Entwicklung einer CRF-Bibliothek für OpenClinica auf Basis von CDISC CDASH

Henrik Dittmann

Institut Jules Bordet, Brüssel

Institut Jules Bordet

Das Institut Jules Bordet

- auf Onkologie spezialisiertes Krankenhaus
- Teil des Netzwerks der öffentlichen Krankenhäuser in Brüssel
- Teil der Université Libre de Bruxelles

Szenario für OpenClinica

- eCRFs für akademisch initiierte klinische Studien
- komplexe CRFs, kurze Laufzeiten, geringe Mittel
- Ansatz: Verwendung von OpenClinica in Verbindung mit CDISC CDASH

  → Standardisierung

  → Wiederverwendbarkeit

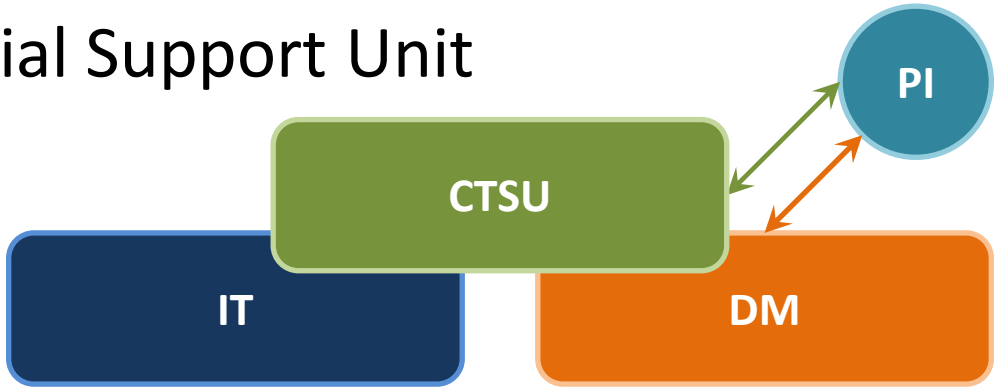
  → zügige Erstellung

Akademisch initiierte klinische Studien am Institut Jules Bordet

- Erwartung: ca. zehn Phase-II-Studien pro Jahr mit OpenClinica
- 20-200 Teilnehmer/innen, in der Regel in mehreren Zentren, teils in mehreren Ländern
- in OpenClinica 30-40 CRFs, verteilt auf 10-15 Study Events
- OpenClinica Enterprise Edition 3.1.3.1 seit Mai 2013
- Aktuell: eCRF für eine Studie in Verwendung, zwei sind im Test, zwei in der Entwurfsphase

Struktur und Ressourcen

- Clinical Trial Support Unit



- eCRFs werden derzeit auf Papier entworfen
- Erfahrung mit großen Phase-III-Studien im Datenzentrum BrEAST
- erstes eCRF maßgeblich implementiert durch Trial Data Solutions, Amsterdam

CDISC CDASH

- CDISC: Standardisierung von Daten und Metadaten in der klinischen Forschung (www.cdisc.org)
- Standards für Zulassungsanträge bei der FDA (SDTM, ADaM, SEND, SDTM-Terminologie)
- CDASH: Standard für die Datenerfassung, eng verbunden mit SDTM

Beispiel: CDASH

	Question Text	Prompt	SDTM or CDASH Variable Name	BRIDG	Definition	CRF Completion Instructions	Information for Sponsors	Core
13	Is this event related to study treatment?	Relationship to Study Treatment	AEREL	EvaluatedActivity Relationship .probabilityCode	Indication of whether the study treatment had a causal effect on the adverse event, as determined by the clinician/investigator.	Indicate if the cause of the adverse event is related to the study treatment and cannot be reasonably explained by other factors (e.g., subject's clinical state, concomitant therapy, and/or other interventions).	Sponsored-defined terminology will be used to indicate the relationship between the AE and the study treatment (e.g. ICH E2B examples: Not Related, Unlikely Related, Possibly Related, Related). *See the BRIDG model for	HR
14	What action was taken with study treatment?	Action Taken with Study Treatment	AEACN	DefinedActivity.name Code *	Changes made to the study treatment in response to the adverse event. {ACN} (See Section 2.2.)	Record changes made to the study treatment resulting from the adverse event.	CDISC controlled terminology should be used to indicate the action taken with the study treatment in response to the AE. *See the BRIDG model for complete path.	HR
15	What other action was taken in response to this adverse event?	Other Action Taken	AEACNOTH	DefinedActivity.name Code *	Describes Other Action(s) taken in response to the adverse event that are unrelated to study treatment dose changes.	Record all other action(s) taken resulting from the adverse event that are unrelated to study treatment.	This field is usually collected as a free text field. Example: Treatment Unblinded, Primary Care Physician Notified. *See the BRIDG model for complete path.	O
16	What was the outcome of this adverse event?	Outcome	AEOUT	PerformedObservation Result.value*	Description of the subject's status associated with an event. {OUT} (See Section 2.2.)	Record the appropriate outcome of the event in relation to the subject's status.	CDISC controlled terminology should be used to indicate the outcome of the event as it relates to the subject's status. The Outcome controlled terminology includes ICH E2B values. *See the BRIDG model for complete path.	HR

Beispiel: Struktur einer Studie

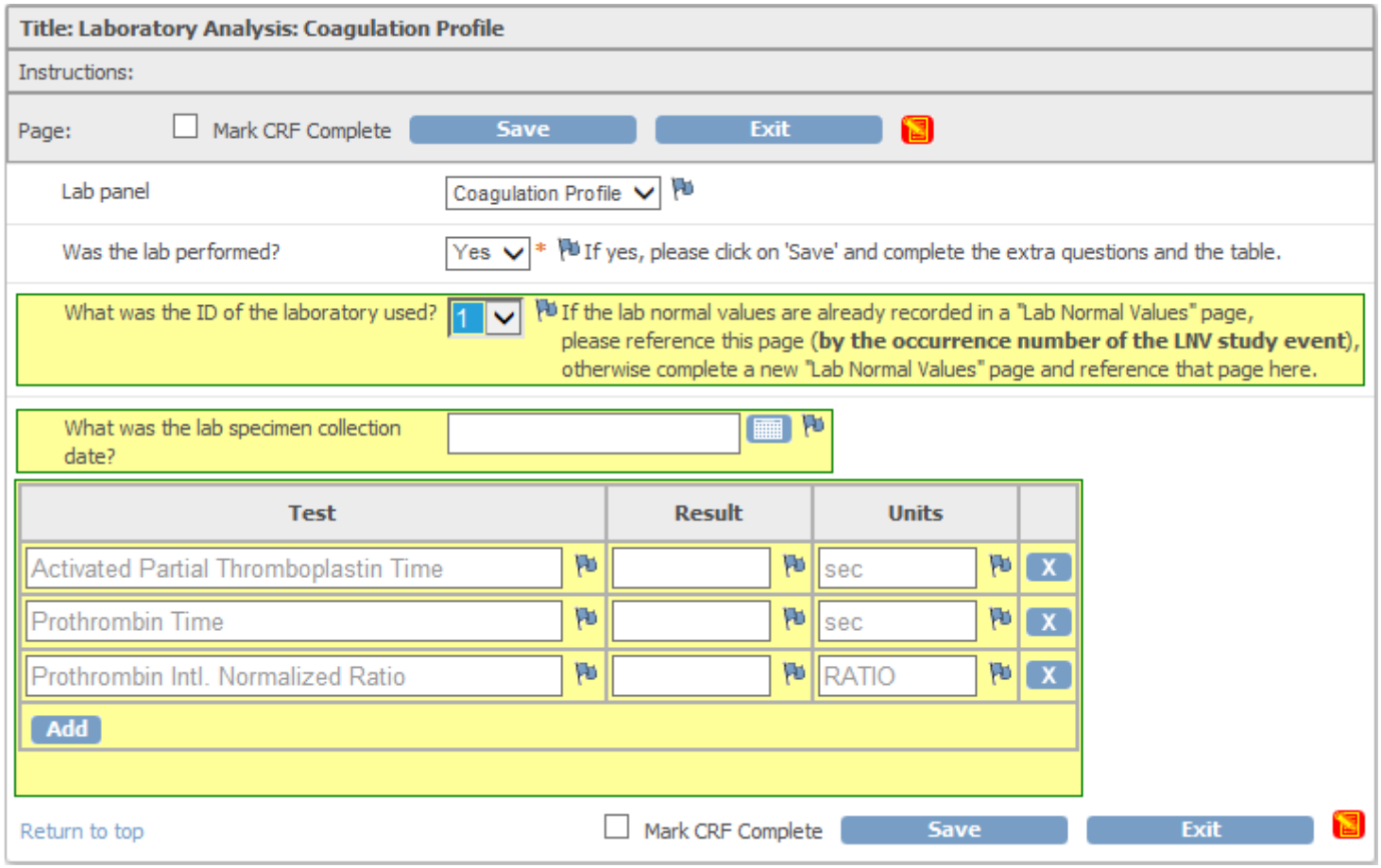
Title	Screening	Treatment				Follow-up		Common and unscheduled events						
	Screening	Cycle 1, Day 1/8	Cycle 1, Day 14	Cycle 2	Cycle *	End of Treatment and Safety Follow-Up	Survival Follow-up	Administration of the Study Drug	Concomitant Medications	Adverse Event	Unscheduled	Lab Normal Values	Progression	Death
	Scre	D1/8	D14	Cyc 2	Cyc *	EoT/Sfty	Svvl *	Drug	ConMed	AE *	Unsched	LNV	PD	Death
Registration / IE Crit.	X													
Phys. Exam. / Vital Signs	X (v1)	X (v2)	X (v2)	X (v2)	X (v2)	X (v2)								
Haematology	X	X		X	X	X								
Coagulation Profile	X	X		X		X								
Liver Function Tests	X	X		X	X	X								
Blood Chemistry	X	X		X	X	X								
Electrolytes	X	X		X	X	X								
Thyroid Function Test	X	X		X		X								
Urine Analysis	X			X		X								
Biological Samples	X (v1)		X (v2)		X (v2)								X (v3)	
^{18}FDG PET/CT	X		X										X	
ECG	X				X									
LVEF	X				X									
Colorectal Cancer History	X													
Colorectal Cancer Surgery	X													
Prior Anti-Cancer Treatm.	X													
Prior Radiotherapy	X													
Medical History	X													
Imaging Examination	X				X	X								
Lesion Sites	X				X	X								
Tumour Response Eval.	X				X	X								

und 11 weitere CRFs

Beispiel: eCRF-Definition

	A	B	C	N	O	P	
1	ITEM_NAME	DESCRIPTION_LABEL	LEFT_ITEM_TEXT	RESPONSE_TYPE	RESPONSE_LABEL	RESPONSE_OPTIONS_TEXT	RESP
2	XPPERF	XPPERF: Whether radiation therapy was performed	Was radiation therapy performed before the subject entered the trial?	single-select	NY	, Yes, No	, Y, N
3	XPLOC	XPLOC: Specifies anatomical site of the radiation therapy	Anatomical Location	single-select	LOC	, Abdominal Cavity, Adrenal Gland, Bladder, Bone, Breast, Central Nervous System, Cervix Uteri, Chest, Colon, Colorectal, Esophagus, Head and Neck, Heart, Kidney, Liver, Lung, Lymph Node, Oral Cavity, Ovary, Pancreas, Pelvis, Peritoneum, Pleural Cavity, Prostate Gland, Rectum, Skin, Small Intestine, Spleen, Stomach, Testis, Thyroid Gland, Other, Whole Body	, ABD BLADI NERV COLO HEAD LUNG, OVAR PERIT PROS INTES THYR
4	XPLAT	XPLAT: Laterality of the anatomical site	Laterality	single-select	LAT	, Left, Right, Bilateral, Not Applicable	, LEFT
5	XPDOSTOT	XPDOSTOT: Total dose of radation therapy	Total Dose	text			
6	XPDOSU	XPDOSU: The unit associated with the radiation therapy	Dose Unit	single-select	UNIT	, Gy, cGy, Rad	, Gy, c
7	XPSTDAT	XPSTDAT: Date when the therapy was first given	Start Date	text			
8	XPENDAT	XPENDAT: Date that the therapy was ended	End Date	text			
9	XPTRTSET	XPTRTSET: Setting of the radiation therapy	Setting	single-select	TRTSET	, Neoadjuvant, Adjuvant, Advanced	, NEO.
10							

Beispiel: Terminologie



Probleme: OpenClinica

- Item names müssen pro CRF eindeutig sein – eine Eindeutigkeit pro Item Group wäre für normalisierte Strukturen wünschenswert
- OIDs ändern sich bei der Übertragung in eine andere Studie, was Konvertierung der Regeldateien erfordert

Probleme: CDISC CDASH etc.

- SDTM-Terminologie erscheint teils ungeeignet zur Abbildung der im CRF erhobenen Daten (v.a., wenn die Codelisten nicht erweiterbar sind)
- Einzelne Terme aus der Terminologie sind nicht an die PIs vermittelbar
- bisher sind vor allem Domänen beschrieben, die allgemein benötigt werden, die Therapeutic Area Standards stehen noch aus

Therapeutic Area Standards

CFAST Program Overview

Therapeutic Area Standards Under Development

	Coordinating Organization(s)	Stage 0	Stage 1	Stage 2	Stage 3a	Stage 3b	Stage 3c
	Project Manager	Scoping & Input	Concept Modeling	Standards Development	Internal Review	Public Review	Publication
Alzheimer's V1.1	CPATH/CDISC Jon Neville	Jan	Mar	Jun	*Jul*	*Sep*	*Q313*
Asthma V1	CDISC Rhonda Facile	Jan	Mar	Jun	Jul	*Sep*	*Q413*
Cardiovascular Endpoints V1	CDISC/DCRI Amy Palmer	Jun	*Jul*	*Aug*			*Q114*
Multiple Sclerosis V1	CPATH/CDISC Bess Leroy	May	*Aug*	*Jul*			*Q114*
Diabetes V1	TCB/CDISC Rachael Zirkle	Mar	*Jun*	Aug	*Sep*		*Q114*
QT Studies V1	TCB/CDISC John Owen	*Jul*	*Sep*				*Q214*
Traumatic Brain Injury V1	CDISC TBD	*Sep*					*Q214*
Hepatitis C V1	TBD	*Sep*					*Q314*
Schizophrenia V1	CDISC/DCRI Amy Palmer	*Oct*					*Q314*
Oncology	TBD	*Oct*					

Project Status: Stage ongoing Stage completed *Italics = Projected*

Quelle:

http://www.cdisc.org/therapeutic

Status und Ausblick

- derzeit noch in einem frühen Stadium
- mittelfristig: Bereitstellung einer Bibliothek standardisierter CRF-Module
- langfristig: konfigurierbare CRF-Module auf Basis standardisierter Datenelemente
- weitere Interessen in diesem Zusammenhang:
  - Best Practices in der eCRF-Erstellung
  - Automatisierung der Regelgenerierung

Diskussion

Vielen Dank für Ihre Aufmerksamkeit!

www.bordet.be

www.br-e-a-s-t.org

henrik.dittmann@bordet.be