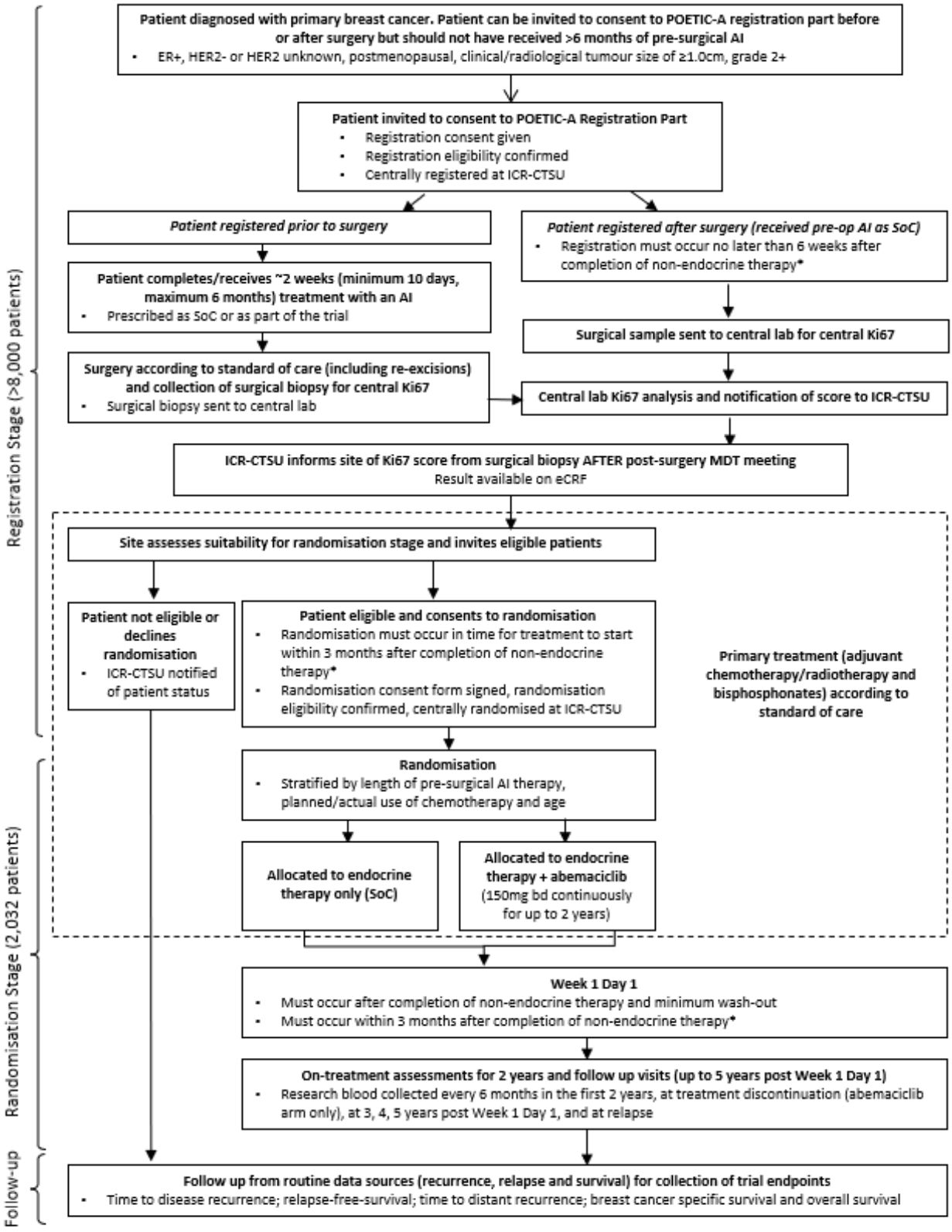
POETIC-A TRIAL SUMMARY

PROTOCOL TITLE	POETIC–A: Pre-Operative Endocrine Therapy for Individualised Care with Abemaciclib
TARGET DISEASE	Operable invasive breast cancer which is ER positive and HER2 negative, with high (20%) 5-year risk of relapse with endocrine therapy (ET) alone in postmenopausal women.
TRIAL OBJECTIVES	Primary Objective: • To determine the benefit of adding abemaciclib to standard adjuvant ET in a sub-population of ER+/HER2- breast cancer who exhibit early evidence suggestive of sub-optimal endocrine responsiveness and high risk of disease relapse. Secondary Objectives: • To determine whether a molecular algorithm can identify those postmenopausal women with ER+/HER2- primary breast cancer and poor anti-proliferative response to an aromatase inhibitor (AI) who may derive greatest benefit from additional adjuvant therapy with abemaciclib. • To compare patient reported quality of life in patients receiving combination treatment with abemaciclib compared to those receiving standard adjuvant ET alone. • To provide an estimate of the cost-effectiveness of combination treatment with abemaciclib in comparison with standard adjuvant ET alone. • To assess the safety and tolerability of abemaciclib combined with ET compared to standard adjuvant ET alone.
TRIAL DESIGN	POETIC-A is a phase III, multi-centre randomised trial. The trial has 2 parts; i) a screening-registration part where patients enriched for the subsequent eligible population receive AI treatment pre-surgery followed by ii) a randomised intervention part where patients whose early AI exposure is indicative of a sub-optimal endocrine response will receive standard endocrine therapy alone or abemaciclib with standard endocrine therapy.
TRIAL POPULATION	Postmenopausal women with non-metastatic operable invasive ER+/HER2- breast cancer.
RECRUITMENT TARGET	2,032 patients randomised. New patients will be registered and screened until a sufficient number of patients for the interventional Randomised Part have been identified. It is estimated that at least 8,000 patients will need to enter the registration part.
TREATMENT REGIMEN	**<u>Registration Part</u>** Patients will have received, or currently be receiving, AI therapy (letrozole or anastrozole) for at least 10 days in the window immediately prior to surgery, up to a maximum of six months, as

	part of standard of care. If the patient has not already received AI as part of standard of care, they should be prescribed 2 weeks (minimum of 10 days) of AI therapy (letrozole or anastrozole) to be taken in the window immediately prior to surgery. Samples taken at the time of the primary surgical procedure - two core cuts (if registration occurred prior to surgery) and/or excision samples - will be sent to the central laboratory for Ki67 analysis. **<u>Randomisation Part</u>** Patients who are eligible by virtue of a centrally assessed high Ki67 at surgery ($Ki67_S$) will be asked to consent to the randomised part of the study where they will be allocated to receive ET alone or ET + abemaciclib (1:1 allocation ratio) stratified by age, use of chemotherapy, and time on pre-surgical AI. Abemaciclib will be prescribed at a standard dose of 150mg bd continuously. ET will be prescribed as per standard of care. Treatment with abemaciclib will be for up to 2 years or until evidence of disease recurrence or other discontinuation criteria are met.
PRIMARY ENDPOINT	Time to tumour (local or distant disease) recurrence (TTR)
SECONDARY ENDPOINTS	• Relapse-free-survival • Time to distant recurrence • Breast cancer specific survival • Overall survival • Patient reported quality of life • Cost-effectiveness (incremental cost per QALY) • Grade 3/4 Adverse Events (AEs), Serious Adverse Events (SAEs) and hospitalisations assessed by Common Terminology Criteria for Adverse Events, version 5 (CTCAEv5) • Treatment related deaths
EXPLORATORY ENDPOINTS	The relationship between the presence of ctDNA and time-to-recurrence
FOLLOW-UP	Patients in the abemaciclib + ET arm will have follow-up visits every 2 weeks in the first 2 months after treatment commencement (Week1 Day1), every 4 weeks until 6 months on treatment, and then every 12 weeks until the end of the 2-year treatment period, followed by a safety visit at 28 days after completion of treatment. Patients in the ET only arm will have follow-up visits every 4 weeks in the first 2 months, and every 24 weeks subsequently until the end of the 2-year treatment period (with a phone consultation half-way between each visit). All patients will have follow-up visits at 3, 4, and 5 years after Week1 Day1.

TRIAL SCHEMA



** Defined as the final fraction of radiotherapy, Day 1 of the final cycle of chemotherapy or the date of the final surgical procedure, whichever is latest*