Disclosure

Robert Zeiser:

Honoraria from Novartis, Mallinckrodt Pharmaceuticals, and Incyte

12 June 2020
Stem cell transplantation - Clinical: Graft Versus Host Disease

EHA-2121/S255

Ruxolitinib Versus Best Available Therapy in Patients with Steroid-Refractory Acute Graft-Versus-Host Disease: Overall Response Rate by Baseline Characteristics in the Phase 3 Randomized REACH2 Trial

Robert Zeiser[1], Nikolas von Bubnoff[2], Dietger Niederwieser[3], Mohamad Mohty[4], Sinem Civriz Bozdag[5], Edouard Forcade[6], Giovanni Grillo[7], Francis Ayuk[8], Domenico Russo[9], Jaime Sanz[10], Friedrich Stölzel[11], Judith Xu[12], Bruyère Mahuzier[13], Celine Wilke[14] and Gérard Socié[15], on behalf of the REACH2 study group

[1]University Hospital Freiburg, Department of Haematology, Oncology and Stem Cell Transplantation, Freiburg, Germany; [2]Department of Haematology and Oncology, University Hospital Schleswig-Holstein, Lübeck, Germany; [3]University of Leipzig, Department of Haematology and Oncology, Leipzig, Germany; [4]Hôpital Saint-Antoine, Paris, France; [5]Department of Haematology, Ankara University School of Medicine, Ankara, Turkey; [6]CHU Bordeaux, Hôpital Haut-Leveque, Pessac, France; [7]Department of Hematology Oncology, Ospedale Niguarda Ca' Granda, Milano, Italy; [8]Department of Stem Cell Transplantation, University Medical Center Hamburg, Hamburg, Germany; [9] Department of Clinical and Experimental Sciences, Spedali Civili of Brescia, Università Brescia, Brescia, Italy; [10] Department of Hematology, Hospital La Fe, Valencia, Spain; [11]Department of Hematology/Oncology, Medical Clinic and Policlinic, University Hospital Carl Gustav Carus Dresden, Technical University Dresden, Dresden, Germany; [12]Novartis Pharmaceutical Corporation, East Hanover, NJ, United States;[13] Novartis Pharma, Rueil-Malmaison, France; [14]Novartis Pharma AG, Basel, Switzerland; [15]APHP, Hématologie-Transplantation, Hôpital St Louis, Université de Paris and INSERM UMR 976, Paris, France

REACH2 Primary Publication

The NEW ENGLAND JOURNAL of MEDICINE

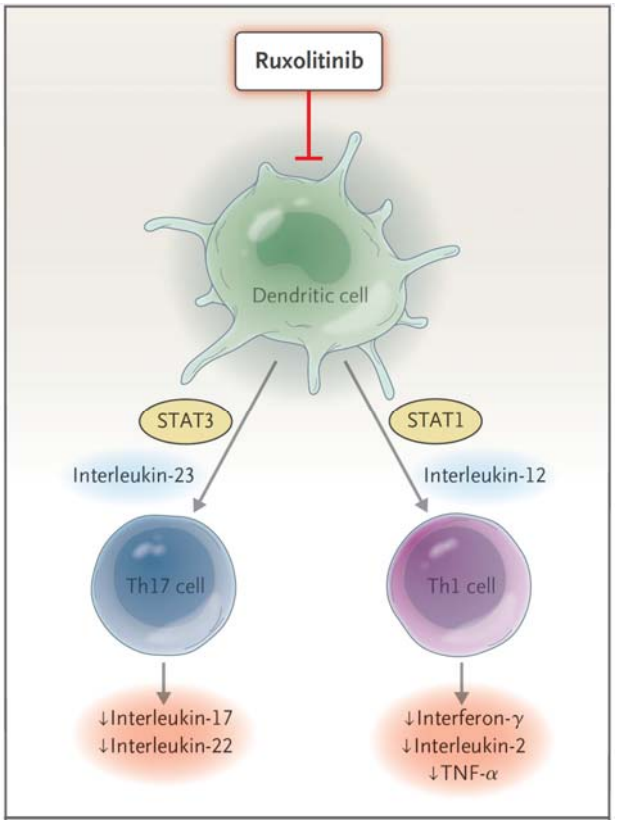
ORIGINAL ARTICLE

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*

Scan for link to publication

Zeiser R, et al *N Engl J Med.* 2020;382:1800–1810



Scan for link to publication

Chao N. *N Engl J Med.* 2020;382:1853–1854.

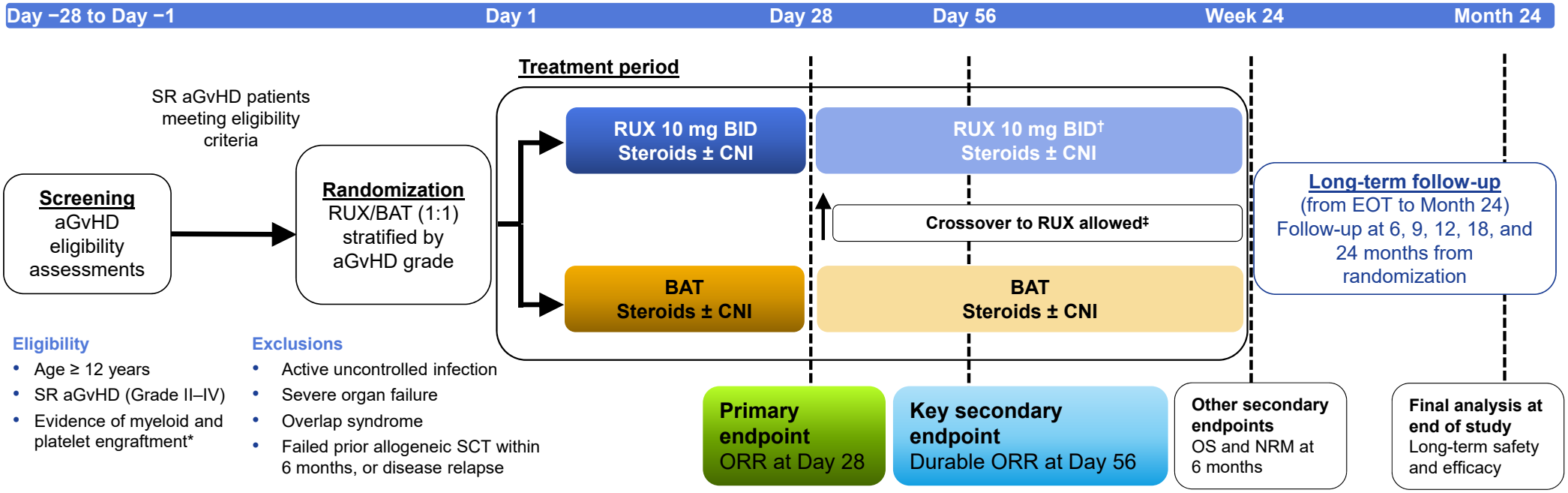
Graft Versus Host Disease

- The use of allogeneic SCT continues to rapidly increase worldwide[1]
- GvHD remains a major limitation of a successful allogeneic SCT[2,3]
  - Up to 50% of patients develop GvHD, despite immunosuppressive prophylaxis[3–5]
  - GvHD is a significant cause of mortality in allogeneic SCT patients[6–9]
- Only half of patients with aGvHD respond to first-line treatment with corticosteroids[9,10]
- There is no optimal second-line treatment for patients with SR aGvHD, though RUX was recently approved in the USA[2,3,11,12]
  - Previous randomized trials evaluating novel therapies have failed to demonstrate superiority to BAT[13,14]

aGvHD, acute GvHD; BAT, best available therapy; RUX, ruxolitinib; SCT, stem cell transplantation; SR, steroid refractory.

1. Niederwieser D, et al. *Bone Marrow Transplant*. 2016;51:778–785. 2. Ruutu T, et al. *Bone Marrow Transplant.* 2014;49:168–173. 3. Zeiser R, Blazar BR. *N Engl J Med.* 2017;377:2167–2179. 4. Martin PJ, et al. *Biol Blood Marrow Transplant.* 2012;18:1150–1163. 5. Jagasia M, et al. *Immunotherapy.* 2018;10:391–402. 6. van Groningen LFJ, et al. *Biol Blood Marrow Transplant.* 2016;22:170–182. 7. Arai S, et al. *Biol Blood Marrow Transplant.* 2002;8:115–160. 8. Van Lint MT, et al. *Blood*. 2006;107:4177–4181. 9. Westin JR, et al. *Adv Hematol.* 2011;2011:601953. 10. MacMillan ML, et al. *Biol Blood Marrow Transplant.* 2002;8:387–394. 11. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-ruxolitinib-acute-graft-versus-host-disease. 12. Jagasia et al. *Blood*. 2020 [Epub ahead of print].13. MacMillan ML, et al. *Blood.* 2007;109:2657–2662. 14. Socié G, et al. *Blood*. 2017;129:643–649.

REACH2 Study Design



The focus of this presentation is data until Day 56

*Absolute neutrophil count > 1,000/mm^3 and platelet count ≥ 20,000/mm^3. †RUX tapering was permitted after Day 56 for responding patients and to continue beyond 6 months and up to 2 years from randomization, as required. ‡Crossover from BAT to RUX was permitted from Day 28 if patients did not respond at Day 28, or if they lost their response thereafter and required additional systemic therapy and did not have signs of cGvHD.

BID, twice daily; cGvHD, chronic graft versus host disease; EOT, end of treatment period; ICF, informed consent form; NRM, non-relapse mortality; ORR, overall response rate; OS, overall survival.

REACH2 Study Design (cont'd)

Randomized, phase 3, open-label, multicenter study comparing the efficacy and safety of RUX with BAT (NCT02913261)[1]

- Age ≥ 12 years, grade II–IV aGvHD that requires systemic immunosuppressive therapy and that became SR
- SR aGvHD is defined based on organ assessment as:
  - Progression after ≥ 3 days of high-dose systemic steroid therapy, with or without CNI; or
  - Lack of response (PR or better) after 7 days; or
  - Failure during steroid taper, defined as
    - Requiring dose increase to ≥ 2 mg/kg/day methylprednisolone*; or
    - Failure to taper dose to < 0.5 mg/kg/day methylprednisolone†

RUX

- 10 mg orally BID
- Tapering permitted no earlier than Day 56 for responding patients, dose modifications permitted for AEs
- Ruxolitinib (optional) tapering steps: 10 mg BID → 5 mg BID → 5 mg QD → Discontinue ruxolitinib

BAT

- By investigators choice at randomization: Antithymocyte globulin, Extracorporeal photopheresis, Mesenchymal stromal cells, Low-dose methotrexate, Mycophenolate mofetil, Everolimus, Sirolimus, Etanercept, Infliximab
- Crossover to RUX permitted from Day 28 if lack of response at Day 28 or loss of response thereafter

*Prednisone equivalent dose ≥ 2.5 mg/kg/day. †Prednisone equivalent dose < 0.6 mg/kg/day. CNI, calcineurin inhibitor; PR, partial response.

1. https://clinicaltrials.gov/ct2/show/NCT02913261.

Patient Disposition*

	RUX (n = 154)	BAT (n = 155)
Patients randomized, n (%)	154 (100)†	155 (100)†
Completed treatment	31 (20.1)	17 (11.0)
Ongoing treatment	12 (7.8)	6 (3.9)
Discontinued treatment	111 (72.1)	132 (85.2)
Reason for discontinuation, n (%)		
Lack of efficacy	32 (20.8)	68 (43.9)
AE	26 (16.9)	5 (3.2)
Death	25 (16.2)	22 (14.2)
Failure to meet protocol continuation criteria	10 (6.5)	9 (5.8)
Malignancy relapse	7 (4.5)	12 (7.7)
Physician decision	6 (3.9)	8 (5.2)
Patient/guardian decision	4 (2.6)	7 (4.5)
Graft loss	1 (0.6)	0
Technical issues	0	1 (0.6)
Crossover to RUX, n (%)	-	49 (31.6)

*At study cut-off date (25 July 2019). †2 patients (1.3%) in the RUX group and 5 patients (3.2%) in the BAT group did not receive treatment.

Baseline Characteristics

Characteristic	RUX (n = 154)	BAT (n = 155)	Total (N = 309)
Age, median (range), years	52.5 (12–73)	54.0 (13–71)	54.0 (12–73)
Aged 12 to < 18 years, n (%)	5 (3.2)	4 (2.6)	9 (2.9)
Aged ≥ 65 years, n (%)	21 (13.6)	25 (16.1)	46 (14.9)
Male, n (%)	92 (59.7)	91 (58.7)	183 (59.2)
Female, n (%)	62 (40.3)	64 (41.3)	126 (40.8)
Ethnicity, n (%)			
White	111 (72.1)	102 (65.8)	213 (68.9)
Black/African American	0	1 (0.6)	1 (0.3)
Asian	19 (12.3)	29 (18.7)	48 (15.5)
Other	8 (5.2)	4 (2.6)	12 (3.9)
Unknown	16 (10.4)	19 (12.3)	35 (11.3)
aGvHD grade at randomization, n (%)			
II	50 (32.5)	54 (34.8)	104 (33.7)
III	68 (44.2)	68 (43.9)	136 (44.0)
IV	30 (19.5)	32 (20.6)	62 (20.1)

Baseline Characteristics (cont'd)

Characteristic	RUX (n = 154)	BAT (n = 155)	Total (N = 309)
aGvHD organ involvement, n (%)			
Skin	93 (60.4)	74 (47.7)	167 (54.0)
Liver	36 (23.4)	26 (16.8)	62 (20.1)
Upper GI	28 (18.2)	37 (23.9)	65 (21.0)
Lower GI	96 (62.3)	115 (74.2)	211 (68.3)
Missing	4 (2.6)	1 (0.6)	5 (1.6)
SR criteria, n (%)			
Progression after at least 3 days	35 (22.7)	43 (27.7)	78 (25.2)
Failure to respond after 7 days	72 (46.8)	63 (40.6)	135 (43.7)
Failure during steroid taper	47 (30.5)	49 (31.6)	96 (31.1)
Donor type, n (%)			
Related	49 (31.8)	55 (35.5)	104 (33.7)
Not related	105 (68.2)	100 (64.5)	205 (66.3)
Prior aGvHD therapy, n (%)			
Steroid + CNI	77 (50.0)	76 (49.0)	153 (49.5)
Steroid + CNI + other systemic aGvHD treatment	56 (36.4)	49 (31.6)	105 (34.0)
Steroid + other systemic aGvHD treatment	9 (5.8)	12 (7.7)	21 (6.8)
Steroid only	12 (7.8)	18 (11.6)	30 (9.7)

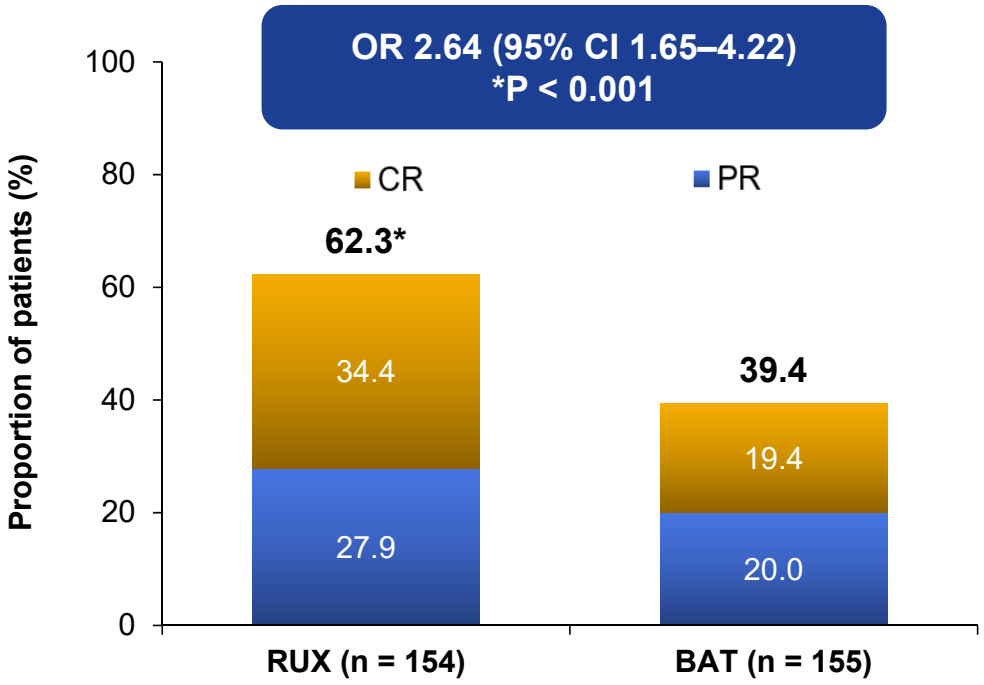
CNI, calcineurin inhibitors; GI, gastrointestinal.

Baseline Characteristics (cont'd)

Characteristic	RUX (n = 154)	BAT (n = 155)	Total (N = 309)
Conditioning regimen, n (%)			
Myeloablative	85 (55.2)	65 (41.9)	150 (48.5)
Non-myeloablative	31 (20.1)	41 (26.5)	72 (23.3)
Reduced intensity	38 (24.7)	49 (31.6)	87 (28.2)
Donor type HLA match status, n (%)			
Not related and match	65 (42.2)	62 (40.0)	127 (41.1)
Not related and mismatch	38 (24.7)	36 (23.2)	74 (23.9)
Not related and missing	2 (1.3)	2 (1.3)	4 (1.3)
Related and match	27 (17.5)	29 (18.7)	56 (18.1)
Related and mismatch	21 (13.6)	21 (13.5)	42 (13.6)
Related and missing	1 (0.6)	3 (1.9)	4 (1.3)
Related and unknown	0	2 (1.3)	2 (0.6)

HLA, Human Leukocyte Antigen.

Overall Response Rate at Day 28 Significantly Higher for Ruxolitinib vs BAT

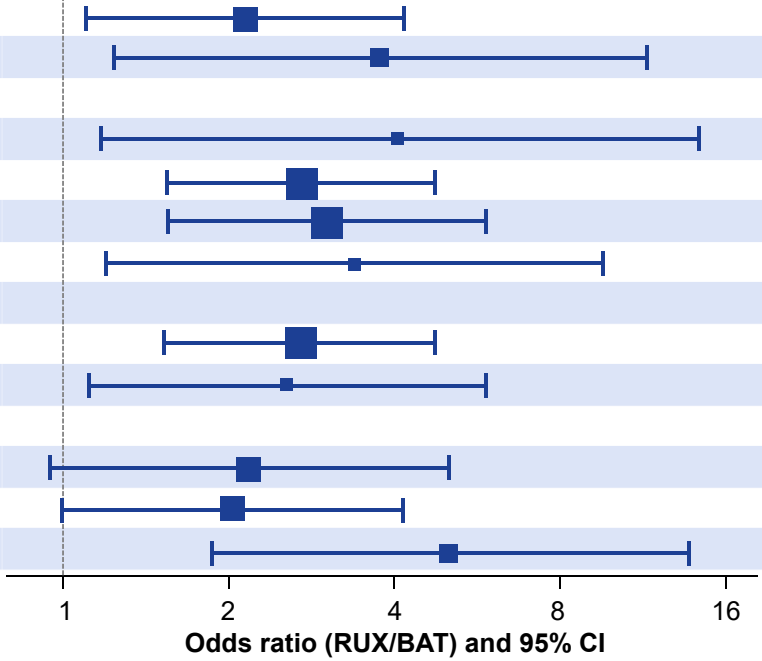


	RUX (n = 154)	BAT (n = 155)
Responders, n (%)		
Complete Response	53 (34.4)	30 (19.4)
Partial Response	43 (27.9)	31 (20.0)
Non-responders, n (%)		
No response	7 (4.5)	10 (6.5)
Mixed response	10 (6.5)	17 (11.0)
Progression	4 (2.6)	13 (8.4)
Other†	1 (0.6)	7 (4.5)
Unknown	36 (23.4)	47 (30.3)

†Other: patient with additional systemic therapies along with CR/PR per investigator assessment.
CI, confidence interval; CR, complete response; OR, odds ratio.

Overall Response Rate at Day 28 Higher for Ruxolitinib vs BAT in all Subgroups

Forest plot of odds ratio with 95% CI interval for ORR at Day 28 from subgroup analysis

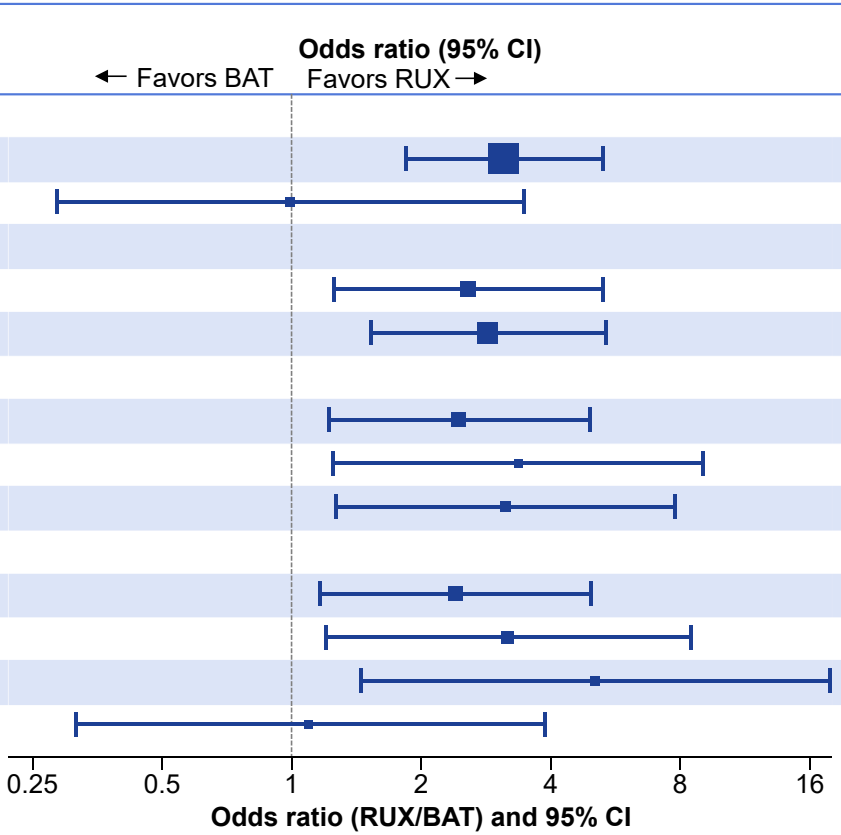


Subgroup	Odds ratio (95% CI)	ORR	
		RUX	BAT
aGvHD grade at randomization per IRT			
Grade II		75.5 (40/53)	50.9 (27/53)
Grade III		56.3 (40/71)	37.5 (27/72)
Grade IV		53.3 (16/30)	23.3 (7/30)
Organ involvement			
Liver		44.4 (16/36)	19.2 (5/26)
Lower GI		57.3 (55/96)	33.0 (38/115)
Skin		72.0 (67/93)	47.3 (35/74)
Upper GI		67.9 (19/28)	37.8 (14/37)
Donor type			
Not related		64.8 (68/105)	41.0 (41/100)
Related		57.1 (28/49)	36.4 (20/55)
Criteria for SR-aGvHD			
Failure on steroid taper		66.0 (31/47)	46.9 (23/49)
Failure to achieve a response after 7 days		56.9 (41/72)	38.1 (24/63)
Progression after at least 3 days		68.6 (24/35)	32.6 (14/43)

IRT, interactive response technology
X-axis values are represented in natural log scale. Dotted line shows no effect point. The area of the box indicates the weight of the sub group, measured by the size of subpopulation.

Overall Response Rate at Day 28 Higher for Ruxolitinib vs BAT in Majority of Subgroups

Forest plot of odds ratio with 95% CI interval for ORR at Day 28 from subgroup analysis

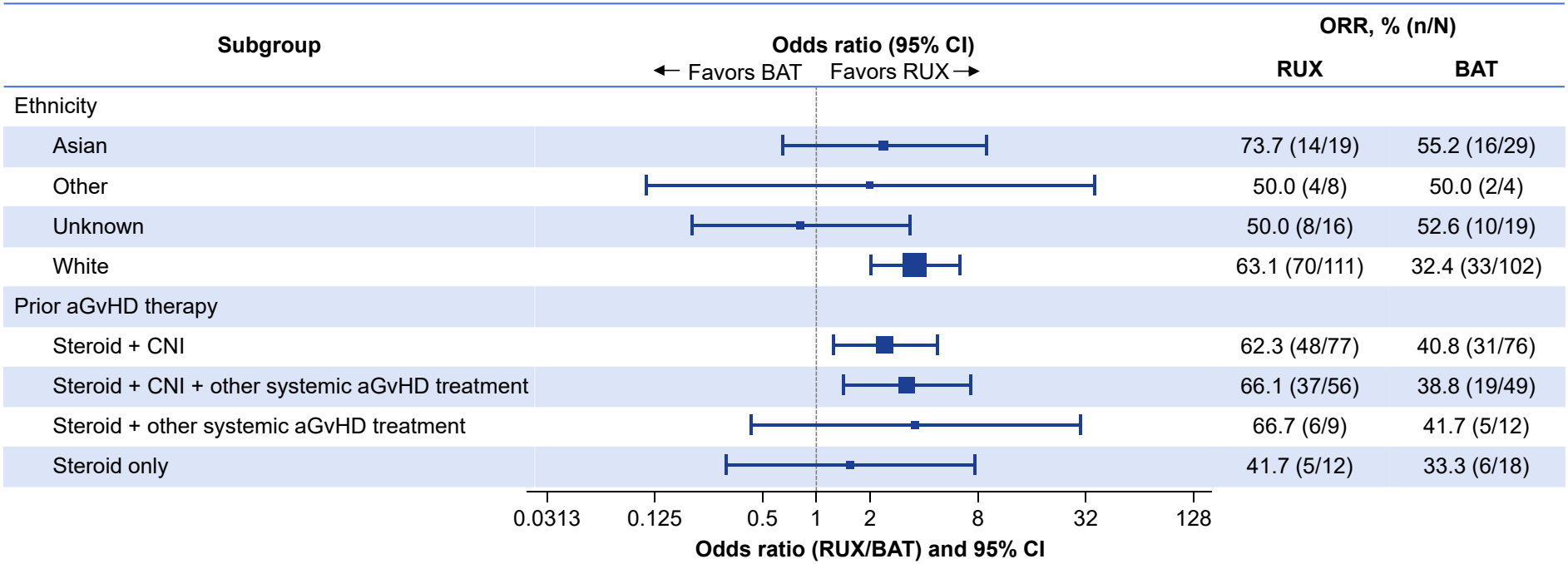


Subgroup	ORR, % (n/N) RUX	ORR, % (n/N) BAT
Age group		
18-65 years	64.8 (83/128)	38.1 (48/126)
> 65 years	42.9 (9/21)	40.0 (10/25)
Gender		
Female	62.9 (39/62)	39.1 (25/64)
Male	62.0 (57/92)	39.6 (36/91)
Conditioning regimen		
Myeloablative	55.3 (47/85)	36.9 (24/65)
Non-myeloablative	71.0 (22/31)	41.5 (17/41)
Reduced intensity	71.1 (27/38)	40.8 (20/49)
Donor source/HLA match status		
Not related and match	61.5 (40/65)	40.3 (25/62)
Not related and mismatch	71.1 (27/38)	44.4 (16/36)
Related and match	59.3 (16/27)	24.1 (7/29)
Related and mismatch	52.4 (11/21)	52.4 (11/21)

IRT, interactive response technology.
X-axis values are represented in natural log scale. Dotted line shows no effect point. The area of the box indicates the weight of the sub group, measured by the size of subpopulation.

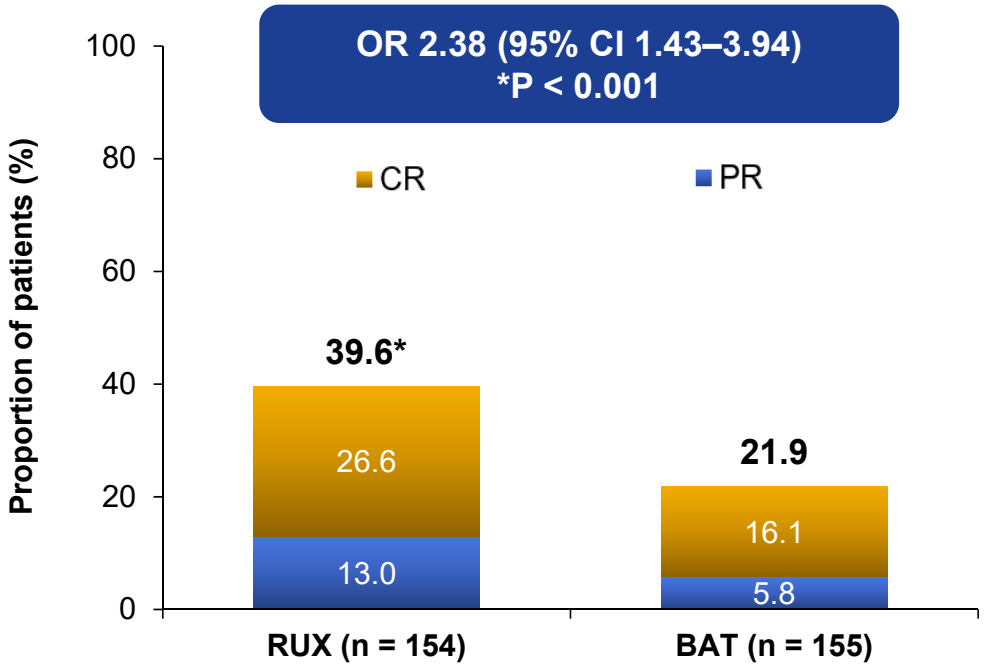
Overall Response Rate at Day 28 Higher for Ruxolitinib vs BAT in Majority of Subgroups(cont'd)

Forest plot of odds ratio with 95% CI interval for ORR at Day 28 from subgroup analysis



IRT, interactive response technology.
X-axis values are represented in natural log scale. Dotted line shows no effect point. The area of the box indicates the weight of the sub group, measured by the size of subpopulation.

Durable Overall Response Rate at Day 56 Significantly Higher for Ruxolitinib vs BAT

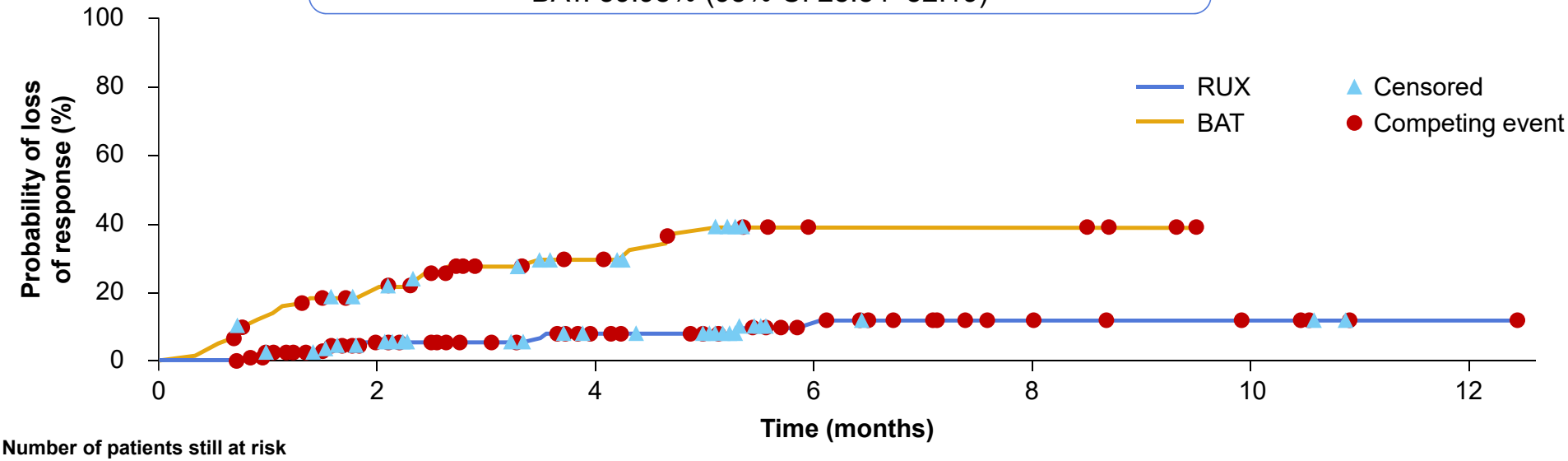


	RUX (n = 154)	BAT (n = 155)
Responders, n (%)		
Complete Response	41 (26.6)	25 (16.1)
Partial Response	20 (13.0)	9 (5.8)
Non-responders, n (%)		
No response	1 (0.6)	1 (0.6)
Mixed response	5 (3.2)	4 (2.6)
Progression	0	0
Other†	0	1 (0.6)
Unknown	29 (18.8)	21 (13.5)

†Other: patient with additional systemic therapies along with CR/PR per investigator assessment.

Duration of Response*

Cumulative incidence of loss of response at 6 months:
RUX: 9.65% (95% CI 4.39–17.40)
BAT: 39.98% (95% CI 25.54–52.19)



Number of patients still at risk

RUX	96	71	47	20	10	7	2
BAT	61	40	21	4	4	0	0

Cumulative number of competing events

RUX	0	13	26	37	45	48	51
BAT	0	5	14	19	19	23	NA

*Only patients achieving a response at Day 28 were included.

Common (≥ 10%) Adverse Events Up to Day 28 by Preferred Term

Event, n (%)	RUX (n = 152)*		BAT (n = 150)*	
	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Thrombocytopenia	50 (32.9)	41 (27.0)	27 (18.0)	23 (15.3)
Anemia	46 (30.3)	33 (21.7)	42 (28.0)	28 (18.7)
Cytomegalovirus infection†	39 (25.7)	11 (7.2)	31 (20.7)	12 (8.0)
Peripheral edema	28 (18.4)	2 (1.3)	26 (17.3)	1 (0.7)
Platelet count decreased	26 (17.1)	22 (14.5)	21 (14.0)	20 (13.3)
Neutropenia	24 (15.8)	20 (13.2)	19 (12.7)	14 (9.3)
Hypokalemia	20 (13.2)	9 (5.9)	25 (16.7)	9 (6.0)
Hypertension	16 (10.5)	9 (5.9)	14 (9.3)	6 (4.0)
Hypoalbuminemia	16 (10.5)	6 (3.9)	15 (10.0)	10 (6.7)
Pyrexia	16 (10.5)	2 (1.3)	17 (11.3)	2 (1.3)
Hypomagnesemia	15 (9.9)	0	20 (13.3)	1 (0.7)
Diarrhea	14 (9.2)	7 (4.6)	15 (10.0)	5 (3.3)
All deaths up to study cut-off date, n (%)‡	72 (47.4)		77 (51.3)	
Deaths during randomized treatment period up to study cut-off date, n (%)	43 (28.3)		36 (24.0)	

*Safety population: all patients who received at least 1 dose of study treatment. †A distinction between cytomegalovirus infection and reactivation was not made due to MedDRA v.22.0 limitations (cytomegalovirus reactivation coded to cytomegalovirus infection). ‡Most common causes of death were aGvHD (34 RUX, 37 BAT), underlying disease progression, including neoplasms (8 RUX, 8 BAT), multiple organ dysfunction syndrome (3 RUX, 1 BAT), sepsis (4 RUX, 3 BAT), and septic shock (3 RUX, 3 BAT).

Conclusions

- **ORR at Day 28 was significantly higher with RUX than with BAT in patients with SR aGvHD** (62.3% vs 39.4%; P < 0.001)
- RUX showed a consistent clinically meaningful treatment benefit for patients compared with BAT across different subgroups of baseline characteristics
  - These included aGvHD grade at randomization, organ involvement, criteria for SR and transplant characteristics
- **Durable ORR at Day 56 was also significantly higher with RUX than with BAT** (ORR 39.6% vs 21.9%; P < 0.001)
  - The 6-month cumulative incidence of loss of response was 9.7% with RUX vs 40.0% with BAT
- The safety profile of RUX was consistent with previous observations in patients with aGvHD
- RUX is the first novel agent to demonstrate superiority to BAT in a phase 3 trial of patients with SR aGvHD

Acknowledgments

- The authors would like to thank the patients who participated in the REACH2 clinical trial and the investigators who were involved in the study

Participating REACH2 Investigators

Trial Site Primary Investigator Name	Trial Site Name
Sung-Soo Yoon	Seoul National University Hospital
Chulwon Jung	Samsung Medical Center
Tobias Gedde-Dahl	Oslo Universitetssykehus HF Rikshospitalet
Marwan Shaheen	King Faisal Specialist Hospital and Research Center Riyadh
Jose Antonio Perez Simon	Hospital Virgen del Rocio
Jose Valentin Garcia Gutierrez	Hospital Ramon Y Cajal
Jaime Sanz Caballer	Hospital Universitario i Politecnico La Fe
Rafael Duarte Palomino	Hospital Universitario Puerta de Hierro
David Valcarcel Ferreiras	Hospital Vall D'Hebron
Cristina Diaz de Heredia Rubio	Hospital Vall D'Hebron
Mi Kwon	Hospital Gregorio Maranon
Maria del Carmen Martinez Munoz	Hospital Clinic I Provincial De Barcelona
Soledad Gonzalez	Hospital General de Asturias
Matilde Rodriguez Ruiz	Hospital Alvaro Cunqueiro
Inmaculada Heras Fernando	Hospital Morales Meseguer
Maria Pascual Cascon	Hospital Regional Univ de Malaga
Yasmina Mozo	Hospital La Paz
Marta Gonzalez Vicent	Hospital Nino Jesus
Jose Maria Fernandez Navarro	Hospital Universitario y Politecnico La Fe
Yvonne Björk	Sahlgrenska Universitetssjukhuset
Kristina Carlson	Akademiska Sjukhuset
Jih-Luh Tang	National Taiwan University Hospital

Trial Site Primary Investigator Name	Trial Site Name
Su-Peng Yeh	China Medical University Hospital
Ronjon Chakraverty	UCLH Hospital
Robert Wynn	Royal Manchester Children's Hospital
Lajos Floro	Kings College Hospital
Brian Thomas Kornblit	Rigshospitalet
Jason Butler	Royal Brisbane and Womens Hospital
David Ritchie	Royal Melbourne Hospital
John Kwan	Westmead Hospital
Jacqueline Fleming	Royal Children's Hospital VIC
Duncan Purtill	Fiona Stanley Hospital
Werner Rabitsch	Universitaetsklinik fuer Innere Medizin I
Hildegard Greinix	Universitätsklinik für Innere Medizin
Johannes Clausen	Krankenhaus der Elisabethinen Linz
Dennis Kim	Princess Margaret Cancer Centre
Natasha Kekre	The Ottawa Hospital Cancer Centre
Imran Ahmad	Hopital Maisonneuve Rosemont
Brian Leber	The Juravinski Cancer Centre
Andrew Daly	Tom Baker Cancer Center
Gizelle Popradi	McGill University Health Center Gen Site
Jennifer White	Vancouver General Hospital
Mohamed Elemary	Saskatoon Cancer Centre
Gerard Socie	Hopital Saint Louis

Participating REACH2 Investigators

Trial Site Primary Investigator Name	Trial Site Name
Valérie Coiteux	CHRU Claude Huriez
Patrice Chevallier	Hopital Hotel Dieu
Claude-Eric Bulabois	Hopital Albert Michallon
Helene Labussiere-Wallet	Centre Hospitalier Lyon Sud
Mohamad Mohty	Hospital Saint Antoine
Pierre-Simon Rohrlich	CHU de Nice Hopital de l'Archet 2
Edouard Forcade	Hopital du Haut-Leveque
Ana Berceanu	CHU Jean Minjoz
Sylvie Francois	CHU d'Angers
Stephanie N'Guyen Quoc	Hopital La Pitie Salpetriere
Marie-Therese Rubio	CHU Nancy Hopital Brabois
Jean-Hughes Dalle	Hopital Robert Debre
Marie Ouachee-Chardin	Institut d'hematologie et d'oncologie pediatrique
Benedicte Bruno	CHRU de Lille - Hopital Jeanne de Flandre
Anne Huynh	IUCT Oncopole
Nathalie Fegueux	CHRU de Montpellier Hopital Saint Eloi
Jerome Cornillon	Institut Cancerologie Loire L Neuwirth
Pascal Turlure	Centre Hospitalier de Limoges
Robert Zeiser	Universitaetsklinikum Freiburg
Georg-Nikolaus Franke	Universitaetsklinikum Leipzig AoR
Friedrich Stoelzel	Universitaetsklinikum Dresden
Matthias Eder	Medizinische Hochschule Hannover

Trial Site Primary Investigator Name	Trial Site Name
Arne Brecht	DKD HELIOS Klinik Wiesbaden
Nicolaus Kroeger	Universitaetsklinikum Hamburg Eppendorf
Nina-Kristin Steckel	Universitaetsklinikum Essen
Eva Wagner	Universitaetsklinikum Mainz
Guido Kobbe	Universitaetsklinikum
Wolfgang Bethge	Universitaetsklinikum Tuebingen
Matthias Stelljes	Universitaetsklinikum Muenster
Donald Bunjes	Universitaetsklinikum Ulm
Igor Blau	Universitaetsmedizin Charite
Ingo Mueller	Universitaetsklinikum Hamburg Eppendorf
Stefan Klein	Universitaetsklinikum Mannheim
Christoph Schmid	Universitaetsklinikum Augsburg
Lena Oevermann	Universitaetsmedizin Charite
Herrad Baurmann	Helios Kliniken GmbH Berlin Buch
Inken Hilgendorf	Universitaetsklinikum Jena
Klaus Daniel Stachel	Universitaetsklinikum Erlangen Nuernberg
Yok-Lam Kwong	Queen Mary Hospital
Ron Ram	Tel Aviv Sourasky Medical Center Ichilov
Batya Avni	Hadassah Medical Organization Ein Karem
Moshe Yeshurun	Rabin Medical Center Belinson
Tsila Zuckerman	Rambam Medical Center
Riccardo Saccardi	Azienda Ospedaliera Universitaria Careggi

Participating REACH2 Investigators

Trial Site Primary Investigator Name	Trial Site Name
Paolo Corradini	Fondazione IRCCS Istituto Nazionale dei Tumori
Franco Locatelli	IRCCS Ospedale Pediatrico Bambino Gesu'
Alessandro Rambaldi	ASST Papa Giovanni XXIII
Simona Sica	Fondaz Policl Univ A Gemelli
Attilio Olivieri	AOU Osp Riuniti Umberto I GM Lancisi G Salesi Univ Studi
Francesca Patriarca	Az.Osped.-Universit.Santa Maria della Misericordia di Udine
Giovanni Grillo	ASST Grande Osp Metropolitano
Francesca Bonifazi	Az Osp di Bologna Policl S Orsola Malpighi Univ degli Studi
Maura Faraci	IRCCS Istituto Giannina Gaslini
Attilio Rovelli	Fondazione Monza e Brianza per il Bambino e la sua Mamma ASST Monza
Benedetto Bruno	P O Molinette AO Citta della Salute e della Scienza Torino
Domenico Russo	ASST degli Spedali Civili di Brescia Univ degli Studi
Maurizio Musso	Casa di Cura di Alta Spec La Maddalena Dip Onc III livel
Marco Zecca	Fondazione IRCCS Policlinico S Matteo Univ.degli Studi Pavia
Franca Fagioli	AO Città della Salute e Scienza-PO Infant. Regina Margherita
Angelo Michele Carella	IRCCS Casa Sollievo della Sofferenza

Trial Site Primary Investigator Name	Trial Site Name
Stefania Bregante	Ospedale Policlinico San Martino IRCCS
Roberto Sorasio	Az Osp S Croce e Carle
Takanori Teshima	Hokkaido University Hospital
Koichi Miyamura	Japanese Red Cross Nagoya Daiichi Hospital
Kiyoshi Ando	Tokai University Hospital
Hirohisa Nakamae	Osaka City University Hospital
Yoshinobu Maeda	Okayama University Hospital
Tadakazu Kondo	Kyoto University Hospital
Masaya Okada	Hyogo College of Medicine Hospital
Kazuhiko Kakihana	Tokyo Metropolitan Komagome Hospital
Koji Kato	Kyushu University Hospital
Yasushi Onishi	Tohoku University Hospital
Kentaro Fukushima	Osaka University Hospital
Shuichi Taniguchi	Toranomon Hospital
Takehiko Mori	Keio University Hospital
Takayuki Ishikawa	Kobe City Medical Center General Hospital
Yoshihiro Inamoto	National Cancer Center Hospital
J. Kuball	University Medical Center Utrecht (UMCU)
C A Lindemans	Prinses Maxima Centrum
Jan Vydra	Ustav hematologie a krevni transfuze
Achilleas Anagnostopoulos	General Hospital of Thessaloniki G PAPANIKOLAOU

Participating REACH2 Investigators

Trial Site Primary Investigator Name	Trial Site Name
Zubeyde Ozkurt	Gazi University Medical Faculty
Zafer Gulbas	Anadolu Saglik Merkezi
Seckin Cagirgan	Izmir Medical Park Hospital
Sinem Civriz Bozdag	Ankara University Medical Faculty
Penka Ganeva	Spec.Hospital for Active Treatment in Hematological Diseases
Dobrin Konstantinov	UMHAT Tsaritsa Yoanna-ISUL EAD
Kazimierz Halaburda	Instytut Hematologii i Transfuzjologii
Jan Zaucha	UCK Klinika Hematologii i Transplantologii
Gergely KrivÃ¡n	DEL PESTI CENTRUMKORHAZ
Isabelina Ferreira	Instituto Portugues de Oncologia de Lisboa
Joao Forjaz de Lacerda	Centro Hospitalar Lisboa Norte
Alexey Maschan	Federal Research Clinical Center for childrens hemotology
Elena Parovichnikova	Hematological Scientific Center of RAMS

Thank you

The authors would like to thank Keisha Peters, MSc, of Excerpta Medica, for writing and editorial assistance, funded by Novartis Pharmaceuticals.