UNIVERSITY OF BIRMINGHAM

EURO EWING Consortium EEC

@CRCTU Cancer Research UK Clinical Trials Unit

Issue 11

rEECur Newsletter

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rEECur reaches 500 patients

rEECur at ASCO!

TRIAL SUMMARY

Welcome to the 11th rEECur newsletter. Since our last edition:

1. 500 patients have been enrolled onto rEECur; the first randomised and largest trial conducted in relapse or refractory Ewing sarcoma
2. The trial has opened at a total of 200 sites in 17 countries across Europe and Australia & New Zealand
3. The outcomes of the phase III analysis of the TC vs IFOS arms were presented at the plenary session at the 2022 ASCO annual meeting, after successfully being selected from over 6,000 abstracts submitted. The rEECur abstract was also included in the ASCO official press programme. https://ascopost.com/videos/2022-asco-annual-meeting/martin-mccabe-on-ewing-sarcoma-assessment-of-topotecan-cyclophosphamide-and-high-dose-ifosfamide/

Summary of Results in rEECur to Date

Thanks to all of the rEECur investigators and the patients who have agreed to take part, the rEECur study has for the first time accrued randomised data for four widely used chemotherapy regimens and is now accruing data for a fifth regimen, (carboplatin/etoposide – CE).

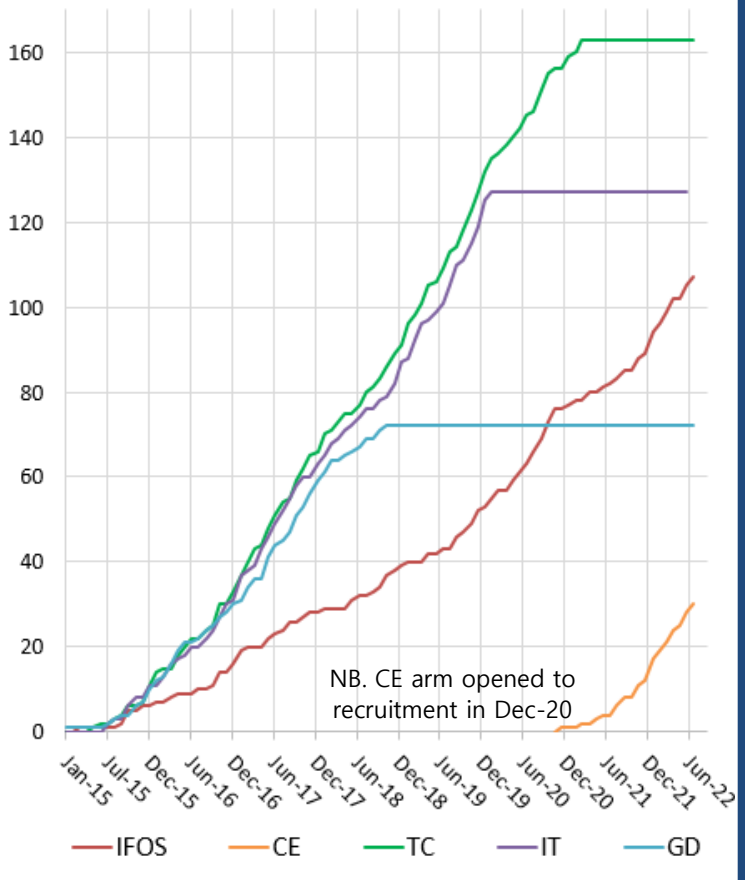
⇒ **GD arm** - closed in November 2018 on the basis that it was performing worse than the remaining three arms and was unlikely to be significantly better than the most effective arm for objective imaging response (OR), event-free survival (EFS) and overall survival (OS) (presented at ASCO 2019). *https://www.doi.org/10.1200/JCO.2019.37.15_suppl.11007*

⇒ **IT arm** - closed in March 2020 on the basis that it was performing worse than the remaining two arms and was unlikely to be significantly better than the most effective arm for OR, EFS and OS (presented at ASCO 2020). *https://www.doi.org/10.1200/JCO.2020.38.15_suppl.11502*

⇒ **TC arm** - suspended in March 2021 based on observed differences between the out-comes of patients randomised to the TC and IFOS arms. Further analysis was performed after six months when additional follow-up data had accrued. IFOS was more effective than TC for EFS and OS, albeit with more renal and CNS toxicity. The TC arm was closed in October 2021.

https://doi.org/10.1200/JCO.2022.40.17_suppl.LBA2

Recruitment over Time by Arm



Upcoming new combination arm - Ifosfamide & Lenvatinib

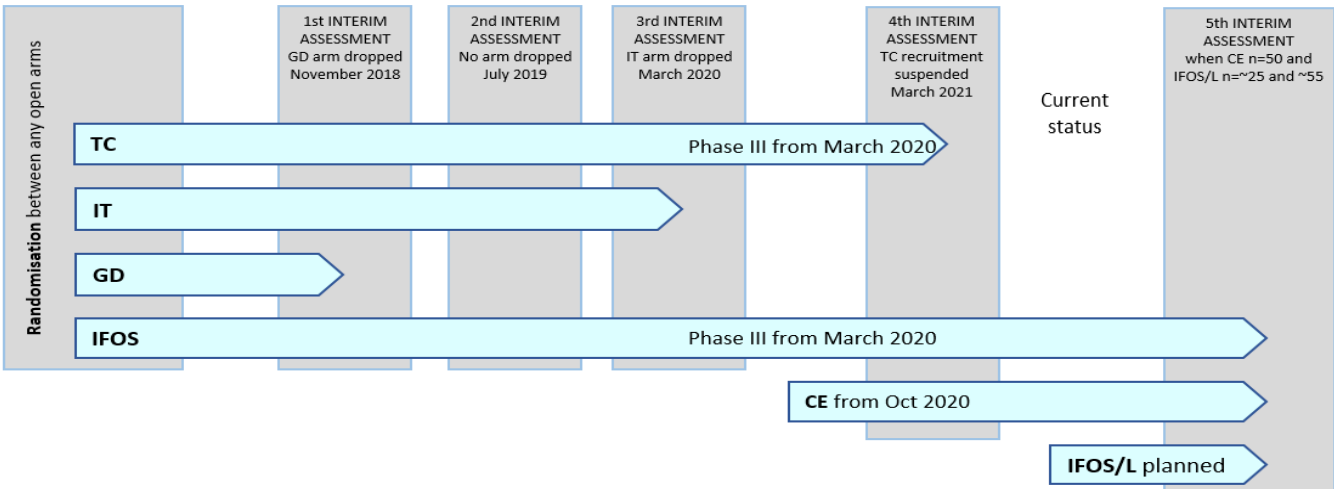
Multi-receptor tyrosine kinase inhibitors (RTKIs) such as lenvatinib, are of particular interest in Ewing sarcoma because of their promising single agent activity in relapsed disease. We propose to study the toxicity, safety and activity of lenvatinib in combination with ifosfamide, as a new arm (IFOS-L) in the rEECur study.

Patients will receive 4 cycles of intravenous ifosfamide (15g/m^2/cycle) and continuous daily oral lenvatinib in the form of a capsule (14mg/m^2, with a max dose of 24mg). Patients will have the option to discontinue ifosmafide or lenvatinib and continue with the other chemotherapy alone, or discontinue both chemotherapies at the same time. Patients who have not progressed will receive up to 2 years' treatment with Lenvatinib.

WHY IFOS?

The phase III comparison concluded that based on the observed data, there was a 95% probability that IFOS was more effective than TC at prolonging EFS and OS. A randomised phase II trial of ifosfamide (9 g/m^2/cycle) and etoposide +/- lenvatinib in relapsed osteosarcoma (the OLIE study, NCT04154189) recently finished recruiting. The ifosfamide/etoposide regimen used in the OLIE study was demonstrated to have acceptable toxicities. Although the rEECur ifosfamide regimen is more intensive, the rEECur regimen does not include etoposide. Therefore, we anticipate the ifosfamide/lenvatinib combination will be tolerable. The DMC has agreed to meet early to review toxicity after the first 10 patients.

The IFOS-L arm will be introduced this year as part of a substantial amendment to the study. Keep an eye out for the new protocol!

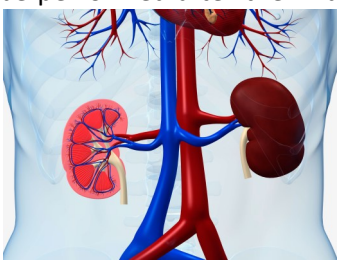


Renal Function Monitoring

GFR (calculated creatinine clearance (Ccrea) or isotopic)) and tubular function **must be assessed before randomisation and monitored prior each cycle of treatment.** They should also be performed after the final cycle of treatment.

Dose modification guideline apply and can be found in section 7 of the protocol.

Investigators are encouraged to use an isotope clearance method to measure GFR in preference to a calculated estimate based on creatinine clearance for both the IFOS and CE regimens, particularly if the calculated GFR is <90ml/min/1.73m^2 since both are nephrotoxic and all calculated methods have inaccuracies.



SciePro / istock / Getty Images

Contact the rEECur Trial Team

Please email the rEECur trial mailbox in the first instance and provide a telephone number for us to call you back on if required/urgent. We operate a mixed model of home and office working

The mailbox is monitored continuously as per office hours below.

Office hours 09:00-17:00 GMT, Monday-Friday ✉ **reecur@trials.bham.ac.uk**

Please continue to report SAEs within 24 hours of becoming aware of the event to **reg@trials.bham.ac.uk**