Paper ET11

iCSR: A Wormhole to Interactive Data Exploration Universe

Chen Yang, Jazz Pharmaceuticals, Cambridge, United Kingdom,
Sudhir Kedare, Jazz Pharmaceuticals, Palo Alto, USA
Steve Wade, Jazz Pharmaceuticals, Kansas City, USA
Matt Travell, Jazz Pharmaceuticals, Cambridge, USA
Jagan Mohan Achi, Jazz Pharmaceuticals, Palo Alto, USA

INTRODUCTION

In this paper, we will demonstrate how a pilot process was developed to begin the first step in the digital transformation journey towards interactive clinical study reporting by moving beyond static Tables, Listing and Figures (TLFs) as the primary way for study teams and key stakeholders to interact with the full set of analysis results generated for a clinical study. We will show how a Shiny based framework was developed to combine both Statistical Analysis Plan (SAP) based formal results and exploratory analysis capabilities into one end-user focused, controlled application.

THE CHALLENGE

Jazz Pharmaceutical is a relatively small but expanding Biopharma company which is going through a rapid transformation internalizing and modernizing its data analytics capabilities plus expanding into new molecule entities. The challenge to the Integrated Data Analytics and Statistical Programming group (IDASP) was to develop a way to improve the experience of study teams in the consumption of formal analysis from clinical trial which historically have only had the CSR appendix formatted non-digital static TLFs available to them to review the full study analysis results. The requirement was to provide both the formal SAP analysis and extended exploratory capabilities while ensuring control over the analysis.

THE OPPORTUNITY

This challenge provided a specific digital transformation use-case where the feasibility of creating a new primary process based around interactive analysis table, listing and figure could be assessed.

THE APPROACH

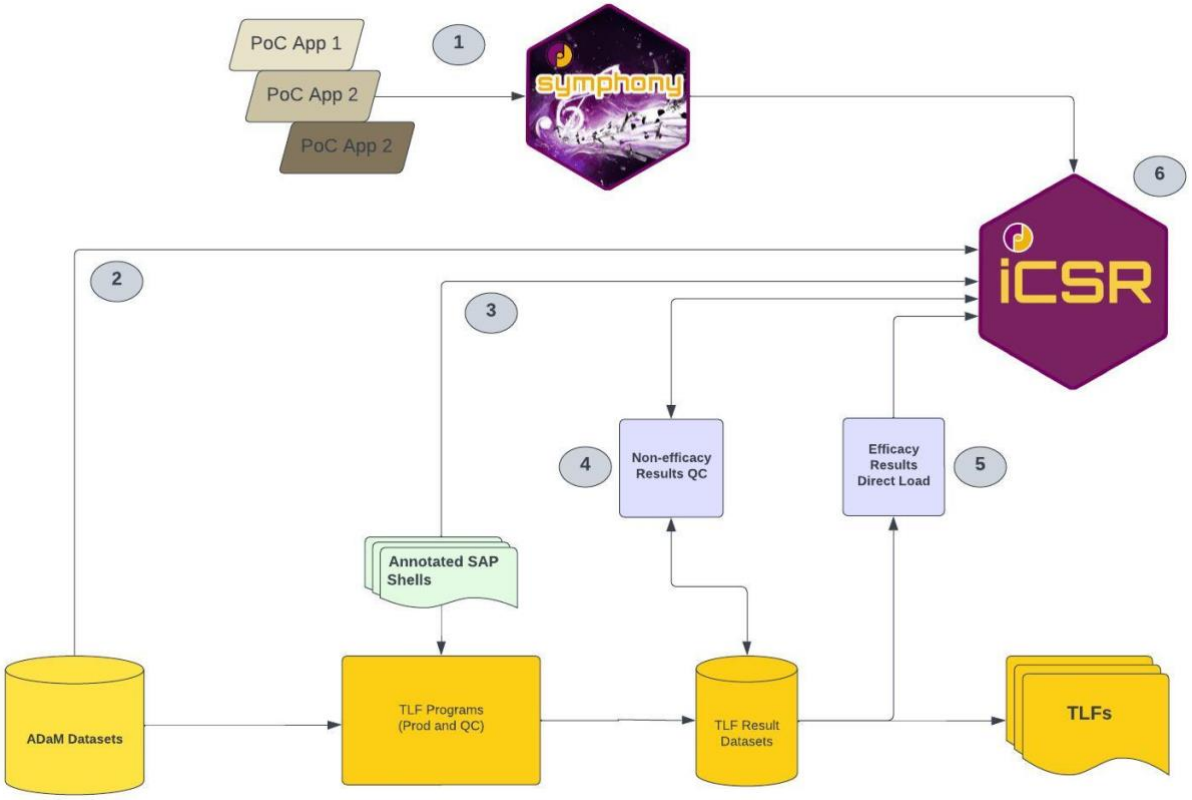
The approach was to identify several key studies from the main therapeutic areas of Neuroscience and Oncology plus early first-in-human Phase 1 studies that had upcoming decision-making read-outs that the new process could be piloted on. This would provide a broad range of study analysis types and provide insight into how differing formal analysis could be handled. It would also provide further insight into the differing exploratory capabilities needs and understanding of the different operational delivery challenges.

An interactive application called the Interactive Clinical Study Reporter (iCSR) would be created from a central template code repository, tailored to study specifics and deployed with each study's main deliveries (Dry Runs, Top Line and Full) in addition to the regular TLFs. This application would have the following features:

- Study ADaM datasets as the input data.
- Summary statistics would be generated with-in the application.
- Efficacy model results would be calculated externally via the SAS formal process then imported via Analysis Results Datasets. This is to preserve the robustness of the analysis and mitigate any programming language differences that might be experienced.

The central template {symphony} was created from several proof-of-concept applications that had been experimented with on previous studies.

WORKFLOW



1) Central template code library {symphony} using a Golem package Shiny framework consisting of Shiny Modules per data endpoint domain.

2) ADaM datasets are the input source data with no post-processing of data allowed (apart from factorizing and other R necessary data processing tasks). These are generated via the regular SAS based process.

3) All summary statistics tables and listing present in the SAP are internally generated in the iCSR application.

4) All summary statistics code in the application is QCed against the TLF analysis results datasets to ensure consistency.

5) All efficacy statistical model results are externally generated and QCed. Then loaded directly into the application.

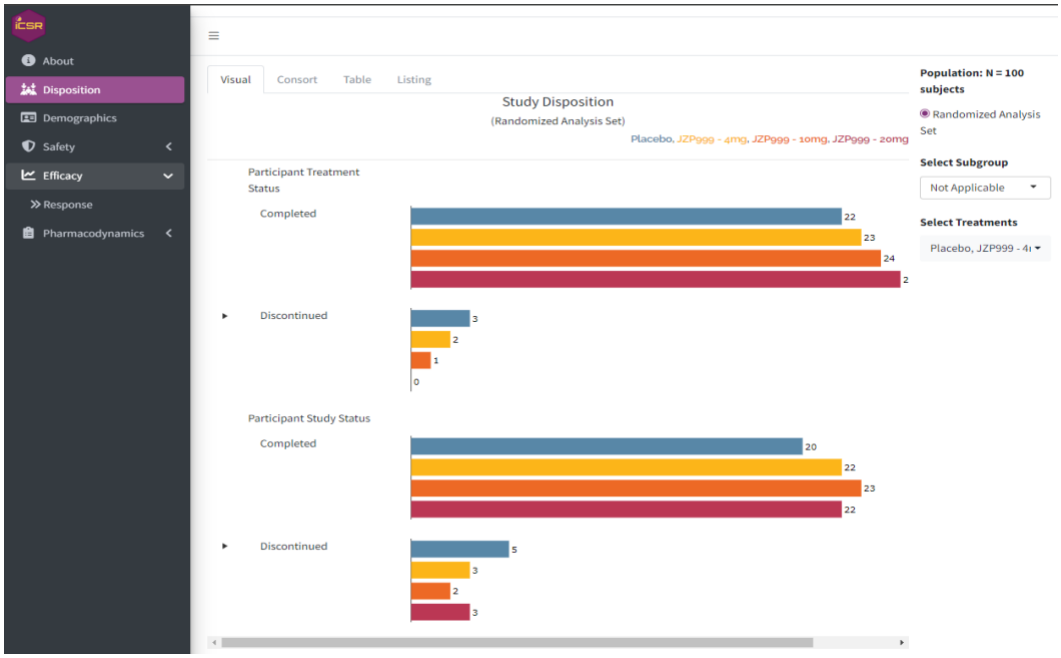
6) Study specific iCSR application includes additional non-SAP visualizations and interactive features.

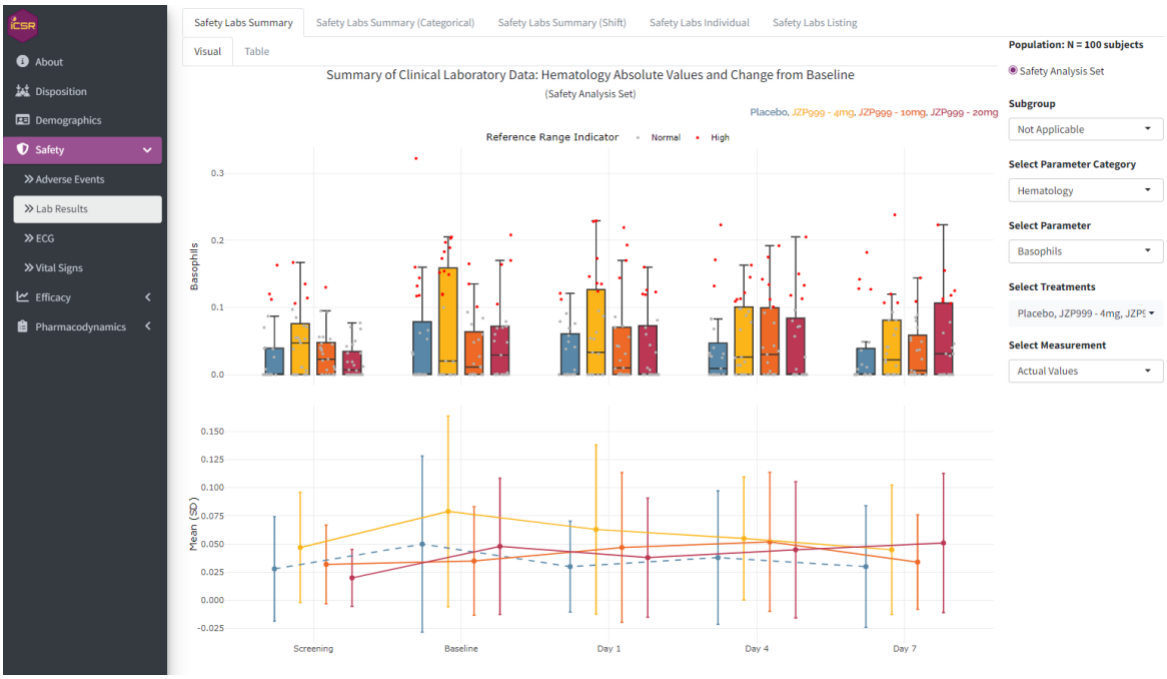
App Design

The app design aimed to provide a simple uncluttered user interface to provide an enhanced digital experience for the study teams navigating the study analysis combined with guardrails on what exploratory analysis would be possible. The goal was not to create a full and open-ended exploratory data analysis tool where the end user could create custom analysis but provide an extension to pre-defined study analysis. Functionality to download or export analysis was not enabled at this point as this was proof of concept and not replacing current processes.

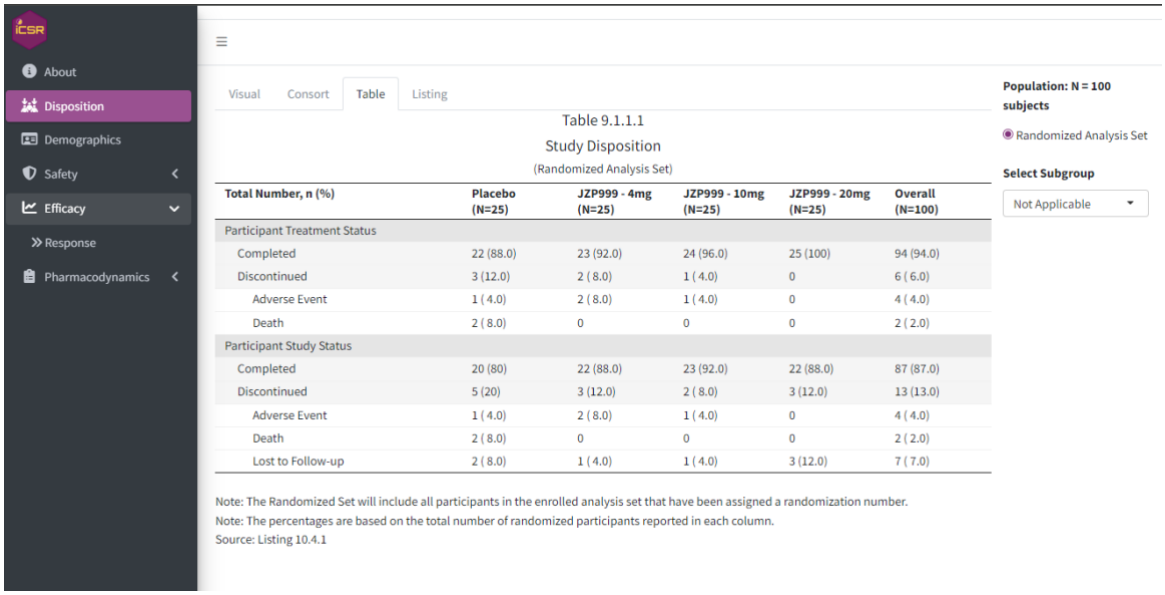
Each module has a uniform design consisting of 3 core areas plus module specifics.

(1) **Visual** – set of exploratory interactive visuals ranging from simple plots to more sophisticated visuals.



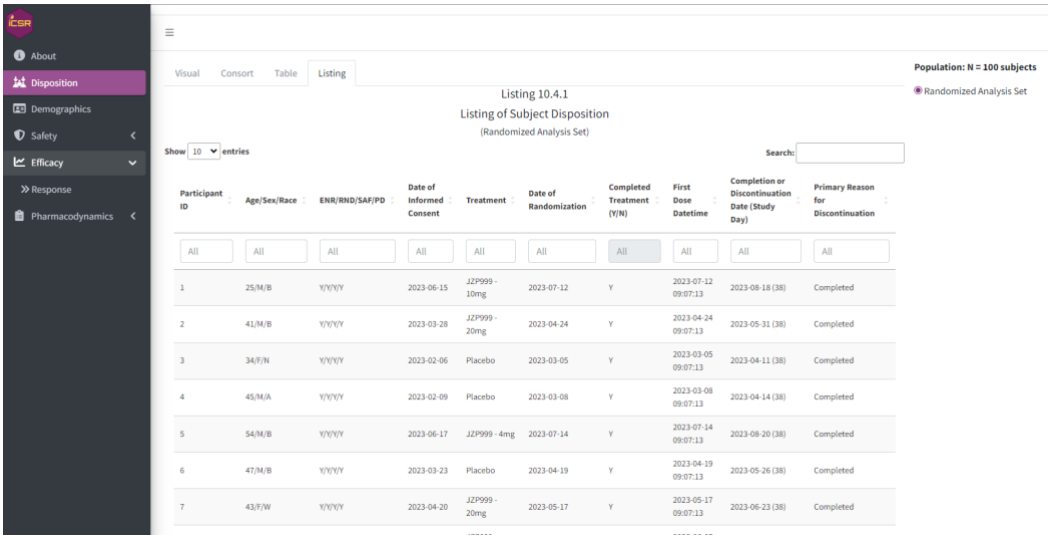


(2) **Table** – SAP specified tables. Summary statistics calculated within the application or statistical model results externally calculated and loaded in. Includes drill-down functionality to specific subject listings for statistics calculated with-in the application.

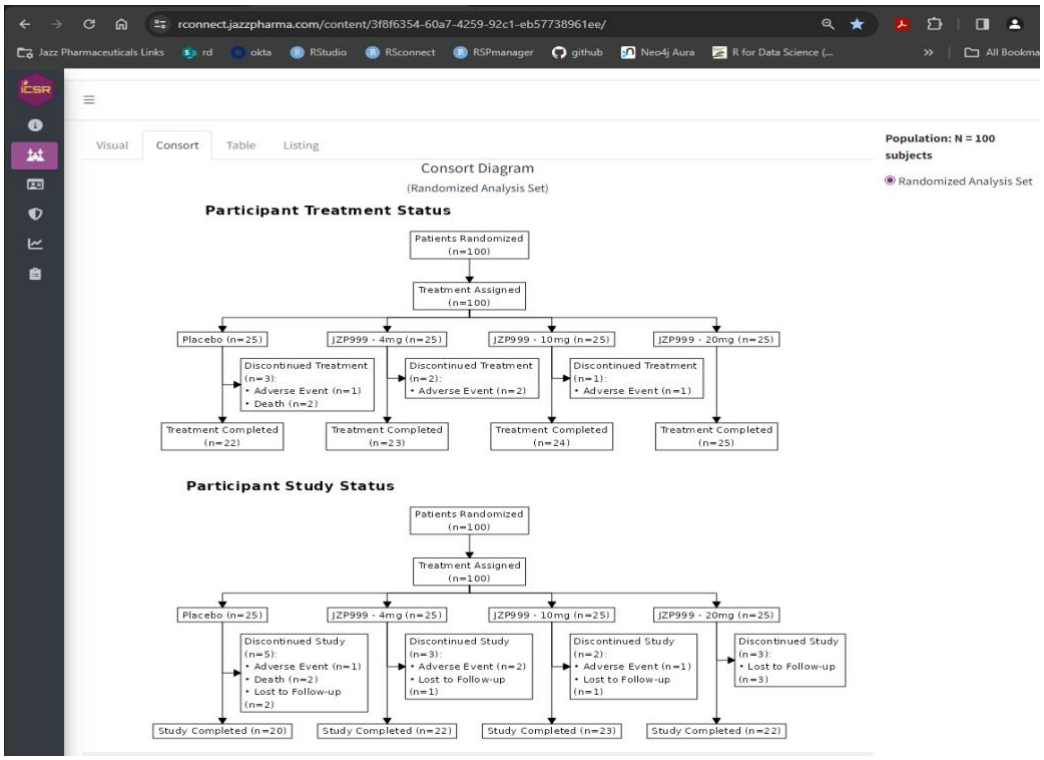


Total Number, n (%)	Placebo (N=25)	JZP999 - 4mg (N=25)	JZP999 - 10mg (N=25)	JZP999 - 20mg (N=25)	Overall (N=100)
Participant Treatment Status					
Completed	22 (88.0)	23 (92.0)	24 (96.0)	25 (100)	94 (94.0)
Discontinued	3 (12.0)	2 (8.0)	1 (4.0)	0	6 (6.0)
Adverse Event	1 (4.0)	2 (8.0)	1 (4.0)	0	4 (4.0)
Death	2 (8.0)	0	0	0	2 (2.0)
Participant Study Status					
Completed	20 (80)	22 (88.0)	23 (92.0)	22 (88.0)	87 (87.0)
Discontinued	5 (20)	3 (12.0)	2 (8.0)	3 (12.0)	13 (13.0)
Adverse Event	1 (4.0)	2 (8.0)	1 (4.0)	0	4 (4.0)
Death	2 (8.0)	0	0	0	2 (2.0)
Lost to Follow-up	2 (8.0)	1 (4.0)	1 (4.0)	3 (12.0)	7 (7.0)

(3) **Listing** – SAP specified listings. With enhanced search functionality.



(4) **Module specifics** – in addition some modules have additional endpoint specific visuals such as the Consort diagram for subject disposition.



THE OUTCOME

The outcome of the pilot was positive with study teams using the application as the main review tool for analysis results discussion, particularly in the early phase studies, with the visualization capabilities being preferred over the traditional tables. Additionally, the ability to easy switch / compare pre-defined subgroups/populations, search listings and have consort type diagrams readily available expediated the review.

THE LESSONS LEARNED

The following insight was taken:

- Technology and internal skillsets have reached a maturity level where we are confident of moving to a digital analysis type platform for TLF generation from the traditional approach.

- Need to move to a software development approach in code development to meet the required scale up needs. Traditional Statistical Programming approaches are will not be adequate. This needs to include more automation in code creation, testing and deployment. New technical skills, tooling and processes will need to be invested in.

- The use of CSR Appendix formatted TLFs is a long established and entrenched process in how study results are provided to stakeholders and in operational systems. There is a large change management effort required to break this and move to a more digital analysis-based approach.

THE NEXT STEPS

To build on the success of the pilot, the following areas are currently being worked on to move the iCSR from a pilot to production use:

- Introduce the iCSR approach as a standard deliverable on all studies.

- Use the iCSR application to replace the static TLFs outputs in non-CSR required output situations.

- Use the iCSR application to replace historically double QC programming in current TLF generation process.

- Use the iCSR application as means for Outsourced work QC/Oversight.

- Enable features to generate CSR ready TLF output directly from the application with supporting code files, this includes qualifying the Shiny required packages in the validated R environment.

- Expand efficacy modelling and visual capabilities.

- Automate app code generation, testing and deployment.

- Working with wider functional group to embed digital study result in traditional workflows.

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author(s) at:

Author Name: Chen Yang
Company: Jazz Pharmaceuticals
Email: chen.yang@jazzpharma.com

Author Name: Sudhir Kedare
Company: Jazz Pharmaceuticals
Email: sudhir.kedare@jazzpharma.com