Real-World Auvelity® (AXS-05) Patient Characteristics in Major Depressive Disorder

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Objective

- To examine how Auvelity is used in the real-world setting for patients with MDD in the US

Conclusions

- Using a large claims database in the US, this initial real-world assessment of Auvelity identified 22,288 patients diagnosed with MDD who began Auvelity treatment within one year of its introduction
- Approximately 10% of patients were treatment-naïve during the 12-month pre-index period
- Nearly 29% of all patients and 98% of treatment-naïve patients initiated Auvelity as monotherapy
- PCPs, NPs, and PAs played a significant role in MDD management, accounting for 27% of initial Auvelity prescriptions
- The majority of patients presented with mental health-related comorbidities and had previously attempted various treatments for MDD, emphasizing the necessity for alternative therapeutic approaches

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Disclosures

A Muzyk and **FZ Syed** report no conflict of interest relevant to this poster
H Zhou and **J Cong** are employees of KMK Consulting, LLC.
H Tabuteau, and **Y Zhao** are employees of Axsome Therapeutics Inc.

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Introduction

- Major depressive disorder (MDD) is a prevalent and chronic disorder associated with decreased quality of life, increased functional impairment, morbidity, and mortality[1-4]
- MDD treatment varies due to differences in presentation, patient demographics, and clinical characteristics, often leading to inadequate patient response to monoamine-targeted therapies[5,6]
- Despite several approved treatment classes, patients often struggle to achieve remission, highlighting the need for new options[6,7]
- N-methyl-D-aspartate (NMDA) receptor antagonism, exemplified by esketamine and now Auvelity (45-mg dextromethorphan/105-mg bupropion), offers novel therapeutic pathways for MDD[8]
- Auvelity, an oral, NMDA receptor antagonist, sigma-1 receptor agonist, and aminoketone CYP2D6 inhibitor, was approved in Aug 2022 for the treatment of MDD in adults[9]
  - The dextromethorphan component of Auvelity is an antagonist of the NMDA receptor, an ionotropic glutamate receptor, and a sigma-1 receptor agonist which modulates glutamatergic neurotransmission
  - The bupropion component of Auvelity is an aminoketone that is a CYP2D6 inhibitor that increases the bioavailability of dextromethorphan, and is a weak norepinephrine and dopamine reuptake inhibitor

METHODS

Study design

- Adult patients initiating Auvelity in the Symphony IDV® claims databases between Aug 2017-Sep 2023 were identified with the first Auvelity claim as the index date
- Eligible patients had ≥1 active claim over the 12-month pre-index period, and ≥1 MDD diagnosis (ICD-10-CM codes: F32.*, F33.*) over the 5-year pre-index period

Outcomes

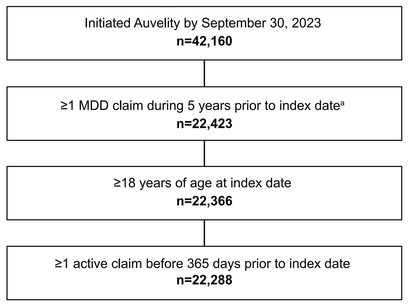
- Patient demographics and clinical characteristics (comorbidities and prior MDD-related medication use) during the 12-month pre-index period
- Initiation status of Auvelity: monotherapy or add-on therapy
  - Therapies that Auvelity was added on to
- Specialty of the prescriber for the initial Auvelity claim
- Characteristics of patients who did not receive any MDD-related treatment during the 12-month pre-index period ("treatment-naïve patients") and their Auvelity initiation status

RESULTS

Patient characteristics

- Overall, 22,288 patients with MDD treated with Auvelity (mean age 45.1 years; 68.1% women) were included (**Figure 1** and **Table 1**)
- The largest proportion of patients were aged 35-44 years (22.6%), lived in the South (40.0%), and were covered by commercial insurance (58.5%)
- Around 70% of patients obtained their initial Auvelity prescription from psychiatrists/mental health specialists, with primary care physicians (PCPs) and nurse practitioners/physician's assistants (NPs/PAs) each accounting for 13.6% of prescriptions
- The most common comorbidities in the 12-month pre-index period were mental health disorders (53.5%; 47.6% had anxiety disorders), followed by metabolic (26.4%) and musculoskeletal/pain (22.6%) (**Table 2**)

Figure 1. Patient Attrition Diagram



[a]ICD-10-CM codes: F32.*, F33.*

Table 1. Patient Demographics

Parameter	All Auvelity Patients (N=22,288)	Treatment-naïve Patients Prior to Auvelity Initiation[a] (n=2,254)
Age, mean (SD), years	45.1 (14.7)	44.0 (14.5)
Age groups, n (%)		
18 to 34 years	6,089 (27.3)	686 (30.4)
35 to 54 years	9,894 (44.4)	988 (43.8)
55 to 64 years	4,005 (18.0)	358 (15.9)
≥65 years old	2,300 (10.3)	222 (9.8)
Female, n (%)	15,188 (68.1)	1,451 (64.4)
U.S. Region, n (%)		
South	8,915 (40.0)	1,042 (46.2)
Midwest	6,860 (30.8)	586 (26.0)
Northeast	3,748 (16.8)	314 (13.9)
West	2,650 (11.9)	295 (13.1)
Health insurance, n (%)		
Commercial	13,035 (58.5)	1,318 (58.5)
Medicaid	3,991 (17.9)	374 (16.6)
Medicare	3,443 (15.4)	284 (12.6)
Initiating healthcare provider specialty, n (%)		
Psychiatry and mental health	15,562 (69.8)	1,427 (63.3)
PCP	3,032 (13.6)	394 (17.5)
NP/PA	3,041 (13.6)	338 (15.0)

[a]Patients who did not receive treatment during the 12-month pre-index period.
NP, nurse practitioner; PA, physician's assistant; PCP, primary care provider.

Table 2. Patient Comorbidities

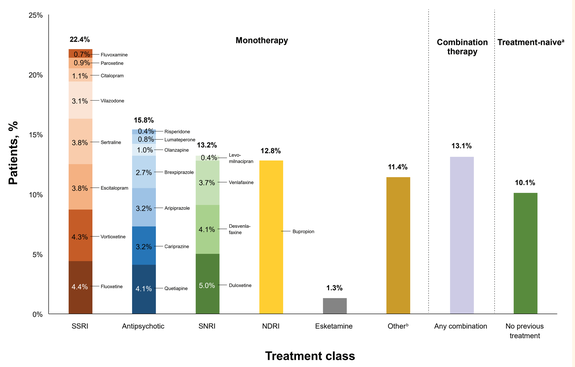
Parameter	All Auvelity Patients (N=22,288)	Treatment-naïve Patients Prior to Auvelity Initiation[a] (n=2,254)
Comorbidities, n (%)[b]		
Mental health disorder	**11,933 (53.5)**	**1,074 (47.6)**
Anxiety	10,606 (47.6)	946 (42.0)
ADHD, conduct disorders, and hyperkinetic syndrome	3,132 (14.1)	283 (12.6)
Bipolar disorder	2,682 (12.0)	187 (8.3)
PTSD	2,548 (11.4)	181 (8.0)
Metabolic	**5,890 (26.4)**	**539 (23.9)**
Hyperlipidemia	3,409 (15.3)	316 (14.0)
Obesity	3,154 (14.2)	287 (12.7)
Diabetes/prediabetes	2,091 (9.4)	181 (8.0)
Musculoskeletal/pain	**5,029 (22.6)**	**446 (19.8)**
Low back pain	2,559 (11.5)	224 (9.9)
Rheumatoid arthritis/osteoarthritis	2,475 (11.1)	208 (9.2)
Migraine and chronic headache	1,657 (7.4)	134 (5.9)
Cardiovascular disease	**4,227 (19.0)**	**382 (16.9)**
Hypertension	3,789 (17.0)	347 (15.4)
Sleep disorders	**4,097 (18.4)**	**347 (15.4)**
Sleep apnea	2,620 (11.8)	223 (9.9)
Insomnia	1,810 (8.1)	145 (6.4)
Substance use disorder	**1,965 (8.8)**	**155 (6.9)**

[a]Patients who did not receive treatment during the 12-month pre-index period. [b]Additional medical conditions included: Mental health - eating disorder, obsessive compulsive disorder, personality disorders, schizoaffective disorder, schizophrenia; Musculoskeletal/pain - arthritis, osteoporosis with or without pathologic fracture; Cardiovascular - heart failure, ischemic heart disease, myocardial infarction, peripheral vascular disease, stroke/transient ischemic attack; Sleep disorders - narcolepsy; Substance use disorder - alcohol use disorder, drug use disorder.
ADHD, attention deficit disorder; PTSD, post-traumatic stress disorder.

MDD treatments prior to Auvelity initiation

- The last MDD-related treatment that was used prior to Auvelity initiation comprised SSRI (22.4%), SNRI (13.2%), and NDRI (12.8%) monotherapies; only 1.3% of patients were treated with esketamine (**Figure 2**)
- A total of 2,254 (10.1%) patients initiated Auvelity without any MDD-related treatment in the 12-month pre-index period

Figure 2. Last MDD-Related Treatment Prior to Auvelity Initiation



[a]Patients who did not receive treatment during the 12-month pre-index period. [b]Other includes MAOI, SARI, TCA, TeCA.
MAOI, monoamine oxidate inhibitor; MDD, major depressive disorder; NDRI, norepinephrine and dopamine reuptake inhibitor; SARI, serotonin antagonist reuptake inhibitor; SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant; TeCA, tetracyclic antidepressant.

MDD treatment during the 12-month pre-index period

- 20,034 (89.9%) patients received any MDD-related treatment and 18,665 (83.7%) patients had received treatment with any SSRI/SNRI/NDRI (**Table 3**)
- Overall, 2.9% of patients utilized esketamine treatment

Table 3. MDD-Related Treatment During the 12-Month Pre-Index Period

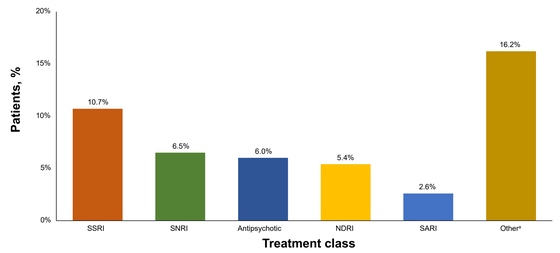
Treatment, n (%)	All Auvelity Patients (N=22,288)
Any MDD-related treatment	**20,034 (89.9)**
Any SSRI/NDRI/SNRI	**18,665 (83.7)**
Any SSRI	**12,234 (54.9)**
Fluoxetine	3,071 (13.8)
Vortioxetine	2,902 (13.0)
Escitalopram	2,849 (12.8)
Sertraline	2,775 (12.5)
Vilazodone	1,948 (8.7)
Citalopram	815 (3.7)
Paroxetine	665 (3.0)
Fluvoxamine	529 (2.4)
NDRI (bupropion only)	**9,015 (40.4)**
Any SNRI	**8,002 (35.9)**
Duloxetine	3,306 (14.8)
Desvenlafaxine	2,683 (12.0)
Venlafaxine	2,608 (11.7)
Levomilnacipran	371 (1.7)
Any antipsychotic	**10,182 (45.7)**
Aripiprazole	3,656 (16.4)
Quetiapine	3,214 (14.4)
Cariprazine	2,422 (10.9)
Brexpiprazole	2,378 (10.7)
Olanzapine	1,186 (5.3)
Lumateperone	700 (3.1)
Risperidone	530 (2.4)
Any SARI	**5,205 (23.4)**
Any TCA	**2,523 (11.3)**
TeCA (mirtazapine only)	**2,150 (9.6)**
Ketamine	**660 (2.9)**
Esketamine	654 (2.9)
Ketamine	8 (0.0)
Any MAOI	**202 (0.9)**

MAOI, monoamine oxidate inhibitor; MDD, major depressive disorder; NDRI, norepinephrine and dopamine reuptake inhibitor; SARI, serotonin antagonist reuptake inhibitor; SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant; TeCA, tetracyclic antidepressant.

Auvelity initiation

- Auvelity was initiated as monotherapy in 6,418 (28.8%) patients and as an add-on therapy in 15,870 (71.2%) patients, most frequently to an SSRI (10.7%) alone or SNRI (6.5%) alone (**Figure 3**)

Figure 3. Initiation of Auvelity as an Add-On Therapy (Frequency ≥2%)



[a]Other includes antipsychotics + SSRI, NDRI + SSRI, antipsychotics + SNRI, NDRI + SNRI, and SARI + SSRI.
MDD, major depressive disorder; NDRI, norepinephrine and dopamine reuptake inhibitor; SARI, serotonin antagonist reuptake inhibitor; SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

Treatment-naïve patients

- Demographics of the 2,254 (10.1%) treatment-naïve patients resembled the overall Auvelity population (mean age 44.0 years; 64.4% women) (**Table 1**)
- The largest proportion of treatment-naïve patients lived in the South (46.2%), had commercial insurance (58.5%), and received their initial Auvelity prescriptions from their psychiatrist/mental health provider (63.3%)
- PCPs and NPs/PAs accounted for a higher proportion of Auvelity prescriptions in treatment-naïve patients than the overall population (32.5% vs 27.2%)
- The prevalence of comorbidities was lower in treatment-naïve patients than the overall Auvelity population (**Table 2**)
- Overall, 2,200 (97.6%) of the treatment-naïve patients initiated Auvelity treatment as monotherapy