



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 | v1 |
| This version publication date | 16 May 2020 |
| First version publication date | 16 May 2020 |

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

| | |
|-----------|-------------------------|
| Arm title | Digital Medicine System |
|-----------|-------------------------|

Arm description:

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

| | |
|--|-------------------------|
| 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 | 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 | 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.

| | |
|--|------------|
| 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 | Digital Medicine System |
|--|-------------------------|
| Started | 44 |
| Received At Least 1 Dose of Study Drug | 43 |
| Completed | 24 |
| Not completed | 20 |
| Physician decision | 1 |
| Consent withdrawn by subject | 7 |
| Participant Noncompliance | 1 |
| Adverse event, non-fatal | 4 |
| Technical Problems | 3 |
| Lost to follow-up | 4 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------------------|
| Reporting group title | Digital Medicine System |
|-----------------------|-------------------------|

Reporting group description:

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

| Reporting group values | Digital Medicine System | Total | |
|------------------------|-------------------------|-------|--|
| Number of subjects | 44 | 44 | |
| Age categorical | | | |
| Units: | | | |

| | | | |
|---|--------|----|--|
| Age continuous | | | |
| Units: Years | | | |
| arithmetic mean | 34.4 | | |
| standard deviation | ± 10.7 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 15 | 15 | |
| Male | 29 | 29 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 0 | 0 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 8 | 8 | |
| White | 35 | 35 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 1 | 1 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | |
| Not Hispanic or Latino | 40 | 40 | |
| Unknown or Not Reported | 4 | 4 | |
| Disease Diagnosis | | | |
| Units: Subjects | | | |
| Schizophrenia: Schizophrenia | 18 | 18 | |
| Schizophrenia: Schizoaffective Disorder | 10 | 10 | |
| Schizophrenia: First Episode Psychosis | 16 | 16 | |

End points

End points reporting groups

| | |
|-----------------------|-------------------------|
| Reporting group title | Digital Medicine System |
|-----------------------|-------------------------|

Reporting group description:

Participants were treated with at least 1 CoEncapsulated (CoE) oral atypical antipsychotic tablet (aripiprazole, olanzapine, or quetiapine), wearing the digital medicine system (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 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.

Primary: Percentage Of Days With Good Patch Coverage

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

End point description:

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 miniature ingestible event marker in tablet (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 (\pm 20.24) | 62.99 (\pm 37.68) | 62.51 (\pm 27.53) | 63.37 (\pm 26.60) |

Statistical analyses

No statistical analyses for this end point

Secondary: Participant Adherence

| | |
|-----------------|-----------------------|
| End point title | Participant Adherence |
|-----------------|-----------------------|

End point description:

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 | 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 | 8 | 16 | 42 |
| Units: percentage of MITs | | | | |
| arithmetic mean (standard deviation) | 88.94 (\pm 8.06) | 72.29 (\pm 25.65) | 91.04 (\pm 7.37) | 86.57 (\pm 14.47) |

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

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|-----------------------|--------------|
| Reporting group title | Aripiprazole |
|-----------------------|--------------|

Reporting group description:

Participants were treated with at least 1 CoE oral aripiprazole tablet, wearing the 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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

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|---------------|
| None reported |
|---------------|

Notes: