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Master Class for Neuroscience Professional Development

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Addressing Your Greatest Concerns in Schizophrenia Management: From Suicide to Relapse Prevention and the Role of LAIs

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Learning Objective

Formulate individualized treatment plans for patients with schizophrenia that consider safety, efficacy, mechanism of action (MOA), and ideal candidates for current and emerging LAIs versus oral therapies.

Veronica

- 28-year-old woman with a diagnosis of schizoaffective disorder; diagnosed at age 21
- Over the years has stopped her medication. When she stops she can become psychotic and suicidal
- Currently prescribed lurasidone 40mg BID and lamotrigine 150mg per day
- Smoked cannabis daily in high school and still uses periodically, for “anxiety”
- Has a supportive boyfriend and they are considering having a baby
- She has noticed some twitching of her fingers now and then

Suicide

- Historical quoted suicide mortality rate is 10%
- Probably closer to 2-5%
- 10X general population
- Risk Factors:
  - Male, early in the illness, substance use, more episodes, better insight
- More deaths by violent means especially jumping off buildings or in some countries by car or train
- High rates in some delusional disorders like body dysmorphic disorder
- Preventing psychosis and depression are key—clozapine (reduced suicidal ideation), LAIs

Suokas JT, et al. *Schizophr Res.* 2010; 124(1-3):22-28.

Cannabis

- Cannabis use prevalence noted to be as high as 43% in patients with schizophrenia
- Cannabis associated with earlier onset of psychosis
- Cannabis predicts onset of psychosis independent of intoxication effects and other confounding effects
- Cannabis use in adolescence increases the likelihood of experiencing symptoms of schizophrenia in adulthood
- An ounce of prevention worth a pound of a cure
  - Educate patient and family about the risks
- The chicken or the egg problem
  - What came first the psychosis or the cannabis?
- Critical to adequately treat the underlying problem
  - Substance abuse treatment, LAIs

Bersani G, et al. *Psychopathology*. 2002;35(5):289-295; Di Forti M, et al. *Schizophr Bull*. 2014;40(6):1509-1517; Donoghue K, et al. *Psychiatry Res*. 2014;215(3):528-532; Stefanis NC, et al. *Addiction*. 2004;99(10):1333-1341.

Pregnancy

- Associated with higher risk of relapse in both schizophrenia and bipolar disorder
- Discontinuation of antipsychotics occurs in a majority of patients with schizophrenia
- American Congress of OB/GYN recommends avoiding discontinuation of antipsychotics
- Newborns smaller for GA, low birth weight
- No increase in fetal or neonatal death in bipolar; mixed results in schizophrenia
- No increase rate of major malformations with SGAs
- OLZ >placental passage, QUE <placental passage
- No obvious pattern of delay in 6 month and 12 month old's
- "At present any comfort we may have in prescribing antipsychotics during pregnancy comes mainly from the absence of negative data rather then the presence of positive data"

GA = gestational age; OLZ = olanzapine; QUE = quetiapine; SGA = second generation antipsychotics

Tosato S, et al. *J Clin Psychiatry.* 2017;78(5):e477-e489.

Tardive Dyskinesia

- Antipsychotics given for a number of disorders
- May occur in untreated patients with schizophrenia
- Prevalence: 13% SGA, 32% FGA, 15% antipsychotic free (at the time)
- Incidence: .8% SGA, 5% FGA
- Risk Factors: Age, female, AA, mood or cognitive disorder, substance abuse, duration of use, FGA, early EPS, DM, HIV
- Renewed interest in treatment may be leading to closer detection
- Stable and lowest doses of antipsychotic optimal (consider LAI)
- Clonazepam, gingko, Vit E, amantadine, VMAT inhibitors (tetrabenazine, valbenazine, deutetrabenazine)

DM = diabetes mellitus; EPS = extrapyramidal symptoms; FGA = first-generation antipsychotic; VMAT = vesicular monoamine transporter.

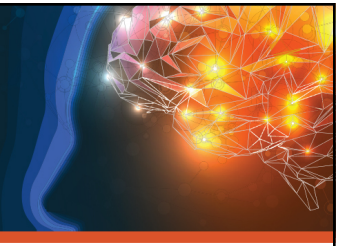
Correll CU. *J Clin Psychiatry.* 2017;78(9):e1426.

Atypical Antipsychotics LAIs for Schizophrenia

Drug	Formulation (Approval)	FDA Approved Dose Range	Mechanism of Action
Risperidone (Risperdal®, Consta®)	Long-Acting IM (2003)	25, 37.5, or 50 mg IM every 2 weeks	Dopamine D2 and serotonin 5-HT_{2A} antagonism
Olanzapine (Zyprexa Relprevv®)*	Long-Acting IM (2009*)	150-300 mg IM every 2 weeks	Primarily dopamine D2 and 5-HT_{2A} antagonism
Aripiprazole (Abilify Maintena®)	Long Acting IM (2013)	160-400mg per month	Dopamine D2 partial agonist, serotonin 5-HT_{1A} partial agonist, 5-HT_{2A} antagonist
Aripiprazole Lauroxil (Aristada®)	Long Acting IM (2015)	441, 662 and 882mg per 4-6 weeks,1064 q8weeks	Dopamine D2 partial agonist, serotonin 5-HT_{1A} partial agonist, 5-HT_{2A} antagonist
Aripiprazole loading (Aristada Initio®)	Long-Acting IM (2018)	675 mg (only as single dose)	Dopamine D2 partial agonist, serotonin 5-HT_{1A} partial agonist, 5-HT_{2A} antagonist
Paliperidone (Invega®, Sustenna®)	Long-Acting IM (2009)	117 to 234 mg per month	Dopamine D2, 5-HT_{2A}, $\alpha_{1,}$ and α_2 adrenergic, H_1 histaminergic antagonist
Paliperidone (Invega Trinza®)	Long-Acting IM (2015)	273-819 every 12 weeks	Dopamine D2, 5-HT_{2A}, $\alpha_{1,}$ and α_2 adrenergic, H_1 histaminergic antagonist
Risperidone SubQ (Perseris®)	Long-Acting SQ (2018)	90 or 120mg q 4weeks	Dopamine D2 and serotonin 5-HT_{2A} antagonism

*Includes Risk Evaluation and Mitigation Strategy (REMS) with approval [Package Inserts]. Drugs@FDA Website.

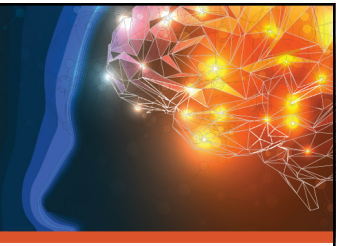
Considerations When Converting Oral Daily Medications to LAIs



- Indications for switching from oral to LAIs
- Who are the ideal candidates?
- Key points to discuss with patients
- Assessing response to orals
- Dose range and frequency of administration (e.g., every 2 weeks, 4 weeks, 12 weeks)
- Discontinue/taper orals to convert to LAIs?

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely



- Personalize the management of schizophrenia by identifying patients in whom long-acting injectables are appropriate.
- Improve the likelihood of your patients with schizophrenia achieving remission and recovery by incorporating the use of long-acting injectables into your treatment regimen.

Questions & Answers

Don’t forget to fill out your evaluations to collect your credit.