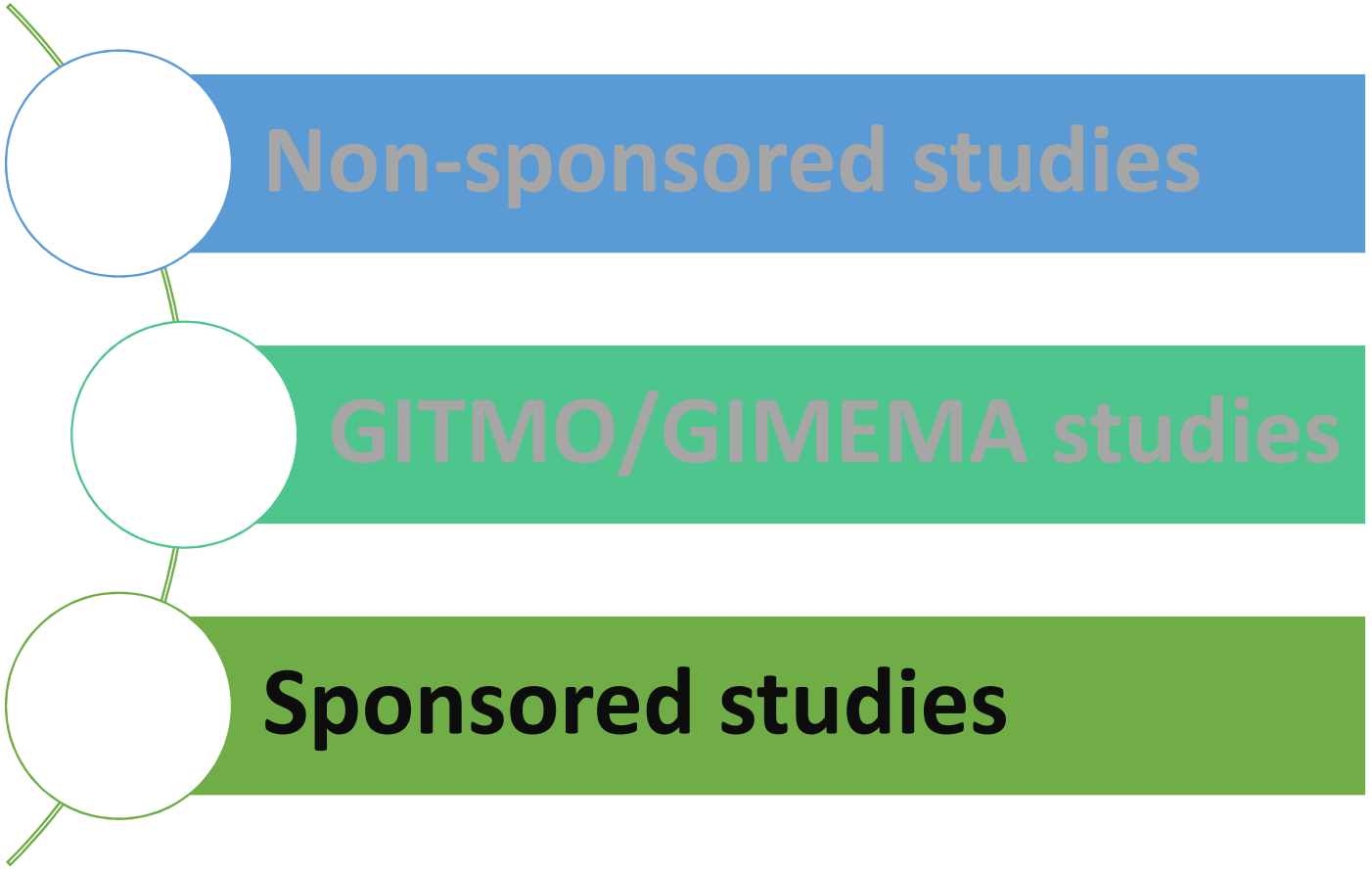
Update Ongoing Trials BS BMT-Unit



Ongoing sponsored studies (2020)

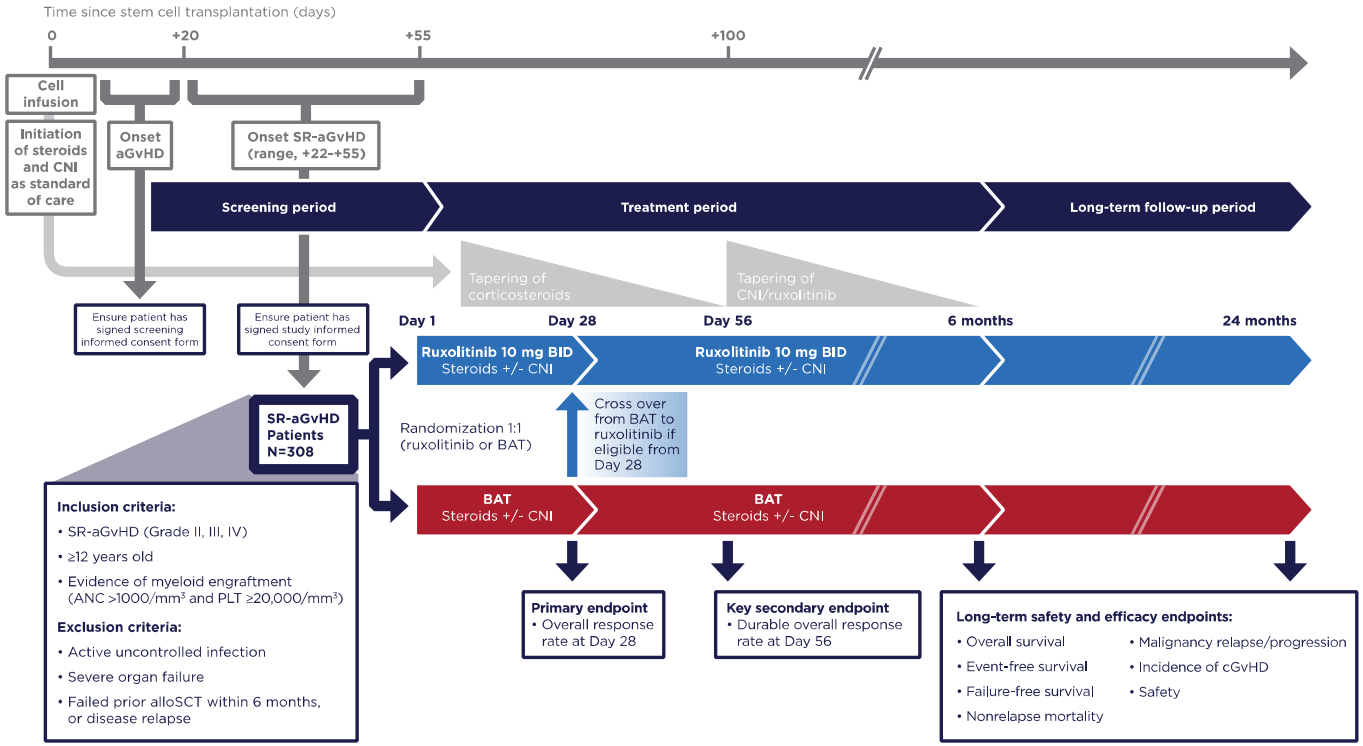
Studies	Submitted EC	EC approval	Enrolled patients	Published abstract	Published full paper
REACH 2	Yes	20/Sep/2017	11	Yes	Yes
REACH 3	Yes	20/Sep/2017	13	Yes	Submitted
REACH ROLLOVER	Yes	23/Jun/2020	2	No	No
LETERMOVIR	Yes	07/Aug/2019	27	No	No
GRAVITAS-309	Yes	20/10/2020	4	No	No
M19-063 (VEN-AZA)	Yes	In approval	20	No	No
M19-753 (NAVITOCLAX)	Yes	In approval	0	No	No
GALINPEPIMUT-S (GPS)	Yes	25/01/2021	0	No	No

REACH 2 – CINC424C2301

A phase III randomized open-label multi-center study of ruxolitinib versus best available therapy in patients with corticosteroid-refractory acute graft vs host disease after allogenic stem cell transplantation

Study phase: III

Primary objective:
To compare the efficacy of ruxolitinib vs Investigator's choice Best Available Therapy in patients with grade II-IV steroid refractory acute graft vs host disease



PI: Prof Domenico Russo

REACH 2 – CINC424C2301

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ruxolitinib for Glucocorticoid-Refractory Acute Graft-versus-Host Disease

Robert Zeiser, M.D., Nikolas von Bubnoff, M.D., Jason Butler, F.R.A.C.P., Mohamad Mohty, M.D., Ph.D., Dietger Niederwieser, M.D., Reuven Or, M.D., Jeff Szer, F.R.A.C.P., Eva M. Wagner, M.D., Tsila Zuckerman, M.D., Bruyère Mahuzier, Pharm.D., Judith Xu, M.Sc., Celine Wilke, M.D., Kunal K. Gandhi, M.D., M.P.H., and Gérard Socié, M.D., Ph.D., for the REACH2 Trial Group*

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Zeiser at the Department of Hematology, Oncology, and Stem Cell Transplantation, University Medical Center Freiburg, Hugstetter Str. 55, 79106 Freiburg, Germany, or at robert.zeiser@uniklinik-freiburg.de.

*A list of the investigators in the REACH2 Trial Group is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Zeiser and von Bubnoff contributed equally to this article.

This article was published on April 22, 2020, at NEJM.org.

N Engl J Med 2020;382:1800-10.
DOI: 10.1056/NEJMoa1917635

ABSTRACT

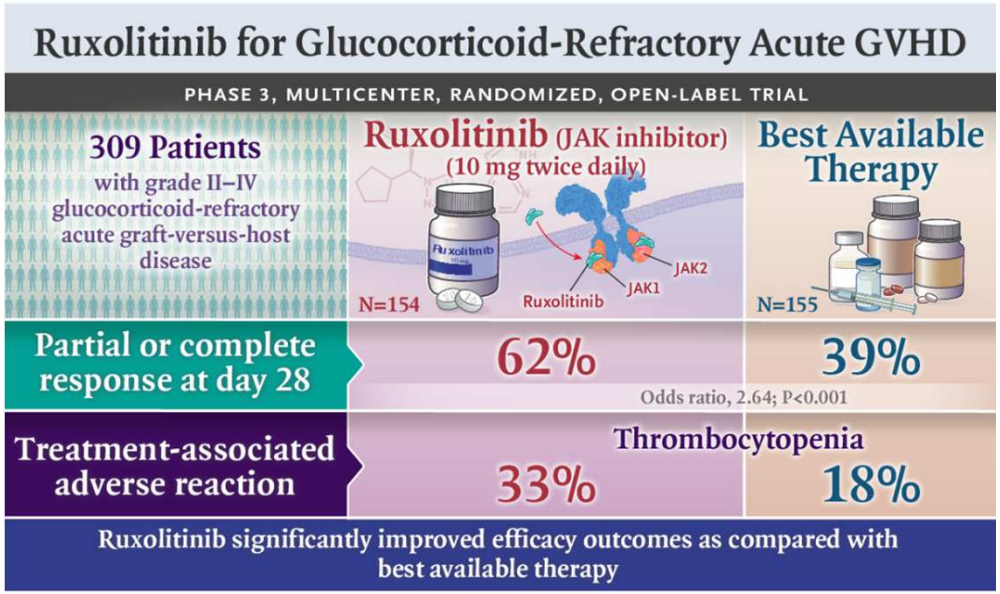
BACKGROUND
Acute graft-versus-host disease (GVHD) remains a major limitation of allogeneic stem-cell transplantation; not all patients have a response to standard glucocorticoid treatment. In a phase 2 trial, ruxolitinib, a selective Janus kinase (JAK1 and JAK2) inhibitor, showed potential efficacy in patients with glucocorticoid-refractory acute GVHD.

METHODS
We conducted a multicenter, randomized, open-label, phase 3 trial comparing the efficacy and safety of oral ruxolitinib (10 mg twice daily) with the investigator's choice of therapy from a list of nine commonly used options (control) in patients 12 years of age or older who had glucocorticoid-refractory acute GVHD after allogeneic stem-cell transplantation. The primary end point was overall response (complete response or partial response) at day 28. The key secondary end point was durable overall response at day 56.

RESULTS
A total of 309 patients underwent randomization; 154 patients were assigned to the ruxolitinib group and 155 to the control group. Overall response at day 28 was higher in the ruxolitinib group than in the control group (62% [96 patients] vs. 39% [61]; odds ratio, 2.64; 95% confidence interval [CI], 1.65 to 4.22; P<0.001). Durable overall response at day 56 was higher in the ruxolitinib group than in the control group (40% [61 patients] vs. 22% [34]; odds ratio, 2.38; 95% CI, 1.43 to 3.94; P<0.001). The estimated cumulative incidence of loss of response at 6 months was 10% in the ruxolitinib group and 39% in the control group. The median failure-free survival was considerably longer with ruxolitinib than with control (5.0 months vs. 1.0 month; hazard ratio for relapse or progression of hematologic disease, non–relapse-related death, or addition of new systemic therapy for acute GVHD, 0.46; 95% CI, 0.35 to 0.60). The median overall survival was 11.1 months in the ruxolitinib group and 6.5 months in the control group (hazard ratio for death, 0.83; 95% CI, 0.60 to 1.15). The most common adverse events up to day 28 were thrombocytopenia (in 50 of 152 patients [33%] in the ruxolitinib group and 27 of 150 [18%] in the control group), anemia (in 46 [30%] and 42 [28%], respectively), and cytomegalovirus infection (in 39 [26%] and 31 [21%]).

CONCLUSIONS
Ruxolitinib therapy led to significant improvements in efficacy outcomes, with a higher incidence of thrombocytopenia, the most frequent toxic effect, than that observed with control therapy. (Funded by Novartis; REACH2 ClinicalTrials.gov number, NCT02913261.)

The NEW ENGLAND JOURNAL of MEDICINE



R. Zeiser et al. 10.1056/NEJMoa1917635

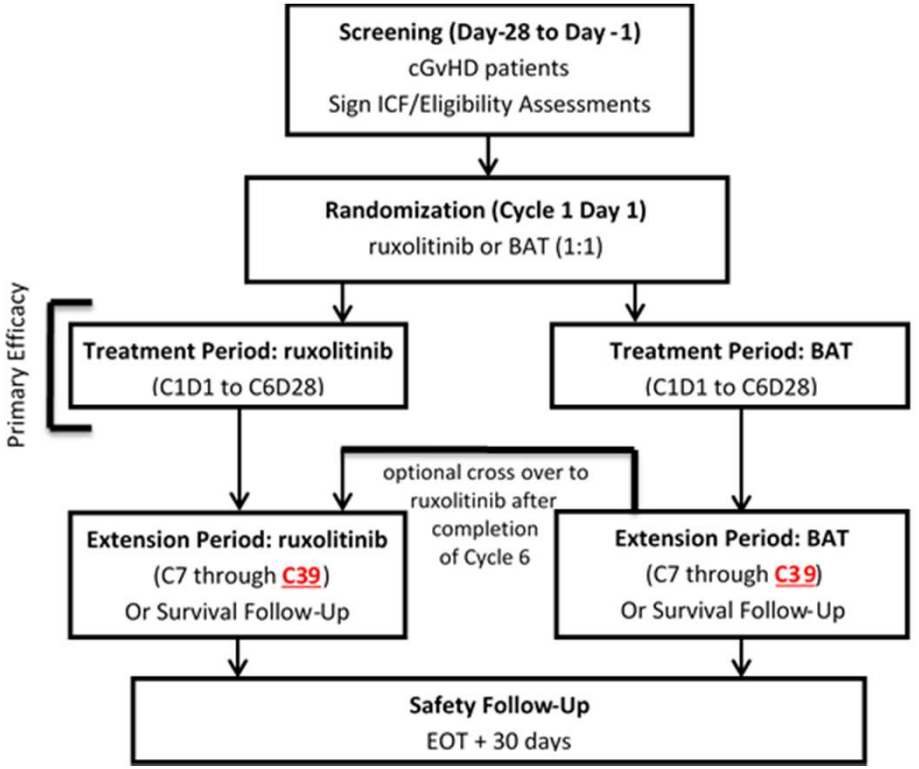
PI: Prof Domenico Russo

REACH 3 – CINC424D2301

A phase III randomized open-label multi-center study of ruxolitinib versus best available therapy in patients with corticosteroid-refractory chronic graft vs host disease after allogenic stem cell transplantation

Study phase: III

Primary objective:
To compare the efficacy of ruxolitinib vs Investigator's choice Best Available Therapy in patients with moderate or severe SR-cGVHD



PI: Prof Domenico Russo

REACH 3 – CINC424D2301

Study Design of a Phase 3, Randomized, Open-Label, Multicenter Study to Evaluate Ruxolitinib Over BAT in Patients with Corticosteroid-Refractory Chronic Graft vs Host Disease after Allogeneic Hematopoietic Stem Cell Transplantation (REACH-3)

Robert Zeiser [1], *Ron Ram* [2,3], *Stephen Ronan Foley* [4], *Moshe Yeshurun* [3,5], *Franco Locatelli* [6,7], *Andrew Artz* [8], *Brian Gadbaw* [9], *Edric Atienza* [9], *Norbert Hollaender* [10], *Patricia Delaite* [11], *Takanori Teshima* [12]. [1] *Department of Hematology, Oncology and Stem Cell Transplantation, University Hospital Freiburg, Freiburg, Germany;* [2] *BMT Unit, Tel Aviv Medical Center, Tel Aviv, Israel;* [3] *Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel;* [4] *Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada;* [5] *Institute of Hematology, Davidoff Cancer Center, Rabin Medical Center, Petah Tikva, Israel;* [6] *Department of Pediatric Hematology/Oncology, Bambino Gesù Children's Hospital, Rome, Italy;* [7] *Department of Pediatric Hematology/Oncology, University of Pavia, Pavia, Italy;* [8] *Section of Hematology/Oncology, Department of Medicine, University of Chicago, Chicago, IL;* [9] *Novartis Pharmaceuticals Corporation, East Hanover, NJ;* [10] *Novartis Pharma AG, Basel, Switzerland;* [11] *Incyte Corporation, Wilmington, DE;* [12] *Department of Hematology, Hokkaido University Faculty of Medicine, Graduate School of Medicine, Sapporo, Japan*

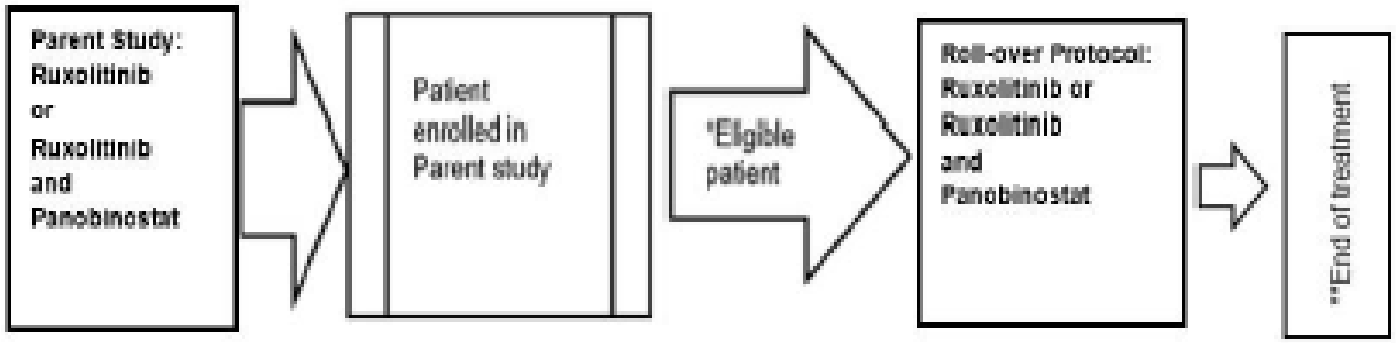
PI: Prof Domenico Russo

REACH ROLLOVER – CINC424A2X01B

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

Study phase: IV

Primary objective:
To evaluate long term safety data i.e. SARs and AEs



PI: Prof Domenico Russo

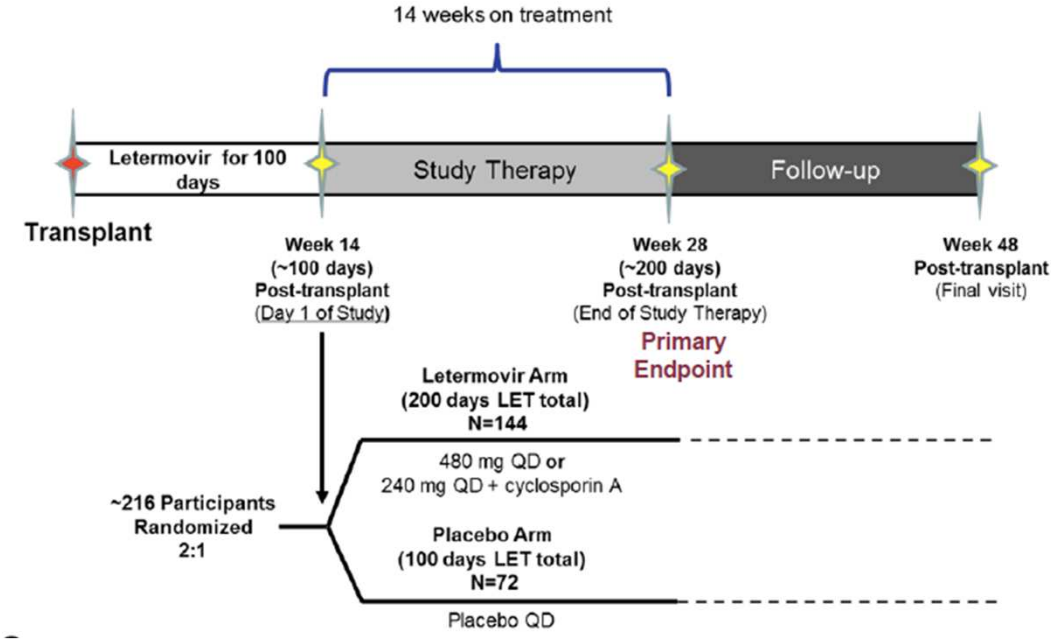
LETERMOVIR – MK-8228

A phase III randomized, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of letermovir (LET) prophylaxis when extended from 100 days to 200 days post-transplant in cytomegalovirus (CMV) seropositive recipients (R+) of an allogenic hematopoietic stem cell transplant (HSCT)

Study phase: III

Primary objective:

To evaluate the efficacy of letermovir (LET) versus placebo when LET prophylaxis is extended from 100 to 200 days post-transplant, as measured by the proportion of participants with clinically significant CMV infection from Week 14 (100 days) post-transplant throught Week 28 (200 days) post transplant



PI: Prof Domenico Russo

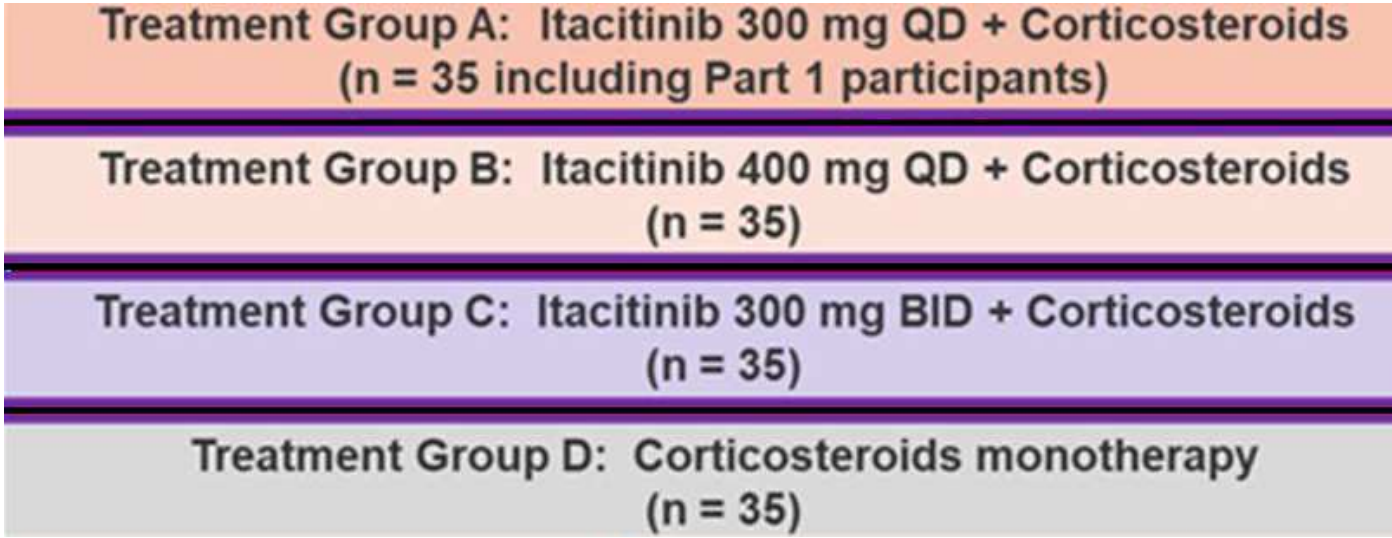
GRAVITAS-309 – INCB39110-309

A phase II/III study of itacinib and corticosteroids as initials treatment for chronic graft-versus-vost disease

Study phase: II/III

Primary objective:
To evaluate the PK of Itacinib when administered in combination with corticosteroids in the study population

Part 1 expantion



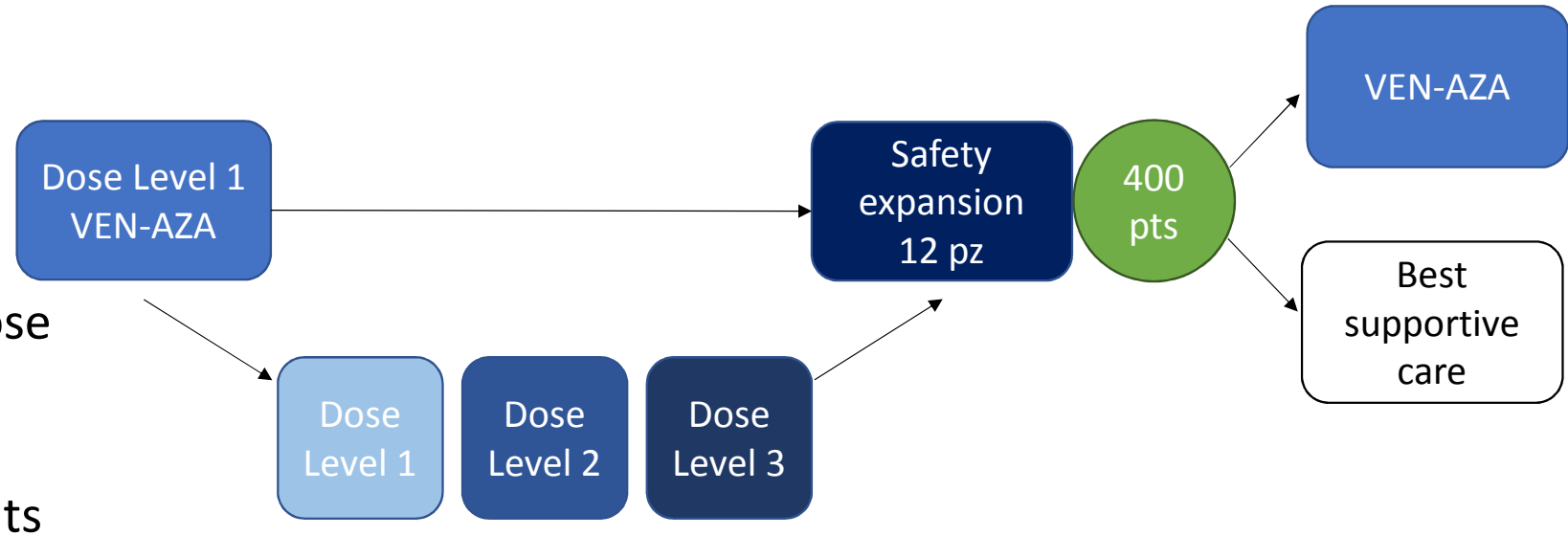
PI: Prof Domenico Russo

M19-063 (VEN-AZA)

A randomized, open label phase 3 study evaluating safety and efficacy of venetoclax in combination with azacitidine after allogenic stem cell transplantation in subjects with acute myeloid leukemia (AML) (VIALE-T)

Study phase: III

Primary objective:
To determinate the recommended Phase 3 dose of venetoclax in combination with azacytidine in AML patients when given as maintenance therapy following allogenic stem cell transplantation



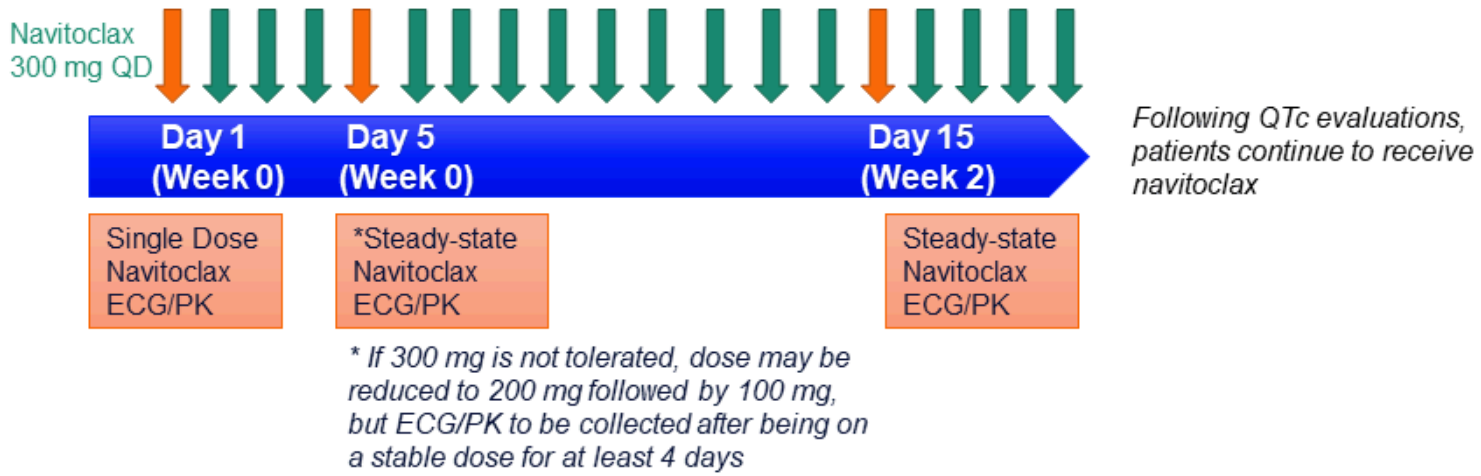
PI: Prof Domenico Russo

M19-753 (NAVITOCLAX)

A phase I open-label evaluating the safety and tolerability, and pharmacokinetics of navitoclax monotherapy and in combinations with ruxolitinib in myeloproliferative neoplasm subjects

Study phase: I

Primary objective:
Evaluate the effect of navitoclax on corrected QTc interval by Fridericia's correction formula (QTcF) in subjects with MPN or CMM



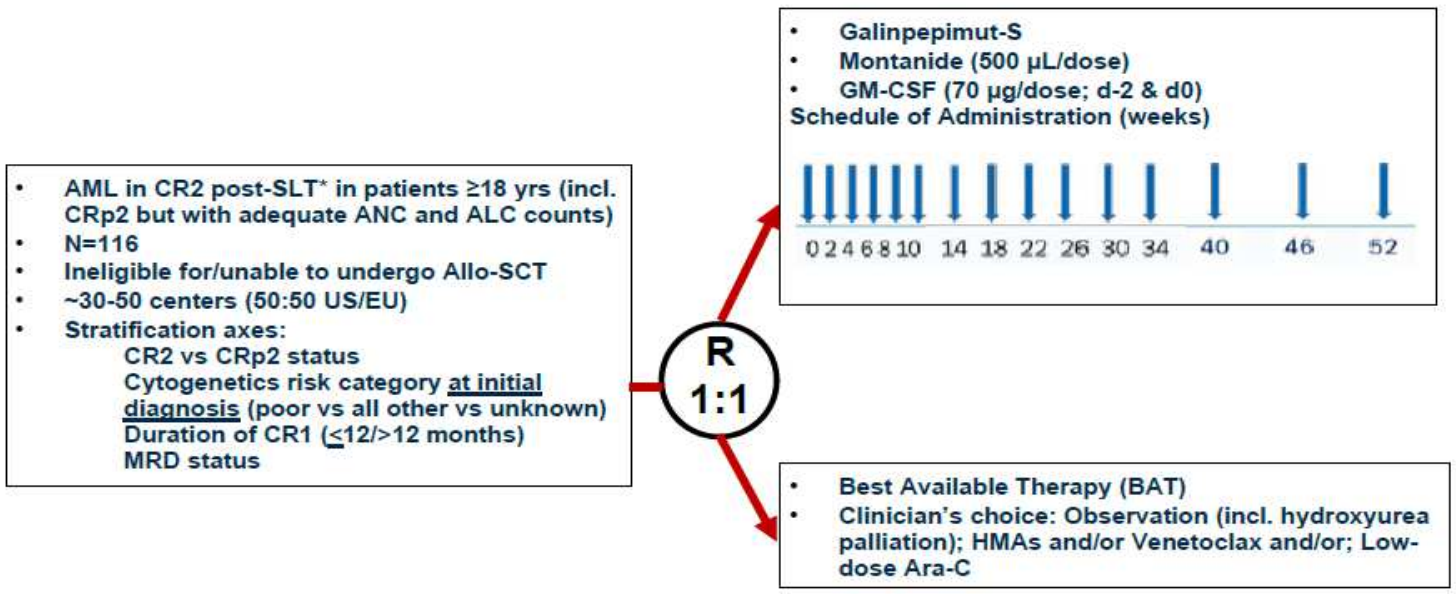
PI: Prof Domenico Russo

GALINPEPIMUT-S (GPS) – SLSG18-301

A randomized, open-label Study of efficacy and safety of galinpepimut-S (GPS) maintenance monotherapy compared to investigator's choice of best available therapy in subjects

Study phase: III

Primary objective:
Compare the efficacy of GPS to Investigator's choice of best available therapy (1:1) on OS in subjects with AML who care in CR2/CRp2



PI: Prof Domenico Russo