Canadian Consortium for Early Intervention in Psychosis

Where do new and emerging pharmacotherapy treatment options fit in our first-episode psychosis treatment algorithms?

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Disclosures

Dr Howard Margolese:

1. Membership on advisory board or speakers' bureaus or consultant: Abbvie, Bausch Health, BI, HLS, Janssen, Newron, Otsuka, Lundbeck, Teva.
2. Funded grants, research, or clinical trials: AIFred, MGH Foundation, SyneuRx

Dr Jason Morrison:

None

Learning Objectives

After participating in this session, participants will be better able to;

- Evaluate new pharmacotherapy options that are currently available in Canada or are expected to become available soon
- Understand where these therapeutic options might best fit among currently available options for our First episode and Early psychosis patients
- Apply an algorithm approach to pharmacotherapy treatments.

Interactivity

Once all of the new medications become available (including Cobenfy, Cariprazine, SC Risperidone and Aripiprazole 2 monthly) , when should you now consider clozapine?

a. After you try at least one medication from every class with a different mechanism of action (i.e., One from each “generation” of antipsychotics)
b. After at least one second and third generation medication or 2 failed trials
c. After 2 or more failed trials of adequate dose and duration in which at least one is an LAI (long-acting injection)
d. Clozapine is not indicated for early psychosis patients.

A Word on Medication Nomenclature

There is no global consensus on nomenclature for psychotropic medications used in schizophrenia and bipolar disorder

Examples	Chlorpromazine, Haloperidol, Perphenazine	Clozapine, Olanzapine, Quetiapine, Risperidone	Aripiprazole, Brexpiprazole, Cariprazine
First used	1950s	1980s	2000s
Typicality / temporality	Typical / Conventional	Atypical	Atypical
Generation	1st generation	2nd generation	3rd generation
Neuroscience-based Nomenclature (Pharmacological target / Mode of action)	Example: Haloperidol Target: DA MOA: Antagonist	Example: Olanzapine Target: DA & 5HT MOA: Antagonist	Example: Aripiprazole Target: DA & 5HT MOA: Partial agonist and antagonist

5HT: serotonin; DA: dopamine

Adapted from King C, *et al. J Psychiatry Neurosci.* 2002; 27(3):168-75; Seifert R, *et al. Naunyn Schmiedebergs Arch Pharmacol*. 2020; 393(8):1331-9.

A Word on Medication Nomenclature

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First used	1950s	1980s	2000s
Typicality / temporality	Typical / Conventional	Atypical	Atypical
Throughout this presentation, we will refer to the various agents by their generation			3rd generation
Neuroscience-based Nomenclature (Pharmacological target / Mode of action)	Example: Haloperidol Target: DA MOA: Antagonist	Example: Olanzapine Target: DA & 5HT MOA: Antagonist	Example: Aripiprazole Target: DA & 5HT MOA: Partial agonist and antagonist

5HT: serotonin; DA: dopamine

Adapted from King C, *et al. J Psychiatry Neurosci.* 2002; 27(3):168-75; Seifert R, *et al. Naunyn Schmiedebergs Arch Pharmacol*. 2020; 393(8):1331-9.

The Evolution of Antipsychotic Therapy

1st generation (1950s & '60s)
Chlorpromazine
Fluphenazine
Haloperidol
Loxapine
Perphenazine
Thioradizine

2nd generation (1970s – 2000s)
Asenapine
Clozapine
Lurasidone
Olanzapine
Paliperidone
Quetiapine
Risperidone
Ziprasidone

3rd generation (2000s – 2020s)
Aripiprazole
Brexpiprazole
Cariprazine

Compared to 1st generation:[1-3]
- ↑ Efficacy for some, but not all agents
- ↓ Risk of EPS
- ↑ Better quality of life for some
- ↑ **likelihood of metabolic side effects**

Compared to 2nd generation:[4,5]
- ↑ Efficacy for negative and cognitive symptoms
- ↓ Risk / severity of metabolic side effects
- ↑ **Risk of akathisia**

*Cariprazine is an investigational agent under review by Health Canada.

Davis JM, *et al. Arch Gen Psychiatry.* 2003; 60:553–64; 2. Leucht S, *et al. Lancet.* 2009; 373:31–41; 3. Gründer G, *et al. Lancet Psychiatry*. 2016 Aug;3(8):717-29.

New and Newer Oral and LAI Options

New and Newer Oral Options

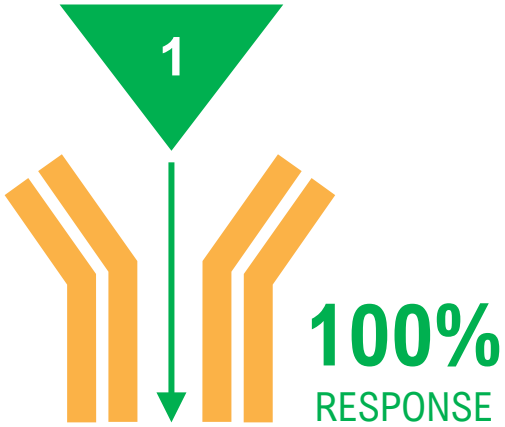
1. Cariprazine (Vraylar)
   Already available but not yet used very much due to reimbursement delays.

2. xanomeline/trospium (Cobenfy)
   Available in US and possibly coming to Canada soon – but as of today there is no specific timeline for when.

3. TAAR 1 agonists (Trace Amine-Associated Receptor 1 Agonists)
   - In phase 3 trials for schizophrenia the treatment arm did not separate from placebo arm.
   - Will not be presented further today.

Pharmacology of 3rd Generation Antipsychotics: What is a Partial Agonist?

Dopamine

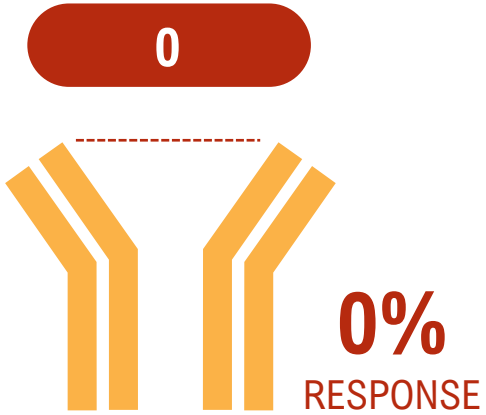


The intrinsic activity of a full agonist (like dopamine) is 1

Produce the maximal effect (100%) at that receptor

1st- and 2nd-generation Antipsychotics

D2 antagonist

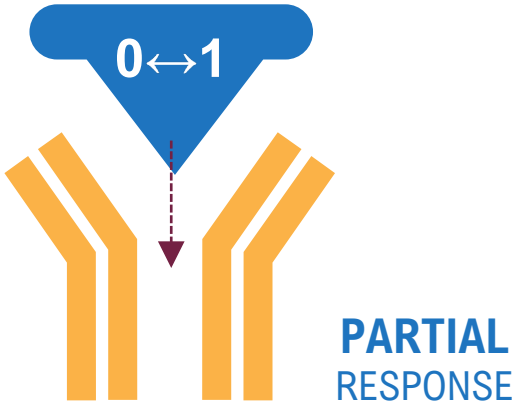


The intrinsic activity of antagonists is 0

Produce no effect (0%) and/or prevent any effect at that receptor

3rd-generation Antipsychotics

Partial D_2 agonist



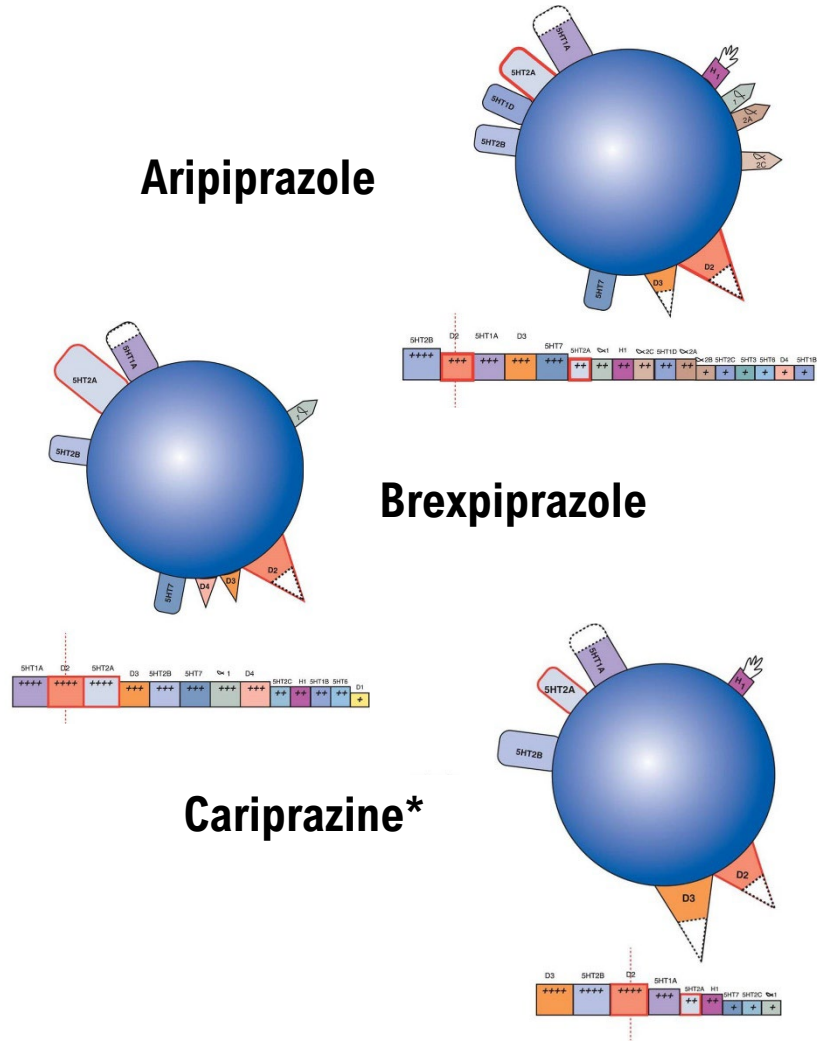
The intrinsic activity of a partial agonist is between 0 and 1

Produce a partial effect at that receptor

Adapted from Stahl S. *Essential Psychopharmacology: Neuroscientific Basis and Practical Applications;* Cambridge University Press, 2000; and Tamminga CA. *J Neural Transm* 2002; 109(3):411-20.

3rd-generation Antipsychotics

- 3rd-generation antipsychotics display different binding profiles and receptor affinities



Similarities and Differences of 3rd-generation Antipsychotics: Summary

- Aripiprazole, brexpiprazole and cariprazine* are all D_2 and D_3 receptor partial agonists

- The 3 agents have differences and similarities in receptor binding affinities, including:
  - Similar affinities for the D_2 receptor
  - Differing affinities for the D_3 receptor
  - Similar affinities for H_1, and M_1 receptors
  - Differing affinities for the $5HT_{1A}$ and $5HT_{2A}$ receptors

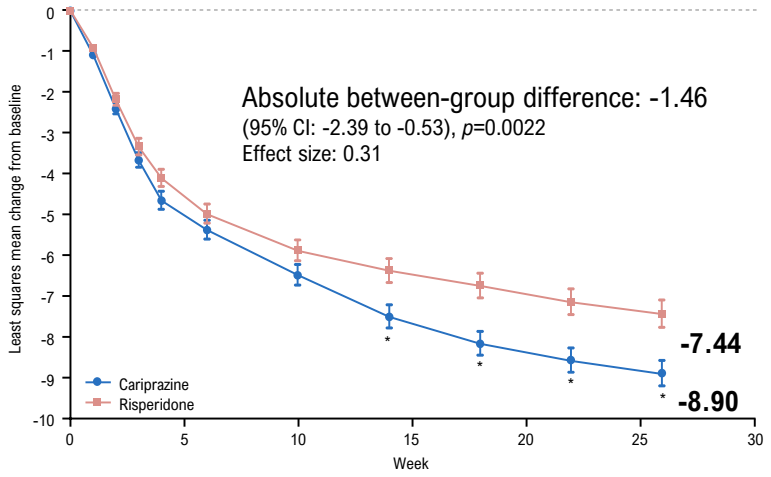
- Differing binding profiles and receptor affinities have potentially important clinical implications in terms of efficacy and potential side effects

*Cariprazine is an investigational agent under review by Health Canada.

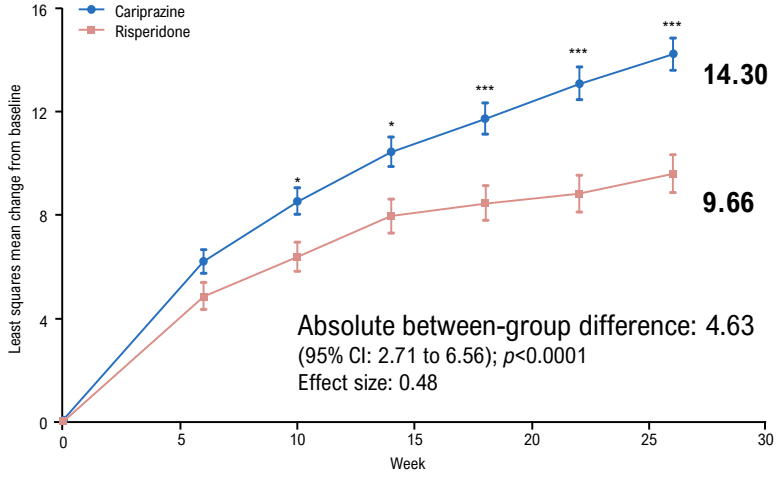
Cariprazine vs. Risperidone in Schizophrenia with Predominant Negative Symptoms: Prospective Head-to-Head Study

N=461 adults aged 18–65 years with long-term (>2 year), stable schizophrenia and predominant negative symptoms (>6 months)

Change in PANSS Factor Score for Negative Symptoms (PANSS-FSNS)



Change in Personal and Social Performance (PSP) Total Score



Proportion with PANSS-FSNS response ≥20% from baseline to 26 weeks: **69% vs. 58%** (*p*=0.0022, NNT=9)

*p<0.01 vs. risperidone; ***p<0.0001 vs. risperidone

Mean daily doses: Cariprazine 4.2 mg; Risperidone 3.8 mg; CI: confidence interval; PANSS: positive and negative syndrome scale

Németh G, *et al. Lancet.* 2017; 389(10074):1103–13.

Cariprazine: Indications in Canada

Cariprazine is an atypical antipsychotic approved by health Canada in April 2022 for:

- Treatment of Schizophrenia in adults
- Bipolar Mania: acute management of manic or mixed episodes associated with bipolar I disorder in adults, and
- Bipolar Depression: acute management of depressive episodes associated with bipolar I disorder in adults.

Dosage and Administration Summary		
Administer cariprazine once daily with or without food		
	Starting Dose	**Recommended Dose**
Schizophrenia	1.5 mg daily	1.5 mg to 6 mg daily
Bipolar I Mania (acute)	1.5 mg daily	3 mg to 6 mg daily
Bipolar I Depression	1.5 mg daily	1.5 mg or 3 mg daily
Schizophrenia and Bipolar I Mania: Dose can be increased from 1.5 mg to 3 mg on Day 2. Depending upon clinical response and tolerability, further dose adjustments can be made in 1.5 mg or 3 mg increments. Dosages above 6 mg daily do not confer significant benefit but increase the risk of dose-related adverse reactions. The maximum recommended dose is 6mg/d.		
Bipolar I Depression: Depending upon clinical response and tolerability, the dosage can be increased to 3 mg once daily on Day 15. The maximum recommended daily dosage is 3 mg.		

VRAYLAR® (cariprazine) [prescribing information]. Madison, NJ: Allergan USA, Inc. May 2019.

Cobenfy (KarXT)

- M1/M4 central agonist (Xanomeline)
- with peripheral M1/M4 antagonist (Trospium)
- Indirect modulator of dopamine, serotonin, and glutamate/GABA
- 4th generation antipsychotic not acting directly on dopamine
- But works by reducing the amount of dopamine that gets into the synapses (Taking your foot off the accelerator of your car as opposed to putting your foot on the brakes)

- Positive results in phase 3 studies including 52-week long term extension studies
- Approved by FDA Sept 2024

Safety and Efficacy of KarXT (Xanomeline–Trospium) in Schizophrenia in the Phase 3, Randomized, Double-Blind, Placebo-Controlled EMERGENT-2 Trial

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NEI Congress

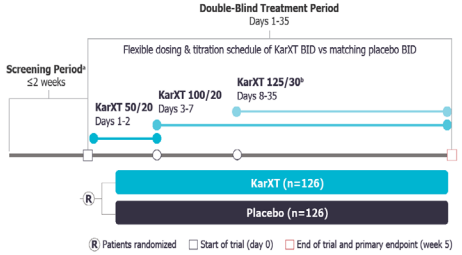
Background

- KarXT combines the dual M_1/M_4 preferring muscarinic receptor agonist xanomeline with the peripherally restricted muscarinic receptor antagonist trospium
- In the 5-week, randomized, double-blind, placebo-controlled, phase 2 EMERGENT-1 trial (NCT03697252), KarXT met the primary endpoint of a significant reduction in Positive and Negative Syndrome Scale (PANSS) total score through week 5 vs placebo, improved other key efficacy measures, and was generally well tolerated[1]

Methods

- EMERGENT-2 (NCT04659161) was a phase 3, randomized, double-blind, placebo-controlled, 5-week trial of KarXT vs placebo (**Figure 1**)

Figure 1. EMERGENT-2 Trial Design



KarXT dose is expressed as xanomeline/trospium (mg/mg). [a]Washout of prior oral lithium and/or antipsychotics. [b]Optional increase in dose based on tolerability determined by a clinician. BID, twice daily.

- Adult patients aged 18-65 years with a confirmed *DSM-5* diagnosis of schizophrenia and a recent worsening of psychotic symptoms warranting hospitalization were enrolled
- Eligible patients were randomized 1:1 to KarXT or matched placebo
- Dosing of KarXT (xanomeline/trospium) started at 50 mg/20 mg twice daily (BID) and increased to a maximum dose of 125 mg/30 mg BID
- Primary efficacy endpoint: change from baseline to week 5 in PANSS total score compared with placebo
- Secondary efficacy endpoints: change from baseline to week 5 in PANSS positive subscale, PANSS negative subscale, and PANSS Marder negative factor subscale scores; Clinical Global Impression–Severity (CGI-S) score at week 5; and percentage of PANSS responders at week 5[a]

Statistical Analyses

- Efficacy analyses were performed in the modified intent-to-treat population, defined as all randomized patients who received ≥1 dose of study medication, had a baseline PANSS assessment, and had ≥1 postbaseline PANSS assessment
- Safety analyses were performed in the safety population, defined as all patients who received ≥1 dose of study drug

[a]Analysis is ongoing and results to be presented at a future meeting.

Results

- A total of 252 patients at 22 study sites in the United States were enrolled
- There were no meaningful differences in baseline demographics and characteristics between treatment groups (**Table 1**)

Table 1. Baseline Demographics and Characteristics (ITT Population)

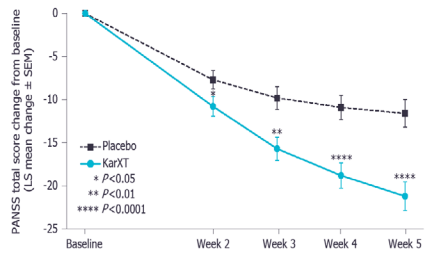
	KarXT (n=126)	Placebo (n=126)
Mean age, years (SD)	45.6 (10.4)	46.2 (10.8)
Sex, n (%)		
Male	95 (75.4)	95 (75.4)
Female	31 (24.6)	31 (24.6)
Race, n (%)		
Asian	2 (1.6)	1 (0.8)
Black	97 (77.0)	92 (73.0)
White	26 (20.6)	31 (24.6)
Other	1 (0.8)	2 (1.6)
PANSS total score, mean (SD)	98.3 (8.9)	97.9 (9.7)
PANSS positive subscale score, mean (SD)	26.8 (3.7)	26.7 (4.0)
PANSS negative subscale score, mean (SD)	22.9 (4.0)	22.9 (3.8)
PANSS Marder negative factor subscale score, mean (SD)	22.9 (5.0)	22.5 (4.7)

ITT defined as all randomized patients.
ITT, intent-to-treat; PANSS, Positive and Negative Syndrome Scale; SD, standard deviation.

Primary Endpoint: Change in PANSS Total Score vs Placebo at Week 5

- KarXT demonstrated a statistically significant and clinically meaningful 9.6-point reduction in PANSS total score compared with placebo at week 5 (-21.2 KarXT vs -11.6 placebo, $P<0.0001$; Cohen's d effect size=0.61) (**Figure 2**)
- KarXT demonstrated a statistically significant improvement in PANSS total score starting at week 2 (first postbaseline rating) and maintained such improvement through all time points in the trial

Figure 2. Change From Baseline in PANSS Total Score vs Placebo at Week 5

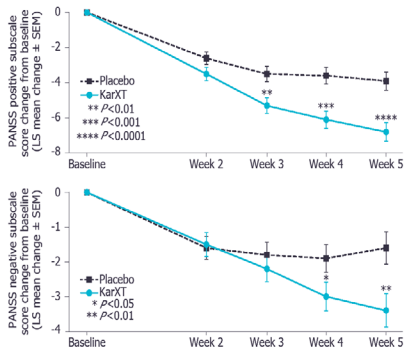


LS, least squares; PANSS, Positive and Negative Syndrome Scale; SEM, standard error of the mean.

Secondary Endpoints: Change in PANSS Subscale Scores and CGI-S Score vs Placebo at Week 5

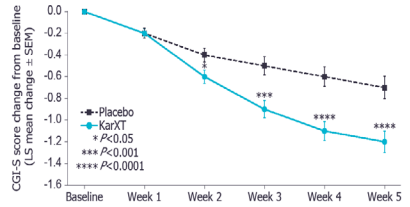
- KarXT met tested secondary endpoints, demonstrating a statistically significant reduction in PANSS positive and negative subscale scores (**Figure 3**) and CGI-S score (**Figure 4**) compared with placebo

Figure 3. Change From Baseline in (A) PANSS Positive Subscale Score and (B) PANSS Negative Subscale Score



LS, least squares; PANSS, Positive and Negative Syndrome Scale; SEM, standard error of the mean.

Figure 4. Change From Baseline in CGI-S Score vs Placebo at Week 5



The difference between KarXT and placebo at week 5 is estimated using mixed-model repeated measures.
CGI-S, Clinical Global Impression–Severity; LS, least squares; SEM, standard error of the mean.

Safety and Tolerability

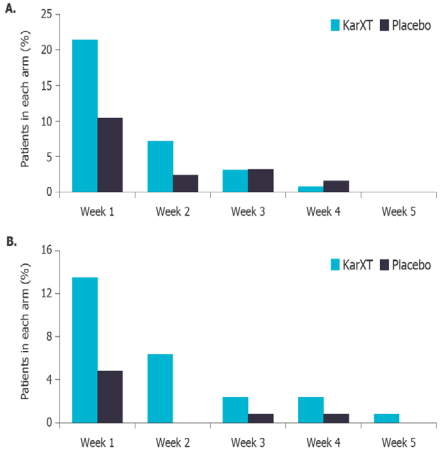
- KarXT was generally well tolerated (**Table 2**), with a side effect profile substantially consistent with prior trials
- Overall discontinuation rates were similar between KarXT and placebo arms (25% vs 21%)
- Common treatment-emergent adverse events (TEAEs; ≥5%) were all mild to moderate in severity and mostly transient in nature
- Commonly reported TEAEs generally began within the first 2 weeks of treatment (**Figure 5**) and were intermittent and time limited in nature
  - Vomiting was intermittent and generally mild. About one-third of vomiting TEAEs were only a single episode of emesis
  - One patient in both the KarXT and placebo arms had an increase in supine systolic blood pressure of ≥15 mmHg or diastolic blood pressure of ≥10 mmHg at day 35
- KarXT was not associated with weight gain, Parkinsonism, dystonia, akathisia, prolactin elevation, or sedation, which are common AEs of current antipsychotic medications

Table 2. Safety and Tolerability During the 5-Week Treatment Period (Safety Population)

Variable	KarXT (n=126)	Placebo (n=125)
Any TEAE, n (%)	95 (75.4)	73 (58.4)
Serious TEAE,[a] n (%)	2 (1.6)	2 (1.6)
TEAE leading to discontinuation, n (%)	9 (7.1)	7 (5.6)
TEAE occurring in ≥5% of patients in the KarXT group, n (%)		
Constipation	27 (21.4)	13 (10.4)
Dyspepsia	24 (19.0)	10 (8.0)
Nausea	24 (19.0)	7 (5.6)
Vomiting	18 (14.3)	1 (0.8)
Headache	17 (13.5)	15 (12.0)
Hypertension[b]	12 (9.5)	1 (0.8)
Dizziness	11 (8.7)	4 (3.2)
Gastroesophageal reflux disease	8 (6.3)	0 (0)
Abdominal discomfort	7 (5.6)	4 (3.2)
Diarrhea	7 (5.6)	4 (3.2)
Mean change from baseline to week 5 in body weight, kg ± SD	2.2 ± 3.62	2.0 ± 4.0
≥7% increase in body weight from baseline, n (%)	16 (12.7)	19 (15.2)
Mean change from baseline to week 5 in Simpson-Angus Scale Score, ±SD	0.4 ± 0.95	0.3 ± 0.76
Mean change from baseline to week 5 in Barnes Akathisia Rating Scale score, ± SD	-0.1 ± 1.09	-0.2 ± 0.98

[a]Serious TEAEs were 2 cases of suicidal ideation in the KarXT group, 1 case of appendicitis in the placebo group, and 1 case of worsening of schizophrenia in the placebo group.
[b]Hypertension is the MedDRA preferred term and is not necessarily reflective of clinical hypertension.
MedDRA, Medical Dictionary for Regulatory Activities; SD, standard deviation; TEAE, treatment-emergent adverse event.

Figure 5. Onset of (A) Constipation/Dyspepsia and (B) Nausea/Vomiting



Conclusions

- In the phase 3 EMERGENT-2 study, KarXT demonstrated a statistically significant and clinically meaningful improvement in PANSS total score vs placebo starting at week 2, which was maintained through all time points in the trial
- KarXT also met tested secondary endpoints, demonstrating a statistically significant reduction in both positive and negative symptoms of schizophrenia vs placebo
- Consistent with prior trials, KarXT was generally well tolerated. The most common TEAEs were all mild to moderate in severity and mostly cholinergic in nature
- KarXT was not associated with common problematic side effects of currently available antipsychotics, including somnolence, weight gain, or extrapyramidal symptoms
- KarXT has the potential to be the first in a new class of treatments for patients with schizophrenia based on muscarinic receptor agonism

Reference

1. Brannan SK, et al. *N Engl J Med.* 2021;384(8):717-726.

Disclosures

CUC has been a consultant and/or advisor to or has received honoraria from AbbVie, Acadia, Alkermes, Allergan, Angelini, Aristo Pharma, Boehringer Ingelheim, Cardio Diagnostics, Cerevel, CNX Therapeutics, Compass Pathways, Damitsa, Gedeon Richter, Hikma, Holmusk, Intra-Cellular Therapies, Janssen/Johnson & Johnson, Karuna Therapeutics, LB Pharma, Lundbeck, MedAvante-ProPhase, MedinCell, Merck, Mindpax, Mitsubishi Tanabe Pharma, Mylan, Neurocrine Biosciences, Newron, Noven, Otsuka, Pharmabrain, PPD, Recordati, Relmada, Reviva, ROVI, Seqirus, SK Life Science, Sunovion, Sun Pharma, Supernus, Takeda, Teva, and Viatris; provided expert testimony for Janssen and Otsuka; served on a data safety monitoring board for Lundbeck, Relmada, Reviva, ROVI, Supernus, and Teva; has received grant support from Janssen and Takeda; received royalties from UpToDate; and is a stock option holder of Cardio Diagnostics, Mindpax, and LB Pharma. ACM, SS, IK, SMP, and SKB are employees of and hold equity in Karuna Therapeutics.

Acknowledgments

The authors thank Matthew Jacobson, CMPP, and Paula Stuckart of Apollo Medical Communications for medical writing and editorial support, which was funded by Karuna Therapeutics. The EMERGENT-2 study was sponsored by Karuna Therapeutics.

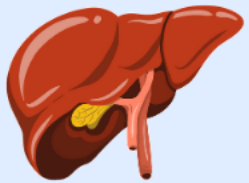
Presented at NEI Congress, November 3-6, 2022, Colorado Springs, Colorado

Cobenfy

- Cobenfy shows efficacy across positive, negative and cognitive symptoms of schizophrenia.
- low risk of side effects (short and long term), particularly extrapyramidal and metabolic side effects (including weight gain) compared to the current standard of care
- Main side effects are GI/GU related due to peripheral muscarinic effects of trospium – Constipation/Urinary retention

XANOMELINE-TROSPIUM CHLORIDE FOR SCHIZOPHRENIA

BEFORE DOSING

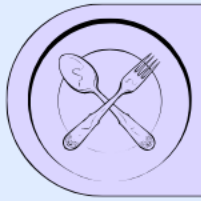


Liver Enzymes & Bilirubin

Heart Rate

HOW TO DOSE?

STARTING DOSE	MAXIMUM DOSE IN GERIATRIC	MAXIMUM DOSE
		
2 DAYS	5 DAYS	
TWICE DAILY	TWICE DAILY	TWICE DAILY
50 mg Xanomeline 20 mg Trospium	100 mg Xanomeline 20 mg Trospium	125 mg Xanomeline 30 mg Trospium



at least **1 hour** before a meal or
at least **2 hours** after a meal

New LAI options

1. Aripiprazole 2 monthly
2. Subcutaneous risperidone – Uzedy
3. Risperidone LAI (IM) – Okedi – approved by Health Canada in March 2024
   - Q 4 weeks
   - will not be discussed further today

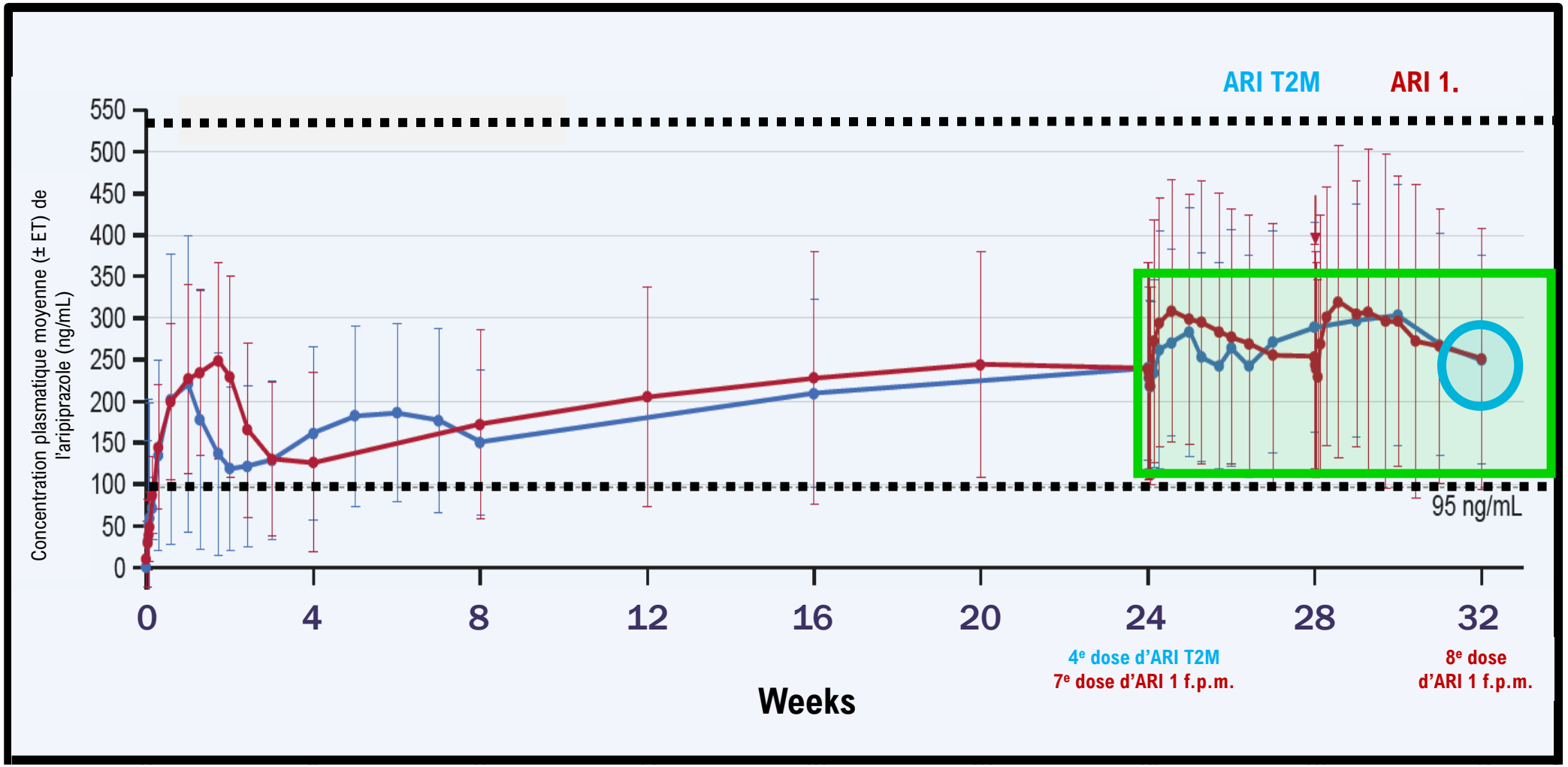
- Essentially these are new formulations of medications you already know and use

Aripiprazole Monthly Versus 2 Monthly

Aripiprazole monthly	Aripiprazole every 2 months
• Powder in vial	• Prefilled syringe
• Reconstitute with sterile water provided in package	• Ready to use
• Syringe to be filled	
• Shake vigorously (30 s)	• Tap (≥ 10 x) and shake vigorously (≥ 10 s)
• IM Injection in deltoid or gluteal muscle	• IM Injection only in gluteal muscle
• Doses: 300 et 400 mg	• Doses: 720 et 960 mg

ARI 1 f.p.m : aripiprazole 1 fois par mois (ABILIFY MAINTENA); ARI T2M : aripiprazole tous les 2 mois; i.m. : intramusculaire.

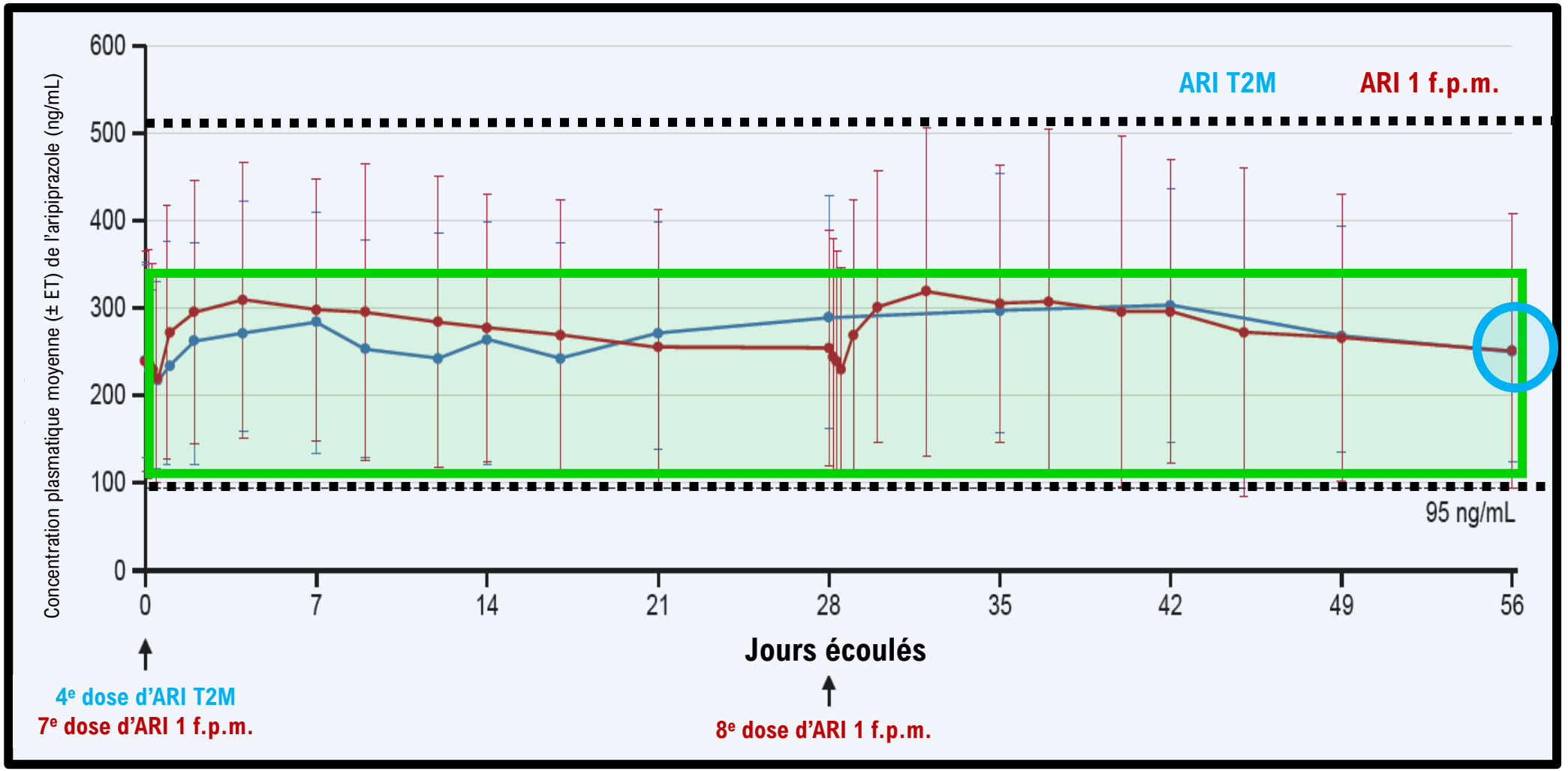
Plasma concentration by time elapsed
(Harlin M et al CNS Drugs 2023)



75e percentile de la $C_{max,éé}$ après la prise orale de 30 mg d'aripiprazole (534 ng/mL)

$C_{min,éé}$ médiane après la prise orale de 10 mg d'aripiprazole (94 ng/mL)

Plasma Concentration by Time Elapsed
(Harlin M et al CNS Drugs 2023)



75e percentile de la $C_{max,éé}$ après la prise orale de 30 mg d'aripiprazole (534 ng/mL)

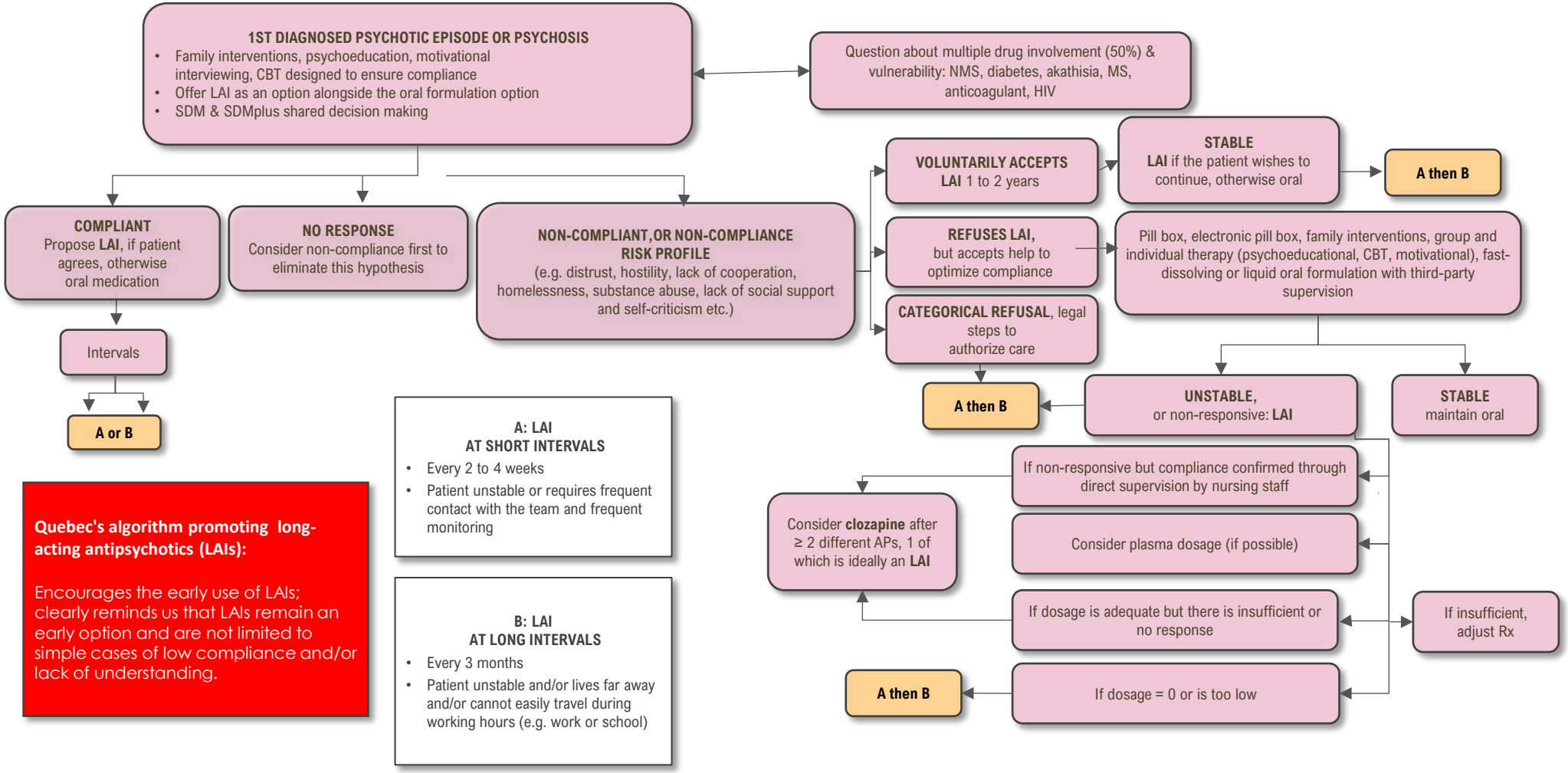
$C_{min,éé}$ médiane après la prise orale de 10 mg d'aripiprazole (94 ng/mL)

ARI 1 f.p.m : aripiprazole 1 fois par mois (ABILIFY MAINTENA); ARI T2M : aripiprazole tous les 2 mois; C_{max} : pic plasmatique; C_{min} : creux plasmatique; éé : à l'état d'équilibre; ET : écart-type.

Uzedy (Risperidone)

- Subcutaneous Risperidone
- Initiate as once monthly (50mg, 75mg, 100mg, 125mg) or once every 2 months (100mg, 150mg, 200mg, 250mg) the day after last dose of oral risperidone
- 2 absorption peaks – early and late so no PO supplementation or initiation regimen needed
- Therapeutic plasma concentrations within 6-24 hours
- Peak plasma concentrations for risperidone and 9-hydroxyrisperidone range from 8-14 days
- Half-life 14-22 days
- Can be administered in upper arm or abdomen

QAAPAPLE Algorithm 2019

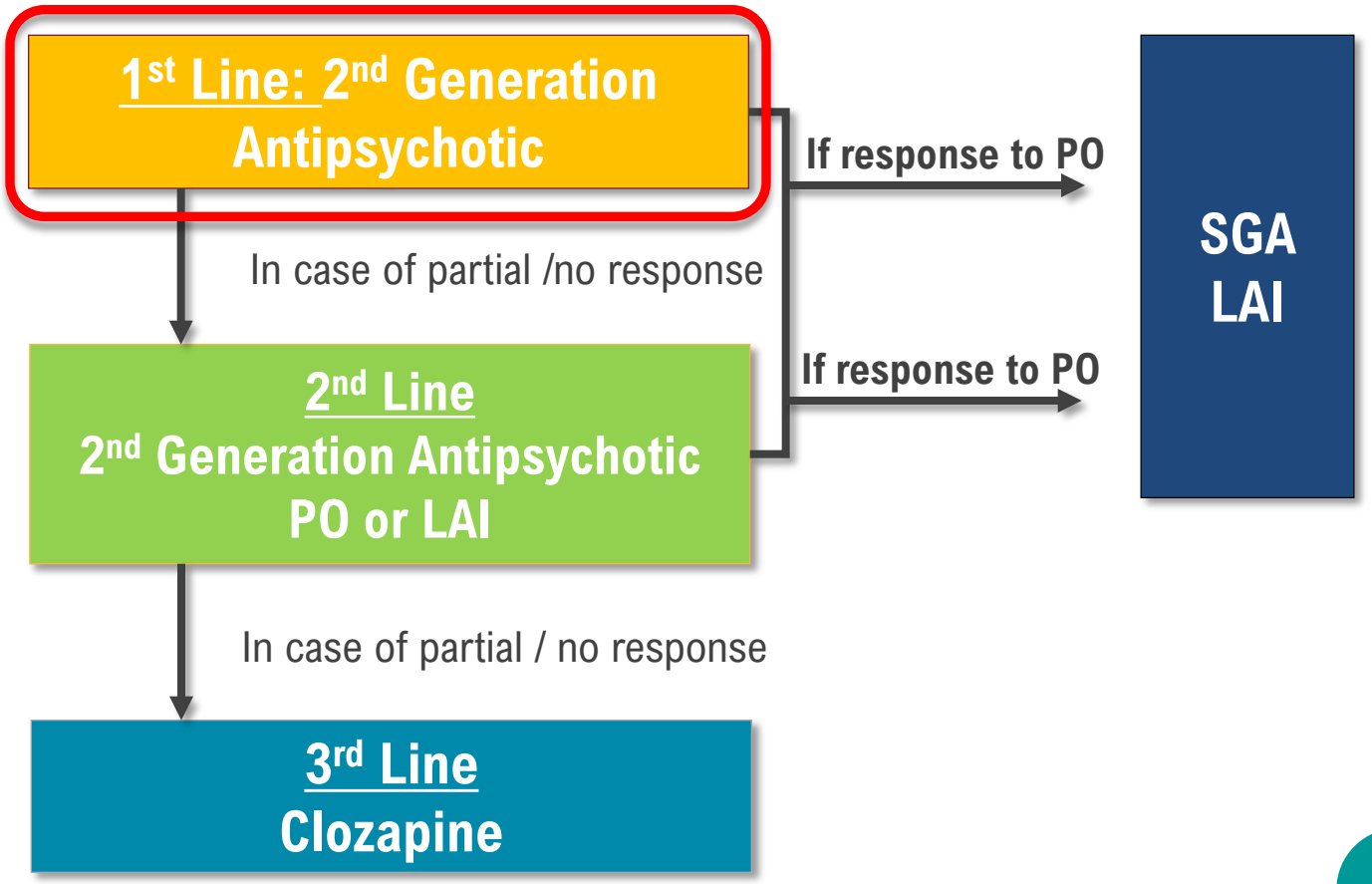


Quebec's algorithm promoting long-acting antipsychotics (LAIs):

Encourages the early use of LAIs; clearly reminds us that LAIs remain an early option and are not limited to simple cases of low compliance and/or lack of understanding.

Stip, Emmanuel, et al. "Antipsychotiques à Action Prolongée: Révision de l'algorithme QAAPAPLE." *The Canadian Journal of Psychiatry*. 2019; 0706743719847193.

Treatment Algorithm for Schizophrenia
What should happen



Where do these new treatments fit in our current treatment algorithms?

Considerations in Adopting New Treatments

- Compared to current treatments, do new agents offer advantages in:
  - Improved efficacy for specific psychotic symptoms, especially negative or cognitive symptoms?
  - Improved efficacy for co-morbid symptoms/disorders including addictions?
  - Improved tolerability / facilitation of medication adherence?
  - Suitability as an adjunctive treatment for clozapine partial responders?
  - Facilitating or augmenting non-pharmacological treatments?

- Any risk that new treatments could distract clinicians from adherence to current treatment guidelines, such as use of LAIs or clozapine?

Value Add to Existing Treatments?

	Efficacy	Neg Sympt	Cognition	Tolerability	Adherence	Other
Risperidone Uzedy	NC	NC	NC	NC	++	
Aripiprazole 2 monthly	NC	NC	NC	NC	++	
Cariprazine	NC	+	NC	+	+/-	Mood symptoms?
Cobenfy	?	NC	?	+	+/-	Augmentation agent?

Current Pharmacological Treatment Algorithm Principles

- Use of a shared decision-making model (CAN)
- Start medication at the lower end of the dose range and titrate up (CAN)
- Preference for agents with:
  - Lower rates of metabolic side effects (ALL)
  - SGA over FGA (AUS, CCEIP)
  - Agents with LAI options (CCEIP)
- Switch if no response at 4 weeks, extend to 8 weeks if partial response (CAN)
- Avoid antipsychotic polypharmacy (CAN)
- Offer patients LAI options early in treatment (CAN)
- Offer clozapine after 2 failed optimized trials of other agents (ALL)
- No specific recommendations for clozapine resistant patients (CAN)

*CAN: Remington et al, 2017; Abidi et al, 2017
AUS: Orygen, 2016 CCEIP: CCEIP 2015

Simplified First Episode Psychosis treatment algorithm

1st antipsychotic trial

Prioritize low metabolic SE, lower dose, SGA

Consider LAI

2nd antipsychotic trial

Use an SGA LAI if not used in first trial

Clozapine trial

Cobenfy

Cariprazine

Summary

- Risperidone SC offers a third SGA LAI option
- Aripiprazole 2 monthly offers a second option for patients interested in fewer clinic visits, and inconsistently adherent patients
- Cariprazine may offer advantage for those with primarily negative symptoms, and is another partial DA agonist option
- Cobenfy offers a novel mechanism of action and its role in the pharmacological armamentarium remains to be elucidated
- None of these new options should delay non-responding patients from being offered clozapine in their third treatment trial

Discussion - Improving Adherence to Existing Treatments

- What are the mix of Oral / LAI / Clozapine prescribing on your teams?
- How do you promote the use of LAIs and clozapine? Any successful strategies?
- Any concerns about discontinuation/modification of treatment during transitions (e.g. outpatient to inpatient, at discharge from your EIP team)