A phase III randomized, open label, multicenter study comparing isatuximab, pomalidomide, and low-dose dexamethasone versus pomalidomide and low-dose dexamethasone in patients with relapsed/refractory multiple myeloma (RRMM).

Presented Sunday, June 2, 2019

Authors:
Paul G. Richardson, Michel Attal, S. Vincent Rajkumar, Jesus San Miguel, Meral Beksac, Ivan Spicka, Xavier Leleu, Fredrik Schjesvold, Philippe Moreau, Meletios A. Dimopoulos, Jeffrey SY. Huang, J[illegible] Minarik, Michele Cavo, H. Miles Prince, Sandrine Macé, Kathryn Penkus Corzo, Frank Campana, Soleni[illegible] Le-Guennec, Franck Dubin, Kenneth Carl Anderson, on behalf of the ICARIA-MM Study Group; Jerome Lipper Multiple Myeloma Center, Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA; IUCT-Oncopole, Toulouse, France; Mayo Clinic, Rochester, MN; Clínica Universidad de Navarra, Navarra, Spain; Ankara University, Ankara, Turkey; Vseobecna Fakultni Nemocnice V Praze, Prague, Czech Republic; CHRU Lille, Lille, France; Oslo University Hospital, Oslo, Norway; CHU de Nantes-Hôtel Dieu, Nantes, France; National and Kapodistrian University of Athens, Athens, Greece; National Taiwan University Hospital, Taipei, Taiwan; University Hospital Olomouc, Olomouc, Czech Republic; Seràgnoli Institute of Hematology, Bologna University School of Medicine, Bologna, Italy; Epworth Healthcare and Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; Sanofi R&D, Oncology, Vitry-Sur-Seine, France; Sanofi, Cambridge, MA; Sanofi US, Cambridge, MA; Sanofi R & D, Vitry-Alfortville, France; Sanofi, Vitry-Sur-Seine, France

View Less

Abstract Disclosures

Background:
The primary objective of this phase 3 trial was to demonstrate progression free survival (PFS) improvement of isatuximab (Isa), a novel anti-CD38 monoclonal antibody, combined with pomalidomide (P)/dexamethasone (d) versus (vs) Pd.

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.

Conclusions:

IsaPd significantly improved PFS and ORR vs Pd, with a manageable safety profile. IsaPd is an important new treatment option for the management of RRMM. Clinical trial information: NCT02990338