



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



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**

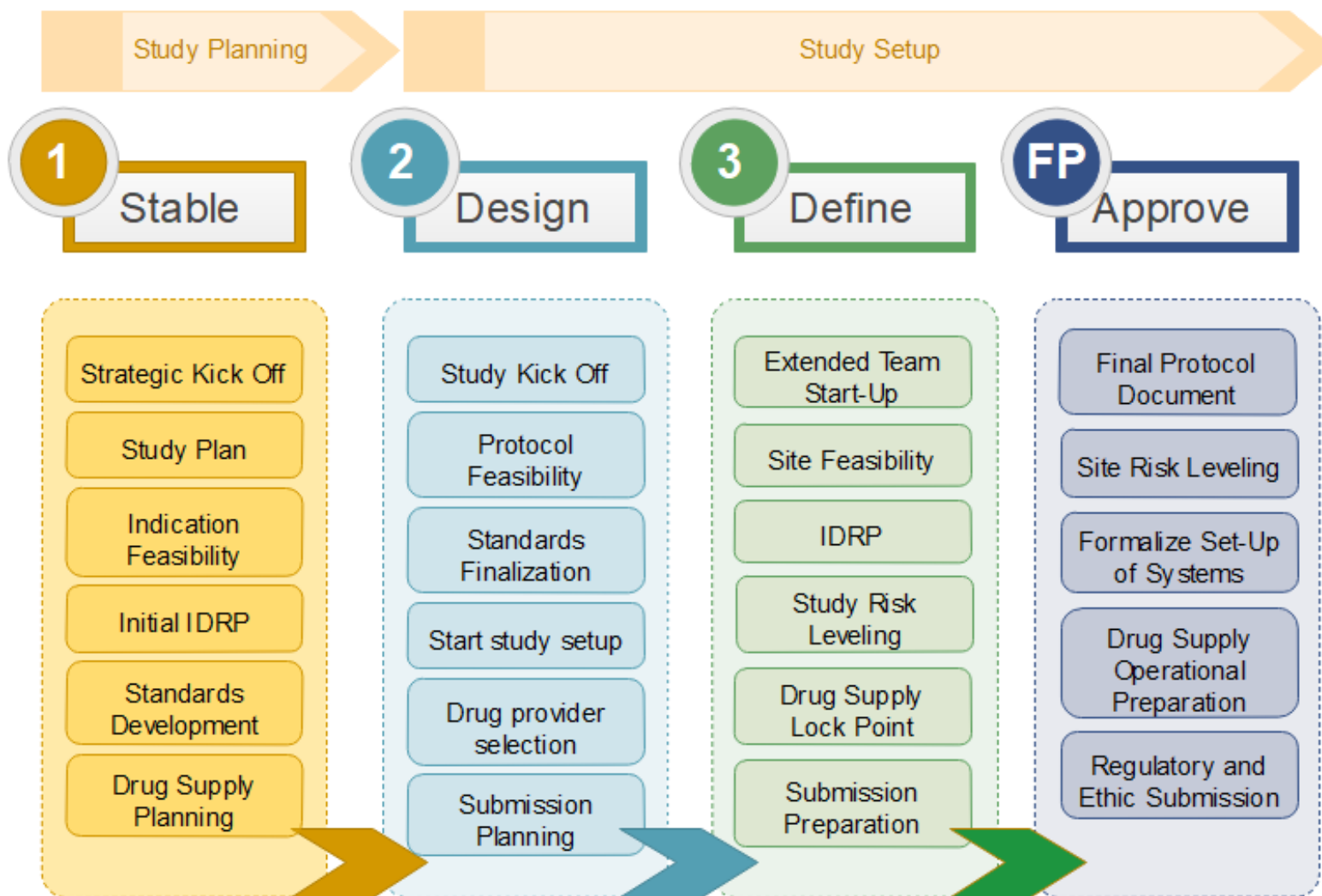
Standardization Gap

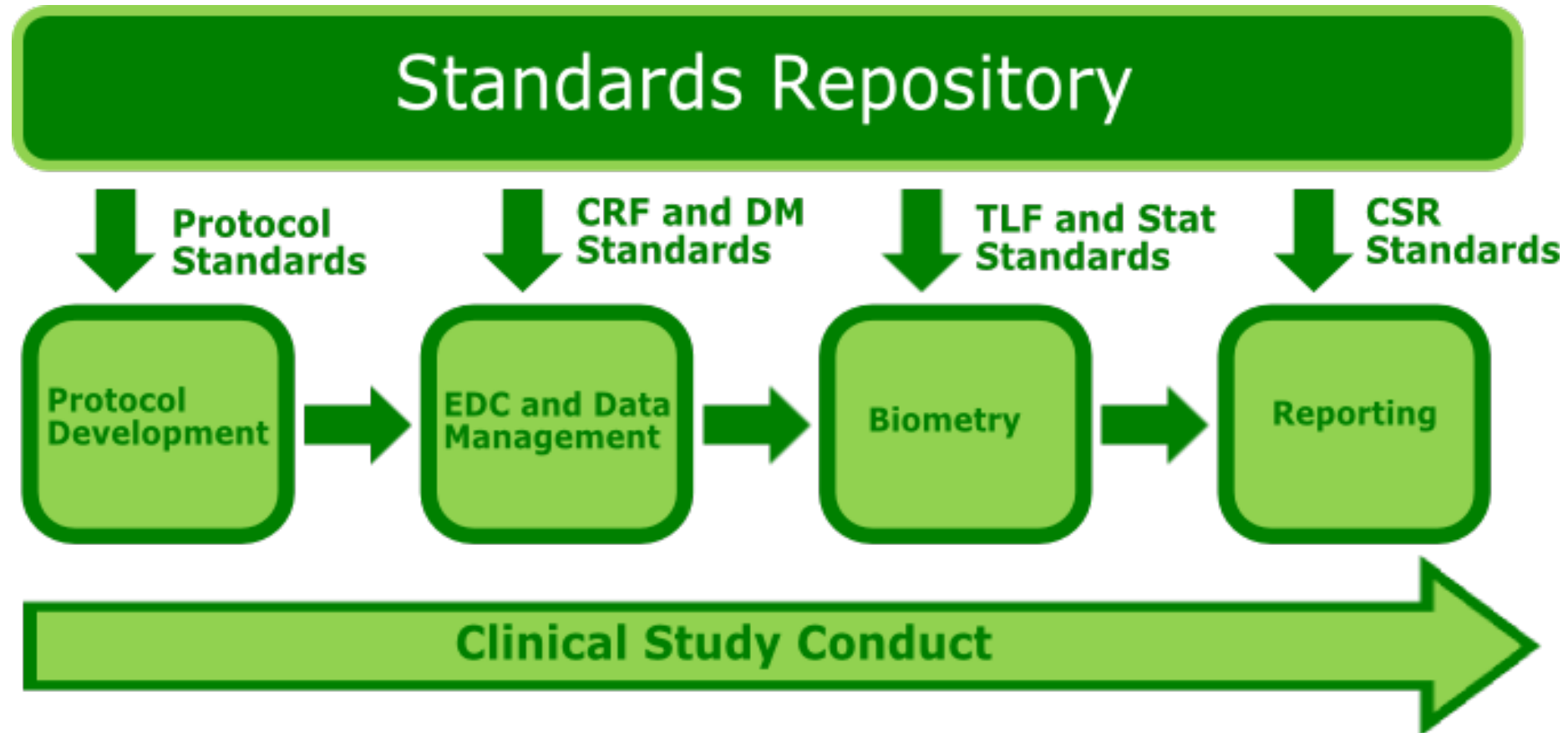
- **Patchy standards across Clinical Development**
- **Fit-for-purpose and E2E linked clinical standards**
- **Requires Standards Repository**

Clinical Data Strategy

Protocol Data Elements

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





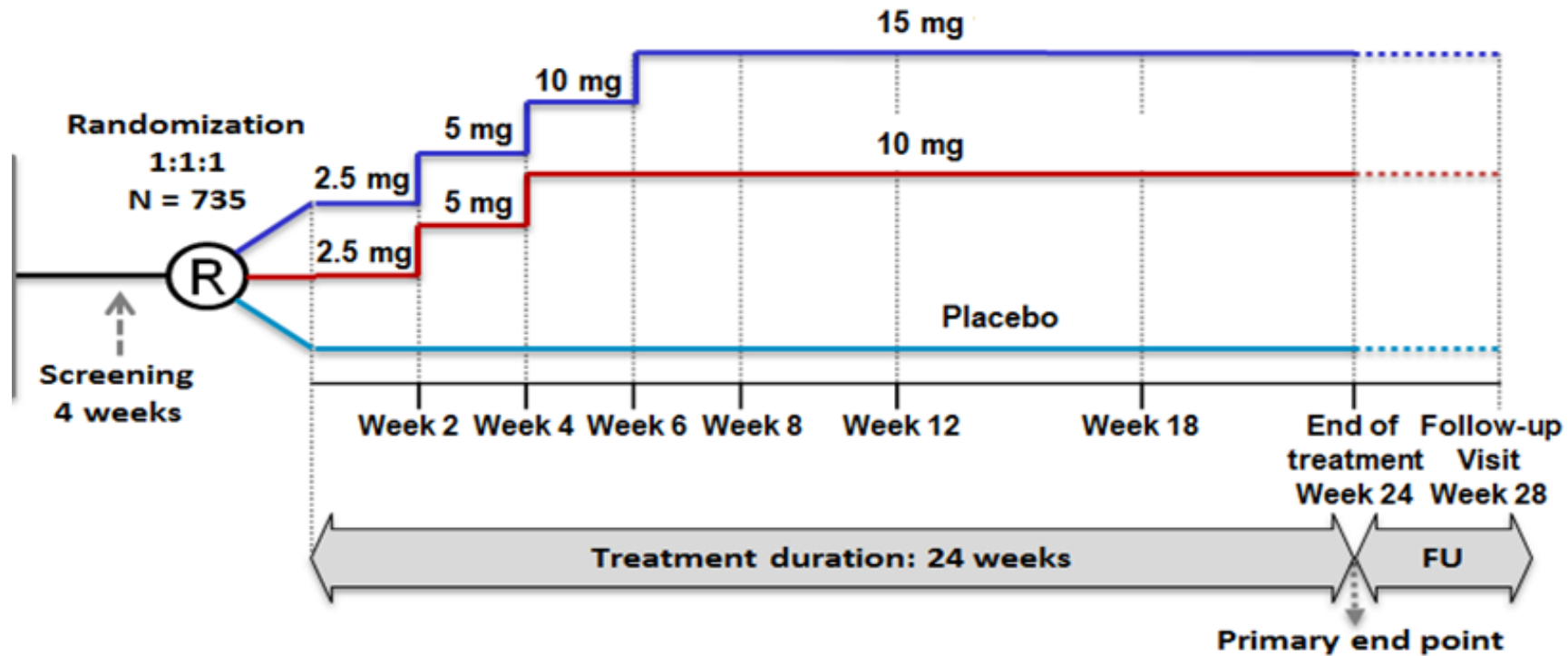
Objectives > Endpoints > Activities > Medical Concepts > Medical Items > Data Standards > Codelists

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

An Example

Example Introduction

Study design Diagram

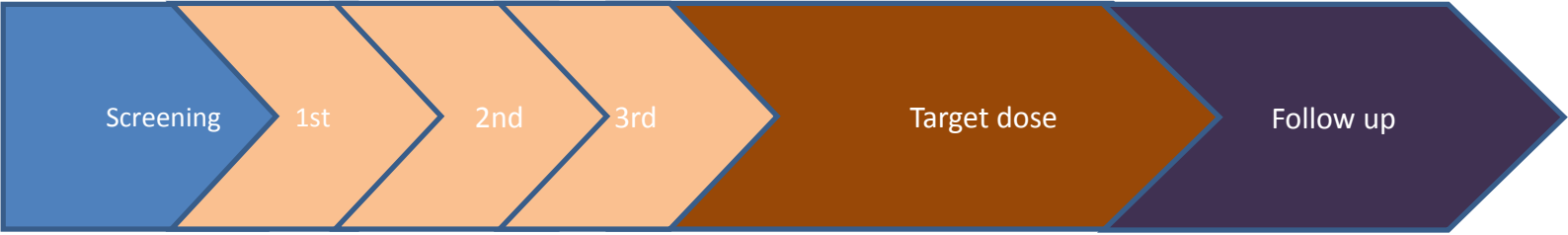


Example Introduction

Assessment schedule table

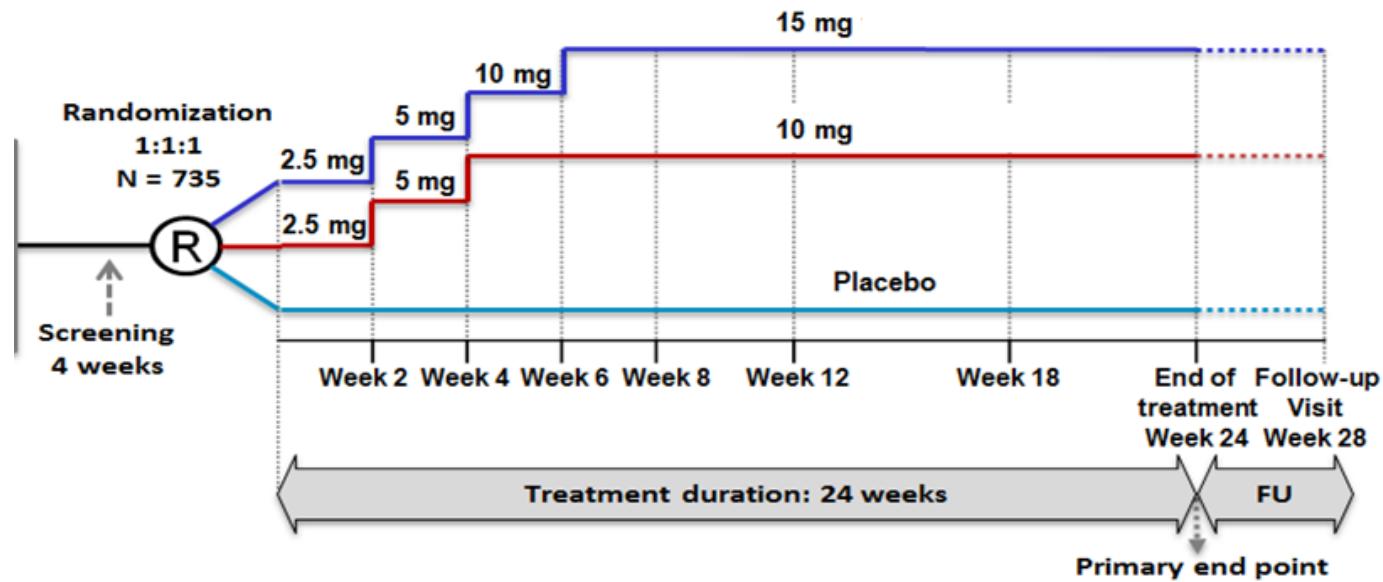
Trial Periods	Screening	Baseline	Titration / Sham titration			Treatment			End of treatment	Safety Follow-Up	Premature Treatment Discontinuation	
Visit Number	1	2	3	4	5	6	7	8	9	10	11	12
Week			2	4	6	8	12	18	24	28		

Subject „knowledge“



EPOCH definition

Nubmer of EPOCHs

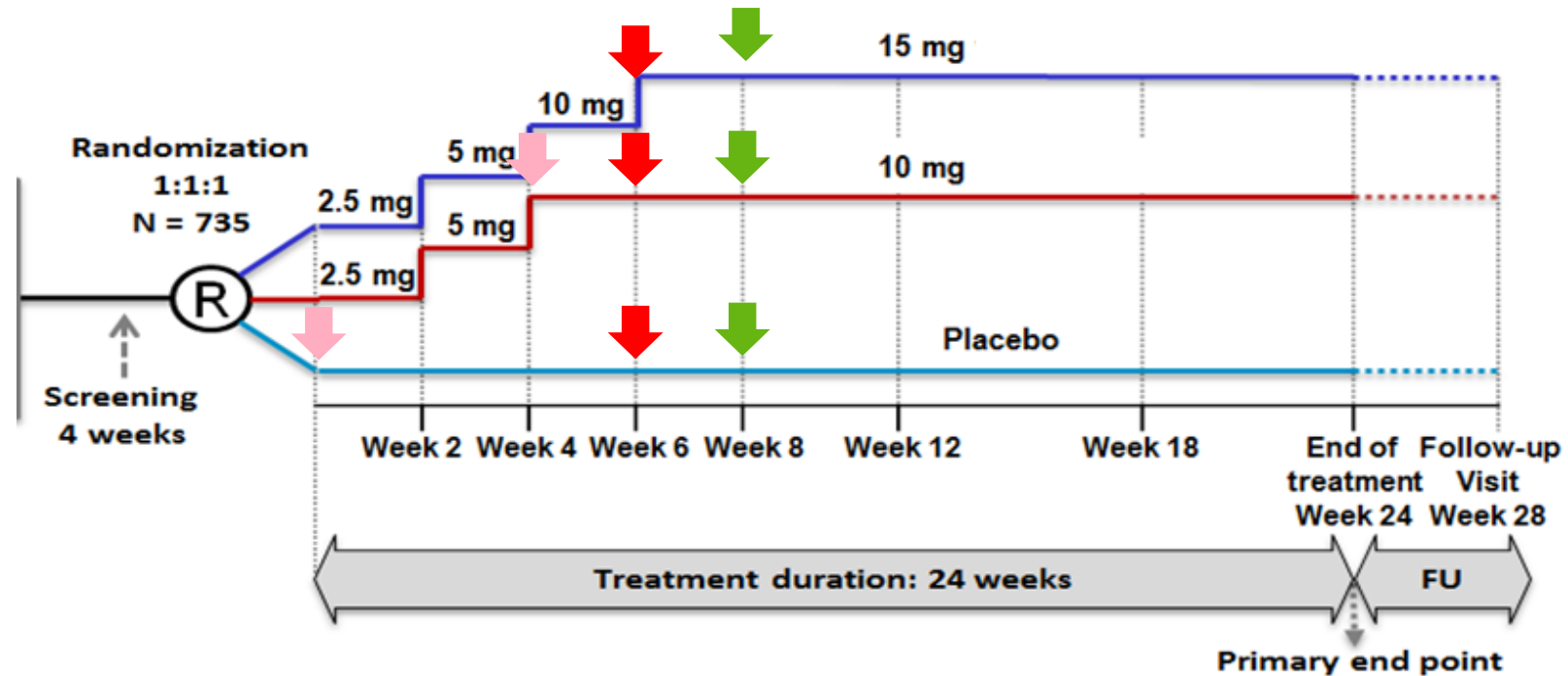


Trial Periods	Screening	Baseline	Titration / Sham titration				Treatment			End of treatment	Safety Follow-Up	Premature Treatment Discontinuation
Visit Number	1	2	3	4	5	6	7	8	9	10	11	12
Week			2	4	6	8	12	18	24	28		

- ❖ One „treatment“ EPOCH in case that titration is the recommended 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



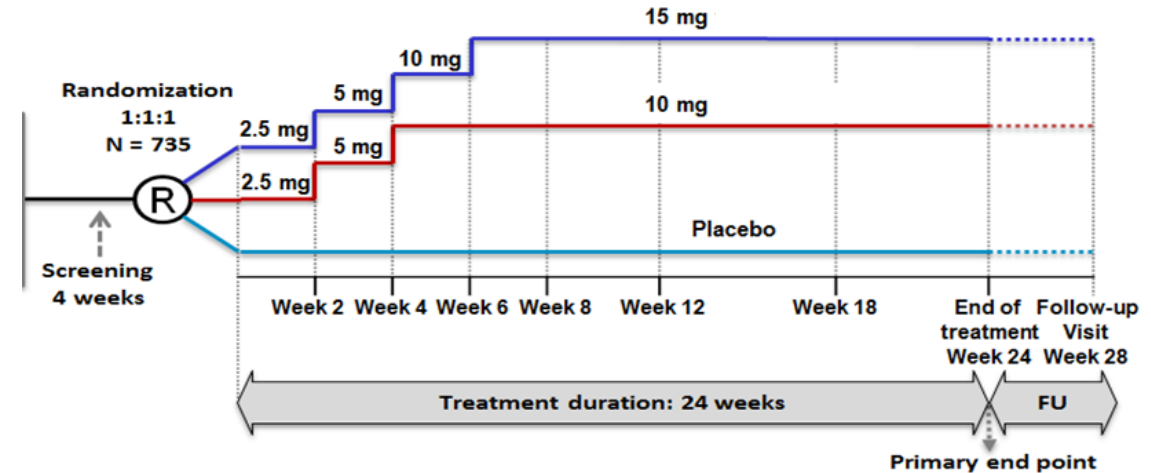
- ❖ Fix dose starts with the last titration step
- ❖ Fix dose starts when also the last dosing step was administered for 2 weeks

Impact of EPOCH and “view” on ELEMENTS

Example: one EPOCH but 2 „views“

1: Prospective view

TREATMENTα			
2.5-mg·(tit)α	5-mg·(tit)α	10-mg·(tit)α	15mg·(fix)α
2.5mg·(tit)α	5-mg·(tit)α	10-mg·(tit)α	10mg·(fix)α
Placebo·(tit)α	Placebo·(tit)α	Placebo·(tit)α	Placebo·(fix)α



2: Retrospective view

TREATMENTα			
2.5-mg·(tit)α	5-mg·(tit)α	10-mg·(tit)α	15mg·(fix)α
2.5mg·(tit)α	5-mg·(tit)α	10mg·(fix)α	
Placeboα			

„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

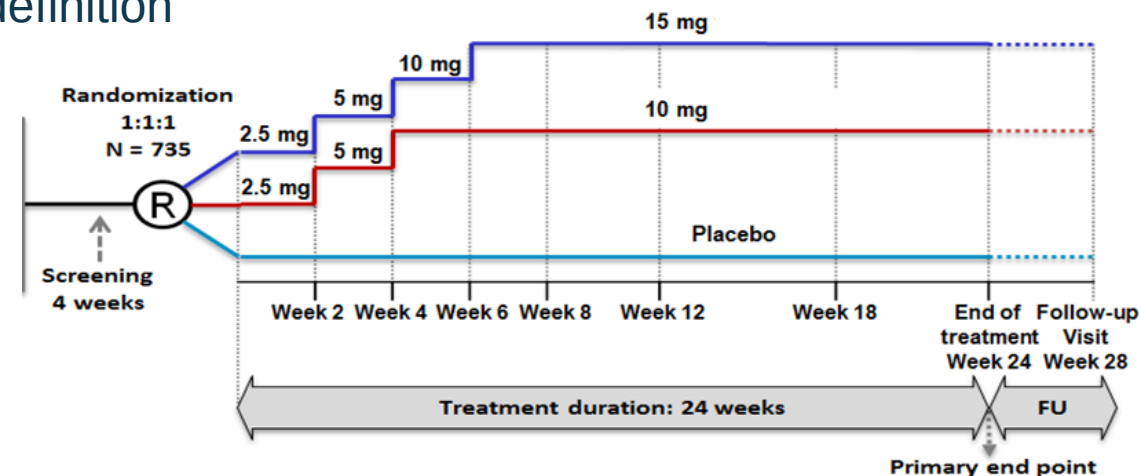
Impact on	
Starting rules	yes
CRF	no
Exposure (EX)	yes

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

TITRATIONα				FIX·DOSEα
2.5-mg·(tit)α	5-mg·(tit)α	10-mg·(tit)α	15mg·(tit)α	15mg·(fix)α
2.5mg·(tit)α	5-mg·(tit)α	10-mg·(tit)·4Wα		10mg·(fix)α
Placebo·(tit)α				Placebo·(fix)α

„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

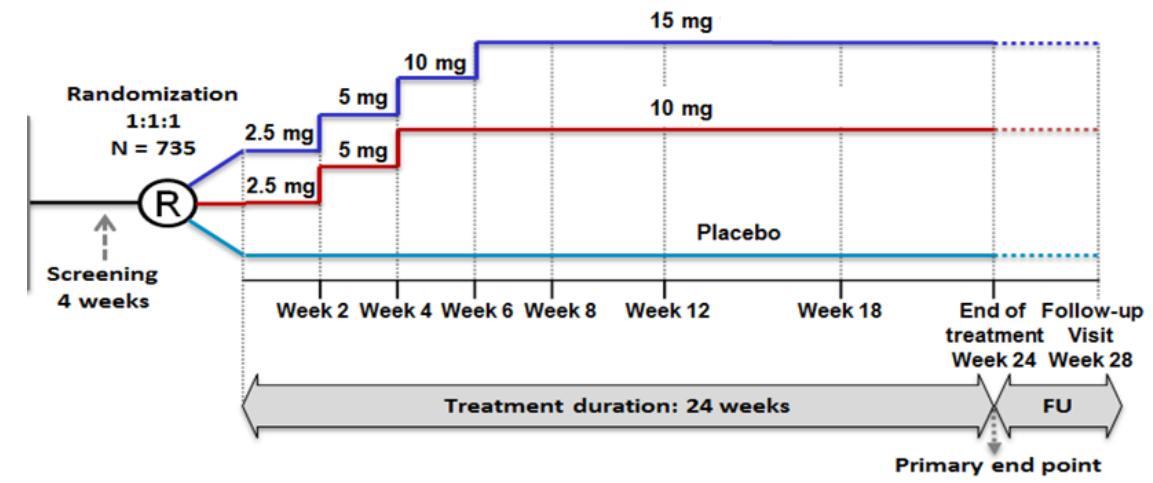
Impact on	
Starting rules	yes
CRF	yes
Exposure (EX)	yes

Impact of EPOCH and “view” on ELEMENTS

Example: impact of different „views“

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

TITRATIONα				FIX·DOSEα
2.5-mg·(tit)α	5-mg·(tit)α	10-mg·(tit)α	15mg·(tit)α	15mg·(fix)α
2.5mg·(tit)α	5-mg·(tit)α	10-mg·(tit)·4Wα		10mg·(fix)α
Placebo·(tit)α				Placebo·(fix)α



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

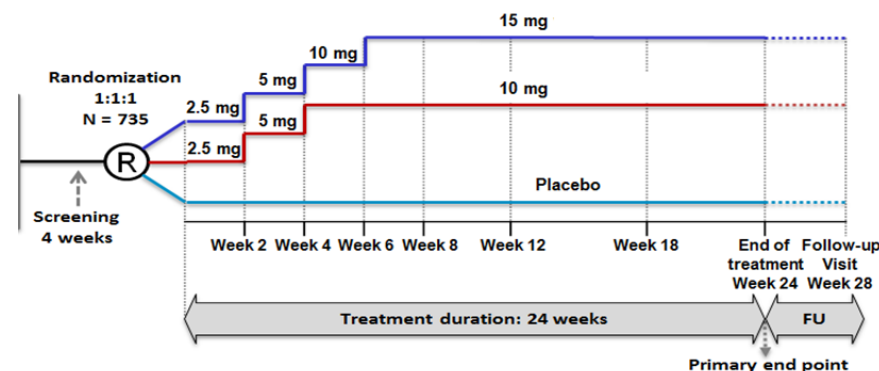
TITRATIONα			FIX·DOSEα
2.5-mg·(tit)α	5-mg·(tit)α	10-mg·(tit)α	15mg·(fix)α
2.5mg·(tit)α	5-mg·(tit)α	10-mg·(tit)α	10mg·(fix)α
Placebo·(tit)α			Placebo·(fix)α

TREATMENTα			
2.5-mg·(tit)α	5-mg·(tit)α	10-mg·(tit)α	15mg·(fix)α
2.5mg·(tit)α	5-mg·(tit)α	10-mg·(tit)α	10mg·(fix)α
Placebo·(tit)α	Placebo·(tit)α	Placebo·(tit)α	Placebo·(fix)α

TITRATIONα				FIX·DOSEα
2.5-mg·(tit)α	5-mg·(tit)α	10-mg·(tit)α	15mg·(tit)α	15mg·(fix)α
2.5mg·(tit)α	5-mg·(tit)α	10-mg·(tit)α	10-mg·sα	10mg·(fix)α
Plc·(tit)α	Plc·(tit)α	Plc·(tit)α	Plc·(tit)α	Placebo·(fix)α

TREATMENTα			
2.5-mg·(tit)α	5-mg·(tit)α	10-mg·(tit)α	15mg·(fix)α
2.5mg·(tit)α	5-mg·(tit)α	10mg·(fix)α	
Placeboα			

TITRATIONα				FIX·DOSEα
2.5·mg·(tit)α	5·mg·(tit)α	10·mg·(tit)α	15mg·(tit)α	15mg·(fix)α
2.5mg·(tit)α	5·mg·(tit)α	10·mg·(tit)·4Wα		10mg·(fix)α
Placebo·(tit)α				Placebo·(fix)α



Conclusions

SSD

- 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

