Targeting Therapy With Diagnostics in Community Care

Nonclinical Factors Affecting Acceptance and Commercial Success
Introduction

The development of targeted therapies has been a key focus of biomedical research in recent years. In 2016, of the 22 new molecular entities (NMEs) and biologics approved by the US Food and Drug Administration (FDA), 27% (6) were targeted therapeutics.1 This demonstrates a marked increase from 2011, when it was 14%,1 and a significant increase from 2005, when only 5% of approvals were targeted therapies.2 However, while the number of targeted therapies as a proportion of overall NME approvals continues to grow, these have been primarily concentrated in oncology, with limited targeting in other disease areas (Figure 1).

This focus on oncology has occurred for a number of reasons. First, even with recent advances, the clinical unmet need in oncology remains high, especially in consideration of the relatively poor clinical responses and significant adverse event profiles of untargeted chemotherapeutic regimens. Critically, the scientific understanding of cancer and its genomic etiology is more advanced than for any other noninfectious disease, and enables diagnostic drug targeting of numerous tumor-driving cellular mechanisms. Finally and perhaps most significant from a societal healthcare perspective, the economic impact of targeted patient selection in oncology is substantial: oncology therapeutics are often very expensive in a concentrated way, creating a highly visible spend where the benefit of targeting therapy to likely responder patients is obvious.
The Case for Diagnostic Targeting in Community Care

While the benefits of targeted therapy in oncology are clear, the potential benefits of a personalized medicine approach to diseases managed in community care should also be recognized. Chronic conditions such as asthma, hypertension, diabetes, and depression are most frequently managed with care delivered in the community setting, through internal medicine or family practices and office-based clinical practices in psychiatry, endocrinology, and the like. These conditions are highly prevalent and have a significant impact on healthcare costs in the long-term, due to both medication cost and high utilization of other healthcare resources (e.g., physician visits, hospitalizations). There are significant clinical and economic benefits that could be realized by targeting drug therapies to improve response rates and adherence to therapy, while minimizing complications in these disease areas. Clearly, then, there is both clinical and commercial opportunity in developing targeted drugs for these conditions.

Despite this opportunity, the application of diagnostic drug targeting for treatment personalization has lagged significantly in these clinical areas. What factors might account for the relative lack of progress in targeted therapy for chronic diseases? Certainly, one cause is scientific: the genetics involved in development of these chronic diseases and patients’ responses to particular drugs is not as well understood as in cancer. Indeed, chronic diseases have complex etiologies that may defy reduction to one or even a small handful of specific genetic variations. Nevertheless, it has proven possible to develop biomarker signatures that can predict response to drug classes in a clinically meaningful way, and we can presume that continued advances in population-based ‘omic analyses (e.g., genomic, proteomic, metabolomic) will permit development of multifactor signatures with increased predictive power for patient targeting in these diseases.

However, in addition to the strength of targeting, other factors in the healthcare ecosystem significantly influence the extent to which targeted therapies are embraced in actual clinical practice. In the US, drugs and services provided by laboratories, physicians, hospitals, and pharmacies are often delivered by unrelated entities and paid for under different systems administered by different organizations, with unrelated and sometimes opposing incentives. For a targeted therapy to be widely adopted, all of the following must occur:

- **The doctor must order the targeting test**
- **The test must be readily available and fit within the typical care paradigm**
- **A payer (or another economic stakeholder) must agree to pay the lab for the test**
- **The test result must get back to the doctor for the decision to prescribe or administer the targeted drug**
- **A payer (potentially different from the test payer) must agree to pay for the drug, presumably with knowledge that the test has been performed and that the result indicates the drug should be effective**
- **The patient must agree to pay his or her contribution for both the test and the drug**
In the US healthcare ecosystem, such an arrangement requires a fairly complex set of interactions among the various stakeholders (Figure 2). If any is blocked or disincentivized, the drug may fail as a commercially viable targeted therapy.

We have examined these interactions for both oncology and community care paradigms and have noted some striking differences related to key aspects of the respective models—including infrastructure and clinical practice management—that tend to erect barriers to targeting chronic disease therapy in community care. We discuss 4 of the most important below:

**Drug Distribution Channel and Test Information Flow:** Except in some fully integrated delivery systems, there is no routine mechanism for evidence of test completion or for the test result to flow directly from the laboratory to the payer making the associated drug’s coverage decision. This has little impact on oncology drugs, which are often dispensed through specialty pharmacies that have established mechanisms to handle the payer prior authorization processes often applied to a targeted therapy, such as reporting a specific test result to authorize access to the drug. In contrast, drugs for community care conditions such as depression are usually dispensed through retail pharmacies, which are ill equipped to deal with this type of complex payer communication, thus creating a barrier to targeted drug access at the point of drug dispensing.
Medical vs Pharmacy Insurance Benefit: Diagnostic testing is usually administered by third-party payers through the health insurance medical benefit. Physician-administered oncology drugs are often administered through the same benefit. Practically speaking, this means that for targeted oncology drugs, both the cost of testing and any drug cost savings from improved patient stratification would be recognized by the same payer entity, with economic incentives aligned at a high level. In contrast, drugs for chronic, community care conditions are almost always paid through the pharmacy benefit. Typically, the medical and pharmacy benefits of a health insurance plan are managed independently (and the pharmacy benefit management may be further outsourced to an independent pharmacy benefit manager). Therefore, for targeted drugs dispensed in the retail pharmacy for community care, the testing cost and the resulting drug cost savings are separated between different payer entities with independent economic incentives. As a result, in community care applications, testing for drug targeting does not return any direct cost offsets to the test’s payer, making the economic justification for test coverage more difficult for the payer to recognize.

Clinical Practice Management: Healthcare providers (HCPs) set up practice management and business processes appropriately designed to optimize patient care and practice profitability within their typical care paradigms. Therefore, an oncology practice and a community care practice are set up and resourced very differently with respect to the administrative staff and its capability to engage with payers in a prior authorization process. Specialty care practices often have dedicated staff members who frequently engage in (and may even be dedicated to) lengthy and complex prior authorization and claims appeal processes. In primary or community care, such staff members are typically not present, leaving the responsibility of responding to payers’ test information requests to the practice’s clinical staff, including the HCPs themselves. This atypical administrative burden is a limiting factor in the ability of a patient to gain access to a test and the associated targeted therapy in the community care setting. Moreover, because in community care there are often multiple alternative drugs that do not require payer authorization for coverage, the need to verify diagnostic test results with the payer may be a powerful disincentive for the HCP to select the targeted therapy.

Key aspects of the community care delivery model, including infrastructure and clinical practice management, tend to erect barriers to targeting chronic disease therapy.
Drug vs Test Costs: Modern targeted oncology drugs cost tens of thousands of dollars per course of therapy. Therefore, even a very expensive targeting test for an oncology drug may be financially attractive for payers if it can avert only a small number of failed treatments. In contrast, branded community care drugs such as antidepressants or antihypertensives typically cost only several hundred dollars per month, and generic equivalents cost even less. Because drug treatment in community care for chronic disease is often determined empirically, if the targeting test’s cost exceeds the cost of several months of treatment—which may be the case even for a moderately priced test—it may be financially more attractive for the payer to require the physician to find an efficacious drug through trial and error than through targeting.

Setting aside issues associated with identifying actionable biomarker signatures for patient stratification in chronic diseases, these and other healthcare ecosystem and infrastructure aspects make it much more difficult to implement targeted therapy in community care as opposed to specialty care such as oncology. The patient stratification and drug-targeting approach that is providing clinical and economic benefits in oncology also has great potential to yield health benefits and cost savings in chronic diseases managed in the community. However, the current care delivery paradigm and infrastructure in the community care setting creates access barriers that will need to be lowered before these benefits can be fully realized. Manufacturers can support the introduction and uptake of precision medicines in these disease areas by fully understanding the access landscape and the challenges faced by all key stakeholders involved in the patient journey, and implementing programs to overcome infrastructure obstacles by lessening the administrative burden for HCPs and supporting the overall patient experience.

References