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IASLC
INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER
Conquering Thoracic Cancers Worldwide

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# What do all those lines and colors mean?
Interpreting cancer data plots

In this webinar, you will learn to:

1. Identify the different types of data plots commonly used to summarize cancer clinical trial results.

2. Understand the layout, terminology, and significant data in each type of plot.

3. Improve ability to communicate clinical trial results to patients and caregivers as well as the public at large.
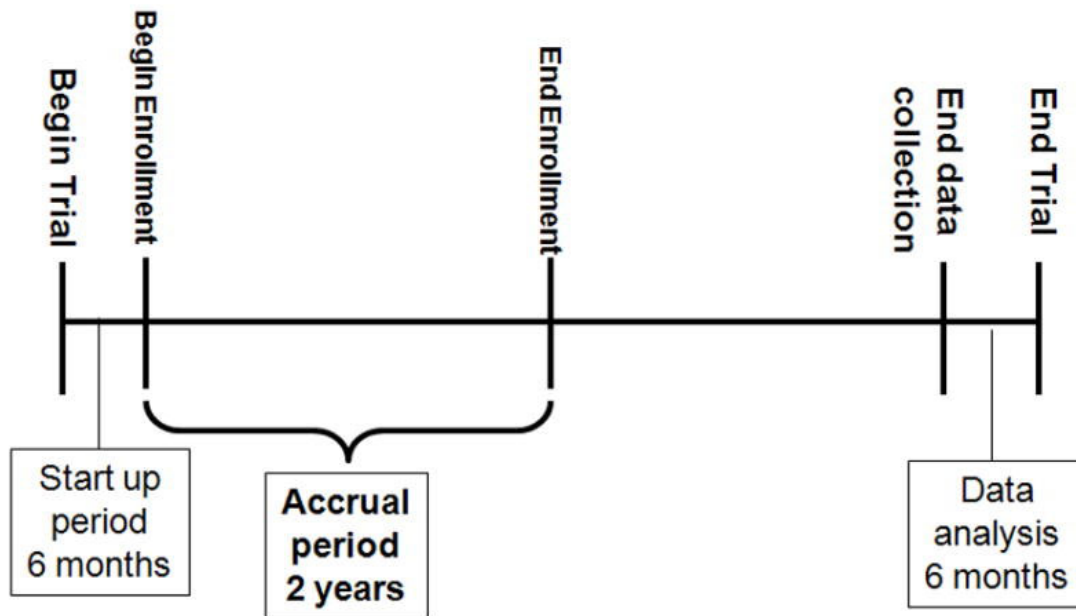
Clinical Trial Overview

Anatomy of a 5-year trial

Rich JT et al. A practical guide to understanding Kaplan-Meier curves. *Otolaryngol Head Neck Surg*. 2010;143(3):331–336. doi:10.1016/j.otohns.2010.05.007
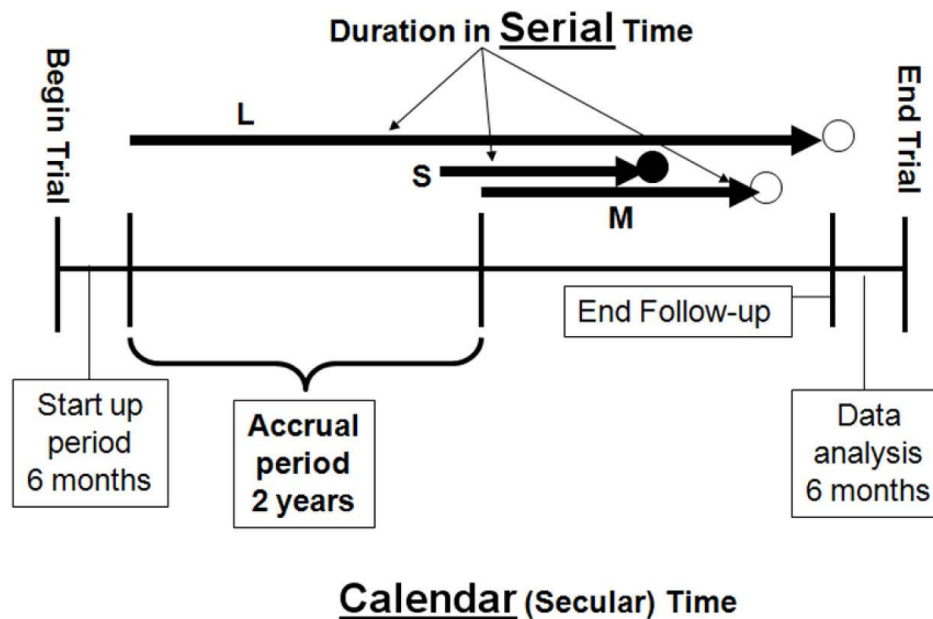
Clinical Trial Overview

Individual subject follow-up until event

Rich JT et al. A practical guide to understanding Kaplan-Meier curves. *Otolaryngol Head Neck Surg.* 2010;143(3):331–336. doi:10.1016/j.otohns.2010.05.007
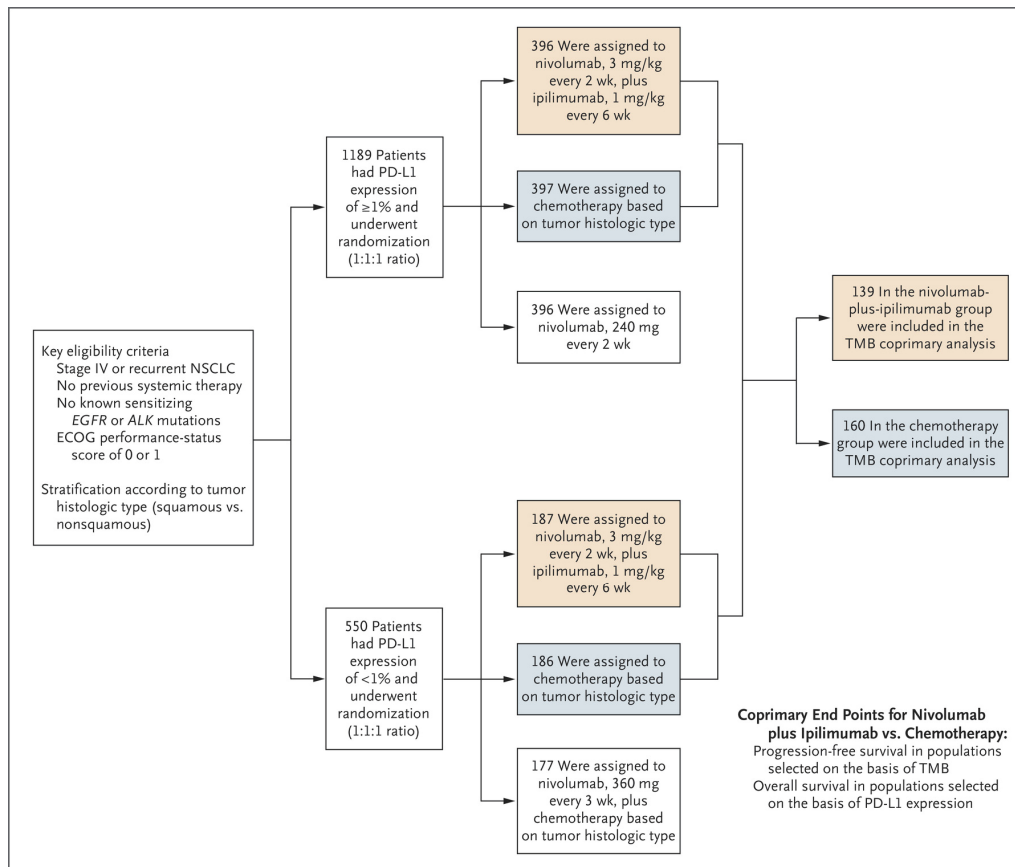
Schema (Clinical Trial Design)

Hellman, MD et al. Nivolumab plus Ipilimumab in Lung Cancer with a High Tumor Mutational Burden. *NEJM*. 2018;378:2093-2104. DOI: 10.1056/NEJMoa1801946

Clinical Trial Endpoints

› **Disease Free Survival (DFS)**
The length of time between treatment and relapse.

› **Progression Free Survival (PFS)**
The length of time between treatment and measurable worsening of the disease.

› **Response Rate (RR)**
The percentage of patients whose cancer shrinks or disappears after treatment.

› **Overall Survival (OS)**
The time between treatment and death.

› **Quality of Life (QoL)**
A drug's impact on pain or other symptoms related to a condition.

Types of Data Plots

› **Survival curve (or Kaplan-Meier curve)**
Survival over time for the entire group of trial participants

› **Forest plot**
Compares survival for two different treatments by subgroups of participants

› **Adverse events**
Summarizes side effect type, severity, and number of participants affected

› **Waterfall plot**
Best change in tumor size for individual trial participants

› **Swimmer plot**
Duration and type of response for individual trial participants

› **Spider plot**
Track the change in tumors over time for individual trial participants

Tips for Identifying Data Plots

› Look at the title
  › The type of study, method or analysis
  › The conclusion

› Look for axis labels
  › X and Y axis
  › These vary from graph to graph

› Look for the legend
  › This will tell you details about colors, shapes, variables, etc

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Survival Curve or Kaplan-Meier (KM) Curve
survival over time for the entire group of trial participants
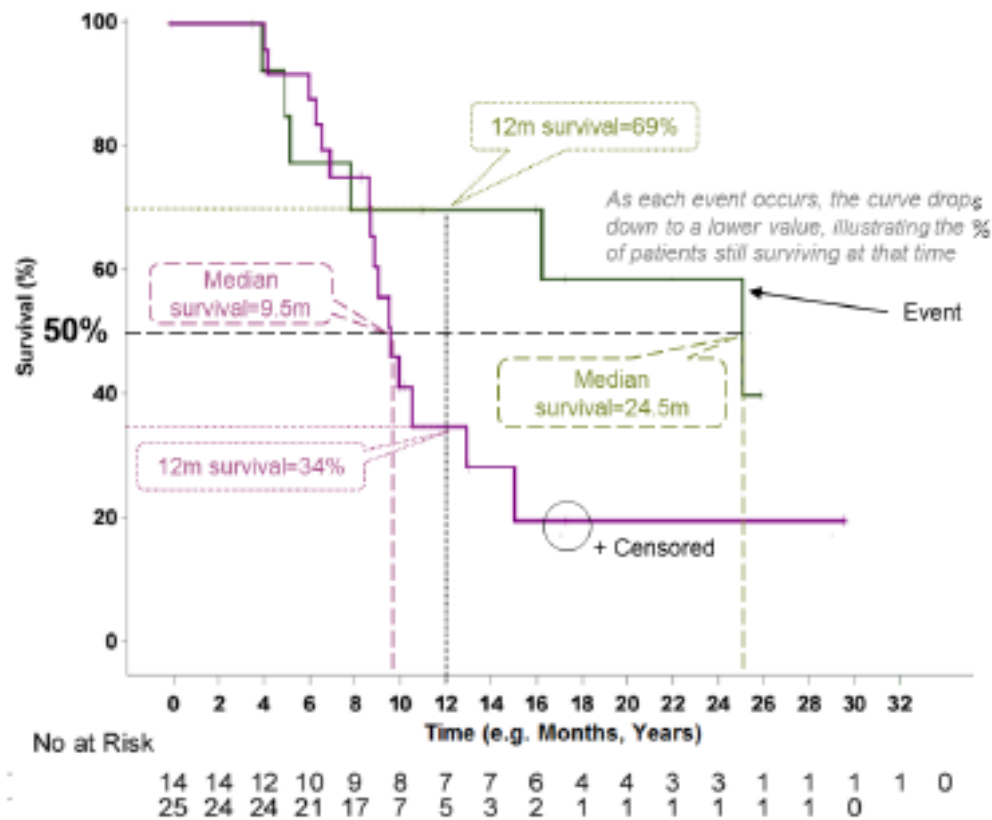
Survival Curve or KM Curve
PFS over time for the entire group of trial participants

A **Tumor PD-L1 Expression**

PD-L1 Expression of ≥1%

Hazard ratio for disease progression or death, 0.62 (95% CI, 0.44–0.88)

Nivolumab+ipilimumab — 42

Chemotherapy — 16

Patients with Progression-free Survival (%) vs *Months*
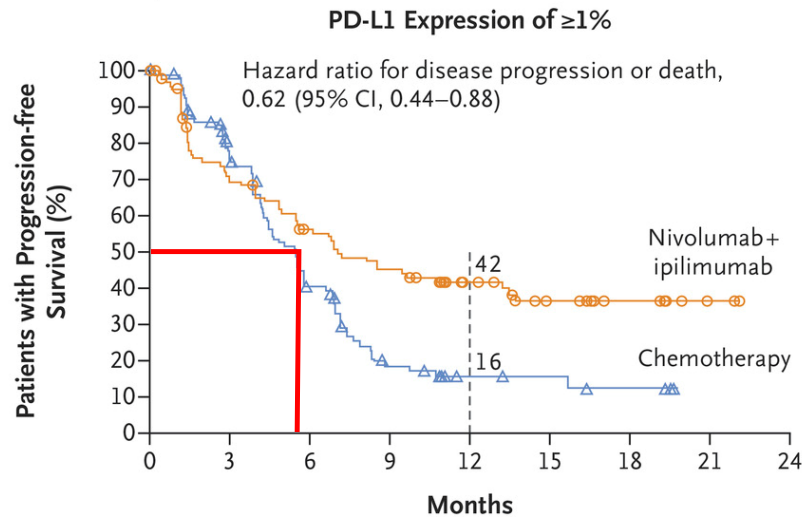
No. at Risk								
Nivolumab + ipilimumab	101	65	50	40	26	16	7	2	0
Chemotherapy	112	73	35	13	6	5	3	0	0

Nivo + Ipi Median PFS
~ 7 months

Chemo Median PFS
~ 5.5 months

Hellman, MD et al. Nivolumab plus Ipilimumab in Lung Cancer with a High Tumor Mutational Burden. *NEJM*. 2018;378:2093-2104. DOI: 10.1056/NEJMoa1801946

Survival Curve or KM Curve
PFS over time for the entire group of trial participants

	Pembrolizumab 200mg Q3W + SOC (N=125)	Standard of Care (N=124)
Events (%)	44 (35.2)	45 (36.3)
Median TTP (Months) (95% CI)	8.1 (5.6, NE)	8.7 (6.6, NE)
Hazard Ratio(95% CI)	1.14 (0.75, 1.74)	

Number of Subjects at Risk

SOC	124	91	61	46	29	17	5	2	0
Pembro+SOC	125	81	50	37	24	12	8	4	0
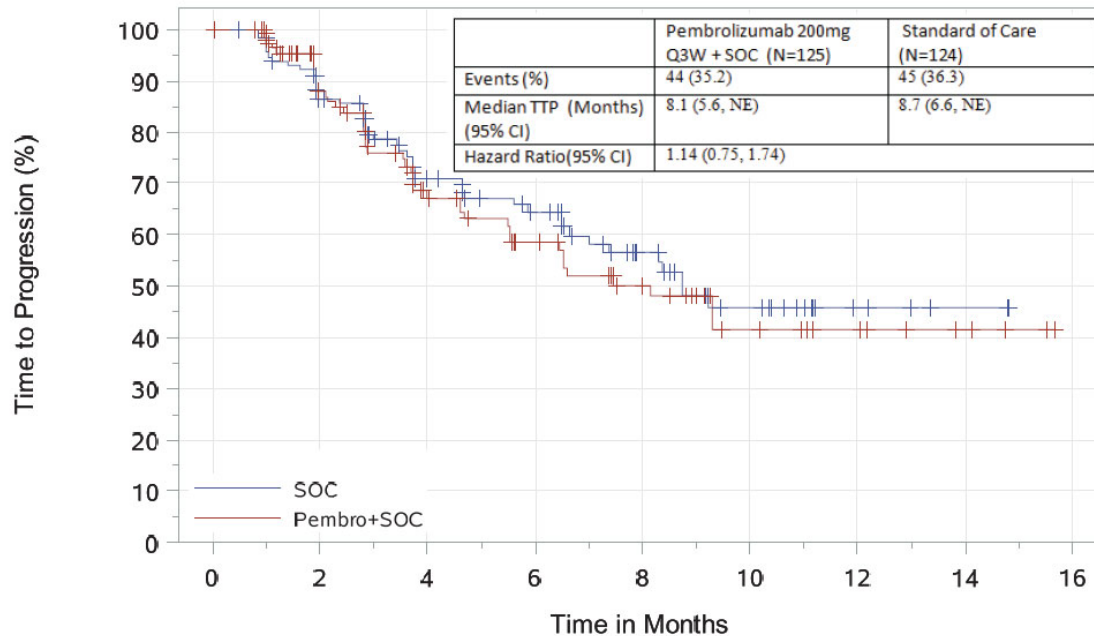
When the lines are very close together, one treatment is not better than the other

https://www.fda.gov/drugs/drug-safety-and-availability/fda-alerts-healthcare-professionals-and-oncology-clinical-investigators-about-two-clinical-trials

Cheat Sheet: Survival Curve or KM Curve
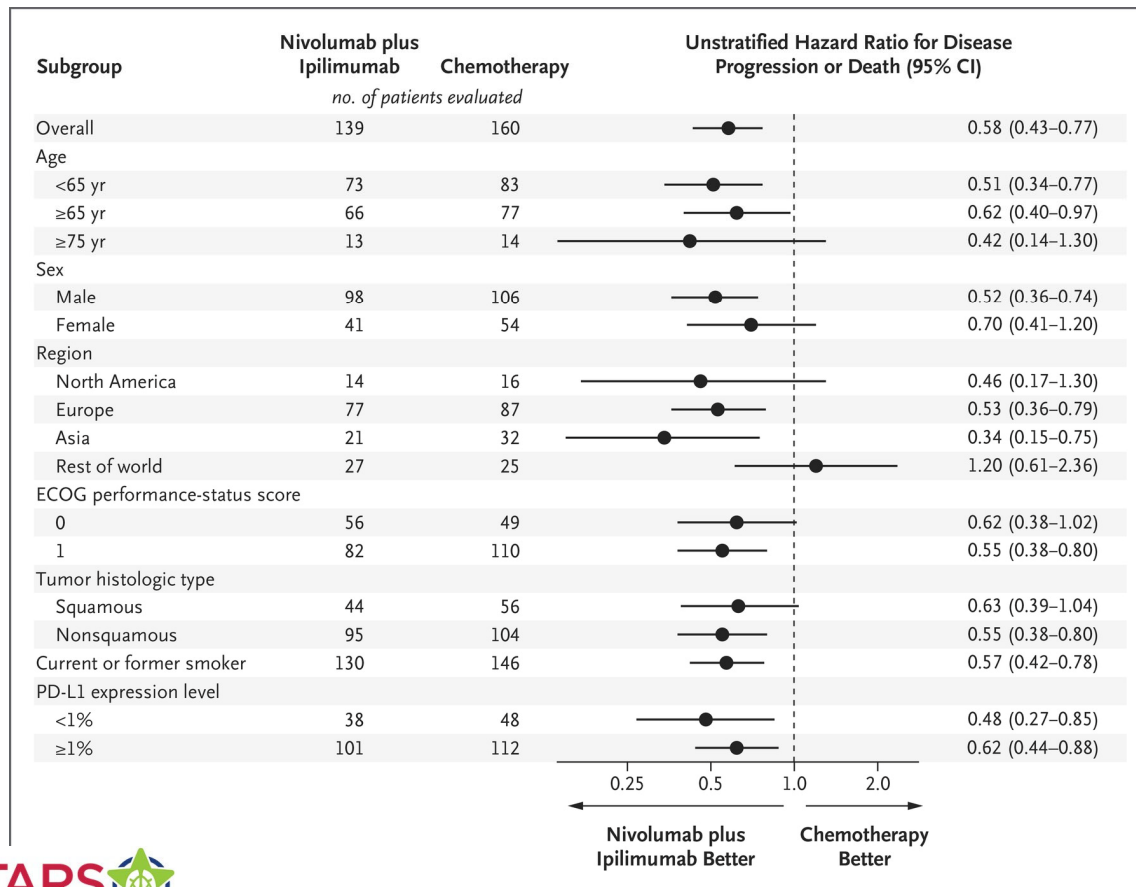
> › Read the title
>
> › Look for space between the lines
>
> › Check the axis to see if survival is what is presented
>
> › Use the "line-drawing" method to estimate median survival

Forest Plot
compares survival for two treatments by subgroups

Hazard Ratio (HR): measure of the effect of an intervention (Nivo + Ipi) on a specific outcome (disease progression or death) over time.

https://www.students4bestevidence.net/tutorial-hazard-ratios/

Hellman, MD et al. Nivolumab plus Ipilimumab in Lung Cancer with a High Tumor Mutational Burden. *NEJM*. 2018;378:2093-2104. DOI: 10.1056/NEJMoa1801946

Cheat Sheet: Forest Plot

› Read the title

› Look to see if dots are more to the left or right

› Check the subgroups to see what they are

› Look to see which subgroups have dots that are outliers

Adverse Events
summarizes side effects by type, severity, number affected

Table 3. Treatment-Related Adverse Events Reported in at Least 10% of Patients Treated with Nivolumab plus Ipilimumab, Nivolumab, or Chemotherapy.*

Event	Nivolumab plus Ipilimumab (N=576)		Nivolumab (N=391)		Chemotherapy (N=570)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
			number of patients (percent)			
Any event	433 (75.2)	180 (31.2)	251 (64.2)	74 (18.9)	460 (80.7)	206 (36.1)
Any serious event	138 (24.0)	102 (17.7)	42 (10.7)	30 (7.7)	79 (13.9)	61 (10.7)
Any event leading to discontinuation†	100 (17.4)	69 (12.0)	45 (11.5)	27 (6.9)	51 (8.9)	28 (4.9)
Rash	96 (16.7)	9 (1.6)	43 (11.0)	3 (0.8)	29 (5.1)	0
Diarrhea	94 (16.3)	9 (1.6)	44 (11.3)	3 (0.8)	55 (9.6)	4 (0.7)
Pruritus	81 (14.1)	3 (0.5)	30 (7.7)	0	5 (0.9)	0
Fatigue	76 (13.2)	8 (1.4)	43 (11.0)	2 (0.5)	105 (18.4)	8 (1.4)
Decreased appetite	73 (12.7)	3 (0.5)	25 (6.4)	0	110 (19.3)	6 (1.1)
Hypothyroidism	67 (11.6)	2 (0.3)	25 (6.4)	1 (0.3)	0	0
Asthenia	56 (9.7)	7 (1.2)	29 (7.4)	2 (0.5)	72 (12.6)	5 (0.9)
Nausea	56 (9.7)	3 (0.5)	21 (5.4)	1 (0.3)	205 (36.0)	12 (2.1)
Vomiting	27 (4.7)	2 (0.3)	10 (2.6)	1 (0.3)	76 (13.3)	13 (2.3)
Constipation	23 (4.0)	0	6 (1.5)	0	86 (15.1)	2 (0.4)
Anemia	23 (4.0)	9 (1.6)	11 (2.8)	2 (0.5)	183 (32.1)	64 (11.2)
Neutrophil count decreased	4 (0.7)	0	0	0	64 (11.2)	36 (6.3)
Neutropenia	1 (0.2)	0	1 (0.3)	0	97 (17.0)	54 (9.5)

* Data are based on a January 24, 2018, database lock. Safety analyses included all the patients who received at least one dose of a trial drug. Included are events reported from the time of the first dose of a trial drug to 30 days after the last dose, as determined by the investigator.
† For nivolumab plus ipilimumab, these events include treatment-related adverse events leading to discontinuation of ipilimumab or both trial drugs; patients could not discontinue nivolumab without discontinuing ipilimumab.

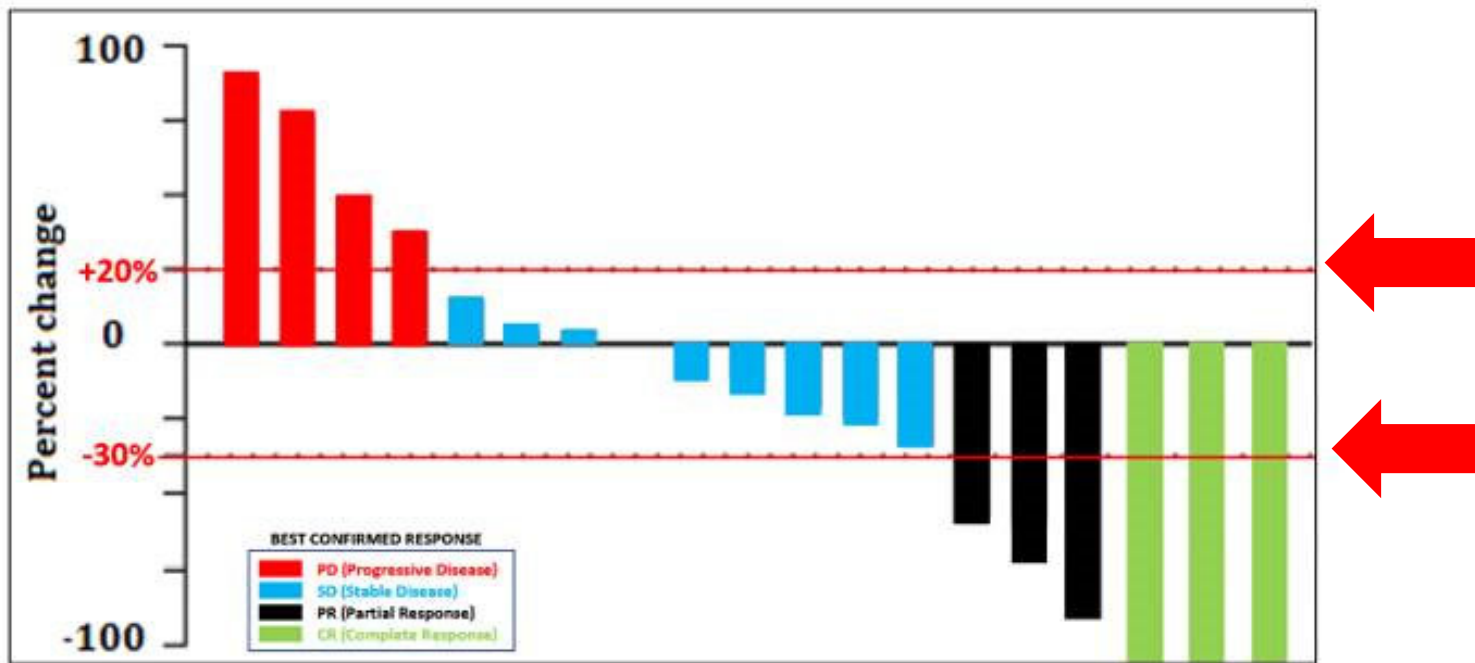Even when plots show the drug is effective, it might not be the best option

RECIST Criteria
defines the patient's response to a drug

› **Complete Response (CR)**
Disappearance of all target lesions

› **Partial Response (PR)**
At least a 30% decrease in the sum of the LD of target lesions

› **Stable Disease (SD)**
Target lesions change in size between a 20% increase and a 30% decrease

› **Progressive Disease (PD)**
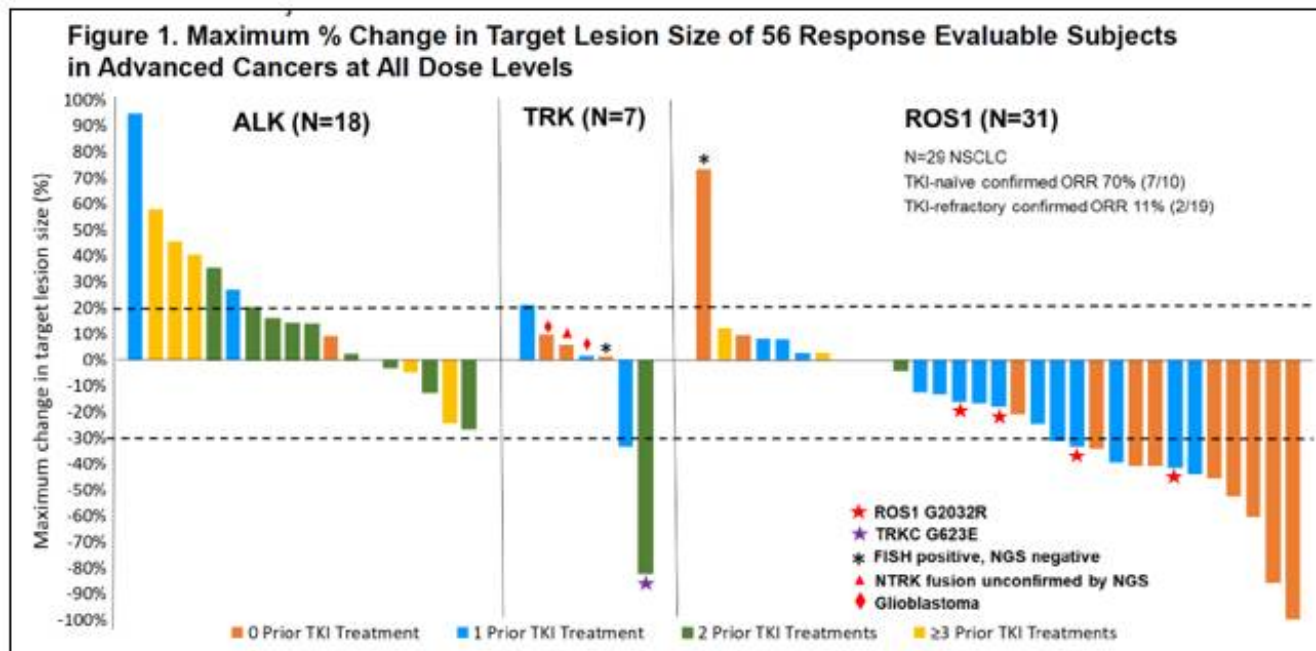At least a 20% increase in a target lesion OR the occurrence of a new lesion

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Waterfall Plot
best change in tumor size for individual participants

Waterfall Plot
best change in tumor size for individual participants

Figure 1. Maximum % Change in Target Lesion Size of 56 Response Evaluable Subjects in Advanced Cancers at All Dose Levels

Drilon A, et al. A Phase 1 Study of the Next-Generation ALK/ROS1/TRK Inhibitor Ropotrectinib (TPX-0005) in Patients with Advanced ALK/ROS1/NTRK+ Cancers (TRIDENT-1). Presented at ASCO 2018.
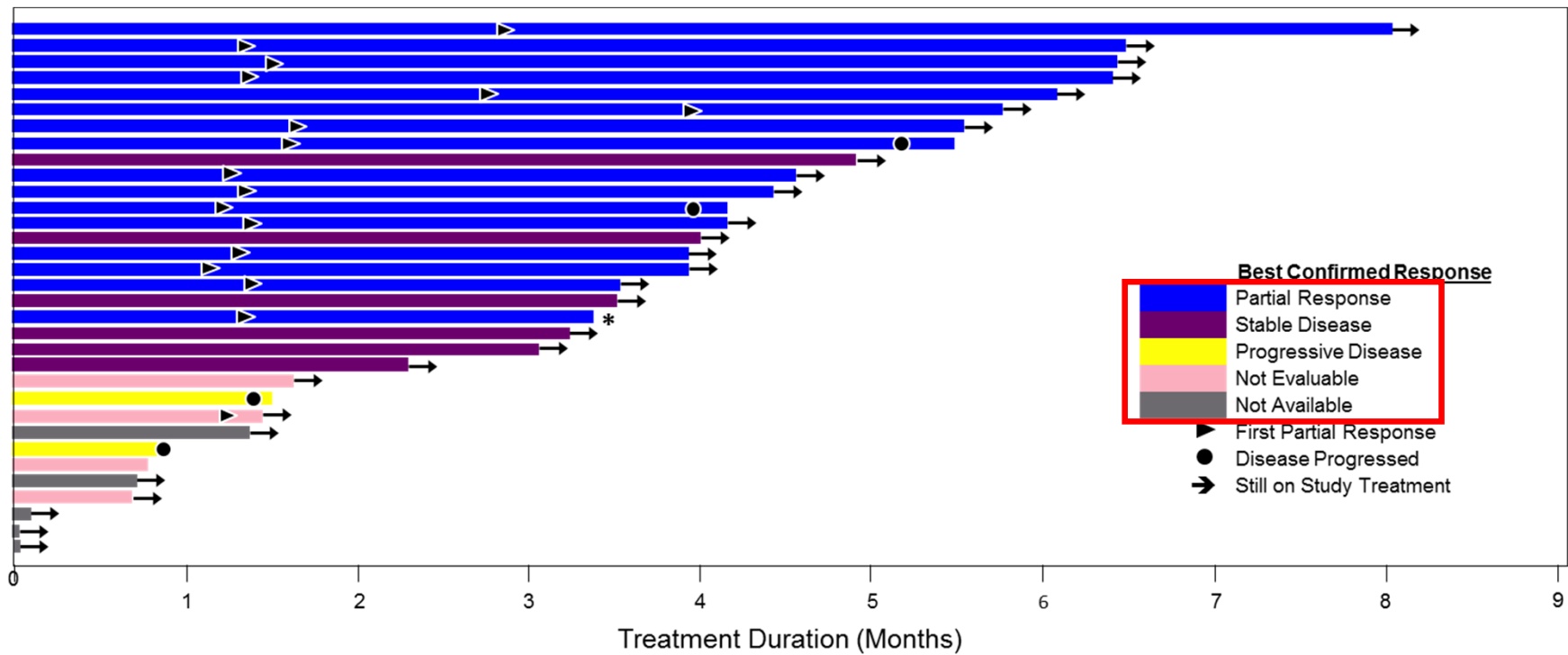
Cheat Sheet: Waterfall Plot

› Read the title

› Look to see if there are more bars pointing up or down

› Look for CR (bars at -100%)

› Look to see how many lines fall above, in the middle, and below the dashed horizontal lines
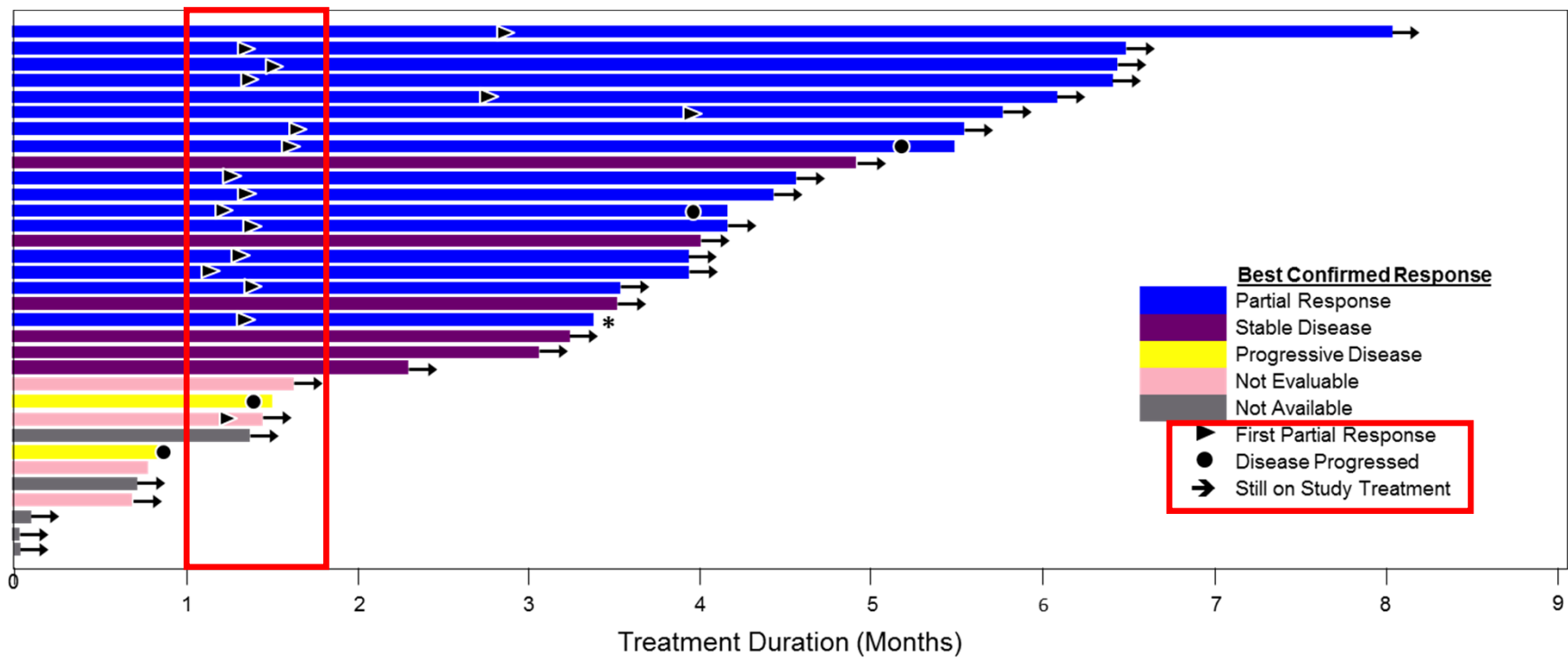
› Read the legend to understand the color coding

Swimmer Plot
duration and type of response for individual participants

Best Confirmed Response
- Partial Response
- Stable Disease
- Progressive Disease
- Not Evaluable
- Not Available
- ▶ First Partial Response
- ● Disease Progressed
- ➔ Still on Study Treatment

Treatment Duration (Months)

Swimmer Plot
duration and type of response for individual participants

Best Confirmed Response
- Partial Response
- Stable Disease
- Progressive Disease
- Not Evaluable
- Not Available

▶ First Partial Response
● Disease Progressed
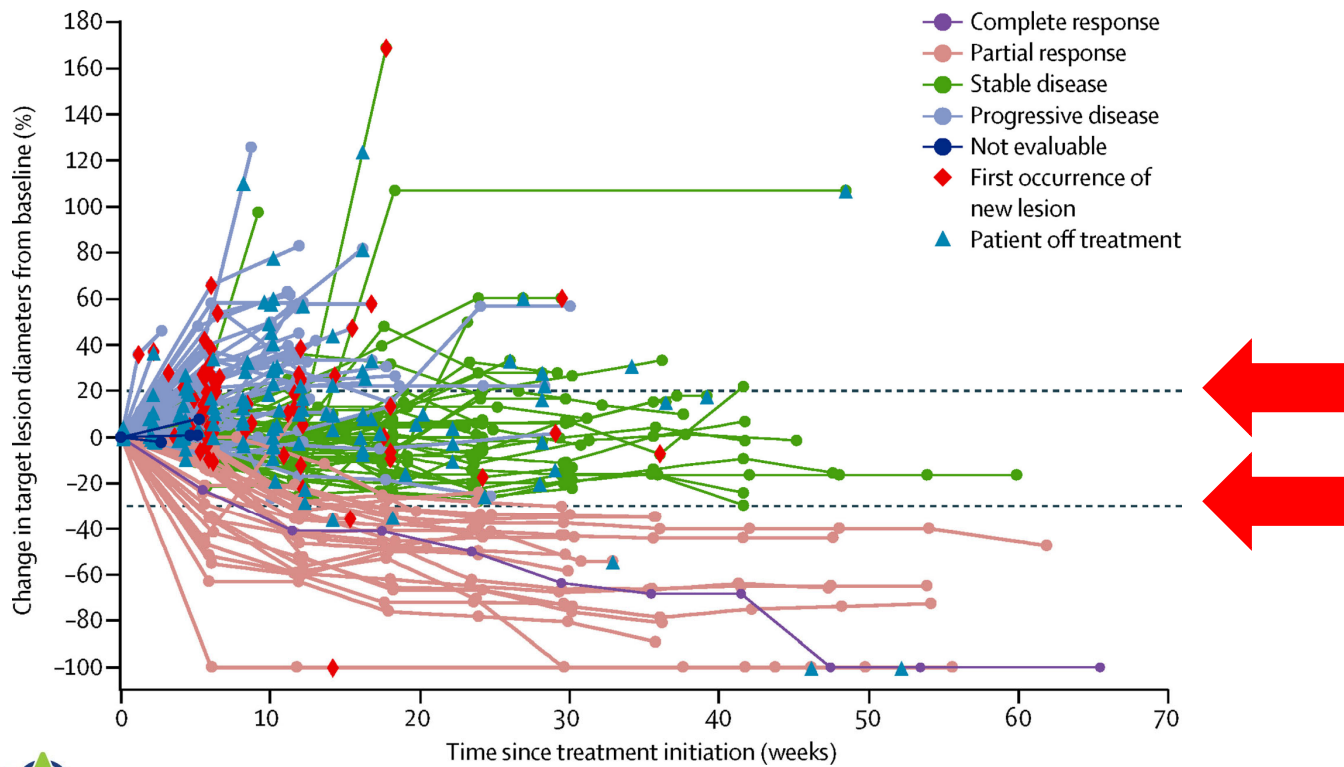➜ Still on Study Treatment

Treatment Duration (Months)

Cheat Sheet: Swimmer Plot

› See how long the bars are

› See if CR is listed in the legend

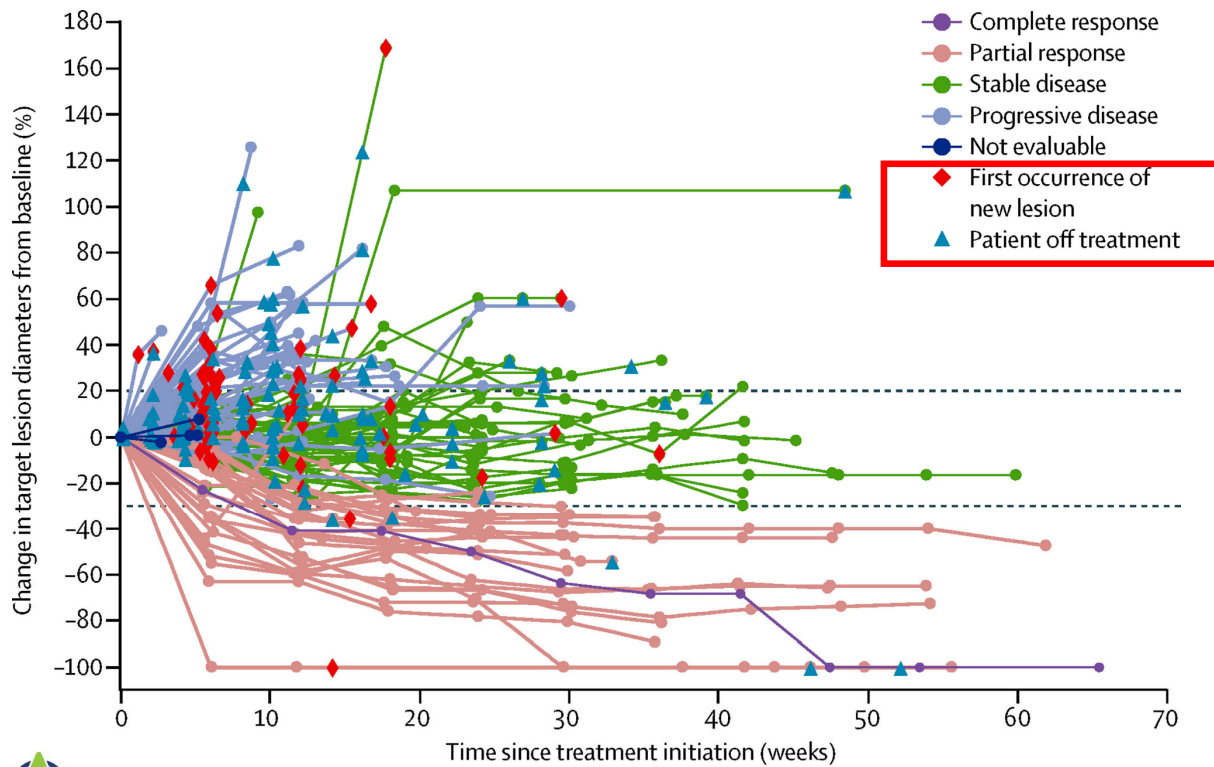› Read the legend to understand the color coding and symbols

Spider Plot
change in tumors over time for individual participants

Spider Plot
change in tumors over time for individual participants

Cheat Sheet: Spider Plot

› Look to see how many lines fall above, in the middle, and below the dashed horizontal lines

› Look for CR (lines at -100%)

› Read the legend to understand the color coding and symbols