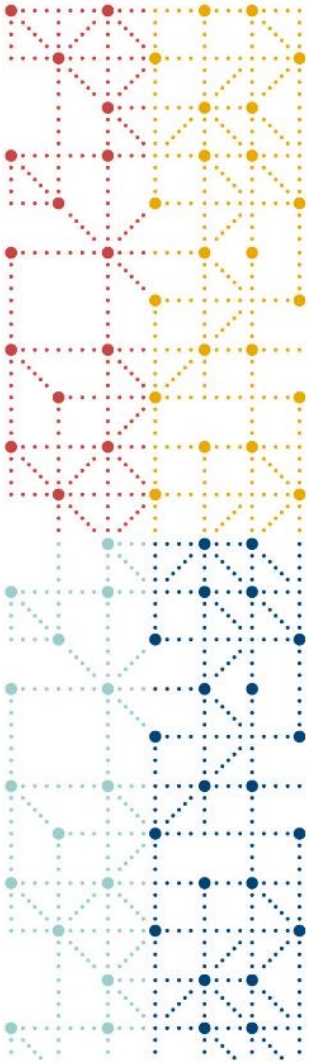
Experience with Implementation of Kidney TAUGs

Presented by Sai Jaya Nagarajan, Zifo RnD Solutions



Meet the Speaker

Sai Jaya Nagarajan

Organization: Zifo RnD Solutions

Disclaimer and Disclosures

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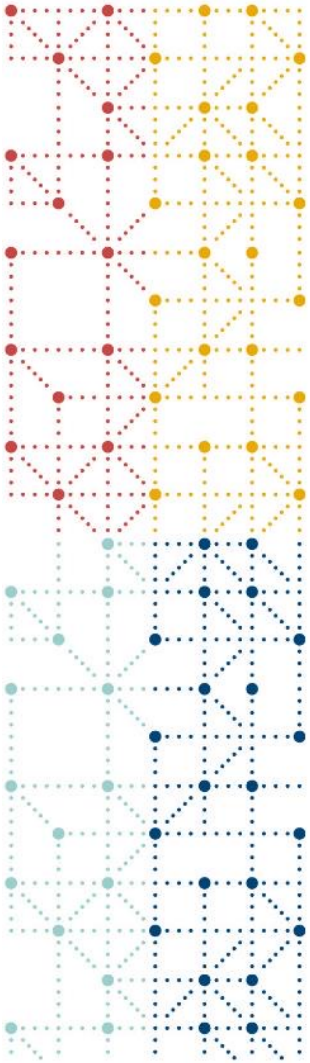

Introduction

The Guidelines Released!!

- Increasing kidney related ailments and transplants across globe
- Three guidelines released related to kidney

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Therapeutic Area User Guide for Polycystic Kidney Disease

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Therapeutic Area Data Standards User Guide for Kidney Transplant
Version 1.0 (Provisional)

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Therapeutic Area User Guide for Acute Kidney Injury

Version 1.0 (Provisional)

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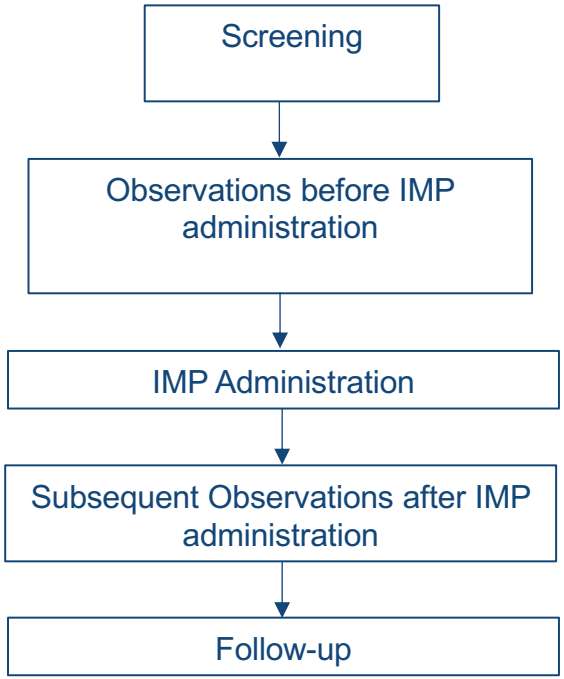
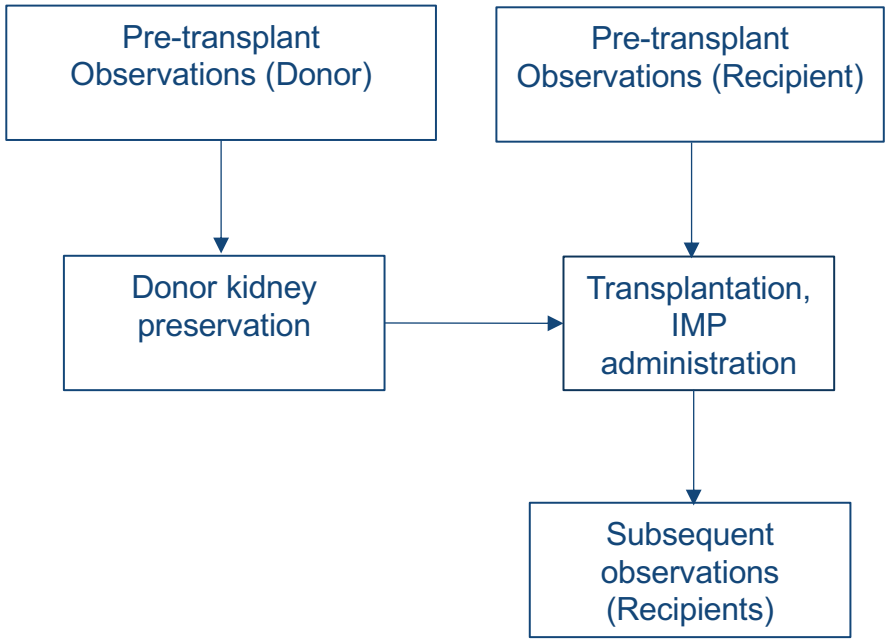
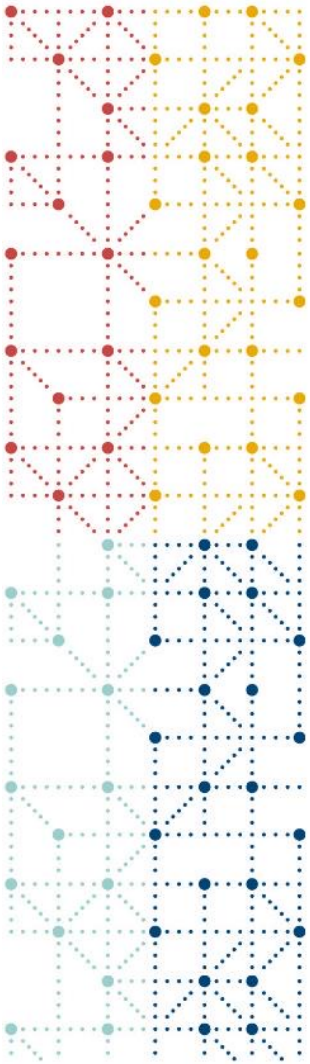
What happens across Kidney related studies?

General Cases



In Case of Transplants





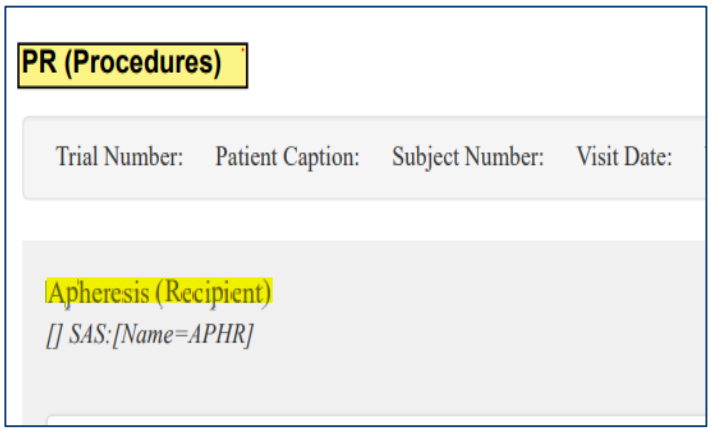
Differentiating Donor and Recipient

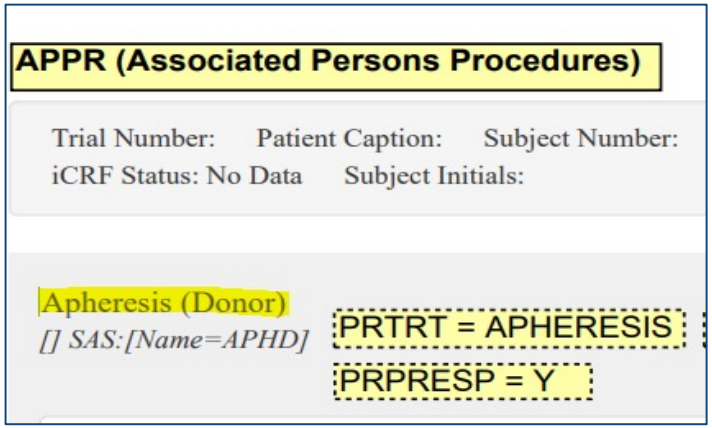
Issue Faced

- The minor difference in CRF gets unnoticed
- CRF appears to be repetitive when seen in the first go

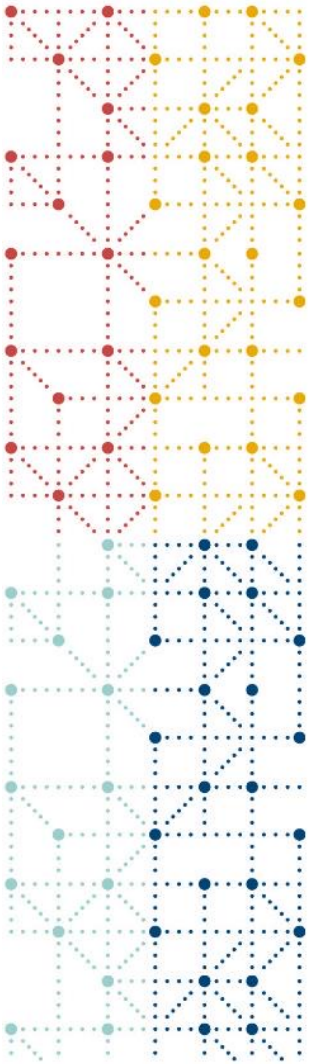
Way Forward

- Attention to detail when protocol specifies donor and recipient information is collected
- Carefully consider the patient type information while annotating and bookmarking the CRF





Sometimes information regarding Donor/Recipient is collected explicitly!!!



Conventional Approach - Nuances

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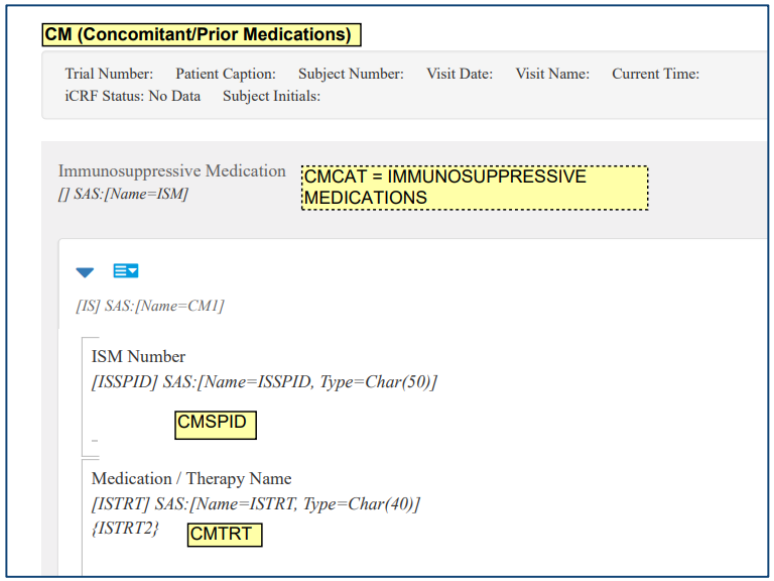
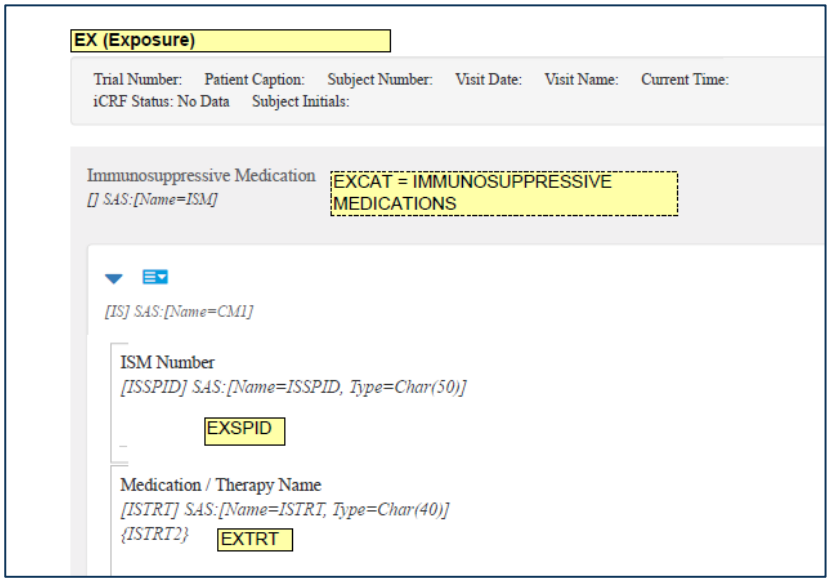
- Immunosuppressant Medications
- HLA Genotyping
- Graft loss, infection or graft rejection
- Relationship between datasets

Immunosuppressant Medications

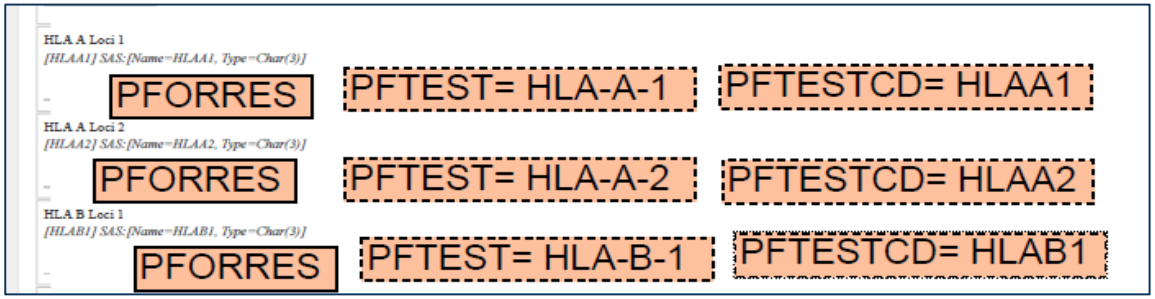




Protocol-specified?

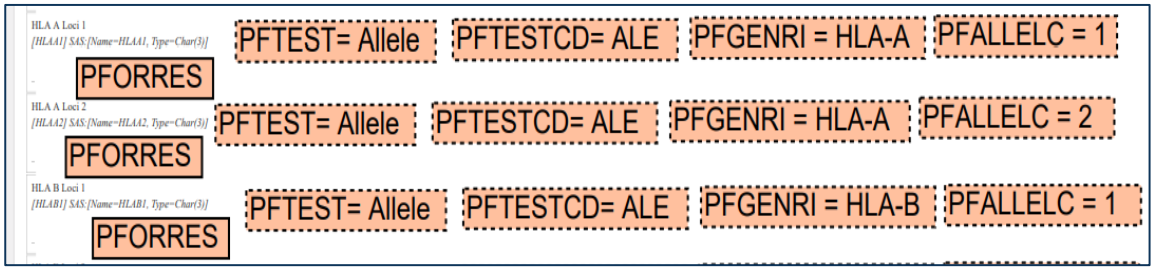
Any protocol-specified medication should be mapped in EX domain

HLA Typing – by Genotyping



Generally, we consider each of these tests to be independent and map each of them to separate TESTCDs

INCORRECT!



As per the guidelines for Pharmacogenomics, mapping all these to the same TESTCD and differentiating using PFGENRI is deemed right

Note:

- The provisional SDTMIG-PGx v1.0 has been deprecated and its content has been subsumed into SDTM IG v3.4
- The provisional PF domain is deprecated and superseded by the GF domain
- HLA Typing by serological methods should be represented in LB

Graft loss, infection or graft rejection

Clinical Event or Adverse Event?

Events of **graft loss, infection and cerebrovascular accident** should be represented in the Adverse Events (AE) domain, unless specified differently in the protocol

ae.xpt

Row	STUDYID	DOMAIN	USUBJID	AESEQ	AETERM	AEDECOD	AELOC	AEOUT	AESER	AESDTH	AESTDTC	CAUSE
1	ABC	AE	ABC-001	1	RENAL GRAFT LOSS	Renal graft loss	KIDNEY		Y		2014-03-03	PRIMARY NON-FUNCTION
2	ABC	AE	ABC-001	2	INFECTION	Infection		FATAL	Y	N	2014-03-20	
3	ABC	AE	ABC-002	1	CEREBROVASCULAR ACCIDENT	Cerebrovascular accident		FATAL	Y	Y	2014-04-16	
4	ABC	AE	ABC-002	2	RENAL GRAFT LOSS	Renal graft loss	KIDNEY				2014-04-16	DEATH

AE NSV Metadata

Variable	Label	Type	Role	Origin
CAUSE	Cause of the Event	text	Non-Standard Record Qualifier	CRF

RELREC

How to represent relationship between Associated Persons domains?

USUBJID vs RSUBJID?
APRELREC?

apex.xpt

Row	STUDYID	DOMAIN	APID	EXSEQ	RSUBJID	SREL	EXTRT	EXDOSE	EXDOSTXT	EXDOSU	EXDOSFRM	EXDOSFRQ	EXROUTE	EXSTDTC
1	Y6AOF7	APEX	AP_01	1	ABC_123	FAMILY MEMBER	DRUG X		SPLASH		LOTION	ONCE	TOPICAL	2005-05-05

apae.xpt

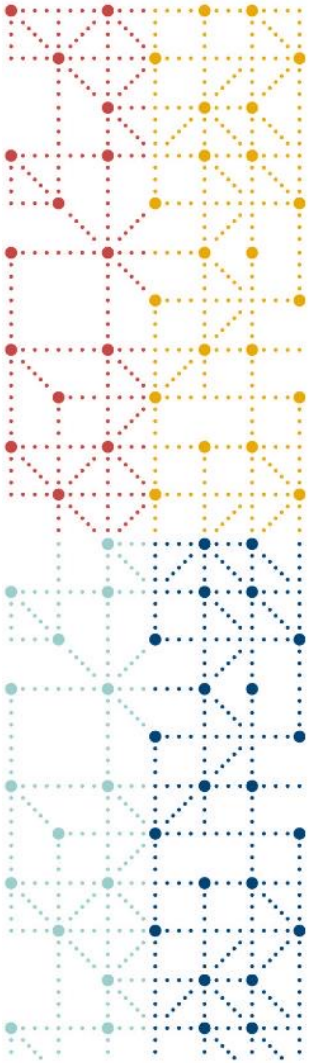
Row	STUDYID	DOMAIN	APID	AESEQ	RSUBJID	SREL	AETERM	AEDECOD	AESEV	AESER	AEREL	AEOUT	AESTDTC	AEENDTC
1	Y6AOF7	APAE	AP_01	1	ABC_123	FAMILY MEMBER	Rash	Rash	MODERATE	N	RELATED	RECOVERED / RESOLVED	2005-05-05	2005-05-08

relrec.xpt

Row	STUDYID	RDOMAIN	USUBJID	APID	RSUBJID	IDVAR	IDVARVAL	RELTYPE	RELID
1	Y6AOF7	APEX		AP_01	ABC_123	EXTRT	DRUG X		1
2	Y6AOF7	APAE		AP_01	ABC_123	AETERM	Rash		1

Comparison

Topic	Conventional Approach	Approach suggested by TAUG
Immunosuppressant Medications	Concomitant Medications (CM)	Exposure (EX)
HLA Genotyping	Incorrect representation using individual TESTCDs for each genes	Single TESTCD with multiple PFGENRI for the genes
Graft loss or rejection	Clinical Events (CE)	Adverse Events (AE)
Relationship between APxx domains	Incorrect or missed representation	Proper representation including APID and RSUBJID variables

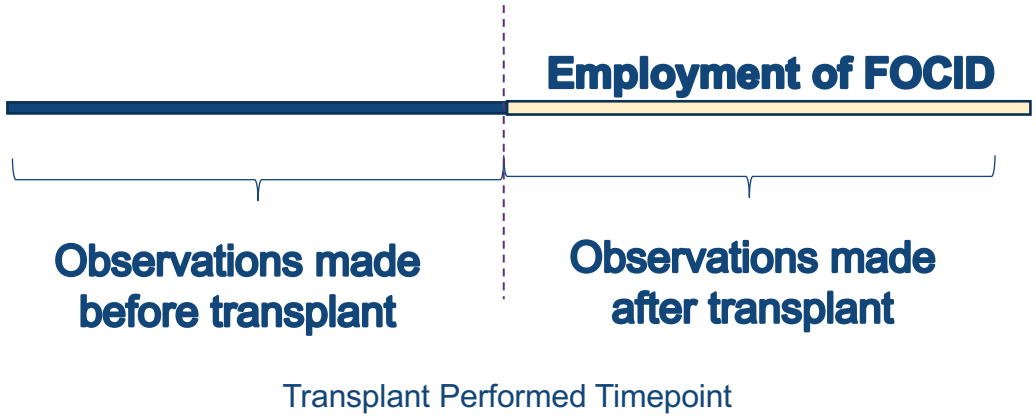


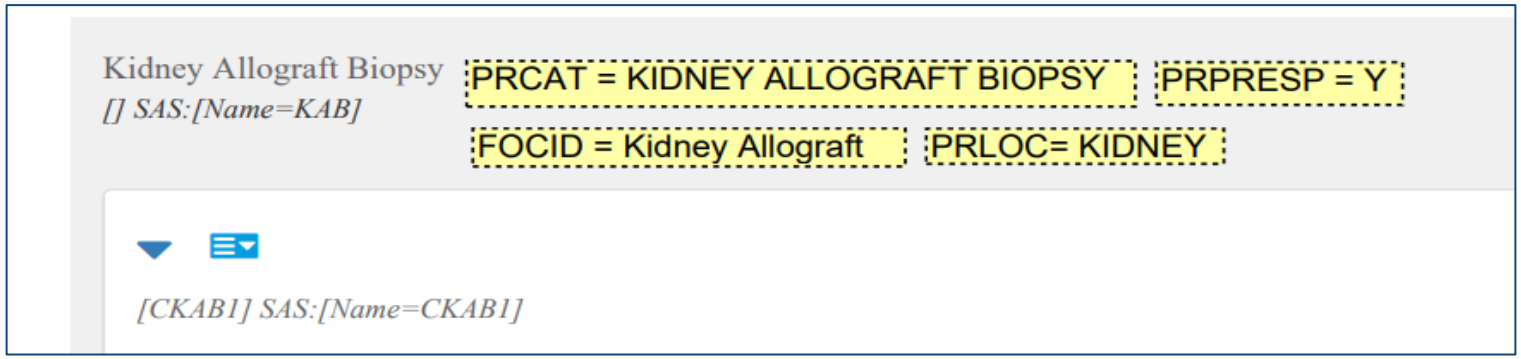
Fill the Bill

Spotlight on FOCID

- Introduced as model permissible variable in SDTM IG v3.3
- Predominantly used in OE domain

- To distinguish observations between original and transplanted tissues/organs





FOCID	PRSEQ	PRTRT	PRCAT	PRPRESP	PROCCUR	PRSTAT	PRINDC
	2	BIOPSY	ILIAC CREST BONE MARROW BIOPSY	Y	Y		Iliac Crest Bone Marrow Biopsy
	3	BIOPSY	ILIAC CREST BONE MARROW BIOPSY	Y	Y		Iliac Crest Bone Marrow Biopsy
KIDNEY ALLOGRAFT	4	BIOPSY	KIDNEY ALLOGRAFT BIOPSY	Y	Y		Other: Initial diagnosis, not research

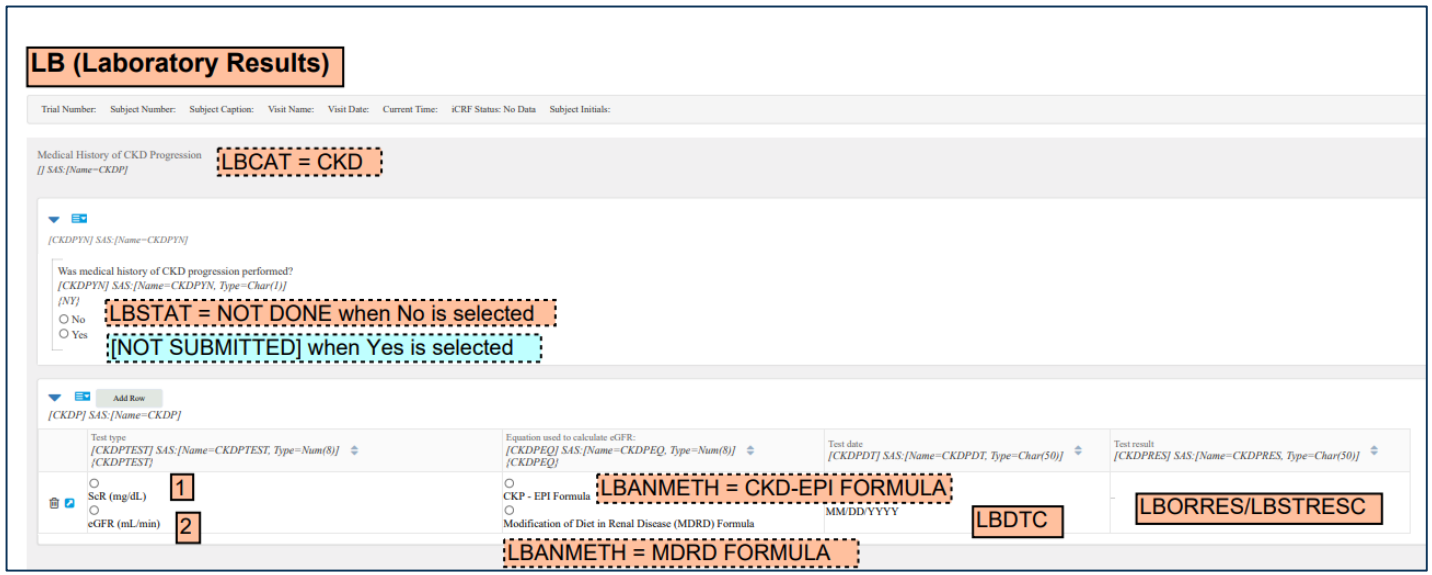
ur.xpt

Row	STUDYID	DOMAIN	USUBJID	FOCID	URSEQ	URTESTCD	URTEST	URORRES	URSTRESC	URMETHOD	URDTC	URTPT
1	KT-101	UR	KT-101-324	KIDNEY ALLOGRAFT	1	COLOR	Color	Pink	PINK	OBSERVATION	2016-03-31	IMMEDIATELY AFTER
2	KT-101	UR	KT-101-566	KIDNEY ALLOGRAFT	1	COLOR	Color	Mottled	MOTTLED	OBSERVATION	2016-04-19	IMMEDIATELY AFTER

Analysis Method- Taking the weight of METHOD

- **LBANMETH** - standard variable in IG 3.4 to supplement the **METHOD** variable
- Used when the results are derived using standard formula Example, MDRD equation for eGFR

Use METHOD="CALCULATION" when LBANMETH employs any formula



TSPARMCD - DGFCRIT

Delayed Graft Function Diagnostic Criteria (DGFCRIT)

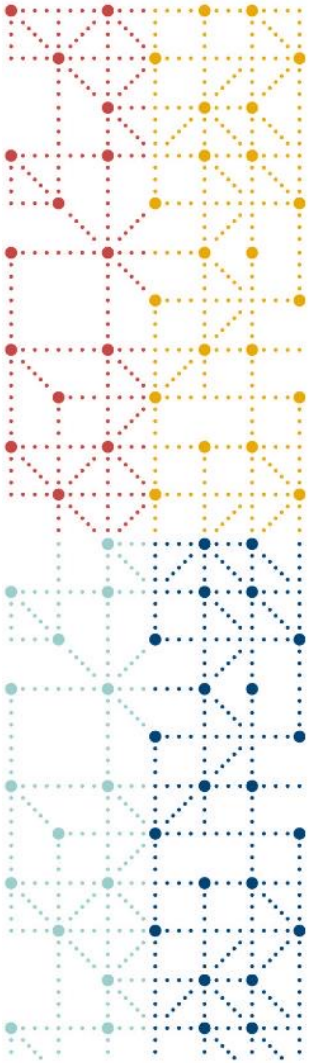
- Vary from protocol to protocol
- Add a record in TS to represent the trial level definition

ae.xpt

Row	STUDYID	DOMAIN	USUBJID	AESEQ	AETERM	AELLT	AEDECOD	AEPRESP	AESTDTC
1	ABC123	AE	ABC123-001	1	DELAYED GRAFT FUNCTION	Renal graft function delayed	Complications of transplanted kidney	Y	2015-07-06

ts.xpt

Row	STUDYID	DOMAIN	TSSEQ	TSPARMCD	TSPARM	TSVAL
1	ABC123	TS	1	DGFCRIT	Delayed Graft Function Criteria	Dialysis required within one week after transplantation



Specific Concepts

Specific Concepts

Specific to kidney transplant studies

- Kidney Donor Profile Index (KDPI)
- Organ handling / Ischemia
- Banff Diagnostic Categories

Kidney Donor Profile Index (KDPI)

- Evaluation of deceased donor organ quality using score
- Involves few facts about the donor, like Age, Height, Weight, etc.

Map **KDPI** Score as a TEST in APRS domain

aprs.xpt

Row	STUDYID	DOMAIN	APID	RSSEQ	USUBJID	SREL	RSTESTCD	RSTEST	RSCAT	RSORRES	RSORRESU	RSSTRESC	RSSTRESN	RSSTRESU	RSDTC
1	ABC	RS	ABC-AP1	1	ABC-001	DONOR, KIDNEY	KDPI0101	KDPI01-KDPI Score	KDPI	40	%	40	40	%	2013-08-06

Organ Handling / Ischemia

Handling of the donor kidney from the point of recovery until anastomosis

Associated Persons Biospecimen Events

Example representation of warm and cold ischemia experienced by the donor kidney between the organ recovery and transplant procedures

apbe.xpt

Row	STUDYID	DOMAIN	APID	BESEQ	RSUBJID	SREL	BEGRPID	BEREFID	BETERM	BEDECOD	BECAT	BELOC	BELAT
1	124	BE	124-KD-001	1	124-001	DONOR, KIDNEY	1	4F678LK	WARM ISCHEMIA		ISCHEMIA	KIDNEY	LEFT
2	124	BE	124-KD-001	2	124-001	DONOR, KIDNEY		4F678LK	COLD ISCHEMIA		ISCHEMIA	KIDNEY	LEFT
3	124	BE	124-KD-001	3	124-001	DONOR, KIDNEY	1	4F678LK	ANASTOMOTIC ISCHEMIA		ISCHEMIA	KIDNEY	LEFT

2009 Banff Classification of Renal Allograft Biopsies

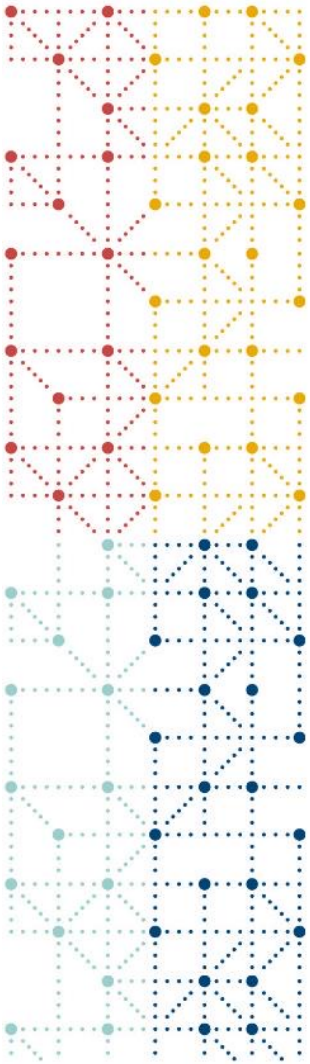
- To determine the level of rejection
- The Banff Classification (for renal allograft biopsies) has undergone multiple revisions since being introduced in 1991
- Findings should be recorded in MI domain
- Version will be populated under non-standard record qualifier variable **VER**

2009 Banff Classification of Renal Allograft Biopsies

mi.xpt

Row	STUDYID	DOMAIN	USUBJID	FOCID	MISEQ	MIGRPID	MIREFID	MITESTCD	MITEST	MITSTDTL	MIORRES
1	KT-101	MI	KT-101-001	KIDNEY ALLOGRAFT	1	1	10100103	INTIMART	Intimal Arteritis	Banff Quantitative Criteria Score 2009 Renal	3
2	KT-101	MI	KT-101-001	KIDNEY ALLOGRAFT	2	1	10100103	BANFRDX	Banff Diagnostic Category Renal		Acute Antibody Mediated Rejection Grade III - Arterial -v3
3	KT-101	MI	KT-101-001	KIDNEY ALLOGRAFT	3		10100103	BANFRDX	Banff Diagnostic Category Renal		Mild interstitial fibrosis and tubular atrophy (<25% of cortical area)
4	KT-101	MI	KT-101-324	KIDNEY ALLOGRAFT	1		10132405	BANFRDX	Banff Diagnostic Category Renal		PTLD
5	KT-101	MI	KT-101-234	KIDNEY ALLOGRAFT	2		10132405	BANFRDX	Banff Diagnostic Category Renal		Drug-induced Neprhotoxicity
6	KT-101	MI	KT-101-099	KIDNEY ALLOGRAFT	3		10109901	BANFRDX	Banff Diagnostic Category Renal		Normal

Row	MISTRESC	MISTRESN	MIRESCAT	MISPEC	VISITNUM	VISIT	MIDTC	VER
1	3	3		KIDNEY	3	VISIT 3	2016-01-25	2009
2	ACUTE ANTIBODY MEDIATED REJECTION GRADE III		ANTIBODY MEDIATED CHANGES	KIDNEY	3	VISIT 3	2016-01-25	2009
3	INTERSTITIAL FIBROSIS AND TUBULAR ATROPHY GRADE I			KIDNEY	3	VISIT 3	2016-01-25	2009
4	POST TRANSPLANT LYMPHOPROLIFERATIVE DISORDER		OTHER CHANGES NOT DUE TO REJECTION	KIDNEY	5	VISIT 5	2016-03-31	2009
5	DRUG INDUCED NEPHROTOXICITY		OTHER CHANGES NOT DUE TO REJECTION	KIDNEY	5	VISIT 5	2016-03-31	2009
6	NORMAL			KIDNEY	1	Visit 1	2015-11-28	2009



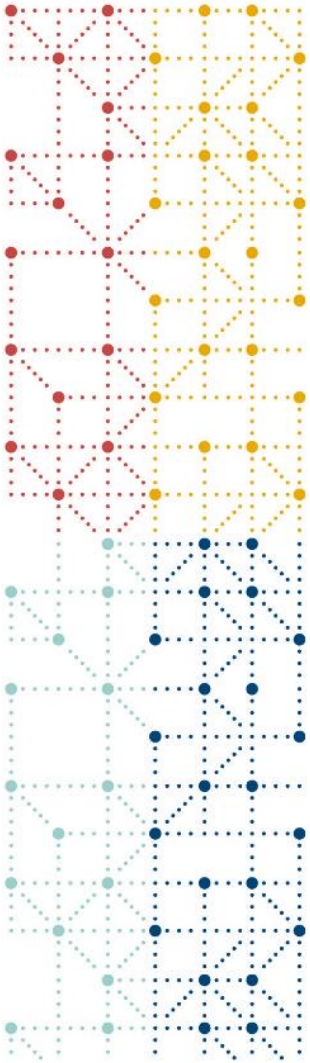
What’s next?

What's next after SDTM?

- Pinnacle validation of SDTM involving AP domains
- Should we include Associated Persons data in ADaM?

Summary

- Please pay attention to every detail in the CRF
- Information provided in the protocol plays a major role in representing the data
- Validate approach against the TAUG, even though it is a conventional domain
- Look for model permissible or newly introduced variables to fill the bill
- Check the TAUG for recommendations before concluding on Custom domains or Supplementary variables



Thank You!

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