Single Day Phuse Event

Automation of the narrative section of the clinical study report for oncology studies

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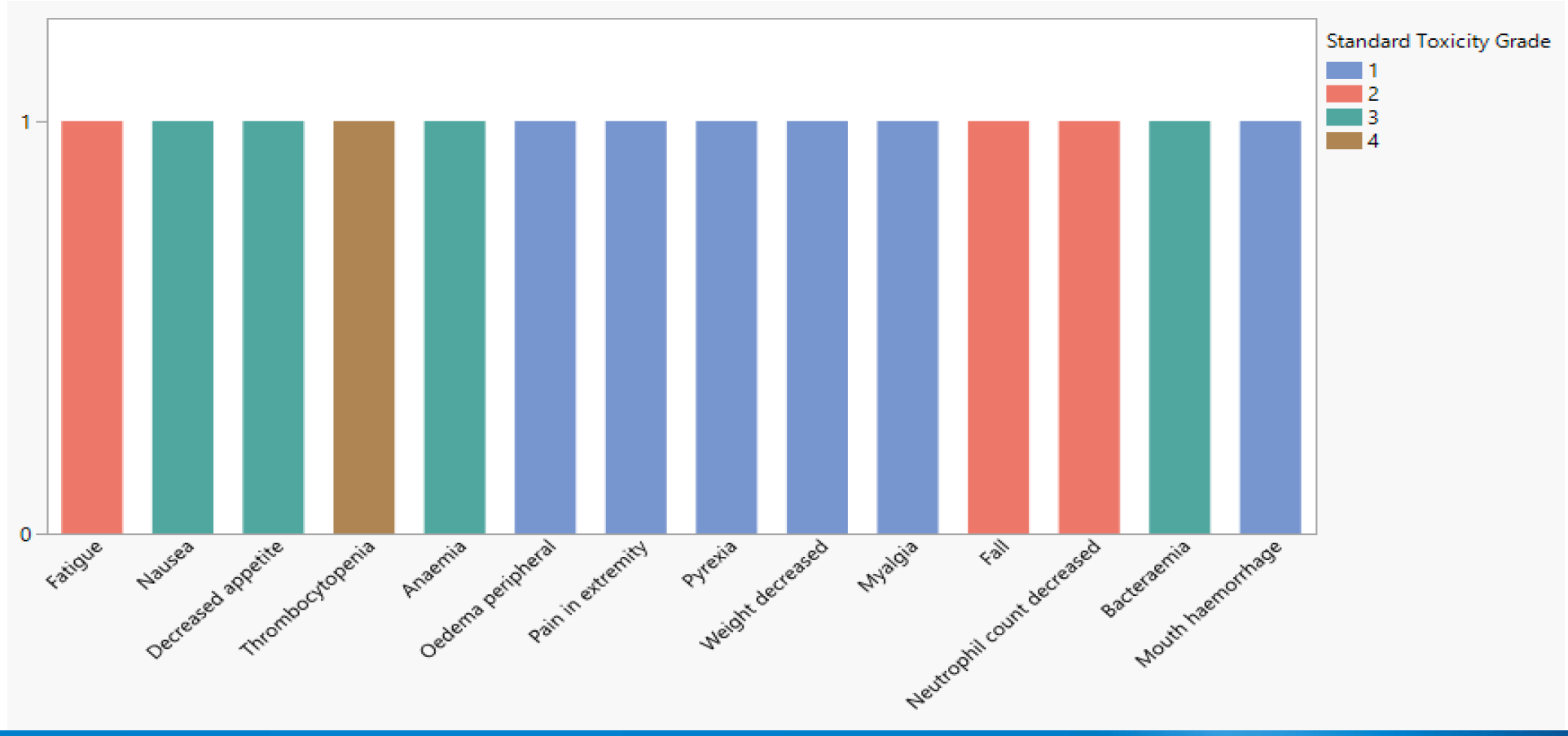
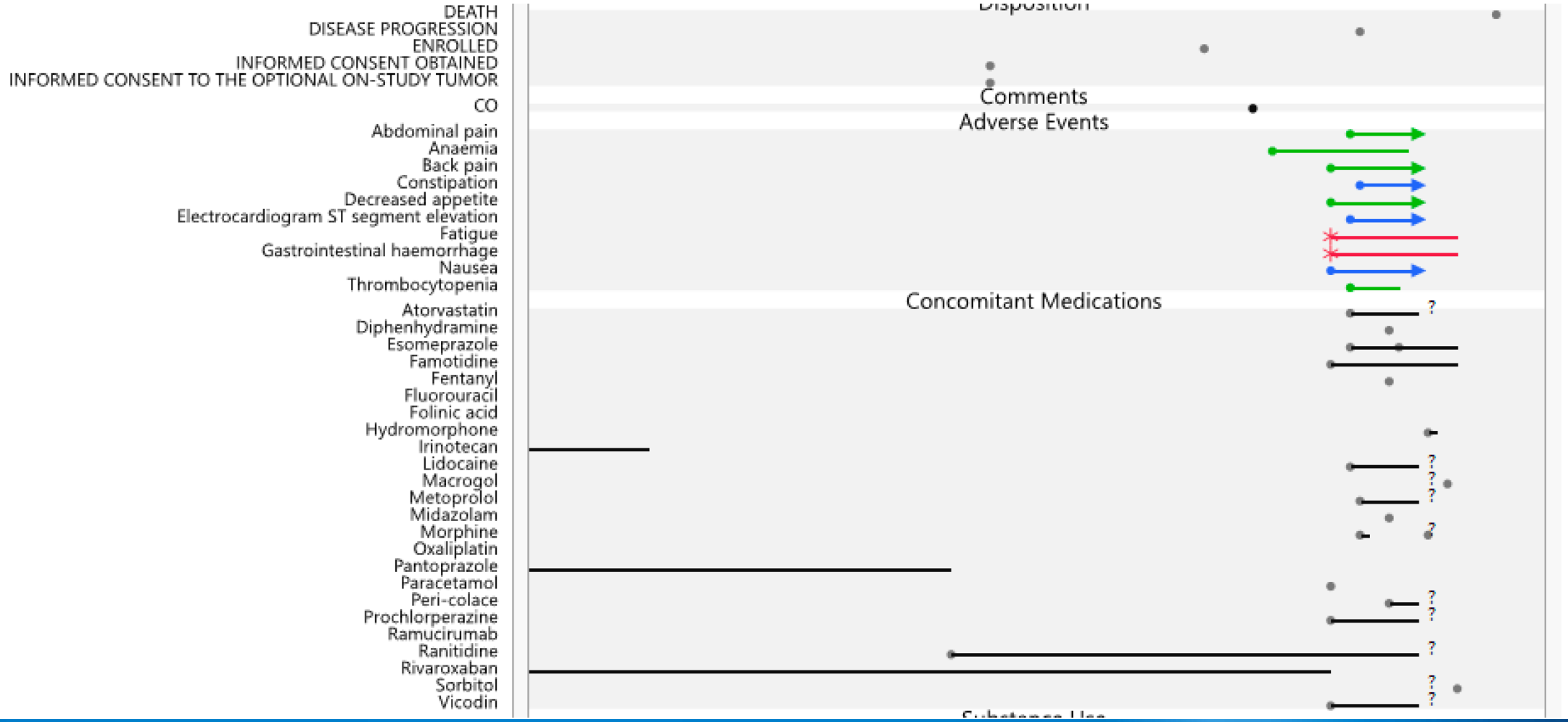
ONCOLOGY NARRATIVES

Oncology adverse event narratives are perhaps the most complicated narratives that a medical writer must deal with. The quantity and complexity of the study data associated with participants on these trials puts a high burden on the writer to be accurate, consistent and discerning as to which information to include for these individuals. Fortunately, software now allows the medical writer to choose from a variety of options as to which content to present as well as how the grammar for each adverse event is written within the paragraphs and tabulated data belonging to each participant. Once the medical writer has selected these options and modified a narrative template, software can generate the narratives for each participant in the trial in a matter of seconds.

THE COMPLEXITY OF AN ONCOLOGY PARTICIPANT



THE COMPLEXITY OF AN ONCOLOGY PARTICIPANT



REQUIREMENTS

ICHE3: Structure and Content of Clinical Study Reports

Clinical Data Interchange Standards Consortium (CDISC) implementation guidelines

- SDTM: Submission Data Tabulation Model
- ADAM: Analysis Data Model

Study Data Technical Conformance Guide from the Food and Drug Administration (FDA)

ICHE3 GUIDELINES

The nature and intensity of event

the clinical course leading up to event, with an indication of timing relevant to test drug/investigational product administration

relevant laboratory measurements

whether the drug was stopped, and when

countermeasures

post-mortem findings

investigator's opinion on causality and sponsor's opinion on causality, if appropriate

ICHE3 GUIDELINES

patient identifier

age and sex of patient; general clinical condition of patient, if appropriate

disease being treated (if this is the same for all patients, this information is not required) with duration (of current episode) of illness

relevant concomitant/previous illnesses with details of occurrence/duration

relevant concomitant/previous medication with details of dosage

test drug administered, including dose, if this varied among patients, and length of time administered

NARRATIVE SECTIONS OF THE CLINICAL STUDY REPORT

15.0 Participants with AEs table

15.1 TEAE with a fatal outcome

15.2 Serious TEAE

15.3 TEAE leading to study drug discontinuation

15.4 TEAE of special interest

CDISC DATA

2.5 The SDTM Standard Domain Models

The following standard domains, listed in alphabetical order by Domain Code, with their respective domain codes have been defined or referenced by the CDISC SDS Team in this document. Note that other domain models may be posted separately for comment after this publication.

Special-Purpose Domains (defined in *Section 5 – Models For Special-Purpose Domains*):

- Comments (CO)
- Demographics (DM)
- Subject Elements (SE)
- Subject Visits (SV)

Interventions General Observation Class (defined in *Section 6.1 - Interventions*):

- Concomitant Medications (CM)
- Exposure as Collected (EC)
- Exposure (EX)
- Substance Use (SU)
- Procedures (PR)

Events General Observation Class (defined in *Section 6.2 - Events*):

- Adverse Events (AE)
- Clinical Events (CE)
- Disposition (DS)
- Protocol Deviations (DV)
- Healthcare Encounters (HO)
- Medical History (MH)

Findings General Observation Class (defined in *Section 6.3 - Findings*):

- Drug Accountability (DA)
- Death Details (DD)
- ECG Test Results (EG)
- Inclusion/Exclusion Criterion Not Met (IE)
- Immunogenicity Specimen Assessments (IS)
- Laboratory Test Results (LB)
- Microbiology Specimen (MB)
- Microscopic Findings (MI)
- Morphology (MO)
- Microbiology Susceptibility Test (MS)
- PK Concentrations (PC)
- PK Parameters (PP)
- Physical Examination (PE)
- Questionnaires (QS)
- Reproductive System Findings (RP)
- Disease Response (RS)
- Subject Characteristics (SC)
- Subject Status (SS)
- Tumor Identification (TU)
- Tumor Results (TR)
- Vital Signs (VS)

Findings About (defined in *Section 6.4 - FA Domain*)

- Findings About (FA)
- Skin Response (SR)

CDISC DATA

Study Identifier	Domain Abbreviation	Unique Subject Identifier	Sequence Number	Lab Test or Examination ...	Lab Test or Examination Name	Result or Finding in Original Units	Original Units	Reference Range Lower Limit in ...
NICSAH1	LB	101001	1	ALP	Alkaline Phosphatase	57	U/L	40
NICSAH1	LB	101001	2	APTT	Activated Partial ...	22	sec	20
NICSAH1	LB	101001	38	APTT	Activated Partial ...	22	sec	20
NICSAH1	LB	101001	3	AST	Aspartate Aminotransferase	19	U/L	10
NICSAH1	LB	101001	4	BILI	Bilirubin	0.40000001	mg/dL	0.3
NICSAH1	LB	101001	5	BUN	Blood Urea Nitrogen	26	mg/dL	7
							mg/dL	7
							mg/dL	7
						9998	mg/dL	7
							U/L	15
							mEq/L	97
							mEq/L	97
							mEq/L	97
							mmol/L	23

Study Identifier	Domain Abbreviation	Unique Subject Identifier	Subject Identifier for ...	Subject Reference Start Date/Time	Subject Reference End Date/Time	Study Site Identifier	Investigator Identifier	Investigator Name	Date/Time of Bir
NICSAH1	DM	101001	101001	1988-01-21T17:15:00	1988-02-02T17:11:00	10	1A	101A	1924-03-02
NICSAH1	DM	101002	101002	1988-01-26T11:30:00	1988-02-05T12:00:00	10	1A	101A	1921-08-11
NICSAH1	DM	101003	101003	1988-01-26T15:10:00	1988-02-04T15:30:00	10	1A	101A	1956-08-03
NICSAH1	DM	101004	101004	1988-01-28T16:00:00	1988-01-28T16:33:00	10	1A	101A	1939-08-17
NICSAH1	DM	101005	101005	1988-04-05T14:45:00	1988-04-17T13:45:00	10	1A	101A	1920-11-14
NICSAH1	DM	101006	101006	1988-04-28T13:40:00	1988-05-08T14:00:00	10	1A	101A	1955-08-10
NICSAH1	DM	101007	101007	1988-06-25T11:05:00	1988-06-27T12:00:00	10	1A	101A	1925-05-29
NICSAH1	DM	101008							
NICSAH1	DM	101009							
NICSAH1	DM	101010							
NICSAH1	DM	101011							
NICSAH1	DM	101012							
NICSAH1	DM	101013							
NICSAH1	DM	101014							
NICSAH1	DM	101015							
NICSAH1	DM	101016							
NICSAH1	DM	101017							
NICSAH1	DM	11001							
NICSAH1	DM	11002							
NICSAH1	DM	11003							
NICSAH1	DM	11004							

Study Identifier	Domain Abbreviation	Unique Subject Identifier	Sequence Number	Reported Term for the Adverse Event	Dictionary-Derived Term	High Level Term	High Level Group Term	Body System or Organ Class
NICSAH1	AE	101001	1	Hydrocephalus	Hydrocephalus	Hydrocephalic ...	Increased intracranial ...	NERVOUS SYSTEM ...
NICSAH1	AE	101001	2	Pyrexia	Pyrexia	Febrile disorders	Body temperature ...	GENERAL DISORDERS AND ...
NICSAH1	AE	101001	3	Vasoconstriction	Vasoconstriction	Peripheral ...	Arteriosclerosis, ...	VASCULAR DISORDERS
NICSAH1	AE	101001	4	Vomiting	Vomiting	Nausea and ...	Gastrointestinal signs ...	GASTROINTESTINAL ...
NICSAH1	AE	101002	1	Alveolitis	Alveolitis	Lower ...	Lower respiratory tract ...	RESPIRATORY, THORACIC ...
NICSAH1	AE	101002	2	Hydrocephalus	Hydrocephalus	Hydrocephalic ...	Increased intracranial ...	NERVOUS SYSTEM ...
NICSAH1	AE	101002	3	Hyperglycaemia	Hyperglycaemia	Hyperglycaemic ...	Glucose metabolism ...	METABOLISM AND ...
NICSAH1	AE	101002	4	Pulmonary oedema	Pulmonary oedema	Left ventricular ...	Heart failures	RESPIRATORY, THORACIC ...
NICSAH1	AE	101002	5	Urinary tract infection	Urinary tract infection	Genitourinary ...	Genitourinary tract ...	INFECTIONS AND ...
NICSAH1	AE	101002	6	Vasoconstriction	Vasoconstriction	Peripheral ...	Arteriosclerosis, ...	VASCULAR DISORDERS
NICSAH1	AE	101002	7	Ventricular extrasystoles	Ventricular extrasystoles	Ventricular ...	Cardiac arrhythmias	CARDIAC DISORDERS
NICSAH1	AE	101004	1	Brain oedema	Brain oedema	Increased ...	Increased intracranial ...	NERVOUS SYSTEM ...
NICSAH1	AE	101004	2	Coma	Coma	Coma states	Neurological disorders ...	NERVOUS SYSTEM ...
NICSAH1	AE	101004	3	Hydrocephalus	Hydrocephalus	Hydrocephalic ...	Increased intracranial ...	NERVOUS SYSTEM ...
NICSAH1	AE	101004	4	Hyperglycaemia	Hyperglycaemia	Hyperglycaemic ...	Glucose metabolism ...	METABOLISM AND ...
NICSAH1	AE	101004	5	Hypotension	Hypotension	Vascular ...	Decreased and ...	VASCULAR DISORDERS
NICSAH1	AE	101004	6	Intracranial pressure increased	Intracranial pressure ...	Increased ...	Increased intracranial ...	NERVOUS SYSTEM ...
NICSAH1	AE	101004	7	Subarachnoid haemorrhage	Subarachnoid ...	Central nervous ...	Central nervous ...	NERVOUS SYSTEM ...
NICSAH1	AE	101004	8	Vasoconstriction	Vasoconstriction	Peripheral ...	Arteriosclerosis, ...	VASCULAR DISORDERS
NICSAH1	AE	101005	1	Alveolitis	Alveolitis	Lower ...	Lower respiratory tract ...	RESPIRATORY, THORACIC ...
NICSAH1	AE	101005	2	Anaemia	Anaemia	Anaemias NEC	Anaemias ...	BLOOD AND LYMPHATIC ...
NICSAH1	AE	101005	3	Heart rate increased	Heart rate increased	Heart rate and ...	Cardiac and vascular ...	INVESTIGATIONS
NICSAH1	AE	101005	4	Hydrocephalus	Hydrocephalus	Hydrocephalic ...	Increased intracranial ...	NERVOUS SYSTEM ...
NICSAH1	AE	101005	5	Hyperglycaemia	Hyperglycaemia	Hyperglycaemic ...	Glucose metabolism ...	METABOLISM AND ...

SUMMARIES

15. PARTICIPANT NARRATIVES

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Participant Number	Fatal TEAE	Other Serious TEAE	TEAE Leading to Study Drug Discontinuation	TEAE of Special Interest
101001			X	
101004		X	X	
101005		X	X	
101007		X	X	
101008			X	
101009			X	
101010		X	X	
101011			X	
101013		X		
101014	X	X	X	
101015	X			
101016	X			
101017	X			
11002		X	X	
11003		X		
11004		X		
11005	X	X		
11008		X	X	
11009		X		
11012		X		
11013		X		
11014		X		
11015	X	X	X	
11016			X	
11018		X		

NARRATIVE

15.1 TEAE with a fatal outcome

Participant Number	001
Arm	Treatment A
Diagnosis	Prostate cancer
Age	62 years
Sex	female
Race	white

Event Type	Preferred Term	Toxicity Grade	Relative Study Day
TEAE with a fatal outcome	septic shock	4	8
Serious TEAE	pleural effusion	3	8

Medical History	anaemia, hypertension, dyspnoea, anxiety, bronchitis chronic, and solid tumor
Baseline Disease Characteristics	Histopathology: None Current Stage: None MYC rearrangement status: None
Oncology Treatment History	Prior systemic therapy: None Number of prior regimens: None Prior radiotherapy: None Prior surgery: None
Prior Medications	None
Concomitant Medications	***uncoded medication****, alprazolam*, diphenhydramine, metoprolol tartrate*, prednisone

On Day 8 the participant experienced a septic shock (Grade 4) which was considered a serious adverse event (SAE). The event was considered serious for the following reasons: requires or prolongs hospitalization. At the time of the event, the participant had completed study medication. Trial medication had an action of drug interrupted as a result of the event. It is not known from the case report form if therapeutic measures were administered to treat the event. Adverse events that occurred within a +/- 3-day window of the onset of the SAE included alanine aminotransferase increased (Grade 1), anaemia (Grade 3), aspartate aminotransferase increased (Grade 1), haematuria (Grade 3), hepatic vein thrombosis (Grade 3), thrombocytopenia (Grade 1), thrombocytopenia (Grade 2), and thrombocytopenia (Grade 3). The investigator considered the AE to be not related to study medication. The event ended on (Day 25) with a final outcome of fatal.

NARRATIVE

15.2 Serious TEAE

Participant Number	40004
Treatment Group / Dose	TRTA / 5 mg
Diagnosis	Breast Cancer
Age	64 years
Sex	female
Race	hispanic

Event Type	Preferred Term	Toxicity Grade	Relative Study Day
Serious TEAE	vasoconstriction		58
Serious TEAE	hydrocephalus		58
Serious TEAE	intracranial pressure increased		58
Serious TEAE	hypotension		58
Serious TEAE	coma		30
Serious TEAE	subarachnoid haemorrhage		88

Medical History	headache associated with sah, and vomiting associated with sah
Baseline Disease Characteristics	Histopathology: None Current Stage: None MYC rearrangement status: None
Oncology Treatment History	Prior systemic therapy: None Number of prior regimens: None Prior radiotherapy: None Prior surgery: None
Prior Medications	None
Concomitant Medications	None

On Day 58 the participant experienced a vasoconstriction (severe) which was considered a serious adverse event (SAE). Though the event was considered serious, no reasons were provided on the case report form. The participant was on treatment when the event occurred. Trial medication had an action of drug withdrawn as a result of the event. It is not known from the case report form if therapeutic measures were administered to treat the event. Adverse events that occurred within a +/- 3-day window of the onset of the SAE included coma (severe), hydrocephalus (severe), hyperglycaemia (mild), hypotension (severe), and intracranial pressure increased (severe). The investigator considered the AE to be not related to study medication. The event ended on (Day 58) with a final outcome of recovered/resolved.

NARRATIVE

15.3 TEAE Leading to Study Drug Discontinuation

Participant Number	40050
Treatment Group / Dose	TRTA / 5 mg
Diagnosis	Prostate Cancer
Age	55 years
Sex	male
Race	white

Event Type	Preferred Term	Toxicity Grade	Relative Study Day
TEAE leading to Discontinuation	intestinal perforation		106

Medical History	focal deficit associated with sah, headache associated with sah, loss of consciousness associated with sah, other medical condition, vomiting associated with sah, and allergies
Baseline Disease Characteristics	Histopathology: None Current Stage: None MYC rearrangement status: None
Oncology Treatment History	Prior systemic therapy: None Number of prior regimens: None Prior radiotherapy: None Prior surgery: None
Prior Medications	None
Concomitant Medications	None

On Day 106 the participant experienced a intestinal perforation (moderate) which was an adverse event leading to study drug discontinuation. Though the event was considered serious, no reasons were provided on the case report form. At the time of the event, the participant had completed study medication. Trial medication had an action of not applicable as a result of the event. It is not known from the case report form if therapeutic measures were administered to treat the event. Adverse events that occurred within a +/- 3-day window of the onset of the SAE included vasoconstriction (moderate). The investigator considered the AE to be not related to study medication. The event ended on (Day 108) with a final outcome of recovered/resolved.

NARRATIVE

15.4 TEAE of Special Interest

Participant Number	40070
Treatment Group / Dose	TRTA / 5 mg
Diagnosis	Breast Cancer
Age	72 years
Sex	female
Race	hispanic

Event Type	Preferred Term	Toxicity Grade	Relative Study Day
TEAE of Special Interest	subarachnoid haemorrhage		177
TEAE of Special Interest	respiratory disorder		183

Medical History	headache associated with sah, and vomiting associated with sah
Baseline Disease Characteristics	Histopathology: None Current Stage: None MYC rearrangement status: None
Oncology Treatment History	Prior systemic therapy: None Number of prior regimens: None Prior radiotherapy: None Prior surgery: None
Prior Medications	None
Concomitant Medications	None

On Day 177 the participant experienced a subarachnoid haemorrhage (severe) which was considered a serious adverse event (SAE). Though the event was considered serious, no reasons were provided on the case report form. The participant was on treatment when the event occurred. Trial medication had an action of drug withdrawn as a result of the event. It is not known from the case report form if therapeutic measures were administered to treat the event. Adverse events that occurred within a +/- 3-day window of the onset of the SAE included cerebral infarction (severe), hypotension (moderate), intracranial pressure increased (severe), phlebitis (moderate), and pyrexia (moderate). The investigator considered the AE to be not related to study medication. The event ended on (Day 178) with a final outcome of not recovered/not resolved.

TABLES

Participant Number	001
Arm	Treatment A
Diagnosis	Prostate cancer
Age	46 year old
Sex	male
Race	white

Event Type	Preferred Term	Toxicity Grade	Relative Study Day
Serious TEAE	dyspnoea	3	53
Serious TEAE	pleural effusion	2	64
TEAE with a fatal outcome	dyspnoea	4	88
TEAE with a fatal outcome	hypoxia	4	88
TEAE with a fatal outcome	respiratory failure	4	88

Medical History	aortic stenosis, arthritis, solid tumor, and gastrooesophageal reflux disease
Baseline Disease Characteristics	Histopathology: None Current Stage: None MYC rearrangement status: None
Oncology Treatment History	Prior systemic therapy: None Number of prior regimens: None Prior radiotherapy: None Prior surgery: None
Prior Medications	None
Concomitant Medications	colecalciferol*, guaifenesin*

DEMOGRAPHICS TABLE

Participant Number	**$SUBJID = 001**
Arm	**$TRT01A = Treatment A**
Diagnosis	**$MHTERM when $MHCAT="CANCER HISTORY" = prostate cancer**
Age	**$AGE = 46**
Sex	**$SEX = male**
Race	**$RACE = caucasian**

USUBJID	Unique Subject Identifier	Char		Identifier	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product. This must be a unique number, and could be a compound identifier formed by concatenating STUDYID-SITEID-SUBJID.	Req
SUBJID	Subject Identifier for the Study	Char		Topic	Subject identifier, which must be unique within the study. Often the ID of the subject as recorded on a CRF.	Req

EVENTS TABLE

Event Type	Preferred Term	Toxicity Grade	Relative Study Day
TEAE leading to study drug discontinuation	**$AEDECOD** = “dyspnea”	**$AETOXGR** = “3”	$AESTDY = 2
Serious TEAE	**$AEDECOD** = “hypoxia”	**$AETOXGR** = “3”	$AESTDY = 4
AE of Special Interest	**$AEDECOD** = “pleural effusion”	**$AETOXGR** = “2”	$AESTDY = 7
TEAE with a fatal outcome	**$AEDECOD** = “cardiac arrest”	**$AETOXGR** = “4”	$AESTDY = 10
TEAE with a fatal outcome	**$AEDECOD** = “respiratory failure”	**$AETOXGR** = “4”	$AESTDY = 10

AETOXGR	Standard Toxicity Grade	Char	*	Record Qualifier	Toxicity grade according to a standard toxicity scale such as Common Terminology Criteria for Adverse Events v3.0 (CTCAE). Sponsor should specify name of the scale and version used in the metadata (see Assumption 6d). If value is from a numeric scale, represent only the number (e.g., “2” and not “Grade 2”).	Perm

MEDICAL HISTORY TABLES

Medical History	**$MHDECOD when $MHCAT = "GENERAL MEDICAL HISTORY"**
Baseline Disease Characteristics	Histopathology: **$FATEST, $FASCAT, $FAORRES** Current Stage: **$FATEST, $FASCAT, $FAORRES** MYC rearrangement status: **$FATEST, $FASCAT, $FAORRES**
Oncology Treatment History	Prior systemic therapy: **$CMDECOD when $CMCAT="PRIOR THERAPY"** Number of prior regimens: None Prior radiotherapy: **$CMDECOD when $CMCAT="PRIOR RADIOTHERAPY"** Prior surgery: **$CMDECOD when $CMCAT="PRIOR SURGERY"**
Prior Medications	**$CMDECOD when $CMCAT = "PRIOR"**
Concomitant Medications	**$CMDECOD when $CMCAT = "CONCOMITANT MEDICATION"**

PARAGRAPHS

Participant **$SUBJID** first received **$EXDOSE when $EXSTDY = “1”** of **$TRTXXA** on **$EXSTDY**, as participant of the **$TRTXXA**, and ended dosing with **$EXDOSE when $EXSTDY is the last day of treatment** of **$TRT01A** on .

On **$AESTDY** the participant experienced a **$AEDECOD** (**$AETOXGR**) which was considered a **$AESER = “Y”** (SAE). The event was considered serious for the following reasons: requires or prolongs hospitalization. On the day of the event, the participant did not take any drug. The SAE occurred 20 days after the first dose of any study medication. Trial medication had an action of **$AEACN** as a result of the event. Other action, unrelated to dose adjustments of study treatment, was not reported. Therapeutic measures administered to treat the event included **$CMDECOD**. No other AEs were recorded within a +/- 3-day window around the onset of the event. The investigator considered the AE to be **$AEREL** to study medication. The event ended on **$AEENDY** with a final outcome of **$AEOUT**.

REFERENCES

- http://drug-dev.com/patient-safety-narratives-clinical-trials-medical-writing-patient-safety-narratives/
- https://www.cognibrain.com/narrative-writing-in-clinical-research-guidelines-for-medical-writer/
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5384400/