FRONTLINE BRENTUXIMAB VEDOTIN AS MONOTHERAPY OR IN COMBINATION FOR OLDER HODGKIN LYMPHOMA PATIENTS

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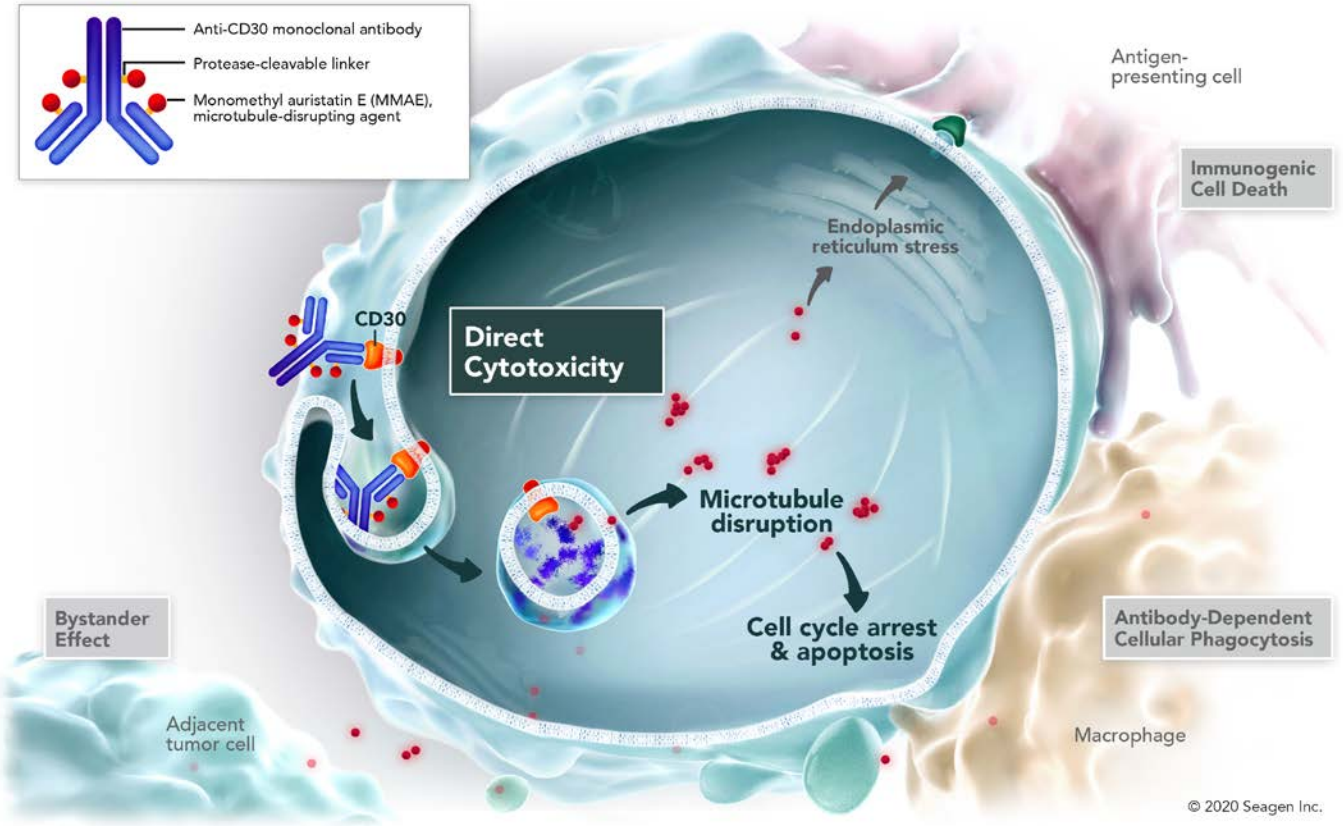
Background and Rationale – Unmet Need in Elderly Hodgkin Lymphoma (HL) Population

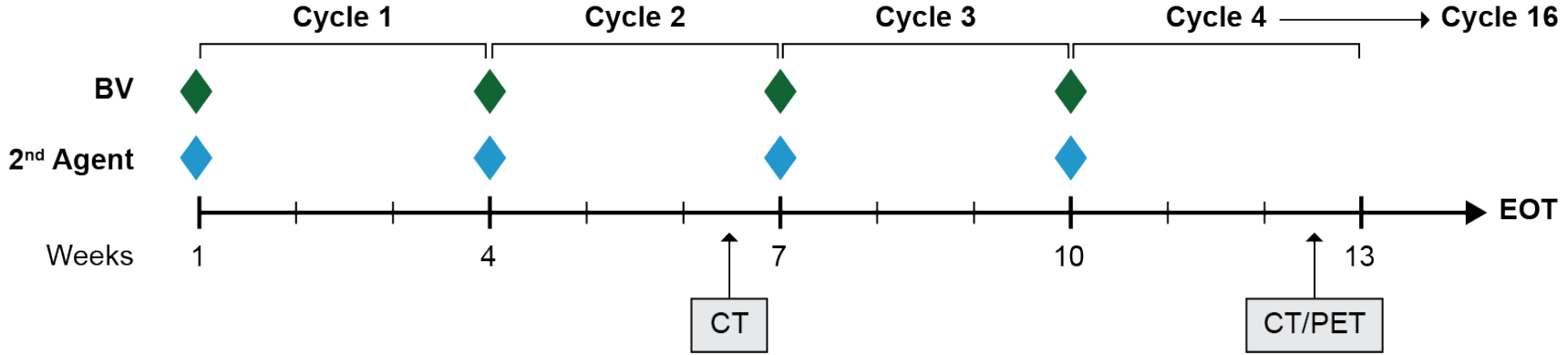
- ~20% of patients with HL are ≥60 years of age[1]
- Older HL patients have markedly inferior outcomes versus younger patients[2]
  - Intrinsic differences in disease/biology
  - Increased rates of advanced disease at presentation
  - Increased comorbidities at baseline
  - Increased treatment-related 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% objective response rate [ORR], 80% complete response [CR]) and well-tolerated in relapsed/refractory classical Hodgkin Lymphoma (cHL)[3]
  - Sequential BV-AVD with BV consolidation demonstrated an ORR of 95% (CR 93%) in a study of older adults[4]
- Potential option for elderly and medically fragile patients

Brentuximab Vedotin Proposed Mechanism of Action



SGN35-015 Study Design: Phase 2, Frontline Therapy in Older cHL Patients

- Eligible patients: ≥60 years of age with cHL, treatment naïve, considered unsuitable or unfit for conventional chemotherapy; fluorodeoxyglucose (FDG)-positron emission tomography (PET)-avid and measurable disease by computed tomography (CT)



- Part A: BV monotherapy (mono; 1.8 mg/kg)
- Part B: BV (1.8 mg/kg) + dacarbazine (DTIC; 375 mg/m^2)
- Part C: BV (1.8 mg/kg) + bendamustine (benda; 70 mg/m^2); *Closed early due to multiple acute toxicities*
- Part D: BV (1.8 mg/kg) + nivolumab (nivo; 3 mg/kg), Part D; *1 patient remaining on treatment*

Study Definitions

- Full Analysis Set: All subjects who received BV at an intended starting dose of 1.8 mg/kg dose
- Efficacy Evaluable Set: All subjects in the full analysis set with at least one post-baseline disease assessment
- Data Set: All results as of the 21 October 2020 data cutoff

Key Demographics and Disease Characteristics

Full analysis set	Part A BV mono N=26	Part B BV+DTIC N=20	Part C BV+benda N=20	Part D BV+nivo N=21	Total N=87
Age in years, median (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 (80)
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 – Full Analysis Set

Full analysis set	Part A BV mono N=26	Part B BV+DTIC[b] N=20	Part C BV+benda[b] N=20	Part D BV+nivo[b] 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
b After stopping BV, the other component of therapy could be continued.

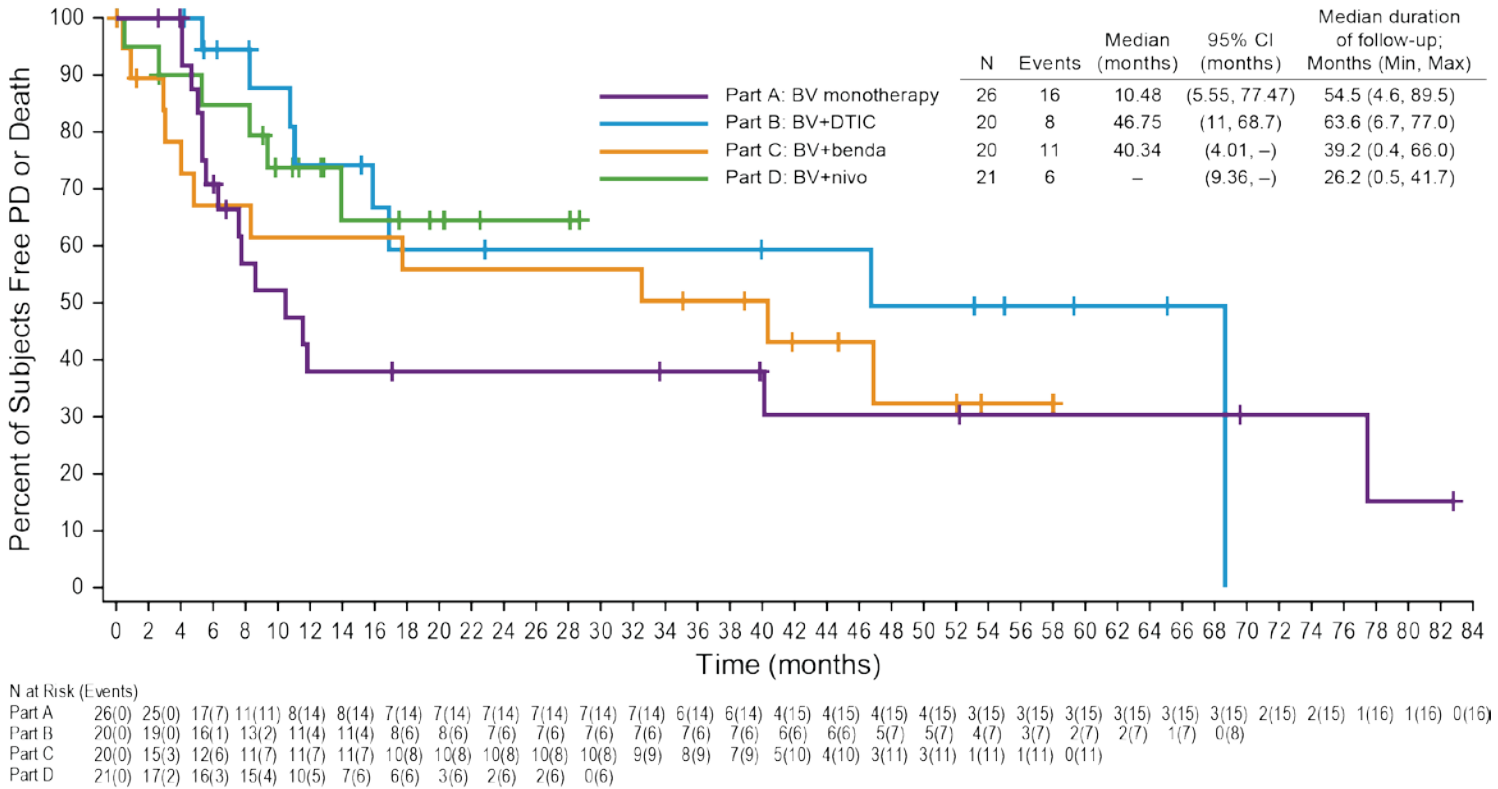
Best Responses per Investigator – Efficacy Evaluable Set

Efficacy Evaluable Set	Part A BV mono N=25	Part B BV+DTIC N=19	Part C BV+benda N=17	Part D BV+nivo N=19
ORR, n (%)	**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, n	23	19	17	18
Median (min, max)	9.1 (2.8, 81.4+)	45.4 (0.0+, 67.3)	39.0 (0.0+, 56.8+)	NR (1.4+, 27.5+)

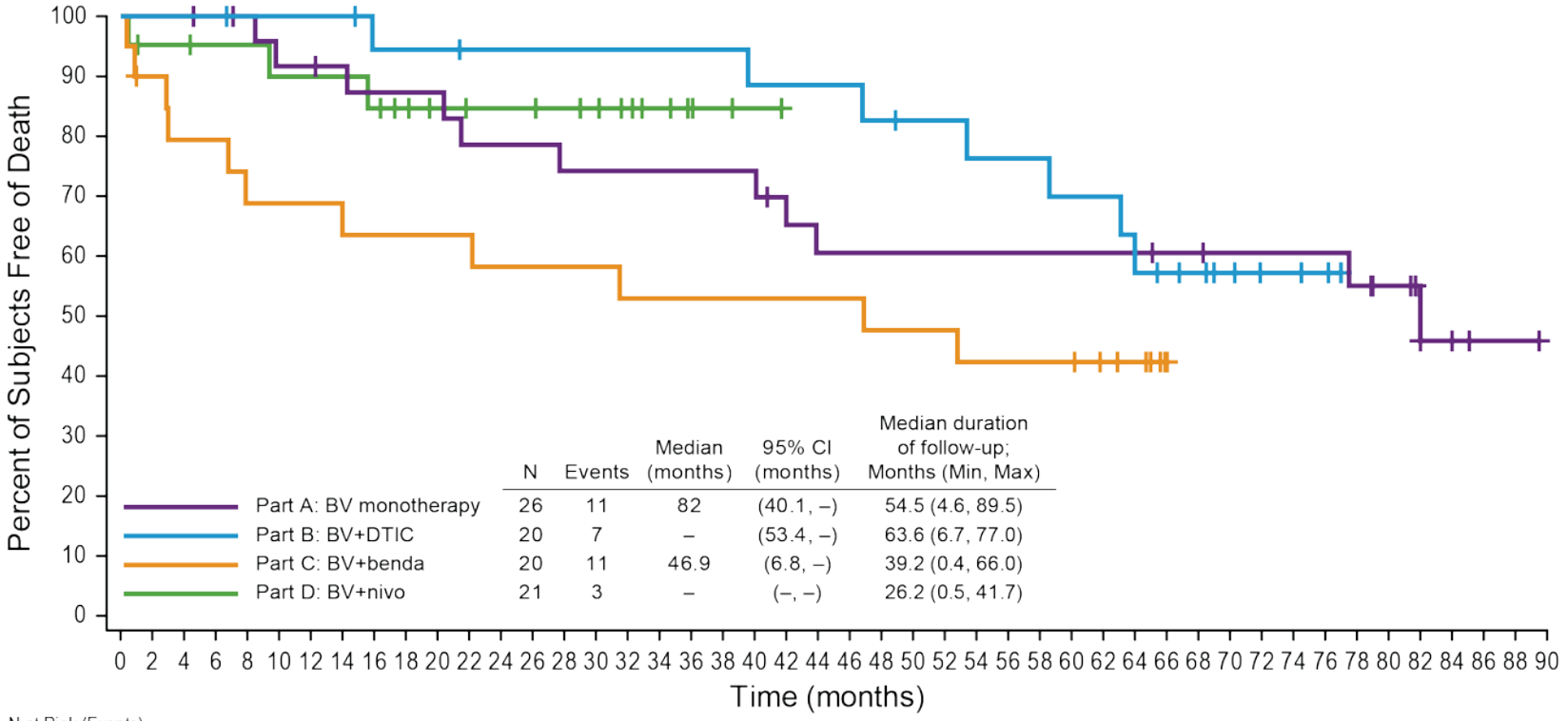
Patients who were not efficacy-evaluable included:

- Patients with no post-baseline response assessment due to deaths (n=3) and patient withdrawal (non-AE related, n=2) on or before the first scheduled post-baseline scan at Cycle 2
- One patient lost to follow-up
- One patient who was not an eligible cHL subtype (nodular lymphocyte-predominant HL) but still achieved partial response after receiving BV

Progression-Free Survival (PFS) – Full Analysis Set



Overall Survival (OS) – Full Analysis Set



	N	Events	Median (months)	95% CI (months)	Median duration of follow-up; Months (Min, Max)
Part A: BV monotherapy	26	11	82	(40.1, –)	54.5 (4.6, 89.5)
Part B: BV+DTIC	20	7	–	(53.4, –)	63.6 (6.7, 77.0)
Part C: BV+benda	20	11	46.9	(6.8, –)	39.2 (0.4, 66.0)
Part D: BV+nivo	21	3	–	(–, –)	26.2 (0.5, 41.7)

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)	13(9)	13(9)	12(9)	11(9)	11(9)	11(9)	10(10)	8(10)	3(11)	2(11)	0(11)
Part B	20(0)	20(0)	20(0)	19(0)	19(0)	18(0)	17(1)	17(1)	16(1)	16(1)	16(1)	16(1)	16(1)	16(1)	15(2)	15(2)	14(3)	13(3)	12(4)	12(4)	11(5)	11(5)	8(7)	5(7)	3(7)	2(7)	0(7)				
Part C	20(0)	15(4)	15(4)	13(6)	13(6)	12(7)	12(7)	12(7)	11(8)	11(8)	11(8)	10(9)	10(9)	10(9)	10(9)	10(9)	9(10)	9(10)	8(11)	8(11)	8(11)	5(11)	0(11)								
Part D	21(0)	19(1)	18(1)	18(1)	17(2)	17(2)	14(3)	12(3)	11(3)	10(3)	9(3)	5(3)	3(3)	1(3)	0(3)																

Treatment-Related Treatment-Emergent Adverse Events (TEAEs) – Full Analysis Set

Full analysis set	Part A BV mono N=26 n (%)	Part B BV+DTIC N=20 n (%)	Part C BV+benda N=20 n (%)	Part D BV+nivo 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 treatment-related TEAEs occurred in 42%, 40%, 60%, and 38% of patients, respectively
- Peripheral neuropathy was the most common treatment-related TEAE leading to treatment discontinuation in all parts (38%, 35%, 30%, and 29%, respectively)

Grade ≥3 Treatment-Related TEAEs – Full Analysis Set

Grade ≥3 treatment-related TEAEs occurring in >5% of all patients (Full analysis set)	Part A BV mono N=26 n (%)	Part B BV+DTIC N=20 n (%)	Part C BV+benda N=20 n (%)	Part D BV+nivo 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 TEAEs – Full Analysis Set

Treatment-related SAEs in ≥2 patients	Part A BV mono N=26 n (%)	Part B BV+DTIC N=20 n (%)	Part C BV+benda N=20 n (%)	Part D BV+nivo 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

Summary

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

- **BV monotherapy**
  - Active regimen in elderly population
    - Median 78 years of age
    - Median follow up of 54.5 months
    - ORR 92% (95% CI: 74%, 99%)
    - Median OS >6 years
  - Notable activity and tolerability in cHL patients unable to tolerate a multi-agent regimen
- **BV combination treatments**
  - BV+nivo and BV+DTIC
    - Promising activity (ORR 95%-100%)
    - Favorable safety profile in older adults with previously untreated cHL
  - BV+benda associated with multiple acute toxicities
  - Additional long-term follow-up is ongoing

Conclusions and Future Directions

- For older patients with cHL and multiple comorbidities, treatment with BV as monotherapy or combined with nivolumab or DTIC resulted in:
  - Improved tolerability for patients unfit for combination chemotherapy
  - High response rates, often durable
- Findings reflect a need for further studies dedicated to the elderly population, along with geriatric assessments

Acknowledgements

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References

1. Stark GL et al. (2002) Br J Haematol 119: 432–40.
2. Evens AM et al. (2013) Br J Haematol 161: 76–86.
3. Advani RH et al. (2018) Blood 132: 1635.
4. Evens AM et al. (2018) J Clin Oncol 36(30): 3015-3022.
5. Friedberg JW et al. (2017) Blood 130(26): 2829–37.