PhUSE US Connect 2019

Paper DV01

Efficacy endpoint visualization of investigational products for cancer patients using R Shiny

Beverly F. Martinez, Sarah Cannon Development Innovations, Nashville, TN, USA
Mukul K. Mittal, Sarah Cannon Development Innovations, Nashville, TN, USA

ABSTRACT

Now that FDA has begun to leverage open source programming languages (see PhUSE US Connect 2018 poster by Li *et al* [1]), we utilized R programming for visualizing efficacy endpoints in our clinical trials. We used newer endpoints rather than the more traditional overall and progression-free survival. With the interactive capabilities of R Shiny web-interface, we examined individual patients with respect to their Best Overall Response, Duration of Response, Best Percentage Change in tumor size down to the lesion level, along with exposure and end-of-study data. Hence, we focused our attention on specific patient(s) by highlighting parts of Waterfall, Swimmer, Spider and Bubble plots in order to understand the treatment outcome and patient management decisions during the trial. In summary, open source R Shiny provides an elegant and powerful framework to turn your analysis into interactive graphs.

INTRODUCTION

In this paper, we show how data visualization using R Shiny can add value to the efficacy analysis of early phase oncology clinical trials. We will use a mock-up data for illustration of the efficacy endpoints in a dose escalation trial. In such a trial a common secondary objective is to evaluate the **Objective Response Rate (ORR)** and **Duration of Response (DoR)** as preliminary evidence of antitumor activity of the investigational product (IP) according to the Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 [2]. Other response criteria, (iRECIST, mRECIST, Cheson, etc.) are not discussed in this paper. Other endpoints, such as Disease Control Rate and Time to Treatment Failure, are also not covered. RECIST v1.1 defines the best overall response (BOR) as "the best response recorded from the start of the study treatment until the end of treatment taking into account any requirement for confirmation." The ORR is calculated as the proportion of patients with a BOR of complete response (CR) or partial response (PR). The DoR is defined as the time between first documentation of a response (CR or PR) and first evidence of progressive disease (PD). The duration of stable disease (SD) is also of interest and is a response metric relevant for the swimmer plot to be depicted later in this paper.

Our mock-up data did not come from independent assessors and do not include any subject with CR. For demographic and baseline variables we will include only the sex, age, primary diagnosis and baseline Eastern Cooperative Oncology Group (ECOG) Performance Status.

The flow of data for the efficacy analysis begins with the identification and measuremen/observations of the size of all available Target Lesions, Non-Target Lesions and New Lesions. The tumor lesion size is measured in 2 diameters in a single plane, and at each visit or timepoint [i], the investigator uses the RECIST algorithm to determine values for TRGRESP[i], NTRGRESP[i], and NEWLPROG[i] and combines these to determine the patient's Overall Response (OVRLRESP[i]). These tumor-related data are mapped into three SDTM domains: Tumor Identification (TU), Tumor Results (TR) and Disease Response (RS). Next, two ADaM data datasets are constructed: measurement records ADTR and response ADRS. The information flow can be represented as follows:

<u>Data flow from tumors:</u>
Tumor identification at each timepoint ➔
Tumor measurements/observation at each timepoint ➔
Assessment of response for each type of lesion at each timepoint ➔
Assessment of overall response across all lesions for each patient at each timepoint ➔
Assessment of best overall response for each patient across all timepoints ➔
Computation of best overall response rate and duration of response

The flow of questions will follow a top-down process using the analogy of going down the waterfall, swimming on the surface like spiders. As this link shows (https://www.livescience.com/14518-underwater-gallery-diving-spiders.html), spiders swim around underwater with air bubbles sticking to their leg hairs, which help them breathe awhile. Last, we will dive deeper to make sure we get answers from accurate detailed data. This flow will be opposite that of the flow of data, beginning with the ORR and DoR at the study level, lingering at the patient and visit levels, and ending with the tumor measurements and observations at the lesion level.

Responder Analysis (endpoint = BOR):
Is evidence of antitumor activity? ➔
What is the best overall response rate? ➔
Which patients are responders and which patients are not? ➔
For each patient, what was their overall response at each timepoint? ➔
For each patient and timepoint, how was the overall response determined? ➔
For each patient, timepoint and type of of lesion, how was the response assessed? ➔
For each patient, timepoint, type and tumor link ID, what was the measurement/observation?

Time-to-event Analysis (endpoint = DoR):
Is evidence of antitumor activity? ➔
What is the best overall response rate? ➔
Which patients are responders and which patients are not? ➔
For each patient, what was their overall response at each timepoint? ➔
For each patient and timepoint, how was the overall response determined? ➔
For each patient, timepoint and type of of lesion, how was the response assessed? ➔
For each patient, timepoint, type and tumor link ID, what was the measurement/observation?

Datasets and Variables:
The table below lists the datasets and variables we examined in this study. Responses in ADRS were linked back to measurements in ADTR and other observations in ADSL.

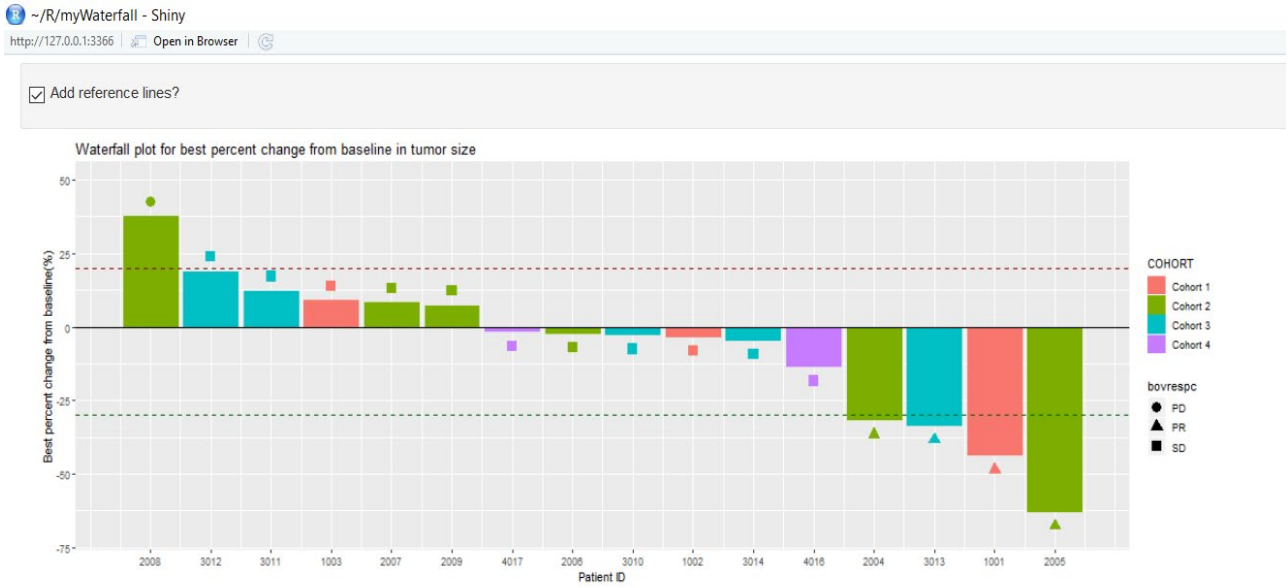
ADaM Data Set	Variables
ADRS	USUBJID, ADY, AVAL, TRGRESP, NTRGRESP, NEWLPROG, OVRLRESP, BOVRADY, BOVRESPC, TRTSDT and TRTEDT
ADTR	USUBJID, ADY, AVAL, PARAMCD in ('LDIAM','SAXIS') for TRGRPID='TARGET', PARAMCD = 'TUMSTATE' for TRGRPID in ('NEW','NON-TARGET'), PARAMTYP = 'DERIVED' only for PARAMCD='SUMDIAM', TRGRPID in ('TARGET','NON-TARGET','NEW'), TRLINKID in ('T01','T02','T03','T04','T05', 'NT01',…, 'NL01',….), TRLOC, TRSMNDVI, BASE, ABLFL, PCHG, NADPCHG.
ADSL	USUBJID, COHORT, AGE, SEX, DIAGP, BLECOG, TDISCFL, STCOMFL, TDISCDT, STCOMDT, TDISCRS and STCOMPRS

TOP VIEW

In our sample study, we have a total of 16 patients, four of whom had a BOR of PR (1001, 2004, 2005 and 3013). To simplify things, we will not require confirmation of PR. So, we calculate our ORR as 4/16 or 0.25. We can easily see this from the waterfall plot. For two of these four responders (1001 and 2004), disease progression occurs, and so the DoR is calculated as 15 months and 7 months , respectively. This can we can see from the swimmer plot. These two visualizations are produced by Shiny code given below.

BOR FROM A WATERFALL PLOT

Note that for some waterfall visualizations in the literature, the vertical bars are ordered from worst percent increase from baseline to the best percent decrease from baseline of the sum of longest diameters of all measurable target tumor lesions (SUMDIAM). However, in this paper, we only report the best percent change from baseline for all subjects, including those subjects whose "best" percent change is the least percent increase from baseline that corresponds to a progressive disease (PD). Per RECIST v1.1 PD is based on at least a 20% increase from Nadir (smallest SUMDIAM value). If that same patient has a Baseline greater than the Nadir, and has a subsequent percent increase from Baseline > 20%, the patient could have a best observed response of PD (for example, patient 2008). So the waterfall bars in this paper will be presenting the best percent change from baseline that match the best observed response for each subject. The ordering will start with the greatest increase on the left and end with the greatest decrease on the right. For a patient with several increases in tumor size, we pick the best tumor burden (smallest value). For a patient with several decreases in tumor size, we pick the best reduction (largest absolute value).

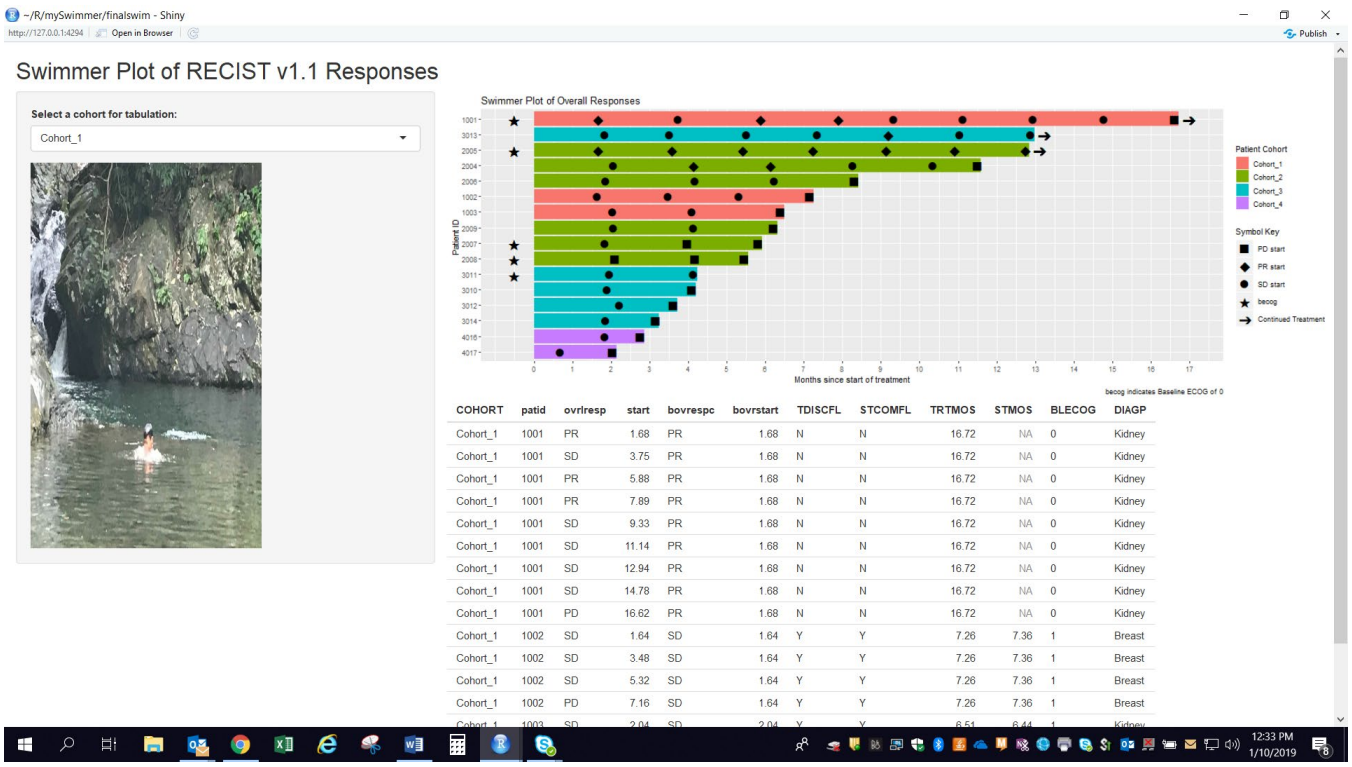



```
ui <- fluidPage(
  inputPanel(
    checkboxInput("reflines", label = "Add reference lines?",
                  value = FALSE)
  ),
  mainPanel(
    plotOutput("wfPlot")
  )
)
server <- function(input, output) {
  output$wfPlot <- renderPlot({
    unicode = list(triangle=sprintf('\u25B2'),circle=sprintf('\u25CF'),
                   square=sprintf('\u25A0'),star=sprintf('\u2605'),
                   diamond=sprintf('\u25C6'),arrow=sprintf('\u2794'))
    myPlot <-
      ggplot(wfp2, aes(x = x, y = bestpchg, fill = COHORT, col = COHORT)) +
      labs(title = "Waterfall plot for best percent change from baseline in tumor size",
           x = "Patient ID", y = "Best percent change from baseline(%)")    +
      coord_cartesian(ylim = c(-70,50)) +
      geom_bar(stat = "identity", width = 0.9) +
      geom_point(data = mydf.shapes, aes(x,ynew, shape = bovrespc), size = 4,

 show.legend = TRUE) +
    scale_x_continuous(breaks = c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16) ,
                       labels = c("2008","3012","3011","1003","2007","2009","4017",

"2006","3010","1002","3014","4016","2004","3013","1001","2005"))
    if(input$reflines){
        myPlot = myPlot +
          geom_abline(slope=0, intercept=0,  col = "black",lty=1) +
          geom_abline(slope=0, intercept=20,  col = "darkred",lty=2) +
          geom_abline(slope=0, intercept=-30,  col = "darkgreen",lty=2)
      }
    print(myPlot)
  })
}
```

SWIM : FOLLOW THE PATIENT JOURNEY

DOR AND OVERALL RESPONSES FROM A SWIMMER PLOT

Out of the 4 patients with BOR of PR shown in the waterfall plot, only two developed PD as shown in the swimmer plot below. Patient 1001 had PR at 2 months and had PD at 17 months, giving a duration of response DoR of 15 months. Patient 2004 had PR and PD at 4 and 11 months, respectively giving a DoR of 7 months.



COHORT	patid	ovrlresp	start	bovrespc	bovrstart	TDISCFL	STCOMFL	TRTMOS	STMOS	BLECOG	DIAGP
Cohort_1	1001	PR	1.68	PR	1.68	N	N	16.72	NA	0	Kidney
Cohort_1	1001	SD	3.75	PR	1.68	N	N	16.72	NA	0	Kidney
Cohort_1	1001	PR	5.88	PR	1.68	N	N	16.72	NA	0	Kidney
Cohort_1	1001	PR	7.89	PR	1.68	N	N	16.72	NA	0	Kidney
Cohort_1	1001	SD	9.33	PR	1.68	N	N	16.72	NA	0	Kidney
Cohort_1	1001	SD	11.14	PR	1.68	N	N	16.72	NA	0	Kidney
Cohort_1	1001	SD	12.94	PR	1.68	N	N	16.72	NA	0	Kidney
Cohort_1	1001	SD	14.78	PR	1.68	N	N	16.72	NA	0	Kidney
Cohort_1	1001	PD	16.62	PR	1.68	N	N	16.72	NA	0	Kidney
Cohort_1	1002	SD	1.64	SD	1.64	Y	Y	7.26	7.36	1	Breast
Cohort_1	1002	SD	3.48	SD	1.64	Y	Y	7.26	7.36	1	Breast
Cohort_1	1002	SD	5.32	SD	1.64	Y	Y	7.26	7.36	1	Breast
Cohort_1	1002	PD	7.16	SD	1.64	Y	Y	7.26	7.36	1	Breast

```
mydf <- data.frame(mytumor)
mydf$isContinued <- if_else(mydf$highcap=="FilledArrow",TRUE,FALSE,missing=FALSE)
mydf <- mydf %>%
  rename(becog=ecog0) %>%
  mutate(TRTMOS = Duration_of_Treatment/30.4375)
mydf.shapes1 <- mydf %>%
  dplyr::select(patid,status,start) %>%
  reshape2::melt(id.vars=c("patid","status"),value.name="time") %>%
  dplyr::filter(!is.na(time)) %>%
  dplyr::select(-variable) %>%
  dplyr::mutate(status=paste(status,"start",sep=" "))
mydf.shapes2 <- mydf.shapes1 %>%
  bind_rows(mydf %>%
              select(patid,becog) %>%
              filter(!is.na(becog)) %>%
              mutate(status="becog") %>%
              rename(time=becog))
mydf.shapes3 <- mydf.shapes2 %<>%
  bind_rows(mydf %>%
              select(patid, high, isContinued) %>%
              filter(isContinued) %>%
              select(-isContinued) %>%
              mutate(status="Continued Treatment") %>%
              mutate(high=high+0.25) %>%
              rename(time=high))
responseLevels = c("PD start","PR start","SD start","CR start",
                   "becog","Continued Treatment")
```

```
mydf.shapes3 %<>%
  dplyr::mutate(status = factor(status,levels=responseLevels))

ui <- fluidPage(
     titlePanel("Swimmer Plot of RECIST v1.1 Responses"),
     inputPanel(
         selectInput("cohort","Select a cohort for tabulation:",
                     c("Cohort_1", "Cohort_2", "Cohort_3", "Cohort_4"))
      ),
      mainPanel(
        fluidRow(
          plotOutput("swimPlot")
        ),
        fluidRow(
          tableOutput("table")
        )
      )
   )
server <- function(input, output, session) {
  unicode = list(triangle=sprintf('\u25B2'),circle=sprintf('\u25CF'),
                 square=sprintf('\u25A0'),star=sprintf('\u2605'),
                 diamond=sprintf('\u25C6'),arrow=sprintf('\u2794'))
   output$swimPlot <- renderPlot({
      mydf %>%
        select(patid, high, COHORT) %>%
        distinct() %>%
        mutate(patid=forcats::fct_reorder(.f=patid, .x=as.numeric(high), .desc = FALSE)) %>%
        ggplot(aes(patid, high)) + # Base axis
        geom_bar(stat="identity", aes(fill=factor(COHORT))) +
        geom_point(data=mydf.shapes3, aes(patid, time, colour=status, shape=status), size=8)
+
        coord_flip() +         scale_colour_manual(values=c("black","black","black","black","
black")) +         scale_shape_manual (values=c(unicode[["square"]], unicode[["diamond"]], un
icode[["circle"]],                                    unicode[["star"]],unicode[["arrow"]])
) +
        scale_y_continuous(limits=c(-0.5, 17), breaks=0:20) +
        labs(fill="Patient Cohort", colour="Symbol Key", shape="Symbol Key",
             x="Patient ID ", y="Months since start of treatment",
             title="Swimmer Plot of Overall Responses",
             caption="becog indicates Baseline ECOG of 0") +
        theme_replace(plot.title = element_text(hjust = 0.5),
              plot.caption = element_text(size=9, hjust=0),
              aspect.ratio = 1,
              plot.margin = margin(0, 0, 0, 0, "cm"))
   })
   output$table <- renderTable(
     filter(mydf, COHORT == input$cohort) %>%
       select(COHORT, patid, ovrlresp, start, bovrespc, bovrstart,
              TDISCFL, STCOMFL, TRTMOS, STMOS, BLECOG, DIAGP)
   )
}
```

DIVE DEEP FOR TUMOR MEASUREMENTS AND OBSERVATIONS

To understand better the overall responses in the preceding swimmer plot, we need to look at target, non-target and new lesions and their respective responses based on the RECIST guidelies presented in Table 1 from Eisenhauer *et al*[2] and reproduced below:

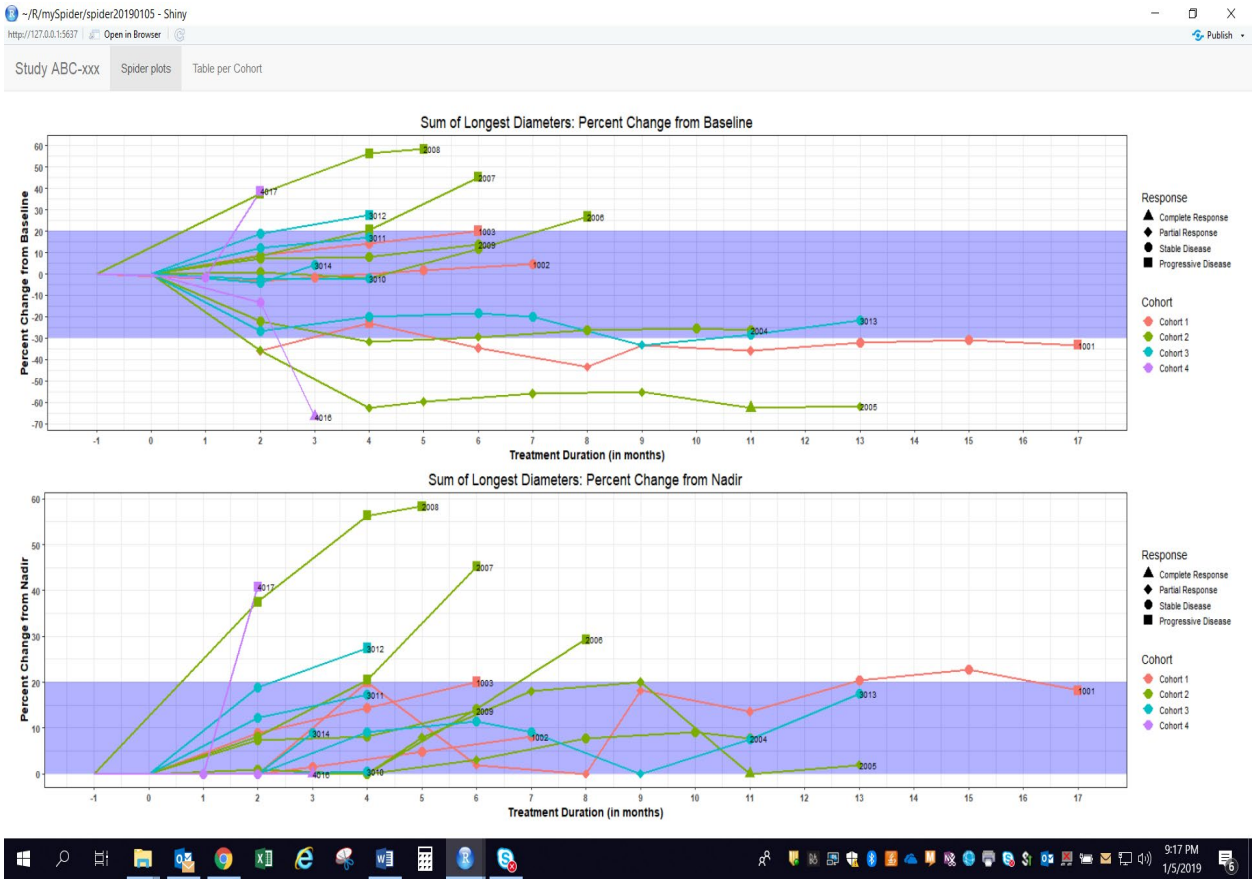
Table 1 – Time point response: patients with target (+/- non-target) disease.

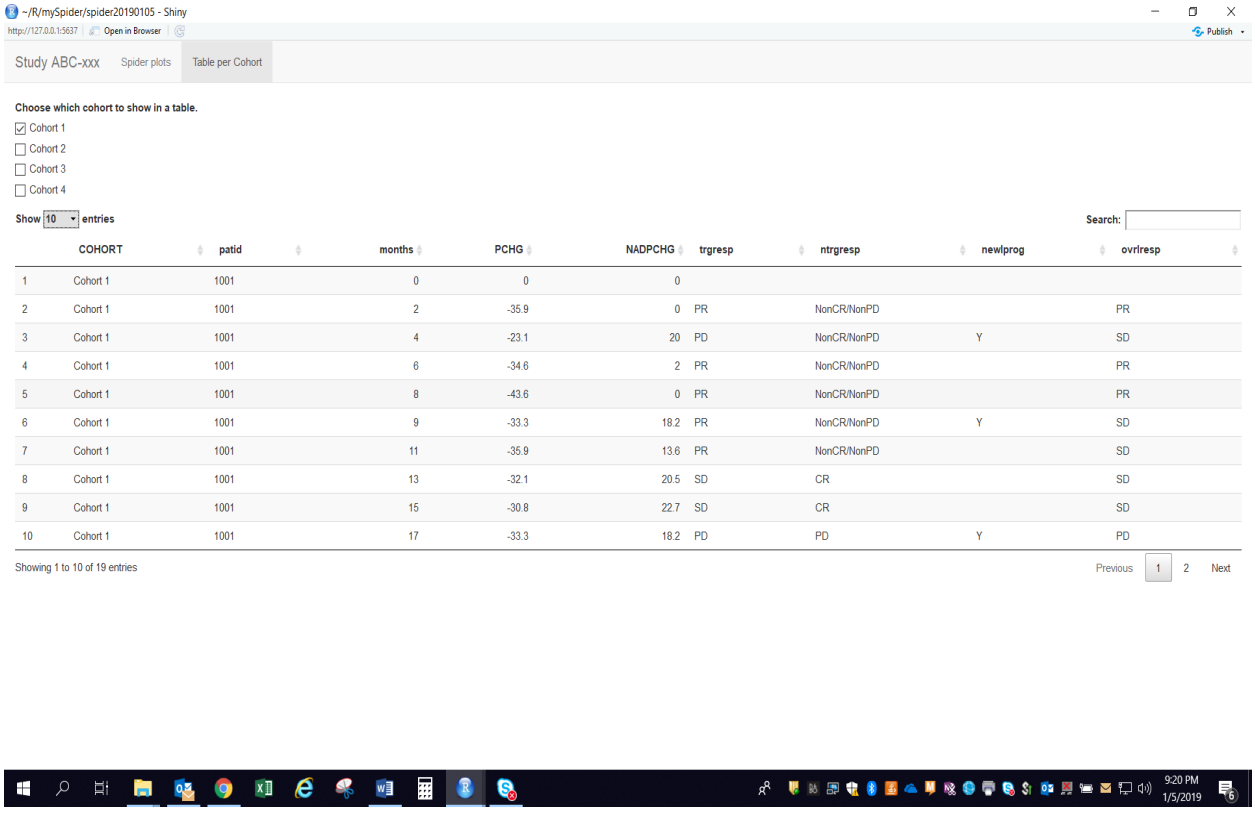
Target lesions	Non-target lesions	New lesions	Overall response
CR	CR	No	CR
CR	Non-CR/non-PD	No	PR
CR	Not evaluated	No	PR
PR	Non-PD or not all evaluated	No	PR
SD	Non-PD or not all evaluated	No	SD
Not all evaluated	Non-PD	No	NE
PD	Any	Yes or No	PD
Any	PD	Yes or No	PD
Any	Any	Yes	PD

CR = complete response, PR = partial response, SD = stable disease,PD = progressive disease, and NE = inevaluable

TARGET LESIONS ON SPIDER PLOTS

Spider plots show the time point measurements of target lesions on which the RECIST responses of CR, PR, SD and PD are based as follows [2]:
CR: All target lesions have disappeared. Any pathological lymph nodes must have reduction in short axis to <10 mm.
PR: The sum of diameters of target lesions has decreased 30% or more, taking as reference the baseline sum.
PD: The sum of diameters of target lesions has increased 20% or more, taking as reference the nadir (smallest sum on study, including the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm.
SD: There is neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum of diameters while on study.


~/R/mySpider/spider20190105 - Shiny
http://127.0.0.1:5637 | Open in Browser
Publish
Study ABC-xxx
Spider plots
Table per Cohort
Sum of Longest Diameters: Percent Change from Baseline
Percent Change from Baseline
Treatment Duration (in months)
Response
Complete Response
Partial Response
Stable Disease
Progressive Disease
Cohort
Cohort 1
Cohort 2
Cohort 3
Cohort 4
Sum of Longest Diameters: Percent Change from Nadir
Percent Change from Nadir
Treatment Duration (in months)
9:17 PM
1/5/2019

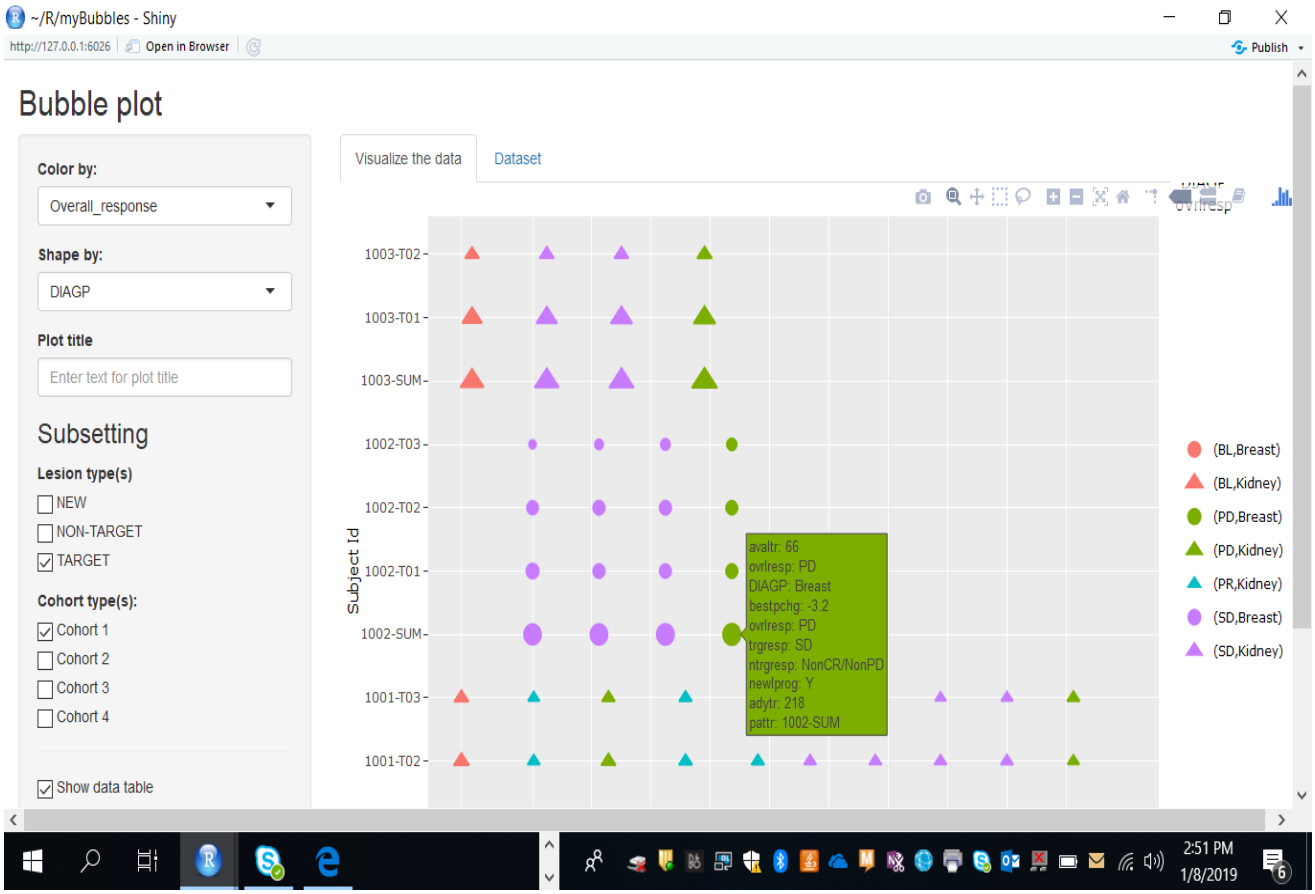

~/R/mySpider/spider20190105 - Shiny
http://127.0.0.1:5637 | Open in Browser
Publish
Study ABC-xxx
Spider plots
Table per Cohort
Choose which cohort to show in a table.
Cohort 1
Cohort 2
Cohort 3
Cohort 4
Show 10 entries
Search:
COHORT
patid
months
PCHG
NADPCHG
trgresp
ntrgresp
newlprog
ovrlresp
1 Cohort 1 1001 0 0 0
2 Cohort 1 1001 2 -35.9 0 PR NonCR/NonPD PR
3 Cohort 1 1001 4 -23.1 20 PD NonCR/NonPD Y SD
4 Cohort 1 1001 6 -34.6 2 PR NonCR/NonPD PR
5 Cohort 1 1001 8 -43.6 0 PR NonCR/NonPD PR
6 Cohort 1 1001 9 -33.3 18.2 PR NonCR/NonPD Y SD
7 Cohort 1 1001 11 -35.9 13.6 PR NonCR/NonPD SD
8 Cohort 1 1001 13 -32.1 20.5 SD CR SD
9 Cohort 1 1001 15 -30.8 22.7 SD CR SD
10 Cohort 1 1001 17 -33.3 18.2 PD PD Y PD
Showing 1 to 10 of 19 entries
Previous
1
2
Next
9:20 PM
1/5/2019

```
ui <- navbarPage("Study ABC-xxx", id = "navBar",
          tabPanel(
                 "Spider plots",
                 plotOutput("spiderBase"),
                 plotOutput("spiderNadir")
          ),
          tabPanel(
                 "Table per Cohort", value = "table",
                 checkboxGroupInput("checkbox", "Choose which cohort to show in a table.",

 choices = c("Cohort 1", "Cohort 2", "Cohort 3", "Cohort 4"),
              selected = "Cohort 4"),
                 DTOutput("cohortPicker")
                )
)
server <- function(input, output, session) {
  dfbase = df %>%
    select(-NADPCHG)
  dfnadir = df %>%
    select(-PCHG)
  dfboth = reactive({
    df %>%
      filter(COHORT == input$checkbox)
  })
  output$spiderBase <- renderPlot({
    ggplot(data = dfbase, aes(x = months, y = PCHG, group=patid))  +
      theme_bw(base_size=14) +
      theme(axis.title.x = element_text(face="bold"), axis.text.x = element_text(face="bold")
) +
      theme(axis.title.y = element_text(face="bold"), axis.text.y = element_text(face="bold")
) +
      theme(plot.title = element_text(size=18, hjust=0.5)) +
      ggtitle("Sum of Longest Diameters: Percent Change from Baseline") +
      xlab("Treatment Duration (in months)") +
      ylab("Percent Change from Baseline") +
      geom_rect(aes(xmin = -Inf, xmax = Inf, ymin = -30, ymax = 20), fill = "blue",

 alpha=0.005) +
      geom_line(aes(color=COHORT), size = 1) +
      geom_point(aes(shape=trgresp, color=COHORT), size = 5, show.legend=TRUE) +
      scale_x_continuous(breaks = seq(-1, 20, by = 1)) +
      scale_y_continuous(breaks = seq(-100, 200, by = 10)) +
      scale_colour_discrete(name="Cohort", labels=c("Cohort 1", "Cohort 2", "Cohort 3",

 "Cohort 4")) +
      scale_shape_manual(name = "Response",
                  breaks = c("CR", "PR", "SD", "PD", "NA"),
                  values = c("SD"=16, "PD"=15, "PR"=18, "CR"=17, "NA"=4),
                  labels=c("CR"="Complete Response", "PR"="Partial Response",
"SD"="Stable Disease", "PD"="Progressive Disease", "NA"="Not Available")) +
      geom_dl(aes(label = patid), method = list("last.points", cex = 0.8))
  })
  output$spiderNadir <- renderPlot({
    ggplot(data = dfnadir, aes(x = months, y = NADPCHG, group=patid))  +
      theme_bw(base_size=14) +
      theme(axis.title.x = element_text(face="bold"), axis.text.x = element_text(face="bold")
) +
      theme(axis.title.y = element_text(face="bold"), axis.text.y = element_text(face="bold")
) +
      theme(plot.title = element_text(size=18, hjust=0.5)) +
      ggtitle("Sum of Longest Diameters: Percent Change from Nadir") +
      xlab("Treatment Duration (in months)") +
      ylab("Percent Change from Nadir") +
      geom_rect(aes(xmin = -Inf, xmax = Inf, ymin = 0, ymax = 20), fill = "blue", alpha=0.005
```

```
) +
      geom_line(aes(color=COHORT), size = 1) +
      geom_point(aes(shape=trgresp, color=COHORT), size = 5, show.legend=TRUE) +
      scale_x_continuous(breaks = seq(-1, 20, by = 1)) +
      scale_y_continuous(breaks = seq(-100, 200, by = 10)) +
      scale_colour_discrete(name="Cohort", labels=c("Cohort 1", "Cohort 2", "Cohort 3",

 "Cohort 4")) +
      scale_shape_manual(name = "Response",
                         breaks = c("CR", "PR", "SD", "PD", "NA"),
                         values = c("SD"=16, "PD"=15, "PR"=18, "CR"=17, "NA"=4),
                         labels=c("CR"="Complete Response", "PR"="Partial Response",
  "SD"="Stable Disease", "PD"="Progressive Disease", "NA"="Not Available")) +
      geom_dl(aes(label = patid), method = list("last.points", cex = 0.8))
  })
  output$cohortPicker <- renderDT({
    filter(dfboth(), COHORT == input$checkbox)[,1:9]
  })
}
```

TUMOR LINK IDS IN BUBBLE PLOTS

Finally, if we want to examine detailed data at the lesion level, we can visualize each individual tumor link IDs with their corresponding measurements and categorizations. The bubble plots below include tooltips which show detailed data on all types of lesions (Target, Non-target, and New) together with the primary diagnosis.



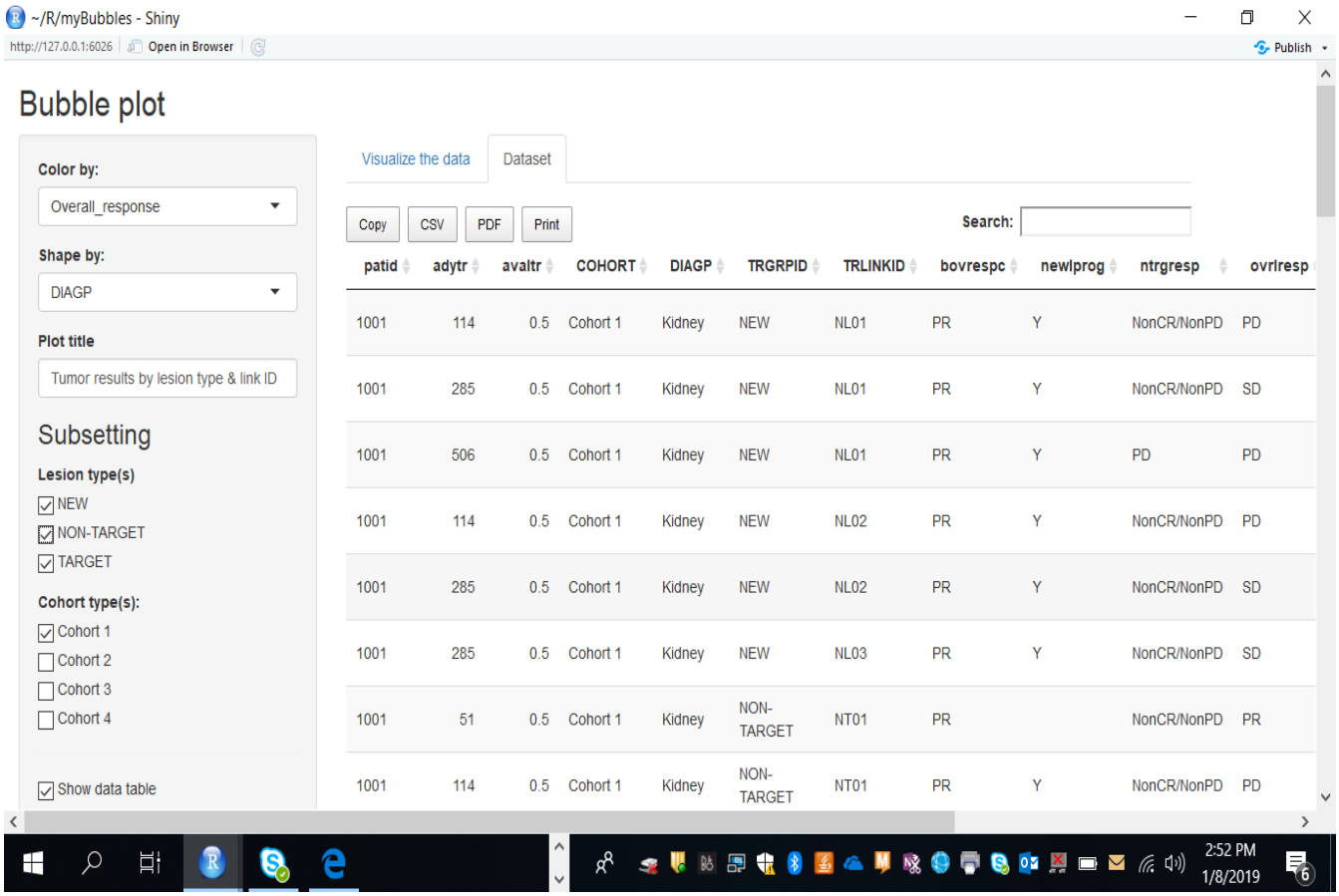

```
ui <- fluidPage(
  titlePanel("Bubble plot"),
  sidebarLayout(
```

```
    sidebarPanel(
      selectInput(inputId = "z",
         label = "Color by:",
       choices = c("Best_response" = "bovrespc",
                   "Overall_response" = "ovrlresp",
                   "Target_response"= "trgresp",
                  "Nontarget_response" = "ntrgresp" ),
       selected = "ovrlresp"),

      selectInput(inputId = "s",
                  label = "Shape by:",
                  choices = c("DIAGP", "COHORT"),
                  selected = "DIAGP"),
      h3("Subsetting"),
      checkboxGroupInput(inputId = "GRPID",
                         label = "Lesion type(s)",
                       choices = c("NEW", "NON-TARGET", "TARGET"),
                         selected = c("TARGET")),
      checkboxGroupInput(inputId = "selected_type",
                         label = "Cohort type(s):",
                      choices = c("Cohort 1","Cohort 2","Cohort 3","Cohort 4"),
                         selected = "Cohort 1"),
      hr(),
      checkboxInput(inputId = "show_data",
                    label = "Show data table",
                    value = TRUE),
      width = 3),
    mainPanel(
      tabsetPanel(type = "tabs",
                  tabPanel(title = "Visualize the data",
                           plotlyOutput(outputId = "scatterplot",height="700px",
 width = "1000px")
                  ),
                  tabPanel(title = "Dataset",
                           br(),
                           dataTableOutput(outputId = "table"))
      )
    )
  )
server <- function(input, output, session) {
  data_selected <- reactive({
    req(input$selected_type)
    filter(df1, COHORT %in% input$selected_type)
  })
  data_selected2 <- reactive({
    req(input$GRPID)
    filter(data_selected(), TRGRPID %in% input$GRPID)
  })
  pretty_plot_title <- reactive({ toTitleCase(input$plot_title) })
  output$scatterplot <- renderPlotly({
    p <- ggplot(data = data_selected2(), aes_string(x = "adytr", y = "pattr",
label2="bestpchg",
            label3="ovrlresp", label4 = "trgresp",label5="ntrgresp", label6 = "newlprog")) +
      geom_point(aes_string(size = "avaltr" , color = input$z, shape = input$s))  +
            scale_x_continuous(name = "Assessment Day",
            breaks = c(-10, 50, 100, 150, 200, 250, 300, 350, 400, 450, 500),
                       limits = c(-10, 550)) +
      theme(axis.text.x = element_text(angle = 60, hjust = 1, face = "bold")) +
      scale_y_discrete( name = "Subject Id") +
      theme(axis.text.y = element_text(face = "bold")) +
      ggtitle ("Change in tumor size") +
      theme(plot.title = element_text(size = 15, face = "bold"))
    ggplotly(p)
  })
```

```
  output$table <- DT::renderDataTable(
    if(input$show_data){
      datatable(data = data_selected2(),
                extensions = 'Buttons',
                options = list(pageLength = 50,
                               dom = 'Bfrtip',
                               buttons = c('copy', 'csv','excel', 'pdf', 'print')),
                rownames = FALSE
      )
    }
  )
}
```

DOWNLOADABLE DATASETS WITH INFORMATION AT THE LESION LEVEL

The second tab of this last shiny application enables users to download and print data sets in different formats.



CONCLUSION

Our experience in employing R Shiny to visualize efficacy endpoints based on RECIST v1.1 has convinced us that the wave of the future in oncology trials includes harnessing the power of both R and Shiny to assist end users in understanding data from top to bottom. In addition to the commonly used ggplot2 and tidyverse, we were able to tap into the strengths of plotly and DT in particular. For example, users can get more detailed answers with the help of tooltips and by hovering and brushing to select and deselect subsets of data to visualize and examine. We can give options for end users to download data which they can search and sort according to their choice of variables. We are optimistic that the R Shiny apps will lead to meaningful visualizations for both exploration and presentation,resulting in actionable insights to help cancer patients.

REFERENCES

[1] Utilizing Visualizations Developed in R Shiny for Exploratory Safety Analysis by Li et al.

https://www.phusewiki.org/docs/2018_US%20Connect18/PP%20STREAM/pp06%20final.pdf
[2] New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1) by Eisenhauer et al. https://www.ncbi.nlm.nih.gov/pubmed/19097774

ACKNOWLEDGMENTS

We gratefully acknowledge the medical expert input of Dr. Nenad Sarapa, and datasets contribution of Jesse Beck and Dan Creswell.

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Please feel free to contact the author at:

Beverly F. Martinez
Sarah Cannon Development Innovations
1100 Martin Luther King Blvd
Nashville , TN, 37203
Work Phone: 615.306.3079
Email: Beverly.Martinez3@SarahCannon.com

Mukul K. Mittal
Sarah Cannon Development Innovations
1100 Martin Luther King Blvd
Nashville , TN, 37203
Work Phone: 615.524.4009
Email: Mukul.Mittal@SarahCannon.com