BRENTUXIMAB VEDOTIN, NIVOLUMAB, DOXORUBICIN, AND DACARBAZINE FOR ADVANCED-STAGE CLASSICAL HODGKIN LYMPHOMA: UPDATED EFFICACY AND SAFETY RESULTS FROM THE SINGLE-ARM PHASE 2 STUDY (SGN35-027 PART B)

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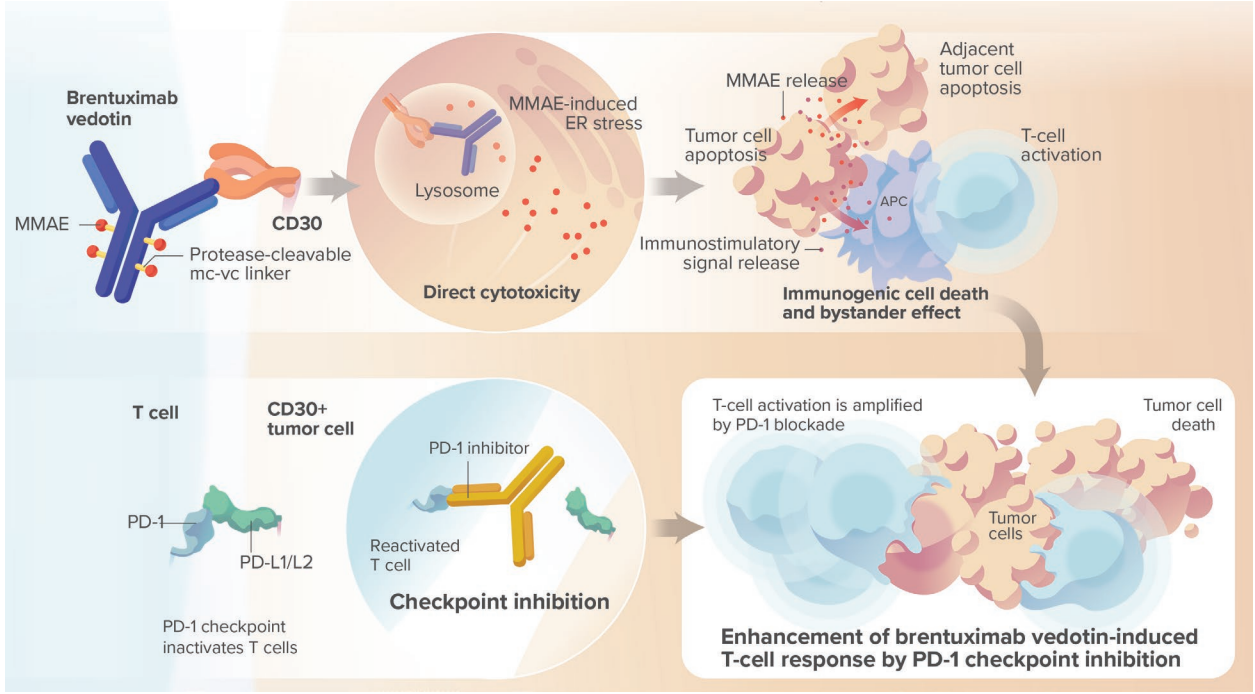
Background

- Brentuximab vedotin (BV) is an antibody-drug conjugate approved for untreated stage III or IV classical Hodgkin Lymphoma (cHL), in combination with doxorubicin, vinblastine, and dacarbazine (A+AVD)

- A+AVD has improved overall survival in advanced stage cHL; however, the regimen is associated with increased neuropathy and neutropenia related to overlap of BV with vinblastine[1-4]
- In earlier studies, BV+nivolumab was well tolerated with promising efficacy[5-6]
- It is hypothesized that BV with nivolumab combined with AD (AN+AD) may result in high response rates and a tolerable safety profile, with less toxicity compared with vinblastine-containing regimens

Here, the efficacy and safety results from Part B of this Phase 2 study of patients with advanced cHL treated with AN+AD are presented

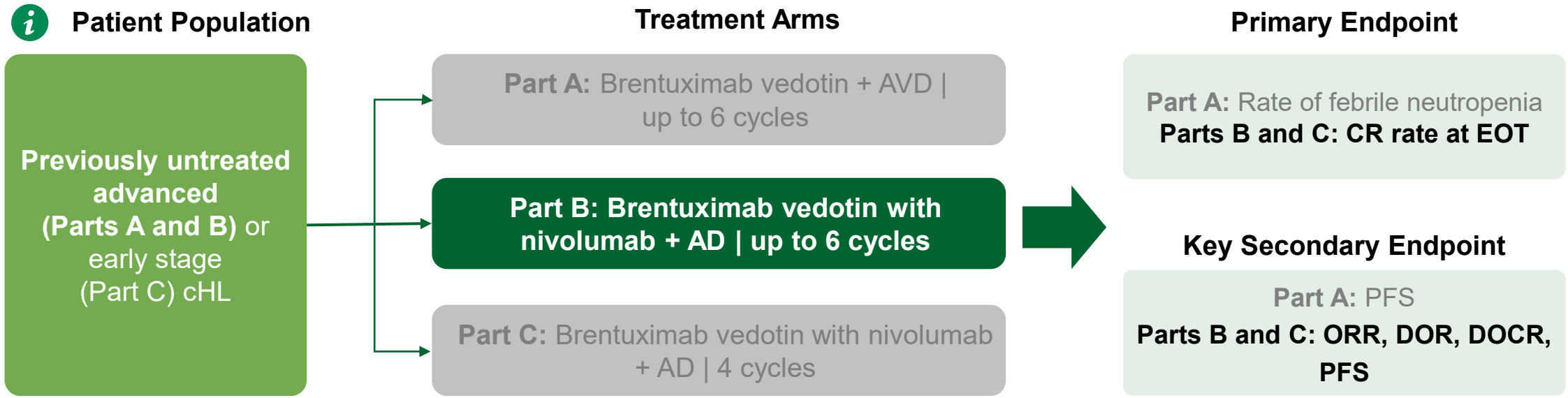


Brentuximab vedotin plus a PD-1 inhibitor is an investigational drug combination; the safety and efficacy of the drug combination has not been established.

1. Connors, J. N Engl J Med. 2018;378:331-344 2. Ansell, S. N Engl J Med. 2022;387:310-320 3. Ramchandren R. J Clin Oncol. 2019;37:1997-2007 4. Abramson, JS. Blood. 2023:7:1130 5. Advani, R. Blood. 2021;138:427-38
6. Yasenchak, CA. Blood. 2020; 136:18-19

Study Design

NCT03646123 | Active, not recruiting



- SGN35-027 is an open-label, multiple part, multicenter, phase 2 trial
- Part B enrolled patients with stage II with bulky mediastinal disease (≥10 cm), and stage III or IV cHL
- Patients received up to 6 cycles of AN+AD (BV 1.2 mg/kg, nivolumab 240 mg, doxorubicin 25 mg/m^2, and dacarbazine 375 mg/m^2)
- Response assessments were taken at Cycle 2 and EOT, including PET and diagnostic-quality CT
  - CR rate at EOT assessed per Lugano[8] with incorporation of LYRIC[9]

Data Cut-off: 05 SEP 2023

[8]Cheson, BD. J Clin Oncol. 2014;32:3058-68, [9]Cheson, BD. Blood. 2016;128:2489-96

Patient Disposition

90% of patients completed intended therapy of 6 cycles

Summary of Disposition, n (%)	Part B N = 58
Patients who received ≥1 dose	57 (98)
Patients on treatment	0
Patients in long-term follow-up	48 (83)
Reasons for treatment discontinuation[a]	
Completed treatment	52 (90)
Progressive disease	0
Adverse event[b]	4 (7)
Investigator decision	1 (2)
Patients off study	10 (17)

[a]Treatment discontinuation includes all study drugs
[b]Adverse events leading to discontinuation: Grade 3 Drug Reaction with Eosinophilia and Systemic Symptoms syndrome (DRESS), Grade 2 pyrexia, Grade 3 pyrexia, Grade 4 hypophysitis

Patient Demographics and Disease Characteristics

Most patients had stage IV disease; 58% had B symptoms present at diagnosis

Patient Demographics and Disease Characteristics	Part B N = 57
Age, median years (range)	35 (19, 78)
Sex, Female, n (%)	27 (47)
Race, White, n (%)	50 (88)
Disease stage at initial diagnosis, n (%)	
II	18 (32)
Bulky[a]	17 (30)
III	10 (18)
IV	29 (51)
Extranodal disease present, n (%)	28 (49)
B symptoms present at initial diagnosis, n (%)	33 (58)
International Prognostic Score, n (%)	
0-1	13 (23)
2-3	32 (56)
4-7	12 (21)

[a]One patient with non-bulky disease was enrolled under a prior amendment

Antitumor Activity

93% of patients experienced a complete or partial response at EOT; 88% had a CR

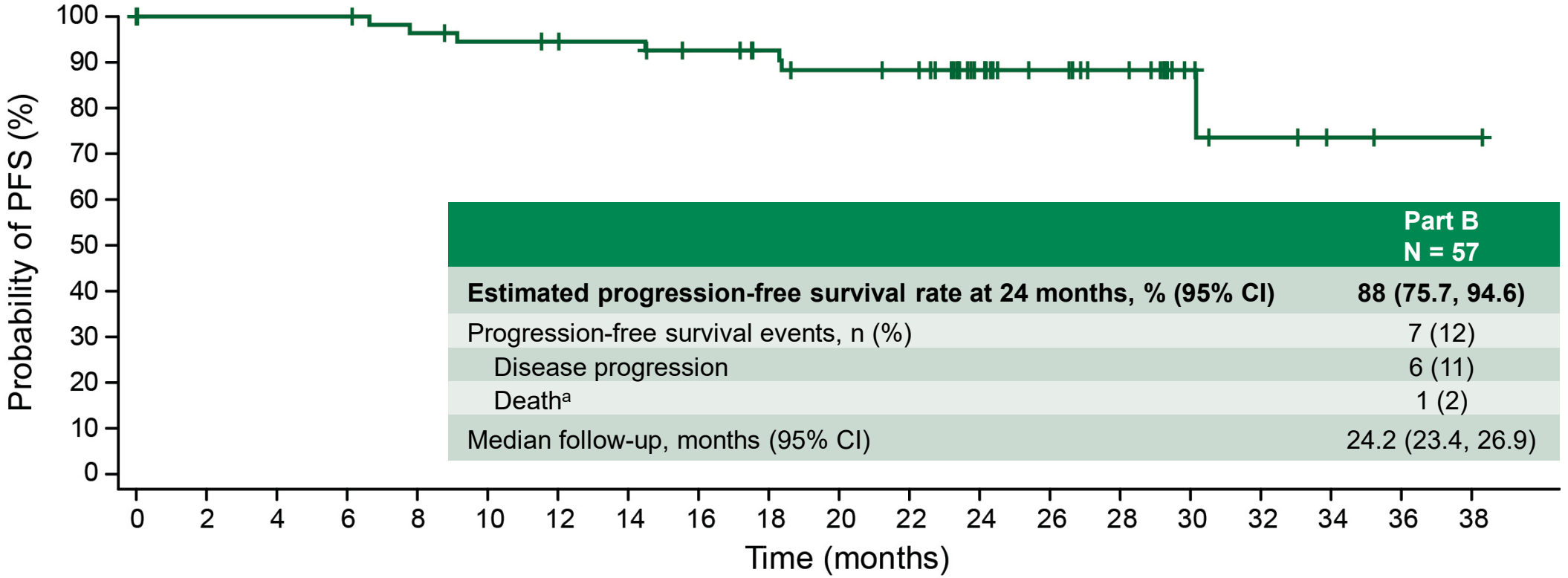
Overall Response at EOT per Investigator, n (%)	All treated patients N = 57	Efficacy evaluable patients[a] N = 56
Objective response rate (complete + partial response)	**53 (93)**	**53 (95)**
95% CI	(83.0, 98.1)	(85.1, 98.9)
Complete response	**50 (88)**	**50 (89)**
95% CI	(76.3, 94.9)	(78.1, 96.0)
Partial response	3 (5)	3 (5)
Stable disease	0	0
Progressive disease	2 (4)	2 (4)
Indeterminate response[b]	1 (2)	1 (2)
Not evaluable[c]	1 (2)	0

[a]Efficacy evaluable includes patients who completed EOT response assessments
[b]1 patient achieved CR in long-term follow-up
[c]1 patient discontinued study treatment after cycle 1 due to a serious adverse event

- Best response of CR at any time point on treatment or in long-term follow-up was 95% (54/57) in all treated patients
- 88% (N=56) (95% CI, 75.7, 94.6) of patients had a **duration of response** beyond 24 months
- 88% (N=54) (95% CI, 76.0, 94.6) of patients had a **duration of complete response** beyond 24 months

Progression-free Survival

88% rate of progression-free survival after 2 years; no patients had subsequent radiation therapy



	Part B N = 57
Estimated progression-free survival rate at 24 months, % (95% CI)	**88 (75.7, 94.6)**
Progression-free survival events, n (%)	7 (12)
Disease progression	6 (11)
Death[a]	1 (2)
Median follow-up, months (95% CI)	24.2 (23.4, 26.9)

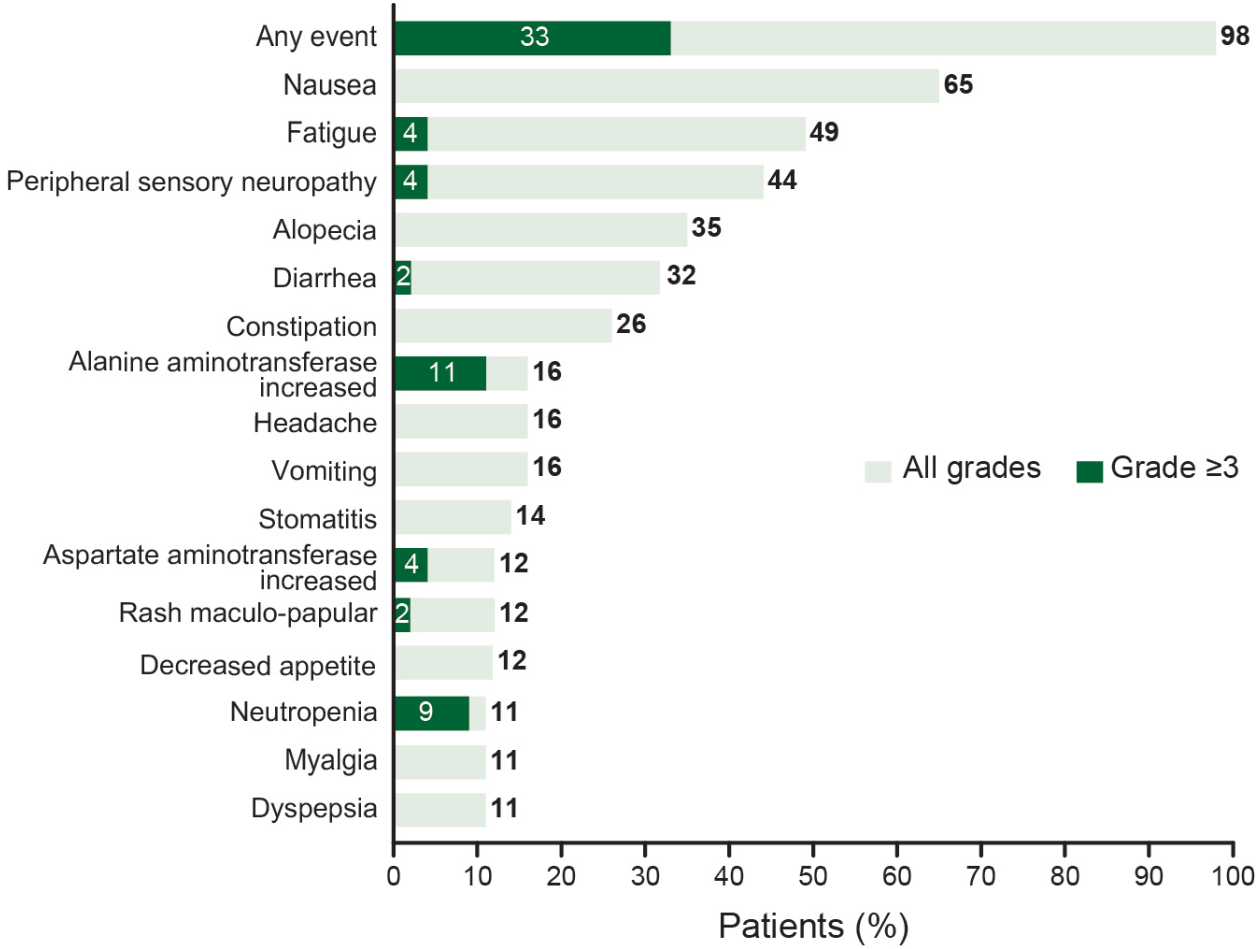
N at risk (events)

Part B	57(0)	56(0)	56(0)	56(0)	53(2)	51(3)	50(3)	49(3)	46(4)	43(4)	40(6)	39(6)	28(6)	21(6)	17(6)	7(6)	4(7)	2(7)	1(7)	1(7)

[a]Patient died due to sepsis approximately 3.5 months following last dose of study drug

Summary of Adverse Events

Most Common Treatment-related TEAEs



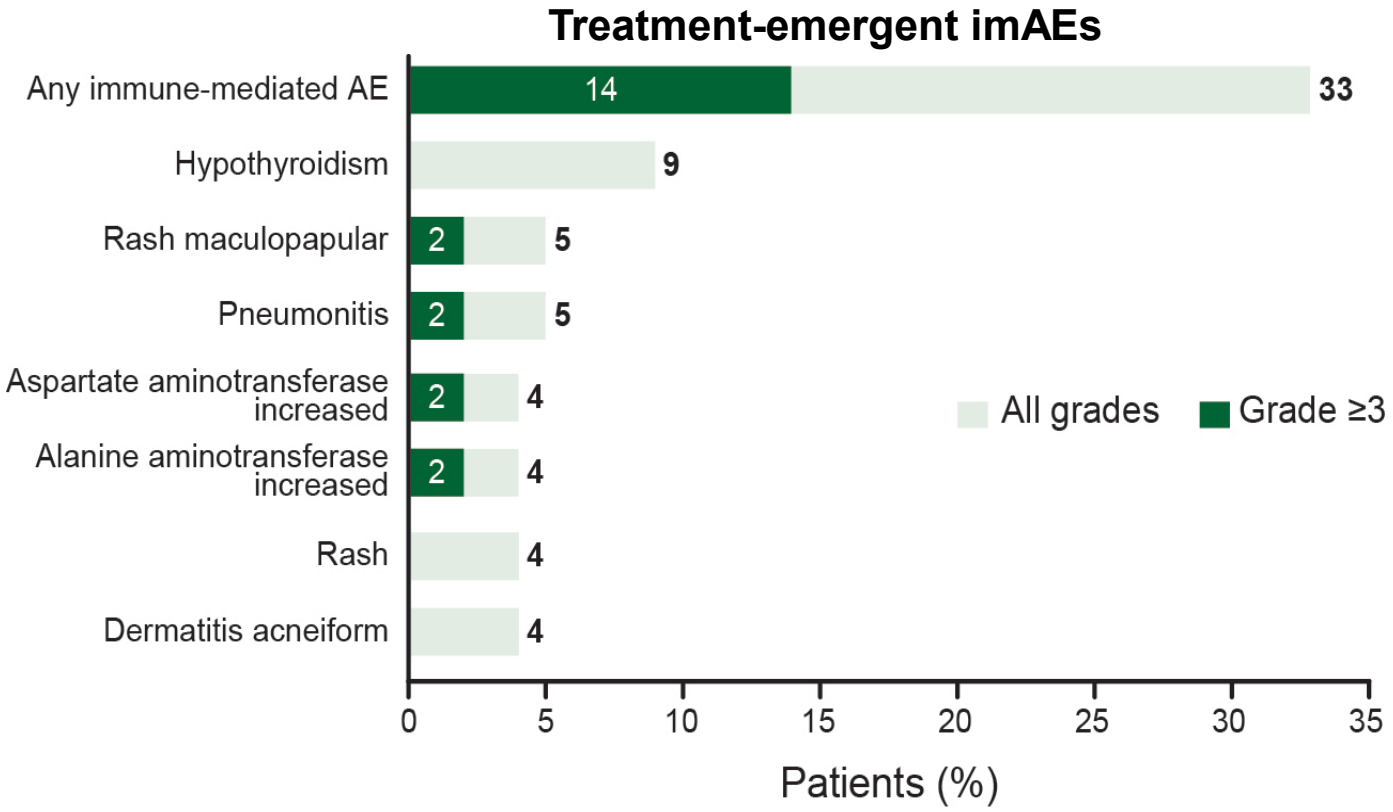
≥10% of patients (all grades) or ≥2% of patients with grade ≥3

Treatment-Emergent Adverse Events (TEAEs)

- No events of febrile neutropenia were reported
  - 28/57 (49%) received G-CSF during treatment, all (28/28, 100%) given as primary prophylaxis
  - G-CSF was not required per protocol
- Peripheral neuropathy[a] (PN) occurred in 32/57 (56%); PN was primarily low grade
  - Grades 1 and 2: 17/57 (30%) and 13/57 (23%), respectively
  - Grade 3: 2/57 (4%)
  - 9/32 (28%) had complete resolution and 2/32 (6%) with improvement of at least one grade at last follow-up. All ongoing PN is ≤ Grade 2
- No grade 5 adverse events were reported
- 7/57 (12%) had TEAEs leading to the discontinuation of BV:
  - Sensory PN (n=2), colitis (n=1), DRESS (n=1), hyperglycemia (n=1), hypophysitis (n=1), pyrexia (n=1)
- 9/57 (16%) had TEAEs leading to discontinuation of nivolumab. Most common reasons were colitis (n=2) and pneumonitis (n=2)

[a]Events include MedDRA SMQ peripheral neuropathy terms

Immune-mediated Adverse Events



≥2% of patients (all grades) or any patients with grade ≥3

- Immune-mediated adverse events (imAEs) were primarily grade 1-2, and were consistent with the safety profile of nivolumab
- 4/57 (7%) had imAEs leading to discontinuation of nivolumab:
  - Colitis (n=1), hypophysitis (n=1), pneumonitis (n=1), Type 1 diabetes (n=1)

Conclusions

- ORR and CR rates at EOT were 93% and 88%, respectively
  - One patient with an indeterminate response at EOT; subsequently achieved a CR during long-term follow-up
- 88% of patients remained progression-free after 2 years with a median follow-up of 24.2 months
- AN+AD was well tolerated
  - No cases of febrile neutropenia
  - Peripheral neuropathy was primarily low grade. 28% of all PN cases completely resolved and 6% improved in grade since last follow-up; all ongoing PN events are grade 2 or lower
  - ImAEs were primarily low-grade
- Follow-up of SGN35-027 Part B is ongoing with 83% of patients in long-term follow-up
- AN + AD shows promising efficacy and tolerability warranting further exploration for the treatment of patients with 1L advanced cHL

Acknowledgments

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