UNIVERSITY OF BIRMINGHAM

EURO EWING Consortium EEC

Cancer Research UK Clinical Trials Unit @CRCTU

Issue 6

15th October 2019

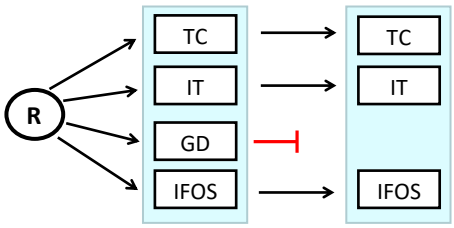
rEECur Newsletter

TRIAL UPDATE

Dear colleagues,

Welcome to the 6th newsletter for the rEECur study. Our two major news items for this newsletter are the results of the second interim assessment and the news that Cancer Research UK has agreed to fund the study in the UK for another three years once the European Commission funding is complete at the end of September.

At the first interim assessment in 2018, the GD arm was closed to recruitment on the grounds that it was unlikely to be competitive with the other arms if recruitment continued, measured either by RECIST imaging response assessment or progression free survival (PFS). In other words, patients in the three remaining arms were more likely to have partial or complete imaging responses at the cycle 4 assessment, or to have better PFS. The second interim assessment took place in July 2019. The data monitoring committee was unable to make a recommendation that one arm was sufficiently worse than the other two arms, judged by either RECIST response (the primary outcome) or PFS (a secondary outcome). Recruitment to the other three arms will therefore continue for another six months. However, at the next interim assessment another arm will almost certainly be dropped.



Recruitment to the IFOS arm is taking place at approximately half the rate of the other two rEECur arms TC and IT. This is particularly true in patients with refractory disease and early relapse, many of whom are not being entered into randomisations that include IFOS. I understand there may be reluctance to randomise patients to a drug that has recently been given during first line treatment. However, the outcomes with IFOS were significantly better than GD at the first assessment, and it remains competitive in the study at the second assessment despite relatively poor recruitment. Therefore, I urge you not to exclude IFOS as a potential arm in patients with refractory disease or early relapse simply because your patients have recently had an ifosfamide-containing regimen.

Finally, thank you for your continued support and recruitment of patients to this important study, the first and largest randomised trial for patients with refractory and recurrent Ewing sarcoma. It is a testament to the UK oncology community that we remain the largest recruiter to rEECur almost five years into recruitment.

Yours,

Dr Martin McCabe

RECRUITMENT

No of patients

- United Kingdom - 103
- Spain - 78
- France - 71
- Italy - 42
- Denmark - 8
- Hungary - 8
- Czech Republic - 6
- Netherlands - 5
- Australia - 5
- Norway - 3
- Belgium - 2
- Switzerland - 2
- Finland - 1
- Poland - 1
- New Zealand - 0
- Germany - 0

UK Site	No of PTs
University College London Hospital	18
Christie Hospital	11
The Queen Elizabeth Hospital	8
Royal Manchester Childrens Hospital	6
Alder Hey Children's Hospital	5
Clatterbridge Cancer Centre	5
Churchill Hospital	5
Addenbrooke's Hospital	5
Leicester Royal Infirmary	5
St James's University Hospital	4
Royal Victoria Infirmary	4
Beatson West of Scotland Cancer Centre	4
Leeds General Infirmary	3
John Radcliffe Hospital	3
Queen's Medical Centre, Nottingham	3
Nottingham City Hospital	2
Weston Park Hospital	2
Royal Marsden Hospital Sutton	2
Royal Marsden Hospital London	2
Birmingham Children's Hospital	2
Royal Hospital for Sick Children Edinburgh	2
Royal Belfast Hospital for Sick Children	1
Freeman Hospital	1
Southampton General Hospital	1
Sheffield Children's Hospital	1
Noah's Ark Children's Hospital for Wales	1

Change of address for Biological Samples - Leeds

	At Diagnosis	After Cycle 2	After Cycle 4	After Cycle 6[a]	Progression/
Frozen tumour – snap frozen. Ship on dry ice to reference centre	●				●
Paraffin embedded tumour block Send at room temperature to pathology reference centre	●				●
Bone marrow aspirate (0.5 ml x 2, right and left) into PAXgene™ Blood RNA Tubes – DO NOT POOL. Store at -80°	●				●
Whole blood (2 ml x 1) into PAXgene™ Blood RNA Tube. Store at -80°C. Ship on dry ice to reference centre.	●	●	●	●	●
Whole blood (5 ml) into EDTA tube; separated into plasma (0.5 ml aliquots) and cellular fraction. Store at -80°C.	●	●	●	●	●
Whole blood (5ml into EDTA) for sequencing of constiutional DNA Store at -80°C. Ship on dry ice to reference	●				

The laboratory in Leeds has recently re-located and this has meant a change of address. Please note the current Sample forms and Laboratory Manual still have the old address and will be amended in due course. Please contact the team at Leeds before shipping any samples at ccrg.reecur@leeds.ac.uk

New address:
Leeds Institute of Medical Research at St. James's
Children's Cancer Research Group, Level 5
Welcome Trust Brenner Building
St. James's University Hospital
Beckett Street, Leeds. LS9 7TF

The **new contact numbers** are:
0113 3438448 and 0113 3438436.

Please remember to record the collection of all biological study samples on the 'Sample form' and fax a copy to CRCTU.

Only patients who have consented to biological studies should have samples taken.

[a] In treatment arms TC, IT, GD only
[b] If appropriate

OTHER IMORTANT MESSAGES

Treatment CRFs—Toxicities

Please note, only specific adverse reactions, or toxicities, are collected on the treatment form. The full CTCAE is no longer available on the eRDC. Please refer to page 3 of Treatment CRF v3.0 for the list of toxicities. It is not necessary to record any other toxicities other than those listed. The below now demonstrates how the eRDC now appears. Toxicities are listed in the table or click "other" to report infection or oedema.

CTCAE Category	CTCAE Toxicity
Gastrointestinal disorders	Vomiting
Gastrointestinal disorders	Nausea
General disorders and administration site conditions	Fatigue
Gastrointestinal disorders	Diarrhea
Gastrointestinal disorders	Colitis
Investigations	Creatinine increased
Renal and urinary disorders	Chronic kidney disease
Renal and urinary disorders	Hematuria
Investigations	Blood bilirubin increased
Investigations	Alanine aminotransferase increased
Investigations	Aspartate aminotransferase increased
Investigations	GGT increased
Blood and lymphatic system disorders	Febrile neutropenia
Nervous system disorders	Peripheral motor neuropathy
Nervous system disorders	Peripheral sensory neuropathy

1 2

Please use other to record infection and oedema

Add Other Toxicity

It is not necessary to record any other toxicities other than those listed above

RECIST Reporting

It is vital that imaging is reported according to RECIST 1.1 criteria. These reports should then be used to complete Tumour Assessment Baseline and Response Forms. The primary outcome measure for phase II is objective imaging response measured according to RECIST 1.1 criteria, so it is imperative we adhere to this. Thank you all in advance!

rEECur Sub-Studies

The quality of life (QoL) and PETCT studies are important secondary outcome measures for rEECur. **Please remember to provide QoL questionnaires to patients and parents/guardians (if applicable) at baseline, after Cycle 2 and after Cycle 4, and organise PETCT scans at baseline and post Cycle 4.** Completed questionnaires should be posted to the rEECur Office. If not done, please notify us.

Contact the rEECur Trial Team
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