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POSTER ABSTRACTS

722.ALLOGENEIC TRANSPLANTATION: ACUTE AND CHRONIC GVHD, IMMUNE RECONSTITUTION

Sitagliptin for Prevention of aGVHD in Patients Received Alternative Donor Transplantations: A Prospective, Multicenter, Open-Label, Randomized Controlled Trial

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Background:
Acute graft versus host disease (aGVHD) remains one of the most frequent complications following allogeneic hematopoietic stem cell transplantation (allo-HSCT) with high mortality. Traditionally, alternative donor transplantation (ADT) from an unrelated donor or a haploidentical family donor has been reported in an increased incidence of aGVHD and severe GvHD. Sitagliptin is a selective inhibitor of dipeptidyl peptidase 4 (DPP-4; also known as CD26), a transmembrane receptor expressed on T cells which has a costimulatory function in activating T cells.
This trial aims to evaluate the safety and efficacy of sitagliptin plus a calcineurin inhibitor, methotrexate (MTX), mycophenolate mofetil (MMF) and antithymocyte globulin (ATG) in the prevention of aGVHD for ADT.
Methods:
We are performing a prospective, multicenter, open-label, randomized controlled trial (NCT05149365). From 5 HSCT centers in China competitively, patients(pts) who underwent their first allo-HSCT in first or second complete remission (CR) state with hematologic malignancies were received busulfan and cyclophosphamide (Bu/Cy) myeloablative conditioning regimen followed by ADT. 190 eligible pts(18-60 years) were planned randomly assigned in a 1:1 ratio to either a sitagliptin group (600mg sitagliptin taken orally every 12 hours on day -1 to +14, plus conventional prophylaxis including Cyclosporin A(CsA)/tacrolimus (FK506), MTX, MMF and ATG) and a conventional prophylaxis control group (CsA/FK506, MTX, MMF and ATG). The randomization was based on a computer-generated priori list of 190 binary numbers, with block-balanced with random

variable block sizes of two or four pts, without stratification. The primary endpoint was grade II to IV aGvHD by day +100. Key secondary endpoints included severe (grade III or IV) aGvHD by day +100, transplant-related mortality (TRM), relapse-free survival (RFS) and GVHD-free, relapse-free survival (GRFS) from HSCT. At present we have completed pts enrollment and are at the stage of follow-up the study endpoints.

Results :

From December 2021 to May 2023, a total of 191 pts were enrolled. The ratio of male to female was 113 to 78 with a median age of 38 years (range, 18-60 years). Pts were randomly assigned to the sitagliptin group of 95 and the control group of 96. The clinical and transplantation characteristics at baseline of the intention to treat (ITT) population of the two groups were well balanced (Table1). The last follow-up was on May 30, 2023 and the median follow-up time was 164 (20-512) days.

Comparison of the sitagliptin group and the control group by day +100, the cumulative incidence rate of grade II-IV aGVHD was 15.1% and 28.6%, respectively (P= 0.019), and the cumulative incidence rate of grade III or IV aGVHD was 7.6% and 15.9% (P= 0.068); median days of neutrophil engraftment were +11.48 and +11.65 days, respectively (P=0. 545); TRM was 3.7% and 7.1% (P=0.454), RFS was 98.7% and 95.9% (P=0.889), respectively and OS of the two groups(96.7% vs 93.6%, P=0.341) was also the same as the RFS. There was no significant difference between the sitagliptin and control groups with regard to cytomegalovirus reactivation, Epstein-Barr virus reactivation, and transplant-related complications (Table 1, Figure 1).

The regimen was well tolerated. Only 5(/95) pts discontinued sitagliptin treatment due to adverse events: 4 patients experienced abdominal pain (CTCAE Grade1-2) undergoing sitagliptin therapy 3-7 days and one of them also exhibited hypoglycemia (CTCAE Grade1), which were deemed by clinicians as probable (WHO-UMC) associated with sitagliptin. Symptoms resolved spontaneously within 2 days of cessation. Another patient discontinued treatment due to mild hematemesis initiating sitagliptin therapy only 2 days, which was determined by the clinician as unlikely (WHO-UMC) associated with sitagliptin.

Conclusions :

Our trial showed sitagliptin combined with conventional prophylaxis (CsA+MTX+MMF+ATG) resulted in a significant reduction of grade II-IV aGVHD in ADT. Furthermore, sitagliptin is ready available, easy of administration, safe, and relatively inexpensive. It remains to be followed up whether it would increase infection and relapse or improve the prognosis of patients after allo-HSCT.

Disclosures No relevant conflicts of interest to declare.

OffLabel Disclosure: Sitagliptin is a selective inhibitor of DPP-4 that is approved for the treatment of type 2 diabetes mellitus. In our trial sitagliptin is for prevention of aGvHD in patients received alternative donor transplantations.

Table 1. Clinical Characteristics at Baseline and Transplantation Outcomes of Two Groups

Characteristic	Sitagliptin group (n=95)	Control group (n=96)	Value	*P* value
Median age (range)-yr	37(18-60)	40(18-59)	-1.180	0.239
Patient gender— no. (%)			0.004	0.952
Male	56(58.9)	57(59.4)		
Disease — no. (%)			3.501	0.478
Acute myeloid leukemia	59	51		
Myelodysplastic syndrome	12	18		
Acute lymphoblastic leukemia	19	24		
Mixed phenotype acute leukaemias	4	3		
Chronic myelomonocytic leukemia	1	0		
Donor type — no. (%)			0.044	0.833
haplo	72(75.8)	74(77.1)		
MUD	23(24.2)	22(22.9)		
10/10 matched unrelated	18(78.3)	17(77.3)	0.006	0.936
9/10 mis-matched	5(21.7)	5(22.7)		
Median donor age, yr(range)	29(10-60)	26.5(8-61)	-0.070	0.946
Donor gender — no. (%)			0.950	0.330
Male donor	75(78.9)	70(72.9)		
Female donor	20(21.1)	26(27.1)		
Donor-recipient gender matching, no. (%)			0.715	0.398
Female to male	10(10.5)	14(14.6)		
Other	85(89.5)	82(85.4)		
Donor-recipient relationships of haplo-transplant,no./no.			10.306	0.112
Brother/sister	14/6	4/6		
Son/daughter	31/10	31/13		
Father/mother	10/0	16/3		
Cousin	1	1		
Graft type — no. (%)			2.008	0.156
Bone marrow + Peripheral blood	4(4.2)	9(9.4)		
Peripheral blood	91(95.8)	87(90.6)		
PBSC graft counts: mean (±SD)				
CD34+: 10^6/kg	4.64(±2.09)	4.30(±1.81)	1.196	0.233
CD3+:10^8/kg	1.44(±0.81)	1.69(±1.20)	-1.648	0.101
Engraftment(ANC) mean days(±SD)	11.48(±1.46)	11.65(±2.16)	-0.606	0.545
CMV infection(%)	36(37.9)	33/96(34.4)	0.256	0.613
EBV infection(%)	18(19.0)	15/96(15.6)	0.369	0.544
HC/BKV infection(%)	21(22.1)	22/96(23.0)	0.018	0.893

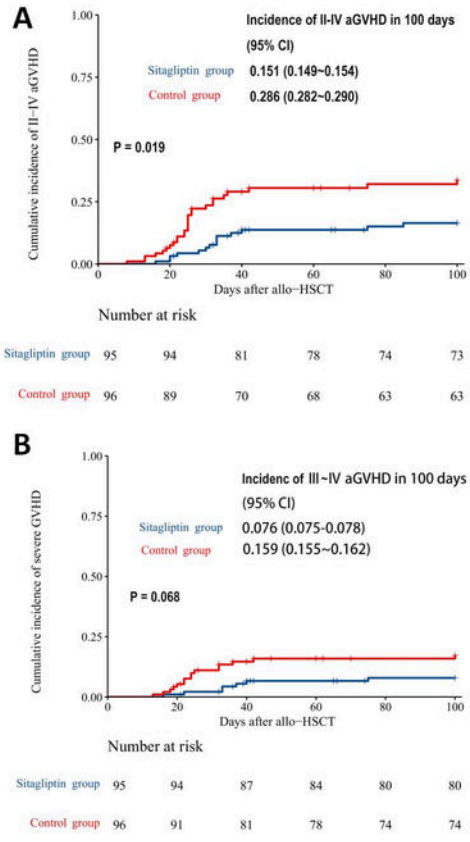

Figure 1. Cumulative incidence of aGVHD of the sitagliptin and control group in 100 days

Figure 1

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