ERS Investor & Analyst Event

Munich
Tuesday 9th September 2014

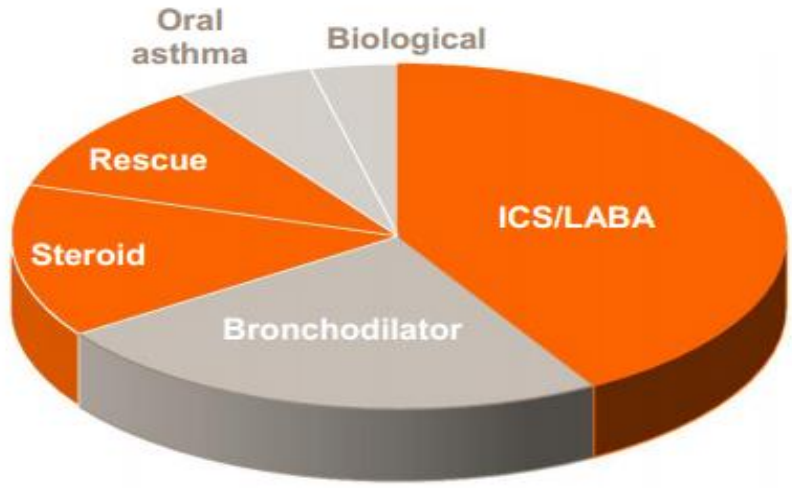
Darrell Baker
SVP, Global Head of Respiratory

Agenda

GSK's Respiratory Portfolio	Darrell Baker, Global Head of Respiratory at GSK	13:45 – 14:00
Eosinophils Research in COPD	Professor Neil Barnes, Respiratory Franchise Medical Head at GSK	14:00 – 14:10
Eosinophils – Clinical Experience in Severe Asthma	Professor Ian Pavord, University of Oxford	14:10 – 14:25
Mepolizumab Phase III data in Severe Asthma	Steven Yancey, Medicine Development Leader at GSK	14:25 – 14:45
Q&A		14:45 – 15:45

Respiratory portfolio in transition – new portfolio provides platform for continued market leadership

£21bn global respiratory market



33% GSK share of global market

Anoro Ellipta allows access to £4.9bn bronchodilator market

Breo Ellipta approved & launched
Anoro Ellipta approved & launched
Incruse Ellipta approved
Arnuity Ellipta approved

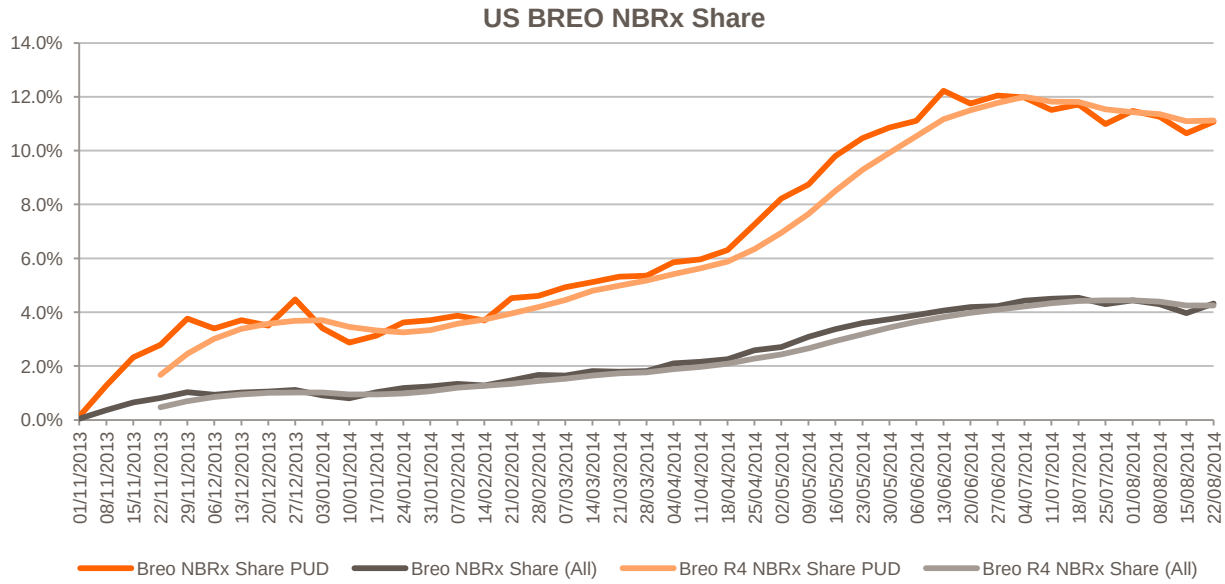
5 additional products in late stage development

- **mepolizumab**
- **ICS/LABA/LAMA (closed triple)**
- **VI monotherapy**
- **ICS/LAMA**
- **MABA**

Source: GSK R3 Model based on IMS Health June 2014

Breo Ellipta / Relvar Ellipta launches underway

- Approved in over 50 markets globally
- Launched in 19 markets including US (for COPD only), Japan (asthma only), UK, Germany, Denmark, Sweden, Mexico, Chile, Brazil.



US access building as at July:

- Commercial: ~50%
- Medicare Part D: ~70%

US market shares (42 weeks to 22 Aug14)

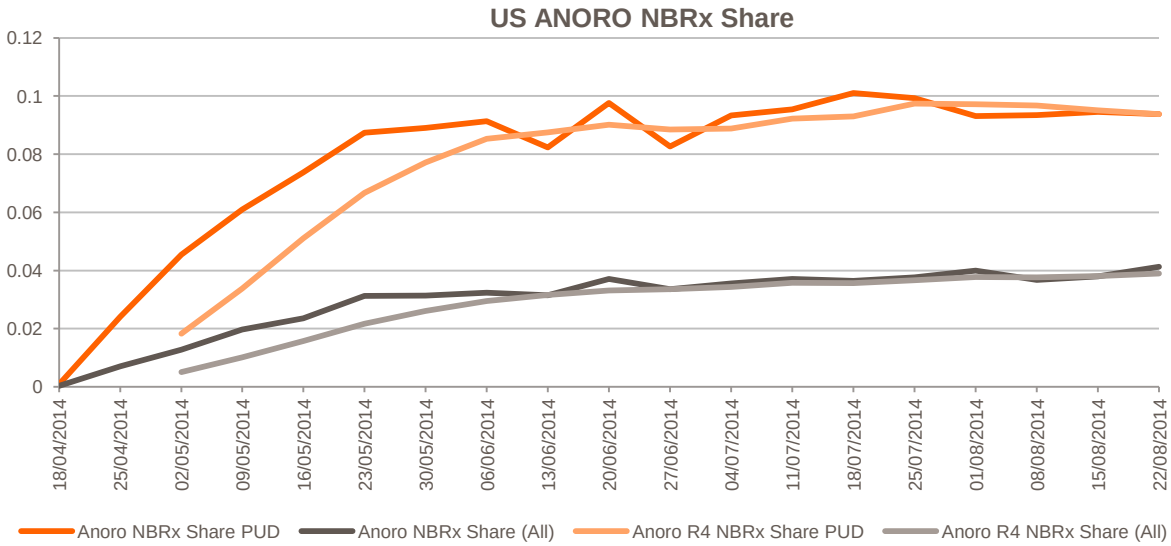
- NBRx is 4.3% overall and 11.1% for pulmonologists
- TRx is 1.18%

- BREO ELLIPTA filed in US for asthma in June 2014
- SUMMIT recruitment complete; data now expected in 2015

Anoro Ellipta launches underway

The first once-daily dual bronchodilator in US for treatment of COPD

- Approved in 38 markets globally
- Launched in 8 markets including US, Canada, UK, Germany, Chile, Denmark & Japan



US access building as at July:

- Commercial: ~75%
- Medicare Part D: ~30%

US market shares (18 weeks to 22 Aug14)

- NBRx is 4.1% overall and 9.4% for pulmonologists
- TRx is 0.8%

- ANORO v tiotropium H2H data – significantly improved lung function (trough FEV_1 at Day 169) compared with tiotropium.

Upcoming catalysts in our respiratory franchise

- *Incruse* approved in US and Europe – launch anticipated by end of the year
- *Arnuity* approved in US – launch anticipated in 2015
- Mepolizumab severe asthma filing by end of 2014
- Phase 3 studies commenced in Eosinophilic Granulomatosis with Polyangiitis in Feb 2014 and COPD in April 2014
- Closed triple for COPD (UMEC/FF/VI) Ph III IMPACT started July 2014
- Breo Ellipta, PDUFA anticipated Q2 for asthma file
- SUMMIT recruitment completed in March 2014, read out in 2015
- Salford Lung Studies:
  - COPD recruitment due to complete end 2014; 12 month treatment period
  - Asthma recruiting

Salford Lung Study

Seretide comparator study DB2116134
Anoro Ellipta vs. Seretide

– A 12-week, randomised, double-blind, double-dummy, multi-centre study to evaluate the efficacy and safety of Anoro Ellipta and Seretide in subjects with COPD[1]

Primary objective

– To compare the efficacy (defined by 0-24hr wm FEV_1) of Anoro Ellipta 55/22mcg* once-daily and Seretide 500/50mcg twice-daily in subjects with COPD who have a history of infrequent exacerbations[1]

Secondary objective

– To compare the effects of Anoro Ellipta and Seretide on safety and patient-reported outcomes relating to health-related quality of life in subjects with COPD[1]

Patients and treatment[1]

– Patients were randomised to Anoro Ellipta 55/22mcg or Seretide 500/50mcg in a 1:1 ratio

Main entry criteria[1]

– Age 40+

– COPD as per American Thoracic Society (ATS)/European Respiratory Society (ERS) definition

– Smoking history ≥10 pack-years

– Post-bronchodilator FEV_1 ≤70% predicted

– No history of ≥1 COPD exacerbations within 12 months, that required oral corticosteroids, antibiotics and/or hospitalisation

– Use of ICS and other ICS/LABA (non-FSC) was not permitted during the trial

– LABAs, LAMAs, theophyllines, PDE4s, LTMs, and ipratropium also not allowed

– mMRC score ≥2 (0–4 point scale) – walks slower than people of the same age because of breathlessness, or has to stop for breath when walking at own pace

– No current diagnosis of asthma

***Each UMEC delivered dose of 55mcg corresponds to pre-dispensed dose of 62.5mcg. Each VI delivered dose of 22mcg corresponds to a pre-dispensed dose of 25mcg**

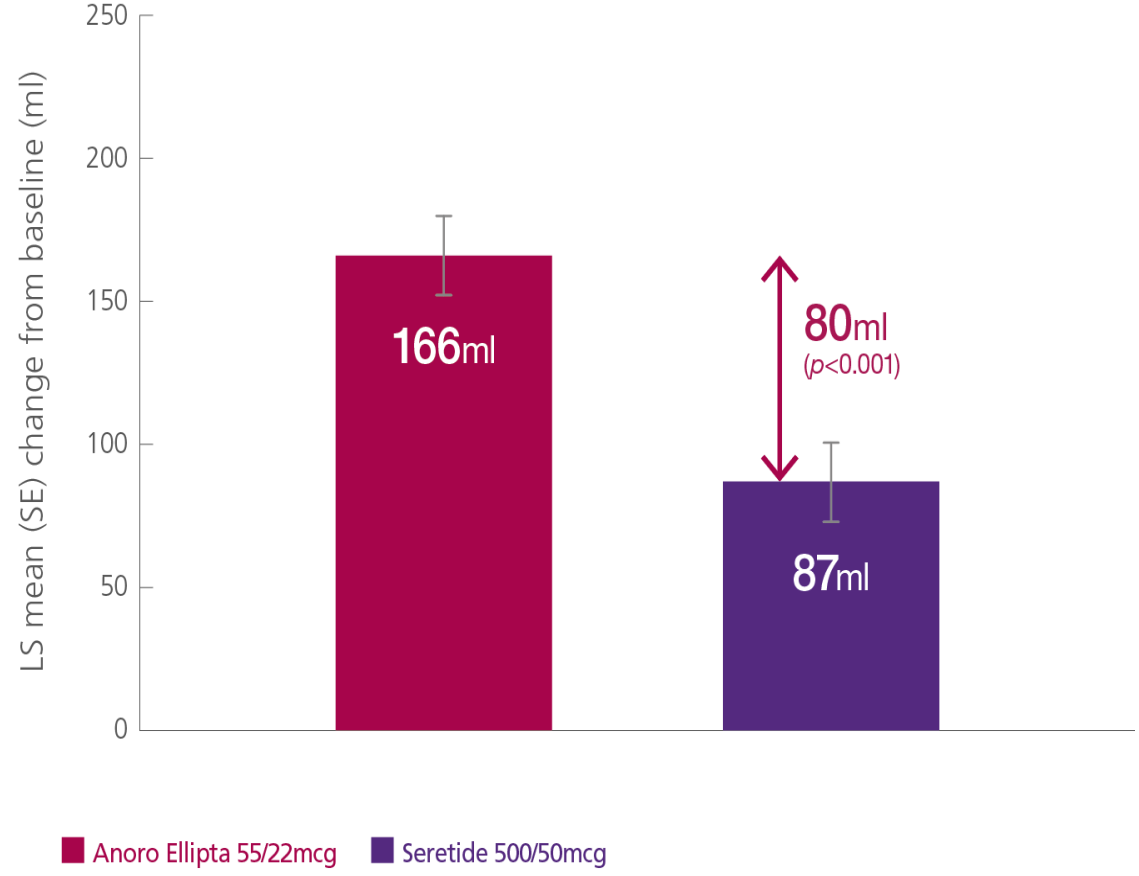
Reference: 1. Data on file. Clinical trial report: CSR-DB2116134.

Anoro Ellipta significantly improved FEV_1 compared with Seretide

Primary endpoint: WM FEV1 (0–24h) on Day 84

– Anoro Ellipta showed a statistically significant improvement in mean change from baseline WM FEV_1 (0–24h) compared with Seretide by 80ml (95% CI: 46, 113; p<0.001) in subjects with moderate to severe COPD and infrequent COPD exacerbations[1]

Least squares mean changes in WM FEV_1 (0–24h) from baseline on Day 84[1]



Reference: 1. Data on file. Clinical trial report: CSR-DB2116134.

Patient profiles for the new portfolio

Anoro®▼ Ellipta®

Initial maintenance bronchodilator treatment for patients with COPD who are breathless[1]

Age: 60

Diagnosed with COPD: 2 years ago

Former smoker: 24 pack-years

FEV_1: 70% predicted

Primary clinical concern: breathlessness

Primary lifestyle concern: being able to continue working until his planned retirement in 5 years

- Until recently enjoyed a relatively active lifestyle as breathlessness was controlled with rescue medication
- Can no longer complete everyday physical activities like walking up stairs or going to the shops, without stopping to catch his breath
- His quality of life is deteriorating, and he needs a treatment that can offer him the chance of continuing to work

Relvar®▼ Ellipta®

For symptomatic treatment of patients with COPD with a FEV_1 <70% predicted normal (post-bronchodilator) and a exacerbation history[1]

Age: 59

Diagnosed with COPD: 6 months ago

Current smoker: 10 cigarettes/day

FEV_1: 54% predicted

Primary clinical concern: a history of exacerbations

Primary lifestyle concern: increasing anxiety about his condition

- Had one course of oral steroids for an exacerbation i the winter months, now using SABA as needed
- Jorge is adjusting to life with a confirmed COPD diagnosis, and trying to quit smoking
- However, his recent exacerbation has set him back considerably. He needs a treatment that will reduce his risk of exacerbating again

Incruse®▼ Ellipta® in combination with an ICS/LABA†

For patients with COPD with a history of exacerbations who require further symptom relief*[1]

Age: 56

Diagnosed with COPD: 8 years ago

Former smoker: 30 pack-years

FEV_1: 44% predicted

Primary clinical concern: continuing symptoms and a history of exacerbations

Primary lifestyle concern: struggling to walk which is preventing her from doing daily activities and is slowly becoming housebound

- Has a history of exacerbations, one of which left her hospitalised
- She is also increasingly breathless when walking
- Due to her breathlessness, her activity levels have fallen, reducing her fitness and increasing her breathlessness further

*Incruse Ellipta for symptom relief, ICS/LABA to reduce exacerbation risk.
†Please note, for the EU, the only ICS/LABA that has been studied in combination with Incruse Ellipta is Relvar Ellipta.

Relvar®▼ Ellipta®

For patients with asthma who are uncontrolled on ICS and 'as needed' SABAs[1]

Age: 39

Diagnosed with asthma: 25 years ago

Former smoker: No

FEV_1: 78%

Primary clinical concern: ongoing asthma symptoms

Primary lifestyle concern: doesn't want to be slowed down by her asthma

- Olivia is a busy mum of three with a full-time job
- She 'puts up' with her symptoms as she doesn't feel she has the time to manage them properly
- Dislikes being on inhalers as she feels tied to asthma, but tries to remember to use them

Steven Yancey
Medicine Development Leader, mepolizumab

Objectives/design of the Phase III asthma programme

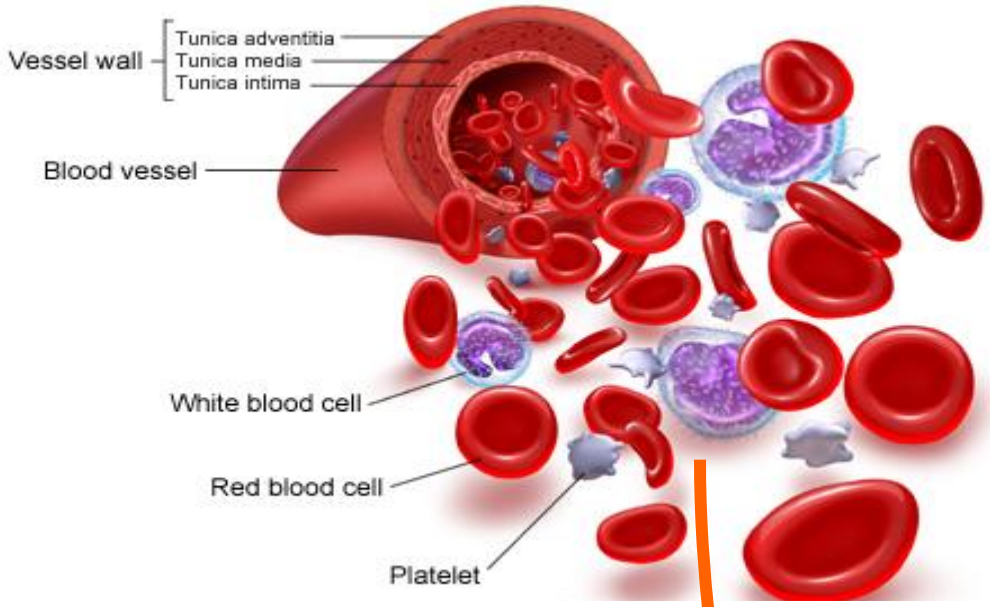
MEA115588 (MENSA)

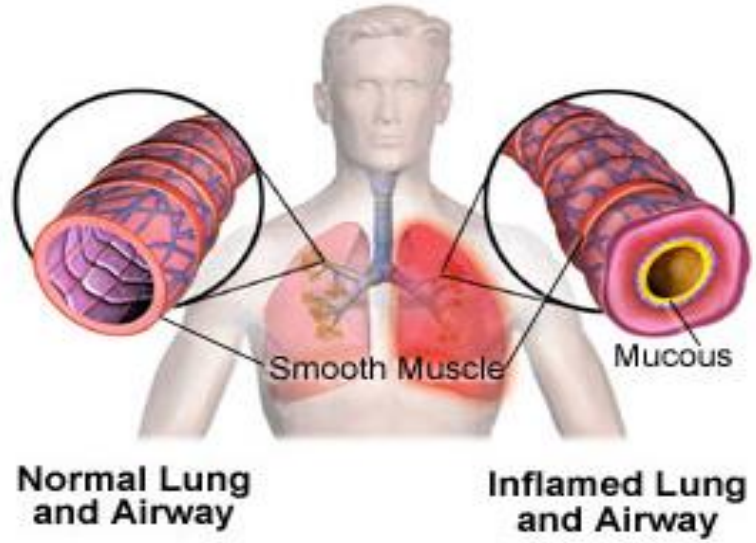
To evaluate the efficacy of mepolizumab 75 mg intravenous (i.v.) or 100 mg subcutaneous (SC) every 4 weeks versus placebo on the frequency of clinically significant exacerbations in adult and adolescent subjects with severe eosinophlic asthma.

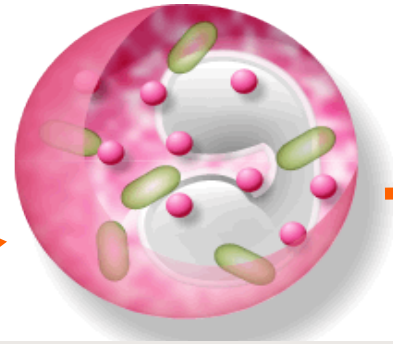
MEA115575 (SIRIUS)

To compare the effects of 100 mg subcutaneous (SC) mepolizumab adjunctive therapy with placebo on reducing the use of maintenance oral corticosteroids (OCS) in systemic corticosteroid dependent subjects with severe eosinophlic asthma.

Asthma and eosinophilic inflammation

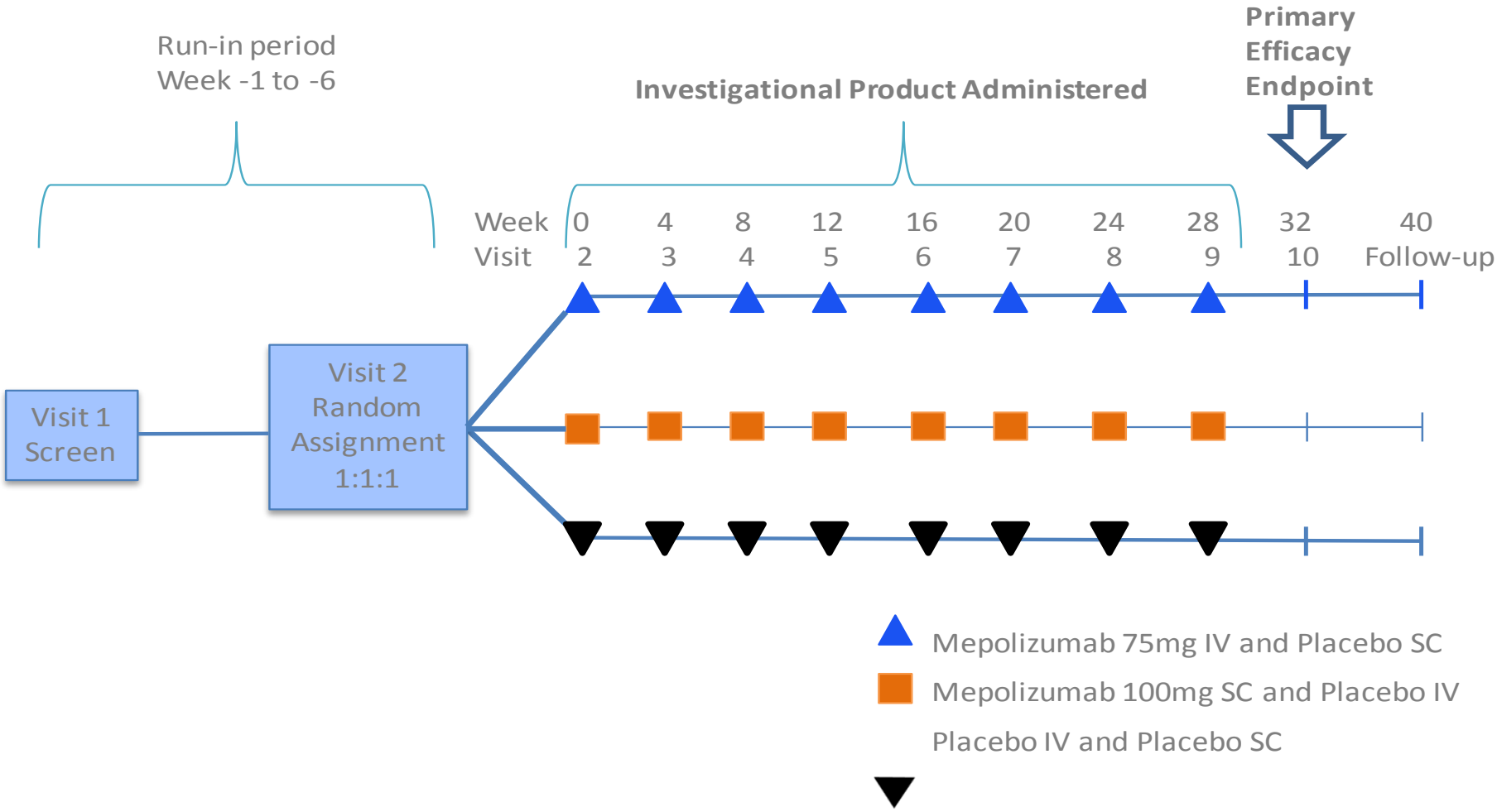






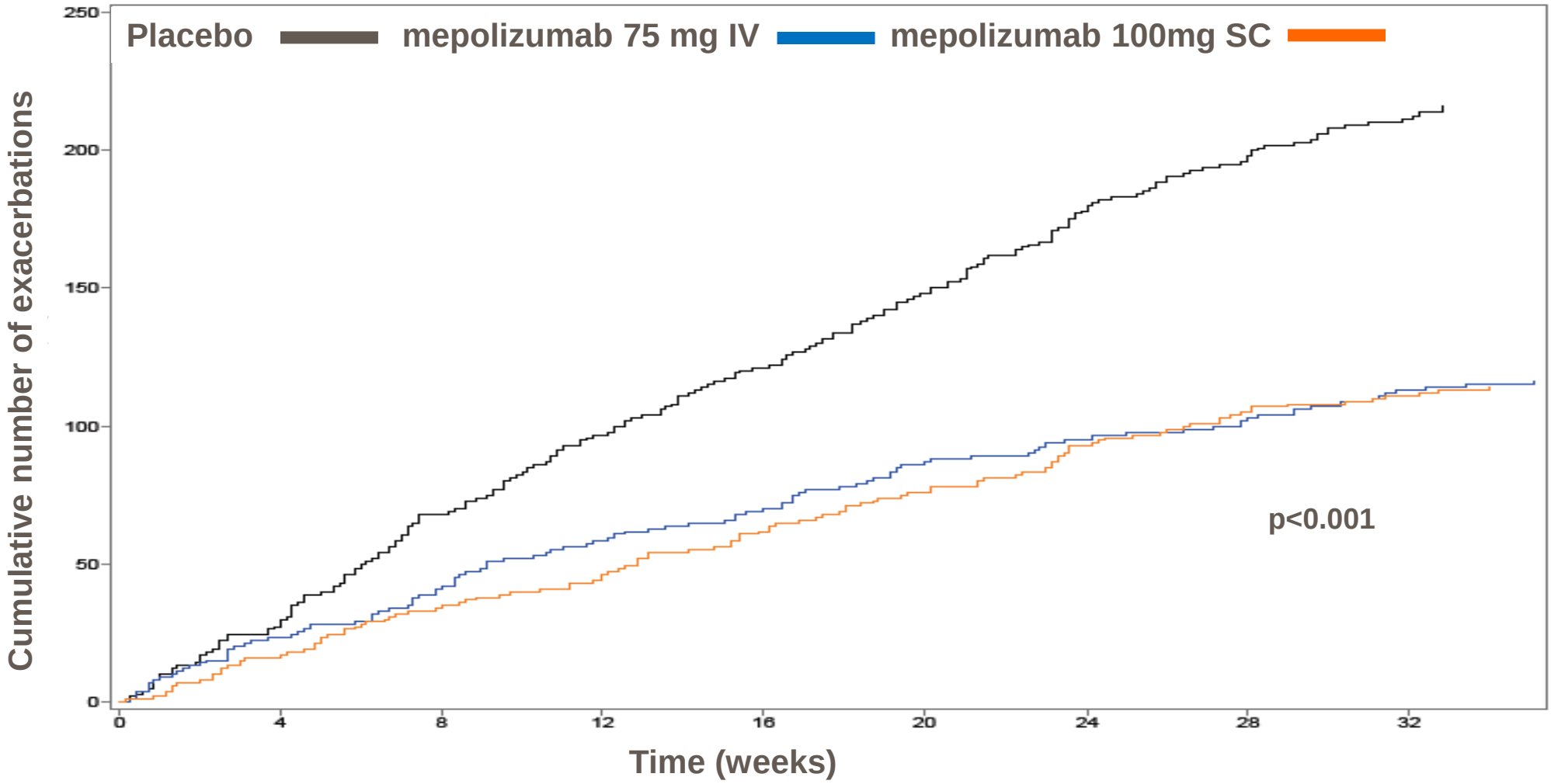
Over-expression of eosinophils

MENSA: Design and patient identification



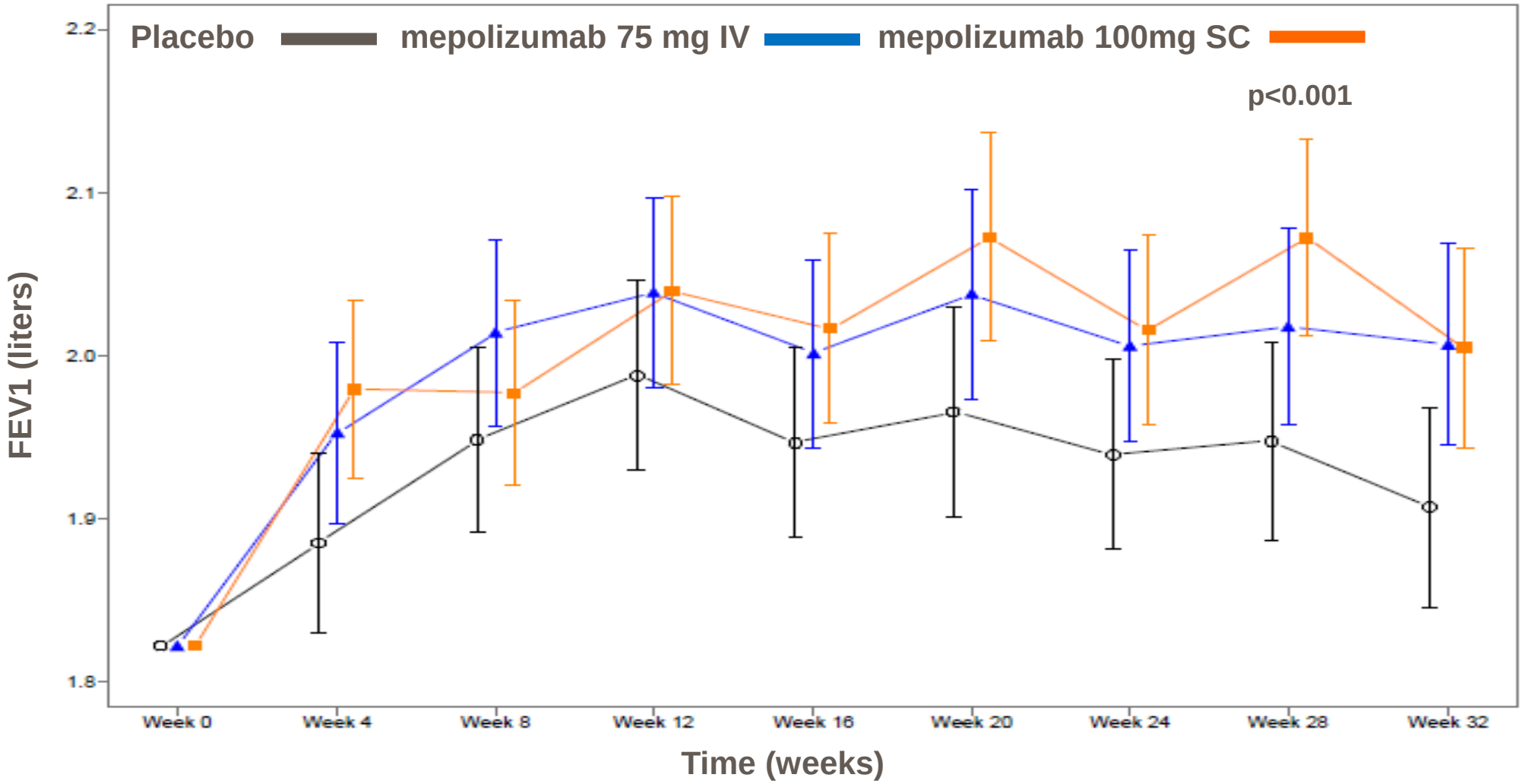
Results: Primary Endpoint

Reduction in Exacerbations



Secondary Endpoint

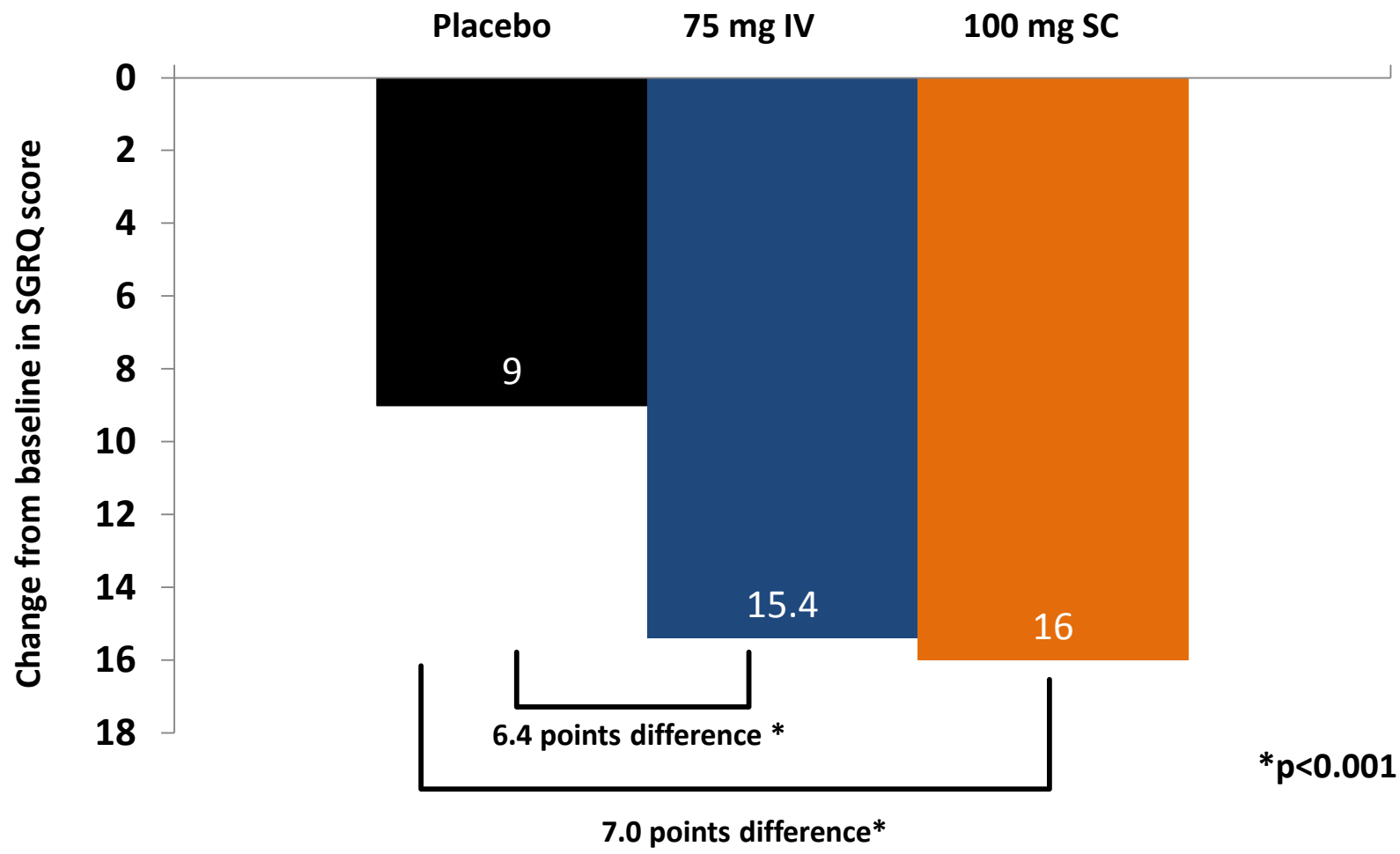
Changes in Pre-BD FEV_1



Errors bars represent 95% CI

Secondary Endpoint

Changes in St George's Respiratory Questionnaire



Key Results by Higher Blood Eosinophil Counts

(≥500 cells/µL)

Figure S4A. Reduction of Clinical Significant Exacerbations Across the Three Treatment Groups at Week 32

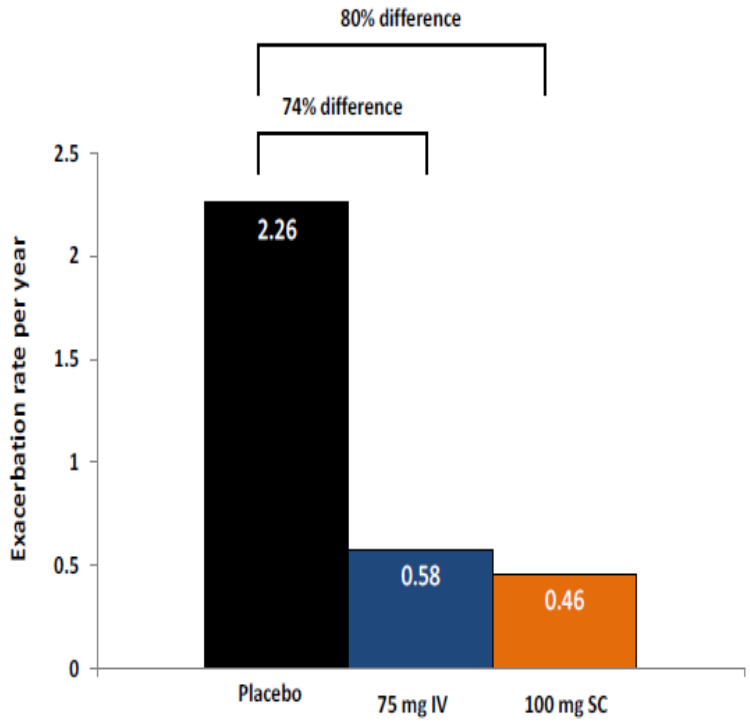
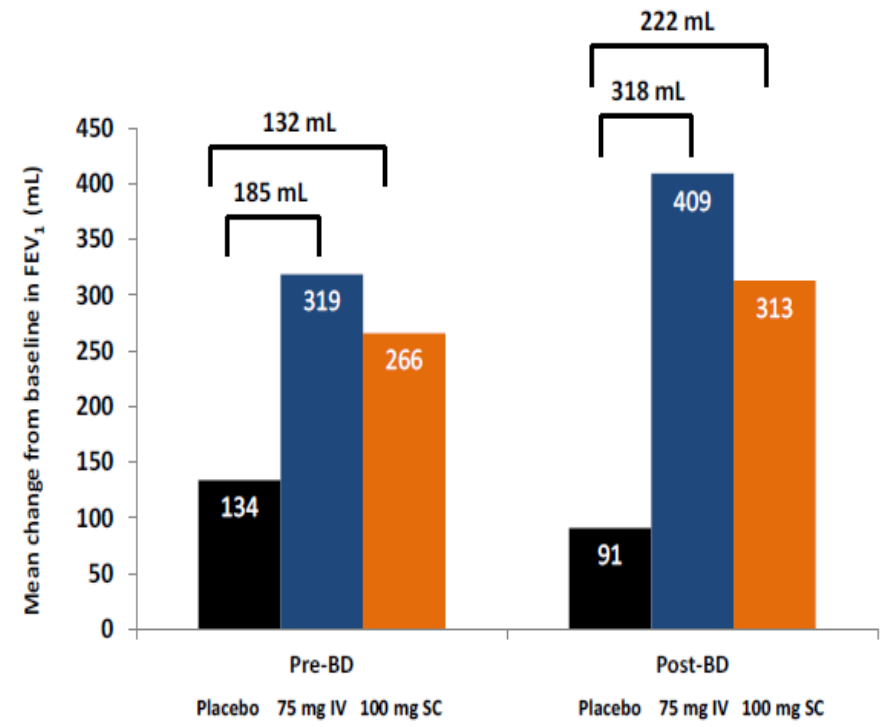


Figure S4B. Change from Baseline in Pre- and Post-bronchodilator FEV_1 Compared to Placebo at Week 32

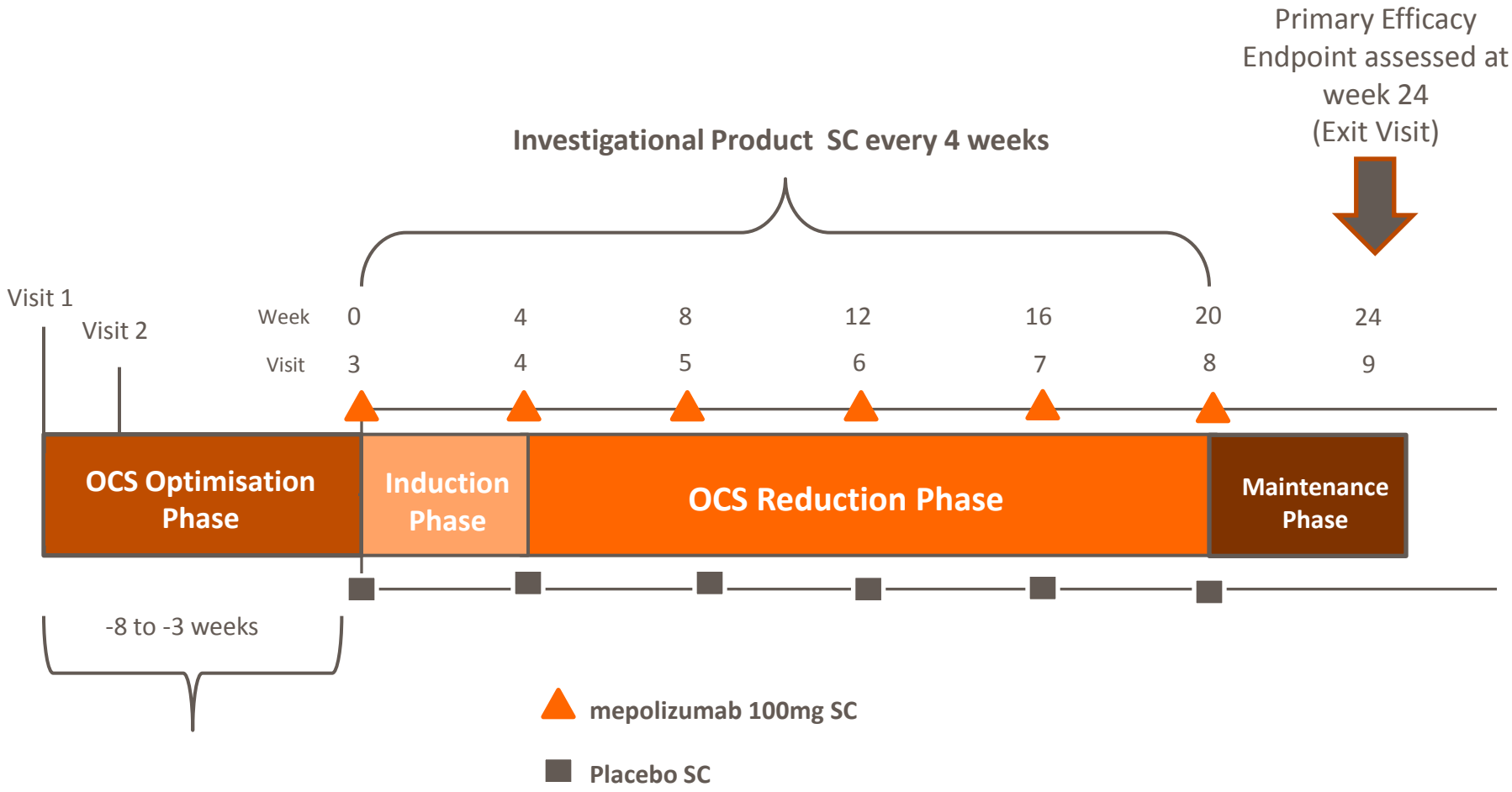


Summary of Adverse Events

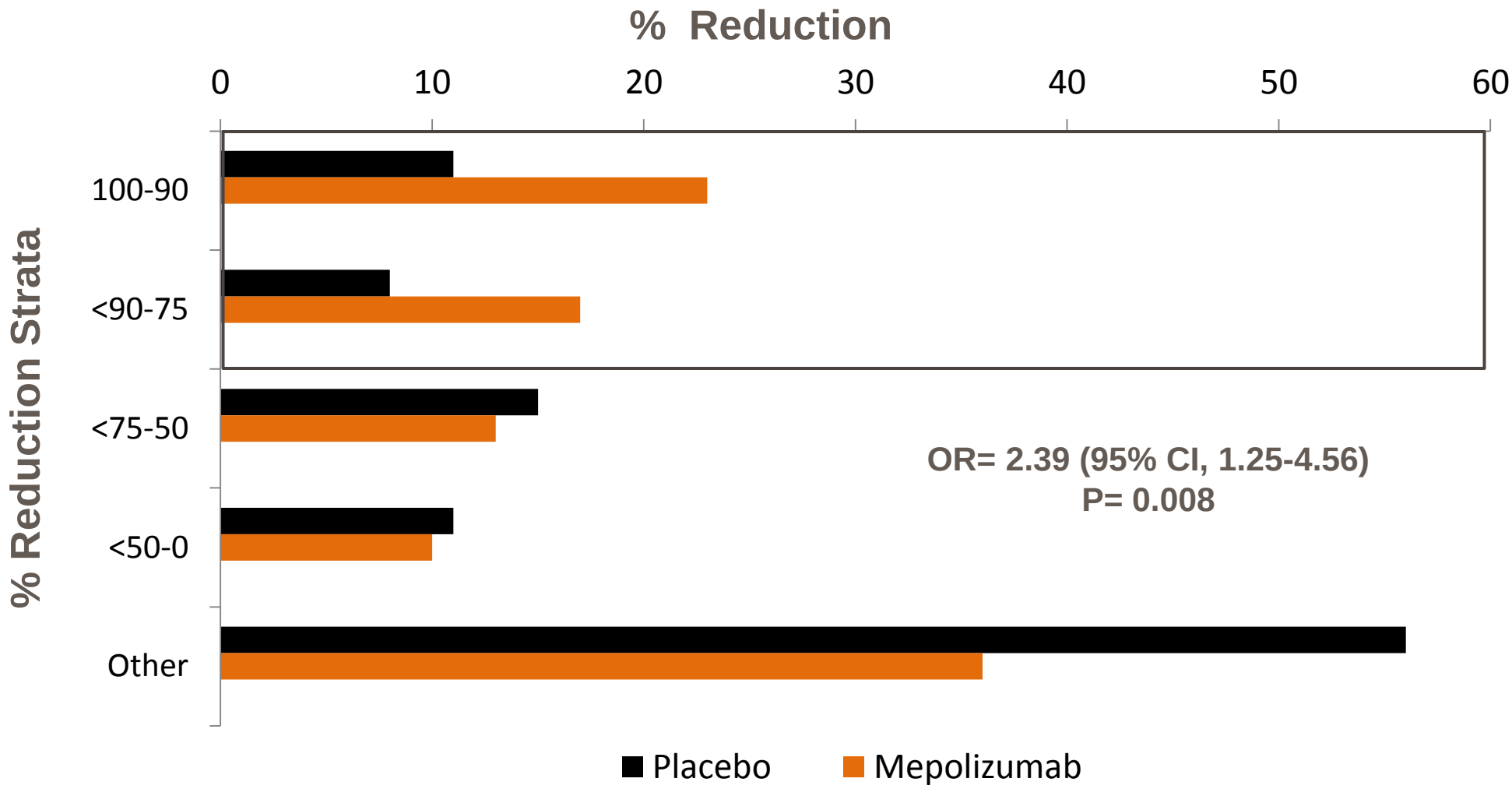
	Placebo N=191	mepolizumab IV N=191	mepolizumab SC N=194
All AEs, n (%)	158 (83)	161 (84)	152 (78)
Non-asthma events	157 (82)	161 (84)	152 (78)
Asthma worsening	29 (15)	18 (9)	13 (7)
Drug-related*	30 (16)	33 (17)	39 (20)
Led to withdrawal	4 (2)	0	1 (<1)
SAEs, n (%)			
On-treatment	27 (14)	14 (7)	16 (8)
Investigator assigned as drug-related	1 (<1)	0	1 (<1)
Fatal	1 (<1)	0	0

*Status assigned by the investigators while masked to treatment group

SIRIUS: Design and patient identification

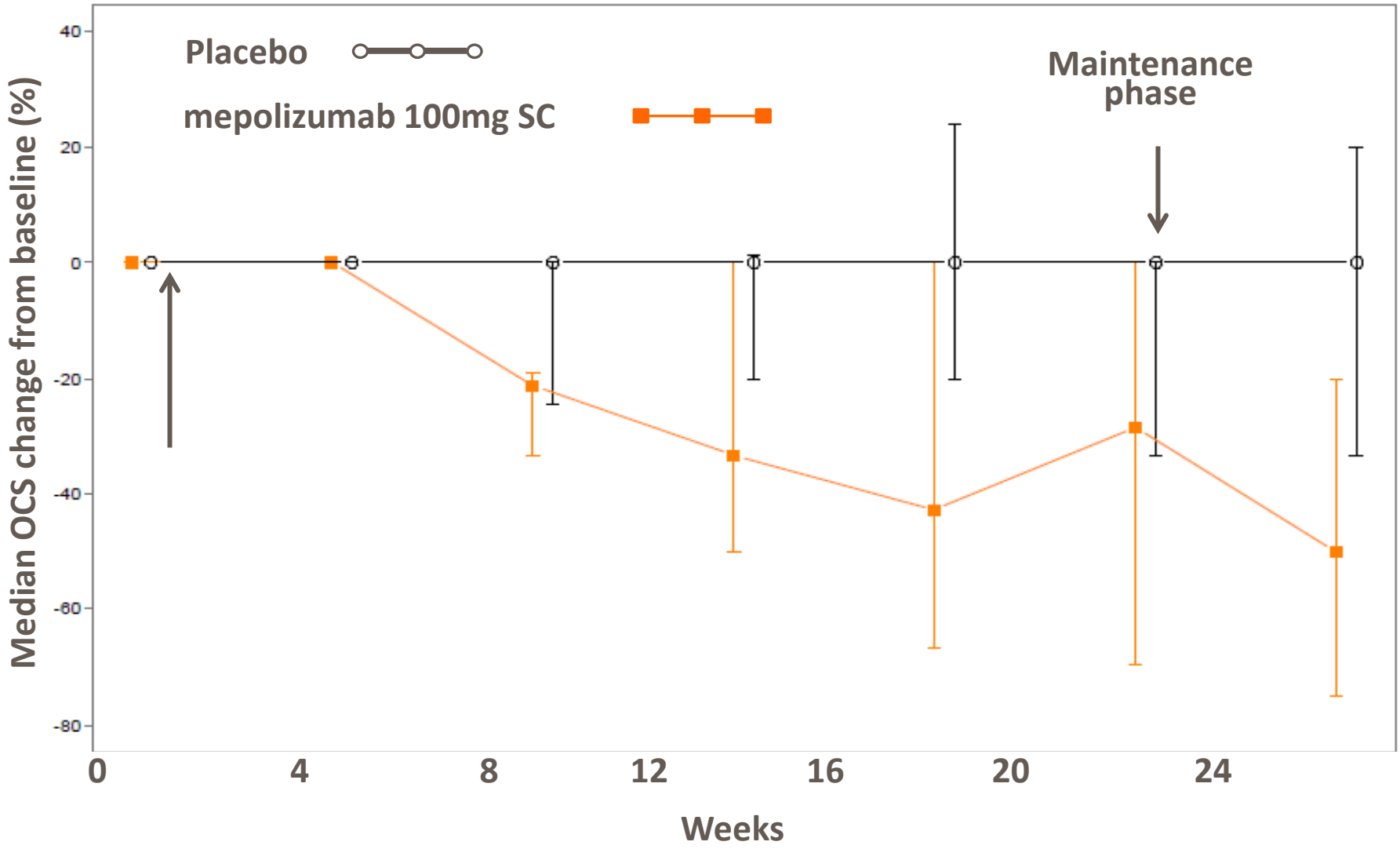


Results: Primary endpoint of OCS reduction



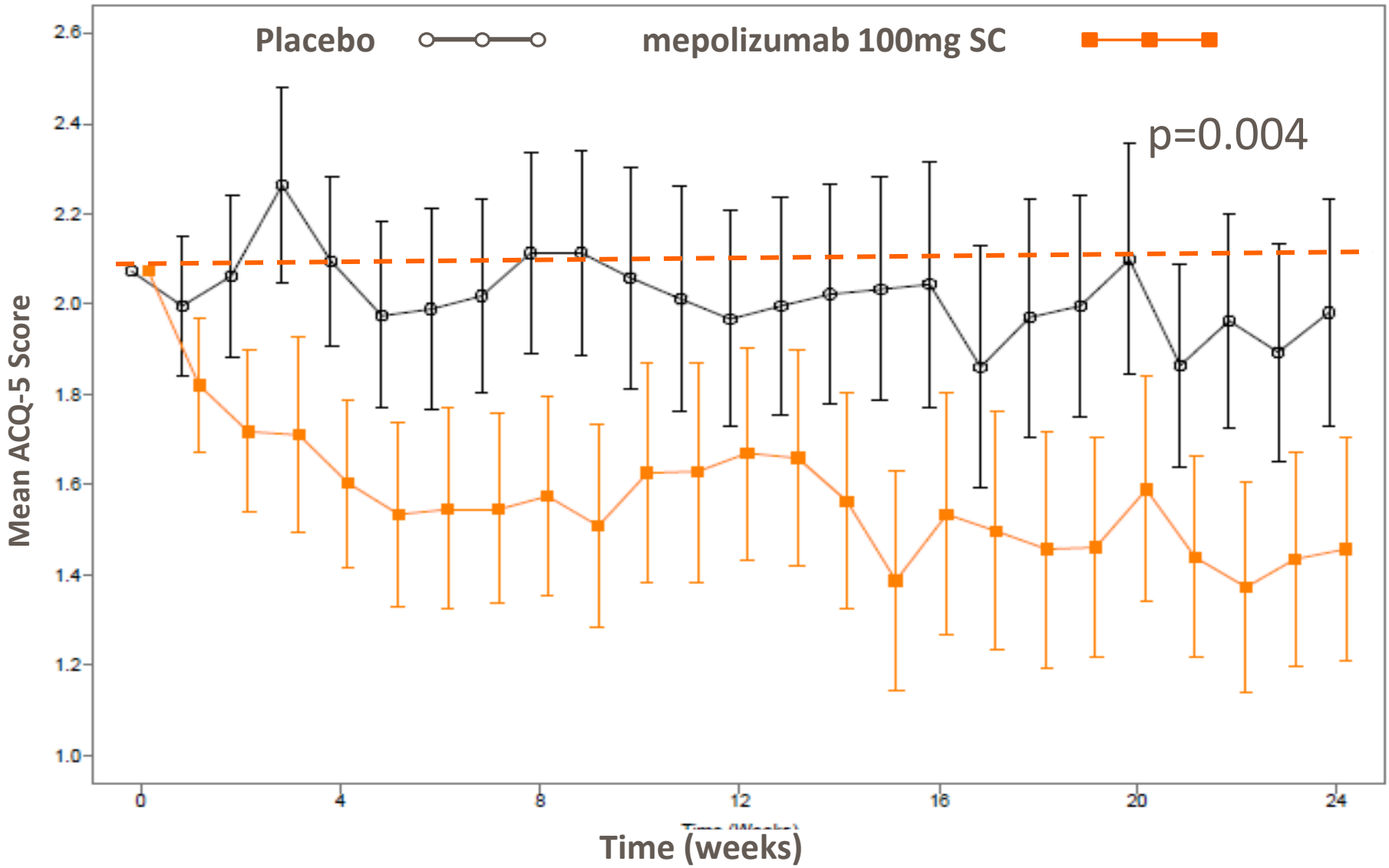
Other: no decrease in OCS dose, or lack of control during weeks 20-24 or withdrawal from treatment

Results: Median OCS reduction during the study

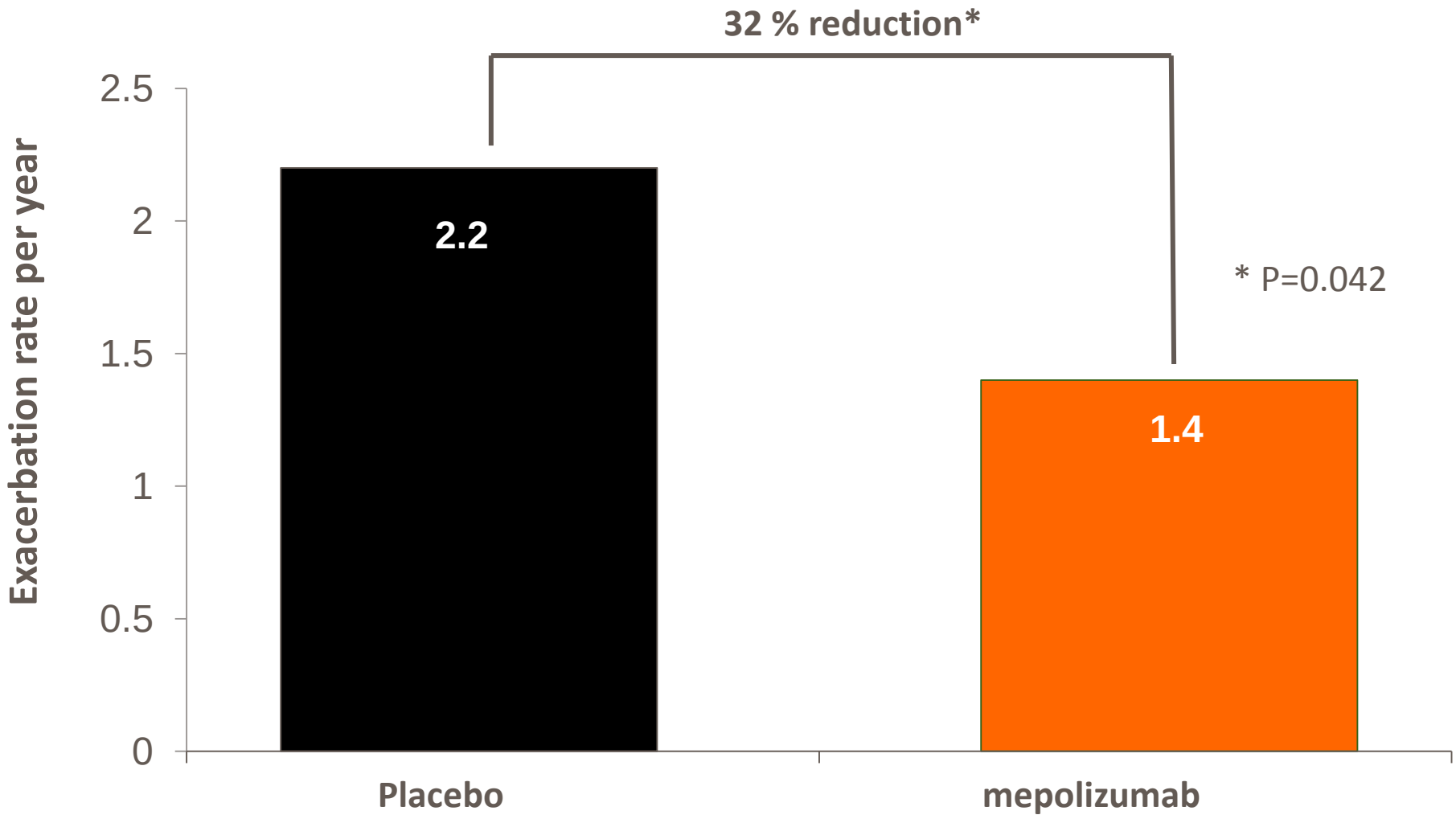


* P=0.007

Changes in Asthma Control Questionnaire



Reduction in Exacerbations



Summary of Adverse Events

Adverse Event Type	Number (%) of Patients	
	Placebo N=66	mepolizumab N=69
All AEs	61 (92)	57 (83)
Non-asthma events	60 (91)	57 (83)
Asthma worsening	8 (12)	2 (3)
Drug-related*	12 (18)	21 (30)
Led to withdrawal from study	3 (5)	3 (4)
SAEs		
On-treatment	12 (18)	1 (1)
Fatal	1 (2)	0
Any on-treatment AE	61 (92)	57 (83)

*Status assigned by the investigators while masked to treatment group

Conclusions – Asthma

MENSA

mepolizumab: PhIII data demonstrated potential as an add-on therapy in patients with severe eosinophilic asthma, producing a **clinically and statistically significant** (~50%) **reduction** in the **exacerbation rate** compared with placebo

mepolizumab produced a **similar treatment effect** in exacerbations, lung function and quality of life measures regardless of the **route of administration (IV or SC)**

mepolizumab was **well-tolerated** with a safety profile similar to that of placebo

SIRIUS

mepolizumab: PhIII data in patients with severe eosinophilic asthma and on daily use of oral corticosteroids, demonstrated potential to **reduce OCS while maintaining control**

The validity of this OCS reduction approach was supported by **stability of FEV_1 and ACQ-5** over the course of the study

mepolizumab was **well-tolerated** with a safety profile similar to that of placebo

mepolizumab is in development for severe eosinophilic asthma in patients who exacerbate despite high-dose oral or inhaled corticosteroids (ICS) and an additional controller such as long-acting beta-2 agonist. In addition, mepolizumab is being investigated in COPD and Eosinophilic Granulomatosis with Polyangiitis (EGPA). mepolizumab is not approved anywhere in the world

Q&A