Abstract 7077

Frontline brentuximab vedotin and CHP in patients with peripheral T-cell lymphoma with <10% CD30 expression: primary analysis results from the phase 2 SGN35-032 study

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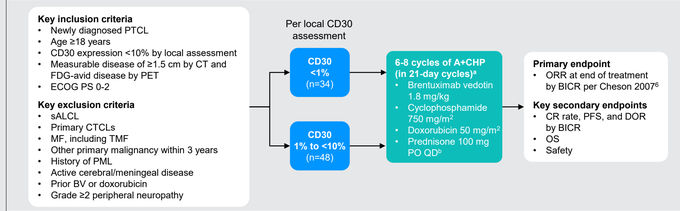
Background

- BV, an antibody-drug conjugate targeting CD30, has shown single-agent activity in several lymphomas regardless of CD30 expression[3,4]
- The BV combination therapy of A+CHP was approved as a frontline treatment for patients with sALCL or other CD30-positive PTCL subtypes based on results from the phase 3 ECHELON-2 study (NCT01777152)[1,4]
  - A+CHP had a 30% risk reduction in PFS (stratified hazard ratio [HR], 0.70; 95% CI, 0.53-0.91; *P*=0.0077) and an OS benefit (HR, 0.72; 95% CI, 0.53-0.99; *P*=0.0424)[1]
- While high CD30 expression is a diagnostic characteristic of sALCL, CD30 expression is more variable in other PTCL subtypes[1]
- The SGN35-032 study is evaluating whether frontline A+CHP may also demonstrate efficacy in patients with non-sALCL PTCL with <10% CD30 expression[5]
- We report primary analysis results of SGN35-032

Methods

- SGN35-032 (NCT04569032; EudraCT 2020-002336-74) is an open-label, dual-cohort, global, multicenter, phase 2 study (**Figure 1**)
- Patients with newly diagnosed non-sALCL PTCL with <10% CD30 expression (by standard immunohistochemistry by local pathology assessment) were enrolled
  - Patients were assigned to either CD30 <1% or CD30 1% to <10% cohorts
- All patients received 21-day cycles of A+CHP for up to 6 to 8 cycles
- The primary endpoint, ORR following the completion of study treatment, was assessed by blinded independent central review (BICR) per Cheson 2007[6]
- Secondary endpoints included safety and complete response (CR) rate, PFS, OS, and duration of response (DOR)
- Efficacy endpoints are reported per central CD30 assessment unless otherwise noted

Figure 1: Study design



CT, computed tomography; CTCL, cutaneous T-cell lymphoproliferative disorders and lymphomas; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG, fluorodeoxyglucose; MF, mycosis fungoides; PET, positron emission tomography; PML, progressive multifocal leukoencephalopathy; PO, orally; QD, once daily; TMF, transformed mycosis fungoides.
[a]Brentuximab vedotin, cyclophosphamide, and doxorubicin were administered by intravenous infusion on day 1 of each cycle. [b]Prednisone was administered orally on days 1 to 5 of each cycle.

Results

- As of July 22, 2024, a total of 82 patients received ≥1 dose of A+CHP, including 34 in the CD30 <1% cohort and 48 in the CD30 1% to <10% cohort (per local assessment)
  - Per central CD30 assessment, 23 patients were included in the CD30 <1% cohort, and 31 were included in the CD30 1% to <10% cohort
- At data cutoff, no patients were still receiving A + CHP; median follow-up was 15.7 months
- Baseline characteristics were generally balanced between the 2 cohorts (**Table 1**)

Table 1: Demographics and baseline disease characteristics

	CD30 <1%[a] (n=34)	CD30 1% to <10%[a] (n=48)	Total (N=82)
Age, median (range), years	63.0 (24-78)	64.0 (32-80)	63.5 (24-80)
Age group, n (%)			
<65 years	19 (56)	28 (58)	47 (57)
≥65 years	15 (44)	20 (42)	35 (43)
Race, n (%)			
Asian	2 (6)	4 (8)	6 (7)
Black or African American	2 (6)	2 (4)	4 (5)
White	26 (76)	37 (77)	63 (77)
Other/unknown/not reportable	4 (12)	5 (10)	9 (11)
ECOG PS, n (%)[b]			
0	15 (44)	21 (44)	36 (44)
1	16 (47)	22 (46)	38 (46)
2	2 (6)	5 (10)	7 (9)
Missing	1 (3)	0	1 (1)
Disease diagnosis, n (%)			
PTCL-NOS	18 (53)	19 (40)	37 (45)
Nodal TFH cell lymphoma	13 (38)	26 (54)	39 (48)
Other	3 (9)	3 (6)	6 (7)
Baseline IPI score, n (%)			
0/1	6 (18)	11 (23)	17 (21)
2/3	22 (65)	33 (69)	55 (67)
4/5	5 (15)	3 (6)	8 (10)
Missing	1 (3)	1 (2)	2 (2)

IPI, International Prognostic Index; PTCL-NOS, peripheral T-cell lymphoma, not otherwise specified; TFH, T-follicular helper.
[a]CD30 expression per local testing. [b]The last nonmissing value before or on the day of first study treatment.

- Overall, the median treatment duration was 18.0 weeks (range, 3-24 weeks)
- At end of treatment, ORR was 77%, with CR rate of 63% (**Table 2**)
  - In the CD30 <1% cohort, ORR was 61%, with CR rate of 52%
  - In the CD30 1% to <10% cohort, ORR was 81%, with CR rate of 71%
- Overall median DOR was 15.9 months but NR in either cohort

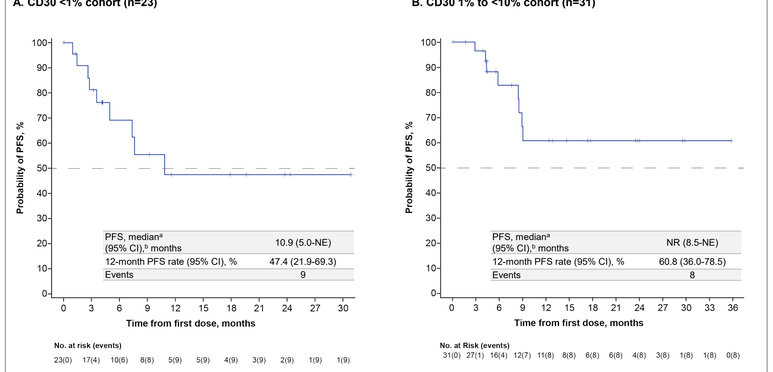
Table 2: Response by BICR by CD30 status

	CD30 <1%	CD30 1% to <10%	Total
Per local CD30[a]	**n=34**	**n=48**	**N=82**
Response at EOT, n (%)[b]			
CR	19 (56)	33 (69)	52 (63)
PR	6 (18)	5 (10)	11 (13)
SD	0	3 (6)	3 (4)
PD	4 (12)	5 (10)	9 (11)
NE[c]	5 (15)	2 (4)	7 (9)
CR rate (95% CI), %[d]	56 (37.9-72.8)	69 (53.7-81.3)	63 (52.0-73.8)
ORR (95% CI), %[d]	74 (55.6-87.1)	79 (65.0-89.5)	77 (66.2-85.4)
Per central CD30[a]	**n=23**	**n=31**	**N=82[e]**
Response at EOT, n (%)[b]			
CR	12 (52)	22 (71)	52 (63)
PR	2 (9)	3 (10)	11 (13)
SD	1 (4)	1 (3)	3 (4)
PD	5 (22)	2 (6)	9 (11)
NE[c]	3 (13)	3 (10)	7 (9)
CR rate (95% CI), %[d]	52 (30.6-73.2)	71 (52.0-85.8)	63 (52.0-73.8)
ORR (95% CI), %[d]	61 (38.5-80.3)	81 (62.5-92.5)	77 (66.2-85.4)

EOT, end of treatment; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.
[a]Based on response either at end of treatment or the first assessment after the last dose of study treatment. [b]CR, PR, SD, and PD per Cheson 2007 per independent assessor. CR, PR, SD, PD, and NE are mutually exclusive. [c]NE includes patient with no postbaseline response assessments. [d]Two-sided 95% exact CI, computed using the Clopper-Pearson method. [e]Per central testing, 28 patients either had CD30 ≥10% or were missing CD30 results.

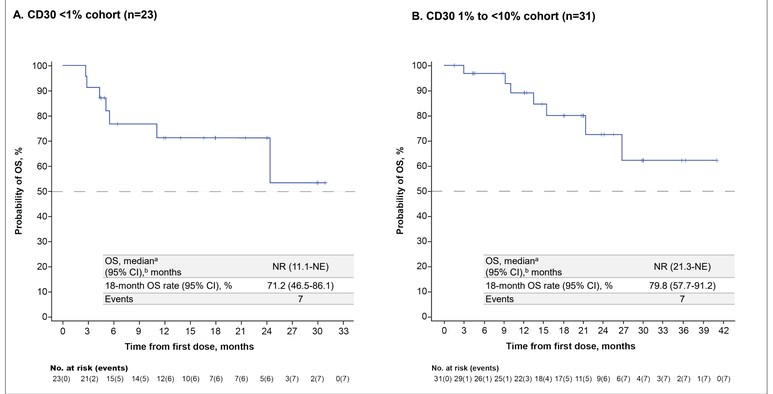
- Median PFS was 10.9 months in the CD30 <1% cohort, NR in the CD30 1% to <10% cohort, and 12.7 months in the overall population (**Figure 2**)
- Median OS was NR in the CD30 <1% cohort, CD30 1% to <10% cohort, and overall population (**Figure 3**)

Figure 2: PFS by central CD30 status



NE, not evaluable.
[a]As estimated using Kaplan-Meier methods. [b]Calculated using the complementary log-log transformation method.

Figure 3: OS by central CD30 status



NE, not evaluable.
[a]As estimated using Kaplan-Meier methods. [b]Calculated using the complementary log-log transformation method.

- Most patients (95%) had a treatment-emergent adverse event (TEAE), with 59% having a grade ≥3 TEAE (**Table 3**)
  - The most common (≥10%) overall grade ≥3 TEAEs were neutropenia (18%), febrile neutropenia (17%), and anemia (10%)
- Treatment-related deaths were reported in 2 patients: decreased appetite and general physical health deterioration
- TRAEs led to treatment discontinuation in 3 patients (4%)
  - Decreased appetite, febrile neutropenia, and pneumonitis (1 patient each)
- After last treatment, 13 patients (38%) and 14 (29%) in the CD30<1% and CD30 1% to <10% cohorts, respectively, received autologous stem cell transplant

Table 3: Summary of TEAEs

	CD30 <1%[a] (n=34)	CD30 1% to <10%[a] (n=48)	Total (N=82)
Any-grade TEAEs, n (%)	32 (94)	46 (96)	78 (95)
Grade ≥3 TEAEs, n (%)	22 (65)	26 (54)	48 (59)
Most common (≥10% of total patients)			
Neutropenia	4 (12)	11 (23)	15 (18)
Febrile neutropenia	6 (18)	8 (17)	14 (17)
Anemia	2 (6)	6 (13)	8 (10)
Treatment-related TEAEs[b]	25 (74)	40 (83)	65 (79)
Most common (≥20% of total patients)			
Peripheral sensory neuropathy	11 (32)	16 (33)	27 (33)
Diarrhea	7 (21)	13 (27)	20 (24)
Nausea	7 (21)	13 (27)	20 (24)
Neutropenia	4 (12)	12 (25)	16 (20)
Serious TEAE, n (%)	15 (44)	16 (31)	31 (38)
Treatment related	9 (26)	12 (25)	21 (26)
BV related	9 (26)	10 (21)	19 (23)
TEAEs leading to dose treatment discontinuation, n (%)	2 (6)	4 (8)	6 (7)[c]
Treatment related	1 (3)	2 (4)	3 (4)[d]
BV related	1 (3)	2 (4)	3 (4)

[a]CD30 expression per local testing. [b]Per investigator determination of relatedness to any study drug. [c]These included anemia, colitis, cutaneous T-cell lymphoma, decreased appetite, febrile neutropenia, and pneumonitis. [d]These included pneumonitis, decreased appetite, and febrile neutropenia.

Conclusions

- Brentuximab vedotin (BV) combined with cyclophosphamide, doxorubicin, and prednisone (A+CHP) demonstrated clinically meaningful efficacy as a frontline therapy in patients with nonsystemic anaplastic large cell lymphoma (non-sALCL) peripheral T-cell lymphoma (PTCL) regardless of CD30 expression
  - Objective response rate (ORR) at end of treatment was comparable for the CD30 <1% (61%) and CD30 1% to <10% (81%) cohorts
  - Progression-free survival (PFS) and overall survival (OS) were similar for the CD30 <1% (10.9 months and not reached [NR], respectively) and 1% to <10% (NR and NR, respectively) cohorts
- Safety was consistent with the known safety profile of A+CHP, with no new safety signals
- This study demonstrated that the efficacy and safety of A+CHP in non-sALCL PTCL with CD30 <10% were comparable to those of a similar population from ECHELON-2 with CD30 ≥10%[1,2]
- Results show that A+CHP is effective for patients with non-sALCL PTCL regardless of CD30 expression, supporting the proposed, multifaceted mechanism of action of BV in combination with CHP

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