340 Subgroup Analyses of Elderly Patients Aged ≥ 70 Years in MAGNIFY: A Phase IIIb Interim Analysis of Induction R2 Followed By Maintenance in Relapsed/Refractory Indolent Non-Hodgkin Lymphoma

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Background

Lenalidomide combined with rituximab (R^2) has shown complimentary clinical activity and is a tolerable regimen in both untreated and relapsed or refractory (R/R) patients with indolent non-Hodgkin lymphoma. Patients with advanced age at diagnosis are considered to be high risk, supporting post-hoc subgroup analyses by age, with a focus on patients aged ≥ 70 years from the MAGNIFY study.

Methods

MAGNIFY is a multicenter, phase IIIb trial in patients with R/R follicular lymphoma (FL) grades 1-3b, transformed FL (tFL), marginal zone lymphoma (MZL), or mantle cell lymphoma (MCL; NCT01996865) exploring optimal lenalidomide duration. Lenalidomide 20 mg on days 1-21 of a 28-day cycle + rituximab 375 mg/m^2/week cycle 1 and then every 8 weeks starting with cycle 3 (R^2) are administered for 12 cycles followed by 1:1 randomization in patients with stable disease,

partial response, or complete response/complete response unconfirmed (CR/CRu) to R^2 vs rituximab maintenance for 18 months. Data presented here focus on induction R^2 in efficacy-evaluable FL grade 1-3a and MZL patients (FL grade 3b, tFL, and MCL not included) receiving ≥ 1 treatment with baseline/postbaseline assessments. The primary end point is progression-free survival (PFS) by 1999 International Working Group criteria. Post-hoc analyses were performed by analyzing data from patients aged ≥ 70 years at time of study entry.

Results

As of November 30, 2019, 393 patients have enrolled and 152 (39%) were aged ≥ 70 years. Baseline characteristics including histology, disease status, and prior treatments of patients ≥ 70 and the overall population are shown in the table. Median PFS in the ≥ 70 subgroup was 36.0 months (95% CI, 28.3-NR). Overall response rate and CR/CRu were 75% and 38%, with a median duration of response that was not reached (95% CI, 27.1-NR). Efficacy results for the overall population are shown in the table. In patients ≥ 70 the most common (≥ 20%) any-grade treatment emergent adverse events (TEAEs) were fatigue (44%), neutropenia (41%), diarrhea (34%), constipation (34%), and nausea (27%). Neutropenia (35%) was the only grade 3/4 TEAE occurring in > 10% of patients (febrile neutropenia occurred in 3 patients [2%]). TEAEs led to lenalidomide dose reduction in 69 patients (46%) and discontinuation in 40 patients (26%). Seventy-eight patients ≥ 70 (51%) completed all 12 cycles of induction treatment, and 72 (47%) have entered the maintenance phase. Sixty-one patients ≥ 70 (40%), compared to 35% of patients in overall population, prematurely discontinued both lenalidomide and rituximab, due to TEAEs (n = 26; 17%), progressive disease (n = 15; 10%), patient withdrawal (n = 12; 8%), death (n = 5; 3%), and other reasons (n = 3; 2%). Neutropenia was the only TEAE leading to discontinuation of lenalidomide in more than 2 patients (n = 10; 7%).

Conclusions

Similar to findings in the overall population, R^2 treatment in advanced-age patients with R/R FL and MZL resulted in encouraging efficacy, and with close attention to dose reduction there is a tolerable safety profile.

MAGNIFY: Baseline Characteristics and Efficacy in the Overall Population and Elderly Population

	Overall (N = 393)	≥ 70 (n = 152)
Baseline characteristics, n (%)		
Median age, y (range) ≥ 70 to < 80 ≥ 80	66 (35-91) 108 (27) 44 (11)	76 (70-91) 108 (71) 44 (29)
FL grades 1-3a	317 (81)	121 (80)
MZL	76 (19)	31 (20)
Ann Arbor stage III-IV	327 (83)	124 (82)
ECOG PS 0-1	384 (98)	148 (97)
Bulky disease	162 (41)	61 (40)
Prior rituximab-containing therapy	372 (95)	142 (93)
Rituximab refractory	137 (35)	48 (32)
Early relapse*	132 (34)	41 (27)
Double refractory†	80 (20)	23 (15)
Efficacy		
Median PFS, mo (95% CI) ‡	40.1 (37.6-NR) (n = 391)	36 (28.3-NR) (n = 151)
ORR, n/N (%)	270/393 (69)	106/141 (75)
CR+CRu, n/N (%)	158/393 (40)	54/141 (38)
Median DOR, mo (95% CI)	39.0 (36.8-NR)	NR (27.1-NR)

CR, complete response; CRu, CR unconfirmed; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; MZL, marginal zone lymphoma; NR, not reached; ORR, overall response rate; PFS, progression-free survival

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