pediatric partner, Hospital Sant Joan de Déu. Although HE for adult ALL patients and compassionate uses (next to indicated commercial products that authorized our center) allow us to use CART19 therapy for treating our patients (our real aim of this development), the good clinical results, and petitions of different centers all around the world (specially from places where commercial products are not available) encouraged us to consider how we should proceed to extend our product to other patients. Our Academic proposal is the result of the work of a multidisciplinary team, a point-of-care (PoC) procedure based on a well stablish protocol in a commercially available bioreactor and our home-developed lentivirus. All the elements of our proposal follow the GMP standards, strictly controlled by the AEMPS and the regulations for Advanced Therapy Medicinal Products (ATMPs) of the EMA; although the product could be developed in our clean-rooms at Barcelona, our aim is to share procedures to allow production as a real PoC product, looking for partners that can reproduce all steps next to the patient. This multi-site cell production has been already accomplished with success in several clinical trials, while for a homogeneous lentiviral production, we decided (by now) to use facilities centralized in our university hospital. We expect to obtain first local authorization for this multicenter production in Spain, and later by EMA and other regulators (India). In fact, this experience is also supported by developing a clinical trial with 60 multiple myeloma patients under the treatment of a new own CART-BCMA (ARI-0002h). We are convinced that it is a possible model, although most of the huge number of rules are mainly thought for pharma-companies and are not easily implemented by Academic entities. But if we want to have the best treatments for our patients, to find solutions with real options for Academic ATMPs developments is the only way to arrive where the commercial companies, the health systems and in general countries will not be able to arrive for different reasons (difficult recover of investments by complex reimbursement, low level of patients, no-sustainable expenses and procedures for economic and ecologic reason, ...).

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Sp15

USA EXPERIENCE: IN-HOUSE PREPARATION: PROSPECTS AND PROBLEMS

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Adoptive Cellular Therapy (ACT) is transitioning from experimental to standard of care. Limited specificities of chimeric antigen receptor T cells (CAR-T) are licensed drugs, with commercial products selling for ~400,000 USD. Tumor infiltrating lymphocytes (TIL) can target multiple cell surface and intracellular tumor antigens. TIL have not been commercialized, due to complex logistics and cost. Our objective is to leverage a single standardized platform (Miltenyi Prodigy) for in-house ACT. We currently manufacture CD19 CAR-T under an FDA IND and are developing a virtually identical TIL protocol minus the lentiviral vector. TIL are manufactured from malignant pleural effusions rich in immune infiltrates. CD4+ and CD8+ cells are enriched and activated with anti-CD3/CD28 beads. CAR-T are transduced, and both CAR-T and TIL are expanded (IL-7/IL-15) for 5 days. The product is infused fresh, avoiding losses associated with cryopreservation and thawing. Developing and validating release tests (absence of replication competent virus, vector copy number, chimeric antigen receptor expression, endotoxin testing) posed an initial challenge. Having completed assay development, our manufacturing process, including release testing, can be performed for less than 1/10 the cost of commercial CAR-T. We expect that the platform that we have validated will be easily transitioned to new chimeric antigen receptor designs and specificities and will likewise be adaptable to TIL manufacture for the wide variety of cancers that metastasize to the pleura of peritoneum. Standardized in-house ACT manufacture may greatly reduce the cost of cellular immunotherapies, making it more widely available to patients.

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