EVALUATION OF PET-CT METRICS AND PHARMACOKINETICS IN ADULTS RECEIVING TISLELIZUMAB FOR RELAPSED/REFRACTORY CLASSICAL HODGKIN LYMPHOMA: ANCILLARY ANALYSES OF LYSA PHASE 2 TIRHOL STUDY BGB-A317-210

Authors: Hervé Ghesquières,[1] Krimo Bouabdallah,[2] Salim Kanoun,[3] Marc André,[4] Philippe Quittet,[5] Cécile Borel,[6] Aspasia Stamatoullas Bastard,[7] Michael Gilbertson,[8] Fabien Le Bras,[9] Catherine Thieblemont,[10] Baptiste Delapierre,[11] Mohamed Touati,[12] Pierre Feugier,[13] Loïc Renaud,[14] Nadine Morineau,[15] Thomas Gastinne,[16] Isabelle Chaillol,[17] Rod Ramchandren,[18] Harsh Shah,[19] Dipenkumar Modi,[20] Heather Allewelt,[21] Pierre Fustier,[22] Xiangyu Liu,[21] Jun Zhang,[21] Richard Delarue,[22] Franck Morschhauser,[23] Cédric Rossi[24]

Affiliations: [1]Lyon Sud Hospital, Pierre Bénite, France; [2]Hôpital Haut-Lévêque, CHU Bordeaux, Pessac, France; [3]Institut Universitaire du Cancer de Toulouse, Toulouse, France; [4]CHU UCL Namur, Yvoir, Belgium; [5]CHU Montpellier, Montpellier, France; [6]IUCT Oncopole, Toulouse, France; [7]Centre Henri Becquerel, Rouen, France; [8]Monash Health, Melbourne, VIC, Australia; [9]CHU Mondor, Creteil, France; [10]AP-HP, Hôpital Saint-Louis, Hemato-oncology, Paris University Paris Cité, Paris, France; [11]Caen University Hospital, Caen, France; [12]CHU Limoges, Limoges, France; [13]CHU Nancy, Nancy, France; [14]Gustave Roussy, Department of Hematology, Villejuif, France; [15]CHD de Vendee, La Roche Sur Yon, France; [16]CHU de Nantes, Nantes, France; [17]Lymphoma Academic Research Organisation, Lyon, France; [18]UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [19]University of Utah, Salt Lake City, UT, USA; [20]Karmanos Cancer Institute, Wayne State University, Detroit, MI, USA; [21]BeOne Medicines, Ltd, San Carlos, CA, USA; [22]BeOne Medicines, Ltd, Basel, Switzerland; [23]CHU de Lille, Lille, France; [24]CHU Dijon, Dijon, France

Background: Conventional methods using PET-CT to assess lymphoma response are suboptimal in patients (pts) treated with PD1 inhibitors; specialized criteria are required to prevent premature treatment discontinuation due to inflammation unrelated to disease progression. In the LYSA phase 2 BGB-A317-210 study (NCT04318080), 45 pts with relapsed/refractory (R/R) classical Hodgkin lymphoma (cHL) were treated with tislelizumab every 3 weeks until progressive disease (PD), unacceptable toxicity, or study withdrawal; disease response was assessed by investigator every 12 weeks according to Lugano 2014 PET-CT classification. At final analysis, the overall response rate (ORR), the primary endpoint of TIRHOL, was 66.7% (95%CI, 51%-80%), and the complete response rate was 31%. PK profiles were comparable between BGB-A317-210 and the prior Chinese study BGB-A317-203.

Methods: For this correlative analysis, PET-CT imaging in pts in the TIRHOL study was evaluated post-hoc by a central, independent reviewer. Relationships were assessed between baseline PET-CT metrics (TMTV4, TLG4, Dmax4, SUVmean, and SUVmax) and response assessments, progression-free (PFS), and overall survival (OS). The longitudinal evolution of TMTV4 and SUV during tislelizumab therapy was also

examined. Tislelizumab PK profiles (cycle 1 post-dose and cycle 2 pre-dose concentrations) were evaluated against baseline clinical and PET-CT characteristics.

Results: Baseline and follow-up PET-CT images were available for post-hoc central review for 37 of the 45 pts in TIRHOL. ORR was 70%, with complete metabolic response (CMR) observed in 15 pts (40%) and partial metabolic response (PMR) in 11 (30%); remaining pts had no metabolic response (NMR; stable disease or PD; n=10, [27%]), or were not evaluated (n=1, [3%]). At the first metabolic evaluation at Week 12, 10 pts had CMR (27%), 13 had PMR (35%), 13 had NMR (35%) and 1 (3%) was not evaluated. Pts with best metabolic response of CMR, PMR and NMR had 1-year PFS rates of 60%, 26%, and 8%, and 1-year OS rates of 100%, 100%, and 77%, respectively. Median baseline PET-CT metrics were comparable across Week 12 and best metabolic response categories and were comparable between pts with PFS or OS events and those who remained event-free. Longitudinal evaluations of TMTV4 and SUV showed a rapid decrease of values at first evaluation for pts with CMR and PMR at Week 12. The patterns of TMTV4 and SUV variations during tislelizumab treatment differed between pts with best metabolic response of CMR, PMR, and NMR. No differences in PK results were observed based on key baseline categorical variables (sex, age, B-symptoms, cohort 1/2, Ann Arbor stage, bulk, refractory vs relapse, IPS score, TMTV4, albumin level).

Summary/Conclusion: Central review of PET-CT imaging confirmed that tislelizumab is an effective therapeutic option for pts with R/R cHL, and efficacy may have been underestimated in the TIRHOL study. Tislelizumab PK and efficacy outcomes did not differ between baseline PET-CT metrics. OS was lower in pts with NMR at Week 12 compared with pts who had CMR or PMR. Analyses of centrally reviewed PET-CT imaging demonstrated a trend for underestimation of local response assessments, and therefore in ORR (70% vs. 66.7%) and CMR rate (40% vs. 31%)—likely due to the presence of non-lymphomatous inflammatory lesions. Variations in PET-CT parameters during anti-PD1 therapy should be interpreted with caution to avoid premature treatment discontinuation.