

Use of Sebetrastat as Short-term Prophylaxis for Patients With Hereditary Angioedema: Results From the KONFIDENT-S Study

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Key Takeaways

97.7% Of Procedures Without HAE Attack when ≥2 600mg doses of oral sebetrastat were used for short-term prophylaxis (STP)

0 Treatment-Related AEs with oral sebetrastat for STP (44 procedures across 16 patients)

These findings support the continued evaluation of sebetrastat as an alternative STP regimen

Background

- International hereditary angioedema (HAE) guidelines recommend STP with intravenous plasma-derived C1 inhibitor (IV pdC1INH) before medical or dental procedures to reduce the risk of perioperative angioedema attacks¹
- IV pdC1INH products are approved for STP in EU,² but no treatment options are indicated for STP in the US
- The use of STP is heterogenous and inconsistent,³ likely due to the burden of IV administration, product availability, and procedure coordination^{1,4}
- Sebetrastat has recently been approved in the US, Europe, Australia, Singapore, and Japan as the first oral on-demand treatment for patients with HAE⁵⁻⁸
- KONFIDENT-S, a 2-year open-label extension (NCT05505916), is investigating the long-term effectiveness and safety of on-demand sebetrastat.⁹ As part of this study, the potential of sebetrastat as an alternative STP regimen is also being evaluated

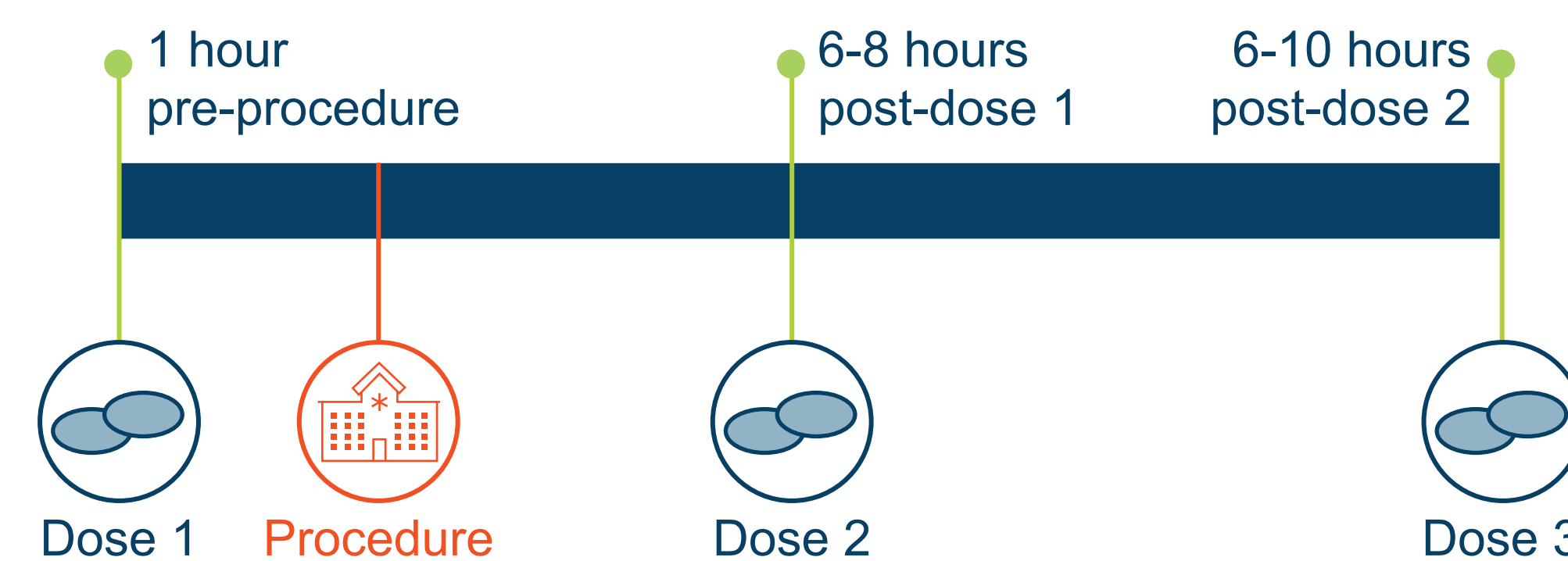
Objective

- Evaluate the effectiveness of sebetrastat for STP of HAE attacks triggered by medical and dental procedures among KONFIDENT-S participants

Methods

- The KONFIDENT-S trial population included patients ≥12 years of age with HAE-C1INH⁹
- Patients scheduled to undergo a medical or dental procedure were instructed to self-administer 3 doses of sebetrastat 600 mg as STP (**Figure 1**)
 - Participants using long-term prophylaxis (LTP) were excluded from the STP evaluation
 - The dosing interval was based on pharmacokinetic data with the goal of providing 24 hours of coverage
- Treatment effectiveness was assessed by the number of HAE attack within 24 hours of procedure start
- Safety was assessed using adverse event (AE) reporting

Figure 1. Sebetrastat dosing schedule for STP



Results

Participant Demographics and Characteristics

- At data cutoff (Sept 30, 2025), 16 of 136 patients (11.8%) in KONFIDENT-S had used sebetrastat as STP for medical or dental procedures (**Table 1**)

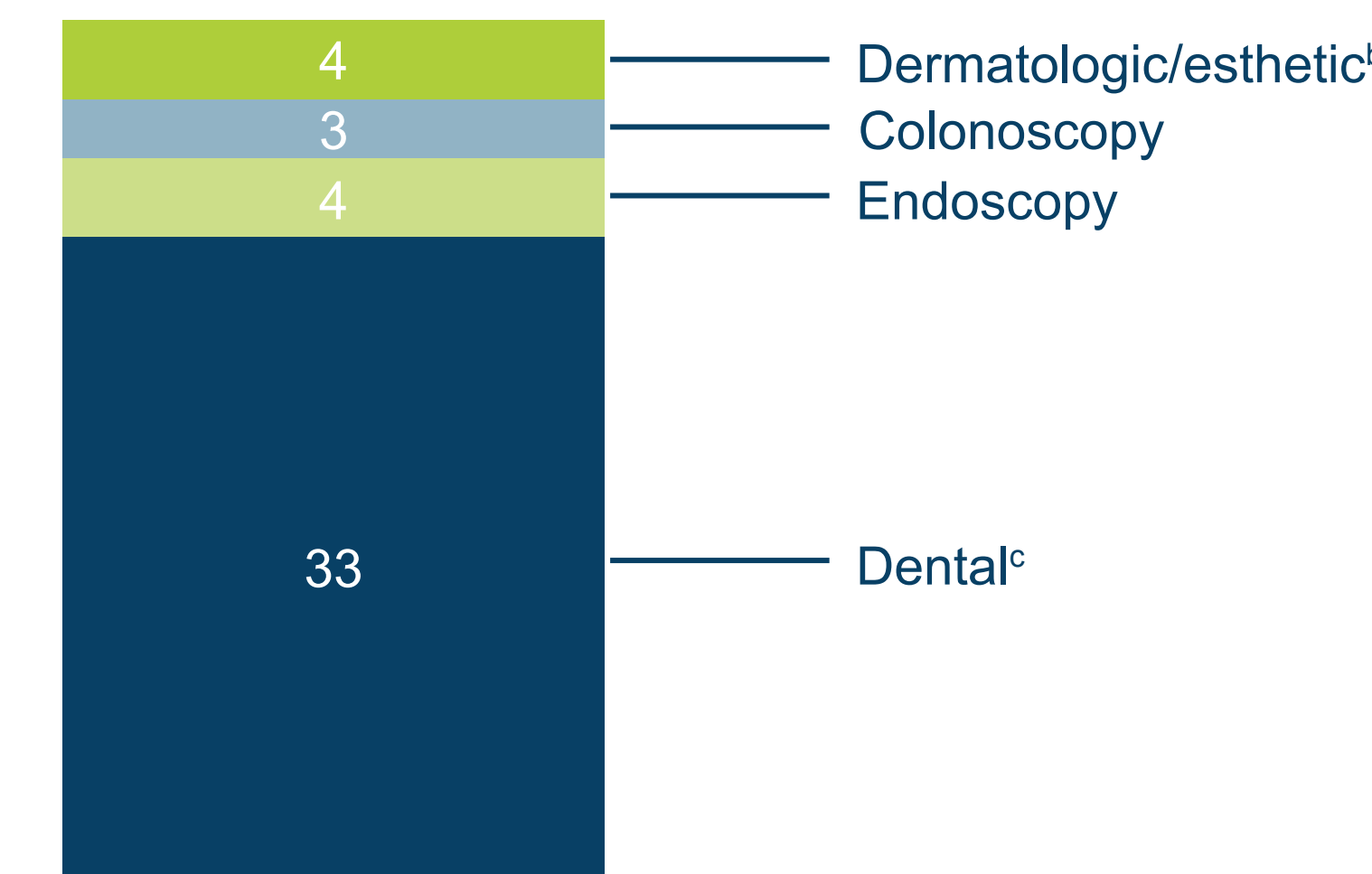
Table 1. Demographics and clinical characteristics of the STP population (N=16)

Age, mean (range), years	34.6 (16–58)
Age-group, n (%)	
<18 years	2 (12.5)
≥18 years	14 (87.5)
Females, n (%)	10 (62.5)
Race, n (%)	
White	11 (68.8)
Asian	5 (31.3)
Type 1 HAE-C1INH, n (%)	16 (100)
Family history of HAE-C1INH, n (%)	12 (75)
Years of diagnosis at screening, mean (range)	13.0 (0–34)

HAE-C1INH, hereditary angioedema with deficiency of functional C1-esterase inhibitor.

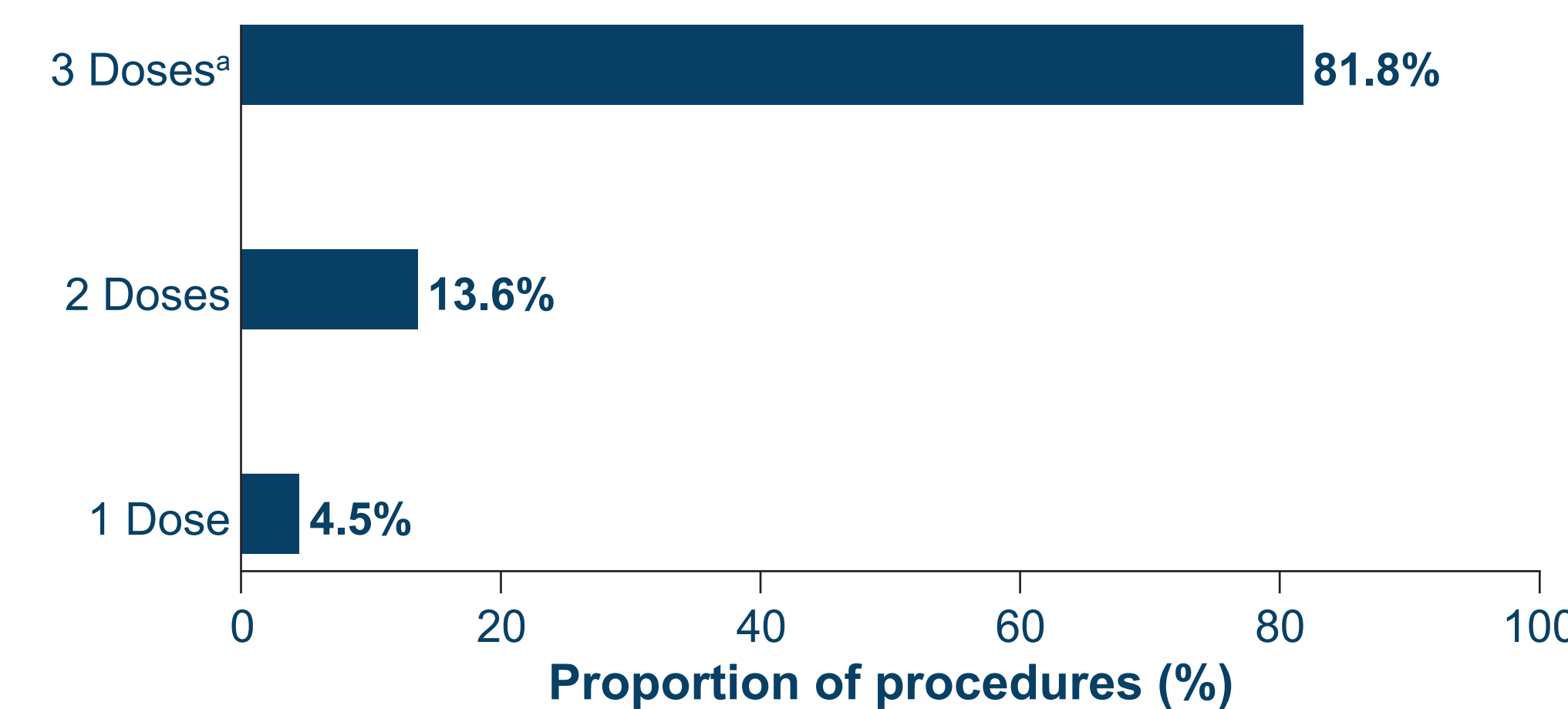
Results (continued)

Figure 2. Sebetrastat STP use by procedure (N=44)^a



^aIn one case, STP was used to cover 2 procedures (colonoscopy and gastroscopy).
^bDermal filler injection, lipoma excision, papilloma excision, and eyebrow microblading.
^cDental procedures (e.g., filling, root canal, extraction): 27; Dental care (other): 6.

Figure 3. Sebetrastat STP doses taken

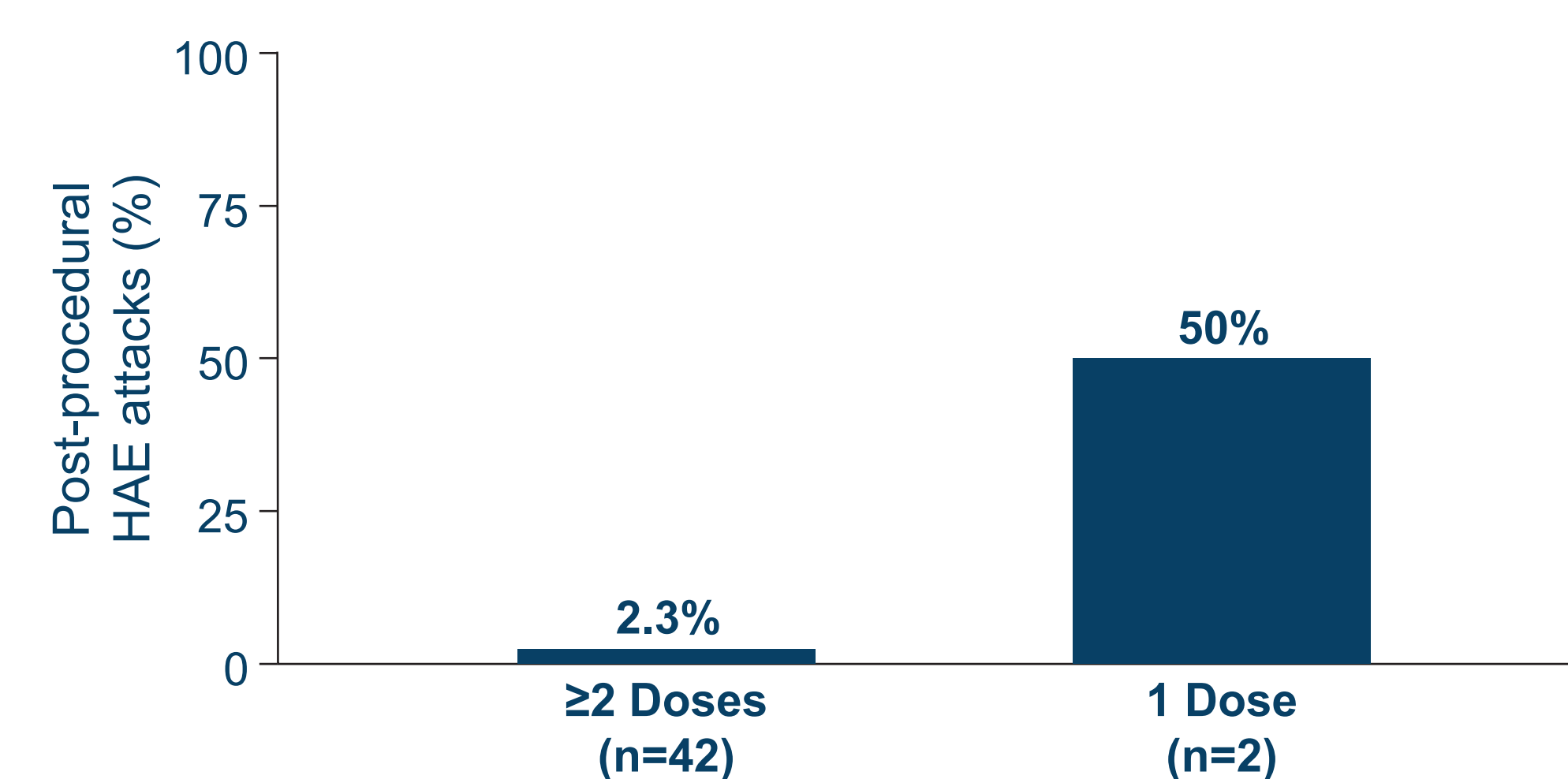


^aPer protocol.

STP Effectiveness Within 24 Hours

- For the 42 procedures in which 2 or 3 scheduled doses of oral sebetrastat STP were administered, 1 HAE attack (2.3%) occurred following dermal filler injection (mild severity) (**Figure 4**)
- For the 2 procedures in which only the first, pre-procedural dose of oral sebetrastat STP was administered, 1 HAE attack was reported following a colonoscopy (attack severity and location unknown)

Figure 4. HAE attack incidence within 24 hours of the procedure

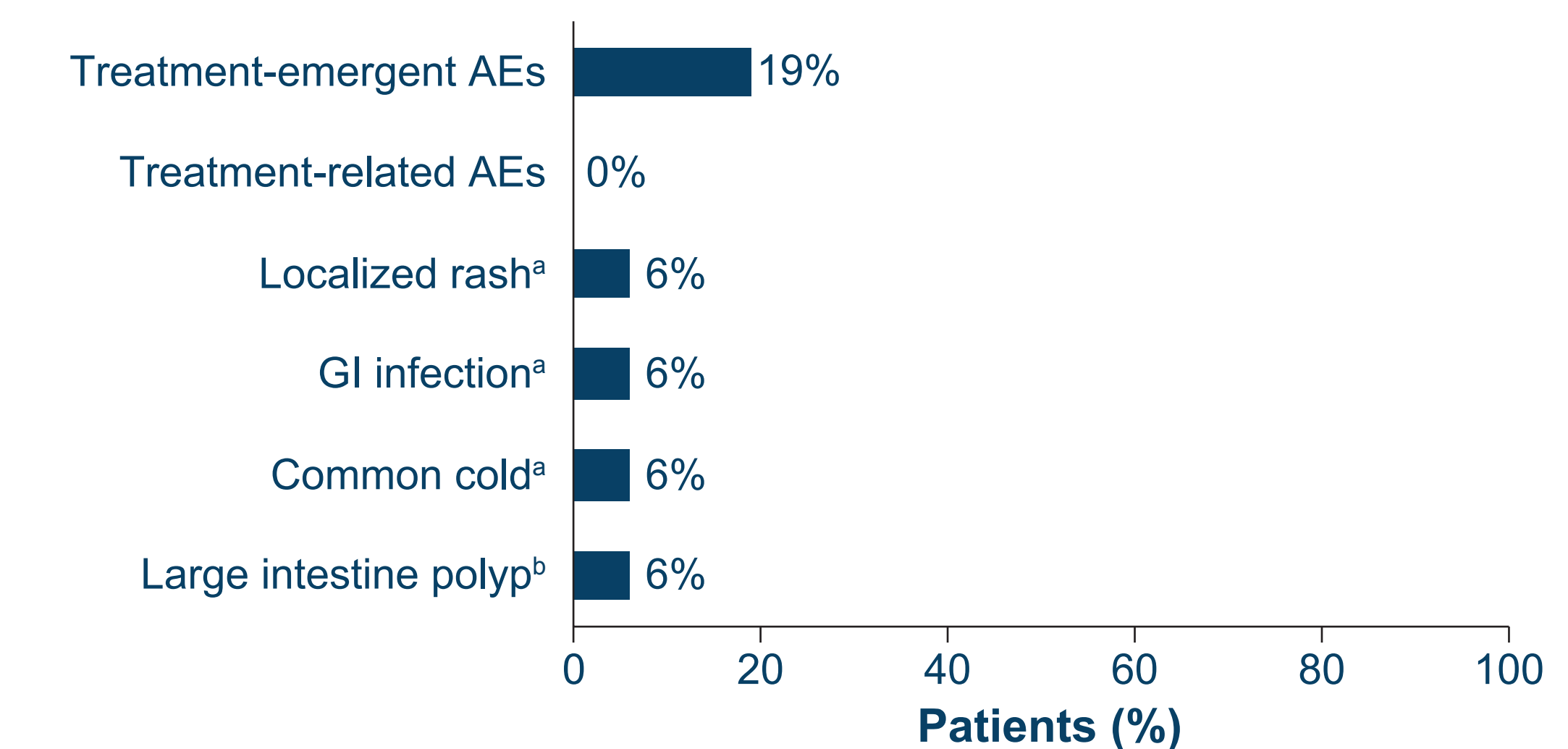


- Of the 44 total routine medical and dental procedures performed during which sebetrastat was used as STP, 2 (4.5%) procedures were accompanied by an HAE attack within 24 hours

Safety

- Five AEs were reported in 3 patients within 72 hours of administering sebetrastat as STP (**Figure 5**)

Figure 5. Adverse events



^aWith the use of 3 doses of sebetrastat.
^bAfter a single dose of sebetrastat.
 AE, adverse event.

Limitations to this study

- Few highly invasive procedures included
- No control arm/comparator
- Limited participant medical history

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