Autologous transplantation of bone marrow mononuclear cells in patients with decompensated cirrhosis

E. Berishvili[1,2,3,4], N. Kipshidze[3], Z. Kakabadze[1,2,3], K. Mardaleishvili[1,4], G. Shatirishvili[4], G. Loladze[4], A. Archvadze[3], M. Janelidze[2,3]

[1]Ilia State University; [2]Division of Cell Transplantation, Georgian National Institute of Medical Research; [3]Cell Transplantation Unit, Central University Hospital; [4]Cell Transplantation Unit, Mardaleishvili Medical Center, Tbilisi, Georgia

CTS 2013, Milan, July 9, 2013

Background

- Liver transplantation is considered as the standard treatment for advanced decompensated liver cirrhosis
- Studies in animal models of liver diseases have demonstrated that BMC transplantation may reduce hepatic fibrosis and improve liver function and survival rate
- Cytokines and growth factors produced by infused hematopoietic cells might support liver function and repair

Aim

To evaluate the safety and feasibility of BMC transplantation in patients with decompensated cirrhosis

Patients and Methods

Inclusion Criteria

- Age 20-70 years
- HCV related liver cirrhosis Child C
- Ability to give informed consent.

Exclusion Criteria

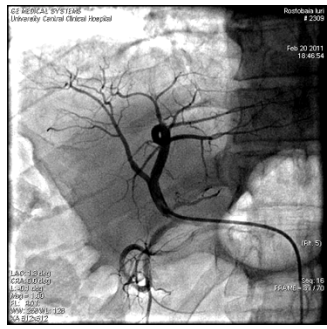
- Age <20 or >70 years
- Hepatopulmonary syndrome
- Liver tumors/history of other cancer
- Hepatic, portal or splenic vein thrombosis
- Autoimmune diseases
- Patients with active infection
- Recurrent gastrointestinal bleeding

Patients and Methods

- The present study comprised 45 patients with advanced liver cirrhosis.
- 40 male and 5 female patients
- Median age 50 years
- The study protocol was approved by the Ethics Committee of Central University Hospital, Tbilisi, Georgia.

Patients and Methods

Infusion of $200x10^6$ BM Cells into the Hepatic Artery



4 w | 8 w | 12 w | 16 w | 20 w | 24 w | 28 w | 32 w

- Aspiration of 80 ml BM
- Preparation of MNC (Ficoll-Hypaque)
- Checking the character of MNC
- Intraarterial administaration of BMCs

Endpoint:
1. Safety & Feasibility
2. 4 weeks and 32 weeks of Liver Function

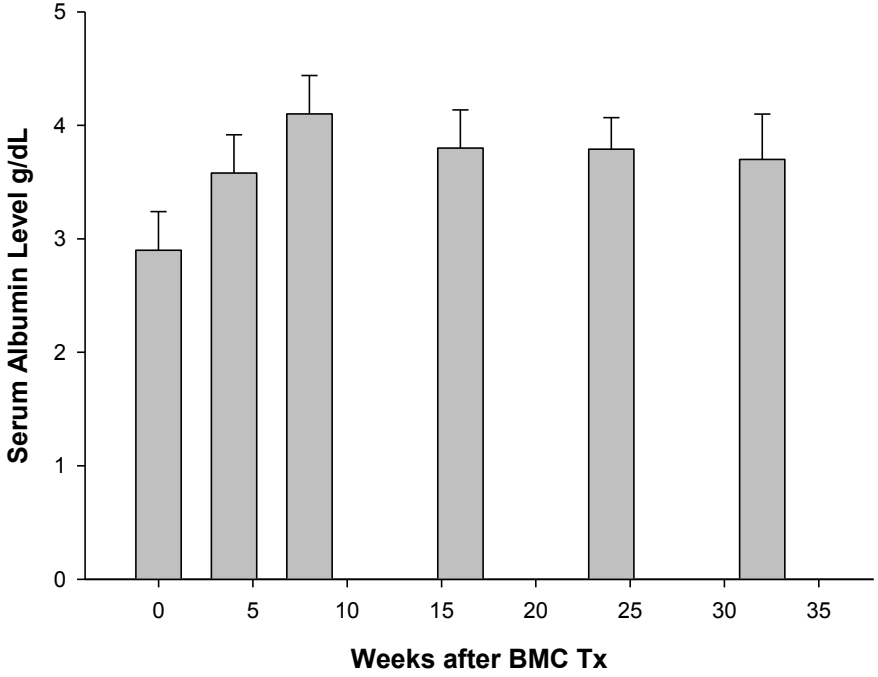
Checking liver functions by serum blood tests, Ultrasonography

Results

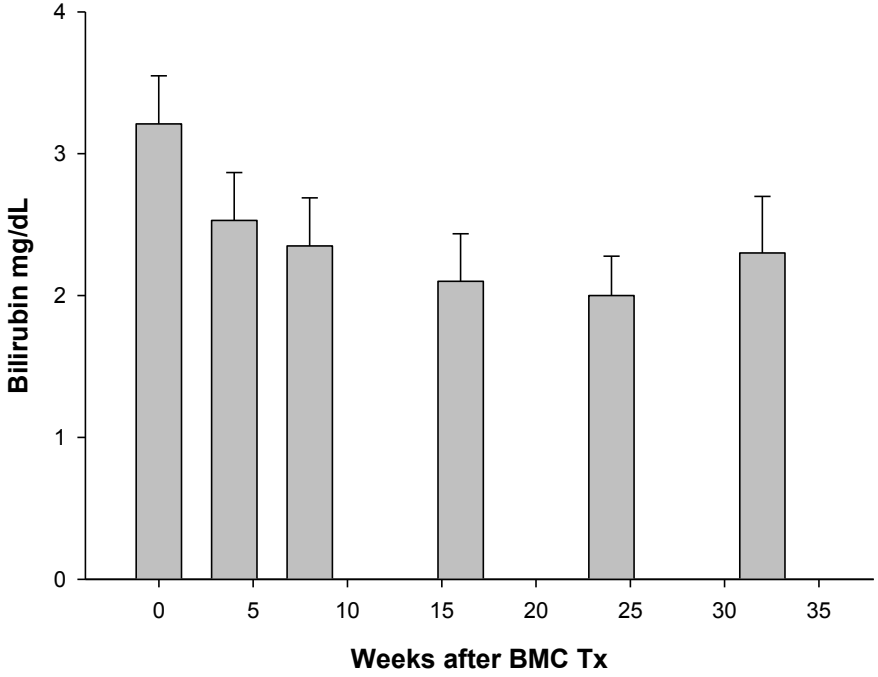
- All patients were discharged 48 h after BMC infusion.
- BMC transplantation was well tolerated by all patients
- 5 patients complained of mild pain at the bone marrow needle puncture site.
- No other complications or specific side effects related to the infusion procedure were reported.

Results

Serum Albumin level before and after BMC Tx

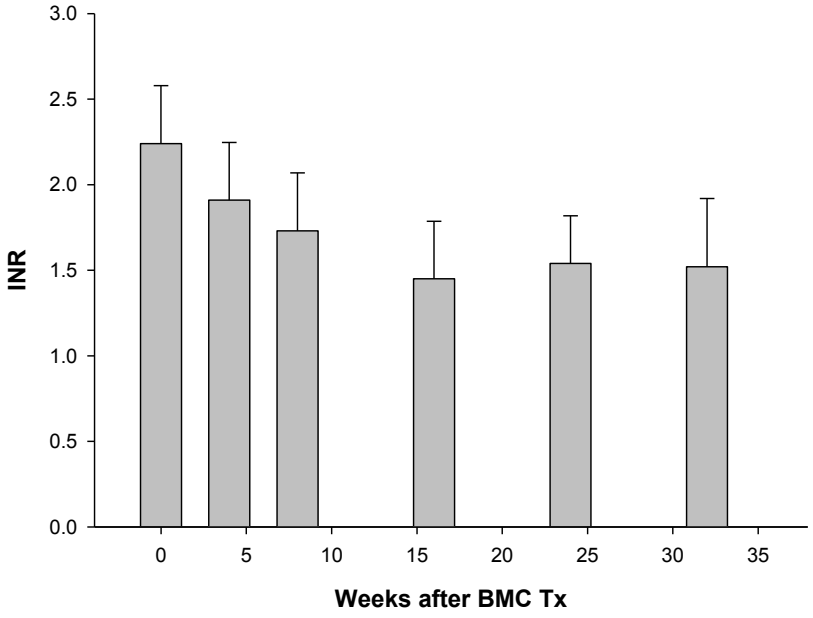


Serum bilirubin level before and after BMC Tx

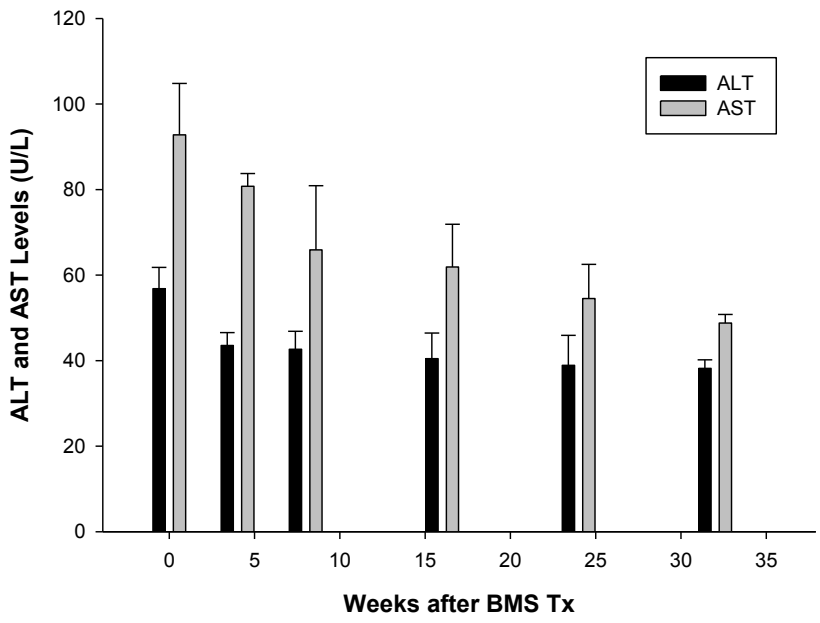


Results

INR level before and after BMC Tx



ALT and AST levels before and after BMC Tx



Characteristics of the distribution of serum bilirubin, albumin and INR levels in 45 patients with chronic liver failure at baseline, 1 and 4 month after transplantation of autologous BMCs

Parameters	Minimum	Maximum	Mean	Median	Standard deviation	Realative change from baseline (%)
Bilirubin (mg/dl)						
Baseline	1.00	6.90	3.21	2.48	2.79	
1 month	0.60	7.0	2.53	1.25	3.57	- 22%
4 month	0.50	6.20	2.10	0.85	2.75	-35%
Albumin (unit)						
Baseline	2.40	3.90	2.90	2.65	0.68	
1 month	3.00	4.20	3.58	3.55	0.28	19%
4 month	3.40	4.90	4.07	4.00	0.69	29%
INR (unit)						
Baseline	1.18	3.63	2.24	2.08	1.03	
1 month	1.24	2.79	1.91	1.79	0.71	15%
4 month	1.20	2.20	1.73	1.76	0.51	23%

Conclusions

- BMC infusion into the hepatic artery of patients with advanced chronic liver disease is safe and feasible
- Transient decrease in mean serum bilirubin and INR levels
- Transient elevation of serum albumin

Next Steps

- **Controlled studies are required to to evaluate the efficacy of BMC infusion in patients with liver disease**
- **Determine the number of BMCs required for achievement of therapeutic effect, which may vary with the patient's age and the etiology of liver disease.**

Acknowledgments

Tbilisi State Medical University:

Dr. Zurab Kakabadze MD, PhD

Dr. Koba Shanava MD

Mardaleishvili Medical Center

Dr. Konstantine Mardaleishvili MD, PhD

Dr. George Loladze MD

Dr. Gocha Shatirishvili MD, PhD

University Hospital:

Dr. Nickolas Kipshidze MD, PhD

Dr. Akaki Archvadze MD, PhD


Thank You!