F. Foss[1]
R. Advani[2]
K. Hymes[3]
B. Pohlman[4]
E. Jacobsen[5]
J. McDonnell[6]
A. Lerner[7]
Y. Kim[2]
R. Mundis[6]
M. Duvic[8]

[1]Yale Univ., New Haven, CT; [2]Stanford Univ., Stanford, CA; [3]New York Univ. Medical Center, New York, NY; [4]Cleveland Clinic, Cleveland, OH; [5]Dana Farber Cancer Inst., Boston, MA; [6]Kansas City Cancer Center, Lenexa, KS; [7]Boston Medical Center, Boston, MA; [8]MD Anderson, Houston, TX, USA

Activity of Belinostat in patients with recurrent or refractory peripheral or cutaneous T-cell lymphoma

Background

Belinostat (PXD101) is a hydroxamate pan HDAC inhibitor which demonstrates broad antineoplastic activity *in vitro* and *in vivo*. Phase I studies have shown that belinostat is well-tolerated and has had activity in T-cell malignancies.

Methods

We conducted a Phase II trial to evaluate the activity of intravenous belinostat in patients with peripheral T-cell lymphoma (PTCL) or cutaneous T-cell lymphoma (CTCL) who failed ≥1 prior systemic therapy. Belinostat (1000 mg/m^2) was administered as a 30-min IV infusion on Days 1-5 of a 3-wk cycle. The primary endpoint was objective response (OR) rate for each study arm. Response for PTCL and CTCL was evaluated using the Cheson criteria and Severity Weighted Assessment Tool (SWAT), respectively. For each study arm, a Simon 2-stage design was used based on target OR rate of 25%, with expansion to 34 pts if ≥2/13 responses were observed.

Results

In the PTCL arm, 12 pts (9 with stage III/IV disease) were enrolled and included: 2 anaplastic large cell lymphoma (ALCL), 2 angioimmunoblastic T-cell lymphoma, 1 NK T-cell lymphoma, and 7 PTCL-unspecified (PTCL-U). Pts were treated for a median of 2 cycles (range 1-8). Of 11 evaluable patients, there were 2 CR and 5 pts with SD. The two CR, both pts with Stage III PTCL-u, have median durations of 11+ and 15+ wks. One pt with PTCL-U (14%) had SD lasting 14 wks and discontinued study due to an adverse event (AE). Both pts with ALCL had stable disease, for 20+ and 14 wks. In the CTCL arm, 16 pts were enrolled, including 9 Mycosis Fungoides (MF), 5 Sezary Syndrome, 2 primary cutaneous ALCL, and treated for a median of 2 cycles (range 1-6). Overall, 8 of 16 had clinically significant improvement in skin disease with ≥35% decrease in skin involvement as measured by SWAT. The response rate was 25% (4 of 16) with 1 CR and 3 PR, one of which was observed 8 days after first dose, with dura-

tion of 10+ wks. Significant improvement in pruritis score by ≥3 on a visual analog scale was reported in 5/6 patients who reported significant pruritus. Overall the drug was well tolerated and most AE were grade I/II (nausea, fatigue, constipation, diarrhea and vomiting). Grade 3 AE attributed to the study drug occurred in 7 pts and included peripheral edema, apraxia, adynamic ileus, and infections. Only 1 related Grade 4 AE was noted (thrombocytopenia).

Conclusions

Belinostat (PXD101) is generally well tolerated and demonstrates encouraging clinical activity in relapsed or refractory PTCL and CTCL. The objective response rate in both arms has met the pre-defined criteria for study expansion to stage II of enrollment. In addition, a study is ongoing to explore the activity of an oral formulation of Belinostat in patients with refractory lymphoma.