RELEVANCE: PHASE III EFFICACY AND SAFETY STUDY OF LENALIDOMIDE PLUS RITUXIMAB (R2) VERSUS RITUXIMAB PLUS CHEMOTHERAPY, FOLLOWED BY RITUXIMAB, IN PREVIOUSLY UNTREATED FOLLICULAR LYMPHOMA

Author(s): Frank Morschhauser, et al.

Abstract: S154

Type: Presidential Symposium

Presentation during EHA23: On Friday, June 15, 2018 from 17:00 - 17:15

Location: Room A1

Background

Standard of care for advanced stage, high tumor burden, previously untreated follicular lymphoma (FL) has been rituximab plus chemotherapy (R-chemo) followed by rituximab maintenance. Combination immunotherapy with lenalidomide and rituximab (R^2) is a chemotherapy-free regimen that has shown promising efficacy and safety in previously untreated patients with FL.

Aims

This is the first report of the co-primary endpoints: i) complete response (CR)/CR unconfirmed (CRu) at 120 weeks and ii) interim analysis of progression-free survival (PFS; ~50% of the target of 456 events by 1999 IWG criteria) for R^2 vs R-chemo followed by rituximab in previously untreated patients with FL.

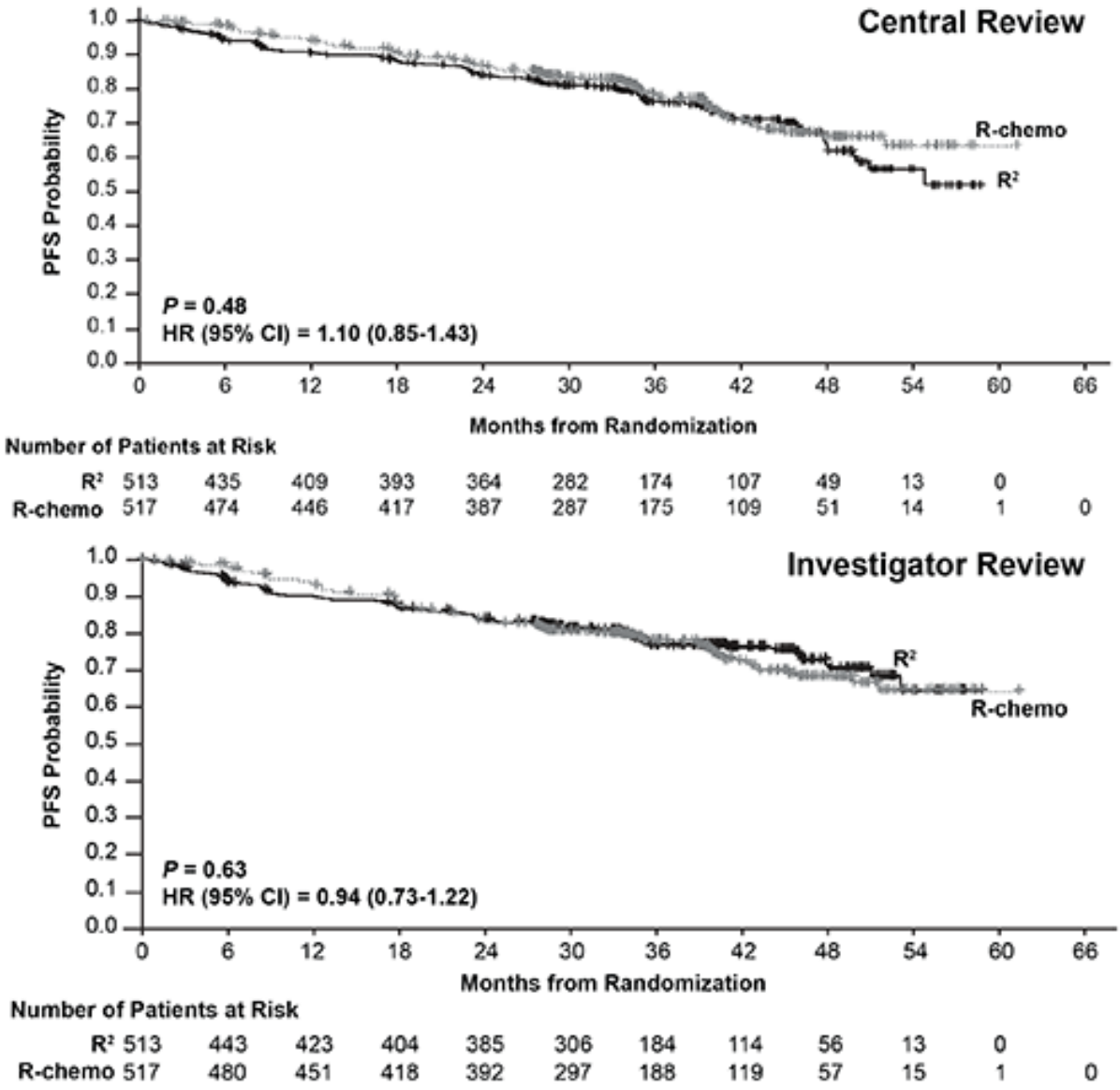
Methods

RELEVANCE is a global, randomized, open-label phase III trial (NCT01650701; EUDRACT2011-002792-42) in patients with grade 1-3a FL who required systemic therapy (per GELF criteria). In the R^2 arm, lenalidomide 20 mg/day on days 2-22/28 was given cycles 1 to 6-12, continued in responders at 10 mg/day for a total of 18 cycles. Rituximab was 375 mg/m^2 weekly in cycle 1, day 1 in cycles 2-6, and continued in responders for 12 additional cycles (q8wk). R-chemo was given per investigator's choice of standard R-CHOP, R-bendamustine (R-B), or R-CVP, followed by 12 cycles of rituximab (q8wk).

Results

As of the cutoff date of 31May2017, 1030 patients with high tumor burden FL were randomized to R^2 (n=513) or R-chemo (n=517; 72% R-CHOP, 23% R-B, 5% R-CVP). Both groups had similar baseline characteristics; overall median age was 59 years (range, 23-89), 49% with FLIPI score ≥3, 93% stage III/IV, and 41% bulky disease (>7 cm). The superiority of both co-primary endpoints for R^2 over R-chemo was not established after a median follow-up of 37.9 months. CR/CRu at 120 weeks was similar in the R^2 v R-chemo groups (48% v 53%, *P*=0.13 per central review; 55% v 58%, *P*=0.38 per investigator assessment). R^2 and R-chemo groups demonstrated similar 3-year PFS rates by both central review (77% v 78%) and investigator assessment (77% v 78%), respectively (Figure). 3-year overall survival was 94% for both arms. The toxicity profiles for R^2v R-chemo were different, with lower rates of any grade fatigue (23% v 29%), nausea (20% v 42%), peripheral neuropathy (11% v 22%), vomiting (7% v 19%), stomatitis (3% v 7%), and alopecia (1% v 9%), and higher rates of cutaneous reactions (43% v 24%), diarrhea (37% v 19%), and tumor flare reaction (6% v 0.2%) associated with R^2. Rates of thromboembolic events were similar in both groups. Higher grade 3/4 lab neutropenia (34% v 50%) and febrile neutropenia (2% v 6%) were associated with R-chemo, whereas higher grade 3/4 cutaneous reactions (7% v 1%) were associated with R^2. Adverse events (AEs) led to treatment discontinuation in 11% of R^2 and 3% of R-chemo patients. Grade 5 AEs were 1% for both arms, and SPMs were reported in 7% (n=38) R^2 and 9% (n=48) R-chemo patients (5% invasive SPMs for both). 69% R^2 and 71% R-chemo patients completed 30 months of treatment. For the R^2 group, 76% of patients completed all 18 cycles of lenalidomide.

Figure. RELEVANCE PFS (Central and Inv. Review)



Conclusion

RELEVANCE is the first randomized phase III trial comparing the chemotherapy-free regimen R^2 v standard R-chemo followed by rituximab maintenance in previously untreated patients with FL. The superiority of R^2over R-chemo was not demonstrated in this phase III trial, however, compared with R-chemo, R^2 appeared to show similar efficacy with a different toxicity profile.

Session topic: 20. Indolent Non-Hodgkin lymphoma – Clinical

Keyword(s): Follicular lymphoma, Imids, Non-Hodgkin's lymphoma