SCHEDULE OF ACTIVITIES

The Schedule of Activities table provides an overview of the protocol visits and procedures. Refer to STUDY PROCEDURES and ASSESSMENTS sections of the protocol for detailed information on each procedure and assessment required for compliance with the protocol. The investigator may schedule visits (unplanned visits) in addition to those listed on the schedule of activities, in order to conduct evaluations or assessments required to protect the wellbeing of the patient.

Protocol Activity	**Screening**	**Active Treatment Phase[a] - One Cycle = 28 days**			**End of Treatment/Withdrawal[c]**	**Post-Treatment Follow-Up[d]**
		Cycles 1 and 2		**Cycles ≥3**		
Study Day	**Within 28 days prior to randomization unless specified otherwise**	**Day 1[b]**	**Day 15**	**Day 1**		
Visit Window		**±-2 days**	**±2 days**	**±7 days[a]**		**±7 days**
Informed Consent[e]	X					
Medical/Oncological History[f]	X					
Baseline Signs/Symptoms[g]		X[g]				
Physical Examination/Vital Signs[h]	X	X[b]		X	X	
Ophthalmic Examination[i]	X			X[i]	X	
ECOG Performance Status	X	X		X	X	
Laboratory Studies						
Hematology[j]	X	X[b]	X	X	X	
Blood Chemistry[j]	X	X[b]	X	X (upon approval of Amendment 3, assessed every 3 cycles)	X	
Pregnancy test, serum estradiol and FSH (if applicable)[j]	X					
12-Lead ECG (in triplicate)	X				X	
Disease Assessment						
CT/MRI Scans of Chest, Abdomen, Pelvis, any clinically indicated sites of disease, and of bone lesions; Clinical evaluation of superficial disease[k]	X	◄--►[k] Upon approval of Amendment 3, performed as per local practice (See tumor assessment requirements flowchart)			X	X
Radionuclide Bone Scan, Whole Body[l]	X	Upon approval of Amendment 3, performed as per local practice (See tumor assessment requirements flowchart)[l]			X	X
Other Clinical Assessments						
Adverse Event Reporting[m]	X	X	X	X	X	X

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		Cycles 1 and 2		**Cycles ≥3**		
Study Day	**Within 28 days prior to randomization unless specified otherwise**	**Day 1[b]**	**Day 15**	**Day 1**		
Visit Window		**±-2 days**	**±2 days**	**±7 days[a]**		**±7 days**
Concomitant Medications/Treatments	◄--► Recorded from 28 days prior to the start of study treatment up to 28 days after the last dose of study treatment					
Pharmacokinetics (PK)[n]		First 40 patients: Sampling at pre-dose on Day 1 and Day 15 of Cycles 1 and 2, and Day 1 of Cycle 3; all other patients: Pre-dose sampling on Day 15 of Cycles 1 and 2				
[redacted]						
EuroQol-5D (EQ-5D)[r]		Pre-dose on Day 1 of Cycles 1, 2, 3, 4 and Day 1 of every other cycle thereafter starting with Cycle 6 (ie, Cycle 6,8, 10, etc)			X	
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30)[r]					X	
European Organisation for Research and Treatment of Cancer Breast Cancer Module (EORTC-QLQ-BR23)[r]					X	
Survival Follow-up[s]						X
Study Treatment						
Randomization		X				
Fulvestrant (both treatment arms)[t]		◄--►[t] IM administration on Days 1 and 15 of Cycle 1, every 28 days (±7 days) thereafter starting from Day 1 of Cycle 1				
Palbociclib or placebo (Arm A only)[u]		◄--►[u] Orally once daily on Days 1 to 21of each Cycle followed by 7 days off treatment (visit windows not applicable to palbociclib/placebo dosing)				
For pre-/peri-menopausal patients only: Goserelin (both treatment arms, if applicable)[v]	SC administration at least 4 weeks before study treatment start[v]	◄--►[v] SC administration every 28 days				

a. **Active Treatment Phase:** Assessments should be performed prior to dosing on the visit day unless otherwise indicated. Acceptable time windows for performing each assessment are described in the column headers. No time window is to be considered for treatment schedule of palbociclib/placebo. One cycle consists of 28 days. A cycle could be longer than 28 days if persistent toxicity delays initiation of the subsequent cycle. **Day 1 of any cycle visit should coincide with the day the palbociclib/placebo treatment begins.** If there are delays due to toxicity, then the start of the next cycle visit will be delayed until the patient has recovered and can begin study treatment again. Fulvestrant injection will be given every 28 days (+/- 7 days) with the exception of Cycle 1 during which it will be administered on Days 1 and 15 (±2 days allowed according to the protocol visit time windows). Goserelin will be administered every 28 days (+/- number of days allowed according to the protocol visit time windows). The active treatment phase is ongoing as long as the patient is receiving both study drugs (ie, palbociclib/placebo and fulvestrant) or fulvestrant alone.
b. **Cycle 1/Day 1:** Blood chemistry, hematology, and physical examination not required if acceptable screening assessment is performed within 7 days prior to randomization.
c. **End of Treatment/Withdrawal:** Visit to be performed as soon as possible but no later than 4 weeks from the last dose of investigational products and prior to initiation of any new anticancer therapy. Obtain assessments if not completed during the previous 4 weeks on study.
d. **Post Treatment Follow-up:** Patients who discontinue study treatment should be contacted 28 calendar days (±7 days) after discontinuation of study treatment (palbociclib/placebo or fulvestrant) to assess if there have been any new adverse events and/or any change to any previously reported adverse events. This follow-up should occur 28 calendar days (±7 days) regardless of any new anti-cancer therapy that may have started. Telephone contact is acceptable. Follow-up visits to assess survival status will be conducted every 3 months going forward after approval of Amendment 3. See table footnote s (Survival Follow-up) below.
e. **Informed Consent:** Informed consent must be obtained prior to any protocol required assessments being performed (with the exception of certain imaging assessments if meeting the criteria defined in the Screening Section).
f. **Medical/Oncological History:** To include information on prior anticancer treatments.
g. **Baseline Signs/Symptoms:** Baseline tumor related signs and symptoms will be recorded at the Cycle 1 Day 1 visit prior to initiating treatment and then reported as adverse events during the trial if they worsen in severity or increase in frequency.
h. **Physical Examination/Vital signs:** A full physical examination including an examination of all major body systems and breasts, height (at screening only), weight, blood pressure and pulse rate, which may be performed by a physician, registered nurse or other qualified health care provider. Physical examinations will be carried out at Screening, Day 1 of every cycle and the End of Treatment/Withdrawal visit.