



Presentation No: DV10
Stream: Data Visualization (DV)

PHUSE US Connect 2021

*Topline Results Dashboard
with R Markdown &
Flexdashboard*



Robert Adams

Harsha Kalikivayi



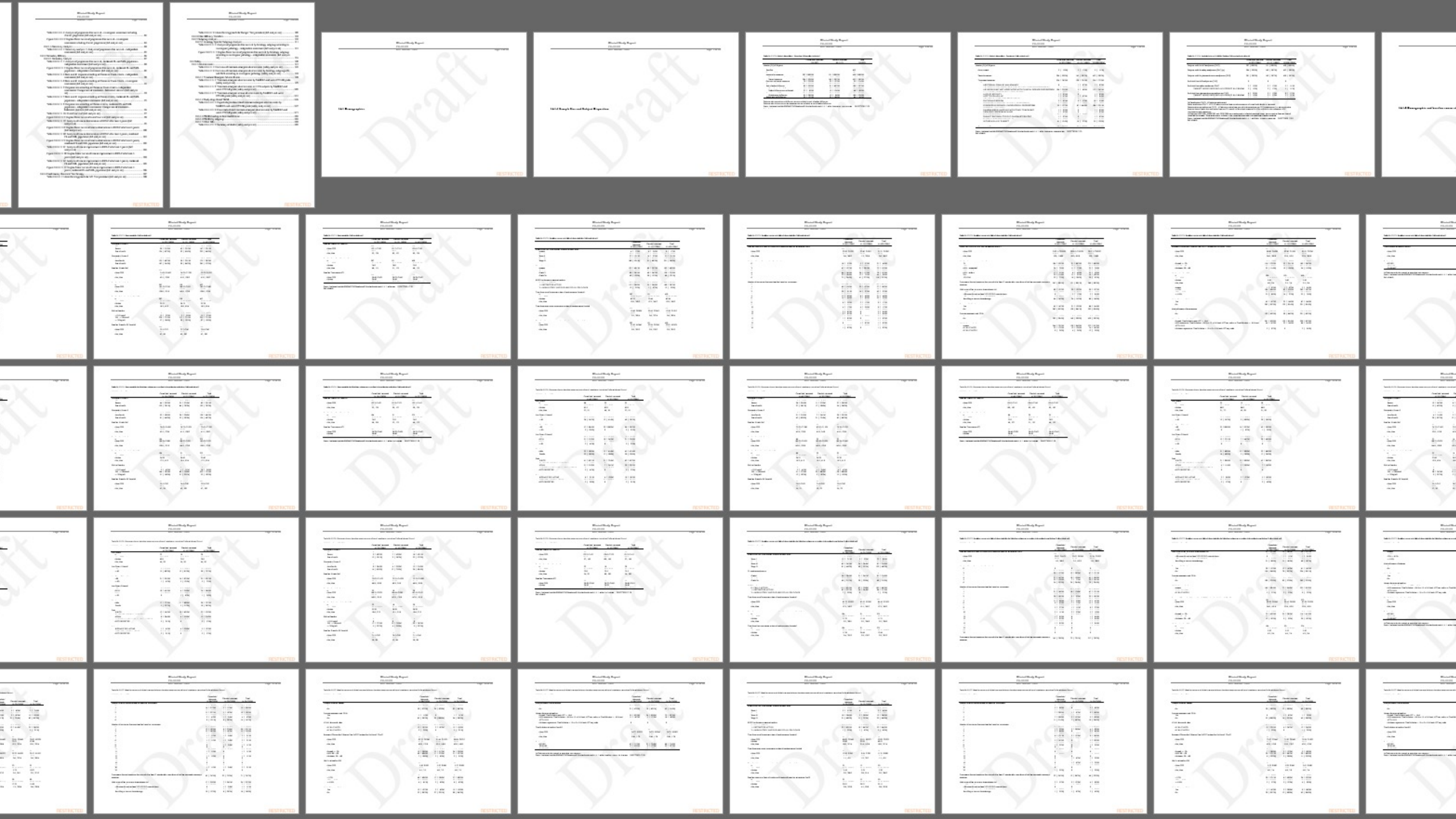


Rationale – Topline Results (TLRs) – Visualization of TLRs

- TLRs are preliminary key results of a clinical trial
 - Pre-selected sets of demographic, safety and efficacy (primary / secondary endpoints) high-level summaries
- Time critical (usually within hours after DB lock / unblinding)
- Usually statistics printed in tables
- Not intuitive to interpret
 - Insights into underlying trends in results not straightforward



- Visualization of TLRs might give faster insights
 - More pleasant to review
- Interactive navigation through document might increase accessibility / foster more vital discussions about results





Rationale – Technology

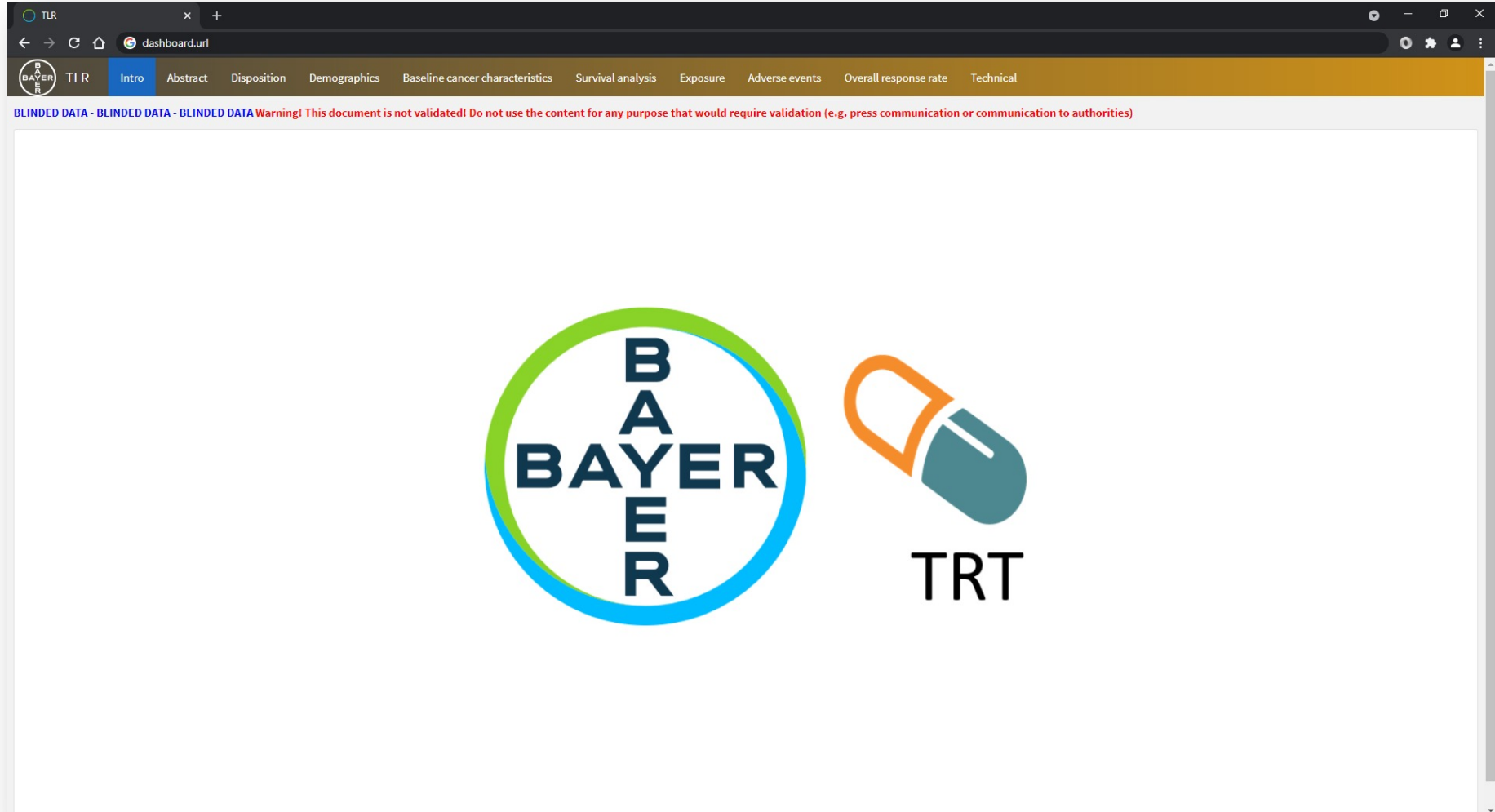


- Self-contained HTML file:
 - Javascript, HTML, CSS, data (tables), visuals
- (HTML / CSS / Javascript) allow creation of interactive standalone files
 - No app; no hosting; no server
 - Still interactive features / navigation possible
- R / R Markdown / Flexdashboard / Flextable
 - R wrapper packages are easy interfaces to web stack – no knowledge of HTML, JS, CSS required (beneficial though)
- Programmatic pipeline decouples data (pre)processing, generation of visual artefacts (tables or figures) & document generation
 - Very flexible use of artefacts in down-stream applications / documents
 - Allows flexible integration in agile frameworks (Git, Team programming)



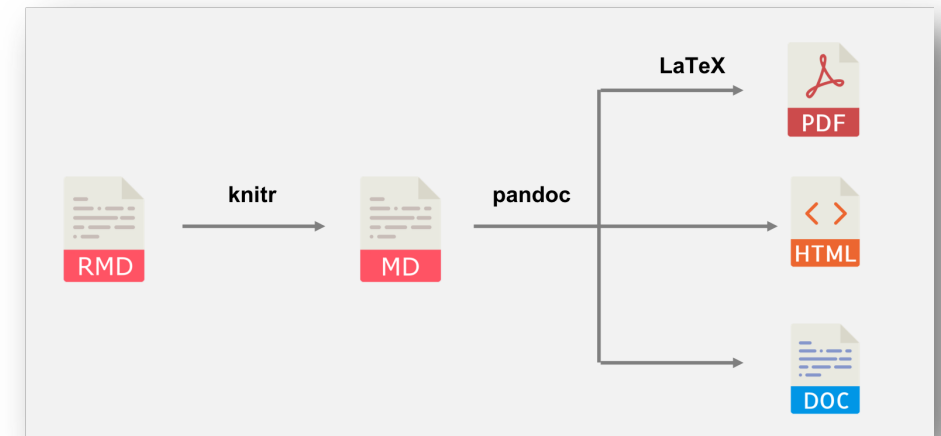
First Look

“App-look & feel” – still just one self-contained HTML file in a modern browser



R / Rmarkdown

- Combine code, results and free text into one document (incl. Figures, Tables, Formulas)
- Analysis steps, documentation, output transparently into one document
- Markdown documents can be compiled into multiple output formats:
 - Output HTML, PDF, Word documents
 - .Rmd file
 - Either code + formatting + text
 - Or formatting and sourcing of .R source scripts
- Could be standardized documentation format for R-projects



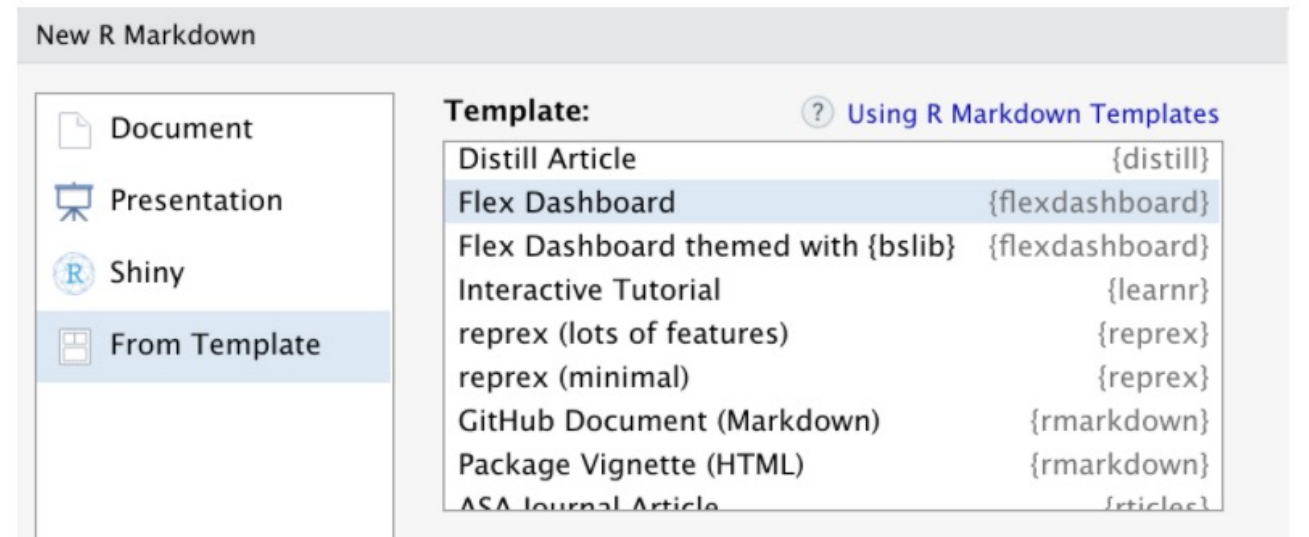
- Human readable, simple syntax, a reminder for your future self (code & documentation), easy to modify, flexible export formats, easy to share*



R / Flexdashboard

- Make it easy to create interactive dashboards for R, using R Markdown
- Flexible and easy to specify row and column-based layouts
 - Intelligent re-sizing to fill the browser and adapted for display on mobile devices
- Customizable
 - Colors, Fonts, Layouts
- Very easy start with RStudio

To author a **flexdashboard** you create an [R Markdown](#) document with the `flexdashboard::flex_dashboard` output format. You can do this from within RStudio using the **New R Markdown** dialog:

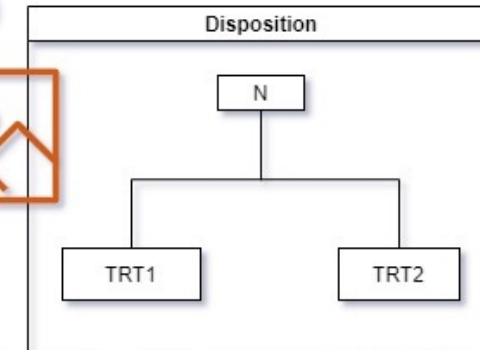


Workflow outline

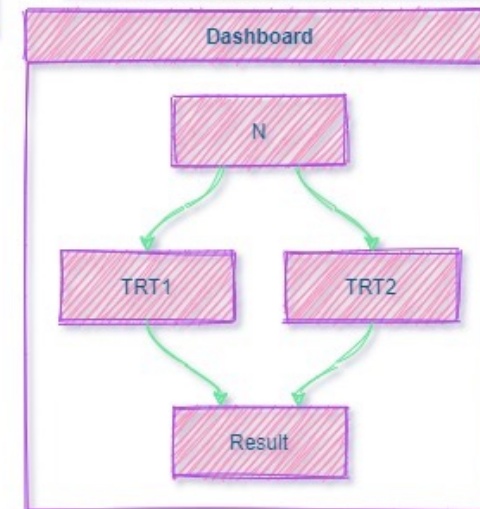


Tables and figures creation

Title 1	Title 2	Title 3
Value 1	Value 2	Value 3
Value 4	Value 5	Value 6
Value 7	Value 8	Value 9
Value 10	Value 11	Value 12



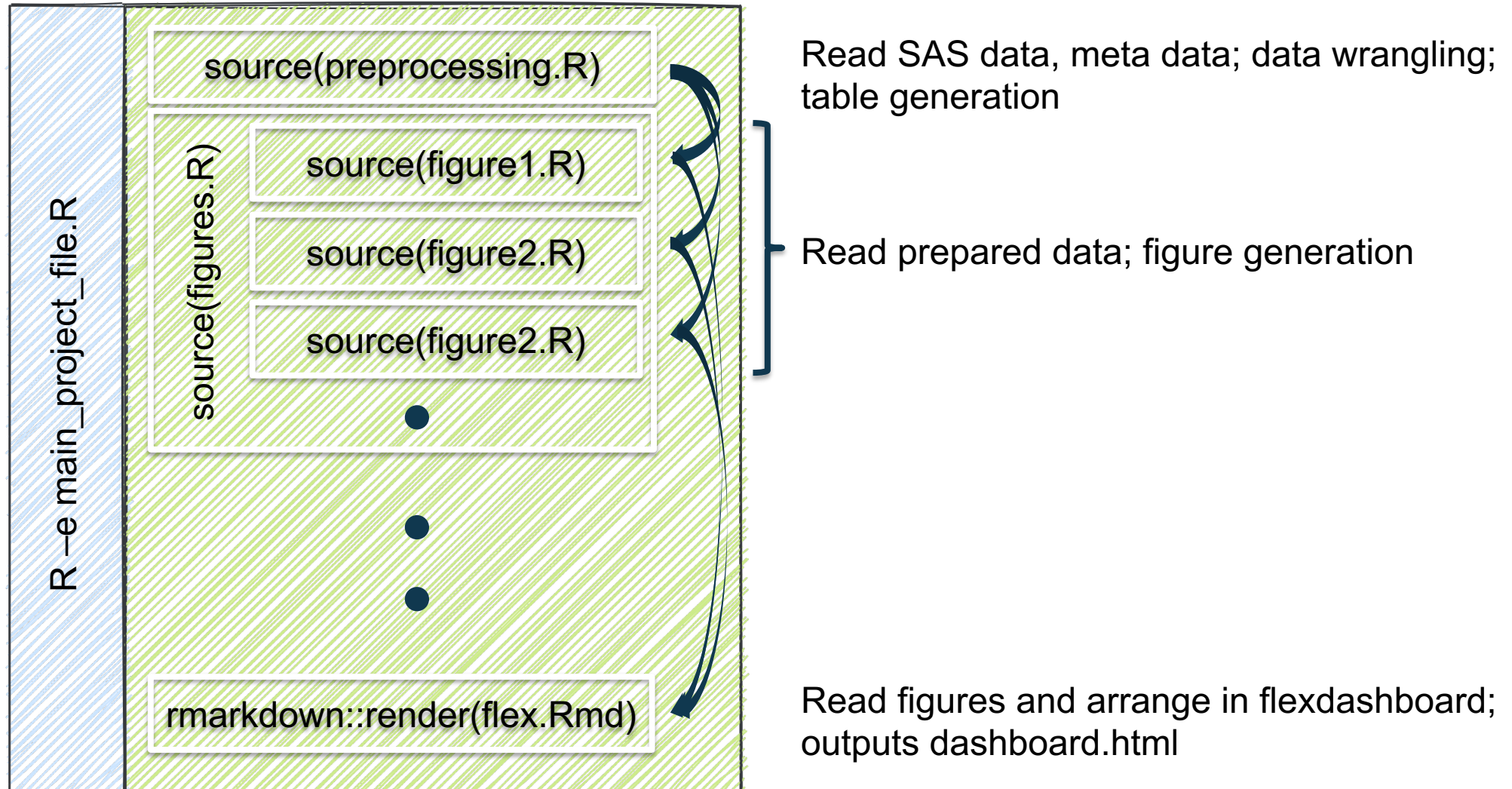
Dashboard creation
(document output)





R – Project organization – easy collaboration & maintenance

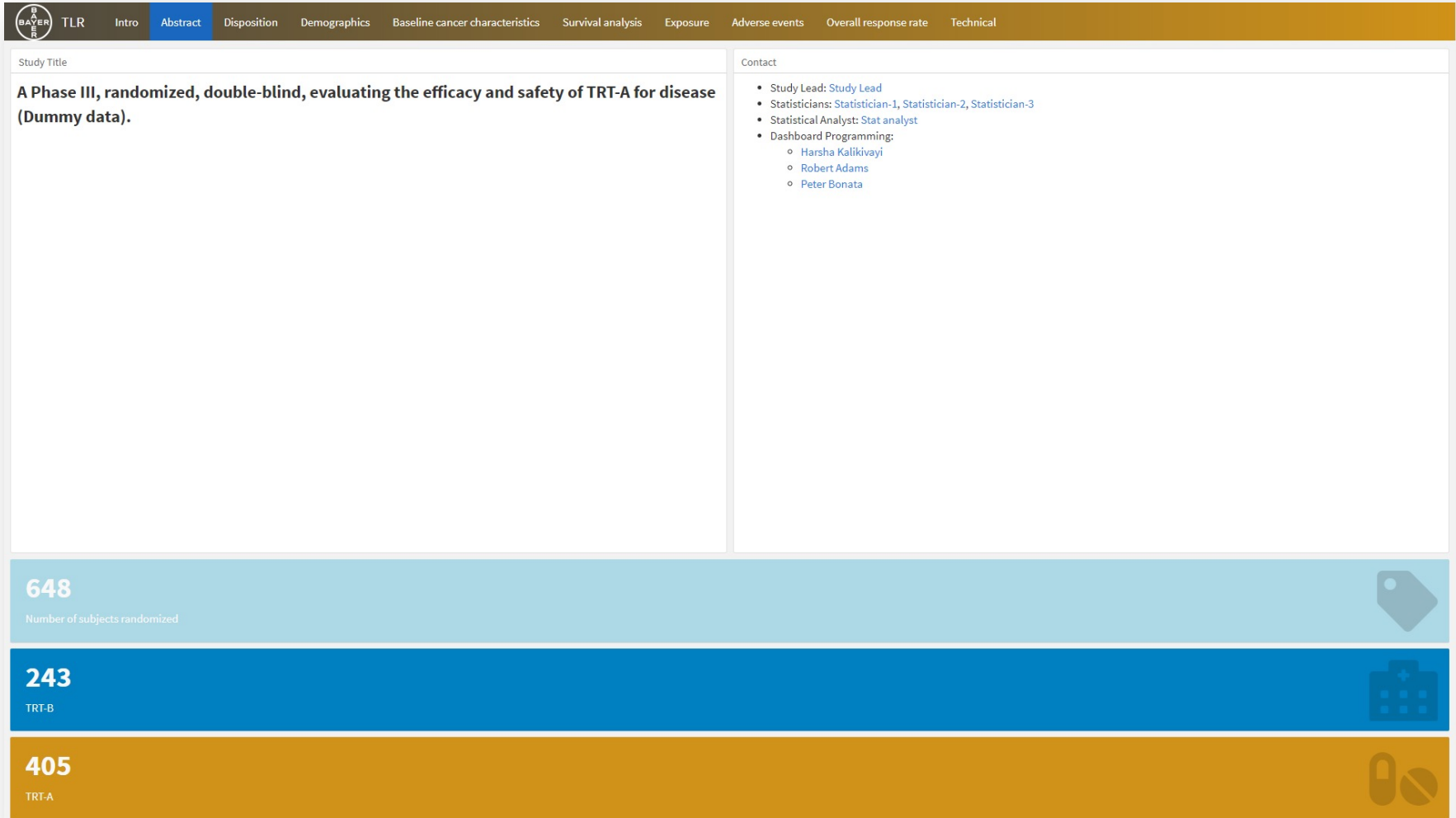
File names are descriptive – not actual file names





Dashboard Details

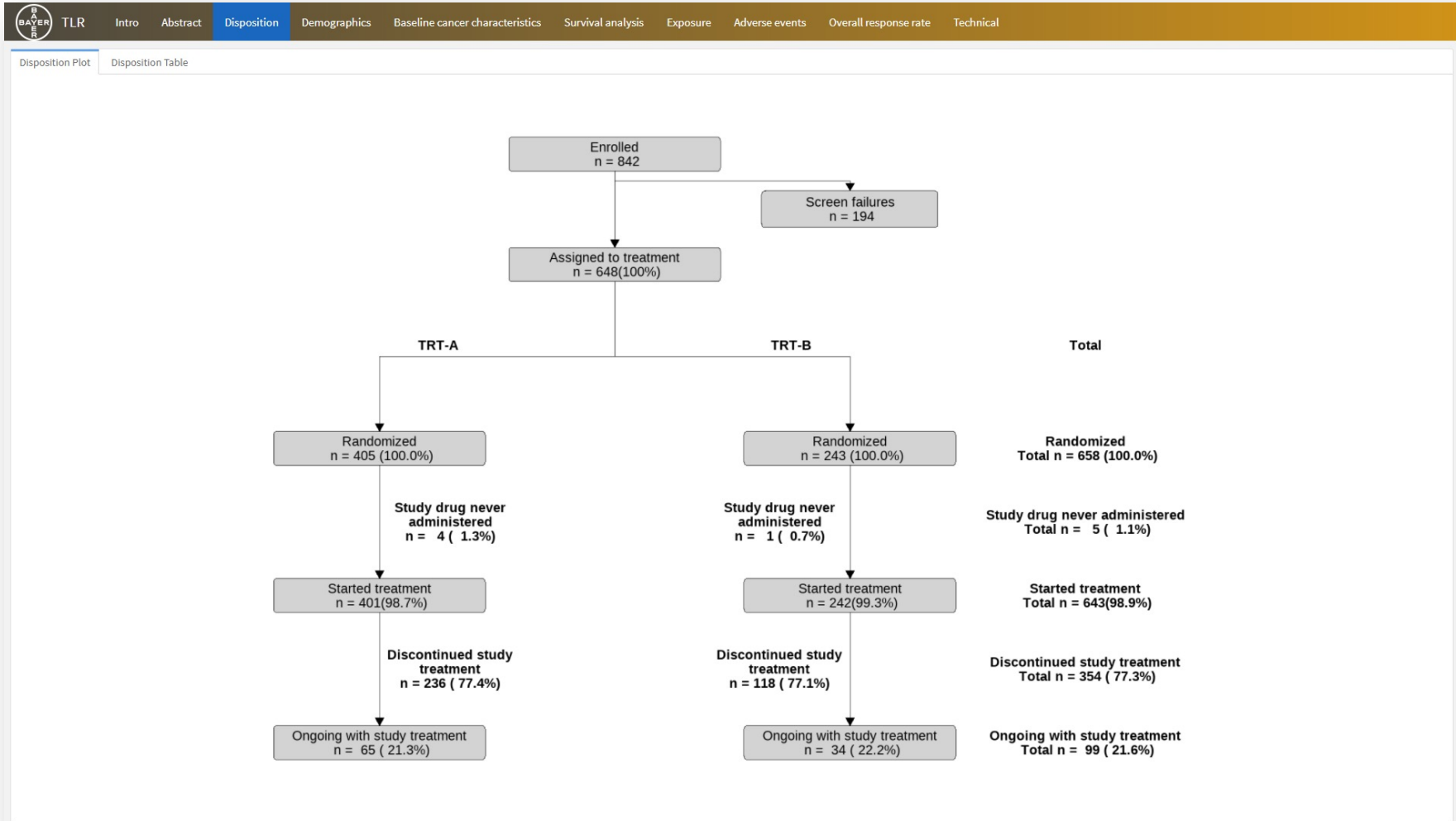
Abstract tab (dummy data - perhaps inconsistent)





Dashboard Details

Disposition tab – plot (dummy data - perhaps inconsistent)





Dashboard Details

Disposition tab – table (dummy data - perhaps inconsistent)

TLR Intro Abstract Disposition Demographics Baseline cancer characteristics Survival analysis Exposure Adverse events Overall response rate Technical			
Disposition Plot Disposition Table			
Subject disposition - Overview (all enrolled subjects)			
	TRT-A	TRT-B	TOTAL
Number (%) of Subjects			
Enrolled			842
Screening failures			194
Assigned to treatment	405(100%)	243(100%)	648(100%)
Study drug never administered	4 (1.3%)	1 (0.7%)	5 (1.1%)
Started treatment	401(98.7%)	242(99.3%)	643(98.9%)
Ongoing with study treatment	65 (21.3%)	34 (22.2%)	99 (21.6%)
Discontinued study treatment	236 (77.4%)	118 (77.1%)	354 (77.3%)
End of safety follow-up	128 (42.0%)	52 (34.0%)	180 (39.3%)
Completed safety follow-up	93 (30.5%)	41 (26.8%)	134 (29.3%)
Safety follow-up not performed	35 (11.5%)	11 (7.2%)	46 (10.0%)
Entered active follow-up	96 (31.5%)	60 (39.2%)	156 (34.1%)
Ended active follow-up	64 (21.0%)	44 (28.8%)	108 (23.6%)
Ended survival follow-up	43 (14.1%)	21 (13.7%)	64 (14.0%)
Subjects who entered active follow-up are not included in end of safety follow-up.			
Subjects who did not receive the treatment are not included in end of safety follow-up.			
/pgms/t_14_1_adds_disposition_overview.sas DDMMYYYY hh:mm			



R / Flextable

- Easy table creation for reporting and publications
- Tables can be embedded in HTML, PDF, Word or PowerPoint from R Markdown documents
- Integrates nicely in tidyverse / pipe syntax of modern data science packages in R

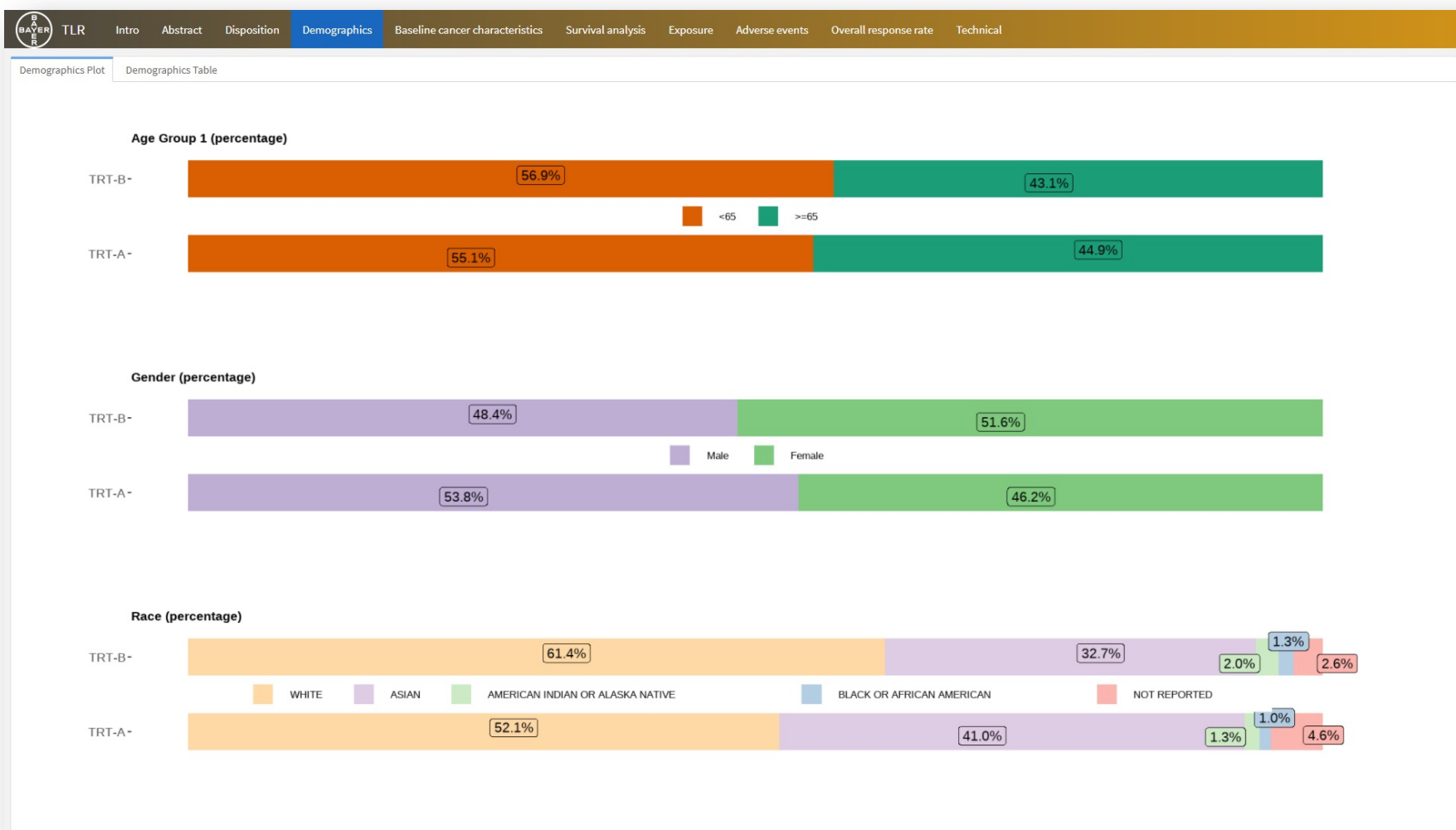
```
haven::read_sas("XXX.sas7bdat") %>%  
  select(-category) %>%  
  flextable() %>%  
  align_text_col(align = "left") %>%  
  autofit() %>%  
  bold(bold = TRUE, part = "header") %>%  
  fontsize(size = 16, part = "all") %>%  
  set_header_labels(text = "") %>%  
  padding(padding.top = 5, part = "all") %>%  
  padding(padding.bottom = 5, part = "all")
```

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/pgms/t_14_1_adds_disposition_overview.sas DDMMYYYY hh:mm			



Dashboard Details

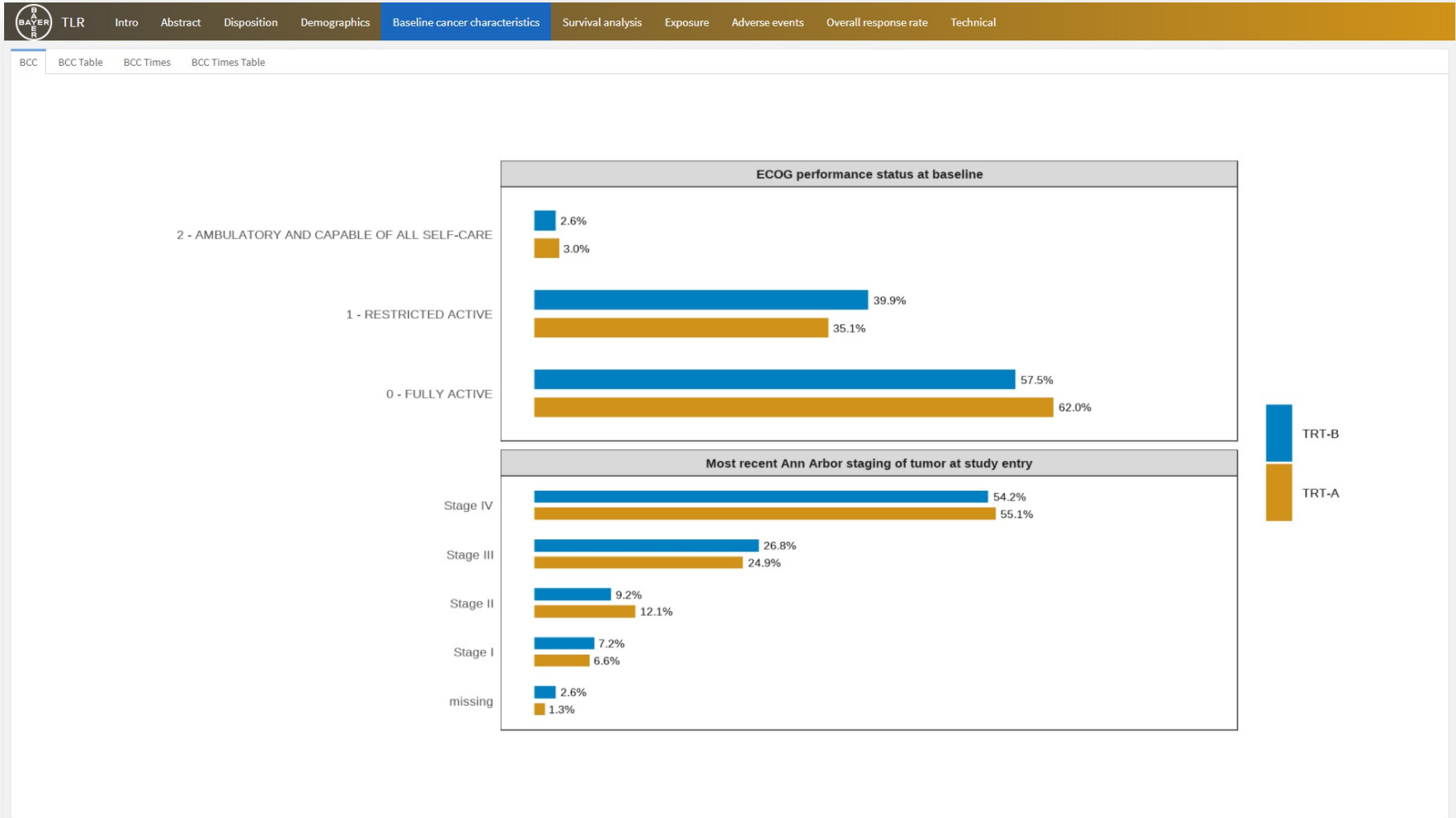
Demographics (dummy data - perhaps inconsistent)





Dashboard Details

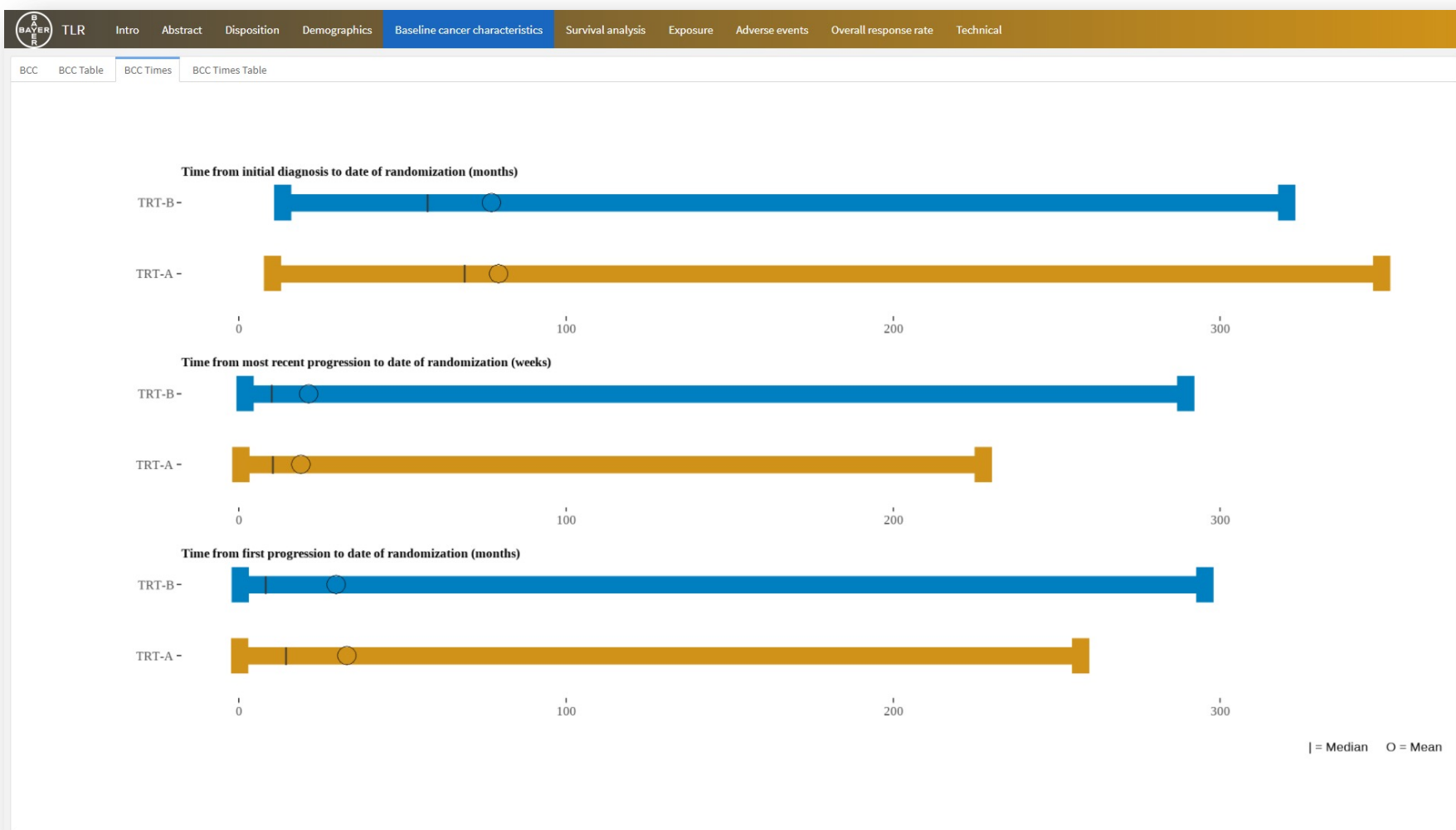
Baseline Cancer Characteristics (dummy data - perhaps inconsistent)





Disposition plot

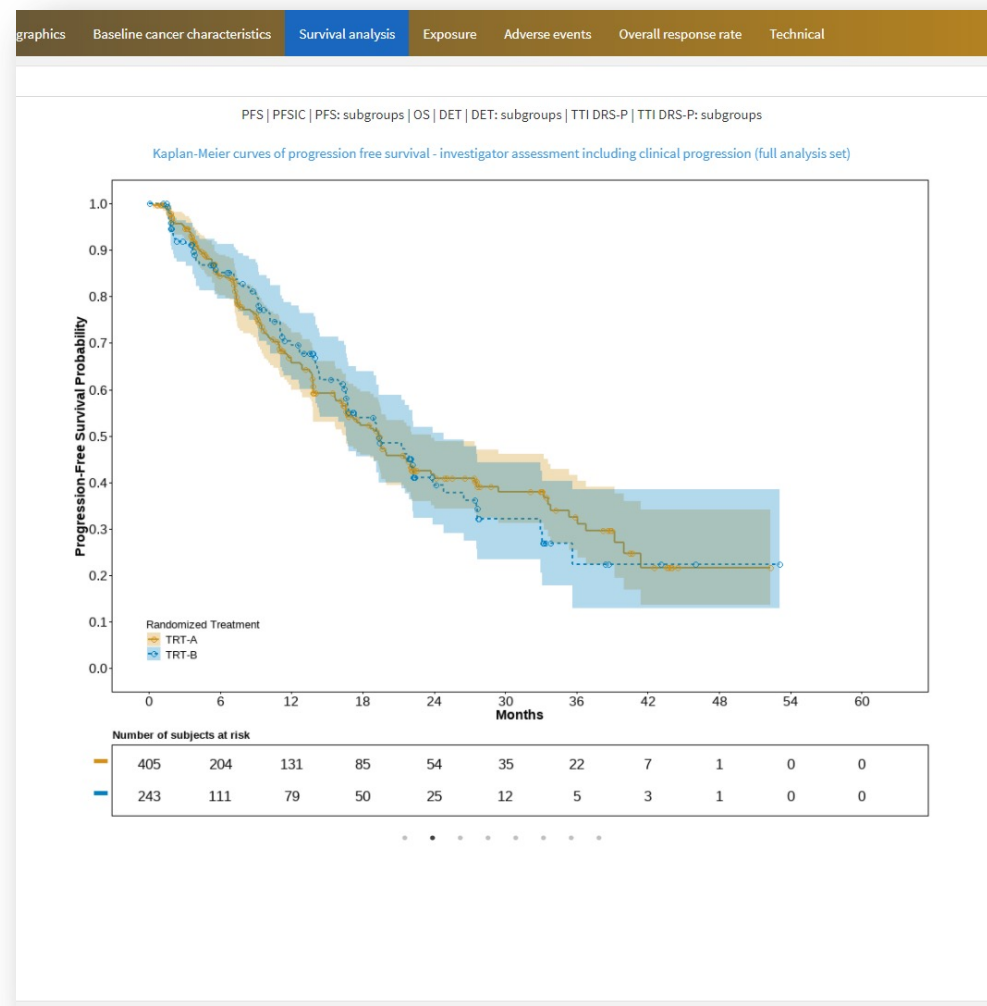
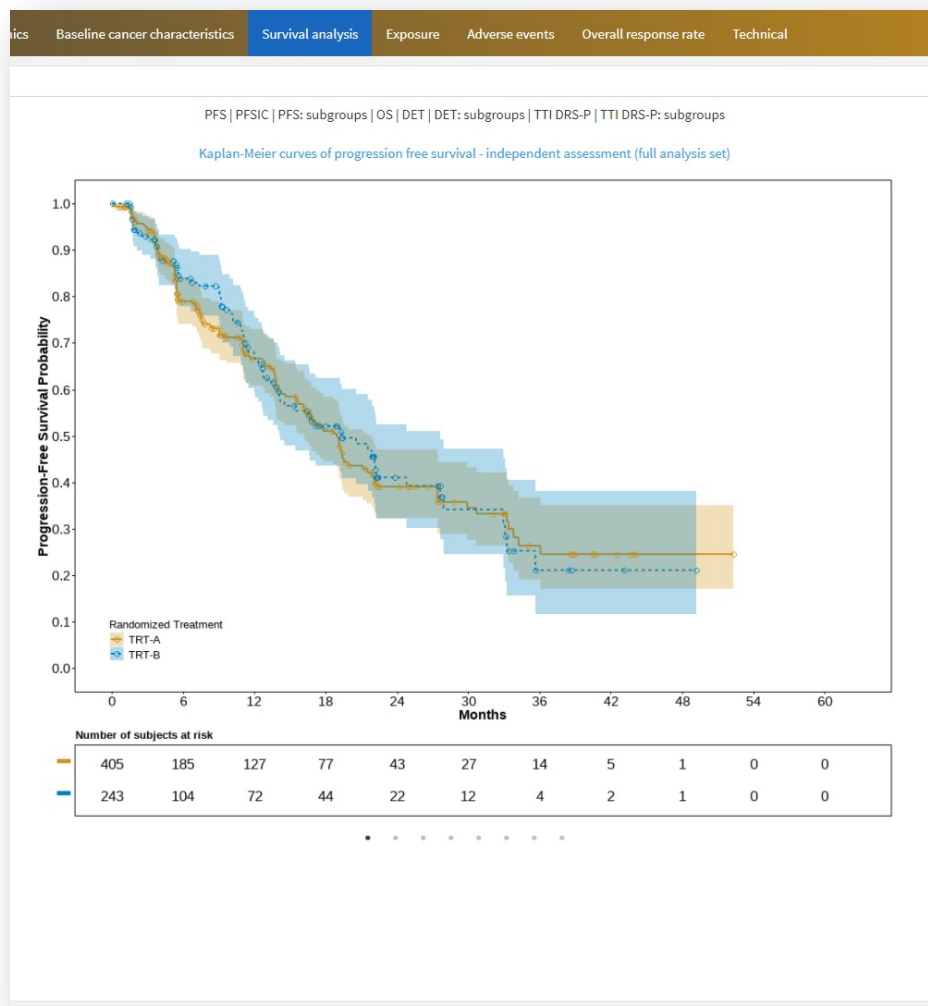
Baseline Cancer Characteristics – ctd (dummy data - perhaps inconsistent)





Dashboard Details

Kaplan Meier Carousel (dummy data - perhaps inconsistent)





Survival Table Carousel (dummy data - perhaps inconsistent)



cancer characteristics	Survival analysis	Exposure	Adverse events	Overall response rate	Technical
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PFS | PFSIC | PFS: subgroups | OS | DET | DET: subgroups | TTI DRS-P | TTI DRS-P: subgroups

Kaplan-Meier curves of progression free survival - investigator assessment including clinical progression (full analysis set)

Analysis of progression free survival - investigator assessment including clinical progression (full analysis set) - Overall					
		TRT-A	TRT-B	TOTAL	
N		405 (100.0%)	243 (100.0%)	648 (100.0%)	
Number (%) of subjects with event		136 (44.6%)	75 (49.0%)	211 (46.1%)	
Number (%) of subjects censored		169 (55.4%)	78 (51.0%)	247 (53.9%)	
25th percentile [95% CI]	(months)	9.2 [7.4, 11.0]	10.2 [8.0, 13.9]	9.5 [7.9, 11.0]	
Median [95% CI]	(months)	19.4 [16.3, 22.1]	19.3 [16.6, 23.9]	19.4 [16.6, 22.0]	
75th percentile [95% CI]	(months)	40.0 [35.4, A]	35.7 [27.6, A]	40.0 [35.4, A]	
Range (including censored values)	(months)	(0.0** - 52.3**)	(0.0** - 53.1**)	(0.0** - 53.1**)	
Range (without censored values)	(months)	(0.4 - 41.4)	(1.5 - 35.7)	(0.4 - 41.4)	
25th percentile [95% CI]	(days)	279 [224, 335]	311 [242, 422]	288 [241, 336]	
Median [95% CI]	(days)	590 [497, 674]	588 [504, 726]	590 [506, 671]	
75th percentile [95% CI]	(days)	1218 [1077, A]	1086 [840, A]	1218 [1077, A]	
Range (including censored values)	(days)	(1** - 1592**)	(1** - 1617**)	(1** - 1617**)	
Range (without censored values)	(days)	(11 - 1260)	(46 - 1086)	(11 - 1260)	
Progression free survival rate at Month 6 [95% CI]		0.845 [0.801, 0.888]	0.852 [0.793, 0.910]	0.847 [0.812, 0.882]	
Progression free survival rate at Month 12 [95% CI]		0.658 [0.597, 0.719]	0.696 [0.616, 0.775]	0.671 [0.623, 0.720]	
Progression free survival rate at Month 18 [95% CI]		0.523 [0.455, 0.591]	0.540 [0.448, 0.631]	0.528 [0.474, 0.583]	
Progression free survival rate at Month 24 [95% CI]		0.417 [0.346, 0.489]	0.395 [0.297, 0.493]	0.409 [0.351, 0.467]	
Hazard ratio [95% CI]		0.979 [0.737, 1.300]			
One-sided p-value from log rank test		0.441446			

PFS is evaluated with the stratified log-rank test based on stratification factors and entry criterion used for randomization.

A: Value cannot be estimated due to censored data.

** censored observation

Median, percentile and other 95% CIs computed using Kaplan-Meier estimates.

Hazard ratio and 95% CI are based on Cox Regression Model, stratified by subgroup and entry criterion used for randomization.

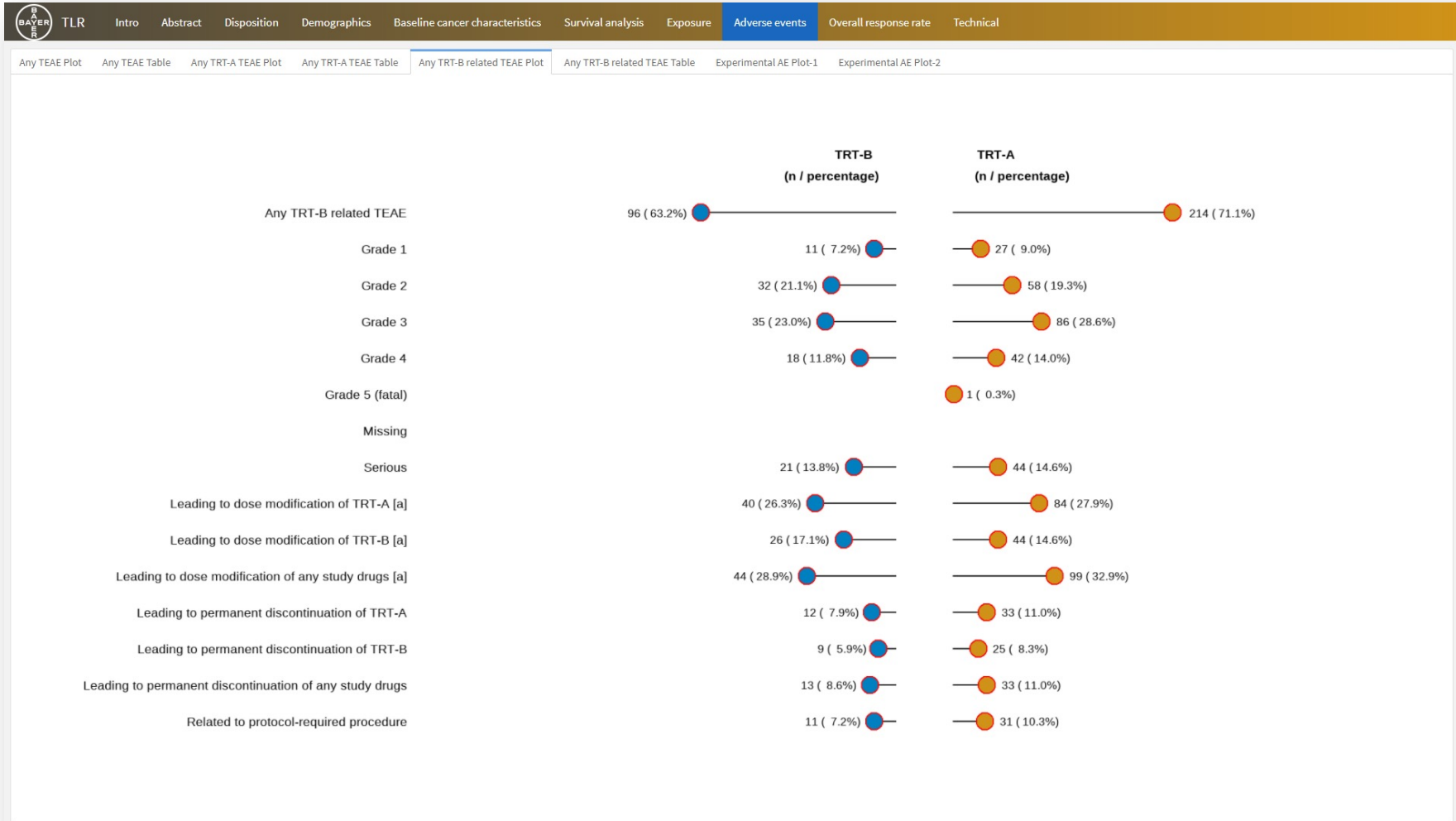
A Hazard ratio < 1 indicates superiority of TRT-A over TRT-B.

pgrm1_14_z_adhs_pfs.sas DOMYYYY hh:mm



Alternative Adverse Events Visualizations

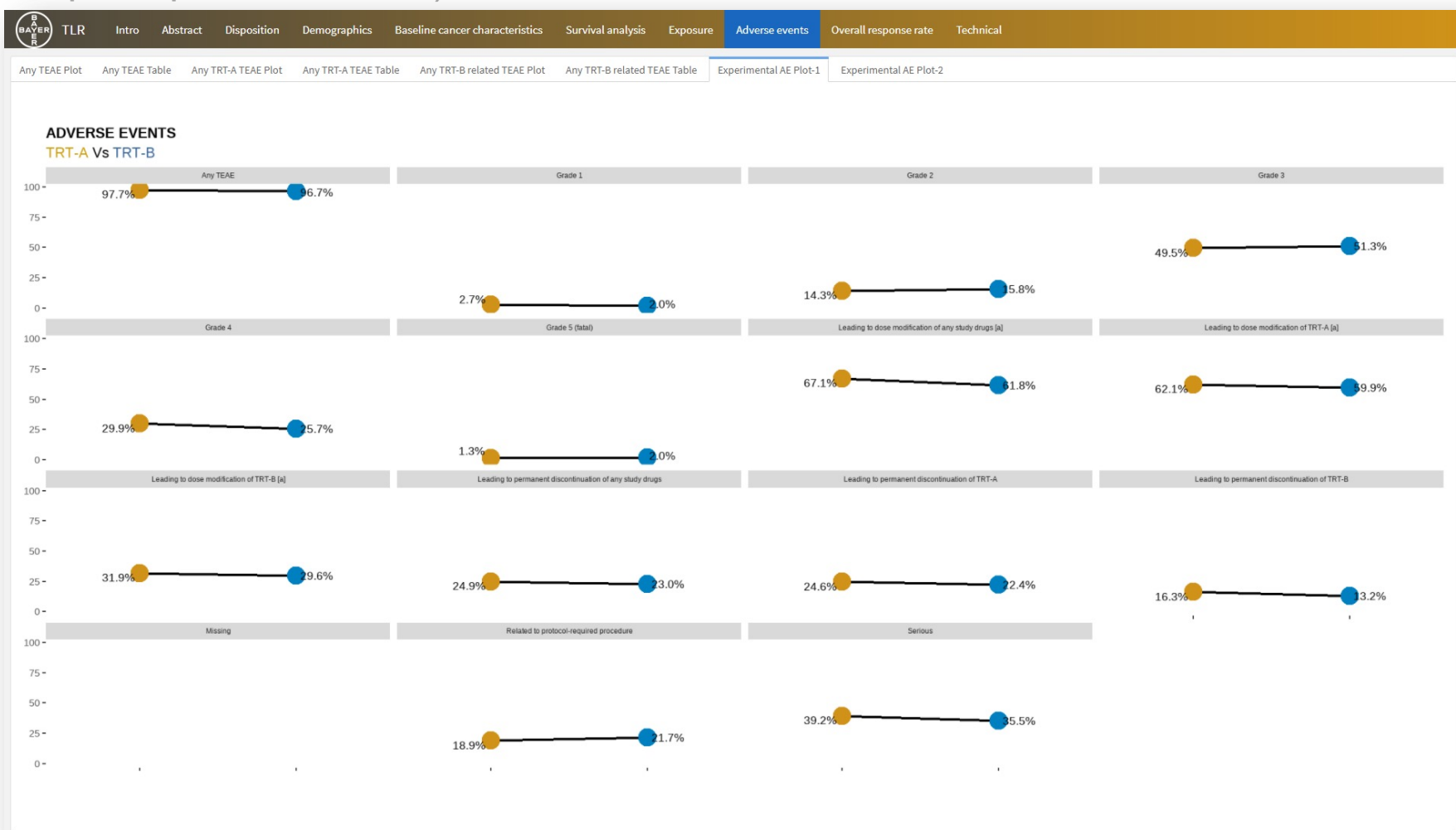
Adverse Events in a lollipop chart – bad idea (diverging geometrics are less comparable)
(dummy data - perhaps inconsistent)





Alternative Adverse Events Visualizations

Adverse Events in a slope chart – slope indicates if your compound did “good“ or “bad“
(dummy data - perhaps inconsistent)





Alternative Adverse Events Visualizations

Adverse Events in a dumbbell chart – position (left or right) indicates if your compound did “good” or “bad” (dummy data - perhaps inconsistent)





Dashboard Details

Technical Information (dummy data - perhaps inconsistent)

TLR

Intro

Abstract

Disposition

Demographics

Baseline cancer characteristics

Survival analysis

Exposure

Adverse events

Overall response rate

Technical

Setup & Session Info

Dashboard created in a demo run on: Thu Apr 29 10:10:29 AM 2021 - CEST

[1] "path TLFMETA: stat\\main01\\results\\tlfmeta"

[1] "path DATA: stat\\main01\\data"

[1] "path RESULTS: stat\\main01\\results"

R version 4.0.3 (2020-10-10)

Platform: x86_64-w64-mingw32/x64 (64-bit)

locale: LC_COLLATE=English_United States.1252, LC_CTYPE=English_United States.1252, LC_MONETARY=English_United States.1252, LC_NUMERIC=C and LC_TIME=English_United States.1252

attached base packages: grid, stats, graphics, grDevices, utils, datasets, methods and base

other attached packages: pander(v.0.6.3), htmlTable(v.2.1.0), Rcpp(v.1.0.6), jpeg(v.0.1-8.1), ggtext(v.0.1.1), ggalt(v.0.4.0), slickR(v.0.5.0), htmlwidgets(v.1.5.3), gridExtra(v.2.3), survival(v.3.2-7), emojiFont(v.0.5.3), survminer(v.0.4.9), zoo(v.1.8-9), tidyR(v.1.1.3), stringr(v.1.4.0), splitstackshape(v.1.4.8), reshape2(v.1.4.4), readxl(v.1.3.1), officer(v.0.3.18), magrittr(v.2.0.1), knitr(v.1.31), patchwork(v.1.1.1), hrbrthemes(v.0.8.0), haven(v.2.3.1), ggcharts(v.0.2.1), ggthemes(v.4.2.4), ggrepel(v.0.9.1), gt(v.0.2.2), flextable(v.0.6.5), ggpubr(v.0.4.0), ggplot2(v.3.3.3), flexdashboard(v.0.5.2) and dplyr(v.1.0.3)

loaded via a namespace (and not attached): colorspace(v.2.0-0), ggsignif(v.0.6.1), ellipsis(v.0.3.1), rio(v.0.5.26), showtext(v.0.9-2), sjlabelled(v.1.1.7), base64enc(v.0.1-3), gridtext(v.0.1.4), rstudioapi(v.0.13), showtextdb(v.3.0), fansi(v.0.4.2), xml2(v.1.3.2), splines(v.4.0.3), extrafont(v.0.17), jsonlite(v.1.7.2), broom(v.0.7.6), km.ci(v.0.5-2), Rttf2pt1(v.1.3.8), compiler(v.4.0.3), backports(v.1.2.1), assertthat(v.0.2.1), Matrix(v.1.2-18), htmltools(v.0.5.1.1), tools(v.4.0.3), gtable(v.0.3.0), glue(v.1.4.2), maps(v.3.3.0), tinytex(v.0.31), carData(v.3.0-4), cellranger(v.1.1.0), jquerylib(v.0.1.3), vctrs(v.0.3.6), extrafontdb(v.1.0), insight(v.0.13.2), xfun(v.0.19), proto(v.1.0.0), openxlsx(v.4.2.3), lifecycle(v.1.0.0), rstatix(v.0.7.0), MASS(v.7.3-53), scales(v.1.1.1), hms(v.1.0.0), proj4(v.1.0-10.1), RColorBrewer(v.1.1-2), yaml(v.2.2.1), curl(v.4.3), KMSurv(v.0.1-5), gdtools(v.0.2.3), sass(v.0.3.1), stringi(v.1.5.3), highr(v.0.8), checkmate(v.2.0.0), zip(v.2.1.1), rlang(v.0.4.10), pkgconfig(v.2.0.3), systemfonts(v.1.0.1), evaluate(v.0.14), lattice(v.0.20-41), purrr(v.0.3.4), tidyselect(v.1.1.0), plyr(v.1.8.6), R6(v.2.5.0), generics(v.0.1.0), DBI(v.1.1.1), pillar(v.1.6.0), foreign(v.0.8-80), withr(v.2.4.1), abind(v.1.4-5), ash(v.1.0-15), tibble(v.3.0.5), crayon(v.1.4.1), car(v.3.0-10), survMisc(v.0.5.5), uuid(v.0.1-4), KernSmooth(v.2.23-17), utf8(v.1.2.1), rmarkdown(v.2.7), sysfonts(v.0.8.3), data.table(v.1.14.0), forcats(v.0.5.1), digest(v.0.6.27), xtable(v.1.8-4), munsell(v.0.5.0) and bslib(v.0.2.4)



Outlook & Summary



- Self-contained HTML files provide quick visual insights and fast navigation in clinical Top Line Results
 - Can be either regarded as a modern alternative “slide-deck” (i.e. sending it via mail / storing it on central storages)...
 - Hosted on a server / SharePoint etc. for secured remote access...
 - Part of a submission package? – PHUSE / FDA looks into possibilities
- Powerful interactive features for faster navigation; visuals allow faster insights for crucial Topline Data
- Programmatic document generation allows traceable, re-usable, fast to adopt pipelines
- R in general: possible validation / peer programming / parallel to SAS
- Limitations
 - Data limitation (file size may be a limiting factor)
 - Infrastructure not yet established (less matured compared to SAS environment)
 - Internal / external acceptance (mind-shift towards SAS alternatives as R & Co)





Acknowledgements



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Bayer – Onc SBU – Statistics



Oliver Wirtz

Bayer – Onc SBU – Statistical Programming



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Stream: Data Visualization (DV)

Main Author: Robert Adams

Co-Author: Harsha Kalikivayi



Thank you for the attention

