

## POSTER 24

### EVALUATION OF HISTOLOGIC CHANGES OF TENOSYNOVIAL GIANT CELL TUMORS FOLLOWING TREATMENT WITH PEXIDARTINIB

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**Background:** Tenosynovial giant cell tumors (TGCT) and pigmented villonodular synovitis (PVNS) are common names for a group of rare, typically benign neoplasms that occur in or around joints. They can have common histologic features and are classified according to growth pattern and behavior as 2 types: localized and diffuse. Localized TGCT (L-TGCT) is the more common form of TGCT representing 90% of TGCT cases. L-TGCT usually affects small joints or tendon sheaths and are limited to a specific portion of the joint, typically confined to the synovium or tendon sheath. Diffuse TGCT (D-TGCT) are more aggressive, typically affecting bone and large joints, and spread widely in or around the entire joint. D-TGCT are less common, representing 10% of TGCT cases, and have a propensity for local recurrence usually resulting in the need for a joint replacement. The median age of patients diagnosed with TGCT is 40 years with a range from 25-50. The localized type has a female preponderance; with a female:male predominance of 2.1:1. There is no sex predilection in the diffuse type. The most common primary sites of TGCT are the digits of the hands and the knees. Clinical presentation varies immensely and is dependent upon the location involved and the type present, but can include limited range of motion, pain, joint effusions and cartilage destruction occurring with more aggressive tumors. Surgical resection was the standard of care for TGCT. However, due to tumor recurrence or unresectable tumors due to location, there is increasing interest in the use of therapeutic agents that target CSF1/CSF1R pathway.

**Question/Purpose:** Are there noticeable histologic changes of TGCT following treatment with Pexidartinib?

**Patients and Methods:** 4 patients were retrospectively reviewed that received Pexidartinib prior to attempted complete surgical resection and open biopsy. Prior to the start of Pexidartinib, all patients had a core needle biopsy. The pre and post-treatment histology were reviewed following resection of the tumor bed. All patients required surgery because of continued pain, secondary to joint involvement and neurologic involvement with TGCT. Patients, because of side effects of the drug, were discontinued at 4 weeks, 3 months, and 6 months.

**Results:** There was 1 male and 3 females in our cohort with an average age of 40 years with a range of 17-62 years. 1 patient only took Pexidartinib for 4 weeks due to elevated liver enzymes that resolved with the discontinuation of medication. Out of the other 3 patients, 2 took Pexidartinib for 3 months and 1 for 6 months. There was little reduction in tumor mass based on CT/MRI for all patients. Comparison of pre and post Pexidartinib treatment histology showed remarkable changes for all patients as early as 4 weeks of treatment, with more dramatic changes demonstrated after 6 months of treatment (Figures 1 and 2).

**Conclusion:** Pexidartinib should be continued for a period of at least 3-6 months preoperatively, if possible, to see the most complete response prior to surgical resection. The effects of this CSF-1 inhibitor is dramatic and aids in the surgical resection of the tumor. Expression of the CFS-1 needs to be quantified comparing pretreatment and posttreatment at 3 months and possibly at 6 months. It appears there is a definite histologic effect as early as 4 weeks with the beginnings of necrosis of the histiocytes and giant cells.

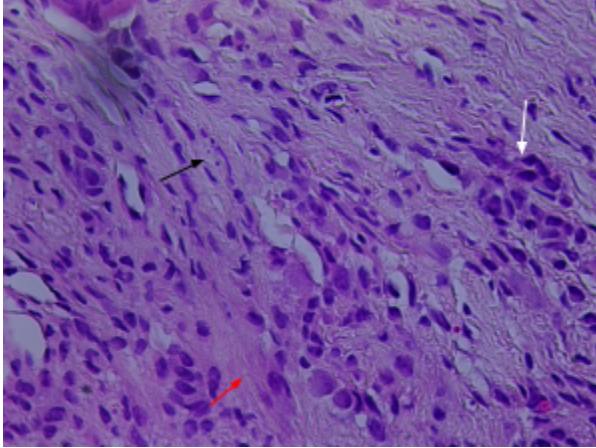


Figure 1: Core needle biopsy demonstrating the classic appearance of TGCT, with multinucleated giant cells (white arrow), histiocytes (black arrow) and fibrous tissue (red arrow) prior to treatment with Pexidartinib.

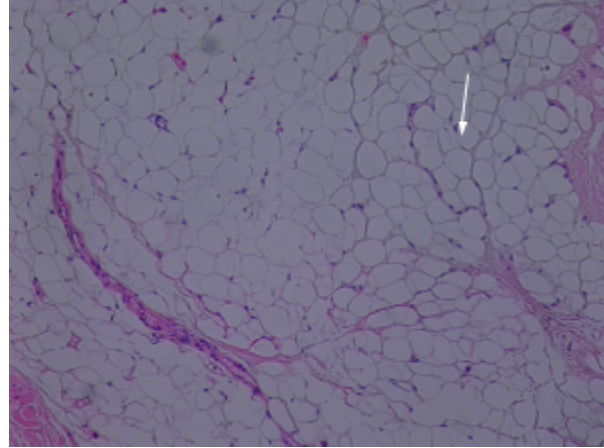


Figure 2: Post 6 month treatment with Pexidartinib from the same patient. This shows fat formation (white arrows) in the same area without histiocytes. The diagnosis of TGCT could not be made histologically at the time of resection.