R^2 诱导后维持治疗复发/难治性惰性 NHL 的 MAGNIFY IIIb 期研究中期分析

MAGNIFY phase IIIb interim analysis of induction R2 followed by maintenance in relapsed/refractory indolent NHL

David Jacob Andorsky, Morton Coleman, Abdulraheem Yacoub, Jason M. Melear, Suzanne R. Fanning, Kathryn S. Kolibaba, Frederick Lansigan, Chris Reynolds, Grzegorz S. Nowakowski, Mecide Gharibo, Jung Ryun Ahn, Ju Li, Mathias J. Rummel, Jeff P. Sharman, on behalf of the MAGNIFY Trial Investigators

背景：复发性惰性非霍奇金淋巴瘤（iNHL）患者的标准治疗方案有限。一项研究显示免疫调节剂来那度胺能增强利妥昔单抗（即 R^2）的活性，该研究近期报道复发/难治性（R / R） iNHL 患者的中位无进展生存期（PFS）为 39.4 个月（AUGMENT; J Clin Oncol.2019 ; 37：1188）。

方法：MAGNIFY 是一项在进展期 1-3a 级复发/难治性滤泡性淋巴瘤（R/R FL）gr1-3a，边缘区淋巴瘤（MZL）或套细胞淋巴瘤(MCL)患者中探索来那度胺的最佳持续时间的多中心、IIIb 期临床试验（NCT01996865）。先给与给予 1 个疗程的来那度胺 20 mg/d（第 1~21 天，每 28 天 1 个疗程），同时联合利妥昔单抗 375 mg/m^2/w，1 个

疗程。然后继续给药 q8wk 3 个疗程 +（R²）12 疗程。随后按 1:1 比例随机将稳定（SD）、部分缓解（PR）或完全缓解（CR）的患者分配给予 R² 或利妥昔单抗维持治疗 18 个月。本文提供的数据集中于在基线/基线后接受≥1 次治疗疗效可评估的 FL 和 MZL 患者（不包括 MCL）中的 R² 诱导，分析主要终点为以 1999 IWG 为标准的客观缓解率（ORR）。

结果：截至 2019 年 6 月 16 日，共有 393 例患者（81% FL gr1-3a；19%MZL）入组，中位随访时间为 23.7 个月（范围 0.6-57.8）（n=335）。随访患者中位年龄为 66 岁（范围：35-91 岁），其中 83％患有 III / IV 期疾病，既往疗法中位数为 2 （95％以前用过利妥昔单抗）。ORR 为 69％，CR / CRu 为 40％（如下表）。缓解持续时间(DOR)中位数为 39.0 个月，PFS 中位数为 40.1 个月。199 例（51%）完成了 12 个疗程的 R²，188 例（48%）随机进入维持治疗。139 例患者（35%）提前中断了来那度胺和利妥昔单抗治疗，主要原因是 AE（n=52,13%）或 PD（n=45,11%）。最常见的 AE 包括疲劳 48％，中性粒细胞减少 43％，腹泻 36％，恶心 31％和便秘 30％。36％出现 3/4 级 AE 中性粒细胞减少（9 例[2％]有发热性中性粒细胞减少）；所有其他 3/4 级 AE 发生率<7%。

结论：R² 在 R/R FL 和 MZL 患者具有可接受的安全性，包括利妥昔单抗耐药、双重难治性和早期复发患者

。临床试验信息：NCT01996865

	ORR, %	CR/CRu, %	DOR, median (95% CI), mo	PFS, median (95% CI), mo*
Overall	69	40	39.0 (36.8-NR)	40.1 (37.6-NR)
Histology FL	70	41	NR (36.8-NR)	39.4 (30.0-NR)
MZL	63	38	38.6 (29.4-NR)	41.2 (38.4-NR)
R-refractory Yes	60	36	35.8 (35.2-NR)	25.9 (18.1-41.6)
No	73	43	NR (38.4-NR)	41.2 (39.4-NR)
Double refractory Yes†	50	26	20.1 (14.6-NR)	17.7 (10.7-23.0)
No	73	44	39.0 (38.4-NR)	41.6 (39.4-NR)
Early relapse Yes‡	66	31	35.8 (22.4-NR)	26.5 (18.1-41.6)
No	70	45	NR (38.4-NR)	41.2 (39.4-NR)

上图：在 R/R iNHL 中 R^2 诱导的效果

原文摘要：

Abstract

Background: Patients (pts) with relapsed iNHL have limited standard treatment options. The immunomodulatory agent lenalidomide shows enhanced activity with rituximab (ie, R^2), which recently reported 39.4-mo median PFS in R/R iNHL pts (AUGMENT; J Clin Oncol. 2019;37:1188). **Methods:** MAGNIFY is a multicenter, phase IIIb trial in pts with R/R FL gr1-3a, MZL, or MCL (NCT01996865) exploring optimal lenalidomide duration. Lenalidomide 20 mg/d, d1-21/28 + rituximab 375 mg/m2/wk c1 and then q8wk c3+ (R^2) are given for 12c followed by 1:1

randomization in pts with SD, PR, or CR to R2 vs rituximab maintenance for 18 mo. Data presented here focus on induction R^2 in efficacy-evaluable FL and MZL pts (MCL not included) receiving $\geqslant$ 1 treatment with baseline/post-baseline assessments to analyze the primary end point of ORR by 1999 IWG criteria.

Results: As of June 16, 2019, 393 pts (81% FL gr1-3a; 19% MZL) were enrolled with a median follow up of 23.7 mo (range, 0.6-57.8) for censored pts (n = 335). Median age was 66 y (range, 35-91), 83% had stage III/IV disease, with a median of 2 prior therapies (95% prior rituximab-containing). ORR was 69% with 40% CR/CRu (Table). Median DOR was 39.0 mo, and median PFS was 40.1 mo. 199 pts (51%) have completed 12c of R^2, and 188 (48%) have been randomized and entered maintenance. 139 pts (35%) prematurely discontinued both lenalidomide and rituximab, primarily due to AEs (n = 52, 13%) or PD (n = 45, 11%). Most common all-grade AEs were 48% fatigue, 43% neutropenia, 36% diarrhea, 31% nausea, and 30% constipation. Grade 3/4 AE neutropenia was 36% (9 pts [2%] had febrile neutropenia); all other grade 3/4 AEs occurred in < 7% of pts.

Conclusions: R^2 is active with a tolerable safety profile in pts with R/R FL and MZL, including rituximab-refractory, double-refractory, and early relapse pts. Clinical trial information: NCT01996865

参考文献：

Andorsky DJ, Coleman M, Yacoub A, Melear JM, Fanning SR, Kolibaba KS, Lansigan F, Reynolds C, Nowakowski GS and Gharibo M, et al: MAGNIFY phase IIIb interim analysis of induction R2 followed by maintenance in relapsed/refractory indolent NHL. J CLIN ONCOL 38: 8046, 2020.