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22 Jan 2024 | **News**

Kisqali 'Live Longer' TV Ad Misrepresents Patient-Reported Outcome Data, US FDA Tells Novartis

by Brenda Sandburg

Untitled letter says advertisement could lead breast cancer patients to believe Kisqali has better overall survival and quality of life than was demonstrated. FDA also criticizes length of time to read claims in superimposed text and competing audio and visual presentations in the TV spot.

The US Food and Drug Administration's Office of Prescription Drug Promotion objected to *Novartis AG*'s television ad claiming its breast cancer drug Kisqali (ribociclib) "preserves qualify of life" and that patients taking it are "living well."

The claims "create a misleading impression that Kisqali has demonstrated a benefit on the patient reported outcome (PRO) measure of global quality of life (QoL). In fact, we note significant limitations to the PRO analysis described in the cited reference (the MONALEESA-2 clinical trial) which preclude the drawing of such conclusions regarding benefits related to QoL," the agency stated in a 18 January *untitled letter*.

"Specifically, while PROs for health-related QoL were included in the trial as secondary endpoints, there was no alpha-allocation. Since there was no alpha-allocation, and, therefore, no specified false positive error rate, it is not known whether the QoL outcome data represents a false positive finding that occurred by chance alone," OPDP stated. Therefore, the PRO data are considered exploratory (i.e., hypothesis generating), and do not demonstrate that Kisqali "helps preserve quality of life" or that it supports patients "living well."

Limitations In PRO Analyses

The agency said the presentation of these data creates a misleading impression regarding the benefits of Kisqali because of the significant limitations to the PRO analysis performed in the

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MONALEESA-2 trial. OPDP said Novartis did not demonstrate that the PRO assessments were frequent enough to collect data to support the claims regarding QoL at the 26-month check-in.

Global QoL was assessed every eight weeks for the first 18 months and then every 12 weeks thereafter. OPDP said Novartis did not account for concerns the QoL could fluctuate significantly between assessment points and that in the context of patients with advanced or metastatic breast cancer, variations in QoL across the assessment period may be greater than in the general population.

In addition, OPDP said there was no assessment to demonstrate the appropriateness of the intervals used to assess global QoL in this study, and that the claims were based on the PRO endpoint of global QoL, which can be confounded by non-treatment and non-disease related factors. And the agency said Novartis did not demonstrate that the time to deterioration endpoint as assessed in the trial is appropriate for evaluating PROs.

The agency noted that Novartis submitted the broadcast ad for review. The untitled letter is the first enforcement letter OPDP has issued this year and reflects the agency's focus on efficacy claims that are inconsistent with labeling. Four of the five letters OPDP issued last year objected to promotions that overstated a product's efficacy and were not in accordance with labeling. (Also see "*FDA Is 'Getting More Aggressive' In Going After Drug Efficacy Claims Outside Label*" - Pink Sheet, 5 Dec, 2023.)

Too Little Time To Read SUPER

The *advertising frames* note that the voice over states that post-menopausal women with HR+ HER2-metastatic breast cancer are living longer with Kisqali. The ad's superimposed text (SUPER) says overall survival was a secondary endpoint of the trial.

However, the agency said the presentation of the SUPER is undermined by multiple, competing presentational aspects that distract the viewer and undermine the communication of material information regarding the overall survival data in the SUPER, which is needed to qualify the amount of time that patients can expect to "live longer" when treated with Kisqali plus a non-steroidal aromatase inhibitor compared to an NSAI alone.

OPDP also took issue with the length of time the "long live" and "live longer" claims appear in the SUPER, noting that the ad presents 48 words in approximately 5 seconds, which translates to a reading speed of 575 words per minute (wpm).

The agency said a recent review and meta-analysis found that the average silent reading rate for adults in English is 238 wpm for uninterrupted non-fiction reading, with most adults falling in a range of 175 to 300 wpm. It noted that the number of words in the SUPER is more than twice the number of words, on average, that an adult can read within five seconds and that during the five-

second period that the SUPER appears, there are multiple competing audio and visual presentations.

“Overall, by presenting compelling and attention-grabbing visuals as well as information in other modalities during the presentation of the SUPER, which itself is presented in a manner that would not allow most viewers to read, process, and comprehend the material information it presents, the TV ad misleadingly undermines the communication of material information about the drug’s efficacy,” OPDP stated.

The FDA addressed the timing of the presentation of risk information in direct-to-consumer television ads in a final rule issued in November. The rule on presenting the “major statement” about a prescription drug’s side effects and contraindications in a “clear, conspicuous, and neutral manner” requires that the statement be presented simultaneously in audio and visual portions of the ad and displayed for sufficient duration to allow it to be easily read. (Also see "*Rx Drug TV Ads Must Present ‘Major Statement’ Simultaneously In Audio & Visual Segments*" - Pink Sheet, 20 Nov, 2023.)

Nine-Month Ad Campaign

Novartis did not respond to a query about when and where the Kisqali TV ad aired. According to iSpot.tv, the *commercial* aired from 5 December 2022 through 12 September 2023 with 6,600 airings and an estimated national TV ad spend of $46.5m.

iSpot.tv, which measures the performance of TV ads, said the ad had 3.29 billion household TV ad impressions and the top networks by ad impressions SOV (share of voice) were CBS (29.9%), ABC (17.2%), NBC (13.7%), Game Show (5.1%) and Fox News (5.0%). And the top programs by ad impressions SOV were CBS Evening News With Norah O’Donnell (6.7%), ABC World News Tonight With David Muir (5.1%), NBC Nightly News With Lester Holt (4.5%), The Price Is Right (4.1%), and Today Third Hour (4.0%).

Novartis’s promotional materials for Kisqali have previously been criticized. *Eli Lilly and Company* brought a complaint to the National Advertising Division of BBB National Programs contending that promotions directed to consumers and health care providers conveyed that Kisqali is superior to Lilly’s Verzenio (abemaciclib). Last year, NAD concluded that the consumer promotions were inappropriate but that a similar claim in health care provider promotional materials did not need to be discontinued. (Also see "*Novartis’ Kisqali Consumer Promos Inappropriately Convey Superiority, NAD Finds In Unusual Ruling*" - Pink Sheet, 19 Jan, 2023.)

In 2012, OPDP objected to Novartis promotional materials for its oncology drug Gleevec (imatinib). The agency sent a “notice of violation” letter citing the company's case highlights that described five-year survival data before it was added to the label. (Also see "*FDA Cites Gleevec For Promoting Unapproved Indications Three Weeks Before Expanding Label*" - Pink Sheet,

15 Mar, 2012.)