Clinical trial results:
A Multicentre, 8-week, Single-arm, Open-label, Pragmatic Trial to Explore Acceptance and Performance of Using a Digital Medicine System with Healthcare Professionals and Adult Subjects with Schizophrenia, Schizoaffective Disorder, or First Episode Psychosis on an Oral Atypical Antipsychotic (Aripiprazole, Olanzapine, Quetiapine, or Risperidone)

Summary

EudraCT number	2017-004602-17
Trial protocol	GB
Global end of trial date	06 September 2019

Results information

Result version number	v2 (current)
This version publication date	25 October 2020
First version publication date	16 May 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	031-201-00186

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03568500
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Otsuka Pharmaceutical Development & Commercialization, Inc.
Sponsor organisation address	2440 Research Boulevard, Rockville, Maryland, United States, 20850
Public contact	Global Clinical Development, Otsuka Pharmaceutical Development & Commercialization, Inc., 609 524-6788, clinicaltransparency@otsuka-us.com
Scientific contact	Global Clinical Development, Otsuka Pharmaceutical Development & Commercialization, Inc., 609 524-6788, clinicaltransparency@otsuka-us.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 May 2019
Global end of trial reached?	Yes
Global end of trial date	06 September 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Explore the acceptance and performance of the digital medicine system (DMS) with healthcare professionals and adult participants with schizophrenia, schizoaffective disorder, or first episode psychosis.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 44
Worldwide total number of subjects	44
EEA total number of subjects	44

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	44

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial enrolled participants with a confirmed clinical diagnosis of schizophrenia, schizoaffective disorder, or first episode psychosis.

Pre-assignment

Screening details:

Participants in this trial received at least 1 CoEncapsulated miniature ingestible event marker in a tablet and a medicinal product originator tablet of either aripiprazole, olanzapine, or quetiapine (participants were allowed to take risperidone, though no participant took risperidone in this trial) as prescribed by their healthcare professional.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Aripiprazole

Arm description:

Participants were treated with at least 1 CoEncapsulated (CoE) oral aripiprazole tablet, wearing the digital medicine system (DMS) patch, and using the associated smartphone app for a total of 8 weeks.

Arm type	Experimental
Investigational medicinal product name	Aripiprazole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral tablet; dosage determined by the healthcare professional.

Investigational medicinal product name	Digital Medicine System
Investigational medicinal product code	
Other name	DMS
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The DMS included a drug-device combination of a CoEncapsulated (CoE) drug, a patch, and application software to convey level of activity and rest, and to mark events through the act of ingestion.

Arm title	Olanzapine

Arm description:

Participants were treated with at least 1 CoE oral olanzapine tablet, wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks.

Arm type	Experimental
Investigational medicinal product name	Digital Medicine System
Investigational medicinal product code	
Other name	DMS
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The DMS included a drug-device combination of a CoEncapsulated (CoE) drug, a patch, and application

software to convey level of activity and rest, and to mark events through the act of ingestion.

Investigational medicinal product name	Olanzapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral tablet; dosage determined by the healthcare professional.

Arm title	Quetiapine

Arm description:

Participants were treated with at least 1 CoE oral quetiapine tablet, wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks.

Arm type	Experimental
Investigational medicinal product name	Digital Medicine System
Investigational medicinal product code	
Other name	DMS
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The DMS included a drug-device combination of a CoEncapsulated (CoE) drug, a patch, and application software to convey level of activity and rest, and to mark events through the act of ingestion.

Investigational medicinal product name	Quetiapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral tablet; dosage determined by the healthcare professional.

Number of subjects in period 1	Aripiprazole	Olanzapine	Quetiapine
Started	18	20	6
Received At Least 1 Dose of Study Drug	18	19	6
Completed	8	14	2
Not completed	10	6	4
Physician decision	1	-	-
Consent withdrawn by subject	4	2	-
Participant Noncompliance	1	1	-
Adverse event, non-fatal	1	1	2
Technical Problems	2	1	-
Lost to follow-up	1	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Aripiprazole
Reporting group description:	
Participants were treated with at least 1 CoEncapsulated (CoE) oral aripiprazole tablet, wearing the digital medicine system (DMS) patch, and using the associated smartphone app for a total of 8 weeks.	
Reporting group title	Olanzapine
Reporting group description:	
Participants were treated with at least 1 CoE oral olanzapine tablet, wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks.	
Reporting group title	Quetiapine
Reporting group description:	
Participants were treated with at least 1 CoE oral quetiapine tablet, wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks.	

Reporting group values	Aripiprazole	Olanzapine	Quetiapine
Number of subjects	18	20	6
Age categorical Units:			
Age continuous Units: Years			
arithmetic mean	31.6	38.0	30.8
standard deviation	± 9.6	± 11.4	± 8.8
Gender categorical Units: Subjects			
Female	8	4	3
Male	10	16	3
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	4	4	0
White	14	15	6
More than one race	0	0	0
Unknown or Not Reported	0	1	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	17	18	5
Unknown or Not Reported	1	2	1
Disease Diagnosis Units: Subjects			
Schizophrenia: Schizophrenia	5	13	0
Schizophrenia: Schizoaffective Disorder	4	4	2

Schizophrenia: First Episode Psychosis	9	3	4

Reporting group values	Total		
Number of subjects	44		
Age categorical Units:			
Age continuous Units: Years arithmetic mean standard deviation	 -		
Gender categorical Units: Subjects			
Female	15		
Male	29		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	8		
White	35		
More than one race	0		
Unknown or Not Reported	1		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	40		
Unknown or Not Reported	4		
Disease Diagnosis Units: Subjects			
Schizophrenia: Schizophrenia	18		
Schizophrenia: Schizoaffective Disorder	10		
Schizophrenia: First Episode Psychosis	16		

End points

End points reporting groups

Reporting group title	Aripiprazole

Reporting group description:

Participants were treated with at least 1 CoEncapsulated (CoE) oral aripiprazole tablet, wearing the digital medicine system (DMS) patch, and using the associated smartphone app for a total of 8 weeks.

Reporting group title	Olanzapine

Reporting group description:

Participants were treated with at least 1 CoE oral olanzapine tablet, wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks.

Reporting group title	Quetiapine

Reporting group description:

Participants were treated with at least 1 CoE oral quetiapine tablet, wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks.

Subject analysis set title	Schizophrenia
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had a confirmed clinical diagnosis of schizophrenia (defined by International Classification of Disease-10 codes F20 and F25). There was no limit on the duration of illness. Participants were treated with at least 1 CoE oral atypical antipsychotic tablet (aripiprazole, olanzapine, or quetiapine), wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks. The treatment medication decision was determined by the healthcare professional.

Subject analysis set title	Schizoaffective Disorder
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had a confirmed clinical diagnosis of schizoaffective disorder (defined by International Classification of Disease-10 codes F20 and F25). There was no limit on the duration of illness. Participants were treated with at least 1 CoE oral atypical antipsychotic tablet (aripiprazole, olanzapine, or quetiapine), wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks. The treatment medication decision was determined by the healthcare professional.

Subject analysis set title	First Episode Psychosis
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had a confirmed clinical diagnosis of first episode psychosis using case note review. The duration of illness was defined as less than 3 years since presentation to the mental health team or first antipsychotic prescription. Participants were treated with at least 1 CoE oral atypical antipsychotic tablet (aripiprazole, olanzapine, or quetiapine), wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks. The treatment medication decision was determined by the healthcare professional.

Subject analysis set title	Total
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were treated with at least 1 CoE oral atypical antipsychotic tablet (aripiprazole, olanzapine, or quetiapine), wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks. The treatment medication decision was determined by the healthcare professional.

Subject analysis set title	Schizophrenia
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had a confirmed clinical diagnosis of schizophrenia (defined by International Classification of Disease-10 codes F20 and F25). There was no limit on the duration of illness. Participants were treated with at least 1 CoE oral atypical antipsychotic tablet (aripiprazole, olanzapine, or quetiapine), wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks. The treatment medication decision was determined by the HCP.

Subject analysis set title	Schizoaffective Disorder
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had a confirmed clinical diagnosis of schizoaffective disorder (defined by International Classification of Disease-10 codes F20 and F25). There was no limit on the duration of illness. Participants were treated with at least 1 CoE oral atypical antipsychotic tablet (aripiprazole, olanzapine, or quetiapine), wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks. The treatment medication decision was determined by the HCP.

Subject analysis set title	First Episode Psychosis
Subject analysis set type	Full analysis

Subject analysis set description:

Participants had a confirmed clinical diagnosis of first episode psychosis using case note review. The duration of illness was defined as less than 3 years since presentation to the mental health team or first antipsychotic prescription. Participants were treated with at least 1 CoE oral atypical antipsychotic tablet (aripiprazole, olanzapine, or quetiapine), wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks. The treatment medication decision was determined by the HCP.

Primary: Percentage Of Days With Good Patch Coverage

End point title	Percentage Of Days With Good Patch Coverage[1]

End point description:

The DMS includes a drug-device combination of a CoE product, a wearable sensor patch, and application software (smartphone) to record activity and rest and mark events through the act of ingestion. The CoE product consists of an approved antipsychotic medication enclosed with an Ingestible Sensor Pill (miniature ingestible event marker in tablet [MIT]). The sensor patch detects and records each MIT ingestion, as well as other physiologic and behavioral data. Good patch coverage for a specific day was defined as having either at least 80% patch data available (80% of the day the patch was worn and data was collected as noted via the accelerometer channel) or the MIT was detected within the 24-hour period, for each day while the participant was in the trial. The percentage of days was calculated as the number of days with good patch coverage divided by the total number of trial days for each participant. Descriptive statistics were performed for this outcome measure.

End point type	Primary

End point timeframe:

Up to 8 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Quantitative statistical analysis (for example, a p-value) was not performed. Descriptive statistics are included (mean and standard deviation).

End point values	Schizophrenia	Schizoaffective Disorder	First Episode Psychosis	Total
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	9	16	43
Units: percentage of days				
arithmetic mean (standard deviation)	64.34 (± 20.24)	62.99 (± 37.68)	62.51 (± 27.53)	63.37 (± 26.60)

Statistical analyses

No statistical analyses for this end point

Secondary: Participant Adherence

End point title	Participant Adherence

End point description:

The DMS includes a drug-device combination of a CoE product, a wearable sensor patch, and application software (smartphone) to record activity and rest and mark events through the act of ingestion. The CoE product consists of an approved antipsychotic medication enclosed with an Ingestible Sensor Pill (MIT). The sensor patch detects and records each MIT ingestion, as well as other physiologic and

behavioral data. Participant adherence was measured as the detected MITs over the expected MITs ingested during the trial days with good patch coverage. The more the participant successfully engaged in a number of processes across the 8-week trial, the greater the measured adherence. Descriptive statistics were performed for this outcome measure.

End point type	Secondary

End point timeframe:

Up to 8 weeks

End point values	Total	Schizophrenia	Schizoaffective Disorder	First Episode Psychosis
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	18	8	16
Units: percentage of MITs				
arithmetic mean (standard deviation)	86.57 (± 14.47)	88.94 (± 8.06)	72.29 (± 25.65)	91.04 (± 7.37)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline to Week 24 (+ 7 days)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	Aripiprazole
Reporting group description: Participants were treated with at least 1 CoEncapsulated (CoE) oral aripiprazole tablet, wearing the digital medicine system (DMS) patch, and using the associated smartphone app for a total of 8 weeks.	
Reporting group title	Olanzapine
Reporting group description: Participants were treated with at least 1 CoE oral olanzapine tablet, wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks.	
Reporting group title	Quetiapine
Reporting group description: Participants were treated with at least 1 CoE oral quetiapine tablet, wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks.	
Reporting group title	Total
Reporting group description: Participants were treated with at least 1 CoE oral atypical antipsychotic tablet (aripiprazole, olanzapine, or quetiapine), wearing the DMS patch, and using the associated smartphone app for a total of 8 weeks. The treatment medication decision was determined by the healthcare professional.	

Serious adverse events	Aripiprazole	Olanzapine	Quetiapine
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	0 / 19 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Total		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Aripiprazole	Olanzapine	Quetiapine
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 18 (22.22%)	2 / 19 (10.53%)	3 / 6 (50.00%)
General disorders and administration site conditions			
Medical device site irritation			
subjects affected / exposed	4 / 18 (22.22%)	2 / 19 (10.53%)	3 / 6 (50.00%)
occurrences (all)	5	2	4

Non-serious adverse events	Total		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 43 (20.93%)		
General disorders and administration site conditions			
Medical device site irritation			
subjects affected / exposed	9 / 43 (20.93%)		
occurrences (all)	11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported