ABSTRACT

In this paper, a SAS reporting system is developed to obtain computer-generated summary tables of adverse events (AE). The system consists of various customized SAS macros that can be applied by SAS users. One major characteristic of the system is that the adverse events summary tables can contain one of two types of p-values from two common statistical tests. Fisher's exact test is used to calculate the p-values comparing the incidence rates among treatment groups for each of the adverse events reported, while the Wilcoxon rank sum test is applied to compute the p-values for evaluating the difference of severity for an adverse event among treatment groups. Both techniques and guidelines to develop the system are presented in detail in this paper. Also, an ongoing application development of user-friendly interface with SAS/AF is discussed with a focus on module design and screen design.

INTRODUCTION

As it has been accepted in the pharmaceutical industry that the collection of comprehensive data on adverse events is a critical part of any well-designed clinical trial, a well-developed reporting system of summary statistics of adverse events provides a solid ground and an efficient approach toward better understanding of what the data represent.

In this paper, a SAS reporting system is developed to efficiently obtain computer-generated summary tables of adverse events by body system, preferred term, treatment group, or severity. First, a customized SAS macro is developed to summarize incidence rates of adverse events by body system (or preferred term) and treatment group. The p-values based on Fisher's exact test are incorporated in the summary statistics to compare the incidence rates among treatment groups for each of adverse events reported. In order to evaluate the difference of severity for an adverse event among treatment groups, another SAS macro is created to calculate the incidence rates and p-values from Wilcoxon rank sum test for different severity (mild, moderate, or severe) among treatment groups by body system (or preferred term). Second, a reporting SAS code is demonstrated in this paper to output those summary statistics into tables whose specifications can be selected from a prespecified format pool. Finally, a discussion about development of user-friendly interface using SAS/AF is presented.

A MACRO TO SUMMARIZE AE BY BODY SYSTEM AND TREATMENT: FISHER'S EXACT TEST

A macro to summarize adverse events by body system (or preferred term) and treatment group is shown in Appendix 1. The options used in this macro are as follows:

Options for data sets:
- inds=input data set containing AE information.
- outds=output data set containing summary statistics.
- patds=patient data set containing complete patient list.

Options for variable names in data sets:
- rxgrp=treatment group variable.
- invvar=investigator variable.
- patva=patient number variable.
- bodysys=body system variable.
- prefterm=preferred term variable.
- idvars=other possible id variables, such as age group.

Options for conditions
- subcond=condition to subset input data set.
- invall=condition for whether to summarize data for overall investigator. Default is YES.
- rxall=condition for whether to calculate summary statistics for an overall treatment group. Default is NO.
- p_value=condition for whether to calculate p-values based on Fisher's exact test. Default is YES.

Many comments are incorporated in the macro in order to let readers understand the underling data steps or procedures. It is worth noting that the following standard macros are used in the program. Three of them, %fisher, %varinfo, and %sort, are general standard macros stored in general macro library at STATPROBE. The %fisher macro is used to calculate p-values based on Fisher's exact test and is demonstrated in detail in Zuo and Haske (1997). The %varinfo macro is created for putting information (number of unique values and those values) about a specific variable in a data set into global macro variables, while %sort is used to sort a data set.

The other three standard macros in the program are protocol-related: %patcount, %rxgrp, and %patmerge. The %rxgrp is used to assign treatment group to each patient in the input data set, while %patcount is employed to calculate patient counts under each treatment group and possible other id variables. Because the AE data set does not contain those patients without AE, the %patmerge is created to add those patients for each adverse event with r1=0 (1=AE, 0=No AE), so that Fisher's exact test can be performed based on complete information for all patients.

In the output data set, four types of summary statistics are presented across investigator, body system (or preferred term), and treatment group: number of patients with at least one AE, proportion of patients with at least one AE, number of a specific adverse event reported, and p-value (based on Fisher's exact test) comparing proportions between two treatment groups. The output data set is sorted by investigator variable, possible id variables, descending number of patients with at least one AE for body systems, descending number of patients with at least one adverse event for treatment groups, and descending number of patients with at least one AE for each adverse event.
Appendix 3 contains a sample SAS code to output AE summary statistics for preferred terms within a body system, and treatment group.

The output data set can then be incorporated with a standard reporting system at STATPROBE to produce various AE summary tables. A sample SAS code will be presented in a following section.

MACRO TO SUMMARIZE AE BY BODY SYSTEM, TREATMENT GROUP, AND SEVERITY: WILCOXON RANK SUM TEST

This macro (see Appendix 2) is used to calculate the summary statistics of adverse events by body system (or preferred term), treatment group, and severity. Many parts (data steps or procedures) in this macro are identical or similar to those discussed in the previous section. The exceptions are resulted from the incorporation of severity in the calculation. For example, an additional option, sevvar=, is used to identify the severity variable, which is also added into many data steps or procedures.

Two other different parts include a data step to retain observations with maximum severity for each patient under each adverse event and a standard macro (%wilcoxon) to calculate p-values based on Wilcoxon rank sum test to compare difference caused by severity among different treatment groups. The %wilcoxon macro can be found in Zuo and Haske (1997).

In the final output data set, the following summary statistics are presented: 1) number (%) of patients with at least one AE across investigator, body system (or preferred term), treatment group, and severity, and 2) p-value (based on the Wilcoxon rank sum test) comparing difference in proportions due to deference in severity between two treatment groups.

SAS CODE TO USE THE AE SUMMARY MACROS

Appendix 3 contains a sample SAS code to output AE summary statistics into a specified table (see Appendix 4) using the above discussed AE summary macros and other reporting-related macros. The SAS code includes the following steps:

1) Reading in required data sets: AE and patient data sets;
2) Subsetting AE data set to treatment-emergent adverse events (TEAE) using %teae macro;
3) Obtaining body system and preferred term from AE dictionary or AE format library using %aemap macro;
4) Assigning global macro variables to identify treatment group for a control drug (&basrxgrp) and treatment group used to obtain sort id (&countgrp);
5) Calling %aesum macro to calculate AE summary statistics;
6) Defining sub head and footnotes for the table (%subhead and %foot);
7) Creating statements to output AE summary statistics (%body);
8) Calling %report macro to execute output statements using data _null_.

The table generated using the SAS code is displayed in Appendix 4. Similarly, another table (Appendix 5) can be created to contain summary statistics across body system (preferred term), treatment group, and severity, using the same AE data set as that for Appendix 4. Both tables are typical AE summary tables used for comparative studies with two treatment groups.

Appendices 6 and 7 contain AE summary statistics for five treatment groups plus an overall treatment group. The tables have different specifications from Appendixes 4 and 5 using different %subhead, %body, and %foot.

FURTHER DEVELOPMENT WITH SAS/AF

The goal in creating the SAS macros discussed here is to develop a user-friendly interface to generate various customized AE summary tables. At the present time, we are working on interface development using SAS/AF. Three major parts have been considered in our application development: module design, screen design, and function implementation.

Two types of modules will be included in our application: screen module and function module. A screen module is used to accept input from users, while a function module performs a specific functional task inside the application. The following screen modules are going to be designated in our application: locating required data sets, subsetting data sets (e.g., in order to focus on treatment emergent adverse events) if necessary, mapping AE dictionary or not, assigning base and count treatment groups, selecting table specification (among different styles), and typing texts for heads, sub heads, and footnotes. Each screen module is corresponding to an icon in menu screen and has its own screen. On the other hand, the function modules are mainly constructed by various SAS macros (AE summary macros and reporting-related macros). All the SAS macros discussed in this paper can be formed as individual function modules. It is noted that all module should be arranged to make the interface natural to the users as well as make programming as simple as possible in that each module can be performed or tested for its particular task without having other modules in place.

While creating those modules is the most important aspect in the development of application for developers, the screen design is another important area of application from a user's perspective. Users do not care about how an application is programmed. Instead, they are interested in whether they can comfortably use it. On the other hand, the developers can use classes provided in SAS/AF software to efficiently design and create those screens.

All screen modules and function modules will be implemented to associated with those designated screens by using screen control language (SCL). The SCL is a sort of assembling tool to link functions together and make the screens work well. Along with function implementation, debugging will be conducted in order to discover potential problems and make the application error free.
CONCLUSION

This paper has presented various customized SAS macros that can be applied by SAS users to generate any types of AE summary tables. Those SAS macros provide programmers an integrated tool to efficiently and effectively design and create those AE summary tables. An ongoing development of interface application with SAS/AF was also discussed in terms of module design, screen design, and function implementation. The application will provide a user-friendly interface for those non-SAS users to produce customized AE summary tables.

REFERENCES


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AUTHORS' ADDRESSES

Jun Zuo, Ph.D.
STATPROBE, Inc.
3885 Research Park Drive
Ann Arbor, MI 48108
Phone: (313) 769-5000 x139
E-Mail: jzuo@statprobe.com or jzuo@ix.netcom.com

Carl R. Haske, Ph.D.
STATPROBE, Inc.
3885 Research Park Drive
Ann Arbor, MI 48108
Phone: (313) 769-5000 x115
E-Mail: chaske@statprobe.com

APPENDIXES

APPENDIX 1 Macro to summarize AE by body system (preferred term) and treatment group

```
*** Create obs for body system and overall ***;
Data reports;
  Set reports;
  Output;
  &prefterm = '0';
  Output;
  &bodysys = 'ZZZZZ';
  Output;
  Run;

*** Create data set for calculating numbers & percents of patients with at least one AE ***;
%sort(data=reports nodupkey out=pats, sortvars=indivar &idvars &bodysys &prefterm &patvar);

*** Create obs for overall investigator ***;
%If &invall=YES %then %do;
  Data reports;
  Set reports;
  &inwar=99;
  Output;
  Run;
  Data patients;
  Set patients;
  &inwar=99;
  Output;
  Run;
%End;

%sort(data=reports, sortvars=indivar &idvars &bodysys &prefterm &rxgrp &patvar);
%sort(data=patients,sortvars=indivar &idvars &bodysys &prefterm &rxgrp &patvar);

*** Calculate number of total AE reports ***;
Proc means data=reports noprint;
  Var r1;
  By &inwar &idvars &bodysys &prefterm &rxgrp;
  Output out=repstat sum=repnum;
Run;

*** Calculate number of patients with at least one AE ***;
Proc means data=patients noprint;
  Var r1;
  By &inwar &idvars &bodysys &prefterm &rxgrp;
  Output out=patstat sum=patnum;
Run;

*** Calculate percent of patients with at least one AE ***;
Data patstat;
  Set patstat;
  totn=symget(n'lltrim(left(&invar»lltrim(left(&rxgrp»);
  If totn ^= 0 then patcnt=round(100*patnum/totn, .1);
  If patcnt= . then patcnt=0.0;
  Drop totn;
  Run;

*** Obtain sort id based on number of patients for body system under a specified treatment group ***;
Data bodyid;
  Set patstat;
  if &rxgrp=&countgrp and &prefterm='0';
  if &bodysys='ZZZZZ' then bodyid=-1;
  else bodyid=patnum;
  Keep &inwar &idvars &bodysys bodyid;
Run;
```

APPENDIX 2 Macro to summarize AE by body system (preferred term) and treatment group

```
%Macro aesum(inds=, outds=, patds=, rxgrp=, inwar=, patvar=, idvars=, bodysys=, prefterm=, subcond=, invall=YES, rxall=NO, p_value=YES);
  *** Calculate denominators for percentage calculation ***;
  %patcount(inds=&patds, invid=&inwar, rxgrp=&rxgrp, rxall=&rxall);

  *** Read in AE data and set r1 as AE indicator variable ***;
  Data reports;
    Set &inds;
    &subcond;
    r1=1;
  Run;

  *** Assign treatment group ***;
  %&rxgrp(inds=reports, rxall=&rxall);
```
*** Obtain sort id based on number of patients for preferred term under a specified treatment group ***;
Data prefid;
    Set patstat;
    If &rxgrp=&countgrp;
    If &prefterm='O' then prefid=9999;
    Else prefid=patnum;
    Keep &invvar &idvars &bodysys &prefterm prefid;
Run;

*** Merge numbers of reports and patients ***;
Data &outds;
    Merge repstat patstat;
    By &invvar &idvars &bodysys &prefterm &rxgrp;
    Keep &invvar &idvars &bodysys &prefterm &rxgrp patnum patnum repnum;
Run;

*** Calculate p-values (Fisher's exact test) ***;
%If %upcase(&p_value)=YES %then %do;
*** Create complete patient list for each AE ***;
%patmerge(inds=patients, outds=fishers, patds=&patds,
    idvars=&idvars &bodysys &prefterm);
Data rxgrp;
    Set fishers;
    If &rxgrpA=&basrxgrp;
    Keep &rxgrp;
Run;

*** Obtain rx group info and put them into a macro variable ***;
%varinfo(inds=rxgrp, var=&rxgrp, id=rx);

*** Calculate p-values ***;
%Do k=1 %to &totrx;
    Data fisher;
    Set fishers;
    If &rxgrp=&basrxgrp or &rxgrp=&&&rx&k;
    Run;
    %fisher(inds=fisher, outds=pout&k, var=r1,
        rxgrp=&rxgrp, 
        byvars=&invvar &idvars &bodysys &prefterm, 
        pvalue=pvalue&&&rx&k);
%End;

*** Merge with p-values ***;
Data &outds;
    Merge &outds %Do k=1 %to &totrx;
        pout&k;
    %End;
    By &invvar &idvars &bodysys &prefterm;
Run;

*** Merge with preferred term id ***;
Data &outds;
    Merge &outds prefid;
        By &invvar &idvars &bodysys &prefterm;
    If prefid= then do;
        If &bodysys='ZZZZZ' then bodyid=-1;
        Else bodyid=0;
    End;
Run;

*** Sort stats by descending sort ids and other variables ***;
%sort(data=&outds, sortvars=&invvar &idvars descending 
    bodysys descending prefid &prefterm &rxgrp);
%Mend aesum;

APPENDIX 2 Macro to summarize AE by body system (preferred term), treatment group, and severity.

%Macro aesumsev(inds=, outds=, patds=, rxgrp=, invvar=,
    patvar=, idvars=, sevvar=, bodysys=, prefterm=, 
    subcond=, invall=YES, rxall=NO);

*** Calculate denominators for percentage calculation ***;
%patcount(inds=&patds, invid=&invvar, rxgrp=&rxgrp, 
    rxall=&rxall);

*** Read in AE data and set r1 as AE indicator variable ***;
Data reports;
    Set &inds;
    &subcond;
    r1=1;
Run;

*** Assign treatment group ***;
%rxgrp(inds=reports, rxall=&rxall);

*** Create obs for body system and overall ***;
Data reports;
    Set reports;
    Output;
    &prefterm='O';
    Output;
    &bodysys='ZZZZZ';
    Output;
Run;

*** Keep maximum intensity of each adverse event for each patient ***;
%sort(data=reports out=severpat, sortvars=&invvar &idvars 
    &bodysys &prefterm &patvar &sevvar);

Data severpat;
    Set severpat;
    By &invvar &idvars &bodysys &prefterm &patvar &sevvar;
    If last.&patvar;
Run;

*** Create data set for calculating numbers & percents of patients with at least one AE ***;
%sort(data=reports nodupkey out=patients, 
    sortvars=&invvar &idvars &bodysys &prefterm &patvar &sevvar);

Data severpat;
    Set severpat;
    By &invvar &idvars &bodysys &prefterm &patvar &sevvar;
Run;

*** Create obs for overall investigator ***;
%If &invall=YES %then %do;
    Data severpat;
        Set severpat;
        Output;
        &invvar=99;
        Output;
Data patients;
  Set patients;
  Output;
  &invar=99;
  Output;
Run;

%End;

%sort(data=severpat,sortvars=&invar &idvars &bodysys &prefterm &rxgrp &sevvar &patvar);
%sort(data=patients,sortvars=&invar &idvars &bodysys &prefterm &rxgrp &patvar);

*** Calculate number of patients with different severity ***;
Proc means data=severpat noprint;
  Var r1;
  By &invar &idvars &bodysys &prefterm &rxgrp &sevvar;
  Output out=sevstat sum=sevnum;
Run;

*** Calculate number of patients with at least one AE ***;
Proc means data=patients noprint;
  Var r1;
  By &invar &idvars &bodysys &prefterm &rxgrp;
  Output out=patstat sum=patnum;
Run;

*** Obtain sort id based on number of patients for body system under a specified treatment group ***;
Data bodyid;
  Set patstat;
  If &rxgrp=&countgrp and &prefterm='O';
  If &bodysys='ZZZZZ' then bodyid=-1;
  Else bodyid=patnum;
  Keep &invar &idvars &bodysys bodyid;
Run;

*** Obtain sort id based on number of patients for preferred term under a specified treatment group ***;
Data prefid;
  Set patstat;
  If &rxgrp=&countgrp;
  If &prefterm='O' then prefid=9999;
  Else prefid=patnum;
  Keep &invvar &idvars &bodysys &prefterm prefid;
Run;

*** Obtain rx group info and put them into a macro variable ***;
%varinfo(inds=severpat, var=&rxgrp, ld=rx);

*** Calculate p-values ***;
%Do k=1 %to &totrx;
  Data wilcox;
  Set severpat;
  If &rxgrp=&basrxgrp or &rxgrp=&&&rx&k;
  Run;
  %wilcoxon(inds=wilcox, outds=pout&K, var=&sevvar, rxgrp=&rxgrp, byvars=&invar &idvars &bodysys &prefterm, pvalue=pvalue&&&rx&k);
%End;

*** Merge two statistics data sets and calculate percent of patients with at least one AE ***;
Data &outds;
  Merge patstat sevstat;
  By &invar &idvars &bodysys &prefterm &rxgrp;
totn=symget('n'lltrim(left(&invvar»lltrim(left(&rxgrp»);If totn ^=0 then do;
  patcnt=round(100*patnum/totn,.1);
  sevcnt=round(100*sevnum/totn,.1);
End;
If patcnt=. then patcnt=0.0;
If sevcnt=. then sevcnt=0.0;
Drop totn;
Run;

*** Merge with p-values ***;
Data &outds;
  Merge &outds prefid;
  By &invar &idvars &bodysys &prefterm;
Run;

*** Merge with prefterm id ***;
Data &outds;
  Merge &outds bodyid;
  By &invar &idvars &bodysys &prefterm;
Run;

*** Merge with bodysys id ***;
Data &outds;
  Merge &outds prefid;
  By &invar &idvars &bodysys &prefterm;
  If prefid=. then do;
    If &bodysys='ZZZZZ' then bodyid=-1;
    Else bodyid=0;
  End;
Run;

%sort(data=&outds,sortvars=&invvar &idvars descending bodyid &bodysys descending prefid &prefterm &rxgrp &sevvar);

%End aseumsev;

APPENDIX 3 Sample SAS code to output summary table

*** Read in data sets ***;
%Let ds1=ae;
%Let keep1=prot inv pt date aesymp aetext aestardt;
%Let subset1=⊂;
%Let ds2=patient;
%Let keep2=prot inv pt;
%Let subset2=⊂;
Readdata;

*** Identify treatment-emergent AE ***;
%eaee(inds=&ds1,aedt=aestardt);

*** Map AE dictionary ***;
%aemap(inds=&ds1,aename=aesymp);

*** Control treatment group ***;
%Let basrxgrp=1;

*** Count treatment group for sort id ***;
%Let countgrp=1;
Calculate summary statistics:
%aesum(inds=&ds1, outds=stats, patds=&ds2, rxgrp=rxgrp,
inwar=inv, patvar=pt, bodysys=bodysys, prefterm=prefterm);

Obtain information about treatment group:
%varinfo(inds=stats, var=rxgrp, id=nx);

Assign width of columns:
%colwids(40, 17, 17, 10);

Treatment group names:
%Let drgname1=DRUG A;
%Let drgname2=DRUG B;

Define sub head for table:
%Macro subhead;
%Do i=1 %to &totrx;
nval&i = symget(i\n'lltrim(left(inv»lItrim(left(&&rx&i)));
%End;
Put @&c1 "BODY SYSTEM"
%Do i=1 %to &totrx;
%Let j=%eval(&i+1);
@&&c&j " &&drgname&i"
%End;
@&c1 "ADVERSE EVENT"
%Do i=1 %to &totrx;
%Let j=%eval(&i+1);
( N = " nval&i 3. ")
%End;
@&c4 "P-VALUE"
%Mend subhead;

Put statements used in data _null_:
%Macro body;
%Let pcol=%eval(&totrx+2);
Retain zero 0;
Select (rxgrp);
%Do i=1 %to &totrx;
When (&&rx&i) col = &&&c&j;
%End;
Otherwise;
End;
If first.prefterm then do;
Put ;
%Do i=2 %to &totrx+1;
@&&&c&i zero 3. (' zero 5.1 ') zero 3.
%End; @;
End;
If bodysys *=ZZZZZ’ then do:
If prefterm = ’0’ then put @&c1 bodysys @;
Else put @&c1+2 prefterm @;
End;
Else if first.prefterm then
put @&c1 %uline / @&c1 "TOTAL" @;
Put @col patnum 3. (" patcnt 5.1 ") repnum 3.
@&c1%pooled pvalue2 8.3 @;
If last.prefterm then put;
If last.bodysys and bodysys”=ZZZZZ’ then put;
%Mend body;

Define footnotes:
%Macro foot;
Put @&c1 "REFERENCE: LISTING X"
/ @&c1 "P-VALUE COMPARING TREATMENT GROUPS"
" USING FISHER’S EXACT TEST."
/ @&c1 "NOTE: (1) TEAES WERE DEFINED AS ALL NEW"
" ADVERSE EVENTS INCLUDING THOSE NOT"
" PRESENT AT BASELINE OR THAT"
APPENDIX 4 Sample summary table incorporated with p-values (Fisher's exact test)

### TABLE X

(PAGE 1 OF 1)

**SUMMARY OF TREATMENT-EMERGENT ADVERSE EVENTS (TEAES) BY BODY SYSTEM**

<table>
<thead>
<tr>
<th>INVESTIGATOR: XYZ</th>
</tr>
</thead>
<tbody>
<tr>
<td>BODY SYSTEM</td>
</tr>
<tr>
<td>GASTROINTESTINAL</td>
</tr>
<tr>
<td>DIARRHEA</td>
</tr>
<tr>
<td>PAIN ABDOMINAL</td>
</tr>
<tr>
<td>DYSPNEA</td>
</tr>
<tr>
<td>ERUCTAT</td>
</tr>
<tr>
<td>RECTAL DISCOMFORT</td>
</tr>
<tr>
<td>FLATULESS</td>
</tr>
<tr>
<td>Nausea</td>
</tr>
<tr>
<td>Vomiting</td>
</tr>
<tr>
<td>URINARY</td>
</tr>
<tr>
<td>Dysuria</td>
</tr>
<tr>
<td>Nocturia</td>
</tr>
<tr>
<td>Body as a Whole</td>
</tr>
<tr>
<td>Pain Chest</td>
</tr>
<tr>
<td>React Aggraviation</td>
</tr>
<tr>
<td>Central Nervous System</td>
</tr>
<tr>
<td>Dizziness</td>
</tr>
<tr>
<td>Headache</td>
</tr>
<tr>
<td>Twitch</td>
</tr>
<tr>
<td>Psychiatric</td>
</tr>
<tr>
<td>Insomnia</td>
</tr>
<tr>
<td>Nervousness</td>
</tr>
<tr>
<td>Metabolic &amp; Nutritional</td>
</tr>
<tr>
<td>Hyperglycemia</td>
</tr>
<tr>
<td>Platelet, Bleeding, Clotting</td>
</tr>
<tr>
<td>Epiptaxis</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

**REFERENCE: LISTING X**

* P-VALUE COMPARING TREATMENT GROUPS USING FISHER'S EXACT TEST.

**NOTE:**

1. TEAES WERE DEFINED AS ALL NEW ADVERSE EVENTS INCLUDING THOSE NOT PRESENT AT BASELINE OR THAT WORSENED DURING TREATMENT.

2. BODY SYSTEM TOTALS ARE NOT NECESSARILY THE SUM OF THE INDIVIDUAL ADVERSE EVENTS SINCE A PATIENT MAY HAVE REPORTED MORE THAN ONE ADVERSE EVENT IN THE SAME BODY SYSTEM.
## Table X

### (Page 1 of 1)

**SUMMARY OF TREATMENT-EMERGENT ADVERSE EVENTS (TEAEs) BY BODY SYSTEM AND SEVERITY**

<table>
<thead>
<tr>
<th>INVESTIGATOR: XYZ</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>BODY SYSTEM</th>
<th>ADVERSE EVENT</th>
<th>DRUG A (N = 26)</th>
<th>DRUG B (N = 26)</th>
<th>P-VALUE*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (MILD)</td>
<td>MODERATE</td>
<td>SEVERE</td>
<td>N (MILD)</td>
</tr>
<tr>
<td>GASTROINTESTINAL</td>
<td>5 (19.2)</td>
<td>3 (11.5)</td>
<td>1 (3.8)</td>
<td>1 (3.8)</td>
</tr>
<tr>
<td>DIARRHEA</td>
<td>3 (11.5)</td>
<td>2 (7.7)</td>
<td>0 (0.0)</td>
<td>1 (3.8)</td>
</tr>
<tr>
<td>PAIN ABDOMINAL</td>
<td>2 (7.7)</td>
<td>1 (3.8)</td>
<td>0 (0.0)</td>
<td>1 (3.8)</td>
</tr>
<tr>
<td>DIABETES</td>
<td>1 (3.8)</td>
<td>1 (3.8)</td>
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<td>0 (0.0)</td>
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**TOTAL**

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**REFERENCE:** LISTING X

*P-VALUE COMPARING TREATMENT GROUPS USING THE WILCOXON RANK SUM TEST.

**NOTE:**

1. TEAEs were defined as all new study events including those not present at baseline or that worsened during treatment.

2. For events reported multiple times with different intensities for the same patient, only the incidence with maximum intensity was summarized.

3. Body system totals are not necessarily the sum of the individual study events since a patient may have reported more than one study event in the same body system.
## Table X

**INCIDENCE RATES OF DRUG RELATED TREATMENT EMERGENT ADVERSE EVENTS (TEAE)**

**BY BODY SYSTEM AND TREATMENT GROUP**

**[NUMBER (%) OF SUBJECTS WITH AT LEAST ONE TEAE]**

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Footnote: A Treatment Emergent Adverse Event is an event that starts on or after the day of randomization. TOTAL is the total number of subjects (not events) that are being tabulated across the body systems.
## TABLE X

**INCIDENCE RATES OF ALL TREATMENT EMERGENT ADVERSE EVENTS (TEAE)**

**BY BODY SYSTEM, SEVERITY AND TREATMENT GROUP**

**[NUMBER (%) OF SUBJECTS WITH AT LEAST ONE TEAE]**

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| **Footnote:** A Treatment Emergent Adverse Event is an event that starts on or after the day of randomization.
TOTAL is the total number of subjects (not events) that are being tabulated across the body systems.