eSafety Data Requirement and Screen Shots

I. Analysis Method Settings: Data Sets, AE Variables and Co-variates

The following factors are typically analyzed in the ISS reports, and are available in eSafety to explore the exposure-safety relationship.

1. Study Pool

   A study pool can be selected by

   i. Study ID
   ii. Study arm
   iii. Treatment regimen
   iv. Study length, size
   v. Clinical development phase

2. Study Design

   The following study designs can be identified and re-grouped by dose level or treatment

   i. Parallel
   ii. Crossover
   iii. Sequential
   iv. Titration
   v. Extension
   vi. Adaptive

3. Patient Subset

   Patient population can be defined by

   i. Demographic variables
   ii. Disease baseline
   iii. Special patient population
   iv. Laboratory results

4. AE of Special Interest

   Specific AE can be identified by

   i. AE preferred term
   ii. Body system
   iii. Composite AE by combining multiple AE terms

5. AE Subset

   A subset of AE's can be determined by

   i. Severity
   ii. Related to treatment or not
   iii. Time of AE occurrence
   iv. Duration of AE

6. Other Criteria

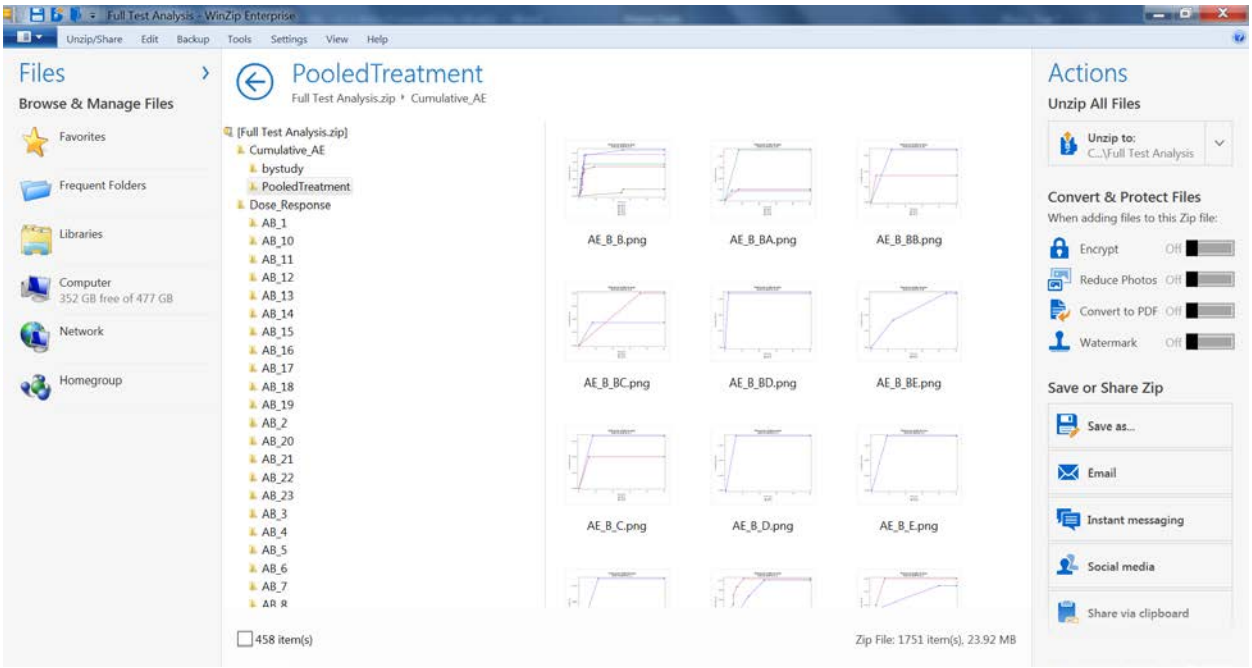
   Additional inclusion and exclusion criteria for patient pool and AE

   i. Patient pool: can be subset by any variable listed in ADSL.xpt
   ii. AE: can be subset by any variable listed in ADAE.xpt

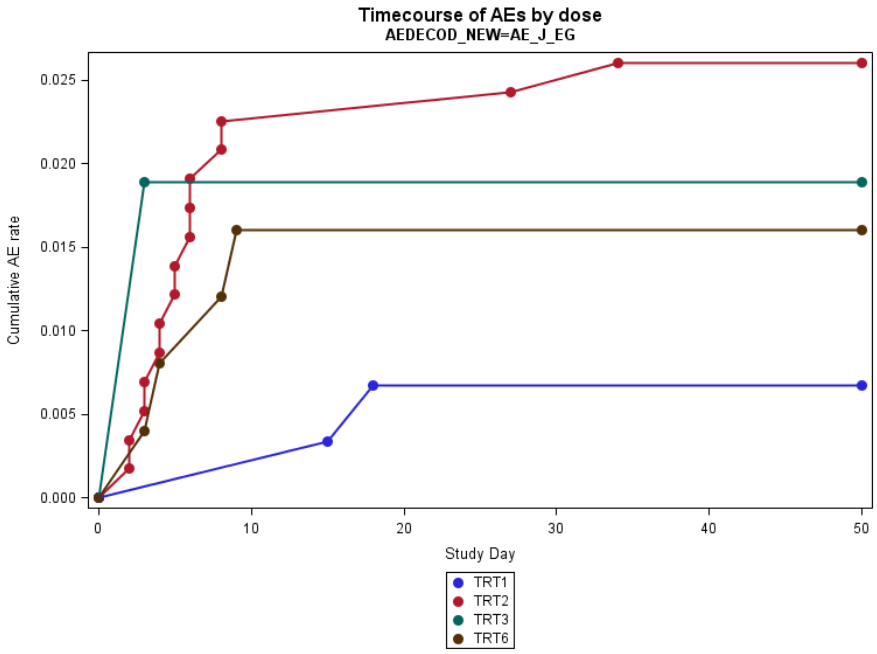
II. Analyses Outputs

1. Cumulative AE Rate

   The cumulative rates of all AEs are available in the "/Cumulative AE" folder and further organized into "/pooled treatment" (which shows pooled study results) and "/bystudy" (which shows individual study results).

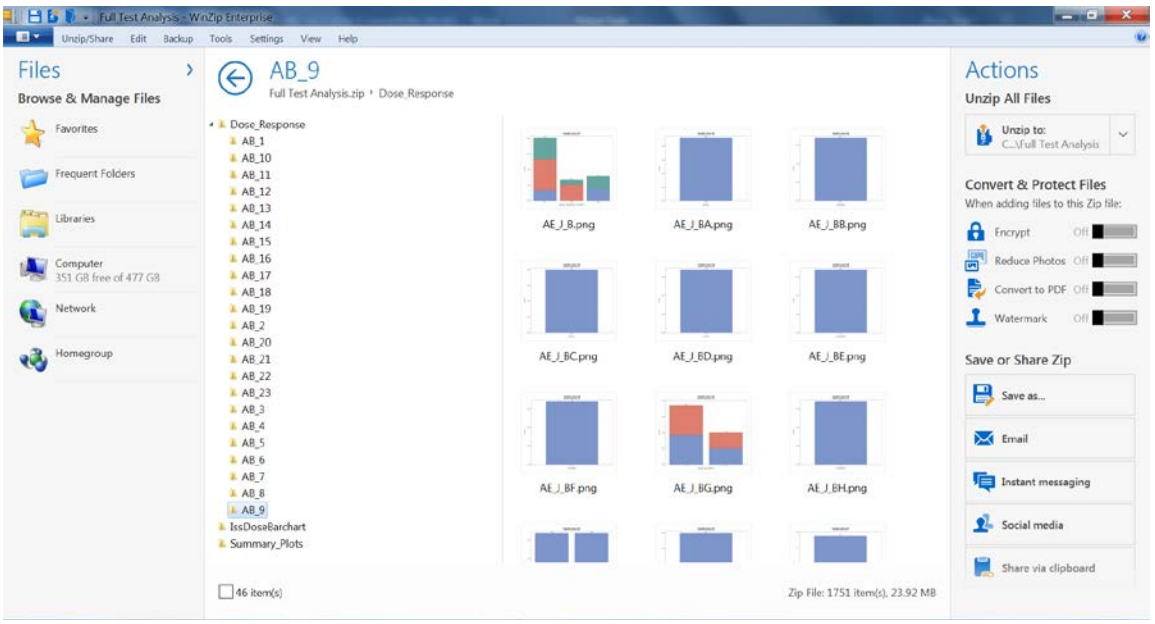


The cumulative rate of an AE term is plotted as a function of time of the first occurrence in each subject. An example is shown below

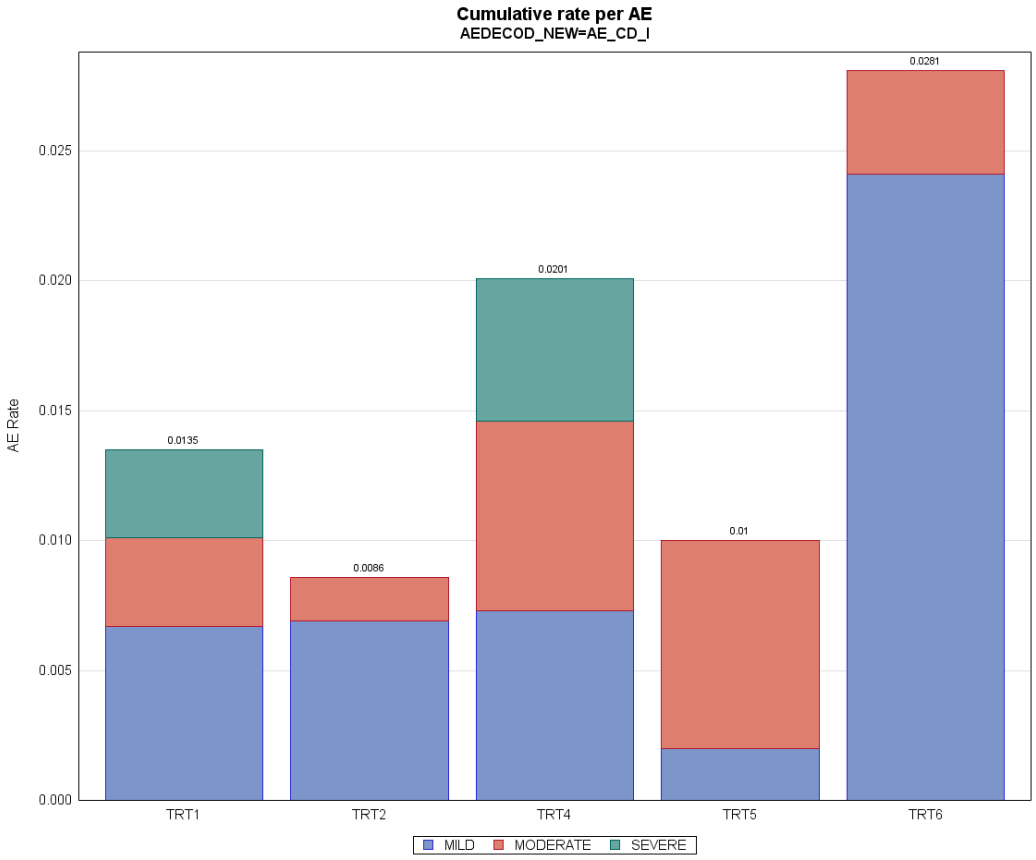


2. Dose Response of AE

The dose response of each AE term is available under the "/Dose Response" folder, and further organized by the body system folders

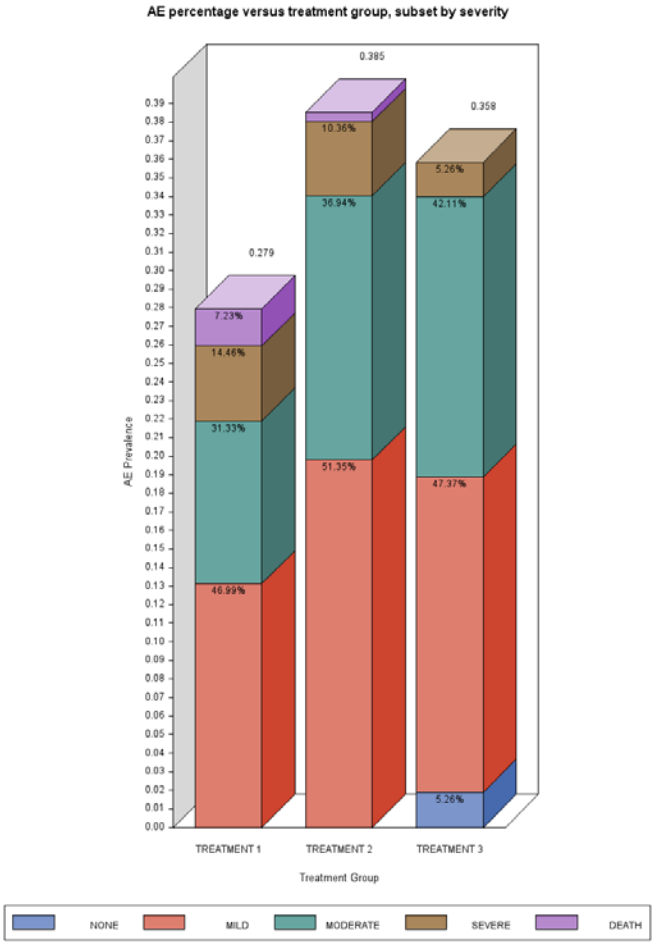


The AE rate is plotted per dose and color coded by severity. An example is shown below



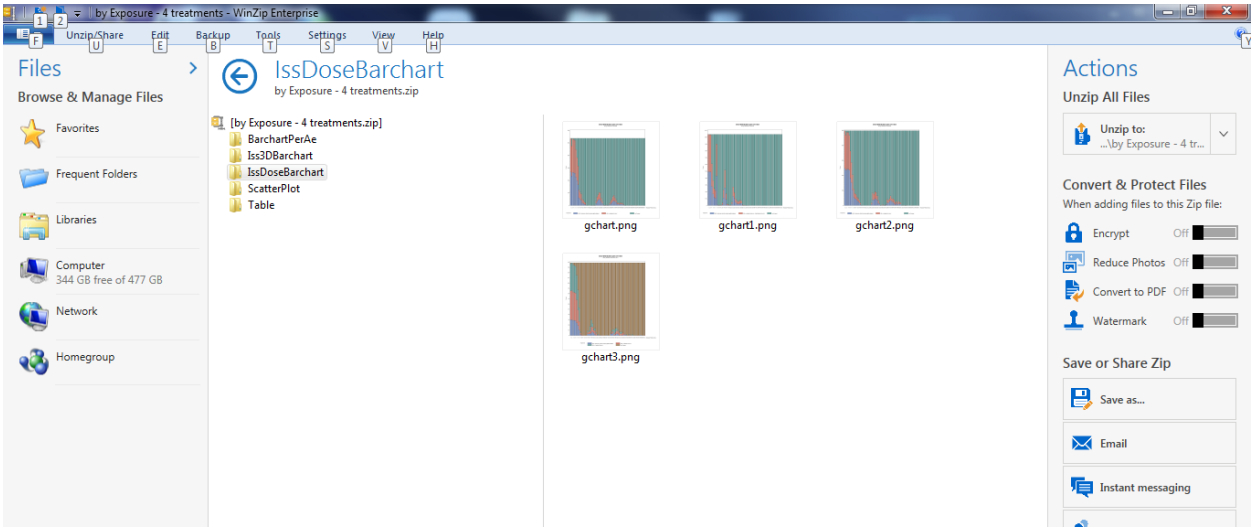
3. Total AE Prevalence

The total AE Prevalence is available in the "/Summary_Plots" folder. The total AE rate is plotted per dose and color coded by severity. An example is shown below

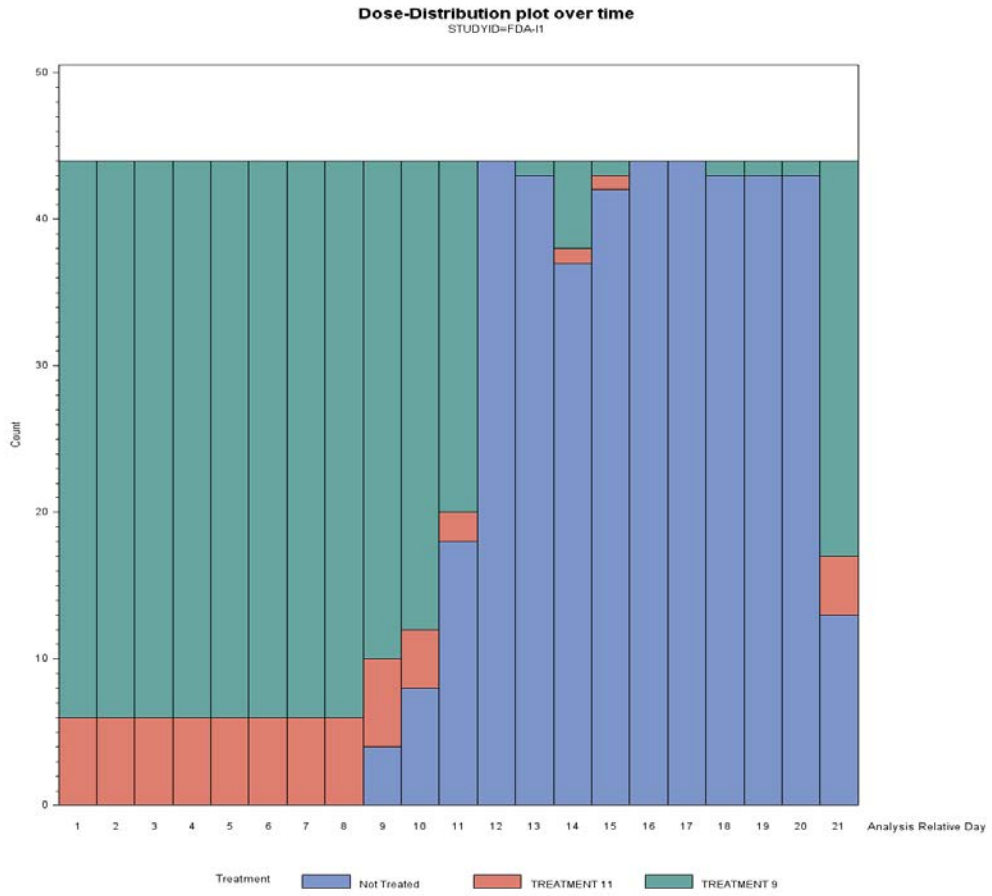


4. The dosing records

   The dosing record as a function of study time is available in the "/IssDoseBarChart" folder.



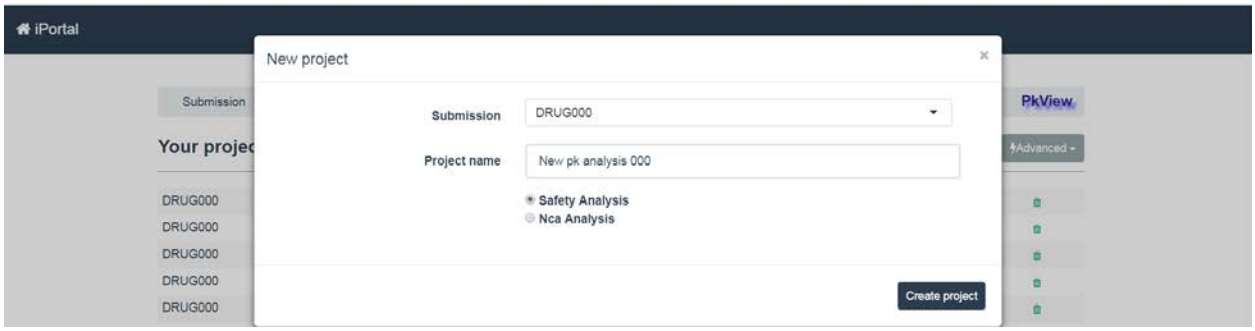
An example of the dosing record plot is shown below:



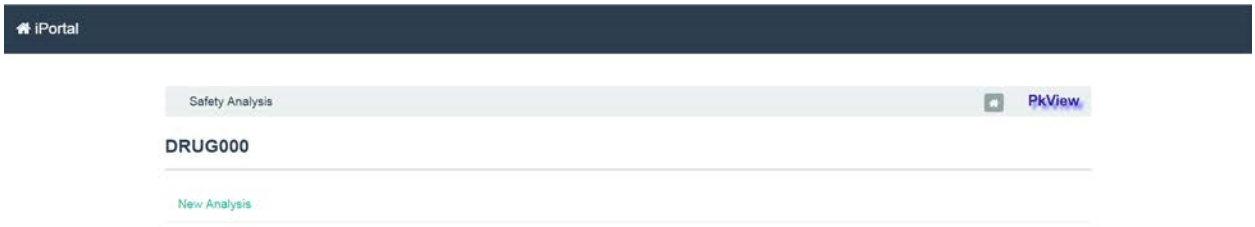
III. User Interface

a. Steps to create a new safety analysis project –

- On the homepage select 'Advanced' tab and click 'New Project'.
- On the 'New Project' screen, select the drug name and enter the project name.
- Select 'Safety Analysis' option and click 'Create Project'.



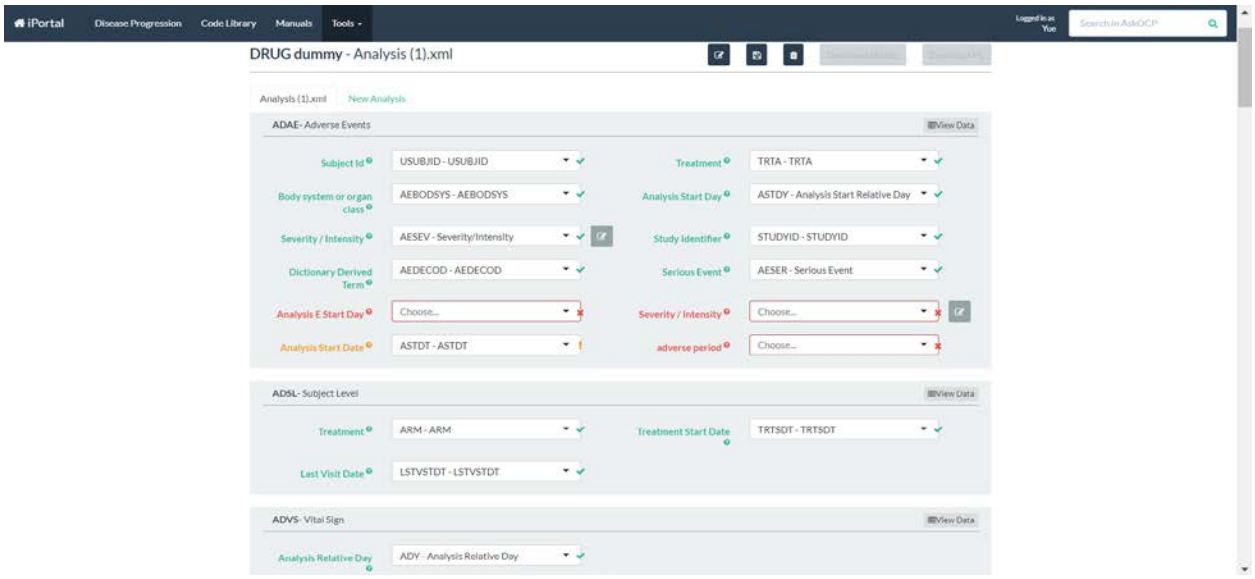
- The project gets created and the 'Safety Analysis' screen appears



- Once the project is created, the user can directly navigate to safety analysis screen from the homepage by clicking on the 'Safety Analysis' icon.

b. Required data files and variables

The user interface will initially load the required variables for the exposure safety analysis based on CDISC ADAM data standard terminology. The three required ADAM data files: ADAE.xpt, ADSL.xpt, and ADVS.xpt. An example of the starting screen of eSafety is shown below.



Here is the definition of each required field:

ADAE:

Variable name	Standard CDISC ADAM Terms
Subject ID	USUBJID
Body system or organ class	AEBODSYS
Severity/Intensity	AESEV
Dictionary derived terms	AEDECOD
Analysis E start day (optional, alternative to 'analysis start day')	AESTDY
Analysis start date (optional, alternative to 'analysis start day')	ASTDT
Treatment	TRTA
Analysis start day	ASTDY
Study identifier	STUDYID
Serious event	AESER
Severity/intensity (optional, alternative to standard 'Severity/intensity' term	ASEV
Adverse period (optional)	APERIOD

ADSL:

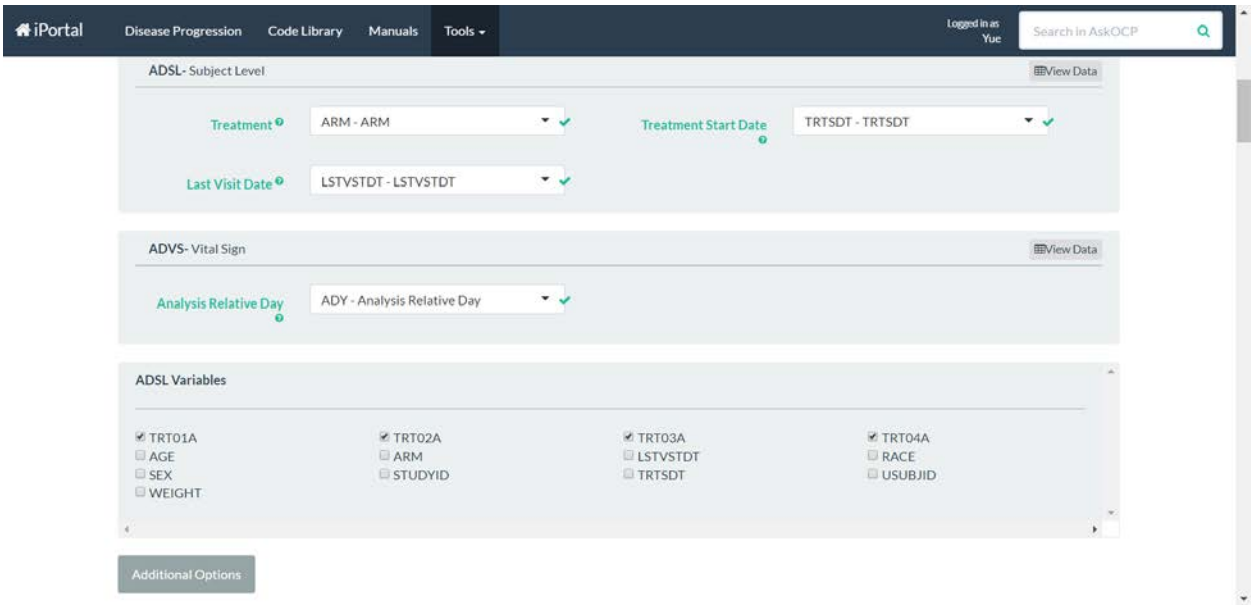
Variable name	Standard CDISC ADAM Terms
Treatment	ARM
Last visit date	TRTED, RFENDT, LSTDTALL, DISCDTC, SFFUPDT, LSTCONDT, ARFENDT
Treatment start date	TRTSDT

ADVS:

Variable name	Standard CDISC ADAM Terms
Analysis relative day	ADY

c. Treatment names from ADAE and ADSL

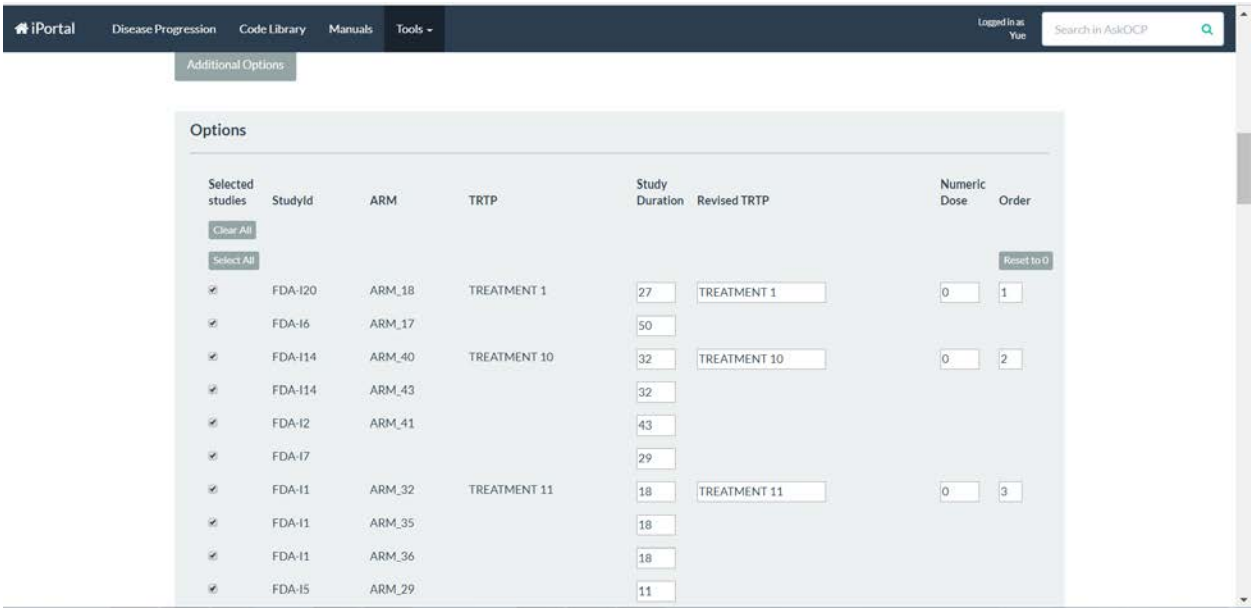
The treatment terms under the treatment variables in ADSL must match the terms under the treatment variable selected for ADAE, so that the two files can be merged. Some studies may have different treatments throughout the trial and the treatment names in the sequential periods are typical defined by TRT001A, TRT002A, TRT003A, etc., respectively in ADSL.

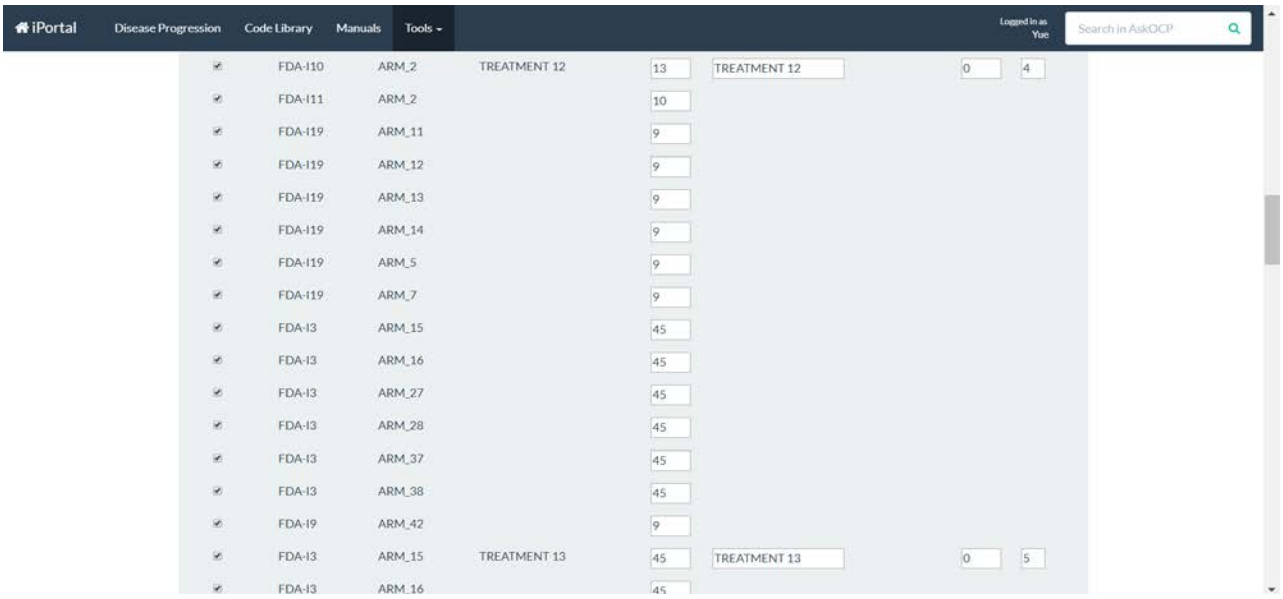


d. Study Pool

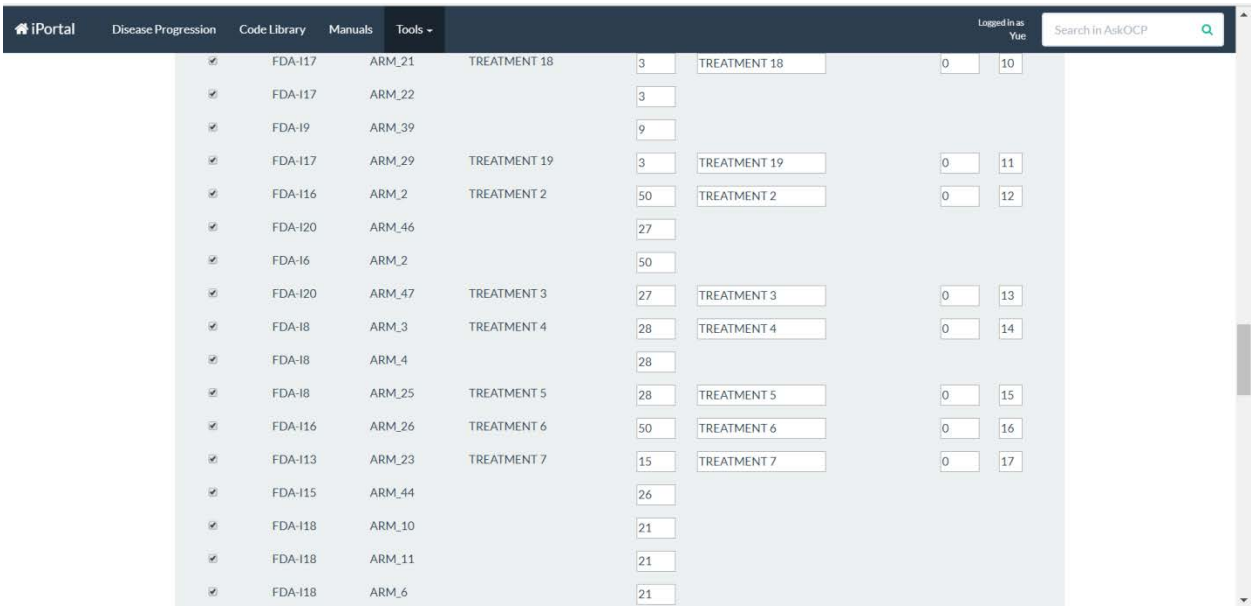
All treatments in all studies listed in the ISS datasets are automatically grouped and ranked by the dose level. For example, in the screen shots below, all treatments from various studies are grouped accordingly and ranked by the dose level. The user can select or deselect study and arm, or re-rank the dose level.

For special study designs with multiple treatments per ARM, such as titration, safety extension, cross over, or sequential studies, different treatment periods from different studies can be combined by specifying the combination of "Study Pool" described in this session and "Treatment names from ADAE and ADSL" described in the previous session.

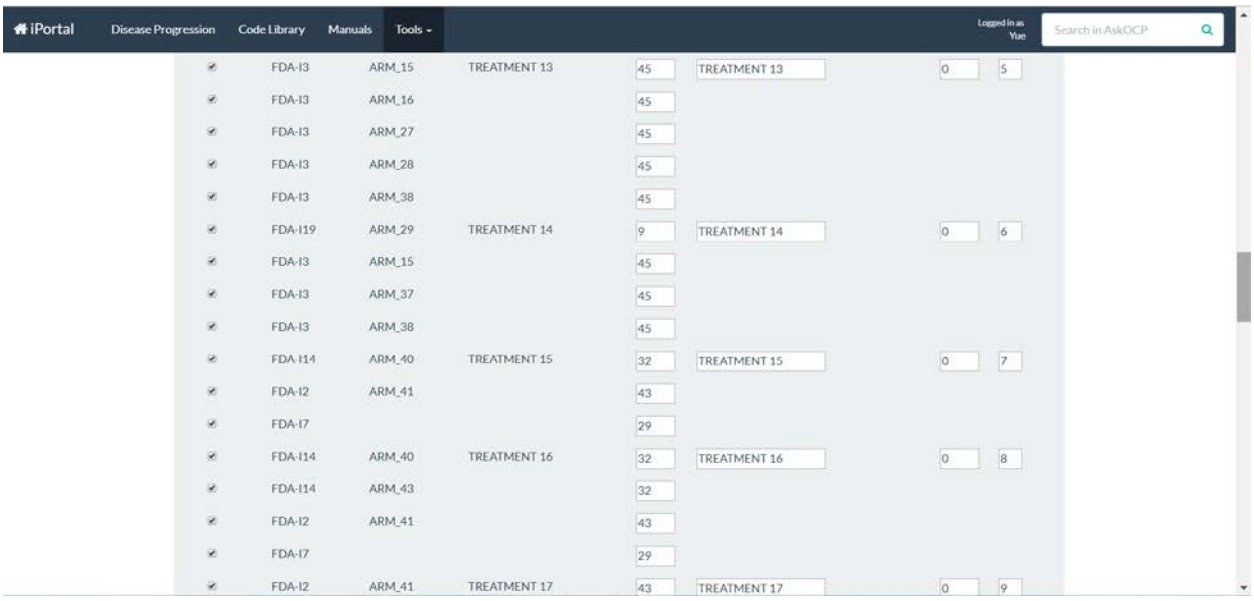




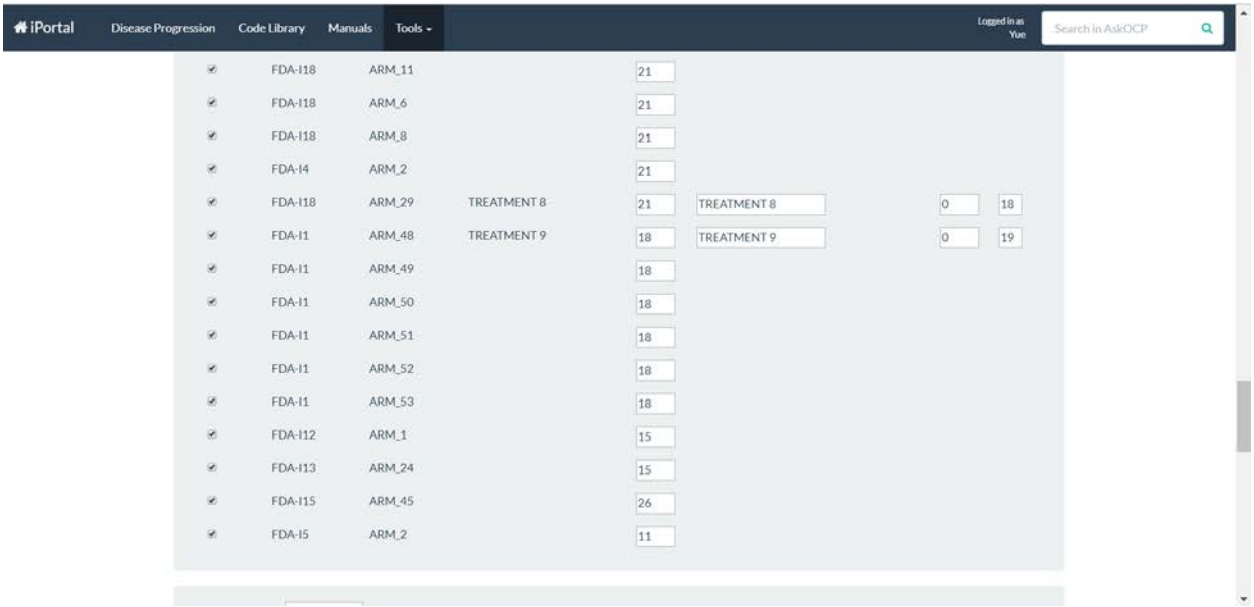
FDA-I10	ARM_2	TREATMENT 12	13	TREATMENT 12	0	4
FDA-I11	ARM_2		10			
FDA-I19	ARM_11		9			
FDA-I19	ARM_12		9			
FDA-I19	ARM_13		9			
FDA-I19	ARM_14		9			
FDA-I19	ARM_5		9			
FDA-I19	ARM_7		9			
FDA-I3	ARM_15		45			
FDA-I3	ARM_16		45			
FDA-I3	ARM_27		45			
FDA-I3	ARM_28		45			
FDA-I3	ARM_37		45			
FDA-I3	ARM_38		45			
FDA-I9	ARM_42		9			
FDA-I3	ARM_15	TREATMENT 13	45	TREATMENT 13	0	5
FDA-I3	ARM_16		45			



FDA-I17	ARM_21	TREATMENT 18	3	TREATMENT 18	0	10
FDA-I17	ARM_22		3			
FDA-I9	ARM_39		9			
FDA-I17	ARM_29	TREATMENT 19	3	TREATMENT 19	0	11
FDA-I16	ARM_2	TREATMENT 2	50	TREATMENT 2	0	12
FDA-I20	ARM_46		27			
FDA-I6	ARM_2		50			
FDA-I20	ARM_47	TREATMENT 3	27	TREATMENT 3	0	13
FDA-I8	ARM_3	TREATMENT 4	28	TREATMENT 4	0	14
FDA-I8	ARM_4		28			
FDA-I8	ARM_25	TREATMENT 5	28	TREATMENT 5	0	15
FDA-I16	ARM_26	TREATMENT 6	50	TREATMENT 6	0	16
FDA-I13	ARM_23	TREATMENT 7	15	TREATMENT 7	0	17
FDA-I15	ARM_44		26			
FDA-I18	ARM_10		21			
FDA-I18	ARM_11		21			
FDA-I18	ARM_6		21			



☑	FDA-I3	ARM_15	TREATMENT 13	45	TREATMENT 13	0	5
☑	FDA-I3	ARM_16		45			
☑	FDA-I3	ARM_27		45			
☑	FDA-I3	ARM_28		45			
☑	FDA-I3	ARM_38		45			
☑	FDA-I19	ARM_29	TREATMENT 14	9	TREATMENT 14	0	6
☑	FDA-I3	ARM_15		45			
☑	FDA-I3	ARM_37		45			
☑	FDA-I3	ARM_38		45			
☑	FDA-I14	ARM_40	TREATMENT 15	32	TREATMENT 15	0	7
☑	FDA-I2	ARM_41		43			
☑	FDA-I7			29			
☑	FDA-I14	ARM_40	TREATMENT 16	32	TREATMENT 16	0	8
☑	FDA-I14	ARM_43		32			
☑	FDA-I2	ARM_41		43			
☑	FDA-I7			29			
☑	FDA-I2	ARM_41	TREATMENT 17	43	TREATMENT 17	0	9



☑	FDA-I18	ARM_11		21			
☑	FDA-I18	ARM_6		21			
☑	FDA-I18	ARM_8		21			
☑	FDA-I4	ARM_2		21			
☑	FDA-I18	ARM_29	TREATMENT 8	21	TREATMENT 8	0	18
☑	FDA-I1	ARM_48	TREATMENT 9	18	TREATMENT 9	0	19
☑	FDA-I1	ARM_49		18			
☑	FDA-I1	ARM_50		18			
☑	FDA-I1	ARM_51		18			
☑	FDA-I1	ARM_52		18			
☑	FDA-I1	ARM_53		18			
☑	FDA-I12	ARM_1		15			
☑	FDA-I13	ARM_24		15			
☑	FDA-I15	ARM_45		26			
☑	FDA-I5	ARM_2		11			

e. Inclusion/Exclusion Criteria for Patient subset and AE of interest

Inclusion and exclusion criteria can be applied to narrow down patient subset or AE of interest. In the example below:

Patient subset

- Include only severity = moderate and severe
- Include only Age>40 y
- Exclude study = FDA-I1 and FDA-I10AE of interest