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UPDATED CLINICAL PROGRESS OF IL-10 EXPRESSING CD19 CAR-T CELLS FOR TREATMENT OF RELAPSED OR REFRACTORY B-CELL HEMATOLOGICAL MALIGNANCIES AT TINY DOSES

Yugang Guo, PhD[1-3], Qianwen Xu, M.S.[1], Lei Xue, M.S.[1], Erlin Chen, M.S.[1], Xuhan Zhang, M.S.[1], Chonglin Liu, M.S.[2], Min Gao, PhD[2,3], Youjia Li, PhD[2], Jingjing Ren, MD, PhD[2], Karthik Sathiyanadan, PhD[2], Li Tang, PhD[4], Xingbing Wang, MD, PhD[1]

[1]Centre for Leading Medicine and Advanced Technologies of IHM, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui, China. [2]Leman Biotech Co., Ltd. Shenzhen, China. [3]Institute of Drug Metabolism and Pharmaceutical Analysis, College of Pharmaceutical Sciences, and State Key Laboratory of Advanced Drug Delivery and Release Systems, Zhejiang University, Hangzhou, China. [4]Institute of Bioengineering, École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland.

INTRODUCTION

Meta10-19, the innovative IL-10 expressing CD19 CAR-T cells, show significant potential in addressing T-cell dysfunction, a major hurdle in current CAR-T therapies. This dysfunction often leads to resistance and relapse in patients with relapsed/refractory (R/R) B-cell hematological malignancies.

AIM

The primary objective of this phase I trial (NCT05715606; NCT05747157) is to assess the safety and tolerability of Meta10-19 among patients diagnosed with R/R diffuse large B-cell lymphoma (DLBCL) and B-cell acute lymphoblastic leukemia (B-ALL). Secondary goals encompass investigating pharmacokinetics and gauging initial efficacy outcomes.

CONCLUSIONS

This first-in-human trial of Meta10-19 has shown encouraging preliminary efficacy and a manageable safety profile even at tiny doses (1~5% doses of commercial products). Ongoing investigations with larger patient cohorts and extended follow-up periods aim to provide further insight into the efficacy and safety parameters.

REFERENCES

- **Guo Y., …, Tang L. et al. Metabolic reprogramming of terminally exhausted CD8+ T cells by IL-10 enhances anti-tumor immunity. Nat Immunol. 2021 Jun;22(6):746-756.**
- **Zhao Y., …, Tang L. et al. IL-10-expressing CAR T cells resist dysfunction and mediate durable clearance of solid tumors and metastases. Nat Biotechnol. 2024 Jan 2.**

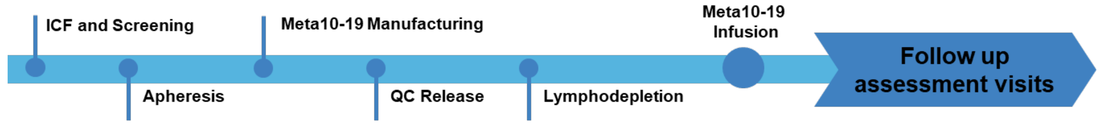
METHOD

Patient Enrollment and Dose Level:

Subjects (n =18)	Cohort	Dose
3	r/r DLBCL	1.0×10^5/ kg (5.0%)
5	r/r DLBCL	0.5×10^5/ kg (2.5%)
1	r/r DLBCL	0.2×10^5/ kg (1.0%)
9	r/r B-ALL	1.0×10^5/ kg (5.0%)

***1%-5% dose* of commercial products**

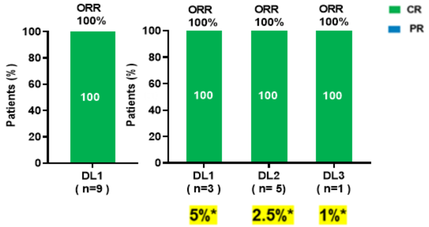
Study Period: February 2023 to March 2024



Cytokine Release Syndrome (CRS): Graded according to Lee 2014 guidelines
Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS): Graded according to ASTCT 2019 guidelines
Adverse Events (AEs): Assessed based on CTCAE 5.0 criteria

RESULTS

Overall Assessment ORR of Meta10-19:



- ORR = 100% (18/18) patients
- CR = 100% (18/18) patients

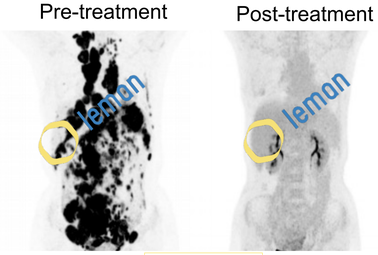
Meta10-19 CR rate and comparison:

CR rate	DLBCL 3M CR	B-ALL 1M CR	B-ALL 3M CR
Meta 10-19	100%	100%	100%
Commercial CD19 CAR-T (average)	~50%	~90%	~70%

- Meta10-19 induce breakthrough efficacy (100% CR) in all patients.

Case Report: DLBCL, Stage IV, NCCN-IPI 4

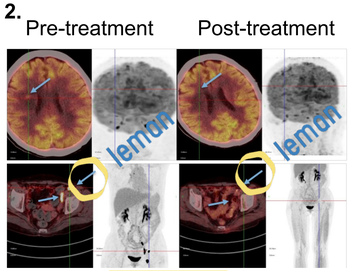
Case 1.



UNPUBLISHED

- Many bulky tumor lesions in the chest and abdominal cavity
- CR achieved at 1M.

Case 2.



UNPUBLISHED

- Multiple tumor lesions in the pelvic cavity with CNS involvement
- CR achieved at 1.5M

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CONTACT INFORMATION

Dr. Li Tang, Co-founder & President
li.tang@lemanbio.com
Dr. Yugang Guo, Co-founder & CEO
Yugang.guo@lemanbio.com

Official Website LinkedIn WeChat