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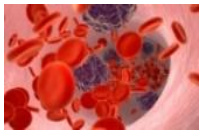
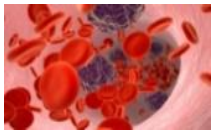


Myeloproliferative Neoplasm (MPN) Clinical Trials Portfolio



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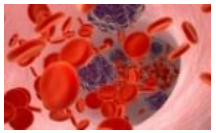
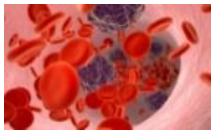
Recruiting MPN Trials

BLU-285-2202 (Interventional) Systemic mastocytosis PI: Dr Deepti Radia	An open-label, single arm, Phase 2 study to evaluate efficacy and safety of Avapritinib (BLU-285), A Selective KIT Mutation-targeted Tyrosine Kinase Inhibitor, in Patients with Advanced Systemic Mastocytosis. ***Eligibility criteria:***-Age 18 or over and have an ECOG performance status of 0-3. must have a diagnosis of AdvSM,ASM,SM-AHN or MCL and patient must have a BM biopsy.
Mithridate (Interventional- All cohorts open) MPN PI: Prof C Harrison	A phase III, randomised, open-label, Multicenter International Trial comparing ruxolitinib with either HydRoxycarbamIDe or interferon Alpha as first line Therapy for high risk polycythaemia vera. ***Eligibility criteria:-*** 1) Patient must be 18 years or over. 2) Diagnosis of PV meeting WHO criteria within past 10 years. 3) Meets criteria of high risk PV: defined as WBC>11 x 10^9/l* and at least one of the following: • Age> 60 years • Prior thrombosis or major haemorrhage related to disease • Platelet count> 1000 x 10^9/l* (* at any time since diagnosis) 4)Patients may have received antiplatelet agents and venesection. 5) Patients may have received one or less cytoreductive therapy for less than 2 years (but they should not be resistant or intolerant to that therapy) 6) Able to provide written consent
PHAZAR (Only observational arm is open) Accelerated or blast phase MPN PI: Prof Claire Harrison	A Phase 1b Study to assess the safety and tolerability of oral Ruxolitinib in combination with Azacitidine in patients with Advanced Phase MPN, including MDS or AML arising from MPN ***Eligibility Criteria:*** -Age 16 and over, Diagnosis of ET,PV or MF with either bone marrow blasts (with or without dysplastic changes) or >20% bone marrow blasts, ECOG performance status:0-3.
Constellation (Interventional- only transfusion dependent and JAK naïve arms open) Myelofibrosis PI: Dr Claire Harrison	A Phase 1/2 Study of CPI-0610, a Small Molecule Inhibitor of BET proteins: Phase 1 (Dose escalation of CPI-0610 in patients with haematological malignancies) and Phase 2 (Dose expansion of CPI-0610 with and without Ruxolitinib in patients with Myelofibrosis. ***Eligibility criteria:***- *Age 18 or over and have an ECOG performance score* ≤2. Diagnosis of AML,ALL,CML in blast crisis, MDS,MDS/MPN or MF.
DCC-2618-01-001 (Interventional) Systemic Mastocytosis PI: Dr Deepti Radia	A multicentre Phase 1, Open-Label Study of DCC-2618 to assess safety, tolerability, efficacy and pharmacokinetics in patients with advanced malignancies. ***Eligibility criteria:-*** Age 18 or over, gastrointestinal stromal tumour patients must have KIT it PDGFRA mutation and must have progressed on or had intolerability to at least 1 but not more than 4 lines of systemic anticancer therapy, Systemic mastocytosis (SM patients) must have a confirmed diagnosis of advanced SM according to 2016 world health organisation (WHO) criteria for SM.
ACE-536 (Interventional) Myelofibrosis PI Prof C Harrison	Phase 2, Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Luspatercept (ACE-536) in Subjects with Myeloproliferative Neoplasm-Associated Myelofibrosis and Anaemia with and without Red Blood Cell-Transfusion Dependence ***Eligibility Criteria:*** -Age 18 or over, subject has MPN-associated myelofibrosis, subject has anaemia and an ECOG performance score ≤2. Includes patients currently on ruxolitinib, but may also not be on the drug
KRT-232-101 (Interventional- All cohorts open) MPN PI: Dr Donal Mclornan	An Open-Label, Phase 2a/2b Study of KRT-232 in Subjects With Primary Myelofibrosis (PMF), Post–Polycythemia Vera MF (Post–PV-MF), Or Post–Essential Thrombocythemia MF (Post–ET-MF) Who Have Failed Ruxolitinib ***Eligibility criteria:***-Age 18 or over and have an ECOG performance status of 0 to 2. Palpable splenomegaly at least 5cm below left costal margin. Confirmed diagnosis of PMF, Post –PV-MF or Post-ET-MF. High –risk intermediate-2 risk, or intermediate-1 risk. Adequate haematological hepatic and renal organ function (within 14 days prior to the first dose of KRT-232)
KRT-232-102 (Interventional- All cohorts open) MPN PI: Prof Claire Harrison	A Two-Part, Randomized, Open-label, Multicenter, Phase 2a/2b Study of the Efficacy, Safety, and Pharmacokinetics of KRT-232 Compared to Ruxolitinib in Patients with Phlebotomy-Dependent Polycythemia Vera ***Eligibility criteria:-*** Age 18 or over and have an ECOG performance status of 0,1 or 2. Documentation that the patient has met the WHO criteria for the diagnosis of PV. Subject must be phlebotomy dependent.

Myeloproliferative Neoplasm (MPN) Clinical Trials Portfolio





Recruiting MPN trials Cont.

Imago-7289-CTP-102 (Interventional) PI Prof C Harrison	A Multi-Center, Open Label Study to Assess the Safety, Steady-State Pharmacokinetics and Pharmacodynamics of IMG-7289 in Patients with Myelofibrosis. ***Eligibility Criteria:-*** Age 18 or over and have an ECOG performance score of 2 or less. Diagnosis of either primary myelofibrosis (PMF) per World Health Organization criteria, post-polycythaemia vera myelofibrosis (PPV-MF), or post-essential thrombocythaemia myelofibrosis (PET-MF) and meet the following additional criteria: a. Classified as high risk (3 prognostic factors) OR intermediate risk-2 (2 prognostic factors): i. Age > 65 years ;ii. Presence of constitutional symptoms (weight loss, fever, night sweats);iii. Marked anaemia (Hgb < 10g/dL)*; iv. History of leukocytosis [WBC > 25 x109/L (25,000/µL)]; v. Circulating blasts > 1%. Be refractory or resistant to, or intolerant of available approved therapy, or in the Investigator's judgment, are not candidates for available approved therapy, Peripheral blast count ≤10% prior to dosing.
Celgene FEDR-MF-002 (Interventional) PI Prof C Harrison	A Phase III, Multicenter, Open-Label, Randomized Study to Evaluate the Efficacy and Safety of Fedratinib Compared to Best Available Therapy in Subjects with DIPPS-Intermediate or High-risk Primary Myelofibrosis, Post-Polycythemia Vera Myelofibrosis or Post-Essential Thrombocythemia Myelofibrosis and Previously Treated with Ruxolitinib. The "FREEDOM 2" trial. ***Eligibility Criteria:-*** Age 18 or over and have an ECOG performance status of 0,1 or 2. Diagnosis of primary myelofibrosis (PMF) according to the 2016 World Health Organisation WHO criteria.. Subject has a DIPSS Risk score of intermediate or high. Subject has a measurable splenomegaly during the screening period. Subject must have been previously exposed to ruxolitinib.
CALLS Study (Non-interventional) CML PI: Dr Deepti Radia	A cohort study to establish the prevalence of mutations in patients With CML who meet the ELN Criteria for warning or failure and patients with Ph+ ALL with detectable BCR-ABL currently being treated with first or subsequent TKI therapy in the UK using next-generation sequencing. ***Eligibility Criteria:-***Age 18 or over, subject has CML (in all phases of disease) or Ph+ ALL with detectable BCR-ABL levels. Patients with CML will be on their first or subsequent TKI and will have met the ELN 2013 criteria for warning or failure. Patients with Ph+ ALL will be on their first or subsequent TKI and are not currently enrolled in UK ALL 14.

MPN Trials on hold

BLU-285-2203 (Interventional) Systemic mastocytosis PI: Dr Deepti Radia	A 3-Part, Randomized, Double-Blind, Placebo-Controlled Phase 2 Study to Evaluate Safety and Efficacy of Avapritinib (BLU-285), a Selective KIT Mutation-Targeted Tyrosine Kinase Inhibitor, in Indolent and Smoldering Systemic Mastocytosis with Symptoms Inadequately Controlled with Standard Therapy. ***Eligibility criteria:-*** Age 18 or over and have an ECOG performance status of 0 to 2. Patient must have SH. Patient must have moderate to severe symptoms. Patient must have failed to achieve symptom control for 1 or more baseline symptoms measured by ISH-SAF.

MPN Trials in Set-up

INForMeD (Observational) PI Prof C Harrison	An observational and biological research study to investigate the genetic and cellular basis of sporadic and familial myeloid disorders. ***Eligibility Criteria:-*** Age 2 or over, patients under investigation for or diagnosed with a myeloid or related disorder, patient willing to give consent to the study.
ACE-536 –LTFU-001 (Interventional) Myelofibrosis PI Prof C Harrison	A Phase 3b, open-label, single-arm, rollover study to evaluate long-term safety in subjects who have participated in other Luspatercept (ACE-536) clinical trials. ***Eligibility Criteria:- Subject must be age 18 and over and willing to adhere to study visit schedule and other protocol requirements.*** Subject has been participating in a luspatercept trial and continues to fulfil all the requirements of the parent protocol and the subject has been either: a. Assigned to luspatercept treatment, continues to receive clinical benefit in the opinion of the investigator and should continue to receive luspatercept treatment, **OR** b. Assigned to placebo arm in the parent protocol (at the time of unblinding or in follow-up) and should cross over to luspatercept treatment, **OR** c. Assigned to the Follow-up Phase of the parent protocol, previously treated with luspatercept or placebo in the parent protocol who shall continue into Long-term Post-treatment Follow-up Phase in the rollover study until the follow-up commitments are met (unless requirements are met as per parent protocol to crossover to luspatercept treatment).

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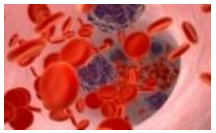

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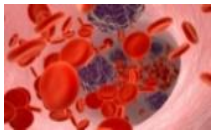

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MPN Trials in Set-up Cont.

CINC424H12201 The "Adore" Study. (Interventional) Myelofibrosis PI: Prof C Harrison	A randomized, open-label, phase I/II open platform study evaluating safety and efficacy of novel ruxolitinib combinations in myelofibrosis patients. The "ADORE" Study. ***Eligibility criteria:-*** Age 18 or over and have an ECOG performance status of 0 to 2,Subjects have diagnosis of primary myelofibrosis (PMF) according to the 2016 World Health Organization (WHO) criteria, or diagnosis of post-ET (PET-MF) or post-PV myelofibrosis (PPV-MF) according to the International Working Group for Myelofibrosis Research and Treatment (IWG-MRT) 2007 criteria. Patients must have a palpable spleen of at least 5 cm or enlarged spleen volume of at least 450 cm3 per MRI or CT scan at Baseline and must have been treated with ruxolitinib for at least 24 weeks prior to first dose of study treatment. Hemoglobin < 10 g/dL, Absolute neutrophil count (ANC) ≥ 1000/µL. Part 1: Platelet counts ≥ 75 000/µL Part 2 and Part 3: Platelet counts ≥ 50 000/µL. Part 2 and Part 3: Subjects who do not require packed red blood cells (PRBC) transfusion at screening and will not require any PRBC transfusions within 4 weeks prior to first dose of study treatment.
SRA-MMB-301 The Momentum Study. (Interventional) Myelofibrosis PI:Dr Donal Mclornan	A Randomized, Double-Blind, Phase 3 Study to Evaluate the Activity of Momelotinib (MMB) versus Danazol (DAN) in Symptomatic, Anaemic Subjects with Primary Myelofibrosis (PMF), Post-Polycythemia Vera (PV) Myelofibrosis, or Post Essential Thrombocythemia (ET) Myelofibrosis who were Previously Treated with JAK Inhibitor Therapy . ***Eligibility criteria:-*** Age 18 or over and have an ECOG performance status of 0 to 2, Subject must have diagnosis of primary myelofibrosis (PMF) according to the 2016 World Health Organization (WHO) criteria, or Post-PV/ET MF in accordance with the International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) criteria, subject must be symptomatic defined as MFSAF TSS of ≥ 10 units, anaemic and previously treated with an approved JAK inhibitor for PMF or Post-PV/ET MF for ≥ 90 days, or ≥ 28 days if JAK inhibitor therapy is complicated by RBC transfusion requirement of ≥ 4 units in 8 weeks, or Grade 3/4 AEs of thrombocytopenia, anaemia, or hematoma. Subject must have a DIPSS Risk score of intermediate or high, a measurable splenomegaly during the screening period and have a life expectancy of more than 24 weeks.
NP39761 (Interventional) MPN PI: Prof C Harrison	A Phase II, single-arm, open-label study to evaluate the efficacy, safety, pharmacokinetics and pharmacodynamics of idasanutlin monotherapy in patients with hydroxyurea-resistant/intolerant polycythaemia vera. ***Eligibility criteria:-*** 1) Patient must be 18 years or over. 2) Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1. 3) There must be documentation that the patient has met the revised 2016 WHO criteria for the diagnosis of polycythaemia vera. 4) Hct at screening and initiation of idasanutlin>40%. 5) Phlebotomy-dependent patients with splenomegaly by magnetic resonance imaging (MRI) or computerized tomography (CT) imaging (more than or equal to 450 cm3) or without splenomegaly (<450 cm3 or prior splenectomy). 6) Resistance to/intolerance to hydroxyurea according to modified *European Leukemia Net (*ELN*)* criteria.
CINC424A2X01B (Interventional) MPN PI: Prof C Harrison	An open label, multi-center, Phase IV rollover protocol for patients who have completed a prior global Novartis or Incyte sponsored ruxolitinib (INC424) study or ruxolitinib and panobinostat (LBH589) combination study, and are judged by the investigator to benefit from continued treatment. ***Eligibility criteria:-*** Patient is currently enrolled in a Novartis-sponsored Global Drug Development (GDD) or Global Medical Affairs (GMA) study or Incyte-sponsored study (where Incyte can delegate the sponsorship to a preferred CRO, if applicable) that is approved to enroll into this rollover study, and are receiving either ruxolitinib or combination of ruxolitinib and panobinostat, and fulfilled all of the requirements of the parent protocol. Patient is currently benefiting from the treatment with ruxolitinib monotherapy or combination of ruxolitinib and panobinostat, as determined by the investigator.

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