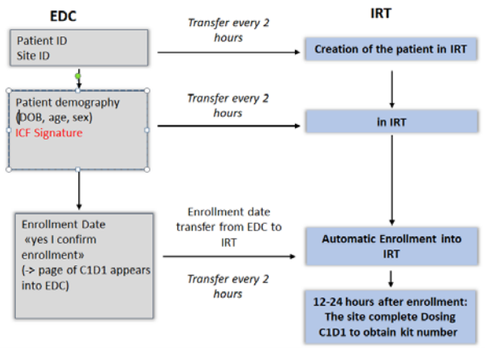
Systems for Enrollment and IMP management

France and Belgium



Safety monitoring and reporting

AE, SAE, AESI, Pregnancy - See Protocol_section 8

To be reported within 24 hours to Beigene using TiRHoL_SAE Form
BeigeneClinicalTrialPVG.sm@ppdi.com
Or fax : +331 53 01 34 49 (France) or +32 27 06 51 35 (Belgium)

- After ICF has been signed but prior to the administration of the study drug: only SAEs should be reported
- After initiation of study drug, AEs and SAEs, regardless of relationship to study drug, will be reported until 90 days after last dose of study treatment or until initiation of new anticancer therapy.
- For patients who begin new anticancer therapy, only irAEs will be reported during the 90-day period after the last dose of study treatment.
- The symptoms, signs, or clinical sequelae, if considered serious in nature that result from disease progression should be reported as SAE.
- **AESI :** Protocol_section 8.7: infusion related reactions, severe hypersensitivity reactions, and irAEs.
- **Pregnancy:** refers to Protocol_section 8.6.6

Primary study objective

To evaluate the efficacy of tislelizumab in patients with R/R cHL, as measured by ORR per the Lugano Classification (Cheson et al 2014—cf Appendix 4) and determined by the investigator

ENROLLMENT: eCRF (CSonline)

The inclusion of a patient must be finalized before starting study treatment:

1. Connect to TiRHOL's eCRF on the website:
   http://study.lysarc.info
2. Create the subject.
3. Enter screening data and confirm enrollment.
4. The site receives an enrollment or screen-failure notification: the subject will only be considered enrolled in the study after receiving the enrollment confirmation.
5. Central pathology confirmation is not required prior to enrollment.
6. Send by email the anonymized pathological report to tirhol@lysarc.org

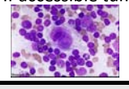
Central review of Tumor Imaging

⇒ PET-CT and CT with contrast at screening
⇒ PET-CT at week 12 from C1D1, then every 12 weeks for 96 weeks and every 24 weeks thereafter (± 14 days)
⇒ CT w/contrast every 24 weeks from C1D1 (± 14 days)
⇒ After EOT, every 90 days (± 7 days) until PD, withdrawal of consent, death, loss to follow-up, or EOS

The images must be uploaded on the Imagys® platform:

1. Access provided after the first patient enrollment
2. Platform training by LYSA-IM (if needed)
3. Loading images and completing the investigator form within 1 week after the exam
4. Quality control by LYSA-IM

Central confirmation of cHL diagnosis

Screening	If PD: optional Biopsy
⇒ Archival tumor tissues mandatory for patients who consent to participate in the study (If no archival sample available, fresh biopsy required.)	⇒ written informed consent is required prior to fresh tumor biopsy ⇒ If accessible tumor sites
⇒ Fresh tumor biopsy optional but strongly recommended.	

Tumor tissue are to be sent at enrollment to:
LYSA-P—Henri Mondor Hospital—Créteil—FRANCE

Biology

Refer to the Biological booklet

TiRHoL

BGB-A317-210

A Phase 2, Multicenter, Open-Label Study of Tislelizumab (BGB-A317) in Patients with Relapsed or Refractory Classical Hodgkin Lymphoma

CONTACTS

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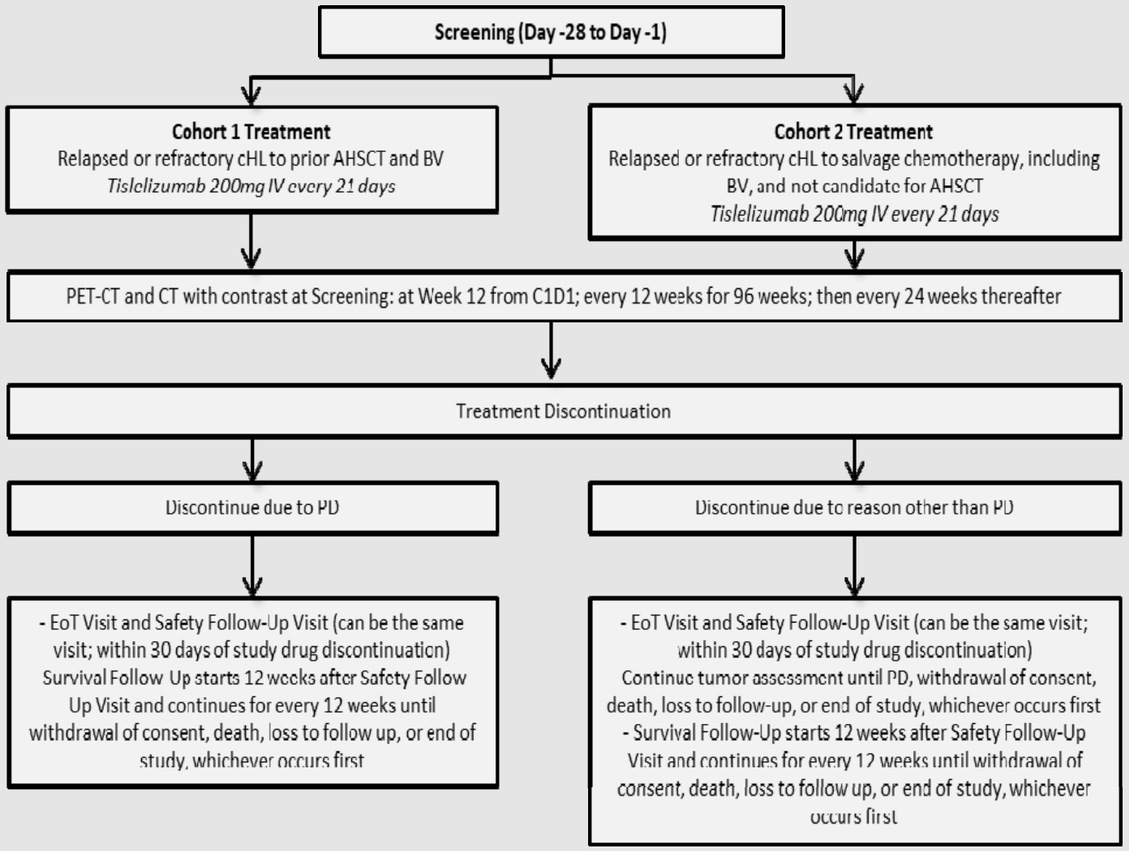
Main inclusion criteria

Cohort 1 R/R to prior autologous hematopoietic stem cell transplant (HSCT) and Bv	Cohort 2 R/R to salvage chemotherapy, including Bv, and has not received prior autologous or allogeneic HSCT
✓ Has failed to achieve a response or progressed after autologous HSCT and failed to achieve a response or progressed after Bv ✓ Not a candidate for additional autologous or allogeneic HSCT	✓ Not a candidate for autologous or allogeneic HSCT ✓ Has received at least 2 prior systemic chemotherapy regimens and failed to achieve a response or progressed after Bv

- ✓ Measurable disease
- ✓ Able to provide fresh or archival tumor tissue
- ✓ ECOG performance status of 0 or 1
- ✓ Histologically confirmed diagnosis of R/R cHL
- ✓ Adequate organ function, as indicated by the lab values

Main exclusion criteria

- ×Nodular lymphocyte-predominant Hodgkin lymphoma or gray zone lymphoma
- ×Prior allogeneic hematopoietic stem cell transplantation
- ×History of severe hypersensitivity reaction to monoclonal antibodies
- ×New York Heart Association (NYHA) class III or IV heart failure, unstable angina, severe uncontrolled ventricular arrhythmia, electrocardiographic evidence of acute ischemia, or myocardial infarction within 6 months of first day of screening
- ×Prior therapy targeting PD-1 or PD-L1, anti-PD-L2 or anti CTLA-4 agent
- ×Prior malignancy within the past 3 years except for curatively treated basal or squamous cell skin cancer, superficial bladder cancer, or carcinoma in situ of the cervix, breast, or other site for which in situ carcinoma has metastatic potential
- ×Active autoimmune disease or history of autoimmune disease that may relapse
- ×Conditions requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalent) or other immunosuppressive medications within 14 days of the first dose of tislelizumab



PRIOR AND CONCOMITANT THERAPY

BGB-A317-210 Protocol_section 6

Prior therapy : sections 4.1 and 4.2

Exclusion criteria: 6, 7 and 9

n°6 : Prior therapy targeting PD-1 or PD-L1, anti-PD-L2, or anti CTLA-4 agent.

n°7: 4 weeks prior to Cycle 1 Day 1:

- Systemic chemotherapy, targeted small molecule therapy, or radiation therapy
- Treatment with monoclonal antibody

n°9: Systemic corticosteroid > 10 mg daily

Prohibited Medications : section 6.2.2

⇒ Immunosuppressive agents

⇒ Systemic corticosteroid > 10 mg daily prednisone equivalent (except to treat a drugrelated AE).

⇒ Any concurrent antineoplastic therapy

⇒ Live vaccines

Permitted Medications : section 6.2.1

⇒ Concomitant medications and therapies deemed necessary for supportive care (eg, antiemetics, antidiarrheals) , safety and patient's welfare are allowed.

⇒ Systemic corticosteroids may be used for the control of irAEs

	Screening [1]	Treatment Period			Safety Follow-up [4]	Safety/Survival/Efficacy Follow-up [5]
		Cycle 1 (21 Days) [2]	Cycle 2 and additional cycles (every 21 days)	EOT [3]		
Days	-28 to -1	1	1 ± 7		30 + 7 (after last dose)	
Informed consent [6]	x					
Inclusion/exclusion criteria	x					
Demographics /Medical history / Prior medications [7]	x					
Vital signs [8]	x	x	x	x	x	
Height and weight [9]	x	x	x	x		
Physical examination	x	x	x	x	x	
Ophthalmic examination [10]	x		x		x	
ECOG performance status	x	x	x	x	x	
12-lead ECG [11]	x					
Pulmonary function test [12]	x					
Review adverse events [13]	x	x	x	x	x	x
Review concomitant medications [14]	x	x	x	x	x	x
CBC with differential [15]	x	x	x [28]	x	x	
Serum chemistry panel [15]	x	x	x [28]	x	x	
Hepatitis B and C and HIV [16]	x					
ESR		x [28]				
Pregnancy test [17]	x		x	x	x	
Thyroid function test [18]		x [28]	x [28] (after C2D1, repeat every 2 cycles)	x	x	
Liver function tests [19]	x	x	x		x	
Pancreatic enzymes [20]	x					
Tumor tissue [21]	x	x [21]		x [21]		
Optional blood collection [22]	x	x	x	x		
Tumor imaging [23]	x	PET-CT: At Week 12 from C1D1, then every 12 weeks for 96 weeks, and every 24 weeks thereafter, ± 14 days CT w/contrast: Every 24 weeks from C1D1, +/- 14 days		x [24]		x [24]
ECHO or MUGA [25]	x					
Survival status						x
Study drug administration		x	x			
Pharmacokinetics [26]		x	x		x	
Anti-drug antibody [27]		x	x		x	
Patient-reported outcomes [29]		x [29]	x [29]		x [29]	