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Patient Perspectives in Multiple Myeloma

Highlights from the 2018 American Society of Hematology Annual Meeting

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TABLE. Efficacy of IRd Based on Pooled Analysis from the INSIGHT MM Observational Study and the Czech Registry of Monoclonal Gammopathies

Efficacy Measure	All IRd Patients (n = 105[a])	Second-Line IRd (n = 58[a])	Third-Line IRd	Fourth-Line IRd
ORR (partial response or better)	74%	91%	57%	47%
VGPR or better	31%	41%	25%	11%
PFS (median)	21 months	NR	23 months	14 months
Patients who were progression free at 12-month time point	65%	70%	NA	NA
Time to next therapy (median)	26 months	NR	NA	NA
Patients needing next therapy at 12-month time point	73%	73%	NA	NA
Overall survival (median)	NR	NR	NA	NA
Patients alive at 12-month time point	81%	89%	NA	NA

[a]Number of patients with best response to therapy data available.

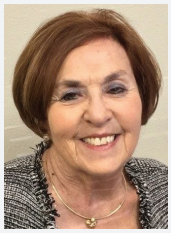
IRd indicates ixazomib/lenalidomide/dexamethasone; NA, not available; NR, not reached; ORR, overall response rate; PFS, progression-free survival; VGPR, very good partial response.

(IRd) in real-world patients with relapsed and refractory multiple myeloma, researchers analyzed patient-level data from the ongoing INSIGHT MM study using data from the Czech Registry of Monoclonal Gammopathies (RMG). INSIGHT MM, the largest global, prospective, observational study of its kind to date, is enrolling approximately 4200 adults with newly diagnosed or relapsed/refractory multiple myeloma from around the world: Europe, United States, Asia, and Latin America. The Czech RMG, which the Czech Myeloma Group initiated in 2007, includes clinical data for more than 6000 patients with multiple myeloma who enrolled at 1 of 19 Czech and 4 Slovak cancer centers.

After data were collected from 9 countries, 163 patients with relapsed or refractory multiple myeloma who received IRd were included in the analysis (50 from the INSIGHT MM database and 113 from the Czech RMG). Of these patients, 90% were from Europe, 10% were from the United States, and 1% were from Taiwan. Patients were aged 67 years (median; range, 39-84 years), and 53% of patients were men. At the time of initial diagnosis with multiple myeloma, 38% of patients had International Staging System (ISS) stage I disease, 36% had ISS stage II disease, and 26% had ISS stage III disease.

Most (61%) patients in this database had received a previous stem-cell transplant. Prior therapy medications included bortezomib (Velcade) in 89% of patients, thalidomide (Thalomid) in 42%, lenalidomide (Revlimid) in 21%, carfilzomib (Kyprolis) in 11%, daratumumab (Darzalex) in 3%, and pomalidomide (Pomalyst) in 2%.

The median time between



"When patients hear that real people use this therapy and these are the results, they feel reassured that real people are actually using it, and this is their experience. This definitely needs to be considered as extremely relevant."—Barbara Kavanagh, MSW, LCSW

have received at least 1 prior therapy. Because its oral administration is potentially more convenient for patients, researchers were interested in learning whether ixazomib could be used as maintenance therapy.

To assess the value of ixazomib maintenance therapy in patients with multiple myeloma, investigators initiated a phase 3, double-blind, placebo-controlled, multicenter clinical trial called TOURMALINE-MM3. This trial compared weekly ixazomib maintenance with placebo in patients with newly diagnosed multiple myeloma who had at least a partial response to their induction therapy with a PI (bortezomib) and/or an IMiD (lenalidomide) followed by single ASCT.

Patients received ixazomib or placebo on days 1, 8, and 15 of 28-day cycles for up to 2 years or until progressive disease or unacceptable toxicity. The ixazomib dose was 3 mg during the first 4 cycles, and then was increased to 4 mg from cycle 5 onward if it was tolerated well during cycles 1 to 4.

The primary measure of the efficacy of ixazomib maintenance was progression-free survival (PFS), which was assessed by an independent review committee of physicians who were blinded to treatment assignment. A key secondary measure of the efficacy of ixazomib maintenance was overall survival. At ASH 2018, researchers reported data from the final assessment of PFS.

A total of 656 patients enrolled in the TOURMALINE-MM3 trial; 395 received ixazomib maintenance and 261 received placebo. Median age in both groups was 57 years (range, 24-73 years), and more than half (59%) had received a PI without an IMiD during their induction therapy. Most (79%) of these patients had achieved a complete response or very good partial response following induction along with ASCT. A minority (18%) of patients in this trial had high-risk cytogenetics (del[17p], t[4;14], or t[14;16]).

"Most patients will say, 'If it is going to prolong my life, I am willing to deal with that.' So, I think, in balance, once the patient and family know both the risks and the benefits of a new therapy, most of them would say, 'I am going to give this a try.'"—Barbara Kavanagh, MSW, LCSW

After following these patients for an average of 31 months, researchers in this trial observed a 28% reduction in the risk for progression or death for those who received ixazomib compared with those who received placebo. Stated differently, there was a 39% improvement in PFS with ixazomib compared with placebo. The median time over which patients were free from progressive disease improved by approximately 6 months for those receiving ixazomib (27 months) compared with those receiving placebo (21 months). This difference in median PFS was statistically significant.

Patients who underwent ASCT after their induction regimen and who received ixazomib had longer PFS compared with those who received placebo maintenance. The median PFS for patients who underwent ASCT and then received ixazomib maintenance was 31 months compared with 25 months for placebo. Ixazomib maintenance also led to a higher percentage of patients with no evidence of minimal residual disease compared with placebo (12% vs 7%).

The benefit in PFS was seen across all subtypes of multiple myeloma, including patients with high-risk disease, those who received a PI as a part of induction, and those who did not receive a PI as a part of induction.

In the TOURMALINE-MM3 trial, 7% of patients in the ixazomib group and 5% of patients in the placebo group discontinued maintenance therapy because of adverse events. Approximately one-quarter (27%) of patients receiving ixazomib experienced 1 or more severe adverse events compared with 20% of patients receiving placebo. Frequently observed severe adverse events associated with ixazomib versus placebo were infections (15% vs 8%), such as pneumonia (6% vs 4%), gastrointestinal disorders (6% vs 1%), low white blood cell count (5% vs 3%), and low platelet count (5% vs <1%). Peripheral neuropathy (any severity level) was reported by 19% of patients in the ixazomib group and 15% of those in

significantly longer progression-free survival (PFS) and higher overall response rate compared with patients with multiple myeloma who received bortezomib plus low-dose dexamethasone (Vd). All patients in this trial had received previous treatment with lenalidomide (Revlimid).

Knowing that HRQoL in relapsed/refractory multiple myeloma is an important consideration, researchers looked further into the data collected to evaluate the effect of PVd and Vd on HRQoL. To understand whether these treatments affected QoL, and if so, how, investigators used a specific survey called the European Organisation for Research and Treatment of Cancer Quality of Life Core 30 questionnaire. A total of 449 patients (240 patients in the PVd group and 209 in the Vd group) completed this survey at multiple time points in the study, including day 1 of each 21-day treatment cycle before treatment administration and at the end of treatment.

Demographic characteristics of the patients, such as age, time since diagnosis, and number of previous treatments, were similar between those who received PVd and those who received Vd. Global QoL scores were also similar between groups at the start of the study.

When comparing the 2 groups' QoL scores over time, researchers found that there were no clinically meaningful differences between patients who received PVd and those who received Vd. There was also no difference in the proportion of patients who experienced clinically meaningful worsening in their global QoL between the treatment groups.

The results from this analysis of the OPTIMISMM trial showed that the triplet regimen of PVd did not worsen HRQoL in patients with relapsed or refractory multiple myeloma.

"My husband (the patient who developed peripheral neuropathy because of therapy) would look at you and say, 'There are side effects to every drug, and you have to adapt.' The family has to adjust. It is not only QoL. Very often, patients cannot continue their normal work, or their activities, but when you speak to that person, he or she would say, 'I am glad I am still alive!'"—Barbara Kavanagh, MSW, LCSW

Source
Weisel K, Dimopoulos MA, Moreau P, et al. Health-related quality of life among patients with relapsed or refractory multiple myeloma who received pomalidomide, bortezomib, and low-dose dexamethasone versus bortezomib and low-dose dexamethasone—results from the phase 3 OPTIMISMM study. Presented at the 2018 ASH Annual Meeting; December 1, 2018; San Diego, CA. Abstract 1960.

"QoL is a very important outcome measure for patients with multiple myeloma. PFS and overall survival (OS) are important too, of course, but if 2 arms of a clinical trial have generally similar PFS and OS results, I would definitely choose the better QoL treatment. However, I would definitely choose a therapy that improved my clinical outcome if it had little or no impact on QoL. I would NOT choose that therapy if it worsened my QoL, even if it modestly improved survival. I do not want to extend my life if the price to do it is feeling miserable for a few more months. On the other hand, if the survival difference was quite large, my decision might be different."—James Omel, MD

Appendix: Resources for Multiple Myeloma Patients and Their Caregivers

Pharmaceutical Reimbursement Assistance Programs

Amgen ASSIST 360™
Products: Kyprolis® (carfilzomib), Xgeva® (denosumab)
www.amgenassist360.com
1-888-4ASSIST (1-888-427-7478)

Bristol-Myers Squibb Access Support®
Product: Empliciti™ (elotuzumab)
www.bmsaccesssupport.bmscustomerconnect.com/patient
1-800-861-0048

Celgene Patient Support®
Products: Revlimid® (lenalidomide), Thalomid® (thalidomide), Pomalyst® (pomalidomide)
www.celgenepatientsupport.com
1-800-931-8691, ext 4091

Janssen CarePath
Product: Darzalex® (daratumumab)
www.janssencarepath.com/patient/darzalex/patient-support
1-844-55DARZA (1-844-553-2792)

Novartis Oncology Patient Support
Products: Farydak® (panobinostat), Zometa® (zoledronic acid)
www.patient.novartisoncology.com/
1-800-282-7630

Takeda Oncology Co-Pay Assistance Program (Takeda Oncology 1Point™)
Product: Ninlaro® (ixazomib)
www.takedaoncologycopay.com
1-844-T1POINT (1-844-817-6468), Option 2

Takeda VELCADE Reimbursement Assistance Program (VRAP)
Product: Velcade® (bortezomib)
www.velcade.com/Paying-for-treatment/
1-866-VELCADE (1-866-835-2233), Option 2

Patient/Caregiver Financial Assistance Services

Benefits.gov
www.benefits.gov

CancerCare Financial Assistance Program
www.cancercare.org/financial

Centers for Medicare & Medicaid Services
www.cms.hhs.gov

HealthWell Foundation Multiple Myeloma - Medicare Access (Medicare patients only)
www.healthwellfoundation.org/fund/multiple-myeloma-medicare-access/

Leukemia & Lymphoma Society (LLS) Financial Support
www.lls.org/support/financial-support

NeedyMeds
www.needymeds.org

Partnership for Prescription Assistance (PPA)
www.pparx.org

Patient Access Network (PAN) Foundation
https://panfoundation.org/index.php/en/

Patient Advocate Foundation (PAF)
www.patientadvocate.org

RxAssist Patient Assistance Program Center
www.rxassist.org

Social Security Disability Insurance & Supplemental Security Income
www.ssa.gov/benefits/disability/

The Bone Marrow Foundation
https://bonemarrow.org/financial-assistance/

Other Resources

Academy of Oncology Nurse & Patient Navigators
CONQUER: the patient voice® magazine (free subscription)
https://conquer-magazine.com/subscribe/

American Association for Cancer Research
Cancer Today magazine (free subscription)
www.cancertodaymag.org/subscriber-services

CURE®: Cancer Updates, Research & Education
CURE magazine (free subscription)
www.curetoday.com/subscription

International Myeloma Foundation
Myeloma Terms and Definitions
www.myeloma.org/sites/default/files/images/publications/tools/glossary.pdf

Myeloma Acronyms and Abbreviations
www.myeloma.org/sites/default/files/images/pages/acronyms.pdf

National Cancer Institute
Eating Hints: Before, during, and after Cancer Treatment
www.cancer.gov/publications/patient-education/eatinghints.pdf