

REal life MAnagement of children with severe haemophilia A and INhibitors: first results of the REMAIN study

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Inhibitors
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Background: Inhibitors are a frequent side effect among previously untreated patients (PUPs) with severe haemophilia A affecting up to 30% of patients. FVIII replacement is still effective in patients with low-titer inhibitors, while by-passing therapy is required for bleeding control in those with high-titer inhibitors. Immune tolerance induction (ITI) is the only proven strategy to eradicate inhibitors, however no standard protocol exists for all patients and treatment optimization is highly warranted.

Aim: This study is aimed at describing the clinical status and the real life management of a large **unselected** cohort of children with severe haemophilia A and inhibitors followed-up for at least 3 years after inhibitor development.

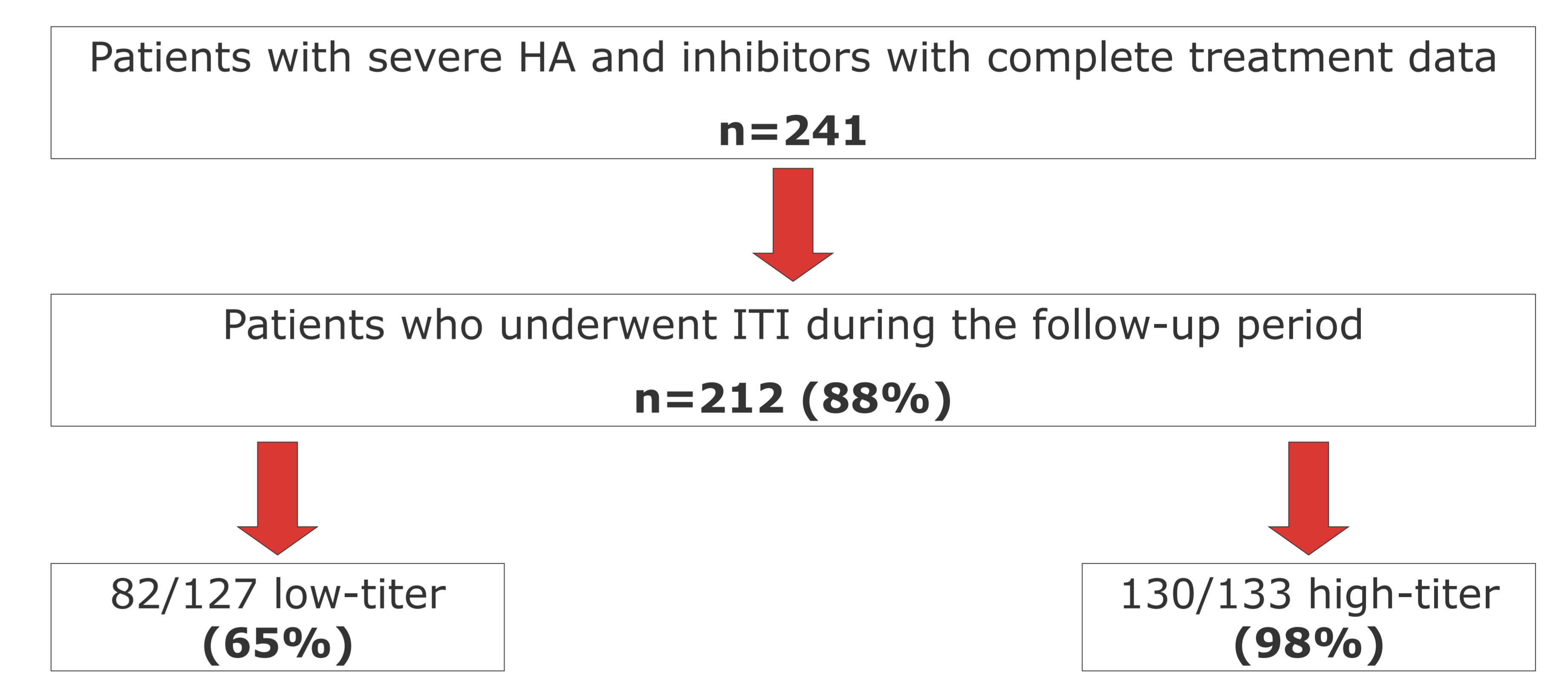
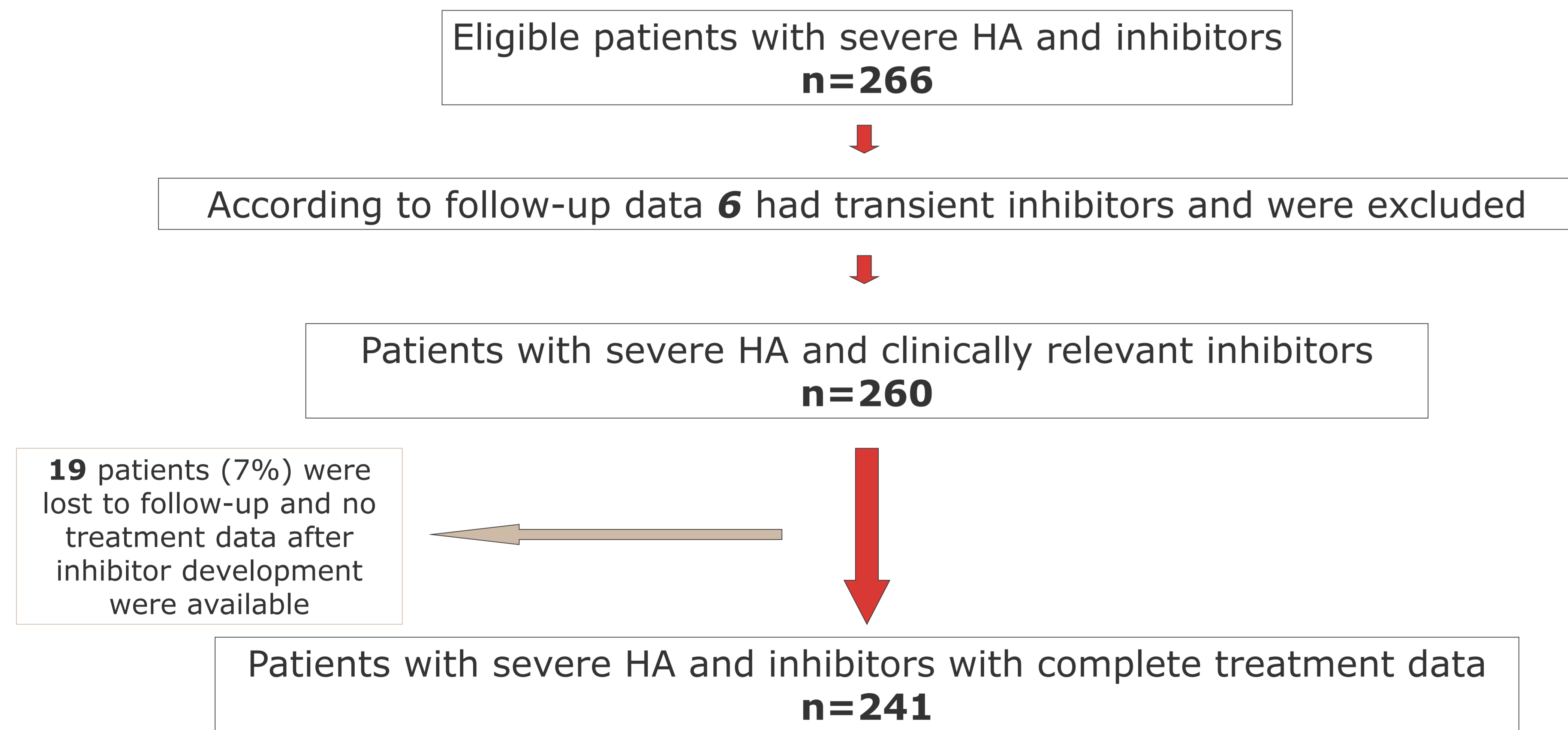
Methods: The REMAIN study is a satellite observational study of the PedNet Registry including all children with severe haemophilia A (FVIII<1 IU/dL) and inhibitors. Previously untreated patients born between January 1990 and December 2009 were consecutively recruited from 31 haemophilia treatment centers in 16 countries. Data on bleeding frequency, treatment of bleeding episodes and details on ITI (regimen, doses, product) were collected from medical files and laboratory data retrieved from local laboratories.

Based on inhibitor titer at diagnosis

127 (49%) had low-titer 133 (51%) had high-titer

Based on inhibitor peak reached during the follow-up period

69 (26%) had low-titers 191 (74%) had high-titers



Conclusions

- In this cohort of 260 unselected children with severe hemophilia A and inhibitors the proportion of low- and high-titer inhibitors at diagnosis was similar
- During follow-up 46% of low-titer inhibitors converted to high-titer upon FVIII re-exposure and high-titer inhibitors represented 75% of cases at the end of follow-up period
- A high proportion of patients underwent ITI both with low- and high-titer inhibitors

The PedNet Study Group

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