soho2023
ELEVENTH ANNUAL MEETING

VENETOCLAX THERAPY IN CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS RELAPSED AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

F. PERUTELLI[1], E. BOCCELLATO[1], G. CATANIA[2], A.M. FRUSTACI[3], I. INNOCENTI[4], R. MOIA[5], G. QUARESMINI[6], G. GAIDANO[5], M. LADETTO[2], L. LAURENTI[4], A. RAMBALDI[6], A. TEDESCHI[3], B. BRUNO[1], C. VITALE[1] and M. COSCIA[1]

1.University Division of Hematology, A.O.U. Città della Salute e della Scienza di Torino and Department of Molecular Biotechnology and Health Sciences, University of Torino, Torino, Italy; 2. Division of Hematology, Azienda Ospedaliera Santi Antonio e Biagio e Cesare Arrigo, Alessandria, Italy; 3. Department of Haematology, Niguarda Cancer Center, ASST Grande Ospedale Metropolitano Niguarda, Milano; 4. Department of Hematology, Università Cattolica del Sacro Cuore, Rome, Italy; 5. Division of Hematology, Azienda Ospedaliero-Universitaria Maggiore della Carità, Novara, Italy; 6. USC Ematologia, ASST Papa Giovanni XXIII, Bergamo, Italy

UNIVERSITÀ DI TORINO

AZIENDA OSPEDALIERO - UNIVERSITARIA Città della Salute e della Scienza di Torino

INTRODUCTION

Allogeneic hematopoietic stem cell transplantation (alloHSCT) remains an option for young and fit chronic lymphocytic leukemia (CLL) patients with high-risk disease features. However, patients who previously underwent alloHSCT are generally excluded from clinical trials, making data regarding the use of targeted agents after alloHSCT extremely rare.

AIM

The aim of the study was to determine the feasibility of venetoclax therapy in allotransplanted CLL patients.

DESIGN AND SETTING

This is an observational, multicenter, retrospective study collecting data from a survey sent to 53 Italian hematology centers. Thirty-five centers responded, among which 7 had patients who received venetoclax in this setting.

INTERVENTIONS

Venetoclax was administered at 400 mg daily to all except two patients, who received 200 mg and 300 mg daily, respectively. All patients received venetoclax as a single agent, except for one patient who received venetoclax plus obinutuzumab.

PATIENTS

The 7 CLL patients were diagnosed between 2002 and 2016 and underwent alloHSCT between 2006 and 2021 after failing chemoimmunotherapy (7/7), ibrutinib (5/7) and idelalisib (1/7). Five of 7 patients underwent alloHSCT from matched unrelated donors and five of 7 patients received a non-myeloablative conditioning regimen. Of note, three of 7 patients had already received venetoclax-based therapy before alloHSCT.

The characteristics of patients and main aspects of alloHSCT and venetoclax therapy are summarized in **Table 1**.

	Date of CLL diagnosis	CLL prognostic features[1]	Date of alloHSCT	Type of alloHSCT	Conditioning regimen of alloHSCT	Date of venetoclax start	Relevant AEs during venetoclax therapy	cGvHD during venetoclax therapy	Best response to venetoclax	Date of venetoclax discontinuation	Reason of venetoclax discontinuation	Duration of venetoclax therapy	Last follow-up
Patient 1	01/06/09	FISH: del13, del17 TP53 NA IgHV NA	14/01/15	MUD 10/10	Non myeloablative	15/04/19	Neutropenia G4	/	NR	16/08/19	Progression disease	4 months	16/08/19
Patient 2	23/12/09	FISH: del13, del17 TP53 MUT IgHV UM	27/04/15	MUD 9/10	Non myeloablative	03/05/19	Neutropenia G3	/	PR	09/09/19	Progression disease	4 months	17/09/19
Patient 3	01/02/11	FISH: del17 TP53 NA IgHV UM	02/04/15	Sibling	Non myeloablative	14/08/21	Neutropenia G4	Skin G2	PR	20/01/22	Progression disease	5 months	31/05/22
Patient 4	20/12/16	FISH: neg TP53 MUT IgHV NA	17/06/20	MUD 7/8	Myeloablative	25/02/21	Infection G2	Skin NA	PR MRD neg	10/03/22	Progression disease	12 months	19/03/23
Patient 5	15/03/08	FISH: del13, del11, del17 TP53 MUT IgHV UM	13/07/17	MUD 10/10	Non myeloablative	11/11/17	/	/	NR	04/06/18	Progression disease	6 months	19/03/23
Patient 6	01/01/05	FISH: del17 TP53 MUT IgHV UM	12/01/21	Sibling	Non myeloablative	01/04/21	Neutropenia G3	Skin G2	PR MRD neg	ongoing	/	21 months, ongoing	20/01/23
Patient 7	01/12/02	FISH: del11, del13 TP53 NA IgHV UM	09/03/06	MUD 10/10	Myeloablative	26/08/20	/	Ocular G3	PR	ongoing	/	35 months, ongoing	18/08/23

Table 1. *Abbreviations: alloHSCT, allogeneic hematopoietic stem cell transplantation; CLL, chronic lymphocytic leukemia; MRD, minimal residual disease; MUD, matched unrelated donor; MUT, mutated; NR, non-responder; PR, partial response; UM, unmutated.*

1 = Last available before venetoclax start

RESULTS

In post-transplant patients, venetoclax was safe, with adverse events (AEs) no different from those registered in clinical trials, neutropenia and infections being the most relevant (5/7 patients). Venetoclax did not impact graft versus host disease (GvHD) course: four out of 7 patients with pre-existing chronic GvHD had no exacerbation after venetoclax start, and only one patient developed GvHD during venetoclax therapy. During treatment, two out of 5 patients had improved GvHD symptoms and in three of 5 patients, the dose of steroid therapy was reduced. No patient needed to start additional immunosuppressive therapy. Five of 7 patients had a clinical response, with two achieving partial response with undetectable minimal residual disease in bone marrow. By the time of data collection, two patients had a persistent response after 2 years of venetoclax treatment.

CONCLUSIONS

To our knowledge, this is the largest reported series of CLL patients treated with venetoclax after alloHSCT. In this cohort of heavily pretreated and high-risk patients, previous alloHSCT did not compromise sensitivity to venetoclax, which was capable of inducing objective responses without exacerbating GvHD.

CONTACT INFORMATION

Francesca Perutelli, MD

francesca.perutelli@unito.it