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Journal

Cancer Research, 83(8_Supplement)

ISSN

0008-5472

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Publication Date

2023-04-14

DOI

10.1158/1538-7445.am2023-ct021

Peer reviewed

ORAL PRESENTATIONS - PROFFERED ABSTRACTS | APRIL 14 2023

Abstract CT021: Assessing clinical and pharmacodynamic (PD) profiles of patients (pts) with chronic lymphocytic leukemia (CLL) on ianalumab (VAY736) + ibrutinib FREE

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Cancer Res (2023) 83 (8_Supplement): CT021.

https://doi.org/10.1158/1538-7445.AM2023-CT021

Abstract

Introduction VAY736 is an afucosylated, human monoclonal antibody engineered to enhance antibody-dependent cellular cytotoxicity that targets BAFF-R+ B cells for elimination. In preclinical CLL models, VAY736 showed antileukemic activity and, when combined with ibrutinib, significantly reduced disease burden, which may allow some pts to discontinue ibrutinib.

Methods This Phase Ib dose-escalation (ESC)/-expansion (EXP) trial (NCT03400176) enrolled pts with CLL who did not achieve a complete response (CR) after >1 year of ibrutinib or had developed a resistance mutation to ibrutinib. Pts received IV VAY736 (ESC: 0.3-9 mg/kg; EXP: 3 mg/kg) once every 2 weeks and oral ibrutinib (420 mg) once daily for up to 8 28-day cycles. Pts achieving undetectable MRD (uMRD) at C9D1 could discontinue ibrutinib at investigator discretion. The study aimed to characterize the safety and tolerability of VAY736 + ibrutinib, assess antitumor activity, PK, and characterize PD profiles.

Results By Jul 29, 2022, 39 pts were enrolled (ESC: n=15; EXP: n=24). **Table 1** shows pt characteristics, safety, and efficacy data. The overall response at C9D1 for 37 evaluable pts was 40.5% CR + CRi and 16.2% PR (1L: 63.6% CR + CRi and 18.2% PR). At C9D1, 17 pts (45.9%) had uMRD in blood or bone marrow (BM). In the 2-year follow-up period, 16 pts discontinued ibrutinib and were off therapy for 4.9-19.8 months. Frequency of peripheral NKp46+ NK cells increased at least 50% after VAY736 in over 50% of pts. Preliminary coverage-based limiting-cell experiment analysis of RNAseq (CLEAR) data from 10 pts supports peripheral NK cell activation with VAY736.

Conclusions VAY736 + ibrutinib appears highly active and has an acceptable safety profile. Multiple pts attained uMRD in blood or BM. Biomarker data suggest NK cell activation with VAY736.

Table 1.

Patient characteristics, safety, and efficacy results.

	All patients (N=39)
Patient demographics and prior treatment	
Median age, years (range)	65.0 (39-82)
ECOG performance status, n (%)	
0	36 (92.3)
1	3 (7.7)
No prior regimens excluding ibrutinib, n (%)	12 (30.8)
Median number of prior regimens, n (range)	1.0 (0.0-14.0)
Median duration of ibrutinib, years (range)	2.95 (0.2-8.3)
Patient baseline characteristics	
Dohner risk by FISH,[a] n (%)	
17p deletion	6 (15.4)
11q deletion	9 (23.1)
Trisomy 12	3 (7.7)
13q deletion	10 (25.6)
IGHV mutant status, n (%)	
Non-mutant	32 (82.1)
Complex karyotype, n (%)	
Yes	20 (51.3)
Safety	
Dose-limiting toxicities, n (%)	0
Patients with at least one AE, any grade, n (%)	38 (97.4)

Patients with at least one Grade ≥3 AE, n (%)	13 (33.3)		
Most common (occurring in ≥2 patients) Grade ≥3 AEs, n (%)			
Neutrophil count decreased	5 (12.8)		
Lymphocyte count decreased	2 (5.1)		
Hypophosphatemia	2 (5.1)		
Lipase increased	2 (5.1)		
Efficacy	**1L[b] n=11**	**R/R n=26**	**Evaluable patients**
Overall response at C9D1 or before discontinuation,[c] n (%)			
Complete response	6 (54.5)	8 (30.8)	14 (37.8)
Complete response with incomplete marrow recovery	1 (9.1)	0	1 (2.7)
Partial response	2 (18.2)	4 (15.4)	6 (16.2)
Stable disease	2 (18.2)	8 (30.8)	10 (27.0)
Progressive disease	0	5 (19.2)	5 (13.5)
uMRD response at C9D1 or before discontinuation,[c] n (%)			
Bone marrow uMRD	6 (54.5)	6 (23.1)	12 (32.4)
Blood uMRD	7 (63.6)	10 (38.5)	17 (45.9)
Blood or bone marrow uMRD	7 (63.6)	10 (38.5)	17 (45.9)
Patients elected to discontinue ibrutinib after achieving CR or uMRD, n (%)	16 (43.2)		

[a]The categories were: patients with a 17p deletion; patients with an 11q deletion without a 17p deletion; patients with trisomy 12 without a 17p deletion or an 11q deletion; and patients with a 13q deletion without a 17p deletion, trisomy 12, or an 11q deletion; [b]Patients with no prior therapies excluding ibrutinib; [c]For evaluable patients (N=37).
1L, first line; AE, adverse event; CR, complete response; C, cycle; D, day; ECOG, Eastern Cooperative Oncology Group; FISH, fluorescence in situ hybridization; IGHV, immunoglobulin heavy chain variable region; R/R, relapsed/refractory; uMRD, undetectable minimal residual disease.

Citation Format: Kerry Anne Rogers, Pearlly Yan, Ian W. Flinn, Deborah M. Stephens, Thomas J. Kipps, Sarah M. Larson, Laura Martz, Xi Chen, Huabao Wang, Ethan Hopping, Ralf Bundschuh, Alexandra Acosta, Daniela Baldoni, Anwesha Chaudhury, Jeanne Whalen, Nadia B. Hassounah,

In: Proceedings of the American Association for Cancer Research Annual Meeting 2023; Part 2 (Clinical Trials and Late-Breaking Research); 2023 Apr 14-19; Orlando, FL. Philadelphia (PA): AACR; Cancer Res 2023;83(8_Suppl):Abstract nr CT021.

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Online ISSN 1538-7445 **Print ISSN** 0008-5472

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