PhUSE EU Connect 2018

Structured and Standardized Study Definition drives early study setup for added business benefits

Djenan Ganic
Tanja Petrowitsch

November 2018

Agenda

- **Structured Study Definition**
  - Structured Data Gap
  - Standardization Gap
  - SSD-MDR
- **Application of SSD to Trial Design discussion**
  - Example introduction
  - Epoch/Element consideration

Structured Study Definition

SSD

Structured data in clinical development

Study Planning and Design

Mainly document driven.

Data Collection

Well known data models utilized by EDC

Data Management

Well defined data structures and standards.

Analysis and Reporting

Well defined data structures, standards and analytics

Why are we not benefiting more from the wealth of CT data?

Because of:

- Structured Data Gaps
- Standardization Gaps

Structured Data Gap

- Study planning, definition and design
- Document centric
- Requires a Structured Protocol Representation

Standardization Gap

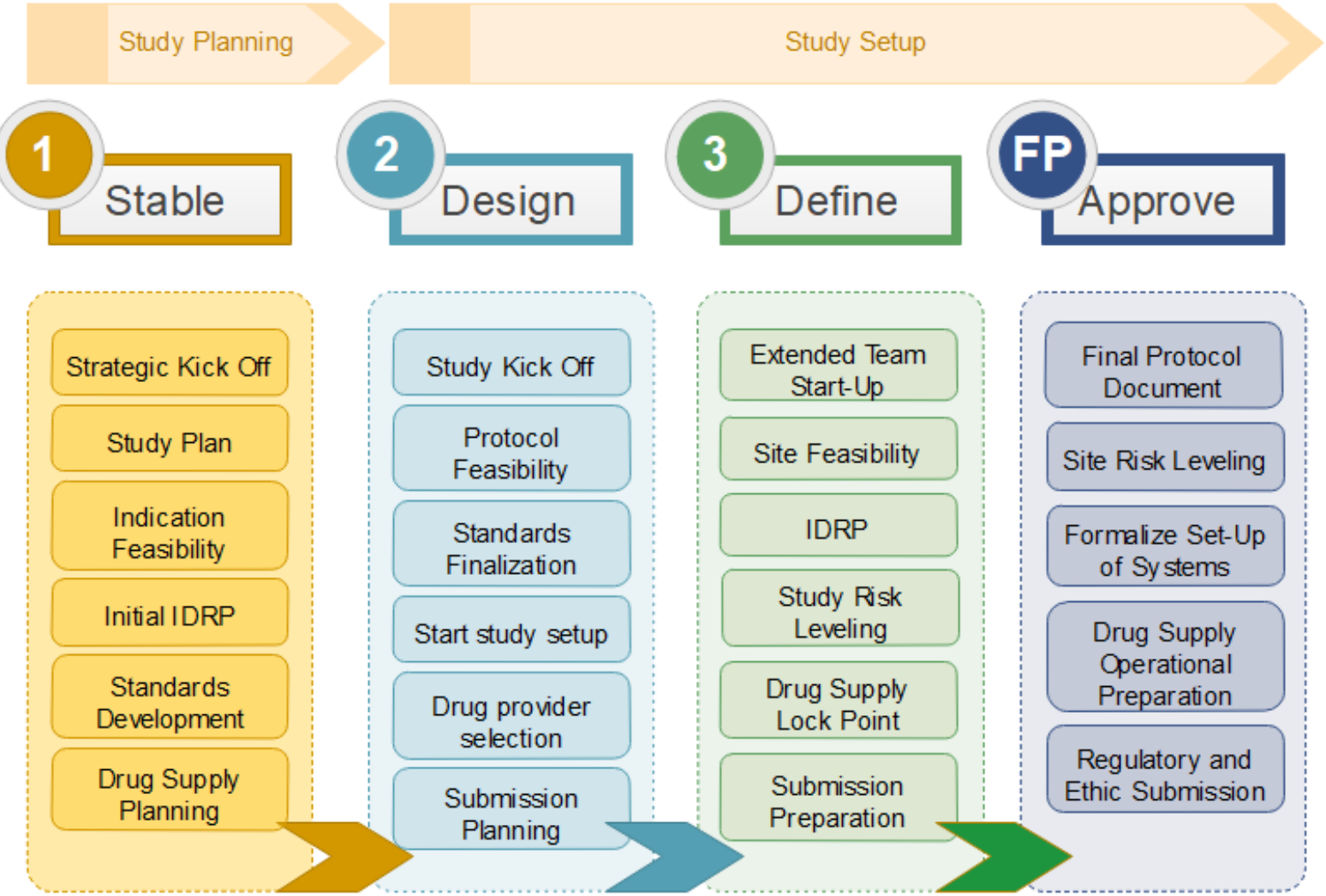
- Patchy standards across Clinical Development
- Fit-for-purpose and E2E linked clinical standards
- Requires Standards Repository

Clinical Data Strategy

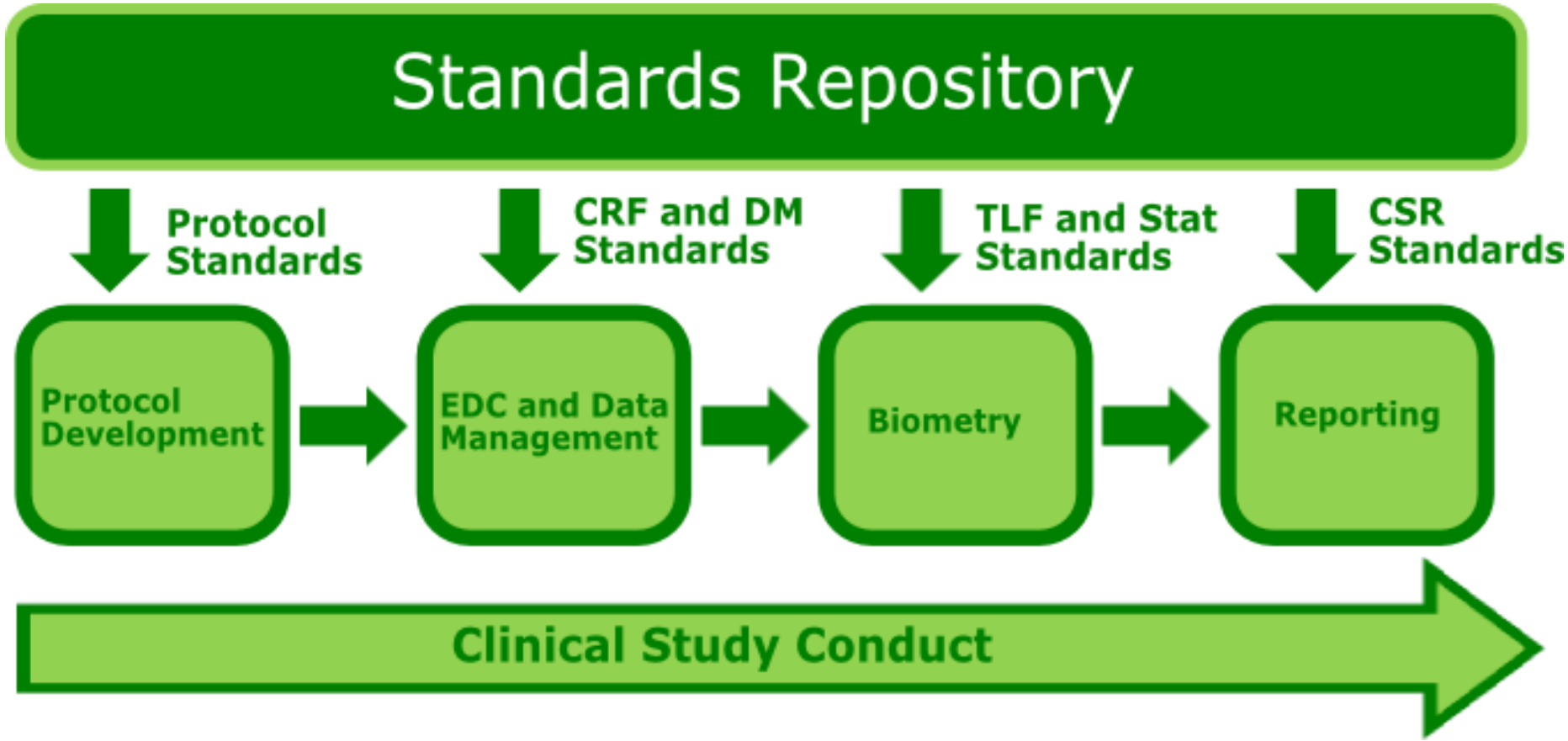
Structured Study Definition – Quality by Design in practice

Protocol Data Elements

- Trial Summary
- Objectives
- Endpoints
- Eligibility
- Treatment
- Protocol Activities
- SOA
- Trial Design
  - Arms
  - Visits
  - Elements



E2E Standardization



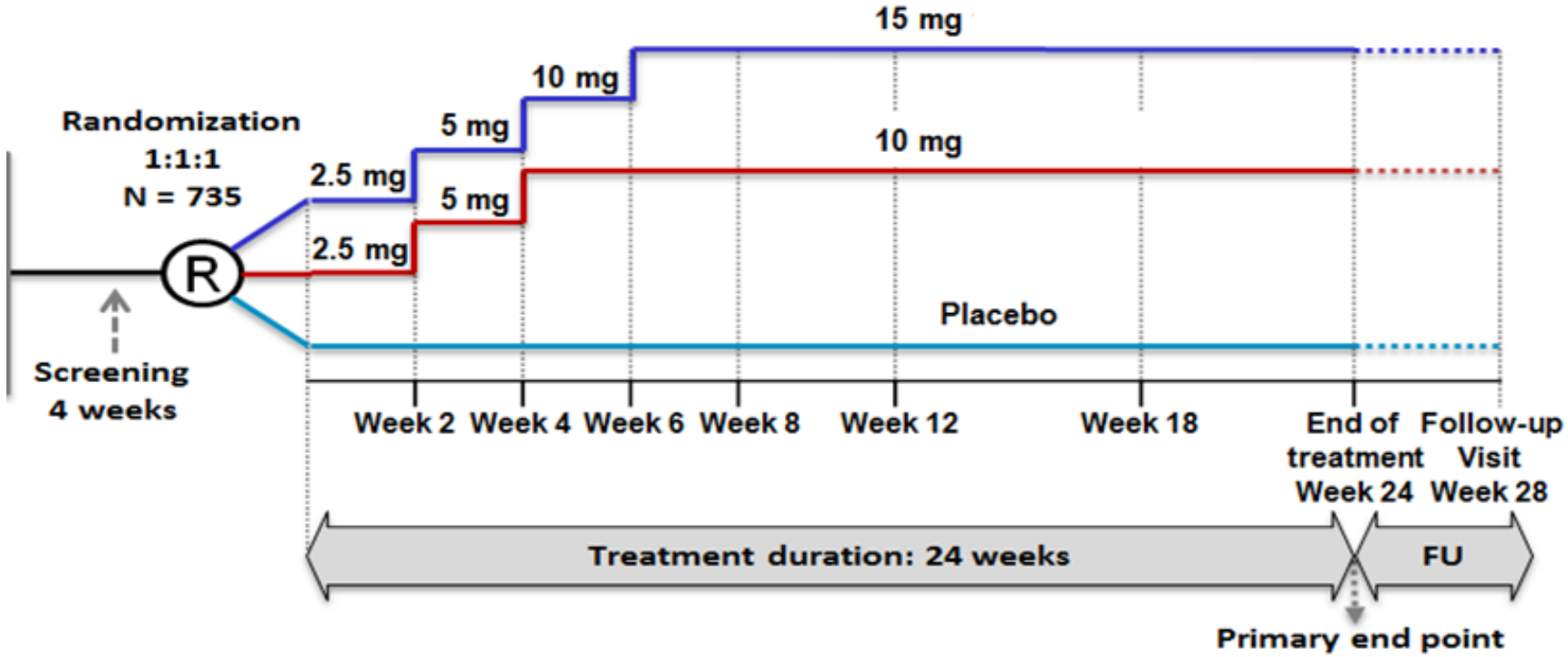
Objectives > Endpoints > Activities > Medical Concepts > Medical Items > Data Standards > Codelists

APPLICATION OF PROTOCOL DEFINITION IN TRIAL DESIGN AND IMPACT ON CRF AND DATABASE

An Example

Example Introduction

Study design Diagram

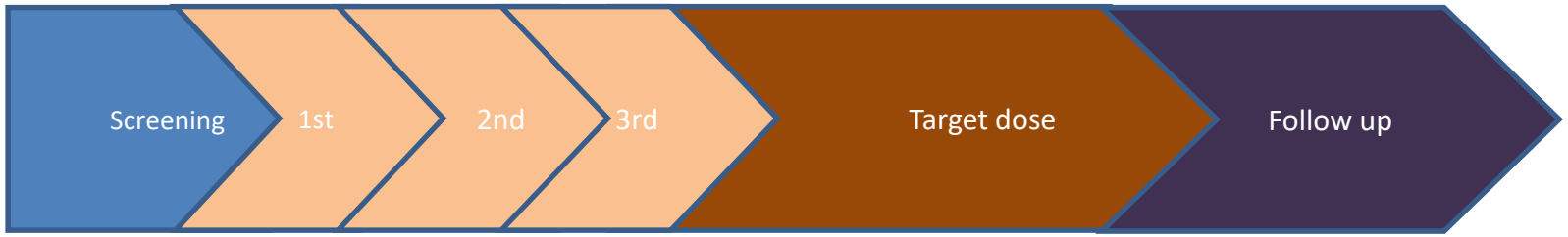


Example Introduction

Assessment schedule table

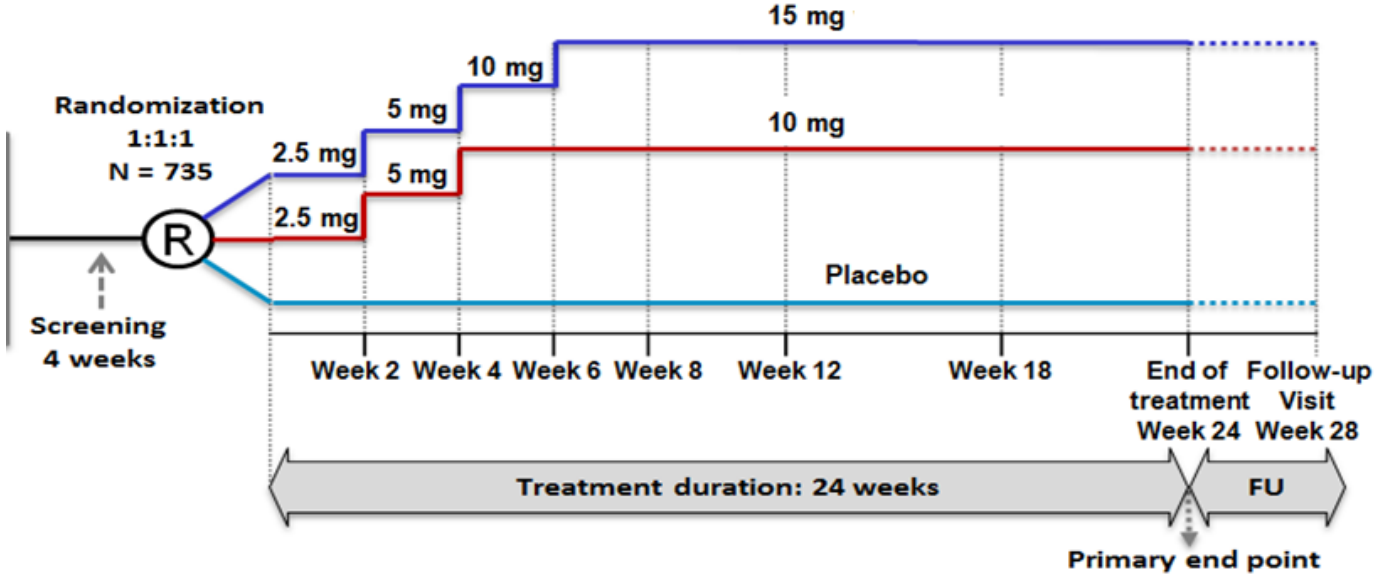
Trial Periods	Screening	Baseline	Titration / Sham titration			Treatment			End of treatment	Safety Follow-Up	Premature Treatment Discontinuation	
Visit Number	1	2	3	4	5	6	7	8	9	10	11	12
Week			2	4	6	8	12	18	24	28		

Subject „knowledge“



EPOCH definition

Nubmer of EPOCHs

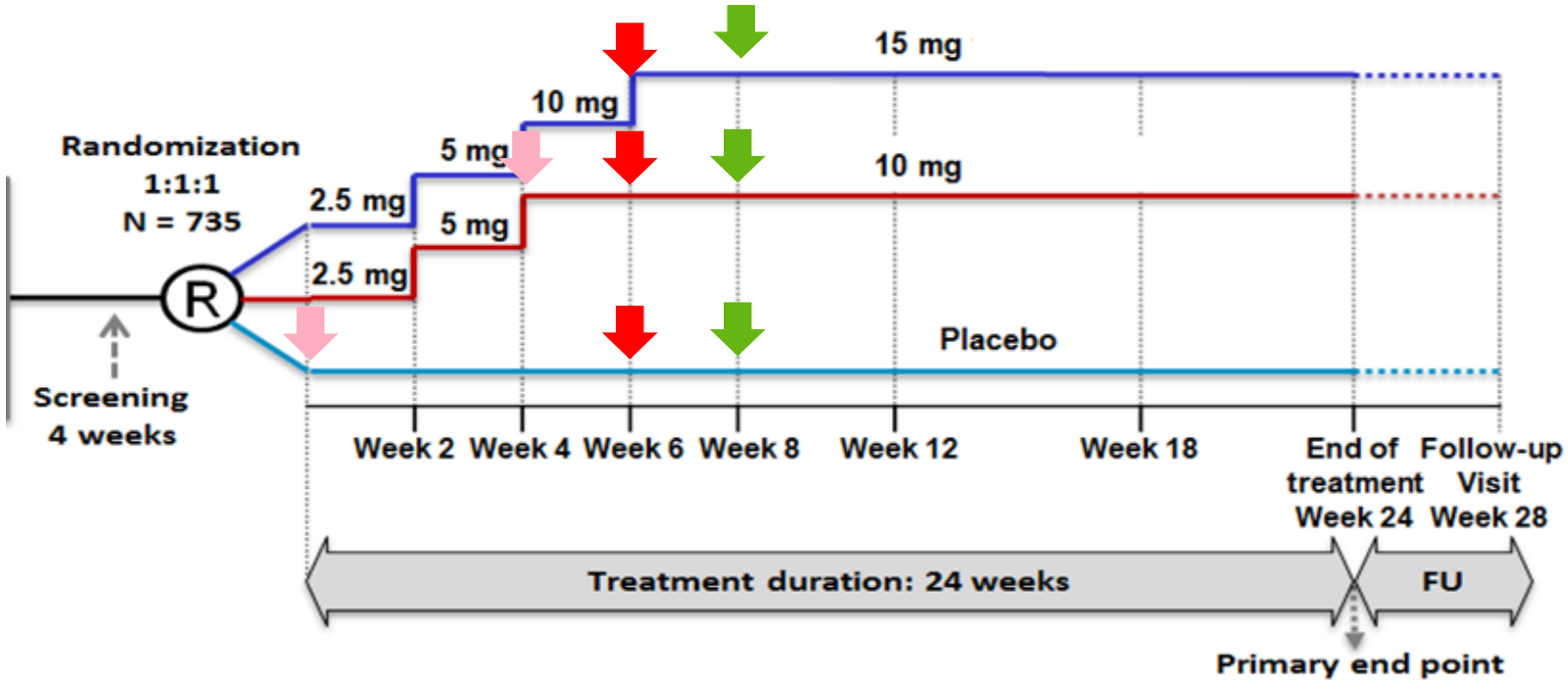


Trial Periods	Screening	Baseline	Titration / Sham titration			Treatment			End of treatment	Safety Follow-Up	Premature Treatment Discontinuation	
Visit Number	1	2	3	4	5	6	7	8	9	10	11	12
Week			2	4	6	8	12	18	24	28		

- One „treatment“ EPOCH in case that titration is the recommanded regimen
- 2 EPOCHS („titration“ – „fix dose“) in case the regimen is also in scope of the trial

EPOCH definition

Stop of titration – start of fix dose



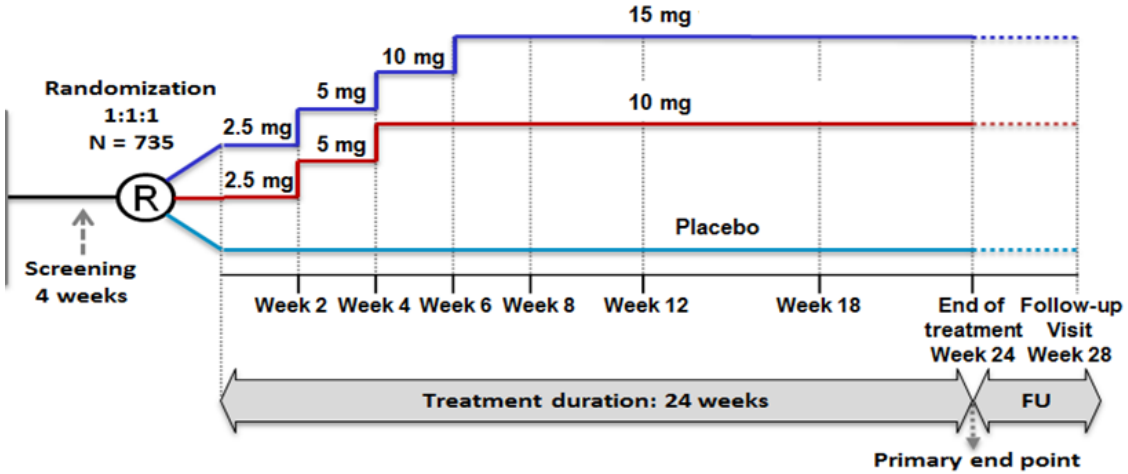
- Fix dose starts with the last titration step
- Fix dose starts when also the last dosing step was administered for 2 weeks

Impact of EPOCH and “view” on ELEMENTS

Example: one EPOCH but 2 „views“

1: Prospective view

TREATMENT¤			
2.5·mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	15mg·(fix)¤
2.5mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	10mg·(fix)¤
Placebo·(tit)¤	Placebo·(tit)¤	Placebo·(tit)¤	Placebo·(fix)¤



2: Retrospective view

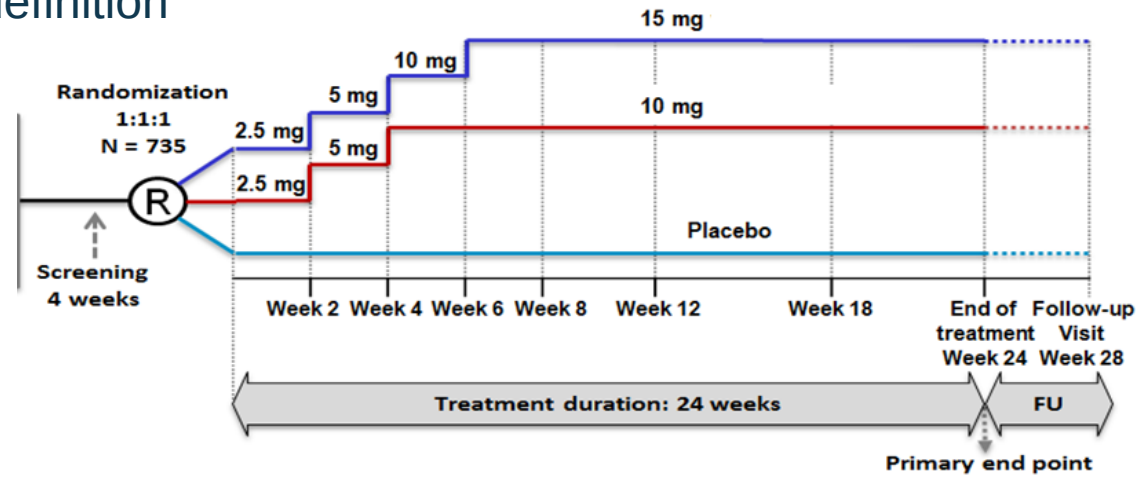
TREATMENT¤			
2.5·mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	15mg·(fix)¤
2.5mg·(tit)¤	5·mg·(tit)¤	10mg·(fix)¤	
Placebo¤			

„Treatment elements“	# in 1	# in 2
2.5 mg	1	1
5 mg	1	1
10 mg	2	2
15 mg	1	1
Placebo	2	1

Impact on	
Starting rules	yes
CRF	no
Exposure (EX)	yes

Impact of EPOCH and “view” on ELEMENTS

Example: impact of different „end of titration“ definition



1: Retrospective view: last dosing step

TITRATION¤			FIX·DOSE¤
2.5·mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	15mg·(fix)¤
2.5mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	10mg·(fix)¤
Placebo·(tit)¤			Placebo·(fix)¤

2 Retrospective view: incl. 2 weeks of target dose

TITRATION¤				FIX·DOSE¤
2.5·mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	15mg·(tit)¤	15mg·(fix)¤
2.5mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)·4W¤		10mg·(fix)¤
Placebo·(tit)¤				Placebo·(fix)¤

„Treatment elements“	# in 1	# in 2
2.5 mg	1	1
5 mg	1	1
10 mg	2	3
15 mg	1	2
Placebo	2	2

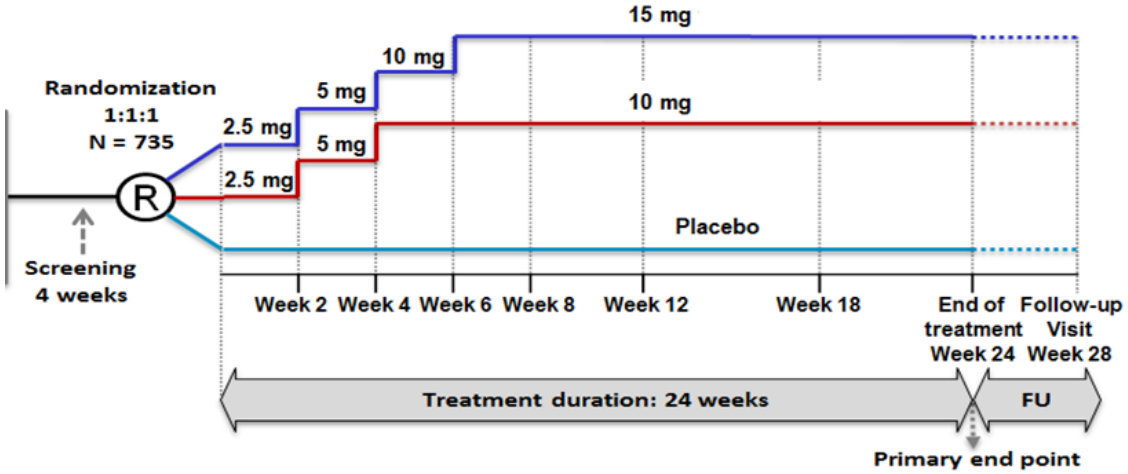
Impact on	
Starting rules	yes
CRF	yes
Exposure (EX)	yes

Impact of EPOCH and “view” on ELEMENTS

Example: impact of different „views“

1: Retrospective view: incl. 2 weeks of target dose

TITRATION¤				FIX·DOSE¤
2.5·mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	15mg·(tit)¤	15mg·(fix)¤
2.5mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)·4W¤		10mg·(fix)¤
Placebo·(tit)¤				Placebo·(fix)¤



2: Prospective view: incl. 2 weeks of target dose

TITRATION¤				FIX·DOSE¤
2.5·mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	15mg·(tit)¤	15mg·(fix)¤
2.5mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	10·mg·s¤	10mg·(fix)¤
Plc·(tit)¤	Plc·(tit)¤	Plc·(tit)¤	Plc·(tit)¤	Placebo·(fix)¤

„Treatment elements“	# in 1	# in 2
2.5 mg	1	1
5 mg	1	1
10 mg	3	3
15 mg	2	2
Placebo	2	2

Impact on	
Starting rules	yes
CRF	no
Exposure (EX)	yes

Summary

1 study – 1 protocol – x interpretations

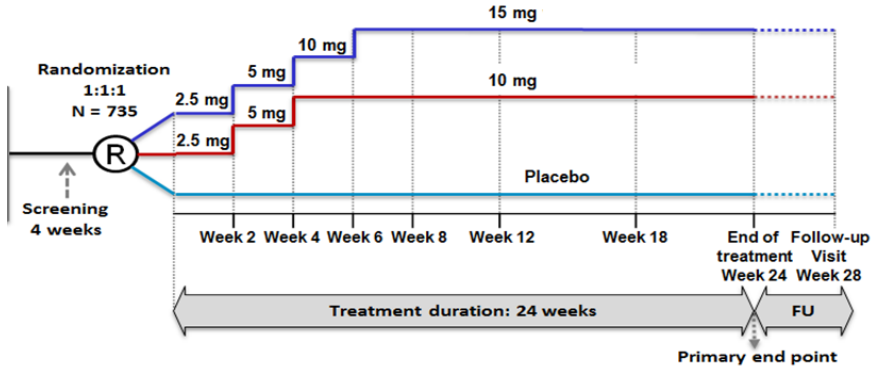
TITRATION¤			FIX·DOSE¤
2.5·mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	15mg·(fix)¤
2.5mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	10mg·(fix)¤
Placebo·(tit)¤			Placebo·(fix)¤

TREATMENT¤			
2.5·mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	15mg·(fix)¤
2.5mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	10mg·(fix)¤
Placebo·(tit)¤	Placebo·(tit)¤	Placebo·(tit)¤	Placebo·(fix)¤

TITRATION¤				FIX·DOSE¤
2.5·mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	15mg·(tit)¤	15mg·(fix)¤
2.5mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	10·mg·s¤	10mg·(fix)¤
Plc·(tit)¤	Plc·(tit)¤	Plc·(tit)¤	Plc·(tit)¤	Placebo·(fix)¤

TREATMENT¤			
2.5·mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	15mg·(fix)¤
2.5mg·(tit)¤	5·mg·(tit)¤	10mg·(fix)¤	
Placebo¤			

TITRATION¤				FIX·DOSE¤
2.5·mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)¤	15mg·(tit)¤	15mg·(fix)¤
2.5mg·(tit)¤	5·mg·(tit)¤	10·mg·(tit)·4W¤		10mg·(fix)¤
Placebo·(tit)¤				Placebo·(fix)¤



Conclusions

SSD

Conclusions

- SSD applied through gated milestones enables the downstream processes to receive focused, precise and executable protocol information earlier than before for their implementations.
- Timely provision of the structured study data is essential to promote the understanding and alignment of the downstream processes to front-load their activities.
- SSD linked to the MDR drives the Clinical Development Operations productivity by re-applying the knowledge through standards.
- late discussions which impact the clinical database can be avoided
- A “good choice” of the Trial design can emphasize similarities of different trials within a project as well as stressing some analysis aspects

Thank you!

Djenan Ganic, intilaris LifeSciences
Tanja Petrowitsch, Bayer AG