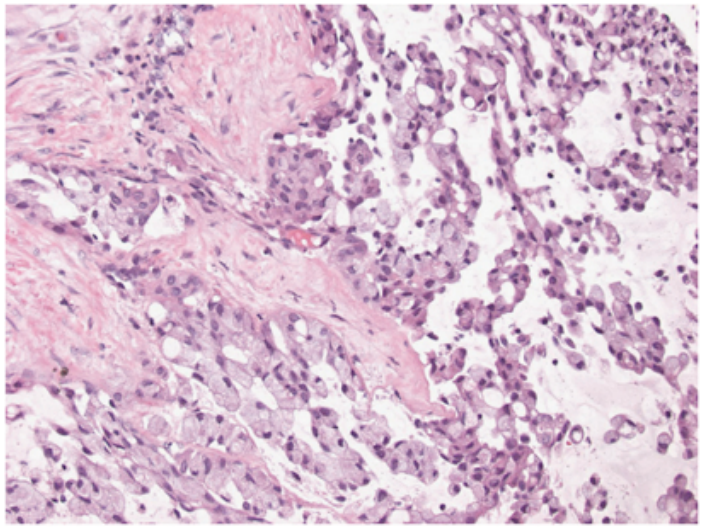
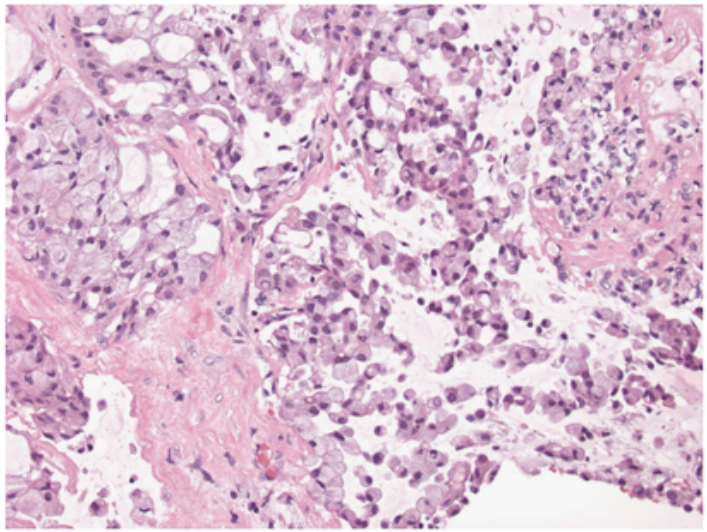
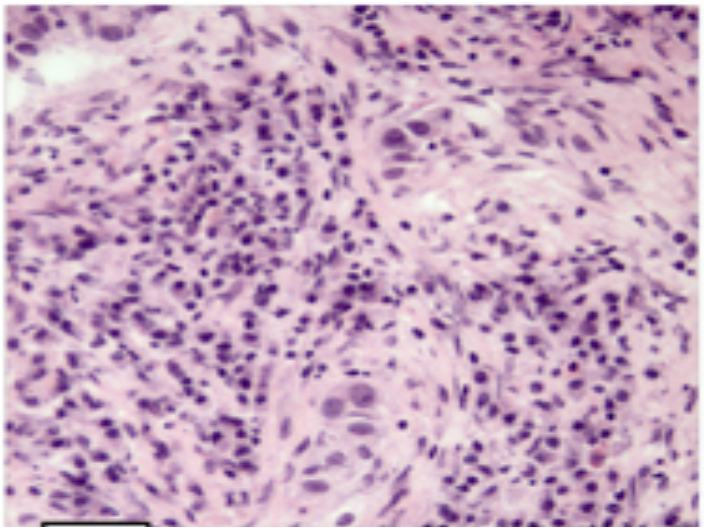


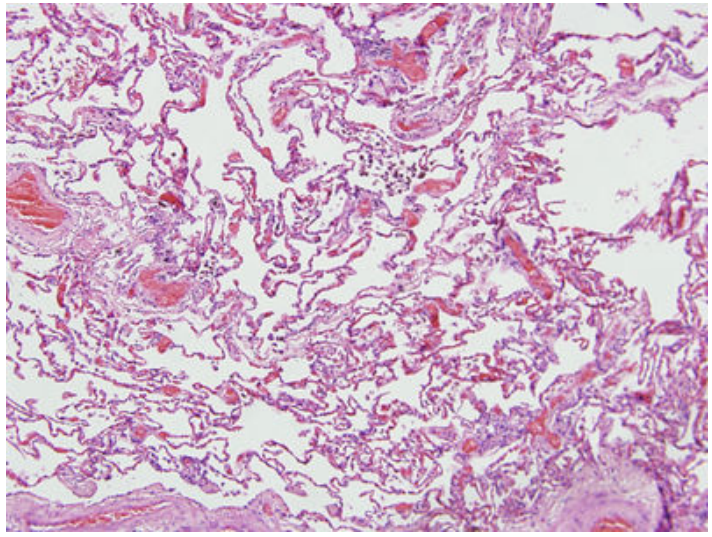
Patient #1



Patient #2



Patient #3



Normal Lung

Images adapted from Yousem, *Mod Pathol*. 2012; Ji et al., *Oncogene,* 2006; http://www.histology-world.com/photoalbum/displayimage.php?album=15&pid=714.

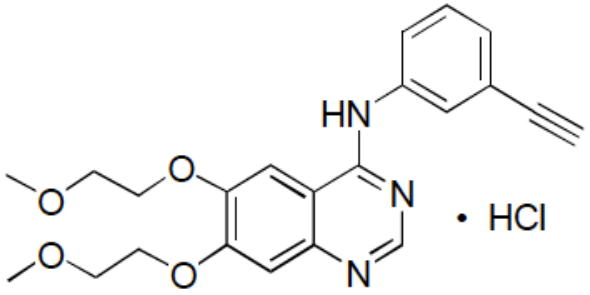
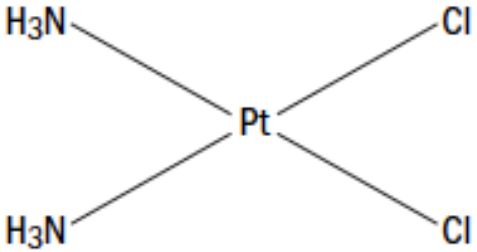
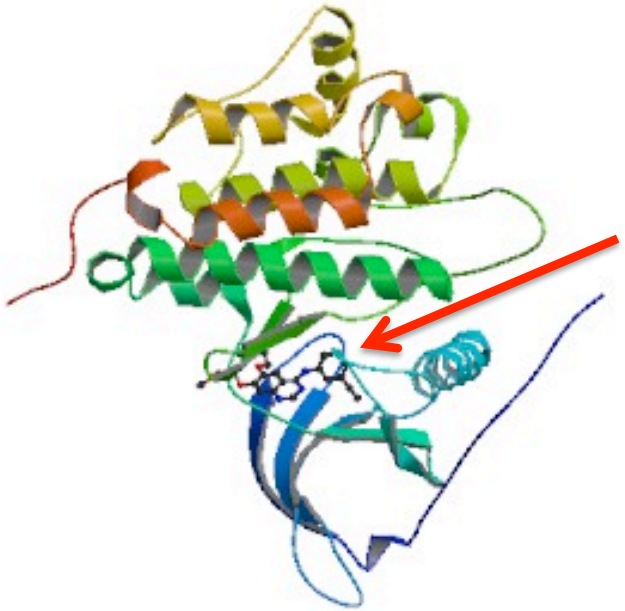
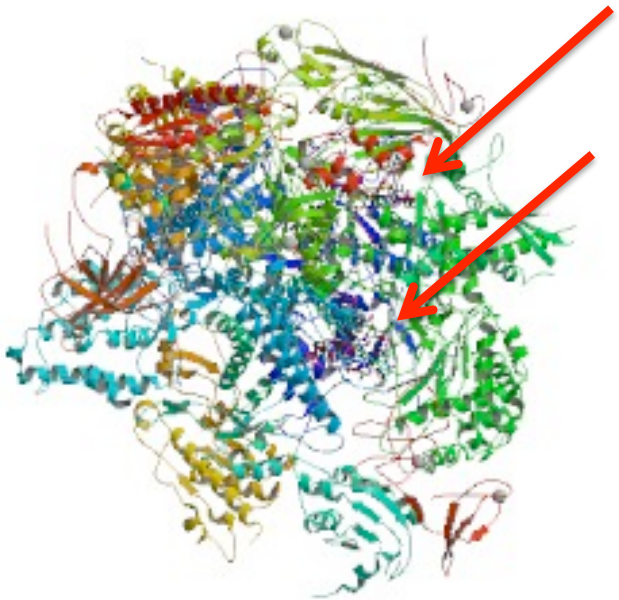
Different Types of Cancer Treatments

Surgery

Radiation

Anti-cancer drugs

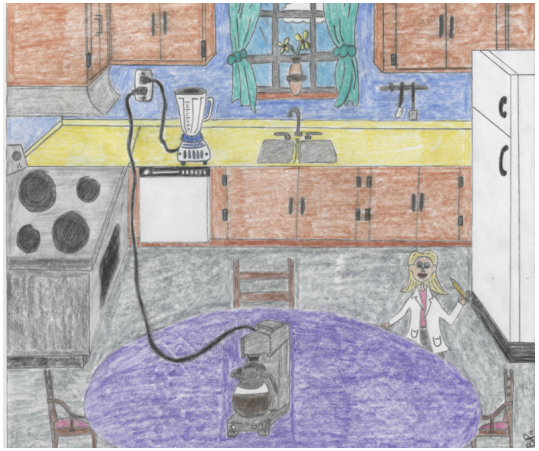
Two types of anti-cancer drugs

	Targeted therapy	Chemotherapy
Drug		
Target Protein		

Erlotinib binding to mutant form of EGFR
(which is a form of EGFR that is only present in cancer)

Cisplatin binding to DNA Polymerase
(an enzyme that replicates DNA, and is active in all growing & dividing cells)

Protein structures adapted from Protein Databank (PDB) http://www.rcsb.org/pdb/home/home.do



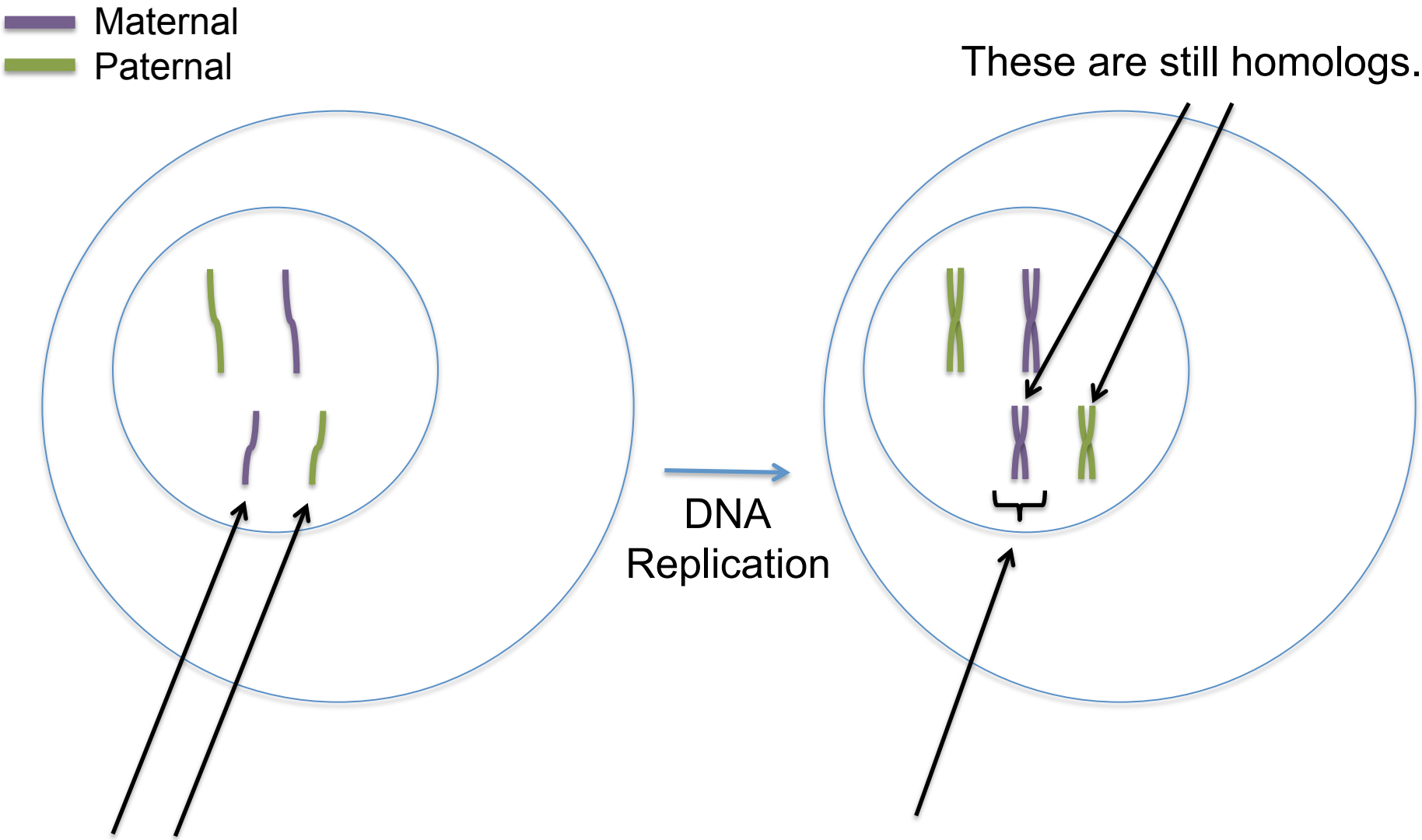
1) Fill in this table with whether each treatment would work, or not work, to treat each kitchen-related problem:

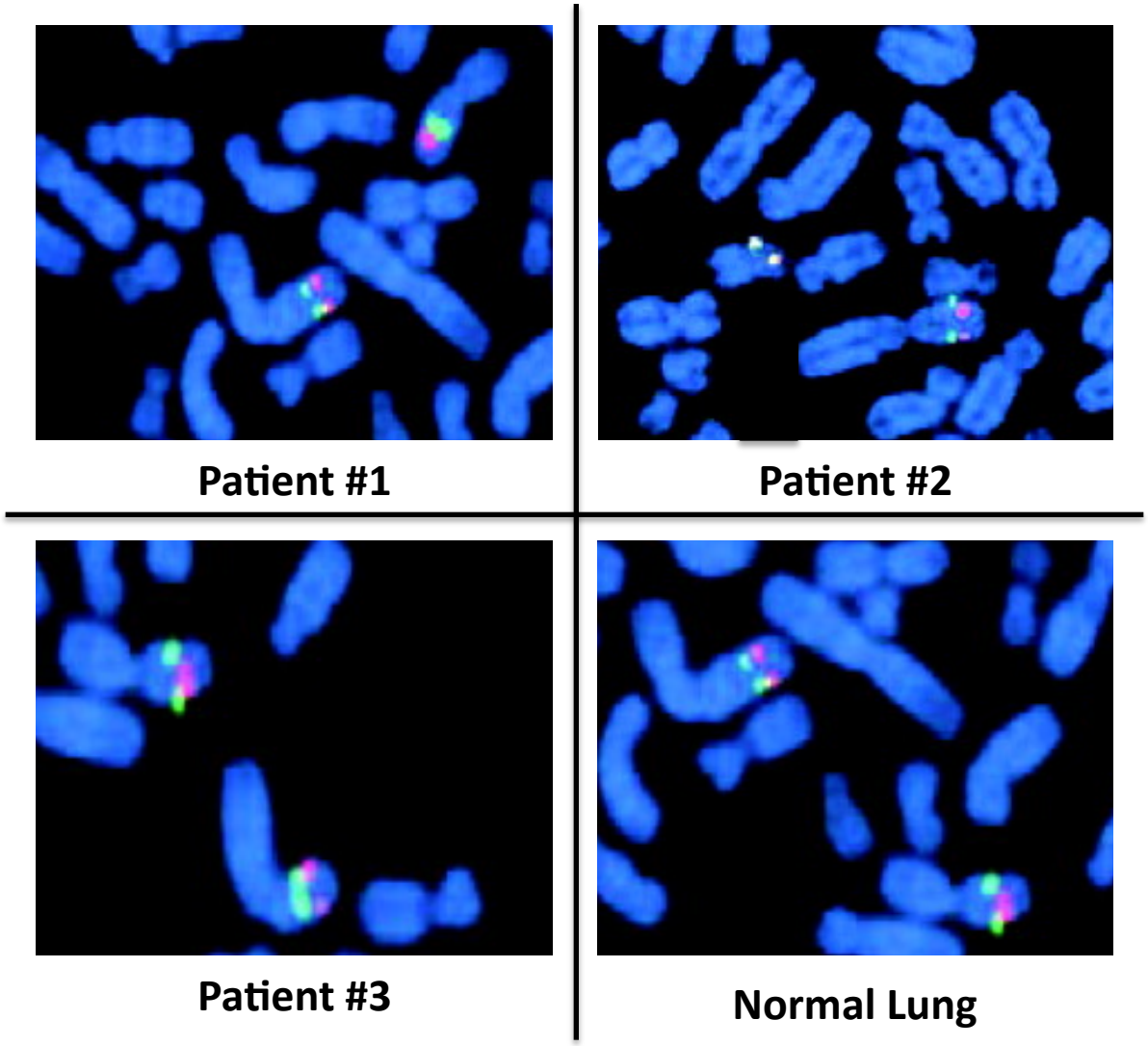
	In a kitchen with an out-of-control coffee maker	In a kitchen with an out-of-control blender
Use a lid		
Use a rubber stopper		
Turn off power to the whole kitchen		

2) Which is the best way to treat a kitchen with an out-of-control coffee maker?

3) Which is the best way to treat a kitchen with an out-of-control blender?

4) Which treatment works to treat the out-of-control appliance, but also yields other negative side effects to the kitchen?


Maternal
Paternal
These are still homologs.
DNA
Replication
"Homologs" are ***versions*** of chromosomes – one from the mother, and one from the father.
"Sisters" are ***replicates*** of each other, and are formed after DNA replication.

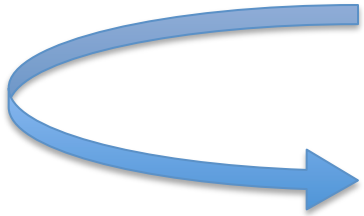


*Gene A has been dyed red and Gene B has been dyed green. If both genes come together at the same location due to a change in the DNA, then the area appears yellow.

Images adapted from Koivunen J P et al. *Clin Cancer Res*, 2008.

Large Rearrangement

CGCATCGAAGTCGATGCGATGCATGCGCTGCATCGATTGCATGTTCAGTACAGATT

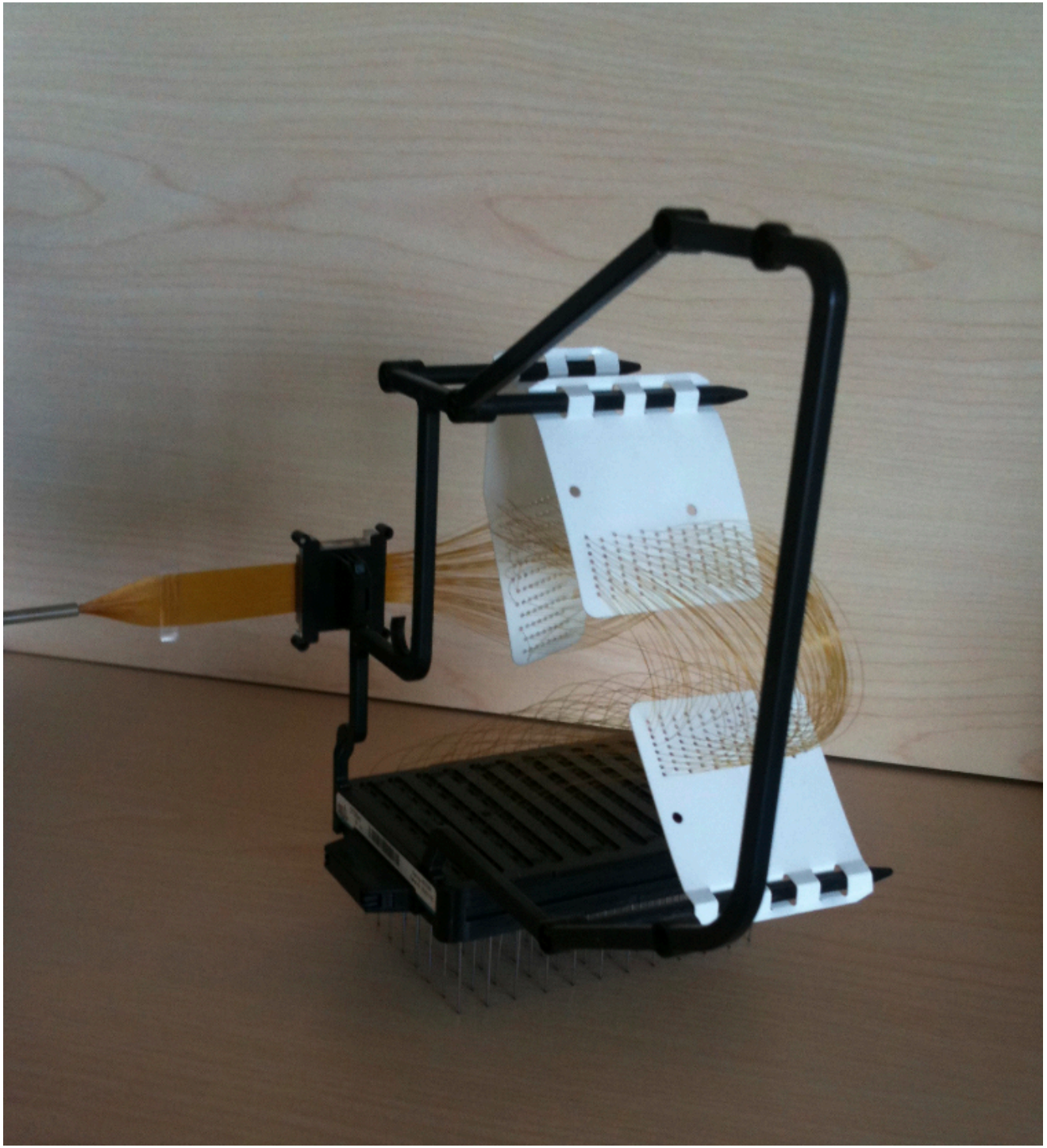


CGCGACATGACTTGTACGTTAGCTACGTCGCGTACGTAGCGTAGCTGAAGCTAATT

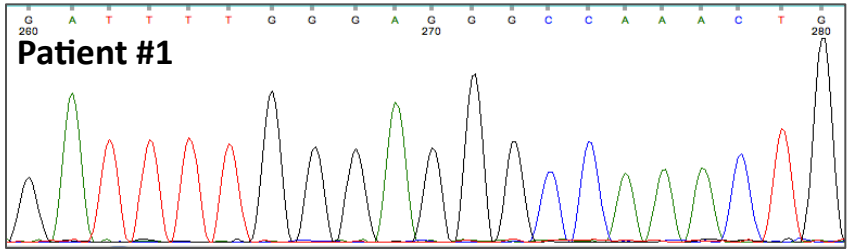
Single Point Mutation

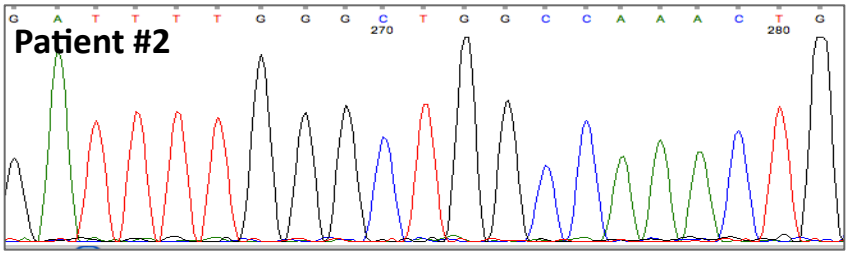
CGCATCGAAGTCGATGCGATGCATGCGCTGCATCGATTGCATGTTCAGTACAGATT

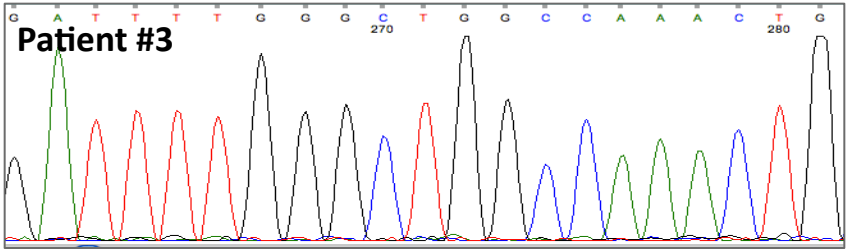
CGCATCGAAGTCGAAGCGATGCATGCGCTGCATCGATTGCATGTTCAGTACAGATT

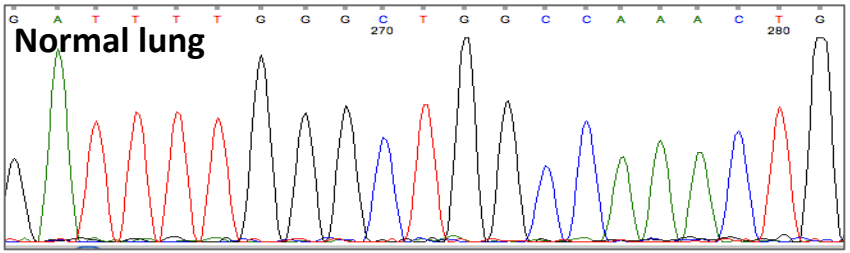


EGFR sequencing chromatograms

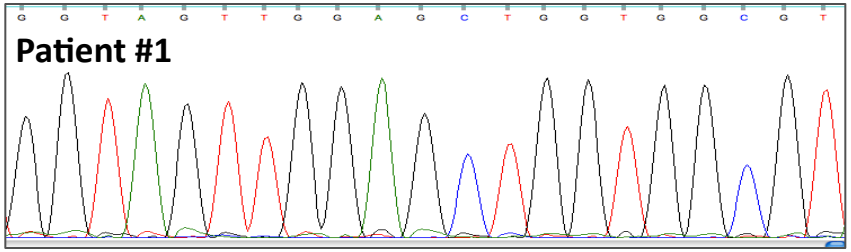


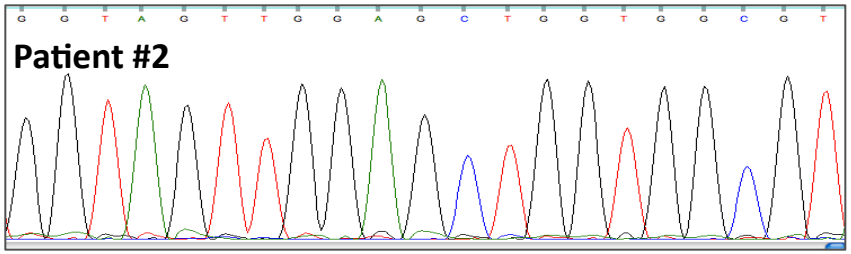


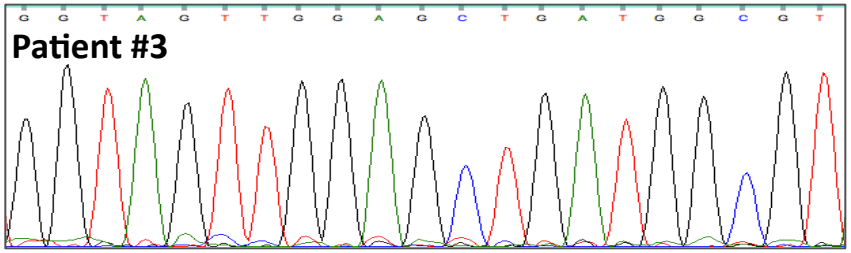


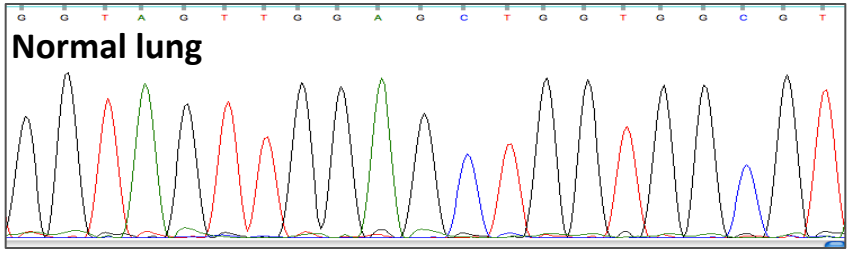


KRAS sequencing chromatograms









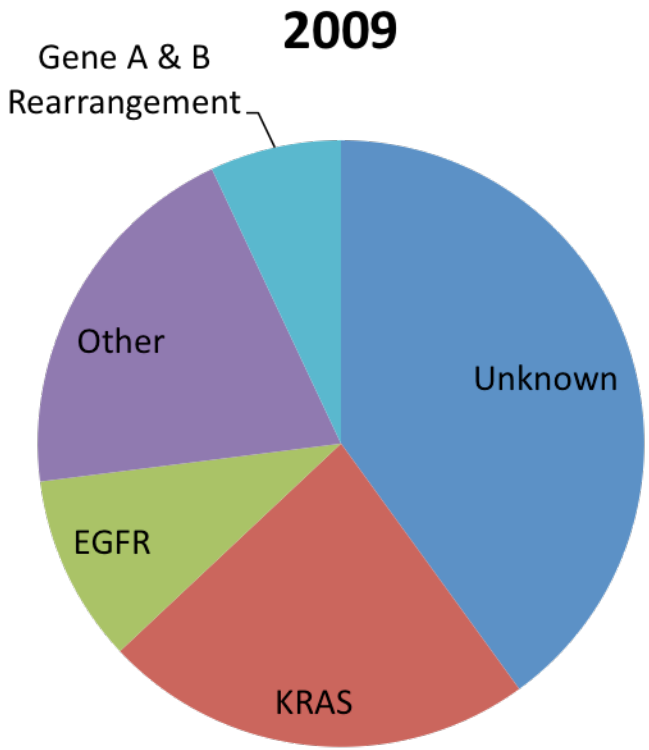
Based on the data that you gathered and the data on the response rates in the table provided, how would you treat each patient?

	Response Rates		
	erlotinib	crizotinib	carboplatin/paclitaxel (chemotherapy)
KRAS mutation	3%	n/a	23%
Rearrangement of Gene A & Gene B	n/a	56%	29%*
EGFR mutation	77%	n/a	37%

n/a: data are not available for these mutation/drug combinations
*includes patients from all categories

Data adapted from Jänne et al., *Clin Cancer Res*. 2006; Jackman et al., *Clin Cancer Res*. 2009; Shaw et al, *Nat Rev Drug Disc*. 2011; Mok et al., *New Eng J Med*. 2009; Eberhard et al., *J Clin Oncol* 2005; Vittorio et al., *J Clin Oncol* 2008.

Distribution of Genetic Mutations Known to Cause Lung Cancer



Data adapted from Pao et al., *Lancet Oncology* 2011.