ELEVAIR™ Endobronchial Coil System Safety Profile

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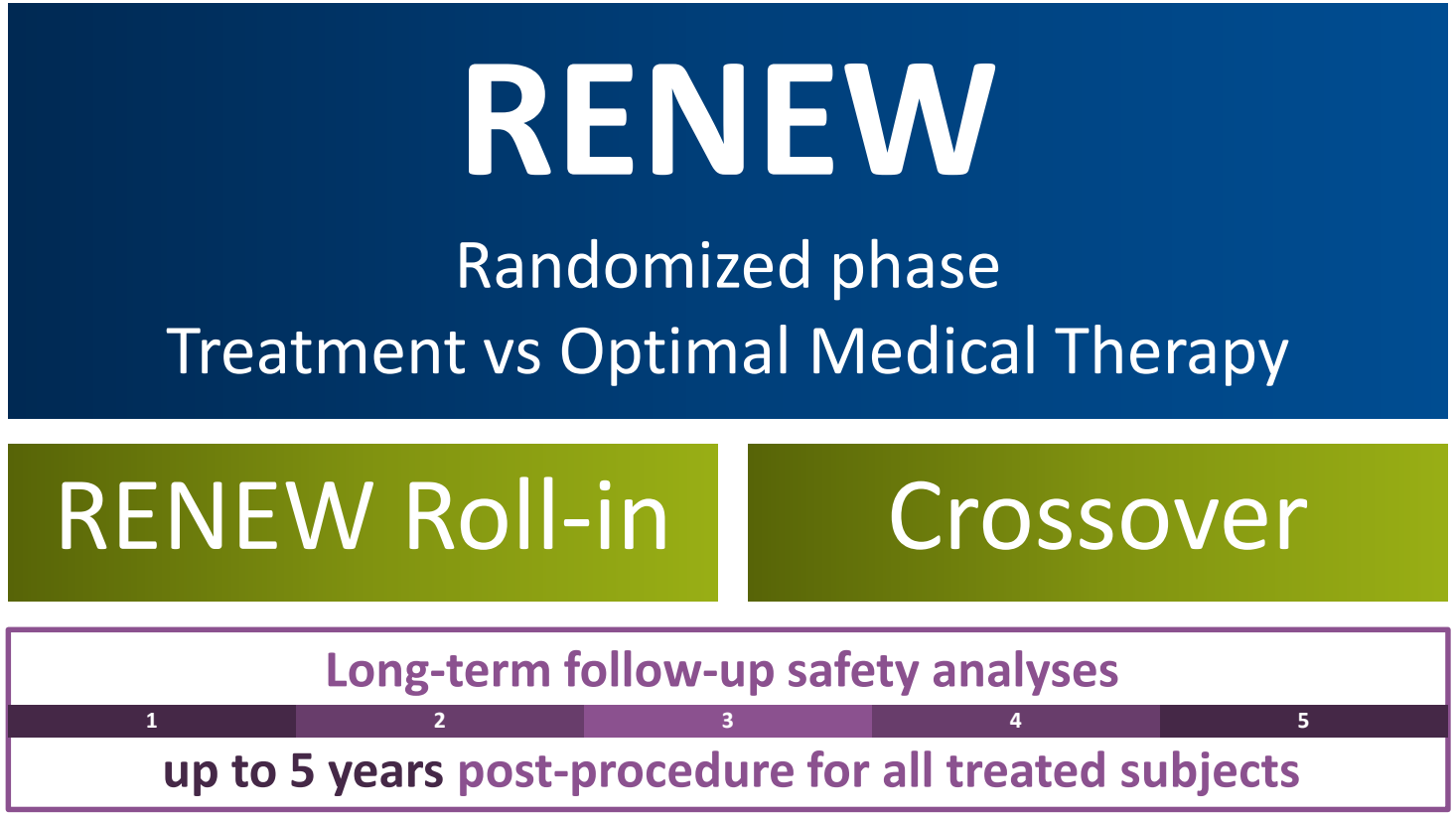
a BTG International group company

Safety Population/Analyses



Overview of Safety Presentation

- Adverse Events and Serious Adverse Events
- Primary Safety Analysis - Major Complications Through 12 Months
- Lower Respiratory Infections
- Additional Safety Events of Interest
- Summary of Long-term Follow-up
- Post-Market Safety
- Safety Conclusions

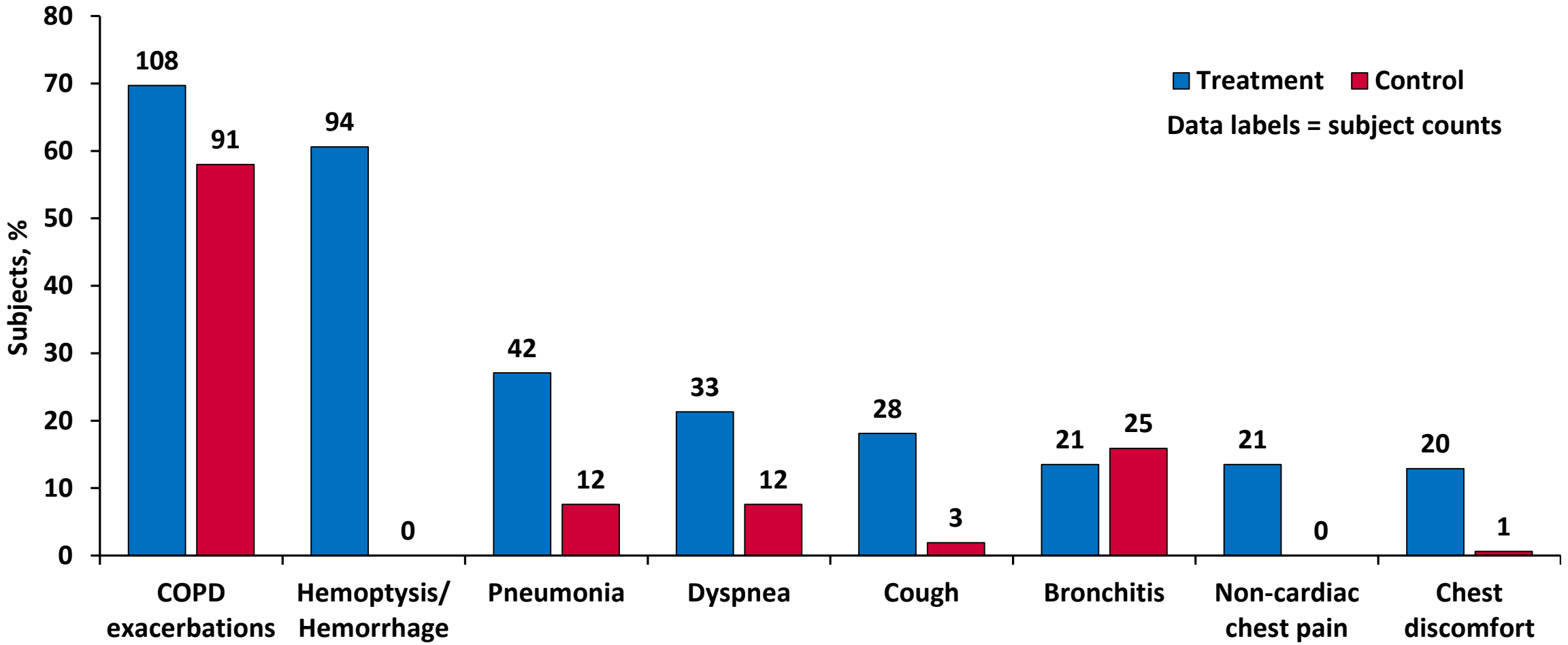
Summary of Adverse Events

RENEW Randomized

	Treatment N=155		Control N=157	
	% Subjects	Events	% Subjects	Events
Total AEs	100.0	1110	88.5	492
SAEs	61.9	211	34.4	92
Death	6.5	10	5.1	8
Device/Procedure-related SAEs	45.8	128	N/A	N/A

Most Frequent Adverse Events Through 12 Months

RENEW Randomized



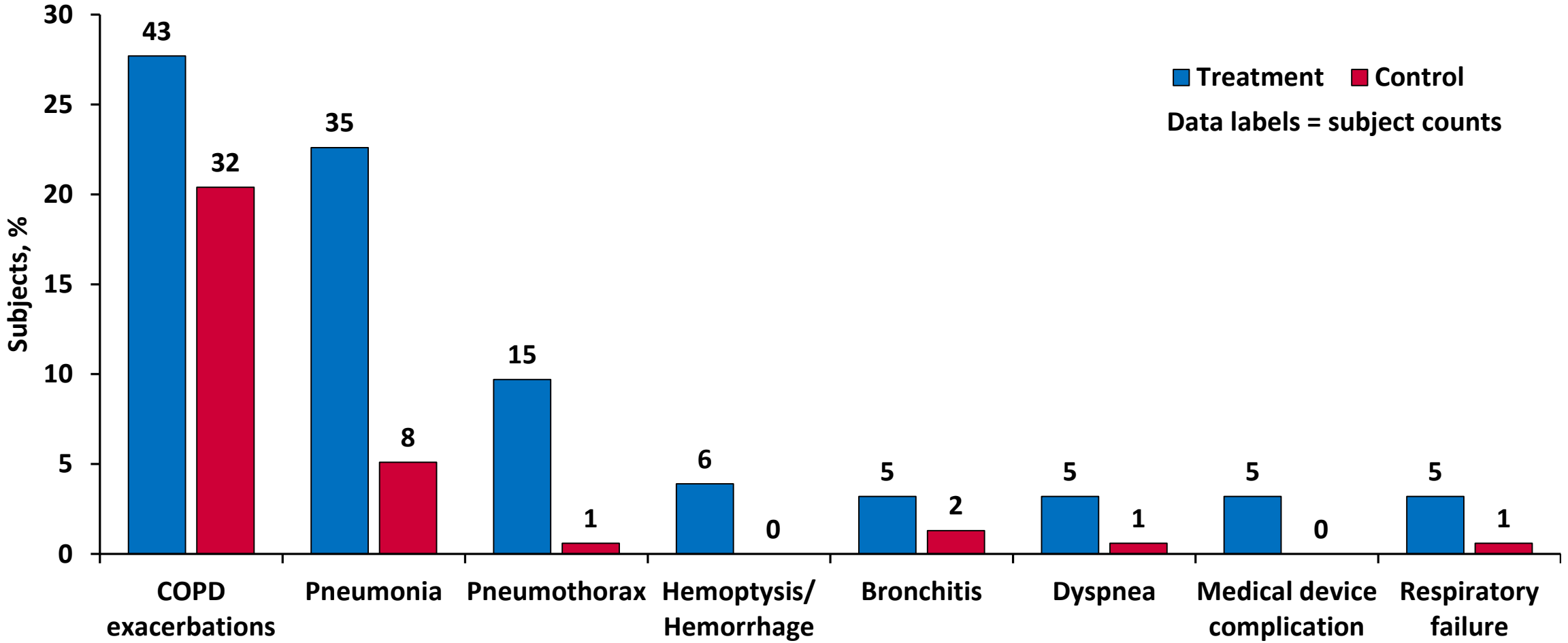
Pneumonia, terms used: Pneumonia, Pneumonia Bacterial, Pneumonia Staphylococcal, Bronchopulmonary Aspergillosis, Pneumonia Necrotizing, Pneumonia Respiratory Syncytial Virus, Lower Respiratory Tract Infection.

Hemoptysis/Hemorrhage, terms used: Hemoptysis, Post Procedural Hemorrhage, Procedural Hemorrhage, Pulmonary Hemorrhage, Respiratory Tract Hemorrhage.

Note: Figure was not provided within the PMA; however, underlying information / analysis was included.

Most Frequent Serious Adverse Events Through 12 Months

RENEW Randomized



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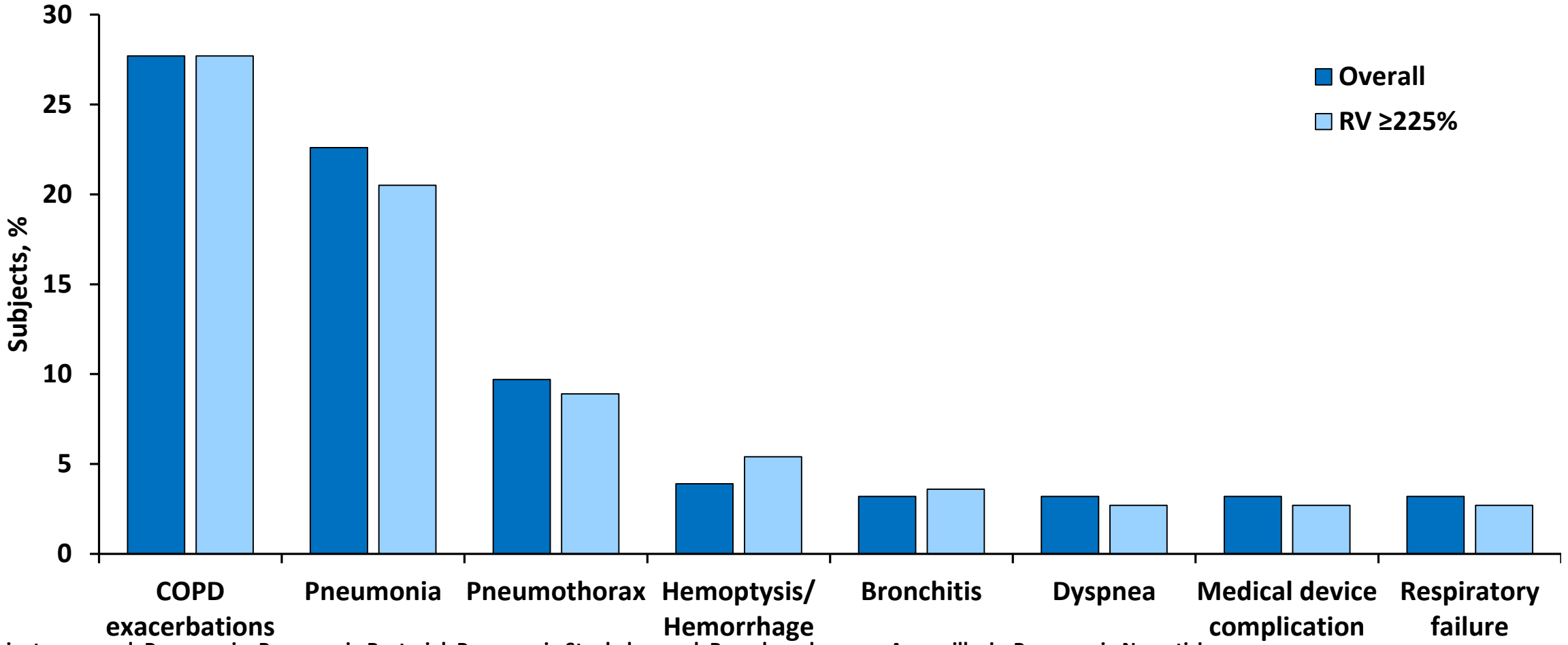
Serious Adverse Events Through 12 Months in Treated Subjects

Overall RENEW Randomized vs Baseline RV ≥225% Predicted



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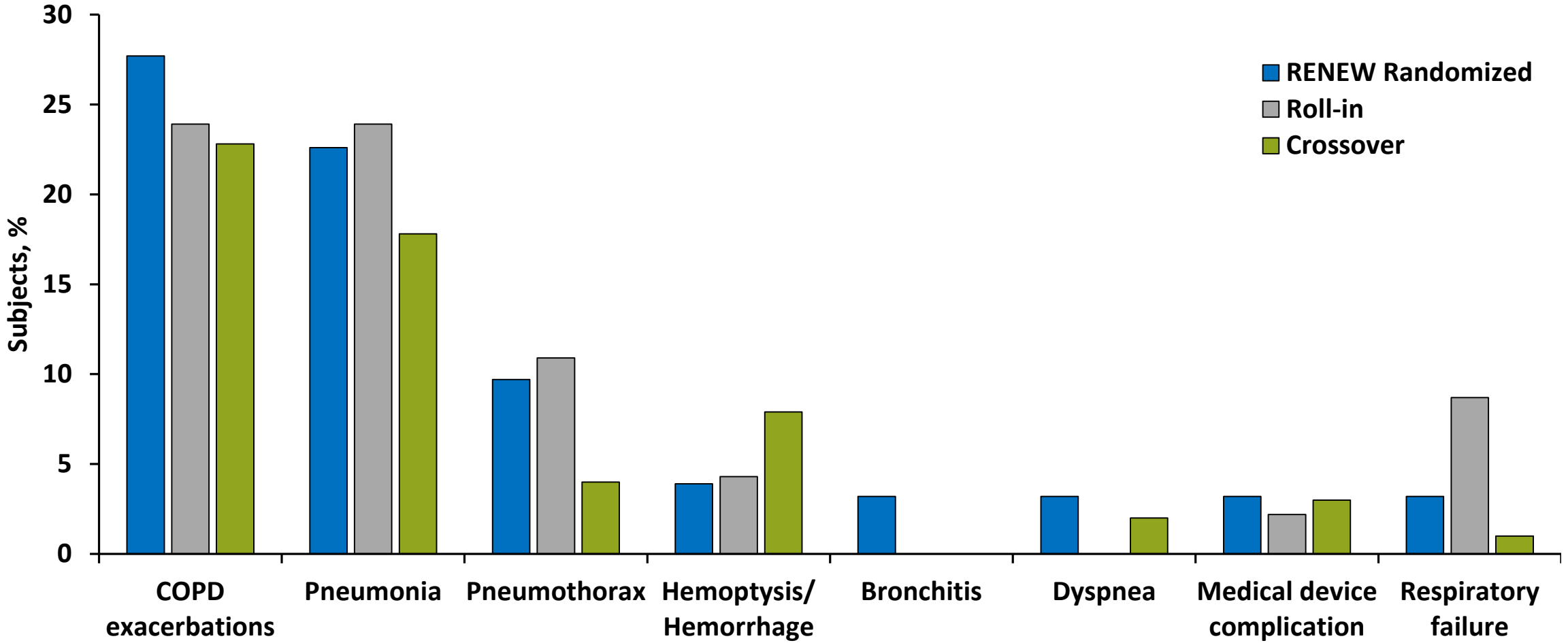
Serious Adverse Events Through 12 Months in Treated Subjects

RENEW Randomized, Roll-in and Crossover



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Primary Safety Analysis: Protocol Defined Major Complications

- **Death**
- **Pneumothorax** requiring a chest drainage tube for >7 days
- **Hemoptysis** requiring blood transfusion(s), arterial embolization, or surgical/endoscopic procedure
- **COPD exacerbation** increase in respiratory symptoms requiring in-patient hospitalization >7 days
- **Lower respiratory infection** (including pneumonia) new or increased symptoms
- **Respiratory failure** requiring mechanical ventilator support for >24 hours
- **Unanticipated bronchoscopy** removal of 1 or more coils due to a device-related AE

Major Complications (MCs) Through 12 Months

RENEW Randomized

Major complication	Subjects, n (%) Treatment N=155	Subjects, n (%) Control N=157	P-value[a]
Total major complication events (95% CI)[b]	54 (34.8) (27.4, 42.9)	30 (19.1) (13.3, 26.1)	0.0021
Death	10 (6.5)	8 (5.1)	NS
Pneumothorax	1 (0.6)	1 (0.6)	NS
Hemoptysis requiring intervention	2 (1.3)	0	NS
COPD exacerbation	18 (11.6)	13 (8.3)	NS
Lower respiratory infections	29 (18.7)	7 (4.5)	<0.0001
Respiratory failure	6 (3.9)	6 (3.8)	NS
Unanticipated bronchoscopy	0	0	N/A

[a] Nominal p value By Fisher's exact test unadjusted for multiplicity.
[b] By Clopper-Pearson method

Fatal Adverse Events Through 12 Months

RENEW Randomized

Adverse event category	Treatment group	Control group
Respiratory, thoracic and mediastinal disorders		
COPD	3***	4
Pulmonary hemorrhage	1*	0
Respiratory arrest	0	1
Respiratory failure	2*	0
Infections and infestations		
Bronchopulmonary aspergillosis	1*	0
Pneumonia	1*	1
Septic shock	0	1
Cardiac disorders		
Cardio-respiratory arrest	0	1
Neoplasms benign, malignant and unspecified		
Bone neoplasm malignant	1	0
Renal and urinary disorders		
Renal failure acute	1	0

*** One death considered possibly or probably device or procedure related.**
***** Three deaths considered possibly or probably device or procedure related.**

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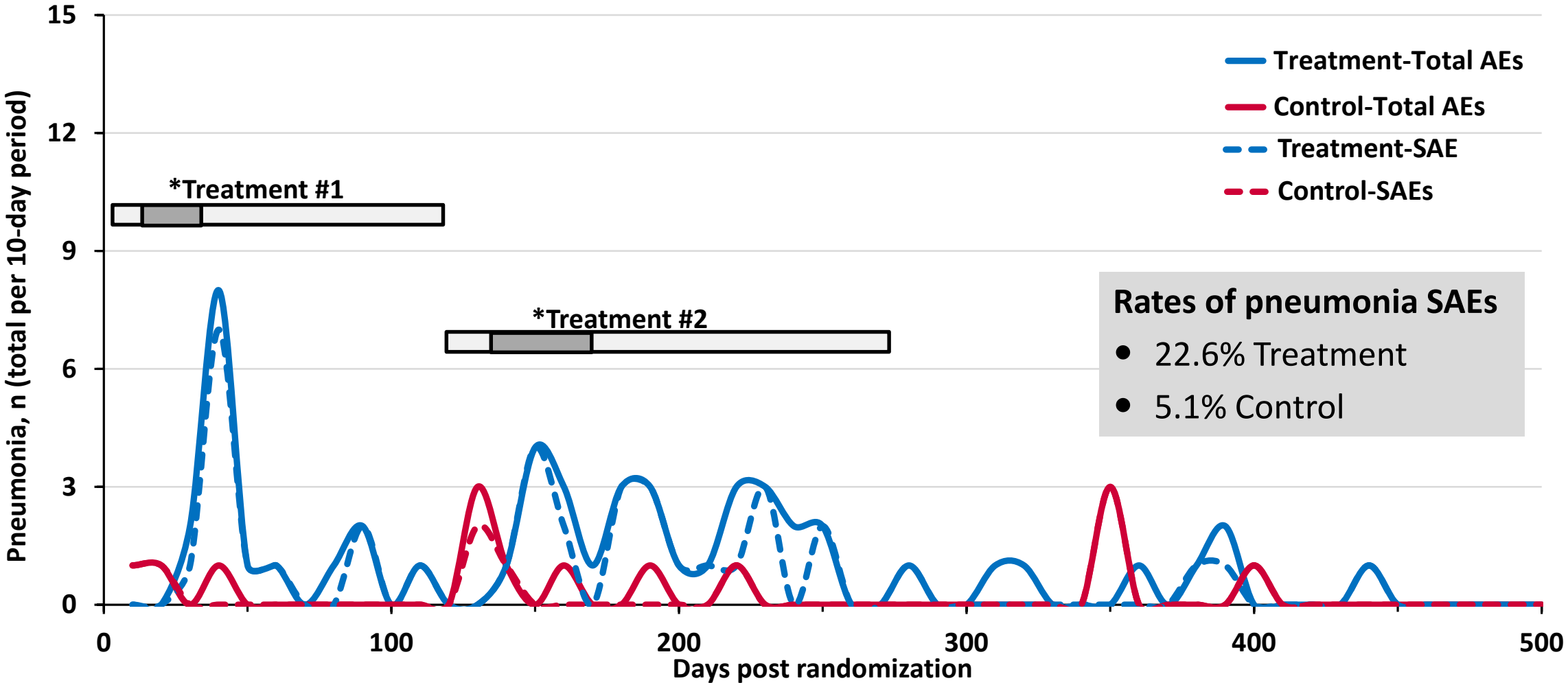
Pneumonia Events Within 12 Months

RENEW Randomized



Pneumonia, terms used: Pneumonia, Pneumonia Bacterial, Pneumonia Staphylococcal, Bronchopulmonary Aspergillosis, Pneumonia Necrotizing, Pneumonia Respiratory Syncytial Virus, Lower Respiratory Tract Infection. *Treatment bar indicates range of days from randomization until treatment, with dark bar indicating time in which the middle 50% of subjects were treated. Note: Figure was not provided within the PMA; however, underlying information / analysis was included.

Pneumonia: Further Details

- Local inflammatory response identified called Coil-Associated Opacity (CAO)
- 28 total events considered CAO
  - 14 pneumonia events determined to be CAO through re-evaluation
  - 14 inflammatory events

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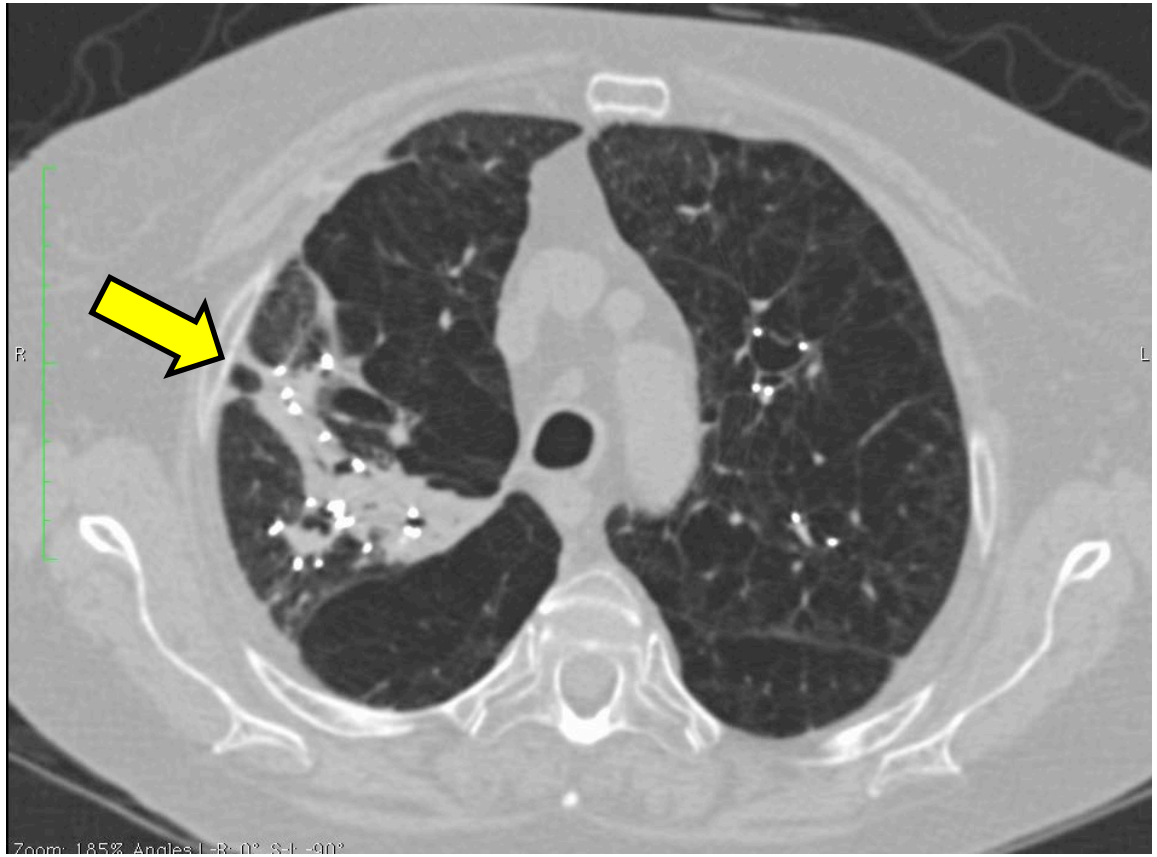
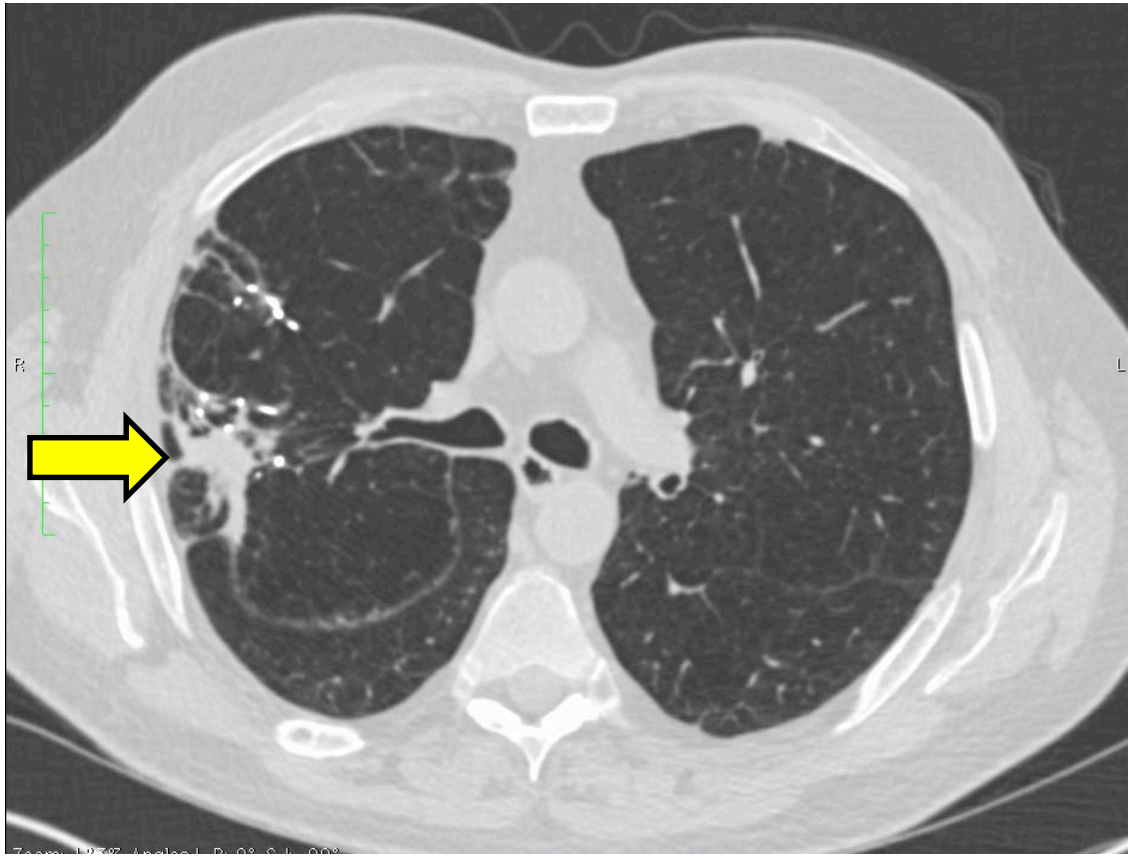
Radiographic Similarities: Pneumonia or Coil-Associated Opacity?



Pneumonia



CAO

Clinical Representation: Pneumonia or Coil-Associated Opacity?

Diagnosis	Suggested treatment course
Pneumonia likely Purulent sputum Fever >100.5 °F Positive blood culture	• Antibiotics
Pneumonia suspected CXR Opacity is central/lobar, segmental Positive sputum culture WBC > 12K with >5% bands, shifts	• Corticosteroids at discretion of treating physician
CAO likely CXR opacity is peripheral, localized to area around Coils Temp <100.5 °F WBC <12K without shifts Negative blood or sputum culture No change from baseline sputum	• Antibiotics at discretion of treating physician • Corticosteroids 30 mg × 5 days • Ibuprofen at treating physician discretion • Suggest follow-up with CXR in 7 days to confirm DX

This treatment course was developed by the RENEW DMC and several Key Opinion Leaders who were investigators in the RENEW trial.

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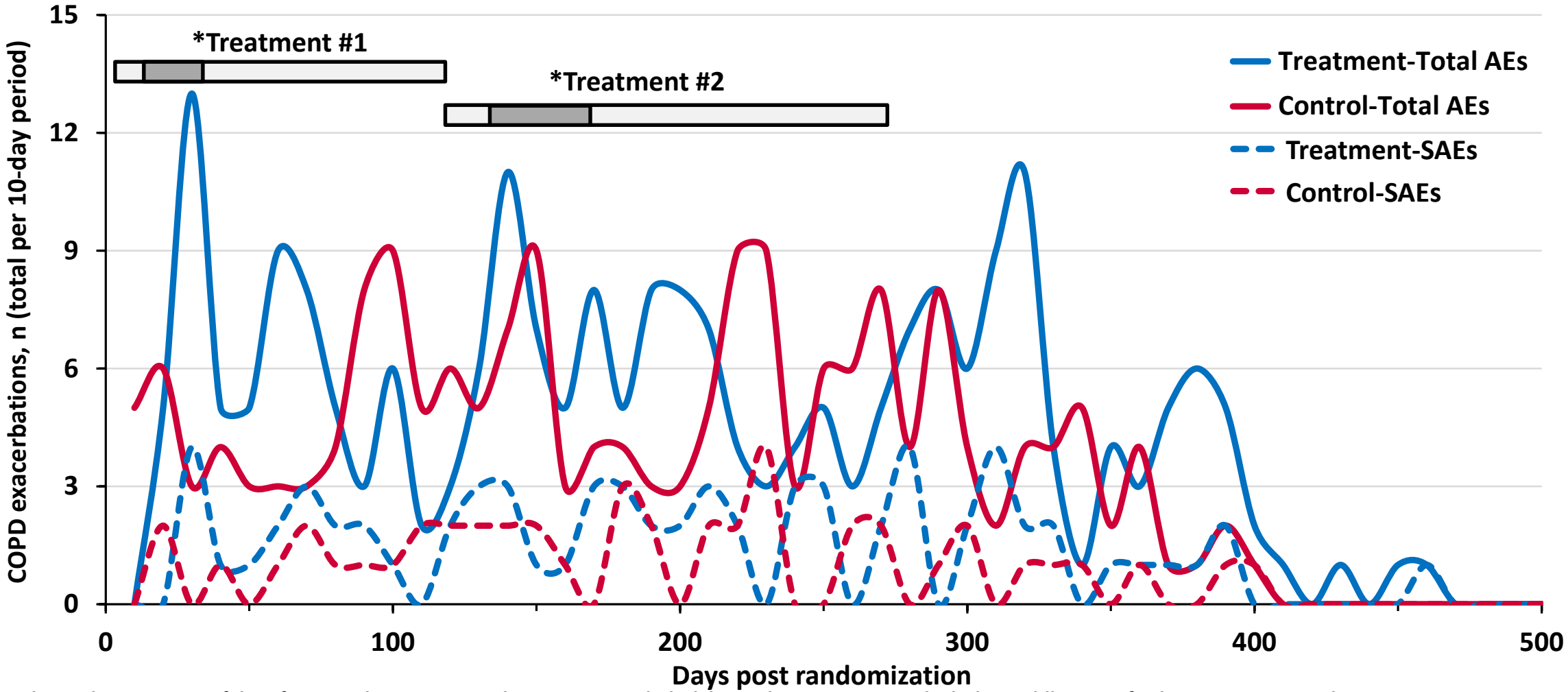
COPD Exacerbation Events Within 12 Months

RENEW Randomized



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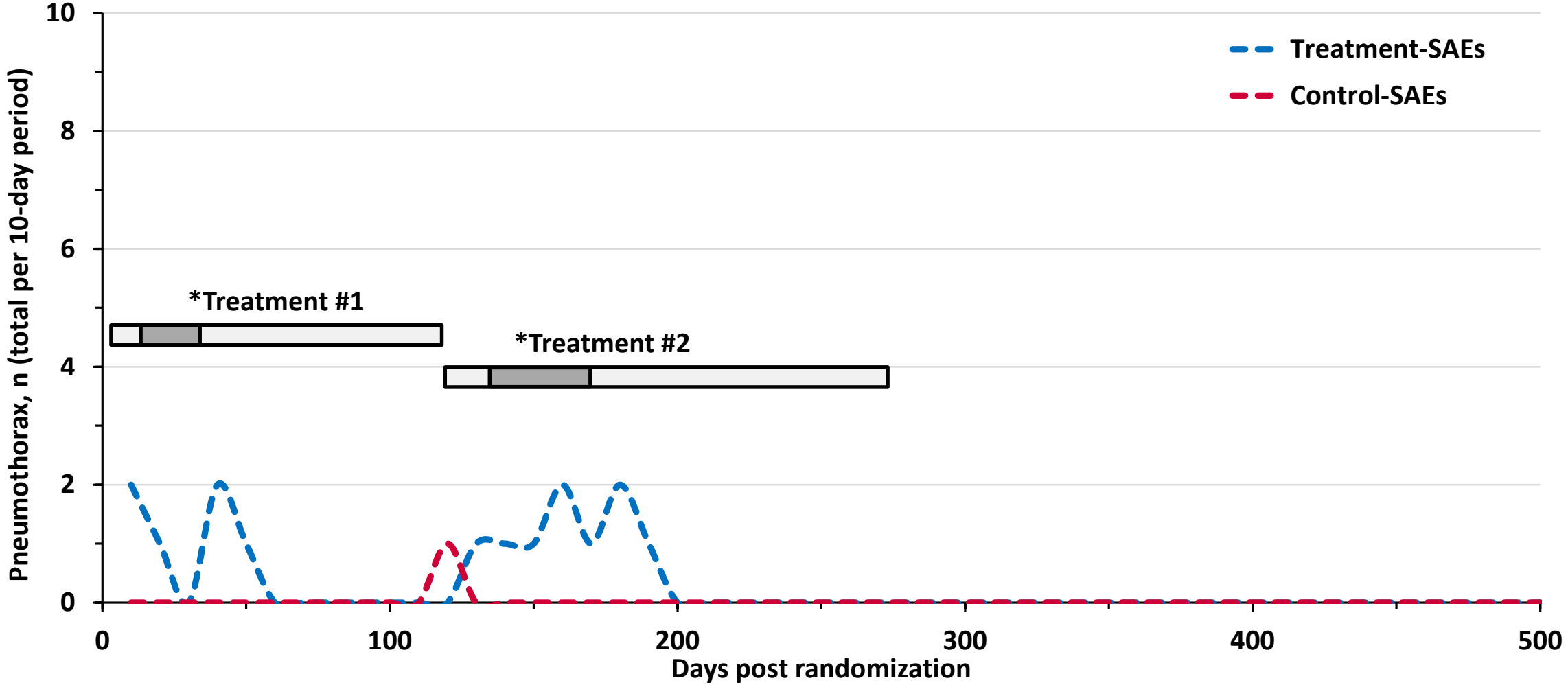
Pneumothorax Serious Adverse Events Within 12 Months

RENEW Randomized



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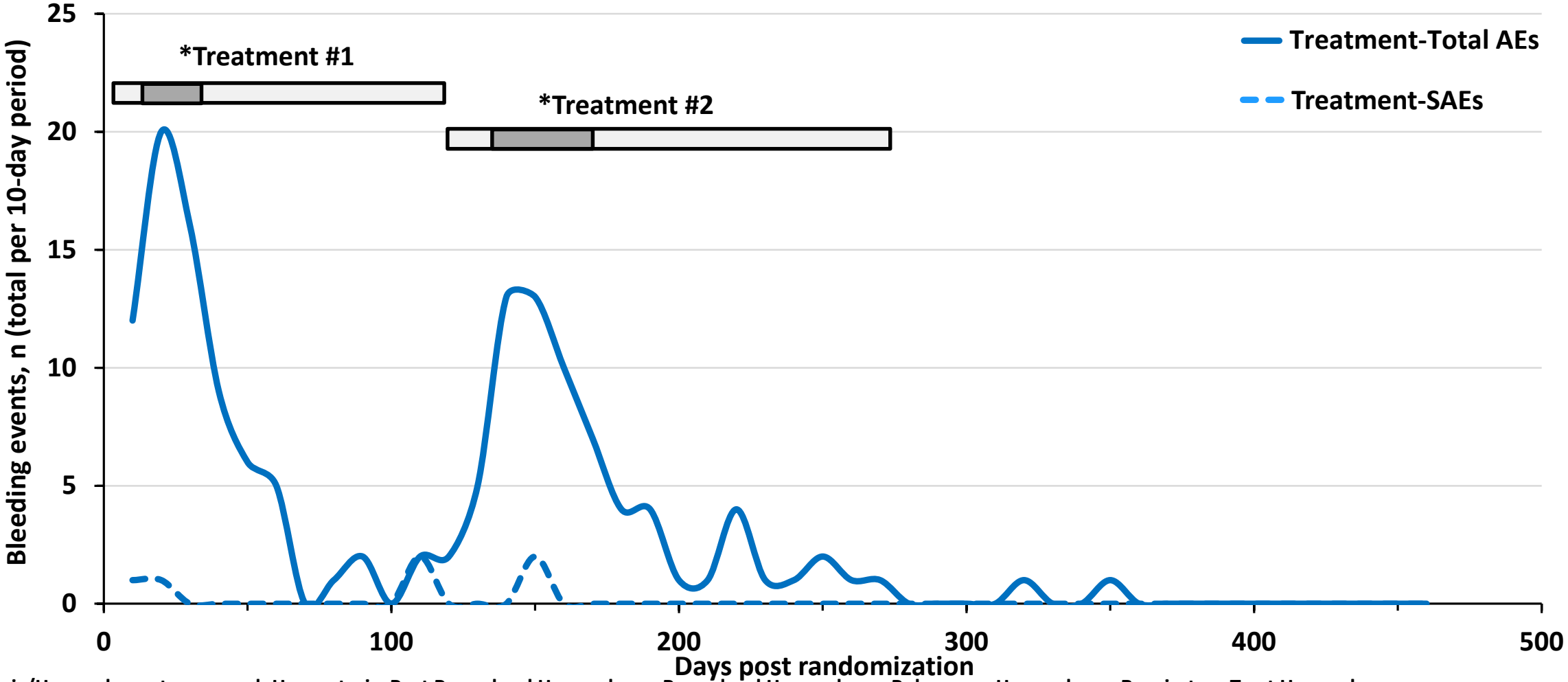
Bleeding (Hemoptysis/Hemorrhage) Events Within 12 Months

RENEW Randomized



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Summary of Long-term Follow-up in RENEW

	Subjects, %		
	Within 12 months		12-24 months
	Treatment N=155	Control N=157	Treatment N=141
Total AEs	100.0	88.5	79.4
SAEs	61.9	34.4	41.1
Death	6.5	5.1	8.5
Device/Procedure-related SAEs	45.8	N/A	9.9

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Post-Marketing Safety Experience
Most Frequently Reported Complaints – Through Feb 2018

Adverse event	Total complaints*	Subject treatments, %**
Pneumothorax	55	0.96
COPD exacerbation	47	0.82
Pneumonia	45	0.79
Hemoptysis	42	0.74
Medical device removal	20	0.35

*Complaints include spontaneously reported adverse events from commercial customers in the EU and other commercial markets, since 2011.
**Subject treatment % based on delivery systems sold.

Safety Conclusions

- Well-characterized safety profile
- COPD exacerbation, pneumonia and pneumothorax were the most frequent SAEs
  - Safety profile similar in the baseline RV ≥225% predicted group; similar rates in SAEs and major complications
- Coil-Associated Opacity (CAO) was recognized to be a treatment specific event, described and incorporated into training
- Device and procedure related complications decrease over time
- Procedure related risks outweighed by benefits of therapy