

Using SAS graphics to help with decision making in Early Clinical Development

PP26

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Introduction:

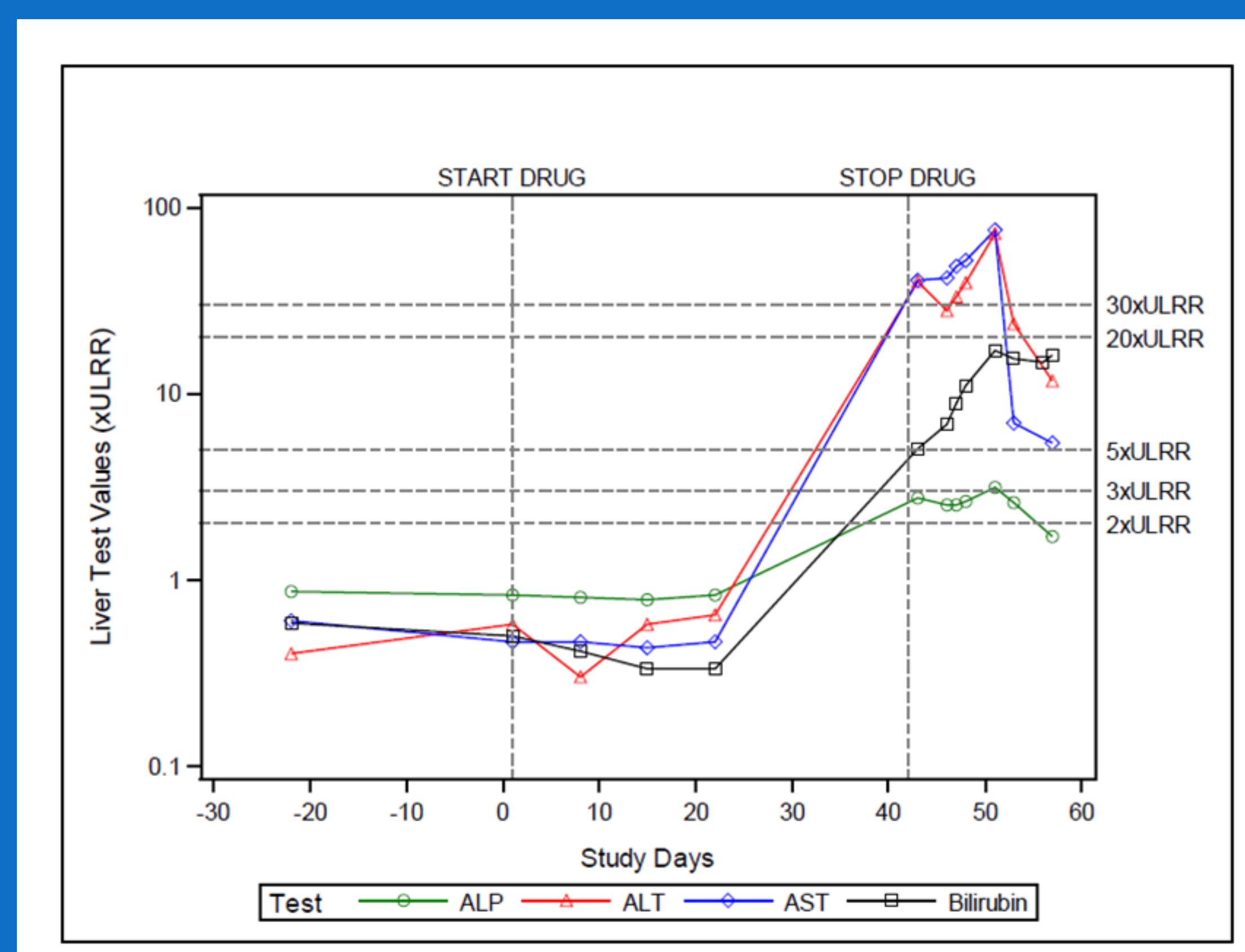
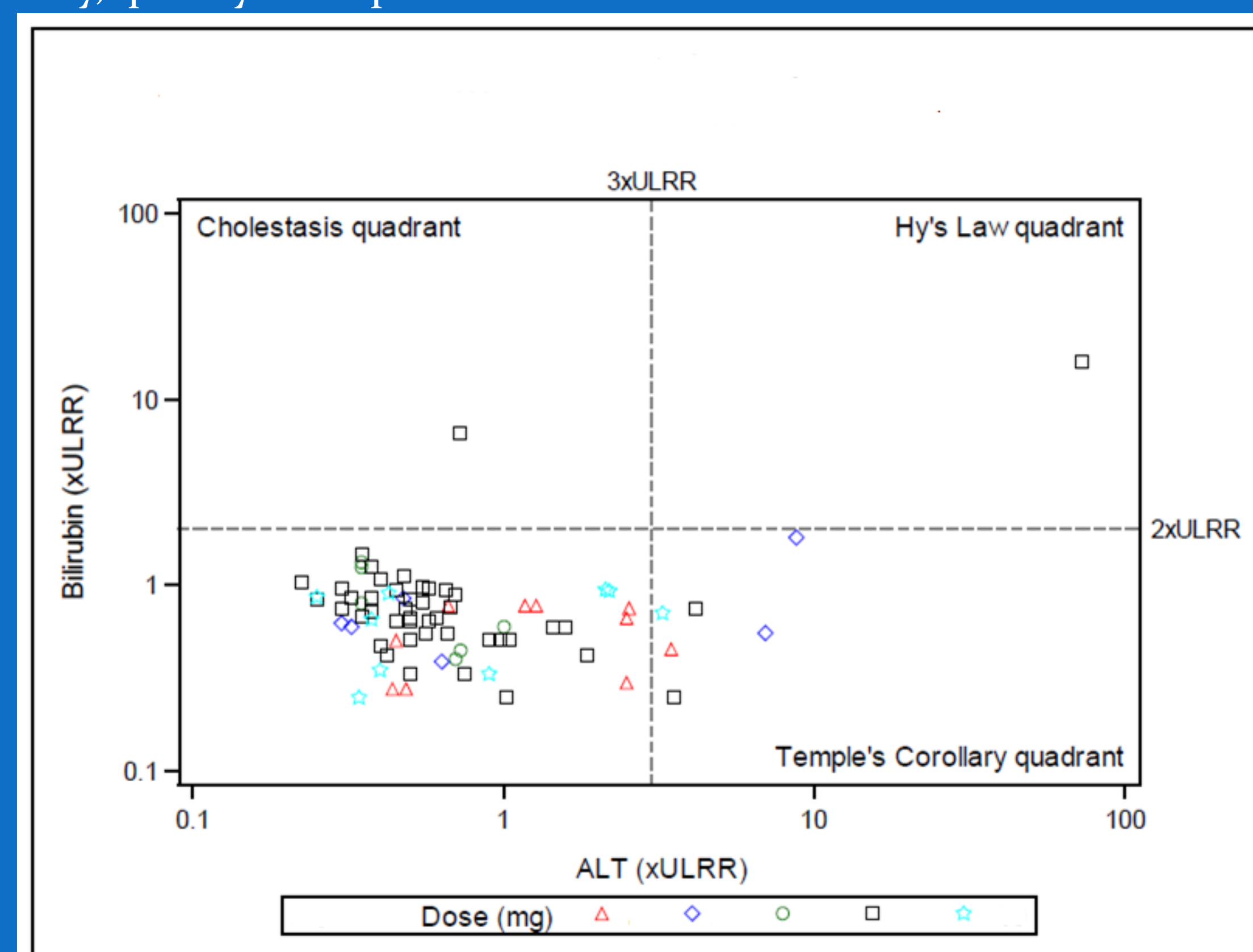
The Early Clinical Biometrics department (ECB) at AstraZeneca (AZ) is part of Early Clinical Development (ECD). ECD is a dedicated resource for the small molecules early stage portfolio. The role of the programming group within ECB is to provide access to clinical analyses which supports strategic decision making in drug projects, e.g. part of the work we do in programming is around providing quick, clear and informative graphical representations to help make these key decision as below. The intention of this poster is to present three examples of decision supportive plots. The poster will illustrate the MDI plot, eDISH plot and Pharmacokinetic Profile plot. Purpose of the three plots will be presented and any special features used in the SAS coding.

MDI(Medicines Differentiation Index) plot

- MDI is a tool that will aid in the setting and evaluation of TPP (Target Product Profile) targets in an efficient way.
- TPP is a strategic level document that describes the characteristics of a drug that would meet the Clinical, Regulatory and Commercial requirements for the covered indication.
- TPP sets the targets for efficacy, safety and other differentiating features of a drug that will treat a given condition and TPP is necessarily a living document.
- MDI plot is a concentrated compilation of current data, modeled data and competitors data. A single image that show how we differentiate the drug projects from the competitors .
- ESPC (Early Stage Product Committee) expects that MDI will be included in all slide sets supporting major investment decisions from FTIM (First Time In Man).
- The benefits of using SAS 9.3® to produce MDI plot are flexibility, consistency and parameter input control.

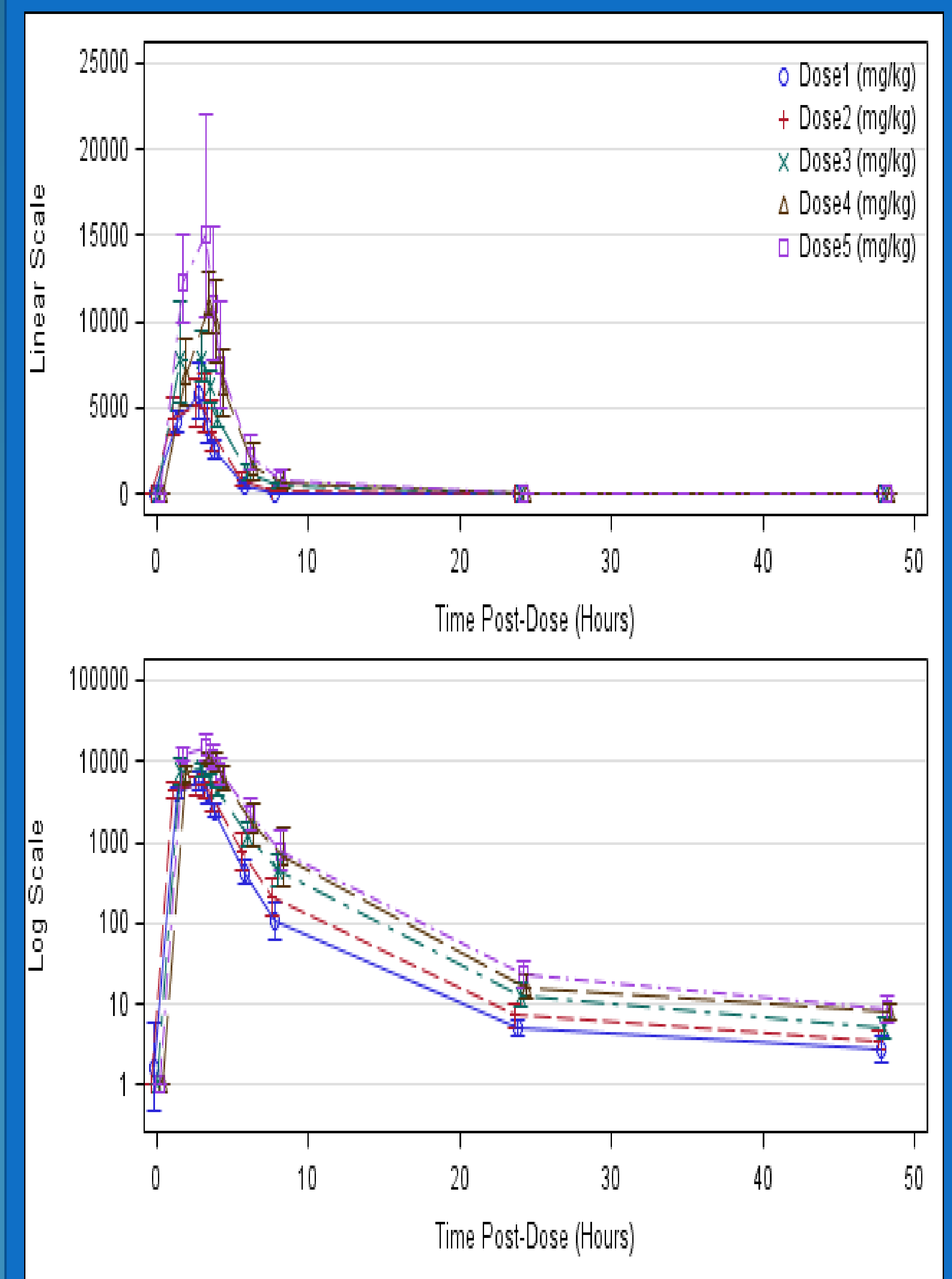
eDISH (Evaluation of Drug-Induced Serious Hepatotoxicity) plot

- A tool for evaluation of DILI (Drug induced liver injury)
- DILI has been the most frequent single cause of safety-related drug marketing withdrawals for the past 50 years
- Hy's Law – a rule of thumb named after Hy Zimmerman which states:
"A drug is at high risk of causing a fatal drug-induced liver injury when given to a large population, if it caused cases of liver injury that satisfied certain criteria when given to a smaller population."
- eDISH plot is a simple but very informative tool for medical reviewers that enables them to view individual lab patient data, study data or pooled data over time.
- eDISH plot allows the project teams to see the lab data trends clearly, quickly to help make informed decision



Pharmacokinetic (PK) profile plot

- Play an important role in interpreting drug concentration-time data as they provide a quick view of the general trend of the drug concentrations over time.
- Normally contains PK profiles of geometric mean concentration with STD bars vs. time
- PROC SGRENDER procedure in SAS 9.3 was used to create a plot. PROC TEMPLATE is efficient tool used for layout control
- Figures of linear scale and log scale are displayed on the same page
- There are options to display side-by-side or top-bottom



Summary

One of ECBs key objective is to deliver the standard data structures to generate recognisable graphical output in order to promote effective internal decision making , e. g. Go/No-go criteria as presented above. Members of the statistical programming group has been tasked with promoting the usage and awareness of ODS functionality. ECB is managing a area of template and code library together with other useful graphics information for easy re-use purposes.

SAS ® is one of the standard tool that is used for graphical presentation of the data, following the SAS/GRAPH® improvement with the release of the ODS procedures. Present in the code library are example code and output for MDI , eDISH, PK profile plot, Scatter plot, Patient Exposure over time plot, Waterfall plots produced by the SAS/GRAPH®