Case 6
Amaya is a 33-year-old patient who notices skin irritation and dimpling around the side of her right breast one morning. Concerned about her discovery, Amaya went to see an oncologist the very next day. The oncologist requested a mammogram for Amaya and upon looking at her results found small, white calcifications clustered together in her breast. Her oncologist then biopsied these calcifications and surrounding breast tissue in order to check for a possible underlying cancer. The results of the biopsy show the tissue is positive for cancer cells with estrogen receptors. After surgical removal of the tumor cells, the doctor recommends long-term treatment with a drug that targets the estrogen receptor.
Case 6

• The prescriber is considering treating Amaya with:

  **Tamoxifen (Soltamox)**

• Question 1: How does this drug work to treat breast cancer?
  
  *Hint: pharmacodynamics; use [https://www.pharmgkb.org/annotatedDrugs](https://www.pharmgkb.org/annotatedDrugs)*
Case 6

- Metabolism of Tamoxifen:

Tamoxifen $\xrightarrow{Liver}$ endoxifen $\xrightarrow{CYP2D6}$

Blocks DNA synthesis in cancer cells

- Key pharmacogene for Tamoxifen: \textit{CYP2D6}
You recommend preemptive testing of Amaya’s CYP2D6 genotype before initiating tamoxifen therapy. In the meantime, you have the genotypes of Amaya’s parents in the electronic medical records.

Dad: *1/*12

Mom: *3/*1
Case 6

• Question 2: What genotypes and phenotypes are possible for Amaya 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/PA451581/guidelineAnnotation/PA166176068
Case 6

- Amaya underwent genotyping and you have received the results from the laboratory.

  **CYP2D6: *1/*12**

- Question 3: What is Amaya’s phenotype?

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