Bisphosphonate therapy in Langerhans cell histiocytosis: An international retrospective descriptive study

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BACKGROUND

- Langerhans cell histiocytosis (LCH) is characterized by reactive clonal proliferation and accumulation of pathological dendritic cells.
- Bone involvement in LCH can be destructive and painful with significant morbidity from pathologic fractures.
- Bisphosphonates are osteoclast inhibitors that can be effective in treating bone Langerhans cell histiocytosis (LCH).

OBJECTIVES

- To describe the outcomes of patients with bone-LCH who received bisphosphonate therapy.
- To evaluate whether bisphosphonates can be effective in non-osseous LCH lesions.

MATERIALS & METHODS

- Retrospective clinical data were collected and analyzed on 18 LCH patients (both pediatric and adult) treated with bisphosphonates from 4 centers world-wide using a standardized data collection sheet.
- Appropriate research ethics approval was obtained from each of the participating centers.

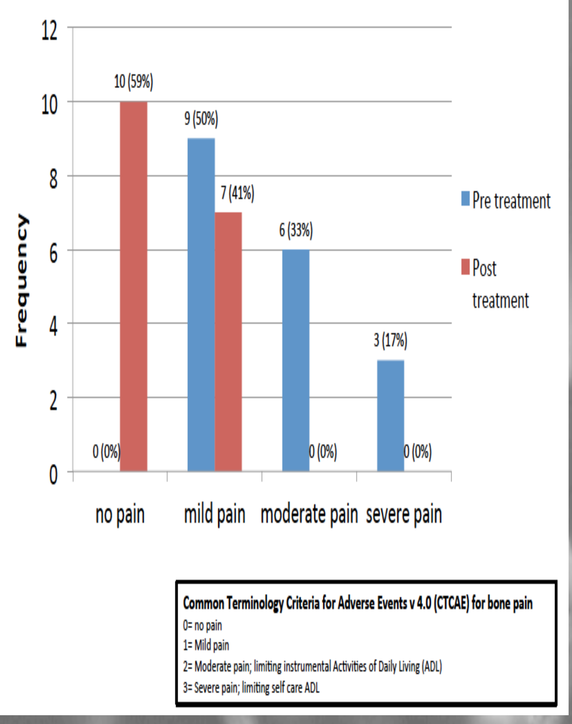
RESULTS

- All 18 patients received bisphosphonates therapy either at diagnosis or at ≥ 1st reactivation.
- Patients had either single system (SS) or multisystem (MS) LCH with or without risk organ involvement.
- Patients were treated with Zoledronic acid (n=10), followed by Pamidronate (n=4) and Alendronate (n= 3); one patient received both pamidronate and zoledronic acid.

Table 1: Patient Characteristics

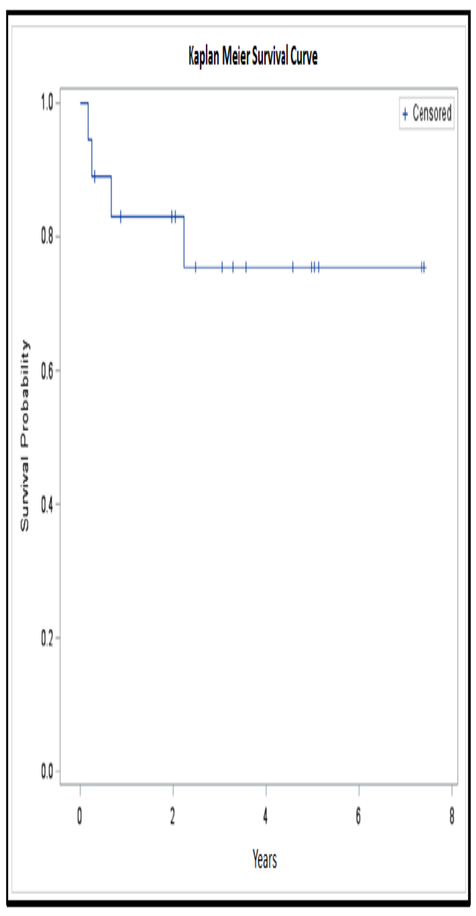
	All patients (N=18)
Median age at diagnosis (Years) (IQR)	15.8 (1.8-28.5)
Median age at the start of bisphosphonate therapy (Years) (IQR)	23.7 (5.7-38.3)
Gender N (%)	
Male	11 (61)
Female	7 (39)
Median Follow Up (Years) (IQR)	2.8 (0.9-5.0)

Pain score pre and post bisphosphonate therapy



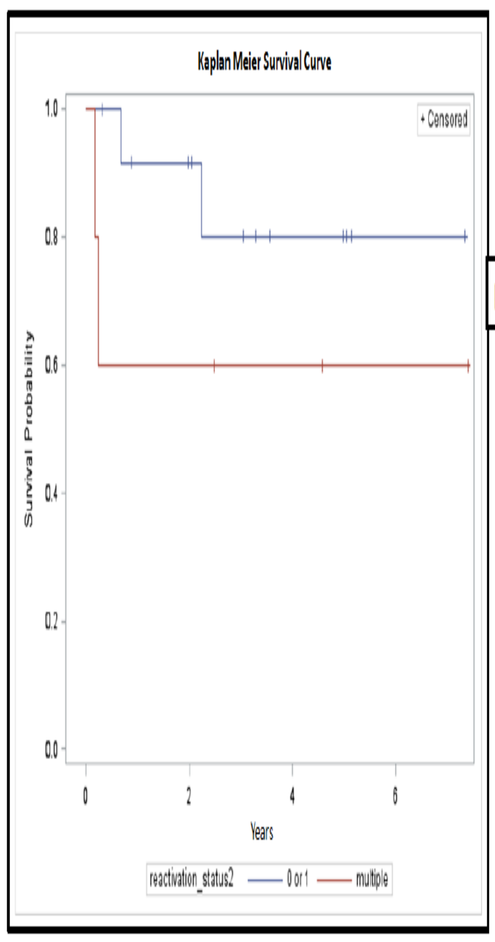
RESULTS

Progression Free Survival post bisphosphonate therapy



PFS at 3 years= 75 ± 11%

Progression Free Analysis by reactivation status at the start of bisphosphonate therapy



P=0.24

- All patients reported significant reduction in pain, to either no or mild pain after administration of bisphosphonates, with none having moderate/severe pain.
- 13/18 patients (72%) achieved complete remission (CR) in the bone lesions, including lesions in skin (n=1), lung (n=1) and pituitary (n=1); 2 had partial response and 3 had no response.
- Among the 13 CR patients, 12 had no active disease for a median of 4.1 years (range 2.8 - 5.1 years) and 1 developed radiographic neurodegeneration after 2 years.
- Bisphosphonate therapy was well tolerated by all patients with no major toxicity.
- Progression-free survival (PFS) was 75 ± 11% at 3 years, with a trend favoring better PFS (P=0.24) in patients with no or first reactivation compared with those having ≥ 2 reactivations.
- Age, gender, system involvement at diagnosis and concomitant medications did not affect the PFS.

CONCLUSIONS

- This is the largest cohort of LCH patients treated with bisphosphonates in the literature so far.
- Bisphosphonates significantly improved bone pain in patients with bone LCH, and may be effective in treating extra-osseous disease.
- A prospective randomized trial evaluating the role of bisphosphonates in multifocal bone LCH is warranted.

There are no relevant conflicts of interest to disclose