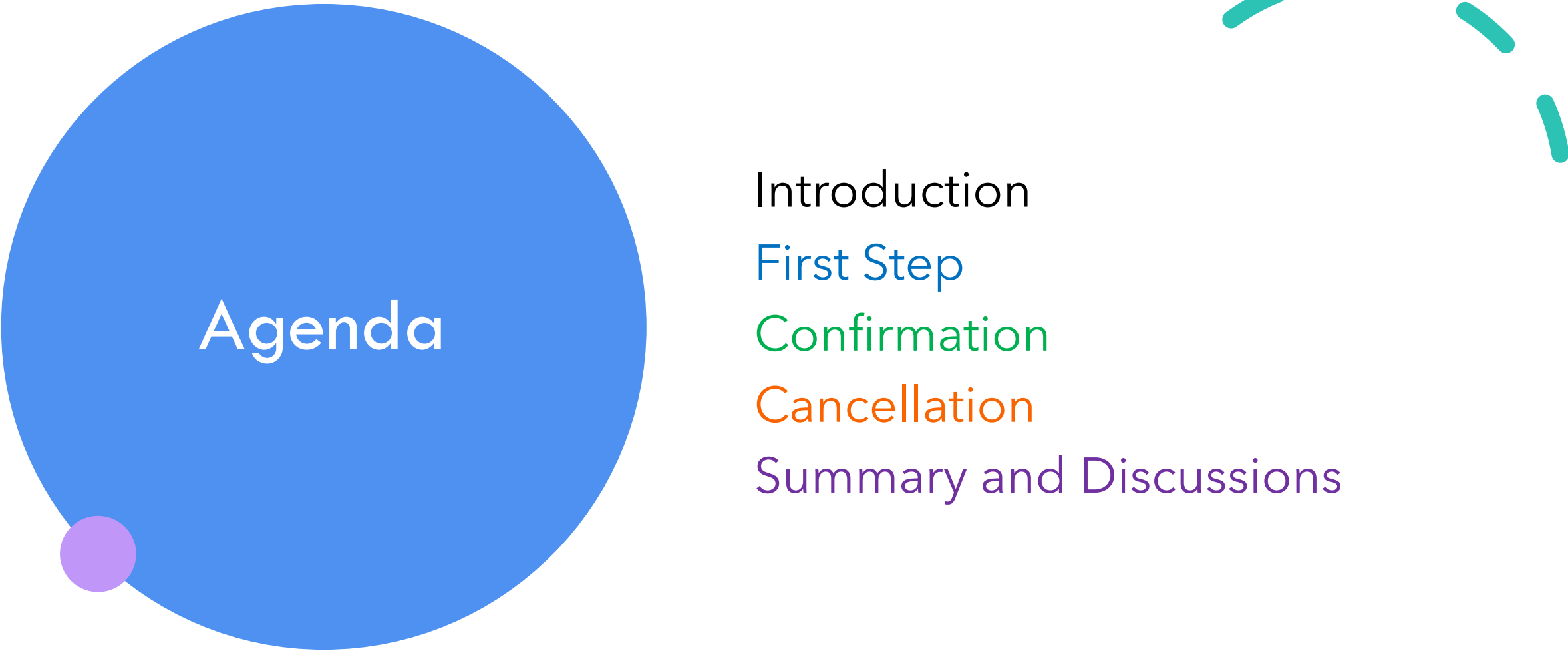




TA03

Confirmation and Cancellation -
Best Strategies for Data Collection
and Handling within Solid Tumor
Studies using RECIST 1.1 and
iRECIST Guidelines

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Agenda

Introduction

First Step

Confirmation

Cancellation

Summary and Discussions

Introduction

RECIST (Response Evaluation Criteria in Solid Tumors) provides a simple and pragmatic methodology to evaluate the activity and efficacy of new cancer therapeutics in solid tumors, using validated and consistent criteria to assess changes in tumor burden.

A consensus guideline—iRECIST—was developed by the RECIST working group for the use of modified Response Evaluation Criteria in Solid Tumors (RECIST version 1.1) in cancer immunotherapy trials, to ensure consistent design and data collection, facilitate the ongoing collection of trial data, and ultimate validation of the guideline.



First Steps

TEAM COLLABORATION: Involve cross-function teams in advance and share learnings from experience.

EARLY QUERIES: Send queries as soon as they were observed. Please bear in mind things might not be resolved therefore more discussion might be needed.





CONFIRMATIONS

Explanation for minimum SD duration and response confirmation

	Baseline Timepoint 0 (Randomization/First Dose Date)	Overall Response First Timepoint	Overall Response Subsequent Timepoint
	Week 0	CR at week 4	PD at week 8
The SD duration	4 weeks - To the 1st Timepoint		
	8 weeks - To the 2nd Timepoint		
Duration of the two timepoints post baseline		4 weeks - Between the 1st & 2nd Timepoints	

Best overall Response when confirmation of CR and PR is required per RECIST 1.1

Scenario	Overall Response First Timepoint	Overall Response Subsequent Timepoint	BEST overall response
1	CR	CR	CR
2	CR	PR	SD, PD, or PR
3	CR	SD	SD provided minimum SD duration are met. Otherwise, PD
4	CR	PD	SD provided minimum SD duration are met. Otherwise, PD
5	CR	NE	SD provided minimum SD duration are met. Otherwise, NE
6	PR	CR	PR
7	PR	PR	PR
8	PR	SD	SD
9	PR	PD	SD provided minimum SD duration are met. Otherwise, PD
10	PR	NE	SD provided minimum SD duration are met. Otherwise, NE
11	NE	NE	NE

CR first, PR second (after query, CR remain as CR / change to PR)

SUBJID	ADT	AVALC	TRTSDT
001	2023-03-01	CR	2023-01-01
001	2023-05-01	PR	2023-01-01
002	2023-03-10	CR	2023-03-01
002	2023-03-15	PR	2023-03-01
002	2023-03-30	PD	2023-03-01

SUBJID	ADT	AVALC	TRTSDT	BOR
001	2023-03-01	CR	2023-01-01	SD
001	2023-05-01	PRPD	2023-01-01	
002	2023-03-10	CR	2023-03-01	PD
002	2023-03-15	PRPD	2023-03-01	
002	2023-03-30	PD	2023-03-01	

SUBJID	ADT	AVALC	TRTSDT	BOR
001	2023-03-01	CRPR	2023-01-01	PR
001	2023-05-01	PR	2023-01-01	
002	2023-03-10	CRPR	2023-03-01	PD
002	2023-03-15	PR	2023-03-01	
002	2023-03-30	PD	2023-03-01	

Consideration for confirmations

- (1) Is the minimum duration of the SD met?
- (2) Once non-PD response was observed, we need to look at the next response- one to check if that goes equal or better to confirm, second is to check the elapsed time between the non-PD exceed the response confirmation duration.
- (3) If unfortunately, the subsequent response is worse, then the queries as well as the minimum duration of SD, perhaps the previous assessment needs to be re-considered.
- (4) The implementations of the 'NE' need to be considered.



Where is best to do in the confirmation?

ADaM as we suggest.

Pros and Cons for RAW, SDTM, ADaM.

Discussions and Thoughts...





CANCELLATIONS

INTRODUCTION ON IPFS within RECIST

The iRECIST usually kicked in by the protocols definition and the first PD would be ideally equivalent to iUPD which need a subsequent confirmed iCPD to confirm. This is used to calculate the censoring and duration of the iPFS.



CANCELLATIONS OF BETTER ASSESSMENTS AFTER IUPD IN IRECIIST WHEN DERIVING IPFS

The iRECIST guideline suggested to cancel out the iUPD if the subsequent is a better assessment (iCR, iPR, iSD) while deriving iPFS.

(1) The progression event date would be the same as RECIST 1.1 date (i.e., first iUPD date) unless iSD, iPR or iCR intervenes which is ultimately date at which progression criteria are met provided that iCPD is confirmed at the next assessment.

(2) However, iUPD would be disregarded if iUPD only occurs before later iSD, iPR, or iCR, that iUPD date should not be used as the event date.



Discussions

1. CAUTION: Do not delete records!
There is a difference between deleting and cancellation / disregarding records per the rule. It is better to flag them and disregard them while deriving for the iPFS.
2. Where is the best place in the data flow to handle these? Again, RAW, SDTM, ADaM...



Summary and Discussions

1. Understand what you need to understand, also reach out if you do not understand.
2. Where is the best workflow to handle such complicated operations in the lifecycle of our data?
3. Are we doing these in a way that is already too complicated? Are there any enhancements that can be suggested to add in the data flow to make the whole process more streamlined?





Questions?

Thank you

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