Introduction
Management of advanced B cell malignancies refractory to standard chemotherapy is challenging with sub-optimal results. Recent clinical reports of durable, objective responses from adoptive transfer of anti-CD19 chimeric antigen receptor (CAR) T cells have accentuated the potential of this therapy.

Here we report the preliminary results of an on-going Phase I clinical trial at our Institution.

Methods
This is a single centre, open label, dose escalation, Phase I study of adoptive transfer of autologous T cells expressing a CD19-specific first generation CAR (aCD19z) with pre-conditioning chemotherapy and intravenous interleukin-2 (IL2), in patients with pre-treated CD19-positive malignancy.

We report data on 2 cohorts: Cohort 1 (4 patients) received 1x10^9 aCD19z T-cells and Cohort 2 (planned 4 patients) 1x10^10. Both cohorts received 100,000 u/kg of IL2.

Results
To date, 6 patients have successfully completed treatment. All patients tolerated treatment well, and experienced anticipated transient grade 1-2 toxicities attributable to pre-conditioning chemotherapy and IL2. 5 patients developed short lived but significant Grade 4 neutropenia and thrombocytopenia.

4 of 5 patients evaluable to date achieved at least stable disease as best response at 6 weeks post aCD19z T cell infusion, with 1 patient maintaining response at 400+ days. 1 patient achieved a very good partial response with a 65% reduction in disease burden. 2 patients died of disease progression (1 of Central Nervous (CN) progression only, not present at baseline); 2 patients died of viral infection over 400 days post infusion; 1 patient with disease control maintained. No patients died of treatment-related complications.

Quantitative polymerase chain reaction (qPCR) analysis of peripheral blood samples detected aCD19z T cells in both cohorts. Levels peaked at days 4-7 post aCD19z T cell infusion (cohort 1 peak 30% of total cells, cohort 2 (results available to date) peak 25%) before falling to lower levels. All patients revealed persisting low frequency levels (< 1%) at week 6; 1 patient at up to 50 weeks. 1 patient received a further course of low dose IL2 at week 6 resulting in a transient increase in zCD19z T cell levels.

All patients demonstrated a significant reduction in peripheral CD19+ T cell numbers post aCD19z T cell infusion, with most substantial results seen in cohort 2 where suppression was seen lasting into week 8 (prior to CN progression).

Discussion
Our data contributes to the encouraging growing body of evidence on antiCD19-specific CAR T cells, suggesting significant clinical responses and sustained persistence. Updated results and immune data will be presented.
Registration Details
www.clinicaltrials.gov NCT01493453

Consent
Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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Published: 6 November 2014


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