Exploratory Analysis of Retreatment with Brentuximab Vedotin (BV) After Frontline Treatment with BV and CHP (A+CHP) for Patients with CD30+ PTCL

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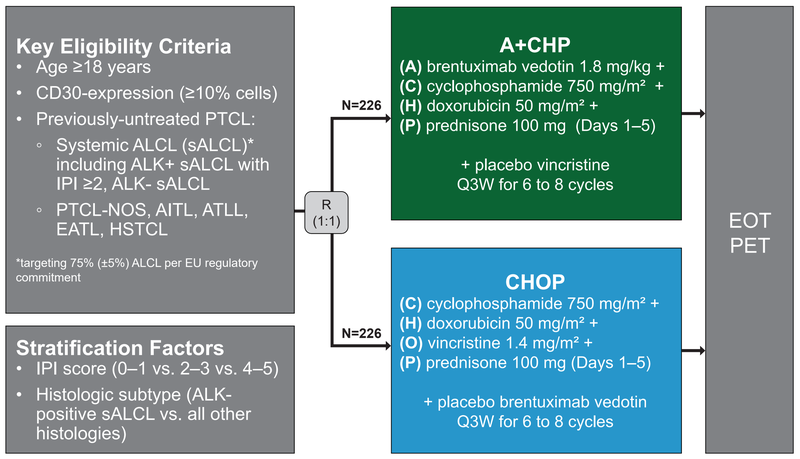
Background: A+CHP Treatment in CD30+ PTCLs

- **Brentuximab vedotin plus cyclophosphamide, doxorubicin, and prednisone (A+CHP) was approved for adults:**
  - In 2018 by FDA for previously untreated patients with sALCL or CD30-expressing PTCL, including AITL and PTCL-NOS
  - In 2019 by Health Canada for previously untreated patients with sALCL, AITL, or PTCL-NOS whose tumors express CD30
- The approvals were based on superior PFS, the primary endpoint, compared to CHOP in the ECHELON-2 study[1] (NCT01777152):
  - PFS (HR=0.71 [95% CI: 0.54, 0.93], p=0.0110)
  - OS (HR=0.66 [95% CI: 0.46, 0.95], p=0.0244)
- Given the historically high relapse rate in PTCLs, retreatment is an option for some patients following relapse after frontline therapy.

Background: BV Retreatment

- Retreatment with BV monotherapy after relapse showed encouraging antitumor activity in patients with cHL or sALCL who had previously responded to BV therapy in the relapsed or refractory setting.[2]
- Antitumor activity was demonstrated in 19 patients with cHL or sALCL (NCT00947856)
  - cHL retreatment: 60% ORR (12 of 20 evaluable patients) and 30% CR rate (6 of 20 evaluable patients)
  - sALCL retreatment: 88% ORR (7 of 8 patients) and 63% CR rate (5 of 8 patients)
  - Estimated median DOR for patients with an objective response was 9.5 months; for patients with a CR, the estimated median DOR was 12.3 months
- Interpretation of results from this study is limited because no patients received BV as part of frontline treatment and no patients were enrolled with non-sALCL PTCL.

ECHELON-2 Study Design (NCT01777152)



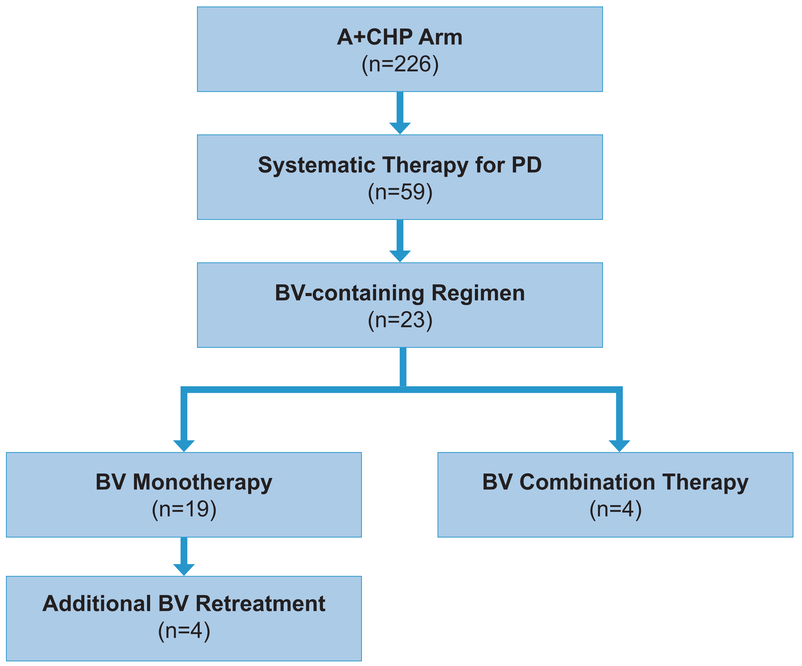
AITL, angioimmunoblastic T-cell lymphoma; ALCL, anaplastic large-cell lymphoma; ALK, anaplastic lymphoma kinase ATLL, adult T-cell leukemia/lymphoma; EATL, enteropathy-associated T-cell lymphoma; EOT, end of treatment; GCSF, granulocyte-colony stimulating factor; HSTCL, hepatosplenic T-cell lymphoma; IPI, international prognostic index

Per investigator discretion:
GCSF primary prophylaxis, consolidative RT and SCT

Methods

- In ECHELON-2, patients were permitted subsequent anticancer therapies, including BV-containing regimens, after frontline treatment with A+CHP or CHOP.
- Response to BV retreatment was assessed by the investigators based on the Revised Response Criteria for Malignant Lymphoma.[3]
- Safety information was not collected for subsequent anticancer therapy.

BV Retreatment in A+CHP Arm of ECHELON-2



Demographic and Disease Characteristics for Patients in A+CHP Arm Receiving BV Retreatment

Patients	N=23
Age (y), median (range)	62 (26, 77)
Gender, n (%)	
Male	16 (70)
Female	7 (30)
Diagnosis, n (%)	
sALCL	17 (74)
ALK positive	1 (6)
ALK negative	16 (94)
PTCL-NOS	3 (13)
AITL	3 (13)
Disease stage at initial diagnosis, n (%)	
II	1 (4)
III	5 (22)
IV	17 (74)
ECOG status 0 or 1, n (%)	20 (86)
Intention of STC following completion of study regimen - yes, n (%)	11 (48)

Summary of Patients in A+CHP Arm Receiving BV Retreatment

Patients	N=23
First BV retreatment, n (%)	
Monotherapy	19 (83)
Combination therapy	4 (17)
Received multiple lines of BV retreatment	4 (17)
Time from start of frontline A+CHP to first BV retreatment months, median (range)	12.3 (3, 50)
Received any SCT after frontline therapy n (%)	13 (57%)
Received autologous SCT after frontline therapy n (%)	12 (52%)
Response at EOT per Investigator after frontline A+CHP n (%)	
Objective response rate	20 (87)
Complete remission	14 (61)
Partial remission	6 (26)
Stable disease	2 (9)
Progressive disease	1 (4)

Objective Response to First BV Retreatment for Patients in A+CHP Arm

	Overall N=23	sALCL N=17	PTCL-NOS N=3	AITL N=3
Objective response rate, n (%)	**13 (57)**	**9 (53)**	**2 (67)**	**2 (67)**
Response, n (%)[a]				
Complete remission	10 (43)	7 (41)	2 (67)	1 (33)
Partial remission	3 (13)	2 (12)	0	1 (33)
Stable disease	1 (4)	1 (6)	0	0
Progressive disease	4 (17)	3 (18)	1 (33)	0
Not evaluable[b]	4 (17)	3 (18)	0	1 (33)
Unknown	1 (4)	1 (6)	0	0

a Responses were assessed by investigators based on Revised Response Criteria for Malignant Lymphoma[3]. Responses are mutually exclusive.
b Patients had no post-baseline response assessment.

Patients Receiving More Than One BV Retreatment (n=4)

Diagnosis	Response at EOT after frontline A+CHP	Response to 1st BV retreatment[a]	Duration of therapy (days)	Response to 2nd BV retreatment[b]	Duration of therapy (days)	Response to 3rd BV retreatment[a]	Duration of therapy (days)
AITL	CR	CR[b]	70	PD[b]	1	–	–
ALK– sALCL	CR	CR	129	Unknown[b,c]	Missing	–	–
ALK– sALCL	CR	PD	22	CR[b]	361	–	–
ALK– sALCL	CR	CR	114	CR	22	CR	1

a Unless otherwise noted, patients received BV monotherapy for retreatment.
b Patient received intervening therapy before BV retreatment.
c Patient received BV in combination with nivolumab.

Limitations

- This exploratory subgroup analysis was post-hoc, which may introduce unknown bias.
- The study was not powered to make an assessment of the antitumor effects of BV retreatment in patients with PTCL.
- Small sample sizes (overall and by histological subtype).

Conclusions and Future Directions

- In patients in ECHELON-2 who were retreated with BV after frontline treatment with A+CHP, 57% had an objective response to initial BV retreatment.
- BV retreatment is currently under investigation in phase 2 study in patients with cHL, sALCL, or other CD30-expressing PTCL (NCT03947255).

Acknowledgments

- The authors thank the patients who participated in this study, their families, and the caregivers.
- Study funded by Seattle Genetics, Inc. and Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited. This research was funded in part through the National Institutes of Health/National Cancer Institute Cancer Center Support Grant P30 CA008748.

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