Frontline Brentuximab Vedotin and CHP (A+CHP) in Patients With Peripheral T-cell Lymphoma With Less Than 10% CD30 Expression: Initial Efficacy and Safety Results From the Phase 2 Study (SGN35-032)

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Objectives

To present initial efficacy and safety results from SGN35-032 (NCT04569032; EudraCT 2020-002336-74), a study of A+CHP for patients with previously untreated PTCL with <10% CD30 expression.

Conclusions

Initial findings show that A+CHP is effective for patients with non-ALCL PTCL regardless of CD30 expression by local testing supporting the proposed, multi-faceted mechanism of action of BV in combination with CHP

Initial efficacy reported for CD30 <1% and CD30 1% to <10% were similar with an **ORR of 84% and 74%** respectively and a **CR rate of 58%** and **59%** respectively per local testing

- By CD30 centrally, data between cohorts were comparable with overlapping confidence intervals

Safety results are consistent with previously reported data from ECHELON-2 and no new safety signals were observed

This study is ongoing and updated results will be presented in the future

Abbreviations

95% CI, 95% confidence interval; A+CHP, cyclophosphamide, doxorubicin, and prednisone; ADC, antibody drug conjugate; AE, adverse event; AITL, angioimmunoblastic T-cell lymphoma; ALCL, anaplastic large cell lymphoma; BICR, blinded independent central review; BV, brentuximab vedotin; CR, complete response; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; EOT, end of treatment; GI, gastrointestinal; IHC, immunohistochemistry; IPI, international prognostic index; INV, investigator; MMAE, monomethyl auristatin E; NE, not evaluable; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; PTCL, peripheral T-cell lymphoma; PTCL-NOS, PTCL-not otherwise specified; SAE, serious adverse event; sALCL, systemic anaplastic large cell lymphoma; SCT, stem cell transplant; SD, stable disease; TE SAE, treatment-emergent serious adverse event; TEAE, treatment-emergent adverse event

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Disclosures

Abbvie; Abcuro, Inc. and Tubulis; Acrotech; ADC Therapeutics; Affimed; American Society of Cellular Therapy and Transplantation speaker; American Society of Hematology speaker; Astra Zeneca; Auxilius Pharma; Beigene; Biocure and Targeted Oncology's speaker bureaus; C4; Celgene; Crispr Therapeutics; Daiichi Sankyo; Dren Bio; Genmab; Gilead; Incyte; Innate Pharma; Janssen; Kite/Gilead; Kyowa Hakko Kirin; Legend; Memorial Sloan Kettering Cancar Center; Merck; Millennium/Takeda; Morphosys, Myeloid; ONO Pharmaceutical; Rhizen; Roche; Sandoz; Seagen; Secura Bio; Servier; Shoreline Biosciences, Inc; Takeda S.A; Takeda; Verastem/SecuraBio; Yingli Pharma Limited

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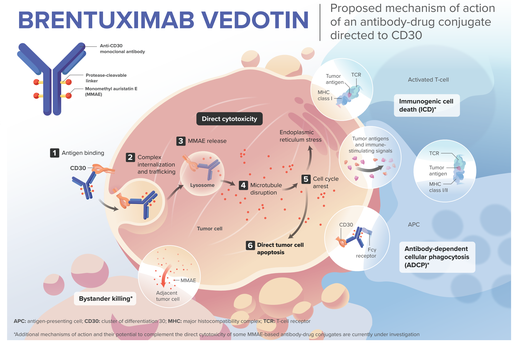
Background

- Brentuximab vedotin (BV) is an CD30-directed ADC approved for multiple cancer types, including previously untreated sALCL and CD30-expressing PTCL[1]
- The unique combination of a CD30-directed monoclonal antibody, protease-cleavable linker, and microtubule-disrupting agent MMAE drives the anticancer activity[2]
  - MMAE-mediated microtubule disruption induces cell cycle arrest and apoptosis[2]
  - Direct cytotoxicity, including the induction of immunogenic cell death, promotes activation and recruitment of immune cells to tumors[2-8]
- The phase 3 ECHELON-2 study evaluated the efficacy and safety of BV in combination with cyclophosphamide, doxorubicin, and prednisone (A+CHP) in patients with ALCL and other types of PTCL with ≥10% CD30 expression
  - Patients treated with A+CHP had a 29% reduction in the risk of a PFS event (stratified HR=0.70 [95% CI: 0.53, 0.91], P=0.0770) and a survival benefit (HR=0.72 [95% CI: 0.53, 0.99], P=0.0424) versus conventional frontline therapy[9]
  - In patients with non-ALCL PTCL treated with A+CHP, there was no correlation between CD30 expression and response, which may be a result of CD30-independent mechanisms (eg. ADCP, ICD, bystander effect, and depletion of CD30+ T regulatory cells)[11]
- It is hypothesized that A+CHP will demonstrate efficacy in patients with non-ALCL PTCL with <10% CD30 expression both due to this lack of correlation and because responses to BV monotherapy can occur in patients with low and undetectable CD30 expression[12]

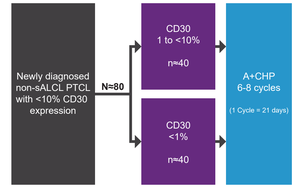


Brentuximab vedotin is an investigational agent in some settings, and its safety and efficacy have not been established.

Methods

- SGN35-032 (NCT04569032; EudraCT 2020-002336-74) is an open-label, dual-cohort, global, multicenter, phase 2 study
- Patients with newly diagnosed non-sALCL PTCL with <10% CD30 expression were enrolled and analyzed as determined by standard IHC by local pathology assessment unless otherwise specified
  - Patients were assigned to either CD30 <1% or CD30 1% to <10% cohorts
- Patients received up to 6-8 cycles of A+CHP
  - BV 1.8 mg/kg, cyclophosphamide 750 mg/m^2, doxorubicin 50 mg/m^2, and prednisone 100 mg
  - Study drugs were administered by IV infusion on Day 1 each 21-day cycle
  - Prednisone was administered orally on Days 1-5 of each cycle
- Primary endpoint is ORR at EOT per BICR using Cheson 2007
- Secondary endpoints include safety, tolerability, ORR per BICR using modified Lugano, OS, DOR, CR rate, and PFS

Study Design - SGN35-032



Results

Patient Characteristics

	CD30 <1% (n = 23)	CD30 1% to <10% (n = 32)	Total (N = 55)
Age, median (range)	61.0 (46, 74)	64.0 (35, 80)	64.0 (35, 80)
Age range, n (%)			
<65 years	14 (61)	18 (56)	32 (58)
≥65 years	9 (39)	14 (44)	23 (42)
Race, n (%)			
White	18 (78)	26 (81)	44 (80)
Black or African American	1 (4)	0	1 (2)
Asian	2 (9)	3 (9)	5 (9)
Unknown/not reported	2 (8)	3 (9)	5 (9)
ECOG performance status[a,b], n (%)			
0	8 (35)	12 (38)	20 (36)
1	13 (57)	16 (50)	29 (53)
2	1 (4)	4 (13)	5 (9)

[a]The last non-missing value before or on the day of first study treatment.
[b]One patient from the CD30 <1% cohort had a missing ECOG performance status value.

- 55 patients received at least 1 dose of study treatment as of January 13, 2023
- 46/55 patients had at least one post-baseline response assessment or discontinued treatment with no post-baseline response assessment
  - Safety results are reported for all treated patients

	CD30 <1% (n = 23)	CD30 1% to <10% (n = 32)	Total (N = 55)
Disease Diagnosis			
PTCL-NOS	12 (52)	12 (38)	24 (44)
AITL	6 (26)	11 (34)	17 (31)
Nodal PTCL with T-follicular helper phenotype	2 (9)	4 (13)	6 (11)
Follicular T-cell lymphoma	1 (4)	4 (13)	5 (9)
Other	2 (8)	1 (3)	3 (6)
Baseline IPI score, n (%)			
0	0	1 (3)	1 (2)
1	2 (9)	6 (19)	8 (15)
2	7 (30)	11 (34)	18 (33)
3	9 (39)	12 (38)	21 (38)
4	5 (22)	1 (3)	6 (11)
5	0	1 (3)	1 (2)

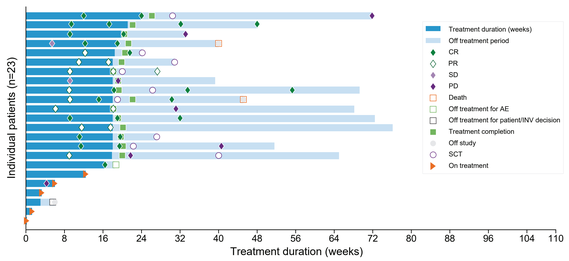
ORR per BICR by Local CD30 Status

	CD30 <1% (n = 19)	CD30 1% to <10% (n = 27)	Total (N = 46)
Best overall response[a,b], n (%)			
CR	11 (58)	16 (59)	27 (59)
PR	5 (26)	4 (15)	9 (20)
SD	1 (5)	3 (11)	4 (9)
PD	1 (5)	3 (11)	4 (9)
NE	1 (5)	1 (4)	2 (4)
ORR (CR+PR), n (%)	16 (84)	20 (74)	36 (78)
95% CI[c] for ORR	(60.4, 96.6)	(53.7, 88.9)	(63.6, 89.1)

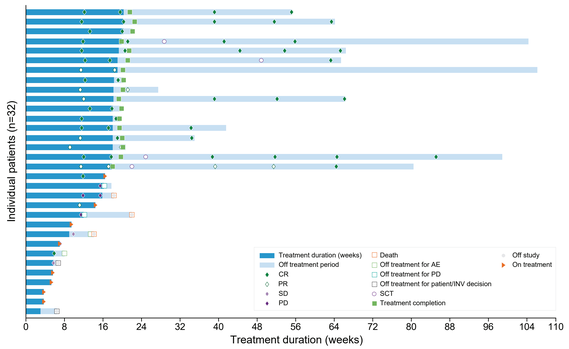
[a]CR, PR, SD and PD per Cheson 2007 per independent assessor.
[b]CR, PR, SD, PD and NE are mutually exclusive.
[c]Two-sided 95% exact confidence interval, computed using the Clopper-Pearson method (1934).

- ORR per INV using Cheson 2007 was 76% (95% CI: 61.2, 87.4) overall with 79% (95% CI: 54.4, 93.9) and 74% (95% CI: 53.7, 88.9) for CD30 <1% and CD30 1% to <10%, respectively

Treatment and Response per BICR for Local CD30 <1%



Treatment and Response per BICR for Local CD30 1% to <10%



ORR per BICR by Central CD30 Status

	CD30 <1% (n = 11)	CD30 1% to <10% (n = 19)	CD30 ≥10% (n = 12)	Total (N = 46)[d]
Best overall response[a,b], n (%)				
CR	5 (45)	11 (58)	8 (67)	27 (59)
PR	1 (9)	5 (26)	2 (17)	9 (20)
SD	1 (9)	2 (11)	1 (8)	4 (9)
PD	3 (27)	0	1 (8)	4 (9)
NE	1 (9)	1 (5)	0	2 (4)
ORR (CR+PR), n (%)	6 (55)	16 (84)	10 (83)	36 (78)
95% CI[c] for ORR	(23.4, 83.3)	(60.4, 96.6)	(51.6, 97.9)	(63.6, 89.1)

[a]CR, PR, SD and PD per Cheson 2007 per independent assessor.
[b]CR, PR, SD, PD and NE are mutually exclusive.
[c]Two-sided 95% exact confidence interval, computed using the Clopper-Pearson method (1934).
[d]4 of 46 patients did not have available CD30 central data. 3 patients had a CR and 1 patient had a PR

- ORR per INV using Cheson 2007 was 76% (95% CI: 61.2, 87.4) overall with 45% (95% CI: 16.7, 76.6) and 84% (95% CI: 60.4, 96.6) for CD30 <1% and CD30 1% to <10%, respectively

Safety

Treatment-related TEAEs (>10% of total patients)	CD30 <1% (n = 23)	CD30 1% to <10% (n = 32)	Total (N = 55)
Patients with any event, n (%)	17 (74)	26 (81)	43 (78)
Diarrhea	7 (30)	9 (28)	16 (29)
Nausea	5 (22)	8 (25)	13 (24)
Peripheral sensory neuropathy	5 (22)	7 (22)	12 (22)
Anemia	5 (22)	6(19)	11 (20)
Febrile neutropenia	4 (17)	7 (22)	11 (20)
Lymphopenia	1 (4)	5 (16)	6 (11)
Stomatitis	1 (4)	5 (16)	6 (11)

- No new safety signals were observed
- Three patients (5%) discontinued study treatment due to TEAE
- Sixteen patients (29%) had BV-related TE SAEs
- One patient (2%) had a treatment-related fatal event of general physical health deterioration

Treatment-emergent SAEs (>5% of total patients)	CD30 <1% (n = 23)	CD30 1% to <10% (n = 32)	Total (N = 55)
Patients with any SAE, n (%)	8 (35)	12 (38)	20 (36)
Febrile neutropenia	4 (17)	7 (22)	11 (20)
Diarrhea	2 (9)	2 (6)	4 (7)

Grade ≥3 TEAEs (>10% of total patients)	CD30 <1% (n = 23)	CD30 1% to <10% (n = 32)	Total (N = 55)
Patients with any event, n (%)	13 (57)	16 (50)	29 (53)
Febrile neutropenia	4 (17)	6 (19)	10 (18)
Neutropenia	2 (9)	7 (22)	9 (16)
Anemia	1 (4)	6 (19)	7 (13)