

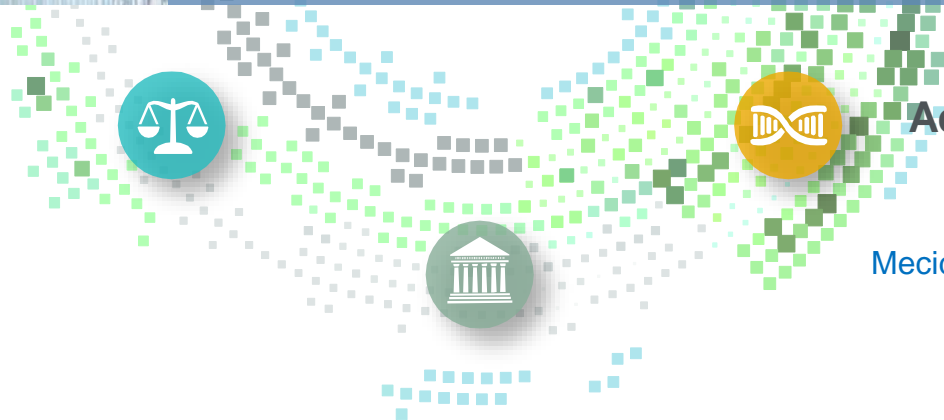


Request for New ICD-10-PCS Code for the Administration of Lisocabtagene Maraleucel

ICD-10 Coordination & Maintenance Committee Meeting

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March 17, 2020



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- All of Celgene's chimeric antigen receptor (CAR) T cell therapy candidates are investigational product candidates and their safety and efficacy have not been established. Celgene has not obtained marketing approval for any product, and there is no certainty that any marketing approvals will be obtained or as to the timelines on which they will be obtained.
- Any data presented pertaining to Celgene CAR T cell therapy candidates are interim data, and may include investigator-reported interim data for which Celgene has not yet independently reviewed the source data. The interim data may not be representative of the final results that may be obtained in the corresponding trial, and results from earlier trials may not be representative of results obtained in later trials or pivotal trials.

Refractory Aggressive B-cell Non-Hodgkin Lymphoma

- Aggressive B-cell Non-Hodgkin Lymphoma (NHL) consists of multiple large B-cell lymphoma subtypes
- Diffuse large B-cell lymphoma (DLBCL) is most common NHL subtype worldwide, 30% of all NHL
 - De novo DLBCL
 - DLBCL transformed from follicular lymphoma (FL) (a low-grade, e.g. indolent, B-cell NHL)
- Disease of the elderly
 - ~50% of DLBCL patients are ≥ 65 years old
 - Comorbidities common, often limiting therapeutic options, and eligibility for clinical trials
 - Characteristics such as older age and comorbidities further portend adverse outcomes but have not been rigorously studied in other clinical trials of novel therapies
- Multiple large B-cell lymphoma subtypes
 - Primary mediastinal B-cell lymphoma (PBMCL): 10% of large B-cell lymphomas
 - Follicular lymphoma Grade 3B (FL3B): 1% of NHL cases
 - DLBCL transformed from indolent lymphomas other than FL
 - Clinically important because of aggressive behavior, limited options for relapsed/refractory (R/R) disease
 - Typically underrepresented in clinical trials

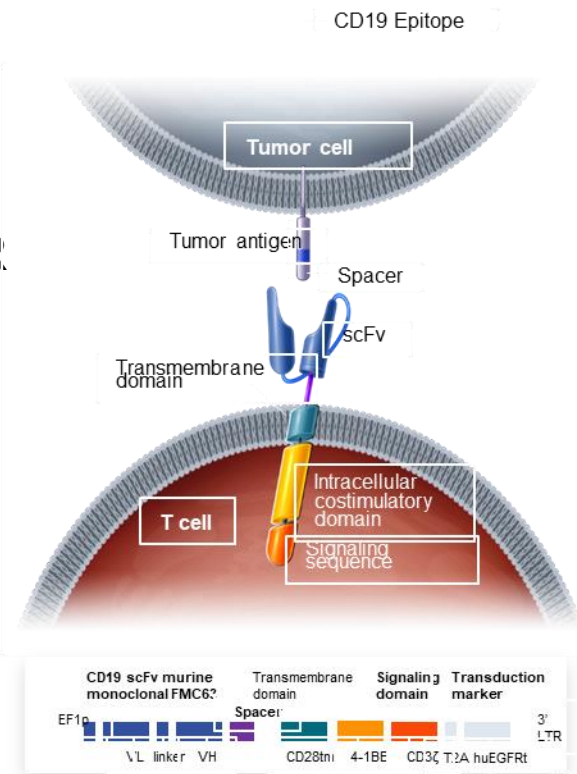
R/R Large B-cell Lymphoma is Associated with High Unmet Need and Poor Outcomes

- Only a few Food and Drug Administration (FDA)-approved therapies currently exist for the treatment of 3L+ large B-cell lymphoma
 - A high unmet medical need persists, given the limited number of approved treatment options available and due to important large B-cell lymphoma subtypes and subpopulations of patients with comorbidities were not represented in the approved therapies
- R/R large B-cell NHL after at least 2 prior therapies has a very poor prognosis
 - Patients with R/R disease already have received 1st and 2nd line standards of care; unlikely to benefit from additional chemoimmunotherapy
 - Overall response rate (ORR) < 40% and complete response (CR) rate < 20% to available traditional salvage therapies
 - Outcomes worse in chemorefractory DLBCL: 26% ORR, 7% CR rate, median overall survival (OS) 6.3 months
- Central Nervous System (CNS) relapse
 - Secondary CNS lymphoma
 - Often excluded from R/R NHL clinical trials because of poor prognosis
 - Median OS < 4 months

Crump et al Blood 2017 130[16]:1800-8

Lisocabtagene Maraleucel (Liso-cel) Overview

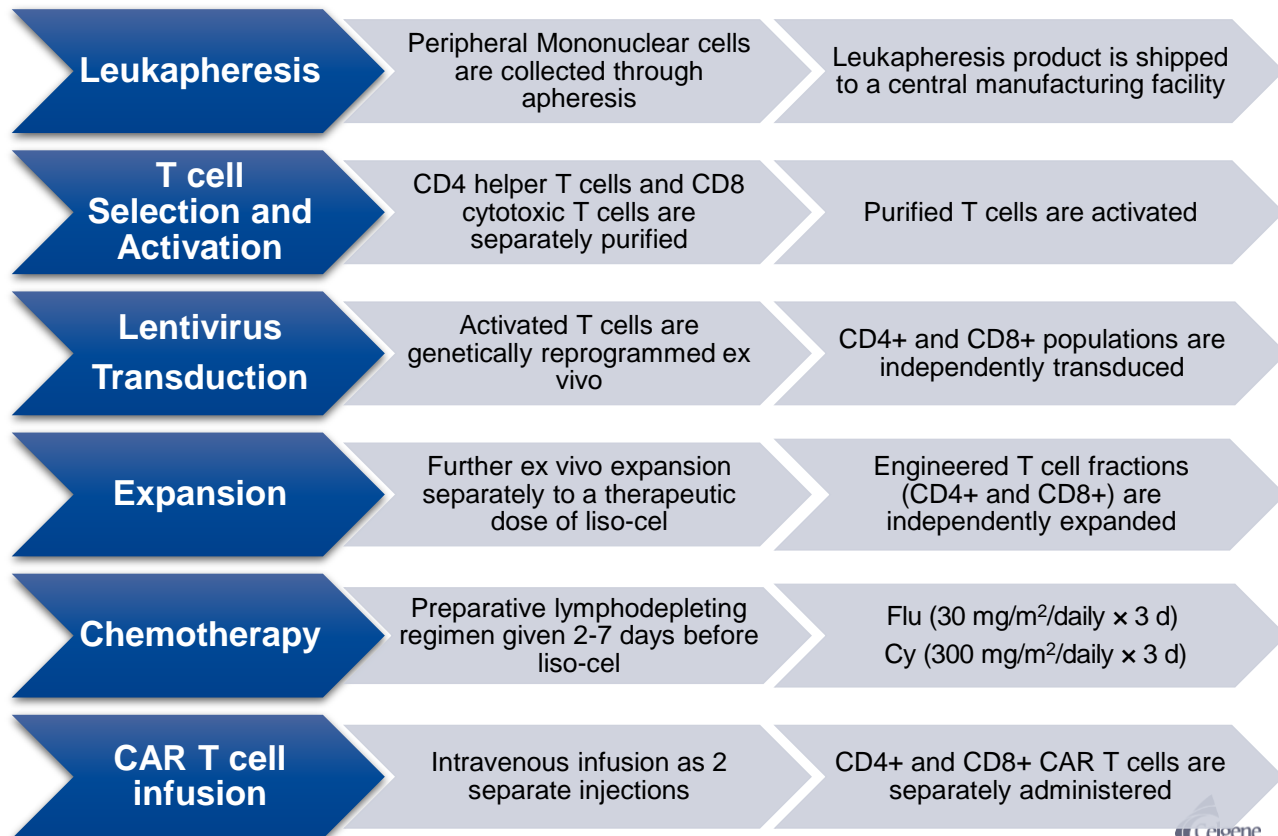
Liso-cel is an investigational, CD19-directed, autologous CAR T-cell immunotherapy comprising individually formulated CD8 and CD4 CAR T cells that is anticipated to be indicated for the treatment of adult patients with R/R large B-cell lymphoma after at least 2 prior therapies. Liso-cel is genetically engineered to have a CAR on the cell surface that directs the immune cell to mount an immune response and destroy the cancerous tumor cells. FDA approval anticipated by July 1, 2020. An application for new technology add-on payment (NTAP) status has been submitted for liso-cel and, if granted, would begin in fiscal year (FY) 2021.



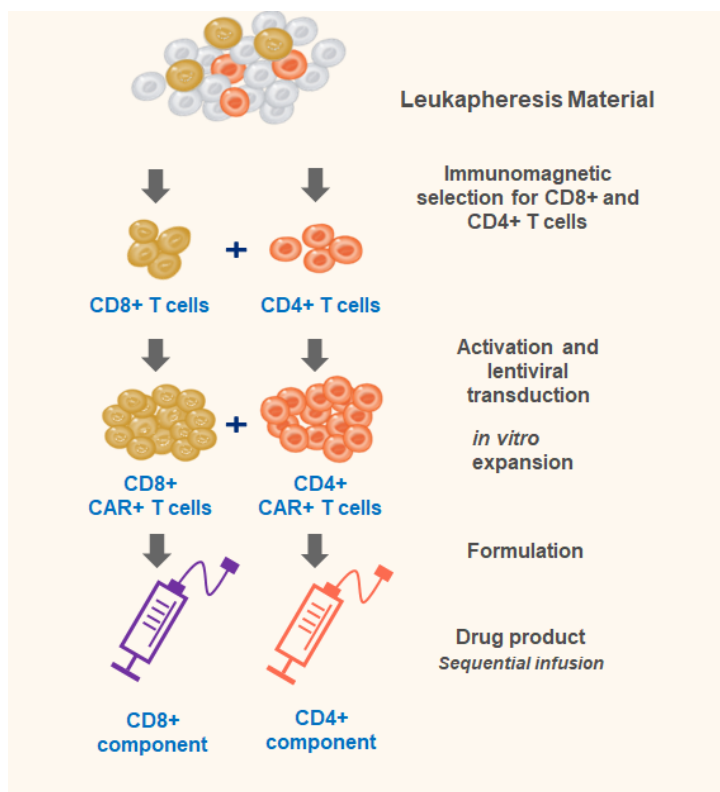
Liso-cel Manufacturing and Delivery Process: Overview

Manufacturing and delivery of liso-cel is a multi-step process

Unlike other current CAR T-cell products, liso-cel's manufacturing process was designed to minimize between-drug product lot variability, relative to currently approved CAR T-cell products



Liso-cel CD19-Directed, Defined Composition, 4-1BB CAR T Cell Product



CD8+ and CD4+ CAR+ T cell components are administered separately at equal target doses of CD8+ and CD4+ CAR+ T cells

The defined composition of liso-cel results in:

- Consistent administered CD8+ and CD4+ CAR+ T cell dose
- Low variability in the CD8+/CD4+ ratio

Dose and ratio of CD8+ and CD4+ CAR+ T cells may influence the incidence and severity of cytokine release syndrome (CRS) and neurological events (NE)¹⁻³

Liso-cel Infusion Procedure

- Unlike current CAR T-cell products, liso-cel is infused through 2 separate injections at equal doses of CD4+ and CD8+ CAR T cells using separate syringes
 - The target dose of liso-cel for each patient is 100×10^6 CAR+ viable T cells (consisting of CD8+ and CD4+ components)
 - The number of cells from each component, the dose, is calculated as a volume of final drug product and is administered, in its entirety, by infusion to the patient
- The CD8 component is administered first at an infusion rate of approximately 0.5 mL/minute
 - If more than one syringe is required for full cell dose of the CD8 component, the volume in each syringe should be administered consecutively without any time between (unless there is a clinical reason to hold the dose, e.g. infusion reaction)
- The CD4 component is administered second using the same steps described for the CD8 component

TRANSCEND NHL 001 Pivotal Phase I, Multicenter Seamless Design Study

Baseline Characteristic

All Liso-cel–Treated Patients (N=269)

Age, median (range), years	63 (18–86)
≥65, n (%)	112 (42)
≥75, n (%)	27 (10)
NHL subtypes, n (%)	
DLBCL NOS	137 (51)
Transformed from FL / other indolent lymphomas	60 (22) / 18 (7)
HGBCL ^a / PMBCL / FL3B	36 (13) / 15 (6) / 3 (1)
Secondary CNS lymphoma, n (%)	7 (3)
ECOG PS of 0–1 / 2 at screening, n (%)	265 (99) / 4 (1)
High disease burden,^b n (%)	103 (38)
Creatinine clearance >30 to <60 mL/min, n (%)	51 (19)
LVEF ≥40% to <50%, n (%)	13 (5)
Prior systemic therapies, median (range)	3 (1–8)
≥4 prior therapies, n (%)	71 (26)
Received prior HSCT, n (%)	94 (35)
Autologous / allogeneic HSCT	90 (33) / 9 (3)
Chemotherapy-refractory,^c n (%)	181 (67)
Never achieved CR with prior therapy, n (%)	119 (44)
Received bridging therapy, n (%)	159 (59)

- **Large cohort of elderly subjects**
- **89% of patients had high-risk features known to portend a shortened overall survival**
 - Double/triple hit
 - Primary refractory disease
 - Refractory to ≥ second-line therapy
 - Never in CR
 - Never undergone autologous stem cell transplant (ASCT)
- **Comorbidities common in elderly lymphoma patients were not excluded**
 - 51 (19%) decreased renal function
 - 13 (5%) decreased cardiac function
 - 39 (15%) Grade ≥3 cytopenias

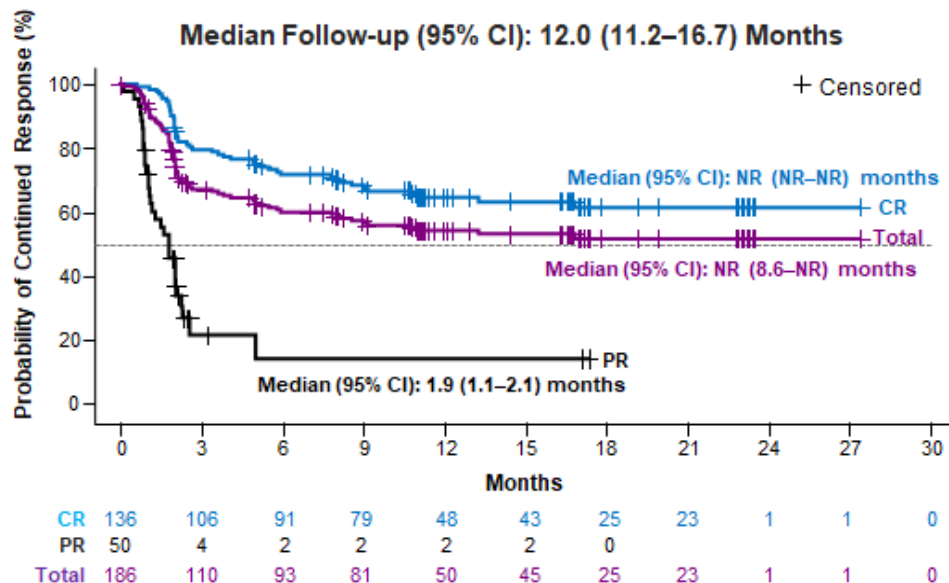
^aPatients with DLBCL transformed from indolent lymphomas with *MYC* and *BCL2* or *BCL6* rearrangements are not included as HGBCL.

^bPatients with LDC SPD ≥50 cm² or LDH ≥500 U/L (N=269). ^cThe status was chemotherapy-refractory if the patient achieved SD or PD to last chemotherapy-containing regimen or relapsed <12 months after autologous HSCT; otherwise the status was chemotherapy-sensitive. ASCT, allogeneic stem cell transplantation; CNS, central nervous system; CR, complete response; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; FL(3B), follicular lymphoma (grade 3B); HGBCL, high-grade B-cell lymphoma; LBCL, large B-cell lymphoma; LDC, lymphodepleting chemotherapy; LVEF, left ventricular ejection fraction; NHL, non-Hodgkin lymphoma; NOS, not otherwise specified; PMBCL, primary mediastinal large B-cell lymphoma; SPD, sum of product of diameter.

Response and Durability by IRC Assessment

Efficacy-Evaluable Patients (N=256)

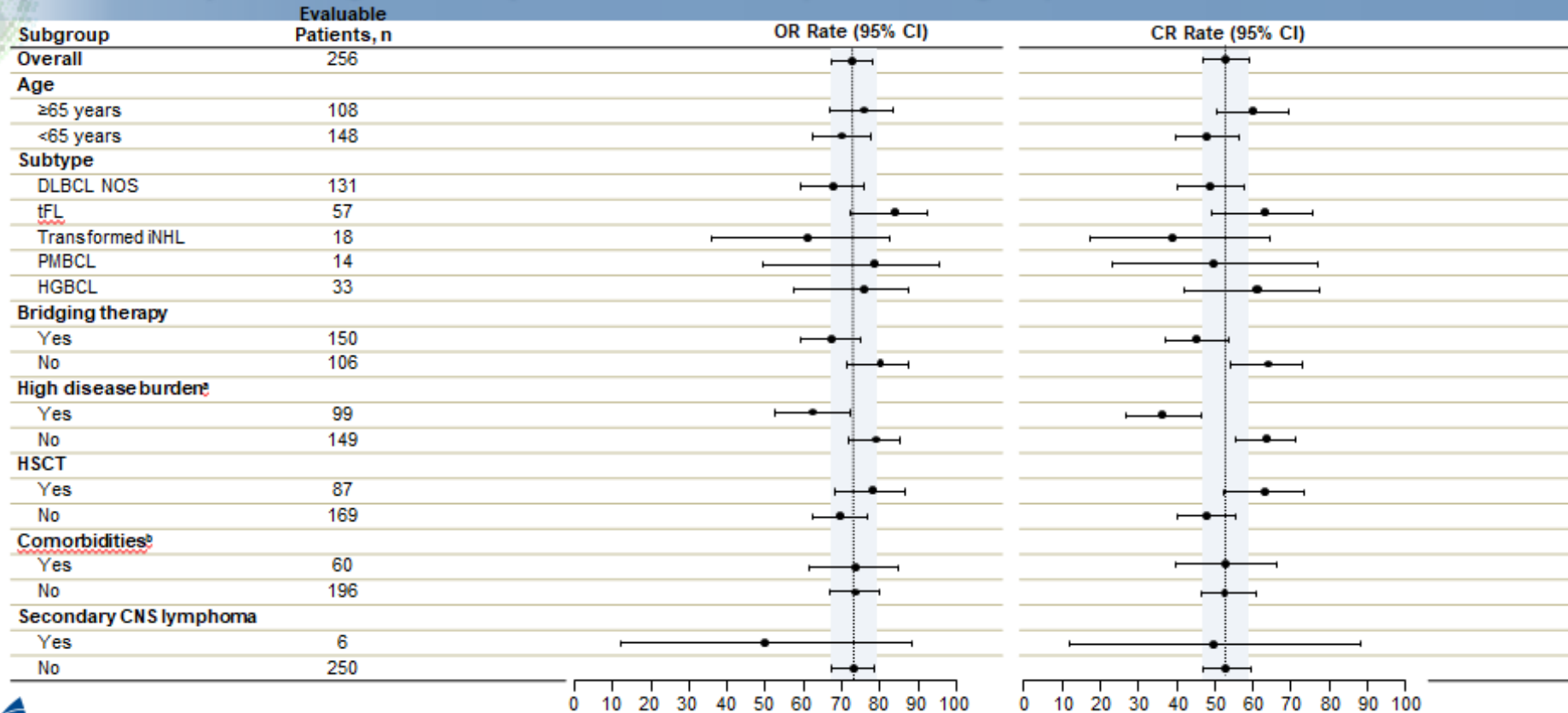
ORR (95% CI)	73% (67–78)
CR rate (95% CI)	53% (47–59)
Time to first CR or PR, median (range), months	1.0 (0.7–8.9)
DOR at 6 months (95% CI), %	60.4 (52.6–67.3)
DOR at 12 months (95% CI), %	54.7 (46.7–62.0)



CI, confidence interval; CR, complete response; DOR, duration of response; IRC, independent review committee; NR, not reached; ORR, objective response rate; PR, partial response.

Objective and CRs by Patient and Clinical Characteristic:

Clinically meaningful activity observed across patient subgroups with unmet medical need



^aPatients with LDC SPD ≥50 cm² or LDH ≥500 U/L. ^bPatients with CrCl >30 but <60 mg/min or with LVEF ≥40% to <50%.

CI, confidence interval; CNS, central nervous system; CR, complete response; DLBCL, diffuse large B-cell lymphoma; HGBCL, high-grade B-cell lymphoma; HSCT, hematopoietic stem cell transplantation; iNHL, indolent non-Hodgkin lymphoma; NOS, not otherwise specified; PMBCL, primary mediastinal large B-cell lymphoma; tFL, transformed from follicular lymphoma.

Liso-cel Efficacy and Safety Data

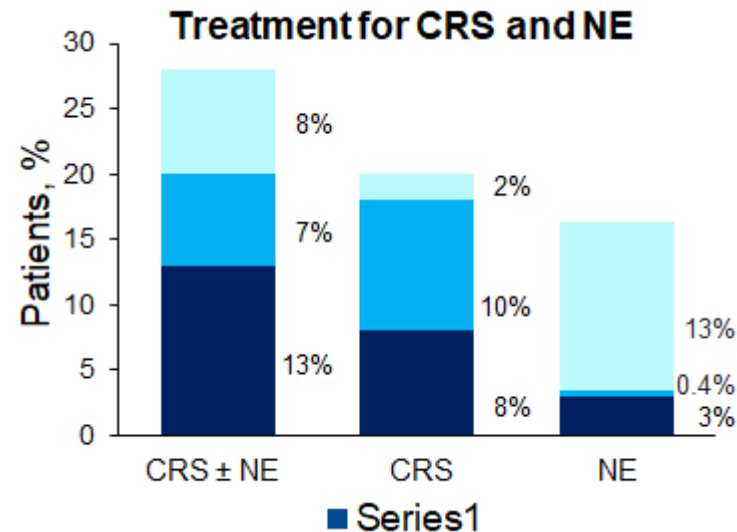
- Liso-cel has, overall, an improved safety profile compared to YESCARTA® and KYMRIA®
- In comparison to liso-cel, both approved CAR T-cell products had higher rates of toxicity
 - In the TRANSCEND NHL 001 registrational study (n=269), 42% and 2% of subjects developed all-grade and Grade ≥ 3 CRS, respectively, and 30% and 10% developed all-grade and Grade ≥ 3 NT, respectively
 - KYMRIA® had higher rates of all-grade and Grade ≥ 3 CRS (74% and 23%, respectively) and all-grade and Grade ≥ 3 NT (58% and 18%, respectively)
 - YESCARTA had higher rates of all-grade and Grade ≥ 3 CRS (94% and 13%, respectively) and all-grade and Grade ≥ 3 NT (87% and 31%, respectively)
- Safety with liso-cel was similar in the subsets of subjects at higher risk for poor outcomes and subjects with comorbidities who were excluded from the registrational studies for YESCARTA and KYMRIA®
 - This includes patients with prior allogeneic hematopoietic stem cell transplantation (allo-HSCT), secondary CNS lymphoma, and reduced renal and cardiac function, as well as in the rare large B-cell NHL subtypes included in TRANSCEND NHL 001 not studied in the other registrational trials



* There is no head-to-head comparison of liso-cel with the other therapies discussed in this presentation, and we acknowledge the caveats inherent with direct cross-study comparisons due to differences between patient populations, baseline comorbidities, and the number and type of prior treatment regimens that subjects have received.

Patient Incidence and Management of CRS and NE

	All liso-cel-Treated Patients (N=269)
CRS^a	
Any grade, n (%)	113 (42)
Grade 3, n (%)	4 (1)
Grade 4, n (%)	2 (1)
Time to onset, median (range), days	5 (1–14)
Time to resolution, median (range), days	5 (1–17)
NE^b	
Any grade, n (%)	80 (30)
Grade 3, n (%)	23 (9)
Grade 4, n (%)	4 (1)
Time to onset, median (range), days	9 (1–66)
Time to resolution, median (range), days	11 (1–86)
CRS or NE, n (%)	127 (47)
ICU admissions,^c n (%)	19 (7)
For CRS and/or NE	12 (4)
Other reasons	7 (3)



- 3% of patients received vasopressors for CRS or NE
- 2 patients received other anti-inflammatory/anticytokine agents

CRS and NE were reversible

- 1 patient had an unresolved NE (grade 1 tremor) at data cutoff
- No grade 5 CRS or NE occurred
- 8 patients had ongoing CRS/NE at time of death from other reasons

^aCRS was graded according to the Lee criteria (Lee DW, et al. *Blood*. 2014;124:188–195). ^bNEs were based on investigator assessment and graded per National Cancer Institute Common Terminology Criteria for Adverse Events v4.03.

^cDuring initial hospital admission following liso-cel administration. CRS, cytokine release syndrome; ICU, intensive care unit; NE, neurological event; toci, tocilizumab.

Liso-cel is a Substantial Clinical Improvement Compared to Existing Technologies

- Liso-cel has a comparable or superior effectiveness compared to existing therapies
- Important large B-cell lymphoma subtypes and subpopulations of patients with comorbidities were not represented in the main clinical studies for YESCARTA and KYMRIA^H or in the main studies for accelerated approval of KEYTRUDA[®] in PMBCL and POLIVY[®] in R/R DLBCL
- Liso-cel, therefore, has demonstrated a comparable or superior effectiveness compared to existing therapies for patients with R/R aggressive large B-cell NHL, a serious and life-threatening disease

Product	<u>Liso-cel</u>	YESCARTA ¹	KYMRIA ^H ²	Keytruda ³	Polivy ⁴	
Study	TRANSCEND NHL 001	ZUMA-1	JULIET	KEYNOTE-170	G029365	
Analysis Population	3L+ large B-cell lymphoma ⁵	3L+ large B-cell lymphoma ⁶	3L+ large B-cell lymphoma ⁷	Refractory or 2L + PMBCL	2L and 3L + DLBCL NOS	
Sample size (N)	256	101	68	53	<u>pola-BR</u> 40	BR 40
ORR, % (95% CI)	73 (67, 78)	72 (62, 81)	50 (38, 62)	45 (32, 60)	63 (46, 77)	25 (13, 41)
CR, % (95% CI)	53 (47, 59)	51 (41, 62)	32 (22, 45)	11 (NA)	50 (34, 66)	23 (11, 38)
PR, % (95% CI)	20	21 (13, 30)	18 (10, 29)	34 (NA)	12 (NA)	2 (NA)
DOR (months)	Median [95% CI]: 13.3 [8.2, NE]	Median [95% CI]: 9.2 [5.4, NE]	Median [95% CI]: NE [5.1, NE]	Median [95% CI]: NR [1.1+, 19.2+]	6-month DOR: 64% 12-month DOR: 48%	6-month DOR: 30% 12-month DOR: 20%
BR = <u>bendamustine + rituximab</u> ; CI = confidence interval; CR = complete response; DLBCL = <u>diffuse large B-cell lymphoma</u> ; DOR = duration of response; HGL = high-grade lymphoma; NA = not available; NE = not estimable; NOS = not otherwise specified; NR = not reached; ORR = objective response rate; PMBCL = primary mediastinal B-cell lymphoma; PR = partial response; R/R = relapsed or refractory; <u>tFL</u> = DLBCL transformed from follicular lymphoma; <u>tiNHL</u> = DLBCL transformed from indolent lymphoma other than FL; USPI = United States prescribing information.						

Liso-cel is a Substantial Clinical Improvement Compared to Existing Technologies (2)

- The totality of the circumstances regarding liso-cel's clinical efficacy and safety data make clear that liso-cel has substantial clinical improvements compared to existing technologies and fills an unmet need for Medicare beneficiaries with R/R NHL
- Liso-cel patient population in its registrational study more accurately reflects real-world NHL patients compared to the existing CAR T-cell therapies
- Liso-cel will offer benefit to patients for whom currently approved products have not been studied
 - The clinical efficacy and safety data from TRANSCEND NHL 001 demonstrate that liso-cel has clinically meaningful results in a real-world population that is more inclusive of patients across multiple large B-cell lymphoma subtypes as well as patients with comorbidities that were not represented in registrational trials for the two currently available CAR T-cell therapies approved by the FDA studies of currently available CAR T-cell therapies
- TRANSCEND NHL 001 enrolled a patient population that was at high risk for worse outcomes, yet despite that had equivalent efficacy and improved safety compared to YESCARTA and improved efficacy and safety compared with KYMRIA[®]