The Right to Try

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ABSTRACT

Patients who request access to investigational drugs are terminally ill and consequently have an increased risk for serious adverse events. Additionally, their terminal illness is a poor indicator for success with future treatment attempts. Drug manufacturers are therefore often hesitant to grant these higher-risk patients access to their product, both inside and outside of their own tightly controlled clinical trial environments. Through the RTT Act, patients with life-threatening illnesses, who have exhausted approved treatment options and do not qualify for any available clinical trials, are able to seek access to investigational drugs without the FDA's approval and direct involvement.

Keywords: right to try, investigational drugs, experimental treatments, end of life, bioethics, access to care

INTRODUCTION

The need for increased access to investigational drugs has consistently been supported by the public, in spite of the fact that the Expanded Access Program (EAP), which is regulated by the Food and Drug Administration (FDA), already exists.[1] As a result, the Right to Try (RTT) Act became a federal law on May 30, 2018. Through the RTT Act, patients with life-threatening illnesses, who have exhausted approved treatment options and do not qualify for any available clinical trials, are able to seek access to investigational drugs without the FDA's approval and direct involvement. Eligible investigational drugs must have already completed a Phase 1 Clinical Trial in order to ensure some, but nonetheless a bare minimum, level of safety.[2] This law was enacted in an

effort to increase terminally ill patients' access to investigational drugs, which could possibly prolong their life that would otherwise surely end in the near future.

ANALYSIS

Opponents of the RTT Act favor the EAP, which is the presumably safer route to gain access to investigational drugs because the FDA provides direct regulatory oversight prior to and throughout the treatment process.[3] The problem with the EAP is that it involves an extensive pre-approval process.[4] Physicians are required to obtain informed consent from the patient, as well as approval from both an Institutional Review Board (IRB) and the drug's manufacturer, prior to completing and submitting the EAP application. Once the EAP application is received by the FDA, it is almost always approved and the patient is granted access to the investigational drug through a clinical trial that is regulated by the FDA.[5] Unfortunately, the pre-application process is tedious and time-consuming for physicians and these terminally ill patients are limited on time as it is.

Difficulties in obtaining access to investigational drugs are not solely a result of the FDA's pre-approval process. Manufacturers of investigational drugs often deny these requests, and it is the manufacturer who ultimately determines whether or not a patient will be granted access to their product.[6] Patients who request access to investigational drugs are terminally ill and consequently have an increased risk for serious adverse events. Additionally, their terminal illness is a poor indicator for success with future treatment attempts. Drug manufacturers are therefore often hesitant to grant these higher-risk patients access to their product, both inside and outside of their own tightly controlled clinical trial environments. This is due to the fact that any adverse event associated with its use, which could be related to the drug or related to the patient's condition, could negatively influence the FDA's decision to ultimately approve the drug. Furthermore, the FDA requires manufacturers to develop and continuously update expanded access protocols that require time and additional resources to produce.[7] Medium to smaller sized companies do not have the personnel nor the financial means to keep up with the requirements of the EAP, and this limits their ability to provide access to their investigational drugs.[8]

The RTT Act attempts to overcome these barriers to investigational drug access. In order to decrease the amount of time physicians spend on the pre-approval process, physicians are able to request and obtain investigational drugs directly from the manufacturer. The physician, rather than the FDA, is responsible for monitoring and managing the patient's clinical progression throughout the treatment process going forward. It addresses manufacturers' concerns by prohibiting clinical outcomes and adverse events associated with drugs taken through the RTT pathway to be used to influence the FDA's review, and ultimately its approval, of the investigational drug. However, manufacturers are required to include a summary of severe adverse events experienced by these patients in the annual report they submit to the FDA for review. Lastly, drug manufacturers, physicians, and other involved parties are liberated of any liability claims associated with drugs administered through the RTT pathway, with the exception of instances where there is a clear act of misconduct or negligence involved.[9]

Many people have voiced their concerns with the RTT pathway. They believe that in removing the FDA's role to provide regulatory oversight throughout the process, it also removes safety nets that are crucial for these

vulnerable patients.[10] The whole point of the issue at hand is that there is no safe and proven effective solution. The fact of the matter is that these patients are at death's door and there is no hope in sight for they have exhausted every available treatment option approved by the FDA. The RTT Act was not developed to replace the EAP. It was developed to provide an additional pathway that terminally ill patients can utilize to obtain access to potentially life-saving drugs. The drug's manufacturer still has the option to provide access to their product through the EAP.[11] If the manufacturer is more inclined to grant access to its drug through the RTT pathway, then this opens a window of opportunity for patients who are faced with dire and limited circumstances.

Another concern people have with the RTT pathway is related to its lax requirements for obtaining informed consent.[12] The EAP requires physicians to obtain written consent from the patient, which is then reviewed by an IRB to ensure that the patient is well informed and comprehends the risks associated with using the investigational drug. The RTT pathway only requires written consent from the patient and as previously mentioned, the physician is protected from liability claims if the information provided prior to obtaining written consent is incorrect or inconclusive. The reason physicians, and manufacturers for that matter, are absolved of liability in this situation is because there is limited information available about the safety and efficacy of these investigational drugs at that point in time. Phase 1 clinical trials involve only a small number of patients and notable adverse events are often first discovered in later clinical trials that involve a larger number of patients.[13] As a result of this, it is impossible to obtain a proper informed consent from patients prior to their use of investigational drugs through the RTT pathway.

It is clear that investigational drugs taken through the EAP are a safer bet, but the EAP has been available for many years and people have consistently continued to support the need for increased access to investigational drugs.[14] The RTT Act is a new law that was enacted in order to help terminally ill patients overcome barriers that have prevented them from accessing investigational drugs in the past. However, because manufacturers are not required to report the total number of individual requests they receive, it is difficult to determine if the RTT Act has effectively increased access to investigational drugs.[15] This also makes it difficult to quantify the extent of the need for increased access among this population. Drug manufacturers should be required to keep track of the total number of requests they receive for access to investigational drugs through both the EAP and RTT pathways, which would provide pertinent insight regarding this matter.

CONCLUSION

Terminally ill patients do not seek access to investigational drugs because they think these drugs are a safe and effective treatment option. They seek access to investigational drugs because there is no other option left. Claiming that the RTT Act may do more harm than good is a moot point considering that the only alternative for these patients is dying. The RTT pathway is not perfect by any means, but it helps to preserve the autonomy of terminally ill patients by affording them the opportunity to decide whether or not they wish to take this extreme and unsafe risk. Every dying patient has the right to choose how they spend their remaining days and if they choose to spend that time trialing an investigational drug on the off-chance that it leads them on a path to recovery, then this is something that I fully support.

[1] Jessica Piel, "Informed Consent in Right-To-Try Cases," *Journal of the American Academy of Psychiatry and the Law* 44, no. 3 (September 1, 2016): 290-96.

[2] This and the preceding three sentences include information from Susan Thaul, *Right to Try: Access to Investigational Drugs,* CRS Report No. R45414 (Washington, DC: Congressional Research Service, 2018), https://www.everycrsreport.com/reports/R45414.html.

[3] Jessica Piel; Susan Thaul; Beth Roxland and Elisa A. Hurley, "Taking a Closer Look at the New Federal 'Right to Try' Law," *Ampersand* (PRIM&R blog), August 21, 2018, https://blog.primr.org/right-to-try-law/; Ellen V. Sigal, "Why Right-to-Try Laws Are Dangerous," *The ASCO Post*, March 5, 2018, https://www.ascopost.com/issues/march-5-2018-special-report/why-right-to-try-laws-are- dangerous/.

[4] Jessica Piel; Susan Thaul; Brian Connelly, "Right to Try Act: Is It the Answer for Terminally Ill Patients?," *Update Magazine*, October 2018, https://www.fdli.org/2018/10/right-to-try-act-is-it-the-answer-for-terminally-ill-patients/; Leah Lawrence, "The Realities of 'Right to Try,'" *ASH Clinical News*, October 1, 2018, https://www.ashclinicalnews.org/features/realities-right-try/.

[5] This and the preceding sentence are from Susan Thaul.

[6] Susan Thaul; U.S. Food & Drug Administration, *Right to Try*, (Silver Spring, MD: U.S. Department of Health and Human Services, 2020), https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/right-try.

[7] This and the preceding five sentences are from Susan Thaul.

[8] Susan Thaul; Brian Connelly.

[9] This entire paragraph includes information from Susan Thaul.

[10] Jessica Piel; Susan Thaul; Beth Roxland and Elisa A. Hurley; Ellen V. Sigal; Leah Lawrence.

[11] Beth Roxland and Elisa A. Hurley; Brian Connelly.

[12] Jessica Piel; Susan Thaul; Beth Roxland and Elisa A. Hurley; Ellen V. Sigal; Leah Lawrence

[13] This and the preceding three sentences are from Susan Thaul.

[14] Jessica Piel.

[15] Susan Thaul; Ellen V. Sigal.