The Role of Claims Analysis During Financial Due Diligence of Aficamten for Hypertrophic Cardiomyopathy (HCM)

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Introduction

Closing a biotech financing round can be challenging in cases where there are no FDA approved products for the target indication. Success requires in-depth analysis of the addressable market, patient dynamics, and unmet need in the absence of approved therapies as anchors for key commercial forecast assumptions.

Cytokinetics and Royalty Pharma entered a diligence process to fund aficamten's pivotal clinical trials for the treatment of hypertrophic cardiomyopathy (HCM).

HCM is a disease in which the heart muscle becomes abnormally thick or enlarged, ultimately limiting the heart's pumping function, resulting in symptoms including chest pain, dizziness, shortness of breath, or fainting during physical activity.

Until recently, HCM patients have been treated with either beta- or calcium-channel blockers, both of which have significant side effects and low patient compliance and persistency compared to other therapies treating cardiovascular diseases such as heart failure. With few treatment options, patients frequently disappear from medical claims data after initial diagnosis, resulting in an under-estimate of HCM patients in medical claims-based epidemiology studies.

In addition, published epidemiology studies vary widely in terms of their HCM patient estimates and with most suggesting a small, diagnosed prevalence of HCM in the US.

To better understand the true epidemiology of HCM, define the addressable market, and find the disappearing patients, each company performed its own medical claims analyses.

Parties Involved

Cytokinetics

Cytokinetics is a late-stage biopharmaceutical company focused on discovering, developing, and commercializing first-in-class muscle activators and best-in-class muscle inhibitors as potential treatments for people with debilitating diseases in which muscle performance is compromised and/or declining.

As a pre-commercial company, Cytokinetics turns to outside funding to support the necessary investments in a growing list of development programs. One such program, currently in Phase 3 trials, is *aficamten*, a cardio myosin inhibitor in development for the treatment of hypertrophic cardiomyopathy (HCM).

At the time of diligence, Cytokinetics was conducting start-up activities for SEQUOIA-HCM, the Phase 3 clinical trial of *aficamten* in patients with obstructive HCM and was interested in a non-dilutive source of financing in support of this clinical development.

ROYALTY PHARMA

Royalty Pharma is the largest buyer of biopharmaceutical royalties and a leading funder of innovation across the biopharmaceutical industry.

The Company has assembled a portfolio of royalties which entitles it to payments based directly on the top-line sales of many of the industry's leading therapies.

Royalty Pharma funds innovation directly in the biopharmaceutical industry as a partner with companies to co-fund late-stage clinical trials and new product launches in exchange for future royalties.

Results

Cytokinetics and Royalty Pharma shared the insights from their independently conducted real-world evidence studies and jointly concluded that a significant contributor to the observed high rate of patient data drop-out after initial diagnosis was the lack of effective and tolerable treatments undermining the motivation of HCM patients to seek on-going care, leaving the underlying condition un(der)treated.

The recent approval of Bristol Myers's Camzyos (mavacamten) and the potential role of Cytokinetics' investigational agent, aficamten, offer new treatment options to patients suffering from hypertrophic cardiomyopathy, a disease with clear unmet medical needs.

As a result of a collaborative approach to defining the addressable market, patient dynamics, and unmet medical needs for a potential next-generation therapy to treat HCM, Royalty Pharma committed $150 million to fund the pivotal clinical trials of aficamten for HCM.

Conclusion

HCM is a serious disease in which the heart muscle thickens (hypertrophies) making it harder for the heart to pump blood. Its epidemiology is not well understood and using commercially available claims data may vastly underestimate the true diagnosed prevalence primarily due to patients not seeking treatment for a disease that, until recently, did not have any approved therapy offering the promise to improve symptoms or treat the underlying disease.

Claims analytics using a longer, 5-6 year time horizon, identify up to 3 times as many diagnosed HCM patients than previous research suggested. Since it is well understood that HCM is a chronic disease with patients experiencing only a slightly higher mortality rate compared to similar age cohorts, it is safe to conclude that the drop off in the number of patients associated with HCM diagnosis codes is related to patients not seeking and/or receiving treatment for their underlying condition in any given year rather than patient mortality. This gives the impression of lower HCM patient numbers in studies that investigate a one-year timeframe and that patients disappear in studies looking at longer timeframes, when there is little reason for physicians to continue to associate patients with the HCM diagnosis code or for patients to seek treatment.

Recommendations

A highly collaborative approach to claims data analysis can be key to a successful biotech financing especially when there are few or conflicting prevalence estimates and helpful for the parties to align on the commercial opportunity. This is often the case for highly innovative therapies that address diseases with no FDA approved treatments.

Analysis

Published medical claims-based epidemiology studies have typically chosen a 1- or 2-year timeframe to estimate the diagnosed prevalence of HCM in the US and identified around 100K patients.

Cytokinetics' analysis of open claims data provided by Symphony Health (Figure 1) and Royalty Pharma's analysis of closed claims data sourced from Healthverity (Figure 2) independently confirm 85-95K patients diagnosed with HCM in any given year.

Independently Conducted Analyses of Diagnosed Prevalence

Figure 1: Analysis based on Symphony Health Open Claims

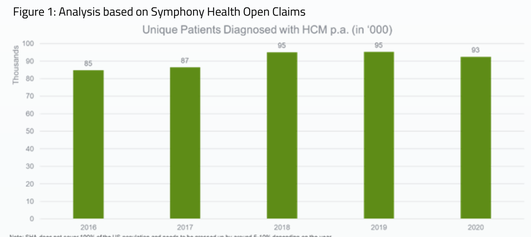
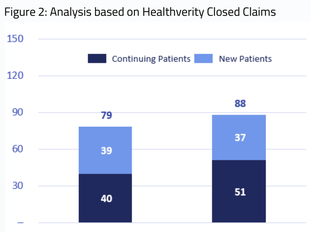


Figure 2: Analysis based on Healthverity Closed Claims



As part of the diligence process, both companies noticed that a large portion of patients diagnosed in one year, are not found in subsequent years after their initial HCM diagnosis.

Using the same data from Symphony Health, Cytokinetics performed a cohort analysis, tracking the annual re-diagnosis rate of HCM patients after the initial diagnosis (Figure 3). Royalty Pharma performed as similar analysis on its closed claims database and found the same dynamic (Figure 4).

Collectively, the Companies acknowledged that approximately 42-52K new HCM patients are diagnosed each year, and that 60-70% do not re-appear in claims databases after this initial diagnosis.

Independently Conducted Analyses of Repeat Diagnoses

Figure 3: Analysis based on Symphony Health Open Claims

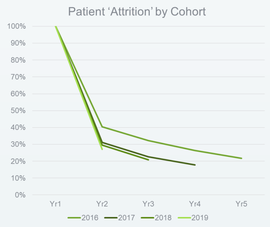
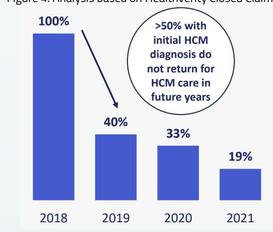


Figure 4: Analysis based on Healthverity Closed Claims



The Companies independently investigated the cause of the 'disappearing' patients using separate, but similar approaches.

Cytokinetics conducted more in-depth claims analyses, primary market research with treating physicians, and a review of clinical guidelines (Figure 5).

Royalty Pharma continued to leverage its closed claims database and retrieved the prescription drugs used by patients after being diagnosed with HCM (Figure 6).

These analyses independently confirmed that the treatment of HCM typically involves a beta blocker followed by calcium channel blockers, disopyramide, and once drug treatment seizes to be effective, septal reduction therapy.

Different Approaches to Modeling Current Treatment Paradigm

Figure 5: Treatment Paradigm Derived From Market Research

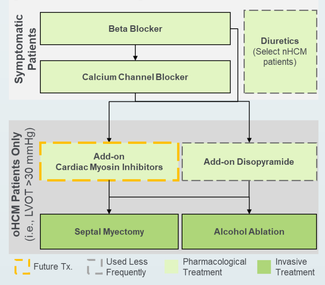
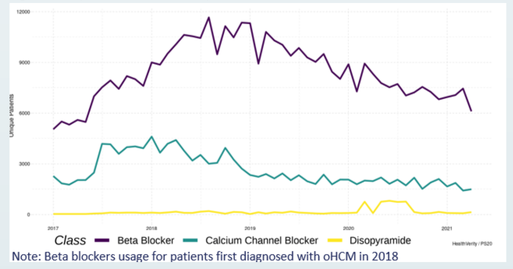


Figure 6: Analysis based on Healthverity Closed Claims



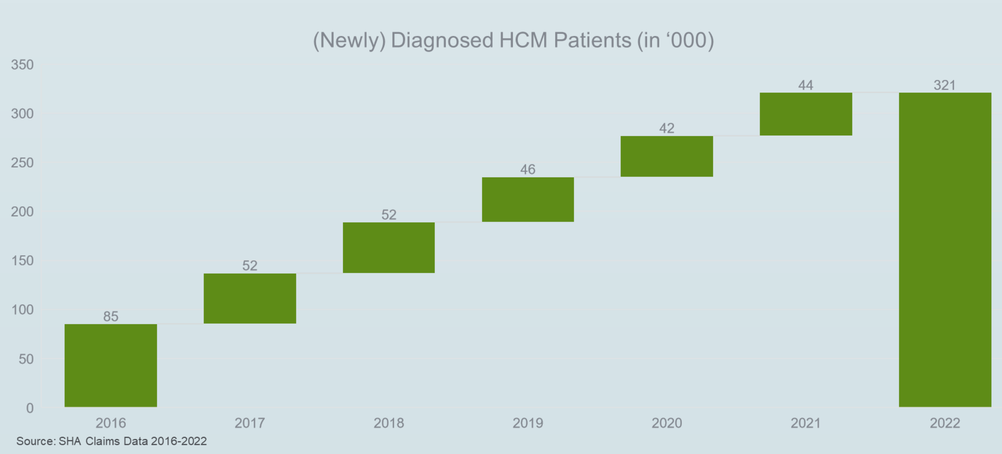
Key Findings

Of those patients diagnosed with HCM, 60-70% do not re-appear in claims databases/ are not associated with a HCM diagnosis code in subsequent years.

This high rate of disappearance cannot be attributed to mortality (Elliot et al 2006 10.1136/hrt.2005.068577) and a majority of diagnosed HCM patients are drug treated, with most patients receiving a betablocker and less frequently a calcium channel blocker or other anti-arrhythmic drug for years after initial diagnosis.

Based on the observations made through independent claims analyses and confirmatory primary market research, Cytokinetics and Royalty Pharma concluded that many of these patients who disappear in the data are still alive and continue to be affected by HCM (Figure 7).

Figure 7: True Diagnosed Prevalence of HCM Potentially Significantly Higher When Considering Newly Diagnosed Over Several Years



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