GALLANT-1: Galectin-3 (Gal-3) inhibitor GB1211 plus atezolizumab (atezo) in patients with non-small cell lung cancer (NSCLC) – a randomized double-blind trial

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Background

- Gal-3 is a member of a protein family defined by high affinity for β-galactosides. Gal-3 binds specifically to N-acetylglucosamine residues, which are upregulated on key tumorigenic cell surface proteins[1]
- Gal-3 is widely over-expressed in the tumor microenvironment[2,3] and is generally linked to poor outcomes.[4] Gal-3 regulates immune cell function of T cells and macrophages, and promotes neovascularization and fibrosis[5–7]
- Gal-3 sequesters interferon γ, reduces T cell influx, and contributes to tumor cell evasion of the immune system via lymphocyte activation gene-3 (LAG-3).[8,9] Gal-3 is also a ligand of LAG-3 and enables signaling in *KRAS*-mutated tumors[10,11]
- Gal-3 has been identified as a marker of resistance to checkpoint inhibitors (CPIs). In a retrospective study, patients with stage IV NSCLC and high Gal-3 levels (>70% Gal-3 immunohistochemical staining) were shown to be resistant to pembrolizumab (a CPI) despite >50% of tumor cells showing programmed death-ligand 1 (PD-L1) staining[12]
- Animal data indicate synergy between CPI therapy and Gal-3 inhibition;[1,13] thus, inhibiting Gal-3 together with CPI-based immunotherapy may enhance tumor-specific immune responses, and overcome CPI resistance

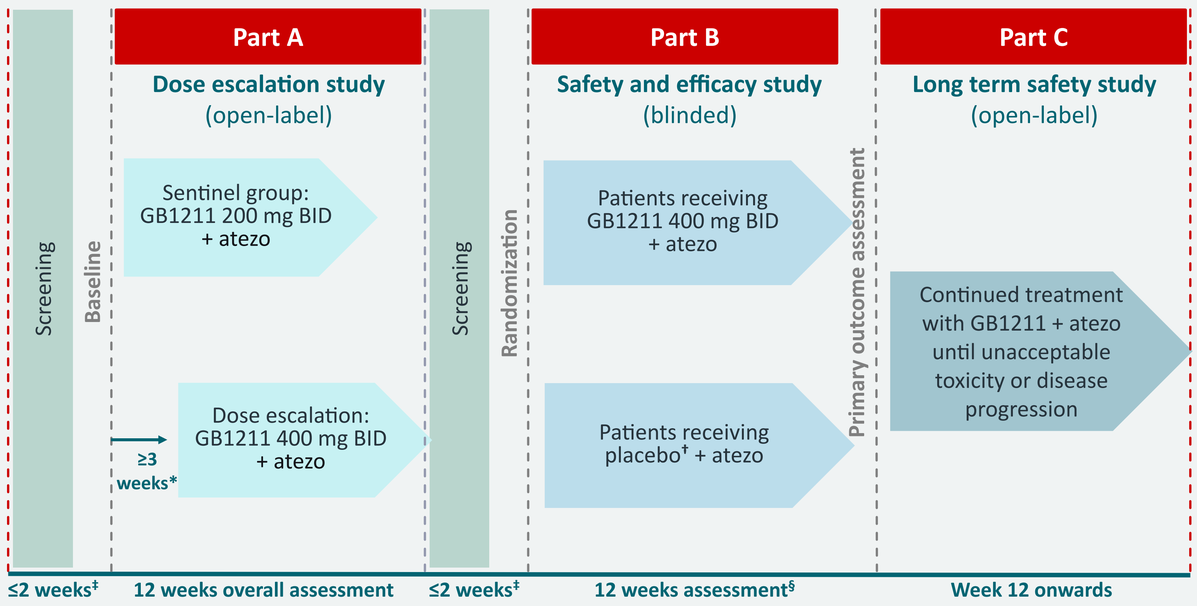
Methods

- GALLANT-1 (ClinicalTrials.gov identifier: NCT05240131) is a 3-part, placebo-controlled, phase IB/IIA trial that will investigate safety and efficacy of GB1211 (a Gal-3 inhibitor) + atezo (a CPI) vs. placebo + atezo in patients with advanced or metastatic NSCLC

GALLANT-1 (NCT05240131)

- An open label study followed by a randomized, double-blind, placebo-controlled trial (**Fig. 1**)
  - **Primary endpoint:** Safety and tolerability (Part A, B and C), tumor shrinkage (Part B)
  - **Secondary endpoints:** Pharmacokinetic measurements, overall response rate (response evaluation criteria in solid tumors)
  - **Exploratory:** Effect of GB1211 on pharmacodynamic markers and biomarkers

Figure 1. Trial design



*After 4 patients in the sentinel group have completed the 1st cycle of 3 weeks treatment, safety will be reviewed to allow dose escalation to 400 mg GB1211 BID; †Matched to GB1211 dosing. ‡Between Day −14 and Day −1. §Continuation of blinded treatment until the last patient has received 12 weeks of treatment. BID, twice-daily

Part A

- **Patient sample:** 8–12 patients
- **Aim:** to determine the safety and tolerability of 200 mg and 400 mg GB1211 BID + atezo, in an open-label design
- **Primary endpoint:** number of adverse events (AEs) after 12 weeks of treatment in patients receiving 200 mg GB1211 compared with those receiving 400 mg GB1211
  - Part A will determine the GB1211 dose for Part B
  - Safety will be evaluated 7 days after the first patient in each treatment group receives the first dose; if no safety concerns arise, the remaining 3 patients will be enrolled
  - Safety review committee meeting will take place after the last patient in each group has been treated for 3 weeks; additional safety review meetings will be scheduled if necessary

Part B

- **Patient sample:** 75 patients
- **Aim:** to determine the safety and efficacy of GB1211 + atezo vs. placebo + atezo in a randomized, double-blind study
- **Primary endpoints:** safety (number of AEs) and efficacy (percentage change from baseline in the sum of longest diameter of target lesions at Week 12)
  - Safety review committee meetings will take place after (i) 10 patients and (ii) 30 patients have been treated for 3 weeks, and at the end of the study; additional safety review meetings will be scheduled if necessary

Part C

- An open-label extension study that includes patients from Parts A and B, who have achieved clinical benefit from the study drug in either Part A or Part B; treatment will continue until disease progression or unacceptable toxicity

Eligibility criteria

Principal inclusion criteria

- Advanced or metastatic stage IIIB or IV NSCLC adenocarcinoma
- Measurable disease (RECIST v1.1)
- Expression of PD-L1 on ≥50% of tumor cells
- Eligible for atezo 1200 mg every 3 weeks

Principal exclusion criteria

- Symptomatic, untreated, or actively progressing central nervous system metastases
- Prior systemic chemotherapy for treatment of recurrent advanced or metastatic disease (except if part of neoadjuvant/adjuvant therapy)
- Prior treatment with immune CPIs and/or GB1211
- Presence of *EGFR* mutation and *ALK*, *ROS1* and *RET* alterations
- Treatment with antineoplastic principal or systemic immunotherapeutic agents prior to first GB1211 dose
- Severe infectious disease <4 weeks prior to first GB1211 dose
- Active hepatitis B or C, human immunodeficiency virus, or COVID-19

Study status

As of May 15, 2022, Part A has been initiated and enrolment is ongoing

References

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