Case 5
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David is a 23-year-old diabetic patient who completed rehabilitation for intravenous drug abuse one month ago. Over the past few weeks, David has experienced flu-like symptoms including a persistent fever (101F), fatigue, chills, swollen lymph nodes and night sweats. David went to an urgent care center four days ago where he tested negative for influenza and SARS-CoV-2 viruses. The clinic discharged him with a recommendation of fluids and a fever reducer such as acetaminophen (Tylenol).

Symptoms have continued and David was able to get an appointment with his doctor. Lab tests to look for blood cancers such as lymphoma and infections were ordered. David’s blood shows an active HIV infection and low numbers of CD4 T lymphocyte immune cells.
Case 5

• The prescriber is considering treating David with:

  **Efavirenz (Sustiva)**

• Question 1: How does this drug work to treat HIV infection?

  *Hint: pharmacodynamics; use* https://www.pharmgkb.org/annotatedDrugs
Case 5

• Metabolism of efavirenz:

Efavirenz $\xrightarrow{Liver} \text{CYP2B6} \xrightarrow{8\text{-hydroxy efavirenz}} \text{Remove from the body}$

• Key pharmacogene for efavirenz: CYP2B6
You recommend preemptive testing of David’s *CYP2B6* genotype before initiating therapy efavirenz. In the meantime, you have the genotypes of David’s parents in the electronic medical records.

**Dad**

*1/*6

**Mom**

*2/*4
Case 5

• Question 2: What genotypes and phenotypes are possible for David based on mom and dad’s genotype?

<table>
<thead>
<tr>
<th>Possible Genotypes (*X/*X)</th>
<th>Phenotype (Poor/Normal/Intermediate/Ultrarapid Metabolizer)</th>
<th>Drug Therapy Recommendation (Use/Don’t Use/Change Dose)</th>
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Use This Website To Look Up Genotype-Based Dosing:
https://www.pharmgkb.org/chemical/PA449441/guidelineAnnotation/PA166182603
• David underwent genotyping and you have received the results from the laboratory.

**CYP2B6: *1/*4**

• Question 3: What is David’s phenotype?

• Question 4: What do you recommend for their treatment? Why (better or worse benefit/toxicity)?