MAGNIFY phase 3B study of lenalidomide + rituximab (R^2) followed by maintenance in relapsed/refractory indolent non-Hodgkin lymphoma: complete induction phase analysis

Frederick Lansigan, MD,[1] David Jacob Andorsky, MD,[2] Morton Coleman, MD, FACP,[3] Abdulraheem Yacoub, MD,[4] Jason M. Melear, MD,[5] Suzanne R. Fanning, DO,[6] Kathryn S. Kolibaba, MD,[7] Chris Reynolds, MD,[8] Grzegorz S. Nowakowski, MD,[9] Mecide Gharibo, MD,[10] Jung Ryun Ahn, MD,[10] Ju Li, PhD,[10] Mathias J. Rummel, MD, PhD,[11] and Jeff P. Sharman, MD,[12] on behalf of the MAGNIFY Trial Investigators

[1]Dartmouth–Hitchcock Medical Center, Lebanon, NH, USA; [2]Rocky Mountain Cancer Centers, US Oncology Research, Boulder, CO, USA; [3]Clinical Research Alliance Inc, Weill Cornell Medicine, New York, NY, USA; [4]University of Kansas Cancer Center, Westwood, KS, USA; [5]Texas Oncology – Austin, US Oncology Research, Austin, TX, USA; [6]Prisma Health, US Oncology Research, Greenville, SC, USA; [7]US Oncology Research, Vancouver, WA, USA; [8]IHA Hematology Oncology Consultants – Ann Arbor, Ypsilanti, MI, USA; [9]Mayo Clinic, Rochester, MN, USA; [10]Bristol Myers Squibb, Princeton, NJ, USA; [11]Justus-Liebig Universität, Giessen, Germany; [12]Willamette Valley Cancer Institute and Research Center, US Oncology Research, Eugene, OR, USA

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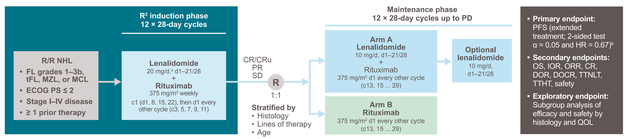
Introduction

- Patients with relapsed indolent non-Hodgkin lymphoma (iNHL) have limited standard treatment options
- iNHL is often initially responsive to chemoimmunotherapy but is considered incurable, and standard treatment options are lacking for patients with relapsed/refractory (R/R) iNHL[1-3]
- Patients with follicular lymphoma (FL) and marginal zone lymphoma (MZL) make up ~35% and ~10% of NHL cases, respectively[4,5]
- The AUGMENT trial showed that combining the immunomodulatory agent lenalidomide with rituximab (R^2) resulted in enhanced activity versus rituximab alone (median progression-free survival [PFS], 39.4 mo vs 14.1 mo) in R/R iNHL[6]

Patients and methods

- MAGNIFY (NCT01996865) is a phase 3b randomized, open-label, multicenter study of R^2 initial treatment followed by R^2 versus rituximab extended treatment in patients with R/R FL, MZL, and mantle cell lymphoma (MCL) (**Figure 1**)

Figure 1. MAGNIFY study design



NCT01996865.
c, cycle; CR, complete response; CRu, complete response unconfirmed; d, day; DOCR, duration of CR/CRu; DOR, duration of response; IOR, improvement of response; ORR, overall response rate; OS, overall survival; PD, progressive disease; PR, partial response; PS, performance status; QOL, quality of life; SD, stable disease; tFL, transformed FL; TTHT, time to histological transformation; TTNLT, time to next antilymphoma treatment.
[a]Lenalidomide is administered at 10 mg if creatinine clearance is > 30 to < 60 mL/min.
[b]Assessed per CT/MRI and 1999 International Working Group (IWG) criteria with modifications to include extranodal disease.
Data cutoff March 5, 2021.

- Data presented here are the complete analysis from the induction phase in patients with FL grades 1–3a or MZL (FL grade 3b, tFL, and MCL not included)
- The focus of this current interim analysis was ORR, DOR, PFS, and safety
- Response was assessed by 1999 IWG criteria

Results

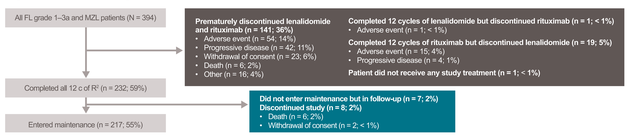
- As of March 5, 2021, 394 patients with FL grades 1–3a and MZL had enrolled in the initial treatment period of MAGNIFY
- At the time of enrollment, patients had a median age of 66 years (range, 35–91) (**Table 1**)
- Most had an ECOG PS of 0 to 1 (n = 385, 98%) and stage III/IV disease at study entry (n = 328, 83%)
- Patients received a median of 2 prior systemic treatments (range, 1–8), and 94% received prior rituximab-containing regimens (**Table 2**)
- 36% were considered rituximab refractory defined as having a best response of PD or SD to rituximab-containing regimen or a response lasting < 6 months after last rituximab dose
- 22% were considered double refractory defined as being refractory to both rituximab and an alkylating agent
- 34% were considered early relapse defined as progressing or relapsing within 2 years of initial diagnosis
- Median follow-up time was 40.6 months (range, 0.6–79.6)
- 59% of patients (n = 232) have completed 12 cycles of initial treatment, and 55% (n = 217) have proceeded to maintenance treatment (**Figure 2**)
- The best overall response during R^2 induction was 71% with 42% achieving a CR or CRu (**Figure 3**)
  - R^2 showed clinical activity in patients with FL or MZL histology and those refractory to rituximab, double refractory, or with early relapse (**Figure 3**)
  - Responses were deep with the majority of patients achieving greater than 50% reduction from baseline in target lesion tumor burden (**Figure 4**)
  - Median time to response in all patients was 2.8 mo (range, 0.5–17.2)

Table 1. Baseline patient characteristics

Characteristic, n (%)	Overall (N = 394)
Age, median (range), y ≥ 65 y	66 (35–91) 221 (56)
Male	210 (53)
ECOG PS at enrollment 0 1 2	 193 (49) 192 (49) 9 (2)
Positive bone marrow involvement	123 (31)
Ann Arbor disease stage at enrollment I/II III IV	 66 (17) 99 (25) 229 (58)
Bulky disease[a]	161 (41)
FL Grade 1 Grade 2 Grade 3a	318 (81) 116 (29) 147 (37) 55 (14)
MZL MALT[b] Nodal Splenic	76 (19) 15 (4) 44 (11) 17 (4)

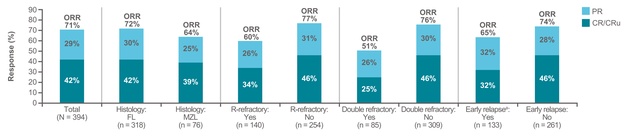
Data cutoff March 5, 2021.
MALT, extranodal MZL of mucosa-associated lymphoid tissue.
[a]Defined as a nodal or extranodal (except spleen) mass > 7 cm in greater diameter or involvement of at least 3 nodal or extranodal sites (each with a diameter > 3 cm).
[b]Three patients had gastric MALT.

Figure 2. Consort diagram



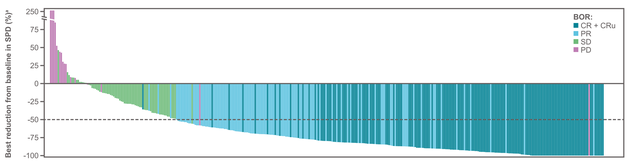
Data cutoff March 5, 2021.

Figure 3. Best overall response in R^2 induction treatment phase



Data cutoff March 5, 2021.
[a]ORR may not equal PR + CR due to rounding.

Figure 4. Change in tumor burden by best overall response



Data cutoff March 5, 2021.
[a]4 patients had change > 100%.
BOR, best overall response; SPD, sum of the products of diameters.

Table 2. Treatment history

Characteristic, n (%)	Overall (N = 394)
Prior lines of antilymphoma treatment, median (range)	2 (1–8)
Prior therapies Rituximab containing Rituximab + chemotherapy Rituximab monotherapy	 372 (94) 289 (73) 159 (40)
Rituximab refractory[a]	140 (36)
Double refractory[b]	85 (22)
Early relapse[c]	133 (34)

Data cutoff March 5, 2021.
[a]Defined as a best response of PD or SD to treatment with rituximab or a rituximab-containing regimen or a response (PR or CR) lasting < 6 months following the last rituximab dose.
[b]Defined as patients who are refractory to both rituximab (as monotherapy or combination therapy) and an alkylating agent.
[c]Defined as patients who progressed or relapsed within 2 years of initial diagnosis after first-line systemic treatment.

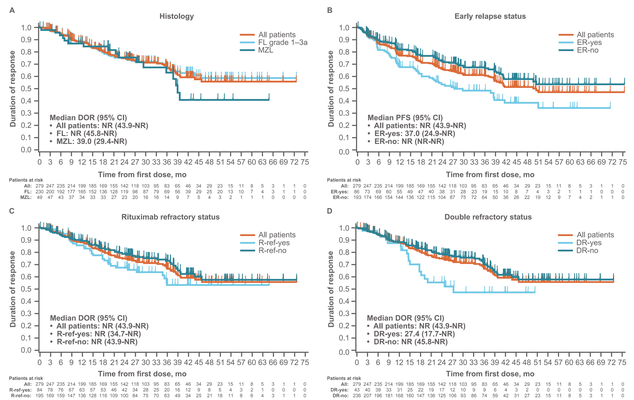
Table 3. Dose modifications due to TEAEs

Patients with ≥ 1 TEAE leading to dose modification in induction period, n (%)	Overall (N = 393)
Early lenalidomide discontinuation	75 (19)
Early rituximab discontinuation	46 (12)
Lenalidomide dose reduction/interruption	252 (64)
Rituximab dose interruption	116 (30)

Data cutoff March 5, 2021.
TEAE, treatment-emergent adverse event.

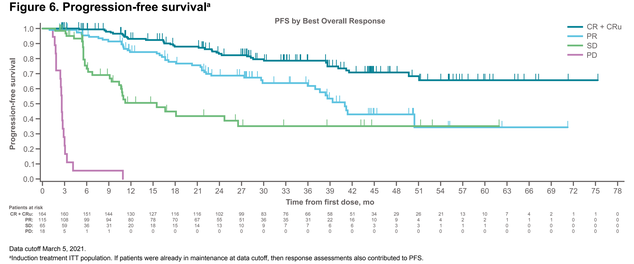
- Median DOR was not reached (NR) for all patients (**Figure 5A**)
  - Median DOR was NR for patients with FL and was 39.0 mo for patients with MZL (**Figure 5A**)
  - Median DOR was 37.4 mo for patients with early relapse (**Figure 5B**), NR for patients rituximab refractory (**Figure 5C**), and 27.4 mo for patients double refractory (**Figure 5D**)

Figure 5. Duration of response[a]



Data cutoff March 5, 2021.
[a]Induction treatment ITT population. If patients were already in maintenance at data cutoff, then response assessments also contributed to DOR.
DR, double relapse; ER, early relapse; R-ref, rituximab refractory.

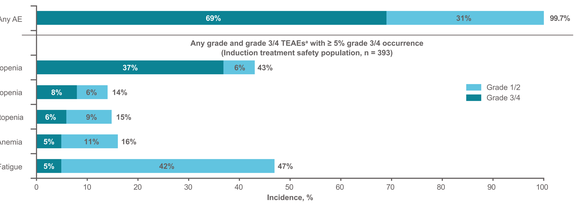
Figure 6. Progression-free survival[a]



Data cutoff March 5, 2021.
[a]Induction treatment ITT population. If patients were already in maintenance at data cutoff, then response assessments also contributed to PFS.

- Median PFS was 50.5 mo (95% CI, 39.4-NR) for all patients
- Grade 3/4 treatment emergent adverse events (TEAEs) occurred in 69% of patients (**Figure 7**)
- The most common grade 3/4 TEAE was neutropenia (37%)
  - Other grade 3/4 AEs that occurred in greater than or equal to 5% of patients included leukopenia (8%), thrombocytopenia (6%), anemia (5%), fatigue (5%)

Figure 7. Treatment emergent adverse events



Data cutoff March 5, 2021.
[a]Assessed per National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03. TEAEs include any AEs occurring on or after first dose date of induction treatment through 28 days after the last dosing date of study treatment.

- Other TEAEs (any grade/grade 3–4) of interest included maculopapular rash (17%/1%), infusion-related reaction (12%/1%), tumor flare reaction (4%/1%), febrile neutropenia (0%/3%), and tumor lysis syndrome (1%/< 1%)
- TEAEs led to early discontinuation of lenalidomide in 19% of patients and rituximab in 12% of patients, and dosing was reduced/interrupted in 64% and 30% of patients for lenalidomide and rituximab, respectively (**Table 3**)
  - Neutropenia was the most common TEAE leading to lenalidomide discontinuation (n = 22, 6%) and reduction/interruption (n = 125, 32%), and rituximab discontinuation (n = 10, 3%)
  - Infusion-related reaction was the most common TEAE leading to rituximab interruption (n = 32, 8%)

Conclusions

- These data represent complete analysis of patients with FL grade 1–3a and MZL in the induction phase of MAGNIFY
- R^2 is active with deep and durable responses in patients with R/R FL grade 1–3a and MZL, including rituximab-refractory, double-refractory, and early relapse patients
- R^2 has a tolerable safety profile in patients with R/R FL grade 1–3a and MZL
- The MAGNIFY trial is ongoing to compare R^2 versus rituximab maintenance treatment in patients with R/R FL and MZL
  - 232 Patients have completed 12 cycles of induction treatment, and 217 have proceeded to maintenance treatment
- Results shown here from MAGNIFY align with those previously shown in AUGMENT of R^2 activity in R/R patients with iNHL

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