ZYNLONTA® (loncastuximab tesirine-lpyl) – Use in Pregnancy and Lactation

Summary

- LOTIS-1 was a Phase 1, open-label, single-arm, multicenter study which evaluated the safety and tolerability of ZYNLONTA monotherapy in 183 male or female patients (≥18 years of age) with relapsed or refractory (R/R) B-Cell Non-Hodgkin's Lymphoma (B-NHL). Pregnant or breastfeeding women were excluded from study enrollment.[1]
- LOTIS-2 was a Phase 2, open-label, single-arm, multicenter study which evaluated the efficacy and safety of ZYNLONTA monotherapy in 145 male or female patients (≥18 years of age) with R/R diffuse large B-cell lymphoma (DLBCL) following ≥2 lines of prior systemic therapy. Pregnant or breastfeeding women were excluded from study enrollment. Women of child-bearing age were required to use effective forms of contraception from the time of providing informed consent until a minimum of 16 weeks following the final dose of ZYNLONTA.[2]
- There is no data on the use of ZYNLONTA in pregnant women to evaluate for drug-associated risk.[5] However, ZYNLONTA can cause fetal harm when administered to pregnant women.
    - Pregnancy testing is recommended for females of reproductive potential prior to initiating ZYNLONTA.
    - Effective methods of contraception during treatment and for 10 months following the last dose of ZYNLONTA is advised for females of reproductive potential, while effective methods of contraception during treatment and for 7 months following the last dose of ZYNLONTA is advised for males with female partners of reproductive potential.
- There is no data on the presence of ZYNLONTA in human milk, the effects on the breastfed child, or milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with ZYNLONTA and for at least 4 months after the last dose.
- See **Relevant Prescribing Information** for additional information.

Background

- LOTIS-1 was a Phase 1, open-label, single-arm, multicenter study which evaluated the safety and tolerability of ZYNLONTA monotherapy in 183 adult patients with relapsed or refractory (R/R) B-Cell Non-Hodgkin's Lymphoma (B-NHL). The study was conducted in two parts, dose-escalation (Part 1) followed by dose-expansion (Part 2).
    - Male or female patients (≥18 years of age) with histologically confirmed R/R B-NHL were enrolled if they failed or became intolerant to established therapies or if they had no other treatment options available.[1]
- LOTIS-2 was a Phase 2, open-label, single-arm, multicenter study which evaluates the efficacy and safety of ZYNLONTA monotherapy in 145 male or female patients (≥18 years of age) with R/R DLBCL following ≥2 lines of prior systemic therapy.[2]

Clinical Data

- Pregnant or breastfeeding women were excluded from enrollment into LOTIS-1 and LOTIS-2. A negative blood or urine beta-human chorionic gonadotropin (β-HCG) pregnancy test within 7 days prior to Day 1 for women of childbearing potential was required.[3,4]
- Additionally, women of childbearing potential were required to use a highly effective method of contraception from the time of providing informed consent until a minimum of 16 weeks following the final dose of ZYNLONTA.[4]
  - Forms of birth control which achieved a failure rate of < 1% per year when used correctly with compliance included hormonal contraceptives (i.e., oral, injectable, patch, intrauterine device). Additional methods of contraception were male partner sterilization or abstinence from heterosexual intercourse.[4]
  - Methods of birth control which were not deemed as "highly effective" were the double barrier method (i.e., synthetic condoms, diaphragm, cervical cap with spermicidal foam, cream, or gel). In addition to this periodic abstinence, symptothermal, post ovulation, withdrawal (coitus interruptus), lactational amenorrhea method, and spermicide-only were not acceptable methods of contraception.[4]
- Men with female partners of childbearing potential had to agree that they or their partners would use a highly effective method of contraception from the time of providing informed consent until a minimum of 16 weeks following the last dose of ZYNLONTA.
- If it was determined that a patient was pregnant while receiving the study drug, the patient could be withdrawn from treatment with ZYNLONTA.[3,4]

Literature search

- A PubMed biomedical literature search conducted on November 5, 2025, yielded no relevant data regarding the use of ZYNLONTA in pregnancy and lactation.

Relevant Prescribing Information[5]

Section 8: Use in Specific Populations

8.1: Pregnancy

Risk Summary

- Based on its mechanism of action, ZYNLONTA can cause embryo-fetal harm when administered to a pregnant woman, because it contains a genotoxic compound (SG3199) and it affects actively dividing cells. There are no available data on the use of ZYNLONTA in pregnant women to evaluate for drug-associated risk. No animal reproduction studies were conducted with ZYNLONTA. Advise pregnant women of the potential risk to a fetus.
- The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

- Animal reproductive or developmental toxicity studies were not conducted with ZYNLONTA. The cytotoxic component of ZYNLONTA, SG3199, crosslinks DNA, is genotoxic, and is toxic to rapidly dividing cells, suggesting it has the potential to cause embryotoxicity and teratogenicity.

8.2: Lactation

Risk Summary

- There is no data on the presence of ZYNLONTA or SG3199 in human milk, the effects on the breastfed child, or milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with ZYNLONTA and for at least 4 months after the last dose.

8.3: Females and Males of Reproductive Potential

- ZYNLONTA can cause fetal harm when administered to pregnant.

Pregnancy Testing

- Pregnancy testing is recommended for females of reproductive potential prior to initiating ZYNLONTA.

Contraception

- Advise women of reproductive potential to use effective contraception during treatment and for 10 months after the last dose. Because of the potential for genotoxicity, advise males with female partners of reproductive potential to use effective contraception during the treatment with ZYNLONTA and for 7 months after the last dose.

Infertility

- Based on the results from animal studies, ZYNLONTA may impair fertility in males. The effects were not reversible in male cynomolgus monkeys during the 12-week drug-free period.

References

[1] Hamadani M, Radford J, Carlo-Stella C, et al. Final Results of a Phase 1 Study of loncastuximab tesirine in relapsed/refractory B-cell Non-Hodgkin Lymphoma. Blood. 2020 Nov 19. DOI: 10.1182/blood.2020007512.
[2] Caimi PF, Ai WZ, Alderuccio JP, et al. Loncastuximab tesirine in relapsed/refractory diffuse large B-cell lymphoma: long-term efficacy and safety from the phase 2 LOTIS-2 study. Haematologica. 2024;109:1184-1193
[3] Data on File, LOTIS 1 Clinical Study Report. ADC Therapeutics.
[4] Data on File, LOTIS 2 Clinical Study Report. ADC Therapeutics.
[5] ZYNLONTA® (loncastuximab tesirine) FDA-approved Prescribing Information. October 2022.

ADC Therapeutics encourages all health care professionals to report any adverse events and product quality complaints to medical information at 855-690-0340. Please consult the ZYNLONTA Prescribing Information.