

FDA Slide Errata

Slide #	FDA Presented Slide	Corrected Slide																																												
64	<div style="border: 1px solid black; padding: 5px;"> <div style="font-size: 8px; margin-bottom: 5px;"> U.S. Food and Drug Administration Protecting and Promoting Public Health www.fda.gov </div> <h3 style="text-align: center;">Uncertainties with Post-hoc Primary Effectiveness Analysis</h3> <ul style="list-style-type: none"> • Prespecified effectiveness endpoint: <ul style="list-style-type: none"> » Model-based: $p < 0.0001$ » Empirical: $p = 0.15$ • Post-hoc effectiveness endpoint: <ul style="list-style-type: none"> » Model-based: $p = 0.056$ » Empirical: $p = 0.012$ • Some alternative post-hoc GEE models do not achieve statistical significance. • None of the prespecified secondary endpoints achieve statistical significance • No observed data analyses achieve statistical significance <p style="text-align: right; font-size: 8px;">Panel Question 2 ⁶⁴</p> </div>	<div style="border: 1px solid black; padding: 5px;"> <div style="font-size: 8px; margin-bottom: 5px;"> U.S. Food and Drug Administration Protecting and Promoting Public Health www.fda.gov </div> <h3 style="text-align: center;">Uncertainties with Post-hoc Primary Effectiveness Analysis</h3> <ul style="list-style-type: none"> • Prespecified effectiveness endpoint: <ul style="list-style-type: none"> » Model-based: $p < 0.0001$ » Empirical: $p = 0.15$ • Post-hoc effectiveness endpoint: <ul style="list-style-type: none"> » Model-based: $p = 0.056$ ← p=0.0056 » Empirical: $p = 0.012$ • Some alternative post-hoc GEE models do not achieve statistical significance. • None of the prespecified secondary endpoints achieve statistical significance • No observed data analyses achieve statistical significance <p style="text-align: right; font-size: 8px;">Panel Question 2 ⁶⁴</p> </div> <p style="margin-top: 10px;">Correction: The model-based p-value that was for the post-hoc model was presented as $p = 0.056$ when it should have been presented as $p = 0.0056$.</p>																																												
66	<div style="border: 1px solid black; padding: 5px;"> <div style="font-size: 8px; margin-bottom: 5px;"> U.S. Food and Drug Administration Protecting and Promoting Public Health www.fda.gov </div> <h3 style="text-align: center;">Secondary Effectiveness Endpoint Results</h3> <table border="1" style="width: 100%; border-collapse: collapse; font-size: 8px;"> <thead> <tr> <th>Effectiveness Endpoint</th> <th>Treatment</th> <th>Sham</th> <th>P-value</th> </tr> </thead> <tbody> <tr> <td>50% Responder Rate</td> <td>29%</td> <td>27%</td> <td>0.727</td> </tr> <tr> <td>% Change in Mean Seizure Frequency</td> <td>-24%</td> <td>-17%</td> <td>0.238</td> </tr> <tr> <td>% Change in Days with Seizures</td> <td>-18.9%</td> <td>-18.3%</td> <td>Not Reported</td> </tr> <tr> <td>Liverpool Seizure Severity Score</td> <td>-4.7</td> <td>-5.8</td> <td>0.574</td> </tr> </tbody> </table> <p style="font-size: 8px; margin-top: 5px;">The study was powered on the expectation of a 20 % difference in responder rates between the treatment and sham groups.</p> <p style="font-size: 8px; margin-top: 5px;">No interim analysis was performed.</p> <p style="text-align: right; font-size: 8px;">Panel Questions 2 & 3a(i) ⁶⁶</p> </div>	Effectiveness Endpoint	Treatment	Sham	P-value	50% Responder Rate	29%	27%	0.727	% Change in Mean Seizure Frequency	-24%	-17%	0.238	% Change in Days with Seizures	-18.9%	-18.3%	Not Reported	Liverpool Seizure Severity Score	-4.7	-5.8	0.574	<div style="border: 1px solid black; padding: 5px;"> <div style="font-size: 8px; margin-bottom: 5px;"> U.S. Food and Drug Administration Protecting and Promoting Public Health www.fda.gov </div> <h3 style="text-align: center;">Secondary Effectiveness Endpoint Results</h3> <table border="1" style="width: 100%; border-collapse: collapse; font-size: 8px;"> <thead> <tr> <th>Effectiveness Endpoint</th> <th>Treatment</th> <th>Sham</th> <th>P-value</th> </tr> </thead> <tbody> <tr> <td>50% Responder Rate</td> <td>29%</td> <td>27%</td> <td>0.727</td> </tr> <tr> <td>Change in Mean Observed Seizure Counts</td> <td>-11.5</td> <td>-5.0</td> <td>0.238</td> </tr> <tr style="color: red;"> <td>% Change in Mean Seizure Frequency</td> <td>-24%</td> <td>-17%</td> <td>0.238</td> </tr> <tr> <td>% Change in Days with Seizures</td> <td>-18.9%</td> <td>-18.3%</td> <td>Not Reported</td> </tr> <tr> <td>Liverpool Seizure Severity Score</td> <td>-4.7</td> <td>-5.8</td> <td>0.574</td> </tr> </tbody> </table> <p style="font-size: 8px; margin-top: 5px;">The study was powered on the expectation of a 20 % difference in responder rates between the treatment and sham groups.</p> <p style="font-size: 8px; margin-top: 5px;">No interim analysis was performed.</p> <p style="text-align: right; font-size: 8px;">Panel Questions 2 & 3a(i) ⁶⁶</p> </div> <p style="margin-top: 10px;">Correction: The pre-specified secondary endpoints did not include % Change in Mean Seizure Frequency but did include Change in Mean Observed seizure Counts.</p>	Effectiveness Endpoint	Treatment	Sham	P-value	50% Responder Rate	29%	27%	0.727	Change in Mean Observed Seizure Counts	-11.5	-5.0	0.238	% Change in Mean Seizure Frequency	-24%	-17%	0.238	% Change in Days with Seizures	-18.9%	-18.3%	Not Reported	Liverpool Seizure Severity Score	-4.7	-5.8	0.574
Effectiveness Endpoint	Treatment	Sham	P-value																																											
50% Responder Rate	29%	27%	0.727																																											
% Change in Mean Seizure Frequency	-24%	-17%	0.238																																											
% Change in Days with Seizures	-18.9%	-18.3%	Not Reported																																											
Liverpool Seizure Severity Score	-4.7	-5.8	0.574																																											
Effectiveness Endpoint	Treatment	Sham	P-value																																											
50% Responder Rate	29%	27%	0.727																																											
Change in Mean Observed Seizure Counts	-11.5	-5.0	0.238																																											
% Change in Mean Seizure Frequency	-24%	-17%	0.238																																											
% Change in Days with Seizures	-18.9%	-18.3%	Not Reported																																											
Liverpool Seizure Severity Score	-4.7	-5.8	0.574																																											