SCRIP
CITELINE COMMERCIAL

13 May 2021 |

CDK4/6 Market: Is A Shakeup Underway?

by Jessica Merrill

Pfizer's Ibrance still dominates the category but sales slowed in the first quarter, while Novartis's Kisqali and Lilly's Verzenio both grew double digits.

Pfizer Inc.'s Ibrance (palbociclib) has dominated the CDK4/6 inhibitor category since it launched in 2015 for hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced or metastatic breast cancer, despite the entry of two competitors. But now it appears Ibrance's momentum may be reaching a plateau.

Ibrance sales were flat in the first quarter at $1.25bn on a worldwide basis and declined 7% in the US to $794m compared with Q1 2020, while sales of *Eli Lilly and Company*'s Verzenio (abemaciclib) and *Novartis AG*'s Kisqali (ribociclib) both grew double digits, though off considerably smaller bases. First quarter sales of Verzenio grew 43% to $269m and Kisqali grew 21% to $195m year-over-year.

Pfizer attributed the slowdown in Ibrance revenue to the COVID-19 pandemic, which has created a challenging commercial dynamic for many cancer drugs with fewer patients seeking out cancer screenings and receiving diagnoses. US prescription volume for Ibrance was relatively stable in the quarter, according to Pfizer, but more patients accessed the drug through Pfizer's patient assistance program due to economic hardship brought on by the pandemic.

"We continue to be the leading product in the CDK class by a wide range with an 84% of total patient share in first-line use," Pfizer CEO Albert Bourla said in a 4 May conference call. "However, we saw increased involvement this quarter in our patient assistance program, which provides Ibrance free of charge to certain low-income patients. We believe this increase is due to COVID-19-related economic hardships that are affecting particularly the demographics of the Ibrance patient population." Bourla said the trend is expected to normalize over time as the pandemic subsides.

Nonetheless, Ibrance has come under new commercial pressure after the drug failed to show a significant survival benefit in advanced HR+/HER2-negative breast cancer in a clinical trial, while

Verzenio and Kisqali both did. Verzenio also succeeded in reducing the risk of breast cancer recurrence in women with HR+, HER2- high risk early breast cancer in the monarchE trial in the adjuvant setting, while Ibrance failed to do so in the PALLAS and PENLOPE-B trials. (Also see "*ESMO: A Tale Of Two CDK 4/6 Inhibitors With monarchE Success and Failure For PALLAS*" - Scrip, 21 Sep, 2020.) An ongoing study with Kisqali in the early adjuvant setting called NATALEE is ongoing and expected to read out in 2022.

The drugs are approved with different hormone regimens, however, and also have different safety profiles. Kisqali, for example, is the only one that carries a warning for risk of QT prolongation, or abnormal heart rhythm, in combination with tamoxifen.

Pfizer Defends Its Market Leadership Position

"Pfizer is on its back foot a bit," Wolfe research analyst Tim Anderson said in comments to *Scrip*. "While the incumbent, it also has been the only one to not show a formal OS benefit in first-line [metastases]. Novartis and Lilly both have it."

Anderson speculated that could be driving increased rebating in the category. "Do I know for sure who is (or whether anyone is) rebating more in the class suddenly? Not specifically. I can only guess that it's Pfizer," he said.

Bernstein analyst Ronny Gal also suspected that the category could be seeing more pricing pressure in a 10 May note. "Commercial price pressure is moving into specialty products previously protected," he said. "Some management comments around BTKi and CDK4/6 suggest these oral oncology categories are beginning to see pressure."

Pfizer, however, said it has not changed the price or rebates for Ibrance.

Cancer is not a category that has generally experienced high rebating and payers have largely taken a hands-off approach to managing drug utilization in the therapy area, so it would be interesting if that were to change substantially. Use of cancer drugs tends to be managed through cancer pathways established by oncology providers, generally protocols for treating cancer patients. Competitive oral cancer drug categories that are reimbursed under Medicare Part D rather than Part B could be an easier target for more aggressive strategies, however.

"We clearly see that this is a class where there are three drugs that have obviously some similarity," said Ed Schoonveld, principal at ZS Associates and author of "The Price of Global Health," a book on drug pricing and access.

"We need to be careful with that because the profile of the drugs are still very different," he said. "This is a delicate balance where obviously providers and payers want to extract some additional savings to make sure they have higher margins in that game."

During Lilly's first quarter sales and earnings call on 4 May, oncology president Anne White confirmed that the category is seeing more competitive dynamics at play but declined to comment on any pricing or rebating specifics.

"It's an incredibly competitive market with the CDK4/6s, and so we and others continue to do what we need to do to make sure that patients get access to the right medicines," she said.

In the US market, she said Verzenio saw a total prescription market share of 17% in the first quarter and new prescription share of over 28% despite a modest decline in category prescriptions year-over-year. *[Editor's note: This story has been updated to accurately reflect Verzenio's market share. A previous version reported the share as growth].*

"Obviously, the data in adjuvant breast cancer reinforced a growing awareness that these medicines are different," White said. "The focus for our execution has been capitalizing on positive OS data and making sure that people are aware of that, and we're seeing more trial, more adoption."

Novartis reported that growth of Kisqali came from outside the US and particularly Europe, while sales in the US were flat to slightly declining.

"The reason is really very different market dynamics, that in the US the market certainly is already quite penetrated with CDK4/6 inhibitors," Novartis oncology president Susanne Schaffert said during the company's quarterly conference call on 27 April. The pandemic has also contributed to a significant slowdown in new prescriptions in the US, she added.

Kisqali has faced some added pressure in the US as well in that the pharmacy benefit manager Express Scripts, owned by *Cigna Corp.*, excluded the medication on its national formulary and listed Ibrance and Verzenio as preferred medications. Novartis, in a statement, said oncologists continue to prescribe and receive medical exception to the policy based on the significant overall survival benefit seen with Kisqali in metastatic breast cancer and pointed to its patient support program that is available to help patients understand their insurance coverage and identify assistance options.

The outcome of Novartis's Phase III NATALEE trial in the adjuvant setting will be an important readout for the category. A positive readout will be valuable to Novartis, but a negative outcome could give Verzenio, in particular, an edge.

"The importance of the Novartis data set (NATALEE) is under-appreciated by investors, in my view, as it will either suggest that all three of the CDKs are more or less the same (if NATALEE is positive) and that Pfizer just had bad luck, or conversely it will suggest that Lilly's is unique (if NATALEE misses)," Anderson said.