CAR T cell therapy trial conducted by Novartis found that 41 of 50 patients had complete remission with no detectable leukemia, confirming the single center trial that Carl had conducted at the University of Pennsylvania. Current FDA regulations require that gene therapy patients be followed for at least 15 years. To detectable leukemia, confirming the single center trial that Carl had conducted at the University of Pennsylvania. Current FDA regulations require that gene therapy patients be followed for at least 15 years. To date, cumulative patient data for CAR T cell therapy has not produced a single side effect with 468 patients and 1586 patient years of safety among them. Leukemia is the first indication for this therapy, but translating this technology for the treatment of solid tumors, pancreatic cancer and autoimmunity are current challenges.

June’s presentation began with an overview of the cancer epidemic and treatment. Cancer is the number one killer in 22 of the 50 U.S. states. In 2010, the first curative therapy for metastatic melanoma, which normally does not respond to chemotherapy, was approved by the FDA. Since the release of this therapy, 20% of people have become long term survivors, living past 10 years. The goal in oncology is to have this be 100%. To achieve this goal, the cancer field is moving away from chemotherapy and towards a combination of immunotherapy and targeted therapy, an approach that is more potent and less toxic. Manipulating the immune system to treat cancer has been explored in the field for the last decade. However, early therapies were ineffective in patients, resulting in policies that made it difficult to obtain funding for such research. Since the breakthrough in 2010 with the first curative therapy for melanoma, funding became widely available from government, industry and philanthropic organizations.

June then discussed the drug his team has developed, CTL019, noting that the underlying idea behind their approach is synthetic biology: “making the immune system do things it never could”. In the case of cancer, this would be repurposing cells to become “cancer killing cells”. The impact of this drug was highlighted through a short video from the Emily Whitehead Foundation. June outlined the drug’s mechanism of action which involves removing white blood cells called T-cells from the patients’ blood; using a modified virus to introduce a synthetic gene into T cells, which cause T cells to target cancer cells rendering them “leukemia-specific killer cells;” these cells are called chimeric antigen receptor T cells or CAR T cells; infusing the CAR T cells back into the patient, where they divide and proliferate, acting as a “living drug;” unlike other drugs that are metabolized and need to be reintroduced.

This therapy is technologically intensive. Each drug is made individually from a patient’s own T cells, instead of mass manufactured for large populations. Consequently, this raises the policy issue of how to price a drug that is expensive to make, for a single patient only, but potentially curative. The first global CAR T cell therapy trial conducted by Novartis found that 41 of 50 patients had complete remission with no detectable leukemia, confirming the single center trial that Carl had conducted at the University of Pennsylvania. Current FDA regulations require that gene therapy patients be followed for at least 15 years. To date, cumulative patient data for CAR T cell therapy has not produced a single side effect with 468 patients and 1586 patient years of safety among them. Leukemia is the first indication for this therapy, but translating this technology for the treatment of solid tumors, pancreatic cancer and autoimmunity are current challenges.

The next steps for this technology include incorporation of CRISPR/Cas9 gene editing to enhance T cells. June’s team is involved in the first-in-human evaluation of safety and feasibility of CRISPR/Cas9 technology. This protocol engineers T cells to be more resistant to autoimmunity issues. While this is the first trial in the US, there is competition with China as to who will be able to demonstrate this technology in humans first. Now that we have the technological ability to conduct genome editing in humans, policy, ethics and risk taking are key issues to consider with its uptake in medical care. Varying risk-taking capabilities mean “people with the same data will make different choices”, as demonstrated by the use of fluoridated water in only some states in the US.

The therapies discovered in the June lab have enormous health policy implications. He noted that countries approach genetic modification with varying degrees of caution, resulting in regulatory policies that have influenced the distribution and scale of clinical trials across the globe: there are now 160 clinical trials, with China recently overtaking the US in number conducted, and Europe conducting very few.

Healthcare challenges include the need for the industry to add a “fourth pillar” of therapeutic - cell therapies - to the current 3 pillars, namely pharmaceuticals, biologics and devices. Compared to other therapeutics, each drug is generated from the individual so a local blood bank model for manufacturing is where the industry may head, compared to the central, controlled manufacturing facility which is what current US regulatory policy requires for genetic modifications. Finally, the cell therapy industry is so new that there are currently no standards. This, combined with the fact that the field is highly multidisciplinary, makes the establishment of standards complex. A consortium at Georgia Institute of Technology and the National Institute of Standards of Technology are currently tackling this.

KEY POINTS

• CAR T cell therapy for leukemia is likely to be the first FDA approved cell therapeutic
• The healthcare industry (nationally and globally) will require new manufacturing standards, pricing models and policies to add a brand new arm of therapeutic delivery.
• Globally, the uptake of this technology will be affected by public perception of risk, affordability, and each country’s regulatory policies regarding genetic modification.