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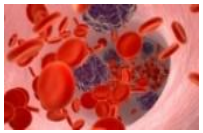
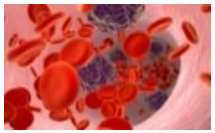


Myeloproliferative Neoplasm (MPN) Clinical Trials Portfolio



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Recruiting MPN Trials

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)
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 PMF, PPVMF, or PETMF 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.
Immunological Effects of Covid-19 Infection and Response to Vaccination PI: Prof C Harrison	Immunological Effects of Covid-19 Infection and Response to Vaccination in Patients with Haematological Malignancy ***Eligibility criteria:-*** Previous confirmed Covid-19 infection at a minimum of 4 weeks after resolution of symptoms or from the time of last positive nasopharyngeal PCR swab if asymptomatic *or* SARS-CoV-2 IgG antibody positive *or* Receiving vaccination against SARS-Cov-2
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.
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)
Constellation Manifest (Interventional) Myelofibrosis PI: Prof C 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. Only Arm 1 'Prior JAKi or ineligible for Rux, Monotherapy' & Arm 2 'Prior JAKi combination transfusion dependent' open
E-MPN (Observational) MPN PI: Prof C Harrison	European Myeloproliferative Neoplasms Network (E-MPN) ***Eligibility criteria:-*** Patients with diagnosis of BCR-ABL1-negative MPN (i.e., ET, PV, PMF, pre-MF, PPV-M, PET-MF) OR diagnosis of secondary accelerated phase or acute leukaemia after MPN. Newly diagnosed at time of registry entry OR diagnosed since 01-Jan-2009 and still alive at time of registry entry. Patients at the age of 18 years or older.

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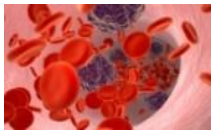
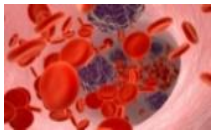


Myeloproliferative Neoplasm (MPN) Clinical Trials Portfolio



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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 'Freedom-2' (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.

Recruiting MPN trials Cont.

Navitoclax (M16-109) Refine (Interventional) Myelofibrosis PI: Prof C Harrison	A Phase 2 Single-Arm, Open-Label Study Evaluating Tolerability and Efficacy of Navitoclax in Combination with Ruxolitinib in Subjects with Myelofibrosis ***Eligibility Criteria:*** Age 18 or over, subject with documented diagnosis of PMF, PPVMF, PETMF as defined by World Health Organization (WHO) classification, Subjects classified as intermediate-2 or high-risk MF, as defined by Dynamic International Prognostic Scoring System (DIPSS), subject ineligible or unwilling to undergo stem cell transplant at time of study entry, ECOG 0, 1 or 2.

MPN Trials on hold

ACE-536-MF-001 (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 **Cohort 3B ONLY** - subjects on ruxolitinib as part of their standard-of care therapy and transfusion dependant ***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
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. ***Eligibility criteria:-*** Age 18 or over and have an ECOG performance status of 0 to 2,Subjects have diagnosis of PMF according to the 2016 (WHO) criteria, or diagnosis of PETMF or PPVMF according to the (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.

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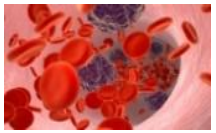

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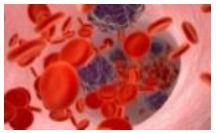

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MPN Trials in Set-up

PACIFICA (PAC303) (Interventional) Myelofibrosis PI: Dr D McLornan	A Randomized, Controlled Phase 3 Study of Pacritinib Versus Physician's Choice in Patients with Primary Myelofibrosis, Post Polycythemia Vera Myelofibrosis, or Post Essential Thrombocythemia Myelofibrosis with Severe Thrombocytopenia (PLT <50,000/µL) ***Eligibility Criteria:*** - age ≥18 years, diagnosis of PMF, PPVMF or PETMF, PLT count of <50,000/uL at screening, DIPSS Intermediate-1, Intermediate-2 or High Risk, Palpable Splenomegaly ≥5cm below LCM, TSS of ≥10 on MPN SAF 2.0 or a single symptom score of >5 or two symptoms of ≥3, including only LUQ pain, bone pain, itching or night sweats. ECOG performance status 0-2. Peripheral blast count of <10%, Absolute neutrophil count ≥500/uL. Left Ventricular cardiac ejection fraction of ≥50%, Adequate liver and renal function, Adequate coagulation. If fertile, willing to use effective birth control methods during the study. Willing to undergo and tolerate frequent MRI and CT scans. Able to understand and willing to complete symptom assessments
IMAGO 201 (IMG-7289-CTP-201) (Interventional) ET PI: Prof C Harrison	A Phase 2 Multi-Center, Open Label Study to Assess the Safety, Efficacy and Pharmacodynamics of IMG-7289 in Patients with Essential Thrombocythemia ***Eligibility Criteria***-Age 18 years or older. Diagnosis of ET per WHO diagnostic criteria. Patients who have failed at leats one standard therapy. Requires treatment in order to lower platelet counts. Platelet count >450 pre dose Day 1, Peripheral blast count <1% pre dose Day1, ANC ≥ 0.5 pre-dose Day. Fibrosis Score < grade 2. Life Expectancy > 36 weeks, able to swallow capsules. Amenable to bone marrow evaluations and peripheral blood sampling. Must have discontinued ET therapy at least 1 week (4 weeks for interferon) prior to study drug initiation.
Transform 1 (M16-191) (Interventional) Myelofibrosis PI: Dr D McLornan	A Randomized, Double-Blind, Placebo Controlled, Phase 3 Study of Navitoclax in Combination with Ruxolitinib versus Ruxolitinib Alone in Subjects with MF ***Eligibility Criteria***-Age 18 years or older. Adequate bone marrow reserve; in the absence of growth factors, thrombopoietic factors or platelet transfusions for at least 14 days prior to Week 1. Platelet Count ≥100, Absolute neutrophil count ≥1. Renal function: calculated creatinine clearance ≥30. Hepatic function and enzymes: AST and ALT ≤3.0 ULN; Total bilirubin ≤1.5 x ULN (exception Gilbert's Syndrome); Coagulation: aPTT and INR ≤1.5 x ULN. Documented diagnosis of PMF or SMF. Classified as Intermediate-2 or high risk MF defined by DIPSS+. Must not have received prior treatment with a JAK2 inhibitor, BH3-mimetic compound or bromodomain and extra-terminal motif (BET) inhibitor. Splenomegaly. Ineligible for SCT. Must not have received splenic irradiation within 6m prior. Must not have leukemic transformation, ECOG PS of 0, 1 or 2
BLU-285-2405 (Observational study). PI: Dr D Radia	Full Title: An External Control, Observational, Retrospective Study Assessing the Effect of Avapritinib Compared with Best Available Therapy for Patients with Advanced Systemic Mastocytosis ***Eligibility Criteria:-*** Diagnosed with AdvSM, with known subtype including SM-AHN, ASM, or MCL1 and Received at least one line of systemic therapy for AdvSM. Adult (≥18 years of age) at the initiation of first systemic line of therapy at the participating site, which must be on or after January 1, 2009. Had available performance status (e.g., ECOG score or Karnofsky score), Had an index date at least 3 months prior to the start of data collection
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
MOSAICC (Observational) MPN PI Prof C	MyelOproliferative neoplasmS: An In-depth Case Control ***Eligibility Criteria:-*** Clinically confirmed MPN diagnosis (PV, ET or PMF. Diagnosed within the previous 24 months. Age 18 years or older. Physically and cognitively capable of completing the questionnaire as determined by the treating clinician.
Transform 2 (M20-178) (Interventional) Myelofibrosis CI: Prof C Harrison	A Randomized, Open-Label, Phase 3 Study valuating Efficacy and Safety of Navitoclax in Combination with Ruxolitinib versus Best Available Therapy in Subjects with Relapsed/Refractory MF ***Eligibility Criteria***-Age 18 years or older. Diagnosis of PMF, PPVMF or PETMF. ECOG PS 0, 1, or 2. Classified as intermediate-2 or high-risk MF defined by DIPSS. Must have received prior treatment with a single JAK2 inhibitor and meet one of the following (in addition to minimum splenomegaly and symptom burden): -Prior treatment with JAK2 inhibitor for ≥24 weeks stopped due to lack of spleen response (refractory), or loss of spleen response or symptom control after prev response (relapsed) -Prior treatment with JAK2 inhibitor for ≥24 weeks with documented disease progression

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