

Abstract geometric lines in the top left corner, consisting of several thin, light brown lines that intersect to form various polygons and shapes, creating a modern, architectural feel.

VISUALIZING YOUR PROTOCOL OBJECTIVES

Varun Tripuraneni

DISCLAIMER

- This presentation is based on publicly available information (including data relating to non-Novartis products or approaches).
- The views presented are the views of the presenter, not necessarily those of Novartis.
- These slides are intended for educational purposes only and for the personal use of the audience.
- These slides are not intended for wider distribution outside the intended purpose without presenter's approval.
- The content of this slide deck is accurate to the best of the presenter's knowledge at the time of production.
- Data shown is purely created for this presentation and does not reflect any actual investigations.

AGENDA

STUDY DESIGNS

Complex study designs and endpoints

VISUAL AIDS

Impact of Figures vs Other modes of data representation

APPROACH

Transforming protocols objectives into graphical elements

CONCLUSION

The big picture !



STUDY DESIGNS

ADAPTIVE TRIALS

BASKET TRIALS

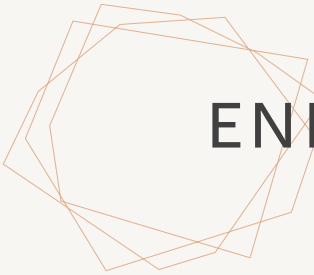
CLUSTER RANDOMISED TRIALS

SMART[#]

UMBRELLA TRIALS

and many more...

#Sequential Multiple Assignment Randomized Trials



END POINTS

BINARY

TIME TO EVENT

COMPOSITE

NET CLINICAL BENEFIT

HIERARCHICAL

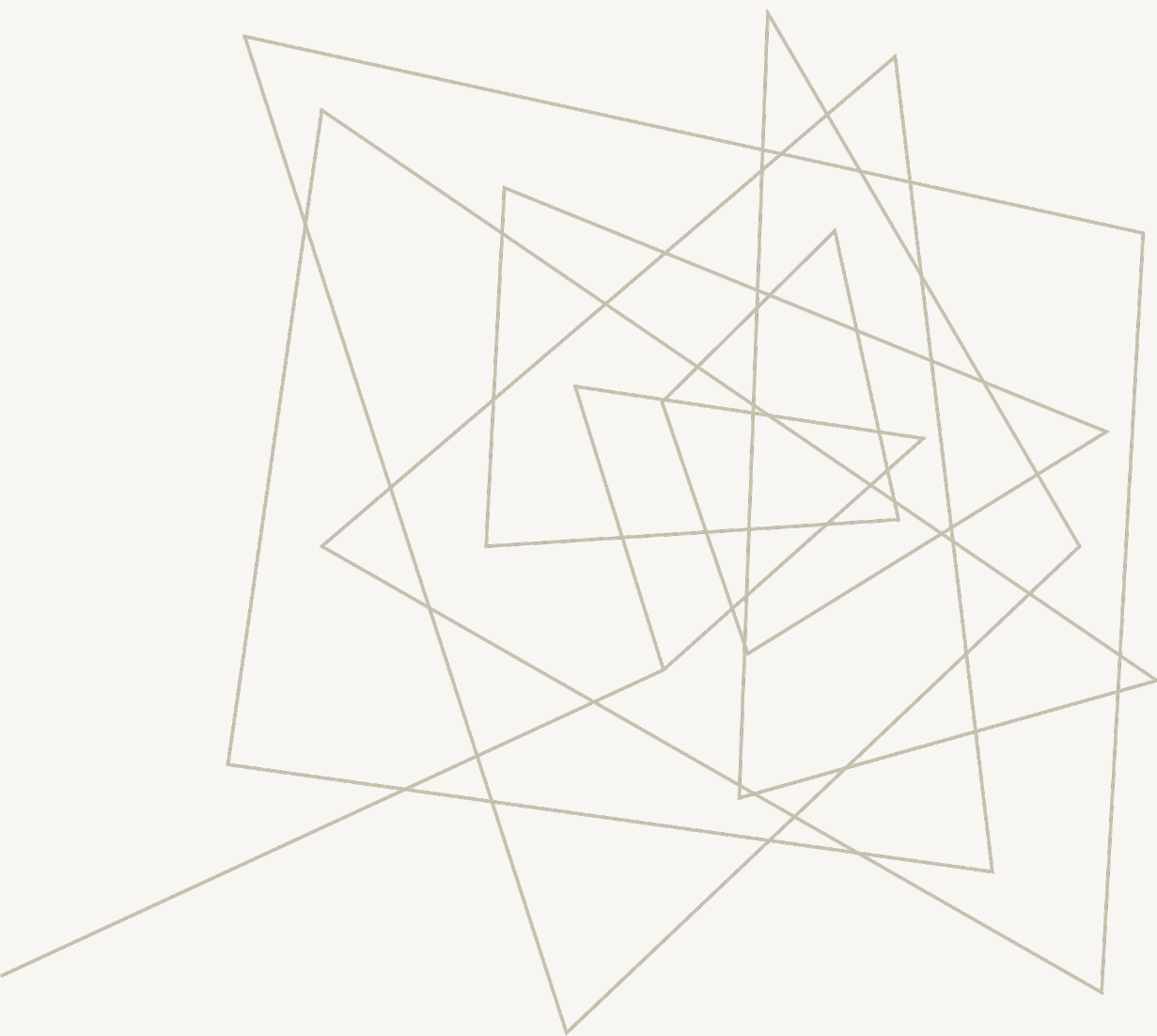
PRO[#]

LONGITUDINAL

#Patient Reported Outcome

WHY VISUAL ?

- COMPREHENSIVE
- STORYTELLING
- COMPARISON
- IMPACT
- EXPLORATION
- RELATIONSHIP
- AESTHETIC



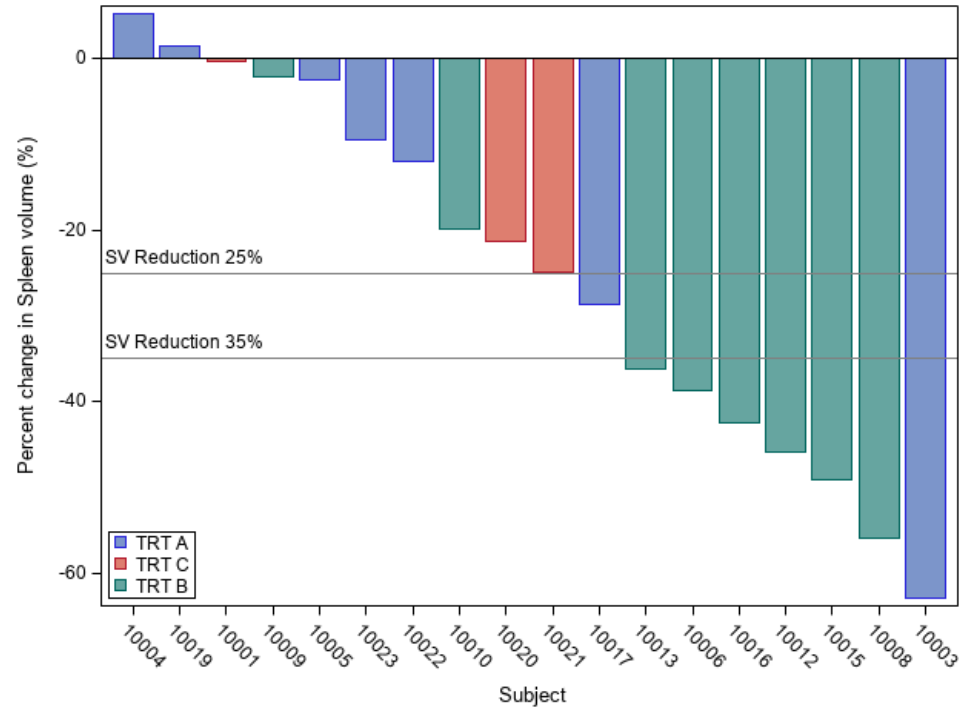
GRAPHICAL APPROACH TO THE PROTOCOL

SCENARIO - 1

Table 2-1 Objectives and related endpoints

Objective(s)	Endpoint(s)
Primary objective(s)	Endpoint(s) for primary objective(s)
To evaluate the efficacy of each combination treatment arm	Response rate for the composite endpoint (anemia improvement of ≥ 1.5 g/dL and no spleen volume progression and no symptom worsening) at the end of Cycle 6.
Secondary objective(s)	Endpoint(s) for secondary objective(s)
- To assess the proportion of subjects in each treatment arm who achieve an Hb improvement of ≥ 1.5 g/dL - To evaluate changes in symptoms in each treatment arm using patient reported outcomes (PROs) - To evaluate the changes in spleen size in each treatment arm	- Proportion of subjects achieving improvement of Hb level of ≥ 1.5 g/dL from baseline - Change in PRO scores from baseline - Change in spleen length from baseline. Change in spleen volume from baseline.

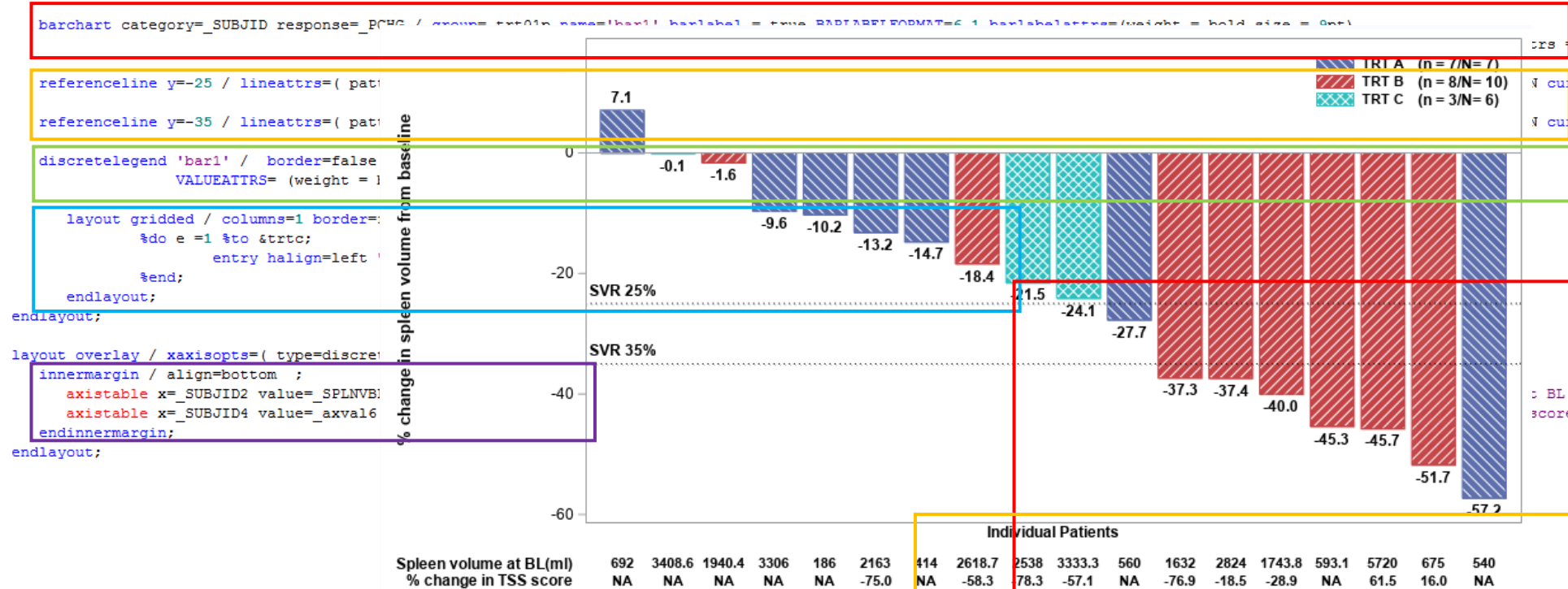
DATA REVIEW FOR THE GRAPH



	PARAMCD	AVAL	BASE	CHG	PCHG				
L)	SPLVOL	3400	3410	-10	-0.293255132				
L)	SPLVOL	200	540	-340	-62.96296296				
L)	SPLVOL	200	190	10	5.2631578947				
L)	SPLVOL	400	410	-10	-2.43902439				
L)	SPLVOL	1000	1630	-630	-38.65030675				
L)	SPLVOL	300	680	-380	-55.88235294				
L)									
L)	SUBJID	TRT01P	AVISIT	PARAM	PARAMCD	AVAL	BASE	CHG	PCHG
L)	10001	TRT C	Cycle 7 Day 1	MFSAF total symptom score (TSS)	TSS	2	2	0	0
L)	10002	TRT C	Cycle 7 Day 1	MFSAF total symptom score (TSS)	TSS	22	14	8	57.142857
L)	10006	TRT B	Cycle 7 Day 1	MFSAF total symptom score (TSS)	TSS	3	13	-10	-76.92308
L)	10007	TRT B	Cycle 7 Day 1	MFSAF total symptom score (TSS)	TSS	61	22	39	177.27273
L)	10008	TRT B	Cycle 7 Day 1	MFSAF total symptom score (TSS)	TSS	29	25	4	16
L)	10009	TRT B	Cycle 7 Day 1	MFSAF total symptom score (TSS)	TSS	4	1	3	300
L)	10010	TRT B	Cycle 7 Day 1	MFSAF total symptom score (TSS)	TSS	5	12	-7	-58.33333
L)	10012	TRT B	Cycle 7 Day 1	MFSAF total symptom score (TSS)	TSS	21	13	8	61.538462
L)	10013	TRT B	Cycle 7 Day 1	MFSAF total symptom score (TSS)	TSS	22	27	-5	-18.51852
L)	10015	TRT B	Cycle 7 Day 1	MFSAF total symptom score (TSS)	TSS	3	0	3	
L)	10016	TRT B	Cycle 7 Day 1	MFSAF total symptom score (TSS)	TSS	22	45	-13	-28.88889

GRAPH DEVELOPMENT

```
layout overlay / xaxisopts= ( label="Individual Patients" display=(LINE LABEL) labelattrs=(weight = bold size = 9pt) )
                    yaxisopts=( label="% change in spleen volume from baseline" display=(TICKS TICKVALUES LINE LABEL)
                    offsetmax = 0.15 labelattrs=(weight = bold size = 10pt));
```



SCENARIO - 2

Table 2-3 Objectives and related endpoints

Objective(s)	Endpoint(s)
Primary objective(s)	Endpoint(s) for primary objective(s)
To measure the activity of treatment in patients with disease assessed by Overall Response Rate (ORR) at Day 28.	Overall response rate (ORR) at Day 28, defined as the proportion of patients demonstrating a complete response (CR) or partial response (PR) without requirement for additional systemic therapies for an earlier progression, mixed response or non-response.
Secondary objective(s)	Endpoint(s) for secondary objective(s)
Key Secondary To assess the rate of durable ORR at Day 56	Proportion of all patients who achieve a CR or PR at Day 28 and maintain a CR or PR at Day 56
To estimate ORR at Day 14	Proportion of patients who achieved ORR (CR+PR) at Day 14
To assess Duration of response	Duration of response (DOR) is assessed for responders only and is defined as the time from first response until disease progression or the date of additional systemic therapies. Progression to chronic condition, or death without prior observation of progression are considered as competing risks

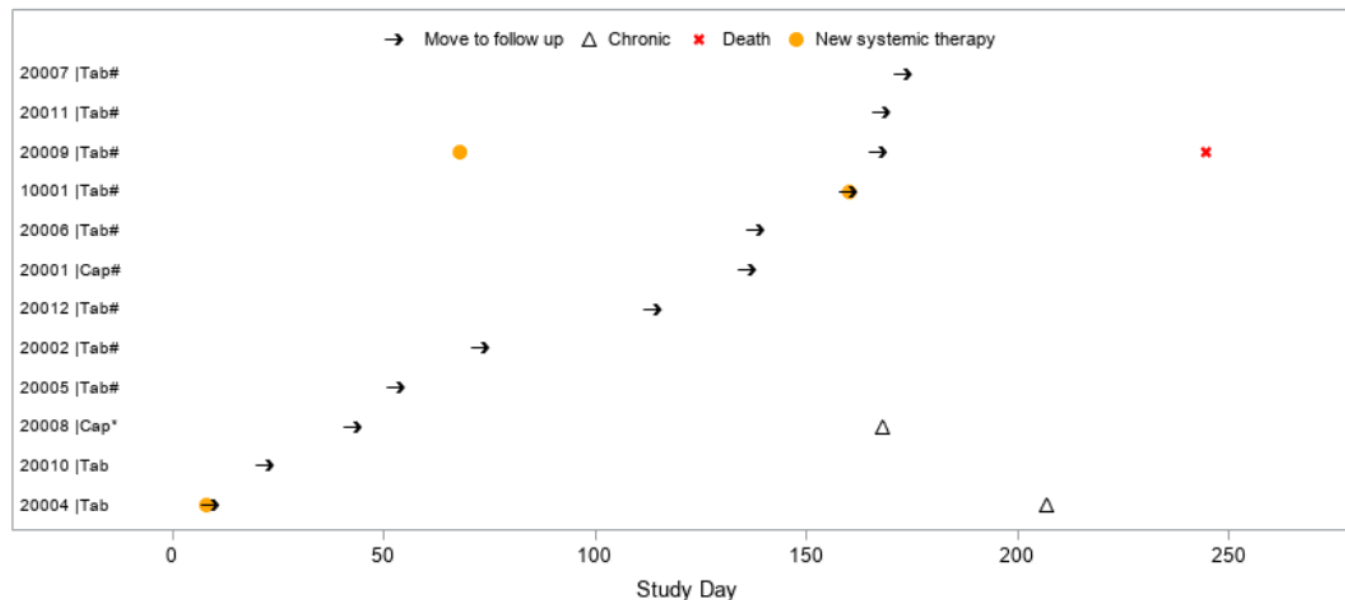
DATA REVIEW & GRAPH DEVELOPMENT

SUBJID	FACAT	FADTC	FADY
10001	PROGRESSION TO CHRONIC	2021-03-12	379

DISEASE PROGRESSION DATA

Age Group : Group 1

Tab: Tablet Cap: Capsule Liq: Liquid



```

/* new sys therapy*/
scatterplot y = usubjid x = sysdy/markerattrs = (symbol = circlefilled size = 10 color = orange) name = 'nst' legendlabel = 'New systemic therapy' ;
/*FUP*/
scatterplot y = usubjid x = fupdy/markerattrs = (symbol = rarrow size = 20 color = black) name = 'fup' legendlabel = 'Move to follow up';
/* Chronic */
scatterplot y = usubjid x = chrndy/markerattrs = (symbol = triangle size = 10 color = black) name = 'chronic' legendlabel = 'Chronic';
/*Death*/
scatterplot y = usubjid x = dthdy/markerattrs = (symbol = cross size = 15 color = red) name = 'death' legendlabel = 'Death';

```

DATA COLLECTED IN DIFFERENT CRF PAGES and DERIVED DATA

SUBJID	New Systemic Therapy Date
10001	2020-08-05

SUBJID	Dosage form	Date of Death
10001	Tab	.

SUBJID	Parameter	Parameter Code	omd28fl
10001	Overall Response Rate at Day 28	ORRD28	Y

SUBJID	Parameter	Parameter Code	durd56fl
10001	Durable Overall Response Rate at Day 56	DURRD56	Y

DATA REVIEW & GRAPH DEVELOPMENT

SUBJID	VISIT	FADTC	FASTRESC	AVAL	FADY
10001	Week 1	2020-03-06	PROGRESSION	4	8
10001	Week 2	2020-03-13	PROGRESSION	4	15
10001	Week 3	2020-03-19	COMPLETE RESPONSE	1	21
10001	Week 4	2020-03-27	COMPLETE RESPONSE	1	29
10001	Week 5	2020-04-03	COMPLETE RESPONSE	1	36
10001	Week 6	2020-04-10	COMPLETE RESPONSE	1	43
10001	Week 7	2020-04-17	COMPLETE RESPONSE	1	50
10001	Week 8	2020-04-23	COMPLETE RESPONSE	1	56
10001	Week 12	2020-05-21	COMPLETE RESPONSE	1	84
10001	Week 16	2020-06-18	COMPLETE RESPONSE	1	112
10001	Week 20	2020-07-16	MIXED RESPONSE/NO RESPONSE	3	140
10001	EOT	2020-08-04	MIXED RESPONSE/NO RESPONSE	3	159

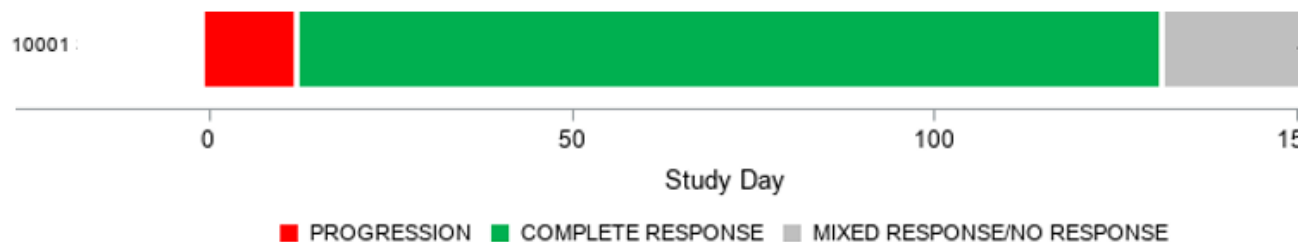
RESPONSE DATA as collected

SUBJID	VISIT	FADTC	FASTRESC	AVAL	FADY	START	END
10001	Week 1	2020-03-06	PROGRESSION	4	8	8	20
10001	Week 3	2020-03-19	COMPLETE RESPONSE	1	21	21	139
10001	Week 20	2020-07-16	MIXED RESPONSE/NO RESPONSE	3	140	140	159



```

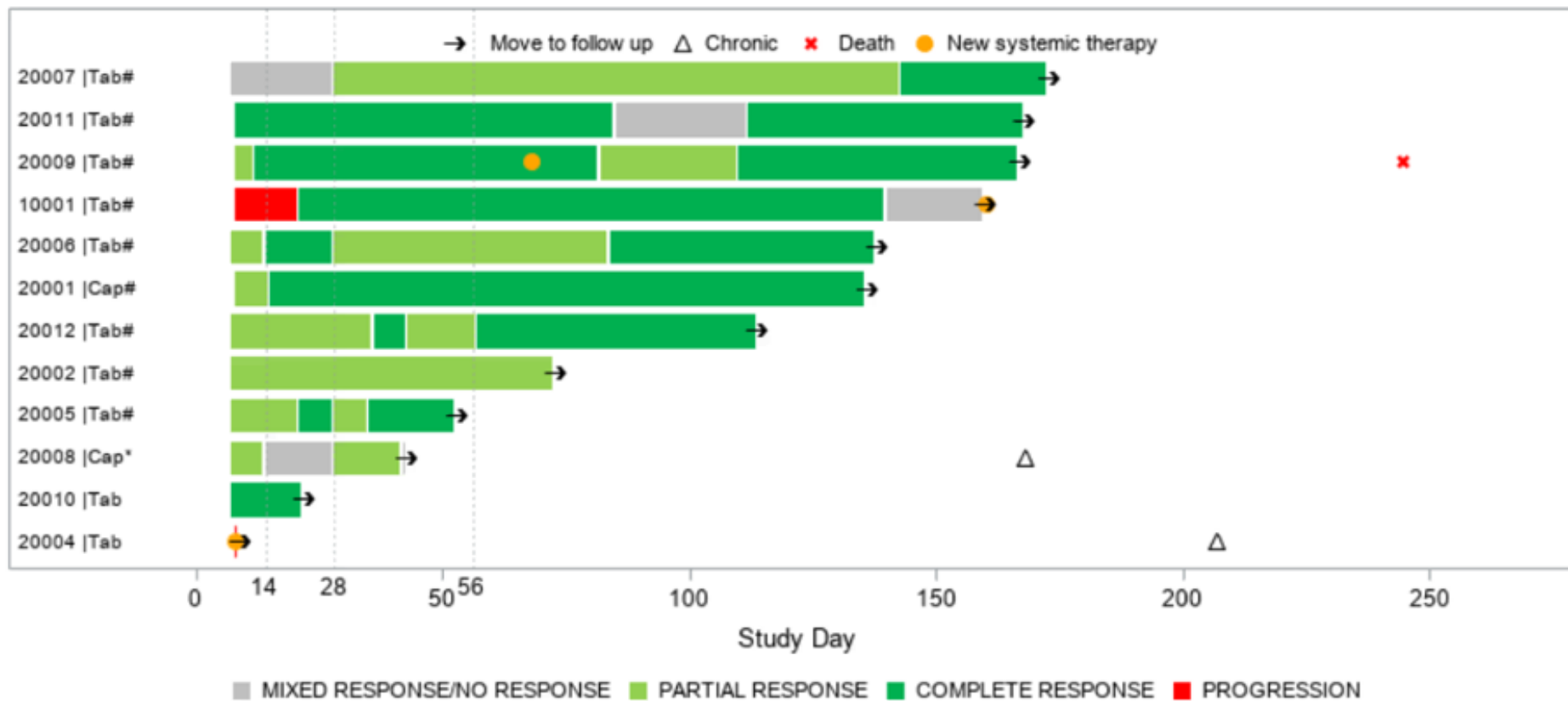
/*Bar plot for response*/
highlowplot y = SUBJID low = START high = END /
type = bar barwidth = 0.75 group = fastresc
outlineattrs = (pattern=solid)
name = 'response';
    
```



GRAPH DEVELOPMENT

Age Group : Group 1

Tab: Tablet Cap: Capsule Liq: Liquid



#: Responder for Durable Overall response at Day 56; *: Responder for Overall response at Day 28

CONCLUSION

- INTERRELATE OBJECTIVES AND ENDPOINT
- IDENTIFY KEY DATA POINTS AND ACCESS THEIR PRACTICALITY IN ANSWERING OUR OUTCOMES
- ASK RIGHT QUESTIONS

QUESTIONS...

Abstract geometric lines in the top left corner of the slide, consisting of several overlapping, irregular polygons and lines in a light brown color.

THANK YOU