Overview of Ongoing Clinical Trials in Prostate Cancer

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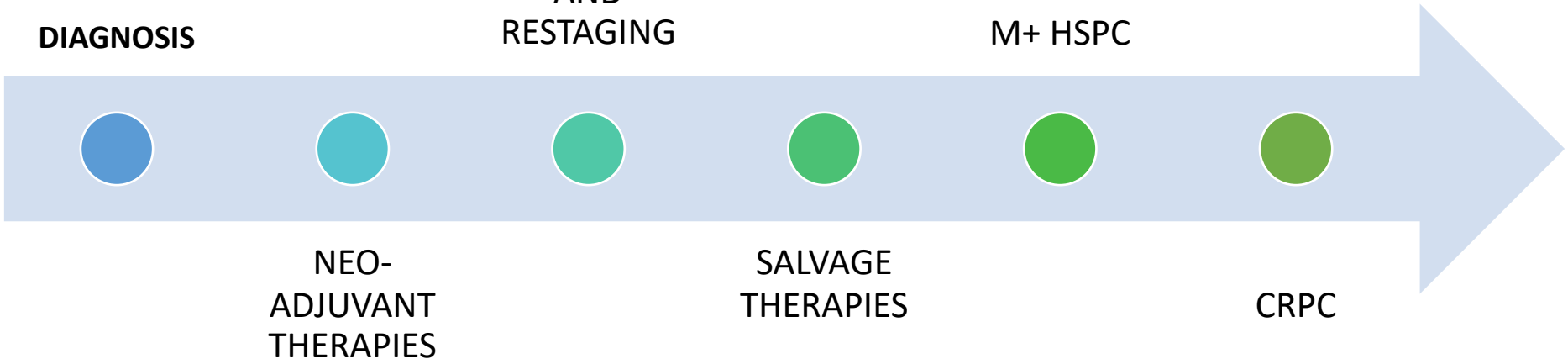
Ongoing Clinical Trials in Prostate Cancer



Fully Hybrid 18F-PSMA PET/MRI as One-stop Approach for the Diagnosis of Clinically Significant Prostate Cancer

AIM: To evaluate the role of fully hybrid PET/MRI with 18F-PSMA and mpMRI as one-stop approach for the diagnosis of clinically significant PCa

Design: Prospective single-arm study

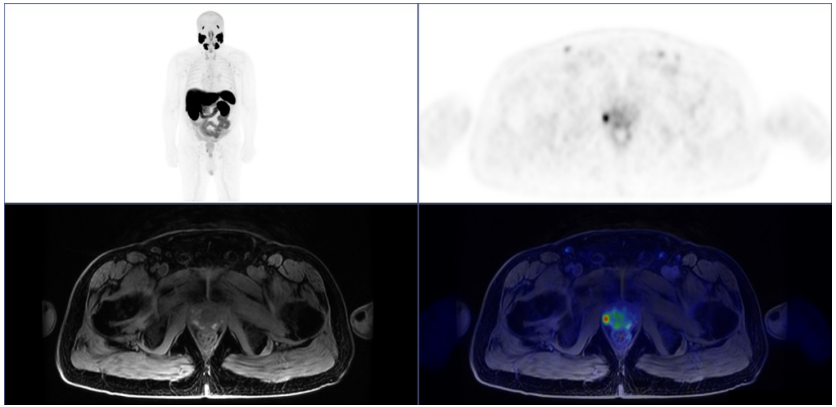
Intervention: 18F-PSMA PET/MRI before biopsy

Primary Endpoint

- Accuracy and the predictive value of fully hybrid 18F-PSMA PET/MRI for the diagnosis of csPCa

Secondary Endpoints

- Proportion of csPCa missed by 18F-PSMA PET scan or mpMRI alone
- Reduction in the detection of clinically insignificant PCa (defined as the presence of prostate cancer with ISUP grade 1) when combining mpMRI and 18F-PSMA PET, and the proportion of biopsies spared



Sample Size: Assuming an average prevalence of csPCa of 56%, a total sample size of 167 patients is sufficient for evaluating a sensitivity of 96% with an absolute precision of 4% (at 95% confident level).

PIs: Prof. Maria Picchio; Prof. Alberto Briganti

Granted by the Italian Ministry of Health – 2022
Waiting for EC approval

Optimizing the Number of Systematic COres during a MRI Target biopsy – (SCOT Trial)

AIM: To identify the optimal biopsy scheme at MRI target biopsy in men with a suspicion of Prostate Cancer

Design: Prospective single-arm study

Intervention: 4 targeted biopsy cores + 20 systematic cores

Primary Endpoint

- Detection rate of csPCa with 6-core vs. 20-core systematic biopsy during a MRI target biopsy

Secondary Endpoints

- Incremental value of any additional systematic core on the detection rate of csPCa during MRI target biopsy
- Incremental value of any additional targeted core on detection rate of csPCa during MRI target biopsy
- Rate of clinically significant PCa missed by MRI target biopsy but detected by 6-core vs 20-core systematic cores

MRI-TBx + S-Bx scheme

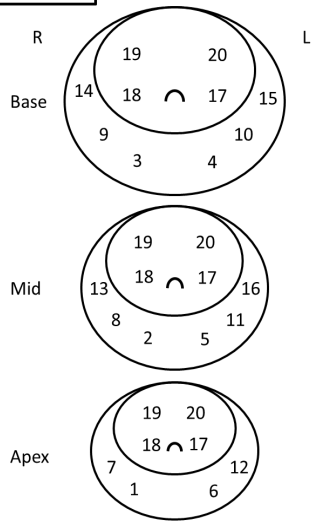
How to biopsy:

- Both transperineal and transrectal approach are allowed
- MRI-TBx first: T1 – T4 cores (1° pot)
- 1° S-Bx Cluster : 1-6 cores (2° pot)
- 2° S-Bx Cluster: 7-20 cores (3° pot)

Notes:

- S-Bx cores must be taken keeping 5-mm margin from IL

- Every single core must be stored in a separate cassette

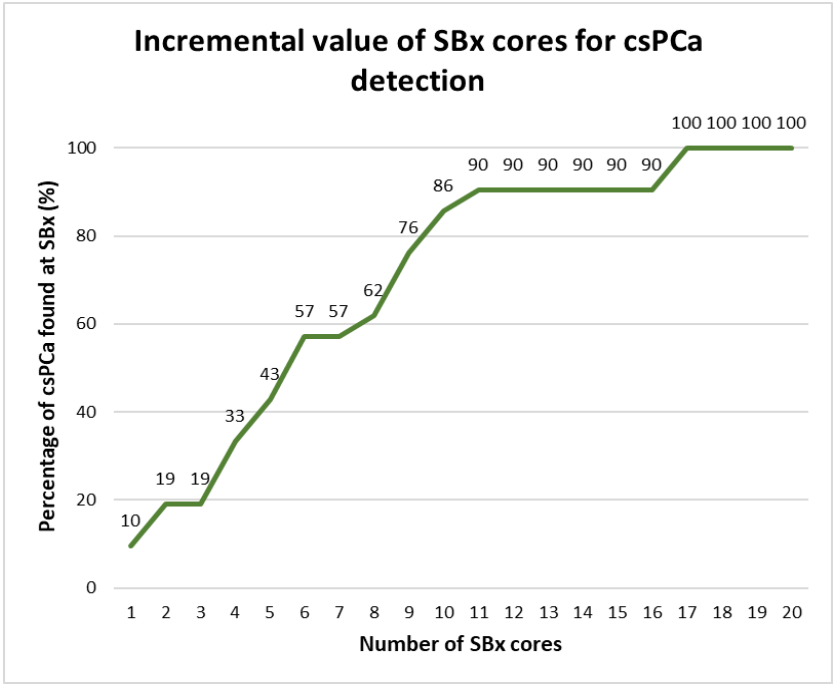


Sample Size: Non-inferiority hypothesis delta: 8%; 380 patients are needed to exclude a difference in favour of 20-core S-Bx vs 6-core S-Bx of more than 8%

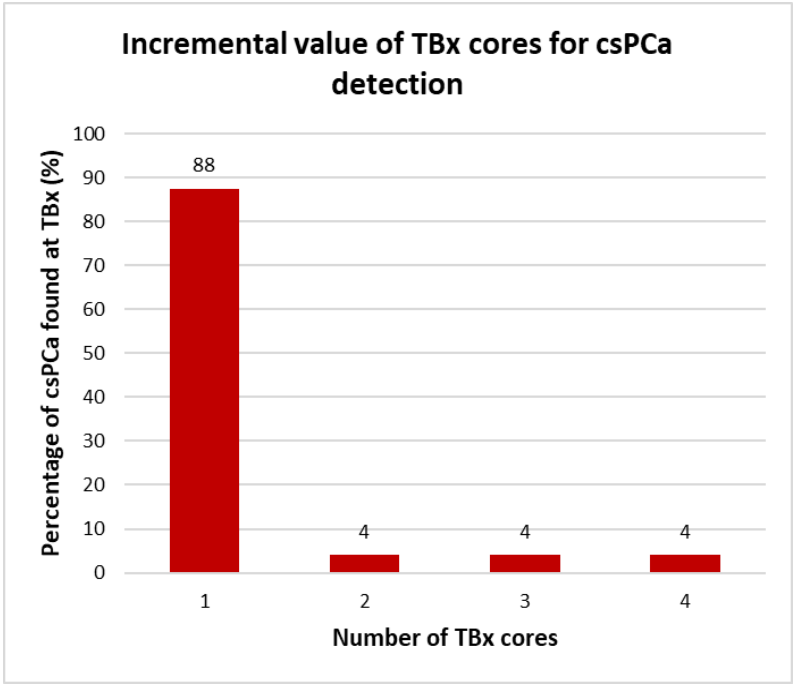
PIs: Prof. Alberto Briganti; Dr. Armando Stabile

EC APPROVED March 2019
Recruiting; Patients enrolled: 77

Optimizing the Number of Systematic COres during a MRI Target biopsy – (SCOT Trial)



12 SBx cores could be sufficient



The majority of csPCa found at TBx were found with the first TBx core

Micro-ultrasound or MRI-targeted Biopsy for Prostate Cancer Diagnosis – US-MIRROR

AIM: To assess the role of micro-ultrasound for the diagnosis of clinically significant prostate cancer

Design: Prospective single-arm study

Intervention:

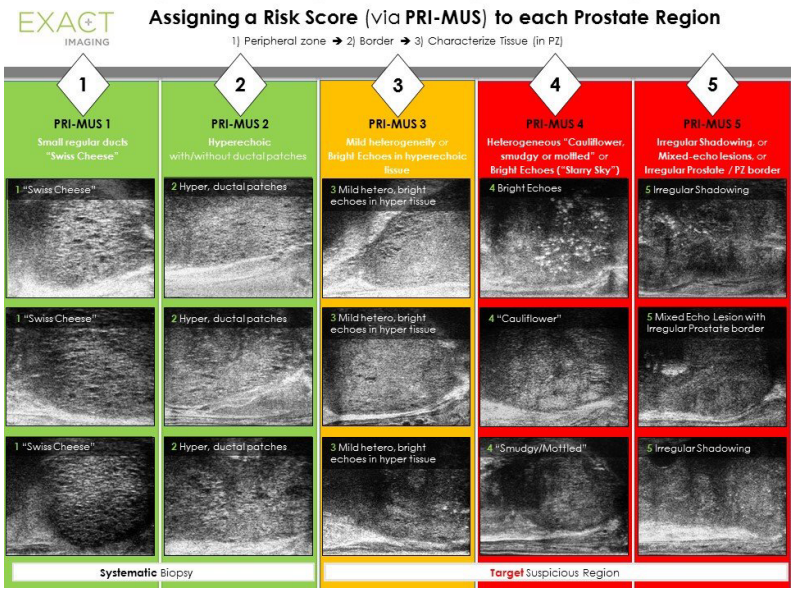
- Both mpMRI and micro-US will be performed in a randomized sequence
- Each mpMRI will be centrally performed by an experienced radiologist that was blinded for micro-US result.
- mpMRIs will be scored using the PI-RADS version 2.1
- Micro-USs will be scored using the PRIMUS
- Subsequent systematic prostate biopsy (12 cores) plus a mpMRI and/or a micro-US targeted biopsy will be performed by transperineal approach

Primary Endpoint

- Sensitivity in detecting clinically significant PCa of Micro-US vs. mpMRI

Secondary Endpoints

- Diagnostic benefit related with the use of Micro-US in the prostate cancer diagnostic pathway



PIs: Prof. Alberto Briganti; Dr. Armando Stabile

EC APPROVED 2021
Recruiting; Patients enrolled: 106

Micro-ultrasound or MRI-targeted Biopsy for Prostate Cancer Diagnosis – US-MIRROR

- Number of ExactVu performed: 106
- Number of mpMRI performed : 82
- Number of biopsies performed: 59

	PIRADS				
PRIMUS	Negative	3	4	5	**Total**
Negative	9	9	1	1	20
3	11	3	2	0	16
4	13	8	4	6	31
5	9	1	3	2	15
Total	42	21	10	9	**82**

49% of positive mpMRI
75% of positive micro-US

- 46% of positivity/negativity concordance
- 30% of positive mpMRI were negative at Micro-US
- 53% of positive Micro-US were negative at mpMRI

csPCa Biopsy Detection

Micro-US

		PRIMUS		
		P+	**P-**	**tot**
BIOPSY	**B+**	11	4	15
	B-	34	10	44
	tot	45	14	59

- Sensibility= 73%
- Specificity= 23%
- PPV= 24%
- NPV= 72%

mpMRI

		PIRADS		
		P+	**P-**	**tot**
BIOPSY	**B+**	14	1	15
	B-	17	27	44
	tot	31	28	59

- Sensibility= 93%
- Specificity= 62%
- PPV= 45%
- NPV= 97%

The Role of Artificial Intelligence in the Assessment of mpMRI of the Prostate

AIM: To compare the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in detecting csPCa of Quantib Prostate vs. traditional radiologist reading of mpMRI

Design: Prospective single-arm study

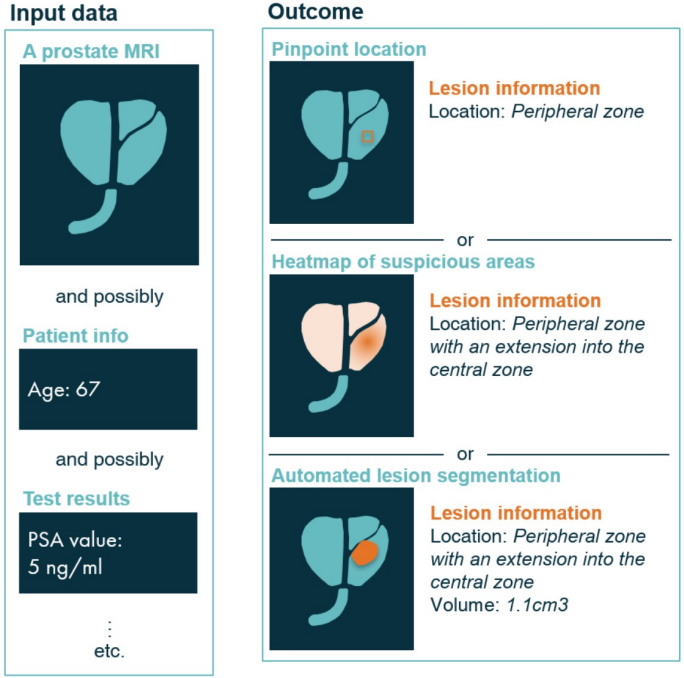
Intervention: All mpMRI images will be retrospectively collected and evaluated using the Quantib Prostate software. In particular, 200 mpMRI with endorectal coil will be read by the expert radiologist and by the Quantib prostate software

Primary Endpoint

- Sensitivity, specificity, negative predictive value, positive predictive value and accuracy of Quantib prostate vs. radiologist in detecting csPCa will be evaluated using the biopsy report as reference standard

Secondary Endpoints

- Correlation of Quantib Prostate vs. traditional radiologist reading of mpMRI with pathologic outcomes
- Differences in diagnostic timing between Quantib Prostate vs. traditional radiologist approach
- Inter-observer variability between Quantib Prostate vs. traditional radiologist approach



PIs: Dr. Giorgio Gandaglia; Dr. Giorgio Brembilla

Quantib

EC APPROVED 2022
Patient Enrolment: December 2022

Molecular Test To sElect biopsy candidates after a negative multiparametRic MRI (MATTER)

AIM: To assess the accuracy of SelectMDx in the identification of csPCa (grade group ≥2 at biopsy) in men with an equivocal or negative mpMRI (PIRADS score ≤3)

Design: Prospective single-arm study

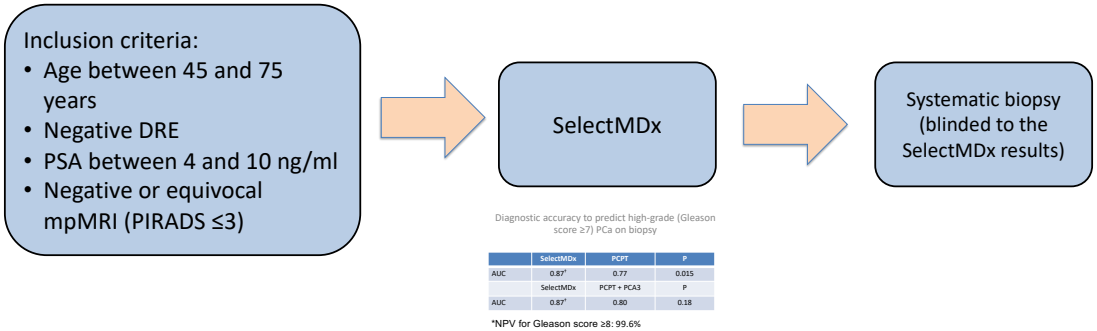
Intervention: SelectMDx before prostate biopsy

Primary Endpoint

- Predictive accuracy of SelectMDx in the identification of csPCa (grade group ≥2 at biopsy) in men with an equivocal or negative mpMRI (PIRADS score ≤3)

Secondary Endpoints

- Rate of complications after both the biopsy procedure and SelectMDx
- Proportion of men who with csPCa and then will receive a definitive treatment
- Proportion of men with clinically insignificant PCa

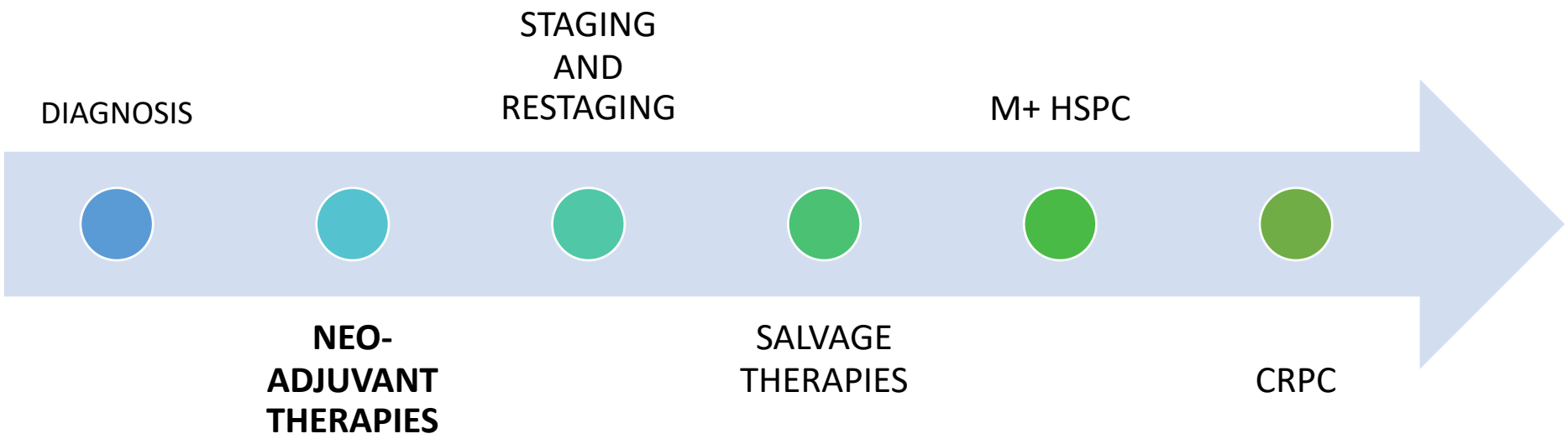


Sample Size: A formal sample size analysis was performed assuming an average prevalence of csPCa of 15%. A total sample size of 314 patients is sufficient for evaluating a sensitivity of 82% with an absolute precision of 11% (at 95% CI)

PI: Dr. Giorgio Gandaglia

EC APPROVED
Patient Enrolment: December 2022

Ongoing Clinical Trials in Prostate Cancer



A Randomized, Double-blind, Placebo-controlled, Phase 3 Study of Apalutamide in Subjects with High-risk, Localized or Locally Advanced Prostate Cancer Who are Candidates for Radical Prostatectomy (PROTEUS)

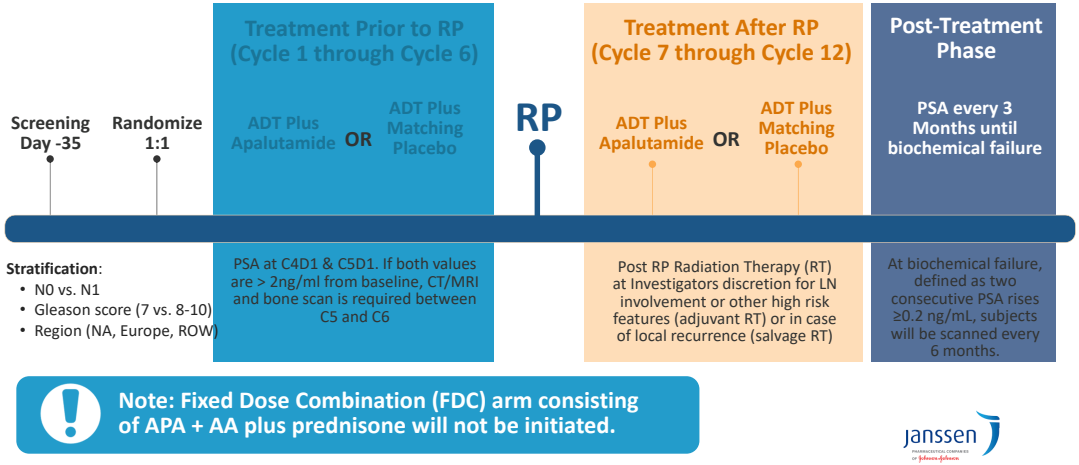
AIM: To determine if apalutamide plus ADT before and after RP with pLND in high-risk localized or locally advanced PCa results in an improvement in pathological complete response (pCR) and MFS compared to placebo plus ADT

Design: Randomized, double-blind, placebo-controlled Phase 3 trial

Intervention: ADT + Apalutamide (12-month perioperative treatment) vs. ADT + placebo

Primary Endpoints
- pCR rate (5% pCR seen with ADT alone, 20% pCR improvement)
- MFS (on conventional imaging)

Secondary Endopoints
- PSA-free survival
- Progression-free survival (on conventional imaging)
- Adverse events, vital signs measurements, clinical laboratory tests, and treatment compliance



Study population: 2000 patients with high-risk localized or locally advanced prostate cancer

Prof. Alberto Briganti; Dr. Vito Cucchiara
IRCCS San Raffaele Hospital Italian Clinical Coordinating Center

Study completed; 10 patients enrolled
Study Completion Date: April 2027

An open label, single-arm, phase 2 study of neoadjuvant PEMbrolizumab before radical PROstatectomy (PEM-PRO) in high-risk prostate cancer patients

AIM: To assess whether pembrolizumab before RP and ePLND induce a pathologic response and reduce by 50% the rate of LNI at final pathology in high-risk PCa

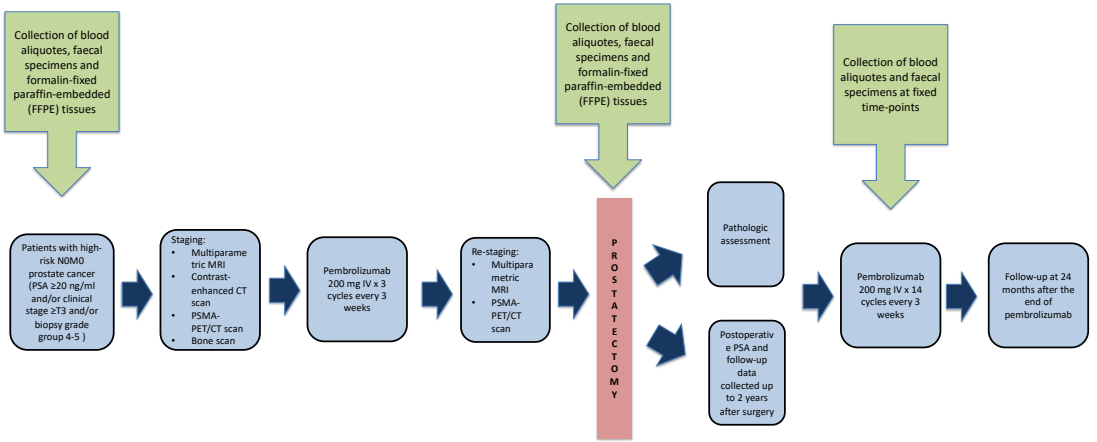
Design: Prospective, single-arm, phase II study

Intervention: Pembrolizumab (neoadv and adv)

Primary Endpoint:
- 50% reduction of the rate of LNI

Secondary Endpoint:
- Pathologic response (absence of cancer in the surgical specimen) or minimal residual disease (i.e., ≤3 mm maximum diameter of residual tumour)
- Radiological response at preoperative mpMRI (tumour reduction of 30%)
- Reduction of positive surgical margins
- PSA persistence and early biochemical recurrence

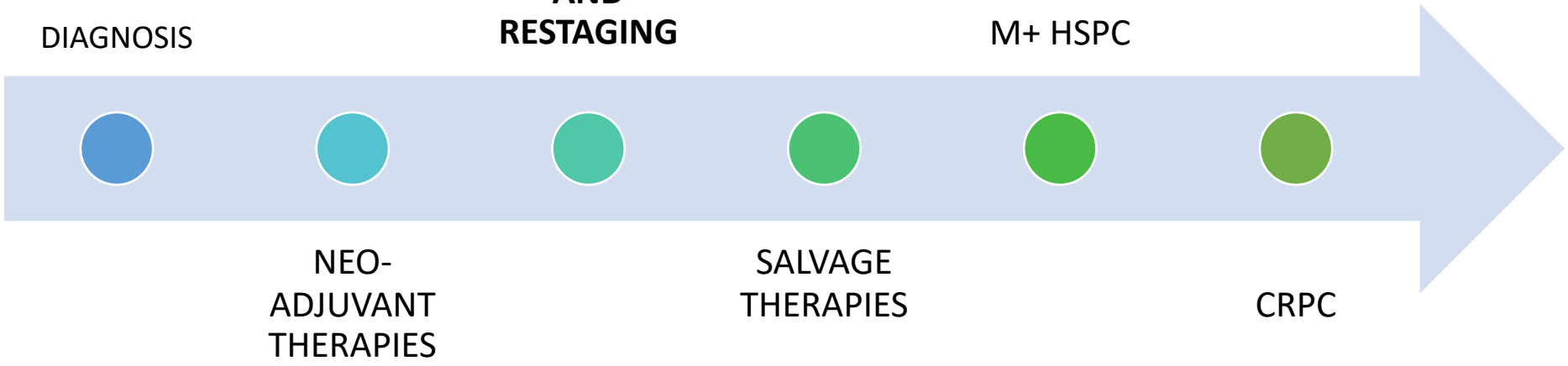
Partecipants	Drug	Dose/Potency	Dose Frequency	Route of Administration	Regimen	Use
59	Pembrolizumab	200 mg	Q3W	IV infusion	Day 1 of each 3 week cycle; 3 cycles (neoadjuvant) + 14 cycles (adjuvant)	Experimental



EC APPROVED
AIFA approval: pending

PIs: Prof. Alberto Briganti; Prof. Andrea Necchi; Dr. Giorgio Gandaglia

Ongoing Clinical Trials in Prostate Cancer



PSMA Radio-Guided Surgery to Detect Nodal Metastases in PCa Patients Candidate to RARP + ePLND

AIM: To assess the accuracy of 99mTc-PSMA Radioguided Surgery to Identify Lymph Node Invasion in patients undergoing RARP

Design: Prospective phase II single-arm study

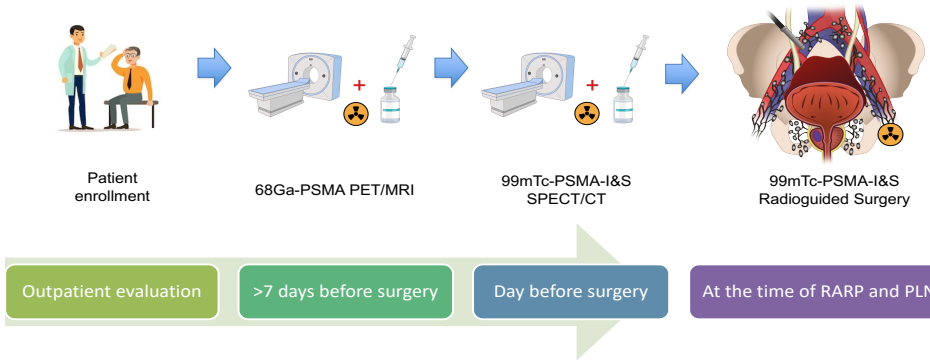
Intervention: 99mTc-PSMA-I&S RGS

Primary Endpoint

- Safety and feasibility of PSMA RGS

Secondary Endpoints

- Sensibility, specificity and accuracy of PSMA RGS for LNI
- Accuracy of PSMA RGS vs available nomograms for LNI
- Detection rate of LNI outside the ePLND template with PSMA RGS
- Number of ePLND spared using PSMA RGS to select ePLND candidates



Accuracy of PSMA-RGS in LNI detection	Per Region	Per Patient
Sensitivity	47%	61%
Specificity	97%	100%
PPV	72%	50%
NPV	91%	100%

PI: Dr. Giorgio Gandaglia
GR2018-12368369

Sample Size: 100 patients with a LNI risk >5%

EC and AIFA APPROVED: May 2021
Recruiting; Patient enrolled: 28;
Completion date: 2024

68Ga-PSMA and 68Ga-DOTA-RM2 PET/MRI in Primary and Recurrent Prostate Cancer: Diagnostic Performance and Association with Clinical and Histopathological Data

AIM: To investigate and compare the performances of ^{68}Ga-PSMA and ^{68}Ga-DOTA-RM2 PET/MRI in identifying primary and recurrent PCa and to explore the association of dual-tracer PET with clinical and histopathological characteristics

Design: Phase II prospective studies

Intervention: 68Ga-PSMA and 68Ga-DOTA-RM2 PET/MRI

Primary Endpoint

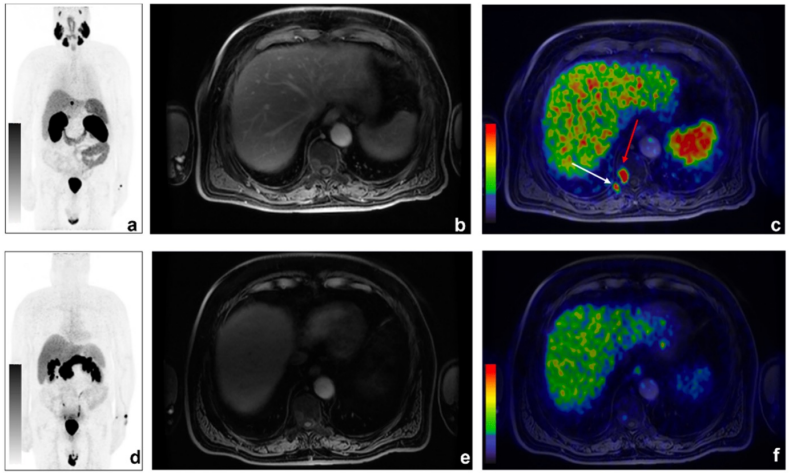
- Accuracy of 68Ga-PSMA PET/MRI for PCa patients and to compare the performance characteristics of 68Ga-PSMA PET/MRI performance to those of 68Ga-bombesin PET/MRI imaging

Secondary Endpoints

- Correlation between 68Ga-PSMA PET/MRI and 68Ga-bombesin-PSMA PET/MRI imaging with clinical and pathological features

Sample size:

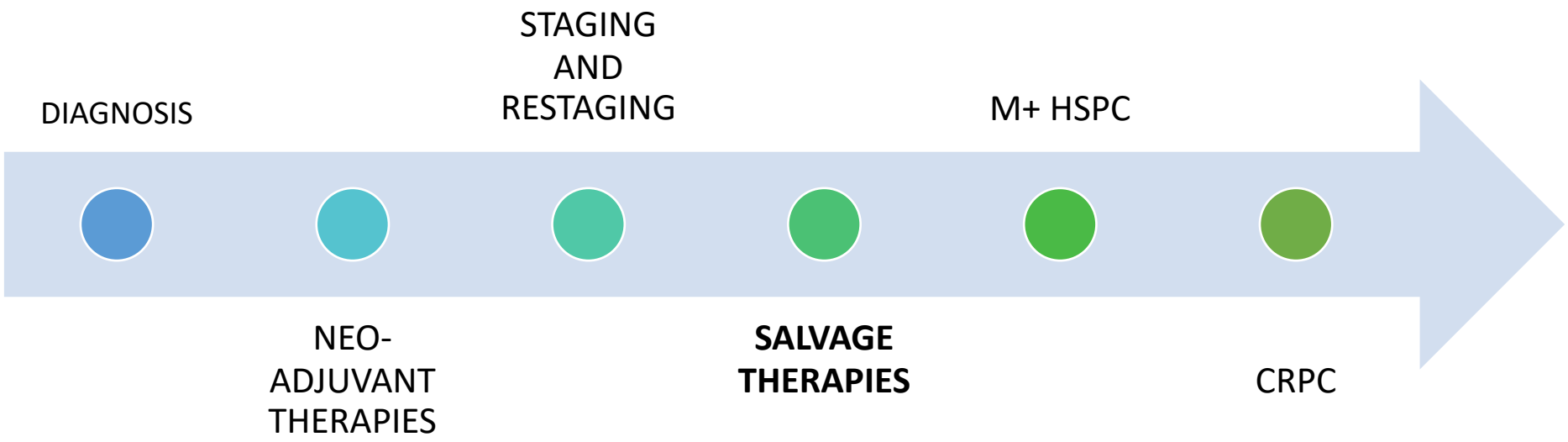
- 50 high-risk patients (primary setting)
- 60 patients with BCR (recurrent setting)



PI: Prof. Maria Picchio
PE2016-02361273; GR-2016-02363991

EC and AIFA APPROVED
Recruiting

Ongoing Clinical Trials in Prostate Cancer



A Study of Adding Apalutamide to Radiotherapy and LHRH Agonist in High-Risk Patients With PSMA-PET Positive Hormone-Sensitive Prostate Cancer Participants (PRIMORDIUM)

AIM: To determine if the addition of apalutamide to RT plus LHRHa delays metastatic progression as assessed by PSMA-PET or death compared with RT plus LHRHa alone

Design: Randomized, controlled, multicenter, open-label trial

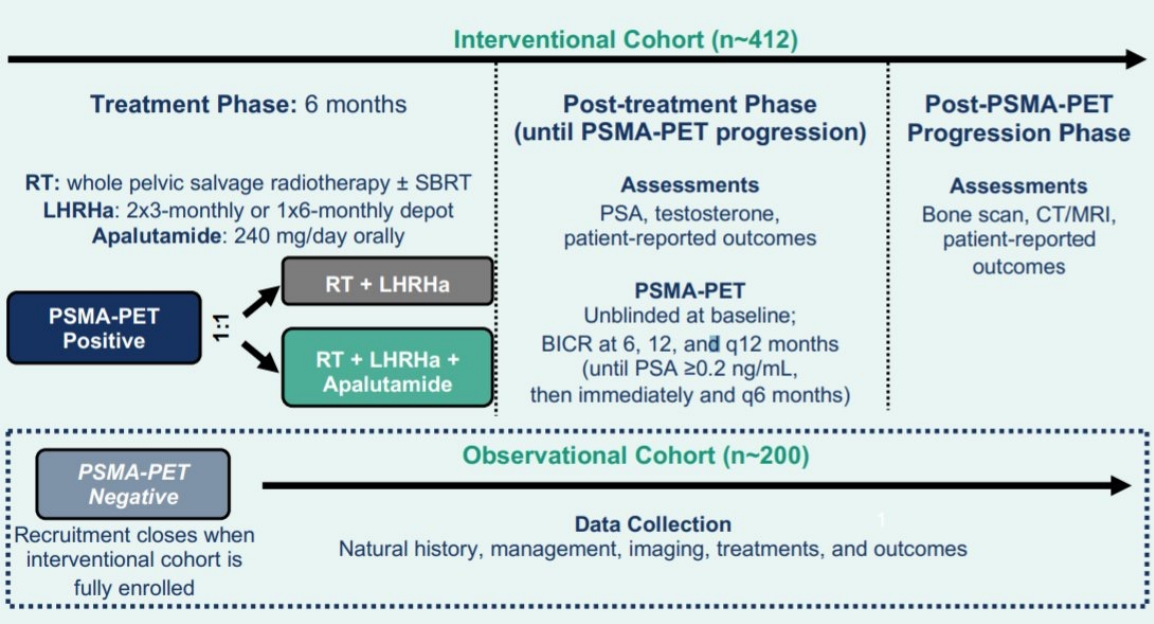
Primary endpoint: Time to PSMA-PET distant metastatic progression or death from any cause

Target cohort:

- High-risk BCR (defined as either PSA doubling time ≤12 months or pathologic Gleason score ≥8) after RP
- Patients with ≥1 locoregional lesion on PSMA-PET

Patients are randomised 1:1 to salvage RT + LHRHa or salvage RT + LHRHa + apalutamide

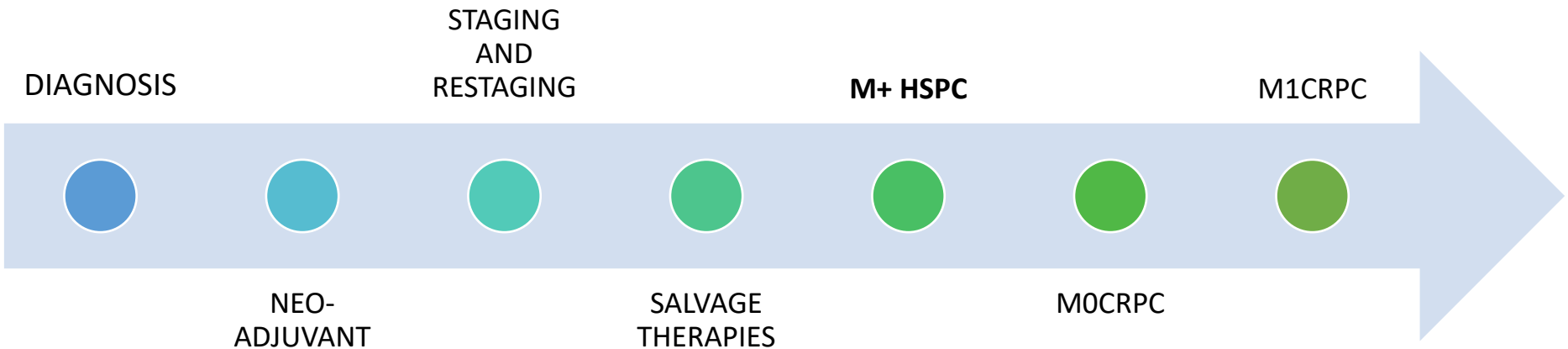
Study population: 412 patients with positive PSMA PET



Prof. Alberto Briganti; Dr. Vito Cucchiara

5 patients enrolled
Study Completion Date: January 2028

Ongoing Clinical Trials in Prostate Cancer



Niraparib in Combination with Abiraterone Acetate and Prednisone Versus Abiraterone Acetate and Prednisone for Patient with Deleterious Germline or Somatic HRR Gene-Mutated mCSPC - AMPLITUDE

AIM: to assess the efficacy and safety of niraparib/placebo added to AAP with androgen deprivation therapy (ADT) in a biomarker-selected population with mCSPC

Design: A Phase 3 Randomized, Placebo-controlled, Double-blind Study

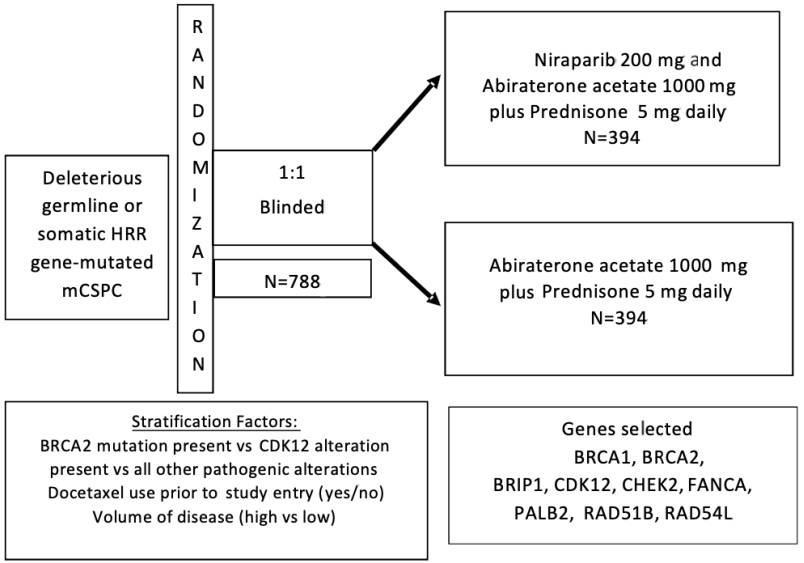
Drug: Niraparib, an orally active poly (ADP-ribose) polymerase (PARP) inhibitor

Setting: patients with mCSPC (documented by conventional imaging) with deleterious germline or somatic HRR gene-mutated mCSPC

Primary endpoint: rPFS as assessed by the investigator which will be evaluated using computed tomography or MRI and whole-body bone scan

Secondary endpoints:

- Overall survival
- Symptomatic progression
- Time to subsequent therapies

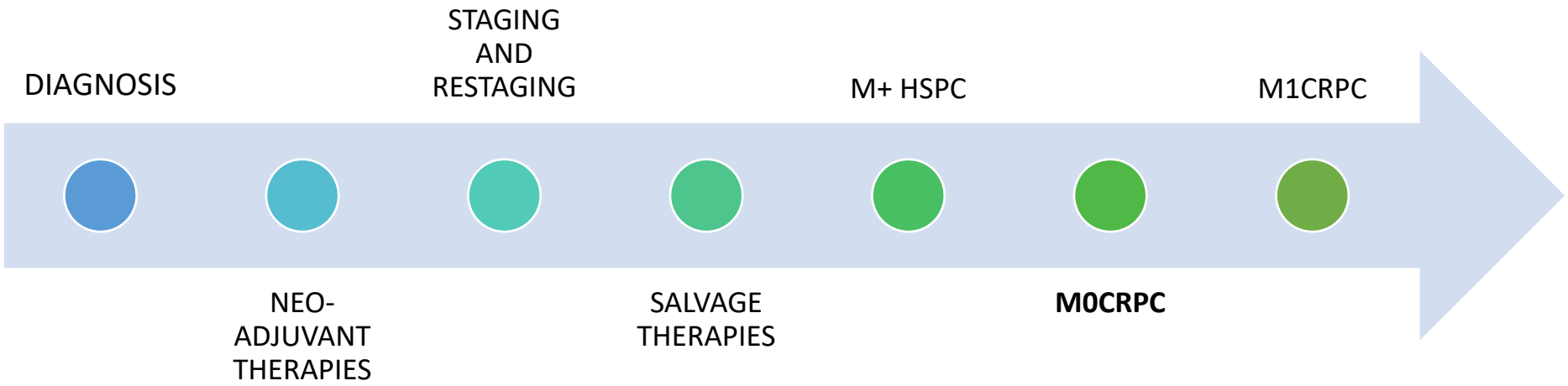


Sample Size: 788 participants will be randomly assigned in a 1:1 ratio to either niraparib and AA, plus prednisone AA plus prednisone

Prof. Andrea Necchi, Dr. Daniele Raggi, Dr. Laura Marandino

Recruiting
Study completion date: May 2027

Ongoing Clinical Trials in Prostate Cancer



A Study in Which nmCRPC Patients for Whom a Decision to Treat With Darolutamide Has Been Made Before Enrollment Are Observed and Certain Outcomes Are Described (DAROL)

AIM: To to find out in the real-world setting, if darolutamide is safe and effective for patients diagnosed with PCa that has not spread to other parts of the body

Design: International, prospective, non-interventional, open-label, multicentric trial

Setting: M0CRPC

Primary endpoint:
- Occurrence of treatment-emergent adverse events

Secondary endpoints:
- patient demographics/characteristics
- utilization patterns of darolutamide
- Oncological efficacy of darolutamide

Sample Size: 1000 patients globally, over a total study period of approximately 5.7 years, including 32 months of enrolment

Milestone	Planned date
Start of data collection	30 Jan 2020
End of data collection (database clean)	30 Dec 2025
Interim analysis 1	After 100 patients complete ≥6 months of treatment or discontinue treatment
Interim analysis 2	After 300 patients complete ≥6 months of treatment or discontinue treatment
Interim analysis 3	After 500 patients complete ≥6 months of treatment or discontinue treatment
Interim analysis 4	After 700 patients complete ≥6 months of treatment or discontinue treatment
Registration in the EU PAS register	08 Oct 2019
Final report of study results	30 Sep 2026

First interim analysis (100 pts) presented at GU-ASCO22: the safety and tolerability was consistent with the favorable profile observed in the ARAMIS trial

Recruiting
Study completion date: September 2026

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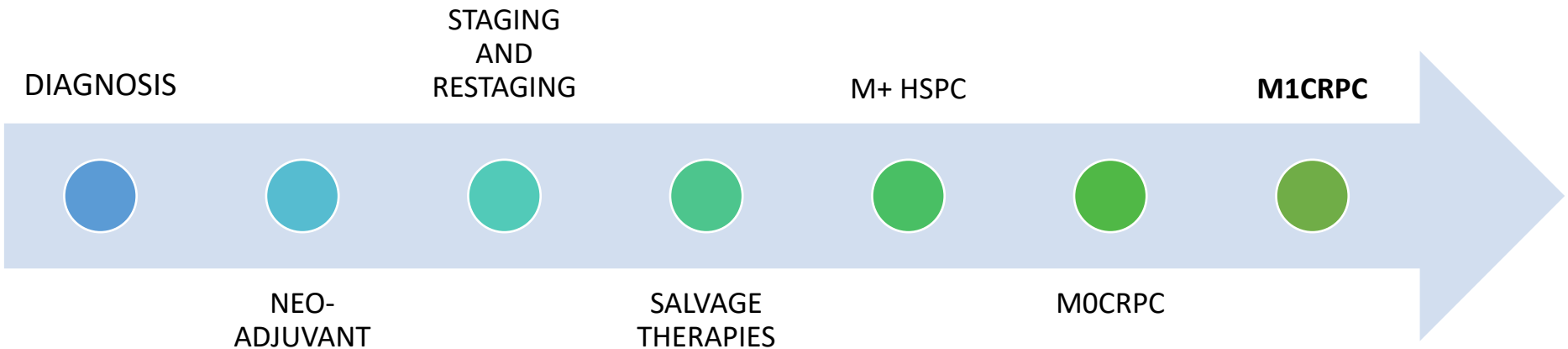
Ongoing Clinical Trials in Prostate Cancer



Study of Cabozantinib in Combination With Atezolizumab Versus Second NHT in Subjects With mCRPC (CONTACT-02)

AIM: To evaluate the efficacy of cabozantinib in combination with atezolizumab vs. a second NHT (abiraterone or enzalutamide) in mCRPC who have previously been treated with one, and only one, NHT

Design: Phase 3, multicenter, randomized, open-label trial

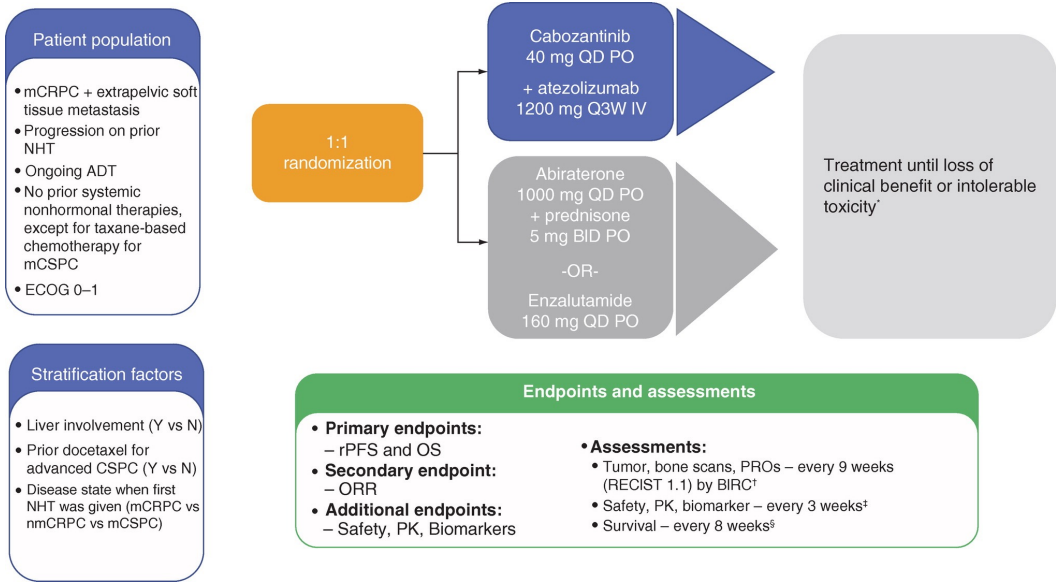
Drug: inhibitor of multiple receptor tyrosine kinases including the VEGFR, MET, KIT, and the TAM family of kinases

Setting: mCRPC patients previously treated with NHT (ABI, APA, DARO or ENZA) who have progressed on that NHT (previous docetaxel is allowed)

Primary endpoints:
- Progression-free survival
- Overall survival

Secondary endpoint:
- Objective response rate

Sample Size: 580 patients



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Recruiting
Study completion date: August 2024

Study of Pembrolizumab (MK-3475) Combination Therapies in Metastatic Castration-Resistant Prostate Cancer (MK-3475-365/KEYNOTE-365)

AIM: To assess the safety and efficacy of pembrolizumab combination therapy in patients with metastatic castrate resistant prostate cancer (mCRPC)

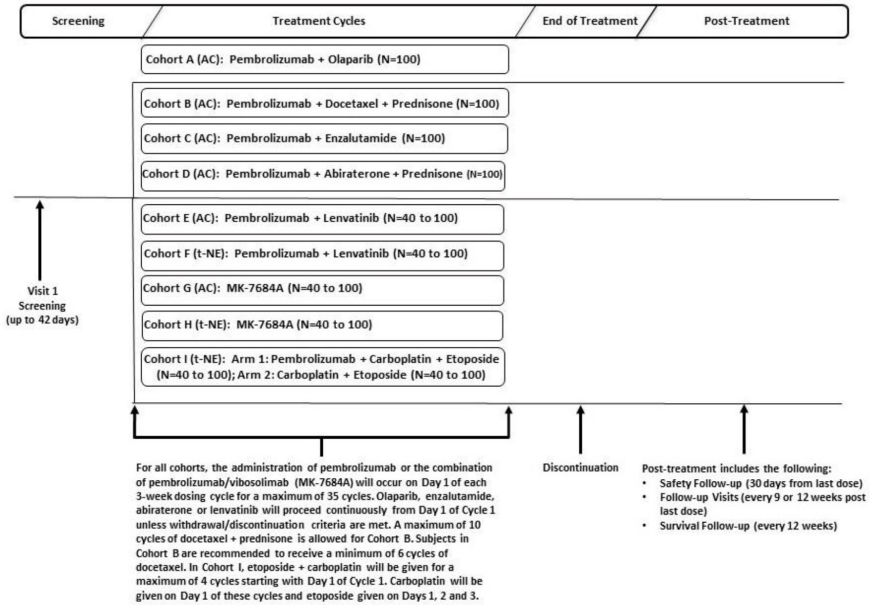
Design: A Phase 1b/2, non-randomized, multi-center trial.

Setting: mCRPC; different combination cohorts according to the treatment received

Intervention: Cohort A: pembro + olaparib, Cohort B: pembro + docetaxel + prednisone, Cohort C: pembro + enzalutamide, Cohort D: pemrbo + abiraterone + prednisone; Cohort E: pembro + Lenvatinib; *Cohort F (neuroendocrine): pembro + Lenvatinib;* Cohort G: pemrbo/vibostolimab coformulation (MK-7684A); *Cohort H (neuroendocrine): pemrbo/vibostolimab coformulation*; *Cohort I (neuroendocrine): pemrbo + carboplatin + etoposide in Arm 1 and carboplatin + etoposide in Arm 2*

Primary endpoint: Decrease of 50% in PSA; AEs; Objective response

Sample Size: 1000 patients



Prof. Andrea Necchi, Dr. Daniele Raggi, Dr. Laura Marandino

Recruiting
Study completion date: May 2025

A Phase II, Multicentre, Open-label, Master Protocol to Evaluate the Efficacy and Safety of Datopotamab Deruxtecan (Dato-DXd) as Monotherapy and in Combination with Anticancer Agents in Patients with Advanced/Metastatic Solid Tumours (TROPION-PanTumor03)

AIM: To assess investigate the safety, tolerability, and anti-tumour activity of Datopotamab Deruxtecan (Dato-DXd) as Monotherapy and in Combination with Anticancer Agents in Patients with Advanced/Metastatic Solid Tumours

Drug: Dato-DXd, an antybody drug coniugate comprised of a recombinant humanised anti-TROP2 IgG1 mAb that is conjugated to a tumour-selective cleavable drug linker

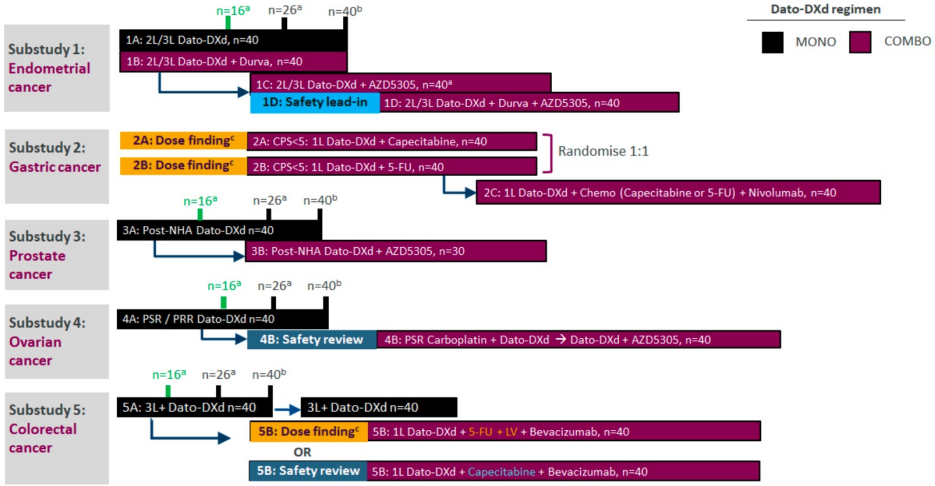
Design: Phase 2, Multicenter, Open-label Trial

Setting: mCRPC that progressed on prior NHA despite of castration level of serum testosterone

Primary endpoints:
- Objective Response Rate
- Adverse events

Secondary endpoints:
- Progression-free survival
- Duration of response
- Disease control rate

Sample Size: 70 men (40 group A and 30 group B)



Prof. Andrea Necchi, Dr. Daniele Raggi, Dr. Laura Marandino

Recruiting
Study completion date: May 2025

A Study of XL092 as Single-Agent and Combination Therapy in Subjects With Solid Tumors (STELLAR-001)

AIM: To assess the safety, tolerability, pharmacokinetics (PK), preliminary antitumor activity, and effect on biomarkers of XL092 administered alone, in combination with atezolizumab, and in combination with avelumab to subjects with advanced solid tumors

Drug: XL092, a novel oral multi-targeted inhibitor of receptor tyrosine kinases MET, VEGFR2, and TAM kinases (AXL, MER)

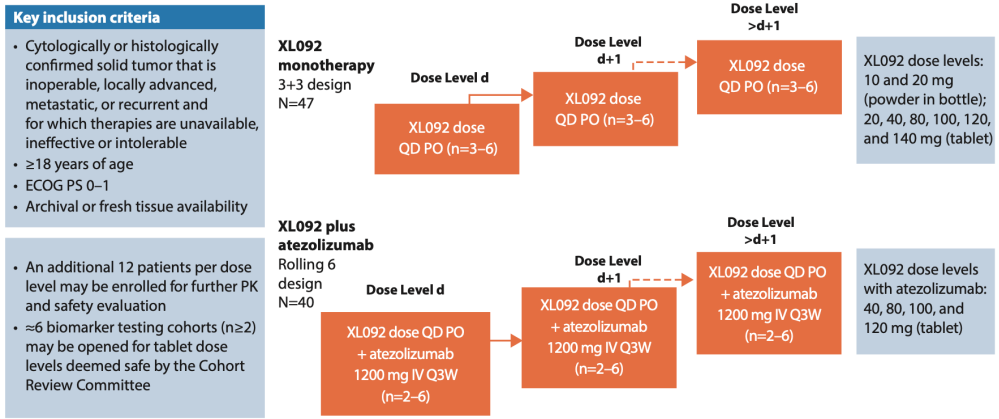
Design: Phase 1, Open-label, Multicentre, Study

Setting: mCRPC; prior treatment with ≥1 novel hormonal therapy and taxane-based chemotherapy, ≤4 prior systemic regimens

Primary endpoints:
- MTD/recommended dose for XL092
- Objective Response Rate (ORR)
- Progression-Free Survival (PFS)
- Overall Survival (OS)

Secondary endpoints:
- Adverse events
- Time to maximum plasma concentrations

Sample Size: 715 participants



Prof. Andrea Necchi, Dr. Daniele Raggi, Dr. Laura Marandino

Recruiting
Study completion date: November 2024

Study of AZD5305 as Monotherapy and in Combination With Anti-cancer Agents in Patients With Advanced Solid Malignancies (PETRA)

AIM: To determine if experimental treatment with PARP inhibitor AZD5305, alone, or in combination with anti-cancer agents is safe, tolerable, and has anti-cancer activity in patients with advanced solid tumors

Drug: AZD5305 (a novel PARPi that has the unique properties to potently and selectively inhibit and trap PARP1)

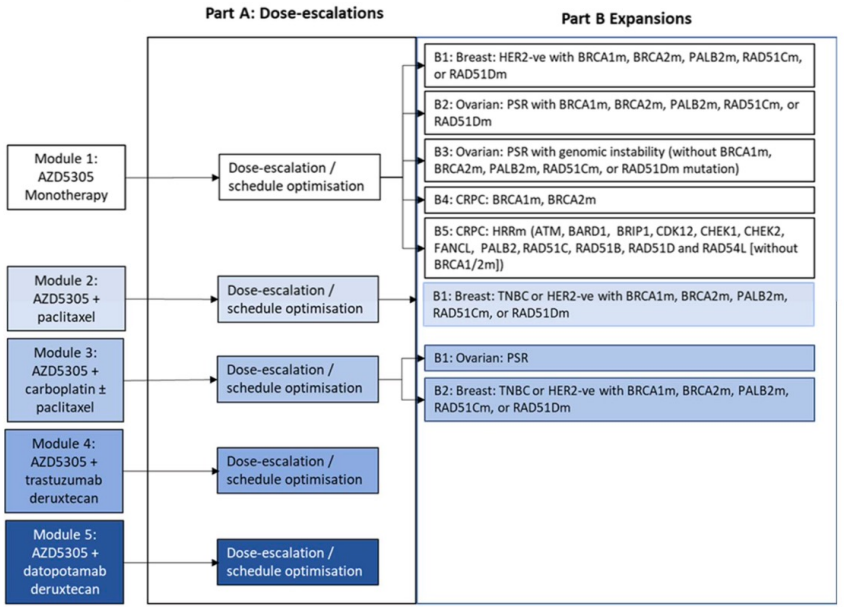
Design: Phase I/IIa, Open-label, Multicentre Study

Setting: Pts with advanced breast (30%), ovarian (33%), prostate (16%) or pancreatic (16%) cancer bearing germline or somatic BRCA1/2, PALB2 or RAD51C/D mutations

Primary endpoint:
- Frequency of AEs

Secondary endpoints:
- Plasma concentrations of AZD5305 and plasma PK parameters
- Best percentage change in target lesion

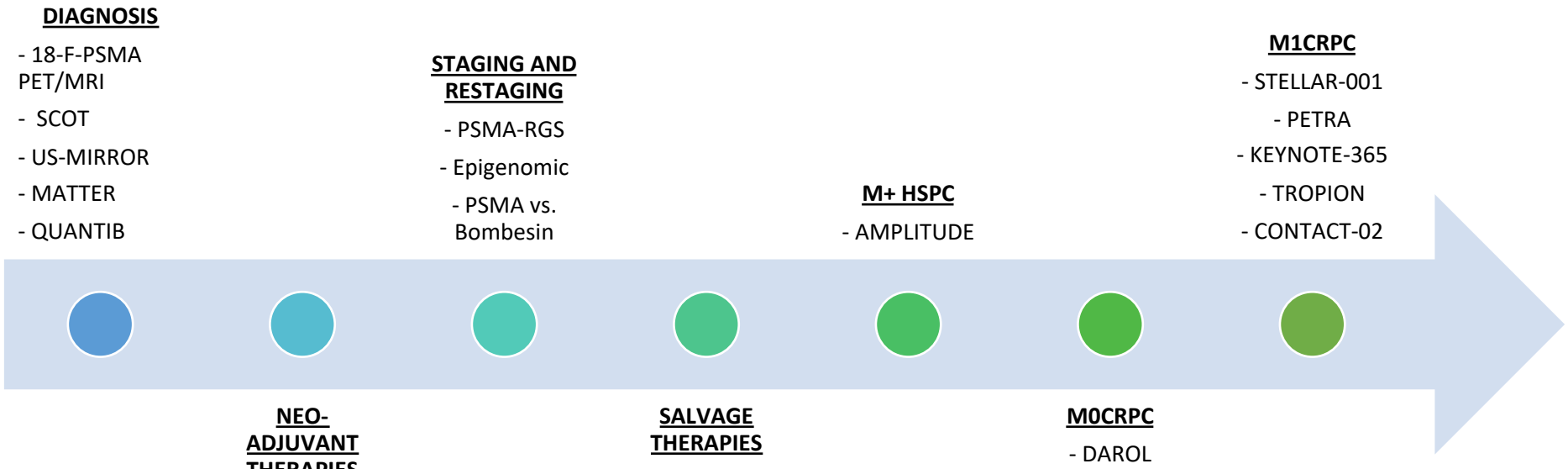
Sample Size: 715 participants



Prof. Andrea Necchi, Dr. Daniele Raggi, Dr. Laura Marandino

Recruiting
Study completion date: July 2025

Ongoing Clinical Trials in Prostate Cancer



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Overview of Ongoing Clinical Trials in Prostate Cancer

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