# EYNOTE-204：pembrolizumab 与 brentuximab vedotin 在复发或难治性经典霍奇金淋巴瘤(R/R cHL)中的随机、开放性、III 期研究。

**KEYNOTE-204: Randomized, open-label, phase III study of pembrolizumab (pembro) versus brentuximab vedotin (BV) in relapsed or refractory classic Hodgkin lymphoma (R/R cHL)**

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**背景：**通过 pembrolizumab（pembro）单药治疗阻断 PD-1 在 R/R cHL 中显示出了抗肿瘤活性。KEYNOTE-204（NCT02684292）是 pembro vs brentuximab vedotin（BV）治疗 R / R cHL 患者的一项国际性、随机、开放标签的 III 期研究。

**方法：**入组自体干细胞移植（auto-SCT）后或不符合 auto-SCT 条件的患者，年龄≥18 岁，有可测量的疾病和 ECOG PS 0 或 1。未接受过 BV

和已接受 BV 的患者均符合条件。患者以 1：1 的比例随机分配至 Pembro 200 mg IV Q3W 或 BV 1.8 mg / kg IV Q3W，并根据既往的 auto-SCT 史（是 vs 否）和一线治疗后的状态（原发难治性 vs 一线治疗后<12 月内复发 vs 一线治疗后≥12 月复发）进行分层。主要终点：按照国际工作组（IWG）的标准进行盲法独立中央评估（BICR）的无进展生存（PFS），包括自体 SCT 或异源 SCT（allo-SCT）和总体生存（OS）后的临床和影像学数据。关键的次要终点：PFS 不包括自体 SCT 或异源 SCT（次要 PFS）后的临床和影像学数据，以及每个 IWG 的 BICR ORR，每个 IWG 研究者评估的 PFS 和安全性。探索性终点：每个 IWG BICR 的 DOR。

**结果：**304 例患者参与随机分组，其中 300 例患者得到了治疗（148 例，pembro；152 例，BV）；256 例中途停药。中位随访：24.7（范围 0.6-42.3）个月。15 例患者接受 BV。pembro 和 BV 治疗的中位时间分别为 305.0（1-814）天和 146.5（1-794）天。Pembro vs BV 在主要 PFS 分析中观察到统计学上的显着改善（HR 0.65 [95％CI 0.48-0.88; P= 0.00271]；中位数为 13.2 vs 8.3 个月）；12 个月 PFS 率分别为 53.9％和 35.6％。在所有接受测试的亚组中均观察到获益，包括无自体 SCT（HR = 0.61）、原发性难治性疾病（HR = 0.52）、既往 BV 治疗（HR = 0.34）和首次 BV 治疗（HR = 0.67）的患者。Pembro vs BV 观察到 PFS 的继发性显着改善（HR 0.62 [95％CI 0.46-0.85]；中位数 12.6 vs 8.2 个月）。根据研究者的评估，pembro 与 BV 相比，PFS 延长（HR 0.49 [95％CI

0.36-0.67]；中位数 19.2 vs 8.2 mo）。pembro 和 BV 的 ORR 分别为为 65.6％和 54.2％；CR 率分别为 24.5％和 24.2％。对于 Pembro，DOR 中位值为 20.7 个月（0.0+至 33.2+），而 BV 为 13.8 个月（0.0+至 33.9+）。3-5 级 TRAE：pembro 的患者为 19.6％，BV 为 25.0％。pembro 组中有 1 例因 TRAE 导致的死亡（肺炎）。

**结论：**在 R / R cHL 患者单药治疗中，pembro 的获益优于 BV，并且在所有亚组中 PFS 均有统计学意义和临床意义的改善，其安全性与先前的报道一致。Pembro 单药治疗应该成为 R/R/cHL 患者的标准治疗方法。临床试验信息：NCT02684292

**原文摘要：**

**Abstract**

**Background:** PD-1 blockade via pembro monotherapy showed antitumor activity in R/R cHL. KEYNOTE-204 (NCT02684292) was a randomized, international, open-label, phase III study of pembro vs BV in R/R cHL.

**Methods:** Patients (pts) were aged ≥18 y, were post−autologous stem cell transplant (auto-SCT) or ineligible for auto-SCT, and had measurable disease and ECOG PS 0 or 1. BV-naive and BV-exposed pts were eligible. Pts were randomized 1:1 to pembro 200 mg IV Q3W or BV 1.8 mg/kg IV Q3W and stratified by prior auto-SCT (yes vs no) and status after 1L therapy (primary refractory vs relapsed <12 mo vs relapsed ≥12 mo

after end of 1L therapy). Primary end points: 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: PFS excluding clinical and imaging data after auto-SCT or allo-SCT (PFS-secondary), and ORR by BICR per IWG, PFS by investigator review per IWG, and safety. Exploratory end point: DOR by BICR per IWG.

**Results:** 304 pts were randomized and 300 were treated (148, pembro; 152, BV); 256 discontinued. Median (range) follow-up: 24.7 (0.6-42.3) mo. 15 pts were BV exposed. Median (range) time on treatment was 305.0 (1-814) and 146.5 (1-794) days with pembro and BV, respectively. Statistically significant improvement was observed with pembro vs BV for primary PFS analysis (HR 0.65 [95% CI 0.48-0.88; P =0.00271]; median 13.2 vs 8.3 mo); 12-mo PFS rates were 53.9% vs 35.6%, respectively. Benefit was observed in all subgroups tested, including pts with no auto-SCT (HR=0.61), primary refractory disease (HR=0.52), prior BV (HR=0.34) and BV naive (HR=0.67). Significant improvement in PFS-secondary was observed with pembro vs BV (HR 0.62 [95% CI 0.46-0.85]; median 12.6 vs 8.2 mo). Per investigator assessment, PFS was longer with pembro vs BV (HR 0.49 [95% CI 0.36-0.67]; median 19.2 vs 8.2 mo). ORR was 65.6% for pembro and 54.2% for BV; CR rates were 24.5% and 24.2%, respectively. Median (range) DOR was 20.7 mo (0.0+

to 33.2+) for pembro and 13.8 mo (0.0+ to 33.9+) for BV. Grade 3-5 TRAEs: 19.6% of pts with pembro and 25.0% with BV. One death due to TRAE occurred with pembro (pneumonia).

**Conclusions:** In pts with R/R cHL, pembro was superior to BV and demonstrated statistically significant and clinically meaningful improvement in PFS across all subgroups, with safety consistent with previous reports. Pembro monotherapy should be standard of care for this pt population with R/R/cHL. Clinical trial information: NCT02684292

参考文献：

Kuruvilla J, Ramchandren R, Santoro A, Paszkiewicz-Kozik E, Gasiorowski R, Johnson N, Melnichenko V, Fogliatto LM, Goncalves I and de Oliveira J, et al: KEYNOTE-204: Randomized, open-label, phase III study of pembrolizumab (pembro) versus brentuximab vedotin (BV) in relapsed or refractory classic Hodgkin lymphoma (R/R cHL). J CLIN ONCOL 38: 8005, 2020.