PIONEER consensus on clinician reported outcome measurements

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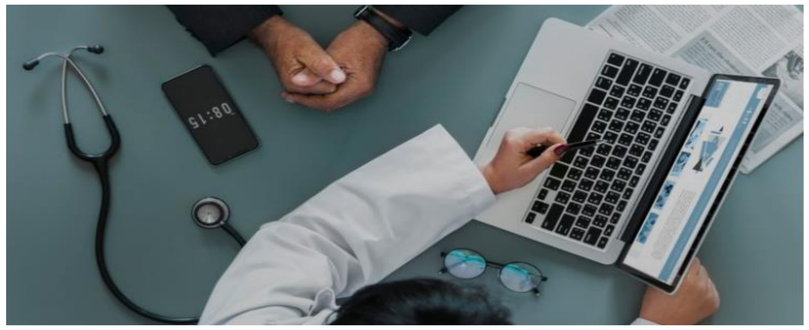
Background

- PIONEER is part of the Innovative Medicine Initiative's (IMI's) "Big Data for Better Outcomes" (BD4BO) umbrella programme.
- PIONEER focuses on improving prostate-cancer related outcomes, health system efficiency and the quality of health and social care across Europe by maximising the potential of Big Data.



Introduction

- Summarising evidence of intervention effectiveness across all stages of prostate cancer (PCa) is currently challenging due to inconsistent outcome definitions.
- In order to address this problem we developed harmonised core outcome sets (COS) for localised and metastatic PCa.
- Here, we report on the identification of definitions for the clinician reported outcomes (ClinROs) identified in the PIONEER COS.

Methods

- We created summary cards of all definitions for each core outcome, identified and adapted from published studies.
- We discussed these during the consensus meeting on 13th November 2019 with a group of 22 participants (urologists, oncologists, imaging specialists, nurses, patients and researchers).
- Participants voted anonymously and consensus was defined as 70% of the participants choosing the same definition.

Figure 1.Example of summary card

Biochemical recurrence

N of studies identified in SR which report directly or indirectly the outcome: 86

Biochemical recurrence	
Applicable Interventions	**ClinRO**
RP	two consecutive PSA measurements ≥ 0.2 ng/mL
RP	detectable serum prostate specific antigen level (> 0.1 ng/mL) at least 6 weeks after surgery, with a confirmatory increase
RP	postprostatectomy serum PSA of 0.4 ng/mL or greater and increasing
RP	increase of PSA after surgery in two subsequent occasions of >1ng/ml
EBRT or FOCAL	rise by 2 ng/mL or more above the nadir PSA be considered the standard definition for biochemical failure after EBRT with or without HT
FOCAL	three consecutive PSA rises after a nadir (ASTRO)
FOCAL	PSA 0.50 ng/mL after nadir
ICHOM	
	• Per AUA definition, PSA>0.2 ng/mL after surgery, with a second confirmatory level of >0.2 ng/ml • Phoenix criteria (nadir + 2 ng/mL) after radiation.

RP: radical prostatectomy; EBRT: external beam radiotherapy; FOCAL: focal therapy

Results

- The group voted separately for localised and metastatic prostate cancer ClinROs.
- Where needed, the outcomes were defined specifically for different interventions.

Figure 2: ClinRO example for localised COS

Definitions of identified core outcomes in the localised setting		
localised COS	**Definitions**	**Consensus**
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).	100%
Prostate cancer specific survival	• Refers to prostate cancer specific death. Reported either at a defined timepoint or as time to event (e.g. 5 years) (depending on study design).	100%
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).	100%
Local 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.	100% 73% 100%
Distant disease recurrence/metastases	• Development of distant metastasis on imaging	86%
Need for curative R/ (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.	100%
Treatment failure (Applicable to ablative procedures (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	77% 82%
Positive surgical margins (surgery)	• Positive when the tumour reached the inked surface of the specimen	
Bowel dysfunction	*Assessed using PROMs*	
- Faecal incontinence		
Urinary dysfunction		
- Stress incontinence		
Sexual dysfunction		
Side effects of hormonal therapy		
Major surgical complications	• RP: presence or absence of early (<30 days) or late complications (≥30 days) according to Clavien Dindo grade 3, 4, 5	86%
- perioperative deaths (surgery specific)	*Assessed using PROMS*	
·thromboembolic disease (surgery specific)		
- bothersome or symptomatic urethral or anastomotic stricture (surgery specific)		
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)	91 %
Overall quality of life	*Assessed using PROMs*	

Conclusion

- Our research identified the most appropriate definitions for clinician reported outcomes in localised and metastatic prostate cancer which should be used for effectiveness trials, clinical audit, real-world evidence and big data.

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