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ADaM Design for Prostate Cancer Efficacy Endpoints Based on PCWG3

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ABSTRACT

Unlike other types of solid tumors that use the RECIST 1.1 [1] tumor response criteria, due to the particularity of prostate cancer, some common oncology efficacy endpoints, such as rPFS, ORR, time to response, and duration of response are usually based on the PCWG3 criteria [2]. Additionally, other specific prostate cancer endpoints like PSA response rate and time to PSA progression are also based on PCWG3, involving more complex data collection and derivation than RECIST 1.1.

In this paper, we will share efficacy endpoints in prostate cancer, such as PSA response and time to PSA progression. We will explain the ADaM design and data flow, and how to ensure traceability and data dependency in derivation. We successfully implemented programming for these complex endpoints, enhancing the speed and quality of effective analysis through the development of macros.

1. INTRODUCTION

There are many articles published on RECIST1.1 for solid tumors. However, for prostate cancer indication, there are limited available articles on PCWG3. CDISC issued the Therapeutic Area User Guide for Prostate Cancer (TAUG-PrCa v1.0) [3], but that is based on PCWG2. Given the complexity of data collection of prostate cancer indication, it is necessary to find a way to design ADaM based on PCWG3 to improve programming efficiency and quality.

Section 2 introduces PCWG3, specifically focusing on the BICR data collection of soft tissue per RECIST 1.1 and bone disease per PCWG3. This section also describes the derivation rule of overall timepoint response by integrating soft tissue and bone timepoint responses. Prostate-specific antigen (PSA) and symptomatic skeletal events (SSEs) are also briefly discussed in this section. Section 3 lists the details on efficacy endpoints based on PCWG3 with a focus on PSA-related endpoints and Blinded Independent Central Review (BICR)-related endpoints. Section 4 illustrates the corresponding efficacy ADaM datasets, including the ADaM data design, data dependency, and detailed description of each ADaM dataset with the purpose of the ADaM dataset and the data flow. In Section 4, detailed examples are provided to illustrate the clear data structure of each ADaM dataset design. Section 5 gives a brief explanation of programming standardization.

2. PCWG3 INTRODUCTION

The Prostate Cancer Clinical Trials Working Group 3 (PCWG3) is an international working group of clinical and translational experts in prostate cancer that convened in June 2012 and worked through February 2015 to update the recommendations of PCWG2 in light of a changing therapeutic landscape and advances in the understanding of disease biology. A synthesized document was developed and approved by all PCWG3 members.

Imaging provides critical information on disease distribution, tumor burden, and the response to the tumor. PCWG3 advises following RECIST 1.1 for extraskeletal disease but recommends that up to 5 lesions per site of metastatic spread. Also, bone lesions should be recorded separately with a quantitative measure of disease burden.

For BICR datasets, two independent readers review the imaging separately. Based on the discrepancy between two readers' results, such as the date of progression or the Best overall response (BOR), adjudication is triggered to favor one of the readers' evaluations. Imaging readers evaluate the soft tissue from target lesion measurement, the status of non-target lesions to evaluate the target lesion response, non-target lesion response, and with information on the presence of new lesions to derive the time point response. Meanwhile, the same readers also assess bone disease by PCWG3, such as identifying bone lesions at screening and whether there are new bone lesions post-treatment. Bone lesions will only be followed as non-target lesions at baseline and as new lesions on-study. The designation of non-target for bone lesions has a different connotation than the use of non-target for soft tissue disease. For instance, bone lesions will not be factored into the soft tissue evaluation but will only be assessed qualitatively. If

superscans are received at baseline, the subject will be considered Not Evaluable (NE) for all bone assessments and subsequent time points. For post-baseline superscans, subjects will be assessed as Progressive Disease (PD).

At each time point, the soft tissue and bone timepoint response will be integrated to determine the overall PCWG3 time point response (TPR), Overall response is assessed according to Table 1:

Table 1: Overall Time Point Response

Soft Tissue (RECIST 1.1) TPR	Bone Lesion (PCWG3) TPR	Overall PCWG TPR
PD	Any	PD
Any	PD	PD
NE	Non-PD, PDu, NED or NE	NE
NED	Non-PD	Non-CR/Non-PD
NED	PDu	PDu
NED	NED	NE
NED	NE	NE
SD	Non-PD, PDu, NED or NE	SD
Non-CR/Non-PD	Non-PD, PDu, NED or NE	Non-CR/Non-PD
PR	Non-PD, PDu, NED or NE	PR
CR	Non-PD, PDu, or NE	PR (1) Non-CR/Non-PD (2)
CR	NED	CR

* When no target and non-target lesions are identified at Baseline, and no new lesions are identified on-study, the response will No Evidence of Disease (NED).

** Progressive Disease Unconfirmed (PDu): Temporary marker of possible PD, at least two (2) new bone lesions are present, but an additional scan is required for confirmation. To be updated to PD or non-PD once a subsequent scan is available. If this is the final visit, the response remains as PDu.

(1) The overall TPR will be PR if target lesions were present at screening.

(2) The overall TPR will be Non-CR/Non-PD if no target lesions were present at screening.

The overall date of progression will also be reported and is defined as the TPR date of the first time point with an overall TPR of PD.

Best overall response (BOR) will be assessed by reviewing all time point response (TPR) prior to the assessment of PD. The best response of CR or PR needs to be confirmed by applying the TPR from two subsequent assessments.

PCWG3 advises reporting skeletal symptomatic events (SSEs) which include asymptomatic fractures. The evaluation of endpoints of SSEs, incorporating rPFS and clinical progression, can determine which endpoint may be most associated with clinical benefit and/or survival after treatment.

A rising PSA is typically the first sign of tumor regrowth, followed later by worsening disease observed through imaging and other clinical symptoms. PCWG3 recommends that PSA should be assessed in all trials in a central laboratory to minimize the variability.

3. EFFICACY ENDPOINTS BASED ON PCWG3

Like endpoints from other tumor types, endpoints for prostate cancer have two types. One type is categorical endpoints, which group the subjects as responders and non-responders. The benefit of experimental drug can be explained from the proportion of responders. Time-to-event endpoints such as rPFS, OS etc., are another common type of endpoint in oncology studies. Unique endpoints for prostate cancer indication include time to PSA progression, time to PSA response, duration of PSA response, and time to skeletal symptomatic event.

3.1 CATEGORICAL ENDPOINTS

ORR-PCWG3 (Objective Response Rate per PCWG3) is the proportion of participants who have a confirmed complete or partial best overall response (BOR) per PCWG3 among randomized participants who have measurable disease at baseline. The BOR is defined as the best response designation, recorded between the date of randomization and the date of objectively documented progression per PCWG3 or the date of subsequent systemic cancer therapy, whichever occurs first. For participants

without documented progression or subsequent systemic cancer therapy, all available response assessments will contribute to the BOR assessment.

PSA-RR (PSA Response Rate) is the proportion of randomized participants with a 50% or greater decrease in PSA from baseline to the lowest post-baseline PSA result. A second consecutive value obtained 3 or more weeks later is required to confirm the PSA response. PSA response will be calculated for all participants with PSA values at baseline and at least one post-baseline assessment.

3.2 TIME-TO-EVENT ENDPOINTS

rPFS (Radiographic Progression Free Survival) is the time between randomization and the first date of documented progression or death due to any cause, whichever occurs first. The radiographic progression will be assessed by Blinded Independent Central Review (BICR) per PCWG3. The rPFS will be censored at the last tumor assessment up to the start of subsequent systemic cancer therapy for those without progression.

TTR-PCWG3 (Time to Response per PCWG3) is the time from randomization to the date of the first documented CR or PR per PCWG3, as determined by BICR.

DOR-PCWG3 (Duration of Response per PCWG3) is the time between the date of first response (CR/PR per PCWG3) to the date of first documented radiographic progression per PCWG3, as determined by BICR, or death due to any cause. Participants who neither progress nor die will be censored at the last tumor assessment up to the start of subsequent systemic cancer therapy.

TTP-PSA (Time to PSA Progression) is the time between randomization to the date of PSA progression per PCWG3 in randomized participants. For participants with an initial PSA decline from baseline, the date of PSA progression is the date that an increase of 25% or more and an absolute increase of 2 ng/mL or more from the nadir are documented and confirmed by a second consecutive PSA value at least 3 weeks later. For participants with no PSA decline from baseline, the date of PSA progression is the date that an increase of 25% or more and an absolute increase of 2 ng/mL or more from baseline are documented beyond Week 13. TTP-PSA will be censored at the date of last PSA evaluation prior to the start of subsequent systemic cancer therapy. The time will be censored at the date of randomization for participants with no post-baseline PSA evaluation.

TTR-PSA (Time to PSA response) is defined for PSA responders as the time from randomization to the date of the first PSA response.

DOR-PSA (Duration of PSA response) is defined for PSA responders as the time between the date of first response and the date of PSA progression. Participants who neither progress by PSA nor die will be censored on the date of last PSA evaluation.

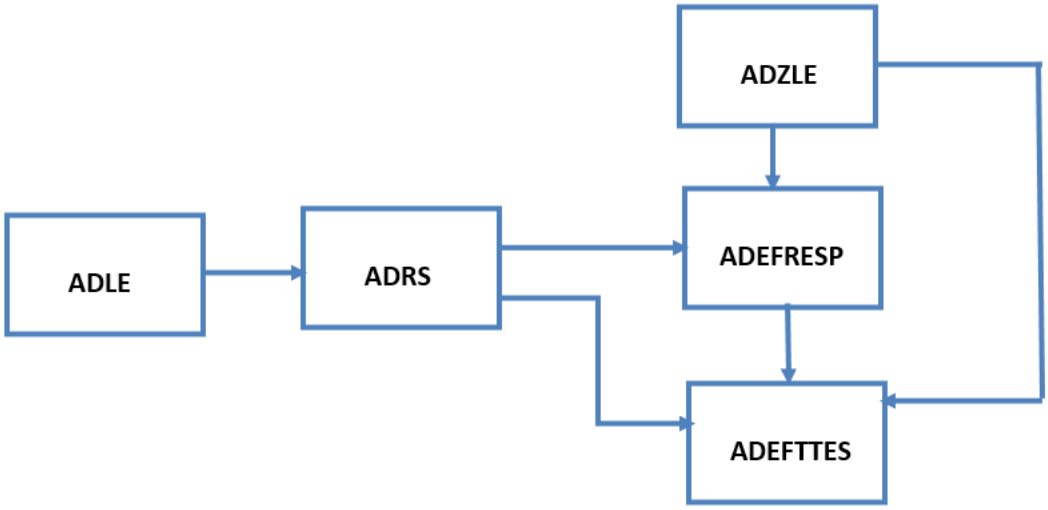
TT-SSE (Time to Skeletal Symptomatic Event) is the time between randomization and the date of first symptomatic fracture, radiation or surgery to bone, or spinal cord compression. Participants without skeletal symptomatic events will be censored at the date of the last SSE assessment by the investigator.

4. ADAM FOR EFFICACY ANALYSES BASED ON PCWG3

4.1 OVERVIEW OF ADAM EFFICACY DATASETS

The input data to drive the PCWG3 efficacy endpoints include the standard SDTM domains such as TU, TR, and RS, as well as additional domains like FAPR, ZL, CE and FACE. Following the CDISC/BMS Oncology ADaM standard, there are five ADaM efficacy datasets used to support efficacy analyses based on PCWG3: ADLE, ADRS, ADZLE, ADEFRESP, and ADEFTTES.

The diagram below shows the derivation order to create the five datasets after SDTM and ADCORE are available. It also illustrates the data dependencies among the five datasets.



All five datasets utilize the ADaM basic data structure (BDS). ADLE and ADZLE are organized as by-visit data, while ADRS and ADEFRESP consist of summary data at the subject level. Additionally, ADEFTTES comprises time-to-event (TTE) data.

- **ADLE:** The dataset contains tumor and bone evaluation data at both baseline and post-baseline time points. The parameter represents lesion codes, indicating whether it is a tumor or bone lesion. The data reference domains for ADLE include SDTM.TR (Tumor Results), SDTM.TU (Tumor Identification), SDTM.SUPPTU, and SDTM.FAPR (Findings About Procedures). Additionally, the dataset includes reference diameters of new lesions.
- **ADZLE:** The dataset contains data related to prostate-specific antigen (PSA), including flags indicating assessments at baseline, post-baseline, or post-baseline after 12 weeks to support PSA analysis. Additionally, it includes information on baseline results, change from baseline, percent change from baseline, and whether there was a decline from baseline. Maximum decrease from baseline results is flagged by a dedicated variable (MDBPSAFL). Nadir value, change, and percent change from nadir are also provided. The dataset also includes data related to progression, including unconfirmed (PSAUPRFL) and confirmed (PSACPRFL), and response: confirmed (PSACRFL) and unconfirmed (PSAUCRFL). ADZLE supports the analysis of time to PSA progression, time to and duration of PSA response, which are efficacy endpoints.
- **ADRS:** The dataset contains one record per subject per parameter per evaluator. Parameters in ADRS support the analysis of the best overall response per Investigator as well as per BICR. Additionally, it includes information about tumor assessment dates, such as the last tumor/bone assessment date up to subsequent therapy, the last tumor/bone assessment prior to an event, and the last tumor/bone assessment and response dates (partial response, complete response, first response). Baseline tumor/bone assessments are marked by dedicated variables. ADRS also contains anti-cancer therapy dates and radiographic progression dates. The analysis of the earliest anti-cancer subsequent therapy is used in censoring for primary efficacy endpoints such as the primary definition of rPFS and sensitivity analysis of rPFS, irrespective of missing tumor assessments. This date is also used in derivations related to secondary efficacy endpoints, such as the derivation of best overall response (BOR), which is necessary to calculate objective response rate (ORR), and time to and duration of response per PCWG3 and time to PSA progression (TTP-PSA).
- **ADEFRESP:** The dataset contains one record per subject per parameter. Parameters in this dataset support the analysis of subject response and include information about the best overall response per Investigator and per BICR, as well as PSA response per Investigator. Additionally, the ADEFRESP dataset includes dates of the first response, first PSA confirmed response, partial response, complete response, and reasons why response assessment was not performed.

Parameters per BICR include results only from the accepted radiologists. The data reference for ADEFRESP is ADRS and ADZLE.

- **ADEFTTES:** The ADEFTTES dataset contains one record per subject per parameter. It includes parameters to support time-to-event analysis of rPFS per BICR and per Investigator, as well as the currentness of follow-up for rPFS per BICR and per Investigator, and the extent of follow-up. Additionally, ADEFTTES includes time-to-objective response per Investigator and per BICR, time to PSA response and PSA progression, duration of PSA response, and time to Skeletal Symptomatic Event.

4.2 ADLE, ADRS AND ADZLE DESIGN

The preparation work for categorical and time-to-event efficacy endpoint derivation starts with ADLE, ADRS, and ADZLE datasets. Below, examples will demonstrate how the information is collected and used as the foundation for efficacy endpoints.

- **ADLE:** Table 2 represents the structure of ADLE dataset. PARAMCDs are assigned based on lesion types, with numbering to make each record unique. In general, "T#" and "NT#" represent target and non-target lesions of soft issues. "N#" refers to new lesions that are only available at post-baseline. The letter "P" indicates bone lesions from bone scans. PARCAT1, LETYPE, and METHOD are also included in the data for grouping or providing supplemental information. TUMSTATE shows the tumor status of each lesion across assessment visits.

Table 2. ADLE - Dummy Records sourced from BICR

USUBJID	AVISIT	PARAMCD	PARCAT1	AVAL	LETYPE	METHOD	TUMSTATE
bms-001	SCREENING	NT01	Soft Tissue per BICR		NON-TARGET	CT SCAN	PRESENT
bms-001	SCREENING	NT02	Soft Tissue per BICR		NON-TARGET	CT SCAN	PRESENT
bms-001	SCREENING	PNT01	Bone per BICR		NON-TARGET	BONE SCAN	PRESENT
bms-001	SCREENING	PNT02	Bone per BICR		NON-TARGET	BONE SCAN	PRESENT
bms-001	SCREENING	T01	Soft Tissue per BICR	15	TARGET	CT SCAN	PRESENT
bms-001	SCREENING	T02	Soft Tissue per BICR	18	TARGET	CT SCAN	PRESENT
bms-001	WEEK 9	NT01	Soft Tissue per BICR		NON-TARGET	CT SCAN	PRESENT
bms-001	WEEK 9	NT02	Soft Tissue per BICR		NON-TARGET	CT SCAN	ABSENT
bms-001	WEEK 9	PN01	Bone per BICR		NEW	BONE SCAN	PRESENT
bms-001	WEEK 9	PNT01	Bone per BICR		NON-TARGET	BONE SCAN	PRESENT
bms-001	WEEK 9	PNT02	Bone per BICR		NON-TARGET	BONE SCAN	PRESENT
bms-001	WEEK 9	T01	Soft Tissue per BICR	10	TARGET	CT SCAN	PRESENT
bms-001	WEEK 9	T02	Soft Tissue per BICR	9	TARGET	CT SCAN	ABSENT

- **ADRS:** Corresponding overall response records of ADLE are displayed below in ADRS (Table 3) for both BICR and Investigator. EVAL and EVALID uniquely identify the source of evaluators. Besides overall responses, a few key dates and flags are included in ADRS for forthcoming time-to-event derivation. However, these details are not presented in below example due to space limitations. The additional information comprises:

  a. Date of partial, complete, and first response.
  b. Date of progression.
  c. Date related to subsequent anti-cancer therapy, including systemic therapy, radiotherapy, and surgery.
  d. Date of the last tumor/bone lesion assessment with subsequent therapy.
  e. Date of the last tumor/bone lesion assessment without subsequent therapy.
  f. Date of the last tumor/bone lesion assessment prior to an event.
  g. Baseline flags for tumor and bone lesion assessments.
  h. Subsequent anti-cancer therapy flags.

Table 3. ADRS - Dummy Records

USUBJID	EVAL	EVALID	PARAMCD	PARAM	AVAL	AVALC	ACPTFL
bms-001	INDEPENDENT ASSESSOR	RADIOLOGIST 1	BORIRC	Best Overall Response per BICR	2	PR	Y
bms-001	INDEPENDENT	RADIOLOGIST 2	BORIRC	Best Overall	2	PR	

USUBJID	EVAL	EVALID	PARAMCD	PARAM	AVAL	AVALC	ACPTFL
	ASSESSOR			Response per BICR			
bms-001	INVESTIGATOR		BORINV	Best Overall Response per Investigator	3	SD	

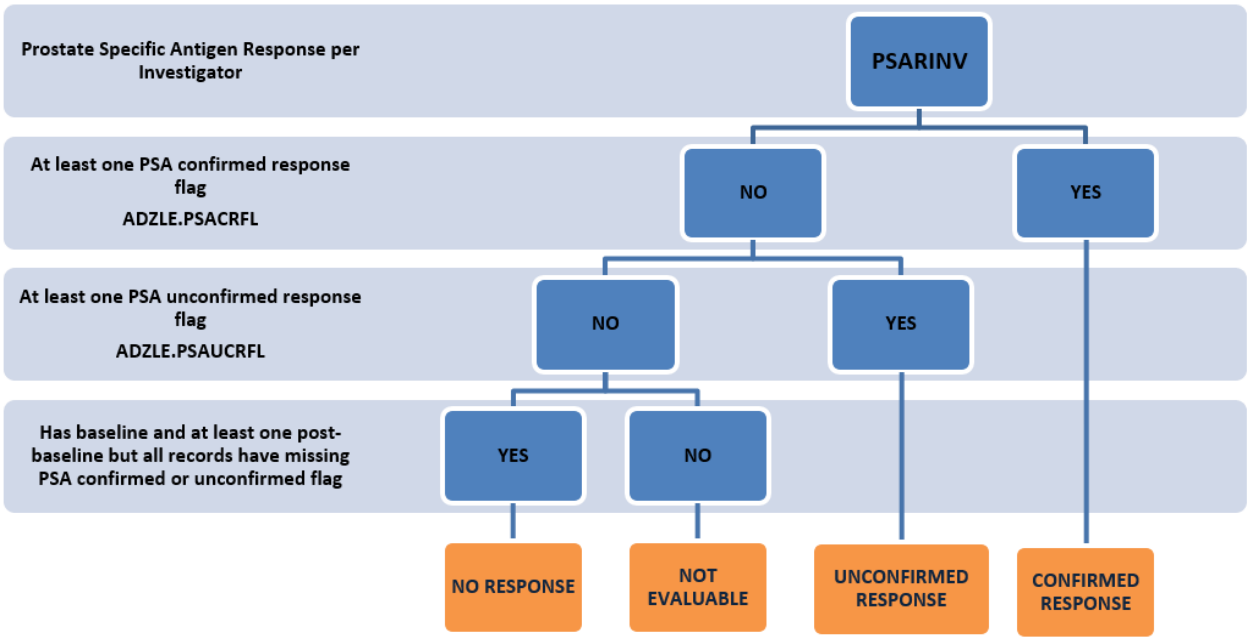
- **ADZLE:** this dataset lists lab values of prostate-specific antigen (PSA) for each visit, along with calculations for BASE, CHG, and PCHG. Additionally, specific flags are derived to determine the PSA responses, as shown in the example of ADEFRESP:
  a. PSAEVFL: Baseline and post-baseline PSA subject flag
  b. MDBPSAFL: Max decrease from baseline in PSA flag
  c. PSADECFL: PSA decline from baseline flag
  d. PSAUPRFL: PSA unconfirmed progression flag
  e. PSACPRFL: PSA confirmed progression flag
  f. PSAURFL: Record qualified for PSA response flag
  g. PSACRFL: PSA confirmed response flag
  h. PSAUCRFL: PSA unconfirmed response flag

Table 4. ADZLE - Dummy Records

USUBJID	APHASE	ADT	PARAMCD	AVAL	SSTHERDT	PSAEVF	PSACRFL	PSAUCRFL	PSACPRFL
bms-001	SCREENING	2021-10-22	PSAG	2030		Y			
bms-001	POST-BASELINE	2021-11-09	PSAG	979		Y	Y	Y	
bms-001	POST-BASELINE	2021-11-30	PSAG	152		Y	Y	Y	
bms-001	POST-BASELINE	2021-12-21	PSAG	64.3		Y	Y	Y	
bms-001	POST-BASELINE	2022-01-11	PSAG	39.6		Y	Y	Y	
bms-004	SCREENING	2022-04-28	PSAG	187.0	2022-12-02	Y			
bms-004	POST-BASELINE	2022-05-17	PSAG	202.7	2022-12-02	Y			
bms-004	POST-BASELINE	2022-06-07	PSAG	177.8	2022-12-02	Y			
bms-004	POST-BASELINE	2022-06-27	PSAG	176.9	2022-12-02	Y			
bms-004	POST-BASELINE	2022-07-19	PSAG	142.7	2022-12-02	Y			
bms-004	POST-BASELINE	2022-09-07	PSAG	249.9	2022-12-02	Y			Y
bms-004	POST-BASELINE	2022-10-05	PSAG	463.1	2022-12-02	Y			Y

4.3 ADEFRESP DESIGN FOR CATEGORICAL ENDPOINTS

ADEFRESP displays the results of categorical endpoints, such as best overall response (BOR) per BICR and the investigator. When acceptance flag ACPTFL in ADRS equals “Y”, the record is pulled to ADEFRESP as final BOR per BICR. Meanwhile, the investigator’s BOR is directly sourced from ADRS. The PSA response per investigator is derived based on prostate-specific antigen values located in the ADZLE dataset. Categorical values for PSA response include confirmed response, unconfirmed response, no response, and not evaluable. The algorithm developed to determine PSA response is displayed in the following chart:



The first response date (FRDT) is shown in the ADEFRESP sample table (Table 5). FRDT is defined as the time point response date when the criteria for CR or PR were first met, for participants whose BOR is either a CR or a PR. The FRDT may not be the same as the date of best response. The objective response rate (ORR) does not have a PARAMCD in ADEFRESP, as the corresponding derivation is completed in its output program.

Table 5. ADEFRESP - Dummy Records

USUBJID	PARAMCD	PARCAT1	AVAL	AVALC	FRDT
bms-001	BORINV	Best Overall Response per Investigator	3	SD	
bms-001	BORIRC	Best Overall Response per BICR	2	PR	2021-12-21
bms-001	PSARINV	Prostate Specific Antigen Response per Investigator	1	CONFIRMED RESPONSE	2021-11-09
bms-004	BORINV	Best Overall Response per Investigator	5	UTD	
bms-004	BORIRC	Best Overall Response per BICR	3	SD	
bms-004	PSARINV	Prostate Specific Antigen Response per Investigator	3	NO RESPONSE	

4.4 ADEFTTES DESIGN FOR TIME-TO-EVENT ENDPOINTS

ADEFTTES contains all time-to-event data. Some time-to-event parameters are summarized below to present the types of endpoints calculated in this dataset. As the preparation of certain key information has already been done in above domains, derivation would be much easier by pulling the necessary dates and flags from the corresponding data and performing the derivation.

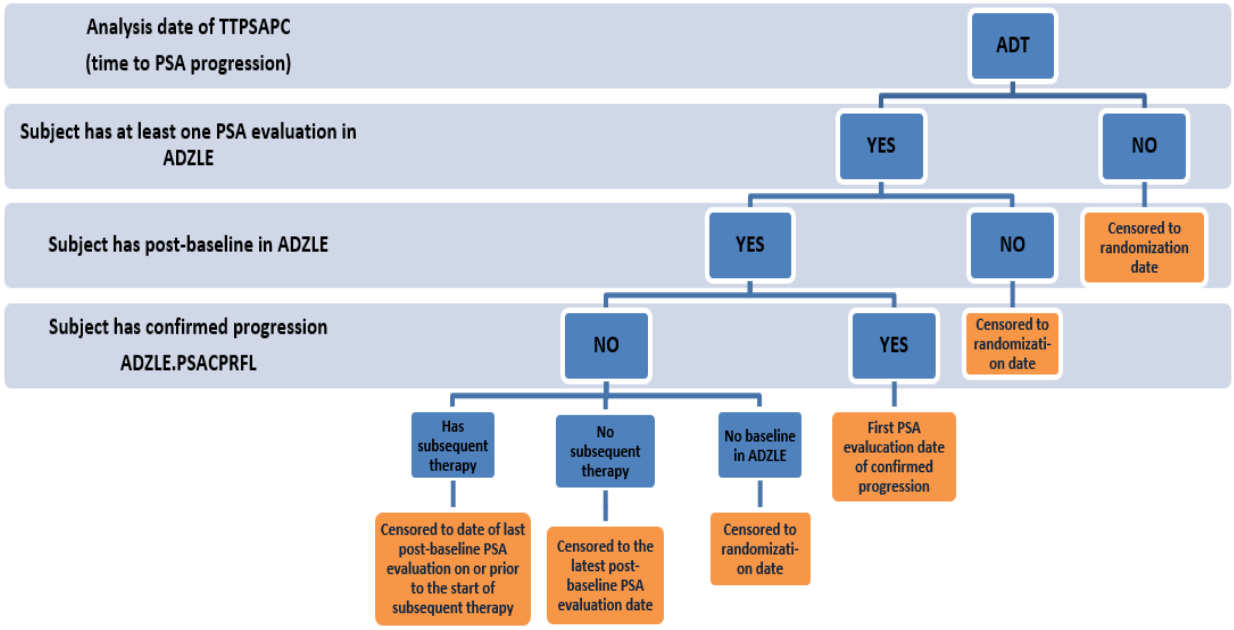
Table 6. Summary of Time-To-Event Parameters in ADEFTTES

PARAMCD	PARAM
DORINV	Duration of Objective Response per Investigator (months)
DORIRC	Duration of Objective Response per BICR (months)
DORPSA	**Duration of PSA Response (months)**
PSFINV	Progression Free Survival (Investigator) Primary (months)
PFSINV2	Progression Free Survival (Investigator) Secondary Definition: Irrespective of Subsequent Therapy (months)
PFSINV2S	Progression Free Survival (Inv) Secondary Definition, Irrespective of Subsequent Therapy and Sensitivity Analyses: Irrespepective of Missing Tumor Assessments (months)
PFSIRC	Progression Free Survival (BICR) Primary (months)
PFSIRC2	Progression Free Survival (BICR) Secondary Definition: Irrespective of Subsequent Therapy (months)
PFSIRC2S	Progression Free Survival (BICR) Secondary Definition, Sensitivity Analyses: Irrespective of Subsequent Therapy and Irrespepective of Missing Tumor Assessments (months)
PFSIRCS	Progression Free Survival (BICR) Primary Definition, Sensitivity Analyses: Irrespepective of Missing Tumor Assessments (months)
TTRINV	Time to Objective Response per Investigator (months)
TTRIRC	Time to Objective Response per BICR (months)

PARAMCD	PARAM
TTPSAPC	Time to PSA Progression (months)
TTRPSA	Time to PSA Response (months)
TTSSE	Time to First Skeletal Symptomatic Event (months)

To represent the PCWG3 efficacy endpoints, we are focusing on PSA and skeletal symptomatic events (SSEs) in the sections below. PSA endpoints include TTPSAPC (Time to PSA Progression), TTRPSA (Time to PSA Response), and DORPSA (Duration of PSA Response). Meanwhile, TTSSE (Time to Skeletal Symptomatic Event) contains the skeletal symptomatic event endpoint.

- **TTPSAPC:** This parameter refers to time to PSA progression. The detailed algorithm to derive ADT presented below:



- **TTRPSA:** To derive time to PSA response, known as TTRPSA, ADT is sourced from ADEFRESP.FRDT (Date of First Response) when PARAMCD is set to “PSARINV” (Prostate-Specific Antigen Response per Investigator), refer to above Table 5 of ADEFRESP for an example. CNSR is set to “0” as censoring is not applicable for this endpoint.
- **DORPSA:** The start date (STARTDT) for duration of PSA response equals the PSA response occur date (where ADEFTTES.ADT corresponds to PARAMCD = ”TTRPSA”). CNSR and ADT are set to ADEFTTES.CNSR where PARAMCD = ”TTPSAPC” and AVAL is not missing.

Table 7a. ADEFTTES - Dummy Records of PSA-Related Endpoints

USUBJID	PARAMCD	PARAM	STARTDT	AVAL	CNSR	ADT
bms-001	TTRPSA	Time to PSA Response (months)	2021-10-19	0.72	0	2021-11-09
bms-001	DORPSA	Duration of PSA Response (months)	2021-11-09	15.67	1	2023-02-28
bms-001	TTPSAPC	Time to PSA Progression (months)	2021-10-19	16.4	1	2023-02-28
bms-004	TTPSAPC	Time to PSA Progression (months)	2022-04-25	4.47	0	2022-09-07

- **TTSSE:** TTSSE stands for time to first skeletal symptomatic event in months. The ADT is sourced from the earliest CEDTC in SDTM.CE (Table 8) where the subject has an SSE event (when CECAT = ”SYMPTOMATIC SKELETAL EVENT” and CE.CEOCCUR = ”Y”). If the subject does not have skeletal symptomatic event but has one or more skeletal symptomatic assessments, the ADT is censored to the latest non-missing FACE.FADTC with FACE.FATESTCD = ”OCCUR”, which is considered as the latest skeletal symptomatic assessment date (Table 9). Otherwise, the ADT is censored to the randomization date.

Table 8. SDTM.CE - Dummy Records of SSE

USUBJID	CECAT	CECERM	CEOCCUR	VISIT	CEDTC
bms-002	SYMPTOMATIC SKELETAL EVENT	SURGERY TO BONE	Y	C3D1	2022-03-28
bms-002	SYMPTOMATIC SKELETAL EVENT	SYMPTOMATIC PATHOLOGIC FRACTURE	Y	C3D1	2022-03-28
bms-002	SYMPTOMATIC SKELETAL EVENT	RADIOTHERAPY TO BONE	Y	SFU	2023-03-19

Table 9. SDTM.FACE - Dummy Records of SSE Assessment

USUBJID	FATESTCD	FAOBJ	FAORRES	FADTC
bms-003	OCCUR	NEW SYMTOMATIC SKELETAL EVENT	NO	2022-09-15
bms-003	OCCUR	NEW SYMTOMATIC SKELETAL EVENT	NO	2022-10-26
bms-003	OCCUR	NEW SYMTOMATIC SKELETAL EVENT	NO	2022-12-22
bms-003	OCCUR	NEW SYMTOMATIC SKELETAL EVENT	NO	2023-03-01

Table 7b. ADEFTTES - Dummy records of TTSSE

USUBJID	PARAMCD	PARAM	STARTDT	AVAL	CNSR	ADT
bms-002	TTSSE	Time to First Skeletal Symptomatic Event (months)	2022-02-14	1.41	0	2022-03-28
bms-003	TTSSE	Time to First Skeletal Symptomatic Event (months)	2022-03-31	11.03	1	2023-03-01

5. ADAM PROGRAMMING STANDARDIZATION

BMS has a company-Oncology therapeutic area (TA) level ADaM specifications in place. Based on the guidance of CDSIC ADaMIG v1.1 [4] and Oncology Core ADaM specifications, we are able to develop and use global vs. Oncology TA macros to ensure that analysis datasets are standardized from various types of data.

5.1 MACROS OF RECIST 1.1 AND PCWG3 RELATED ENDPOINTS

Oncology TA level macros play a crucial role in supporting statistical programming for generating various efficacy measurements. These macros include, but are not limited to:

- Creating the ADLE dataset from TU/TR along with their supplemental domains from the SDTM level, ensuring inclusion of all necessary analysis variables.
- Populating flags and key assessment dates in ADRS, which is sourced different analysis datasets.
- Deriving time-to-event parameters such as PFS and DOR in ADEFTTES dataset.

As the PCWG3 criteria are limited to prostate cancer indication, BMS programming team has developed study level macros to facilitate the creation of ADZLE data and its key flags within the dataset. These efforts contribute significantly to efficient and accurate data processing.

6. CONCLUSION

This paper discusses the ADaM data design for prostate cancer indication based on PCWG3 guidance. Considering the complexity of data collection, such as integrating soft tissue and bone disease to derive the overall time point response, deriving PSA-related endpoints, and determining time to SSEs, key endpoints are created in efficacy ADaM datasets with programming efficiency and quality.

With the implementation of this ADaM data structure, we successfully enable traceability and streamline the development of efficacy ADaM datasets for prostate cancer indication. The corresponding outputs can be easily created from these ADaM datasets and fulfill the needs of easy review.

7. REFERENCES

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[4] CDISC Analysis Data Model Implementation Guide version v1.1 https://www.cdisc.org

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