# Immunological alterations induced by HBV-TCR T cell immunotherapy associates with treatment response of primary HBV related-HCC

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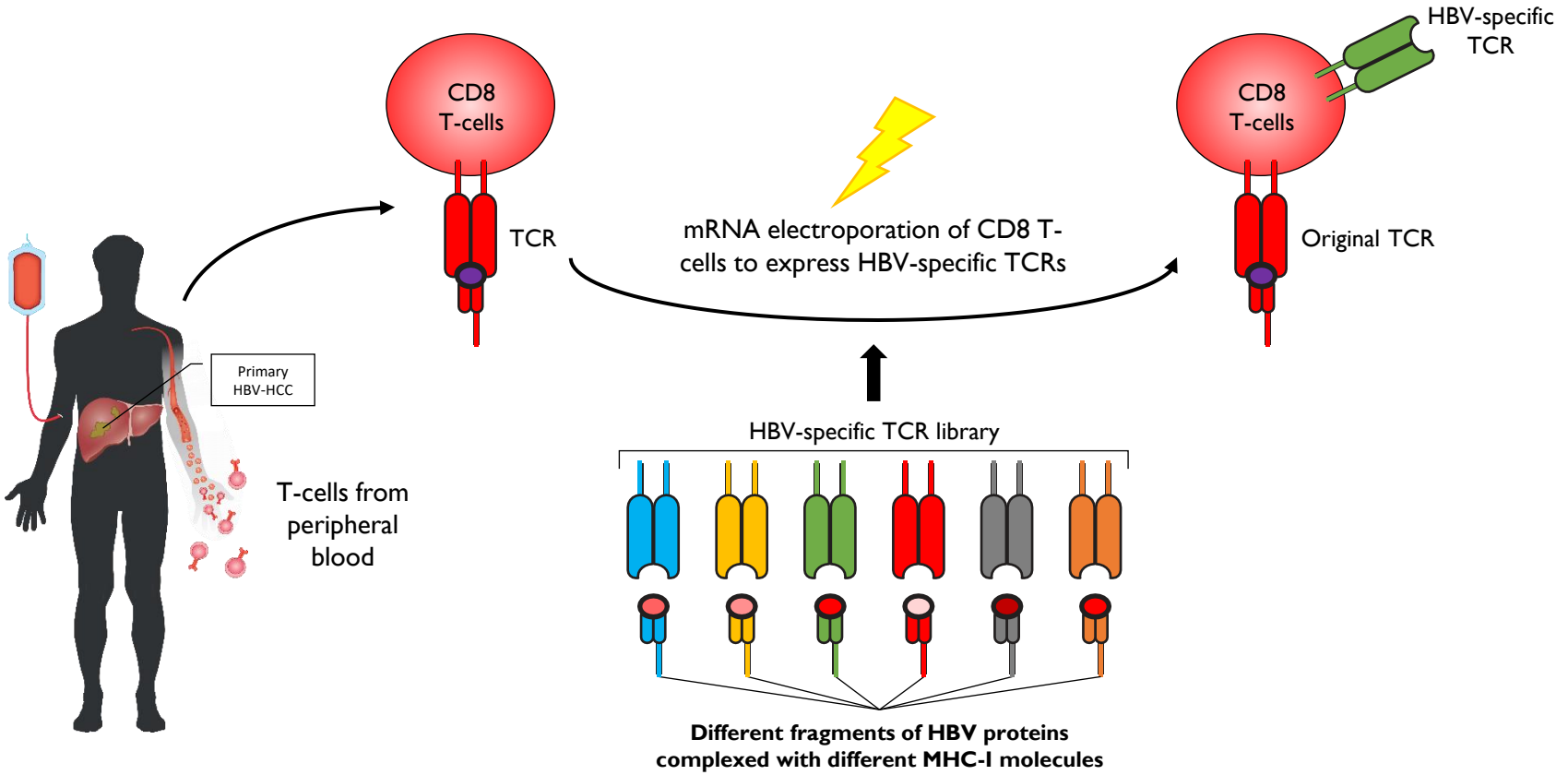
# COI Disclosure

- A.B. is a co-founder and A.T.T. consults for Lion TCR, a biotech company developing T cell receptors for the treatment of virus-related diseases and cancers.  None of the other authors has any competing interest related to the study.

# Background and Aims

- HBV-TCR T cell immunotherapy is potentially associated with increased risk of on-target, off-tumour severe liver inflammatory events in patients with primary HBV-HCC
- This response may indicate a less compromised immune system that can better respond to treatment




**AIM:** To longitudinally analyze immunological, virological, biochemical and radiological alterations in patients with primary HBV-HCC receiving HBV-TCR T cell immunotherapy and its association with treatment response

# Methods

**Patients with diffuse. non-operable HBV-HCC (n=8)**

↓

**mRNA electroporated HBV-TCR T cells**
Escalating doses at weekly intervals

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**Serum and PBMCs collected at baseline and regular intervals post-T cell infusion**

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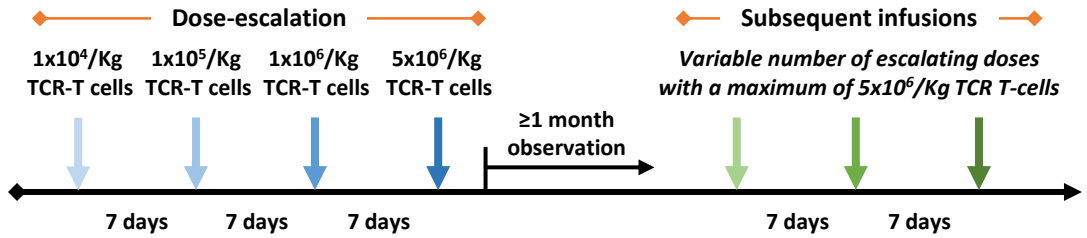
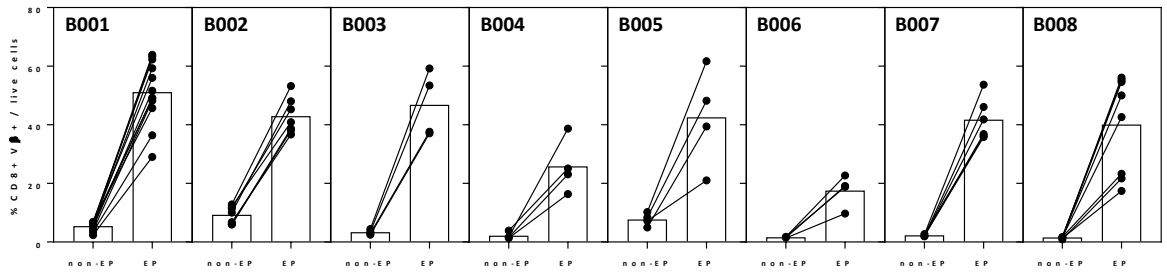
**Retrospective analysis for liver inflammation, cytokine levels, activation phenotype of T cells and anti-tumour response***

*Evaluated primarily by radiological imaging or by detection of serum HBV pgRNA as a surrogate

## Planned dosing schedule

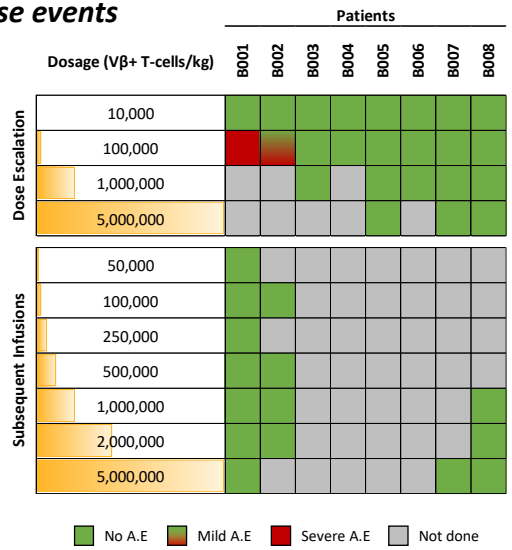



## mRNA Electroporation efficiency (Quality control)

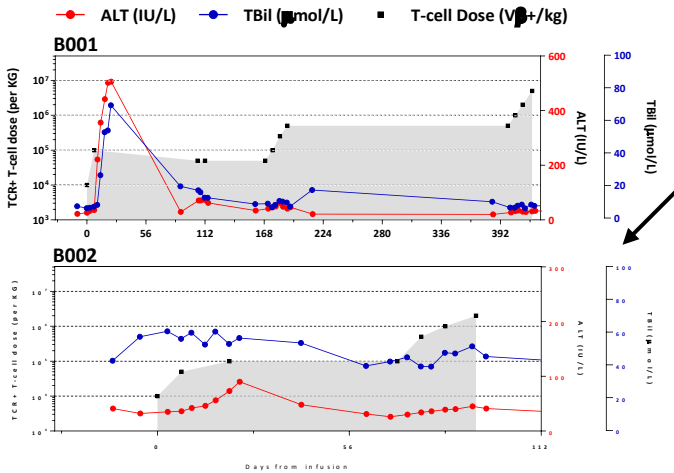


# Results

## Adverse events




## Liver inflammation markers

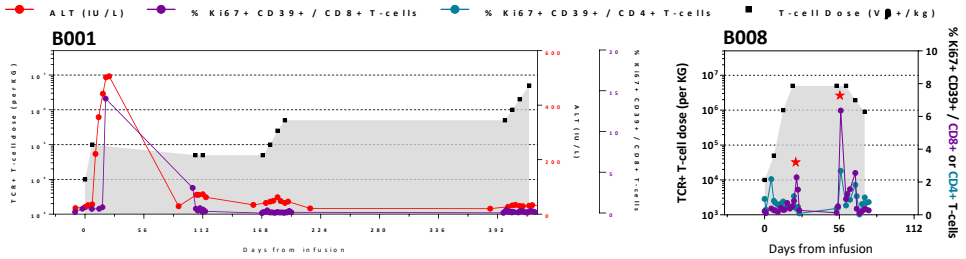



## Summary

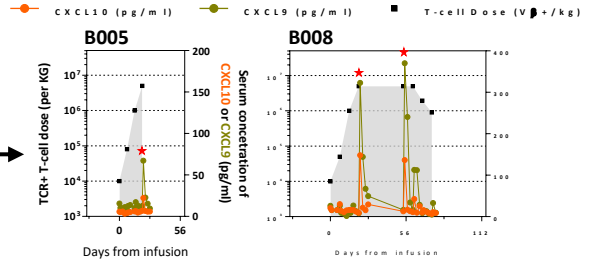
| Patient No. | Adverse Events (Y/N) | T-cell response | Serum chemokine response | Radiological response | HBV virological response |
|---|---|---|---|---|---|
| **B001** | Y | + | - | + | ‡<LLOD |
| **B002** | Y | - | - | - | + |
| B003 | N | - | - | - | <LLOD |
| B004 | N | - | - | - | <LLOD |
| **B005** | N | - | + | *± | <LLOD |
| B006 | N | - | - | - | <LLOD |
| B007 | N | - | - | - | <LLOD |
| **B008** | N | + | + | + | <LLOD |

*Both target lesions remain stable during therapy
‡Below lower limit of detection

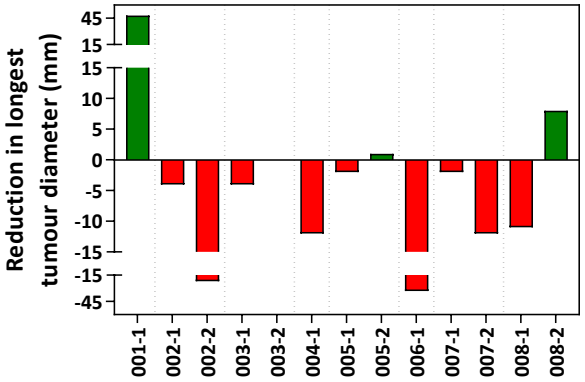
## T cell activation markers

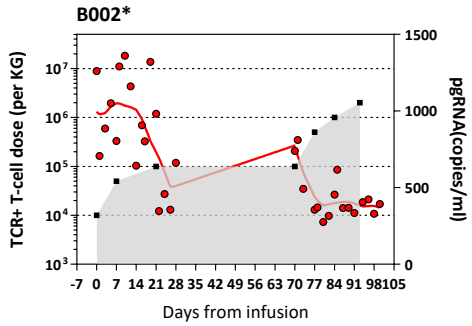



## Serum chemokine levels




## Anti-tumour response



# Conclusion

- Multiple infusions of HBV-TCR T cells with limited functional lifespan in patients with primary HBV-HCC did not induce frequent adverse events.

- Immunological alterations in the peripheral blood induced by HBV-TCR T cell immunotherapy is associated with treatment response.
    1. Patient with major adverse event after HBV-TCR T cell infusion has subsequent dramatic reduction of tumour volume
    2. Patients with post-infusion elevations of serum chemokines or activated T cell frequencies have a stable tumour load

- These findings has important implications in the monitoring of primary HBV-HCC patients receiving T cell immunotherapy.