VIRTUAL 2020 ESMO congress

Pooled Analysis of Patient-Reported Quality of Life in the MONALEESA-2, -3, and -7 Trials of Ribociclib Plus Endocrine Therapy to Treat Hormone Receptor–Positive, HER2-Negative Advanced Breast Cancer

Peter A. Fasching,[1] Aditya Bardia,[2] Arnd Nusch,[3] Guy Jerusalem,[4] Arlene Chan,[5] Nagi El Saghir,[6] Emilio Alba,[7] Seock-Ah Im,[8] Wolfgang Janni,[9] David Chandiwana,[10] Brad Lanoue,[10] Astrid Thuerigen,[11] Anil Gaur,[12] Nadia Harbeck[13]

[1]University Hospital Erlangen, Comprehensive Cancer Center Erlangen–European Metropolitan Region of Nuremberg, and Department of Gynecology and Obstetrics, Friedrich-Alexander University Erlangen-Nuremberg, Erlangen, Germany; [2]Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, USA; [3]Practice for Hematology and Internal Oncology, Velbert, Germany; [4]Centre Hospitalier Universitaire Liège and Liege University, Liege, Belgium; [5]Breast Cancer Research Centre–WA and School of Medicine, Curtin University, Perth, WA, Australia; [6]American University of Beirut Medical Center, Beirut, Lebanon; [7]Hospital Regional y Universitario Virgen de la Victoria, IBIMA, Málaga, Spain; [8]Seoul National University Hospital Cancer Research Institute, Seoul National University College of Medicine, Seoul, South Korea; [9]Department of Gynecology and Obstetrics, Ulm University Hospital, Ulm, Germany; [10]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [11]Novartis Pharma AG, Basel, Switzerland; [12]Novartis Healthcare Pvt Ltd, Hyderabad, India; [13]Breast Center, Department of Obstetrics and Gynecology, Ludwig-Maximilians-University Munich, Munich, Germany

VIRTUAL 2020 ESMO congress

Disclosures

Peter A. Fasching

- Advisory/steering board: Novartis
- Ad board: Roche, Pfizer, Celgene, Teva, Myelo Therapeutics, Macrogenics, Eisai, Puma, Astra Zeneca
- Research support: BionTech, Cepheid, Novartis
- Ad board/lectures: Merck Sharp & Dohme, Lilly, Daiichi-Sankyo

These studies and medical editorial assistance were funded by Novartis.

Pooled QoL MONALEESA Analysis: Background

- Patient-reported outcome results provide important guidance for clinical decision-making; in fact, the ESMO-MCBS includes QoL impact as an important consideration for grading clinical benefit[1]
- MONALEESA-2, -3, and -7 tested efficacy and safety of ribociclib with different ET combination partners as first- or second-line treatment for HR+/HER2− ABC
- In each separate Phase III trial, patient-reported QoL results indicated that treatment with ribociclib + ET maintained or improved global health scores, along with other QoL subscores[2-4]
- Pooling the MONALEESA trial data enables a robust analysis of QoL that includes pre- and postmenopausal patients with HR+/HER2− ABC receiving ribociclib with different ET combination partners

ABC, advanced breast cancer; ESMO-MCBS, European Society for Medical Oncology-Magnitude of Clinical Benefit Scale; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; QoL, quality of life.

1. Cherny NI, et al. *Ann Oncol*. 2017;28:2340-2366. 2. Verma S, et al. *Breast Cancer Res Treat*. 2018;170:535-545. 3. Fasching PA, et al. *Breast*. Accepted August 2020. 4. Harbeck N, et al. *Ther Adv Medical Oncol*. 2020;12:1-8.

VIRTUAL 2020 ESMO congress

Pooled QoL MONALEESA Analysis: Objective and Methods

- Objective: assess time to deterioration by at least 10% in global health status, as well as pain, fatigue, and physical, emotional, and social functioning subscores of the EORTC-QLQ C30
    - Change from baseline in global health score and pain were also examined, as was QoL in patients with and without progressive disease
- Patient populations in this pooled analysis:
    - MONALEESA-2: all patients (letrozole +/- ribociclib as first-line endocrine therapy)
    - MONALEESA-3: only patients receiving fulvestrant +/- ribociclib as first-line endocrine therapy
    - MONALEESA-7: only patients receiving an NSAI +/- ribociclib[a] as first-line endocrine therapy
- Patient-reported outcomes were collected via the EORTC-QLQ C30
- Data are reported for visits during which at least 50 patients completed the questionnaire in one arm
- Compliance rates for RIB vs PBO were 92%-94% in cycles 3, 15, and 25, and 70%-86% in cycles 40, 55, and EOT

EORTC-QLQ C30, European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire C30; EOT, end of treatment; NSAI, nonsteroidal aromatase inhibitor; PBO, placebo; QoL, quality of life; RIB, ribociclib.

[a] Ribociclib is not indicated in combination with tamoxifen; therefore, results of patients treated with tamoxifen in the MONALEESA-7 trials were not considered here.

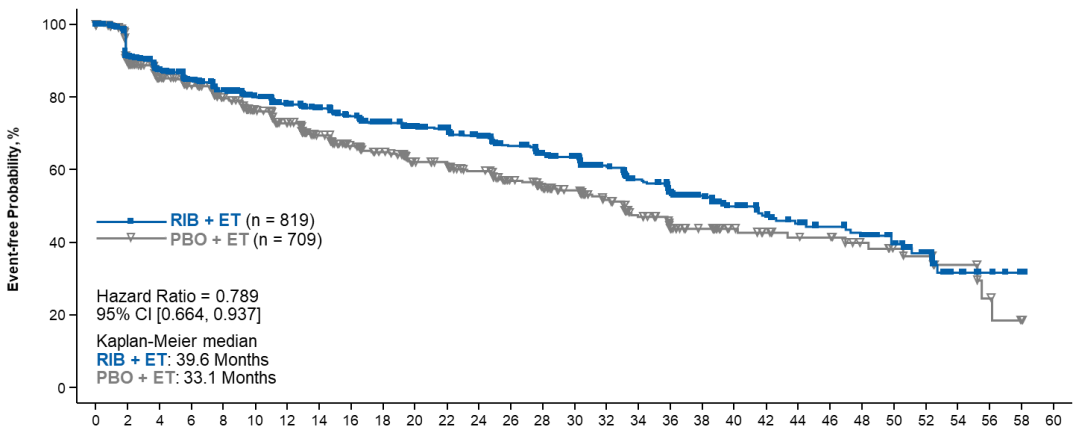
Pooled QoL MONALEESA Analysis: Select Baseline Characteristics

	Category	RIB + ET (n = 819), %	PBO + ET (n = 709), %
Race[a]	Asian	16.6	16.6
	White	73.6	74.3
	Other	5.7	4.8
	Unknown	4.0	4.2
ECOG performance status	0	64.7	68.0
	1	35.0	31.9
	Missing	0.2	0.1
Progression/metastasis status in relation to primary diagnosis	De novo[b]	34.1	31.7
	Non-de novo	65.9	68.3
	DFI ≤ 12 months[c]	3.1	2.8
	DFI > 12 months and ≤ 24 months[c]	6.1	6.2
	DFI >24 months[c]	56.8	59.1
	DFI Unknown[c]	0	0.1
Metastatic sites	Bone only	21.4	22.0
	Visceral	59.1	58.7
	Lung	39.1	37.0
	Liver	23.1	25.8
	CNS	0.5	0.1
Age, years, median (range)		57.0 (23-91)	55.0 (29-88)

CNS, central nervous system; DFI, disease-free interval; ECOG, Eastern Cooperative Oncology Group; ET, endocrine therapy; PBO, placebo; QoL, quality of life; RIB, ribociclib.
[a] Other race includes patients who identified as Black, Native American, Pacific Islander, and other. [b] De novo disease in the MONALEESA-2 study referred to no date of first recurrence/progression or the first recurrence/progression occurring within 90 days of initial diagnosis with no prior antineoplastic therapy received, including medication and radiation. De novo disease in the MONALEESA-3 and -7 studies followed the same definition as MONALEESA-2, except that the criterion of no prior antineoplastic therapy was restricted to medication only. [c] Disease-free interval was defined as time from initial diagnosis to first recurrence/progression.

Pooled QoL MONALEESA Analysis: TTD ≥ 10% in Global Health Score

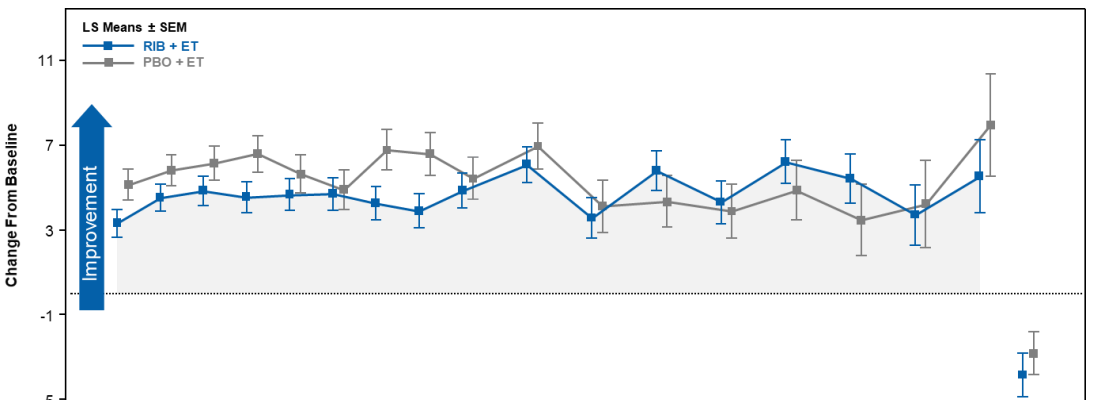
RIB + ET treatment delayed deterioration by ≥ 10% in GHS vs PBO + ET



ET, endocrine therapy; GHS, global health score; PBO, placebo; QoL, quality of life; RIB, ribociclib; TTD, time to deterioration.

Pooled QoL MONALEESA Analysis: Change From Baseline in Global Health Score

GHS was maintained at all time points during treatment

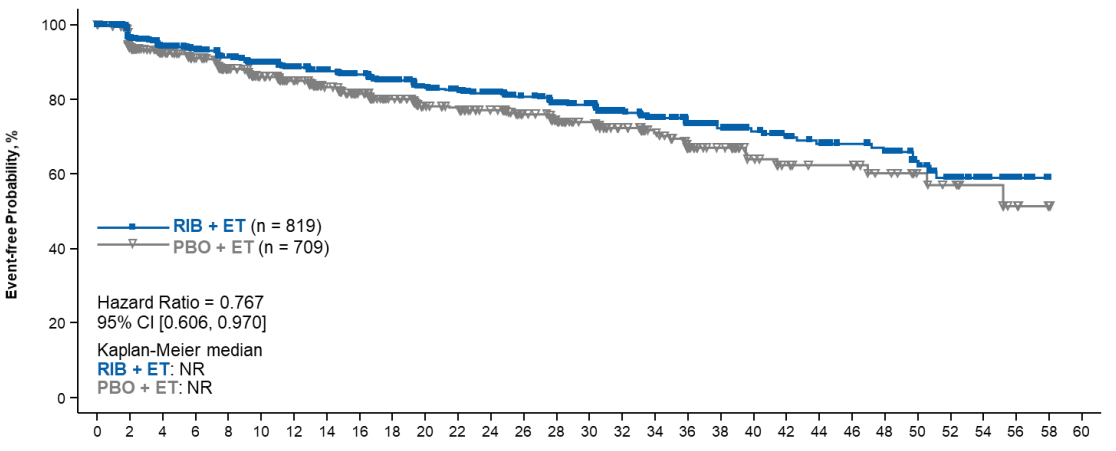


RIB + ET n =	690	630	606	574	537	500	466	447	409	382	362	325	296	265	223	187	131	441
PBO + ET n =	586	519	491	447	402	375	343	306	281	236	219	201	186	145	106	89	60	484

EOT, end of trial; ET, endocrine therapy; GHS, global health score; LS, least squares; PBO, placebo; QoL, quality of life; RIB, ribociclib; SEM, standard error of the mean.

Pooled QoL MONALEESA Analysis: TTD ≥ 10% in Pain Score

RIB treatment delayed TTD ≥ 10% in pain vs PBO



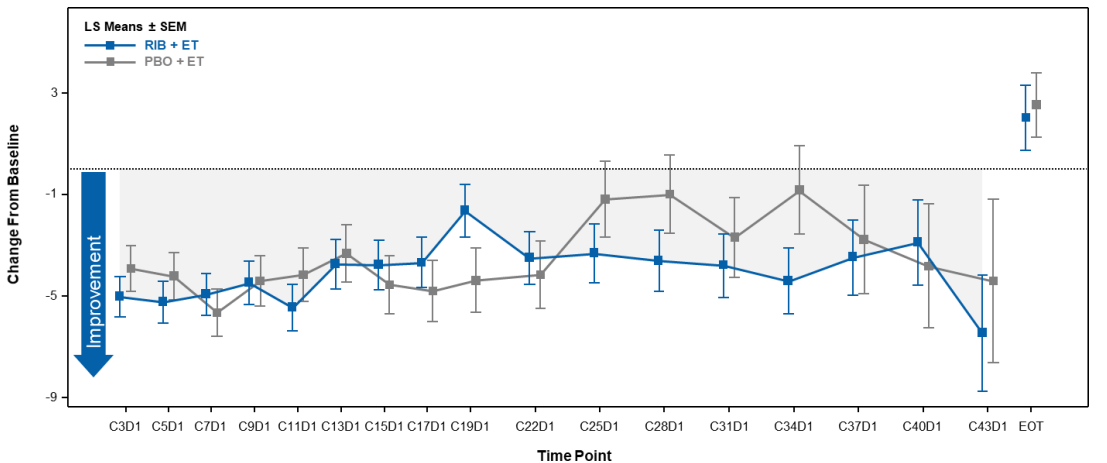
Number of patients still at risk

RIB + ET	819	688	635	598	560	521	486	453	428	401	376	365	342	318	286	274	233	195	158	131	98	84	77	66	61	45	35	18	8	0	0
PBO + ET	709	571	522	483	435	400	368	325	295	265	236	230	210	191	169	153	119	97	71	60	41	35	32	32	26	19	16	10	5	1	0

ET, endocrine therapy; NR, not reached; PBO, placebo; QoL, quality of life; RIB, ribociclib; TTD, time to deterioration.

Pooled QoL MONALEESA Analysis: Change From Baseline in Pain Score

Pain scores were maintained at all time points during treatment



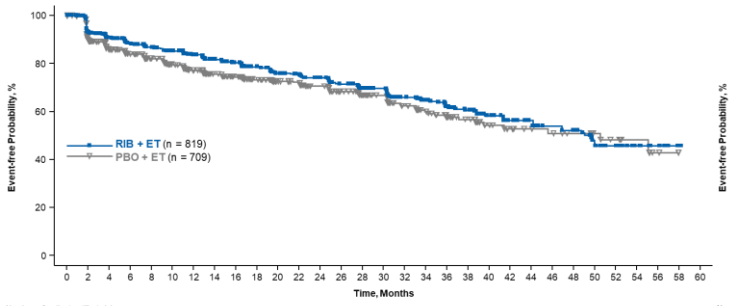
EOT, end of trial; ET, endocrine therapy; LS, least squares; PBO, placebo; QoL, quality of life; RIB, ribociclib; SEM, standard error of the mean.

Pooled QoL MONALEESA Analysis: TTD ≥ 10% in Fatigue and Physical Function

TTD ≥ 10% in fatigue and physical functioning was similar for RIB vs PBO

Fatigue

49.7 vs **50.6** months; HR, 0.833 (95% CI, 0.684-1.013)

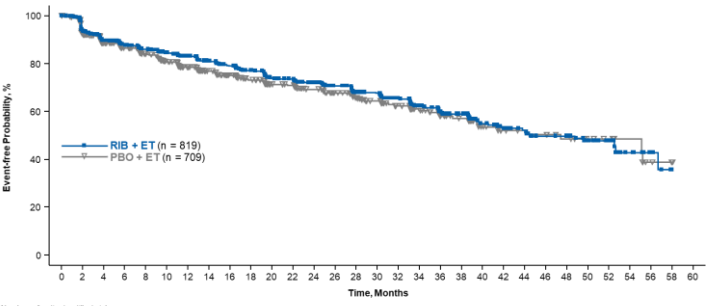


Number of patients still at risk

RIB + ET	819	670	614	573	537	502	467	438	413	383	352	343	319	293	267	258	216	183	145	124	93	77	71	59	55	42	31	15	8	1	0
PBO + ET	709	555	494	456	416	380	346	307	278	252	225	219	197	177	160	147	109	89	66	56	39	33	29	27	24	19	16	9	3	0	0

Physical Functioning

44.5 vs **47.4** months; HR, 0.886 (95% CI, 0.730-1.076)



Number of patients still at risk

RIB + ET	819	678	621	581	541	505	469	432	408	383	354	345	321	296	265	257	218	180	146	124	89	75	67	55	53	40	31	13	7	0	0
PBO + ET	709	571	509	469	425	386	352	308	276	250	221	216	193	174	154	140	106	86	66	57	39	33	31	30	26	19	16	10	4	1	0

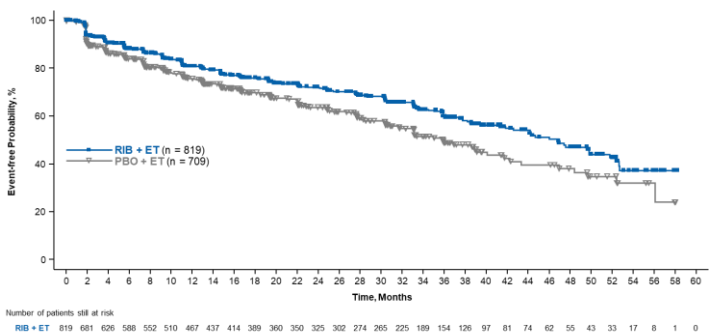
ET, endocrine therapy; HR, hazard ratio; PBO, placebo; QoL, quality of life; RIB, ribociclib; TTD, time to deterioration.

Pooled QoL MONALEESA Analysis: TTD ≥ 10% in Emotional and Social Function

TTD ≥ 10% in emotional functioning was delayed for RIB vs PBO

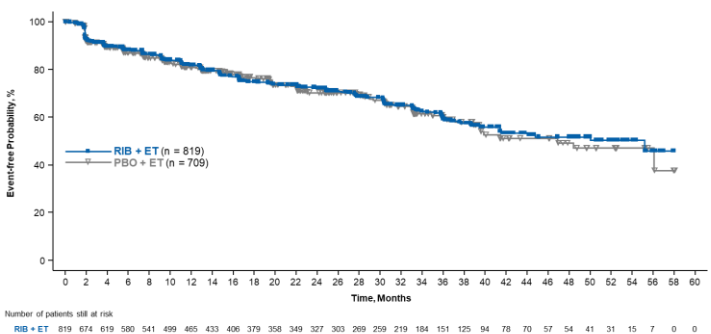
Emotional Functioning

46.9 vs 35.9 months; HR, 0.711 (95% CI, 0.593-0.854)



Social Functioning

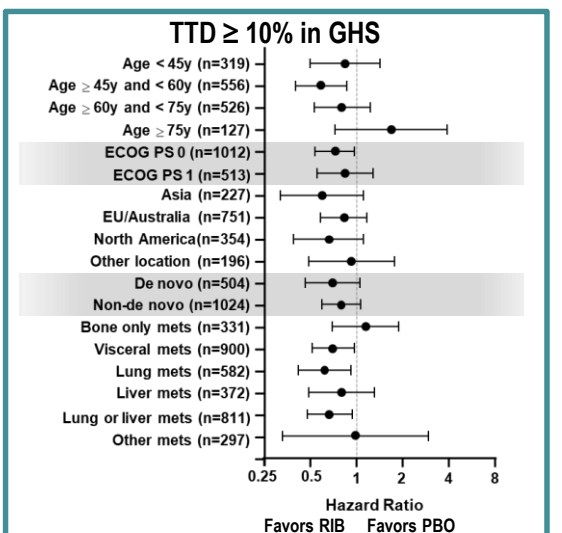
55.2 vs 46.9 months; HR, 0.971 (95% CI, 0.797-1.184)

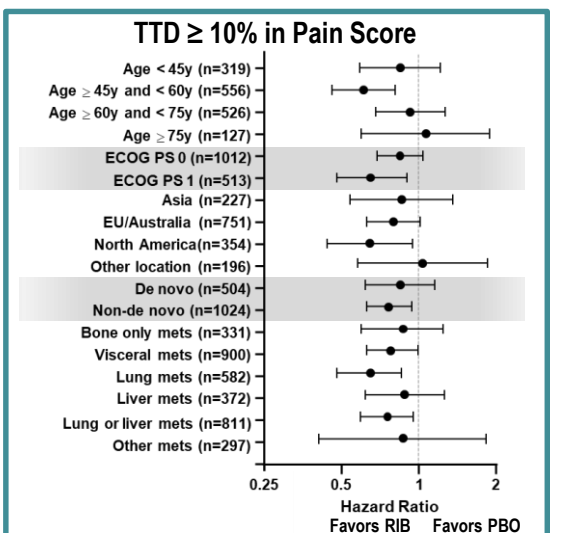


ET, endocrine therapy; HR, hazard ratio; PBO, placebo; QoL, quality of life; RIB, ribociclib; TTD, time to deterioration.

Pooled QoL MONALEESA Analysis: Subgroup Analysis of TTD ≥ 10% in GHS and Pain

TTD ≥ 10% in GHS and pain score was generally consistent across subgroups



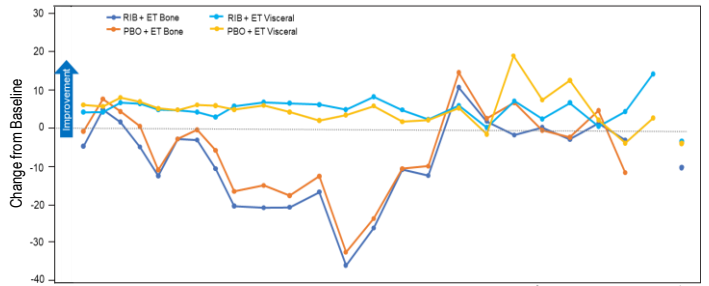


ECOG PS, Eastern Cooperative Oncology Group performance status; GHS, global health score; mets, metastases; PBO, placebo; QoL, quality of life; RIB, ribociclib; TTD, time to deterioration.

Pooled QoL MONALEESA Analysis: Subgroup Analysis of Change From Baseline

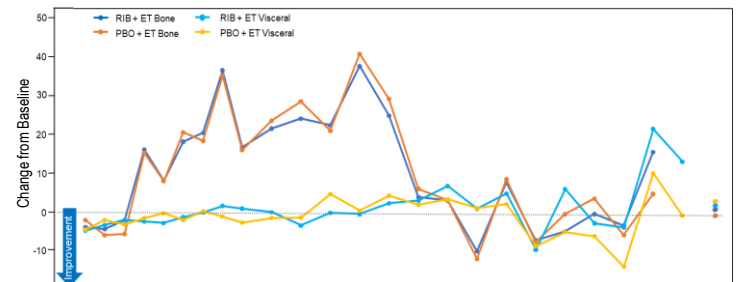
GHS and pain scores were generally maintained in those with visceral metastases

Change from baseline in GHS by metastatic site



No. at Risk	C3D1	C5D1	C7D1	C9D1	C11D1	C13D1	C15D1	C17D1	C19D1	C22D1	C25D1	C28D1	C31D1	C34D1	C37D1	C40D1	C43D1	C46D1	C49D1	C52D1	C55D1	C58D1	C61D1	C64D1	EOT
Bone RIB	149	131	127	123	113	113	103	102	93	87	86	79	71	61	52	47	33	22	15	13	11	8	4	-	84
Bone PBO	140	127	121	106	102	92	88	84	72	62	52	50	46	34	26	26	20	10	10	8	6	4	1	-	113
Visceral RIB	406	370	354	330	312	284	264	255	235	218	205	185	168	152	125	99	72	54	39	35	31	20	11	3	269
Visceral PBO	329	288	268	246	218	202	180	154	149	121	120	110	102	81	57	45	30	19	15	17	15	11	8	2	284

Change from baseline in pain by metastatic site



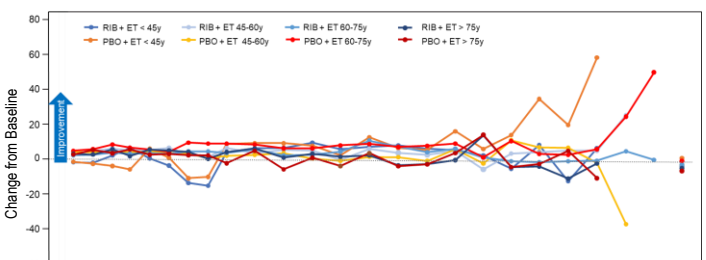
No. at Risk	C3D1	C5D1	C7D1	C9D1	C11D1	C13D1	C15D1	C17D1	C19D1	C22D1	C25D1	C28D1	C31D1	C34D1	C37D1	C40D1	C43D1	C46D1	C49D1	C52D1	C55D1	C58D1	C61D1	C64D1	EOT
Bone RIB	150	132	127	123	114	113	103	103	93	87	86	79	72	61	52	47	33	22	15	13	11	8	4	-	84
Bone PBO	141	129	122	107	103	94	89	85	73	63	53	51	47	35	26	26	20	10	10	8	6	4	1	-	114
Visceral RIB	406	370	355	330	313	284	264	255	236	218	205	185	168	153	125	99	73	54	39	35	31	20	11	3	268
Visceral PBO	332	293	270	249	222	207	183	157	151	122	121	111	103	82	58	46	31	20	15	17	15	11	8	2	287

ET, endocrine therapy; GHS, global health score; PBO, placebo; QoL, quality of life; RIB, ribociclib.

Pooled QoL MONALEESA Analysis: Subgroup Analysis of Change From Baseline

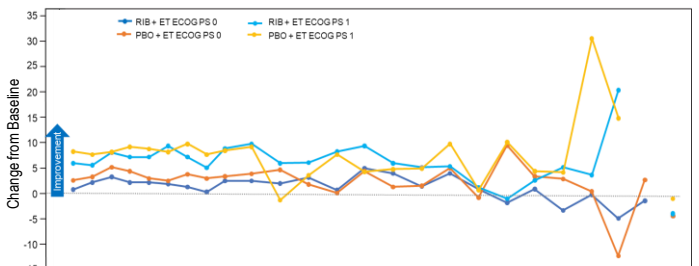
GHS was generally maintained during treatment regardless of age or ECOG PS

Change from baseline in GHS by age



No. at Risk	C1D1	C2D1	C3D1	C4D1	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1	C12D1	C13D1	C14D1	C15D1	C16D1	C17D1	C18D1	C19D1	C20D1	C25D1	C26D1	C31D1	C34D1	C37D1	C40D1	C43D1	C46D1	C49D1	C52D1	C55D1	C58D1	C61D1	C64D1	EOT
<45y RIB	151	140	137	124	116	102	98	92	84	78	74	67	65	53	34	25	13	6	5	4	3	3	-	-	100
< 45y PBO	123	105	99	85	77	72	65	55	49	39	39	32	31	22	17	11	6	3	2	1	1	1	-	-	99
45-60y RIB	248	231	219	203	193	185	175	163	149	141	132	122	109	98	82	65	49	35	19	19	18	13	6	-	156
45-60y PBO	214	191	184	167	150	141	127	118	111	94	82	80	69	54	35	25	18	7	4	6	5	5	3	-	187
60-75y RIB	237	213	204	201	187	171	155	154	138	126	123	108	99	94	89	78	58	42	34	29	25	11	6	3	149
60-75y PBO	205	183	171	159	141	133	125	110	99	88	80	73	71	56	43	43	31	21	18	18	14	8	3	2	162
>75y RIB	54	46	46	46	41	42	38	38	38	37	33	28	23	20	18	19	11	9	7	5	3	4	3	-	36
>75y PBO	44	40	37	36	34	29	26	23	22	15	18	16	15	13	11	10	5	5	5	6	3	2	2	-	36

Change from baseline in GHS by ECOG PS



No. at Risk	C1D1	C2D1	C3D1	C4D1	C5D1	C6D1	C7D1	C8D1	C9D1	C10D1	C11D1	C12D1	C13D1	C14D1	C15D1	C16D1	C17D1	C18D1	C19D1	C20D1	C25D1	C26D1	C31D1	C34D1	C37D1	C40D1	C43D1	C46D1	C49D1	C52D1	C55D1	C58D1	C61D1	C64D1	EOT
ECOG 0 RIB	457	413	404	381	360	337	317	306	286	262	249	227	212	187	155	121	85	57	40	34	30	17	10	5	300
ECOG 0 PBO	405	355	341	312	280	267	249	227	209	175	166	152	141	110	79	66	43	26	21	23	16	13	7	3	337
ECOG 1 RIB	232	216	201	193	176	162	148	140	122	120	112	97	84	78	68	66	46	35	25	23	19	14	5	-	140
ECOG 1 PBO	180	164	150	135	122	108	94	79	72	61	53	49	45	35	27	23	17	10	8	8	7	3	2	-	146

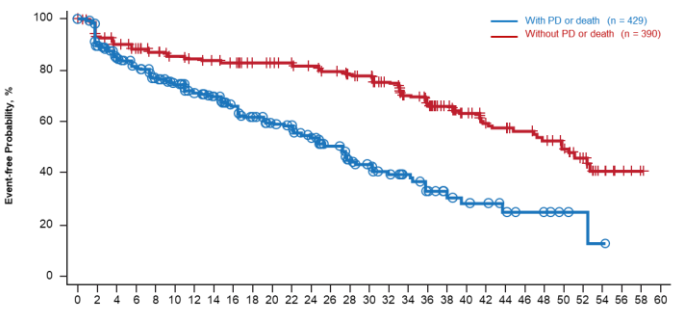
ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; GHS, global health score; PBO, placebo; QoL, quality of life; RIB, ribociclib.

Pooled QoL MONALEESA Analysis: Subgroup Analysis of TTD ≥ 10% GHS by PD

Patients without vs with PD had a delay in TTD ≥ 10% in GHS

RIB + ET (PD vs no PD)

27.2 vs 49.8 months; HR, 2.72 (95% CI, 2.10-3.52)

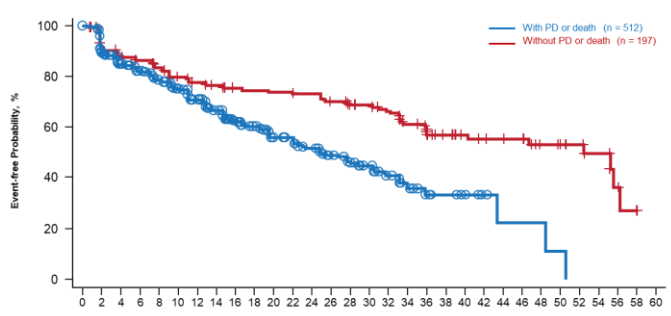


Number of patients still at risk

With PD or death	429	343	306	277	245	221	194	170	151	133	113	105	90	70	52	47	37	30	20	15	12	11	8	6	6	3	2	1	0	0	0
Without PD or death	360	324	303	291	281	269	262	257	252	244	240	238	231	223	207	203	175	147	125	102	75	61	56	48	43	32	25	10	6	1	0

PBO + ET (PD vs no PD)

25.0 vs 52.4 months; HR, 2.12 (95% CI, 1.56-2.89)



Number of patients still at risk

With PD or death	512	395	340	313	276	245	216	177	150	131	104	100	82	65	53	44	28	18	12	10	8	4	2	2	2	1	0	0	0	0	0
Without PD or death	197	154	147	142	135	126	119	113	108	107	106	106	104	99	93	89	78	66	51	45	33	31	29	28	22	18	17	9	5	1	0

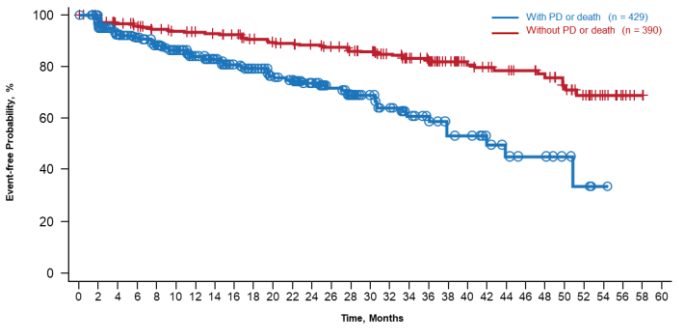
ET, endocrine therapy; GHS, global health score; HR, hazard ratio; PBO, placebo; PD, progressive disease; QoL, quality of life; RIB, ribociclib; TTD, time to deterioration.

Pooled QoL MONALEESA Analysis: Subgroup Analysis of TTD ≥ 10% in Pain Score by PD

Patients without vs with PD had a delay in TTD ≥ 10% in pain

RIB + ET (PD vs no PD)

41.9 months vs not reached, HR 2.80 (95% CI 1.97-3.98)

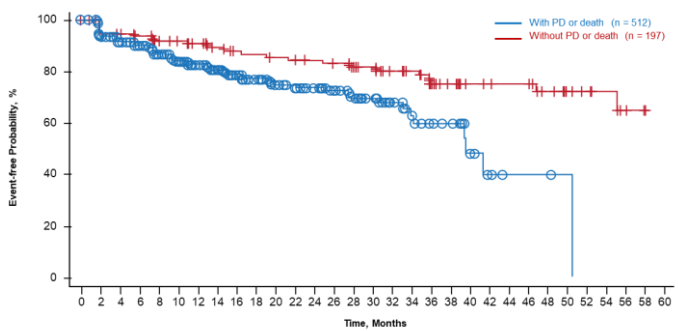


Number of patients still at risk

With PD or death	429	356	318	293	266	237	209	179	158	143	123	115	98	80	64	56	46	35	26	20	18	13	10	8	8	5	3	1	0	0	0
Without PD or death	390	332	317	305	294	284	277	274	270	258	253	250	244	238	222	218	186	160	132	111	80	71	67	58	53	40	32	17	8	0	0

PBO + ET (PD vs no PD)

39.6 months vs not reached, HR 2.19 (95% CI 1.44-3.33)



Number of patients still at risk

With PD or death	512	407	361	327	287	258	232	196	171	143	117	112	94	78	64	54	34	23	17	14	8	4	2	2	2	1	0	0	0	0	0
Without PD or death	197	164	161	156	148	142	136	129	124	122	119	118	116	113	105	99	85	74	54	46	33	31	30	30	24	18	16	10	5	1	0

ET, endocrine therapy; HR, hazard ratio; PBO, placebo; PD, progressive disease; QoL, quality of life; RIB, ribociclib; TTD, time to deterioration.

VIRTUAL 2020 ESMO congress

Pooled QoL MONALEESA Analysis: Conclusions

- This robust pooled analysis of 1528 patients in the MONALEESA-2, -3, and -7 trials demonstrated improvement in quality of life in patients receiving ribociclib + endocrine therapy
- Ribociclib treatment was associated with longer maintenance of global quality of life compared with placebo
- Pain score was maintained from baseline at all time points during treatment, and time to deterioration by at least 10% in pain score was delayed with ribociclib vs placebo treatment
- Times to deterioration by at least 10% in emotional and social functioning were numerically longer with ribociclib vs placebo treatment, whereas those of fatigue and physical functioning were not significantly different
- Results for global health scores and pain scores were generally consistent across most subgroups
- Patients without progressive disease had a delay in deterioration by at least 10% in global health score and pain compared with patients with progressive disease
- The addition of ribociclib to endocrine therapy improved overall survival in patients with HR+/HER2– ABC, and was associated maintained quality of life[1,2]

ABC, advanced breast cancer; HR+/HER2−, hormone receptor-positive, human epidermal growth factor receptor-negative.

1. Im SA, et al. *N Engl J Med*. 2019;381:307-316. 2. Slamon DJ, et al. *N Engl J Med*. 2020;382:514-524.

VIRTUAL 2020 ESMO congress

Acknowledgements

We thank the patients who participated in these trials, their families and caregivers, data monitoring committee members, study steering committee members, and staff who assisted with the trials at each site.

We also thank the team that supported this analysis. Writing assistance was provided by MediTech Media, funded by Novartis.

Ribociclib was discovered by Novartis Institutes for BioMedical Research in collaboration with Astex Pharmaceuticals.

VIRTUAL 2020 ESMO congress

Scan the QR code below for additional materials including a plain language summary

Text: Qef2e7

To: 8NOVA (86682) US Only
+18324604729 North, Central, and South Americas; Caribbean; China
+447860024038 UK, Europe, and Russia
+46737494608 Sweden and Europe

Visit the web at:

http://novartis.medicalcongressposters.com/Default.aspx?doc=ef2e7

Scan this QR code

Presenter email address: peter.fasching@fau.de