Abstract TPS7562: A Phase I Clinical Trial Testing the Safety of IL-21-Expanded, Off-the-Shelf, Natural Killer Cells for Relapsed/Refractory Acute Myeloid Leukemia

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Relapsed/Refractory AML

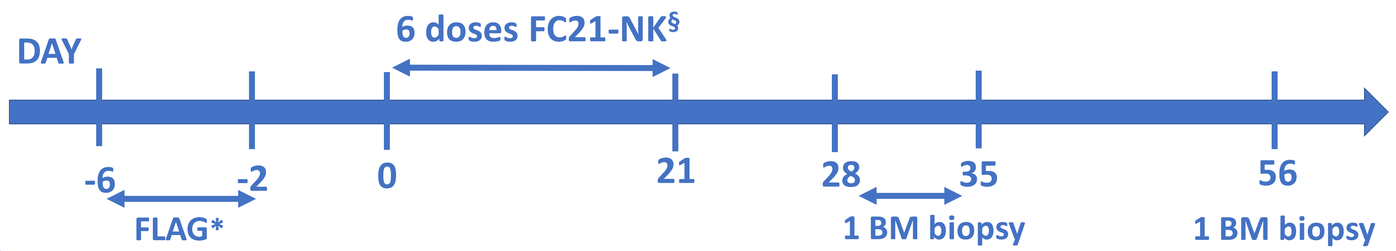
- Allogeneic transplantation (allo-HCT) is an effective treatment for many patients with Acute Myeloid Leukemia (AML) and Myelodysplastic Syndrome(MDS)[1,2]
- DFS for relapsed AML patients without HCT is only 5-10%[3]
- Many relapsed patients have refractory chemo-resistant disease and do not attain remission
- These patients also have comorbidities that preclude allo-HCT
- Attrition of patients while waiting for manufacturing of donor-derived cellular therapies
- Need for readily-available immune cell therapies that can be used for transplant-ineligible patients

Natural Killer (NK) Cells

- NK cells in patients with cancer can be dysfunctional and reduced in number
- *Ex vivo* expanded haploidentical FC21-NK cells (feeder cells) have been safely administered before/after haplo-HCT and following induction chemotherapy for poor prognosis AML/MDS patients with promising outcomes[4-7]
- NK alloreactivity plays a critical role in mediating anti-leukemia effects. The major obstacle for adoptive NK cell immunotherapy is obtaining sufficient cell numbers and having them readily available for patients. This trial determines the safety of FC21 expanded Off-the-shelf (OTS), Third-party donor-derived NK cells for relapsed/refractory AML patients .

First-in-man assessment of OTS FC21-NK cells derived from universal allogeneic donors in R/R AML

Schematic treatment plan



Study Objective:

Establish the safety of OTS FC21-NK cells for the induction of remission in patients with R/R AML & MDS

3+3 Design with two cohorts:

3-18 pts/cohort for dose determination and 10 patients for each cohort during the expansion phase. N_{tot}= 56

* Cohort 1	* Cohort 2
< 60 years old and able to tolerate intensive chemo and disease not insensitive to Cytarabine.	≥ 60 years old, or < 60 years old and unable/unwilling to tolerate intensive chemo, or disease insensitive to Cytarabine (tp53, TET2 mutations).
Fludarabine 30 mg/m2/day (day -6 to day -2) and Cytarabine 2g/m2/day (days -6 to day -2	Fludarabine 30mg/m2/day (day -5 to day -2) and Decitabine 20 mg/m2/day (day -6 to day -2)

§FC21-NK dosing

Six doses of third-party, ideal-donor, mbIL-21 expanded NK cells given thrice weekly for two weeks.
Days may vary and NK cells can be given from days 0-21.
Three dose levels in NK cell/kg (±20%) for each dose : 1) $1x10^7$ NK cell/kg ; 2) $3x10^7$ NK cell/kg ; 3) $1x10^8$ NK cell/kg

Inclusion Criteria:

- Primary refractory AML
- Relapsed AML
- MDS
- Patient age ≥18 to ≤80 years
- Karnofsky or Lansky Performance Scale ≥70

Exclusion Criteria:

- Active GVHD
- Patients with donor-specific antibodies with MFI > 5000
- Patients on systemic steroids for asthma and prednisone dose is > 20 mg/day or >0.25mg/kg, whichever is higher will be excluded
- Asymptomatic viremia is NOT considered as an exclusion criteria

Primary Endpoints:

- Determine RP2D
- Overall response rate (CR, CRi & MLFS)

Secondary Endpoints:

- % pts MRD negative remission
- % pts proceeding to allo-HCT
- Median time to neutrophil and platelet recovery
- Median duration of remission
- Incidence of infectious complications
- % pts with Progression Free Survival and with Overall Survival

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1. Litzow MR, et al. Br J Haematol 2002: 119:1115-1124 **2.** Graef T, et al. Hematol Oncol 2007: 25:170-177. **3.** Hiddemann W, et al. J Clin Oncol 1999: 17:3569-3576. **4.** Ciurea SO, et al. Blood 2017: 130:1857-1868 **5.** Ciurea SO, et al. ASCO Annual Meeting 2018, Abs#7008 6. **NCT**NCT01787474 7. NCT02809092