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[1] and 6–11[2] 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.

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

n (%)	Tiotropium Respimat® 5 µg QD	Tiotropium Respimat® 2.5 µg QD	Placebo Respimat® QD
VivaTinA-asthma®, 6–11 years	**n = 130**	**n = 136**	**n = 134**
Overall AEs			
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)
AEs in >5% pts in any treatment group, by preferred term			
Asthma[a]	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)
PensieTinA-asthma® and RubaTinA-asthma®:	**n = 264**	**n = 252**	**n = 273**
12–17 years			
Overall AEs			
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)
AEs in >5% pts in any treatment group, by preferred term			
Asthma[a]	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
[a]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.[1] To further assess the efficacy and safety of once-

REFERENCES

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

Abstract P156 Table 1 Peak $FEV_{1(0–3\ h)}$, trough FEV_1,FEV_1 $AUC_{(0–3\ h)}$, and Peak $FVC_{(0–3\ h)}$ responses at Week 24 (full analysis set); and overall AEs in treated set

Responses at Week 24			
		Tiotropium Respimat® 5 µg[a] n = 135	Tiotropium Respimat® 2.5 µg[a] n = 135
		Adjusted mean difference versus placebo Respimat®[a] ± standard error[1]	
Background maintenance therapy		Medium-dose ICS (200–400 µg budesonide or equivalent) alone or in combination with another controller medication	
Peak $FEV_{1(0–3h)}$ response, mL		164 ± 31 P < 0.0001 n = 134	170 ± 31 P < 0.0001 n = 131
Trough FEV_1 response, mL[b]		118 ± 36 P = 0.0010 n = 134	116 ± 36 P = 0.0012 n = 131
FEV_1 $AUC_{(0–3h)}$ response, mL		157 ± 30 P < 0.0001 n = 134	154 ± 30 P < 0.0001 n = 131
Peak $FVC_{(0–3h)}$ response, mL		91 ± 37 P = 0.0152 n = 134	110 ± 38 P = 0.0036 n = 131
Adverse Events (AEs)[2]			
	Placebo Respimat®[a] n = 131	Tiotropium Respimat® 5 µg[a] n = 135	Tiotropium Respimat® 2.5 µg[a] n = 135
		n (%)	
Patients with any AE	89 (67.9)	82 (60.7)	86 (63.7)
Patients with investigator-defined drug-related AEs	2 (1.5)	0	0
Patients with AEs leading to discontinuation	0	0	0
Patients with serious AEs	6 (4.6)	1 (0.7)	3 (2.2)

[1]Full analysis set. Placebo Respimat®, N = 131; Placebo Respimat®, Week 24, n = 126. Mean baseline values (± standard deviation): ICS dose, 310.0 ± 112.0 µg; ACQ-IA total score, 1.87 ± 0.31; FEV_1, 1629 ± 393 mL; FVC, 2121 ± 564 mL.
[a]Add-on to background maintenance therapy.
[b]Measured 10 minutes before next dose of trial medication.
ACQ-IA, interviewer-administered Asthma Control Questionnaire
[2]Treated set. Percentages calculated using total number of patients per treatment group as denominator.

daily tioR add-on therapy, a Phase III trial was carried out in patients aged 6–11 years with moderate symptomatic asthma.

Methods This 48-week, Phase III, randomised, double-blind, placebo-controlled, parallel-group study (CanoTinA-asthma®; NCT01634139) was performed in patients aged 6–11 years with moderate symptomatic asthma. Patients received once-daily tioR 5µg (2 puffs, 2.5 µg), tioR 2.5 µg (2 puffs, 1.25 µg) or placebo Respimat® (pboR; 2 puffs) as add-on to maintenance treatment of at least medium-dose inhaled corticosteroid (ICS) (200–400 µg budesonide or equivalent) alone or in combination with another controller medication. The primary end point was peak FEV1 within 3 hours post-dosing (FEV1(0–3 h)). Secondary end points included trough FEV1 (key end point), FEV1 area under the curve (AUC) (0–3 h), and peak FVC (0–3 h); all measured as response (change from baseline) at Week 24. Adverse events (AEs) were analysed descriptively.

Results Of 403 patients randomised, 401 were treated. Baseline demographics and disease characteristics were balanced between treatment groups. TioR 5 µg and 2.5 µg provided statistically significant improvements in lung function versus pboR at Week 24 (Table) with adjusted mean difference ± standard error peak FEV1 (0–3 h) improvements of 164 ± 31 ml ($p < 0.0001$) and 170 ± 31 ml ($p < 0.0001$), respectively. The frequency of patients with AEs was similar across treatment arms, with a low incidence of drug-related and serious AEs (Table); no deaths occurred. The most common AEs were asthma worsening/exacerbation (lower incidence in tioR 5µg and 2.5 µg [34.1% and 36.3%] vs pboR [43.5%]), decreased peak expiratory flow rate (21.5% and 23% vs 20.6%), nasopharyngitis (8.9% and 11.1% vs 9.9%) and respiratory tract infection (9.6% and 8.1% vs 12.2%).

Conclusion In patients aged 6–11 years with moderate symptomatic asthma, once-daily tioR add-on to ICS with or without other maintenance therapy significantly improves lung function compared with pboR. The safety profile of tioR was similar to that of pboR.

REFERENCE

1 Vogelberg C, *et al. Respir Res* 2015;***16***(1):20.

Please refer to page A272 for declarations of interest in relation to abstract P156.

P157 SEASONAL VARIABILITY OF SEVERE ASTHMA EXACERBATIONS AND CLINICAL BENEFIT FROM LEBRIKIZUMAB

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Introduction and objectives Epidemiologic studies have implicated aeroallergens and respiratory infections as triggers underlying seasonal increases in asthma exacerbations in spring and autumn months. These seasonal factors may trigger or amplify airway inflammation in atopic, Type 2 high asthma patients that precipitates acute worsening of symptoms. Biologic therapies targeting Type 2 cytokine pathways have demonstrated efficacy in reducing the rate of severe asthma exacerbations, particularly in patients selected on the basis of Type 2 biomarkers. In children with asthma, increased inhaled corticosteroid or anti-IgE therapy has been found to reduce the rate of seasonal exacerbations. We hypothesised that lebrikizumab (anti-IL-13) therapy would likewise be effective in reducing seasonal exacerbations in adults with asthma.

Methods We conducted *post-hoc* analyses of the Phase III LAVOLTA studies (NCT01867125 and NCT01868061) to assess the seasonal dependence of exacerbations and efficacy of lebrikizumab in 2,148 adults with moderate to severe asthma. We employed Poisson regression utilising linear mixed models to estimate the per-month (normalised by hemisphere) annualised exacerbation rate and treatment effect of lebrikizumab in reducing exacerbations (percent rate reduction).

Results Per-month exacerbation rates in placebo treated eosinophil-low (<300/µL) patients were lower and less variable (0.34 to 0.72 per year) than in eosinophil-high (≥300/µL) patients; (0.63/