Frontline Brentuximab Vedotin as Monotherapy or in Combination for Older Hodgkin Lymphoma Patients

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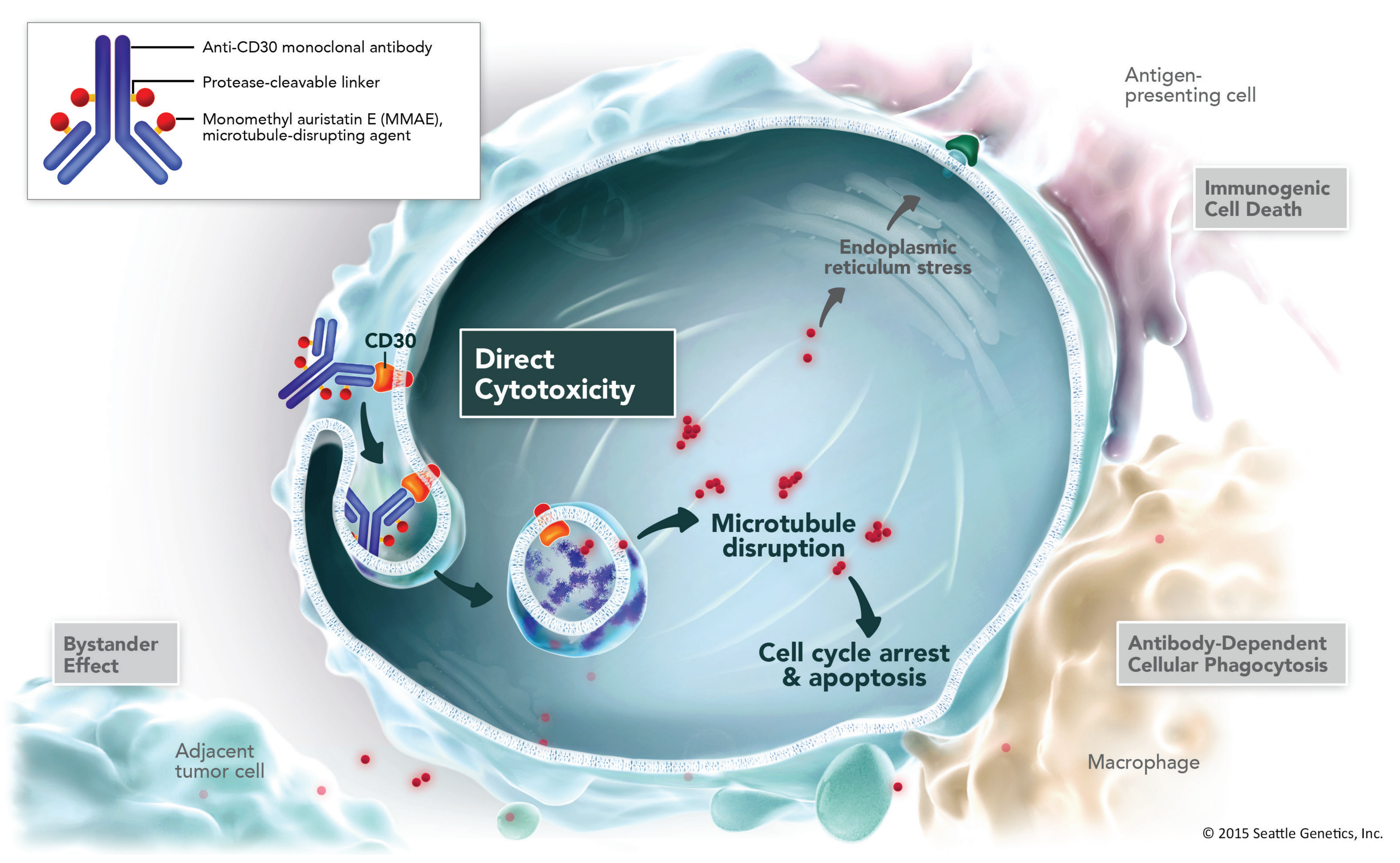
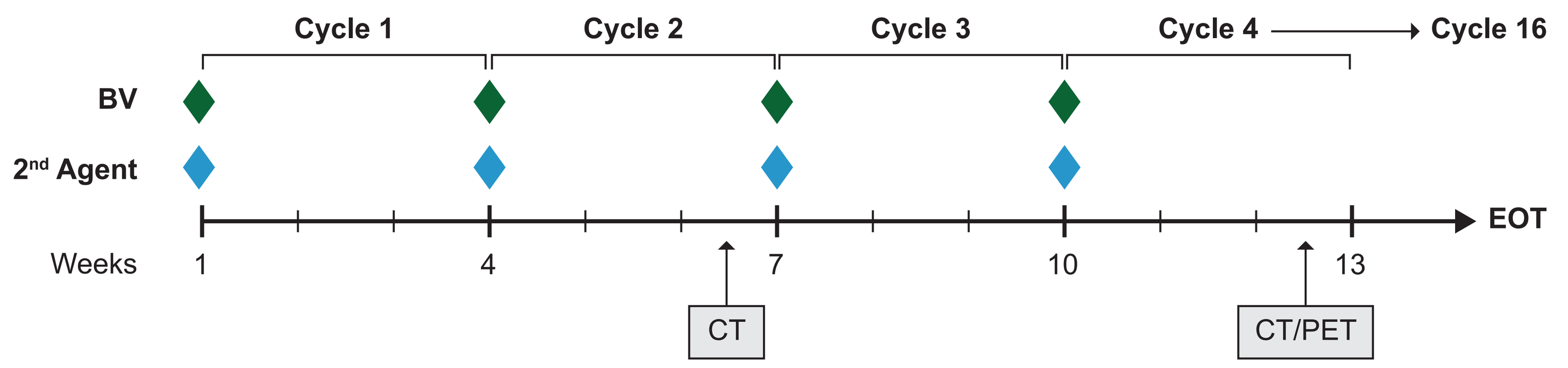
Unmet Need in Elderly HL Population

- ~20% of patients with Hodgkin lymphoma (HL) are ≥60 years[1]
- Older HL patients have markedly inferior outcomes versus younger patients[2]
  - Intrinsic differences in disease/biology
  - Increased rates of advanced disease at presentation
  - Increased comorbidities at baseline
  - Increased treatment-related morbidity and mortality
- Brentuximab vedotin (BV)
  - High single-agent response rates in heavily pretreated patient with relapsed/refractory HL
  - BV combined with other single-agents, such as nivolumab, is active (93% ORR, 80% CR) and well-tolerated in relapsed/refractory classical Hodgkin Lymphoma (cHL)[3]
  - Potential option for elderly and medically fragile patients

Brentuximab Vedotin Proposed Mechanism of Action



Study Design: Phase 2, Frontline Therapy in Older cHL Patients



- Part A: BV monotherapy (1.8 mg/kg)
- Part B: BV (1.8 mg/kg) + dacarbazine (DTIC; 375 mg/m²)
- Part C: BV (1.8 mg/kg) + bendamustine (benda; 70 mg/m²); *Closed early due to multiple acute toxicities[4]*
- Part D: BV (1.8 mg/kg) + nivolumab (nivo; 3 mg/kg), Part D; *1 patient remaining on treatment*

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Treatment for older adults with cHL that may not be considered for conventional combination therapy:

- **BV monotherapy**
  - Active regimen (92% ORR, median OS ≥6 yr) in an elderly patient population (median 78 yr)
  - BV monotherapy has notable activity and tolerability in cHL patients unable to tolerate a multi-agent regimen
- **BV combination treatments**
  - Additional long-term follow-up is ongoing
  - BV+nivo or BV+DTIC are BV-based regimens with promising activity and tolerability in older adults with previously untreated cHL

Study Definitions

- Safety Set: All subjects who received any BV at 1.8 mg/kg dose
- Efficacy Evaluable Set: All subjects in the Safety Set who had at least one post-baseline disease assessment
- Data Set: All results as of the 06 April 2020 data cutoff

Key Demographics and Disease Characteristics - Safety Set

Patients who received any BV (Safety Set)	Part A N=26	Part B N=20	Part C N=20	Part D N=21	Total N=87
Median age years (range)	78 (64-92)	69 (62-88)	75 (63-86)	72 (60-88)	74 (60-92)
Male, n (%)	14 (54)	14 (70)	10 (50)	15 (71)	53 (61)
ECOG ≤1, n (%)	20 (77)	14 (70)	16 (80)	20 (95)	70 (87)
Main histologic subtype of HL, n (%)					
Nodular sclerosis	12 (46)	7 (35)	10 (50)	7 (33)	36 (41)
Mixed cellularity	4 (15)	9 (45)	4 (20)	2 (10)	19 (22)
cHL not otherwise specified	4 (15)	3 (15)	4 (20)	8 (38)	19 (22)
Disease stage III-IV, n (%)	16 (62)	14 (70)	15 (75)	16 (77)	61 (70)
Extra-nodal involvement, n (%)	13 (50)	7 (35)	8 (40)	8 (38)	36 (41)
B symptoms, n (%)	9 (35)	7 (35)	10 (50)	9 (43)	35 (40)
Patients reporting "limited a lot" with ≥1 tasks, n(%)	17 (65)	14 (70)	14 (70)	9 (43)	54 (62)

Duration of Treatment with BV - Safety Set

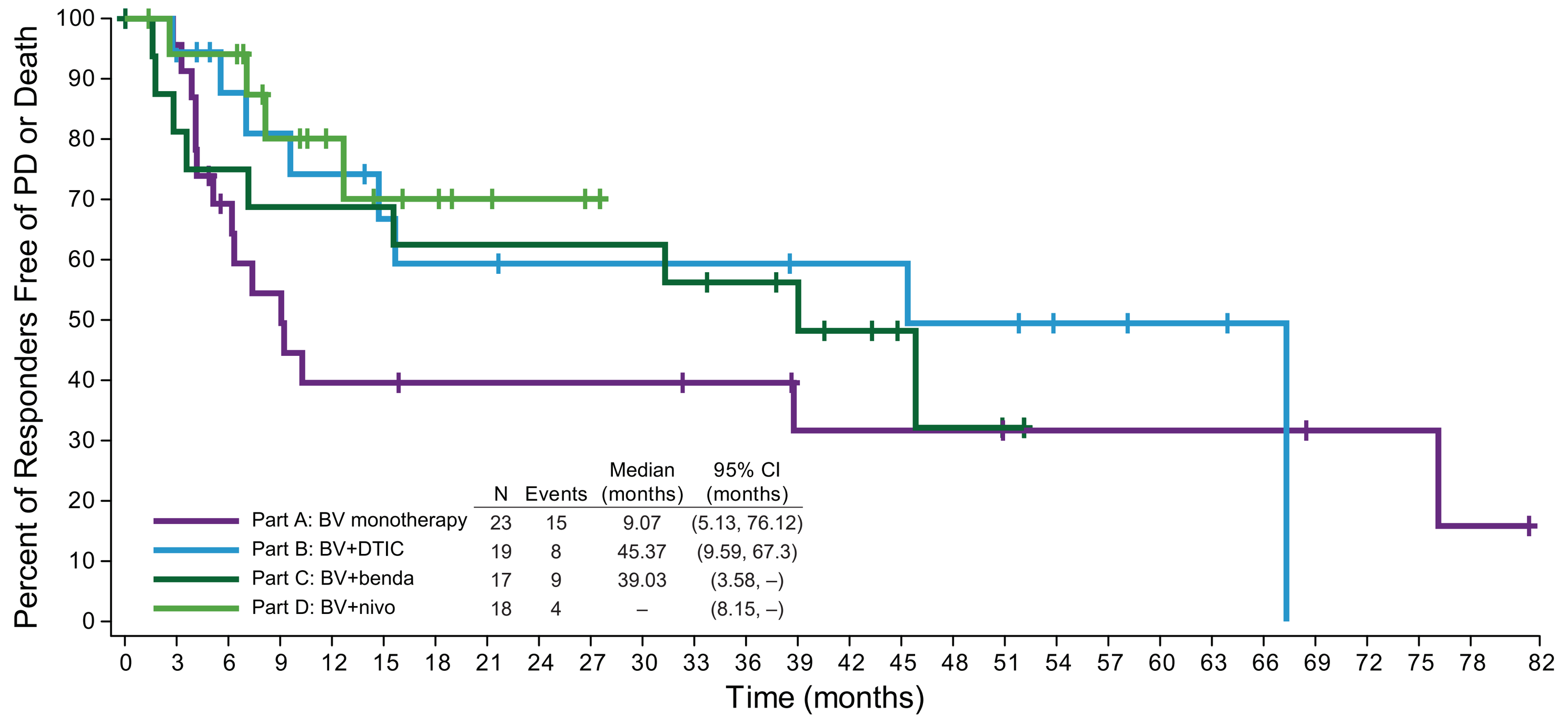
Patients who received any BV (Safety Set)	Part A N=26	Part B N=20	Part C N=20	Part D N=21
Duration of treatment in weeks; Median (min, max)	25.6 (11, 85)	33.9 (6, 82)	15.4 (2, 60)	34.9 (2, 56)
BV treatment cycles[a] per patient; Median (min, max)	8.0 (3, 23)	10.5 (2, 27)	5.0 (1, 16)	10.0 (1, 16)

a Treatment cycle = 21 days

Best Responses per Investigator - Efficacy Evaluable Set

Patients who received ≥1 dose of BV	Part A N=25 n (%)	Part B N=19 n (%)	Part C N=17 n (%)	Part D N=19 n (%)
ORR	**23 (92)**	**19 (100)**	**17 (100)**	**18 (95)**
Best Overall Response				
Complete Response	18 (72)	13 (68)	15 (88)	15 (79)
Partial Response	5 (20)	6 (32)	2 (12)	3 (16)
Stable Disease	2 (8)	0	0	1 (5)
Progressive Disease	0	0	0	0

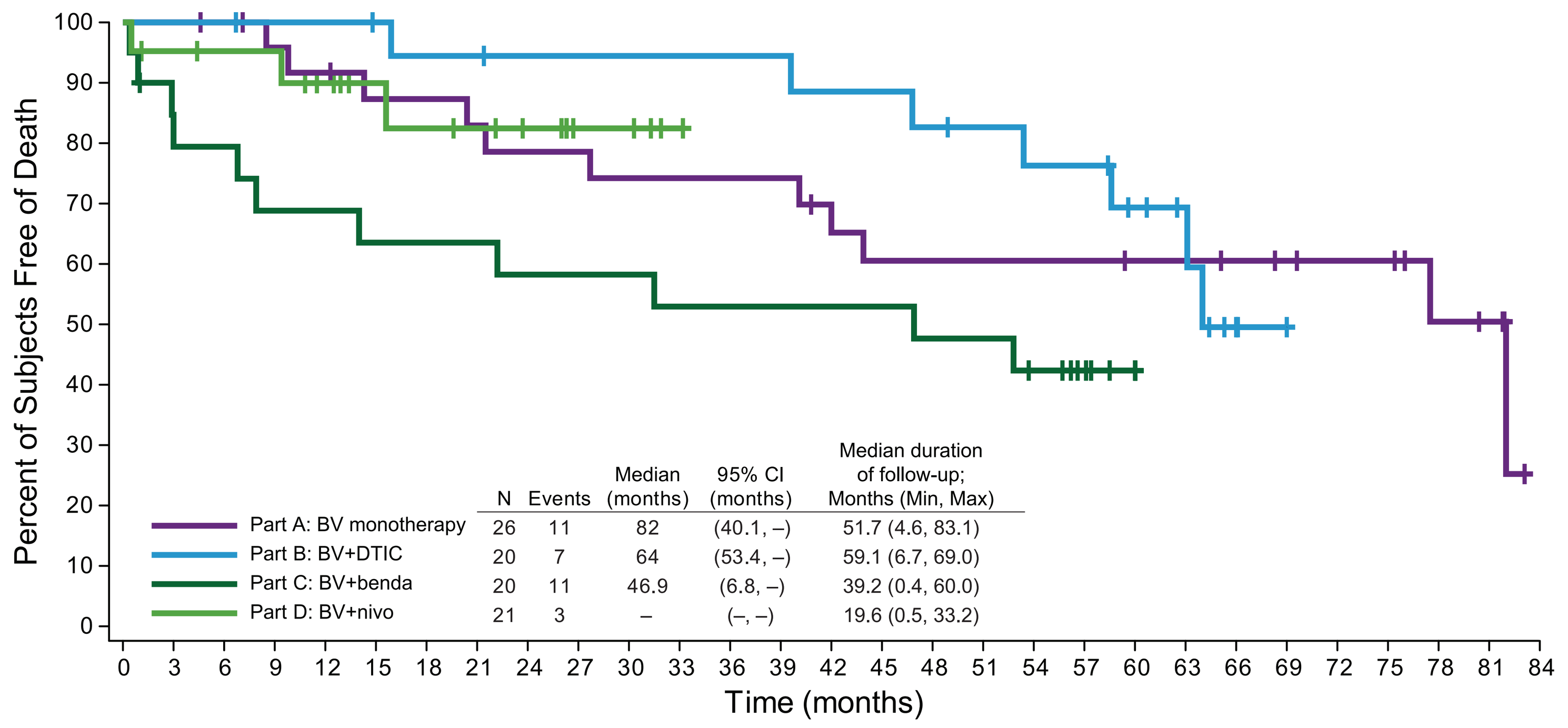
Duration of Response - Efficacy Evaluable Set



N at Risk (Events)

Part A 23(0) 22(1) 14(7) 11(10) 8(13) 8(13) 7(13) 7(13) 7(13) 7(13) 7(13) 6(13) 6(13) 4(14) 4(14) 4(14) 4(14) 3(14) 3(14) 3(14) 3(14) 3(14) 3(14) 2(14) 2(14) 2(14) 1(15) 1(15)
Part B 19(0) 16(1) 13(2) 12(3) 11(4) 9(5) 8(6) 8(6) 7(6) 7(6) 7(6) 7(6) 7(6) 6(6) 6(6) 6(6) 5(7) 5(7) 3(7) 3(7) 2(7) 2(7) 1(7) 0(8)
Part C 17(0) 13(3) 12(4) 11(5) 11(5) 11(5) 10(6) 10(6) 10(6) 10(6) 10(6) 9(7) 8(7) 7(7) 5(8) 3(8) 2(9) 1(9) 0(9)
Part D 18(0) 16(1) 16(1) 11(3) 8(3) 6(4) 5(4) 3(4) 2(4) 1(4) 0(4)

Overall Survival - Safety Set



N at Risk (Events)

Part A 26(0) 26(0) 25(0) 23(1) 22(2) 20(3) 20(3) 19(4) 18(5) 18(5) 17(6) 17(6) 17(6) 17(6) 14(8) 13(9) 13(9) 13(9) 13(9) 13(9) 12(9) 12(9) 11(9) 10(9) 9(9) 9(9) 5(10) 4(10) 0(11)
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Part D 21(0) 19(1) 18(1) 18(1) 15(2) 12(2) 11(3) 10(3) 8(3) 4(3) 4(3) 1(3) 0(3)

Treatment-related Adverse Events - Safety Set

Treatment-related Adverse Events (TRAE) occurring in ≥20% of patients (Safety Set)	Part A N=26 n (%)	Part B N=20 n (%)	Part C N=20 n (%)	Part D N=21 n (%)
Any Event	24 (92)	20 (100)	19 (95)	19 (90)
Peripheral sensory neuropathy	20 (77)	14 (70)	8 (40)	10 (48)
Fatigue	9 (35)	7 (35)	7 (35)	11 (52)
Nausea	8 (31)	7 (35)	10 (50)	3 (14)
Diarrhea	4 (15)	5 (25)	9 (45)	5 (24)
Decreased appetite	5 (19)	5 (25)	8 (40)	1 (5)

- Treatment discontinuation due to TRAE occurred in 42%, 40%, 60%, and 38% of patients
- Peripheral neuropathy was the most common TRAE leading to treatment discontinuation in all Parts (39%, 35%, 30%, and 28%, respectively)

Grade ≥3 Treatment-related Adverse Events - Safety Set

Grade ≥3 TRAE occurring in >5% patients (Safety Set)	Part A N=26 n (%)	Part B N=20 n (%)	Part C N=20 n (%)	Part D N=21 n (%)
Any Event	13 (50)	8 (40)	16 (80)	13 (62)
Peripheral sensory neuropathy	7 (27)	5 (25)	3 (15)	4 (19)
Neutropenia	1 (4)	2 (10)	2 (10)	1 (5)
Peripheral motor neuropathy	2 (8)	0	1 (5)	3 (14)
Lipase increased	0	0	0	5 (24)
Fatigue	0	0	2 (10)	2 (10)
Rash	3 (12)	0	1 (5)	0

Treatment-related Serious Adverse Events - Safety Set

Treatment-related Serious Adverse Events in ≥2 patients (Safety Set)	Part A N=26 n (%)	Part B N=20 n (%)	Part C N=20 n (%)	Part D N=21 n (%)
Any Event	3 (12)	3 (15)	9 (45)	1 (5)
Pyrexia	1 (4)	0	1 (5)	1 (5)
Asthenia	1 (4)	0	1 (5)	0
Febrile neutropenia	0	0	2 (10)	0
Hypotension	0	1 (5)	1 (5)	0

Acknowledgements

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References

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