

## INTRODUCTION

Thrombotic thrombocytopenic purpura (TTP) is a thrombotic microangiopathy due to reduced activity of ADAMTS13 (a disintegrin and metalloprotease with thrombospondin type 1 motif, 13). This disorder can be due to a congenital deficiency or acquired due to an autoantibody against ADAMTS13.

Immune mediated TTP (iTTP) is due to antibody inhibiting or causing clearance of ADAMTS13.

The aim of our study was to determine whether ADAMTS 13 inhibitor titer at initial presentation could serve as a predictor of refractory disease and relapse in iTTP. We also measured clinical outcomes across different gender and racial subgroups.

## MATERIALS & METHODS

The United States Thrombotic Microangiopathy (USTMA) iTTP registry was used to extract patient information for two academic institutions in Eastern North Carolina.

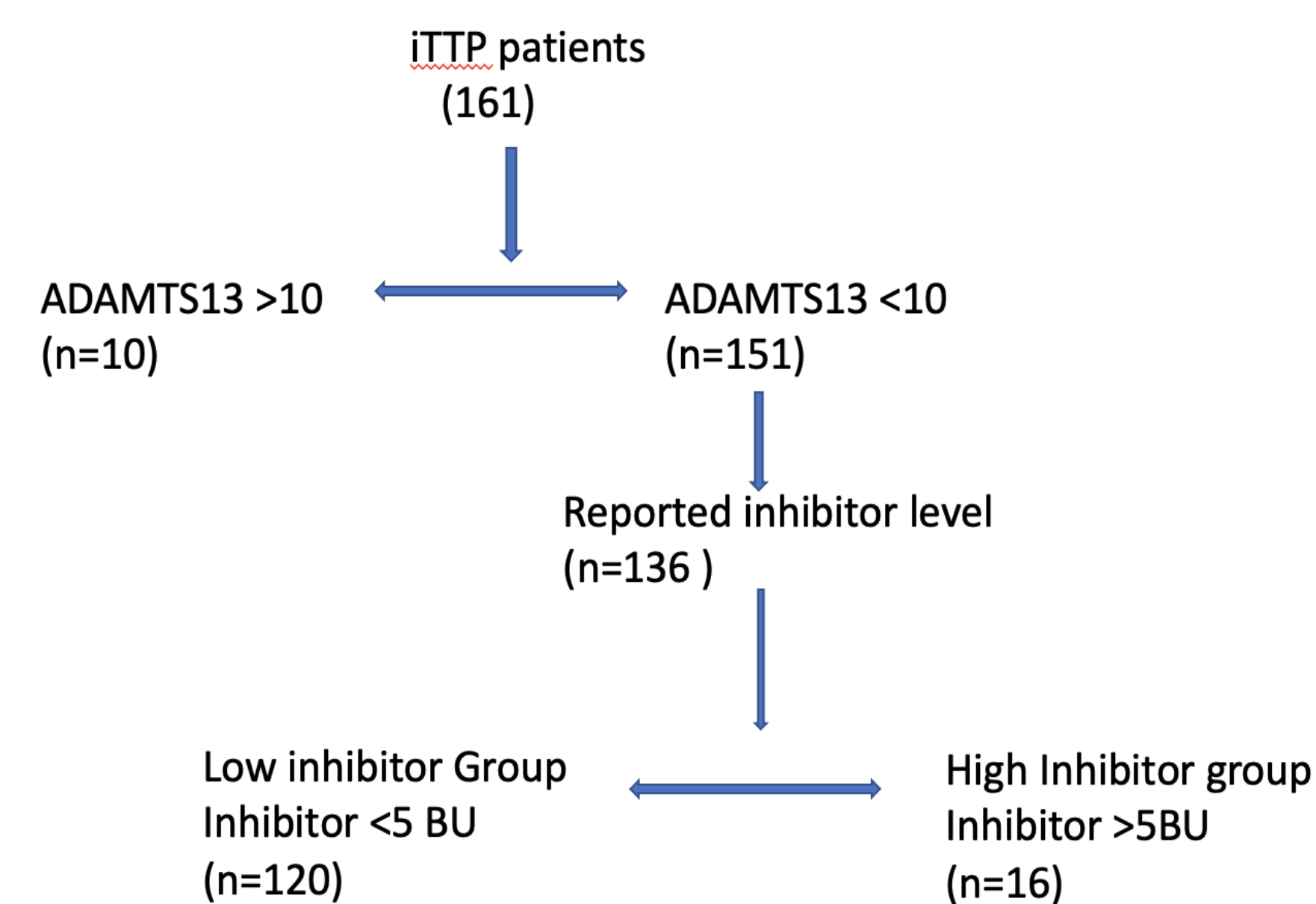
Descriptive statistics were used to analyze the data.

The first iTTP episode recorded in the data base was used as the index episode.

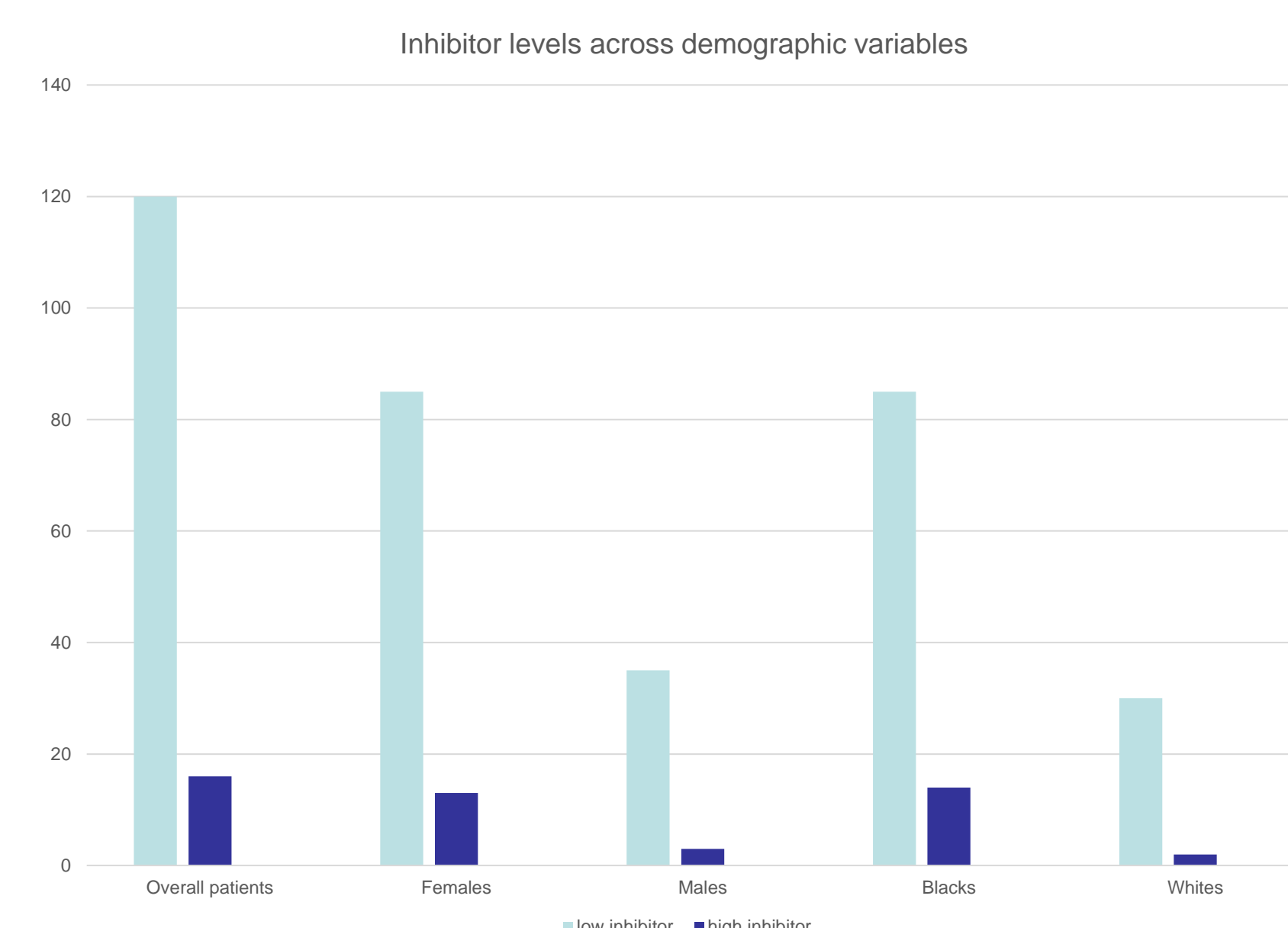
All patients included in the final analysis had an ADAMTS13 activity of <10%. An inhibitor level of 5 Bethesda units was arbitrarily chosen as the cutoff between low (<5) and high (≥5) inhibitor level.

- Response time was defined as the number of days of plasma exchange (PEX) required to achieve a platelet count of 150,000 for two consecutive days. Relapse was defined as occurrence of a new episode of iTTP 30 days after achievement of response (1).
- Refractory disease was defined as persistence of thrombocytopenia or absence of a sustained platelet count increment or platelet counts of < 50,000 despite 4-7 days of plasma exchanges and steroid treatment (2).
- Rituximab resistance was defined as lack of platelet recovery to > 150,000 within 11 to 14 days of administration of the first dose of Rituximab (3).

## RESULTS



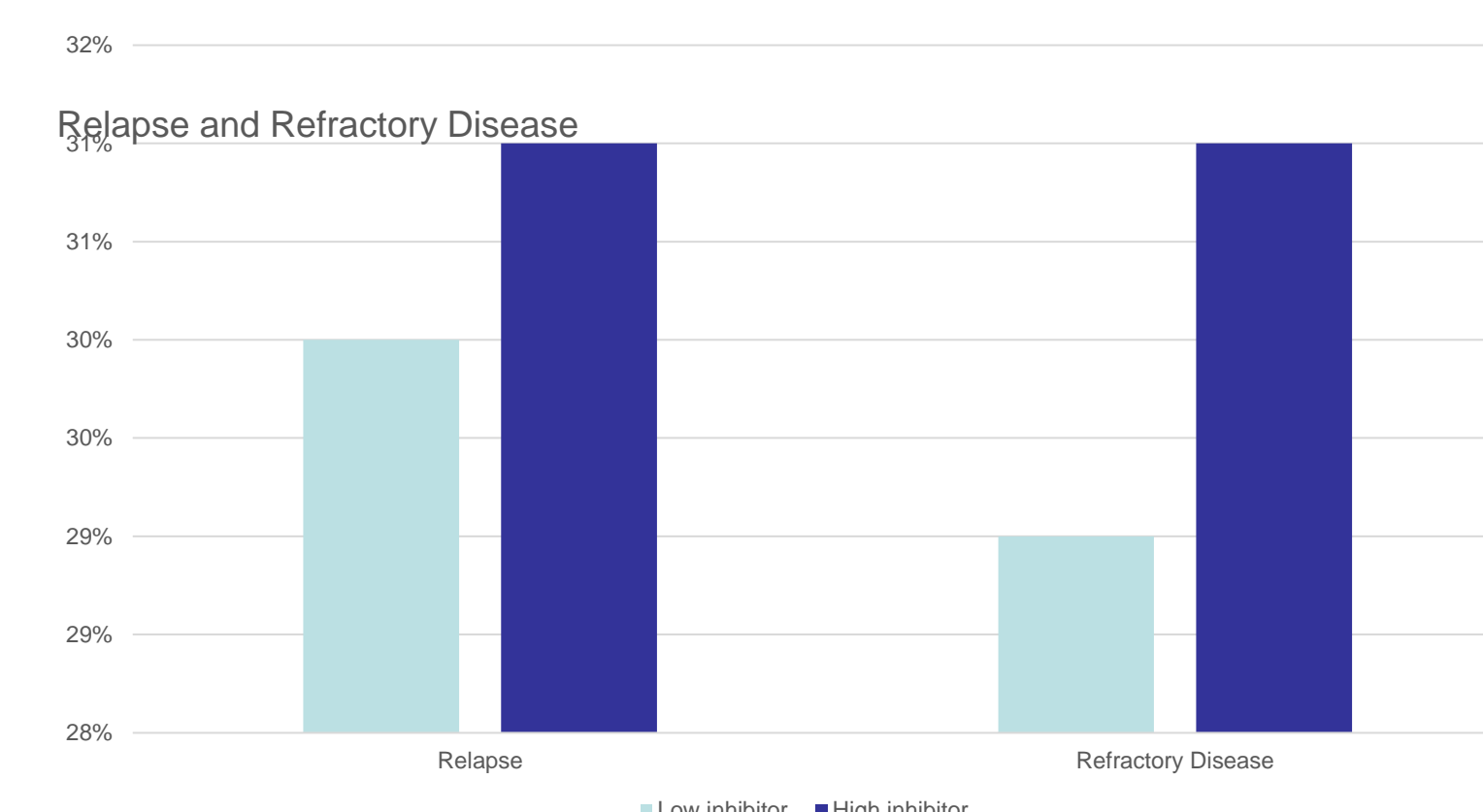
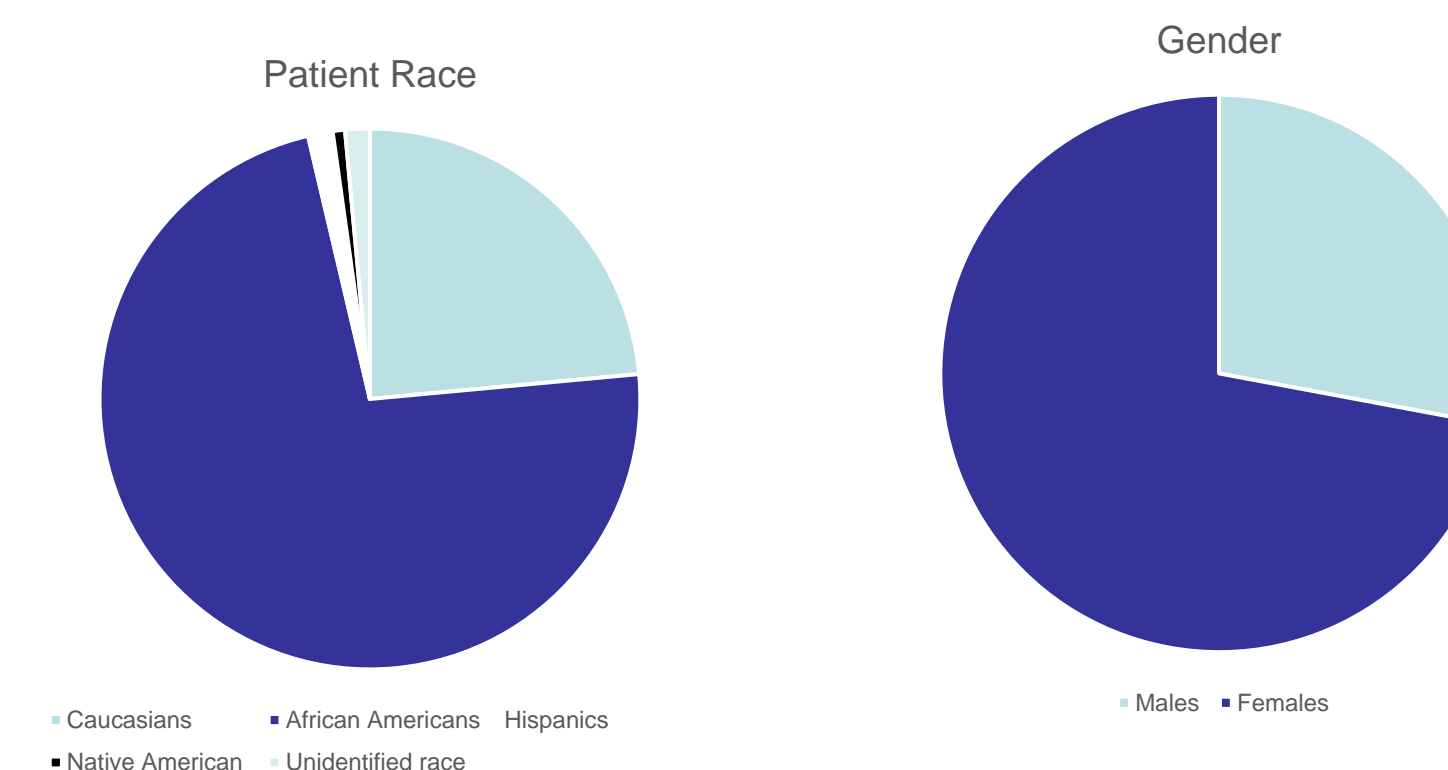
Forty-Three patients with ADAMTS13 activity <10 % had an inhibitor level of 0 (i.e undetectable). They were included in the low inhibitor group.



Overall, 88% patients (n=120/136) had low inhibitor level and only 12% (n=16/136) had a high inhibitor. Thirteen percent females (n=13/98) and 8% (n=3/38) males had a high inhibitor level (p=0.387). Fourteen percent (n=14/99) African Americans and 6 % (n=2/32) Caucasians had a high inhibitor, p=0.23.

At the time of enrollment in the registry, Rituximab was not a part of first line therapy. Only 26/136 patients had received Rituximab. In the low inhibitor group 5 patients displayed Rituximab resistance whereas there were no patients in the high inhibitor group with Rituximab resistance.

The cohort had 28% male (n =38/136) and 72% (n=98/136) female patients. There were more African American patients 73% (n=99/136) than Caucasians, 24% (n=32/136). There were also 2 Hispanic, 1 Native American and 2 patients with unidentified race.



Median ADAMTS3 inhibitor titer was value was 1.05 (Range 0-87).

In the low inhibitor group 30% (n=36/120) patients suffered at least one episode of relapse whereas 31% (n=5/16) had relapsed in the high inhibitor group.

The frequency of refractory disease was 31 % (n=5/16) in the high inhibitor group and 29% (n=34/119) in the low inhibitor group.

## RESULTS

The median time to response was 6 days (range 1-76) in the low inhibitor group and 7 days (range 4-20) in the high inhibitor group (p=0.61). While looking at the various subgroups, median time to response for males was 6 days (range 4-21), females 6 days (range 1-76) , African Americans 6 days (range 3-29) , and Caucasians 6 days (range 1-76).

## DISCUSSION

When evaluating patients presenting with iTTP in two centers in North Carolina, no correlation was found between a high inhibitor levels of ≥ 5 Bethesda units and risk of relapse or refractory disease.

There is a paucity of data looking at the correlation between ADAMTS13 inhibitor level and clinical outcomes.

A study published Hovenga et al suggested that patients with ADAMTS13 activity < 10% and an inhibitor titer of 2 or more Bethesda units/mL was associated with lower survival. However, they did not explore this further in terms or relapse/ refractory disease.

Another study by Zhang et al identified 20 patients with iTTP , out of these 16 had severe ADAMTS-13 deficiency i.e <5 (n=16). Seven patients had a detectable inhibitor level and 4 were noted to have a high inhibitor level of >5 units/ml. 3 out of these 4 patients had recurrent disease and 1 died. Our study results did not suggest a significant difference between low and high inhibitor patients in regards to relapse.

Conclusion: A larger study is needed to evaluate this further.

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