PIONEER Core Outcome Sets (COSs)

The public-private consortium PIONEER updates and integrates Core Outcome Sets for Localised, Locally Advanced, Metastatic, and Nonmetastatic Castration-resistant Prostate Cancer (PCa)

The five experts Mieke Van Hemelrijck, Jihong Zong, Katharina Beyer, Lisa Moris, and Michael Lardas give an insight into their work and explain what COSs are, why they are important, which stakeholders have been involved in their development, and how are they going to be used.

First of all, please briefly introduce yourselves and your role in the work on the Core Outcome Sets?

Mieke Van Hemelrijck: *"I am a Professor in Cancer Epidemiology at King's College London and also lead of the Guy's Cancer Real World Evidence Programme. In PIONEER, I am the academic lead for WP2. This means that I had the pleasure to oversee a fantastic multidisciplinary team of researchers across Europe who have done an outstanding job in defining the COS for prostate cancer as well as a tool to assess diagnostic and prognostic factors for prostate cancer."*

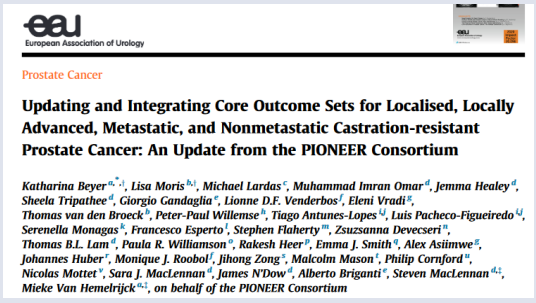
Jihong Zong: *"I am a physician epidemiologist within the Real-World Evidence group in the Global Medical Affairs Oncology department at Bayer. In PIONEER, I am the EFPIA lead and co-lead with our public partner King's College London for Work Package 2 (WP2)."*

Katharina Beyer: *"I am working as the Research Associate under Mieke Van Hemelrijck for WP2 of the PIONEER project where we developed a core outcome set of clinically relevant standardised prostate cancer-related outcomes and prognostic and diagnostic factors. We have finalised the work around the development of the core outcome sets and are currently linking this work to answer three questions of the PIONEER prioritised Research Questions."*

Lisa Moris: "*I am a urology resident and (senior) associate of the European Association of Urology, with a special interest in prostate cancer research. I was introduced to PIONEER during my PhD on high-risk prostate cancer and this international big data project immediately got my attention. For PIONEER, I was involved in WP2 of where I collaborated in the development of core outcome sets of clinically relevant standardised prostate cancer-related outcomes and prognostic and diagnostic factors.*"

Michael Lardas: *"I am a Urology Consultant working at the Second Department of Urology in Sismanoglio Hospital, Athens, Greece, and a Senior Associate member of EAU Guidelines Office. In PIONEER, I am working for WP2 and had the pleasure to help in the development of a core outcome set for prostate cancer."*

Click here to read the PIONEER COS publication in Eur Urology



European Association of Urology

Prostate Cancer

Updating and Integrating Core Outcome Sets for Localised, Locally Advanced, Metastatic, and Nonmetastatic Castration-resistant Prostate Cancer: An Update from the PIONEER Consortium

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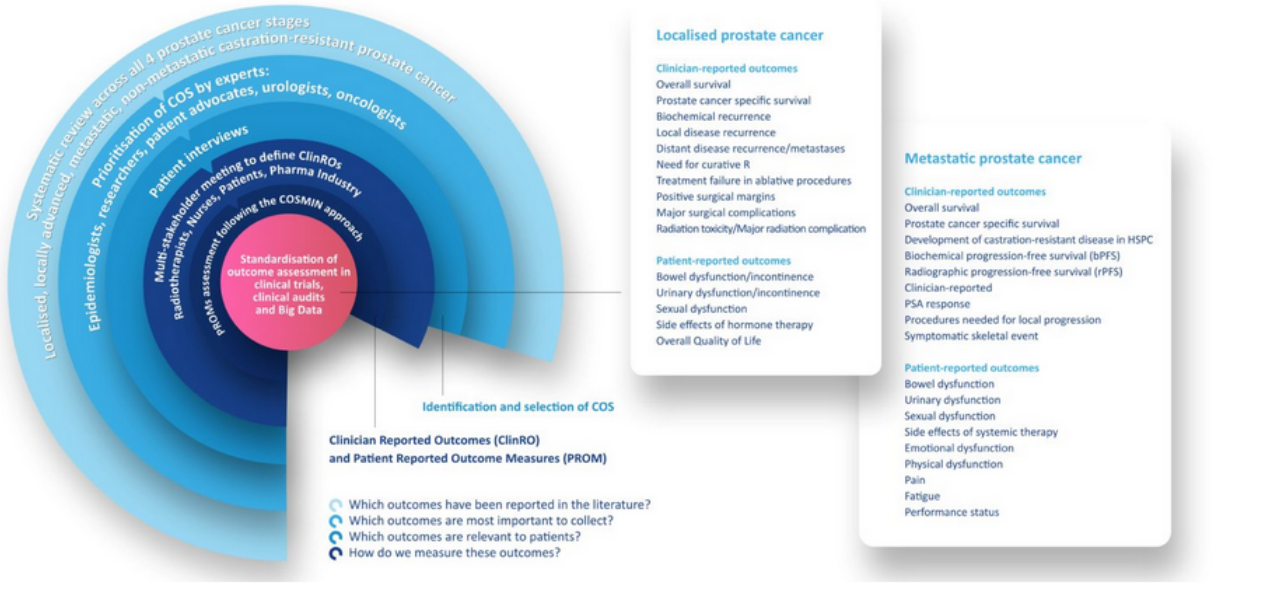
PIONEER Core Outcome Sets (COSs) - 2

Can you briefly summarise what the PIONEER Prostate Cancer COSs exactly are and why they are important?

Katharina Beyer: *"The PIONEER COS is an agreed standardised collection of outcomes prioritised by patients, clinicians and researchers which should be reported as a minimum in all trials for a specific clinical area. Outcomes which have been determined by patients and healthcare professionals to be important should be chosen to be reported in clinical trials and observational studies to increase the impact in clinical practice."*

Jihong Zong: *The PIONEER COSs is a set of consolidated outcomes with their definitions and measurements harmonized. In the past decade, the number of studies or trials in prostate cancer area has been increased significantly. These were not only from clinical trials of potential new therapies but were also from observational studies conducted in real world setting. To draw meaningful conclusions or to make sound clinical decision for patients based on findings from these studies, a standardized set of outcome definitions and measurements is needed, which has been lacking so far. This makes the WP2 work an important task.*

Click here to read the easy to understand overview of what Core Outcome Sets are and why they are important



PIONEER Core Outcome Sets (COSs) - 3

Which stakeholder groups have been involved in the consensus finding process?

Mieke Van Hemelrijk: "*Patients are at the heart everything we do in PIONEER. Hence, in addition to health care professionals and researchers, they were a vital component of the consensus finding process."*

Jihong Zong: *"This project is a multidisciplinary collaboration involving researchers both from academia and private sectors, clinicians, patients, patient advocates, and policy makers. Each stakeholder has a voice in the census process."*

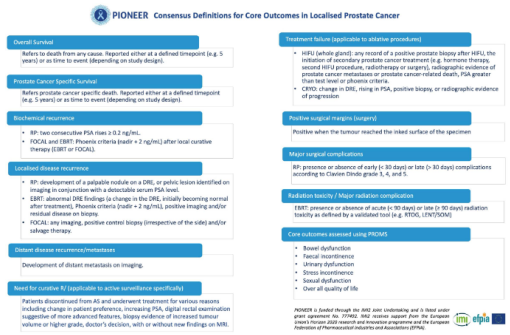
For which conditions have you defined COSs?

Katharina Beyer: *"Across all stages of prostate cancer."*

Lisa Moris: "W*e developed separate COSs for localised and locally advanced prostate cancer and for metastatic and nonmetastatic castration-resistant prostate cancer.*

Click below to read the developed PIONEER consensus definitions for:

Localised PCa


PIONEER Consensus Definitions for Core Outcomes in Localised Prostate Cancer

Overall Survival
Refers to death from any cause. Reported either at a defined timepoint (e.g. 5 years) or as time to event (depending on study design).

Prostate Cancer Specific Survival
Refers prostate cancer specific death. Reported either at a defined timepoint (e.g. 5 years) or as time to event (depending on study design).

Biochemical recurrence
- RP: two consecutive PSA rises ≥ 0.2 ng/mL.
- FOCAL and EBRT: Phoenix criteria (nadir + 2 ng/mL) after local curative therapy (EBRT or FOCAL).

Localised disease recurrence
- RP: development of a palpable nodule on a DRE, or pelvic lesion identified on imaging in conjunction with a detectable serum PSA level.
- EBRT: abnormal DRE findings (a change in the DRE, initially becoming normal after treatment), Phoenix criteria (nadir + 2 ng/mL), positive imaging and/or residual disease on biopsy.
- FOCAL: any imaging, positive control biopsy (irrespective of the side) and/or salvage therapy.

Distant disease recurrence/metastases
Development of distant metastasis on imaging.

Need for curative RT (applicable to active surveillance specifically)
Patients discontinued from AS and underwent treatment for various reasons including change in patient preference, increasing PSA, digital rectal examination suggestive of more advanced features, biopsy evidence of increased tumour volume or higher grade, doctor's decision, with or without new findings on MRI.

Treatment failure (applicable to ablative procedures)
- HIFU (whole gland): any record of a positive prostate biopsy after HIFU, the initiation of secondary prostate cancer treatment (e.g. hormone therapy, second HIFU procedure, radiotherapy or surgery), radiographic evidence of prostate cancer metastases or prostate cancer-related death, PSA greater than test level or phoenix criteria.
- CRYO: change in DRE, rising in PSA, positive biopsy, or radiographic evidence of progression

Positive surgical margins (surgery)
Positive when the tumour reached the inked surface of the specimen

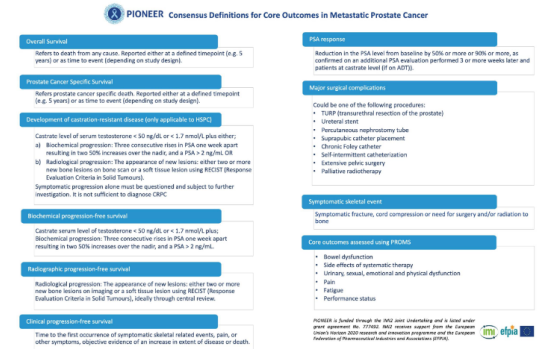
Major surgical complications
RP: presence or absence of early (≤ 30 days) or late (> 30 days) complications according to Clavien Dindo grade 3, 4, and 5.

Radiation toxicity / Major radiation complication
EBRT: presence or absence of acute (< 90 days) or late (≥ 90 days) radiation toxicity as defined by a validated tool (e.g. RTOG, LENT/SOM).

Core outcomes assessed using PROMS
- Bowel dysfunction
- Faecal incontinence
- Urinary dysfunction
- Stress incontinence
- Sexual dysfunction
- Over all quality of life

PIONEER is funded through the IMI2 Joint Undertaking and is listed under grant agreement No. 777492. IMI2 receives support from the European Union's Horizon 2020 research and innovation programme and the European Federation of Pharmaceutical Industries and Associations (EFPIA).

Metastatic PCa


PIONEER Consensus Definitions for Core Outcomes in Metastatic Prostate Cancer

Overall Survival
Refers to death from any cause. Reported either at a defined timepoint (e.g. 5 years) or as time to event (depending on study design).

Prostate Cancer Specific Survival
Refers prostate cancer specific death. Reported either at a defined timepoint (e.g. 5 years) or as time to event (depending on study design).

Development of castration-resistant disease (only applicable to HSPC)
Castrate level of serum testosterone < 50 ng/dL or < 1.7 nmol/L plus either;
a) Biochemical progression: Three consecutive rises in PSA one week apart resulting in two 50% increases over the nadir, and a PSA > 2 ng/mL OR
b) Radiological progression: The appearance of new lesions: either two or more new bone lesions on bone scan or a soft tissue lesion using RECIST (Response Evaluation Criteria in Solid Tumours).
Symptomatic progression alone must be questioned and subject to further investigation. It is not sufficient to diagnose CRPC

Biochemical progression-free survival
Castrate serum level of testosterone < 50 ng/dL or < 1.7 nmol/L plus; Biochemical progression: Three consecutive rises in PSA one week apart resulting in two 50% increases over the nadir, and a PSA > 2 ng/mL.

Radiographic progression-free survival
Radiological progression: The appearance of new lesions: either two or more new bone lesions on imaging or a soft tissue lesion using RECIST (Response Evaluation Criteria in Solid Tumours), ideally through central review.

Clinical progression-free survival
Time to the first occurrence of symptomatic skeletal related events, pain, or other symptoms, objective evidence of an increase in extent of disease or death.

PSA response
Reduction in the PSA level from baseline by 50% or more or 90% or more, as confirmed on an additional PSA evaluation performed 3 or more weeks later and patients at castrate level (if on ADT).

Major surgical complications
Could be one of the following procedures:
- TURP (transurethral resection of the prostate)
- Ureteral stent
- Percutaneous nephrostomy tube
- Suprapubic catheter placement
- Chronic Foley catheter
- Self-intermittent catheterization
- Extensive pelvic surgery
- Palliative radiotherapy

Symptomatic skeletal event
Symptomatic fracture, cord compression or need for surgery and/or radiation to bone

Core outcomes assessed using PROMS
- Bowel dysfunction
- Side effects of systematic therapy
- Urinary, sexual, emotional and physical dysfunction
- Pain
- Fatigue
- Performance status

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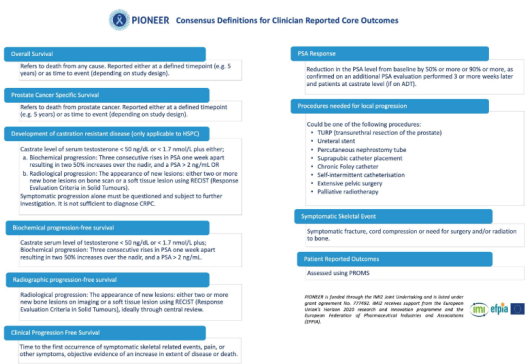
Clinician reported COSs


PIONEER Consensus Definitions for Clinician Reported Core Outcomes

Overall Survival
Refers to death from any cause. Reported either at a defined timepoint (e.g. 5 years) or as time to event (depending on study design).

Prostate Cancer Specific Survival
Refers to death from prostate cancer. Reported either at a defined timepoint (e.g. 5 years) or as time to event (depending on study design).

Development of castration resistant disease (only applicable to HSPC)
Castrate level of serum testosterone < 50 ng/dL or < 1.7 nmol/L plus either;
a. Biochemical progression: Three consecutive rises in PSA one week apart resulting in two 50% increases over the nadir, and a PSA > 2 ng/mL OR
b. Radiological progression: The appearance of new lesions: either two or more new bone lesions on bone scan or a soft tissue lesion using RECIST (Response Evaluation Criteria in Solid Tumours).
Symptomatic progression alone must be questioned and subject to further investigation. It is not sufficient to diagnose CRPC.

Biochemical progression-free survival
Castrate serum level of testosterone < 50 ng/dL or < 1.7 nmol/L plus; Biochemical progression: Three consecutive rises in PSA one week apart resulting in two 50% increases over the nadir, and a PSA > 2 ng/mL.

Radiographic progression-free survival
Radiological progression: The appearance of new lesions: either two or more new bone lesions on imaging or a soft tissue lesion using RECIST (Response Evaluation Criteria in Solid Tumours), ideally through central review.

Clinical Progression Free Survival
Time to the first occurrence of symptomatic skeletal related events, pain, or other symptoms, objective evidence of an increase in extent of disease or death.

PSA Response
Reduction in the PSA level from baseline by 50% or more or 90% or more, as confirmed on an additional PSA evaluation performed 3 or more weeks later and patients at castrate level (if on ADT).

Procedures needed for local progression
Could be one of the following procedures:
- TURP (transurethral resection of the prostate)
- Ureteral stent
- Percutaneous nephrostomy tube
- Suprapubic catheter placement
- Chronic Foley catheter
- Self-intermittent catheterisation
- Extensive pelvic surgery
- Palliative radiotherapy

Symptomatic Skeletal Event
Symptomatic fracture, cord compression or need for surgery and/or radiation to bone.

Patient Reported Outcomes
Assessed using PROMS

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PIONEER Core Outcome Sets (COSs) - 4

Click below to listen to Dr. Steven MacLennan and Prof. Mieke Van Hemelrijck explain what core outcome sets are and why they are important. Followed by Dr. Elena Sisca and Dr. Monica Ratti discussing patient reported outcome measures and their impact on clinical research and patient care.

What was your motivation in the work on the development of the PIONEER Core Outcome Sets?

M. Van Hemelrijck

"A core outcome set not only facilitates policy making and patient experience improvement, but also is a testimony to the need for a multidisciplinary approach when conducting clinical research."

J. Zong

"This is an unique project with the opportunity of working with colleagues from academic institutions and having patients engagement throughout the process. The output of this work could have impact on future research, patient care and their quality of life. This has been the main drive of my commitment."

PIONEER Core Outcome Sets (COSs) - 5

What was your motivation in the work on the development of the PIONEER Core Outcome Sets?

M. Lardas

"Core Outcome Sets (COS) can help us determine which outcomes to measure and how to measure them, when assessing the benefits and risks of interventions for specific conditions. The overall aim of a core outcome set is to contribute to improvements in health and social care by helping patients and the public, practitioners, and policy makers to make informed decisions about the available healthcare treatments. Having that in mind working for the COSs development in prostate cancer was an honor for me."

K. Beyer

Choosing outcomes which are important to patients, will empower patients in treatment decision making, improve their Quality of Life and overall will help to improve the patient journey when diagnosed with prostate cancer.

L. Moris

"The heterogeneity in the use of outcomes used in research and clinical trials limits the interpretation of the data as a whole. I believe that with COS we will create an opportunity to improve homogeneous data reporting and increase the quality of the data/results that can be used for general conclusion on clinical relevant questions."