

MK-0518 Expanded Access Study

Presented by:

Study Design

- Expanded access
- Non-comparative
- Multi-center
- Open-labeled
- Treatment study
- Using MK-0518 400 mg po BID in combination with an Optimized Background Antiretroviral Therapy (OBT) X 6 months

MK-0518

- Classification:
 - HIV Integrase inhibitor in phase IIIb of clinical development
- Use:
 - Highly experienced HIV + patients
 - Patients with advanced HIV and limited therapeutic options

Current Studies

- Clinical trials are currently ongoing
- MK0815 is generally safe + well tolerated
- Potential to be a clinically effective therapeutic option for chronic HIV infection in highly experienced patients
- Need to assess risks vs. potential benefits

Protocol Objectives

- To provide expanded access to MK-0518 prior to FDA approval and availability on the market.
- To monitor the safety and tolerability of MK-0518 for the treatment of HIV-1 infection.

Inclusion Criteria

- HIV-1 infection
- 16 yrs of age (M/F)
- Limited RX options:
 - Resistance
 - To at least 1 drug in each of 3 ART classes (NNRTI, NRTI and PI)
 - Intolerance
 - Defined as having had a significant adverse event which provides a contraindication to the use of any drug in that class

Inclusion Criteria (con't)

- Not achieving adequate virologic suppression on current regimen
- Clinically stable at time of entry into study
 - All chronic meds (except antiretroviral agents) should be unchanged for 2 weeks prior to the start of RX
- If of reproductive potential patient must agree to use an acceptable form birth control including:
 - IUD
 - Diaphragm
 - Condom
 - Abstinence

Exclusion Criteria

- Hypersensitivity or other contraindication to any of the components in MK-0518
- Prior participation in MK-0518 clinical trial
- Inability to obtain informed consent
- Patient requires or is anticipated to require any of the prohibited medications
 - Hormones
 - Phenobarbital
 - Phenytoin
 - Rifampin

Exclusion Criteria (con't)

- Patients with Acute Hepatitis
 - Cirrhosis
 - Ascites
 - Encephalopathy
 - Hypoalbuminemia
 - Prolonged PT/PTT
 - Esophageal varices
 - HCV or HBV positive patients are not excluded if stable

Exclusion Criteria (con't)

- Female patients who are pregnant or breastfeeding
 - All female patients must have a negative pregnancy test at treatment day 1
- Any condition which would interfere with compliance or safety
 - Alcohol abuse (on-going)
 - Substance abuse (on-going)
- Severe renal insufficiency
 - Creatinine clearance <30 ml/min

Treatment Plan

- Each patient will receive MK-0518 400 mg po BID (without regard to food) by medline.
- The investigator will select an OBT based on the patient's prior RX history and geno/phenotypic antiretroviral resistance testing. Patient's must take OBT via medline for study period as well.
 - if not available, must be done at screen

Treatment Plan (con't)

- The investigator will follow patients according to the standard of care
- Laboratory testing will be done locally per study flow chart
 - At screen
 - Week # 4
 - Week # 12 and
 - At the investigator's discretion
- A pregnancy test must be performed on all women of childbearing potential
 - If patient becomes pregnant during the course of the study must immediately be discontinued from all study medication
 - All pregnancies must be reported to the sponsor/representative and must be followed to completion of /termination of the pregnancy

Safety

- Safety data will be collected on case report forms for the following:
 - Serious adverse effects and drug related adverse experiences that result in grade 3 or greater lab toxicity,
 - Lead to RX interruptions or discontinuation

Laboratory Safety Assessment

- Per Standard of care:
 - Chemistry (including serum creatinine)
 - LFTs
 - CBC
- In addition all patients who discontinue from the study early should have a 14-day post therapy follow-up visit

Procedure

- Visits should be planned at weeks 4 and 12 following initiation of RX
- Assessment of serious adverse experiences will be made at visits
- All serious adverse events must be reported immediately to the sponsor/representative and the principal investigator, Dr. Mary Sabolsi.

Informed Consent

- The investigator must obtain documented informed consent from each potential patient (see consent form)
- A copy of the signed and dated consent form must be given to the patient before participating in the trial
- The investigator shall discuss with each patient the:
 - Nature of the study
 - It's requirements
 - It's restrictions
- In the first phase of the study, all screening will be done by Dr. Sabolsi, either at the Shattuck or MCI-Concord.
- Once a potential patient has been identified, the ID physician or case manager should contact Dr. Sabolsi to arrange for screening.

Identification

- Each patient will be assigned a number from the group of numbers provided to each site by the sponsor's representative on day 1 of treatment
- The allocated number will be used to identify the patient for all procedures occurring after enrollment

Case Report

- All patients will be asked about the following and this information will be recorded on the case report form:
 - Prior use of antiretroviral agents
 - Length of time on RX with these agents
 - AIDS defining illness,
 - Hepatitis B and C history,
 - Local geno or phenotype data,
 - Supporting viral load history of virological failure

Contact Information

- If a participant develops a serious adverse event **or** is transferred to another institution, please notify Dr. Sabolsi and the State Pharmacy immediately (preferably prior to transfer).
- Dr. Mary Sabolsi (Sue Galvin, RN Shattuck 617-971-3621), (Sarah Maria, RN Concord 1-508-405-6100, ext. 376), msabolsi@partners.org, pager 617-522-8110.

Distribution

- This medication is designed to be given in the community by the patients.
- There are no known adverse effects from handling the medication.
- The person handling the medication on the med-line has two options that may decrease any potential risk:
 - Wear gloves when handling the medication.
 - Hand the bottle to the inmate, who will remove the medication and hand it back.
- There will be a drug accountability log that should be completed to document that each dose was taken.