HemaSphere

EHA EUROPEAN HEMATOLOGY ASSOCIATION

P905 IXAZOMIB-THALIDOMIDE-DEXAMETHASONE INDUCTION FOLLOWED BY IXAZOMIB OR PLACEBO MAINTENANCE IN NON-TRANSPLANT ELIGIBLE NEWLY DIAGNOSED MULTIPLE MYELOMA PATIENTS; LONG-TERM RESULTS OF HOVON-126/NMSG 21.13

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

Kaz Groen[1], Maarten R. Seefat[1], Bronno van der Holt[2], Fredrik H. Schjesvold[3, 4], Claudia. A.M. Stege[1], Mark-David Levin[5], Markus Hansson[6, 7], Rineke B.L. Leys[8], Josien Regelink[9], Anders Waage[10], Damian Szatkowski[11], Per Axelsson[12], Trung Hieu Do[13], Asta Svirskaite[14], Ellen van der Spek[15], Einar Haukas[16], Dorota Knut-Bojanowska[17], Paula F. Ypma[18], Celine Blimark[19], Ulf-Henrik Mellqvist[20], Niels W.C.J. van de Donk[1], Pieter Sonneveld[21], Anja Klostergaard[22], Annette J. Vangsted[23], Niels Abdilgaard[24, 25], Sonja Zweegman[1]

[1] Hematology, Amsterdam UMC, Amsterdam, Netherlands;[2] HOVON Data Center, Department of Hematology, Erasmus MC Cancer Institute, Rotterdam, Netherlands;[3] Hematology, Oslo Myeloma Center, Oslo, Norway;[4] KG Jebsen center for B Cell malignancies, University of Oslo, Oslo, Norway;[5] Department of Internal Medicine, Albert Schweitzer Hospital, Dordrecht, Netherlands;[6] Skane University Hospital, Lund, Sweden;[7] Sahlgrenska Academy, Göteborg, Sweden;[8] Department of Internal Medicine, Maasstad Ziekenhuis, Rotterdam, Netherlands;[9] Department of Internal Medicine, Meander Medisch Centrum, Amersfoort, Netherlands;[10] IKOM, Norwegian University of Science and Technology, Trondheim, Norway;[11] Førde Central Hospital, Førde, Norway;[12] Skanes University Hospital, Lund, Sweden;[13] Herlev Hospital, Herlev, Denmark;[14] Aalborg Hospital, Aalborg, Denmark;[15] Department of Internal Medicine, Rijnstate, Arnhem, Netherlands;[16] Stavanger University Hospital-Rogaland Hospital, Stavanger, Norway;[17] NU-Hospital - Uddevalla Hospital, Uddevalla, Sweden;[18] Department of Hematology, Haga Ziekenhuis, Den Haag, Netherlands;[19] Sahlgrenska University Hospital, Gothenburg, Sweden;[20] Sodra Alvsborgs Sjukhus Boras, Boras, Sweden;[21] Erasmus Medical Center Cancer Institute, Rotterdam, Netherlands;[22] Aarhus University Hospital, Aarhus, Denmark;[23] Department of Hematology, Rigshospitalet, Copenhagen, Denmark;[24] Department of Hematology, Odense University Hospital, Odense, Denmark;[25] Academy or Geriatric Cancer Research, Odense University Hospital, Odense, Denmark

Background: In the HOVON 126/NMSG 21.13 trial non-transplant eligible newly diagnosed multiple myeloma (NTE-NDMM) patients were treated with 9 induction cycles of ixazomib, thalidomide and dexamethasone (ITd), followed by randomization between either ixazomib or placebo until progression or unacceptable toxicity. The overall response rate and PFS data have been previously published.

Aims:

We here present the long-term PFS2 and overall survival data.

Methods:

Patients were treated with 9 induction cycles (28 days) of ixazomib (4mg on day 1, 8 and 15), thalidomide (100mg on day 1-28) and dexamethasone (40mg on day 1, 8, 15 and 22), followed by maintenance with either ixazomib or placebo (4mg, both on day 1, 8 and 15, every 28 days). Patients were classified as fit, intermediate fit or frail, based on a modified IMWG frailty index which incorporated age, the Charlson Comorbidity Index (CCI) and the WHO performance as a proxy for (instrumental) Activities of Daily Living (iADL) (scoring WHO 0 as 0 points, WHO 1 as 1 point, and WHO 2-3 as 2 points).

Results:

From registration: 143 eligible patients were included in the study. After a median follow-up (FU) of 67.4 months (m), the median PFS was 14.3m (95% CI 11.5-16.8), median PFS2 was 34.6m (30.7-41.5) and median OS was 58.3m (50.5-65.0). There was no difference in PFS between frailty subgroups. In contrast, median PFS2 and OS were longer in fit patients (PFS2: 49.1m (34.6-74.1), OS: NR (66.6-NR)) versus intermediate-fit (30.1m (25.1-39.0); 51.2m (32.3-63.9)

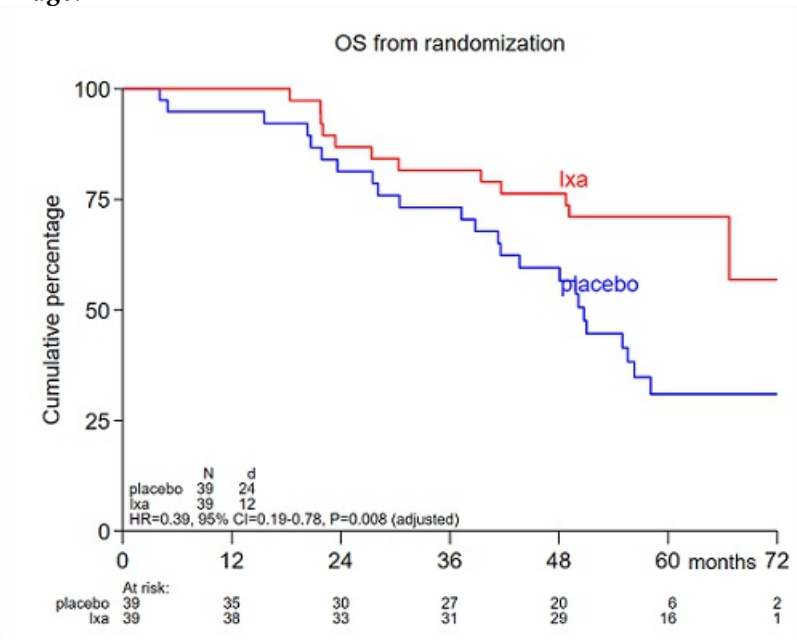
resp.) and frail patients (30.9m (24.0-42.3); 50.5m (32.9-59.4) resp.).

From randomization: 78 (55%) patients were randomized, 39 patients in each arm. After a median FU of 60 months from randomization, there was no difference in PFS between the ixazomib-arm (median 9.5m; 95% CI 5.5-14.8) and the placebo-arm (8.4m; 3.0-13.8). Median PFS2 was 39.8m (28.8-60.0) for patients on ixazomib, as compared to 28.7m (22.8-43.2) for patients in the placebo arm, although this difference was not statistically significant. Median OS was not reached for the ixazomib arm and was 50.7m (41.3-58.1) for the placebo arm (HR 0.39; 95% CI 0.19-0.78, p=0.008).

In both arms 32 (82%) patients received 2nd line treatment. With the caveat of low numbers and heterogeneous treatment regimens, more patients in the ixazomib arm received daratumumab-lenalidomide-dexamethasone (4 patients, 13%) and panobinostat-bortezomib-dexamethasone (6 patients, 19%), compared to the placebo arm (2 patients (6%) and 3 patients (9%) respectively).

In order to explain the difference in OS, subsequent lines of therapy are currently being investigated.

Image:



Summary/Conclusion: With longer FU, we here confirm that ixazomib maintenance therapy did not improve PFS, compared to placebo. However, PFS2 tends to be longer and OS was superior in patients treated with ITd followed by maintenance with ixazomib versus placebo.