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APREMILAST: A POSSIBLE NEW TREATMENT FOR VULVAR PAIN—CLINICAL TRIAL RESULTS

Hypothesis / aims of study

Studies show that more than 14 million women have vulvar pain in the U.S. Vulvar vestibulitis tissue samples show IL-1β is elevated 2.3-fold, and TNF-α is elevated 1.8-fold over controls [1]. Apremilast is a well tolerated, novel, orally available small molecule that specifically inhibits PDE4 and modulates multiple pro- and anti-inflammatory mediators. However it has not been studied with vulvar pain. Our hypothesis was that Apremilast would be effective in treating vulvar pain. The aims of this study were to evaluate the efficacy, safety and quality of life associated with Apremilast in patients with vulvar pain.

Study design, materials and methods

This phase II, open label, single arm, single site study evaluated an oral dose of Apremilast 20 mg twice a day for 12 weeks in 10 women ages 18-69. Women with vulvar pain at 2 or more vulvar sites tested with a q-tip scoring ≥3 (0-10 pain scale), with vulvar pain for at least 3 months prior to enrollment, and no history of tuberculosis or confounding medicines or medical problems were included. Post-screening visits were at 1, 2, 4, 6, 8, 10 and 12 weeks, with a 1-month off drug visit at week 16. Disease activity was measured as the change between weeks 0 (Visit 1) and 12 (Visit 9) on the primary outcome Global Response Assessment (GRA), a 7 item scale from markedly worse to markedly improved. Pain was measured using the Visual Pain Analog Scale 0-100 (VAS); quality of life was measured using the SF-12 Health Survey, Female Sexual Function Index 2000 (FSFI) and the Female Sexual Distress Scale (FSDS). Safety monitoring used the NCI Common Toxicity Criteria.

Results

Complete data was available for 7 women (3 withdrew: 2 for lack of efficacy; 1 for side effect to med—lactose intolerance). The mean age= 49 (range =21-63); BMI: mean=24.6(range =21-30); 2/3 were postmenopausal. GRA responders: 56% moderately or markedly improved at visit 6; 71% at visit 9(end of drug) and 29% at visit 10 (1 month off drug).

Means	VAS (0-100)	SF-12 PCS	SF-12-MCS	FSFI	FSDS
Visit 1	44.7±23	45.6±13	41.7±16	14.4±5.6	25.7±18
Visit 6	19.9±21	47.0±15	46.2±13	18.4±11.1	21.2±16
Visit 9 end of drug	17.3±18	50.8±15	46.6±10	21.8±9.7	15.4±15
Visit 10 one month off drug	32.7±22	47.9±14	42.4±15	13.5±8.9	21.9±14
Pvalues for change over time	0.0014	0.46	0.34	0.021	0.019

The FSFI changed significantly over time. The FSFI at visit 9 was significantly improved from visit 1 (p=0.04), then decreased when off drug from visit 9 to 10 approaching statistical significance (p=0.054).The FSDS changed significantly over time and significantly improved from visit 1 to visit 6 (p=0.015) and visit 9 (p=0.017). VAS dropped significantly over time (visit 1 to visit 6 p=0.0003) and from visit 1 to visit 9 (p=0.0015).There was no significant change in lab values over time, and no significant adverse effects (temporary mood change, GI disturbance found not related to drug).

Interpretation of results

It appears that apremilast may be a useful treatment for vulvar pain, however with a small sample size in an open label trial, statistical significance is difficult to determine and conclusions cannot be made. Of note is the improvement in subjects while on drug over time, with the return to almost baseline levels on all parameters tested when off the drug for one month.

Concluding message

Apremilast needs further study to determine efficacy, safety, dosing and frequency in a randomized controlled trial before efficacy as a treatment for vulvar pain can be determined.

References

1. Foster, DC, Hasday JD. Elevated Tissue Levels of Interleukin-1ß and Tumor Necrosis Factor-alpha in Vulvar Vestibulitis. Obstet Gynecol 89: 291-6, 1997.

Specify source of funding or grant	**Celgene Corporation**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**Yes**
Specify Name of Public Registry, Registration Number	**www.ClinicalTrials.gov NCT00814632**
Is this a Randomised Controlled Trial (RCT)?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**William Beaumont Hospital Human Investigation Committee**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**