ANONYMOUS v GLAXOSMITHKLINE

SUMMIT study press release

An anonymous complainant, who was initially contactable but later could no longer be contacted at the email address provided and who described him/herself as a respiratory physician, alleged that a press release detailing results of the SUMMIT study issued by GlaxoSmithKline was deliberately misleading.

The SUMMIT [Study to Understand Mortality and Morbidity] in COPD [chronic obstructive pulmonary disease] study used, *inter alia*, Relvar (fluticasone 100mcg/vilanterol 25mcg) Ellipta. Relvar Ellipta's indications included the symptomatic treatment of adults with COPD with a FEV1<70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy.

The complainant was particularly concerned about a reference in the press release to 'survival' given that the study had failed to demonstrate a survival benefit for Relvar. The complainant was also concerned that the press release did not include a black triangle given that Relvar was subject to additional monitoring.

The complainant alleged that GlaxoSmithKline's attempt to disguise the failed results of the study could mislead clinicians. Further, by overtly promoting in the public press, such statements could raise unfounded hopes for patients. The complainant alleged that GlaxoSmithKline had brought disrepute to the whole industry.

The detailed response from GlaxoSmithKline is given below.

The Panel noted that the SUMMIT baseline publication (Vestbo *et al,* 2012) described the study as a multicentre, randomised, double-blind, parallel group, placebo-controlled trial to investigate the impact of Relvar 100/25mcg and its components on the survival of patients with moderate COPD and either a history or increased risk of cardiovascular disease.

The Panel noted the complainant's allegation that referring in the press release to the study previously termed SUMMIT as a 'survival' study following release of the results which failed to demonstrate a survival benefit, along with the assertion that 'the risk of dying on [Relvar] 100/25mcg was 12.2% lower than on placebo', was an attempt to mislead health professionals, patients and the public.

The Panel noted that the press release was headed 'GSK and Theravance announce results from the SUMMIT COPD CV Survival Study'. Below the title and the issue date was the statement 'Issued: London, UK and South San Francisco, CA, USA – LSE [London Stock Exchange] announcement'. The first paragraph referred to the LSE, NYSE [New York Stock Exchange] and NASDAQ; the Panel considered that it was clear from the outset that the press release was aimed at financial markets; the intended audience was not clinicians, patients or the public. The first paragraph also briefly explained the study and the SUMMIT acronym but did not refer to survival. The second paragraph read 'For the primary endpoint of the study, the risk of dying on [Relvar] 100/25mcg was 12.2% lower than on placebo over the study period which was not statistically significant (p=0.137)'. The third paragraph referred to the results of the two secondary endpoint. Although one endpoint showed statistical significance in favour of Relvar, it stated that as the primary endpoint was not met, statistical significance could not be inferred from the result. The second secondary endpoint showed a trend in favour of Relvar which was not statistically significant.

The Panel noted that the study was referred to as the SUMMIT study in the title and throughout. The study was designed to investigate the impact of Relvar 100/25mcg and its components on risk of death/survival in selected COPD patients. In the Panel's view it was not unreasonable to refer to survival in the heading when describing the study provided that in doing so, readers would not be misled. In the Panel's view it was stated at the outset and throughout the press release that the study failed to meet its primary endpoint and the secondary endpoints were placed in the context of the failed primary outcome. The Panel did not consider that the title of the press release or description of the results implied a survival claim for Relvar. In that regard, the Panel noted that press articles appeared to show that the target audience had understood the results of the study. The Panel thus did not consider that the press release was misleading as alleged. No breaches of the Code were ruled.

The Panel noted the complainant's concern that the press release did not display a black triangle. The Panel considered that as the press release was not promotional, there was no requirement under the Code for it to include a black triangle. No breach of the Code was ruled.

The Panel noted GlaxoSmithKline's submission that the press release was specifically directed at shareholders and the financial community, not patients. The Panel noted that the press release contained information that might be of interest to patients but in the Panel's view it had not been directed at them. Furthermore, the results were presented in a balanced manner and the fact that the study failed to show a survival benefit was understood by the complainant, the financial journalists and it was therefore, in the Panel's

view, unlikely that the press release would raise unfounded hopes in patients who searched for it. The Panel ruled no breach of the Code. The Panel noted that the Code only required a statement about reporting side effects to be included on material which related to a medicine and was intended for patients taking that medicine. Although it might have been helpful to include information about reporting side effects, as the press release was not intended for patients the Panel ruled no breach of the Code.

The Panel noted its rulings above and considered that high standards had been maintained. No breach of the Code was ruled including no breach of Clause 2.

An anonymous complainant, who was initially contactable but later could no longer be contacted at the email address provided and who described him/herself as a respiratory physician, alleged that a press release entitled 'GSK and Theravance announce results from the SUMMIT [**S**tudy to **U**nderstand **M**ortality and **M**orbid**IT**y] COPD [chronic obstructive pulmonary disease] CV [cardiovascular] Survival Study' issued by GlaxoSmithKline was deliberately misleading. The complainant provided a link to the press release.

The study involved 16,485 COPD patients from 43 countries; each patient had moderate airflow limitation and either a history or increased risk of cardiovascular disease (CVD). Patients were randomly assigned to once daily treatment with GlaxoSmithKline's product Relvar Ellipta (100/25mcg fluticasone furoate/vilanterol (FF/VI)) FF (100mcg), VI (25mcg) or matched placebo. The primary endpoint of the study was the risk of dying on Relvar. Secondary endpoints were the rate of lung function decline and the risk of experiencing an on-treatment cardiovascular event (CV death, myocardial infarction, stroke, unstable angina and transient ischaemic attack).

Relvar Ellipta (100/25mcg) indications included the symptomatic treatment of adults with COPD with a FEV1<70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy.

COMPLAINT

The complainant submitted that in its attempt to fool the medical community and the public, GlaxoSmithKline labelled the latest failed fiasco study a COPD CV 'survival' study. The complainant alleged that use of the word survival was clearly intended to mislead the audience; the study had so far been referred to as the SUMMIT study however, at the release of the results, contrary to what the results showed, it had now been termed 'survival' study.

The complainant noted that the study clearly showed that Relvar failed to demonstrate a survival benefit compared with placebo. Nonetheless, use of the term 'survival' study along with GlaxoSmithKline's assertion that 'the risk of dying on [Relvar] 100/25mcg was 12.2% lower than on placebo' was a calculated attempt to mislead clinicians, patients and the public. In addition it was appalling that the press release failed to display a black triangle for Relvar, a legal requirement for the medicine which was subject to additional monitoring due to the several serious risks that it carried to patients including severe and fatal pneumonia.

The complainant stated that for years, GlaxoSmithKline promoted its medicine Seretide with the claim that it prolonged life in COPD, despite the failed TORCH trial and had been found in breach multiple times last year in relation to such promotion. However, it seemed that the lessons had not been learnt and the complainant alleged that GlaxoSmithKline continued to operate in a wilfully unethical manner both in the UK and abroad, referring to recent events in China and the previous findings by the US government. The complainant submitted that GlaxoSmithKline, as the largest pharmaceutical organisation in Britain, was morally obliged to lead by example, but it brought nothing other than disrepute to the whole industry.

The complainant alleged that GlaxoSmithKline's latest attempt to disguise the failed results of the study could mislead the clinicians. Further, by overtly promoting in the public press, such statements could raise unfounded hopes for patients.

When writing to GlaxoSmithKline, the Authority asked it to respond in relation to Clauses 2, 4.11, 7.2, 7.4, 9.1, 26.2, and 26.3.

RESPONSE

GlaxoSmithKline submitted that it took compliance with the Code very seriously and denied that the press release was in breach of Clauses 2, 4.11, 7.2, 7.4, 9.1, 26.2 or 26.3.

GlaxoSmithKline noted that the complainant referred to a press release issued by GlaxoSmithKline Corporate Communications on 8 September 2015, in London and San Francisco, and which was placed in the 'Press Releases' section of the corporate website. It was also distributed to financial, medical and business institutions which had specifically asked to be informed of any new GlaxoSmithKline press releases.

GlaxoSmithKline stated that the press release was issued because the newsworthy study results were share price sensitive and of potential interest to shareholders and financial institutions. As such, before issuing the press release, the Stock Exchange listing for both companies (NYSE [New York Stock Exchange] and NASDAQ]) were informed of its release and were referred to in the first paragraph of the press release. The press release was also in line with the company's standard operating procedure on press releases which stated, 'We announce Phase III data via a corporate press release, regardless of outcome, upon first presentation or publication in a peer-review journal. Study results for material assets are disclosed via Stock Exchange Announcement when data analysis is complete'.

GlaxoSmithKline noted that the complainant had sourced the material from the press section of its website, either on the day it was released or shortly thereafter and had referred to it as a 'press release'.

Reference to 'survival' study

GlaxoSmithKline submitted that 'survival' was used once in the press release title, and only then as to describe the study design, as follows; 'GSK and Theravance announce results from the SUMMIT COPD CV Survival study'. The study was never simply referred to as a '... COPD CV "survival" study' as alleged. Furthermore the study was referred to as 'SUMMIT' six times; in the title in large and bold font, in the first paragraph to explain the acronym, by the senior vice president and head global respiratory franchise for GlaxoSmithKline, the study's principal investigator, and the chief executive officer for Theravance, as well as in the section which provided further information about the study itself.

GlaxoSmithKline noted that the study was officially listed on clinical trials.gov as:

> 'Study to Evaluate the Effect of Fluticasone Furuoate/Vilanterol on Survival in Subjects With Chronic Obstructive Pulmonary Disease' (emphasis added).

The rationale for the study in a baseline publication for the study design was given as:

> 'The "Study to Understand Mortality and Morbidity in COPD" (SUMMIT) aims at determining the impact of Fluticasone Furoate/ Vilanterol combination (FF/VI), and the individual components on the survival of patients with moderate COPD and either a history of CVD or at increased risk for CVD' (emphasis added).

The keywords to be used when searching for the study were: COPD; CVD; protocol; study design; mortality; survival; Fluticasone Furoate; Vilanterol; combination therapy (emphasis added).

GlaxoSmithKline explained that SUMMIT was an event-driven study designed to have 90% power to detect a 30% reduction in the risk of all-cause mortality. 'Survival' was frequently referred to in the baseline publication, eg 'Survival status of each subject will be recorded at every visit. For any subject who prematurely withdraws, survival status will be captured at 3-monthly intervals by means of telephone calls or other forms of contact' (emphasis added) (Vestbo *et al* 2012). Aside from that, 'survival' could be considered an acceptable descriptor for the study design, particularly as the financial community and shareholders, to whom the press release was directed, would probably not be familiar with the acronym, SUMMIT. Also where 'survival' was used in the title, there were no statements about the outcome of the study; it was used purely as an adjective for the study design, not as a claim.

GlaxoSmithKline therefore denied a breach of Clause 7.2 as well as Clause 7.4.

Alleged attempt to mislead the clinicians, patients and the public.

GlaxoSmithKline submitted that the complainant indicated that he/she had read the press release and understood its contents as he/she used such phrases as 'the study clearly showed' and 'failed to demonstrate a survival benefit'; the complainant thus demonstrated that even a 'critical reader' had understood that the study did not achieve its primary endpoint.

The fact that 'the primary endpoint was not statistically significant' was mentioned four times in the press release and that 'statistical significance could not be inferred from the secondary endpoints, as the primary endpoint was not met', twice. GlaxoSmithKline noted that the complainant's comment that the 'risk of dying on [Relvar] 100/25mcg was 12.2% lower than on placebo', failed to complete the sentence from the press release which continued '... over the trial period which was not statistically significant (p=0.137)'.

The complainant therefore clearly understood the results and significance for the SUMMIT study as did the audience for whom the release was intended, the global financial community, judging from the headlines and analyst reports which appeared worldwide on either the same, or following day after the announcement was made eg:

> 'Overnight GSK has reported that the SUMMIT COPD cardiovascular survival trial failed to meet its primary endpoint. SUMMIT compared [Relvar] to placebo in 16,485 patients with COPD and a history of or increased risk of cardiovascular disease. The aim was to show that treatment with [Relvar] improved cardiovascular survival. If successful, [Relvar] would have been the only COPD drug to have shown a survival benefit and the data would have provided a significant commercial boost to [Relvar] relative to competitors, especially in the face of generic Advair over time' Credit Suisse 9 September 2015.
>
> 'Respiratory drug trial failure deals blow to GSK revival plan' Financial Times and
>
> 'Study finds key GSK-Theravance Lung drug didn't extend lives' Washington Post.

GlaxoSmithKline therefore denied a breach of Clause 7.2 as well as Clause 7.4.

Failure to display a black triangle

GlaxoSmithKline submitted that the press release was targeted at shareholders and the financial community in line with Clause 26.2 'Information made available in order to inform shareholders, the Stock Exchange and the like by way of annual reports and announcements etc may relate to both existing medicines and those not yet marketed'. In addition, the press release was examined in line with the supplementary information to Clause 14.3 which stated 'Other material issued by companies which relates to medicines but which is not intended

as promotional material for those medicines per se, such as corporate advertising, press releases, market research material, financial information to inform ....' and signed as being fair, accurate, balanced and capable of substantiation by thirteen senior members of GlaxoSmithKline, including two statisticians.

As the press release was not a promotional item and was not specifically intended for prescribers or patients, it did not require a black triangle against the first/most prominent mention of the brand name, the significance of which would in any case not have been known to most of the financial community. This was in accordance with guidance from the Medicines and Healthcare products Regulatory Agency (MHRA) about the yellow card scheme.

GlaxoSmithKline therefore denied a breach of Clause 4.11.

GlaxoSmithKline submitted the complainant's assumption that the 'additional monitoring (was) due to the several serious risks that [Relvar] carried to patients including severe and fatal pneumonia' was incorrect. GlaxoSmithKline stated that the black triangle was a requirement for all newly available medicines in the UK and could only be removed once the MHRA believed that the benefit:risk ratio of that medicine had been fully characterised. With regard to statements concerning 'severe and fatal pneumonia' GlaxoSmithKline noted that detailed safety information was given on pages 1 and 2 (relating to the study itself) and on pages 4-6 (relating to a more general overview of Relvar) of the press release.

Clauses 26.2 and 26.3

GlaxoSmithKline submitted that the press release gave an accurate, balanced view of a large important study, which failed to meet its primary endpoint, and within that context it provided information regarding the secondary endpoints. The press release was also balanced and fair in terms of the safety/tolerability information provided both with respect to the study and Relvar. The press release was specifically directed at shareholders and the financial community, not at patients who might have been prescribed Relvar.

GlaxoSmithKline therefore denied that the press release was in breach of Clause 26.2. GlaxoSmithKline did not consider that Clause 26.3 'Any material which relates to a medicine and which is intended for patients taking that medicine must include ...' was applicable as the press release was not specifically distributed to patients taking the medicine (or to potential prescribers); it was principally for the attention of shareholders and the financial community as well as the medical press.

In view of the above GlaxoSmithKline, therefore submitted that high standards had been maintained and that it had not brought the industry into disrepute as claimed; it denied breaches of Clauses 9.1 and 2.

PANEL RULING

The Panel noted that Vestbo *et al* described the SUMMIT study as a multicentre, randomised, double-blind, parallel group, placebo-controlled trial to investigate the impact of Relvar 100/25mcg and its components on the survival of patients with moderate COPD and either a history or increased risk of cardiovascular disease.

The Panel noted the complainant's allegation that referring in the press release to the study previously termed SUMMIT as a 'survival' study following release of the results which failed to demonstrate a survival benefit, along with the assertion that 'the risk of dying on [Relvar] 100/25mcg was 12.2% lower than on placebo', was an attempt to mislead health professionals, patients and the public.

The Panel noted that the press release was dated 8 September 2015 and was headed 'GSK and Theravance announce results from the SUMMIT COPD CV Survival Study'. Below the title and the issue date was the statement 'Issued: London, UK and South San Francisco, CA, USA – LSE [London Stock Exchange] announcement'. The first paragraph referred to the LSE, NYSE and NASDAQ; the Panel considered that it was clear from the outset that the press release was aimed at financial markets; the intended audience was not clinicians, patients or the public as implied by the complainant. The first paragraph also briefly explained the study and the SUMMIT acronym but did not refer to survival. The second paragraph read 'For the primary endpoint of the study, the risk of dying on [Relvar] 100/25mcg was 12.2% lower than on placebo* over the study period which was not statistically significant (p=0.137)'. The asterisk was not explained. The third paragraph referred to the results of the two secondary endpoints; the rate of lung function decline which was reduced by 8ml/year in patients taking Relvar 100/25mcg compared with placebo (p=0.019). It stated that as the primary endpoint was not met, statistical significance could not be inferred from the result; and the risk of experiencing an on-treatment cardiovascular event (CV death, myocardial infarction, stroke, unstable angina and transient ischaemic attack) was 7.4% lower in patients taking Relvar 100/25mcg compared with placebo (p=0.475) which was noted as not being statistically significant.

The Panel noted GlaxoSmithKline's submission that 'survival' was used once in the press release title, and then only as a descriptor for the study design ie 'the SUMMIT COPD CV Survival Study' as opposed to 'a COPD CV survival study' as alleged. 'Survival' was otherwise only used three times more in the eight page press release. Furthermore, the study was referred to as 'SUMMIT' six times throughout the press release.

The Panel noted that the study was referred to as the SUMMIT study in the title and throughout. The study was designed to investigate the impact of Relvar 100/25mcg and its components on risk of death/survival in COPD patients with moderate airflow limitation and either a history or increased risk of cardiovascular disease. In the Panel's view it was

not unreasonable to refer to survival in the heading when describing the study provided that in doing so, readers would not be misled. In the Panel's view it was stated at the outset and throughout the press release that the study failed to meet its primary endpoint and the secondary endpoints were placed in the context of the failed primary outcome. The Panel did not consider that the title of the press release or description of the results implied a survival claim for Relvar. In that regard, the Panel noted that the articles quoted by GlaxoSmithKline appeared to show that the target audience had understood the results of the SUMMIT study as reported in the press release. The Panel thus did not consider that the press release was misleading as alleged. No breach of Clauses 7.2 and 7.4 was ruled.

The Panel noted the complainant's concern that the press release did not display a black triangle. Clause 4.11 of the Code stated that when required by the licensing authority, all promotional material must show an inverted black triangle to denote that special reporting was required in relation to adverse reactions. The Panel considered that as the press release was not promotional, there was no requirement under the Code for it to include a black triangle. No breach of Clause 4.11 of the Code was ruled.

The Panel noted that Clause 26.2 stated 'Information about prescription only medicines which is made available to the public either directly or indirectly must be factual and presented in a balanced way. It must not raise unfounded hopes of successful treatment or be misleading with respect to the safety of the product. Statements must not be made for the purpose of encouraging members of the public to ask their health professional to prescribe a specific prescription only medicine'. The Panel noted GlaxoSmithKline's submission that the press release was specifically directed at shareholders and the financial community, not patients who might have been prescribed Relvar. The Panel noted that the press release contained information that might be of interest to patients but in the Panel's view it had not been directed at them. Furthermore, the results were presented in a balanced manner and the fact that the study failed to show a survival benefit was understood by the complainant, the financial journalists and it was therefore, in the Panel's view, unlikely that the press release would raise unfounded hopes in patients who searched for the press release on GlaxoSmithKline's website. The Panel ruled no breach of Clause 26.2. The Panel noted that Clause 26.3 only required a statement about reporting side effects to be included on material which related to a medicine and was intended for patients taking that medicine. Although it might have been helpful to include information about reporting side effects, as the press release was not intended for patients the Panel ruled no breach of Clause 26.3.

The Panel noted its rulings above and considered that high standards had been maintained. No breach of Clause 9.1 was ruled.

The Panel noted its rulings above and consequently ruled no breach of Clause 2.

Complaint received **25 September 2015**

Case completed **7 October 2015**