前言

2020 年 5 月 13 日，美国临床肿瘤学会（ASCO®）2020 年会公布了研究摘要，在淋巴瘤治疗领域，多种新药的研究成果获得关注，其中来那度胺治疗惰性淋巴瘤的多项研究最新数据公布。来那度胺的化学结构与沙利度胺相似，具有抗肿瘤、免疫调节和抗血管生成等多重作用，由我国自主创新药企百济神州研发。百济神州在2018年2月宣布来那度胺获得中国药品监督管理局(NMPA)批准与地塞米松合用，治疗此前未经治疗且不适合接受移植的多发性骨髓瘤(MM)成年患者。此前另一获批适应症为骨髓异常综合症，用于具有 5q 缺失细胞遗传学异常的骨髓增生异常综合征所致的输血依赖性再生障碍性贫血患者的治疗。现将 ASCO 2020 摘要中泽布替尼最新临床数据整理报道如下。

那度胺联合 R-GDP（R2-GDP）在复发/难治性弥漫性大 B 细胞淋巴瘤中的作用：R2-GDP-GOTEL 试验的最终结果

受新型冠状病毒肺炎疫情影响，作为全球肿瘤领域的年度盛会，今年的美国临床肿瘤学会（ASCO）年会改为线上模式，于 2020 年 5 月 29 日顺利召开。 2020 ASCO 摘要已公布，今年各个领域又有哪些新亮点？大医编将以专题的形式，定期推送，带大家一览为快！

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Lenalidomide plus R-GDP (R2-GDP) in relapsed/refractory diffuse large B-cell lymphoma: Final results of the R2-GDP-GOTEL trial.

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背景：来那度胺是一种免疫调节药物，可以逆转淋巴瘤患者的利妥昔单抗耐药性。研究团队进行了一项开放标签的多中心 2 期试验，评估来那度胺和利妥昔单抗（R2）联合 GDP（吉西他滨+顺铂+地塞米松）方案（R2-GDP）在不符合自体干细胞移植（ASCT）条件的复发/难治性弥漫性大 B 细胞淋巴瘤（R / R DLBCL）病人中的疗效和药物毒性。

方法：纳入先前接受过至少 1 项免疫化疗方案（包含利妥昔单抗）治疗的 R / R DLBCL 患者（不符合 ASCT 条件）。在试验导入期（run-in phase）结束后，诱导期给予来那度胺（LEN）口服 10 mg d1-14，利妥昔单抗 375 mg / m^2 iv d1，顺铂 60 mg / m^2 iv d1，吉西他滨 750 mg / m^2 iv d1 和 d8 和地塞米松 20 mg d1-3 治疗，最多达 6 个周期。无疾病进展（DP）的患者进入维持期，每 28 天为一个周期，给予 LEN 10 mg 或用诱导期最后一次的 LEN 剂量，d1-21。主要终点是研究者评估的客观缓解率（ORR）。次要终点包括无病生存期（DFS），无事件生存期（EFS），总体生存期（OS），来源细胞安全性和反应性（COO），DLBCL 类型(double-triple hit，二次或三次打击)和其他微环境和基因组生物标志物。

结果：2015 年 4 月至 2018 年 9 月间共入组 79 例患者。中位年龄为 70 岁（范围 23-86），其中女性占 48.7％。在意向性治疗（ITT）分析中评估了 78 位病人的疗效和安全性。截止到 2019 年 11 月，中位随

访时间为 13 个月，ORR 为 59.0％，完全缓解（CR）率为 32.1％，部分缓解（PR）率为 26.9％。在原发性难治性人群（n = 33）中，ORR 为 45.5％，CR 为 21.2％，PR 为 24.3％。COO，ORR 没有统计学上的显着差异。在二次打击 R / R DLBCL（n = 16）中，ORR 为 37.5％，CR 为 25％。OS 中位数为 12.0 个月（6.9-17.0）。最常见的 3/4 级不良事件为血小板减少症（60.2％），中性粒细胞减少症（60.2％）和贫血（26.9％）。发热性中性粒细胞减少症发生率为 14.1％。最常见的非血液 3/4 级事件为乏力（19.2％），感染（15.3％）和肾功能不全（6.4％）。4 例中毒死亡与 R2-GDP 方案有关。

结论：来那度胺和利妥昔单抗（R2）联合 GDP 方案在复发/难治性弥漫性大 B 细胞淋巴瘤中是可行和有效的，在原发性难治性 DLBCL 人群中的结果尤其令人期待。对 COO 的分析未显示缓解率的差异。免疫生物标志物的结果将在会议上公布。临床试验信息：EudraCT 2014-001620-29

原文摘要：

Abstract

Background: Lenalidomide is an immunomodulatory drug that could reverse rituximab refractoriness in lymphoma patients (pts). We conducted an open label multicenter phase 2 trial testing the efficacy and toxicity of a combination of lenalidomide and rituximab (R2) plus

GDP schedule (R2-GDP) in Relapsed/Refractory Diffuse Large B Cell Lymphoma (R/R DLBCL) pts, not suitable for autologous stem cell transplant (ASCT).

Methods: Patients with R/R DLBCL previously treated with at least 1 prior line of immunochemotherapy including rituximab, and not candidates for ASCT, were eligible. After a run-in phase period, treatment consisted of an induction phase with lenalidomide (LEN) 10 mg po d1-14, rituximab 375 mg/m2 iv d1, cisplatin 60 mg/m2 iv d1, gemcitabine 750 mg/m2 iv d1 and d8 and dexamethasone 20 mg d1-3, up to a maximum of 6 cycles. Pts without disease progression (DP) entered into a maintenance phase with LEN 10 mg, or last LEN dose received in the induction phase, d1-21 in cycles every 28 days. Primary endpoint was overall response rate (ORR) by investigator assessment. Secondary endpoints included disease free survival (DFS), event free survival (EFS), overall survival (OS), safety and response by cell of origin (COO), type of DLBCL (double-triple hit) and other microenvironment and genomic biomarkers.

Results: 79 pts were enrolled between April 2015 and September 2018. Median age was 70 years (range 23-86), 48,7% women. 78 pts were considered for efficacy and safety in the intention to treat (ITT) analysis. With a median follow-up of 13 months at the time of cut-off (November 2019), ORRwas 59.0%, with 32.1% complete responses (CR) and 26.9%

partial responses (PR). In the primary refractory population (n = 33), ORR was 45.5%, with 21.2% CR and 24.3% PR. There were no statistically significant differences in ORR with respect to COO. In Double-Hit R/R DLBCL (n = 16), ORR was 37.5% with 25% CR. Median OS was 12.0 months (6.9-17.0). Most common grade 3/4 (G3/4) adverse events were thrombocytopenia (60.2%), neutropenia (60.2%) and anemia (26.9%). Febrile neutropenia occurred in 14.1% pts. Most frequent non-hematologic G3/4 events were asthenia (19.2%), infection (15.3%) and renal insufficiency (6.4%). There were 4 toxic deaths related to the R2-GDP schedule.

Conclusions: LEN with Rituximab and GDP (R2-GDP) is feasible and active in R/R DLBCL. Results in the primary refractory DLBCL population are particularly promising. Analysis of COO did not revealed differences in response rates. Immune biomarkers results will be showed at the meeting. Clinical trial information: EudraCT 2014-001620-29

参考文献：

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