MALLINCKRODT (MNK) VTS-270 TRIAL:

GLOBAL COMMUNITY QUESTIONS SUBMITTED TO MNK TUESDAY 13TH NOVEMBER 2018

COMMUNICATION

1. WHY WEREN'T THE PI'S IN EACH COUNTRY NOTIFIED OF THE RELEASE BEFOREHAND?

2. WHY DIDN'T MNK REACH OUT TO PATIENTS AND FAMILIES TO ANNOUNCE THEIR FINDINGS IMMEDIATELY AFTERWARDS?

3. HOW DOES MNK INTEND TO SHARE INFORMATION GOING FORWARD, WITH FAMILIES, PI'S INVOLVED WITH THE TRIAL AND THE BROADER COMMUNITY?

4. HOW WILL MNK REASSURE PARENTS AND PATIENTS THAT THEY ARE COMMITTED TO THE TRIAL AND TO COMMUNICATING EFFECTIVELY WITH THE COMMUNITY?

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TRIAL DATA

1. WHEN WILL A DEEPER ANALYSIS OF THE DATA BE COMPLETED?

2. WAS DATA COLLECTED FROM EVERY COUNTRY INVOLVED IN THE TRIAL, FOR DIFFERENT AGE GROUPS E.G. PAEDIATRIC /ADULT ONSET OF DISEASE AND WILL YOU INCLUDE DATA FROM THOSE IN THE SHAM GROUP (EVEN THOSE WHO PROGRESSED AND RECEIVED TREATMENT EARLY)?

3. HOW AND BY WHOM WILL THE DATA BE EVALUATED?

4. THE INFORMATION SHARED SO FAR IS A STATEMENT ABOUT THE PRIMARY ENDPOINT. WHEN WILL YOU SHARE THE DATA ON THE PRIMARY ENDPOINT?

5. WHEN WILL YOU SHARE DATA ON SECONDARY ENDPOINTS AND OTHER OUTCOME MEASURES / BIOMARKER MEASUREMENTS?

6. WILL YOU PROVIDE A BREAKDOWN OF DIFFERENCES ACROSS THE DOMAINS OF THE SEVERITY SCORE, ANY SUBGROUP (BASED ON BASELINE DISEASE SEVERITY) ANALYSIS TRENDS - EVEN IF NOT OF STATISTICAL SIGNIFICANCE? ARE THERE OUTLIER PATIENTS IN THE PLACEBO GROUP THAT COULD BE IMPACTING THE TOP LINE DATA?

7. WHAT IS TAKEN INTO CONSIDERATION WHEN EVALUATING DATA - ONLY THE SEVERITY SCORES OR ALSO THE "SUBJECTIVE PERCEPTIONS" OF FAMILIES, ESPECIALLY FAMILIES OF PATIENTS ON EXPANDED ACCESS?

8. IF CHILDREN RECEIVING TREATMENT DID NOT SHOW DISEASE PROGRESSION, ISN'T THAT EVIDENCE ENOUGH THAT THE TREATMENTS HELPED?

9. HOW WILL DATA FROM THE UNBLINDED TRIAL BE USED?

10. WHY HAS IT TAKEN SO LONG FOR MNK TO RELEASE THE TOP LINE DATA RESULTS SINCE THE END OF THE TRIAL?

11. WILL FAMILIES BE ABLE TO ACCESS THEIR OWN DATA? IF SO, WHEN, AND HOW WILL THEY DO THIS?

12. IS COMPASSIONATE USE PATIENT DATA BEING USED IN EVIDENCE TO THE FDA? IS THE FDA INDICATING THEY ARE WILLING TO LOOK AT IT AS A PERSUASIVE FACTOR?

13. HOW MANY PATIENTS WERE ON MIGLUSTAT IN THE ACTIVE AND PLACEBO COHORT? CAN THE RESULTS PROVIDE SOME INFORMATION ON THE EFFICIENCY OF THE COMBINATION VTS-270 / MIGLUSTAT IN HUMANS, ON VTS-270 ALONE AND ON MIGLUSTAT ALONE?

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TRIAL DESIGN

1. HOW IS IT POSSIBLE TO EVALUATE THE NATURAL HISTORY IN SUCH A SMALL GROUP OF PATIENTS EVALUATED IN SUCH A SHORT PERIOD OF TIME ESPECIALLY WITH REGARD TO THE DIFFERENT PHENOTYPES AND THE PRESUMABLY SLOWED DEGENERATION DUE TO MIGLUSTAT?

2. WILL THE TRIAL DESIGN BE CHANGED?

3. WOULD YOU CONSIDER LOWERING THE DOSE FOR YOUNGER PATIENTS? ALMOST ALL COMPASSIONATE USE CHILDREN ARE ON LOWER DOSES - WILL YOU CONSIDER CHANGING YOUR PROTOCOL?

4. HOW WILL YOU TELL IF THE DRUG IS WORKING AND SHOWS IMPACT?

5. ARE ALL PATIENTS ENROLLED IN THE TRIAL NOW RECEIVING DRUG?

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FUTURE OF THE VTS-270 TRIAL

1. WILL THE TRIAL CONTINUE?

2. WHAT WILL HAPPEN IF THE FDA/EMA DOES NOT APPROVE TREATMENTS?

3. WHAT STAGE OF THE REVIEW PROCESS IS THE DRUG IN WITH THE FDA/EMA?

4. IS IT POSSIBLE THE FDA/EMA MAY WANT TO SEE THE TRIAL EXTENDED AND IF SO IS MNK WILLING TO DO SO?

5. HOW LONG CAN CHILDREN IN THE TRIAL STAY ON THE TREATMENT?

6. WILL VTS-270 REMAIN AVAILABLE FOR TRIAL AND ILND/COMPASSIONATE USE PATIENTS? WILL NEW PATIENTS HAVE THE OPTION OF COMPASSIONATE USE?

7. WILL THE 0 TO 4 TRIAL STILL GO FORWARD AND IF SO WHEN IS IT ANTICIPATED TO BEGIN?

8. IF THE TRIAL CONTINUES, WHAT WILL BE THE FUTURE FREQUENCY OF TREATMENT? COULD MNK CONSIDER PROVISION OF LOCAL/HOME CARE TO BETTER SUPPORT PATIENTS AND TREATING PHYSICIANS?

9. IS MNK INVESTIGATING USE OF A NEW PORT, AND IF SO WHEN MIGHT THESE BE INTRODUCED?