Interim Results from the ELiPSE-1 Study: A Phase 1, Multicenter, Open-Label Study of CNTY-101 in Subjects with Relapsed or Refractory CD19-Positive B-Cell Malignancies

Abstract #7023

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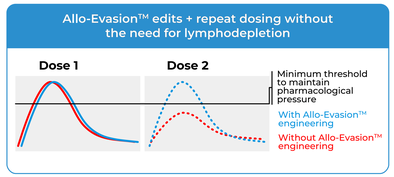
BACKGROUND

CNTY-101 aims to deliver durable responses in R/R B-cell NHL via repeat dosing facilitated by Allo-Evasion™

- Autologous CD19 CAR-T is curative in 40 percent of patients
- Autologous CD19 CAR-T access is limited and/or can fail in manufacturing as quality is dependent on patient-derived starting material
- Limited options and poor prognosis for patients who fail autologous CAR-T

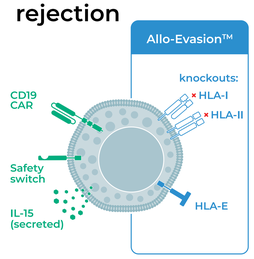
- Off-the-shelf product offers immediate access and consistency
- Multiple doses to increase pharmacological pressure to increase durability
- Host rejection addressed by Allo-Evasion™ edits



Aim: Extending the period of pharmacologic pressure on tumor cells

R/R: relapsed or refractory, NHL: non-Hodgkin lymphoma, CAR-T: chimeric antigen receptor T cell therapy, iPSC: induced pluripotent stem cell, MCB: master cell bank

CNTY-101 is an iPSC-derived NK cell therapy with CD19 CAR and Allo-Evasion™ edits to avoid host rejection



CNTY-101 is an allogeneic anti-CD19 iPSC-derived NK cell therapy

Century's technology for multiple step editing using CRISPR in iPSC allowed 6 edits (2 KO, 4 KI) to enable multiple functions

- Avoid host T cell rejection: Knockout of beta-2 microglobulin (b2M) and HLA Class II Transactivator (CIITA) to eliminate HLA-I & HLA-II
- Avoid host NK cell rejection: Knock-in of HLA-E
- Tumor elimination: CD19 CAR with FMC63 binder
- Safety switch: truncated Epidermal Growth Factor Receptor (EGFRt) containing Cetuximab binding epitope
- Secreted IL-15: to enhance cell persistence and modulate the tumor microenvironment

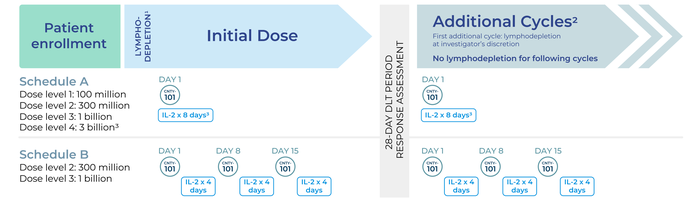
NK: natural killer, FMC63: CD19 binding portion of CAR, HLA: human leukocyte antigen, KO: knockout, KI: knock-in

STUDY DESIGN

CNTY-101: ELiPSE-1 (NCT05336409) Phase 1 BOIN Design

Patients with CD19+ aggressive and high-risk indolent R/R B-NHL
- DLBCL, HGBL, MCL, PMBCL, FL3B, HRFL, MZL
- ≥ 2 prior lines of therapy
- Prior CD19-targeted cell therapy allowed

Part 1 - Dose escalation
Schedule A: single dose
Schedule B: 1 dose per week x 3 weeks
Part 2 - Dose expansion



¹Standard lymphodepletion regimen: fludarabine (30 mg/m²/d) and cyclophosphamide IV (300 mg/m²/d) for 3 days
²Subjects who are assessed as stable disease or better may receive additional cycles of CNTY-101
³Subjects at DL4A did not receive IL-2 on the day of CNTY-101 infusion but did receive daily for 7 days

BOIN: Bayesian Optimal Interval, DLT: dose limiting toxicity; IL-2: Interleukin-2 (dose: 3e6 IU; subcutaneous)

RESULTS

Baseline disease characteristics

Heavily pre-treated R/R B-NHL patients treated across 7 sites

	N=12 safety evaluable[1]
Median Age (range, years)	70 (60-76)
Male, n (%)	9 (75)
NHL subtype, n (%)	
DLBCL	7 (58)
HRFL	1 (8)
MCL	2 (17)
MZL	2 (17)
Prior therapies, median (range)	4 (2-5)
Response to last line of treatment	
Relapsed	3 (25)
Refractory	9 (75)
Received prior autologous CAR-T	3(25)
If no, why	
Manufacturing fail	1
Not eligible	3
Not willing to wait	4[2]
Financial or reimbursement constraints	1

[1]As of 27 March 2024 data cutoff date, data collection ongoing [2]One subject received allogeneic CAR-T

Treatment Emergent Adverse Events (TEAEs)

Manageable safety profile to date; No DLTs or GVHD observed
8/12 subjects received at least one cycle of CNTY-101 in an outpatient setting

	Any Grade n (%)	Grade 3+ n(%)	Related Gr 3+ n(%)
# of subjects with TEAEs	**12 (100)**	**11 (92)**	**2 (17)**
Neutropenia	10 (83)	10 (83)	1 (8)
Nausea	6 (50)	1 (8)	
Anaemia	6 (50)	4 (33)	1 (8)
Thrombocytopenia	6 (50)	1 (8)	
Hypotension	5 (42)	1 (8)	
Constipation	4 (33)		
Febrile neutropenia	4 (33)	4 (33)	1 (8)
Fatigue	4 (33)		
Pyrexia	4 (33)		
Chills	4 (33)		
Cytokine release syndrome	4 (33)		
Diarrhoea	3 (25)		
Hyperhidrosis	3 (25)		
Injection site reaction	3 (25)		
Muscular weakness	3 (25)	2 (17)	
Vomiting	3 (25)		

- Only TEAEs in at least n=3 subjects of any grade are shown
- 12 subjects evaluable for safety across 4 dose levels and two dosing schedules[1]

EVENT		n=12
CRS, n(%)		
	Any Grade	4 (33)
	Grade 1	2 (17)
	Grade 2	2 (17)
Median days to onset, days (range)		0 (0-6)
	Fever >24 hrs	1 (8)
	Hypotension	1 (8)
	Hypoxia	1 (8)

- Only one Gr 1 CRS event in n=1 subject was associated with a fever that lasted more than 24 hrs
- Hypotension (n=1) and hypoxia (n=1) lasted less than 24 hrs

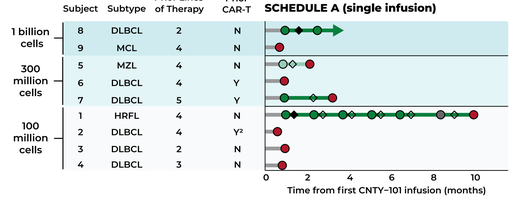
EVENT		n=12
ICANS, n(%)		
	Any Grade	1 (8)
	Grade 1	1 (8)
Days to onset		6
	Fatigue	1 (8)
	Aphasia	1 (8)

ICANS duration was 1 day

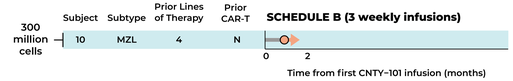
[1]As of 27 March 2024 data cutoff date, data collection ongoing. Grading based on CTCAE v5; CRS and ICANS graded per ASTCT.

CNTY-101 preliminary efficacy

30% CRR; 40% ORR



10 subjects evaluable for efficacy across 3 dose levels and two dosing schedules[1]



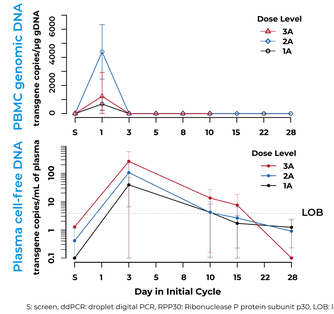
CR
PR
SD
PD
NE
Dose (with LDC)
Dose (no LDC)

HRFL: high risk follicular lymphoma
DLBCL: diffuse large B cell lymphoma
MZL: marginal zone lymphoma
MCL: mantle cell lymphoma

[1]As of 27 March 2024 data cutoff date, data collection ongoing, efficacy based on Lugano criteria [2]Subject received prior allogeneic CAR-T

CRR: complete response rate, ORR: overall response rate

CNTY-101 rapidly traffics out of circulation and persists in extravascular space



CNTY-101 has limited duration in circulation; maxiÂ mum concentration is observed at Day 1 post-infusion

Transgene copies per µg genomic DNA were deterÂ mined using ddPCR with primers targeting transgene and RPP30. Data is shown for initial cycle across subÂ jects at each dose level; mean ± SD. LLOQ is 5 copies.

CNTY-101 persistence is detected via cell-free DNA[1] on Day 3 and beyond

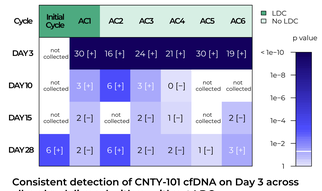
Transgene copies per mL of plasma were determined using ddPCR. Data is shown for initial cycle across subjects at each dose level; mean ± SD (error bar: low values are truncated at 0.1). Positivity values are determined to be significantly above LOB using two sample Poisson test, p < 0.05.

[1]Cell-free DNA has short half-life in circulation, ranging from minutes to hours (Khier and Lohan, Future Science 2018)

S: screen, ddPCR: droplet digital PCR, RPP30: Ribonuclease P protein subunit p30, LOB: limit of blank, SD: standard deviation, LLOQ: lower limit of quantification

Patient 1 (Schedule A 100 million) Case Study - No signs of allo-rejection observed after multiple treatment cycles without LDC

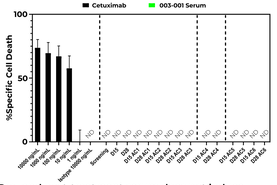
Detection of CNTY-101 cell-free DNA (cfDNA)



Consistent detection of CNTY-101 cfDNA on Day 3 across all cycles delivered with or without LDC

Transgene copies detected in 1 mL of plasma is indicated. Detectable signal [+] was determined to be significantly above negative controls using two sample Poisson test, p < 0.05.

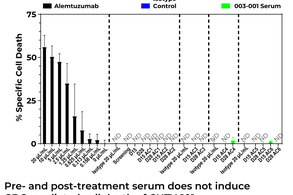
Antibody-dependent cellular cytotoxicity (ADCC)



Pre- and post-treatment serum does not induce ADCC-mediated cell death of CNTY-101

ADCC-mediated cell death of CNTY-101 targets was measÂ ured by pre-incubation with monoclonal control antibodÂ ies or patient serum, followed by the addition of NK-92-CD16-V158 effectors. Controls were pooled across plates; individual plate runs are separated by dashed vertiÂ cal bars. Results are represented as mean +/- SD.

Complement-dependent cytotoxicity (CDC)



Pre- and post-treatment serum does not induce CDC-mediated cell death of CNTY-101

CDC-mediated cell death of CNTY-101 targets was measÂ ured by pre-incubation with control monoclonal antiÂ bodies or patient serum, followed by addition of human complement. Positive controls were pooled across plates; individual plate runs are separated by dashed vertical bars. Results are represented as mean +/- SD.

AC: additional cycle, ND: not detected

SUMMARY

- CNTY-101 is the first iPSC-derived NK cell therapy engineered with six precision gene edits including Allo-evasion™ edits.
- Infusions of up to 1 billion CNTY-101 cells per cycle (as single 1 billion or 3 x 300 million) in patients with R/R NHL demonstrate a manageable safety profile, including in the outpatient setting, with no GvHD or DLTs to date.
- Preliminary efficacy shows 30% CRR rate (n=10) in heavily pretreated, mostly refractory patients with preÂ dominantly aggressive or high-risk histologies.
- Utilizing a novel cell-free DNA method for detecting total body PK of CNTY-101, we show that CNTY-101 rapidly traffics out of circulation and persists in the extravascular space. AUC is trending to increase with dose.
- Patient 1 received five cycles of CNTY-101 (100 million) without LDC and allo-rejection was not observed.
- Overall, in 3 out of 4 patients who received CNTY-101 in cycles without LDC, positive detection of CNTY-101 was observed on Day 3 at minimum.

Current study status: Enrollment is ongoing; in dose escalation phase
Enrolling at dose level 3B (1 billion x 3 doses) and 4A (3 billion x 1 dose)

Clinical data as of 27 March, 2024; translational data as of 1 May, 2024

GvHD: graft versus host disease, DLT: dose limiting toxicities, PK: pharmacokinetics, AUC: area under the curve

Acknowledgements: We thank Thomas Brigman, Sam Kelly, Kile McFadden and Brenda Salantes for their contributions.