CASE AUTH/3241/8/19

VOLUNTARY ADMISSION BY BRISTOL-MYERS SQUIBB

Data error in advertisement

Bristol-Myers Squibb Pharmaceuticals Limited, voluntarily admitted that overall survival (OS) results published in a promotional article was incorrect. The material at issue, published online and in the hard copy version of Urology News, was about the combination of Opdivo (nivolumab) and Yervoy (ipilimumab) for the first line treatment of adults with intermediate/poor-risk advanced renal cell carcinoma.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Bristol-Myers Squibb.

The detailed response from Bristol-Myers Squibb appears below.

The Panel noted that the original article published online and in the hard copy version of Urology News stated that the 30 month OS for the intermediate and poor-risk renal cell carcinoma patients was 64%, (for nivolumab plus ipilimumab) compared with 56% of patients treated with sunitinib (Sutent). The Panel noted that this data was for the Intention-to-Treat (ITT) population which included the favourable risk subgroup rather than only the intermediate and poor risk population. The correct data for the intermediate and poor-risk population should have stated 60% and 47% for the two arms respectively. The Panel noted that the information was inaccurate and ruled a breach as acknowledged by the company.

Bristol-Myers Squibb Pharmaceuticals Limited, voluntarily admitted that data published in a promotional article (ref 7356UK900405-02) was incorrect. The material at issue published online and in the hard copy version of Urology News v23 (5) July/August 2019, featured an interview with a professor of oncology and related to the combination of Opdivo (nivolumab) and Yervoy (ipilimumab) for the first line treatment of adults with intermediate/poor-risk advanced renal cell carcinoma (aRCC).

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Bristol-Myers Squibb.

VOLUNTARY ADMISSION

Bristol-Myers Squibb submitted that on 9 July it identified an error in the online version of Urology News (published 8 July) relating to the overall survival (OS) results quoted within the promotional article. The hazard ratio published in the article (HR 0.66, 95%CI 0.54-0.80; P<0.0001) was correct; however, the article stated that the 30 month OS for the intermediate and poor-risk renal cell carcinoma (RCC) patients was 64%, (for nivolumab plus ipilimumab) compared with 56% of patients treated with sunitinib (Sutent, marketed by Pfizer). The data was erroneously quoted for the Intention-to-Treat (ITT) population. The correct data for the

intermediate and poor-risk group should have read 60% and 47% respectively. Unfortunately, the hard copy journal was already in circulation when the error was noted.

Bristol-Myers stated that as immediate actions the online version had been removed and remedial steps had been taken to re-publish the article, with the correct data, in the next issue of Urology News (to be published 1st week of September) with a clear apology, and an explanation for the reprint. The corrected article would also appear online.

The company acknowledged that the matter constituted a breach of Clause 7.2 of the Code.

RESPONSE

Bristol-Myers Squibb reiterated the error in the article and noted that the ITT population included the favourable-risk aRCC subgroup rather than only the intermediate and poor-risk population. The correct data for the intermediate and poor-risk population should have stated 60% and 47% for the two arms respectively rather than the 64% and 56% cited.

Bristol-Myers Squibb noted that, while the OS figures given in the article were inaccurate, the difference between the two arms of the study did not over-state the benefit, as the difference was smaller than the true value.

Bristol-Myers Squibb explained that the material was developed by a communications agency after an interview with a professor of oncology. It was then uploaded by the Bristol-Myers Squibb originator into the company's internal approval system for accuracy review (conducted by an external vendor), and internal Code review.

At the accuracy review stage, the data in question was initially correctly stated; however, because no supporting reference was provided the material was returned to the originator. The missing reference was subsequently inserted by the communications agency as requested, however, at this point the data in the article was incorrectly updated. Unfortunately, at the next accuracy review this error was not identified as the data amendment had not been initially requested nor was it appropriately highlighted to the accuracy reviewer. When it was certified, the erroneous data change was also not identified by the Bristol-Myers Squibb Code reviewer for the same reason and therefore the error was carried through to final certification.

Timeline

8 July: The online version of the article was published on the Urology News website.

9 July: The data error was identified and the communications agency was contacted to arrange immediate withdrawal of the online article by Urology News. Unfortunately, the hard copy journal was already in circulation and so the print version could not be recalled.

12 July: On checking the Urology News website to confirm the removal of the incorrect article, it was noted, that an amended article with corrected data had been placed online (containing the original job code). During the course of the investigation, it was determined that in the interests of acting with speed and urgency, the originator had provided the agency with the corrected data; in the meantime, the amended article was sent for certification. However, this amended article was re-published online before certification. Bristol-Myers Squibb contacted the communications agency to request removal of the amended (uncertified) version.

15 July: Bristol-Myers Squibb identified that the article was still accessible on the website and was informed by Urology News that removal would not be straightforward due to technical complexity (the online article had to be extracted from the whole digital issue of the journal). Urology News confirmed the article was fully removed on 17 July.

To correct the error within the printed version of the article, the Bristol-Myers Squibb originator arranged for an article reprint in the September edition of Urology News to contain a clear apology and identify the error for the readership. This was mailed to readers on 30 August.

Bristol-Myers Squibb noted that following electronic certification, neither the original nor the corrected article was sent in its final form for check and signature prior to publication.

Bristol-Myers Squibb acknowledged a breach of Clause 7.2 as noted above. Furthermore, through the investigation into this matter, the company also considered that it had breached Clause 14.1.

Bristol-Myers Squibb stated that it took compliance extremely seriously and was committed to abiding by the Code. The matter had been investigated in depth and a corrective and preventive action (CAPA) plan had been implemented:

- Bristol-Myers Squibb contacted the communications agency and subsequently contacted Urology News directly to ensure immediate removal of the online article.

- Corrective steps had been taken regarding the distributed print version, by publishing the corrected version of the article in the September print edition of Urology News, with a clear apology identifying the error. This was distributed to those who received the original article to ensure the entire audience was reached.

- The activity originator had been retrained in relation to the company's promotional materials standard operating procedure (SOP), which included the expectations for certification. Furthermore, as an additional future-looking measure, all potential originators and the Code signatories had been reminded of their responsibilities in this regard. The communication reinforced the responsibilities of employees in relation to the Code, particularly when working with third party agencies and to ensure Bristol-Myers Squibb staff continued to abide by the relevant SOPs. Originators and agencies must highlight any change made to materials during the course of review.

- Bristol-Myers Squibb would not work with the communications agency contracted to this piece in the future and had a new agency in place to support future projects. The new agency had been briefed on its obligations, including the specifics of the promotional materials and non-promotional materials SOPs and the need to ensure that any changes made in documents were highlighted and detailed notes were provided for review.

- The external vendor contracted to perform accuracy and technical checks on materials had been informed about this incident to ensure appropriate corrective and preventative plans were put in place. A face-to-face meeting was urgently arranged, following an initial call, to understand how and why the error was missed. Although

the key contributing factor was human error, remedial steps were agreed to prevent re-occurrence, including:

- Using the same accuracy reviewer where possible for each round of review to maintain continuity and reduce the risk of error;
- requesting continuous feedback from signatories regarding the accuracy reviewers, to facilitate a better understanding of any omissions identified during Code review and any internal decisions made;
- reminding the vendor of his\her responsibilities under the Code and relevant company SOPs.

- External audits of approved materials were undertaken for compliance with the Code. Given the above incident, the company was currently undertaking an audit of accuracy reviews undertaken by the external accuracy review agency.

Bristol-Myers Squibb submitted that it had robust SOPs in place to govern promotional material review and approval including referencing and certification. The sequence of events that occurred was not acceptable. Whilst the company recognised that occasionally human error did occur, it considered that it had taken well-considered and appropriate measures to ensure that it continued to demonstrate its commitment to self-regulation and the principles of the Code.

PANEL RULING

The Panel noted that the original article published online and in the hard copy version of Urology News published in July 2019 stated that the 30 month OS for the intermediate and poor-risk renal cell carcinoma (RCC) patients was 64%, (for nivolumab plus ipilimumab) compared with 56% of patients treated with sunitinib (Sutent). The Panel noted that this data was for the ITT population which included the favourable-risk aRCC subgroup rather than only the intermediate and poor-risk population. The correct data for the intermediate and poor-risk population should have stated 60% and 47% for the two arms respectively. The Panel noted that the information was inaccurate and ruled a breach of Clause 7.2 as acknowledged by the company.

The Panel noted that in its response Bristol-Myers Squibb submitted that to correct the error within the printed version of the article, the originator arranged for an article reprint in the September edition of Urology News to contain a clear apology and identify the error for the readership. Following electronic certification, neither the original nor the corrected article was sent in its final form for check and signature prior to publication. The Panel noted that this voluntary admission was being taken up in Case AUTH/3286/12/19.

Complaint received **21 August 2019**

Case completed **20 December 2019**