

# Skill Blitz Pre-Work: Dissecting a Research Article

Name: \_\_\_\_\_

Using the glossary provided and the figure legend and description, please answer the following questions about this figure.

This figure is figure 4, parts A from this paper:

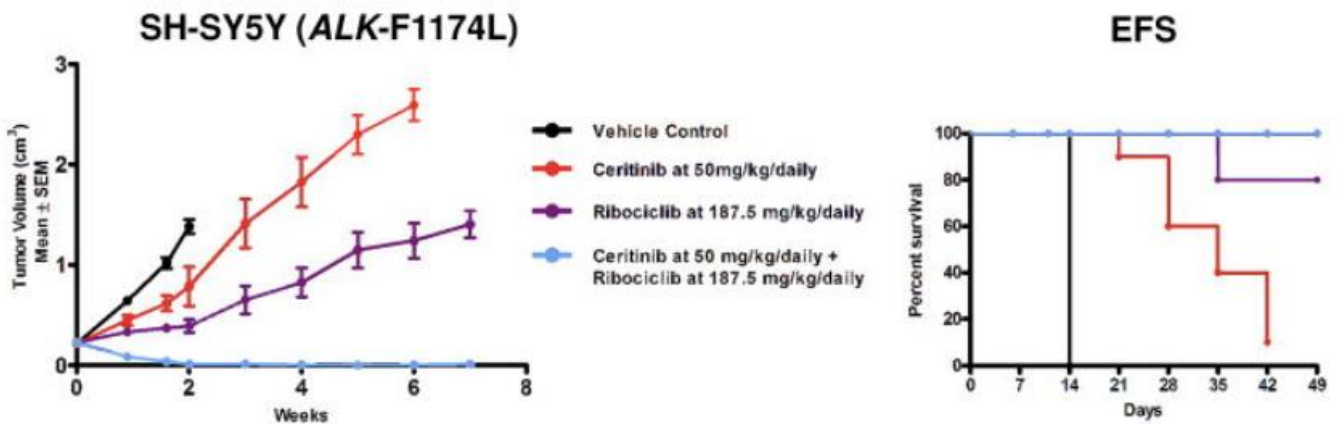
Dual ALK and CDK4/6 inhibition demonstrates synergy against neuroblastoma

Wood et al. 2016

You do not need to read this paper to answer the questions, but the introduction and methods may be helpful to understand the figure.

Don't panic when you see unfamiliar words in this graph. Try to understand the figure in small pieces and use the glossary. Answer as many of the questions as you can.

**A**



## Figure legend:

Dual ALK and CDK4/6 inhibition displays marked anti-tumor activity in several in vivo models of neuroblastoma. Mice harboring (A) SH-SY5Y were treated with vehicle or Ceritinib (50 mg/kg) + doses of Ribociclib (187.5 mg/kg) for 3 weeks.

## Glossary:

- **ALK:** Anaplastic Lymphoma Kinase. A protein that is frequently mutated when patients have the pediatric cancer neuroblastoma.
- **ALK-F1174L:** A mutation in the ALK gene that is found in a particular place in the genome. This mutation makes the mutant ALK resistant to treatment by some cancer drugs, including Ceritinib.
- **CDK4/6:** Cyclin-Dependent Kinase 4 and 6. Two proteins that are important for controlling how fast cells grow. If they are too active, cells can grow out of control.
- **Ceritinib:** A drug that inhibits ALK and is used to treat some cancers.
- **EFS:** Event free survival. After a treatment, this is how long a patient or animal lives without other complications or events.
- **In-Vivo:** A process or experiment done in a live animal.
- **Neuroblastoma:** A cancer that often occurs in children. The cancer develops from early forms of nerve cells. It most often starts in the abdomen and can spread throughout the body.
- **Percent Survival:** The percentage of people or animals in a study that are still alive after a given period of time.
- **Ribociclib:** A drug that inhibits CDK4/6 and is used to treat some cancers.
- **SEM:** Standard Error of the Mean. A term in statistics. This is a type of variation found in data.
- **SH-SY5Y:** Human cells line originally taken from a woman who had neuroblastoma. Can be grown and used for biological research.
- **Vehicle Control:** A harmless substance with no drugs used in research as a control. Used to test if the process which you give a drug (for example, injection) is having an effect other than the drug itself.
- **Xenograft:** Tissue or organ from a donor of a different species.

## Description of the figure results from the paper:

We focused initial *in vivo* experiments on the resistant *ALK* F1174L mutation using SH-SY5Y xenografts. The dose of Ceritinib 50 mg/kg/daily was selected as murine drug exposures were comparable to Ceritinib exposures at the recommended dose in human adults. SH-SY5Y xenografts treated with Ceritinib alone had prolonged event free survival (EFS) (Figure 4A,  $p < 0.0001$ ) compared to vehicle, but not growth delay ( $p = 0.3$ , Supplementary Table 2). SH-SY5Y xenografts treated with ribociclib (CDK4/6i) showed tumor growth delay ( $p < 0.0001$ ) and prolonged median EFS ( $p < 0.0001$ ) versus vehicle controls (Figure 4A and Supplementary Table 2). All SH-SY5Y xenografts treated with combination Ceritinib and Ribociclib achieved complete and sustained regressions, and prolonged EFS versus either single agent ( $p < 0.0001$ ) (Figure 4A). At predefined cessation of the study at 7 weeks, mice came off treatment and all eventually relapsed.

## Questions:

1. In your own words and in less than 3 sentences, describe the first graph (on the left) .
2. In your own words and in less than 3 sentences, describe the second graph (on the right).
3. Why is the black line shorter than the other lines in the first graph?
4. If you were a doctor and you wanted to prescribe medication based on this figure, what would you recommend? How often should you give the medication?
5. Bonus question: Now that you know about this experiment and its results, what would you want to know next? Describe an experiment to test it.