Collaborator Data Index Document

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SUMMARY

This document summarises the datasets that have been generated through the "WINGMEN: Windows trial of INsulin-like Growth factor neutralising antibody Xentuzumab in MEN scheduled for radical prostatectomy" study and has been uploaded into the Oxford Cancer Translational Data Platform

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3 Introduction

WINGMEN (ethics number 21/SC/0170) is a Phase 0 study of IGF antibody Xentuzumab in men with prostate cancer in the 3-4-week window prior to their scheduled radical prostatectomy. The trial tested the feasibility of recruiting men with early prostate cancer, the tolerability of Xentuzumab in the pre-operative setting, and provided pre- and post-treatment samples for assessment of circulating and tissue markers of prostate cancer progression.

The total duration of participant involvement in the trial was approximately 12 weeks. Treatment duration was 3.5-4 weeks but patients may have received up to 10 treatments if standard of care surgery is delayed for any reason. Patients attended an end-of-study follow-up visit 6 weeks after surgery, which coincided with the standard of care post-surgery assessment.

4 Study Population

The study population is Men with localised biopsy proven prostate adenocarcinoma, scheduled to be treated by radical prostatectomy.

4.1 Inclusion critera

- Men with prostate adenocarcinoma confirmed on prostate biopsy and with sufficient cancer-containing biopsy tissue surplus to diagnostic need to provide ³2 sections for primary endpoint analysis.
- Scheduled for open or robotic radical prostatectomy
- Age ≥ 18 years
- ECOG performance score of 0 or 1.
- The patient is willing and able to comply with the protocol scheduled follow-up visits and examinations for the duration of the study
- Patient is willing and able to give informed consent
- Participants whose partner is of child bearing potential must be willing to ensure that they or their partner use effective contraception during the trial and 70 days thereafter
- Adequate haematologic, renal and hepatic function

4.2 Exclusion criteria

- Treated with systemic corticosteroids, insulin, metformin, other oral hypoglycemic agent, or anti-androgens in the 28 days prior to first dose of study drug
- Diabetes mellitus
- Previous prostate radiotherapy
- Current or previous treatment with xentuzumab or other IGF or GH -modifying therapy
- Patients who are known to be serologically positive for Hepatitis B, Hepatitis C or HIV

- Treatment with any other investigational agent, or treatment in another interventional clinical trial within 28 days prior to enrolment
- Other psychological, social or medical condition, physical examination finding or a laboratory abnormality that the Investigator considers would make the patient a poor trial candidate or could interfere with protocol compliance or the interpretation of trial results

5 Study Schema

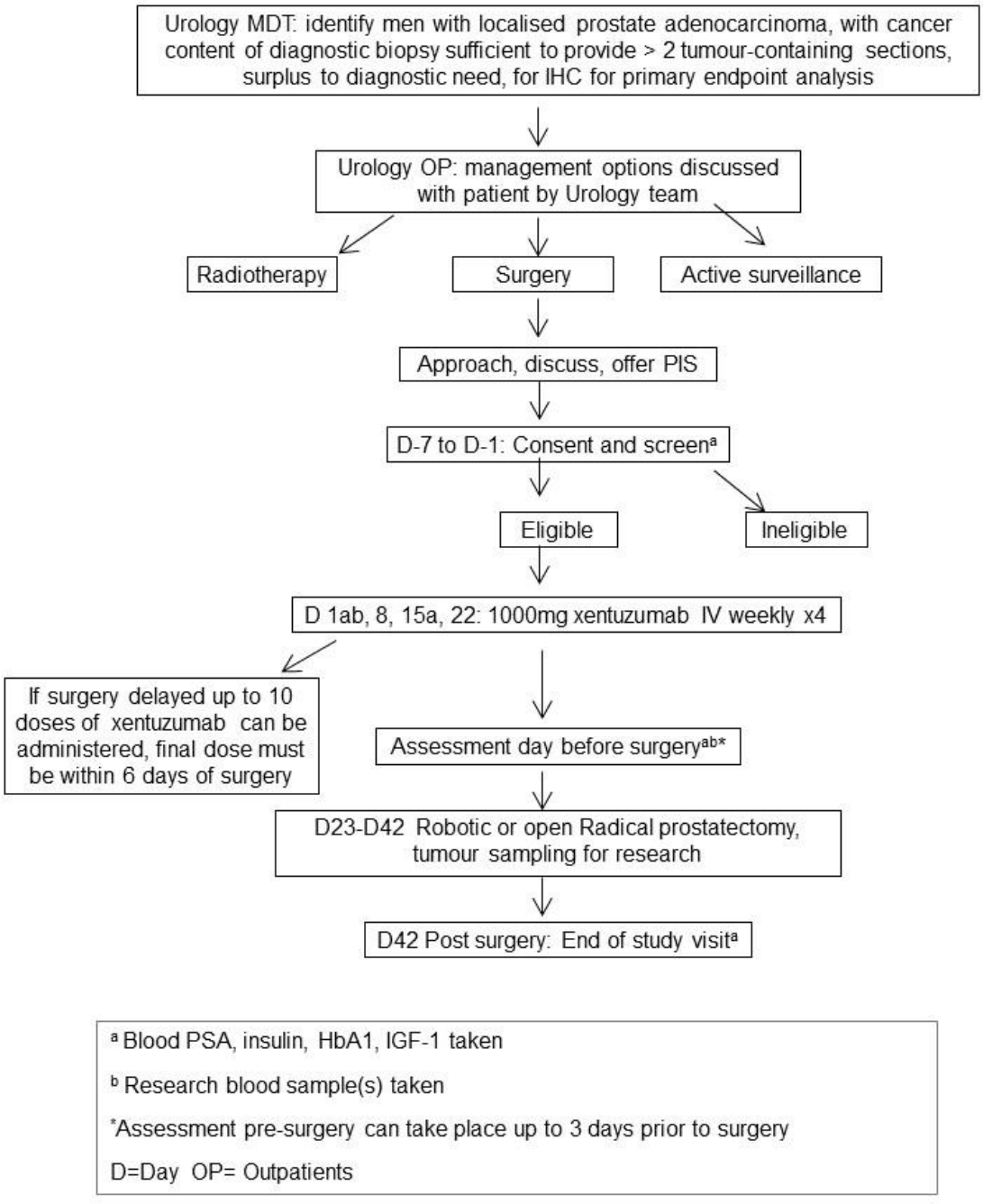

Figure 1: schematic of patient path in the study

6 Clinical trial endpoints

6.1 Primary

Percentage change of phosphor-IGF-1R positive tumour cells following treatment with Xentuzumab - -8.28(-97.94 to 481.68)

Percentage change of phosphor-S5 positive tumour cells following treatment with Xentuzumab - -52.55(-87.61 to 60.11)

6.2 Secondary

Number of participants who had at least 4 doses of Xentuzumab and proceeded to have surgery per the protocol schedule – 26 (100%)

Median delay in surgery in paricipants who had more than 4 doses of Xentuzumab (and whose surgery was delayed by factors other than trial treatment) – 2 (2 to 9)

Number of patients experiencing an adverse event or serious adverse event while on trial – any AE grade 1 or 2 23 (58.2%), any AE grade 3,4, or 5 1 (3.7%)

Number of participants with any adverse event assessed as treatment related (TRAE) while on trial – TRAE grade 1 or 2 17 (63%)

7 Clinical data available on the platform

27 patients were enrolled in the study, 25 of whom completed the study. One patient was lost to follow up and one had disease progression prior to surgery.

Table 1: Clinical data fields available

Demographic:	
	Age
	Sex
	Smocking status
	Ethnicity
Vital signs:	
	Blood pressure
	Pulse
	Temperature
ECG	
	Abnormalities
Characteristics	
	Weight
	Height
Blood test	
	Insulin

	PSA
	Hba1C
	IGF-1
Blood counts	
	Haemoglobin
	White blood cell count
	Neutrophil count
	Platelet count
	Lymphocytes count
Biochemistry	
	Sodium
	Potassiun
	Calcium
	Phosphate
	Urea
	Creatinine
	Total protein
	Albumin
	Bilirubin
	Glucose
	Alkphos
	AST
	ALT
	LDH
	Bilirubin
	EGFR
Diagnosis:	
	Date of diagnosis
	Histology
	T/N/M
	Gleeson Score
	Grade
	Prior Treatment
MRI	
	Date pelvic MRI
	Date marrow MRI
Surgery	
	Date of surgery
	Histology
	T/T1/T2/T3/N
	Gleeson score
	Grad group
	Margins
Progression:	
	Date of progression
	Confirmation method

8 Molecular data available on the platform

8.1 RNA

RNA expression profile of 37 samples, 18 pre- and 19 post-Xentuzumab treatment.

RNA was extracted from FFPE tumour blocks, extracted in the Macaulay lab and sequenced by Azenta.

8.1.1 RNA sequencing

Bulk RNAseq was performed using poly(A) enrichment protocol. Sequencing was performed on an Illumina platform, generating **paired-end 150 bp reads**.

8.1.2 RNAseq analysis

Raw sequencing data were quality-assessed with **FastQC**, adapter-trimmed with **Cutadapt**, and further analysed using the **nf-rnaseq** pipeline (STAR for alignment and Salmon for transcript quantification ver. 0.0.0.9000) against the **Homo sapiens GRCh38** reference genome and annotation.

9 Images available on the platform

9.1 Immunohistochemistry (IHC)

Formalin-Fixed Paraffin Embedded (FFPE) samples from 27 patients collected at diagnostic biopsy (DB), in-theatre core (ITC) or from surgical resections (SR) were used for IHC staining.

Samples were stained for:

- pIGF-1R -nuclear phosphorylated IGF-1R
- pS6 - phosphorylated ribosomal protein S6
- Ki67 - Antigen Kiel 67
- RRM2 - Ribonucleoside-diphosphate reductase subunit M2
- PTEN - phosphatase and tensin homolog

As illustrated in Table 2.

Table 2: List of staining for each patient - Cells marked with "x" indicate that the images are available

Patient ID	Sample type	pIGF1R	pS6	Ki67	RRM2	PTEN
1	DB	x	x			
1	ITC	x	x			
1	SR					x
2	DB	x	x	x	x	
2	ITC	x	x	x	x	
2	SR					x
3	DB	x	x	x	x	
3	ITC	x	x	x	x	
3	SR					x
4	DB	x	x	x	x	
4	ITC	x	x	x	x	
4	SR					x
5	DB	x	x	x	x	
5	ITC	x	x	x	x	
5	SR					x
6	DB	x	x	x	x	
6	ITC	x	x	x	x	
6	SR					x
7	DB	x	x	x	x	
7	ITC	x	x	x	x	
7	ITC	x	x			
7	SR					x
8	DB	x	x	x	x	
8	ITC	x	x	x	x	
8	SR					x
9	DB	x	x	x	x	
9	ITC	x	x	x	x	
9	SR					x
10	DB	x	x	x	x	
10	ITC	x	x	x	x	
10	SR					x
11	DB	x	x	x	x	
11	ITC	x	x	x	x	
11	SR					x
12	DB	x	x	x	x	
12	ITC	x	x	x	x	
12	SR					x
13	DB	x	x	x	x	
13	ITC	x	x	x	x	

13	SR					x
14	DB	x	x	x	x	
14	ITC	x	x	x	x	
14	SR					x
15	DB	x	x	x	x	
15	ITC	x	x	x	x	
15	SR					x
16	DB	x	x	x	x	
16	ITC	x	x	x	x	
16	SR					x
17	DB	x	x			
17	ITC	x	x			
17	SR					x
18	DB	x	x	x	x	
18	ITC	x	x	x	x	
18	SR					x
19	DB	x	x	x	x	
19	ITC	x	x	x	x	
19	SR					x
20	DB	x	x			
20	ITC					
20	SR					
21	DB	x	x	x	x	
21	ITC	x	x	x	x	
21	SR					x
22	DB	x	x	x	x	
22	ITC	x	x	x	x	
22	SR					x
23	DB	x	x			
23	ITC	x	x			
23	SR					x
24	DB	x	x			
24	ITC	x	x			
24	SR					x
25	DB	x	x	x	x	
25	ITC	x	x	x	x	
25	SR					x
26	DB	x	x	x	x	
26	ITC	x	x	x	x	
26	SR					x
27	DB	x	x	x	x	
27	ITC	x	x	x	x	
27	SR					x

10 Study results

All study results available on ClinicalTrial.gov here: Study Results | NCT05110495 | IGF Inhibition With Xentuzumab Prior to Radical Prostatectomy | ClinicalTrials.gov