

چهاردهمین کنگره انجمن علمی پیوند سلولهای بنیادی خونساز
همراه با بیست و سومین کنگره سراسری هماتولوژی

A review of clinical and preclinical cell therapy studies at Shariaty Hospital

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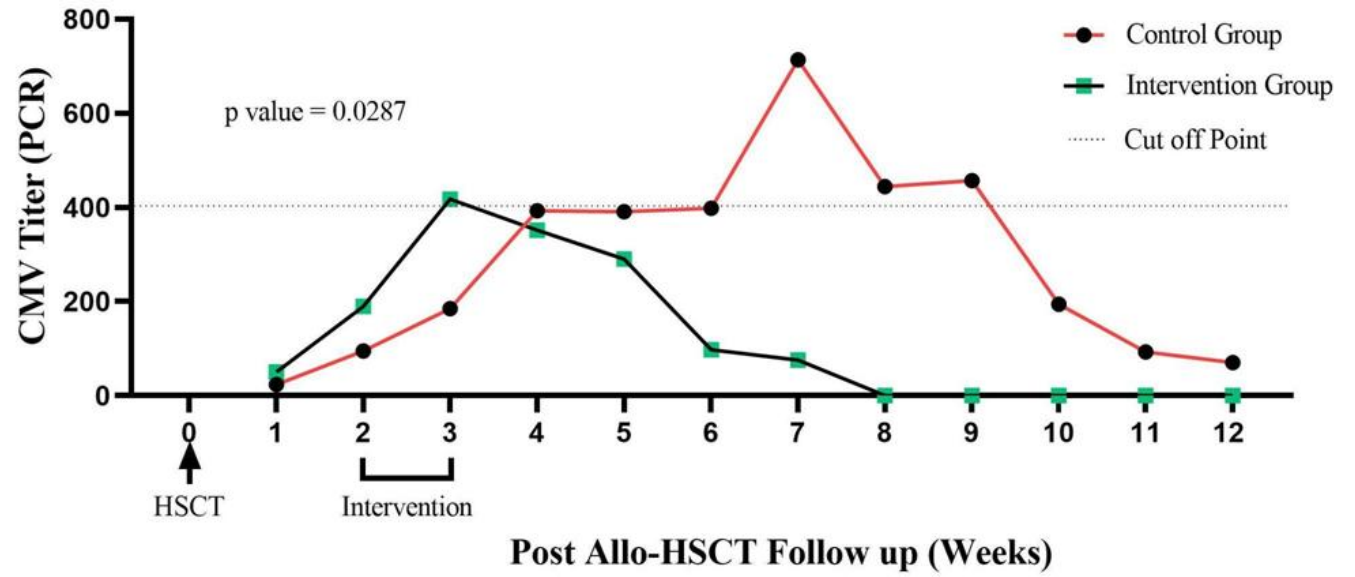
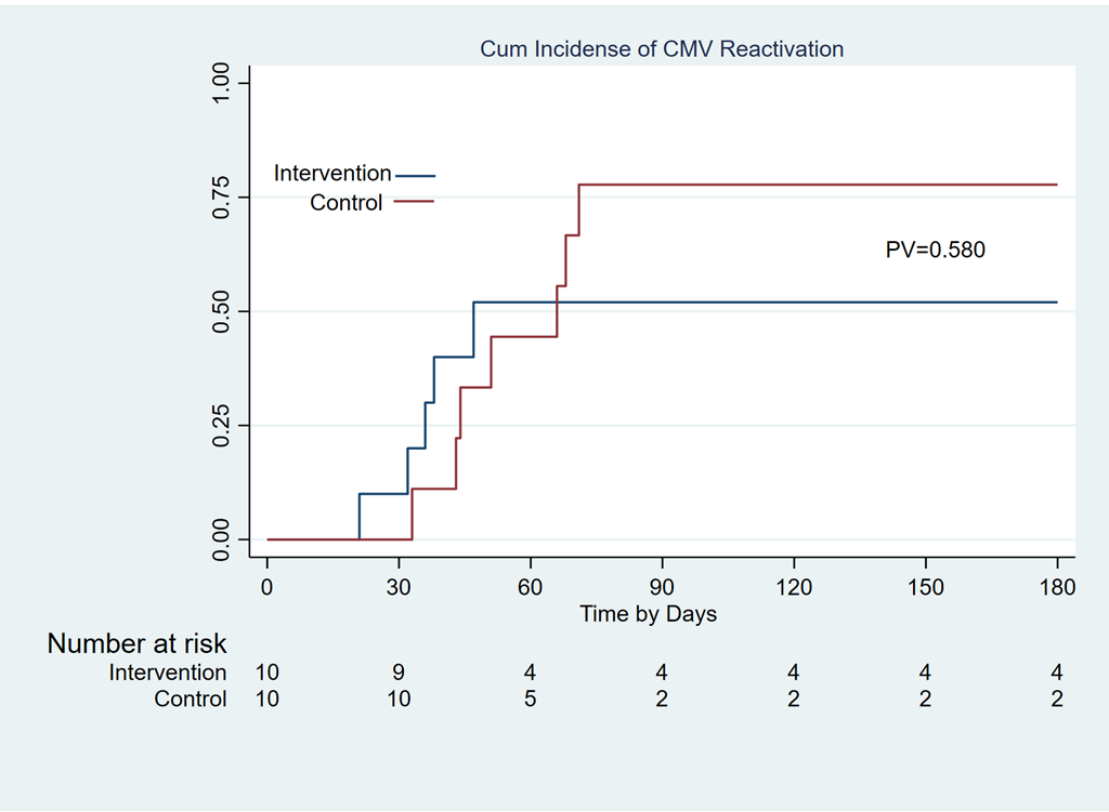
The Use of Donor-Derived CMV-Specific Cytotoxic T Cells

- CMV reactivation is a major complication in allogeneic stem cell transplant (allo-SCT) recipients.
- Adoptive transfer of CMV-specific cytotoxic T cells (CMV-CTLs) is a promising strategy to prevent CMV reactivation.
- This study evaluates the safety and efficacy of donor-derived CMV-CTLs in preventing CMV reactivation post-transplant.

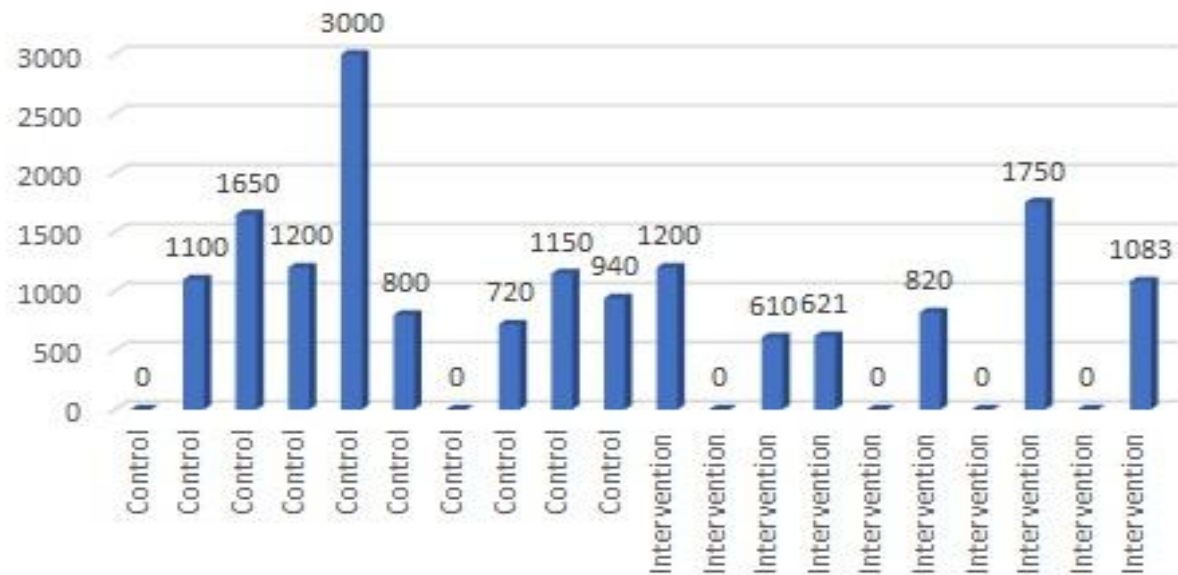
The Use of Donor-Derived CMV-Specific Cytotoxic T Cells

Characteristics		Control Group	ATC Group
Number of Participants		10	10
Recipient Age		32.70 (±7.97)	35.90 (±10.38)
Donor Age		34.90 (±15.54)	35.30 (±9.70)
Recipient Gender	Female	4 (40%)	6 (60%)
Donor Gender	Female	6 (60%)	7 (60%)
ABO Compatibility	Matched	6 (60%)	6 (60%)
	Mismatched	4 (40%)	4 (40%)
Background Disease	AML	6 (60%)	5 (50%)
	ALL	4 (40%)	5(50%)
Remission Status pre HSCT	CR1	4 (60%)	6 (60%)
	CR>=2	6 (40%)	4 (40%)
HSCT Type	Haploidentical	7 (70.0%)	7 (70.0%)
	Full matched	3 (30.0%)	3 (30.0%)
CD3*10^6		333.55 (±88.02)	250.13 (±76.50)
CD34*10^6		8.64 (±1.66)	6.54 (±1.54)
Donor Relation	Sibling	7 (70.0%)	10 (100%)
	Parents	1 (10%)	0 (0%)
	Offspring	2 (20)	0 (0%)
Disease Risk Index	Low/Intermediate	3 (30%)	3 (30.0%)
	Intermediate/High	7 (70%)	7(70%)

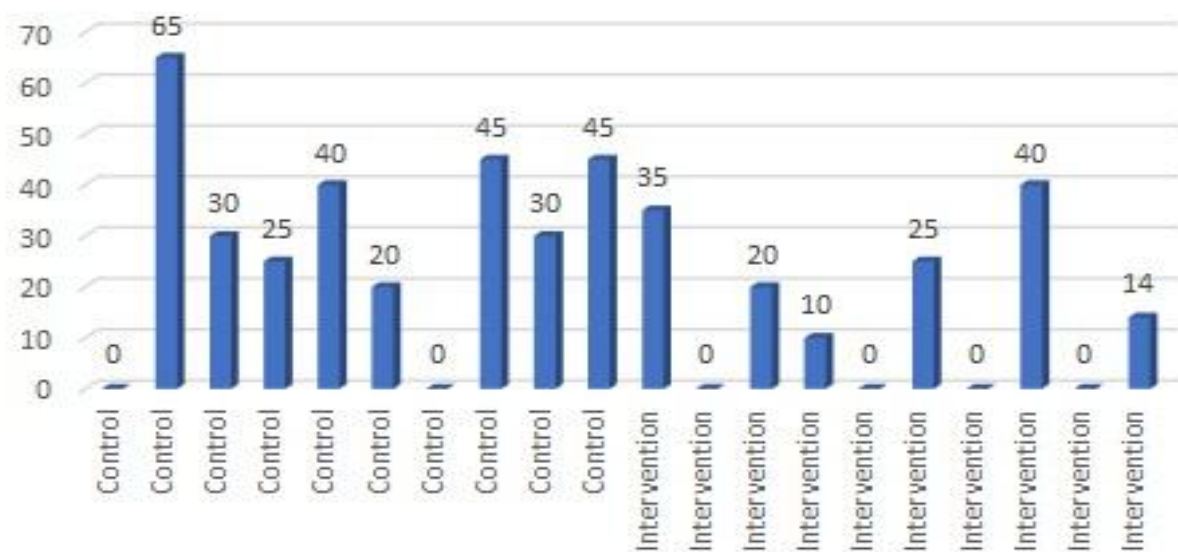
Id	Arm	R. Age	D. Age	R-D Sex Matching	ABO Matching	Prim Dis	Remission Status Pre HSCT	HSCT Type	CMV Reactivati on	Acute GVHD grading	Survival Status	Couse of Death	Follow up Time by Days
1	ATC	27	36s	F-F	Matched	AML	CR1	Haplo	+	2	Alive	-	472
2	Control	29	39	M-F	Bidirectional	AML	CR>=2	MRD	-	2	Alive	-	476
3	ATC	25	38	M-F	Minor MM	ALL	CR>=2	Haplo	-	0	Alive	-	460
4	Control	31	32	F-F	Matched	AML	CR1	MRD	+	2	Alive	-	443
5	ATC	51	43	F-F	Matched	ALL	CR>=2	Haplo	+	0	Alive	-	453
6	ATC	44	53	F-F	Minor MM	AML	CR1	Haplo	-	2	Death	Infectio n	151
7	ATC	34	28	F-F	Matched	ALL	CR1	MRD	-	2	Death	GvHD	453
8	ATC	44	44	M-F	Matched	ALL	CR1	Haplo	+	0	Alive	-	446
9	ATC	34	29	M-M	Matched	ALL	CR1	Haplo	-	1	Alive		404
10	Control	47	20	M-M	Matched	AML	CR1	Haplo	+	1	Alive	-	425
11	Control	20	49	M-F	Matched	ALL	CR>=2	Haplo	+	1	Alive	-	367
12	ATC	18	19	M-F	Minor MM	AML	CR>=2	Haplo	+	0	Alive	-	439
13	ATC	45	31	F-M	Major MM	AML	CR1	MRD	-	0	Alive	-	366
14	ATC	37	32	F-M	Matched	AML	CR>=2	MRD	+	0	Alive	-	401
15	Control	40	55	F-M	Matched	AML	CR>=2	Haplo	+	0	Death	Infectio n	95
16	Control	24	14	M-F	Minor MM	ALL	CR>=2	Haplo	-	0	Alive	-	453
17	Control	35	42	F-M	Matched	AML	CR>=2	Haplo	-	1	Alive	-	480
18	Control	35	10	M-F	Matched	ALL	CR1	Haplo	+	2	Death	Relapse	289
19	Control	28	39	M-F	Minor MM	ALL	CR>=2	Haplo	+	2	Death	Infectio n	163
20	Control	38	49	F-M	Major MM	AML	CR1	MRD	+	0	Alive	-	474



Maximum Titer of CMV by copy number/ml



Duration of CMV reactivation by days



RESEARCH

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Phase I non-randomized clinical trial of allogeneic natural killer cells infusion in acute myeloid leukemia patients

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Abstract

Introduction A new type of immune cell transplantation called allogeneic NK cell infusion is proposed as a potential universal off-the-shelf cell product for adoptive immune cell therapy in hematologic malignancies.

Design A multicentral phase I non-randomized clinical trial was conducted to assess the safety, feasibility, and potential efficacy of adoptively infused NK cells in patients with refractory/relapsed AML. We evaluated the feasibility of the trial by considering cell production, patient selection, and treatment protocol.

Method Allogeneic NK cells were produced from random healthy unrelated donors; 10 patients were selected according to the inclusion criteria and were included in two groups in case of NK cell dose escalation. Two cell infusions were given, spaced 7 days apart, following a lymphodepletion conditioning regimen of fludarabin-endoxan administered 7 days before the first infusion. The intervention safety was scored using Common Terminology Criteria for Adverse Events (CTCAE) based on variations in vital signs due to cell infusion. NK cell chimerism, tumor burden, and duration of relapse were considered to be components of efficacy. The pilot feasibility evaluation was checked using the CONSORT platform.

Results The NK cell infusion procedure was well tolerated, and no grade 2–5 toxicities related (possible or probable) to PB-NK cell infusion were observed. Four patients developed grade 1 transient chills, headaches, vomiting, and bone pain following each PB-NK cell infusion that were not required hospitalization. One of these patients (p01) died because of severe acute respiratory syndrome. Of 9 evaluable patients, 6 (66.6%) showed stable disease (SD) and 3 (33.3%) presented progressive disease (PD). Of 6 SD patients, 2 (p08 and p09) remained alive in SD and 3 patients (p04,

Introduction

Acute Myeloid Leukemia (AML) is a hematologic malignancy with a poor survival rate.

Objective: Investigate the feasibility, safety, and efficacy of allogeneic NK cell infusion as a novel immunotherapy approach.

Study Design & Methods

Multicenter Phase I Non-Randomized Clinical Trial

- 10 refractory/relapsed AML patients
- Two NK cell infusions from random healthy unrelated donors
- Lymphodepletion with fludarabine and cyclophosphamide

Dosing:

- Cohort 1: $2 \times 10^6/\text{kg}$ (1st), $5 \times 10^6/\text{kg}$ (2nd)
- Cohort 2: $5 \times 10^6/\text{kg}$ (1st), $10 \times 10^6/\text{kg}$ (2nd)

Results & Findings

Key Observations:

- No Grade 2-5 toxicities due to NK cell infusion
- 66.6% achieved stable disease (SD)
- 33.3% showed progressive disease (PD)

Clinical Outcomes:

- Transient NK cell engraftment observed (2-28 days)
- Stable liver enzymes, electrolyte levels, and kidney function

Effective Targeting of CD19-Positive Primary B-ALL Cells Using CAR-NK Cells Generated with mRNA-LNPs

Effective targeting of CD19 positive primary B-ALL cells using CAR-NK cells generated with mRNA-LNPs

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1. Abstract

Chimeric antigen receptor natural killer (CAR-NK) cell therapy is recognized as a promising modality for the treatment of hematologic malignancies, particularly B-cell malignancies. In this study, we developed “off-the-shelf” anti-CD19 CAR-NK cells using anti-CD19 CAR mRNAs formulated in proprietary ionizable lipid nanoparticles (LNPs). The efficiency of mRNA-LNP delivery into umbilical cord blood (UCB)-derived NK cells and primary T cells was evaluated in an in-vitro setting, demonstrating superior delivery efficiency in NK cells. Further investigation showed a probable role for an endocytic mechanism, macropinocytosis, in efficient transfection of NK cells with LNPs. Nevertheless, CAR-NK cells generated through this mRNA-LNP platform exhibited significantly enhanced cytotoxicity against CD19⁺ target cells, such as EGFP⁺Raji stable cell line and primary malignant B cells derived from refractory/relapsed B-cell acute lymphoblastic leukemia (B-ALL) patients. These findings highlight the promise of the mRNA-LNP platform in advancing CAR-NK therapies against B-cell malignancies.

Effective Targeting of CD19-Positive Primary B-ALL Cells Using CAR-NK Cells Generated with mRNA-LNPs

CAR-T Therapy: Effective for B-cell Malignancies but presents challenges such as high cost, toxicity (CRS, GvHD).

CAR-NK Therapy:

- 'Off-the-shelf' potential.
- Reduced risks of CRS and GvHD.
- Expands treatment options for hematologic and solid tumors.
- Objective: To develop anti-CD19 CAR-NK cells using mRNA-LNPs and assess their efficacy.

Effective Targeting of CD19-Positive Primary B-ALL Cells Using CAR-NK Cells Generated with mRNA-LNPs

- **mRNA-LNP Platform:**

- Proprietary ionizable lipid nanoparticles (LNPs) for CAR mRNA delivery.
- Higher transfection efficiency in NK cells (94.7%) vs. T cells (21.8%).

- **Cytotoxicity Assessment:**

- CAR-NK cells show enhanced cytotoxicity against EGFP+Raji cells and primary B-ALL cells.
- Higher IFN- γ secretion and LDH release confirm improved efficacy.

- **Macropinocytosis Mechanism:**

- Imipramine (macropinocytosis inhibitor) reduces LNP transfection, suggesting a key role in uptake.

Effective Targeting of CD19-Positive Primary B-ALL Cells Using CAR-NK Cells Generated with mRNA-LNPs

- Key Takeaways:**

- mRNA-LNPs offer an efficient, non-viral method for CAR expression in NK cells.**
- CAR-NK cells demonstrate significant cytotoxicity against CD19+ target cells.**

- Potential Optimizations:**

- Use of stable mRNA variants (circRNA, samRNA) for prolonged expression.**
- Engineering NK cells with IL-15 for enhanced persistence and function.**

- Next Steps:**

- Preclinical validation and clinical trials to establish therapeutic potential.**
- Expansion to other cancer types and immune cell subsets.**

Cell Therapy Using Third-Party Natural Killer Cells in Patients with Advanced Gastrointestinal Cancers

Abstract

Introduction: Natural killer (NK) cells possess the unique ability to target and destroy tumor cells without prior sensitization. The cytotoxic activity of NK cells is modulated by a balance between activating and inhibitory receptors, with inhibitory receptors such as NKG2A playing a significant role. This study evaluates the safety and efficacy of anti-NKG2A-pretreated NK cells for the treatment of advanced gastrointestinal adenocarcinoma in patients who have not responded to at least two lines of therapy.

Materials and Methods: A phase I non-randomized clinical trial was conducted to assess the safety, feasibility, and potential efficacy of adoptive infusion of ex vivo expanded anti-NKG2A-pretreated NK cells in patients with advanced gastrointestinal adenocarcinoma. Patients received a lymphodepletion regimen of fludarabine and cyclophosphamide 7 days before the first infusion. Adoptive transfer of IL-2-activated third-party NK cells was administered on days 0, +5, and +10 post-conditioning at a dose of 7×10^8 cells per injection. Safety was evaluated using the Common Terminology Criteria for Adverse Events (CTCAE).

Results: Six adult patients with advanced gastrointestinal adenocarcinoma, unresponsive to at least two lines of therapy and with a median age of 65 years, were included. The therapy was well tolerated with no reported adverse events according to CTCAE. At the last follow-up, all patients were alive and exhibited stable disease, with a median follow-up duration of three months. Additionally, all patients showed a relative decrease in tumor diameter and tumor markers.

Conclusion: This study demonstrated that the infusion of anti-NKG2A-pretreated NK cells is safe and feasible. The treatment was associated with minimal adverse effects and led to a relative reduction in tumor size and tumor markers in all patients. These promising results warrant further investigation into the potential of NK cell therapy in managing solid tumors.

The study was approved by the Ethics Committee of the Hematology-Oncology and Stem Cell Transplantation Research Center at Tehran University (IR.TUMS.TIPS.REC.1403.015 and IR.TUMS.TIPS.REC.1402.080) and was registered with the Iranian Registry of Clinical Trials (IRCT20140818018842N36).

Original Article



Cell Therapy Using Anti-NKG2A Pretreated Natural Killer Cells in Patients with Hepatocellular Carcinoma

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NKG2A, Inhibitory receptor

Abstract

Purpose: The activities and functions of natural killer (NK) cells are regulated by a limited repertoire of activating and inhibitory receptors. Thus, we provided a study of inhibition of the NKG2A using monoclonal antibodies (mAbs), and as a primary endpoint, we evaluated whether it can be translated to enhance adoptive NK cell immunotherapy, as the secondary endpoint, we investigated safety and feasibility.

Method: In this study, we investigated the safety of anti-NKG2A-pretreated NK cells in improving ADCC function to manage hepatocellular carcinoma (HCC). After a conditioning regimen, we initiated a pilot study of expanded donor haploidentical NK cell infusion. Patients received a fludarabine/cyclophosphamide conditioning followed by adoptive immunotherapy with IL2-activated haploidentical NK cells. Anti-NKG2A pretreated NK cells were infused on days 0, + 5, and + 10 post-conditioning regimens at a dose of 7×10^8 cells ($n=3$). The median follow-up was 4 months for all patients.

Results: Although all patients were alive at the last follow-up, two of them showed progressive disease and an increase in tumor size. In addition, all patients showed a relative decrease in alpha-fetoprotein (AFP) expression levels after one month.

Conclusion: This study demonstrated the safety and feasibility of infusing high doses of ex vivo expanded NK cells after conditioning with transient side effects.

Cell Therapy Using
Anti-NKG2A
Pretreated Natural
Killer Cells in Patients
with Hepatocellular
Carcinoma

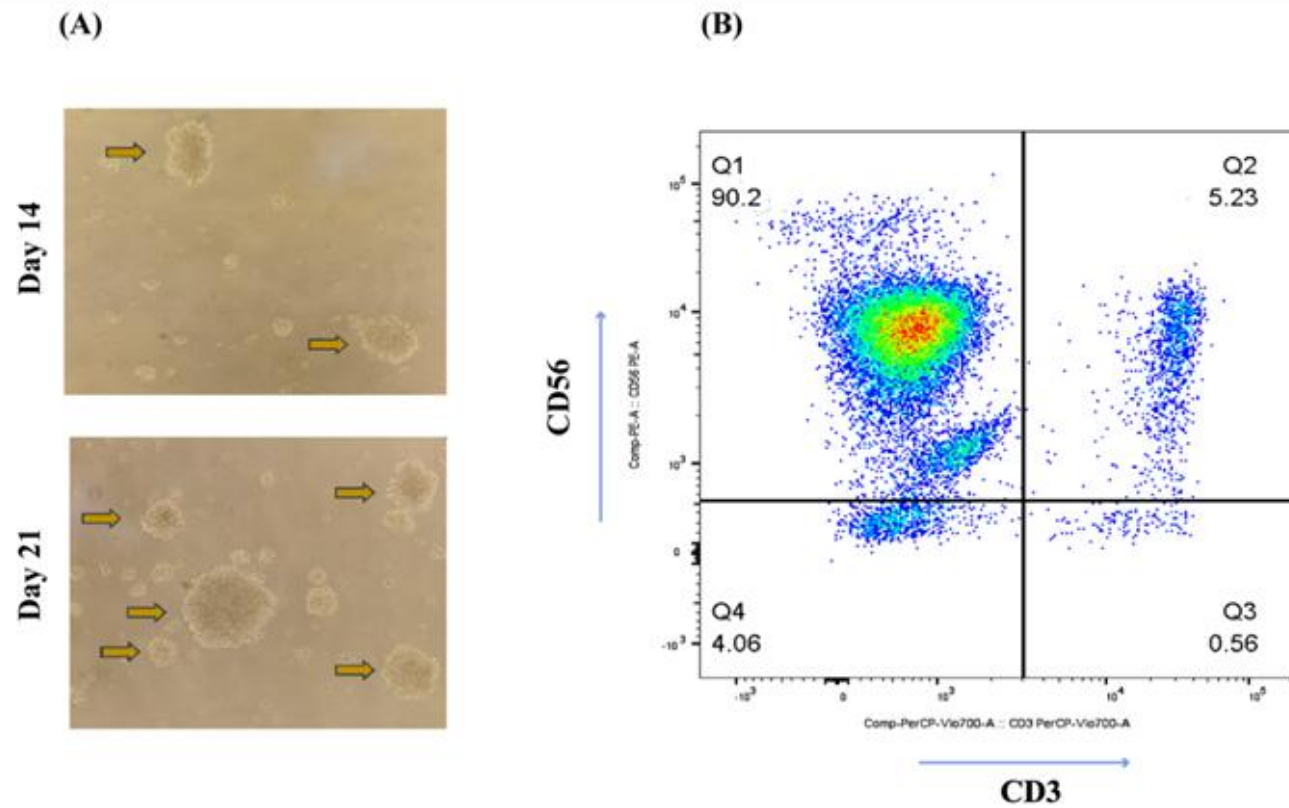


Figure 1. Human NK cell isolation and characterization. (A) NK cells exhibited round colonies as depicted by the arrows after 14 and 21 days of cultivation. (B) CD56+ CD3- PBMC-derived NK cells' frequency was 90.2% after MACS isolation

Table 1. Patient characteristics

Case	Age/Gender	Diagnosis	ECOG	Disease Stage	Prior treatment	NK cell administration
1	51/M	Hepatocellular carcinoma	≤2	Metastasis to lungs, lymph nodes	Sorafenib	Completed
2	59/M	Hepatocellular carcinoma	≤2	Metastasises to lungs	Sorafenib	Completed
3	49/F	Hepatocellular carcinoma	≤2	Metastasises to lungs	Sorafenib	Completed

Cell Therapy Using Anti-NKG2A Pretreated Natural Killer Cells in Patients with Hepatocellular Carcinoma

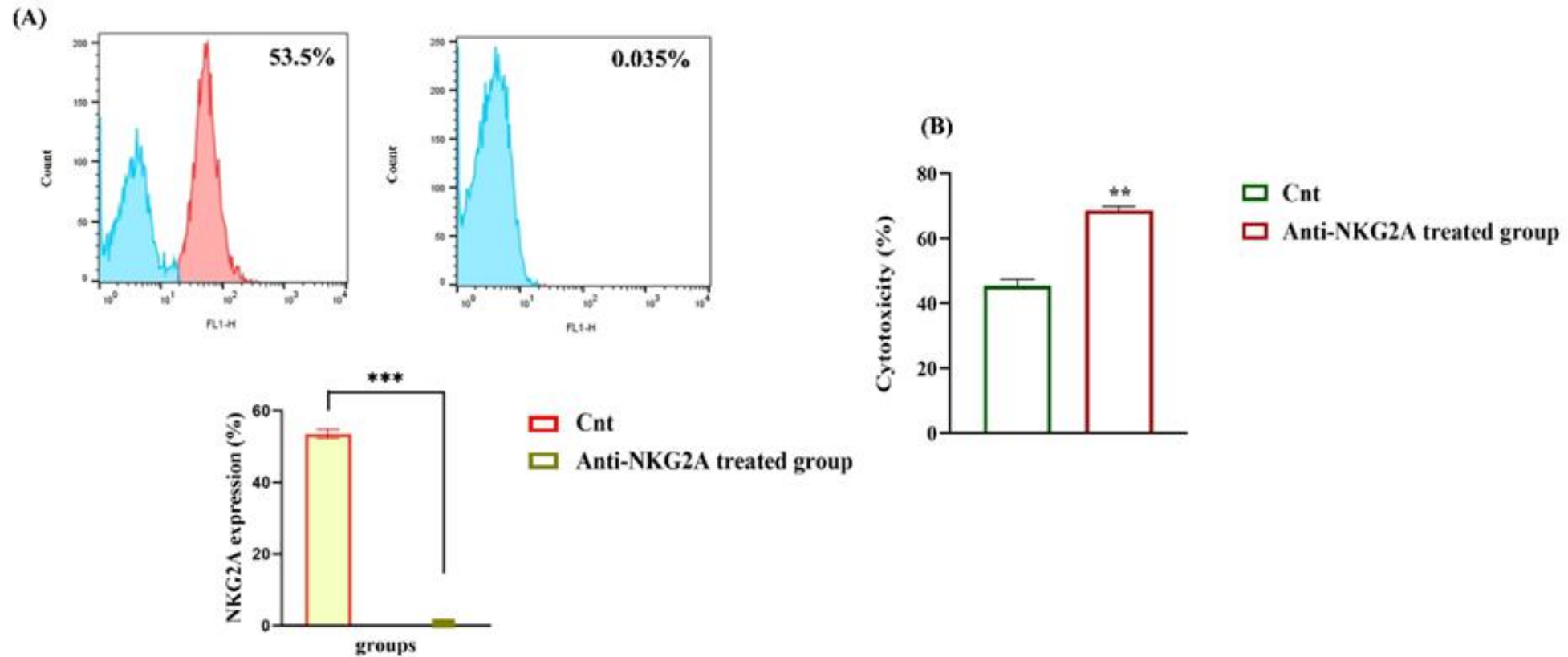


Figure 3. The effect of NKG2A blocking on NK cells. (A) Quantification of positive cells for NKG2A demonstrated a significant decrease in NKG2A expression following treatment of activated NK cells with anti-NKG2A Ab. (B) The cytotoxicity of anti-NKG2A-pretreated NK cells toward K562 cells at an E: T ratio of 10:1 showed a significant increase in their cytotoxicity compared with the control group. The results are displayed as mean \pm SD for three independent experiments. ** $P \leq 0.01$, and *** $P \leq 0.001$

Cell Therapy Using Anti-NKG2A Pretreated Natural Killer Cells in Patients with Hepatocellular Carcinoma

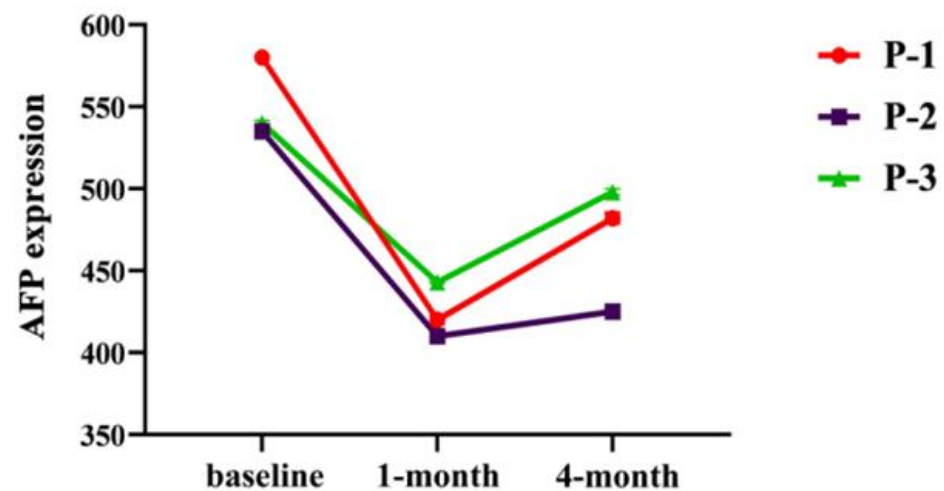


Figure 4. Expression of AFP. Administration of anti-NKG2A pretreated NK cells decreased AFP serum levels after 1 month in all 3 patients (not significant, $P>0.05$). However, two patients showed an increase in their expression level after 4 months ($P>0.05$)

Table 3. Tumor response

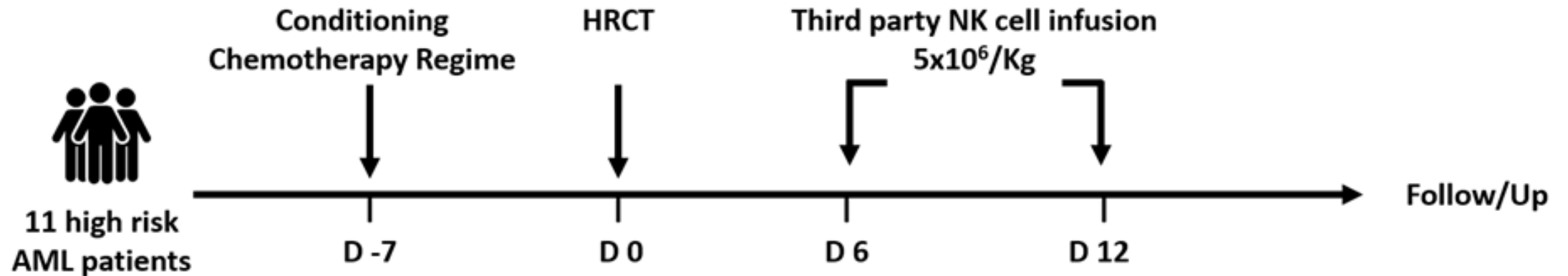
Patients	Response				Response rate (%) (95 % CI)	Disease control rate (%) (95 % CI)
	CR	PR	SD	PD		
1-month follow-up						
n=3	-	-	3	0	0	100%
4-months follow-up						
n=3	-	-	1	2	0	33.3%

CR: Complete Response, PR: Partial Response, SD: Stable Disease, PD: Progressive Disease

Safety and Feasibility of Intravenous Systemic Infusion of Allogeneic NK Cells in Patients with Relapsed or Refractory Lymphoma

Patients	NK infusion dose ($\times 10^6/\text{kg}$)	No. Of doses	Status during transplantation	Clinical response evaluation, 3 months	Clinical response evaluation, 6 months
P-1	5	1	Remission	Remission	Remission
P-2	5	1	PR	Remission	Remission
P-3	5	1	Remission	CR	CR
P-4	5	1	PR	SD	SD
P-5	5	1	Remission	CR	CR
P-6	5	1	PR	Remission	CR
P-7	5	1	Remission	Remission	Remission
P-8	5	1	Remission	Remission	Remission

**Evaluating the Safety and Efficacy of
Prophylactic Third-party NK Cell Administration
in High-Risk AML Patients Post-HSCT**



Patients	Age	Sex	Diagnose	Donor type	Remission status	MRD Remission status before HSCT	NPM1	FLT3_ITD	CD34_10p 6	CD3_10p6	Cytogenetic
P-1	50	male	AML M4-5	Full-match	CR2	Positive 0.6%	NA	NA	7.00	280.00	NA
P-2	35	male	AML M7	Full-match	PIF and CR1	Negative	NA	Wild Type	7.50	164.00	inv(3)
P-3	17	male	AML M1-2	haploidenti cal	CR2	Positive 0.8%	Wild Type	Mutant	8.28	218.00	t(6;9)
P-4	45	male	AML non-M3	haploidenti cal	PIF and CR2	Negative	Mutant	Mutant	9.57	262.00	Normal
P-5	45	male	AML M1-2	haploidenti cal	Not in Remission	Positive 9%	Wild Type	Wild Type	8.54	243.00	Normal
P-6	44	femal e	AML M1-2	Full-match	Not in Remission	Positive 6%	NA	NA	7.82	221.00	Normal
P-7	51	male	AML non-M3	haploidenti cal	CR1	Positive 0.9%	Wild Type	Wild Type	10.00	325.00	Normal
P-8	27	femal e	AML M4-5	Full-match	CR1	Positive 0.2%	NA	NA	8.00	172.00	Normal
P-9	54	male	AML Non- specific	Full-match	CR1	Positive 0.3%	NA	NA	6.00	280.00	NA
P-10	43	male	AML M4-5	Full-match	Not in Remission	Positive 5.24%	NA	NA	7.00	161.50	-7

Patient s	Mucositi s	aGvHD		cGvHD	Did HC	CMV reactivati on	Relapse status	Surviva l status	Cause of death	ANC engraft	PLT engraft	FU	Diseas e free FU
P.01	-	-	-	-	-	-	Relapse	Alive	-	17	11	479	159
P.02	Grade2	Grade 1	Grade 2- moderate	-	-	-	No-Relapse	Alive	-	13	9	482	482
P.03	Grade2	-	-	-	-	-	Relapse	Dead	Relapse	13	12	54	34
P.04	Grade2	-	-	-	Positive	-	No-Relapse	Alive		13	13	256	256
P.05	-	Grade 2	-	-	Positive	-	No-Relapse	Dead	PTLD	12	10	144	144
P.06	-	-	Grade1- severe	Grade 4	-	-	No-Relapse	Dead	GVHD	11	9	210	210
P.07	-	-	-	-	Positive	-	No-Relapse	Alive	-	12	12	514	514
P.08	Grade4	Grade 2	Grade1- moderate	Grade 1	Positive	-	No-Relapse	Alive	-	10	11	463	463
P.09	Grade3	-	-	-	-	-	No-Relapse	Alive	-	14	13	132	132
P.10	Grade3	Grade 2	Grade1- mild	-	Positive	-	Relapse	Dead	-	13	8	234	111
P.11	Grade3	-	-	-	-	-	No-Relapse	Dead	graft failure	15	15	166	166

Osteoarthritis Treatment Based on Interventional Radiology, Using Umbilical Cord Mesenchymal Stem Cells

Maedeh Ruzbahani, Hossein Ghanaati, Ardeshtir Ghavamzadeh, Ramin Sarramiforooshani, Maryam Barkhordar, Mohammad Vaezi, Ahmadsreza Jamshidi, Mohsen Nikbakht, Masud Yunesian, Ali Ghanaati

According to our inclusion and exclusion criteria (in short, they should not be in very advanced stages of the disease), 30 patients were selected. They were hospitalized and then using the slinger technique angiography was done. So, after evaluation of the superficial femoral artery, descending genicular artery has been catheterized and with proper evaluation, mesenchymal stem cell injection was done. Finally, patients were discharged with some oral medications, including painkillers.

Result(s): The critical measure to access the improvement is the WOMAC score, which was filed before and every week after intervention, also MRI was taken before the operation and then 3 months after the process to access cartilage content and cartilage thickness. **In all cases, WOMAC scores were reduced obviously.**

Conclusion(s): This is a primary report of the way, which has been safe and very effective for all 30 cases. Article published online:

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A Phase I/II Study Evaluating the Safety and Efficacy of Prophylactic **Natural Killer Cells Early After Hematopoietic Cell Transplantation** for patients with MRD positive acute Lymphoblastic leukemia at HSCT (MRD + ALL)

بیماران مورد مطالعه افراد مبتلا به ALL با MRD مثبت قبل پیوند می باشند که کاندید دریافت پیوند سلول های بنیادی خون ساز آلون هستند (طبق پروتکل مرکز). (جهت آماده سازی سلولهای NK از ۲۰ روز قبل از اولین انفوزیون NK، از دهنده ۲۰ الی ۵۰ سی سی خون محیطی گرفته شده و بعد از جداسازی PBMC سلولهای CD ۴۵+ با کمک Feeder و ۲- IL تکثیر داده می شوند. تست مربوط به Viability با استفاده از تریپان بلو صورت گرفته و فنوتایپینگ جهت بررسی تعداد مطلق و خلوص سلولهای CD ۳+، CD ۴۵+ و CD ۴۵+ بکار می رود.

سلولهای NK پس از آماده سازی در محیط آزمایشگاه، در روزهای ۶+ و ۱۲+ پیوند) یعنی ۶ روز و ۱۲ روز بعد از انجام پیوند به بیماران واجد شرایط ورود به مطالعه تزریق میشوند.

Evaluating the safety and feasibility of human placenta-derived mesenchymal stem cell injection in systemic sclerosis. A pilot study

کد طرح: ۶۶۴۴۵-۴۱۵-۳-۱۴۰۲

کد اخلاق: IR.TUMS.HORCSCT.REC.1402.047

طرح مشترک پژوهشکده انکولوژی، هماتولوژی و سل تراپی/م ت. سلول درمانی و پیوند سلولهای بنیادی خون ساز و جهاد دانشگاهی دانشگاه تهران

ارزیابی بیخطری و تحمل پذیری تزریق سلولهای بنیادی مزانشیمی مشتق از جفت انسان بعد از کشت در محیط آزمایشگاه در بیماران مبتلا به اسکروزیس سیستمیک بر اساس معیارهای

Common Terminology Criteria for Adverse Events (CTCAE)

شرکت کنندگان سلول های بنیادی مزانشیمی مشتق از جفت انسان را به تعداد یک میلیون سلول به ازای هر کیلوگرم وزن بدن در یک تزریق دریافت خواهند کرد. نتایج در ماه های ۳، ۶، ۹ و ۱۲ پس از تزریق ارزیابی خواهند شد.

Autologous hematopoietic stem cell transplantation in relapsing multiple sclerosis

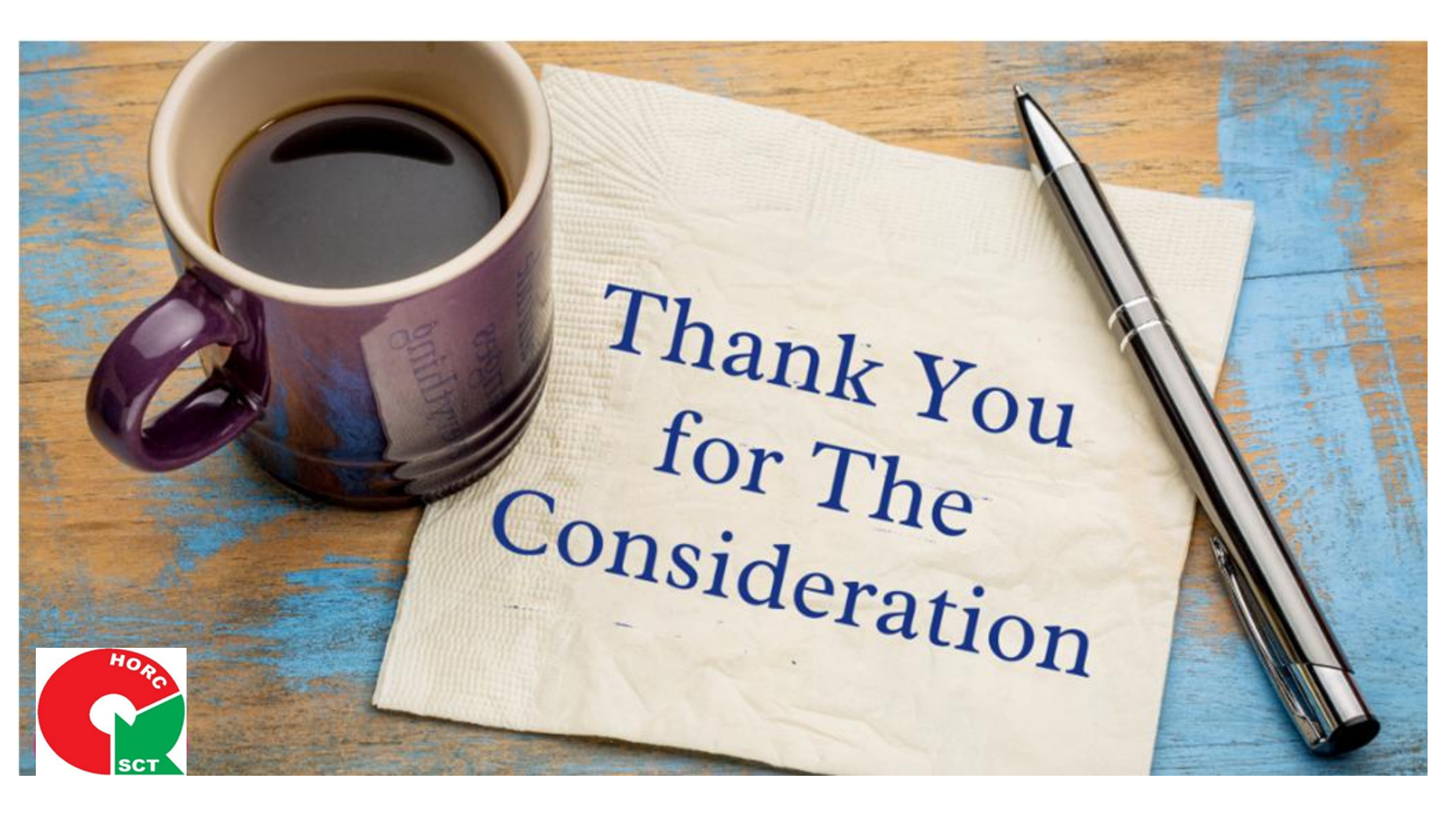
مرکز هدف اول: پژوهشکده انکولوژی، هماتولوژی و سل ترابی/م ت. سلول درمانی و پیوند سلولهای بنیادی خون ساز
مرکز هدف دوم: پژوهشکده بازتوانی عصبی/م ت. ام اس بیمارستان سینا

▪ Inclusion criteria:

1. Relapsing remitting (RRMS) patients (MS diagnosis confirmed by McDonald criteria)
2. Age between 18 and 45 years
3. Expanded Disability Status Scale (EDSS) ≤ 5.5
4. Disease duration ≤ 10 years from MS diagnosis
5. Treatment failure after at least one highly effective treatment *

After harvesting, participants will receive **cyclophosphamide 50mg/kg/day -5 to -2, and rabbit antithymocyte globulin (rATG) 2mg/kg/day -4 to -2**, as a conditioning regimen. This is followed by transplantation of the autologous hematopoietic cell graft.

بیمار مبتلا به مالتیپل اسکلروزیز تحت پیوند اتولوگ با رژیم کاندیشنینگ فوق قرار گرفته اند که هیچ 8 از زمان شروع مطالعه تا کنون مورییدی و مورتالیتی خاصی مشاهده نشد و همچنین هیچ کدام از بیماران شواهدی از عود بیماری یا هر گونه تظاهرات نورولوژیک نداشتند.

A photograph of a purple ceramic mug filled with dark coffee, a silver and black ballpoint pen, and a white paper napkin. The napkin is placed on a rustic wooden surface with blue-painted sections. The text "Thank You for The Consideration" is printed in blue on the napkin. The mug has some faint, illegible text on it.

Thank You
for The
Consideration

