ELSEVIER

Blood 142 (2023) 4753–4754

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

653.MULTIPLE MYELOMA: PROSPECTIVE THERAPEUTIC TRIALS

A Phase 1 Trial Evaluating the Addition of Lenalidomide to Relapsed/Refractory Multiple Myeloma Patients Progressing on Ruxolitinib and Methylprednisolone

James R Berenson, MD[1,2,3], Andrea Limon[3], Stephanie Rice[3], Tahmineh Safaie[3], Ralph Boccia, MD[4], Honghao Yang, MD PhD[5], Mehdi M. Moezi, MD[6], Stephen Lim, MD[7], Gary Schwartz, MD[1], Shahrooz Eshaghian, MD[8], Matthew Brobeck[3], Regina Swift[1], Benjamin M. Eades[1], Sean Bujarski[1], Yohana Sebhat[1], Rudra Ray[1], Susanna Kim, PharmD[3], Robert Allen Vescio, MD[9]

[1] Berenson Cancer Center, West Hollywood, CA
[2] Institute for Myeloma and Bone Cancer Research, West Hollywood, CA
[3] Oncotherapeutics, West Hollywood, CA
[4] Center for Cancer and Blood Disorders, Bethesda, MD
[5] Global Oncology, Alhambra, CA
[6] Cancer Specialists of North Florida, Fleming Island, FL
[7] Cedars-Sinai Samuel Oschin Cancer Center, Los Angeles, CA
[8] LA Cancer Network, Los Angeles, CA
[9] Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA

Background
Ruxolitinib (RUX), an orally administered selective JAK 1/2 inhibitor, has received approval for the treatment of myelofibrosis, polycythemia vera, and graft-versus-host disease. We have previously demonstrated the anti-multiple myeloma (MM) effects of RUX alone and in combination with the immunomodulatory agent lenalidomide (LEN) and glucocorticosteroids both pre-clinically and clinically. Although we have previously demonstrated that LEN and steroid refractory MM patients respond to the addition of RUX, no studies have evaluated whether LEN can achieve clinical activity among those progressing on the combination of RUX and methylprednisolone.
Methods
Patients included those with MM showing progressive disease (PD) who had previously received a proteasome inhibitor, LEN, glucocorticosteroids, and at least three prior regimens. Initially, subjects received oral RUX 15 mg twice daily and oral methylprednisolone 40 mg every other day. Those patients who developed PD according to International Myeloma Working Group criteria had LEN 10 mg once daily days 1-21 on a 28-day cycle added to RUX and methylprednisolone which were administered at the same doses they were receiving at the time of PD.
Results
A total of 29 subjects were enrolled and initially received the combination of RUX and methylprednisolone. Follow up was until June 30, 2023. The median number of prior therapies was 6 (range, 3-12). The overall response rate (ORR) was 31% and the clinical benefit rate (CBR) was 34%. The best responses were 1 very good partial response (VGPR), 8 partial responses (PR), 1 minor response (MR), 12 stable disease (SD), and 7 PD. The median progression-free survival (PFS) was 3.5 mo (range, 0.5-36.2 mo). The median time to response was 3.0 mo (n=10). The median duration of response (DOR) was 12.5 mo (range, 2.8-36.2 mo). Twenty (69%) showed PD and had LEN added to the RUX and methylprednisolone combination: all of these patients were refractory to their last LEN-containing regimen. After the addition of LEN, the ORR was 30% and CBR was 40%. The best responses of patients following the addition of LEN were 2 VGPR, 4 PR, 2 MR, 8 SD, and 4 PD. The majority of patients (71%) who initially achieved a > MR to the two-drug combination responded following the addition of LEN whereas only 23% of patients who did not initially achieve a > MR responded to the addition of the third drug. The median time to response was 2.6 mo (range, 0.7-15 mo). The median DOR was undefined (range, 1.2-10.9 mo). The median PFS was 3.5 mo (range, 0.3-25.9 mo). The median PFS2 (including time from first treatment to end of study or June 30, 2023) was 7.3 mo (range, 0.5-39.9). Treatment was well tolerated with no additional toxicity identified following the addition of LEN. Interestingly, PFS2 was predicted by the patient's baseline serum B-cell maturation level; patients with values above the median (128 ng/mL) had significantly shorter PFS2 than those below it (3.5 mo vs. undefined, $p = 0.0337$).

Conclusion
The addition of LEN to heavily, previously treated relapsed/refractory MM patients progressing on RUX and methylprednisolone shows significant clinical activity. This three-drug combination is well tolerated and is able to extend the benefit of RUX-based treatment for these patients. The promising results from this phase 1 clinical trial demonstrate a potential novel, all oral therapeutic approach for treating RRMM patients.

Disclosures Berenson: *Incyte Corporation:* Research Funding. **Vescio:** *Bristol Myers Squib:* Speakers Bureau; *Amgen:* Speakers Bureau; *Alnylam:* Speakers Bureau.

https://doi.org/10.1182/blood-2023-180287