ASCO®
AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

ASCO TAPUR™

Increasing Efficiency in DSMB Report Generation Using R Markdown

Michael Rothe, MS; Mallory Connors; Amber Boose, MPH

American Society of Clinical Oncology (ASCO)

May 21, 2024

Disclosures and Disclaimers

- I am an employee of the American Society of Clinical Oncology (ASCO).
  - ASCO receives funding from the following pharmaceutical companies to support the TAPUR Study: AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly and Company, Genentech, Merck, Seagen, now a wholly owned subsidiary of Pfizer Inc, and Taiho Oncology.
- All opinions expressed here are my own and not necessarily those of ASCO.

Statement of Purpose

- The aim of this presentation is to describe:
  - The utilization of R Markdown to create Monthly DSMB Reports
  - The benefits and process improvements derived from using R Markdown

Cohort Maturation and Review

- Simon's optimal two-stage design.
- 10 patients enrolled in stage I.
  - DSMB reviews for futility and recommends either closure or expansion to stage II.
  - If fewer than two patients have met the primary outcome, the cohort is permanently closed for futility, otherwise the cohort expands to stage II.
- 18 additional patients enrolled in stage II.
  - DSMB confirms the maturity of the efficacy results and approves release of the findings.
  - The null hypothesis is rejected if at least seven patients out of 28 have met the primary outcome.

Scope of DSMB Reporting

- Over 250 cohorts that require reporting.
- Monthly reporting to the DSMB in two reports.
  - Cohorts that have reached stage I review.
  - Cohorts that have reached stage II review.
- Two to three cohorts for review per report.
- Seven tables and listings per cohort (14-21 total tables and listings per report).
- Supporting text and footnotes for each cohort.
- Two data locks per report (internal review and official review).

Process Comparison

Previously

- Tables created in rtf file format, copied and pasted into a Word document, and formatted manually.
- Data updates require rerunning the tables and repeating the above process to add them to the report.
- Footnotes included in the template but cannot be easily added and removed based on reviewer feedback.
- Report created and edited in Word then converted to pdf.

Currently

- Tables created and formatted in the report using programming.
- Data updates require rerunning the R Markdown program.
- Footnotes included in the template and can be commented out to not appear but can be added back easily by removing the comment.
- Report created in pdf.

Monthly Report QC Process

- Tables can be reviewed directly in the report, rather than as outputs that may change when copied and pasted into the report.
- Additional QC outputs (such as a full demographics listing) can still be generated for comparison either from R or SAS.
- Footnotes and text can be reviewed in conjunction with the tables, rather than being reviewed in a separate step later.

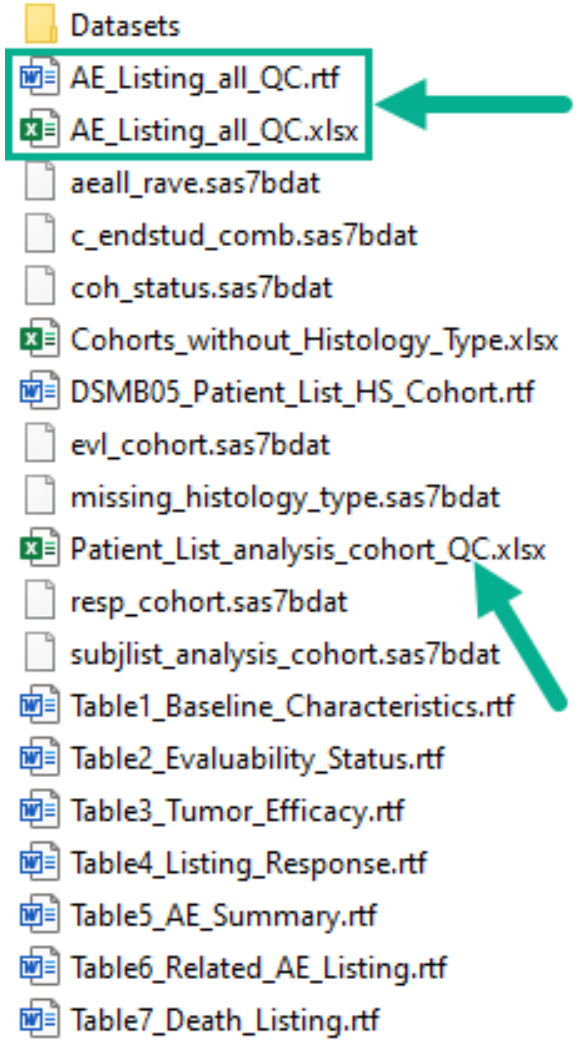


Table Programming Example

```
## Table 1.1.  Baseline Characteristics of Cohort
``r drug1``; ``r cancer1``; ``r mutation1``

Baseline characteristics were collected through screening and enrollment.
Race and ethnicity were collected by self-report. No further information was collected or provided regarding Other race.

```{r table1_1, echo=FALSE}

test<-table1(~  regtage + diagage + Sex + Race + Ethnicity + `Tumor Type`,
      caption="",
       data=dataTable_1_2_Base)
test2 <- as.data.frame(test)

test2 %>%
  kable() %>%
  row_spec(0,bold=TRUE) %>%
  row_spec(1,bold=TRUE) %>%
  column_spec(1,bold=TRUE) %>%
  kable_styling(bootstrap_options = "bordered",
                full_width = FALSE,latex_options = "HOLD_position") %>%
  add_indent(c(3,4,6,7,9,10,12,13,14,16,17,18,20,21,22,23,24,25,26,27,28,29,30))%>%
  add_footnote(c(footnoteTable_1_1a,footnoteTable_1_1b,footnoteTable_1_1c,footnoteTable_1_1d), notation = "none")
```
```

Title Text.

Defined earlier in the program.

Body Text.

Only these rows and columns will be bold.

Can be commented out.

Table Example in the Report

Table 1.1. Baseline Characteristics of Cohort

Pertuzumab (PERJETA) + Trastuzumab (HERCEPTIN); Histology Pooled; ERBB2/ERBB3 amplification or overexpression

Baseline characteristics were collected through screening and enrollment. Race and ethnicity were collected by self-report.
No further information was collected or provided regarding Other race.

	Overall (N=26)
Age at time of registration/enrollment (years)	
Mean (SD)	61.3 (12.0)
Median [Min, Max]	63.0 [31.0, 86.0]
Age at initial cancer diagnosed (years)	
Mean (SD)	59.1 (13.0)
Median [Min, Max]	61.5 [22.0, 85.0]
Sex	
Female	14 (53.8%)
Male	12 (46.2%)
Race	
Black or African American	4 (15.4%)
Prefer not to answer	2 (7.7%)
White/Caucasian	20 (76.9%)
Ethnicity	
Hispanic or Latino	3 (11.5%)
Not Hispanic or non-Latino	21 (80.8%)
Prefer not to answer	2 (7.7%)
Tumor Type	
Cervical Cancer	5 (19.2%)
Cancer of the small intestine	3 (11.5%)
Esophagus Cancer	3 (11.5%)
Malignant neoplasm of eye and adnexa	2 (7.7%)
Malignant neoplasm of other and unspecified urinary organs	2 (7.7%)
Malignant neoplasm of retroperitoneum and peritoneum	2 (7.7%)
Malignant neoplasm without specification of site	2 (7.7%)
Other and unspecified malignant neoplasm of skin	2 (7.7%)
Testicular Cancer	2 (7.7%)
Vaginal Cancer	2 (7.7%)
Malignant Neoplasm of Thymus	1 (3.8%)

The sites entered the following comments for the three participants with esophagus cancer:
ID 775: Pathologist notes cancer in the upper esophagus.
ID 1002: Pathologist notes cancer in the middle esophagus.
ID 2357: Pathologist notes cancer in the lower esophagus.

Limitations

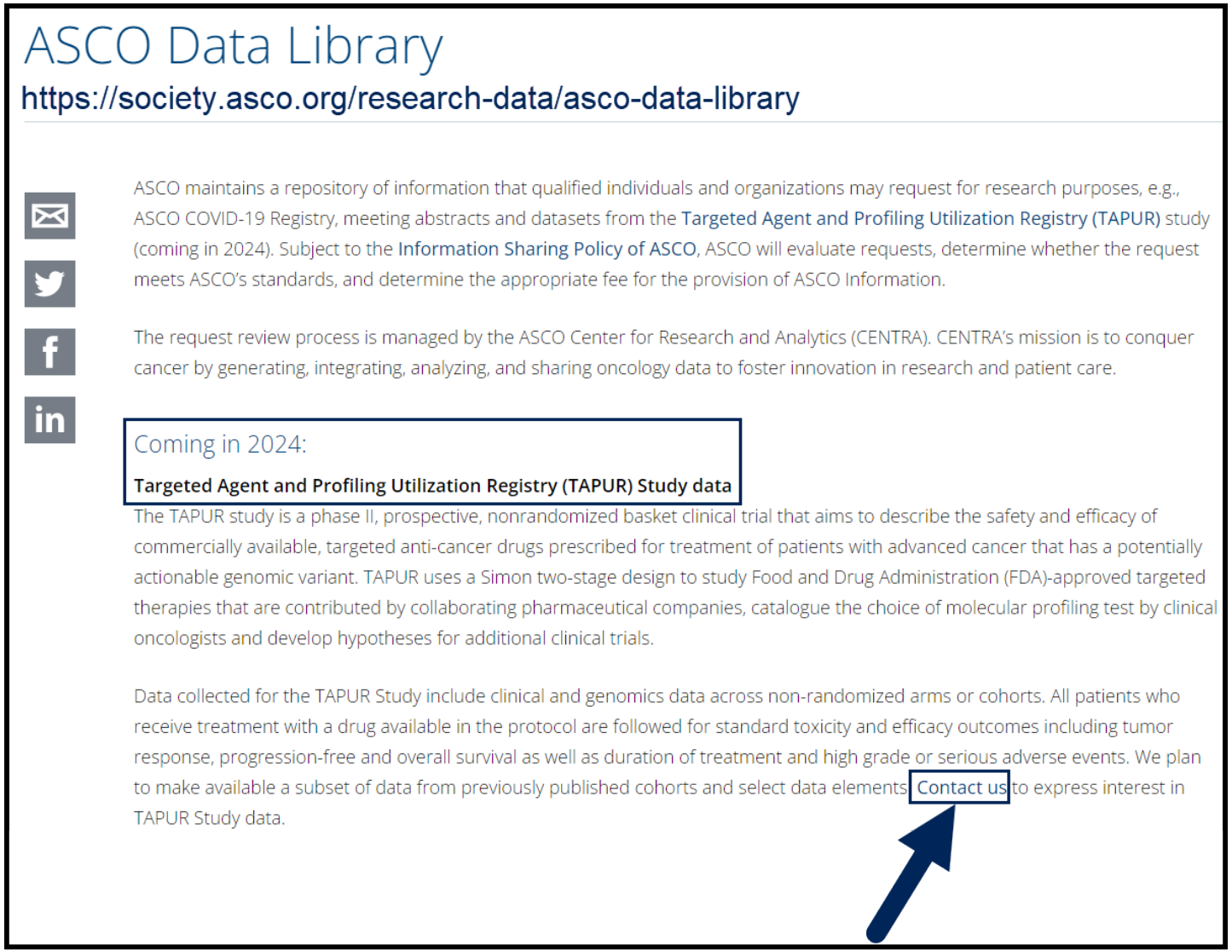
- Not useful for reports that will only need to be generated once or will have many table and formatting changes throughout the life of the trial.
- Needs to be identified early in the study, ideally before study start, so that all programming can be completed before the first report.
- Using programming from multiple different packages may result in not all programming working, such as an inability to add footnotes to tables that span multiple pages.

Conclusions

- Implementation of R Markdown to generate reports has saved the team time and reduced error while generating Monthly DSMB Reports.
- This process should be implemented early in the study to shift the time burden to the start of the study.

Thank you!

- Questions? Please contact TAPUR@asco.org
- The authors thank the patients who participated, the clinical centers, staff, and the TAPUR Study Team for study conduct and support
- Published TAPUR cohorts are being added to ASCO Data Library this year



ASCO Data Library

https://society.asco.org/research-data/asco-data-library

ASCO maintains a repository of information that qualified individuals and organizations may request for research purposes, e.g., ASCO COVID-19 Registry, meeting abstracts and datasets from the Targeted Agent and Profiling Utilization Registry (TAPUR) study (coming in 2024). Subject to the Information Sharing Policy of ASCO, ASCO will evaluate requests, determine whether the request meets ASCO's standards, and determine the appropriate fee for the provision of ASCO Information.

The request review process is managed by the ASCO Center for Research and Analytics (CENTRA). CENTRA's mission is to conquer cancer by generating, integrating, analyzing, and sharing oncology data to foster innovation in research and patient care.

Coming in 2024:

Targeted Agent and Profiling Utilization Registry (TAPUR) Study data

The TAPUR study is a phase II, prospective, nonrandomized basket clinical trial that aims to describe the safety and efficacy of commercially available, targeted anti-cancer drugs prescribed for treatment of patients with advanced cancer that has a potentially actionable genomic variant. TAPUR uses a Simon two-stage design to study Food and Drug Administration (FDA)-approved targeted therapies that are contributed by collaborating pharmaceutical companies, catalogue the choice of molecular profiling test by clinical oncologists and develop hypotheses for additional clinical trials.

Data collected for the TAPUR Study include clinical and genomics data across non-randomized arms or cohorts. All patients who receive treatment with a drug available in the protocol are followed for standard toxicity and efficacy outcomes including tumor response, progression-free and overall survival as well as duration of treatment and high grade or serious adverse events. We plan to make available a subset of data from previously published cohorts and select data elements. Contact us to express interest in TAPUR Study data.