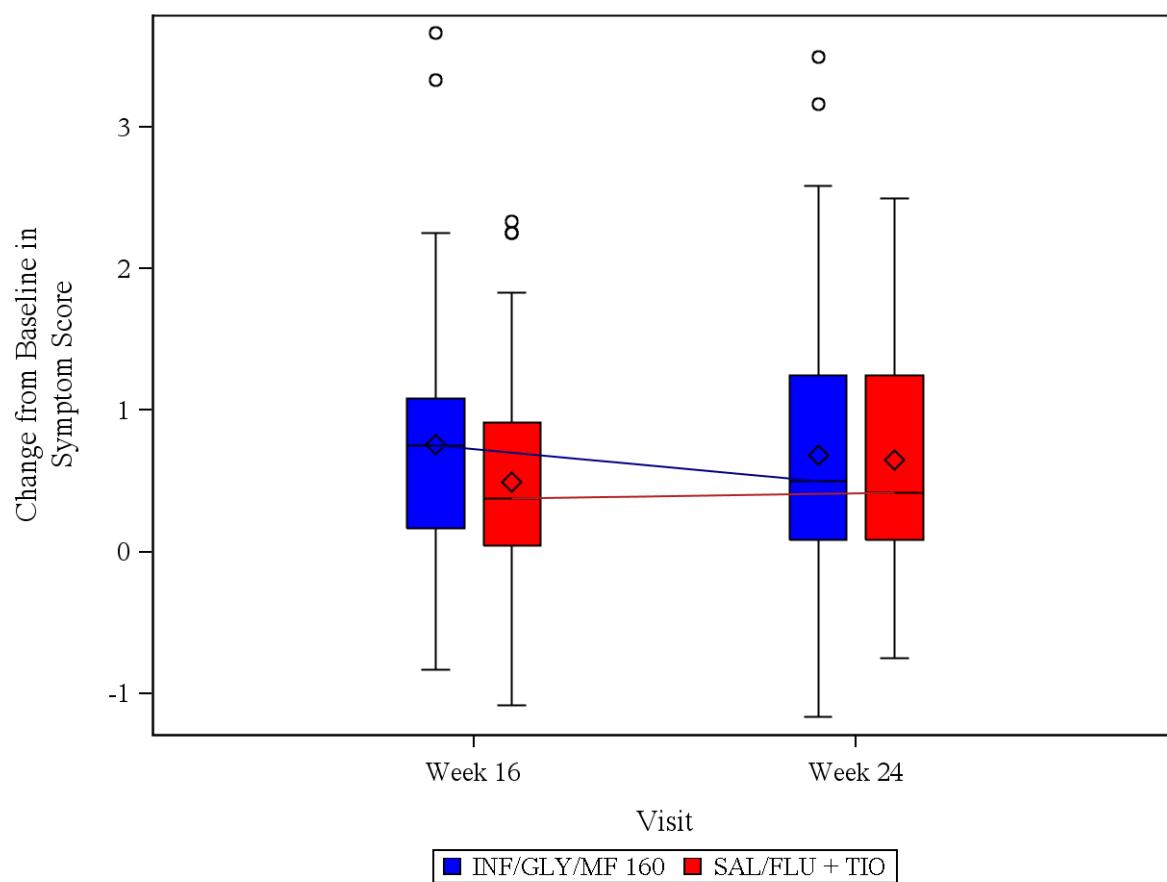
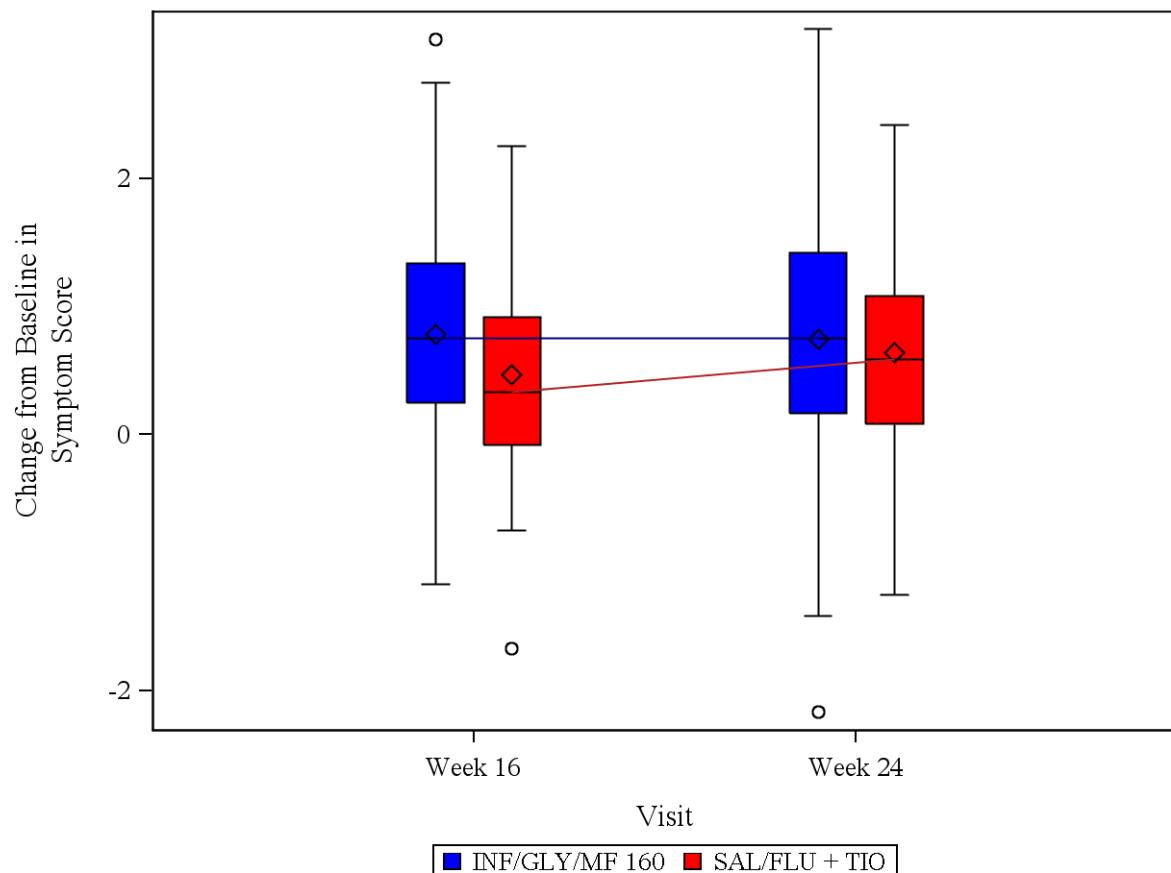


Figure 5.8.3 AQLQ-S (Symptom Score) - Change from Baseline by Age (FAS), Age = ≥ 65 years

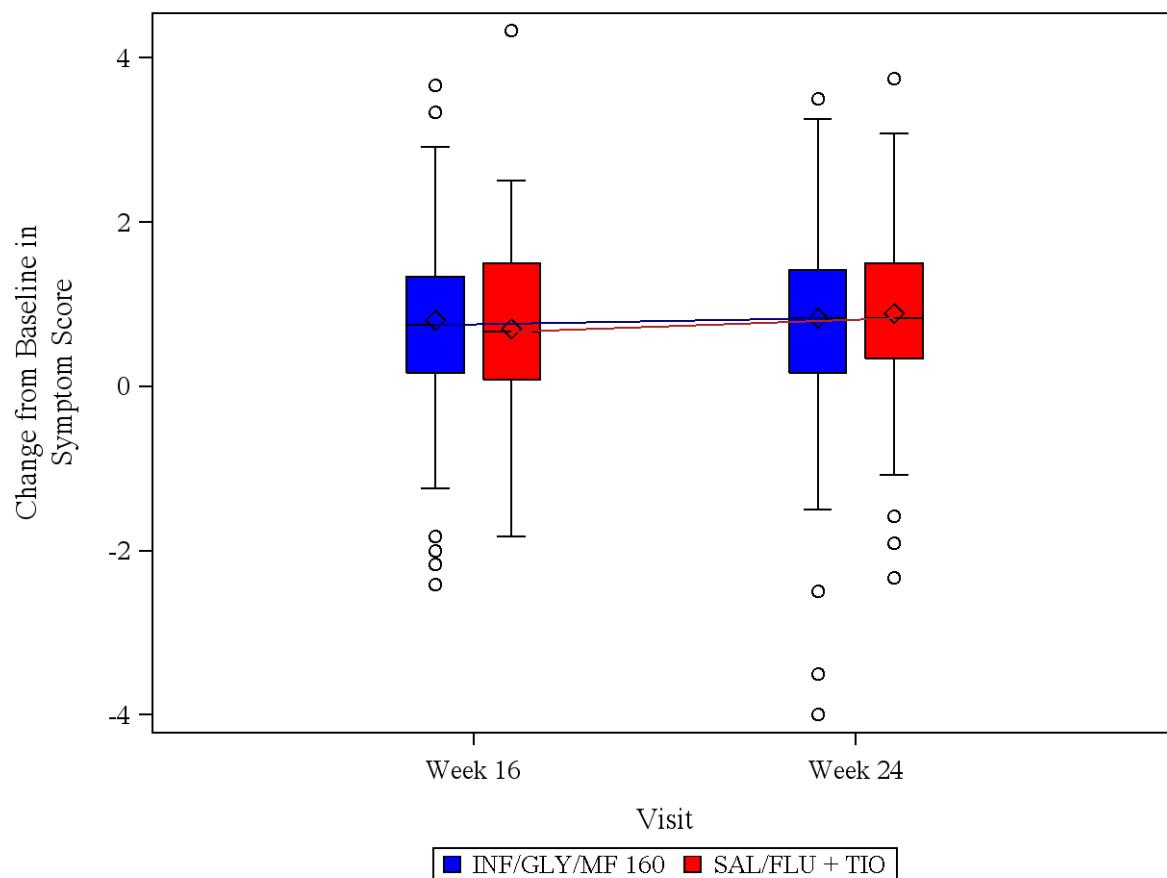


5.9 Boxplot: AQLQ-S (Symptom Score) - Change from Baseline by Gender (FAS)

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

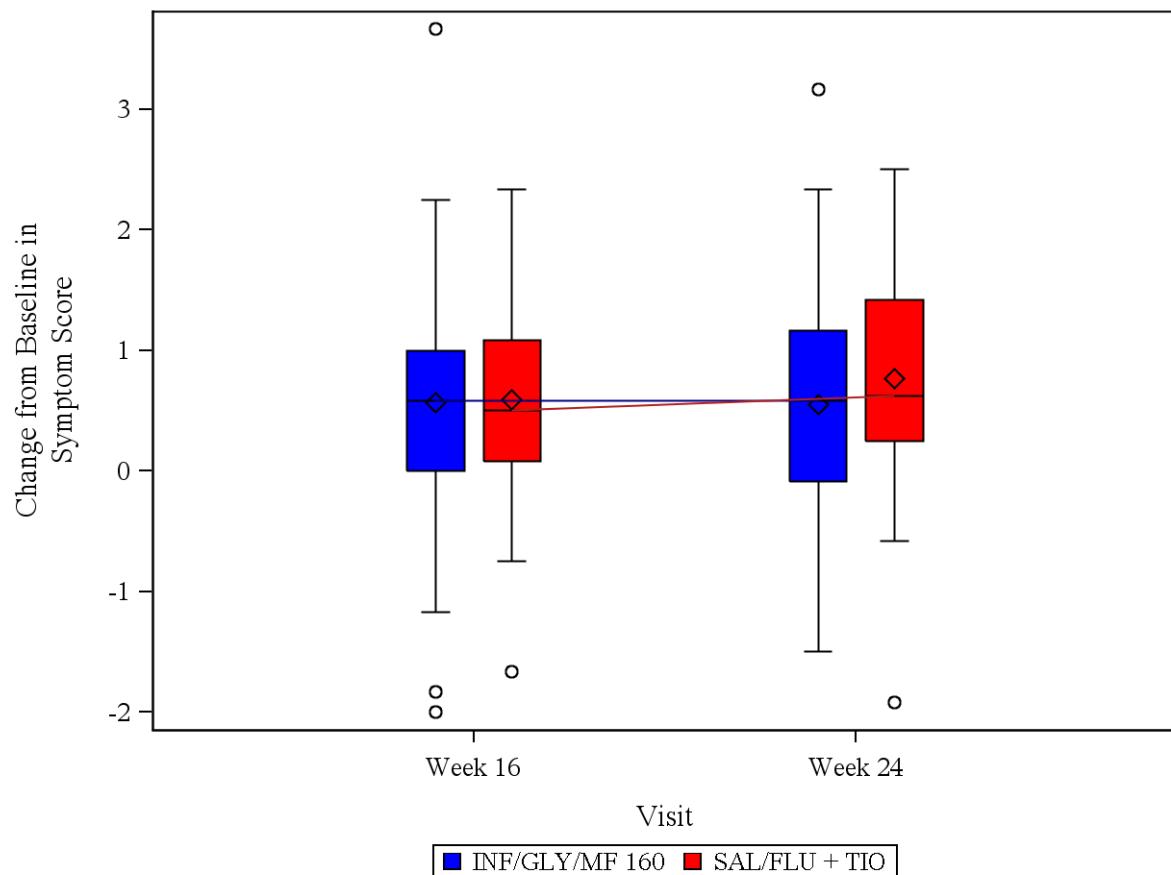


**Figure 5.9.2 AQLQ-S (Symptom Score) - Change from Baseline by Gender (FAS),
Gender = Female**

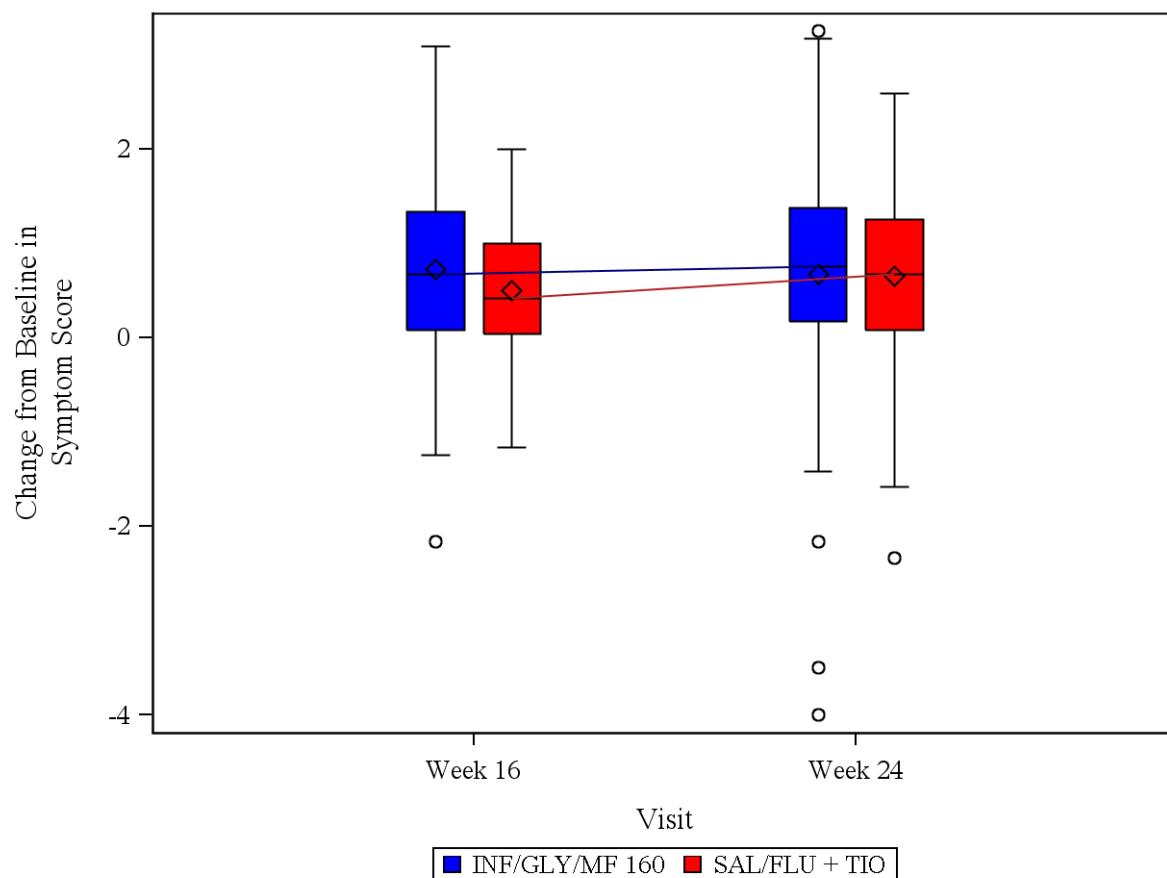


5.10 Boxplot: AQLQ-S (Symptom Score) - Change from Baseline by Region (FAS)

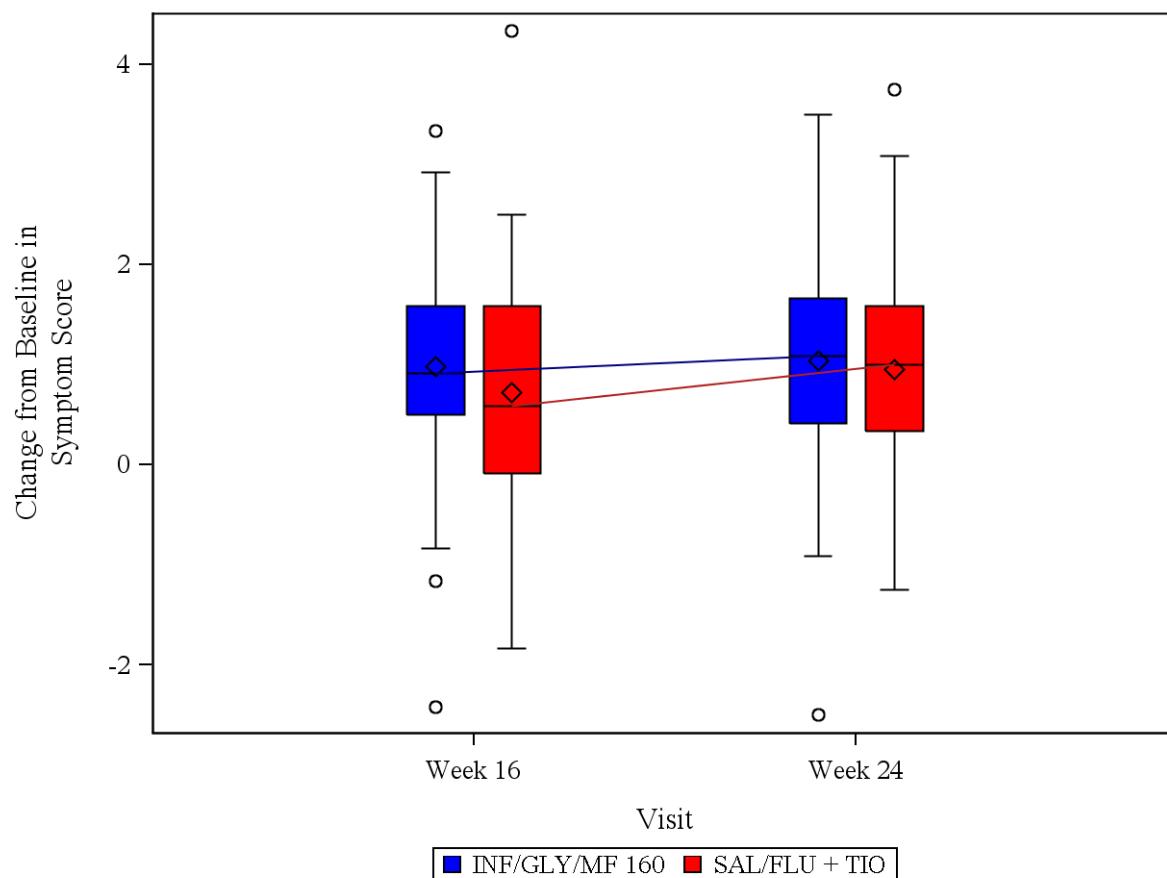
Figure 5.10.1 AQLQ-S (Symptom Score) - Change from Baseline by Region (FAS), Region = Asia



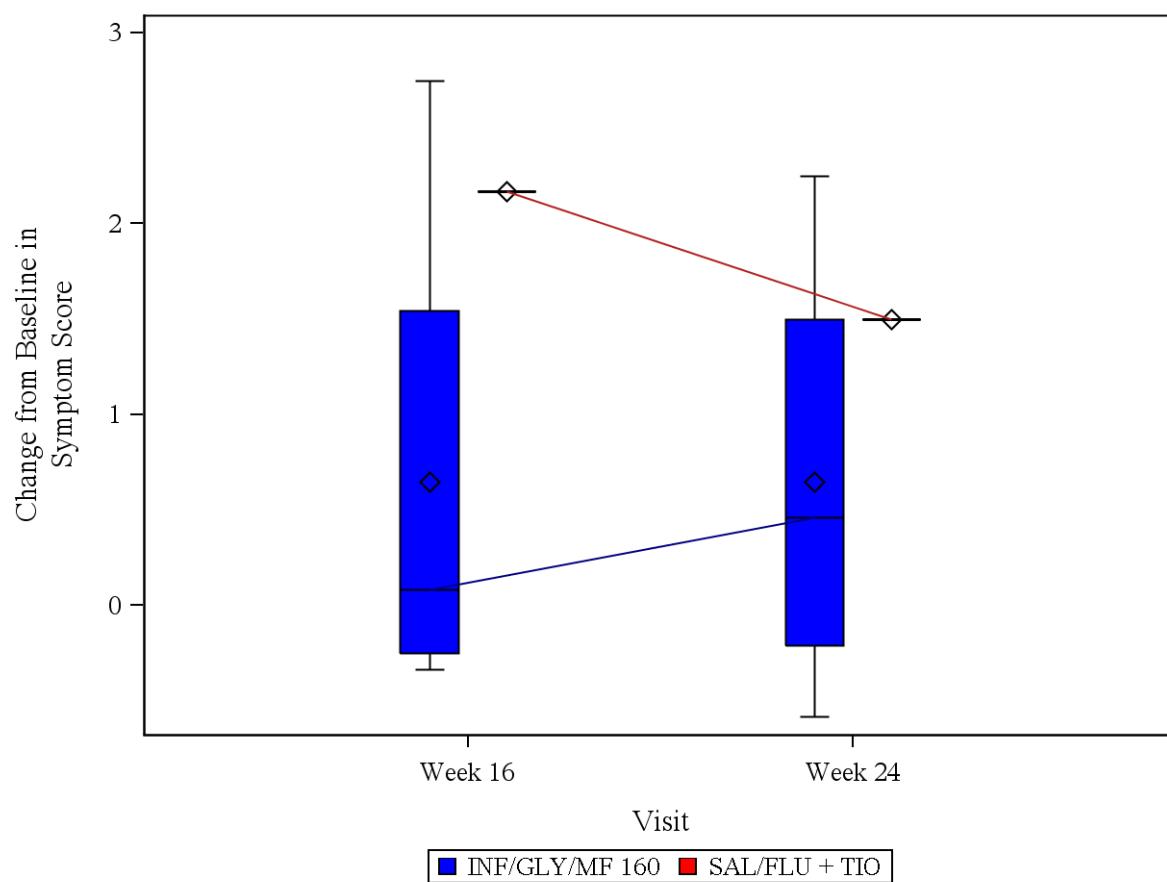
**Figure 5.10.2 AQLQ-S (Symptom Score) - Change from Baseline by Region (FAS),
Region = Europe**



**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

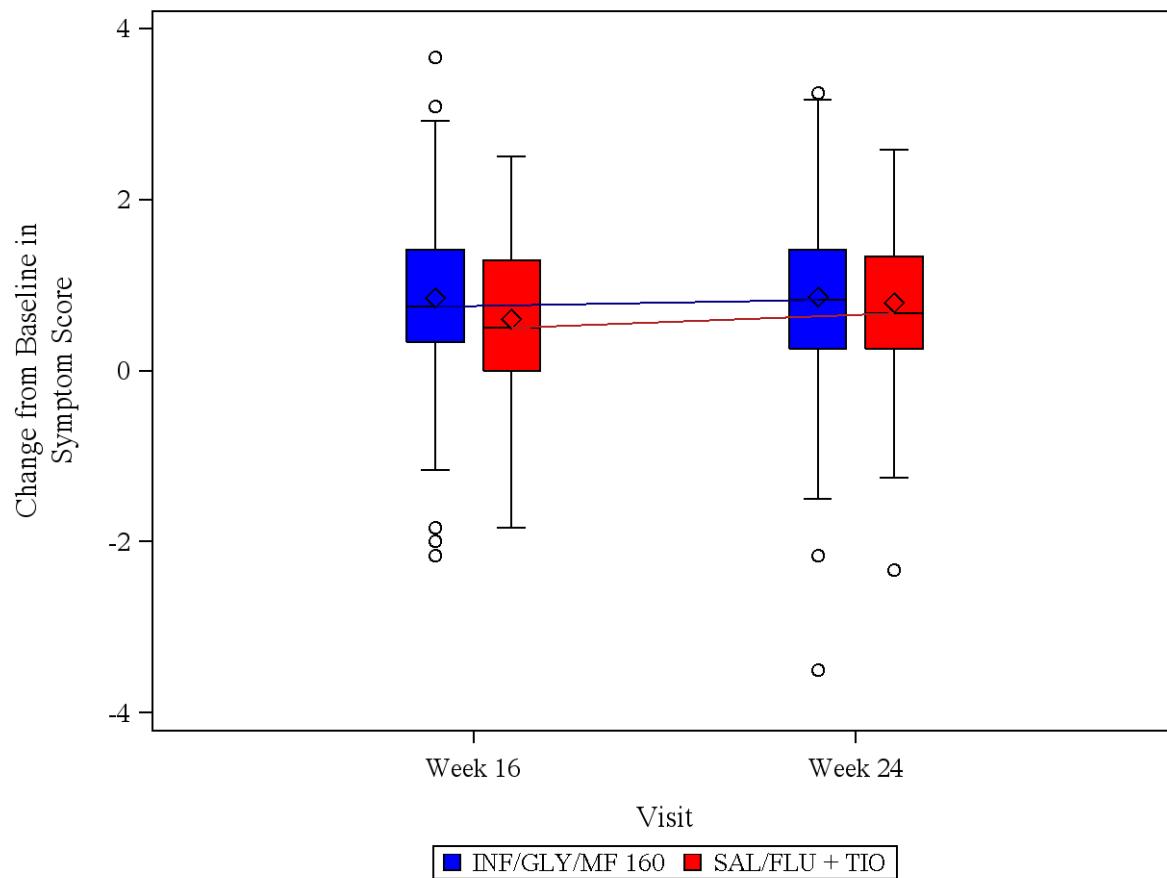
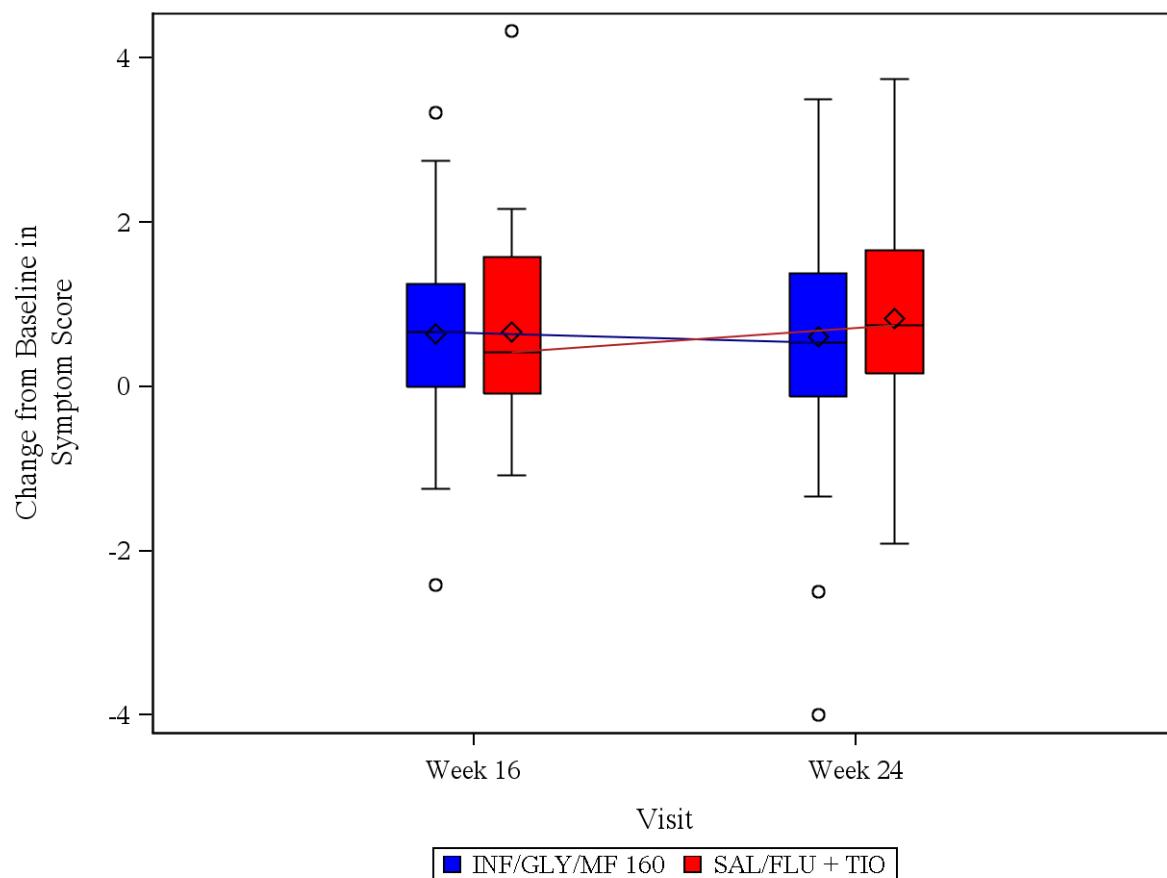
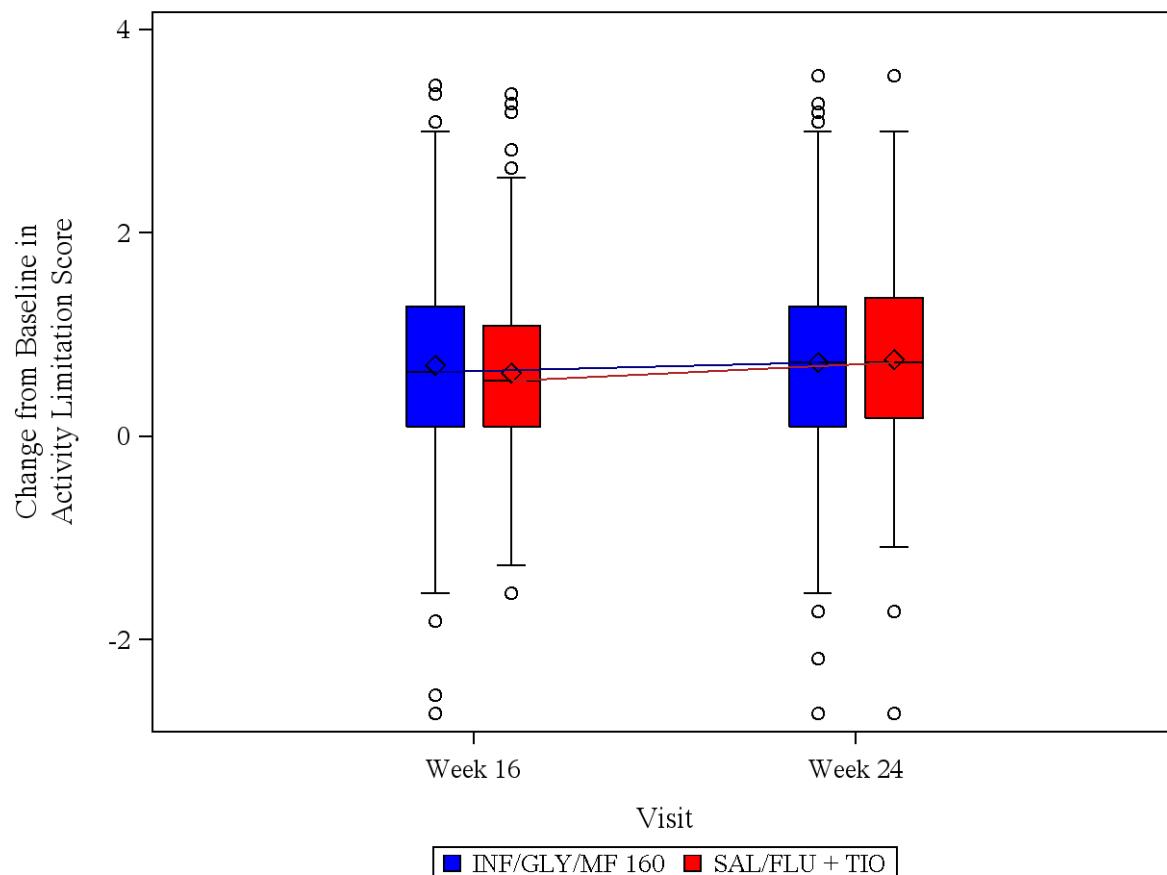


Figure 5.11.2 AQLQ-S (Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



5.13 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

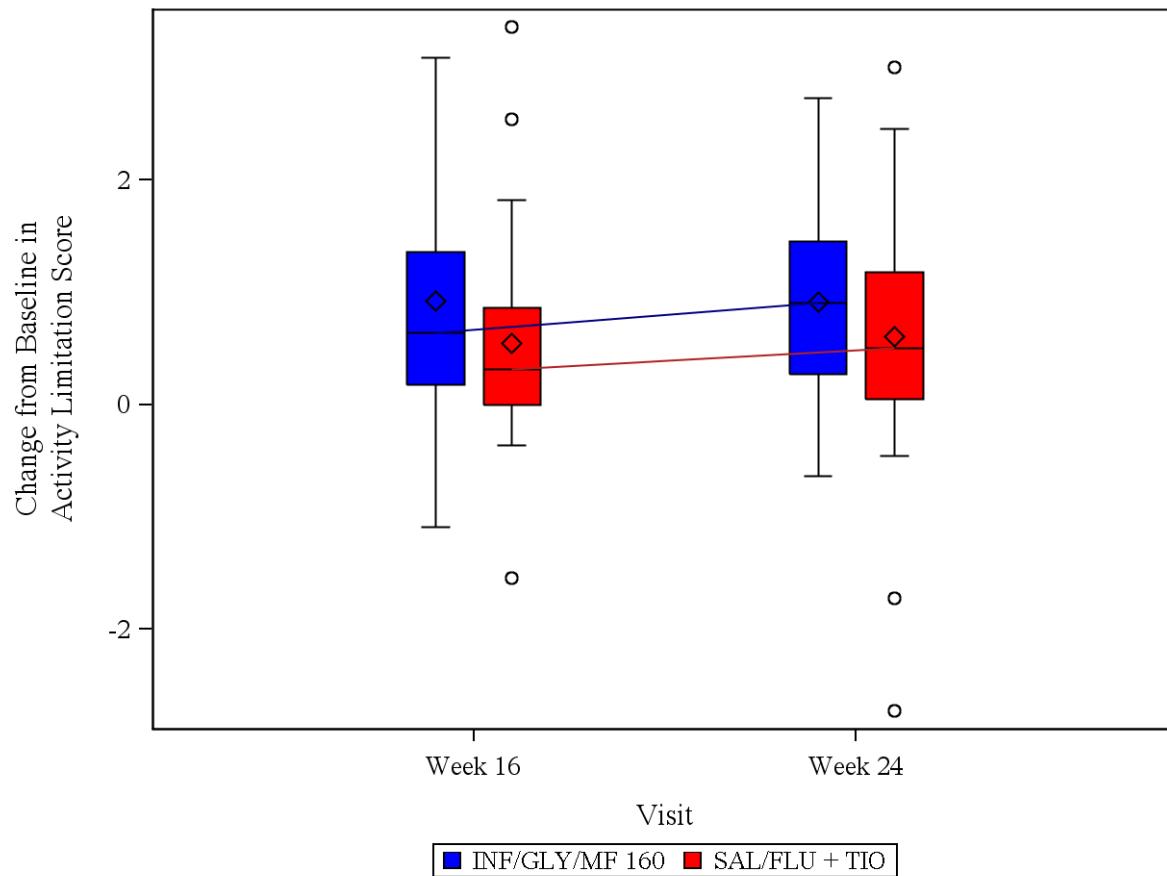


Figure 5.14.2 AQLQ-S (Activity Limitation Score) - Change from Baseline by Age (FAS), Age = 40-64 years

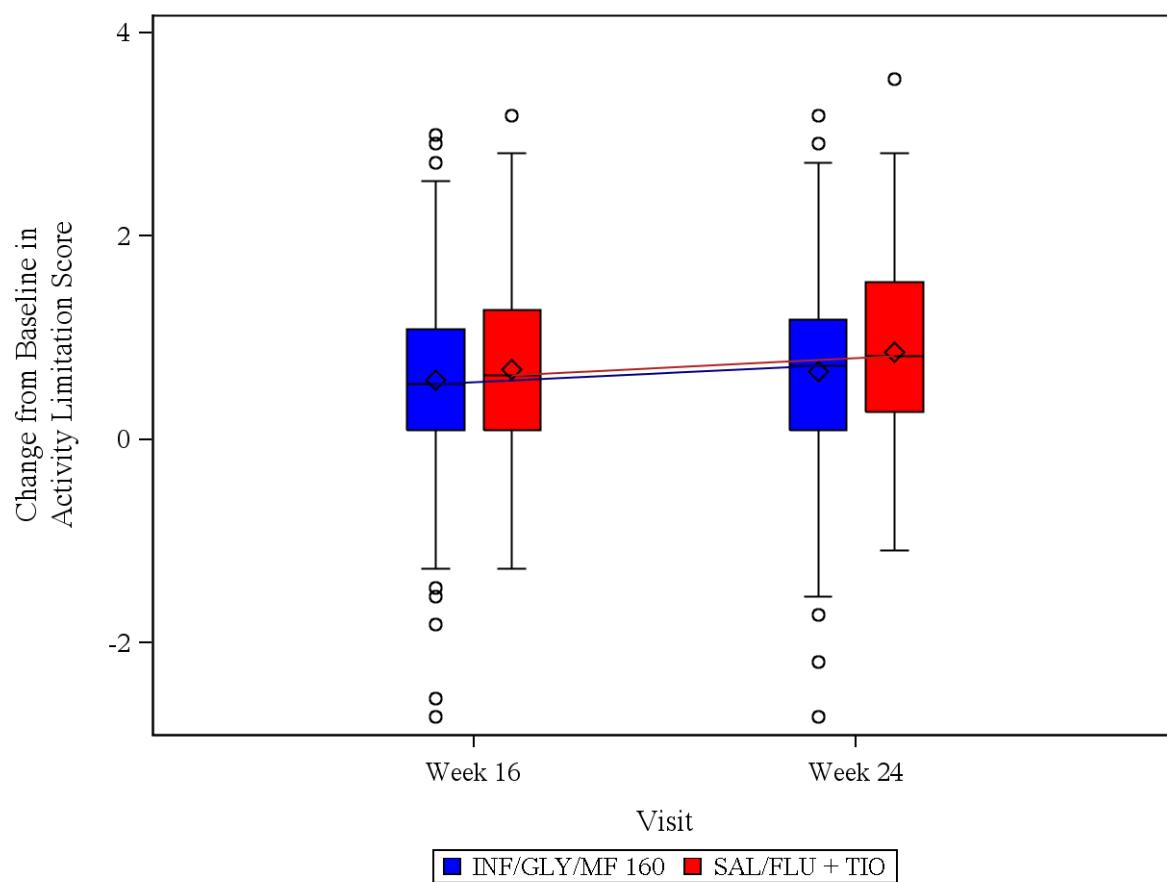
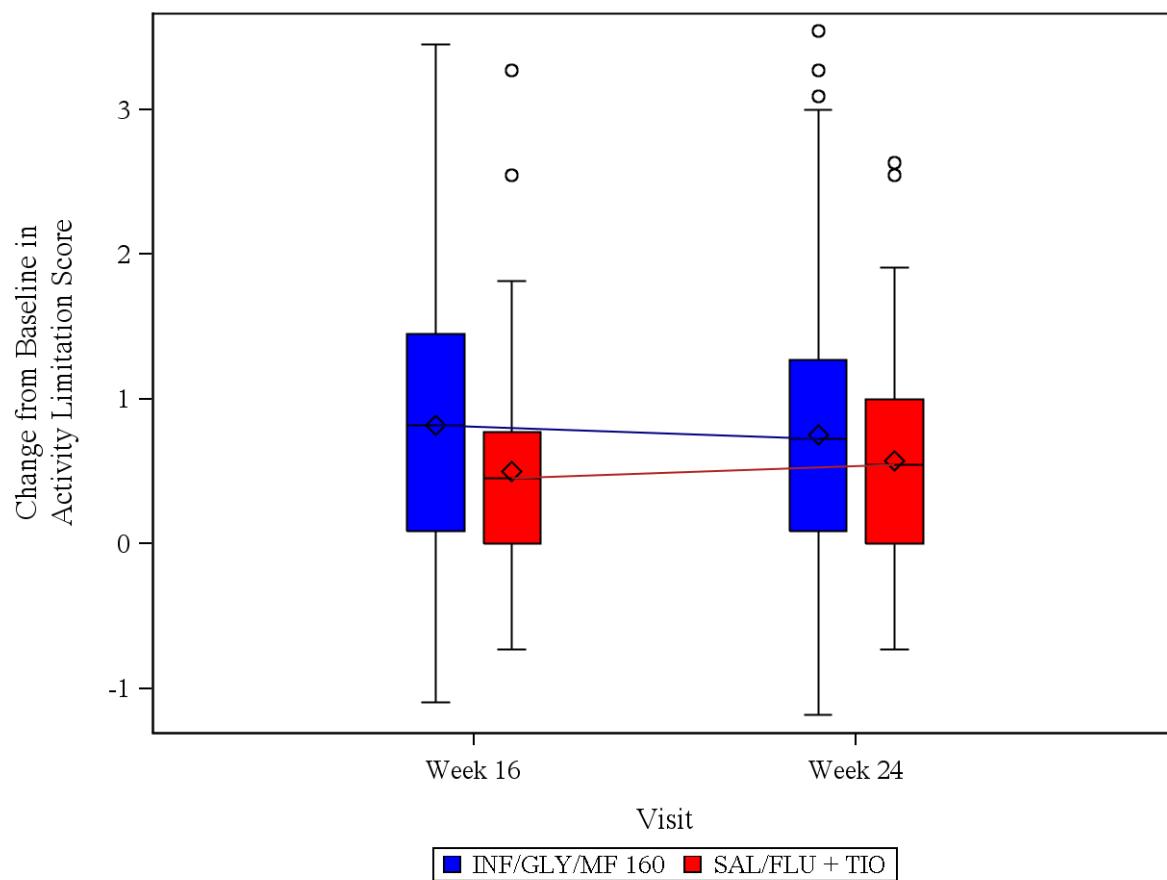


Figure 5.14.3 AQLQ-S (Activity Limitation Score) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

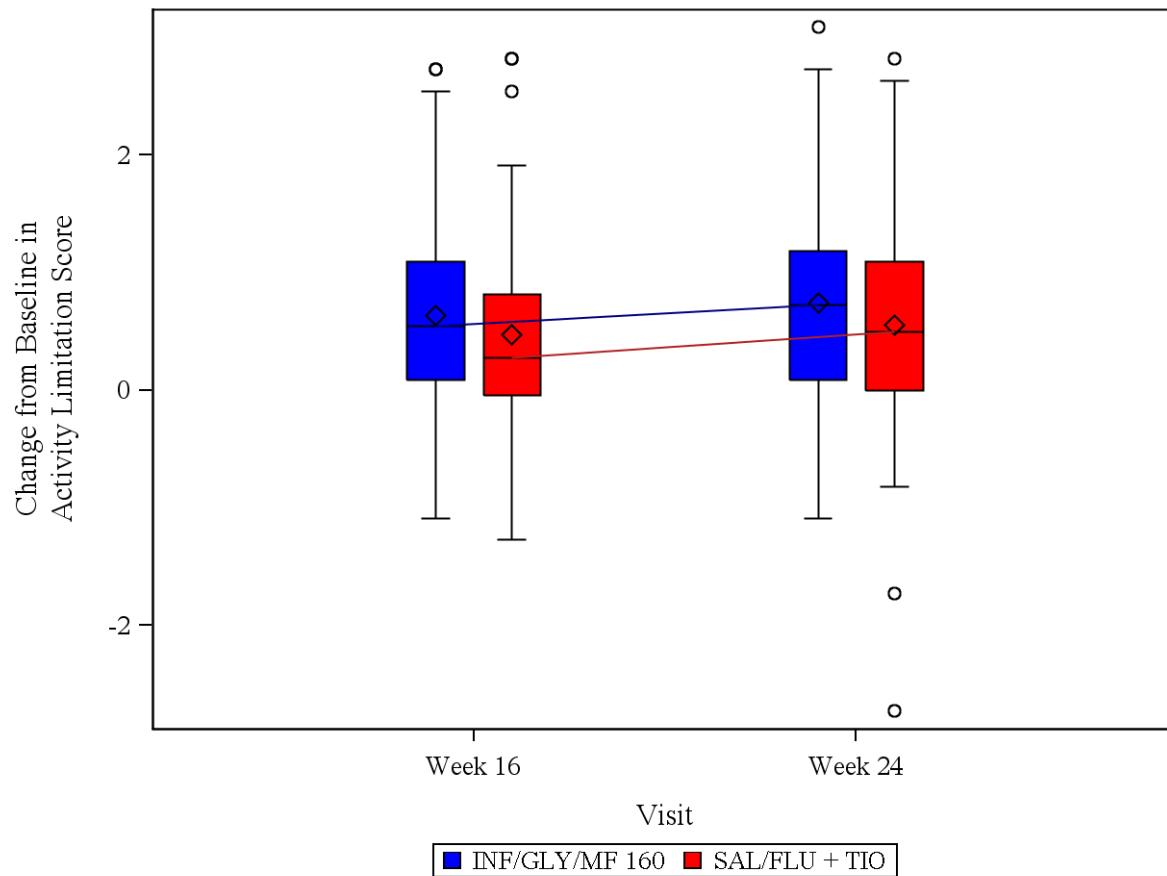
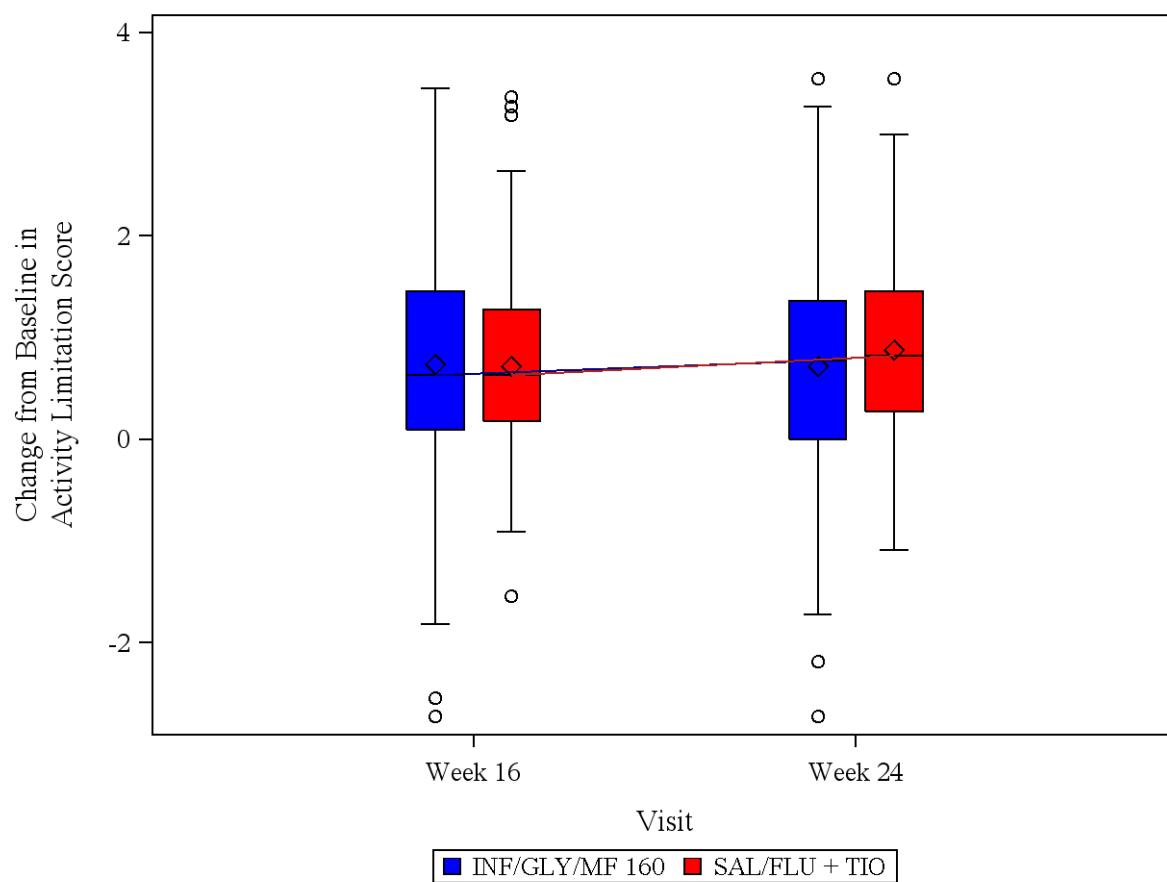


Figure 5.15.2 AQLQ-S (Activity Limitation Score) - Change from Baseline by Gender (FAS), Gender = Female



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

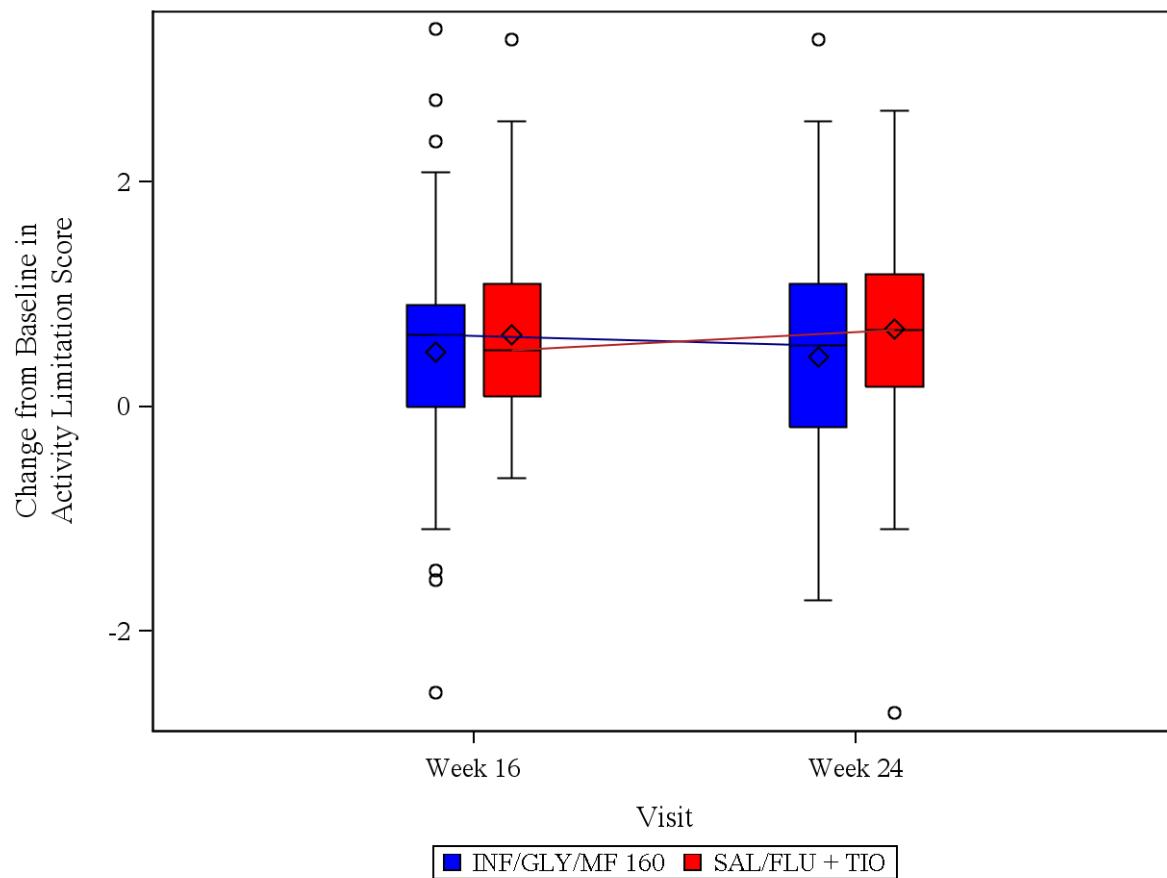


Figure 5.16.2 AQLQ-S (Activity Limitation Score) - Change from Baseline by Region (FAS), Region = Europe

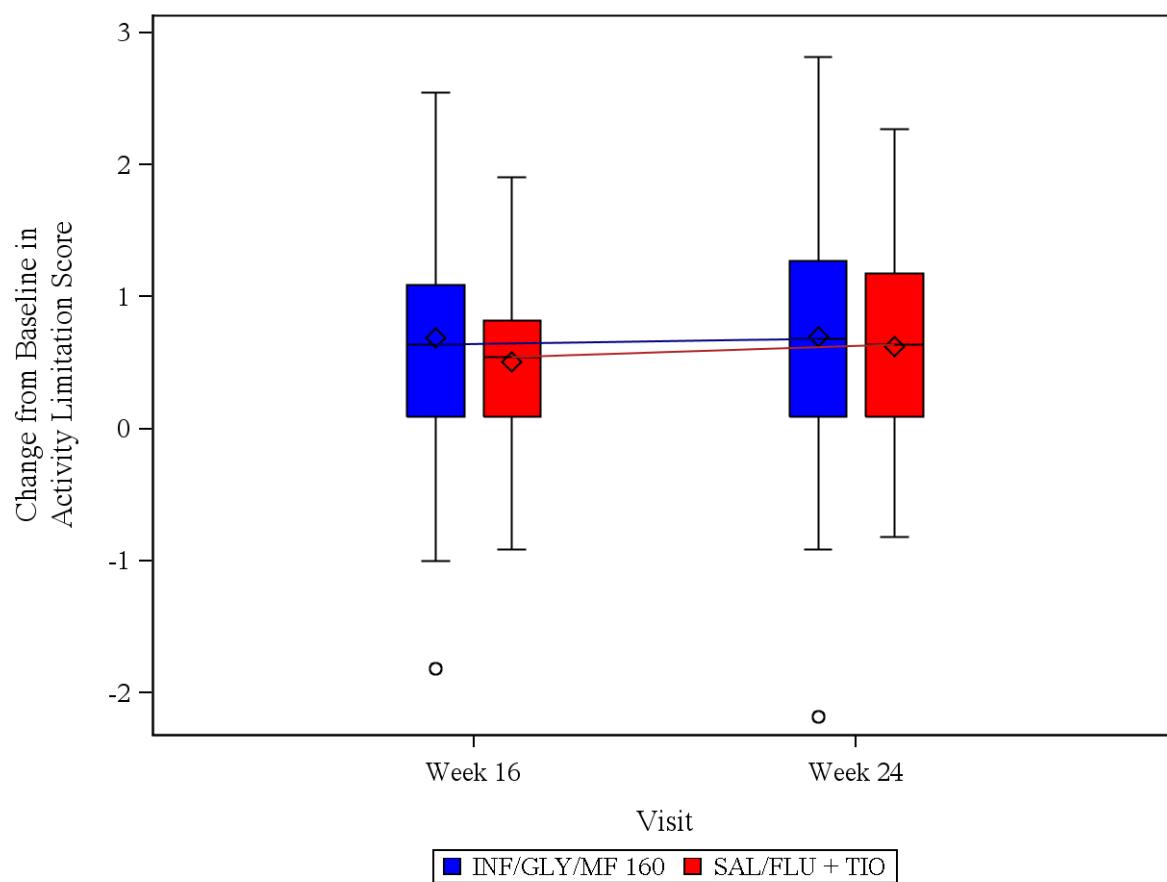


Figure 5.16.3 AQLQ-S (Activity Limitation Score) - Change from Baseline by Region (FAS), Region = Latin America

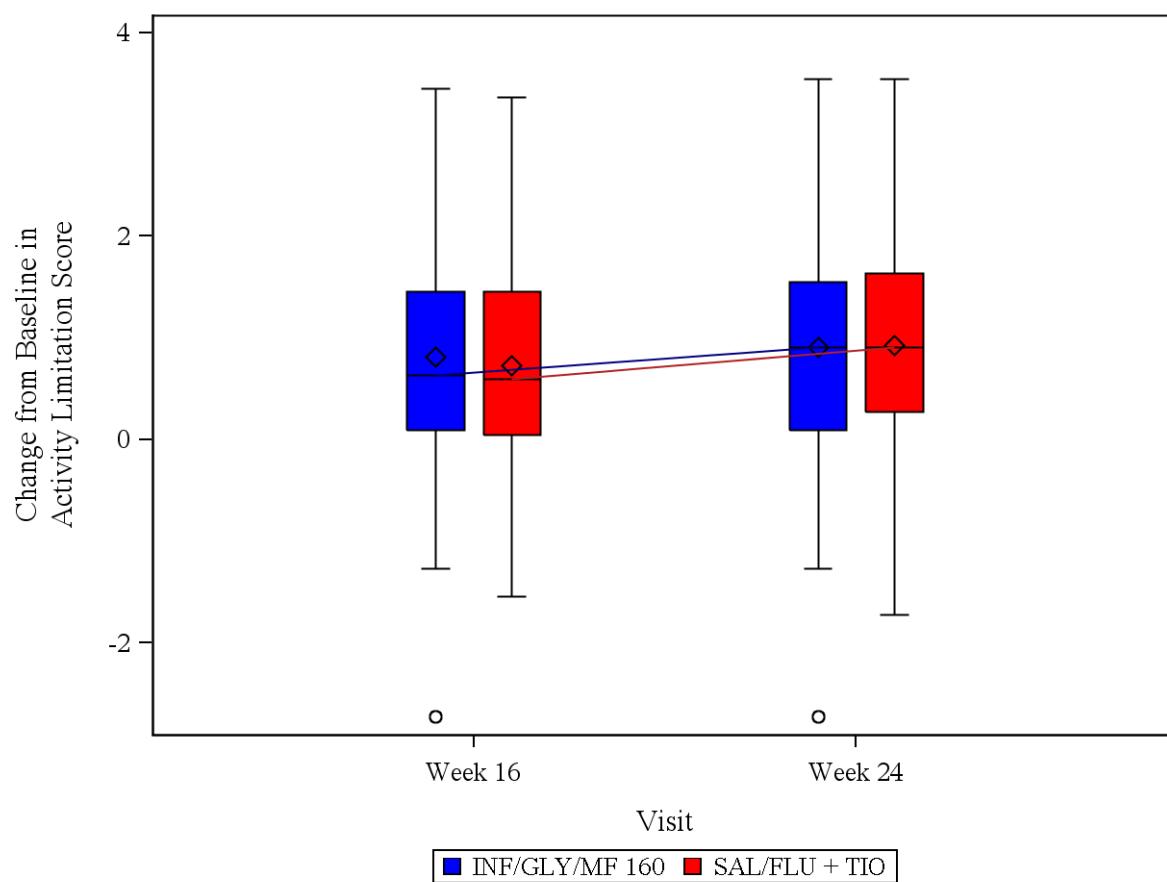
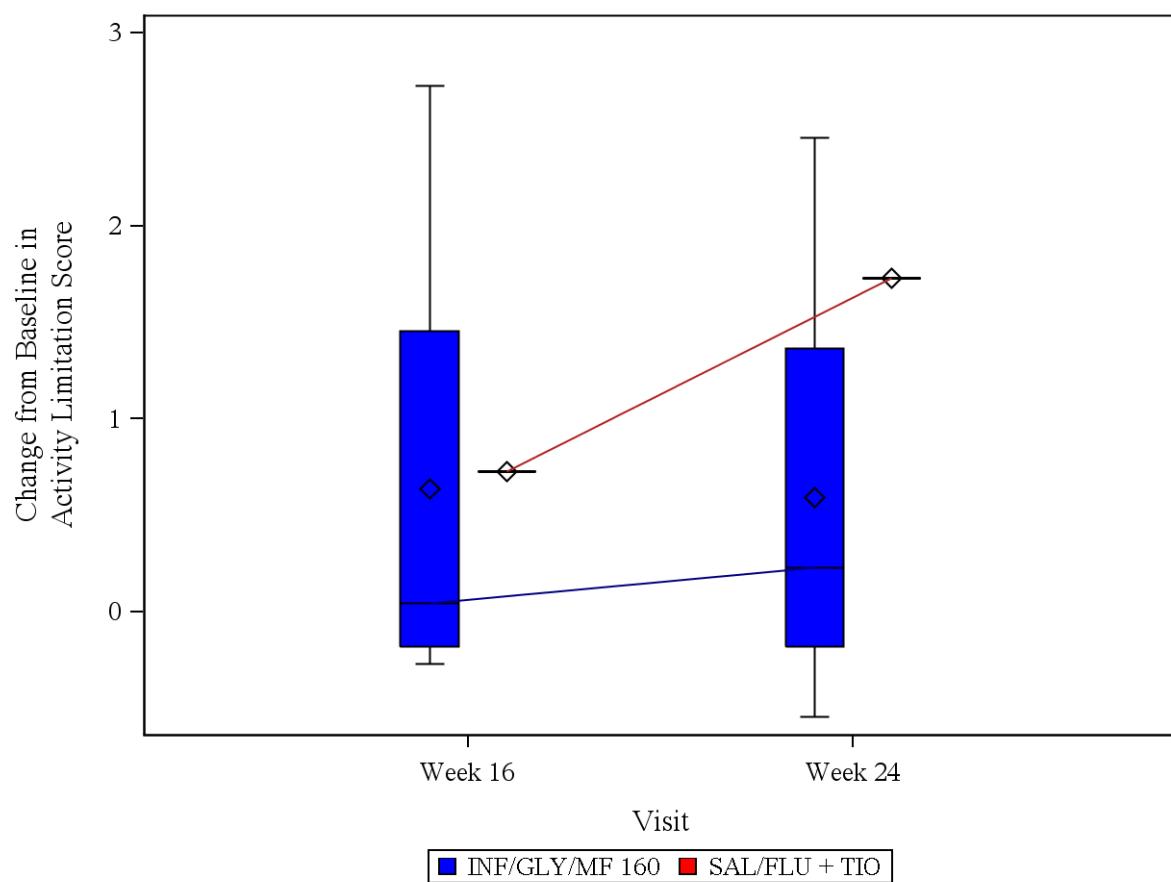


Figure 5.16.4 AQLQ-S (Activity Limitation Score) - Change from Baseline by Region (FAS), Region = Others



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

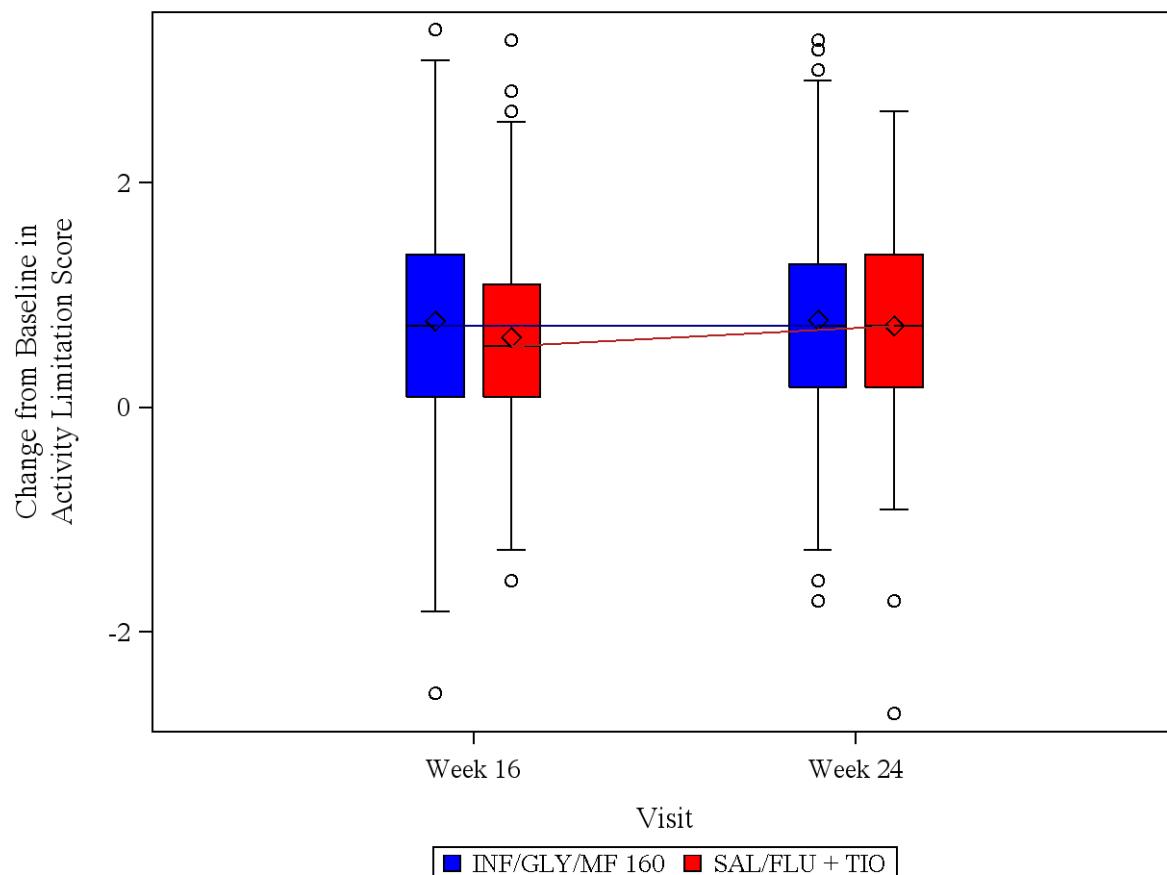
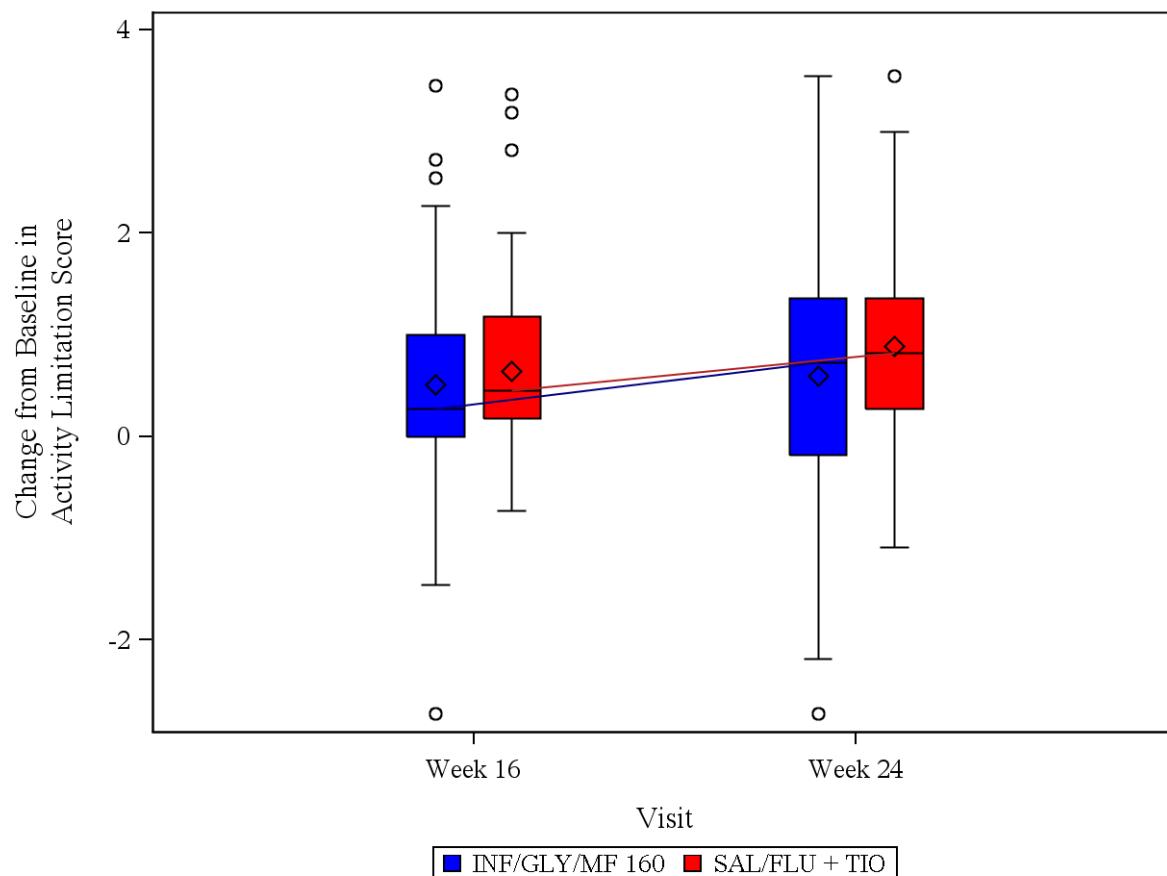
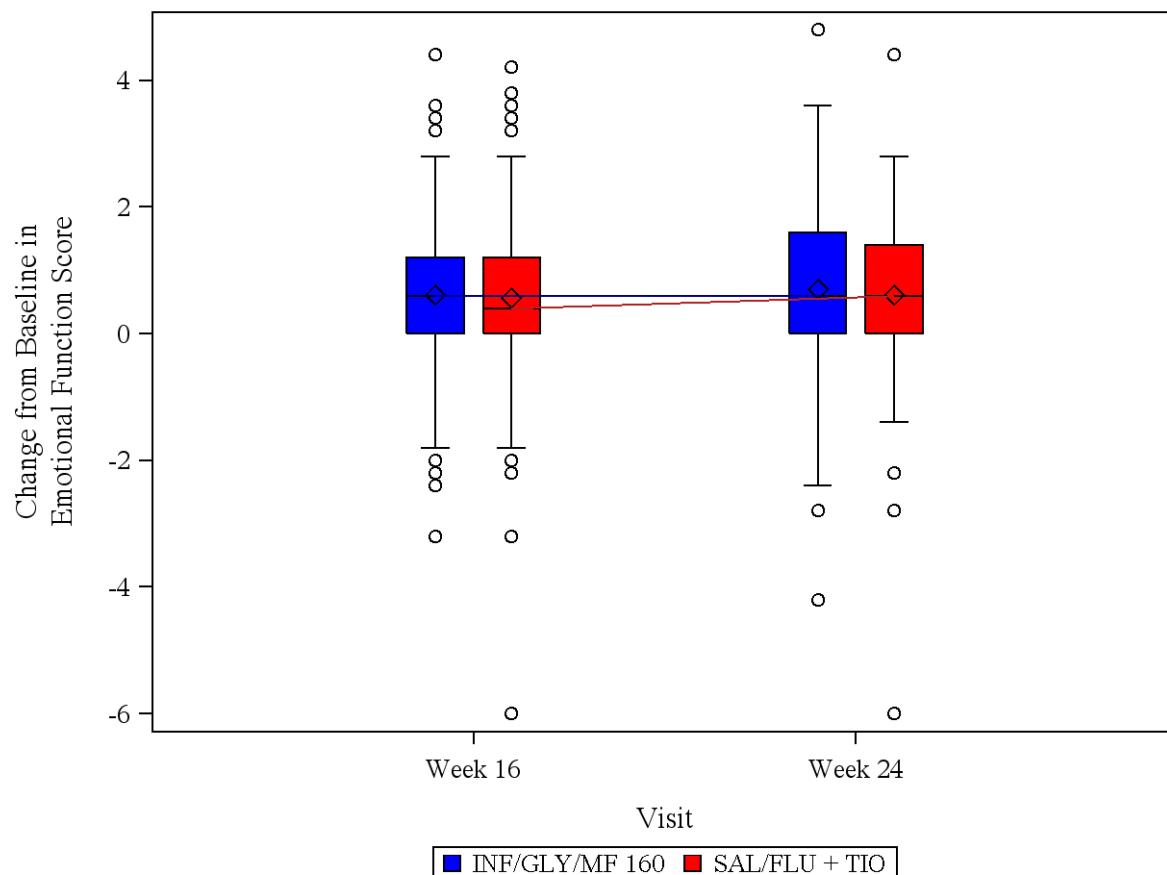


Figure 5.17.2 AQLQ-S (Activity Limitation Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



5.19 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

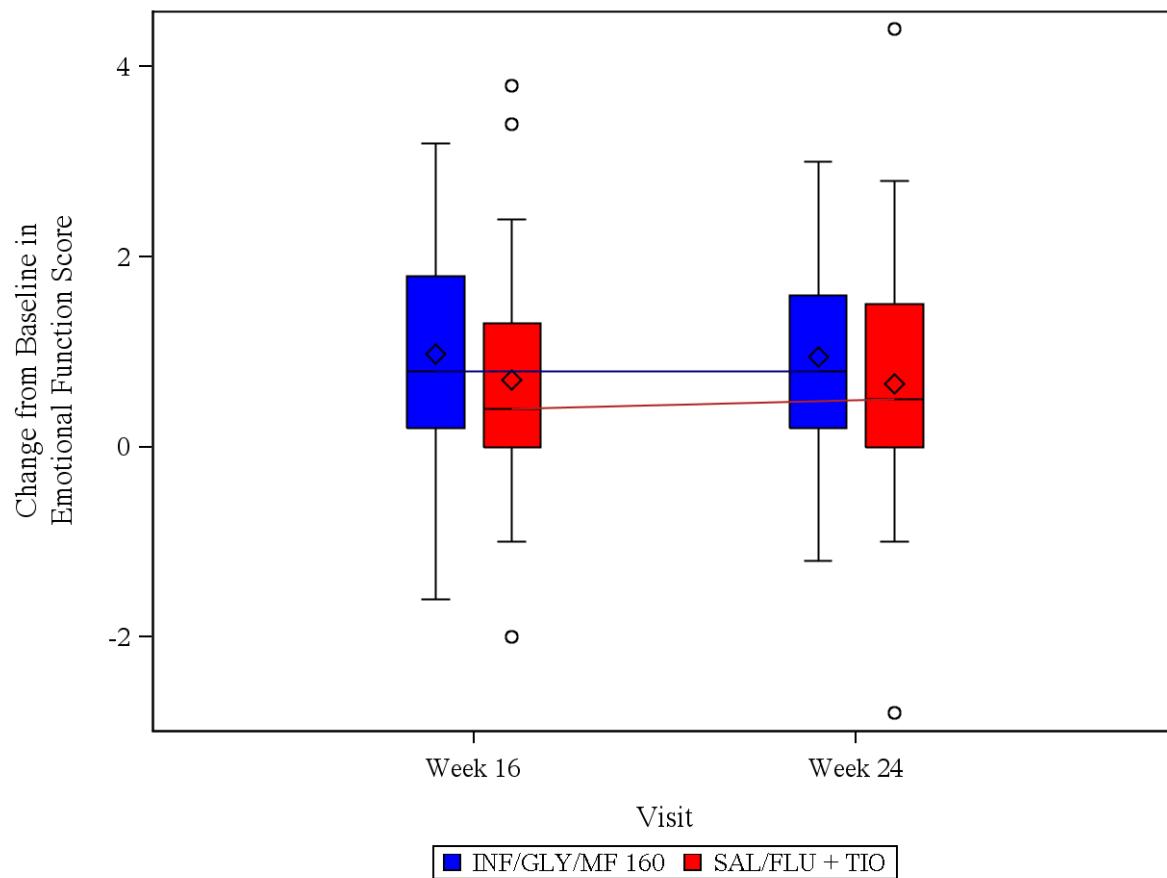


Figure 5.20.2 AQLQ-S (Emotional Function Score) - Change from Baseline by Age (FAS), Age = 40-64 years

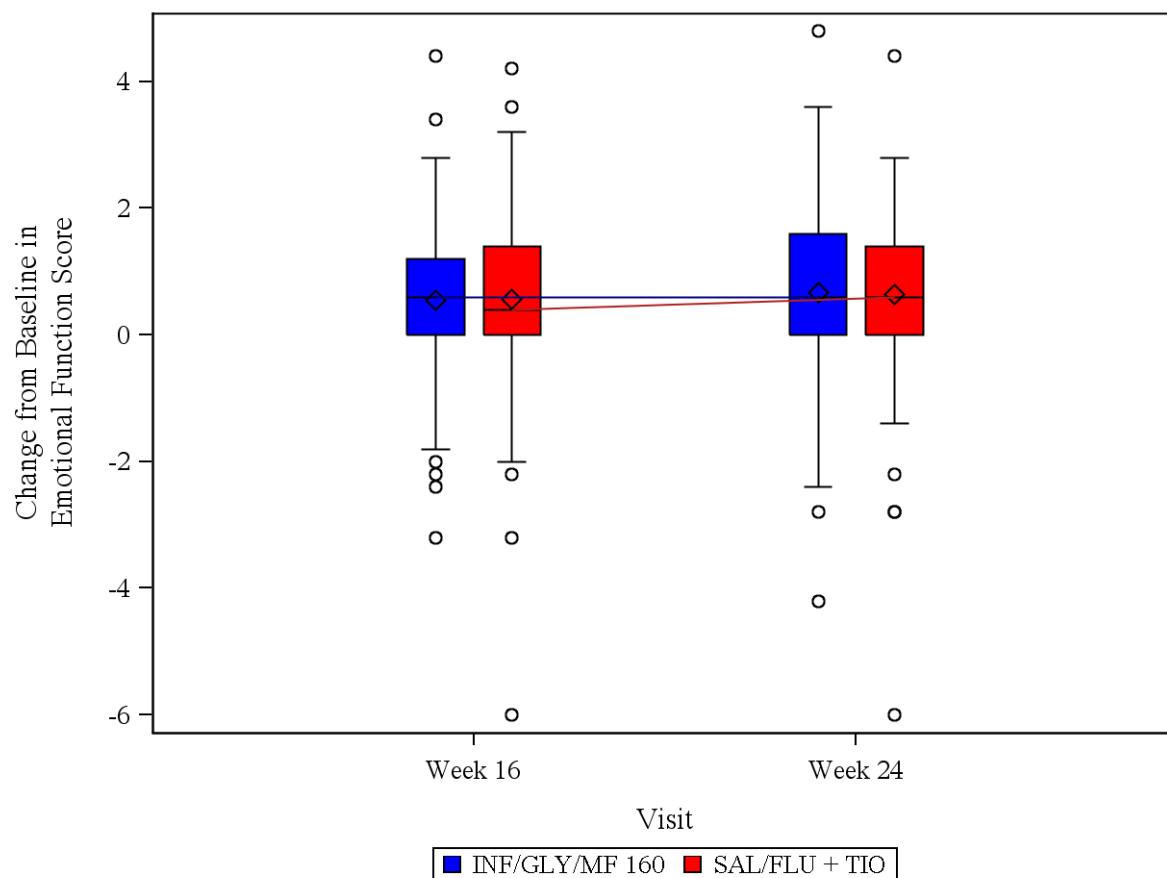
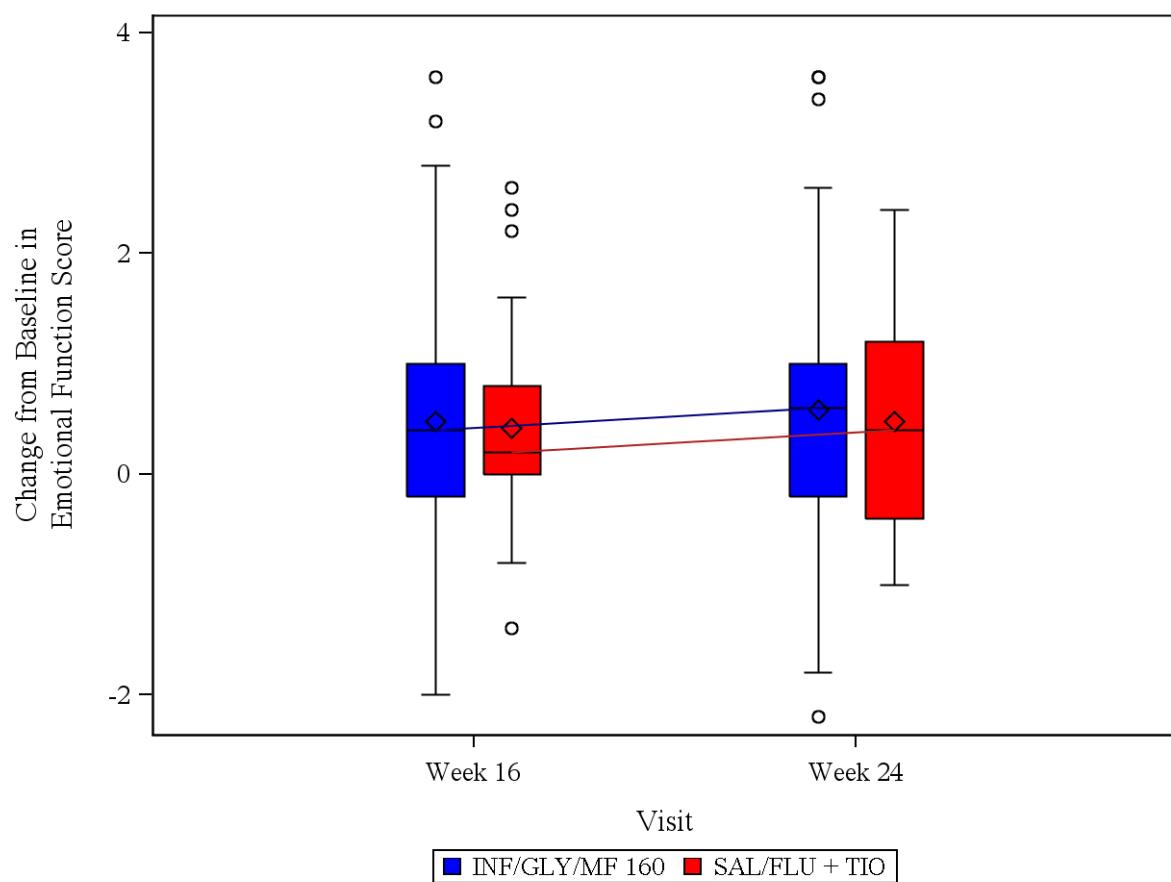


Figure 5.20.3 AQLQ-S (Emotional Function Score) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

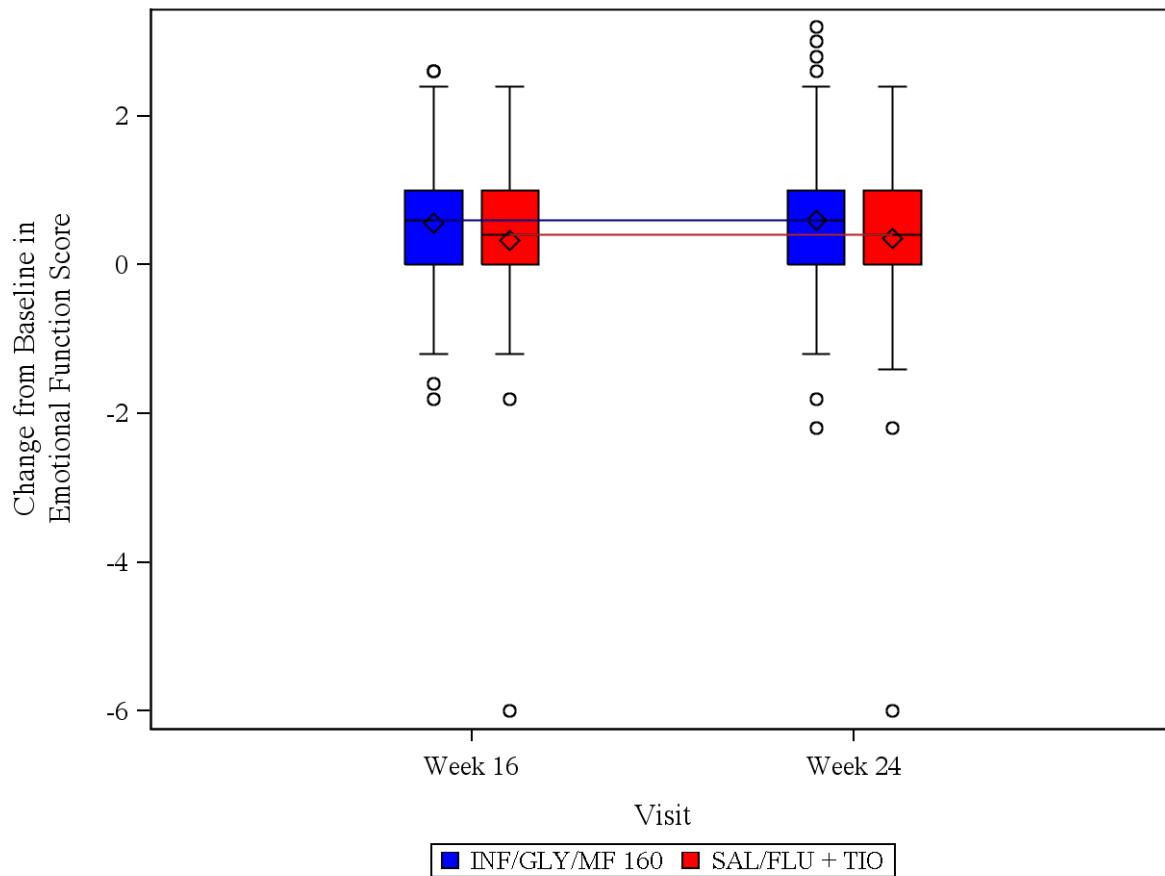
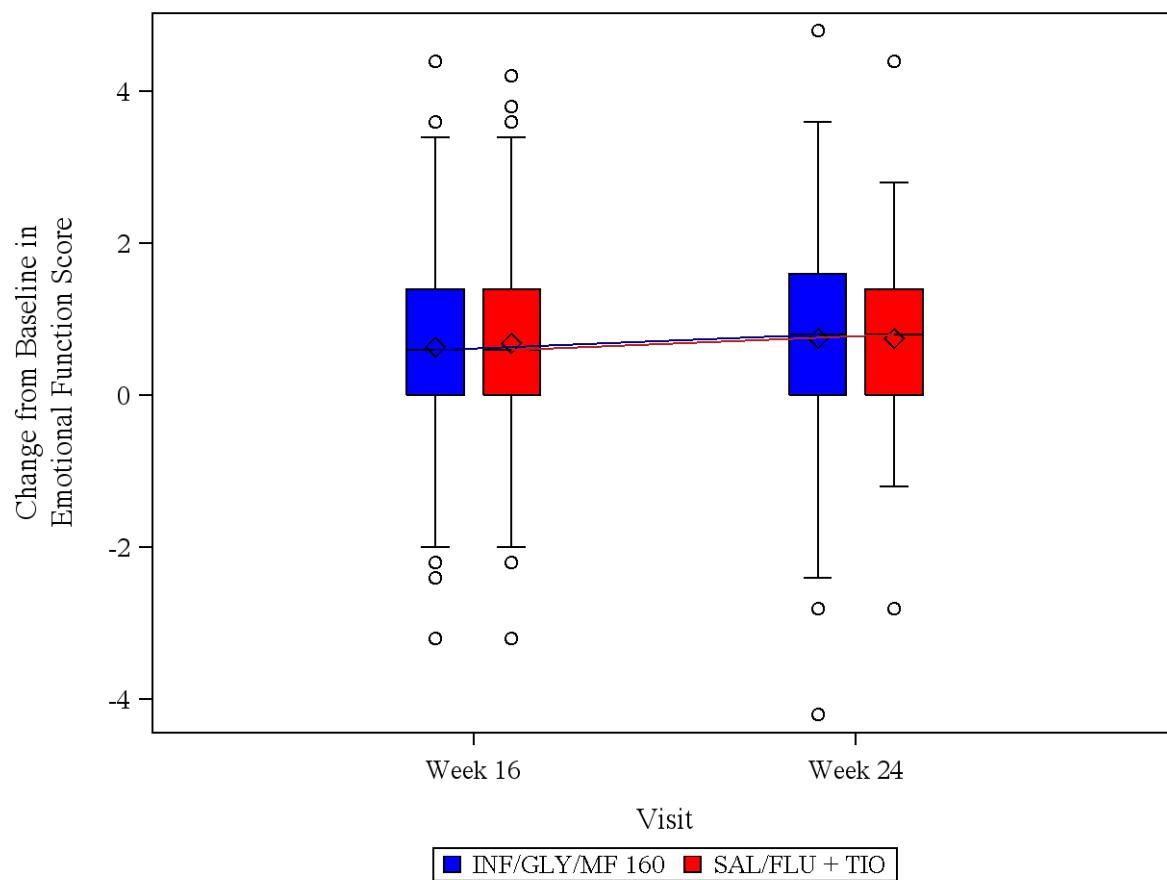


Figure 5.21.2 AQLQ-S (Emotional Function Score) - Change from Baseline by Gender (FAS), Gender = Female



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

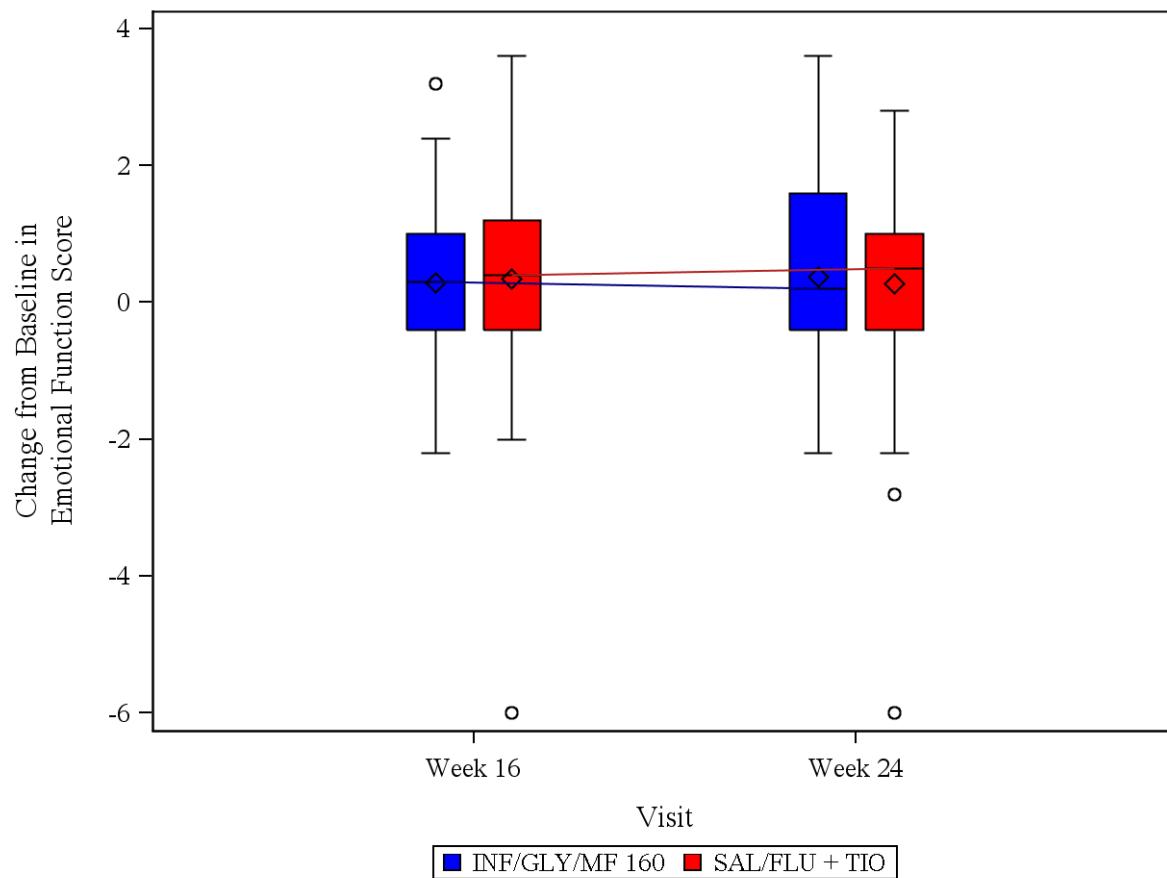


Figure 5.22.2 AQLQ-S (Emotional Function Score) - Change from Baseline by Region (FAS), Region = Europe

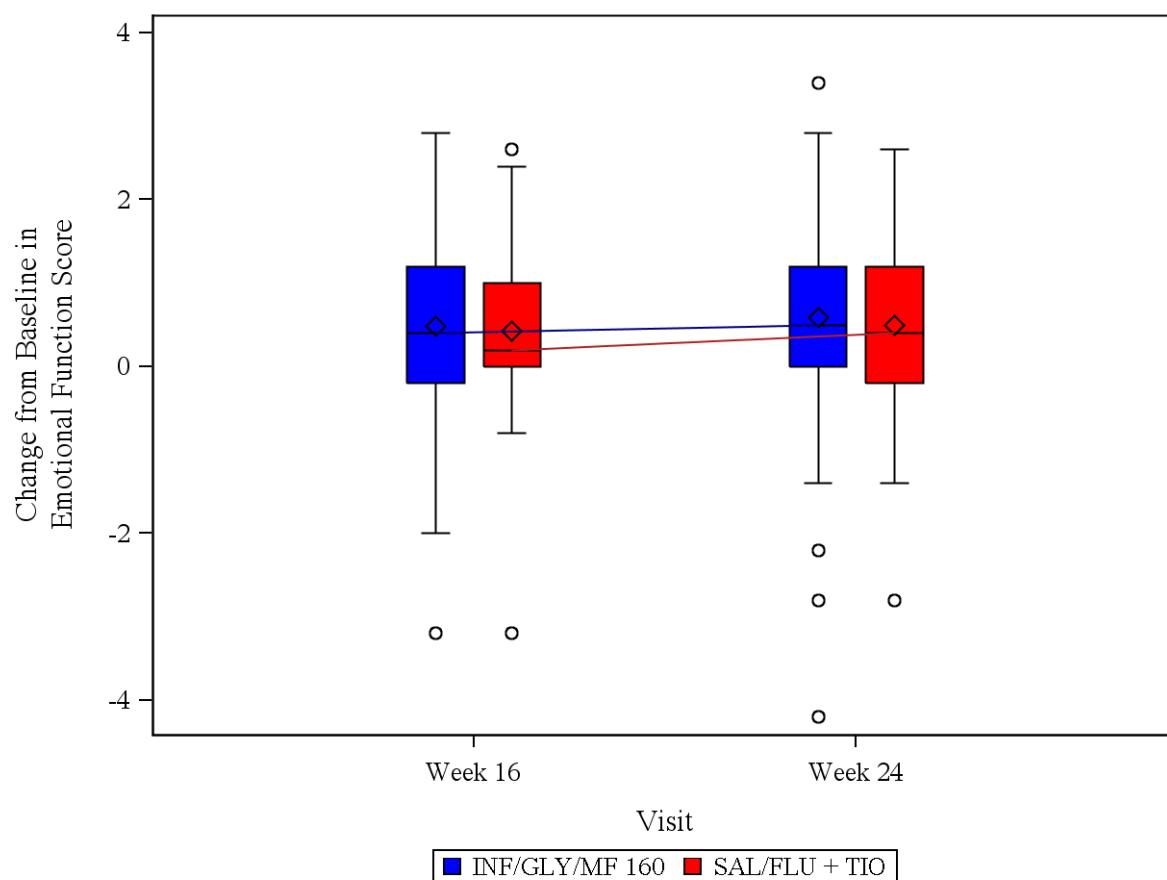


Figure 5.22.3 AQLQ-S (Emotional Function Score) - Change from Baseline by Region (FAS), Region = Latin America

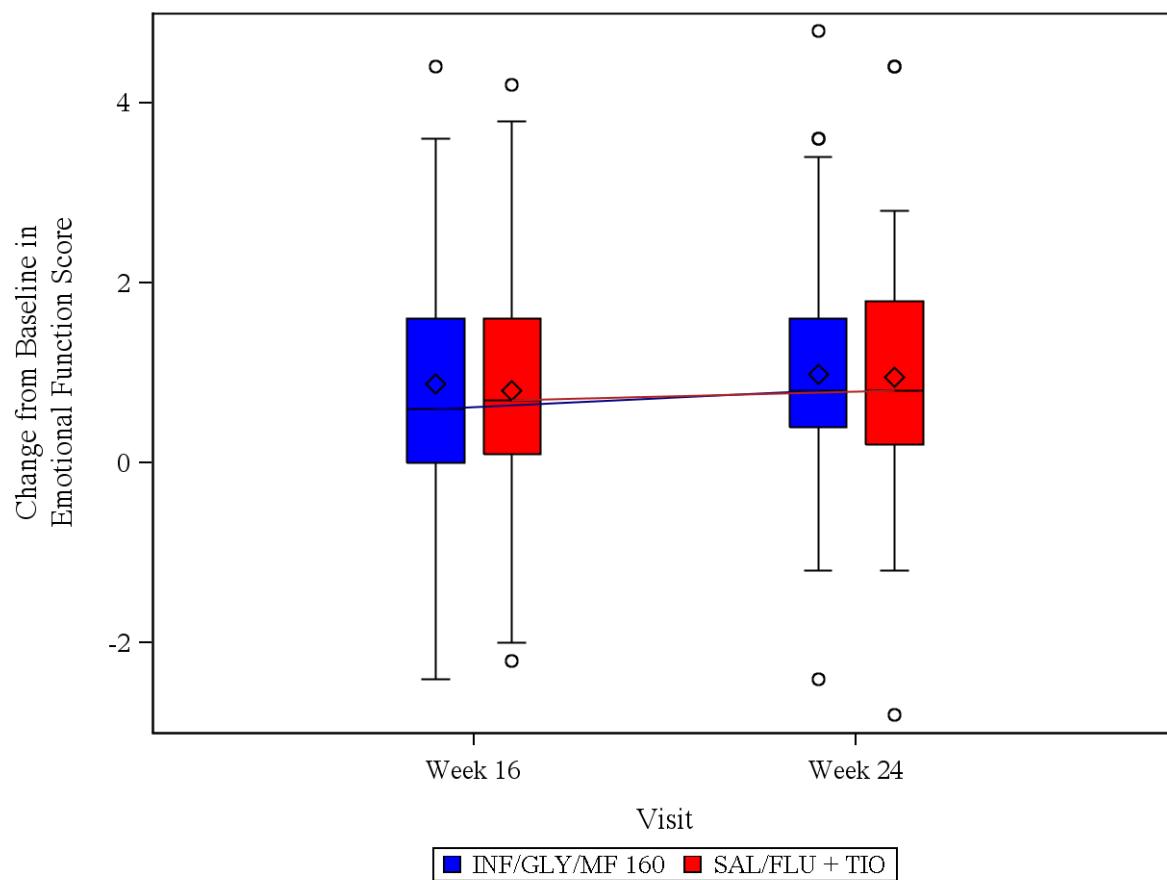
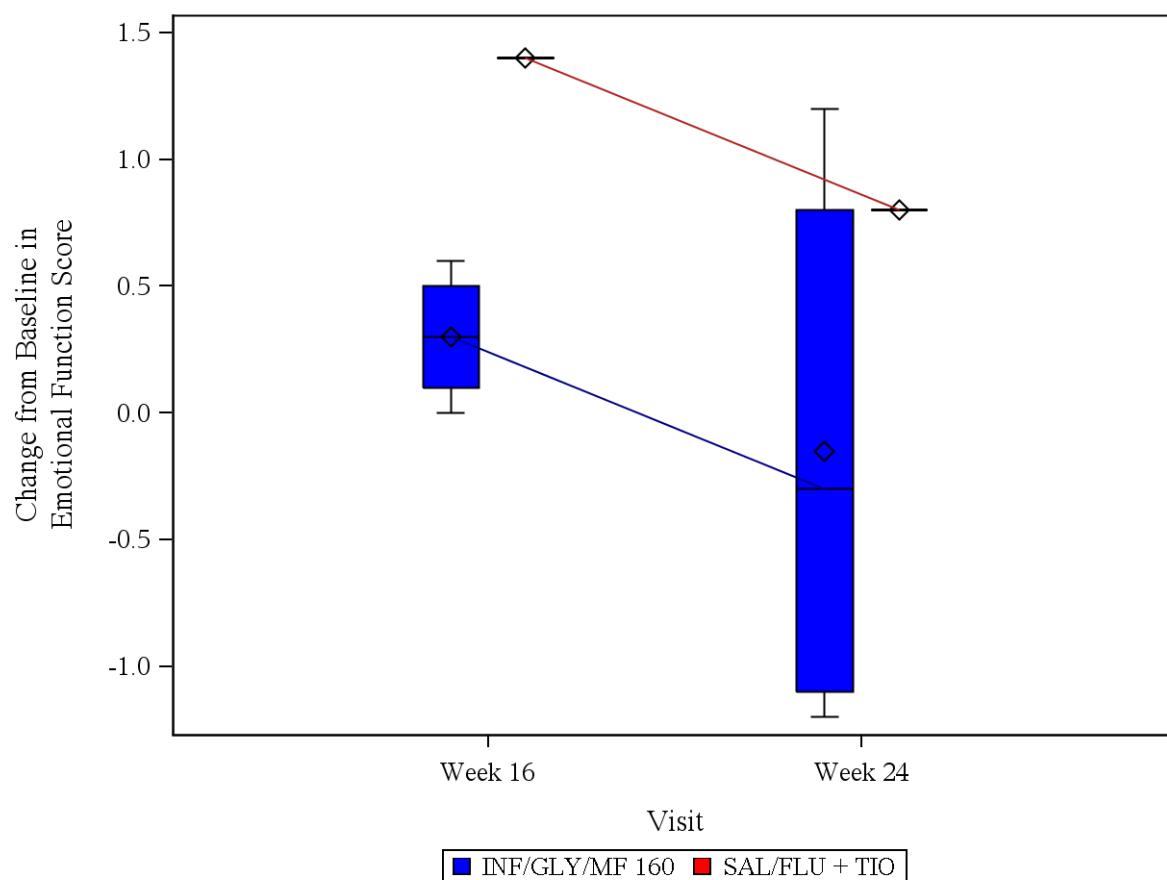


Figure 5.22.4 AQLQ-S (Emotional Function Score) - Change from Baseline by Region (FAS), Region = Others



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

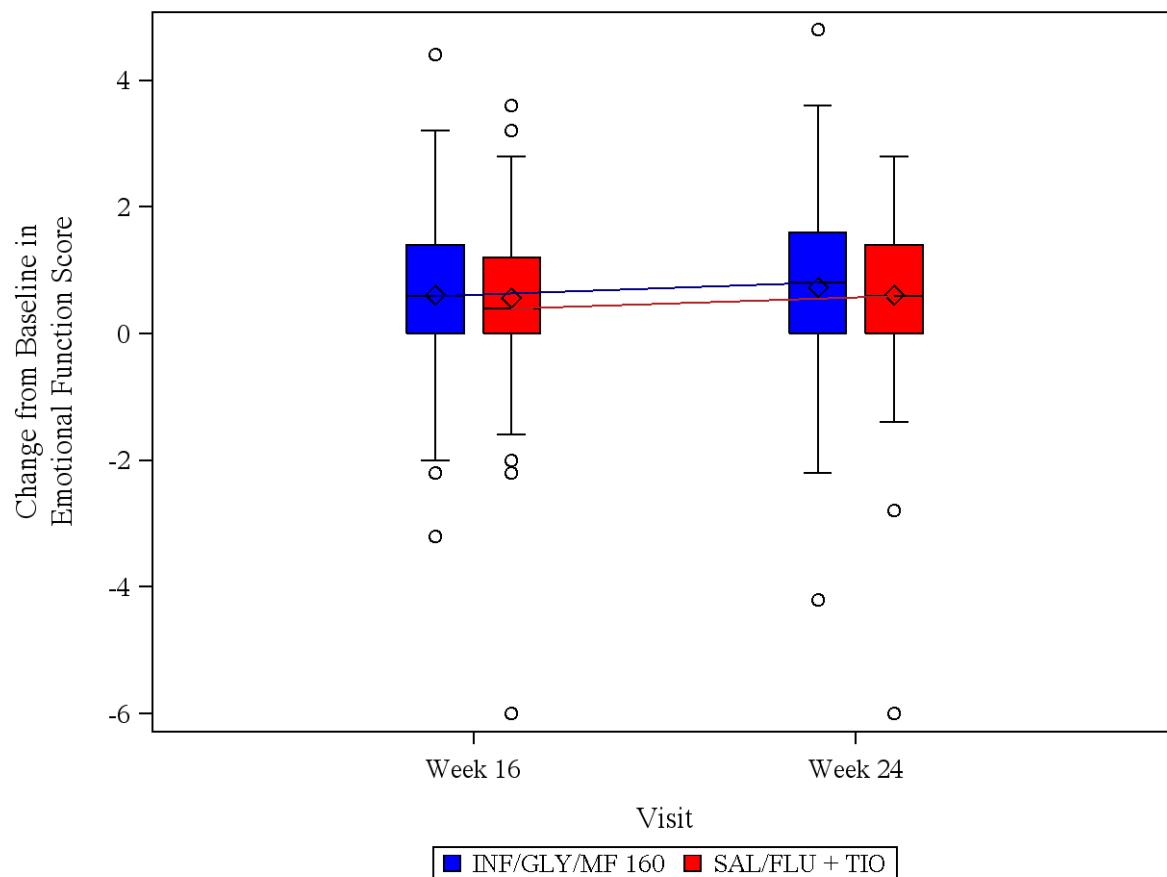
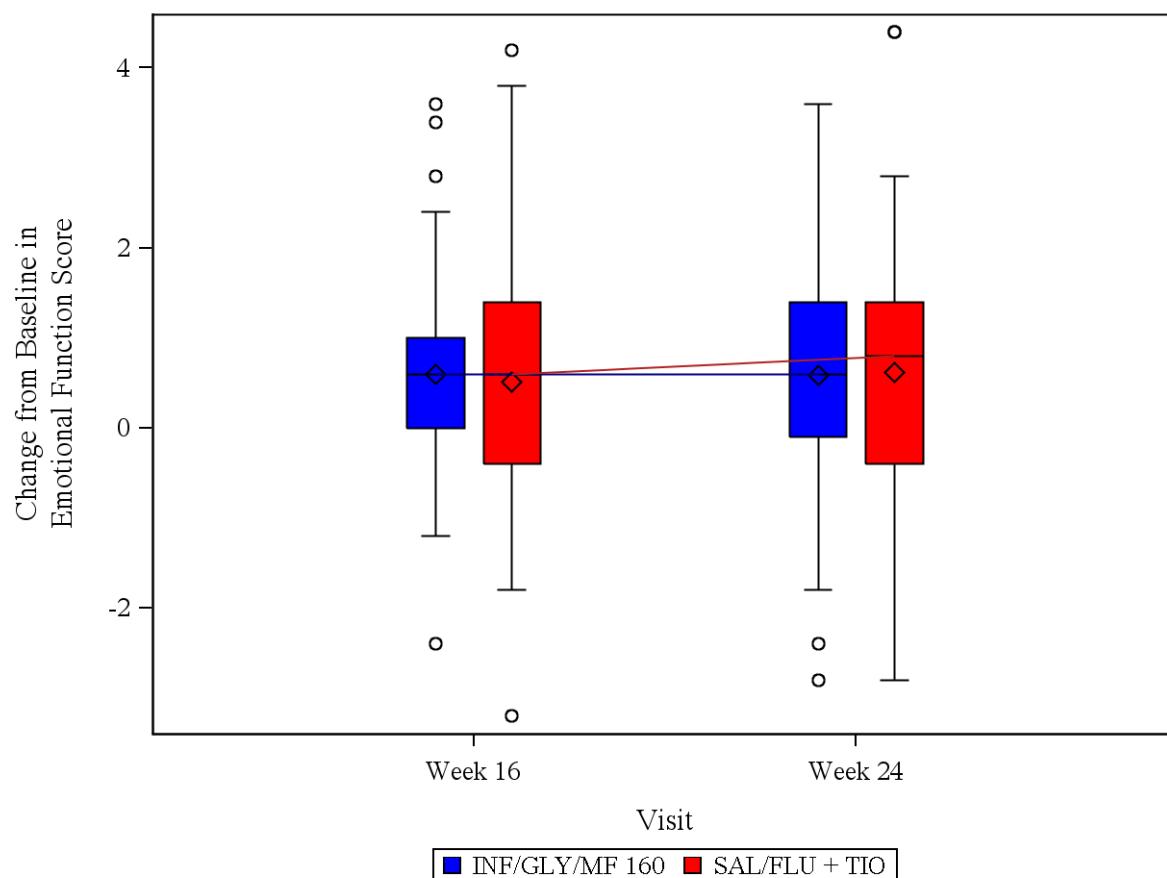
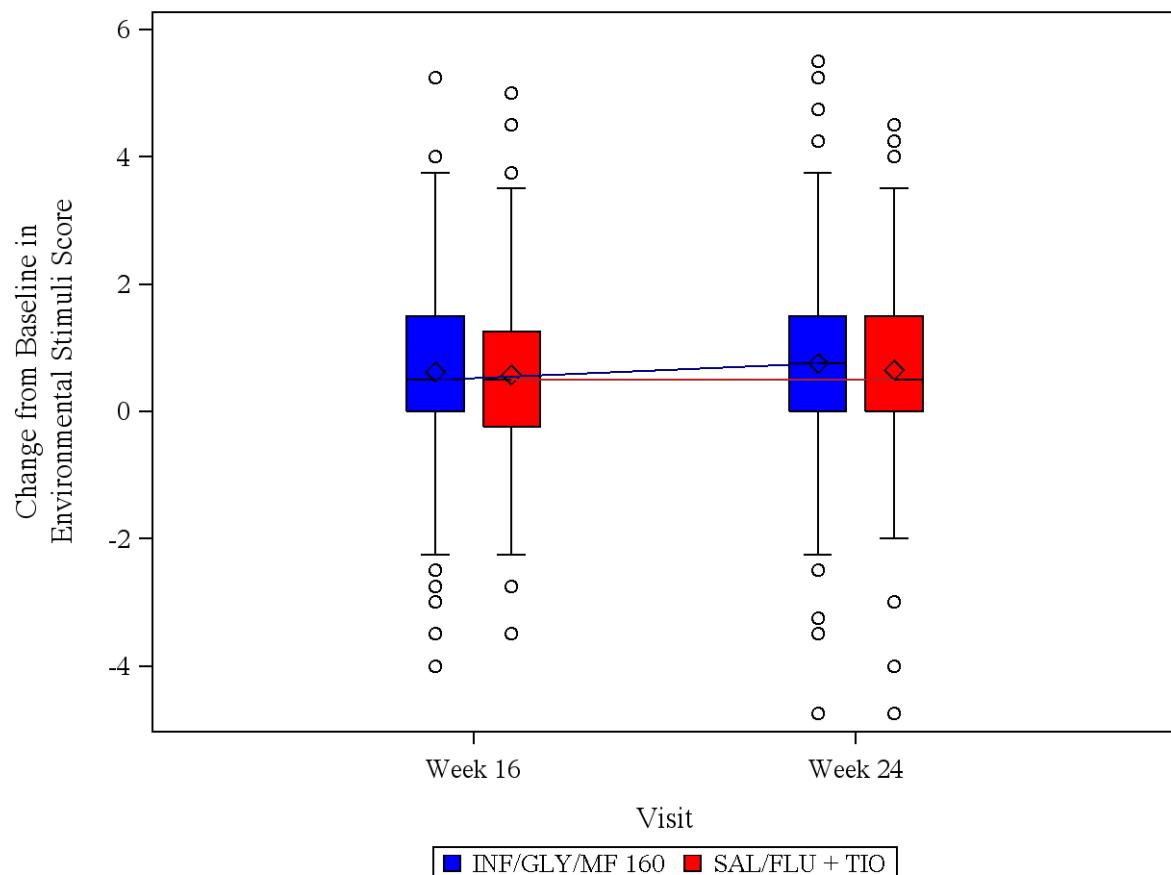


Figure 5.23.2 AQLQ-S (Emotional Function Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



5.25 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

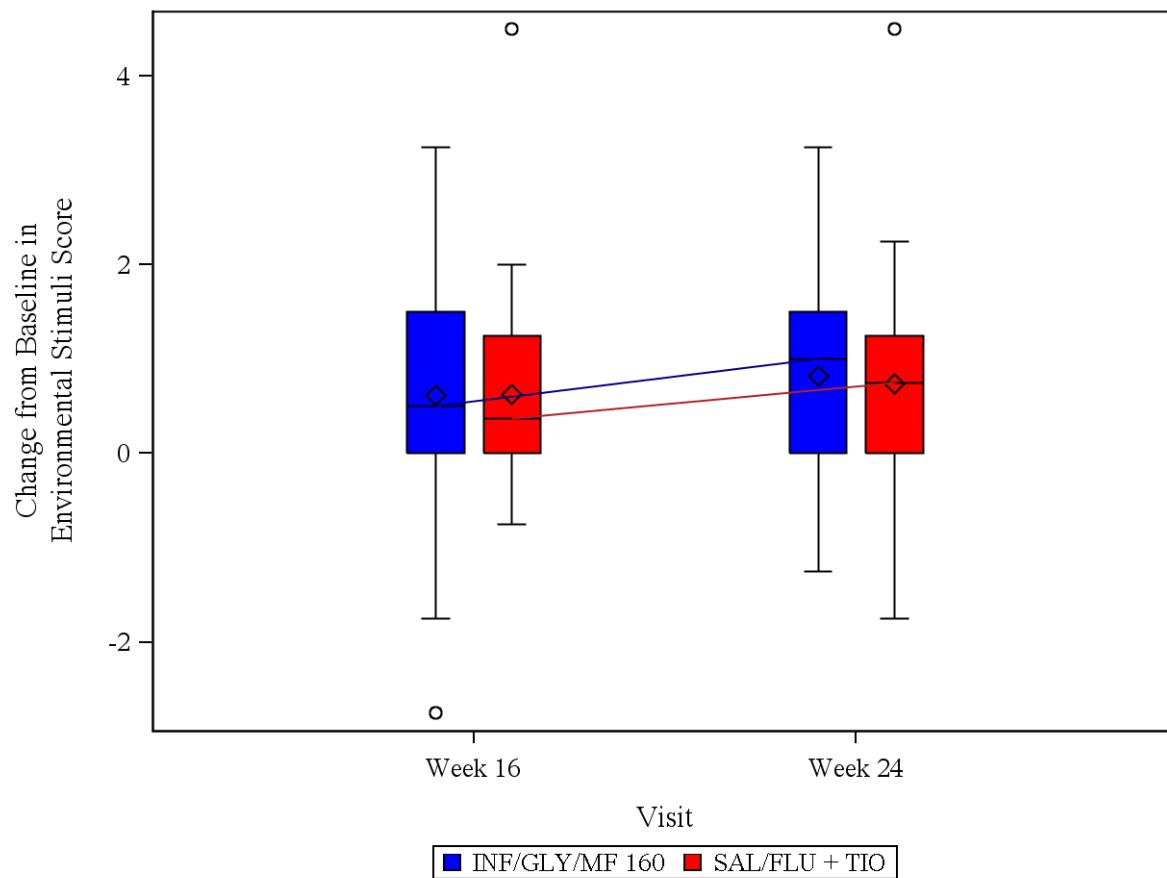


Figure 5.26.2 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Age (FAS), Age = 40-64 years

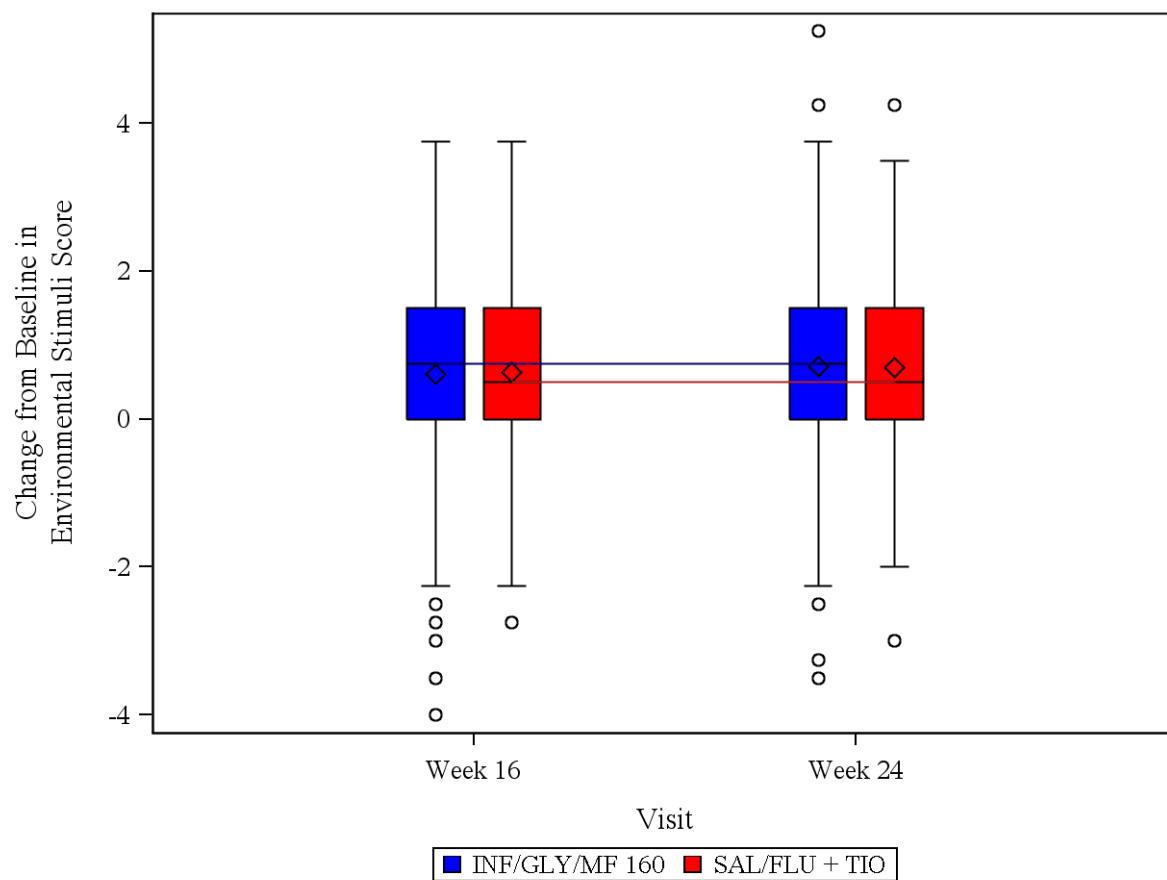
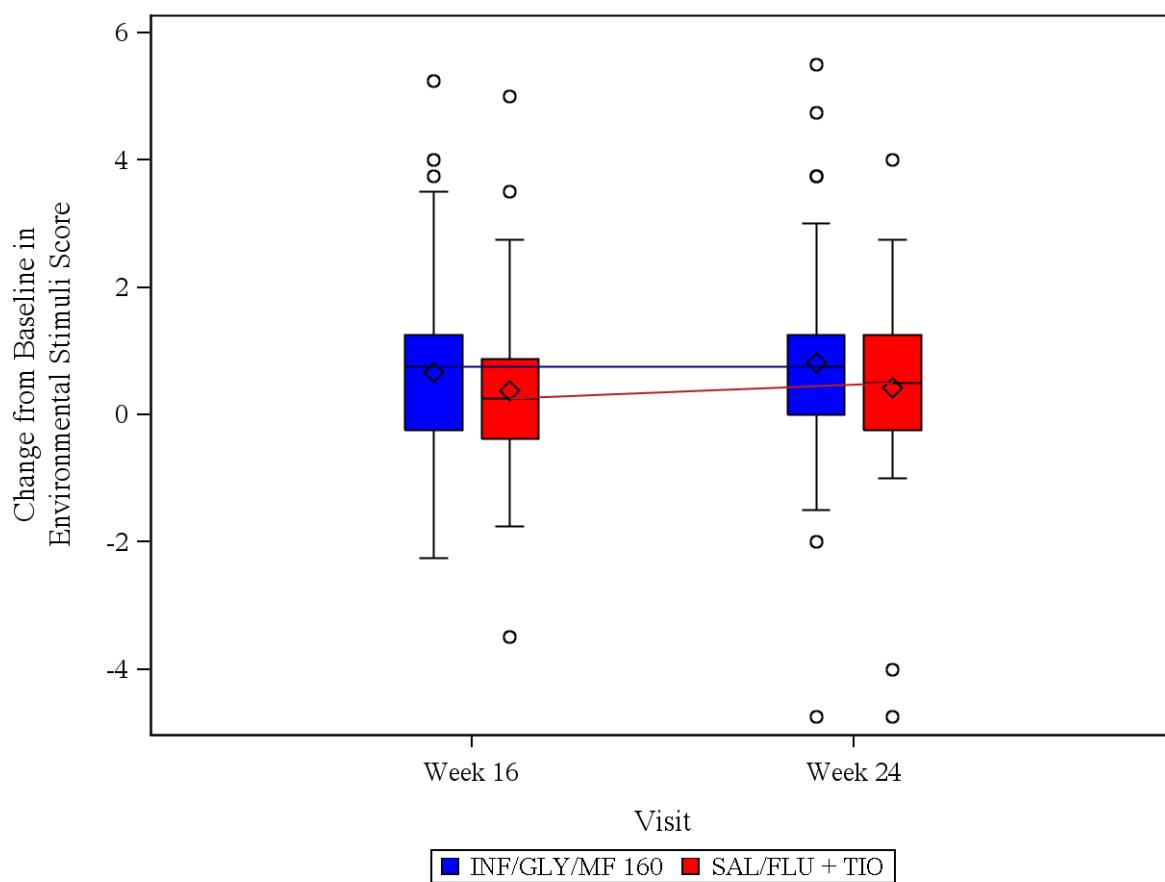


Figure 5.26.3 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

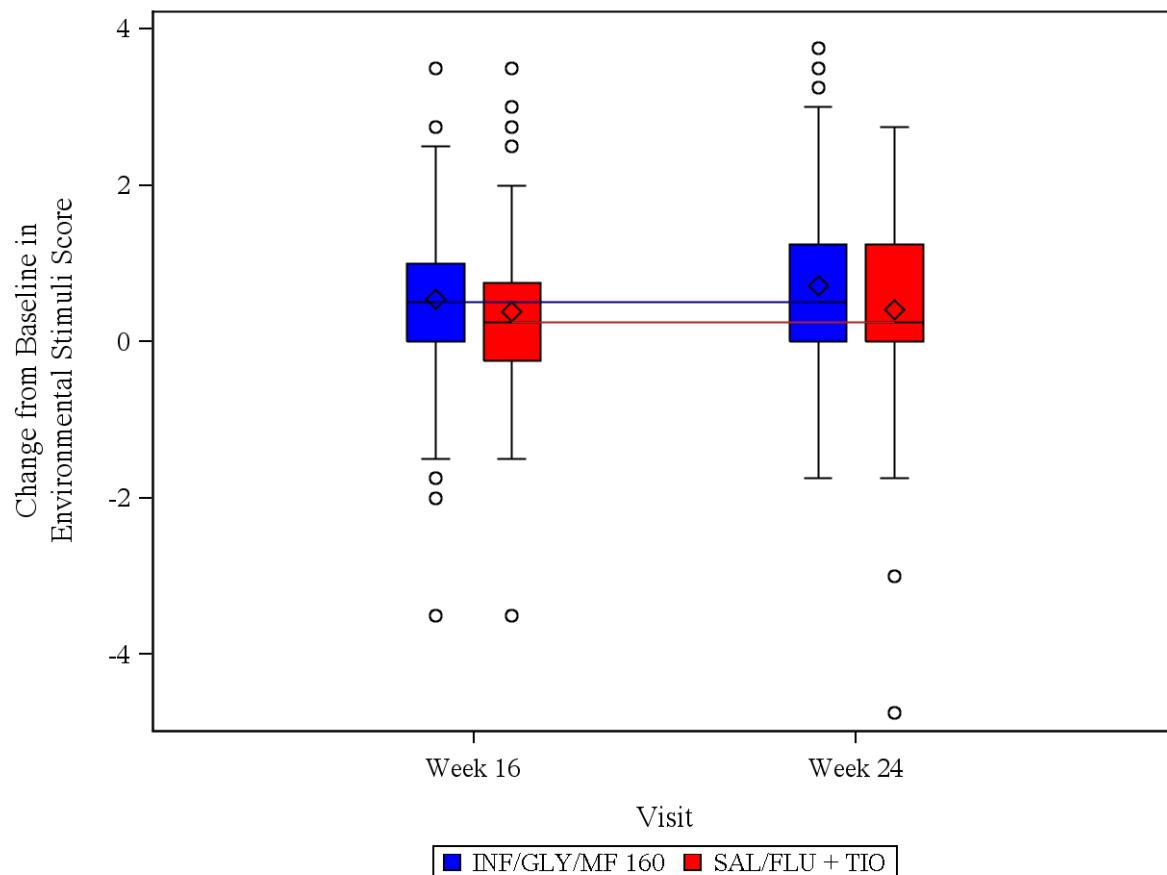
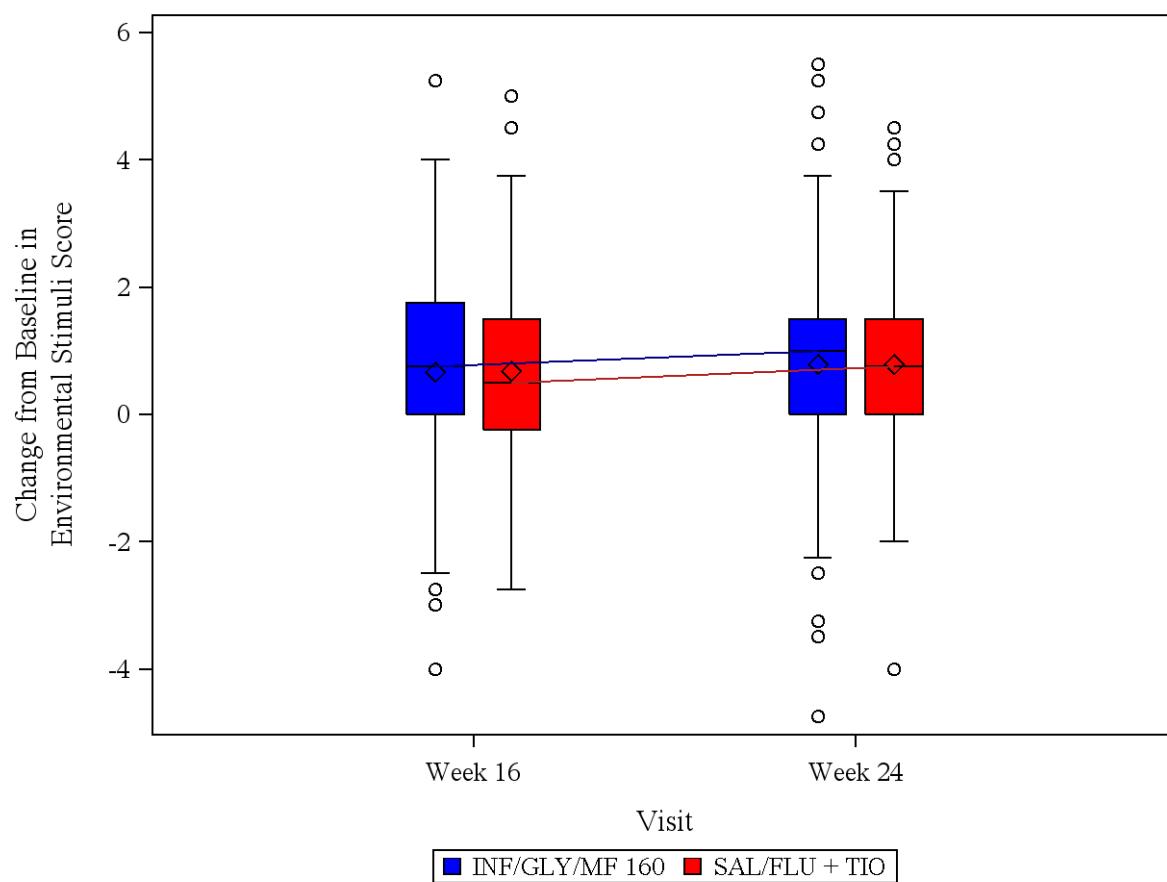


Figure 5.27.2 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Gender (FAS), Gender = Female



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

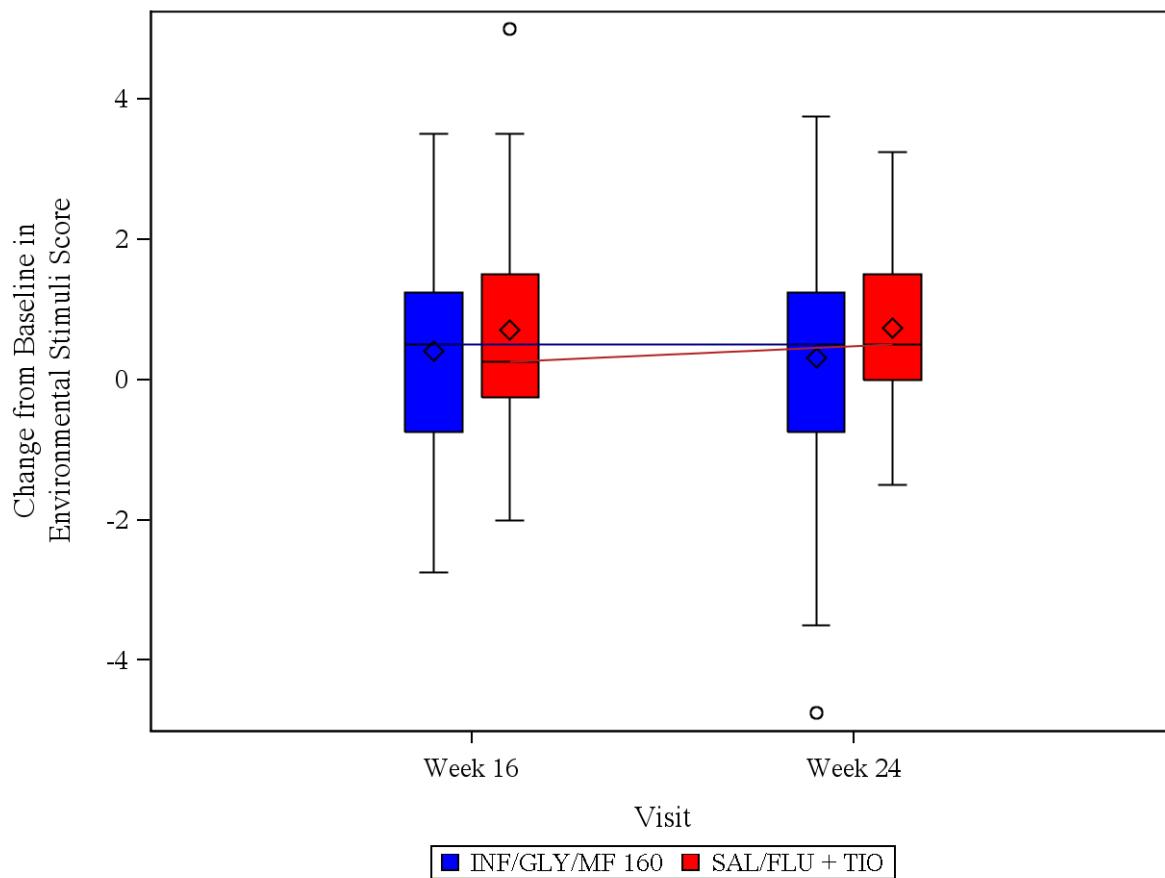


Figure 5.28.2 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Region (FAS), Region = Europe

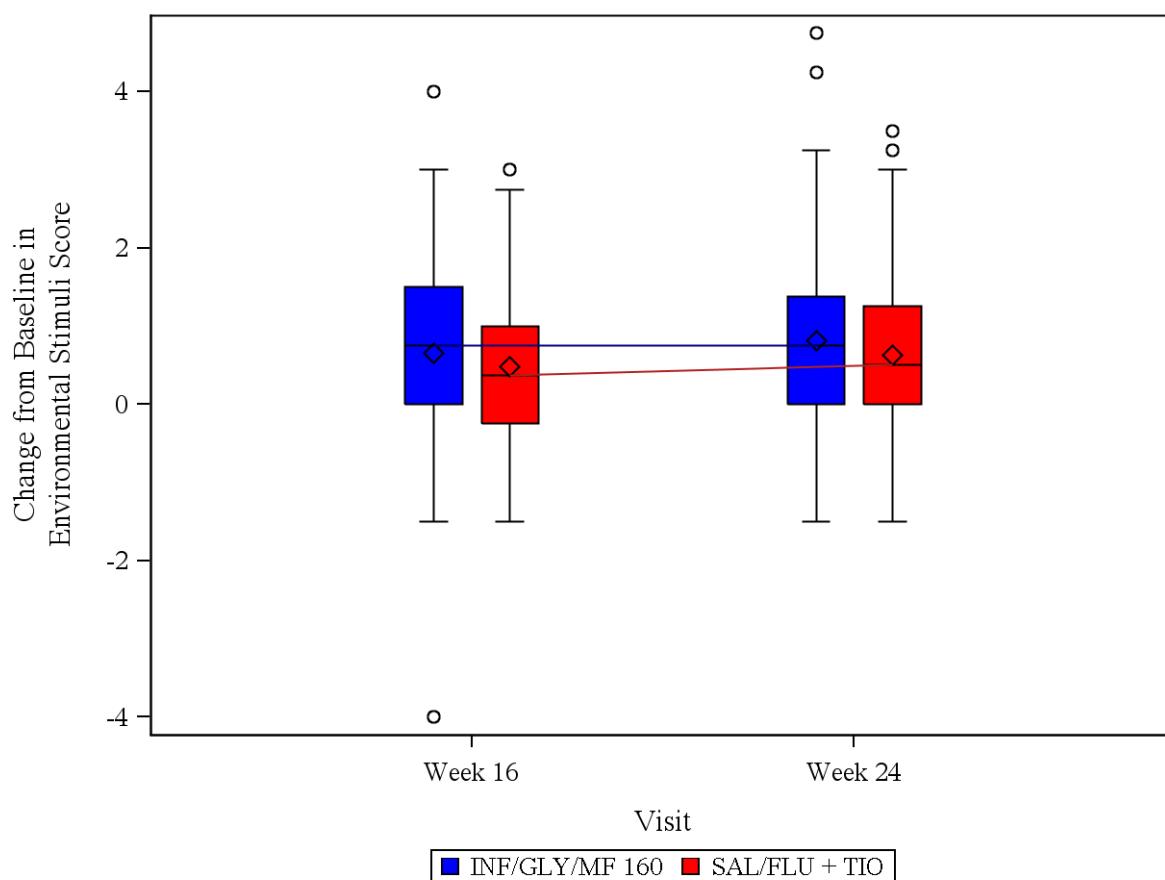


Figure 5.28.3 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Region (FAS), Region = Latin America

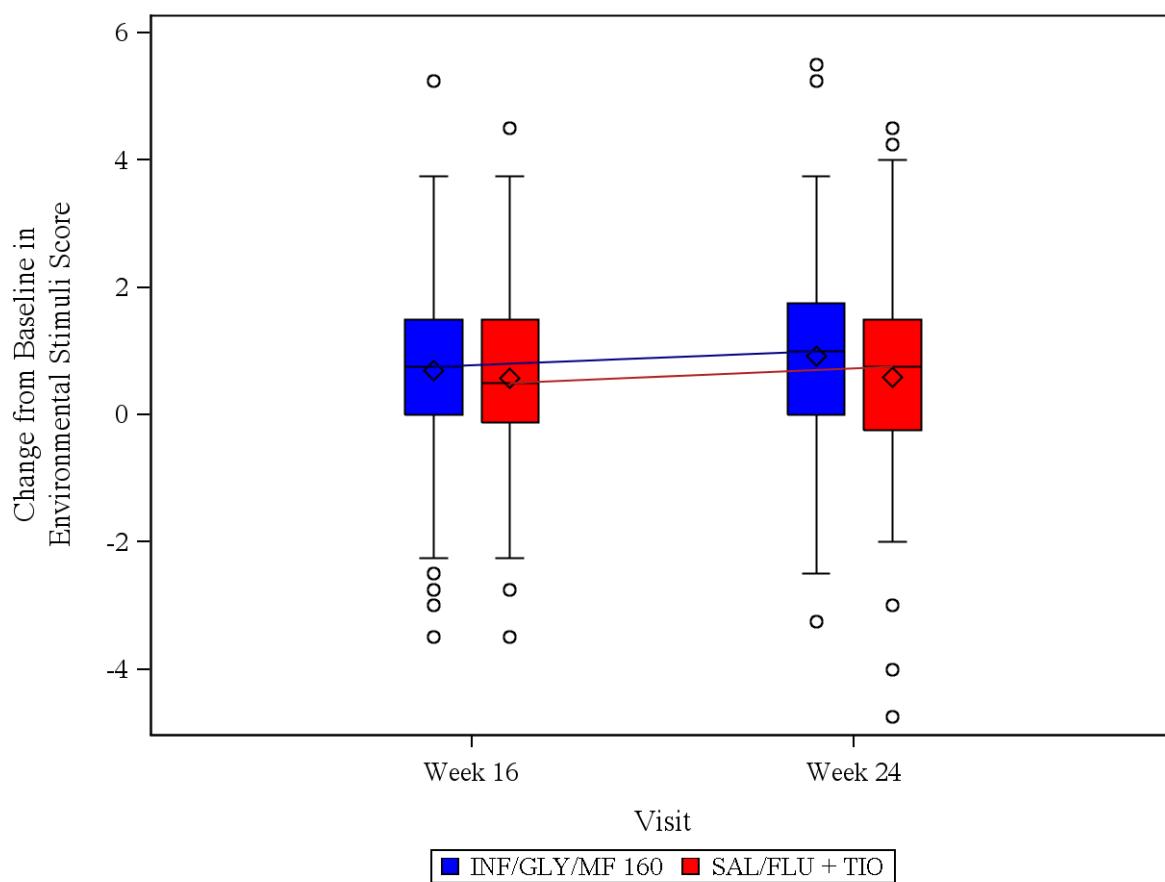
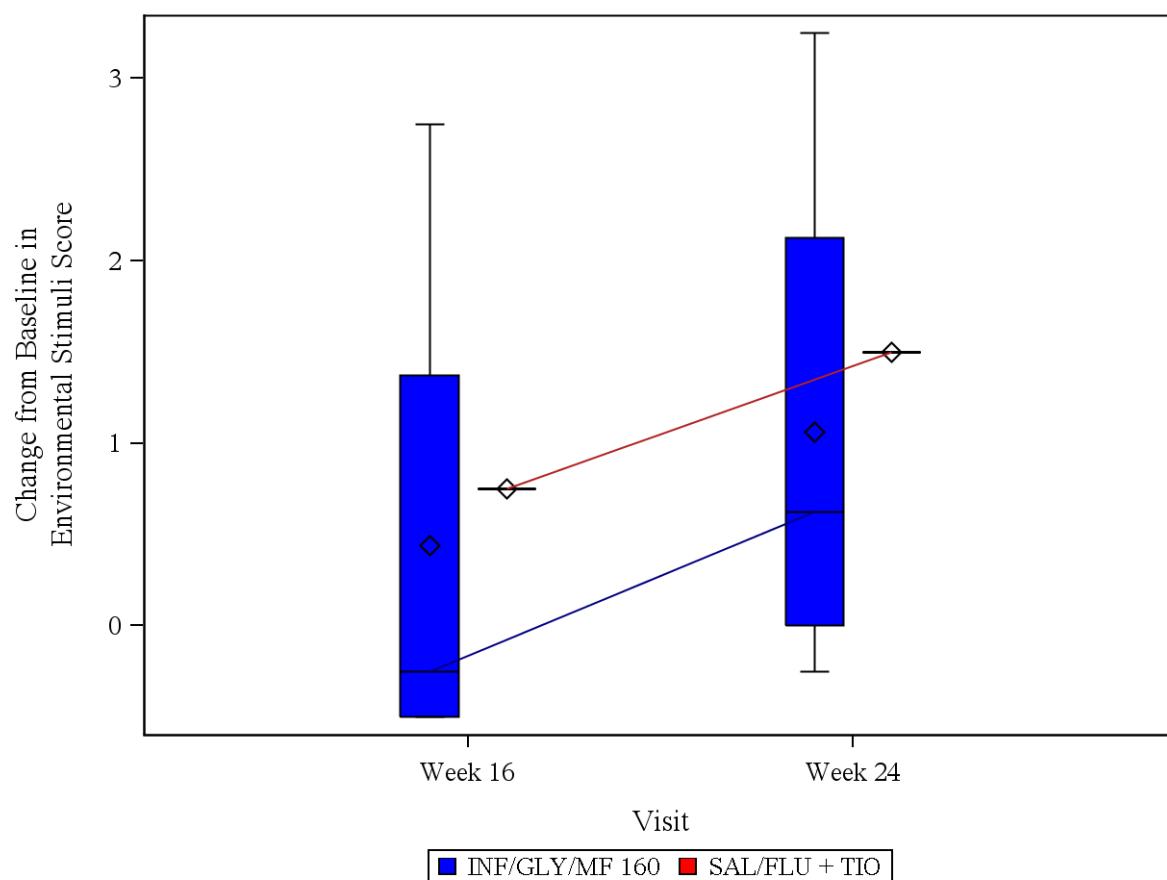


Figure 5.28.4 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by Region (FAS), Region = Others



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

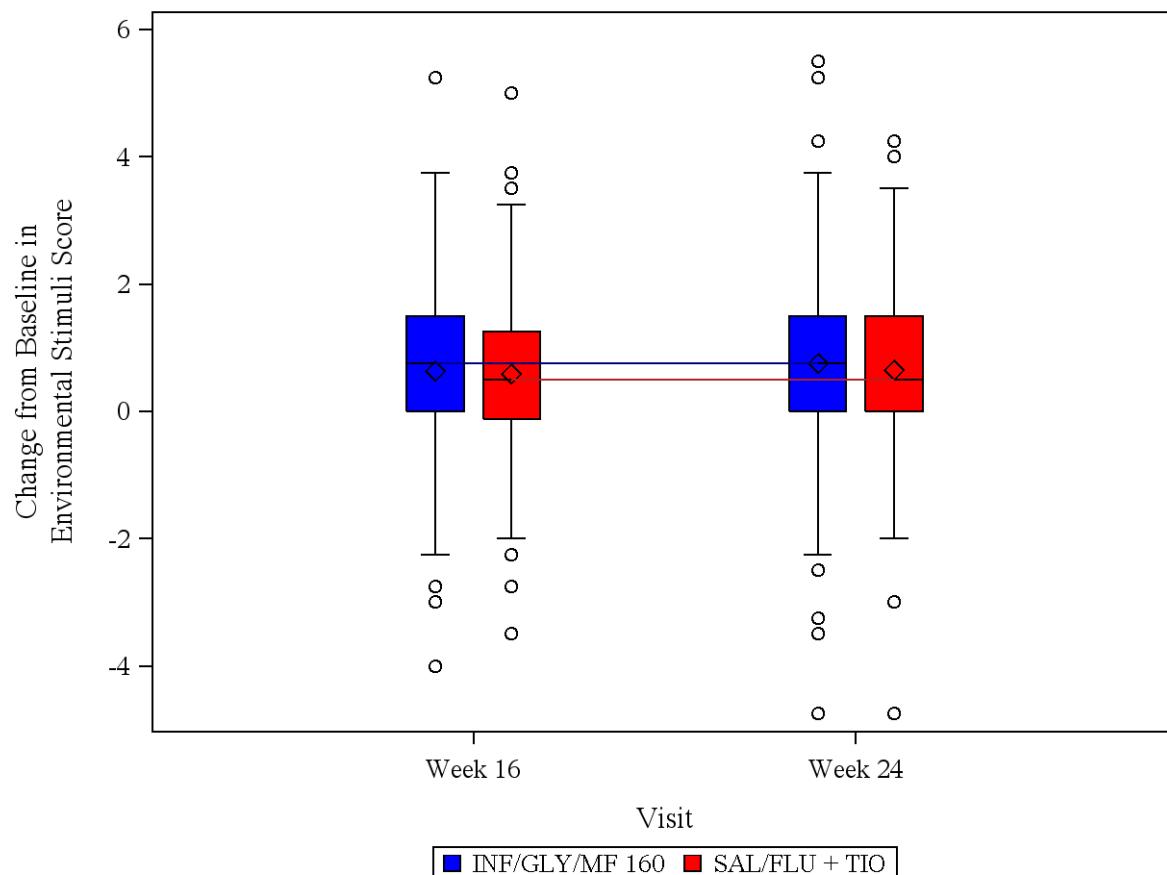
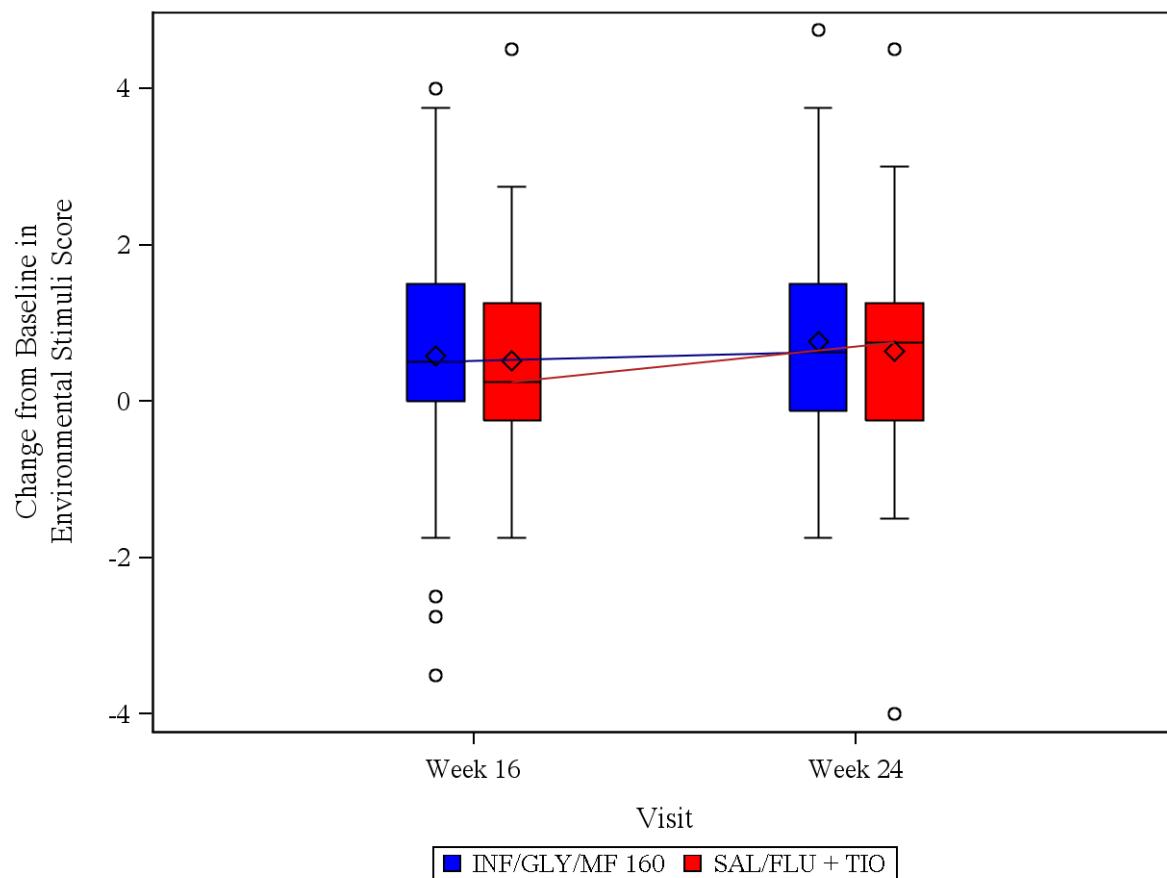


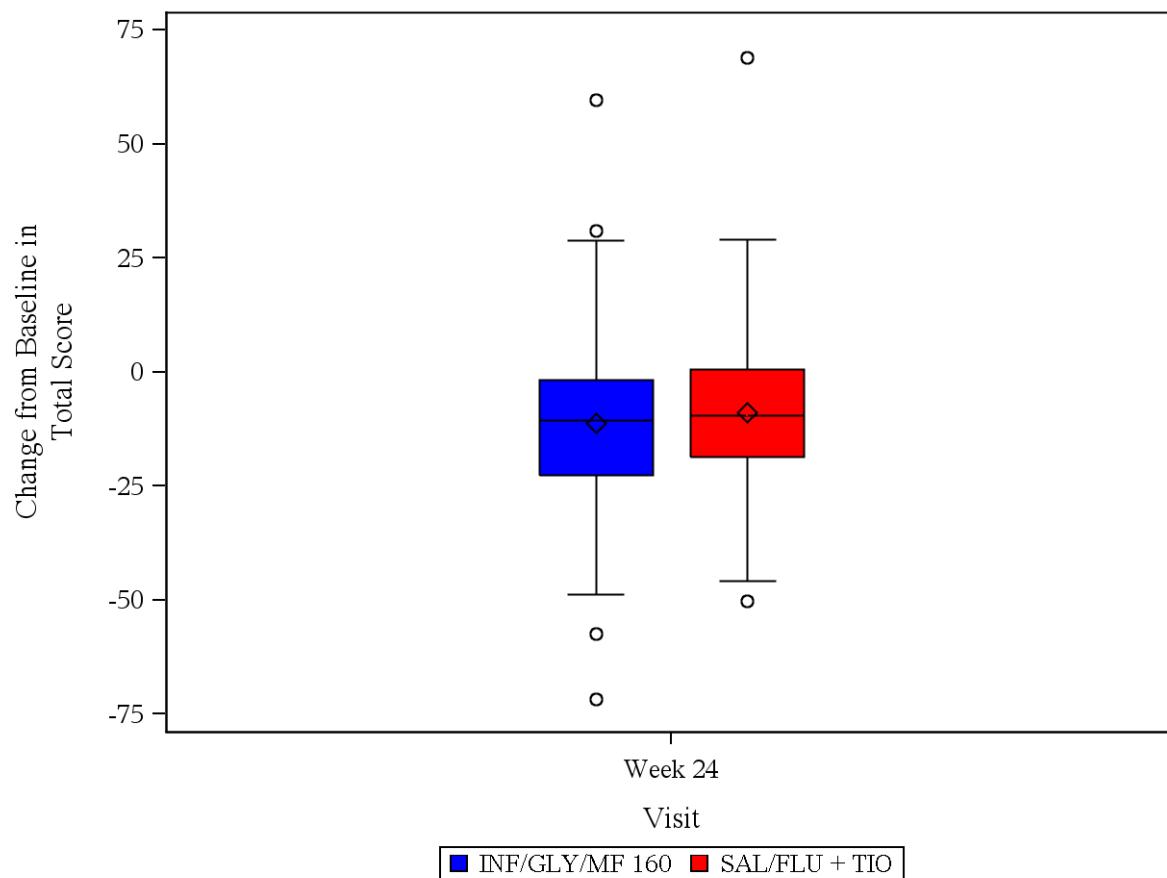
Figure 5.29.2 AQLQ-S (Environmental Stimuli Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



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

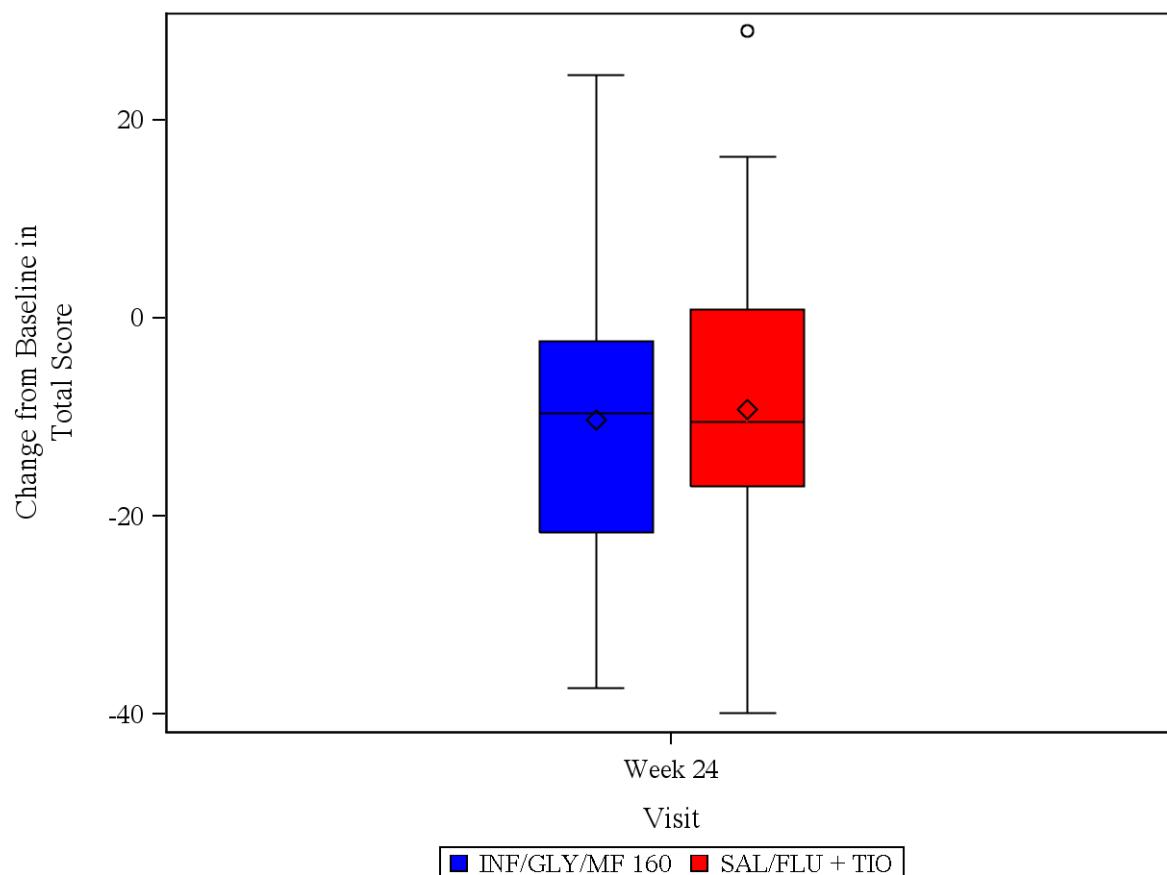


Figure 7.2.2 SGRQ (Total Score) - Change from Baseline by Age (FAS), Age = 40-64 years

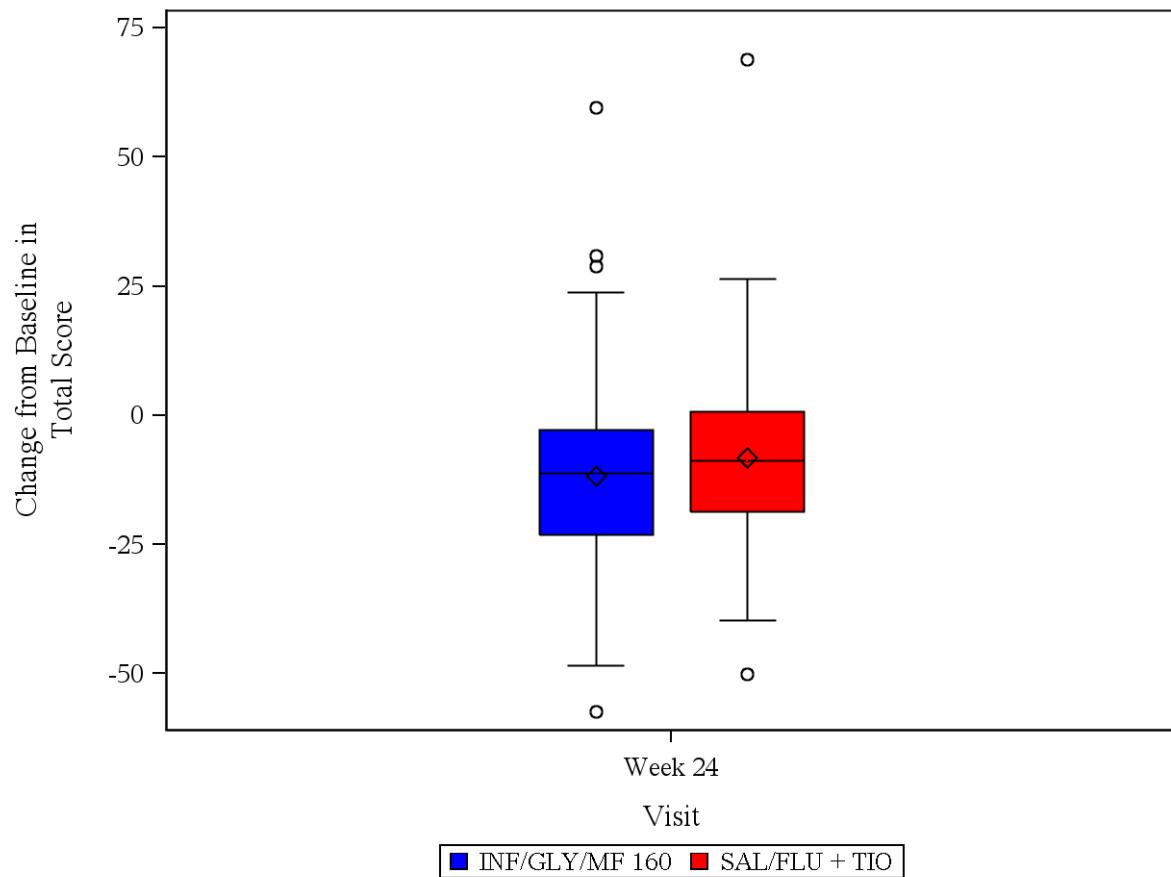
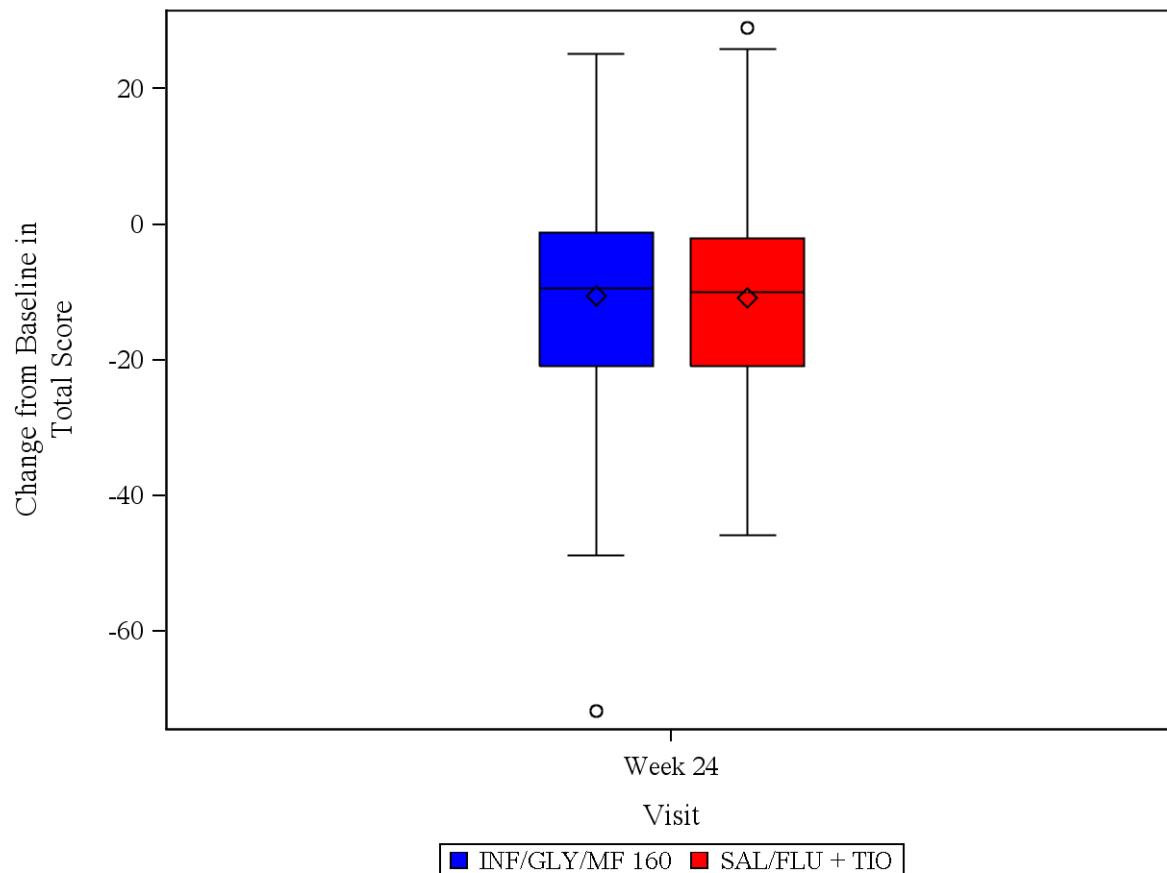


Figure 7.2.3 SGRQ (Total Score) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

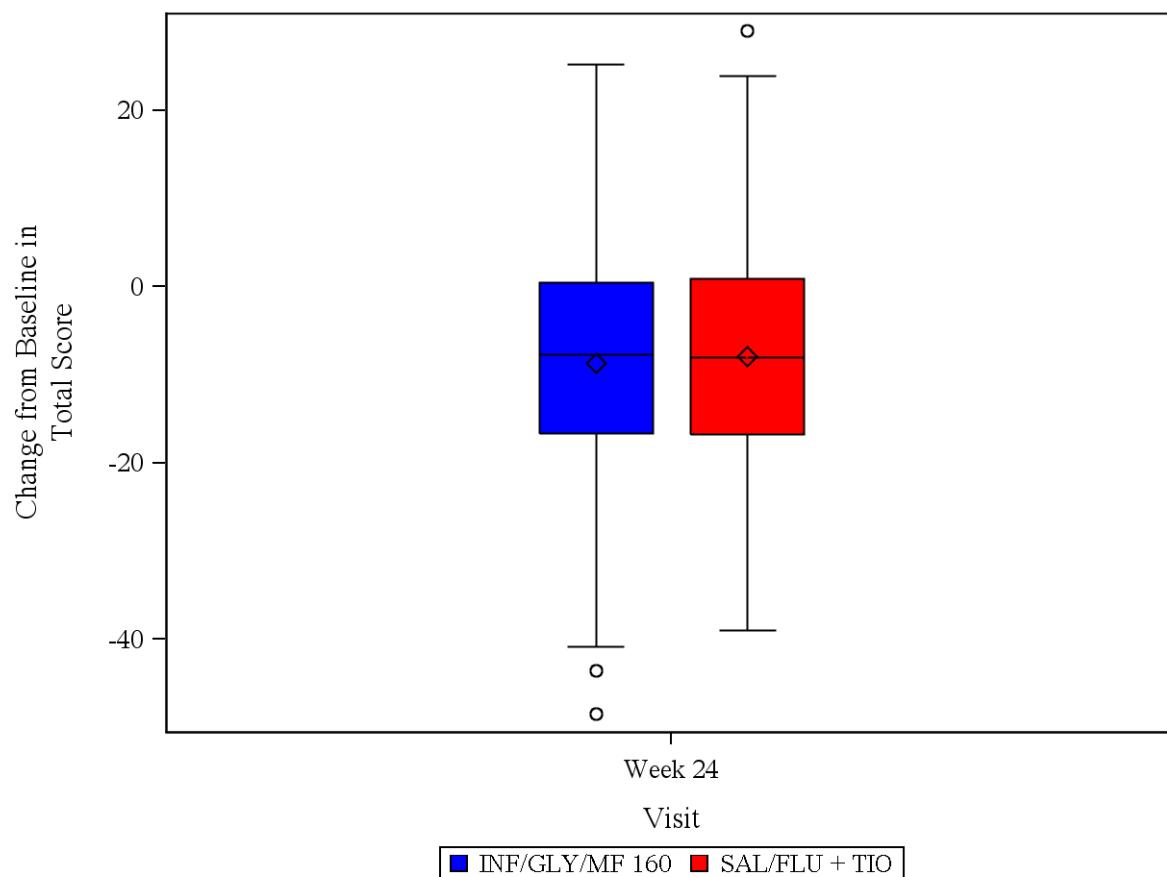
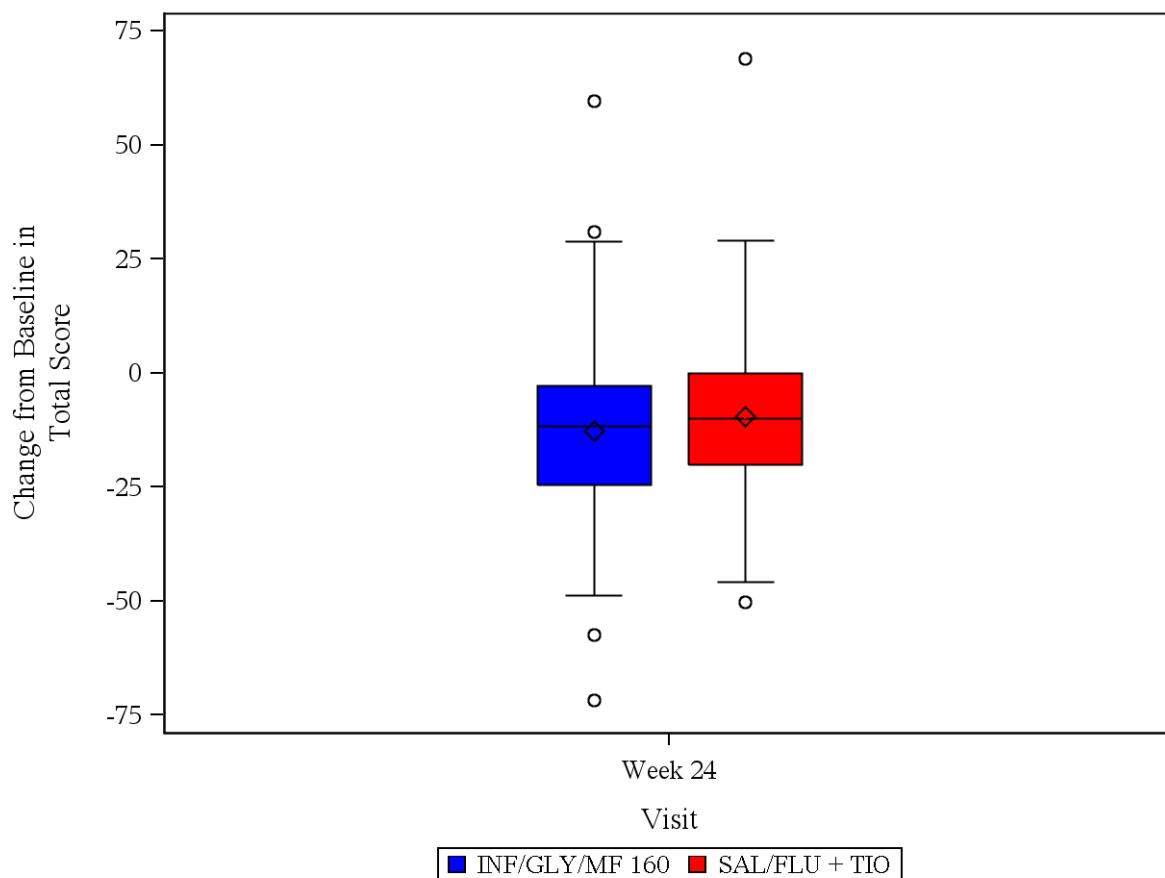


Figure 7.3.2 SGRQ (Total Score) - Change from Baseline by Gender (FAS), Gender = Female



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

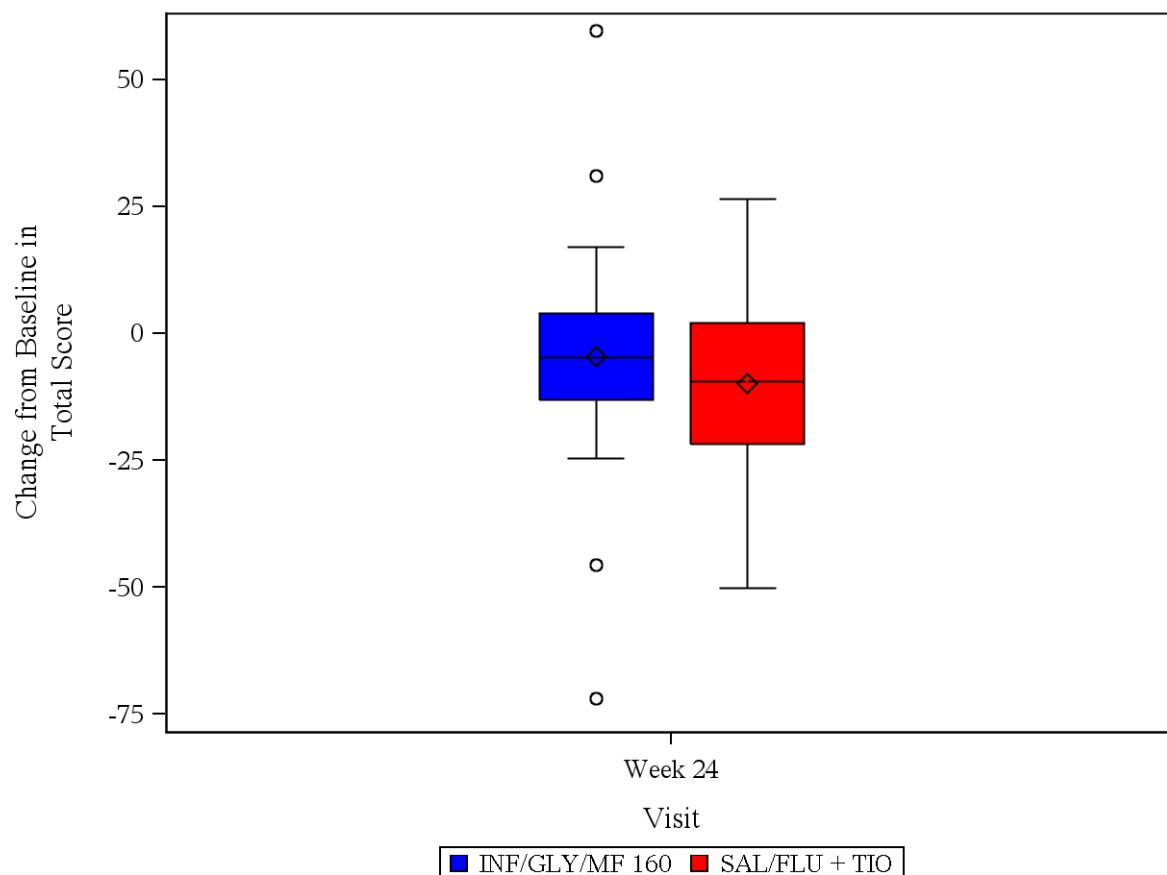


Figure 7.4.2 SGRQ (Total Score) - Change from Baseline by Region (FAS), Region = Europe

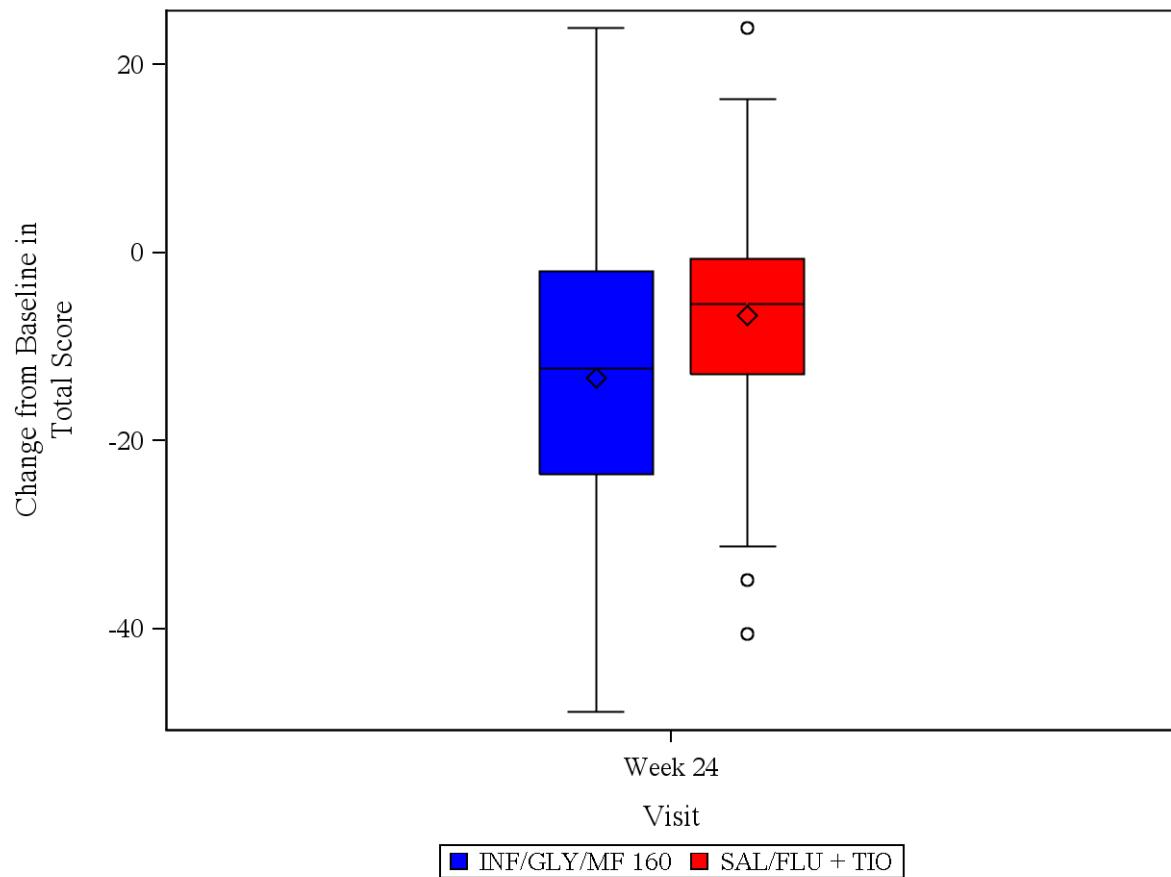


Figure 7.4.3 SGRQ (Total Score) - Change from Baseline by Region (FAS), Region = Latin America

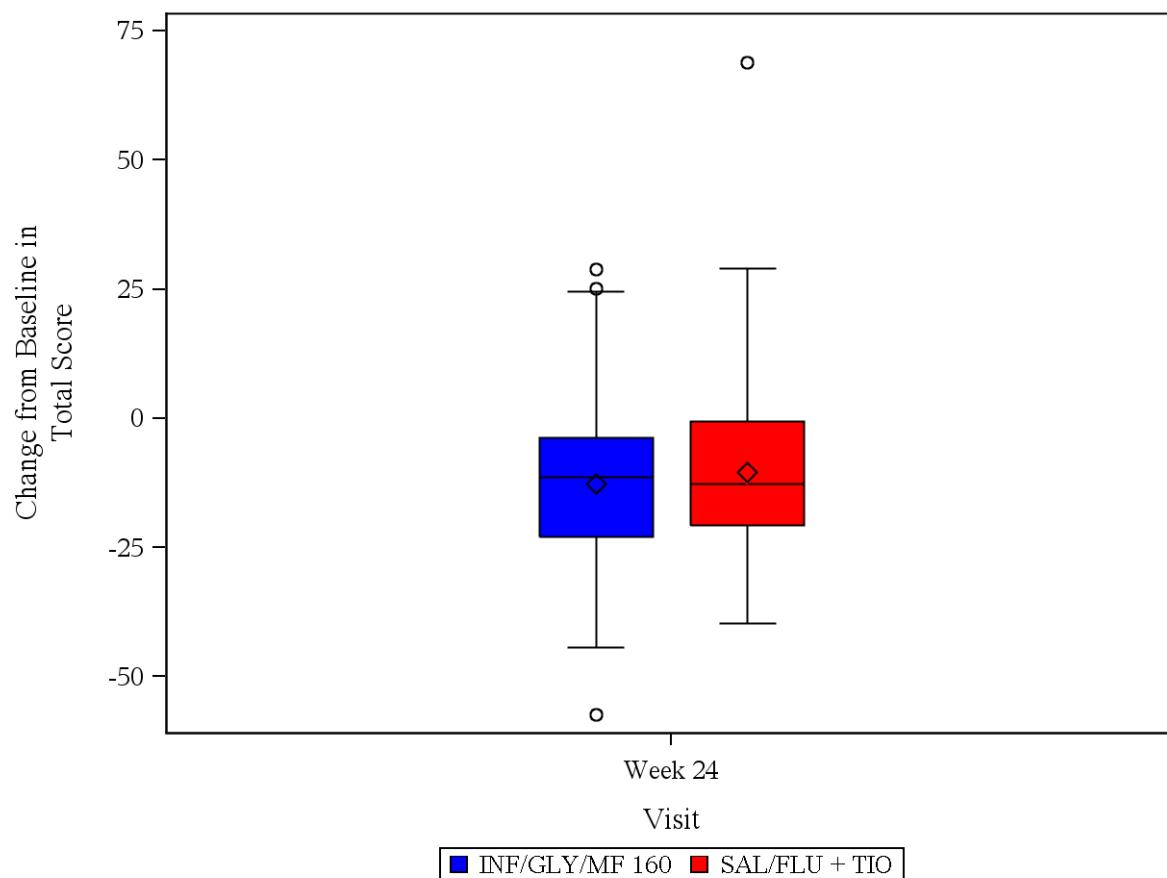
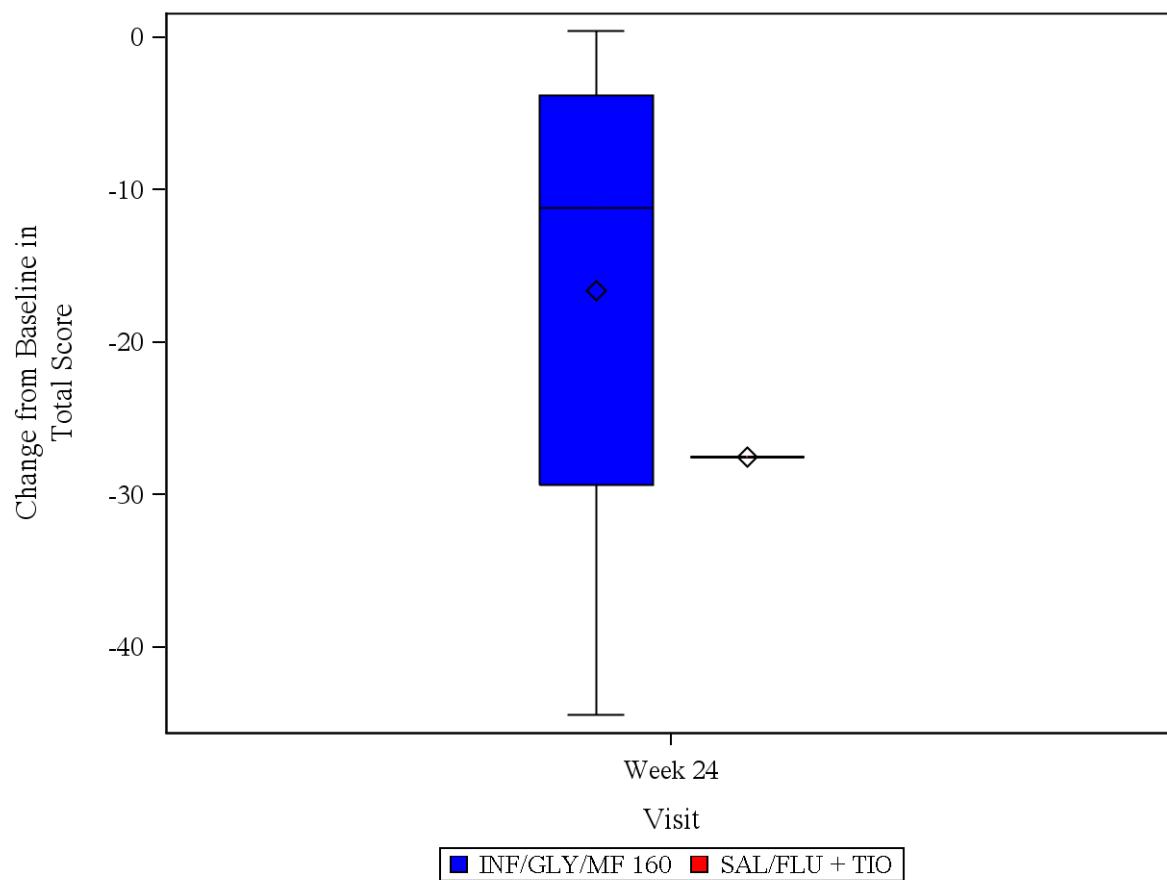


Figure 7.4.4 SGRQ (Total Score) - Change from Baseline by Region (FAS), Region = Others



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

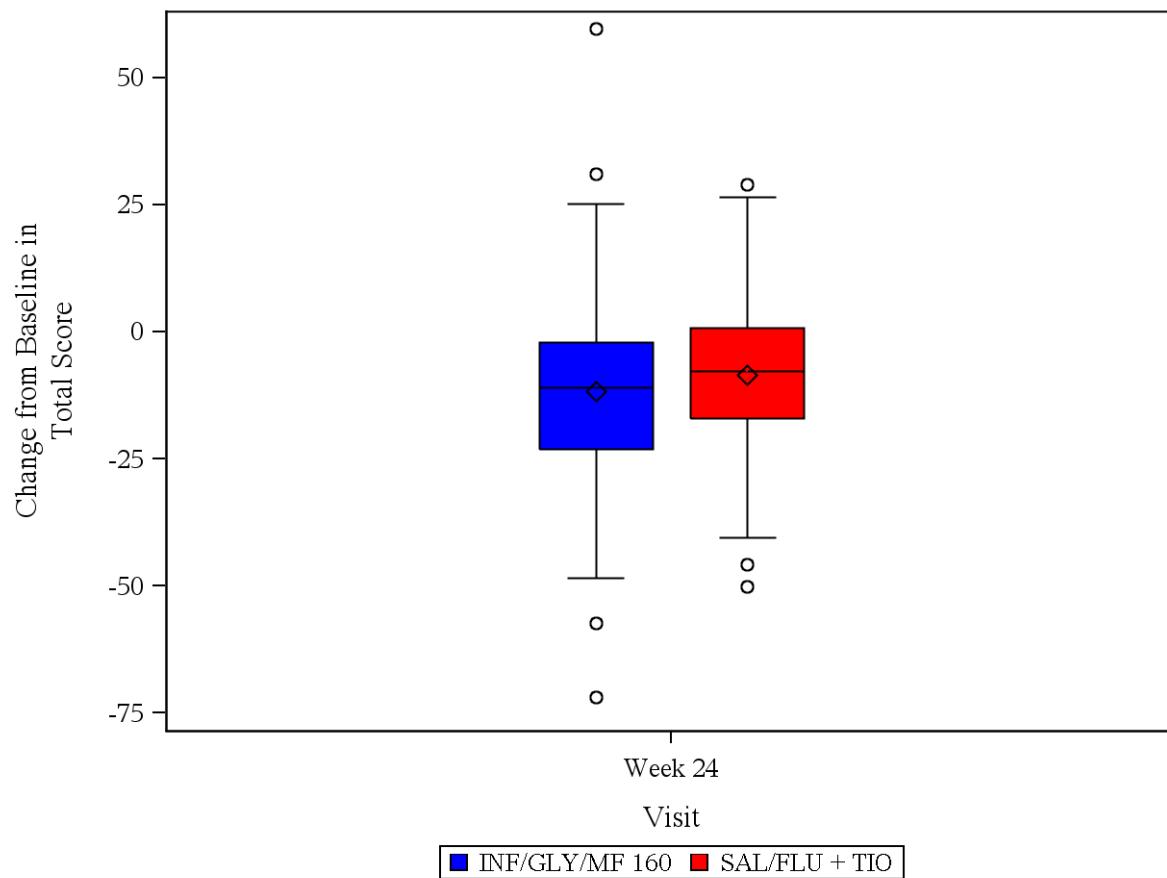
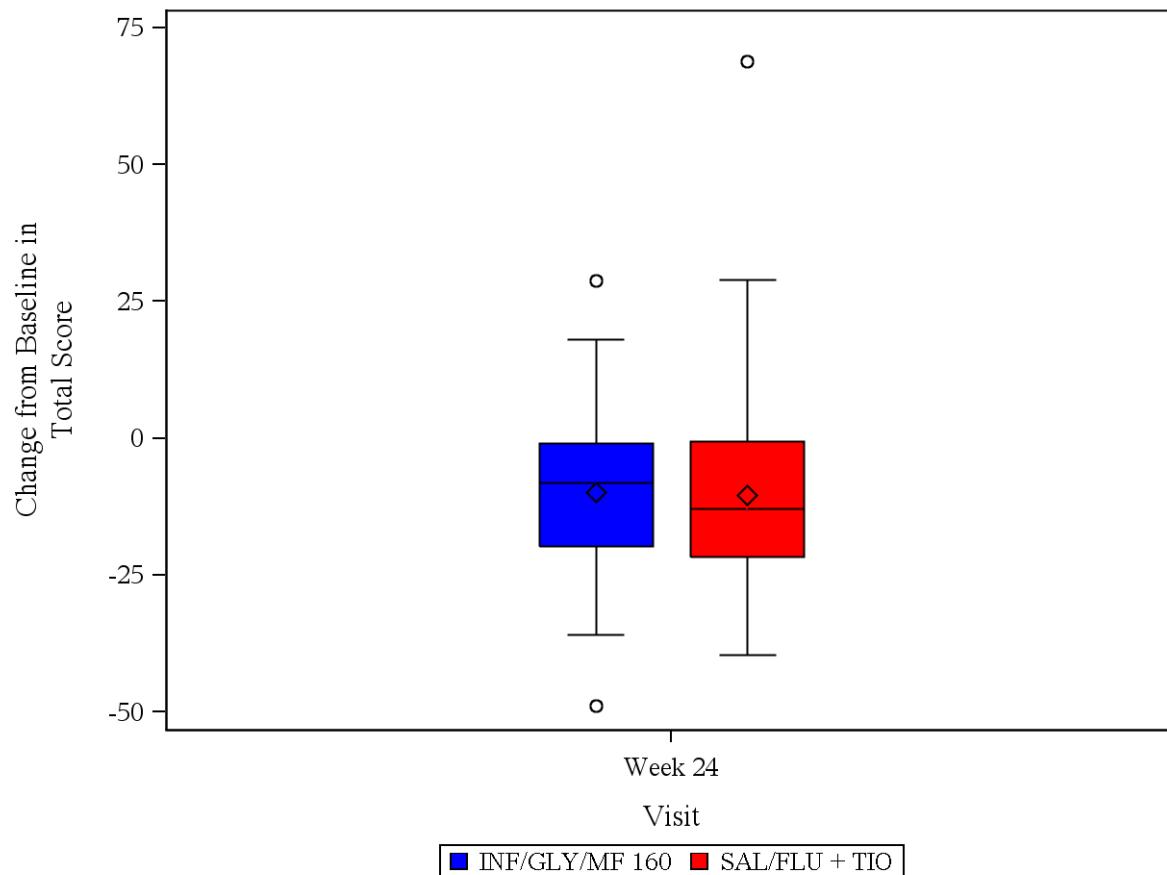
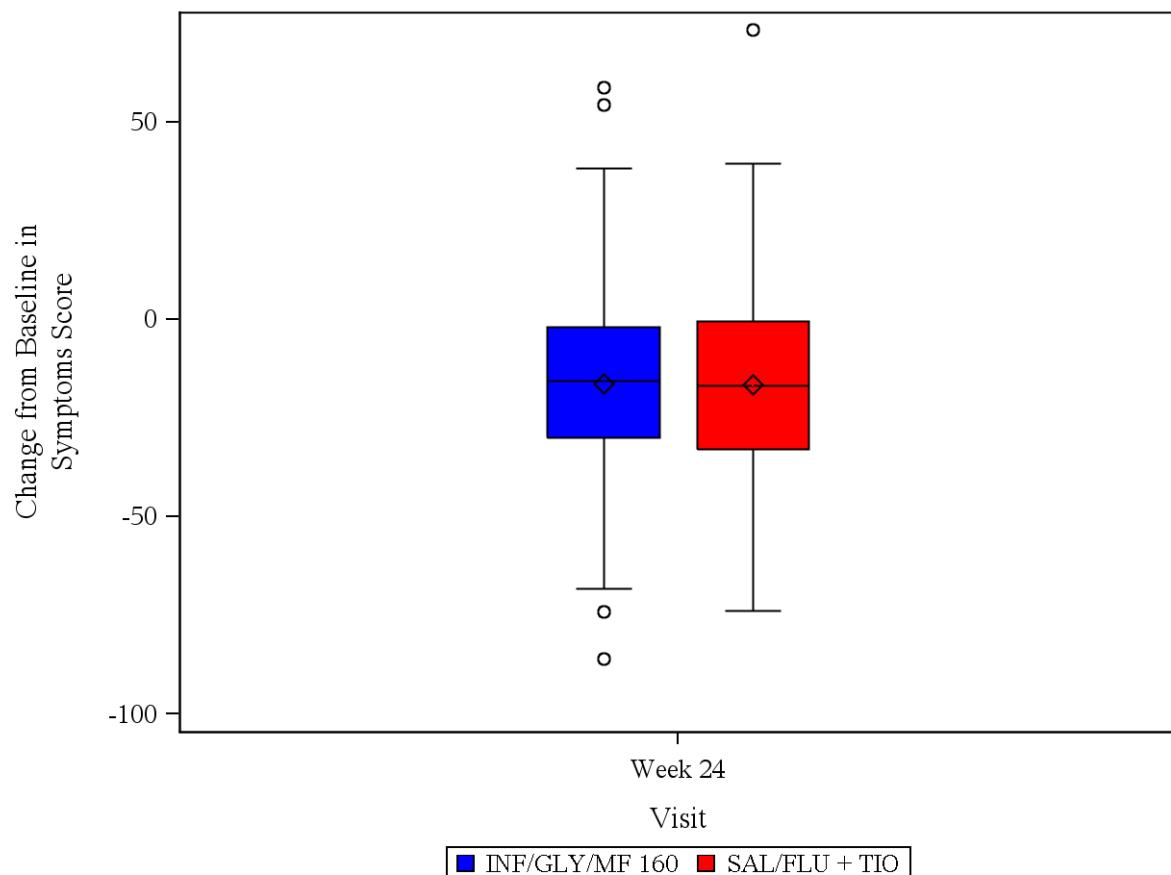


Figure 7.5.2 SGRQ (Total Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



7.7 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

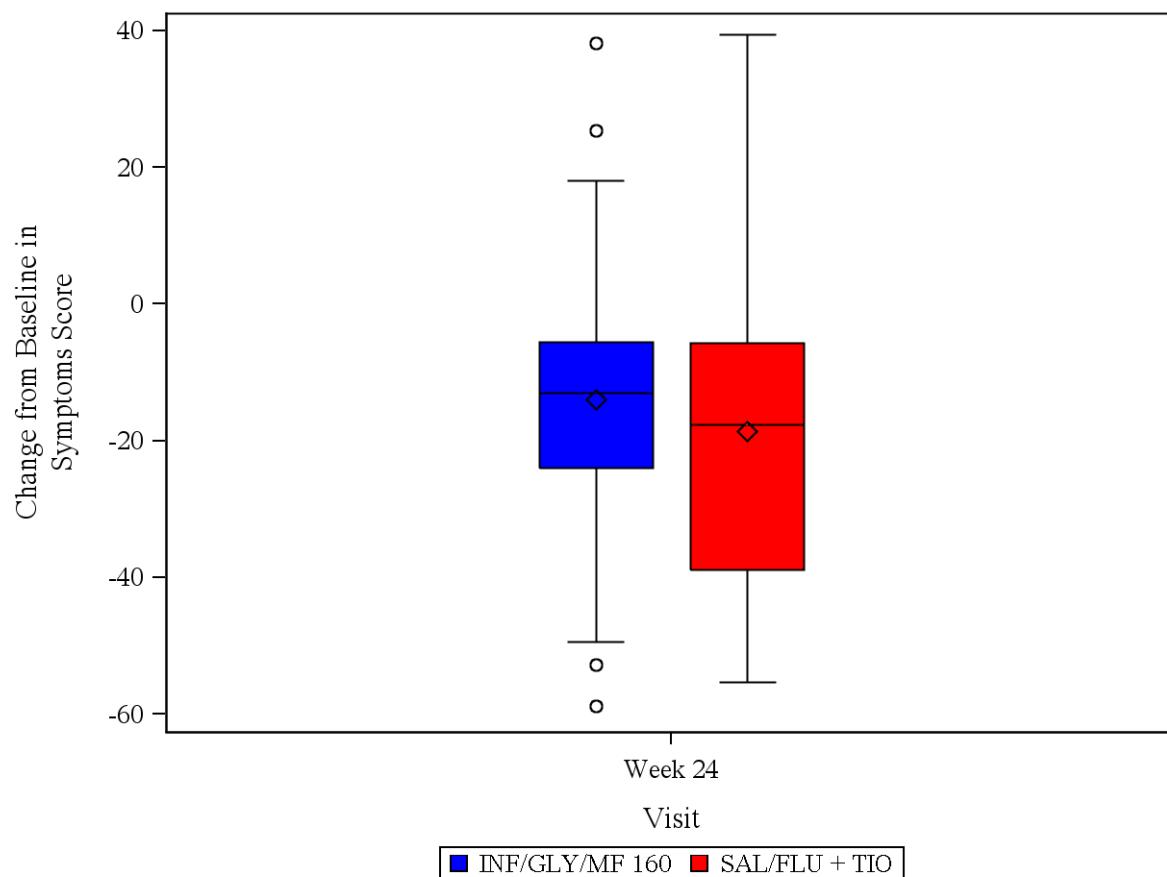


Figure 7.8.2 SGRQ (Symptoms Score) - Change from Baseline by Age (FAS), Age = 40-64 years

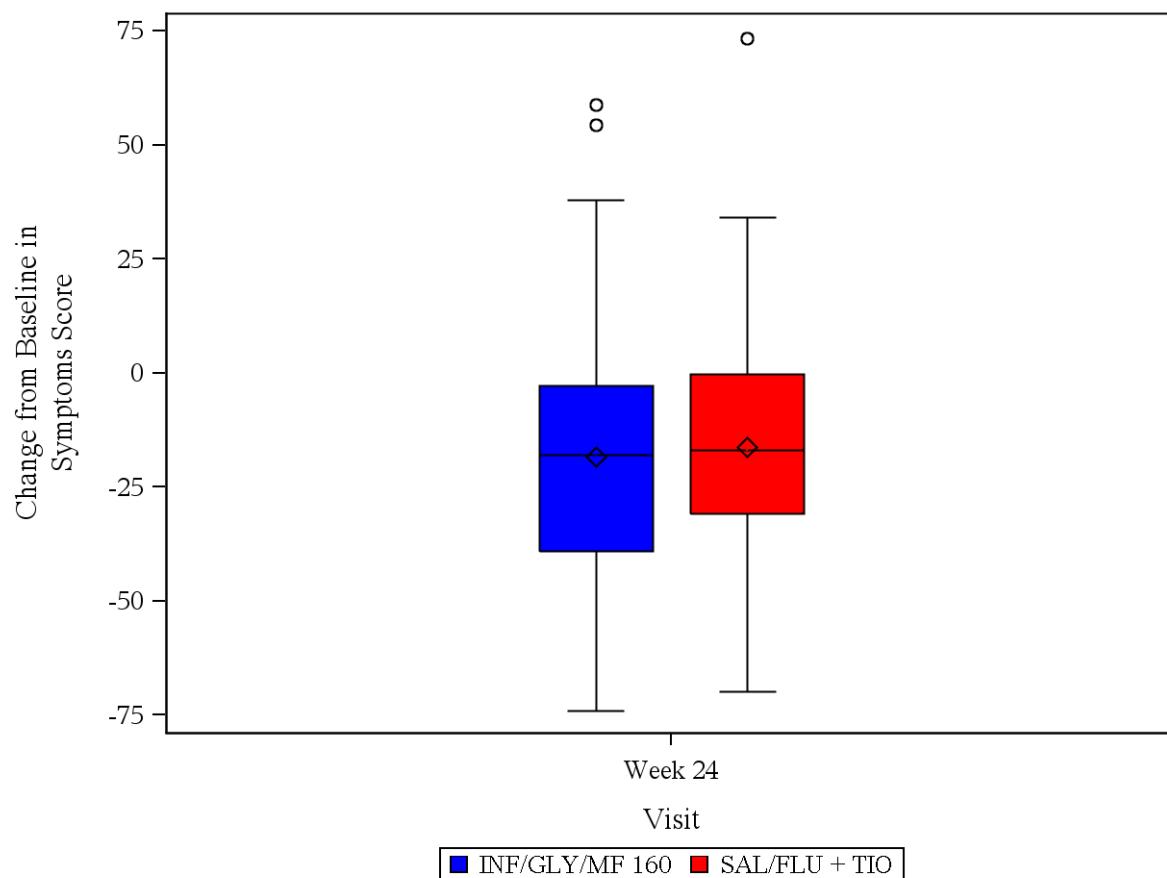
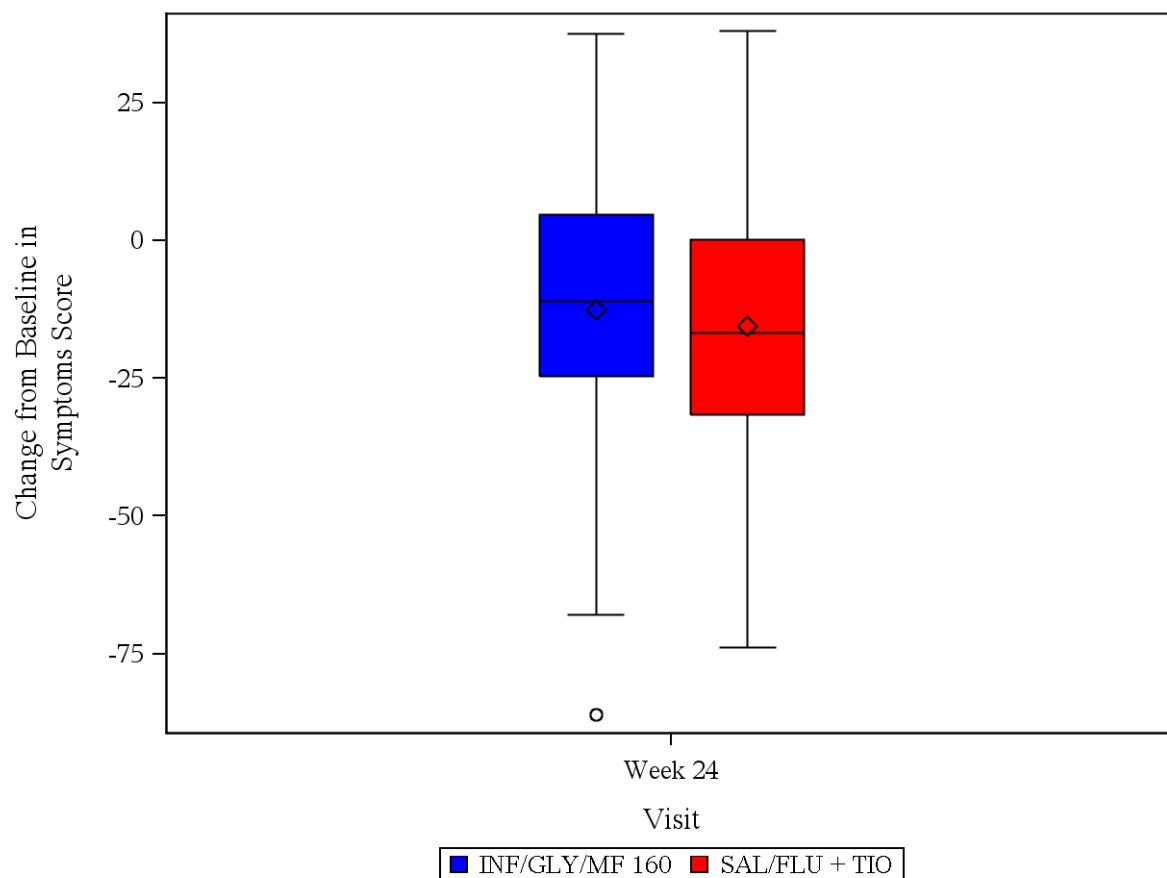
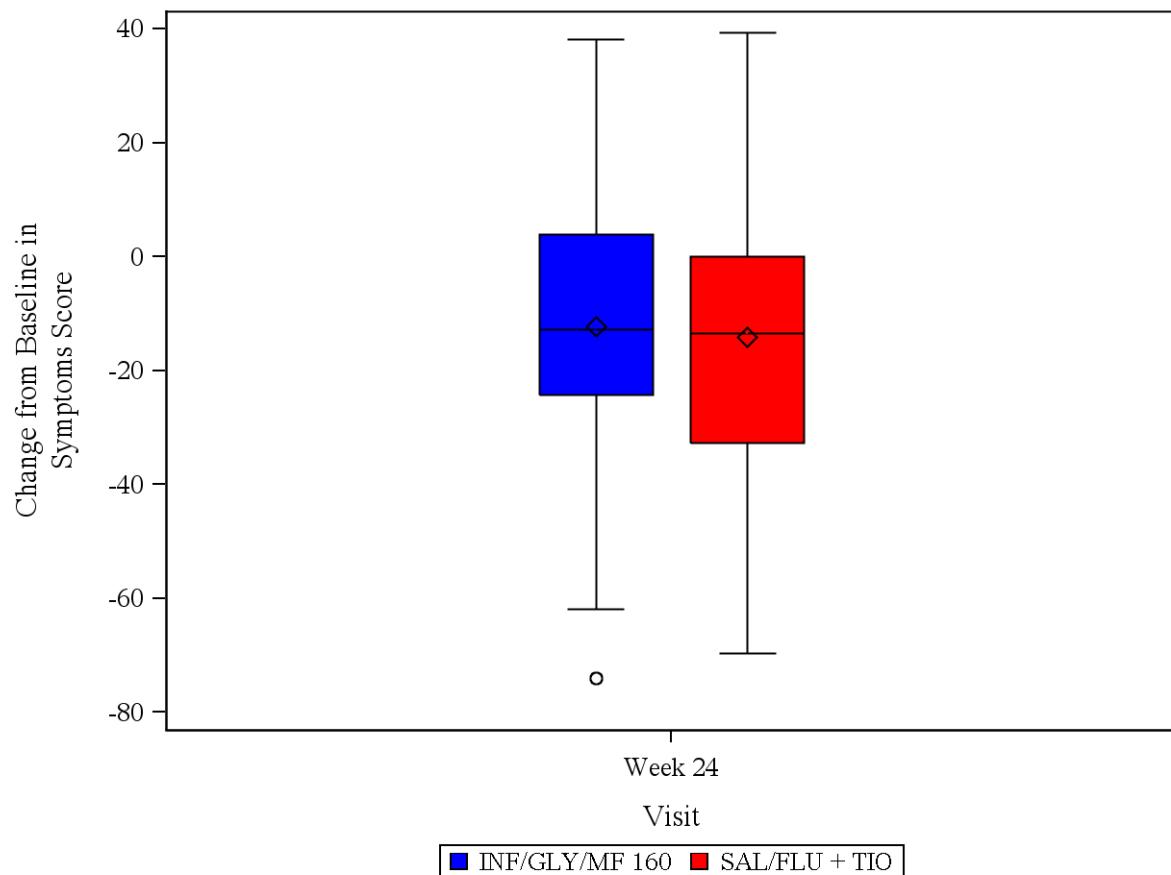


Figure 7.8.3 SGRQ (Symptoms Score) - Change from Baseline by Age (FAS), Age = ≥ 65 years

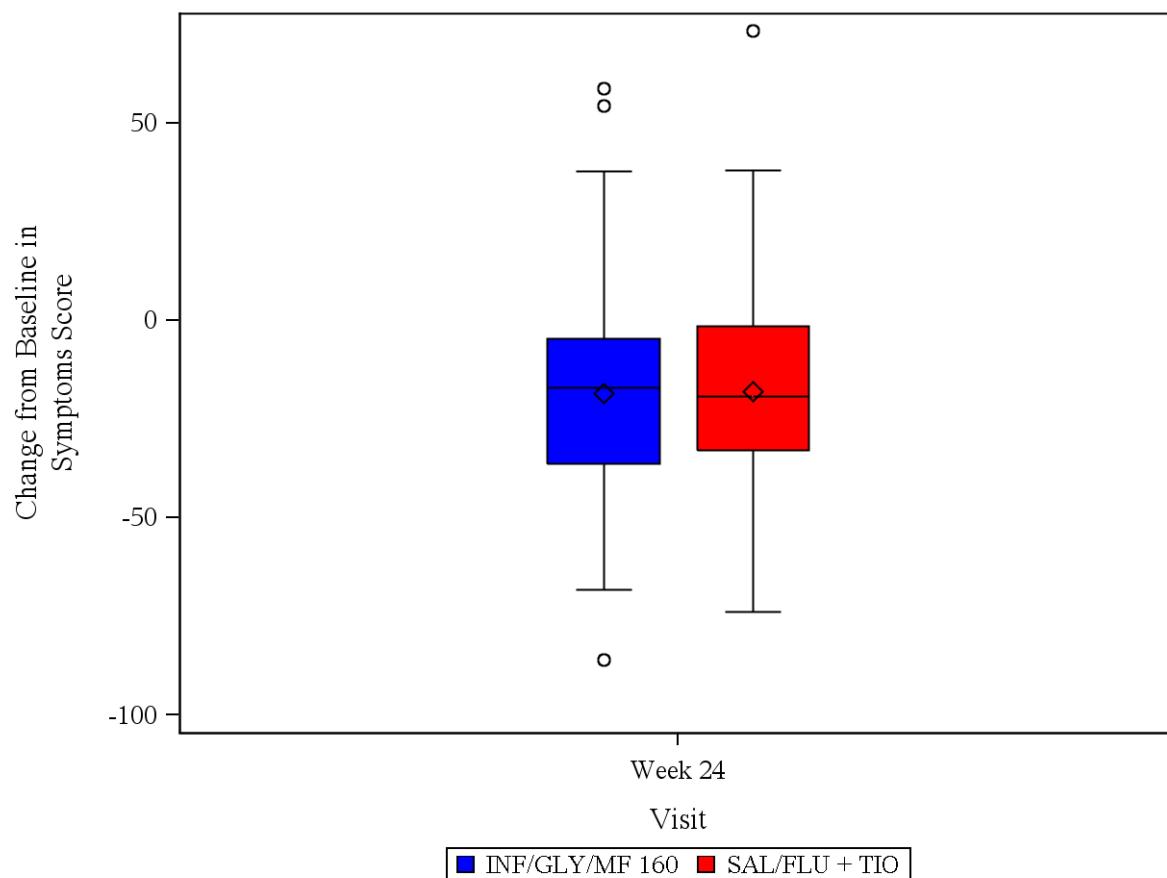


7.9 Boxplot: SGRQ (Symptoms Score) - Change from Baseline by Gender (FAS)

**Figure 7.9.1 SGRQ (Symptoms Score) - Change from Baseline by Gender (FAS),
Gender = Male**

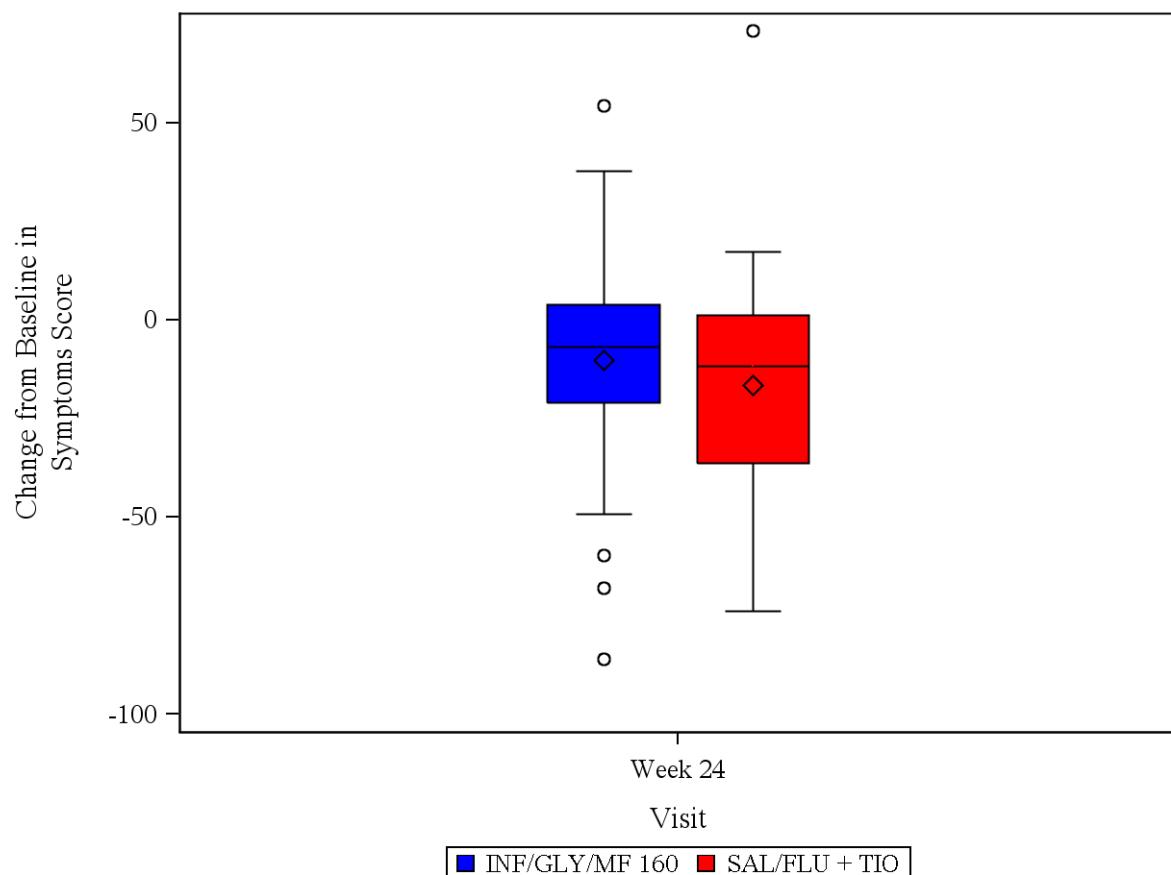


**Figure 7.9.2 SGRQ (Symptoms Score) - Change from Baseline by Gender (FAS),
Gender = Female**

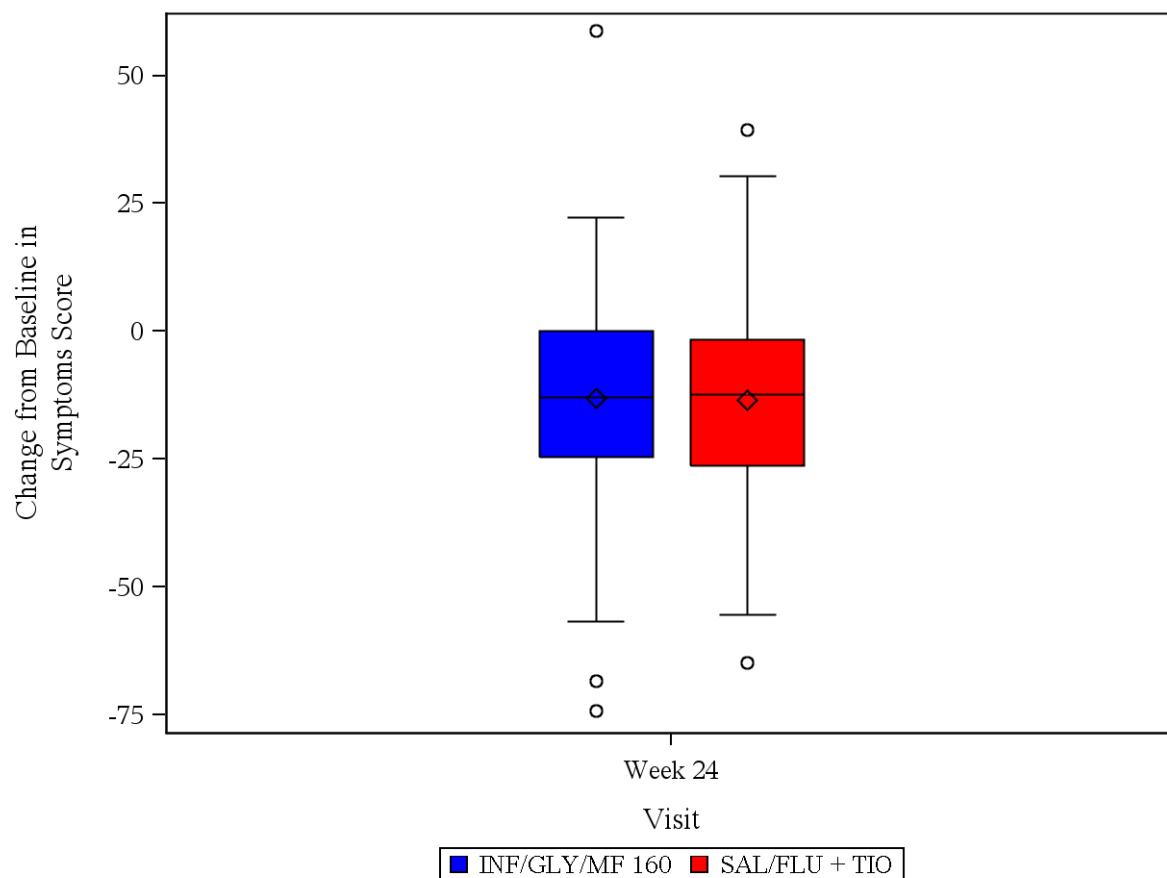


7.10 Boxplot: SGRQ (Symptoms Score) - Change from Baseline by Region (FAS)

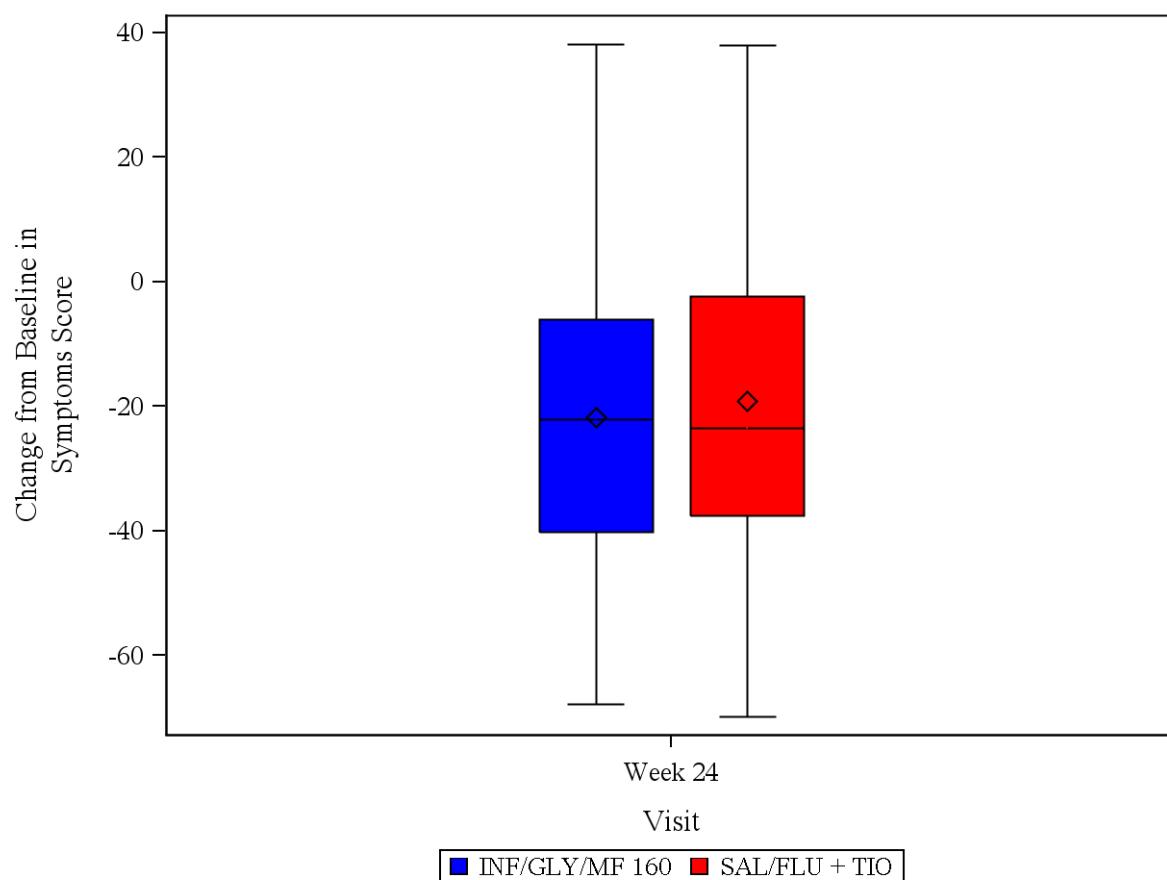
Figure 7.10.1 SGRQ (Symptoms Score) - Change from Baseline by Region (FAS), Region = Asia



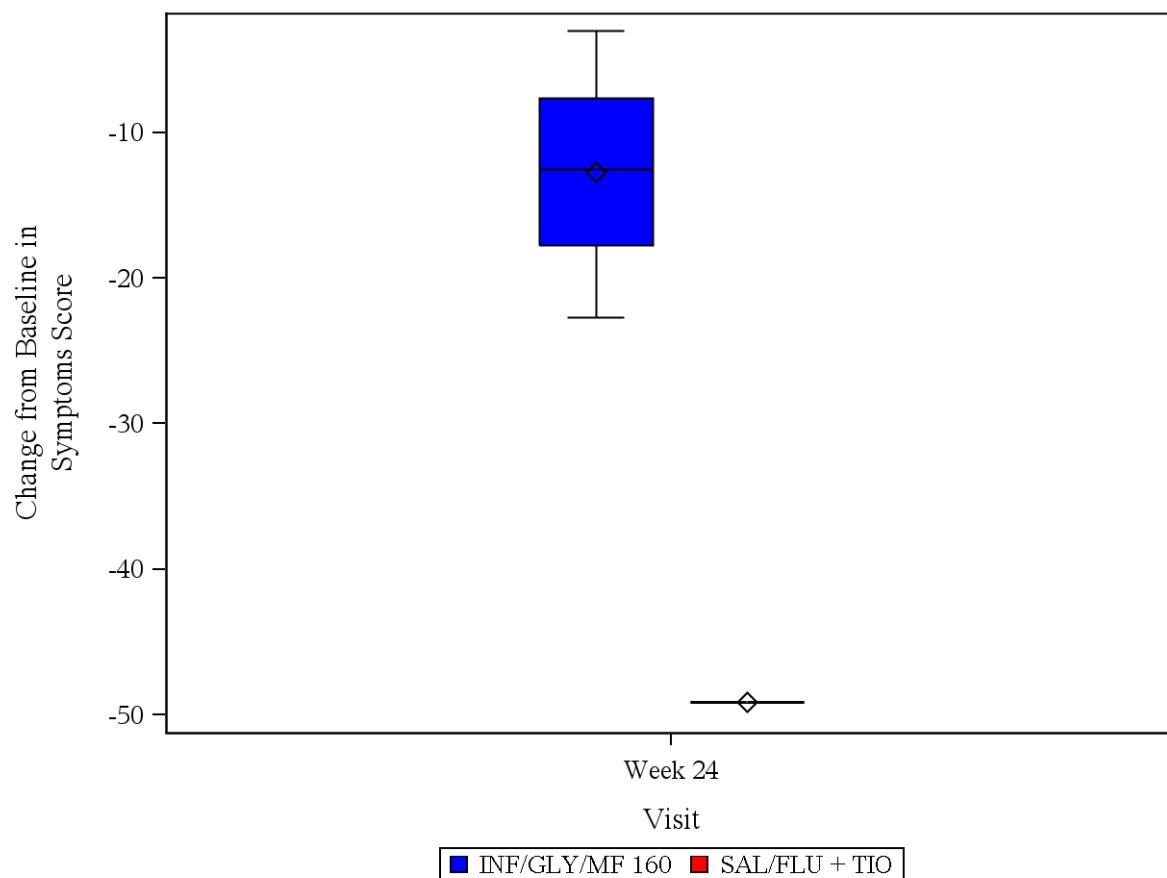
**Figure 7.10.2 SGRQ (Symptoms Score) - Change from Baseline by Region (FAS),
Region = Europe**



**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

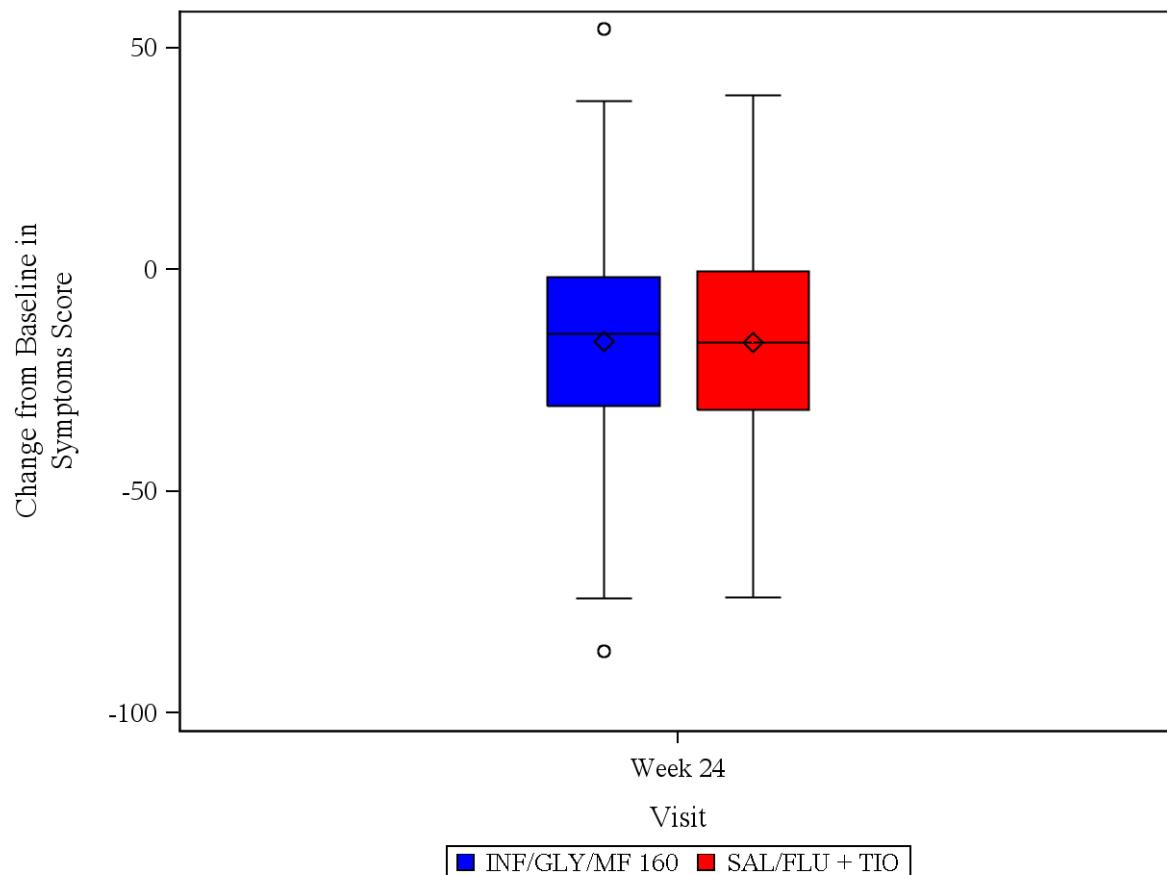
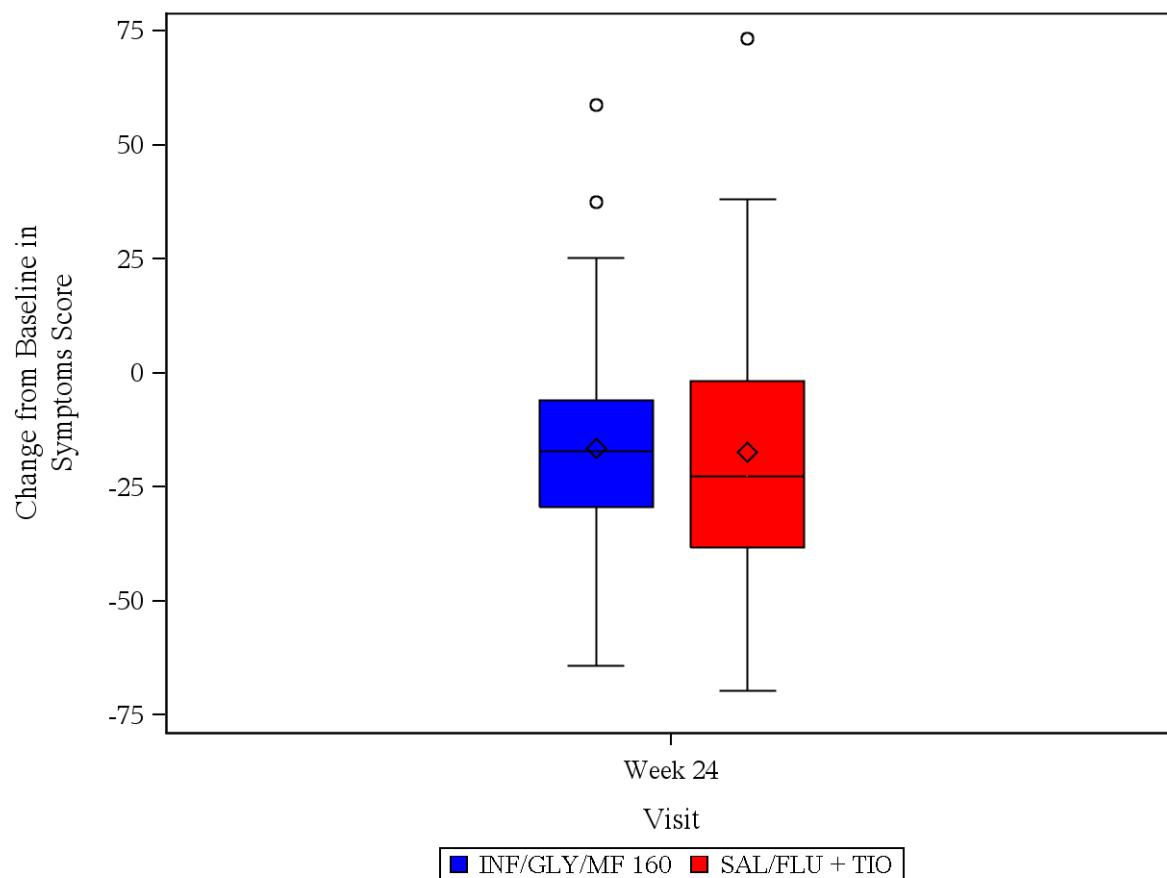
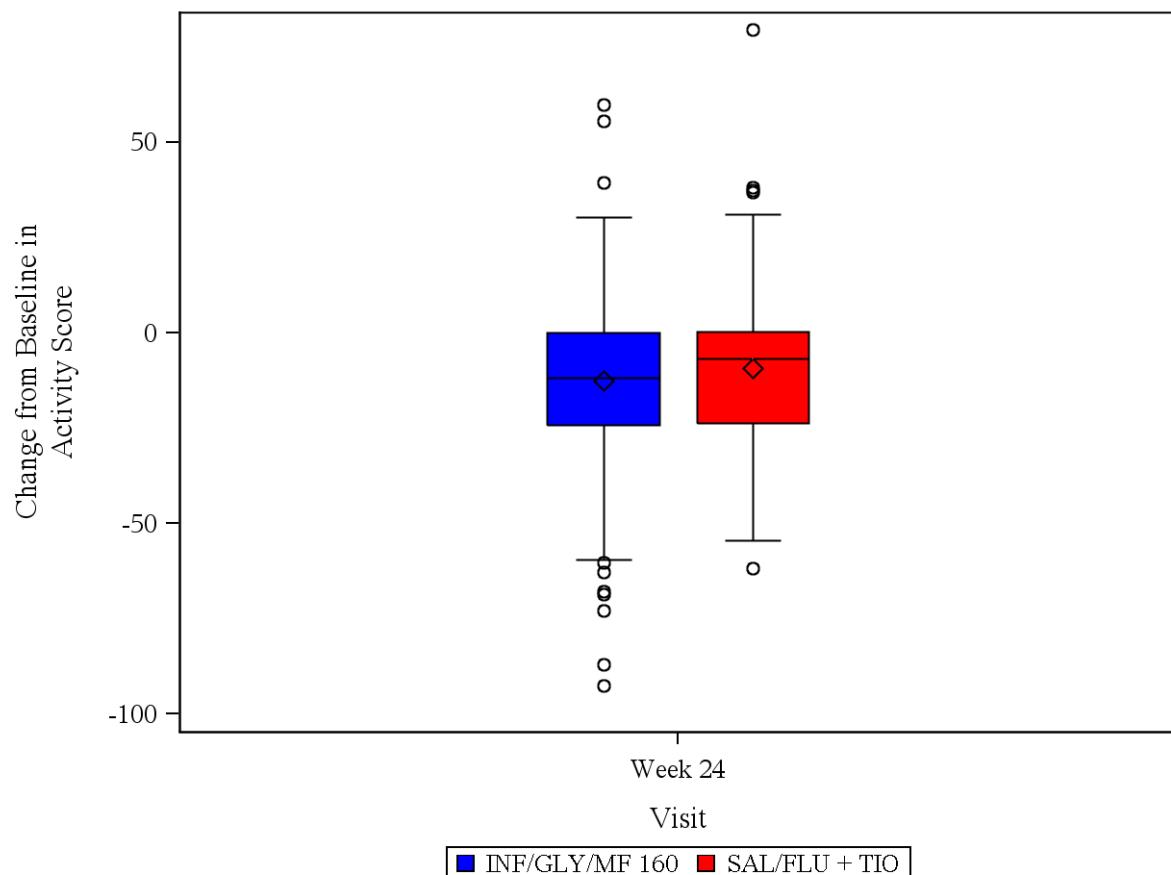


Figure 7.11.2 SGRQ (Symptoms Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



7.13 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

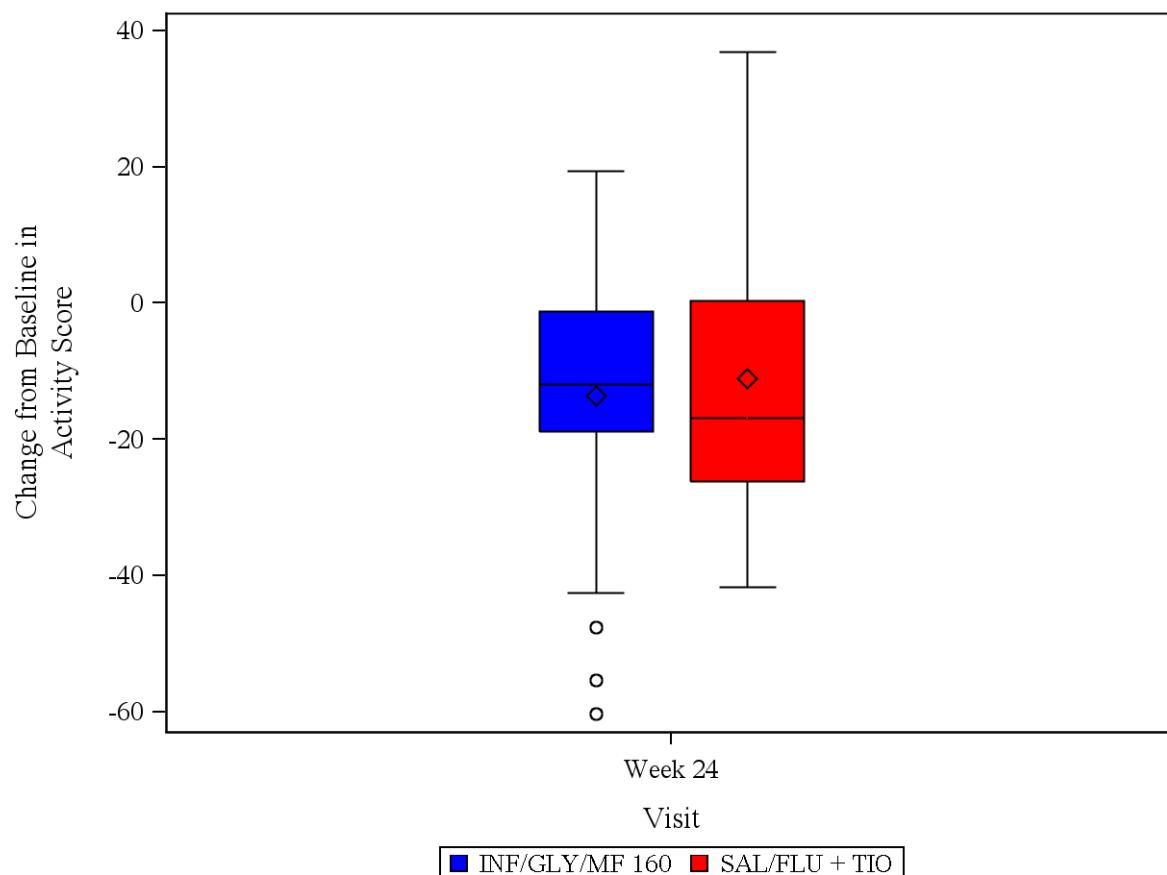


Figure 7.14.2 SGRQ (Activity Score) - Change from Baseline by Age (FAS), Age = 40-64 years

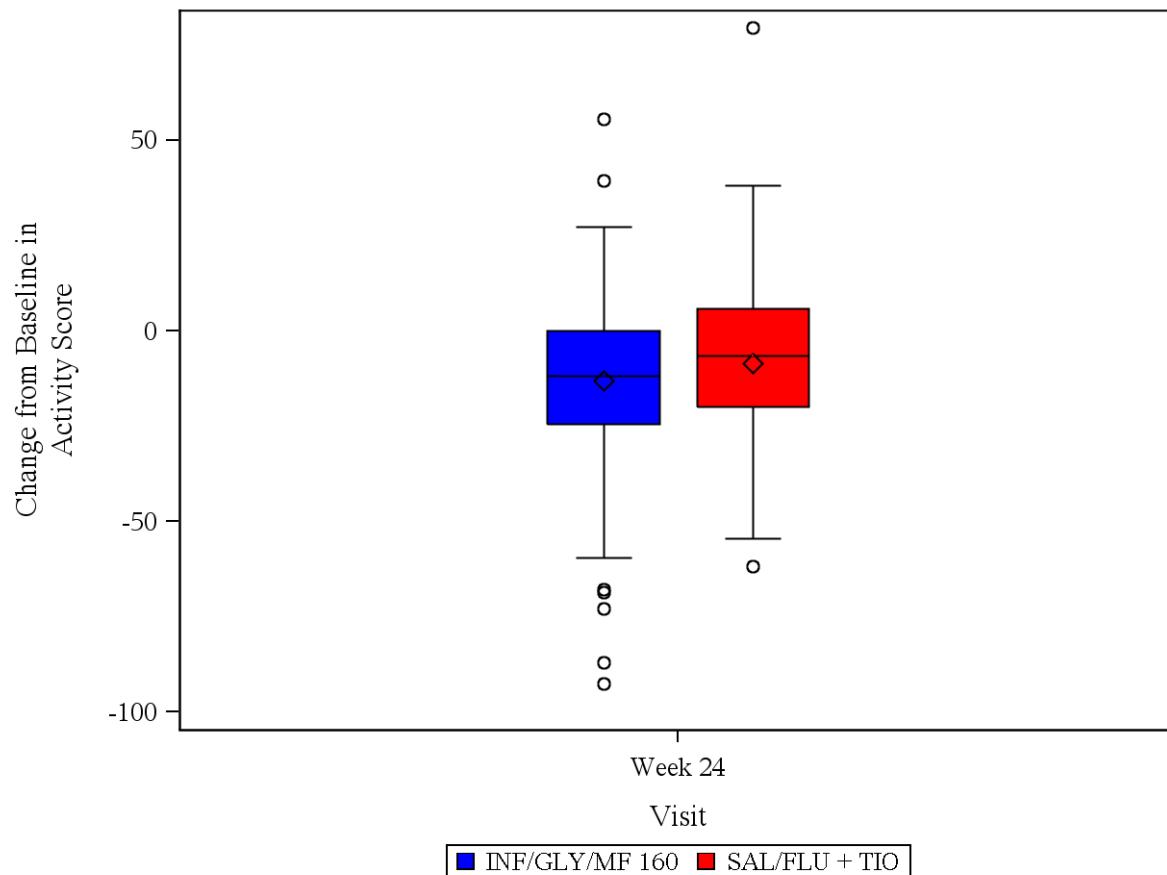
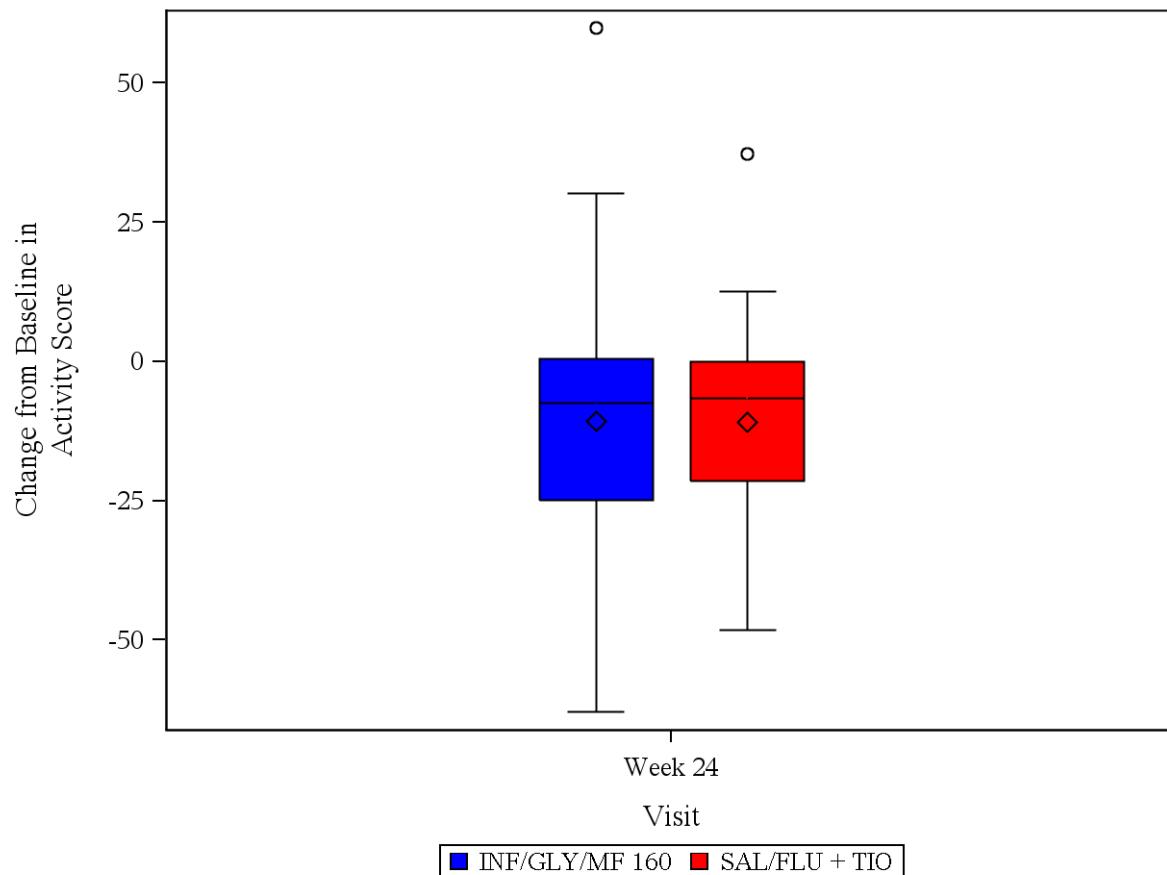


Figure 7.14.3 SGRQ (Activity Score) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

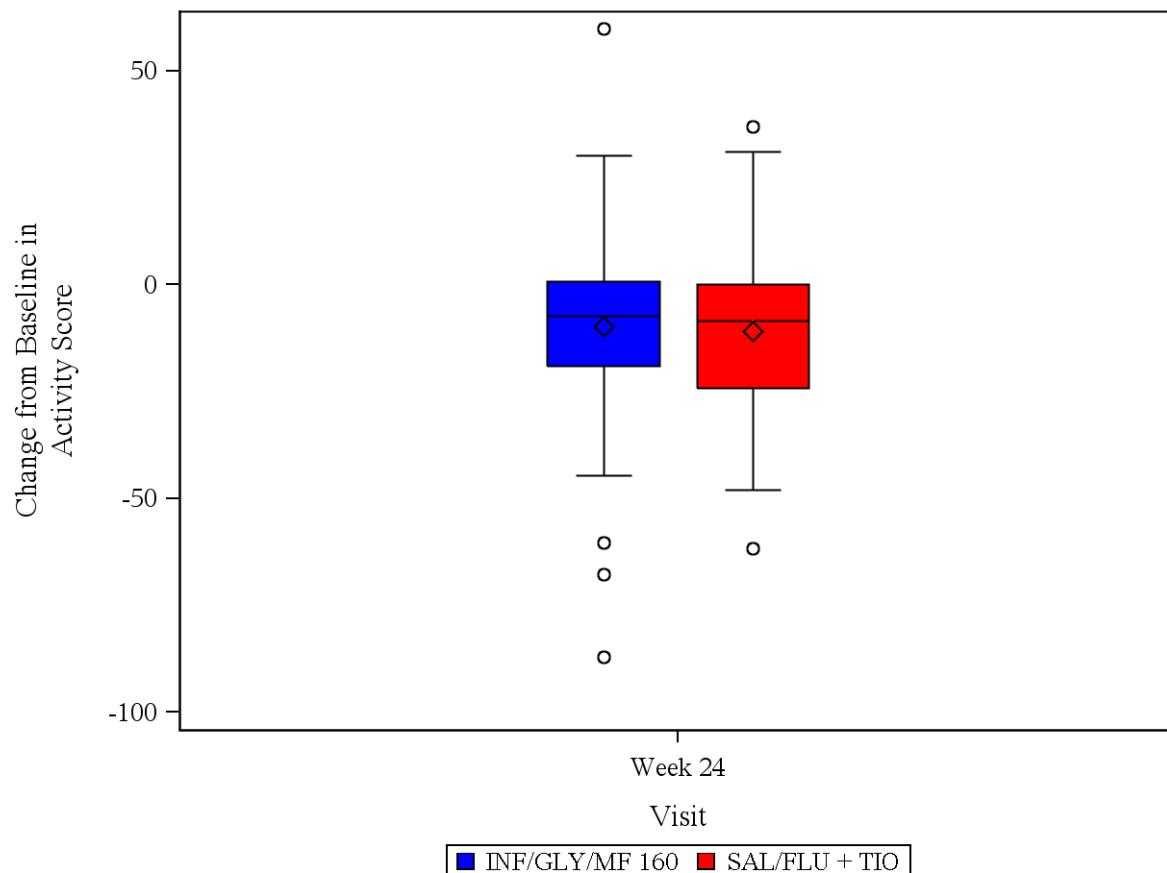
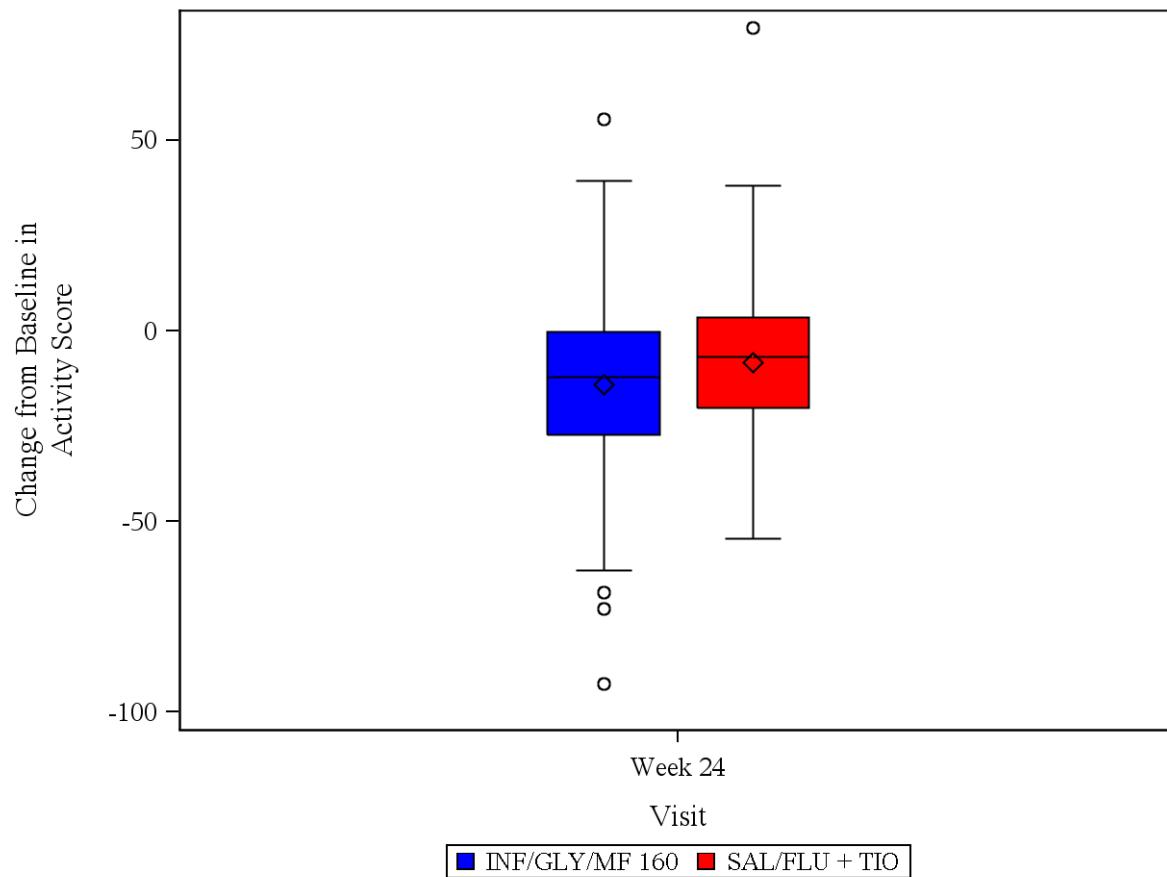


Figure 7.15.2 SGRQ (Activity Score) - Change from Baseline by Gender (FAS), Gender = Female



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

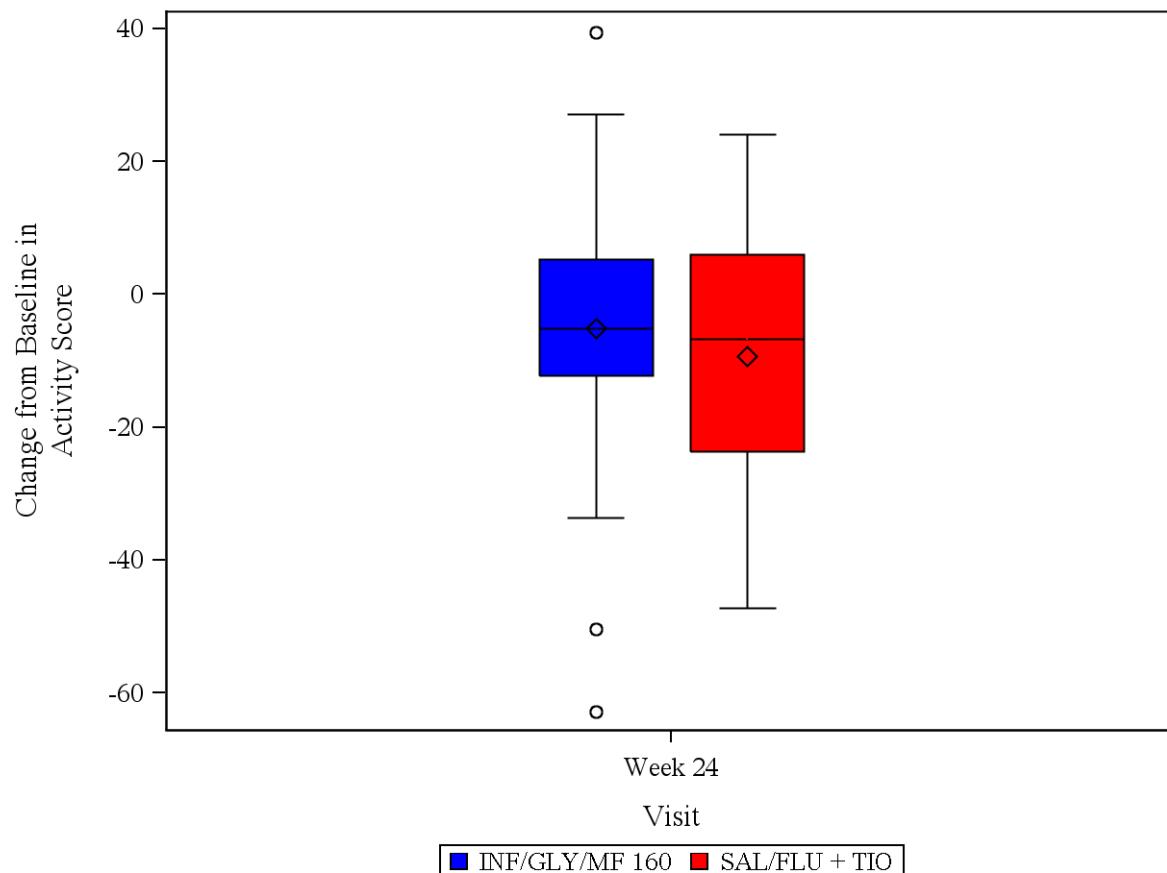


Figure 7.16.2 SGRQ (Activity Score) - Change from Baseline by Region (FAS), Region = Europe

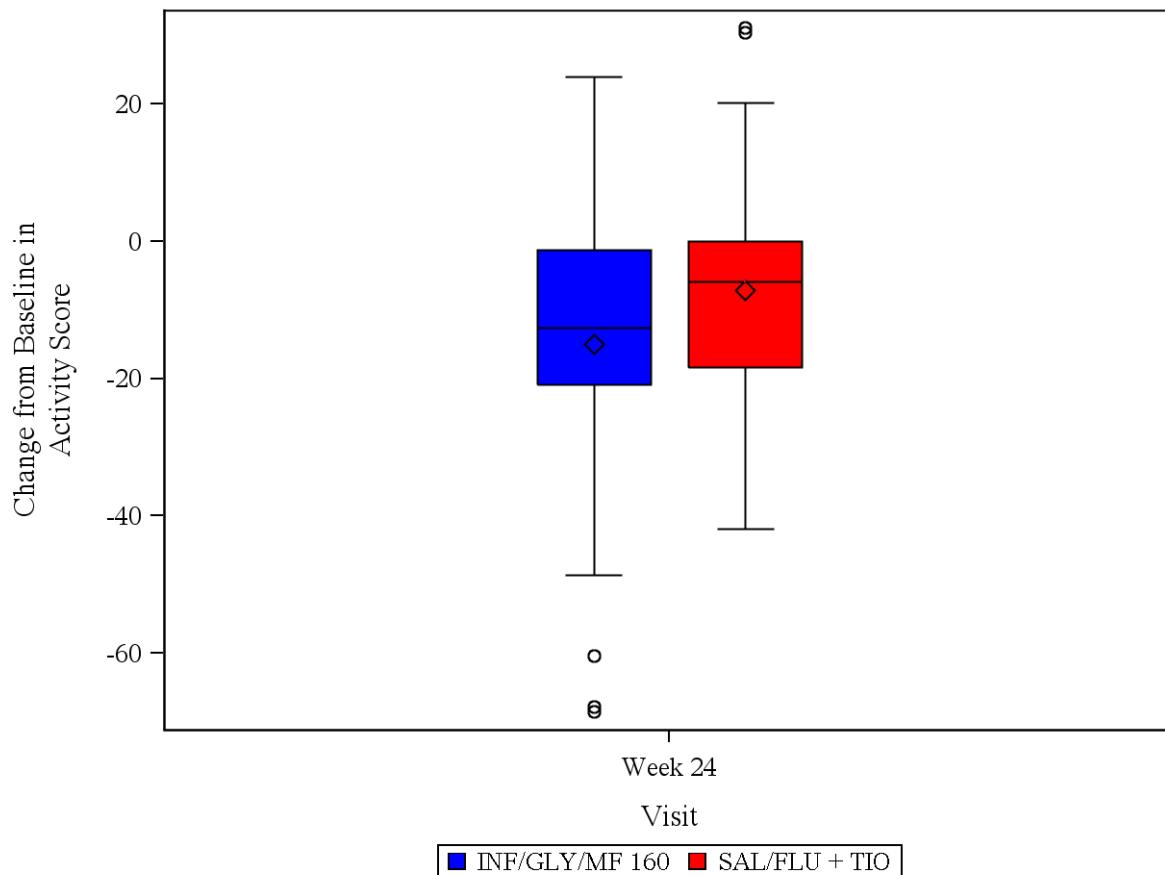


Figure 7.16.3 SGRQ (Activity Score) - Change from Baseline by Region (FAS), Region = Latin America

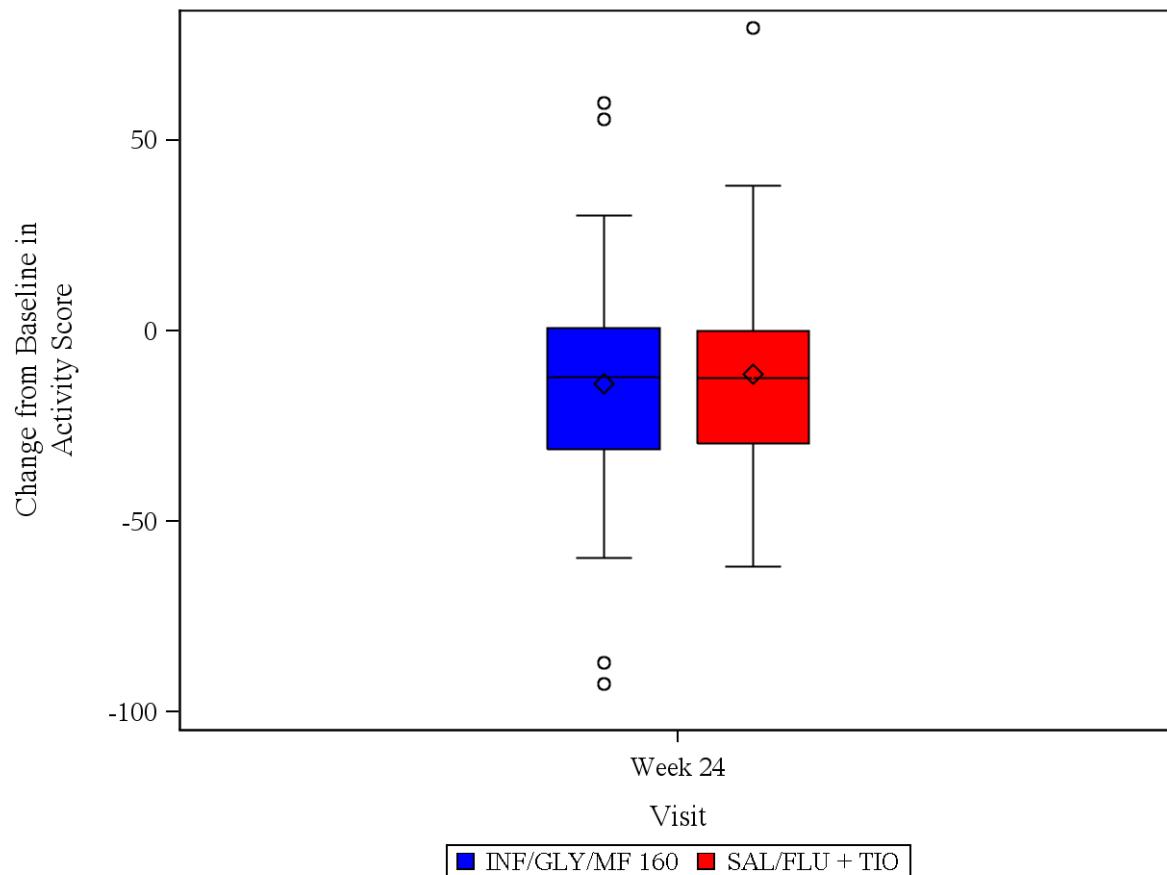
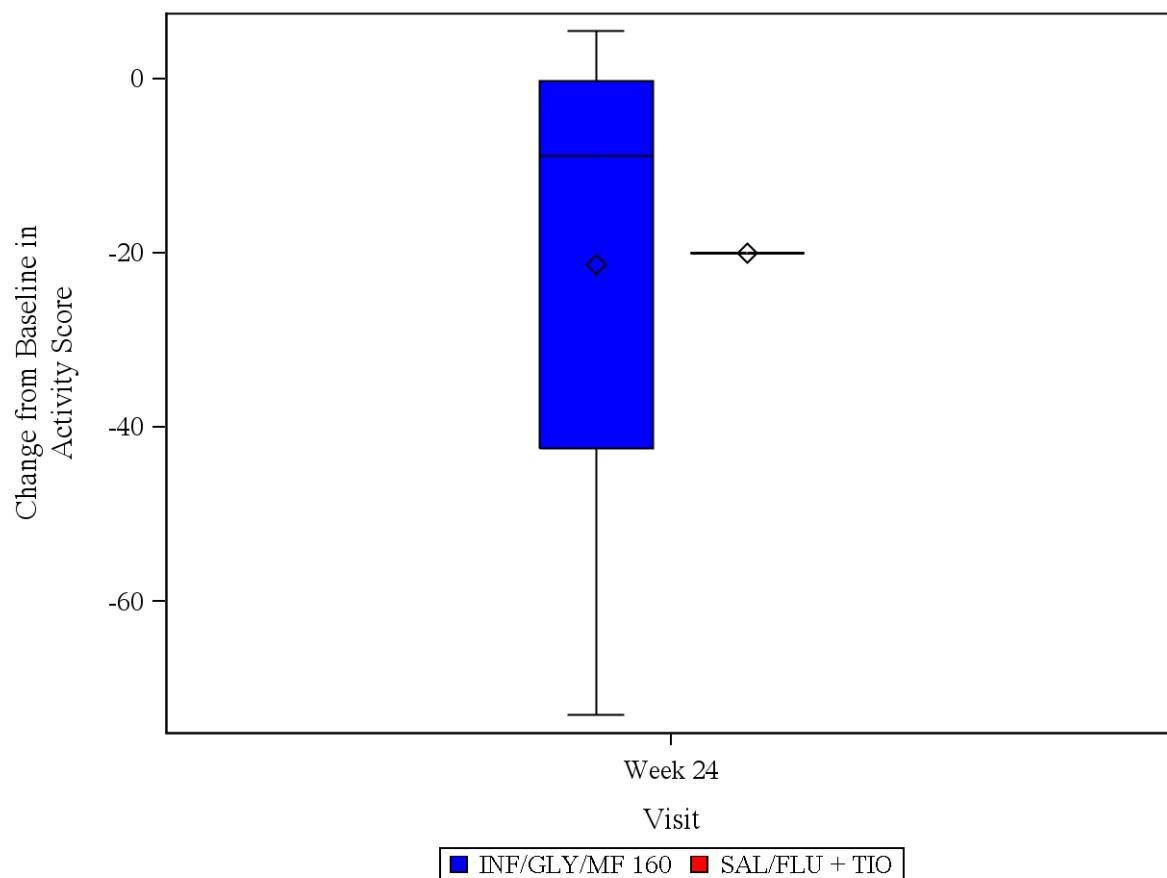


Figure 7.16.4 SGRQ (Activity Score) - Change from Baseline by Region (FAS), Region = Others



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

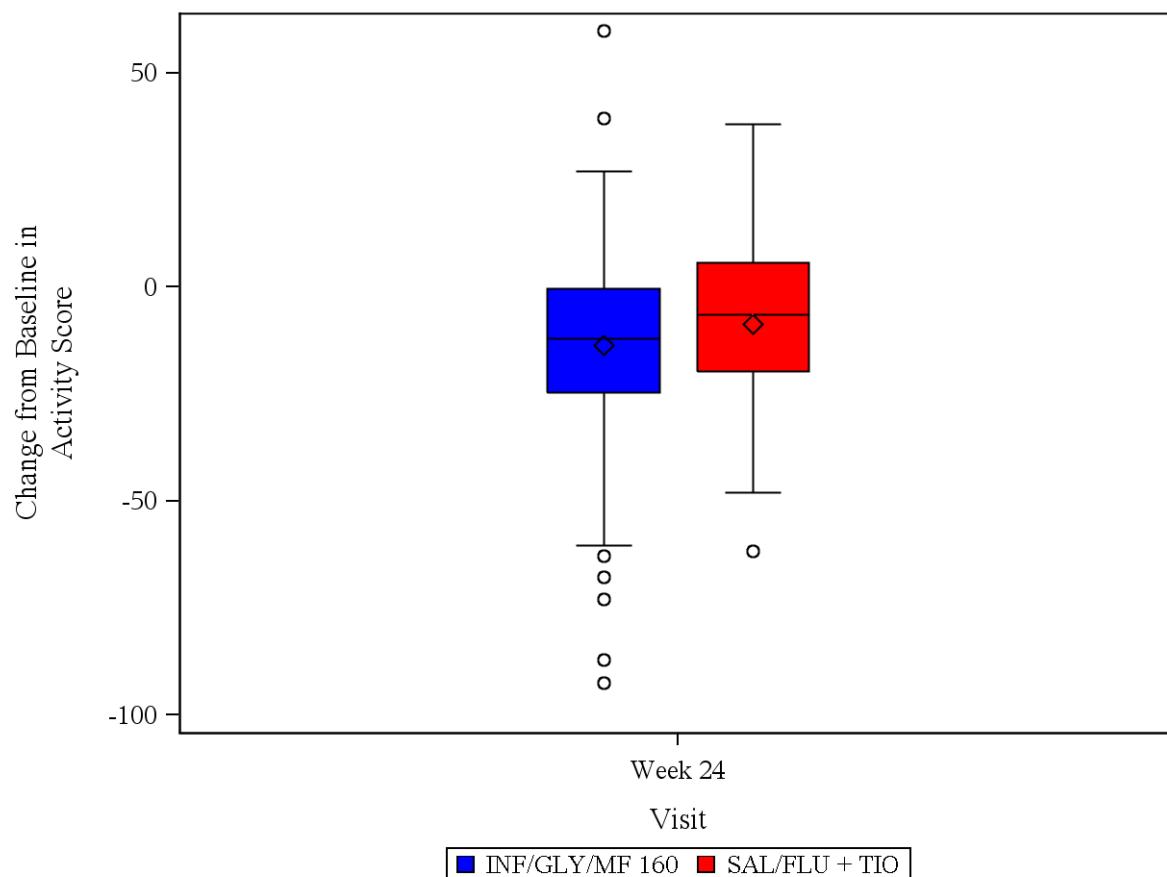
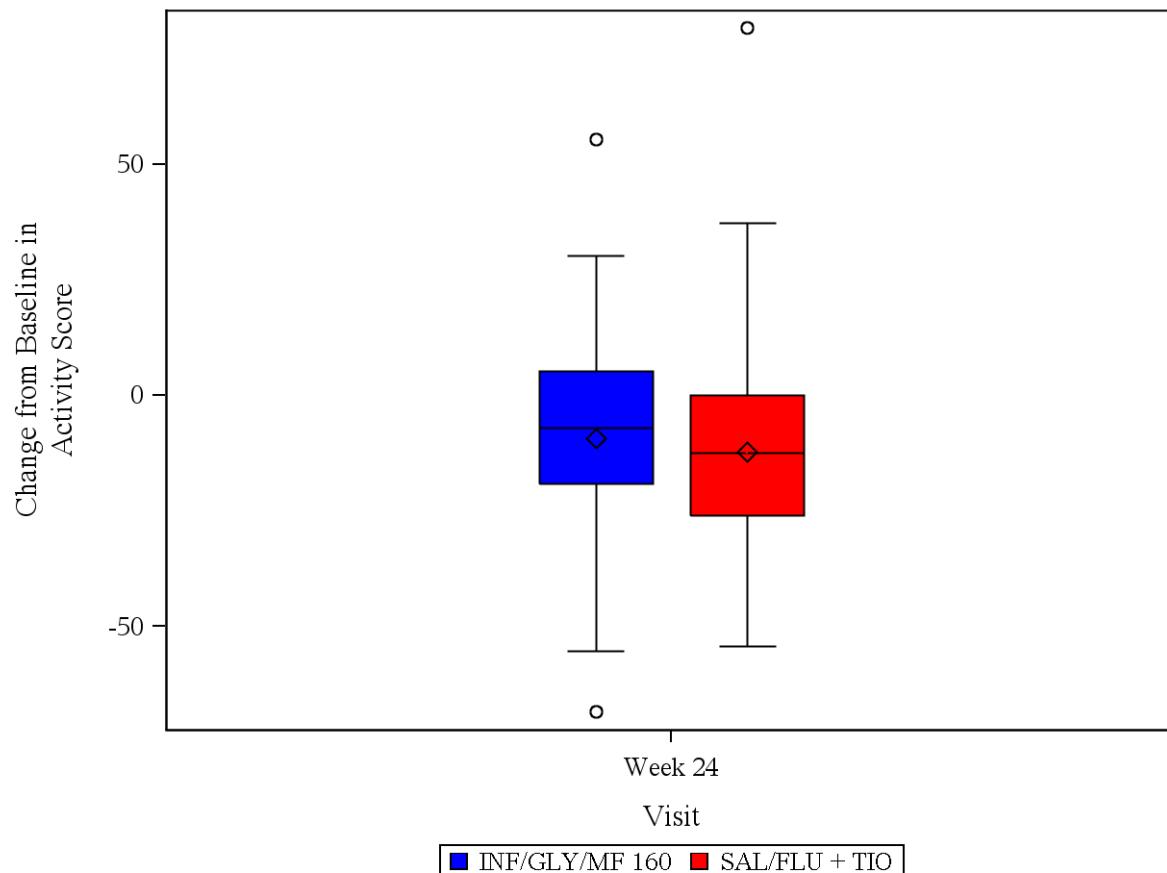
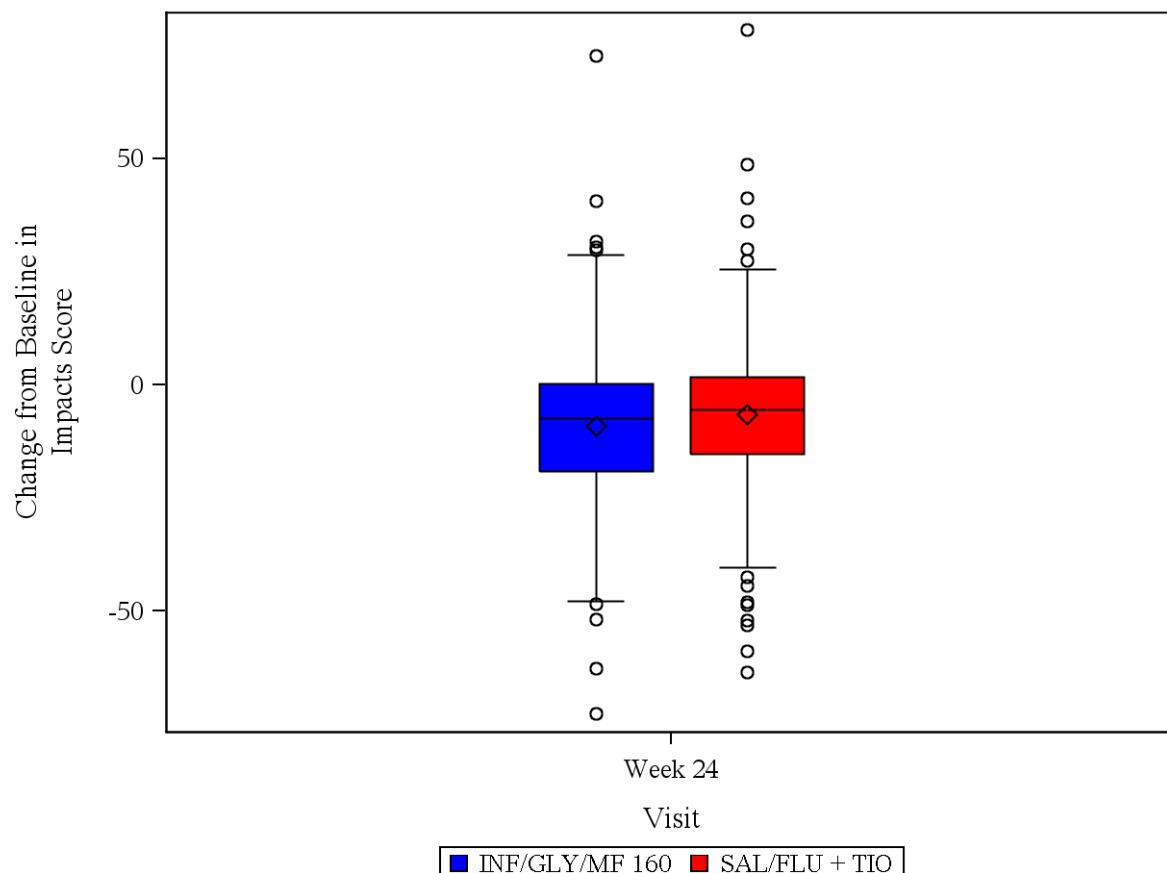


Figure 7.17.2 SGRQ (Activity Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



7.19 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

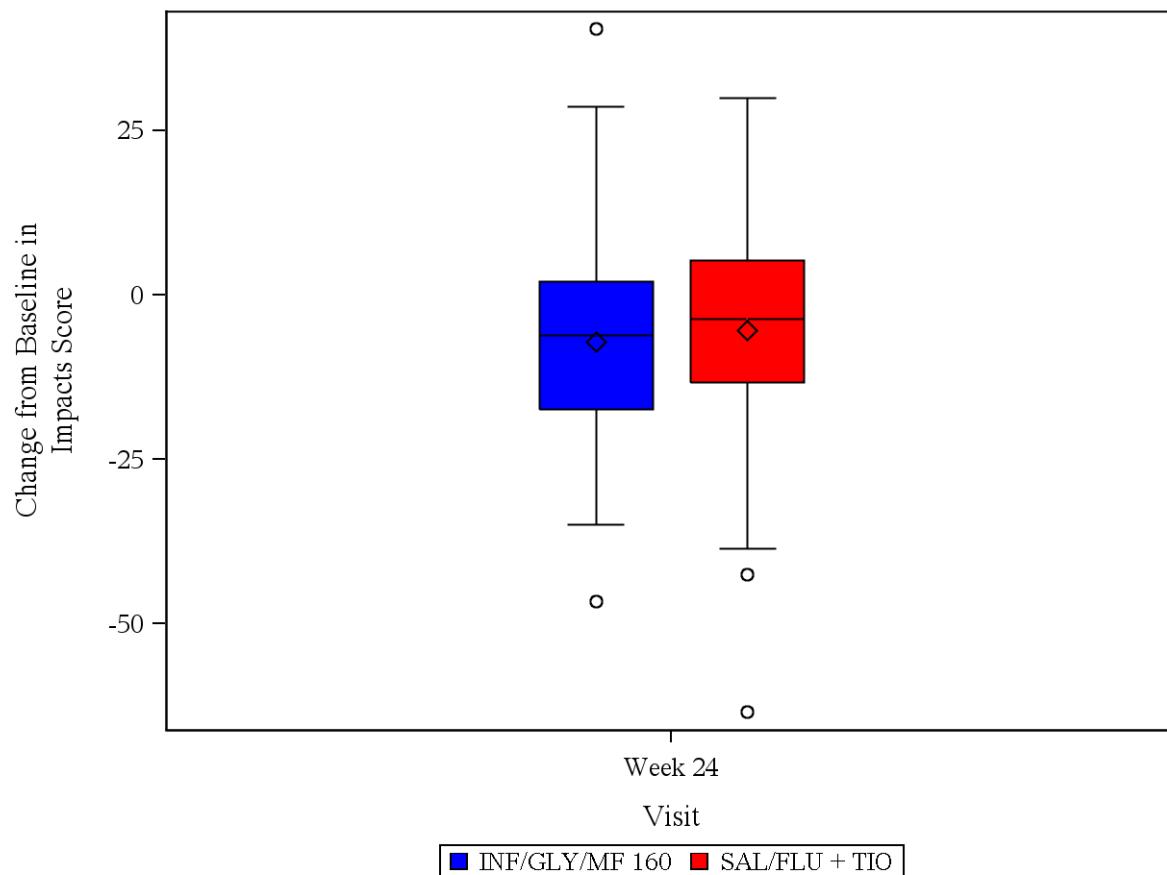


Figure 7.20.2 SGRQ (Impacts Score) - Change from Baseline by Age (FAS), Age = 40-64 years

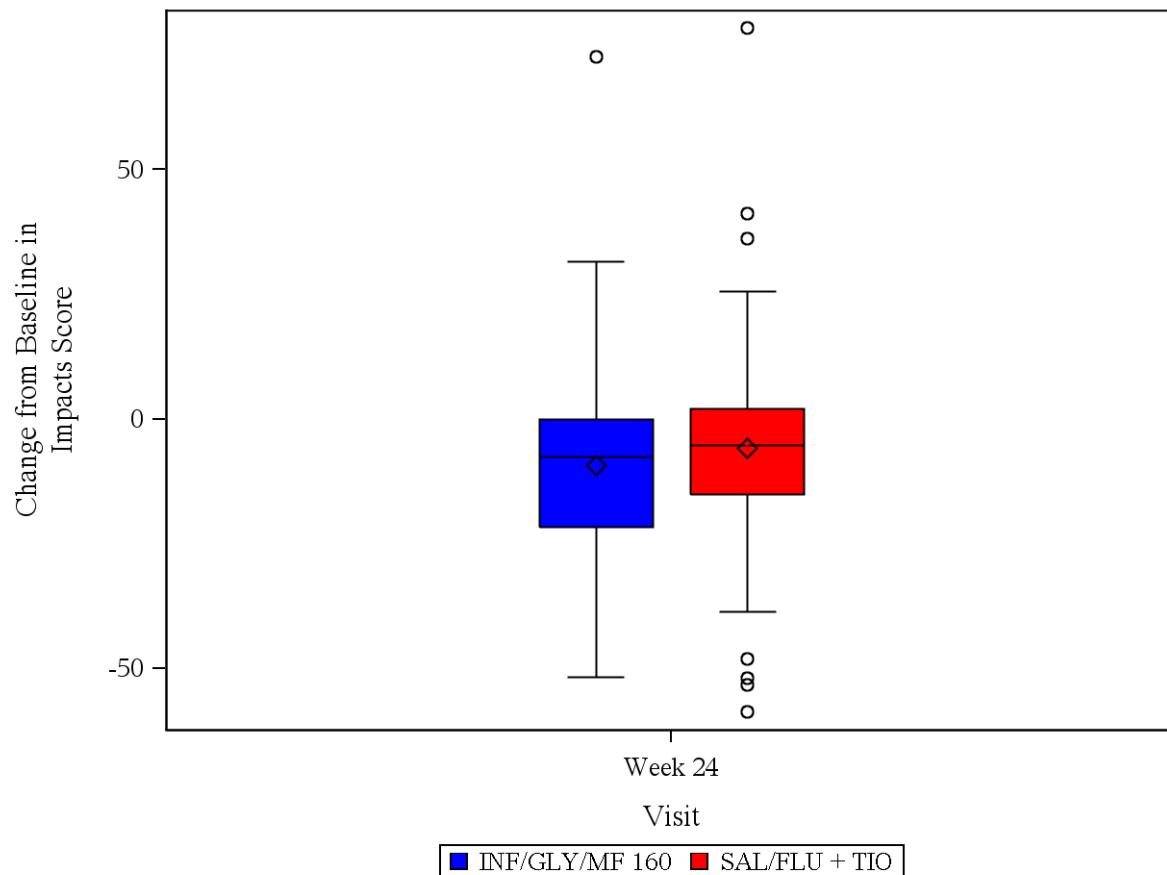
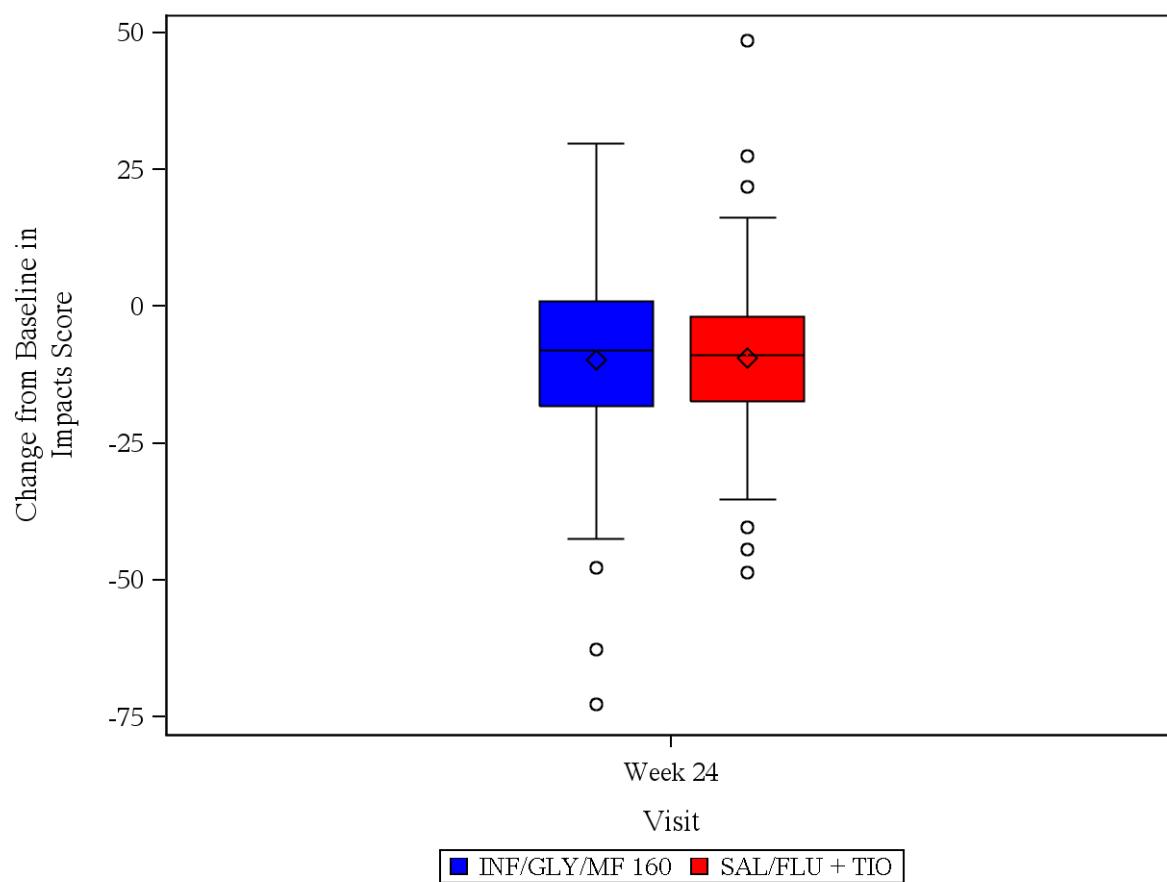


Figure 7.20.3 SGRQ (Impacts Score) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

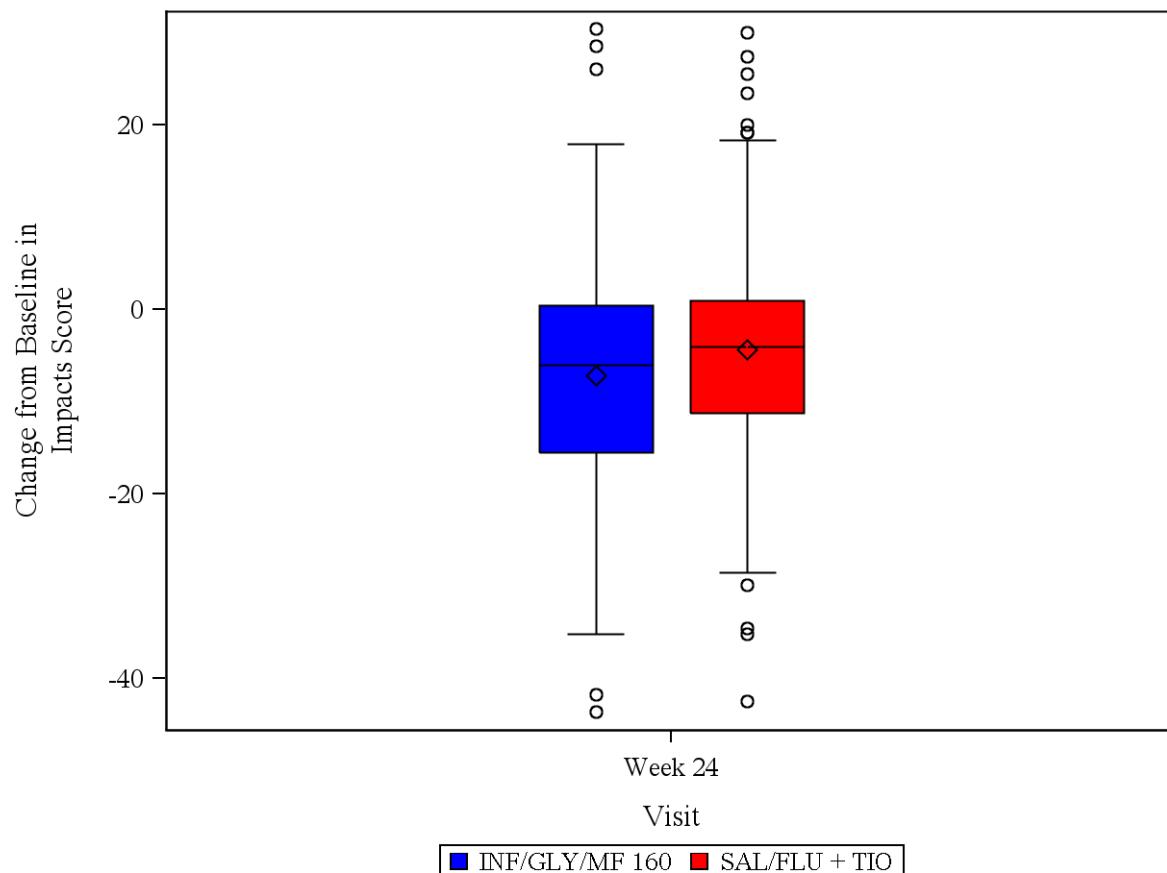
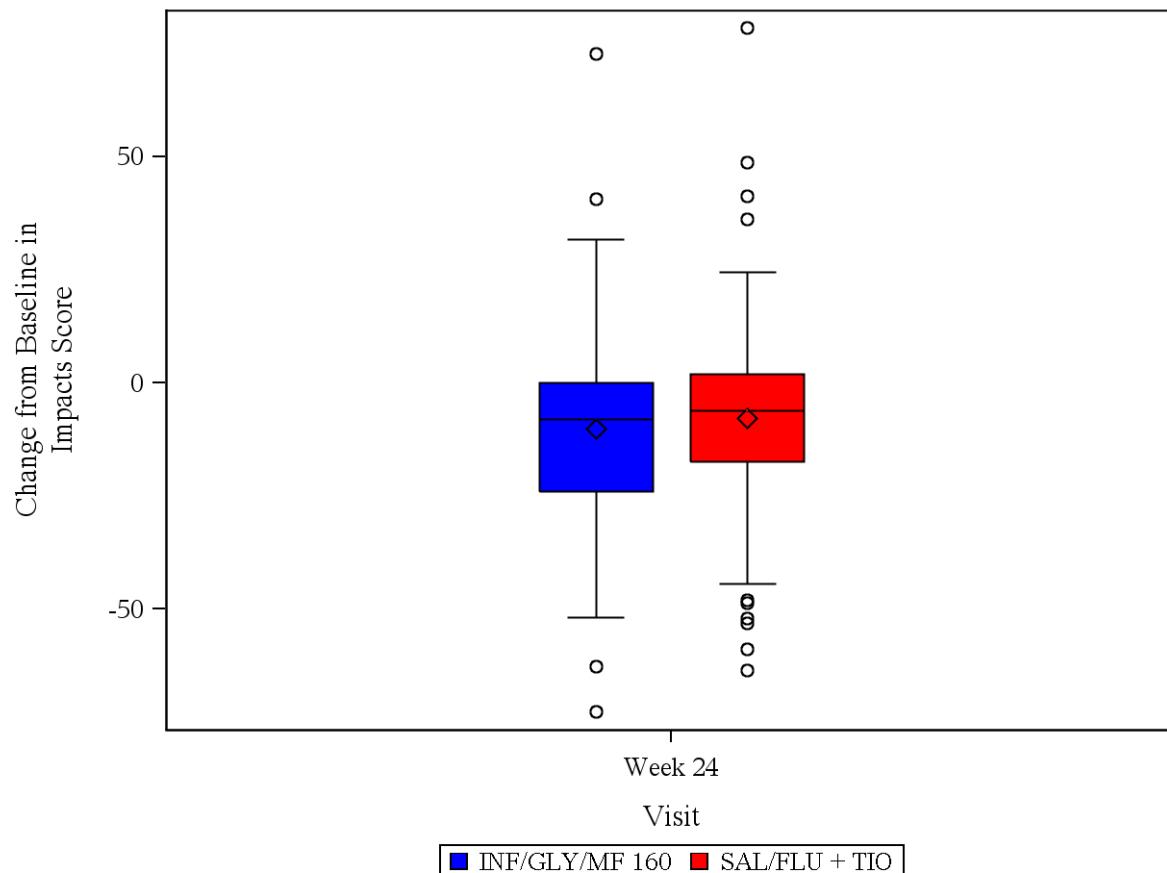


Figure 7.21.2 SGRQ (Impacts Score) - Change from Baseline by Gender (FAS), Gender = Female



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

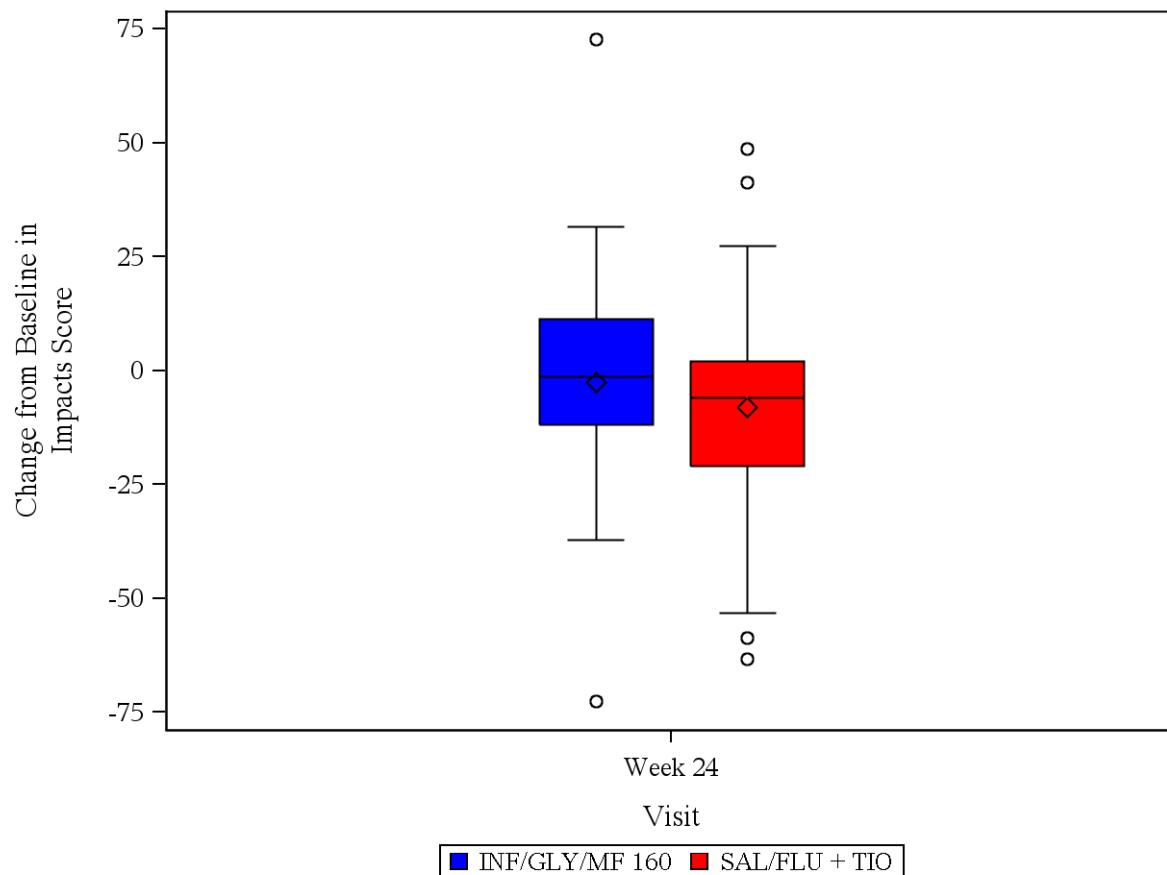


Figure 7.22.2 SGRQ (Impacts Score) - Change from Baseline by Region (FAS), Region = Europe

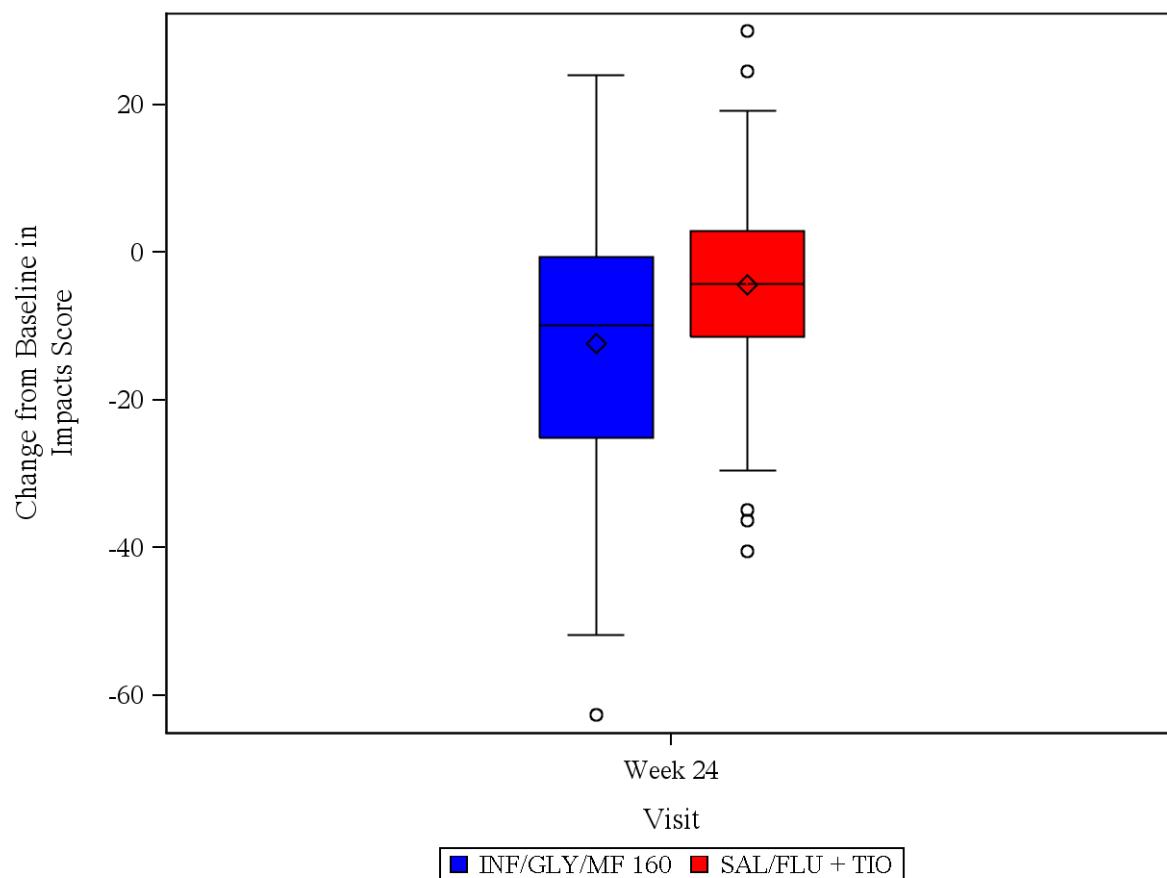


Figure 7.22.3 SGRQ (Impacts Score) - Change from Baseline by Region (FAS), Region = Latin America

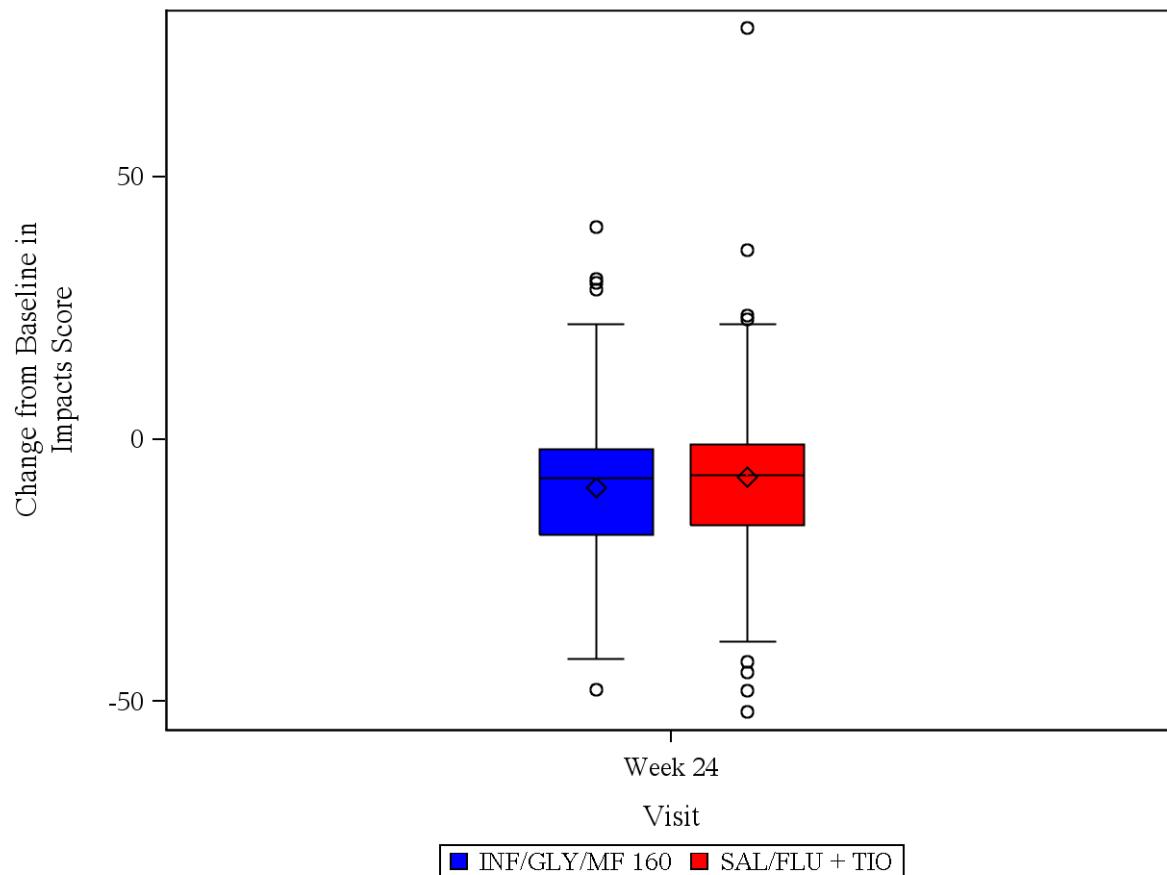
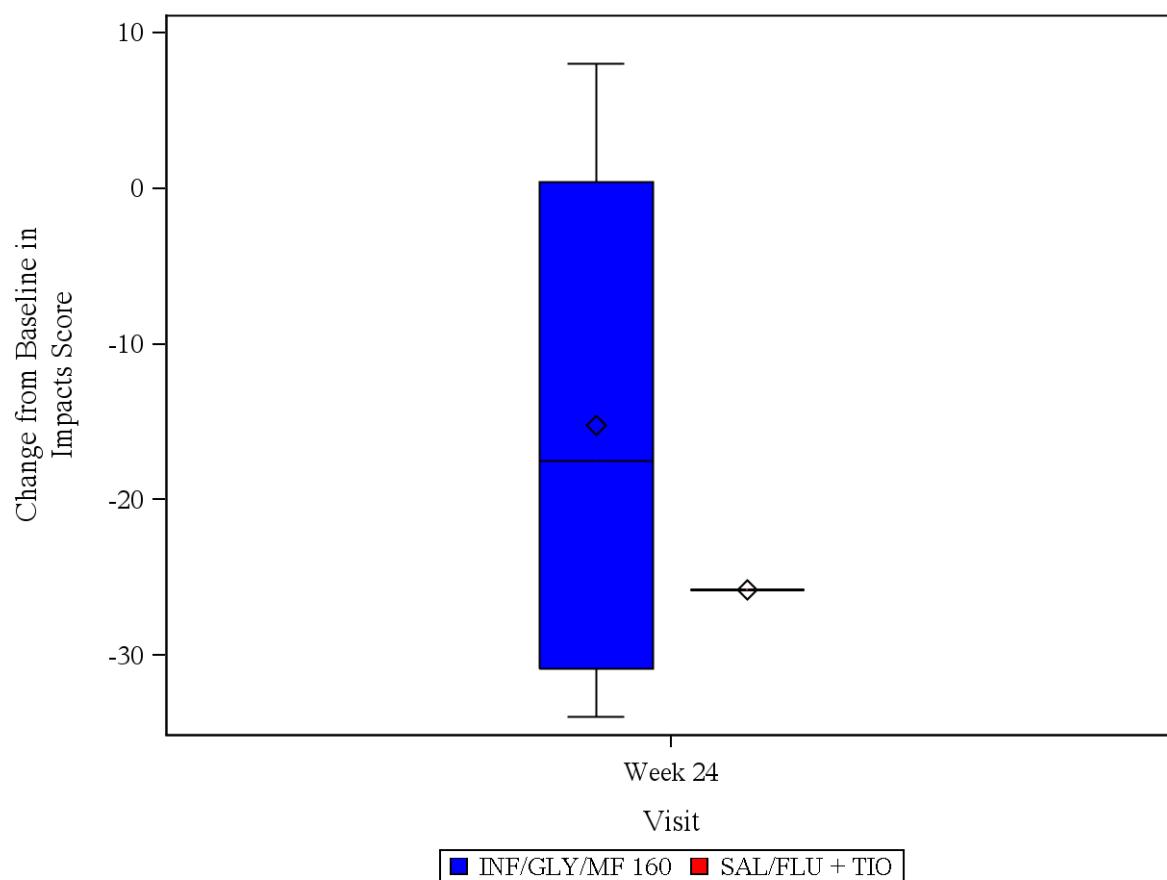


Figure 7.22.4 SGRQ (Impacts Score) - Change from Baseline by Region (FAS), Region = Others



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

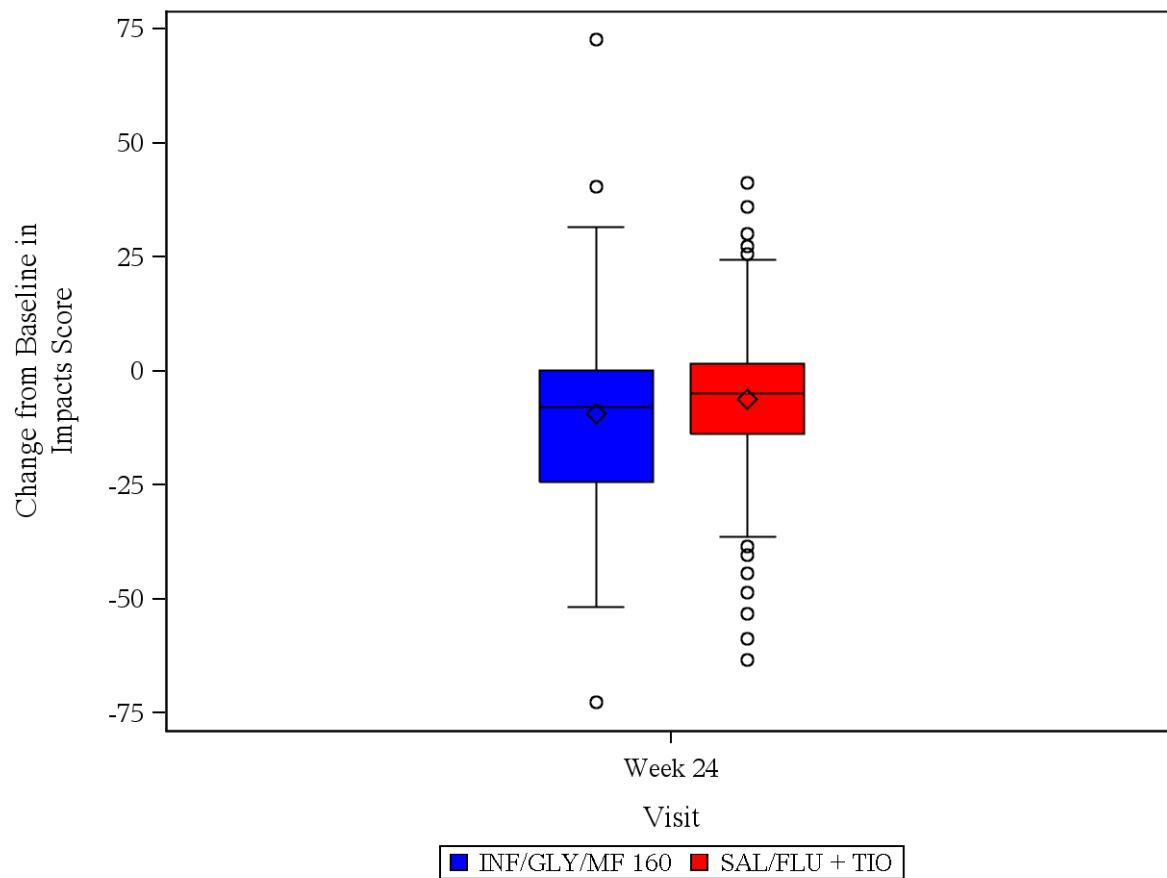
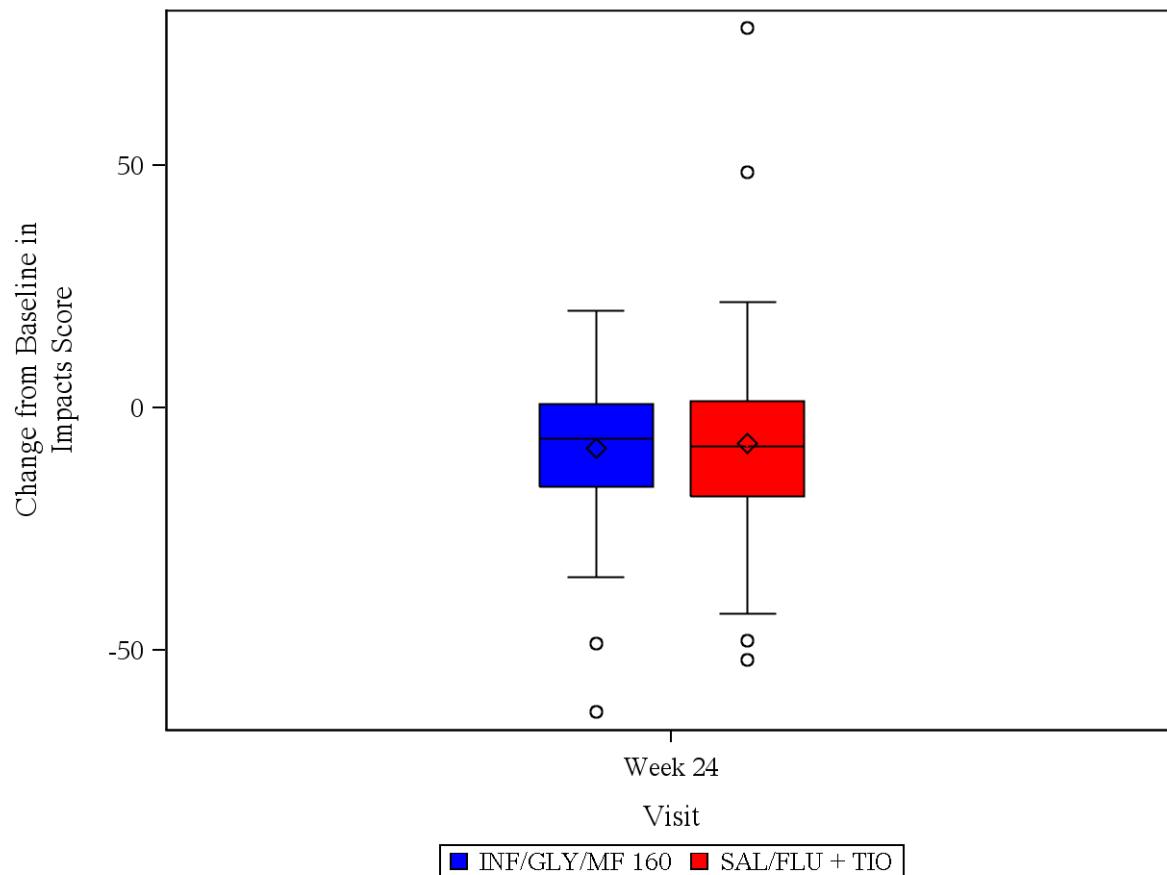


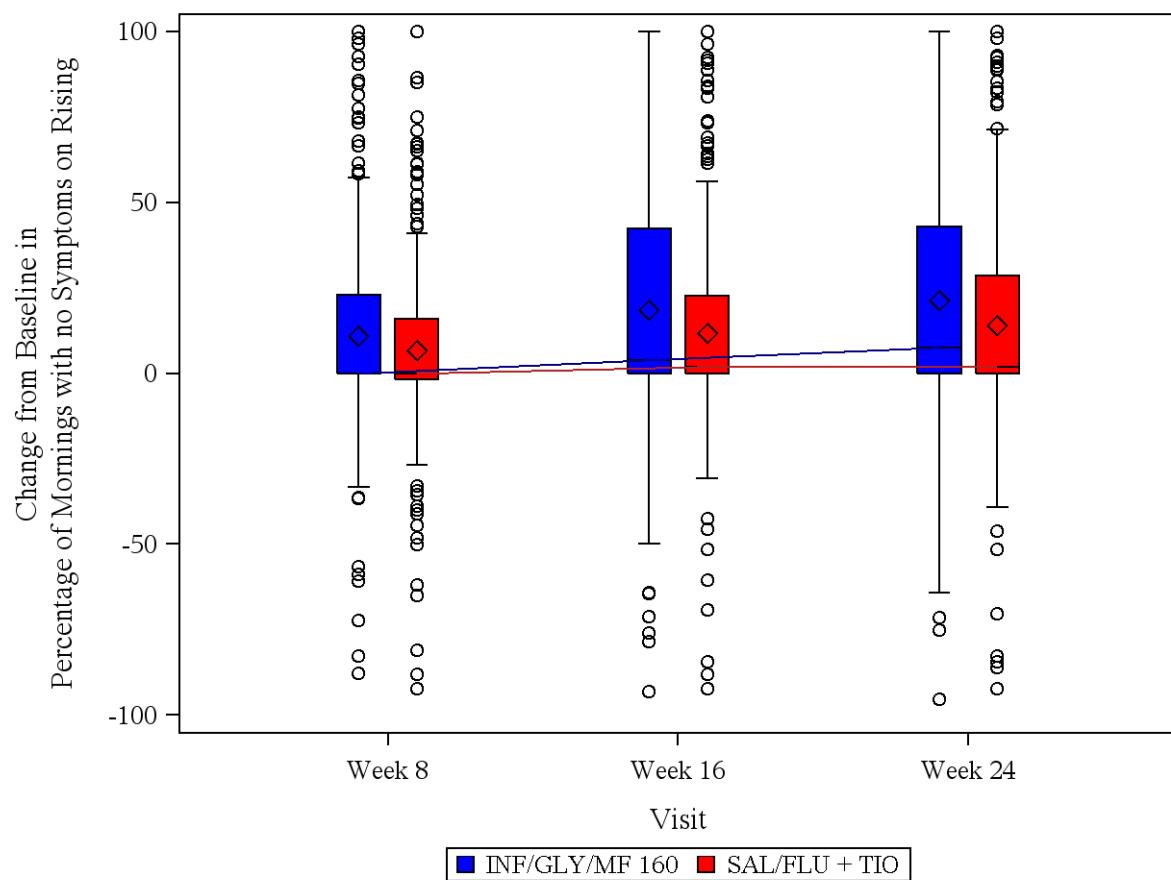
Figure 7.23.2 SGRQ (Impacts Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



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

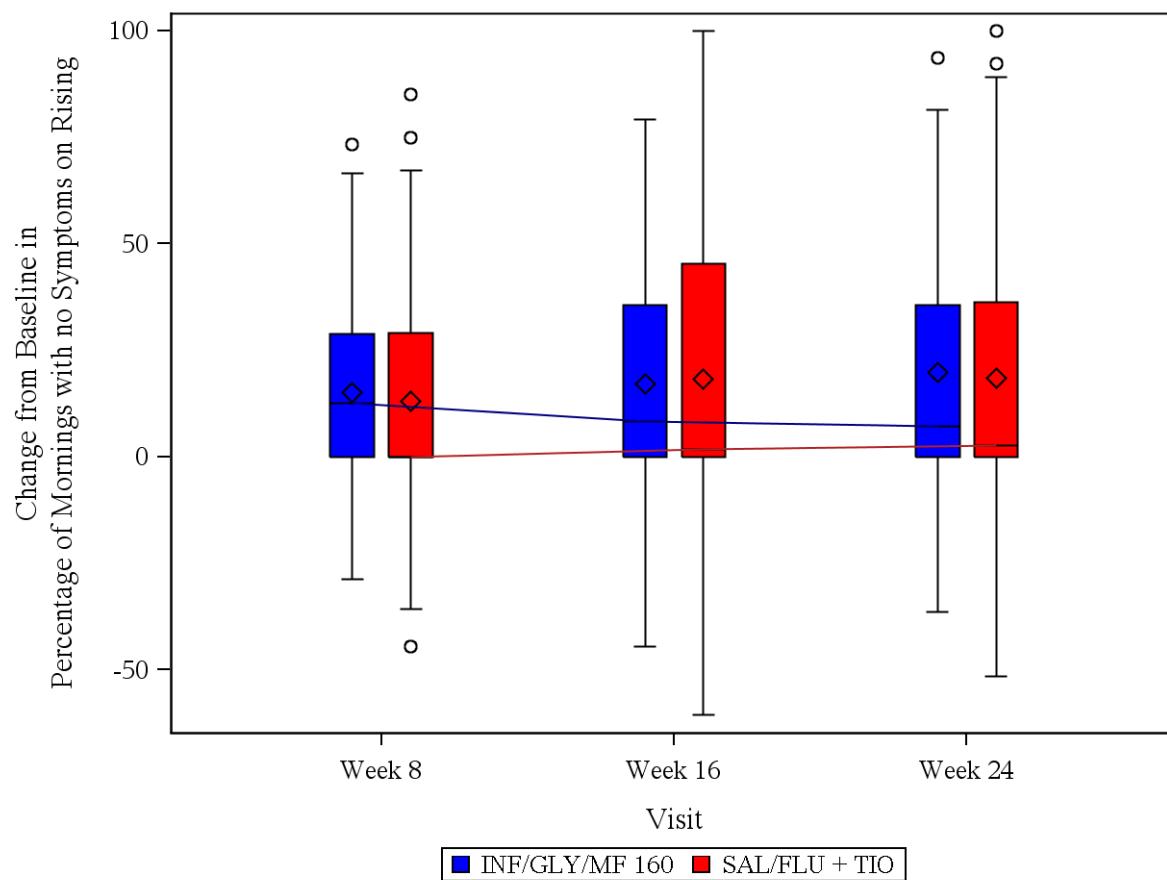


Figure 9.2.2 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Age (FAS), Age = 40-64 years

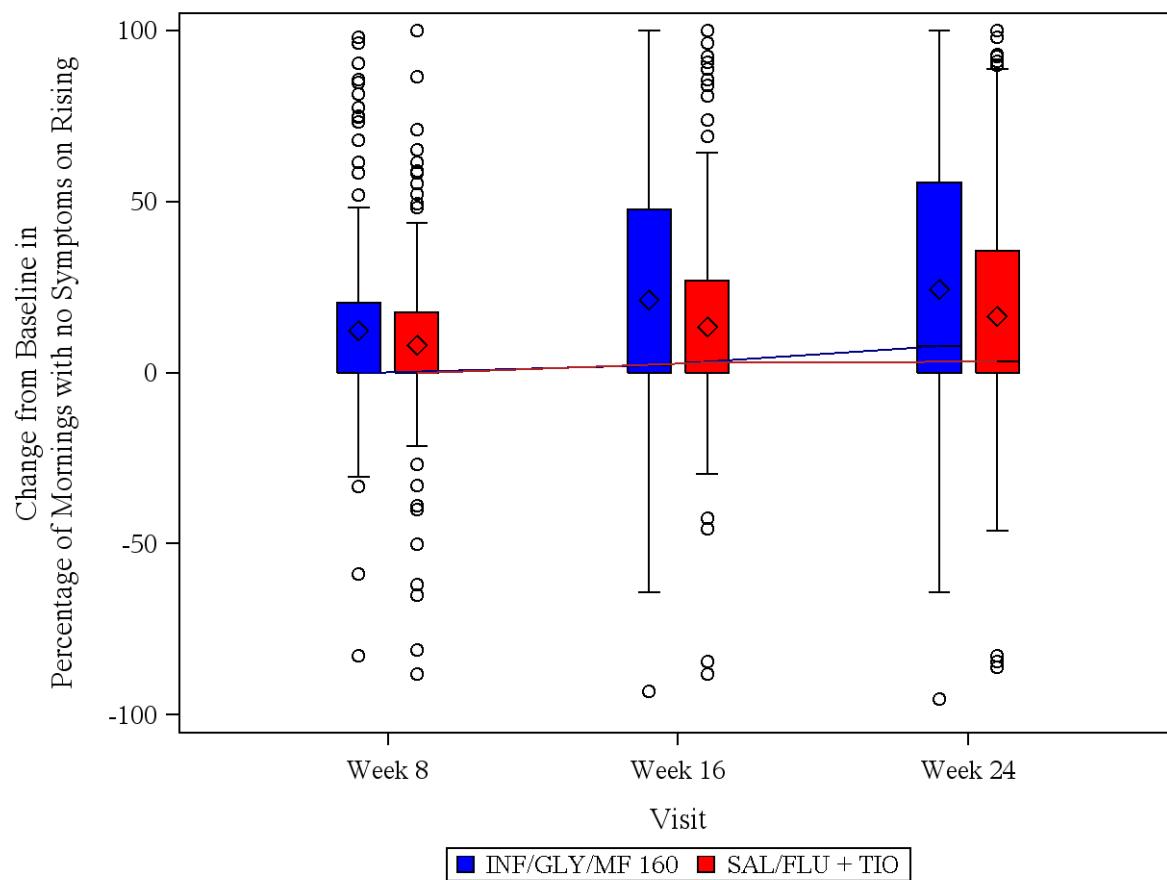
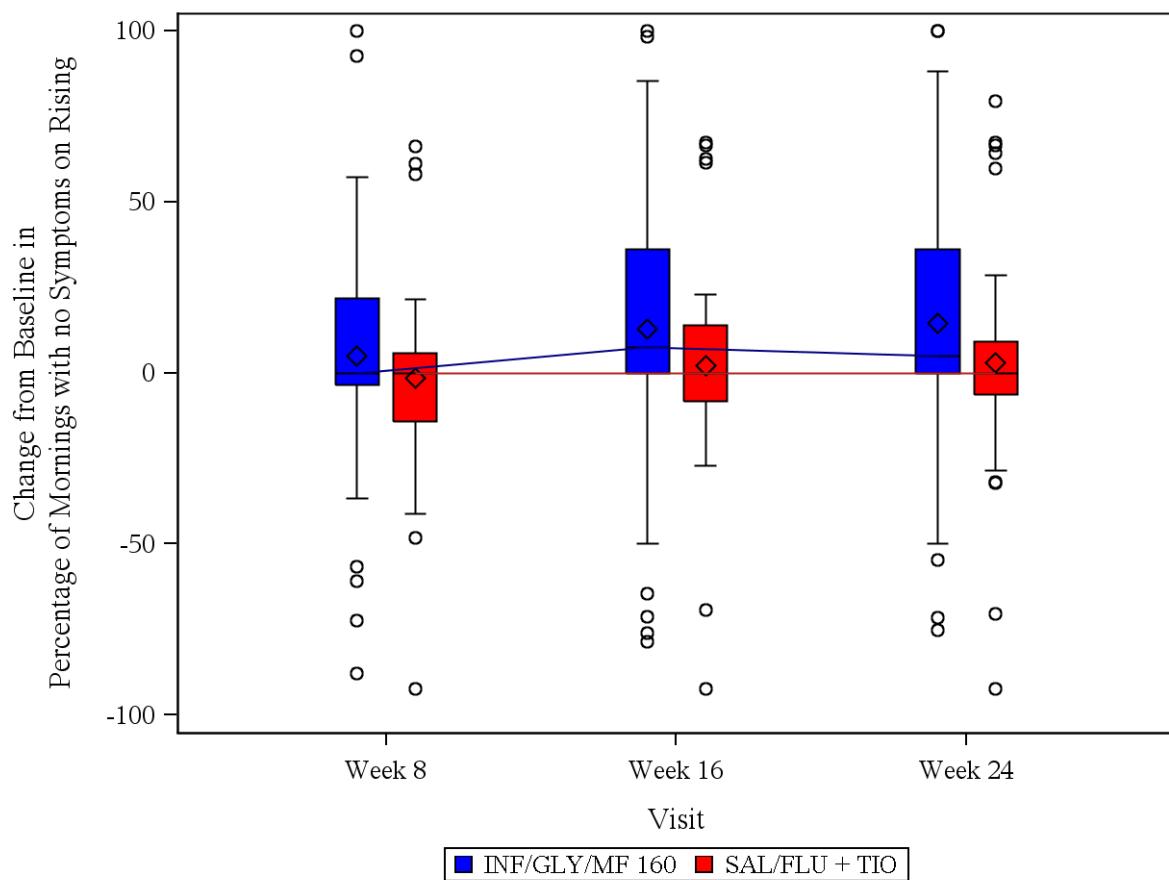


Figure 9.2.3 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

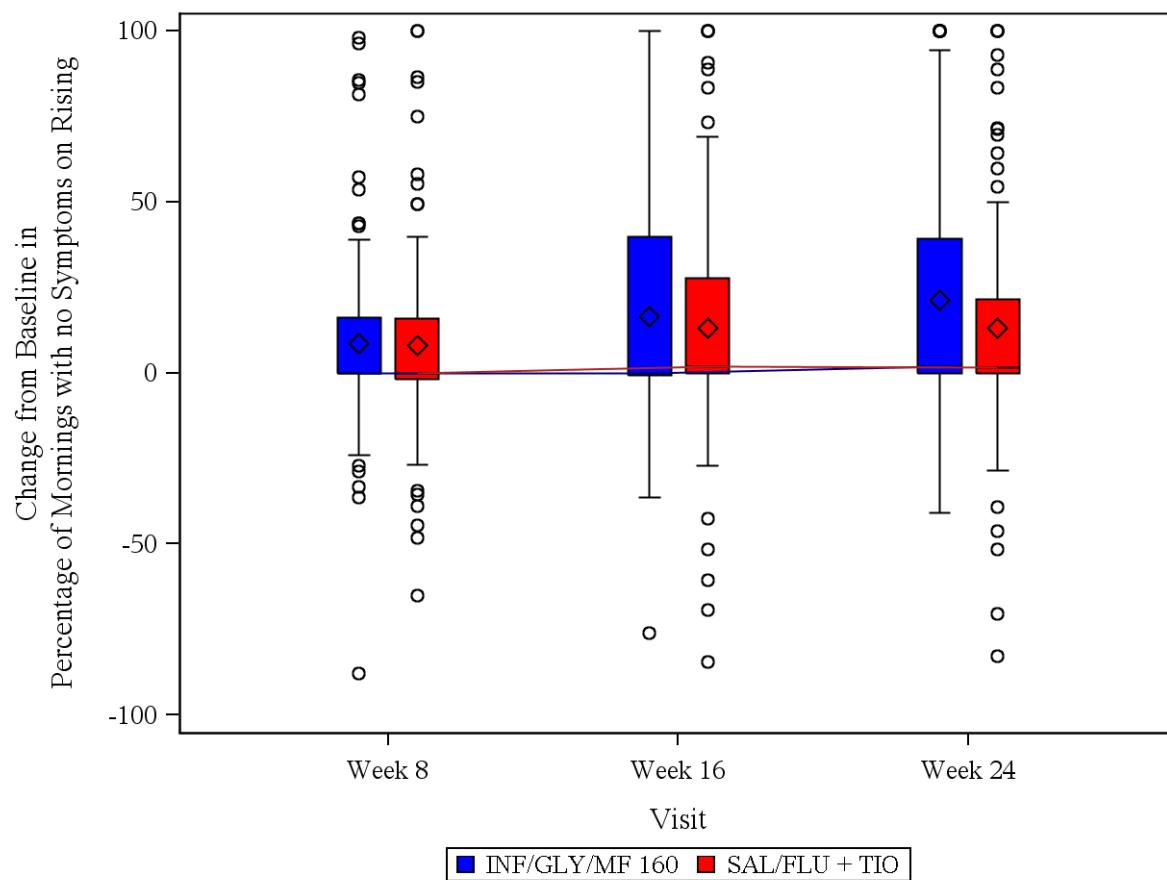
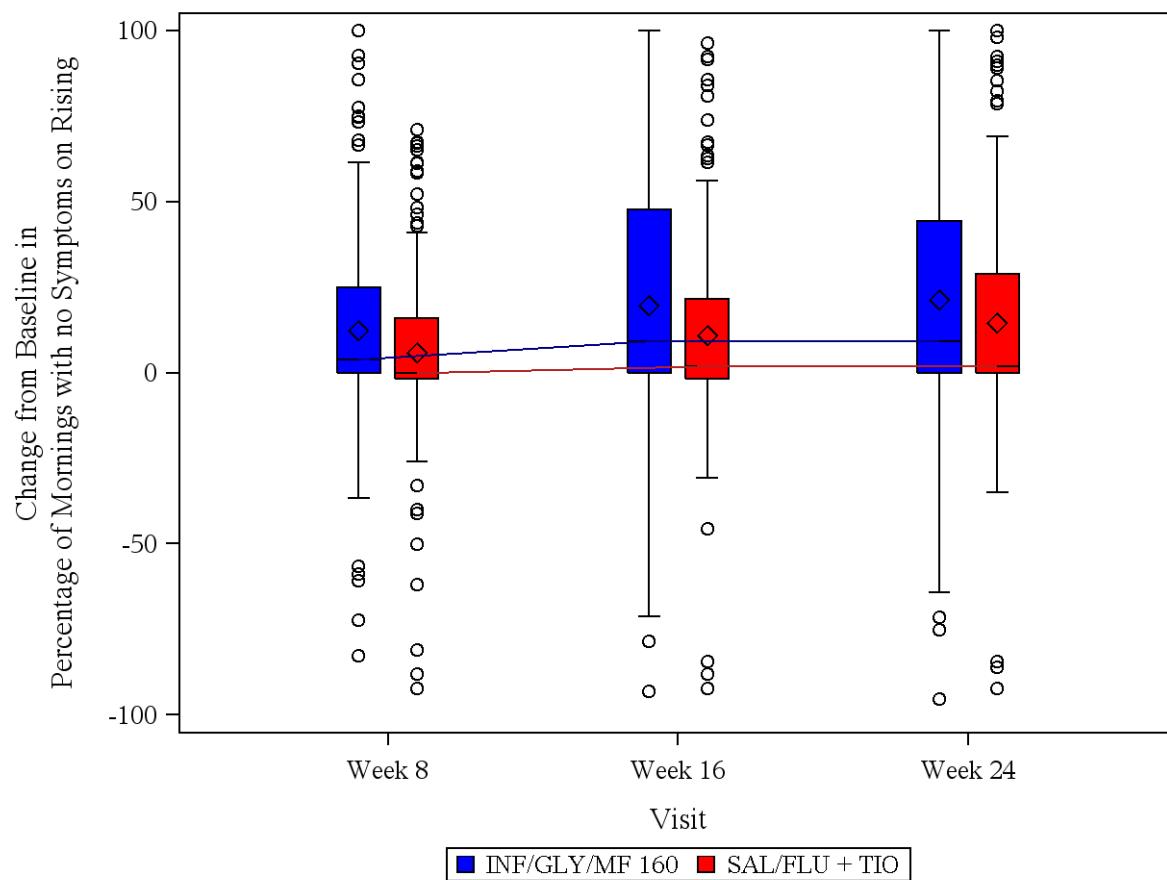


Figure 9.3.2 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Gender (FAS), Gender = Female



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

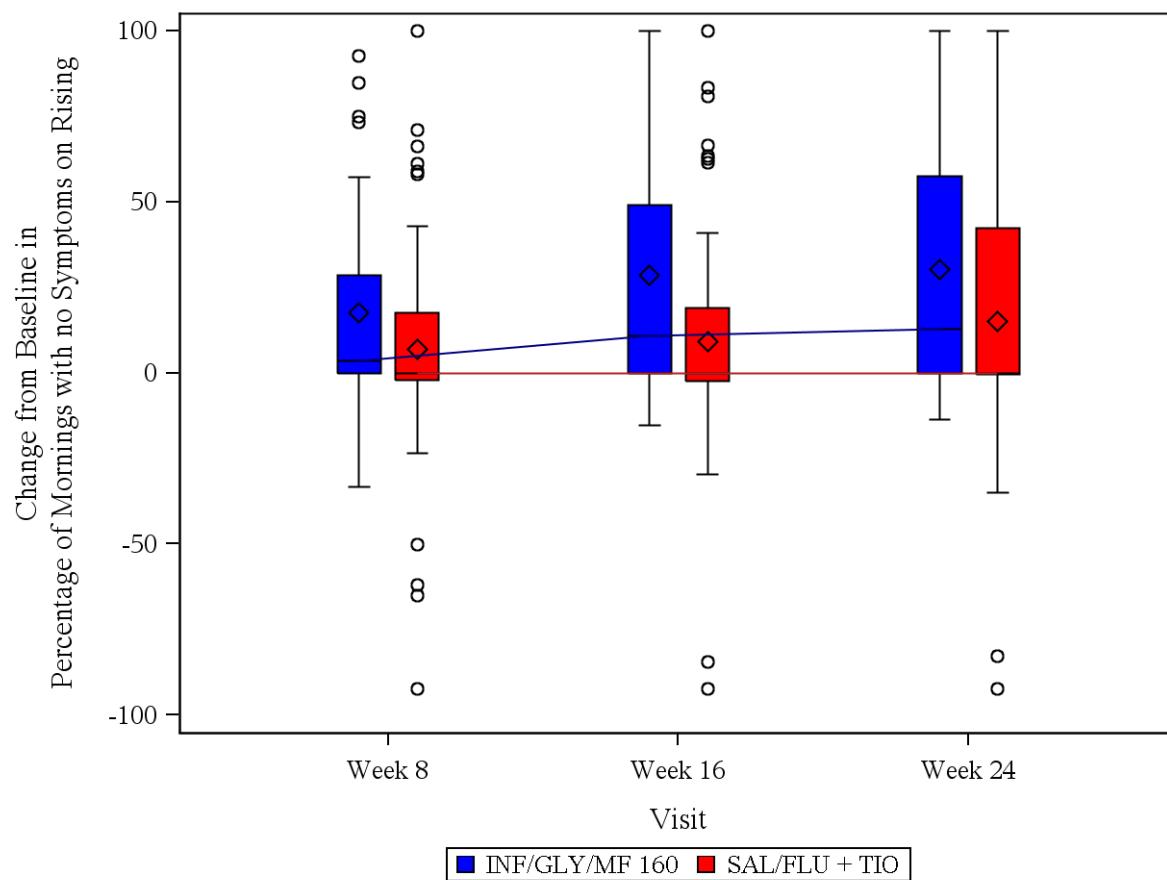


Figure 9.4.2 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Region (FAS), Region = Europe

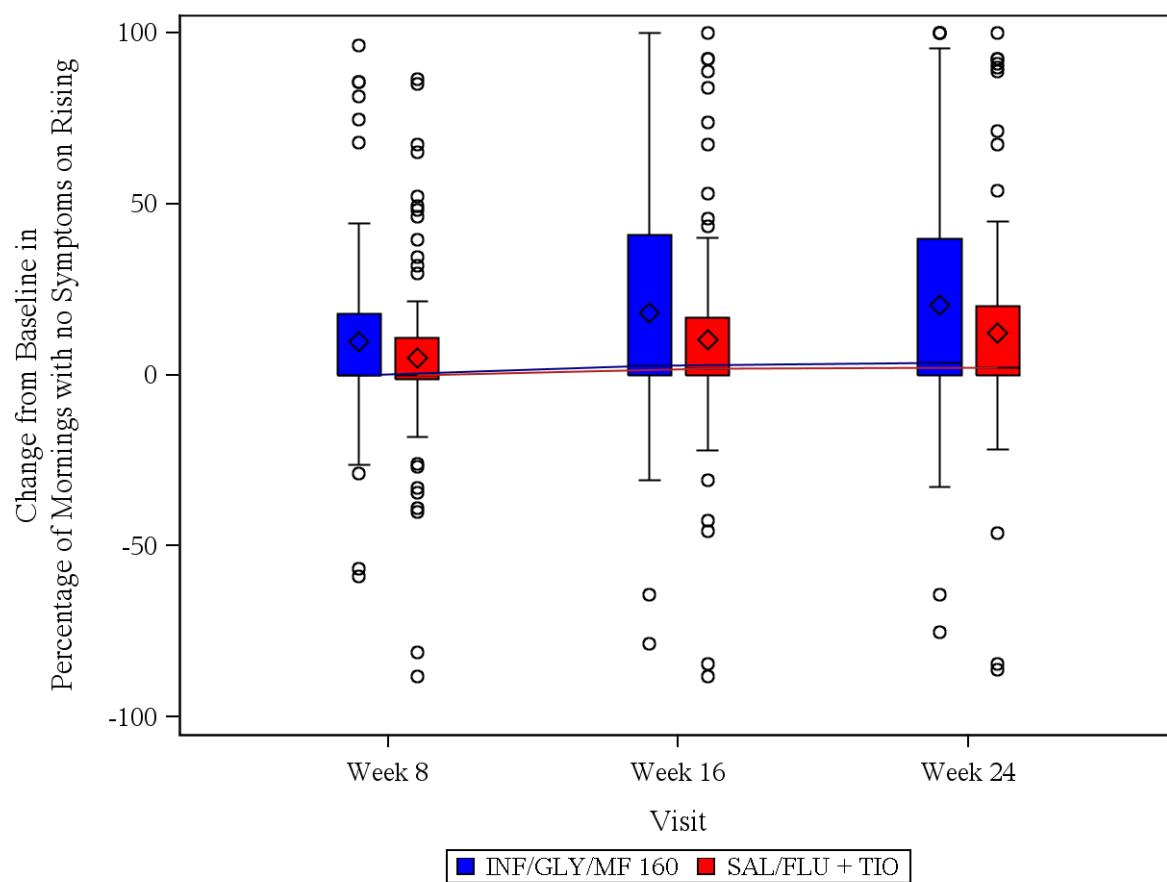


Figure 9.4.3 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Region (FAS), Region = Latin America

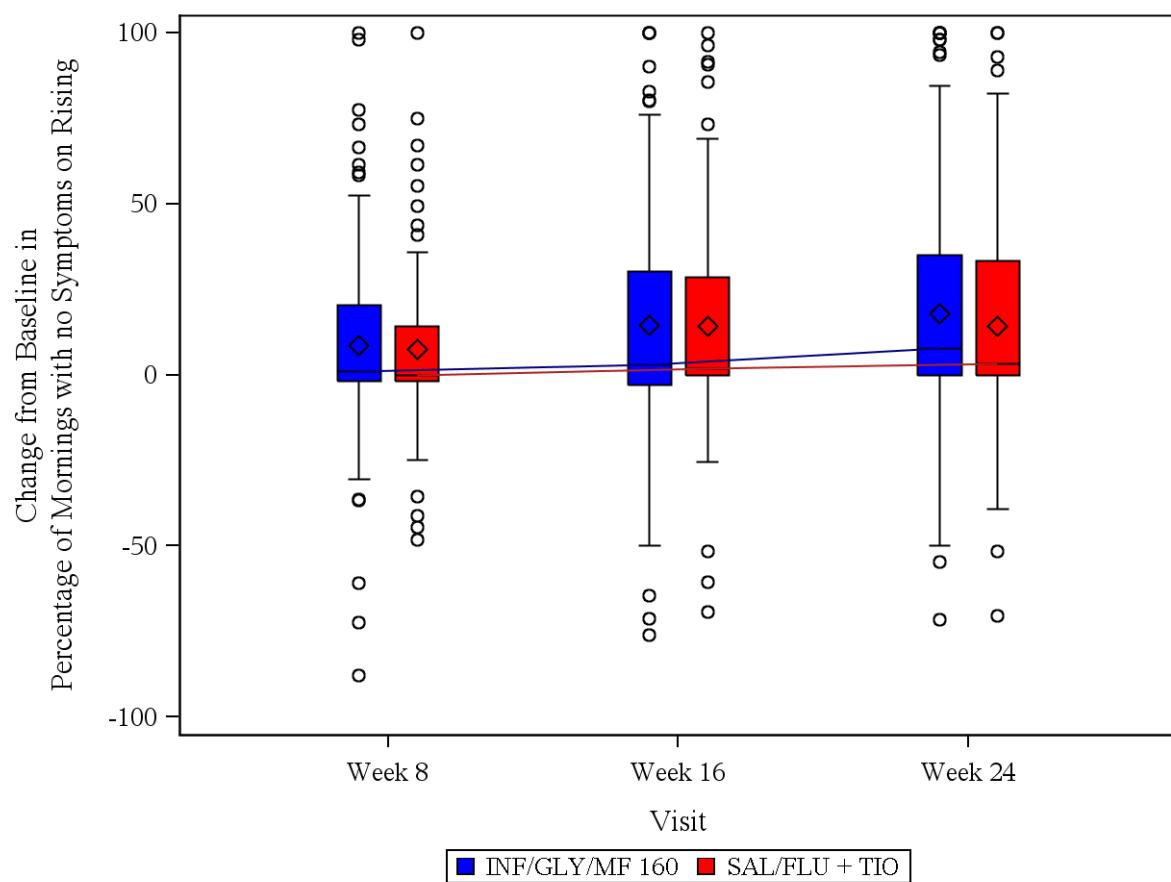
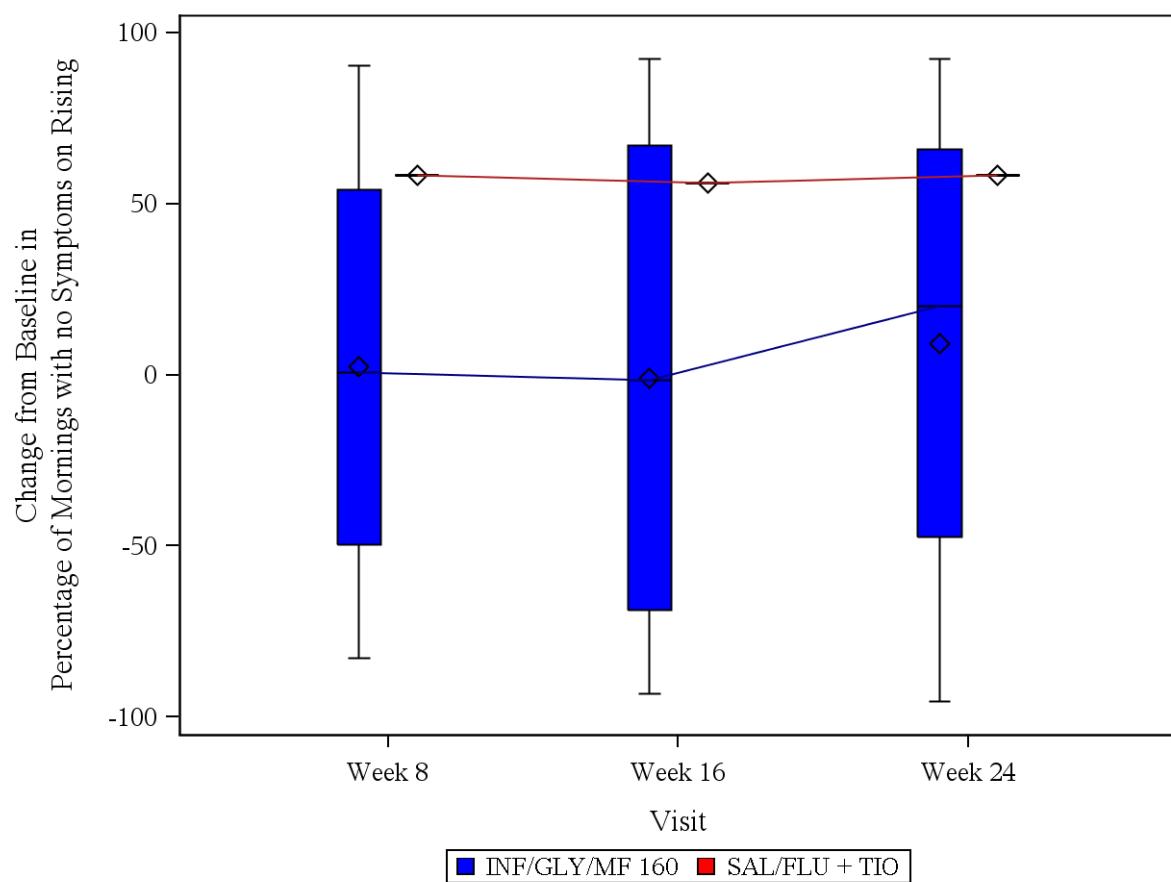


Figure 9.4.4 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by Region (FAS), Region = Others



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

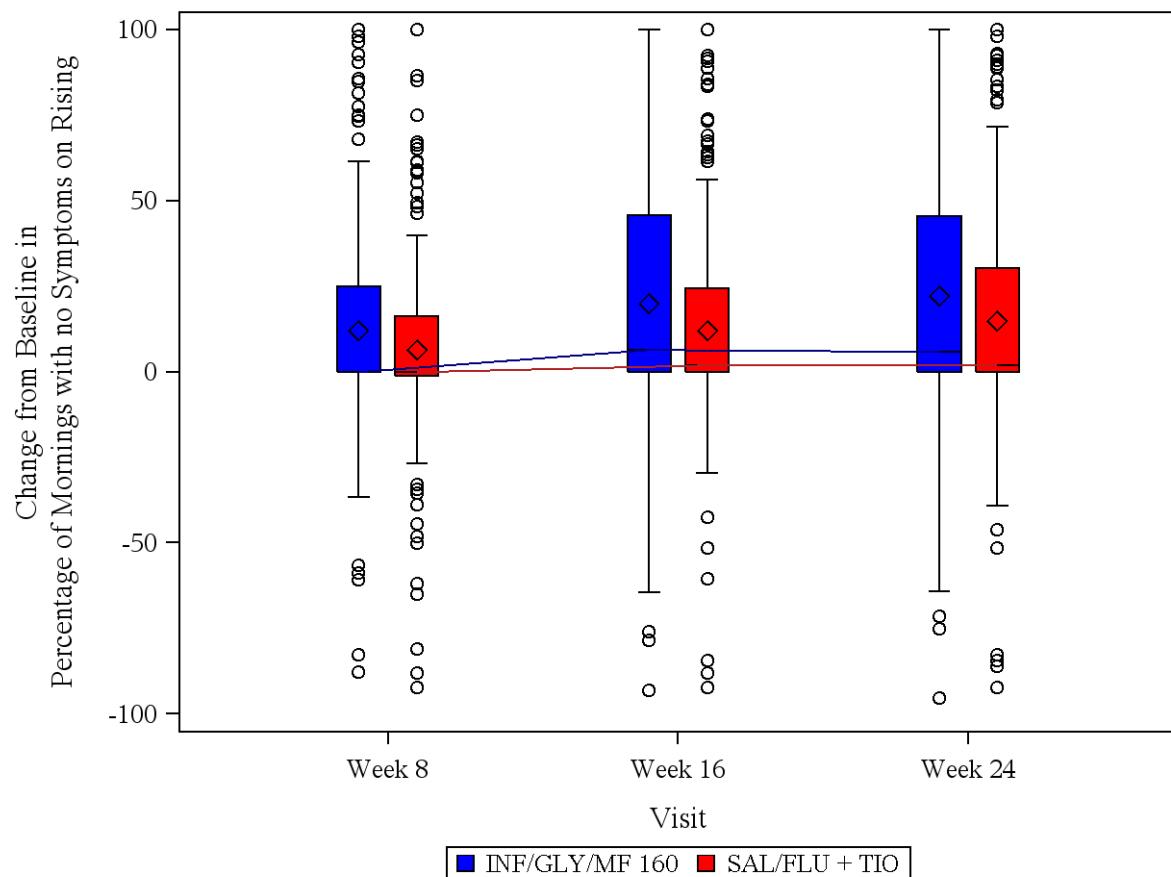
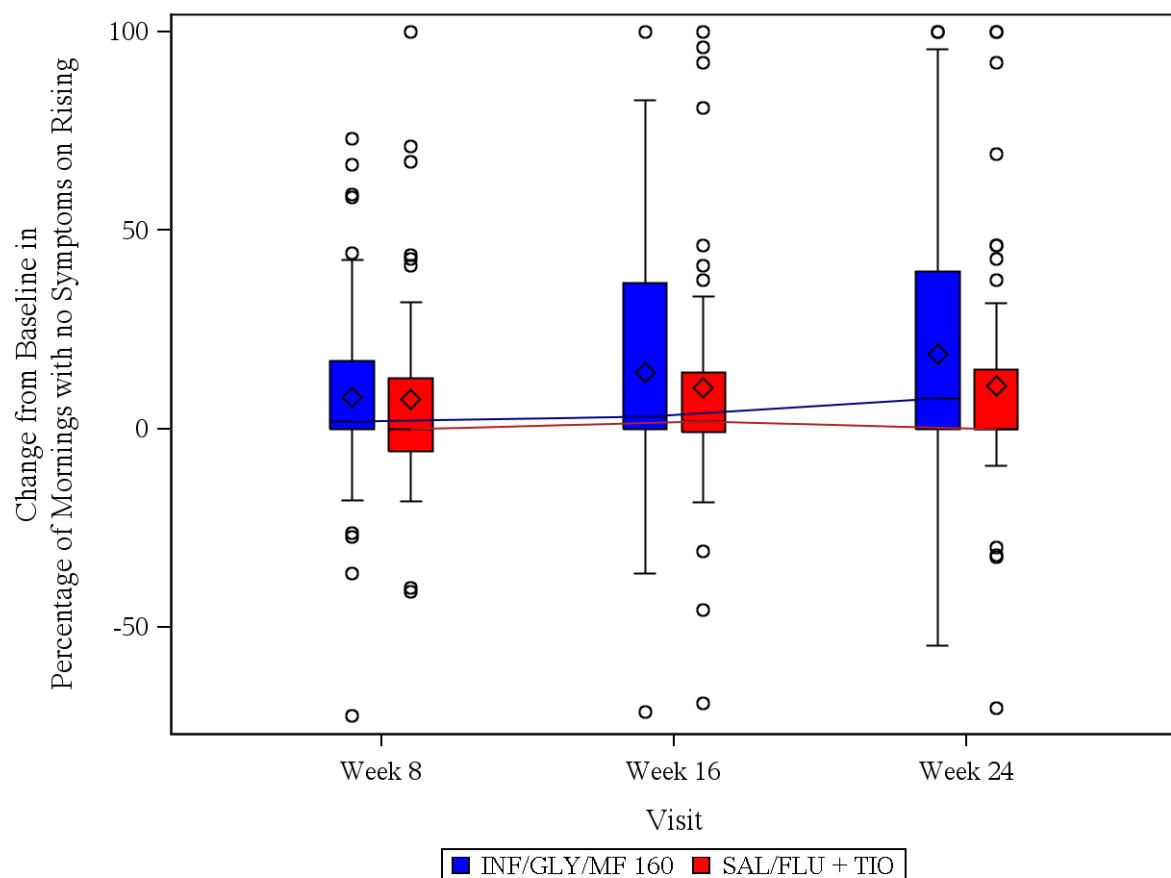
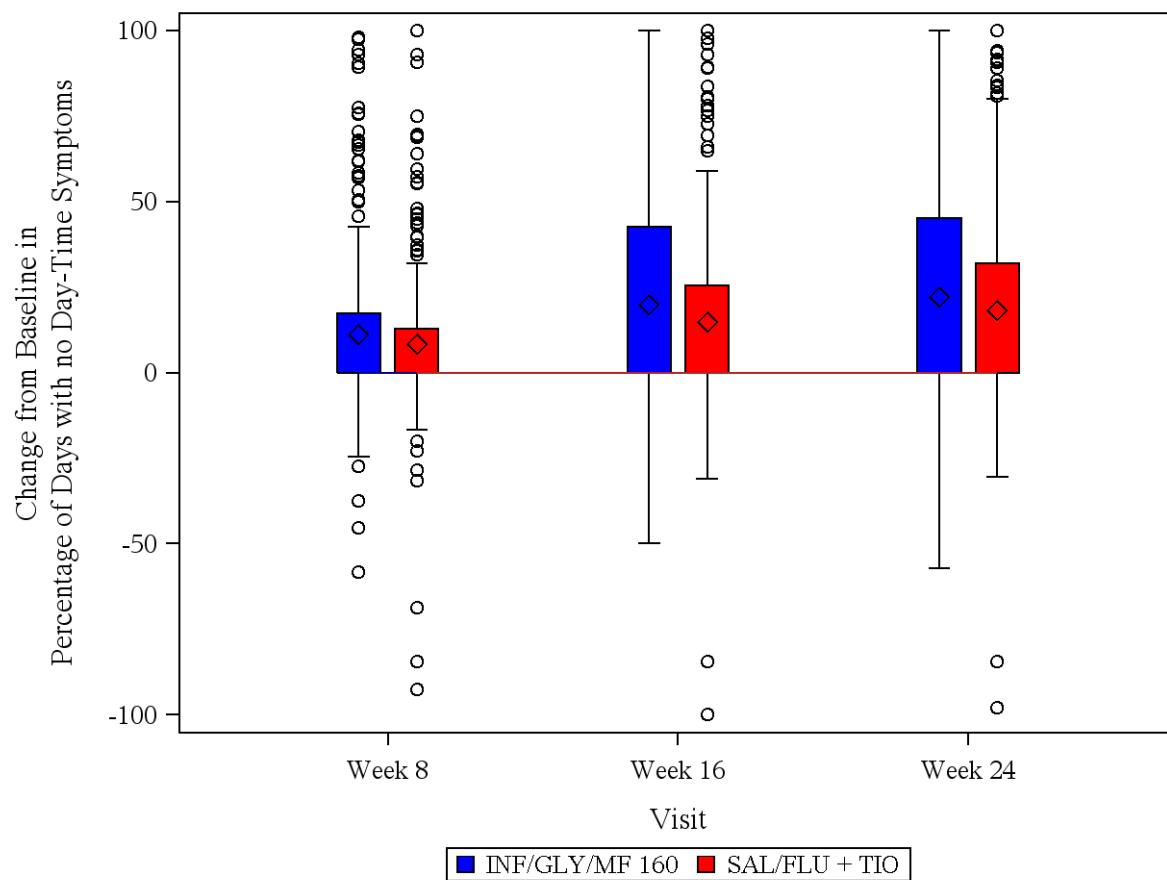


Figure 9.5.2 Symptoms (Percentage of Mornings with no Symptoms on Rising) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.7 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

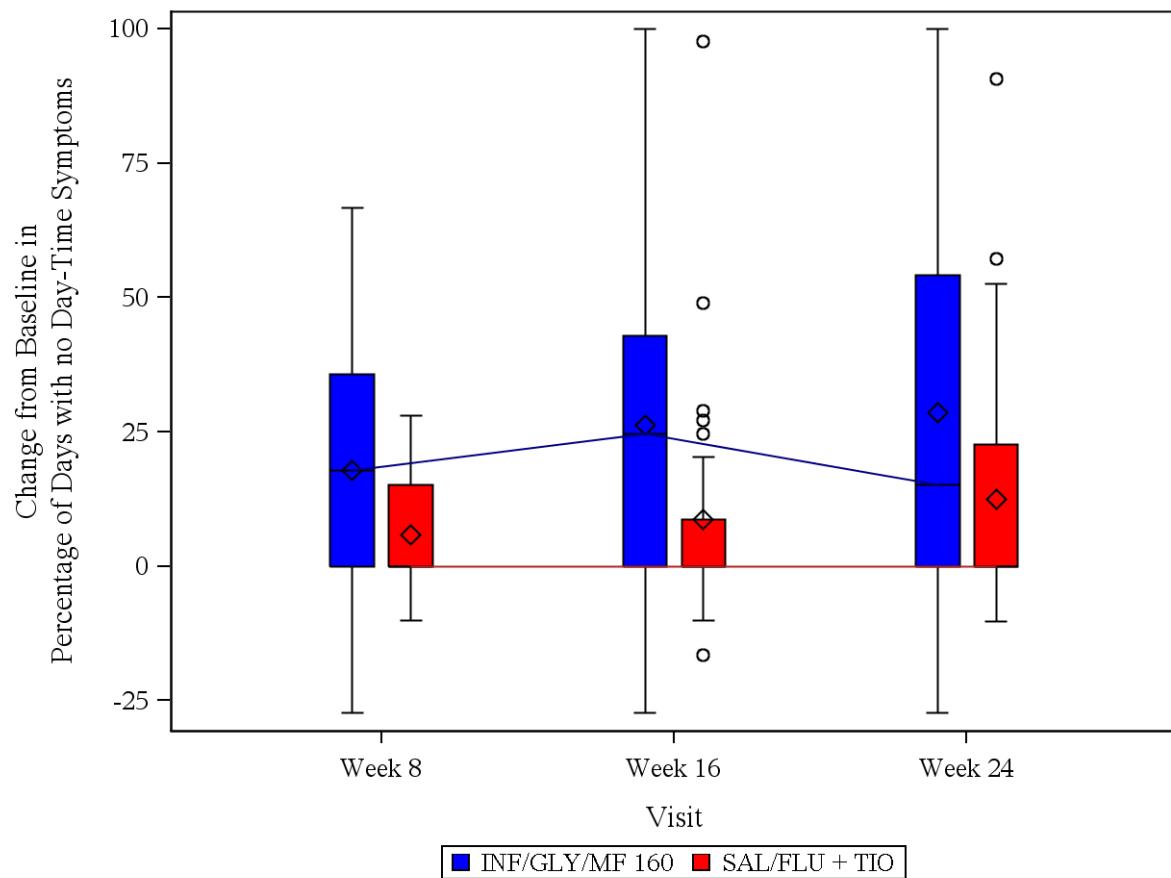


Figure 9.8.2 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Age (FAS), Age = 40-64 years

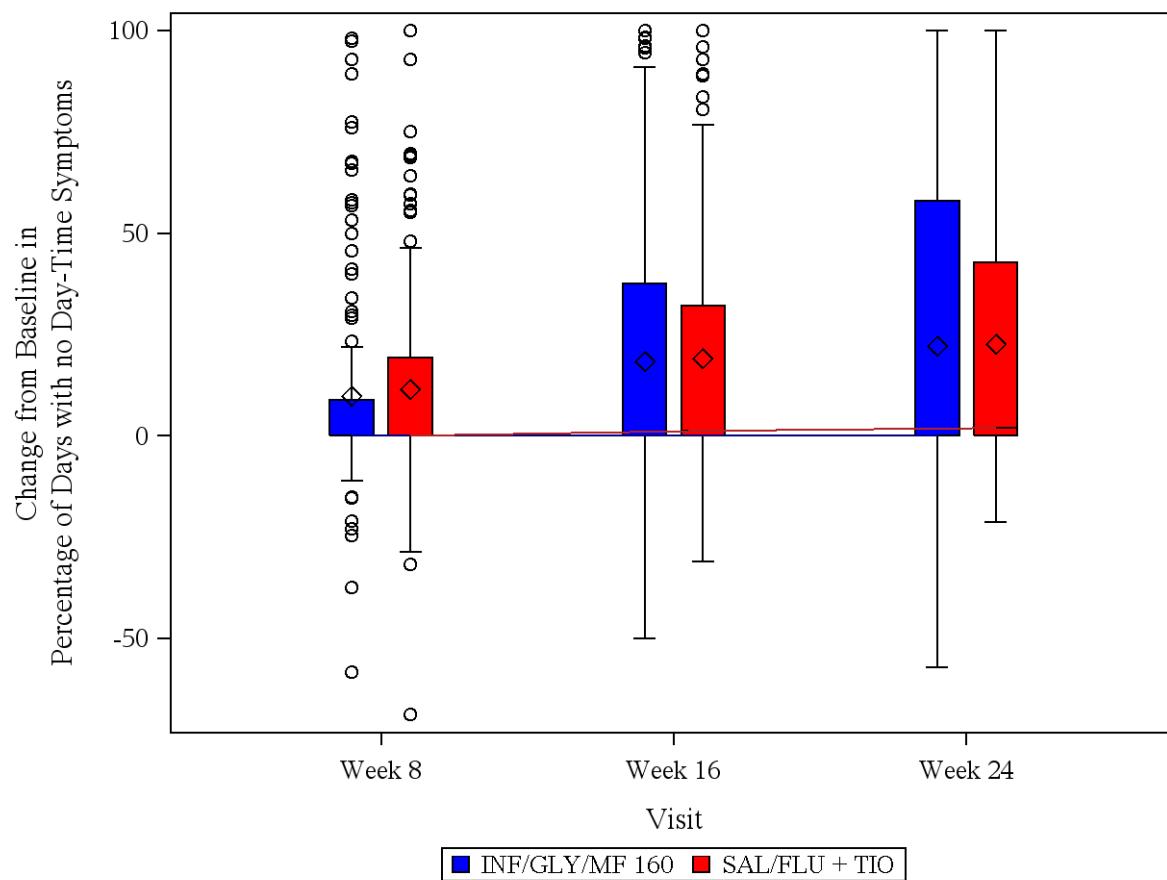
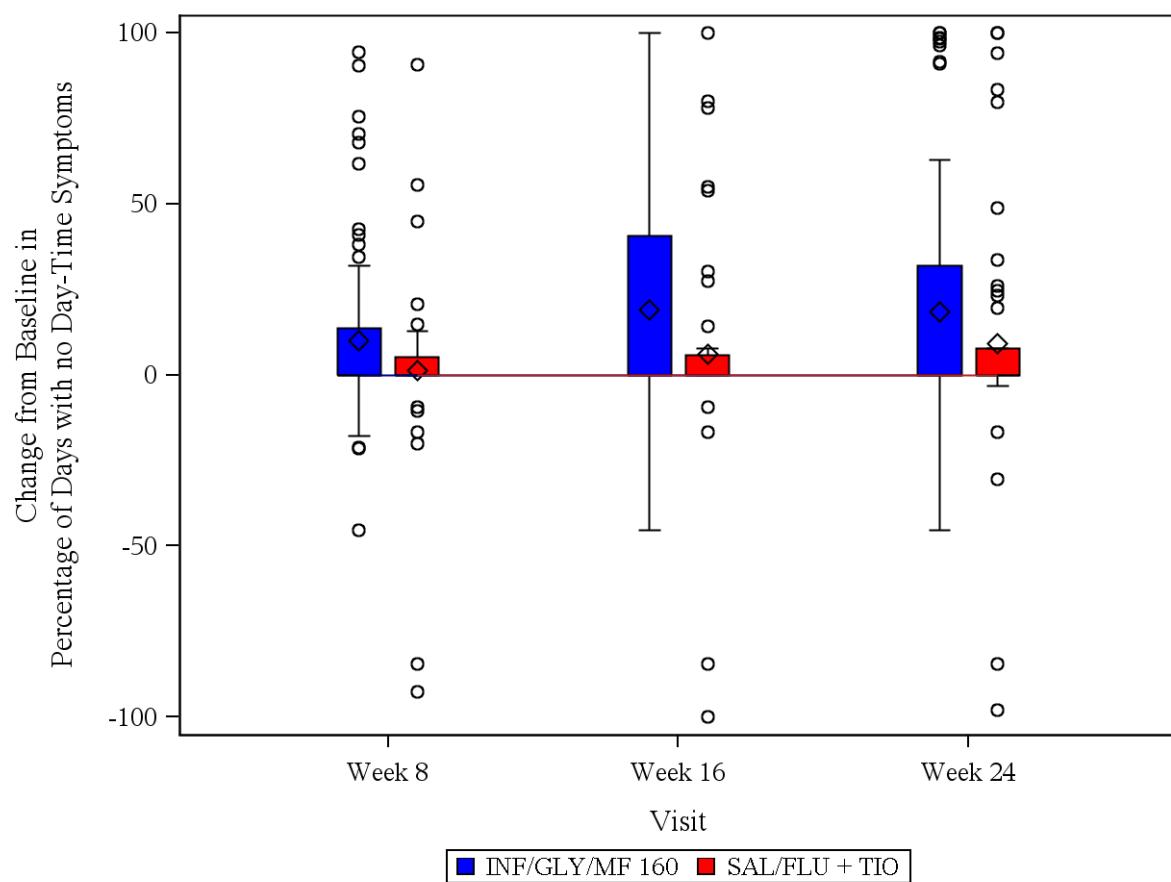


Figure 9.8.3 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

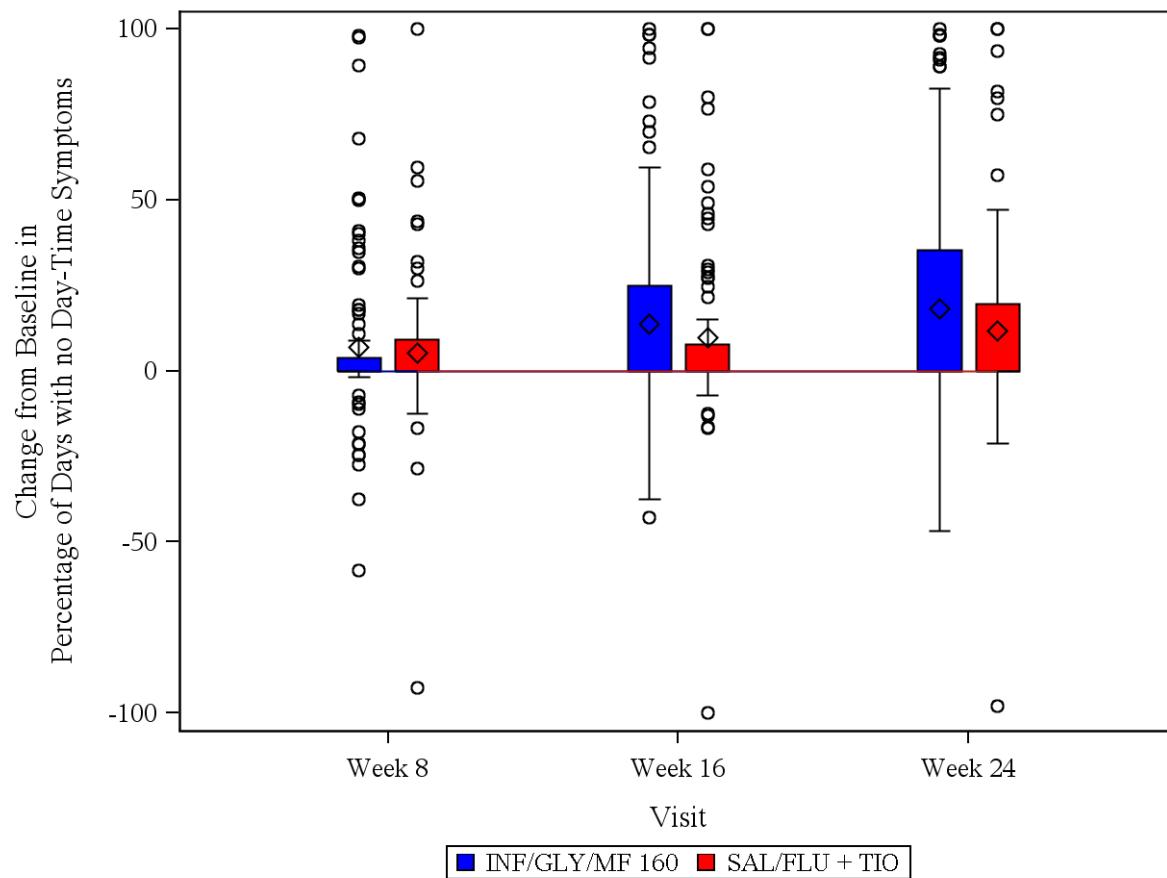
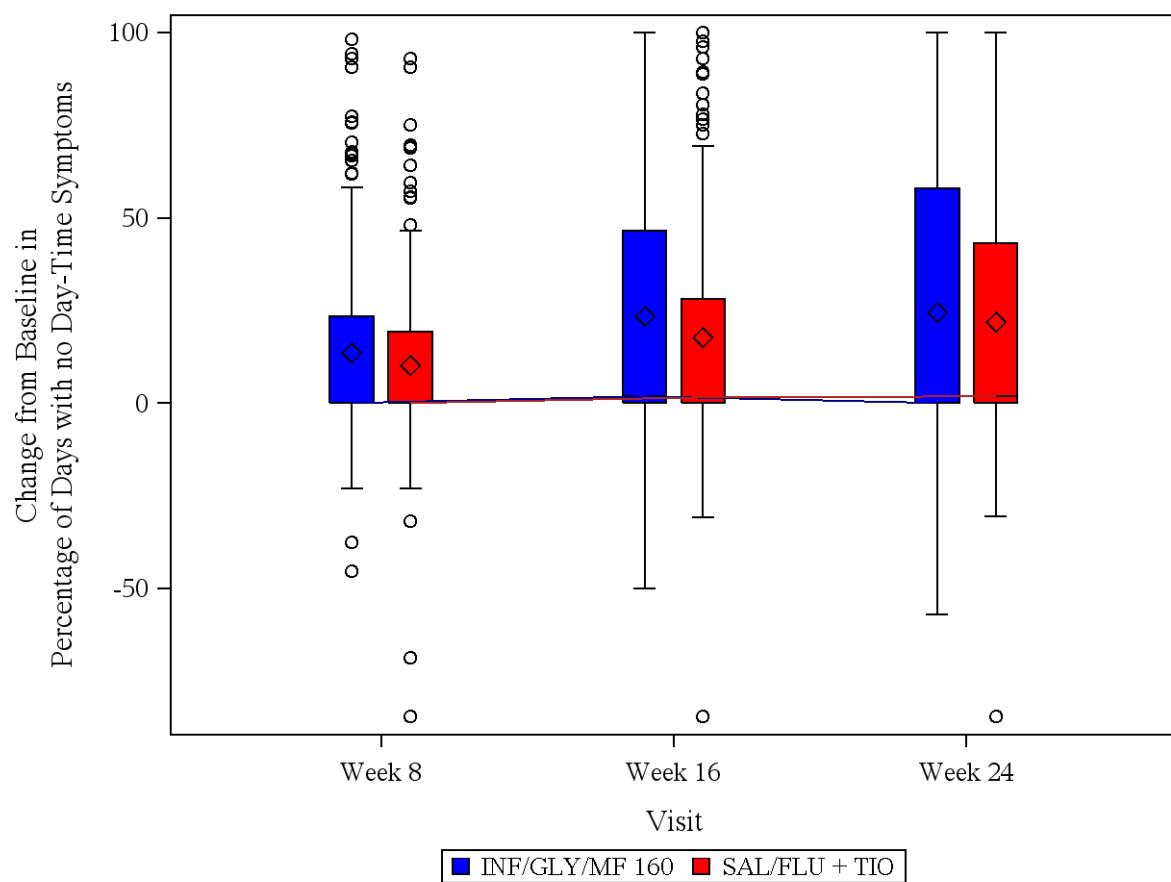


Figure 9.9.2 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Gender (FAS), Gender = Female



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

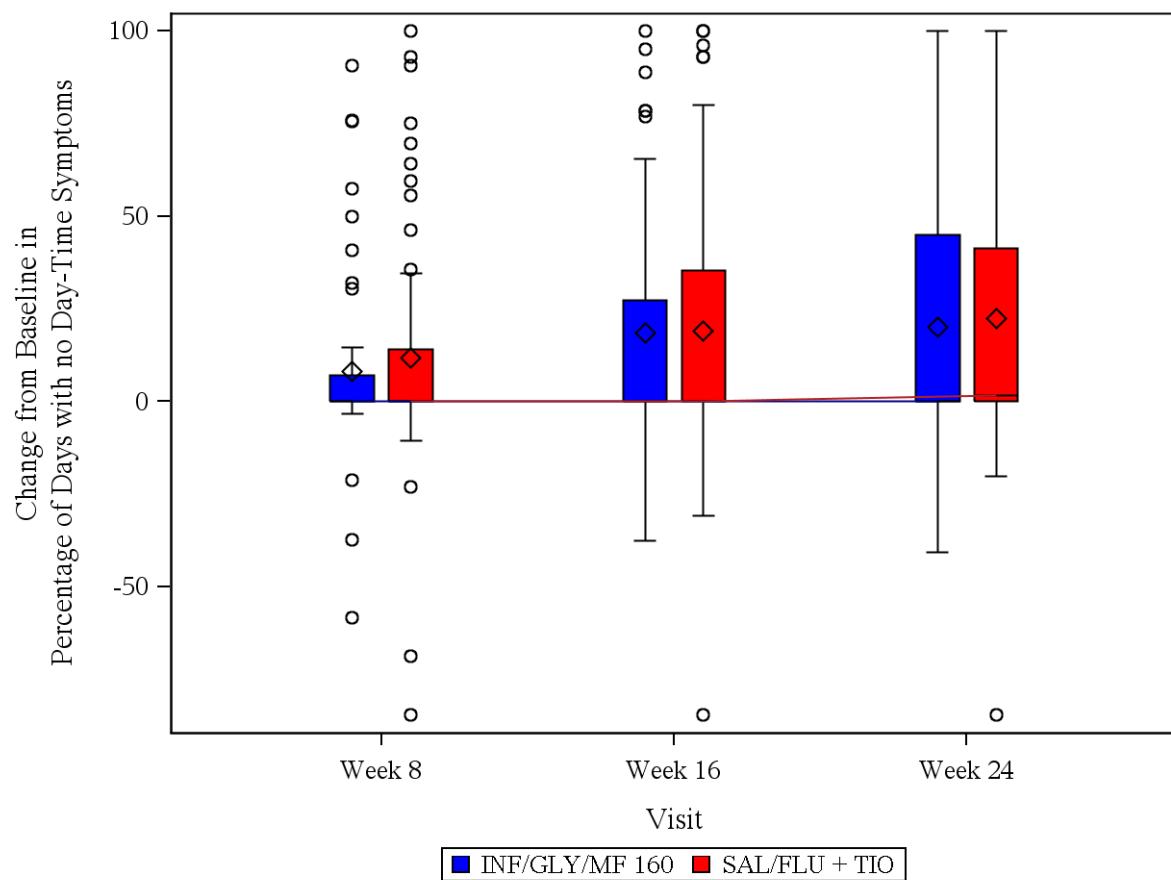


Figure 9.10.2 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Region (FAS), Region = Europe

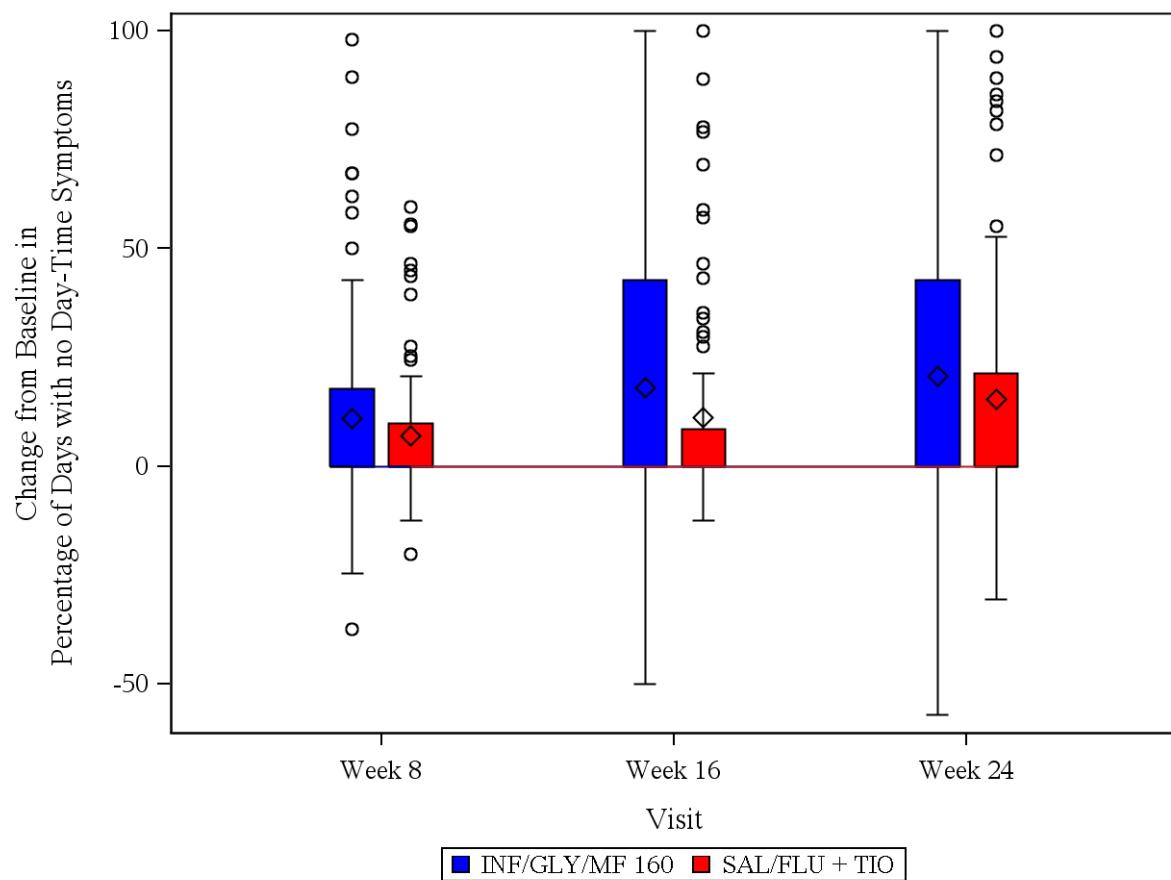


Figure 9.10.3 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Region (FAS), Region = Latin America

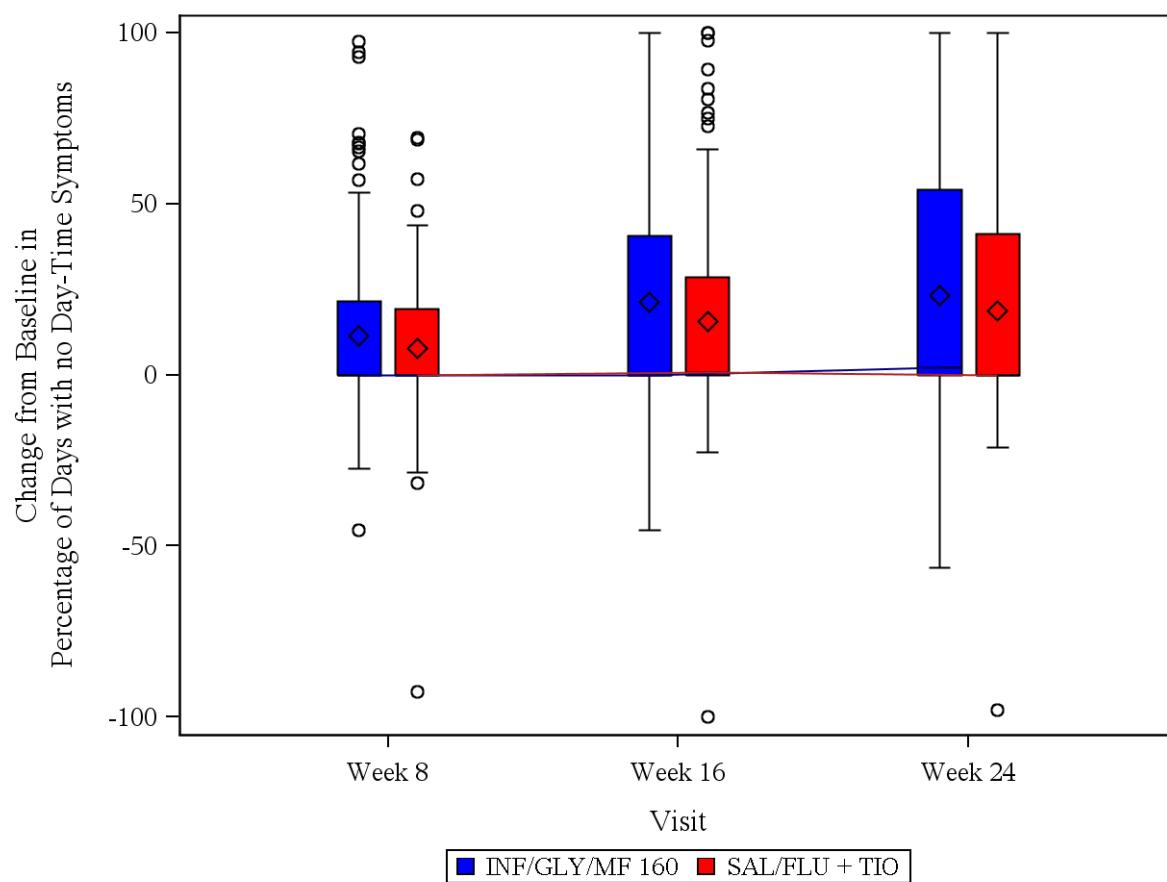
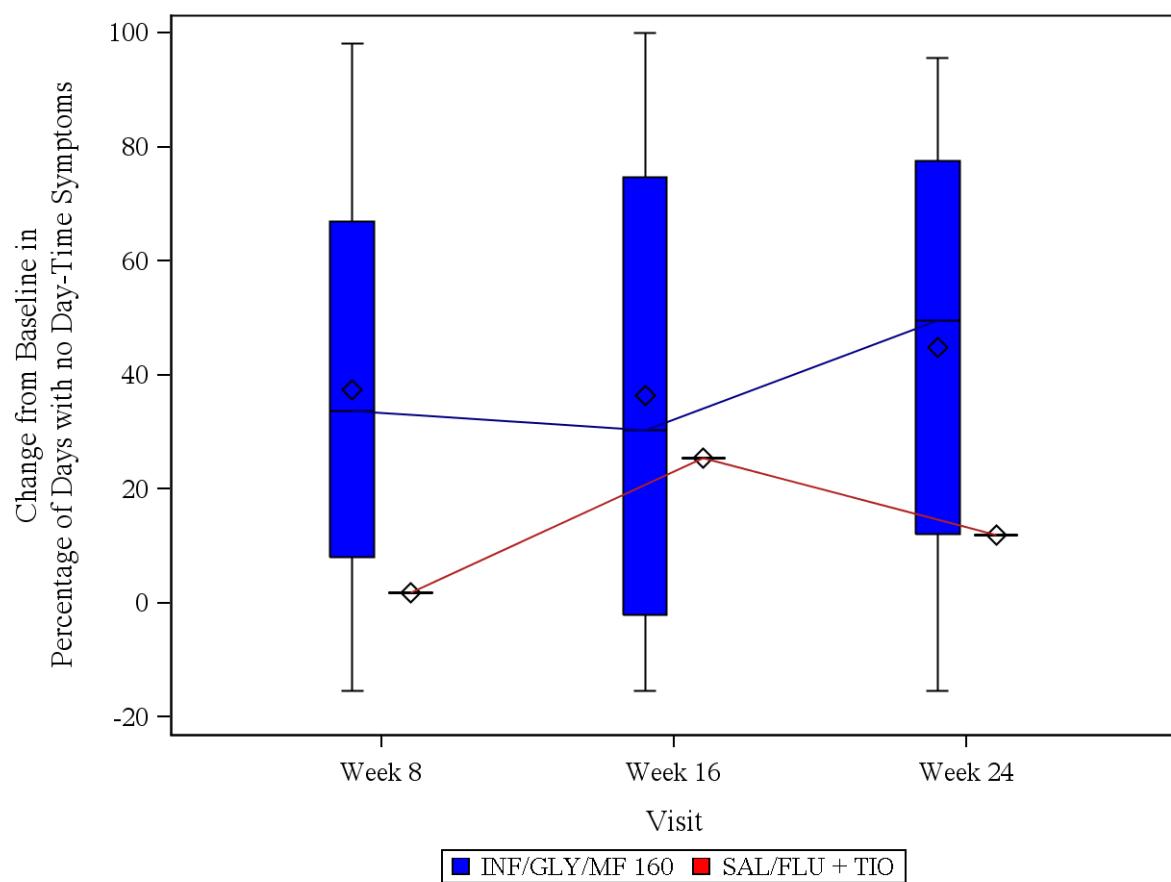


Figure 9.10.4 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by Region (FAS), Region = Others



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

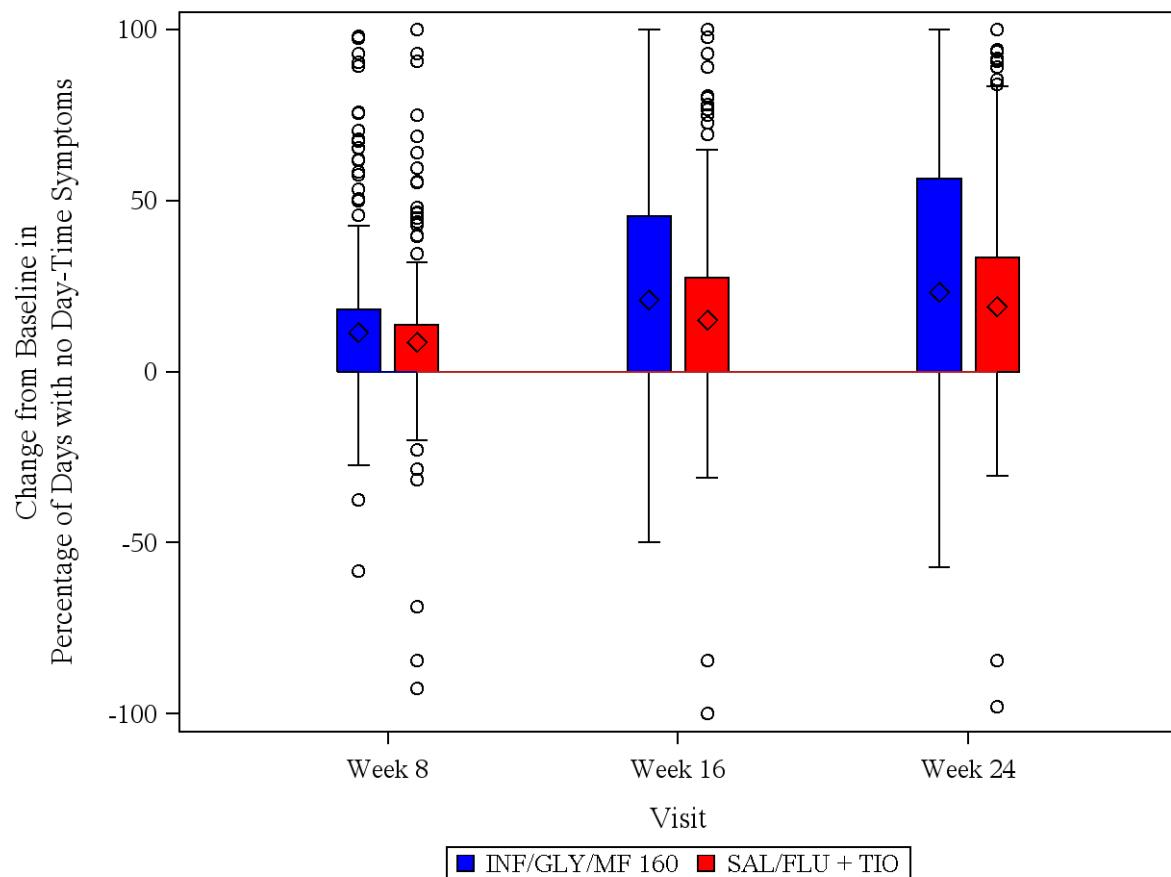
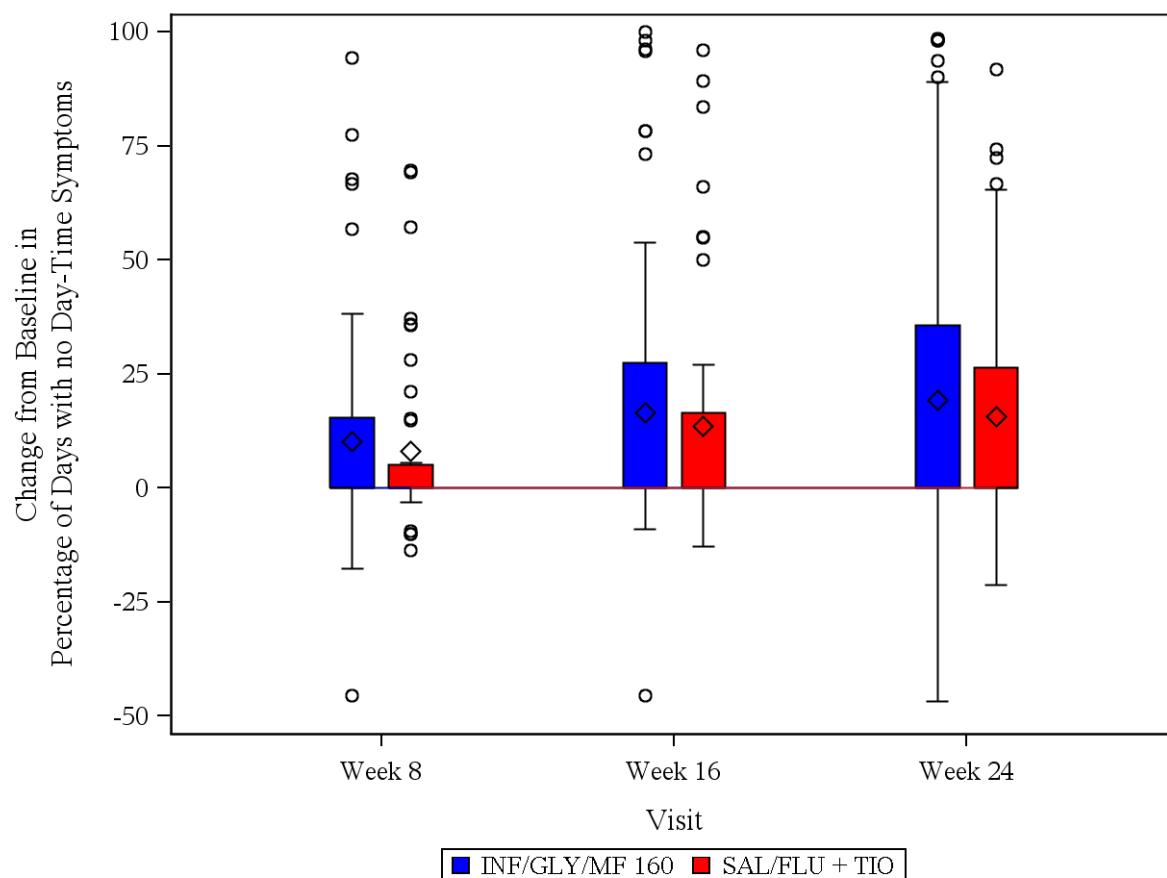
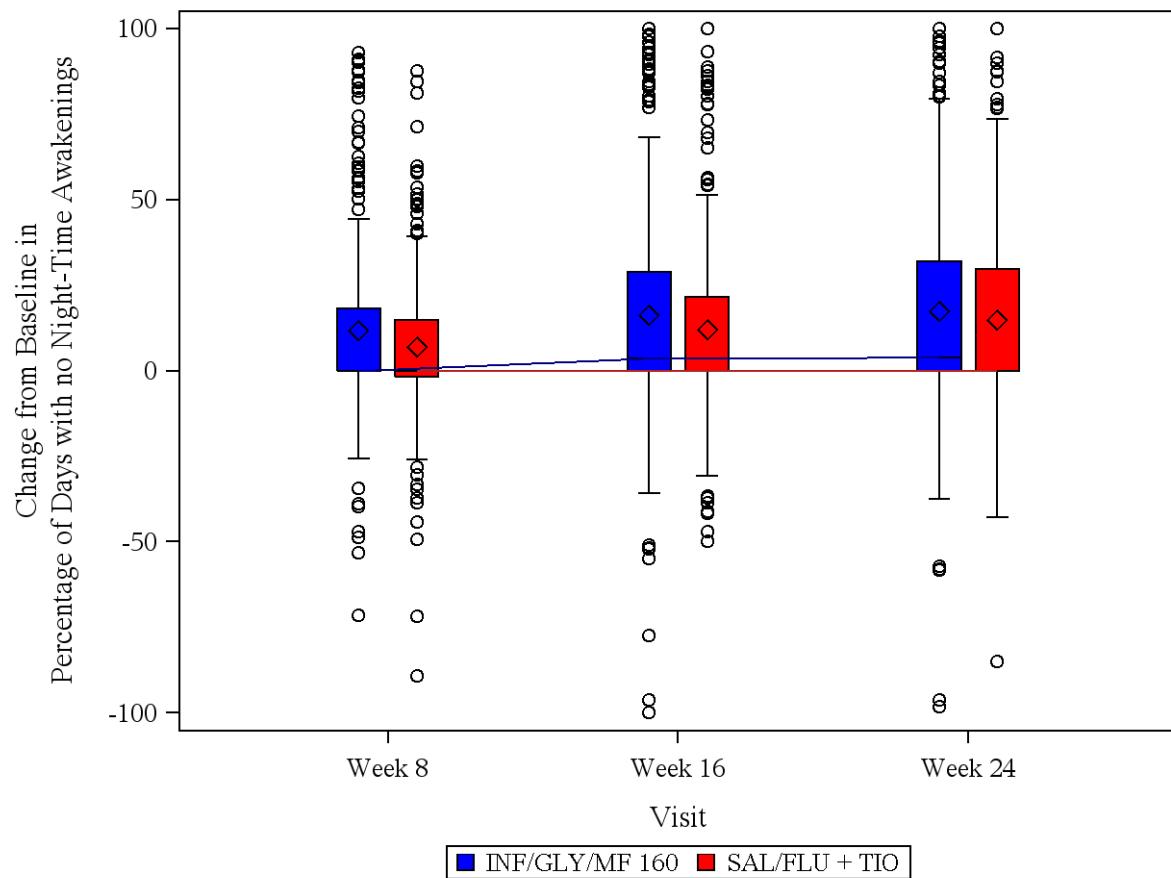


Figure 9.11.2 Symptoms (Percentage of Days with no Day-Time Symptoms) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.13 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

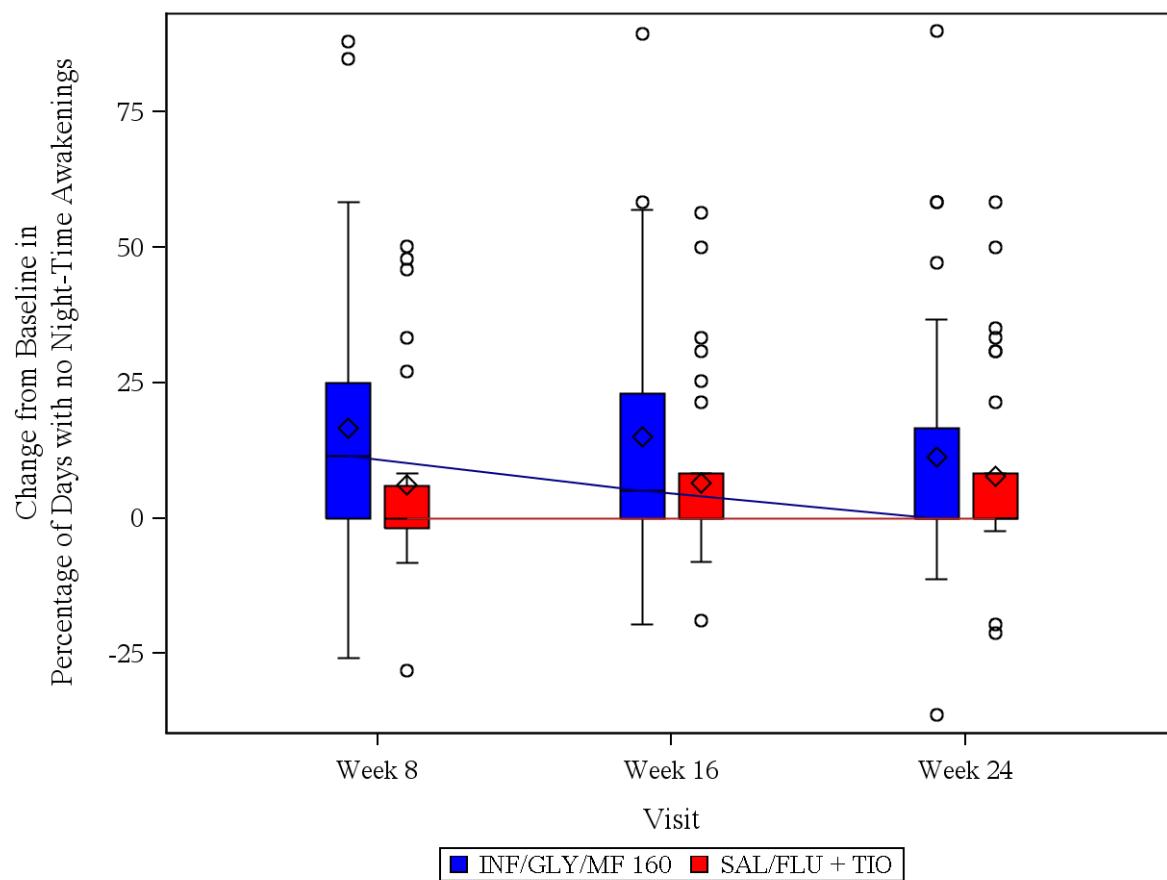


Figure 9.14.2 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Age (FAS), Age = 40-64 years

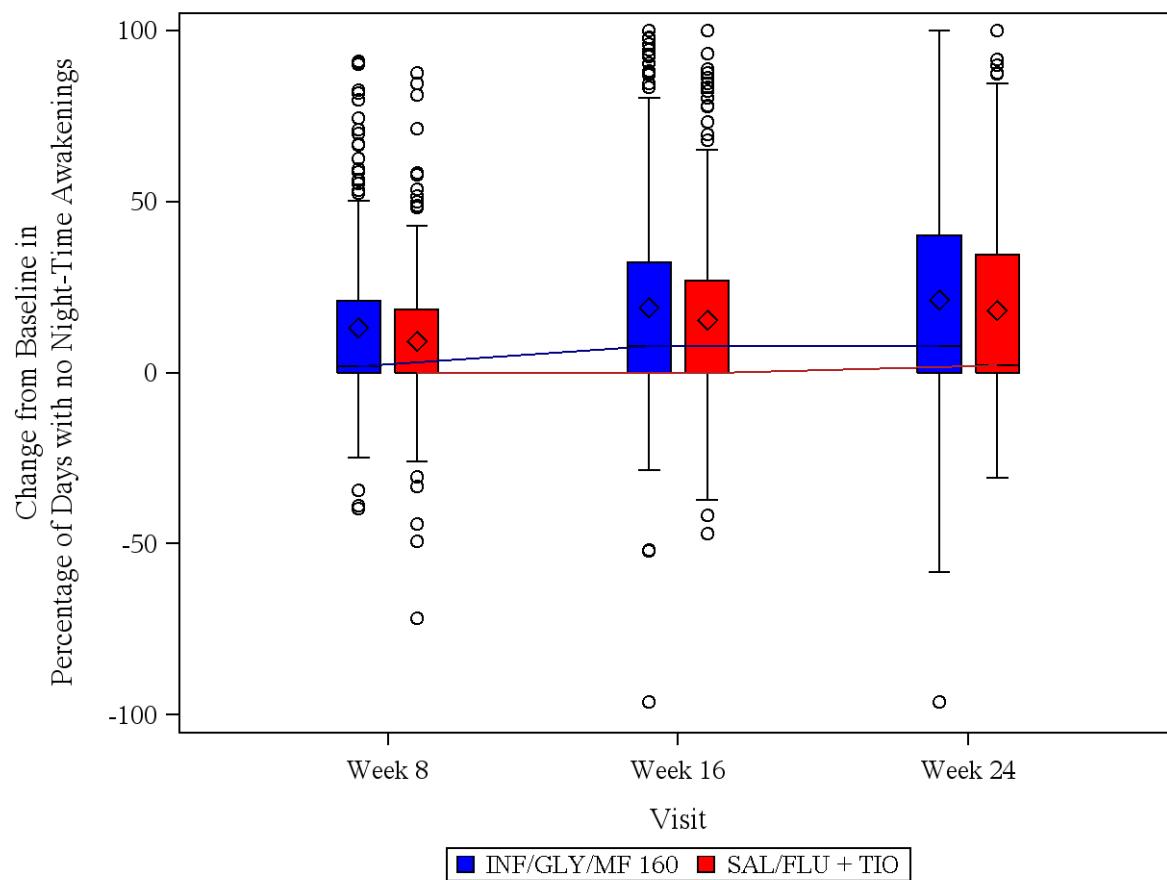
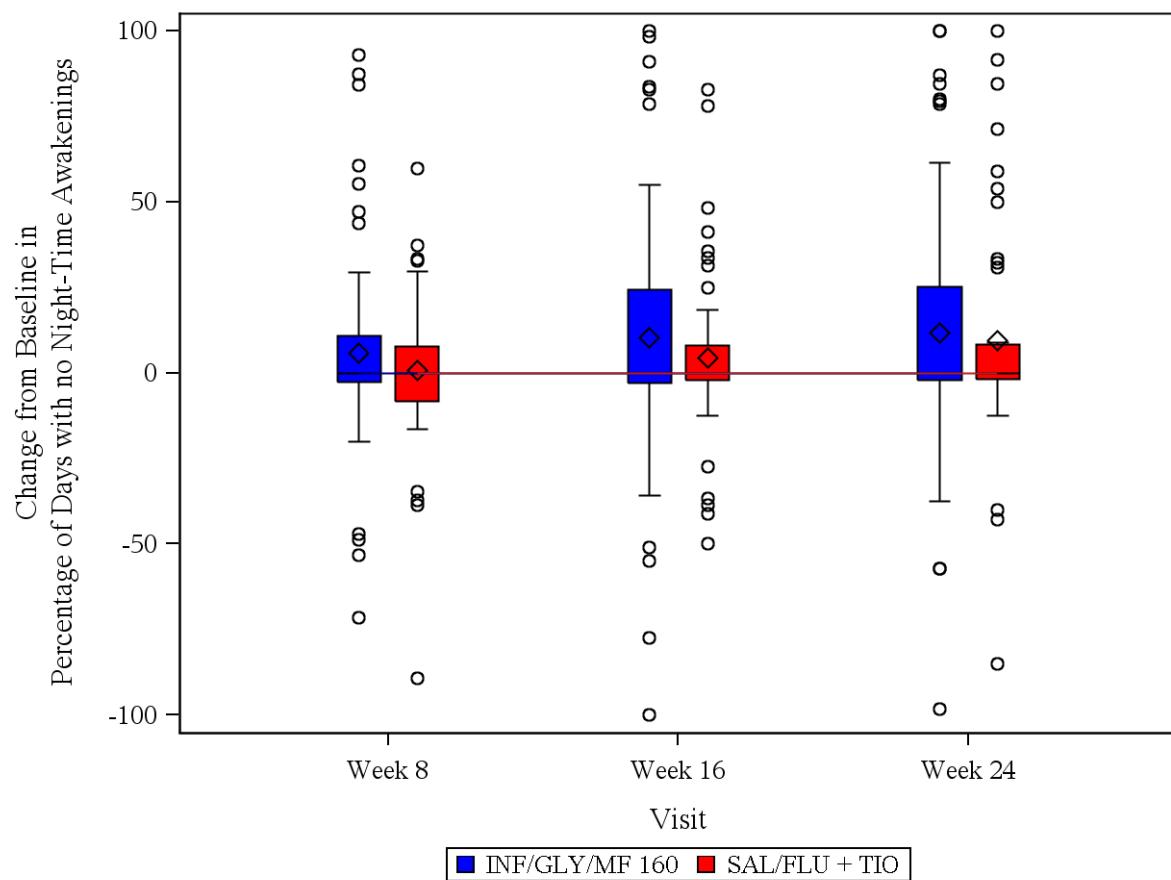


Figure 9.14.3 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

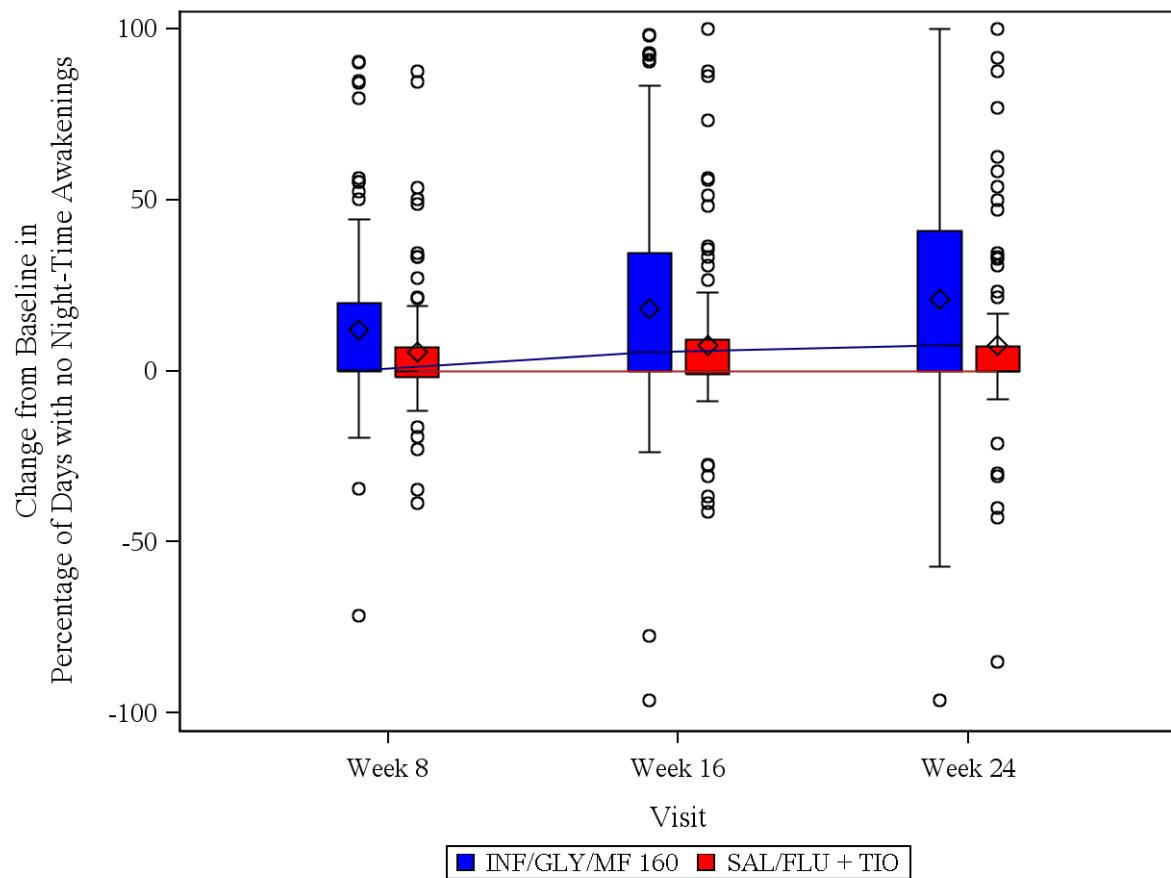
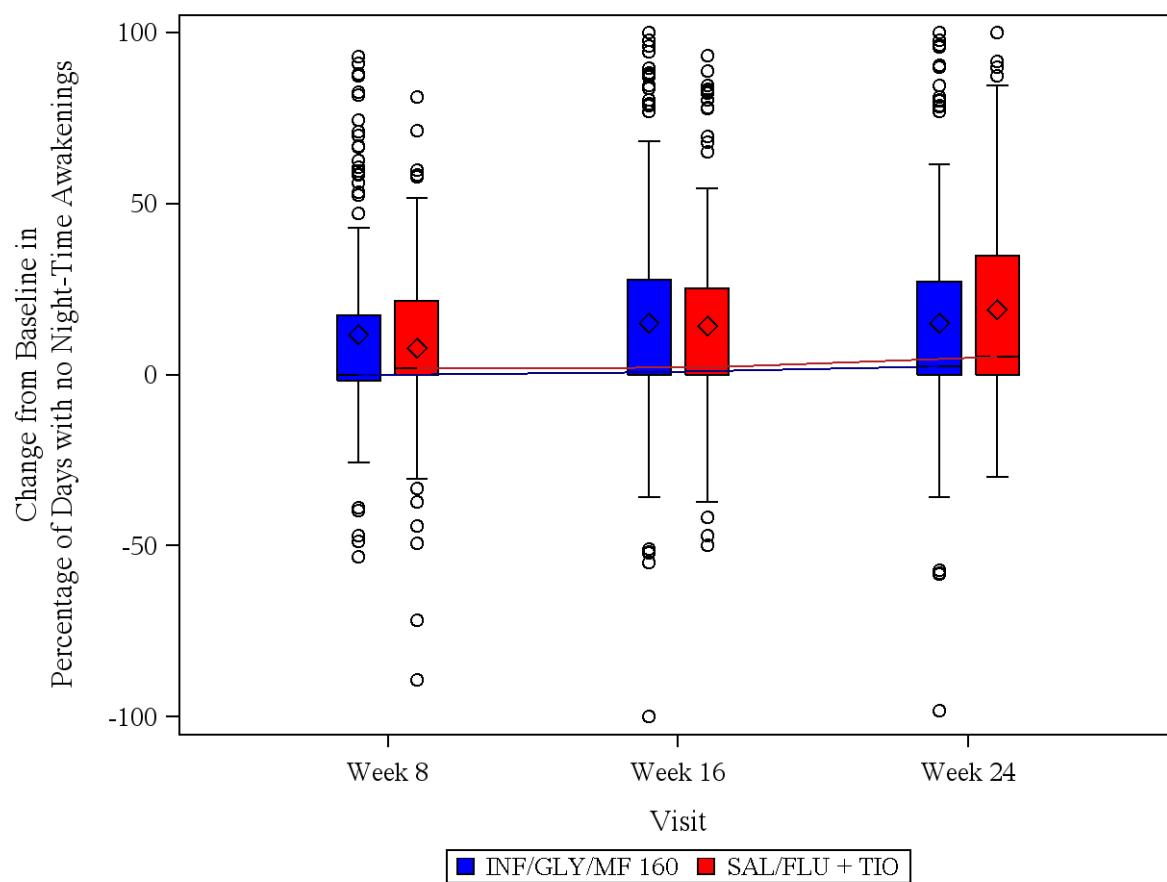


Figure 9.15.2 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Gender (FAS), Gender = Female



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

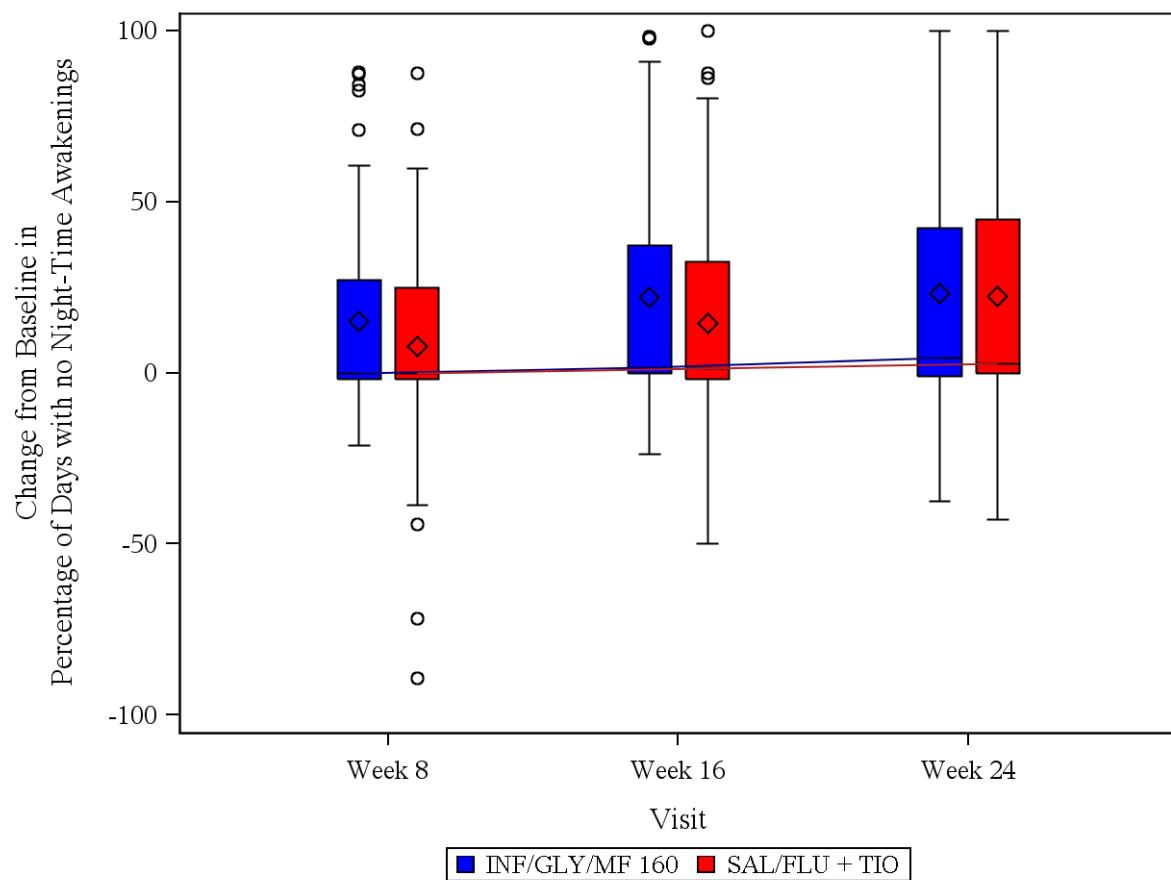


Figure 9.16.2 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Region (FAS), Region = Europe

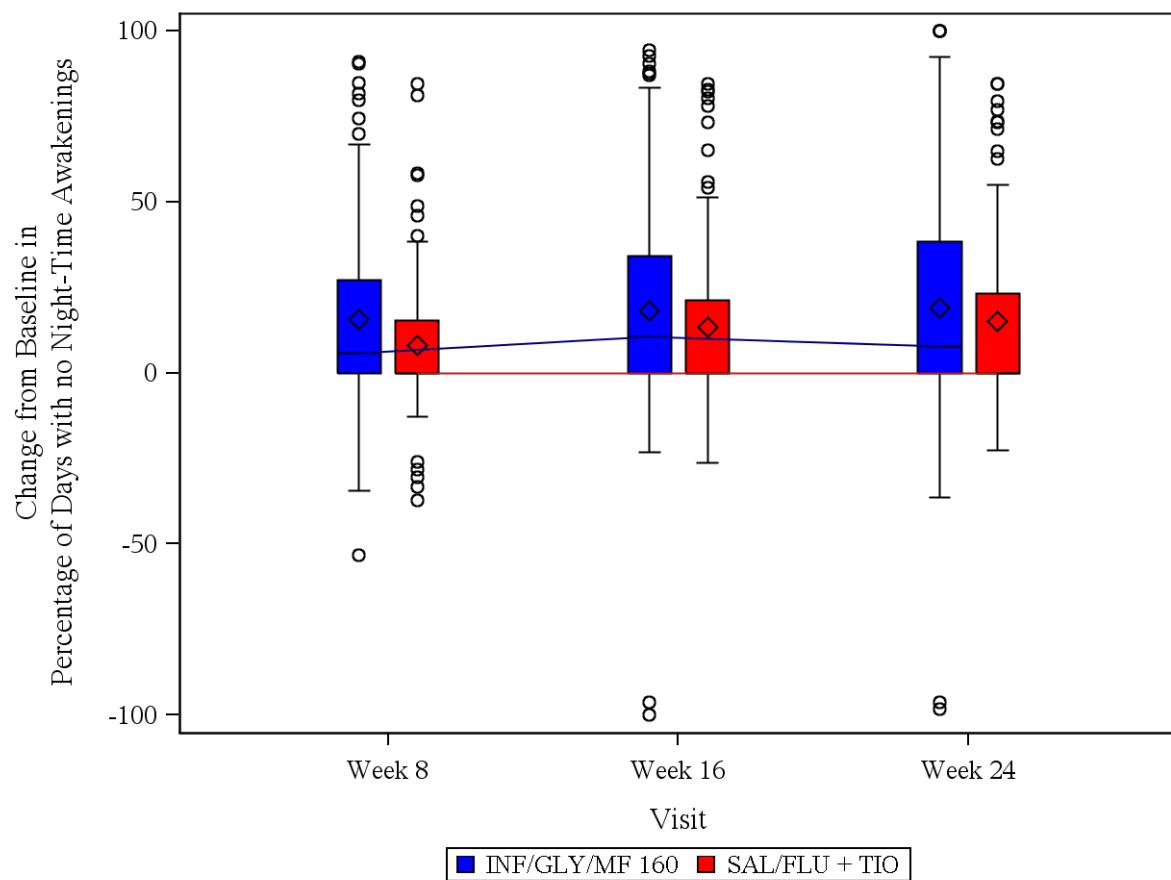


Figure 9.16.3 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Region (FAS), Region = Latin America

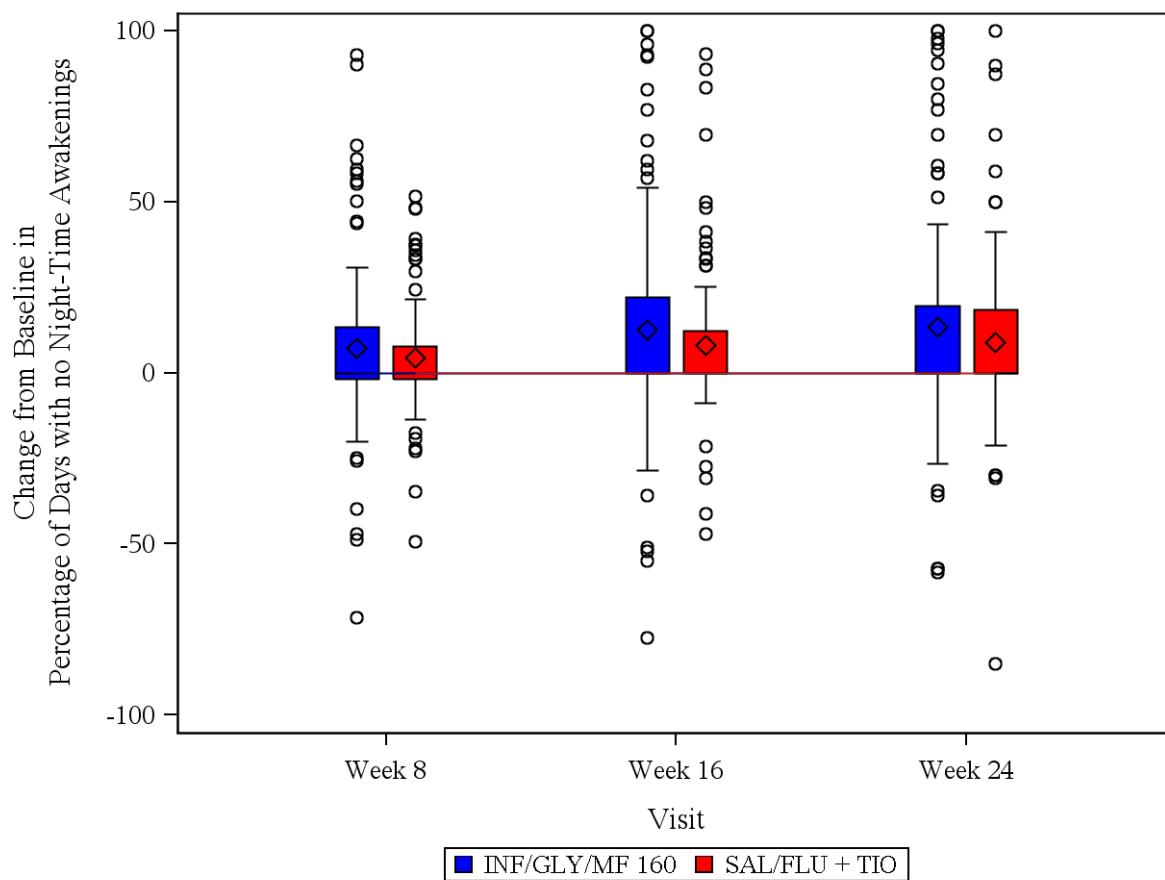
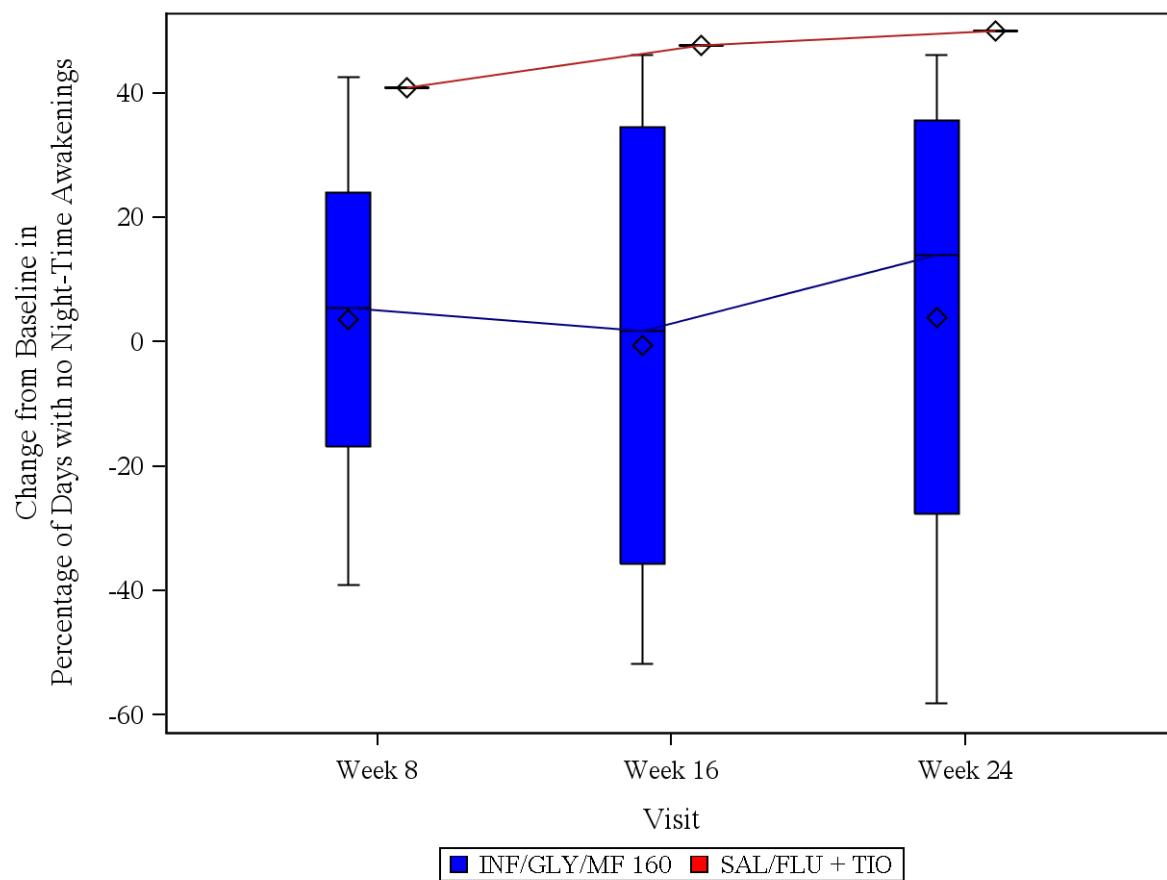


Figure 9.16.4 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by Region (FAS), Region = Others



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

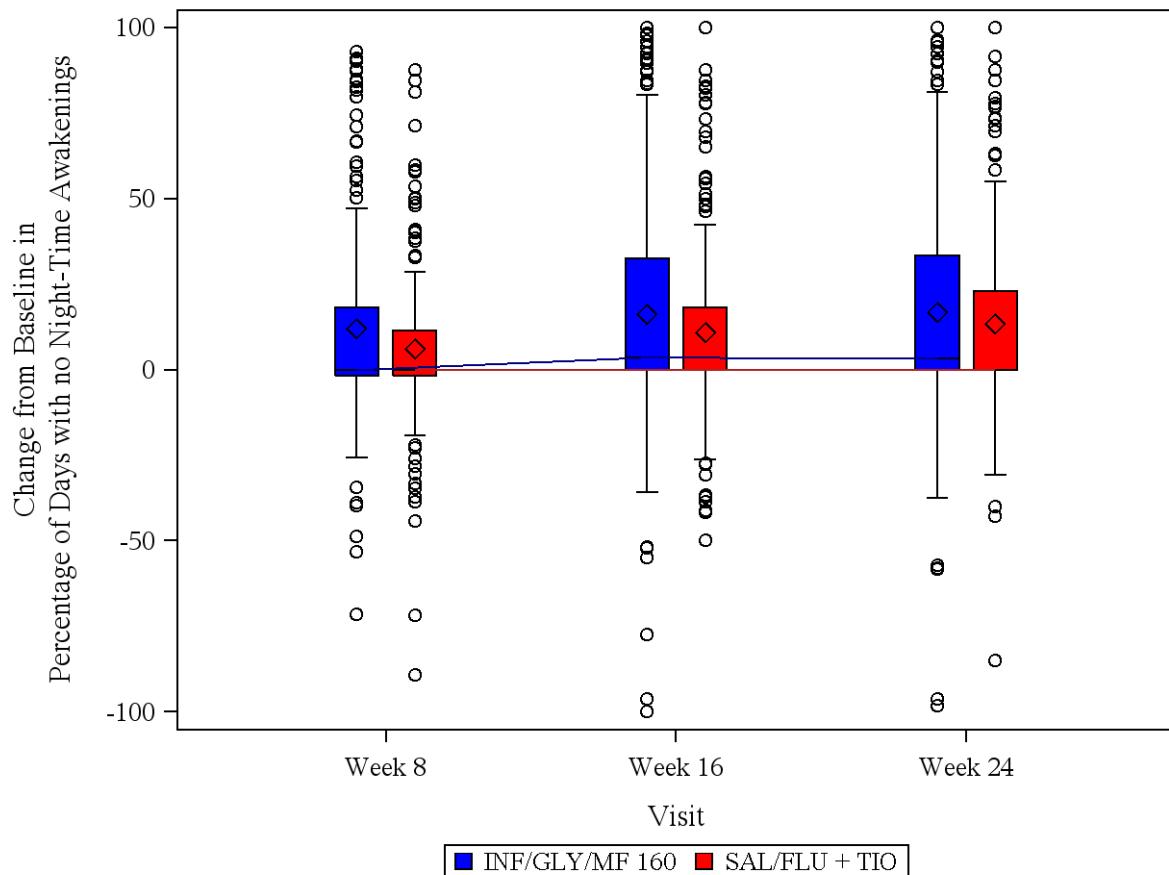
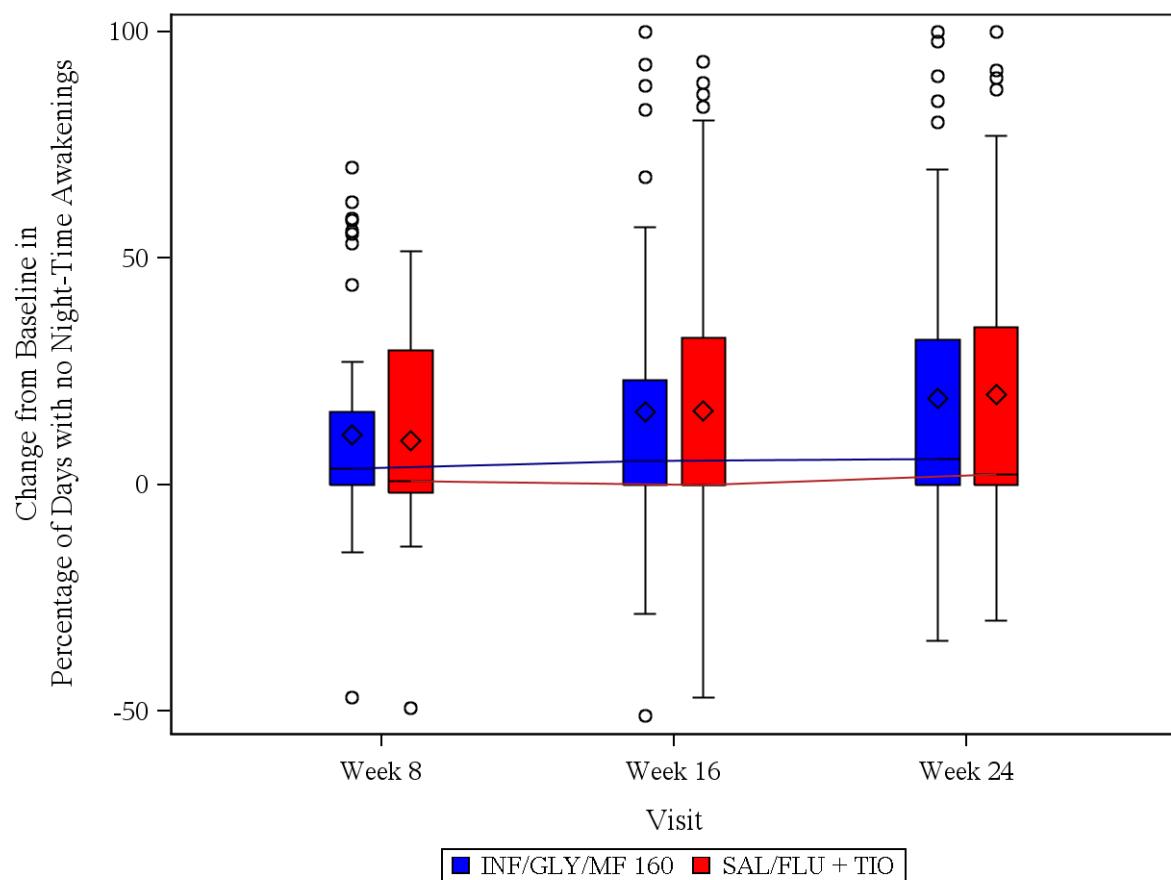
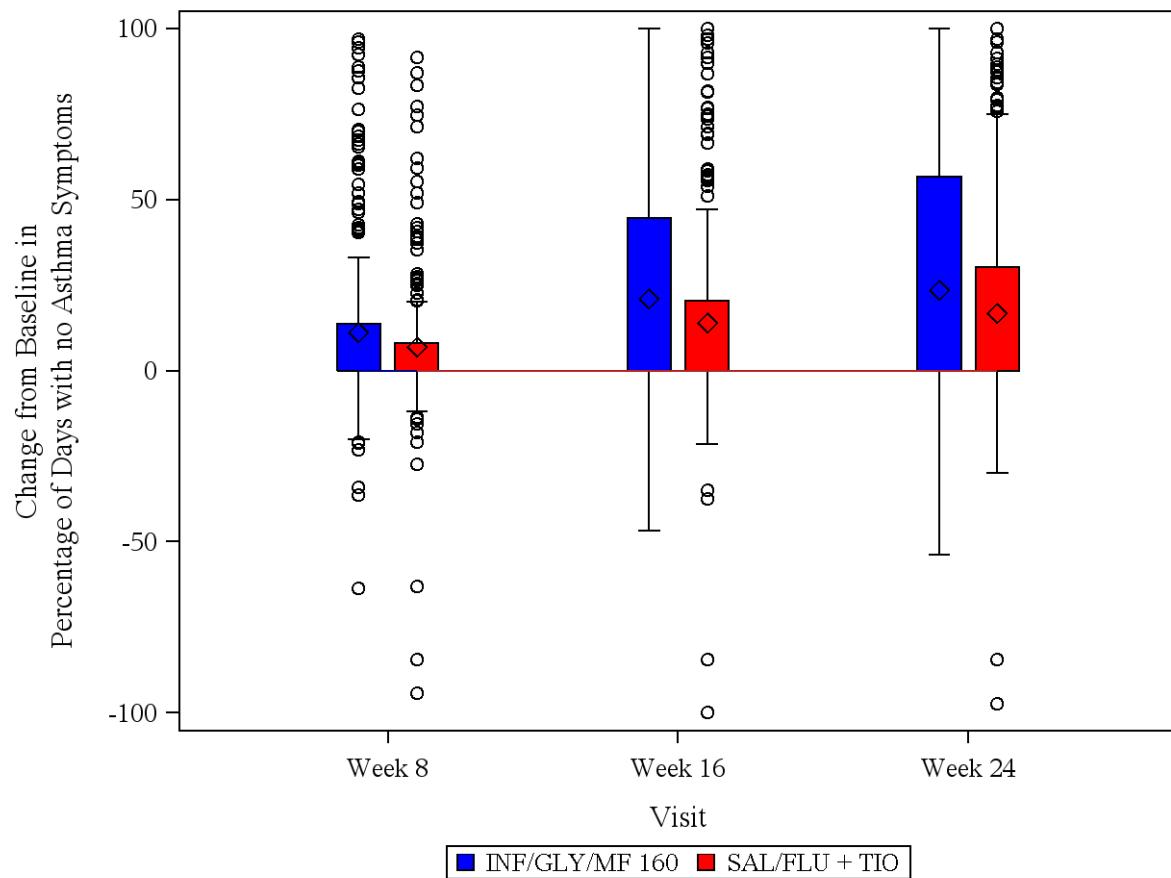


Figure 9.17.2 Symptoms (Percentage of Days with no Night-Time Awakenings) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



9.19 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

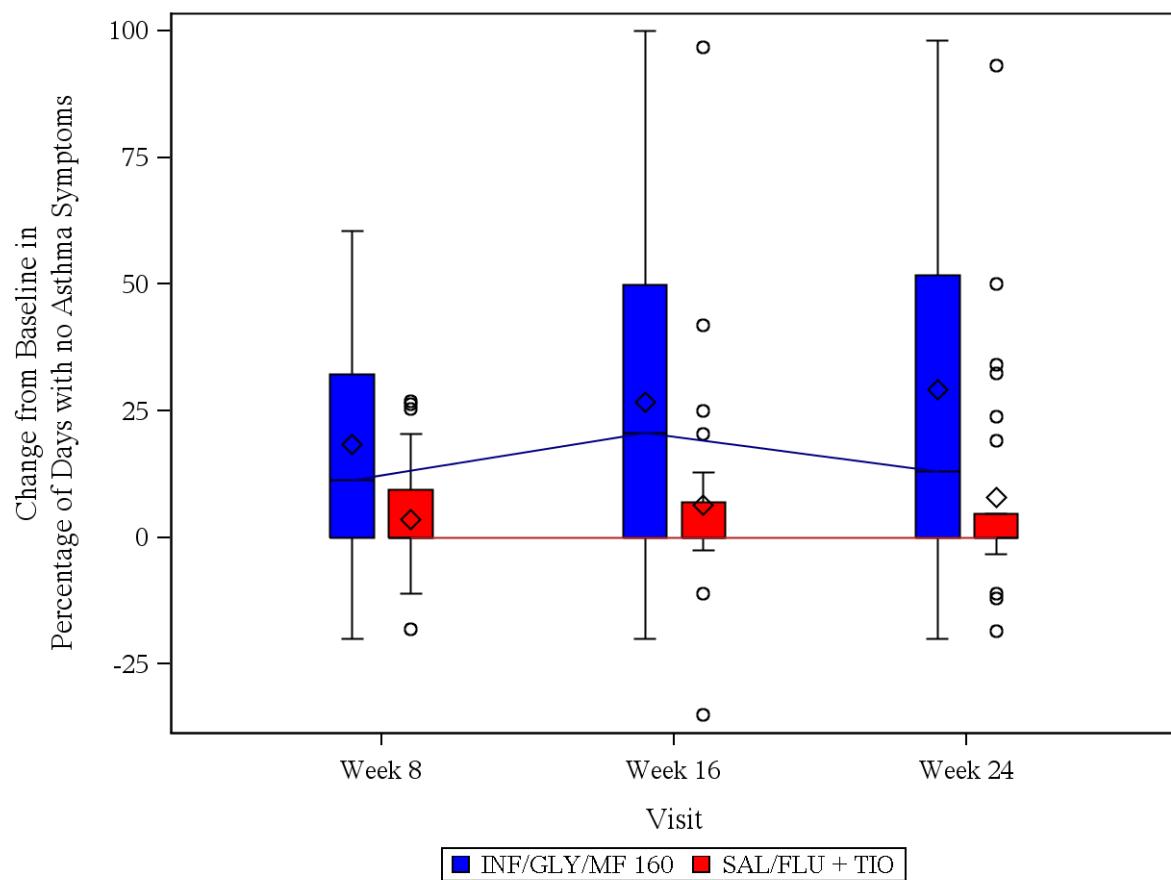


Figure 9.20.2 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Age (FAS), Age = 40-64 years

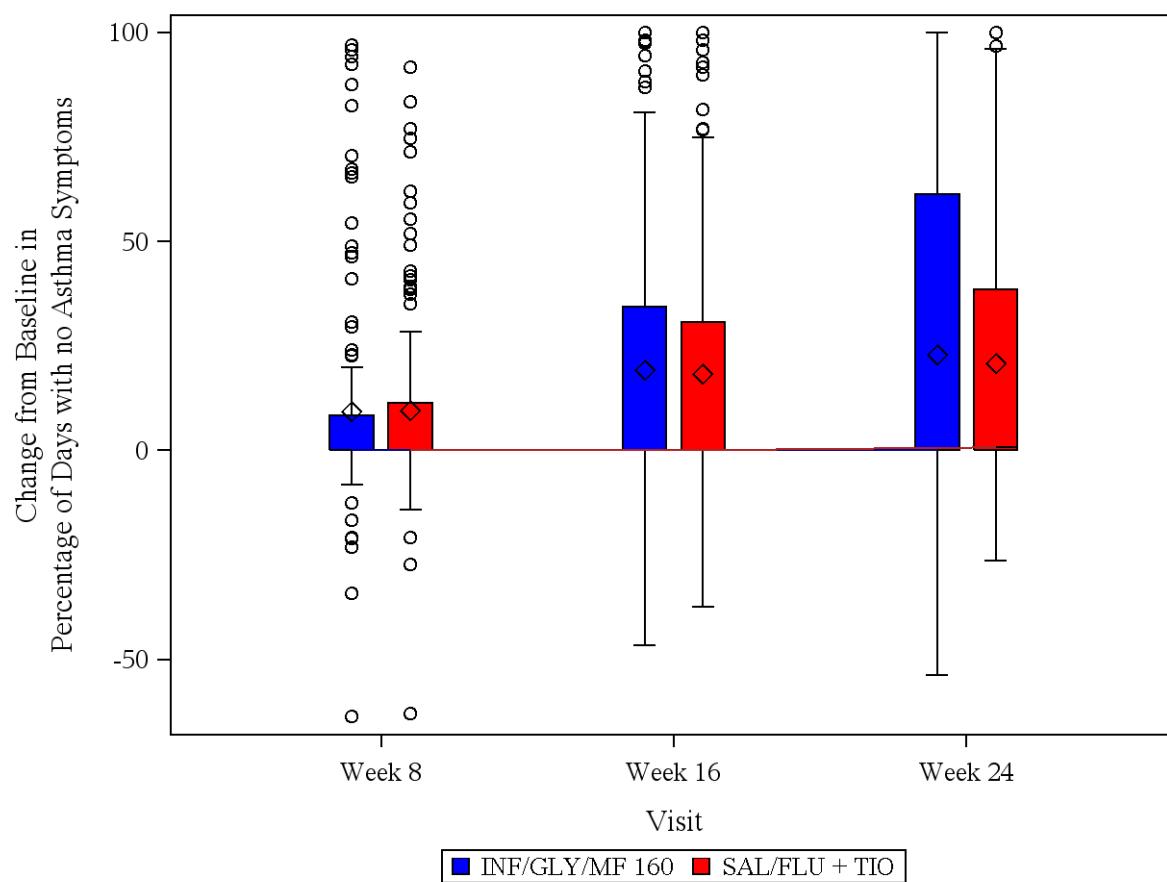
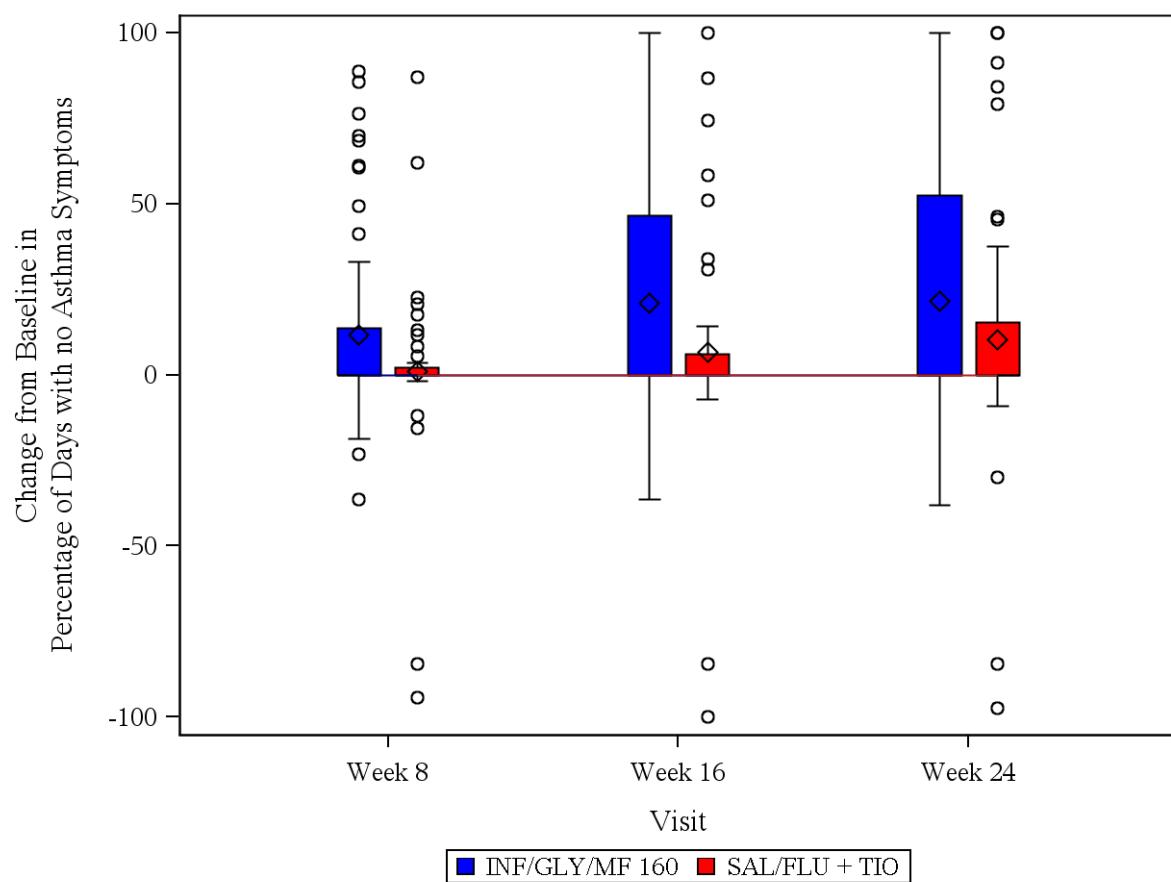


Figure 9.20.3 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

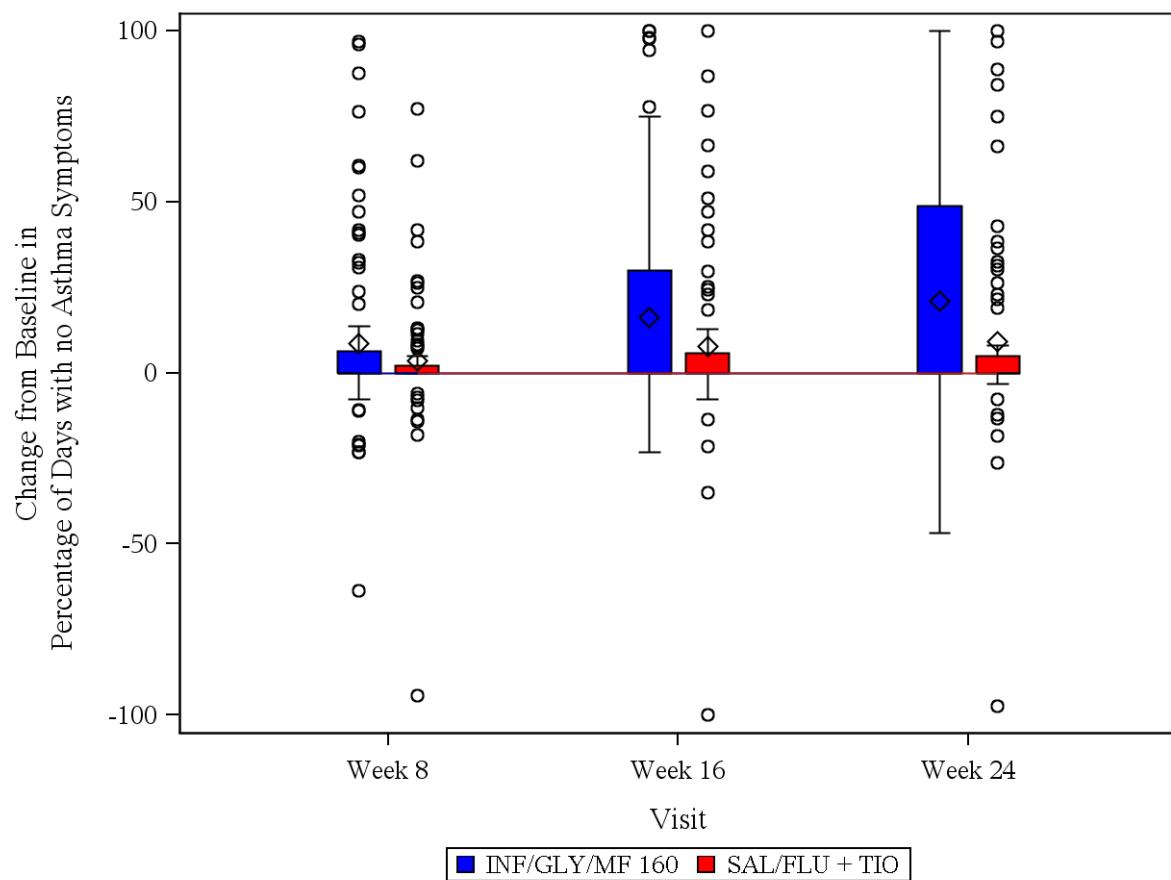
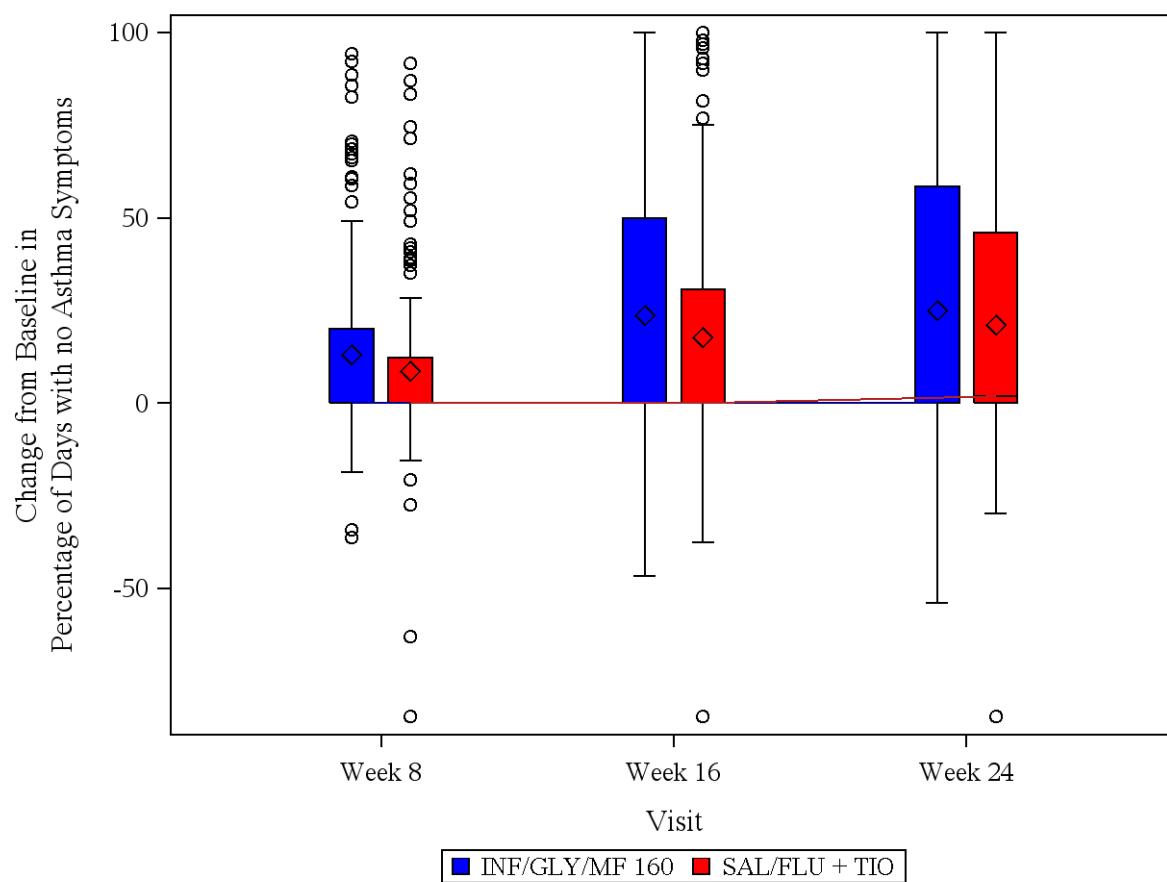


Figure 9.21.2 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Gender (FAS), Gender = Female



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

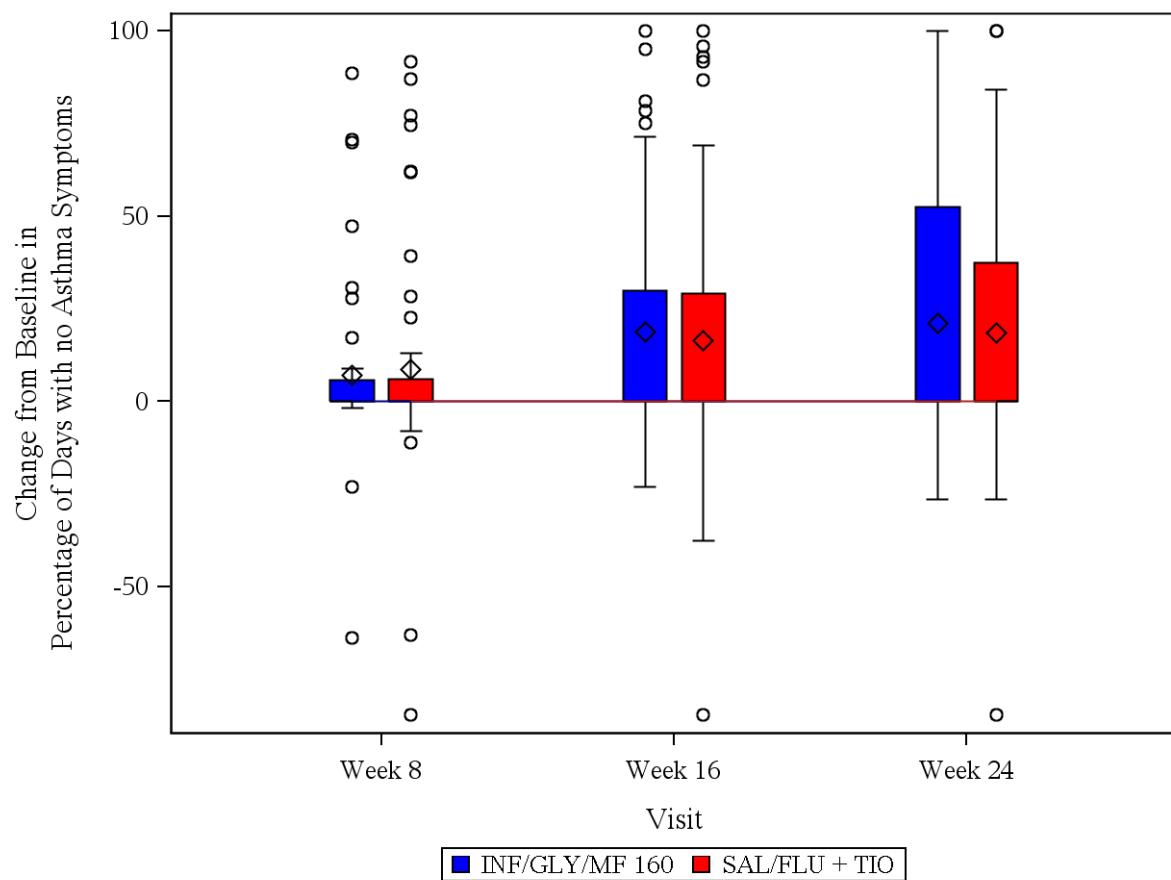


Figure 9.22.2 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Region (FAS), Region = Europe

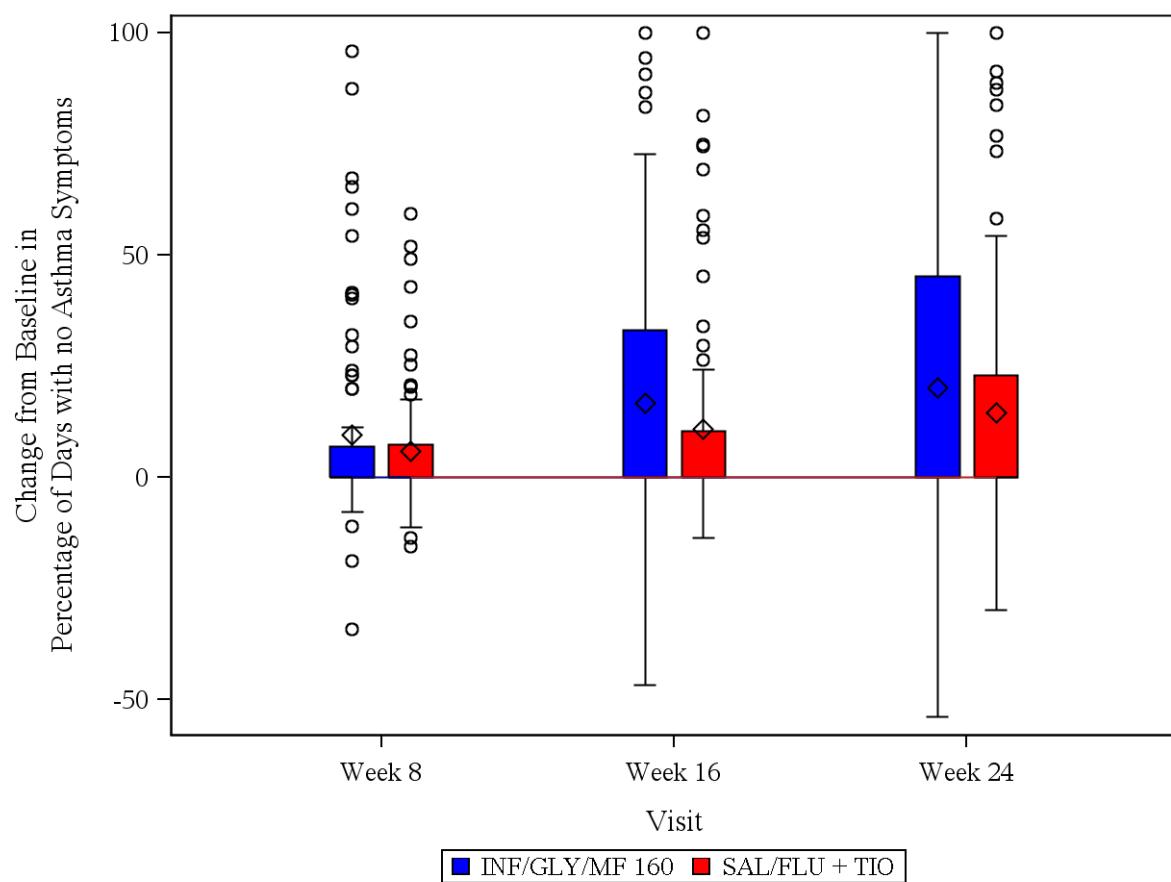


Figure 9.22.3 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Region (FAS), Region = Latin America

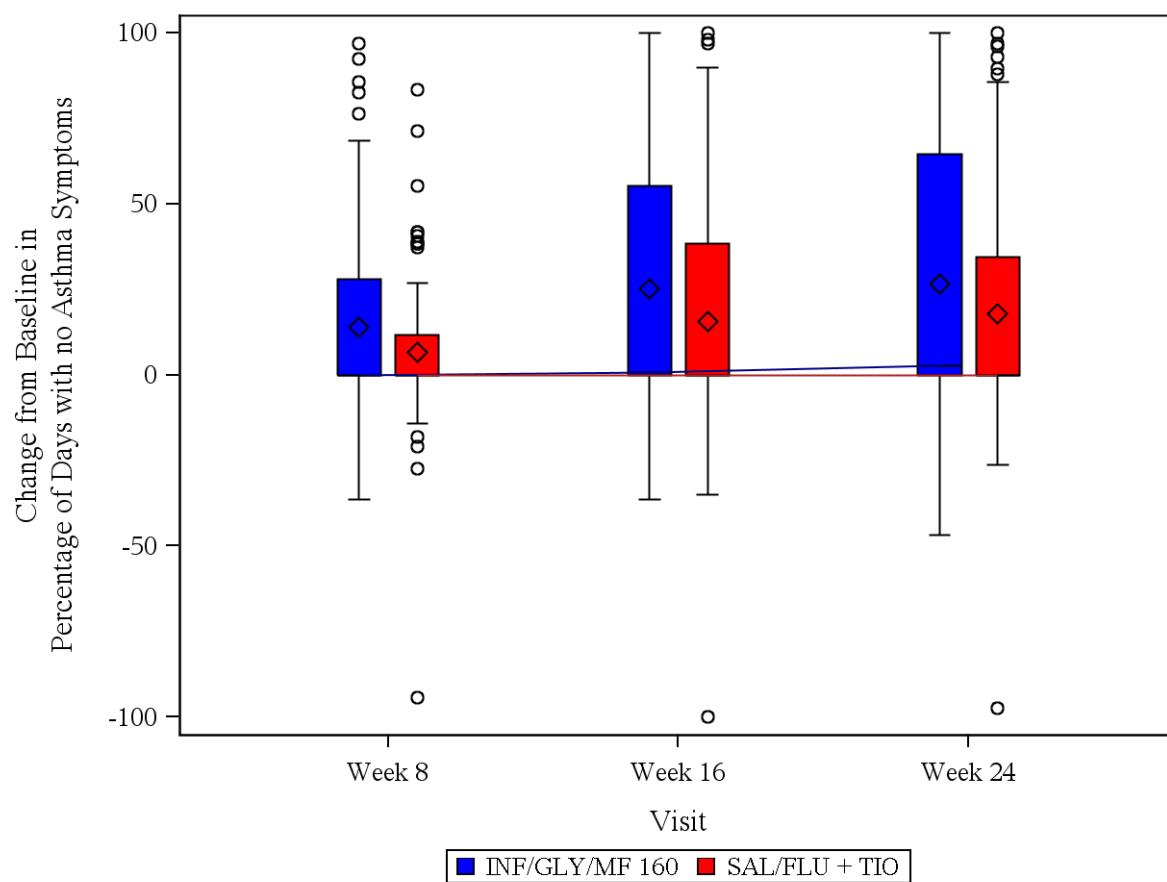
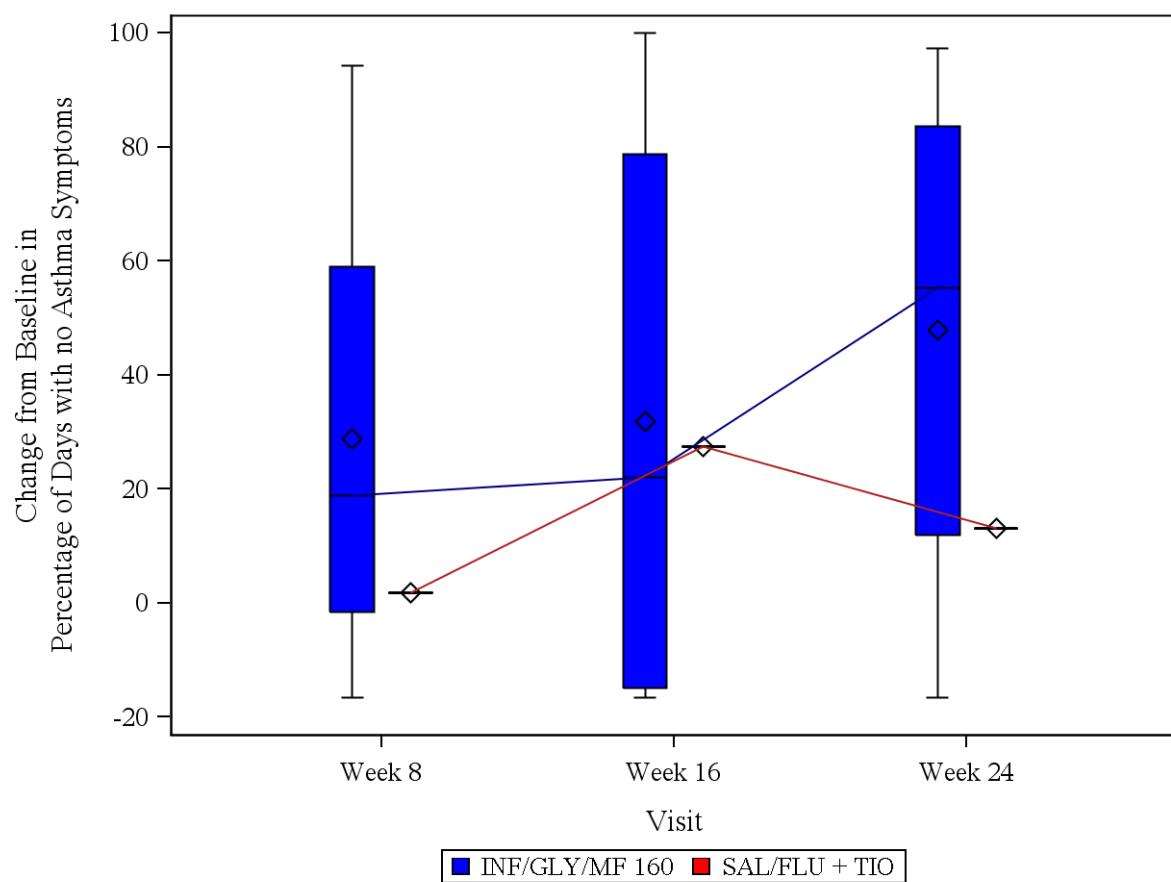


Figure 9.22.4 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by Region (FAS), Region = Others



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

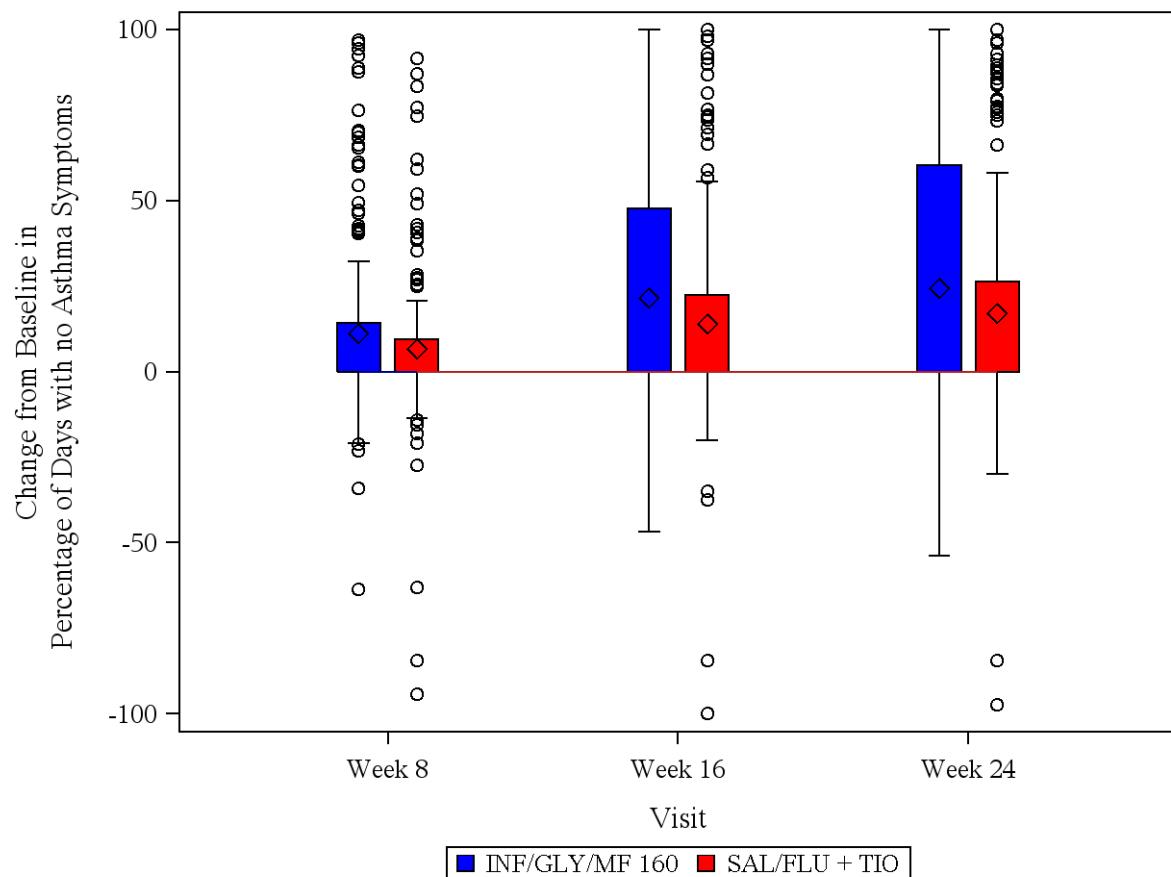
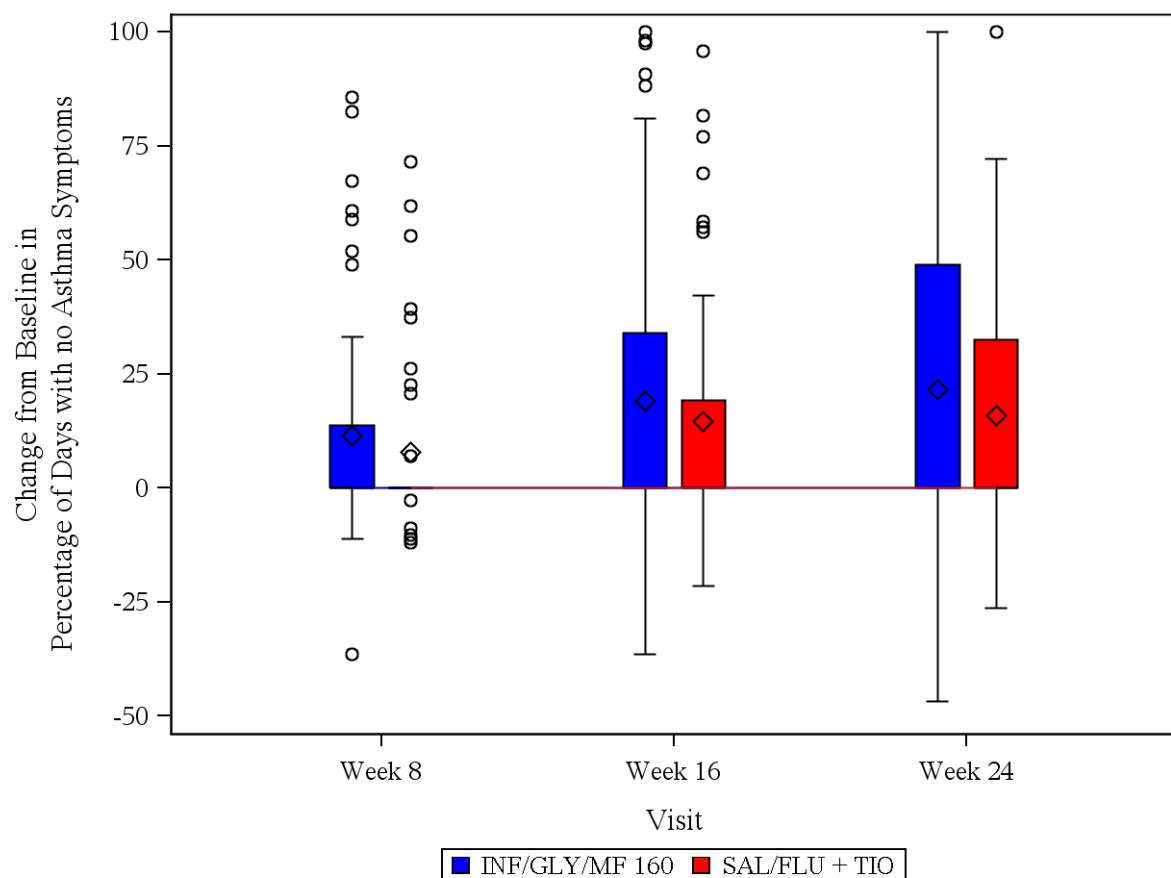
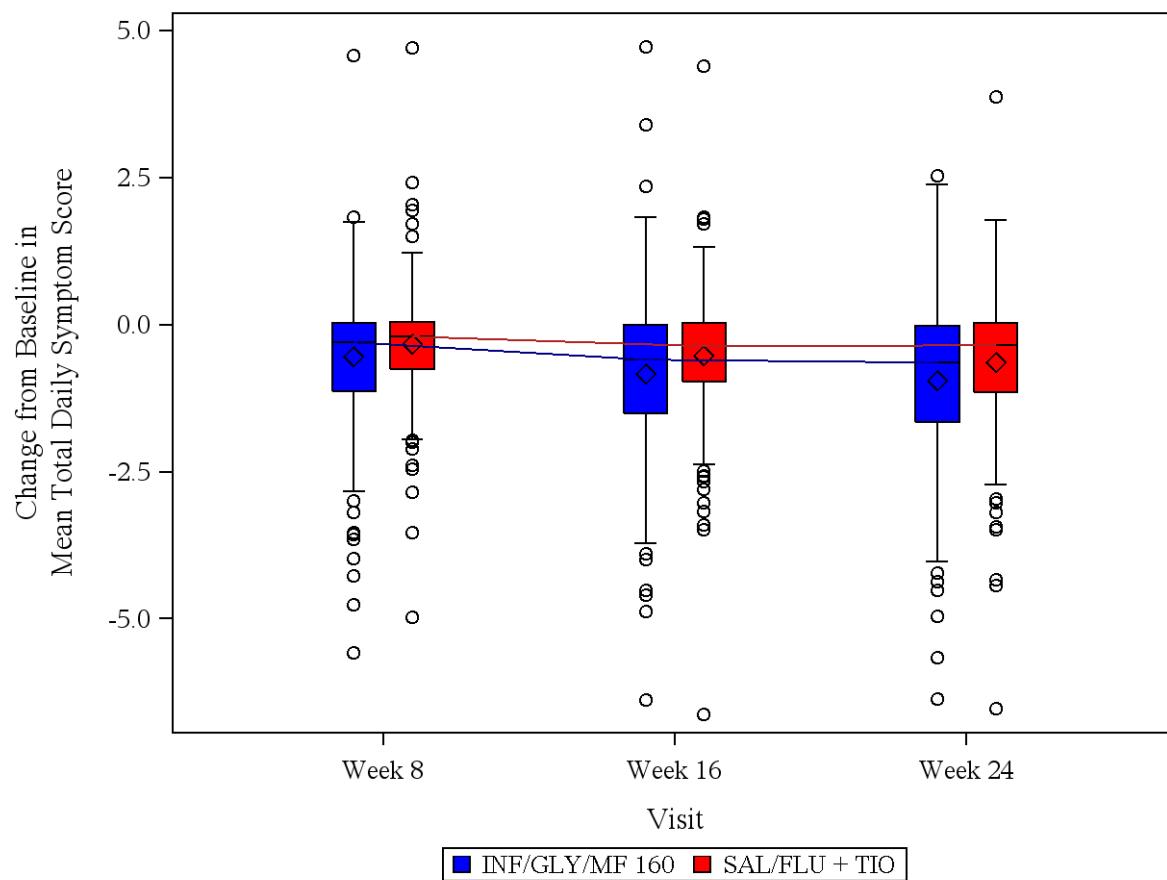


Figure 9.23.2 Symptoms (Percentage of Days with no Asthma Symptoms) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.25 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

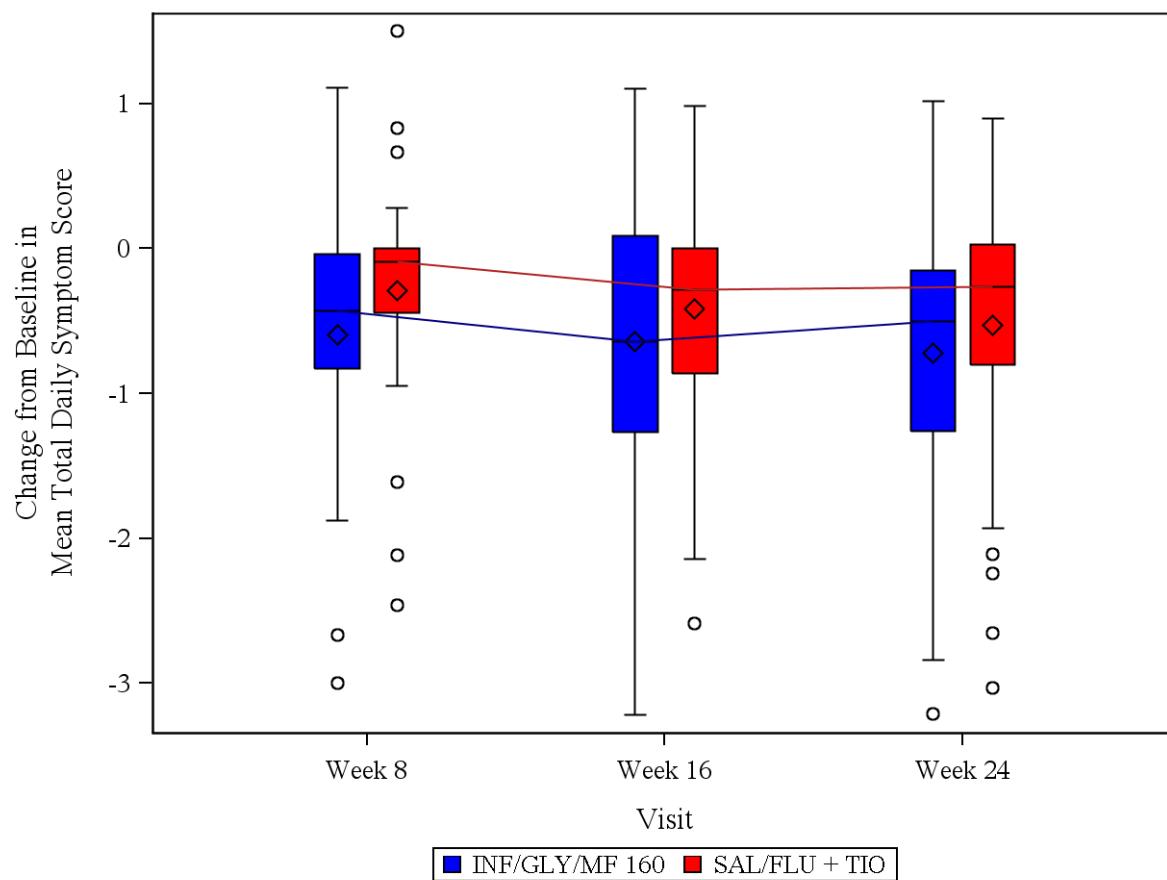


Figure 9.26.2 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Age (FAS), Age = 40-64 years

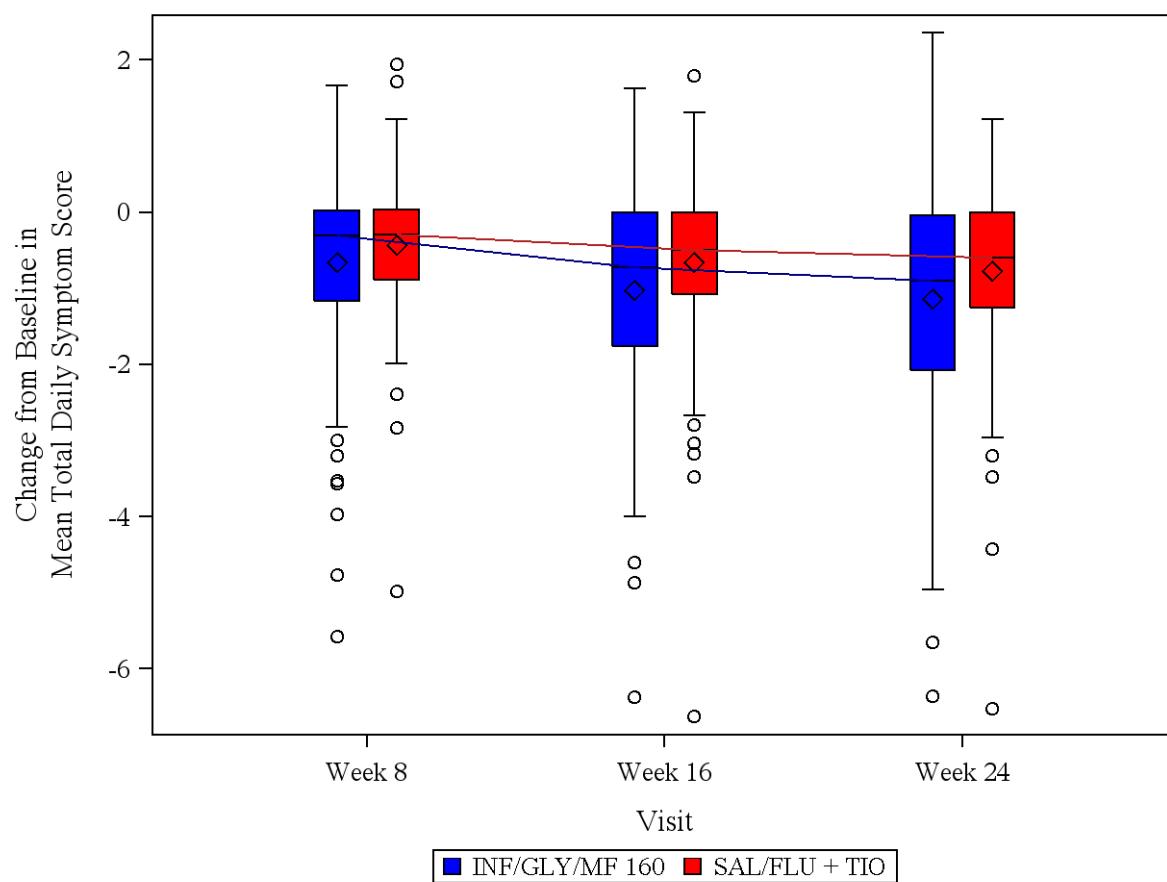
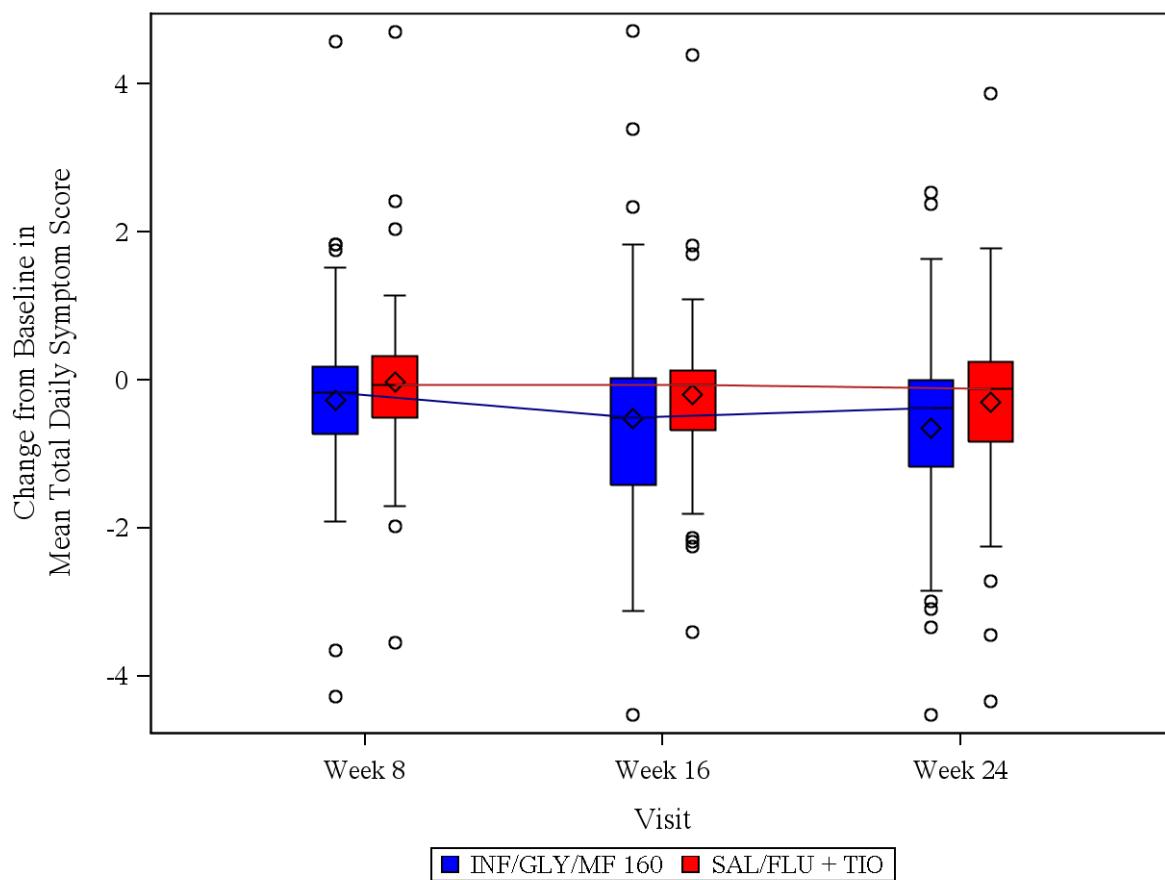


Figure 9.26.3 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

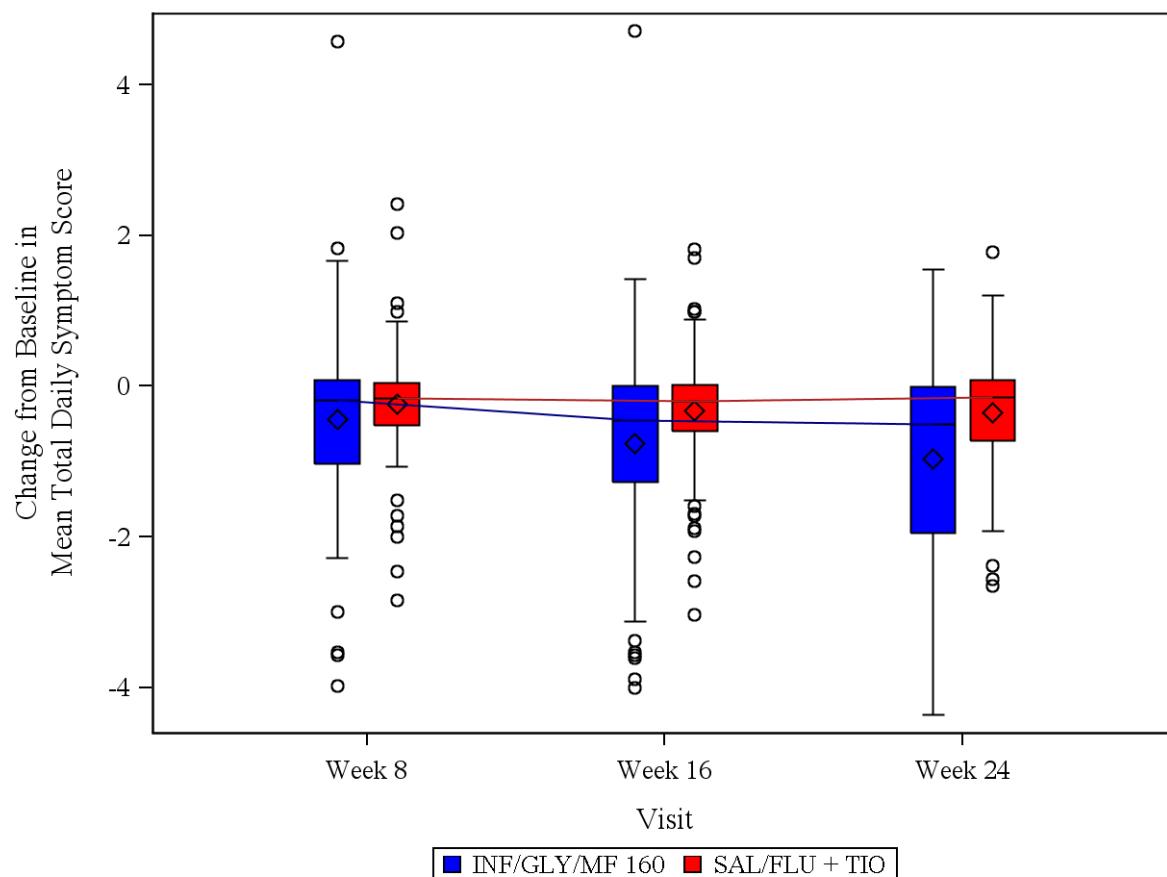
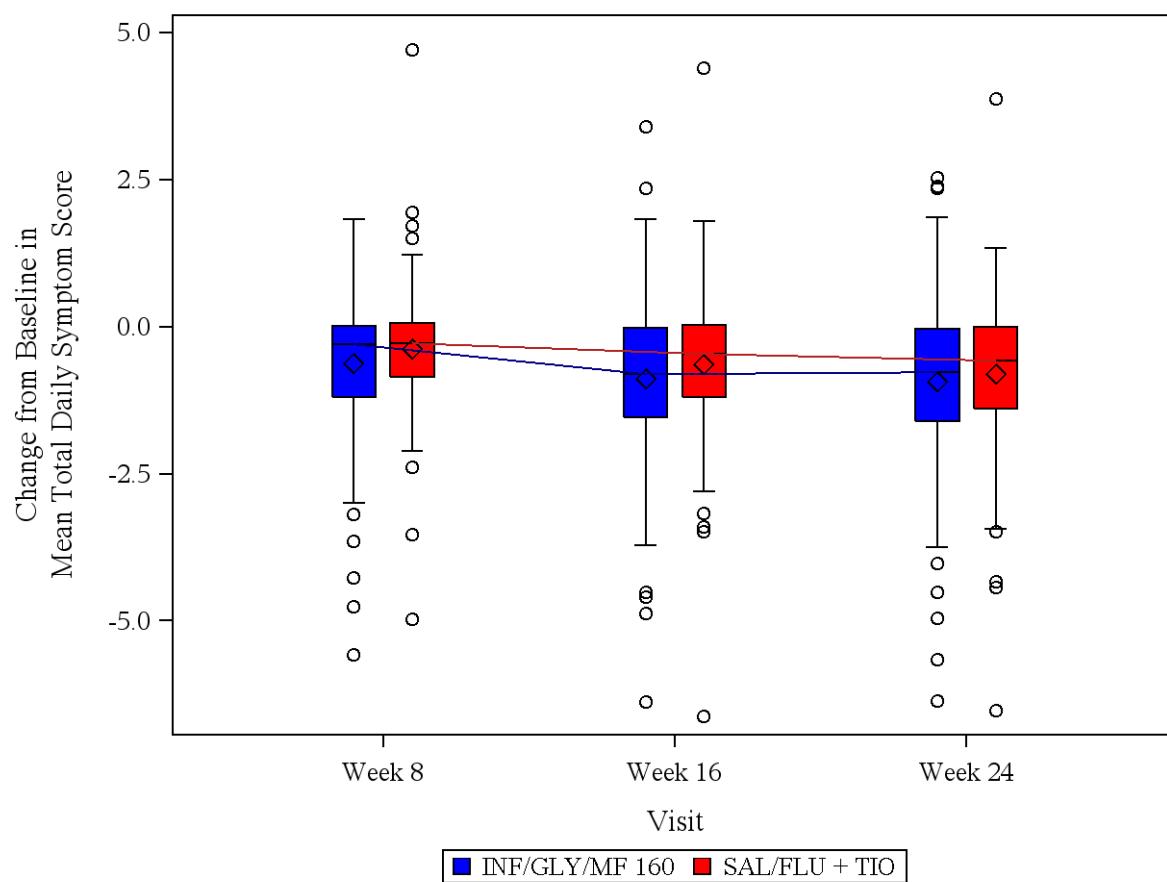


Figure 9.27.2 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Gender (FAS), Gender = Female



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

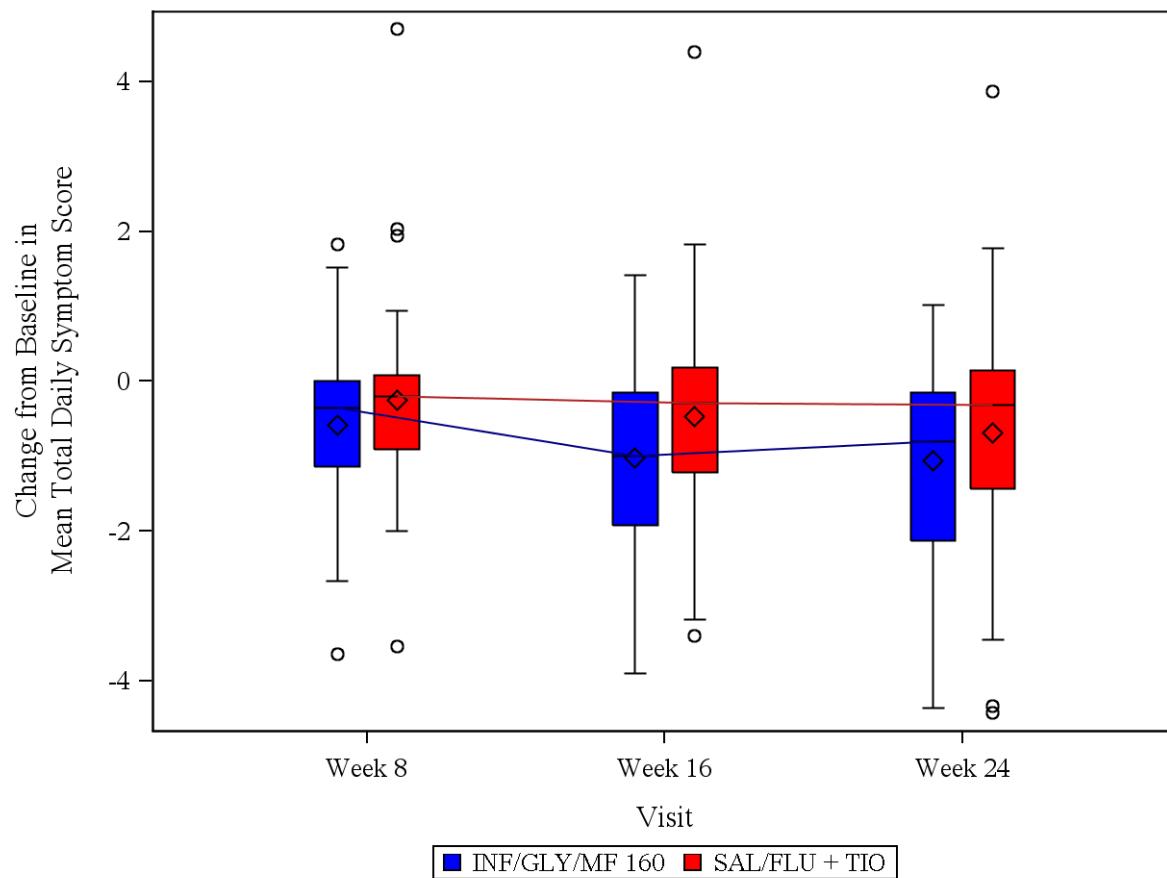


Figure 9.28.2 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Region (FAS), Region = Europe

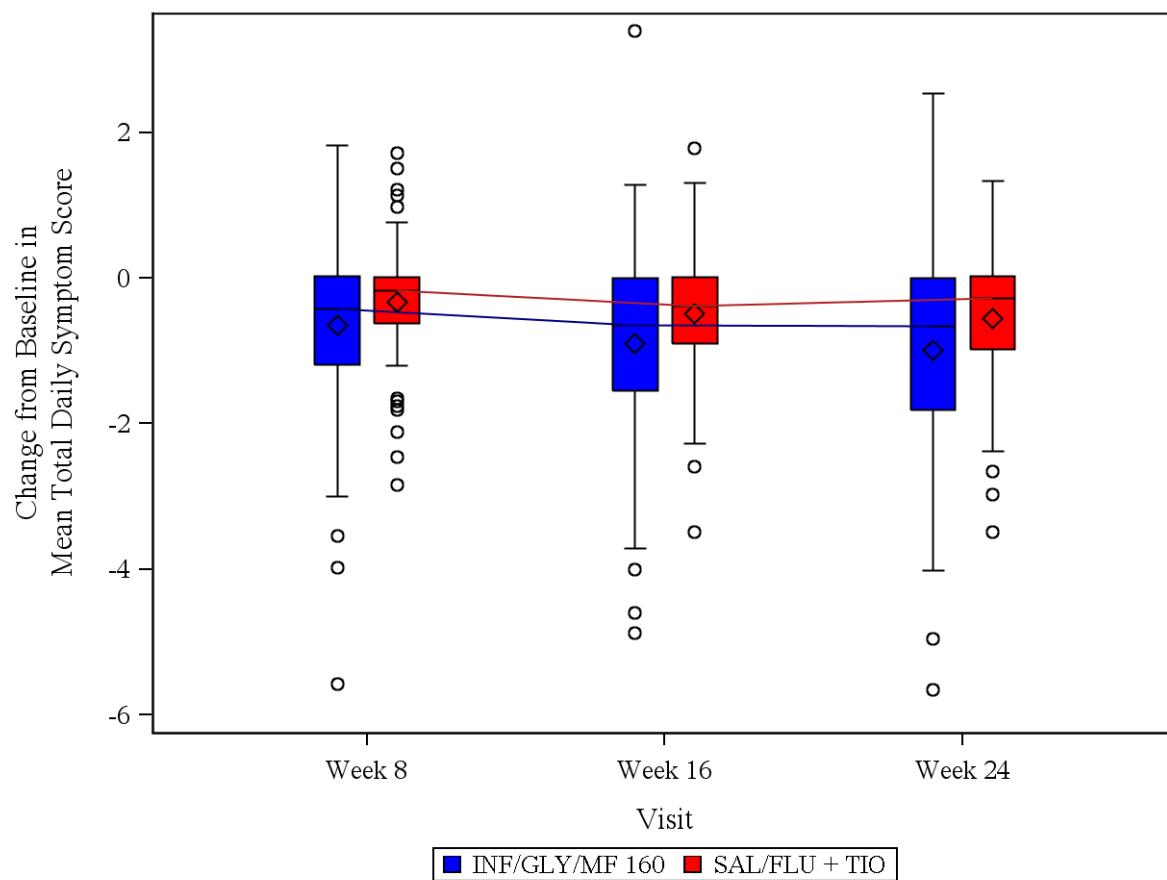


Figure 9.28.3 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Region (FAS), Region = Latin America

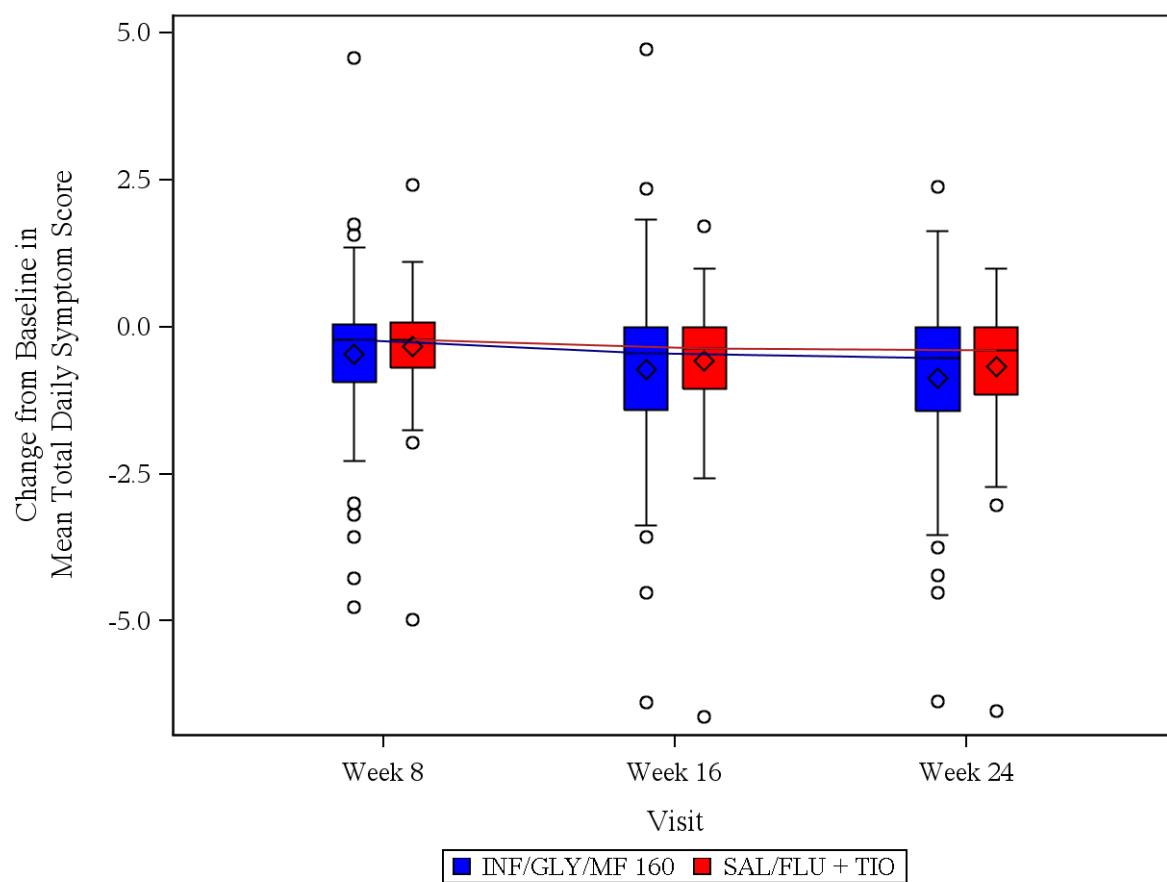
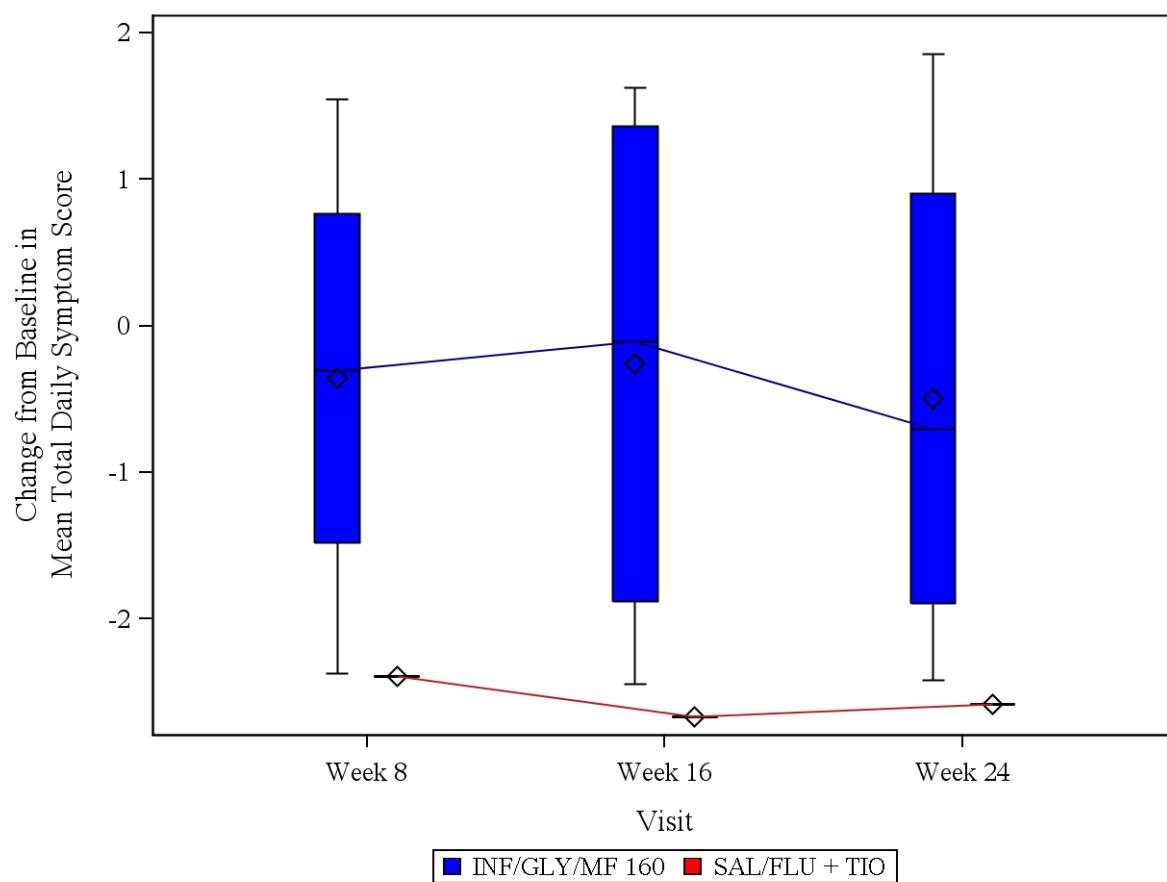


Figure 9.28.4 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by Region (FAS), Region = Others



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

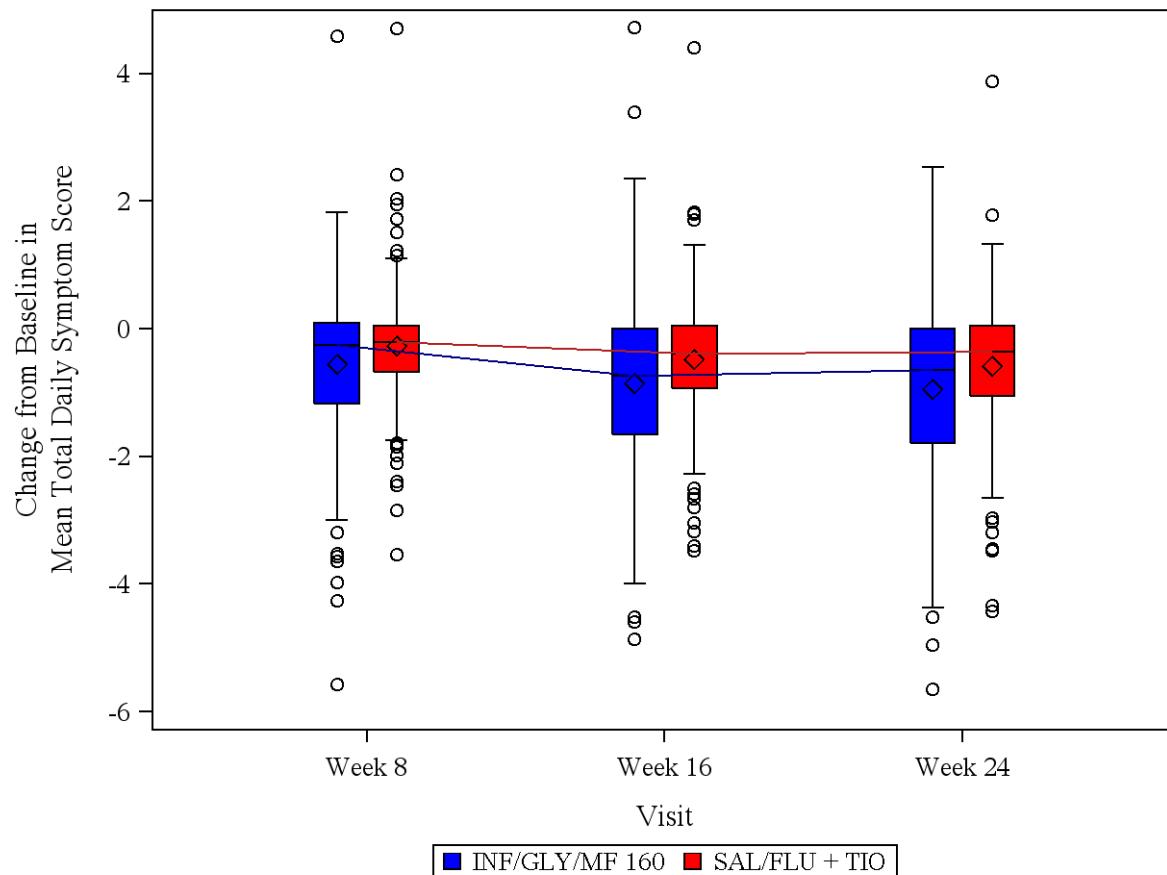
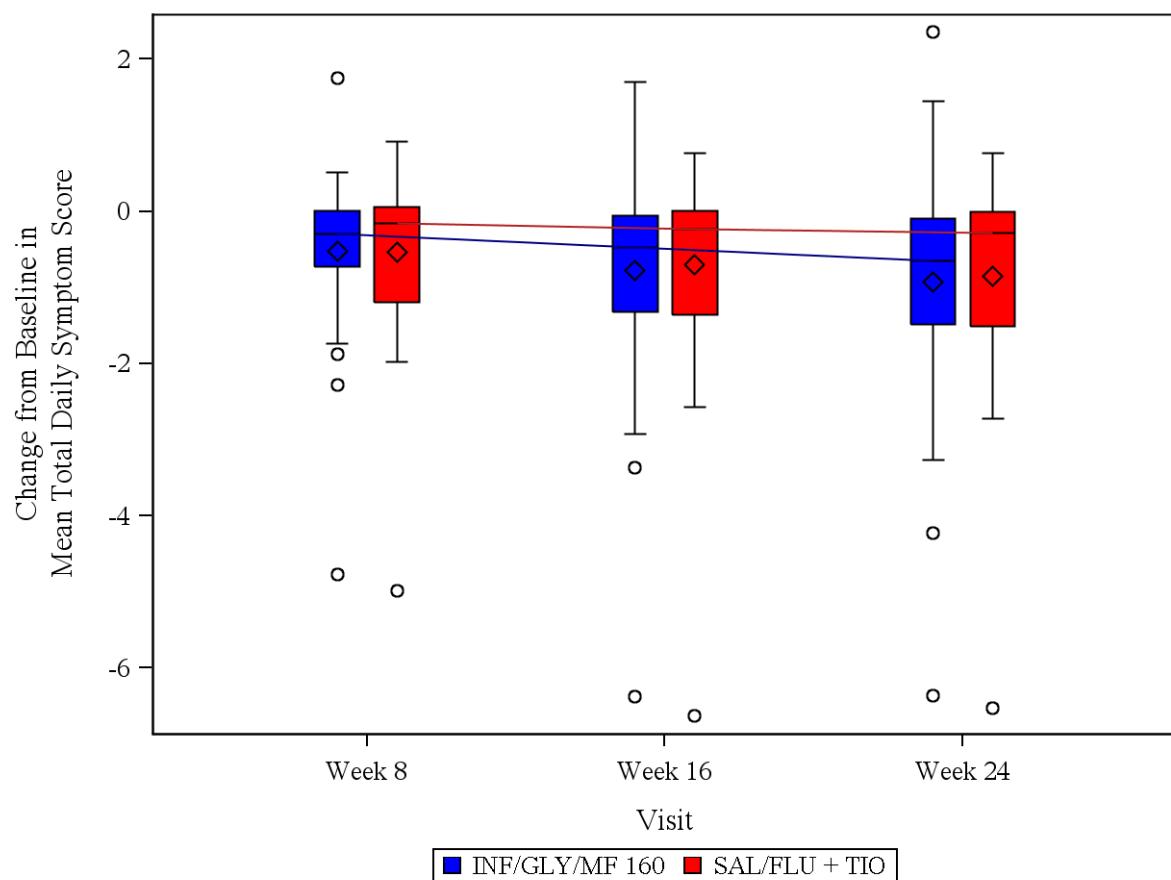
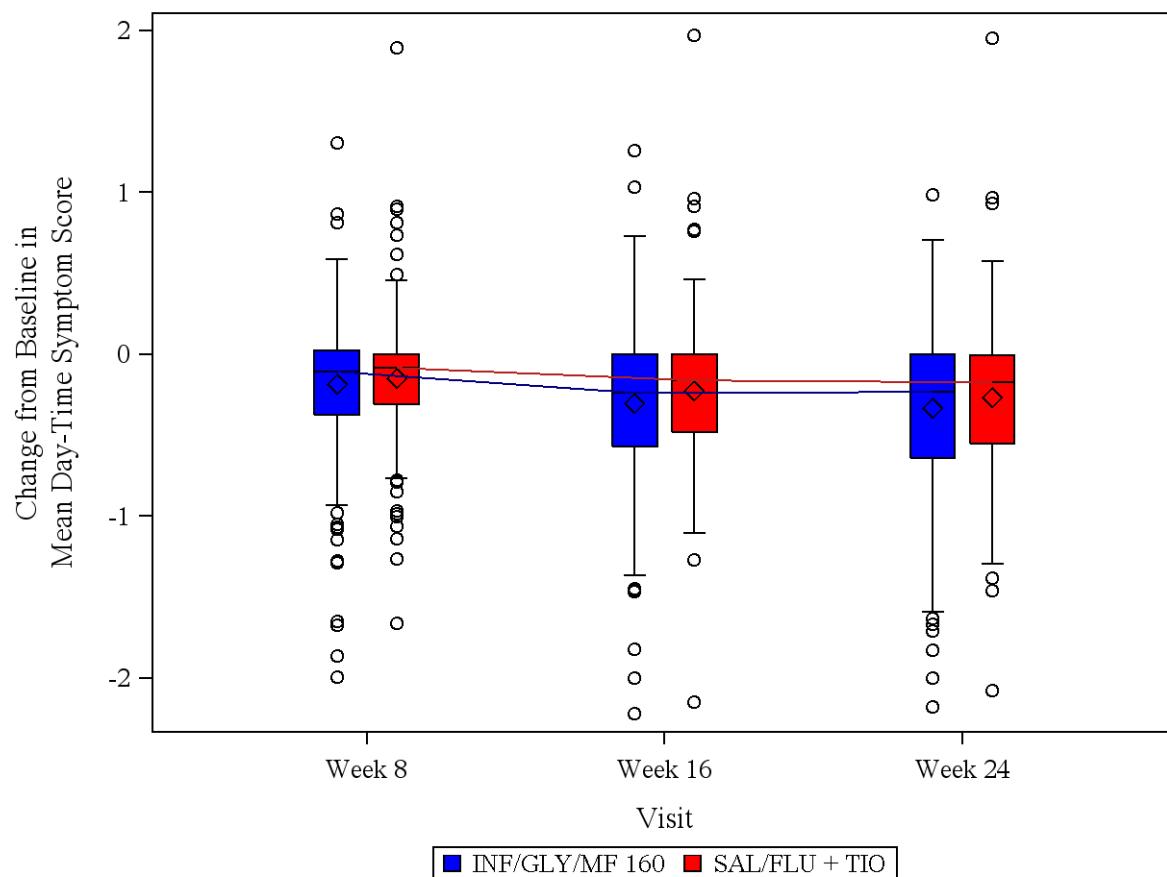


Figure 9.29.2 Symptoms (Mean Total Daily Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



9.31 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

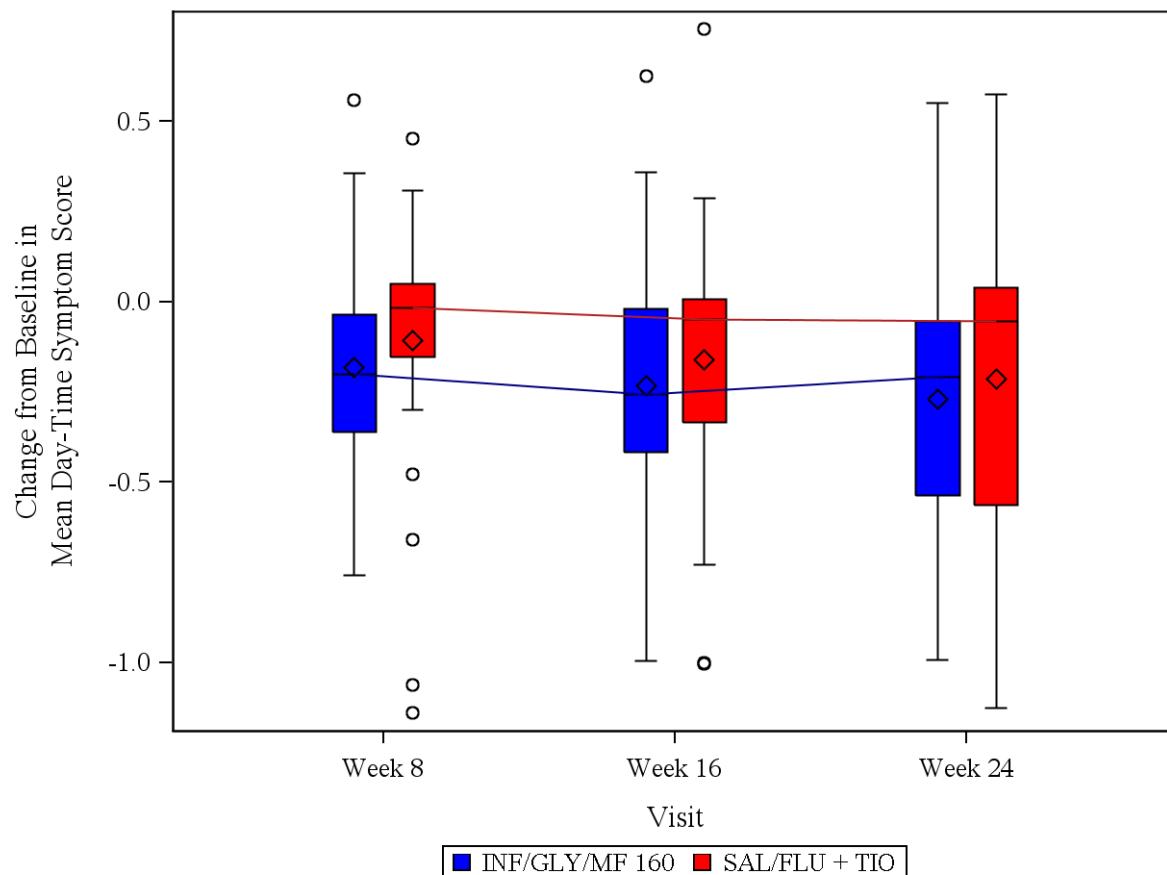


Figure 9.32.2 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Age (FAS), Age = 40-64 years

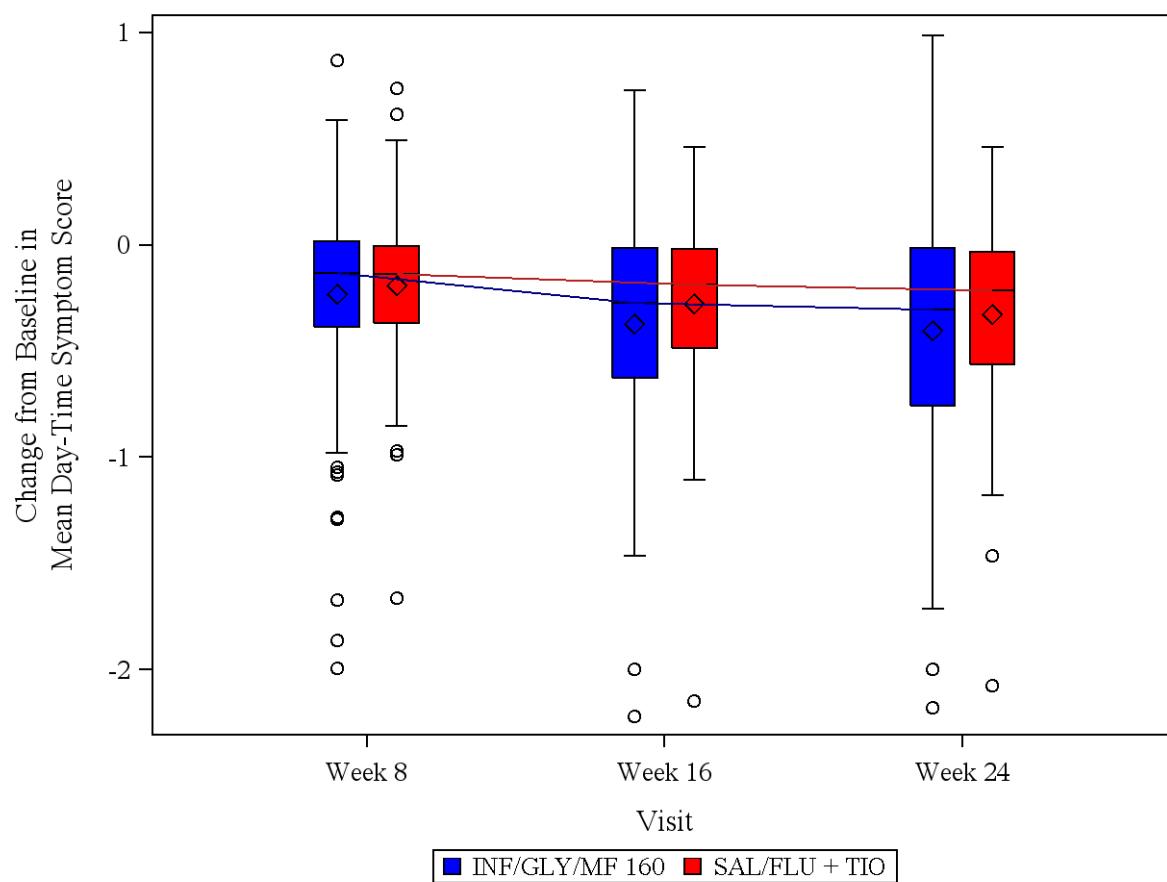
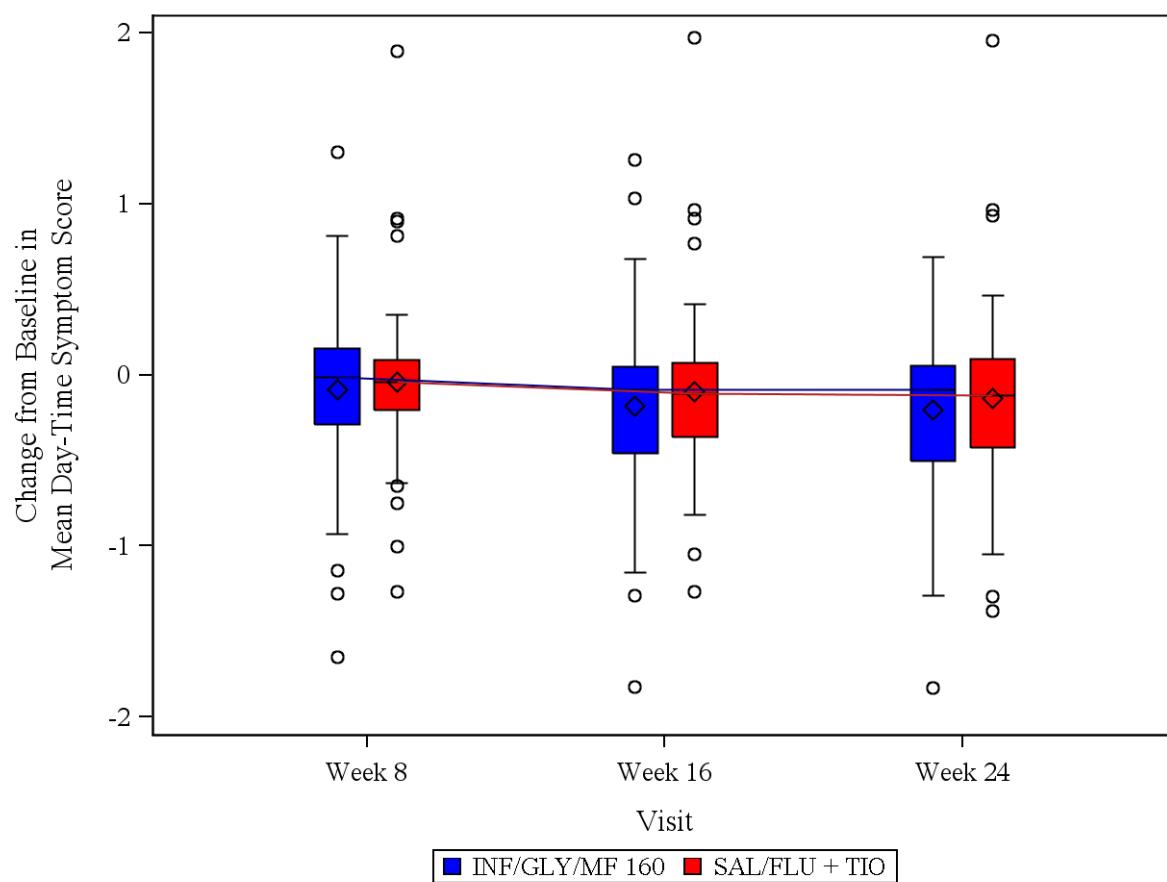


Figure 9.32.3 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

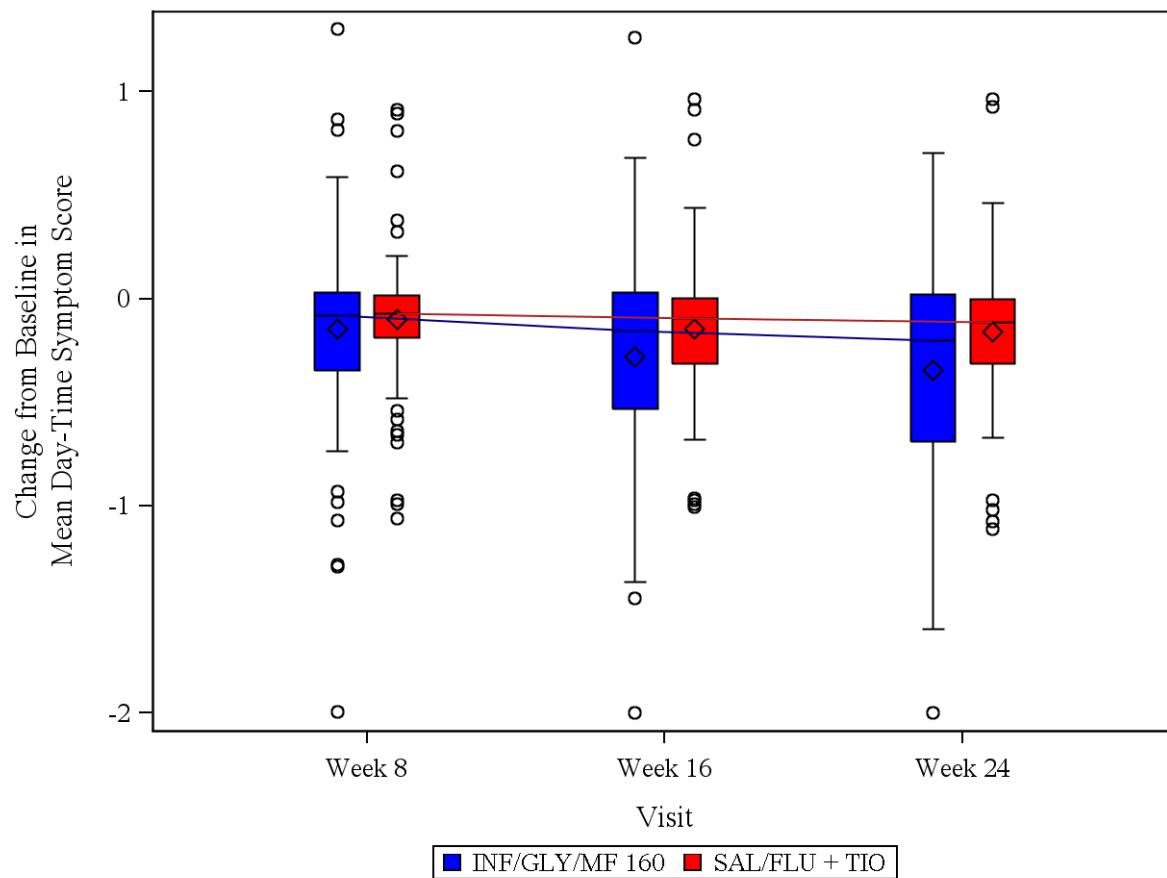
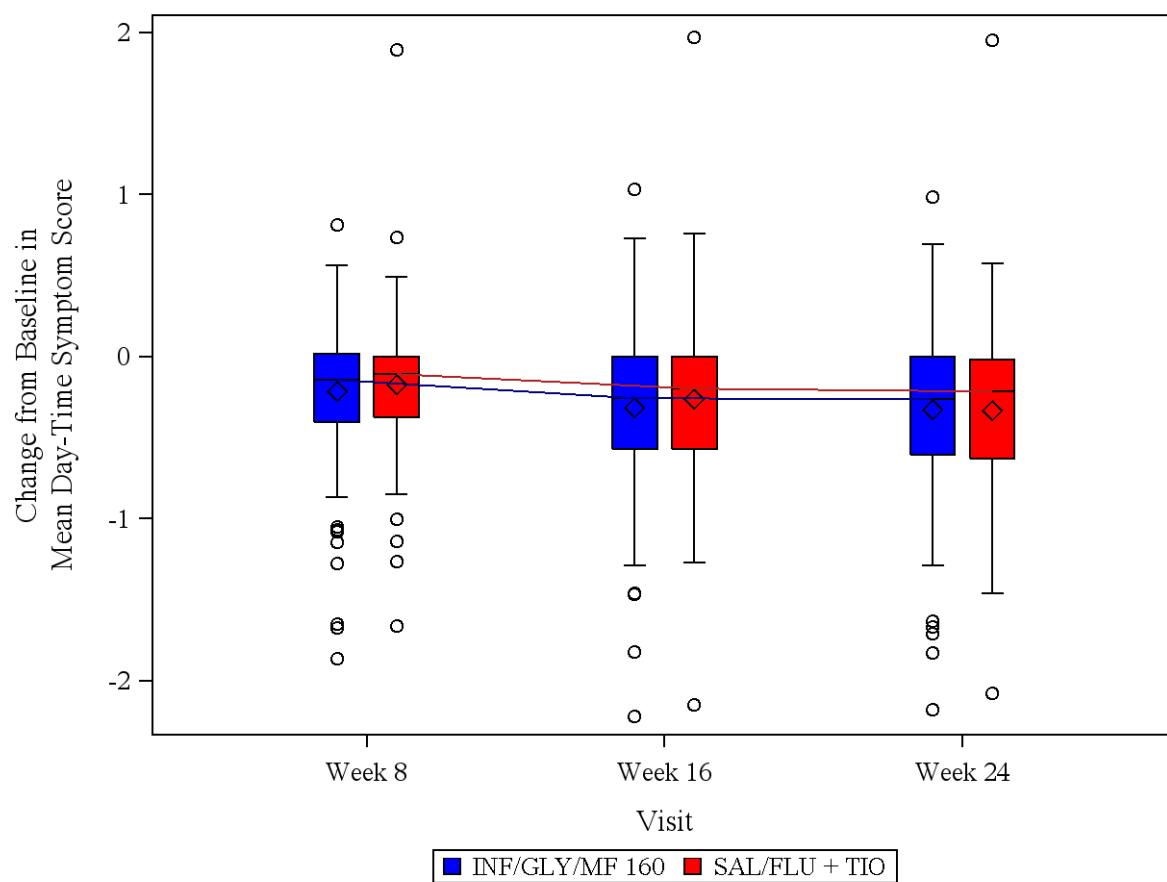


Figure 9.33.2 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Gender (FAS), Gender = Female



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

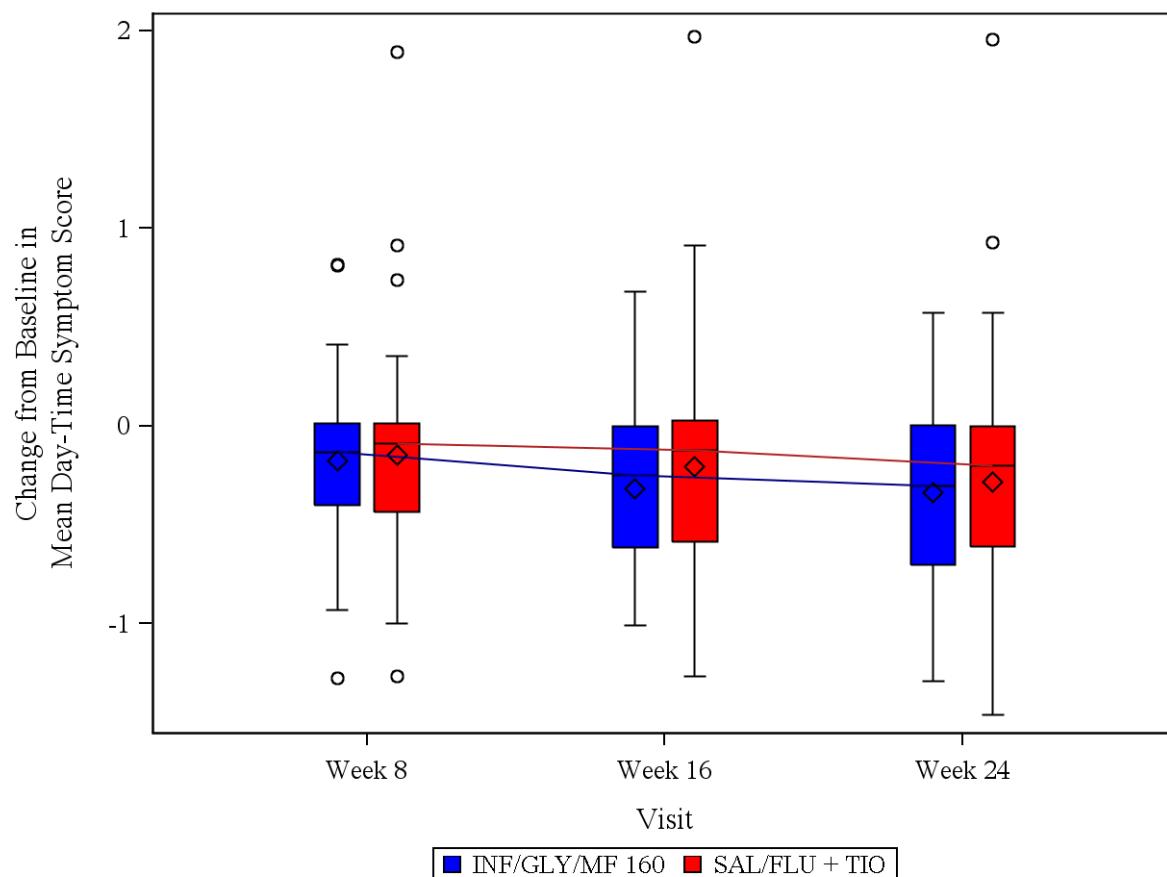


Figure 9.34.2 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Region (FAS), Region = Europe

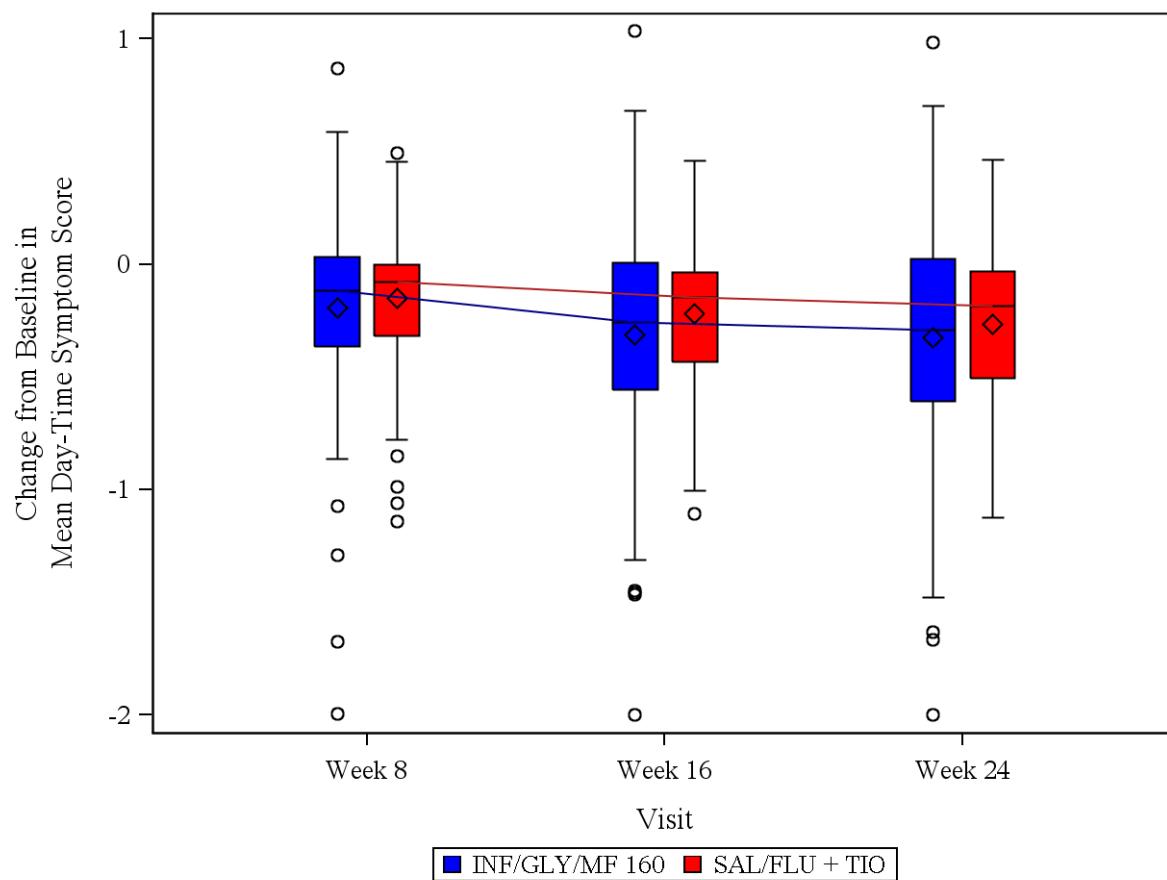


Figure 9.34.3 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Region (FAS), Region = Latin America

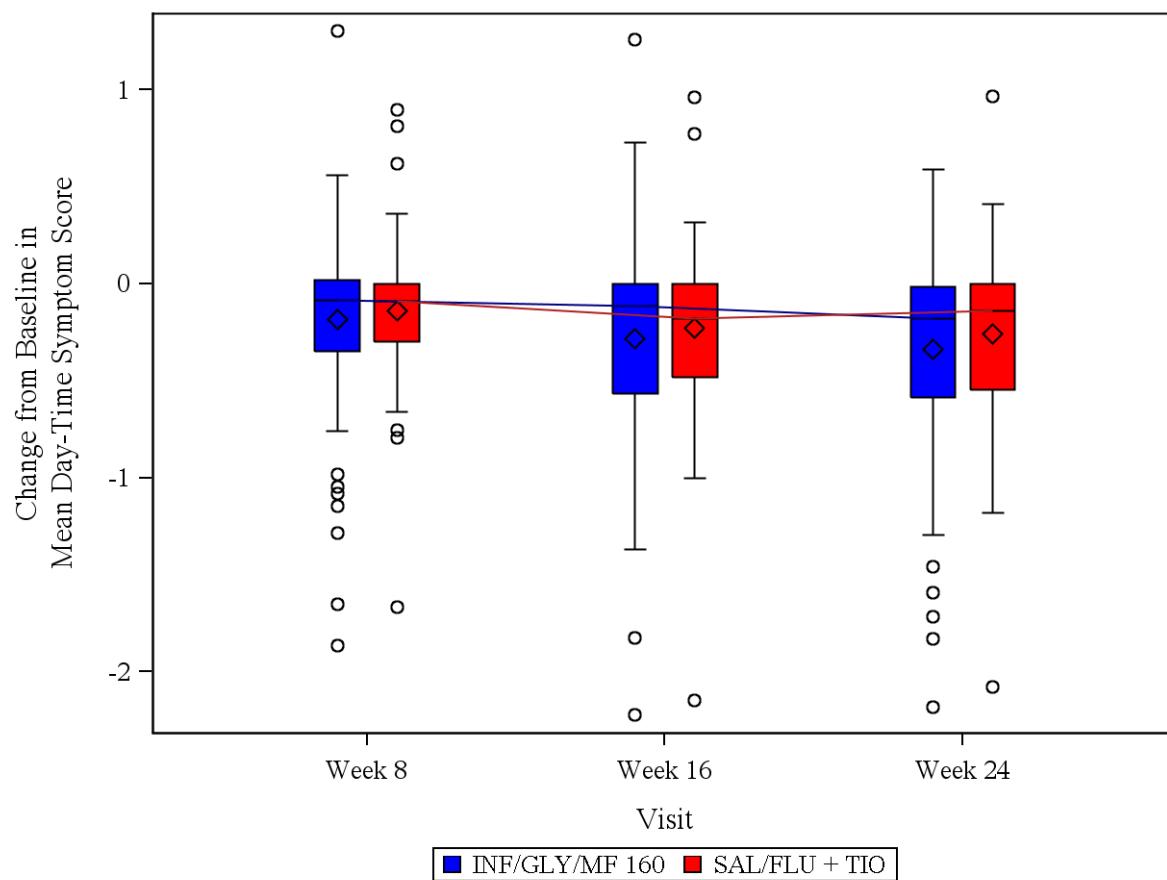
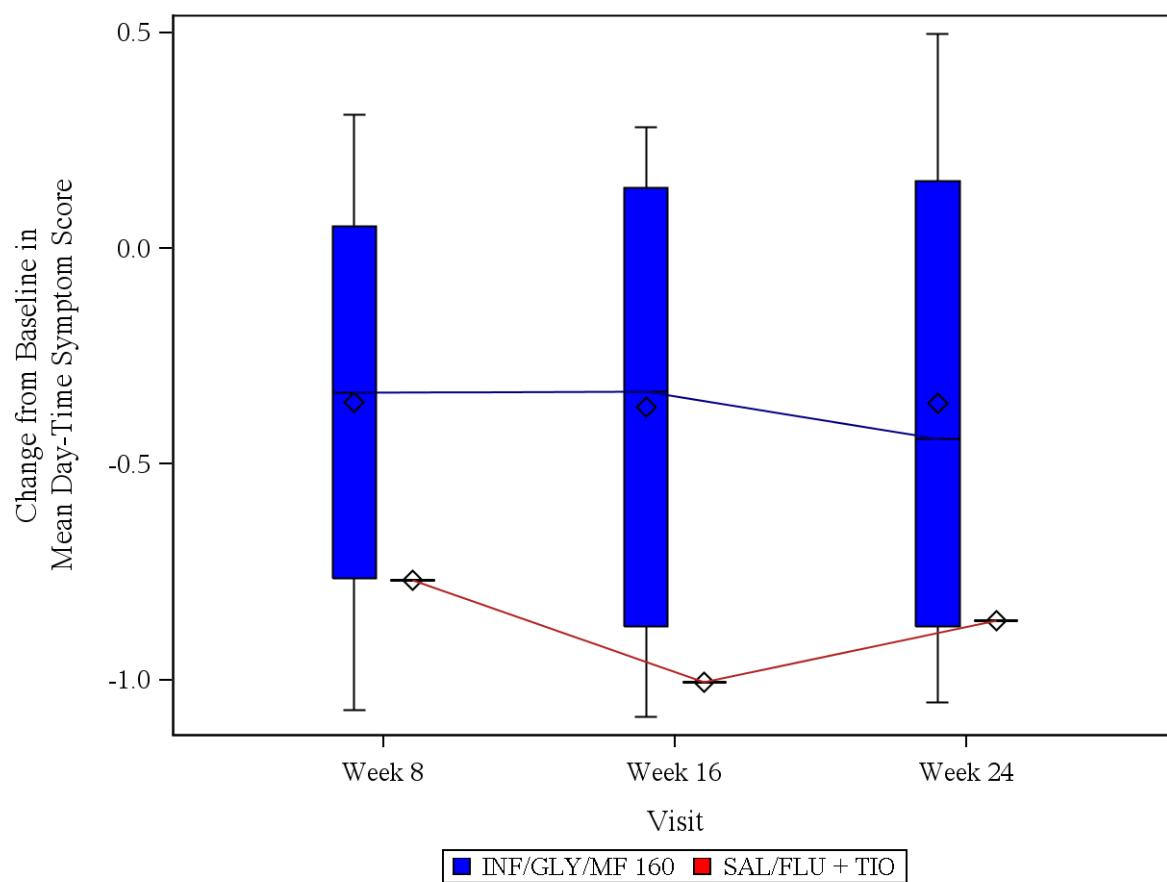


Figure 9.34.4 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by Region (FAS), Region = Others



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

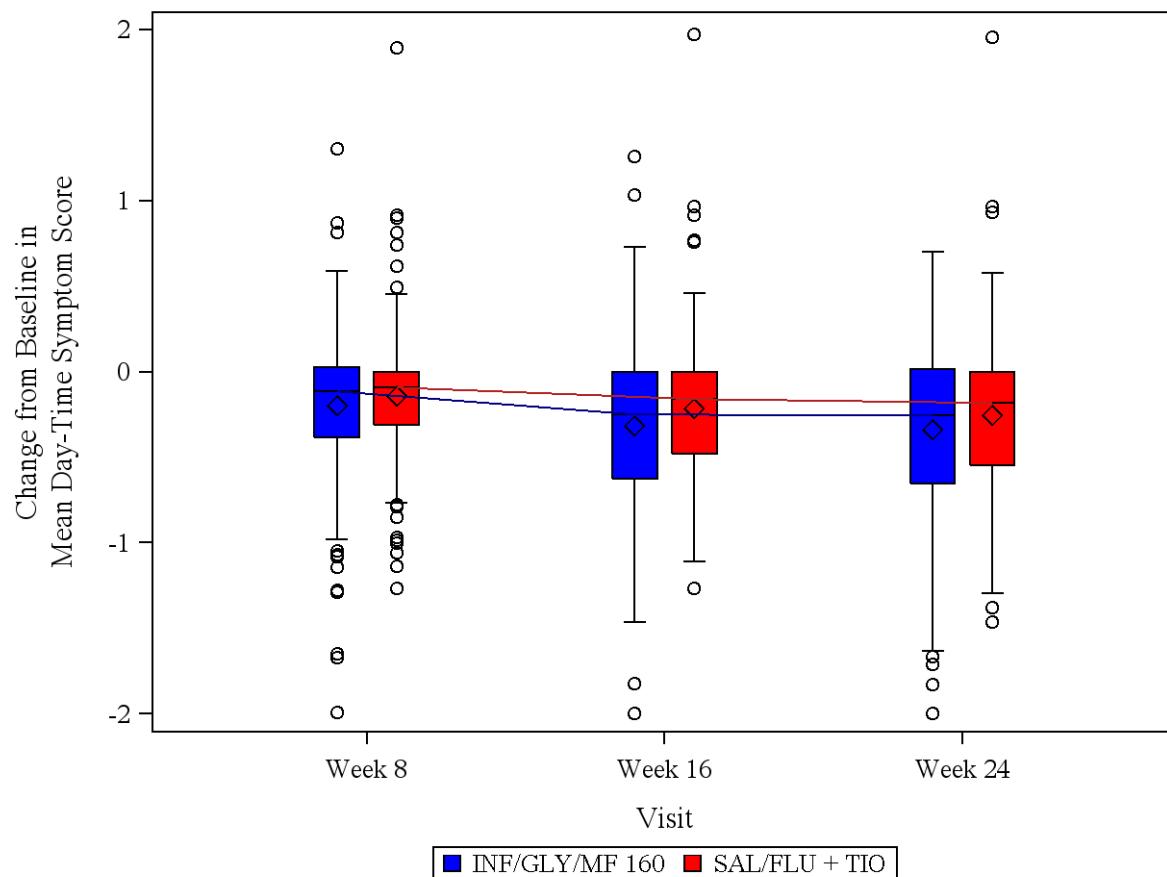
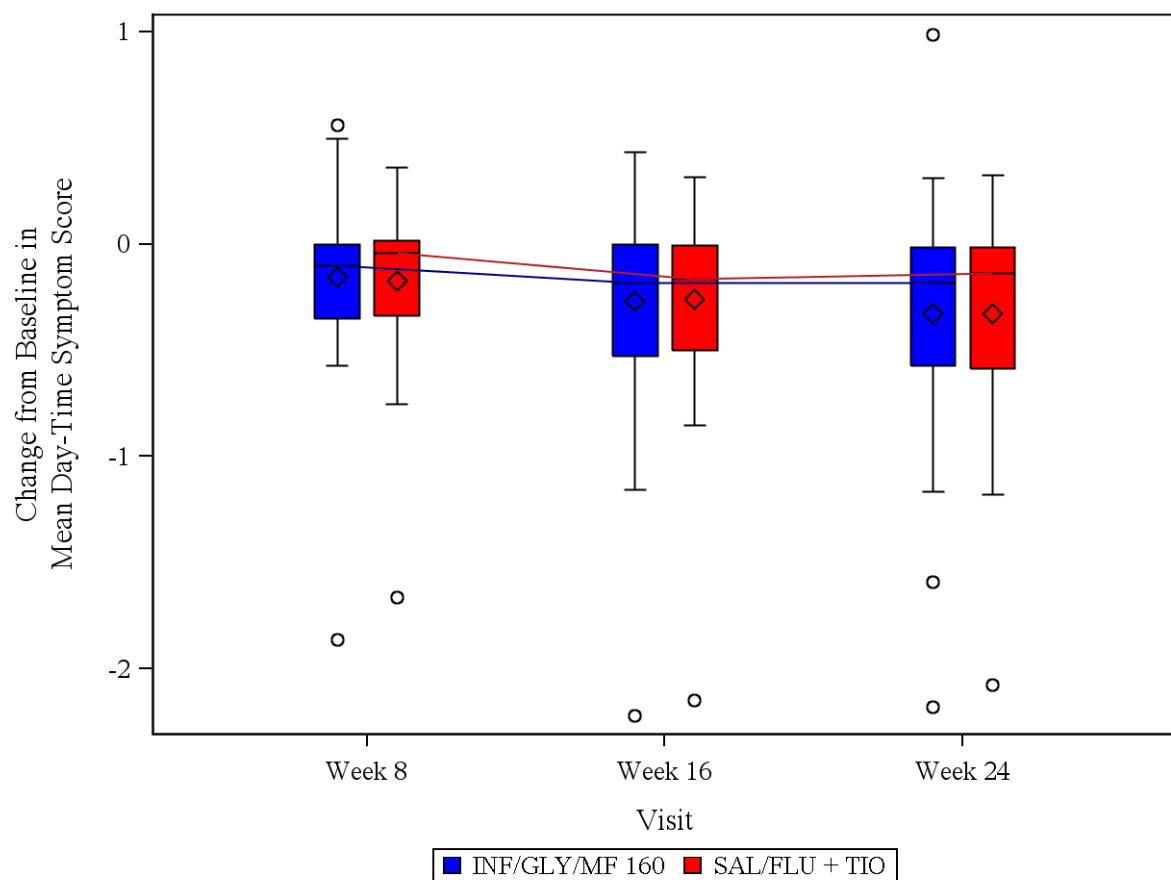
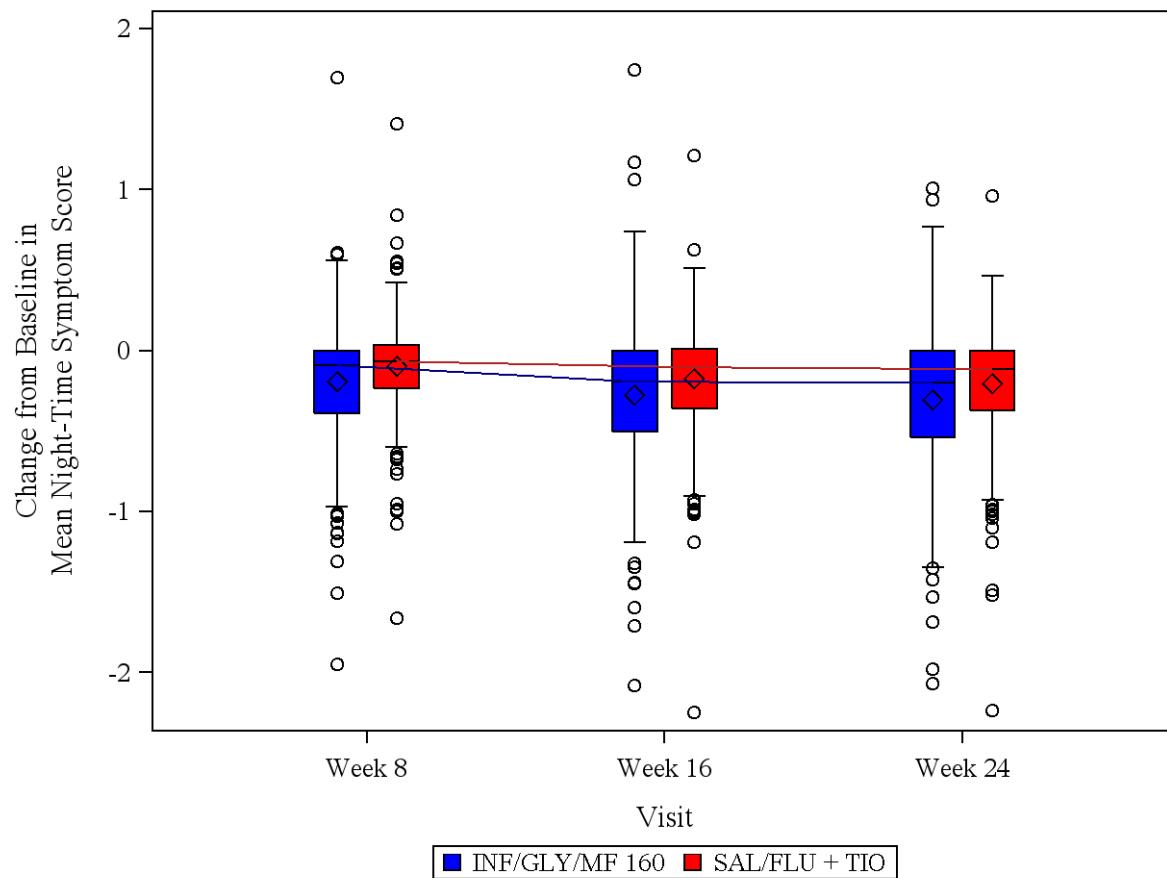


Figure 9.35.2 Symptoms (Mean Day-Time Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



9.37 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

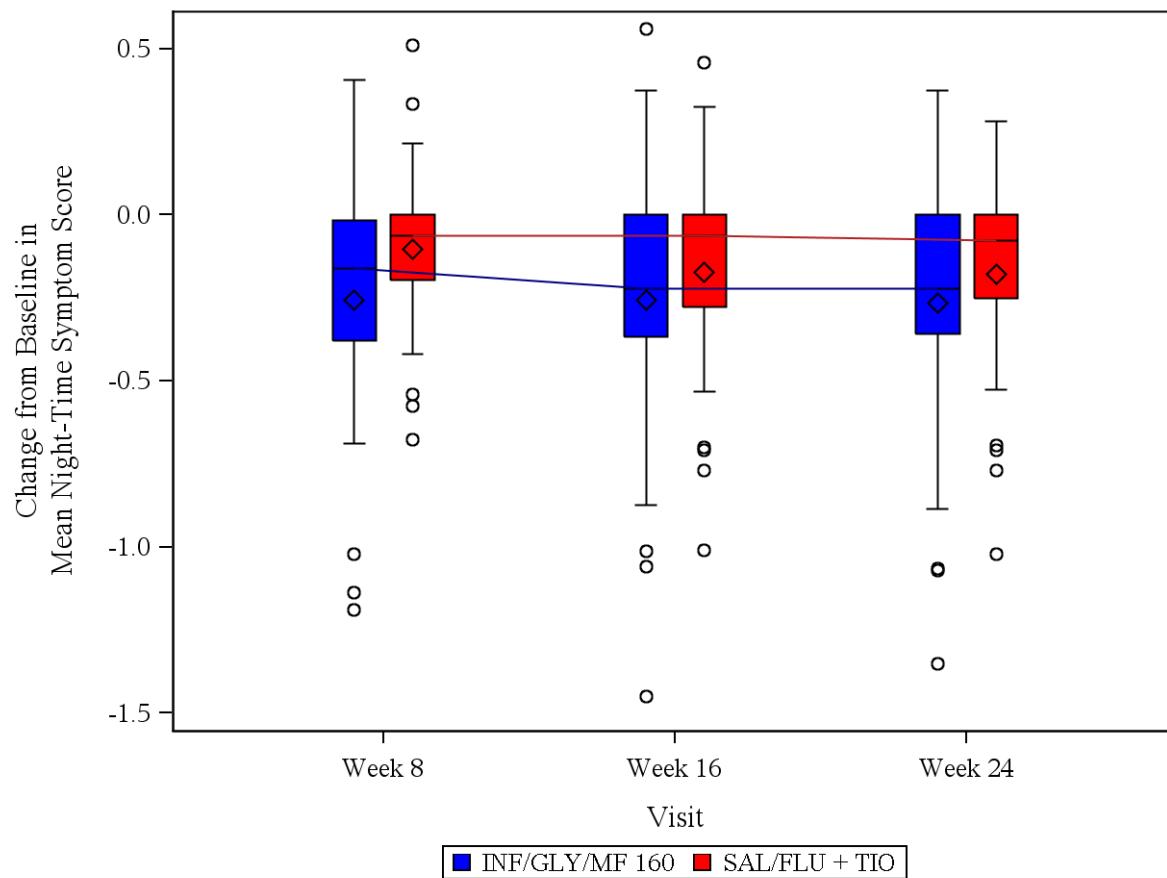


Figure 9.38.2 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Age (FAS), Age = 40-64 years

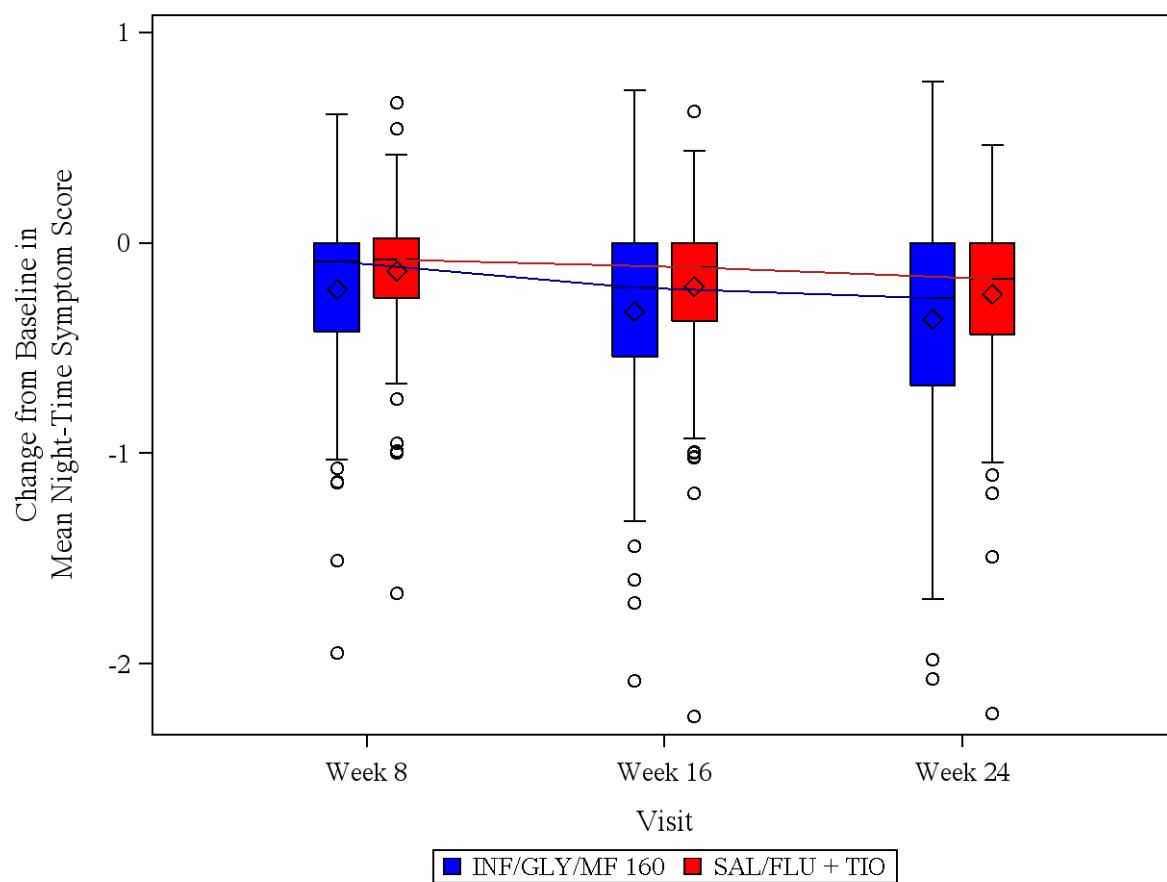
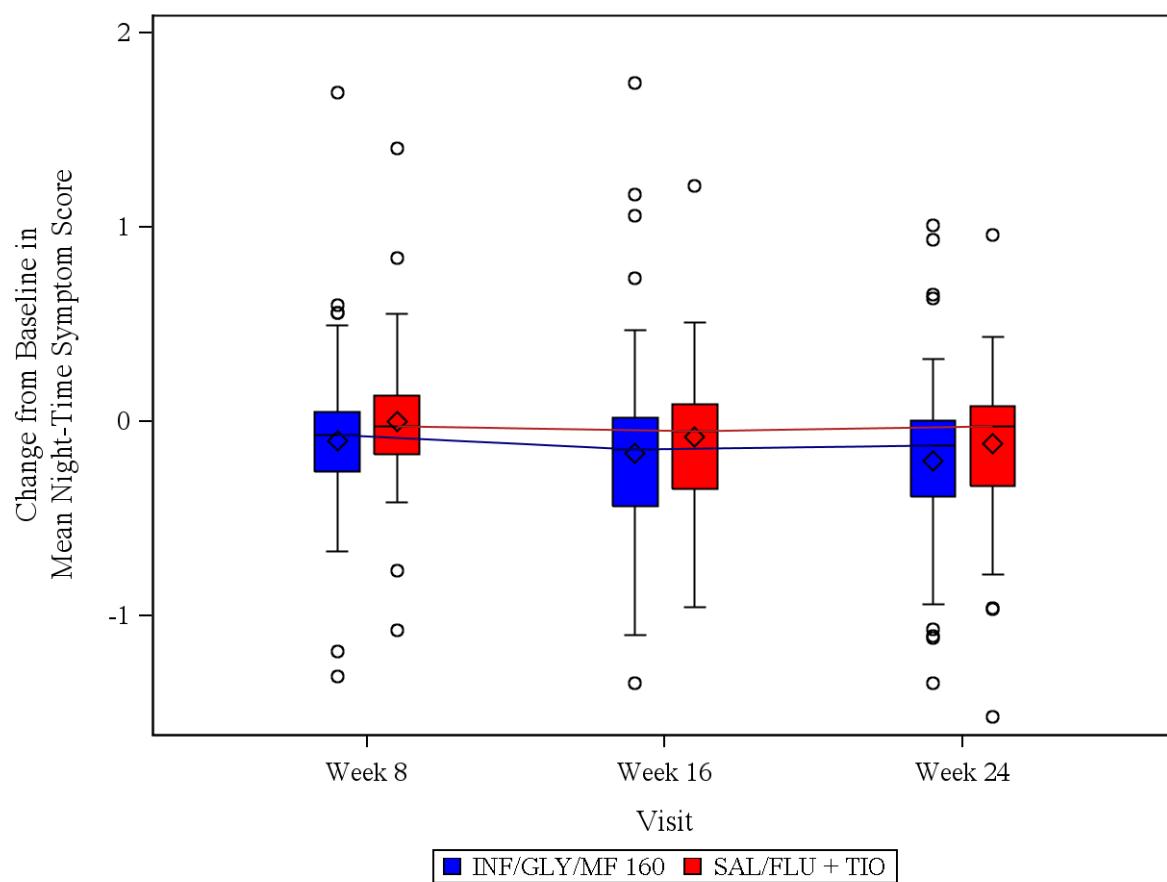


Figure 9.38.3 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

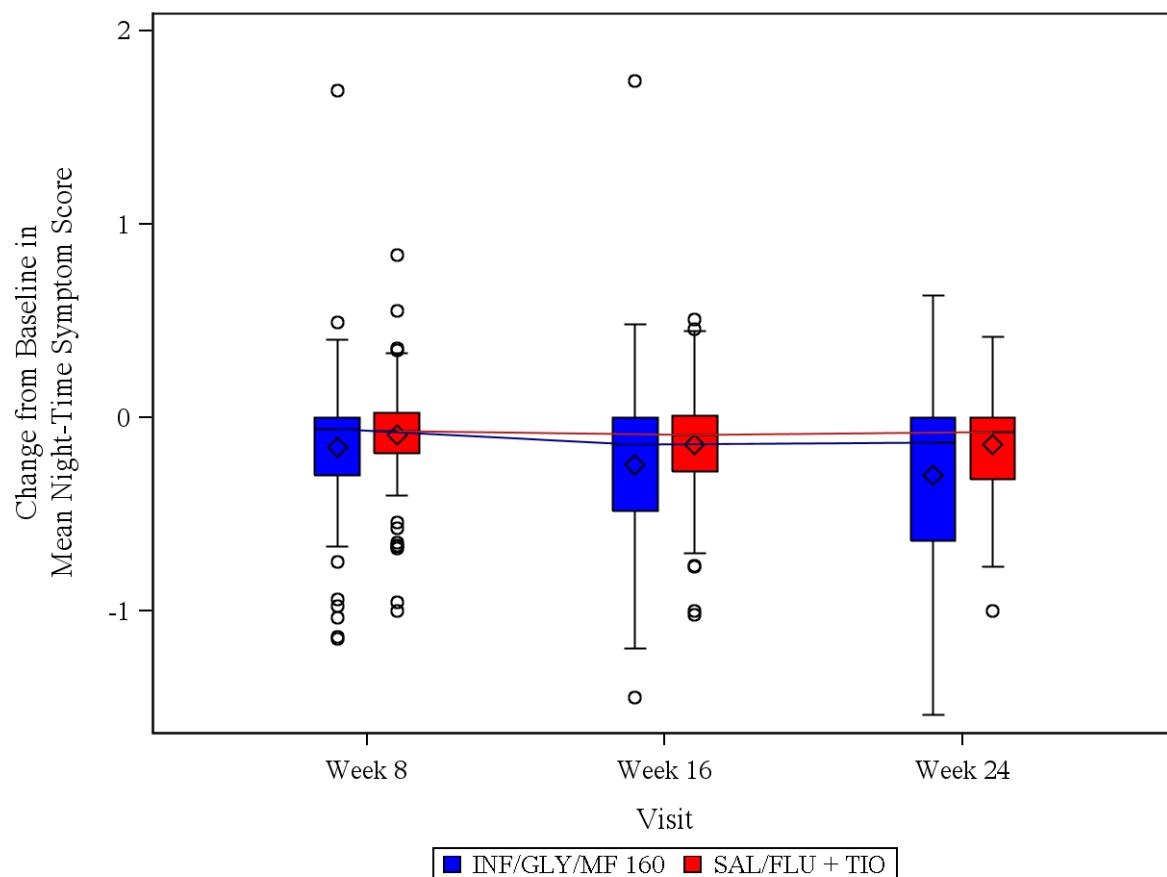
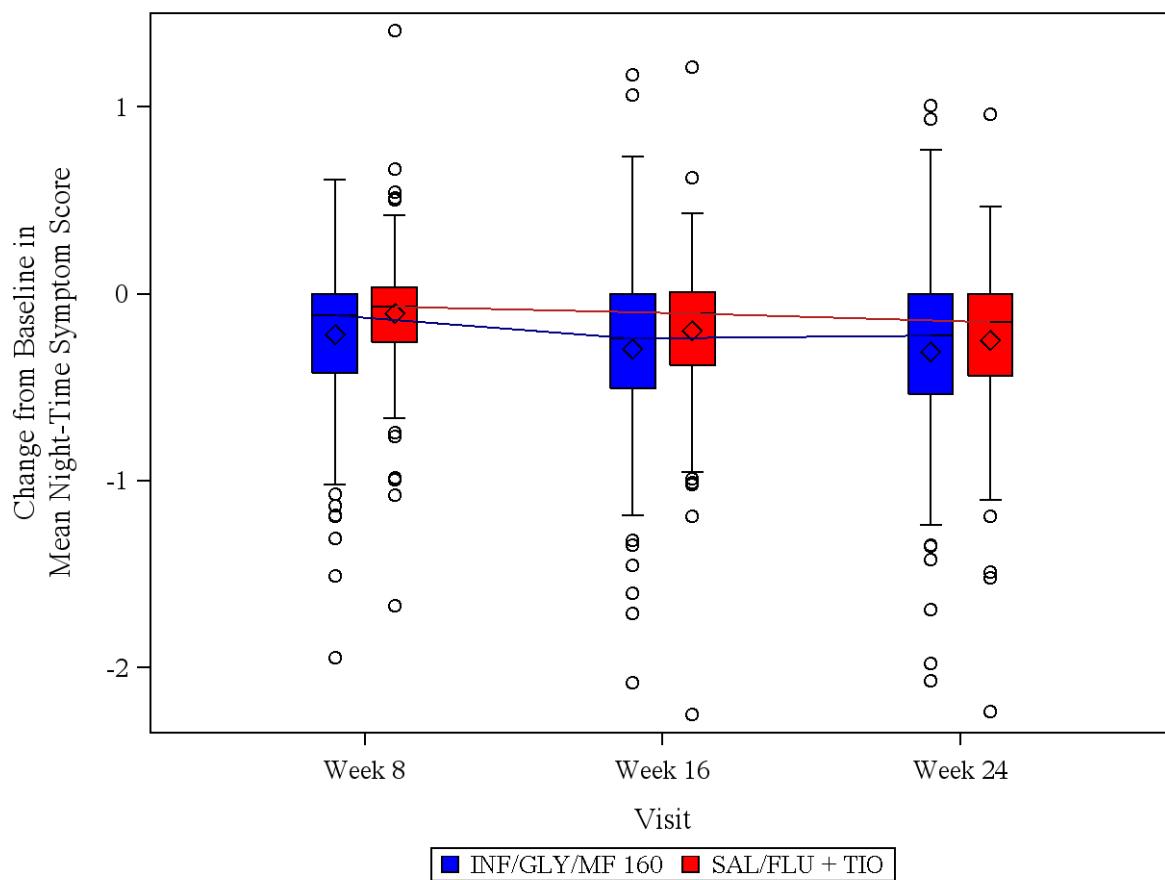


Figure 9.39.2 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Gender (FAS), Gender = Female



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

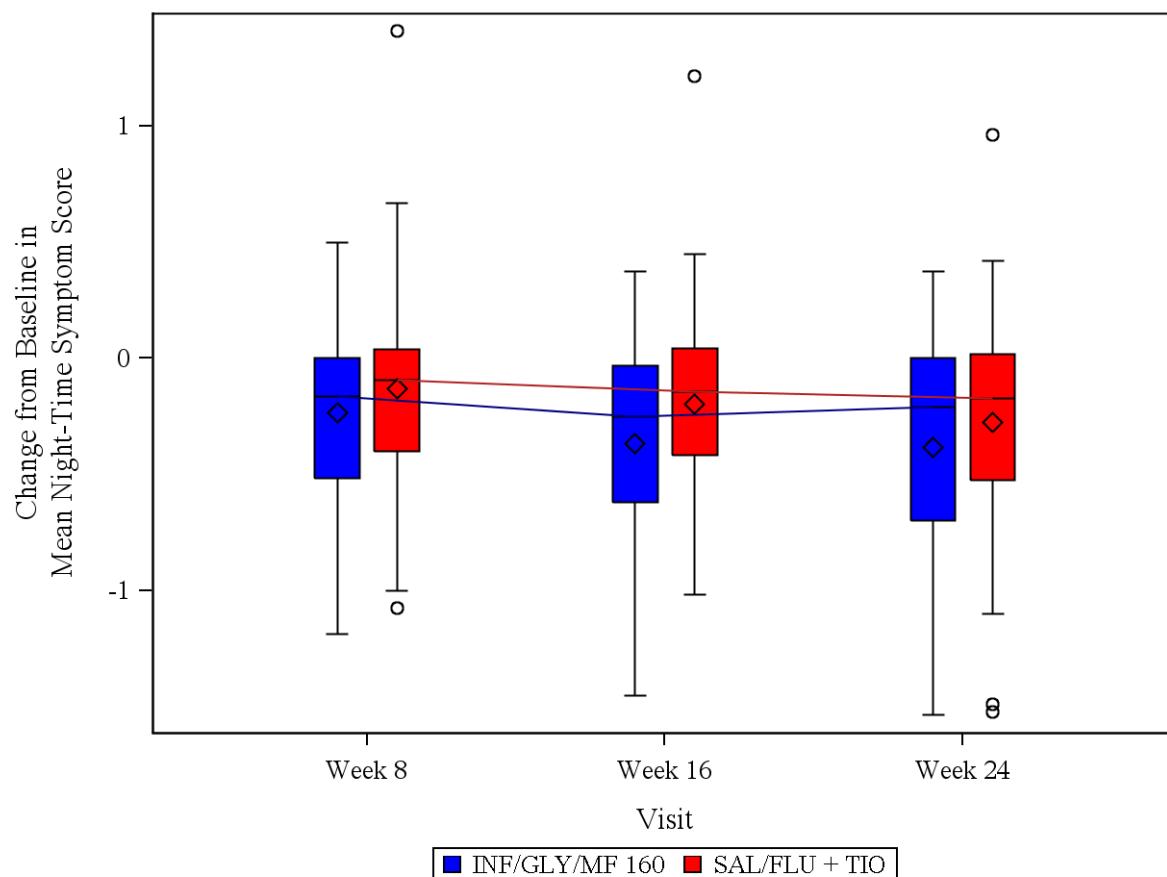


Figure 9.40.2 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Region (FAS), Region = Europe

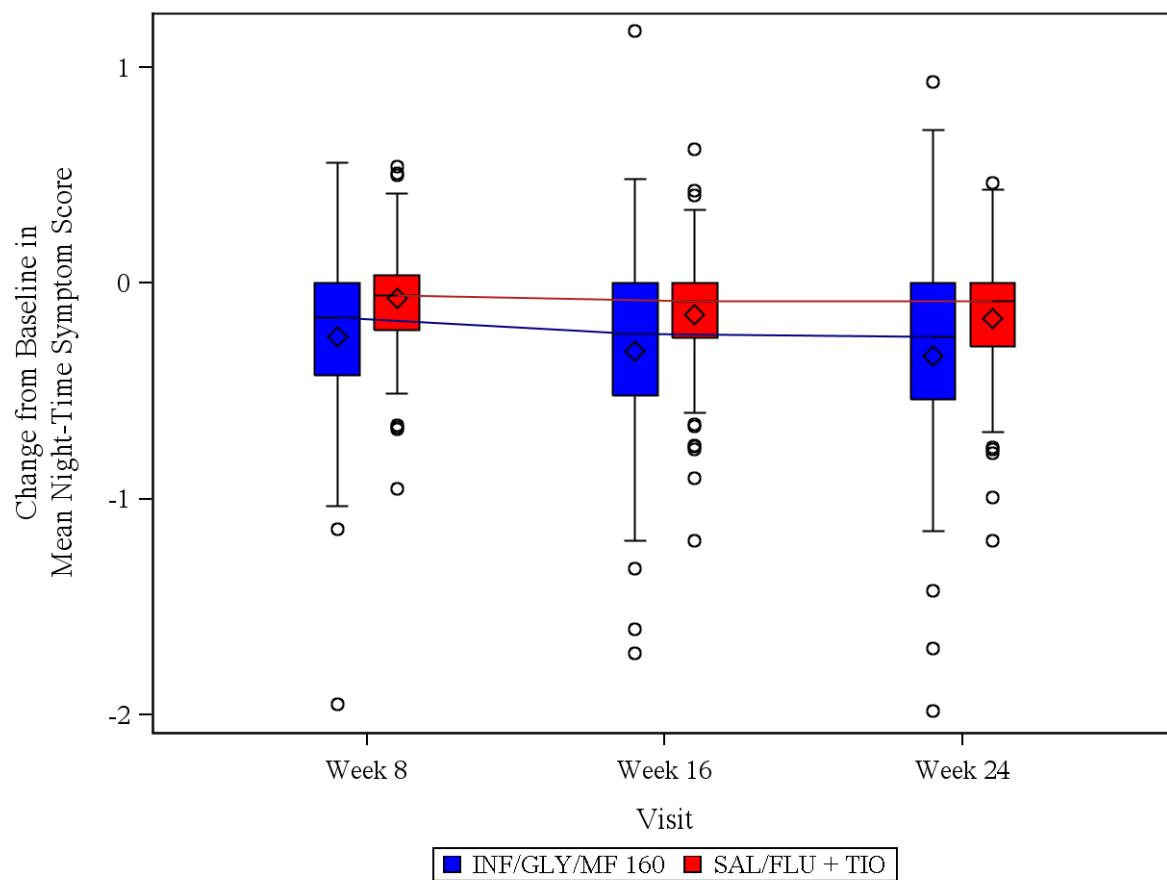


Figure 9.40.3 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Region (FAS), Region = Latin America

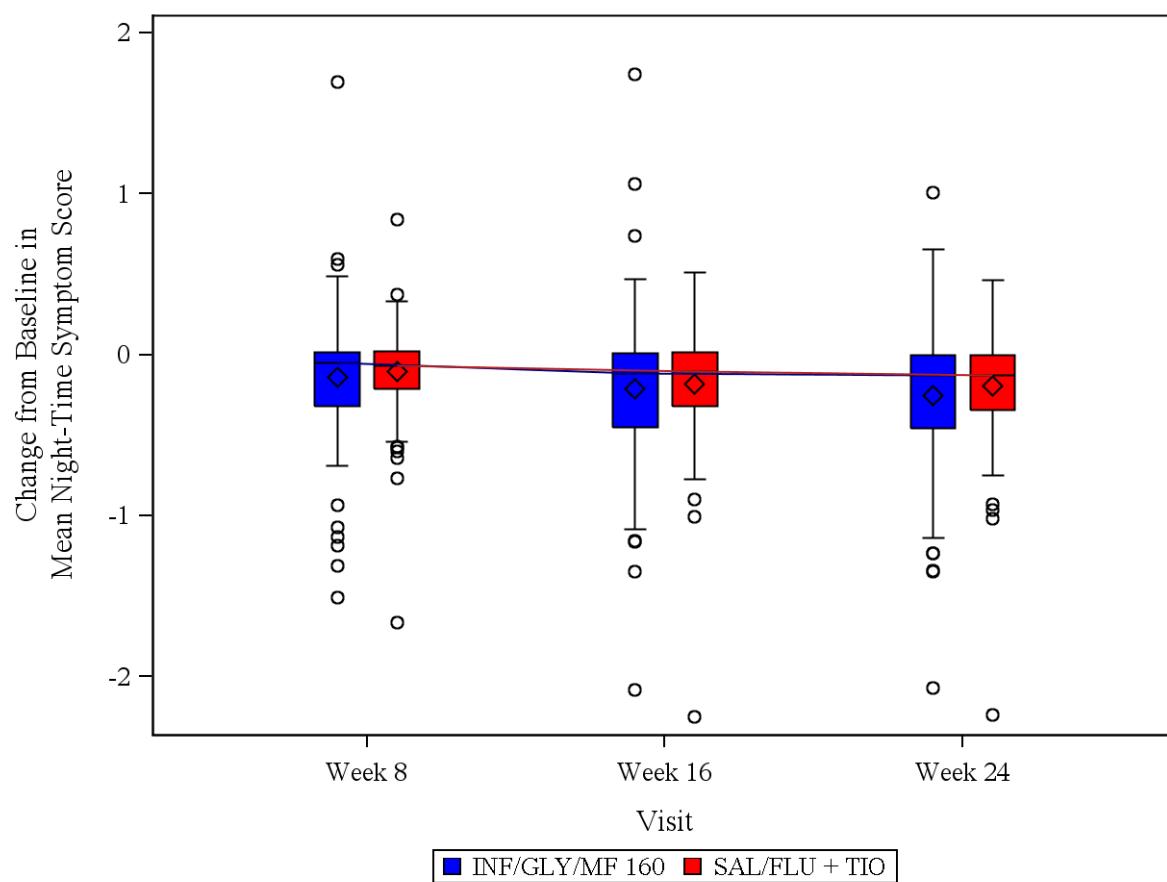
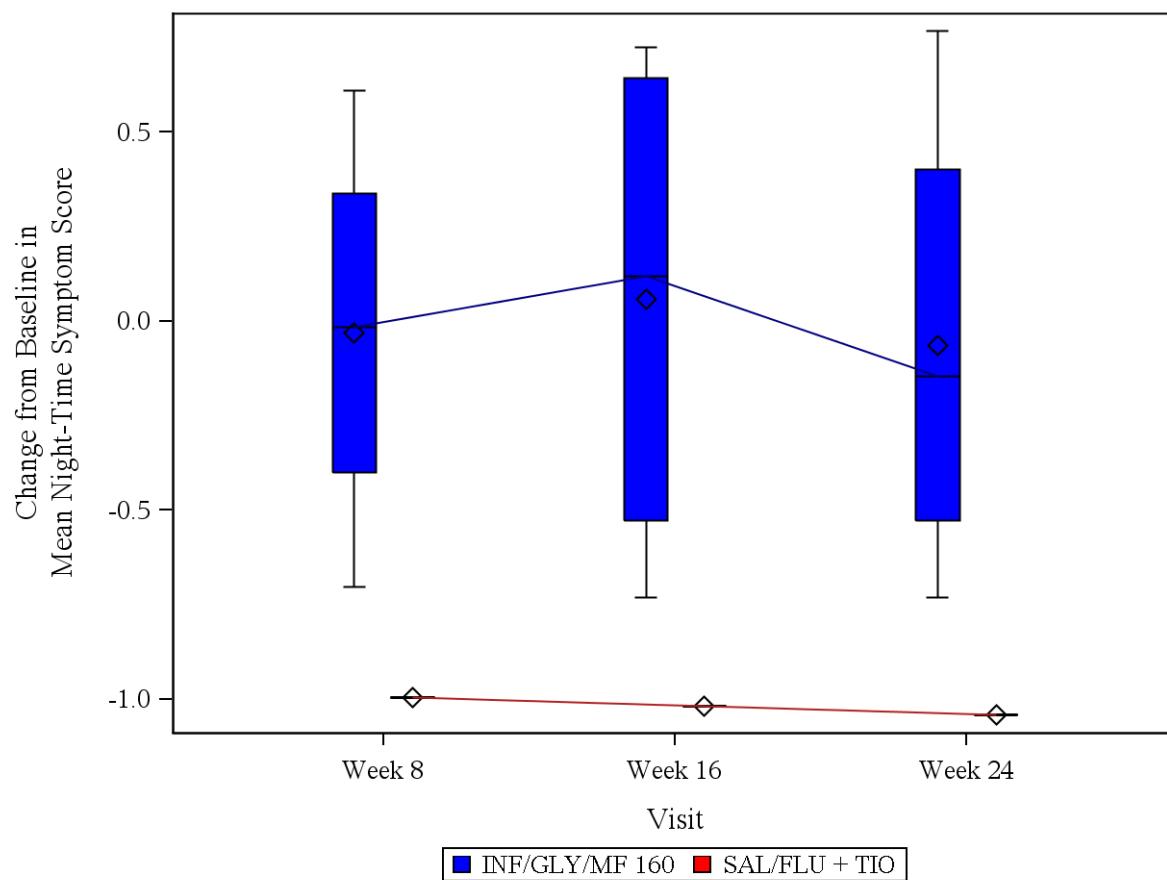


Figure 9.40.4 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by Region (FAS), Region = Others



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

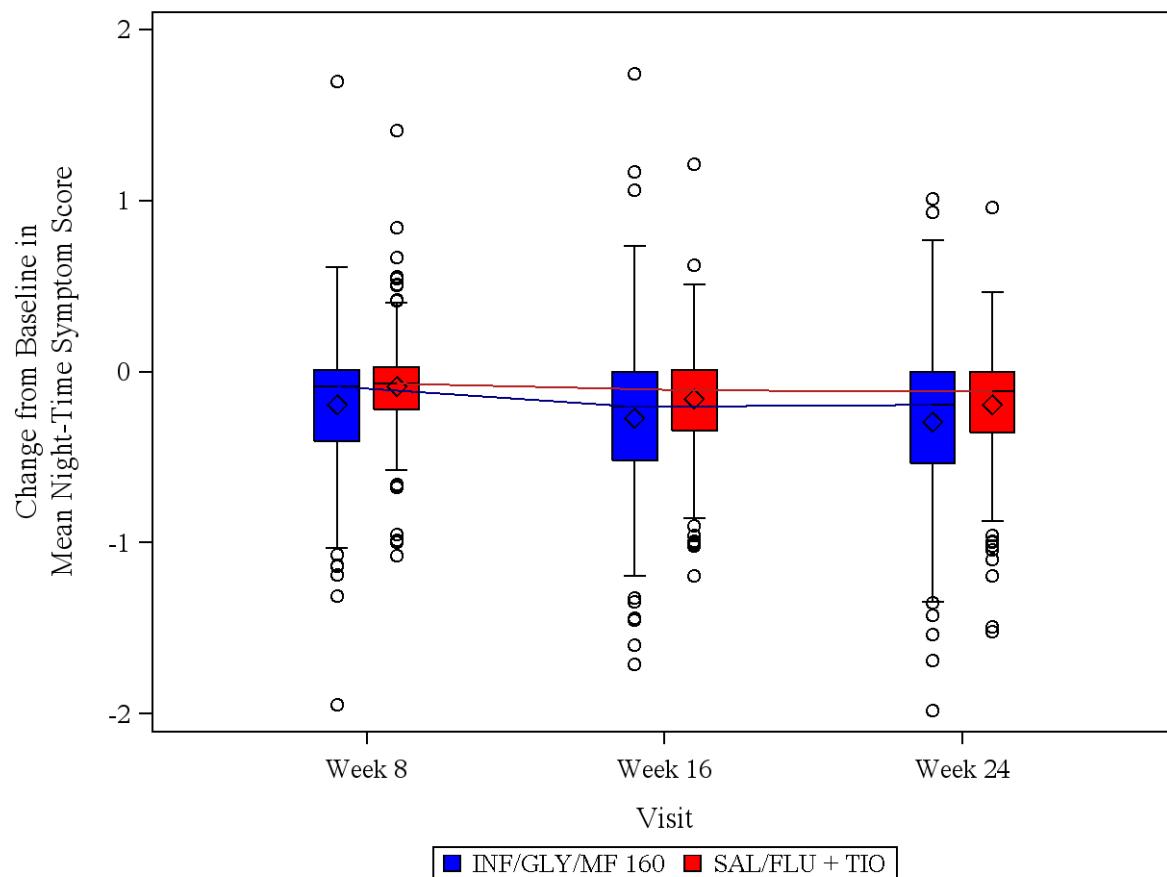
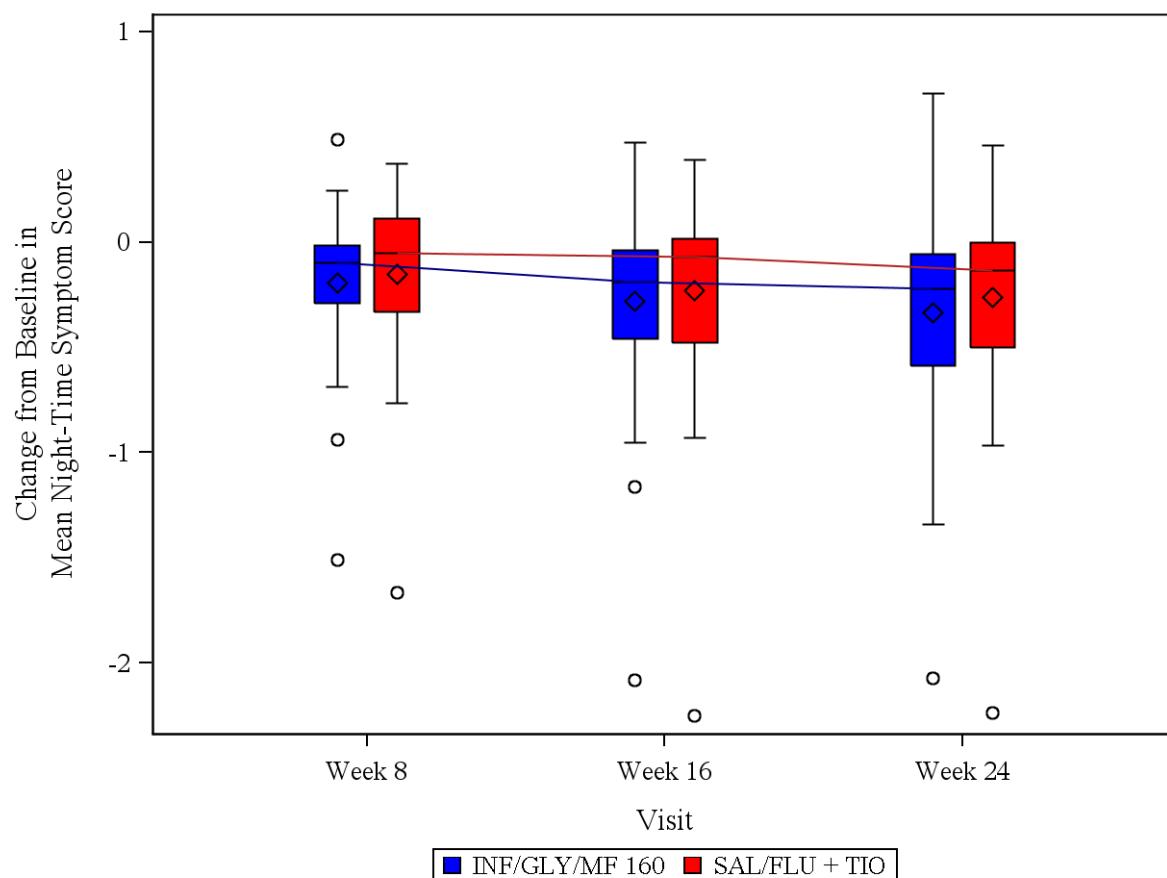
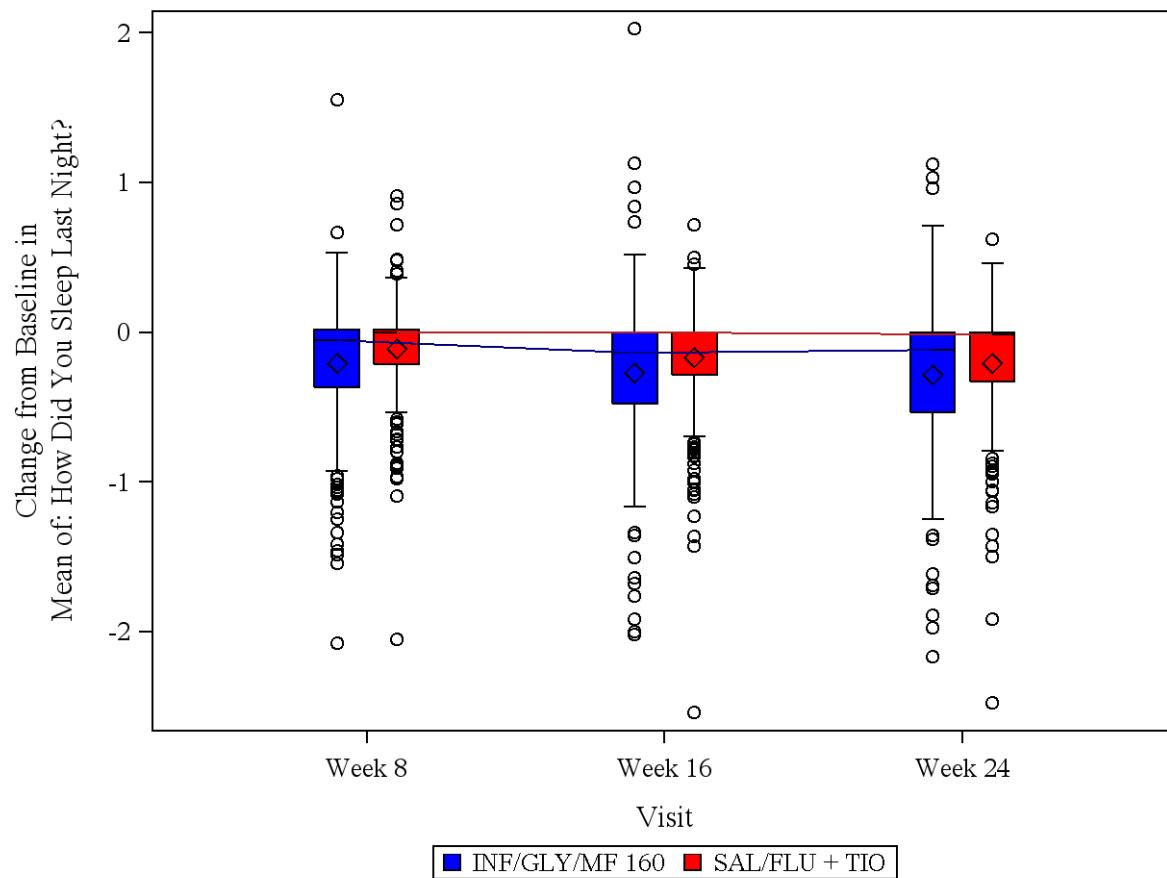


Figure 9.41.2 Symptoms (Mean Night-Time Symptom Score) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



9.43 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

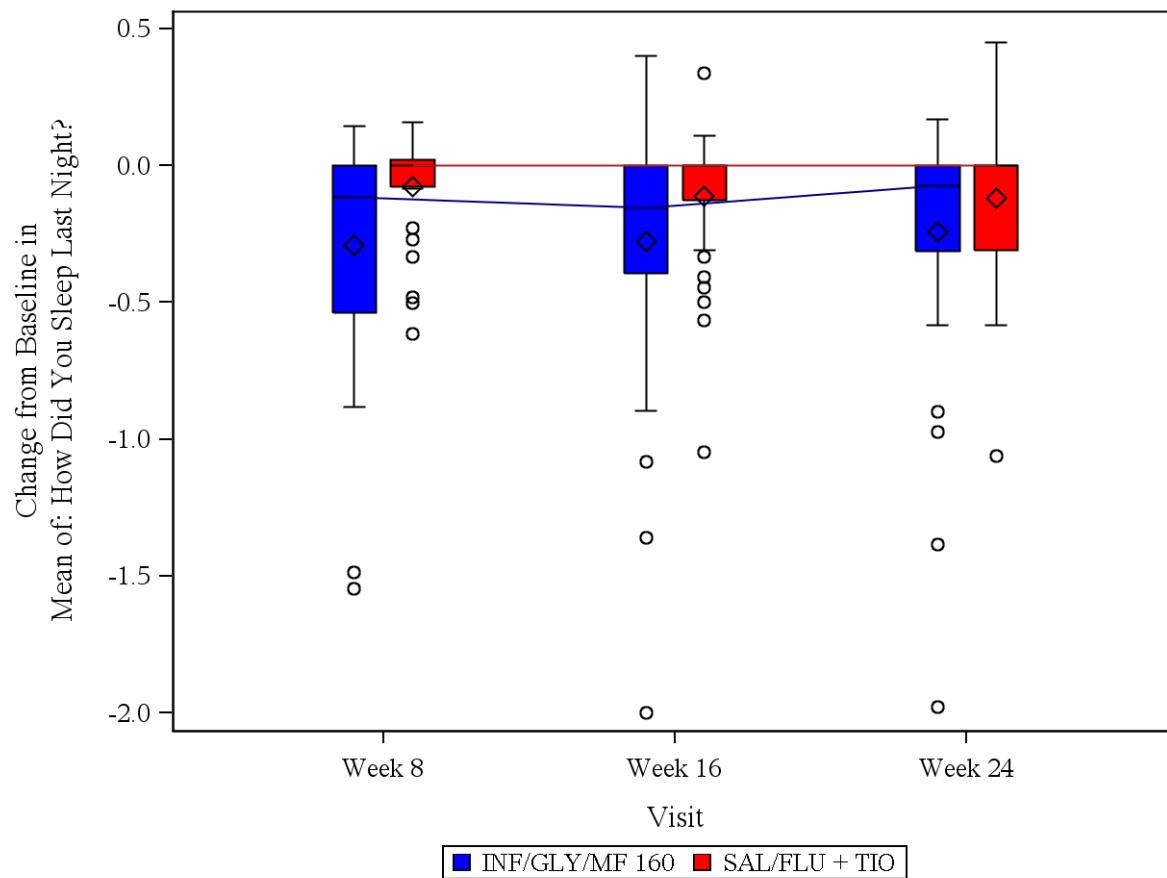


Figure 9.44.2 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Age (FAS), Age = 40-64 years

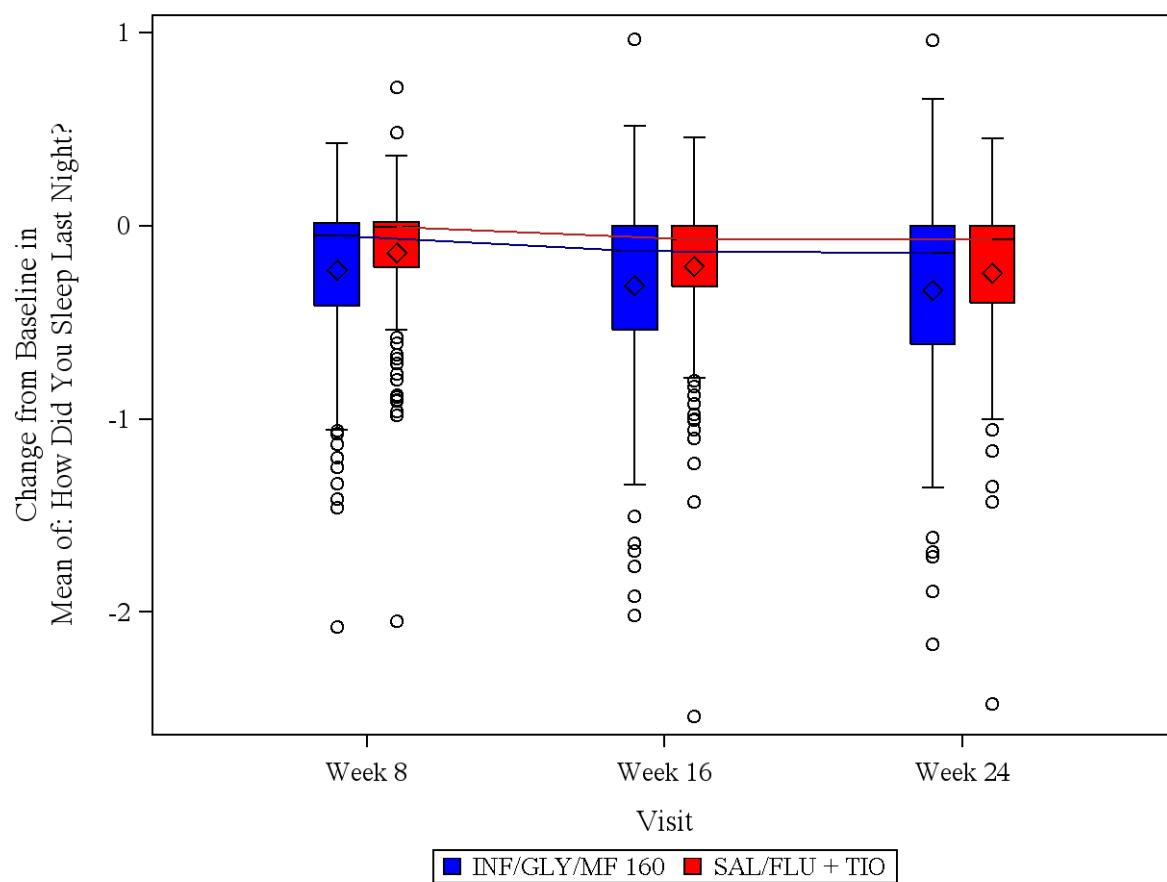
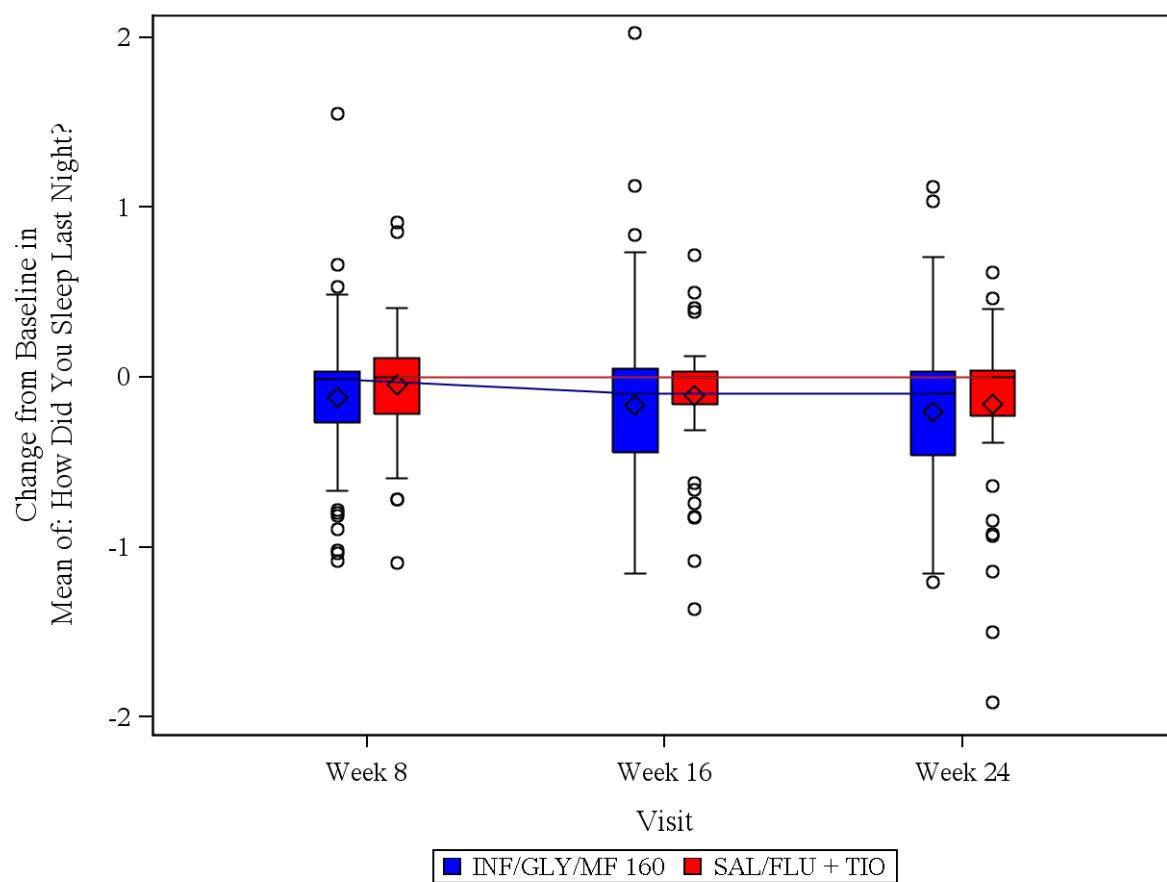


Figure 9.44.3 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

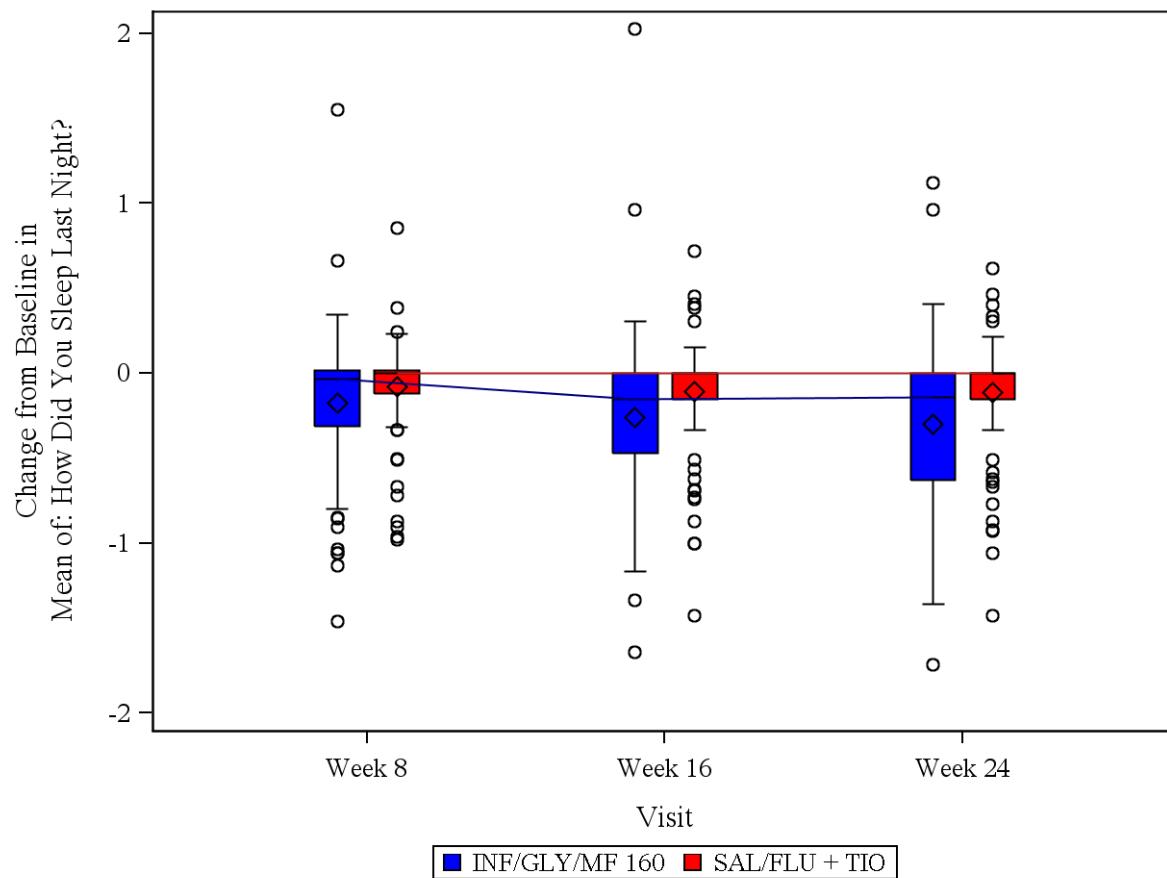
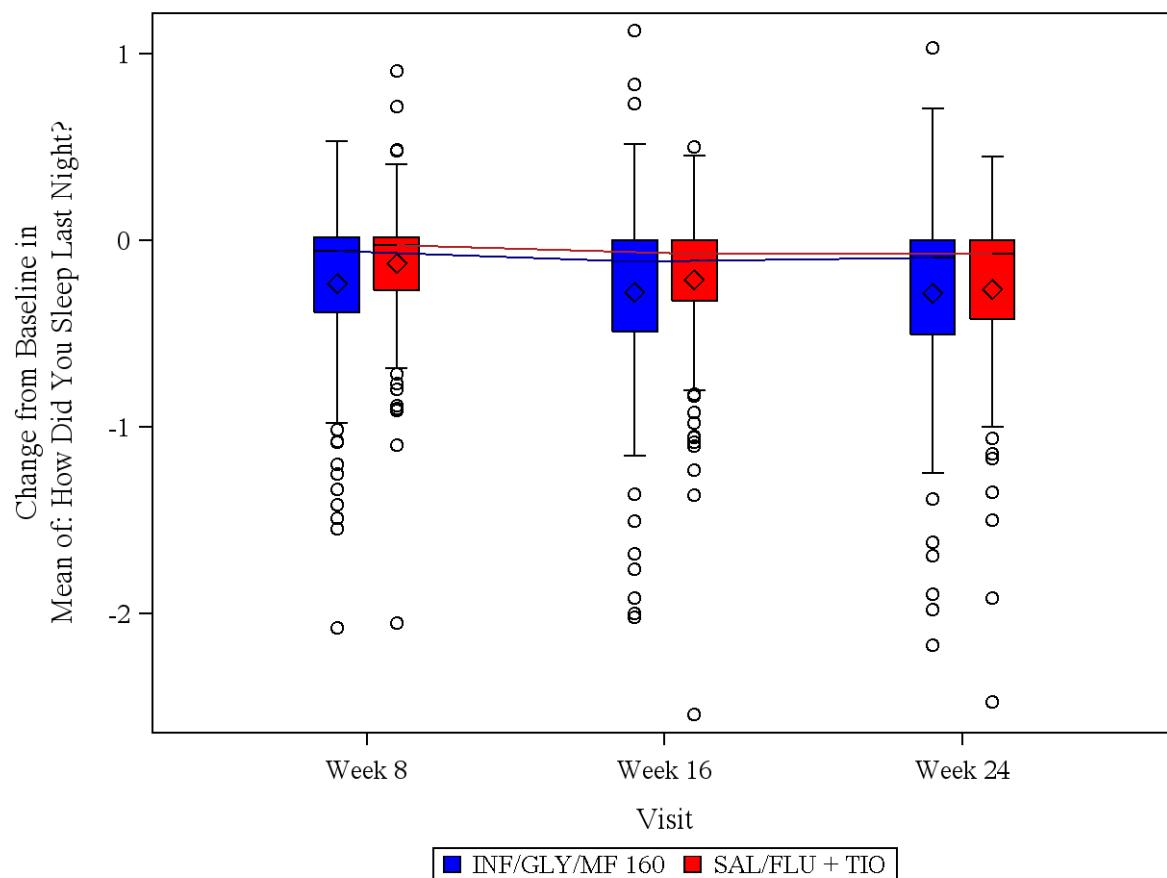


Figure 9.45.2 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Gender (FAS), Gender = Female



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

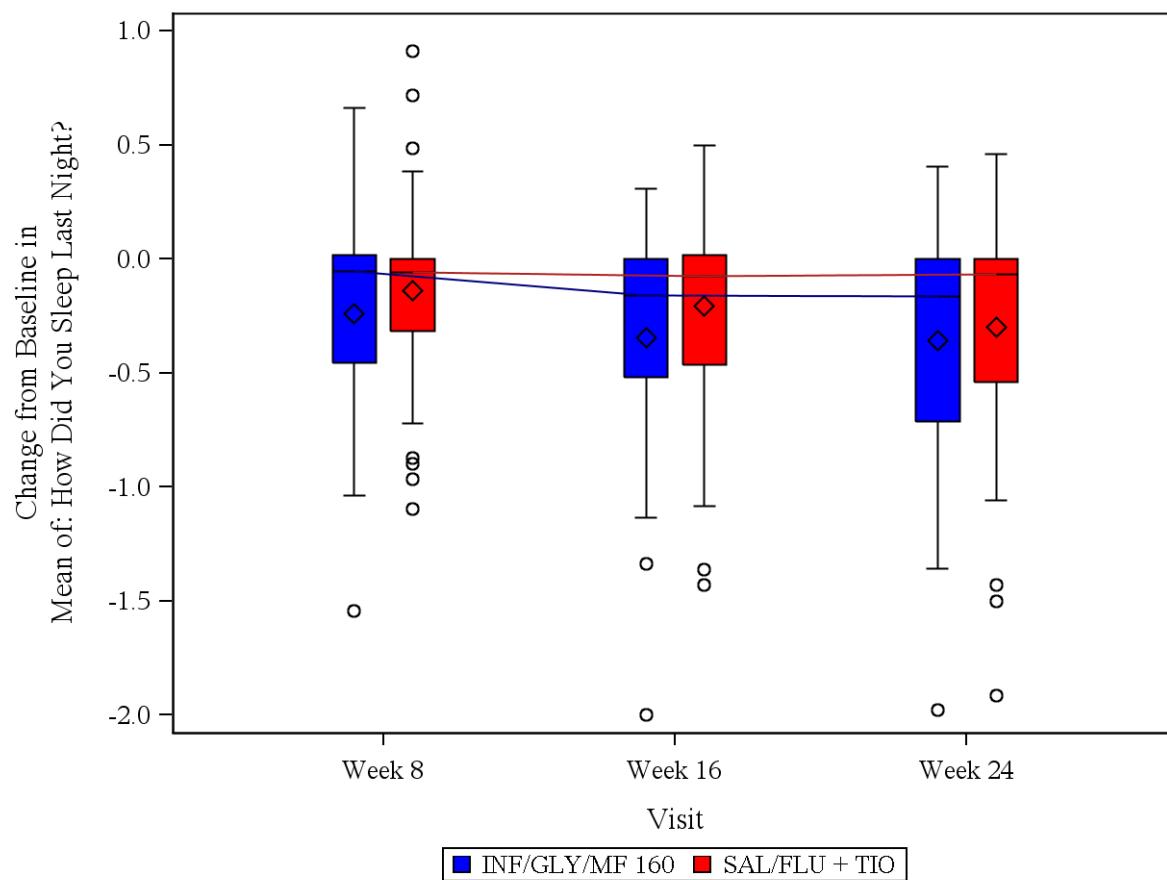


Figure 9.46.2 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Region (FAS), Region = Europe

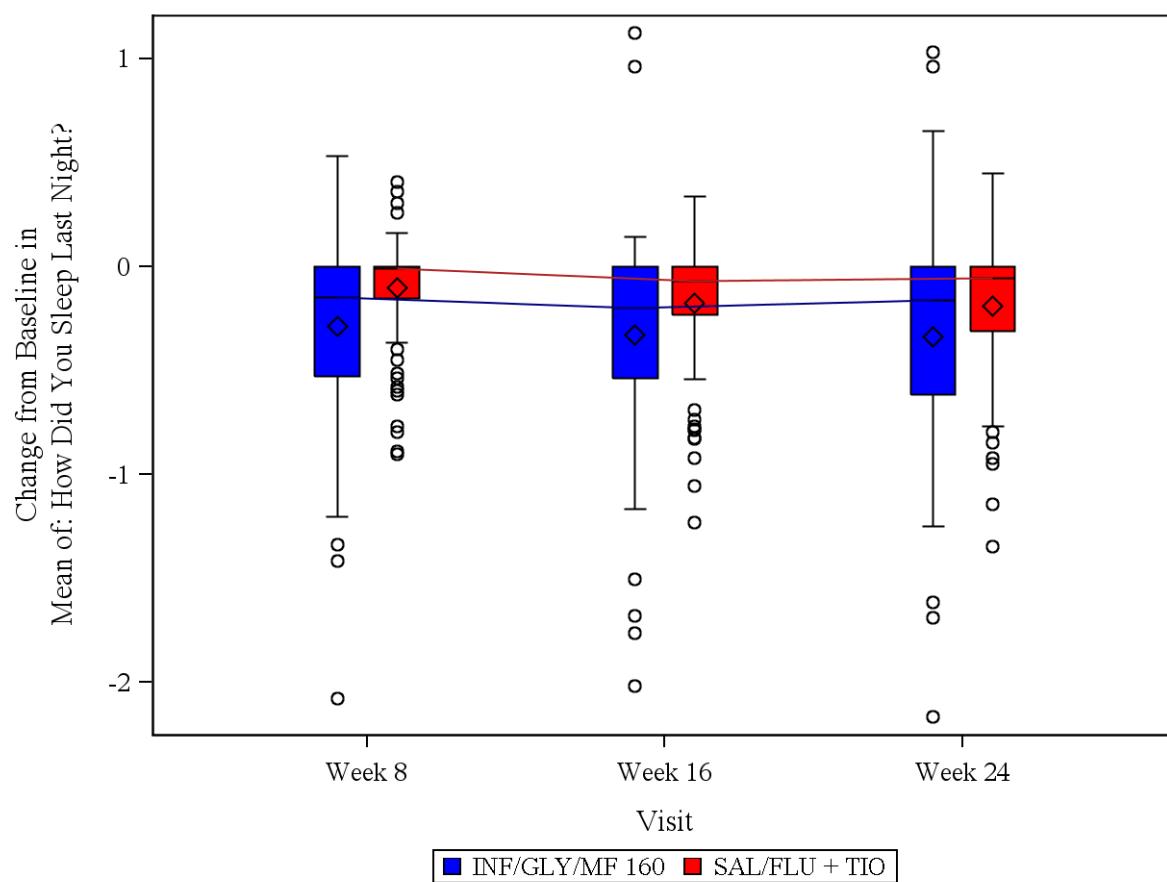


Figure 9.46.3 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Region (FAS), Region = Latin America

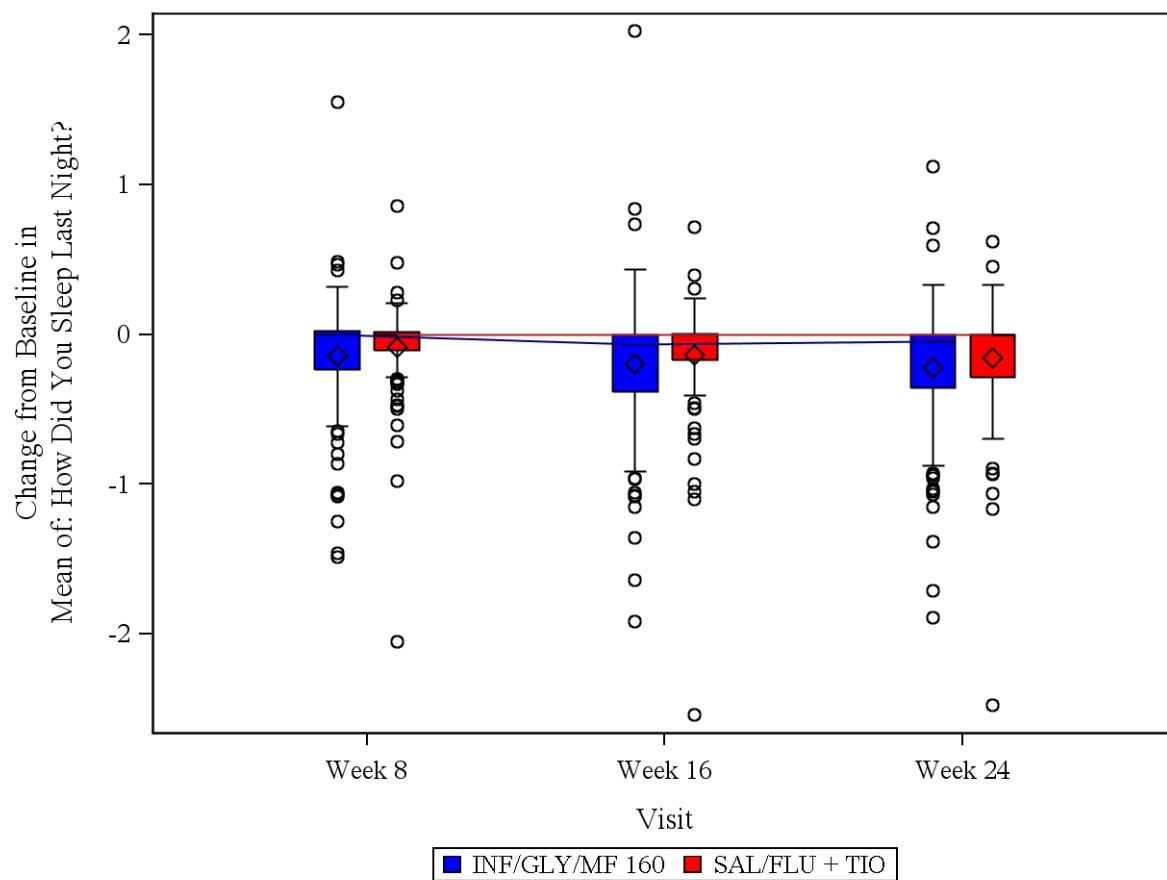
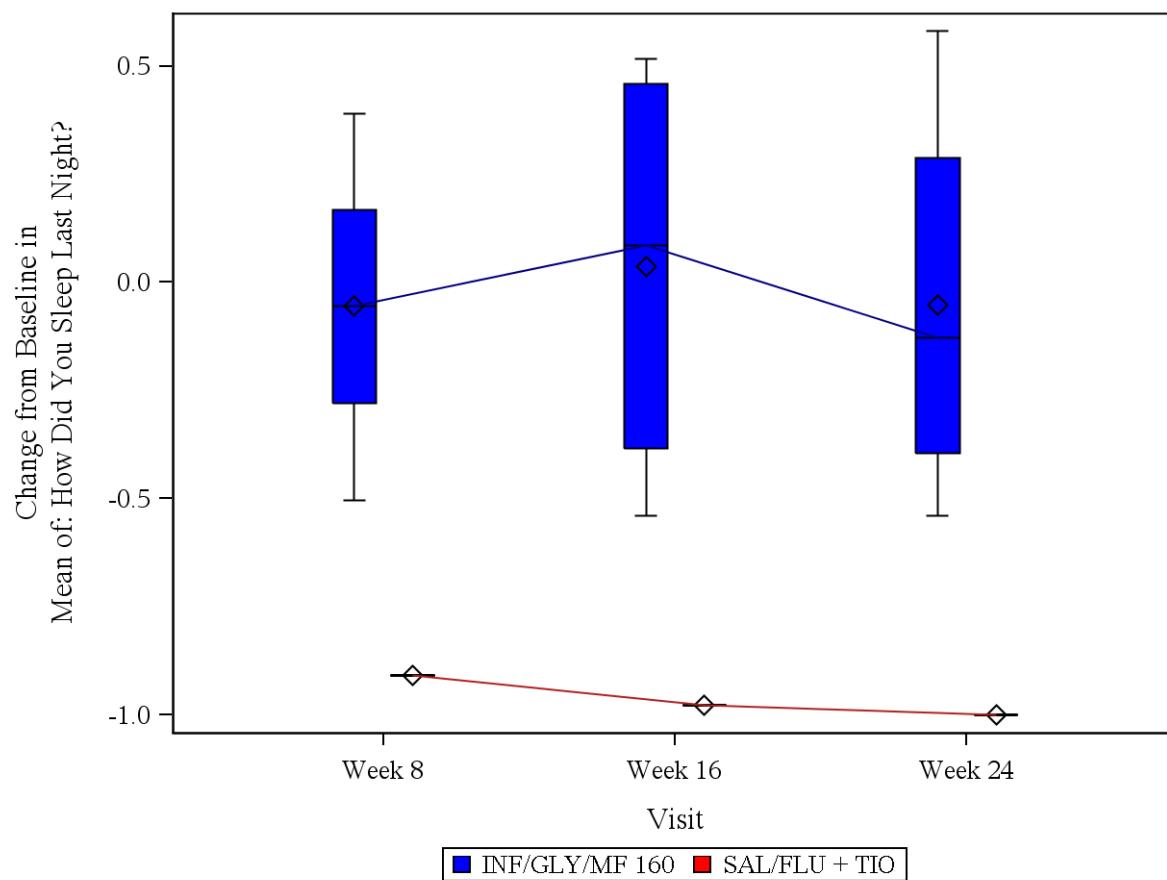


Figure 9.46.4 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by Region (FAS), Region = Others



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

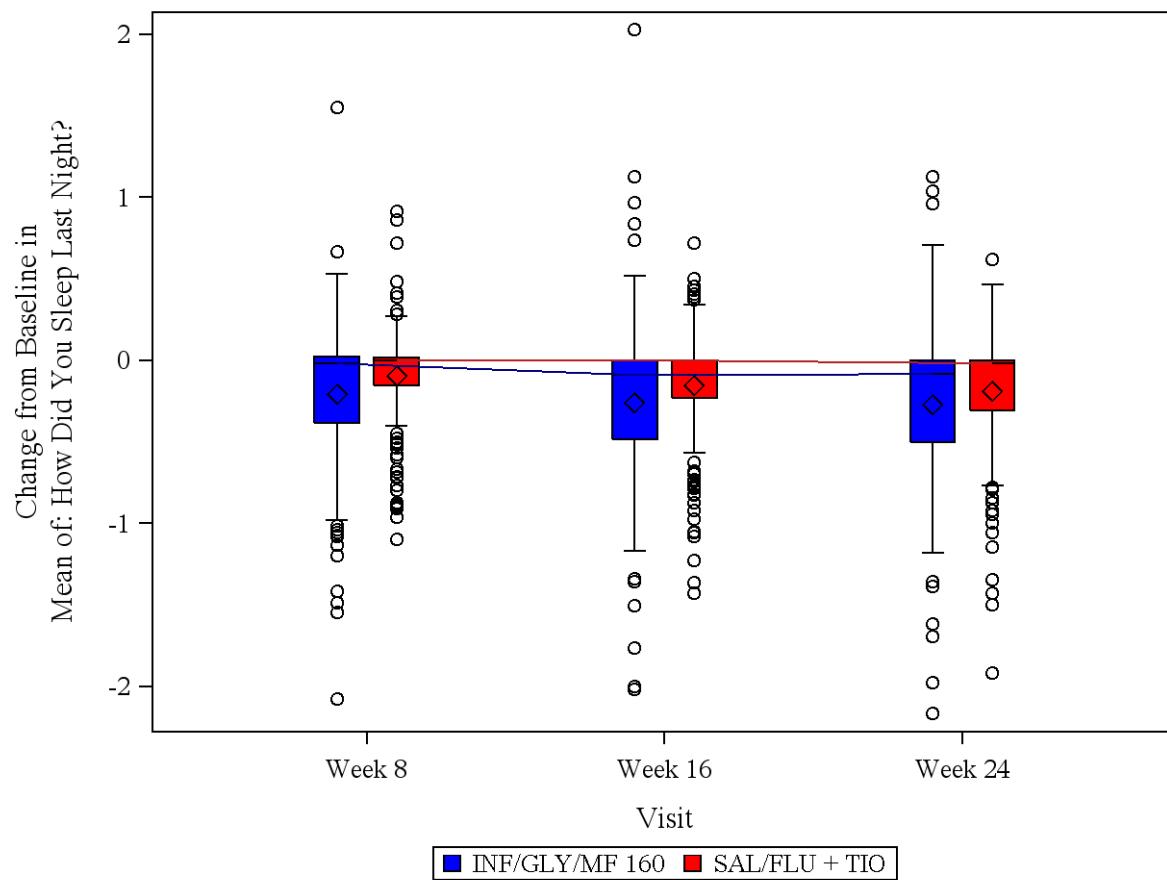
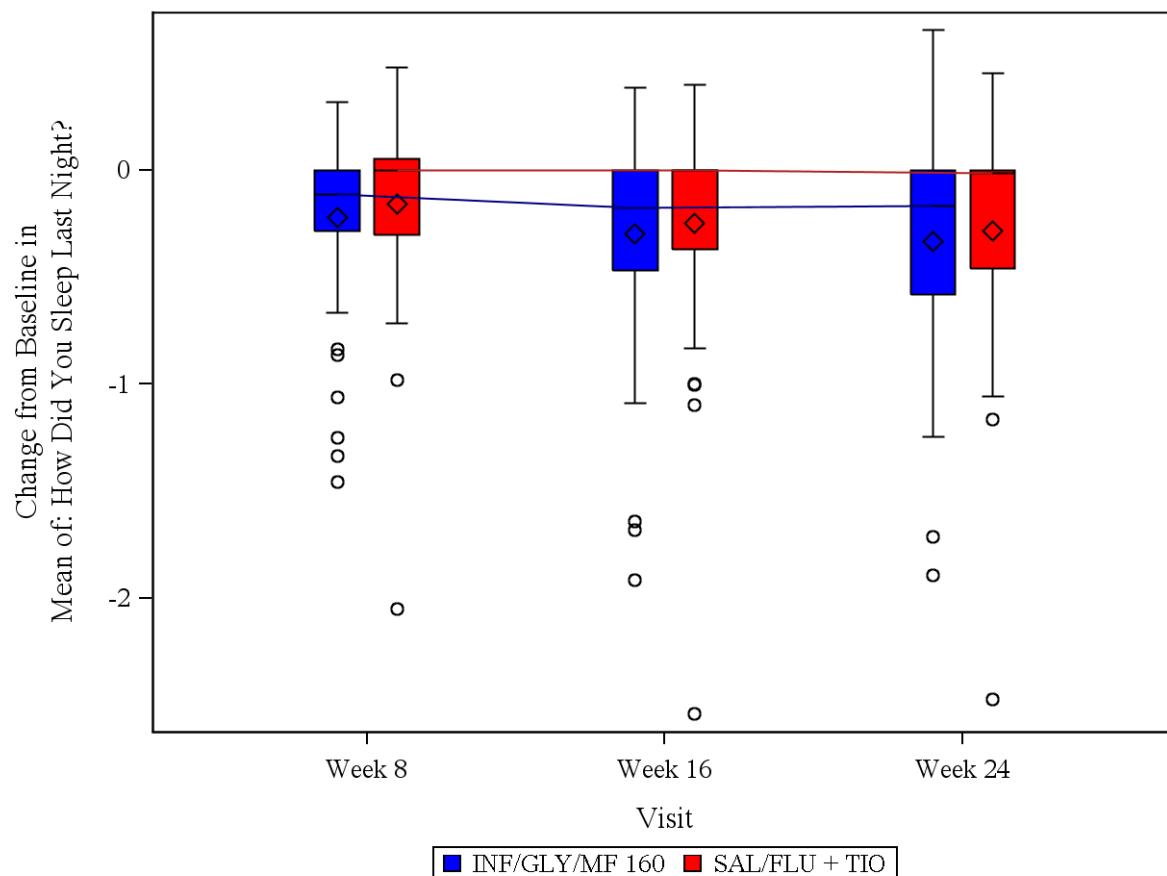
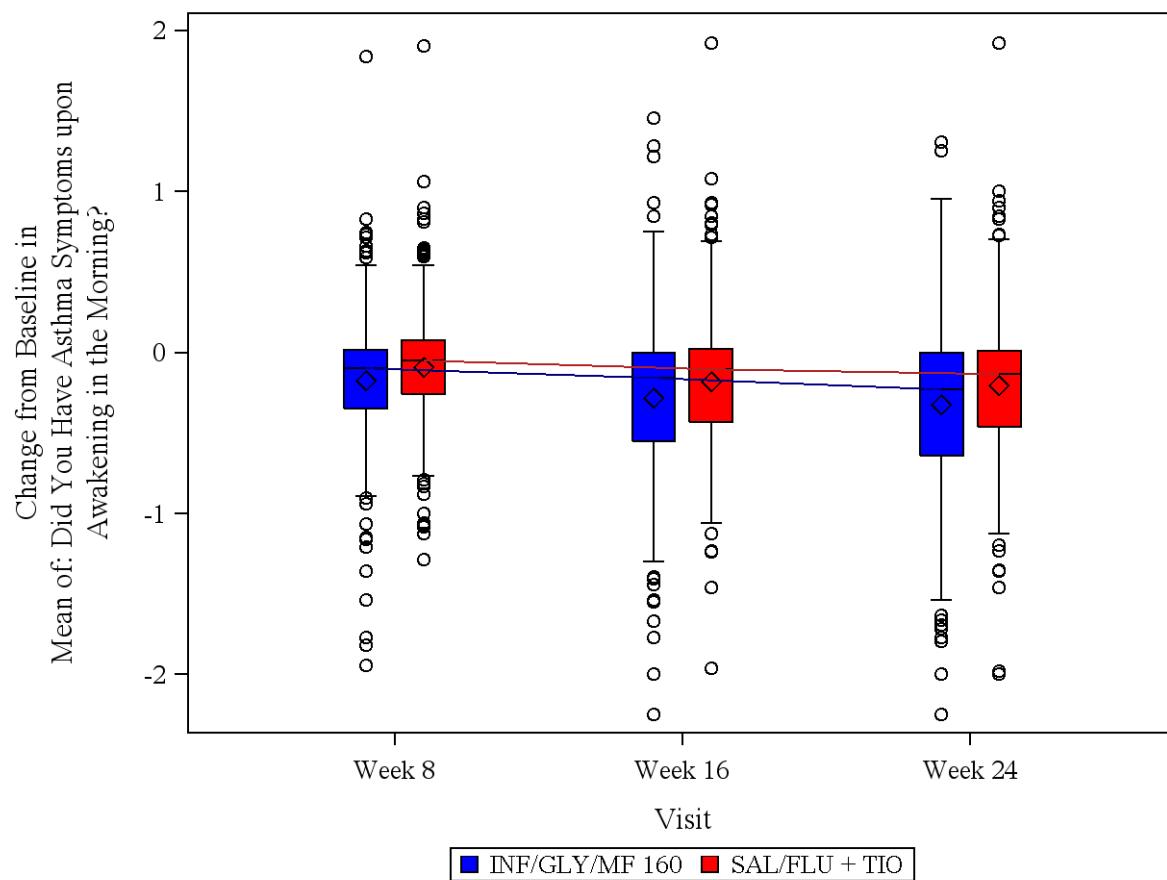


Figure 9.47.2 Symptoms (Mean of: How Did You Sleep Last Night?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



9.49 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

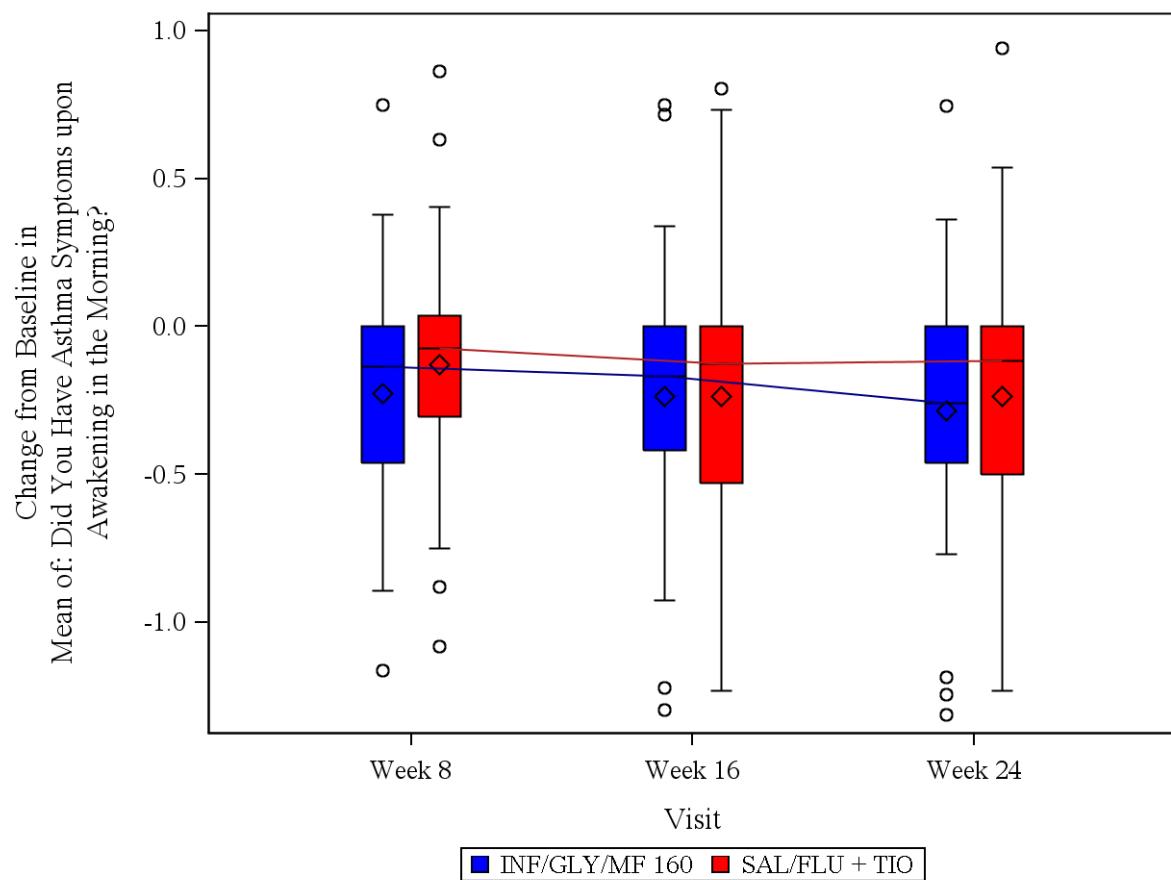


Figure 9.50.2 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Age (FAS), Age = 40-64 years

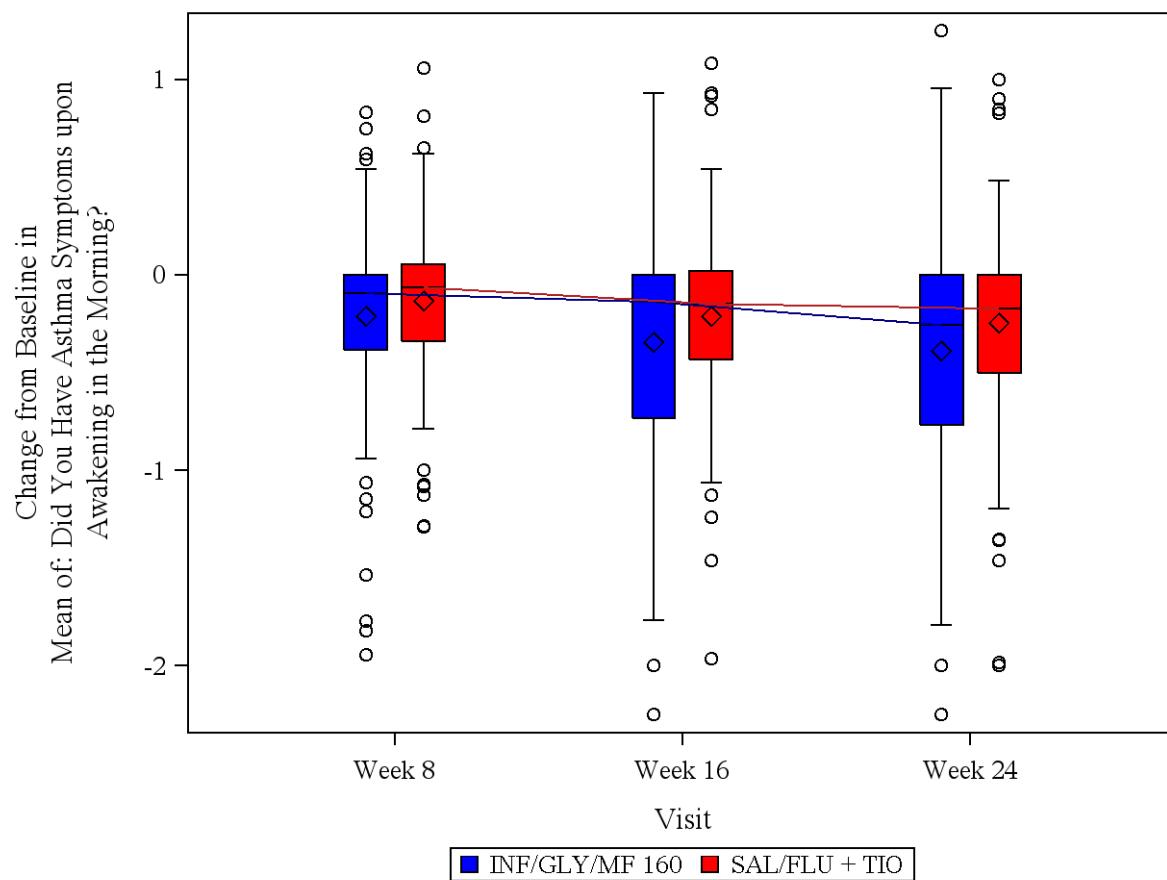
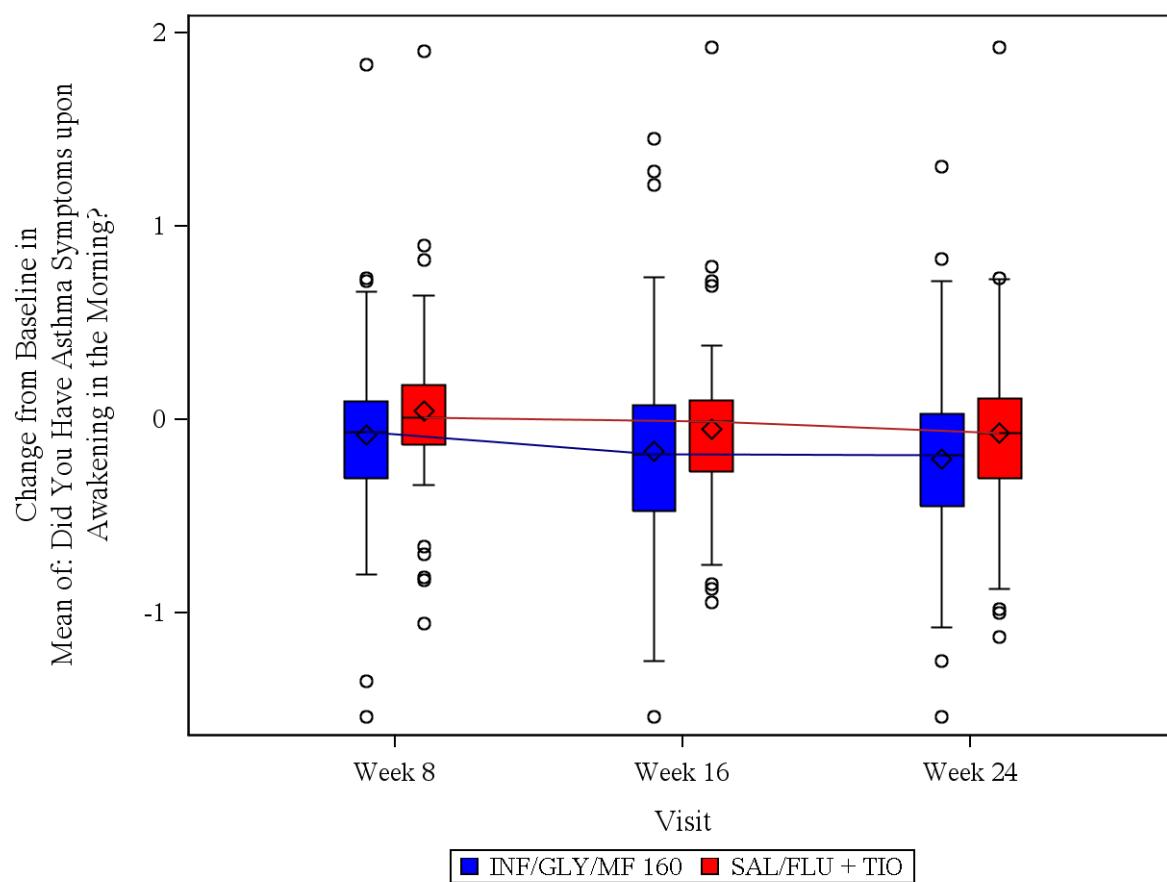


Figure 9.50.3 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

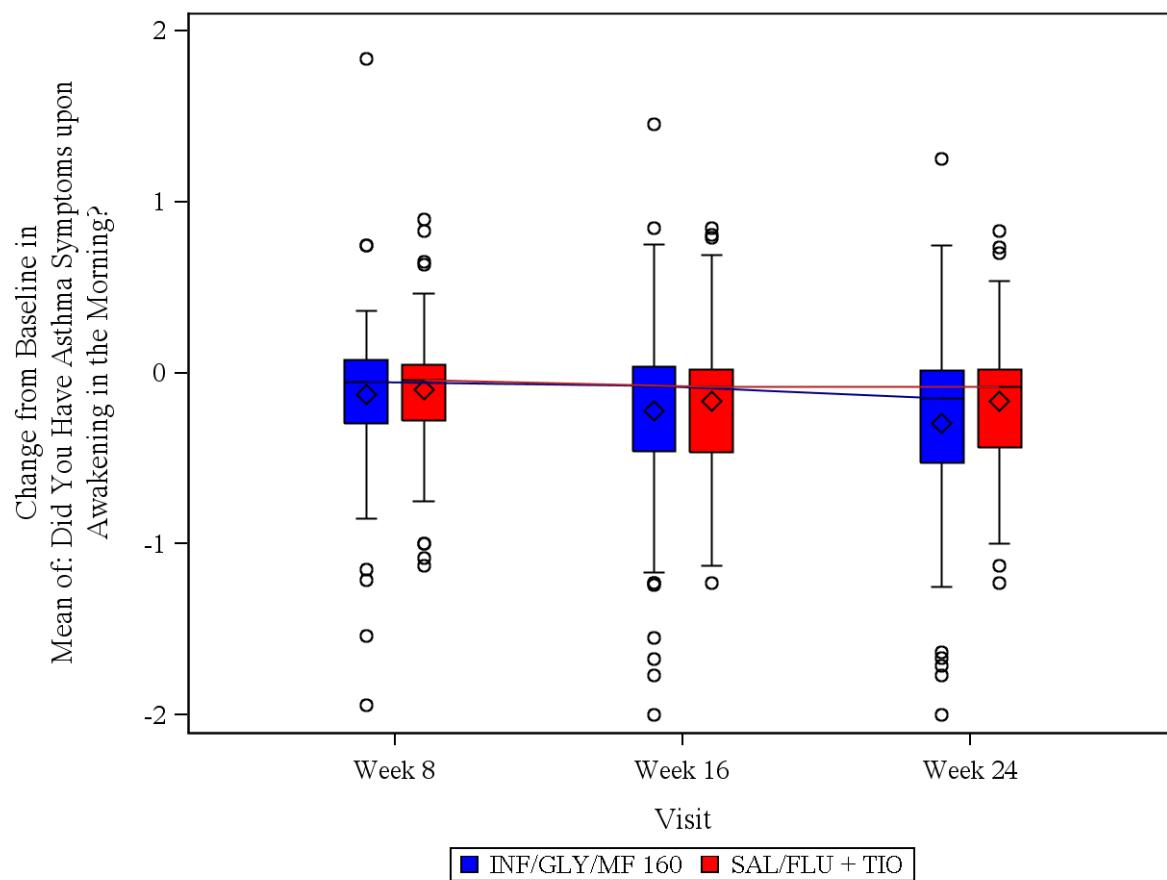
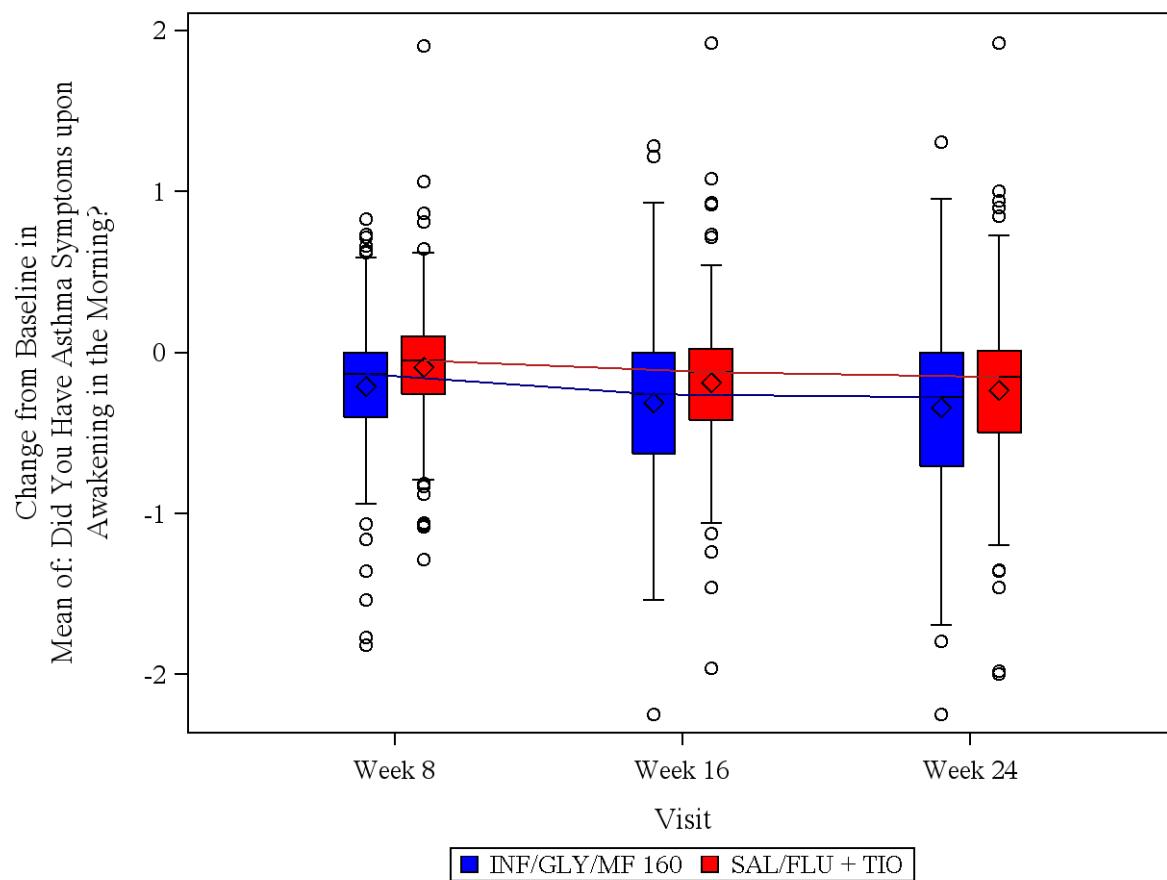


Figure 9.51.2 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Gender (FAS), Gender = Female



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

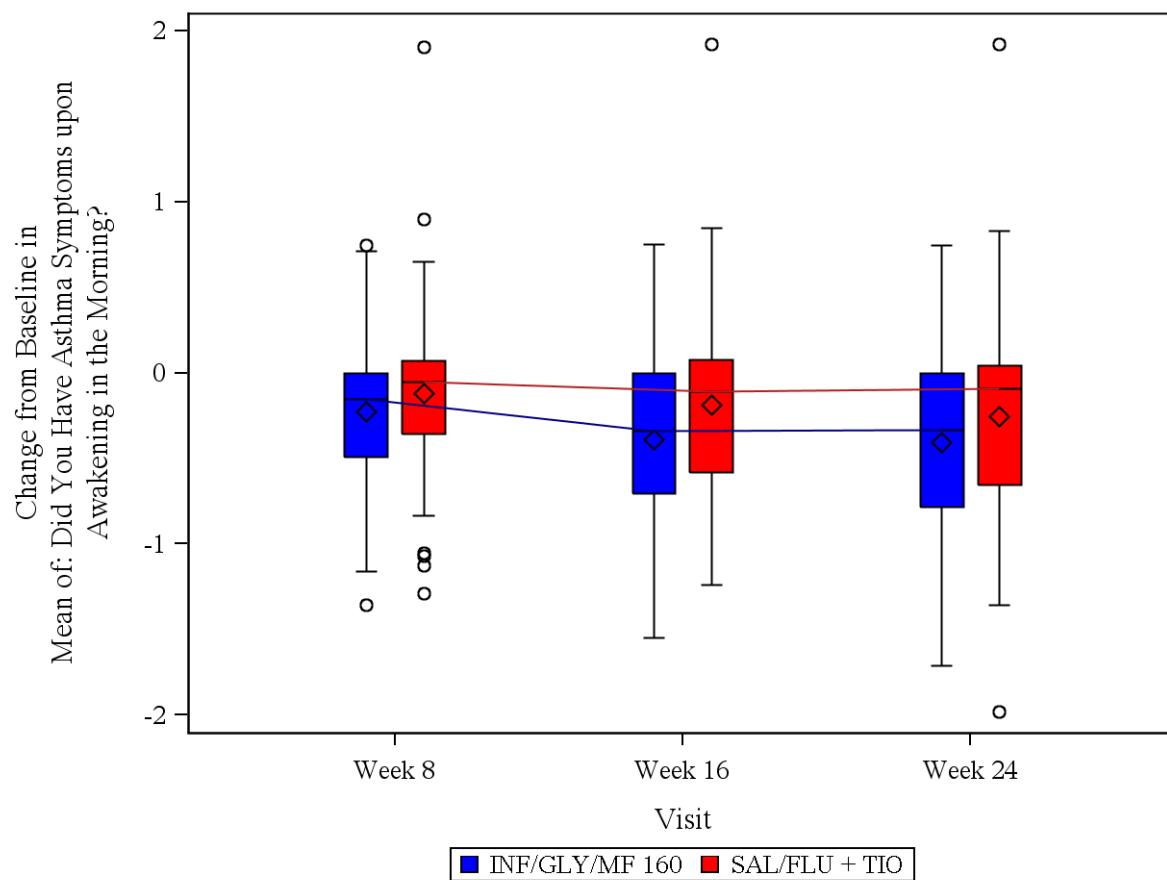


Figure 9.52.2 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Region (FAS), Region = Europe

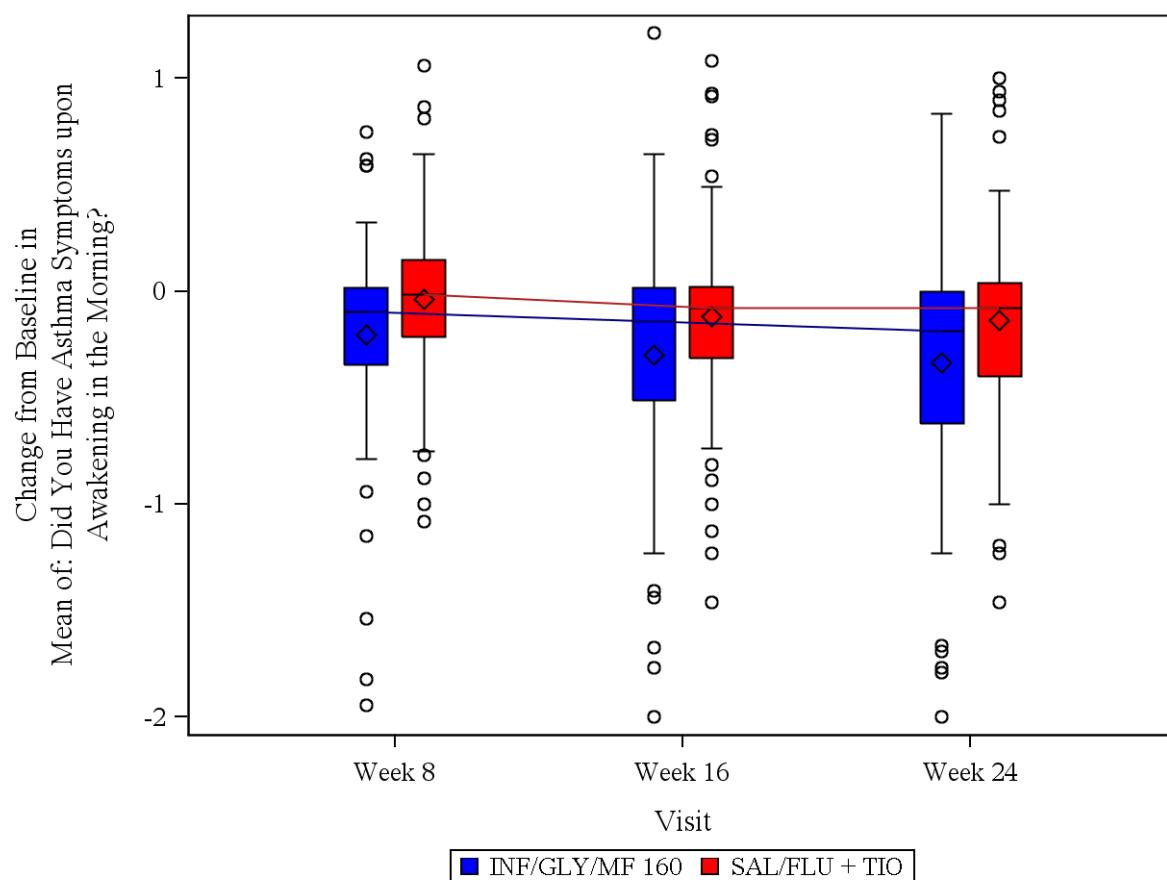


Figure 9.52.3 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Region (FAS), Region = Latin America

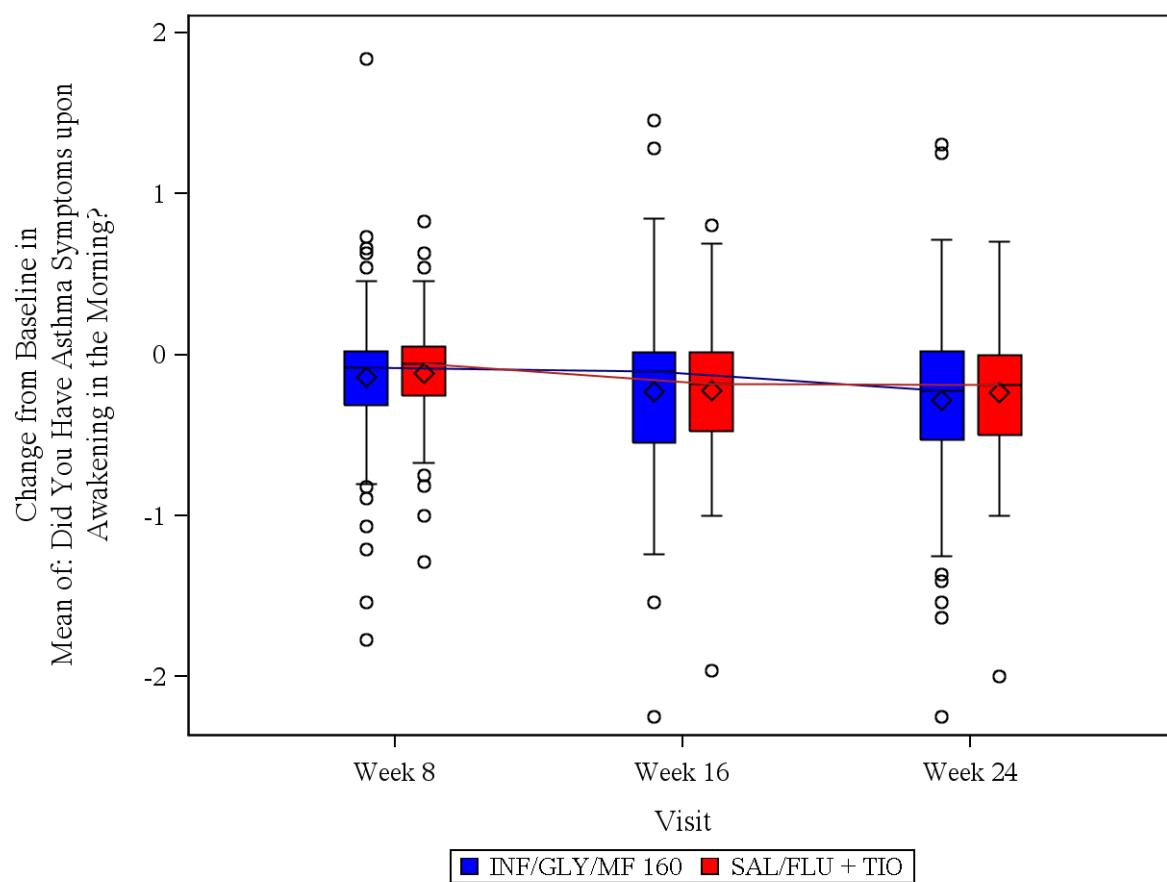
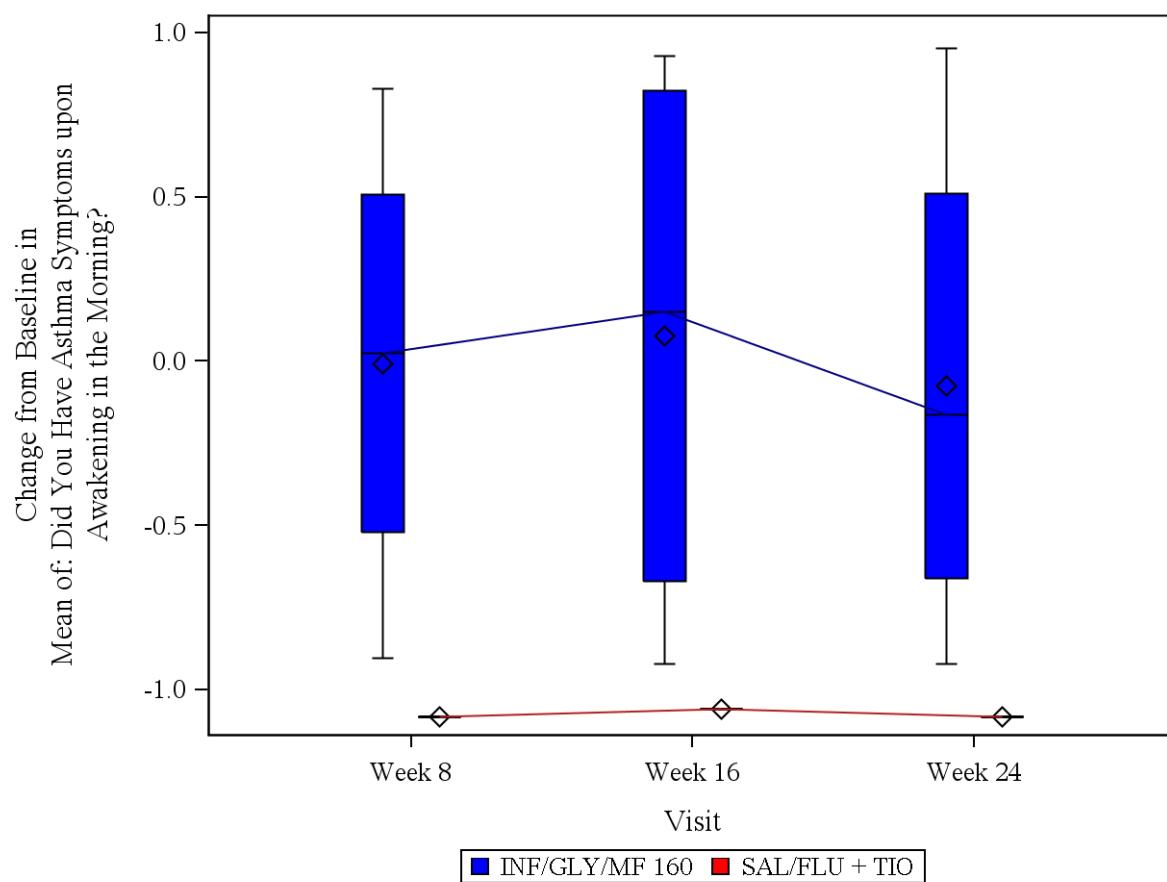
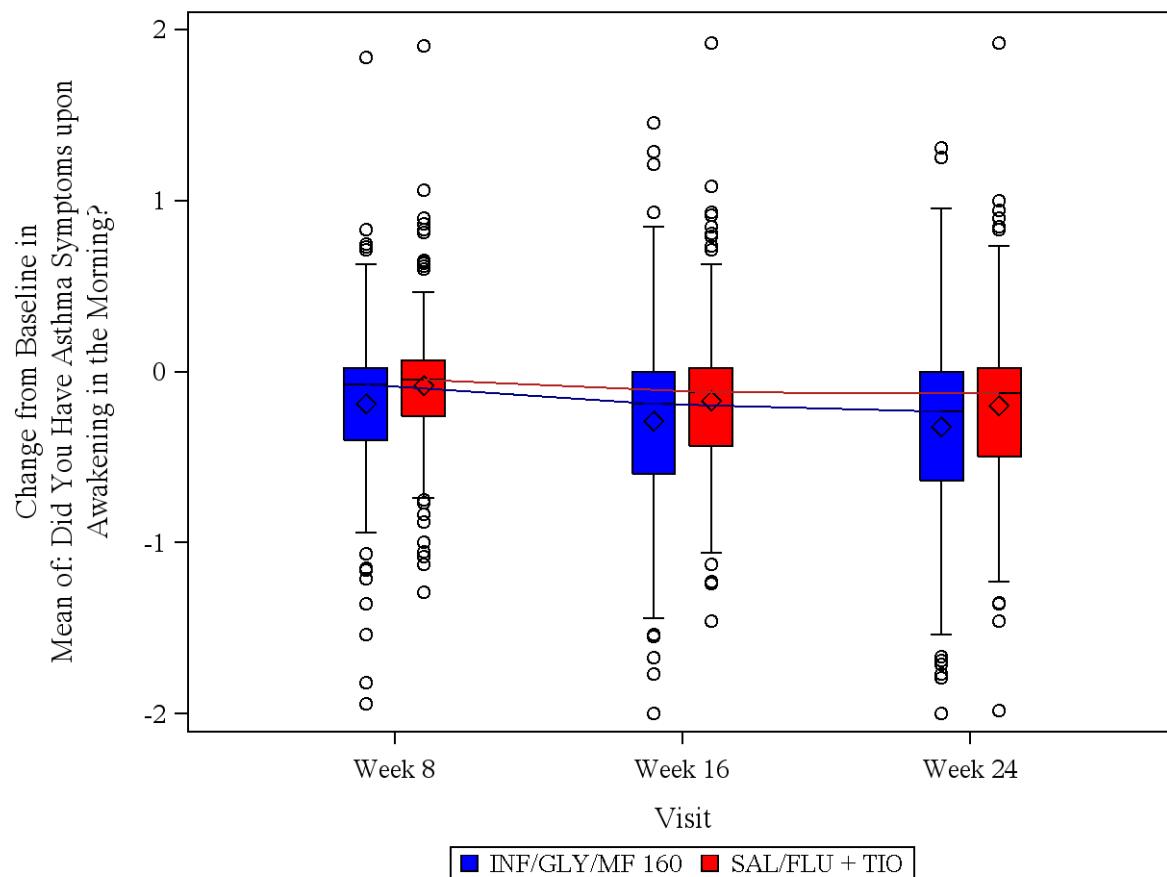


Figure 9.52.4 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by Region (FAS), Region = Others

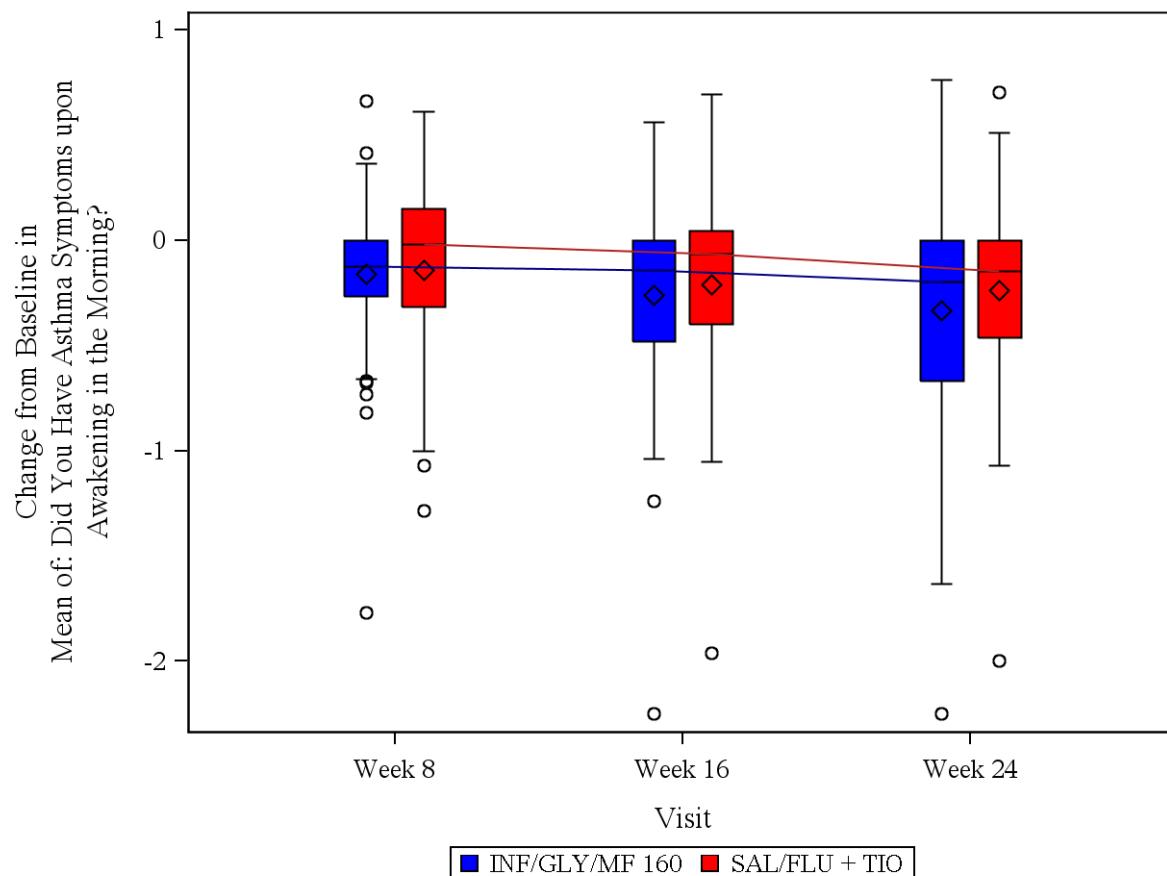


9.53 Boxplot: Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by History of Asthma Exacerbation (FAS)

**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**

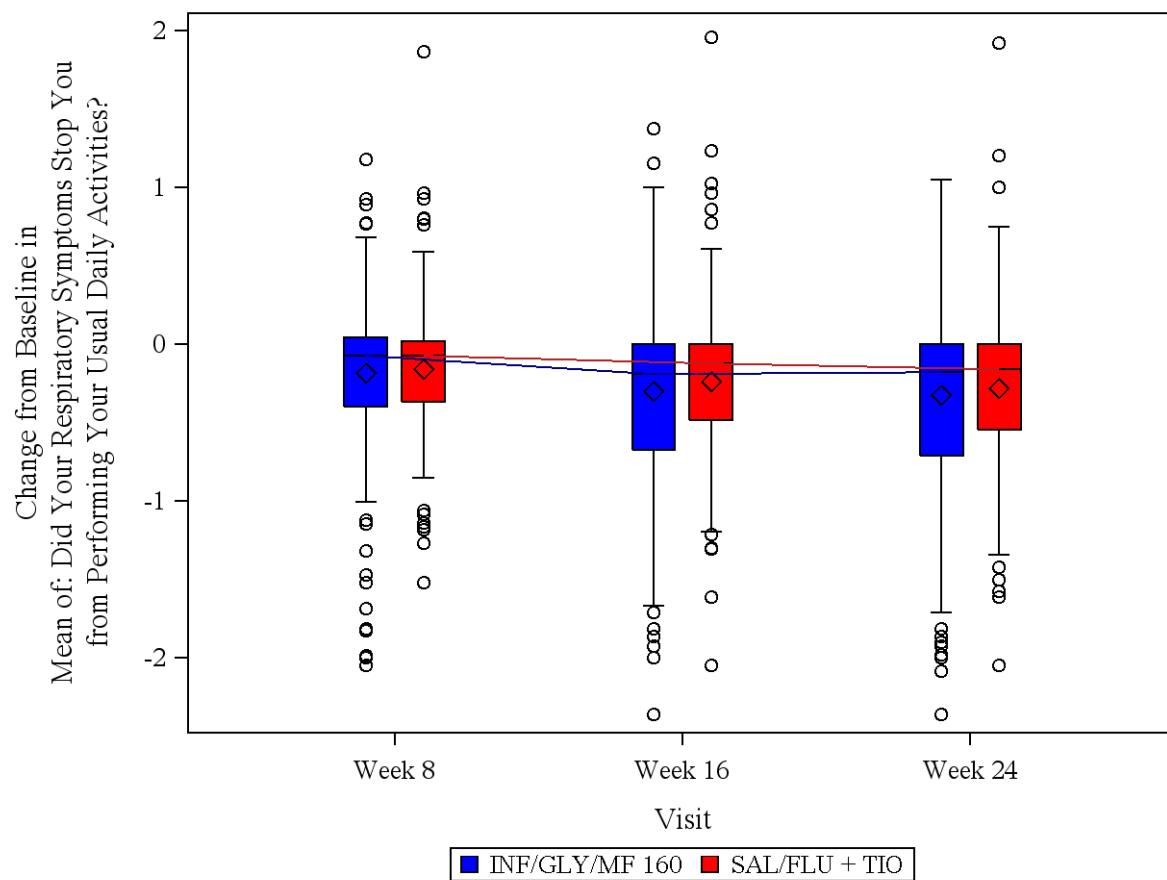


**Figure 9.53.2 Symptoms (Mean of: Did You Have Asthma Symptoms upon Awakening in the Morning?) - Change from Baseline by History of Asthma Exacerbation (FAS),
Asthma exacerbations in the 12 months prior to screening = ≥ 2**



9.55 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

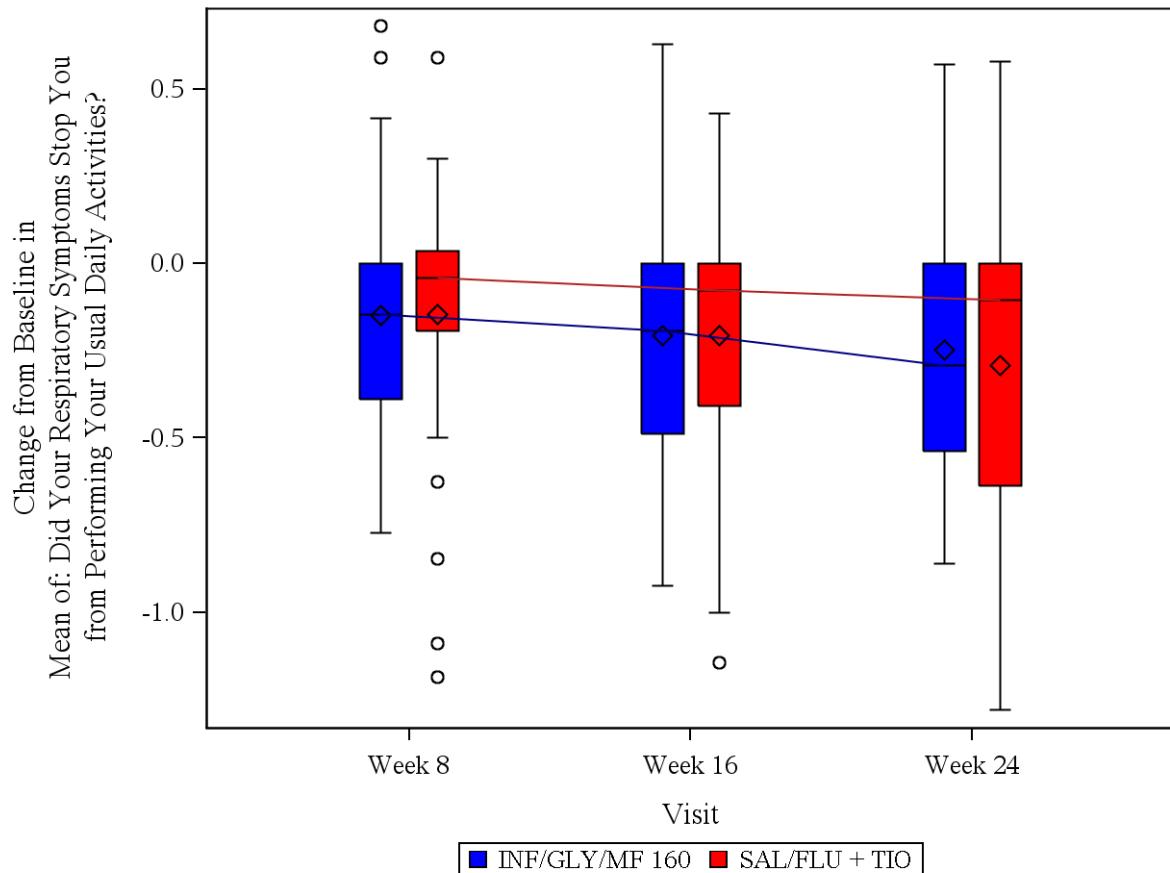


Figure 9.56.2 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Age (FAS), Age = 40-64 years

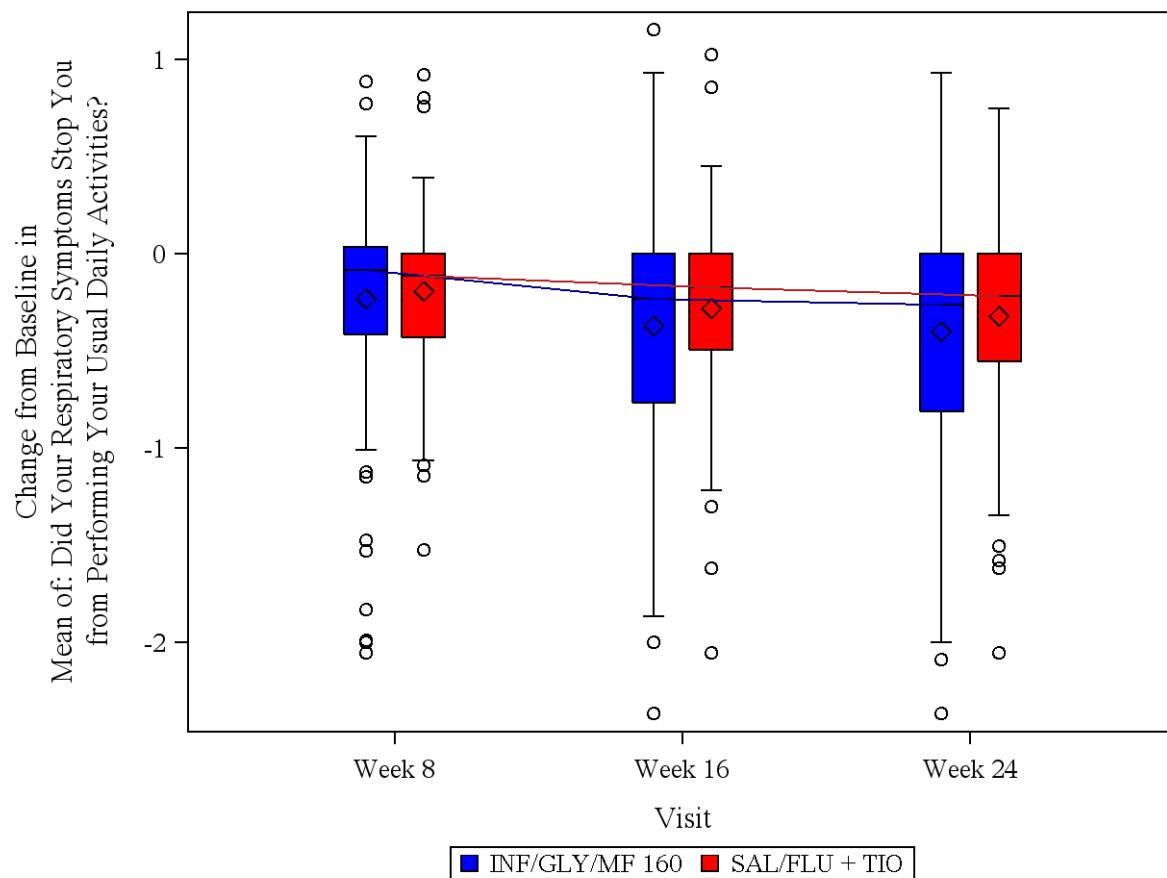
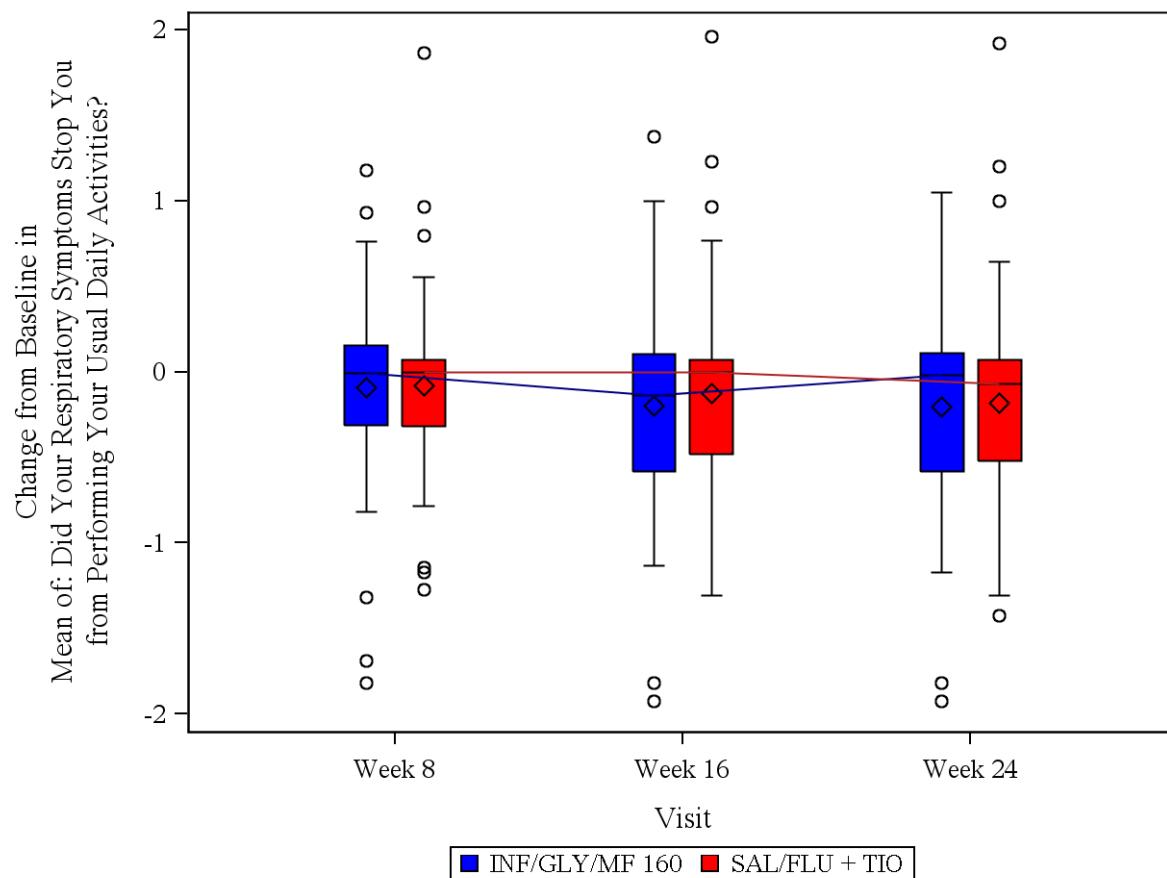


Figure 9.56.3 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

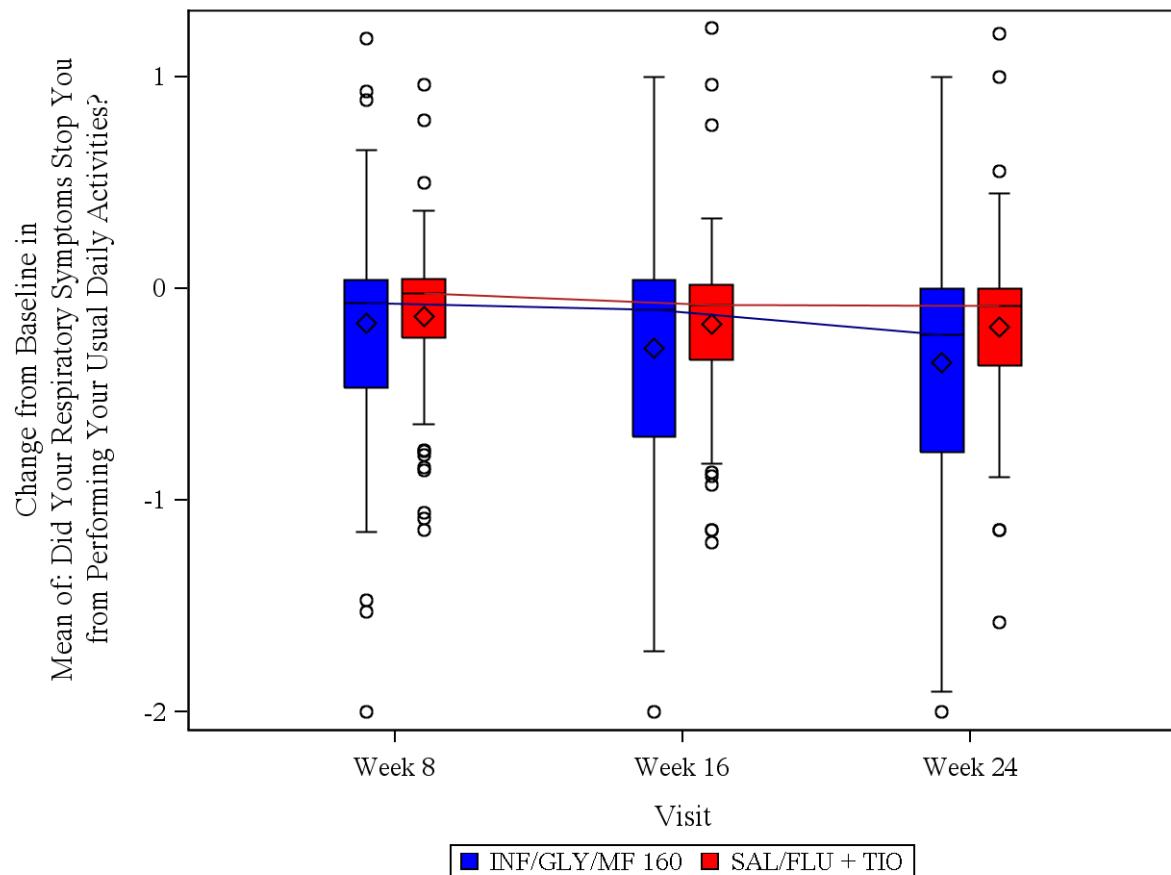
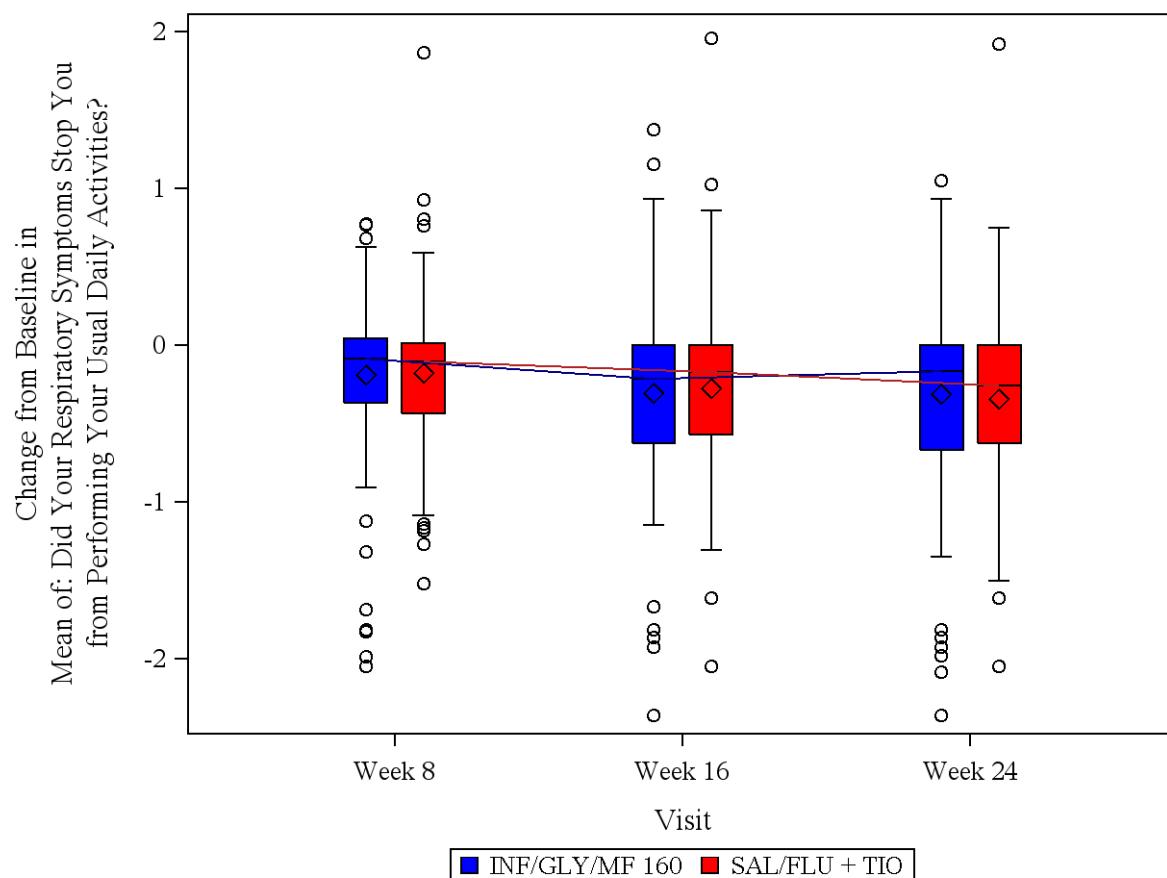


Figure 9.57.2 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Gender (FAS), Gender = Female



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

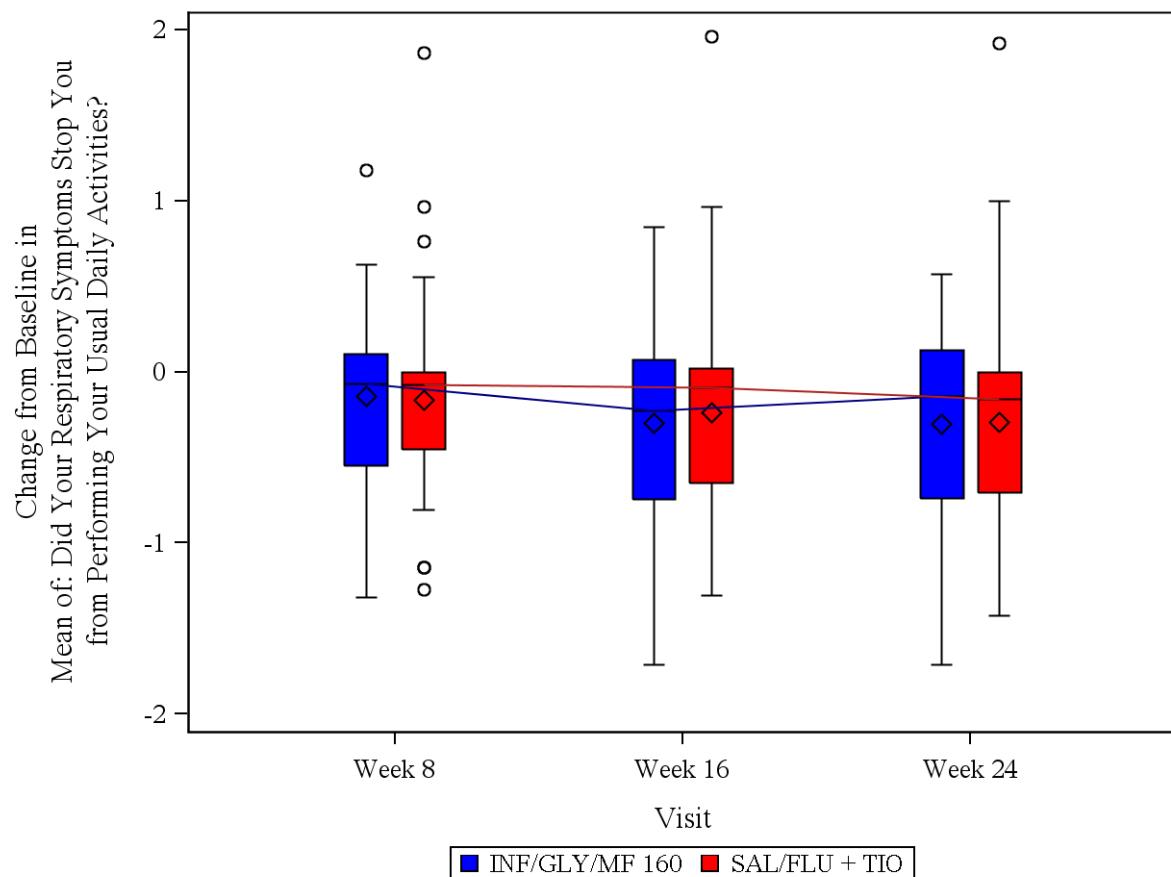


Figure 9.58.2 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Region (FAS), Region = Europe

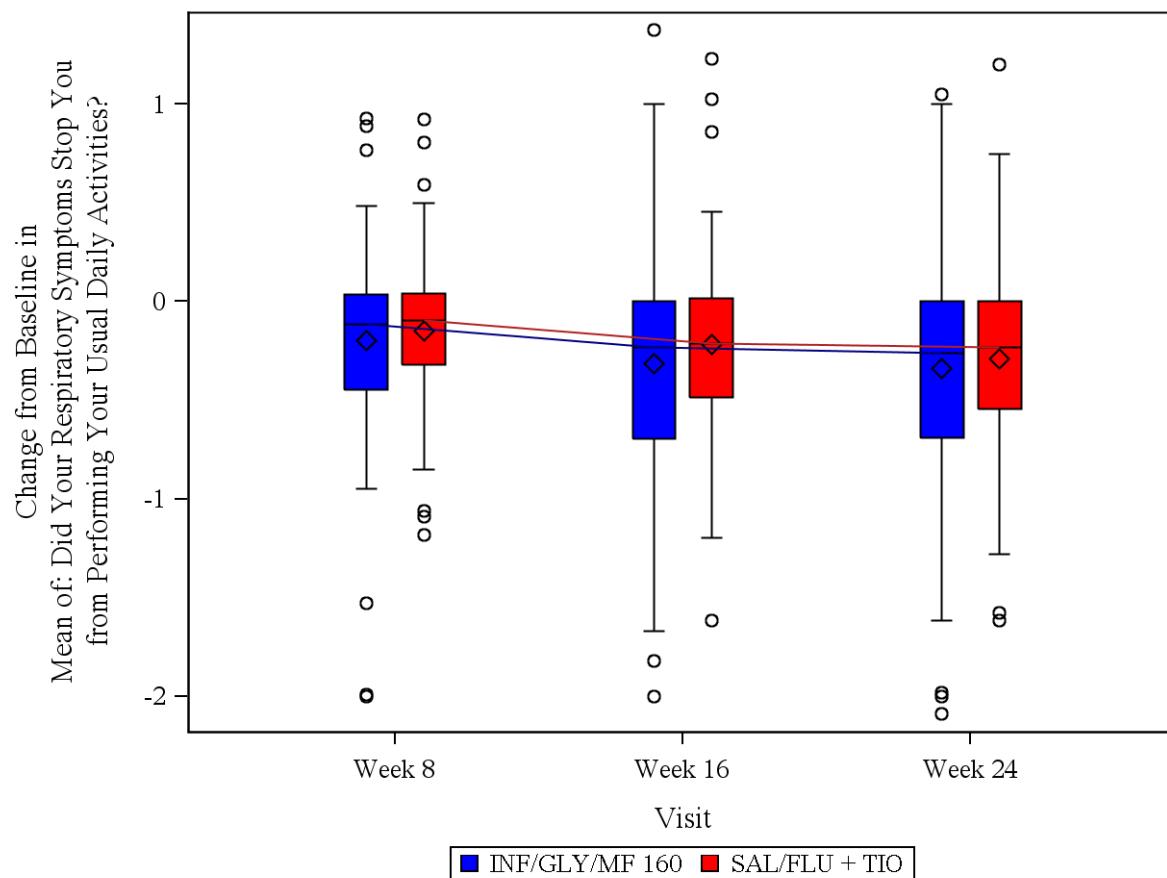


Figure 9.58.3 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Region (FAS), Region = Latin America

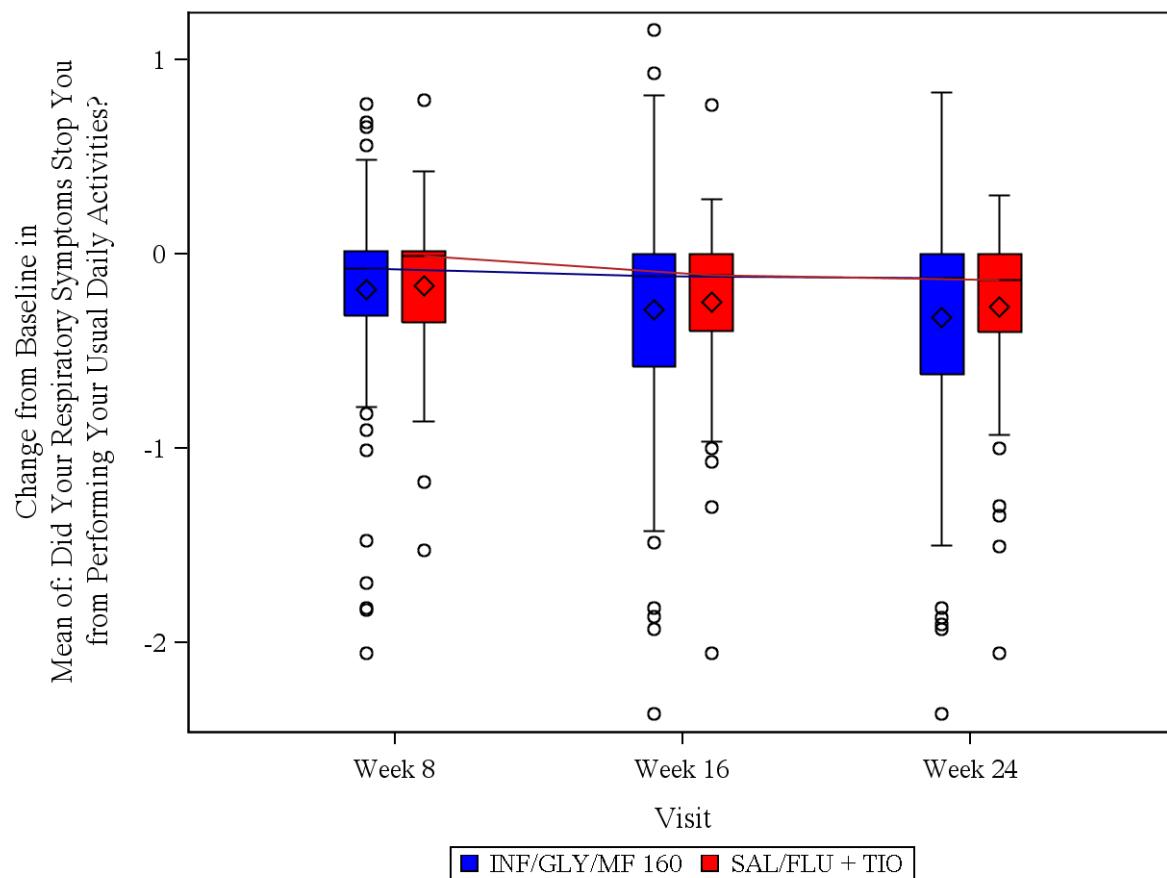
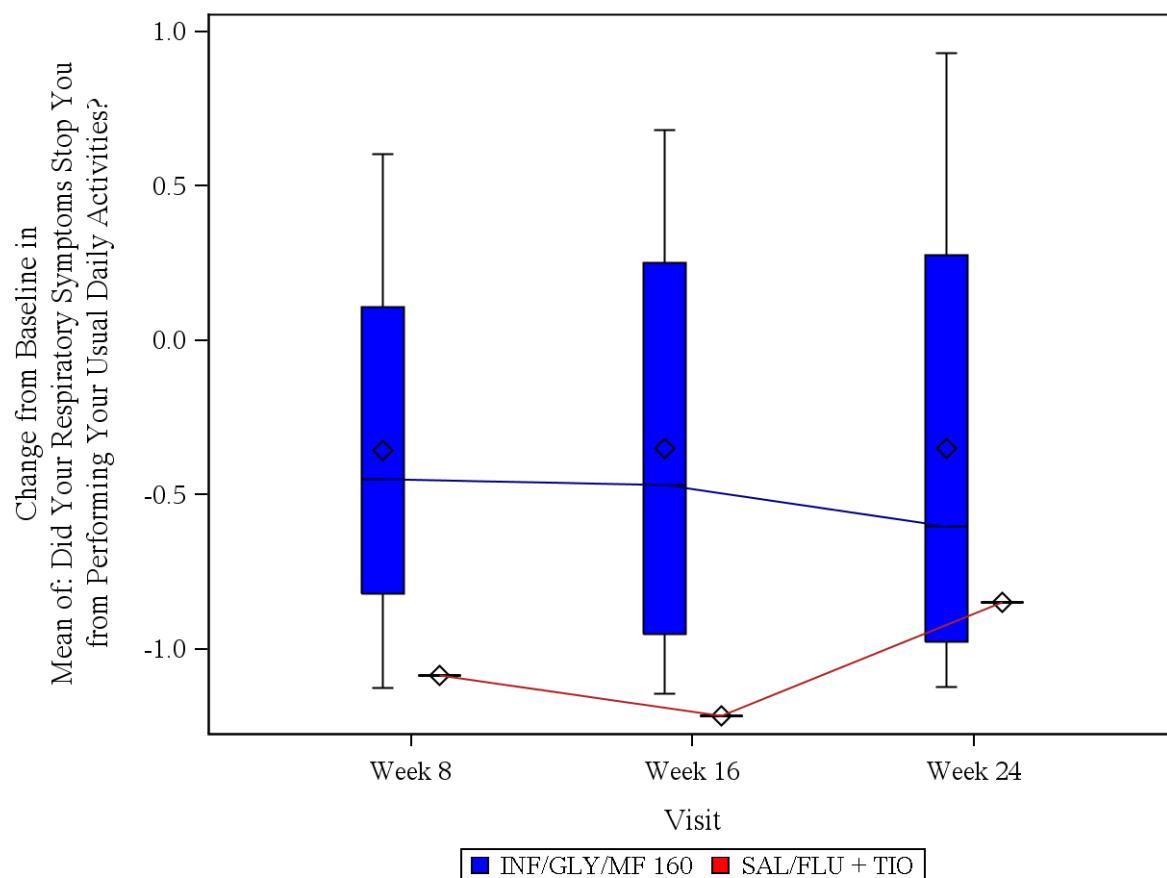


Figure 9.58.4 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by Region (FAS), Region = Others



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

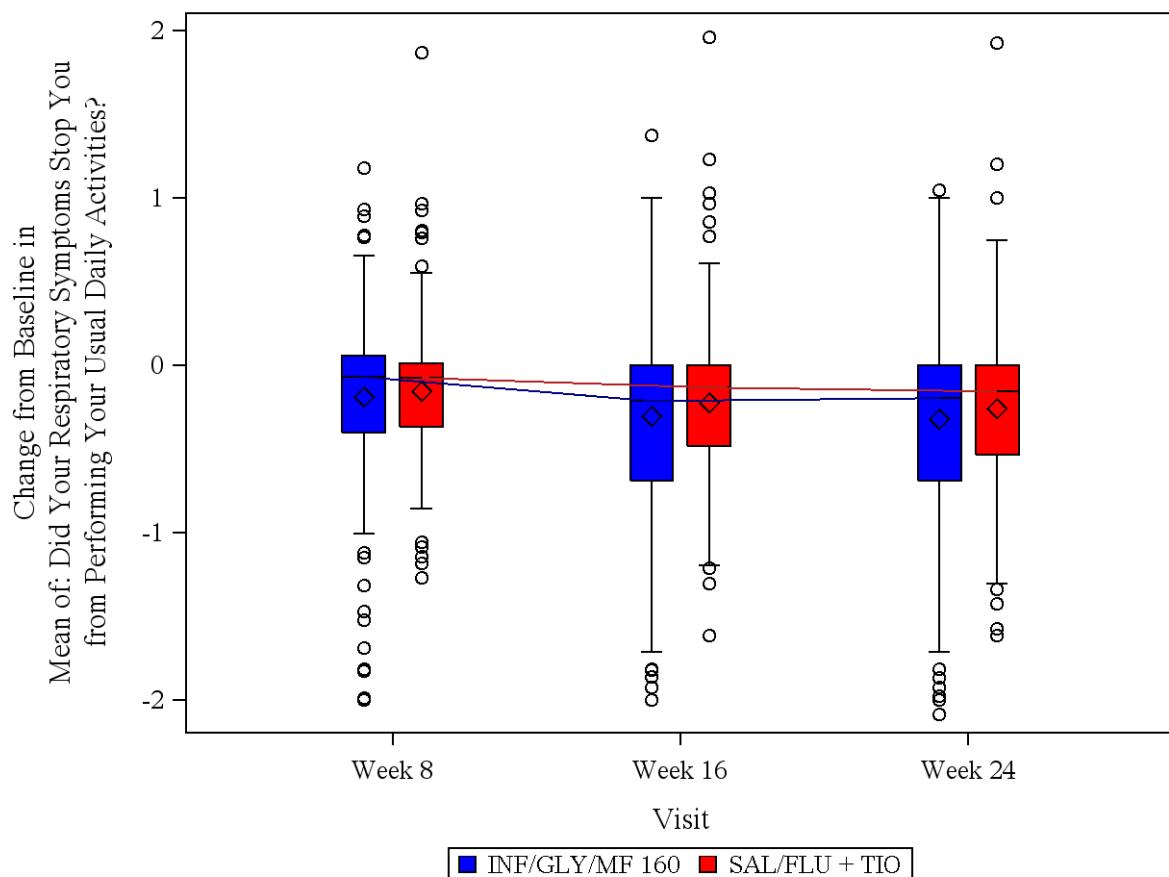
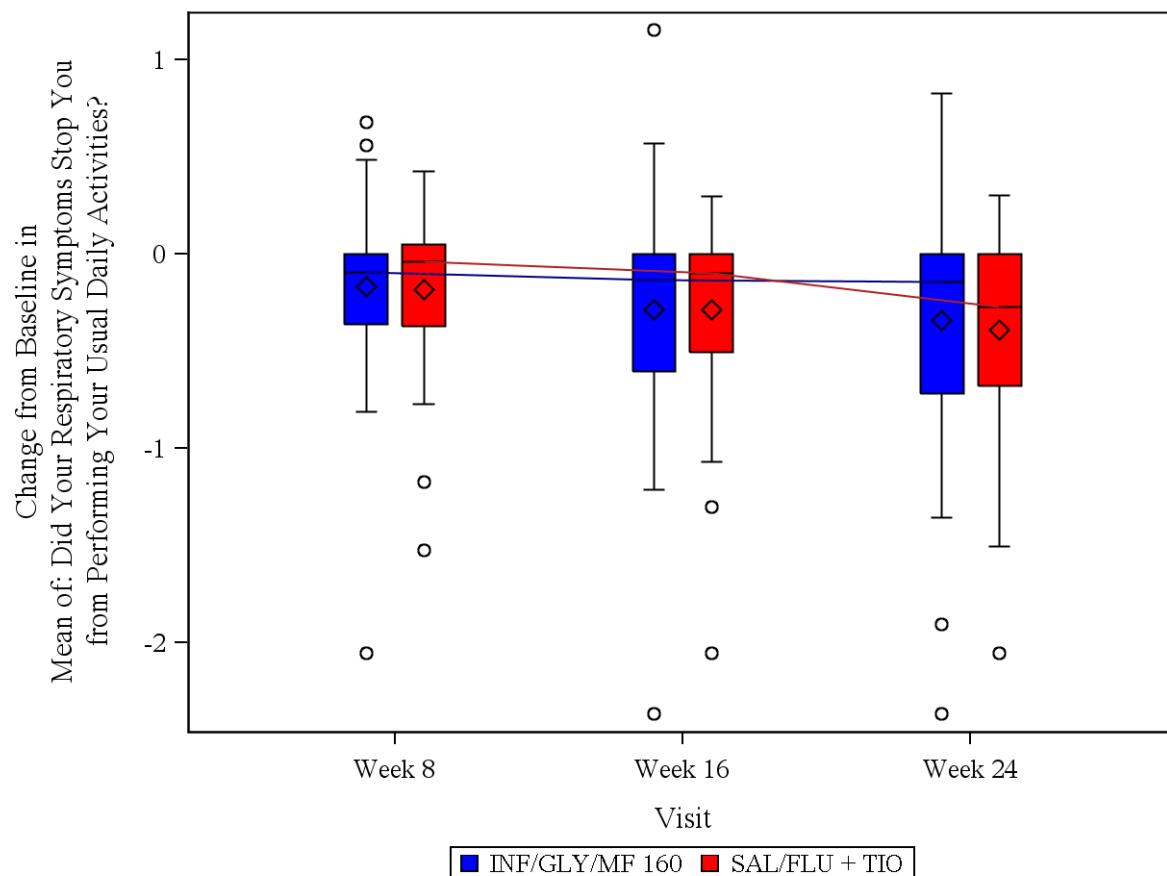
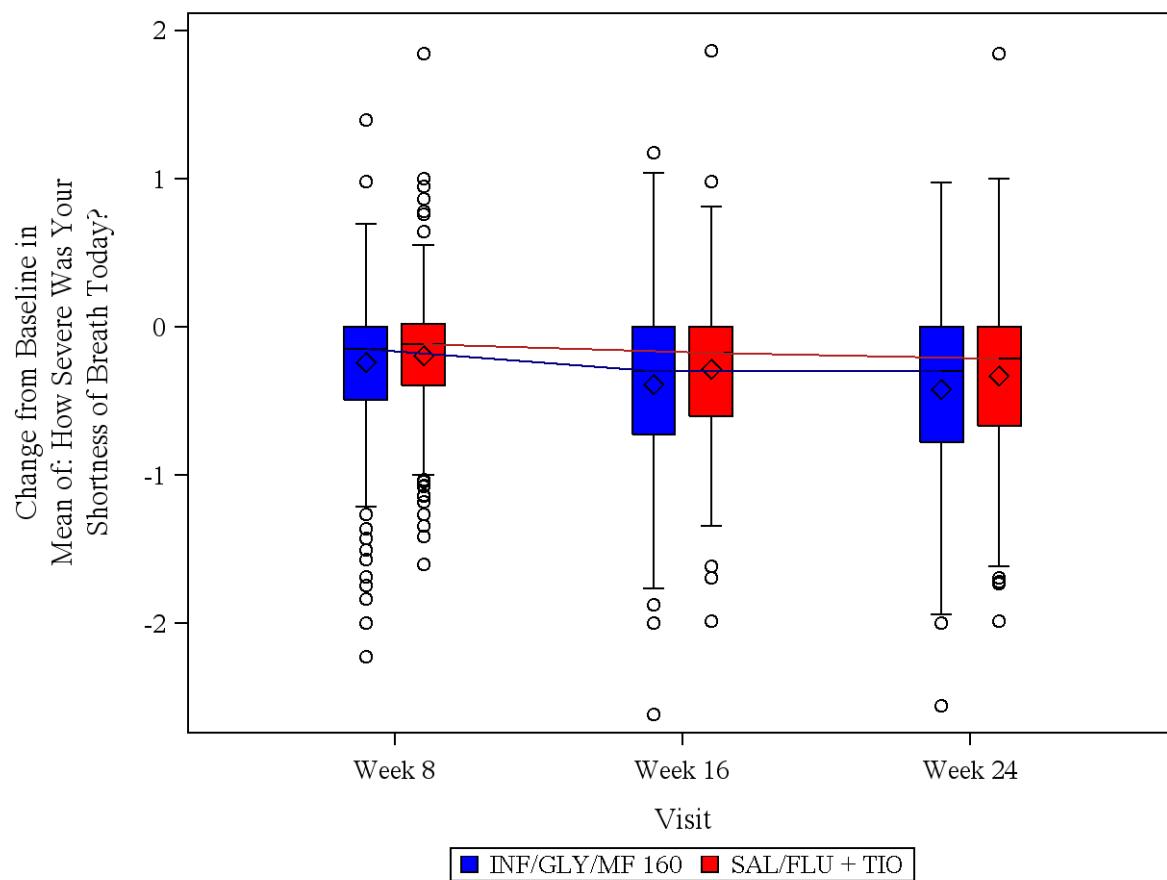


Figure 9.59.2 Symptoms (Mean of: Did Your Respiratory Symptoms Stop You from Performing Your Usual Daily Activities?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



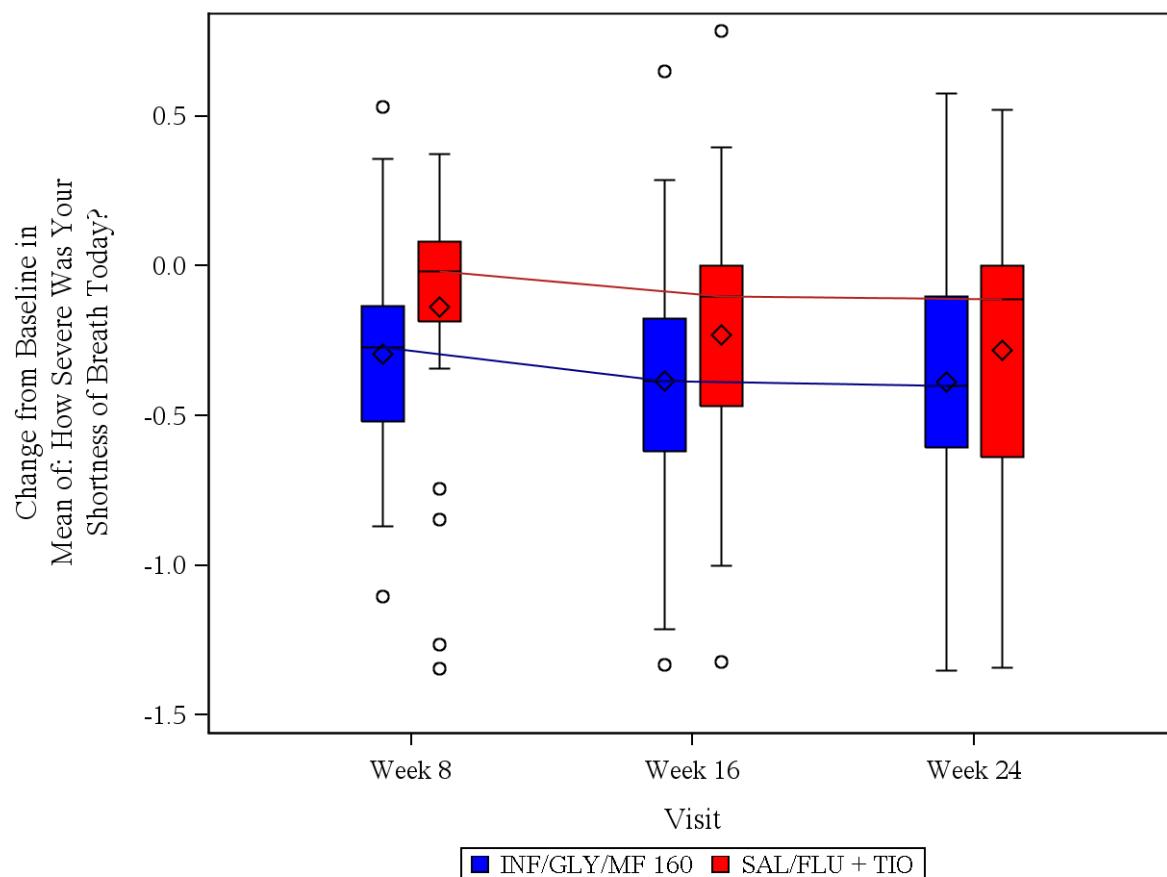
9.61 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline (FAS)

Figure 9.61 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?) - Change from Baseline (FAS)

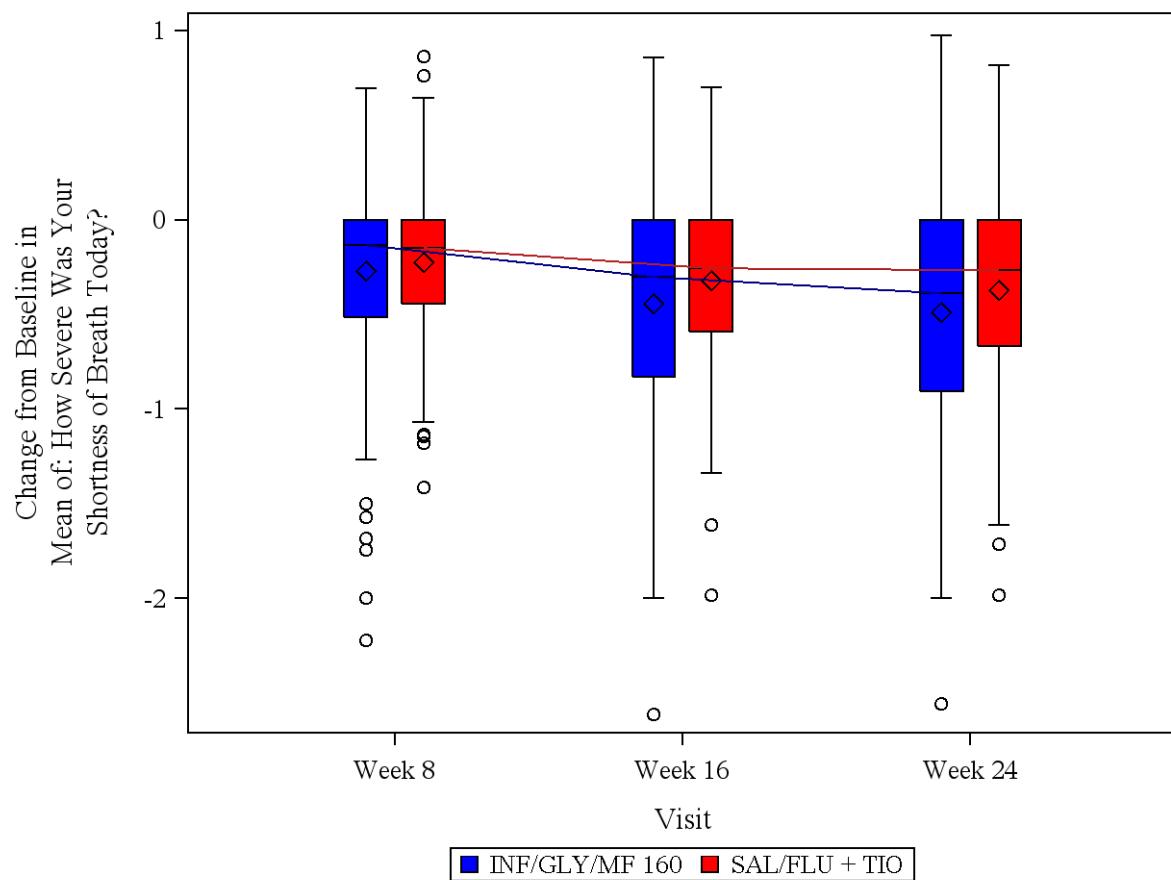


**9.62 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?)
- Change from Baseline by Age (FAS)**

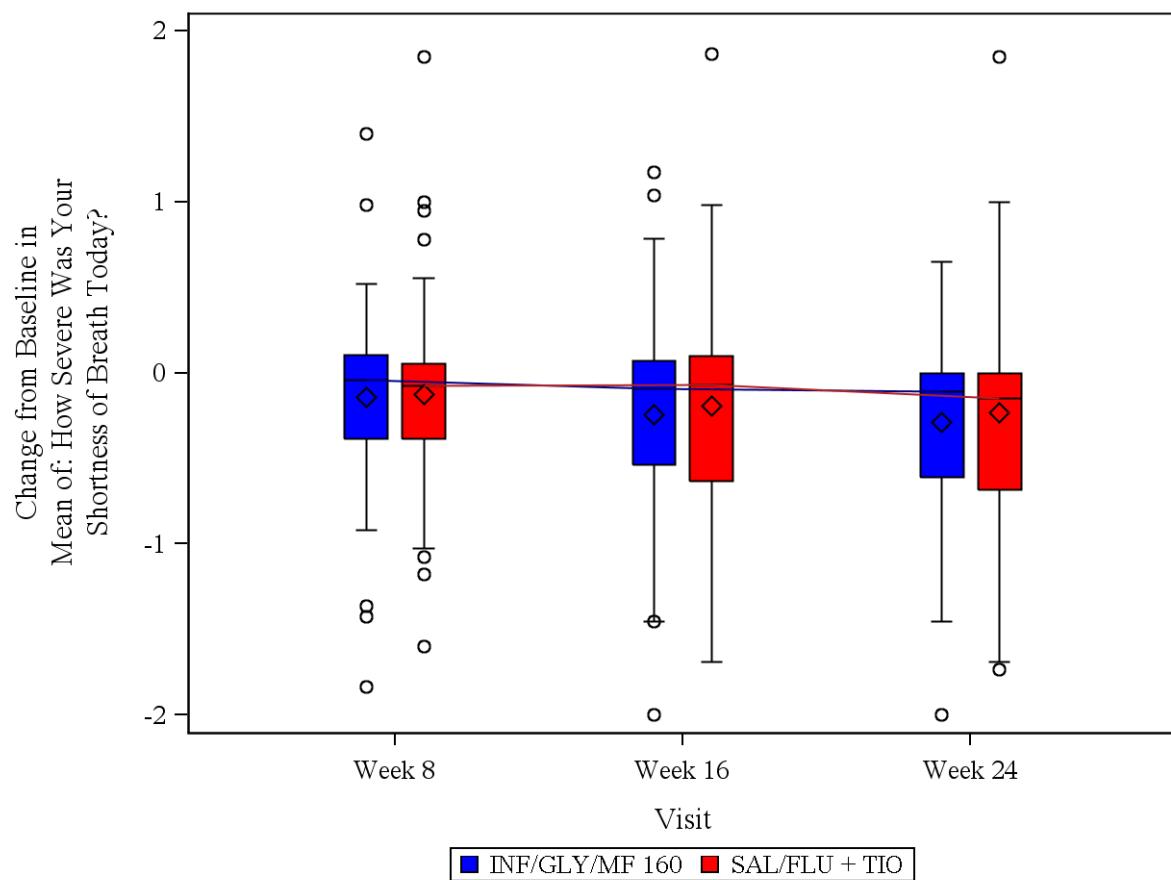
**Figure 9.62.1 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?)
- Change from Baseline by Age (FAS), Age = 18-39 years**



**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**

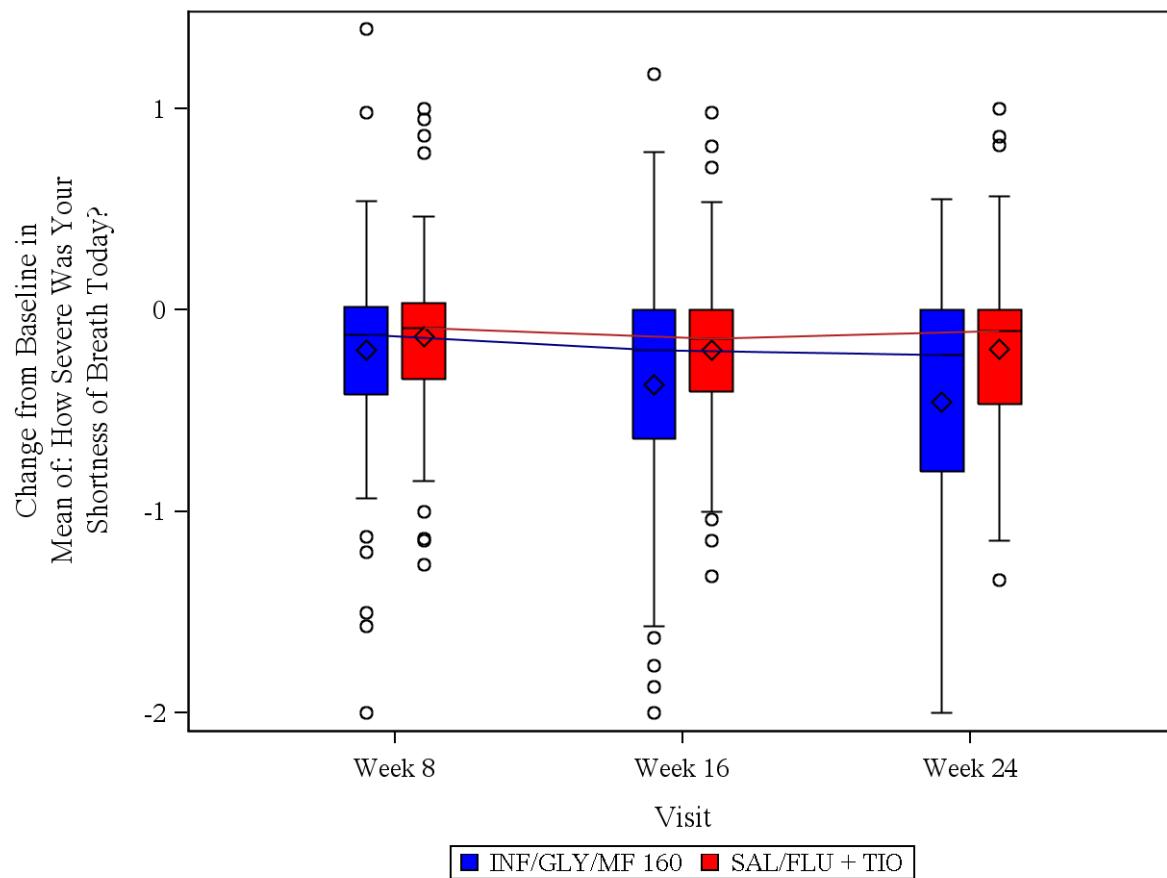


**Figure 9.62.3 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?)
- Change from Baseline by Age (FAS), Age = ≥ 65 years**

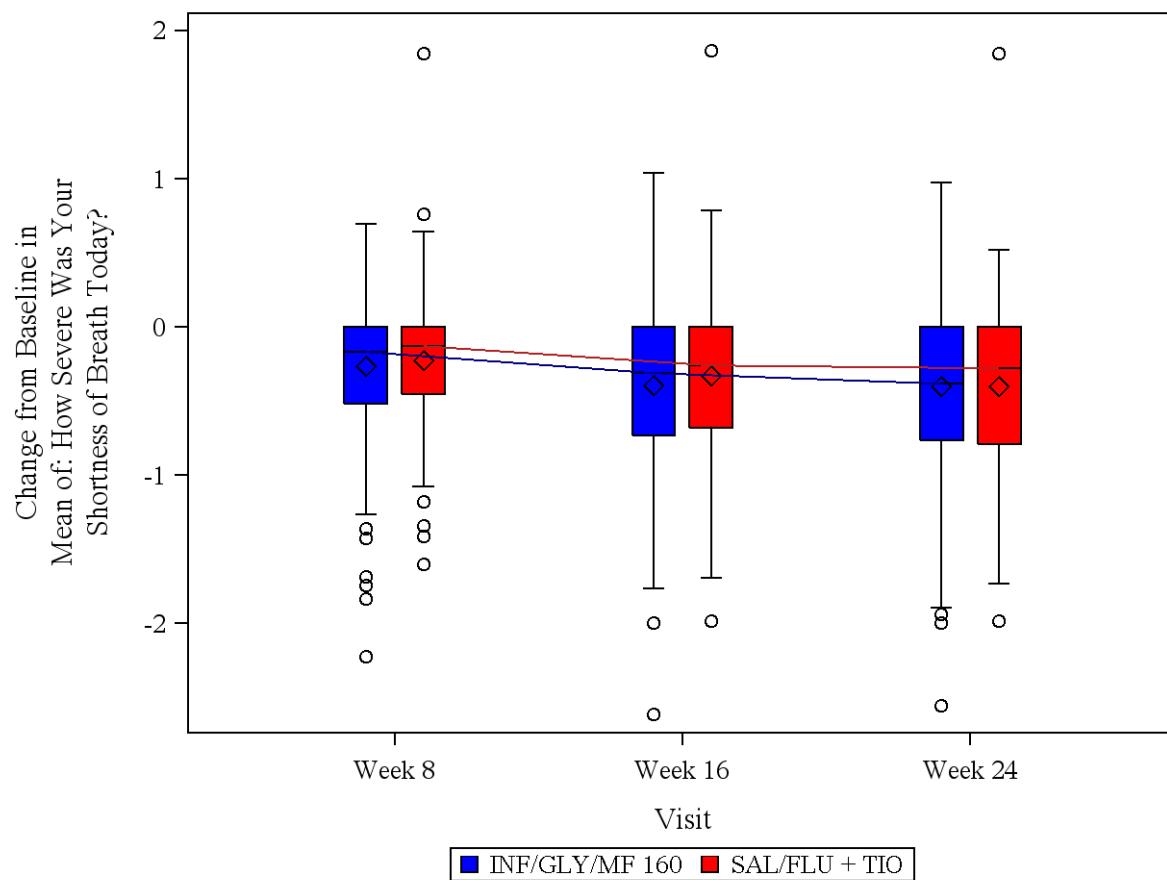


**9.63 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?)
- Change from Baseline by Gender (FAS)**

**Figure 9.63.1 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?)
- Change from Baseline by Gender (FAS), Gender = Male**

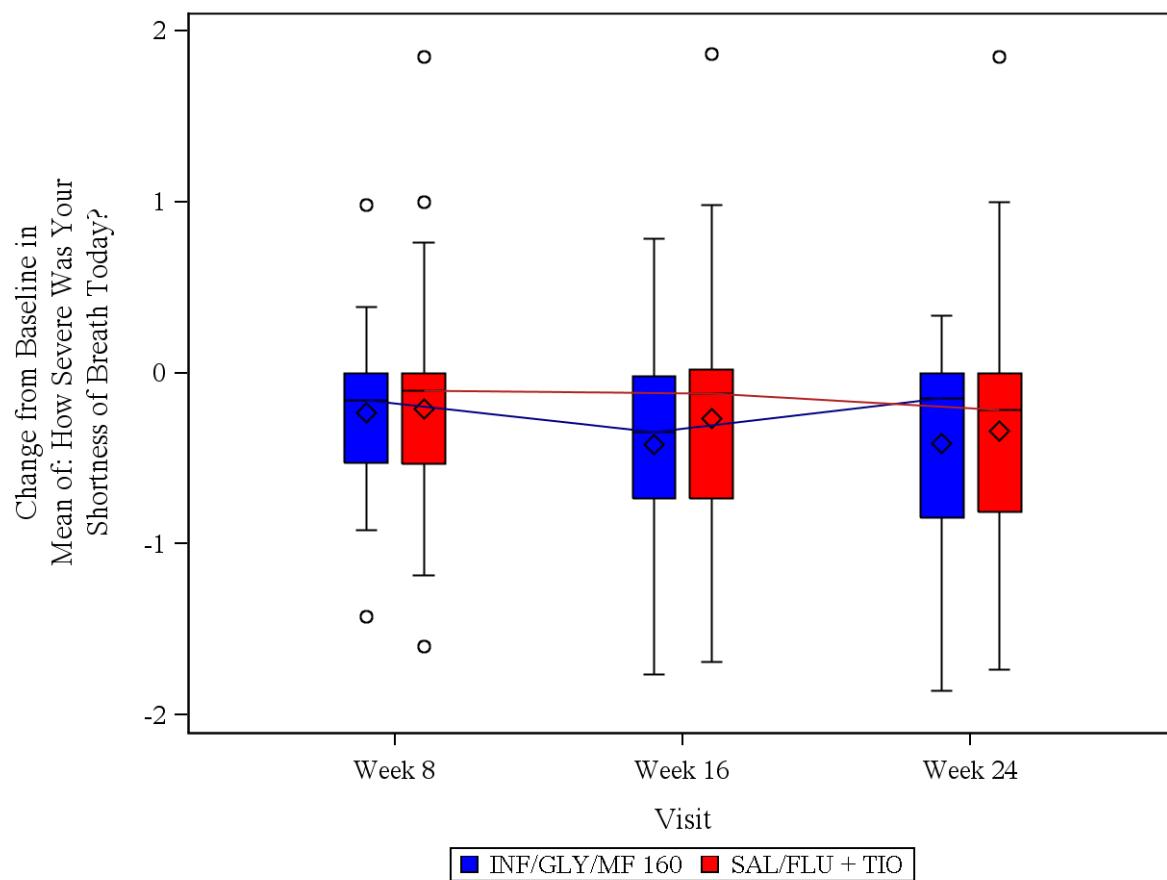


**Figure 9.63.2 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?)
- Change from Baseline by Gender (FAS), Gender = Female**

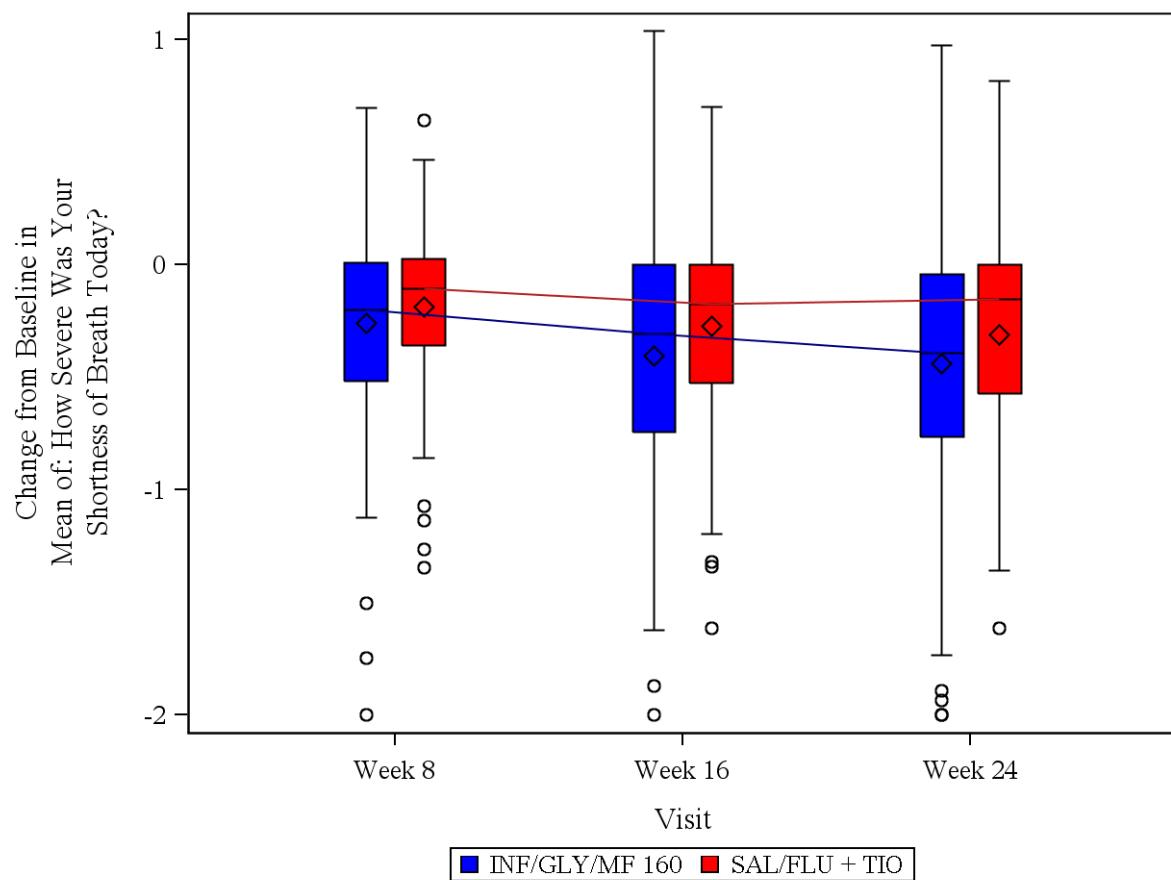


**9.64 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?)
- Change from Baseline by Region (FAS)**

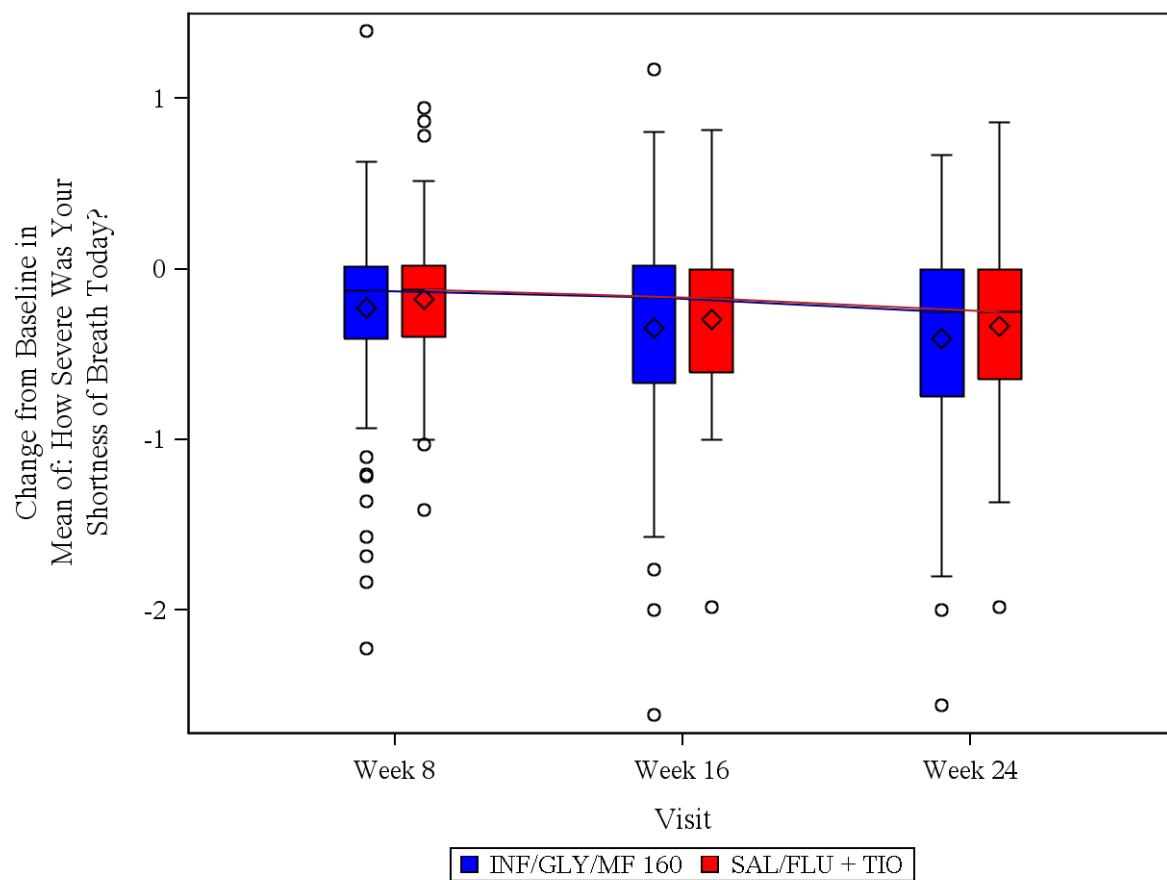
**Figure 9.64.1 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?)
- Change from Baseline by Region (FAS), Region = Asia**



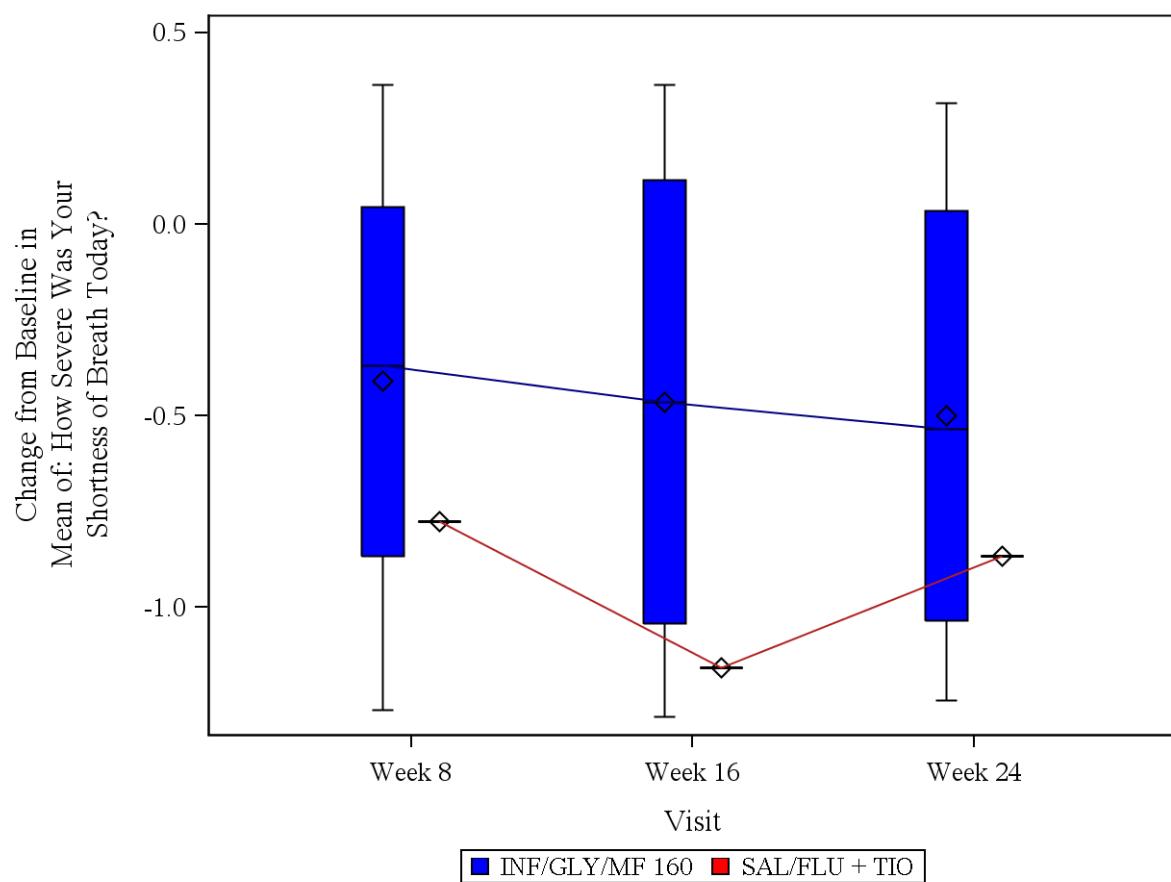
**Figure 9.64.2 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?)
- Change from Baseline by Region (FAS), Region = Europe**



**Figure 9.64.3 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?)
- Change from Baseline by Region (FAS), Region = Latin America**

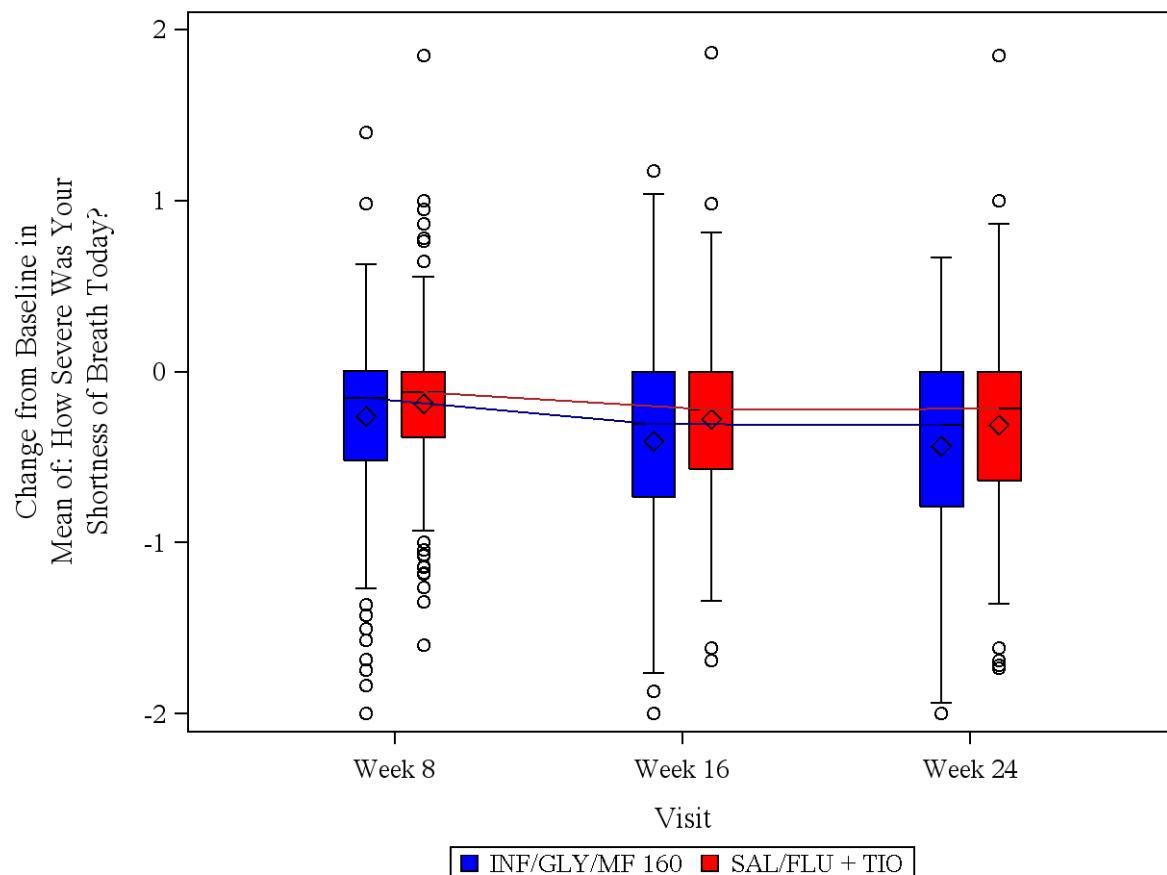


**Figure 9.64.4 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?)
- Change from Baseline by Region (FAS), Region = Others**

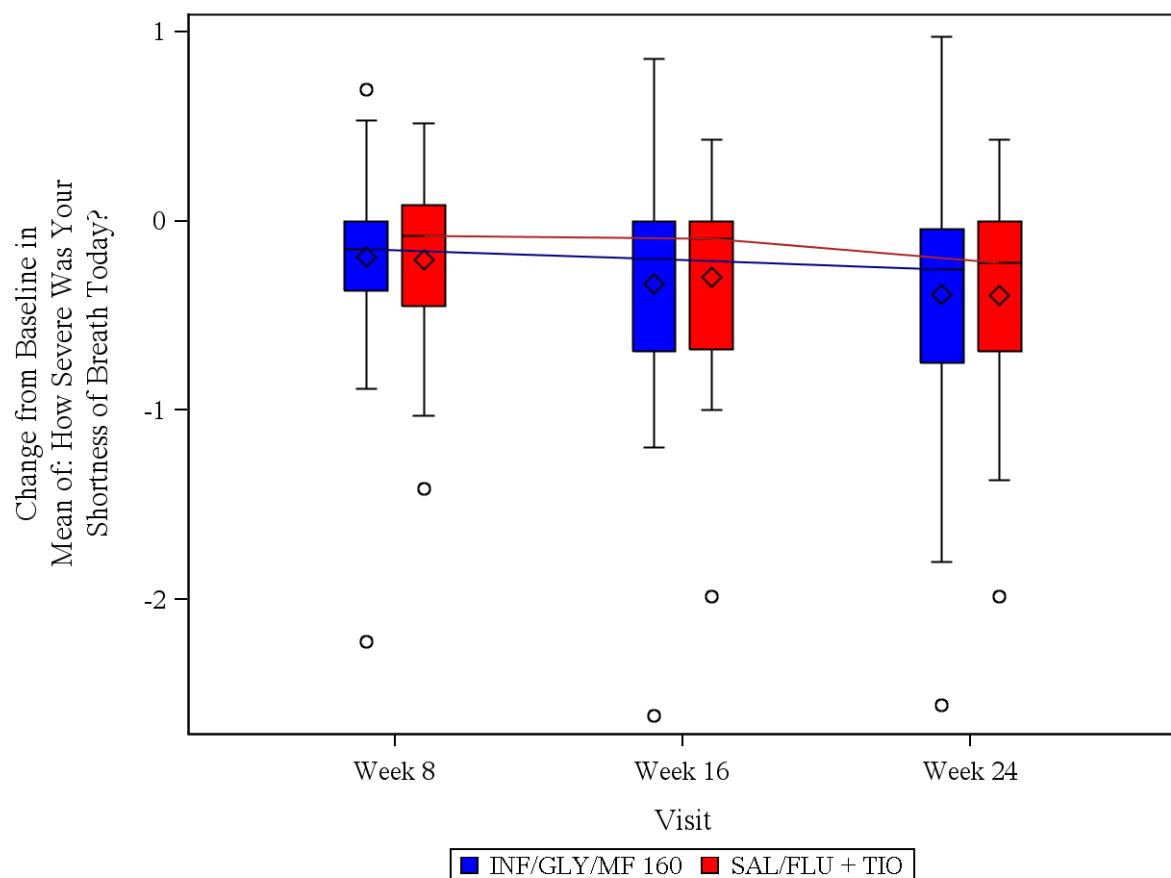


**9.65 Boxplot: Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?)
- Change from Baseline by History of Asthma Exacerbation (FAS)**

**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**

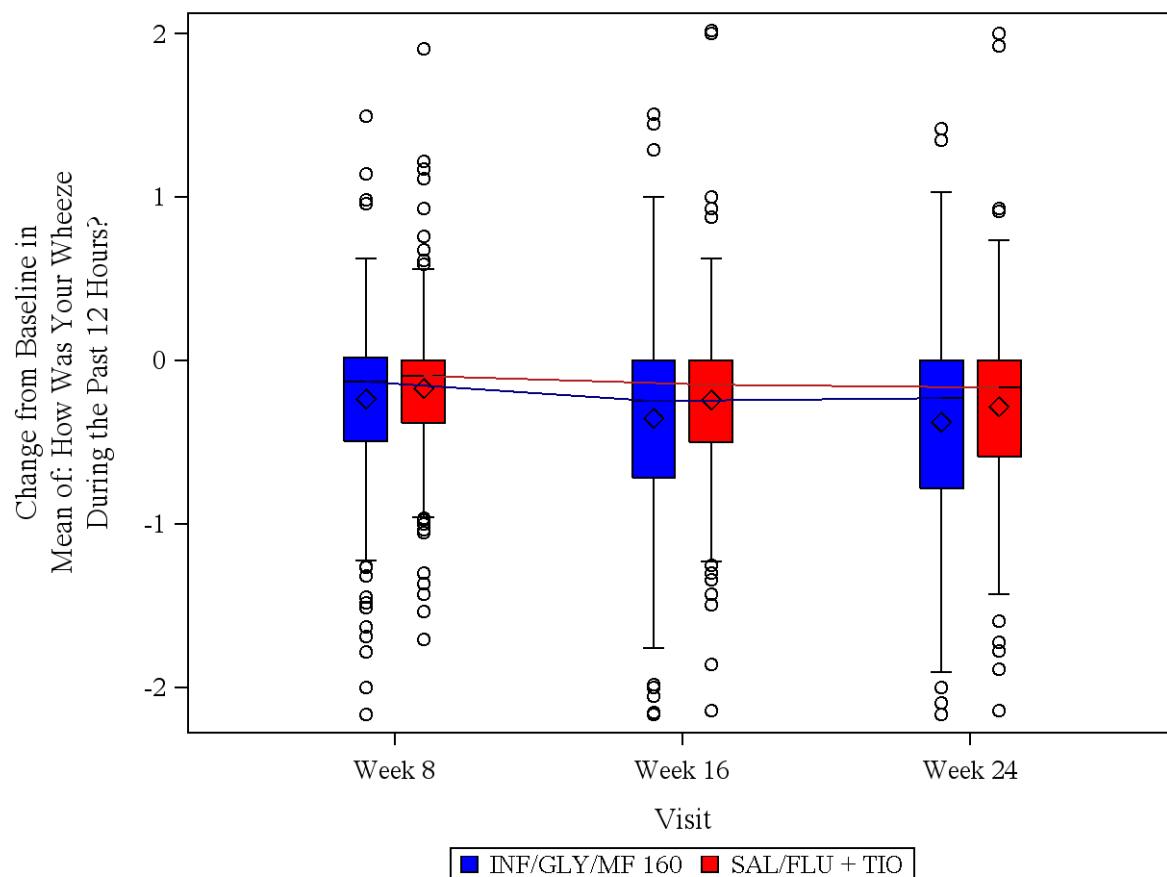


**Figure 9.65.2 Symptoms (Mean of: How Severe Was Your Shortness of Breath Today?)
- Change from Baseline by History of Asthma Exacerbation (FAS), Asthma
exacerbations in the 12 months prior to screening = ≥2**



9.67 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

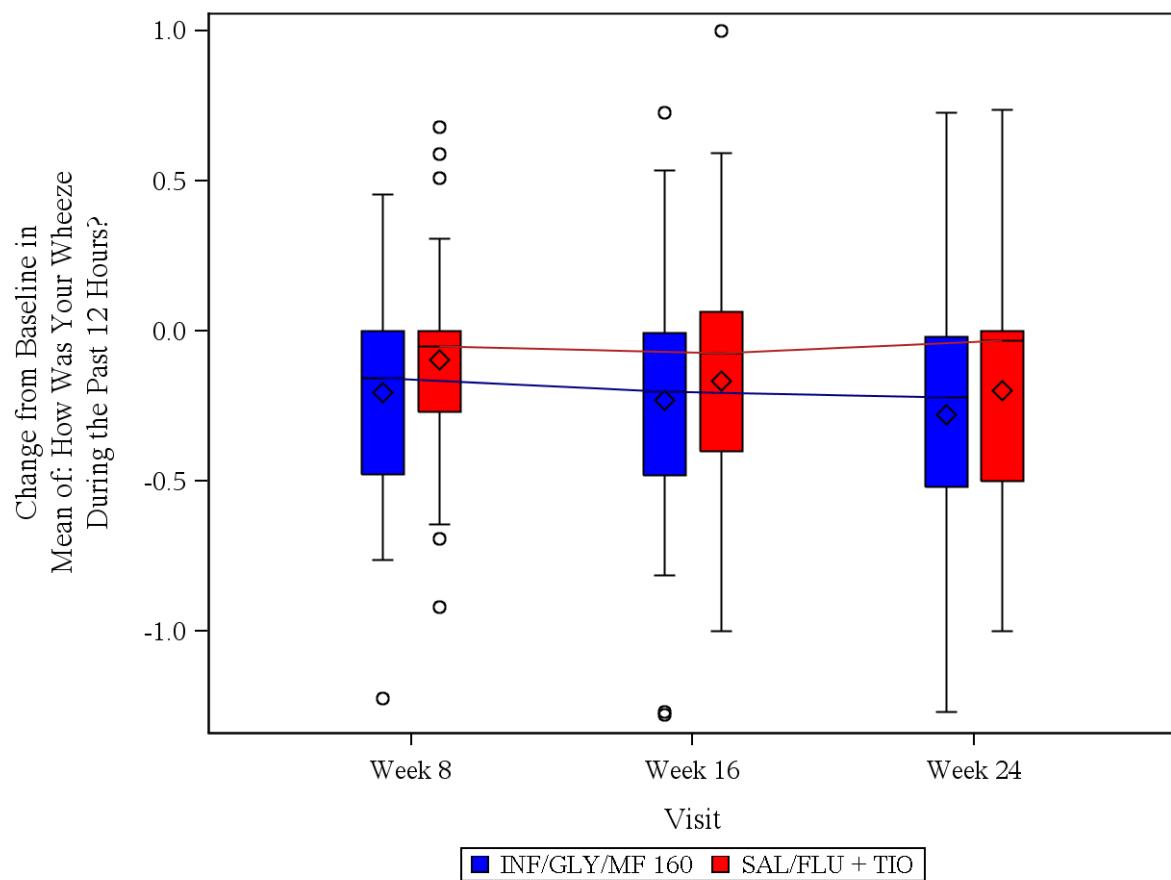


Figure 9.68.2 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Age (FAS), Age = 40-64 years

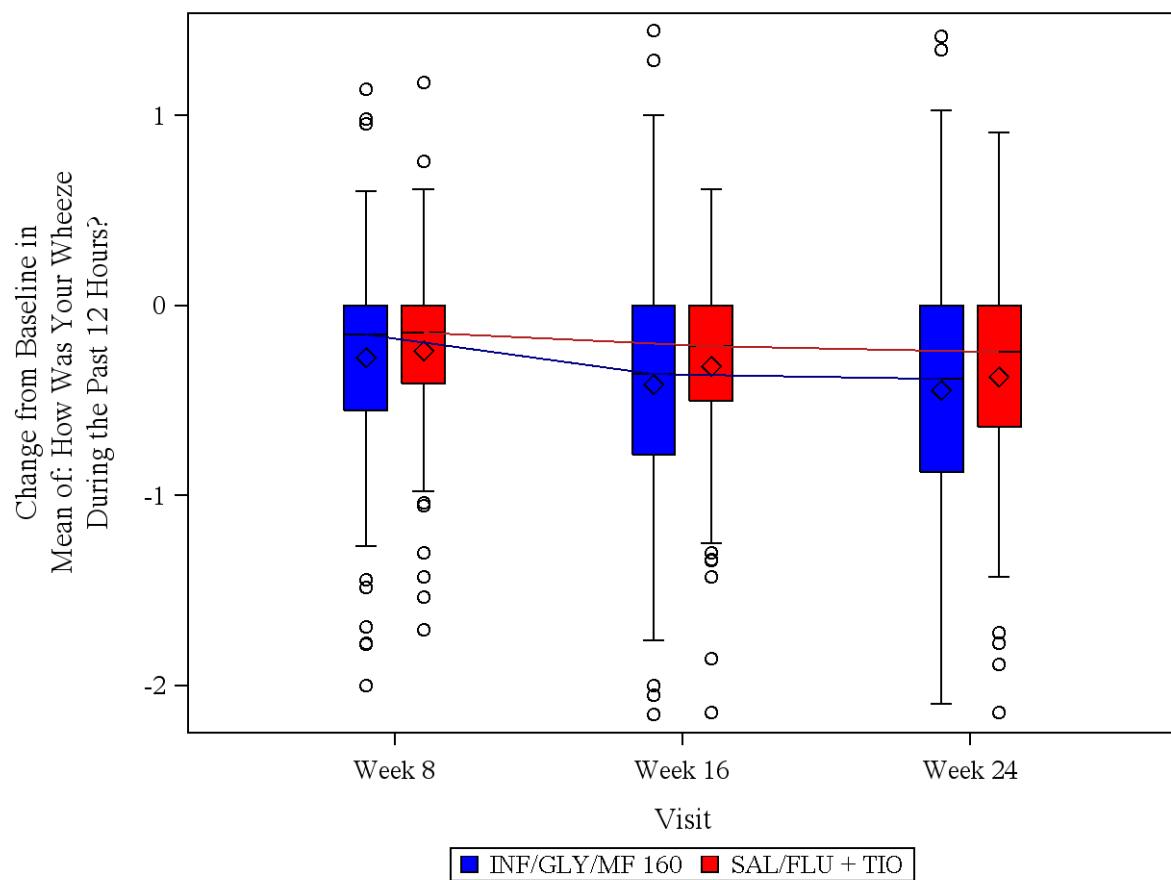
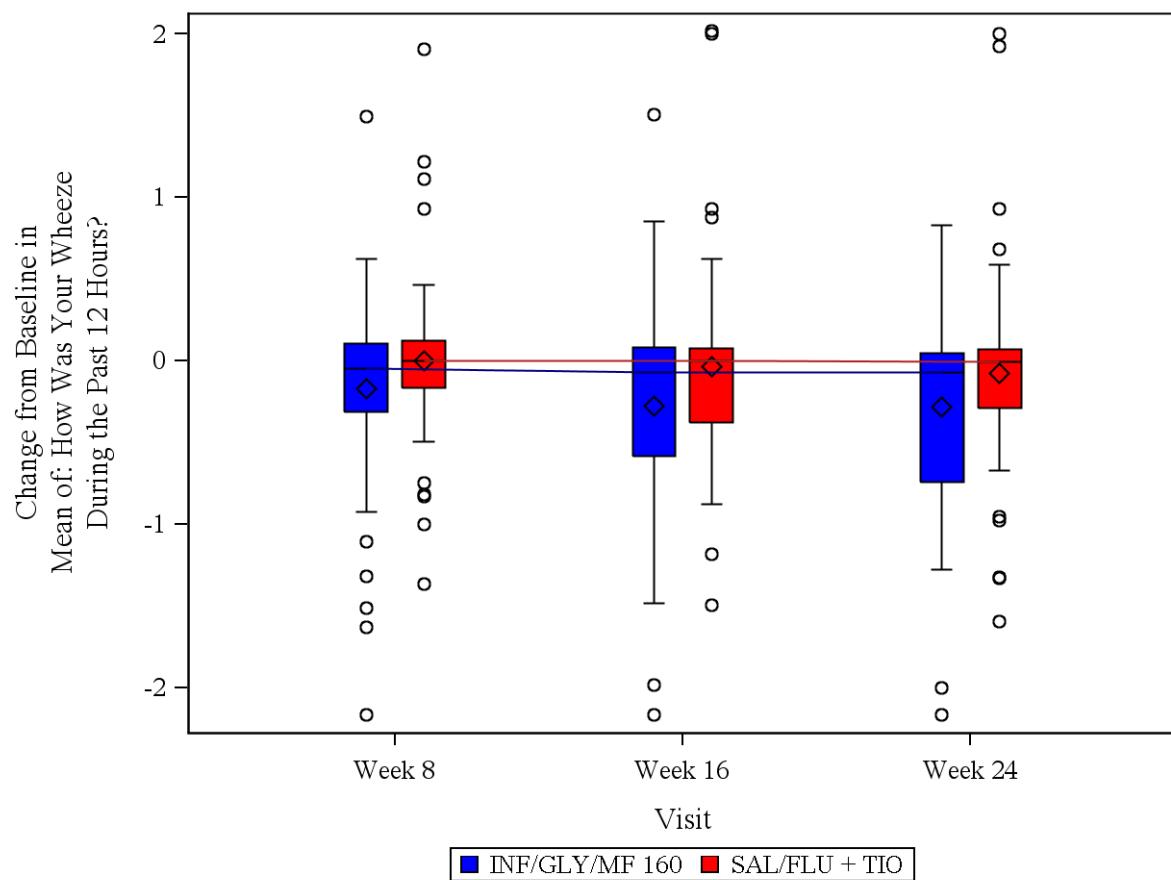


Figure 9.68.3 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

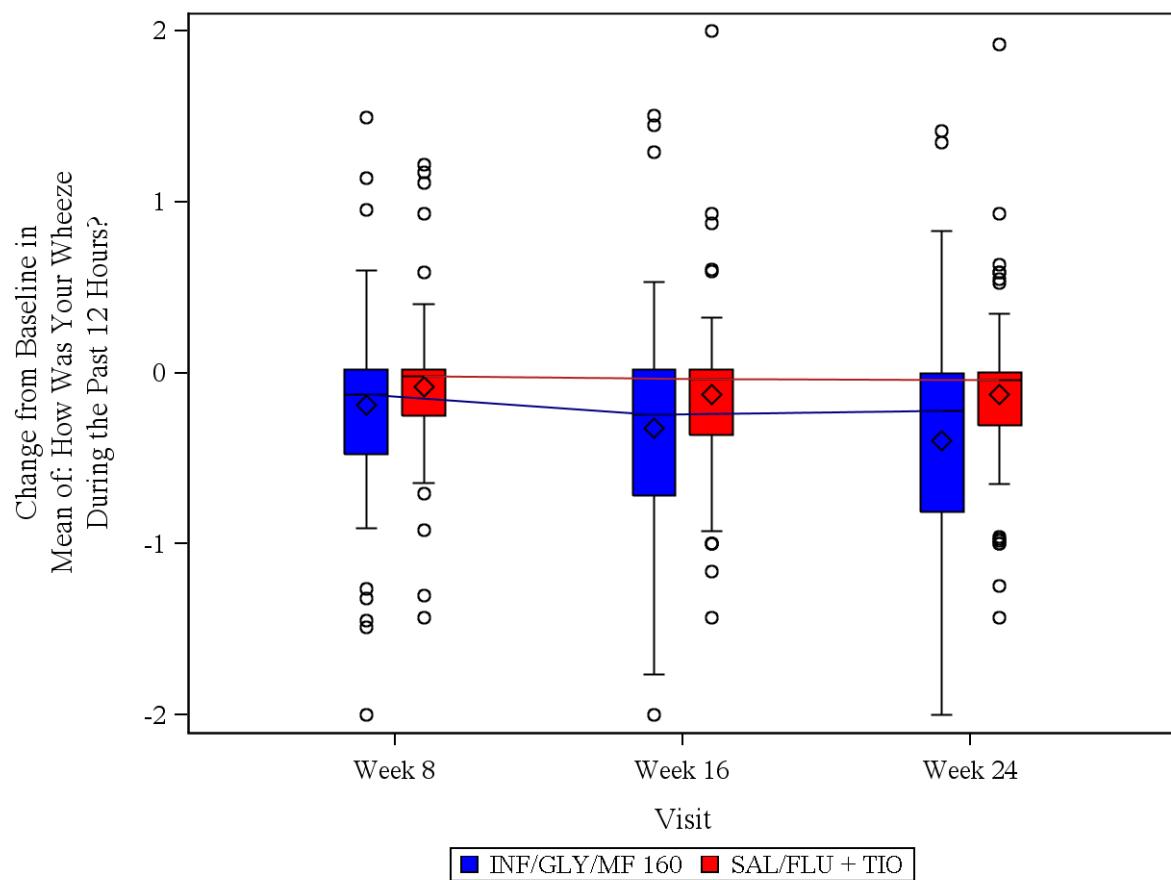
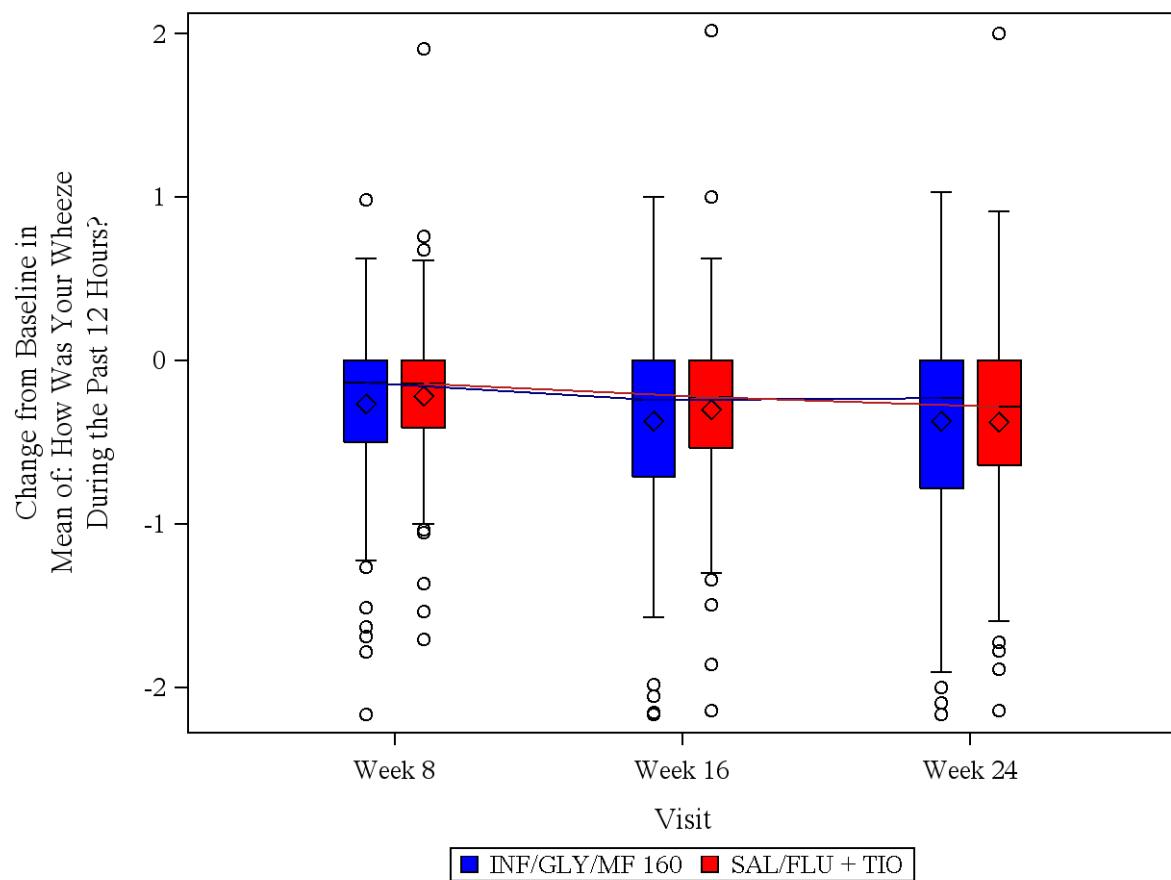


Figure 9.69.2 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Gender (FAS), Gender = Female



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

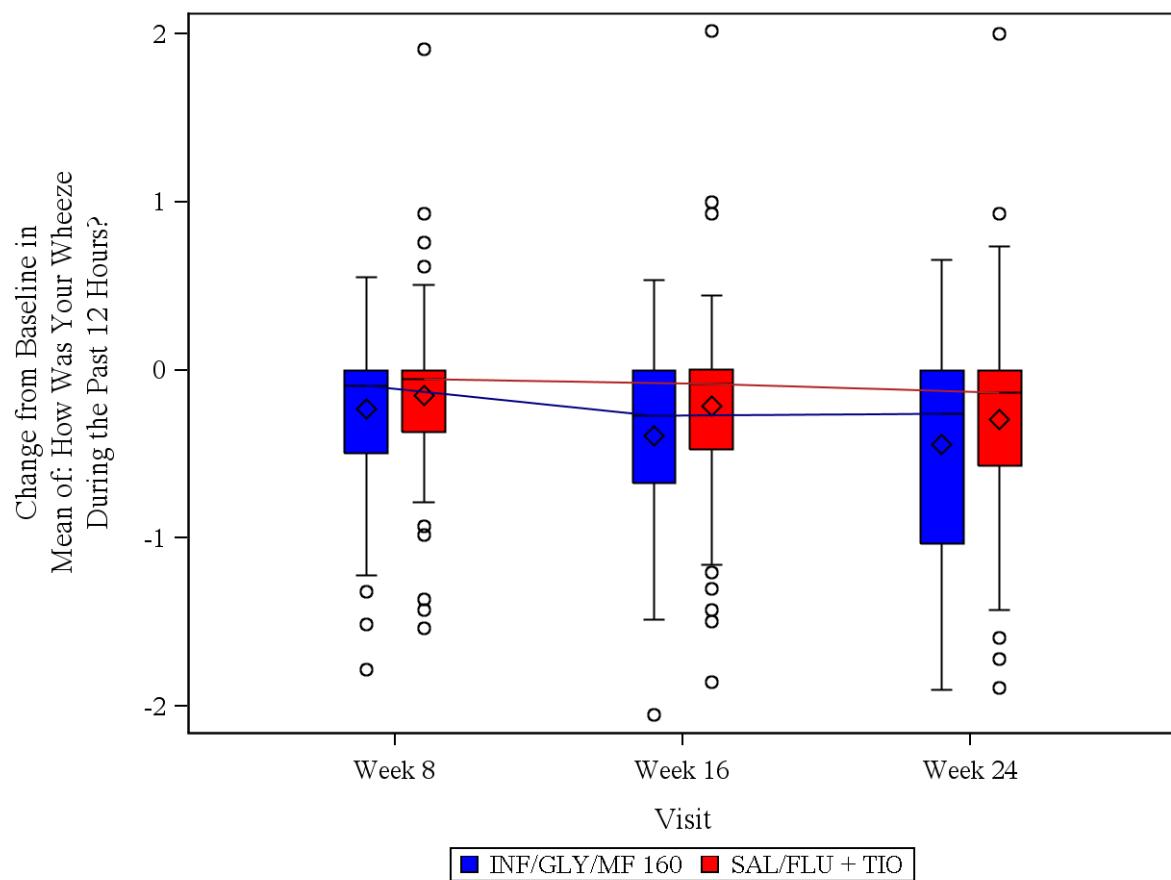


Figure 9.70.2 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Europe

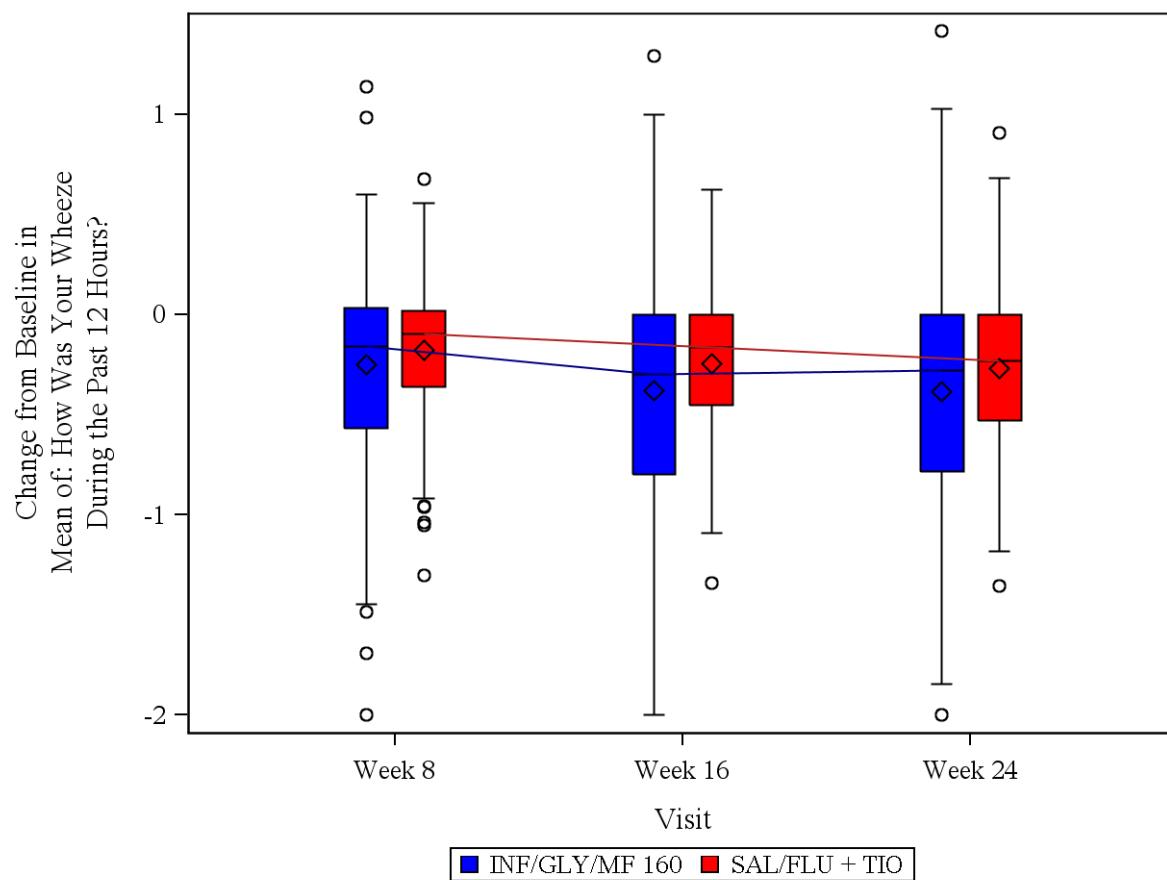


Figure 9.70.3 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Latin America

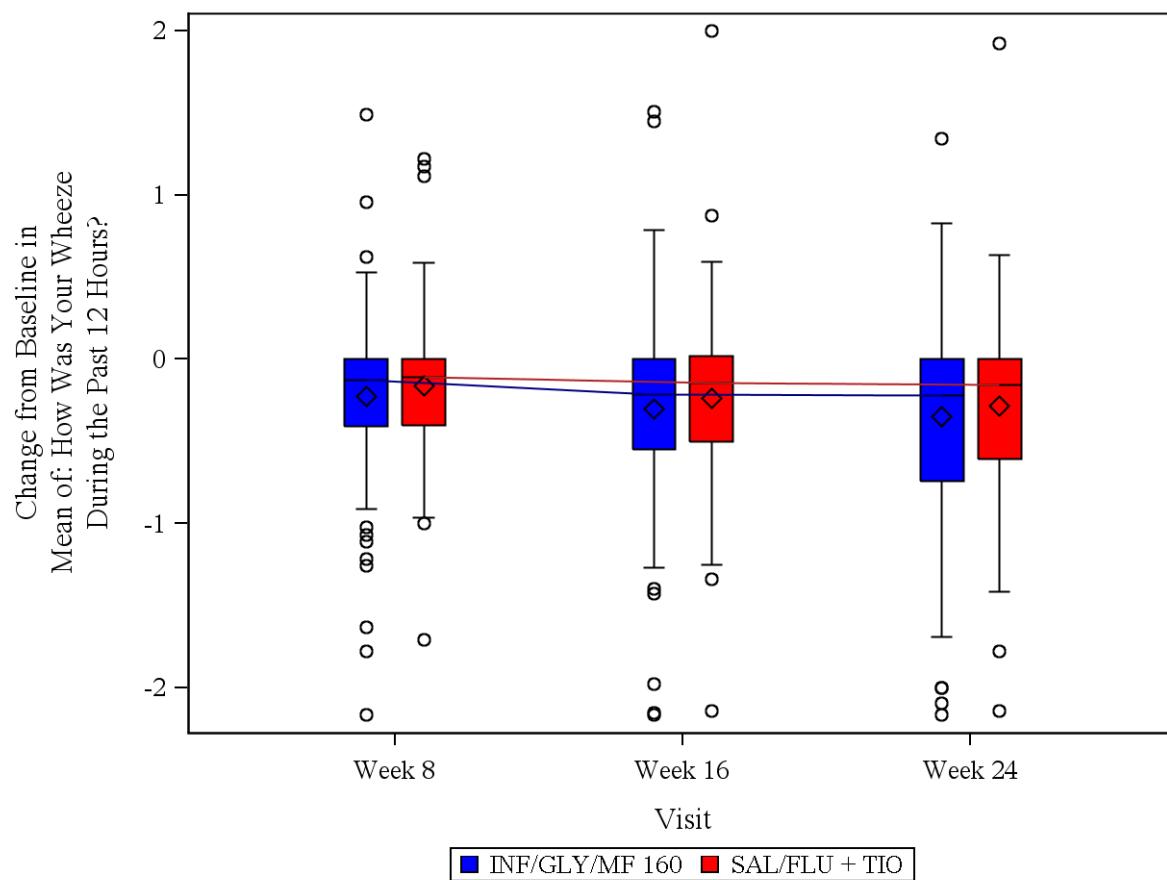
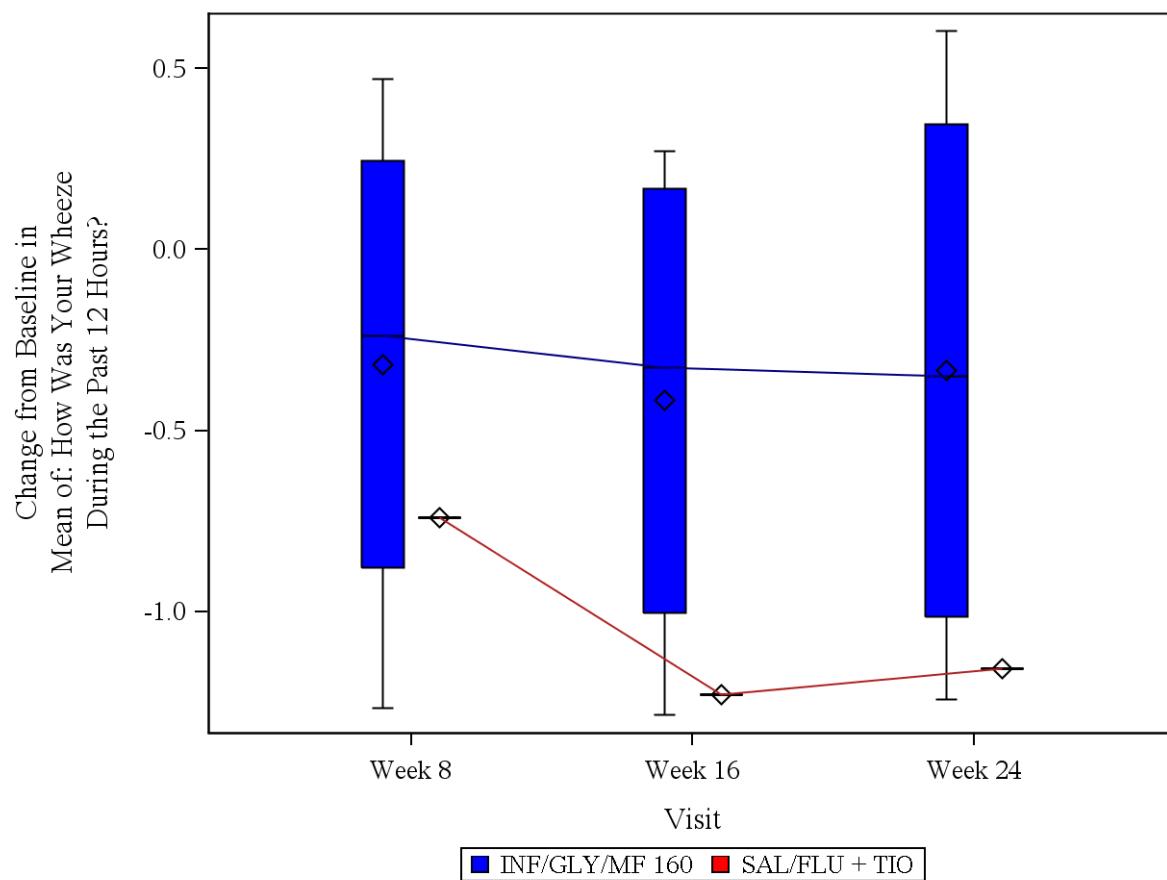


Figure 9.70.4 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Others



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

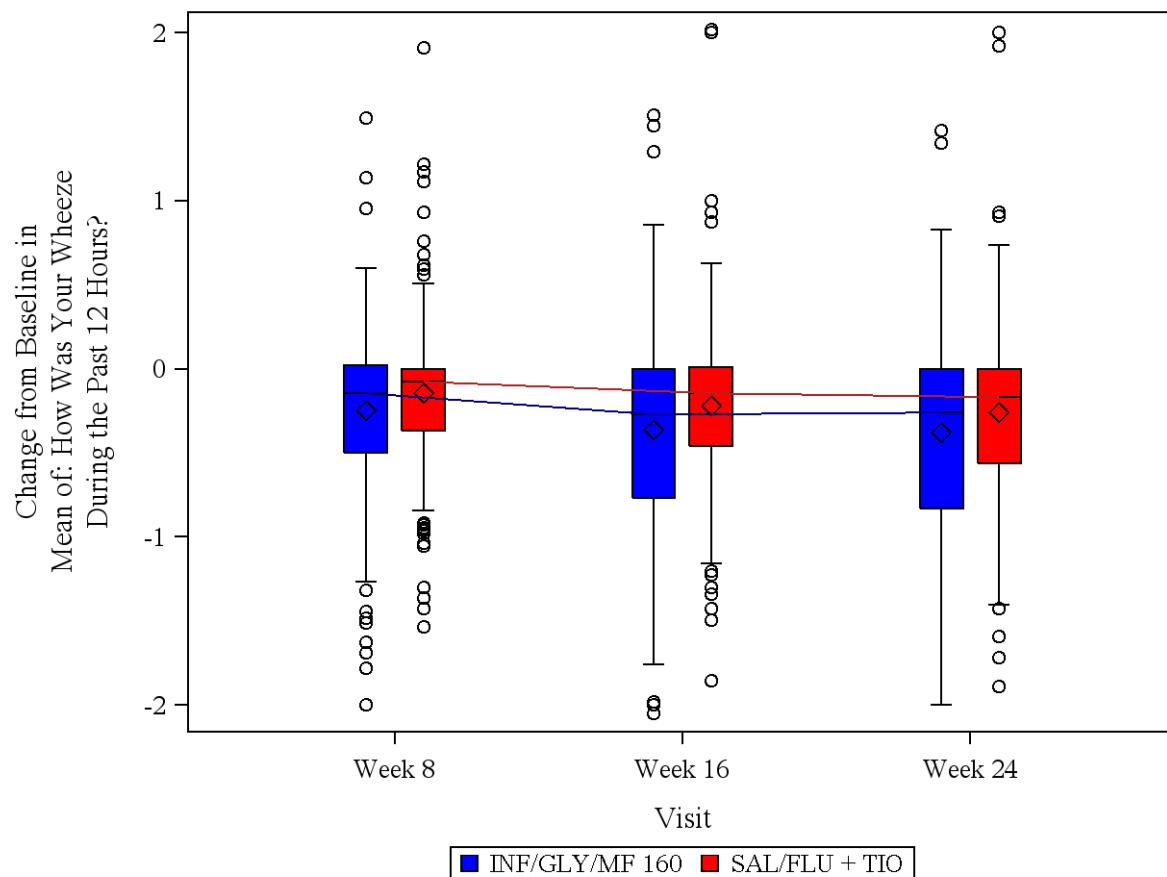
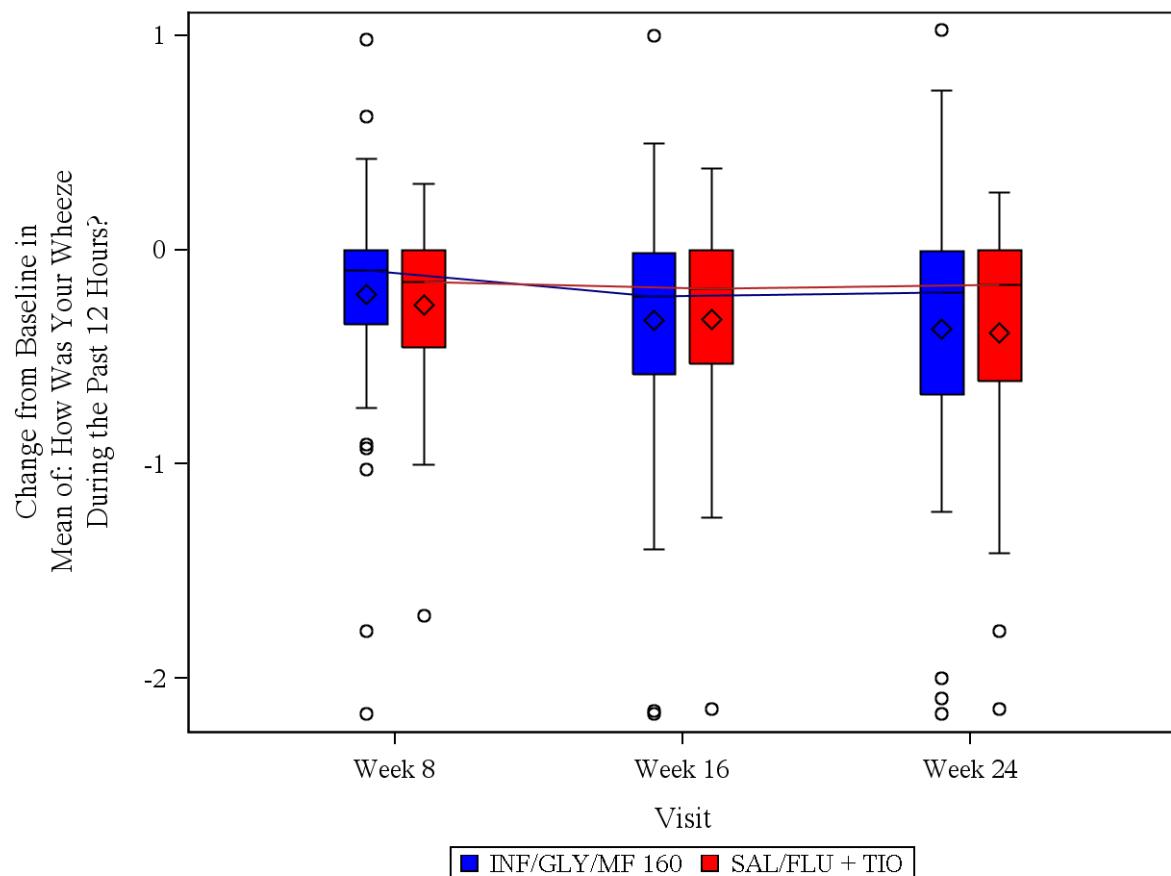
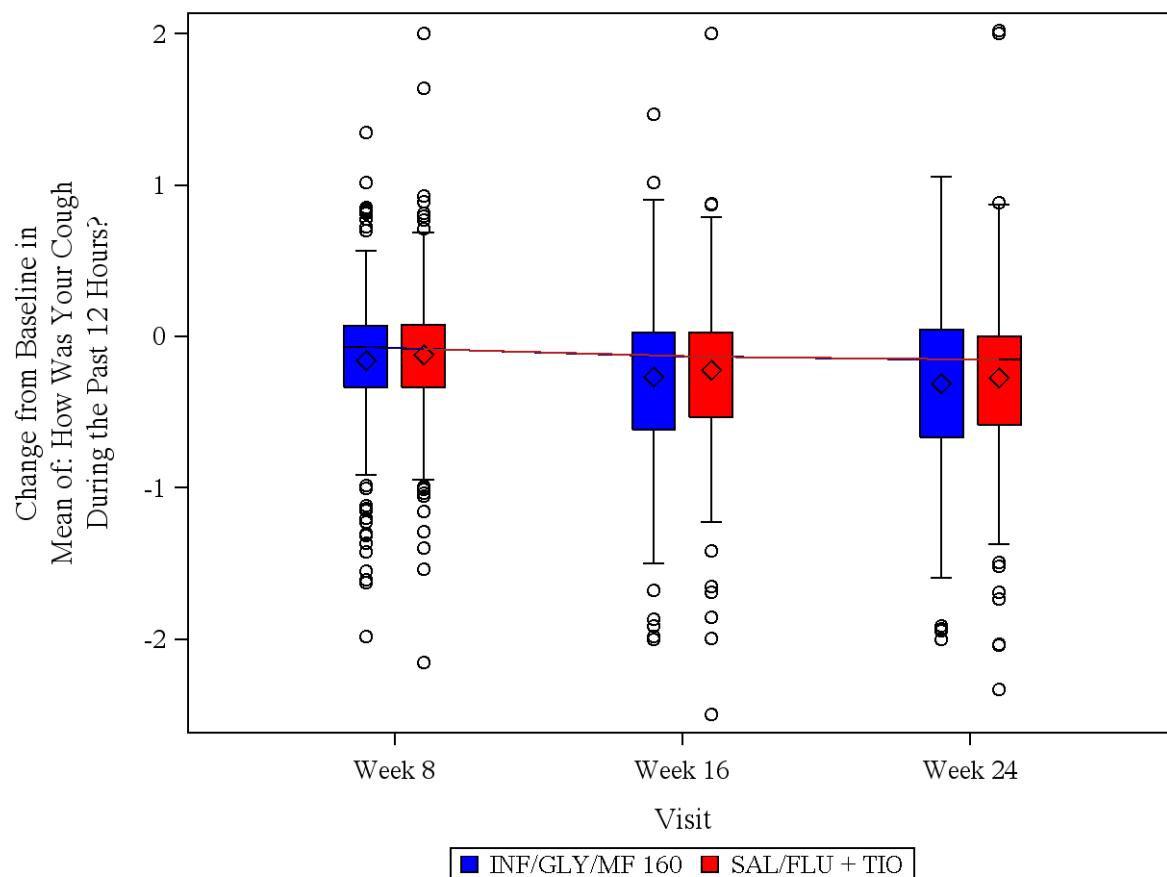


Figure 9.71.2 Symptoms (Mean of: How Was Your Wheeze During the Past 12 Hours?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



9.73 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

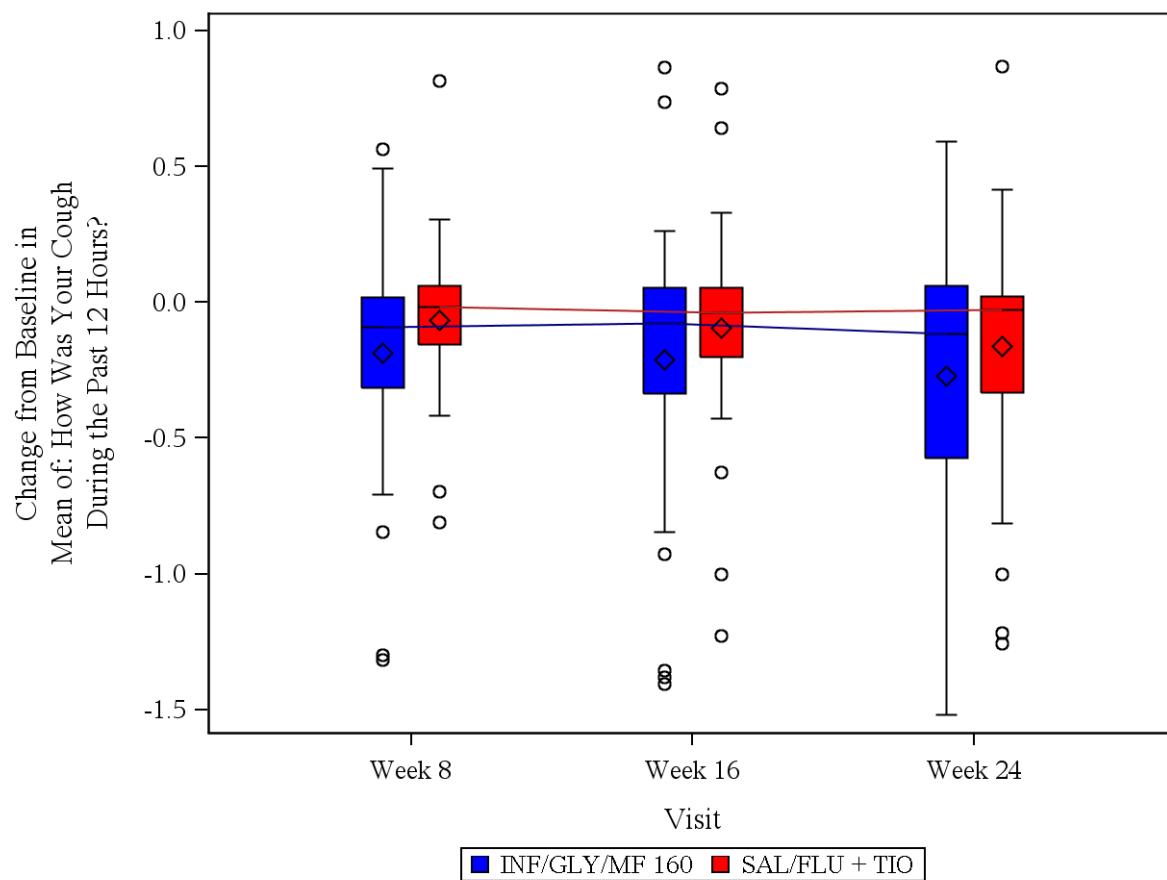


Figure 9.74.2 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Age (FAS), Age = 40-64 years

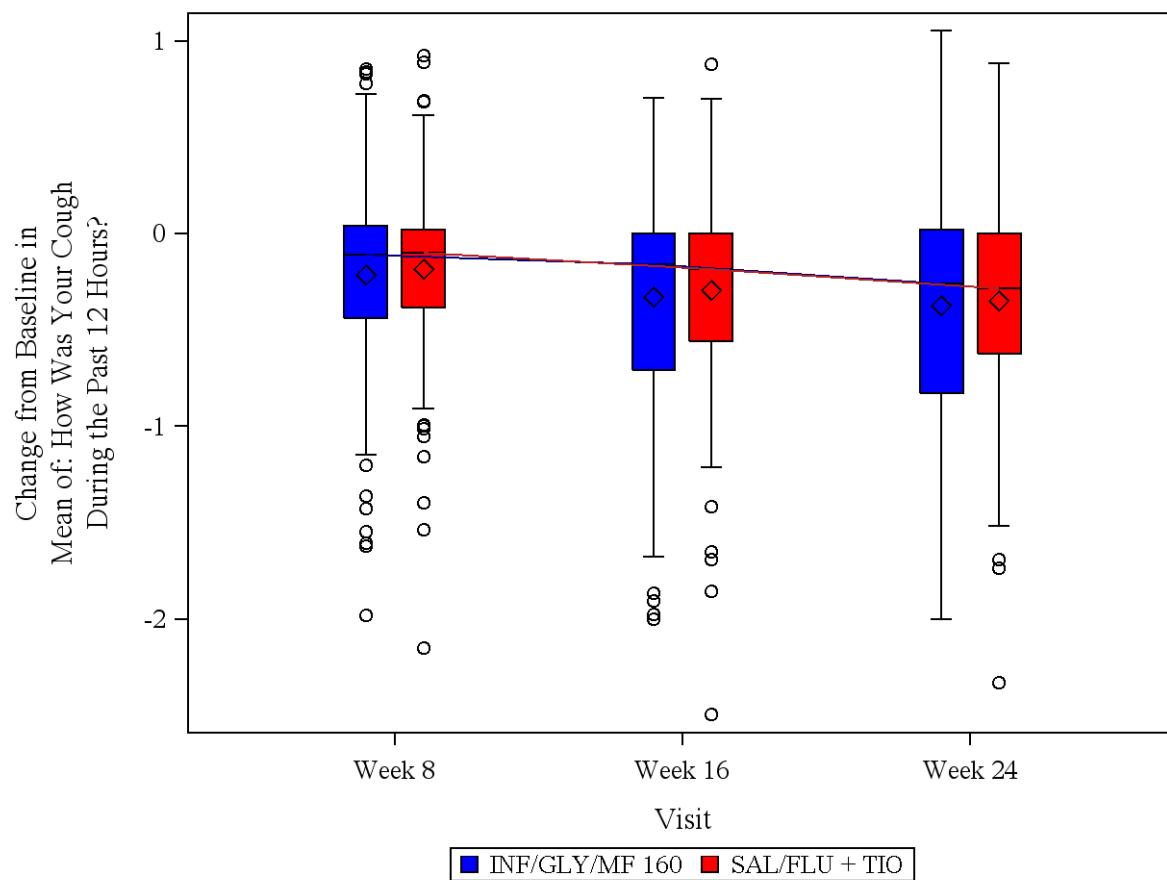
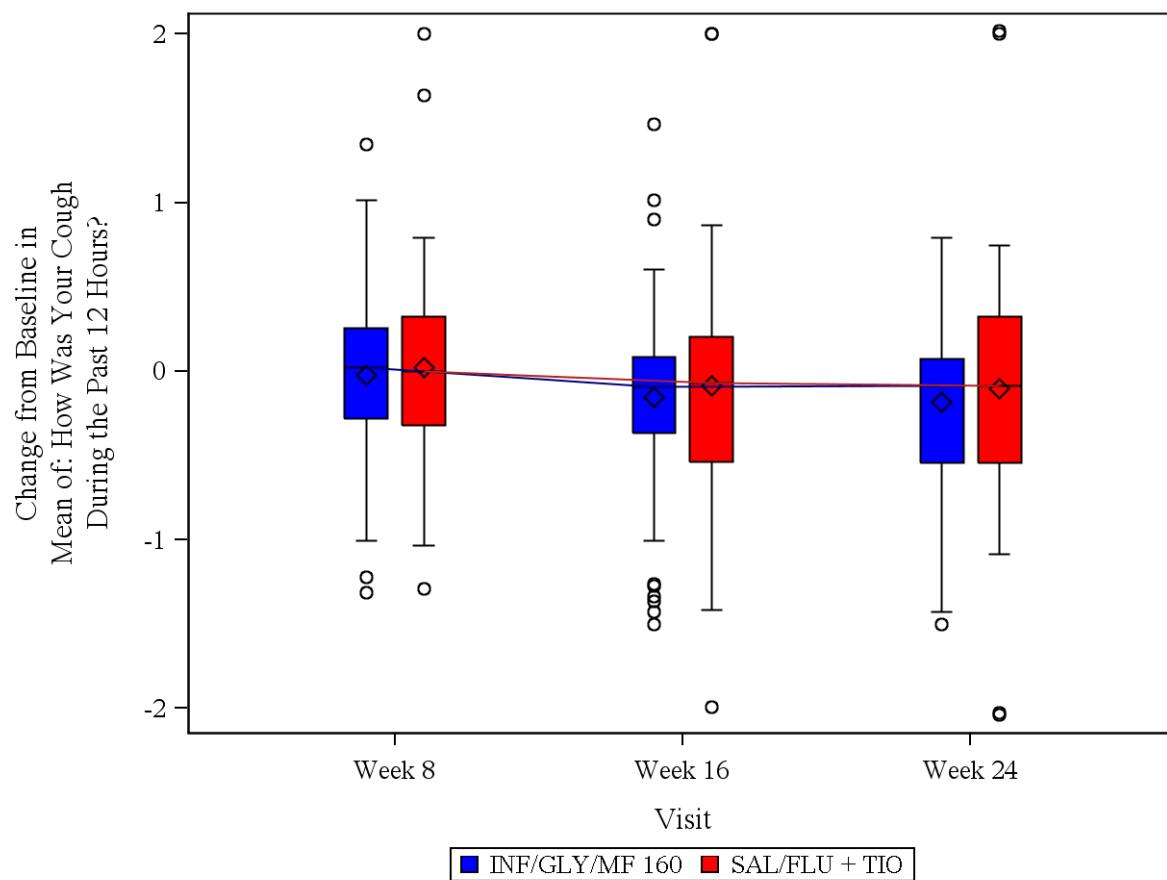


Figure 9.74.3 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

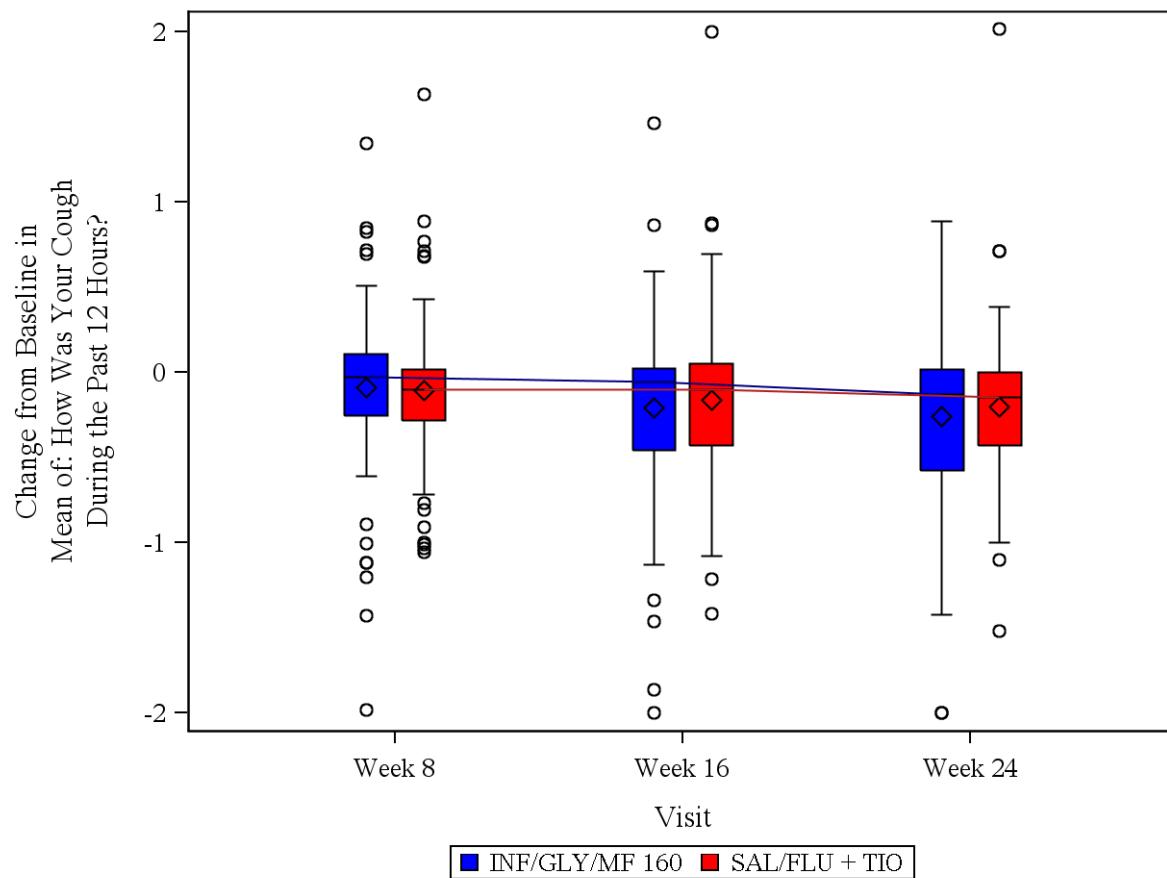
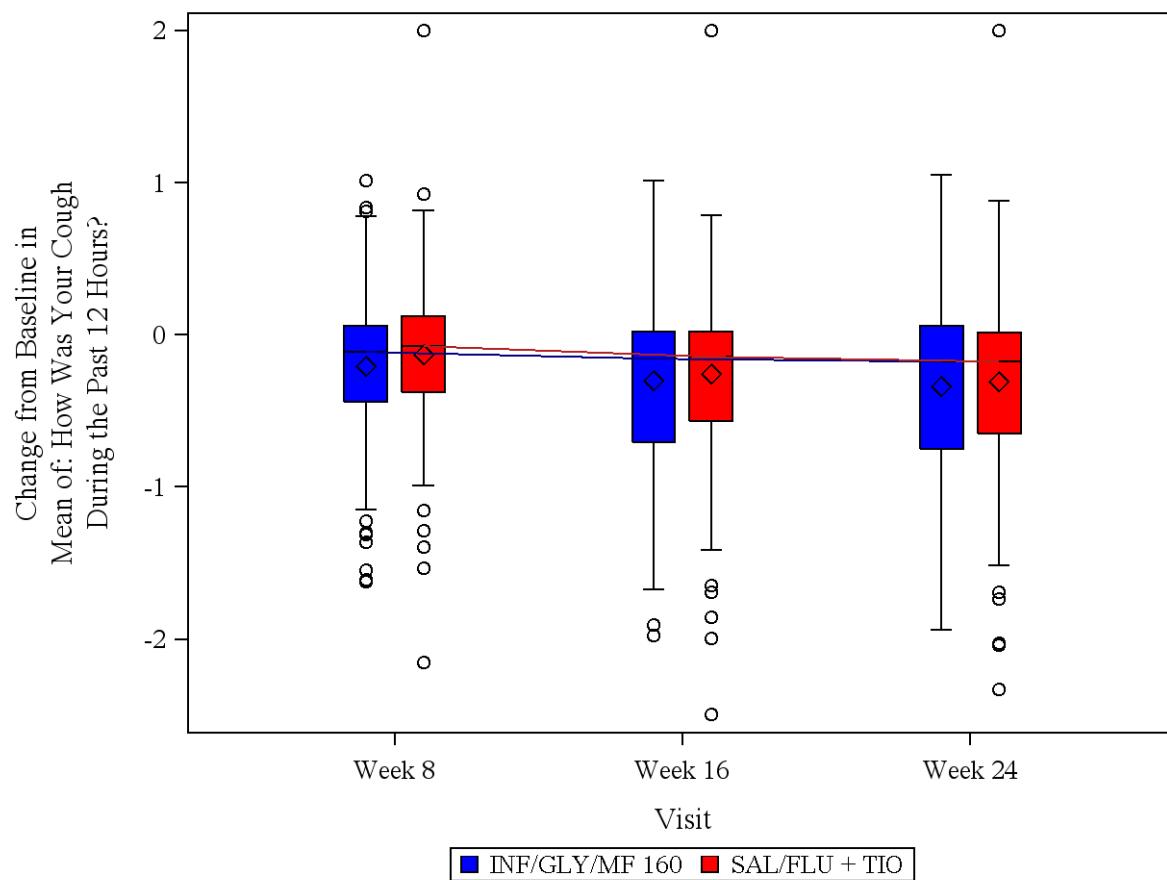


Figure 9.75.2 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Gender (FAS), Gender = Female



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

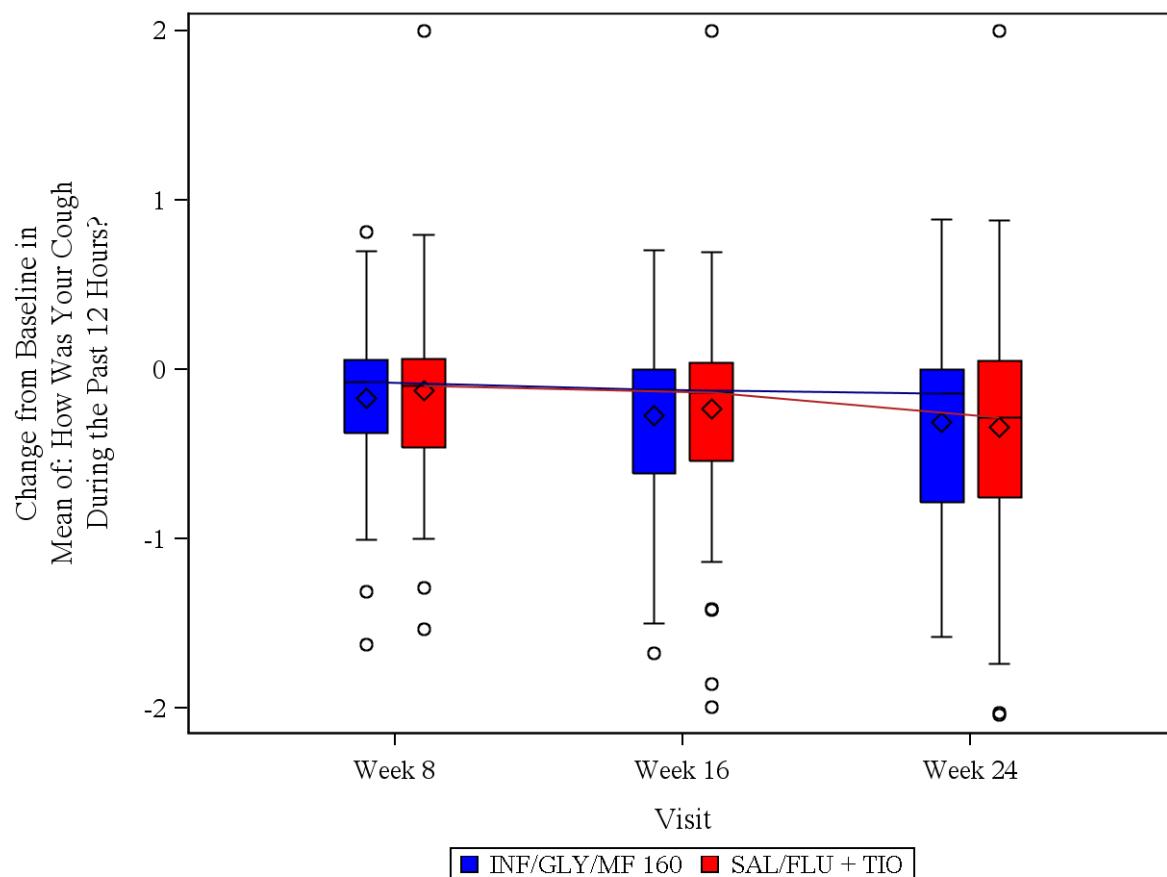


Figure 9.76.2 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Europe

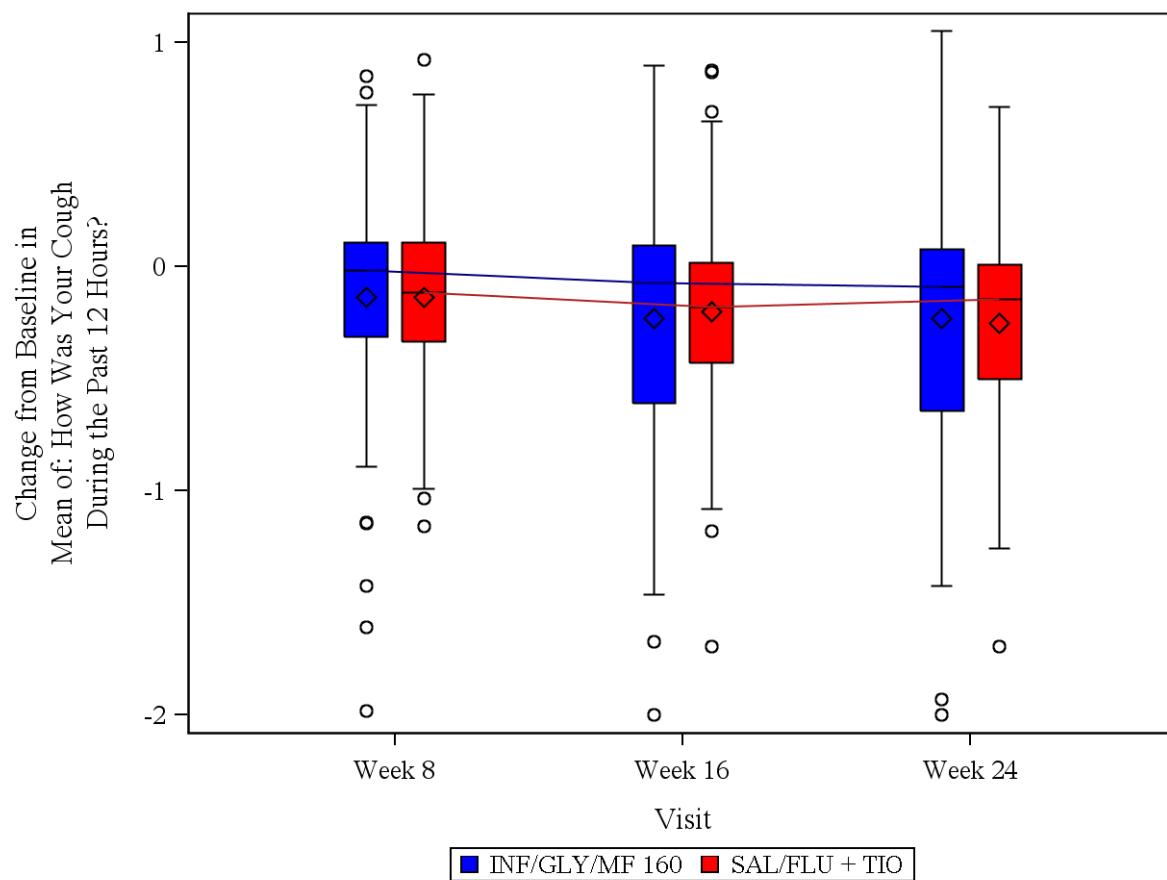


Figure 9.76.3 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Latin America

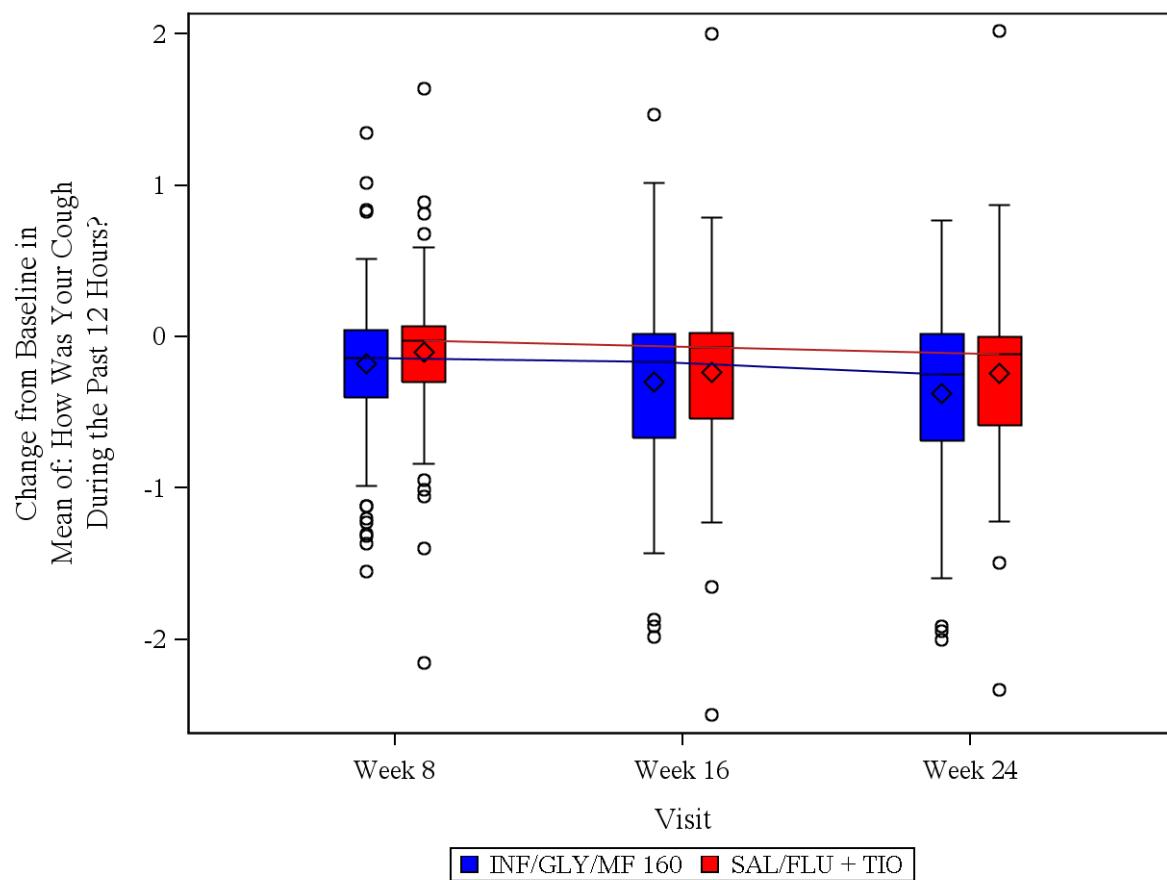
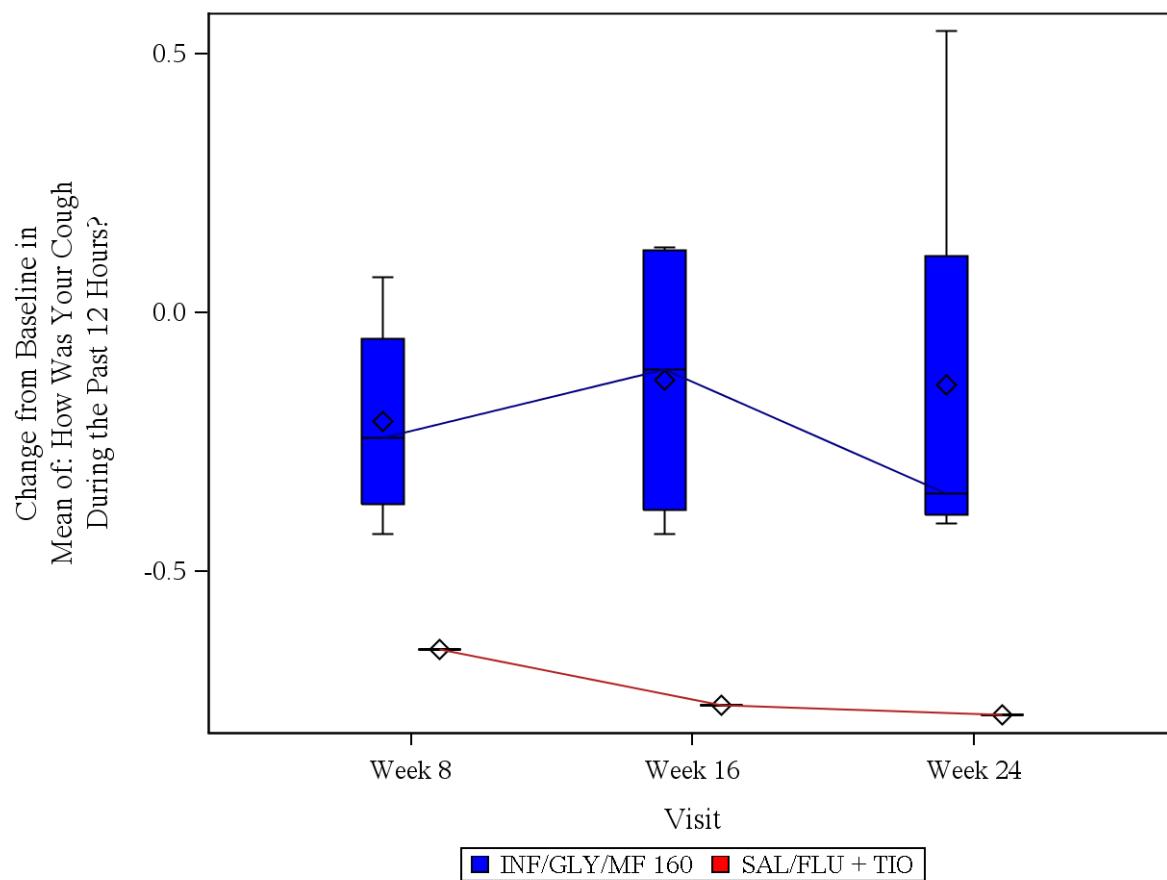


Figure 9.76.4 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Others



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

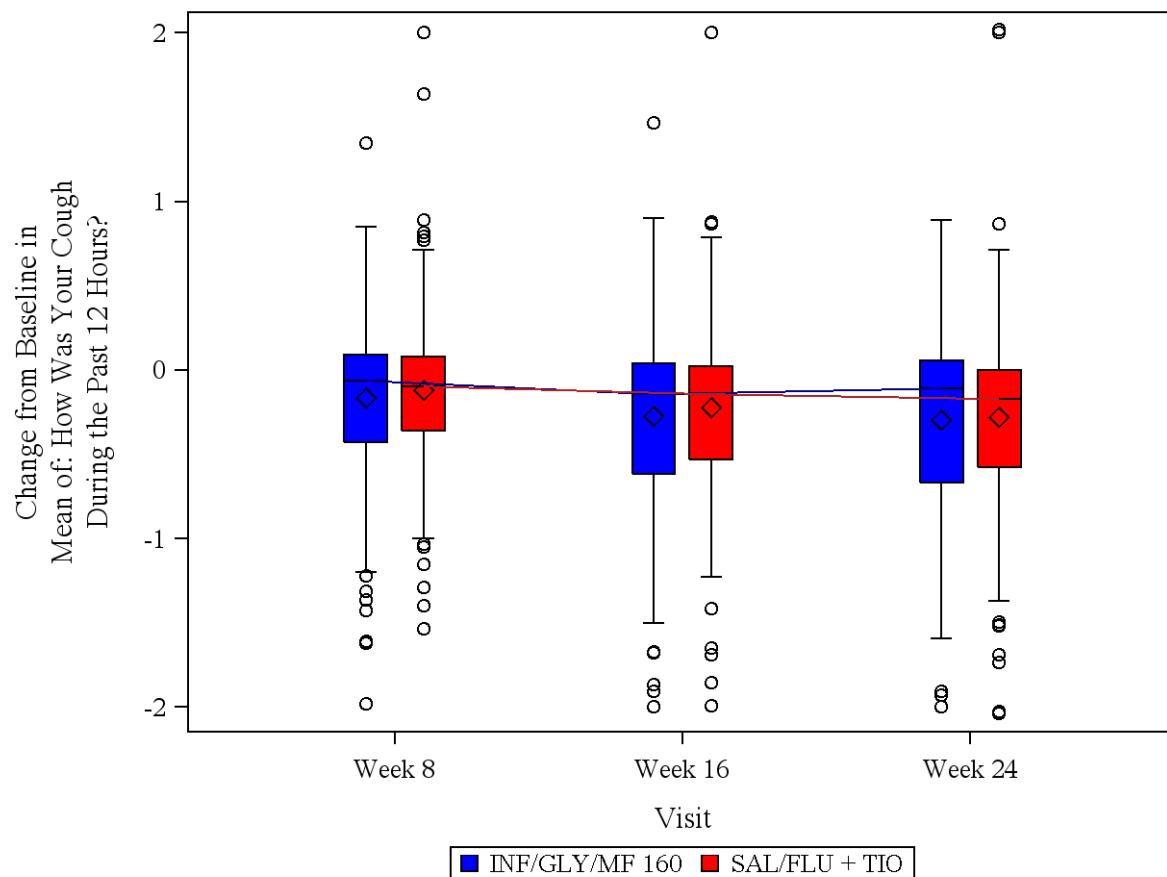
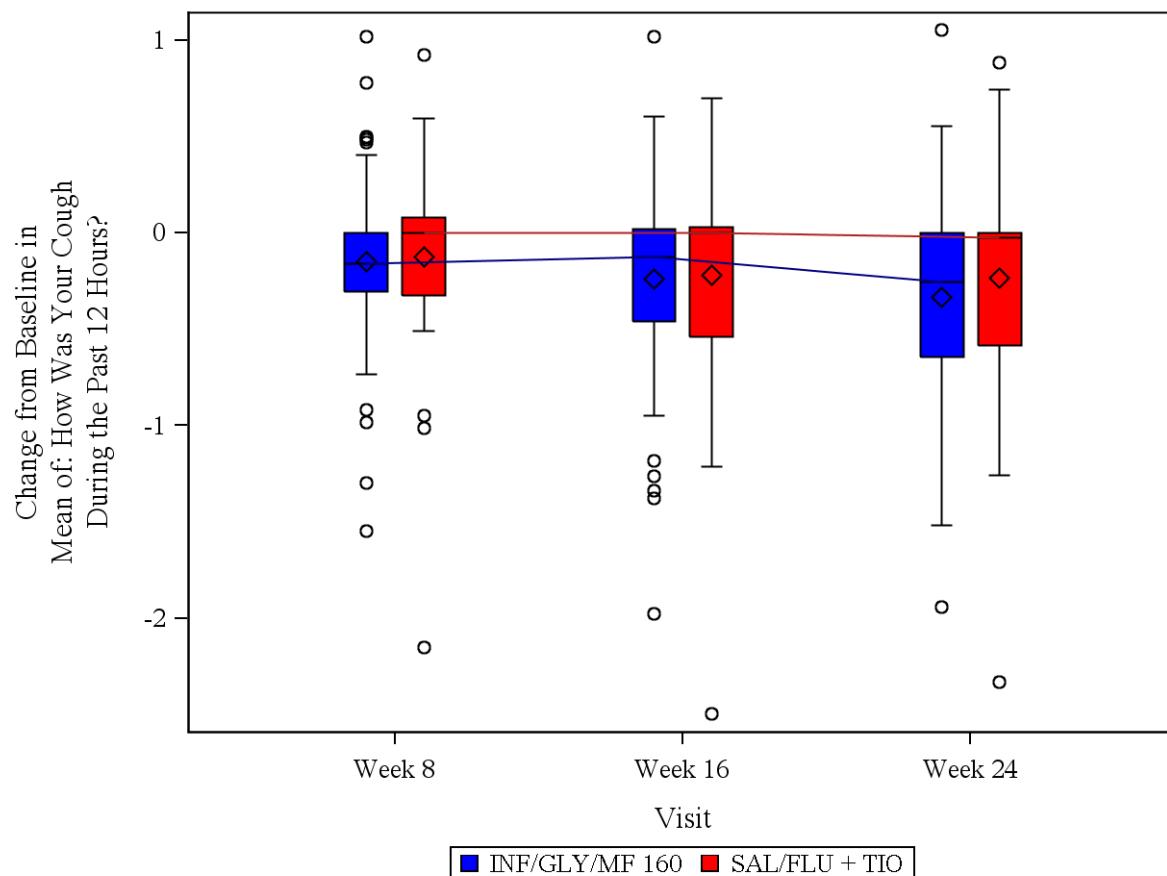
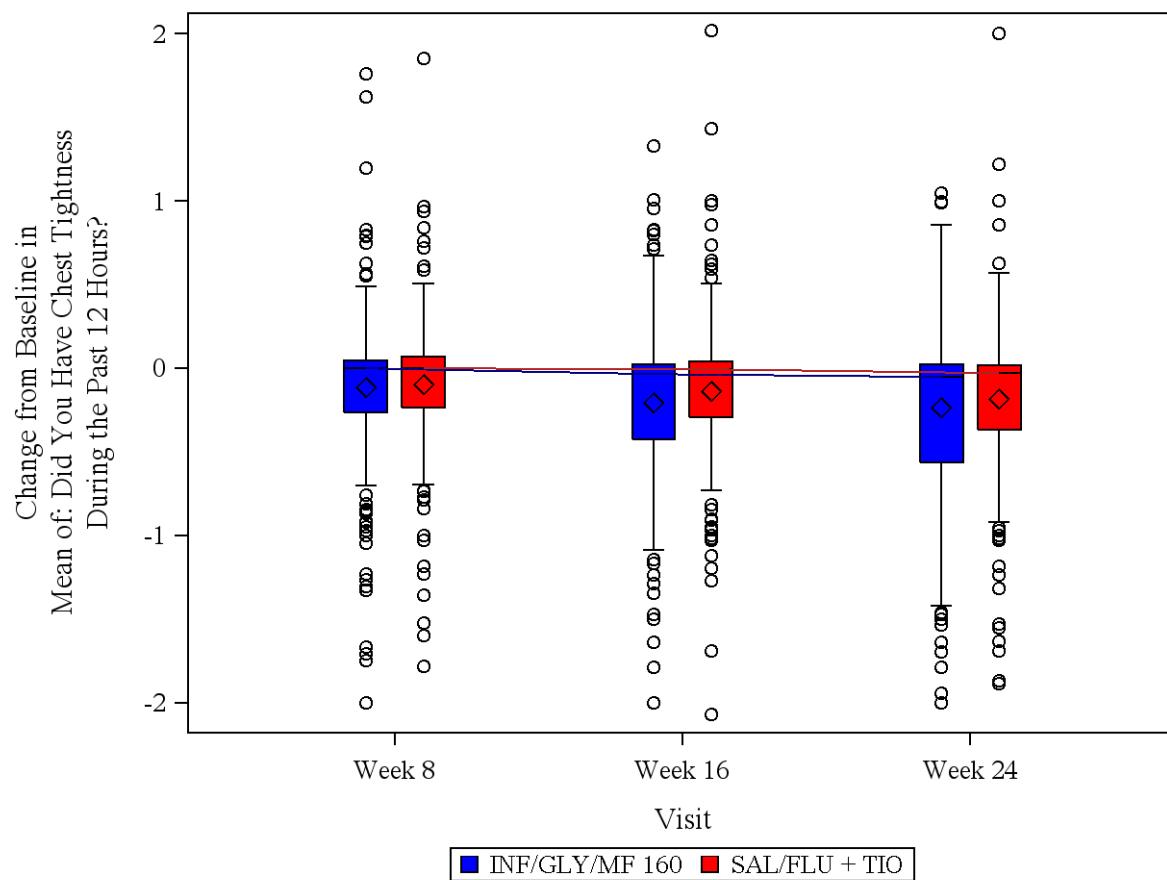


Figure 9.77.2 Symptoms (Mean of: How Was Your Cough During the Past 12 Hours?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



9.79 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

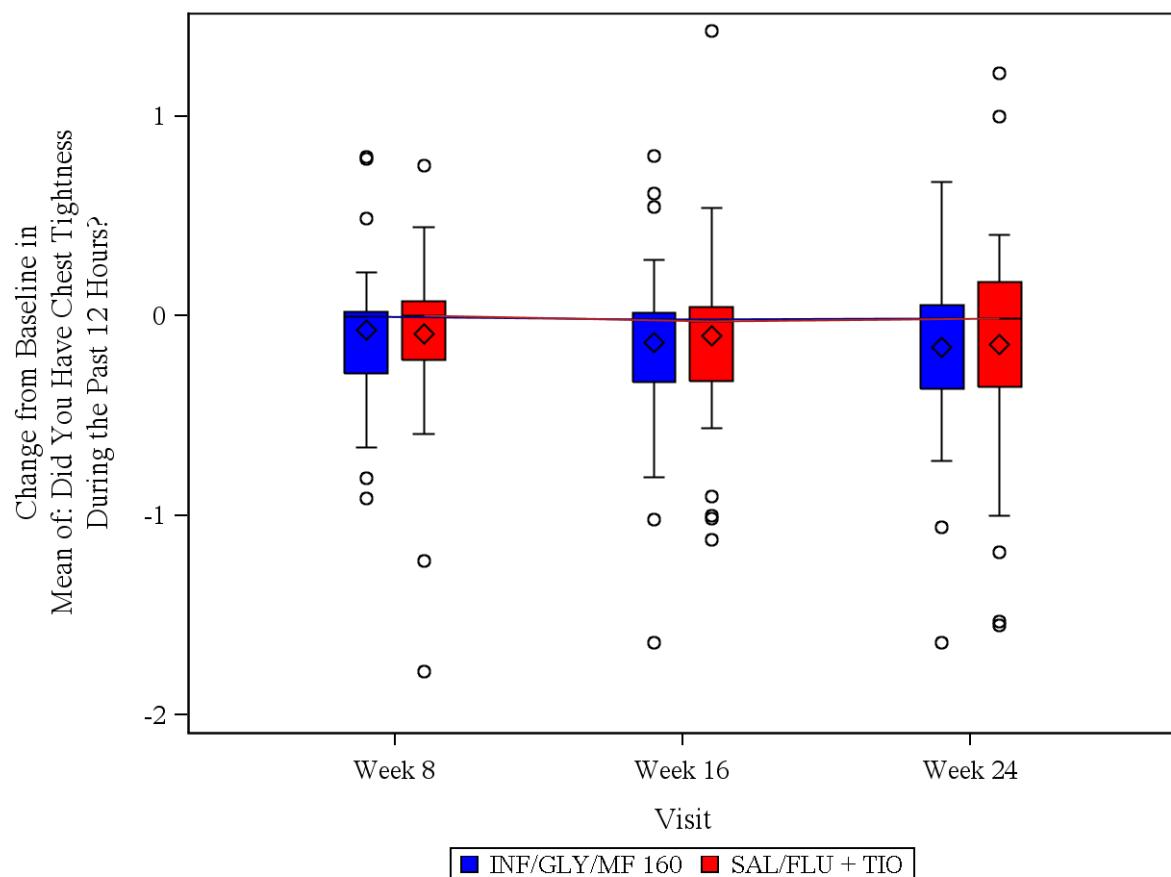


Figure 9.80.2 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Age (FAS), Age = 40-64 years

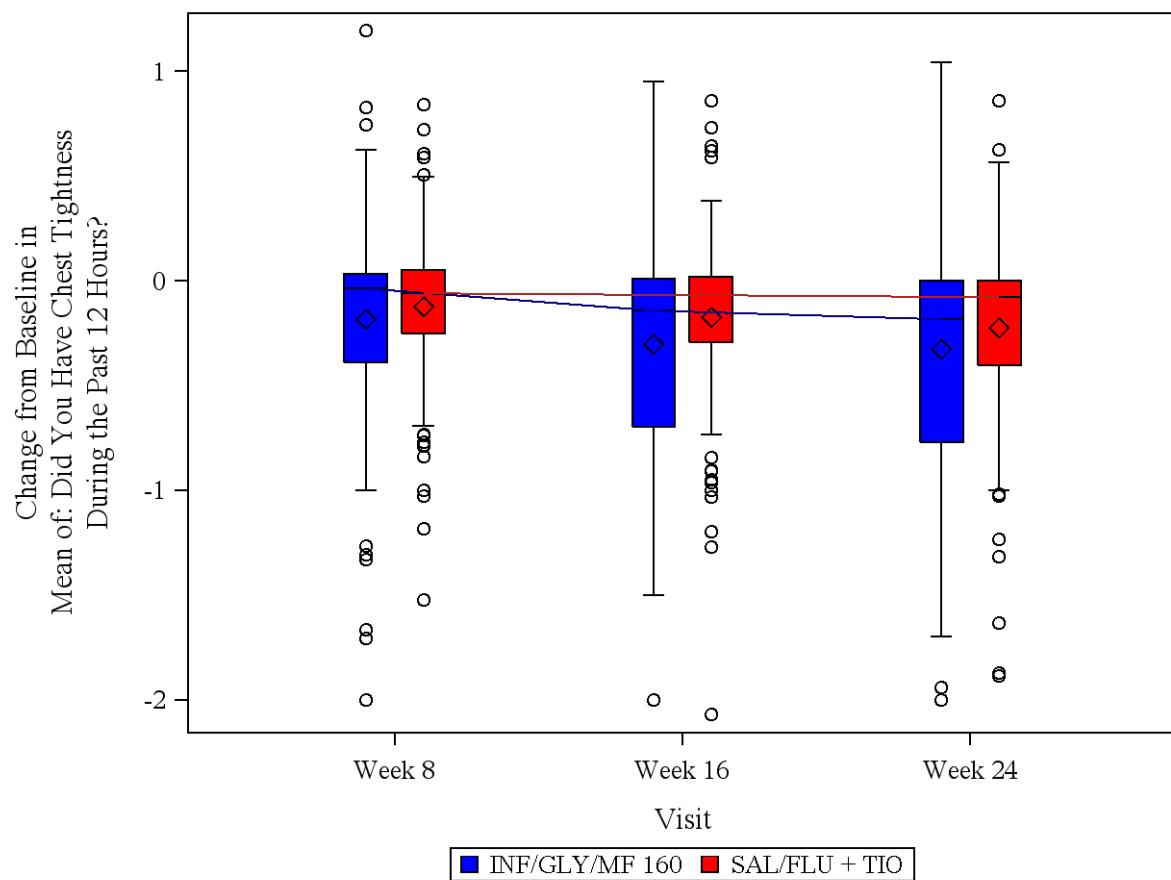
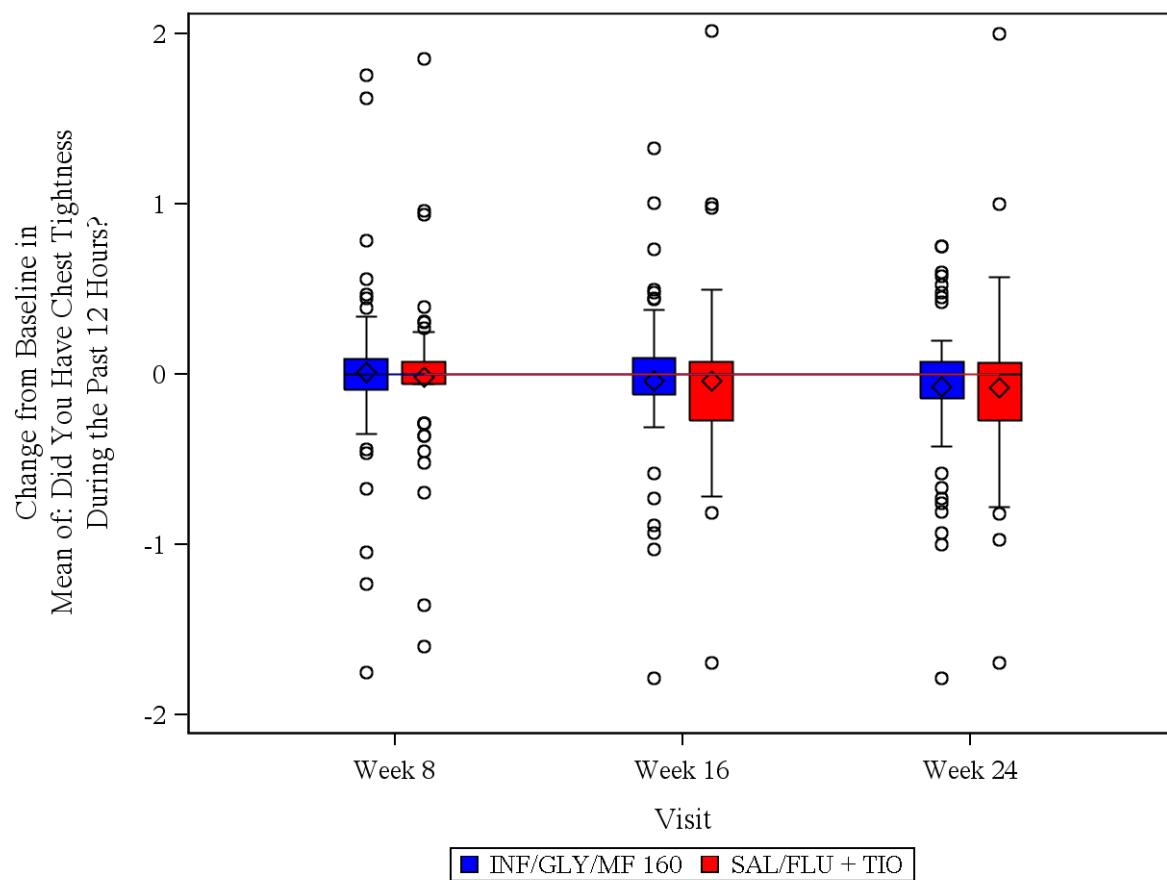


Figure 9.80.3 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

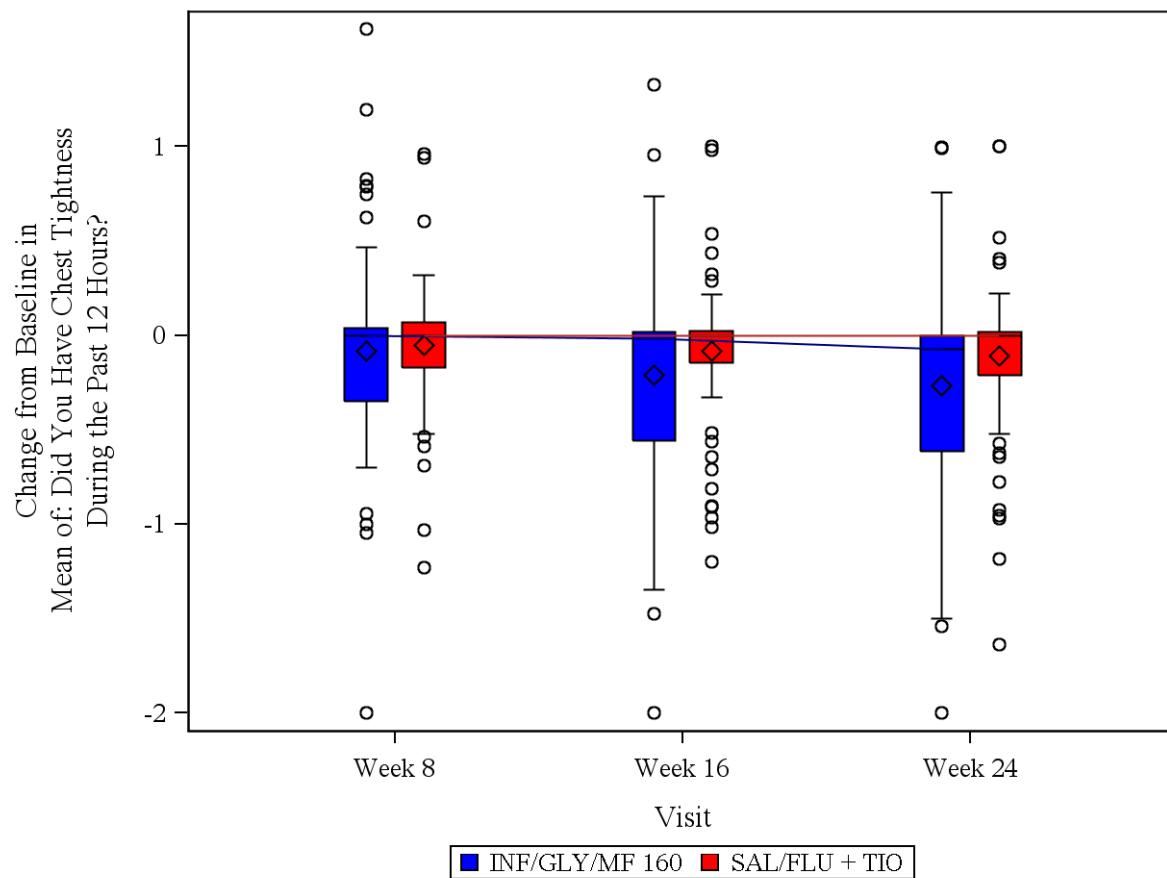
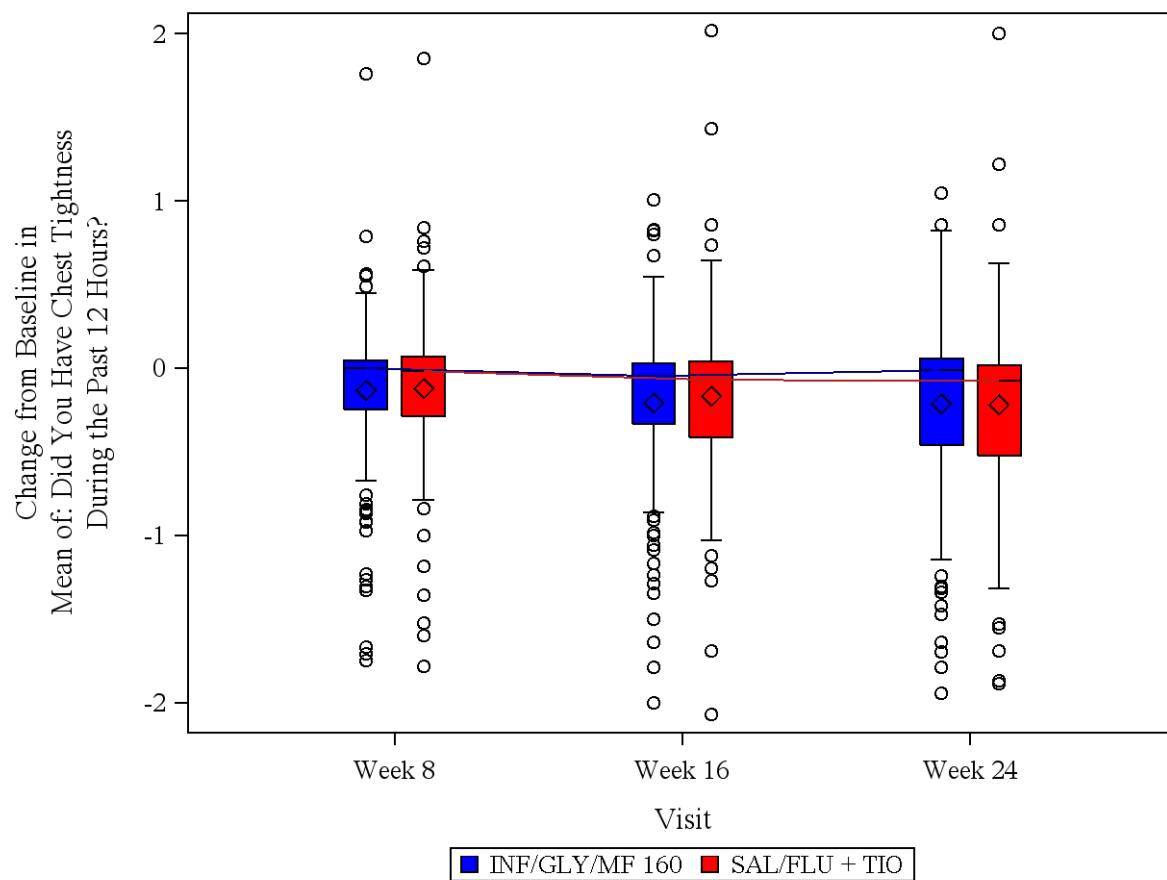


Figure 9.81.2 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Gender (FAS), Gender = Female



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

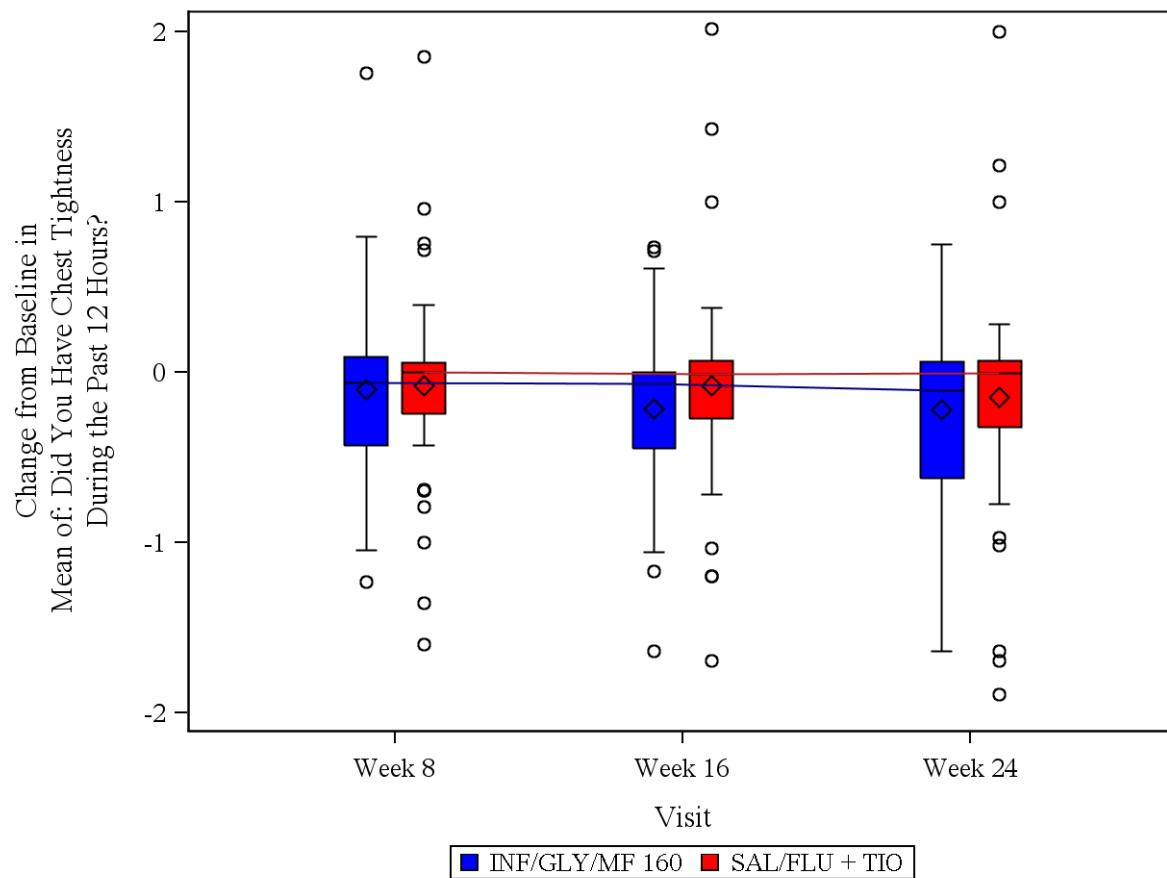


Figure 9.82.2 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Europe

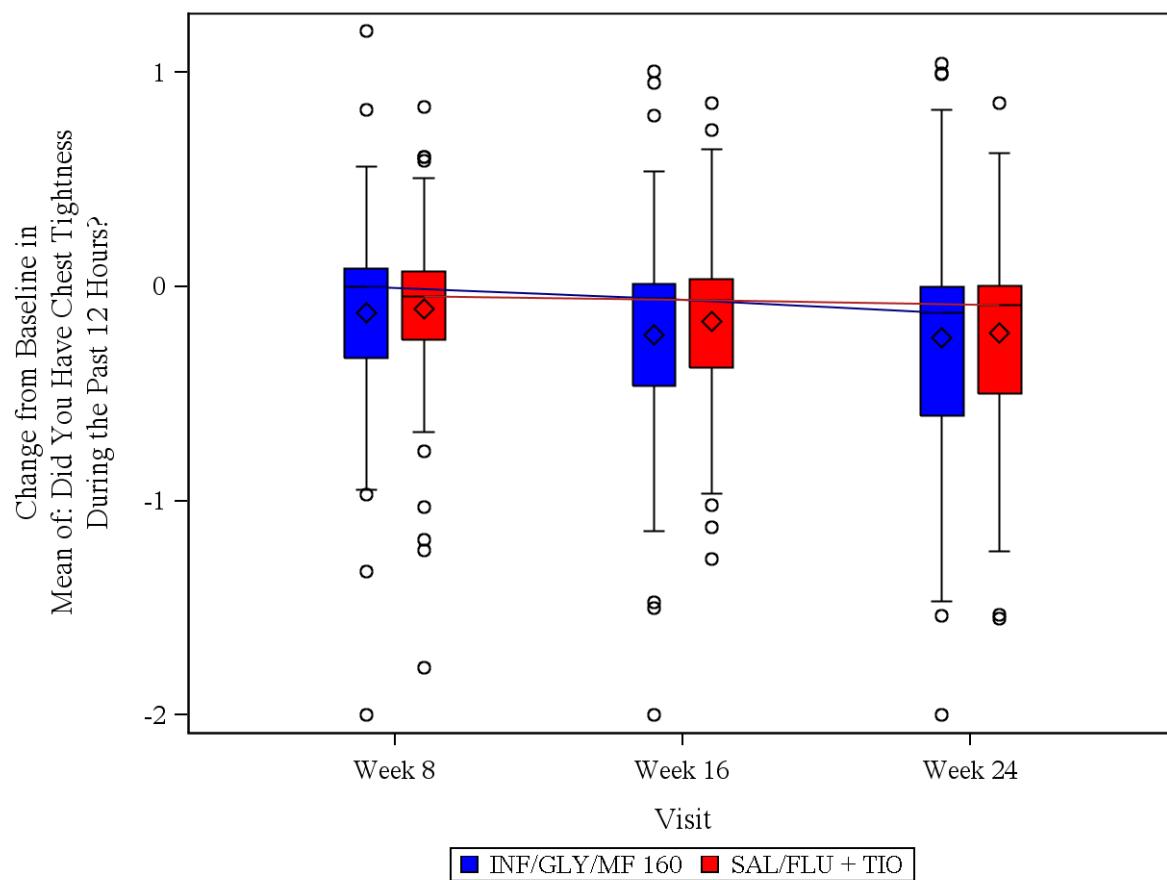


Figure 9.82.3 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Latin America

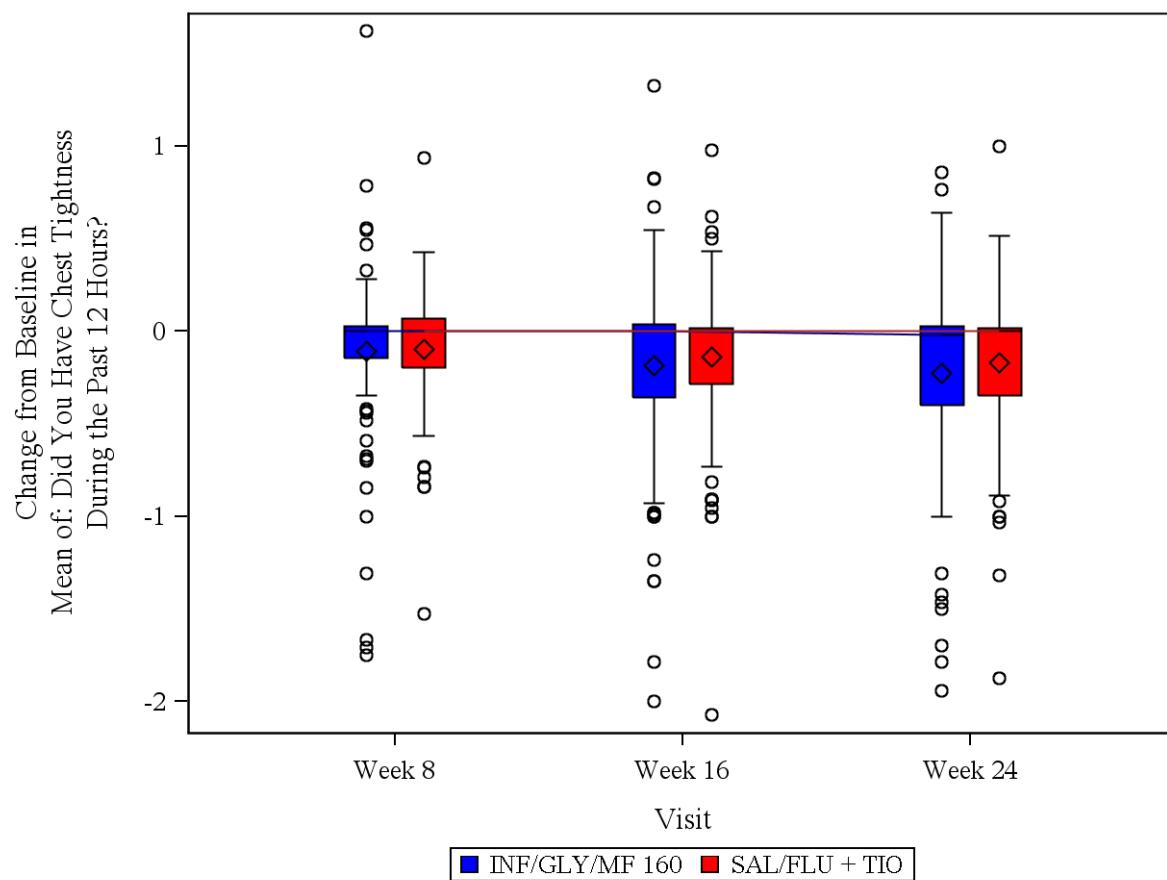
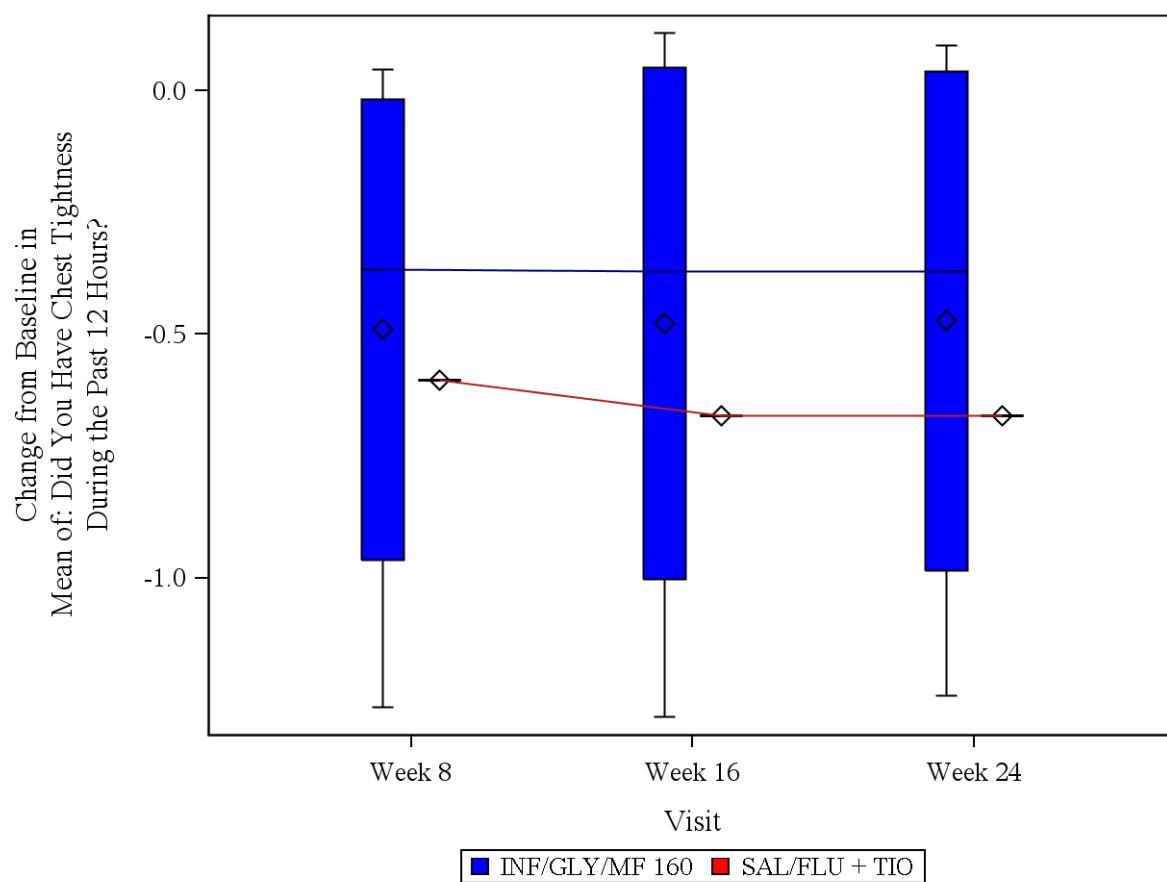


Figure 9.82.4 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by Region (FAS), Region = Others



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

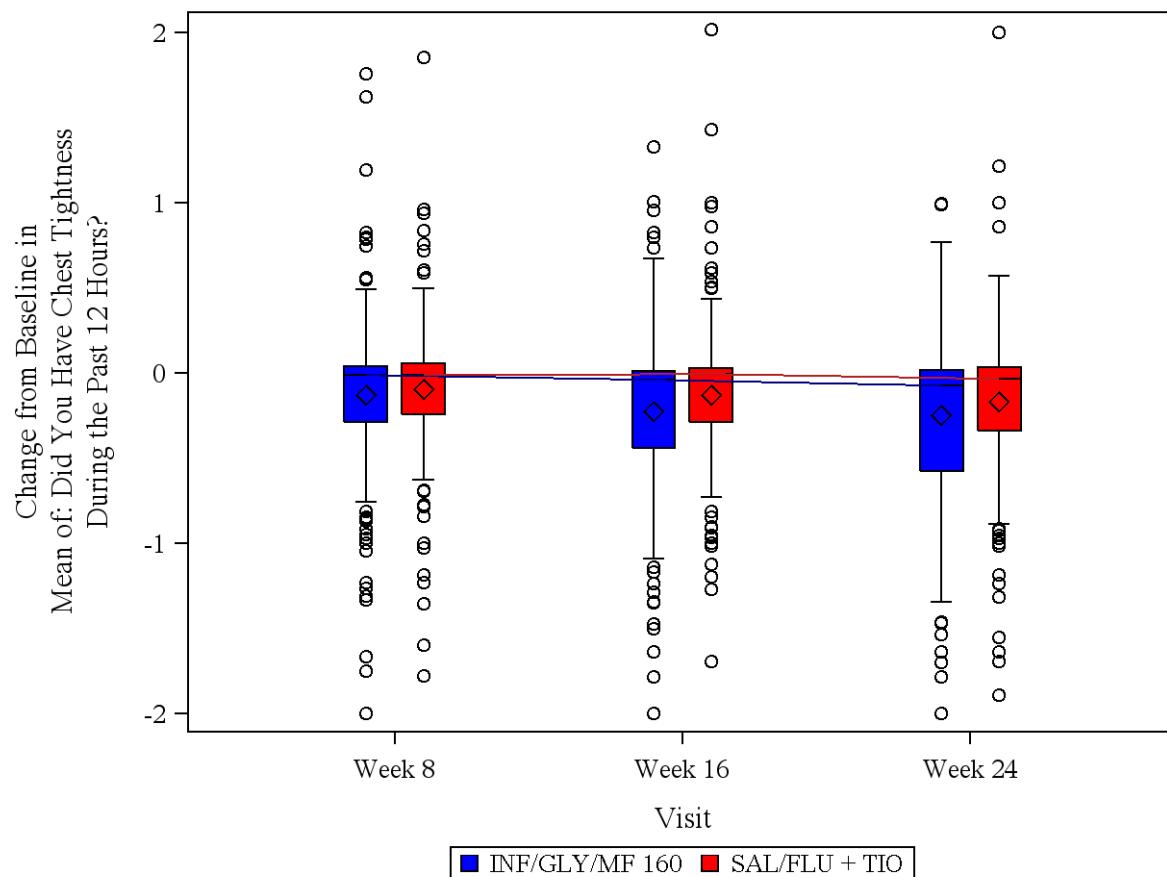
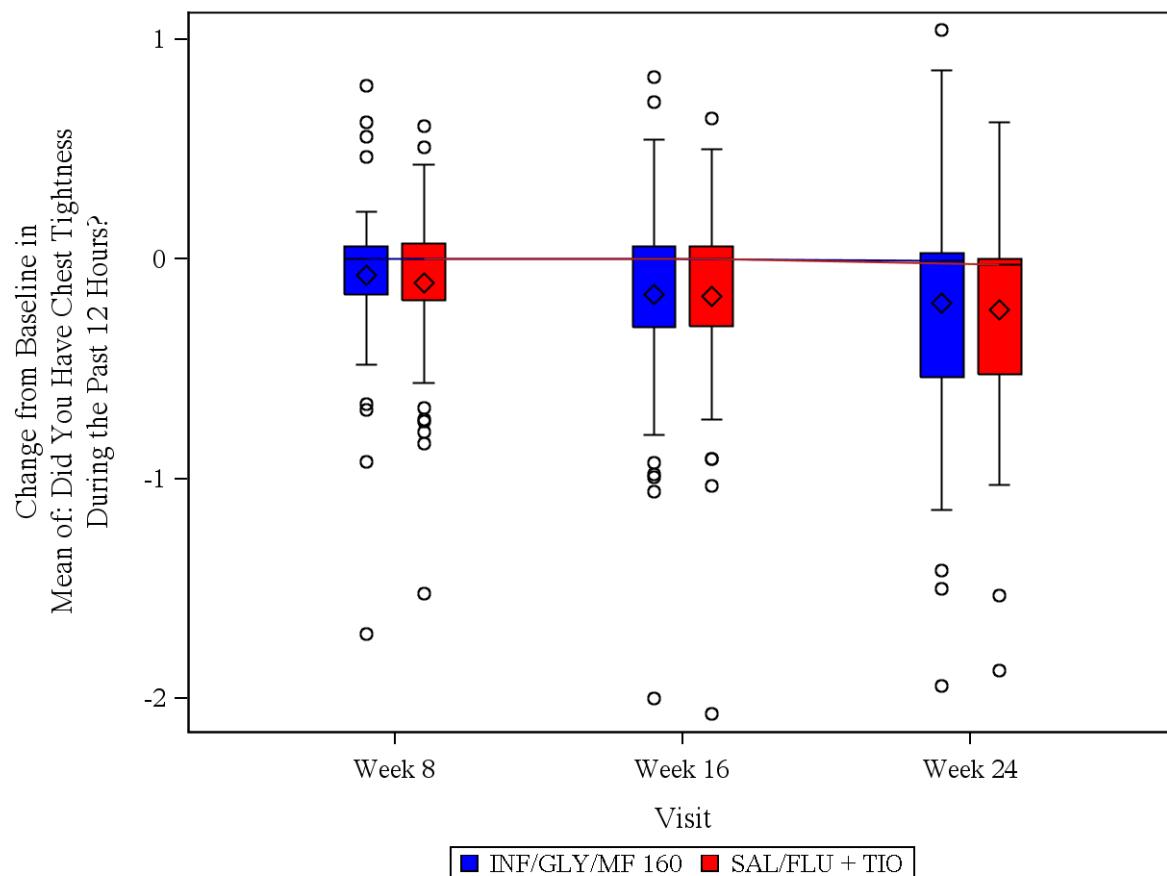


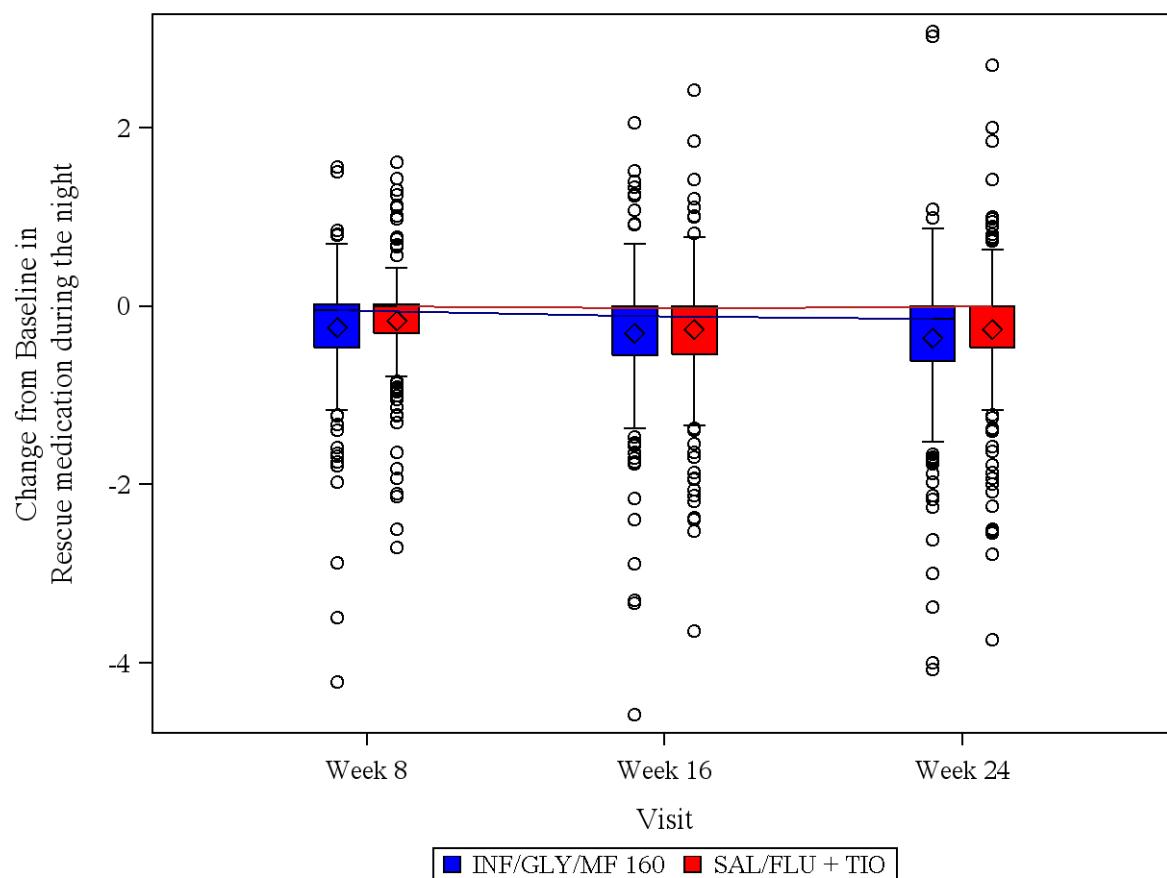
Figure 9.83.2 Symptoms (Mean of: Did You Have Chest Tightness During the Past 12 Hours?) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



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

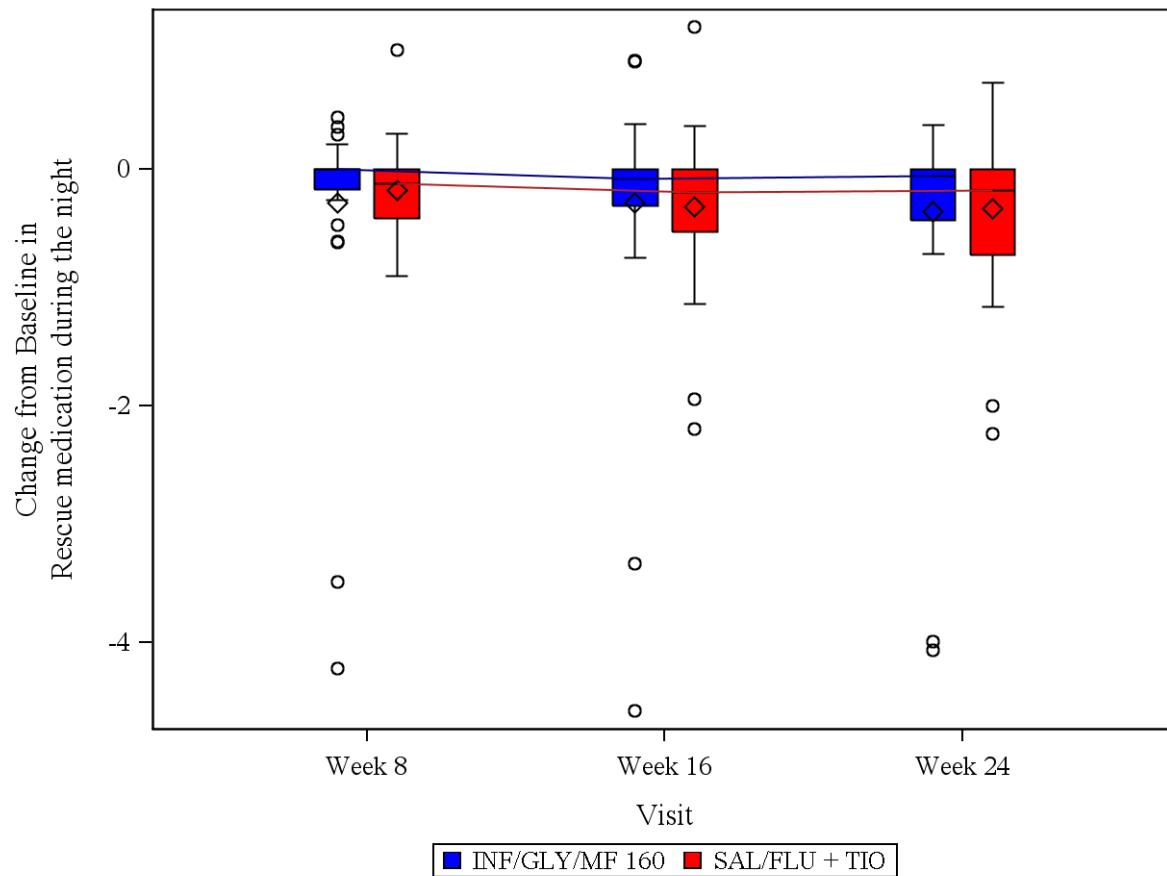


Figure 5.2.2 Rescue Medication (Rescue medication during the night) - Change from Baseline by Age (FAS), Age = 40-64 years

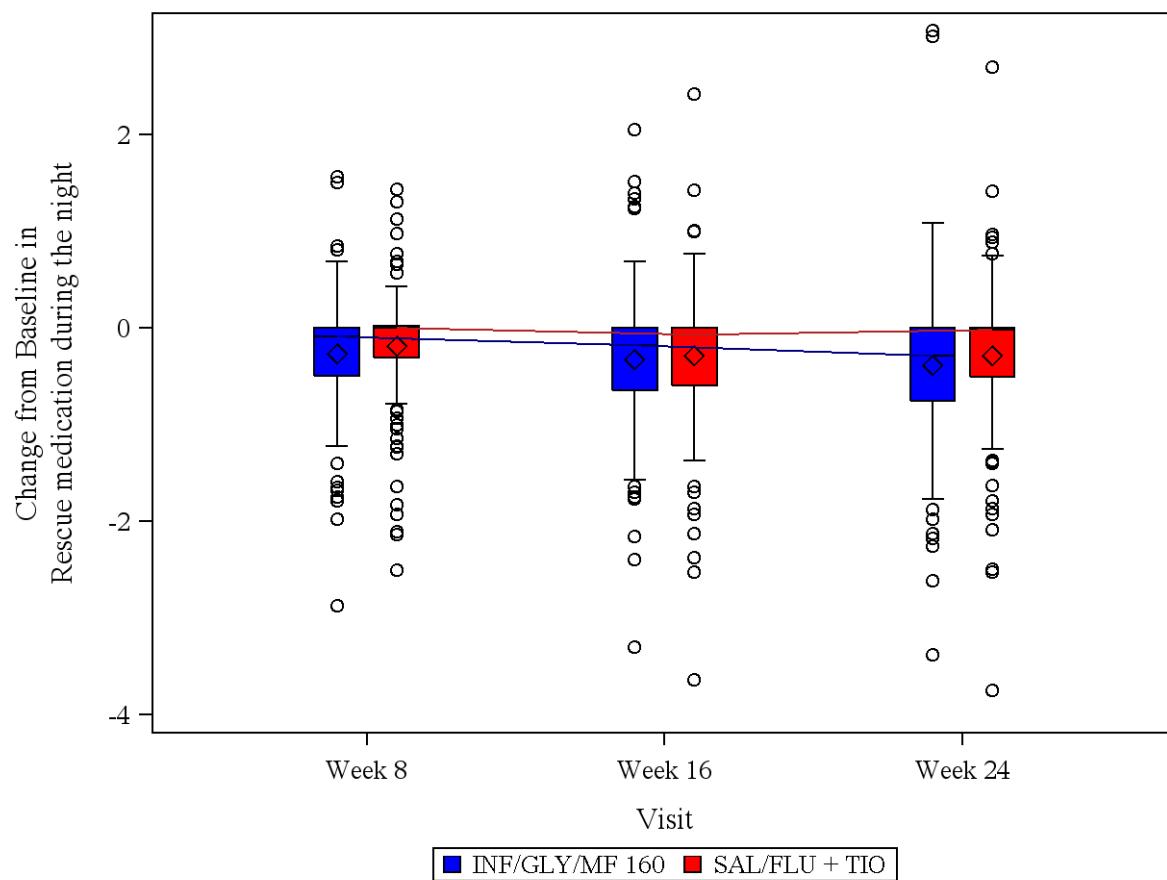
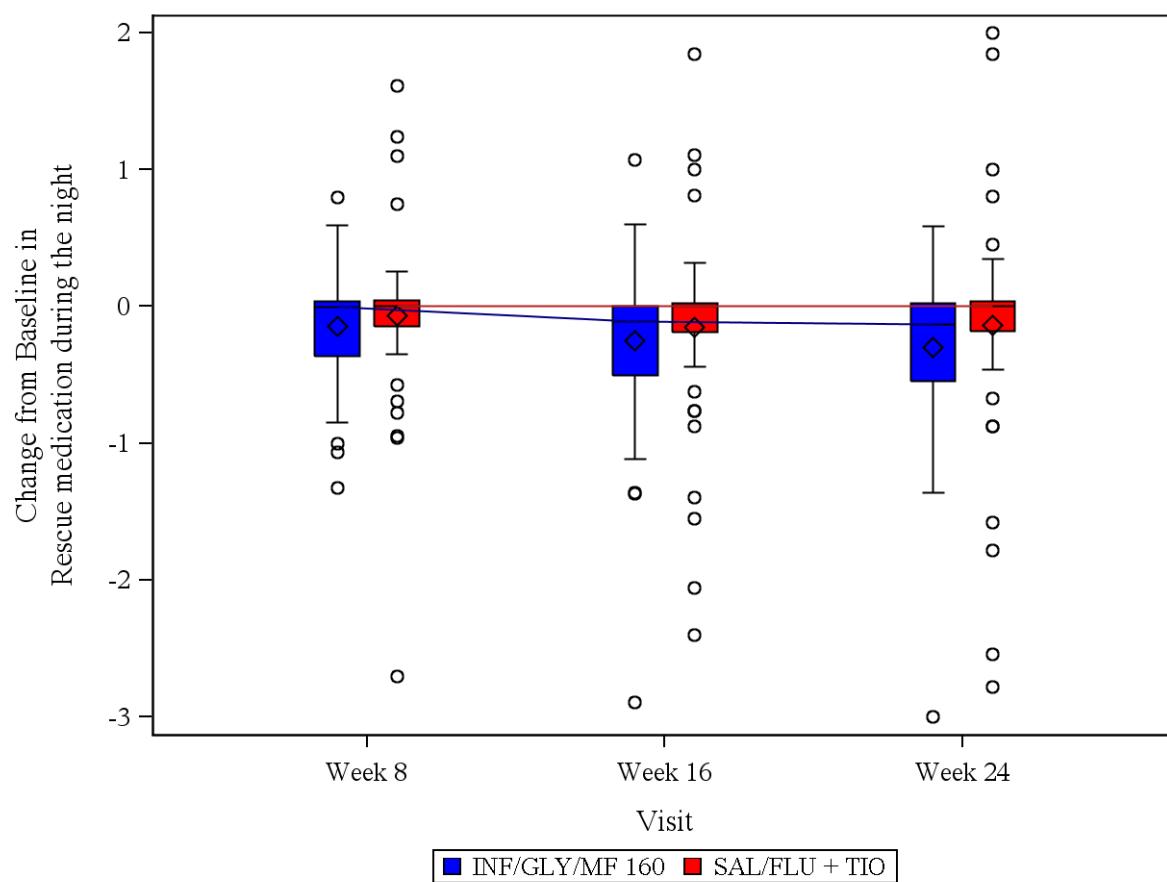


Figure 5.2.3 Rescue Medication (Rescue medication during the night) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

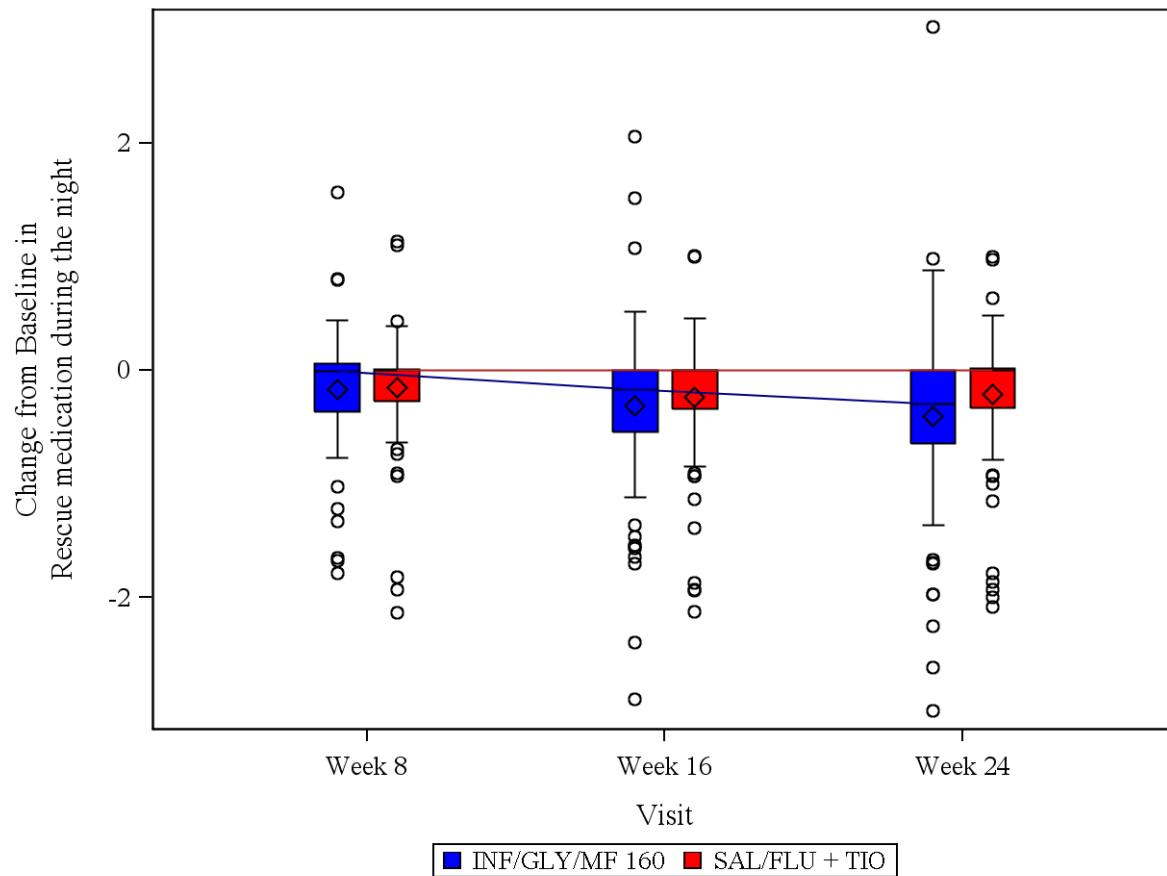
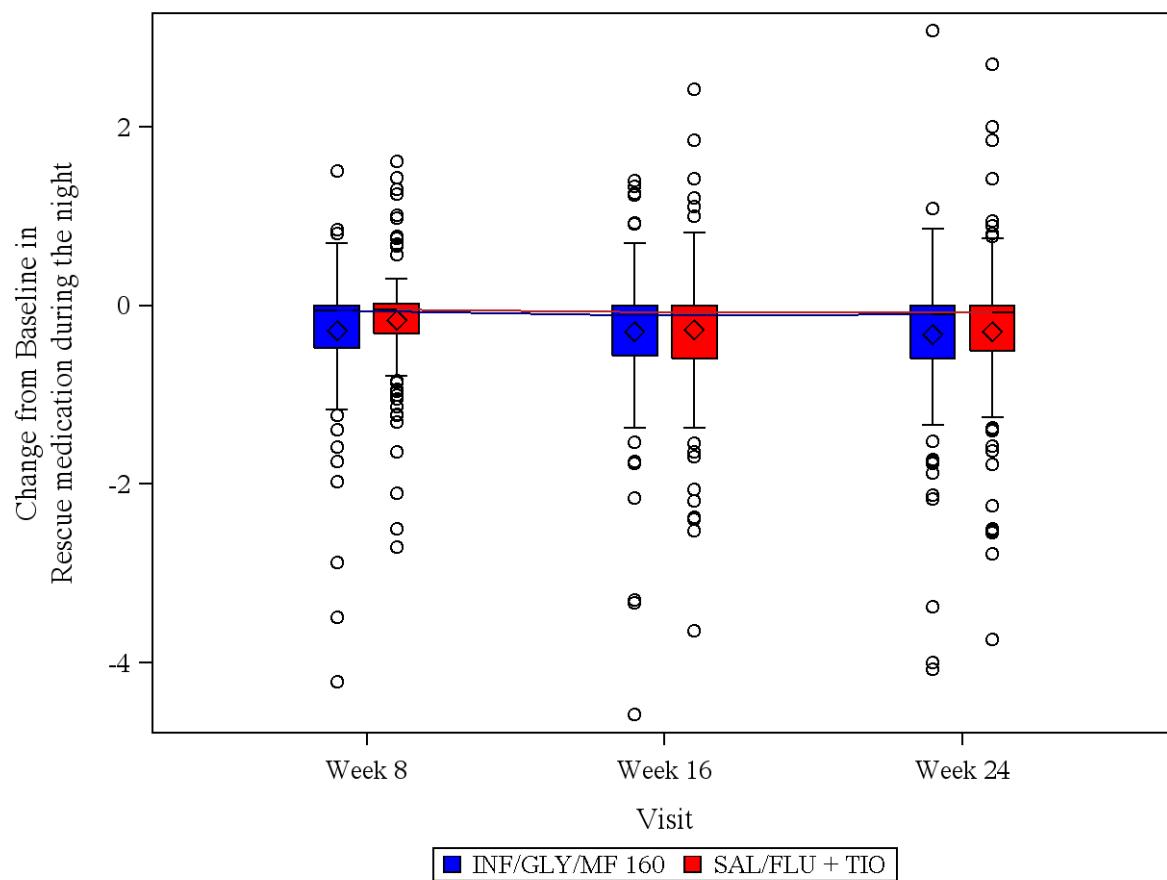


Figure 5.3.2 Rescue Medication (Rescue medication during the night) - Change from Baseline by Gender (FAS), Gender = Female



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

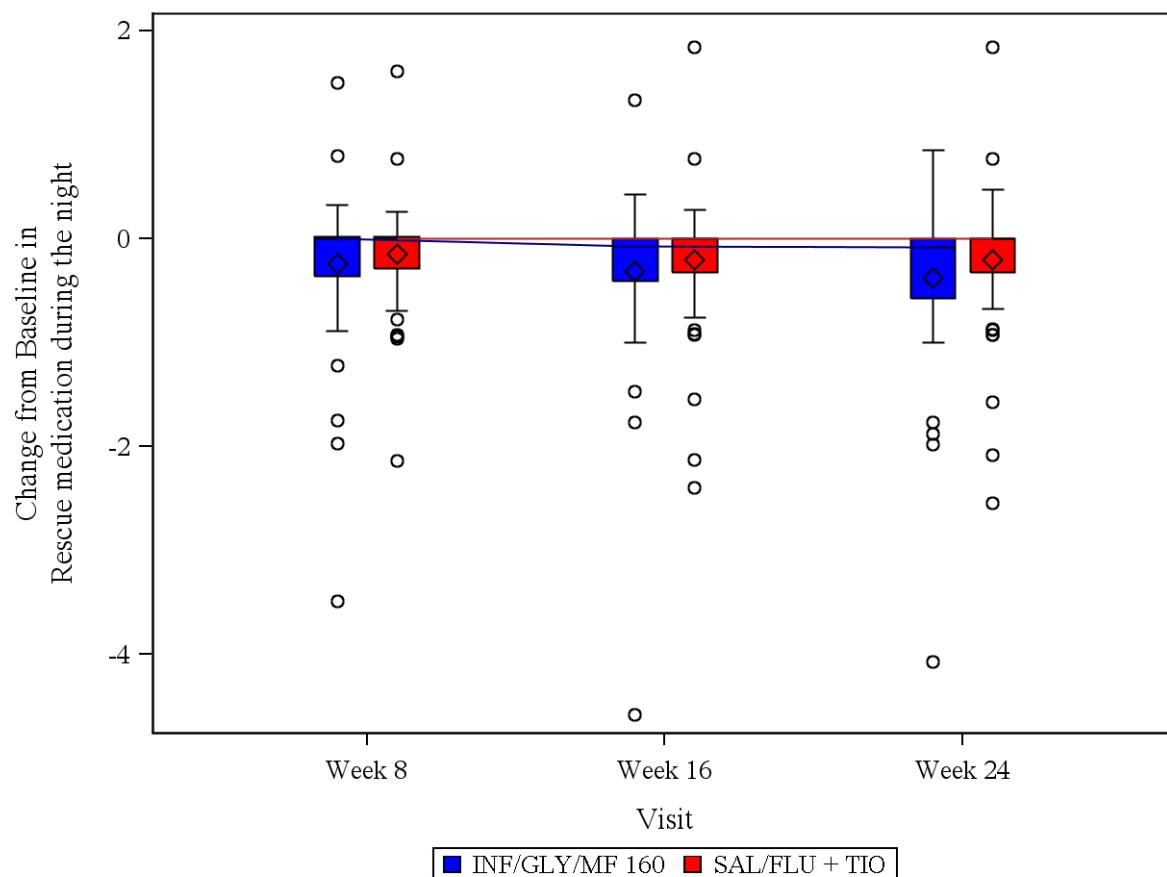


Figure 5.4.2 Rescue Medication (Rescue medication during the night) - Change from Baseline by Region (FAS), Region = Europe

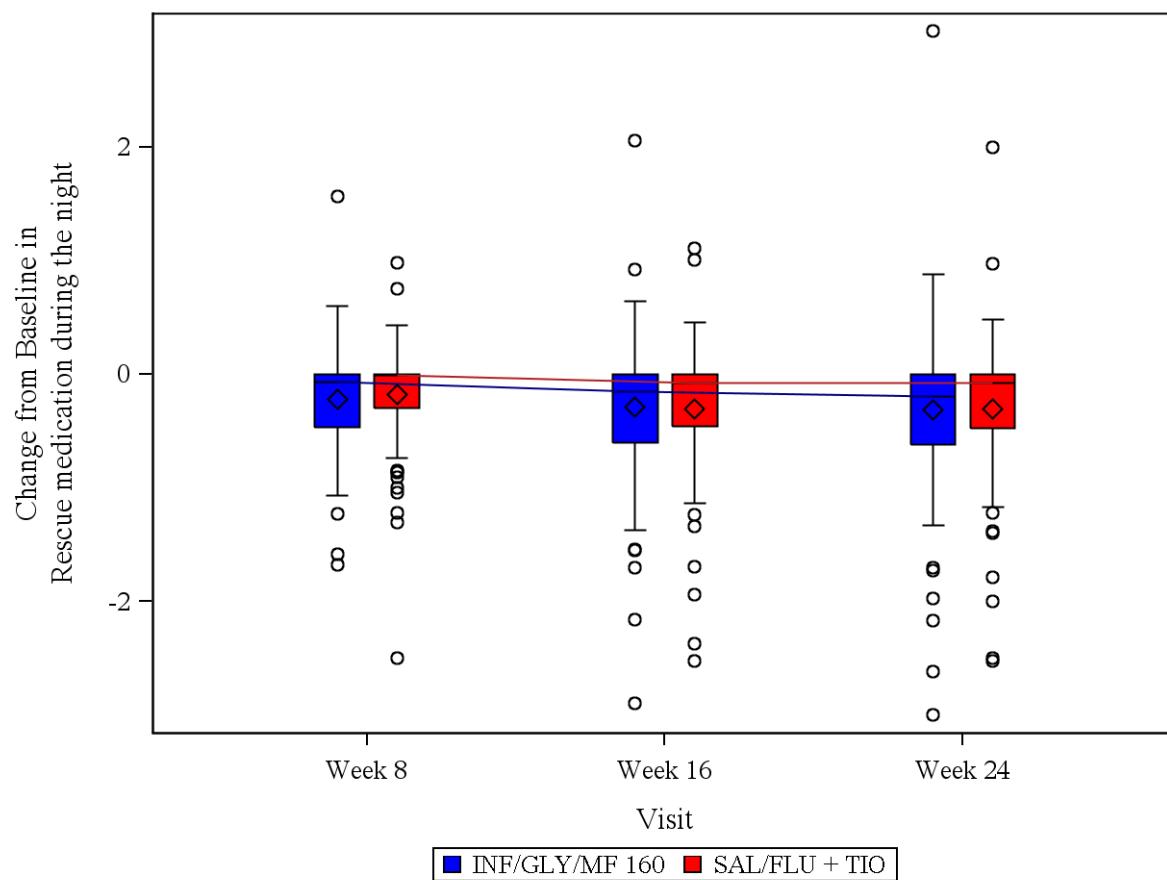


Figure 5.4.3 Rescue Medication (Rescue medication during the night) - Change from Baseline by Region (FAS), Region = Latin America

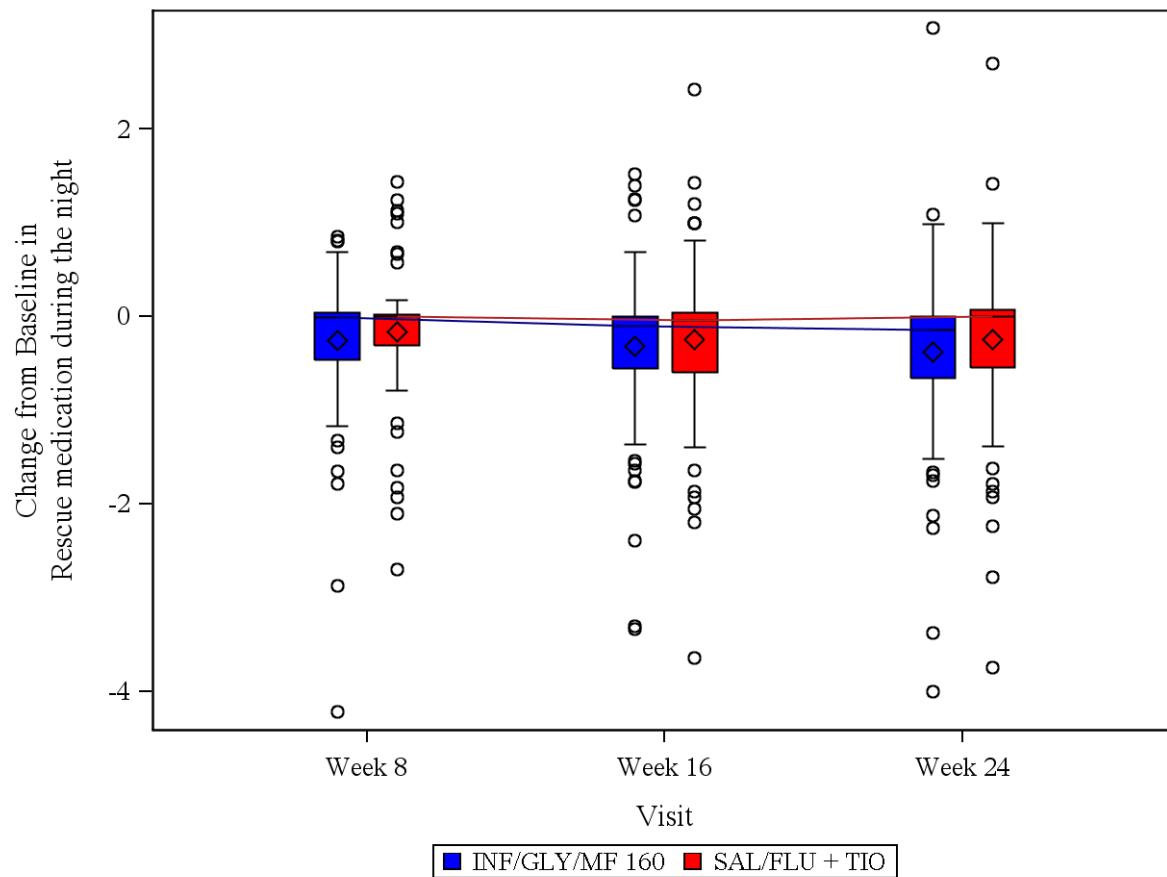
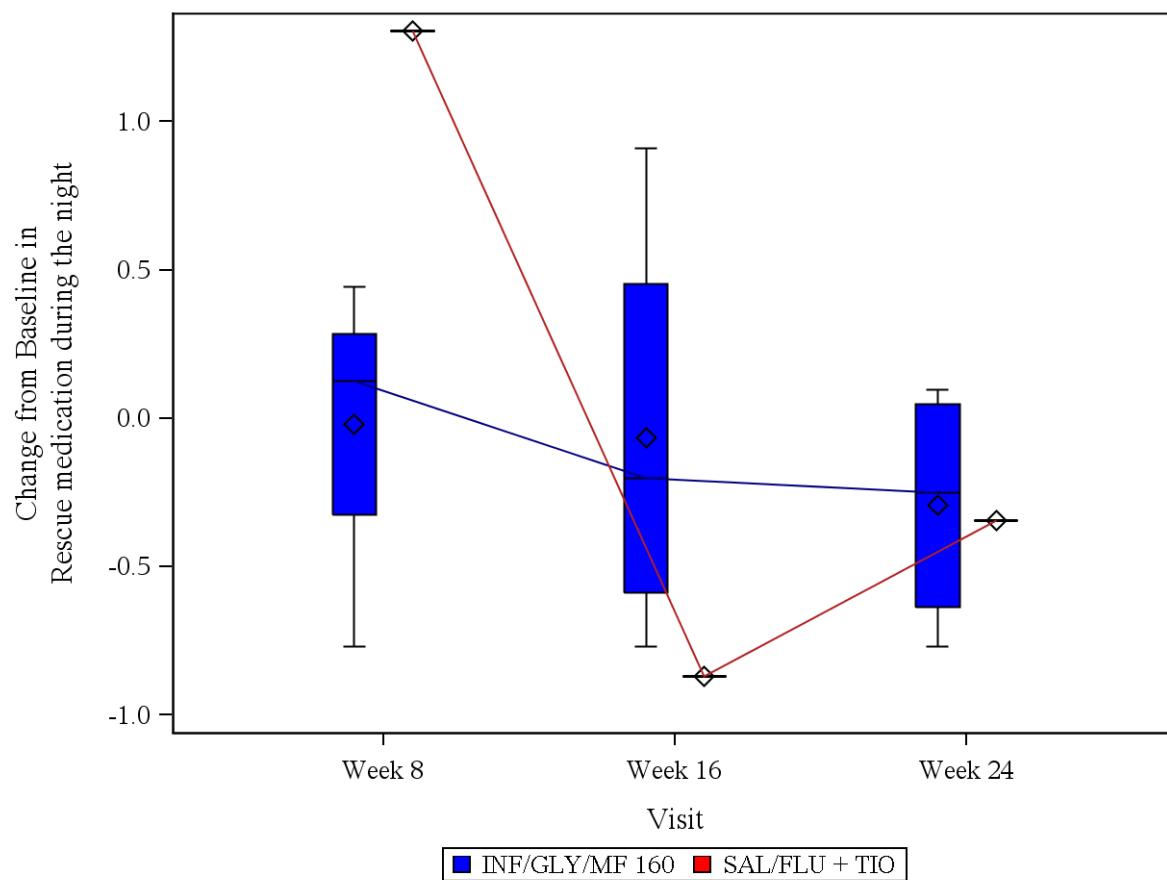


Figure 5.4.4 Rescue Medication (Rescue medication during the night) - Change from Baseline by Region (FAS), Region = Others



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

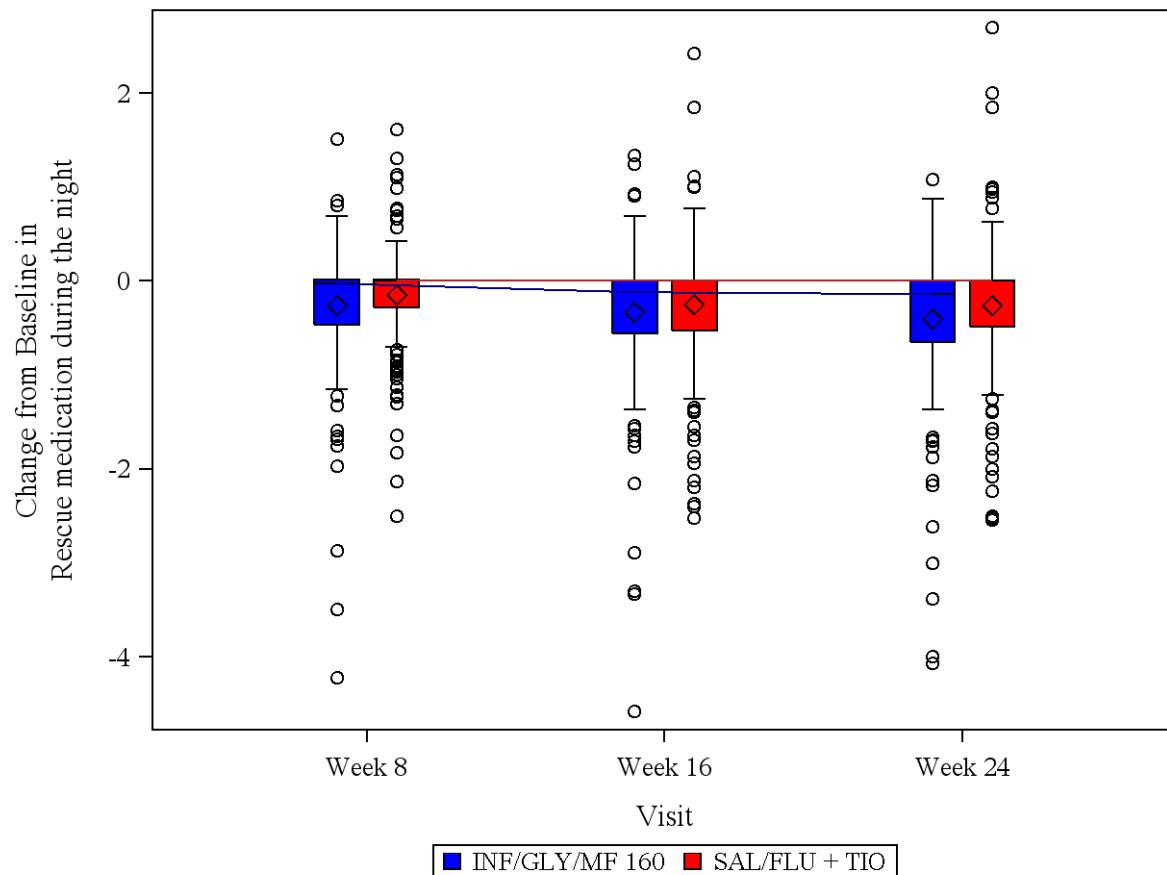
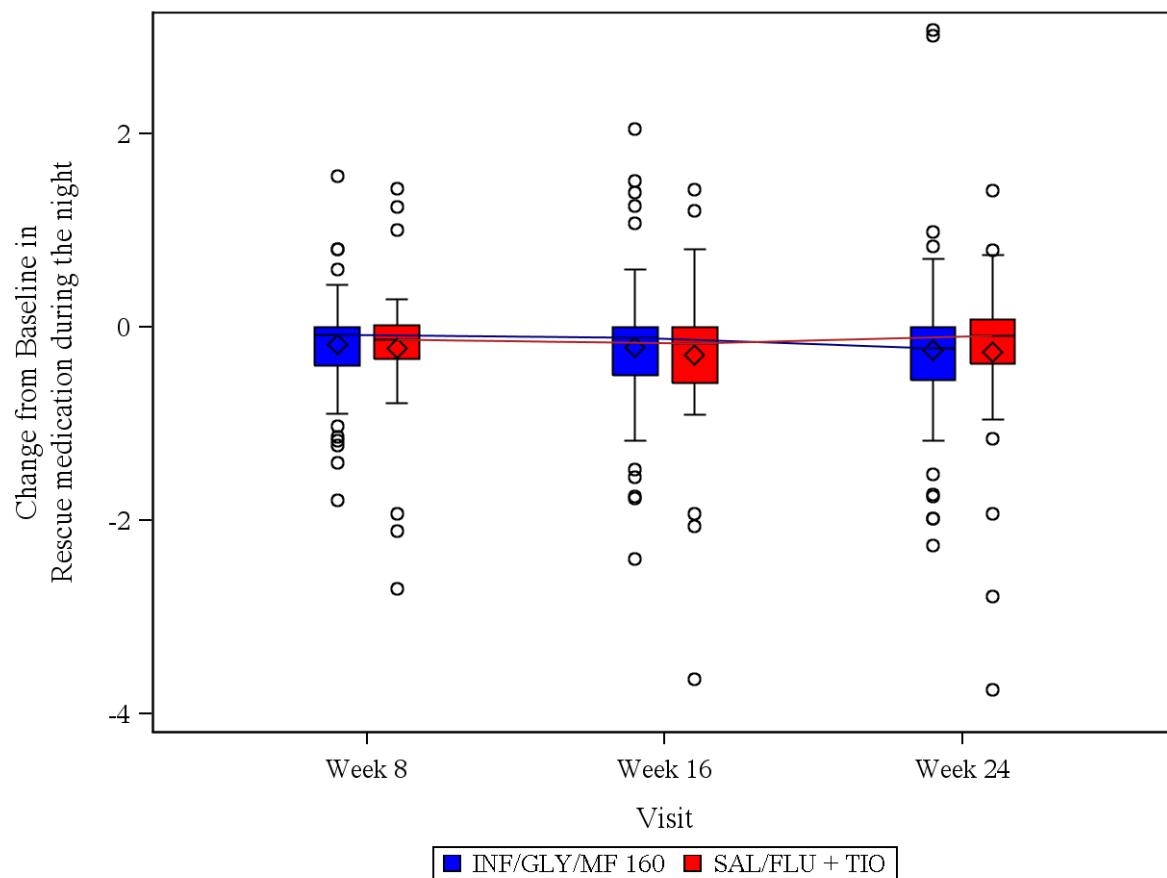
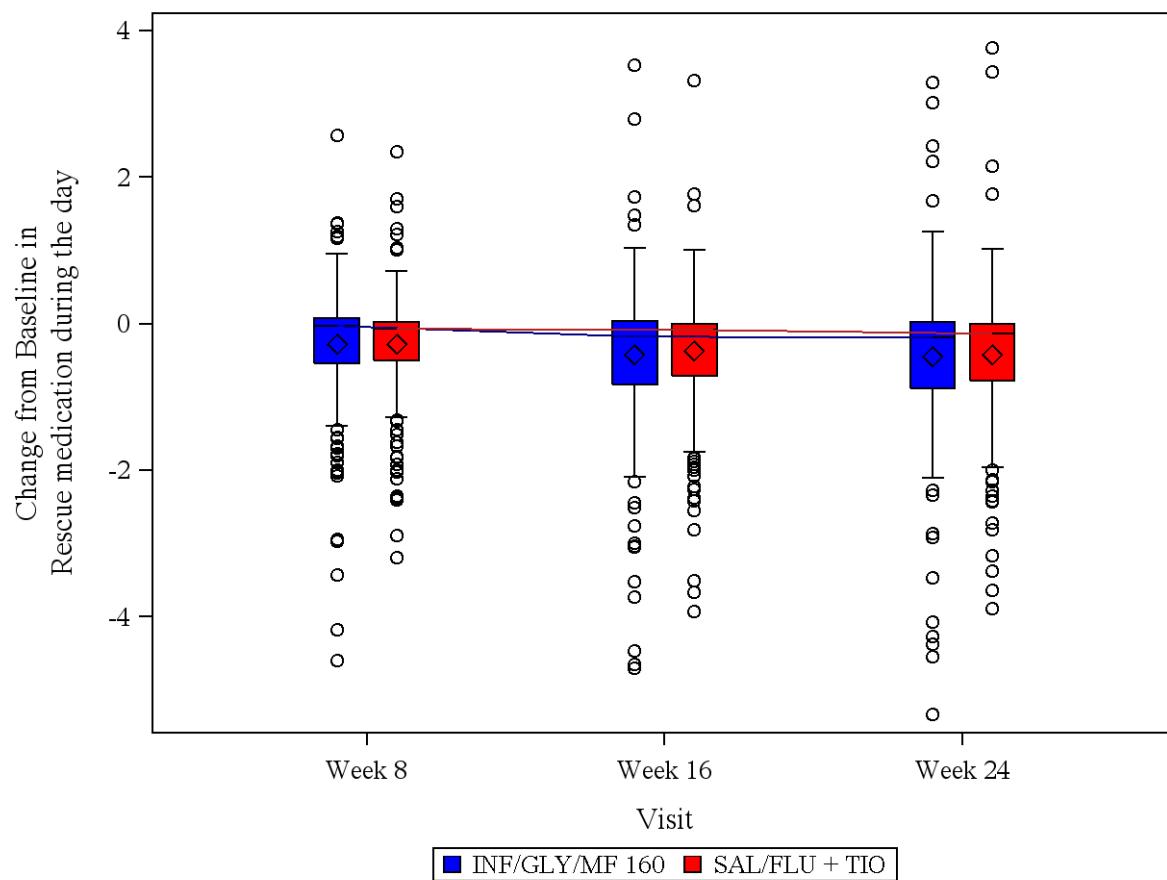


Figure 5.5.2 Rescue Medication (Rescue medication during the night) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



10.7 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

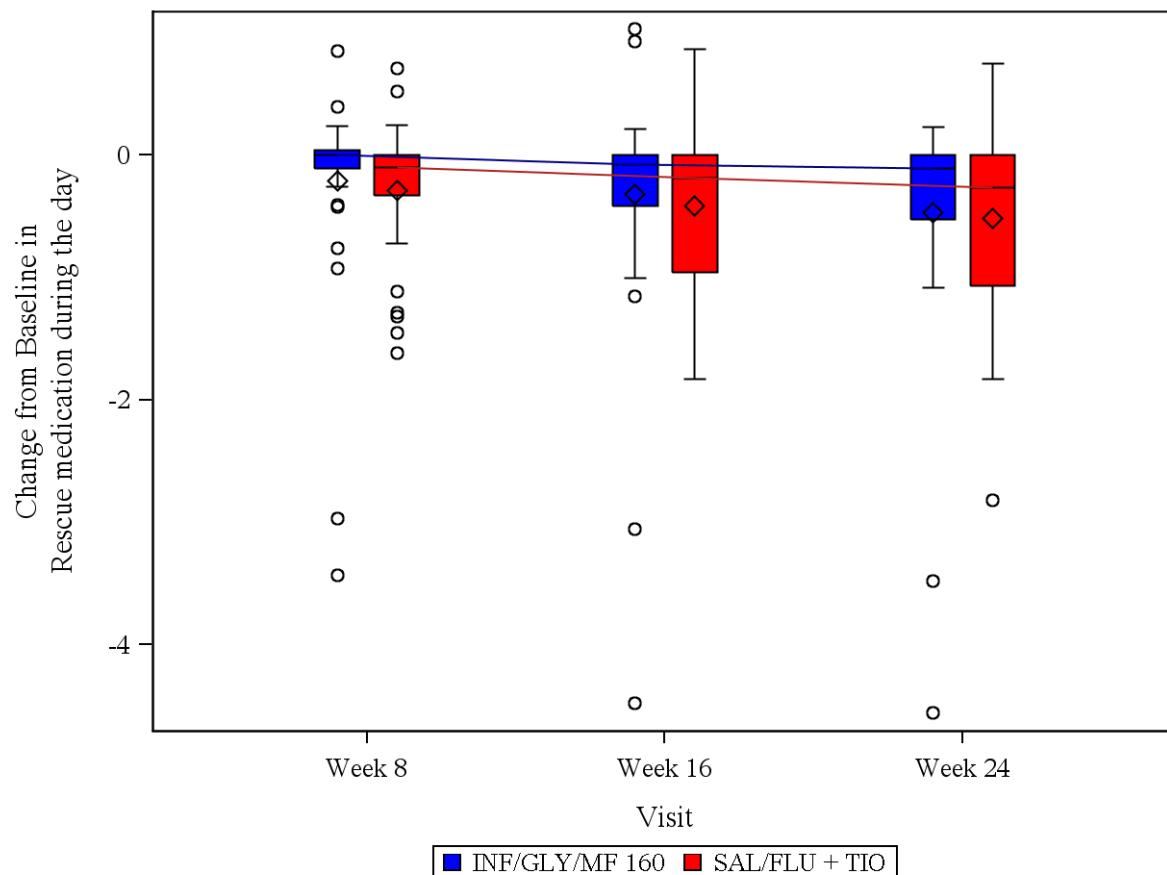


Figure 5.8.2 Rescue Medication (Rescue medication during the day) - Change from Baseline by Age (FAS), Age = 40-64 years

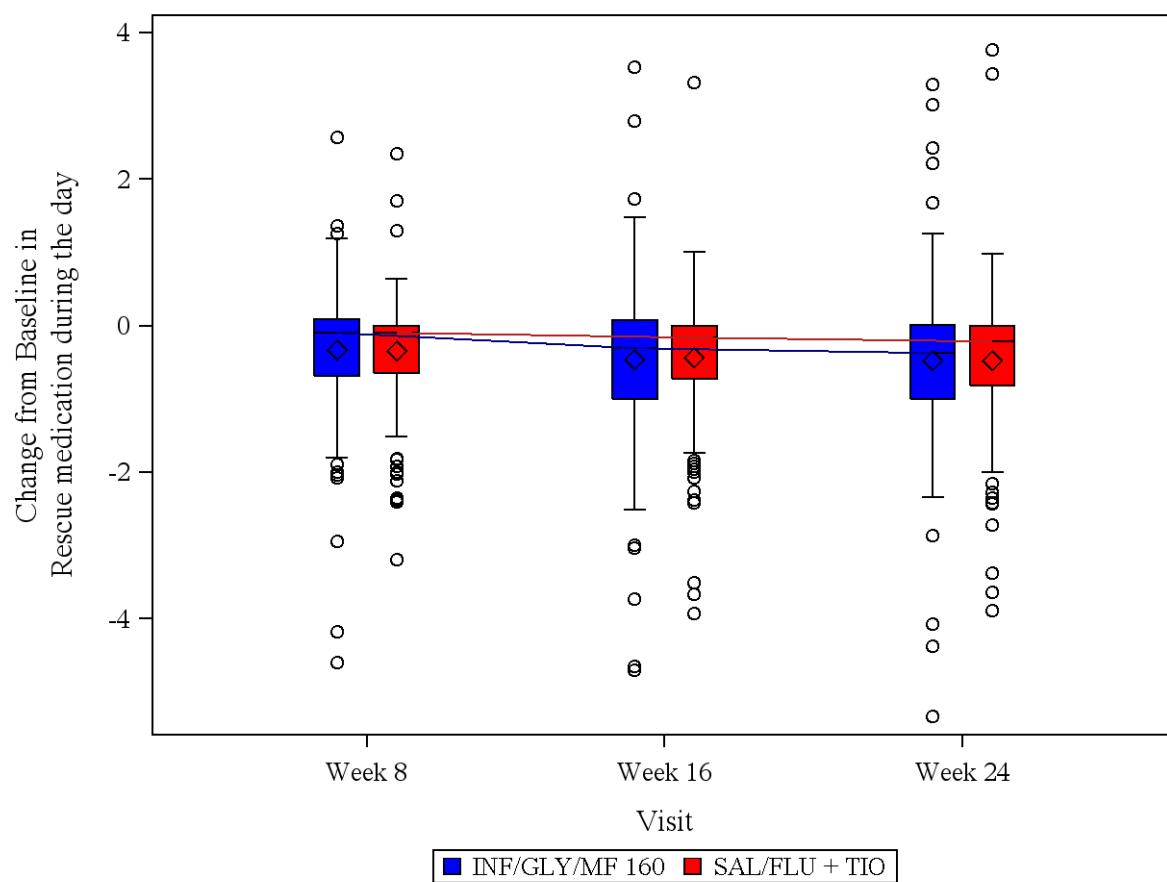
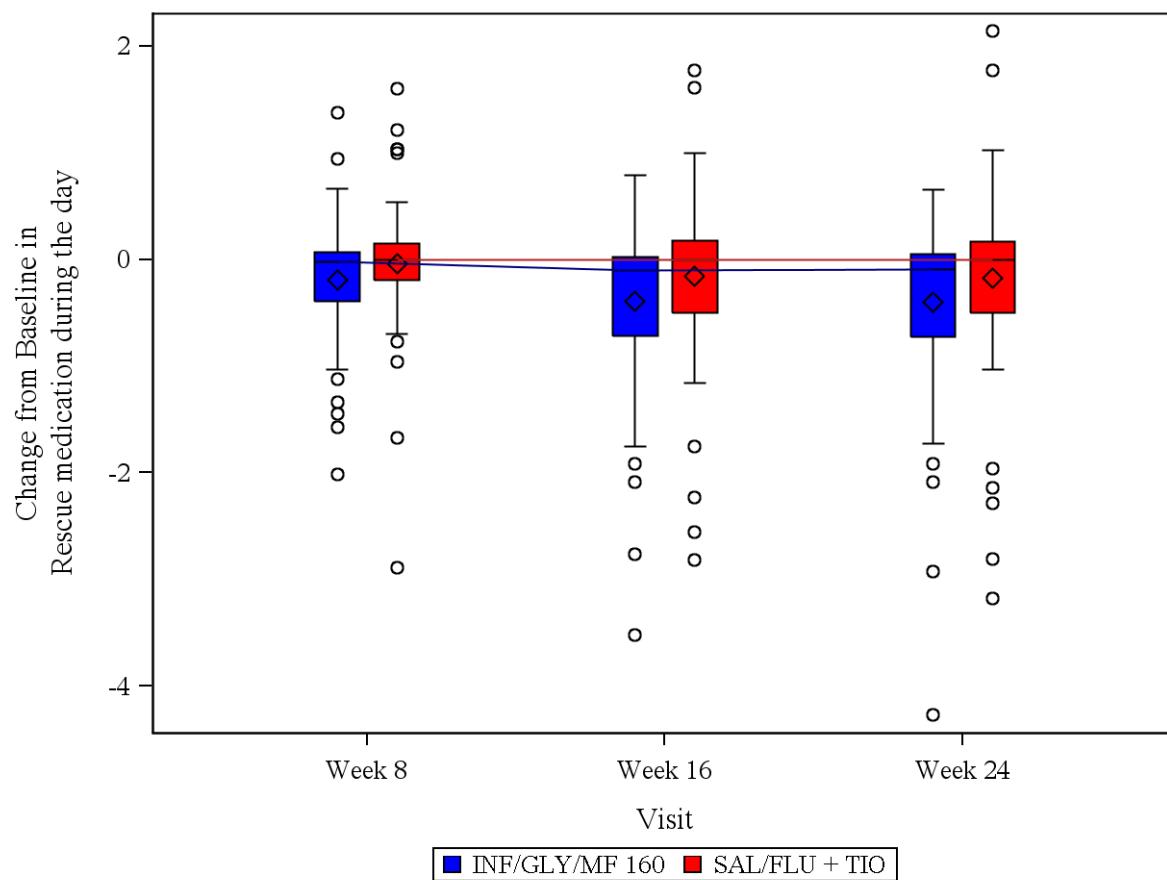


Figure 5.8.3 Rescue Medication (Rescue medication during the day) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

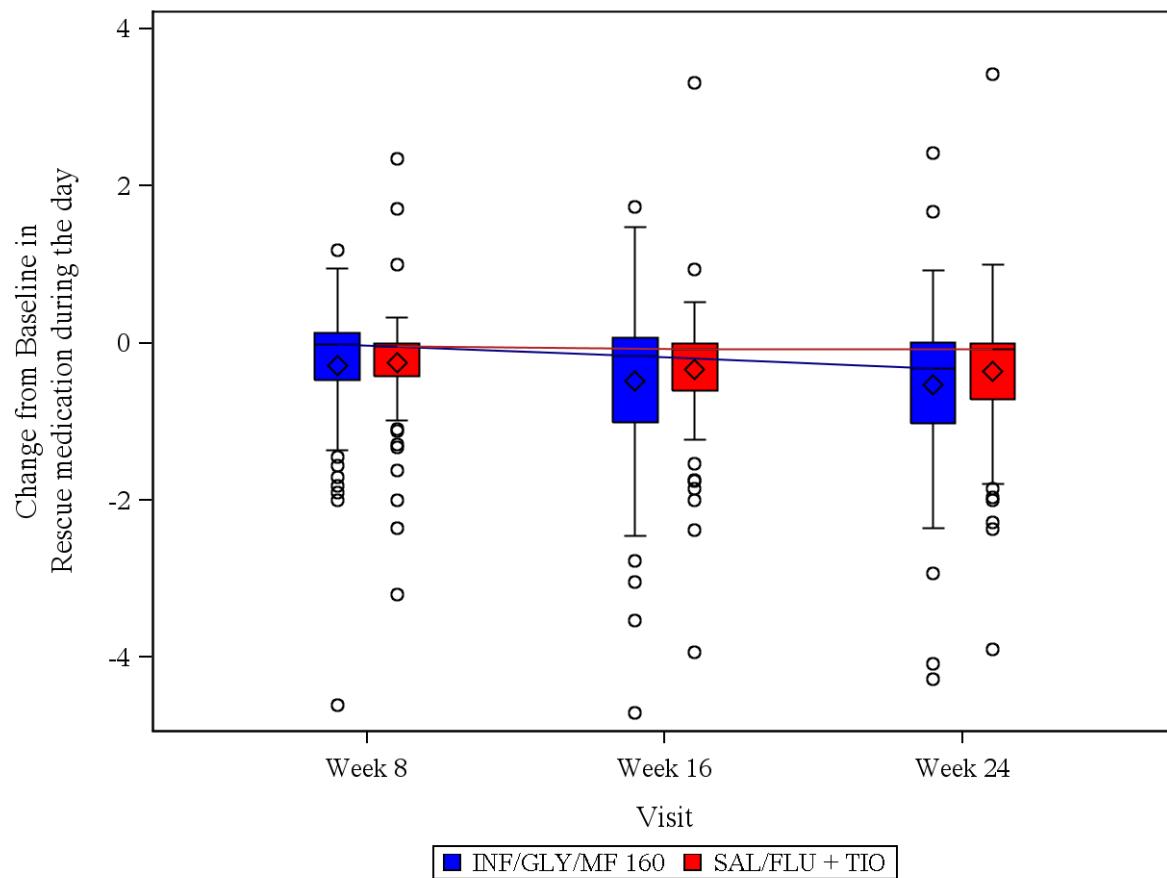
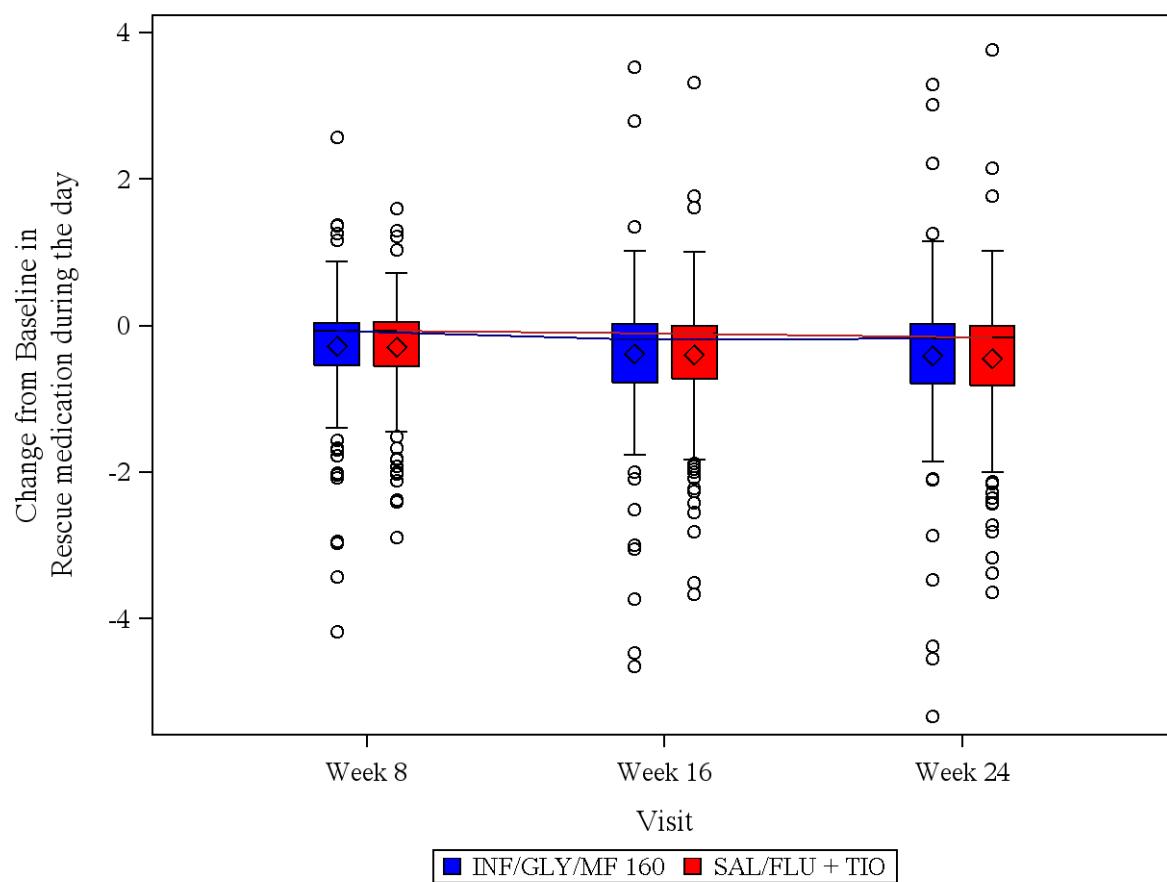


Figure 5.9.2 Rescue Medication (Rescue medication during the day) - Change from Baseline by Gender (FAS), Gender = Female



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

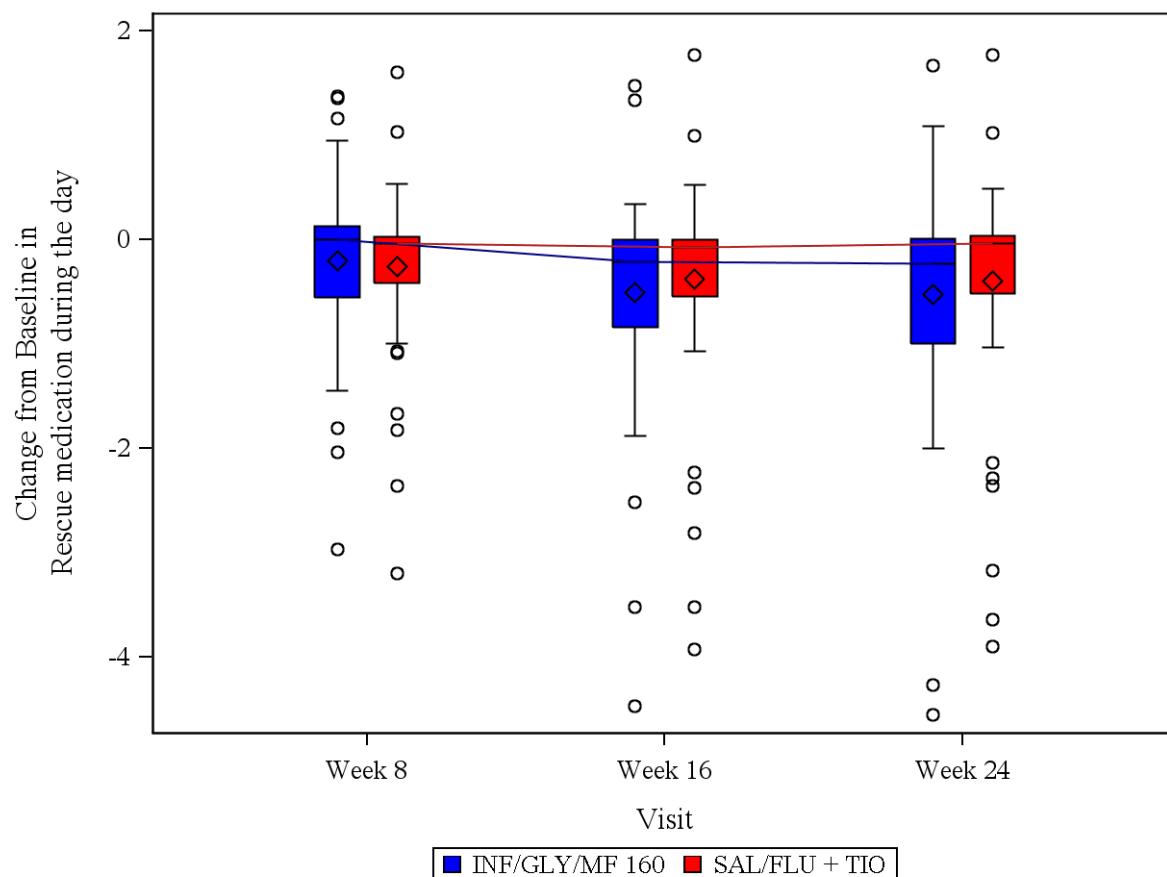


Figure 5.10.2 Rescue Medication (Rescue medication during the day) - Change from Baseline by Region (FAS), Region = Europe

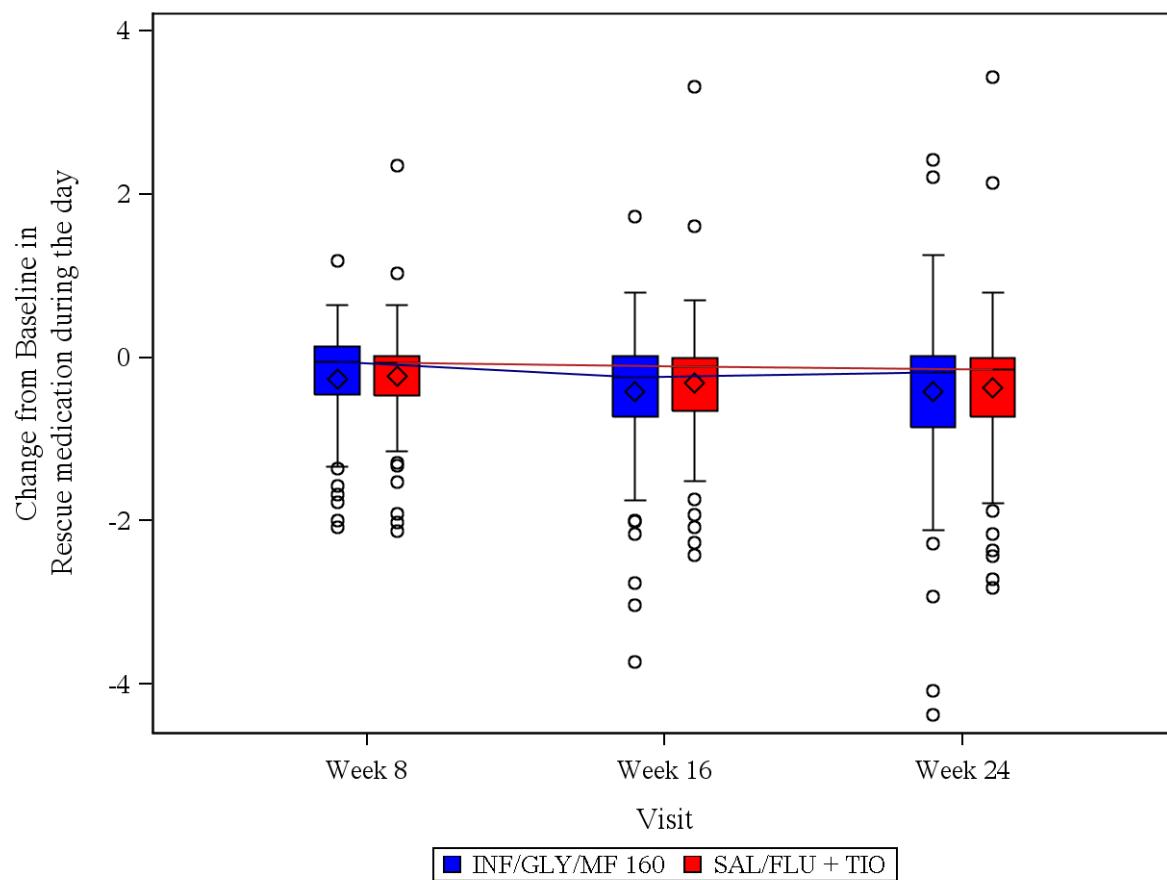


Figure 5.10.3 Rescue Medication (Rescue medication during the day) - Change from Baseline by Region (FAS), Region = Latin America

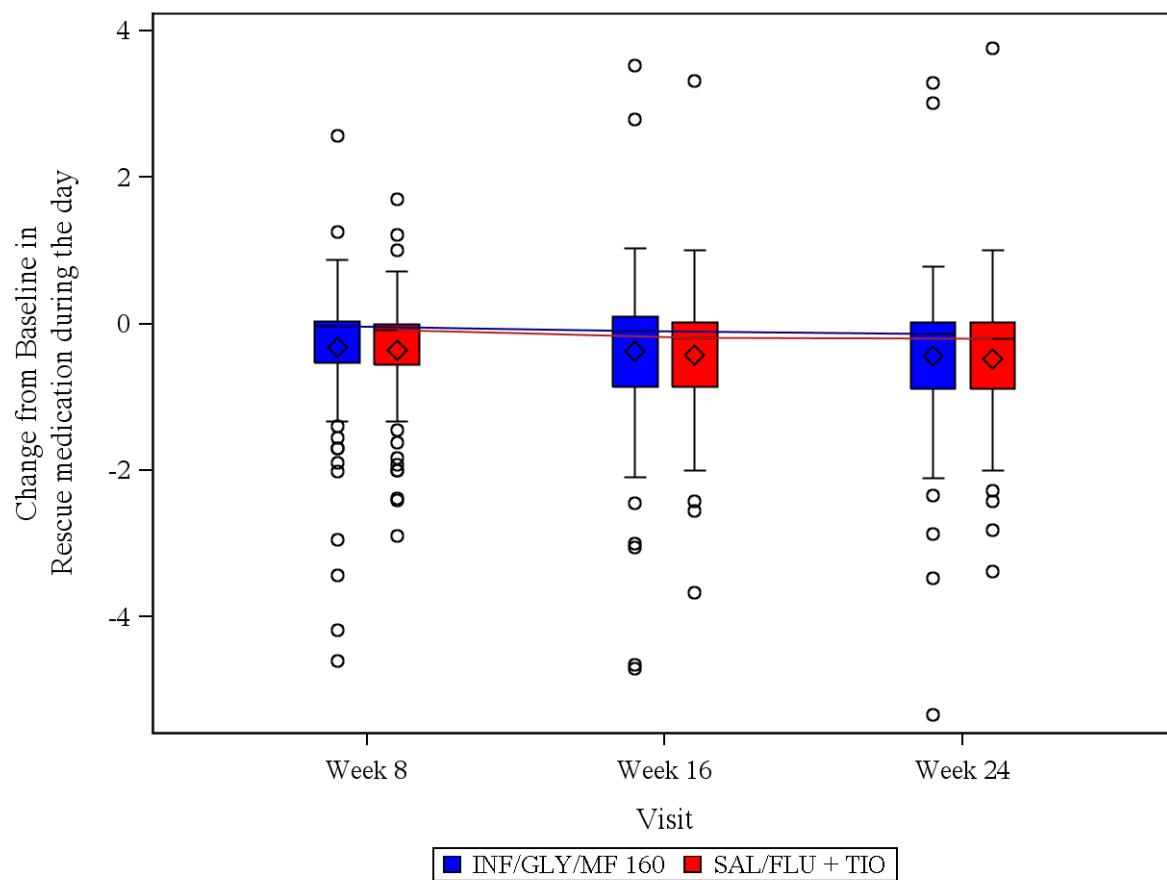
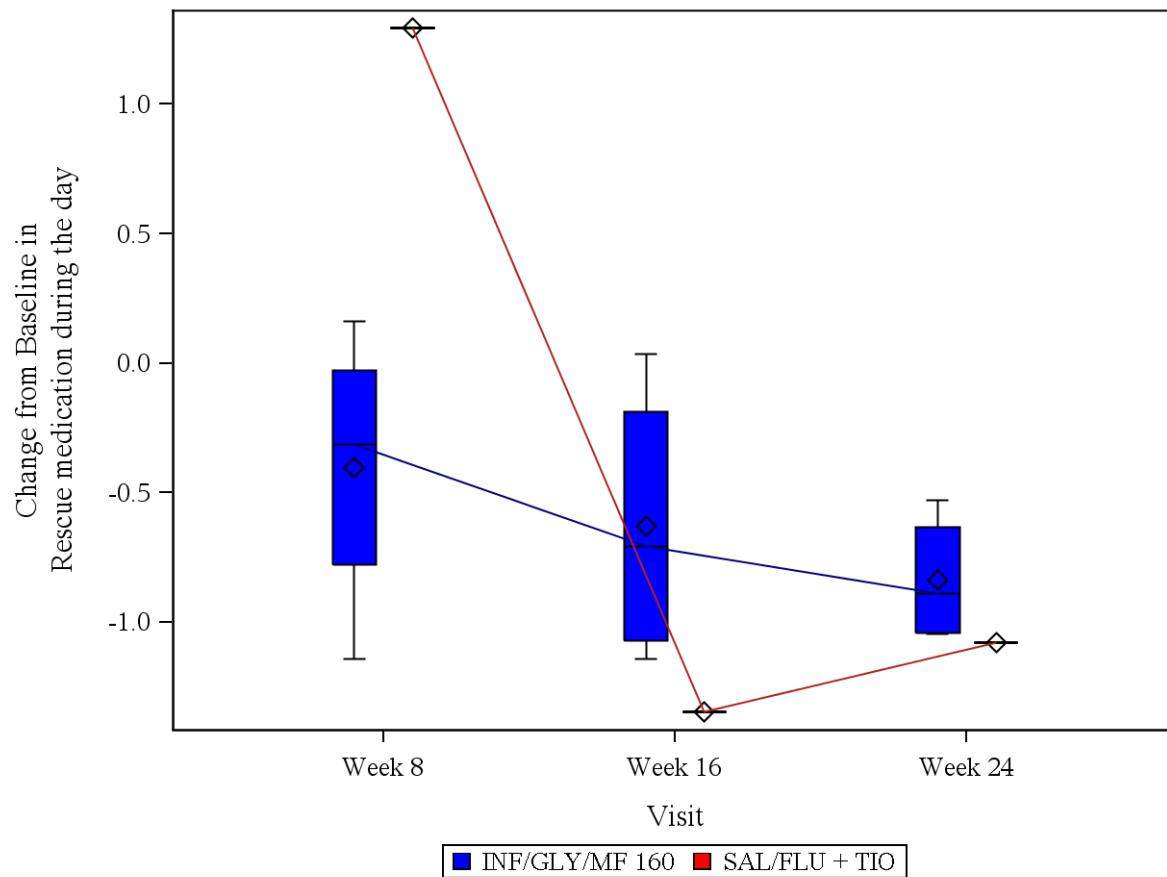


Figure 5.10.4 Rescue Medication (Rescue medication during the day) - Change from Baseline by Region (FAS), Region = Others



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

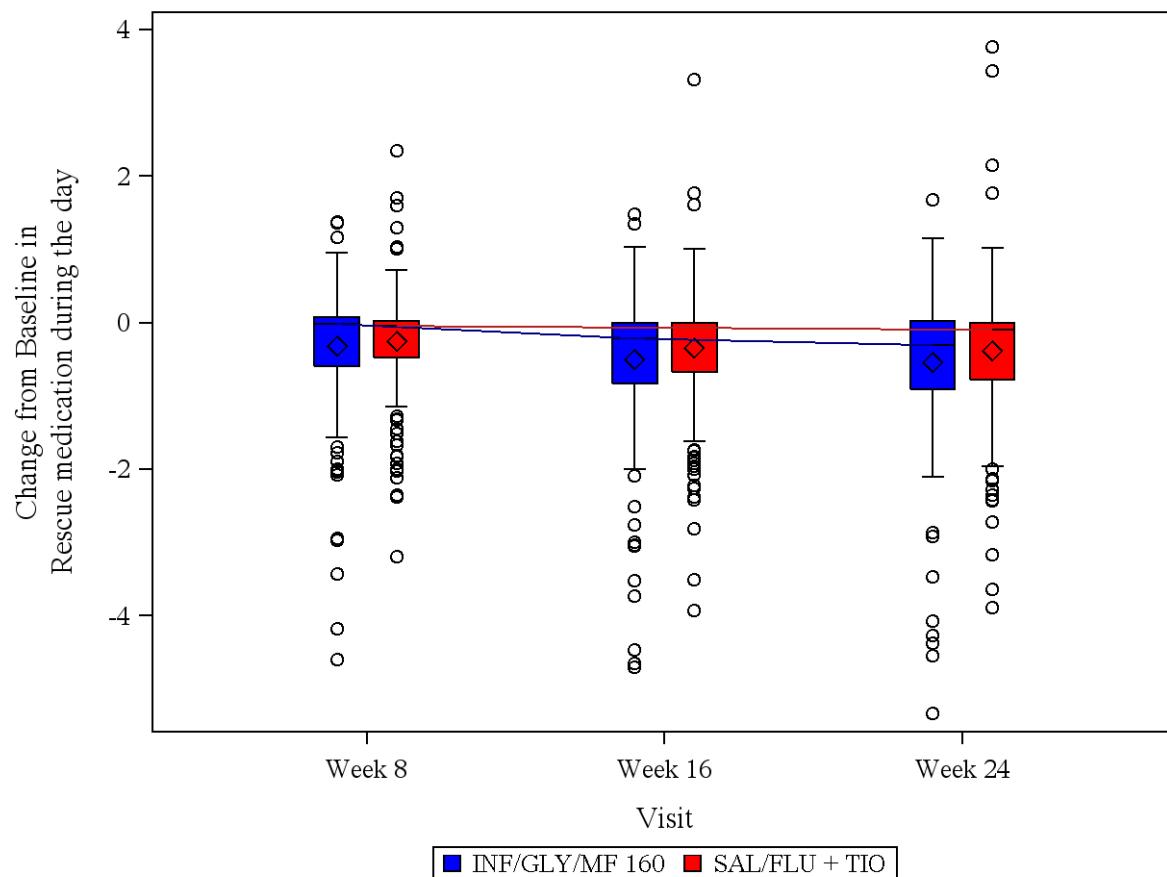
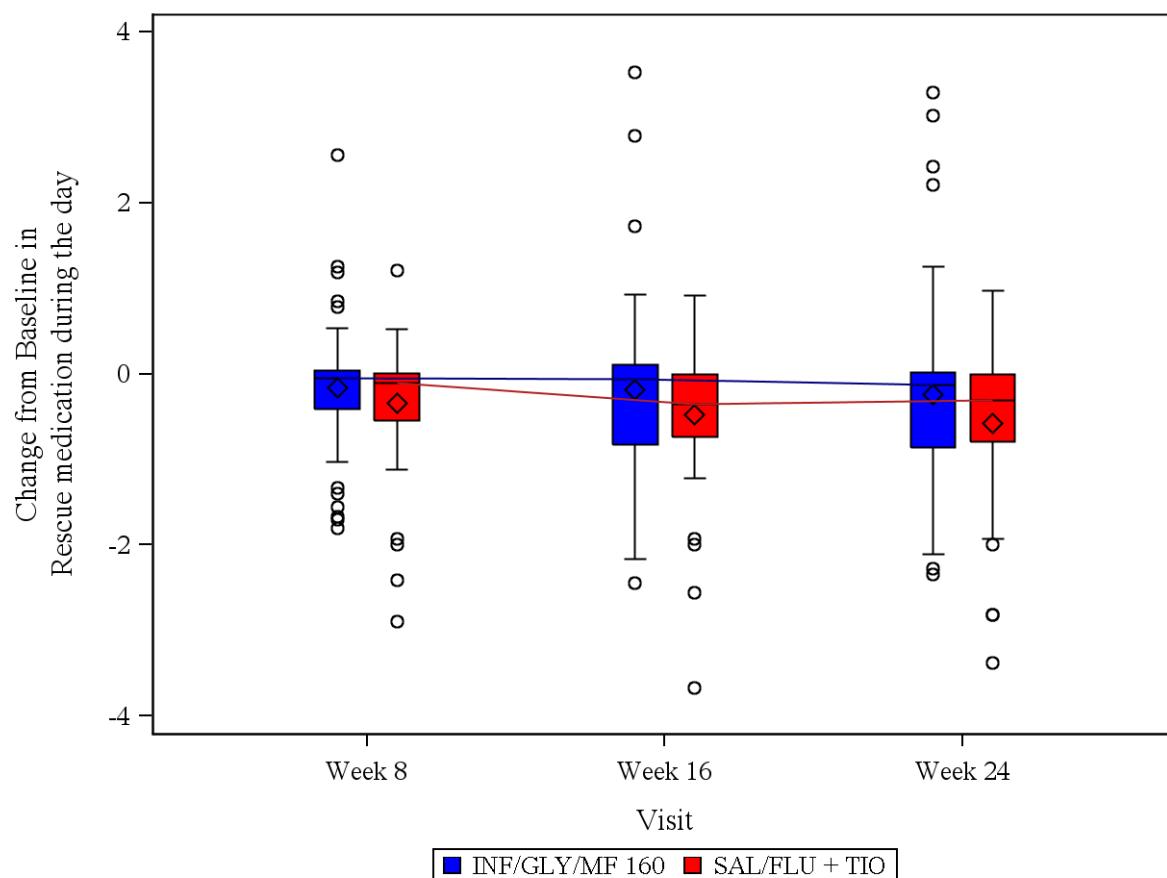
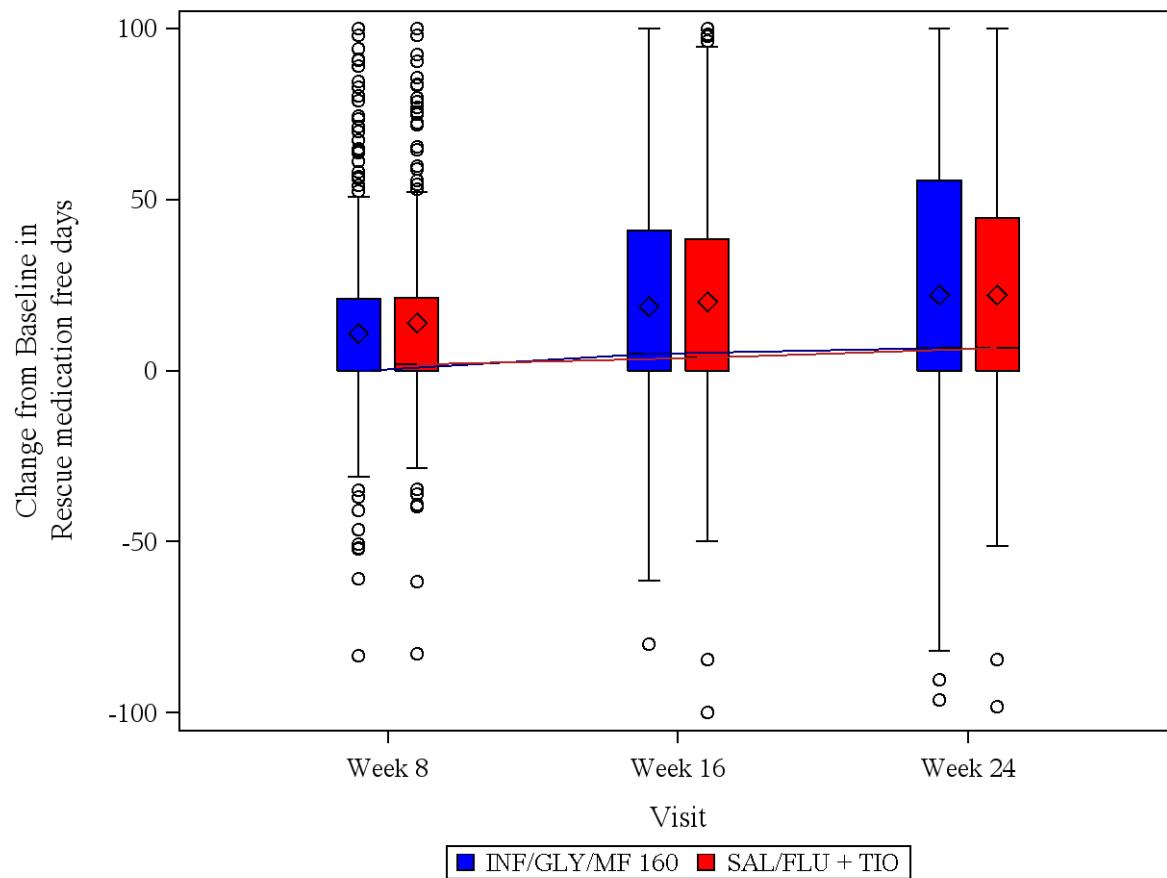


Figure 5.11.2 Rescue Medication (Rescue medication during the day) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥2



10.13 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

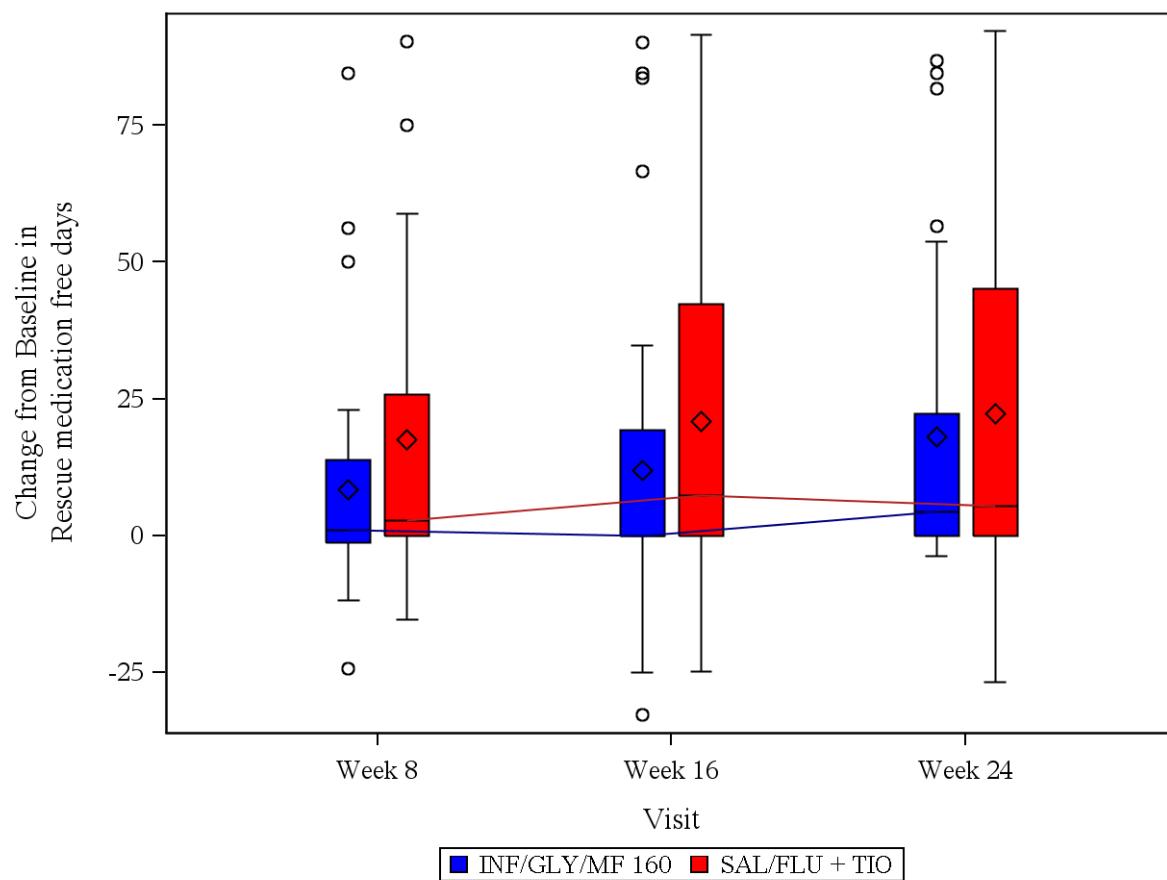


Figure 5.14.2 Rescue Medication (Rescue medication free days) - Change from Baseline by Age (FAS), Age = 40-64 years

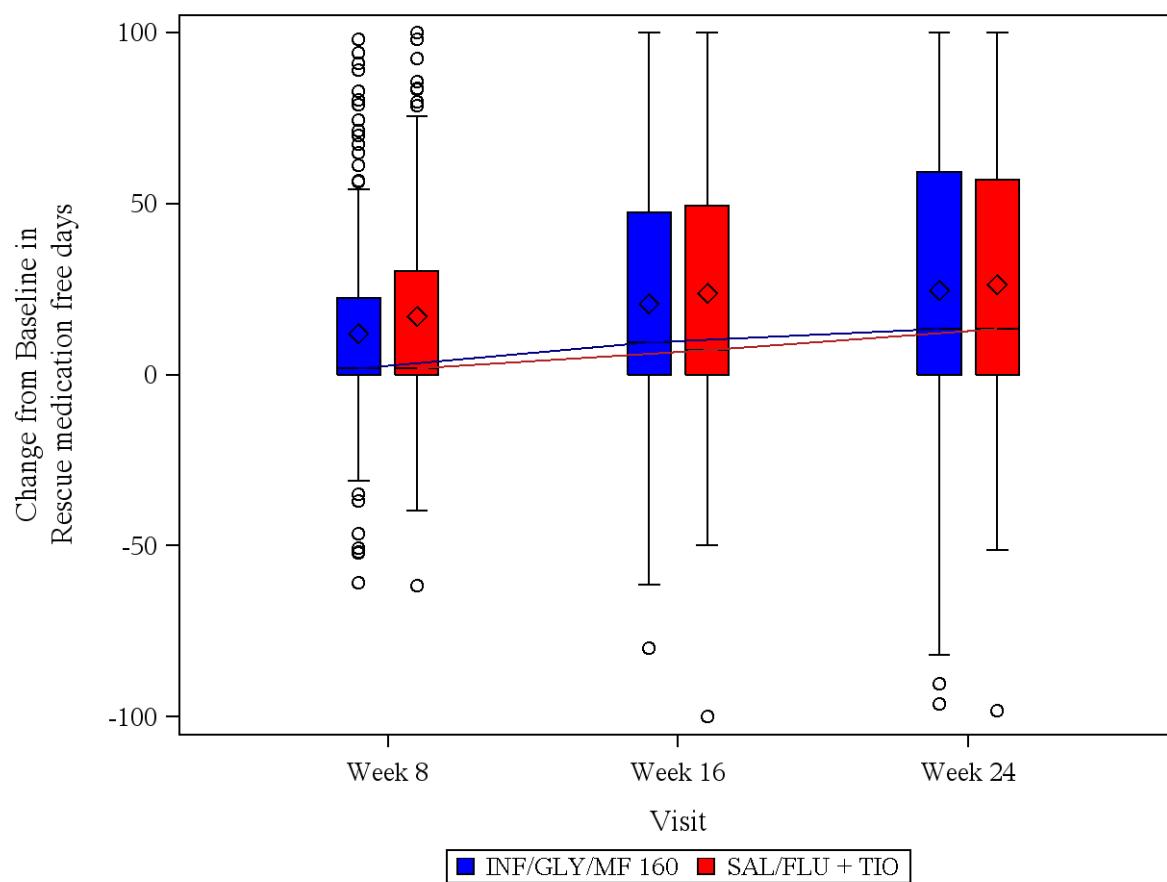
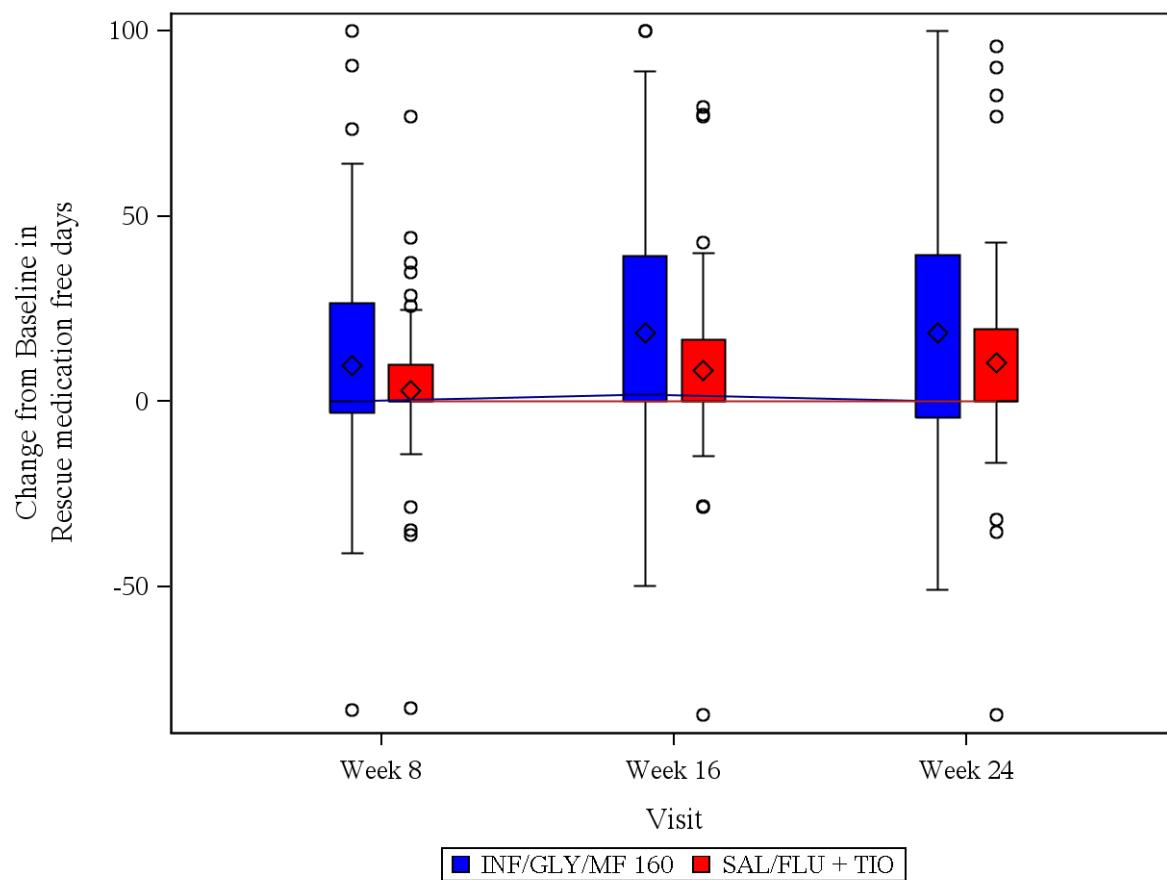


Figure 5.14.3 Rescue Medication (Rescue medication free days) - Change from Baseline by Age (FAS), Age = ≥ 65 years



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

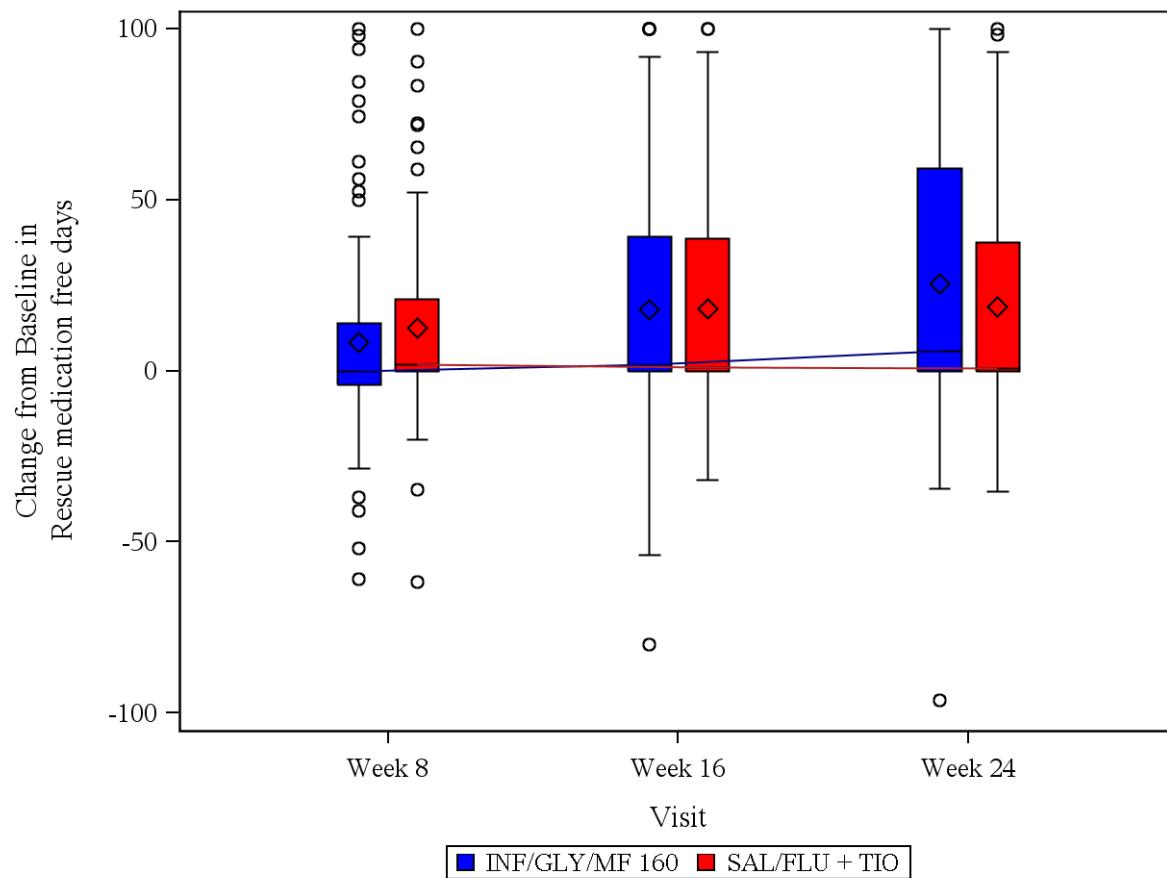
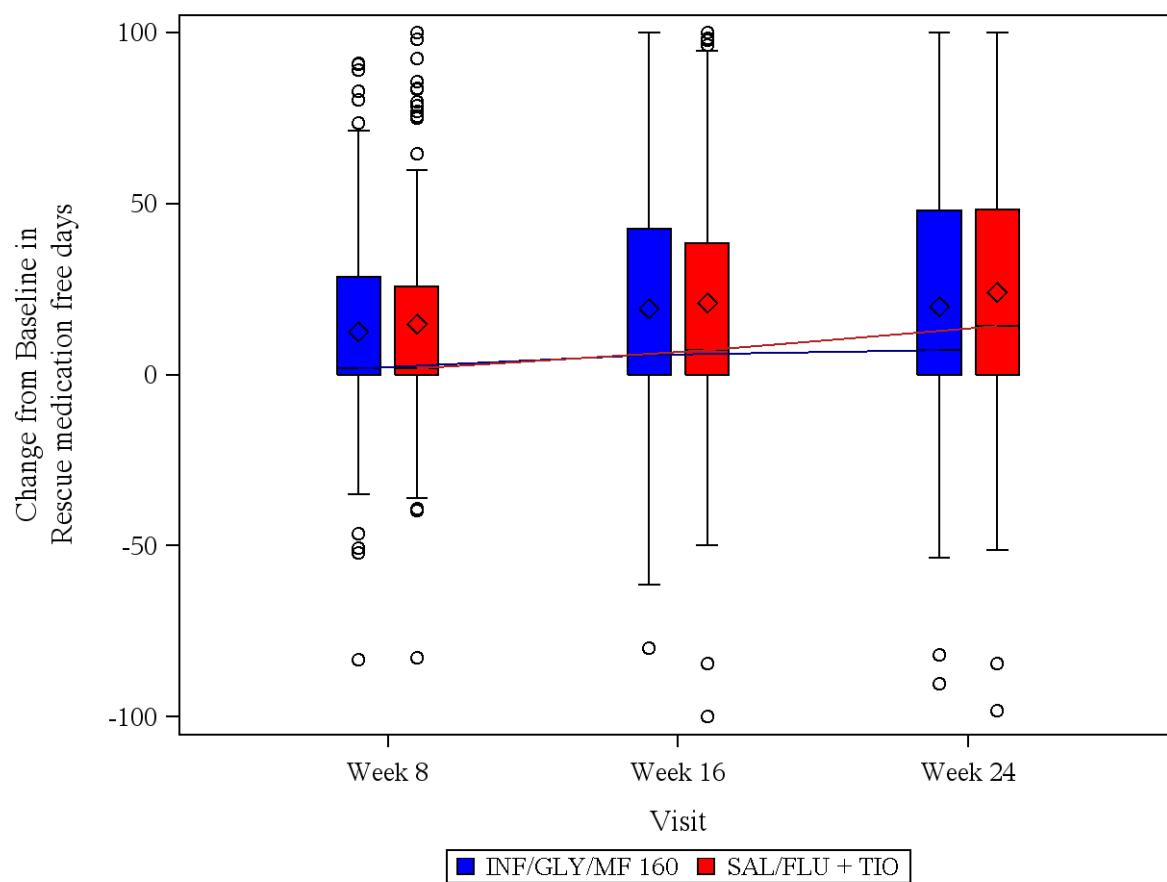


Figure 5.15.2 Rescue Medication (Rescue medication free days) - Change from Baseline by Gender (FAS), Gender = Female



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

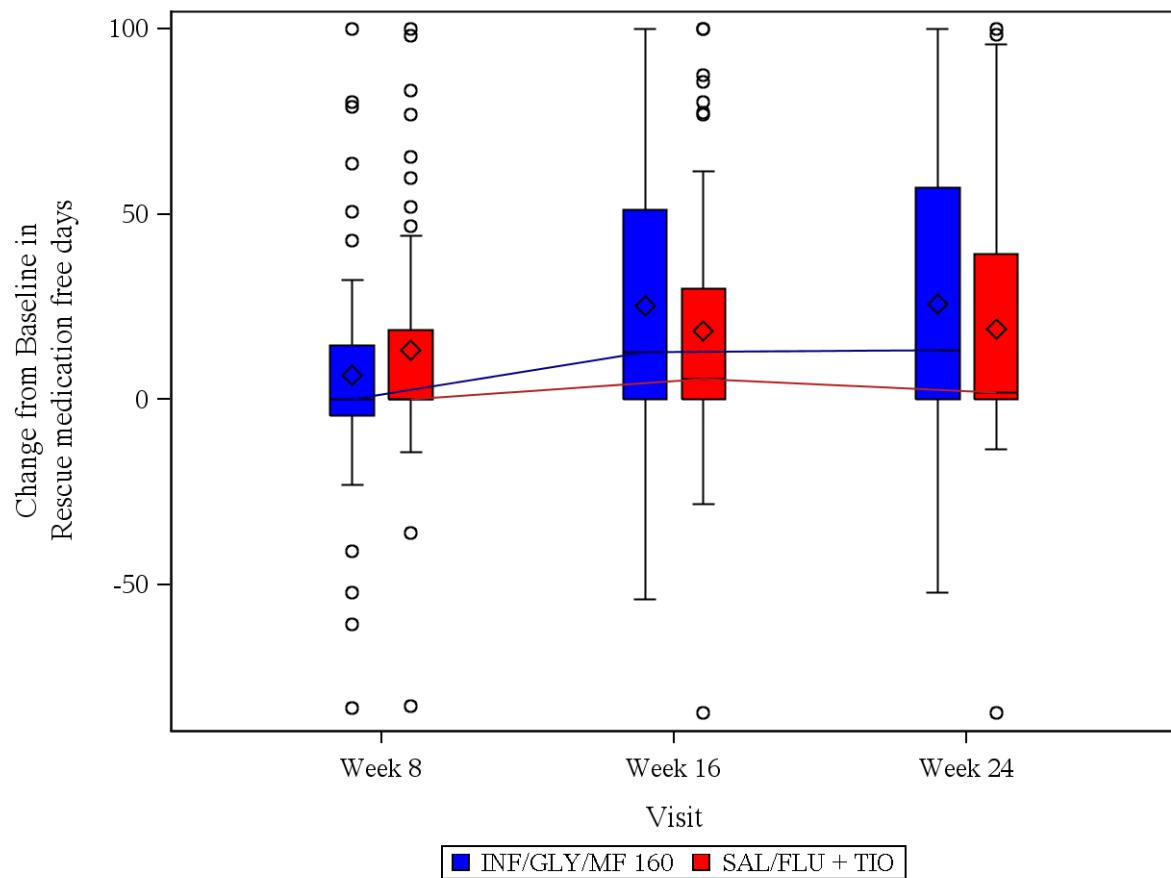


Figure 5.16.2 Rescue Medication (Rescue medication free days) - Change from Baseline by Region (FAS), Region = Europe

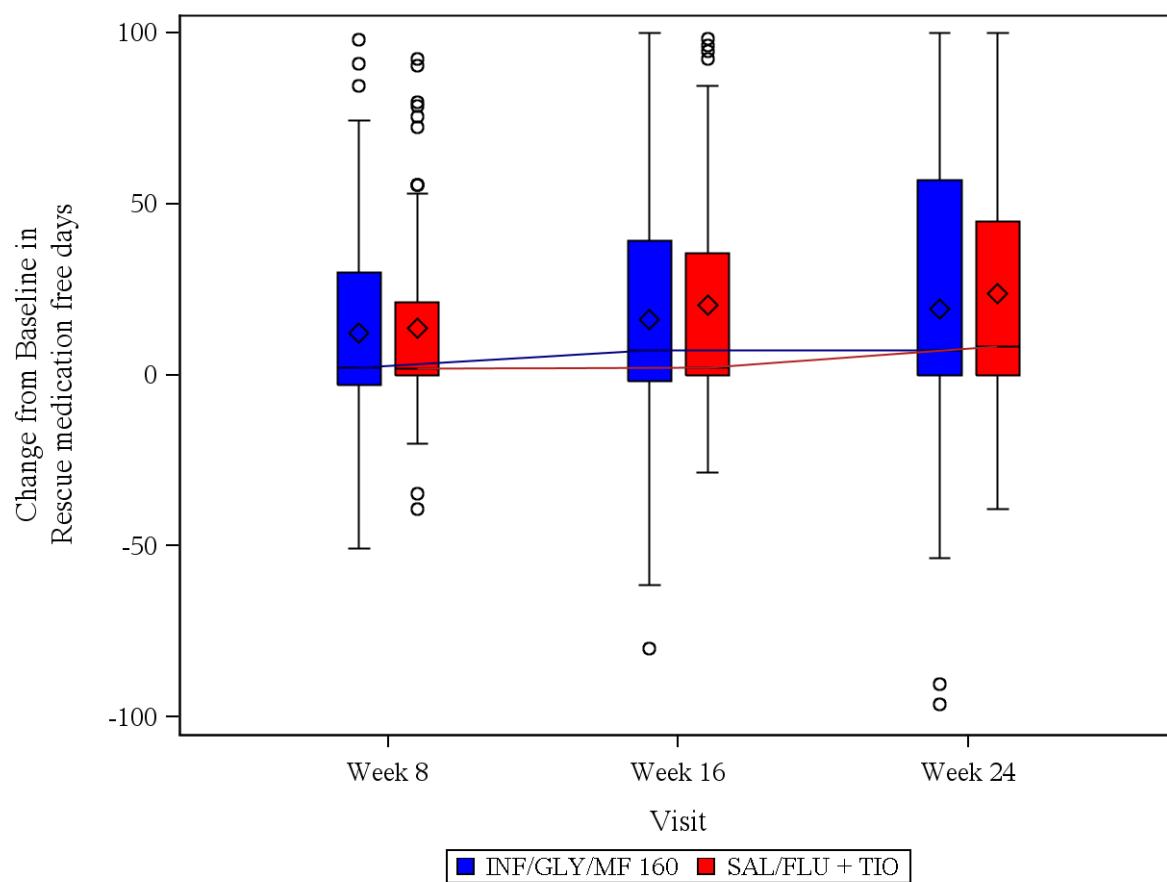


Figure 5.16.3 Rescue Medication (Rescue medication free days) - Change from Baseline by Region (FAS), Region = Latin America

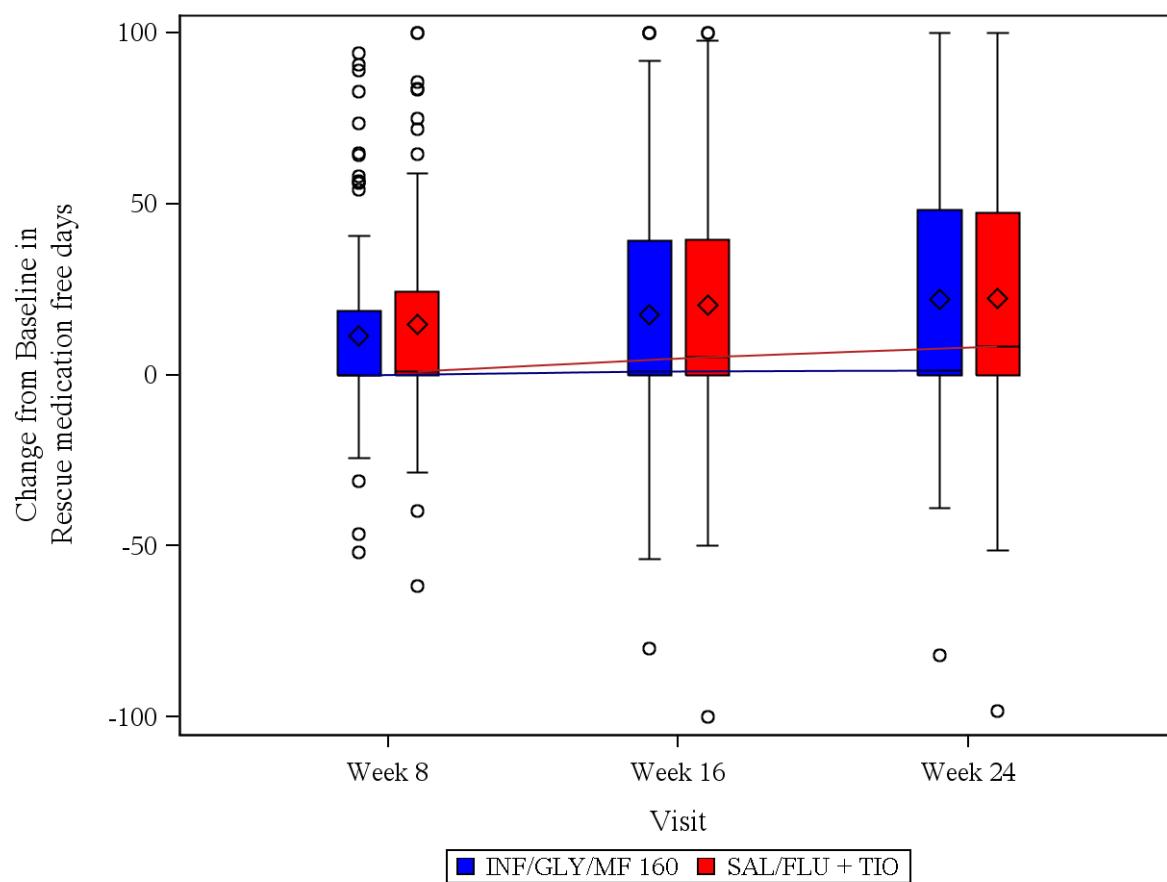
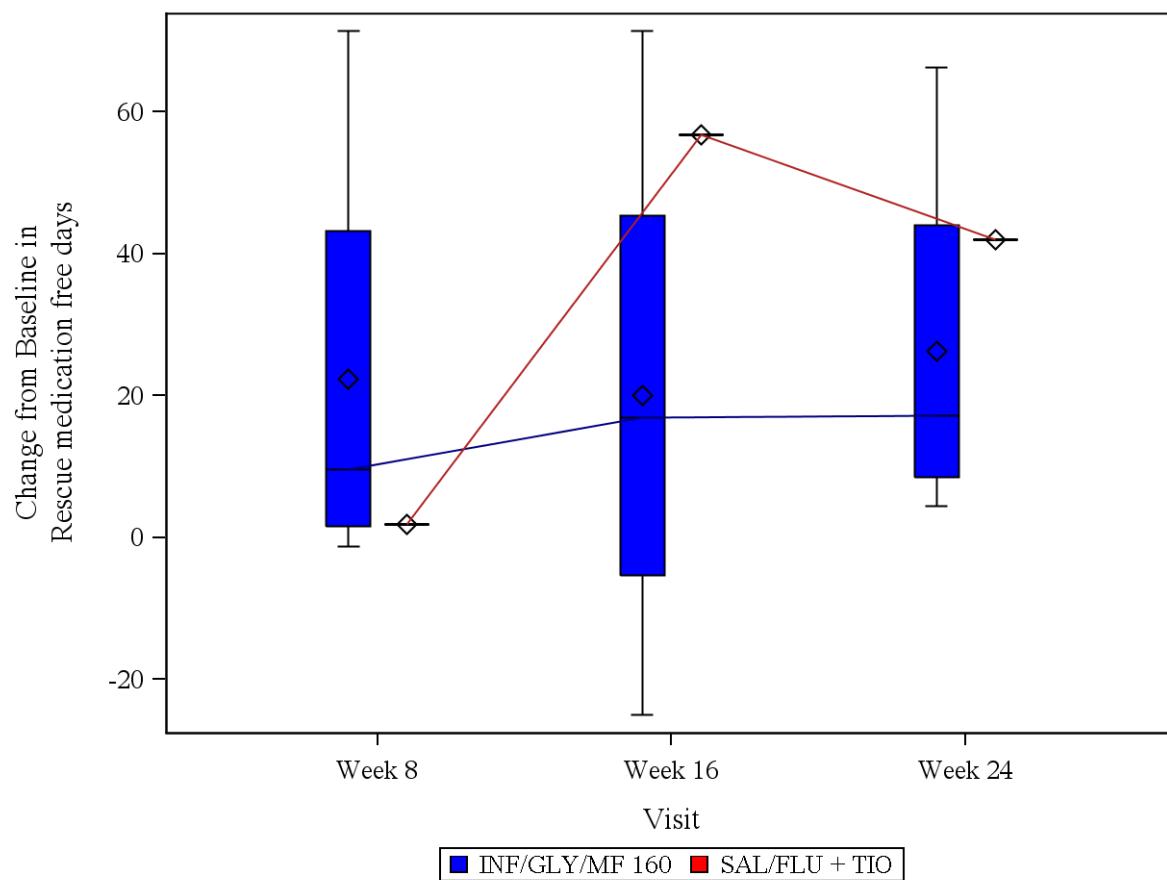


Figure 5.16.4 Rescue Medication (Rescue medication free days) - Change from Baseline by Region (FAS), Region = Others



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

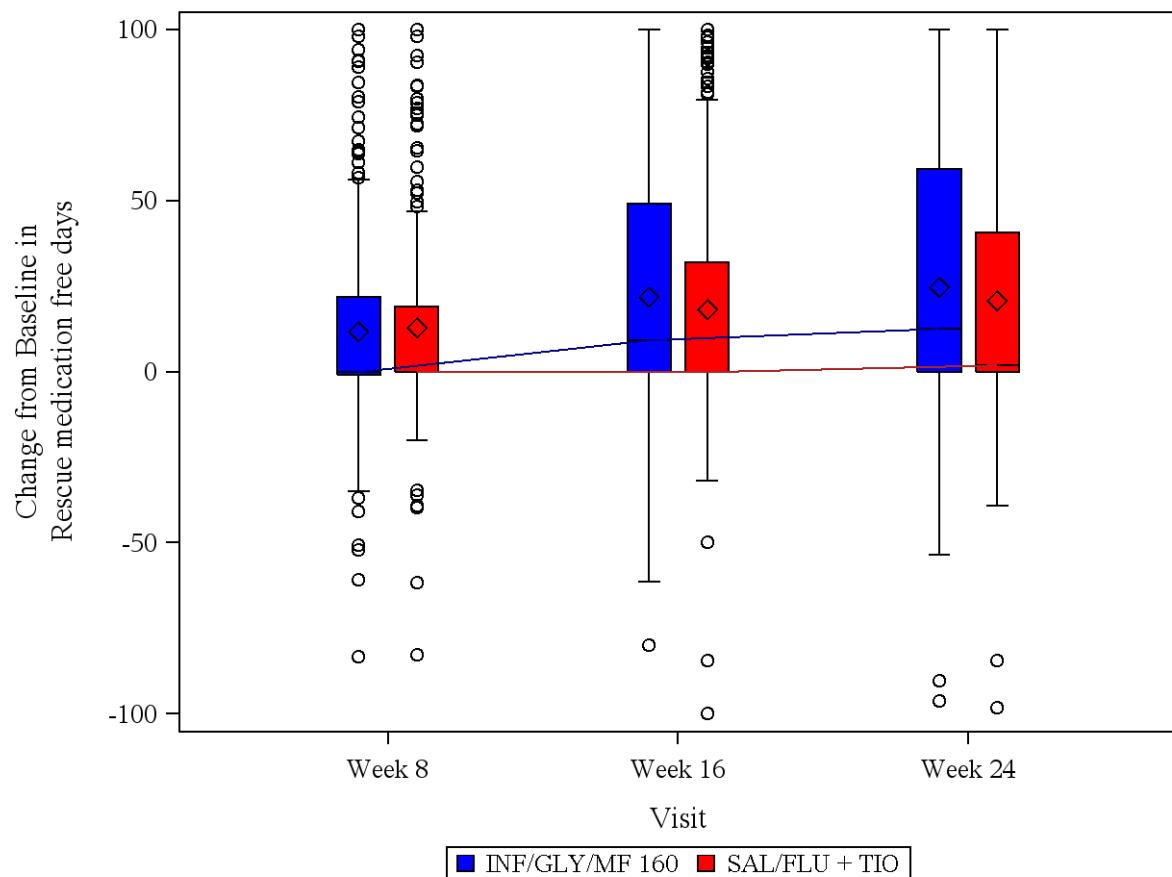
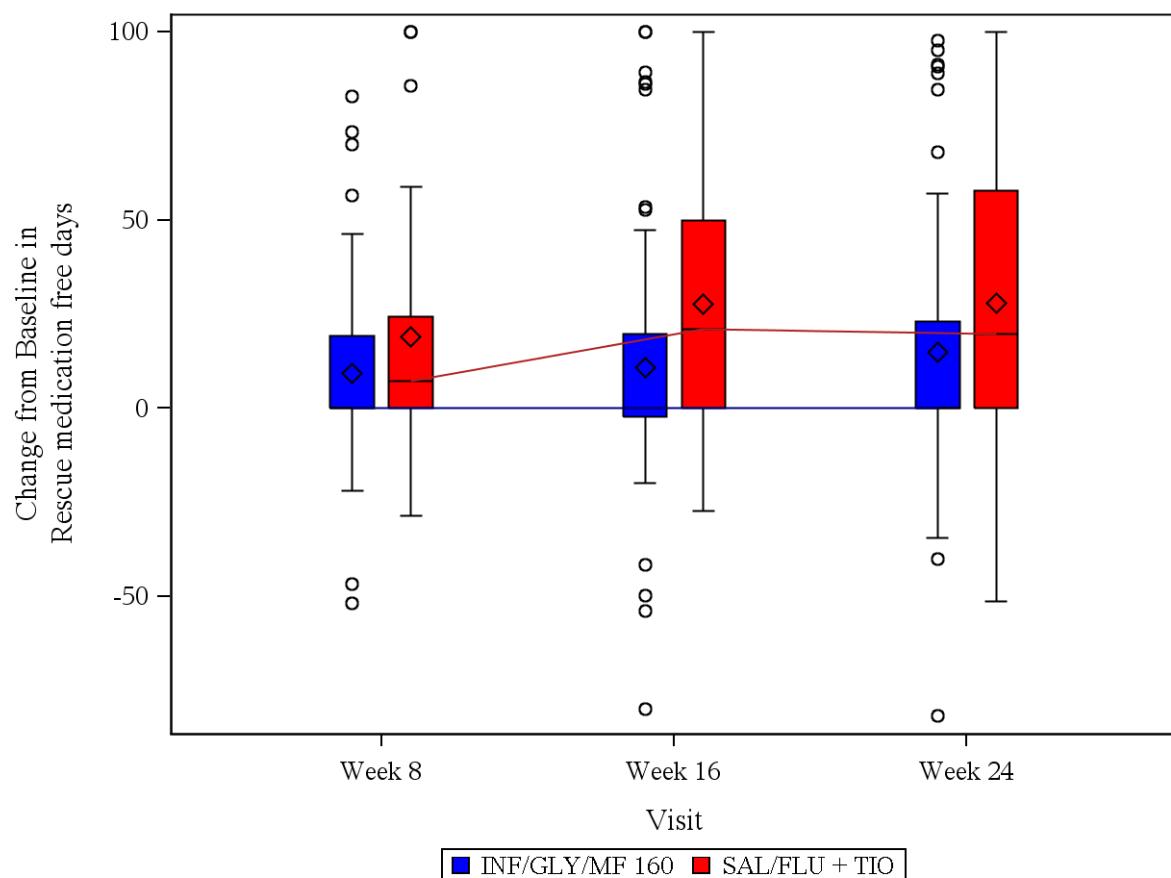


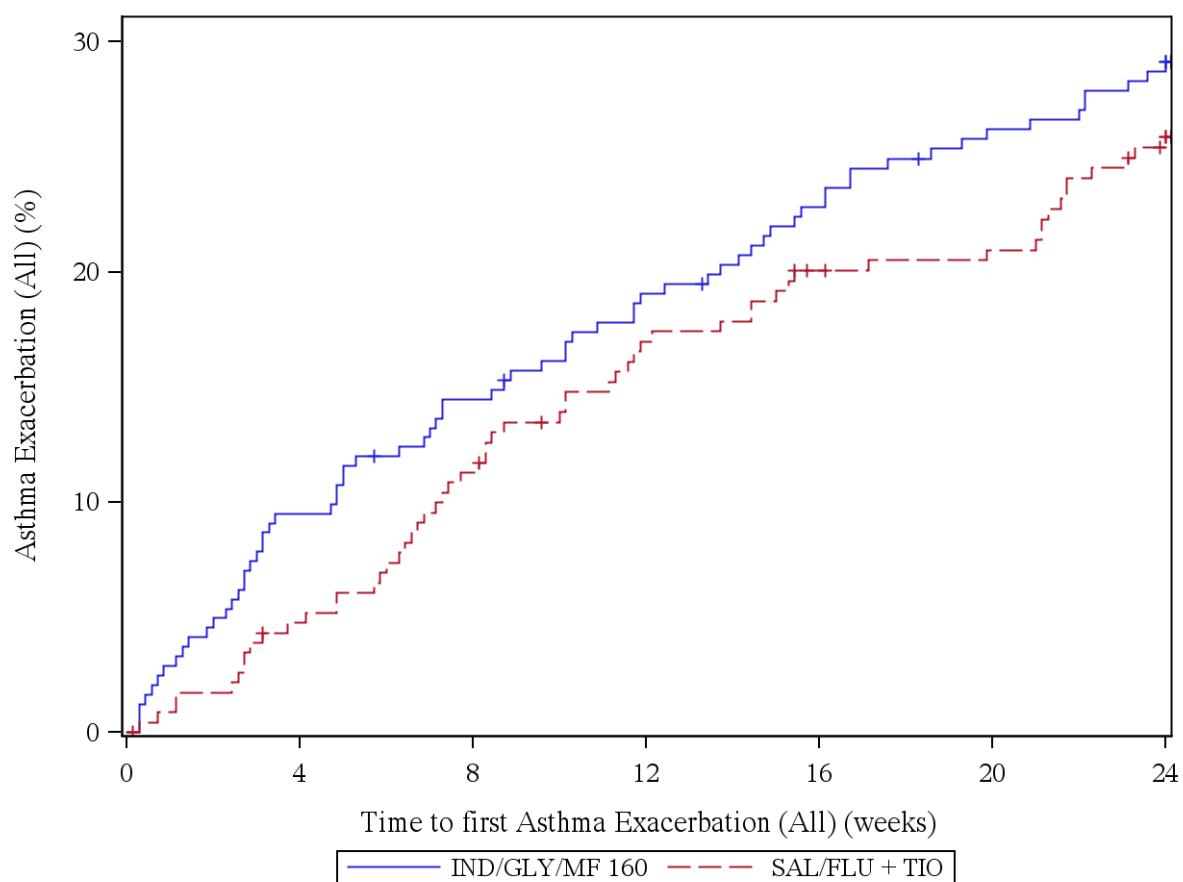
Figure 5.17.2 Rescue Medication (Rescue medication free days) - Change from Baseline by History of Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2



11. Kaplan-Meier-Plot: Asthma exacerbations (FAS)

11.1 Kaplan-Meier-Plot: Asthma Exacerbation (All) (FAS)

Figure 11.1 Asthma Exacerbation (All) (FAS)

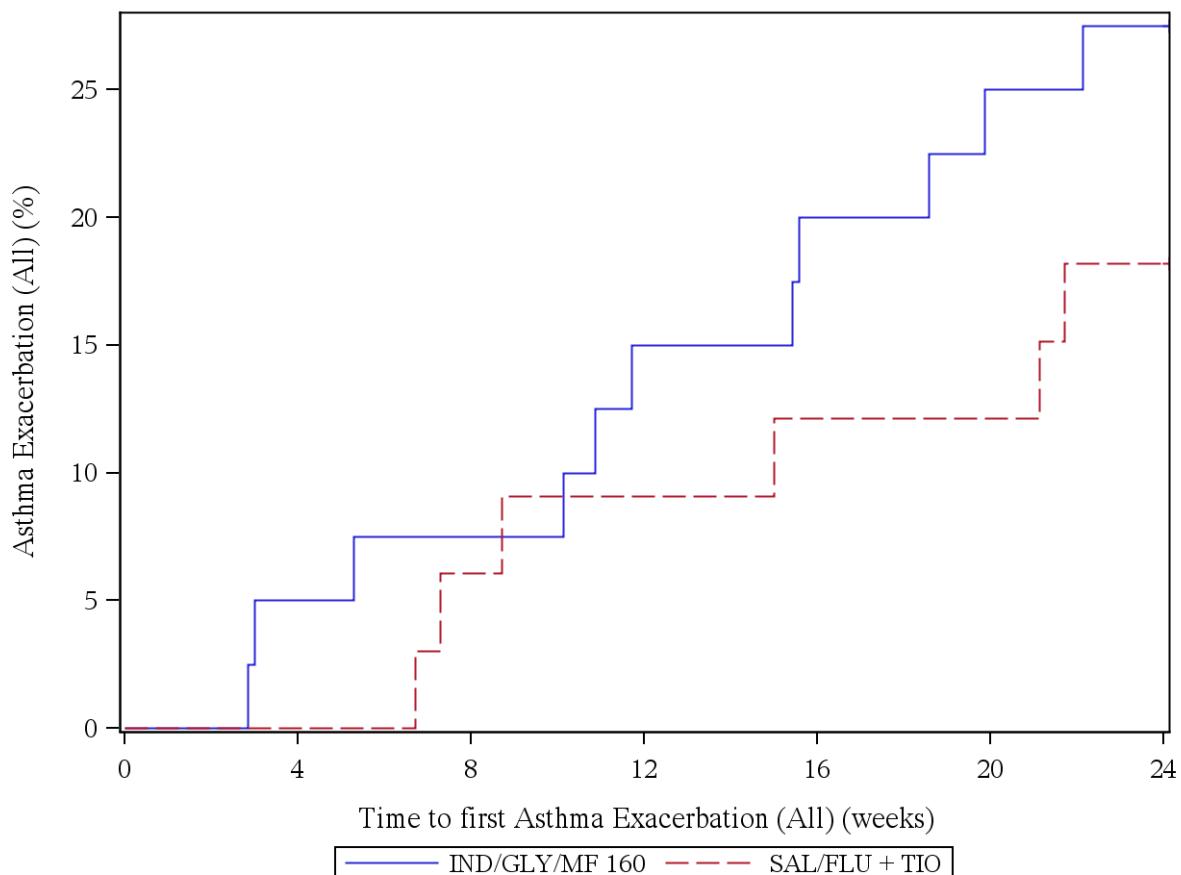


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 242/232, Week 8: 206/204, Week 16: 184/180, Week 24: 166/162

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.2 Kaplan-Meier-Plot: Asthma Exacerbation (All) by Age (FAS)

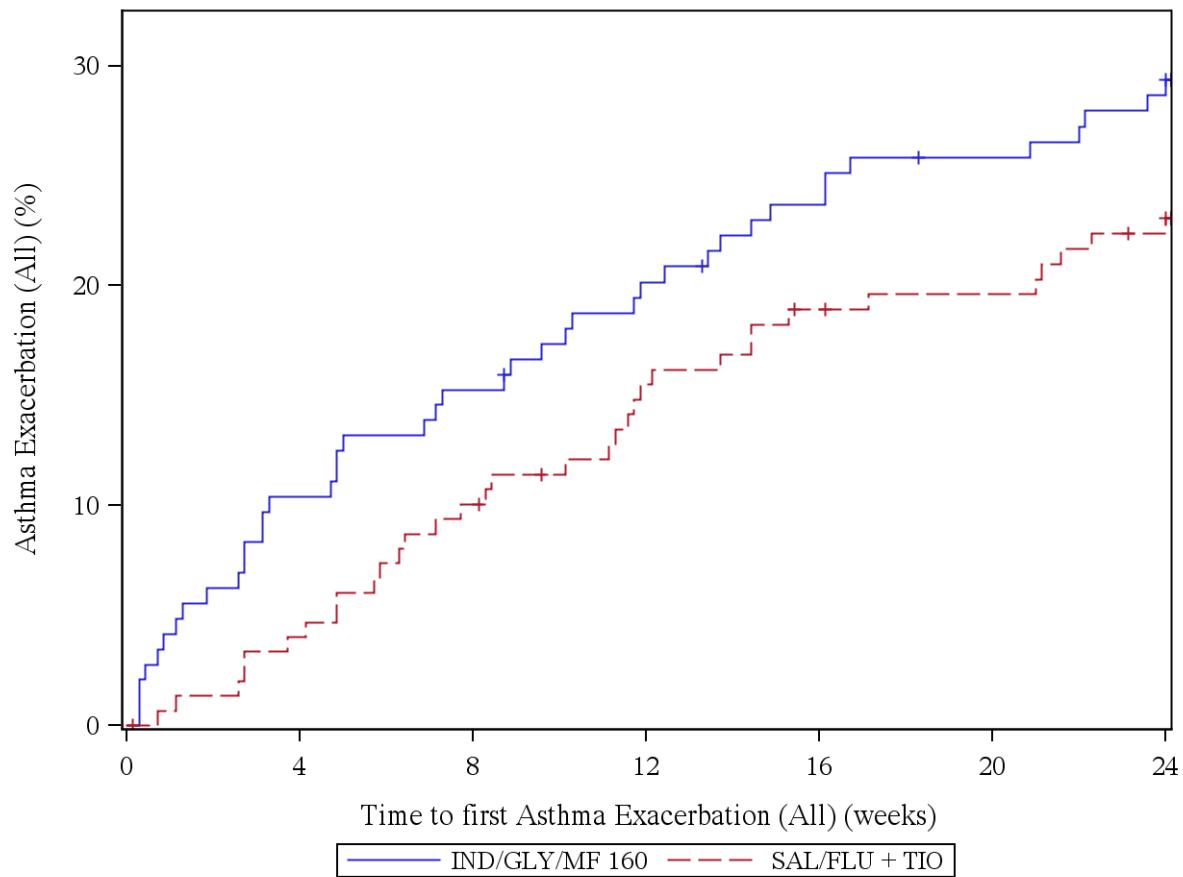
Figure 11.2.1 Asthma Exacerbation (All) (FAS), Age = 18-39 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 40/33, Week 8: 37/31, Week 16: 32/29, Week 24: 29/27

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

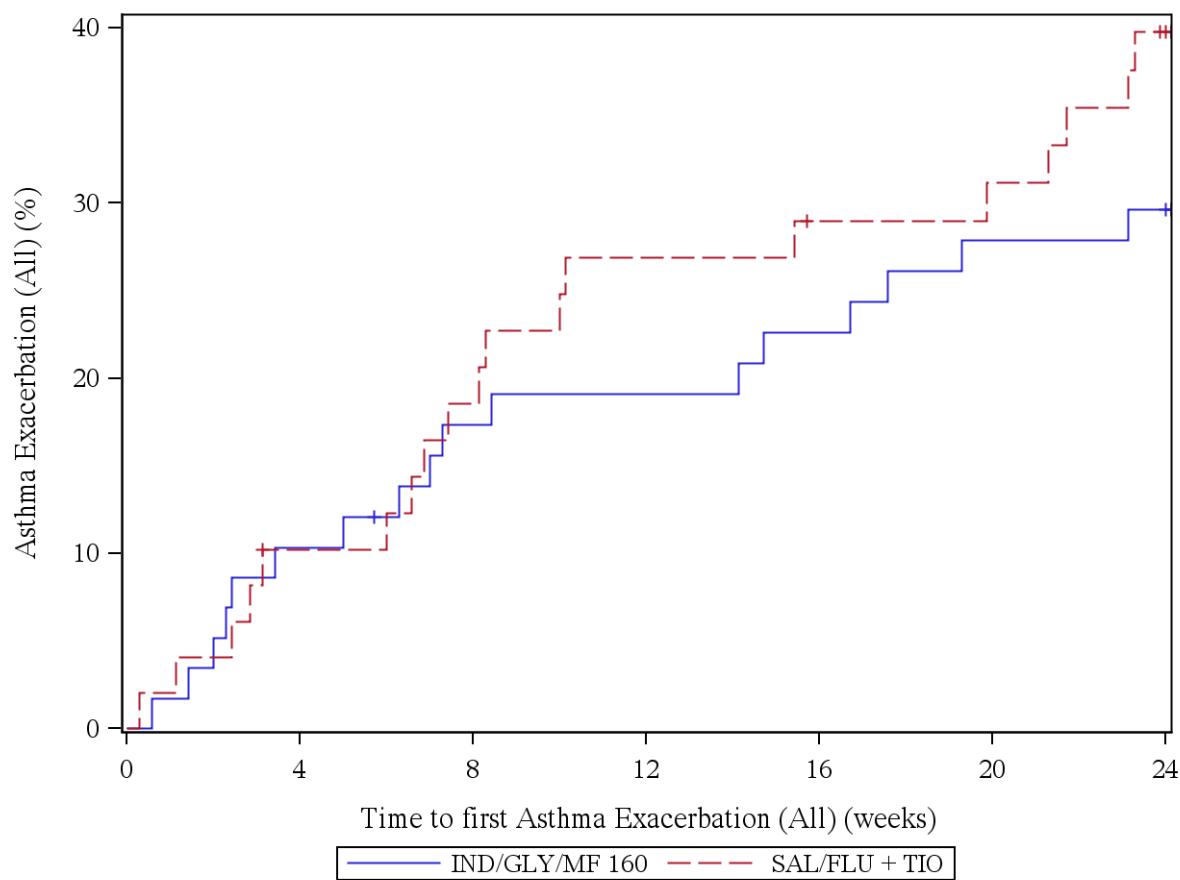
Figure 11.2.2 Asthma Exacerbation (All) (FAS), Age = 40-64 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 144/150, Week 8: 122/134, Week 16: 108/118, Week 24: 98/109

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.2.3 Asthma Exacerbation (All) (FAS), Age = ≥ 65 years

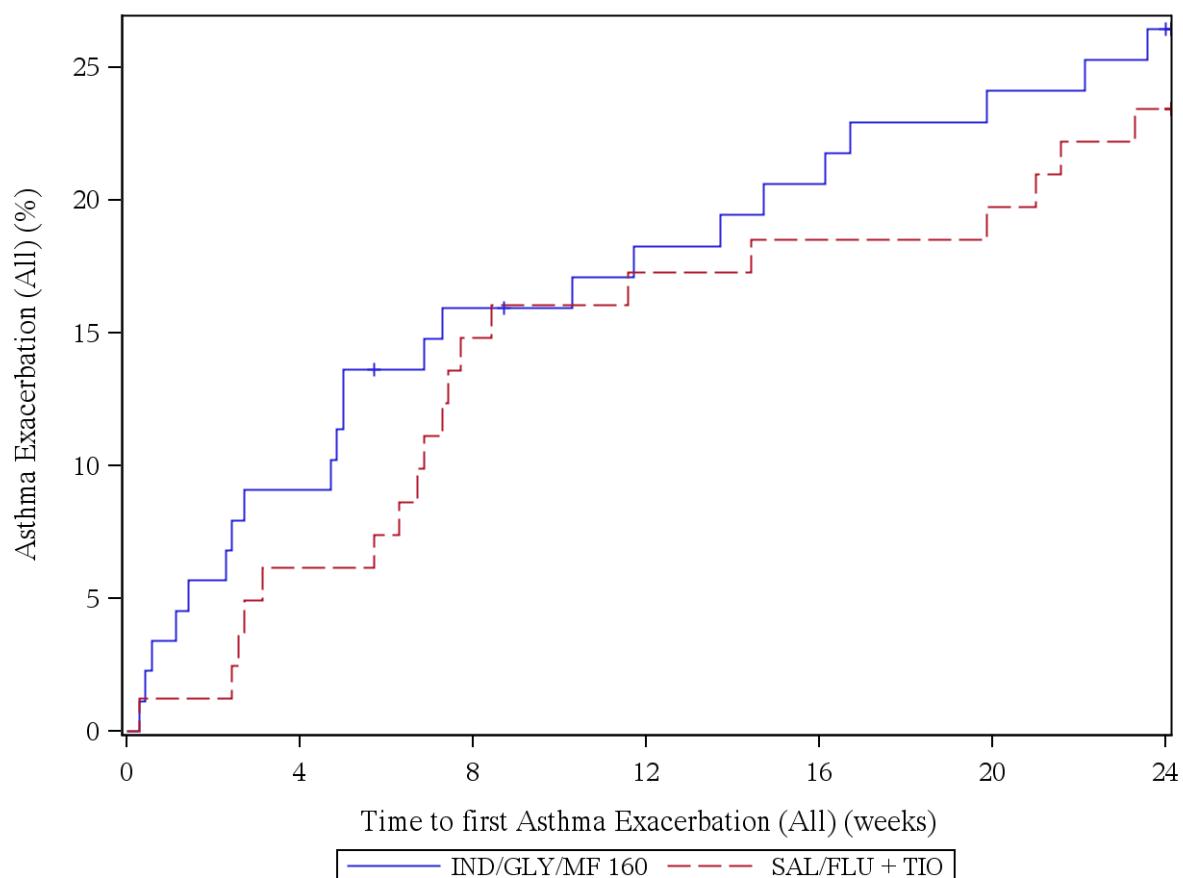


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 58/49, Week 8: 47/39, Week 16: 44/33, Week 24: 39/26

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.3 Kaplan-Meier-Plot: Asthma Exacerbation (All) by Gender (FAS)

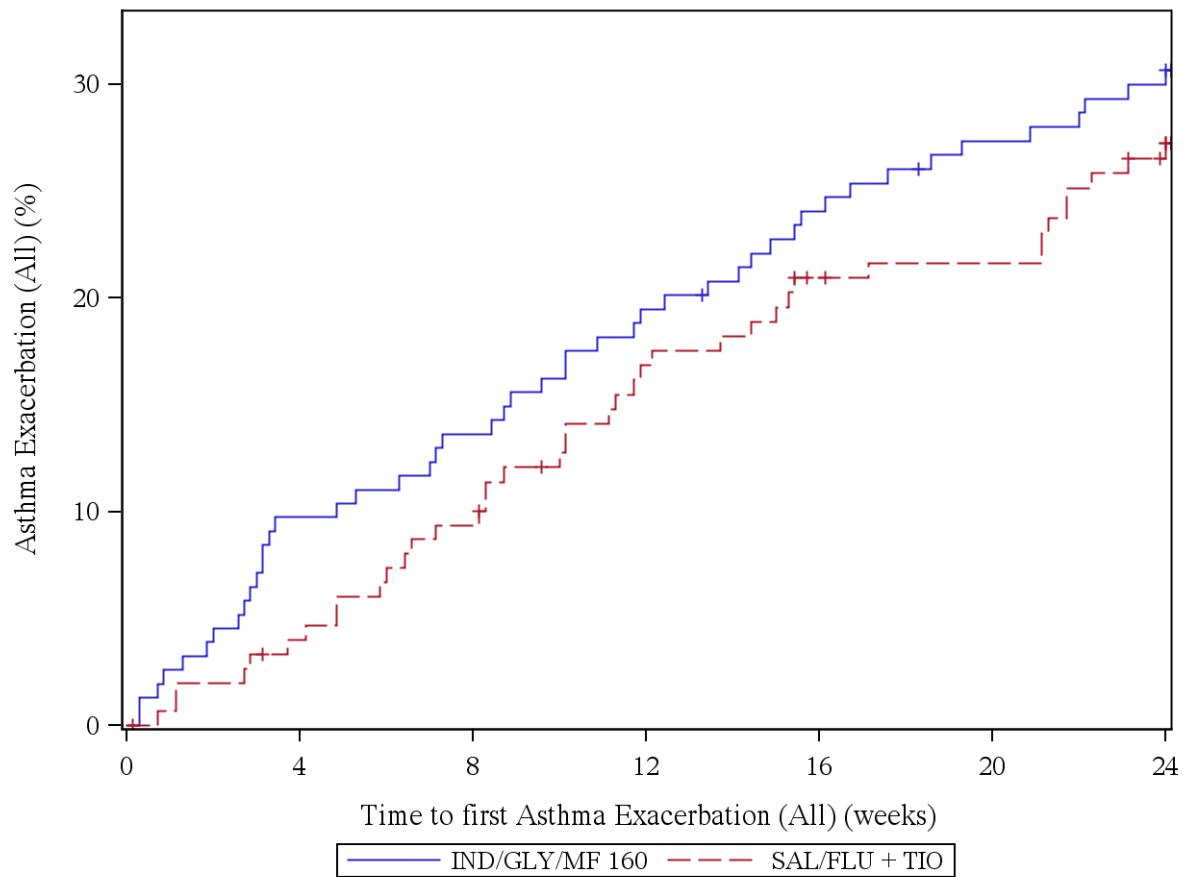
Figure 11.3.1 Asthma Exacerbation (All) (FAS), Gender = Male



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 88/81, Week 8: 73/69, Week 16: 68/66, Week 24: 62/62

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.3.2 Asthma Exacerbation (All) (FAS), Gender = Female

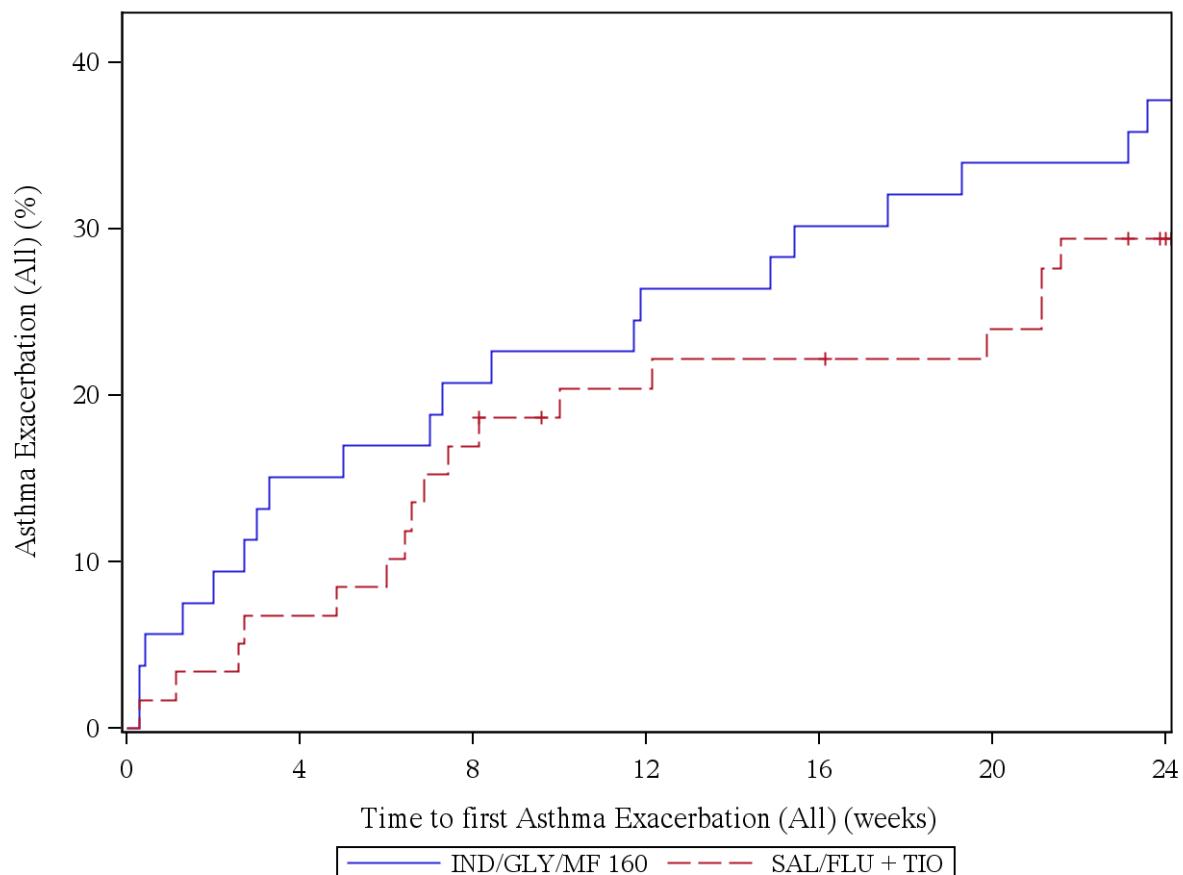


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 154/151, Week 8: 133/135, Week 16: 116/114, Week 24: 104/100

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.4 Kaplan-Meier-Plot: Asthma Exacerbation (All) by Region (FAS)

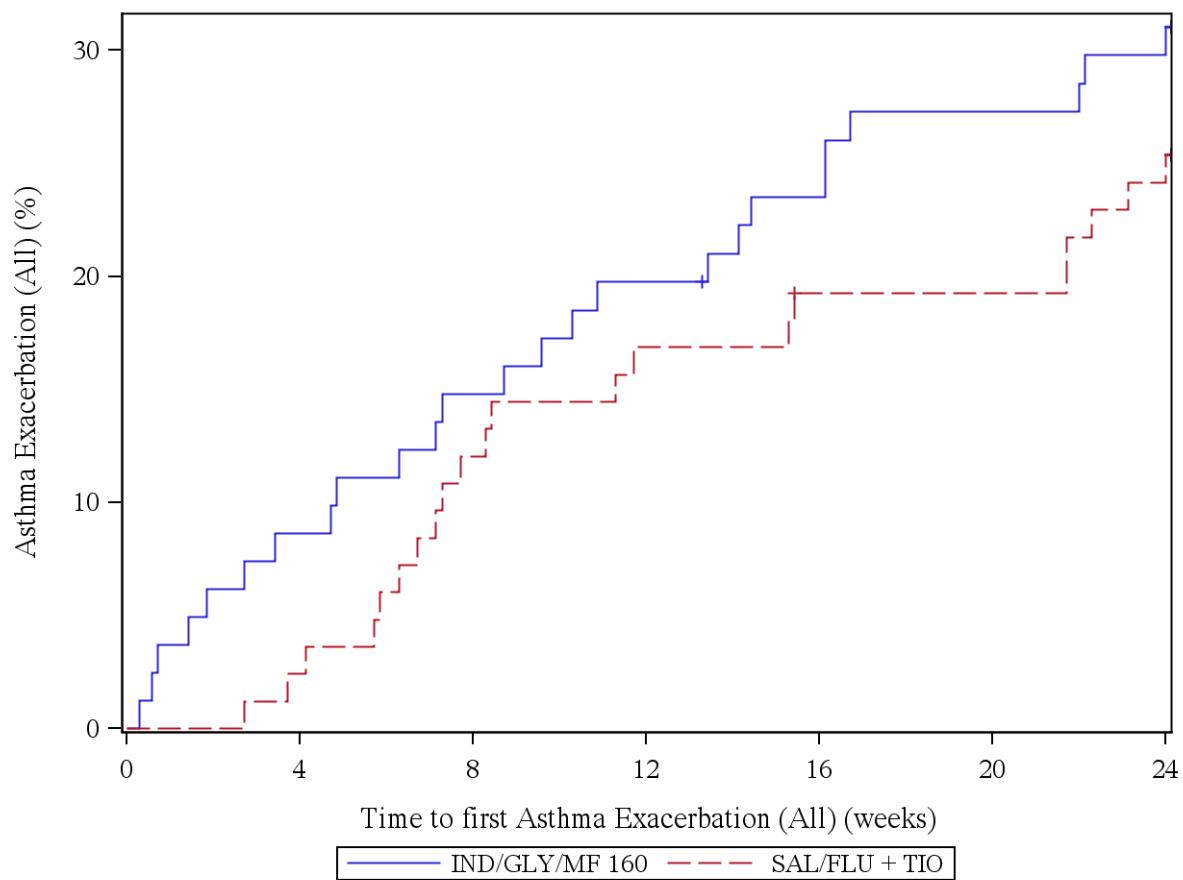
Figure 11.4.1 Asthma Exacerbation (All) (FAS), Region = Asia



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 53/59, Week 8: 42/49, Week 16: 37/44, Week 24: 33/36

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

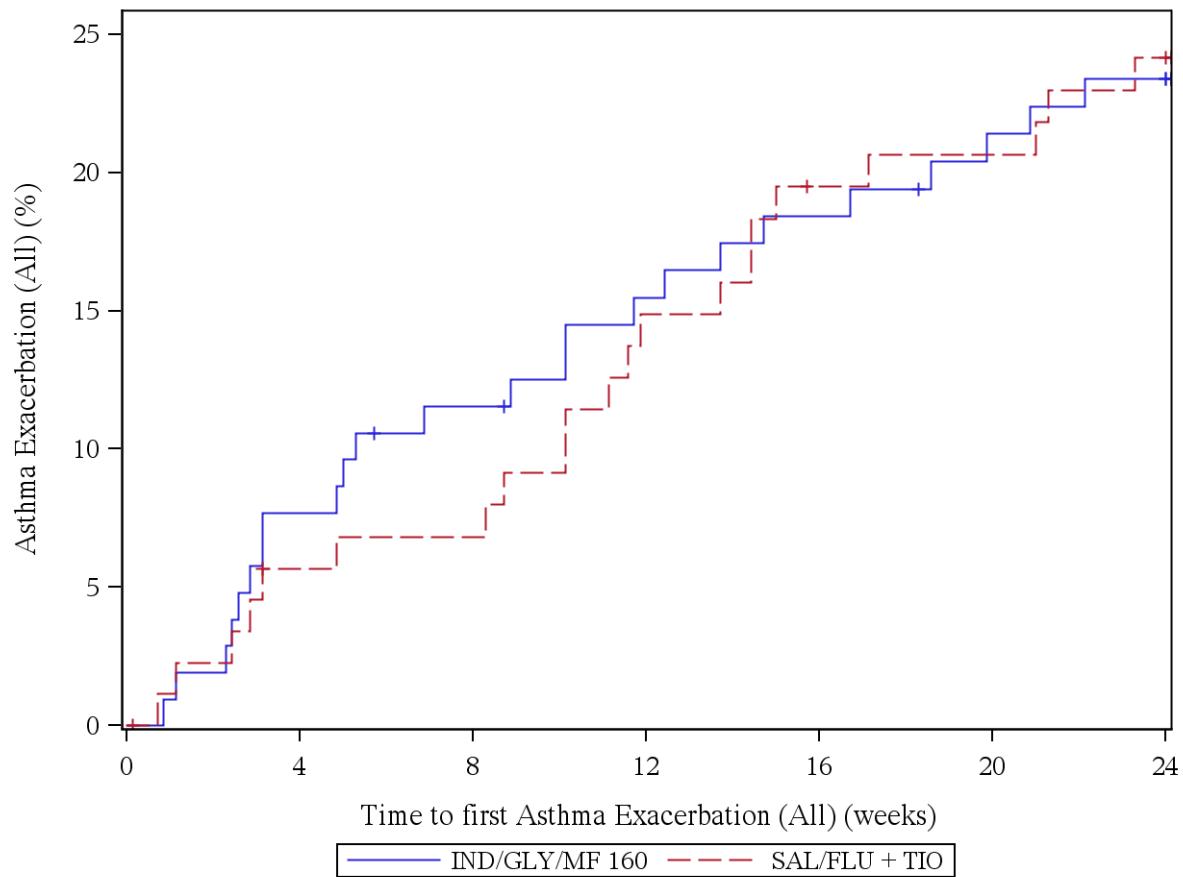
Figure 11.4.2 Asthma Exacerbation (All) (FAS), Region = Europe



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 81/83, Week 8: 69/73, Week 16: 61/66, Week 24: 55/61

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

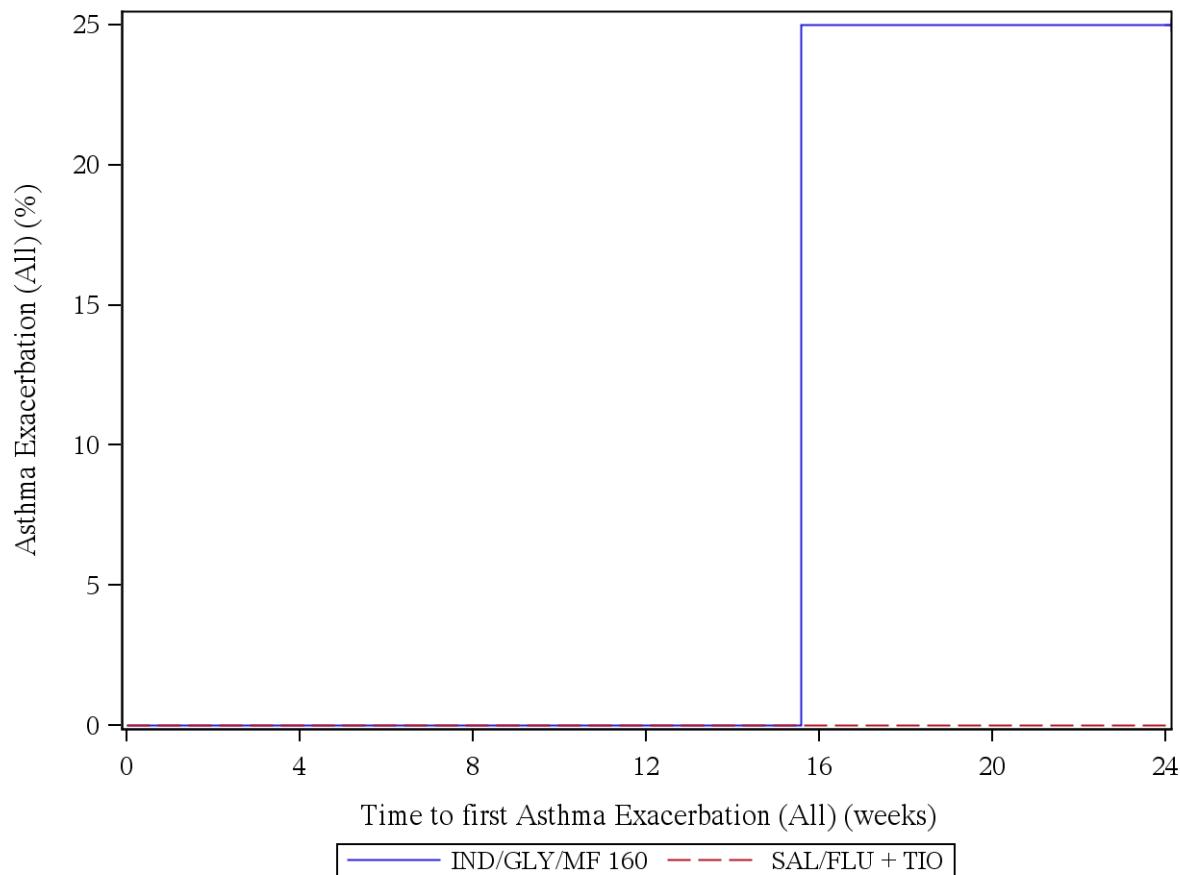
Figure 11.4.3 Asthma Exacerbation (All) (FAS), Region = Latin America



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 104/89, Week 8: 91/81, Week 16: 83/69, Week 24: 75/64

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.4.4 Asthma Exacerbation (All) (FAS), Region = Others

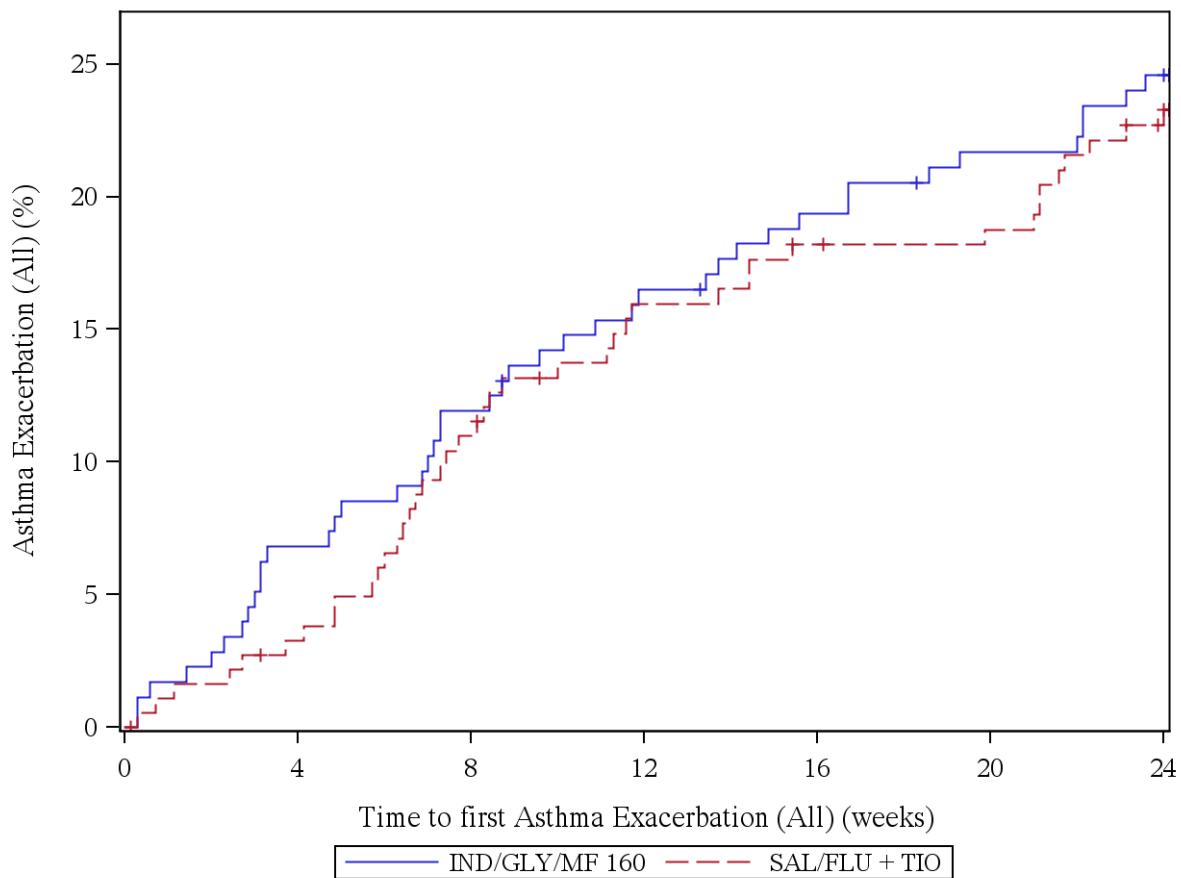


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 4/1, Week 8: 4/1, Week 16: 3/1, Week 24: 3/1

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.5 Kaplan-Meier-Plot: Asthma Exacerbation (All) by History of Asthma Exacerbation (FAS)

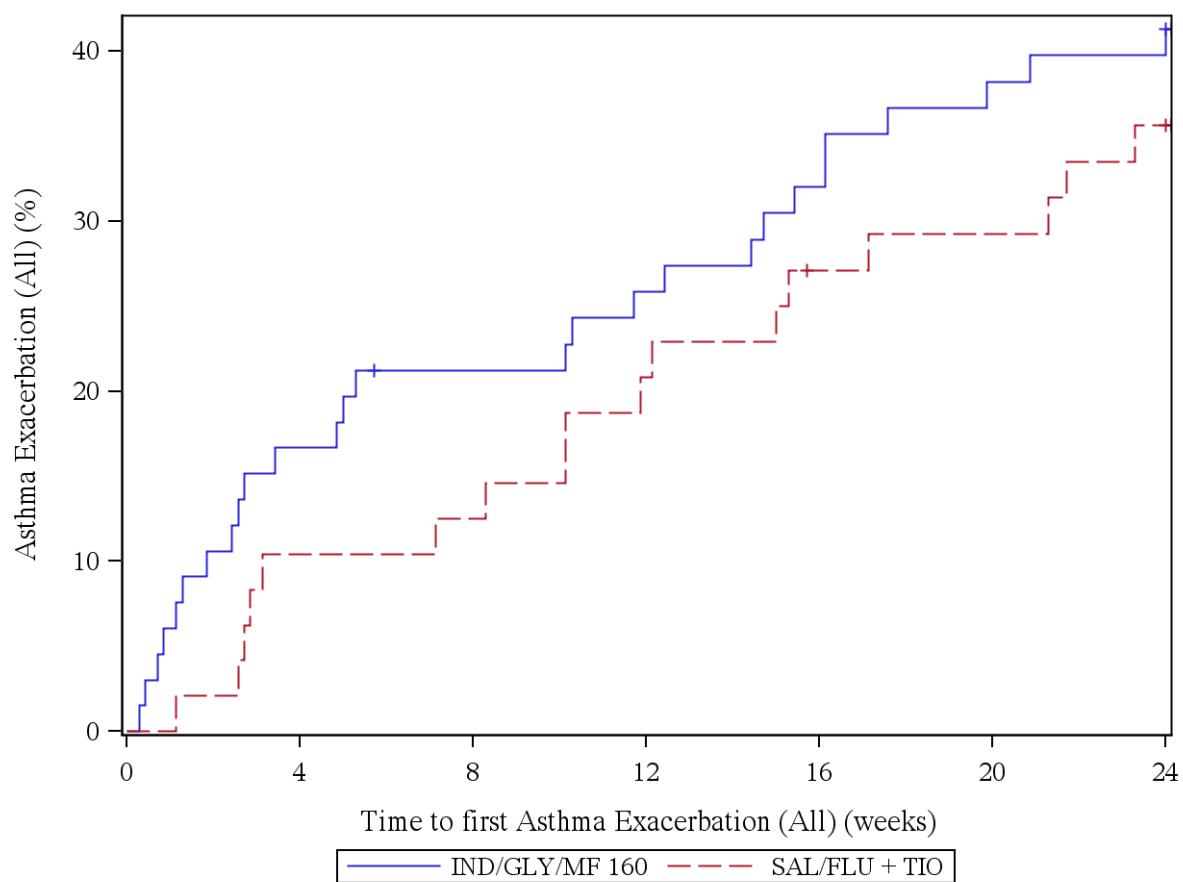
Figure 11.5.1 Asthma Exacerbation (All) (FAS), Asthma exacerbations in the 12 months prior to screening = 1



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 176/184, Week 8: 155/162, Week 16: 140/146, Week 24: 129/133

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.5.2 Asthma Exacerbation (All) (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2

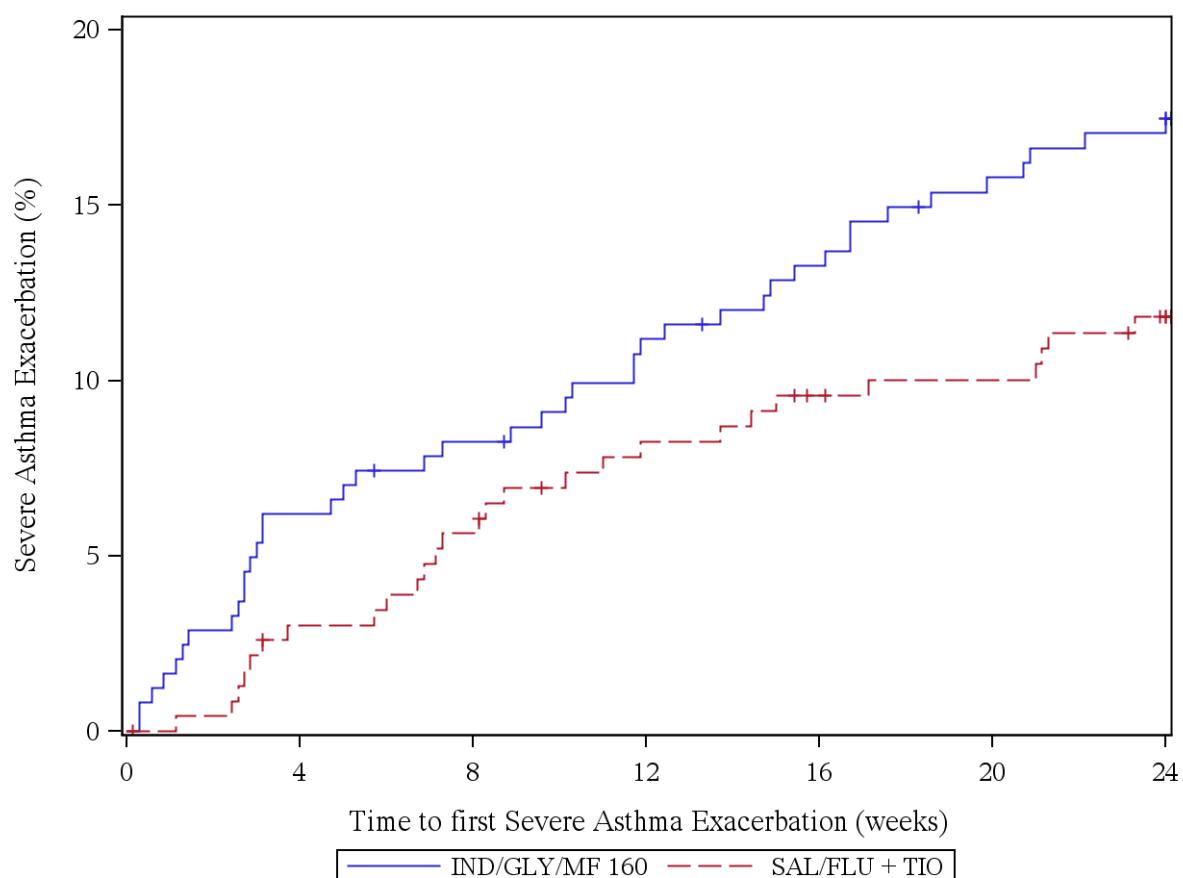


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 66/48, Week 8: 51/42, Week 16: 44/34, Week 24: 37/29

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.7 Kaplan-Meier-Plot: Severe Asthma Exacerbation (FAS)

Figure 11.7 Severe Asthma Exacerbation (FAS)

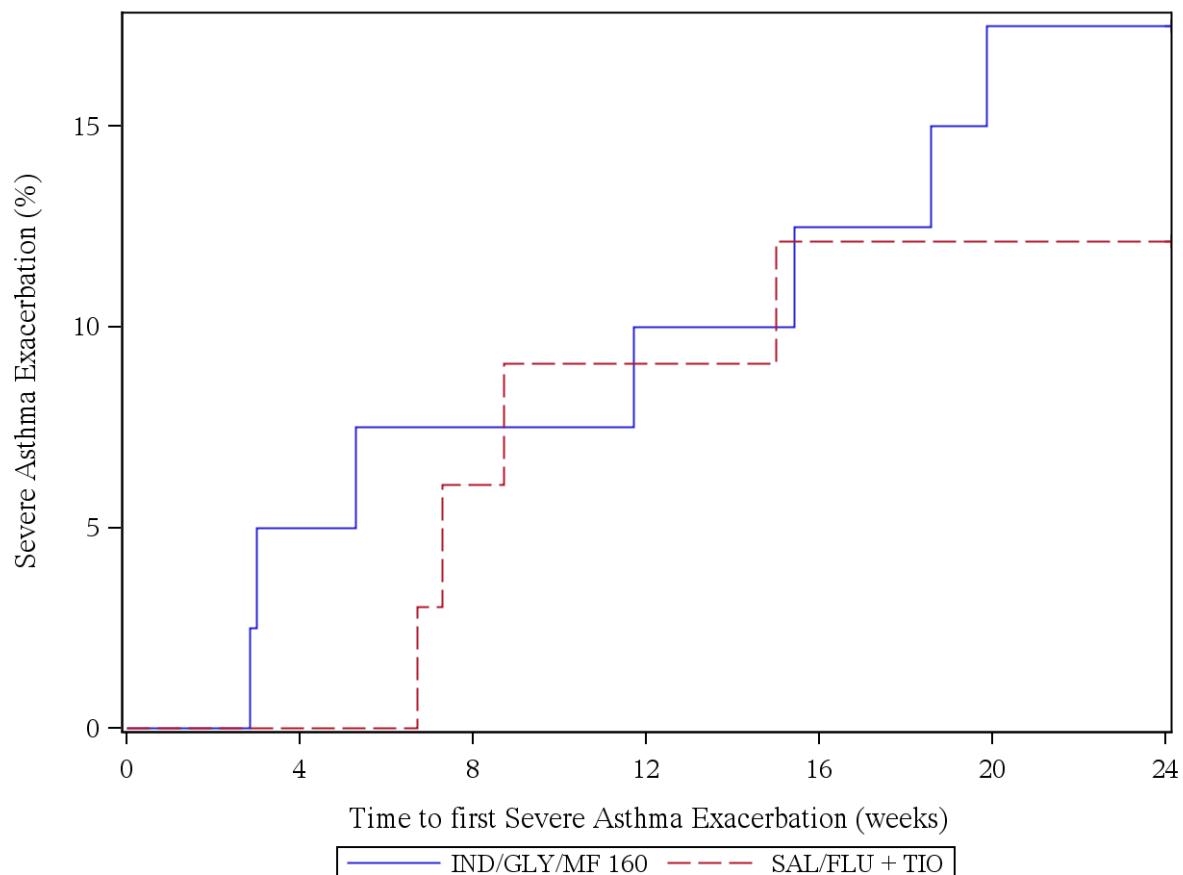


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 242/232, Week 8: 221/217, Week 16: 207/204, Week 24: 194/194

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.8 Kaplan-Meier-Plot: Severe Asthma Exacerbation by Age (FAS)

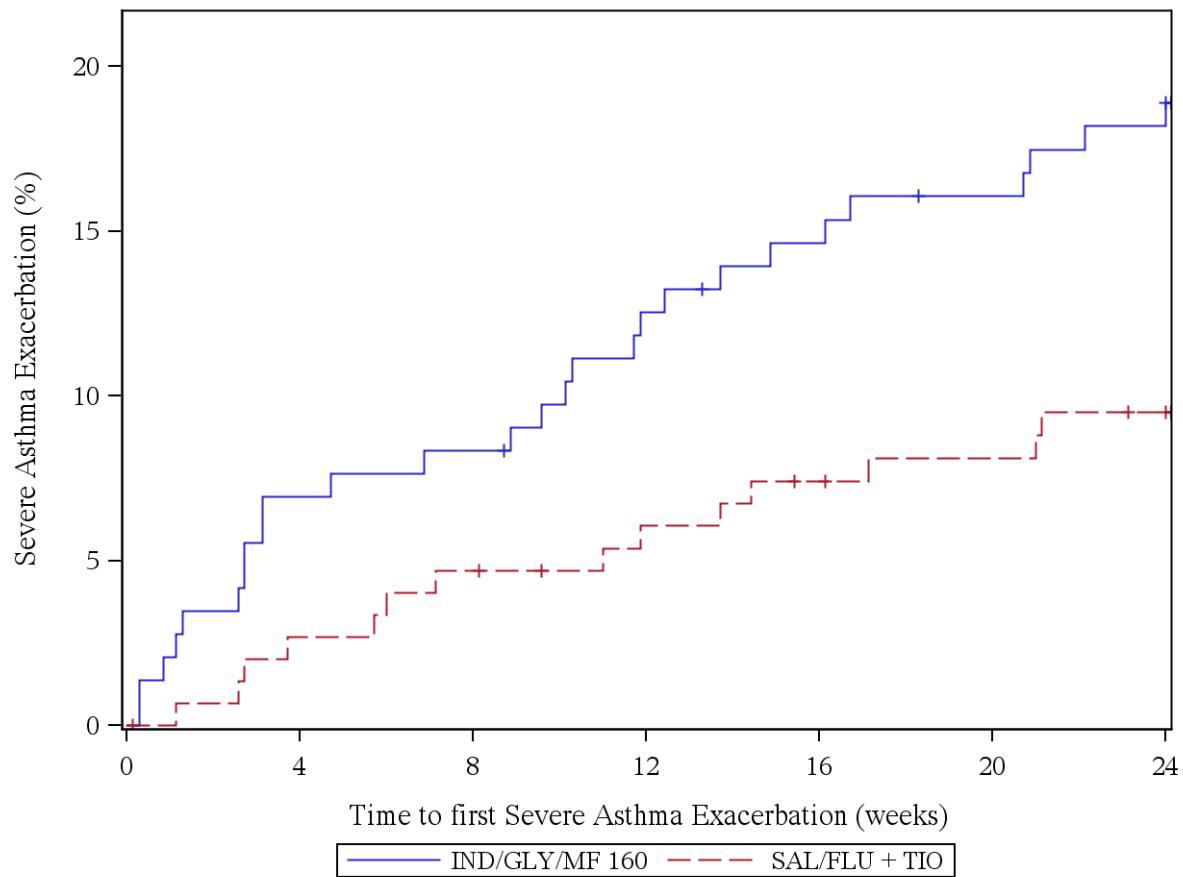
Figure 11.8.1 Severe Asthma Exacerbation (FAS), Age = 18-39 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 40/33, Week 8: 37/31, Week 16: 35/29, Week 24: 33/29

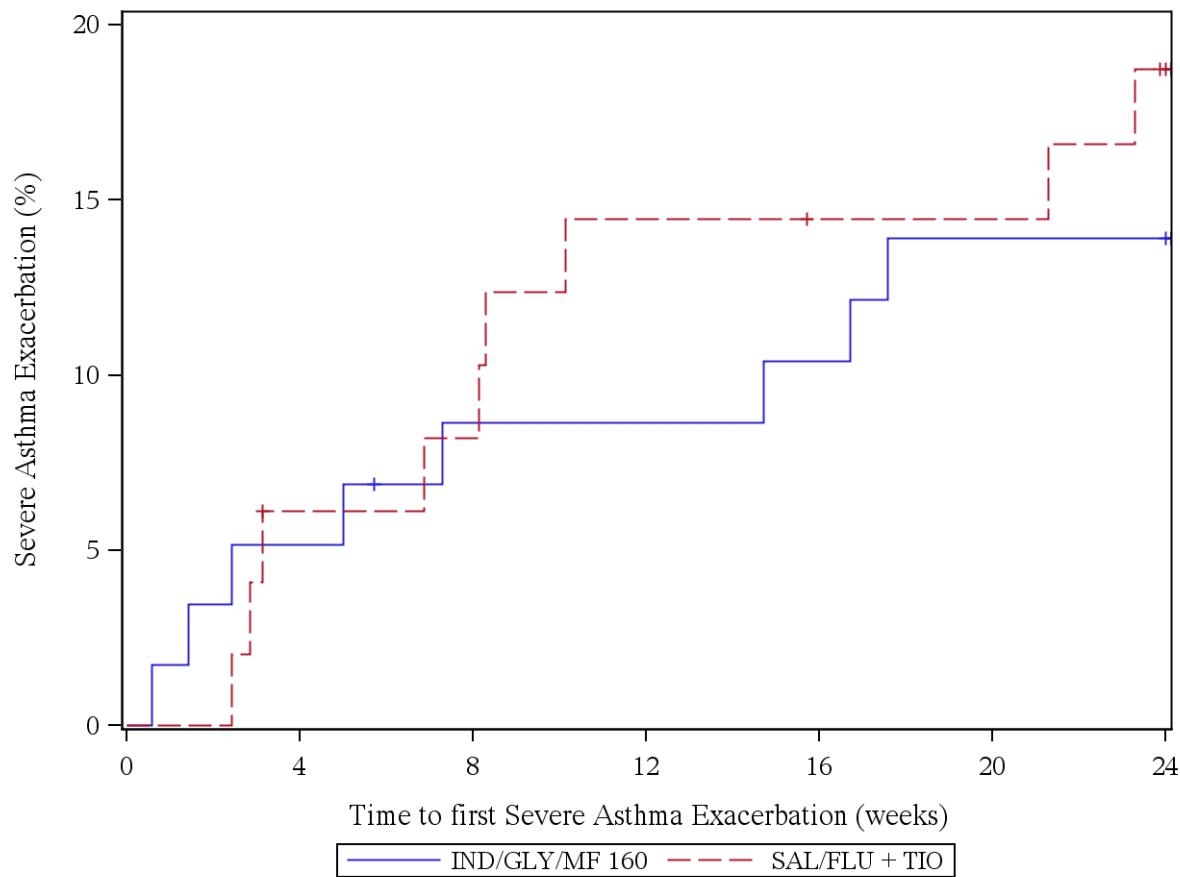
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.8.2 Severe Asthma Exacerbation (FAS), Age = 40-64 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 144/150, Week 8: 132/142, Week 16: 121/135, Week 24: 113/129
Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.8.3 Severe Asthma Exacerbation (FAS), Age = ≥ 65 years

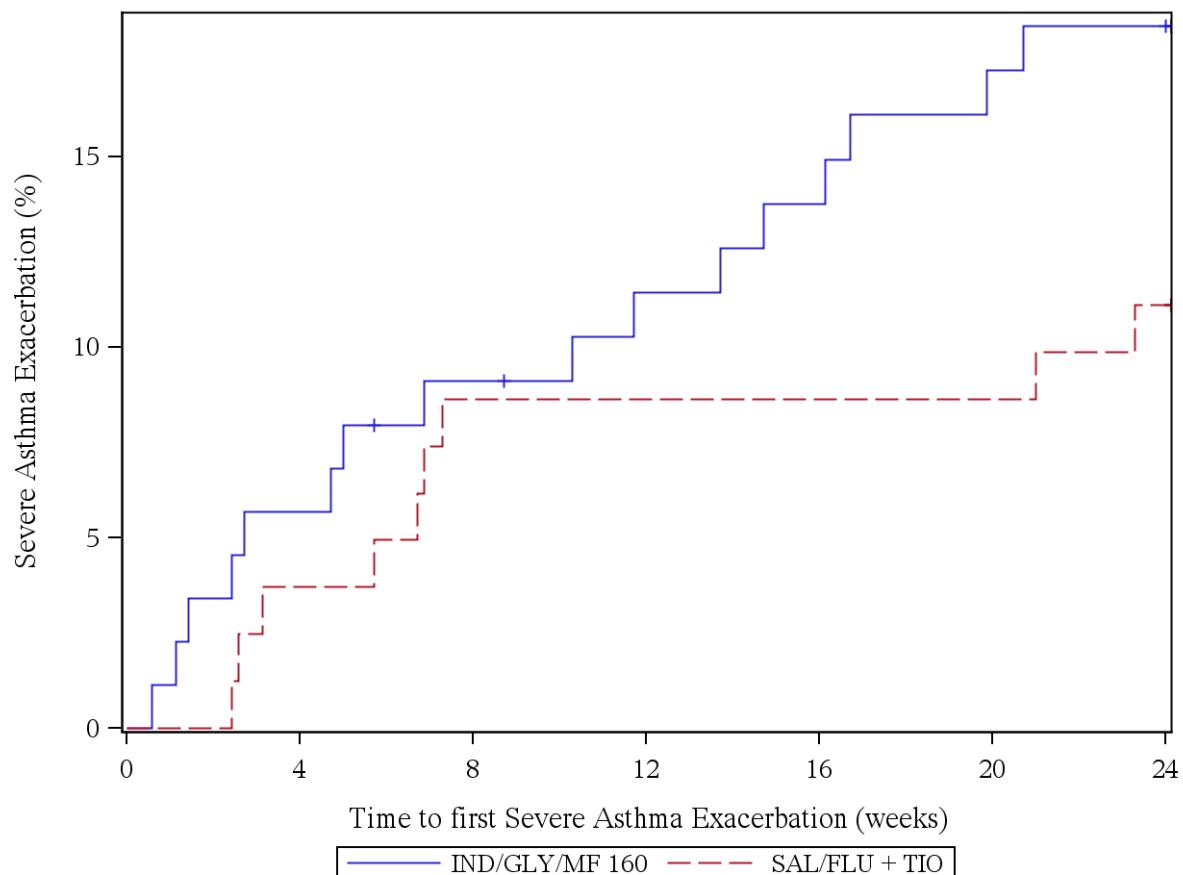


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 58/49, Week 8: 52/44, Week 16: 51/40, Week 24: 48/36

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.9 Kaplan-Meier-Plot: Severe Asthma Exacerbation by Gender (FAS)

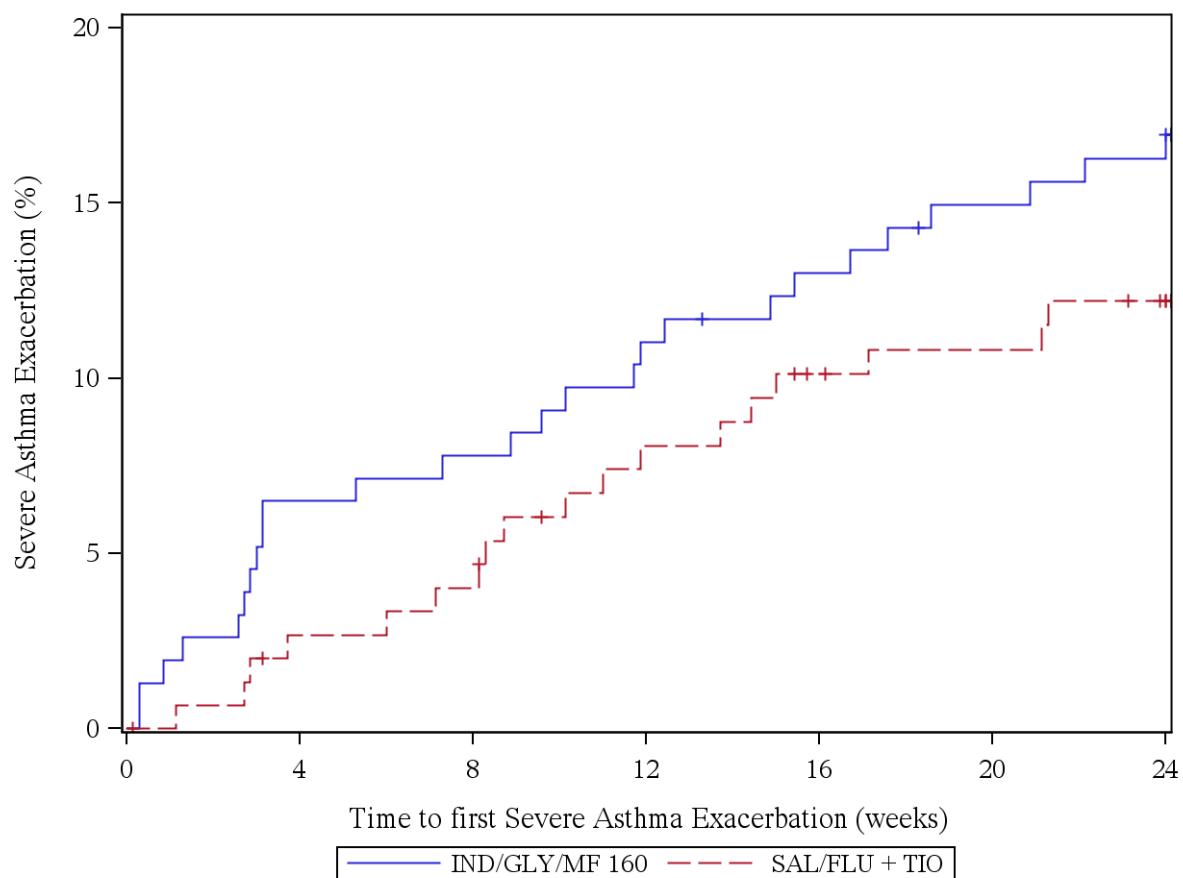
Figure 11.9.1 Severe Asthma Exacerbation (FAS), Gender = Male



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 88/81, Week 8: 79/74, Week 16: 74/74, Week 24: 69/72

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.9.2 Severe Asthma Exacerbation (FAS), Gender = Female

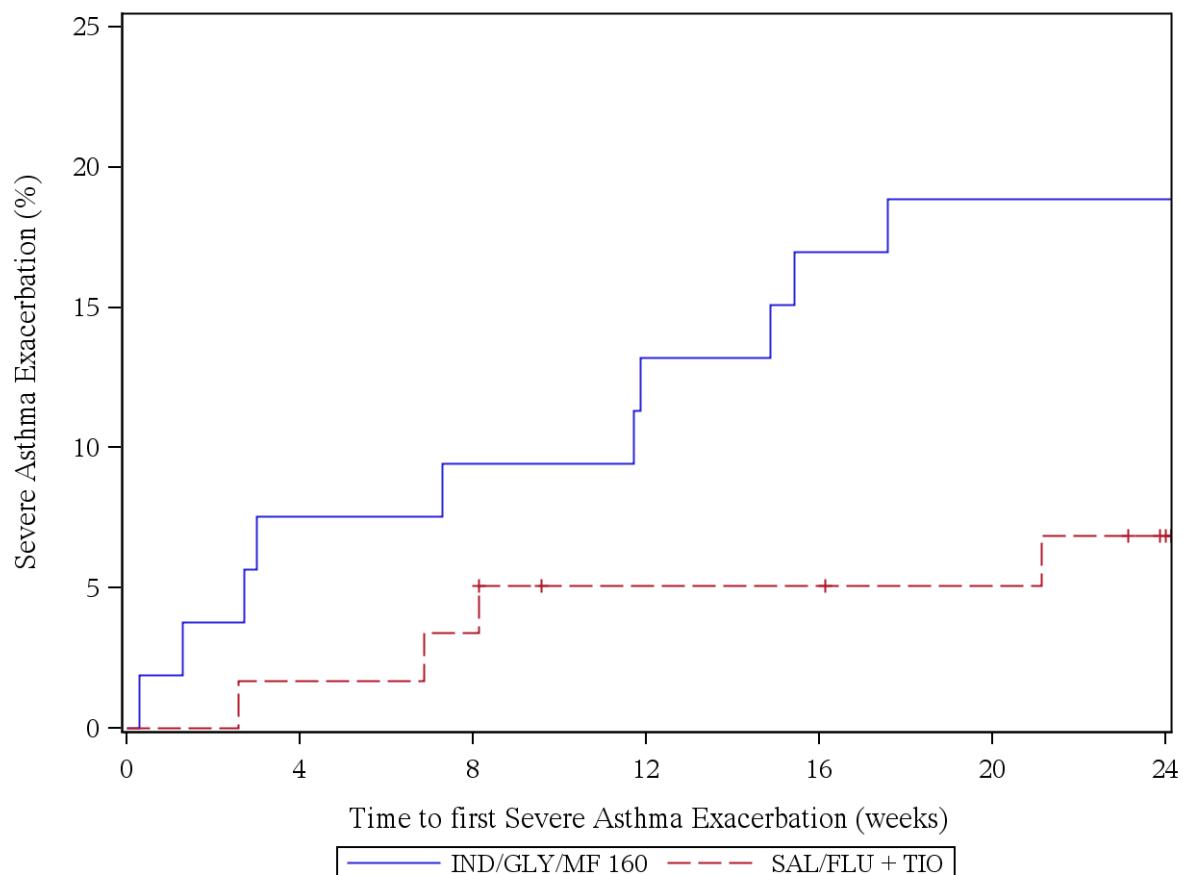


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 154/151, Week 8: 142/143, Week 16: 133/130, Week 24: 125/122

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.10 Kaplan-Meier-Plot: Severe Asthma Exacerbation by Region (FAS)

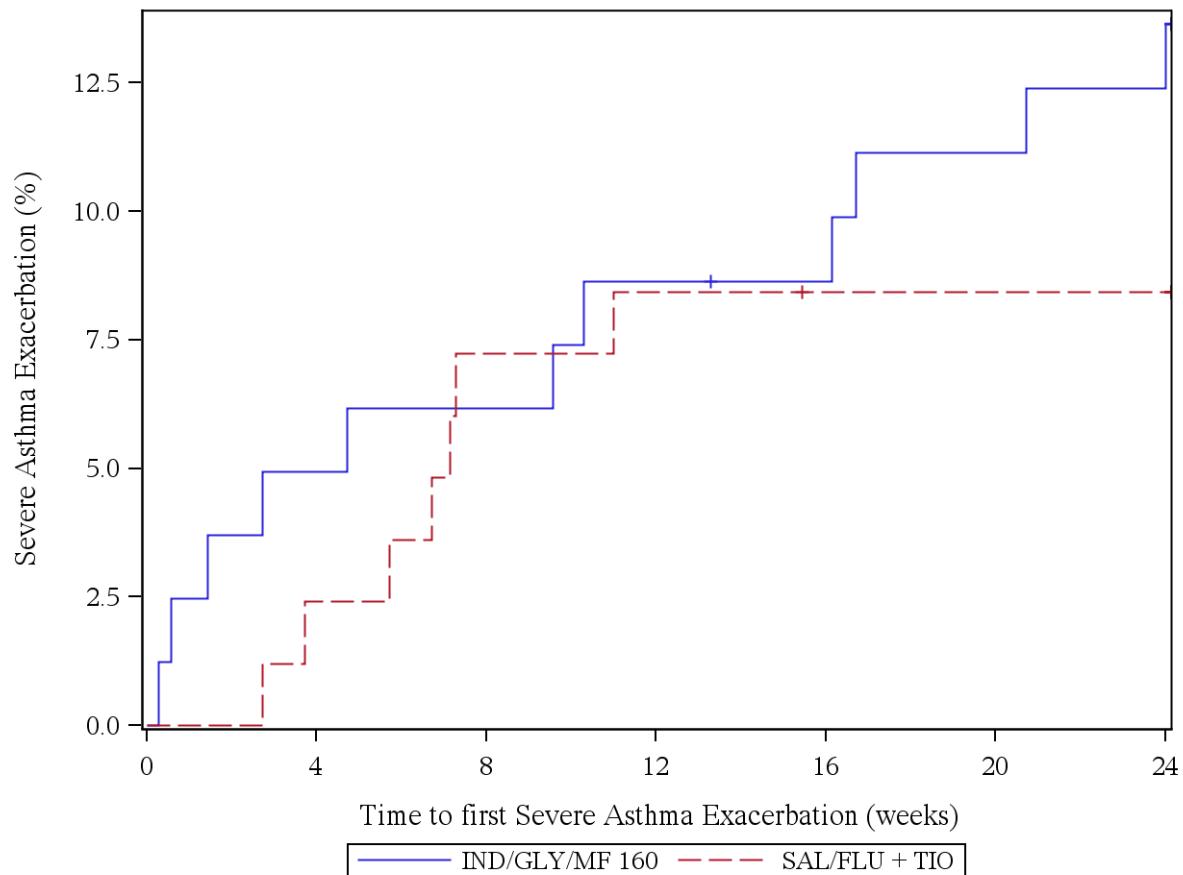
Figure 11.10.1 Severe Asthma Exacerbation (FAS), Region = Asia



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 53/59, Week 8: 48/57, Week 16: 44/54, Week 24: 43/49

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

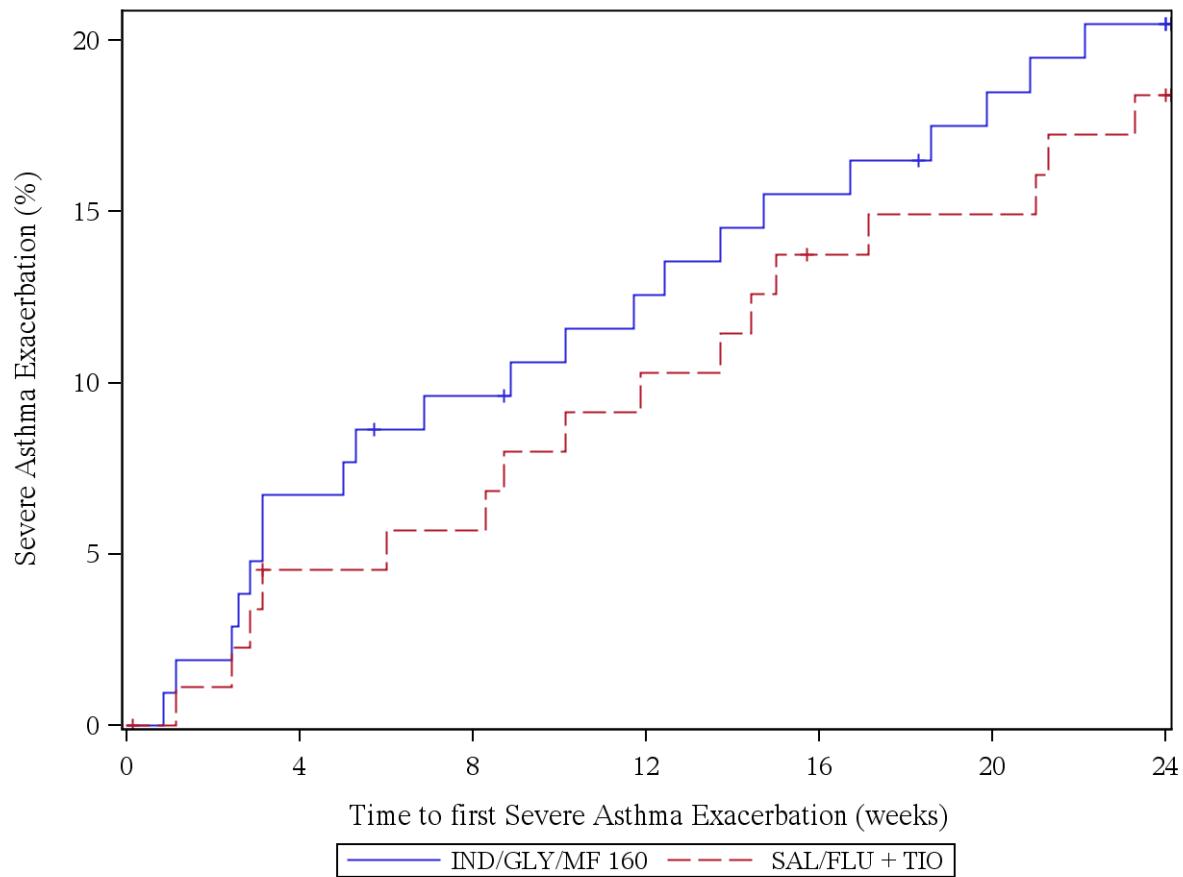
Figure 11.10.2 Severe Asthma Exacerbation (FAS), Region = Europe



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 81/83, Week 8: 76/77, Week 16: 73/75, Week 24: 69/75

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

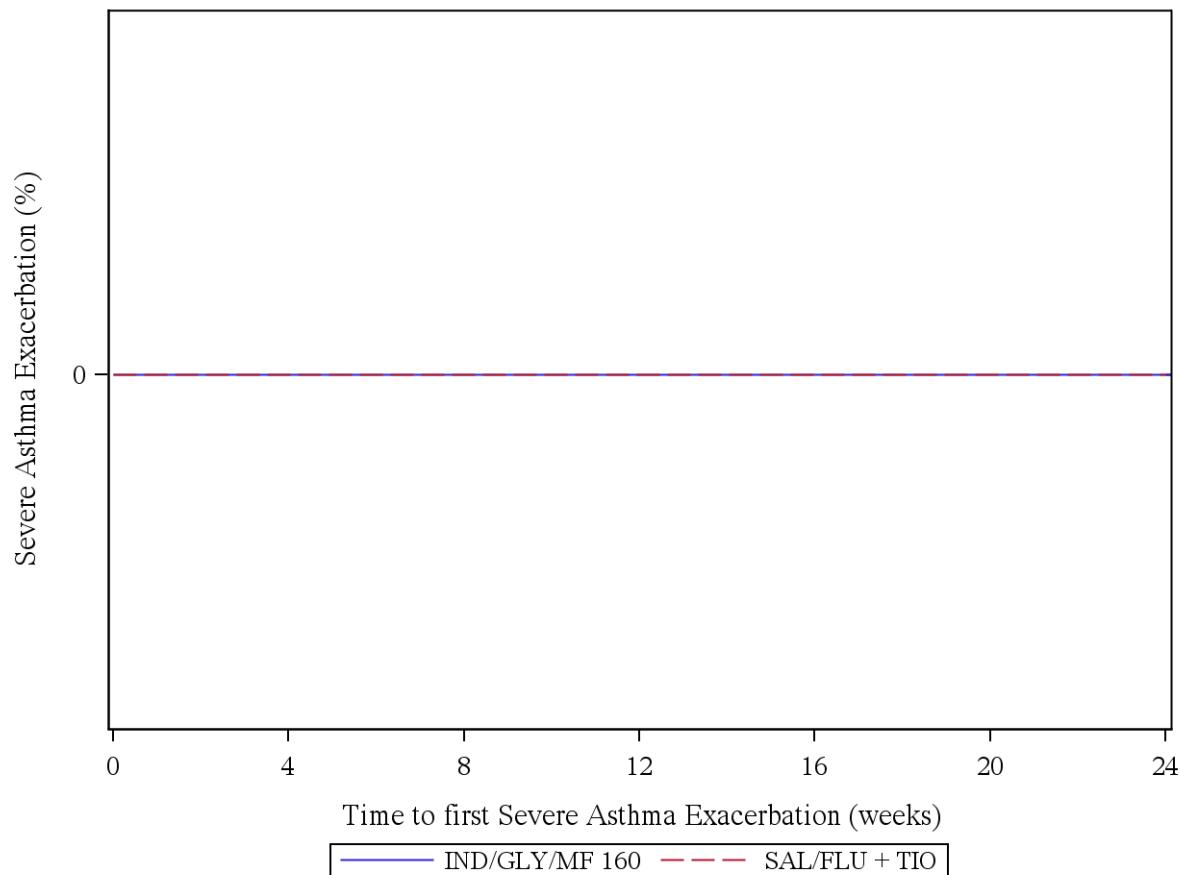
Figure 11.10.3 Severe Asthma Exacerbation (FAS), Region = Latin America



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 104/89, Week 8: 93/82, Week 16: 86/74, Week 24: 78/69

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.10.4 Severe Asthma Exacerbation (FAS), Region = Others

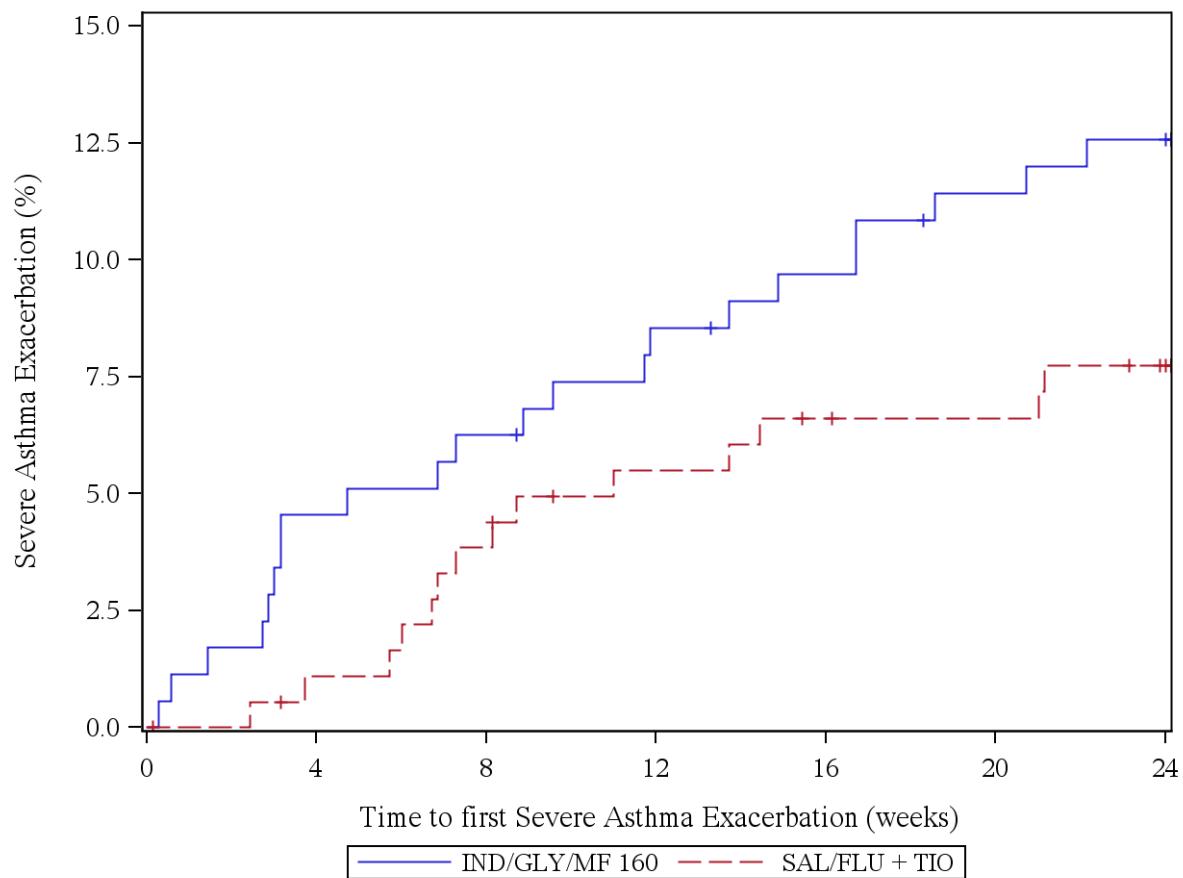


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 4/1, Week 8: 4/1, Week 16: 4/1, Week 24: 4/1

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.11 Kaplan-Meier-Plot: Severe Asthma Exacerbation by History of Asthma Exacerbation (FAS)

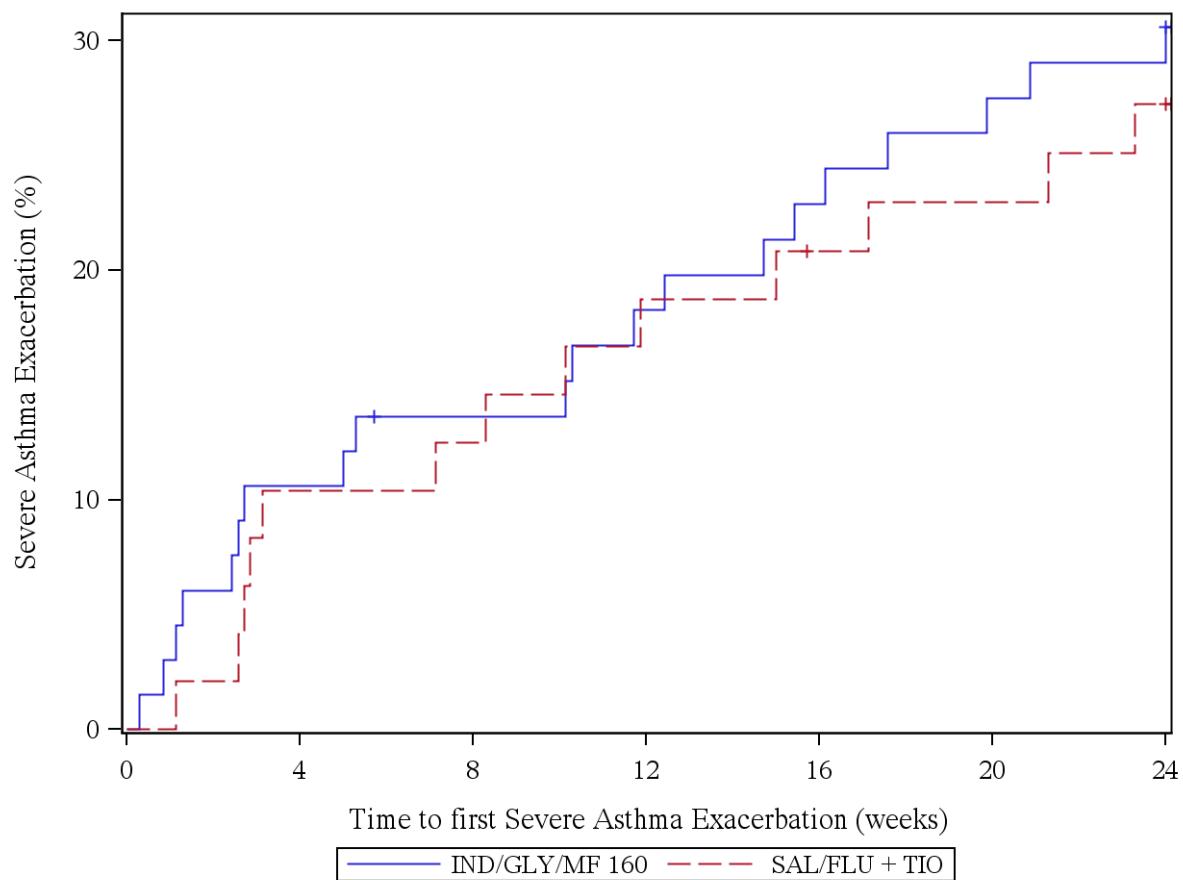
Figure 11.11.1 Severe Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 176/184, Week 8: 165/175, Week 16: 157/167, Week 24: 150/161

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.11.2 Severe Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2

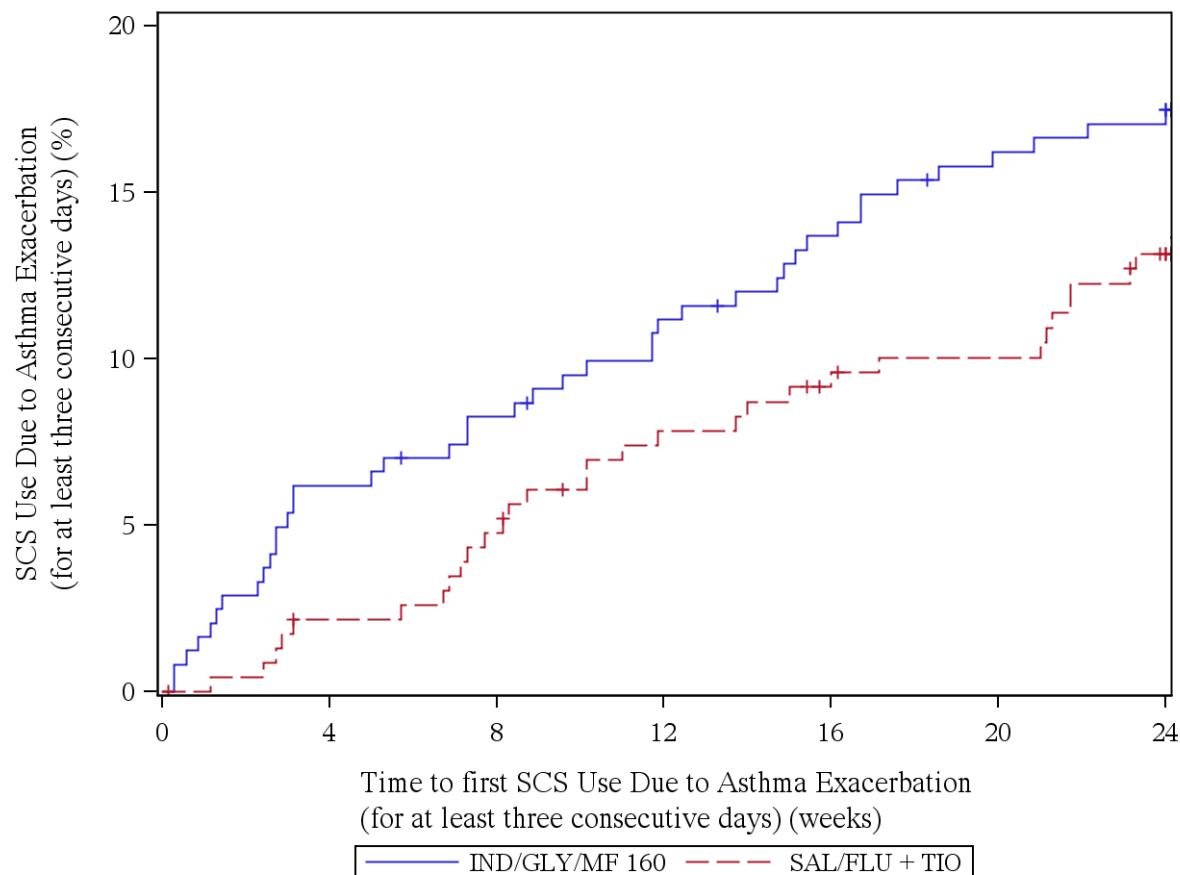


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 66/48, Week 8: 56/42, Week 16: 50/37, Week 24: 44/33

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

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)

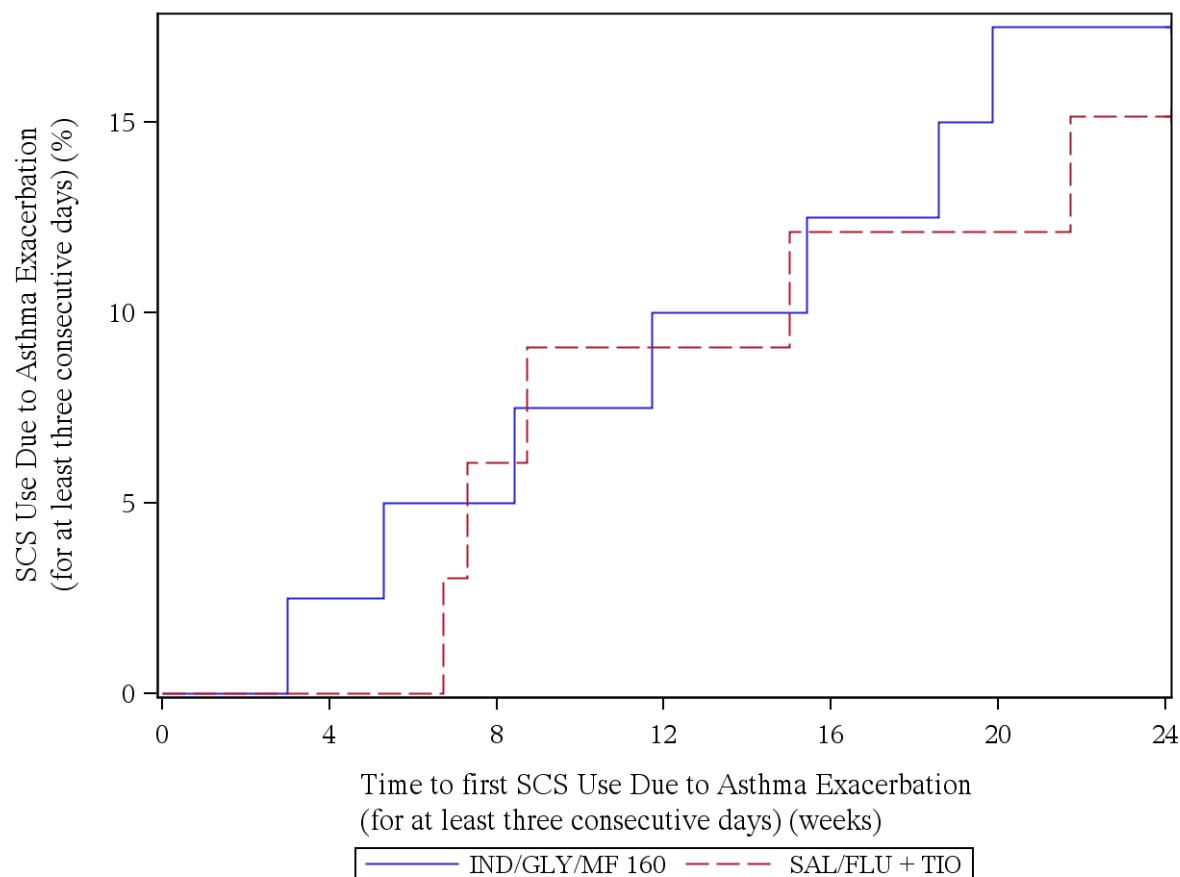


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 242/232, Week 8: 221/219, Week 16: 206/204, Week 24: 194/191

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.14 Kaplan-Meier-Plot: SCS Use Due to Asthma Exacerbation (for at least three consecutive days) by Age (FAS)

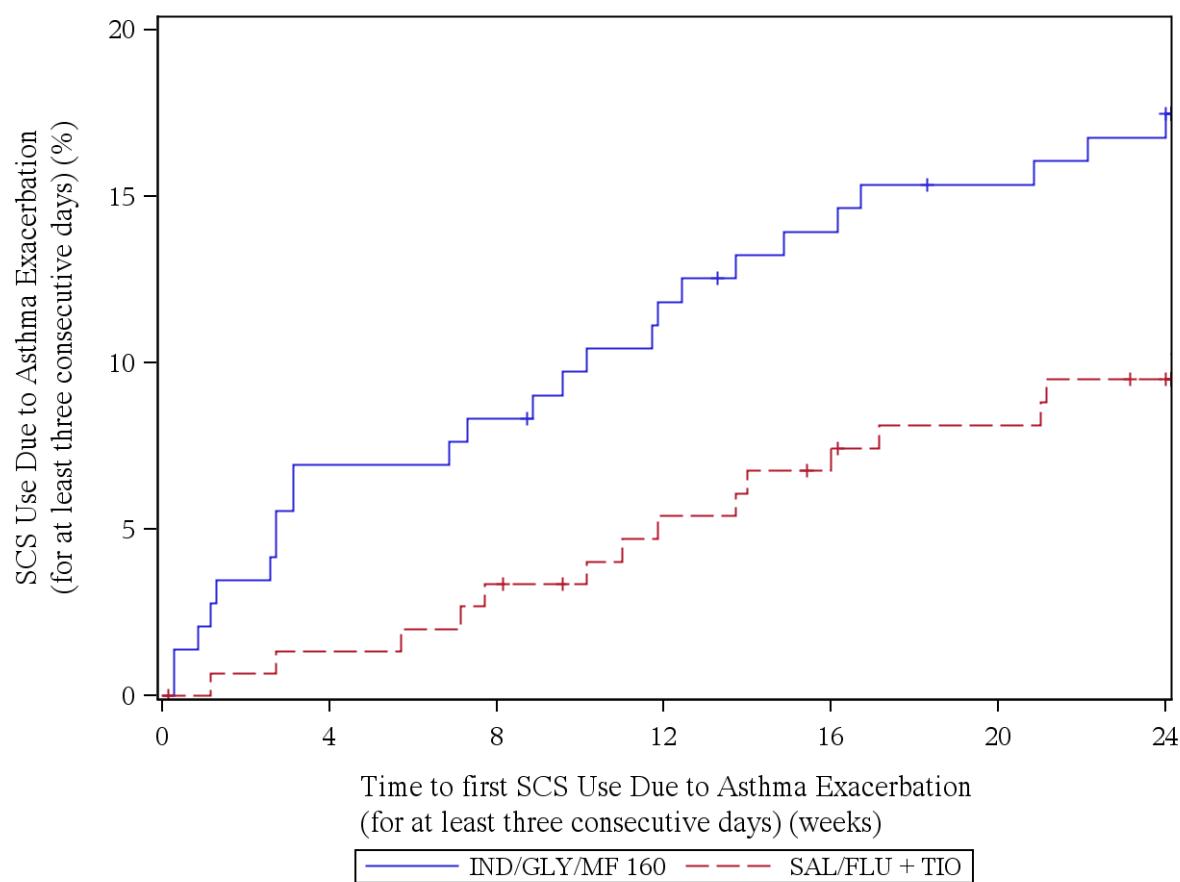
Figure 11.14.1 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Age = 18-39 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 40/33, Week 8: 38/31, Week 16: 35/29, Week 24: 33/28

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

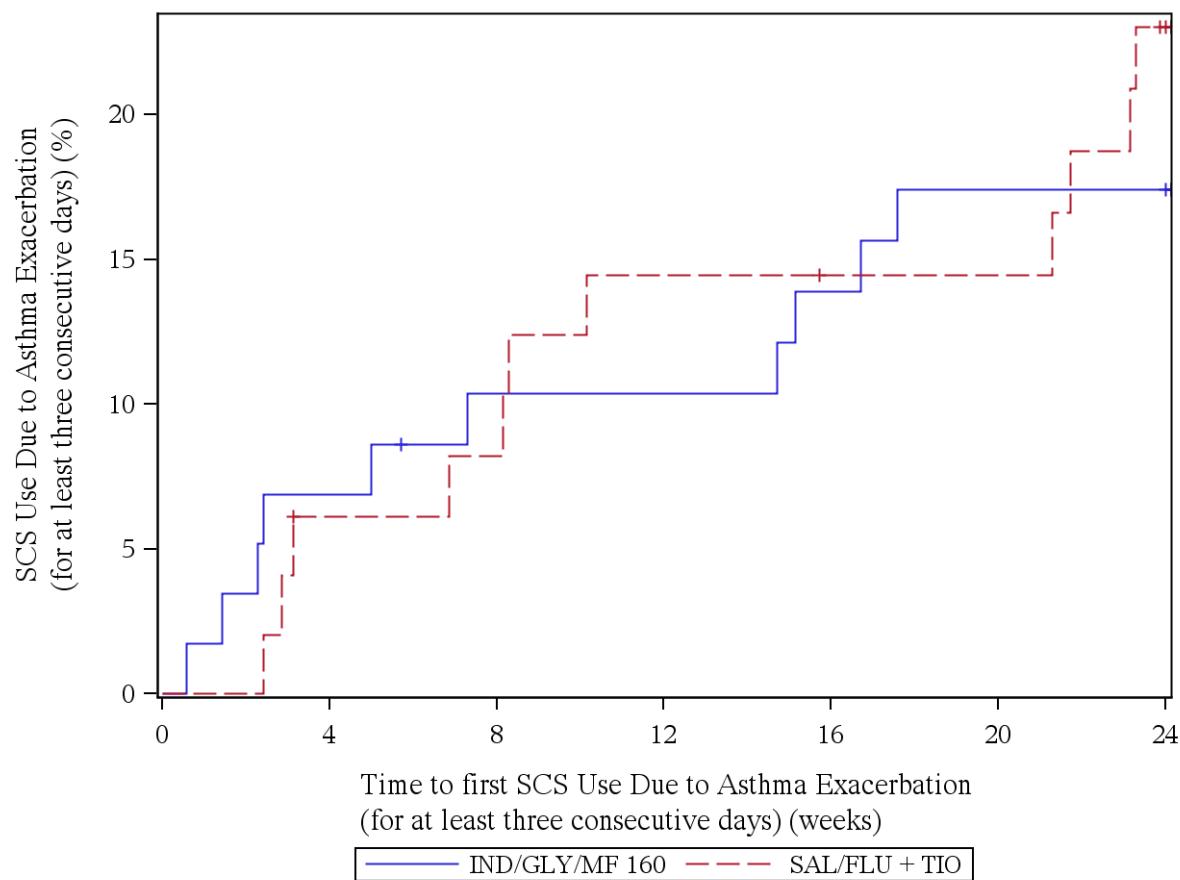
Figure 11.14.2 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Age = 40-64 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 144/150, Week 8: 132/144, Week 16: 122/135, Week 24: 115/129

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.14.3 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Age = ≥ 65 years

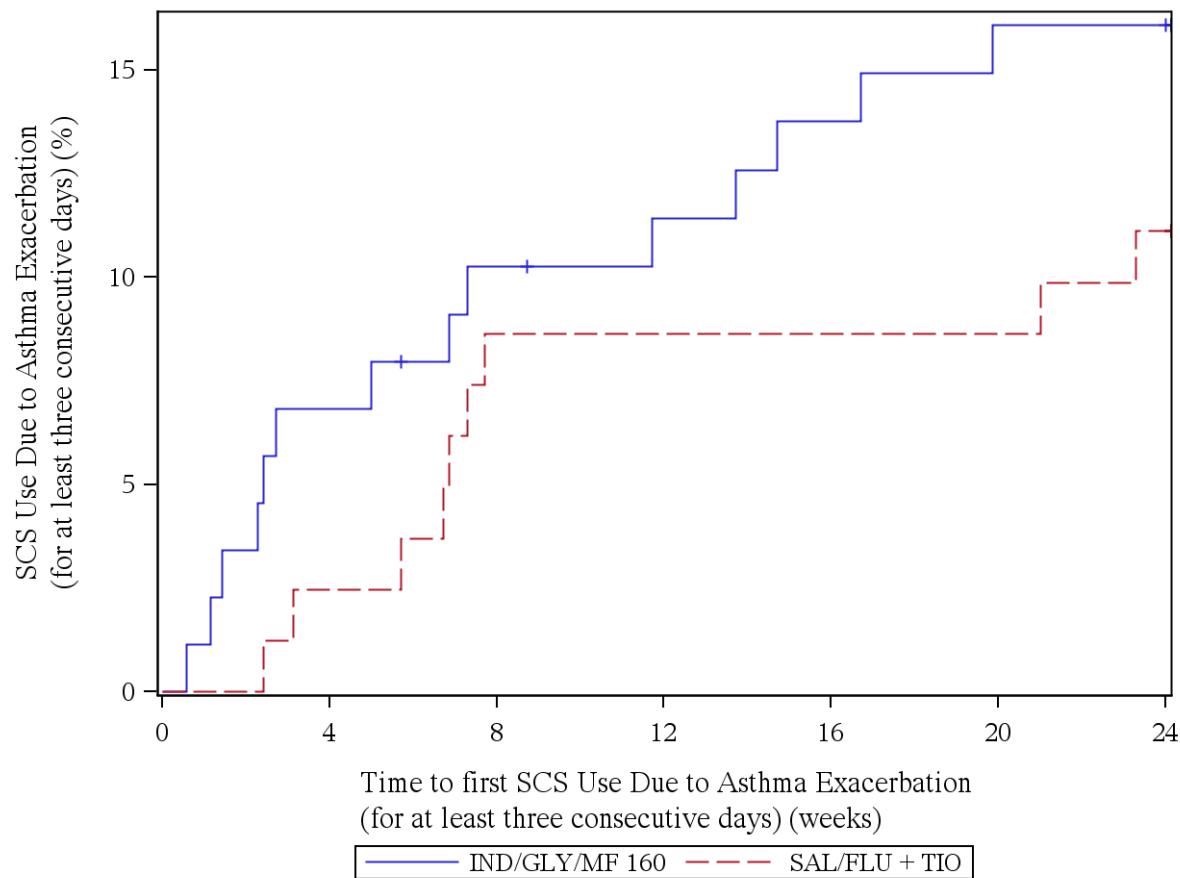


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 58/49, Week 8: 51/44, Week 16: 49/40, Week 24: 46/34

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.15 Kaplan-Meier-Plot: SCS Use Due to Asthma Exacerbation (for at least three consecutive days) by Gender (FAS)

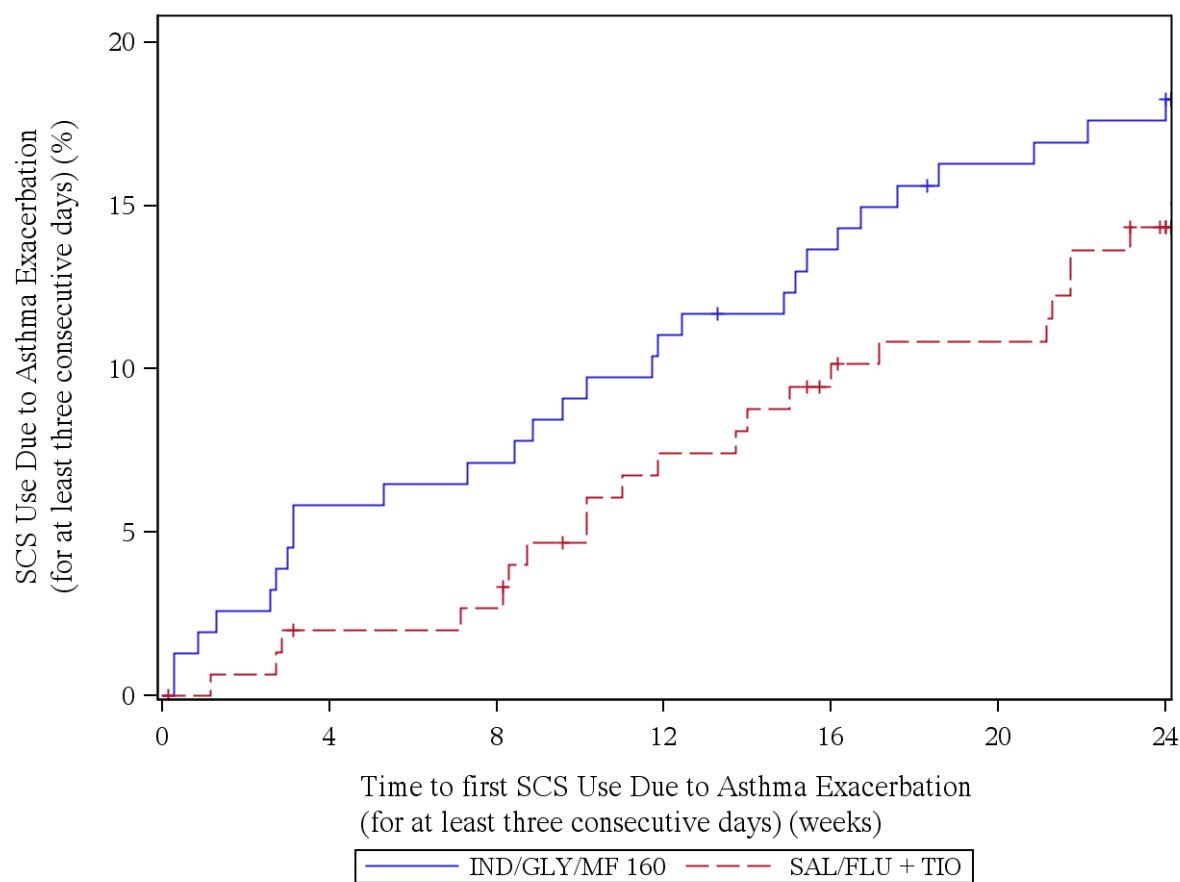
Figure 11.15.1 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Gender = Male



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 88/81, Week 8: 78/74, Week 16: 74/74, Week 24: 71/72

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.15.2 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Gender = Female

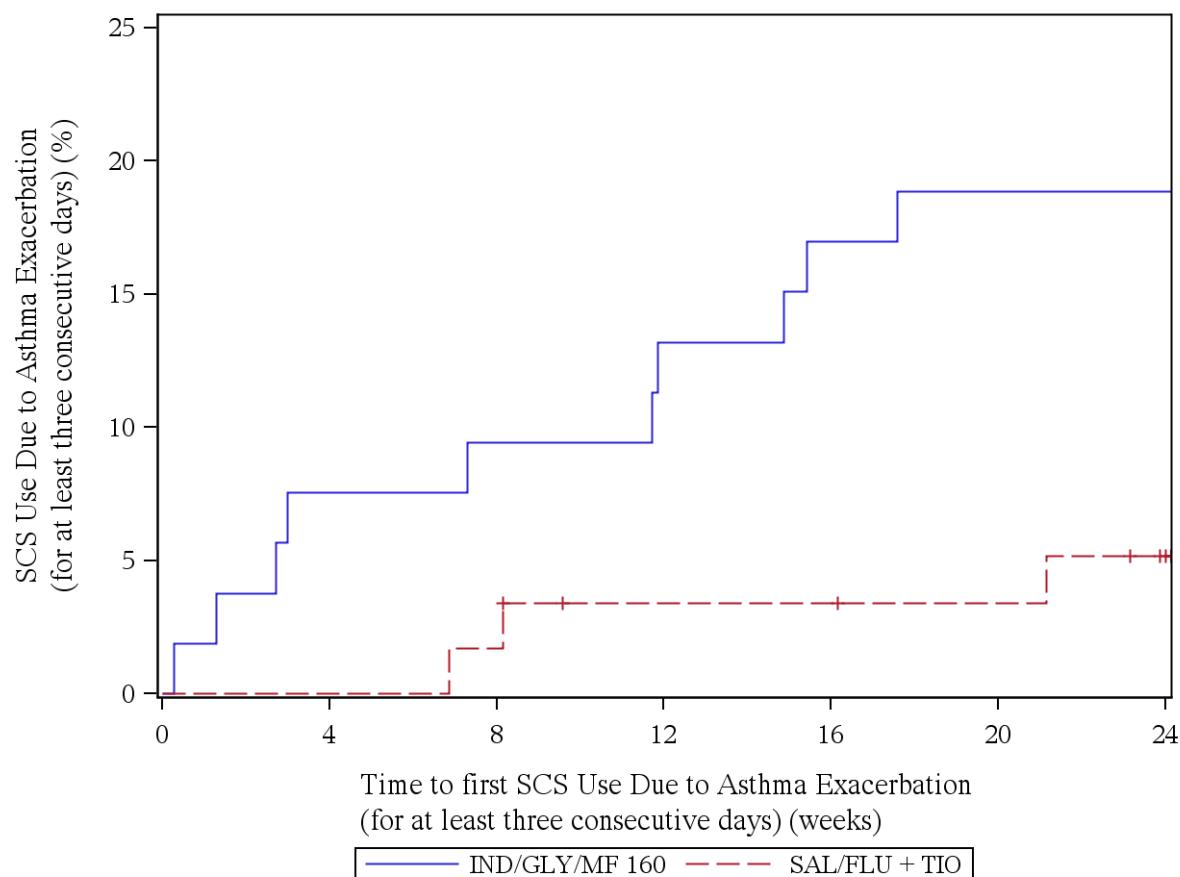


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 154/151, Week 8: 143/145, Week 16: 132/130, Week 24: 123/119

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.16 Kaplan-Meier-Plot: SCS Use Due to Asthma Exacerbation (for at least three consecutive days) by Region (FAS)

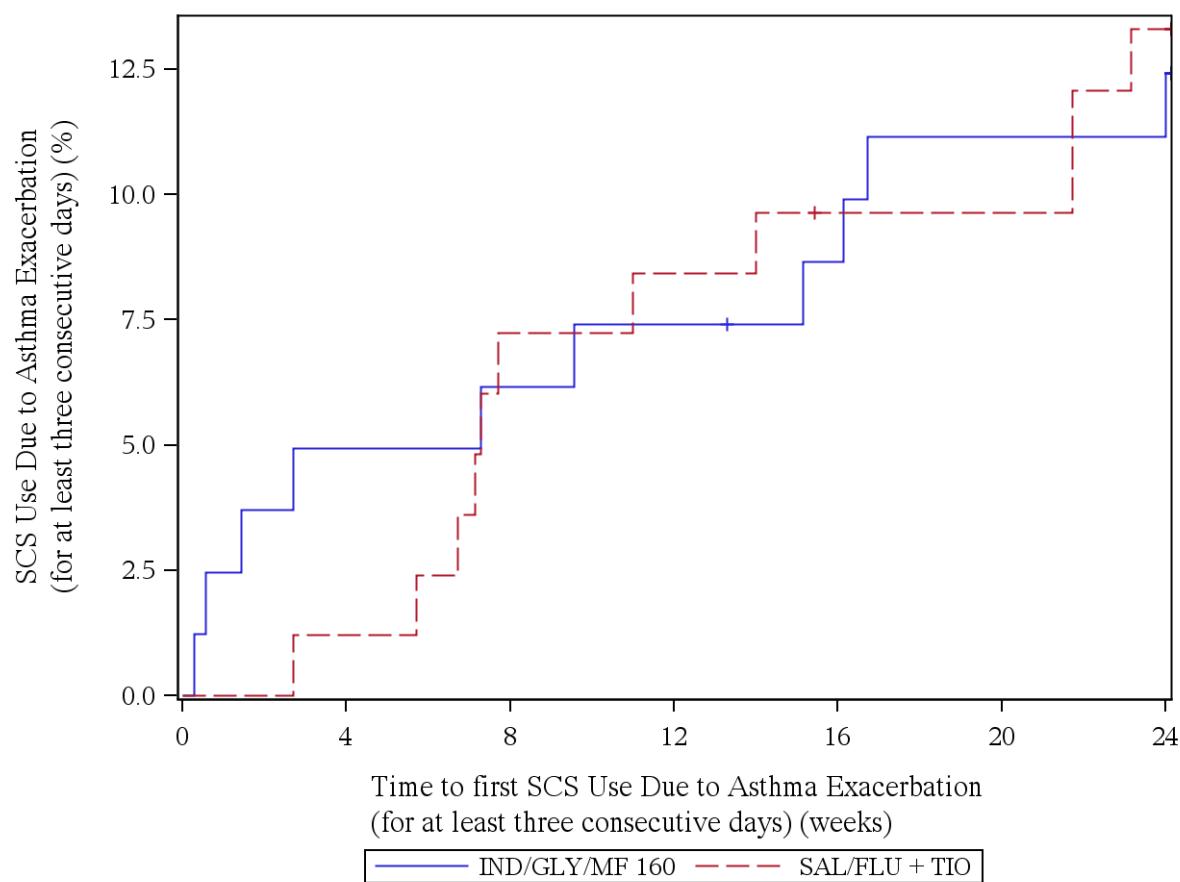
Figure 11.16.1 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Region = Asia



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 53/59, Week 8: 48/58, Week 16: 44/55, Week 24: 43/50

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

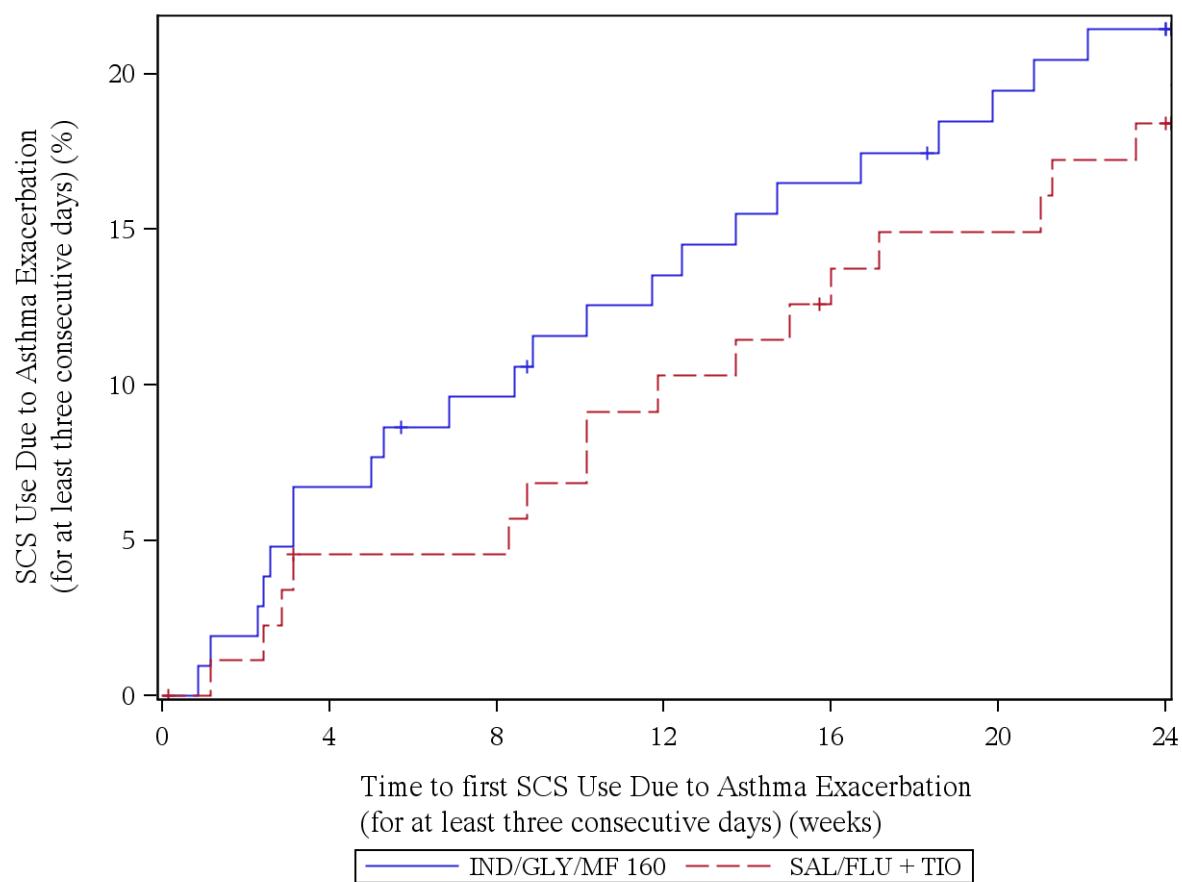
Figure 11.16.2 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Region = Europe



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 81/83, Week 8: 76/77, Week 16: 73/74, Week 24: 70/71

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

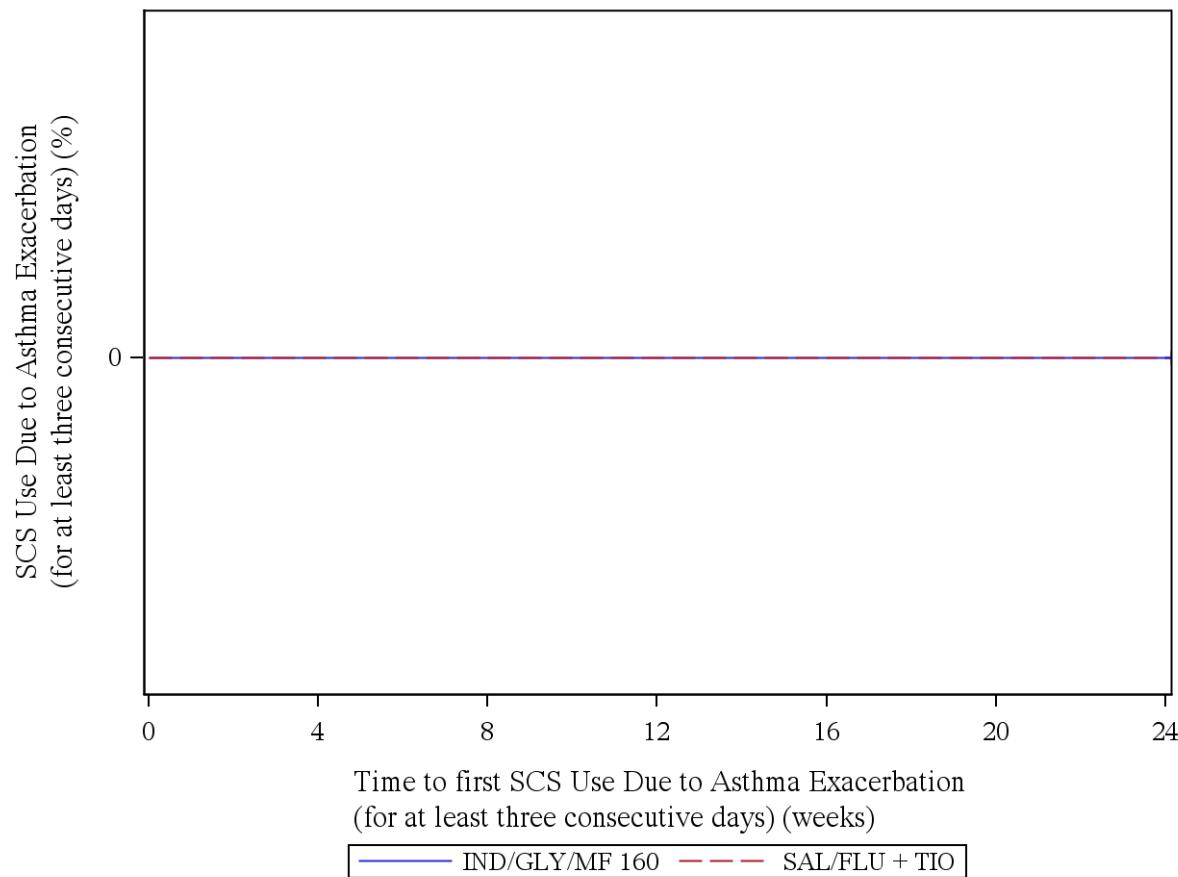
Figure 11.16.3 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Region = Latin America



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 104/89, Week 8: 93/83, Week 16: 85/74, Week 24: 77/69

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.16.4 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Region = Others

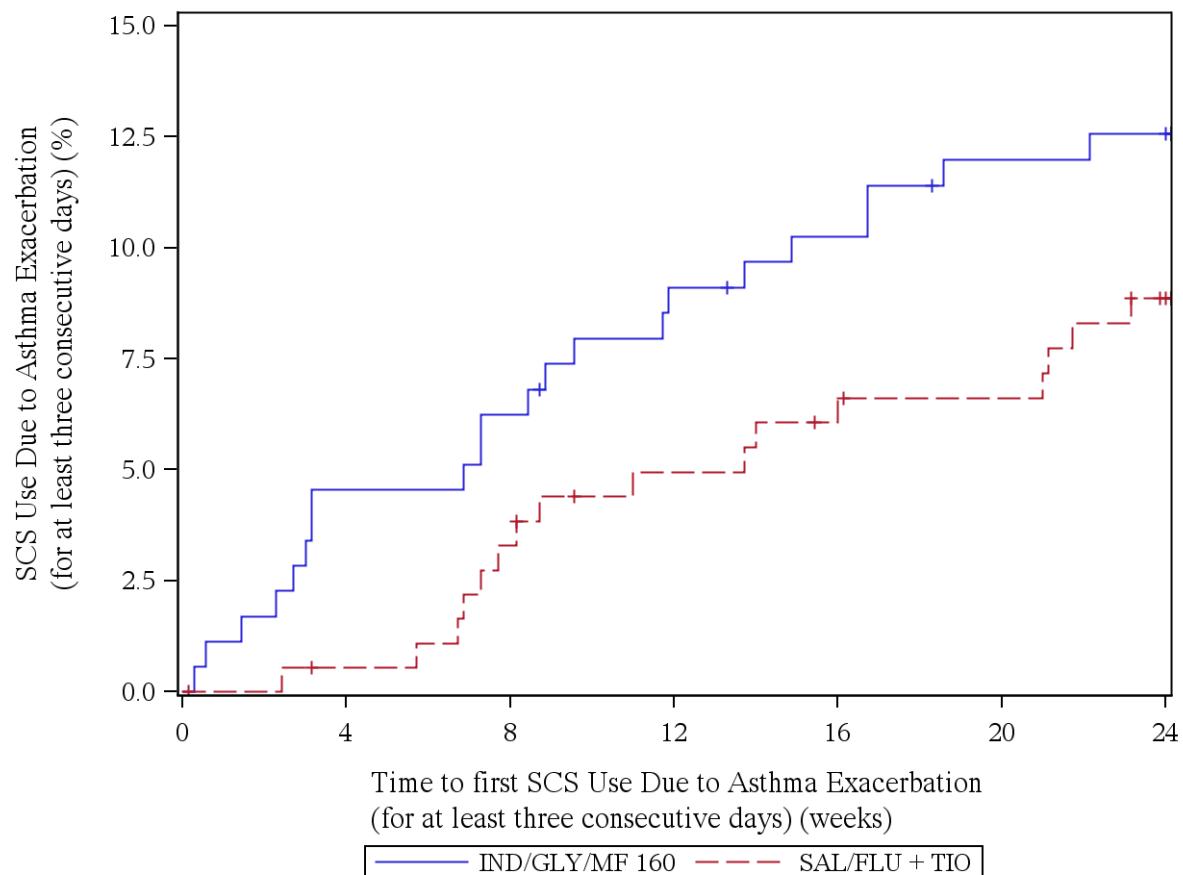


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 4/1, Week 8: 4/1, Week 16: 4/1, Week 24: 4/1

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.17 Kaplan-Meier-Plot: SCS Use Due to Asthma Exacerbation (for at least three consecutive days) by History of Asthma Exacerbation (FAS)

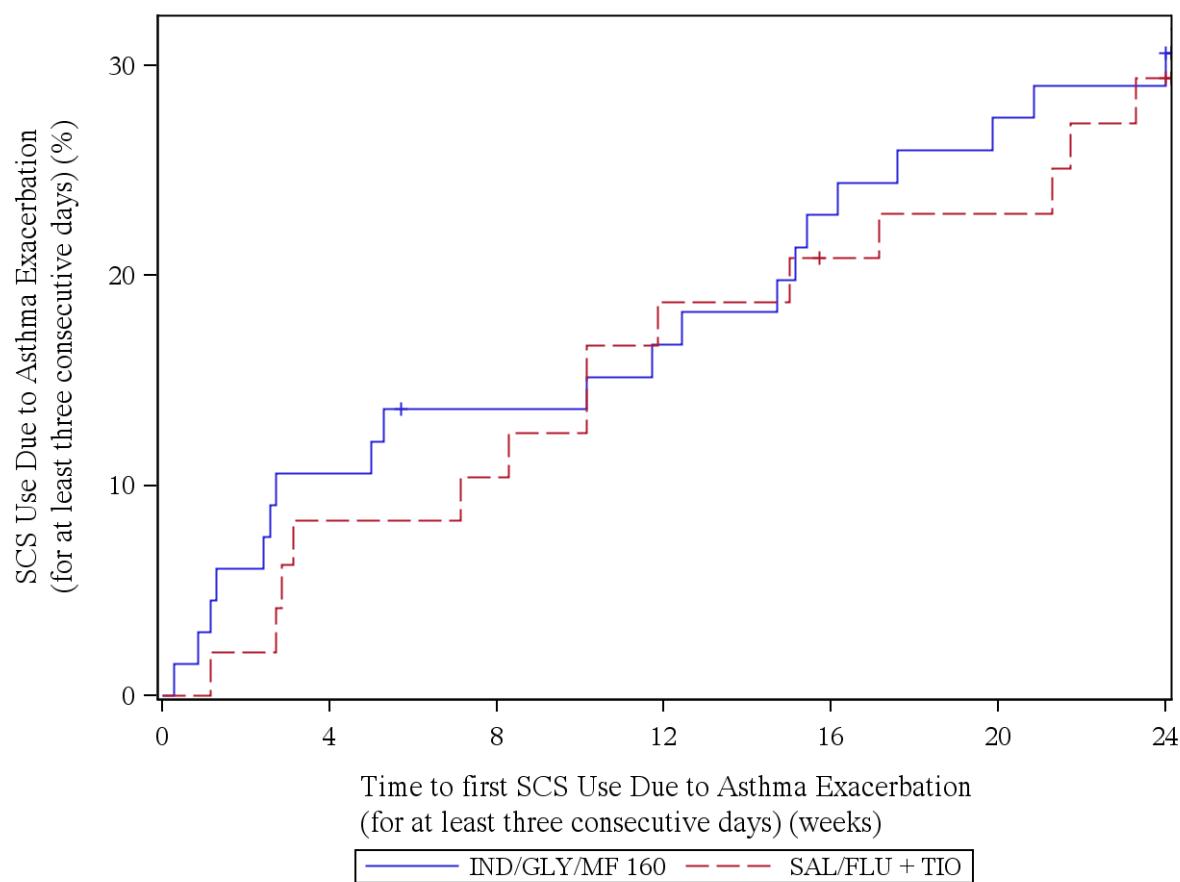
Figure 11.17.1 SCS Use Due to Asthma Exacerbation (for at least three consecutive days) (FAS), Asthma exacerbations in the 12 months prior to screening = 1



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 176/184, Week 8: 165/176, Week 16: 156/167, Week 24: 150/159

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

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

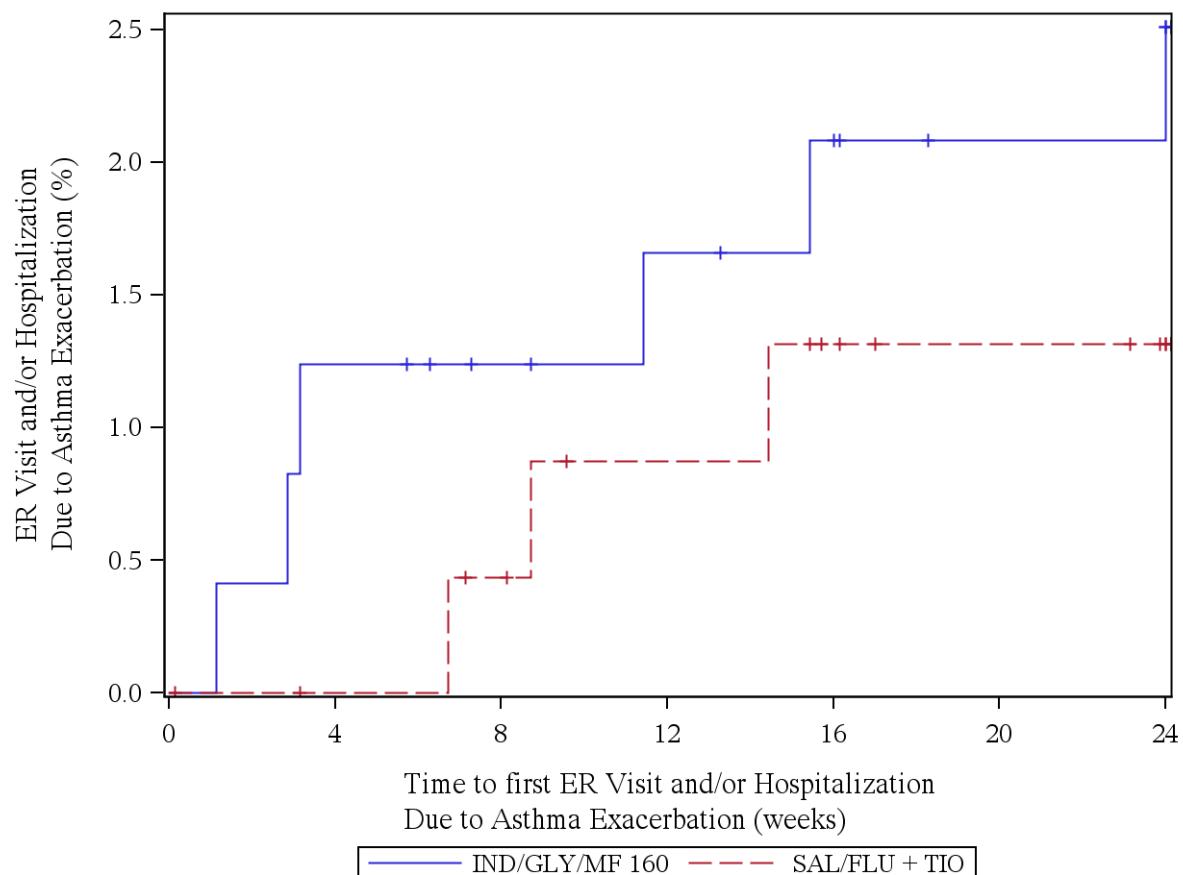


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 66/48, Week 8: 56/43, Week 16: 50/37, Week 24: 44/32

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

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)

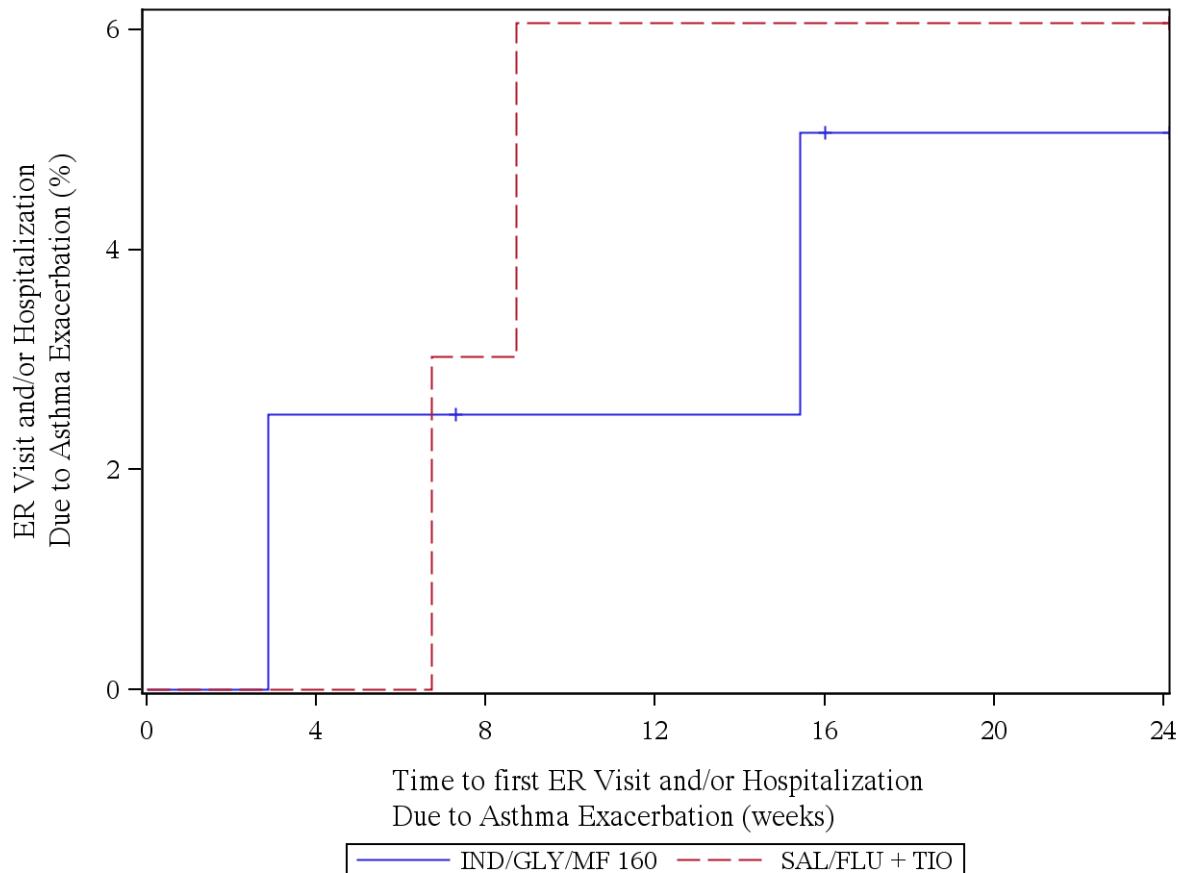


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 242/232, Week 8: 236/228, Week 16: 231/222, Week 24: 226/216

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.20 Kaplan-Meier-Plot: ER Visit and/or Hospitalization Due to Asthma Exacerbation by Age (FAS)

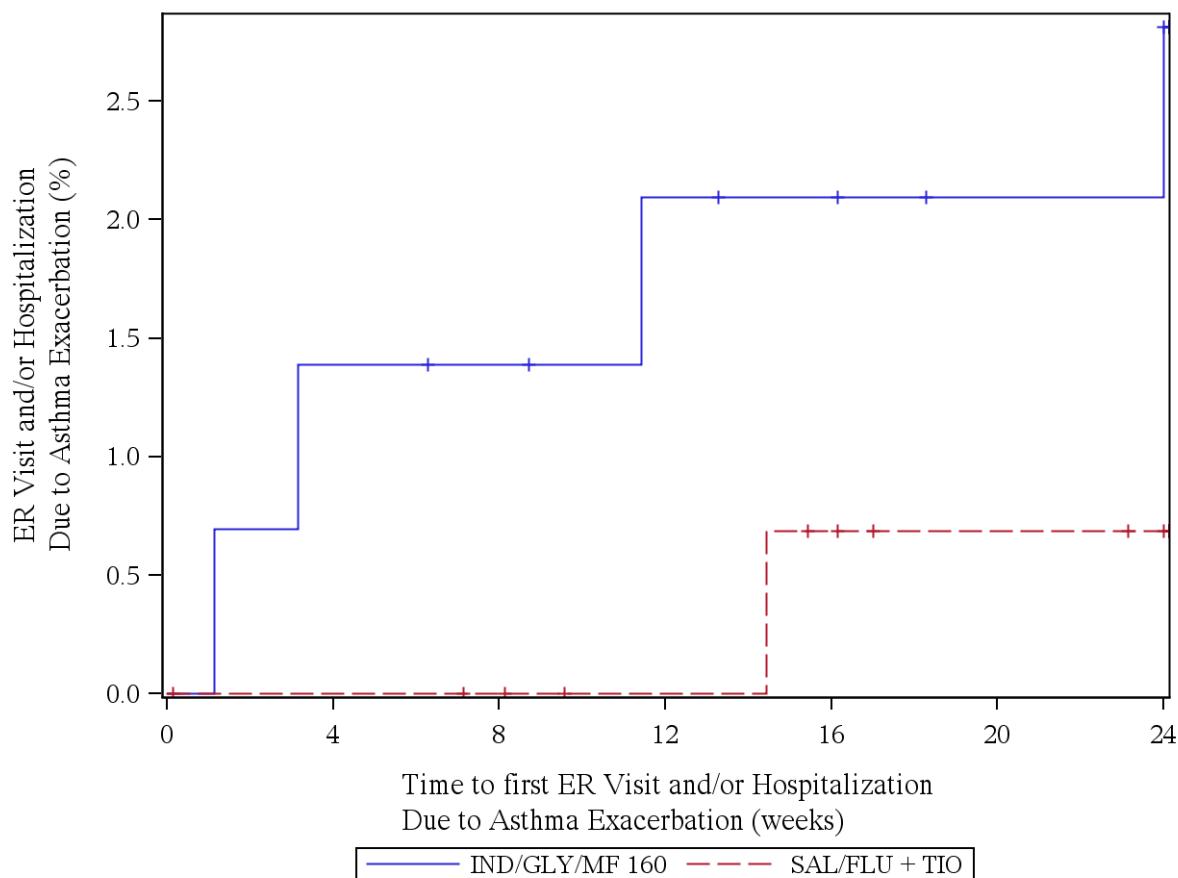
Figure 11.20.1 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Age = 18-39 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 40/33, Week 8: 38/32, Week 16: 36/31, Week 24: 36/31

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

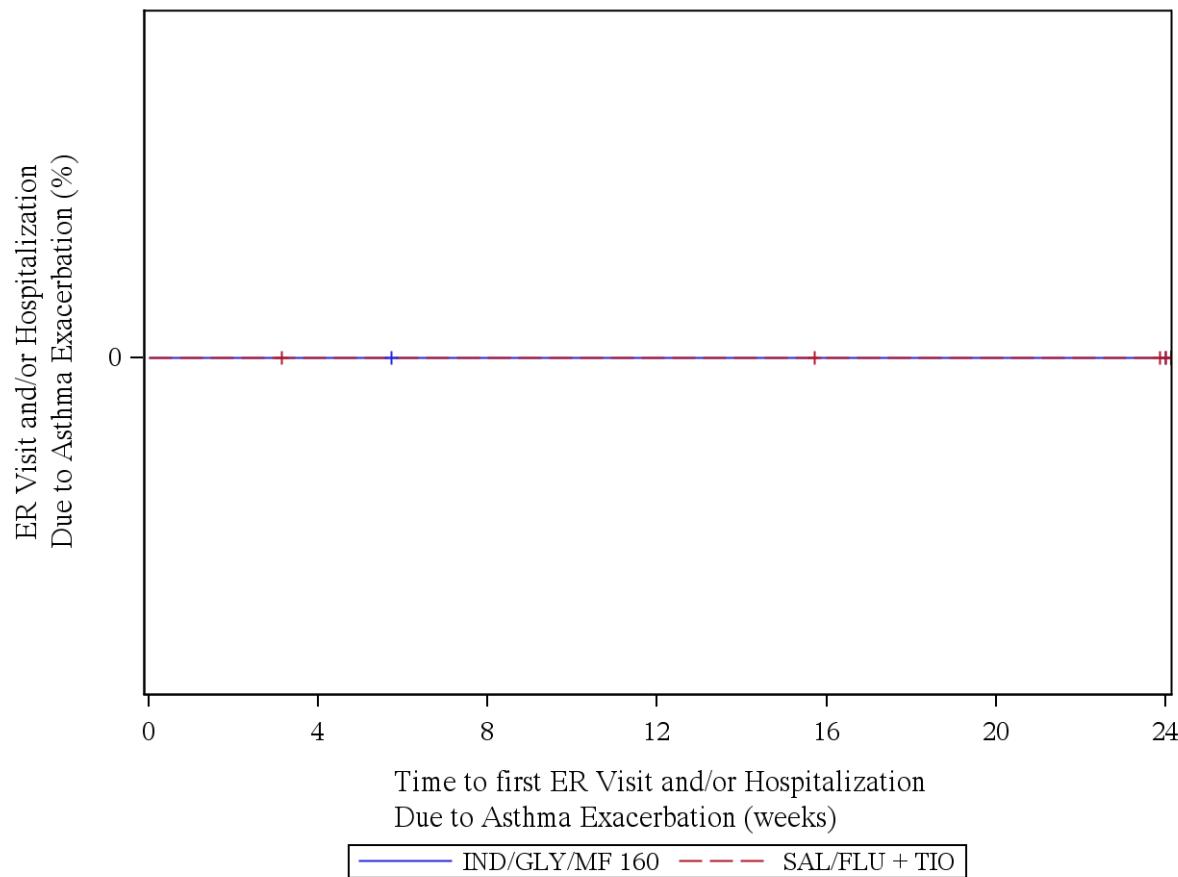
Figure 11.20.2 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Age = 40-64 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 144/150, Week 8: 141/148, Week 16: 138/144, Week 24: 134/140

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.20.3 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Age = ≥ 65 years

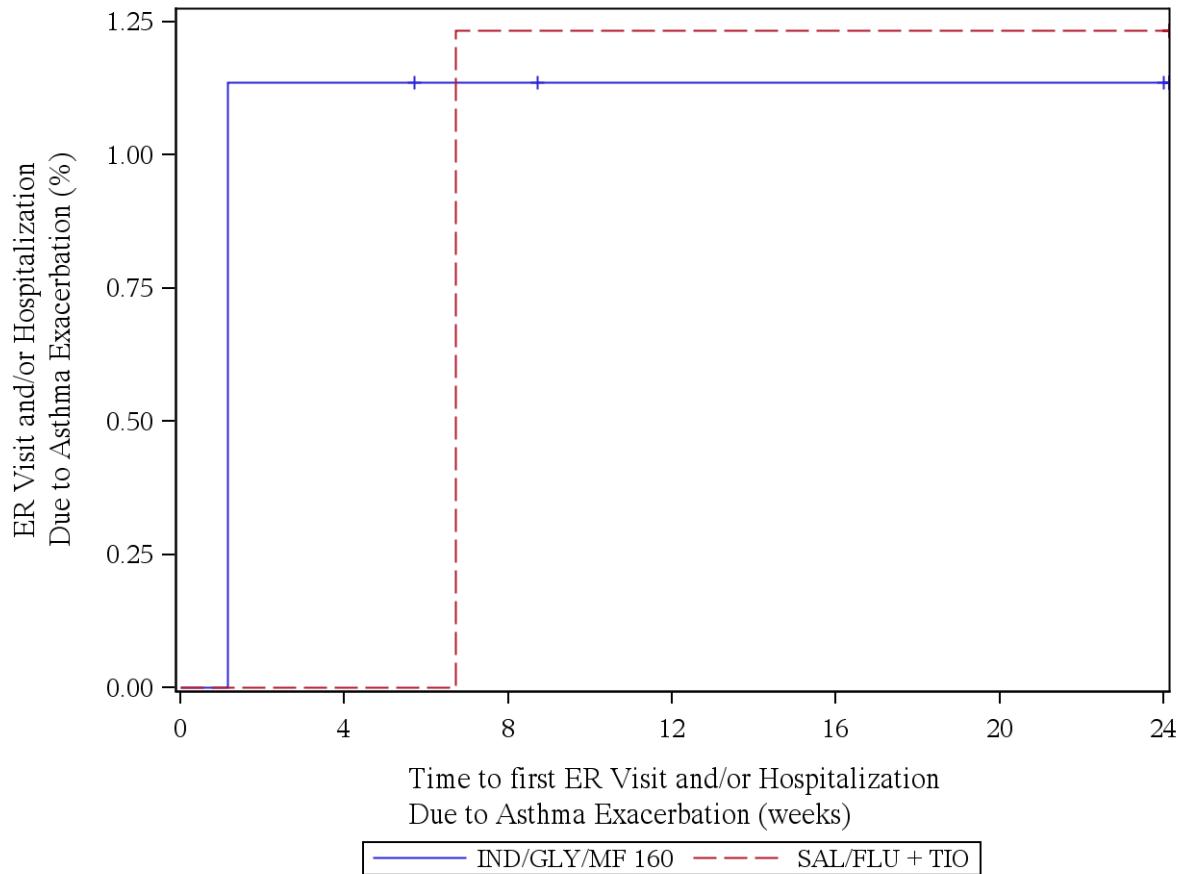


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 58/49, Week 8: 57/48, Week 16: 57/47, Week 24: 56/45

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.21 Kaplan-Meier-Plot: ER Visit and/or Hospitalization Due to Asthma Exacerbation by Gender (FAS)

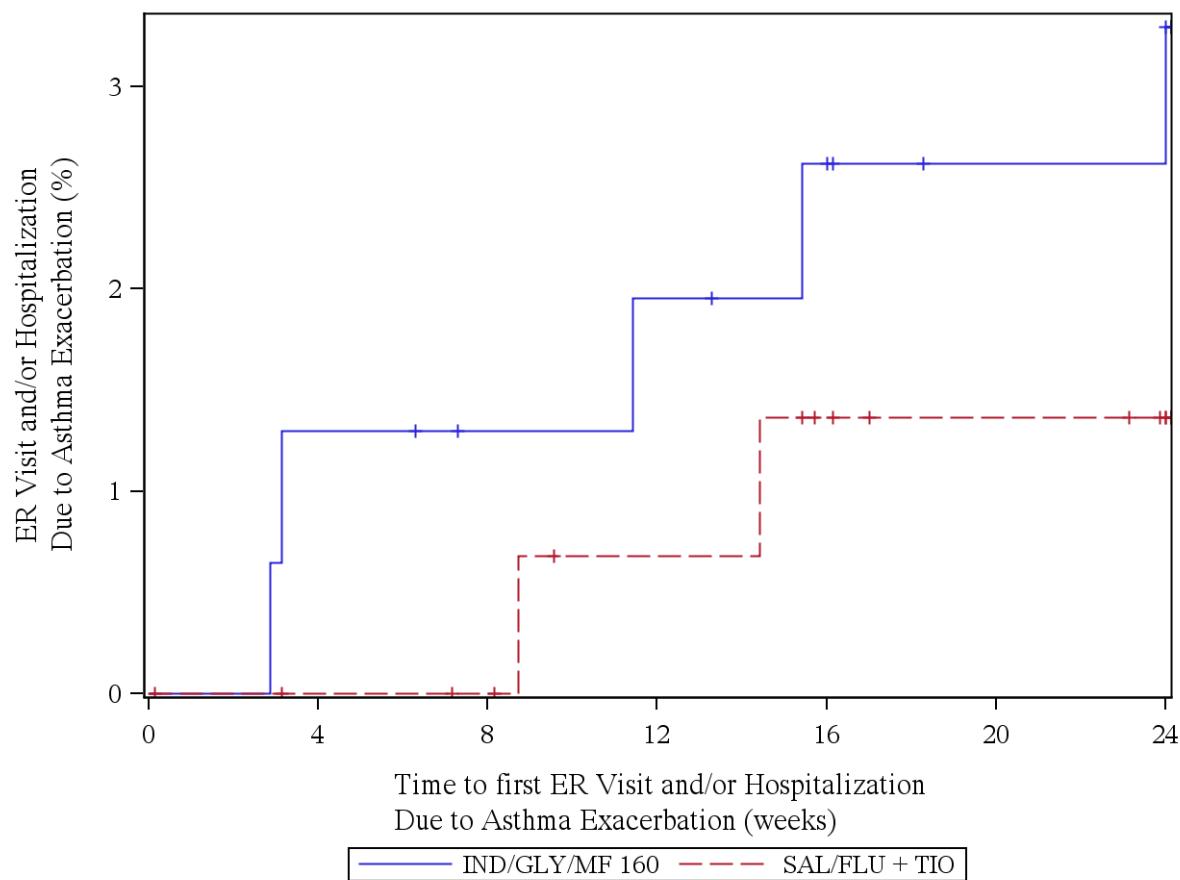
**Figure 11.21.1 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS),
Gender = Male**



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 88/81, Week 8: 86/80, Week 16: 85/80, Week 24: 84/80

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

**Figure 11.21.2 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS),
Gender = Female**

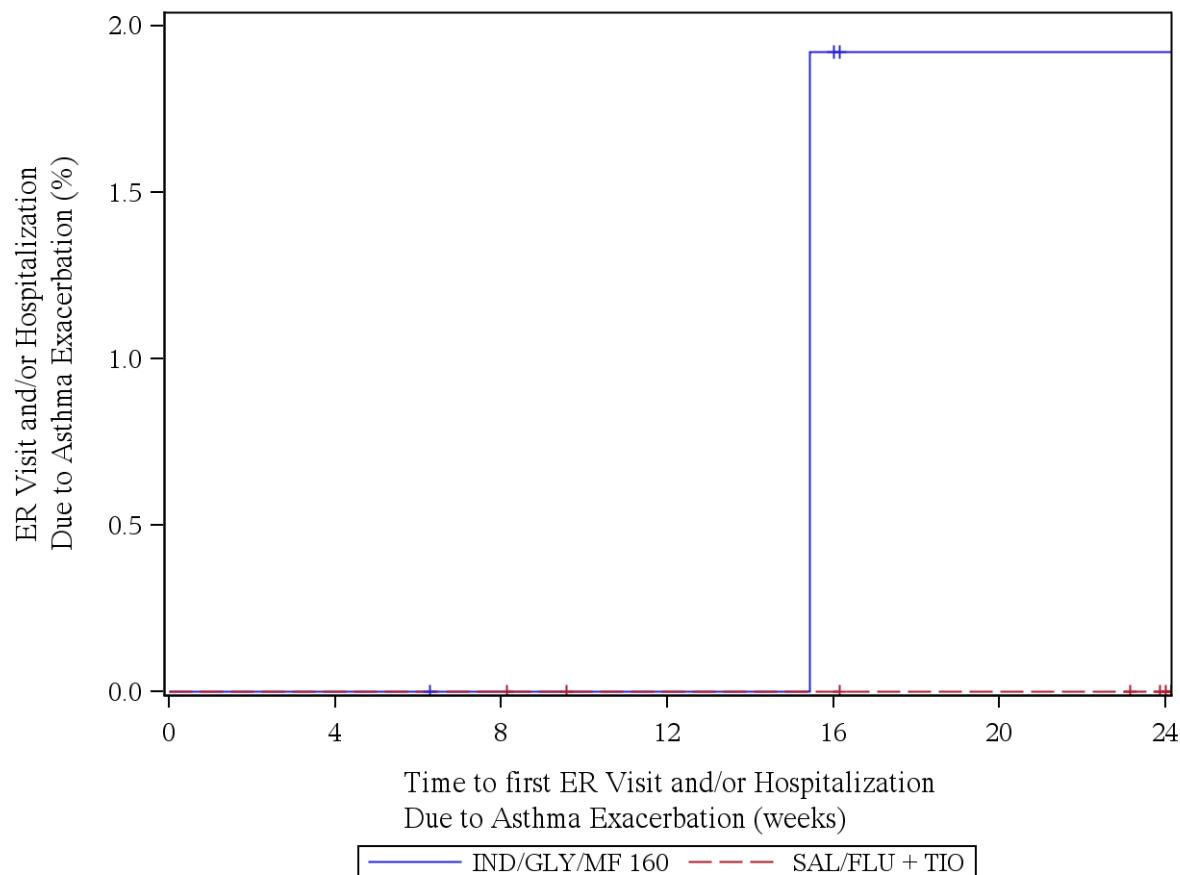


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 154/151, Week 8: 150/148, Week 16: 146/142, Week 24: 142/136

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.22 Kaplan-Meier-Plot: ER Visit and/or Hospitalization Due to Asthma Exacerbation by Region (FAS)

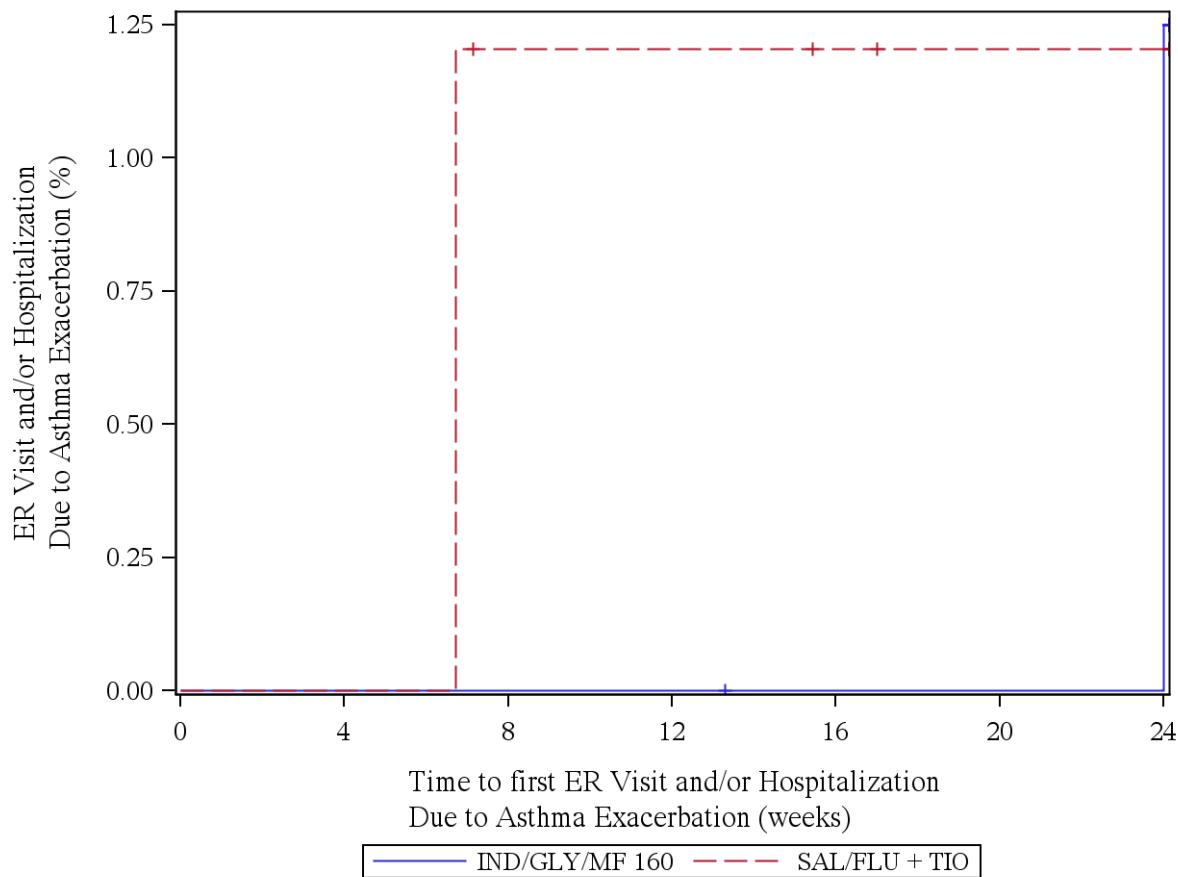
Figure 11.22.1 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Region = Asia



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 53/59, Week 8: 52/59, Week 16: 50/57, Week 24: 49/53

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

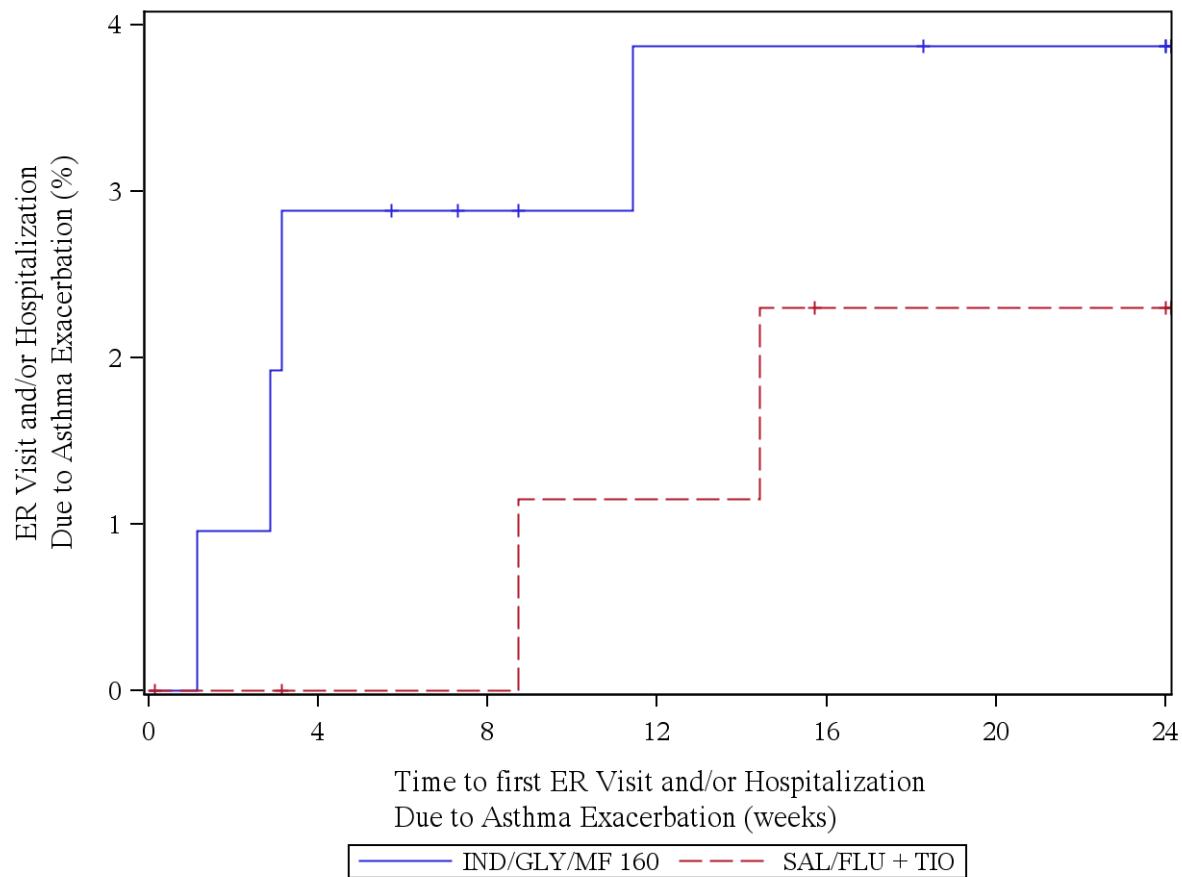
Figure 11.22.2 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Region = Europe



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 81/83, Week 8: 81/81, Week 16: 80/80, Week 24: 79/79

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

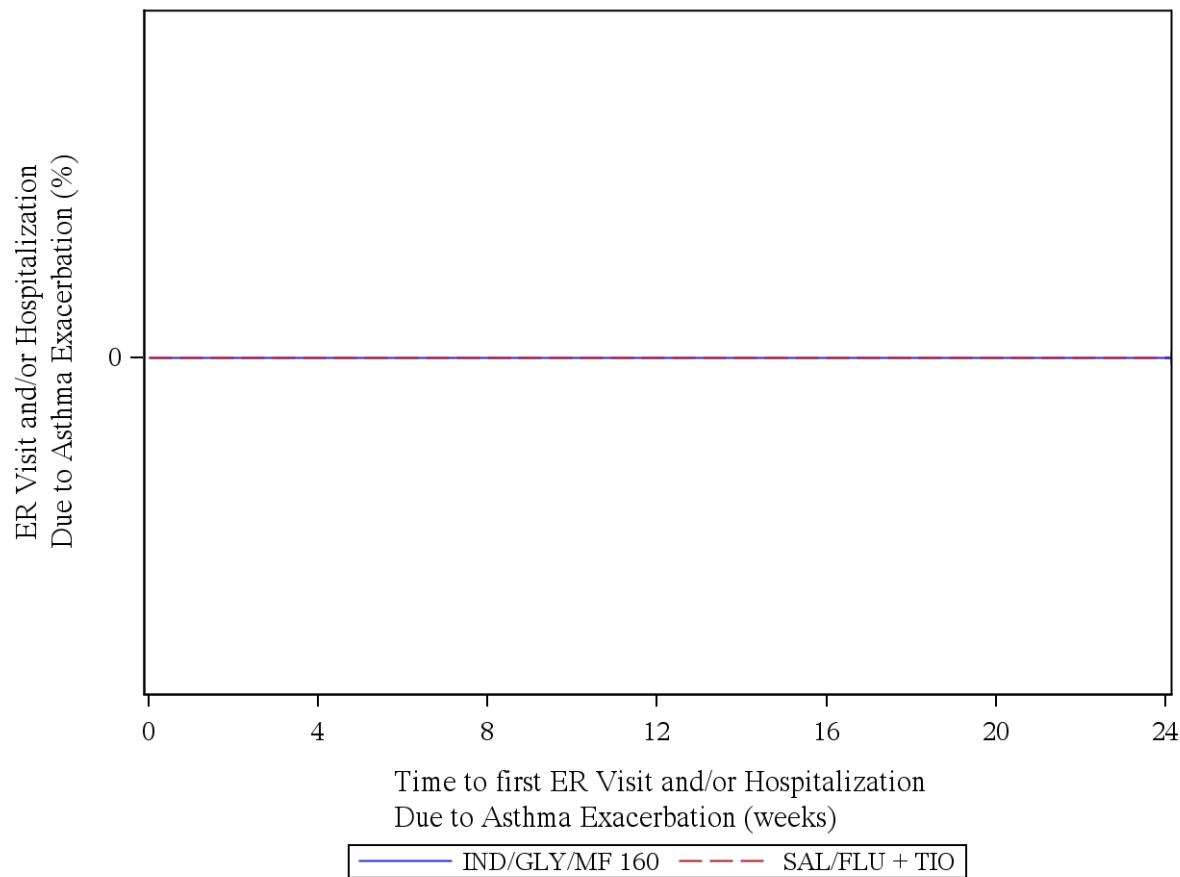
Figure 11.22.3 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Region = Latin America



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 104/89, Week 8: 99/87, Week 16: 97/84, Week 24: 94/83

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.22.4 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS), Region = Others

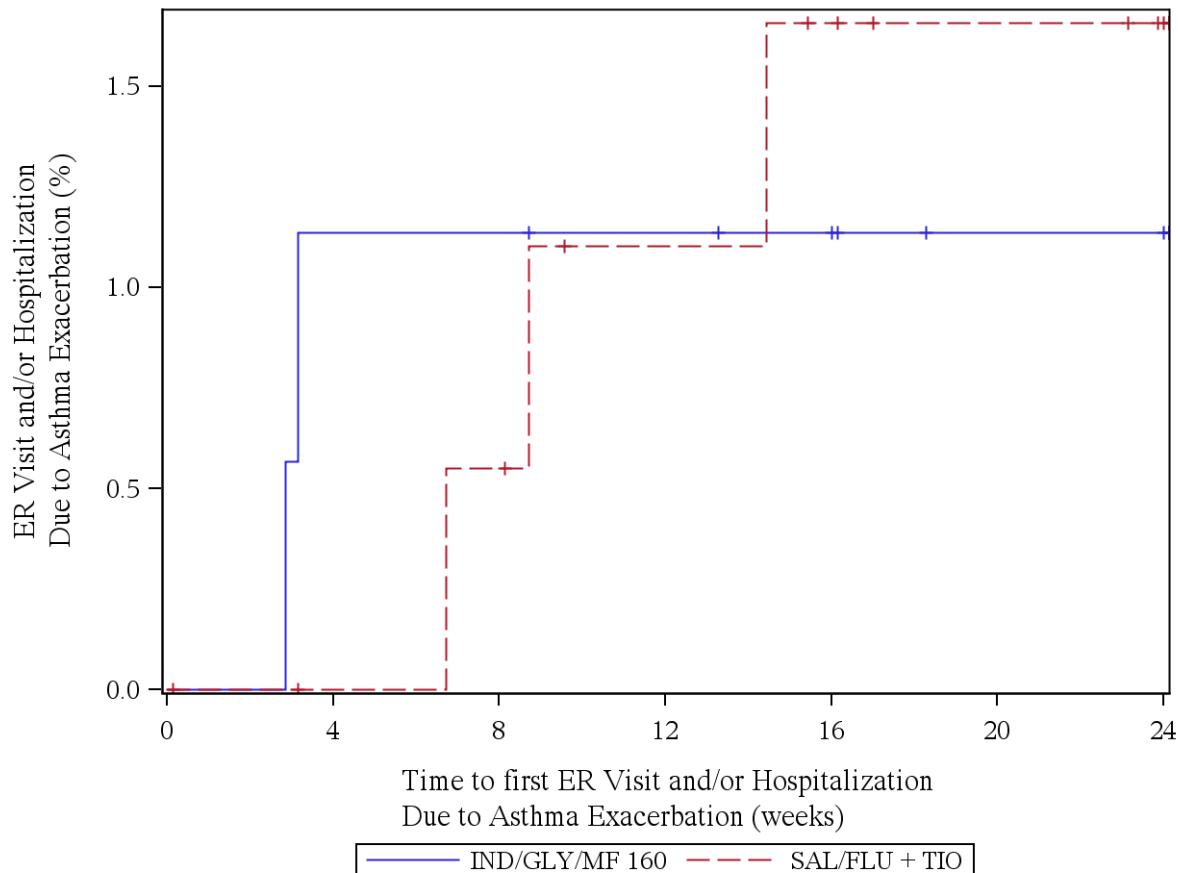


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 4/1, Week 8: 4/1, Week 16: 4/1, Week 24: 4/1

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.23 Kaplan-Meier-Plot: ER Visit and/or Hospitalization Due to Asthma Exacerbation by History of Asthma Exacerbation (FAS)

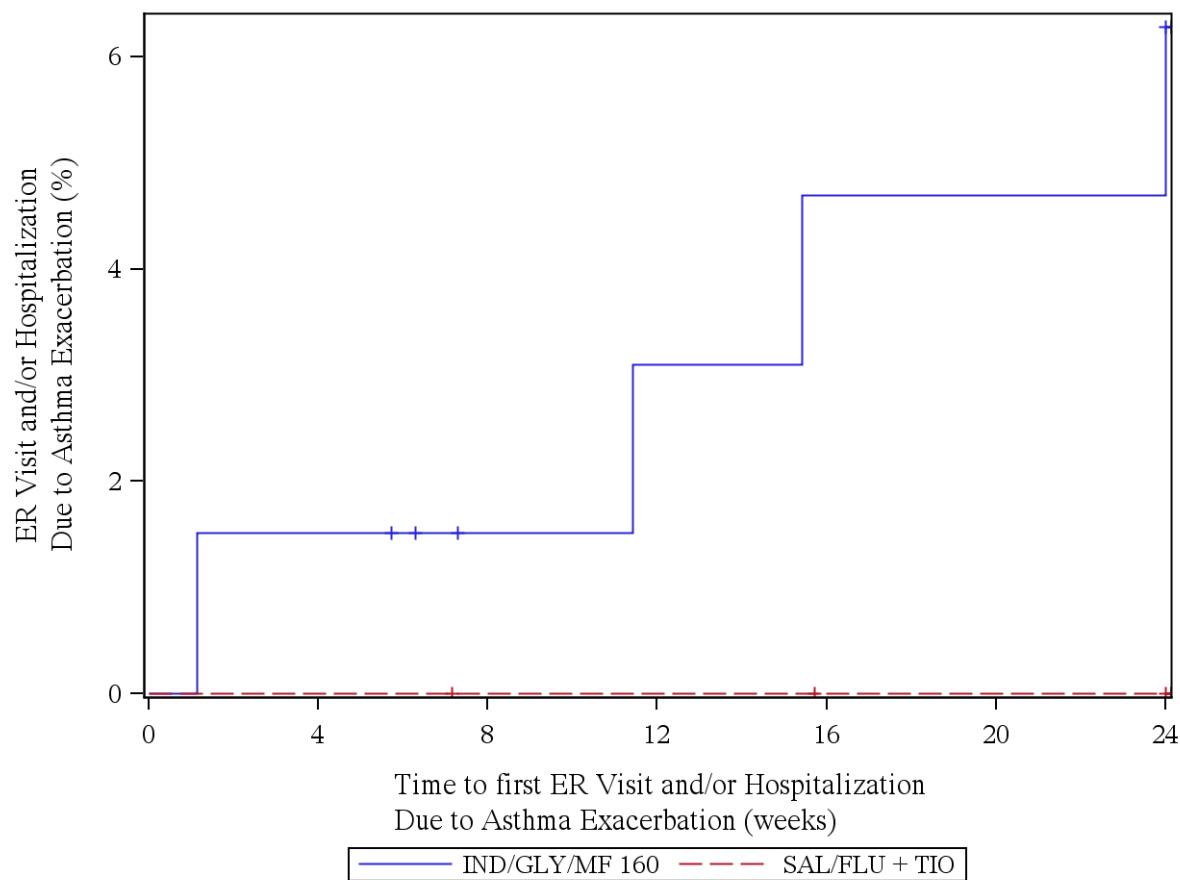
**Figure 11.23.1 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS),
Asthma exacerbations in the 12 months prior to screening = 1**



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 176/184, Week 8: 174/181, Week 16: 171/176, Week 24: 168/171

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

**Figure 11.23.2 ER Visit and/or Hospitalization Due to Asthma Exacerbation (FAS),
Asthma exacerbations in the 12 months prior to screening = ≥ 2**

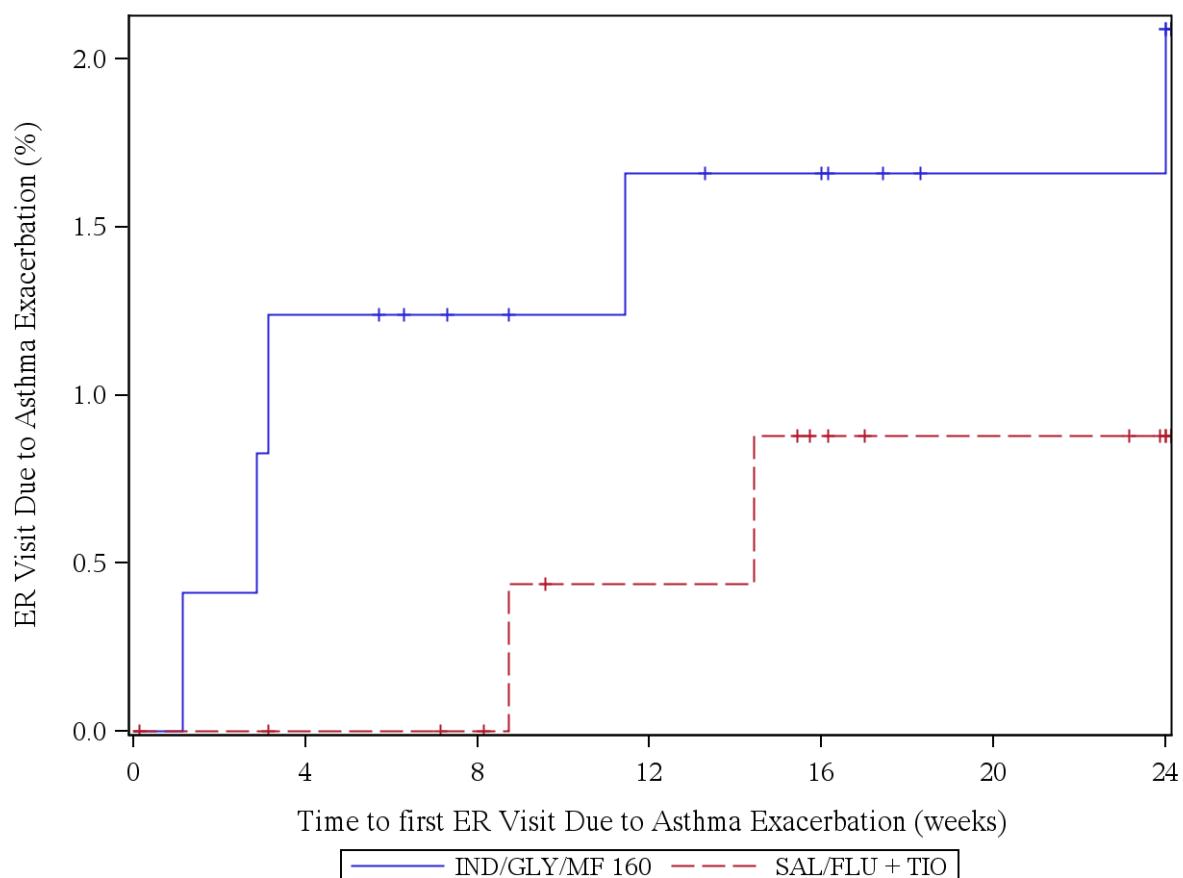


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 66/48, Week 8: 62/47, Week 16: 60/46, Week 24: 58/45

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.25 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation (FAS)

Figure 11.25 ER Visit Due to Asthma Exacerbation (FAS)

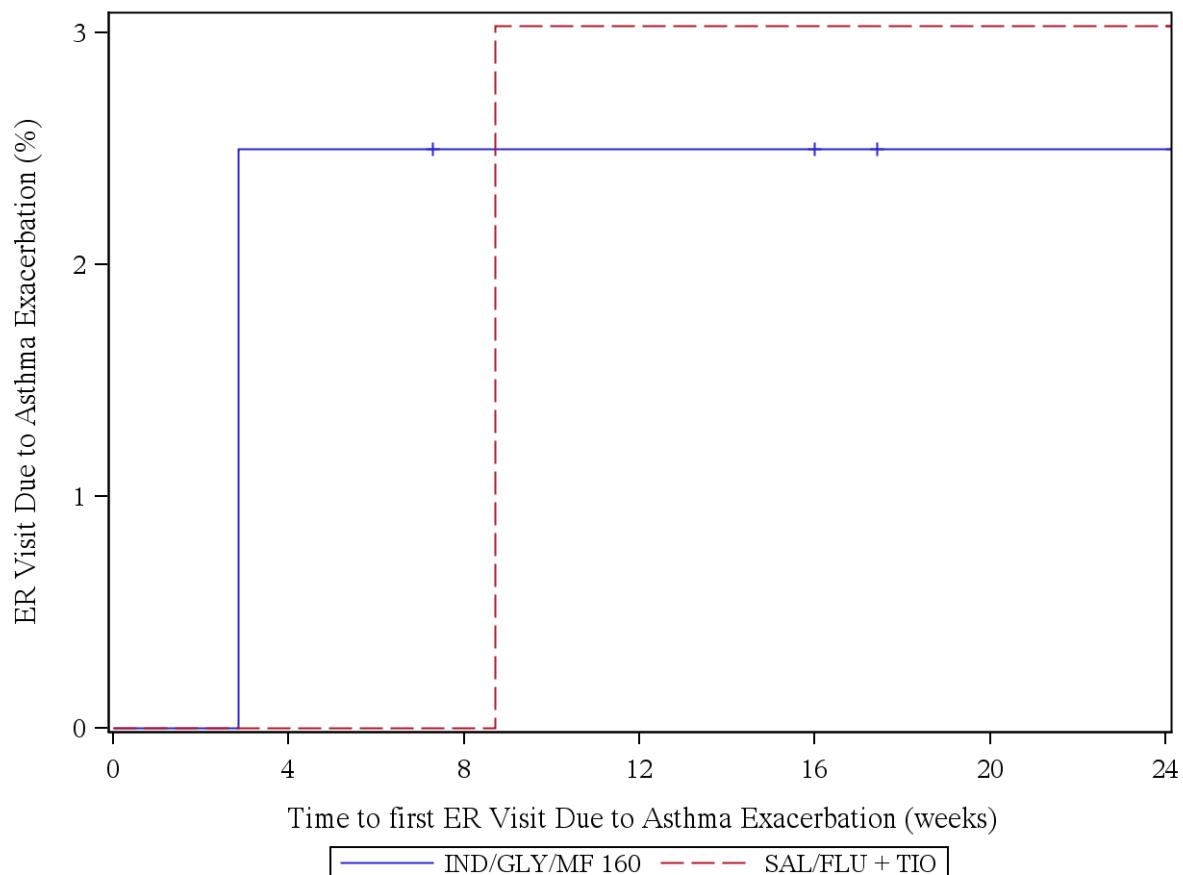


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 242/232, Week 8: 236/229, Week 16: 232/223, Week 24: 226/217

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.26 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation by Age (FAS)

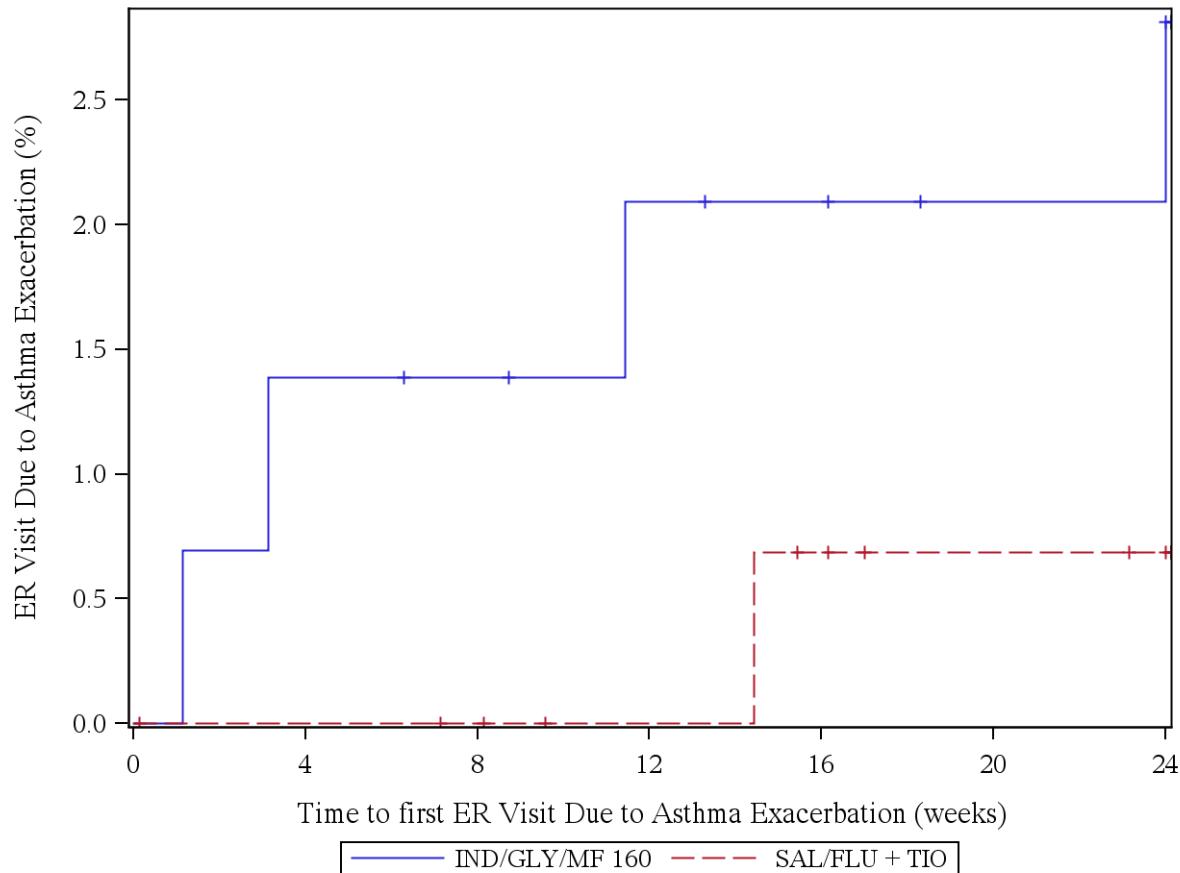
Figure 11.26.1 ER Visit Due to Asthma Exacerbation (FAS), Age = 18-39 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 40/33, Week 8: 38/33, Week 16: 37/32, Week 24: 36/32

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

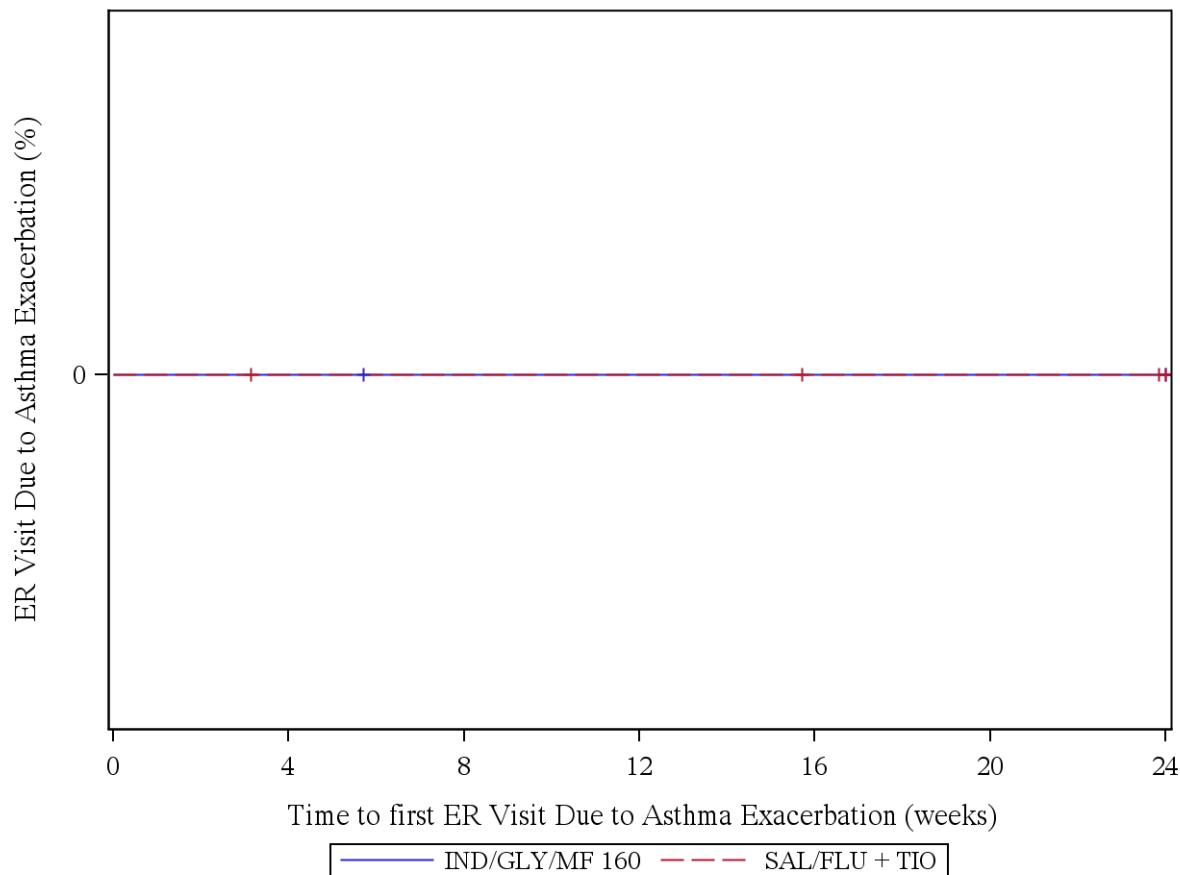
Figure 11.26.2 ER Visit Due to Asthma Exacerbation (FAS), Age = 40-64 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 144/150, Week 8: 141/148, Week 16: 138/144, Week 24: 134/140

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.26.3 ER Visit Due to Asthma Exacerbation (FAS), Age = ≥ 65 years

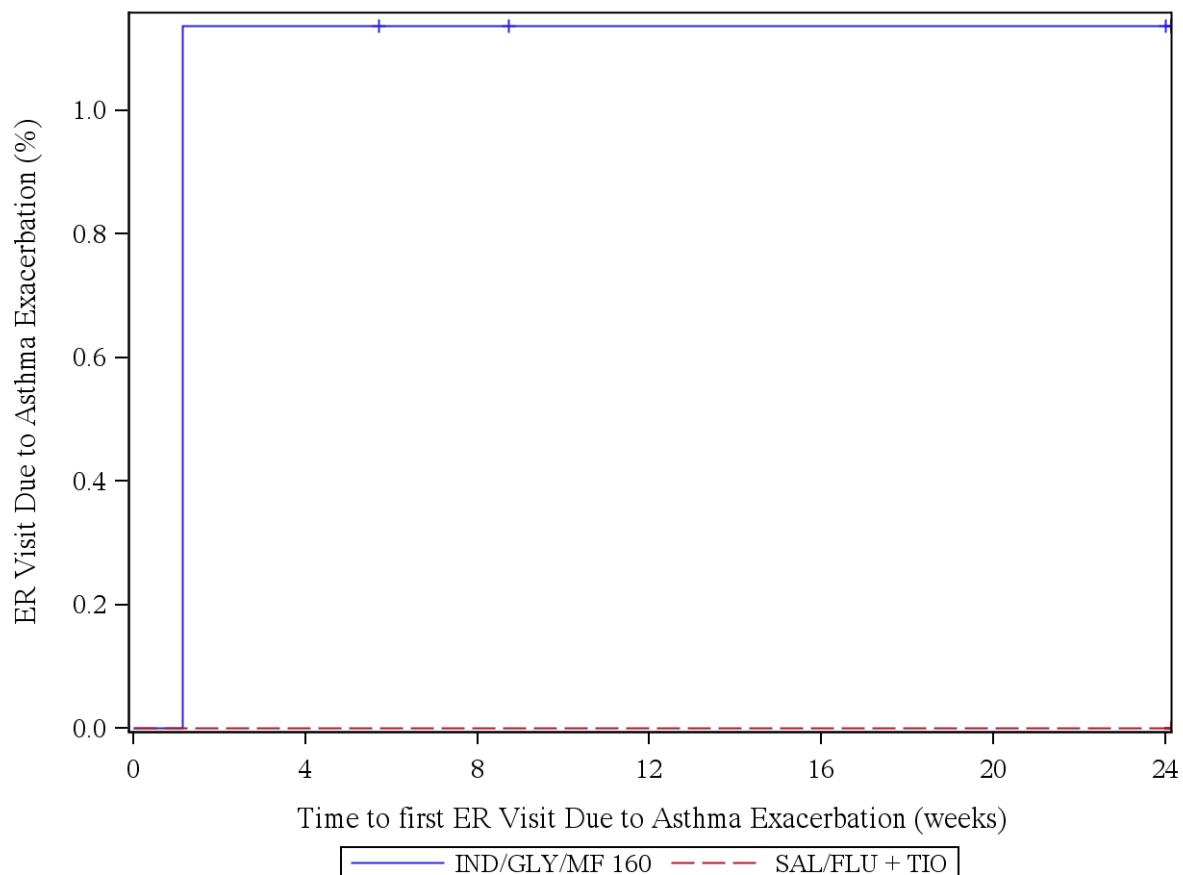


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 58/49, Week 8: 57/48, Week 16: 57/47, Week 24: 56/45

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.27 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation by Gender (FAS)

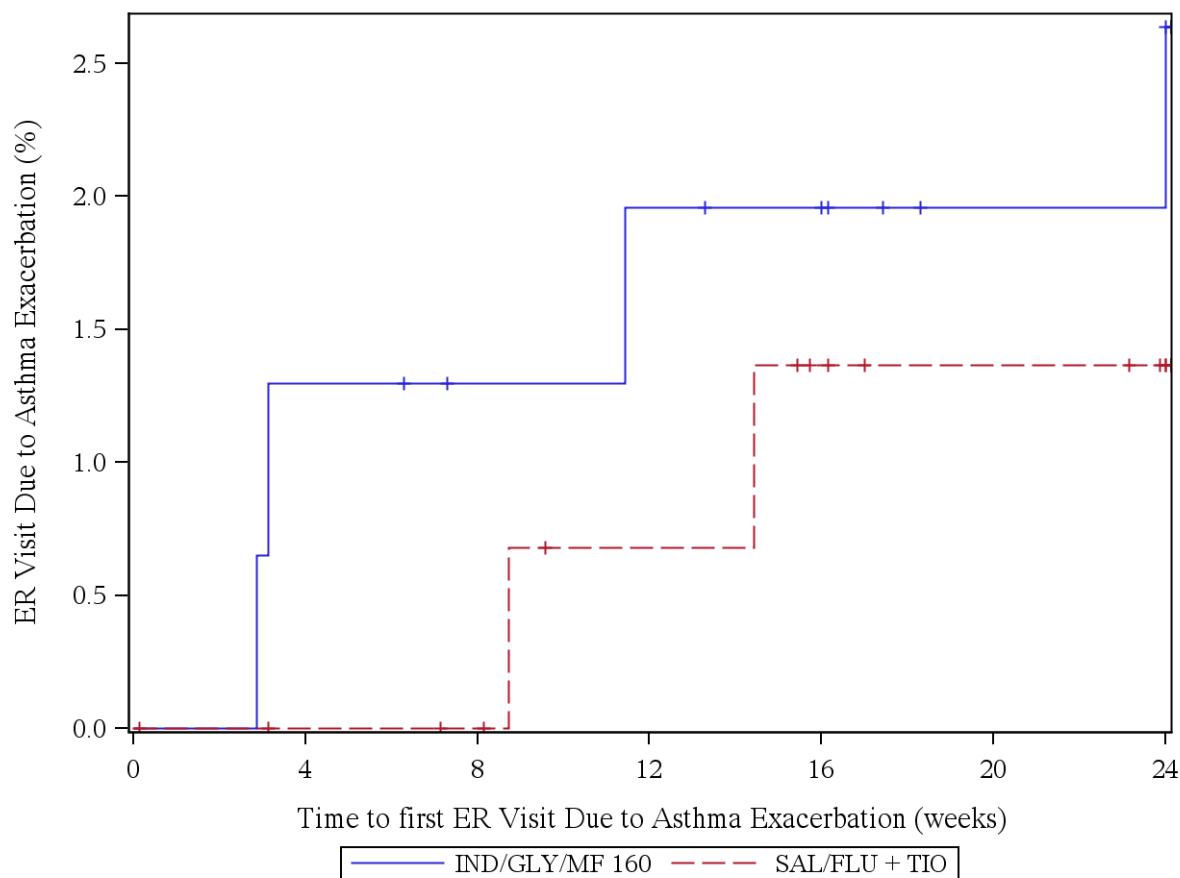
Figure 11.27.1 ER Visit Due to Asthma Exacerbation (FAS), Gender = Male



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 88/81, Week 8: 86/81, Week 16: 85/81, Week 24: 84/81

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.27.2 ER Visit Due to Asthma Exacerbation (FAS), Gender = Female

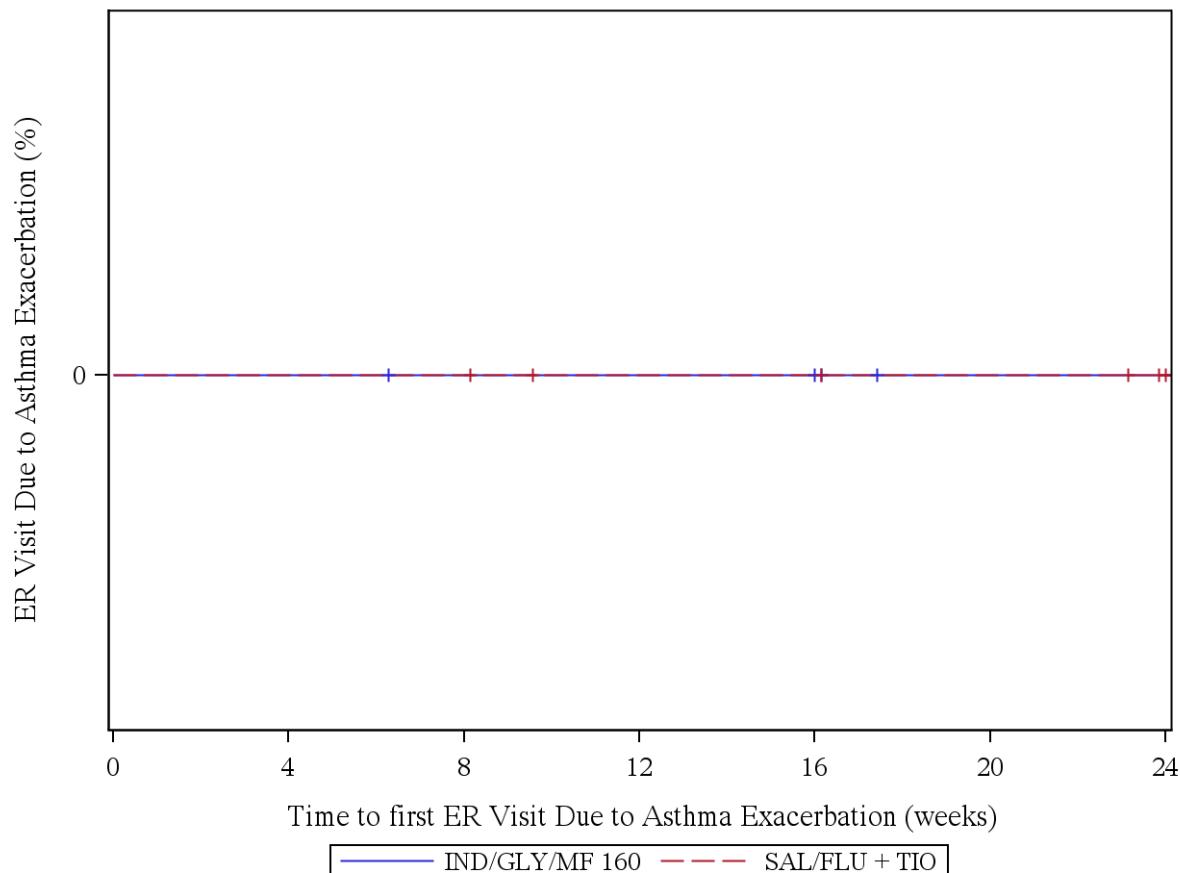


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 154/151, Week 8: 150/148, Week 16: 147/142, Week 24: 142/136

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.28 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation by Region (FAS)

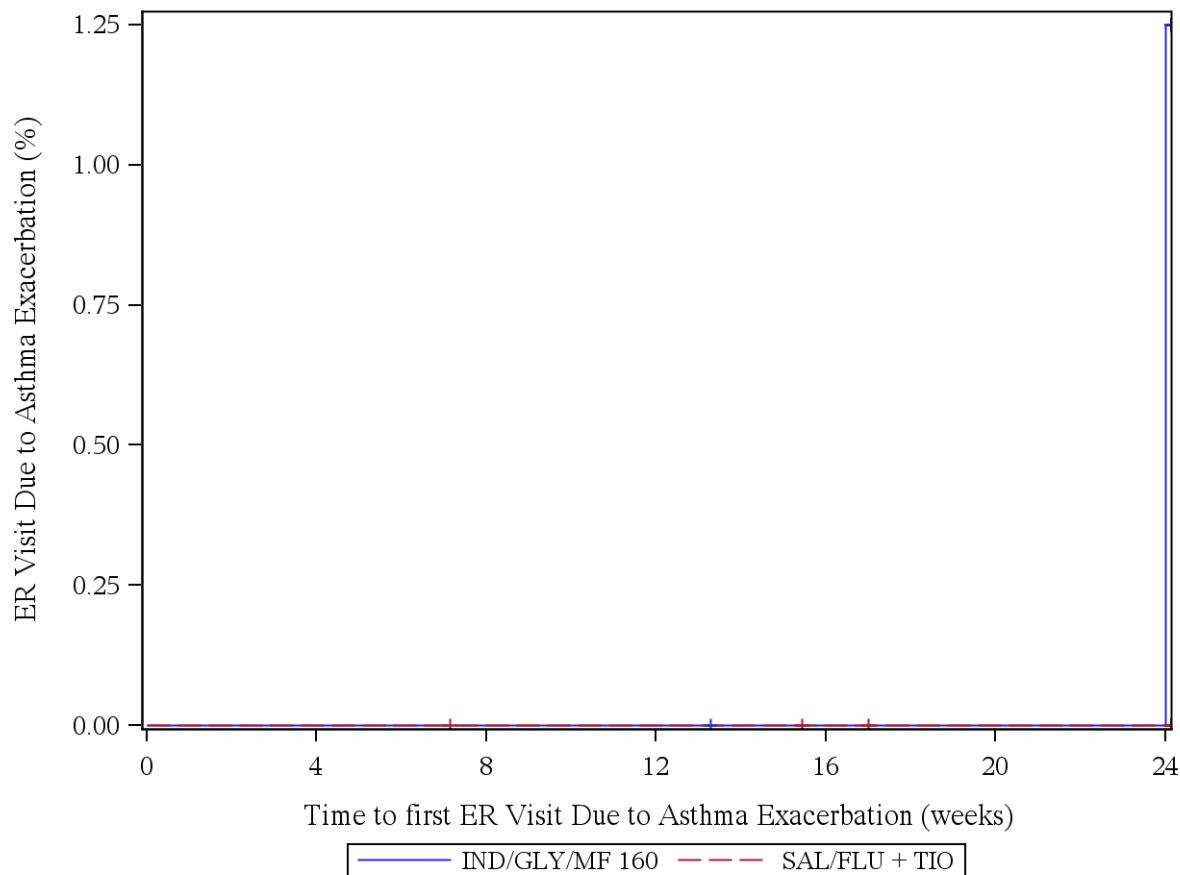
Figure 11.28.1 ER Visit Due to Asthma Exacerbation (FAS), Region = Asia



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 53/59, Week 8: 52/59, Week 16: 51/57, Week 24: 49/53

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

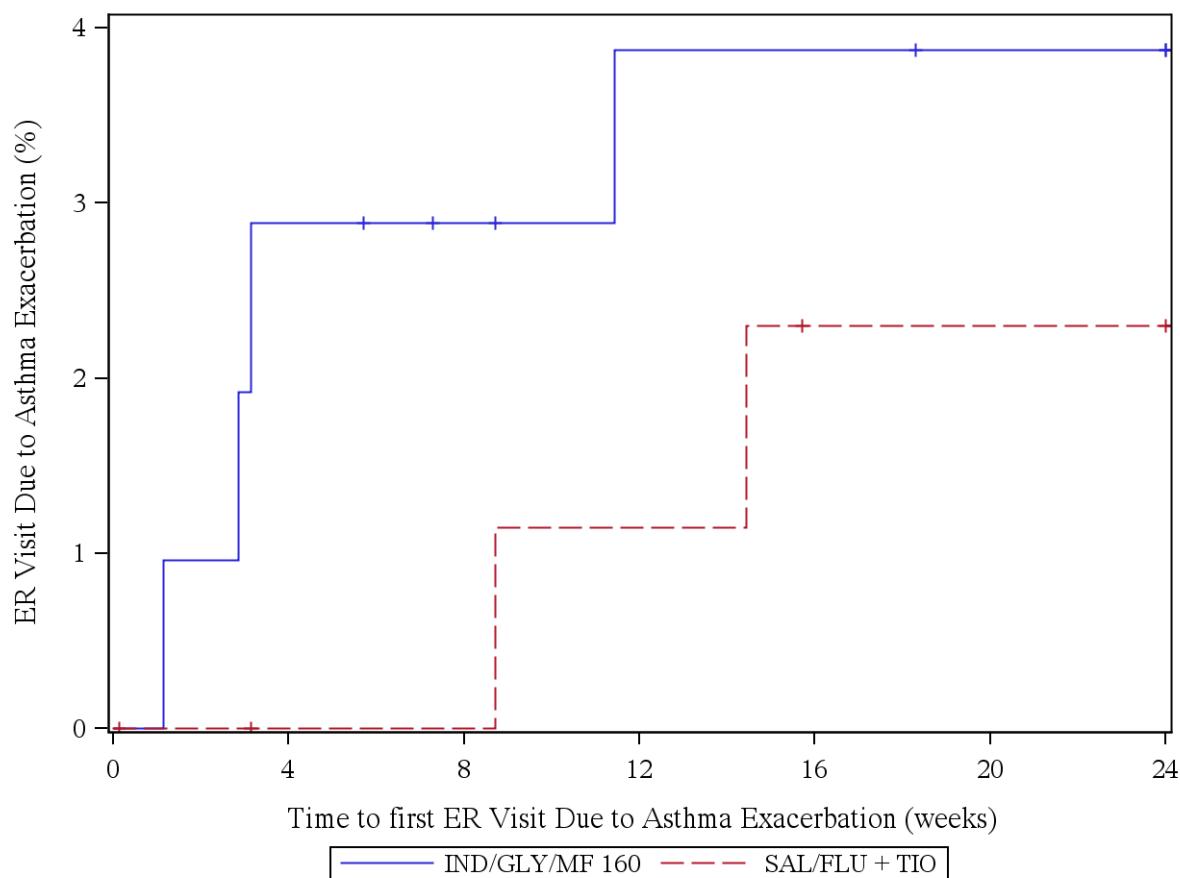
Figure 11.28.2 ER Visit Due to Asthma Exacerbation (FAS), Region = Europe



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 81/83, Week 8: 81/82, Week 16: 80/81, Week 24: 79/80

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

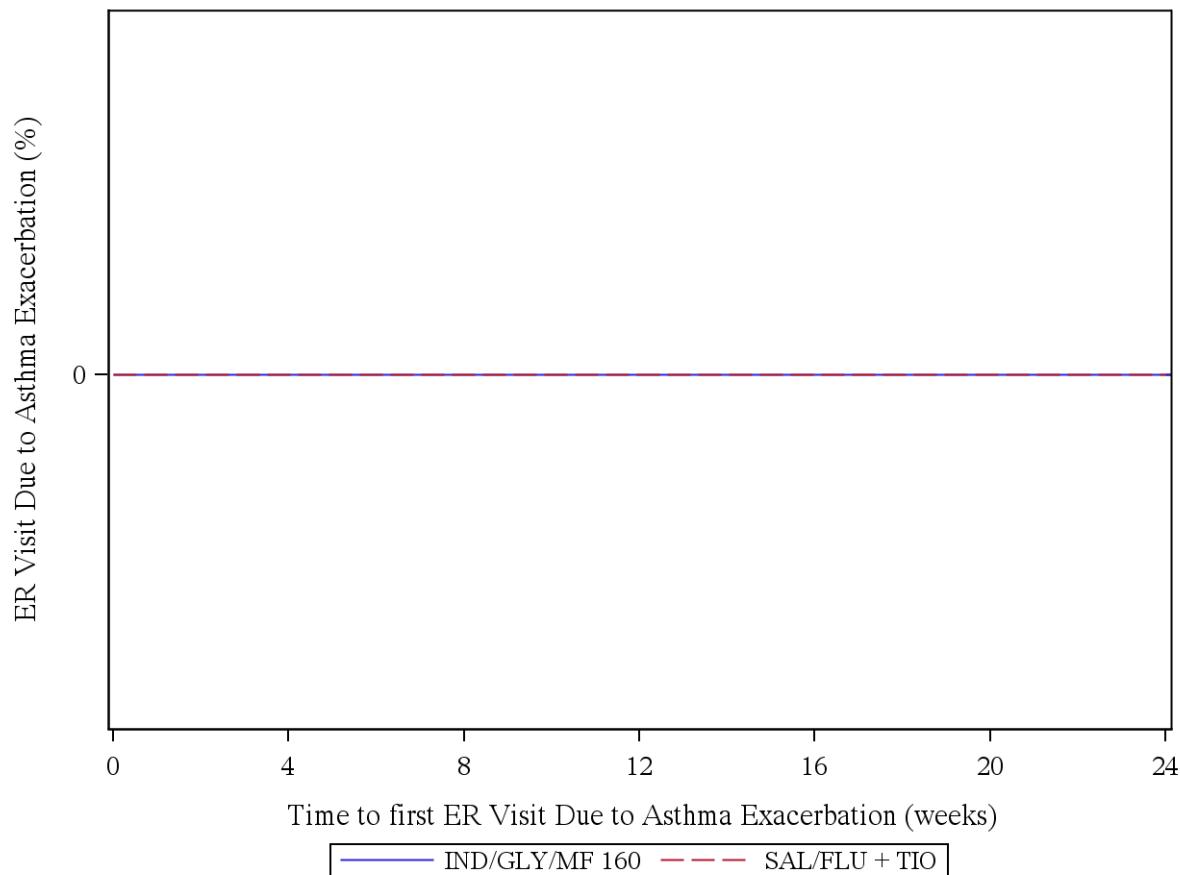
Figure 11.28.3 ER Visit Due to Asthma Exacerbation (FAS), Region = Latin America



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 104/89, Week 8: 99/87, Week 16: 97/84, Week 24: 94/83

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.28.4 ER Visit Due to Asthma Exacerbation (FAS), Region = Others

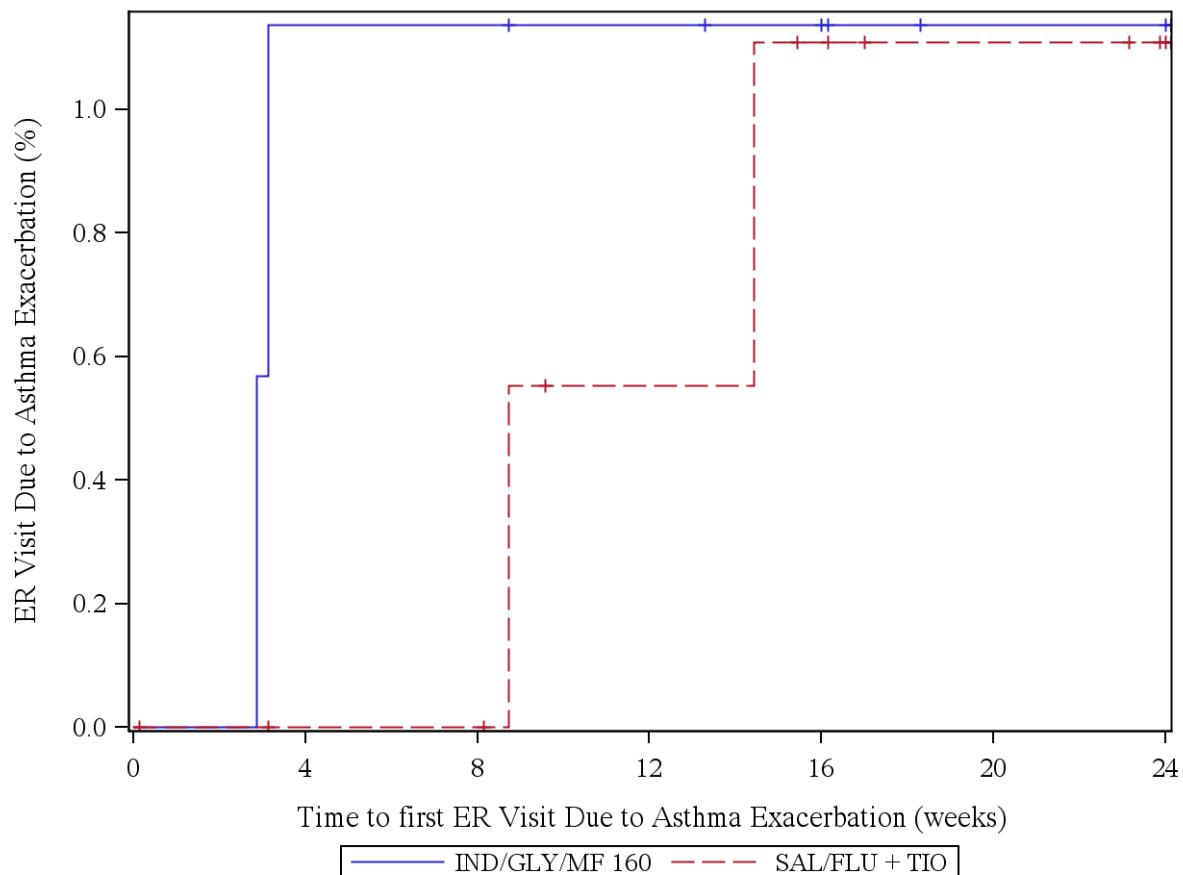


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 4/1, Week 8: 4/1, Week 16: 4/1, Week 24: 4/1

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.29 Kaplan-Meier-Plot: ER Visit Due to Asthma Exacerbation by History of Asthma Exacerbation (FAS)

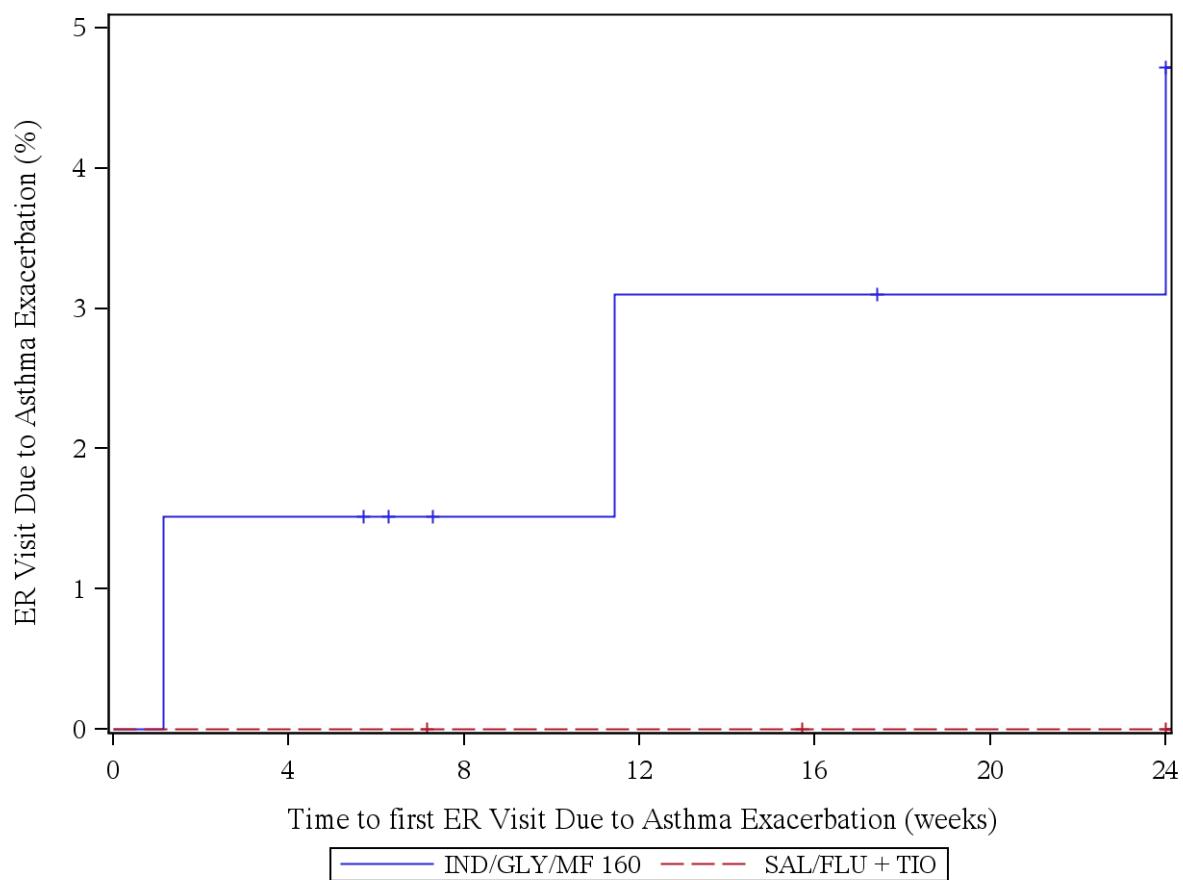
Figure 11.29.1 ER Visit Due to Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 176/184, Week 8: 174/182, Week 16: 171/177, Week 24: 168/172

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.29.2 ER Visit Due to Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = ≥ 2

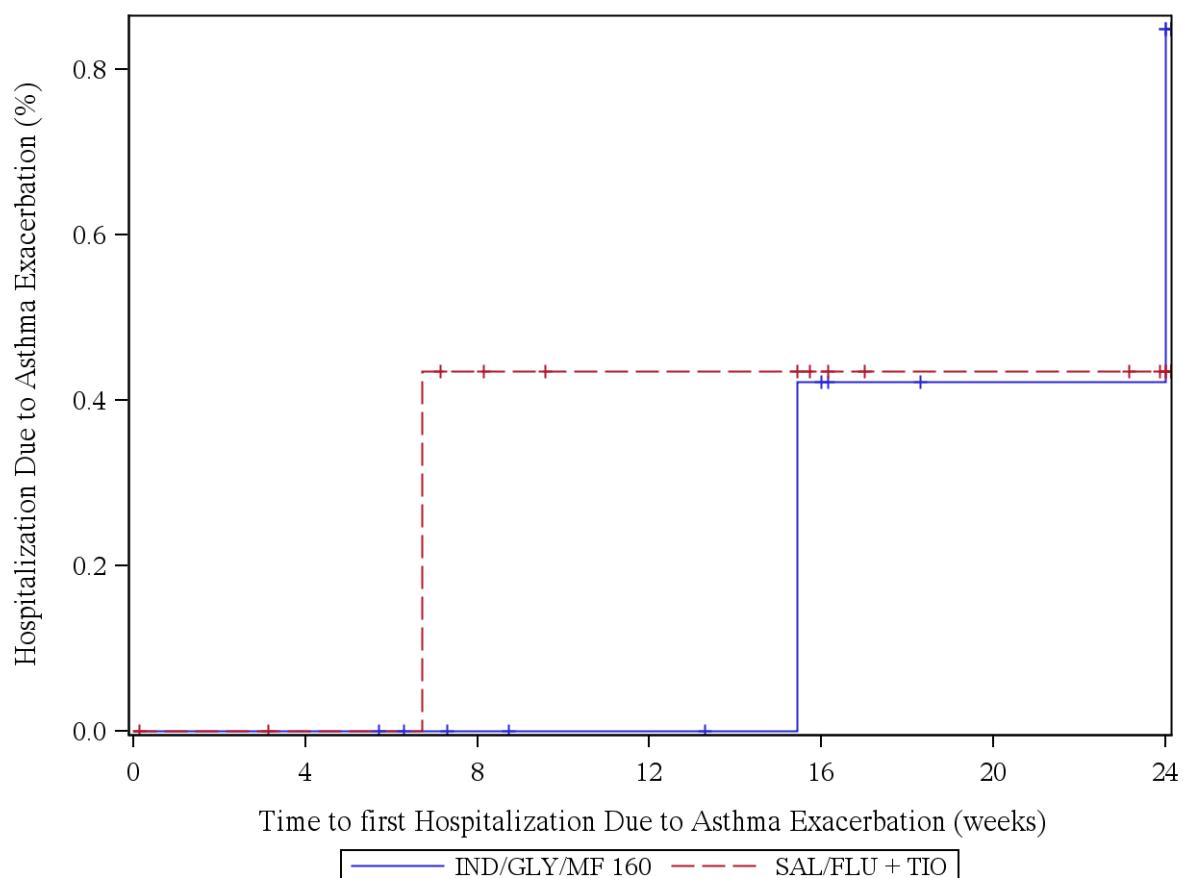


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 66/48, Week 8: 62/47, Week 16: 61/46, Week 24: 58/45

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.31 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation (FAS)

Figure 11.31 Hospitalization Due to Asthma Exacerbation (FAS)

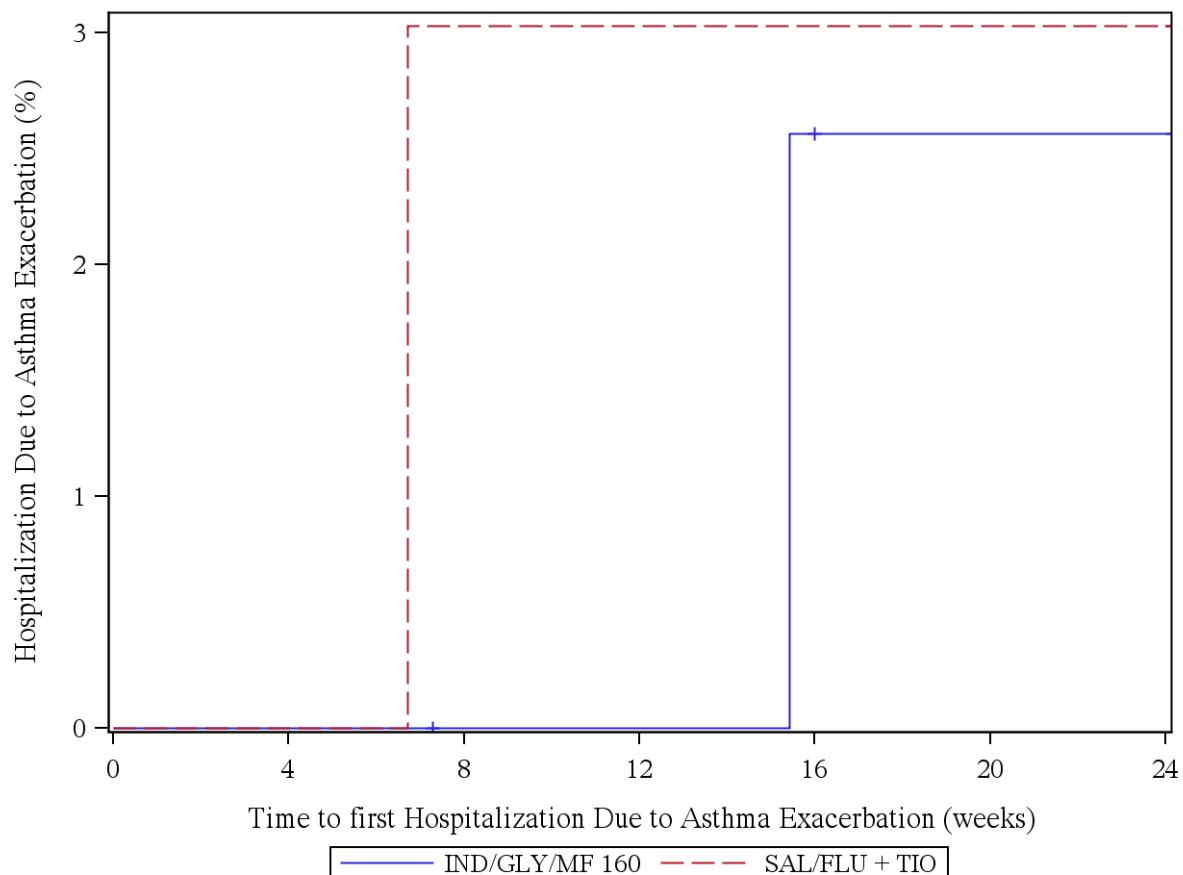


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 242/232, Week 8: 239/228, Week 16: 235/224, Week 24: 230/218

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.32 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation by Age (FAS)

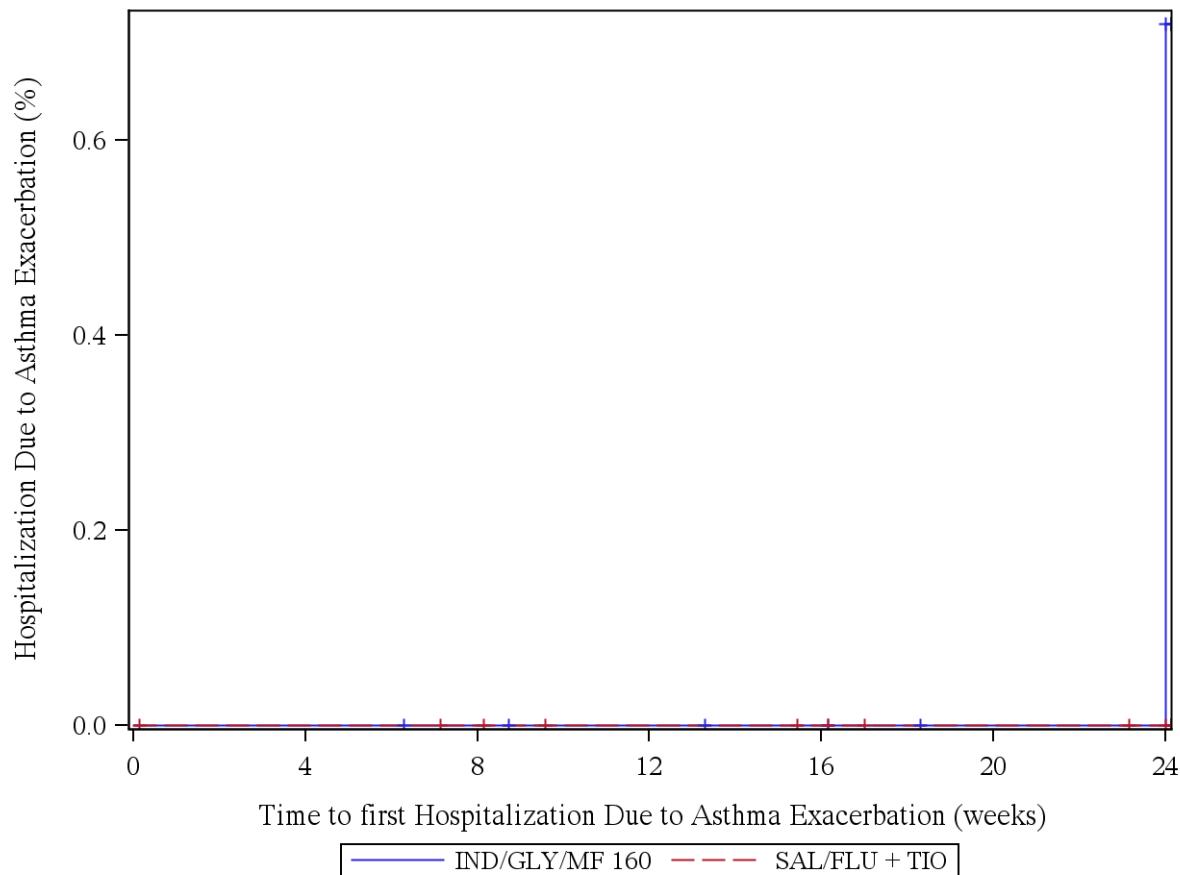
Figure 11.32.1 Hospitalization Due to Asthma Exacerbation (FAS), Age = 18-39 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 40/33, Week 8: 39/32, Week 16: 37/32, Week 24: 37/32

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

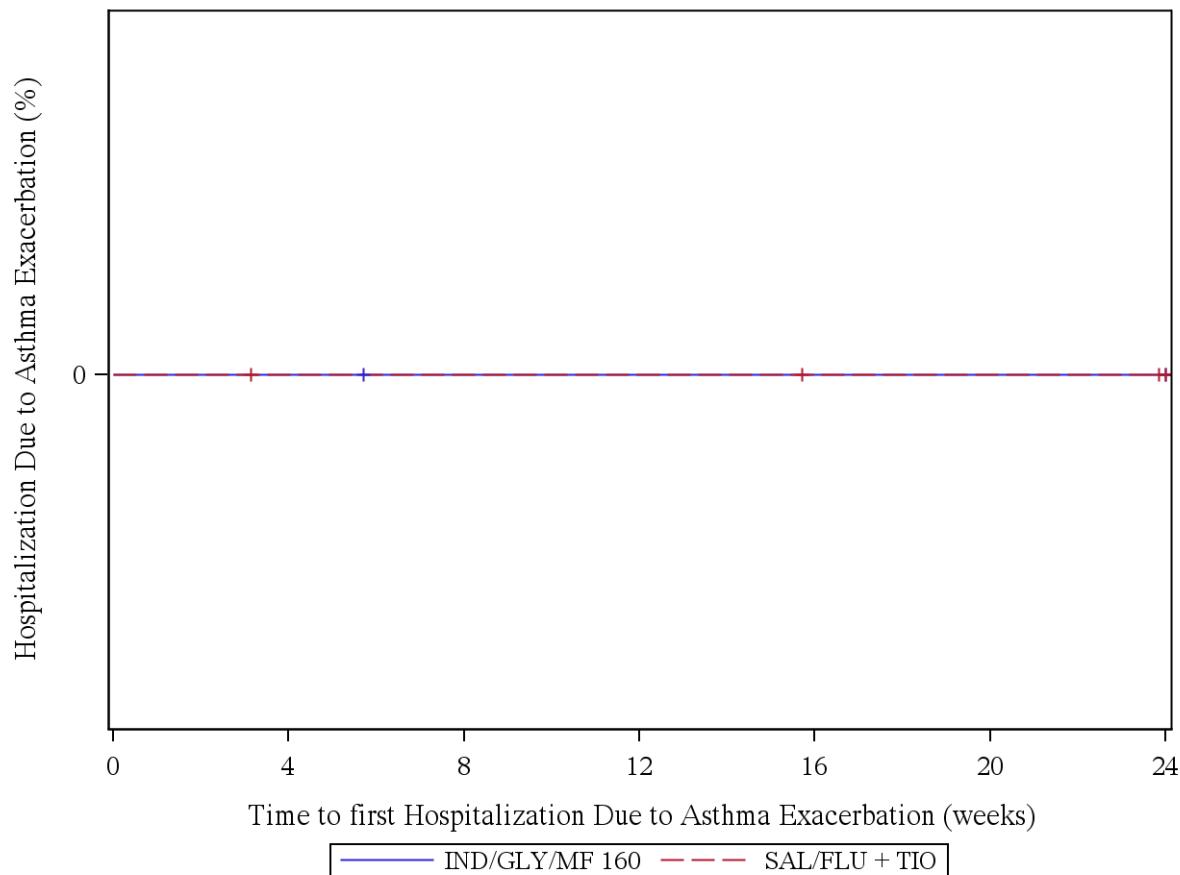
Figure 11.32.2 Hospitalization Due to Asthma Exacerbation (FAS), Age = 40-64 years



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 144/150, Week 8: 143/148, Week 16: 141/145, Week 24: 137/141

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.32.3 Hospitalization Due to Asthma Exacerbation (FAS), Age = ≥ 65 years

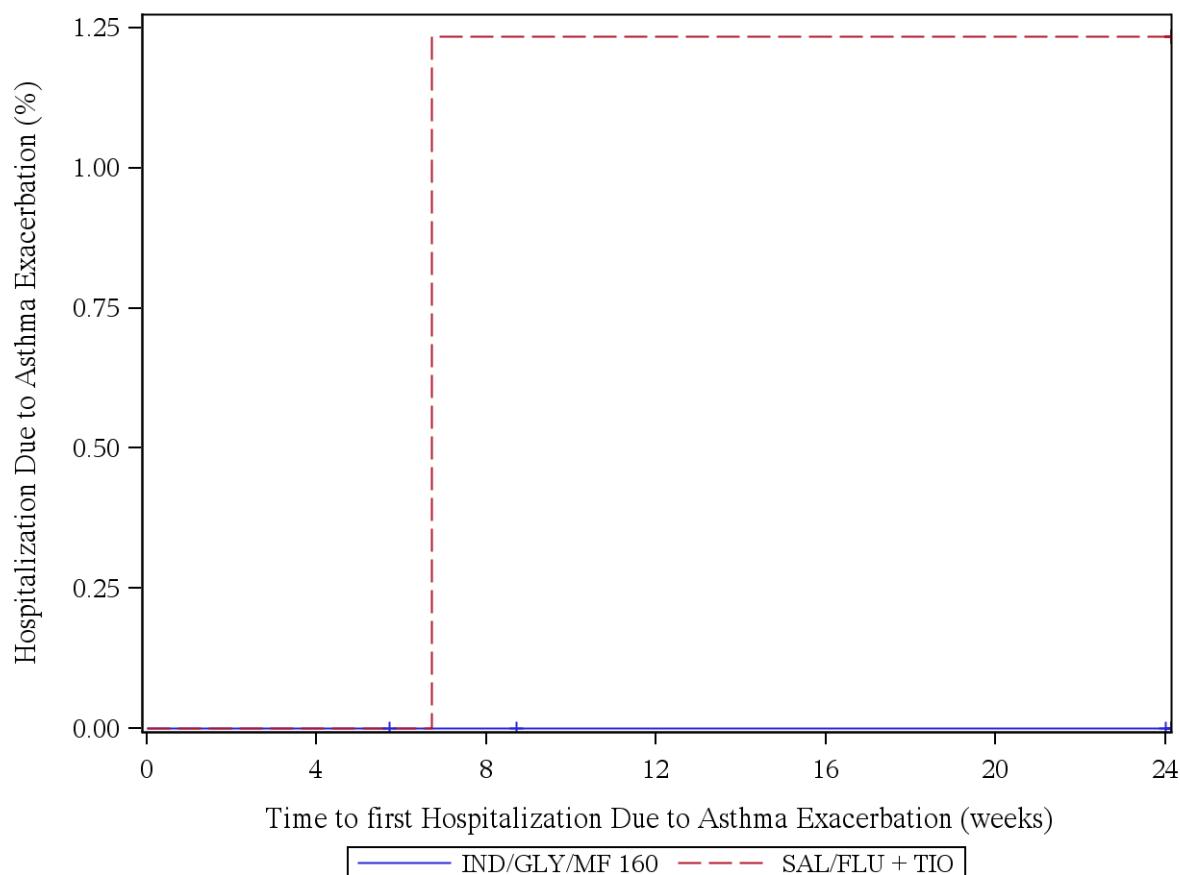


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 58/49, Week 8: 57/48, Week 16: 57/47, Week 24: 56/45

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.33 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation by Gender (FAS)

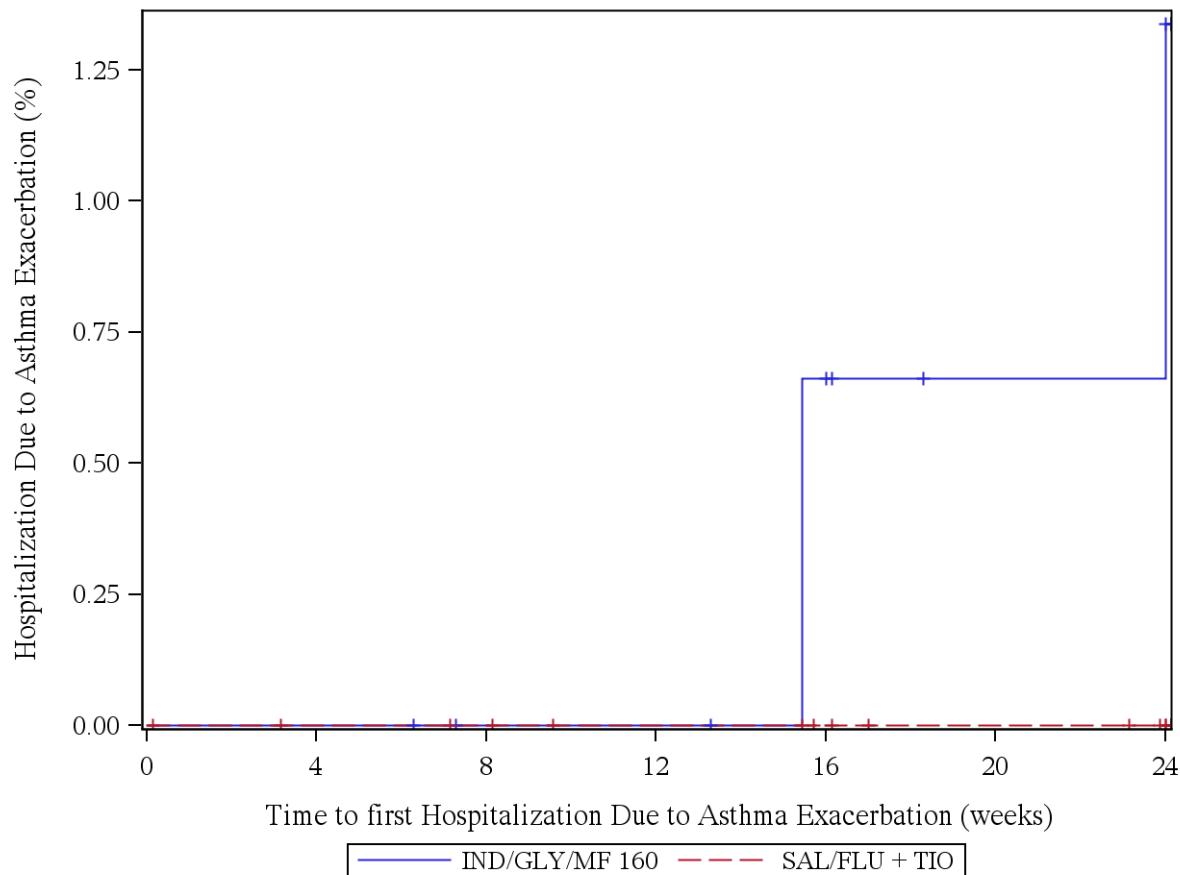
Figure 11.33.1 Hospitalization Due to Asthma Exacerbation (FAS), Gender = Male



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 88/81, Week 8: 87/80, Week 16: 86/80, Week 24: 85/80

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.33.2 Hospitalization Due to Asthma Exacerbation (FAS), Gender = Female

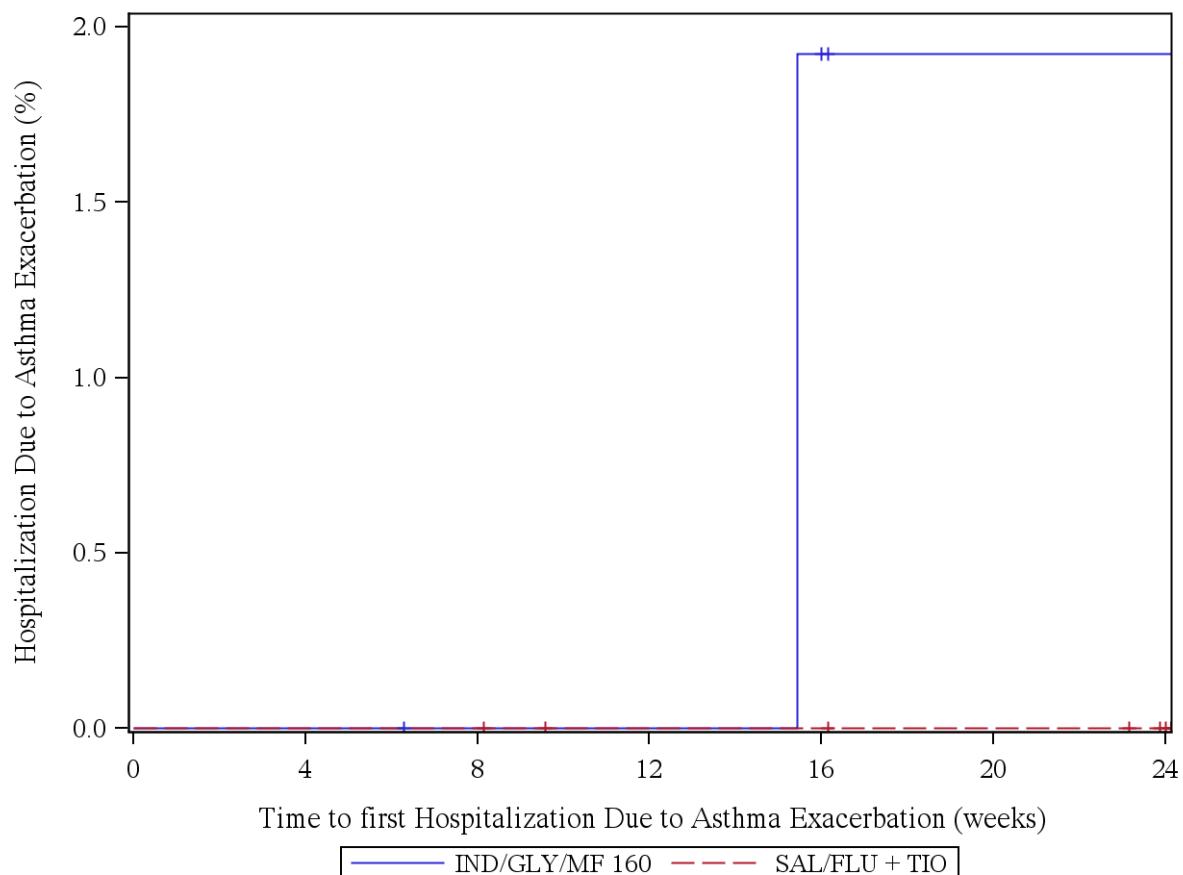


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 154/151, Week 8: 152/148, Week 16: 149/144, Week 24: 145/138

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.34 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation by Region (FAS)

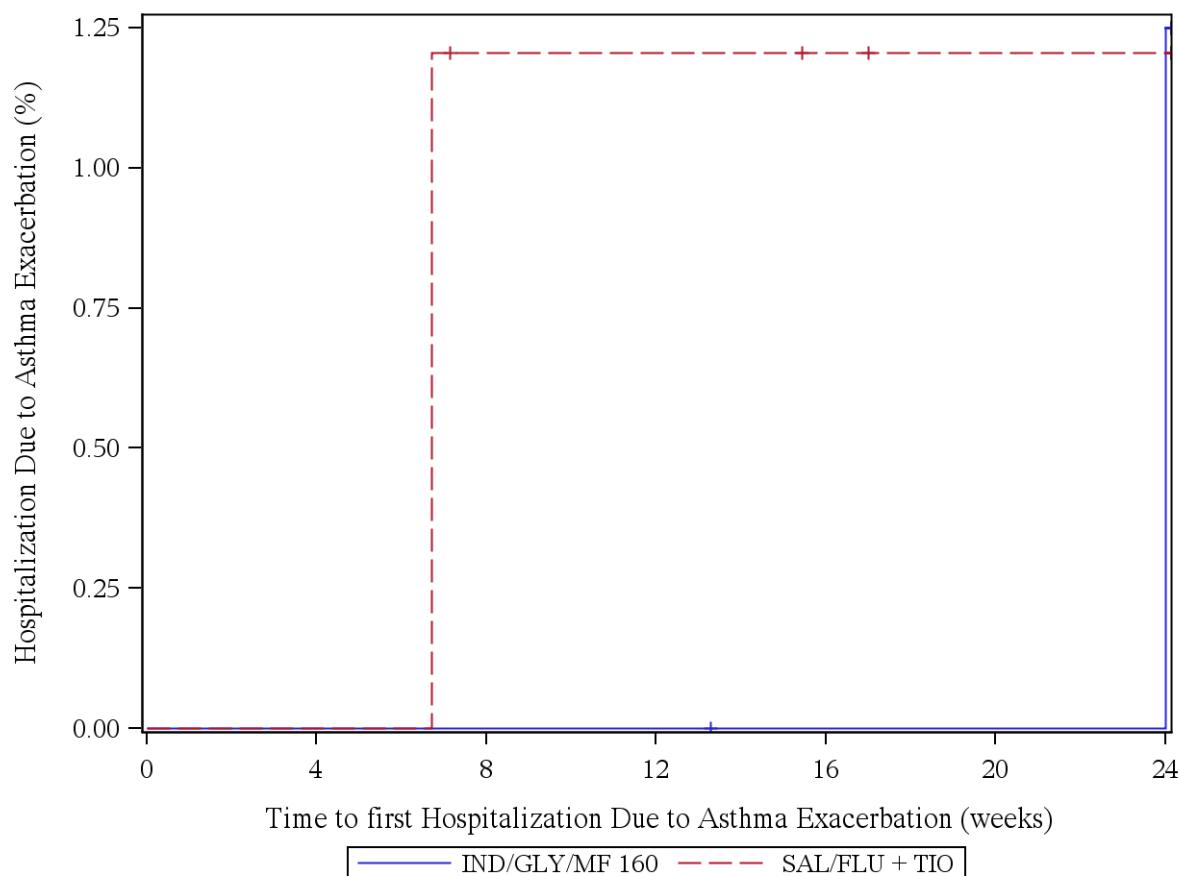
Figure 11.34.1 Hospitalization Due to Asthma Exacerbation (FAS), Region = Asia



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 53/59, Week 8: 52/59, Week 16: 50/57, Week 24: 49/53

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

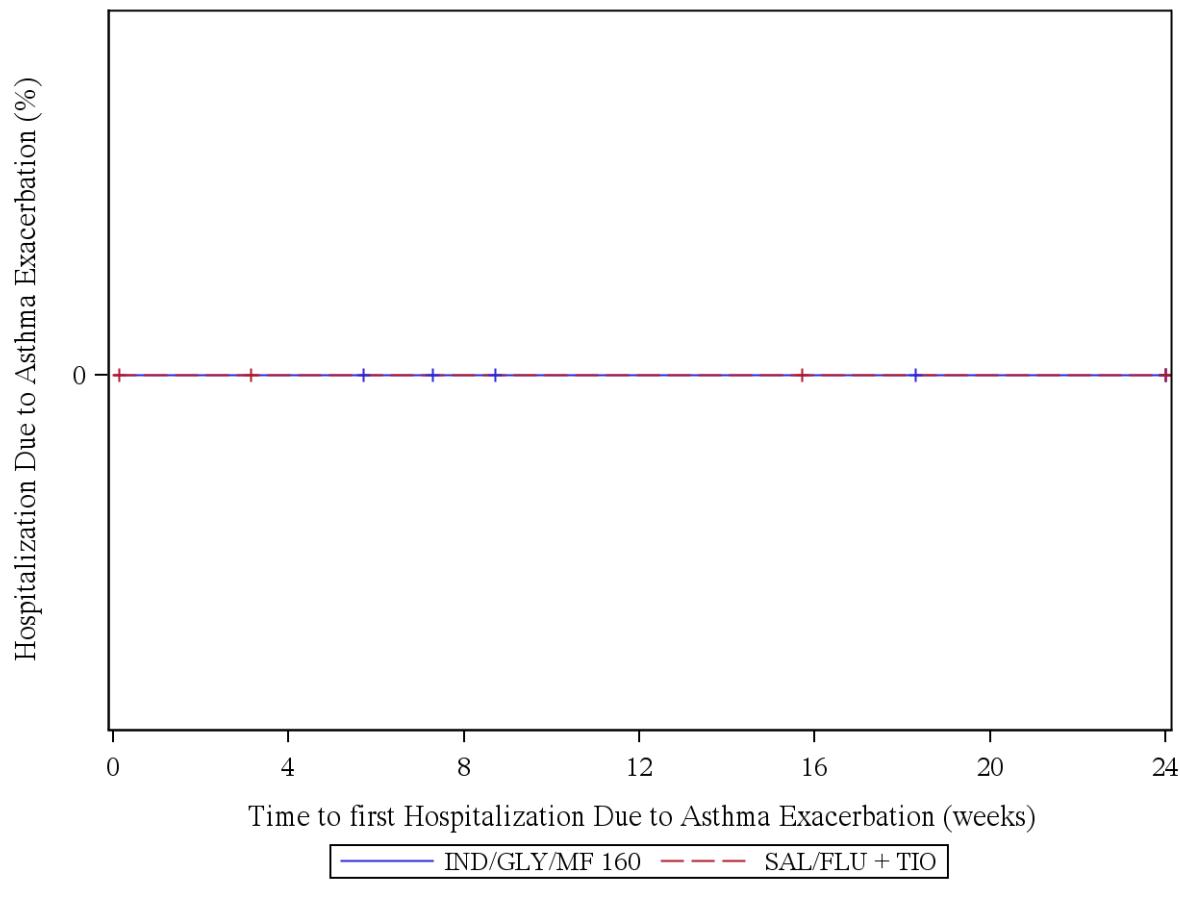
Figure 11.34.2 Hospitalization Due to Asthma Exacerbation (FAS), Region = Europe



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 81/83, Week 8: 81/81, Week 16: 80/80, Week 24: 79/79

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

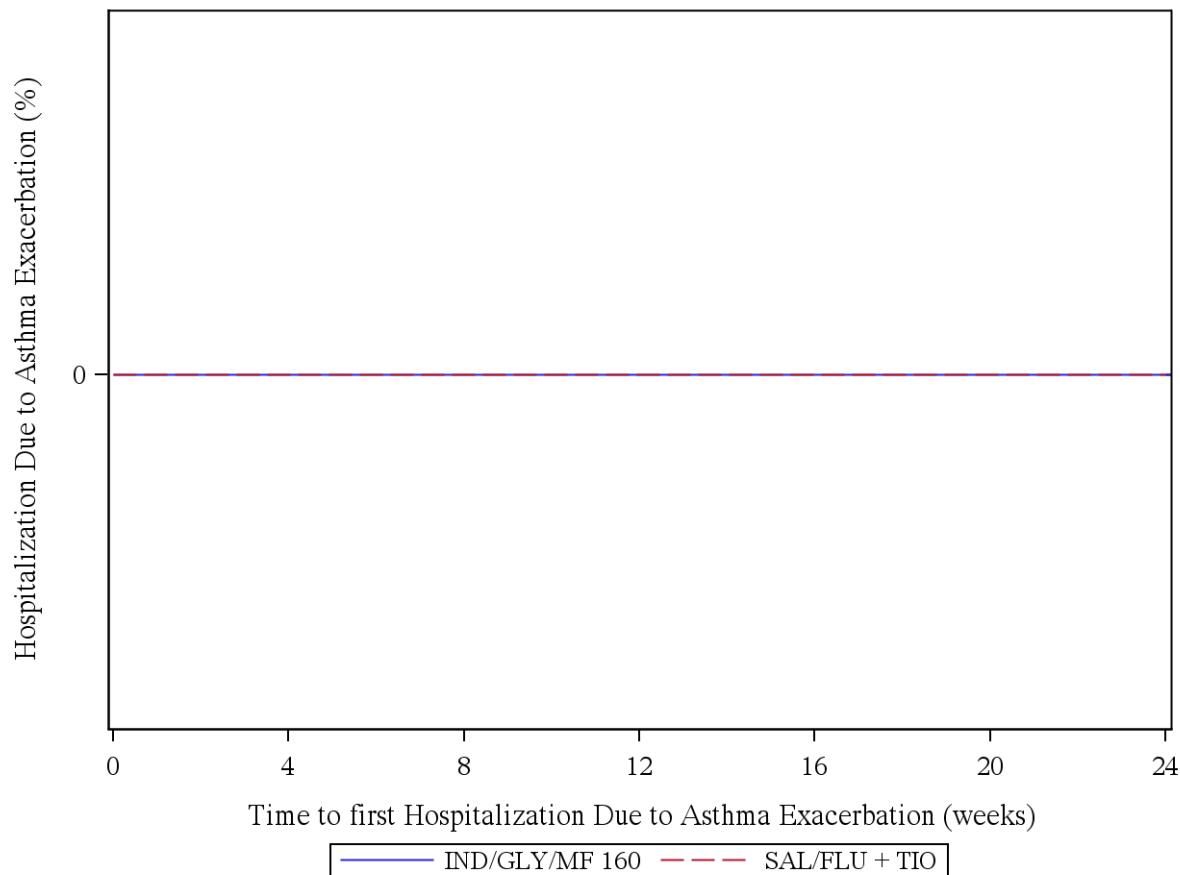
Figure 11.34.3 Hospitalization Due to Asthma Exacerbation (FAS), Region = Latin America



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 104/89, Week 8: 102/87, Week 16: 101/86, Week 24: 98/85

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

Figure 11.34.4 Hospitalization Due to Asthma Exacerbation (FAS), Region = Others

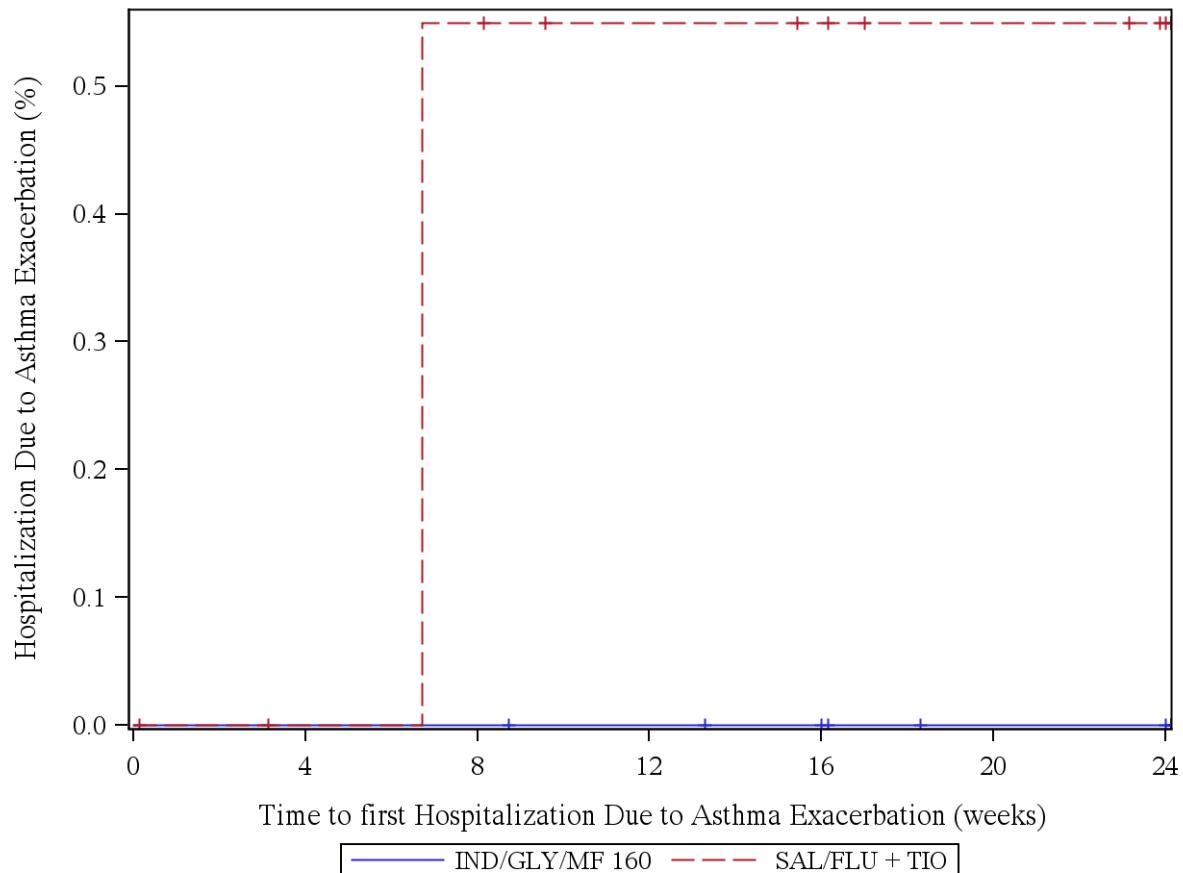


Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 4/1, Week 8: 4/1, Week 16: 4/1, Week 24: 4/1

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

11.35 Kaplan-Meier-Plot: Hospitalization Due to Asthma Exacerbation by History of Asthma Exacerbation (FAS)

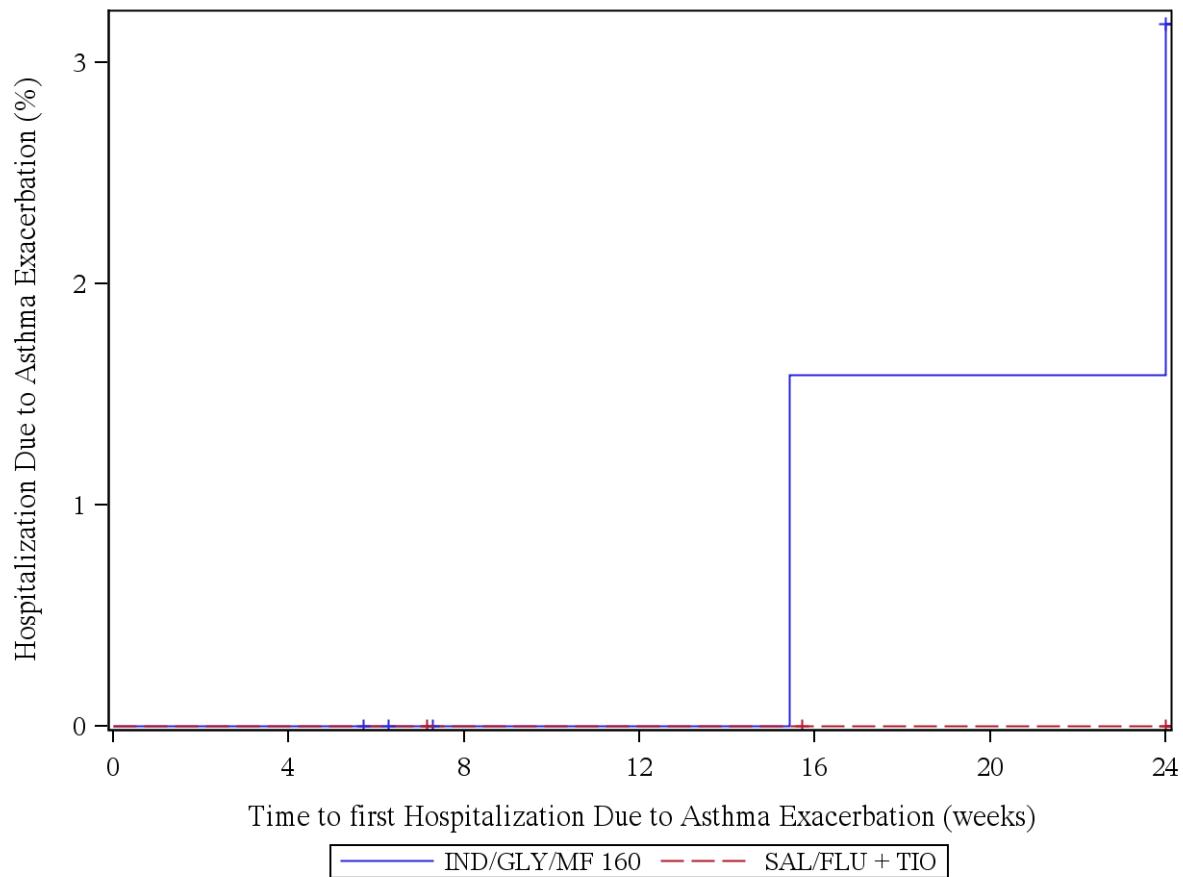
Figure 11.35.1 Hospitalization Due to Asthma Exacerbation (FAS), Asthma exacerbations in the 12 months prior to screening = 1



Patients at risk (IND/GLY/MF 160 / SAL/FLU + TIO): Week 0: 176/184, Week 8: 176/181, Week 16: 173/178, Week 24: 170/173

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"

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: 66/48, Week 8: 63/47, Week 16: 62/46, Week 24: 60/45

Analysis population: B2306 FAS subpopulation "high-dose ICS/LABA"