**CD5^{bright}/CD16^{bright} FC21-NK-cell adoptive immunotherapy in patients with concurrent CNS disease and relapsed or refractory (R/R) AML**

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**INTRODUCTION**

- Patients with relapsed or refractory acute myeloid leukemia (R/R AML) and concurrent central nervous system (CNS) disease rarely respond to chemotherapy and have a dismal prognosis.
- Gene expression profiling was performed by next-generation sequencing.
- In a phase I study (NCT02809092), we investigated multiple doses of DB FC21-NK cells following induced, and granulocyte colony stimulating factor (FLG) induction in patients with R/R AML.

**OBJECTIVE**

- To investigate preliminary safety and efficacy data in a subgroup of patients with R/R AML and concurrent CNS disease from this phase I study.

**METHODS**

- This open-label, phase I study was performed in patients treated at a single center in Brazil.
- Eligible patients were 18 years old, with R/R AML, a Karnofsky or Lansky performance status score ≥ 70, and adequate renal, liver, and pulmonary function.
- Eligible donors were a human leukocyte antigen (HLA)-identical sibling or histocompatible related donor selected for HLA NK allodonor.
- CD5^{bright}/CD16^{bright} was determined according to European Haematological (S樨) guidelines.
- FC21-NK cells were expanded from donor on FC21 feeder cells as previously described.
- The treatment scheme is shown in Figure 1.
- Results are presented as median (range).

**RESULTS**

**Patient characteristics**

- Of 13 patients treated with FLAG chemotherapy followed by FC21-NK, 9 patients had concurrent CNS disease and were included in this analysis.
- Characteristics of patients with CNS disease are summarized in Table 1.
- All four patients had received a prior dose of FLAG and were heavily pretreated.
- Two patients had primary refractory disease.

**Treatment exposure and safety**

- Table 2: all patients completed ≥6 infusions of FC21-NK.
- All patients experienced grade 3/4 neutropenia attributable to hematologic toxicity secondary to FLAG.
- ADAs could be related to treatment are shown in Table 3. all were manageable.
- No FC21-NK cell infusion-related toxicities or cytotoxic syndrome were reported.
- Patient 5 experienced grade-4 hypersensitivity reaction (GHR).
- Re-injection of FC21-NK cells was managed with atropine and high-dose steroids.
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- Table 3: adverse events considered to be related to FC21-NK cell treatment.

**CONCLUSIONS**

- Multiple IV infusions of ex vivo-expanded FC21-NK cells were well tolerated and demonstrated unprecedented CNS responses in patients with R/R AML.
- These data demonstrate the potential of FC21-NK to traverse the BBB and mediate therapeutic anti-leukemic effect.

**DISCLOSURES**

- Site: Nothing to disclose
- Paz: Nothing to disclose
- Hammond: Nothing to disclose
- Efthimos: Nothing to disclose

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**REFERENCES**


**Figure 1: Treatment scheme**

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**Figure 3: CNS responses in patients treated with FC21-NK after FLAG chemotherapy**

- CNS responses as indicated by cellular infiltration or the resolution of CNS lesions, were observed in all patients with nervous system lesions (including probable aspergillosis), shown in Figure 3:
- Complete resolution of bone and nerve root leukaemic infiltration was observed in patient 4 and 5, and patient 1 experienced no relapse of pulmonary or CNS leukaemia.
- Almost complete resolution of bone and nerve root leukaemic infiltration was observed in patient 4 and 5, and patient 1 experienced a 35% reduction of CNS chloromas.

**Figure 4: Gene expression profiling in FC21-NK cells**

- Depression profiles of genes with increased expression identified in FC21-NK cells are shown in Figure 4.