Approved for the first version: 13th April, 2017
Approved for the latest version: 26th February, 2020

Summary of statistical analysis plan (SAP) for post-marketing surveillance (031-101-00116)
- Aripiprazole for irritability associated with pediatric autism spectrum disorder (ASD) in Japan

1. Definition

1.1. Patient disposition

Patient disposition	Definition
Enrolled	Enrolled cases.
Case report failures	Case reports were unavailable among the enrolled cases.
Case reports collected	Case reports were collected and locked the data among the enrolled cases.
Exclusion criteria for safety analysis	1. Treatment not administered 2. Lost to follow-up 3. First dose before registration 4. Others
Safety analysis	Cases do not meet exclusion criteria for safety analysis among the case reports collected.
Exclusion criteria for efficacy analysis	1. Registration after Day 15 2. Other indications (not for irritability associated with pediatric ASD) 3. Assessment failures (all effectiveness measures were not assessed after treatment) 4. Others (all effectiveness measures were assessed over 7 days after last dose or after Day 393, overdose: > 15 mg/day)
Efficacy analysis	Cases do not meet exclusion criteria for efficacy analysis among the safety analysis.

1.2. Timing of assessment and acceptable ranges

Timing of assessment is Baseline, Week 4, Week 8, Week 16, Week 24, Week 52, End-point (LOCF). If more than one data is present within each period, calculate the absolute difference in days from the reference day and employ the smallest absolute value as the data for the time of assessment. If the absolute value is the same, data for the later assessment date will be employed. In addition, data evaluated after the 8th day of the last dose of drug will not be included. Day 1 is the starting day of drug administration for the elapsed days from the starting day of drug administration.

Time point	Record Date	Acceptable range
Baseline	First dose	Day -30 to Day 1
Week 4	Day 28	≥Day 15, < Day 43
Week 8	Day 56	≥Day 43, < Day 71

Time point	Record Date	Acceptable range
Week 16	Day 112	≥Day 85, < Day 141
Week 24	Day 168	≥Day 141, < Day 197
Week 52	Day 364	≥Day 337, < Day 393
End-point (LOCF)	Date [a)] closest to Day 364	-

a) Data outside the acceptable range will also be included. However, the all effectiveness measures, which were assessed over 7 days after last dose or after Day 393 should be excluded.

2. Software for analysis

The following software is used for the analysis.

- SAS 9.2 or later (SAS Institute Japan Ltd.)
- Microsoft Office Excel 2007 or later

3. Analysis

3.1.1. Patient disposition

Prepare the Patient disposition figure.

3.2. Patient demographics

The following items will be tabulated in Safety analysis sample:

Item	Classification	Tabulation and analysis method
Gender	Male and Female	Frequency tabulation
Age	- < 6 years old - ≥ 6 years old, < 13 years old - ≥ 13 years old, < 18 years old - ≥ 18 years old - Unknown	Summary statistics, frequency tabulation
Baseline ABC-J Score	Baseline Subscale Score [Irritability Subscale Score]	Summary statistics

3.3. Safety analysis

Safety analyses are for Safety analysis sample.

3.3.1. Adverse events

1) Adverse events will be coded according to the latest version of MedDRA/J at the time of analysis or its previous version. SOC and PT will be tabulated by case number.
2) If more than one adverse event (PT) is observed within the same case, the data will be

summarized as one subject.

3) If more than one adverse event (SOC) is observed within the same case, the data will be summarized as one subject.

3.3.1.1. Frequency of adverse reactions

The number of cases with adverse events and the incidence of adverse events will be calculated by serious/non-serious and total. In addition, the frequency by SOC and PT is tabulated.

3.4. Efficacy analysis

Efficacy analyses are for Efficacy analysis sample.

Observed Case (OC) will be used for the analysis of each assessment time point. Last Observation Carried Forward (LOCF) is also used to analyze End-point.

3.4.1. ABC-J

Efficacy analysis sample consisted of all participants who received at least one dose of study medication and have Baseline and at least one Post-Baseline efficacy evaluation.

1) Irritability Subscale Score

The total scores for 15 items in item No. 2, 4, 8, 10, 14, 19, 25, 29, 34, 36, 41, 47, 50, 52 and 57 of ABC-J shall be calculated.

However, if at least one missing value is observed during the observation period, the total score will not be calculated.

Summary statistics will be calculated for the changes in subscale scores by time of assessment.

End of document