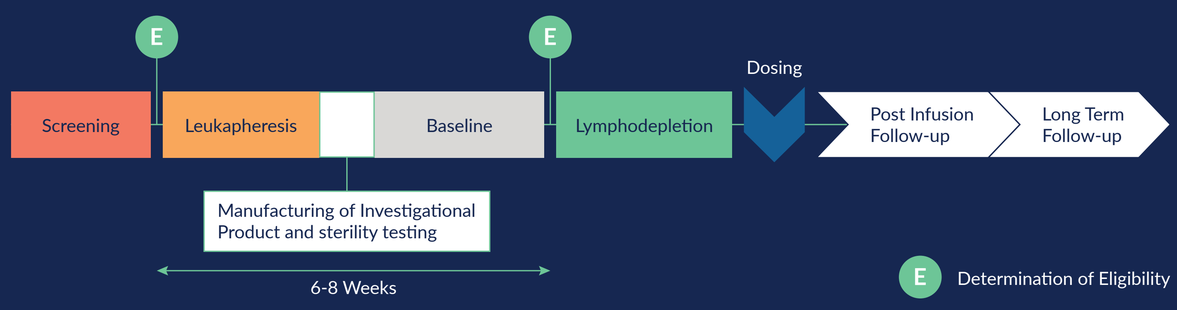
OPERATIONALIZING CELL THERAPY STUDIES: CHALLENGES AND OPPORTUNITIES

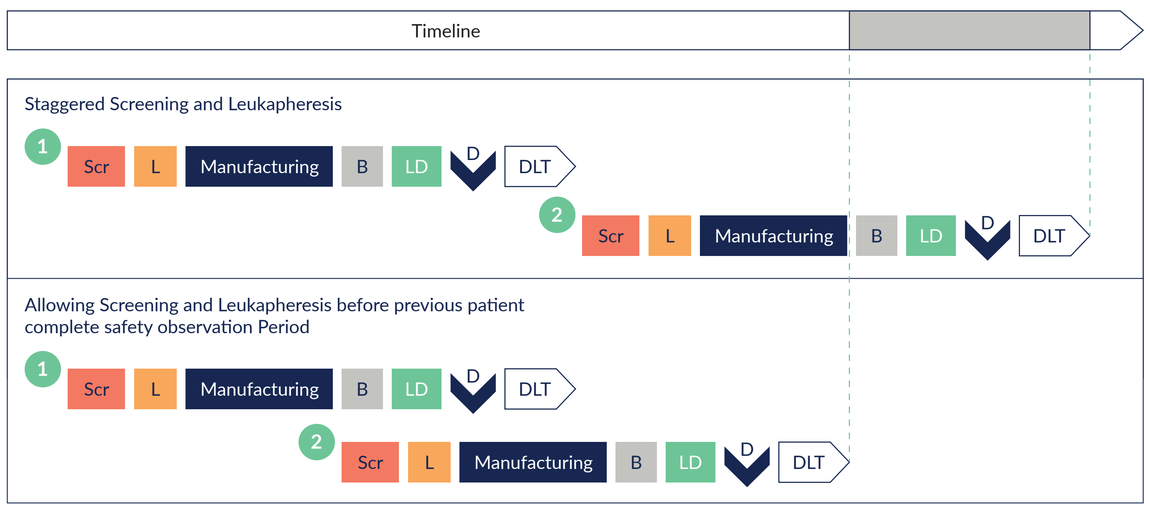
A case study of genetically modified autologous cell therapy oncology trial

STUDY DESIGN



PROTOCOL CONSIDERATIONS

1. **Optimal Enrollment Strategy**
   - Minimizes loss of patients while waiting for treatment
   - Shortens enrollment timelines
   - Reduces investigator frustration



Scr-Screening; L-Leukapheresis; B-Baseline; LD-Lymphodepletion; D-Dosing and DLT-Dose limiting toxicity

2. **Eligibility Criteria**

   For cell therapy trials, subjects often must meet more than one set of eligibility criteria to proceed through the study; therefore, careful consideration must be given to:
   - Avoid unnecessary duplication of assessments
   - Ensure alignment with standard of care procedures
   - Feasibility of performing assessments within the described eligibility window
3. **Visit Windows**
   - Account for potential toxicity of lymphodepletion therapies and possible delays to dosing
   - Take into consideration the feasibility of the procedures within the window
   - Accommodate site scheduling and staff coordination across multiple departments
4. **Defining and reporting of Adverse Events (AEs)**
   - Clear definition of the windows and the type of serious AEs to be collected within the windows must be specified
   - Protocol must provide guidance regarding grading criteria used for cytokine release syndrome, neurotoxicity, and other adverse events

SITE SELECTION AND START-UP STRATEGIES

Experience

- Prior and current experience in conducting cell therapy trials

Infrastructure

- FACT accreditation
- Multi-disciplinary teams (HCT, oncology and other departments)
- Alignment of site SOPs with the protocol
- Cell Therapy Unit/Pharmacy capabilities
- Investigators enthusiastic about therapeutic approach
- Staff availability

Start-up

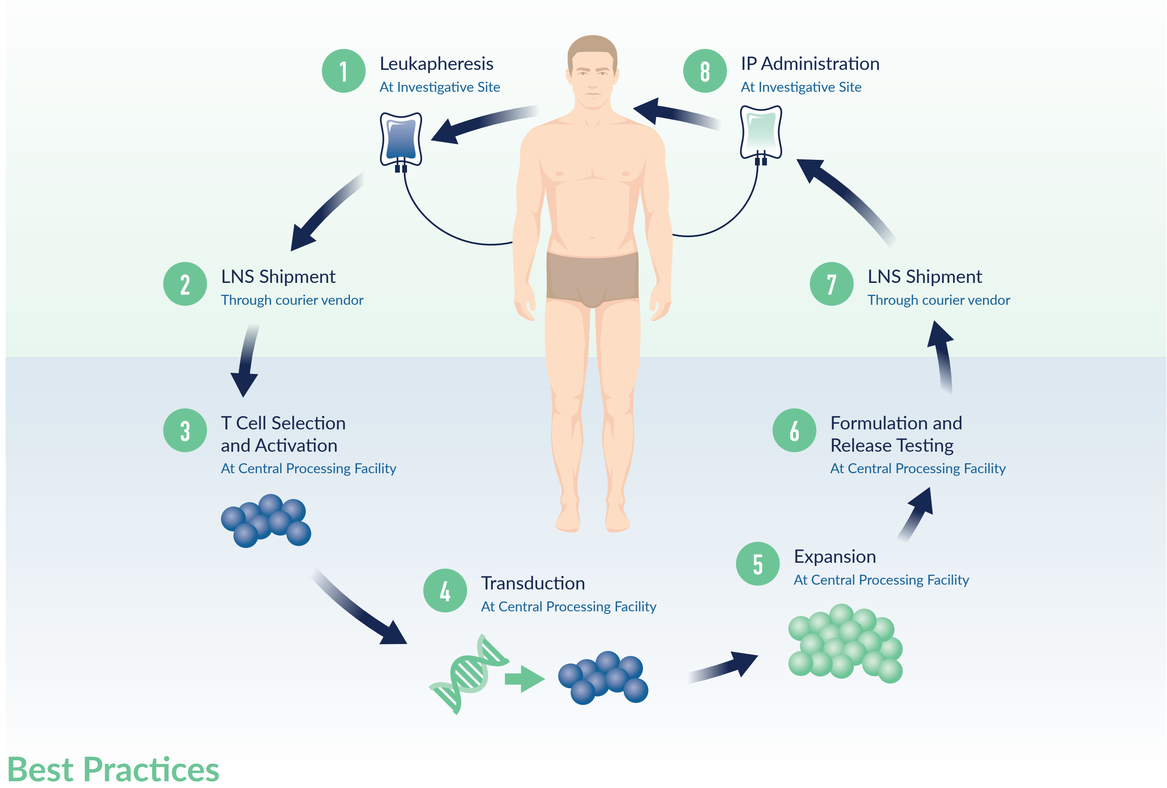
- Central/Local IRB
- Contract process
- Prior start-up timelines
- Institutional Biosafety committee

Recruitment Potential

- Number of patients in site's database
- Other competing studies
- Prior recruitment metrics

INVESTIGATION PRODUCT MANAGEMENT

Leukapheresis and Autologous Cell Therapy Product Manufacturing



Best Practices

- Leukapheresis and Cell therapy manual
  - Visual and intuitive
  - Defers to institutional standards where appropriate
- Cell Tracking
  - 21 CFR Part 1271.290 requires establishment and maintenance of a tracking system that enables the tracking of HCT/P* from donor to consignee and the return of the HCT/P (vein-to-vein)
- Feasibility
  - Conduct site feasibility to understand site IP handling and process requirements
- Dry run
  - Conduct dry run of logistics process with every site and all stakeholders prior to activation

*HCT/P: human cells, tissues, and cellular and tissue-based products

Cell Tracking

- Hybrid approach

ClinTrak® Cell Tracking
Server-based system enabling real-time tracking, Chain of Custody and key quality indicator oversight, and notification of stakeholders

Cell Tracking Worksheets & Forms
Paper-based, monitored source worksheets and forms documenting key handoffs in Chain of Custody and details of leukapheresis and Investigational Product administration

Stakeholder Training & Logistics Dry Run
Hands-on dry run of the logistics process with each site and all stakeholders, including shipments of mock leukapheresis product and Investigational Product

RECRUITMENT AND RETENTION

Recruitment and Retention Strategies

- Understand the site recruitment processes
  - Database and/or referral process
- Retention
  - Include hospitalization costs in the budget
  - Consider vendor for providing travel arrangements
  - Patient facing materials, such as the Patient Journey, help inform the patients of study visit requirements

CONCLUSION

Clinical trials involving Advanced Therapy Medicinal Products (ATMPs) are complex. A tailored-approach must be adopted during protocol development, site selection, investigational product management, and other aspects of study management.

MEDPACE