Comments on the paper authored by Group 23 as Refereed by Group 22

Overall, the method of analysis seems to be correct. Linear regression is a great option in this setting. However,

1. How does the frequency-based test fit into the question of interest? Seems like only the grade-based test is described.

2. Model selection-- it seems strange that site or sex should be adjusted for--as long as the treatment groups are comparable, it shouldn't matter?

Since you are not using the NCI classification to stratify patients, it may be better to mention it in a more concise manner, rather than describe the classification in detail.

General spelling errors (see spell check), but also some not found by spell check:

-in Frequency Based Tests, consider changing “rational” to “rationale”

-general editing technique: we recommend reading the paper out loud to see how the sentences sound

Consider stating more demographic information before discussion of the results.

“We estimated that the mean hearing loss in men and women was significantly different with a 95% confidence threshold at 500 Hz ant 1000 Hz. with men having greater hearing loss in both cases.”

-What was the estimate? P-value?

-From same paragraph, two instances of conjunctive adverb “however”

-Consider changing “, however,” to “; however,” since it connects two closely related but independent clauses

“After adjusting for the patient variables to add precision and avoid any potential confounding, in the frequency based linear regression we observed the estimated difference in mean threshold increase for every mg of LG-03812 per day in all of the measured frequencies. However, this linear increase is only statistically significant for 3 of the 8 measured frequencies.”

-This is an impact statement. At this point the reader is deciding if they want to continue reading. Consider making the statement more explicit, or stating what you mean more plainly, to give a solid introduction to rest of the results.

When stating regression results, consider highlighting the direction of change. It’s fairly clear to a trained reader what is meant (minimum threshold increases between groups differing in one mg/day). However, to non-trained readers the relationship between changes in dose and changes in minimum threshold may not be as clear.

Discussion and Summary (we assume you intend to complete these sections by the final draft)

Table 1: consider using only percentages or only proportions (we prefer proportions) for binary variables site 2 and female.

General table formatting suggestions:

-Make all alignments similar (e.g. make everything left-aligned)

 -Use fewer decimal places (2 or 3 should be fine, maybe 5 for p-values)

Figure 1:

-Unable to obtain information from figure due to small size of plots. Consider making them larger.

-If space is an issue consider what plots are most important and omit others.

Figure 2:

-Not described in text.
-Any association between dose and stopping drug?

-Consider adding axis labels and making the legend more explicit (give units to numbers)

-Consider using a different set of colors or line types to accommodate all varieties of vision

Table 2: Consider grouping all correlation measures by frequency instead of splitting by treatment time/age and sex/site.

What sources were used for background? If any, please cite them.