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

A 2021 IASLC STARS Webinar
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

Begin Trial

Begin Enrollment

Start up period 6 months

Accrual period 2 years

Calendar (Secular) Time

End Enrollment

End Trial

End data collection

Data analysis 6 months

Clinical Trial Overview

doi:10.1016/j.otohns.2010.05.007
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
Survival Curve or Kaplan-Meier (KM) Curve survival over time for the entire group of trial participants

https://oncologypro.esmo.org/content/download/72962/1300141/file/Tips-Tricks-Understanding-Clinical-Trials-Statistics.pdf
Survival Curve or KM Curve
PFS over time for the entire group of trial participants

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

When the lines are very close together, one treatment is not better than the other

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

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Nivolumab plus Ipilimumab</th>
<th>Chemotherapy</th>
<th>Unstratified Hazard Ratio for Disease Progression or Death (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>139</td>
<td>160</td>
<td>0.58 (0.43–0.77)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 yr</td>
<td>73</td>
<td>83</td>
<td>0.51 (0.34–0.77)</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>66</td>
<td>77</td>
<td>0.62 (0.40–0.97)</td>
</tr>
<tr>
<td>≥75 yr</td>
<td>13</td>
<td>14</td>
<td>0.42 (0.14–1.30)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>98</td>
<td>106</td>
<td>0.57 (0.36–0.74)</td>
</tr>
<tr>
<td>Female</td>
<td>41</td>
<td>54</td>
<td>0.70 (0.41–1.20)</td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>North America</td>
<td>14</td>
<td>16</td>
<td>0.46 (0.17–1.30)</td>
</tr>
<tr>
<td>Europe</td>
<td>77</td>
<td>87</td>
<td>0.53 (0.36–0.79)</td>
</tr>
<tr>
<td>Asia</td>
<td>21</td>
<td>32</td>
<td>0.34 (0.15–0.75)</td>
</tr>
<tr>
<td>Rest of world</td>
<td>27</td>
<td>25</td>
<td>1.20 (0.61–2.36)</td>
</tr>
<tr>
<td>ECOG performance-status score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>56</td>
<td>49</td>
<td>0.62 (0.38–1.02)</td>
</tr>
<tr>
<td>1</td>
<td>82</td>
<td>110</td>
<td>0.55 (0.38–0.80)</td>
</tr>
<tr>
<td>Tumor histologic type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous</td>
<td>44</td>
<td>56</td>
<td>0.63 (0.39–1.04)</td>
</tr>
<tr>
<td>Non-squamous</td>
<td>95</td>
<td>104</td>
<td>0.55 (0.38–0.80)</td>
</tr>
<tr>
<td>Current or former smoker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD-L1 expression level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1%</td>
<td>38</td>
<td>48</td>
<td>0.48 (0.27–0.85)</td>
</tr>
<tr>
<td>≥1%</td>
<td>101</td>
<td>112</td>
<td>0.62 (0.44–0.88)</td>
</tr>
</tbody>
</table>

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/](https://www.students4bestevidence.net/tutorial-hazard-ratios/)

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

<table>
<thead>
<tr>
<th>Event</th>
<th>Nivolumab plus Ipilimumab (N = 576)</th>
<th>Nivolumab (N = 391)</th>
<th>Chemotherapy (N = 570)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any Grade</td>
<td>Grade 3 or 4</td>
<td>Any Grade</td>
</tr>
<tr>
<td>Any event</td>
<td>413 (75.2)</td>
<td>180 (31.2)</td>
<td>251 (64.2)</td>
</tr>
<tr>
<td>Any serious event</td>
<td>118 (20.0)</td>
<td>102 (17.7)</td>
<td>42 (10.7)</td>
</tr>
<tr>
<td>Any event leading to discontinuation(^\d)</td>
<td>100 (17.4)</td>
<td>69 (12.0)</td>
<td>45 (11.5)</td>
</tr>
<tr>
<td>Rash</td>
<td>96 (16.7)</td>
<td>9 (1.6)</td>
<td>43 (11.0)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>94 (16.3)</td>
<td>9 (1.6)</td>
<td>44 (11.3)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>81 (14.1)</td>
<td>3 (0.5)</td>
<td>30 (7.7)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>76 (13.2)</td>
<td>8 (1.4)</td>
<td>43 (11.0)</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>73 (12.7)</td>
<td>3 (0.5)</td>
<td>25 (6.4)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>67 (11.6)</td>
<td>2 (0.3)</td>
<td>25 (6.4)</td>
</tr>
<tr>
<td>Asthenia</td>
<td>56 (9.7)</td>
<td>7 (1.2)</td>
<td>29 (7.4)</td>
</tr>
<tr>
<td>Nausea</td>
<td>56 (9.7)</td>
<td>3 (0.5)</td>
<td>21 (5.4)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>27 (4.7)</td>
<td>2 (0.3)</td>
<td>10 (2.6)</td>
</tr>
<tr>
<td>Constipation</td>
<td>23 (4.0)</td>
<td>0</td>
<td>6 (1.5)</td>
</tr>
<tr>
<td>Anemia</td>
<td>23 (4.0)</td>
<td>9 (1.6)</td>
<td>11 (2.8)</td>
</tr>
<tr>
<td>Neutrophil count decreased</td>
<td>4 (0.7)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>1 (0.2)</td>
<td>0</td>
<td>1 (0.3)</td>
</tr>
</tbody>
</table>

\(^\d\) 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.

\(\d\) 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
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

ALK (N=18)
- N=26 NSCLC
- TKI-naïve confirmed ORR 70% (7/10)
- TKI-refractory confirmed ORR 11% (2/19)

TRK (N=7)
- ROS1 (N=31)
- ROS1 G2032R
- TRKC G623E
- FISH positive, NGS negative
- NTRK fusion unconfirmed by NGS
- Glioblastoma

0 Prior TKI Treatment 1 Prior TKI Treatment 2 Prior TKI Treatments 3 Prior TKI Treatments

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
Swimmer Plot
duration and type of response for individual participants
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