Abstract: S216

Title: CD47/PD-L1 BISPECIFIC ANTIBODY (IBI322) IN ANTI-PD-1 OR PD-L1 TREATMENT-RESISTANT CLASSICAL HODGKIN LYMPHOMA: A PHASE I STUDY

Abstract Type: Oral Presentation

Session Title: Hodgkin Lymphoma - Clinical

Background:

IBI322 is an anti-CD47/PD-L1 bispecific antibody that blocks both the PD-1/PD-L1 and CD47/SIRP-α pathways. By an "imbalanced" design with a lower binding affinity to CD47 and higher binding affinity to PD-L1, preclinical models showed IBI322 tended to bind CD47+PD-L1+ tumor cells rather than CD47+ cells, which could significantly reduce the toxicity to red blood cells. Despite the excellent efficacy of PD-1 or PD-L1 inhibitors and brentuximab vedotin (BV) in relapsed or refractory classical Hodgkin lymphoma (cHL), some patients (pts) still have disease progression. These pts have a poor prognosis and new treatment options are urgently needed.

Aims:

This phase I study is designed to evaluate the safety, tolerability and efficacy of IBI322 monotherapy in anti-PD-1 or PD-L1 treatment-resistant cHL pts.

Methods:

Eligible pts (18-75 years of age, ECOG PS 0-2) had histologically/cytologically confirmed cHL that was either primary resistant (best objective response was SD or PD after at least 2 doses) or secondary resistant (best objective response was CR, PR or SD and progressed or within 24 weeks of last dose) during anti-PD-1/PD-L1 treatment. Pts received IBI322 45mg/kg intravenously Q2W until unacceptable toxicity or documented disease progression, or for up to 24 months. The primary objectives of this study were to evaluate the safety and preliminary anti-tumor activity of IBI322 according to the Lugano 2014 criteria. Adverse events (AEs) were reported according to CTCAE v5.0.

Results:

Twenty-four cHL pts (median age: 35 years, range: 25-68 years; male: 17 (70.8%) pts; ECOG PS=0: 15 (62.5%) pts) who have failed anti-PD-1 or PD-L1 treatment were enrolled, 8 pts were primary resistant and 16 pts were secondary resistant. Among them, 4 pts progressed even after BV treatment. Among 23 cHL pts with at least one tumor assessment, the objective response rate (ORR) and disease control rate (DCR) were 47.8% (11/23; 95% CI: 26.8-69.4) and 91.3% (21/23; 95% CI: 72.0-98.9), respectively. For primary resistant pts, the ORR was as high as 57.1% (4/7; 95% CI: 18.4-90.1), and 3 pts achieved CR. For all 24 treated patients, treatment-related adverse events (TRAEs) of any grade occurred in 22 (91.7%) pts. The most frequent TRAEs (≥ 20%) were lymphocyte count decreased (n=15, 62.5%), anaemia (n=15, 62.5%), white blood cell count decreased (n=5, 20.8%) and platelet count decreased (n=5, 20.8%). Grade ≥3 TRAEs occurred in 10 (41.7%) pts, the most frequent grade ≥ 3 TRAEs (≥ 5%) was lymphocyte count decreased (n=7, 29.2%). Four (16.7%) pts experienced investigator-defined immune-related AEs (irAEs). No grade ≥ 3 irAEs occurred. No pt experienced TRAE leading to drug discontinuation or death. As of data cut-off date, 12 pts remained on IBI322 monotherapy.

Summary/Conclusion:

IBI322 monotherapy showed a promising anti-tumor effectivity with a manageable safety profile in anti-PD-1 or PD-L1 treatment-resistant classical Hodgkin Lymphoma patients.

Clinical trial information: NCT04795128

Keywords: Hodgkin's lymphoma, Resistance, Immune therapy