Beneficial effect of autologous macrophage therapy on clinical outcomes in patients with compensated cirrhosis: extended follow up data from a randomised controlled phase 2 trial

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Introduction

Preclinical models and early human studies using macrophage cel therapy for liver cirrhosis have produced promising results.
We recently performed a multicentre, open-label, Phase 2, randomized controlled trial of autologous monocyte-derived macrophage therapy for cirrhosis (MATCH01; ISRCTN10368050)[1] which followed on from our original phase I trial assessing the safe and feasibility of a novel cell therapy for compensated ACLD.[2]

Aim

The long-term outcomes of advanced cellular therapies are vital to understanding the efficacy, duration of response, and adverse safety signals in relation to treatment, but are poorly described.

In this study, we present an interim analysis of an extended follow-up of participants from the MATCH01 study, to assess for differences in clinical outcomes between those who underwent treatment with autologous macrophage therapy and controls.

Method

In MATCH01, autologous monocyte-derived macrophage therapy was compared with standard medical care in adults (18 to 75 years inclusive) with compensated cirrhosis (MELD score ≥10 and ≤17)
Treatment comprised leukapheresis, cell isolation and maturation with reinfusion of macrophages up to a maximum dose of 1 x 10^9 cells.
Participants were followed-up for 12 months as part of the original trial which was reported.[3]
Time-to-event analysis over 30 months post-randomization was estimated for each group using the Kaplan-Meier method and compared statistically using the log-rank test.

Results

In total participants were randomized to triple infusion (n=3), single infusion (n=23) or standard medical care (n=24).
After 18 months of additional follow-up (i.e., 30 months post-randomization)- there were 7 deaths, 2 liver transplants, 1 patient listed for transplant, and 3 malignancies (no HCC) in the control group
Compared to 2 deaths, no liver transplants, no patients listed for transplant, and 1 malignancy (HCC) in the macrophage infusion group.
The macrophage treated groups had significantly improved overall survival (Chi-square=4.35; p=0.037) and transplant-free survival (Chi-square=7.07; p=0.0078).

Conclusion

This study demonstrates proof-of-concept for the beneficial effect of macrophage therapy on clinical outcomes in patients with compensated cirrhosis and reinforces their longer-term safety profile.
Further development of macrophage therapy for cirrhosis/end-stage liver disease is warranted, including larger trials which also incorporate long follow up intervals.
Future trials should also focus on assessing durability of response and consideration for repeated infusions.

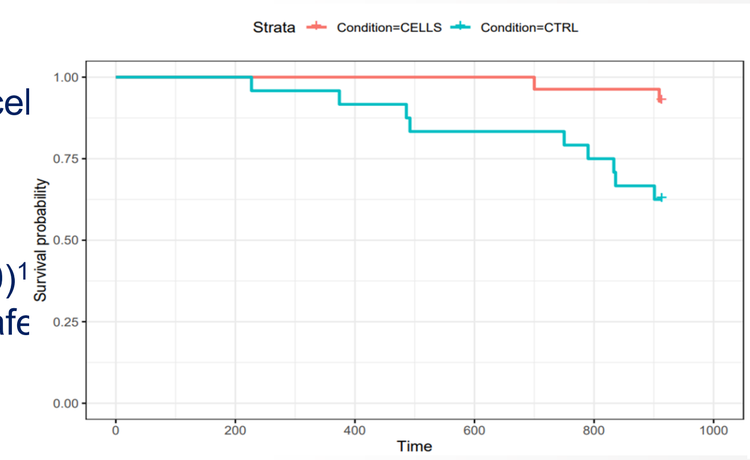

Fig 1: *Kaplan-Meier Curve demonstrating difference in time to death or transplantation between cell group (red) or control (blue*

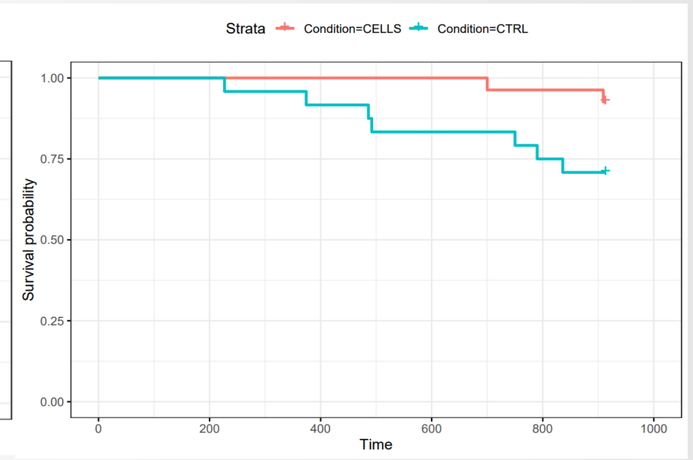

Fig 2: *Kaplan-Meier Curve demonstrating difference in time to death between cell group (red) or control (blue*

Subjects	Aetiology	Cause of Death
Cell Group		
1	ArLD	Acute GI bleed , Group B strep discitis
2	ArLD	Decompensated, Ascites, HE
Control		
1	NAFLD	dACLD, Lymphoma, LVSD
2	ArLD	Multi organ failure, HE, CRC
3	NAFLD	Oesophageal Ca, dACLD
4	ArLD	Anoxic brain injury, E.Coli Bacteraemia dACLD, HE, Ascites
5	NAFLD	dACLD, HE, Ascites
6	ArLD	Cardiopulmonary Arrest, PE
7	NAFLD	HFrEF, SARS-Cov2, COPD

Table 1*Overview of cause of death in patients in the MATCH01 trial in both treatment group (cells) and controls.* **:**

References

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