



Programming and Reporting on a Master Protocol in Cell & Gene Therapy

Paper DS-05

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- There is a lack of industry guidance and standards for programming and reporting for master protocol & cell and gene therapy (CGT) studies.
 - Both have unique characteristics requiring novel programming methods and mindset.

 - The purpose is to:
 - Share few challenges faced working on master protocol TCR-T studies to the wider programming community.
 - Explore collaboration possibilities within the industry to develop guidance, standards, and training materials for programming and reporting.

Master Protocol – An Overview



Basket

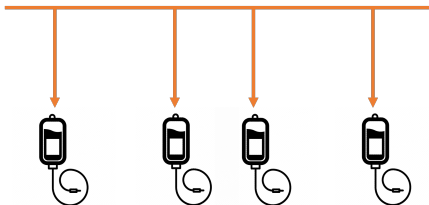
Multiple Indications/Biomarkers/Patient Characteristics



Single Intervention

Umbrella

Single Indication/Biomarker/Patient Characteristic



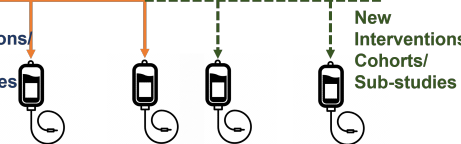
Multiple Interventions

Platform

Multiple Indications/Biomarkers/Patient Characteristics



Multiple Interventions/
Cohorts/
Sub-studies



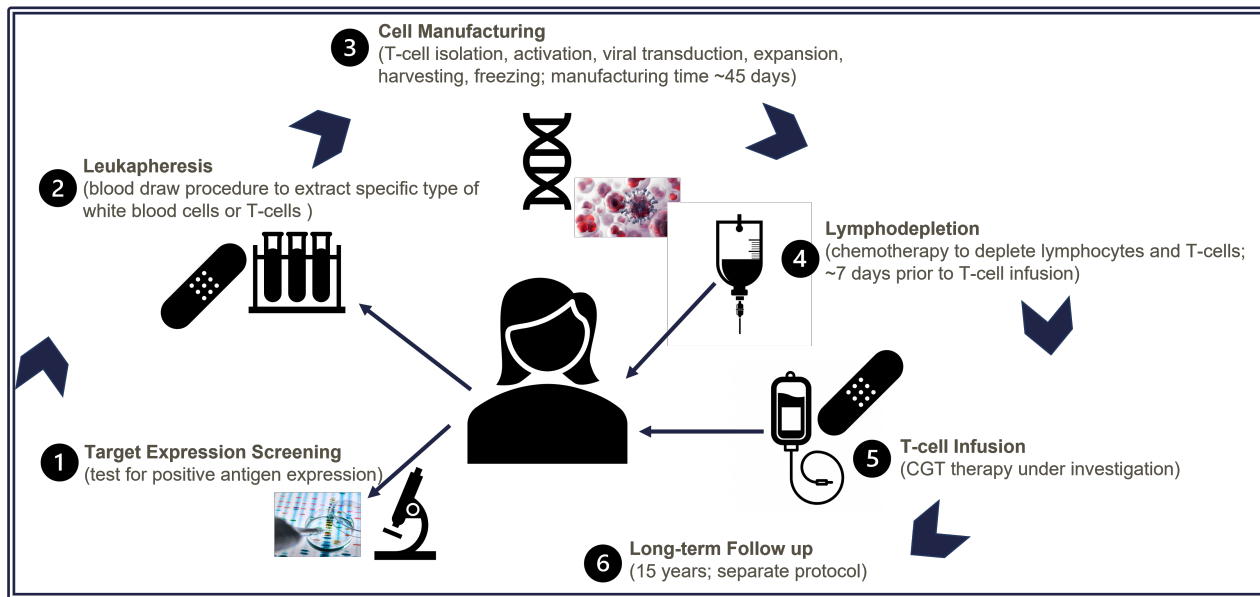
Protocol defined
milestone,
e.g., interim analysis

Drop interventional arms/
cohorts/sub-studies

Adoptive T-Cell Therapy Study Design



- Unique design characteristics:
 - Multiple eligibility screenings
 - Length of time between Leukapheresis and lymphodepletion
 - Single infusion
- Long-term follow up of 15 years per FDA guidelines on human gene therapy studies





Key Challenges Related to Master Protocols

Three Key Challenges Presented in the Paper



1

**Designing Master-Level
SDTM Trial Arm
Domains**

2

**Creating Separate SDTM
Packages for Individual
Substudies Based on
Master Database**

3

**Managing Differences in
Efficacy and Safety
Analyses Mockups**

Designing Master-Level SDTM Trial Arm Domains



Assigning ARM & ARMCD
in TA domain

Domain	ARMCD	ARM	TAETORD	ETCD
TA	S1A	Substudy 1, TxUI		1 SCREEN
TA	...	Substudy 1, TxUI		
TA	.S1A	Substudy 1, TxUI		n FUPP
TA	S2B	Substudy 2, TxUI		1 SCREEN
TA	...	Substudy 2, TxUI		
TA	S2B	Substudy 2, TxUI		n FUPP

ARM & ARMCD assignment in SDTM.TA domain
"TxUI" refers to Treatment under Investigation

Domain	IETESTCD	IETEST	IECAT	TIVERS
TI	I02	IETESTx.	INCLUSION	YYYYID_00
TI	I03	IETESTx.	INCLUSION	YYYYID_00

SDTM.TI mapping for traditional studies

Domain	IETESTCD	IETEST	IECAT	IESCAT	TIVERS
TI	I0102	IETESTx. s1	INCLUSION	SUBSTUDY 1	YYYYID_00
TI	I0203	IETESTx. s2	INCLUSION	SUBSTUDY 2	YYYYID_00

SDTM.TI mapping for Master Protocol studies with multiple sub-studies

Adding substudy specific
inclusion/exclusion criteria in TI domain



Key Challenges Related to T-cell Therapy Design

Three Key Challenges Presented in the Paper



1

**Defining Reference Start
Dates for Different
Analysis**

2

**Reporting Adverse
Events in Different
Phases of a T-cell
Therapy Study**

3

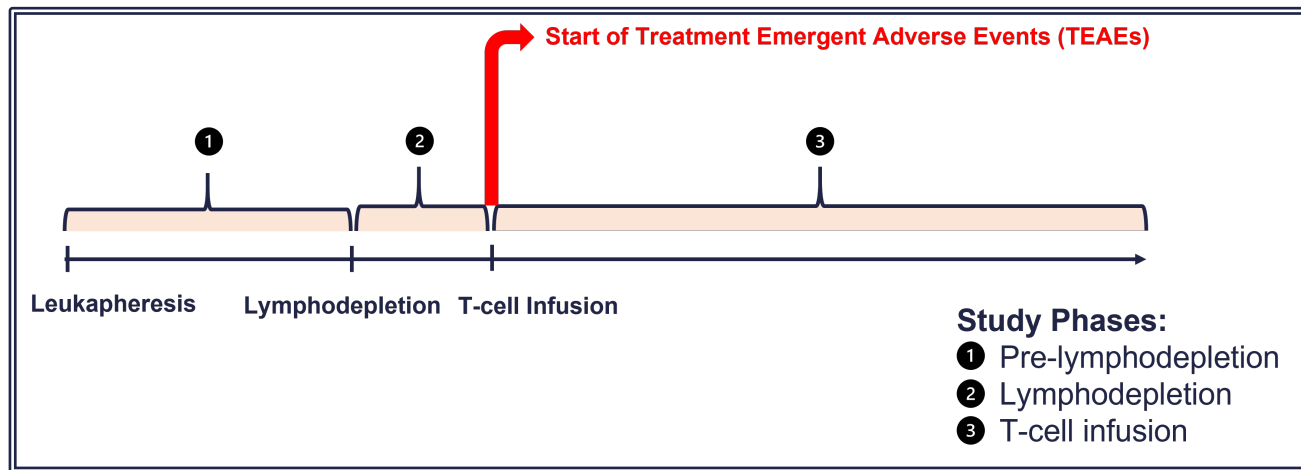
**Receiving Full Line
Systemic Therapy
during Time between
Leukapheresis and
Lymphodepletion**

Reporting AEs in Different Phases of a T-cell Therapy Study

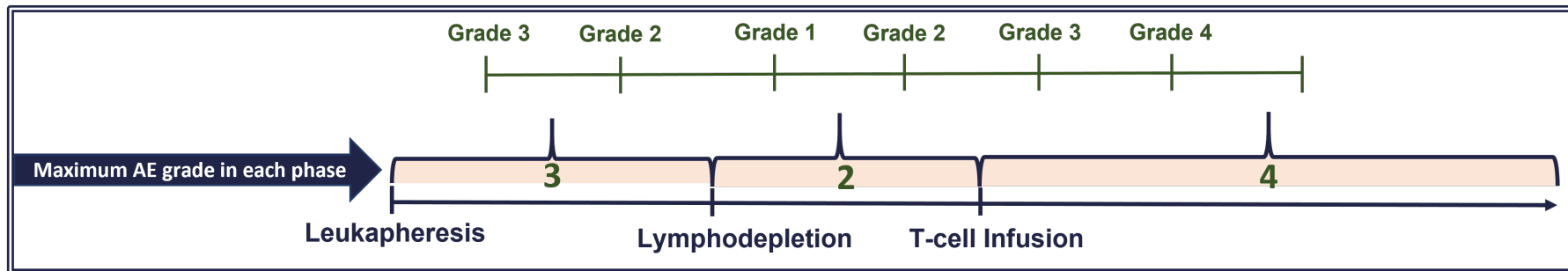


Defining TEAEs

Using “actual” vs.
“planned” treatment

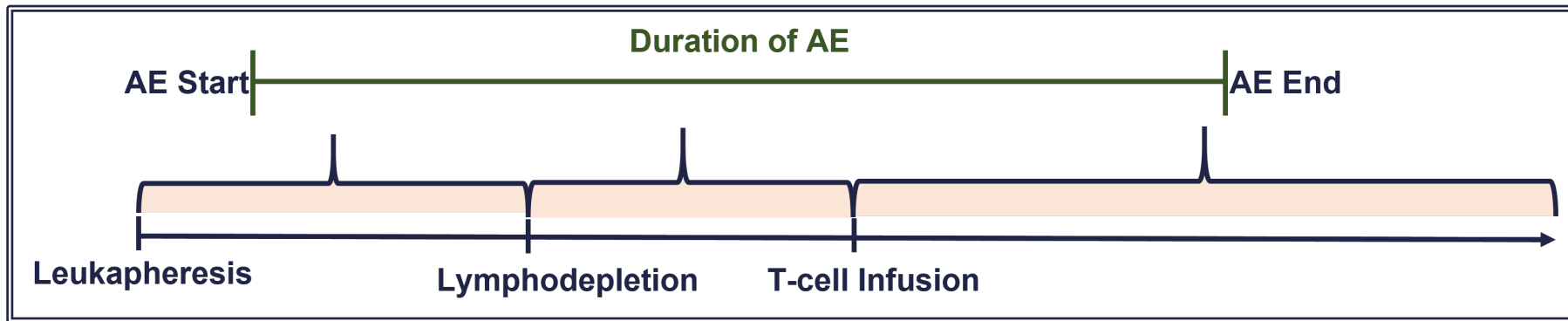


Reporting AEs in Different Phases of a T-cell Therapy Study



Worsening of adverse events spanning multiple study phases

Reporting AEs in Different Phases of a T-cell Therapy Study



Duration of adverse events spanning multiple study phases



Closing Remarks

Closing Remarks



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- Develop robust standards, best practices, and guidance for master protocol and TCR-T studies, in order to:
 - Support programming activities.
 - Facilitate operational efficiencies and expedited regulatory reviews.
 - Invest in resources internally to develop CGT specific end-to-end standards.
 - GSK CGT programmers are working on two initiatives to standardize CGT specific reporting standards based on current learnings
 - Involve the programming team early in the process, preferably during protocol development phase

Contact Information



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