LOTIS

Loncastuximab Tesirine Clinical Assessments

For information about the LOTIS Clinical Trial Program, visit www.adctmedical.com or email ADC Therapeutics at medicalinformation@ADCTherapeutics.com

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ADC™ THERAPEUTICS

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Loncastuximab tesirine (Lonca; loncastuximab tesirine-lpyl) indication

Loncastuximab tesirine-lpyl (Zynlonta®, ADC Therapeutics SA) is a CD19-directed antibody and alkylating agent conjugate indicated for the treatment of adult patients with R/R large B-cell lymphoma after ≥2 lines of systemic therapy, including DLBCL not otherwise specified, DLBCL arising from low grade lymphoma, and high-grade B-cell lymphoma.

This indication is FDA-approved under accelerated approval based on ORR. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

The LOTIS Clinical Development Program

LOTIS·1
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 1, open-label, dose-escalation, dose-expansion study to evaluate the tolerability, safety, PK, and efficacy of loncastuximab tesirine in patients with R/R B-NHL

NCT02669017
COMPLETED

LOTIS·2
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 2, open-label, single-arm study to evaluate the efficacy and safety of loncastuximab tesirine in patients with R/R DLBCL

NCT03589469
ACTIVE, NOT RECRUITING

LOTIS·3
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 1/2, open-label study to evaluate the safety and efficacy of loncastuximab tesirine and ibrutinib in patients with advanced DLBCL or MCL

NCT03684694
RECRUITING

LOTIS·4
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 1, open-label study to evaluate the safety and efficacy of loncastuximab tesirine and durvalumab in patients with advanced DLBCL, MCL, or FL

NCT03685344
TERMINATED

LOTIS·5
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 3, randomized, open-label study to evaluate the efficacy and safety of loncastuximab tesirine and rituximab versus immunochemotherapy in patients with R/R DLBCL

NCT04384484
RECRUITING

LOTIS·6
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 2, randomized, open-label study to evaluate the efficacy and safety of loncastuximab tesirine versus idelalisib in patients with R/R FL

NCT04699461
RECRUITING

LOTIS·7
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 1b, open-label study to evaluate the safety and efficacy of loncastuximab tesirine in combination with other anticancer agents in patients with R/R B-NHL

NCT04970901
NOT YET RECRUITING

LOTIS·8
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 1b, open-label study to evaluate the tolerability, safety, PK, and efficacy of loncastuximab tesirine and R-CHOP in patients with previously untreated DLBCL

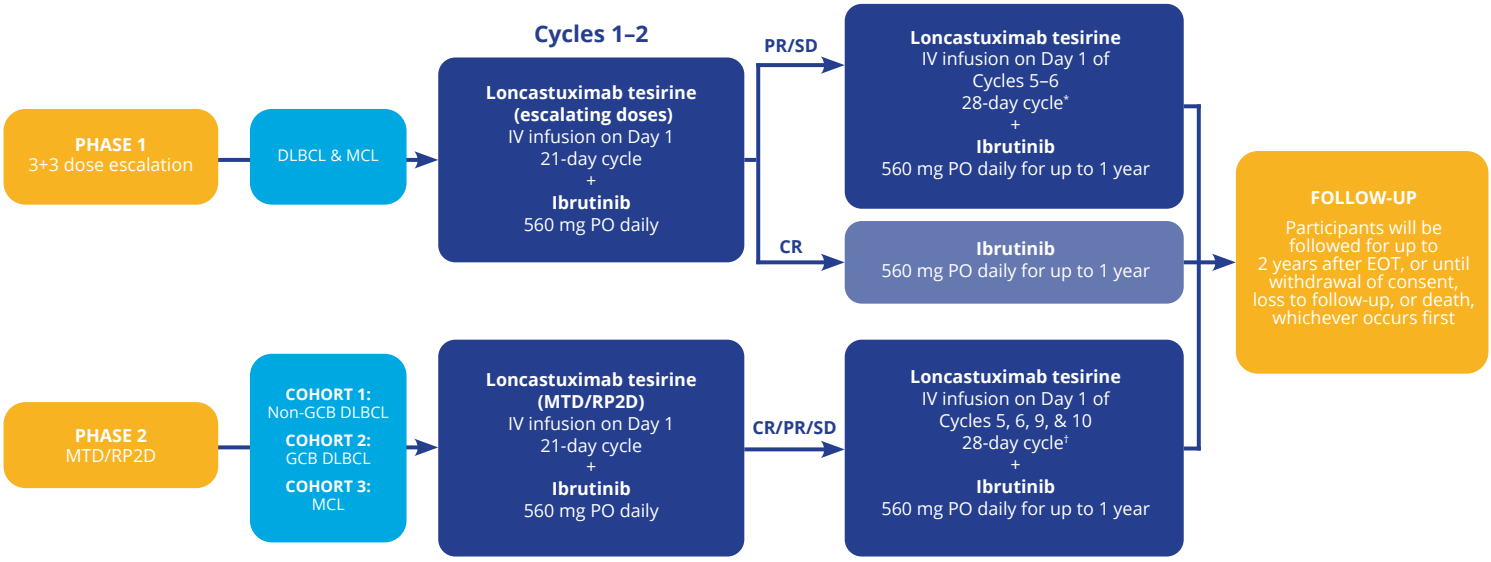
NCT04974996
NOT YET RECRUITING

LOTIS·9
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 2/3, open-label study to evaluate the efficacy and safety of loncastuximab tesirine and rituximab in unfit/frail patients with previously untreated DLBCL

NCT PENDING
NOT YET RECRUITING

A Phase 1/2, open-label study to evaluate the safety and efficacy of loncastuximab tesirine and ibrutinib in patients with advanced DLBCL or MCL



KEY PRIMARY ENDPOINTS

- Phase 1: AEs, AEs ≥Grade 3, SAEs, SAEs ≥Grade 3; DLTs, dose modifications
- Phase 2: CRR‡ determined by the IRC. CRR, defined as the number of participants with a BOR of CR in the non-GCB DLBCL cohort only

KEY SECONDARY ENDPOINTS

- Phase 1: ORR‡, defined as the number of participants with a BOR of CR or PR; DOR; RFS; PFS; OS; PK
- Phase 2: ORR‡, defined as the number of participants with a BOR of CR or PR
- Phase 2: CRR in GCB DLBCL, all DLBCL, and MCL participants. CRR determined by the investigator and/or IRC. CRR‡, defined as the number of participants with a BOR of CR in non-GCB DLBCL, GCB DLBCL, all DLBCL, and MCL participants
- Phase 2: ORR; DOR; RFS; PFS; OS; PK; CRR in subgroups; HRQoL, safety (AEs, AEs ≥Grade 3, SAEs, SAEs ≥Grade 3)

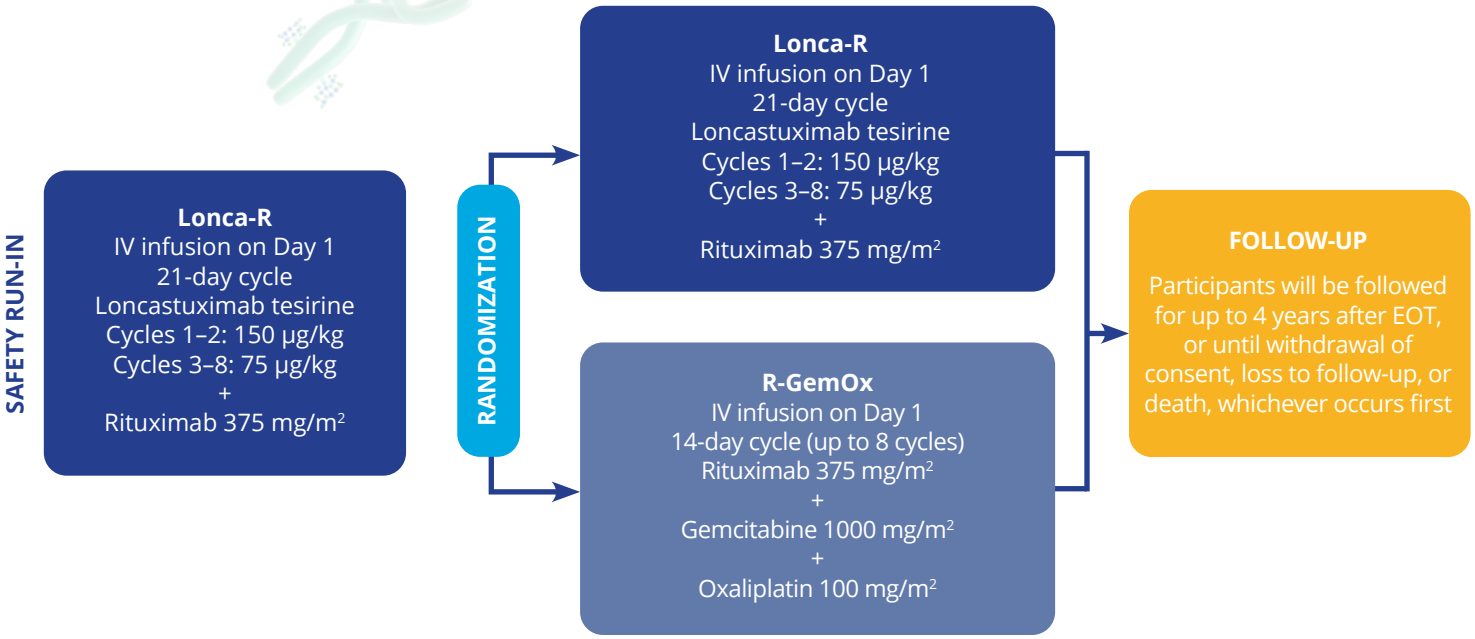
KEY ELIGIBILITY CRITERIA

- ECOG PS 0 to 2
- Pathologic diagnosis of DLBCL or MCL
- Participants with DLBCL must have R/R disease and have failed, or been intolerant to, available standard therapy
- Participants with MCL must have R/R disease and have received ≥1 prior line of therapy
- Lymphoma with active CNS involvement, including leptomeningeal disease, is not eligible
- AHCT or alloHCT permitted if received ≥60 days prior to the start of study drug
- No prior loncastuximab tesirine or BTK inhibitors
- Prior CD19-directed therapy permitted if biopsy confirms CD19 expression

*Break from loncastuximab tesirine treatment on cycles 3–4.
†Break from loncastuximab tesirine treatment on cycles 3–4 and 7–8.
‡According to the 2014 Lugano Classification.
Ibrutinib is supplied by Pharmacyclics LLC.

LOTIS-3
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 3, randomized, open-label study to evaluate the efficacy and safety of loncastuximab tesirine and rituximab versus immunochemotherapy in patients with R/R DLBCL



PRIMARY ENDPOINT

- PFS

KEY SECONDARY ENDPOINTS

- OS
- ORR*
- CRR*
- DOR
- Number of participants who experience ≥1TEAE and/or SAE
- PK
- HRQoL

KEY ELIGIBILITY CRITERIA

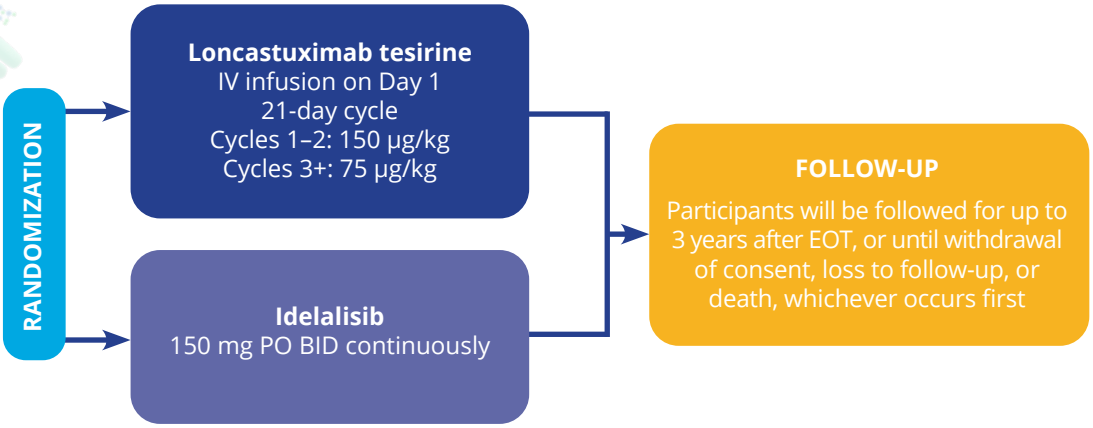
- ECOG PS 0 to 2
- Pathologic diagnosis of DLBCL, as defined by the 2016 WHO Classification, or high-grade B-cell lymphoma with *MYC* and *BCL-2* and/or *BCL-6* rearrangements
- R/R disease following ≥1 multi-agent systemic treatment regimens
- Lymphoma with active CNS involvement, including leptomeningeal disease, is not eligible
- AHCT or alloHCT permitted if received ≥30 days or ≥60 days prior to the start of study drug, respectively
- No prior loncastuximab tesirine or R-GemOx
- Prior CD19-directed therapy permitted if biopsy confirms CD19 expression

*According to the 2014 Lugano Classification.

LOTIS-5

LOncastuximab Tesirine ClinIcal AsSessment

A Phase 2, randomized, open-label study to evaluate the efficacy and safety of loncastuximab tesirine versus idelalisib in patients with R/R FL



PRIMARY ENDPOINT

- CRR*

KEY SECONDARY ENDPOINTS

- ORR*
- PFS
- OS
- DOR
- Number of participants who experience ≥1 TEAE and/or SAE
- PK
- HRQoL

KEY ELIGIBILITY CRITERIA

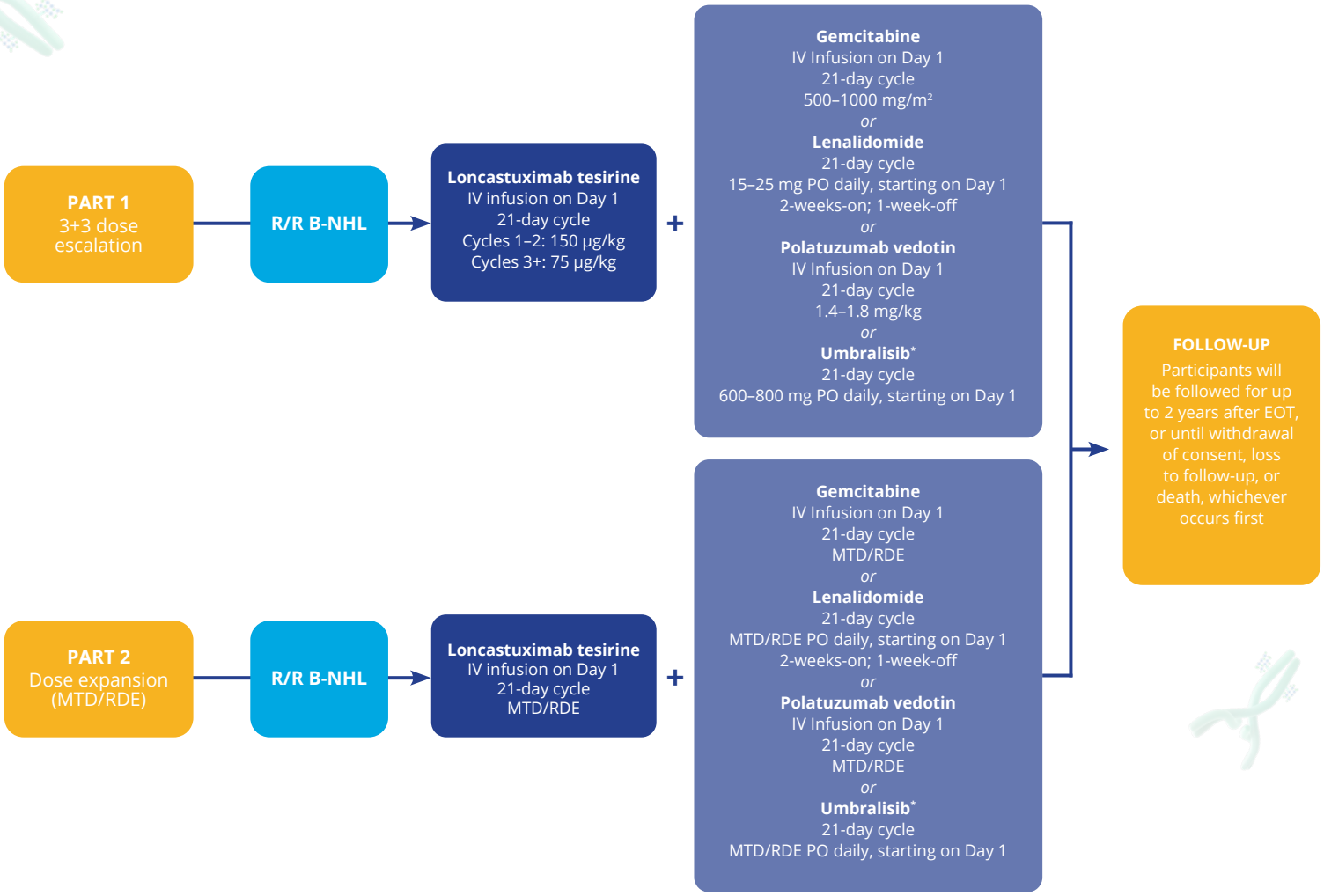
- ECOG PS 0 to 2
- Pathologic diagnosis of FL (Grade 1, 2, 3a)
- Participants with FL that has transformed to DLBCL or other aggressive lymphomas are not eligible
- Lymphoma with active CNS involvement, including leptomeningeal disease, is not eligible
- R/R disease following ≥2 prior treatment regimens, including ≥1 anti-CD20 therapy
- AHCT or alloHCT permitted if received ≥30 or ≥60 days prior to start of study drug, respectively
- No prior loncastuximab tesirine or idelalisib
- Prior CD19-directed therapy permitted if biopsy confirms CD19 expression

*According to the 2014 Lugano Classification.

LOTIS-6

LOncastuximab Tesirine ClinIcal AsSessment

A Phase 1b, open-label study to evaluate the safety and efficacy of loncastuximab tesirine in combination with other anticancer agents in patients with R/R B-NHL



KEY PRIMARY ENDPOINTS

- Number of participants who experience ≥1 TEAE and/or SAE; DLTs; AEs leading to dose delay, interruption or reduction

KEY SECONDARY ENDPOINTS

- ORR†
- DOR
- CRR†
- PFS
- RFS
- OS
- PK

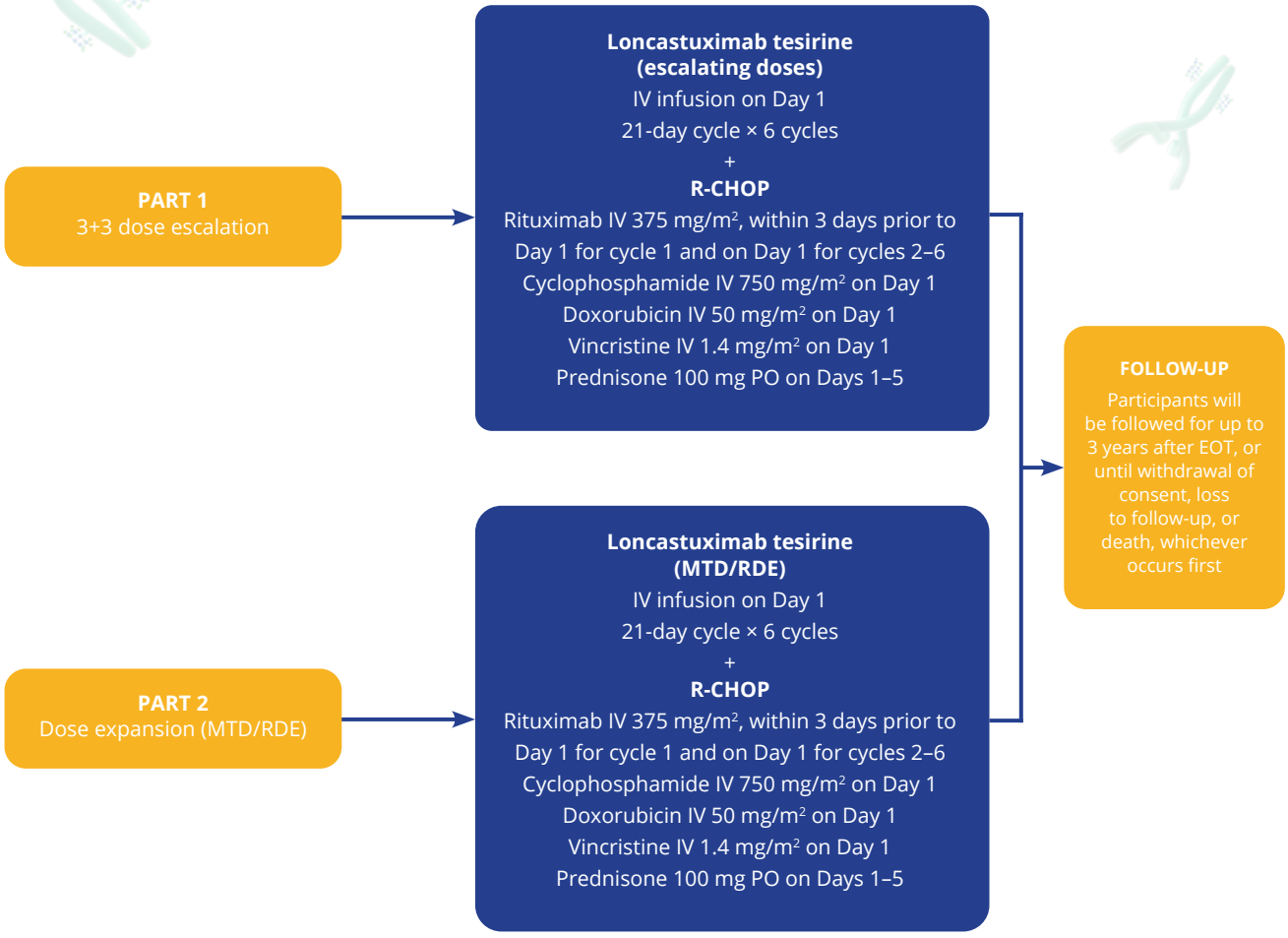
KEY ELIGIBILITY CRITERIA

- ECOG PS 0 to 2
- Pathologic diagnosis of B-NHL, as defined by the 2016 WHO Classification (including DLBCL, HGBCL, FL, MCL, MZL, and BL)
- Lymphoma with active CNS involvement, including leptomeningeal disease, is not eligible
- R/R disease, have failed, or been intolerant to, any approved therapy, and have received ≥2 prior systemic treatment regimens
- AHCT or alloHCT permitted if received ≥60 days prior to start of study drug
- No prior loncastuximab tesirine, gemcitabine, lenalidomide, polatuzumab vedotin or umbralisib (applied to relevant arm and/or cohort of the specific drug administered)
- Prior CD19-directed therapy permitted if biopsy confirms CD19 expression

*Patients with a history of (or ongoing) inflammatory bowel disease, or confirmed CMV infection (CMV IgG-positive or IgM-positive and CMV DNA-positive) are not eligible for enrollment into this treatment arm.
†According to the 2014 Lugano Classification.

LOTIS·7
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 1b, open-label study to evaluate the tolerability, safety, PK, and efficacy of loncastuximab tesirine in combination with R-CHOP in patients with previously untreated DLBCL



KEY PRIMARY ENDPOINTS

- DLTs (part 1); number of participants who experience ≥1 TEAE and/or SAE; AEs leading to dose delay, interruption or reduction

KEY SECONDARY ENDPOINTS

- ORR*
- DOR
- PFS
- OS
- CRR*
- PK

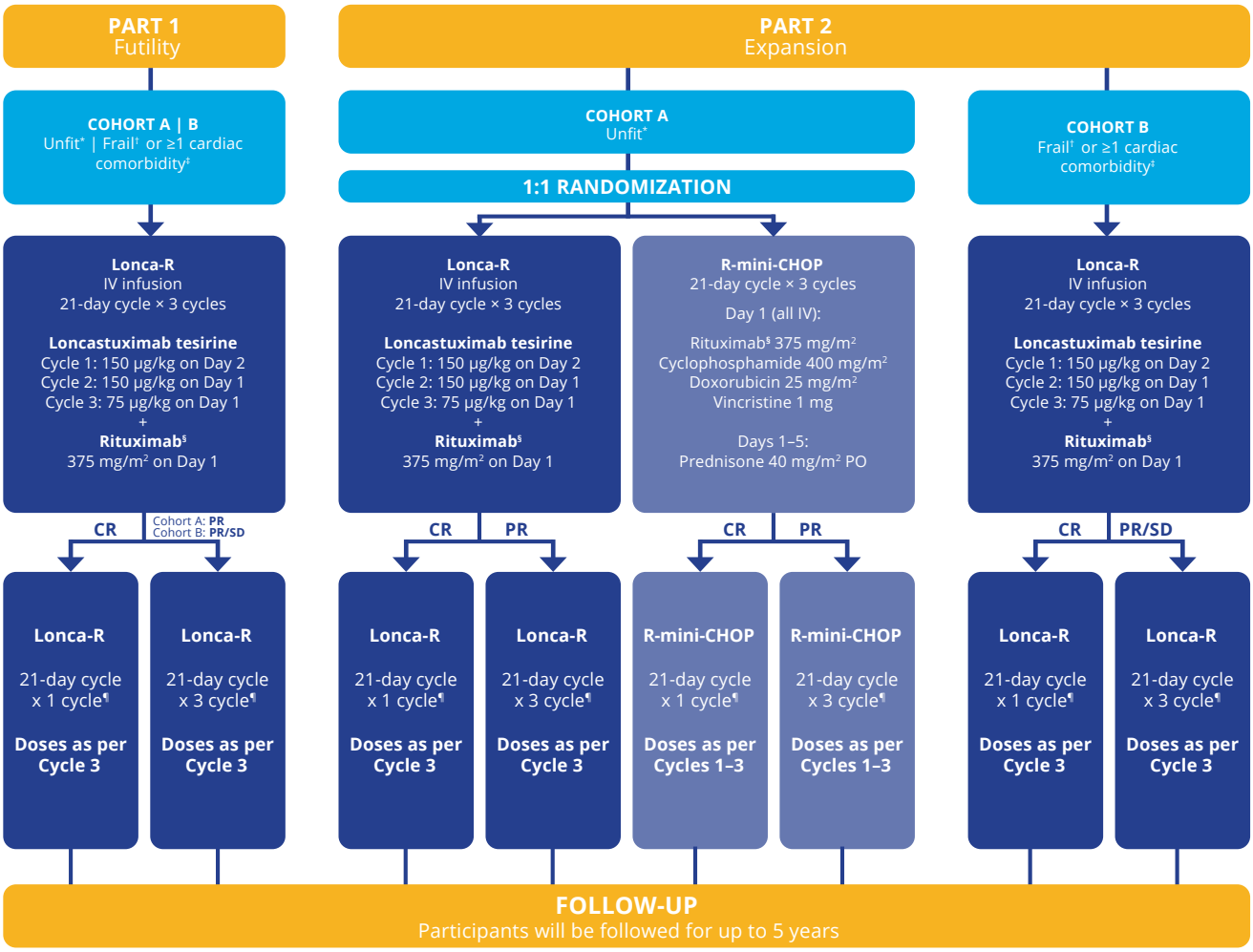
KEY ELIGIBILITY CRITERIA

- ECOG PS 0 to 2
- LVEF ≥50%
- Pathologic diagnosis of DLBCL, as defined by the 2016 WHO Classification, or HGBCL
- Lymphoma with active CNS involvement, including eptomeningeal disease, is not eligible
- No prior loncastuximab tesirine, rituximab, anthracycline, or CHOP
- No prior treatment for aggressive lymphoma, except for up to 7 days of corticosteroids for symptom management

*According to the 2014 Lugano Classification.

LOTIS-8
LOncastuximab Tesirine ClinIcal AsSessment

A Phase 2/3, open-label study to evaluate the efficacy and safety of loncastuximab tesirine and rituximab in unfit/frail patients with previously untreated DLBCL



KEY PRIMARY ENDPOINTS

- Part 1: CR rate#; tolerability
- Part 2: CR rate#; 2-year PFS

KEY SECONDARY ENDPOINTS

- ORR#
- DOR
- 3-year OS
- Safety
- HRQoL

KEY ELIGIBILITY CRITERIA

- Age ≥80 years or ≥65 years with ≥1 cardiac comorbidity‡
- Unfit* & Frail† patients as defined by sGA
- ECOG PS 0 to 2, or ECOG PS 3 if decline in status is deemed related to lymphoma and potentially reversible
- Pathologic diagnosis of DLBCL, as defined by the 2016 WHO Classification, HGBCL, or FL (Grade 3b)
- No prior therapy for DLBCL, HGBCL, or FL (Grade 3b)
- No prior loncastuximab tesirine or R-CHOP for any indication
- No prior treatment for aggressive lymphoma, except for up to 14 days of corticosteroids for symptom management

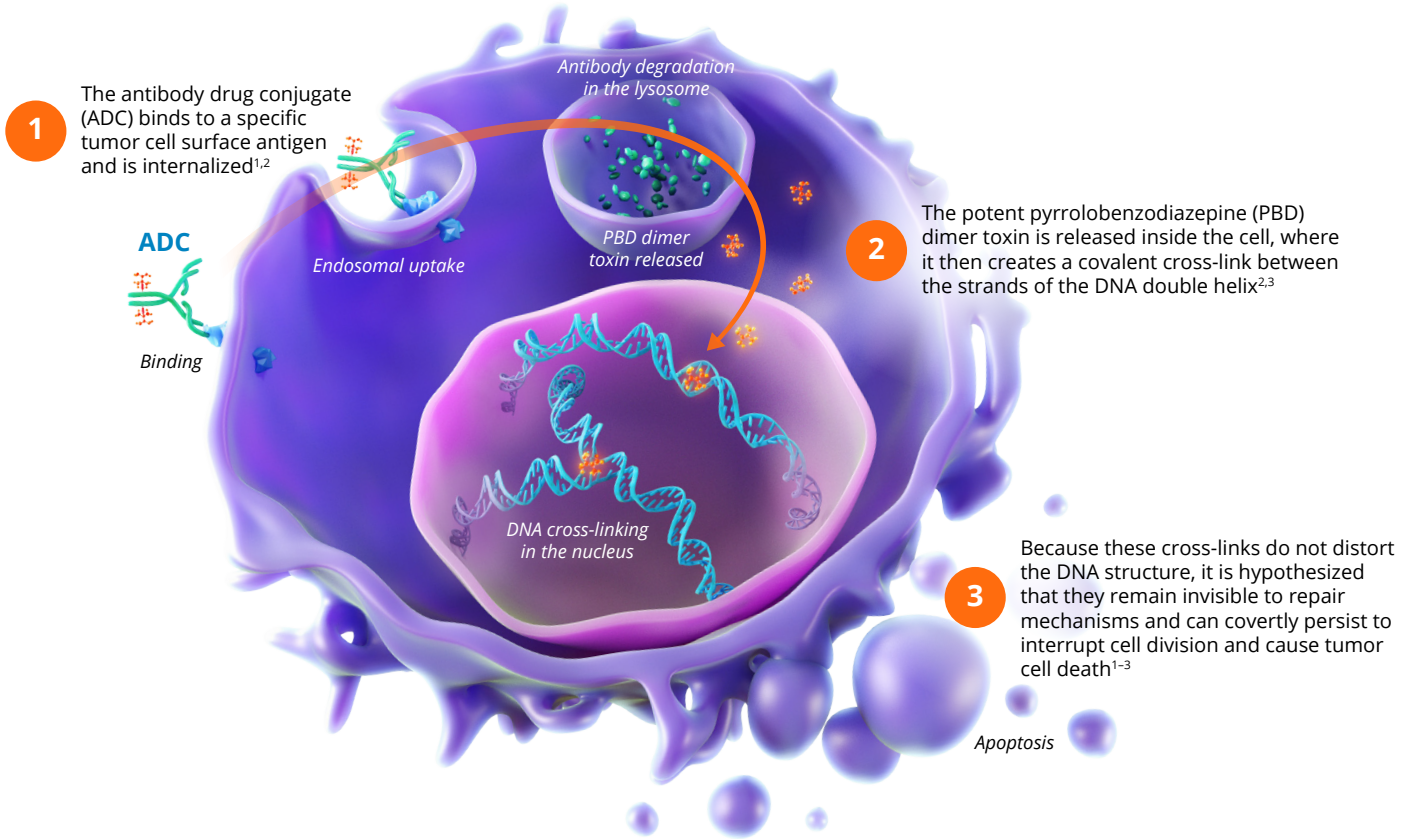
*Defined by the sGA as ≥80 years of age, an ADL score of 6, an IADL score of 8, and for CIRS-G: no score of 3-4 and <5 scores of 2 based on the FIL tool.
†Defined by the sGA as ≥80 years of age, an ADL score of <6, an IADL score of <8, and for CIRS-G: ≥1 score of 3-4 and ≥5 scores of 2 based on the FIL tool.
‡≥65 years of age with at least one of the following cardiac comorbidities: LVEF ≥30 to <50%; history of MI within 6 months prior to screening;IHD; history of stroke within 12 months prior to screening.
§A subcutaneous formulation of rituximab may be used at a flat dose of 1400 mg, starting from Cycle 2.
¶Up to 6 cycles of either Lonca-R or R-mini-CHOP may be ad
#Responses according to the 2014 Lugano Classification.

LOTIS-9
LOncastuximab Tesirine ClinIcal AsSessment

ADC Therapeutics is advancing next-generation PBD-based ADCs

ADC Therapeutics is a commercial-stage biotechnology company dedicated to delivering next-generation PBD-based ADCs for those affected by cancer. With a deep understanding of ADC technology and of the oncology treatment landscape, ADC Therapeutics intends to address significant unmet medical needs and improve outcomes for those with difficult-to-treat cancers

An MOA that features the "stealth-like" properties of PBD dimer toxins



LOTIS

LOncastuximab Tesirine ClinIcal AsSessment

Abbreviations

ADC, antibody drug conjugate
ADL, Activities of Daily Living
AE, adverse event
AHCT, autologous hematopoietic cell transplantation
AlloHCT, allogeneic hematopoietic cell transplantation
BID, twice daily
B-NHL, B-cell non-Hodgkin lymphoma
BOR, best overall response
BL, Burkitt lymphoma
BTK, Bruton tyrosine kinase
CD, cluster of differentiation
CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone
CIRS-G, Cumulative Illness Rating Scale-Geriatric
CMV, cytomegalovirus
CNS, central nervous system
CR, complete response
CRR, complete response rate
DLBCL, diffuse large B-cell lymphoma
DLT, dose-limiting toxicities
DOR, duration of response
ECOG PS, Eastern Cooperative Oncology Group performance status
EOT, end of treatment
FDA, US Food and Drug Administration
FIL, Fondazione Italiana Linformi
FL, follicular lymphoma
GCB, germinal center B-cell-like
HGBCL, high grade B-cell lymphoma
HRQoL, health-related quality of life
IADL, Instrumental Activities of Daily Living
IgG, immunoglobulin G
IgM, immunoglobulin M
IHD, ischemic heart disease
IRC, Independent Review Committee
IV, intravenous
Lonca-R, loncastuximab tesirine and rituximab
LVEF, left ventricular ejection fraction
MCL, mantle cell lymphoma
MI, myocardial infarction
MOA, mechanism of action
MTD, maximum tolerated dose
MZL, marginal zone lymphoma
ORR, overall response rate
OS, overall survival
PBD, pyrrolobenzodiazepine
PFS, progression-free survival
PK, pharmacokinetics
PO, taken orally
PR, partial response
R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone
R-mini-CHOP, rituximab and a reduced dose regimen of cyclophosphamide, doxorubicin, vincristine, and prednisone
RDE, recommended dose for expansion
RFS, relapse-free survival
R-GemOx, rituximab, gemcitabine, and oxaliplatin
RP2D, recommended Phase 2 dose
R/R, relapsed or refractory
SAE, serious adverse event
SD, stable disease
sGA, simplified geriatric assessment
TEAE, treatment-emergent adverse event
WHO, World Health Organization

References

1. Kaplon H, et al. mAbs. 2020;12:e1703531.
2. Zammarchi F, et al. Blood. 2018;131:1094–1105.
3. Hartley JA, et al. Sci Rep. 2018;8:10479.

LOTIS

Learn more about the LOTIS Clinical Development Program

For additional outcome measures and inclusion/exclusion criteria, and a list of active study sites, visit www.ClinicalTrials.gov

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ADC Therapeutics Head Office | Route de la Corniche 3B, 1066 Epalinges, Switzerland
ADC Therapeutics America | 430 Mountain Avenue, Suite #404, New Providence, NJ 07974, USA.
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