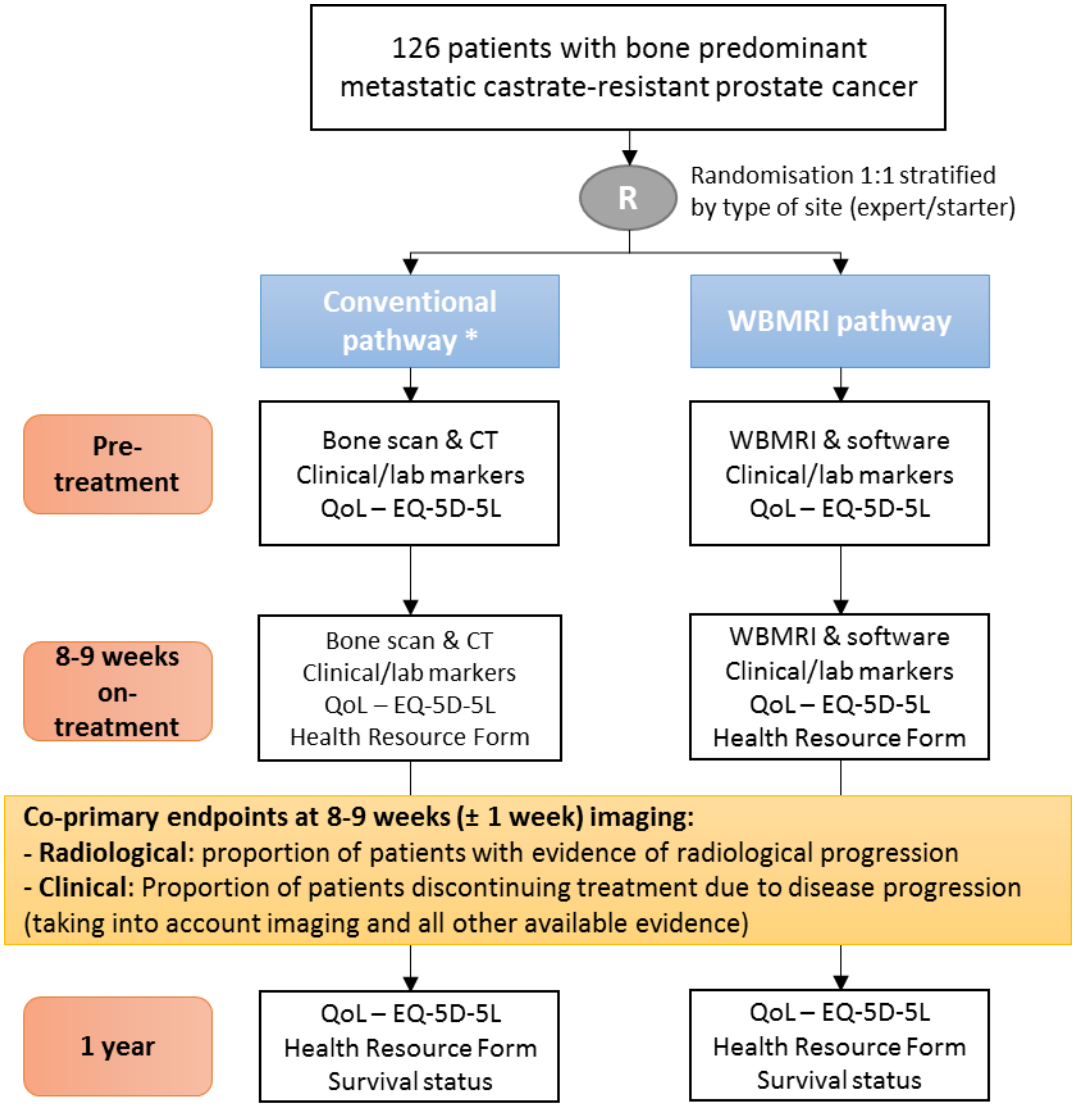
POETIC-A TRIAL SUMMARY

PROTOCOL TITLE	Real-world testing of software for measuring bone disease on whole-body MRI in patients with prostate cancer – WISER-P
TARGET DISEASE	Advanced prostate cancer
TRIAL OBJECTIVES	**Primary objective:** To compare the clinical performance of whole-body MRI (WBMRI), used with the novel software, and conventional imaging, to assess treatment response of bone disease in patients with bone predominant metastatic castration resistant prostate cancer (mCRPC). Clinical performance will be assessed by a) documenting evidence of radiological progression as assessed by imaging performed at 8-9 weeks from start of therapy, b) documenting treatment discontinuation due to progression of disease based on imaging, laboratory and clinical data at the same timepoint. **Secondary objectives** include to assess and compare the following between the conventional imaging and WBMRI plus software pathway groups: 1. Clinician's confidence in clinical decision making (continue/discontinue treatment) after first on-treatment imaging assessment (8-9 weeks from start of treatment) 2. Response to treatment according to clinician perspective at the first on-treatment imaging (8-9 weeks from start of treatment) 3. Time to treatment discontinuation judged to be due to patient no longer clinically benefitting from treatment 4. Patient quality of life at baseline, at first on-treatment imaging assessment (8-9 weeks from start of treatment) and at 12-months from start of treatment 5. Overall survival at 12 months 6. Radiological progression-free survival and progression-free survival 7. Association between radiological progression and time to PSA progression And: 8. In the WBMRI group, to estimate proportion of patients with radiological response. 9. To evaluate the budget impact and cost-effectiveness of WBMRI to assess radiological progression of bone disease
TRIAL DESIGN	Prospective, randomised, multi-centre, controlled trial

TRIAL POPULATION	Patients with metastatic castrate-resistant prostate cancer (mCRPC) with bone-predominant disease about to start systemic therapy (any line approved for this indication) and planned for treatment of disease progression in accordance with standard clinical practice at their centre.
RECRUITMENT TARGET	126 patients (1:1 allocation) will provide 94% power to show a difference of 30% in the proportion of patients with radiological progression at the first on-treatment scan at 8-9 weeks (from 15% in the conventional to 45% in the WBMRI groups), assuming a 10% dropout. *Power for the clinical endpoint:* In the conventional pathway, it is estimated that the proportion who will discontinue treatment due to disease progression at 8-9 weeks is 25% while this can be >50% in the WBMRI group. With 10% dropout, 126 patients would ensure >80% power to find such a difference.
TRIAL INTERVENTION	Patients will be randomised in a 1:1 ratio to the following: 1. Conventional imaging pathway (bone scan plus CT as per local practice). 2. WBMRI (and associated software) imaging pathway All patients will undergo imaging, according to randomised group, prior to commencement of systemic treatment and again at 8-9 weeks (± 1 week) from start of treatment as per PCWG3 guidelines. Radiological assessment afterwards will be as per local practice, and/or as clinically indicated. Clinical and laboratory assessments including disease symptoms, will be according to local practice and as clinically indicated. Patients will be followed up for a minimum 12 months from start of treatment to assess survival status.
CO-PRIMARY ENDPOINTs	Co-primary endpoints are: • The proportion of patients with evidence of radiological progression as assessed in the first on-treatment imaging performed at 8-9 weeks after start of treatment. • Proportion of patients for whom decision is made to discontinue treatment due to disease progression following the first on-treatment imaging (8-9 weeks) and before start of subsequent cycle, taking into account imaging and all other available evidence.
SECONDARY ENDPOINTS	1. Clinician's confidence in clinical decision making (continue/discontinue treatment) after first on-treatment scan (8-9 weeks from start of therapy).

	2. Proportion of patients who respond to treatment according to clinician perspective at the first on-treatment imaging (8-9 weeks from start of treatment) 3. Time to treatment discontinuation and the specific reason(s) a therapy was ultimately discontinued. 4. Health-related quality of life (using EQ-5D-5L) at baseline, at first on-treatment scan (8-9 weeks) and 12 months from start of treatment. 5. Overall survival at 12 months 6. Radiological Progression Free Survival (rPFS) and Progression Free Survival (PFS) 7. Association between time to radiological progression and time to PSA progression 8. In the WBMRI group, proportion of patients with radiological response 9. Health economic evaluation with budget impact and cost-effectiveness of WBMRI
EXPLORATORY ENDPOINTS	1. Number of and time to skeletal-related events defined as either the use of external beam radiotherapy to relieve skeletal symptoms or the occurrence of new symptomatic bone fractures (vertebral or non-vertebral) or the occurrence of spinal cord compression or a tumour related orthopaedic surgical intervention. 2. In the WBMRI group, software report parameters and quantitative histogram parameters derived from the WBMRI software 3. In the WBMRI group, concordance correlation coefficient between local and central WBMRI software report parameters including but not limited to %change in ADC and TDV. 4. In the WBMRI group, proportion of cases where software identifies disease progression at the first on-treatment scan but treatment is continued.
FOLLOW UP	Patients will be followed up for up to 12 months from start of treatment

TRIAL SCHEMA



CT: computer tomography; MRI: magnetic resonance imaging; WBMRI: whole body MRI; QoL: Quality of life;
** MRI (limited to pelvis) is permitted if local practice and/or if clinically indicated*
Clinical/lab markers include disease symptoms (e.g. pain) & PSA, as per local practice.