Anaphylaxis Analysis using the Sampson Criteria

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IASCT 2020

ABSTRACT

Anaphylaxis is a severe, potentially fatal, systemic allergic reaction that occurs suddenly after contact with an allergy-causing substance. Although immediate recognition and treatment of anaphylaxis are crucial, both patients and healthcare professionals often fail to diagnose early signs and symptoms of anaphylaxis. Clinical criteria were proposed and emphasized the need for heightened suspicion of anaphylaxis in patients with a previous history of allergic reactions to a specific allergen and a known exposure, as well as patients in whom there is no known history of allergic reactions. Even though anaphylaxis was described around 100 years ago and is one of the most alarming disorders encountered in medicine, there is no universal agreement on its definition or criteria for diagnosis. This lack of specific criteria for anaphylaxis diagnosis has led to confusion on the part of healthcare professionals and resulted in a failure to diagnose and treat anaphylaxis in a consistent manner. A team of clinicians, statisticians and programmers in Pfizer helped develop the programming algorithm based on a paper by Sampson et al on the Second Symposium on the Definition and Management of Anaphylaxis. This poster is from a programmer's point-of-view in drafting the programming algorithm and standardizing codes and formats to be used across biosimilar studies.

INTRODUCTION

There is no universal agreement on the definition of anaphylaxis or the criteria for diagnosis. In July 2005, the National Institute of Allergy and Infectious Disease and Food Allergy and Anaphylaxis Network convened a second meeting on anaphylaxis to continue working toward a universally accepted definition of anaphylaxis, establish clinical criteria that would accurately identify cases of anaphylaxis with high precision, further review the evidence on the most appropriate management of anaphylaxis, and outline the research needs in this area.

Participants at the Symposium on the Definition and Management of Anaphylaxis agreed that a brief, broad definition of anaphylaxis that reflected its course and potential severity would be most useful to both medical and lay community: "Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death." It was agreed that the diagnostic criteria must provide the emergency responder or treating physician with a relatively simple and rapid means to make the diagnosis of anaphylaxis. It was also acknowledged that no criteria will provide 100% sensitivity and specificity, but it was believed that the criteria proposed are likely to capture more than 95% of cases of anaphylaxis.

PROGRAMMATIC ALGORITHM

A subject is said to have an episode fulfilling the Sampson Criteria if **at least one** of the following criteria is met:

Criterion 1

The subject experienced an onset of both Condition 1 and Condition 2 up to 24 hours (or 1 calendar day if exact times were not collected) post dosing with study drug

- **Condition 1**: a skin or mucosal membrane adverse event (Group 1)
- **Condition 2**:
  - a respiratory compromise AE (Group 2) or
  - an end-organ dysfunction/reduced blood pressure AE (Group 3), or
  - reduced systolic blood pressure (characterized by systolic blood pressure under 90 mmHg or a greater than 30% decrease from baseline based on the vital signs data

Criterion 2

The subject experienced an onset of any 2 or more conditions up to 24 hours (or 1 calendar day if exact times were not collected) post dosing with study drug

- **Condition 1**: a skin or mucosal membrane adverse event (Group 1)
- **Condition 2**: a respiratory compromise AE (Group 2)
- **Condition 3**:
  - an end-organ dysfunction/reduced blood pressure AE (Group 3), or
  - reduced systolic blood pressure
- **Condition 4**: a gastrointestinal AE (Group 4)

Criterion 3

The subject experienced reduced systolic BP up to 24 hours (or 1 calendar day) post dosing with study drug, and at least 1 qualifying event*

A qualifying event is defined as any of the following occurring during the current study, after the first administration of the study drug and before the administration of the same study drug associated with the current reduced systolic blood pressure event

- **Condition 1**: An event meeting Criterion 1 or Criterion 2
- **Condition 2**: An Infusion Related Reaction (IRR) or an Injection Site Reaction (ISR)
- **Condition 3**: AE under the Anaphylactic Reaction SMQ or the Angioedema SMQ or the Hypersensitivity SMQ considered to be related to the study drug as reported by the investigator

ADVERSE EVENTS GROUPINGS

Adverse events will be grouped under the following based on the latest MedDRA Preferred Terms. The list will be confirmed by the clinicians of the study.

1. Skin and mucous membrane involvement
2. Respiratory compromise
3. End-organ dysfunction
4. Gastrointestinal symptoms

APPLICATION ON BIOSIMILARS STUDIES

Sampson Criteria Anaphylaxis Analysis is currently being used in Biosimilar studies in Pfizer.

STATUS/CURRENT DIRECTION

Next step: Application to other TAs outside Biosimilars

SAMPLE OUTPUTS

Listings of Adverse Events fulfilling the Sampson Criteria output

Study Drug Details								Adverse Events Details				
Subject/Age/ Race/Gender	Dose Number	Injection Date	Sampson Criteria[a] Flag	Vital Signs[d]	PTs related to reduced BP[e]	Qualifying Event[f]	ISR Flag	AE Onset Date (Study Day)	Preferred Term (PT Group)[g]	Max Severity /SAE	Outcome	Action Taken with Study Drug/ Other Action Taken
21331009/ 50/ WHITE/ F	Dose 1	05FEB2016	Criterion 2					FEB2016	Dry skin (1)	Grade 2/ No	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED
								FEB2016	Skin exfoliation (1)	Grade 2/ No	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED
								06FEB2016 (2)	Abdominal pain (4)	Grade 1/ No	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED
								06FEB2016 (2)	Abnormal faeces (4)	Grade 1/ No	RECOVERED/RESOLVED	DOSE NOT CHANGED
21581002/ 73/ WHITE/ F	Dose 3	19FEB2016	Criterion 2					20FEB2016 (30)	Abdominal pain upper (4)	Grade 2/ No	RECOVERED/RESOLVED	DOSE NOT CHANGED
								20FEB2016 (30)	Asthenia (3)	Grade 2/ No	RECOVERED/RESOLVED	DOSE NOT CHANGED
								20FEB2016 (30)	Vomiting (4)	Grade 2/ No	RECOVERED/RESOLVED	DOSE NOT CHANGED

Summary of the Sampson Criteria output

	Treatment A n (%)	Treatment B n (%)	Total n (%)
Subjects Evaluable for Adverse Events	297	299	596
Subjects Meeting any Sampson Criteria	2 (0.7)	3 (1.0)	5 (0.8)
Subjects Meeting Criterion 1	1 (0.3)	0	1 (0.2)
Subjects Meeting Criterion 2	1 (0.3)	2 (0.7)	3 (0.5)
Subjects Meeting Criterion 3	0	1 (0.3)	1 (0.2)

The following were created:

- SAS codes for creation of analysis datasets (AR and ADAR) and summary tables and listings
- Templates for the SAP, A&R Plan, summary tables and listings
- Work instruction on using the codes and templates

REFERENCE

Sampson H.A., et al. [2006]. Second Symposium on the Definition and Management of Anaphylaxis: Summary Report – Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network Symposium. Annals of Emergency Medicine, 47. 373 - 380.

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