Initial results of a phase I study of TNB-383B, a BCMA x CD3 bispecific T-cell redirecting antibody, in relapsed/refractory multiple myeloma

Cesar Rodriguez, Anita D'Souza, Nina Shah, Peter M. Voorhees, Ben Buelow, Ravi Vij, and Shaji Kumar

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Disclosures

Cesar Rodriguez: *Consultancy*: BMS, Takeda, Amgen

Anita D'Souza: *Consultancy*: Akcea, Imbrium, Janssen, Pfizer; *Research Funding*: Amgen, Merck, Teneobio

Nina Shah: *Consultancy*: GSK, Amgen, Indapta, Sanofi, BMS, CareDx, Kite, Karyopharm; *Research Funding*: BMS, Janssen, Bluebird bio, Sutro, Teneobio, Poseida, Nektar; *Equity*: Indapta

Peter Voorhees: *Personal fees*: Adaptive, BMS, Celgene, Janssen, Novartis, Oncopeptides, Teneobio; *Current employment*: Levine Cancer Institute

Ben Buelow: *Current Employment*: Teneobio

Ravi Vij: *Research Funding*: BMS, Celgene, Takeda; Honoraria: BMS, Celgene, Genentech, Janssen, Karyopharm, Sanofi, Takeda

Shaji Kumar: *Consultancy*: Abbvie, Takeda, Janssen, Amgen, Merck, Adaptive, Celgene, Genentech, Oncopeptides, Kite, Karyopharm, BMS, Genecentrix; *Research Funding*: Amgen, Merck, Kite, Novartis, Sanofi, Medimmune, BMS, Teneobio, Carsgen; *Other*: Abbvie, Takeda, Janssen, Amgen, Celgene, Genentech, Teneobio, Cellectar, Carsgen

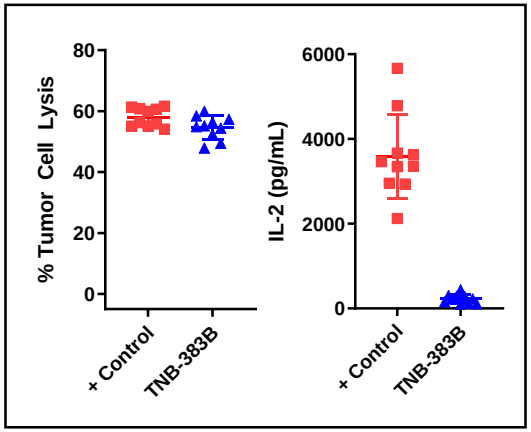
Novel Therapies are Needed in Relapsed/Refractory Myeloma (RRMM)

- **Multiple Myeloma (MM) Patients refractory to available therapies have a median OS of < 1 year[1]**
- **B-Cell Maturation Antigen (BCMA) is a cell-surface protein widely expressed in MM**
- **BCMA-Targeted approaches show promise but also have limitations**
  - **Chimeric Antigen Receptor T-Cells (CAR-Ts)[2]**
    - ORR 80%+
    - CRS 76 – 90% (Grade ≥ 3 in 5 – 9%)
  - **Antibody-Drug Conjugates (ADCs)[2]**
    - ORR 31%
    - Keratopathy Grade ≥ 3 in 21 – 26%
  - **Existing T-Cell Engaging Bispecific Antibodies (TCEs)[3 - 6]**
    - ORR 60 – 80% at active doses
    - CRS 37 – 80% (Grade ≥ 3 in 5 – 9%)
    - Q1W dosing

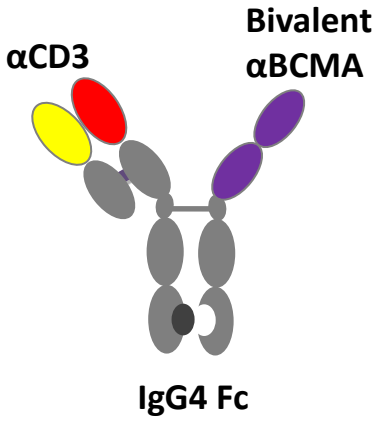
[1]Gandhi UH, *et al.* Leukemia. 2019; 33:2266-75
[2]Shah N, *et al*. Journal for ImmunoTherapy of Cancer 2020;8:e000734.
[3]Harrison et al. Abstract #181. ASH 2020
[4]Lesokhin et al. Abstract #3206. ASH 2020
[5]Garfall et al. Abstract #180. ASH 2020
[6]Madduri et al. Abstract #291. ASH 2020

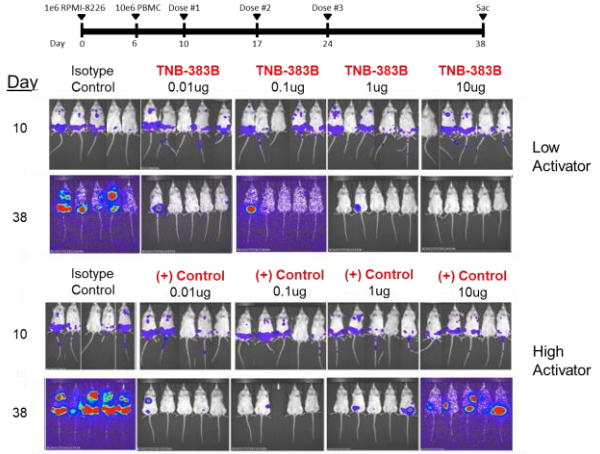
TNB-383B is a Novel BCMA x CD3 TCE to Treat RRMM

- **TNB-383B is a fully-human triple-chain BCMA x CD3 antibody designed to overcome the limitations of existing therapies**
  - Unique αCD3 moiety: Target lysis with minimal cytokine release
  - 2 αBCMA domains: Favors cell surface BCMA binding
  - Silenced IgG4 backbone: Prevents nonspecific T-cell activation, 2 – 3 week half-life
- **Activity in *in vitro, in vivo*, and *ex vivo* models of MM without toxic cytokine secretion**
  - Compared to positive control incorporating a strong αCD3



Cytokine Release and Tumor Cell Lysis mediated by Positive Control or TNB-383B by PBMCs in 10 healthy donors.
Trinklein, ND, et al. mAbs. 2019; mAbs, 11:4, 639-652





TNB383B.0001: NCT03933735

Phase 1 Escalation/Expansion Study of TNB-383B in RRMM

Key Eligibility Criteria

- 3 Prior lines including a PI, an IMiD, and an anti-CD38 mAb
- Hgb ≥ 8 g/dL, ANC ≥ 1 x 10^9 / L, Platelets ≥ 50 x 10^9 / L
- ECOG ≤ 2
- eGFR ≥ 30 mL/min
- Prior BCMA-targeted therapy prohibited

Key Design Features

- 3 + 3 with backfilling to 9 subjects permitted
- IV Administration over 1 – 2 hours
- Fixed (as opposed to weight-based) dosing
- Q3W Schedule
- Intra-patient dose escalation permitted, to highest safe dose
- No mandatory on-study biopsies

Cohort	Dose (mg Q3W)	Enrolled
1	0.025	3
2	0.075	3
3	0.2	3
4	0.6	3
5	1.8	3
6	5.4	6
7	10	9
8	20	7
9	30	6
10a	40	6
10b	50	3
11	60	6
12+	Up to +50%	

Expand at MTD or RP2D

Escalation data through 60 mg / dose are presented (NCT03933735)

Demographics, Disease Characteristics and Disposition

Demographics	Enrolled (n = 58)
Age, median (range)	66 (37 - 88)
Gender	
Female, n (%)	23 (40)
Male, n (%)	35 (60)
Race	
Black or African American, n (%)	12 (21)
White, n (%)	45 (78)
Not Reported, n (%)	1 (2)

Subject Disposition	Enrolled (n = 58)
Continuing Treatment, n (%)	25 (43)
Discontinued, n (%)	33 (57)
Progressive Disease, n (% of Discontinued)	30 (91)
Dose-limiting Toxicity, n (% of Discontinued)	1 (3)
COVID-19, n (% of Discontinued)	2 (6)

Disease Characteristics	Enrolled (n = 58)
MM Subtype	
IgG, n (%)	30 (52)
IgA, n (%)	12 (21)
Light Chain, n (%)	13 (22)
Other, n (%)	3 (5)
ECOG at Screening	
Grade 0, n (%)	15 (26)
Grade 1, n (%)	33 (57)
Grade 2, n (%)	9 (16)
ISS Stage III, n (%)	19 (33)
Prior Lines of Therapy, median (range)	6 (3 - 15)
Triple-class Exposed[a], n (%)	58 (100)
Penta-drug Exposed[b], n (%)	44 (76)
Triple-class Refractory, n (%)	37 (64)
Penta-drug Refractory, n (%)	20 (34)
Progressed on Last Line[c], n (%)	47 (81)

[a]PI, IMiD, and anti-CD38 mAb (Daratumumab or Isatuximab)
[b]PI x2, IMiD x2, and anti-CD38 mAb (Daratumumab or Isatuximab)
[c]Progressive disease on or within 60 days of last regimen

CRS Was the Most Common AE on Study

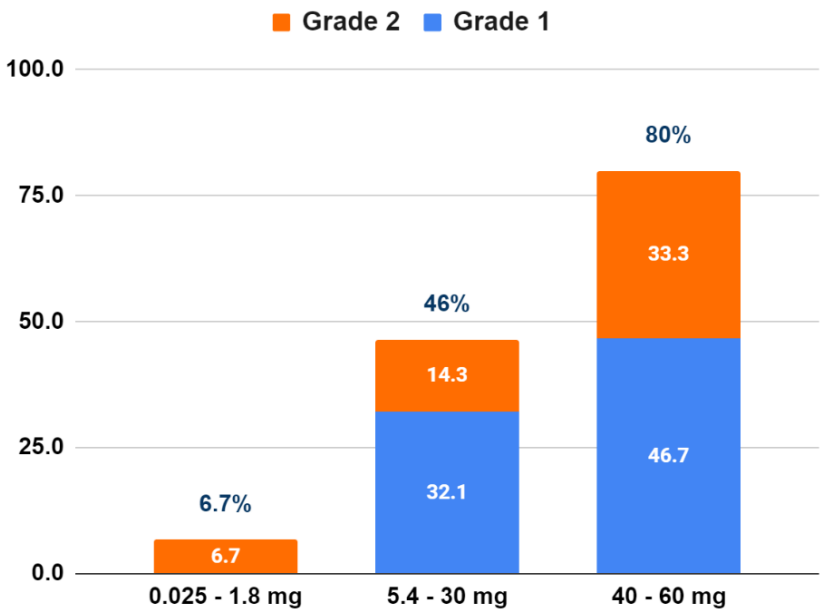
Common AEs[a], n (%)	Enrolled (n = 58)	
	All Grade	≥ Grade 3
Hematological		
Anemia	12 (21)	10 (17)
Neutropenia[b]	11 (19)	9 (16)
Thrombocytopenia[c]	10 (17)	8 (14)
Nonhematological		
Cytokine release syndrome	26 (45)	0 (0)
Fatigue	14 (24)	1 (2)
Headache*	13 (22)	1 (2)
Infection[d]	12 (21)	8 (14)
Nausea	12 (21)	0 (0)
Fever*	9 (16)	1 (2)
Vomiting	8 (14)	0 (0)
Chills*	7 (12)	0 (0)
Diarrhea	7 (12)	0 (0)
Hypomagnesemia	7 (12)	0 (0)

[a]Adverse events of any grade that occur in ≥ 10% of subjects
[b]Includes neutrophil count decrease
[c]Includes platelet count decrease
[d]Includes bacterial, fungal, viral, and unspecified pathogens
*CRS associated AEs

Adverse Events, n (%)	All	0.025 - 1.8 mg	5.4 - 30 mg	≥ 40 mg
Subjects	n=58	n=15	n=28	n=15
TEAE of any Grade	51 (88)	13 (87)	26 (93)	12 (80)
TEAE ≥ Grade 3	33 (57)	9 (60)	18 (64)	6 (40)
SAE	19 (33)	5 (33)	10 (36)	4 (27)
TRAE	36 (62)	10 (67)	14 (50)	12 (80)

- **No marked increase in incidence of non-CRS AEs with higher doses of TNB-383B**
- **TRAE increased at doses ≥ 40mg due to ↑ CRS**
- **2 DLTs observed. Both resolved without sequelae.**
  - Gr3 Confusion at 20 mg: not ICANS-related
  - Gr4 Thrombocytopenia at 60 mg
- **2 Deaths on study, both due to COVID-19**
  - Not study drug-related

No Grade 3 CRS Observed at Any Dose



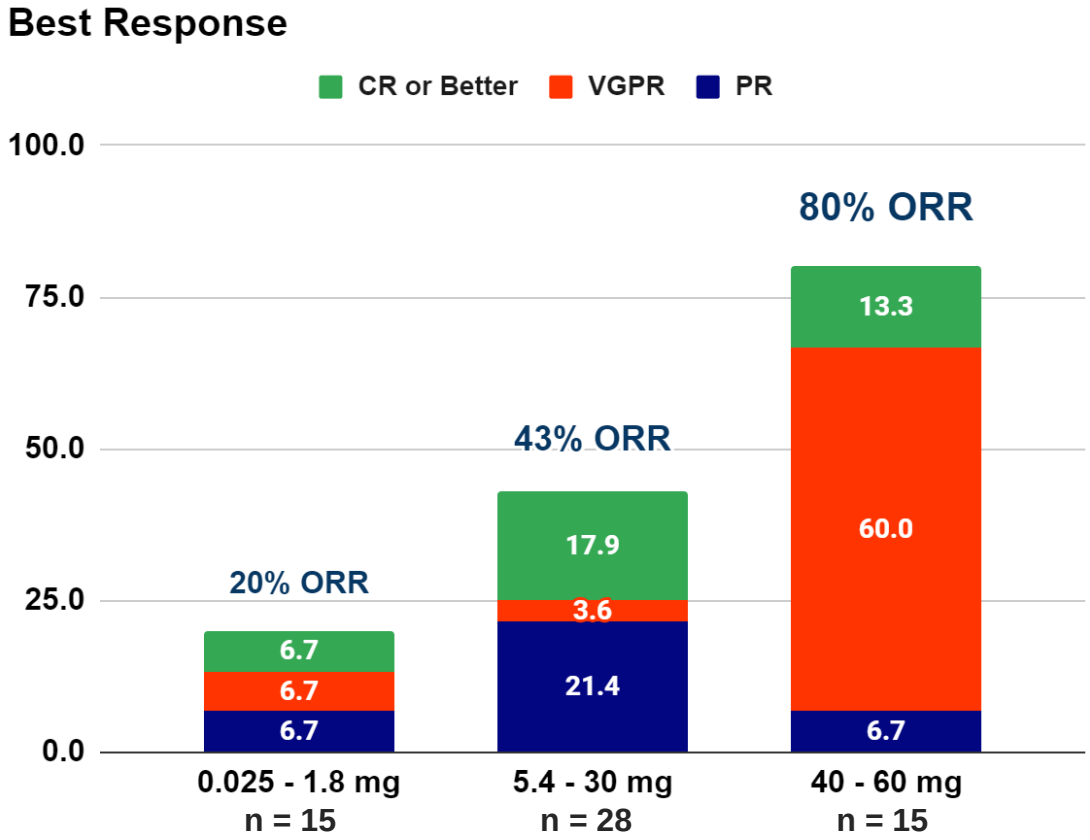
Graded according to CTCAE v5.0

CRS Summary	Enrolled (n = 58)
Subjects with CRS, n (%)	26 (45)
Onset time, median days (range)	<1 (0 - 7)
Duration of CRS, median days (range)	1 (1 - 7)
Subjects treated with Tocilizumab, n (%)	5 (9)
Subjects treated with Dexamethasone*, n (%)	0 (0)

*Does not include use for premedication

- **Minimally worsening severity of CRS with increased doses of TNB-383B**
- **Re-occurrence of CRS post-C1 in only one subject**
  - No CRS in subjects undergoing intra-patient dose escalation
- **Step- / split-dosing not required**
  - TNB-383B administered as bolus at all dose levels

80% ORR Seen at Doses ≥ 40 mg of TNB-383B



- 3 / 4 MRD-evaluable subjects MRD-Negative (2 at 10^{-6} , 1 at 10^{-5})
- Responses continue to deepen with ongoing treatment

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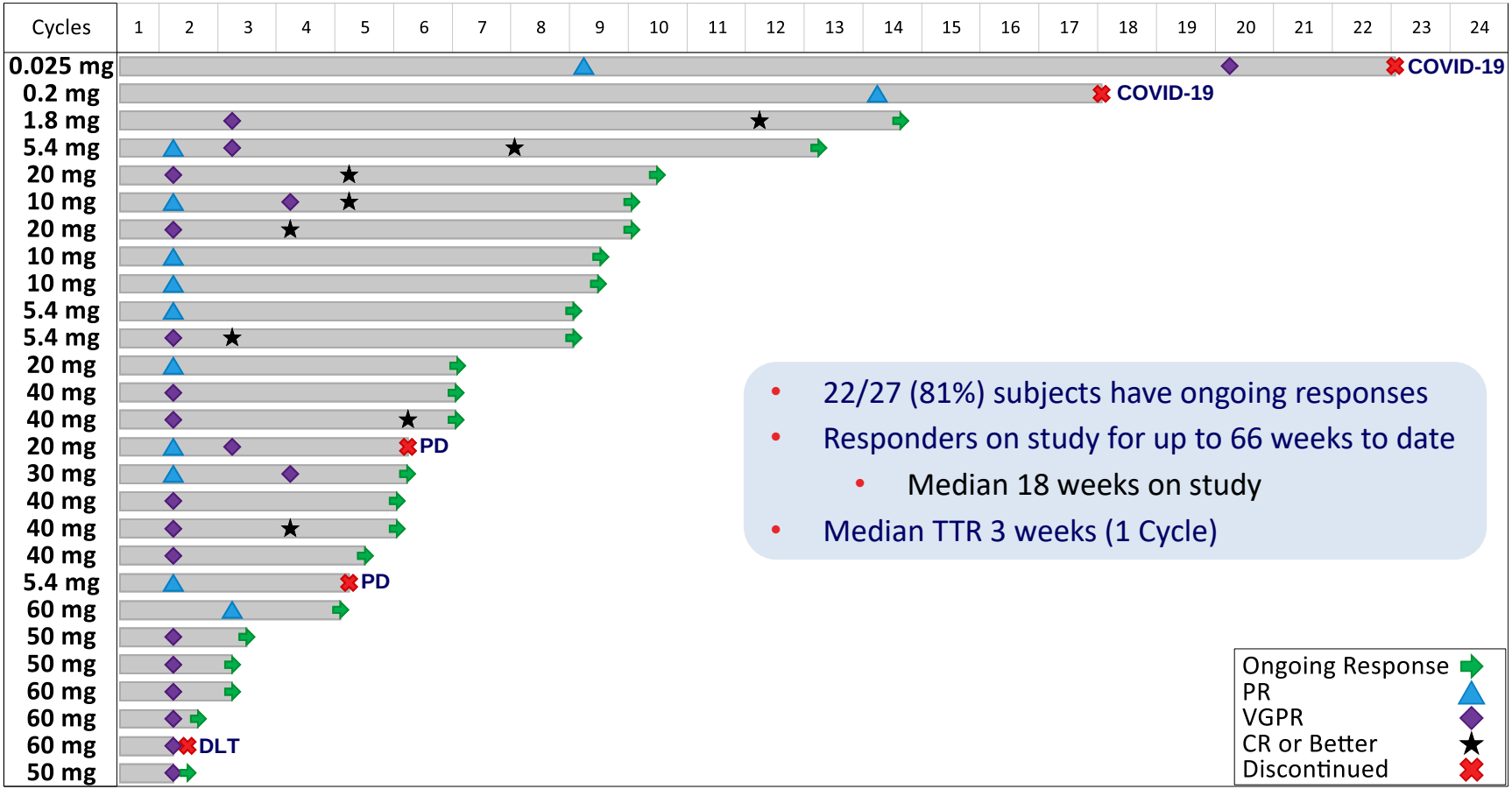
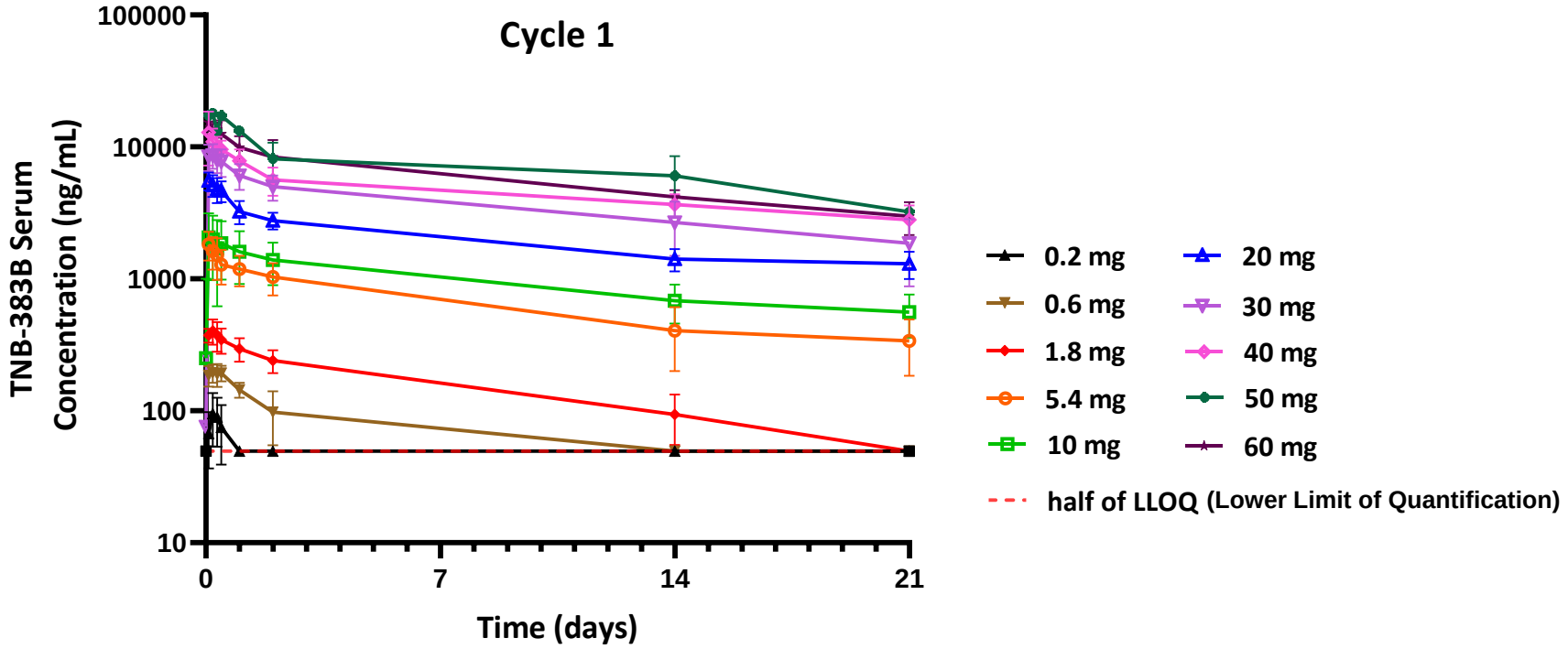
[1]Activity assessment based performed centrally

Durable Ongoing Responses Up to 39 Weeks Observed



- 22/27 (81%) subjects have ongoing responses
- Responders on study for up to 66 weeks to date
  - Median 18 weeks on study
- Median TTR 3 weeks (1 Cycle)

15 – 18 Day Preliminary Half-Life Supports Q3W Dosing



- Preliminary Half-life of 15-18 days at doses ≥ 20 mg supports Q3W dosing schedule
- PK approximately dose proportional from 5.4 – 60 mg

Case Study: Subject receiving 40 mg / Dose

Demographics

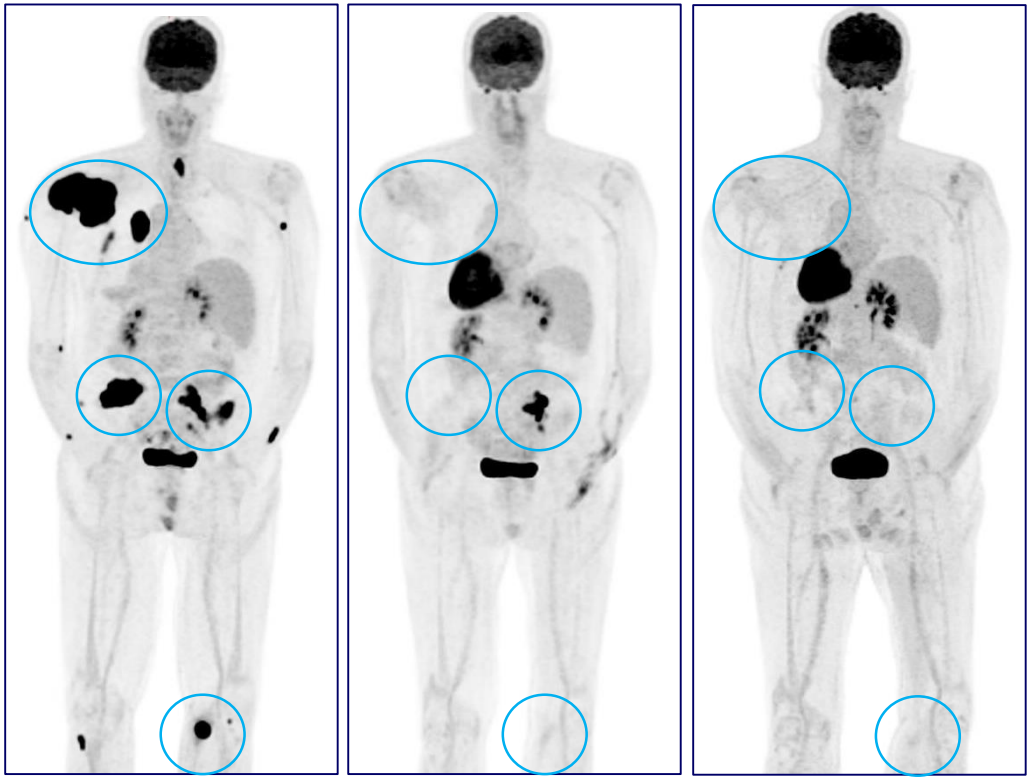
- 59 years old
- Male
- African-American

Medical Hx, Disease Type, Prior Rx

- Initial Diagnosis Date: Apr 2019
- R-ISS Stage: II
- Type: Lambda Light Chain
- High-risk cytogenetics (incl. del17p)
- 5 Prior lines of therapy
- Refractory to: Car, Pom, Dara, Len

Study Course

- CRS Grade 2 in Cycle 1, Grade 1 in Cycle 3
- VGPR at C2D1, ongoing x12 weeks
- Soft tissue plasmacytomas up to 15 cm resolved after 1 dose



Screening | Cycle 2 | Cycle 5

TNB-383B is a Novel BCMA x CD3 TCE to Treat RRMM

- **TNB-383B was well tolerated at all tested doses**
  - **CRS seen in 26 (45%) subjects**
    - Grade 1 – 2 in all cases
    - No Step- or Split-dosing
    - Confined to Cycle 1 in all but one subject
    - Tocilizumab used in 5 (<10%) subjects
  - **Most common Gr ≥ 3 TEAEs: Anemia (17%), Neutropenia (19%), Thrombocytopenia (17%), and Infection (14%)**
- **ORR 80% at doses ≥ 40 mg / dose in heavily pretreated subjects with a median of 6 prior lines**
  - **73% VGPR or better at ≥ 40 mg**
  - **22/27 responses ongoing; responses appear durable (up to 39 weeks to date)**
- **Q3W Dosing starting at C1D1**
  - **48 hours inpatient at <u>C1D1 only</u>**
- **The Escalation and Expansion portions of the study are ongoing**

Acknowledgments

- **The patients taking part in TNB383B.0001 and their families/caregivers**
- **The doctors, nurses, pharmacists, lab-, and research-staff caring for study patients and who have made this study a success**
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