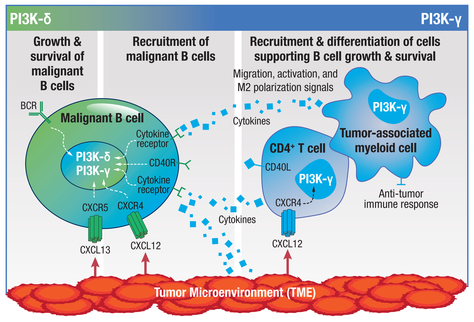
Abstract No. 3146

Characterization of the Long-Term Efficacy and Safety of Duvelisib Monotherapy in Patients with CLL/SLL On Treatment for More Than 2 Years Across 4 Clinical Studies

Ian W. Flinn[1], Marco Montillo[2], Zsolt Nagy[3], Zoltán Gasztonyi[4], Matthew S. Davids[5], Jose J. Rifon Roca[6], Leanne Berkhan[7], Klaus Geissler[8], Fritz Offner[9], Stephanie Lustgarten[10], Julio Delgado[11]

[1]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; [2]Niguarda Cancer Center, ASST Grande Ospedale Metropolitano Niguarda, Milan, ITA; [3]Semmelweis University, Budapest, HNG; [4]Petz Aladár County Hospital, Györ, HNG; [5]Dana-Farber Cancer Institute, Boston, MA; [6]Clínica Univ. de Navarra, Pamplona, ESP; [7]Auckland City Hospital, Auckland, New Zealand; [8]Krankenhaus Lainz, Vienna, AUT; [9]Ghent University Hospital, Ghent, BEL; [10]Verastem Oncology, Needham, MA; [11]Hospital Clínic de Barcelona, Barcelona, ESP

BACKGROUND



- Duvelisib (DUV) is a first-in-class, oral dual inhibitor of PI3K-δ,γ approved by the US FDA for treatment of relapsed/refractory (RR) CLL/SLL in patients who have received 2 or more prior therapies
- The Phase 3 DUO Study (NCT02004522) in RR CLL/SLL showed favorable benefit-risk in patients who had received 2 or more prior therapies[1,2]
- Gr 3+ hematologic adverse events (AEs) included neutropenia (30%), anemia (13%), and thrombocytopenia (8%); the most common Gr 3+ non-hematologic AEs were diarrhea (15%), pneumonia (14%), and colitis (12%)[1]

Efficacy from the DUO Study in Patients Who Received ≥ 2 Prior Therapies[2]

Category	Duvelisib Monotherapy (N = 95)	Ofatumumab Monotherapy (N = 101)
Median PFS (months)	16.4*	9.1
95% CI	12.0, 20.5	7.9, 10.7
Hazard Ratio (95% CI)	0.4 (0.27, 0.59)	
ORR, %	78.9*	38.6
95% CI	70.7, 87.1	29.1, 48.1

*Statistically significant vs ofatumumab: p < 0.0001. All results per blinded independent review committee. ORR = overall response rate; PFS = progression-free survival.

- To date 304 patients with RR CLL/SLL have been treated with DUV monotherapy 25 mg BID in 4 studies
- Here we present pooled efficacy and safety analyses from these 4 studies in RR CLL/SLL in the subset of patients who received DUV monotherapy for > 2 years

METHODS

- Response based on investigator assessment per IWCLL/IWG criteria
- Treatment-emergence (TE) = AEs that occurred from first dose to 30 days post last dose of DUV
- AEs coded using MedDRA version 16.1
- Severity assessed by investigators according to the National Cancer Institute-Common Terminology Criteria for Adverse Events version 4.03.

ANALYSIS POPULATION AND DISPOSITION

Analysis Population

Study	Phase	Patients Receiving DUV Monotherapy ≥ 2 Years, n
IPI-145-02 [NCT01476657]	Phase 1 in advanced hematologic malignancies	3
IPI-145-06 (DYNAMO™) [NCT01882803]	Phase 2 in RR iNHL, including SLL	1
IPI-145-07 (DUO™) [NCT02004522]	Phase 3 in RR CLL/SLL	32
IPI-145-12 IPI-145-12 [NCT02049515]	Phase 3 crossover, extension from DUO	10
	Total:	46

References: 1) Flinn, *Blood* 2018. **2)** COPIKTRA™ Prescribing Information 2018.

Disclosures: Author information is available on the ASH website: https://ash.confex.com/ash/2018/webprogram/Paper120027.html.

DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Disposition

Characteristic	Patients Treated ≥ 2 years N = 46
On Treatment, n (%)	21 (46)
Off Treatment, n (%)	25 (54)
Reason for Discontinuation, n (%)	
Progressive Disease	12 (26)
Adverse Event	7 (15)
Investigator Decision	2 (4)
Voluntary Withdrawal by Patient	1 (2)
Death	1 (2)
Other	2 (4)

Demographics

Category	Patients Treated < 2 Years N = 258	Patients Treated ≥ 2 years N = 46
Median Age (years)	68	69
Min, Max	39, 86	45, 90
≥ 65 years, %	64	63
Male, %	65	59
Race, %		
White/Caucasian	93	94
Black/African American	2	0
Other/Unknown	5	7
Baseline BMI, median	27	25

Baseline Disease Characteristics and Prognostic Features

Characteristic	Patients Treated < 2 Years N = 258	Patients Treated ≥ 2 years N = 46
CLL/SLL, %	87 / 13	91 / 9
ECOG PS 2, %	9	2
Rai Stage ≥ 3 / Binet Stage C, %	56	47
Bulky disease (≥ 5 cm target lesion), %	49	42
Grade 4 Cytopenia(s), %	6	0
Molecular features (per central laboratory), %		
17p deletion	27	22
TP53 mutation	25	14
17p deletion and TP53 mutation	33	24
Unmutated IGHV	81	83

Prior Anticancer Therapy

Characteristic	Patients Treated < 2 Years N = 258	Patients Treated ≥ 2 years N = 46
Median prior therapies	2	2
Median months from prior therapy	9	10
Purine Analog, %	59	50
Alkylator, %	85	89
Monoclonal antibody, %	80	74

Dose Intensity and Dose Reductions with DUV Over Time in Patients Treated > 2 Years

	0-6 Mo	>6-12 Mo	>12-18 Mo	>18-24 Mo	>24 Mo
Relative Dose Intensity, mean (SD)[1]	90.2 (16.5)	85.6 (19.2)	84.2 (21.9)	79.4 (26.1)	74.6 (29.7)
Patients on Reduced Dose, %[2]	35	33	41	48	54

[1] Dose Intensity calculated as actual accumulated total dose divided by prescribed dose for study 06, 07, and 12, and number of days on treatment divided by number of days prescribed for study 02. [2] Includes any patients who received a reduced dose (< 25 mg BID) of DUV. SD = standard deviation

- Median exposure 34 months; 26 patients on DUV > 36 cycles (~3 years); 4 patients on DUV > 48 cycles (~4 years)

For more information:
+1-781-292-4200 or MedicalAffairs@verastem.com

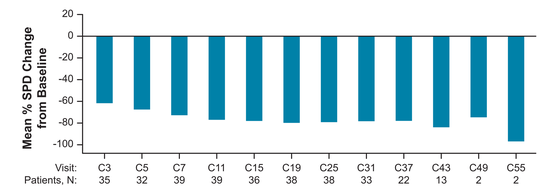
EFFICACY

Overall Response Rate (Per Investigator Assessment)

Response	All Patients Treated ≥ 2 Years N = 46	Patients with del(17p)/TP53 Mutation N = 10
ORR, n (%)	41 (89)	10 (100)
CR/CRi	9 (20)	3 (30)
PR	32 (70)	7 (70)
SD	5 (11)	0
LNRR, %	87	80
Median PFS (months)	40	38

CR = complete response; CRi = complete response with incomplete marrow recovery; LNRR = lymph node response rate (i.e. ≥ 50% reduction in target lesion); PR = partial response; SD = stable disease

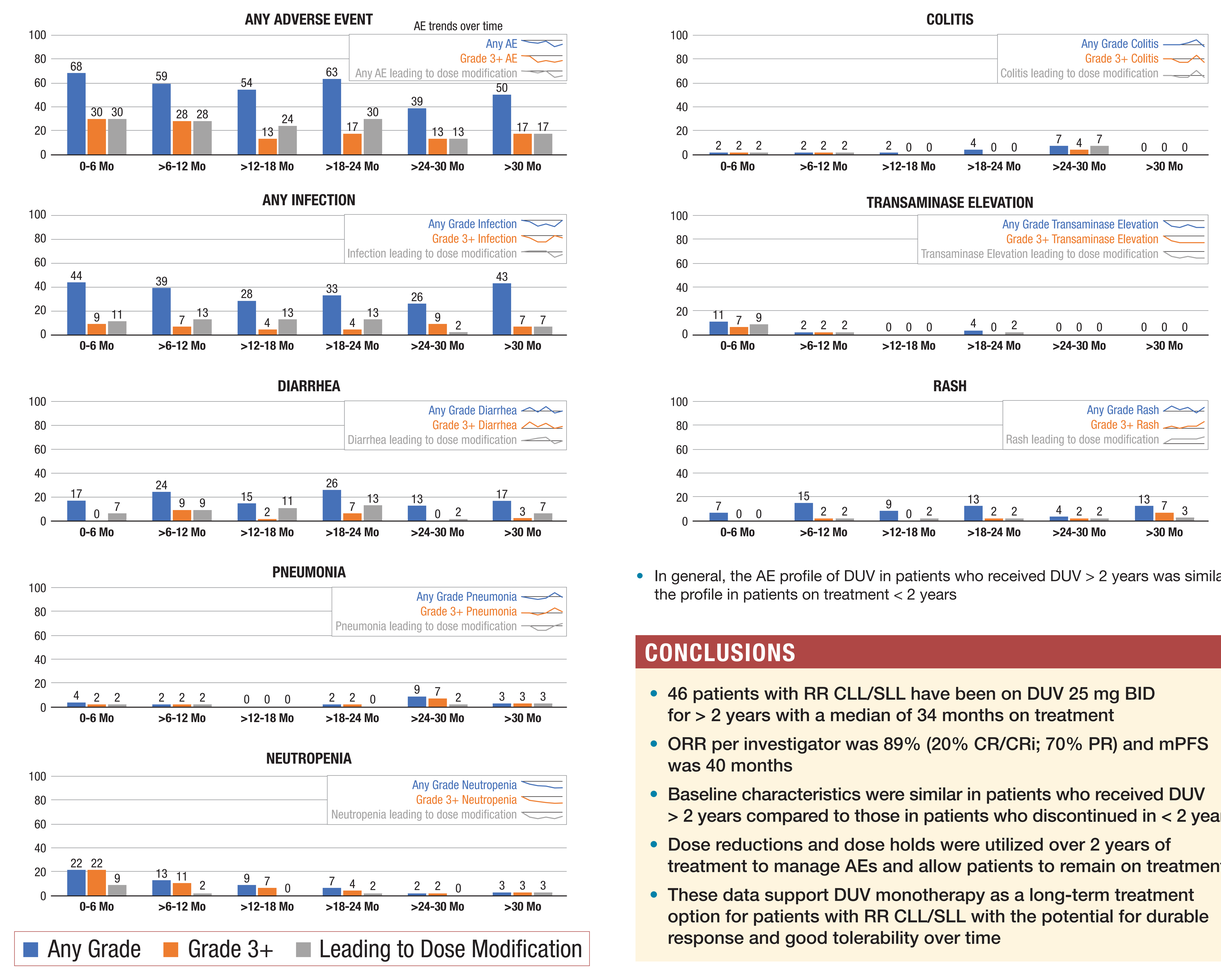
Nodal SPD Change from Baseline over Time in Patients Treated ≥ 2 Years



C = cycle; SPD = Sum of the product of greatest diameter

SAFETY

Adverse Events of Interest in Long-Term Patients Treated with Duvelisib Over Time (% Patients) (N = 46)



- In general, the AE profile of DUV in patients who received DUV > 2 years was similar to the profile in patients on treatment < 2 years

CONCLUSIONS

- 46 patients with RR CLL/SLL have been on DUV 25 mg BID for > 2 years with a median of 34 months on treatment
- ORR per investigator was 89% (20% CR/CRi; 70% PR) and mPFS was 40 months
- Baseline characteristics were similar in patients who received DUV > 2 years compared to those in patients who discontinued in < 2 years
- Dose reductions and dose holds were utilized over 2 years of treatment to manage AEs and allow patients to remain on treatment
- These data support DUV monotherapy as a long-term treatment option for patients with RR CLL/SLL with the potential for durable response and good tolerability over time

American Society of Hematology; San Diego, CA; December 1 – 4, 2018