FDA Questions for the Neurological Devices Advisory Panel

December 10, 2021

Ischemic Stroke System (ISS500)
for Acute Ischemic Stroke

BrainsGate

Panel Discussion Question #1

1. The ImpACT-24B pivotal study was conducted from 2011-2018. The sponsor selected the CCI subgroup as an analysis cohort in 2018 after a large proportion of the patients had been randomized and completed the study, and the selection may have altered the comparability of the treatment groups. Further influencing the comparability of the CCI treatment groups, 34 patients (12%) were removed from the SPG stimulation group after randomization, compared to 0 from the sham group.

   Please discuss the effect on the external validity of the trial results.

Panel Discussion Question #2

2. US patients comprised 6% of the patients in the 24B trial and the patients treated at US sites demonstrated a smaller clinical effect (2.6% effect in CCI subgroup) compared to those treated OUS (9.9% effect in CCI subgroup). Additionally, there were many low enrollment countries with a large variability in responder rates across countries.

   Can the overall results of the trial be generalized to the U.S. indicated population?

Panel Discussion Question #3

3. The sliding dichotomous scale used a prognostic model (VISTA) to predict 3-month disease natural history outcome of all subjects in the ImpACT-24B study. Considering the accuracy of the VISTA model, to what extent does the evidence show that treatment with the ISS500 causes the difference from sham observed in the clinical study?

Panel Discussion Question #4

4. A change in device design and how it was studied may have an impact on the effectiveness observed in clinical trials. The device studied in the ImpACT-24B trial is not the final device the sponsor intends to market in the US.

   Given the uncertainties raised from the device changes, study design changes, and statistical analysis plan changes implemented during the conduct of the ImpACT-24B trial, do you believe the evidence from the clinical studies is sufficient to accurately predict the effectiveness of the current version of the ISS500 in the proposed indications for use population?

Panel Discussion Question #5

5. The clinical trials included information on the adverse events experienced by the subjects.

   a. Based on the design of the study and amount of data collected, was the information collected sufficient to adequately assess the probable risks to health? For example, are the risks of increasing cerebral blood flow in the target population adequately addressed with the existing data?

   b. The rate of hemorrhage was quite a bit lower than expected in this population. Was the imaging data sufficient to assess this adverse event?

   c. Although there were no reports in the trials, based on the intended use of the device, how serious are the risks of bleeding and swelling at the implantation site, airway endangerment, laryngospasm, microaspiration, chronic neuropathic pain, acute pain, among other risks to health with use of the device?

Panel Discussion Question #6

6. The injectable neurostimulator (INS) is implanted through an image guided procedure using the Guide View optical navigation system. There are multiple steps to use this system, including the pre-procedural CT, optical targeting, and obtaining dental impressions of the gums and teeth.

   a. What concerns are there regarding safety, accuracy, and reliability of using the system to implant the INS in a location near the sphenopalatine ganglion (SPG)?

   b. What expertise would be needed to implant the device, and is the training program proposed by the sponsor sufficient?