PEARL

A window of opportunity study to assess the biological effect of progesterone in premenopausal Estrogen Receptor-positive, Progesterone Receptor-positive early breast cancer

EudraCT number: 2017-001521-41
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Final Analysis Report

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Protocol Version and Date	V4.0 05/09/2019		

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3. Introduction

The trial was concluded early and any samples taken have not yet been analysed. The planned analysis outlined in the Protocol and SAP was therefore not possible and this report instead presents the baseline, compliance and safety data as line listings.

4. Recruitment

4.1 Withdrawals

A single patient withdrew consent after being randomised. The remaining 6 patients completed the study as per the protocol.

Table 4.1-1: Withdrawals from Study

Allocation	Reason	Timepoint
Arm A: Tamoxifen	Patient did not want to take the high dose of tamoxifen. She has, in the past, had lots of side effects to treatment and she was very anxious about this dose.	Baseline

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5. Tables

5.1 Baseline Characteristics

5.1.1 Age and Demographic Details

Patient age is the recorded age at randomisation.
The information was taken from screening data as the baseline visit was incomplete.

Table 5.1-1: Age and Demographic Details

Patient	Allocation	Age	ECOG Performance Status	Tumour Size (mm)	Tumour Type	Tumour Grade	ER Positive	PgR Positive	Her2 Negative
Patient 1	Arm A: Tamoxifen	45	0	20	Ductal	1	6	8	1+
Patient 2	Arm B: Tamoxifen plus Utrogestan	47	0	40	Ductal	1	7	8	1+
Patient 3	Arm A: Tamoxifen	45	0	35	Lobular	3	8	8	1+
Patient 4	Arm B: Tamoxifen plus Utrogestan	34	0	16	Ductal	3	8	8	1+
Patient 5	Arm A: Tamoxifen	40	0	44	Ductal	1	8	8	1+
Patient 6	Arm B: Tamoxifen plus Utrogestan	44	0	15	Invasive Micropapillary	2	8	8	1+
Patient 7	Arm A: Tamoxifen	49	0	47	Ductal	2	8	8	2+

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5.1.2 Biochemistry Details

No biochemistry data was recorded at baseline. The table below summarizes the biochemistry data that was instead collected at Screening.

Table 5.1-2: Biochemistry Details

Patient	Allocation	Creatinine (µmol/l)	Sodium (mmol/l)	Potassium (mmol/l)	Corrected Calcium (mmol/l)	Bilirubin (µmol/l)	Albumin (g/l)	Alk Phosphatase (IU/l)	GGT (IU/l)	AST (U/l)	ALT (U/l)
Patient 1	Arm A: Tamoxifen	48	140	4.7	2.14	2	46	72	10	13	9
Patient 2	Arm B: Tamoxifen plus Utrogestan	48	139	4.8	2.45	4	47	65	104	28	33
Patient 3	Arm A: Tamoxifen	75	140	4.8	2.37	11	41	46	.	17	20
Patient 4	Arm B: Tamoxifen plus Utrogestan	63	142	4.1	2.41	4	40	58	18	.	25
Patient 5	Arm A: Tamoxifen	70	139	3.6	2.39	22	46	47	.	.	11
Patient 6	Arm B: Tamoxifen plus Utrogestan	69	139	4	2.28	6	49	25	18	13	11
Patient 7	Arm A: Tamoxifen	72	140	4.5	2.26	8	47	69	21	.	21

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5.1.3 Haematology Details

Haematology data was recorded for only one patient at baseline and so the results listed below are those recorded at screening.

Table 5.1-3: Haematology Details

Patient	Allocation	Haemoglobin (g/l)	WBC (10^9/l)	Absolute Neutrophil Count	Lymphocytes (10^9/l)	Platelets (10^9/l)
Patient 1	Arm A: Tamoxifen	12.7	7.7	4.7	1.9	369
Patient 2	Arm B: Tamoxifen plus Utrogestan	13.2	7.9	5.8	1.3	493
Patient 3	Arm A: Tamoxifen	13.4	6.3	3.6	1.9	351
Patient 4	Arm B: Tamoxifen plus Utrogestan	14.1	8.5	6.1	1.7	259
Patient 5	Arm A: Tamoxifen	12.5	6	4.6	0.9	256
Patient 6	Arm B: Tamoxifen plus Utrogestan	14.2	6.5	5.1	0.9	178
Patient 7	Arm A: Tamoxifen	15.1	7.7	6	1.2	260

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5.1.4 Protocol Deviations

There were a total of 8 protocol deviations across two sites. The "major" deviations related to the same site.

Table 5.1-4: Protocol Deviations

	Details	Category	Action	Deviation Date	Report Date
1	Patient source document specifies that the patient wore knee high stockings pre-surgery. The protocol says that the patient must wear thigh high stockings.	5: Major: Major protocol deviation in patient management and/or assessment	Site staff informed the monitor that knee high stockings are part of the site's standard care. This has been raised with the trial co ordinator to inform the site staff if knee high stockings can be allowed in place of thigh high stockings.	07/10/2019	28/11/2019
2	Haematology tests were not completed as part of patient's follow up as the research nurse completed the process forms and bottle labels incorrectly so the laboratory did not run the tests.	13: Major: Patient Management/Assessment - Blood Results	The research nurses are now aware of the requirements for completing labels to ensure that the laboratory staff can accept the samples.	07/10/2019	28/11/2019
3	Haematology test were not completed as part of patient's tissue collection as the research nurse used the wrong vacutainer to obtain the blood sample and the tests could not be completed.	13: Major: Patient Management/Assessment - Blood Results	Research nurses were reminded to check the protocol prior to taking blood samples to ensure that to correct vacutainers are used.	07/10/2019	28/11/2019
4	Mid-treatment Visit (Biochemistry) - Magnesium and glucose blood test was not carried out, as it was not requested in error.	30: Minor: Patient examination/test	RN reminded to request all tests required for the trial.	22/03/2019	28/05/2019
5	ALT not done at mid treatment and follow up visits.	24: Minor: blood results	Protocol to be amended to allow for either AST or ALT to completed at visits.	08/04/2019	28/05/2019
6	Surgery Visit translational blood samples - Blood samples were taken 16 hours following the last dose of Tamoxifen (+1 hour deviation).	25: Minor: translational	RN reminded that translation blood samples should be taken 3 - 15 hours following last dose of tamoxifen.	22/03/2019	28/05/2019
7	Surgery Visit (Haematology & Biochemistry) - PT, magnesium and glucose tests not completed as not requested in error.	30: Minor: Patient examination/test	RN reminded to carry out all tests required for trial.	22/03/2019	28/05/2019
8	Corrected calcium and phosphate not done within 28-day window of randomisation.	24: Minor: blood results	Site staff reminded to complete all relevant test results as per protocol.	08/04/2019	28/05/2019

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5.2 Compliance with Treatment

A single patient, allocated to the intervention, failed to take both drugs on one of the days. All other patients, not withdrawn, adhered to the allocated treatments.

Table 5.2-1: Compliance with Treatment

Patient	Allocation	TAMOXIFEN: Number of pills taken	Total dose received (mg)	Proportion of sufficient dose (%)	UTROGESTAN: Number of pills taken	Total dose received (mg)	Proportion of sufficient dose (%)
Patient 1	Arm A: Tamoxifen	18	360	100	.		
Patient 2	Arm B: Tamoxifen plus Utrogestan	17	340	94	9	3900	93
Patient 3	Arm A: Tamoxifen	18	360	100			
Patient 4	Arm B: Tamoxifen plus Utrogestan	18	360	100	42	4200	100
Patient 5	Arm A: Tamoxifen	.	.	.			
Patient 6	Arm B: Tamoxifen plus Utrogestan	18	360	100	42	4200	100
Patient 7	Arm A: Tamoxifen	18	360	100			

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5.3 Safety Data

A total of 8 AEs were recorded across 5 patients, with one patient recorded 2 AEs and another recording 3 AEs. All events recorded were considered low in severity and largely unrelated to either drug received. Fatigue and nausea were possibly related to Utrogestan and tamoxifen, respectively.

Table 5.3-1: Summary of Adverse Events

	Description	CTCAE	Onset (Days since Randomisation)	Allocation	Relationship to Tamoxifen	Relationship to Utrogestan	Action
1	Back Pain	1	1	Arm B: Tamoxifen plus Utrogestan	None	None	None
2	Constipation	1	41	Arm A: Tamoxifen	Unlikely		None
3	Cramping Lower Abdominal Pain	1	0	Arm A: Tamoxifen	Unlikely		None
4	Fatigue	1	10	Arm A: Tamoxifen	None		None
5		1	1	Arm B: Tamoxifen plus Utrogestan	None	Possible	None
6	Fluttering Sensation In Right Thigh	1	8	Arm A: Tamoxifen	None		None
7	Nausea	1	17	Arm A: Tamoxifen	Possible		None
8	Tingling/Numbness In Fingers	1	10	Arm A: Tamoxifen	None		None

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5.4 Efficacy Outcomes

5.4.1 Primary Outcome

At the time of writing this report sample data had not been analysed and therefore the primary outcome cannot be assessed.

5.4.2 Secondary Outcome

At the time of writing this report sample data had not been analysed and therefore the secondary outcomes cannot be assessed.