



Drug exposure plot

Tailored approach to display ongoing data

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A tailored approach to display ongoing data

- **Tailored approach:** adapted specifically to address dose escalation trial needs
- **Display:** graphical representation with condensed information
- **ongoing data:** ability to produce reports based on recently captured data to assess drug impact on patients

Clinical questions / needs



How long does a patient stay on study?

How often a dose interruption and/or a dose change occur?

What is the effect of a dose reduction on the efficacy response?

Is Patient discontinued?

Occurrence of serious adverse event related to a specific dose level?

Clinical questions / needs



How long does a patient stay on study?

How often a dose interruption and/or a dose change occur?

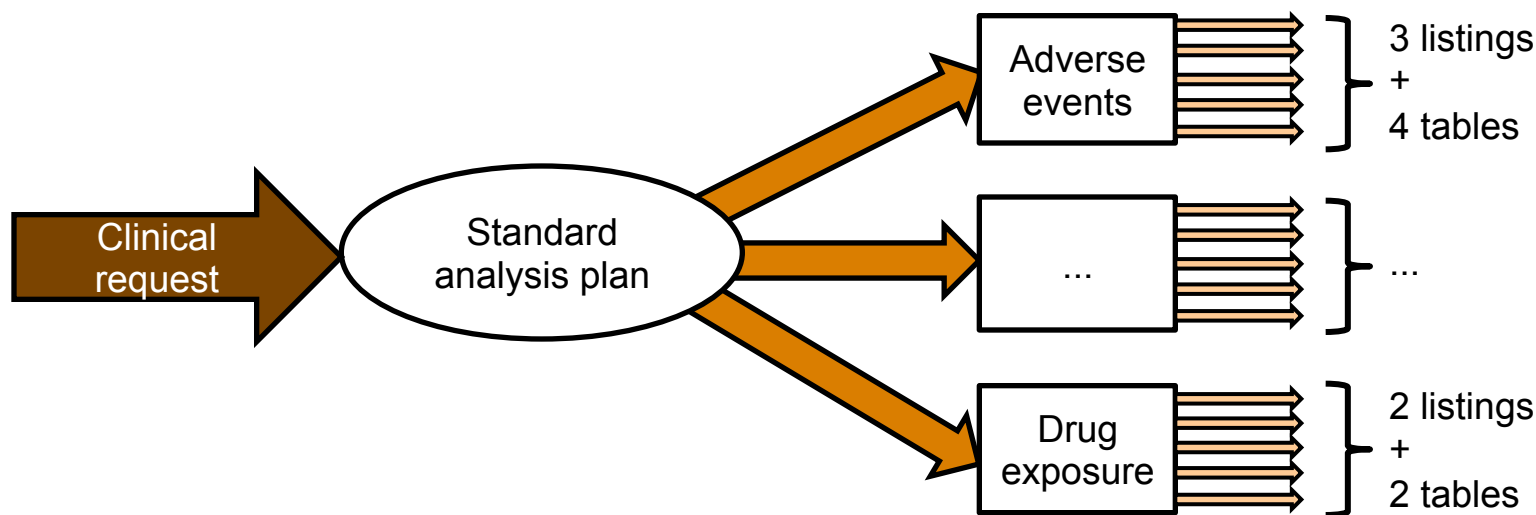
What is the effect of a dose reduction on the efficacy response?

Is Patient discontinued?

Occurrence of serious adverse event related to a specific dose level?

Usual / Standard Approach

- E.g. Relationship between the occurrence of serious adverse event and a specific dose level



- Content and purpose of initial request are spread
 - Need to work with several outputs
 - No cross analysis

Prioritize...



How long does a patient stay on study?

How often a dose interruption and/or a dose change occur?

What is the effect of a dose reduction on the efficacy response?

Is Patient discontinued?

Occurrence of serious adverse event related to a specific dose level?

Prioritize...



How long does a patient stay on study?

How often a dose interruption and/or a dose change occur?

What is the effect of a dose reduction on the efficacy response?

Primary area of interest:
Display the drug information

Is Patient discontinued?

Occurrence of serious adverse event related to a specific dose level?

... and investigate further

How long does a patient stay on study?

How often a dose interruption and/or a dose change occur?

What is the effect of a dose reduction on the efficacy response?

Secondary area of interest:
Additional cross analysis

Occurrence of serious adverse event related to a specific dose level?

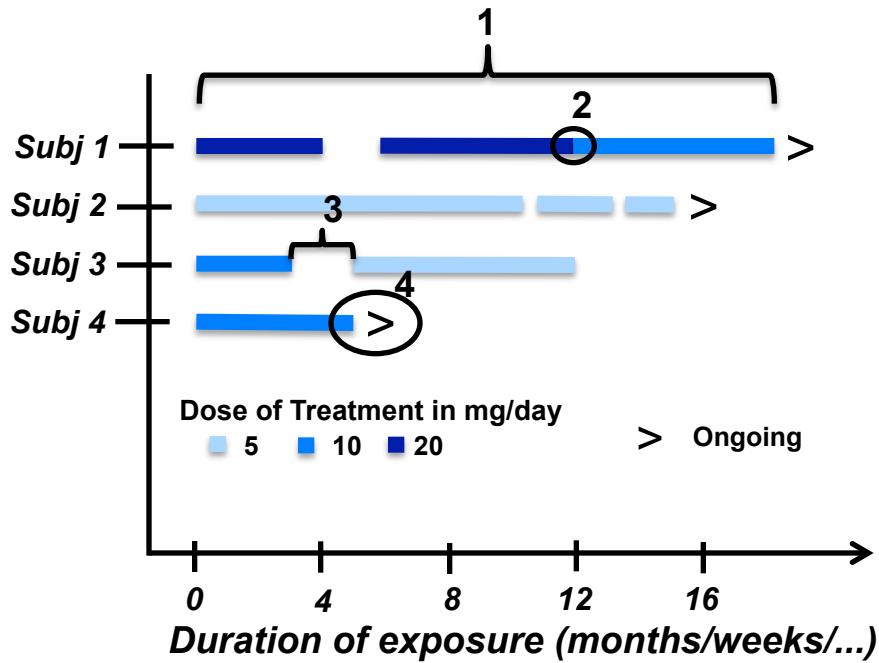


- Need to know exactly what the patient receives effectively.
- Visualize data, patient by patient
- Display exposure, drug intake level, as well as AE at risk or efficacy responses

Drug exposure plot :

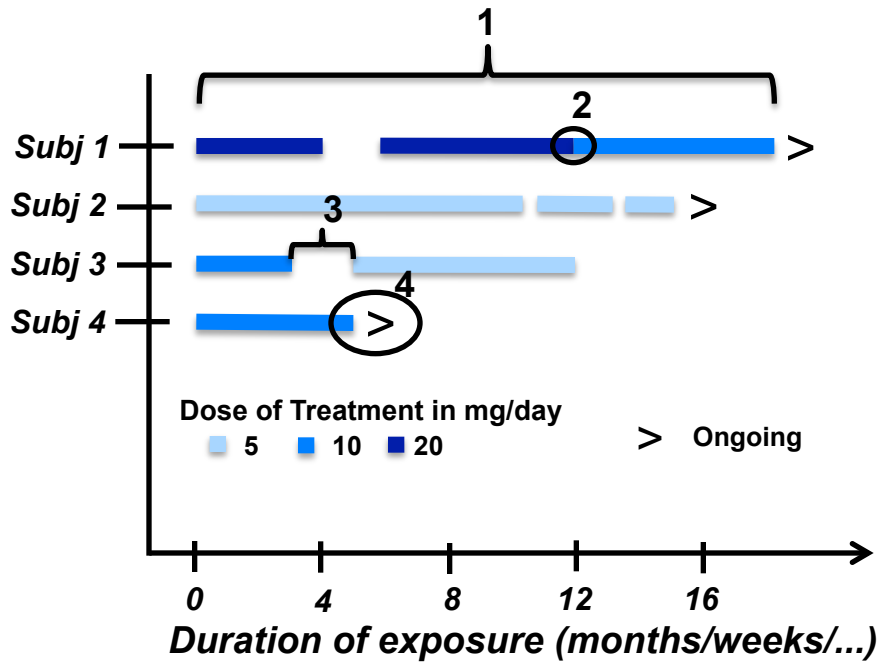
**A tailored plot that could be interpreted at a glance
and help clinicians to find areas of investigation
in order to help for decision**

- **Primary area of interest: Drug information**



- 1) Total exposure
 - Duration
 - Actual dose intake
- 2) Dose change
 - When?
 - # of occurrence?
 - Increase/decrease?
- 3) Dose interruption
 - When?
 - # of occurrence?
 - Duration?
- 4) Subject ongoing/discontinued

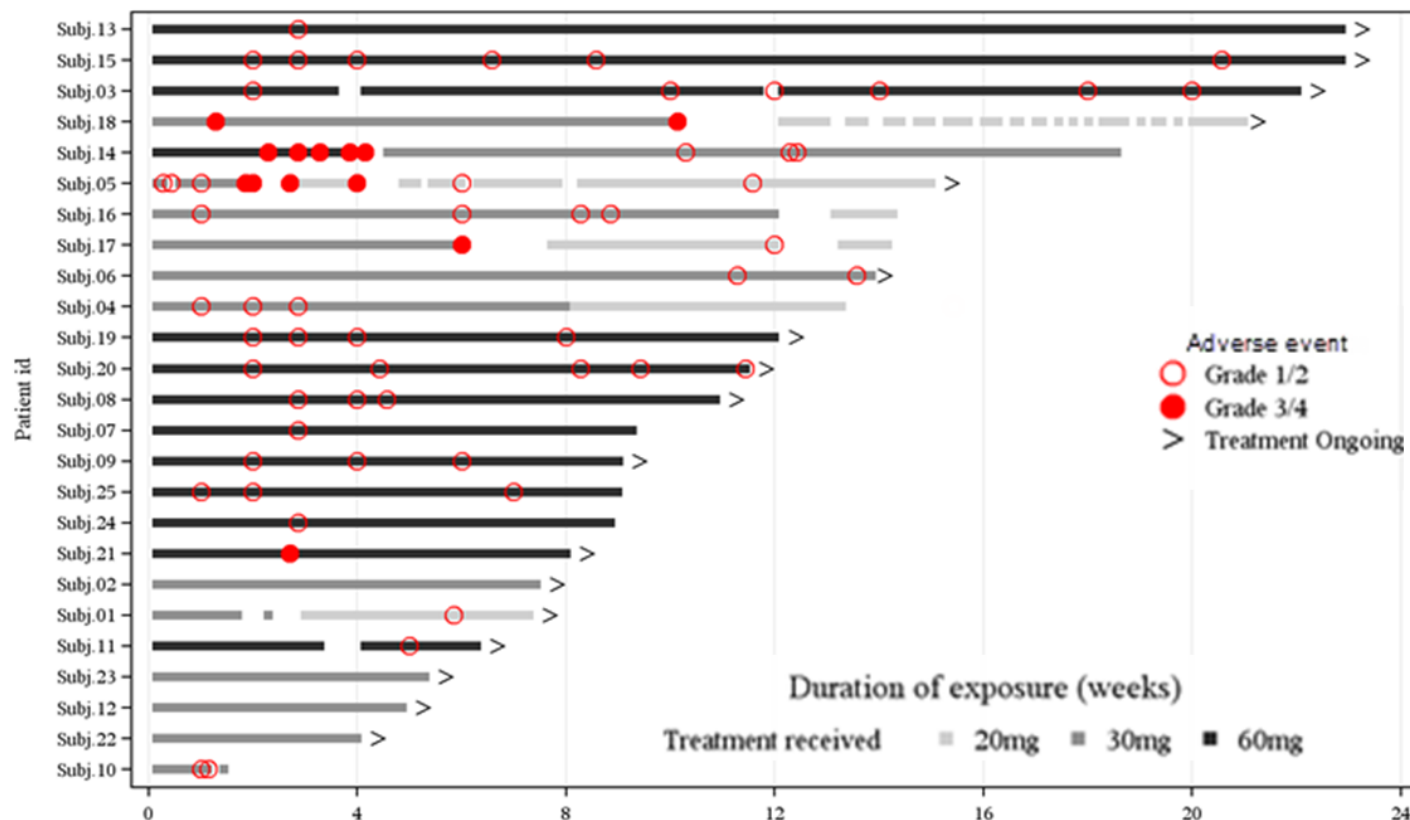
- **Primary area of interest: Drug information**



- 1) Total exposure
 - Duration
 - Actual dose intake
- 2) Dose change
 - When?
 - # of occurrence?
 - Increase/decrease?
- 3) Dose interruption
 - When?
 - # of occurrence?
 - Duration?
- 4) Subject ongoing/discontinued

Exposure plot: Additional events

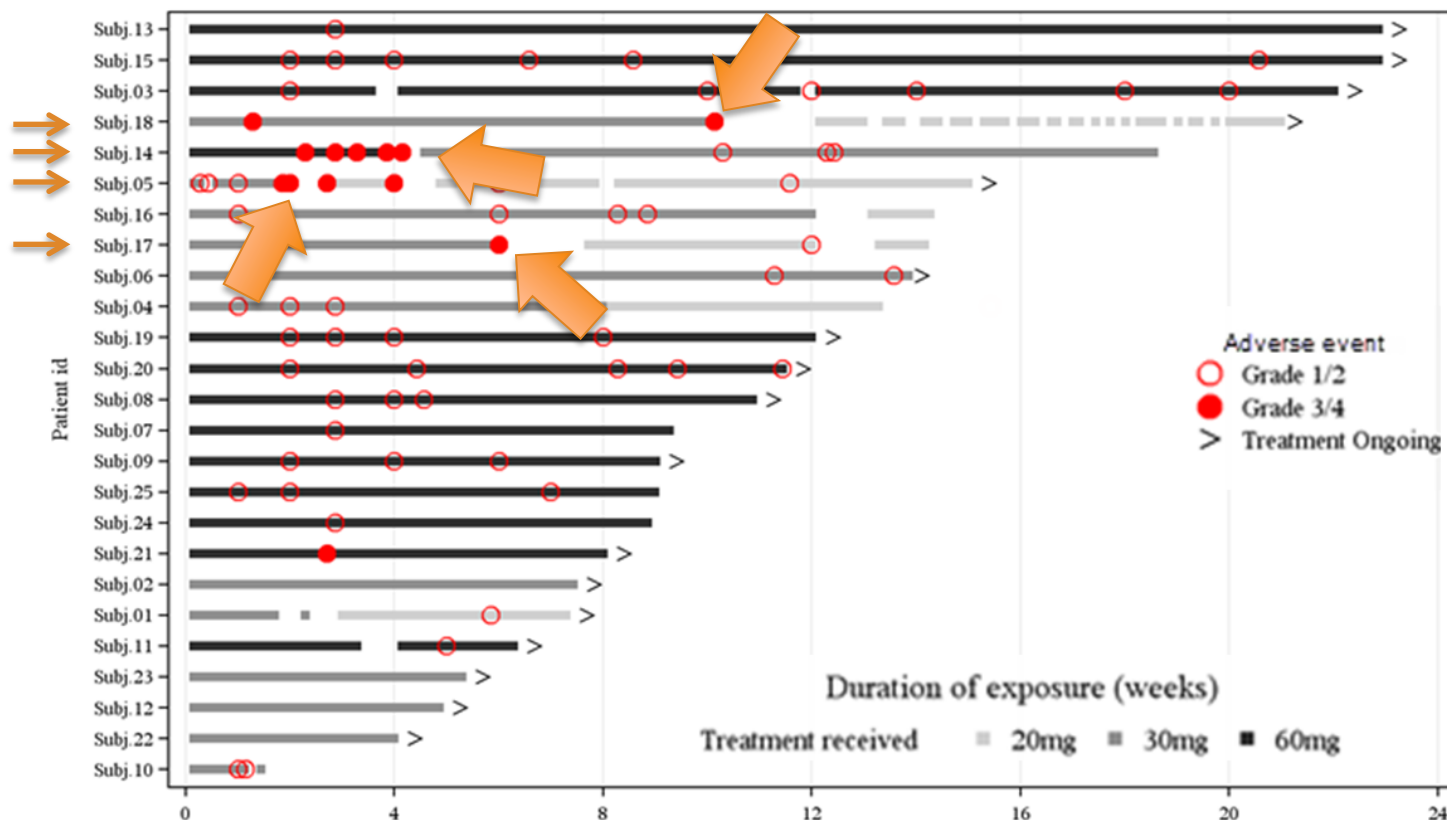
■ Safety: Drug exposure and adverse event by 'severity grade'



Grade 3/4 adverse event usually lead to a dose change and/or interruption

Exposure plot: Additional events

- **Safety: Drug exposure and adverse event by 'severity grade'**



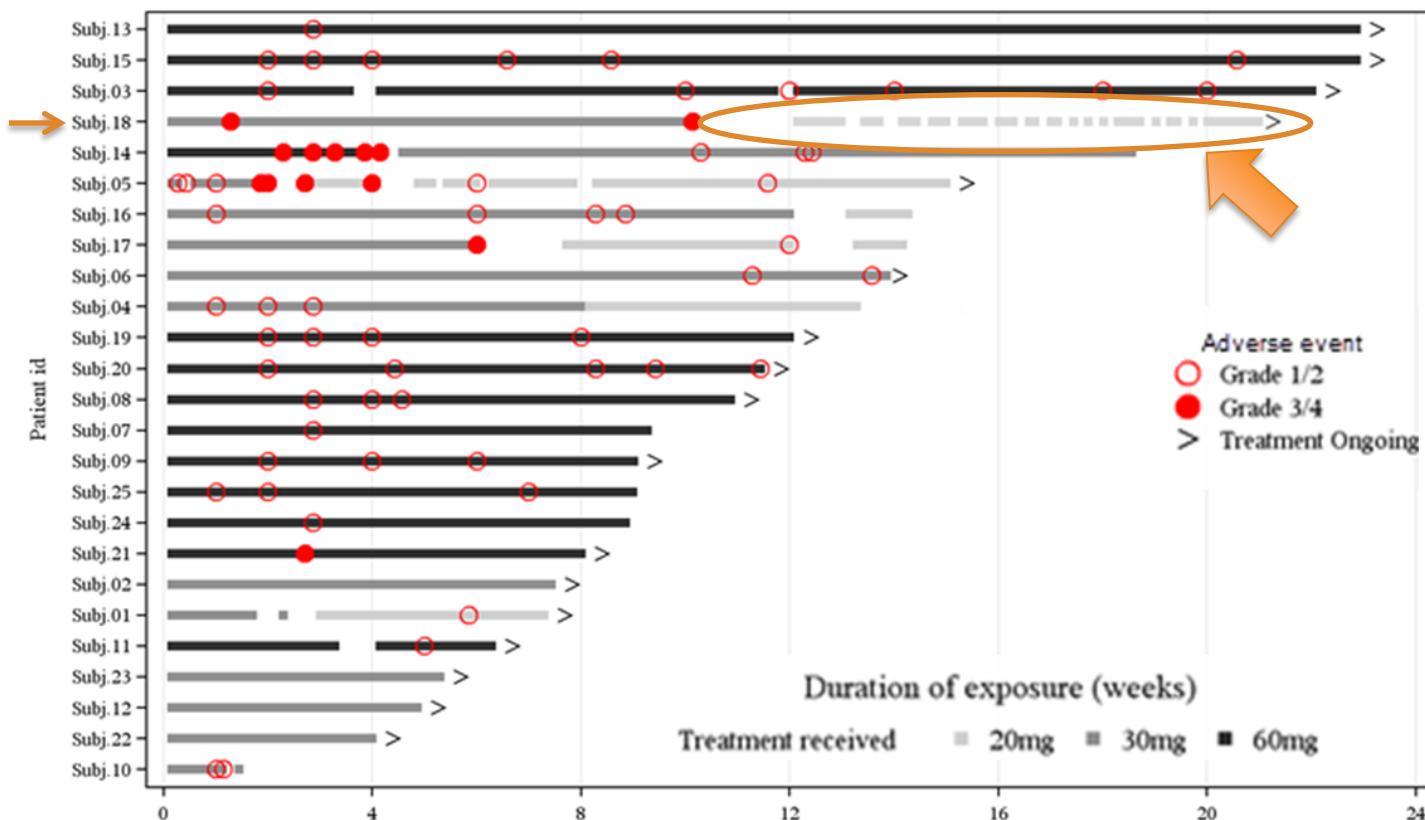
- **Subjects 18, 14, 05, 17: grade 3/4 adverse events leading to a dose decrease**

- **Potential protocol deviation:** Subjects 18 and 21 have a grade 3/4 adverse event with no dose change



Exposure plot: Additional events

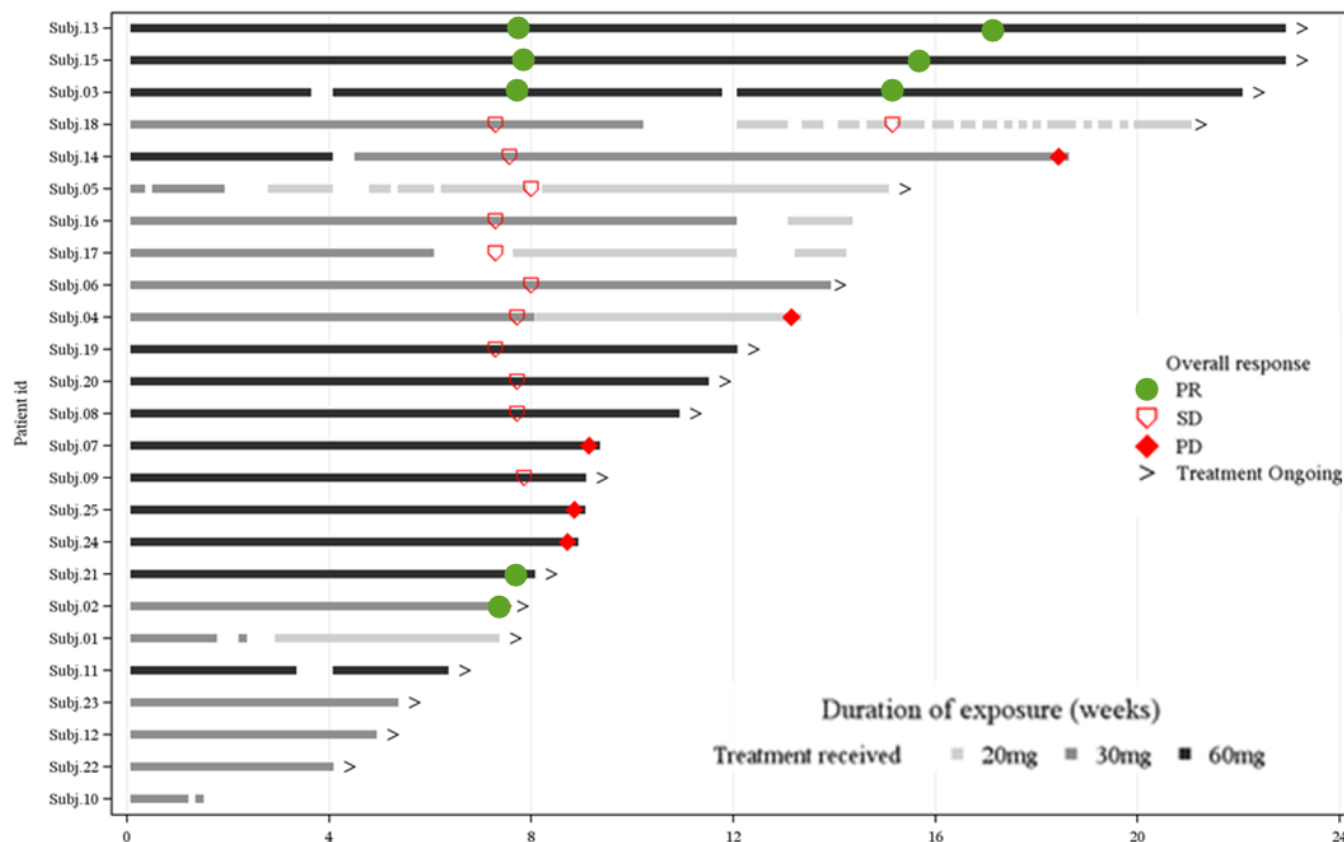
- **Safety: Drug exposure and adverse event by 'severity grade'**



- **Potential data issue: Subject 18 has a significant number of interruptions**

Exposure plot: Additional events

■ Efficacy: Drug exposure and RECIST overall response

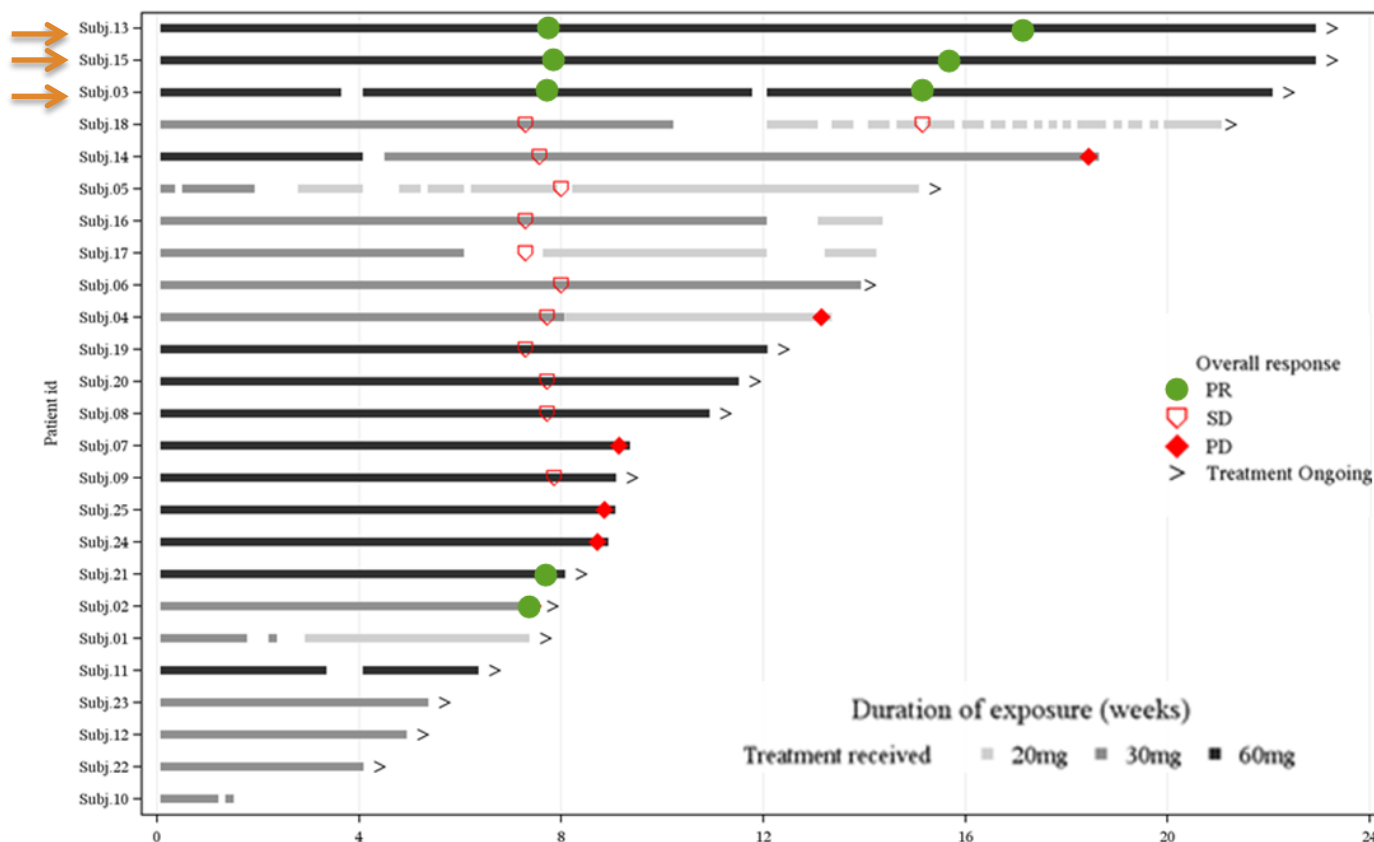


Response Evaluation Criteria In Solid Tumors:

- Complete response (CR) > Partial Response (PR) > Stable Disease (SD) > Progressive Disease (PD)
- One assessment every 8 weeks
- Progressive disease leads to a discontinuation

Exposure plot: Additional events

■ Efficacy: Drug exposure and RECIST overall response

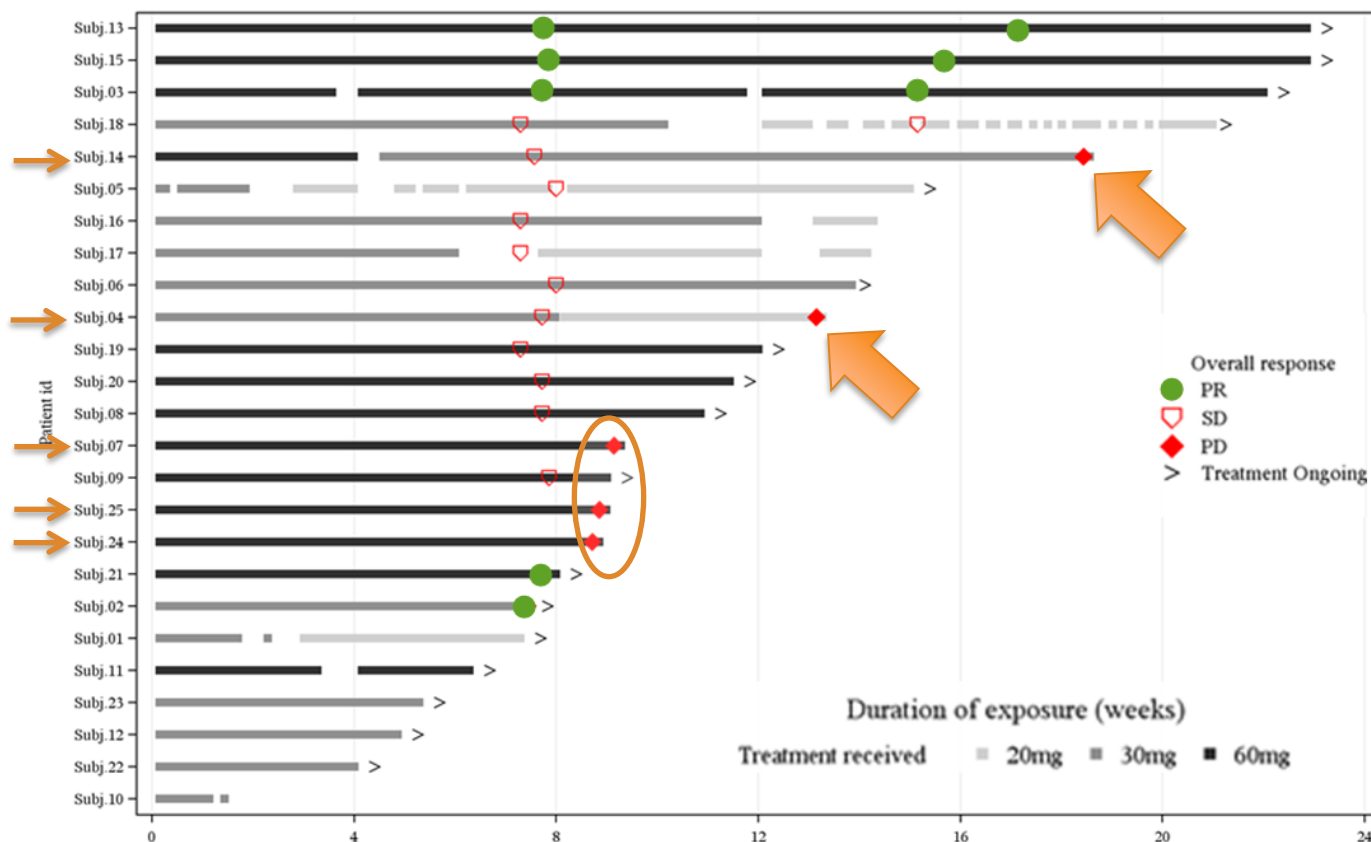


First efficacy interpretations: Subjects 13, 15, 03 have the longest exposure + PR

➤ potential effect at 60 mg on efficacy responses

Exposure plot: Additional events

■ Efficacy: Drug exposure and RECIST overall response



Potential protocol deviation: Subjects 14 and 04 not assessed at week 16

Subject 07, 25 and 24: Discontinue after a PD



■ **SG plot procedure:**

- Easier for those who are not familiar with GTL
- GTL code of SG plot can be generated by the option TMPLOUT if needed

■ **SG plot statement : Series or Histogram?**

- Draw a continuous line or bar
- Unique colour per subject
- Not tailored to display interruption and dose change

■ **Scatter (succession of dots = a bar)**



- Draw a dot whenever a subject is exposed to a treatment drug
- Color of dot is controlled by the dose level



■ SG plot procedure:

```
Proc sgplot data = input-dataset;
```

Drug exposure

```
Scatter Y= Subject ID X= Duration for dose level 1
      /Markerattrs=(symbol=squarefilled size=5 color=color1) legendlabel="Dose level label 1" name="trt1";
Scatter Y= Subject ID X= Duration for dose level 2
      /Markerattrs=(symbol=squarefilled size=5 color=color2) legendlabel="Dose level label 2" name="trt2";
```

Additional events

```
Scatter Y= Subject ID X=Secondary category1
      / Markerattrs=(symbol=symbol1 size=9 color=red) legendlabel="Category label1" name="cat1";
Scatter Y= Subject ID X=Secondary category2
      / Markerattrs=(symbol=symbol2 size=9 color=red) legendlabel="Category label2" name="cat2";
```

Ongoing flag

```
Scatter Y= Subject ID X=Ongoing variable
      /Markerattrs =(symbol=greaterthan size=7 color=black) legendlabel="Treatment Ongoing" name="ong";
```

Legend part

```
Keylegend "trt1" "trt2" ... /location=outside position=bottom noborder title="Treatment received" titleattrs=(size=7)
valueattrs=(size=7);
Keylegend "cat1" "cat2" ... "ong" /location=inside position=right noborder title="category label" titleattrs=(size=7)
valueattrs=(size=7);
```

```
Xaxis statement;
Yaxis statement;
```

```
run;
```



- **Exposure plot shows:**

- Overall exposure and its events (interruption, dose change)
- Additional events (adverse event, efficacy outcomes, ...)
- Data trends

- **Clinical teams are using it for:**

- Internal and External presentations
- Data review
- Decision making

- **Flexible enough, it can be generated:**

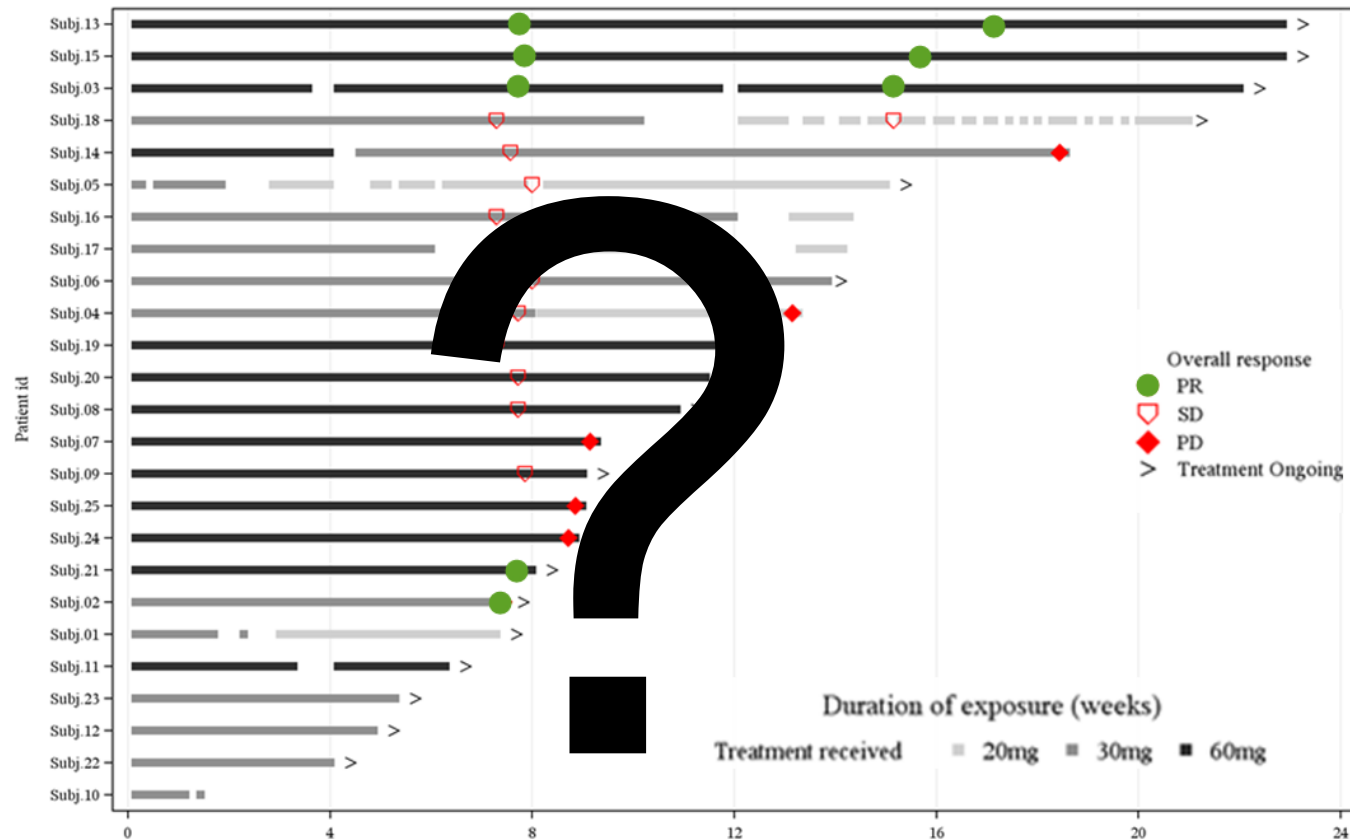
- For any type of study design
- For any combination of treatments
- With any type of event

One of our most popular and powerful graphs in early phase studies !

Thank you !



Any Questions



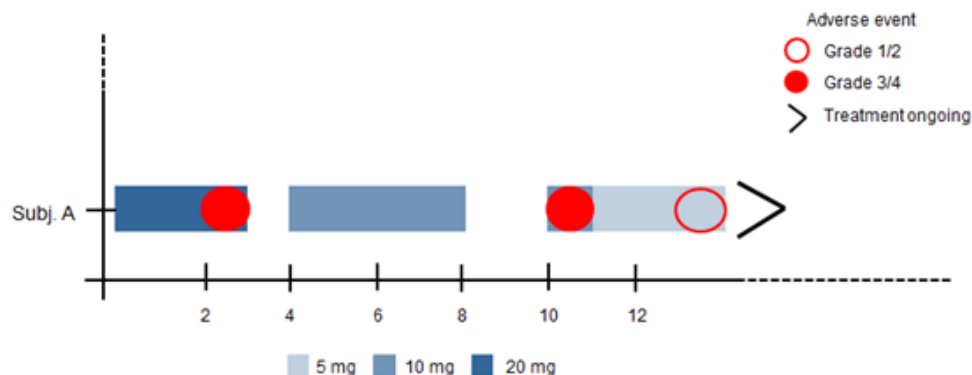
Back-up slide 1/3



Input dataset:

Subj_ID	Trt5	Trt10	Trt20	AE1	AE2	Ong
A			1			
A			2			
A			3			
A		5				
A		6				
A		7				
A		8				
A		11				
A	12					
A	13					
A	14					
A					3	
A					11	
A				14		
A						15

output:





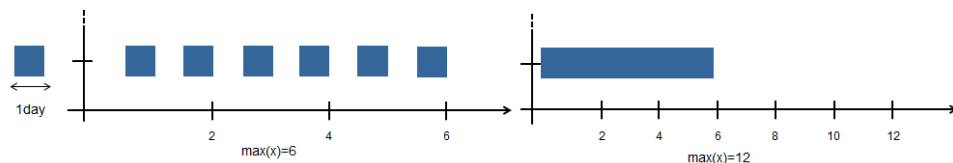
■ Procedure example:

```
Proc sgplot= final_input_dataset;
  Scatter Y= Subj_ID X= Trt5
    /Markerattrs=(symbol=squarefilled size=5 color=GREYE0) legendlabel="5 mg"
    name="doslvl1";
  Scatter Y= Subj_ID X= Trt10
    /Markerattrs=(symbol=squarefilled size=5 color=GREYA0) legendlabel="10 mg"
    name="doslvl2";
  Scatter Y= Subj_ID X= Trt20
    /Markerattrs=(symbol=squarefilled size=5 color= GREY50) legendlabel="20 mg"
    name=" doslvl3";
  Keylegend "doslvl1" "doslvl2" "doslvl3"
    /location=outside position=Top noborder titleattrs=(size=7) valueattrs=(size=7);

  Scatter Y= Subj_ID X= AE1
    /Markerattrs=(symbol=circlefilled size=9 color=RED) legendlabel="Grade 1/2"
    name="_ae1";
  Scatter Y= Subj_ID X= AE2
    /Markerattrs=(symbol=starfilled size=9 color=RED) legendlabel="Grade 3/4"
    name="_ae2";
  Scatter Y= Subj_ID X= Ong
    /Markerattrs=(symbol=greaterthan size=7 color=Black)
    legendlabel="Treatment ongoing" Name= "_Ong";
  Keylegend "_ae1" "_ae2" "_Ong"
    / location=inside position=right noborder title="Adverse event"
    titleattrs=(Size=7) valueattrs =(Size=7);
  /*Xaxis ...*/
  /*Yaxis ...*/
Run;
```



■ X axis control:



Max(x)=6



Max(x)=12

■ Y axis control:

- The size of the marker is set to a value (previous example size=5), from that we can determine the number max of subject ($\max(y)=25$).