

Considerations for the Use of Novel HIV Medications: To Injectables and Beyond!

Milena Murray, PharmD, MSc, BCIDP, AAHIVP
Associate Professor of Pharmacy Practice
Midwestern University – Chicago College of Pharmacy
HIV/ID Clinical Pharmacist
Northwestern Memorial Hospital

All clip art images are through subscriptions.



Disclosures

- Milena Murray is a speaker for Merck & Co. All conflicts were resolved through peer review of the material.



Objectives – Pharmacists

1. Review novel injectable agents for the treatment of HIV including clinical data, pharmacokinetic data, and appropriate patient populations for treatment.
2. Develop an action plan for the implementation of an injectable agent treatment program.
3. Discuss HIV medications currently in the pipeline and their potential place in clinical therapy.



Objectives – Pharmacy Technicians

1. Review novel injectable agents for the treatment of HIV including important logistical considerations for dispensing.
2. Develop an action plan for the implementation of an injectable agent treatment program.
3. Discuss HIV medications currently in the pipeline and any special requirements needed for dispensing.



Which of the following best describes your role?

- A. Pharmacist
- B. Pharmacy Technician
- C. Other

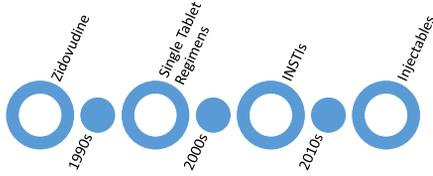


Please rate your level of comfort with antiretrovirals including the new injectable treatments.

- A. Expert
- B. Comfortable with most aspects
- C. Working knowledge
- D. I avoid these medications!



Back at One



The Backstory

- Cabotegravir/rilpivirine (Cabenuva™) submitted for FDA approval 4/29/2019
- Cabotegravir tablets (Vocabria™)
- On 12/21/2019, FDA informed approval would not be granted due to unspecified manufacturing issues
 - Later clarified as issues related to scaling up production
- Approved in Canada on 3/20/2020 for “switch” patients

Cabotegravir



- Investigational integrase strand transfer inhibitor
 - Structural analogue of dolutegravir
 - HIV treatment and pre-exposure prophylaxis
- Long Acting Injectable Cabotegravir
 - Half-life: 20-40 days
 - Measurable concentrations seen up to one year after a single dose
 - Detectable but sub-therapeutic
 - How to provide therapeutic coverage to prevent occurrence of drug resistance during the “tail-phase” needs to be addressed

Clinical Trial Data



ATLAS

- N=616 patients
- HIV RNA < 50 copies/mL for at least 6 months
- Randomized to continue oral therapy or switch to monthly IM injections of cabotegravir + rilpivirine
- Week 48
 - Oral therapy: 96% HIV RNA < 50 copies/mL
 - IM injections: 93% HIV RNA < 50 copies/mL

FLAIR

- N=566 patients
- Treatment naïve patients
- 20 weeks of oral therapy with dolutegravir-abacavir-lamivudine
 - If HIV RNA < 50 copies/mL after 16 weeks
 - Continue oral therapy or switch to monthly IM injections of cabotegravir + rilpivirine
- Week 48
 - Oral therapy: 93% HIV RNA < 50 copies/mL
 - IM injections: 94% HIV RNA < 50 copies/mL

Srinivasan S, et al. ATLAS N Engl J Med 2020; 382:1122-32.
Olsen C, et al. FLAIR N Engl J Med 2020; 382:1124-33.

2020 ICDP Annual Meeting **OUR TEAM CAN**

Clinical Trial Data

Injection Site Reactions

- ATLAS – 81%
- FLAIR – 86%
- ~2% withdrawals for this reason

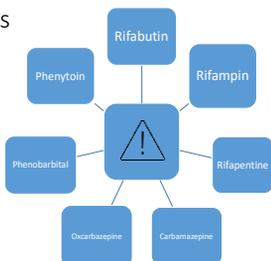
Patient Satisfaction

- IM therapies > oral therapy

Srinivasan S, et al. ATLAS N Engl J Med 2020; 382:1122-32.
Olsen C, et al. FLAIR N Engl J Med 2020; 382:1124-33.

2020 ICDP Annual Meeting **OUR TEAM CAN**

Contraindications



Forness D, et al. ICDP Abstracts CD 409-405 (Abstract) 2020:11-179-180.

2020 ICDP Annual Meeting **OUR TEAM CAN**

Adverse Events

- Main adverse events are injection site reactions
- Satisfaction surveys indicate that even with these reactions, the injections are preferred over daily medications



Fernandez, C, van Hattena CL, WVA02 (AUSA) 2019.11.179.132

2020 QIP Annual Meeting

OUR TEAM CAN

Treatment Phases



Cabotegravir and Rilpivirine Extended Release Injectable Suspensions (Cabotrova), VIV Healthcare LLC, Lovel, Quebec, Canada, 2020

2020 QIP Annual Meeting

OUR TEAM CAN

Treatment



- If greater than 1 month and 7 days since the last injection
 - Start oral medications
- If greater than 2 months since last injection
 - Start at initiation injection doses
- When starting or resuming injections, oral therapy should be taken on the same day as injections
- When discontinuing injections, another fully active HIV regimen should be started within one month after the final injection

Cabotegravir and Rilpivirine Extended Release Injectable Suspensions (Cabotrova), VIV Healthcare LLC, Lovel, Quebec, Canada, 2020

2020 QIP Annual Meeting

OUR TEAM CAN

Have you started discussions regarding an implementation strategy for injectable HIV medications?

- A. Yes
- B. No
- C. I just discovered these existed today.

Logistical Considerations

- Timing of injections
 - 7 days before or after target
 - Consider entire year of target dates
- Flagging missed visits
- Rescheduling missed injections
- Patient parking
- Check-in for patients in busy clinics



Dispensing Considerations

- Cold chain requirement
 - White bag or Buy and Bill
 - Rilpivirine must be refrigerated
 - Bring to room temperature prior to injection
- Size of refrigerator for storage



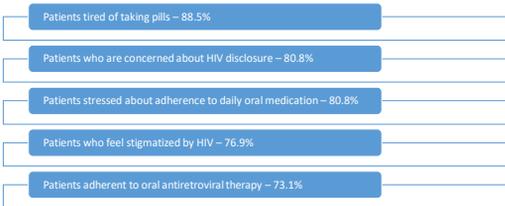
Patient Considerations



- Monthly commitment
 - Transportation issues
 - Every 2-month injections may be in the future
 - Consider travel schedule, etc.
- Discussion regarding resistance if injections missed
 - Bridging with oral medications needed
- Consider patients who attend clinic appointments but may struggle with adherence

2020 ICFP Annual Meeting **OUR TEAM CAN**

Characteristics of Patients Appropriate for Injectable Therapy



<http://www.cfnhs.org/2020/ICFIC/46.htm>
2020 ICFP Annual Meeting **OUR TEAM CAN**

Patient Case – Part #1

CJ is a 35 y/o female who has been living with HIV for 5 years and struggles with medication adherence. She has 2 young children and finds it difficult to prioritize her own health needs such as picking up her prescription each month at the pharmacy and she does not have a safe space for medication delivery through the mail. She also struggles with remembering to take her medication each day and because of disclosure issues she does not want to leave her medication where she can see it or have her children help her remember. She regularly attends all her clinic appointments.

When offered injectable medications once monthly as a treatment option, she is very enthusiastic and motivated for this change. After a benefits investigation, it is determined that the treatment is covered. You are getting set up to call CJ for medication teaching.

What logistical aspects do you need to consider?



2020 ICFP Annual Meeting **OUR TEAM CAN**

Patient Case – Part #2

CJ has completed her oral lead-in phase of medication. She needs to schedule her first injection appointment.

What are the important considerations when scheduling CJ's first injection appointment?



2020ICP Annual Meeting	OUR	TEAM	CAN
---------------------------	-----	------	-----

Patient Case – Part #3

CJ has successfully received her first injection and it is now 3 weeks later and a pharmacy technician is calling to remind her of her upcoming appointment for her next injection. CJ states that "something has come up" and wants to push the appointment out by about 2 weeks.

How should the pharmacy technician respond?



2020ICP Annual Meeting	OUR	TEAM	CAN
---------------------------	-----	------	-----

Patient Case – Part #4

Because of the education provided by the pharmacy technician, CJ has decided to keep her original appointment and has returned to the clinic. She is only here for her injections and no other services.

How might this visit differ from her other clinic visits?



2020ICP Annual Meeting	OUR	TEAM	CAN
---------------------------	-----	------	-----

Patient Case – Part #5

Six months into treatment, CJ does not make her appointment and does not return the outreach calls. A week later CJ returns the call to reschedule her appointment and asks for guidance.

What guidance should you give CJ?





Continuing to Look Forward



Fostemsavir (Rukobia™)

- Mechanism of action: gp120 directed attachment inhibitor
- Indication: In combination with other antiretrovirals, the treatment of HIV-1 infection in heavily treatment-experienced adults with multidrug-resistant HIV-1 infection failing their current ARV regimen due to resistance, intolerance, or safety considerations
- Dose: 600 mg PO twice daily with or without food



Approved 7/2/2020



Fostemsavir (Rukobia™)

- Do not chew or crush
- Most common side effect is nausea
- Tablets may have a slight vinegar-like odor
- Store at room temperature
- Dispense in original, child-resistant bottle (60 tablets)

Fostemsavir (Rukobia) ViiV Healthcare, GlaxoSmithKline, Research Triangle Park, NC, 2020

2020 IAPAC Annual Meeting OUR TEAM CAN

Islatravir

- Mechanism of action: nucleoside reverse transcriptase translocation inhibitor (NRTTI)
- Studied for treatment and pre-exposure prophylaxis
 - Potential for once yearly long acting implant
- Dose: 0.75 mg selected for further development
 - Unprecedented potency
- Once daily dual regimen with doravirine 100 mg
 - Treatment naïve
 - Virologically suppressed
 - Heavily treatment experienced



Dhillon C. et al. 23rd International AIDS Conference, Abstract OAB0202, 2020.
 Dhillon C. et al. 23rd International AIDS Conference, Abstract OAB0205, 2020.
https://www.hivma2020.org/wp-content/uploads/2020/12/Abstract_OAB_2020.pdf

2020 IAPAC Annual Meeting OUR TEAM CAN

Lenacapavir

Phase II/III



- Mechanism of action: HIV capsid inhibitor
- Unaffected by mutations associated with mutations to most approved antiretrovirals
- CAPELLA (Phase II/III) – Evaluation in heavily treatment experienced patients with multidrug resistance
 - Lead in oral lenacapavir for 14 days then subcutaneous dosing every six months
- CALIBRATE (Phase II) – Evaluation in treatment naïve patients
 - Lead in oral lenacapavir for 14 days then subcutaneous dosing every 26 weeks

https://www.hivma2020.org/wp-content/uploads/2020/12/abstract_APR_2020.pdf

2020 IAPAC Annual Meeting OUR TEAM CAN

Which of the following statements regarding fostemsavir is the most correct?

- A. As fostemsavir is indicated for patients with resistant virus, dispense in a pill box to assist patients with adherence
- B. Fostemsavir should be taken in combination with other antiretrovirals and always with food
- C. Patients who are failing their current therapy due to an intolerance would be a candidate for fostemsavir
- D. The most common side effect of fostemsavir is diarrhea which is alleviated by chewing the tablet



Summary

- Injectable agents will have many logistical considerations for treatment implementation
- Patients should be carefully counseled regarding injectable therapy
- New and pipeline agents will offer options for patients with resistant virus and push treatment beyond monthly dosing





Considerations for the Use of Novel HIV Medications: To Injectables and Beyond!

Milena Murray, PharmD, MSc, BCIDP, AAHIVP
 Associate Professor of Pharmacy Practice
 Midwestern University – Chicago College of Pharmacy
 HIV/ID Clinical Pharmacist
 Northwestern Memorial Hospital

