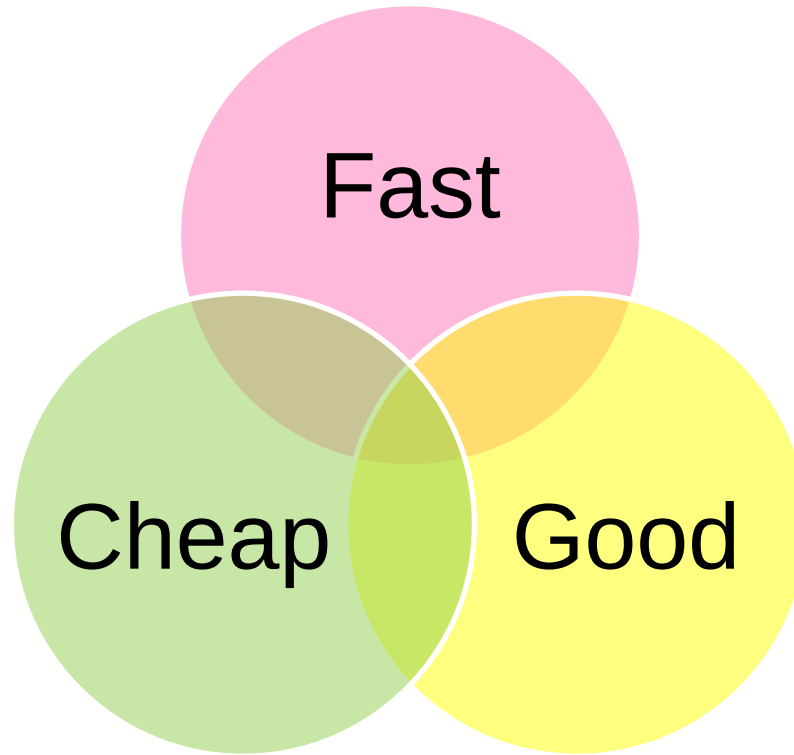
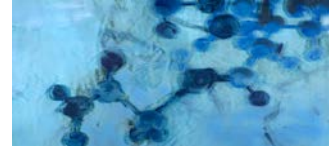


A close-up photograph of a young man and woman smiling and looking off-camera to the right. They are outdoors in a desert-like environment with a clear blue sky and sandy ground in the background. The man is in the foreground, and the woman is slightly behind him, her face partially visible as she smiles.

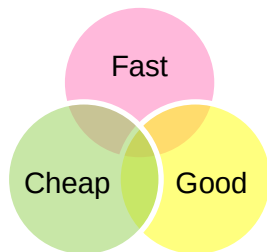
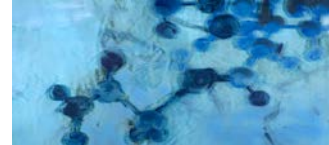
Metadata & ADaM Implementation STREAMing Deliverables @ Ferring

Bjarke Klein, Ferring Pharmaceuticals A/S

Fast Track to Approval: Speed and Efficiency

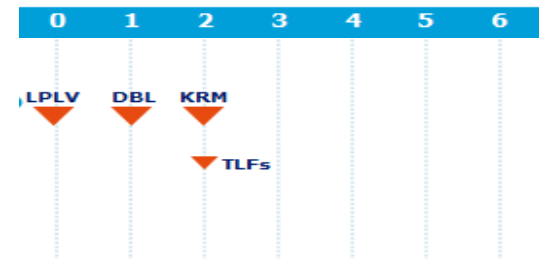


Ferring Global Biometrics Target KPI

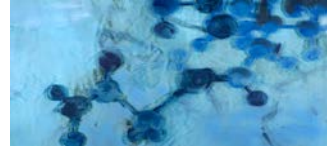


Activity	Date	Day
Database lock / unblinding	12JAN2016	0
Locked SDTM	14JAN2016	+2
Locked validated ADaM	14JAN2016	+2
TLF production + validation	14JAN2016	+2
Internal biometrics review / cross check	15JAN2016	+3
Delivery of end-of-text tables/listings	15JAN2016	+3
Delivery of in-text tables/figures	15JAN2016	+3

3 days



Item	Count
ADaM data sets	23
End-of-text tables	289
End-of-text listings	41
In-text tables	56
In-text figures	8



SDTM



ADaM

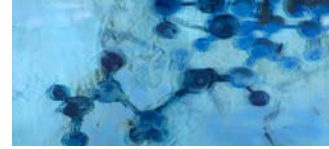


TLF
development



TLF

ADaM Metadata

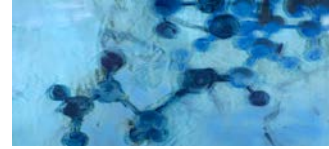


Dataset Name	Description	Structure	Key Variables	Class	Core
ADEF	Efficacy analysis dataset	One record per subject per parameter	USUBJID, PARAMCD	BDS	Yes

Dataset Name	Variable Name	Variable Label	Variable Type	Display Format
ADEF	PARCAT1N	Parameter Category 1 (N)	Num	
ADEF	PARCAT1	Parameter Category 1	Char	\$200
ADEF	PARAMN	Parameter (N)	Num	
ADEF	PARAMCD	Parameter Code	Char	\$200
ADEF	PARAM	Parameter	Char	\$8
ADEF	AVALC	Analysis Value (C)	Char	\$200
ADEF	AVAL	Analysis Value	Num	
ADEF	AROUND	Rounding of results	NUM	

PARCAT1N	PARCAT1	PARAMN	PARAM	PARAMCD	AVALC	AVAL	AROUND
10	Pregnancy	11	Positive blood sample	POSBLOOD	Yes / No	1 / 2	
10	Pregnancy	12	Ongoing pregnancy	ONGPREG	Yes / No	1 / 2	
20	Live birth	21	Live birth	LIVEBRTH	Yes / No	1 / 2	
20	Live birth	22	Duration of pregnancy	DURPREG		Num	1

ADaM Production based on Metadata



Dataset Name	Description	Structure	Key Variables	Class	Core
ADEF	Efficacy analysis dataset	One record per subject per parameter	USUBJID, PARAMCD	BDS	Yes

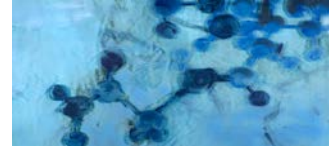
USUBJID	POSBLOOD	ONGPREG	LIVEBRTH	DURPREG
101	Yes	Yes	Yes	240
102	No	No	No	.

PARCAT1N	PARCAT1	PARAMN	PARAM	PARAMCD	AVALC	AVAL	AROUND
10	Pregnancy	11	Positive blood sample	POSBLOOD	Yes / No	1 / 2	
10	Pregnancy	12	Ongoing pregnancy	ONGPREG	Yes / No	1 / 2	
20	Live birth	21	Live birth	LIVEBRTH	Yes / No	1 / 2	
20	Live birth	22	Duration of pregnancy	DURPREG		Num	1

RING

PHARMACEUTICALS

ADaM Production based on Metadata

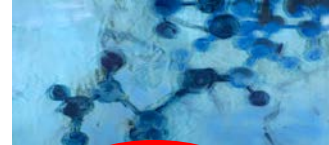


Dataset Name	Description	Structure	Key Variables	Class	Core
ADEF	Efficacy analysis dataset	One record per subject per parameter	USUBJID, PARAMCD	BDS	Yes

USUBJID	PARAMCD	VALUE
101	POSBLOOD	Yes
101	ONGPREG	Yes
101	LIVEBRTH	Yes
101	DURPREG	240
102	POSBLOOD	No
102	ONGPREG	No
102	LIVEBRTH	No
102	DURPREG	.

PARCAT1N	PARCAT1	PARAMN	PARAM	PARAMCD	AVALC	AVAL	AROUND
10	Pregnancy	11	Positive blood sample	POSBLOOD	Yes / No	1 / 2	
10	Pregnancy	12	Ongoing pregnancy	ONGPREG	Yes / No	1 / 2	
20	Live birth	21	Live birth	LIVEBRTH	Yes / No	1 / 2	
20	Live birth	22	Duration of pregnancy	DURPREG		Num	1

ADaM Production based on Metadata

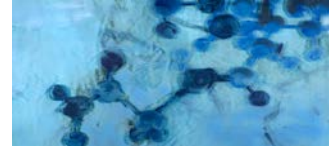


Dataset Name	Description	Structure	Key Variables	Class	Core
ADEF	Efficacy analysis dataset	One record per subject per parameter	USUBJID, PARAMCD	BDS	Yes

USUBJID	PARAMCD	VALUE	PARCAT1N	PARCAT1	PARAMN	PARAM
101	POSBLOOD	Yes	10	Pregnancy	11	Positive blood sample
101	ONGPREG	Yes	10	Pregnancy	12	Ongoing pregnancy
101	LIVEBRTH	Yes	20	Live birth	21	Live birth
101	DURPREG	240	20	Live birth	22	Duration of pregnancy
102	POSBLOOD	No	10	Pregnancy	11	Positive blood sample
102	ONGPREG	No	10	Pregnancy	12	Ongoing pregnancy
102	LIVEBRTH	No	20	Live birth	21	Live birth
102	DURPREG		20	Live birth	22	Duration of pregnancy

PARCAT1N	PARCAT1	PARAMN	PARAM	PARAMCD	AVALC	AVAL	AROUND
10	Pregnancy	11	Positive blood sample	POSBLOOD	Yes / No	1 / 2	
10	Pregnancy	12	Ongoing pregnancy	ONGPREG	Yes / No	1 / 2	
20	Live birth	21	Live birth	LIVEBRTH	Yes / No	1 / 2	
20	Live birth	22	Duration of pregnancy	DURPREG		Num	1

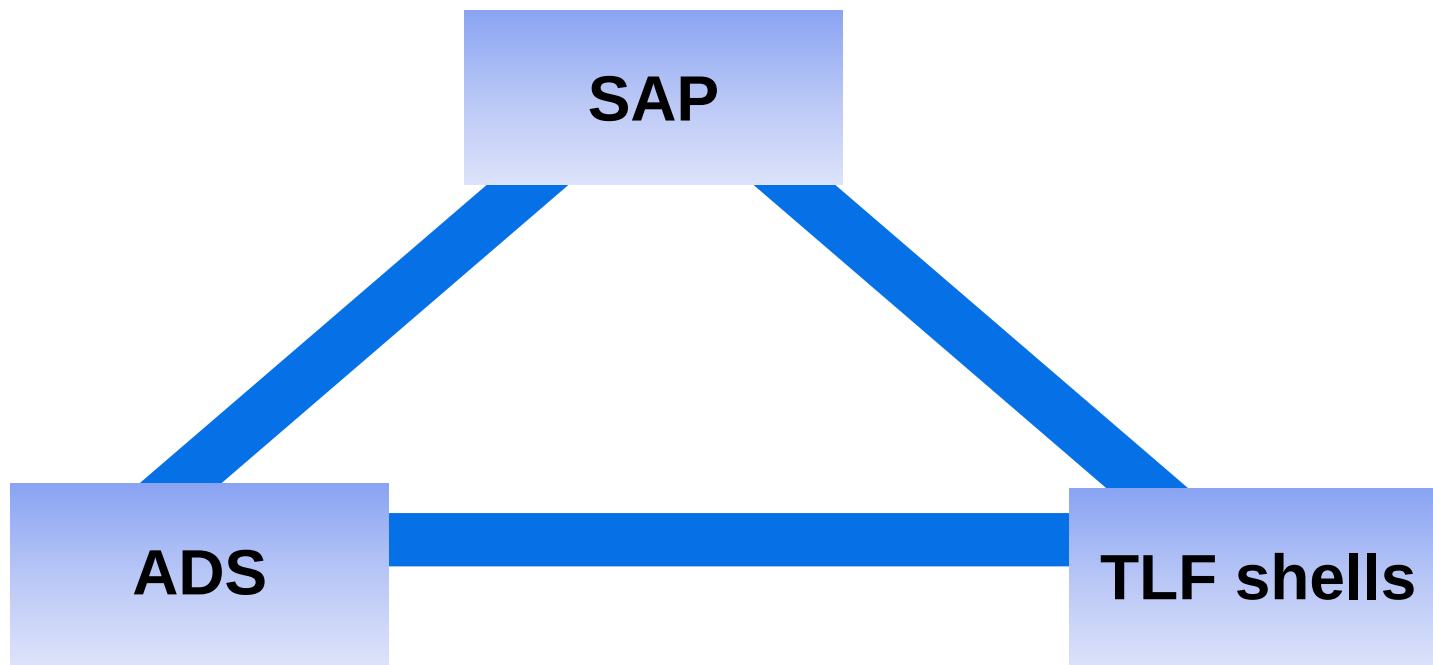
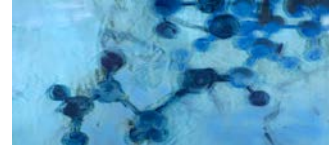
ADaM Production based on Metadata



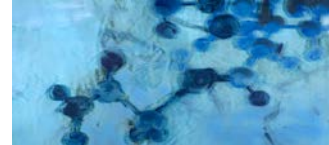
Dataset Name	Variable Name		Variable Label		Variable Type	Display Format			
ADEF	PARCAT1N		Parameter Category 1 (N)		Num				
ADEF	PARCAT1C		Parameter Category 1		Char	\$200			
ADEF	PARAMN		Parameter (N)		Num				
ADEF	PARAMCD		Parameter		Char	\$200			
ADEF	PARAMCD		Parameter Code		Char	\$8			
ADEF	AVALC		Analysis Value (C)		Char	\$200	Yes	1	
ADEF	AVAL		Analysis Value		Num		Yes	1	
ADEF	AROUND		Rounding of results		NUM		Yes	1	
101	DURPREG	20	Live birth	22	Duration of pregnancy			240	1
102	POSBLOOD	10	Pregnancy	11	Positive blood sample	No	2		
102	ONGPREG	10	Pregnancy	12	Ongoing pregnancy	No	2		
102	LIVEBRTH	20	Live birth	21	Live birth	No	2		
102	DURPREG	20	Live birth	22	Duration of pregnancy		.		1

Take control using
ADaM Metadata

Link between ADaM, SAP and tables



Link between ADaM, SAP and tables



7.1.4 Infertility History

The following data on infertility history obtained at the screening visit will be tabulated: Number of subjects with primary infertility, duration of infertility (months), and primary reason for infertility

PARCAT1	PARCAT1	PARAM1	PARAM1	PARAMCD
N				
10	Infertility history	11	Primary infertility	PRIMNF
10	Infertility history	12	Duration of infertility (months)	INFDUR
10	Infertility history	13	Primary reason for infertility	PREASON

Infertility History - Full Analysis Set

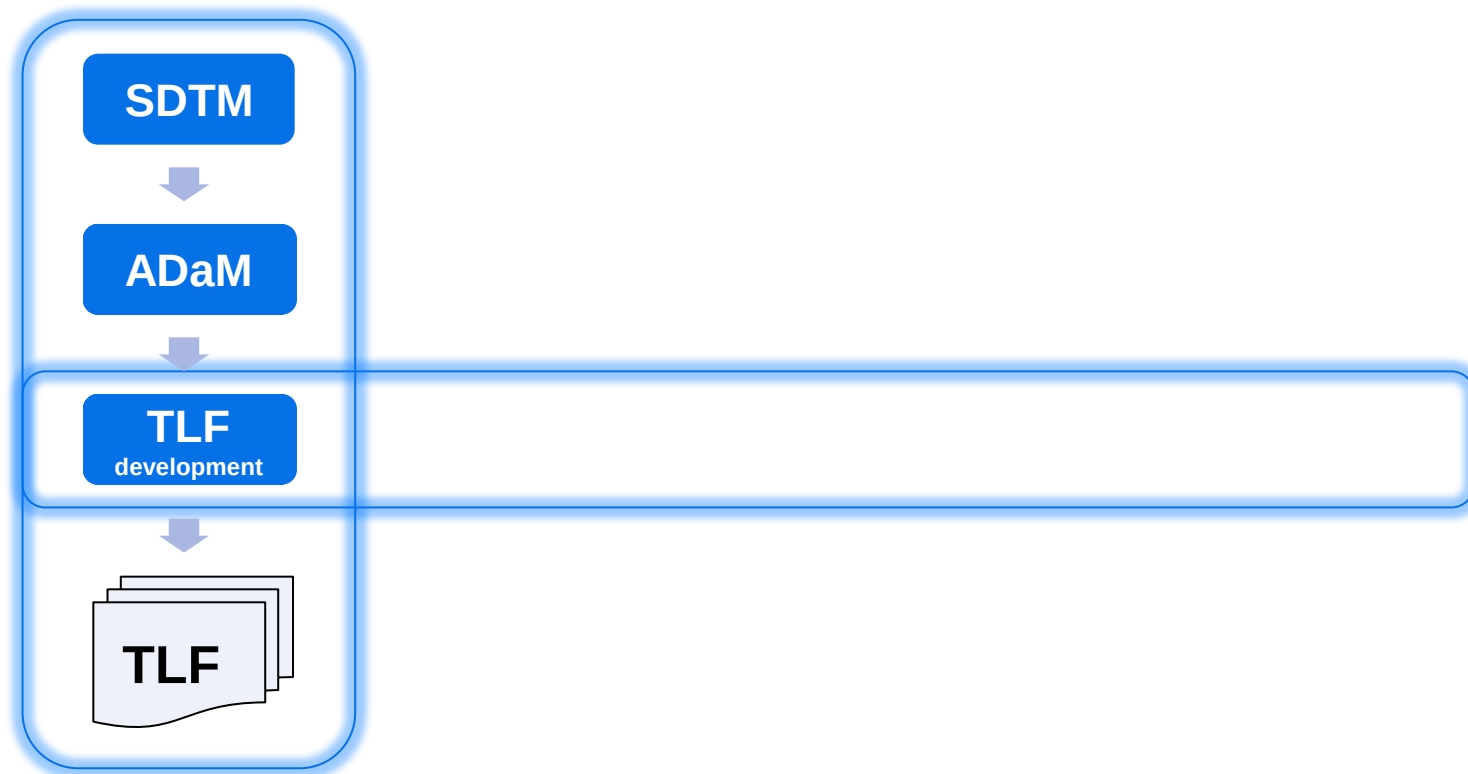
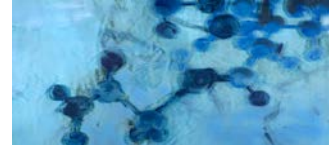
Primary infertility

Duration of infertility (months)

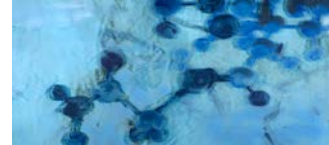
N
Mean (SD)
Median (P25;P75)
Min;max

Primary reason for infertility

Production of End-of-Text Material



Production of End-of-Text Material



Transvaginal Ultrasound: Endometrium • Intention-To-Treat Analysis Set

FORMATS

Treatme 1 Treatme 2 Total

Endometrial triple-layer structure, N (%)

Yes	58 (93.2%)	68 (94.4%)	127 (94.8%)
No	3 (4.8%)	4 (5.6%)	
Total	62 (100%)	72 (100%)	

Endometrial thickness (mm)

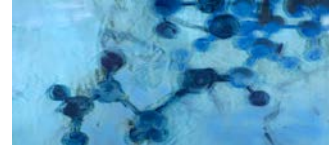
n	62	72	
Mean (SD)	12.1 (4.6)	11.9 (4.5)	
Median	12.0	11.8	
IQ-range	5; 16	5; 15	
Range	2; 22	1; 27	

n: Number of observations
%: Percentage of observations

127 (94.8%)

Dataset Name	Variable Name	Variable Label
ADXX	PARCAT1N	Parameter Category 1 (N)
ADXX	PARCAT1	Parameter Category 1
ADXX	PARAMN	Parameter (N)
ADXX	PARAMCD	Parameter
ADXX	PARAM	Parameter Code
ADXX	AVALL	Analysis Value (C)
ADXX	AVALL	Analysis Value
ADXX	AROUND	Rounding of results

Production of End-of-Text Material



<PARCAT1 by PARCAT1N> - <ANALYSIS SET FORMAT>

<ACTARM 1>	PARCAT1N	PARCAT1	PARAMN	PARAM	PARAMCD
	10	Description	Full control using ADaM Metadata		XXXXXXXXXX
	10	Description			YYYYYYYYYY
	10	Description	13	Parameter	ZZZZZZZZZ

<PARAM by PARAMN>

If PARAM is categorical then present as

<PARAM>, n (%)

<AVALC by AVAL>	xxx (xx%)	xxx (xx%)	xxx
Total	xxx (100%)	xxx (100%)	xxx

If PARAM is continuous then present as

<PARAM>

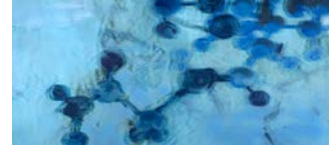
n	xxx	xxx
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)
Median	xx.x	xx.x
IQ-range	xxx; xxx	xxx; xxx
Range	xxx; xxx	xxx; xxx

n: Number of observations

?: Percentage of observations

Dataset Name	Variable Name	Variable Label
ADXX	PARCAT1N	Parameter Category 1 (N)
ADXX	PARCAT1	Parameter Category 1
ADXX	PARAMN	Parameter (N)
ADXX	PARAMCD	Parameter
ADXX	PARAM	Parameter Code
ADXX	AVALC	Analysis Value (C)
ADXX	AVAL	Analysis Value
ADXX	AROUND	Rounding of results

Production of End-of-Text Material



Endometrial Ultrasound: Treatment Analysis Set

Treatment	PARCAT1N	PARCAT1	PARAMN	PARAM	PARAMCD
Treatment 1	10	Endometrium	12	Tripple-layer structure	ENDOTLS
Treatment 2	10	Endometrium	11	Thickness (mm)	ENDOTHCK

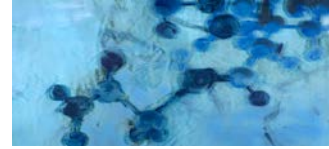
Endometrial Ultrasound: Treatment Analysis Set

Endometrial Ultrasound: Treatment Analysis Set	Endometrial Ultrasound: Treatment Analysis Set	Endometrial Ultrasound: Treatment Analysis Set
Yes	52 (95.2%)	52 (94.4%)
Mean (SD)	12.1 (4.8%)	14.9 (8.6%)
Median	62.0 (100%)	12.5 (100%)
IQ-range	5; 16	5; 15
Endometrial thickness (mm)	22	1; 27
n	62	72
Tripple-layer structure, N (%)	12.1 (4.6%)	11.9 (4.3%)
Mean (SD)	12.1 (4.6%)	11.9 (4.3%)
Median	62.0 (95.2%)	62.5 (94.4%)
IQ-range	5; 16 (4.8%)	5; 15 (5.6%)
Range	0; 22 (100%)	1; 27 (100%)

n: Number of observations
%: Percentage of observations

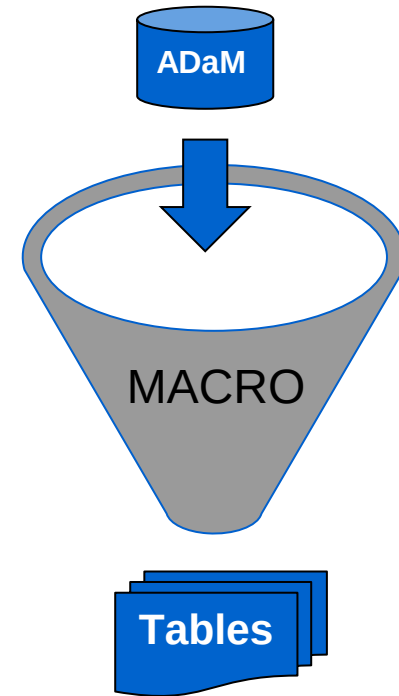
127 (94.8%)

Dataset Name	Variable Name	Variable Label
ADXX	PARCAT1N	Parameter Category 1 (N)
ADXX	PARCAT1	Parameter Category 1
ADXX	PARAMN	Parameter (N)
ADXX	PARAMCD	Parameter
ADXX	PARAM	Parameter Code
ADXX	AVALC	Analysis Value (C)
ADXX	AVAL	Analysis Value
ADXX	AROUND	Rounding of results

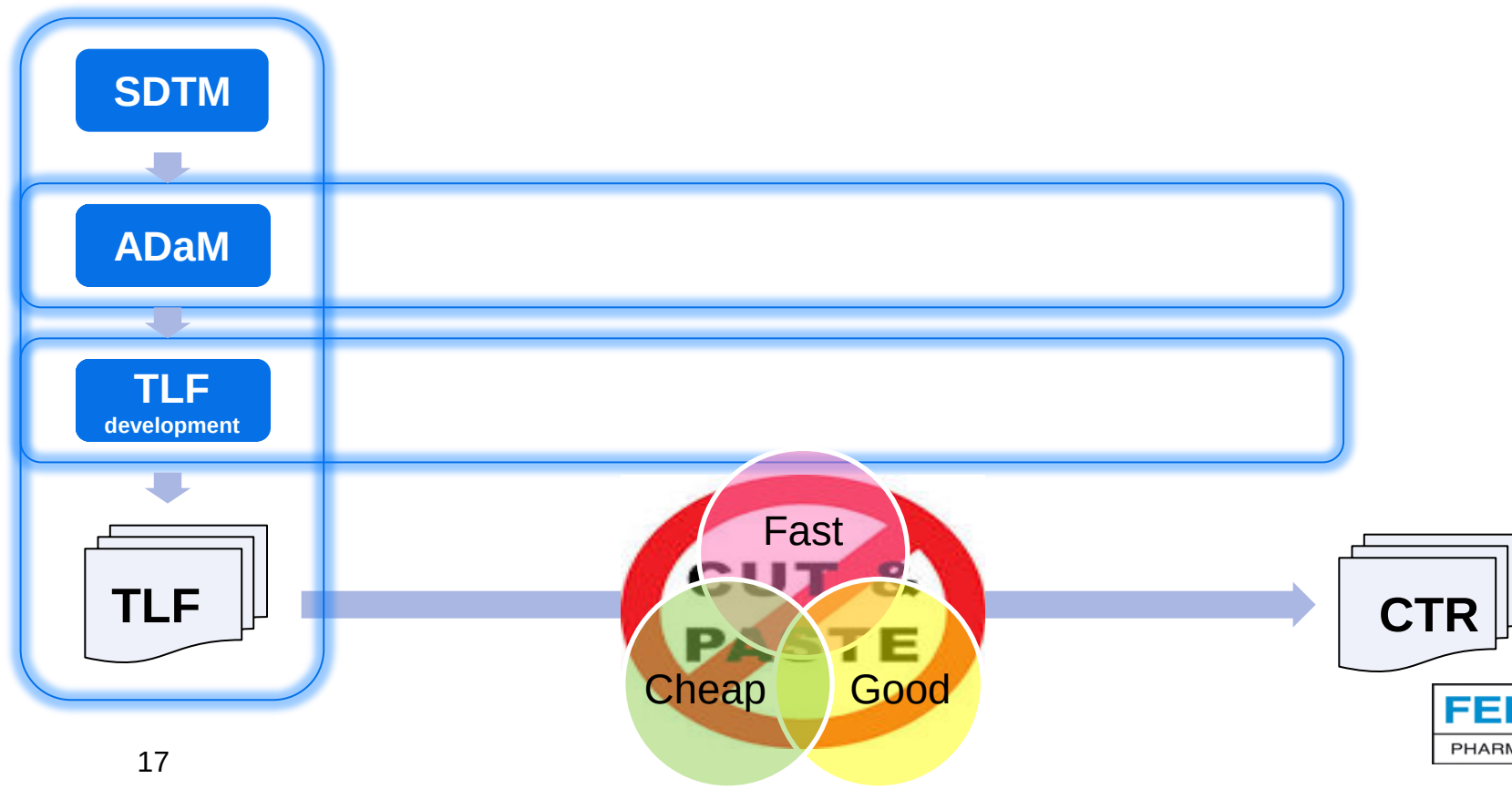
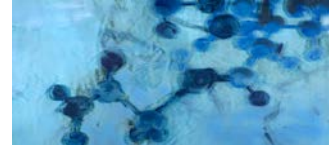


Standard programs

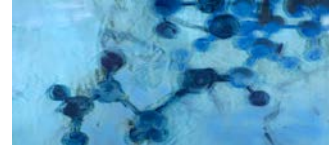
- ▶ 2 types of datasets:
 - ▶ ODS (ADAE, ADMH, ADCM, ...)
 - ▶ BDS (ADEF, ADLB, ADEG, ADVS, ...)
- ▶ 7 Generic table layouts -> 7 validated macros
- ▶ ~90% of summary tables directly from ADaM



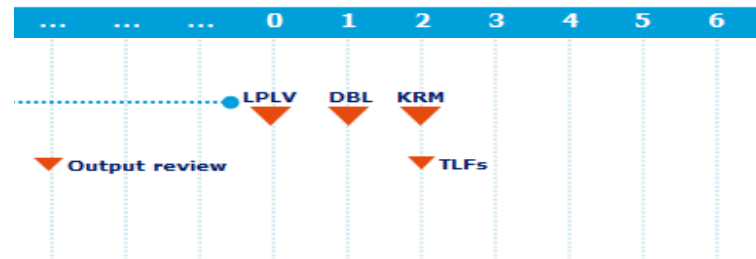
Input to Clinical Trial Report



Fast Track to Approval: Speed and Efficiency

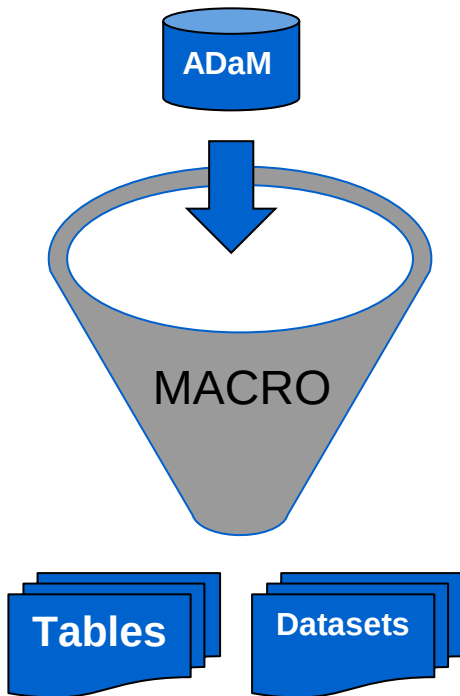
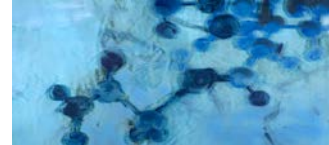


Output review



- ▶ When
 - ▶ Sufficient data is available
- ▶ Who
 - ▶ Statistician
 - ▶ Programmer
 - ▶ Medical writer
 - ▶ Pharmacovigilance physician
 - ▶ Medical responsible
- ▶ Why
 - ▶ Agree on final end-of-text deliverables
 - ▶ Agree on in-text tables
 - ▶ Agree if narratives are needed

In-text Tables



7.4.2 Body Measurements

A summary of the main body measurements is shown in Table 7-6 for the mITT population.

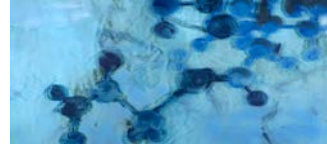
Table 7-6 Body Measurements

	BEM99049 (N=666)	GONAL02 (N=661)
Weight (kg) Mean (SD)	64.2 (10.73)	63.4 (10.44)
BMI (kg/m ²) Mean (SD)	23.7 (3.42)	23.3 (3.23)
BMI, n (%)		
<18.5	15 1.0%	16 2.0%
18.5-<25.0	356 68.0%	360 70.6%
25.0-<30.0	160 20.0%	140 21.0%
>=30.0	35 7.0%	40 6.0%
Maximum abdominal circumference (cm) Mean (SD)	88.1 (9.53)	87.2 (9.39)
Waist-to-hip ratio Mean (SD)	0.77 (0.078)	0.77 (0.077)

[EOT Table 3.1.3]

Treatment groups were comparable in terms of body measurements at baseline. On average, the body weight was 64.0 ± 10.6 kg. The mean BMI was 23.5 ± 3.4 kg/m². While 69% of the subjects were normal weight (BMI 18.5-24.9 kg/m²), the trial population also included 22% overweight subjects (BMI 25.0-29.9 kg/m²), 7% obese subjects (BMI ≥30.0 kg/m²), and 2% underweight subjects (BMI <18.5 kg/m²). The average maximum abdominal circumference was 87.9 ± 9.5 cm. The mean waist-to-hip ratio was 0.77 ± 0.08.

Production of Narratives



ADaM

Subject ID: 0202-103

Event of special interest: Positive β hCG

Trial code: 000004

Treatment allocation: FE 999049

COS#: 1

A 34-year old woman (weight at randomisation: 87.1 kg; AMH at screening: 8 pmol/L) with primary reason for infertility being unexplained infertility, was randomised to treatment with FE 999049 at a daily start dose of 12 μ g while enrolled in the 000004 trial. Duration of stimulation was 9 days starting 03 Apr 2014 and ending 11 Apr 2014. Triggering of final follicular maturation was done with 250 μ g hCG on 12 Apr 2014 and 11 oocytes were retrieved on 14 Apr 2014. Transfer of 1 blastocyst took place on 19 Apr 2014.

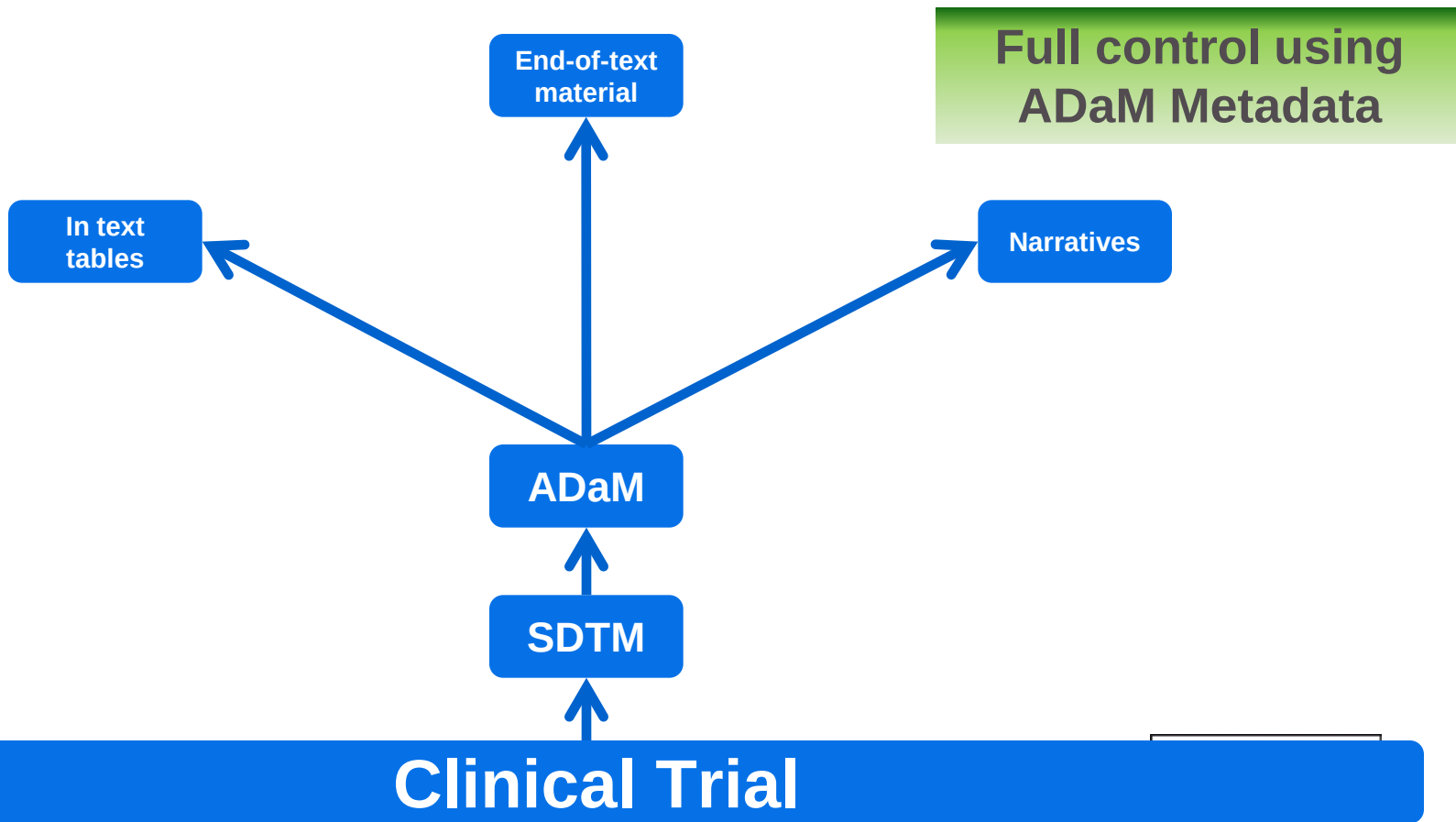
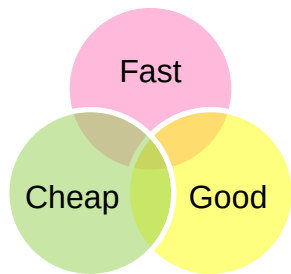
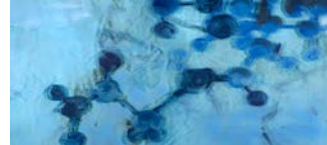
- β hCG: Positive, 1718 mIU/mL, 03 May 2014
- Clinical pregnancy (gestational sac): Positive, 29 May 2014
 - Intrauterine pregnancy: Yes
 - Ectopic pregnancy: No
- Vital pregnancy (intrauterine gestational sac with fetal heart beat): Positive, 29 May 2014
 - Intrauterine gestational sac(s) with fetal heart beat: 1
 - Intrauterine gestational sac(s) without fetal heart beat: 0
 - Intrauterine fetal heart beat: 1
- Ongoing pregnancy (intrauterine viable fetus(es)): Positive, 07 Jul 2014
 - Number of viable fetus(es): 1
- Live birth: Yes, singleton, 18 Dec 2014

Trial Treatment	Start dose (daily)	Start date	Stop date
FE 999049	12 μ g	03 Apr 2014	11 Apr 2014
CETROTIDE	0.25 mg	08 Apr 2014	11 Apr 2014
OVITRELLE	250 μ g	12 Apr 2014	
ENDOMETRIN/LUTINUS	300 mg	15 Apr 2014	21 Apr 2014
	300 mg	22 Apr 2014	28 Apr 2014
	300 mg	29 Apr 2014	03 May 2014

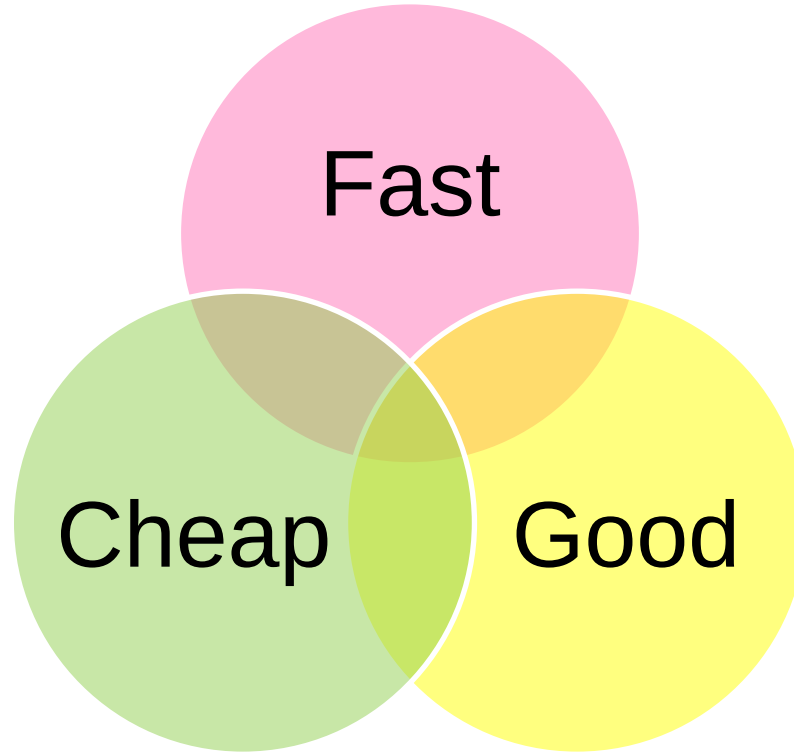
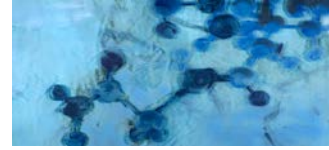
FERRING

PHARMACEUTICALS

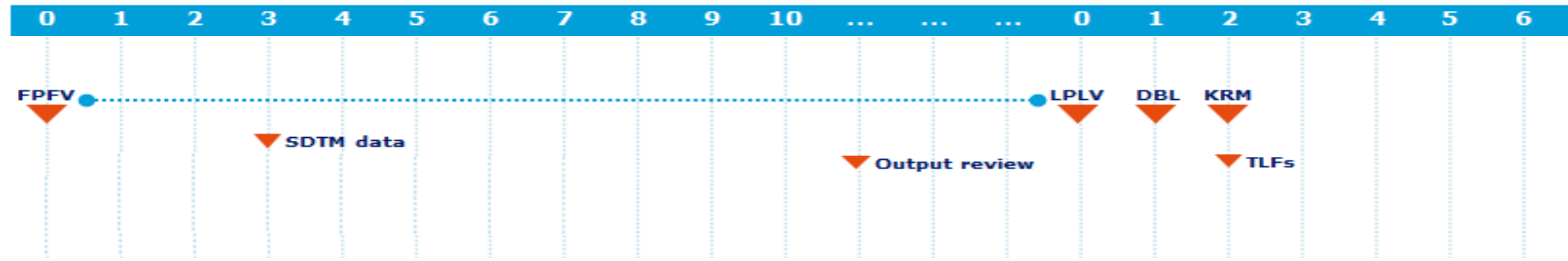
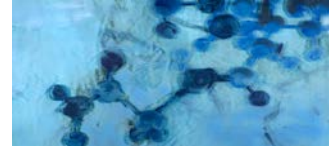
End-of-trial Deliverables



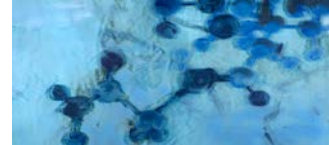
Fast Track to Approval: Speed and Efficiency



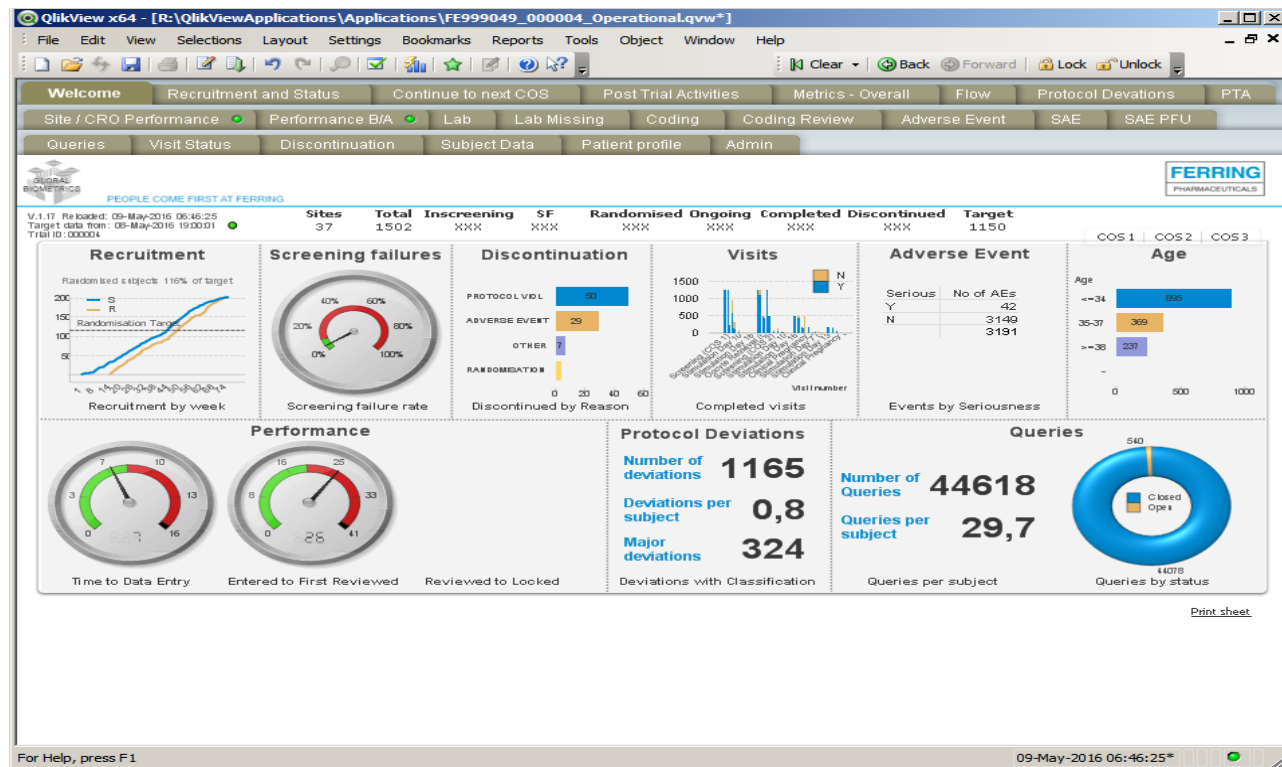
Fast Track to Approval: Speed and Efficiency



Central Monitoring: QlickView Operational

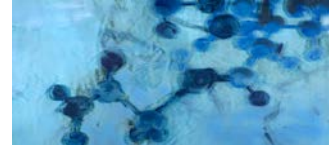


SDTM

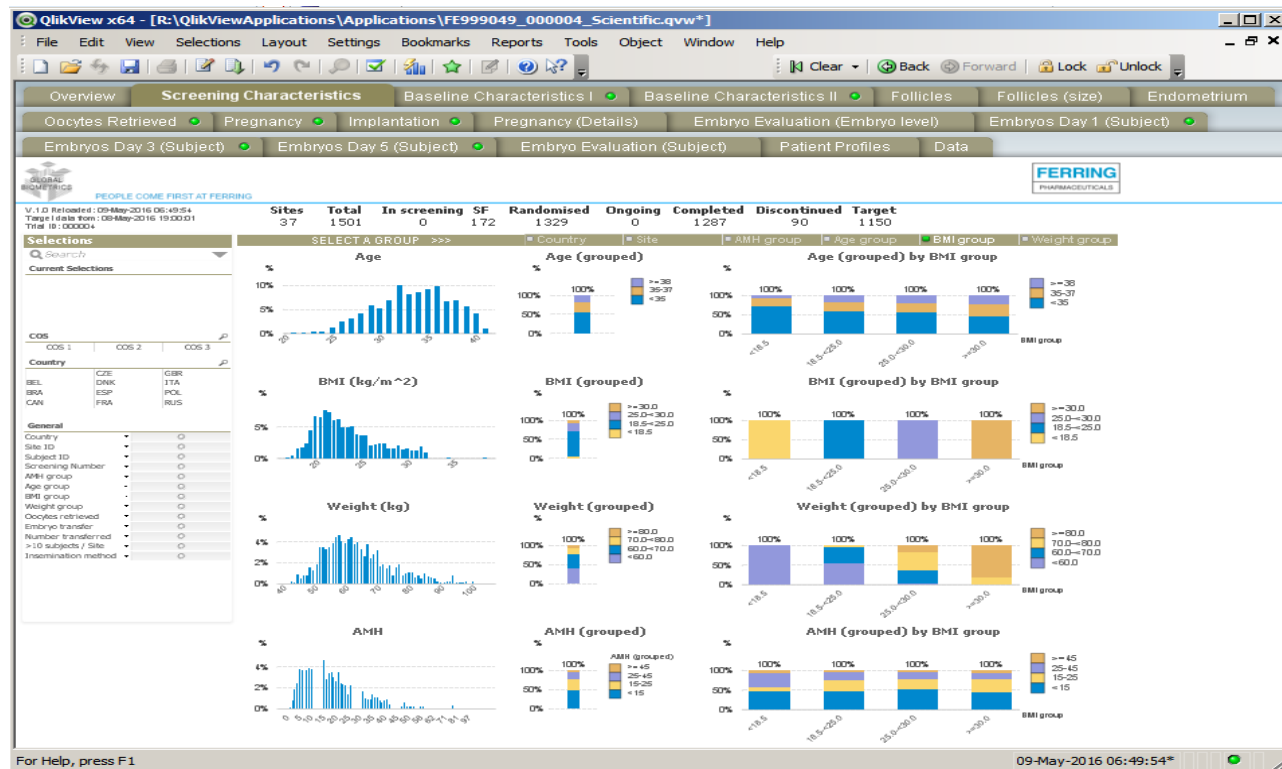


FERRING
PHARMACEUTICALS

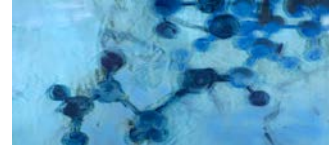
Central Monitoring: QlickView Scientific



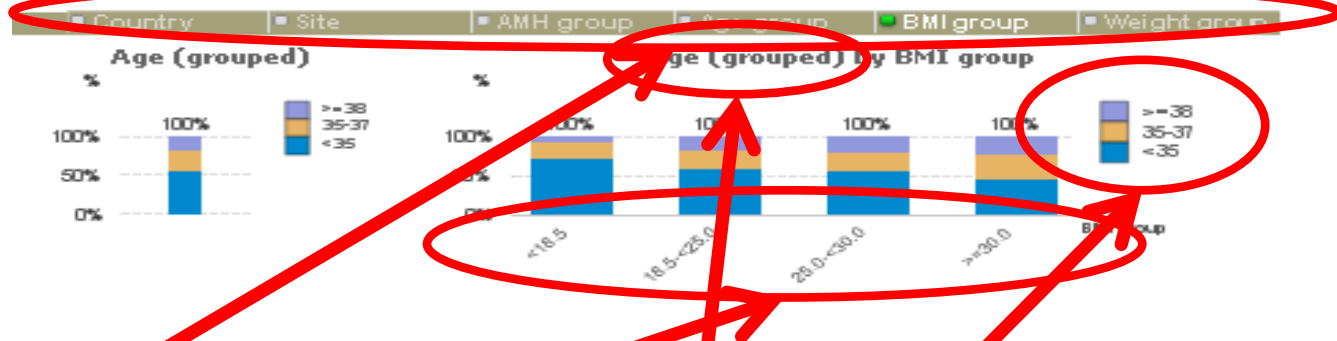
ADaM



Central Monitoring: QlickView Scientific



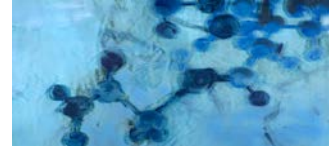
ADaM



Dataset Name	Variable Name	Variable Label
ADSUB	PARCAT1N	Parameter Category 1 (N)
ADSUB	PARCAT1	Parameter Category 1
ADSUB	PARAMN	Parameter (N)
ADSUB	PARAMCD	Parameter
ADSUB	PARAM	Parameter Code
ADSUB	AVALC	Analysis Value (C)
ADSUB	AVAL	Analysis Value
ADSUB	AROUND	Rounding of results

Dataset Name	Variable Name	Variable Label
ADBL	PARCAT1N	Parameter Category 1 (N)
ADBL	PARCAT1	Parameter Category 1
ADBL	PARAMN	Parameter (N)
ADBL	PARAMCD	Parameter
ADBL	PARAM	Parameter Code
ADBL	AVALC	Analysis Value (C)
ADBL	AVAL	Analysis Value
ADBL	AROUND	Rounding of results

Central Monitoring: Patient Profiles



SDTM

ADaM

FE999049 EUPHIII
Patient Profile Safety - 0203-501 0203S0029

07:05 Tuesday, November 10, 2015 1

COS 1

1 - SCREENING				
Age	Primary reason for infertility	Duration of infertility	Clinical pregnancy natural conception	Previous fertility treatment
38	ENDOMETRIOSIS			

1a - PREVIOUS FERTILITY TREATMENT					
Cycle Number	Start Date	Type of fertility treatment	Gonadotropin (trade name)	Positive BhCG	Clinical Pregnancy
1	2012-06	OI+LUI	PUREGON	N	
2	2013-01	OI+LUI	PUREGON	N	

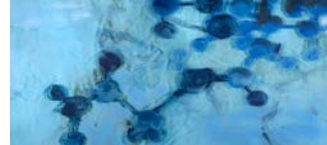
1b - PREVIOUS CLINICAL PREGNANCY(ES)						
Cycle	Cycle Number	Number of fetuses	Fetus Number	Outcome Result	Date of outcome	
REPRODUCTIVE HISTORY	1	1	1	MISABORTION/STILLBORN	2014	

1c - END OF TRIAL	
Date of EOT/Discontinuation	
05MAY2014	
1d - Weight at Randomization	
Weight (kg)	
73.8	

Dataset Name	Variable Name	Variable Label
ADBL	PARCAT1N	Parameter Category 1 (N)
ADBL	PARCAT1	Parameter Category 1
ADBL	PARAMN	Parameter (N)
ADBL	PARAMCD	Parameter
ADBL	PARAM	Parameter Code
ADBL	AVALC	Analysis Value (C)
ADBL	AVAL	Analysis Value
ADBL	AROUND	Rounding of results

AdBkred\SAS\Workspaces\transient\patient_profile_job-72

Central Monitoring: SAS JMP Clinical



ADaM

Central Statistical Monitoring

Site Performance

Subject Population by Study Site

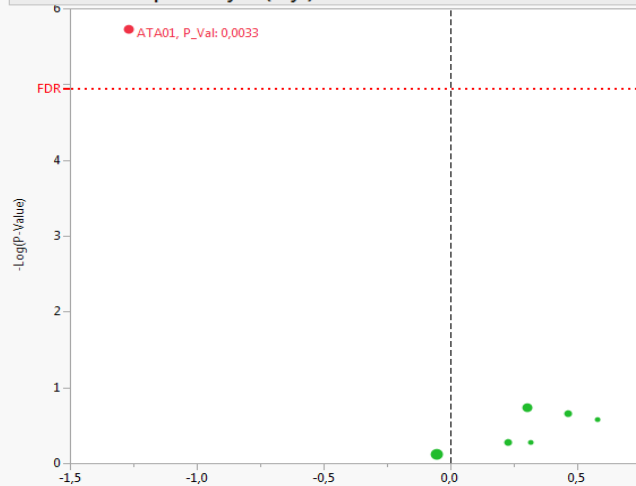
Count						
Study Site Identifier						
ATA01	BRA01	BRA02	NLD01	RUS01	RUS02	USA01
9	27	10	6	7	22	7
All						88

Primary

Primary End Points

Time to death up until day 30 (days)

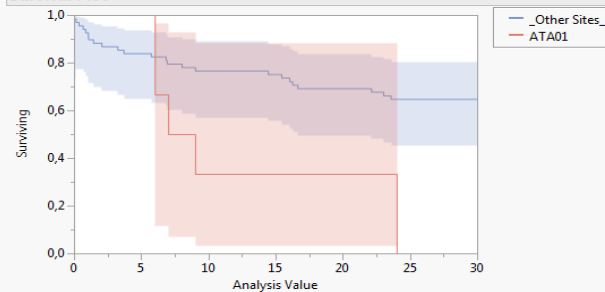
Time to death up until day 30 (days)



Kaplan-Meier

Product-Limit Survival Fit

Survival Plot



Time to event: Analysis Value

Censored by Censor

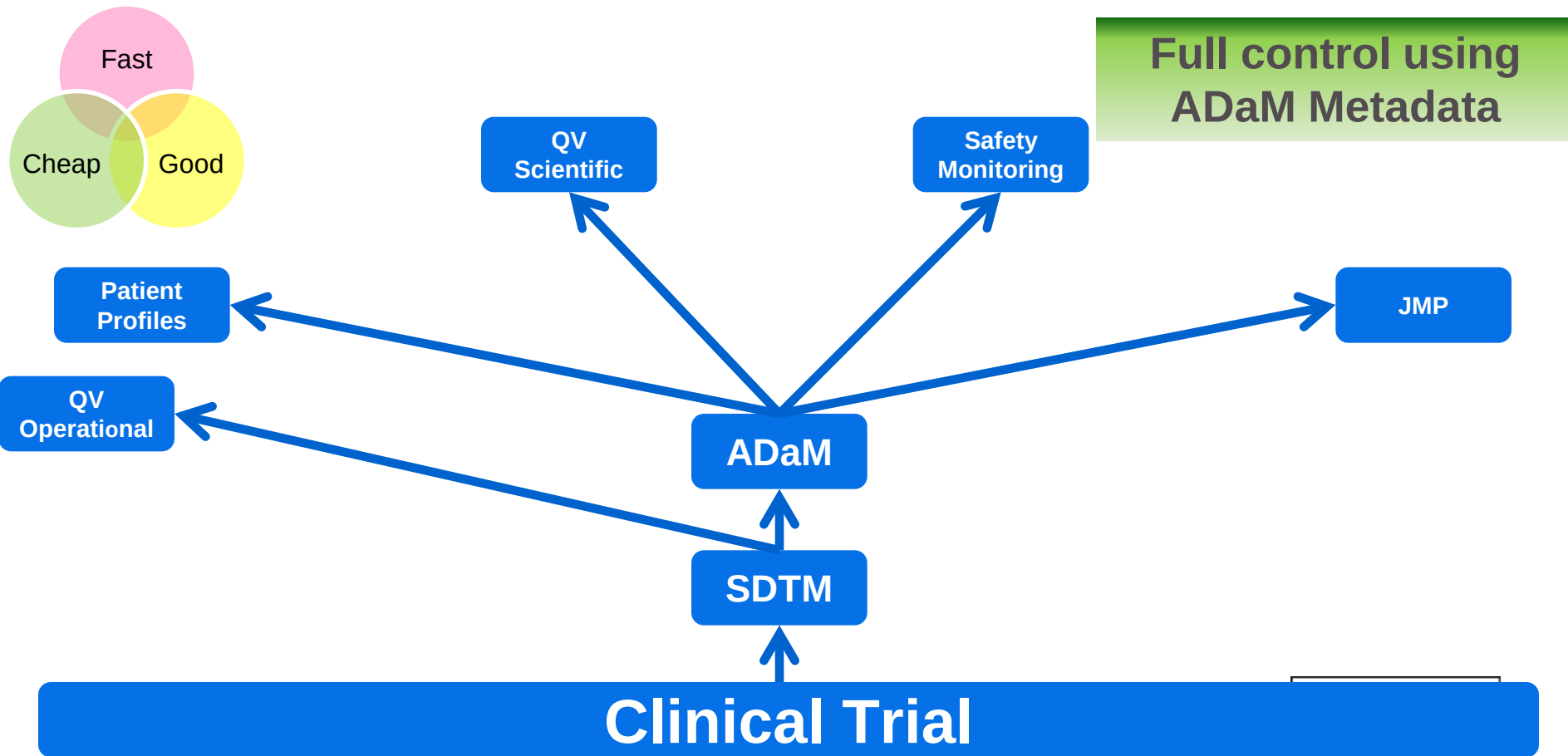
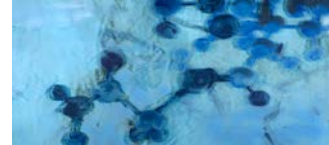
Censor Code 1

Grouped by Group

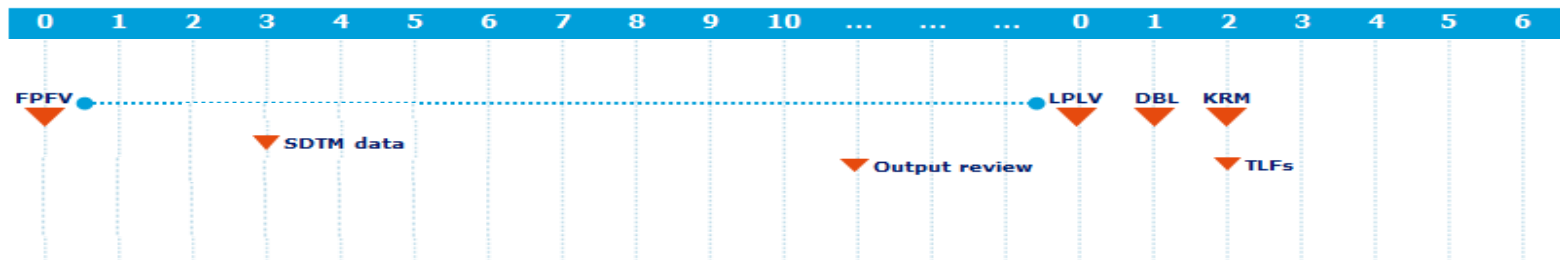
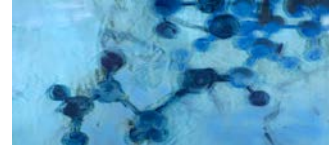
Tests Between Groups

Test	ChiSquare	DF	Prob>ChiSq
Log-Rank	8,6556	1	0,0033*

STREAMing Deliverables @ Ferring



Test Data



- ▶ When
 - ▶ During user acceptance testing of eCRF
- ▶ Why
 - ▶ Start early on development

- ▶ Who
 - ▶ Statistician
 - ▶ Programmer
 - ▶ Data manager
 - ▶ Trial manager / coordinator

STREAMing Deliverables @ Ferring

