新型抗 PD-1 单克隆抗体 Gls-010，用于中国复发或难治性经典型霍奇金淋巴瘤（cHL）患者 II 期临床试验的初步结果

Gls-010, a novel anti-PD-1 mAb in Chinese patients with relapsed or refractory classical Hodgkin lymphoma: Preliminary impressive result of a phase II clinical trial.

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背景：经典型霍奇金淋巴瘤（cHL）的特征是 9p24・1 基因片段的遗传改变和 PD-L1 配体的过度表达。GLS-010 是新型的全人源抗 PD-1 单克隆抗体，在此前的 I 期研究中显示出良好的活性。这项多中心单臂 II 期临床试验旨在进一步评估 GLS-010 在中国复发性或难治性 cHL 患者中的安全性和有效性。

方法：所有入选的患者每 2 周接受 GLS-010 240mg，直到疾病进展、死亡、出现不可接受的毒性或退出研究为止。主要终点是根据 Lugona 2014 独立评估委员会（IRC）评估的客观缓解率（ORR）。根据 NCI CTCAE v4.03 分级的不良事件（AEs）。

结果：85 名先前至少接受过二线系统化疗的复发或难治性 cHL 患者入组并接受治疗。数据截止至 2019 年 8 月 2 日，患者接受治疗周期的中位数为 8 个（1 个周期包括 2 次注射），其中 12 名患者中断治疗，而 73 名患者仍在治疗中。在中位随访时间为 6.57 个月时，通过 IRC 评估报告了 85 例患者中的 78 例（91.76％，95％CI，83.77-96.62）的 ORR，其中 30 例（35.3％）达到完全缓解（CR ）和 48 例（56.5％）部分缓解（PR）。尚未达到中位缓解持续时间（DoR）和无进展生存期（PFS）。85 名患者中有 77 名（90.6％）发生了任何级别的治疗相关不良事件（TRAE），其中大多数为 1-2 级。最常见的 TRAE 是发热（26/85，30.6％），中性粒细胞计数降低（ 16/85，18.82％）和白细胞计数下降（15/85，17.65％）。23 例（27.06％）发生 3 级 TRAE，最常见的是肝功能异常（5/85，5.88％）和高尿酸血症（4/85，4.71％）。

结论：GLS-010 在中国复发或难治性 cHL 患者中显示出令人印象深刻的抗肿瘤活性（ORR = 91.96％）和可控的安全性，GLS-010 可能是在这类患者一种新的安全有效的治疗选择。临床试验信息：NCT03655483

原文摘要

Abstract

Background: classical Hodgkin lymphoma (cHL) are characterized by

genetic alterations at the 9p24 •1 locus and PD-L1 ligand overexpression. GLS-010 is a novel fully human anti-PD-1 mAb and exhibited favorable result in previous Phase I study. This multi-center, single-arm Phase II clinical trial is aimed to further evaluate the safety and efficacy profile of GLS-010 in Chinese patients (pts) with relapsed or refractory cHL.

Methods: All pts enrolled received GLS-010 240mg every 2 weeks until disease progression, death, unacceptable toxicity or withdraw from the study. The primary endpoint was objective response rate (ORR) by independent review committee (IRC) per Lugona 2014. Adverse events (AEs) were graded by NCI CTCAE v4.03.

Results: 85 pts with relapsed or refractory cHL who had received at least 2 lines of prior systemic chemotherapies were enrolled and treated. As of August 2 2019, data cutoff, pts received a median of 8 treatment cycles (1 cycle include 2 injections), with 12 pts discontinued and 73 pts were still in treatment. At a median follow-up of 6.57 months, an ORR was reported in 78 of 85 patients (91.76%, 95%CI, 83.77-96.62), by an IRC assessment, including 30(35.3%) pts with a complete response (CR) and 48 pts (56.5%) with a partial response (PR). Median duration of response (DoR) and progression free survival (PFS) were not reached yet. Treatment-related adverse events (TRAEs) of any grade occurred in 77 (90.6%) of 85 patients, most of which were Grade 1-2.The most common TRAEs were fever (26/85, 30.6%), neutrophil count decreased (16/85,

18.82%), white blood cell count decreased (15/85, 17.65%). ≥ Grade 3 TRAEs occurred in 23 (27.06%) pts, most commonly, hepatic function abnormal (5/85, 5.88%), hyperuricaemia (4/85, 4.71%).

Conclusions: GLS-010 showed impressive anti-tumor activity (ORR = 91.96%) and manageable safety profile in Chinese patients with relapsed or refractory cHL, which could be a new safe and effective treatment option in this setting. Clinical trial information: NCT03655483

参考文献：

Song Y, Zhu J, Lin N, Zhang M, Bai H, Liu H, Cui J, Ke X, Zhang H and Liu L, et al: Gls-010, a novel anti-PD-1 mAb in Chinese patients with relapsed or refractory classical Hodgkin lymphoma: Preliminary impressive result of a phase II clinical trial. J CLIN ONCOL 38: 8033, 2020.