**Statistical Analysis**

Statistical analysis was performed using R statistical software (version 3.6). Linear models or linear mixed effect models were fitted using lm (stats package) or lmer (lme4 package version 1.1-23 and lmerTest package version 3.1-2) functions, respectively. For dose- and time-response curves linear, quadratic or cubic models were tested. The final model was chosen by the Akaike information criterion (bbmle package version 1.0.23.) and by diagnostics of the residuals (DHARMa package version 0.3.1). Plots were generated by ggplot2 package (version 3.3.1). Model summaries are provided in Supplementary Table XX. Detailed analysis code is available on github: (<https://github.com/tschauer/Juhasz_etal_2020>).

**Legend**

(1D) Clonogenic survival assay … Graph includes all datapoints (n=4) and fitted curves with confidence intervals (grey shading). Asterisks indicate p-values derived from a linear model comparing coefficients of the fitted curves (\* p<0.05, \*\* p<0.01 and \*\*\* p<0.001). Model summary is provided in Supplementary Table XX.

(3B-E) … Asterisks on top of the panels indicate the interaction across MMS and Olaparib curves comparing genotypes (\* p<0.05, \*\* p<0.01 and \*\*\* p<0.001). Model summary is provided in Supplementary Table XX.

(2B) The number of chromosome breaks … Bar graph includes all datapoints and mean ± SEM (n=3). Asterisks indicate p-values derived from a linear model comparing mean differences (\* p<0.05, \*\* p<0.01 and \*\*\* p<0.001). Model summary is provided in Supplementary Table XX.

**Rebuttal**

We thank the reviewer for the comments on statistical analysis, we now completely revised the statistical methods. We put all the analyses into a linear model framework using R statistical software. This allows us the flexibility of choosing the best model fit for each dataset. For dose-response curves we fitted various models using linear, quadratic or cubic terms. We selected the final model based on Akaike information criterion to avoid the risk of overfitting. We carefully investigated the residuals to fulfil model assumptions. A model summary of the coefficients is now provided for each dataset in a supplementary table. We also changed the data visualization by showing the fitted curves whenever applicable. If the reviewer has further questions, we made the detailed analysis code available on github:

(<https://github.com/tschauer/Juhasz_etal_2020>).