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637. MYELODYSPLASTIC SYNDROMES-CLINICAL STUDIES:
LOWER RISK MDS CLINICAL STUDIES | DECEMBER 02, 2016

Lenalidomide with or without Erythropoietin and Granulocyte-Colony Stimulating Factor Shows Efficacy in Patients with Low and Intermediate-1 Risk Myelodysplastic Syndrome with or without Del 5q, Refractory or Unlikely to Respond to Erythropoietin. Results of a HOVON89 Phase II Randomized Multicenter Study. (EudraCT 2008-002195-10)

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Abstract

Purpose: This randomized phase II study (HOVON89) in patients with low/int-1 risk MDS refractory or unlikely to respond to erythropoietin and granulocyte-colony stimulating factor (EPO/G-CSF) assessed efficacy and safety of lenalidomide without (Arm A) or with EPO+/-G-CSF (Arm B) in case of no erythroid response after 4 cycles.

Patients and methods: In total 200 patients were randomly 1:1 assigned to either Arm A or Arm B. All patients were treated with lenalidomide (10 mg/day/day 1-21) for a minimum of 6 months in arm A and 12 months in arm B or until loss of response or disease progression. Patients in arm B without hematological improvement-erythroid (HI-E) after 4 cycles received EPO (30,000 IU/wk). In those patients who did not show HI-E after 6 months, EPO was increased to 60,000 IE/wk. G-CSF (3x 300-480 µg/wk) was added if no HI-E was reached at 8 month. The current pre-final evaluation was based on the first180 patients and included 85% non-del5q MDS and15% patients with isolated del5q. The median age was 71years (range 38-89). No differences were observed between both arms regarding sex (55% male), WHO PS, WHO diagnostic subgroup and IPSS, baseline Hb, WBC, platelets, endogenous erythropoietin level, pretreatment with EPO+/-G-CSF (67% of the patients were pretreated) and pre-study transfusions. Patients had received a median of 13 (range 0-72) units of RBC and 4 (range 0-13) within 8 weeks for prior study entry.

Results: Adverse events were consistent with the known safety profile of lenalidomide/EPO/G-CSF. HI-E according to IWG criteria was achieved in 38% and 41% of the patients for arm A and B, respectively ($p = 0.46$). HI-E was significantly lower in non-del5q versus del5q patients (33% vs 78%, respectively). Time-to-HI-E was 3.1 months (median; range 1.6-12.3) for both arms with a median duration of 10 months (range 1 - 76). The median PFS was 14.4 vs 15.4 months in arms A and B ($p=0.43$). OS was 51.1 and 37.7 months for arm A and B ($p=0.09$). At 2 years 17% of patients had progressed to AML (no differences between arms). The median FU of patients still alive is 31 months. PFS and OS was significantly longer in those who achieved HI-E, (median 13 vs 19 months, $p=0.02$ for PFS and median 31 vs 63 months for OS, $p<0.001$); non-responders vs responders). A Landmark analysis at 12 month

confirms a significant prolonged OS in patients who achieved HI-E (28 and 51 months, p<0.002, non-responders vs responders). Endogenous erythropoietin level, pretreatment with EPO/G-CSF, and WHO subgroup did not predict for HI-E, PFS and OS. However, an IPSS of 0 was favorable in comparison to a score of 0.5-1.0 (p=0.02). To better predict response we are currently analyzing baseline flowcytometry and NGS data.

Conclusion: Lenalidomide yields sustained HI-E in 33% of patients with non-del5q low/int-1 risk MDS refractory or unlikely to respond on EPO/G-CSF. The addition of EPO/G-CSF did not improve HI-E. Achievement of HI-E significantly improves PFS and OS.

Disclosures

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Author notes

*Asterisk with author names denotes non-ASH members.


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