

Activity 2: Structure

- Handouts given out upon entry to workshop
- Matt introduces Activity 2 on last slide of Part 2
- Participants discuss with others at their table for 12 minutes
- Discussion prompts:
 - Determine the column variable names based on the excerpts from PHUSE *Implementation of ICH E9(R1) Estimands Framework using Data Standards* white paper (May 2025)
 - List pros and cons of creating an Intercurrent Events Analysis Dataset (ADICE)
- Group sharing: Volunteers share insights and questions from their groups.

Intercurrent events structure (OCCDS-ICE) – Workshop Example

Question of interest from workshop part 1:

What would the **hazard ratio for progression free survival by 24 months** be if **all patients with refractory or relapsed Follicular Lymphoma (Grade 1, 2, 3A) and meeting the additional ELARA eligibility criteria** were prescribed **optional bridging therapy and lymphodepleting therapy followed by tisagenlecleucel infusion** compared to if they were prescribed standard of care, if patients were not able to initiate a new anticancer therapy before progression, but regardless of treatment discontinuation.

Initiation of new anticancer therapy before progression.

- CR: ICE reflected in Variable (Composite; Estimand 01)
- PFS: Hypothetical strategy (Estimand 02)
- OS: Treatment policy strategy (Estimand 03)

Fill in the column headers below based on the excerpts from *Implementation of ICH E9(R1) Estimands Framework using Data Standards* white paper (May 2025)

Col 1	Col 2	Col 3	Col 4	Col 5	Col 6	Col 7	Col 8	Col 9	Col 10	Col 11	Col 12
						AENDT					
ABC001	1	ELARA (single arm)	Breyanzi	Initiating a new anticancer therapy before progression	2018-04-20		COMPOSITE	HYPOTHETICAL	TREATMENT POLICY	CM	1
ABC002	1	RW Cohort (FHRD)	Yescarta	Initiating a new anticancer therapy before progression	2019-04-03		COMPOSITE	HYPOTHETICAL	TREATMENT POLICY	CM	1

Excerpts from PHUSE *Implementation of ICH E9(R1) Estimands Framework using Data Standards* white paper (May 2025)

Table 1: ADICE Define-XML Metadata

Dataset	Description	Class – Subclass	Structure	Purpose	Keys	Documentation	Location
ADICE ¹	Intercurrent Events Analysis Dataset ¹	OCCURRENCE DATA STRUCTURE – INTERCURRENT EVENTS	One record per subject per intercurrent event	Analysis	STUDYID, USUBJID, ATERM, ASTDT ²	Presents the consolidated lists of intercurrent events related to the different estimands and the strategy to handle them. Based on [...]	adice.xpt

1. The name and label could be different, and several datasets could be used.

2. Alternative identifiers other than ATERM and ASTDT could be used. See 6.2.2 Variable-Level Implementation.

Table 3: ADICE Structure Variables List

Variable	Label	Type	Codelist/ Controlled Terms	Core	CDISC Notes
Identifiers					
STUDYID	Study Identifier	Char		Req	
USUBJID	Unique Subject Identifier	Char		Req	
Sequence numbers					
ASEQ		Num		Req	Unique record number within a subject. Within a subject, each intercurrent event record is assigned a unique value.

defined in this white paper.

Record topic (event)					
*TERM	{Reported Term}	Char		Cond ²	Original intercurrent event term.
*TRT	{Reported Name of Drug, Med, or Therapy}	Char		Cond ²	Original intercurrent event name, when the intercurrent event is a treatment.
ATERM	Analysis Term	Char		Cond ²	Analysis term describing the intercurrent event. The most granular description of the intercurrent event, close or identical to the source term/name of the event. This variable is especially useful when: • There are intercurrent events that are not directly an SDTM-reported event or intervention, e.g. a lab finding above some threshold, an AE that is severe. In such cases, an intercurrent event is derived, e.g. lab test <xxx> above <yyy> threshold, <aeterm> with grade <y>. • In general, when there are multiple sources of intercurrent event from different SDTM domain classes – such as events, interventions, findings, e.g. if occurrence of some AEs or intake of some concomitant medications are intercurrent events – then ATERM is used and could contain either an AE or a medication. When present, it must be filled for all records.

Source code and classifications					
ADECODy	Analysis Dictionary Derived Term {y}	Char	*	Perm	Coded version of the intercurrent event, at the more granular level needed according to the intercurrent event definition, per protocol/SAP. It is used to present the intercurrent events in a standardised way, related to the intercurrent event definition and policies. Writers of the white paper foresee that typically one such variable will be used in most situations. However, implementers are free to add ones if they have a need to provide different labels to intercurrent events, e.g. different labels for different estimands or tables/listings.
ACATy	Analysis Category {y}	Char	*	Perm	Categorisation of the intercurrent events. Useful when there are different levels of granularity of intercurrent event across estimands, e.g. some estimands may differentiate "Treatment Discontinuation due to Adverse Events" and "Treatment Discontinuation due to Lack of Efficacy", while others may be interested only in "Treatment Discontinuation" in general. In that case, the more granular labelling would go to an ADECODy variable and the less granular, higher-level grouping to an ACATy variable.
Record start/end date and time					
ASTDT	Analysis Start Date	Num		Cond ⁴	Source start date of the intercurrent event in numerical format. One of ASTDT/ASTDTM must be present.
AENDT	Analysis End Date	Num		Perm	Source end date of the intercurrent event in numerical format. Included if the intercurrent event end date is relevant to assess the impact of the intercurrent event on datapoints.

Intercurrent event handling strategy					
ESTzz*STP ¹	Estimand zz* planned handling strategy	Char	(ICESTRG) ³	Req	Documents the planned strategies for handling the intercurrent events related to estimand zz*, as described in the protocol and/or analysis plan. Blank if the intercurrent event is not related to estimand zz*.
ESTzz*STA ¹	Estimand zz* actual handling strategy	Char	(ICESTRG) ³	Req	Documents the actual strategies for handling the intercurrent events related to estimand zz*. Blank if the intercurrent event is not related to estimand zz* or if the intercurrent event handling strategy is masked by the strategy of another intercurrent event that has a higher precedence. Initially, ESTzz*STA is filled as ESTzz*STP. Then, in a second step, the other intercurrent events for the same estimand are considered, subject by subject, along with their strategy and priority rules. Typically, for a given subject, if an intercurrent event is preceded by another one AND that one has a higher precedence in terms of handling strategy, the handling strategy of that intercurrent event will prevail and mask the strategy of the current intercurrent event. In that case, ESTzz*STA of that event will be set to blank. Note that priority rules are decided and documented by the sponsor.