

Engineered T cell Therapy

Trials in Manchester

Robert Hawkins

MANCHESTER
1824

The Christie
NHS Foundation Trust



Overview of Trials

- Using **first generation** receptors aim to generate **engrafted** cells
 - Target 1% at 28 days based on NCI trials
- MFEz
 - First generation receptor targeting CEA
- aCD19z
 - First generation receptor targeting CD19

Proposed Dose Escalation

Cohort	Expected no of patients per cohort	Chemotherapy Cyclophosphamide (C) 60mg/kg d-7 and d-6 Fludarabine (F) 25mg/m ² d-5 to d-1	Number of MFEz T-cells	IL2 (IU/kg IV)
1	3	F	10 ⁹	600 000
2	3	F	10 ¹⁰	600 000
3	3	F	Up to 5 x 10 ¹⁰	600 000
4	4	C+F	Up to 5 x 10 ¹⁰	600 000

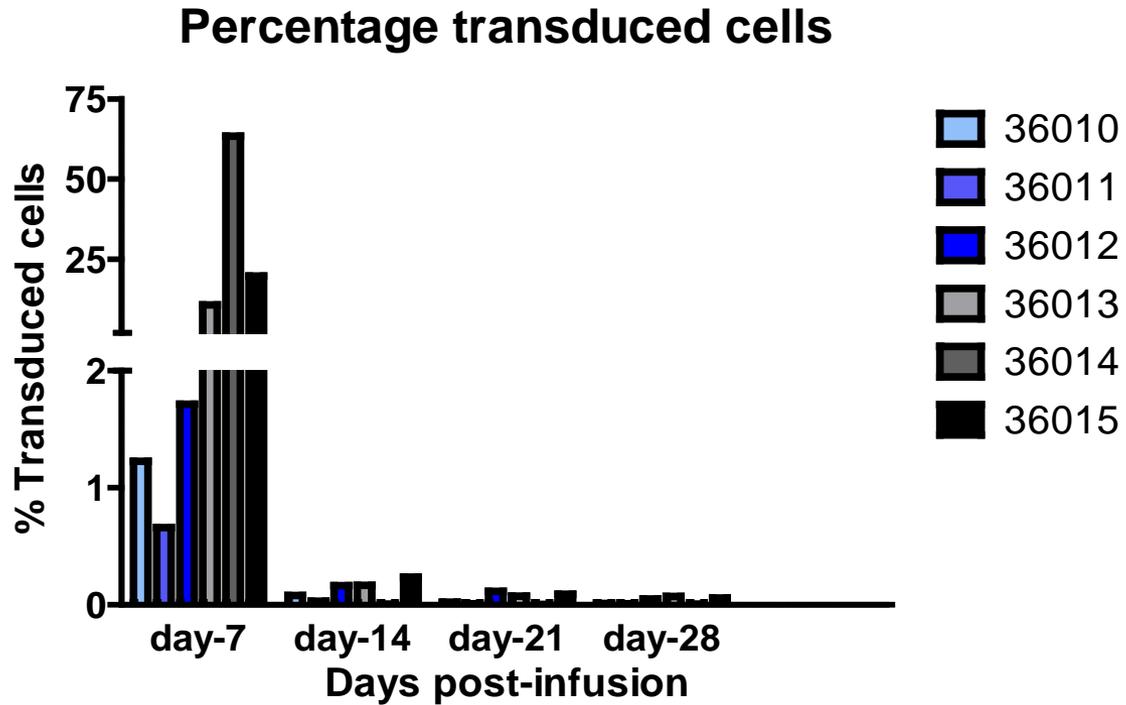
Cohorts 1-3

- Toxicity
 - No (or mild) toxicity related to T cells
 - Some toxicity from infections post chemo
 - Expected IL2 toxicity
- Patients generally discharged after expected inpatient stay of 2-3 weeks
- No evidence of clinical activity
- No evidence of significant cell persistence beyond 7 days

Dose Escalation

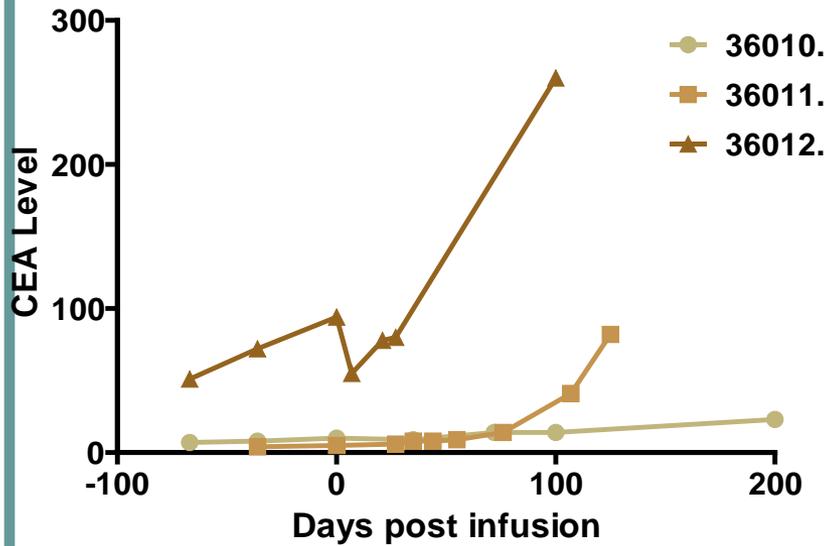
Cohort	Expected no of patients per cohort	Chemotherapy Cyclophosphamide (C) 60mg/kg d-7 and d-6 Fludarabine (F) 25mg/m ² d-5 to d-1	Number of MFEz T-cells	IL2 (IU/kg IV)
1	3	F	10 ⁹	600 000
2	3	F	10 ¹⁰	600 000
3	3	F	Up to 5 x 10 ¹⁰	600 000
4	4	C+F	Up to 5 x 10 ¹⁰	600 000

T-cell Persistence

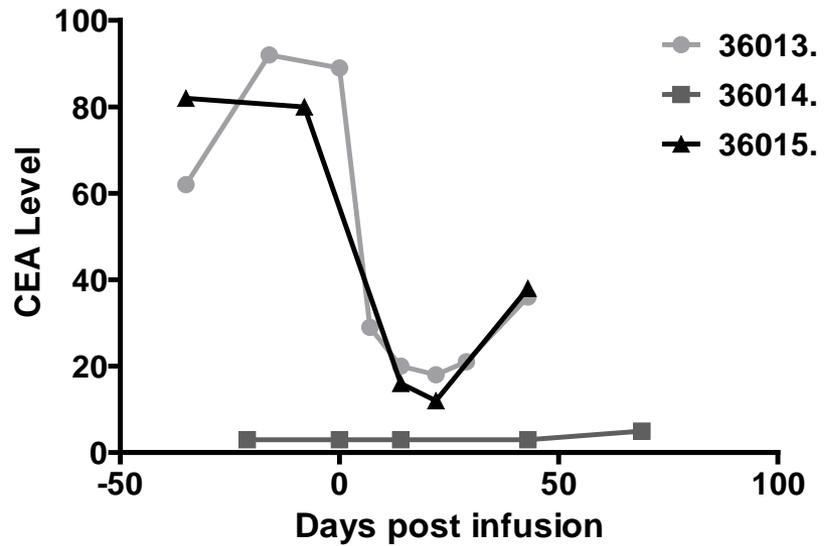


Tumour marker levels: CEA

Cohort-3 CEA Levels



Cohort-4 CEA Levels



Cohort 4 CTC AE gradings

Adverse Event	Max Grade	No of patients
Respiratory		
SOB/hypoxia	3	4
Infective		
C diff colitis	3	1
Throat infection	2	1
GI		
N+V	2	2
Diarrhoea	3	1
Weight loss/reduced appetite	2	2
	3	1

Outcome of CIRB safety review

- Phase I study of MFEz T cells in CEA positive tumours was reviewed at a full CIRB meeting held on Friday 30th April.
 - “External reviews of the data were also provided by two independent experts. These reviews focused on the safety and efficacy data arising from the study. The unanimous decision at CIRB was that, taking into account the potential risks vs benefits of the experimental treatment, the study should be immediately closed to recruitment.”

Targeting B Cell Malignancies

A Phase I Study of Adoptive Transfer of
Autologous Tumour Antigen-Specific T Cells
with Pre-conditioning Chemotherapy
and Intravenous IL2
in Patients with CD19 Positive Malignancy

A Phase I Study of CD19 Specific T cells in CD19 Positive Malignancy

Cohort	Chemotherapy Cyclophosphamide (C) 15mg/kg d-7 and d-6 Fludarabine (F) 25mg/m ² d-5 to d-1	Number of aCD19z T Cells	IL2 IU/kg IV bolus tds max 12 doses
1	C+F	10 ⁹	100 000
2	C+F	10 ¹⁰	100 000
3	C+F	Up to 5 x 10 ¹⁰	100 000
4	C+F	Up to 5 x 10 ¹⁰	300 000
5	C+F	Up to 5 x 10 ¹⁰	600 000

Summary of Outcomes to date

- 3 patients treated (10^9 cells)
- C (1/4 dose)+F
- No major toxicity
- T cell survival better (10% at 14 days)
 - Still no significant long term T cell survival
- 2 /3 Partial responses
 - One brief consistent with chemotherapy effect
 - One prolong > 6 months ? Cell effect