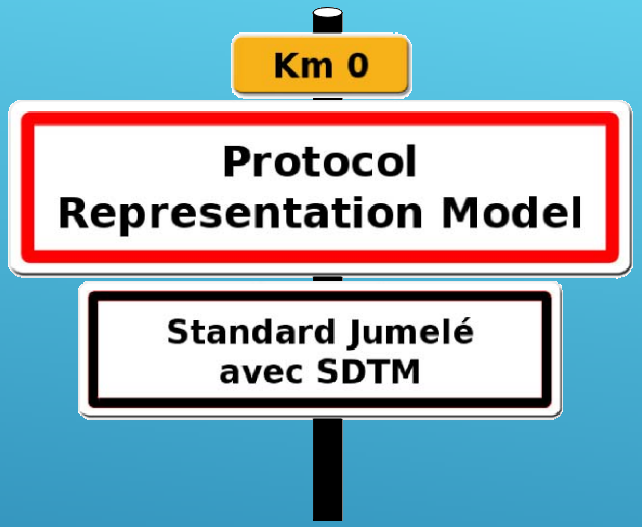
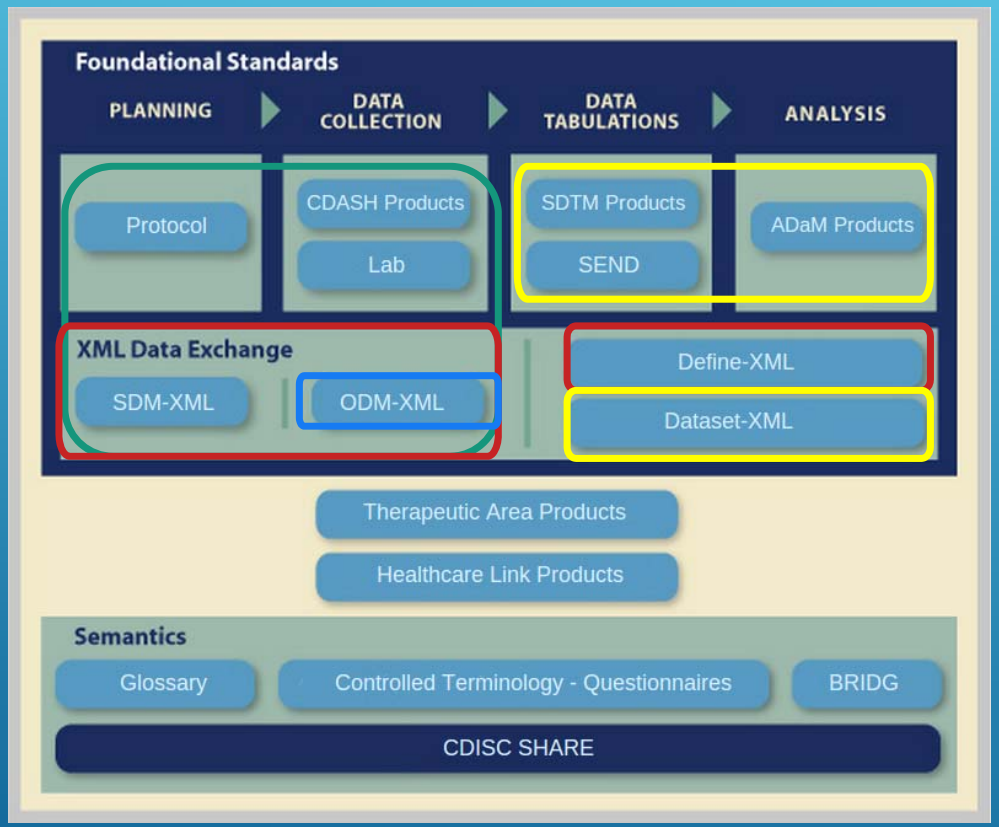


DE PRM VERS ODM ET SDTM VIA SDM

Réunion des Utilisateurs Francophones des Standards CDISC
(a subgroup of CDISC)
8 décembre 2014

LES 4 MISSIONS DE CDISC…



L'acquisition de Données

L'échange de Données

La soumission de Données

L'archivage de Données

Un Protocole Pour Les Gouverner Tous…

AVEC PRM

Mise au point de plus de 100 concepts standards (trial objective, phase): des méta-informations

PRM

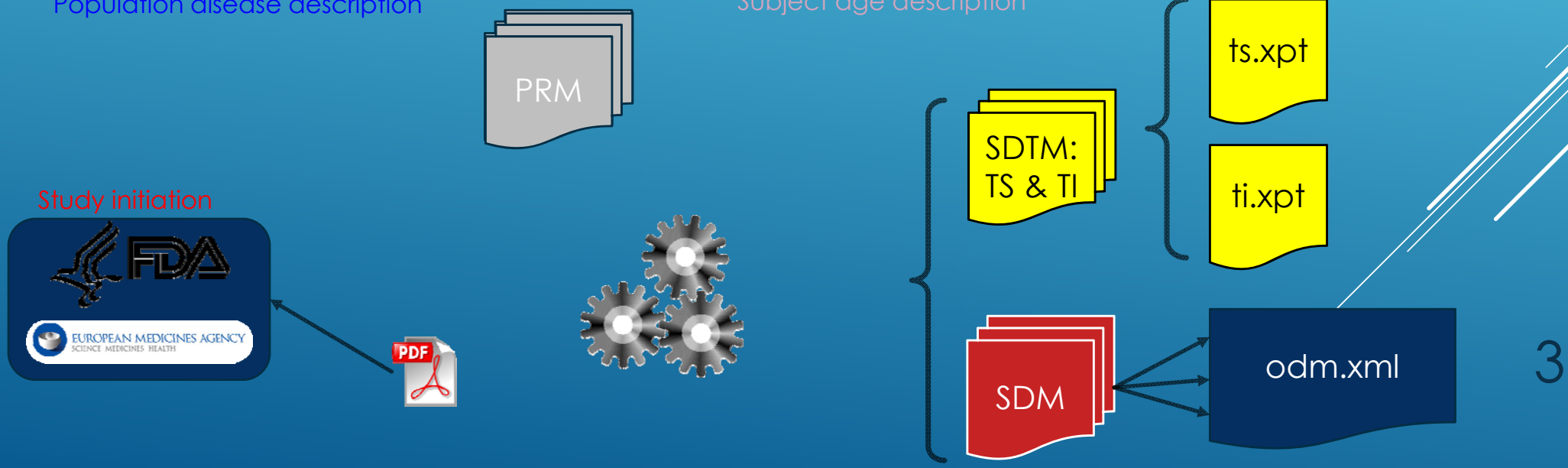
Degree of blind

Configuration

This is a prospective, randomized, double-blind, double-dummy, placebo controlled, forced-titration, multicenter, parallel group trial. Stage I or II hypertensive patients, age 18 years of age or older, who meet all other inclusion and exclusion criteria and successfully complete the placebo run-in period will be randomized at the site level.

Population disease description

Subject age description



PROTOCOL REPRESENTATION MODEL V1.0

- Document téléchargeable sur le site www.cdisc.org
- 4 grands chapitres:
  - Clinical Trial / Study Registry: toutes les informations d'une étude (Study type, Registration ID, Sponsor name, …)
  - Eligibility: tous les critères d'éligibilités (age min et max, …)
  - Study Design part 1: tous les éléments de 'design' de l'étude (Arms et Epochs)
  - Study Design part 2: tous les éléments en rapport avec les activités de l'étude et avec la planification des évènements de l'étude
- En développement: un nouveau chapitre sur « Statistical Aspects of the Protocol »

Study Registry: en relation avec ICH E6, E3 et E9

+ spécifications de EudraCT et de WHO + clinicaltrials.gov

PRM EN UML (Unified Modeling Language)

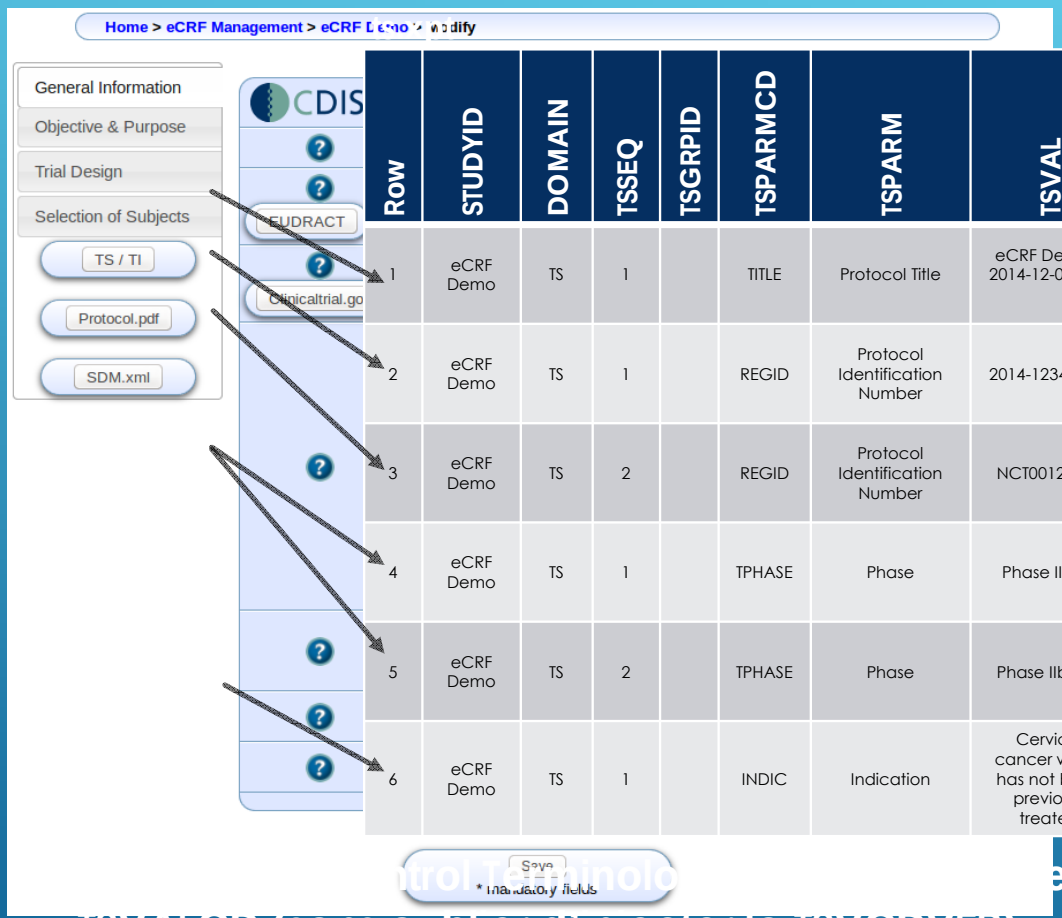
- Exemple de la 'Class' Study:

Cette spécification permet de définir un modèle de données pour stocker les méta-données d'une étude

Nom de la classe

Types de donnée
(basés sur les spécifications de type de données de HL7):
'TX' pour 'Text'
'ST' pour 'String'
'CD' pour 'Concept descriptor'
'DSET' pour 'Multiple coded concepts'
'BL' pour 'Boolean'
'ED' pour 'Encapsulated data'
…

EXEMPLE PRATIQUE D'UTILISATION DE PRM



Row	STUDYID	DOMAIN	TSSEQ	TSGRPID	TSPARMCD	TSPARM	TSVAL	TSVALNF	TSVALCD	TSVCDREF	TSVCDVER
1	eCRF Demo	TS	1		TITLE	Protocol Title	eCRF Demo – 2014-12-08 / V1				
2	eCRF Demo	TS	1		REGID	Protocol Identification Number	2014-123456-89		2014-123456-89	Eudrac	
3	eCRF Demo	TS	2		REGID	Protocol Identification Number	NCT00123456		NCT00123456	Clinicaltrials.gov	
4	eCRF Demo	TS	1		TPHASE	Phase	Phase II Trial		C15601	CDISC Control Terminology	2014-03-28
5	eCRF Demo	TS	2		TPHASE	Phase	Phase IIb Trial		C49688	CDISC Control Terminology	2014-03-28
6	eCRF Demo	TS	1		INDIC	Indication	Cervical cancer which has not been previouly treated		15540006	Snomed	2014-09-01

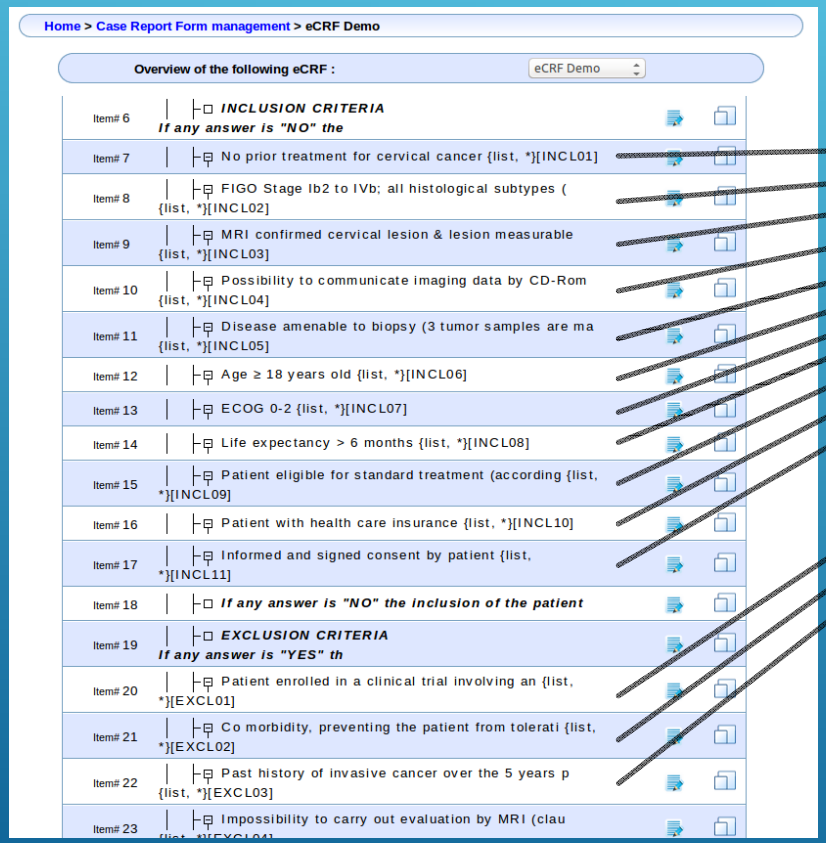
TSVALCD (sans oublier d'injecter la TSVCDVER)

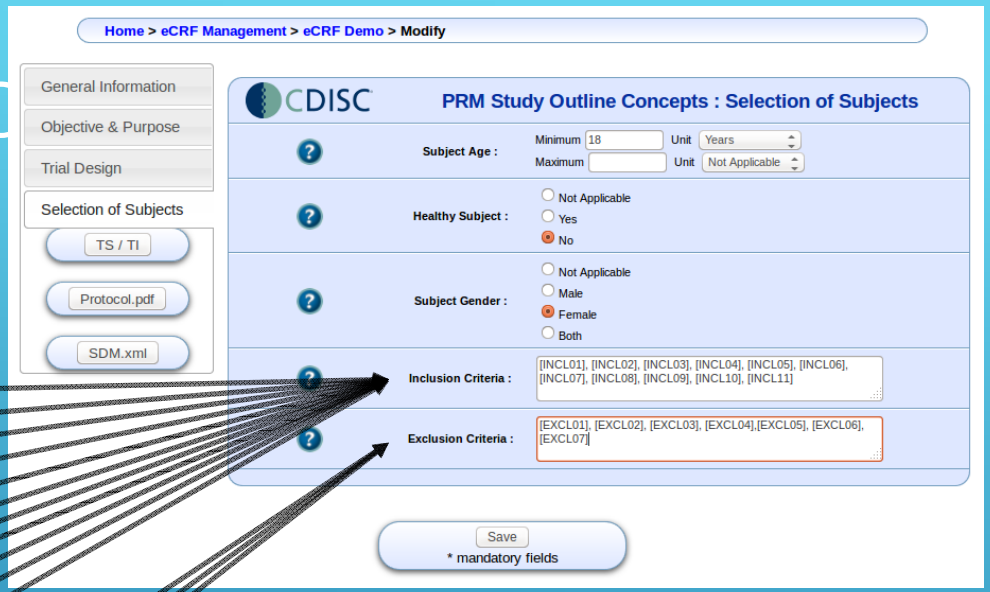
ET TOUJOURS LA TERMINOLOGIE CONTROLÉE!!!

	A	B	C	D	E	F	G	H
1	Code	Codelist Code	Codelist Extensible (Yes/No)	Codelist Name	CDISC Submission Value	CDISC Synonym(s)	CDISC Definition	NCI Preferred Term
7492	C49653	C66736		Trial Indication Type	DIAGNOSIS		A type of study protocol designed to evaluate intervention(s) aimed at identifying a disease or condition. (NCI)	Diagnosis Study
7493	C49655	C66736		Trial Indication Type	MITIGATION		A type of study designed to identify actions necessary to eliminate or reduce the risk to human life or well-being as a result of a particular medication or treatment regimen. (NCI)	Adverse Effect Mitigation Study
7494	C49657	C66736		Trial Indication Type	PREVENTION		A type of study designed to identify actions necessary to permanently eliminate or reduce the long-term risk to human life as a result of a particular medication or treatment regimen.	Prevention Study
7495	C49656	C66736		Trial Indication Type	TREATMENT		A type of study protocol designed to evaluate intervention(s) for treatment of disease, syndrome or condition.	Treatment Study
7496	C66737		Yes	Trial Phase	TPHASE	Trial Phase	Clinical trials are broken into three or four phases: Phase I tests a new drug or treatment for safety in a small group; Phase II expands the study to a larger group of people; Phase III expands the study to an even larger group of people to measure whether the treatment actually benefits patients, and whether its benefits exceed its risks; and Phase IV takes place after the drug or treatment has been licensed and marketed. (NCI)	CDISC SDTM Trial Phase Terminology
7497	C48660	C66737		Trial Phase	NOT APPLICABLE	NA; Not Applicable	Determination of a value is not relevant in the current context. (NCI)	Not Applicable
7498	C15600	C66737		Trial Phase	Phase I Trial	1; Trial Phase 1	The initial introduction of an investigational new drug into humans. Phase 1 studies are typically closely monitored and may be conducted in patients or normal volunteer subjects. NOTE: These studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. During Phase 1, sufficient information about the drug's pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid, Phase 2 studies. The total number of subjects and patients included in Phase I studies varies with the drug, but is generally in the range of 20 to 80. Phase 1 studies also include studies of drug metabolism, structure-activity relationships, and mechanism of action in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes. [After FDA CDER Handbook, ICH E8] (CDISC glossary)	Phase I Trial
7499	C15693	C66737		Trial Phase	Phase I/II Trial	1-2; Trial Phase 1-2	A class of clinical study that combines elements characteristic of traditional Phase I and Phase II trials. See also Phase I, Phase II.	Phase I/II Trial
	C15601	C66737		Trial Phase	Phase II Trial	2; Trial Phase 2	Phase 2. Controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or	Phase II Trial

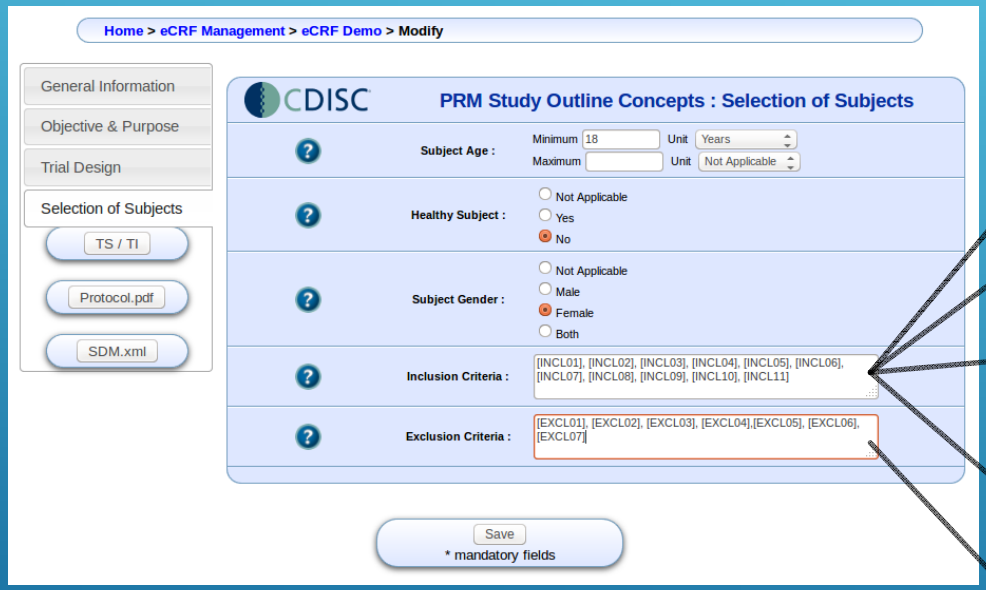
Référence pour la notion de 'Phase de l'étude'

INCLUSION / EXCLUSION C





VERS TI.XPT…



ti.xpt

Row	STUDYID	DOMAIN	IETESTCD	IETEST	IECAT	TIRL	TIVERS
1	eCRF Demo	TI	INCL01	No prior treatment for cervical cancer	INCLUSION		1
2	eCRF Demo	TI	INCL02	FIGO Stage Ib2 to IVb; all histological subtypes (excluding neuro-endocrine type)	INCLUSION	[INCL02] >= [ib2] AND [INCL02] < [IVb]	1
3	eCRF Demo	TI	INCL03	MRI confirmed cervical lesion & lesion measurable by T2 (MRI must be performed using ultrasound gel in vagina)	INCLUSION		1
…							
11	eCRF Demo	TI	INCL11	Age ≥ 18 years old	INCLUSION	[INCL11 >= 18	1
12	eCRF Demo	TI	EXCL01	Patient enrolled in a clinical trial involving an experimental new agent	EXCLUSION		1

PRM VERS ODM VIA SDM

- SDM est une
- Les différents
  ODM (Opera
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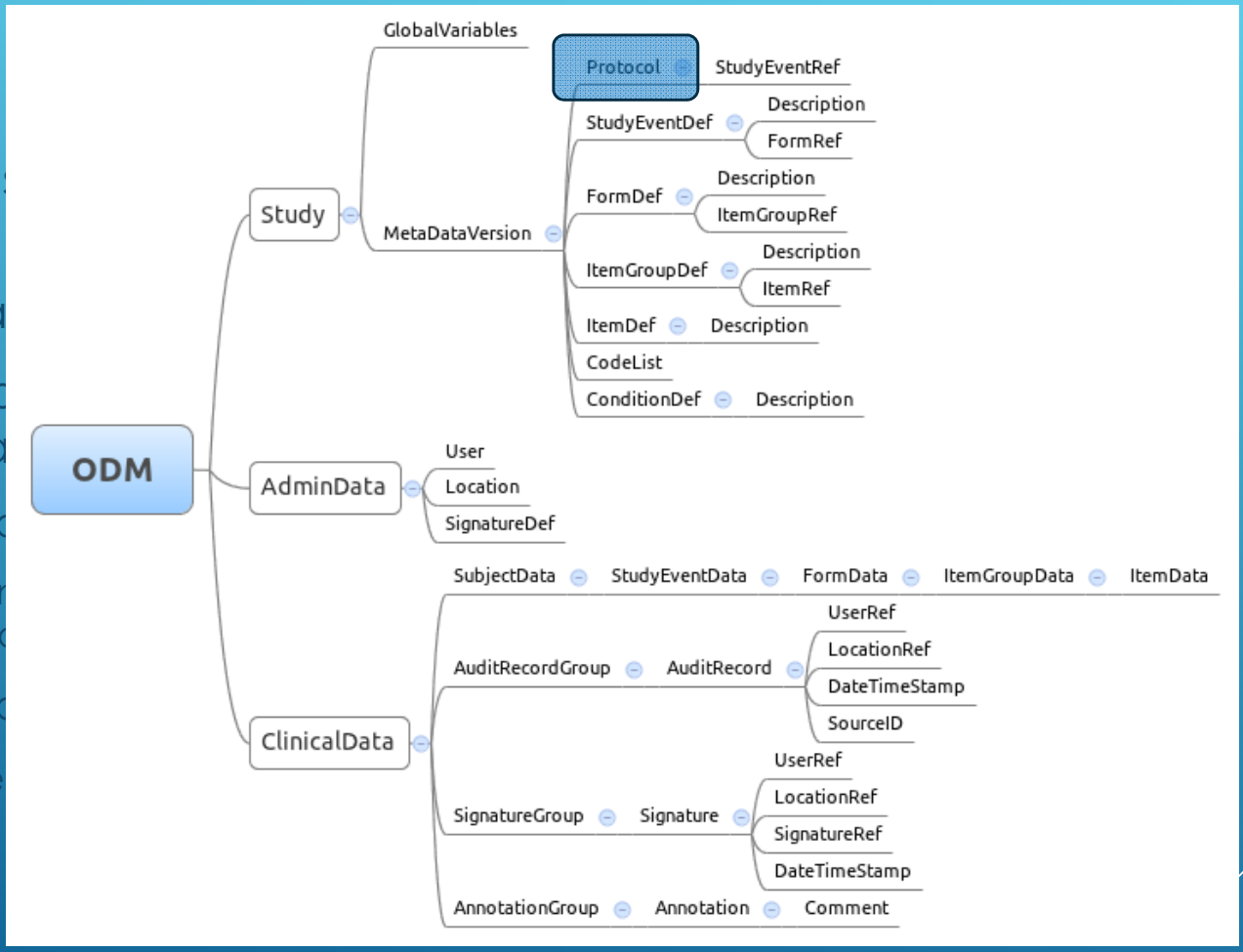
  un fichier d'a
  - Les méta-
    - Les do
      le nive
  - Les méta-
  - Les donné



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sdm:structure
- **sdm:epoch**
- **sdm:arm**
- **sdm:celldef (blind ou unblind)**
- **sdm:segmentdef**
- **sdm:activitydef**

sdm:workflow
- **sdm:studystart**
- **sdm: studyfinish…**

sdm:timing
- **sdm:absolutetimingconstraint**

…

PRM VIA SDM @ EUDRACT / CLINCALTRIAL.GOV

eCRF Demo 2014-12-08 / V1

Description: Biomarker evaluation in advanced stage cervical cancer by an International Working Group. Tumor Stages 1B2 - 4

Trial Parameters
Inclusion and Exclusion

Trial Parameters

Short Name	Term	Value(s)
TITLE	Protocol Title	• eCRF Demo - 2014-12-08 / V1
REGID	Protocol Identification Number	• 2014-123456-89
TPHASE	Trial Phase	• Trial Phase 2 • Trial Phase 2B
INDIC	Indication	• Cervical cancer which has not been previously treated
OBJPRIM	Primary Objective	• Assess dominant mutations and pathway activations in cervical cancer predictive for resistance to treatment.
OBJSEC	Secondary Objectives	• Determination of PFS at 18 months in correlation with dominant genetic or protein alterations • Descriptional analysis of standard treatment modalities applied in participating European countries • Descriptional analysis of grade 3 and 4 treatment associated side effects and toxicities • Descriptional analysis of frequency in geographic distribution of molecular alterations

Inclusion and Exclusion

Inclusion and Exclusion Criteria

Inclusion Criteria

Criterion	Condition
No prior treatment for cervical cance	
FIGO Stage Ib2 to IVb; all histological subtypes (excluding neuro-endocrine type)	FIGO Stage Ib2 to IVb
MRI confirmed cervical lesion and lesion measurable by T2 (MRI must be performed using ultrasound gel in vagina)	
Possibility to communicate imaging data by CD-Rom (DICOM format 3.0 or more)	
Disease amenable to biopsy (3 tumor samples are mandatory prior to treatment)	
...	
Age ≥ 18 years old	Minimum Age

C) General informations about the study

Indication

Cervical cancer which has not been previously treated

Methodology

Prospective Multicentric Observational European trial with tumour biopsies, PBMC and serum collection for molecular analyses at predetermined time points.

Main Objective :

Assess dominant mutations and pathway activations in cervical cancer predictive for resistance to treatment.

Secondary Objectives :

Determination of PFS at 18 months in correlation with dominant genetic or protein alterations

Descriptional analysis of standard treatment modalities applied in participating European countries

Descriptional analysis of grade 3&4 treatment associated side effects and toxicities

Descriptional analysis of frequency in geographic distribution of molecular alterations

Inclusion Criteria :

- No prior treatment for cervical cancer.
- FIGO Stage IB2 to IVB
- IRM confirmed cervical lesion & lesion measurable by T2 (+ ultrasound gel in vagina)
- Possibility to transmit imaging data by CD ROM (format DICOM 3.0 or more)
- ANY Histological type (excluding neuro-endocrine type)
- Patients willing to have at least 3 biopsies
- Age ≥ 18 years
- Life expectancy > 6 months
- Normal hematopoietic and renal function tests compatible with standard therapies
- Patient having health care insurance
- Informed and signed consent by patient or legal representative
- ECOG 0-2

CONCLUSION

- Les standards CDISC sont utiles surtout lorsqu'ils sont utilisés en cascade!
- PRM est assez complexe à mettre en œuvre au départ car il fait appel à d'autres standards (SDM, ODM, SDTM, Control Terminology mais également BRIDGE) – il faut une vision d'ensemble
- Il existe toujours des différences entre les standards de CDISC – Exemple de la variable GENDER de PRM qui donne SEXPOP dans SDTM…
- PRM permet d'automatiser et de réutiliser un ensemble de méta-données d'une première étude vers les suivantes
- PRM organise dès le début de la planification de l'étude un ensemble de méta-données que l'on réutilise dans toute la chaine de production de notre étude (jusqu'à l'archivage en ODM)

Merci pour votre attention…

Pour me joindre: n.desaintjorre@quanticsoft.com