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来那度胺在淋巴瘤中的研究

来那度胺联合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

8019 Poster Discussion Session; Displayed in Poster Session (Board #352), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Lenalidomide plus R-GDP (R2-GDP) in relapsed/refractory diffuse large B-cell lymphoma: Final results of the R2-GDP-GOTEL trial. *First Author: Luis de la Cruz Merino, Clinical Oncology Department, Hospital Universitario Virgen Macarena, Seville, Spain*

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. Research Sponsor: CELGENE.

RE-MIND研究:以倾向评分为基础的1:1配对比较tafasitamab + 来那度胺 (L-MIND)与来那度胺单药治疗(真实数据)在不符合移植条件的复发/难治性弥漫性大b细胞淋巴瘤(DLBCL)患者中的应用

8020 Poster Discussion Session; Displayed in Poster Session (Board #353), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

RE-MIND study: A propensity score-based 1:1 matched comparison of tafasitamab + lenalidomide (L-MIND) versus lenalidomide monotherapy (real-world data) in transplant-ineligible patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL). *First Author: Grzegorz S. Nowakowski, Division of Hematology, Mayo Clinic, Rochester, MN*

Background: Patients with R/R DLBCL ineligible for autologous stem cell transplant (ASCT) have a poor prognosis. In these patients, tafasitamab (anti-CD19 antibody) plus lenalidomide (LEN) has shown encouraging results in the open-label, single-arm, phase II L-MIND study (n = 81; NCT02399085). To evaluate the contribution of tafasitamab to the activity of this doublet, we conducted a global, real-world study of patients treated with LEN monotherapy (RE-MIND; NCT04150328). Here we present the primary analysis of a 1:1 patient-level matched comparison between the L-MIND and RE-MIND cohorts. **Methods:** Patients treated with LEN monotherapy for R/R DLBCL were enrolled in the observational, retrospective RE-MIND cohort. As in L-MIND, patients had 1–3 prior systemic therapies, including ≥1 CD20-targeting regimen; were aged ≥18 years; and were not eligible for ASCT. A 1:1 estimated propensity score (ePS) matching methodology ensured balancing of nine pre-specified baseline covariates. The primary analysis set, Matched Analysis Set 25 (MAS25), included patients who received a LEN starting dose of 25 mg/day. The primary endpoint was investigator-assessed best objective response rate (ORR). Key secondary endpoints included overall survival (OS) and complete response (CR) rate. **Results:** 490 patients were enrolled in RE-MIND across 58 centers in the US and Europe, of which 140 fulfilled the ePS matching criteria. The MAS25 included 76 patients each from the two cohorts. Baseline characteristics between cohorts were comparable. The primary endpoint was met with a significantly better ORR of 67.1% (95% CI: 55.4–77.5) for the L-MIND cohort versus 34.2% (95% CI: 23.7–46.0) for the RE-MIND cohort (odds ratio 3.89; 95% CI: 1.90–8.14; $p < 0.0001$). The CR rate was 39.5% (95% CI: 28.4–51.4) in the L-MIND cohort and 13.2% (95% CI: 6.5–22.9) in the RE-MIND cohort. A significant difference in OS favored the L-MIND cohort (HR = 0.499; 95% CI: 0.317–0.785). ORR and CR outcomes in the RE-MIND cohort were similar to the published literature for LEN monotherapy in R/R DLBCL. **Conclusions:** Significantly better ORR, CR and OS indicate potential synergistic effects of the tafasitamab + LEN combination in ASCT-ineligible R/R DLBCL. ePS-based 1:1 matching allows robust estimation of the treatment effect of tafasitamab when added to LEN. RE-MIND demonstrates the utility of real-world data in interpreting non-randomized trials. Clinical trial information: NCT04150328. Research Sponsor: MorphoSys AG.

R²诱导、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 R^2 followed by maintenance in relapsed/refractory indolent NHL. *First Author: David Jacob Andorsky, Rocky Mountain Cancer Centers/The US Oncology Network, Boulder, CO*

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/m^2/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 R^2 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 ≥ 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. Research Sponsor: Bristol-Myers Squibb, Summit, NJ.

Efficacy for induction R^2 in R/R iNHL.

	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)

*If pts in maintenance at cutoff, response assessments also contributed to PFS †Refractory to both rituximab (monotherapy or combo) and alkylating agent ‡Progressed or relapsed ≤ 2 y of initial diagnosis after 1L systemic treatment

R-ICE (利妥昔单抗-异环磷酰胺-卡铂-依托泊苷)联合来那度胺(R2-ICE)在首次复发/原发性难治弥漫性大B细胞淋巴瘤(DLBCL)患者中的I/II期研究。

Phase I/II study of R-ICE (rituximab-ifosfamide-carboplatin-etoposide) with lenalidomide (R2-ICE) in patients with first-relapse/primary refractory diffuse large B-cell lymphoma (DLBCL) in academic and community cancer research united (ACCRU) network. *First Author: Francis Guerra-Bauman, Mayo Clinic, Rochester, MN*

Background: Response rates to salvage immunochemotherapy in patients with DLBCL relapsing after or refractory (R/R DLBCL) to front line therapy remain unsatisfactory. Lenalidomide (Len) has significant single agent activity in relapsed/refractory DLBCL. The addition of lenalidomide (Len) days 1-7 to rituximab plus ifosfamide-carboplatin-etoposide (RICE) was shown to be feasible with promising efficacy in phase 1b study (Feldman T, et al. BJH, 2014). We developed phase I/II study to evaluate the safety and efficacy of the addition of Len (extended to 14 day schedule) to RICE (R2-ICE) for R/R-DLBCL patients who are candidates for stem cell transplant. **Methods:** The phase I portion was designed to determine the maximally tolerated dose Len in combination with RICE using the standard cohort 3+3 design. The escalation dose levels were 15 mg and 20 mg daily x 14 days. Prophylactic aspirin and growth factor support is mandatory. After 2 cycles of therapy response is evaluated with a PET/CT scan; the responding patients are eligible for 1-2 additional cycles of R2ICE as a bridging before HDC/SCT. The estimated overall response rate for two cycles of R-ICE in R/R DLBCL to RCHOP was estimated to be approximate 45%. We hypothesize that the addition of lenalidomide in the relapse setting could increase the overall response rate by approximately 20%. The one-stage design with an interim analysis being utilized in phase 2 requires 45 evaluable patients (one sided alpha = 0.09, power 90%). For Phase I, all types of B-cell lymphomas were eligible. For phase II portion only DLBCL patients are eligible per central pathology review. Other eligibility criteria include: received one line of previous anti-lymphoma therapy, ≥ 2 weeks from completion of prior anti-lymphoma therapy, candidate for HDC and SCT, adequate organ (creatinine clearance ≥ 60ml/min by Cockcroft-, total bilirubin ≤ 2 × ULN) and bone marrow function (ANC) ≥1500/mm^3; platelet count ≥75,000/mm3). The use of steroids and/or rituximab up to 1 week prior to registration for management of symptoms is allowed. 9 patients cleared phase 1 without DLT and dose of 20 mg days 1 -14 was recommend for phase 2 part (RP2D) of the study. The phase 2 study passed interim futility analysis and accrual continues. Correlatives include cell of origin by Nanostring, Myc/bcl2 expression and by FISH and minimal residual disease. PET scans are centrally reviewed including metabolic tumor volume. Clinical trial information: NCT02628405. Research Sponsor: Celgene/BMS.