National Research Ethics Committee

NREC-CT B

22nd of June 2022

Attendance

Name	Role
Dr Cliona McGovern	Chairperson, NREC-CT B
Dr Jean Saunders	Deputy Chairperson, NREC CT-B
Ms Serena Bennett	Committee Member, NREC-CT B
Mr Philip Berman	Committee Member, NREC-CT B
Dr Enda Dooley	Committee Member, NREC-CT B
Dr John Hayden	Committee Member, NREC-CT B
Mr Gavin Lawler	Committee Member, NREC-CT B
Prof. Colm O'Donnell	Committee Member, NREC-CT B
Ms Caoimhe Gleeson	Committee Member, NREC-CT B
Prof. Abhay Pandit	Committee Member, NREC-CT B
Prof. John Faul	Committee Member, NREC-CT B
Dr Mark Robinson	Committee Member, NREC-CT B
Ms Mandy Daly	Committee Member, NREC-CT B
Prof Andrew Green	Committee Member, NREC-CT B
Ms Susan Kelly	Committee Member, NREC-CT B
Ms Deirdre MacLoughlin	Committee Member, NREC-CT B
Prof Seamus O'Reilly	Committee Member, NREC-CT B
Dr Christina Skourou	Committee Member, NREC-CT B
Dr Susan Quinn*	Programme Manager, National Office for RECs
Dr Emma Heffernan*	Project Officer, National Office for RECs

Dr Jane Bryant*	Project Officer, National Office for RECs
Dr Laura Mackey	Project Officer, National Office for RECs
Ms Rachel McDermott	Project Administrator, National Office for RECs
Dr Emily Vereker	Head of Office, National Office for RECs

*Drafted minutes

Apologies: Prof David Smith, Dr Eimear McGlinchey, Ms Paula Prendeville, Dr Lorna Fanning, Dr Mary McDonnell Naughton, Ms Mandy Daly, Prof Abhay Pandit

Quorum for decisions: Yes

Agenda

Welcome & Apologies

Application 22-NREC-CT-104

Application 22-NREC-CT-109

Application 21-NREC-CT-099_AMEND-2

Application 22-NREC-CT-059_AMEND-2

Application 21-NREC-CT-073_AMEND-3

Application 21-NREC-CT-122_AMEND-2

AOB

The Chair welcomed the NREC-CT B.

The Minutes from the NREC-CT B meeting on the 25th of May were approved.

Applications

22-NREC-CT-104

Principal Investigator: Dr Paula Calvert

Study title: A Randomized, Open-Label, Phase 3 Trial of Tisotumab Vedotin vs Investigator's Choice Chemotherapy in Second- or Third-Line Recurrent or Metastatic Cervical Cancer

Lead institution: University Hospital Waterford

EudraCT No.: 2019-001655-39

- NREC-CT comments:

- The Committee noted this clinical trial application represents an open-Label, Phase 3 Trial of Tisotumab Vedotin vs Investigator's Choice Chemotherapy in Second- or Third-Line Recurrent or Metastatic Cervical Cancer
- The Committee noted the merit of the study and quality of the protocol.
- The Committee was unable to give a favourable ethics opinion on the research

  - NREC-CT Decision:

- Unfavourable

  - Additional Information Required

- The Committee considers the protocol for the study of high scientific merit and recognises its importance to the cohort of potential participants. However, the Committee found the submission to be of poor quality and substandard. The NREC application and PIL/ICF contain substantial errors, and do not align with the protocol submitted. The Committee had strong concerns regarding the PIL/ICF deeming it misaligned with the protocol, unclear particularly regarding genetic testing, biological sampling and storage. The PIL/ICF needs major revisions, review and input from an expert to bring it to an acceptable level appropriate to distribute to patients in Ireland. Particular focus is required to correct typographical errors, grammar and to ensure that potential participants are adequately informed regarding the protocol in order to be able give their informed consent to participate in the study. The Committee concluded that in its current format the PIL/ICF is not fit to present to the vulnerable population of potential participants and is a disservice to the trial and its potential participants.

- This decision is based on the application form, protocol and supporting documentation outlined in Appendix 1.
- The Committee asked that the Sponsor and Investigator at each site in Ireland is informed of the outcome of this review.

22-NREC-CT-109

Principal Investigator: Dr Kamal Fadalla

Study title: A Phase 1/2 Open-label Study to Investigate the Safety and Tolerability, Efficacy, Pharmacokinetics, and Immunogenicity of Modakafusp Alfa (TAK-573) as a Single Agent in Patients with Relapsed Refractory Multiple Myeloma

Lead institution: St Vincent's University Hospital

EudraCT No.: 2021-006038-037

- NREC-CT comments:

- The Committee noted this clinical trial application represents an open-label Study to Investigate the Safety and Tolerability, Efficacy, Pharmacokinetics, and Immunogenicity of Modakafusp Alfa (TAK-573) as a Single Agent in Patients with Relapsed Refractory Multiple Myeloma
- The Committee commented that the PIL/ICF was comprehensive and noted the quality of the plain English language style.
- The Committee agreed that additional information was required to inform its deliberations and therefore, was not yet in a position to return a final ethics decision

- NREC-CT Decision:
- Request for further information

- Additional Information Required:
- The Committee considered the PIL to be comprehensive but lengthy and requested a separate plain English executive summary of the salient points of the study (Summary PIL) is provided.
- The Committee queried whether the participant is required to cease other cancer medication when commencing this trial drug, and if so requested that this needs to be made more explicit to potential participants. This should be stated early on in the PIL/ICF and include information on the implications and associated risks.
- The Committee requested that images/diagrams are included in the Main and Summary PIL/ICF to aid the participant in understanding the envisaged procedure for the project.
- The Committee recommended that for listed side effects, in addition to stating '1 in 10/10%' it is helpful to state 'very common/ common/ uncommon' etc, to help the participant to understand the risks.
- The Committee requested that information regarding contraception is clarified for participants. Specifically, the reference to a surgically sterilised male requiring barrier contraception (p.13 PIL/ICF) does not align with the advice to female participants that they are required to use barrier contraception if their partner if not sterilised.
- The Committee noted that there are references to the UK and NHS in the ICF and pregnant partner PIL/ICF, and requests that all participant materials be adapted for Irish audience/law/sites.
- The Committee queried the role of the 'witness' in the consent section (p.22 PIL/ICF), they noted this is not standard practice in Ireland wherein a person is blind or has literacy issues. Efforts should be made to enable the person, who has capacity, to consent for themselves without the need for a witness. Information should be made

accessible e.g., brail or using ‘browse aloud’ software which reads the content to the blind person. Such persons should have a facility to verbally record their consent which can be noted on any such consent forms.

- The Committee requested that the sentence (p.16 PIL/ICF) “You also can ask that all samples that are kept which can be identified as coming from you are destroyed to prevent further analyses” should be built into the consent form.
- The Committee requested confirmation that the data referred to is anonymised rather than pseudo-anonymised in the statement “The data provided to external researchers will not include information that identifies you” (p.19 PIL/ICF)
- The Committee noted that the application for consent of further use is not in line with national regulations on ‘explicit consent’. The Committee requests that the consent form for future research is separate from the main PIL, and that the applicant provides participants with specific choices, in line with national regulations, as to how their samples and underlying data will be used for future purposes.
- The Committee requested the CVs of all site Principal Investigators are included – these were absent for Vitaliy Mykytiv (Cork University Hospital) and Peter O’Gorman (Mater Misericordiae University Hospital).
- The Committee noted the DPIA provided is not study specific, and requested a comprehensive study specific DPIA is provided, compiled with an input from the site DPO.

21-NREC-CT-099_AMEND-2

Principal Investigator: Dr Richard Bambury

Study title: A PHASE III, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER TRIAL TESTING IPATASERTIB PLUS ABIRATERONE PLUS PREDNISONE/PREDNISOLONE RELATIVE TO PLACEBO PLUS ABIRATERONE PLUS PREDNISONE/PREDNISOLONE IN ADULT MALE PATIENTS WITH ASYMPTOMATIC OR MILDLY SYMPTOMATIC, PREVIOUSLY UNTREATED, METASTATIC CASTRATERESISTANT PROSTATE CANCER

Lead institution: Cork University Hospital

EudraCT No.: 2016-004429-17

- NREC-CT comments:

- The Committee noted this clinical trial application represents a substantial amendment to a placebo-controlled trial of Ipatasertib in combination with other therapies in treatment of metastatic prostate cancer

- The NREC-CT B agreed that while some clarifications were required, this application could be designated as Favourable with Conditions.

- NREC-CT Decision:
- Favourable with Conditions

- Additional Information Required:
- The Committee requests that the PIL is amended to provide clarification regarding Irish law surrounding the sharing of study results.

22-NREC-CT-059_AMEND-2

Principal Investigator: Dr Ray McDermott

Study title: A Phase 2 Clinical Trial of Nivolumab and Nivolumab Plus Ipilimumab in Recurrent and Metastatic Microsatellite High (MSI-H) Colon Cancer and non-MSI-H Colon Cancer

Lead institution: St Vincent's Hospital

EudraCT No.: 2013-003939-30

- NREC-CT comments:
- The Committee noted this clinical trial application represents a substantial amendment to a Trial of Nivolumab and Nivolumab Plus Ipilimumab in Recurrent and Metastatic Microsatellite High (MSI-H) Colon Cancer and non-MSI-H Colon Cancer

- NREC-CT Decision:
- Favourable

21-NREC-CT-073_AMEND-3

Principal Investigator: Dr Amjad Hayat

Study title: A Phase 3, Multicenter, Open-Label, Long-Term Trial to Evaluate the Safety and Efficacy of Efgartigimod (ARGX-113) PH20 Subcutaneous in Adult Patients with Primary Immune Thrombocytopenia

Lead institution: University Hospital Galway

EudraCT No.: 2020-004033-20

- NREC-CT comments:

- The Committee noted this clinical trial application represents a substantial amendment to a Long-Term Trial to Evaluate the Safety and Efficacy of Efgartigimod (ARGX-113) PH20 Subcutaneous in Adult Patients with Primary Immune Thrombocytopenia
- The Committee agreed that while some clarifications were required, this application could be designated as Favourable with Conditions.

- NREC-CT Decision:
- Favourable with Conditions

- Additional Information Required:
- The Committee request that page 5 of the ICF includes a clear explanation of the word ‘lipid’.

21-NREC-CT-122_AMEND-2

Principal Investigator: Prof Noel Gerard (Gerry) McElvaney

Study title: A Prospective Phase III Multi-center, Placebo Controlled, Double Blind Study to Evaluate the Efficacy and Safety of “Kamada-AAT for Inhalation” 80 mg per day in Adult Patients with Congenital Alpha-1 Antitrypsin Deficiency with Moderate and Severe Airflow Limitation (40% ≤ FEV1 ≤ 80% of predicted; FEV1/SVC ≤ 70%)

Lead institution: Beaumont Hospital

EudraCT No.: 2019-000602-30

- NREC-CT comments:
- The Committee noted this clinical trial application represents a substantial amendment to a study to evaluate the efficacy and safety of “Kamada-AAT for Inhalation” in Adult Patients with Congenital Alpha-1 Antitrypsin Deficiency with Moderate and Severe Airflow Limitation
- The Committee agreed that additional information was required to inform its deliberations and therefore, was not yet in a position to return a final ethics decision

- NREC-CT Decision:
- Request for Further Information

- Additional Information Required:
- The Committee requested discrepancies in storage details for the medication be clarified across submitted document

- AOB:

- Deputy Chair Dr Jean Saunders gave an update on the Bootcamp process to Committee members.
- Dr Laura Mackey from the National Office gave a presentation on the CTR legislation and the CTIS system, and questions on this were discussed.

The Chair closed the meeting.