People and ideas for innovation in healthcare

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PRESS RELEASE

TWO PHASE III STUDIES, TRIMARAN AND TRIGGER, SHOW POSITIVE RESULTS FOR SINGLE-INHALER TRIPLE THERAPY OF INHALED CORTICOSTEROID PLUS LONG-ACTING B_2-AGONIST PLUS LONG-ACTING MUSCARINIC ANTAGONIST[1]

Parma, Italy, October 1, 2019 – Today, Chiesi Farmaceutici, an international research-focussed healthcare group (Chiesi Group), has announced that the results of two Phase III studies, TRIMARAN and TRIGGER, have been published in ***The Lancet***. These are the first studies to evaluate the relative efficacy and safety of extrafine formulation single-inhaler triple therapy compared with extrafine formulation inhaled corticosteroid (ICS) and long-acting β2 agonist (LABA) in adults with asthma.[1]

The two 52-week studies, TRIMARAN (N=1,155) and TRIGGER (N=1,437), compared the efficacy and safety of medium-ICS dose beclometasone dipropionate (BDP; 100mcg) / formoterol fumarate (FF; 6mcg) / glycopyrronium (G; 10mcg) versus BDP/FF 100/6mcg (TRIMARAN) and high-ICS dose BDP/FF/G 200/6/10mcg versus BDP/FF 200/6mcg and BDP/FF 200/6mcg plus tiotropium 2.5mcg (TRIGGER) in adult patients with asthma uncontrolled on medium-dose (TRIMARAN) or high-dose (TRIGGER) ICS/LABA.[1]

At week 26, BDP/FF/G improved pre-dose FEV_1 (forced expiratory volume in the 1st second), a co-primary endpoint, by 57mL (95% CI 15–99; p=0.0080) and 73mL (26–120; p=0.0025) versus BDP/FF in TRIMARAN and TRIGGER, respectively. A 15% (rate ratio 0.85 [0.73–0.99]; p=0.033) and 12% (0.88 [0.75–1.03]; p=0.11) reduction in the moderate-to-severe exacerbation rate over 52 weeks (co-primary endpoint) was also observed in TRIMARAN and TRIGGER, respectively.[1] Furthermore, in the key secondary endpoint analysis of data pooled from both studies, BDP/FF/G reduced the annualised rate of severe exacerbations versus BDP/FF by 23% (p=0.0076), the rate of moderate exacerbations by 12% (p=0.043) and combined moderate and severe exacerbations by 14% (p=0.0083).[1]

Prof. J. Christian Virchow, one of the principal investigators of the TRIMARAN and TRIGGER studies, from Rostock, Germany, said, *"Some patients with uncontrolled asthma are required to use two different inhalers, of different design and with different instructions for use – and often with different dosing regimens. This is not only inconvenient for patients and healthcare providers who provide instruction on correct inhaler use but can negatively impact treatment adherence and persistence, leading to poor disease control. So, these findings are exciting for patients and healthcare providers alike because they provide first time evidence of the potential benefits of a single-inhaler triple combination of BDP/FF/G for those with uncontrolled asthma."*

Alessandro Chiesi, **Region Europe Head**, **Chiesi Group** said, *"Today's publication in **The Lancet** highlights Chiesi's commitment to providing efficacious, well-tolerated and convenient treatment options for a disease that affects 8% of adults across Europe.[2] We are proud to be supporting these innovative studies which provide us with key evidence on the potential benefits of single-inhaler triple therapy over other combination inhaler therapies. We look forward to continuing to showcase the potential benefits that our triple therapy in a single inhaler can bring to adult patients with asthma uncontrolled on ICS/LABA therapy."*

Adverse events were reported by 410 (72%) and 431 (75%) patients with BDP/FF/G and 443 (77%) and 455 (79%) with BDP/FF, in TRIGGER and TRIMARAN respectively.[1] The majority of events were mild or moderate in severity, and few were considered related to treatment.[1] The most common adverse event in all groups was asthma exacerbation, the occurrence of which was lower with BDP/FF/G than with BDP/FF.[1]

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About the TRIMARAN study
TRIMARAN is a 52-week, two-arm, parallel-group, double-blind, randomised, active-controlled, Phase III trial comparing a fixed combination of BDP/FF/G (100/6/10mcg) with BDP/FF (100/6mcg) in patients with asthma uncontrolled on medium dose ICS/LABA.[1] Eligible patients were adults (aged 18–75 years) with uncontrolled asthma, a history of one or more exacerbations in the previous year, and previously treated with medium-dose ICS/LABA. Between Feb 17, 2016, and May 17, 2018, 1,155 patients in TRIMARAN were randomly assigned (1:1) to 52 weeks of BDP/FF/G (n=579) or BDP/FF (n=576), two inhalations twice-daily. Co-primary endpoints (BDP/FF/G vs BDP/FF) were: pre-dose FEV_1 at week 26; rate of moderate-to-severe exacerbations over 52 weeks. Key secondary endpoints included severe exacerbation rate over 52 weeks (using pooled data).[1]

About the TRIGGER study
TRIGGER is a 52-week, three-arm, parallel-group, double-blind, randomised, active-controlled, Phase III trial comparing a fixed combination of BDP/FF/G (200/6/10mcg) with BDP/FF (200/6mcg), or BDP/FF (200/6mcg) plus tiotropium (2.5µg) in patients with asthma uncontrolled on high dose ICS/LABA.[1] Eligible patients were adults (aged 18–75 years) with uncontrolled asthma, a history of one or more exacerbations in the previous year, and previously treated with high-dose ICS/LABA. Between April 6, 2016, and May 28, 2018, 1,437 patients in TRIGGER were randomly assigned (2:2:1) BDP/FF/G (n=573), BDP/FF (n=576), two inhalations twice-daily, or open-label BDP/FF two inhalations twice-daily plus tiotropium (n=288) two inhalations once-daily.[1] Co-primary endpoints (BDP/FF/G vs BDP/FF) were: pre-dose FEV_1 at week 26; rate of moderate-to-severe exacerbations over 52 weeks. Key secondary endpoints included severe exacerbation rate over 52 weeks (using pooled data).[1]

About Asthma
Asthma is a common long-term condition that can affect people of all ages and causes inflammation in the airways.[3] The prevalence of asthma in the European Union (EU) is 8.2% in adults.[2] Difficult-to-treat or severe asthma occurs in 24% of patients.[4] The direct and indirect costs of asthma to society are substantial.[5] Recent calculations estimate direct costs within the EU to be nearly €20 billion, indirect costs to be €14 billion and a monetised value of DALYs (disability-adjusted life years) lost to be €38 billion, which totals €72 billion.[6]

About Chiesi Group
Based in Parma, Italy, Chiesi Farmaceutici is an international research-focussed Healthcare Group, with over 80 years of experience in the pharmaceutical industry, and with presence in 28 countries. Chiesi researches, develops and markets innovative drugs in the respiratory therapeutics, specialist medicine and rare disease areas. Its R&D organisation is headquartered in Parma (Italy), and integrated with 4 other key R&D groups in France, the USA, the UK and Sweden to advance Chiesi's pre-clinical, clinical and registration programmes. Chiesi employs over 5,600 people. Chiesi Group is a certified Benefit corporation. Chiesi Limited is the UK affiliate, for more information please visit www.chiesi.uk.com.

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