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ASH 2018 | Results from the HOVON 130 trial: Lenalidomide and R-CHOP for B-cell lymphoma with *MYC* rearrangements

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On Monday 3 December 2018, Oral Session 626 took place at the 60th American Society of Hematology (ASH) Annual Meeting, San Diego, CA. During that session, results from the phase II HOVON 130 trial (Abstract #786) were presented by Martine Chamuleau from the University Medical Center, Amsterdam, NL.

In this prospective phase II trial (HOVON 130) the combination of lenalidomide and R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), was assessed for efficacy and safety in patients with large B-cell lymphoma (except Burkitt lymphoma) with *MYC* rearrangements. R-CHOP alone leads to poor response rates and outcomes in these patients. The primary endpoint of the study was end of treatment complete metabolic response rate (CMR), as detected by positron emission tomography and computed tomography (PET/CT). The secondary endpoint of the trial was the predictive value of PET/CT for patient outcomes.

Study design

- N = 82 eligible newly-diagnosed patients with proven *MYC* rearrangement by fluorescence *in situ* hybridization (FISH), Ann Arbor stage II-IV, aged ≥ 18 and single, double or triple *MYC* rearrangement
- Patients with Burkitt lymphoma, transformed lymphoma or central nervous system localization were excluded
- Median age (range) = 63 (28–82) years
- Dosing: R2-CHOP regimen every 3 weeks:
  - Six cycles R-CHOP:
    - Rituximab: 750 mg/m^2 intravenously (i.v) on Day 1
    - Cyclophosphamide: 750 mg/m^2v on Day 1
    - Doxorubicin: 50 mg/m^2v on Day 1
    - Vincristine: 1.4 mg/m^2v (maximum 2 mg) on Day 1
    - Prednisone: 100 mg orally on Day 1-5
  - Six cycles lenalidomide (15 mg) orally on Day 1–14 followed by two rituximab administrations
- All patients received intrathecal methotrexate prophylaxis
- PET/CT scans were performed at baseline, after 3 treatment cycles (interim) and at the end of treatment (EOT)

Results

- Interim PET/CT:

    - Revealed that 70% of patients (n = 57) achieved CMR, 28% (n = 23) reached a partial metabolic response and 2% (n = 2) progressed to disease (PD)
- EOT PET/CT
    - Revealed that overall 67% of patients (n = 55) achieved CMR
- Interim PET/CT scans were not predictive of patient outcomes in this trial
- Age, International Prognostic Index (IPI) or *MYC* rearrangement status were not significant prognostic factors for CMR
- There was a tendency for higher risk of death for double and triple hit patients when compared to single hit (HR = 6.35; *P* = 0.07; 95% CI, 0.84–75)
- Median follow-up = 15.9 months
- One-year estimates:
    - Progression-free survival (PFS) = 66%
    - Overall survival (OS) = 85%

Safety

- Adverse events (AEs) of Grade 2 were seen in 32%, of Grade 3 in 39% and of Grade 4 in 16% of patients
- The most common Grade 3–4 AEs were:
    - Neutropenia: 18%
    - Infections: 14%
    - Gastrointestinal disorders: 14%
- Serious AEs (n = 72) were observed in 37 patients, leading to 67 hospitalizations and one death due to PD
- No treatment-related deaths occurred

Conclusions

- R2CHOP and lenalidomide are well tolerated by newly-diagnosed B-cell lymphoma patients with *MYC* rearrangements
- R2CHOP and lenalidomide led to promising CMR and survival rates and this combination treatment might be considered in the future as the new standard of care for *MYC*-positive B-cell lymphoma patients

References

1. Chamuleau M. *et al.* Successful Treatment of MYC rearrangement Positive Large B Cell Lymphoma Patients with R-CHOP21 Plus Lenalidomide: Results of a Multicenter Phase II HOVON Trial. Oral Abstract #786: *ASH 60th Annual Meeting and Exposition, December 2018*, San Diego, CA.