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# A Phase II international, multicenter study of oral panobinostat (LBH589) in patients with refractory cutaneous T-cell lymphoma

## Background

Panobinostat (LBH589) is a potent pan-deacetylase inhibitor (DACi) which has demonstrated activity in patients (pts) with CTCL in a Phase I study (Prince *et al.,* ASCO 2007).

## Methods

This Phase II open-label multicenter study is enrolling CTCL patients (Stage IB–IVA), with mycosis fungoides (MF) or Sézary syndrome (SS), who have failed ≥2 prior systemic therapies, have adequate organ function and ECOG PS ≤2. Pts with significant cardiovascular abnormalities or QTcF >450 msec on screening ECG are excluded. Pts are stratified by either previous oral bexarotene (Group 1) or bexarotene-naïve (Group 2) status; both following a Simon 2-stage design. Panobinostat (20 mg) is administered orally on Days 1, 3, and 5 weekly until disease progression or intolerance. The primary endpoint is response rate measured by a composite of score derived from assessment of skin disease using modified Severity-Weighted Assessment Tool [mSWAT], and the evaluation of viscera and lymph nodes using CT. Intensive ECG monitoring for QTcF prolongation is performed.

## Results

Eighty-three pts (Grp 1=57; Grp 2=26) have been treated, with a median age of 58 yrs [range 25-88]; 50 male, 33 female; 62 MF, 21 SS. Median number of prior treatment regimens for Grp 1 pts is 4. Preliminary results for the primary endpoint show that 8 of the evaluable patients in Grp 1 achieved confirmed skin response, including 1 complete response. Seven of the 8 responders by mSWAT and CT scan also responded by PGA with 1 SD. Preliminary safety data have been analyzed for all patients who received at least one dose of study drug (N=83). Most common (>15%) AEs (all grades) include nausea, diarrhea, thrombocytopenia, fatigue, pruritus, abdominal pain, hypertriglyceridaemia, neutropenia, and headache. Twenty one of 57 pts in Grp 1 achieved improvement in pruritus. Among 3671 ECGs analyzed, there has been no QTcF >500 ms, two QTcF >480 ms, and three QTcF >60 ms increased from baseline.

## Conclusions

Preliminary efficacy as documented by improvement in composite score (mSWAT + CT) has been observed. Ongoing review of preliminary safety data demonstrates that panobinostat is generally well tolerated, with a manageable safety profile. Enrollment for Group 1 and Group 2 is ongoing.