Phase 2 study with Tafasitamab and Zanubrutinib in newly diagnosed chronic lymphocytic leukemia/small lymphocytic lymphoma – TaZa CLL

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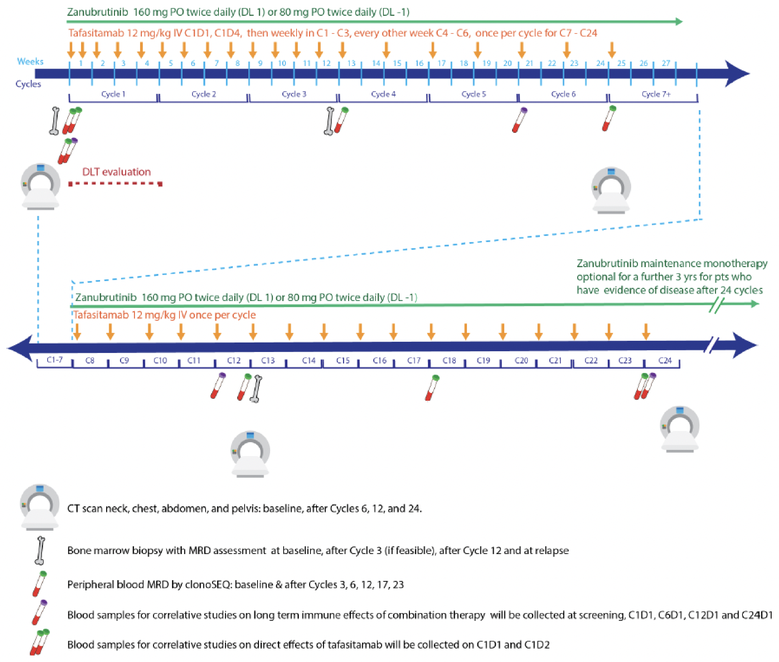
Background: Chronic lymphocytic leukemia (CLL) is the most common type of adult leukemia in the Western countries and is characterized by the clonal expansion of monoclonal CD5+ and CD19+ B lymphocytes. Despite the advances of the clinical outcomes with the Bruton tyrosine kinase inhibitors (BTKi) and the BCL2 inhibitors (BCL2i), relapses and acquisition of resistance remain a clinical challenge. Therefore, novel therapies in the front-line setting are urgently needed to prolong the survival of the CLL patients and delay the development of progression. CD19 is a B-cell surface antigen expressed in CLL cells which makes it an attractive target for drug development. Tafasitamab is a humanized, FC-enhanced anti-CD19 monoclonal antibody, which has demonstrated favorable response rates and toxicity profile when combined with venetoclax or idelalisib in relapsed and refractory CLL (R/R CLL) (Staber PB et al, ASH 2019). We hypothesized that a time-limited doublet combination of Tafasitamab with Zanubrutinib (TaZa) could achieve high efficacy with good tolerability. Herein, we report for first time, the safety and initial preliminary results of TaZa in previously untreated CLL/SLL

METHODS

Figure 1. Treatment Schema



RESULTS

Table 1. Patient and Disease Characteristics

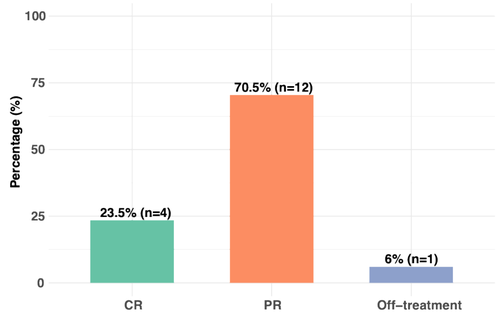
Baseline data	Total N=21
Age at TX start (median/rage)	65 (41-80)
Male	17 (81%)
Race	
White	15 (71%)
Asian	3 (14%)
Black	1 (5%)
Unknown/Not-disclosed	2 (10%)
ECOG	
0	15 (71%)
1	6 (29%)
WBC	93 (2.5-648)
Hemoglobin	12.1 (7-15)
Platelet	154 (89-301)
ANC	4 (0.9-12.6)
Rai Stage	
0-1	6 (29%)
2	7 (33%)
3	7 (33%)
4	1 (5%)
Complex Karyotype	
Yes	9 (43%)
No	7 (33%)
No/UNK Cytogenetic test or inadequate tissue	5 (24%)
Chromosome 17p deletion	
Yes	3 (14%)
No	13 (62%)
No/UNK Cytogenetic test or inadequate tissue	5 (24%)
TP53 mutation	
Yes	4 (19%)
No	14 (67%)
No molecular test	3 (14%)
IGHV mutation	
Mutated (>=2%)	6 (29%)
Unmutated (< 2%)	12 (57%)
Unknown	3 (14%)

Table 2. Adverse Events of Tafasitamab and Zanubrutinib

	Total AE (%) (N=21)	Grade 3-4 (%)
Infusion related reaction	16 (76%)	4 (19%)
Neutrophils	11 (52%)	6 (29%)
Bruising	10 (48%)	0
Lymphocyte count increased	6 (29%)	0
Diarrhea	5 (24%)	0
Platelets	5 (24%)	0
Arthralgia	4 (19%)	0
HgB (Anemia)	4 (19%)	0
Lymphocyte count decreased	4 (19%)	0
Headache	3 (14%)	0
Rash maculopapular	3 (14%)	0
Alkaline phosphatase increased	3 (14%)	0
Constipation	2 (10%)	0
Papulopustular rash	2 (10%)	0
Creatinine increased	2 (10%)	0
White blood cell decreased	2 (10%)	0
Pruritus	2 (10%)	0
Hematoma	2 (10%)	0
Abdominal pain	2 (10%)	0
Lung infection	2 (10%)	1 (5%)
Peripheral sensory neuropathy	2 (10%)	0
Cough	2 (10%)	0
Back pain	2 (10%)	0
Hypertension	2 (10%)	2 (10%)
Flushing	2 (10%)	0

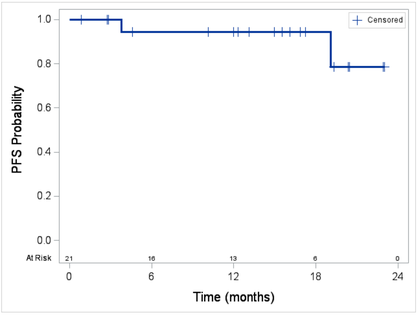
Treatment was discontinued in 2 patients due to grade 5 toxicities: one from pulmonary and brain aspergillus infection, and one from end-stage liver disease related to pre-existing alcoholic cirrhosis

Figure 2. Response Rates



Response assessments have been completed for 17 patients. The median number of cycles is 15 (2-26). CR= complete response, PR= partial response.

Figure 3. Progression Free survival



Nineteen patients (90%) remain on therapy, whereas 2 patients (10%) have discontinued therapy. The PFS and OS was 94% during a median follow up of 14.9 months (0.9-23). There has been no disease progression. Median PFS has not been reached.

CONCLUSIONS

- Our preliminary results suggest that the combination of Tafasitamab and Zanubrutinib leads to high overall response rate, including patients with unfavorable prognostic factors.
- TaZa is well tolerated. Infusion-related reactions secondary to tafasitamab were well-managed and at expected rates.

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