THE PURSUIT OF HOPE

TENNESSEANS' RIGHT TO TRY POTENTIALLY LIFE-SAVING MEDICINES

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INTRODUCTION

"What would you do if [a] smart, beautiful, 25 year old woman, who is the love of your life, is dying?" That was the question asked by Good Morning America when covering one husband's desperate mission to save his young wife's life.

Keith and Mikaela Knapp met in sixth grade and were high school sweethearts before marrying after college graduation. Both shared a love of travel, tying the knot in Maui, and taking trips around the world together.[1] Yet neither anticipated the painful journey they would embark on just two years into their marriage: Mikaela was diagnosed with State IV kidney cancer. In March 2014, Mikaela's plight gained national attention when Keith took her story to social media. By bringing awareness to Mikaela's condition, Keith hoped she could be granted access to potentially life-saving medicine that was in the clinical trial phase of the Food and Drug Administration's (FDA) approval process.

Before long, Mikaela's Facebook Cause petition received over 200,000 signatures, and national television networks contacted the Knapps to tell their story. "Mikaela has always been my rock…she's in a lot of pain and facing death at the age of 25," Keith described on Good Morning America in March. "She's just such a fighter," he added, as he begin to explain his mission to access alternative treatments.

Mikaela was enduring tremendous lower back pain from where her tumor was harbored on her kidneys. Despite a pain regimen that included a multitude of high-dose painkillers, the trauma persisted. To make matters worse, she also contracted pneumonia, which made it even more difficult on her lungs to process enough oxygen to her blood.

Unfortunately, Mikaela was not eligible to participate in clinical trials due to the pervasiveness of the cancer to her brain and history of pneumonia.[2] Out of options, Keith appealed to the FDA via the "compassionate use" clause available to unqualified trial applicants that, if granted, would allow Mikaela use of an experimental gene therapy that produced successful results in clinical trials. With renewed vigor, he devoted precious moments that could otherwise be spent with his ailing wife to instead pursue the FDA's cumbersome compassionate use channels. The race against time began.

HOW WE GOT HERE

Since the Food, Drug, and Cosmetic Act was signed into law by President Franklin D. Roosevelt in 1938, the FDA has been empowered by the federal government to require pre-market safety testing before drugs are available to the public.[3] However, 1962 saw a vast expansion of the FDA's roll by enacting the Kefauver-Harris Amendments that mandated efficacy testing of drugs before market availability. These new regulations significantly reduced the freedoms of doctors and patients, making the FDA the ultimate arbitrator of access to treatment. With this new power came great expansion of the agency; the FDA's staff expanded from 1,000 members in 1951 to approximately 6,500 in just two decades. Not only did these amendments impose new standards for developing drugs, but also required the launch of an investigative audit into the efficacy of all previously approved drugs on the market.[4]

After the passage of the 1962 amendments, the average time and cost associated with obtaining FDA approval for new drugs skyrocketed. Compounded by bureaucratic testing and red tape, these regulations have significantly stifled the productivity and innovation of the pharmaceutical industry. It takes between $500 million and $2 billion for a drug to travel from the laboratory to the market.[5] Drug development has consequently declined since 1962, and the wait time for potentially life-saving drugs increased to more than a decade by the end of the 1970s—where it remains today.[6]

"PHASES" OF ALLOWANCE

Continuous innovation of pharmaceutical treatments has tremendous consequences for our national welfare and security. As Americans grapple with our own solutions to a spreading Ebola virus from

Western Africa, the realities of pharmaceutical's vital roll in society have become even more apparent.

In slightly over a decade—between 1986 and 2000—new drug development was responsible for 40 percent of the total increase in U.S. life expectancy. Yet, the majority of specialists polled on the efficiency of FDA provisions believe the agency's clinical trial process is too slow, and most of these physicians report a hindrance to their treatment of patients due to the FDA approval process.[7]

To begin the clinical trial process, a drug developer must submit an Investigational New Drug Application (IND) to the FDA for review. Prior to granting permission to proceed, the FDA will determine whether the trial would expose patients to "unreasonable risk of harm." Once drug companies receive the green light to begin testing, the clinical trial enters three mandatory human testing phases.

Phase I of the FDA approval process is otherwise known as the "safety phase," during which trial participants are monitored for any serious side effects. Although over 60 percent of investigational drugs in Phase I testing are deemed safe enough to continue, it costs an average of $15.2 million and about 22 months to proceed to Phase II.[8]

During Phase II, safety continues to be monitored as researchers analyze the appropriate dosage for treating targeted conditions. The cost of this phase skyrockets to an average of $23.4 million and approximately 26 months before moving to the third and final phase.

Once a drug surpasses the hurdles in the previous two phases, it goes through a tediously time-intensive and costly final process. If a drug developer has managed to finance the costs associated with Phases I and II, Phase III's associated financial burdens and lengthy process—an average of $86.5 million and 30 months—can often be the determining factor of whether companies proceed to market. During Phase III, the drug is dispensed to a much wider pool of individuals as means of aggregating data to support the safety, efficacy, and prescriptive nature of the drug before ultimate approval. Afterwards, it can take between six months and two years before the new treatment is available for patients.[9]

Thus concludes the long journey for pharmaceuticals, from a newborn invention to pharmacy shelves.

WHO GETS A SNEAK PREVIEW?

Of course, not everyone must wait an average of 10 years to access a new drug. Those chosen for clinical trials as part of the FDA's phased approval process are given potentially game-changing treatments for their conditions before the drug hits the marketplace.

Unfortunately, 97 percent of the sickest patients are deemed ineligible and prohibited from participating in the standard clinical trials.[10] Instead, these individuals must seek alternative options of petitioning the FDA for access to experimental medications.

In 1987, as a response to the AIDS epidemic and increasing pressure for treatment, the FDA began its first programs to allow patients to access experimental drugs outside the clinical-trial setting. This expansion also marked the beginning of the "compassionate use" program, which enabled desperately ill, and in most cases terminally ill, patients to petition the FDA for access to pre-approved drugs.

However, the expanded access has proven ineffective at connecting the most needy patients with access to promising treatments. In fact, from 1987 until 2002, the FDA approved only 44 pre-market drug treatment applications for conditions ranging from AIDS to chronic pain—an average of less than three drugs per year.[11]

In response to concerns that the compassionate use process was inconsistent and arbitrarily administered, the FDA introduced the Food and Drug Administration Modernization Act of 1997.[12] The new law defined the parameters for approval of compassionate use applications, based on the following conditions:

1) The patient's doctor determines the patient's condition has no comparable or sufficient alternative therapy;

2) The FDA deems there is sufficient evidence of safety and efficacy to support the use of the experimental drug;

3) The FDA determines that the experimental drug will not interfere with clinical trials; and

4) The sponsor or clinical investigator submits necessary information to meet FDA requirements.

FDA's approval is also contingent upon the experimental drug developer's willingness to allow a patient to access the drug. Once that permission is obtained, the patient's doctor must be willing to submit the compassionate use application, the patient's medical history, current treatment, and acknowledge that they have informed consent from the patient before proceeding.

While the FDA claims the paperwork burden placed on doctors acting as sponsors for a patient applicant is "non-labor intensive, straightforward, and appropriate," the burden is actually tremendously time-consuming and extensive.[13] In fact, the application states "the burden of time for this collection of information is estimated to average 100 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information."[14]

In measuring the impact of compassionate use's expanded access, a Goldwater Institute study, "Everyone Deserves the Right to Try: Empowering the Terminally Ill to Take Control of their Treatment," concluded, "In 2011, just shy of 1,200 patients received expanded access through either a single-patient or treatment IND. While the total had slightly increased from 1,014 patients in 2010, this is a very small number considering that, in that same year, there were 1,529,560 new cancer cases. In 2012, the number of patients granted expanded access dropped down to a mere 940. The onerous process the FDA requires a patient to go through to request expanded access contributes to the number being so low."[15]

MIKAELA'S LONG BATTLE

This onerous and demoralizing process is the same one that greeted Keith Knapp when he embarked on his mission to save Mikaela's life in the fall of 2013.

Speaking of first meeting Mikaela in sixth grade at a small school near Sacramento, California, Keith reflected, "I eschewed sports at recess that year to swing on the swings with Mikaela... I liked her right away."[16] Facing a future without his bride, Keith partnered with Mikaela's physicians to lobby the drug companies and FDA for access to the experimental gene therapy that had been rendering such promising results.

Tragically, Keith was unable to gain permission from the FDA for this experimental treatment, despite exhaustive and dedicated efforts from Keith and the sponsoring doctors. On April 24, 2014, Mikaela passed away, surrounded by loved ones, and with her devoted husband by her side.[17]

WE ALL DESERVE THE "RIGHT-TO-TRY"

Patients and their families should not be relegated to the mercies of bureaucracy to determine whether they have the right to fight for their own lives. Each one of us knows the pain and devastation that comes with watching a loved one battle a terminal disease. Every moment we have with that person is precious. Imagine the heartache of knowing that your child, parent, husband, or wife's terminal condition could be alleviated or reversed through a potentially life-saving, but experimental treatment. What would you do?

We owe Tennesseans facing these circumstances the opportunity to fight. Instead of demanding extensive amounts of paperwork, placing unreasonable requirements upon local physicians already overburdened by case loads, and restricting the invaluable time left for families to be by the side

of an ailing patient, we must act to ensure that all terminally ill Tennessee patients have the right to access potentially life-saving medication.

The Beacon Center of Tennessee challenges the Tennessee General Assembly to stand up for the rights of patients in our state and adopt "Right-to-Try" legislation in 2015. Right-to-Try declares that a patient diagnosed with a terminal illness may access available investigational medications, devices, or biological products.[18]

Right-to-Try legislation seeks to address the very specific and special needs that terminally ill patients encounter in their treatment process. It would allow access to medications that have passed basic FDA safety testing (Phase I), under the following parameters:

1) The patient has been diagnosed with a terminal disease;

2) The patient has considered all available treatment options;

3) The patient's doctor has recommended that the investigational drug, device, or biological product represents the patient's best chance at survival;

4) The patient or the patient's guardian has provided informed consent; and

5) The sponsoring company chooses to make the investigational drug available to patients outside the clinical trial.

For Mikaela Knapp and Tennessee patients battling a life-ending condition for which there is no approved known cure, the FDA's traditional role of protecting patients from unapproved treatments due to lack of completed efficacy testing is superfluous.

Under Right-to-Try's provisions, these medications have already been deemed safe enough to administer to patients in Phase II clinical testing. The requirement for informed consent ensures that terminally ill patients fully acknowledge the associated risks. Right-to-Try also preserves drug manufacturers' ability to decide whether to provide the treatments to the patients. If a company does not wish to make a medication available for any reason, it will not be obligated to do so.

Right-to-try legislation will give terminally ill patients a fighting chance, restore their family's hope, and unleash innovation to life-saving treatments. Ultimately, it will say that Tennesseans have a right to survive.

ENDNOTES

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