

Forecasting Success: The Misperceived Influence of FDA Approval

By Ed Kissel

It is natural to assume that sales of oncology drugs will start climbing soon after FDA approval of an sNDA. Surprisingly, according to analysts at IntrinsicQ, up to 80% of ‘peak’ usage for cancer drugs’ expanded indications is already realized by the time of the supplemental approval. By correlating market share with clinical events and sNDA approvals, we can view the true nature of adoption and uptake in oncology.

The oncology segment of pharmaceutical markets can be particularly difficult to predict, and prior misconceptions in the oncology market have led to some outlandish forecasts.

Analysts may often confuse perceived market value with real value simply by misinterpreting market conditions, market uptake rates, perception of cost savings, impact of j-codes, unmet need, and a host of other factors. One area that often leads to much uncertainty is the market opportunity for an oncology drug in an expanded indication when it is already commercially available—largely because market penetration has been almost completely realized at the time of U.S. Food and Drug Administration (FDA) approval.

The true art to oncology market predictions is to better understand which events—all of which transpire long before FDA approval—will actually affect product usage, positively or negatively.

By the time FDA approval has occurred for a new indication three phases of influence have already

taken place: presentation of peer-reviewed clinical data, publication of these clinical data, and listing in approved compendia. The usage of oncology drugs

during these phases is meaningful because it increases the predictability of success; likewise, it also increases the predictability of failure.

While FDA approval may be the culmination of successful steps taken in the clinical process, the sole market impact is often the elimination of any lingering perceived reimbursement hurdles for a relatively small and insignificant physician segment.

The following investigation looks at the specific timing of the expanded FDA approval and its impact on oncology product usage. The analysis compares actual market share rates and product usage performance, and the timing of the other market

events to measure the meaningful market events prior to approval. These examples clearly show the possible errors made by ignoring the three phases of influence and overestimating the real market impact.

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Case Scenario 1: Avastin [bevacizumab; Genentech]

Avastin was approved for use in non-small cell lung cancer (NSCLC) in October 2006, its second tumor market; yet its market uptake occurred more than a year earlier through a series of events that follow a very consistent pattern. In March 2005, and nearly a year after Avastin was first approved for treatment in colorectal cancer, Genentech effectively communicated Phase 3 trial findings that met the pre-specified endpoints, and the drug was seen as clinically meaningful for NSCLC. These data were made widely available at ASCO two months later, driving a dramatic increase in the number of patients receiving the drug. By November 2005 when Avastin was officially listed on NCCN compendia, approximately 3,000 NSCLC patients were already being treated—representing nearly 40% of its ‘peak’ market share for this market. The compendia listing removed most of the additional perceived reimbursement hurdles for the late majority of physicians

and contributed an additional 25% to Avastin’s peak performance.

The trend of these two market events—significant clinical findings presented at ASCO and the compendia listing—directly influenced more than two-thirds of Avastin’s peak performance in NSCLC, based on analysis of actual market share rates and product usage performance. The additional growth after FDA approval was not able to meet the lofty sales expectations of analysts.

Likewise, Avastin in breast cancer also saw increased use prior to FDA approval. Usage in this patient population increased significantly after the initial publication of Phase 3 clinical data. The compendia listing that followed gave Avastin an additional 50% push within the breast cancer market. It can be argued effectively that the subsequent FDA approval did not contribute any additional uptake of the product and initial sales expectations went unrealized.

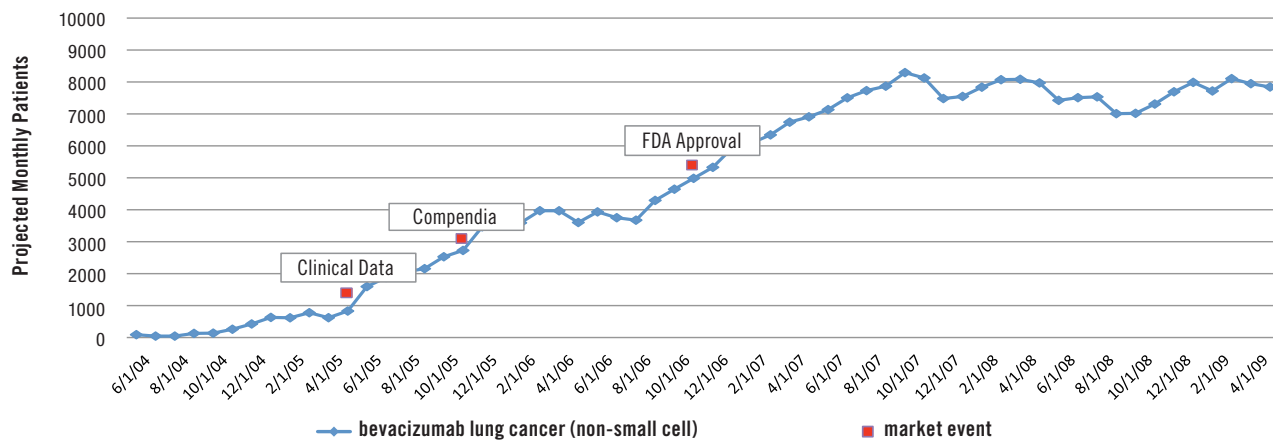


Figure 1. Avastin Use in NSCLC

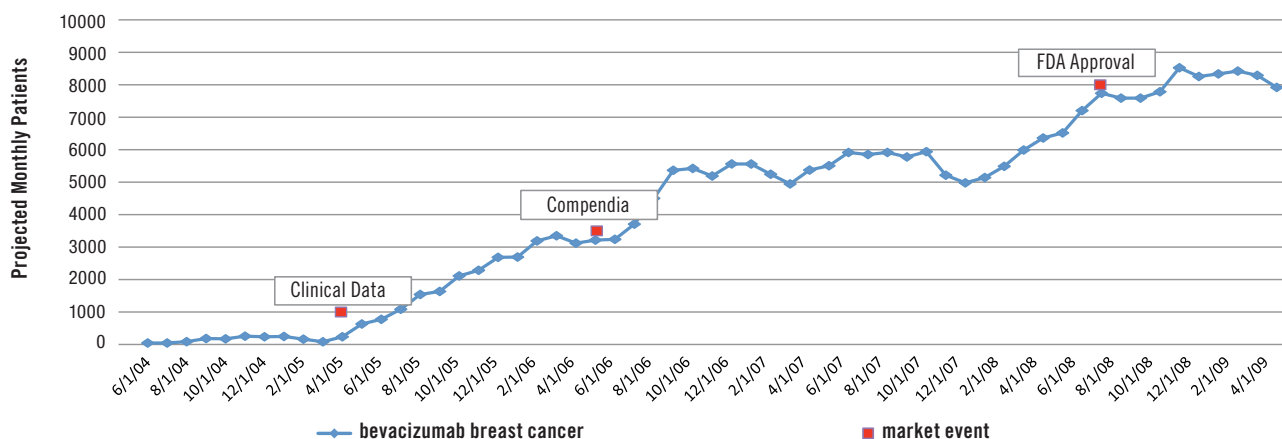


Figure 2. Avastin Use in Breast Cancer

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Case Scenario 2: Alimta [pemetrexed; Eli Lilly & Co.]

Alimta was approved for use in NSCLC in August 2004, its second tumor market; however, unlike Avastin, it hadn't already had significant time to establish itself in its initial indication, mesothelioma. As a result, the indication drove usage similar to uptake seen in launched products but peak market performance was driven by significant clinical and marketing events as the product continued to mature in NSCLC.

Physicians accepted initial clinical data on Alimta for a specific patient population, most notably relapsed NSCLC, with the original message of safety with comparable efficacy. However, because the benefit of efficacy far outweighs that of safety in swaying physician behavior, this early market positioning subdued and evolved into erratic market share over the next 24 months in a highly fragmented market.

In June 2006, additional clinical data began to build a strong case on Alimta's efficacy mes-

sage, signaling the beginning of a strategic shift away from the safety messaging. Over the subsequent 12 months, Alimta's patient base grew an additional 25% while efficacy messages matured. Ultimately, more than 3 years after launch, physicians started to see the clinical benefits of the product allowing Alimta to further penetrate available markets, migrate usage into earlier lines of therapy and defend itself against existing competitive threats. Alimta has grown an additional 60% in first line of therapy prior to its official approval in first-line NSCLC, especially in patients with poor or borderline performance statuses (PS 1-2).

When FDA approval in front-line NSCLC was finally granted in September 2008, most of the adoption in this patient setting already occurred. Any additional growth would be slower than what was previously realized and marketing focus shifted to a new market opportunity: maintenance NSCLC.

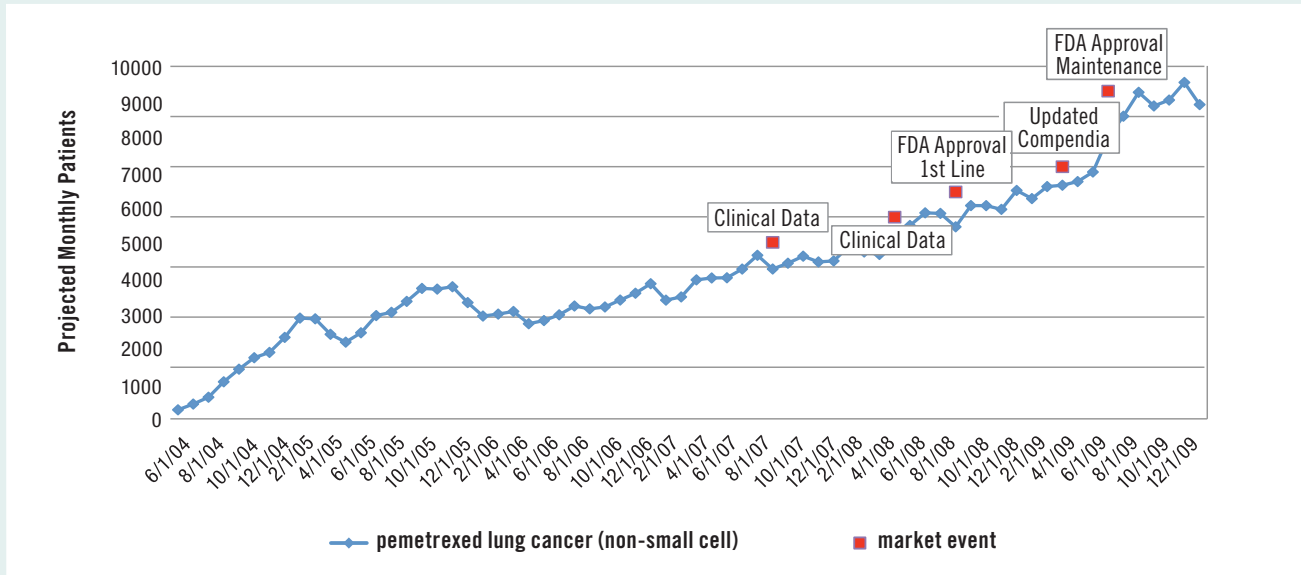


Figure 3. Alimta Use in NSCLC Transition From Second- to First-Line and Maintenance

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The extent of cancer overdiagnosis based on large randomized screening trials?: 25% for mammographically detected breast cancers, 50% for chest x-ray and/or sputum-detected lung cancers, and 60% for PSA-detected prostate cancers. (*JNCI, Online 4/23/10*)

Major clinical news from Roche at ASCO 2010 will include Phase 3 data on Avastin in three separate tumor types: first-line ovarian cancer, gastric cancer and prostate cancer. (*Roche 1Q10 Presentation, 4/15/10*)

Case Scenario 3: Nexavar [sorafenib; Bayer HealthCare, Onyx Pharmaceuticals]

In cancer care, oral drug manufacturers must analyze the complete market landscape, not just the oral drug market. The most successful oral products are launched in defined, custom markets with clinically significant data targeting a high degree of unmet medical need i.e., Nexavar in kidney cancer (renal cell carcinoma or RCC), its first indication, and in liver cancer (hepatocellular carcinoma or HCC), its second market.

Prior to the FDA approval, Nexavar's clinical data in HCC had the immediate ability to significantly grow the

treated patient population further, defining new custom markets that built on specific efficacy or safety messages. Market share also quickly responded and the product achieved almost 60% of its peak performance prior to the FDA approval. Lofty analyst expectations for the product in HCC didn't take into account the swiftness of the adoption and the over saturation of the market prior to FDA approval.

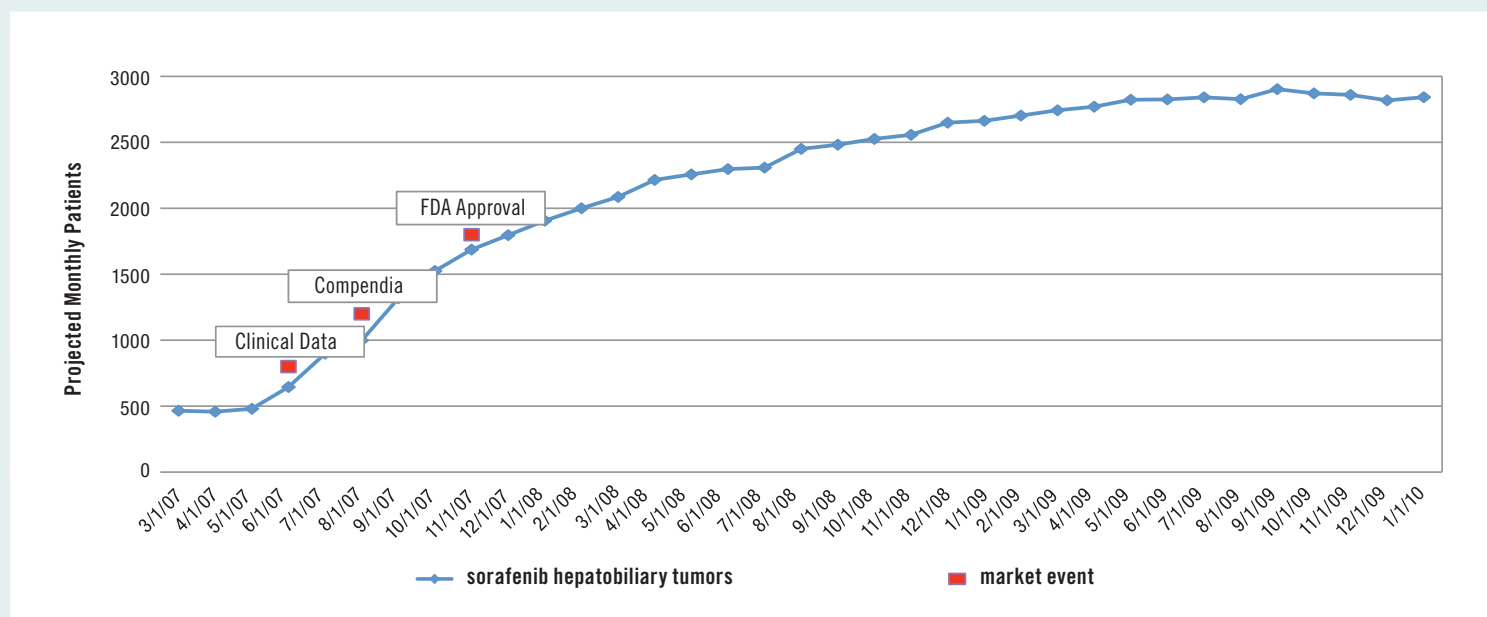


Figure 4. Nexavar Use in Hepatobiliary Tumors

Conclusions

There are many analogs that one could analyze to better understand the impact between FDA approval and the key events that precede the decision, like Erbitux [cetuximab; ImClone, Bristol-Myers Squibb, Merck] in head and neck cancers and Herceptin [trastuzumab; Genentech] in adjuvant breast cancer. Most consistently, analysis shows the significant meaningful use before FDA approval.

The inverse also holds true. When the uptake is non-existent or shows great variability in market share, we are able to confidently conclude that regardless of the expected FDA approval, the product is not likely to effectively penetrate the market.

The art to marketing a new therapy indication lies in convincing physicians with meaningful statistical and clinical findings—long prior to an FDA decision.

FDA approval will—and should—always remain the ultimate goal in a drug development lifecycle. In fact, it may be the ultimate determinant in decisions that drug development and marketing teams make to expand the use of a product and reinforces that companies should pursue areas where clinical data will be indisputably strong enough to garner FDA approval. If so, the reward is that physician adoption will occur much earlier than any FDA decision. Then, the biggest cautionary consideration is in accurate forecasting as the drug will have already approached near-saturation.

About the Contributor



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