ONE-YEAR FOLLOW-UP OF A PHASE I CLINICAL TRIAL ON THE USE OF BONE MARROW MESENCHYMAL STROMAL CELLS IN ADPKD PATIENTS

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Introduction

ADPKD is a genetic ciliopathy disease characterized by progressively formation and enlargement of cysts in multiple organs specially kidney which eventually may lead to ESRD. It affects approximately 4 to 7 million individuals[1]. Although there is no cure the supportive treatment couldn't control the progression of the disease. We hypothesized that BMMSCs are renotropic and could increase the vasculature of the damaged kidney and subsequently increase eGFR[2]. We aimed to assess the safety and potential efficacy of the BMMSC injection in ADPKD.

Methods

We performed single arm phase I clinical trial at one trial center with 12-month follow-up among 6 ADPKD patients (table 1). Twenty seven ADPKD patients diagnosed with ravine's criteria evaluated for participation in the trial, six eligible genetically confirmed ADPKD patients with eGFR 25-60 enrolled the study between June 2014 and January 2015. They received autologous cultured BMMSCs (2 million cells per kilogram) through cubital vein regarding our infusion protocol. We investigated the safety concerns & kidney function during the follow-up visits compared to baseline and a year prior to the intervention. Primary outcomes were the type and the severity of adverse events related to cell injection such as mass formation. Secondary endpoints were changes in eGFR from baseline to 12 months after cell injection. We evaluated total kidney volume & the largest cyst size by ultrasound imaging, eGFR by MDRD (IDMS traceable)formula and DMSA scan. Kidney function of patients were compared to baseline and a year prior to the intervention.

Table 1. Demographic Data

Patient Number	1	2	3	4	5	6
Sex	F	M	M	M	F	F
Age	45	37	39	28	51	54
Race	Caucasian	Caucasian	Caucasian	Caucasian	Caucasian	Caucasian
DM	-	-	-	-	-	-
HTN	-	-	-	-	-	-
Smoking	-	-	-	-	-	-
Controlled Diet	+	+	+	+	+	+
Baseline GFR	25	32	25	25	25	29

Result

There were no patients lost to follow-up. There were no cell related adverse events after 12 months follow-up. There were no detectable changes of kidney volume or largest cyst size in all patients. Kidney function of the patients didn't change noticeably during one year follow-up except one patient (Fig 1); One month following cell injection serum creatinine rise was observed in one patient with lumbar disc herniation history, probably due to taking single dose NSAID. The serum creatinine dropped down to previous level after a week.

Fig 1. eGFR changes of ADPKD patients, a year before to one year after BMMSC infusion

Conclusions

This trial demonstrated that intravenous transplantation of autologous BMMSCs was safe and well tolerated. We couldn't assess the exact efficacy of the treatment due to design of the trial; though BMMSCs may somehow decrease the progression rate of CKD in ADPKD patients, needed to be investigated in a randomized placebo-controlled trial with a larger population which we are going to perform.

The trial has been funded by Royan Institute, Clinical Trials number NCT02166489.

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53 ERA 17--SP
Renal development and cystic diseases.
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DOI: 10.3252/pso.eu.53era.2016
ePosters supported by F. Hoffmann- La Roche Ltd.
53rd CONGRESS ERA-EDTA VIENNA AUSTRIA MAY 21st-24th, 2016
Held jointly with Österreichische Gesellschaft für Nephrologie
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