PHASE 3, RANDOMIZED, OPEN-LABEL STUDY OF PEMBROLIZUMAB (PEMBRO) VERSUS BRENTUXIMAB VEDOTIN (BV) FOR TREATMENT OF RELAPSED OR REFRACTORY CLASSICAL HODGKIN LYMPHOMA (R/R CHL): KEYNOTE-204

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Background

Patients (pts) with R/R cHL have few treatment options when they are no longer eligible for standard curative therapies. PD-1 blockade via pembro monotherapy has demonstrated antitumor activity and tolerable safety in these pts.

Aims

KEYNOTE-204 (NCT02684292) was an open-label, international, randomized, phase 3 study evaluating the efficacy and safety of pembro vs BV in R/R cHL.

Methods

Eligible patients were aged ≥18 years, had measurable disease and ECOG PS 0 or 1, and were post−autologous stem cell transplant (auto-SCT) or ineligible for auto-SCT. Pts who were BV-naive or -exposed were also eligible. Pts were randomized 1:1 to pembro 200 mg IV Q3W or BV 1.8 mg/kg IV Q3W. Randomization was stratified by status after 1L therapy (primary refractory vs relapsed <12 months vs relapsed ≥12 months after end of 1L therapy) and prior auto-SCT (yes vs no). Primary end points were PFS by blinded independent central review (BICR) per International Working Group (IWG) criteria including clinical and imaging data after auto-SCT or allogeneic SCT (allo-SCT) and OS. Key secondary end points were PFS excluding clinical and imaging data after auto-SCT or allo-SCT, ORR by BICR per IWG, PFS by investigator review per IWG, and safety. An exploratory end point was duration of response (DOR) by BICR per IWG.

Results

304 pts were randomized and 300 were treated (148 received pembro and 152 received BV). 256 pts discontinued. Median (range) time from randomization to data cut off was 25.7 (18.2-42.3) months. 15 (4.9%) pts received prior BV, 112 (36.8%) received prior auto-SCT, and 123 (40.5%) had primary refractory disease. Median (range) time on treatment was 305.0 (1-814) with pembro and 146.5 (1-794) days with BV; median (range) number of administrations were 15.0 (1.0-35.0) and 7.0 (1.0-35.0), respectively. 25 pts (16.9%) receiving pembro and 3 pts (2.0%) receiving BV completed 35 cycles of treatment. For the primary PFS analysis, statistically significant

improvement was observed with pembro vs BV (HR 0.65 [95% CI 0.48–0.88; *P*=0.00271]; median 13.2 vs 8.3 months); 12-month PFS rates were 53.9% vs 35.6%, respectively. All subgroups tested demonstrated benefit, including pts with primary refractory disease (HR=0.52), no auto-SCT (HR=0.61), prior BV (HR=0.34), and BV naive (HR=0.67). For the secondary PFS analysis, pembro exhibited improvement over BV (HR 0.62 [95% CI 0.46–0.85]; median 12.6 vs 8.2 months). PFS per investigator assessment was longer with pembro vs BV (HR 0.49 [95% CI 0.36–0.67]; median 19.2 vs 8.2 months). ORR for pembro was 65.6% and for BV was 54.2%; complete response rates were 24.5% and 24.2%, respectively. Median (range) DOR for pembro was 20.7 (0.0–33.2) months and for BV was 13.8 (0.0–33.9) months. 62.4% of pts on pembro and 50.0% of pts on BV had a response of ≥12 months. 74.3% of pts with pembro and 77.0% of pts with BV experienced a treatment-related adverse event (TRAE), most commonly hypothyroidism (15.5%) with pembro and peripheral neuropathy (18.4%) with BV. 19.6% of pts with pembro and 25.0% with BV had grade 3–5 TRAEs, most frequently pneumonitis (4.1%) in pts with pembro and neutropenia (7.2%) with BV. One death due to a TRAE (pneumonia) occurred in a pt receiving pembro.

Conclusion

Pembro was superior to BV in pts with R/R cHL and demonstrated across all subgroups statistically significant and clinically meaningful improvement in PFS. Safety was consistent with previous reports. These results support pembro monotherapy as the new standard of care for pts with R/R/cHL.

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