Low Rates of High-Grade Toxicities With GLPG5101, a Fresh, Stem-Like, Early Memory Phenotype Anti-CD19 CAR T-Cell Therapy With a 7-Day Vein-to-Vein Time in Patients With Non-Hodgkin Lymphoma in the ATALANTA-1 Study

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CONCLUSIONS

- **High-grade toxicities were rare. Low-grade cases of CRS and ICANS were experienced by 41% and 18% of patients, respectively. Only a single Grade ≥ 3 event was observed for each of CRS and ICANS during the study**
- **The most common Grade ≥ 3 TEAEs were cytopenias, with most patients recovering by 30 days after infusion**
- **The low dropout rates observed in ATALANTA-1, with rapid manufacturing and the 7-day vein-to-vein delivery paradigm, potentially facilitated treatment of patients who would otherwise not be able to receive CAR T-cell therapy**
- **In ATALANTA-1, the 7-day vein-to-vein time eliminated the need for bridging chemotherapy in patients receiving fresh product, reducing the burden of additional therapies during CAR T-cell treatment**
- **The favorable safety profile of GLPG5101 suggests the potential for future use in an outpatient setting**

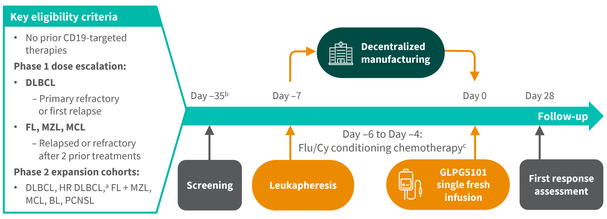
Introduction

- CD19-directed chimeric antigen receptor (CAR) T-cell therapy has changed the treatment paradigm and improved outcomes for patients with relapsed/refractory (R/R) non-Hodgkin lymphoma (NHL).
- Reducing the risk of severe toxicities before and during CAR T-cell therapy may help lower barriers to patient access, and support outpatient treatment.
- Overall attrition rates, including dropout of patients post-leukapheresis, have been reported to be as high as 33% in clinical trials[1] and 32% in real-world clinical settings,[2] with many patients not receiving planned CAR T-cell treatment[3]; rapid disease progression is a primary reason for attrition and dropout.
- Short vein-to-vein time and improved safety profile/characteristics of CAR T-cell therapy may reduce overall attrition rates, including patient dropouts, enable broader use of CAR T-cell therapy, and improve outcomes.[4–6]

Methods

- ATALANTA-1 (CTIS: 2022-502661-23-00; NCT06561425) is an ongoing Phase 1/2 study of GLPG5101 in patients with R/R NHL, including diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), marginal zone lymphoma (MZL), mantle cell lymphoma (MCL), Burkitt lymphoma (BL), and primary central nervous system lymphoma (PCNSL) (**Figure 1**).
- The Phase 1 primary objectives are safety and determination of a recommended Phase 2 dose; the Phase 2 primary objective is efficacy (objective response rate).
- Safety, pharmacokinetics, pharmacodynamics, and the feasibility of decentralized manufacturing are assessed as secondary endpoints.

Figure 1. Study Design



[a]Patients with no prior therapies and IPI 3–5, or double/triple-hit lymphoma on interim PET scan. [b]Screening could take place within 28 days prior to leukapheresis. [c]Conditioning chemotherapy: fludarabine IV (30 mg/m^2/day); cyclophosphamide IV (300 mg/m^2/day).
BL, Burkitt lymphoma; Cy, cyclophosphamide; FL, follicular lymphoma; Flu, fludarabine; (HR) DLBCL, (high-risk) diffuse large B-cell lymphoma; IPI, international prognostic index; IV, intravenous; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; PCNSL, primary central nervous system lymphoma; PET, positron emission tomography.

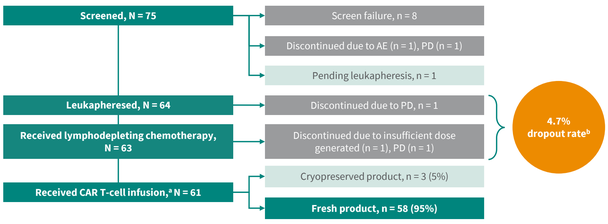
- CAR T-cell expansion and persistence were quantified by quantitative or digital PCR.
- Data are presented for all patients who received an infusion, pooled across dose levels:
  - DL1: 35–50 × 10^6 CAR$^+$ T cells.
  - DL2: 85–110 × 10^6 CAR$^+$ T cells.
  - DL3: 200–250 × 10^6 CAR$^+$ T cells.

Results

Patient Disposition

- As of 14 October 2024, 61 patients had received a CAR T-cell infusion (**Figure 2; Table 1**).
- 95% (58/61) of infused patients received a fresh product.
- Of the 58 patients who received a fresh product, none required bridging chemotherapy.
- 93% (54/58) of patients who received a fresh product had a vein-to-vein time of 7 days.

Figure 2. Patient Disposition



[a]Data are pooled across DLs: DL1: 35–50 × 10^6, DL2: 85–110 × 10^6, DL3: 200–250 × 10^6. [b]% dropout rate calculated as: (100 – [number of patients who received CAR T-cell infusion/number of patients who were leukapheresed] × 100). Data cutoff: 14 October 2024. AE, adverse event; DL, dose level; PD, progressive disease.

Demographics and Baseline Characteristics

- ATALANTA-1 includes high-risk and heavily pretreated patients across all NHL subtypes (**Table 1**).

Table 1. Baseline Demographics and Disease Characteristics

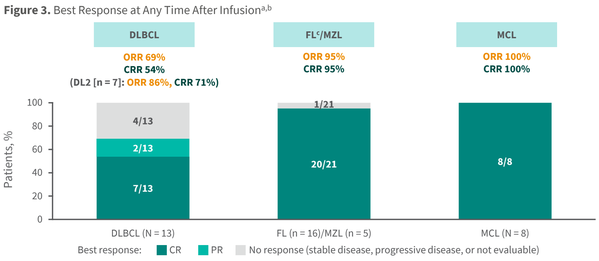
	Phase 1 n = 24	Phase 2 n = 37	All patients N = 61
Age, median (range), years	67 (25–78)	67 (36–81)	**67 (25–81)**
Sex, n (%)			
Male	15 (63)	23 (62)	**38 (62)**
Female	9 (38)	14 (38)	**23 (38)**
NHL subtype, n (%)			
DLBCL	17 (71)	0	**17 (28)**
MCL	3 (13)	9 (24)	**12 (20)**
FL	3 (13)	24 (65)	**27 (44)**
MZL	1 (4)	4 (11)	**5 (8)**
(M, FL)IPI score at screening, high risk, n/n available (%)	10/23 (43)	21/36 (58)	**31/59 (53)**
ECOG PS, n (%)			
0	7 (29)	19 (51)	**26 (43)**
1	15 (63)	13 (35)	**28 (46)**
2	2 (8)	5 (14)	**7 (11)**
Prior systemic therapies, median (range)	3 (1–9)	3 (2–7)	**3 (1–9)**
Ann Arbor disease stage: II/III–IV, n (%)	2 (8)/22 (92)	6 (16)/31 (84)	**8 (13)/53 (87)**
Tumor burden (SPD), median (range),* cm^2	20 (1–115)	22 (3–112)	**20 (1–115)**

[a]Median and range given for 59/61 patients for whom data are available. Data cutoff: 14 October 2024.
DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; (M, FL)IPI, (MCL, FL) international prognostic index; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; NHL, non-Hodgkin lymphoma; SPD, sum of the products of diameters.

Efficacy

- High objective response and complete response rates were observed (best response at any time after infusion) (**Figure 3**).

Figure 3. Best Response at Any Time After Infusion[a,b]



[a]Data for 42 patients. [b]Two patients who received cryopreserved product were not included in the efficacy analyses; both were in CR at data cutoff. [c]Three patients with FL were not included in the Phase 2 response outputs as the first response assessment data were not available at data cutoff. Data cutoff: 25 April 2024.
CR, complete response; CRR, complete response rate; DL, dose level; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; ORR, objective response rate; PR, partial response.

Safety

- Treatment-emergent adverse events (TEAEs) reported up to 14 weeks post-infusion are summarized in **Table 2**.
- Dose-limiting toxicities occurred in 5 patients in Phase 1.
- Of the 15/61 (25%) patients hospitalized, median (range) duration of hospitalization, excluding protocol mandated post-infusion visits, was 9 (3–41) days; 1 patient was intubated and 1 patient required dialysis.

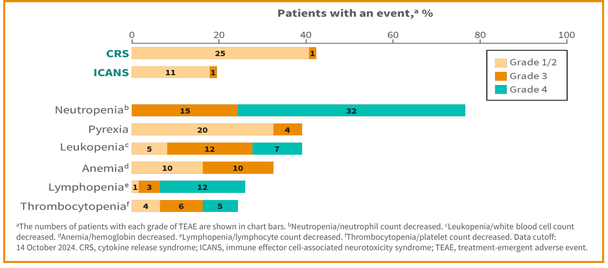
Table 2. Treatment-Emergent Adverse Events Reported up to 14 Weeks Post-Infusion

	Phase 1 n = 24	Phase 2 n = 37	All patients N = 61
Any TEAE, n (%)	24 (100)	35 (95)	**59 (97)**
GLPG5101-related TEAE, n (%)	24 (100)	32 (87)	**56 (92)**
Serious TEAEs, n (%)	7 (29)	9 (24)	**16 (26)**
TEAEs leading to death, n (%)	2 (8)	0	**2 (3)**
Grade ≥ 3 TEAE, n (%)	24 (100)	28 (76)	**52 (85)**

Data cutoff: 14 October 2024. TEAE, treatment-emergent adverse event.

- There were 6 deaths, 2 due to progressive disease and 4 due to TEAEs:
  - Two deaths due to TEAEs were reported ≤ 14 weeks post-infusion: 1 due to intra-abdominal hemorrhage considered related to infusion; 1 due to pneumonia/respiratory distress, considered unrelated to infusion.
  - Two deaths due to TEAEs were reported during follow-up (> 14 weeks post-infusion): 1 due to COVID-19 pneumonia and 1 due to *E. coli* sepsis, both considered possibly related to infusion.
- The most common TEAEs of any grade were hematologic (**Figure 4**).
- Cases of CRS and ICANS were few and predominantly low grade (any grade: 26 patients [43%] and 12 patients [20%], respectively); Grade ≥ 3 CRS and ICANS occurred in 1 patient each (**Figure 4**).
  - Median (range) time to CRS onset was 7.0 (1–20) days and duration of CRS was 3.0 (1–17) days.
  - Median (range) time to ICANS onset was 11.5 (2–30) days and duration of ICANS was 2.0 (1–47) days.
  - The most common treatments used for CRS/ICANS toxicity were dexamethasone and tocilizumab in 18% and 25% of patients with CRS and 10% and 5% of patients with ICANS, respectively.

Figure 4. Treatment-Emergent Adverse Events of Any Grade Occurring in ≥ 20% of Patients (N = 61)



[a]The numbers of patients with each grade of TEAE are shown in chart bars. [b]Neutropenia/neutrophil count decreased. [c]Leukopenia/white blood cell count decreased. [d]Anemia/hemoglobin decreased. [e]Lymphopenia/lymphocyte count decreased. [f]Thrombocytopenia/platelet count decreased. Data cutoff: 14 October 2024. CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; TEAE, treatment-emergent adverse event.

- B-cell aplasia (normalized B-cell count < 0.10 × 10^9/L) was observed in 45/61 (74%), 57/57 (100%), and 45/46 (98%) patients at baseline, Day 28, and Week 14, respectively.
  - One patient had an adverse event of Grade ≥ 3 B-cell aplasia (**Table 3**).
- Hypogammaglobulinemia (IgG < 4 g/L) was observed in 14/61 (23%), 15/59 (25%), and 12/47 (26%) patients at baseline, Day 28, and Week 14, respectively.
- 15/61 (25%) patients had intravenous immunoglobulin administered at any time during the study.

Table 3. Adverse Events of Special Interest Reported up to 14 Weeks Post-Infusion

	Phase 1 n = 24	Phase 2 n = 37	All patients N = 61
Prolonged cytopenias,[a] Grade ≥ 3, n/n available (%)			
30 days after infusion	8/21 (38)	11/37 (30)	**19/58 (33)**
60 days after infusion	5/21 (24)	9/33 (27)	**14/54 (26)**
90 days after infusion	4/20 (20)	8/30 (27)	**12/50 (24)**
180 days after infusion	2/20 (10)	3/27 (11)	**5/47 (11)**
Infections, Grade ≥ 3, n (%)	2 (8)	1 (3)	**3 (5)**
B-cell aplasia, Grade ≥ 3, n (%)	0	1 (3)	**1 (2)**
HLH, Grade 3, n (%)	2 (8)	0	**2 (3)**

[a]Includes all events related to neutropenia, thrombocytopenia, anemia, and lymphopenia. Data cutoff: 14 October 2024.
HLH, hemophagocytic lymphohistiocytosis.

Product Characterization and Pharmacokinetics

- CAR T-cell peak expansion and exposure were higher in patients experiencing CRS than in patients with no CRS.
- Peak expansion and exposure was similar in patients experiencing ICANS versus those with no ICANS.

Disclosures: J.S.P.V. has nothing to declare. **S.A.** has nothing to declare. **M.T.K.** reports consultancy/advisory role for Adicet Bio, Biotec, BMS, Galapagos, Janssen, Kite/Gilead, Miltenyi, Mustang Bio, and Novartis; honoraria from Beigene, BMS, Kite/Gilead, and Roche; and travel grants from AbbVie, BMS, and Roche. **P.G.N.J.M.** has nothing to declare. **E.W.** reports travel support from Beigene and Takeda. **M.R.B.** reports consultancy/advisory role for Autolus Therapeutics, AvenCell Therapeutics, BMS/Juno Therapeutics, Chimeric Therapeutics, CRISPR Therapeutics, Galapagos, Kite/Gilead, in8bio, Incyte, Iovance Biotherapeutics, Novartis, and Sana Biotechnology; honoraria from AbbVie, ADC Therapeutics, AstraZeneca, Autolus Therapeutics, AvenCell Therapeutics, BMS, BMS/Juno Therapeutics, Chimeric Therapeutics, CRISPR Therapeutics, Galapagos, GenmAb, in8bio, Incyte, Iovance Biotherapeutics, Kite/Gilead, Novartis, Sana Biotechnology, and Servier; and speaker fees from AbbVie, ADC Therapeutics, AstraZeneca, BMS, GenmAb, Incyte, Kite/Gilead, and Servier. **T.J.A.D.** has nothing to declare. **M.D.** reports consultancy/advisory role for AbbVie, AstraZeneca, Beigene, BMS/Celgene, Janssen, Kite/Gilead, Lilly/Loxo, Novartis, and Roche; honoraria from AstraZeneca, Beigene, Janssen, Kite/Gilead, Lilly, Novartis, and Roche; and research support (institution) from AbbVie, Bayer, BMS/Celgene, Janssen, Kite/Gilead, Lilly, and Roche. **C.J.** reports consultancy/advisory role for AbbVie, ADC Therapeutics, Aleta, Appia, AstraZeneca, BMS, Caribou, Galapagos, Genentech, GenmAb, Janssen, Kite/Gilead, Kyverna, Miltenyi, Novartis, Sana Biotechnology, and Synthekine. **S.B., O.F., H.K., E.S., J.S.** are employees of Galapagos. **K.V.H.** is an employee of Open Analytics and Galapagos. **M.J.K.** reports consultancy/advisory role for Adicet Bio, Biotec, BMS, Galapagos, Janssen, Kite/Gilead, Miltenyi, Mustang Bio, and Novartis; honoraria from Beigene, BMS, Kite/Gilead, and Roche; and travel grants from AbbVie, BMS, and Roche.

References: 1. Schuster SJ, et al. Blood. 2017;130:577; **2.** Wuliji N, et al. Transplant Cell Ther. 2024;30(2):S362–S363; **3.** Chen AJ, et al. Value Health. 2022;25:1344–1351; **4.** Morris EC, et al. Nat Rev Immunol. 2022;22:85–96; **5.** Locke FL, et al. Blood Adv. 2025;9:2663–2676; **6.** Jallouk AP, et al. Haematologica. 2024;109:1460–1468.

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