Case 4
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Ismel is a 62-year-old patient who was taken to the emergency room after presenting with symptoms of confusion, lack of coordination, and numbness on one side of his body. He was unable to speak. At the hospital, Ismel’s doctor concludes that he has suffered a stroke.

After clearing the blood clot in Ismel’s brain, his doctor discusses steps that Ismel can take to prevent future stroke. This includes medication that prevents further blood clots in his brain.
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• The prescriber is treating Ismel with:

  Clopidogrel (Plavix)

• Question 1: How does this drug work to prevent stroke?
  
  Hint: pharmacodynamics; use https://www.pharmgkb.org/annotatedDrugs
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• Metabolism of Clopidogrel:

  Clopidogrel $\xrightarrow{\text{Liver}}$ 2-oxo-Clopidogrel $\xrightarrow{\text{CYP2C19}}$ Inhibition of clot formation

• Key pharmacogene for Clopidogrel: $CYP2C19$
You recommend preemptive testing of Ismel’s CYP2C19 genotype before initiating clopidogrel therapy. In the meantime, you have the genotypes of Ismel’s parents in the electronic medical records.

- Dad: *1/*3
- Mom: *17/*2
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• Question 2: What genotypes and phenotypes are possible for Ismel 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/guidelineAnnotation/PA166104948
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• Ismel underwent genotyping and you have received the results from the laboratory.

  **CYP2C19: *3/*2**

• Question 3: What is Ismel’s phenotype?

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