

Issue

This poster shows two tools that have been developed to help in the cleaning and visualisation of data in a HNC study, where P118 was given to reduce incidence of oral mucositis in patients receiving adjuvant radio and chemotherapy.

Introduction

The P118 study features a complex visit schedule and a set of several oral mucositis (OM) grading scales, and checking these for consistency and accuracy was becoming increasingly difficult the more data we received.

Instead of the usual review of tables and data listings, several tools were developed to aid in this checking using a graphical representation of the data.

Tool #1: Study Schedule

Motivation

The scheduling for the P118 study is complicated – there are Chemotherapy (CT), Radiotherapy (RT), Investigational Product Dosing (IP), Oral Mucositis (OM) and Patient Reported Outcome (PRO) assessment schedules all running in parallel, but are not necessarily tied together. Any delay in one schedule can easily put the schedules out of synchronisation.

In general this isn't an issue, however it was noticed that occasionally subjects completed their course of IP while still undergoing RT and CT.

Subjects were scheduled to receive only 7 or 8 doses of IP, but standard practice is to keep treating patients with RT/CT until they have received the full dose of RT.

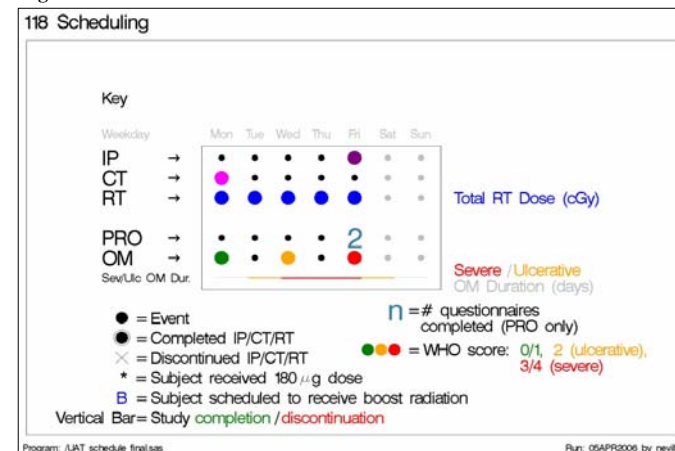
The team felt this was a problem, receiving RT/CT without the protective effect of the P118 drug could prolong OM and increase its severity. However, it was felt that this was probably a very rare occurrence and was therefore unlikely to confound the analysis of this study.

Implementation

This tool was put together to enable the team to visualise each individual's schedule, and identify cases where IP administration ceased while RT/CT was still ongoing. It creates a complete patient schedule overview, without the need to cross-check several listings.

For each subject there are several rows, each representing a different schedule with coloured dots indicating when events occurred (see **Figure 1**). Other information such as study completion/withdrawal, total RT dose, and duration of ulcerative and severe OM are also incorporated into the display.

Figure 1



The tool generates a MS Word document, displaying scheduling information for up to 10 patients per page (**Figure 2**).

Figure 2



Outcome

As a result the team realised that subjects receiving RT/CT without the potential protection of P118 was a bigger problem than anticipated

When a protocol amendment was required, the opportunity was taken to make IP available to subjects for as long as needed to cover their entire course of RT/CT.

The tool underwent subsequent development as new questions arose, amongst other things it has been used to:

- 1) Aid in defining clinically relevant breaks in RT and CT (important secondary endpoints for this study).
- 2) Explore site compliance with the schedules as specified in the protocol.

Tool #2: Oral Mucositis Scales

Motivation

The P118 study uses 3 main scales for assessing OM, as shown in **Figure 3**.

Figure 3

Abbreviated oral mucositis assessment scales			
	WHO	CTCAE clinical	CTCAE functional
Grade 0	None	None	None
Grade 1	Soreness	Erythema	Ability to eat solids
Grade 2	Ulceration	Patchy ulcerations or pseudomembranes	Requires liquid diet
Grade 3	Ulceration Requires liquid diet	Confluent ulcerations or pseudomembranes	Alimentation not possible
Grade 4	Ulceration Alimentation not possible	Tissue necrosis	Life threatening consequences

One very simple data quality check is to make sure that the different measures of OM are consistent with each other.

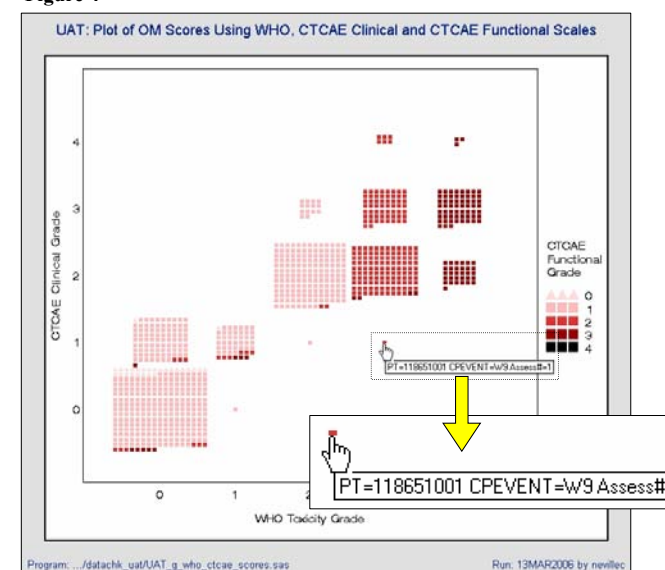
Implementation

Our approach was to create a plot which shows all three OM scales at once. (Since the scales were all discreet, a simple plot could be produced).

The WHO scale was assigned to the x-axis, the CTCAE clinical scale to the y-axis, and the CTCAE functional scale is shown by the colour of the plotted points, with a darker shade indicating a higher score. Every assessment is then plotted.

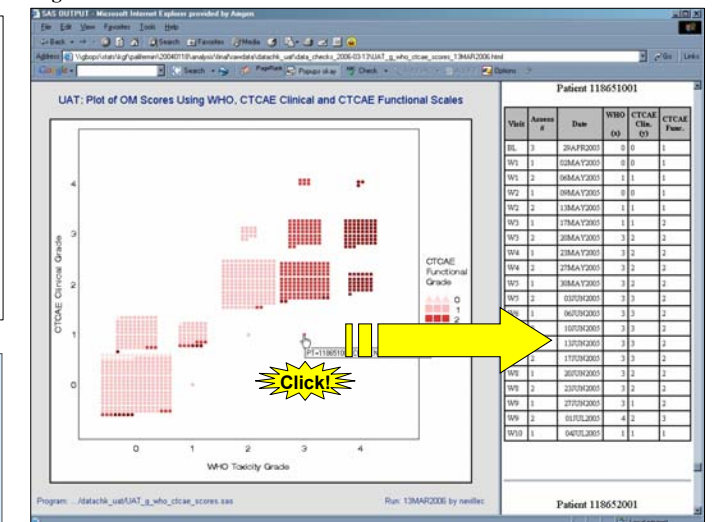
Outliers and unusual patterns in the data can be investigated further by hovering the mouse over the data point. This will display a box by the pointer showing the patient number and visit that the result occurred (See **Figure 4**)

Figure 4



Clicking on the data point displays all information for that particular patient in the right-hand panel (see **Figure 5**). This helps to identify if the data point is part of a trend or a possible data error.

Figure 5



Outcome

Inconsistencies were identified in the data, the source of these errors were tracked down, and processes have been put in place to eliminate further errors.

For the P118 study investigators complete a worksheet as part of the OM assessment process, this worksheet is the source data for assigning an OM score, and this score is QCd by an independent organisation who have access to the source worksheets.

The QCd scores are then transcribed onto the CRF and submitted to Amgen.

It is at this transcription stage that most of the errors were occurring, and additional checks have been put in place to pick up on these errors.

Conclusion

While database listing reviews are helpful in looking at individual data points, data visualisation tools such as these two examples can speed up the overall review process and allow for easier identification of common quality issues in data.

"A picture paints a thousand words..."

For further information on these tools please contact the authors:

nevillec@amgen.com

mwhiley@amgen.com