CARDIFF

Partnership

Increased partnership working between NHS organisations across Wales

Recognition of effective working partnership

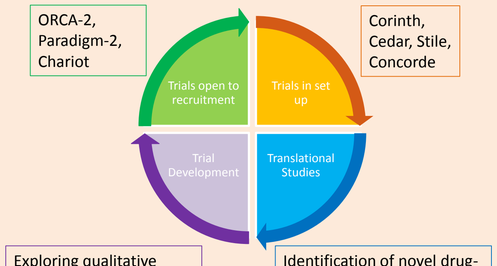
- Shortlisted in the Clinical Research Nursing Category, Nursing Times Award 2018

- Many of the Research Nurses working in Cardiff facilities funded by ECMC

ECMC Network Activity

- **Initiated and led ECMC Haematology Network Group** (involves most ECMC centres and two non-ECMC centres)
- **JING** (Annual Meeting Cardiff Jan 19)
- **Increased interactions with ECMC Paediatric Network**
- **ECMC Network PPI group** (Deputy Chair, Cardiff)
- **Research Nurses Network Group** (Member, Cardiff)

Drug/RT trials



- Developing a drug/RT clinical trial portfolio.
- Working in partnership with other centres, including Liverpool and ECMC network members; Glasgow, Oxford around the UK.
- Developing translational studies together with ECMC centres and industry.

Key Trial: MONOCLE

Chief Investigator: Dr Steven Knapper, Cardiff University and Cardiff & Vale UHB.

A Phase 2 Trial of the monocyte-targeted histone deacetylase inhibitor tefinostat (CHR-2845) in chronic myelomonocytic leukaemia (CMML)

Background

- Pre-clinical in vitro studies characterising properties of Tefinostat in monocytoid AML funded by ECMC.

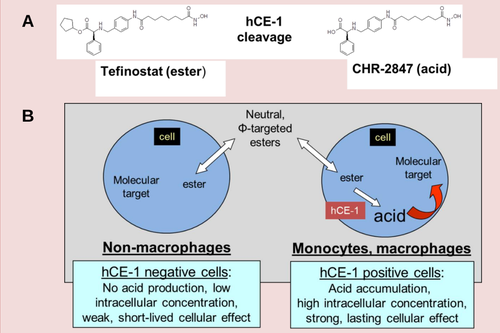


Fig 1. A) Structures of Tefinostat and CHR-2847. **B)** Schematic representation of 'esterase sensitive motif' mechanism of drug activation.

- Trial managed by the Centre for Trials Research, Cardiff University.
- Sponsor was Cardiff University.
- Patients were enrolled at 9 trial centres, 6 of which were members of the ECMC network.

Trial Design

- Single arm phase 2 trial conducted to a Bryant and Day 2-stage design with **dual-primary-endpoints** of **safety** and **clinical efficacy**.

Results (Stage 1)

- 20 patients received 'Tefinostat treatment'.

Table 1. Summarised clinical outcomes.

Outcome	No. (% of evaluable)	
BM response (partial)	1	(8%)
Stable disease	9	(69%)
Progressive disease	3	(23%)
(Non evaluable)	7	(n/a)

Table 2. Details of clinical responses

Age Sex	FAB	Genetics	Response	Description of response
71M	Proliferative (WBC 34.3)	ASXL1 NRAS SETBP1 SRSF2	Partial bone marrow response	CMML-2 with 14% marrow blasts at baseline; red cell transfusion dependency. After 6 cycles, <5% BM blasts, with persisting marrow hypercellularity and peripheral leucocytosis/ low level monocytosis. Achieved red cell transfusion independence from cycle 1 - 14. Received 15 cycles of Tefinostat prior to disease progression.
75M	Proliferative (WBC 19.9)	ASXL1 IDH2 NRAS SRSF2	Clinical Benefit*	CMML-1 with 2% blasts, fibrotic marrow (gd 2-3 reticulin); red cell transfusion dependency. Reduction in MPN/SAF total symptom score from 112 to 31 after 3 cycles of Tefinostat (*not sustained to end of cycle 6). Reduction in WBC from 35.9 to 7.6x10^9/l and monocyte count from 7.6 to 2.0x10^9/l. No impact on bone marrow appearances or transfusion dependency. Stopped Tefinostat treatment after 6 cycles.

Summary/Conclusions

- Trial endpoint for safety was satisfied; Tefinostat was generally well tolerated.
- Trial endpoint for clinical efficacy did not achieve the pre-defined minimum number of clinical responses to Tefinostat.
- Patient recruitment was not continued into stage 2 of this phase 2 study.

Presented at American Society of Haematology, San Diego, December 2018.

Key Trial: FAKTION

Chief Investigators: Dr Rob Jones, Cardiff University and Velindre Cancer Centre, Cardiff and Dr Sacha Howell, The University of Manchester and The Christie NHS Foundation Trust

Results of a Phase 1b/2 randomised placebo-controlled trial of Capivasertib (AZD5363) plus fulvestrant versus placebo plus fulvestrant after relapse or progression on an aromatase inhibitor in metatastic ER-positive breast cancer (FAKTION).

Background

- PI3K and AKT cell signalling network deregulated in cancer.
- AKT activation mediates resistance to treatment.
- Capivasertib is a pan-AKT kinase inhibitor.

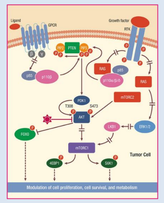


Fig 1. Modulation of cell proliferation, cell survival and metabolism.

- Trial managed by the Centre for Trials Research, Cardiff University.
- Sponsor was Velindre Cancer Centre, Cardiff.

Research questions

- Does the addition of capivasertib to fulvestrant increase the progression free survival in women with ER+ve advanced or metastatic breast cancer?
- Is capivasertib safe, tolerable, and feasible to deliver when combined with fulvestrant?
- What is the efficacy of capivasertib plus fulvestrant in sub-populations of patients with or without activation of the tumour PI3K/Akt/PTEN pathway?
- What is the impact of capivasertib on the pharmacokinetics of fulvestrant?

Results

- Phase I study confirmed starting dose of capivasertib of 400mg.

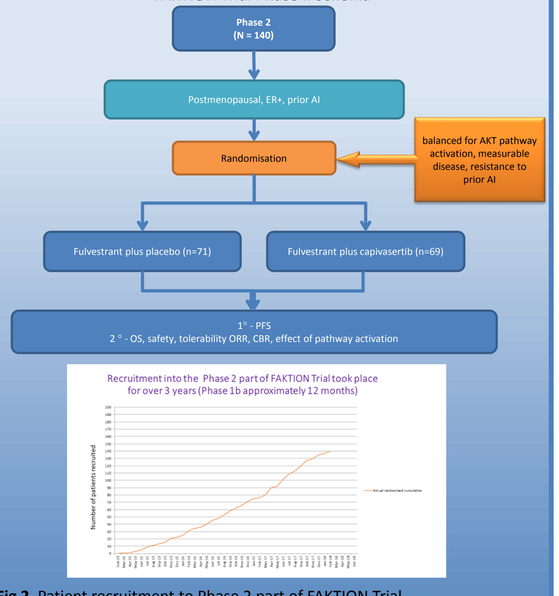


Fig 2. Patient recruitment to Phase 2 part of FAKTION Trial

This data will be presented as an Oral presentation: at the American Society of Clinical Oncology, Chicago on 4th June, 2019.

Cardiff ECMC: The Future

Advanced Therapies → Drug/RT Trials → Haematology Network → Paediatric Studies

Continuing and developing partnerships and networks

- Cellular and gene therapies
- ECMC Haematology Network
- Drug/RT trials
- Paediatric studies
- Development of Cardiff University Integrated Cancer Research (CUICR)
- Development of Cancer Research Strategy

CReSt Cymru Cancer Research Strategy for Wales

- Working partnership with Wales Cancer Network

Rhwydwaith Canser Cymru Wales Cancer Network

Building on translational work

- Drug/RT studies

Our Partners

Contact Us:

Centre Manager: Jo Baker ✉ CardiffECMC@Cardiff.ac.uk

https://www.ecmcnetwork.org.uk/cardiff