P1055 CLINICAL AND GENETIC RESULTS OF THE PHASE IB/II TRIAL MPNSG-0212: RUXOLITINIB PLUS POMALIDOMIDE IN MYELOFIBROSIS WITH ANEMIA

Topic: 16. Myeloproliferative neoplasms - Clinical

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Background: Ruxolitinib (RUX) alleviates disease-associated symptoms including splenomegaly in patients (pts) with myelofibrosis (MF). However, management of cytopenia remains challenging.

Aims: As single-agent pomalidomide (POM) improved cytopenia in 14-29% of MF pts in our previous MPNSG-0109 trial, we sought to investigate the combination of RUX plus POM in MF pts with anemia (Hb <10 g/dL and/or RBC transfusion dependency [RBC-TD]).

Methods: MPNSG-0212 is a multicenter, open-label, phase-Ib/II trial (NCT01644110) comprising 39 pts in cohort 1 (co1, recruited 2013-2017) and 52 pts in co2 (2017-2021). Co1 pts received RUX 10 mg BID plus POM 0.5 mg QD, while POM was intended to be increased in co2 to 1 and 2 mg QD after 3 and 6 28-day-cycles, respectively. Primary endpoint was response according to IWG-MRT and RBC-TI criteria at end of cycle 12 (EOC12). In addition, genomic landscape was characterized in all pts using targeted NGS of 269 candidate genes (Illumina NextSeq550).

Results:

Co1 and co2 pts had similar characteristics: median age was 71 years (range 49-86), median Hb level 8.6 g/dL (5.4-11.7), and median spleen size 17.5 cm (11.4-36); 30% were RBC-TD, 66% intermediate-2, and 25% high-risk according to DIPSS; mutations (muts) in JAK2, CALR, or MPL were identified in 57%, 23%, and 20%, respectively; 55% had ≥1 high-molecular risk (HMR) mut, with ASXL1 being the most common (41%), followed by SRSF2 (24%), EZH2 (10%) and IDH2 (9%). Of note, pts in co2 were more frequently pre-treated with RUX compared to co1 (44% vs 24%)

Median treatment time at data cut-off was 12 cycles in co1 (2-98) and co2 (3-46); 3 pts of co2 have not yet reached EOC12.

In co1, 8/39 pts (21%) achieved response at EOC12: partial remission (PR, n=1), clinical improvement (CI, n=6), or RBC-TI (n=1); 18/39 pts (46%) were treated for >12 cycles due to response (n=8), clinical benefit (CB, n=5) defined as Hb increase ≥1 g/dL or >50% improvement of ≥1 quality of life (QoL) symptom according to MPN-SAF, or stable...
disease (SD, n=5). Median Hb level at EOC12 was 9.3 g/dL; 15/39 pts (38%) were on treatment for >30 cycles, and 3 pts remained on long-term treatment (cycle 76, 97, and 98).

In 73% and 40% of pts in co2, POM dose was increased to 1 mg and 2 mg QD after cycle 3 and 6, respectively. 5/49 pts (10%) showed response at EOC12 (Cl, n=3 and RBC-TI, n=2), while 14 additional pts (29%) had CB; median Hb level at EOC12 was 8.6 g/dL; 22/49 pts (45%) were treated for >12 cycles; 3 pts were still on treatment (cycle 21, 36, and 46).

Targeted NGS did not reveal a distinct mutational pattern associated with treatment response. Median overall survival (OS) of co1 and co2 was 3.6 and 2.6 years, respectively (p=.66). Among all, CALR, but not JAK2 or MPL muts were associated with better OS (p=.04), whereas HMR muts were in trend prognostically adverse (p=.057). Pts with more than 3 muts had a worse median OS (1.2 vs 4 years, p=.002).

Combination therapy was well tolerated in both cohorts. Most common grade 1/2 adverse events (AE) were dyspnea (28%) and fatigue (23%), while the most frequent grade 3 AE was worsening of anemia (32%) in the first weeks of combination treatment not limiting therapy.

**Summary/Conclusion:** Treatment with RUX and POM was safe and feasible in our study of advanced MF with an adverse genetic profile. Almost half of co1 and co2 pts were treated >12 cycles due to clinical benefit of the combination therapy with a subset of 38% of pts in co1 receiving treatment for >30 cycles. Dose increase of POM in co2 did not result into better anemia response or improvement of OS.

Authors FS and EJ contributed equally.