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NEWSLETTER – VOL. VI

CONTENTS

BIOSIMILARS: SEPARATING HYPE FROM REALITY

The term biosimilar has been buzzing around the biopharma industry owing to their potential for savings across the healthcare system and the potential threat they pose to major brand name drugs. While their arrival has been portended for many years, their approval, launch, and commercial adoption in the US has been slower than initial expectations. Now, with seven approved biosimilar products (three of which having been commercially launched) and an October 2016 FDA presentation noting 66 new products enrolled in the agency's Biosimilar Product Development program, they appear to be gaining some momentum. Here we will provide an overview of some of the salient issues which are governing their availability and success in the marketplace.

WHAT IS A BIOSIMILAR?

Biosimilars are analogous to generic drugs. Generic drugs are copycats of branded drugs, with the same active ingredient, dosage form, safety, strength, route of administration, quality, and performance characteristics. In the same way, biosimilars are copycats of biologic drugs. While generics of branded drugs are small molecules you can swallow, synthesized by an organic chemistry process, biosimilars are biologics and typically need to be injected. They are most commonly produced in yeast, bacterial or mammalian cells which have been engineered to produce the desired protein drug product. Because the organisms that produce the drug products can vary in ways that are difficult to assay, there are complexities in proving equivalence that do not exist with synthetic chemical products.

REGULATORY PATHWAY

The Hatch-Waxman Act of 1984 allowed for the introduction of generic drugs to the market, but biosimilars only obtained their own path to market in 2009 with the passage of the Biologics Price Competition and Innovation Act (BPCIA). BPCIA created an abbreviated licensure pathway for biological products shown to be *biosimilar* or *interchangeable* (emphasis added) with an FDA-approved reference/innovator product. This abbreviated pathway, known as a 351(k) application, allows biosimilar sponsors to submit their products with less than the standard full suite of preclinical and clinical data that a biologics innovator sponsor would be expected to produce. Biosimilar and interchangeable products are different. Biosimilar implies a product which may have some differences when compared to the innovator product, but none which are clinically meaningful with respect to safety, purity, or potency. An interchangeable product (sometimes referred to as bio-identical or biogeneric) meets all the characteristics of a biosimilar, while also clearing higher hurdles: they can be expected to produce the same clinical results as the reference product in any given patient.

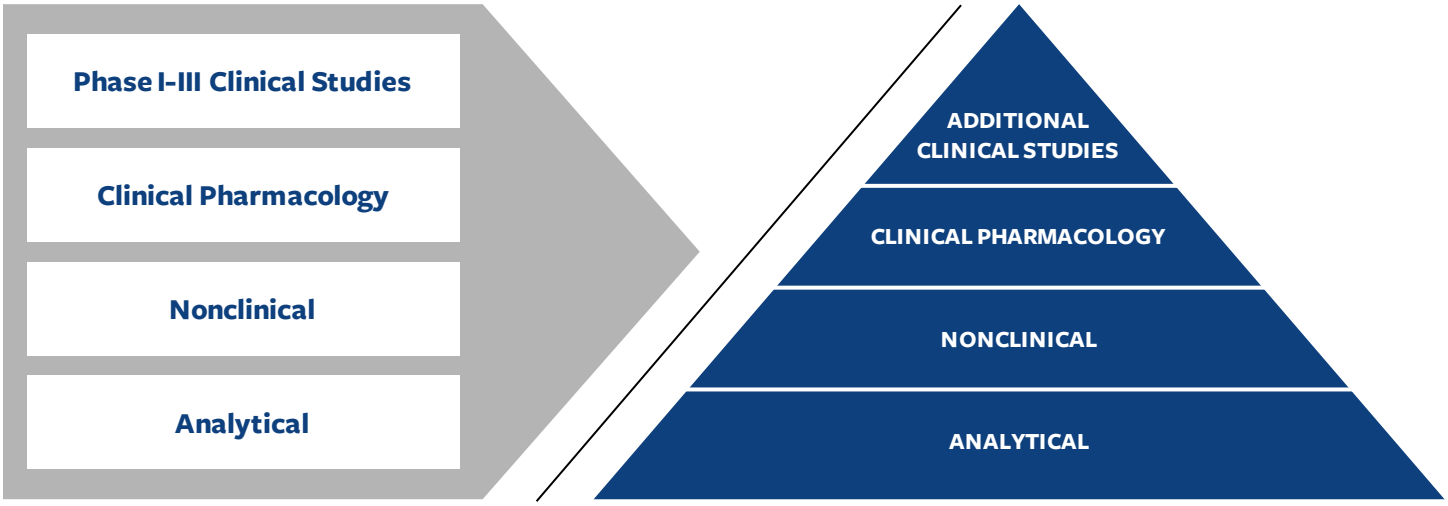

Figure 1: Evidence paradigms for standalone vs biosimilar development programs. Adapted from FDA

The agency has released some guidance on the development of biosimilars, in both draft and final form, a full list of which is available here[1]. The agency guidance on demonstrating interchangeability was released in draft form in January 2017 and has not yet been finalized. So far, no products in the US have been approved as interchangeable as the FDA is still struggling with what is required.

In terms of what is required for approval, the FDA has indicated it would like different degrees of evidence for analytical, nonclinical, clinical pharmacology and clinical studies for 351(k) applications compared to standalone development programs (those meant to establish safety and efficacy of a new product). For 351(k) programs, the agency would like to see the greatest amount of analytical data as the foundation of the application, followed by nonclinical and clinical pharmacology data, with additional clinical studies as the icing on the cake to mitigate any concerns the other three categories were unable to resolve (Figure 1[2]). This is somewhat flipped compared to conventional development paradigms where Phase I-III clinical trials are of utmost importance, particularly large, randomized controlled trials.

Different levels of concern will apply to 351(k) applications depending on the actual drug. For instance, recombinant versions of naturally occurring proteins probably do not merit the same levels of concern as non-naturally occurring biologics, like those commonly used to treat inflammatory diseases, or certain oncology drugs. Another area of uncertainty relates to drugs with approvals in multiple indications – it is still unclear if biosimilar sponsors can run a trial in one indication, but win approval for all indications of the innovator product. We will likely see an ability to extrapolate but this depends on how good the analytical portion of the filing is, and if there is a narrow therapeutic index or key adverse events in a different indication than the one studied.

Neutralizing antibodies present a concern for both interchangeable and biosimilar products, which both have the same risk with respect to safety or diminished efficacy related to alternating and/or switching biosimilar with the reference product. Neutralizing antibodies produced in the patient can render a drug no longer effective. As such, should a patient on a biologic be switched to a biosimilar (or vice versa), and then start producing neutralizing antibodies after switching, the patient would no longer respond to the innovator biologic or biosimilar.

One final sticky wicket is that BPCIA was passed as part of the Affordable Care Act (ACA). Given multiple attempts by

[1] https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm290967.htm

[2] https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM526935.pdf

the current administration to repeal the ACA does somewhat put BPCIA in gray area. However, given the bipartisan interest in curbing drug costs and overall healthcare costs, there would likely be sufficient interest to keep BPCIA alive in some way.

LEGAL CONUNDRUM

As noted earlier, while seven biosimilar are approved, only three have been launched. This is in part due to the "patent dance" that biosimilar and innovator sponsors have been required to engage in under BPCIA. BPCIA requires biosimilars sponsors to provide "notice" to innovators at least 180 days "before the date of first commercial marketing" to allow the innovator to sue for patent infringement on still applicable patents. The Federal Circuit interpreted the statute in a way that this notice can only be given after the approval date.

Overruling the Federal Circuit, the Supreme Court has ruled in *Sandoz v. Amgen* in June 2017 that the 180-day notice can be given prior to the biosimilar approval date, as the notice period beginning the date of approval in practice gave innovators another six months of market exclusivity. In some cases, this ruling should help biosimilars come to market six month earlier.

COMMERCIAL CONSIDERATIONS

Biosimilar products probably fall somewhere in the range of $200-$500 million to develop when all development, regulatory, IP, and manufacturing (both the technical aspects of manufacturing, as well as at scale) costs are added up – far greater than the costs to develop generics. Because of this, biosimilars are unlikely to ever reach the same low cost thresholds of generic drugs and therefore the system will not realize the same degree of savings as it did with the introduction and uptake of generic drugs. Europe's experience with approval and uptake does provide some proxy for what might happen in the US, but is probably the upper bounds of any expectations for total savings. Certain EU countries have seen price decreases greater than 60% since the introduction of biosimilars for epoetin and granulocyte colony-stimulating factor, according to a 2017 QuintilesIMS report.

Because of the way they are reimbursed in the U.S., biosimilars face different barriers than typical generic drugs as well. These are largely based on the channel the innovator is reimbursed under, for instance whether they are Medicare Part B or Medicare Part D drugs. Medicare Part B covers certain doctors' services, outpatient care, medical supplies and preventive services. Non-self-administered drugs are reimbursed under Part B, and considered medical benefit under a scheme known as buy-and-bill. Buy-and-bill drugs are purchased by the office/institution who take the upfront risk of laying out costs, and are subsequently reimbursed once prescribed to a patient. Medicare Part D adds prescription drug coverage on top of original Medicare (Parts A (inpatient services) and B). These plans cover the types of drugs which a patient would pick up at the pharmacy, (and thusly dubbed pharmacy-benefit) and can be heavily managed by both Prescription Benefit Managers (PBMs) like CVS and Express Scripts, as well as managed care plans (the Humanas, Aetnas, and Anthems of the world).

MOLECULE (GENERIC NAME)	INNOVATOR BIOLOGIC PRODUCT	BIOSIMILAR	APPROVAL DATE	LAUNCH DATE
Filgastim	Neupogen (Amgen)	Zarxio (Novartis)	3/6/2015	9/3/2015
Infliximab	Remicade (Johnson & Johnson/Janssen)	Inflectra (Pfizer)	4/4/2016	11/28/2016
		Renflexis (Biogen/Merck)	4/21/2017	7/24/2017
Etanercept	Enbrel (Amgen)	Erelzi (Novartis)	8/30/2016	expected 2018
Adalimumab	Humira (AbbVie)	Amjevita (Amgen)	9/23/2016	expected 2018
		Cyltezo (Boehringer Ingelheim)	8/29/2017	pending patent litigation
Bevacizumab	Avastin	Mvasi (Amgen)	9/14/2017	not disclosed

Table 1: US approved biosimilars - approval and launch dates

In general there is much more discounting and contracting for drugs in the Part D/pharmacy benefit channel than in the Part B/medical benefit channel. This creates an expectation for biosimilars to need to be priced about 50% less than list price of the innovator in order to get market traction to take into account all of the rebates and discounts throughout the value chain. As a bit of a double-edged sword, biosimilars sponsors will probably need about 30% market penetration in order to have enough negotiating power with PBMs. Despite these barriers, price erosion to innovators is expected to happen faster in Part D/pharmacy benefit than under Part B/medical benefit given the power of PBMs and their mandate of offering lower prices to their health plan customers.

Additionally, oncology is probably the largest biologics expenditure in Part B, creating some added reticence to move to biosimilars for what are viewed as life-saving drugs, whereas Part D is generally viewed as housing more "supportive care"-type drugs. The buy-and-bill structure in Part B gives more decision making power to doctors and their institutions, making it more fragmented in terms of adoption of biosimilars compared to the power that PBMs and health plans have in the Part D channel to make more broad sweeping changes.

Regardless of reimbursement channel, it is reasonable to expect stronger adoption of interchangeables over biosimilars as the former might be deemed as a "better copycat". Drugs deemed interchangeable can automatically be substituted for the innovator product unless the prescribing healthcare provider expressly stipulates the branded product.

The recent approval and launch of a second biosimilar to Remicade will probably be an important case study for the industry as it is the first example of two approved biosimilars to the same reference product, and now starts to create more competition for a single drug. Deep contracting by innovators has so far largely kept biosimilar competition at bay, but it will be interesting to see additional biosimilars try to gain share given the dynamics thus far. In the generics world, there has been a rule of thumb that prices for a branded drug and its generics plummet once there are at least three approved generics. The analogous is likely to be true for biosimilars as well.

There are clearly still many moving parts related to biosimilars but things have started to take on more clarity as the FDA has issued guidance and approved products, the recent Supreme Court decision, and now the approval of two biosimilars with the same reference product. We continue to watch this space and hope to comment on further developments, particularly on the commercial front, in future issues.

- by Sumner Anderson, Partner, Pharmaceuticals team and Christine Livoti, Senior Research Manager

RETHINKING THE SALES FORCE BUSINESS MODEL IN A DRAMATICALLY CHANGING ENVIRONMENT

Pharma sales representatives (reps) are one of the most integral components to a manufacturer's commercialization plan. They have long been the voice in determining and shaping the adoption curve of a new drug. However, the "good ol days" are in the rearview mirror for reps as there have been efforts to curb dollars and gifts that reps can shower upon physicians and their staffs, as well as both fewer and lower quality touch points with the decision makers with purchasing power and/or authority on drug choice, particularly when there are multiple options in the same therapeutic category. Here, we will try to put the role of the rep in context and provide some perspective, conceptually, on where the sales model may migrate in the future, and what issues will need to be addressed.

Companies spend significant amounts of time, energy and resources dedicated to planning and building out the sales force optimization plan. Specifically, the commercial team oversees multiple teams to plan the success of the sales rep. Activities that contribute to this success include:

- Market research to quantify the opportunity and understand the behaviors and triggers of doctors to prescribe:
  - Identify potential points of push back from doctors

  - Segmentation of doctor mindsets that can drive training of the sales reps – i.e. identifying high vs low likelihood to prescribe and pyschological drivers that sales reps can use to trigger prescription activation
- Sales training to ensure the rep is knowledgeable and help drive rep performance
- Analytic teams analyze physician productivity to ensure reps are calling on doctors that will yield the greatest return:
  - Spending time with doctors who are loyalists to the therapeutic class and/or may have affinity to a certain type of therapy within a therapeutic area
  - Identify high density geographic areas that may require heavy sales force deployment
- Sales leadership teams develop:
  - Incentive compensation plans (performance-based plans above base salaries) to further drive excellence
  - Determine call planning strategies (who to target, and at what frequency)
  - Ensure operational effectiveness and execution is in line with overall strategy
- Managed care teams drive appropriate reimbursement coverage and facilitate sales training around reimbursement-centric adoption strategies:
  - How to combat doctors wary of reimbursement issues
  - Selling the value of the drug in relation to reimbursement coverage
  - Help the doctor navigate the prescription journey from their office to the pharmacy counter for their patients

In the past, the sales rep had many tools at their disposal to engage and sell their products to physicians:

- Dinner meetings
- Grand Rounds (sponsored lecture series in the hospital setting)
- Lunch and learns
- Golf outings
- Literature leave behinds
- Sampling

The rep had the ability to access the majority of not just physicians, but importantly those with autonomy and decision-making authority, and the nature of the detail (industry lingo for reps providing doctors with the details of a drug, including approved scientific information, benefits, adverse events, etc) evolved around the clinical efficacy and utility of the product. Reps were trained on the mechanism of action of their product as well as competitors, all the key clinical data in the therapeutic area, and how to convey their product's differentiation. This last part is significant as training also focused on breaking down clinical studies, with successful reps well-trained in how to handle any objections raised by doctors around use of their product (ideally identified ahead of time by the manufacturer's market research), and able to rattle off why one product may have a better p-value (measure of statistical significance used in clinical trials) or better efficacy at symptom resolution, among other product features.

Figure 2: Simplified schematic of common commercial team structure

LEVEL AND TYPES OF REP-DOCTOR INTERACTION HAVE CHANGED

Reps historically had an environment that was for the most part without many restrictions, which is increasingly no longer the case. The ability of the sales rep to develop a

relationship with doctors they called upon was easy and simple due to the tools at their disposal. However, over the past two decades, there have been considerable changes in both the ability to access and the types of activities the reps can use to engage with doctors. These changes have come about in an effort to clamp down on what has been viewed as inappropriate influence over docs by industry reps.

Any payments made to physicians by drug and device companies must be reported under the Physician Payment Sunshine Act, signed into law in 2010 along with the Affordable Care Act, and the data is made public by the Centers for Medicare and Medicaid. While these payments can be as seemingly benign as research grants, it can also include things like travel and accommodations around medical conferences and scientific or advisory board meetings, food and beverage, and consulting fees. Details on the types of payments are included in the public data set. Now the public can see if physicians are receiving what might be perceived as healthy sums of money, which whether innocently or not, can be perceived as doctors being "in the pocket" of big pharma, and a potential PR concern for their institutions.

PHYSICIAN ACCESS HAS BEEN ON THE DECLINE DUE TO CONSOLIDATION OF INDEPENDENT PHYSICIANS INTO HEATH SYSTEMS

Most academic medical centers do not allow reps to call on their physicians on site, though there may still be some level of doctor-rep interaction if the doctor maintains an off-campus practice location. One industry report from ZS Associates found that 56% of physicians in the US have either restricted or severely restricted who can visit them, with some specialties even more restrictive. Integrated delivery networks (IDNs), systems where the provider network is also the payer, and group practices, are also increasingly locking out reps. Further, physicians' prescribing autonomy in IDNs and group practices is not the same as in an independent practice, with decisions around drug purchase and utilization instead made by higher level management.

This trend is likely to continue as cost pressures have made it more and more difficult for independent physician practices to remain financially viable. Independent physician practices have been on the decline since 2000, according to a 2016 analysis by inVentiv Health Consulting. While 57% of physicians were independent in 2000, this decreased to 37% in 2013 and was expected to continue sliding to 33% by the end of 2016.

THE SALES CALL HAS MIGRATED FROM A PURE CLINICAL SELL TO ADDRESSING REIMBURSEMENT

When reps are still able to get interactions with doctors, the nature of the sales call has shifted from a clinical sell to putting the rep more in the role of a reimbursement navigator. Price never came up as a major topic of the sales detail, whereas now it may be the primary focus of the conversation, as it is often easier for a doctor to simply pick the drug that is cheapest for their patient – "is it covered by insurance and how much will the patient need to pay?" The use of co-pay cards, which reps can drop at the physician office to reduce financial burden for patients (discussed in a past issue of this newsletter), was largely unheard of until more recent years. Still, co-pay cards are not a panacea, and doctors remain skeptical of the overall utility of these cards. Patients often encounter issues at the pharmacy when they try to use these cards, and may ultimately abandon any attempts to get the drug they were prescribed in the first place. These co-pay cards are off-limits to Medicare patients by law (but fair game for those with private insurance), and so might only benefit a fraction of the doctor's patients.

Put this all together, and reps now have less time to discuss more complicated topics like reimbursement during their detail. The question now to ponder is how will the rep model evolve with the environmental dynamics at play. Specialty reps in the device sector that are required to train docs in the surgical area will continue their business as usual, but there will be a need to evolve the model overall in many sectors.

There is probably not a one size fits all strategy, and that current strategies in the therapeutics sector need to be adjusted to address some of the key challenges outlined below.

- The model needs to pivot from a single point of contact between rep and doctor to one where the sales team has a multi-touch point strategy to various customers in the ecosystem.
  - Customer will be cross functional, including buyers and influencers, not just the physician:
    - Administrators
    - Business/purchasing mangers
    - Chief medical officers
    - CFOs
- The ability to both articulate what constitutes value for patients, doctors, and their institutions, and to create a more holistic approach that drives value throughout all key customers will inform overarching strategy.
  - What services, tools, and business offerings can the commercial team offer to doctors and institutions to drive pull through and adoption of their products?
  - How to generate a more ambitious patient-centric approach?
- Realignment of commercial organizations and build out of the talent pool in key functionalities and responsibilities will take on added significance.
  - Need to create cross-functional business operational teams vs. more independent/siloed groups
    - Re-calibration of the managed markets and sales force groups to more of an account management team that can foster relationships with all key stake holders
    - Ability to trouble shoot and bring customized approaches to physician groups
  - More sophisticated sales rep that can work with a cross functional team and have stronger business acumen:
    - Upgrade to drive toward more sophisticated approach to independent docs
    - Move away from reliance on business-to-business like model that some pharma companies have started to adopt (while acknowledging there are some specific areas where this may still have utility)

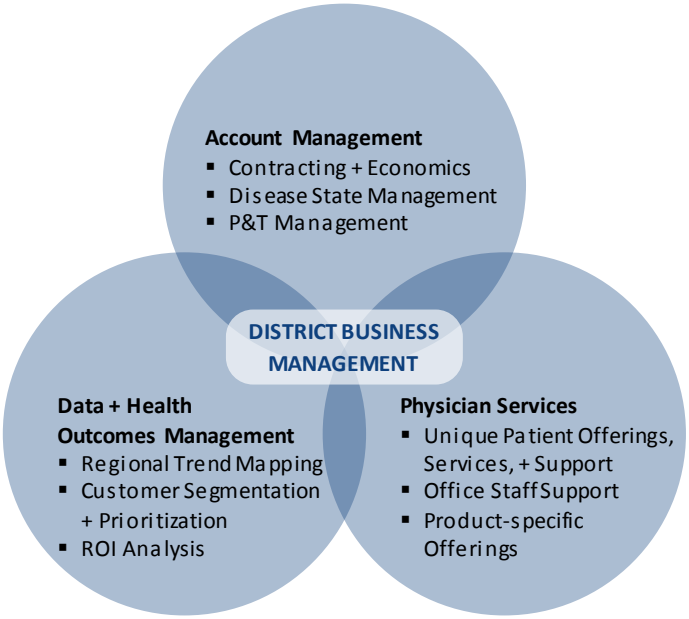

Figure 3: Hypothetical schematic for business management-centric approach to commercial organization where a more integrated team overseen by a district business manager who drives business planning, data analysis, insight mapping, and touch point strategy

Where are we in the continuum with the shift to a more holistic approach? Our observation is that manufacturers acknowledge and discuss that we are at a tipping point, with some having piloted various more integrated approaches to drive behavioral change. Some of these pilot approaches have yielded positive returns but we have not yet seen a full migration over to a new model. What we do believe, however, is that the environmental factors at play will eventually force a significant change for all pharma.

- by Brent Bernstein, Commercialization, and Christine Livoti, Senior Research Manager

PEER-REVIEWED ABSTRACTS

As part of Deerfield's mission of advancing healthcare, the Deerfield Institute is committed to publishing its proprietary research in peer-reviewed, open access scientific journals. Below is a selection of some of our recently published work. More information on the Deerfield Institute, and copies of certain past publications are available on the web at Deerfield.com/Institute.

FRIENDS OF CANCER RESEARCH

TRENDS IN THE MOLECULAR DIAGNOSIS OF LUNG CANCER, RESULTS FROM AN ONLINE MARKET RESEARCH SURVEY

CÉLINE AUDIBERT, MICHAEL SHEA, DANIEL GLASS, MARINA KOZAK, ALEXIS CAZÉ, RYAN HOHMAN, JEFF ALLEN, ELLEN V. SIGAL, JONATHAN LEFF

Abstract

Survey Goals

To better understand the challenges that practices face in testing patients for oncogenic drivers, as well as the uptake of various testing technologies, a questionnaire was developed to obtain the opinions and experiences of practicing medical oncologists regarding the molecular testing process. Numerous specialties are involved in decisions about when and how to test patients and rarely does a single individual have full knowledge of all the steps in the process. However, as the primary point of contact with the patient, the medical oncologist was identified as the person most likely to provide insight into the entire process, from diagnosis, to testing, to treatment. The setting of non-small cell lung cancer (NSCLC) was identified as an area of focus due to the presence of multiple known oncogenic drivers and approved targeted agents, as well as the existence of several approved molecular diagnostics in that setting.

Characteristics of Respondents

The final sample included 157 respondents who both met the eligibility criteria and completed the survey (Appendix Table 2, page 18). The clear majority of respondents were medical oncologists (148, 94%), with an additional 6% either nurses or physician assistants. More than half of respondents reported spending most of their time in a private practice (88, 56%), while the remaining were split between community (36, 23%) and academic settings (29, 18%). The region with the largest number of respondents was the southern United States (63, 40%), with an additional 24% (37) from the Northeast and 18% from the Midwest and West, respectively.

Characteristics of Treated Patient Populations

Respondents reported diagnosing on average 63 patients with NSCLC in the past 12 months, with an average of 53% presenting with stage IV disease (Appendix Table 1, page 17). Among their patients with stage IV disease, respondents reported an average histology breakdown of 62% adenocarcinoma and 29% squamous cell carcinoma.

Conclusion

Despite widespread concerns regarding the adequacy of tissue samples to support molecular testing, we found that for most respondents, acquisition of adequate tumor tissue was not a rate-limiting step in molecular testing. However, timing of testing does appear to be preventing a sizable portion of patients from receiving targeted treatment prior to chemotherapy,

highlighting the need for more early-stage testing. Finally, use of NGS is still primarily concentrated in academic research institutions, indicating that its use outside a research setting is not yet widespread.

ONLINE INFORMATION REVIEW

ADVERSE DRUG REACTION EARLY WARNING USING USER SEARCH DATA

WEI SHANG, HSINCHUN CHEN, CHRISTINE LIVOTI

Abstract:

Purpose

This research proposes a framework to detect adverse drug reactions using Internet user search data, so that adverse drug reaction events can be identified early. Empirical investigation of Avandia, a type II diabetes treatment, is conducted to illustrate how to implement the proposed framework.

Design/methodology/approach

Typical adverse drug reaction identification measures and time series processing techniques are used in the proposed framework. Google Trends Data is employed to represent user searches. The baseline model is a disproportionality analysis using official drug reaction reporting data from the U.S. Food and Drug Administration's (FDA) Adverse Event Reporting System (FAERS).

Findings

Results show that Google Trends series of Avandia side effects search reveal a significant early warning signal for the side effect emergence of Avandia. The proposed approach of using user search data to detect adverse drug reactions is proved to have a longer leading time than traditional drug reaction discovery methods. Three more drugs with known adverse reactions are investigated using the selected approach, and two are successfully identified.

Research limitations/implications

Validation of Google Trends data's representativeness of user search is yet to be explored. In future research, user search in other search engines and in healthcare web forums can be incorporated to obtain a more comprehensive adverse drug reaction early warning mechanism.

Practical implications

Using Internet data in drug safety management with a proper early warning mechanism may serve as an earlier signal than traditional drug adverse reaction. This has great potential in public health emergency management.

Originality/value

Our research work proposes a novel framework of using user search data in adverse drug reaction identification. User search is a voluntary drug adverse reaction exploration behavior. Further, user search data series are more concise and accurate than text mining in forums. The proposed methods as well as the empirical results will shed some light on incorporating user search data as a new source in pharmacovigilance.

IP CORNER

Intellectual Property (IP) is a vital asset to any emerging company in the healthcare space. Here, we highlight noteworthy trends and events in the IP realm with implications for both young and established healthcare companies alike.

UK SUPREME COURT BROADENS THE SCOPE OF PATENT PROTECTION

Historically, British courts had ruled that patent infringement was to be determined by a strictly literal reading of the patent claims. Patent claims are numbered paragraphs at the end of the patent that define the scope of the rights granted by the patent and specify technological solutions that should not be used without prior authorization. However, words are often imprecise and inadequate to describe complex technologies. For example, a minor change to the product could be deemed non-infringing as long as it fell outside the specific words of the claims. In recognition of the unfairness of this scenario, the courts created a doctrine of equivalents, which made it possible to hold a party liable for patent infringement even though the infringing product or process did not fall within the literal scope of a patent claim but nevertheless was equivalent to the claimed invention.

The doctrine of equivalents was generally recognized in the UK, but the test of equivalence established in 2005 was so stringent that it rendered the doctrine practically meaningless. The test required the courts to look at "what the person skilled in the art would have understood the patentee to be claiming." *Kirin-Amgen Inc v Hoechst Marion Roussel Ltd*, 2005 RPC 9. A person of ordinary skill in the art looking at the words of the patent claims would usually interpret the words narrowly in a way that leaves little room for equivalents.

In July of 2017, the UK highest court revitalized the application of the doctrine of equivalents. *Actavis UK Limited & Ors v Eli Lilly and Company,* 2017 UKSC 48 (12 July 2017). To correct for the shortcomings of the prior test, Lord Neuberger, writing for the court in *Actavis*, established a two-prong test for patent infringement under the doctrine of equivalents: "... (i) does the variant infringe any of the claims as a matter of normal interpretation; and, if not, (ii) does the variant nonetheless infringe because it varies from the invention in a way or ways which is or are immaterial?" While the first prong of the test requires interpretation similar to the analysis under prior test, the second prong expands a court's ability to analyze the materiality of the changes based on the facts and expert evidence.

The expansion of patent rights brings the UK law closer to the US law. U.S. Judge Learned Hand has described the purpose of the doctrine as to "prevent an infringer from stealing the benefit of the invention." *Royal Typewriter Co. v. Remington Rand, Inc.*, 168 F.2d 691, 692 (2d Cir. 1948). In the U.S., the courts consider whether "the accused product performs substantially the same function in substantially the same way with substantially the same result as each claim limitation of the patented product." *Warner-Jenkinson Company, Inc. v. Hilton Davis Chemical Co.*, 520 U.S. 17 (1997). While not perfect for chemical cases (for example, aspirin and ibuprofen are equivalent under this test as discussed by the Federal Circuit), the test strives to promote fairness and innovation. This test has restored power to the doctrine of equivalents in the UK and is a welcome development for patent owners.

- by Mark Shtilerman, Senior Counsel

CAUGHT OUR EYE

NICE, the UK health agency, has launched a competition for small or medium-sized companies, charities, and academic research groups in the early stages of clinical development of potentially transformative products. Dubbed the NICE AdviSeME Prize, the winner will receive free scientific advice that usually costs £15,000 to support discussions between the company and payers to enable market access for their product. Applications are due by 13 October 2017. *NICE*

The battle for control of CRISPR-related patents took another turn as the Broad Institute, along with joint owners Harvard University, Massachusetts Institute of Technology and Rockefeller University submitted 22 patents for evaluation to a proposed patent pool. The Broad is one of two main camps in the CRISPR patent debate, along with UC Berkeley. The Broad move is seen as one stemming from concerns the rights over the gene-editing technology may hinder further research toward disease treatment. *The Wall Street Journal*.

Also on the CRISPR front, UC Berkeley moved more recently to appeal the recent Patent Trial and Appeals Board decision that there is no interference between the key Berkeley and Broad CRISPR patents. Broad's opening brief is due October 25th. *The Broad Institute*

Each summer, the Centers for Medicare and Medicaid Services (CMS) rolls out its proposed payment scheme updates for the following calendar year. This year, CMS proposed cutting the discounted drug rates available to 340B Drug Pricing Program eligible institutions and providers. While they are able to purchase drugs at a heavily discounted rate, they are still reimbursed the average sales price (ASP) of the drug plus 6%. The new proposed plan would pay 340B providers far less, at 22.5% less than ASP. CMS is soliciting comments on the proposed rule, with further updates expected later this year. *Modern Healthcare*

The American Academy of Neurology recently formed a Neurology Drug Pricing Task Force to help neurologists navigate use of new, high cost drugs. The goal is to find a realistic middle ground between what patients are eligible for a drug, based on its label, and who insurance companies say they will cover. The task force plans to look at Spinraza in spinal muscular atrophy, Exondys 51 in Duchenne Muscular Dystrophy, and Brienura for Batten's disease. The 18-member group includes 16 neurologists with expertise in clinical practice guidelines, medical economics and ethics, and two advanced practice providers. *SMA News Today*

The FDA announced its first ever Patient Engagement Advisory Committee meeting, slated for October 11-12. The meeting is part of larger agency efforts to better incorporate the patient perspective into the drug and device development process. The inaugural meeting agenda includes challenges of clinical trial design, conduct, and reporting identified by patients. *FDA Voice Blog*

Novartis won approval for the first ever chimeric antigen receptor (CAR)-T cell therapy, one month ahead of its anticipated approval date. Dubbed Kymriah, the cell therapy is approved for certain pediatric and young adult patients with a form of acute lymphoblastic leukemia (ALL) but is also expected to later seek approval for adult patients with relapsed and refractory diffuse large B-cell lymphoma (DLBCL). With a price tag of $475,000 for the one-time infusion, Novartis has said it struck a novel payment scheme deal with CMS where CMS will only reimburse the cell therapy for patients who respond to Kymriah by the end of the first month. As it seeks approval in other indications like DLBCL, Novartis also plans to pursue follow on indication-based pricing. *FDA* and *Novartis*

Allergan made waves over its move to shield patents related to its eye drug Restasis from the U.S. Patent and Trademark Office's *inter partes review* (IPR) process by transferring ownership to the Saint Regis Mohawk Tribe. The tribe then exclusively licensed the drug back to Allergan in exchange for tens of millions of dollars in upfront fees and annual royalties. The tribe is filing a motion to dismiss ongoing IPR challenges to the patents filed by Mylan, citing its sovereign immunity as a recognized tribal government. State universities whose patents end up in IPRs have successfully used the sovereign immunity argument. *STAT News*

DEERFIELD FOUNDATION

The Foundation has formed 34 partnerships and invested and committed over $30 million for the advancement of children's health in its 10 years, ranging from health clinics in Nepal to a mobile medical home for children in the South Bronx. In this newsletter we would like to highlight just one of the organizations that we feel is helping us fulfill our mission of advancing healthcare. We are proud to be critical supporters of Project STAY at the Harlem Health Promotion Center.

PROJECT STAY AT THE HARLEM HEALTH PROMOTION CENTER

Mission:	The mission of the Harlem Health Promotion Center at Columbia University's Mailman School of Public Health is to address health inequities in vulnerable communities through research, education, training, service and advocacy.
Partner since:	2014
Description:	Project STAY (Services to Assist Youth) is the service delivery arm of HHPC, and is designed to engage marginalized youth in community settings and provide needed sexual health education, screening for HIV and sexually-transmitted infections, treatment, and linkages to primary care.
Total Funding:	$103,500
The Deerfield Perspective:	Much like many partners of the Deerfield Foundation, Harlem Health fills a void for a service that the Foundation sees as necessary for advancing healthcare and its awareness. They have been able to navigate the politics of New York City by providing a needed service to heterosexual youths of color that fall outside the mandated focus of the Department of Health programs directed toward gay, bisexual and transgender youth. Their community-based outreach approach to engage youths regarding STI/HIV risks and treatments provides the personal perspective and interaction that is often missing from government-mandated programs, thus appealing to the Foundation's philosophy.
Project STAY Perspective:	One of the most important public health issues affecting us both globally and locally is HIV. People of color, particularly adolescents and young adults, are disproportionately affected, and New York City is one of the epicenters for the epidemic. Support from the Deerfield Foundation has been crucial in helping expand Project STAY to enhance service delivery to New York City youth with providers who specialize in adolescent health. Among those served in 2017: 97% were youth of color; 30% had no health insurance and 60% had Medicaid; 83% were sexually active and many reported not using condoms regularly, yet most had not been tested for HIV recently (or ever) and the majority said they were not normally comfortable talking to a doctor about issues like sex, drugs, HIV, or depression. Funding from the Deerfield Foundation provided on-site risk assessments, HIV and STI screening, and referrals for medical and psychosocial care that these youth would likely not otherwise access.
Most Recent Project Funded:	In 2016-17, Deerfield provided support allowing Project STAY to serve youth in alternative high schools, community colleges, and programs serving young people involved in the criminal justice system. Although at high-risk for sexually-transmitted infections and HIV, youth in these programs would have had limited ability to access care were it not for this novel program. These expanded services also provided practical training opportunities to allow us to help educate the next generation of providers in medicine, nursing and public health.

FROM OUR FOUNDATION PARTNERS

LSA Family Health service is hosting the Spirit of East Harlem Gala where they will be honoring the Deerfield Foundation with its Corporate Spirit Award. Also being honored at the same event are actress, dancer and singer Chita Rivera with the Lifetime Spirit Award, and LSA Board Member and former Board Chair Ralph A. Siciliano, Esq. with its Community Spirit Award.

When: October 16, 2017, 6pm – 9pm
Where: Guastavino's
409 E 59th St at 1st Avenue
New York, NY 10022

For more information and to register if you would like, please visit SpiritofEastHarlem.com

The Spirit of East Harlem is an annual celebration to support LSA Family Health Service's programs for children and families. Founded by the Little Sisters of the Assumption, LSA has been an anchor in the East Harlem community since 1958, annually serving over 2,000 families through health, education, and family support services.

The Deerfield Foundation has been a supporter of Little Sisters of the Assumption since 2008.

The Family Center is hosting its 2017 Fall Benefit Gala, the inaugural Harvest Ball, where they will be honoring the Deerfield Foundation, along with Dr. Joseph Ruggiero of Weill Cornell Medicine, and Bernadette Herward Davida of Polsinelli, PC.

When: October 19, 2017, 7pm – 9pm
Where: Prince George Ballroom
15 East 27th Street
New York, NY 10016

This black tie-optional gala will be emceed by Emmy award-winning WABC7 journalist Lauren Glassberg. Guests will hear about The Family Center's impact from former clients who received its services as children and have now grown and gone on to give back to the NYC community.

If you would like more information on tickets and sponsorship, please visit gala.thefamilycenter.org/

The Deerfield Foundation has been a supporter of The Family Center since 2008.

MEET THE ASSOCIATES

Beginning in 2015, Deerfield started the Deerfield Fellows program, designed to attract students with interest in pursuing healthcare or finance fields from local NYC-area colleges and universities from diverse backgrounds for an immersive summer internship program. Successful summer interns are invited to stay through a yearlong Deerfield Fellowship program, with the most successful of those graduating to become Associates at Deerfield. We are extremely proud of the work our Associates do, and here will highlight an Associate in each issue.

MEET KATE BUSKO:

WHAT INITIALLY DREW YOU TO THE FELLOWS PROGRAM?

I was a pre-pharmacy student when I found out about the Fellows program from my college professor. At that time I was planning to get a PharmD degree and work in the industry upon graduation. When I learned about the Deerfield Fellowship, it was different from any possible scenarios I had imagined for myself by that time, and tempting because it resonated so well with the vision I had for my future. It seemed like a perfect balance between everything that I knew and wanted to know. There is no doubt that this program changed my academic and career track by 180 degrees. All I can say - it was worth it.

WHAT IN YOUR EXPERIENCE HAS MATCHED YOUR EXPECTATIONS ABOUT BEING A DEERFIELD FELLOW AND NOW ASSOCIATE?

Genuine willingness of the team to share their experiences, and the amount of knowledge we gained during the fellowship year – these are the bigger ones. Joining the program with the science background, I was hoping to learn a lot about Wall Street and finance in general during this training, and I did. To our advantage, the program was focused not only on mastering business terminology and basic concepts, but on learning how to approach investment decisions in general - by recognizing our own and companies' biases, identifying the unknown and the knowable, etc. As an associate now, I have a chance to work with different institute and investment teams, which allows me to continue building a well-rounded and profound understanding of the Deerfield investment approach.

DESCRIBE A TIME OR TIMES YOU FOUND TO BE UNEXPECTED.

The first thing that comes to mind is when we got involved into a discussion during the analysts' morning meeting. There was a discussion of potential scenarios in terms of the company valuation, when Jim [Flynn] asked what we, fellows, thought about it. We've just had a meeting with the company management and were working on the company valuation using it as a case study. It was absolutely unexpected (!) for us, but there was no other way rather than to engage into the conversation and summarize our standpoint. In fact, that was the first time we spoke up in front of the team, and I think it worked out relatively well. At least it eliminated a fair amount of bashfulness and made us more comfortable exchanging our views with the senior team members moving forward.

DESCRIBE YOUR MOST MEMORABLE EXPERIENCE AT DEERFIELD.

The whole fellowship experience is quite memorable. I am still getting excited about having unlimited access to talented people here who are willing to share their knowledge and guide us into our professional future.

WHAT ADVICE WOULD YOU GIVE TO FUTURE FELLOWS?

Not to be afraid of being vocal and proactive. If there is a question or an idea worth discussing, to not leave it to yourself since most of the people at Deerfield are genuinely open and eager to talk and to guide the younger members of the company, even

though there might be a professional and academic gap in between. To stay humble, but not intimidated by the senior team members. At the end of the day, if enough energy and diligence is dedicated to the projects, it will be noticed and respected.

WHEN NOT AT DEERFIELD, I CAN BE FOUND:
Cycling, working out, meditating.

ONE FUN FACT ABOUT YOU!
Well, this one is a top secret. I was playing drums in a girl's band when I was a teenager. I am still having a weird feeling that it happened in a parallel life.

Photo courtesy of Kate Busko

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