A PHASE 3 RANDOMIZED, OPEN-LABEL, MULTICENTER STUDY OF ISATUXIMAB, POMALIDOMIDE, AND LOW-DOSE DEXAMETHASONE VS POMALIDOMIDE AND LOW-DOSE DEXAMETHASONE IN RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM)

Author(s): Michel Attal , Paul G. Richardson , S. Vincent Rajkumar , Jesus San-Miguel , Meral Beksac , Ivan Spicka , Xavier Leleu , Fredrick Schjesvold , Philippe Moreau , Meletios A. Dimopoulos , Jeffrey Shang-Yi Huang , Jiri Minarik , Michele Cavo , H. Miles Prince , Sandrine Mace , Kathryn P. Corzo , Frank Campana , Solenn Le-Guennec , Franck Dubin , Kenneth C. Anderson EHA Library. Richardson P.

Jun 15, 2019; 267407

Abstract: S824

Type: Oral Presentation

Presentation during EHA24: On Saturday, June 15, 2019 from 11:45 - 12:00

Background
Despite recent advances, multiple myeloma (MM) remains incurable, and new treatment options are needed to continue to improve patient outcomes. This is the first randomized, phase 3 trial of an anti-CD38 antibody in combination with pomalidomide (P) and dexamethasone (d) in RRMM.

Aims
The primary objective of this phase 3 trial (NCT02990338) was to demonstrate progression free survival (PFS) improvement of isatuximab (Isa), a novel anti-CD38 monoclonal antibody targeting a specific epitope, combined with Pd versus (vs) Pd in RRMM.

Methods
Patients (pts) with RRMM who received ≥2 prior lines, including lenalidomide (len) and a proteasome inhibitor (PI), refractory to last therapy were enrolled. IsaPd arm received Isa 10 mg/kg IV weekly for first 4 weeks (wks), then every 2 wks. Both arms received approved schedules of pom and dex (4mg PO days 1-21; 40mg [20mg if >75 yrs] PO or IV weekly) every 28 days until progression or unacceptable toxicity.

Results
307 pts (154 IsaPd, 153 Pd) were randomized and analyzed (ITT). Patient characteristics were well balanced across arms. Median age: 67 (36-86) yrs; median prior lines of therapy: 3 (2-11); estimated GFR: <60ml/min in 33.9% pts; 92.5% refractory to len, 75.9% to PI; and 19.5% pts had high-risk cytogenetics. At median follow-up of 11.6 months (mos), median PFS was 11.5 mos IsaPd vs 6.5 mos Pd; HR 0.596 (95% CI 0.44-0.81), *P*=0.001. PFS benefit was consistent across all major subgroups. ORR (≥PR) was 60.4% IsaPd vs 35.3% Pd, *P*<0.0001. VGPR rate or better was 31.8% IsaPd vs 8.5% Pd, and MRD negativity (NGS, 10^{-5}) was seen in 5.2% IsaPd pts vs 0% Pd. At analysis date, overall survival (OS) was immature (99 events) but a trend to OS improvement in IsaPd (vs Pd) was observed (HR 0.687; 95% CI 0.461-1.023). Median treatment duration was 41 wks IsaPd vs 24 wks Pd; median Isa infusion (inf.) duration was 3.3h at 1st inf. and 2.8h at subsequent inf. Grade ≥3 AEs were observed in 86.8% IsaPd vs 70.5% Pd; 7.2% IsaPd and 12.8% Pd pts discontinued due to AEs; 7.9% IsaPd and 9.4% Pd pts died due to AEs. Inf. reactions were reported in 38.2% (2.6% grade 3-4) IsaPd. Grade ≥3 infections were seen in 42.8% IsaPd and 30.2% Pd, grade ≥3 neutropenia in 84.9% (febrile 11.8%) IsaPd and 70.1% (febrile 2.0%) Pd.

Conclusion
Isatuximab in combination with pomalidomide and dexamethasone significantly improved PFS and ORR vs pomalidomide and dexamethasone, with a manageable safety profile. Isatuximab in combination with pomalidomide and dexamethasone is an important new treatment option for the management of RRMM.