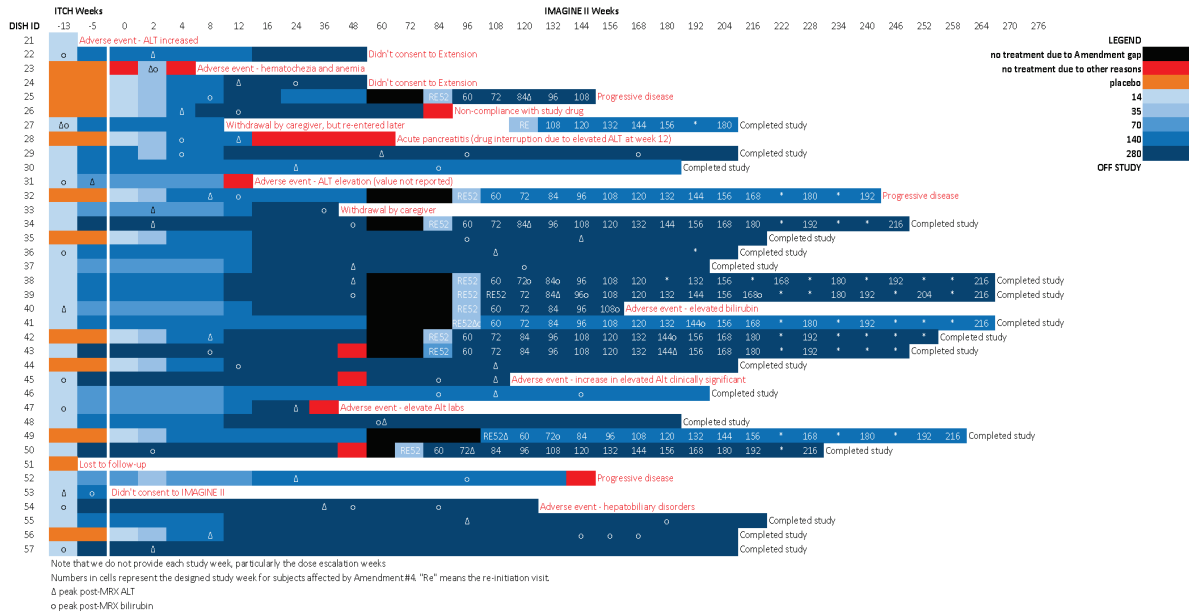
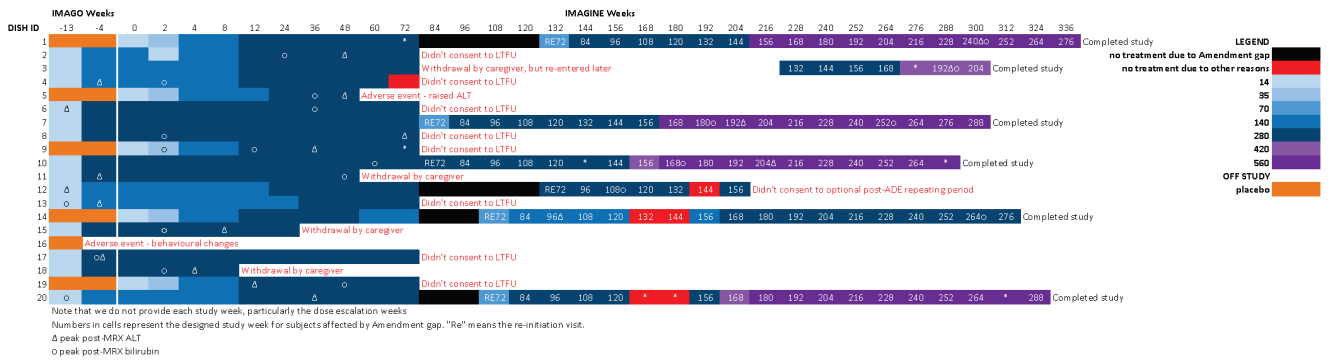


# Supplemental Figure 1. Swimmer Plot of Trial Conduct

A



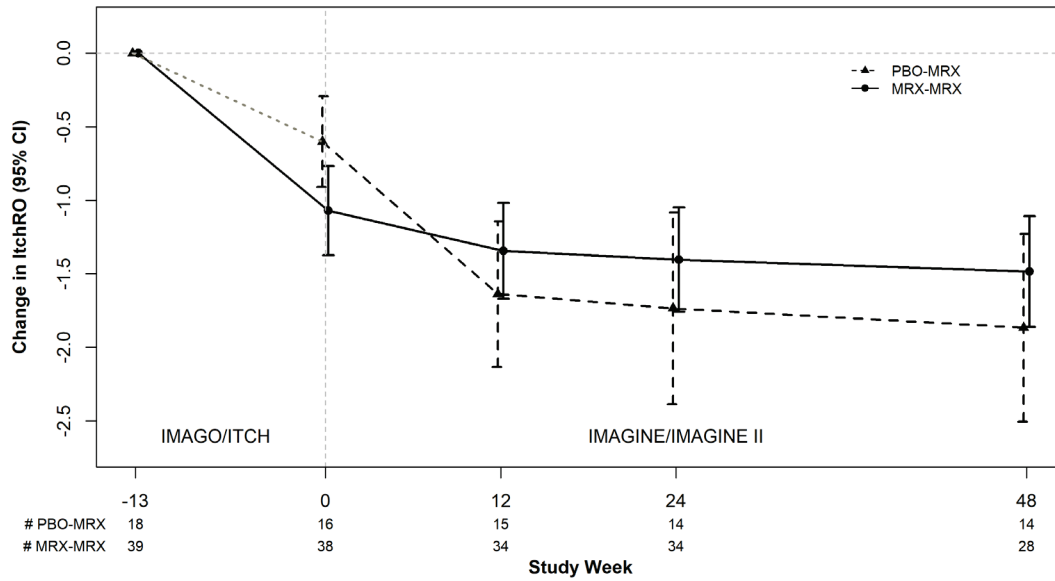
B



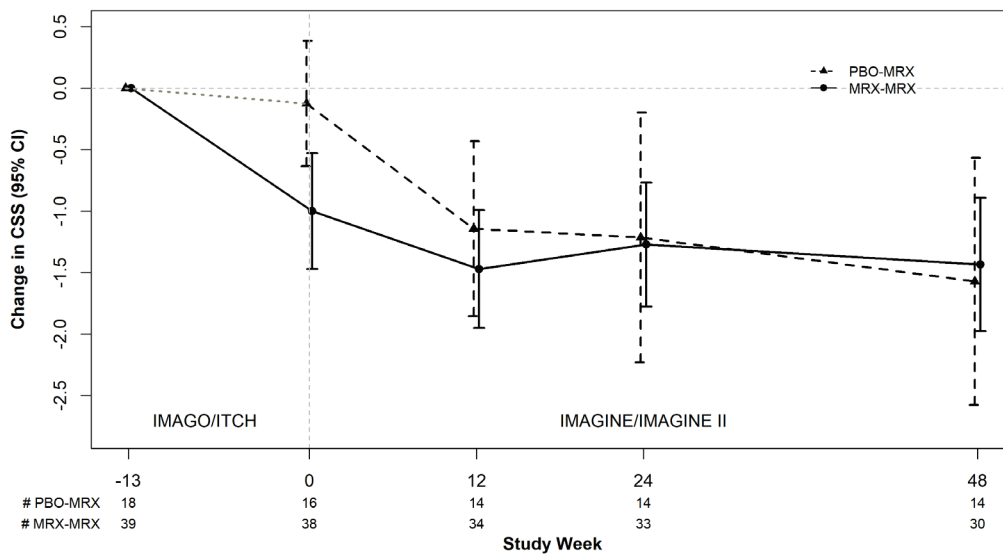
**Supplemental Figure 1. Swimmer Plot of Trial Conduct.** 1A – ITCH and IMAGINE II. Each line represents a single participant. Dose of study drug received is indicated according to the colors in the legend and the time period for the dose correlates with the weeks indicated at the top of the figure. The reason for study discontinuation or completion is indicated. Open circles represent the time of peak total bilirubin, while open triangles represent the time of peak ALT. The numbers in white represent the weeks of study drug administration (i.e., with drug discontinuation time subtracted). RES2 is time of re-entry into study after study drug interruption noted in black. Numbers in each cell represent the designated study week, which may differ from the cumulative week on study because of study drug interruptions. 1B – IMAGO and IMAGINE.

**Supplemental Figure 2. Change in ItchRO(Obs) (2A) or Clinician Scratch Score (CSS) (2B)**

**A**



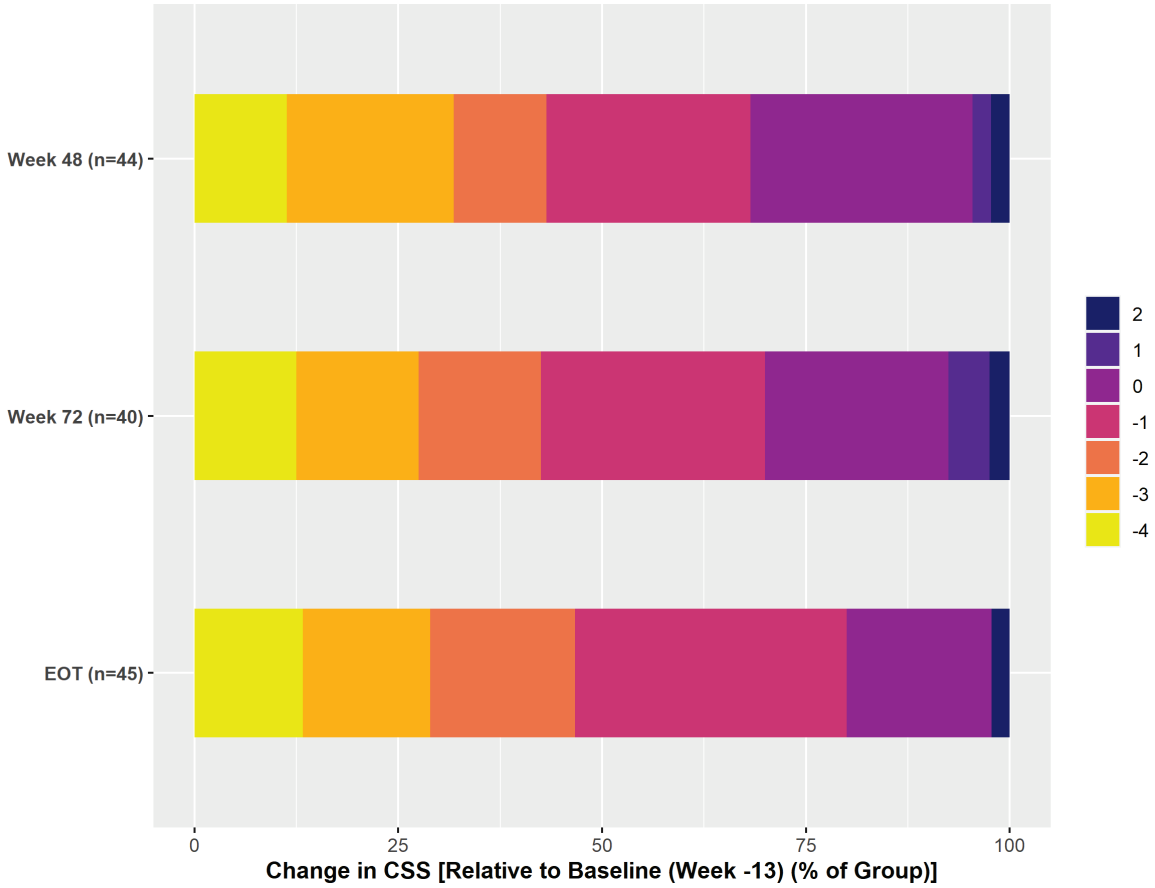
**B**



**Supplemental Figure 2. Change in ItchRO(Obs) (2A) or Clinician Scratch Score (CSS) (2B).**

The mean and 95% confidence interval (CI) for change in measure relative to ITCH/IMAGO baseline (week -13) for individual participants is shown at various time points up to week 48. Participants initially receiving placebo (PBO) are depicted by a dashed line and triangles, while those initially receiving maralixibat (MRX) are depicted by a solid line and circles. The number of participants in the study at a given time point is shown below the graph.

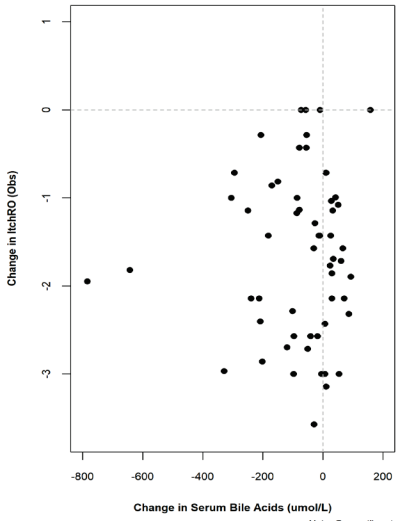
**Supplemental Figure 3. Heatmap of Change in Clinician Scratch Score (CSS) at Weeks 48 and 72 and End of Treatment (EOT).**



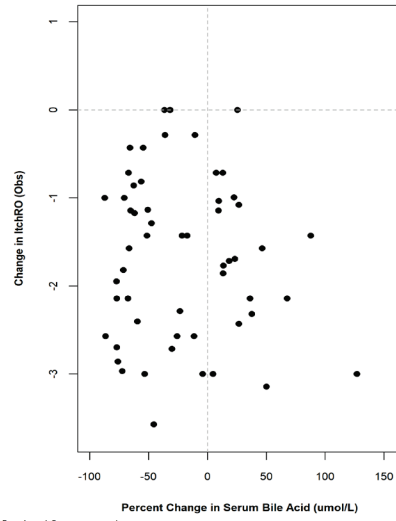
**Supplemental Figure 3. Heatmap of Change in Clinician Scratch Score (CSS) at Weeks 48 and 72 and End of Treatment (EOT).** The number of percentage of participants with changes as noted by the legend relative to baseline CSS is shown.

**Supplemental Figure 4. Scatterplot of Change in ItchRO (4A) or Clinician Scratch Score (CSS) (4B) Relative to Change in Serum Bile Acids**

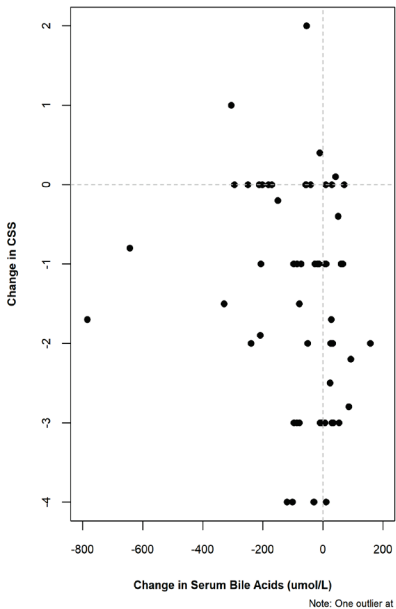
**A**



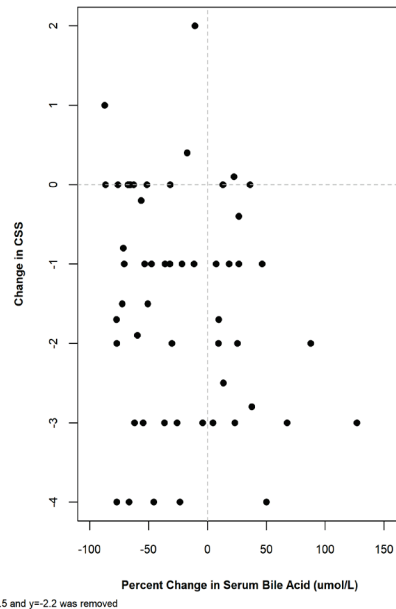
**B**



**C**

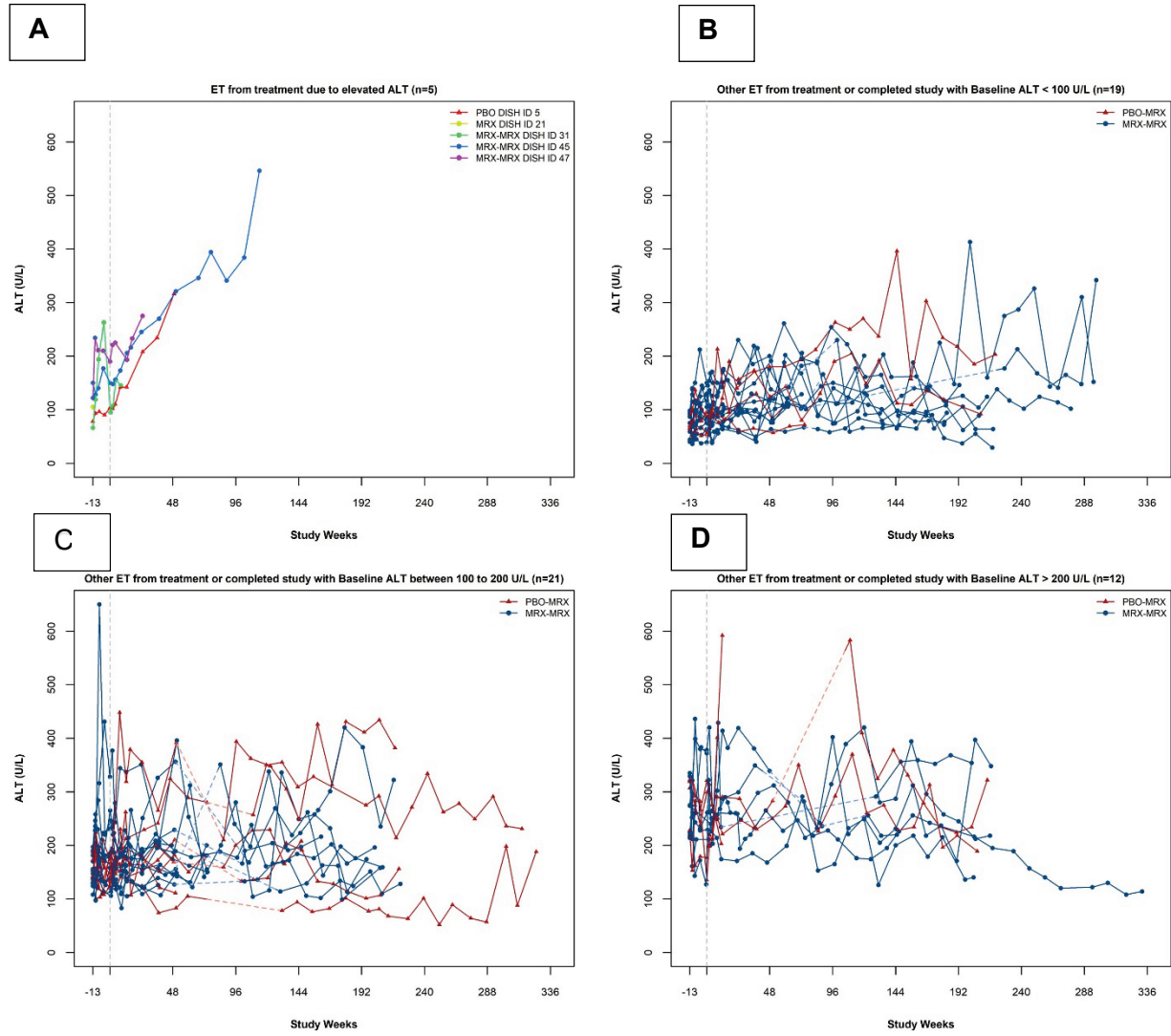


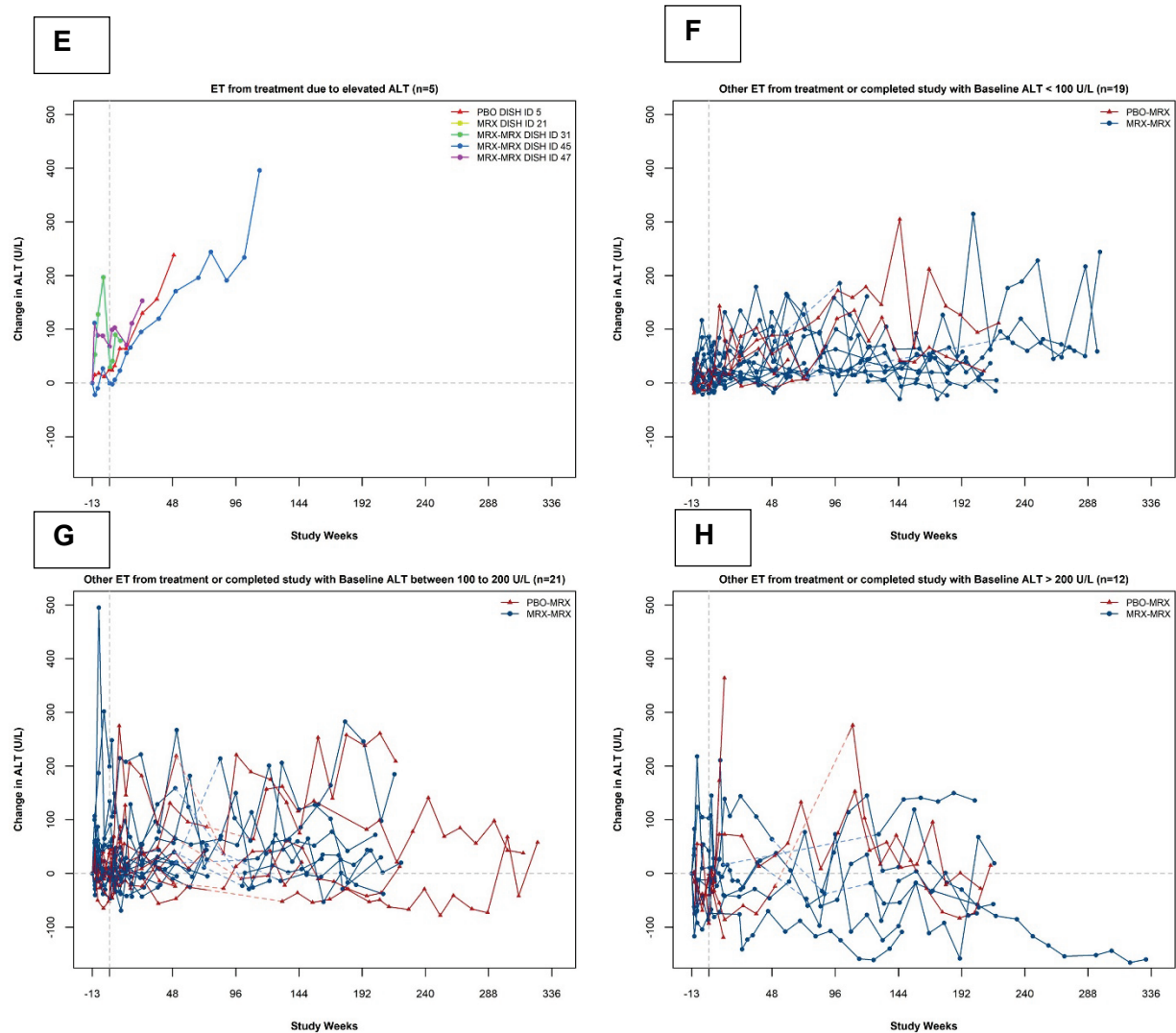
**D**



**Supplemental Figure 4. Scatterplot of Change in ItchRO (4A) or Clinician Scratch Score (CSS) (4B) relative to Change in Serum Bile Acids.** Each point represents a single participant at week 48. Week 48 values were actual values or derived by multiple imputation. The panel on the left indicates absolute change in serum bile acids, while the panel on the right indicates percent change in serum bile acids. The correlation and associated p-value for each of the plots is 4A is  $r = -0.01$ ,  $p = 0.93$ , 4B is  $r = -0.05$ ,  $p = 0.74$ , 4C is  $r = -0.20$ ,  $p = 0.13$ , 4D is  $r = -0.20$ ,  $p = 0.14$ .

**Supplemental Figure 5A. Spaghetti Plots of ALT over Time (5A-5D – actual value, 5E-5H– change from baseline).**

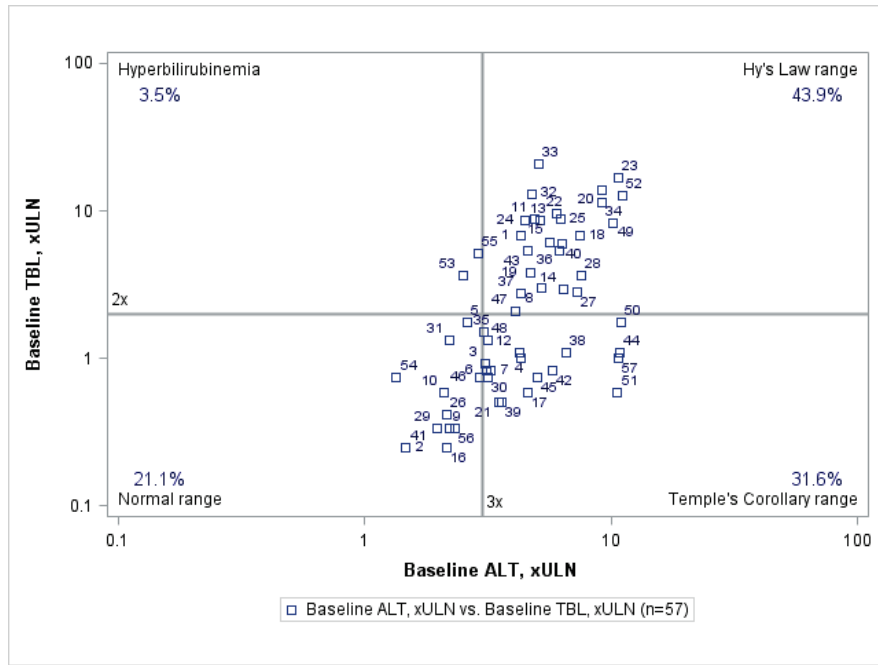




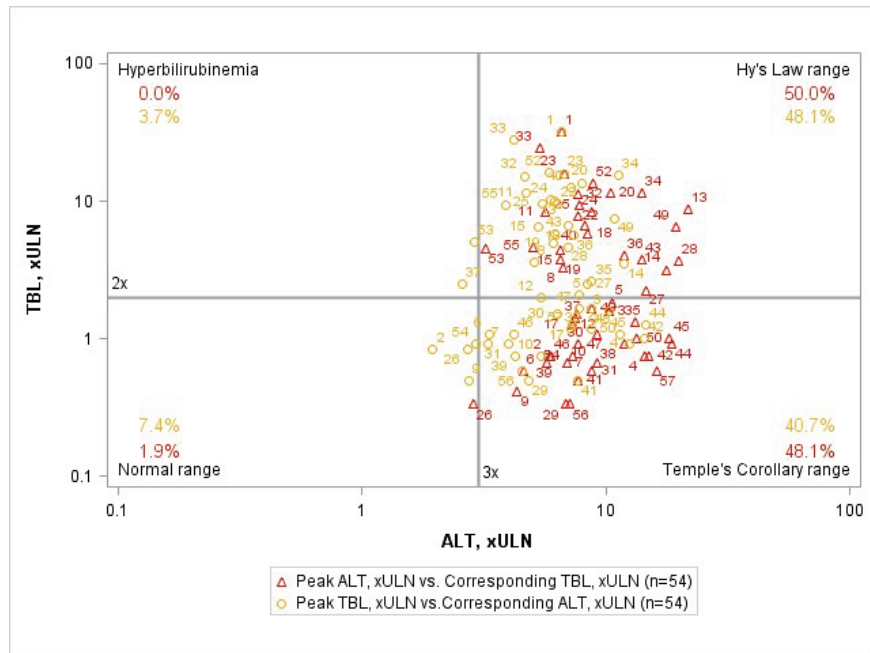
**Supplemental Figure 5. Spaghetti Plots of ALT over time (5A-5D – actual value, 5E-5H – change from baseline).** Panels A and E indicate participants where discontinuation from study medication for increased ALT occurred. Panels B and F indicate participants with baseline ALT < 100 U/L, C and G baseline ALT between 100 and 200 U/L, and D and H baseline ALT > 200 U/L.

**Supplemental Figure 6. Drug-Induced Serious Hepatotoxicity (DISH) Plot of Changes in Alanine Aminotransferase (ALT) and Total Bilirubin (TB) During the Course of the Study.**

**A**

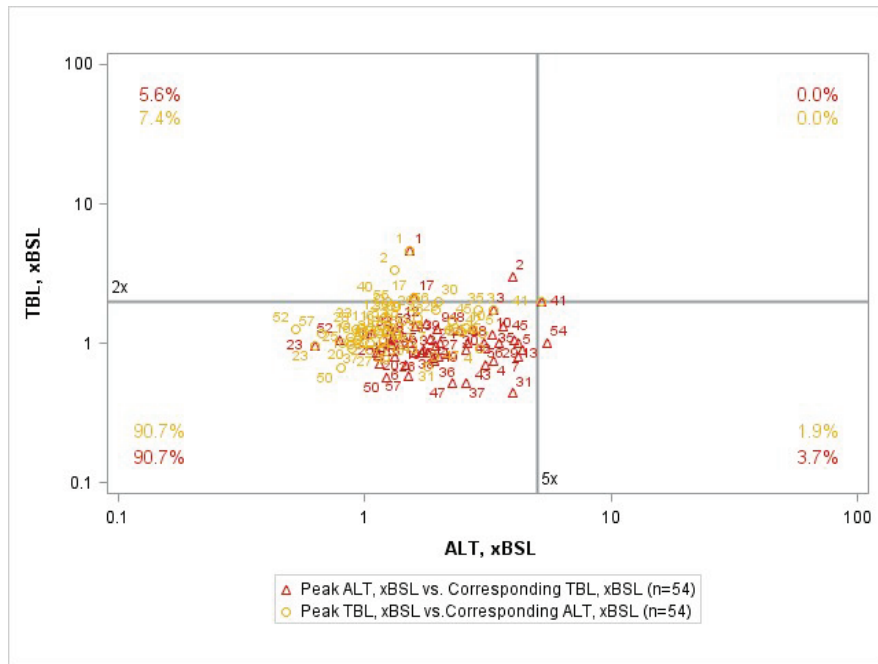


**B**





C



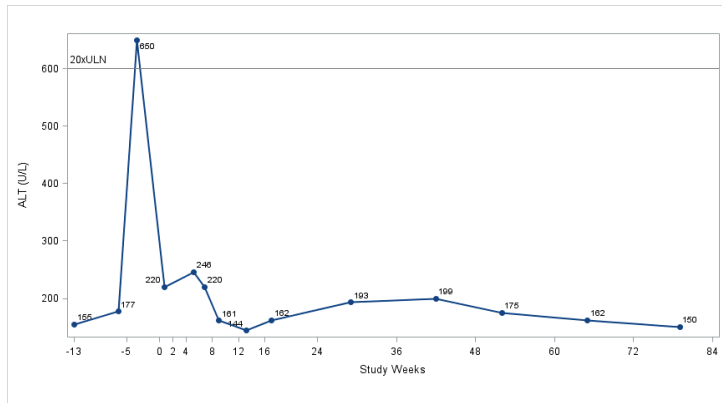
D



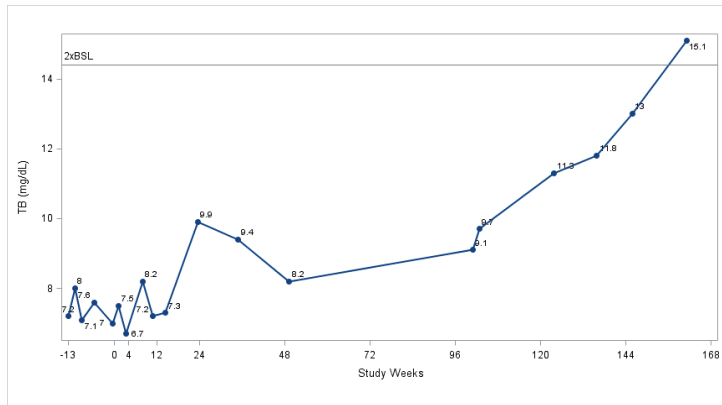
**Supplemental Figure 6. Drug-Induced Serious Hepatotoxicity (DISH) Plot of Changes in Alanine Aminotransferase (ALT) and Total Bilirubin (TB) During the Course of the Study.** The graphs are identical to Figure 4 with the exception that coded identifiers for the participants as noted in Supplemental Figures 1A and 1B.

**Supplemental Figure 7. Spaghetti Plots of Participants Meeting Stopping Guidelines for ALT or TB.**

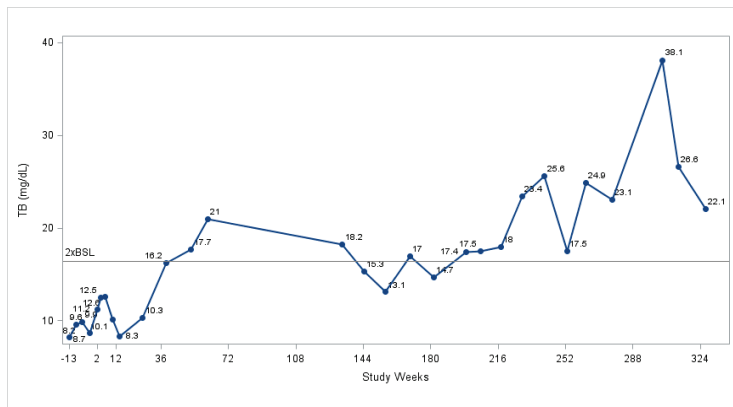
**A**



**B**



**C**



**Supplemental Figure 7. Spaghetti Plots of Participants Meeting Stopping Guidelines for ALT or TB.** Spaghetti plots of participants whose of ALT or TB met stopping guidelines for these parameters. A = DISH ID 13. B = DISH ID 40. C = DISH ID