LymphomaHub

CLL/SLL

EHA 2019 | Investigating liso-cel in R/R chronic lymphocytic leukemia and small lymphocytic lymphoma

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On 14 June 2019, at the 24th European Hematology Association Congress, Tanya Siddiqi presented results of the ongoing phase I/II TRANSCEND CLL 004 study. The study assessed the safety, pharmacokinetics and efficacy of lisocabtagene maraleucel (liso-cel, JCAR017). Liso-cel is an anti-CD19 chimeric antigen receptor (CAR) T-cell product administered as a defined composition of CD4+/CD8+ CAR T-cells.

The primary objectives of the study were safety and determination of the recommended phase II dose.

Patient Characteristics

- Predominantly female patients (52.2%), median age 66
- Patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)
- Previously received ≥2 lines of therapy
- ECOG score of ≤1

Baseline characteristics	All patients (n = 23)	DL1 (n = 9)	DL2 (n = 14)
Received bridging therapy	17 (73.9%)	5 (55.6%)	12 (85.7%)
High-risk features	19 (82.6%)	6 (66.7%)	13 (92.9%)
Del (17p)	8 (34.8%)	3 (33.3%)	5 (35.7%)
Tp53 mutation	14 (60.9%)	4 (44.4%)	10 (71.4%)
Complex karyotype[b]	11 (47.8%)	5 (55.6%)	6 (42.9%)
Previous therapy	5 (2 – 11)	5 (3 – 8)	5 (2 – 11)

Prior ibrutinib	23 (100%)	9 (100%)	14 (100%)
Ibrutinib relapsed/refractory	21 (91.3%)	9 (100%)	12 (85.7%)
Ibrutinib progression and prior venetoclax	13 (56.5%)	5 (55.6%)	8 (57.1%)

Methods

- After three days of lymphodepleting chemotherapy, patients received liso-cel infusion at either dose level 1 or 2 (one: 50 x 10^6; two: 100 x 10^6)
- Patients monitored for dose-limiting toxicities
- Minimal residual disease (MRD) was assessed using flow cytometry in blood, and through next-generation sequencing in bone marrow

Key findings

- 16 patients received liso-cel (n = 6 in dose level one, and n = 10 in dose level two)
- One dose-limiting toxicity, grade four hypertension at dose level 2
- The most common adverse events (AEs) were cytopenias:
  - Thrombocytopenia, 75%
  - Anemia, 69%
  - Neutropenia, 63%
  - Leukopenia, 56%
- One patient had grade 3 cytokine release syndrome (CRS), three patients had grade 3 neurological events
- 83% of patients with complete response (CR) at 6 months remained in CR
- Durable objective responses (67%) and undetectable MRD (64%) maintained at 6 months

Conclusion

Dr Siddiqi mentioned how toxicities related to liso-cell were manageable, with promising clinical activity in patients who had been heavily pre-treated with ibrutinib and venetoclax. At both dose levels, adverse events were manageable, with a follow-up of 9 months showing a high proportion of durable responses that improved over time. The majority of responses and undetected MRD were achieved by day 30, with a large proportion of patients remaining in CR at 6 months, remaining in CR.

A phase II study is currently enrolling patients at dose level 2, stemming from the results of this phase I trial. Patients in this trial will be treated with liso-cel in combination with ibrutinib.

Reference

Siddiqi, T. *et al*. TRANSCEND CLL 004: Minimal residual disease negative response after lisocabtagene maraleucel (liso-cel) in patients with relapsed/refractory chronic lymphocytic leukemia or small lymphocytic lymphoma. Abstract S109. 24th European Hematology Association Congress, Amsterdam, NL. 2019 Jun 14.