

# Interactive clinical study visualisation in enabling the faster decision making

BBS Seminar: Graphics for decision-making in biomedical research and drug development *Tadeusz Lewandowski, Roche Basel* 





**Exploratory Biomarker Analysis** 

**Implementation example** 

Demo



- The exploratory analysis of clinical trials requires flexibility in the results exploration
- The decision making process especially based on biomarker exploratory analysis might be time consuming based on the number of potential candidates and might require the alternative hypothesis generation in the short time
- Visualisation and tabulation of those results in across different biomarkers candidates and ability of cross checking different type of analysis is a key in effective exploration



# Problem statement: regulatory v. exploratory

The exploratory biomarker analysis within the clinical trial usually provides the large number of reports, which using presented flexible framework, allows to reduce the number outputs required for regulatory purposes.

Based on the saem implementation using the *R* Shiny Applications within Ophthalmology 1:

- Efficiency gain by combining study results exploration and code generation
- Flexible and agile solution in increasingly growing complexity of studies and number of biomarker candidates
- Customisations of study specific implementations using the R packages

1 - https://www.lexjansen.com/phuse-us/2020/as/AS01.pdf



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# **Exploratory Biomarker analysis**

- This presentation will focus on the unique capability in visualising the study results of the primary endpoints and the flexibility in exploring different baseline biomarkers, based on the randomly generated data, but reflects the real study analysis scenario.
- In the real study, there might be a good predictive biomarker candidate based on the protocol, which might fail after the study unblinding
- Exploring and finding a new good candidate in short term requires a robust hypothesis generation process



# **Exploratory Biomarker analysis**

- In rider to explore different aspect of analysis, provided example provides a set of standard visualizations:
- Data Table
- Variable Browser
- Selection Bias
- Cross Table
- Uni- and Bivariate Plot
- Response Module
- Time-to-event Analysis
- Forest Response
- Forest Survival
- Overlap Module

- the raw data viewer
- variable data browser
- demographic analysis and selection bias
- cross tabulation of chosen variables and biomarkers
- plotting the variables
- exploration of biomarker using response variable
- exploration of biomarker using Time to event
- exploration using forest for response
- exploration using the forest for time ti event
- cross checking available biomarker populations



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# Implementation example: Data table

ata		select varia	ables				Acuve Fliter Variables
ASL	○ ARS ○ ATE	SUBJID	STUDYID SITEID USUBJID	AGE WEIGHT			
show	only distinct rows						Add Filter Variables
ow 3	0 ❤ entries SUBJID	STUDYID	SITEID	USUBJID	AGE 🖗	WEIGHT	ARS
1	id-1	AB12345	XYZ2	AB12345-XYZ2-id-1	76	67	
2	id-2	AB12345	XYZ1	AB12345-XYZ1-id-2	80	84	ATE
3	id-3	AB12345	XYZ2	AB12345-XYZ2-id-3	23	110	
4	id-4	AB12345	XYZ2	AB12345-XYZ2-id-4	20	79	
5	id-5	AB12345	XYZ2	AB12345-XYZ2-id-5	73	63	
6	id-6	AB12345	XYZ2	AB12345-XYZ2-id-6	55	78	
7	id-7	AB12345	XYZ1	AB12345-XYZ1-id-7	63	93	
8	id-8	AB12345	XYZ1	AB12345-XYZ1-id-8	45	65	
9	id-9	AB12345	XYZ2	AB12345-XYZ2-id-9	46	88	
10	id-10	AB12345	XYZ2	AB12345-XYZ2-id-10	48	71	
11	id-11	AB12345	XYZ1	AB12345-XYZ1-id-11	40	91	
12	id-12	AB12345	XYZ2	AB12345-XYZ2-id-12	81	65	
13	id-13	AB12345	XYZ1	AB12345-XYZ1-id-13	57	81	
14	id-14	AB12345	XYZ2	AB12345-XYZ2-id-14	33	57	
15	id-15	AB12345	XYZ2	AB12345-XYZ2-id-15	36	108	
16	id-16	AB12345	XYZ2	AB12345-XYZ2-id-16	55	88	
17	id-17	AB12345	XYZ1	AB12345-XYZ1-id-17	40	84	
18	id-18	AB12345	XYZ1	AB12345-XYZ1-id-18	34	79	
.ps://sh	iny.roche.com/3.5.1/users/w	olowskv/biom_analysis_final/#ta	ab-5533-2				



# Implementation example: Variable browser

ASL ARS	ATE		ASLAGE remove
now 10 v entries Variable	Search:	10	20 20 27 54 41 46 55 62 69 76 83
SUBJID	Subject Identifier for the Study		
STUDYID	Study Identifier		Add Filter Variables
SITEID	Study Site Identifier		ASL
JSUBJID	Unique Subject Identifier	Real Provide State	
AGE	Age		ARS
VEIGHT		40	
ECOG			ATE
SEX	Sex		
RMCD	Planned Arm Code	20	
OUNTRY	Country	0 20 40	60
nowing 1 to 10 of 34	entries Previous 1 2 3 4 Next		

### Implementation example: Selection bias

									Active Filter Variables
Analysis data: ASL		F	F	M	M	U	U	All Patients	
Biomarker-Evaluable Population (BEP)		(N=219)	(N=201)	(N=175)	(N=163)	(N=6)	(N=6)	(N=400)	Add Filter Variables
RED RMDK1	Age								ASL
	n	219	201	175	163	6	6	400	
Table Comparison	Mean (SD)	40.95 (18.13)	41.03 (18.23)	42.87 (17.71)	43.06 (17.78)	39.83 (13.27)	39.83 (13.27)	41.77 (17.88)	
ALL vs BEP	Median	39	39	42	42	47	47	40	
BEP vs Non-BEP	Min - Max	20 - 90	20 - 90	20 - 81	20 - 81	20 - 51	20 - 51	20 - 90	
) ALL	SEX								
Group Variable	n	219	201	175	163	6	6	400	
SEX •	F	219 (100%)	201 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	219 (54.75%)	
Summarize Variables	м	0 (0%)	0 (0%)	175 (100%)	163 (100%)	0 (0%)	0 (0%)	175 (43.75%)	
AGE SEX	U	0 (0%)	0 (0%)	0 (0%)	0 (0%)	6 (100%)	6 (100%)	6 (1.5%)	
	UNDIFFERENTIATED	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	

https://shiny.roche.com/3.5.1/users/wolowskv/biom\_analysis\_final/#tab-5533-1



# Implementation example: Cross table

Encodings	Note that the columns UN	DIFFERENTIATED were removed a	is they have 0 count			
Analysis data: ASL		F	M U All Patie		All Patients	
		(N=219)	(N=175)	(N=6)	(N=400)	Add Filter Variables
SEX	Age					ASL
Summarize Variables	n	219	175	6	400	
AGE COUNTRY	Mean (SD)	40.95 (18.13)	42.87 (17.71)	39.83 (13.27)	41.77 (17.88)	
	Median	39	42	47	40	
	Min - Max	20 - 90	20 - 81	20 - 51	20 - 90	
	Country					
	n	219	175	6	400	
	BES	51 (23.29%)	54 (30.86%)	2 (33.33%)	107 (26.75%)	
	cuw	59 (26.94%)	51 (29.14%)	1 (16.67%)	111 (27.75%)	
	SXM	58 (26.48%)	38 (21.71%)	2 (33.33%)	98 (24.5%)	
	AFG	51 (23.29%)	32 (18.29%)	1 (16.67%)	84 (21%)	

### Implementation example: Uni- and Bivariate plot



# Implementation example: Response analysis



### Implementation example: Time to Event analysis



# Implementation example: Forest response

Add Filter Variables
Add Filter Variables
Add Filter Variables
Add Filter Variables ASL
ASL
ARS

# Implementation example: Forest Survival

incodings	graph needs to be of a ce	rtain w	idth to	be dis	played							ASL.AGE remove
nalysis data: ATE												20
ARAMCD												O
elect an endpoint to analyze.												20 27 54 41 48 55 62 69 76
				A: Drug	x	B	Placebo	o/C:			B: Placebo/C:	
os 👻	Deselles Disk	Tetal	-	Fuente	Madian	0	ombinat	tion	Henned	05%	Combination A: Drug X	
	Factors	n	n	Evenus	(days)	0.0	Events	(days)	Ratio	Wald CI	better	
m Variable												Add Filter Variables
ABM -	All Patients SEX	400	148	90	82.48	252	164	73.57	1.09	(0.84, 1.42)		ASL
	F	219	88	54	78.49	131	91	67.37	1.19	(0.84, 1.67)		
eference Arm	M	175	59	36	82.48	116	71	86.5	0.98	(0.65, 1.46)		
	U	6	1	0	NA	5	2	136.54	NA	(NA, NA)		
A: Drug X	RACE											ATE
	BLACK OR AFRICAN	40	15	9	60 57	25	10	62.28	0.67	(0.28.1.57)		
fultiple arms automatically combined into a	AMERICAN	40	10		00.07	20	15	OF FO	0.07	(0.20, 1.07)		
ingle arm if more than one value selected.	NATIVE HAWAIIAN OR	20	14	0	76.00	25	15	09.92	0.92	(0.24.2.02)		
omparison Arm	ISLANDER	00	14		10.00	20	10	00.00	0.00	(0.04, 2.00)		
B: Discobo, C: Combination	AMERICAN INDIAN OR	53	18	13	70.01	35	22	75 74	1.04	(0.51, 2.12)		
B: Placebo C: Combination	ALASKA NATIVE				10.01			10.14	1.04	(0.01, 2.12)		
	WHITE	56	23	15	93.09	31	18	41.88	0.71	(0.87, 3.2)		
ultiple arms automatically combined into a	UNKNOWN	53	17	10	68.15	36	24	73.57	0.81	(0.38, 1.71)		
ngie arm il more man one value selected.	OTHER	58	20	9	147.4	38	22	102.65	1.3	(0.59, 2.85)		
ubgroup Variables	MULTIPLE	47	19	10	110.93	28	19	68.62	1.74	(0.8, 3.78)		
e taken from ASL	[0.6314.5.687)	184	68	42	76.99	116	80	67.37	1.21	(0.83, 1.77)		
SEX RACE BMRK1	[5.687,24.12]	186	69	41	83.25	117	73	70.18	1.2	(0.81, 1.76)		
ITTGEFL										0.1	1	10
ITTWIFL												
ITTGE2EI												
ITTOFAEL												
IIIGE3FL												
ARM												
ACTARM												

### Implementation example: Overlap module





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# Acknowledgments

Internal software development team for providing the flexible framework and author of presented shiny implementation based on the random data: Vincent Wolowski



# Doing now what patients need next