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Efficacy of novel endoscopic hemostatic agent for bleeding control and prevention: Results from a prospective, multicentric national registry

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Abstract:
Background: Topical hemostatic agents emerged as a new treatment modality for gastrointestinal bleeding. The aim of the study is to assess the safety and efficacy of PuraStat for control of active bleeding and for prevention of bleeding after different operative endoscopy procedures.
Methods: A national, multicenter, observational registry was established to collect data from ten Italian centers from June 2021 to February 2023. Demographics, type of application (active gastrointestinal bleeding or prevention after endoscopic procedures, site, amount of gel used, completeness of coverage of the treated area), outcomes (rates of intraprocedural hemostasis and bleeding events during a 30-day follow-up) and adverse events were prospectively analyzed.
Results: 401 patients were treated for an active gastrointestinal bleeding or as a preventive measure after different types of operative endoscopy procedures. 91 treatments for active bleeding and 310 preventive applications were included. In 174/401 (43.4%) PuraStat was the primary treatment modality. A complete coverage was possible in 330/401 (82.3%) with difficulty in the application in 7/401 (1.7%) of cases. Hemostasis of active bleedings was achieved in 90/91 patients (98.9%). In the 30-day follow-up 3.9% patients in whom PuraStat was used for prophylaxis had a bleeding event as compared with 7.7% after hemostasis. No adverse events related to the use of PuraStat were reported.
Conclusions: PuraStat is a safe and effective hemostat both for bleeding control and for bleeding prevention after different operative endoscopy procedures. Our results suggest that the possible applications for the use of PuraStat may be wider compared to current indications.

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1. Introduction

Acute gastrointestinal (GI) bleeding, from either an upper or lower source, is a common clinical entity that may frequently require hospitalization and that is associated with substantial morbidity and mortality. Although risk assessment protocols and treatment algorithms have been implemented, GI bleeding still represents a relevant economic burden for healthcare systems[1].

Endoscopy is a cornerstone in the management of GI bleeding, both for assessment and for treatment. The endoscopic armamentarium for hemostasis is wide, but it can be broadly categorized into injective, mechanical and thermal methods[2, 3].

In recent years topical hemostatic agents emerged as a new treatment modality that may have a role in challenging situation, such as management of diffuse bleeding or hemostasis of lesions located in regions difficult to reach endoscopically[4]. These agents (ie. Hemospray, EndoClot) are provided as powder, that is propelled endoscopically via a compressed gas onto the bleeding site. After contact with bodily fluid, the powder turns into a gel and promotes hemostasis through sealing of the bleeding site and enhancement of clot formation[5].

The use of hemostatic powders, however, is hampered by 2 main limitations: the risk of clogging of the delivery catheter and the limitation of visibility after application, due to the opaque nature of the hemostatic agent.

A novel type of topical hemostatic agent has been recently developed for the treatment of oozing bleedings. PuraStat (3D-Matrix Europe SAS, France) consist in a viscous and transparent biocompatible synthetic peptide solution that, upon exposure to blood due to a change in pH and ions concentration, undergoes self-assembly into fibers and forms a hydrogel barrier that both has an hemostatic effect and works as an extracellular matrix scaffold for subsequent healing[6, 7].

First clinical applications of PuraStat were described in various fields such as cardiac surgery[8, 9], vascular surgery[10], ear, nose and throat surgery[11–13] and general surgery[14, 15].

With regard to gastrointestinal endoscopy, PuraStat has proved effective and its use was approved for postprocedural oozing and bleeding from small blood vessels in the gastrointestinal tract as an adjunct

hemostatic modality and for reduction of delayed bleeding after colonic endoscopic submucosal dissection (ESD)[16–18].

Further studies investigated the potential role of PuraStat in other indications, such as spontaneous acute GI bleeding[19–21], post-sphincterotomy bleeding[22–26], post-papillectomy bleeding[27, 28], gastric antral vascular ectasia (GAVE)[29], hemorrhagic radiation proctopathy[30], walled-off pancreatic necrosis[31], solitary rectal ulcer syndrome[32], acute intrahepatic biliary duct bleeding[33], bleeding after endoscopic ultrasound-guided hepaticogastrostomy[34], delayed percutaneous endoscopic gastrostomy (PEG) bleeding[35], with very limited data but initial results seeming promising.

In order to further investigate the role of PuraStat for various applications, we established a national, multicenter, observational registry with the aim to collect data on feasibility, effectiveness and safety profile and to identify any possible additional field of use other than current indications.

2. Patients and methods

Patients

All patients that underwent endoscopy and for whom PuraStat was used were eligible for recruitment in the registry. The study protocol was approved by the institutional review board for human research at Humanitas Research and Clinical Center as coordinating center. Written informed consent was obtained from all patients before they underwent the endoscopic procedure at the respective institutions.

Inclusion criteria were age > 18 years and consent of the patient to be included in the study. Exclusion criterion was the presence of a known coagulopathy likely to affect the risk of bleeding.

Data on patient demographics, comorbidities (i.e. cardiovascular disease, diabetes mellitus, liver disease, renal disease), antithrombotic treatment (antiplatelets, anticoagulants), blood tests (complete blood count and coagulation parameters) and need for blood product transfusion were collected.

PuraStat use was possible in the setting of both active gastrointestinal bleeding (spontaneous or related to endoscopic procedure) and bleeding prevention after endoscopic procedures.

In case of active bleeding data were collected regarding bleeding severity (mild: ooze from mucosa or resection base; moderate: bleeding visible vessel or clot; severe: arterial spurt), cause and location, whether hemostasis was possible, if PuraStat was the primary or secondary hemostatic treatment and what other modality of hemostatic therapy was used (i.e. injective, thermal, mechanical).

In case of the use of PuraStat for prevention after endoscopic procedures data were collected regarding the type of procedure (i.e. endoscopic mucosal resection (EMR), knife assisted resection (KAR), endoscopic submucosal dissection (ESD), sphincterotomy, endoscopic papillectomy, treatment of radiation proctopathy), lesion size and extension (where applicable), length of the procedure, if PuraStat was the primary or secondary hemostatic treatment and if any other hemostatic modality was used.

The patient then entered a follow-up period of 30 days in order to collect data on rebleeding after previous hemostasis with PuraStat or post-procedural bleeding after prophylactic application of PuraStat, and how the bleeding event was managed.

The primary endpoints of the studies were the rate of successful hemostasis with PuraStat in case of active bleeding and the rate of post-procedural bleeding after prophylactic PuraStat application. Secondary endpoints were represented by the rebleeding rate after hemostasis with PuraStat in case of active bleeding and completeness of coverage of the area treated with PuraStat for either hemostasis or postprocedural bleeding prevention. Furthermore, data on difficulty of PuraStat application were analyzed. Finally, data on safety and adverse events (AE) related to PuraStat were collected.

PuraStat application

Before the start of the study, training sessions regarding the application of PuraStat were provided to the investigators involved in the recruiting centers. The investigators from each center were endoscopists with a high experience in therapeutic endoscopic procedures.

The decision to whether employ PuraStat was left to the discretion of the operator, based on the clinical scenario.

The use of PuraStat could be either as the primary and sole hemostatic treatment, or as a secondary additional modality after other treatment options (i.e. mechanical, injective, thermal). In consideration of

the effectiveness of PuraStat being proven in previous studies especially for oozing and nonspurting bleeding, in the event of an arterial spurting the application of PuraStat was allowed solely as a secondary therapy after a different primary hemostatic modality.

PuraStat was supplied in prefilled syringes available in different volumes (1 ml, 3 ml and 5 ml), according to the extent of the surface that needed covering. Delivery of PuraStat was carried out with the use of a dedicated endoscopic catheter (Nozzle System Type E), 220 cm long and compatible with a 2.8 mm endoscopic working channel.

Data on the total amount of PuraStat applied and percentage of coverage of the treated area were collected, as well as difficulty of application and the reason for it (i.e. position of the endoscope, blockage or kinking of the catheter).

Statistical analysis

Patient data were collected in a dedicated electronic case report form (eCRF).

Descriptive statistics were calculated: mean value with standard deviation and median value with range were determined for continuous variables; percentages and proportions were determined for categorical variables.

Statistical analysis was performed using chi-squared, Fisher's exact test and Student's t test, when appropriate. P-values were considered significant when < 0.05.

Potential factors influencing rebleeding rate after previous hemostasis with PuraStat and delayed bleeding rate after prophylactic application of PuraStat were tested in a univariate logistic regression model and results were expressed in terms of odds ratio (OR) and 95% confidence intervals (CI).

The inferential analysis for time to event data, namely the factors influencing time to rebleeding, was conducted using the Cox univariate regression model to estimate hazard ratios (HRs) and 95% CI.

The statistical analysis was performed with the R Statistical Software 3.0.2, *Survival* package (Foundation for Statistical Computing, Vienna, Austria).

3. Results

A total of 403 patients were recruited in 10 Italian centers from June 2021 to February 2023, with 2 patients being subsequently excluded for missing essential data.

91 patients with active gastrointestinal bleeding and 310 patients undergoing postprocedural bleeding prevention were included.

Baseline patients' characteristics, sorted by indication, are shown in **Table 1** and **Table 2**.

No AEs or complications related to PuraStat use were reported.

Acute active Bleeding

The most relevant cause for acute gastrointestinal bleeding was iatrogenic with 45 cases, 39 of which during an endoscopic intervention. The remaining cases were represented by spontaneous bleedings, such as ulcer bleeding (28), angiodysplasia (11), followed by other less common ethiologies (further details are provided in **Table 1** and **Table 3**).

For active bleeding PuraStat was used as primary treatment modality in 30 patients (33%) and as secondary treatment modality in 61 patients (67%). Hemostasis was achieved in 90 cases (98.9%), with a single case (1.1%) of ineffective hemostasis due to a diverticular bleeding that required subsequent radiological embolization.

In the setting of active bleeding the mean and median volumes of PuraStat used were 3.37 ml (±1.51 ml) and 3 ml (range: 1-10 ml) respectively, with a complete coverage of the treated area being possible in 76 patients (83.5%) and with a mean percentage of coverage of 95 (±12.4).

Difficulty in application was reported in 3 cases (3.3%), all due to endoscope position.

During the follow-up period 7 cases (7.7%) of rebleeding took place, of which 5 required endoscopic reintervention and 1 required treatment with interventional radiology.

Details on the outcomes after hemostasis with PuraStat are provided in **Table 3** and **Table 5**.

Logistic regression analysis was performed for rebleeding events after previous use of PuraStat for hemostasis of active bleeding. The threshold for significance, however, was reached for none of the variables taken into account (details are provided in **Table 6**).

Bleeding Prophylaxis

Prophylactic application of PuraStat was performed after the following endoscopic procedures: ESD (172), EMR (94), ERCP (8), endoscopic papillectomy (8), KAR (8), WOPN drainage (7), treatment of GAVE (4), polypectomy (3), treatment of gastric mass lesion (3), treatment of radiation proctopathy (2), and pneumatic colo-rectal anastomosis dilation (1) (further details are provided in **Table 2** and **Table 4**).

For bleeding prevention PuraStat was used as primary treatment modality in 144 patients (46.5%) and as secondary treatment modality in 166 patients (53.5%).

In the setting of bleeding prevention, the mean and median volumes of PuraStat used were 3.32 ml (±1.23 ml) and 3 ml (range: 1-6 ml) respectively, with a complete coverage of the treated area being possible in 254 patients (81.9%) and with a mean percentage of coverage of 98.8 (±5.2).

Difficulty in application was reported in 4 cases (1.3%), all due to endoscope position.

During the follow-up period 12 cases (3.9%) of delayed bleeding took place, of which 7 required endoscopic reintervention and 1 required treatment with interventional radiology.

Details on the outcomes after prophylaxis with PuraStat are provided in **Table 4** and **Table 7**.

Predictive factors for postprocedural delayed bleeding

Logistic regression analysis was performed for delayed bleeding events after previous use of PuraStat for postprocedural bleeding prevention.

In particular, although not with a statistically significance, upper GI bleeding showed an OR 1.49 (0.91-1.88; p=0.09). The threshold for significance, however, was reached for none of the variables considered (details are provided in **Table 8**). Time to event analysis confirmed this trend, with an HR 0.38 (0.12-1.21; p=0.09) (**Figure 1)**.

Logistic regression analysis was performed for delayed bleeding events in patients under antithrombotic and antiplatelets therapy. Even in these cases, the threshold for significance was reached for none of the variables taken into account (details are provided in **Table 8**). In the case of rebleeding within 30 days after hemostasis with PuraStat antiplatelet drug use showed a OR 1.43 (0.91-2.32; p=0.21) and anticoagulant use OR 1.35 (0.71-2.30; p=0.77); in the case of delayed bleeding within 30 days after bleeding prevention with

PuraStat antiplatelet and anticoagulant use showed OR 1.41 (0.76-2.51; p=0.78) and OR 2.64 (0.88-3.67; p=0.18) respectively.

4. Discussion

Gastrointestinal bleeding is a condition frequently encountered in clinical practice associated with high morbidity and mortality. Furthermore, with operative endoscopy procedures becoming more advanced and complex, bleeding is a well-known and common adverse event that may present either during the procedure or up to several days after it and that may be the cause for longer hospital stay.

In recent years and since its introduction, PuraStat is emerging as an effective and safe hemostatic agent that may be helpful both in providing hemostasis for acute bleeding and in the prevention of rebleeding or delayed bleeding events after various operative endoscopy procedures.

To the best of our knowledge, this registry collects the largest study population in which PuraStat has been used either as a hemostat for acute GI bleeding or as a prophylaxis for delayed bleeding following an endoscopic procedure.

PuraStat proved to be an excellent hemostatic agent for acute GIB both as primary and secondary modality, with an overall rate of successful hemostasis of 98.9%. Its effectiveness was shown in different bleeding settings: upper GI, lower GI and biliopancreatic, spontaneous or related to different kinds of operative endoscopy procedures.

With regard to previous hemostasis with PuraStat, the rebleeding rate was low (7.7%) and in the majority of patients (85.7%) it was self-limiting or it could be managed with an endoscopic reintervention.

In the context of postprocedural bleeding prevention the data appeared promising as well, with a delayed bleeding occurring in only 3.9% of patients, typically following endoscopic resection (ER) procedures (i.e. EMR, ESD, endoscopic papillectomy) and once again self-limiting in nature or manageable with an endoscopic reintervention in the vast majority of patients (91.7%). The effectiveness of PuraStat application for bleeding prevention was studied in a wide array of endoscopic procedures involving the upper, lower and biliopancreatic tract.

Of note, in the setting of prevention of post-procedural bleeding PuraStat showed a higher magnitude of effect in lower GI (OR 1.49, 0.91-1.88) thus meaning that PuraStat use led to a 49% decrease in terms of post-procedural bleeding in lower GI as compared to upper GI although the significance threshold was not reached (p=0.09) probably because the study was underpowered to detect this difference. Larger cohorts are needed to assess this important clinical issue. However, given the low event rate and the specific subsets of patients (prevention of postprocedural bleeding), a sample size of more than 1000 patients would be required to register a significant difference; unfortunately, such a huge sample size is very difficult to collect.

Regarding the technical aspect, PuraStat delivery proved simple, with only few cases of difficult application due to complex endoscope position. Nonetheless a near to complete coverage of the treated lesion was possible in almost all patients. Moreover, the safety profile of PuraStat proved excellent, with no reported cases of AEs related to its application.

This noncomparative study is inevitably limited by the nature of its own design that does not include a control group and the non random treatment assignment, which on the contrary was solely left to the discretion of the operator both for acute bleeding hemostasis and for bleeding prophylaxis, therefore implying a potential risk for selection bias. In this regard this study can therefore only provide real-world data.

In addition, due to the very low rates of both rebleeding after previous hemostasis and delayed bleeding after operative endoscopy procedures, it is not possible to draw any specific conclusion regarding any potential risk factor for PuraStat inefficacy. However, albeit not reaching the threshold for statistical significance, we can surmise two potential trends: one that favors the use of PuraStat for hemostasis of intraprocedural bleeding rather than its use for bleeding not related to endoscopic procedures; the other that supports the use of PuraStat for bleeding prevention after endoscopic procedures on the lower GI tract, rather than the upper GI tract.

Nonetheless, we suggest that comparative studies may be necessary in order to mitigate the impact of confounding variables and enhance the broader applicability of the study findings.

Overall, our data further corroborate the effectiveness of PuraStat both as a treatment modality for both hemostasis and bleeding prevention for the indication it is approved for as of today. Moreover, our study provides for the first time additional evidence for the efficacy and safety of PuraStat for different indications than the ones it is currently approved, such as in treatment and prevention of bleeding related to ERCP with sphincterotomy, endoscopic papillectomy, radiation proctopathy, GAVE, EUS-guided WOPN drainage and pneumatic dilation of colorectal anastomoses.

In conclusion, PuraStat appears to be a safe and effective addition to the endoscopic therapeutic armamentarium both for hemostasis and for bleeding prevention, with more and more evidence suggesting a potential wider field for application compared to current indications. As a consequence, clinical data from further studies are needed in order to expand the indications for the use of PuraStat and its place in the therapeutic bleeding algorithms.

Table 1. Baseline characteristics of patients treated for active bleeding

Patients characteristics	
Number of patients	91
Sex (n,%)	Male 62 (68.1) Female 29 (31.9)
Age (mean, SD)	68.7 ± 14
Comorbidities (n,%)	None 18 (19.8) Cardiovascular 55 (60.4) Diabetes 21 (23.1) Renal disease 12 (13.2) Liver disease 6 (6.6)
Antithrombotic therapy (n,%)	Antiplatelet 18 (19.8) Anticoagulant 18 (19.8) Both 3 (3.3)
Bleeding location (n,%)	Upper location 62 (68.2) Esophagus 6 (6.6) Stomach 17 (18.7) Duodenum 21 (23.1) Ampulla 18 (19.8) Lower location 26 (28.6) Caecum 5 (5.5) Right colon 6 (6.6) Left colon 4 (4.4) Rectum 11 (12.1) Biliopancreatic 2 (2.2) Ileum 1 (1.1)

Cause of bleeding (n,%)	Iatrogenic 45 (49.5) Endoscopic intraprocedural 39 (42.9) ERCP 15 (16.5) EMR 13 (14.3) Gastric EMR 1 (1.1) Duodenal EMR 1 (1.1) Caecal EMR 2 (2.2) Right colon EMR 5 (5.5) Left colon EMR 2 (2.2) Rectal EMR 2 (2.2) ESD 4 (4.4) Gastric ESD 1 (1.1) Rectal ESD 3 (3.3) Papillectomy 3 (3.3) Duodenal EFTR 2 (2.2) WOPN drainage 1 (1.1) Intrahepatic lithotripsy 1 (1.1) Postsurgical 5 (5.5) Post PEG placement 1 (1.1) Ulcer 28 (30.8) Esophageal ulcer 4 (4.4) Gastric ulcer 11 (12.1) Duodenal ulcer 9 (9.9) Rectal ulcer 4 (4.4) Angiodysplasia 11 (12.1) Mass lesion 3 (3.3) Mallory-Weiss tear 1 (1.1) Radiation proctopathy 1 (1.1) Diverticular bleeding 1 (1.1) Duodenal necrosis 1 (1.1)
Bleeding severity (n,%)	Mild 34 (37.4) Moderate 52 (57.1) Severe 5 (5.5)

Table 2. Baseline characteristics of patients undergoing postprocedural bleeding prevention

Patients characteristics	
Number of patients	310
Sex (n;%)	Male 165 (53.2) Female 145 (46.8)
Age (mean, SD)	69 ± 12.2
Comorbidities (n,%)	None 107 (34.5) Cardiovascular 178 (57.4) Diabetes 40 (12.9) Renal disease 13 (4.2) Liver disease 7 (2.3)
Antithrombotic therapy (n,%)	Antiplatelet 57 (18.4) Anticoagulant 32 (10.3) Both 4 (1.3)
Bleeding location (n,%)	Upper location 103 (33.2) Esophagus 10 (3.2)

	Stomach 53 (17.1) Duodenum 22 (7.1) Ampulla 18 (5.8) Lower location 200 (64.5) Ileocaecal valve 2 (0.6) Caecum 20 (6.5) Right colon 32 (10.3) Transverse colon 11 (3.6) Left colon 27 (8.7) Rectum 108 (34.8) Biliopancreatic 7 (2.3)
Endoscopic procedure (n,%)	ESD 172 (55.5) Esophageal ESD 6 (1.9) Gastric ESD 42 (13.6) Caecal ESD 5 (1.6) Right colon ESD 7 (2.3) Transverse colon ESD 6 (1.9) Left colon ESD 10 (3.2) Rectal ESD 96 (31) EMR 94 (30.3) Esophageal EMR 3 (1) Gastric EMR 2 (0.6) Duodenal EMR 20 (6.5) Ileo-caecal valve EMR 2 (0.6) Caecal EMR 15 (4.9) Right colon EMR 25 (8.1) Transverse colon EMR 5 (1.6) Left colon EMR 13 (4.2) Rectal EMR 9 (2.9) ERCP 8 (2.6) Papillectomy 8 (2.6) KAR 8 (2.6) Esophageal KAR 1 (0.3) Gastric KAR 3 (1) Left colon KAR 4 (1.3) WOPN drainage 7 (2.3) Treatment of GAVE 4 (1.3) Polypectomy 3 (1) Duodenal polypectomy 2 (0.6) Rectal polypectomy 1 (0.3) Treatment of gastric mass lesion 3 (1) Treatment of radiation proctopathy 2 (0.6) Pneumatic anastomotic dilation 1 (0.3)

Table 3. Details on treatments for active bleeding

Hemostatic treatments for active bleeding	
Number of patients	91
PuraStat as primary modality Other primary treatment modality + PuraStat as secondary modality	30 (33) 61 (67)

Injective Thermal Mechanical Combination of different modalities	17 (18.7) 6 (6.6) 16 (17.6) 22 (24.1)
Cause of bleeding treated with Purastat alone	Endoscopic intraprocedural 16 EMR 7 Gastric EMR 1 Duodenal EMR 1 Right colon EMR 3 Rectal EMR 2 ESD 2 Rectal ESD 2 ERCP 6 Papillectomy 1 Ulcer 7 Esophageal ulcer 2 Gastric ulcer 2 Duodenal ulcer 1 Rectal ulcer 2 Angiodysplasia 2 Esophageal angiodysplasia 1 Rectal angiodysplasia 1 Mallory Weiss tear 1 Anastomotic bleeding 1 Duodenal mass lesion 1 Duodenal necrosis 1 Post PEG placement 1
Cause of bleeding treated with injective hemostasis + PuraStat	Endoscopic intraprocedural 7 EMR 1 Right colon EMR 1 ERCP 5 Papillectomy 1 Ulcer 8 Gastric ulcer 3 Duodenal ulcer 5 Duodenal angiodysplasia 1 Radiation proctopathy 1
Cause of bleeding treated with thermal hemostasis + PuraStat	Endoscopic intraprocedural 2 EMR 2 Right colon EMR 1 Left colon EMR 1 Angiodysplasia 3 Caecal angiodysplasia 1 Right colon angiodysplasia 2 Duodenal mass lesion 1
Cause of bleeding treated with mechanical hemostasis + PuraStat	Endoscopic intraprocedural 5 EMR 2 Caecal EMR 1 Left colon EMR 1 ESD 1 Gastric ESD 1 ERCP 1

	WOPN drainage 1 Ulcer 4 Gastric ulcer 3 Rectal ulcer 1 Angiodysplasia 3 Gastric angiodysplasia 1 Duodenal angiodysplasia 2 Anastomotic bleeding 3 Diverticular bleeding 1
Cause of bleeding treated with combination modality + PuraStat	Endoscopic intraprocedural 9 EMR 1 Caecal EMR 1 ESD 1 Rectal ESD 1 ERCP 4 Papillectomy 1 Duodenal EFTR 2 Ulcer 9 Esophageal ulcer 2 Gastric ulcer 3 Duodenal ulcer 3 Rectal ulcer 1 Angiodysplasia 2 Duodenal angiodysplasia 1 Caecal angiodysplasia 1 Gastric mass lesion 1 Anastomotic bleeding 1
Cases of rebleeding within 30 days	After PuraStat as primary treatment 3 Gastric ulcer 1 Duodenal ulcer 1 Anastomotic bleeding 1 After mechanical hemostasis + PuraStat 1 Gastric ESD 1 After injective hemostasis + PuraStat 1 Duodenal ulcer 1 After combination modality + PuraStat 2 Rectal ESD 1 Duodenal angiodysplasia 1

Table 4. Details on treatments for bleeding prevention

Treatments for bleeding prevention	
Number of patients	310
PuraStat as primary modality	144 (46.5)
Other primary treatment modality + PuraStat as secondary modality	166 (53.5)
Injective	1 (0.3)
Thermal	92 (29.7)
Mechanical	31 (10)
Combination of different modalities	42 (13.5)
Endoscopic procedure followed by bleeding	EMR 53

prevention with PuraStat alone	Esophageal EMR 2 Duodenal EMR 10 Caecal EMR 5 Ileo-caecal valve EMR 1 Right colon EMR 17 Transverse colon EMR 2 Left colon EMR 9 Rectal EMR 7 ESD 56 Esophageal ESD 4 Gastric ESD 28 Caecal ESD 1 Right colon ESD 3 Transverse colon ESD 2 Left colon ESD 3 Rectal ESD 15 KAR 6 Gastric KAR 2 Left colon KAR 4 Polypectomy 2 Duodenal polypectomy 1 Rectal polypectomy 1 Papillectomy 8 ERCP 7 WOPN drainage 7 Treatment of gastric mass lesion 2 Treatment of GAVE 1 Treatment of radiation proctopathy 1 Pneumatic anastomotic dilation 1
Endoscopic procedure followed by bleeding prevention with injective modality + PuraStat	ERCP 1
Endoscopic procedure followed by bleeding prevention with thermal modality + PuraStat	EMR 20 Esophageal EMR 1 Duodenal EMR 3 Caecal EMR 7 Right colon EMR 3 Transverse colon EMR 2 Left colon EMR 4 ESD 65 Esophageal ESD 2 Gastric ESD 8 Caecal ESD 2 Right colon ESD 2 Transverse colon ESD 1 Left colon ESD 4 Rectal ESD 46 KAR 2 Esophageal KAR 1 Gastric KAR 1 Treatment of GAVE 3 Treatment of gastric mass lesion 1 Treatment of radiation proctopathy 1

Endoscopic procedure followed by bleeding prevention with mechanical modality + PuraStat	EMR 17 Gastric EMR 2 Duodenal EMR 7 Caecal EMR 2 Ileo-caecal valve EMR 1 Right colon EMR 3 Transverse colon EMR 1 Rectal EMR 1 ESD 14 Gastric ESD 3 Caecal ESD 1 Right colon ESD 1 Left colon ESD 3 Rectal ESD 6
Endoscopic procedure followed by bleeding prevention with combination modality + PuraStat	EMR 4 Caecal EMR 1 Right colon EMR 2 Rectal EMR 1 ESD 37 Gastric ESD 3 Caecal ESD 1 Right colon ESD 1 Transverse colon ESD 3 Rectal ESD 29 Duodenal polypectomy 1
Cases of bleeding within 30 days	After PuraStat as primary modality 5 Gastric ESD 3 Transverse colon EMR 1 Papillectomy 1 After mechanical modality + PuraStat 3 ESD 2 Gastric ESD 1 Rectal ESD 1 After thermal modality + PuraStat 3 EMR 2 Duodenal EMR 1 Caecal EMR 1 Rectal ESD 1 After combination modality + PuraStat 1 Right colon EMR 1

Table 5. Outcomes after hemostasis (active bleeding) with PuraStat

Outcomes after hemostasis with PuraStat	
Effectiveness of hemostasis (n,%)	Effective 90 (98.9) Not effective 1 (1.1)
Rebleeding within 30 days (n,%)	7 (7.7)
Previously treated lesion	Duodenal ulcer 2 Gastric ESD 1 Gastric ulcer 1 Duodenal angiodysplasia 1

	Rectal ESD 1 Colorectal anastomosis bleeding 1
Previous bleeding severity	Mild 2 Moderate 5 Severe 0
Antithrombotic therapy	None 3 On therapy (discontinued) 4
Previous coverage with PuraStat	Complete 6 Incomplete (50%) 1

Table 6. Logistic regression analysis for rebleeding within 30 days after hemostasis

Variable	
Sex	OR 1.45 (0.78-3.11), p=0.51
Age	OR 0.78 (0.56-2.16), p=0.67
Antiplatelet drug use	OR 1.43 (0.91-2.32), p=0.21
Anticoagulant drug use	OR 1.35 (0.71-2.30), p=0.77
Upper GI tract origin of bleeding	OR 1.13 (0.76-1.87), p=0.94
Bleeding related to endoscopic procedure	OR 1.78 (0.93-2.87), p=0.12
PuraStat as primary treatment modality	OR 1.34 (0.77-1.87), p=0.56
Complete coverage	OR 1.34 (0.79-2.13), p=0.87
Difficult application	OR 1.11 (0.89-2.33), p=0.33

Table 7. Outcomes after bleeding prevention with PuraStat

Outcomes after bleeding prevention with PuraStat	
Delayed bleeding (n,%)	12 (3.9)
Previously treated lesion	ESD 6 Gastric ESD 4 Rectal ESD 2 EMR 4 Duodenal EMR 1 Caecal EMR 1 Right colon EMR 1 Transverse colon EMR 1 Endoscopic papillectomy 2
Antithrombotic therapy	None 7 On therapy (discontinued) 5
Previous coverage with PuraStat	Complete 12 Incomplete 0

Table 8. Logistic regression analysis for delayed bleeding within 30 days after bleeding prevention

Variable	
Sex	OR 1.64 (0.71-3.23), p=0.81
Age	OR 1.98 (0.88-3.07), p=0.17
Antiplatelet drug use	OR 1.41 (0.76-2.51), p=0.78
Anticoagulant drug use	OR 2.64 (0.88-3.67), p=0.18

Upper GI tract origin of bleeding	OR 1.49 (0.91-1.88), p=0.09
PuraStat as primary treatment modality	OR. 1.45 (0.71-2.03), p=0.73
Complete coverage	OR 1.38 (0.75-1.88), p=0.79
Difficult application	OR 1.18 (0.73-2.97), p=0.87

Figure 1. Bleeding-free survival probability

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