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Informed Consent: A Clinical Trials Perspective

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In 2015 there were almost 220,000 open clinical trials across disease states (ClinicalTrials.gov, 2015). There are currently over 5,500 registered clinical trials in cancer research alone (ClinicalTrials.gov, 2016). With the primary goal of survival, clinical trials to test the efficacy, safety, and tolerability of pharmacological agents is the gold standard (Ording et al., 2016). For many patients with a poor prognosis, such trials can be extremely appealing. Many patients, however, are hesitant to sign on. As noted in a 2010 clinical research workshop, a number of barriers exist including fears about quality-of-life alterations, receiving the placebo instead of the drug, side effects, the new drug potentially not being the best treatment, inconveniences in being part of the study, feeling coerced, wanting the physician to make the decision, and feeling a loss of control (English RA, Lebovitz Y, & Giffin RB, 2010).

Indeed, deciding to enroll is an informed gamble and in many cases, the advancements may be minimal. For example, a study evaluating survival, safety, and prognostic factors for the use of Regorafenib in patients with metastatic colorectal cancer refractory to standard therapies boasted a median survival rate of 5.6 months with 80% of patients experiencing at least one adverse event (Adenis et al., 2016). This type of outcome suggests the need to assess patient preferences of quality-of-life verses a few extra months of life with potential poorer quality. Such decisions are certainly individual. Being part of a research study, in such cases, is a necessity for potential life extension, though a possible lack of consideration for the contribution to science. Very much noted, however, is that many patients at any stage do enroll for altruistic reasons.

For these types of clinical trials and all research studies, it is important to review the Belmont Report's focus on ensuring respect of persons, beneficence, and justice (HHS, 2016). Examining two famous cases, we will explore the application of these ethical tenets for patients who signed informed consents to receive gene therapy. The first case involved an 18-year old male with a rare immunological disease in which he was lacking an enzyme (ornithine transcarbamylase) needed to disassociate ammonia. He was fairly well managed with medication. The patient, Jesse Gelsinger, with agreement from his father, took part in a phase I clinical trial using a viral vector to introduce healthy DNA into Jesse's system with the hope of improving his own system's ability to produce the enzyme and decrease the need for the meds (Somia & Verma, 2000). He was also aware that it was likelier that the trial would lead to improved methods for the then nascent protocol and direct benefit to him would only be a future possibility (Wilson, 2010). Jesse had an adverse reaction to the vector

and died just two days after receiving the treatment (Somia & Verma, 2000). Other patients in the same trial did not have such a reaction. A number of questions were raised, however, and even law suits ensued (Wilson, 2010). In terms of respect of persons, Jesse made a seemingly clearly informed decision to enter the trial, with support from his father. Beneficence is a greyer area, though the expectation was not an immediate and direct cure for the disease. Justice – meaning equal opportunity for all – is also questionable. The patient's condition was being managed by a renowned physician at a major academic medical center in a major city.

The second scenario boasted a truly celebratory outcome. More than a decade following the tragic outcome of the young 18-year-old, gene therapy was introduced in a male adult who had been initially diagnosed with chronic lymphocytic leukemia in 1996. It is interesting to note that the completion and publications of the human genome sequencing took place in 2001, two years following Jesse's death. With the advanced information and technology, in 2009, this gentleman was able to have his DNA evaluated with the finding that he had a deletion of the *TP53* gene (Porter, Levine, Kalos, Bagg, & June, 2011) – a gene that produces an anti-tumor protein. Using a specific chimeric antigen receptor gene in a lentivirus vector transduced into autologous T-cells, the patient received a chemotherapy condition regimen followed by an infusion of his altered T-cells (Porter et al., 2011). Although some adverse reactions occurred, he ultimately recovered and went into remission (Porter et al., 2011). In this scenario, the tenets of the Belmont Report in respect of persons and beneficence were certainly upheld. But what about justice? Would a marginalized patient with poor access to health care have had such an opportunity or even enough access to care and resources to have had his CLL so well managed for over 20 years? Importantly, would it take a highly educated patient to even understand the process and potential risks and benefits enough to truly be informed?

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