FIG. 1

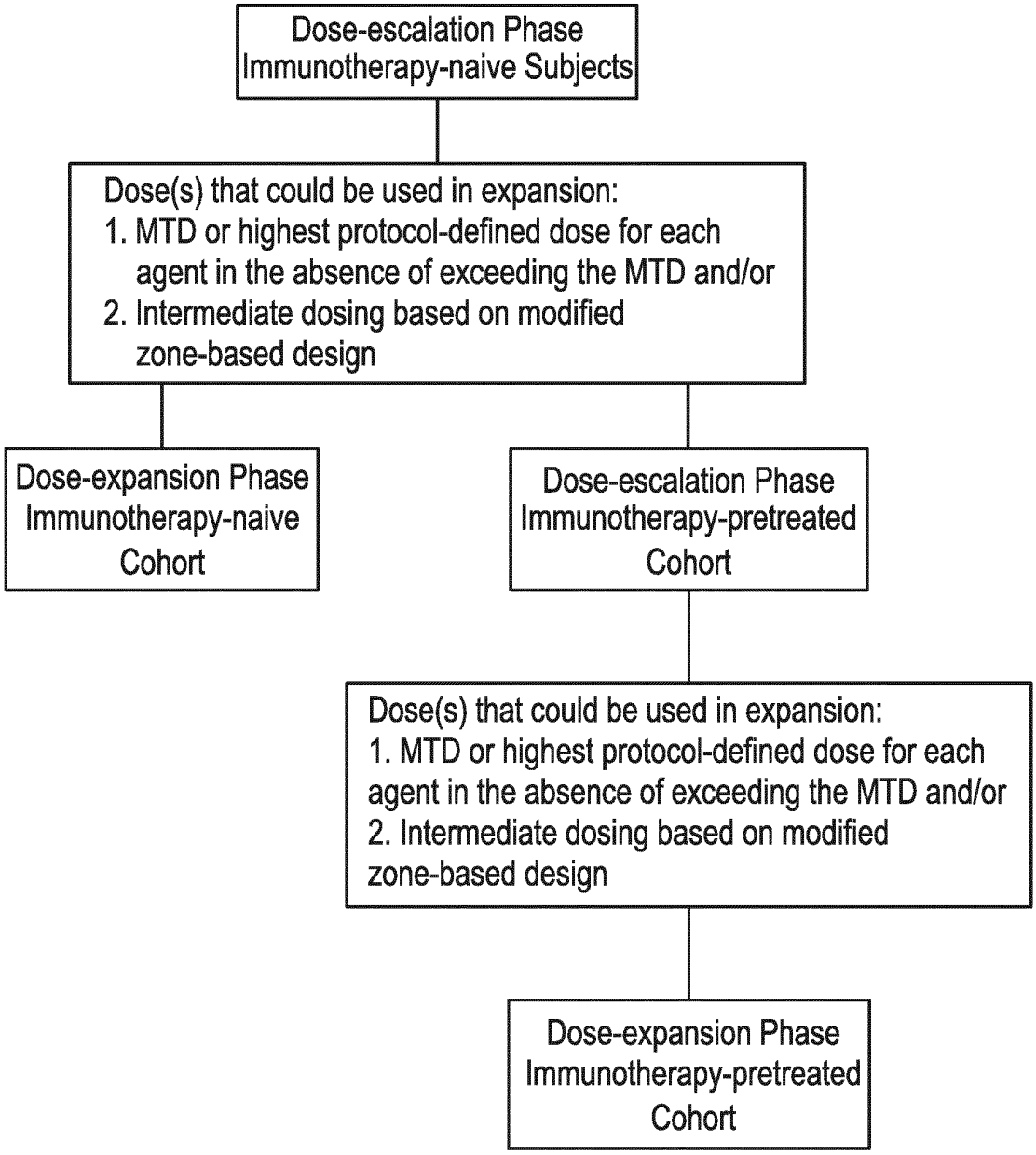

Dose-escalation Phase
Immunotherapy-naive Subjects
Dose(s) that could be used in expansion:
1. MTD or highest protocol-defined dose for each agent in the absence of exceeding the MTD and/or
2. Intermediate dosing based on modified zone-based design
Dose-expansion Phase
Immunotherapy-naive
Cohort
Dose-escalation Phase
Immunotherapy-pretreated
Cohort
Dose(s) that could be used in expansion:
1. MTD or highest protocol-defined dose for each agent in the absence of exceeding the MTD and/or
2. Intermediate dosing based on modified zone-based design
Dose-expansion Phase
Immunotherapy-pretreated
Cohort

FIG. 2

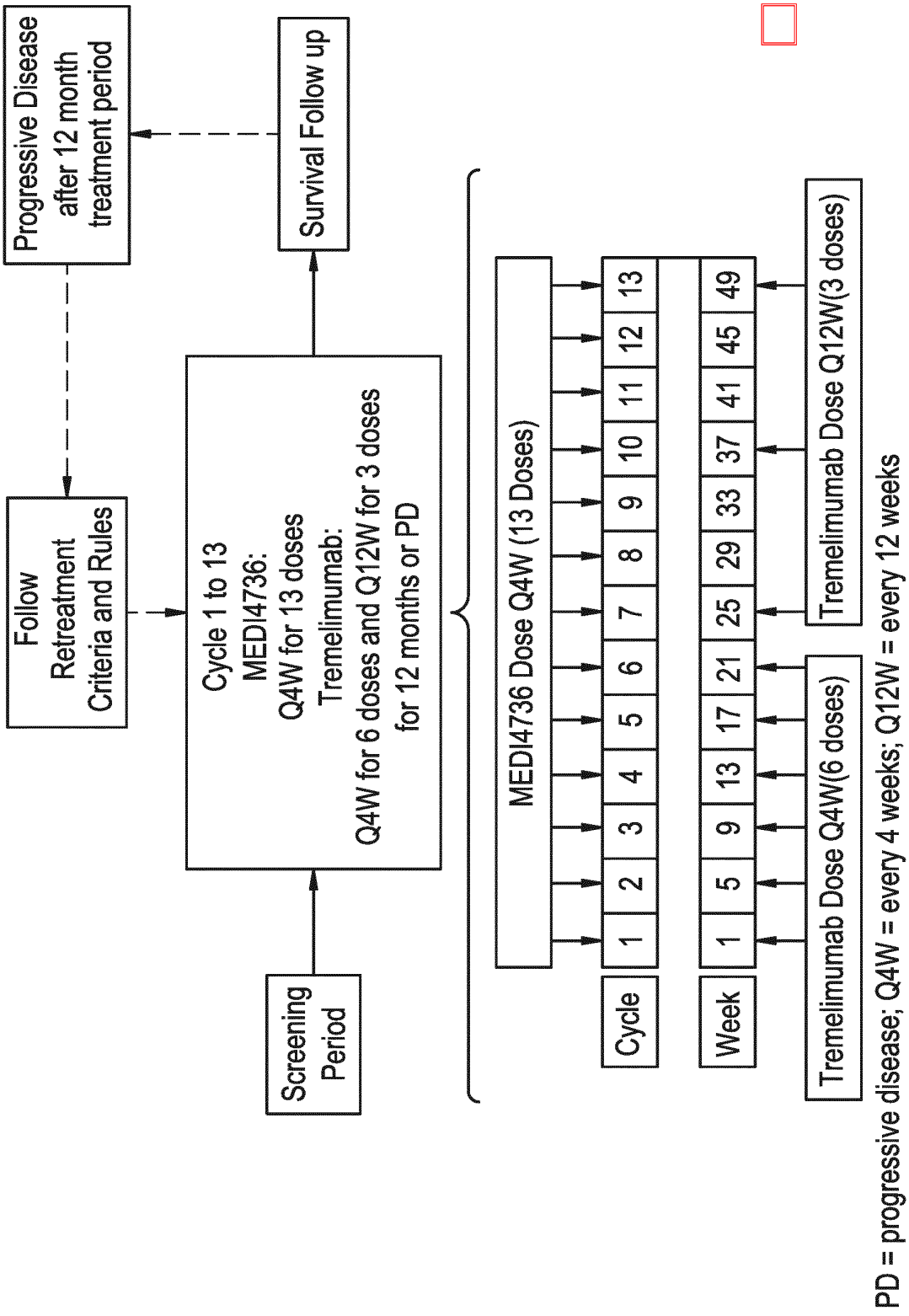

Screening Period
Cycle 1 to 13
MEDI4736:
Q4W for 13 doses
Tremelimumab:
Q4W for 6 doses and Q12W for 3 doses
for 12 months or PD
Follow Retreatment Criteria and Rules
Progressive Disease after 12 month treatment period
Survival Follow up
MEDI4736 Dose Q4W (13 Doses)
Cycle
1 2 3 4 5 6 7 8 9 10 11 12 13
Week
1 5 9 13 17 21 25 29 33 37 41 45 49
Tremelimumab Dose Q4W(6 doses)
Tremelimumab Dose Q12W(3 doses)
PD = progressive disease; Q4W = every 4 weeks; Q12W = every 12 weeks

FIG. 3

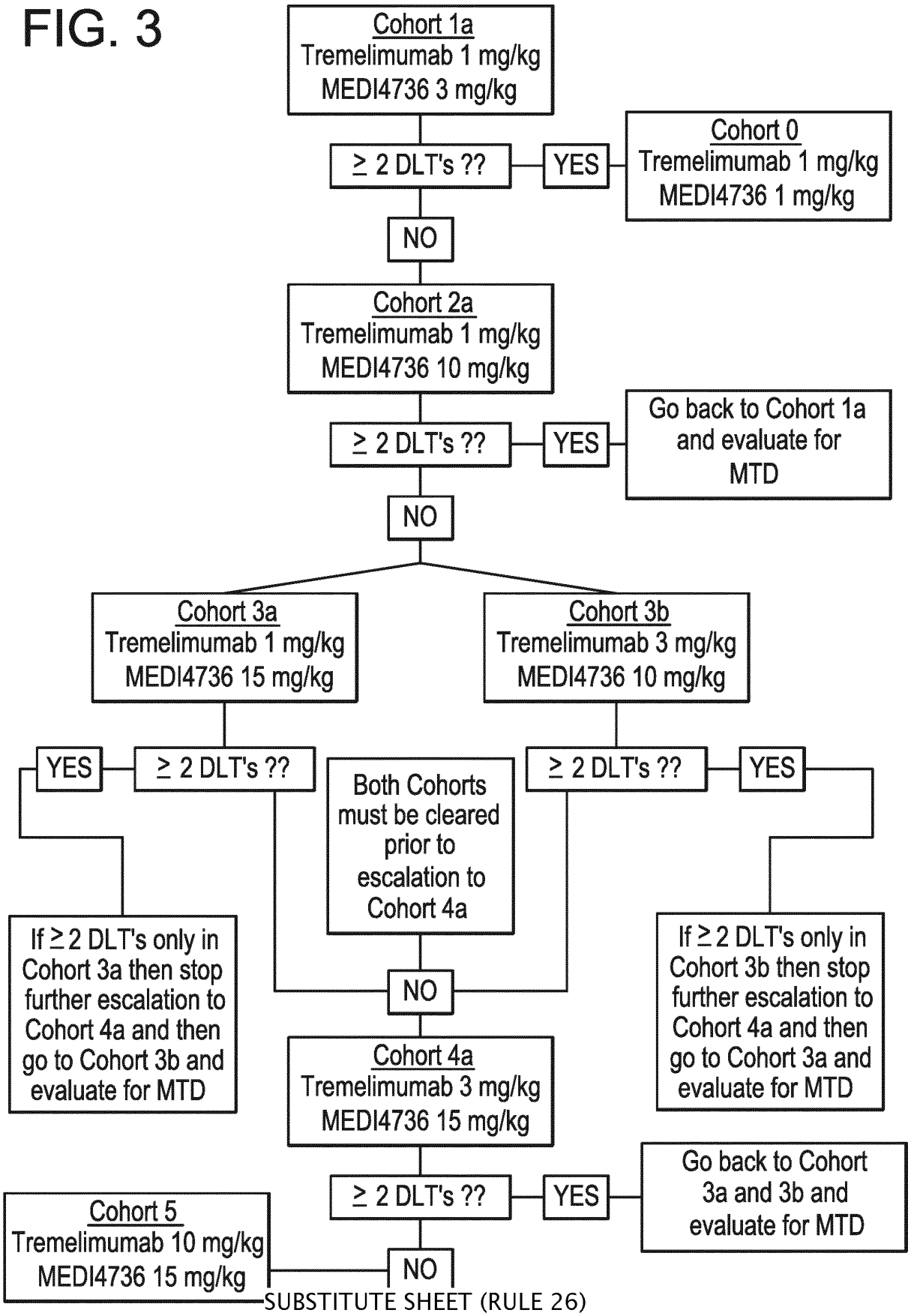
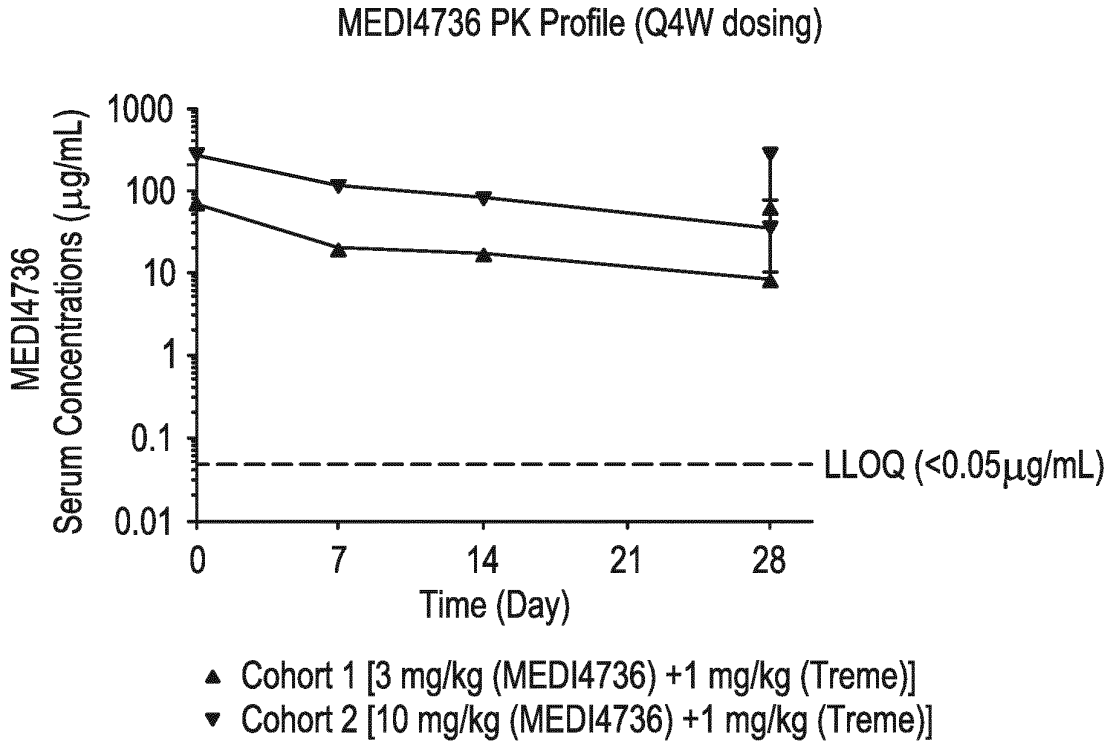

Cohort 1a
Tremelimumab 1 mg/kg
MEDI4736 3 mg/kg
≥ 2 DLT's ??
YES
Cohort 0
Tremelimumab 1 mg/kg
MEDI4736 1 mg/kg
NO
Cohort 2a
Tremelimumab 1 mg/kg
MEDI4736 10 mg/kg
≥ 2 DLT's ??
YES
Go back to Cohort 1a and evaluate for MTD
NO
Cohort 3a
Tremelimumab 1 mg/kg
MEDI4736 15 mg/kg
Cohort 3b
Tremelimumab 3 mg/kg
MEDI4736 10 mg/kg
YES
≥ 2 DLT's ??
Both Cohorts must be cleared prior to escalation to Cohort 4a
≥ 2 DLT's ??
YES
If ≥ 2 DLT's only in Cohort 3a then stop further escalation to Cohort 4a and then go to Cohort 3b and evaluate for MTD
If ≥ 2 DLT's only in Cohort 3b then stop further escalation to Cohort 4a and then go to Cohort 3a and evaluate for MTD
NO
Cohort 4a
Tremelimumab 3 mg/kg
MEDI4736 15 mg/kg
≥ 2 DLT's ??
YES
Go back to Cohort 3a and 3b and evaluate for MTD
Cohort 5
Tremelimumab 10 mg/kg
MEDI4736 15 mg/kg
NO

FIG. 4

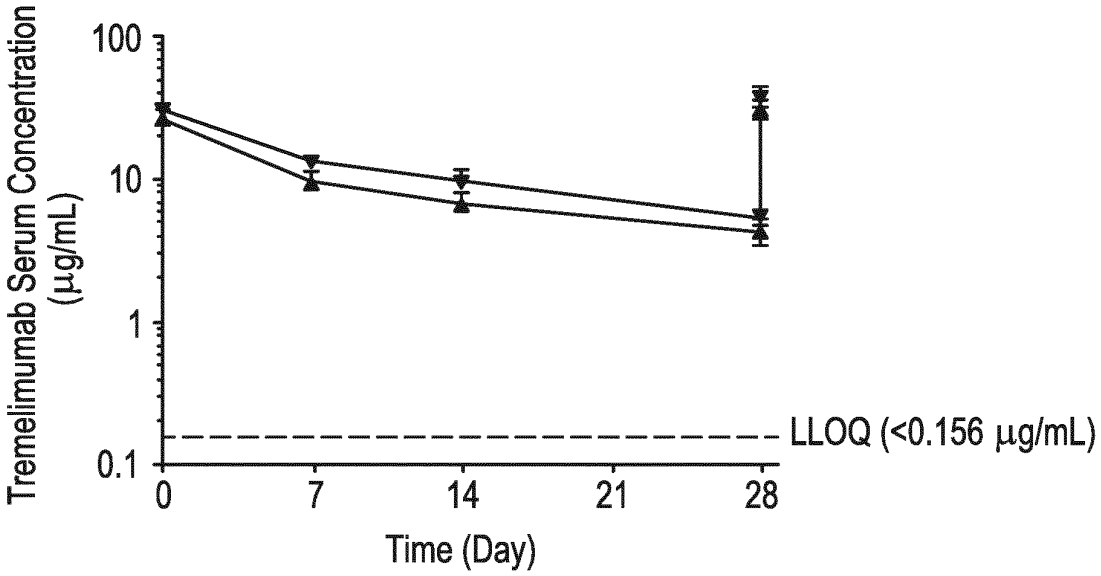


MEDI4736 PK Parameters

Cohort	C_{max} (μg/mL)	AUC_T (μg/mL*day)	C_{trough} (μg/mL)
1 (3 mg/kg) (N=3)	67.36 (7.085)	625.3 (47.98)	8.85 1.80
2 (10 mg/kg) (N=2)	266.7 (72.15)	2860 (286.2)	35.65 (4.65)

FIG. 5

Tremelimumab PK Profile (Q4W dosing)



Tremelimumab PK Parameters

Cohort	C_{max} (µg/mL)	AUC_T (µg/mL*day)	C_{trough} (µg/mL)
1 (1 mg/kg) (N=3)	27.07 (3.669)	262.2 (9.347)	4.21 (1.05)
2 (1mg/kg) (N=2)	30.40 (0.6557)	338.8 (27.20)	5.33 (0.75)

FIG. 6

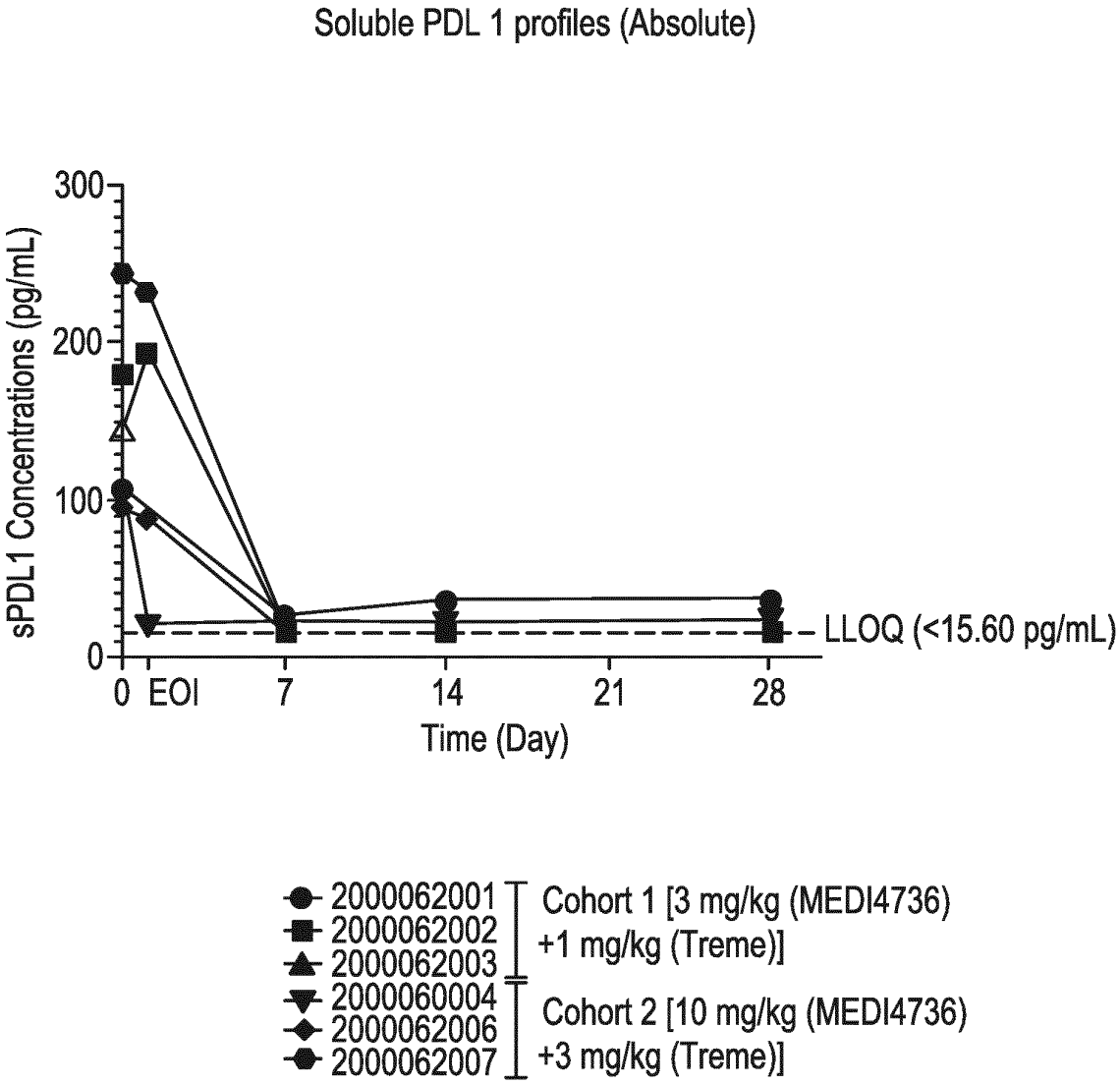

Soluble PDL 1 profiles (Absolute)
sPDL1 Concentrations (pg/mL)
300
200
100
0
0 EOI
7
14
21
28
Time (Day)
LLOQ (<15.60 pg/mL)
2000062001
2000062002
2000062003
Cohort 1 [3 mg/kg (MEDI4736) +1 mg/kg (Treme)]
2000060004
2000062006
2000062007
Cohort 2 [10 mg/kg (MEDI4736) +3 mg/kg (Treme)]

FIG. 7

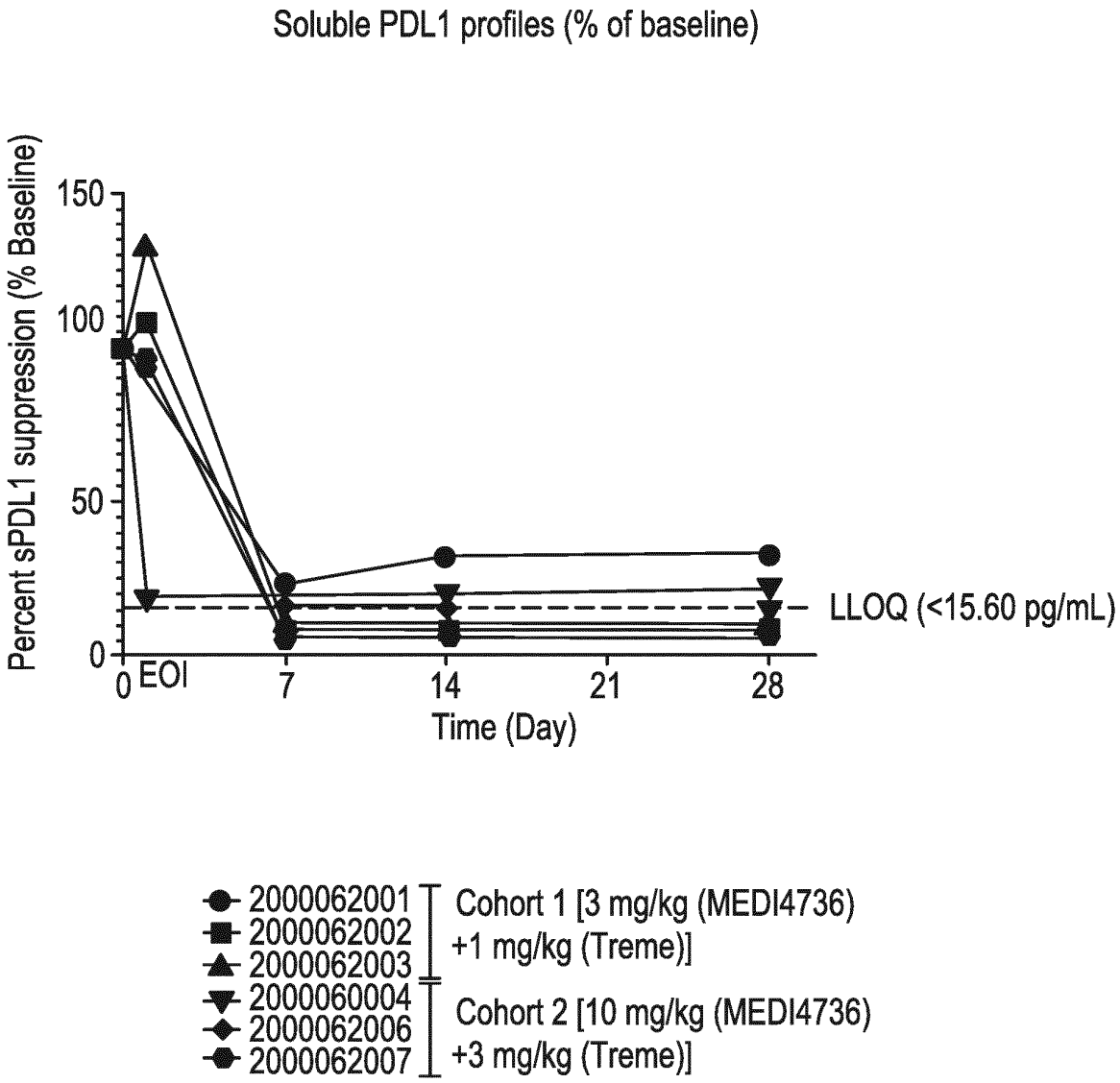

Soluble PDL1 profiles (% of baseline)
Percent sPDL1 suppression (% Baseline)
150
100
50
0
0 EOI
7
14
21
28
Time (Day)
LLOQ (<15.60 pg/mL)
2000062001
2000062002
2000062003
Cohort 1 [3 mg/kg (MEDI4736)
+1 mg/kg (Treme)]
2000060004
2000062006
2000062007
Cohort 2 [10 mg/kg (MEDI4736)
+3 mg/kg (Treme)]

FIG. 8

MEDI4736 Individual PK Profiles

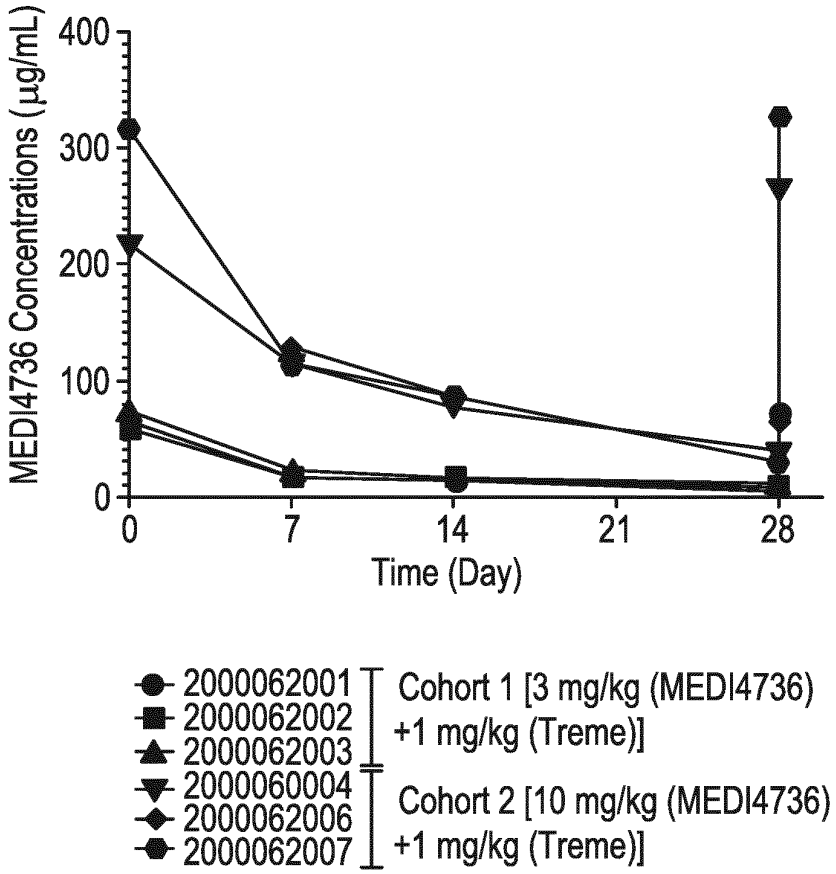


FIG. 9

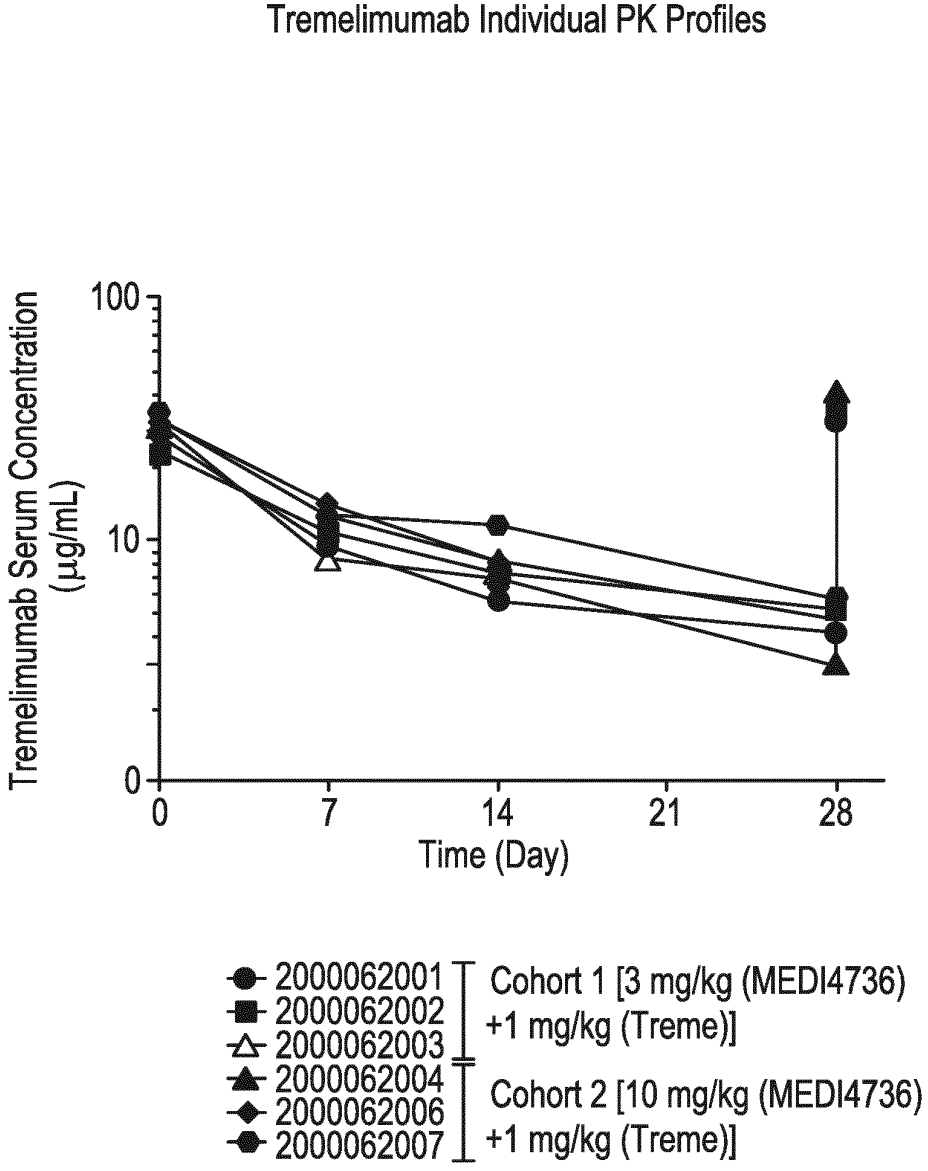

Tremelimumab Individual PK Profiles
Tremelimumab Serum Concentration (µg/mL)
100
10
0
0
7
14
21
28
Time (Day)
2000062001
2000062002
2000062003
Cohort 1 [3 mg/kg (MEDI4736) +1 mg/kg (Treme)]
2000062004
2000062006
2000062007
Cohort 2 [10 mg/kg (MEDI4736) +1 mg/kg (Treme)]

FIG. 10A

Severity	irAEs [a]	All Other Events
Grade 1	None	<u>For infusion-related reactions:</u> • The infusion rate of MEDI4736 or tremelimumab may be decreased by50% or temporarily interrupted until resolution of the event • Acetaminophen and/or antihistamines may be administered per institutional standard at the discretion of the investigator • Consider premedication prior to subsequent doses For all other AEs: no dose adjustment is required
Grade 2	<u>For endocrinopathy</u> • Hold MEDI4736 and tremelimumab • When endocrinopathy is controlled, resume MEDI4736 and tremelimumab For dermatologic irAEs Do not hold MEDI4736 and tremelimumab dose For pneumonitis • Hold MEDI4736 and tremelimumab until resolution to ≤ Grade 1 If resolution to ≤ Grade 1 occurs within 3 days of the initiation of maximal supportive care (including corticosteroids), resume MEDI4736 and tremelimumab administration at next scheduled dose. Otherwise, discontinue MEDI4736 and tremelimumab <u>For all irAEs</u> • Hold MEDI4736 and tremelimumab until resolution to ≤ Grade 1 • If resolution to ≤ Grade 1 does not occur within 30 days, discontinue MEDI4736 and tremelimumab	<u>For infusion-related reactions:</u> • The infusion rate of MEDI4736 or tremelimumab may be decreased by 50% or temporarily interrupted until resolution of the event • Acetaminophen and/or antihistamines may be administered per institutional standard at the discretion of the investigator • Consider premedication prior to subsequent doses All Other AEs • Hold MEDI4736 and tremelimumab until resolution to ≤ Grade 1 or baseline If resolution to ≤ Grade 1 does not occur within 30 days, discontinue MEDI4736 and tremelimumab

AE = adverse event; irAE = immune-related adverse event; ULN = upper limit of normal. [a] Management of irAEs may require administration of immunosuppressive medications (and/or hormone replacement therapy for endocrinopathies). Resolution of irAEs managed in this manner in the timeframes specified is acceptable.

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FIG. 10B

Severity	irAEs [a]	All Other Events
Grade 3	For endocrinopathy • Hold MEDI4736 and tremelimumab When endocrinopathy is controlled, resume MEDI4736 and tremelimumab administration at next scheduled dose For dermatologic irAEs • Hold MEDI4736 and tremelimumab until resolution to ≤ Grade 1 or baseline If resolution to ≤ Grade 1 or baseline does not occur within 30 days, discontinue MEDI4736 and tremelimumab For elevations in transaminases • For elevations in transaminases ≤ 8 × ULN, hold MEDI4736 and tremelimumab until resolution to ≤ Grade 1 or baseline. If elevations downgrade to ≤ Grade 2 within 7 days or resolve to ≤ Grade 1 or baseline within 14 days, resume MEDI4736 and tremelimumab administration at next scheduled dose. Otherwise, discontinue MEDI4736 and tremelimumab • For elevations in transaminases > 8 × ULN, discontinue MEDI4736 and tremelimumab For elevations in total bilirubin • For elevations in total bilirubin ≤ 5 × ULN, hold MEDI4736 and tremelimumab until resolution to ≤ Grade 1 or baseline. If elevations downgrade to ≤ Grade 2 (< 3 × ULN) within 7 days or resolve to ≤ Grade 1 or baseline within 14 days, resume MEDI4736 and tremelimumab administration at next scheduled dose. Otherwise, discontinue MEDI4736 and tremelimumab • For elevations in total bilirubin > 5 × ULN, discontinue MEDI4736 and tremelimumab For all other irAEs: Discontinue MEDI4736 and tremelimumab	For hypersensitivity and infusion- related reactions: • Discontinue MEDI4736 and tremelimumab For all other AEs: • Hold MEDI4736 and tremelimumab until resolution to ≤ Grade 1 or baseline For AEs that downgrade to ≤ Grade 2 within 7 days or resolve to ≤ Grade 1 or baseline within 14 days, resume MEDI4736 and tremelimumab administration at next scheduled dose. Otherwise, discontinue MEDI4736 and tremelimumab
Grade 4	Discontinue MEDI4736 and tremelimumab	Discontinue MEDI4736 and tremelimumab

AE = adverse event; irAE = immune-related adverse event; ULN = upper limit of normal. [a] Management of irAEs may require administration of immunosuppressive medications (and/or hormone replacement therapy for endocrinopathies). Resolution of irAEs managed in this manner in the timeframes specified is acceptable.

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FIG. 11

Cohort	MEDI4736 x 12 doses	Tremelimumab Q4W X6 doses and Q12W x 3 doses
1a	3	1
2a	10	1
3a	15	1
3b	10	3
4a	15	3
5	15	10

Key Study Criteria	
Key Eligibility	Escalation 1. Locally Advanced Unresectable or Metastatic NSCLCa Relapsed/Refractory 2. Immunotherapy Naive Expansion 1. Locally Advanced Unresectable or Metastatic NSCLCa Relapsed/Refractory 2. Immunotherapy Naive and Pre-Treated Cohorts
Objective	1. Primary: MTD or highest protocol-defined dose for each agent in the absence of exceeding the MTD and the safety profile 2. Secondary: Antitumor activity, Immunogenecity, PK/PD
Safety Assessments	1. Cycle 1: Weekly for 4 weeks 2. Cycle 2-6: Every 1-2 weeks 3. Cycle 7-12: Every 1 week
Response Criteria	1. Primary response criteria every 8 weeks using RECIST 1.1 with modifications

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FIG. 12

	MEDI4736 (M) and Tremelimumab (T) in NSCLCa Q4W April 23, 2014 cut-off				
	Cohort				
	1a	2a	3a	3b	4a
	3 mg/kg (M) 1 mg/kg (T) Q4W	10 mg/kg (M) 1 mg/kg (T) Q4W	15 mg/kg (M) 1 mg/kg (T) Q4W	10 mg/kg (M) 3 mg/kg (T) Q4W	15 mg/kg (M) 3 mg/kg (T) Q4W
Subjects enrolled	3	3	3	3	Week of 28th
No. of Lines	1,2,3	4,3,3	4,5,3	2,1,3	
Tumor	1-Sq, 2-Non-sq, 1-KRAS	3-Non-sq	1-Sq, 2-Non-sq, 1-EGFR (T790)	3-Non-sq	
Subjects on treatment	0	2	3	2	
Cohort fully enrolled	07Nov13	17Jan14	14Feb14	26Feb14	
DLT Period (days)	56	28	28 (protocol) 56 (extended due to one AE in prior cohort)	28 (protocol) 56 (extended due to one AE in prior cohort)	28 days
Next Cohort Planned Enrollment			Week of 4/28	Week of 4/28	

Q4W = every 4 weeks

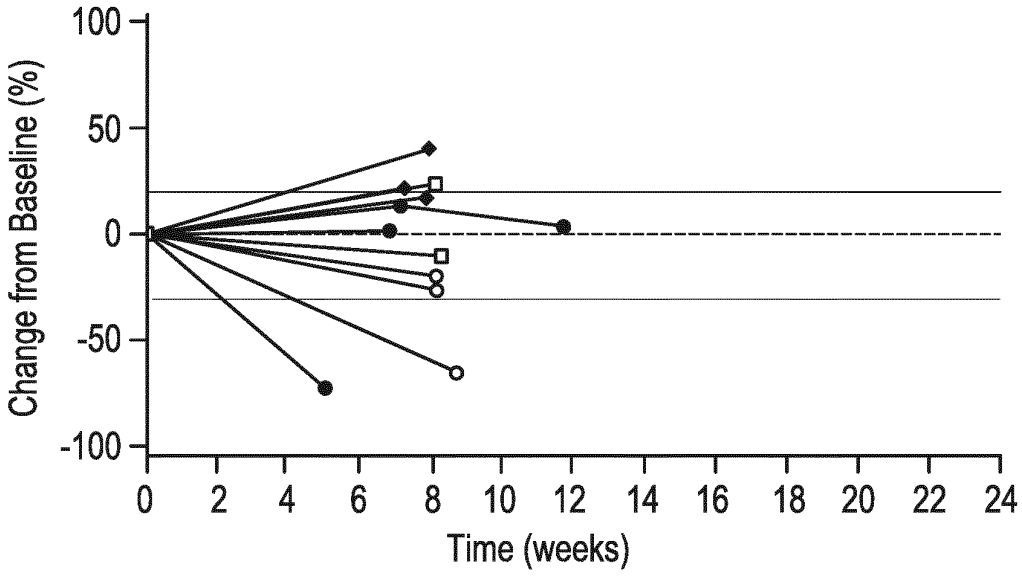
FIG. 13

	Related AE's MEDI4736 (M) and Tremelimumab (T) Q4W April 23, 2014 cut-off				
	Cohort				
	1a	2a	3a	3b	4a
	3 mg/kg (M) 1 mg/kg (T) N=3	10 mg/kg (M) 1 mg/kg (T) N=3	15 mg/kg (M) 1 mg/kg (T) N=3	10 mg/kg (M) 3 mg/kg (T) N=3	15 mg/kg (M) 3 mg/kg (T) N=3 (started week 28th)
Any AE (N)	3	3	3	2	
Any G3/G4 AE	0	1*	1	1	
SAE	1	1*	1	1	
AE to D/C	1	1	0	1	
Related AE	1	2	3	1	
Related G3/G4	0	1*	1	1	
G5	0	1*	0	0	
Related AE to D/C	0	1*	0	1	

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FIG. 14

Tumor Size Change from Baseline
(First Four Cohorts)



1 MG/KG TREME + 3 MG/KG MEDI4736
1 MG/KG TREME + 10 MG/KG MEDI4736
1 MG/KG TREME + 15 MG/KG MEDI4736
3 MG/KG TREME + 10 MG/KG MEDI4736

n-/n = 5/11

- One additional subject in Cohort 3b with 38% reduction at week 7

FIG. 15

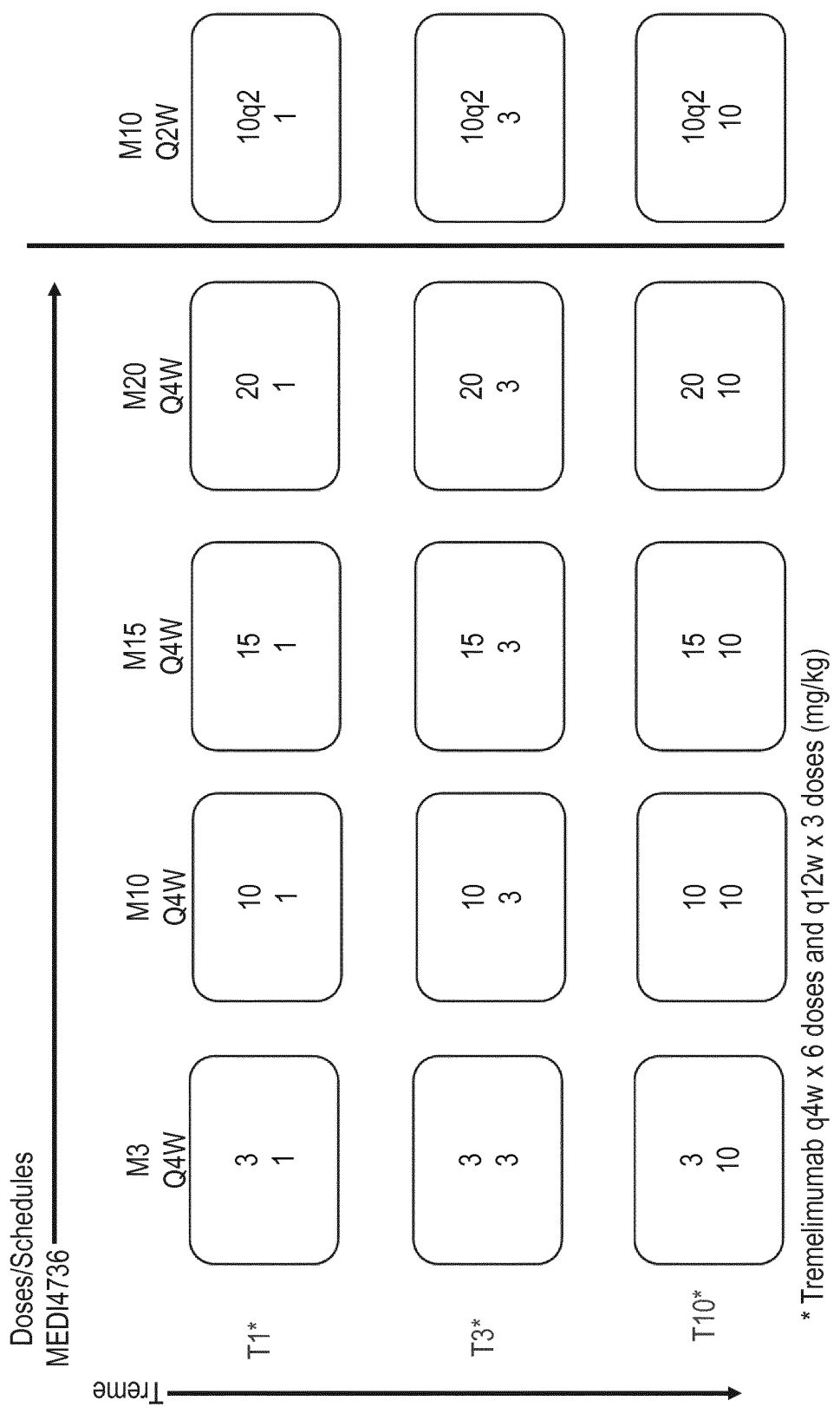
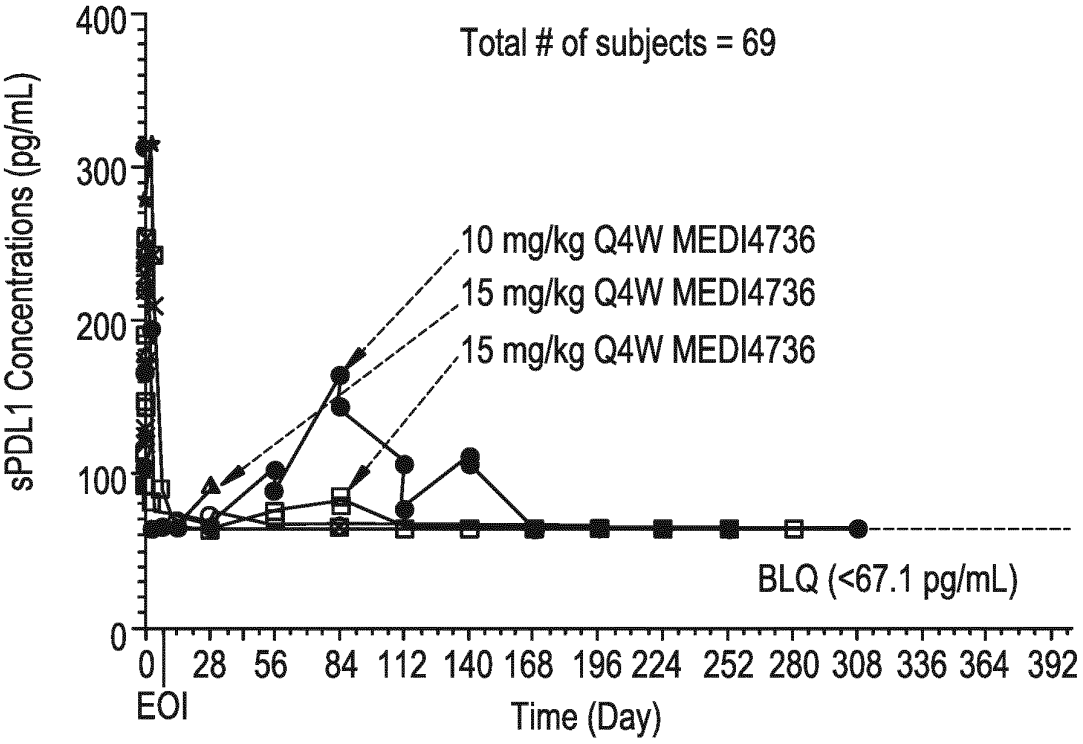

Doses/Schedules
MEDI4736
Treme
M3 Q4W
M10 Q4W
M15 Q4W
M20 Q4W
M10 Q2W
T1*
T3*
T10*
3 1
10 1
15 1
20 1
10q2 1
3 3
10 3
15 3
20 3
10q2 3
3 10
10 10
15 10
20 10
10q2 10
* Tremelimumab q4w x 6 doses and q12w x 3 doses (mg/kg)

FIG. 16

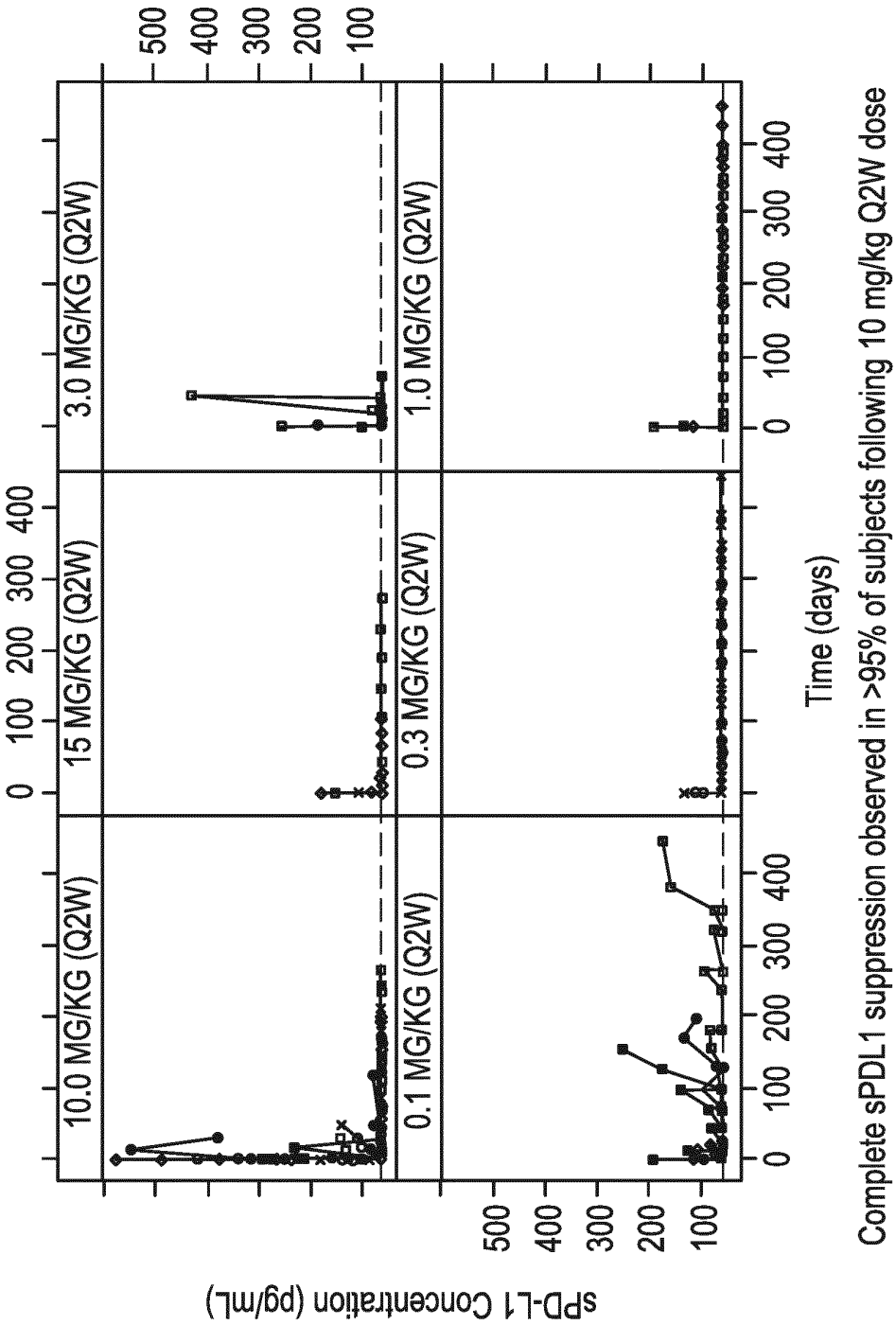
Individual sPD-L1 Profiles in Combination



- Complete sPD-L1 suppression at doses ≥ 15 mg/kg Q4W MEDI4736
  - 1 subject each at 10 mg/kg Q4W and 15 mg/kg Q4W showed partial sPD-L1 suppression at some visits followed by complete suppression after repeated dosing
    - 1 subject following 15 mg/kg Q4W was not suppressed at Day 29 (limited data available)
  - Complete suppression observed with single-agent MEDI4736 (Study 1108) at doses > 3 mg/kg Q2W

FIG. 17

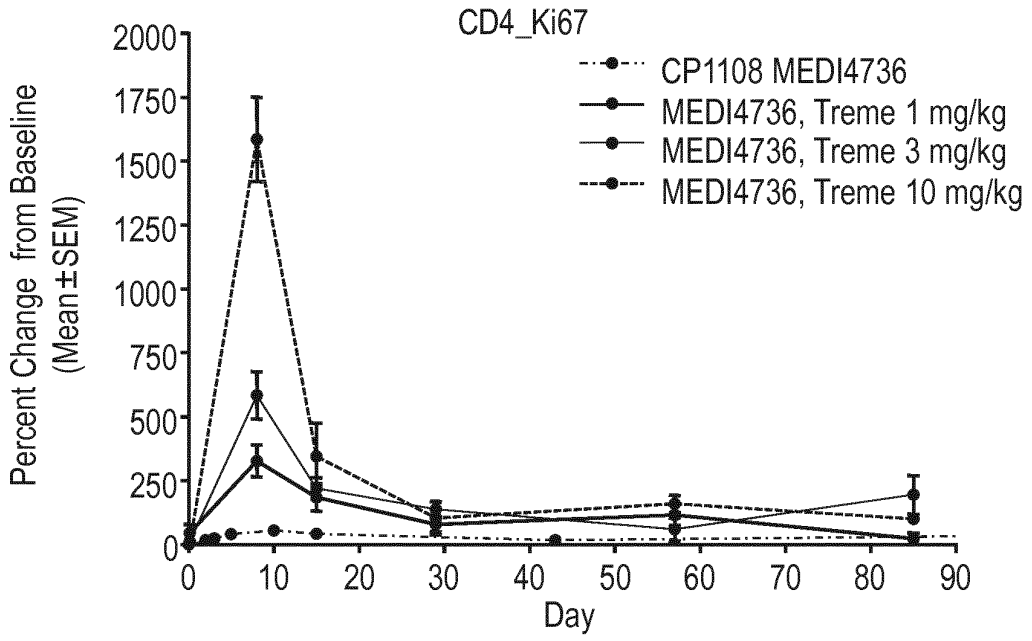
MEDI4736 Individual sPD-L1 Profiles by Cohort
(Study 1108)

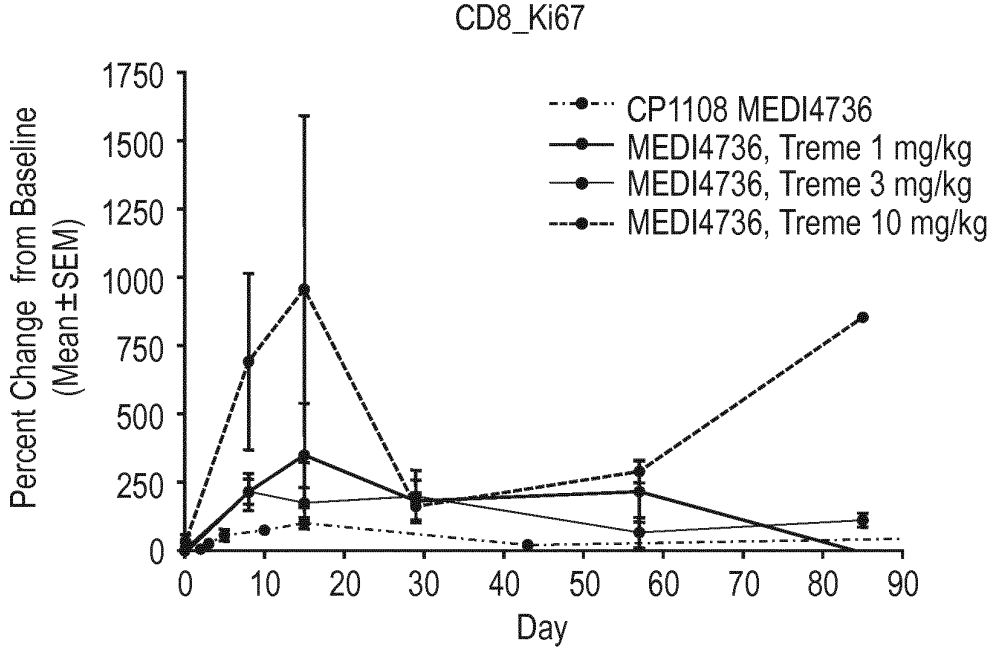


Complete sPDL1 suppression observed in >95% of subjects following 10 mg/kg Q2W dose

FIG. 18

CD4 Ki67+ and CD8_Ki67 proliferating cells: All MEDI4736 doses combined

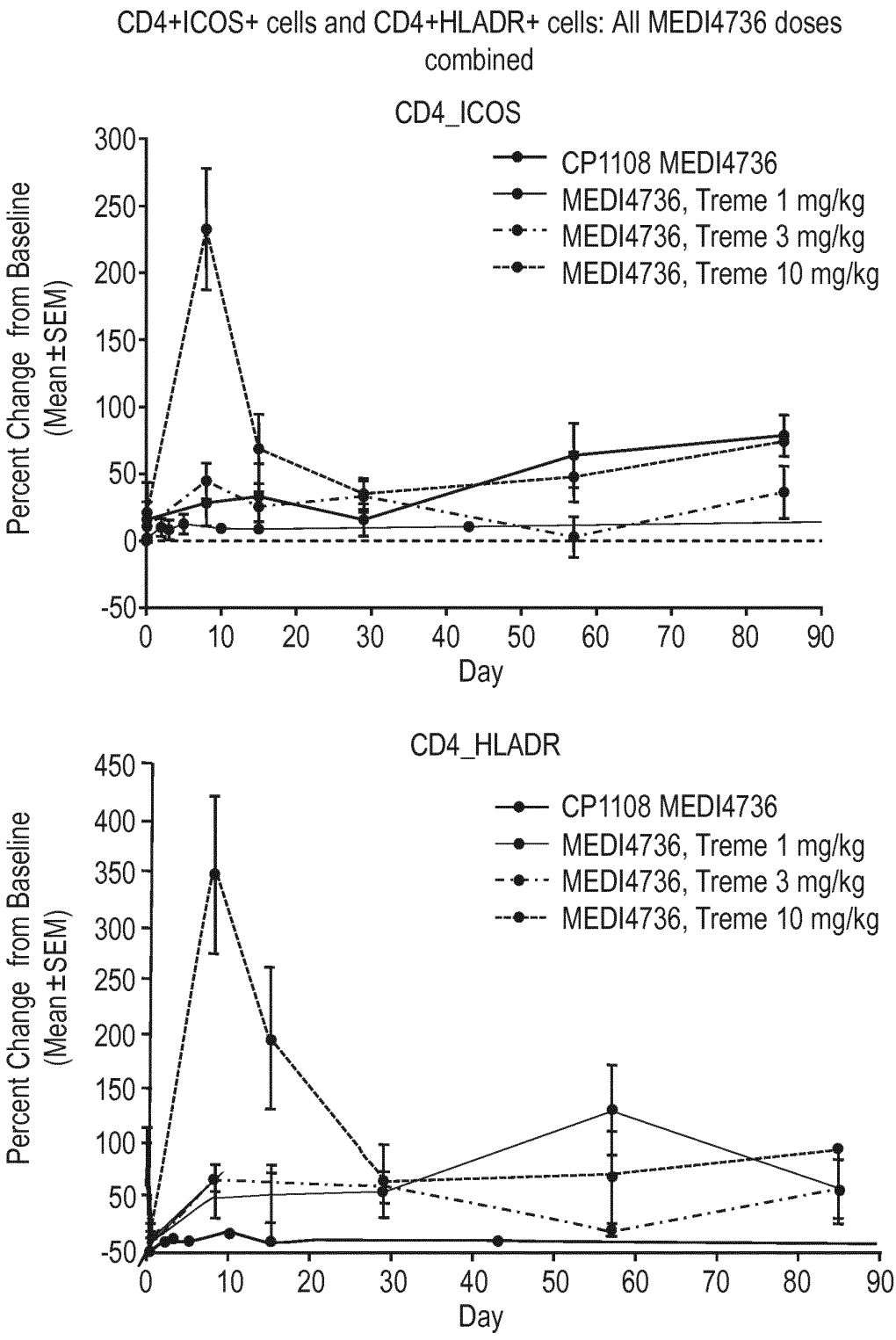




- Monotonic increase in peak CD4+Ki67+ cells with increasing treme dose
- Increase greater than observed with MEDI4736 alone
- CD8+ proliferative response is greater with combinations than that observed with MEDI4736 alone

SEM only provided for time points with n ≥3

FIG. 19



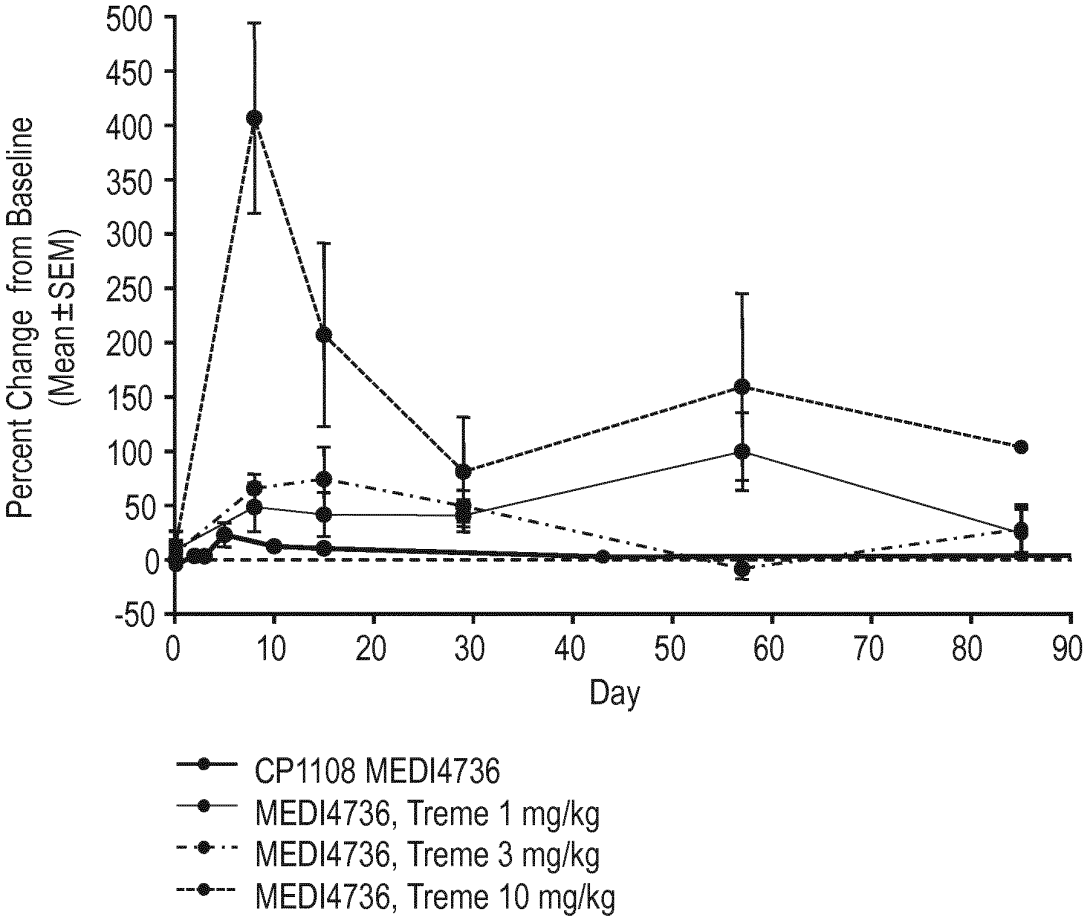
- Minimal change was observed with MEDI4736 alone
- All tested combination doses have a pattern distinguishable from MEDI4736
- Maximal increase observed with 10mg Treme

ided for time points with n≥3

FIG. 20

CD4+T effector cells: All MEDI4736 doses combined

CD4_T effector memory

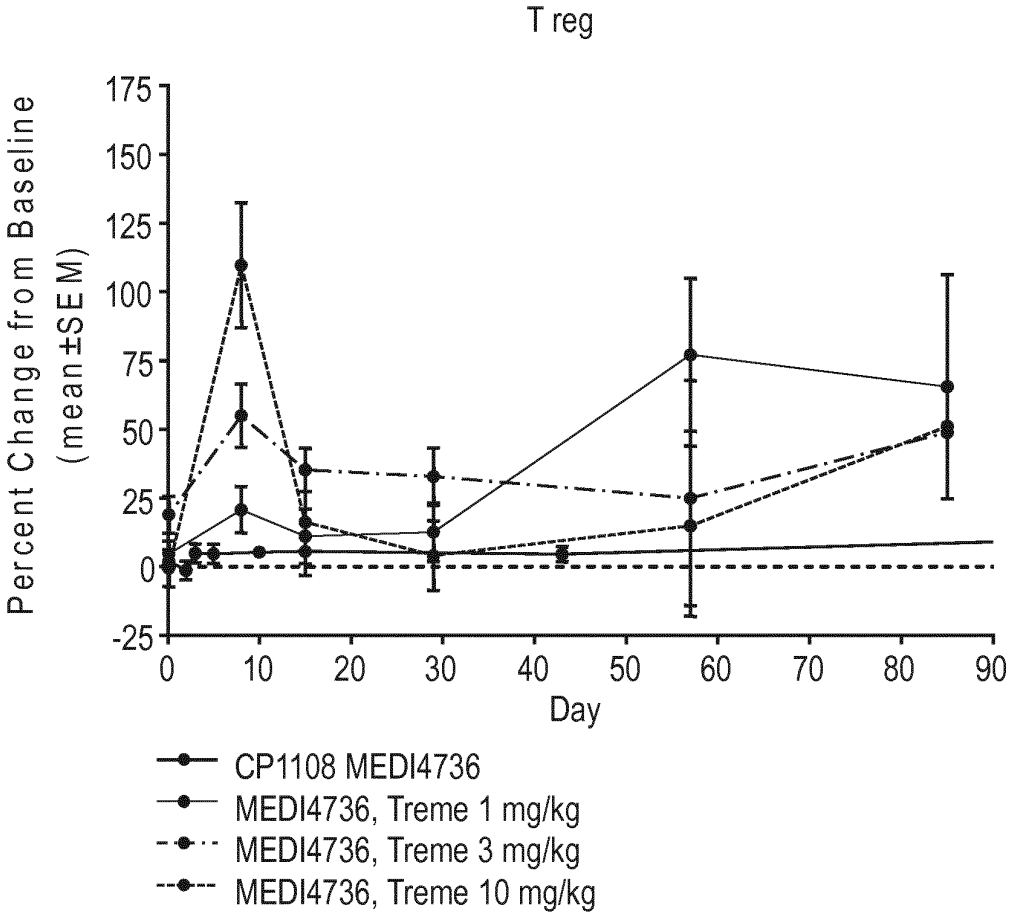


- Increase in CD4+ effector memory cells is greater with combination doses than that observed with MEDI4736 alone

SEM only provided for time points with n ≥3

FIG. 21

Treg cells: All MEDI4736 doses combined



- Treme dose-dependent increase in Treg cells*

  *CD25hi CD127lo phenotype may also include some activated T cells
- T Increase greater than observed with MEDI4736 alone

SEM only provided for time points with n≥3

FIG. 22

Clinical Activity: COMBINATION VS MEDI4736 MONOTHERAPY

	MEDI4736/Treme Combo (All Doses)		MEDI4736 10 mg/kg Q2W CP1108 (NSCLC)	
	ORR n/N, % (95%CI)	SD n/N, % (95%CI)	ORR n/N, % (95%CI)	SD n/N, % (95%CI)
Response Evaluable	12/53 23% (12.3, 36.2)	14/53 26% (15.3, 40.3)	25/166 15% (10.0, 21.4)	41/166 25% (18.3, 32.0)
PD-L1+	4/11 36% (10.9, 69.2)	3/11 27% (6.0, 61.0)	14/56 25% (14.4, 38.4)	10/56 18% (8.9, 30.4)
PD-L1-	6/24 25% (9.8, 46.7)	7/24 29% (12.6, 51.1)	6/83 7% (2.7, 15.1)	28/83 34% (23.7, 44.9)
PD-L1 Unknown	2/18 11% (1.4, 34.7)	4/18 22% (6.4, 47.6)	5/27 19% (6.3, 38.1)	3/27 11% (2.4, 29.2)

- Data as of Jan 27, 2015 for MEDI4736/Treme combo. Data as of Oct 31, 2014 for MEDI4736 NSCL(CP1108).
- Response Evaluable: treated patients with measurable disease at baseline + ≥1 follow-up scan (includes discontinuations due to disease progression or death prior to first follow-up scan). For MEDI4736 NSCLC (CP1108), only patients with >=12 weeks follow-up were included.
- ORR includes **confirmed and unconfirmed CR or PR**. For MEDI4736 NSCLC (CP1108), BOR of SD with minimum duration of 12 weeks. For MEDI4736/Treme combo, BOR of SD with minimum duration of 7 weeks

FIG. 23

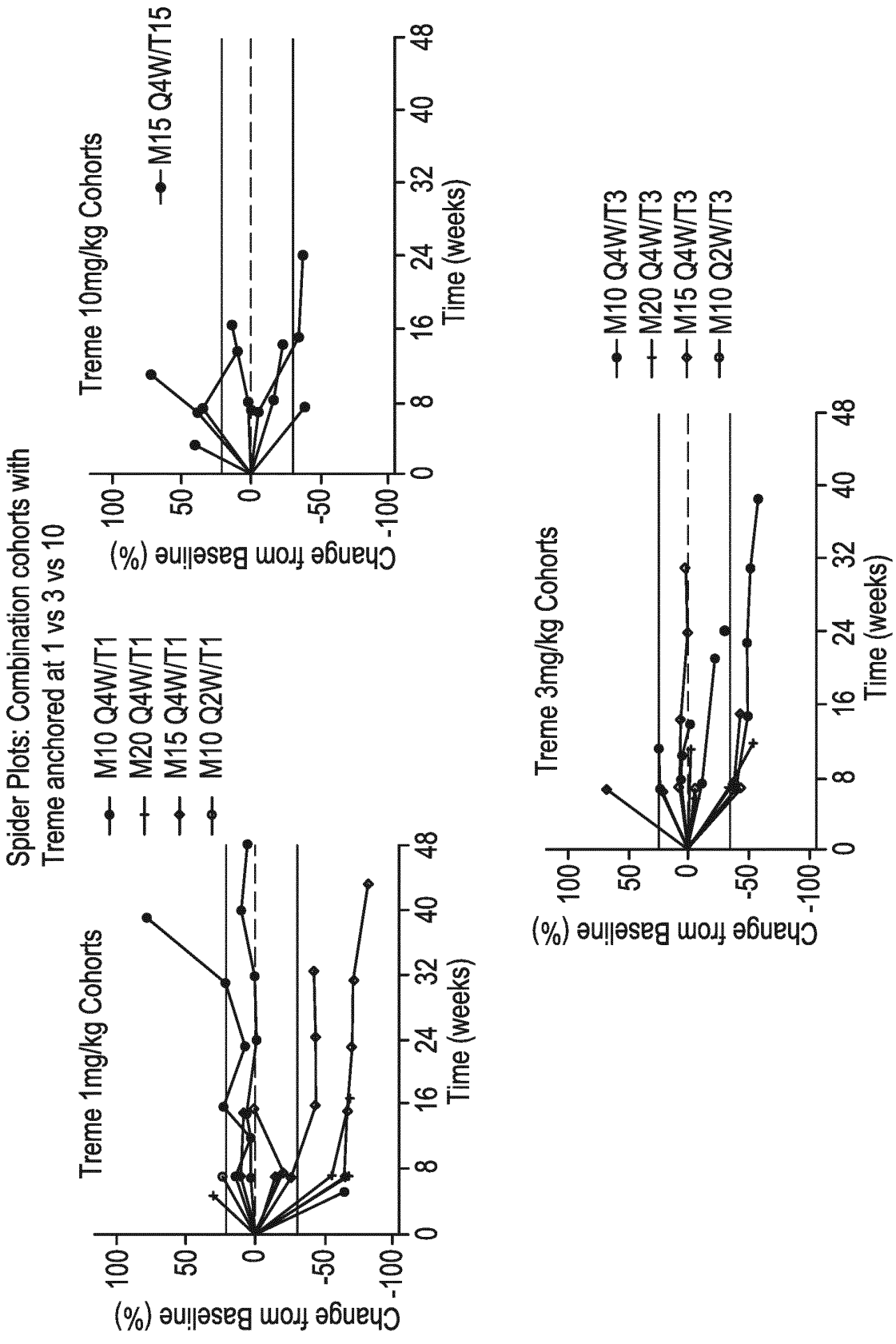

Spider Plots: Combination cohorts with
Treme anchored at 1 vs 3 vs 10
M10 Q4W/T1
M20 Q4W/T1
M15 Q4W/T1
M10 Q2W/T1
Treme 1mg/kg Cohorts
Change from Baseline (%)
Time (weeks)
Treme 10mg/kg Cohorts
M15 Q4W/T15
Change from Baseline (%)
Time (weeks)
Treme 3mg/kg Cohorts
M10 Q4W/T3
M20 Q4W/T3
M15 Q4W/T3
M10 Q2W/T3
Change from Baseline (%)
Time (weeks)

FIG. 24

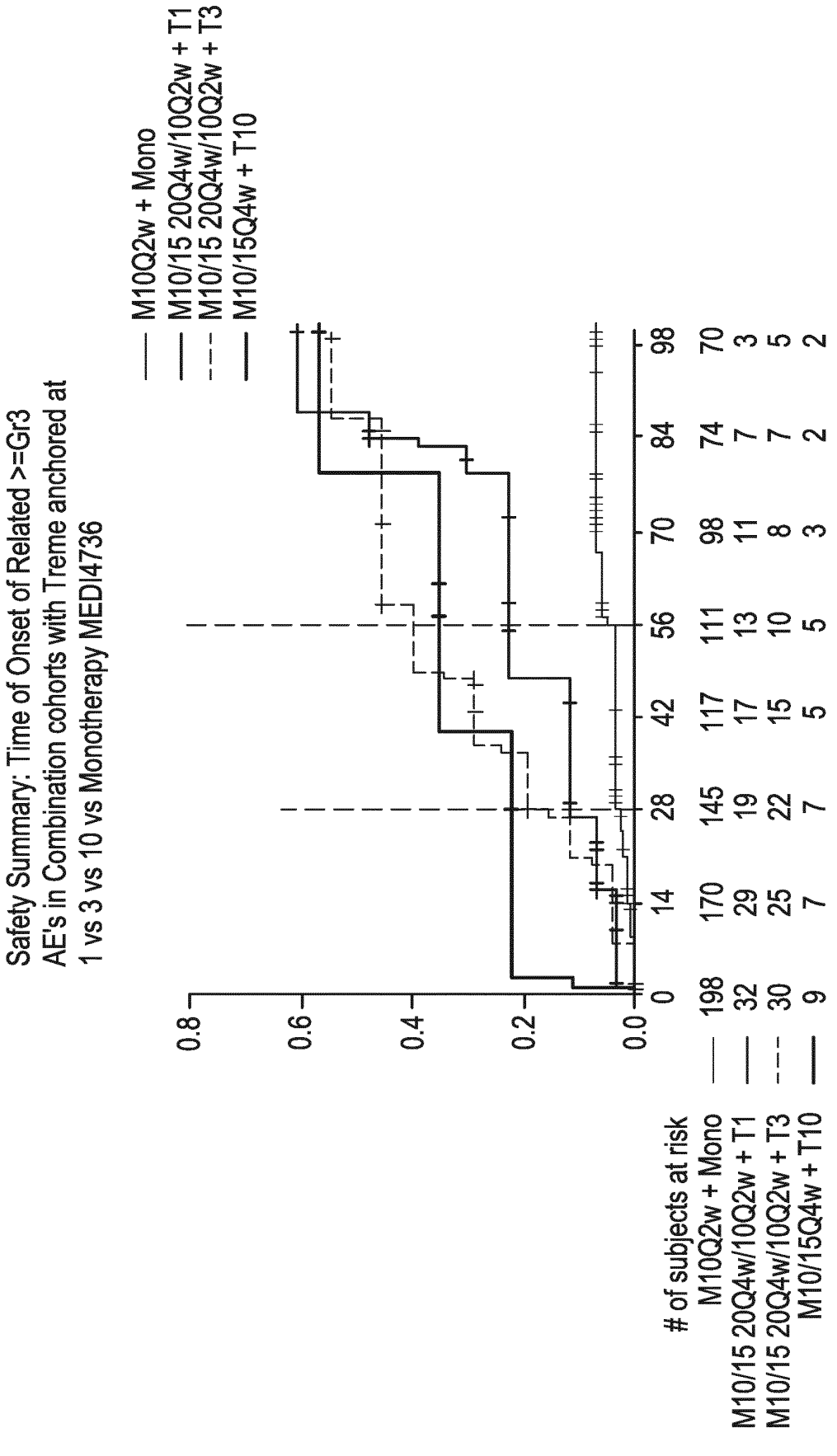

Safety Summary: Time of Onset of Related >=Gr3
AE's in Combination cohorts with Treme anchored at
1 vs 3 vs 10 vs Monotherapy MEDI4736
M10Q2w + Mono
M10/15 20Q4w/10Q2w + T1
M10/15 20Q4w/10Q2w + T3
M10/15Q4w + T10
0.8
0.6
0.4
0.2
0.0
0 14 28 42 56 70 84 98
# of subjects at risk
M10Q2w + Mono 198 170 145 117 111 98 74 70
M10/15 20Q4w/10Q2w + T1 32 29 19 17 13 11 7 3
M10/15 20Q4w/10Q2w + T3 30 25 22 15 10 8 7 5
M10/15Q4w + T10 9 7 7 5 5 3 2 2

FIG. 25

Spider Plots: Combination cohorts with MEDI4736 anchored at 10 vs 15 vs 20 Q4W 10 Q2W

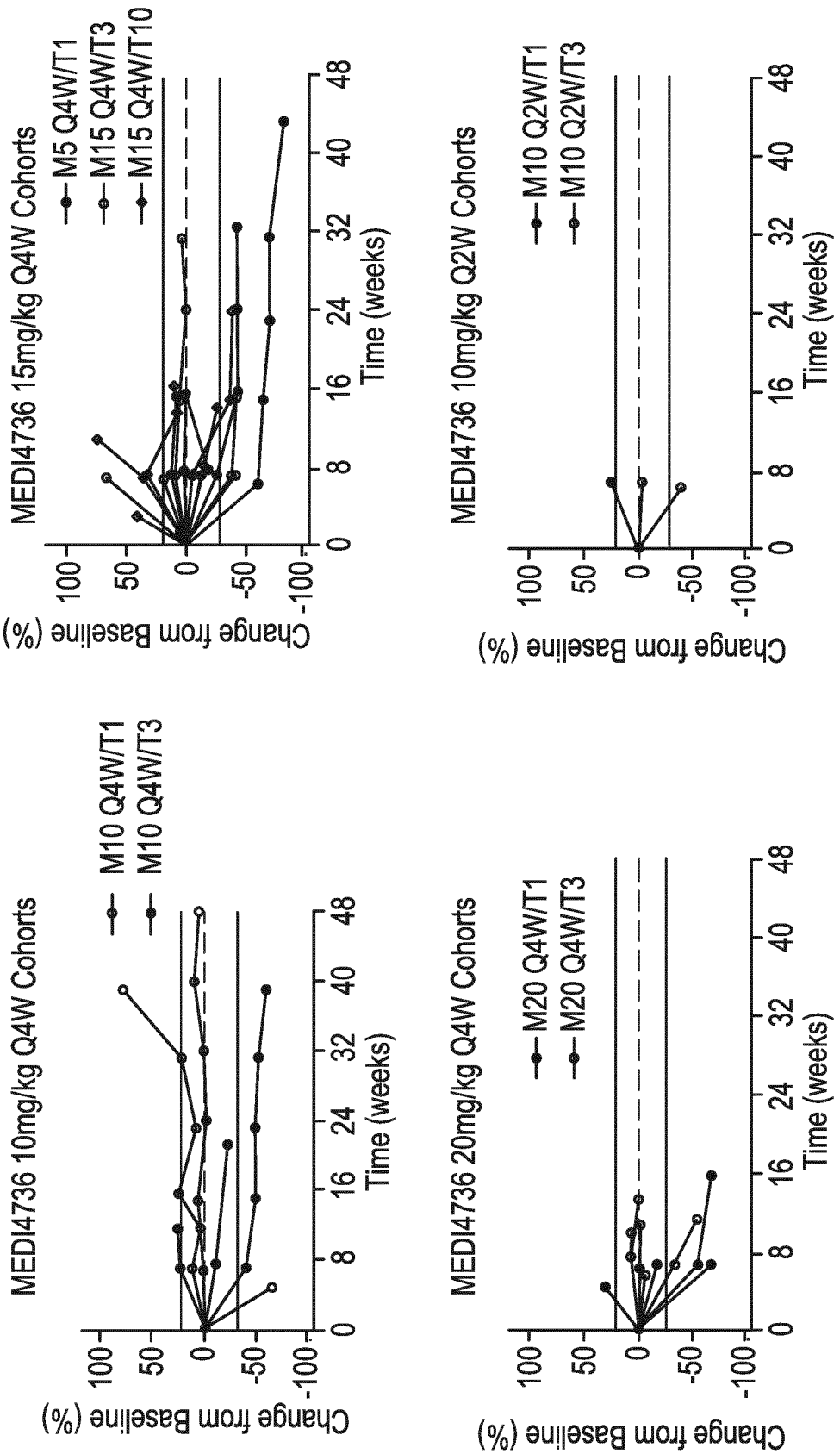


FIG. 26

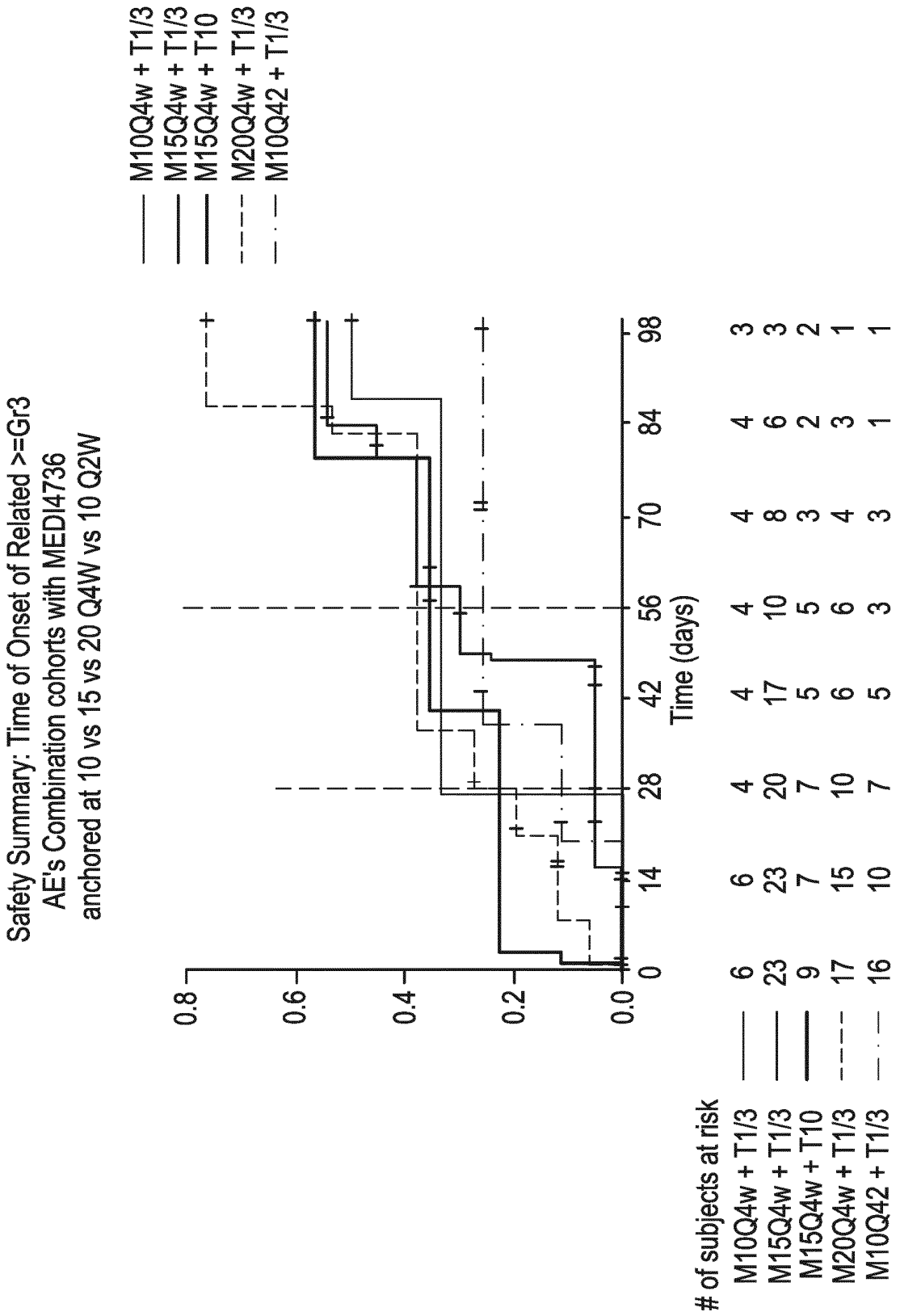

Safety Summary: Time of Onset of Related >=Gr3
AE's Combination cohorts with MEDI4736
anchored at 10 vs 15 vs 20 Q4W vs 10 Q2W
M10Q4w + T1/3
M15Q4w + T1/3
M15Q4w + T10
M20Q4w + T1/3
M10Q42 + T1/3
0.8
0.6
0.4
0.2
0.0
0
14
28
42
56
70
84
98
Time (days)
# of subjects at risk
M10Q4w + T1/3 6 6 4 4 4 4 4 3
M15Q4w + T1/3 23 23 20 17 10 8 6 3
M15Q4w + T10 9 7 7 5 5 3 2 2
M20Q4w + T1/3 17 15 10 6 6 4 3 1
M10Q42 + T1/3 16 10 7 5 3 3 1 1

FIG. 27

Clinical Activity: Combination vs MEDi4736 Monotherapy

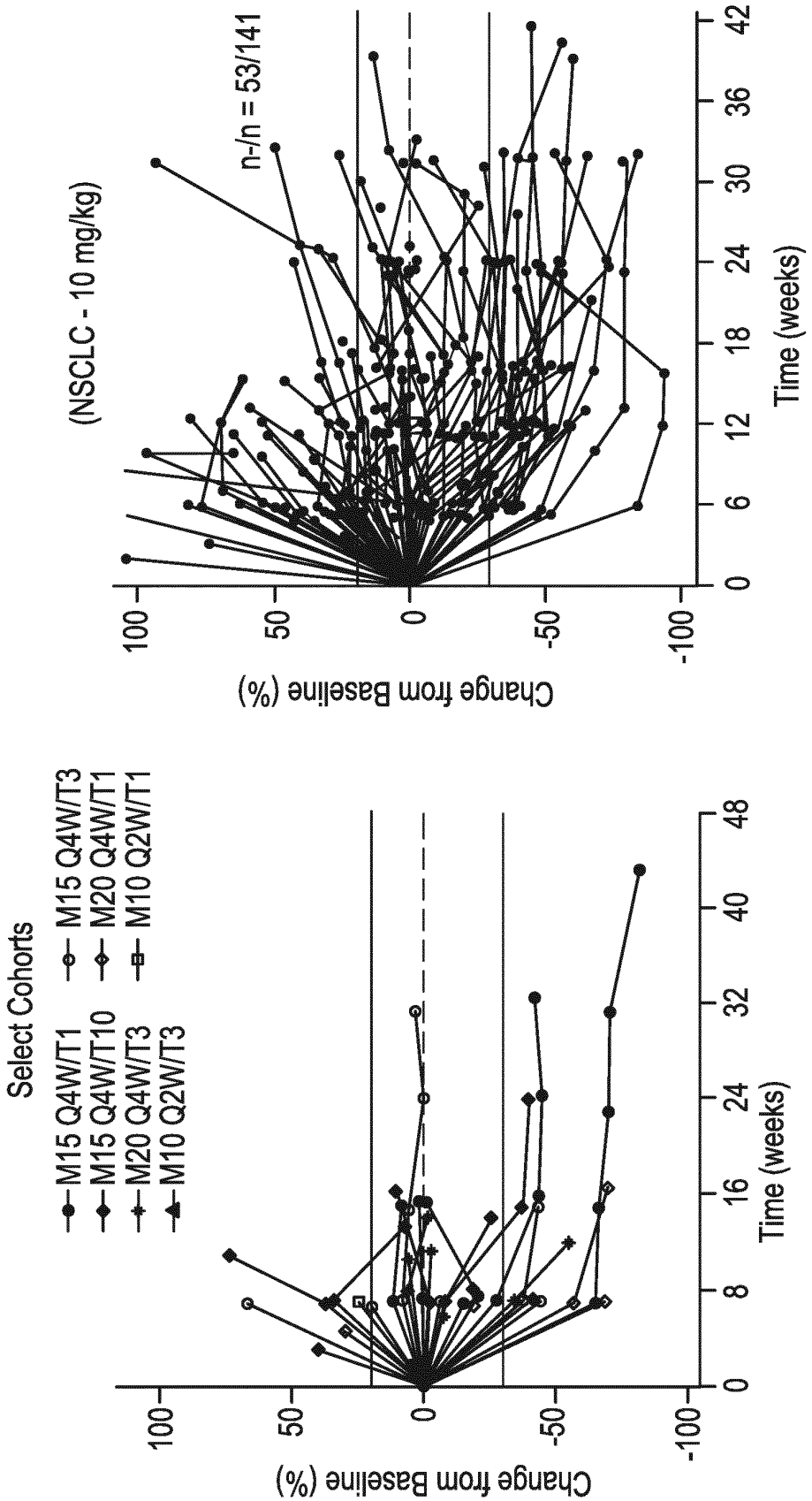


FIG. 28

Safety Summary: Time of Onset of Related >=Gr3
AE's in Selected Combination Cohorts vs.
Monotherapy MEDI4736

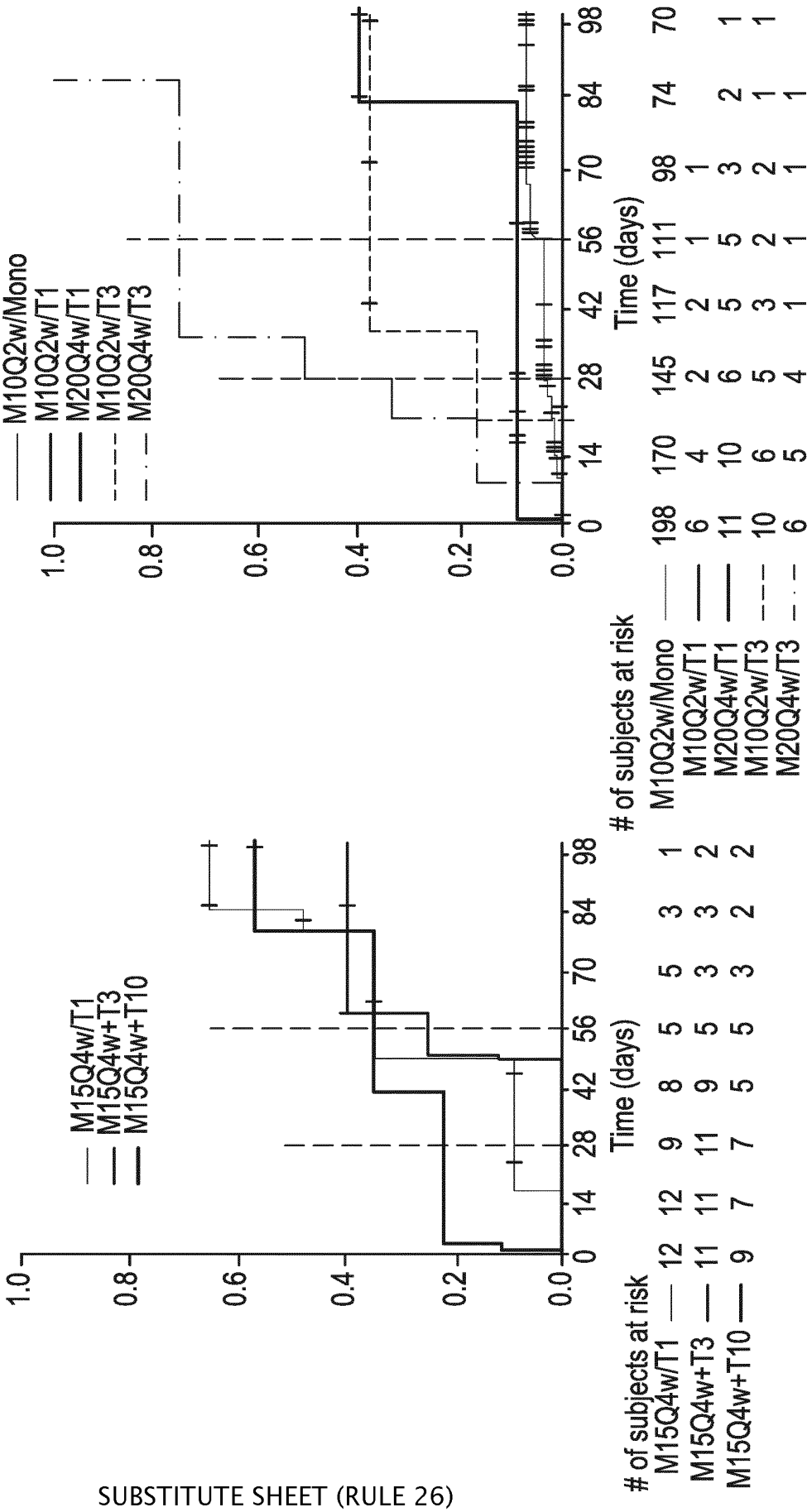


FIG. 29

Tumor Size Change from Baseline

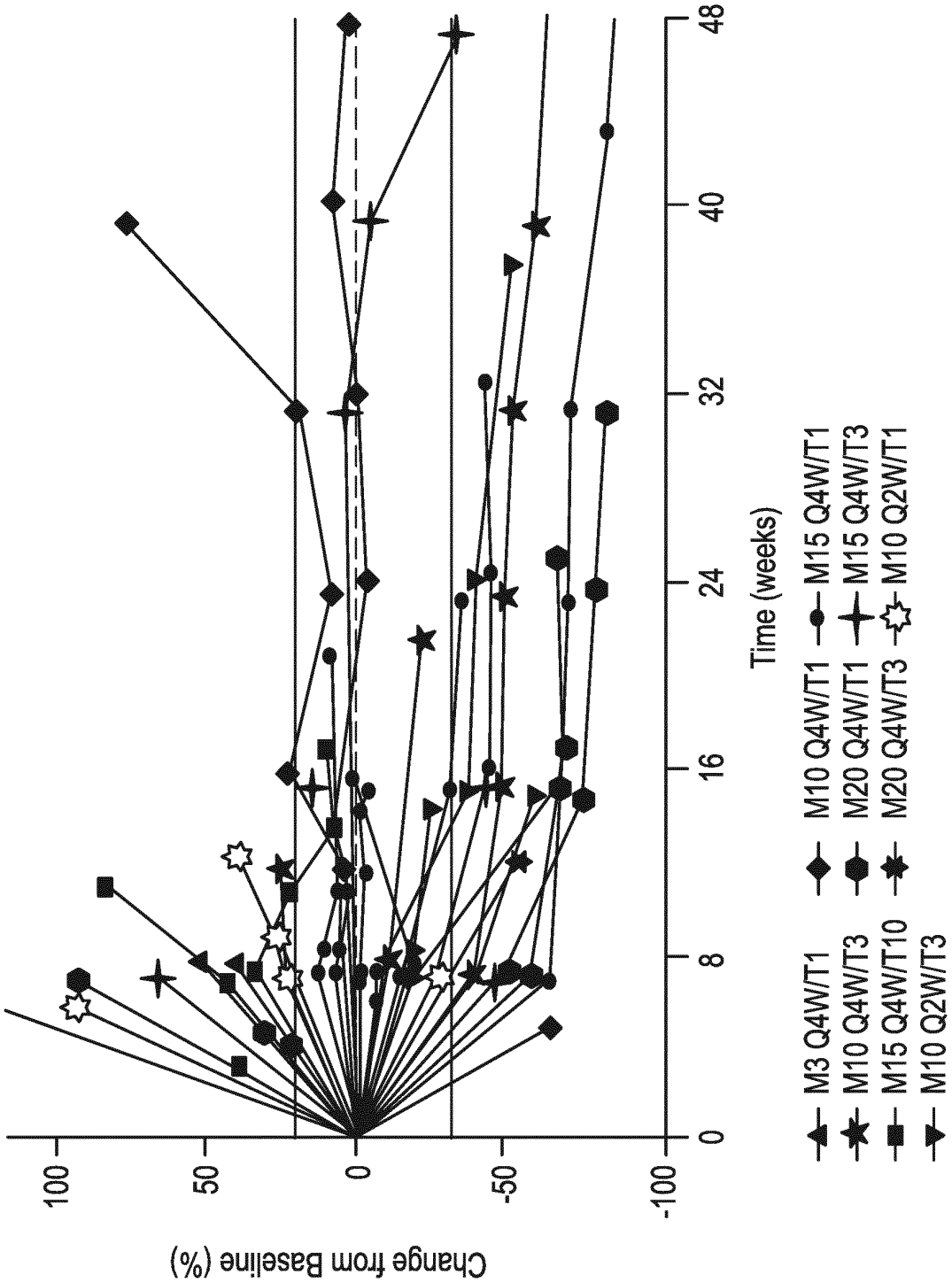


FIG. 30

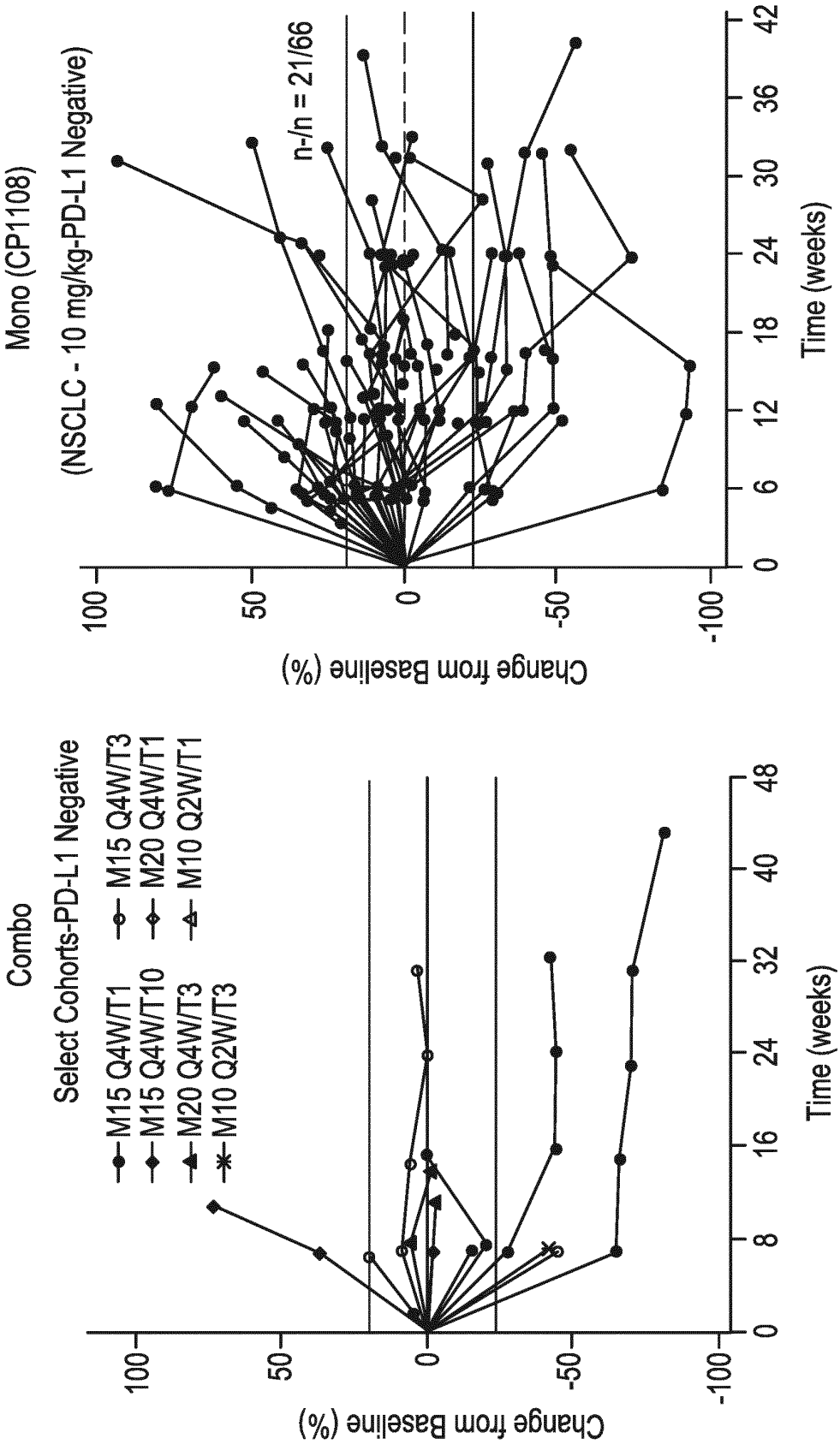

Mono (CP1108)
(NSCLC - 10 mg/kg-PD-L1 Negative)
n-/n = 21/66
Change from Baseline (%)
Time (weeks)
Combo
Select Cohorts-PD-L1 Negative
M15 Q4W/T1
M15 Q4W/T10
M20 Q4W/T3
M10 Q2W/T3
M15 Q4W/T3
M20 Q4W/T1
M10 Q2W/T1
Change from Baseline (%)
Time (weeks)

FIG. 31

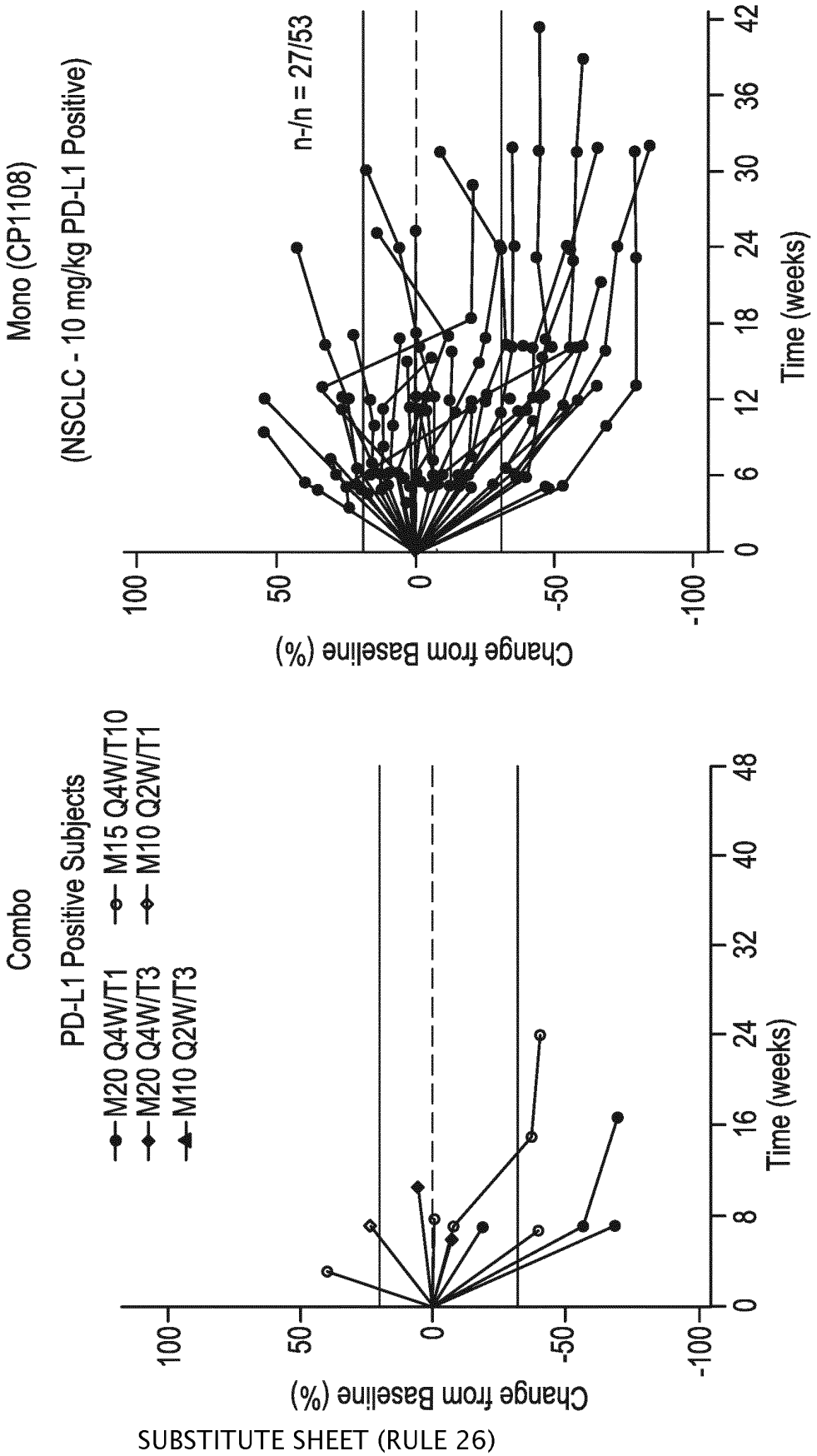

Mono (CP1108)
(NSCLC - 10 mg/kg PD-L1 Positive)
n-/n = 27/53
Change from Baseline (%)
100
50
0
-50
-100
0
6
12
18
24
30
36
42
Time (weeks)
Combo
PD-L1 Positive Subjects
M20 Q4W/T1
M20 Q4W/T3
M10 Q2W/T3
M15 Q4W/T10
M10 Q2W/T1
Change from Baseline (%)
100
50
0
-50
-100
0
8
16
24
32
40
48
Time (weeks)

FIG. 32

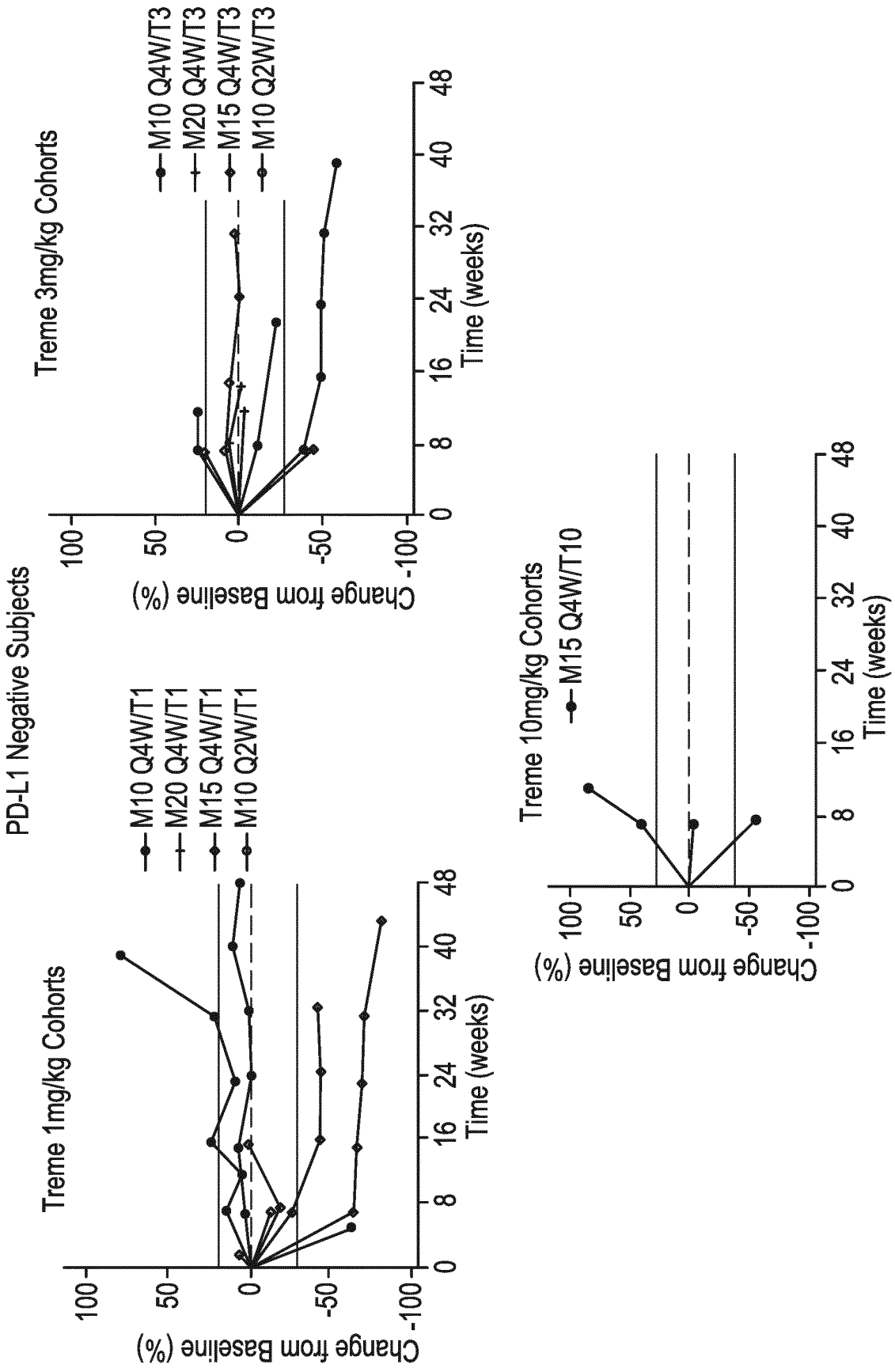
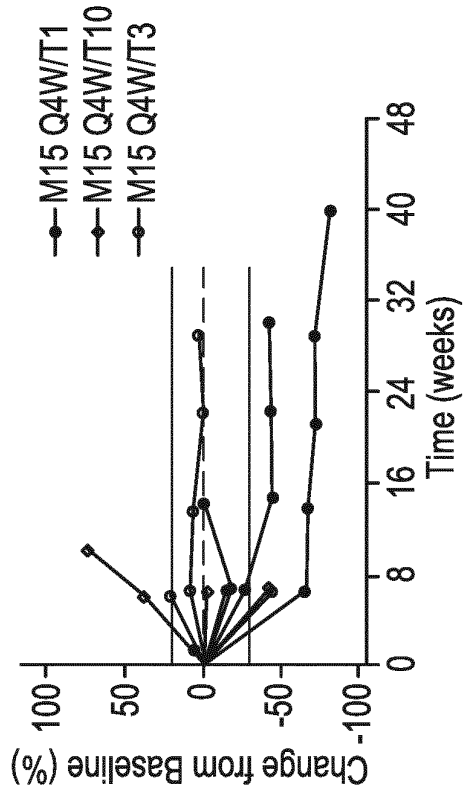
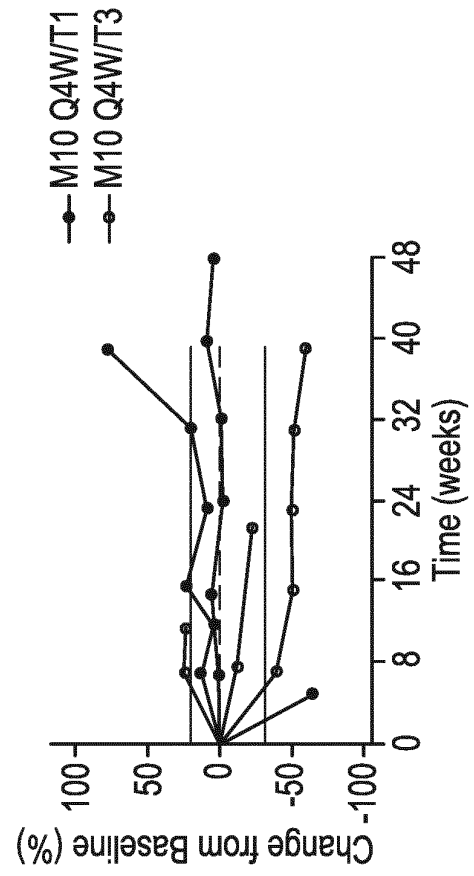
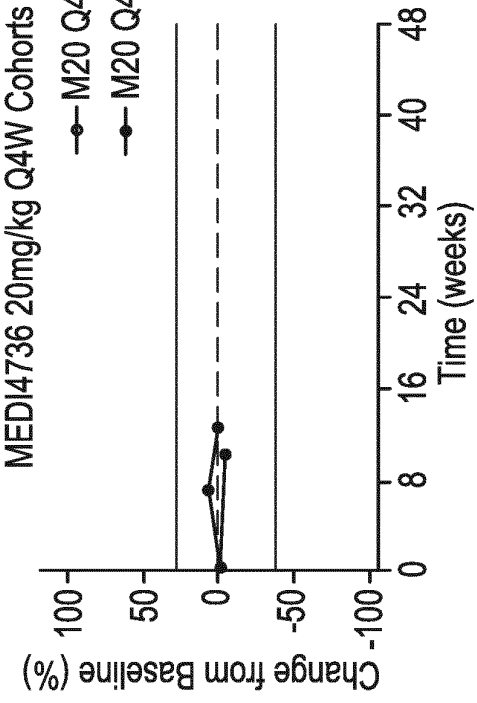

PD-L1 Negative Subjects
Treme 1mg/kg Cohorts
M10 Q4W/T1
M20 Q4W/T1
M15 Q4W/T1
M10 Q2W/T1
Change from Baseline (%)
Time (weeks)
Treme 3mg/kg Cohorts
M10 Q4W/T3
M20 Q4W/T3
M15 Q4W/T3
M10 Q2W/T3
Change from Baseline (%)
Time (weeks)
Treme 10mg/kg Cohorts
M15 Q4W/T10
Change from Baseline (%)
Time (weeks)

FIG. 33

PD-L1 Negative Subjects







No PD-L1 negative subjects in MEDI4736 10mg/kg Q2W cohorts with post-baseline disease assessment data available

FIG. 34A

Tumor Size Change from Baseline

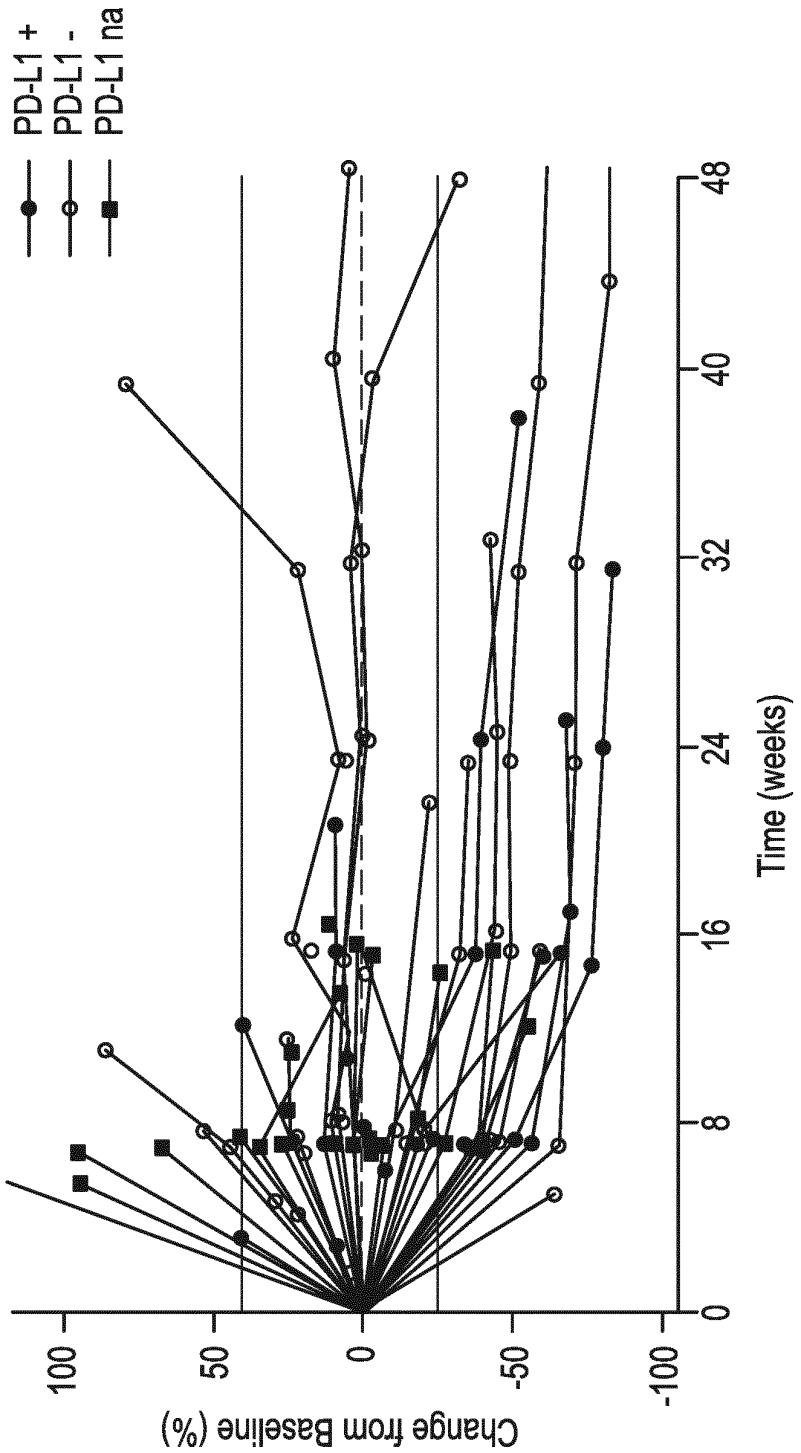


FIG. 34B

Tumor Size Change from Baseline - PD-L1 Negative Subjects

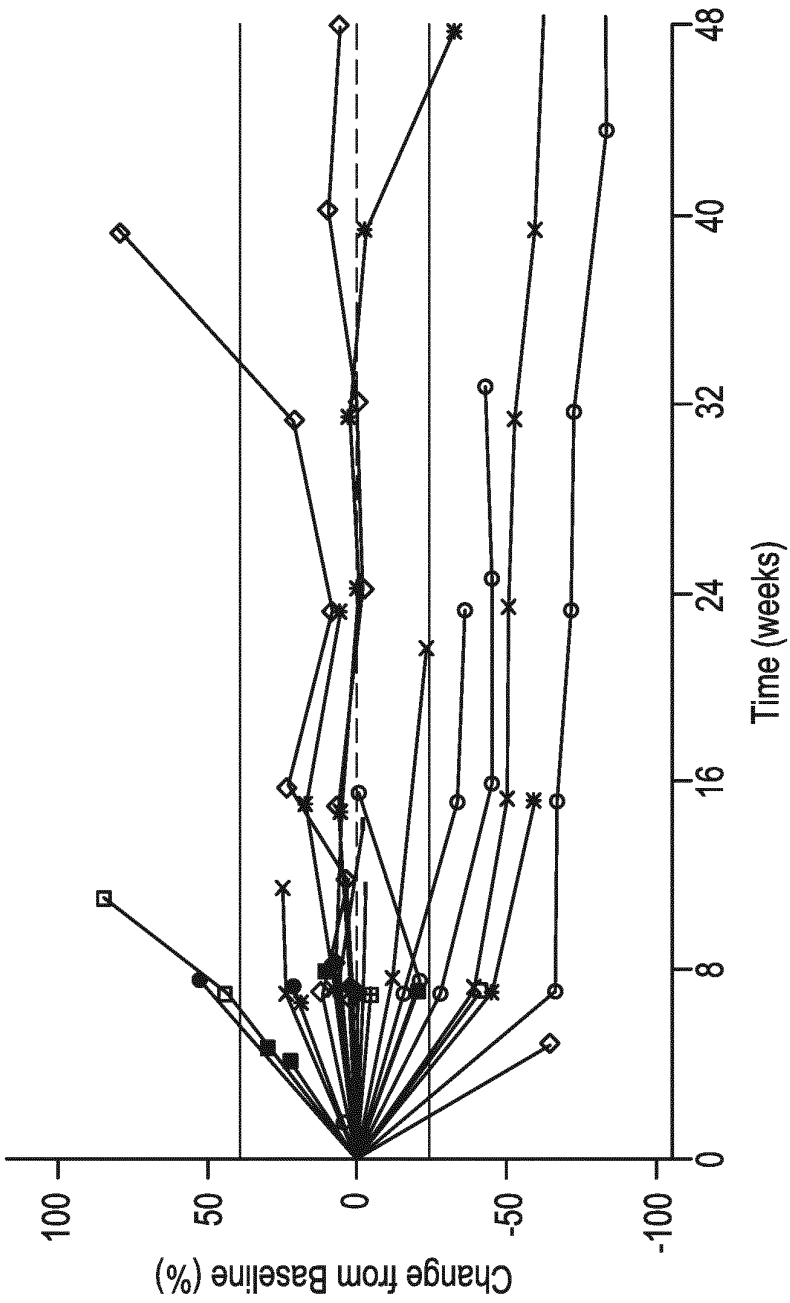


FIG. 34C

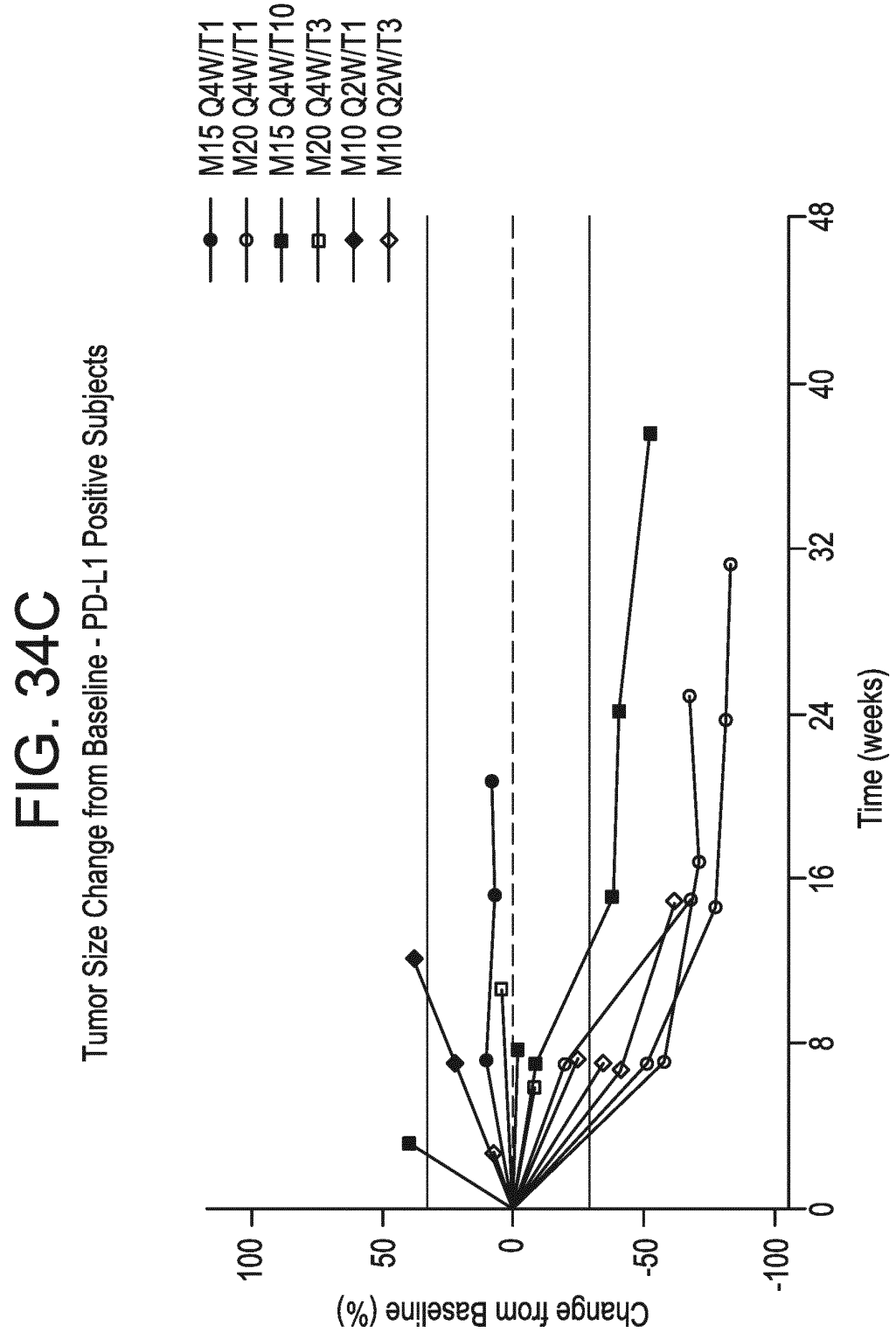

Tumor Size Change from Baseline - PD-L1 Positive Subjects
M15 Q4W/T1
M20 Q4W/T1
M15 Q4W/T10
M20 Q4W/T3
M10 Q2W/T1
M10 Q2W/T3
Change from Baseline (%)
100
50
0
-50
-100
0
8
16
24
32
40
48
Time (weeks)

FIG. 34D

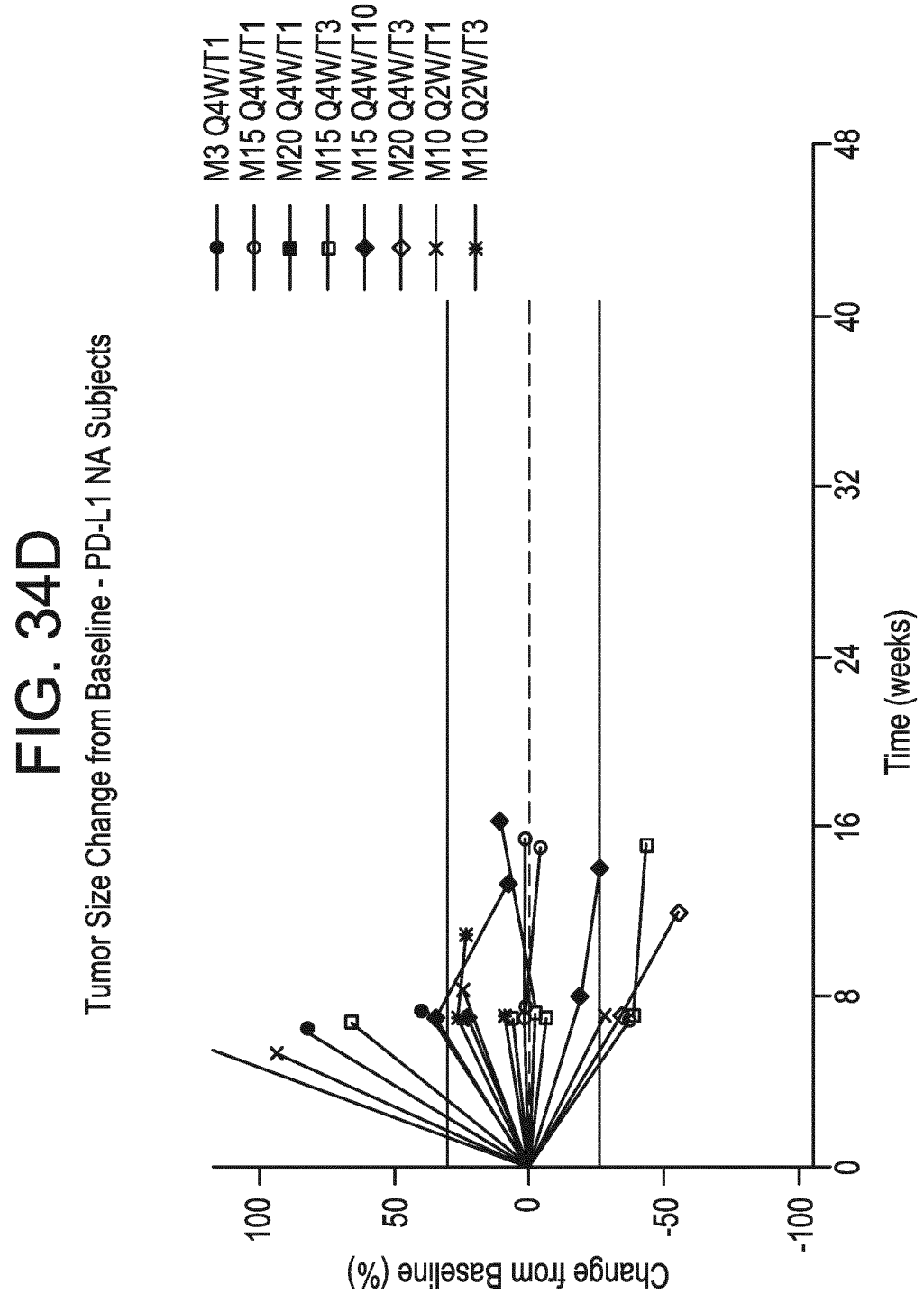

Tumor Size Change from Baseline - PD-L1 NA Subjects
M3 Q4W/T1
M15 Q4W/T1
M20 Q4W/T1
M15 Q4W/T3
M15 Q4W/T10
M20 Q4W/T3
M10 Q2W/T1
M10 Q2W/T3
Change from Baseline (%)
100
50
0
-50
-100
0
8
16
24
32
40
48
Time (weeks)

FIG. 35

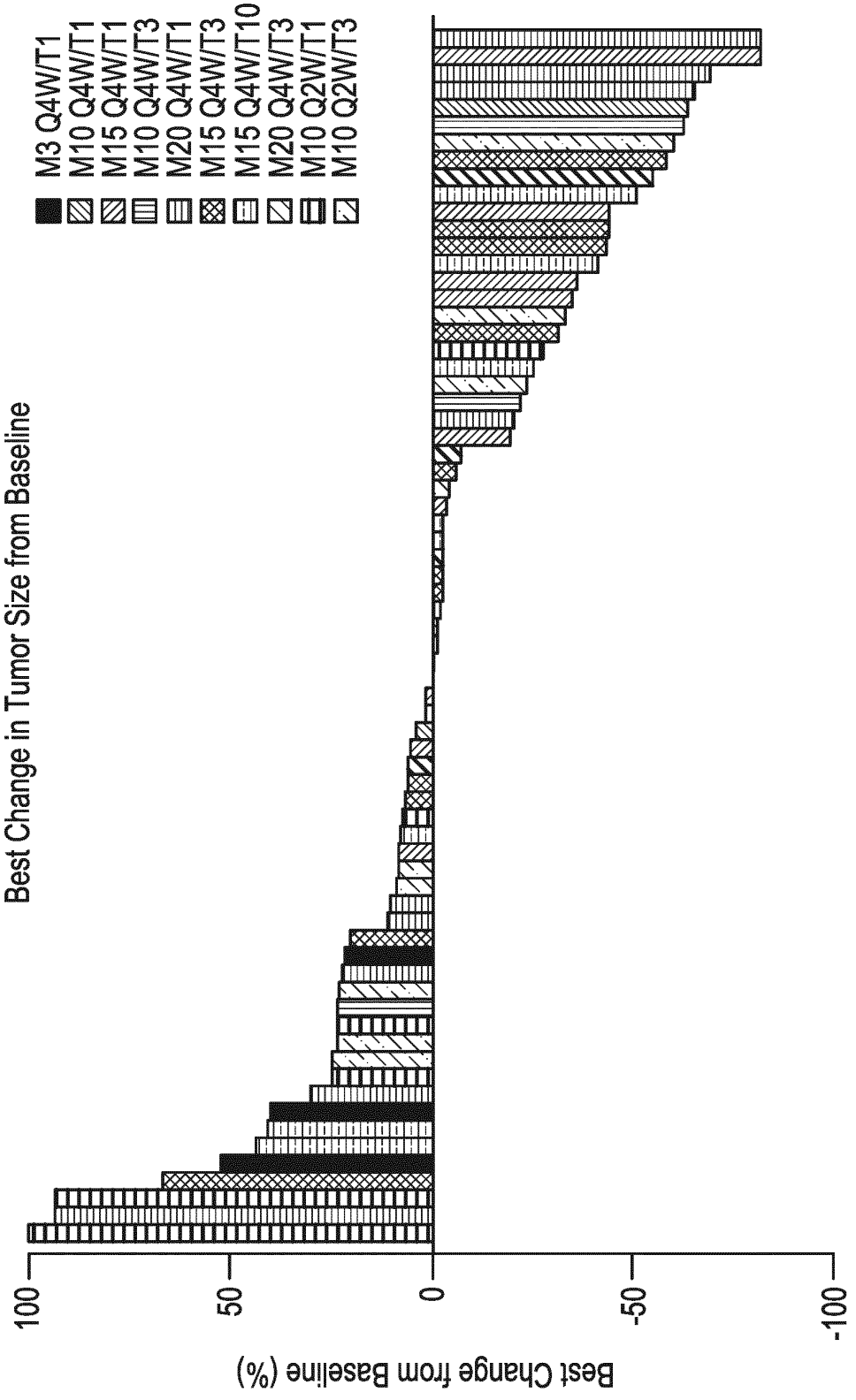

Best Change in Tumor Size from Baseline
M3 Q4W/T1
M10 Q4W/T1
M15 Q4W/T1
M10 Q4W/T3
M20 Q4W/T1
M15 Q4W/T3
M15 Q4W/T10
M20 Q4W/T3
M10 Q2W/T1
M10 Q2W/T3
100
50
0
-50
-100
Best Change from Baseline (%)

FIG. 36

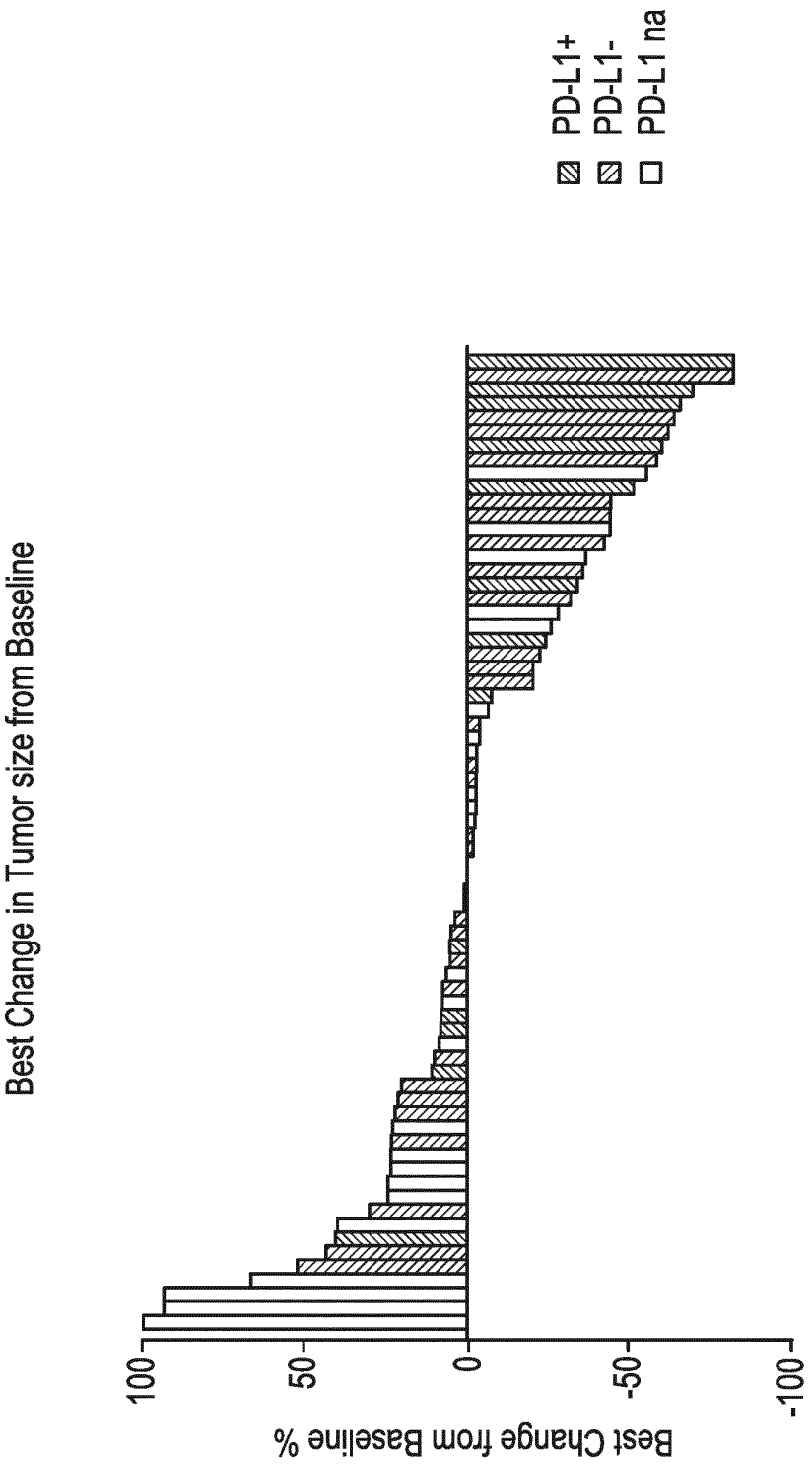
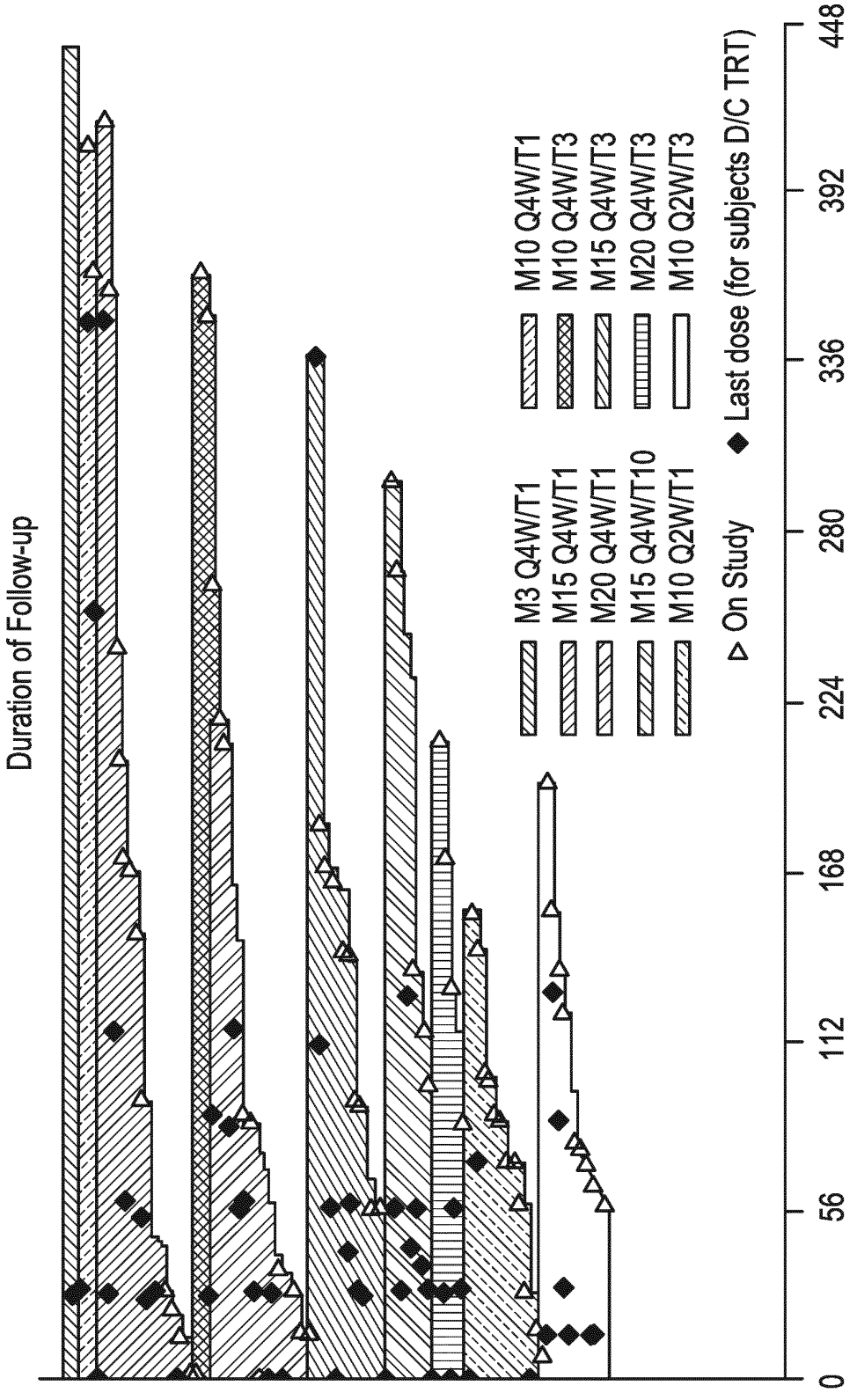

Best Change in Tumor size from Baseline
PD-L1+
PD-L1-
PD-L1 na
100
50
0
-50
-100
Best Change from Baseline %

FIG. 37


Duration of Follow-up
M3 Q4W/T1
M15 Q4W/T1
M20 Q4W/T1
M15 Q4W/T10
M10 Q2W/T1
M10 Q4W/T1
M10 Q4W/T3
M15 Q4W/T3
M20 Q4W/T3
M10 Q2W/T3
On Study
Last dose (for subjects D/C TRT)
0
56
112
168
224
280
336
392
448
Days since Treatment Initiation