

regard to adherence and exacerbation measurements, designs and analysis precluded a formal meta-analysis. Although effect measures varied, good adherence was associated with fewer severe asthma exacerbations in high-quality studies.

**Conclusion** Good adherence is associated with a lower risk of severe asthma exacerbations. Future studies should use standardised methodology to assess adherence and inhaler technique.

### P153 DOES ASTHMA CONTROL, MOOD DISTURBANCE OR HEALTH STATUS INFLUENCE DAILY PHYSICAL ACTIVITY LEVELS IN PATIENTS WITH SEVERE ASTHMA?

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**Introduction** We aimed to assess the level of daily physical activity and investigate the relationship with asthma control, mood disturbance and health status in patients with severe asthma.

**Methods** Patients with severe asthma (step 4–5 of the British Thoracic Society guidelines), MRC dyspnoea grade  $\geq 2$ , were recruited from specialists in difficult-to-treat asthma. All patients were asked to wear Senseware<sup>TM</sup> activity monitor for seven days during waking hours with a minimum data requirement of eight hours per day for four days.<sup>1</sup> Participants completed the Asthma Control Questionnaire (ACQ), Hospital Anxiety and Depression Scale (HADS), Chronic Respiratory Questionnaire (CRQ) and Asthma Quality of Life Questionnaire (AQLQ). Pearson's correlation coefficient was used to assess the relationship between physical activity, asthma control, mood disturbance and health status.

**Results** 45 participants (24 female, mean [SD] age 54 [13] yr, BMI 32 [7] kg/m<sup>2</sup>) provided written consent and physical activity data was available for 41 patients. The mean (SD) number of days of physical activity data available was 6.1 [1.9] days. The mean (SD) number of steps per day was 5258 [3030] with only 84 [82] active minutes. Only 16 patients achieved any moderate physical activity (3–4.5 metabolic equivalents [METs]) and for less than six minutes per day.

The mean [SD] ACQ was 13.6 [6.1], HADS anxiety and depression domains 6.5 [4.9] and 4.5 [2.8], respectively, CRQ Dyspnoea domain 3.4 [1.5], AQLQ environmental, symptoms, activity and emotional domains of 4.9 [1.4], 5.0 [1.4], 5.0 [1.2] and 4.9 [1.5], respectively. Table 1 shows the correlations between steps per day, and measures of asthma control, mood disturbance, and health status.

**Abstract P153 Table 1** Relationship between steps per day and asthma control, mood disturbance and health status

| Questionnaire      | Correlation coefficient | P value |
|--------------------|-------------------------|---------|
| ACQ                | −0.16                   | 0.28    |
| HADS – Anxiety     | −0.17                   | 0.28    |
| HADS – Depression  | −0.13                   | 0.41    |
| CRQ – Dyspnoea     | 0.23                    | 0.14    |
| AQLQ Activity      | 0.34                    | 0.02    |
| AQLQ Emotional     | 0.17                    | 0.26    |
| AQLQ Symptoms      | 0.10                    | 0.51    |
| AQLQ Environmental | 0.06                    | 0.71    |
| AQLQ mean          | 0.15                    | 0.33    |

**Conclusions** Patients with severe asthma demonstrated low levels of physical activity but there were no relationships with asthma control, mood disturbance or health status.

### REFERENCE

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### P154 SAFETY OF TIOTROPIUM IN PRE-SCHOOL CHILDREN WITH SYMPTOMATIC PERSISTENT ASTHMA

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**Introduction and objectives** Asthma is the most common chronic disease of childhood (GINA 2015). For pre-school children whose asthma symptoms are not well controlled on inhaled corticosteroids, limited options are available for further treatment. Here, we evaluated the safety of once-daily (QD) tiotropium Respimat<sup>®</sup> (tioR) in patients aged 1–5 years with symptomatic persistent asthma.

**Methods** A Phase II/III, randomised, double-blind, placebo-controlled, parallel-group trial (NCT01634113) of tioR 5 µg, tioR 2.5 µg or placebo Respimat<sup>®</sup> (pboR), administered QD in the afternoon for 12 weeks, each as add-on to usual maintenance therapy. Safety data, including *post hoc* analysis of a composite exacerbation end point derived from adverse events (AEs), are reported.

**Results** No AEs leading to treatment discontinuation or death were reported. The proportion of patients with any AEs was higher with pboR (73.5%) than with tioR 5 µg (58.1%) and 2.5

**Abstract P154 Table 1** Composite asthma endpoint: Asthma exacerbation (broad) with pneumonia plus asthma worsening

| Composite end point                               | Patients, n (%)                                   |   |   |
|---|---|---|---|
|   | Tiotropium Respimat <sup>®</sup> 5 µg QD (n = 31) | Tiotropium Respimat <sup>®</sup> 2.5 µg QD (n = 36) | Placebo Respimat <sup>®</sup> QD (n = 34) |
| Asthma exacerbation (broad)/worsening + pneumonia | 9 (29.0)  | 12 (33.3)   | 19 (55.9)                                 |
| Asthma  | 2 (6.5)   | 5 (13.9)  | 10 (29.4)                                 |
| Bronchitis  | 2 (6.5)   | 1 (2.8)   | 4 (11.8)                                  |
| Bronchopneumonia                                  | 0   | 0   | 1 (2.9)                                   |
| Cough   | 2 (6.5)   | 4 (11.1)  | 3 (8.8)                                   |
| Dyspnoea  | 1 (3.2)   | 0   | 0   |
| Pneumonia   | 0   | 1 (2.8)   | 2 (5.9)                                   |
| Viral respiratory tract infection                 | 3 (9.7)   | 3 (8.3)   | 4 (11.8)                                  |
| Wheezing  | 0   | 2 (5.6)   | 0   |

Treated set. Percentages calculated using total number of patients per treatment as denominator. AE preferred terms defined by Medical Dictionary for Regulatory Activities version 17.1.

µg (55.6%). Two patients each in the tioR 5 µg (6.5%) and pboR (5.9%) groups were reported with drug-related AEs. Three patients, all in the pboR group, were reported with serious AEs. Asthma exacerbation/worsening was reported by fewer patients in the tioR 5 µg and tioR 2.5 µg groups compared with the pboR group (Table).

**Conclusion** Once-daily tiotropium RespiMat® add-on to maintenance therapy is well tolerated and may reduce exacerbations in pre-school children with symptomatic persistent asthma.

Please refer to page A272 for declarations of interest in relation to abstract P154.

# **P155 SAFETY OF TIOTROPIUM RESPIMAT® ADD-ON THERAPY IN PATIENTS AGED 6–17 YEARS WITH SYMPTOMATIC ASTHMA**

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**Introduction and objectives** Two Phase II trials have shown tiotropium RespiMat® (tioR) to be a well-tolerated bronchodilator in patients aged 12–17<sup>1</sup> and 6–11<sup>2</sup> years with symptomatic asthma. Here, we further assessed the safety and tolerability of once-daily (QD) tioR add-on therapy in Phase III trials in patients aged 6–17 years with symptomatic asthma.

**Methods** Data was analysed from three completed Phase III, randomised, double-blind, placebo-controlled, parallel-group trials: VivaTinA (NCT01634152), 12-week trial, patients aged 6–11 years; PensieTinA (NCT01277523), 12-week trial, patients aged 12–17 years; RubaTinA (NCT01257230), 48-week trial, patients aged 12–17 years. Patients received QD tioR 5 µg (2 puffs, 2.5 µg), QD tioR 2.5 µg (2 puffs, 1.25 µg) or QD placebo RespiMat® (pboR; 2 puffs) as add-on to background therapy. Adverse events (AEs) were recorded and analysed descriptively by age: 6–11 years; 12–17 years.

**Results** 1189 patients were treated: 6–11 years, n = 400; 12–17 years, n = 789. The frequency of patients with AEs was similar across all treatment arms, with a low incidence of drug-related and serious AEs; asthma and decreased peak expiratory flow rate were the most common AEs (Table). No deaths occurred.

**Conclusion** The AE profile and AE incidences were similar between tioR 5 µg, tioR 2.5 µg and pboR, as add-on to inhaled corticosteroid ± other controllers, in patients aged 6–17 years with symptomatic asthma.

## **REFERENCES**

- 1 Vogelberg C, et al. *Respir Med* 2014;**108**:1268–76.
- 2 Vogelberg C, et al. *Respir Res* 2015;**16**:20.

## **Abstract P155 Table 1 Summary of adverse events in the VivaTinA-asthma, PensieTinA-asthma and RubaTinA-asthma trials**

| n (%)  | Tiotropium<br>RespiMat®<br>5 µg QD | Tiotropium<br>RespiMat®<br>2.5 µg QD | Placebo<br>RespiMat®<br>QD |
|--|------------------------------------|--------------------------------------|----------------------------|
| <b>VivaTinA-asthma®, 6–11 years</b>                                |                                    |                                      |                            |
| <b>Overall AEs</b>   |                                    |                                      |                            |
| Patients with any AE   | 56 (43.1)                          | 59 (43.4)                            | 66 (49.3)                  |
| Patients with investigator-defined drug-related AEs                | 1 (0.8)                            | 0                                    | 2 (1.5)                    |
| Patients with AEs leading to discontinuation                       | 2 (1.5)                            | 0                                    | 2 (1.5)                    |
| Patients with serious AEs  | 4 (3.1)                            | 2 (1.5)                              | 2 (1.5)                    |
| <b>AEs in &gt;5% pts in any treatment group, by preferred term</b> |                                    |                                      |                            |
| Asthma <sup>a</sup>  | 24 (18.5)                          | 20 (14.7)                            | 30 (22.4)                  |
| Decreased peak expiratory flow rate                                | 15 (11.5)                          | 15 (11.0)                            | 20 (14.9)                  |
| Nasopharyngitis  | 6 (4.6)                            | 6 (4.4)                              | 11 (8.2)                   |
| <b>PensieTinA-asthma® and RubaTinA-asthma®</b>                     |                                    |                                      |                            |
| <b>12–17 years</b>   |                                    |                                      |                            |
| <b>Overall AEs</b>   |                                    |                                      |                            |
| Patients with any AE   | 127 (48.1)                         | 121 (48.0)                           | 130 (47.6)                 |
| Patients with investigator-defined drug-related AEs                | 4 (1.5)                            | 1 (0.4)                              | 2 (0.7)                    |
| Patients with AEs leading to discontinuation                       | 0                                  | 0                                    | 3 (1.1)                    |
| Patients with serious AEs  | 5 (1.9)                            | 3 (1.2)                              | 2 (0.7)                    |
| <b>AEs in &gt;5% pts in any treatment group, by preferred term</b> |                                    |                                      |                            |
| Asthma <sup>a</sup>  | 38 (14.4)                          | 41 (16.3)                            | 46 (16.8)                  |
| Decreased peak expiratory flow rate                                | 11 (4.2)                           | 18 (7.1)                             | 21 (7.7)                   |
| Nasopharyngitis  | 25 (9.5)                           | 19 (7.5)                             | 21 (7.7)                   |
| Viral respiratory tract infection                                  | 11 (4.2)                           | 11 (4.4)                             | 14 (5.1)                   |

Treated set. Percentages calculated using total number of patients per treatment as denominator. AE preferred terms defined by Medical Dictionary for Regulatory Activities version 16.1 or 18.0. Tiotropium RespiMat® or placebo RespiMat® administered as add-on to background therapy

<sup>a</sup>Represents asthma worsening or exacerbation

Please refer to page A272 for declarations of interest in relation to abstract P155.

# **P156 EFFICACY, SAFETY AND TOLERABILITY OF ONCE-DAILY TIOTROPIUM RESPIMAT® ADD-ON THERAPY IN CHILDREN WITH MODERATE SYMPTOMATIC ASTHMA**

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**Introduction and objectives** A Phase II trial has shown that tiotropium RespiMat® (tioR) is an effective, safe, and well-tolerated bronchodilator in patients aged 6–11 years with moderate symptomatic asthma.<sup>1</sup> To further assess the efficacy and safety of once-