

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Belzutifan (WELIREG®)

MSD Sharp & Dohme GmbH

Modul 4A

Monotherapie zur Behandlung des fortgeschrittenen klarzelligen Nierenzellkarzinoms bei Erwachsenen, deren Erkrankung nach zwei oder mehreren Therapien, darunter ein PD-(L)1-Inhibitor und mindestens zwei zielgerichtete VEGF-Therapien, fortgeschritten ist

Medizinischer Nutzen und
medizinischer Zusatznutzen,
Patientengruppen mit therapeutisch
bedeutsamem Zusatznutzen

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Anhang 4-G1: Ergänzende Morbiditätsendpunkte

Ergänzend zu Abschnitt 4.3.1.3.1.2.4 werden die Zeit bis zum Ansprechen, die Dauer des Ansprechens und die Ergebnisse zum Ansprechen dargestellt.

Tabelle 4G-1: Zeit bis zum Ansprechen und Dauer des Ansprechens RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan N ^b = 188	Everolimus N ^b = 182
Number of participants with response ^c	48	6
Time to Response (Months)		
Mean (SD)	5.72 (4.83)	3.12 (1.40)
Median (Q1; Q3)	3.73 (1.87; 7.98)	2.96 (1.81; 3.81)
Min; Max	1.68; 22.01	1.77; 5.39
Response Duration (Months)		
Median ^d (Q1; Q3)	17.48 (11.73; Not reached)	10.94 (5.62; 17.18)
Min ^e ; Max ^e	1.87+; 39.75+	3.84; 28.42+
Number (%^d) of Participants with Extended Response Duration		
≥ 6 Months	43 (91.5)	4 (66.7)
≥ 9 Months	39 (83.0)	3 (50.0)
≥ 12 Months	33 (70.2)	3 (50.0)
≥ 15 Months	28 (59.6)	2 (33.3)
≥ 18 Months	21 (48.7)	1 (16.7)
≥ 21 Months	16 (41.4)	1 (16.7)
a: Database Cutoff Date: 15APR2024 b: Number of participants: intention-to-treat population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies c: Includes participants with confirmed complete response or partial response d: From product-limit (Kaplan-Meier) method for censored data e: '+' indicates there is no progressive disease by the time of last disease assessment Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation; PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor		

Tabelle 4G-2: Ergebnisse zum Ansprechen aus RCT mit dem zu bewertenden Arzneimittel

	Belzutifan			Everolimus		
	n	(%)	95% CI ^a	n	(%)	95% CI ^a
Number of Participants in Population	188			182		
Complete Response (CR)	7	(3.7)	(1.5, 7.5)	0	(0.0)	(0.0, 2.0)
Partial Response (PR)	41	(21.8)	(16.1, 28.4)	6	(3.3)	(1.2, 7.0)
Overall Response (CR+PR)	48	(25.5)	(19.5, 32.4)	6	(3.3)	(1.2, 7.0)
Stable Disease (SD)	60	(31.9)	(25.3, 39.1)	116	(63.7)	(56.3, 70.7)
Disease Control (CR+PR+SD)	108	(57.4)	(50.0, 64.6)	122	(67.0)	(59.7, 73.8)
Progressive Disease (PD)	65	(34.6)	(27.8, 41.8)	43	(23.6)	(17.7, 30.5)
Not Evaluable ^b	4	(2.1)	(0.6, 5.4)	5	(2.7)	(0.9, 6.3)
No Assessment ^c	11	(5.9)	(3.0, 10.2)	12	(6.6)	(3.5, 11.2)
Responses are based on BICR assessment per RECIST 1.1. ^a Based on the binomial exact confidence interval method for binomial data. ^b Not Evaluable (NE) includes participants with insufficient data for assessment of response per RECIST 1.1. ^c No Assessment includes participants without post-baseline assessment on the data cutoff date. Stable Disease (SD) includes both SD and Non-CR/Non-PD. Database Cutoff Date: 15APR2024 PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death Ligand 1; VEGF: Vascular Endothelial Growth Factor.						

Anhang 4-G2: Rücklaufquoten des EORTC QLQ-C30, FKSI-DRS und EQ-5D VAS

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1.2.2 die Rücklaufquoten des EORTC QLQ-C30, die Rücklaufquoten des FKSI-DRS und die Rücklaufquoten des EQ-5D VAS dargestellt.

Alle Ergebnisse beziehen sich auf den finalen Datenschnitt (15. April 2024).

Anhang 4-G2.1: Rücklaufquoten des EORTC QLQ-C30

Tabelle 4G-3: Gründe für das Fehlen von Werten im EORTC QLQ-C30

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
BASELINE	Expected to Complete Questionnaires	182	(100.0)	174	(100.0)
	Completed	178	(97.8)	164	(94.3)
	Compliance (% in those expected to complete questionnaires)	178	(97.8)	164	(94.3)
	Not completed	4	(2.2)	10	(5.7)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	2	(1.1)	2	(1.1)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	6	(3.4)
	With visit, no record	0	(0.0)	2	(1.1)
	Missing by Design	0	(0.0)	0	(0.0)
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
BASELINE	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 3	Expected to Complete Questionnaires	181	(99.5)	173	(99.4)
	Completed	159	(87.4)	145	(83.3)
	Compliance (% in those expected to complete questionnaires)	159	(87.8)	145	(83.8)
	Not completed	22	(12.1)	28	(16.1)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	11	(6.0)	10	(5.7)
	Subject in hospital or hospice	2	(1.1)	2	(1.1)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	1	(0.6)
	Other	9	(4.9)	13	(7.5)
	With visit, no record	0	(0.0)	1	(0.6)
	Missing by Design	1	(0.5)	1	(0.6)
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	0	(0.0)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	1	(0.5)	1	(0.6)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 5	Expected to Complete Questionnaires	173	(95.1)	171	(98.3)
	Completed	152	(83.5)	156	(89.7)
	Compliance (% in those expected to complete questionnaires)	152	(87.9)	156	(91.2)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 5	Not completed	21	(11.5)	15	(8.6)
	Subject did not complete due to disease under study	2	(1.1)	1	(0.6)
	Not completed due to site staff error	4	(2.2)	4	(2.3)
	Subject in hospital or hospice	3	(1.6)	2	(1.1)
	Subject was physically unable to complete	1	(0.5)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	1	(0.5)	1	(0.6)
	Other	10	(5.5)	7	(4.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	9	(4.9)	3	(1.7)
	Discontinued due to adverse event	1	(0.5)	1	(0.6)
	Discontinued due to clinical progression	2	(1.1)	2	(1.1)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	1	(0.5)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	0	(0.0)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	3	(1.6)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	2	(1.1)	0	(0.0)
WEEK 9	Expected to Complete Questionnaires	165	(90.7)	158	(90.8)
	Completed	147	(80.8)	142	(81.6)
	Compliance (% in those expected to complete questionnaires)	147	(89.1)	142	(89.9)
	Not completed	18	(9.9)	16	(9.2)
	Subject did not complete due to disease under study	1	(0.5)	1	(0.6)
	Not completed due to site staff error	2	(1.1)	5	(2.9)
	Subject in hospital or hospice	3	(1.6)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	1	(0.5)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 9	Subject refused for other reasons	1	(0.5)	4	(2.3)
	Other	10	(5.5)	6	(3.4)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	17	(9.3)	16	(9.2)
	Discontinued due to adverse event	0	(0.0)	2	(1.1)
	Discontinued due to clinical progression	7	(3.8)	4	(2.3)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	1	(0.6)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	6	(3.3)	1	(0.6)
	Discontinued due to withdrawal by subject	1	(0.5)	0	(0.0)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	3	(1.6)	3	(1.7)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	5	(2.9)
WEEK 13	Expected to Complete Questionnaires	148	(81.3)	138	(79.3)
	Completed	130	(71.4)	116	(66.7)
	Compliance (% in those expected to complete questionnaires)	130	(87.8)	116	(84.1)
	Not completed	18	(9.9)	22	(12.6)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	1	(0.5)	5	(2.9)
	Subject in hospital or hospice	2	(1.1)	1	(0.6)
	Subject was physically unable to complete	1	(0.5)	1	(0.6)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.6)
	Subject did not complete due to side effects of treatment	1	(0.5)	0	(0.0)
	Subject refused for other reasons	2	(1.1)	6	(3.4)
	Other	11	(6.0)	6	(3.4)
	With visit, no record	0	(0.0)	1	(0.6)
	Missing by Design	34	(18.7)	36	(20.7)
	Discontinued due to adverse event	5	(2.7)	5	(2.9)
	Discontinued due to clinical progression	9	(4.9)	6	(3.4)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	1	(0.6)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 13	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	19	(10.4)	21	(12.1)
	Discontinued due to withdrawal by subject	1	(0.5)	0	(0.0)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	3	(1.7)
WEEK 17	Expected to Complete Questionnaires	127	(69.8)	100	(57.5)
	Completed	114	(62.6)	92	(52.9)
	Compliance (% in those expected to complete questionnaires)	114	(89.8)	92	(92.0)
	Not completed	13	(7.1)	8	(4.6)
	Subject did not complete due to disease under study	1	(0.5)	1	(0.6)
	Not completed due to site staff error	3	(1.6)	1	(0.6)
	Subject in hospital or hospice	4	(2.2)	1	(0.6)
	Subject was physically unable to complete	0	(0.0)	1	(0.6)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.6)
	Subject did not complete due to side effects of treatment	1	(0.5)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	1	(0.6)
	Other	4	(2.2)	2	(1.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	55	(30.2)	74	(42.5)
	Discontinued due to adverse event	5	(2.7)	10	(5.7)
	Discontinued due to clinical progression	9	(4.9)	10	(5.7)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	3	(1.7)
	Discontinued due to physician decision	0	(0.0)	1	(0.6)
	Discontinued due to progressive disease	38	(20.9)	42	(24.1)
	Discontinued due to withdrawal by subject	2	(1.1)	2	(1.1)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	3	(1.7)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	3	(1.7)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 21	Expected to Complete Questionnaires	114	(62.6)	87	(50.0)
	Completed	106	(58.2)	78	(44.8)
	Compliance (% in those expected to complete questionnaires)	106	(93.0)	78	(89.7)
	Not completed	8	(4.4)	9	(5.2)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	1	(0.5)	3	(1.7)
	Subject in hospital or hospice	0	(0.0)	1	(0.6)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	6	(3.3)	3	(1.7)
	With visit, no record	1	(0.5)	1	(0.6)
	Missing by Design	68	(37.4)	87	(50.0)
	Discontinued due to adverse event	6	(3.3)	14	(8.0)
	Discontinued due to clinical progression	10	(5.5)	11	(6.3)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	3	(1.7)
	Discontinued due to physician decision	0	(0.0)	1	(0.6)
	Discontinued due to progressive disease	48	(26.4)	52	(29.9)
	Discontinued due to withdrawal by subject	3	(1.6)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	2	(1.1)
WEEK 25	Expected to Complete Questionnaires	103	(56.6)	76	(43.7)
	Completed	96	(52.7)	72	(41.4)
	Compliance (% in those expected to complete questionnaires)	96	(93.2)	72	(94.7)
	Not completed	7	(3.8)	4	(2.3)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	1	(0.5)	2	(1.1)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 25	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	1	(0.5)	0	(0.0)
	Other	5	(2.7)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	79	(43.4)	98	(56.3)
	Discontinued due to adverse event	6	(3.3)	18	(10.3)
	Discontinued due to clinical progression	11	(6.0)	11	(6.3)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	57	(31.3)	59	(33.9)
	Discontinued due to withdrawal by subject	3	(1.6)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	1	(0.5)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 29	Expected to Complete Questionnaires	97	(53.3)	64	(36.8)
	Completed	92	(50.5)	59	(33.9)
	Compliance (% in those expected to complete questionnaires)	92	(94.8)	59	(92.2)
	Not completed	5	(2.7)	5	(2.9)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	1	(0.5)	2	(1.1)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.6)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	4	(2.2)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	85	(46.7)	110	(63.2)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 29	Discontinued due to adverse event	7	(3.8)	18	(10.3)
	Discontinued due to clinical progression	11	(6.0)	11	(6.3)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	61	(33.5)	68	(39.1)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	1	(0.6)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	2	(1.1)
	Expected to Complete Questionnaires	91	(50.0)	58	(33.3)
WEEK 33	Completed	86	(47.3)	55	(31.6)
	Compliance (% in those expected to complete questionnaires)	86	(94.5)	55	(94.8)
	Not completed	5	(2.7)	3	(1.7)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	2	(1.1)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	2	(1.1)
	Other	3	(1.6)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	91	(50.0)	116	(66.7)
	Discontinued due to adverse event	7	(3.8)	18	(10.3)
	Discontinued due to clinical progression	11	(6.0)	11	(6.3)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	66	(36.3)	75	(43.1)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 33	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	2	(1.1)
WEEK 37	Expected to Complete Questionnaires	89	(48.9)	53	(30.5)
	Completed	81	(44.5)	50	(28.7)
	Compliance (% in those expected to complete questionnaires)	81	(91.0)	50	(94.3)
	Not completed	8	(4.4)	3	(1.7)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	2	(1.1)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	5	(2.7)	1	(0.6)
	With visit, no record	1	(0.5)	1	(0.6)
	Missing by Design	93	(51.1)	121	(69.5)
	Discontinued due to adverse event	7	(3.8)	18	(10.3)
	Discontinued due to clinical progression	11	(6.0)	11	(6.3)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	67	(36.8)	78	(44.8)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	1	(0.5)	0	(0.0)
	Subject died	0	(0.0)	1	(0.6)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	3	(1.7)
WEEK 41	Expected to Complete Questionnaires	82	(45.1)	47	(27.0)
	Completed	80	(44.0)	43	(24.7)
	Compliance (% in those expected to complete questionnaires)	80	(97.6)	43	(91.5)
	Not completed	2	(1.1)	4	(2.3)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 41	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	1	(0.6)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	3	(1.7)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	100	(54.9)	127	(73.0)
	Discontinued due to adverse event	8	(4.4)	20	(11.5)
	Discontinued due to clinical progression	11	(6.0)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	73	(40.1)	82	(47.1)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	2	(1.1)	3	(1.7)
WEEK 45	Expected to Complete Questionnaires	78	(42.9)	48	(27.6)
	Completed	71	(39.0)	46	(26.4)
	Compliance (% in those expected to complete questionnaires)	71	(91.0)	46	(95.8)
	Not completed	7	(3.8)	2	(1.1)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	1	(0.5)	0	(0.0)
	Subject was physically unable to complete	1	(0.5)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	1	(0.5)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 45	Other	4	(2.2)	2	(1.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	104	(57.1)	126	(72.4)
	Discontinued due to adverse event	8	(4.4)	20	(11.5)
	Discontinued due to clinical progression	12	(6.6)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	77	(42.3)	84	(48.3)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 49	Expected to Complete Questionnaires	74	(40.7)	36	(20.7)
	Completed	69	(37.9)	35	(20.1)
	Compliance (% in those expected to complete questionnaires)	69	(93.2)	35	(97.2)
	Not completed	5	(2.7)	1	(0.6)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	5	(2.7)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	108	(59.3)	138	(79.3)
	Discontinued due to adverse event	8	(4.4)	22	(12.6)
	Discontinued due to clinical progression	12	(6.6)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 49	Discontinued due to progressive disease	82	(45.1)	94	(54.0)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Expected to Complete Questionnaires	73	(40.1)	32	(18.4)
WEEK 53	Completed	70	(38.5)	32	(18.4)
	Compliance (% in those expected to complete questionnaires)	70	(95.9)	32	(100.0)
	Not completed	3	(1.6)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	1	(0.5)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	109	(59.9)	142	(81.6)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	12	(6.6)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	83	(45.6)	97	(55.7)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Expected to Complete Questionnaires	70	(38.5)	31	(17.8)
WEEK 57					

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 57	Completed	68	(37.4)	30	(17.2)
	Compliance (% in those expected to complete questionnaires)	68	(97.1)	30	(96.8)
	Not completed	2	(1.1)	1	(0.6)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	1	(0.6)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	112	(61.5)	143	(82.2)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	12	(6.6)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	86	(47.3)	98	(56.3)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 61	Expected to Complete Questionnaires	68	(37.4)	26	(14.9)
	Completed	63	(34.6)	24	(13.8)
	Compliance (% in those expected to complete questionnaires)	63	(92.6)	24	(92.3)
	Not completed	5	(2.7)	2	(1.1)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	1	(0.6)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 61	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	4	(2.2)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	114	(62.6)	148	(85.1)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	12	(6.6)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	88	(48.4)	102	(58.6)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	1	(0.6)
WEEK 65	Expected to Complete Questionnaires	66	(36.3)	22	(12.6)
	Completed	63	(34.6)	21	(12.1)
	Compliance (% in those expected to complete questionnaires)	63	(95.5)	21	(95.5)
	Not completed	3	(1.6)	1	(0.6)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	116	(63.7)	152	(87.4)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 65	Discontinued due to clinical progression	13	(7.1)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	89	(48.9)	106	(60.9)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	1	(0.6)
	Expected to Complete Questionnaires	61	(33.5)	20	(11.5)
WEEK 69	Completed	57	(31.3)	20	(11.5)
	Compliance (% in those expected to complete questionnaires)	57	(93.4)	20	(100.0)
	Not completed	4	(2.2)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	3	(1.6)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	121	(66.5)	154	(88.5)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	13	(7.1)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	93	(51.1)	108	(62.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 69	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 73	Expected to Complete Questionnaires	60	(33.0)	20	(11.5)
	Completed	55	(30.2)	20	(11.5)
	Compliance (% in those expected to complete questionnaires)	55	(91.7)	20	(100.0)
	Not completed	5	(2.7)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	1	(0.5)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	4	(2.2)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	122	(67.0)	154	(88.5)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	13	(7.1)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	94	(51.6)	108	(62.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	1	(0.5)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 77	Expected to Complete Questionnaires	59	(32.4)	20	(11.5)
	Completed	56	(30.8)	18	(10.3)
	Compliance (% in those expected to complete questionnaires)	56	(94.9)	18	(90.0)
	Not completed	3	(1.6)	2	(1.1)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 77	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	1	(0.6)
	Other	2	(1.1)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	123	(67.6)	154	(88.5)
	Discontinued due to adverse event	9	(4.9)	23	(13.2)
	Discontinued due to clinical progression	13	(7.1)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	95	(52.2)	108	(62.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 81	Expected to Complete Questionnaires	56	(30.8)	15	(8.6)
	Completed	52	(28.6)	15	(8.6)
	Compliance (% in those expected to complete questionnaires)	52	(92.9)	15	(100.0)
	Not completed	4	(2.2)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	3	(1.6)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 81	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	126	(69.2)	159	(91.4)
	Discontinued due to adverse event	9	(4.9)	23	(13.2)
	Discontinued due to clinical progression	13	(7.1)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	97	(53.3)	112	(64.4)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	1	(0.5)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 85	Expected to Complete Questionnaires	53	(29.1)	11	(6.3)
	Completed	50	(27.5)	10	(5.7)
	Compliance (% in those expected to complete questionnaires)	50	(94.3)	10	(90.9)
	Not completed	3	(1.6)	1	(0.6)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	1	(0.6)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	3	(1.6)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	129	(70.9)	163	(93.7)
	Discontinued due to adverse event	9	(4.9)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	99	(54.4)	115	(66.1)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 85	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	1	(0.6)
WEEK 89	Expected to Complete Questionnaires	52	(28.6)	12	(6.9)
	Completed	47	(25.8)	10	(5.7)
	Compliance (% in those expected to complete questionnaires)	47	(90.4)	10	(83.3)
	Not completed	5	(2.7)	2	(1.1)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	2	(1.1)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	1	(0.6)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	1	(0.6)
	With visit, no record	1	(0.5)	0	(0.0)
	Missing by Design	130	(71.4)	162	(93.1)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	100	(54.9)	115	(66.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 93	Expected to Complete Questionnaires	49	(26.9)	11	(6.3)
	Completed	47	(25.8)	11	(6.3)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 93	Compliance (% in those expected to complete questionnaires)	47	(95.9)	11	(100.0)
	Not completed	2	(1.1)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	133	(73.1)	163	(93.7)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	103	(56.6)	116	(66.7)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 97	Expected to Complete Questionnaires	46	(25.3)	10	(5.7)
	Completed	44	(24.2)	10	(5.7)
	Compliance (% in those expected to complete questionnaires)	44	(95.7)	10	(100.0)
	Not completed	2	(1.1)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 97	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	136	(74.7)	164	(94.3)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	105	(57.7)	117	(67.2)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 101	Expected to Complete Questionnaires	43	(23.6)	10	(5.7)
	Completed	42	(23.1)	9	(5.2)
	Compliance (% in those expected to complete questionnaires)	42	(97.7)	9	(90.0)
	Not completed	1	(0.5)	1	(0.6)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	1	(0.6)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	139	(76.4)	164	(94.3)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 101	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	106	(58.2)	117	(67.2)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	3	(1.6)	0	(0.0)
WEEK 105	Expected to Complete Questionnaires	46	(25.3)	7	(4.0)
	Completed	43	(23.6)	7	(4.0)
	Compliance (% in those expected to complete questionnaires)	43	(93.5)	7	(100.0)
	Not completed	3	(1.6)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	1	(0.5)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	1	(0.5)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	136	(74.7)	167	(96.0)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	106	(58.2)	120	(69.0)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 105	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 109	Expected to Complete Questionnaires	46	(25.3)	7	(4.0)
	Completed	42	(23.1)	7	(4.0)
	Compliance (% in those expected to complete questionnaires)	42	(91.3)	7	(100.0)
	Not completed	4	(2.2)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	3	(1.6)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	136	(74.7)	167	(96.0)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	106	(58.2)	120	(69.0)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 113	Expected to Complete Questionnaires	44	(24.2)	5	(2.9)
	Completed	39	(21.4)	5	(2.9)
	Compliance (% in those expected to complete questionnaires)	39	(88.6)	5	(100.0)
	Not completed	5	(2.7)	0	(0.0)
	Subject did not complete due to disease under study	1	(0.5)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 113	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	1	(0.5)	0	(0.0)
	Missing by Design	138	(75.8)	169	(97.1)
	Discontinued due to adverse event	11	(6.0)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	106	(58.2)	122	(70.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 117	Expected to Complete Questionnaires	42	(23.1)	5	(2.9)
	Completed	37	(20.3)	5	(2.9)
	Compliance (% in those expected to complete questionnaires)	37	(88.1)	5	(100.0)
	Not completed	5	(2.7)	0	(0.0)
	Subject did not complete due to disease under study	1	(0.5)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	1	(0.5)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 117	Missing by Design	140	(76.9)	169	(97.1)
	Discontinued due to adverse event	11	(6.0)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	108	(59.3)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 121	Expected to Complete Questionnaires	38	(20.9)	3	(1.7)
	Completed	38	(20.9)	3	(1.7)
	Compliance (% in those expected to complete questionnaires)	38	(100.0)	3	(100.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	144	(79.1)	171	(98.3)
	Discontinued due to adverse event	11	(6.0)	24	(13.8)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	110	(60.4)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 121	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	1	(0.5)	1	(0.6)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 125	Expected to Complete Questionnaires	34	(18.7)	3	(1.7)
	Completed	33	(18.1)	3	(1.7)
	Compliance (% in those expected to complete questionnaires)	33	(97.1)	3	(100.0)
	Not completed	1	(0.5)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	1	(0.5)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	148	(81.3)	171	(98.3)
	Discontinued due to adverse event	11	(6.0)	24	(13.8)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	112	(61.5)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	3	(1.6)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 129	Expected to Complete Questionnaires	31	(17.0)	3	(1.7)
	Completed	29	(15.9)	3	(1.7)
	Compliance (% in those expected to complete questionnaires)	29	(93.5)	3	(100.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 129	Not completed	2	(1.1)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	151	(83.0)	171	(98.3)
	Discontinued due to adverse event	11	(6.0)	24	(13.8)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	113	(62.1)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	4	(2.2)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 133	Expected to Complete Questionnaires	28	(15.4)	2	(1.1)
	Completed	27	(14.8)	2	(1.1)
	Compliance (% in those expected to complete questionnaires)	27	(96.4)	2	(100.0)
	Not completed	1	(0.5)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 133	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	154	(84.6)	172	(98.9)
	Discontinued due to adverse event	12	(6.6)	24	(13.8)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	113	(62.1)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	6	(3.3)	1	(0.6)
	Visit not scheduled	0	(0.0)	1	(0.6)
WEEK 137	Expected to Complete Questionnaires	22	(12.1)	3	(1.7)
	Completed	21	(11.5)	3	(1.7)
	Compliance (% in those expected to complete questionnaires)	21	(95.5)	3	(100.0)
	Not completed	1	(0.5)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	1	(0.5)	0	(0.0)
	Missing by Design	160	(87.9)	171	(98.3)
	Discontinued due to adverse event	12	(6.6)	24	(13.8)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 137	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	115	(63.2)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	9	(4.9)	1	(0.6)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 141	Expected to Complete Questionnaires	22	(12.1)	0	(0.0)
	Completed	21	(11.5)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	21	(95.5)	0	(0.0)
	Not completed	1	(0.5)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	160	(87.9)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	116	(63.7)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	9	(4.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 145	Expected to Complete Questionnaires	20	(11.0)	0	(0.0)
	Completed	20	(11.0)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	20	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	162	(89.0)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	10	(5.5)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 149	Expected to Complete Questionnaires	18	(9.9)	0	(0.0)
	Completed	18	(9.9)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	18	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 149	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	164	(90.1)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	12	(6.6)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 153	Expected to Complete Questionnaires	17	(9.3)	0	(0.0)
	Completed	17	(9.3)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	17	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	165	(90.7)	174	(100.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 153	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	13	(7.1)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Expected to Complete Questionnaires	12	(6.6)	0	(0.0)
WEEK 157	Completed	12	(6.6)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	12	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	170	(93.4)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 157	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	18	(9.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 161	Expected to Complete Questionnaires	11	(6.0)	0	(0.0)
	Completed	11	(6.0)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	11	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	171	(94.0)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	19	(10.4)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 165	Expected to Complete Questionnaires	9	(4.9)	0	(0.0)
	Completed	9	(4.9)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	9	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 165	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	173	(95.1)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	21	(11.5)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 169	Expected to Complete Questionnaires	8	(4.4)	0	(0.0)
	Completed	8	(4.4)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	8	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 169	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	174	(95.6)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	22	(12.1)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 173	Expected to Complete Questionnaires	7	(3.8)	0	(0.0)
	Completed	7	(3.8)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	7	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	175	(96.2)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 173	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	23	(12.6)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Expected to Complete Questionnaires	6	(3.3)	0	(0.0)
WEEK 177	Completed	6	(3.3)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	6	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	176	(96.7)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	24	(13.2)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Expected to Complete Questionnaires	4	(2.2)	0	(0.0)
WEEK 181					

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 181	Completed	4	(2.2)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	4	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	178	(97.8)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	25	(13.7)	1	(0.6)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 185	Expected to Complete Questionnaires	3	(1.6)	0	(0.0)
	Completed	3	(1.6)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	3	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 185	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	179	(98.4)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	27	(14.8)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 189	Expected to Complete Questionnaires	1	(0.5)	0	(0.0)
	Completed	1	(0.5)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	1	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	181	(99.5)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 189	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	29	(15.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Expected to Complete Questionnaires	0	(0.0)	0	(0.0)
WEEK 193	Completed	0	(0.0)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	0	(.)	0	(.)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	182	(100.0)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	118	(64.8)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 193	Visit not reached	29	(15.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 197	Expected to Complete Questionnaires	0	(0.0)	0	(0.0)
	Completed	0	(0.0)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	0	(.)	0	(.)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	182	(100.0)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	118	(64.8)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	29	(15.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 201	Expected to Complete Questionnaires	0	(0.0)	0	(0.0)
	Completed	0	(0.0)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	0	(.)	0	(.)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 201	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	182	(100.0)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	118	(64.8)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	29	(15.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
Expected to complete questionnaire includes all patients who do not have missing data due to a missing by design reason Compliance is the proportion of patients who completed the PRO questionnaire among those who are expected to complete the questionnaire at this time point, excluding those missing by design. All the other categories are defined as the proportion of patients in the analysis population (N) Missing by design includes adverse event, death, discontinuation, translations not available, and no visit scheduled Number of participants: full-analysis-set population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor Database Cutoff Date: 15APR2024					

Anhang 4-G2.2: Rücklaufquoten des FKSI-DRS

Tabelle 4G-4: Gründe für das Fehlen von Werten im FKSI-DRS

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
BASELINE	Expected to Complete Questionnaires	182	(100.0)	174	(100.0)
	Completed	179	(98.4)	164	(94.3)
	Compliance (% in those expected to complete questionnaires)	179	(98.4)	164	(94.3)
	Not completed	3	(1.6)	10	(5.7)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	2	(1.1)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	6	(3.4)
	With visit, no record	0	(0.0)	2	(1.1)
	Missing by Design	0	(0.0)	0	(0.0)
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	0	(0.0)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 3	Expected to Complete Questionnaires	181	(99.5)	173	(99.4)
	Completed	159	(87.4)	143	(82.2)
	Compliance (% in those expected to complete questionnaires)	159	(87.8)	143	(82.7)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 3	Not completed	22	(12.1)	30	(17.2)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	11	(6.0)	12	(6.9)
	Subject in hospital or hospice	2	(1.1)	2	(1.1)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	1	(0.6)
	Other	9	(4.9)	13	(7.5)
	With visit, no record	0	(0.0)	1	(0.6)
	Missing by Design	1	(0.5)	1	(0.6)
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	0	(0.0)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	1	(0.5)	1	(0.6)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 5	Expected to Complete Questionnaires	173	(95.1)	171	(98.3)
	Completed	152	(83.5)	154	(88.5)
	Compliance (% in those expected to complete questionnaires)	152	(87.9)	154	(90.1)
	Not completed	21	(11.5)	17	(9.8)
	Subject did not complete due to disease under study	2	(1.1)	1	(0.6)
	Not completed due to site staff error	4	(2.2)	4	(2.3)
	Subject in hospital or hospice	3	(1.6)	2	(1.1)
	Subject was physically unable to complete	1	(0.5)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 5	Subject refused for other reasons	1	(0.5)	1	(0.6)
	Other	10	(5.5)	9	(5.2)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	9	(4.9)	3	(1.7)
	Discontinued due to adverse event	1	(0.5)	1	(0.6)
	Discontinued due to clinical progression	2	(1.1)	2	(1.1)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	1	(0.5)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	0	(0.0)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	3	(1.6)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	2	(1.1)	0	(0.0)
WEEK 9	Expected to Complete Questionnaires	165	(90.7)	158	(90.8)
	Completed	147	(80.8)	141	(81.0)
	Compliance (% in those expected to complete questionnaires)	147	(89.1)	141	(89.2)
	Not completed	18	(9.9)	17	(9.8)
	Subject did not complete due to disease under study	1	(0.5)	1	(0.6)
	Not completed due to site staff error	2	(1.1)	6	(3.4)
	Subject in hospital or hospice	3	(1.6)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	1	(0.5)	0	(0.0)
	Subject refused for other reasons	1	(0.5)	4	(2.3)
	Other	10	(5.5)	6	(3.4)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	17	(9.3)	16	(9.2)
	Discontinued due to adverse event	0	(0.0)	2	(1.1)
	Discontinued due to clinical progression	7	(3.8)	4	(2.3)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	1	(0.6)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 9	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	6	(3.3)	1	(0.6)
	Discontinued due to withdrawal by subject	1	(0.5)	0	(0.0)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	3	(1.6)	3	(1.7)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	5	(2.9)
WEEK 13	Expected to Complete Questionnaires	148	(81.3)	138	(79.3)
	Completed	130	(71.4)	116	(66.7)
	Compliance (% in those expected to complete questionnaires)	130	(87.8)	116	(84.1)
	Not completed	18	(9.9)	22	(12.6)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	1	(0.5)	5	(2.9)
	Subject in hospital or hospice	2	(1.1)	1	(0.6)
	Subject was physically unable to complete	1	(0.5)	1	(0.6)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.6)
	Subject did not complete due to side effects of treatment	1	(0.5)	0	(0.0)
	Subject refused for other reasons	2	(1.1)	6	(3.4)
	Other	11	(6.0)	6	(3.4)
	With visit, no record	0	(0.0)	1	(0.6)
	Missing by Design	34	(18.7)	36	(20.7)
	Discontinued due to adverse event	5	(2.7)	5	(2.9)
	Discontinued due to clinical progression	9	(4.9)	6	(3.4)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	1	(0.6)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	19	(10.4)	21	(12.1)
	Discontinued due to withdrawal by subject	1	(0.5)	0	(0.0)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	3	(1.7)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 17	Expected to Complete Questionnaires	127	(69.8)	100	(57.5)
	Completed	113	(62.1)	92	(52.9)
	Compliance (% in those expected to complete questionnaires)	113	(89.0)	92	(92.0)
	Not completed	14	(7.7)	8	(4.6)
	Subject did not complete due to disease under study	1	(0.5)	1	(0.6)
	Not completed due to site staff error	3	(1.6)	1	(0.6)
	Subject in hospital or hospice	4	(2.2)	1	(0.6)
	Subject was physically unable to complete	0	(0.0)	1	(0.6)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.6)
	Subject did not complete due to side effects of treatment	1	(0.5)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	1	(0.6)
	Other	5	(2.7)	2	(1.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	55	(30.2)	74	(42.5)
	Discontinued due to adverse event	5	(2.7)	10	(5.7)
	Discontinued due to clinical progression	9	(4.9)	10	(5.7)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	3	(1.7)
	Discontinued due to physician decision	0	(0.0)	1	(0.6)
	Discontinued due to progressive disease	38	(20.9)	42	(24.1)
	Discontinued due to withdrawal by subject	2	(1.1)	2	(1.1)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	3	(1.7)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	3	(1.7)
WEEK 21	Expected to Complete Questionnaires	114	(62.6)	87	(50.0)
	Completed	106	(58.2)	78	(44.8)
	Compliance (% in those expected to complete questionnaires)	106	(93.0)	78	(89.7)
	Not completed	8	(4.4)	9	(5.2)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	1	(0.5)	3	(1.7)
	Subject in hospital or hospice	0	(0.0)	1	(0.6)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 21	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	6	(3.3)	3	(1.7)
	With visit, no record	1	(0.5)	1	(0.6)
	Missing by Design	68	(37.4)	87	(50.0)
	Discontinued due to adverse event	6	(3.3)	14	(8.0)
	Discontinued due to clinical progression	10	(5.5)	11	(6.3)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	3	(1.7)
	Discontinued due to physician decision	0	(0.0)	1	(0.6)
	Discontinued due to progressive disease	48	(26.4)	52	(29.9)
	Discontinued due to withdrawal by subject	3	(1.6)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	2	(1.1)
WEEK 25	Expected to Complete Questionnaires	103	(56.6)	76	(43.7)
	Completed	96	(52.7)	72	(41.4)
	Compliance (% in those expected to complete questionnaires)	96	(93.2)	72	(94.7)
	Not completed	7	(3.8)	4	(2.3)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	1	(0.5)	2	(1.1)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	1	(0.5)	0	(0.0)
	Other	5	(2.7)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	79	(43.4)	98	(56.3)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 25	Discontinued due to adverse event	6	(3.3)	18	(10.3)
	Discontinued due to clinical progression	11	(6.0)	11	(6.3)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	57	(31.3)	59	(33.9)
	Discontinued due to withdrawal by subject	3	(1.6)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	1	(0.5)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Expected to Complete Questionnaires	97	(53.3)	64	(36.8)
WEEK 29	Completed	91	(50.0)	59	(33.9)
	Compliance (% in those expected to complete questionnaires)	91	(93.8)	59	(92.2)
	Not completed	6	(3.3)	5	(2.9)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	2	(1.1)	2	(1.1)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.6)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	4	(2.2)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	85	(46.7)	110	(63.2)
	Discontinued due to adverse event	7	(3.8)	18	(10.3)
	Discontinued due to clinical progression	11	(6.0)	11	(6.3)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	61	(33.5)	68	(39.1)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 29	Subject died	0	(0.0)	1	(0.6)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	2	(1.1)
WEEK 33	Expected to Complete Questionnaires	91	(50.0)	58	(33.3)
	Completed	86	(47.3)	55	(31.6)
	Compliance (% in those expected to complete questionnaires)	86	(94.5)	55	(94.8)
	Not completed	5	(2.7)	3	(1.7)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	2	(1.1)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	2	(1.1)
	Other	3	(1.6)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	91	(50.0)	116	(66.7)
	Discontinued due to adverse event	7	(3.8)	18	(10.3)
	Discontinued due to clinical progression	11	(6.0)	11	(6.3)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	66	(36.3)	75	(43.1)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	2	(1.1)
WEEK 37	Expected to Complete Questionnaires	89	(48.9)	53	(30.5)
	Completed	81	(44.5)	49	(28.2)
	Compliance (% in those expected to complete questionnaires)	81	(91.0)	49	(92.5)
	Not completed	8	(4.4)	4	(2.3)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 37	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	2	(1.1)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	5	(2.7)	2	(1.1)
	With visit, no record	1	(0.5)	1	(0.6)
	Missing by Design	93	(51.1)	121	(69.5)
	Discontinued due to adverse event	7	(3.8)	18	(10.3)
	Discontinued due to clinical progression	11	(6.0)	11	(6.3)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	67	(36.8)	78	(44.8)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	1	(0.5)	0	(0.0)
	Subject died	0	(0.0)	1	(0.6)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	3	(1.7)
WEEK 41	Expected to Complete Questionnaires	82	(45.1)	47	(27.0)
	Completed	80	(44.0)	43	(24.7)
	Compliance (% in those expected to complete questionnaires)	80	(97.6)	43	(91.5)
	Not completed	2	(1.1)	4	(2.3)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	1	(0.6)
	Subject refused for other reasons	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 41	Other	2	(1.1)	3	(1.7)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	100	(54.9)	127	(73.0)
	Discontinued due to adverse event	8	(4.4)	20	(11.5)
	Discontinued due to clinical progression	11	(6.0)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	73	(40.1)	82	(47.1)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	2	(1.1)	3	(1.7)
WEEK 45	Expected to Complete Questionnaires	78	(42.9)	48	(27.6)
	Completed	71	(39.0)	46	(26.4)
	Compliance (% in those expected to complete questionnaires)	71	(91.0)	46	(95.8)
	Not completed	7	(3.8)	2	(1.1)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	1	(0.5)	0	(0.0)
	Subject was physically unable to complete	1	(0.5)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	1	(0.5)	0	(0.0)
	Other	4	(2.2)	2	(1.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	104	(57.1)	126	(72.4)
	Discontinued due to adverse event	8	(4.4)	20	(11.5)
	Discontinued due to clinical progression	12	(6.6)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 45	Discontinued due to progressive disease	77	(42.3)	84	(48.3)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	0	(0.0)
	Expected to Complete Questionnaires	74	(40.7)	36	(20.7)
WEEK 49	Completed	69	(37.9)	35	(20.1)
	Compliance (% in those expected to complete questionnaires)	69	(93.2)	35	(97.2)
	Not completed	5	(2.7)	1	(0.6)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	5	(2.7)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	108	(59.3)	138	(79.3)
	Discontinued due to adverse event	8	(4.4)	22	(12.6)
	Discontinued due to clinical progression	12	(6.6)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	82	(45.1)	94	(54.0)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 53	Expected to Complete Questionnaires	73	(40.1)	32	(18.4)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 53	Completed	69	(37.9)	32	(18.4)
	Compliance (% in those expected to complete questionnaires)	69	(94.5)	32	(100.0)
	Not completed	4	(2.2)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	1	(0.5)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	109	(59.9)	142	(81.6)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	12	(6.6)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	83	(45.6)	97	(55.7)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 57	Expected to Complete Questionnaires	70	(38.5)	31	(17.8)
	Completed	68	(37.4)	30	(17.2)
	Compliance (% in those expected to complete questionnaires)	68	(97.1)	30	(96.8)
	Not completed	2	(1.1)	1	(0.6)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 57	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	1	(0.6)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	112	(61.5)	143	(82.2)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	12	(6.6)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	86	(47.3)	98	(56.3)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 61	Expected to Complete Questionnaires	68	(37.4)	26	(14.9)
	Completed	63	(34.6)	24	(13.8)
	Compliance (% in those expected to complete questionnaires)	63	(92.6)	24	(92.3)
	Not completed	5	(2.7)	2	(1.1)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	1	(0.6)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	4	(2.2)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	114	(62.6)	148	(85.1)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 61	Discontinued due to clinical progression	12	(6.6)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	88	(48.4)	102	(58.6)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	1	(0.6)
	Expected to Complete Questionnaires	66	(36.3)	22	(12.6)
WEEK 65	Completed	63	(34.6)	21	(12.1)
	Compliance (% in those expected to complete questionnaires)	63	(95.5)	21	(95.5)
	Not completed	3	(1.6)	1	(0.6)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	116	(63.7)	152	(87.4)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	13	(7.1)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	89	(48.9)	106	(60.9)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 65	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	1	(0.6)
WEEK 69	Expected to Complete Questionnaires	61	(33.5)	20	(11.5)
	Completed	57	(31.3)	20	(11.5)
	Compliance (% in those expected to complete questionnaires)	57	(93.4)	20	(100.0)
	Not completed	4	(2.2)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	3	(1.6)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	121	(66.5)	154	(88.5)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	13	(7.1)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	93	(51.1)	108	(62.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 73	Expected to Complete Questionnaires	60	(33.0)	20	(11.5)
	Completed	55	(30.2)	20	(11.5)
	Compliance (% in those expected to complete questionnaires)	55	(91.7)	20	(100.0)
	Not completed	5	(2.7)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 73	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	1	(0.5)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	4	(2.2)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	122	(67.0)	154	(88.5)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	13	(7.1)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	94	(51.6)	108	(62.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	1	(0.5)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 77	Expected to Complete Questionnaires	59	(32.4)	20	(11.5)
	Completed	55	(30.2)	18	(10.3)
	Compliance (% in those expected to complete questionnaires)	55	(93.2)	18	(90.0)
	Not completed	4	(2.2)	2	(1.1)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	1	(0.6)
	Other	3	(1.6)	1	(0.6)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 77	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	123	(67.6)	154	(88.5)
	Discontinued due to adverse event	9	(4.9)	23	(13.2)
	Discontinued due to clinical progression	13	(7.1)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	95	(52.2)	108	(62.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 81	Expected to Complete Questionnaires	56	(30.8)	15	(8.6)
	Completed	52	(28.6)	15	(8.6)
	Compliance (% in those expected to complete questionnaires)	52	(92.9)	15	(100.0)
	Not completed	4	(2.2)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	3	(1.6)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	126	(69.2)	159	(91.4)
	Discontinued due to adverse event	9	(4.9)	23	(13.2)
	Discontinued due to clinical progression	13	(7.1)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	97	(53.3)	112	(64.4)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 81	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	1	(0.5)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 85	Expected to Complete Questionnaires	53	(29.1)	11	(6.3)
	Completed	50	(27.5)	10	(5.7)
	Compliance (% in those expected to complete questionnaires)	50	(94.3)	10	(90.9)
	Not completed	3	(1.6)	1	(0.6)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	1	(0.6)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	3	(1.6)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	129	(70.9)	163	(93.7)
	Discontinued due to adverse event	9	(4.9)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	99	(54.4)	115	(66.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	1	(0.6)
WEEK 89	Expected to Complete Questionnaires	52	(28.6)	12	(6.9)
	Completed	47	(25.8)	10	(5.7)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 89	Compliance (% in those expected to complete questionnaires)	47	(90.4)	10	(83.3)
	Not completed	5	(2.7)	2	(1.1)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	2	(1.1)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	1	(0.6)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	1	(0.6)
	With visit, no record	1	(0.5)	0	(0.0)
	Missing by Design	130	(71.4)	162	(93.1)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	100	(54.9)	115	(66.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 93	Expected to Complete Questionnaires	49	(26.9)	11	(6.3)
	Completed	47	(25.8)	11	(6.3)
	Compliance (% in those expected to complete questionnaires)	47	(95.9)	11	(100.0)
	Not completed	2	(1.1)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 93	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	133	(73.1)	163	(93.7)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	103	(56.6)	116	(66.7)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 97	Expected to Complete Questionnaires	46	(25.3)	10	(5.7)
	Completed	44	(24.2)	10	(5.7)
	Compliance (% in those expected to complete questionnaires)	44	(95.7)	10	(100.0)
	Not completed	2	(1.1)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	136	(74.7)	164	(94.3)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 97	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	105	(57.7)	117	(67.2)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 101	Expected to Complete Questionnaires	43	(23.6)	10	(5.7)
	Completed	42	(23.1)	9	(5.2)
	Compliance (% in those expected to complete questionnaires)	42	(97.7)	9	(90.0)
	Not completed	1	(0.5)	1	(0.6)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	1	(0.6)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	139	(76.4)	164	(94.3)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	106	(58.2)	117	(67.2)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 101	Visit not scheduled	3	(1.6)	0	(0.0)
WEEK 105	Expected to Complete Questionnaires	46	(25.3)	7	(4.0)
	Completed	43	(23.6)	7	(4.0)
	Compliance (% in those expected to complete questionnaires)	43	(93.5)	7	(100.0)
	Not completed	3	(1.6)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	1	(0.5)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	1	(0.5)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	136	(74.7)	167	(96.0)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	106	(58.2)	120	(69.0)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 109	Expected to Complete Questionnaires	46	(25.3)	7	(4.0)
	Completed	42	(23.1)	7	(4.0)
	Compliance (% in those expected to complete questionnaires)	42	(91.3)	7	(100.0)
	Not completed	4	(2.2)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	3	(1.6)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 109	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	136	(74.7)	167	(96.0)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	106	(58.2)	120	(69.0)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 113	Expected to Complete Questionnaires	44	(24.2)	5	(2.9)
	Completed	39	(21.4)	5	(2.9)
	Compliance (% in those expected to complete questionnaires)	39	(88.6)	5	(100.0)
	Not completed	5	(2.7)	0	(0.0)
	Subject did not complete due to disease under study	1	(0.5)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	1	(0.5)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 113	Missing by Design	138	(75.8)	169	(97.1)
	Discontinued due to adverse event	11	(6.0)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	106	(58.2)	122	(70.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 117	Expected to Complete Questionnaires	42	(23.1)	5	(2.9)
	Completed	37	(20.3)	4	(2.3)
	Compliance (% in those expected to complete questionnaires)	37	(88.1)	4	(80.0)
	Not completed	5	(2.7)	1	(0.6)
	Subject did not complete due to disease under study	1	(0.5)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	1	(0.6)
	With visit, no record	1	(0.5)	0	(0.0)
	Missing by Design	140	(76.9)	169	(97.1)
	Discontinued due to adverse event	11	(6.0)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	108	(59.3)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 117	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 121	Expected to Complete Questionnaires	38	(20.9)	3	(1.7)
	Completed	38	(20.9)	3	(1.7)
	Compliance (% in those expected to complete questionnaires)	38	(100.0)	3	(100.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	144	(79.1)	171	(98.3)
	Discontinued due to adverse event	11	(6.0)	24	(13.8)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	110	(60.4)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	1	(0.5)	1	(0.6)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 125	Expected to Complete Questionnaires	34	(18.7)	3	(1.7)
	Completed	33	(18.1)	3	(1.7)
	Compliance (% in those expected to complete questionnaires)	33	(97.1)	3	(100.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 125	Not completed	1	(0.5)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	1	(0.5)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	148	(81.3)	171	(98.3)
	Discontinued due to adverse event	11	(6.0)	24	(13.8)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	112	(61.5)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	3	(1.6)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 129	Expected to Complete Questionnaires	31	(17.0)	3	(1.7)
	Completed	28	(15.4)	3	(1.7)
	Compliance (% in those expected to complete questionnaires)	28	(90.3)	3	(100.0)
	Not completed	3	(1.6)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 129	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	151	(83.0)	171	(98.3)
	Discontinued due to adverse event	11	(6.0)	24	(13.8)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	113	(62.1)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	4	(2.2)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 133	Expected to Complete Questionnaires	28	(15.4)	2	(1.1)
	Completed	27	(14.8)	2	(1.1)
	Compliance (% in those expected to complete questionnaires)	27	(96.4)	2	(100.0)
	Not completed	1	(0.5)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	154	(84.6)	172	(98.9)
	Discontinued due to adverse event	12	(6.6)	24	(13.8)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 133	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	113	(62.1)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	6	(3.3)	1	(0.6)
	Visit not scheduled	0	(0.0)	1	(0.6)
WEEK 137	Expected to Complete Questionnaires	22	(12.1)	3	(1.7)
	Completed	21	(11.5)	3	(1.7)
	Compliance (% in those expected to complete questionnaires)	21	(95.5)	3	(100.0)
	Not completed	1	(0.5)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	1	(0.5)	0	(0.0)
	Missing by Design	160	(87.9)	171	(98.3)
	Discontinued due to adverse event	12	(6.6)	24	(13.8)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	115	(63.2)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	9	(4.9)	1	(0.6)
	Visit not scheduled	1	(0.5)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 141	Expected to Complete Questionnaires	22	(12.1)	0	(0.0)
	Completed	21	(11.5)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	21	(95.5)	0	(0.0)
	Not completed	1	(0.5)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	160	(87.9)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	116	(63.7)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
WEEK 145	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	9	(4.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Expected to Complete Questionnaires	20	(11.0)	0	(0.0)
	Completed	20	(11.0)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	20	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 145	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	162	(89.0)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	10	(5.5)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 149	Expected to Complete Questionnaires	18	(9.9)	0	(0.0)
	Completed	18	(9.9)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	18	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	164	(90.1)	174	(100.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 149	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	12	(6.6)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Expected to Complete Questionnaires	17	(9.3)	0	(0.0)
WEEK 153	Completed	17	(9.3)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	17	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	165	(90.7)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 153	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	13	(7.1)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 157	Expected to Complete Questionnaires	12	(6.6)	0	(0.0)
	Completed	12	(6.6)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	12	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	170	(93.4)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	18	(9.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 161	Expected to Complete Questionnaires	11	(6.0)	0	(0.0)
	Completed	11	(6.0)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	11	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 161	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	171	(94.0)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	19	(10.4)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 165	Expected to Complete Questionnaires	9	(4.9)	0	(0.0)
	Completed	9	(4.9)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	9	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 165	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	173	(95.1)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	21	(11.5)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 169	Expected to Complete Questionnaires	8	(4.4)	0	(0.0)
	Completed	8	(4.4)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	8	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	174	(95.6)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 169	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	22	(12.1)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Expected to Complete Questionnaires	7	(3.8)	0	(0.0)
WEEK 173	Completed	7	(3.8)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	7	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	175	(96.2)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	23	(12.6)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 177	Expected to Complete Questionnaires	6	(3.3)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 177	Completed	6	(3.3)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	6	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	176	(96.7)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	24	(13.2)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 181	Expected to Complete Questionnaires	4	(2.2)	0	(0.0)
	Completed	4	(2.2)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	4	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 181	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	178	(97.8)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	25	(13.7)	1	(0.6)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 185	Expected to Complete Questionnaires	3	(1.6)	0	(0.0)
	Completed	3	(1.6)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	3	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	179	(98.4)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 185	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	27	(14.8)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Expected to Complete Questionnaires	1	(0.5)	0	(0.0)
WEEK 189	Completed	1	(0.5)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	1	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	181	(99.5)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 189	Visit not reached	29	(15.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 193	Expected to Complete Questionnaires	0	(0.0)	0	(0.0)
	Completed	0	(0.0)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	0	(.)	0	(.)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	182	(100.0)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	118	(64.8)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	29	(15.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 197	Expected to Complete Questionnaires	0	(0.0)	0	(0.0)
	Completed	0	(0.0)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	0	(.)	0	(.)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 197	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	182	(100.0)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	118	(64.8)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	29	(15.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 201	Expected to Complete Questionnaires	0	(0.0)	0	(0.0)
	Completed	0	(0.0)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	0	(.)	0	(.)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 201	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	182	(100.0)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	118	(64.8)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	29	(15.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
Expected to complete questionnaire includes all patients who do not have missing data due to a missing by design reason Compliance is the proportion of patients who completed the PRO questionnaire among those who are expected to complete the questionnaire at this time point, excluding those missing by design. All the other categories are defined as the proportion of patients in the analysis population (N) Missing by design includes adverse event, death, discontinuation, translations not available, and no visit scheduled Number of participants: full-analysis-set population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor Database Cutoff Date: 15APR2024					

Anhang 4-G2.3: Rücklaufquoten des EQ-5D VAS

Tabelle 4G-5: Gründe für das Fehlen von Werten im EQ-5D VAS

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
BASELINE	Expected to Complete Questionnaires	182	(100.0)	174	(100.0)
	Completed	179	(98.4)	164	(94.3)
	Compliance (% in those expected to complete questionnaires)	179	(98.4)	164	(94.3)
	Not completed	3	(1.6)	10	(5.7)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	2	(1.1)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	6	(3.4)
	With visit, no record	0	(0.0)	2	(1.1)
	Missing by Design	0	(0.0)	0	(0.0)
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	0	(0.0)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 3	Expected to Complete Questionnaires	181	(99.5)	173	(99.4)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 3	Completed	159	(87.4)	143	(82.2)
	Compliance (% in those expected to complete questionnaires)	159	(87.8)	143	(82.7)
	Not completed	22	(12.1)	30	(17.2)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	11	(6.0)	12	(6.9)
	Subject in hospital or hospice	2	(1.1)	2	(1.1)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	1	(0.6)
	Other	9	(4.9)	13	(7.5)
	With visit, no record	0	(0.0)	1	(0.6)
	Missing by Design	1	(0.5)	1	(0.6)
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	0	(0.0)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	1	(0.5)	1	(0.6)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 5	Expected to Complete Questionnaires	173	(95.1)	171	(98.3)
	Completed	152	(83.5)	154	(88.5)
	Compliance (% in those expected to complete questionnaires)	152	(87.9)	154	(90.1)
	Not completed	21	(11.5)	17	(9.8)
	Subject did not complete due to disease under study	2	(1.1)	1	(0.6)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 5	Not completed due to site staff error	4	(2.2)	4	(2.3)
	Subject in hospital or hospice	3	(1.6)	2	(1.1)
	Subject was physically unable to complete	1	(0.5)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	1	(0.5)	1	(0.6)
	Other	10	(5.5)	9	(5.2)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	9	(4.9)	3	(1.7)
	Discontinued due to adverse event	1	(0.5)	1	(0.6)
	Discontinued due to clinical progression	2	(1.1)	2	(1.1)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	1	(0.5)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	0	(0.0)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	3	(1.6)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	2	(1.1)	0	(0.0)
WEEK 9	Expected to Complete Questionnaires	165	(90.7)	158	(90.8)
	Completed	147	(80.8)	141	(81.0)
	Compliance (% in those expected to complete questionnaires)	147	(89.1)	141	(89.2)
	Not completed	18	(9.9)	17	(9.8)
	Subject did not complete due to disease under study	1	(0.5)	1	(0.6)
	Not completed due to site staff error	2	(1.1)	6	(3.4)
	Subject in hospital or hospice	3	(1.6)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 9	Subject did not complete due to side effects of treatment	1	(0.5)	0	(0.0)
	Subject refused for other reasons	1	(0.5)	4	(2.3)
	Other	10	(5.5)	6	(3.4)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	17	(9.3)	16	(9.2)
	Discontinued due to adverse event	0	(0.0)	2	(1.1)
	Discontinued due to clinical progression	7	(3.8)	4	(2.3)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	1	(0.6)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	6	(3.3)	1	(0.6)
	Discontinued due to withdrawal by subject	1	(0.5)	0	(0.0)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	3	(1.6)	3	(1.7)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	5	(2.9)
WEEK 13	Expected to Complete Questionnaires	148	(81.3)	138	(79.3)
	Completed	130	(71.4)	116	(66.7)
	Compliance (% in those expected to complete questionnaires)	130	(87.8)	116	(84.1)
	Not completed	18	(9.9)	22	(12.6)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	1	(0.5)	5	(2.9)
	Subject in hospital or hospice	2	(1.1)	1	(0.6)
	Subject was physically unable to complete	1	(0.5)	1	(0.6)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.6)
	Subject did not complete due to side effects of treatment	1	(0.5)	0	(0.0)
	Subject refused for other reasons	2	(1.1)	6	(3.4)
	Other	11	(6.0)	6	(3.4)
	With visit, no record	0	(0.0)	1	(0.6)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 13	Missing by Design	34	(18.7)	36	(20.7)
	Discontinued due to adverse event	5	(2.7)	5	(2.9)
	Discontinued due to clinical progression	9	(4.9)	6	(3.4)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	1	(0.6)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	19	(10.4)	21	(12.1)
	Discontinued due to withdrawal by subject	1	(0.5)	0	(0.0)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	3	(1.7)
WEEK 17	Expected to Complete Questionnaires	127	(69.8)	100	(57.5)
	Completed	113	(62.1)	92	(52.9)
	Compliance (% in those expected to complete questionnaires)	113	(89.0)	92	(92.0)
	Not completed	14	(7.7)	8	(4.6)
	Subject did not complete due to disease under study	1	(0.5)	1	(0.6)
	Not completed due to site staff error	3	(1.6)	1	(0.6)
	Subject in hospital or hospice	4	(2.2)	1	(0.6)
	Subject was physically unable to complete	0	(0.0)	1	(0.6)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.6)
	Subject did not complete due to side effects of treatment	1	(0.5)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	1	(0.6)
	Other	5	(2.7)	2	(1.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	55	(30.2)	74	(42.5)
	Discontinued due to adverse event	5	(2.7)	10	(5.7)
	Discontinued due to clinical progression	9	(4.9)	10	(5.7)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	3	(1.7)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 17	Discontinued due to physician decision	0	(0.0)	1	(0.6)
	Discontinued due to progressive disease	38	(20.9)	42	(24.1)
	Discontinued due to withdrawal by subject	2	(1.1)	2	(1.1)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	3	(1.7)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	3	(1.7)
WEEK 21	Expected to Complete Questionnaires	114	(62.6)	87	(50.0)
	Completed	106	(58.2)	78	(44.8)
	Compliance (% in those expected to complete questionnaires)	106	(93.0)	78	(89.7)
	Not completed	8	(4.4)	9	(5.2)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	1	(0.5)	3	(1.7)
	Subject in hospital or hospice	0	(0.0)	1	(0.6)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	6	(3.3)	3	(1.7)
	With visit, no record	1	(0.5)	1	(0.6)
	Missing by Design	68	(37.4)	87	(50.0)
	Discontinued due to adverse event	6	(3.3)	14	(8.0)
	Discontinued due to clinical progression	10	(5.5)	11	(6.3)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	3	(1.7)
	Discontinued due to physician decision	0	(0.0)	1	(0.6)
	Discontinued due to progressive disease	48	(26.4)	52	(29.9)
	Discontinued due to withdrawal by subject	3	(1.6)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 21	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	2	(1.1)
WEEK 25	Expected to Complete Questionnaires	103	(56.6)	76	(43.7)
	Completed	96	(52.7)	72	(41.4)
	Compliance (% in those expected to complete questionnaires)	96	(93.2)	72	(94.7)
	Not completed	7	(3.8)	4	(2.3)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	1	(0.5)	2	(1.1)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	1	(0.5)	0	(0.0)
	Other	5	(2.7)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	79	(43.4)	98	(56.3)
	Discontinued due to adverse event	6	(3.3)	18	(10.3)
	Discontinued due to clinical progression	11	(6.0)	11	(6.3)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	57	(31.3)	59	(33.9)
	Discontinued due to withdrawal by subject	3	(1.6)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	1	(0.5)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 29	Expected to Complete Questionnaires	97	(53.3)	64	(36.8)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 29	Completed	91	(50.0)	59	(33.9)
	Compliance (% in those expected to complete questionnaires)	91	(93.8)	59	(92.2)
	Not completed	6	(3.3)	5	(2.9)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	2	(1.1)	2	(1.1)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	1	(0.6)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	4	(2.2)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	85	(46.7)	110	(63.2)
	Discontinued due to adverse event	7	(3.8)	18	(10.3)
	Discontinued due to clinical progression	11	(6.0)	11	(6.3)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	61	(33.5)	68	(39.1)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	1	(0.6)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	2	(1.1)
WEEK 33	Expected to Complete Questionnaires	91	(50.0)	58	(33.3)
	Completed	86	(47.3)	55	(31.6)
	Compliance (% in those expected to complete questionnaires)	86	(94.5)	55	(94.8)
	Not completed	5	(2.7)	3	(1.7)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 33	Not completed due to site staff error	2	(1.1)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	2	(1.1)
	Other	3	(1.6)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	91	(50.0)	116	(66.7)
	Discontinued due to adverse event	7	(3.8)	18	(10.3)
	Discontinued due to clinical progression	11	(6.0)	11	(6.3)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	66	(36.3)	75	(43.1)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	2	(1.1)
WEEK 37	Expected to Complete Questionnaires	89	(48.9)	53	(30.5)
	Completed	81	(44.5)	49	(28.2)
	Compliance (% in those expected to complete questionnaires)	81	(91.0)	49	(92.5)
	Not completed	8	(4.4)	4	(2.3)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	2	(1.1)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 37	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	5	(2.7)	2	(1.1)
	With visit, no record	1	(0.5)	1	(0.6)
	Missing by Design	93	(51.1)	121	(69.5)
	Discontinued due to adverse event	7	(3.8)	18	(10.3)
	Discontinued due to clinical progression	11	(6.0)	11	(6.3)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	67	(36.8)	78	(44.8)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	1	(0.5)	0	(0.0)
	Subject died	0	(0.0)	1	(0.6)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	3	(1.7)
WEEK 41	Expected to Complete Questionnaires	82	(45.1)	47	(27.0)
	Completed	80	(44.0)	43	(24.7)
	Compliance (% in those expected to complete questionnaires)	80	(97.6)	43	(91.5)
	Not completed	2	(1.1)	4	(2.3)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	1	(0.6)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	3	(1.7)
	With visit, no record	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 41	Missing by Design	100	(54.9)	127	(73.0)
	Discontinued due to adverse event	8	(4.4)	20	(11.5)
	Discontinued due to clinical progression	11	(6.0)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	73	(40.1)	82	(47.1)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	2	(1.1)	3	(1.7)
WEEK 45	Expected to Complete Questionnaires	78	(42.9)	48	(27.6)
	Completed	71	(39.0)	46	(26.4)
	Compliance (% in those expected to complete questionnaires)	71	(91.0)	46	(95.8)
	Not completed	7	(3.8)	2	(1.1)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	1	(0.5)	0	(0.0)
	Subject was physically unable to complete	1	(0.5)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	1	(0.5)	0	(0.0)
	Other	4	(2.2)	2	(1.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	104	(57.1)	126	(72.4)
	Discontinued due to adverse event	8	(4.4)	20	(11.5)
	Discontinued due to clinical progression	12	(6.6)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 45	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	77	(42.3)	84	(48.3)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 49	Expected to Complete Questionnaires	74	(40.7)	36	(20.7)
	Completed	69	(37.9)	35	(20.1)
	Compliance (% in those expected to complete questionnaires)	69	(93.2)	35	(97.2)
	Not completed	5	(2.7)	1	(0.6)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	5	(2.7)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	108	(59.3)	138	(79.3)
	Discontinued due to adverse event	8	(4.4)	22	(12.6)
	Discontinued due to clinical progression	12	(6.6)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	82	(45.1)	94	(54.0)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 49	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 53	Expected to Complete Questionnaires	73	(40.1)	32	(18.4)
	Completed	69	(37.9)	32	(18.4)
	Compliance (% in those expected to complete questionnaires)	69	(94.5)	32	(100.0)
	Not completed	4	(2.2)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	1	(0.5)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	109	(59.9)	142	(81.6)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	12	(6.6)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	83	(45.6)	97	(55.7)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 57	Expected to Complete Questionnaires	70	(38.5)	31	(17.8)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 57	Completed	68	(37.4)	30	(17.2)
	Compliance (% in those expected to complete questionnaires)	68	(97.1)	30	(96.8)
	Not completed	2	(1.1)	1	(0.6)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	1	(0.6)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	112	(61.5)	143	(82.2)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	12	(6.6)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	86	(47.3)	98	(56.3)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 61	Expected to Complete Questionnaires	68	(37.4)	26	(14.9)
	Completed	63	(34.6)	24	(13.8)
	Compliance (% in those expected to complete questionnaires)	63	(92.6)	24	(92.3)
	Not completed	5	(2.7)	2	(1.1)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 61	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	1	(0.6)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	4	(2.2)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	114	(62.6)	148	(85.1)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	12	(6.6)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	88	(48.4)	102	(58.6)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	1	(0.6)
WEEK 65	Expected to Complete Questionnaires	66	(36.3)	22	(12.6)
	Completed	63	(34.6)	21	(12.1)
	Compliance (% in those expected to complete questionnaires)	63	(95.5)	21	(95.5)
	Not completed	3	(1.6)	1	(0.6)
	Subject did not complete due to disease under study	0	(0.0)	1	(0.6)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 65	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	116	(63.7)	152	(87.4)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	13	(7.1)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	89	(48.9)	106	(60.9)
	Discontinued due to withdrawal by subject	5	(2.7)	4	(2.3)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	1	(0.6)
WEEK 69	Expected to Complete Questionnaires	61	(33.5)	20	(11.5)
	Completed	57	(31.3)	20	(11.5)
	Compliance (% in those expected to complete questionnaires)	57	(93.4)	20	(100.0)
	Not completed	4	(2.2)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	3	(1.6)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 69	Missing by Design	121	(66.5)	154	(88.5)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	13	(7.1)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	93	(51.1)	108	(62.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 73	Expected to Complete Questionnaires	60	(33.0)	20	(11.5)
	Completed	55	(30.2)	20	(11.5)
	Compliance (% in those expected to complete questionnaires)	55	(91.7)	20	(100.0)
	Not completed	5	(2.7)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	1	(0.5)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	4	(2.2)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	122	(67.0)	154	(88.5)
	Discontinued due to adverse event	8	(4.4)	23	(13.2)
	Discontinued due to clinical progression	13	(7.1)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 73	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	94	(51.6)	108	(62.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	1	(0.5)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 77	Expected to Complete Questionnaires	59	(32.4)	20	(11.5)
	Completed	55	(30.2)	18	(10.3)
	Compliance (% in those expected to complete questionnaires)	55	(93.2)	18	(90.0)
	Not completed	4	(2.2)	2	(1.1)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	1	(0.6)
	Other	3	(1.6)	1	(0.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	123	(67.6)	154	(88.5)
	Discontinued due to adverse event	9	(4.9)	23	(13.2)
	Discontinued due to clinical progression	13	(7.1)	12	(6.9)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	95	(52.2)	108	(62.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 77	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 81	Expected to Complete Questionnaires	56	(30.8)	15	(8.6)
	Completed	52	(28.6)	15	(8.6)
	Compliance (% in those expected to complete questionnaires)	52	(92.9)	15	(100.0)
	Not completed	4	(2.2)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	3	(1.6)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	126	(69.2)	159	(91.4)
	Discontinued due to adverse event	9	(4.9)	23	(13.2)
	Discontinued due to clinical progression	13	(7.1)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	97	(53.3)	112	(64.4)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	1	(0.5)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 85	Expected to Complete Questionnaires	53	(29.1)	11	(6.3)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 85	Completed	50	(27.5)	10	(5.7)
	Compliance (% in those expected to complete questionnaires)	50	(94.3)	10	(90.9)
	Not completed	3	(1.6)	1	(0.6)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	1	(0.6)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	3	(1.6)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	129	(70.9)	163	(93.7)
	Discontinued due to adverse event	9	(4.9)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	99	(54.4)	115	(66.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	1	(0.6)
WEEK 89	Expected to Complete Questionnaires	52	(28.6)	12	(6.9)
	Completed	47	(25.8)	10	(5.7)
	Compliance (% in those expected to complete questionnaires)	47	(90.4)	10	(83.3)
	Not completed	5	(2.7)	2	(1.1)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 89	Not completed due to site staff error	2	(1.1)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	1	(0.6)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	1	(0.6)
	With visit, no record	1	(0.5)	0	(0.0)
	Missing by Design	130	(71.4)	162	(93.1)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	100	(54.9)	115	(66.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 93	Expected to Complete Questionnaires	49	(26.9)	11	(6.3)
	Completed	47	(25.8)	11	(6.3)
	Compliance (% in those expected to complete questionnaires)	47	(95.9)	11	(100.0)
	Not completed	2	(1.1)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 93	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	133	(73.1)	163	(93.7)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	103	(56.6)	116	(66.7)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 97	Expected to Complete Questionnaires	46	(25.3)	10	(5.7)
	Completed	44	(24.2)	10	(5.7)
	Compliance (% in those expected to complete questionnaires)	44	(95.7)	10	(100.0)
	Not completed	2	(1.1)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 97	Missing by Design	136	(74.7)	164	(94.3)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	105	(57.7)	117	(67.2)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 101	Expected to Complete Questionnaires	43	(23.6)	10	(5.7)
	Completed	42	(23.1)	9	(5.2)
	Compliance (% in those expected to complete questionnaires)	42	(97.7)	9	(90.0)
	Not completed	1	(0.5)	1	(0.6)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	1	(0.6)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	139	(76.4)	164	(94.3)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 101	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	106	(58.2)	117	(67.2)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	3	(1.6)	0	(0.0)
WEEK 105	Expected to Complete Questionnaires	46	(25.3)	7	(4.0)
	Completed	43	(23.6)	7	(4.0)
	Compliance (% in those expected to complete questionnaires)	43	(93.5)	7	(100.0)
	Not completed	3	(1.6)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	1	(0.5)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	1	(0.5)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	136	(74.7)	167	(96.0)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	106	(58.2)	120	(69.0)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 105	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 109	Expected to Complete Questionnaires	46	(25.3)	7	(4.0)
	Completed	42	(23.1)	7	(4.0)
	Compliance (% in those expected to complete questionnaires)	42	(91.3)	7	(100.0)
	Not completed	4	(2.2)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	3	(1.6)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	136	(74.7)	167	(96.0)
	Discontinued due to adverse event	10	(5.5)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	106	(58.2)	120	(69.0)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 113	Expected to Complete Questionnaires	44	(24.2)	5	(2.9)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 113	Completed	39	(21.4)	5	(2.9)
	Compliance (% in those expected to complete questionnaires)	39	(88.6)	5	(100.0)
	Not completed	5	(2.7)	0	(0.0)
	Subject did not complete due to disease under study	1	(0.5)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	1	(0.5)	0	(0.0)
	Missing by Design	138	(75.8)	169	(97.1)
	Discontinued due to adverse event	11	(6.0)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	106	(58.2)	122	(70.1)
	Discontinued due to withdrawal by subject	5	(2.7)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 117	Expected to Complete Questionnaires	42	(23.1)	5	(2.9)
	Completed	37	(20.3)	4	(2.3)
	Compliance (% in those expected to complete questionnaires)	37	(88.1)	4	(80.0)
	Not completed	5	(2.7)	1	(0.6)
	Subject did not complete due to disease under study	1	(0.5)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 117	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	1	(0.6)
	With visit, no record	1	(0.5)	0	(0.0)
	Missing by Design	140	(76.9)	169	(97.1)
	Discontinued due to adverse event	11	(6.0)	23	(13.2)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	108	(59.3)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
WEEK 121	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Expected to Complete Questionnaires	38	(20.9)	3	(1.7)
	Completed	38	(20.9)	3	(1.7)
	Compliance (% in those expected to complete questionnaires)	38	(100.0)	3	(100.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 121	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	144	(79.1)	171	(98.3)
	Discontinued due to adverse event	11	(6.0)	24	(13.8)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	1	(0.5)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	110	(60.4)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	1	(0.5)	1	(0.6)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 125	Expected to Complete Questionnaires	34	(18.7)	3	(1.7)
	Completed	33	(18.1)	3	(1.7)
	Compliance (% in those expected to complete questionnaires)	33	(97.1)	3	(100.0)
	Not completed	1	(0.5)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	1	(0.5)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 125	Missing by Design	148	(81.3)	171	(98.3)
	Discontinued due to adverse event	11	(6.0)	24	(13.8)
	Discontinued due to clinical progression	14	(7.7)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	112	(61.5)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	3	(1.6)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 129	Expected to Complete Questionnaires	31	(17.0)	3	(1.7)
	Completed	28	(15.4)	3	(1.7)
	Compliance (% in those expected to complete questionnaires)	28	(90.3)	3	(100.0)
	Not completed	3	(1.6)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	2	(1.1)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	151	(83.0)	171	(98.3)
	Discontinued due to adverse event	11	(6.0)	24	(13.8)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 129	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	113	(62.1)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	4	(2.2)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Expected to Complete Questionnaires	28	(15.4)	2	(1.1)
WEEK 133	Completed	27	(14.8)	2	(1.1)
	Compliance (% in those expected to complete questionnaires)	27	(96.4)	2	(100.0)
	Not completed	1	(0.5)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	1	(0.5)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	154	(84.6)	172	(98.9)
	Discontinued due to adverse event	12	(6.6)	24	(13.8)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	113	(62.1)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 133	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	6	(3.3)	1	(0.6)
	Visit not scheduled	0	(0.0)	1	(0.6)
WEEK 137	Expected to Complete Questionnaires	22	(12.1)	3	(1.7)
	Completed	21	(11.5)	3	(1.7)
	Compliance (% in those expected to complete questionnaires)	21	(95.5)	3	(100.0)
	Not completed	1	(0.5)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	1	(0.5)	0	(0.0)
	Missing by Design	160	(87.9)	171	(98.3)
	Discontinued due to adverse event	12	(6.6)	24	(13.8)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	115	(63.2)	122	(70.1)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	9	(4.9)	1	(0.6)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 141	Expected to Complete Questionnaires	22	(12.1)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 141	Completed	21	(11.5)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	21	(95.5)	0	(0.0)
	Not completed	1	(0.5)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	1	(0.5)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	160	(87.9)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	116	(63.7)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	9	(4.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 145	Expected to Complete Questionnaires	20	(11.0)	0	(0.0)
	Completed	20	(11.0)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	20	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 145	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	162	(89.0)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	10	(5.5)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 149	Expected to Complete Questionnaires	18	(9.9)	0	(0.0)
	Completed	18	(9.9)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	18	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 149	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	164	(90.1)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	12	(6.6)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 153	Expected to Complete Questionnaires	17	(9.3)	0	(0.0)
	Completed	17	(9.3)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	17	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 153	Missing by Design	165	(90.7)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	13	(7.1)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 157	Expected to Complete Questionnaires	12	(6.6)	0	(0.0)
	Completed	12	(6.6)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	12	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	170	(93.4)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 157	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	18	(9.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Expected to Complete Questionnaires	11	(6.0)	0	(0.0)
WEEK 161	Completed	11	(6.0)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	11	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	171	(94.0)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 161	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	19	(10.4)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 165	Expected to Complete Questionnaires	9	(4.9)	0	(0.0)
	Completed	9	(4.9)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	9	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	173	(95.1)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	21	(11.5)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 169	Expected to Complete Questionnaires	8	(4.4)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 169	Completed	8	(4.4)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	8	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	174	(95.6)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	22	(12.1)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 173	Expected to Complete Questionnaires	7	(3.8)	0	(0.0)
	Completed	7	(3.8)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	7	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 173	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	175	(96.2)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	23	(12.6)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 177	Expected to Complete Questionnaires	6	(3.3)	0	(0.0)
	Completed	6	(3.3)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	6	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 177	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	176	(96.7)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	24	(13.2)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 181	Expected to Complete Questionnaires	4	(2.2)	0	(0.0)
	Completed	4	(2.2)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	4	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 181	Missing by Design	178	(97.8)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	25	(13.7)	1	(0.6)
	Visit not scheduled	1	(0.5)	0	(0.0)
WEEK 185	Expected to Complete Questionnaires	3	(1.6)	0	(0.0)
	Completed	3	(1.6)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	3	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	179	(98.4)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 185	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	27	(14.8)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 189	Expected to Complete Questionnaires	1	(0.5)	0	(0.0)
	Completed	1	(0.5)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	1	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	181	(99.5)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
WEEK 189	Discontinued due to progressive disease	117	(64.3)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 193	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	29	(15.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Expected to Complete Questionnaires	0	(0.0)	0	(0.0)
	Completed	0	(0.0)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	0	(.)	0	(.)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	182	(100.0)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	118	(64.8)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	29	(15.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 197	Expected to Complete Questionnaires	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 197	Completed	0	(0.0)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	0	(.)	0	(.)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)
	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	182	(100.0)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	118	(64.8)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	29	(15.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
WEEK 201	Expected to Complete Questionnaires	0	(0.0)	0	(0.0)
	Completed	0	(0.0)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	0	(.)	0	(.)
	Not completed	0	(0.0)	0	(0.0)
	Subject did not complete due to disease under study	0	(0.0)	0	(0.0)

Treatment Visit	Category	Belzutifan N=182		Everolimus N=174	
		n	(%)	n	(%)
WEEK 201	Not completed due to site staff error	0	(0.0)	0	(0.0)
	Subject in hospital or hospice	0	(0.0)	0	(0.0)
	Subject was physically unable to complete	0	(0.0)	0	(0.0)
	Subject lost to follow-up/unable to contact	0	(0.0)	0	(0.0)
	Subject did not complete due to side effects of treatment	0	(0.0)	0	(0.0)
	Subject refused for other reasons	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	182	(100.0)	174	(100.0)
	Discontinued due to adverse event	12	(6.6)	25	(14.4)
	Discontinued due to clinical progression	15	(8.2)	13	(7.5)
	Discontinued due to non-study anti-cancer therapy	2	(1.1)	4	(2.3)
	Discontinued due to physician decision	0	(0.0)	2	(1.1)
	Discontinued due to progressive disease	118	(64.8)	124	(71.3)
	Discontinued due to withdrawal by subject	6	(3.3)	5	(2.9)
	Translation not available in subjects language	0	(0.0)	0	(0.0)
	Subject died	0	(0.0)	0	(0.0)
	Visit not reached	29	(15.9)	1	(0.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
Expected to complete questionnaire includes all patients who do not have missing data due to a missing by design reason Compliance is the proportion of patients who completed the PRO questionnaire among those who are expected to complete the questionnaire at this time point, excluding those missing by design. All the other categories are defined as the proportion of patients in the analysis population (N) Missing by design includes adverse event, death, discontinuation, translations not available, and no visit scheduled Number of participants: full-analysis-set population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death Ligand 1; VEGF: Vascular Endothelial Growth Factor Database Cutoff Date: 15APR2024					

Anhang 4-G3: Auswertung über den Studienverlauf: Krankheitssymptomatik und Gesundheitszustand

Ergänzend zu Abschnitt 4.3.1.3.1.2.3 werden die Auswertung über den Studienverlauf dargestellt. Hierzu werden zu jedem Erhebungszeitpunkt die Anzahl an verfügbaren Daten, der Mittelwert (inkl. Standardabweichung), der Median (inkl. Q1; Q3) und Minimum und Maximum zum jeweiligen Zeitpunkt tabellarisch dargestellt. Zusätzlich erfolgt eine grafische Darstellung des Mittelwerts und des Standardfehlers über den Studienverlauf.

EORTC QLQ-C30

EORTC QLQ-C30: Symptomskala Erschöpfung

Tabelle 4G-6: Auswertung über den Studienverlauf der Symptomskala Erschöpfung des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Erschöpfung	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	178	164
Mittelwert (SD)	29,3 (23,4)	32,5 (21,9)
Median (Q1; Q3)	33,3 (11,1; 44,4)	33,3 (22,2; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	159	145
Mittelwert (SD)	32,7 (26,9)	31,6 (23,8)
Median (Q1; Q3)	33,3 (11,1; 44,4)	33,3 (11,1; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	152	156
Mittelwert (SD)	32,1 (26,2)	34,1 (24,4)
Median (Q1; Q3)	33,3 (11,1; 44,4)	33,3 (11,1; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	147	142
Mittelwert (SD)	33,1 (27,0)	38,8 (26,3)
Median (Q1; Q3)	33,3 (11,1; 55,6)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 13		
N ^c	130	116
Mittelwert (SD)	32,3 (25,0)	37,5 (25,2)
Median (Q1; Q3)	33,3 (11,1; 44,4)	33,3 (22,2; 55,6)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	92
Mittelwert (SD)	31,6 (24,9)	34,8 (22,9)
Median (Q1; Q3)	33,3 (11,1; 44,4)	33,3 (22,2; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 21		
N ^c	106	78

EORTC QLQ-C30 Erschöpfung	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Mittelwert (SD)	30,6 (25,9)	34,8 (25,0)
Median (Q1; Q3)	33,3 (0,0; 44,4)	33,3 (22,2; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 25		
N ^c	96	72
Mittelwert (SD)	27,9 (23,0)	31,8 (21,6)
Median (Q1; Q3)	33,3 (5,6; 33,3)	33,3 (22,2; 33,3)
Min, Max	0,0; 100,0	0,0; 88,9
Woche 29		
N ^c	92	59
Mittelwert (SD)	26,0 (22,8)	30,9 (23,1)
Median (Q1; Q3)	22,2 (0,0; 33,3)	33,3 (11,1; 33,3)
Min, Max	0,0; 88,9	0,0; 88,9
Woche 33		
N ^c	86	55
Mittelwert (SD)	25,6 (20,0)	31,9 (20,8)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (22,2; 44,4)
Min, Max	0,0; 77,8	0,0; 88,9
Woche 37		
N ^c	81	50
Mittelwert (SD)	26,2 (21,8)	33,1 (26,0)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (11,1; 44,4)
Min, Max	0,0; 88,9	0,0; 100,0
Woche 41		
N ^c	80	43
Mittelwert (SD)	27,9 (21,7)	29,2 (23,1)
Median (Q1; Q3)	33,3 (5,6; 33,3)	33,3 (11,1; 33,3)
Min, Max	0,0; 77,8	0,0; 100,0
Woche 45		
N ^c	71	46
Mittelwert (SD)	26,8 (22,5)	32,9 (22,2)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (22,2; 44,4)
Min, Max	0,0; 77,8	0,0; 100,0
Woche 49		
N ^c	69	35
Mittelwert (SD)	25,1 (20,4)	26,0 (19,2)
Median (Q1; Q3)	22,2 (0,0; 33,3)	22,2 (11,1; 33,3)
Min, Max	0,0; 77,8	0,0; 88,9
Woche 53		
N ^c	70	32
Mittelwert (SD)	24,3 (21,4)	26,4 (18,9)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (11,1; 33,3)
Min, Max	0,0; 88,9	0,0; 66,7
Woche 57		
N ^c	68	30
Mittelwert (SD)	26,1 (24,6)	30,0 (20,7)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (11,1; 44,4)

EORTC QLQ-C30 Erschöpfung	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Min, Max	0,0; 100,0	0,0; 66,7
Woche 61		
N ^c	63	24
Mittelwert (SD)	25,2 (23,3)	25,0 (19,2)
Median (Q1; Q3)	22,2 (0,0; 33,3)	33,3 (5,6; 33,3)
Min, Max	0,0; 88,9	0,0; 66,7
Woche 65		
N ^c	63	21
Mittelwert (SD)	26,6 (21,4)	32,8 (24,2)
Median (Q1; Q3)	22,2 (0,0; 33,3)	33,3 (22,2; 33,3)
Min, Max	0,0; 77,8	0,0; 100,0
Woche 69		
N ^c	57	20
Mittelwert (SD)	28,7 (24,4)	36,1 (21,3)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (27,8; 50,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 73		
N ^c	55	20
Mittelwert (SD)	29,9 (25,5)	39,4 (27,6)
Median (Q1; Q3)	33,3 (0,0; 44,4)	33,3 (27,8; 44,4)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 77		
N ^c	56	18
Mittelwert (SD)	29,6 (23,3)	27,2 (18,8)
Median (Q1; Q3)	33,3 (0,0; 44,4)	33,3 (11,1; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 81		
N ^c	52	15
Mittelwert (SD)	29,5 (24,5)	28,1 (24,1)
Median (Q1; Q3)	33,3 (0,0; 44,4)	33,3 (0,0; 33,3)
Min, Max	0,0; 77,8	0,0; 66,7
Woche 85		
N ^c	50	10
Mittelwert (SD)	29,6 (27,2)	30,0 (20,3)
Median (Q1; Q3)	33,3 (0,0; 44,4)	33,3 (22,2; 44,4)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 89		
N ^c	47	10
Mittelwert (SD)	28,8 (25,8)	31,1 (23,3)
Median (Q1; Q3)	33,3 (0,0; 55,6)	33,3 (11,1; 33,3)
Min, Max	0,0; 77,8	0,0; 66,7
Woche 93		
N ^c	47	11
Mittelwert (SD)	28,6 (22,8)	29,3 (18,8)
Median (Q1; Q3)	33,3 (0,0; 44,4)	33,3 (22,2; 33,3)
Min, Max	0,0; 88,9	0,0; 66,7

EORTC QLQ-C30 Erschöpfung	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Woche 97		
N ^c	44	10
Mittelwert (SD)	24,7 (20,9)	25,6 (12,9)
Median (Q1; Q3)	27,8 (0,0; 33,3)	33,3 (11,1; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 101		
N ^c	42	9
Mittelwert (SD)	32,5 (26,4)	28,4 (20,1)
Median (Q1; Q3)	33,3 (0,0; 55,6)	33,3 (22,2; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 105		
N ^c	43	7
Mittelwert (SD)	30,5 (23,6)	23,8 (20,7)
Median (Q1; Q3)	33,3 (0,0; 55,6)	33,3 (0,0; 33,3)
Min, Max	0,0; 88,9	0,0; 55,6
Woche 109		
N ^c	42	7
Mittelwert (SD)	29,6 (25,5)	23,8 (23,5)
Median (Q1; Q3)	33,3 (0,0; 55,6)	22,2 (0,0; 33,3)
Min, Max	0,0; 88,9	0,0; 66,7
Woche 113		
N ^c	39	5
Mittelwert (SD)	29,6 (24,2)	37,8 (9,9)
Median (Q1; Q3)	33,3 (0,0; 44,4)	44,4 (33,3; 44,4)
Min, Max	0,0; 77,8	22,2; 44,4
Woche 117		
N ^c	37	5
Mittelwert (SD)	24,6 (24,4)	42,2 (16,5)
Median (Q1; Q3)	22,2 (0,0; 33,3)	44,4 (33,3; 44,4)
Min, Max	0,0; 88,9	22,2; 66,7
Woche 121		
N ^c	38	3
Mittelwert (SD)	28,9 (27,2)	63,0 (28,0)
Median (Q1; Q3)	22,2 (0,0; 55,6)	66,7 (33,3; 88,9)
Min, Max	0,0; 88,9	33,3; 88,9
Woche 125		
N ^c	33	3
Mittelwert (SD)	25,3 (24,3)	37,0 (33,9)
Median (Q1; Q3)	22,2 (0,0; 33,3)	44,4 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 129		
N ^c	29	3
Mittelwert (SD)	26,8 (27,9)	55,6 (19,2)
Median (Q1; Q3)	22,2 (0,0; 33,3)	66,7 (33,3; 66,7)
Min, Max	0,0; 100,0	33,3; 66,7
Woche 133		

EORTC QLQ-C30 Erschöpfung	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
N ^c	27	2
Mittelwert (SD)	26,3 (26,0)	38,9 (39,3)
Median (Q1; Q3)	22,2 (0,0; 33,3)	38,9 (11,1; 66,7)
Min, Max	0,0; 100,0	11,1; 66,7
Woche 137		
N ^c	21	3
Mittelwert (SD)	27,5 (28,7)	59,3 (12,8)
Median (Q1; Q3)	33,3 (0,0; 33,3)	66,7 (44,4; 66,7)
Min, Max	0,0; 100,0	44,4; 66,7
Woche 141		
N ^c	21	0
Mittelwert (SD)	27,0 (26,4)	- (-)
Median (Q1; Q3)	33,3 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 145		
N ^c	20	0
Mittelwert (SD)	23,3 (26,0)	- (-)
Median (Q1; Q3)	27,8 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 88,9	-; -
Woche 149		
N ^c	18	0
Mittelwert (SD)	21,6 (28,1)	- (-)
Median (Q1; Q3)	5,6 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 153		
N ^c	17	0
Mittelwert (SD)	25,5 (25,7)	- (-)
Median (Q1; Q3)	22,2 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 88,9	-; -
Woche 157		
N ^c	12	0
Mittelwert (SD)	26,9 (29,0)	- (-)
Median (Q1; Q3)	27,8 (0,0; 44,4)	- (-; -)
Min, Max	0,0; 88,9	-; -
Woche 161		
N ^c	11	0
Mittelwert (SD)	28,3 (26,0)	- (-)
Median (Q1; Q3)	33,3 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 77,8	-; -
Woche 165		
N ^c	9	0
Mittelwert (SD)	22,2 (28,9)	- (-)
Median (Q1; Q3)	22,2 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 88,9	-; -
Woche 169		
N ^c	8	0
Mittelwert (SD)	25,0 (26,4)	- (-)

EORTC QLQ-C30 Erschöpfung	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	27,8 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 77,8	-; -
Woche 173		
N ^c	7	0
Mittelwert (SD)	31,7 (29,7)	- (-)
Median (Q1; Q3)	33,3 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 88,9	-; -
Woche 177		
N ^c	6	0
Mittelwert (SD)	27,8 (28,8)	- (-)
Median (Q1; Q3)	27,8 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 77,8	-; -
Woche 181		
N ^c	4	0
Mittelwert (SD)	22,2 (20,3)	- (-)
Median (Q1; Q3)	22,2 (5,6; 38,9)	- (-; -)
Min, Max	0,0; 44,4	-; -
Woche 185		
N ^c	3	0
Mittelwert (SD)	40,7 (44,9)	- (-)
Median (Q1; Q3)	33,3 (0,0; 88,9)	- (-; -)
Min, Max	0,0; 88,9	-; -
Woche 189		
N ^c	1	0
Mittelwert (SD)	33,3 (-)	- (-)
Median (Q1; Q3)	33,3 (33,3; 33,3)	- (-; -)
Min, Max	33,3; 33,3	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Items; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		

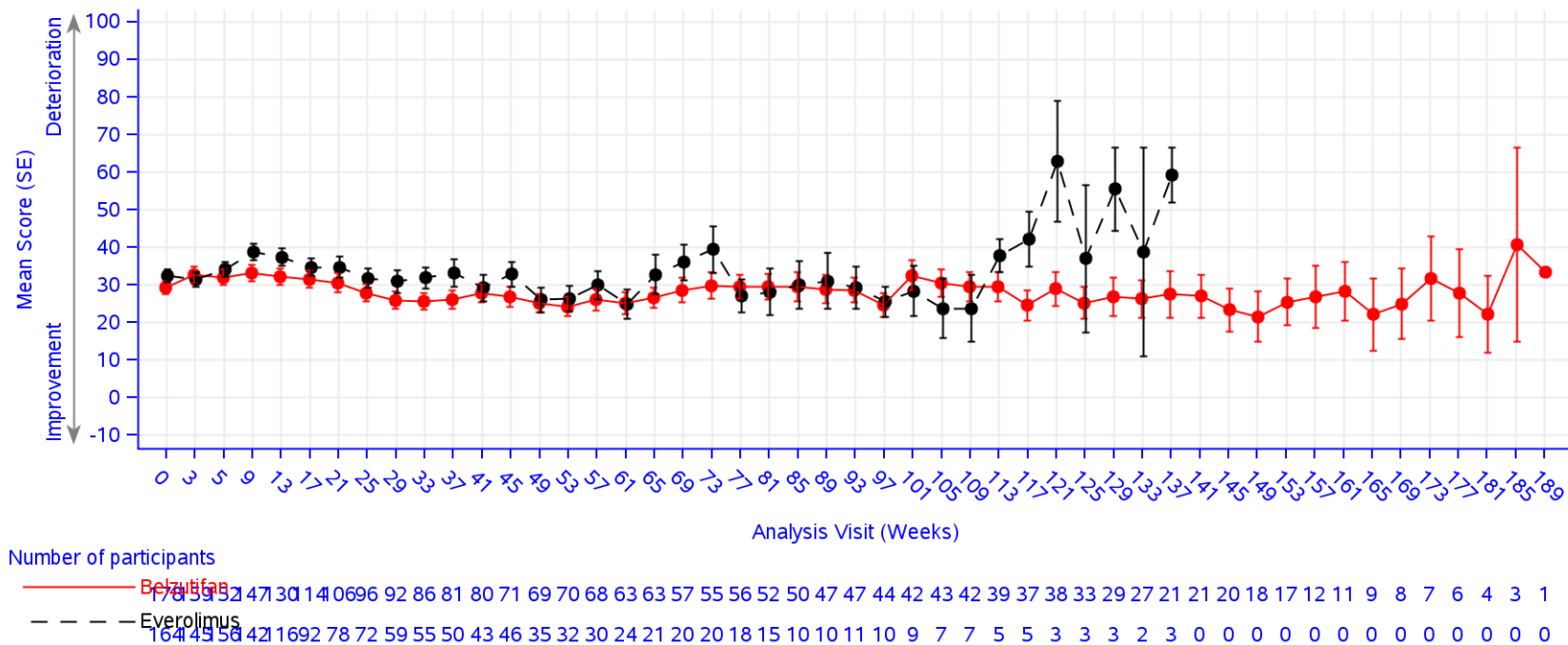


Abbildung 4G-1 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Erschöpfung zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Symptomskala Übelkeit und Erbrechen

Tabelle 4G-7: Auswertung über den Studienverlauf der Symptomskala Übelkeit und Erbrechen des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	178	164
Mittelwert (SD)	5,3 (11,5)	7,5 (17,5)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 100,0
Woche 3		
N ^c	159	145
Mittelwert (SD)	7,1 (14,1)	4,9 (12,3)
Median (Q1; Q3)	0,0 (0,0; 16,7)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 83,3
Woche 5		
N ^c	152	156
Mittelwert (SD)	6,4 (16,5)	6,8 (13,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 83,3
Woche 9		
N ^c	147	142
Mittelwert (SD)	5,9 (13,3)	7,2 (13,8)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 13		
N ^c	130	116
Mittelwert (SD)	6,9 (15,4)	5,3 (12,9)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 83,3	0,0; 100,0
Woche 17		
N ^c	114	92
Mittelwert (SD)	6,9 (16,6)	4,9 (11,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 21		
N ^c	106	78
Mittelwert (SD)	6,3 (15,2)	4,7 (12,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 25		
N ^c	96	72
Mittelwert (SD)	3,8 (10,4)	3,2 (8,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 33,3
Woche 29		
N ^c	92	59

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: LITESPARK 005 ^a	
	Belzutifan	Everolimus
	N ^b = 182	N ^b = 174
Mittelwert (SD)	4,7 (14,0)	4,0 (10,9)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 83,3	0,0; 66,7
Woche 33		
N ^c	86	55
Mittelwert (SD)	4,1 (11,7)	4,8 (11,9)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 37		
N ^c	81	50
Mittelwert (SD)	3,5 (10,1)	5,0 (12,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 41		
N ^c	80	43
Mittelwert (SD)	4,0 (9,7)	2,3 (6,9)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 33,3
Woche 45		
N ^c	71	46
Mittelwert (SD)	3,3 (9,2)	5,1 (11,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 50,0
Woche 49		
N ^c	69	35
Mittelwert (SD)	3,9 (12,5)	3,3 (7,9)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 83,3	0,0; 33,3
Woche 53		
N ^c	70	32
Mittelwert (SD)	3,3 (7,8)	1,6 (6,5)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 33,3
Woche 57		
N ^c	68	30
Mittelwert (SD)	3,7 (9,5)	2,8 (7,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 33,3
Woche 61		
N ^c	63	24
Mittelwert (SD)	4,5 (11,7)	1,4 (4,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 16,7
Woche 65		
N ^c	63	21
Mittelwert (SD)	3,4 (9,5)	4,0 (9,0)

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: LITESPARK 005 ^a	
	Belzutifan	Everolimus
	N ^b = 182	N ^b = 174
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 33,3
Woche 69		
N ^c	57	20
Mittelwert (SD)	4,7 (11,7)	4,2 (7,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 8,3)
Min, Max	0,0; 66,7	0,0; 16,7
Woche 73		
N ^c	55	20
Mittelwert (SD)	6,7 (14,9)	9,2 (19,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 66,7	0,0; 83,3
Woche 77		
N ^c	56	18
Mittelwert (SD)	5,4 (11,9)	2,8 (6,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 16,7
Woche 81		
N ^c	52	15
Mittelwert (SD)	6,4 (15,2)	4,4 (9,9)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 85		
N ^c	50	10
Mittelwert (SD)	5,0 (11,8)	5,0 (15,8)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 50,0
Woche 89		
N ^c	47	10
Mittelwert (SD)	6,0 (13,6)	1,7 (5,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 16,7
Woche 93		
N ^c	47	11
Mittelwert (SD)	3,5 (11,5)	1,5 (5,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 16,7
Woche 97		
N ^c	44	10
Mittelwert (SD)	3,0 (9,7)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 0,0
Woche 101		
N ^c	42	9
Mittelwert (SD)	4,4 (11,1)	1,9 (5,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: LITESPARK 005 ^a	
	Belzutifan	Everolimus
	N ^b = 182	N ^b = 174
Min, Max	0,0; 50,0	0,0; 16,7
Woche 105		
N ^c	43	7
Mittelwert (SD)	5,0 (10,6)	2,4 (6,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 16,7
Woche 109		
N ^c	42	7
Mittelwert (SD)	3,2 (9,2)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 0,0
Woche 113		
N ^c	39	5
Mittelwert (SD)	5,1 (10,9)	6,7 (9,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 50,0	0,0; 16,7
Woche 117		
N ^c	37	5
Mittelwert (SD)	3,6 (8,9)	6,7 (9,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 33,3	0,0; 16,7
Woche 121		
N ^c	38	3
Mittelwert (SD)	5,3 (12,3)	5,6 (9,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 50,0	0,0; 16,7
Woche 125		
N ^c	33	3
Mittelwert (SD)	3,5 (10,8)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 0,0
Woche 129		
N ^c	29	3
Mittelwert (SD)	2,9 (10,0)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 50,0	0,0; 0,0
Woche 133		
N ^c	27	2
Mittelwert (SD)	2,5 (10,0)	8,3 (11,8)
Median (Q1; Q3)	0,0 (0,0; 0,0)	8,3 (0,0; 16,7)
Min, Max	0,0; 50,0	0,0; 16,7
Woche 137		
N ^c	21	3
Mittelwert (SD)	7,1 (22,1)	11,1 (9,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	16,7 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 16,7

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: LITESPARK 005 ^a	
	Belzutifan	Everolimus
	N ^b = 182	N ^b = 174
Woche 141		
N ^c	21	0
Mittelwert (SD)	4,0 (14,8)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 145		
N ^c	20	0
Mittelwert (SD)	1,7 (5,1)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 16,7	-; -
Woche 149		
N ^c	18	0
Mittelwert (SD)	2,8 (8,6)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 153		
N ^c	17	0
Mittelwert (SD)	2,0 (5,5)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 16,7	-; -
Woche 157		
N ^c	12	0
Mittelwert (SD)	1,4 (4,8)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 16,7	-; -
Woche 161		
N ^c	11	0
Mittelwert (SD)	1,5 (5,0)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 16,7	-; -
Woche 165		
N ^c	9	0
Mittelwert (SD)	5,6 (11,8)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 169		
N ^c	8	0
Mittelwert (SD)	8,3 (23,6)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 173		
N ^c	7	0
Mittelwert (SD)	2,4 (6,3)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 16,7	-; -
Woche 177		

EORTC QLQ-C30 Übelkeit und Erbrechen	Studie: LITESPARK 005 ^a	
	Belzutifan	Everolimus
	N ^b = 182	N ^b = 174
N ^c	6	0
Mittelwert (SD)	5,6 (8,6)	- (-)
Median (Q1; Q3)	0,0 (0,0; 16,7)	- (-; -)
Min, Max	0,0; 16,7	-; -
Woche 181		
N ^c	4	0
Mittelwert (SD)	0,0 (0,0)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 0,0	-; -
Woche 185		
N ^c	3	0
Mittelwert (SD)	22,2 (38,5)	- (-)
Median (Q1; Q3)	0,0 (0,0; 66,7)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 189		
N ^c	1	0
Mittelwert (SD)	0,0 (-)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 0,0	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Items; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		

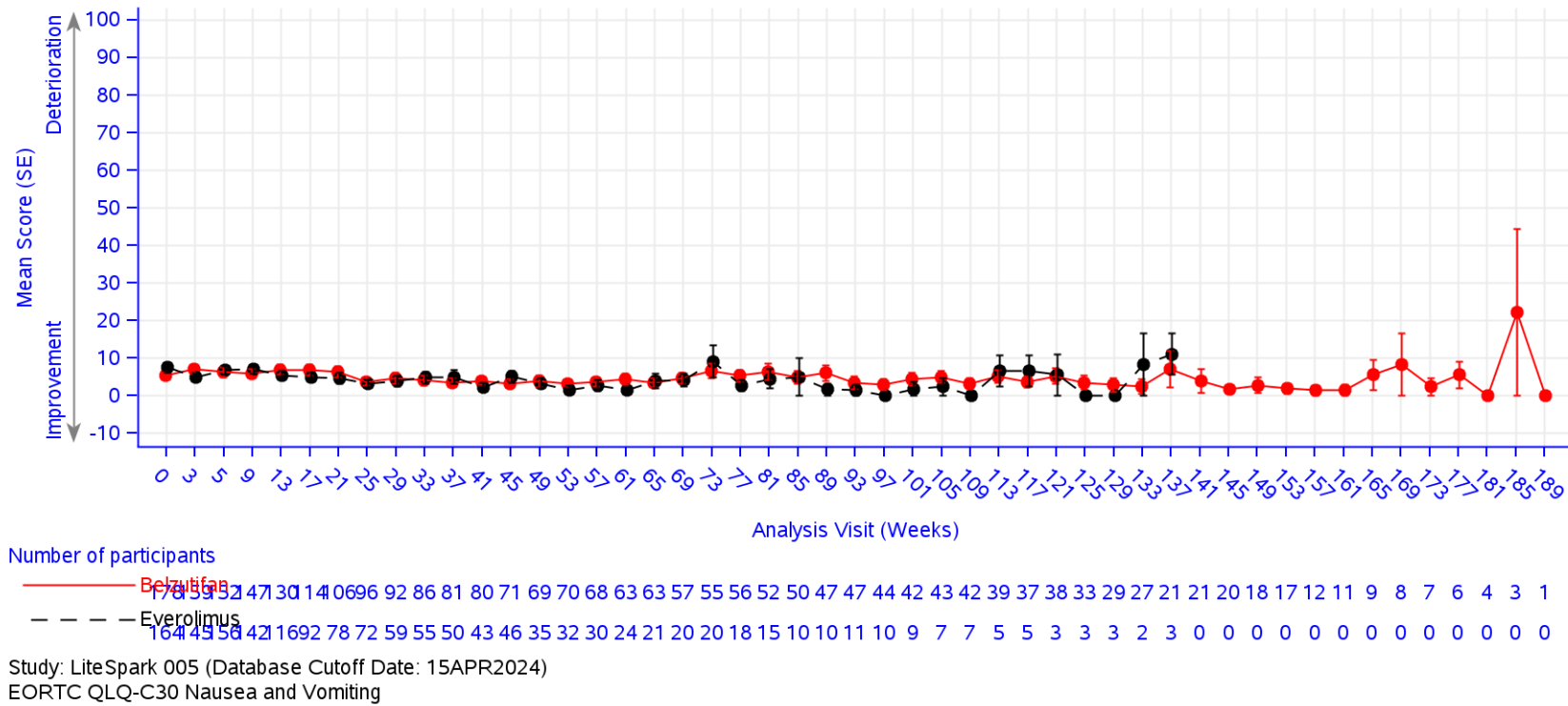


Abbildung 4G-2 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Übelkeit und Erbrechen zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Symptomskala Schmerzen

Tabelle 4G-8: Auswertung über den Studienverlauf der Symptomskala Schmerzen des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Schmerzen	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	178	164
Mittelwert (SD)	26,0 (27,3)	25,8 (28,6)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	159	145
Mittelwert (SD)	27,6 (29,2)	26,6 (27,0)
Median (Q1; Q3)	16,7 (0,0; 50,0)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	152	156
Mittelwert (SD)	23,6 (27,4)	26,5 (26,7)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	147	142
Mittelwert (SD)	24,3 (27,5)	27,8 (27,1)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 13		
N ^c	130	116
Mittelwert (SD)	20,0 (23,3)	27,7 (26,6)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 41,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	92
Mittelwert (SD)	23,4 (27,5)	28,3 (27,8)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 21		
N ^c	106	78
Mittelwert (SD)	22,8 (26,2)	25,9 (28,8)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 25		
N ^c	96	72
Mittelwert (SD)	17,9 (22,5)	25,0 (25,3)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	92	59
Mittelwert (SD)	17,8 (23,7)	22,6 (24,3)

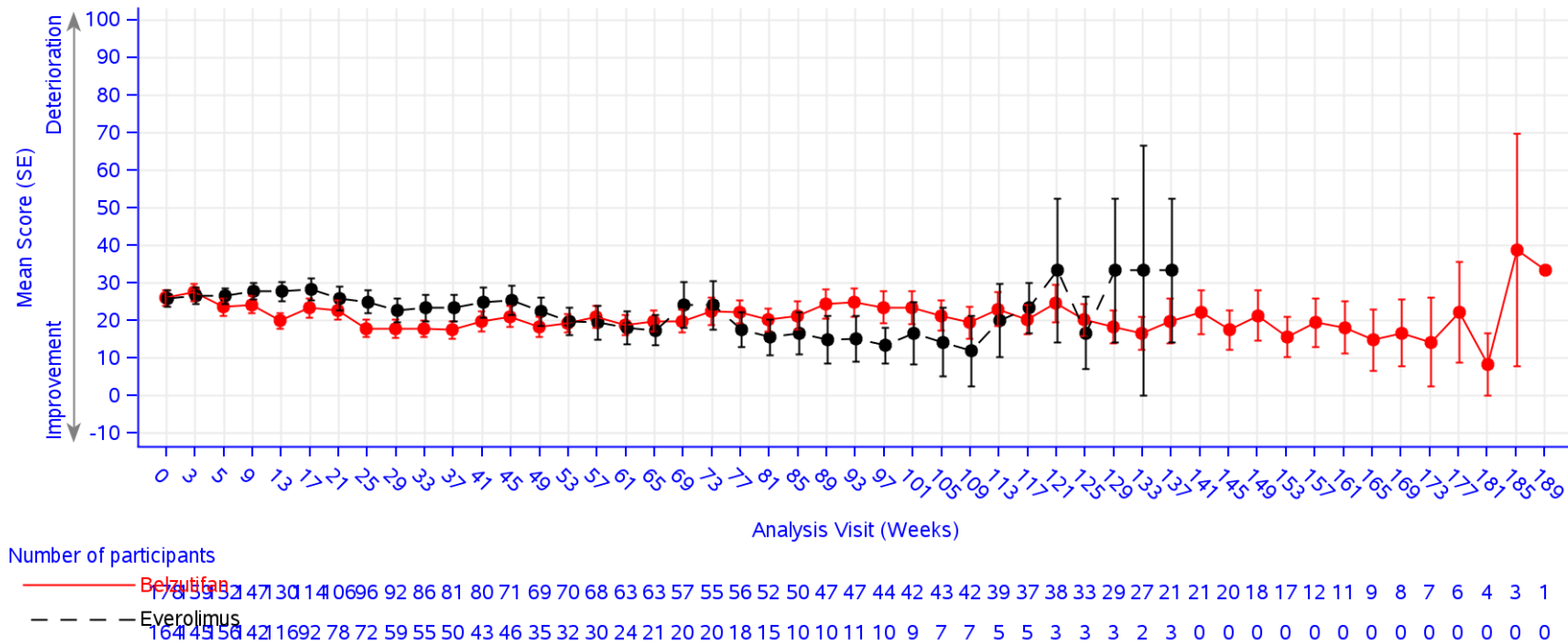
EORTC QLQ-C30 Schmerzen	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 33		
N ^c	86	55
Mittelwert (SD)	17,8 (20,1)	23,3 (26,2)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 37		
N ^c	81	50
Mittelwert (SD)	17,5 (20,9)	23,3 (24,5)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 41		
N ^c	80	43
Mittelwert (SD)	19,8 (23,4)	24,8 (26,8)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 45		
N ^c	71	46
Mittelwert (SD)	21,1 (23,7)	25,4 (26,5)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 49		
N ^c	69	35
Mittelwert (SD)	18,4 (22,0)	22,4 (22,8)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 83,3
Woche 53		
N ^c	70	32
Mittelwert (SD)	19,3 (21,0)	19,8 (21,4)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 83,3
Woche 57		
N ^c	68	30
Mittelwert (SD)	21,1 (24,4)	19,4 (24,8)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 61		
N ^c	63	24
Mittelwert (SD)	18,8 (21,3)	18,1 (21,9)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 83,3	0,0; 83,3
Woche 65		
N ^c	63	21
Mittelwert (SD)	19,8 (22,6)	17,5 (18,6)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)

EORTC QLQ-C30 Schmerzen	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Min, Max	0,0; 83,3	0,0; 66,7
Woche 69		
N ^c	57	20
Mittelwert (SD)	19,9 (23,0)	24,2 (27,3)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 41,7)
Min, Max	0,0; 83,3	0,0; 83,3
Woche 73		
N ^c	55	20
Mittelwert (SD)	22,4 (26,9)	24,2 (28,9)
Median (Q1; Q3)	16,7 (0,0; 33,3)	25,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 77		
N ^c	56	18
Mittelwert (SD)	22,3 (22,8)	17,6 (19,4)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 83,3	0,0; 66,7
Woche 81		
N ^c	52	15
Mittelwert (SD)	20,2 (22,2)	15,6 (18,3)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 16,7)
Min, Max	0,0; 83,3	0,0; 66,7
Woche 85		
N ^c	50	10
Mittelwert (SD)	21,3 (26,3)	16,7 (17,6)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 50,0
Woche 89		
N ^c	47	10
Mittelwert (SD)	24,5 (26,7)	15,0 (20,0)
Median (Q1; Q3)	16,7 (0,0; 50,0)	8,3 (0,0; 16,7)
Min, Max	0,0; 83,3	0,0; 50,0
Woche 93		
N ^c	47	11
Mittelwert (SD)	24,8 (26,4)	15,2 (20,4)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 97		
N ^c	44	10
Mittelwert (SD)	23,5 (28,1)	13,3 (15,3)
Median (Q1; Q3)	16,7 (0,0; 33,3)	8,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 101		
N ^c	42	9
Mittelwert (SD)	23,4 (28,5)	16,7 (25,0)
Median (Q1; Q3)	16,7 (0,0; 33,3)	0,0 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 66,7

EORTC QLQ-C30 Schmerzen	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Woche 105		
N ^c	43	7
Mittelwert (SD)	21,3 (26,1)	14,3 (24,4)
Median (Q1; Q3)	16,7 (0,0; 33,3)	0,0 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 109		
N ^c	42	7
Mittelwert (SD)	19,4 (28,3)	11,9 (24,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 113		
N ^c	39	5
Mittelwert (SD)	23,1 (28,3)	20,0 (21,7)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 50,0
Woche 117		
N ^c	37	5
Mittelwert (SD)	20,3 (24,3)	23,3 (14,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (16,7; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 121		
N ^c	38	3
Mittelwert (SD)	24,6 (30,4)	33,3 (33,3)
Median (Q1; Q3)	8,3 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 125		
N ^c	33	3
Mittelwert (SD)	20,2 (24,6)	16,7 (16,7)
Median (Q1; Q3)	16,7 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 83,3	0,0; 33,3
Woche 129		
N ^c	29	3
Mittelwert (SD)	18,4 (23,7)	33,3 (33,3)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 83,3	0,0; 66,7
Woche 133		
N ^c	27	2
Mittelwert (SD)	16,7 (22,6)	33,3 (47,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 83,3	0,0; 66,7
Woche 137		
N ^c	21	3
Mittelwert (SD)	19,8 (27,2)	33,3 (33,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 141		

EORTC QLQ-C30 Schmerzen	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
N ^c	21	0
Mittelwert (SD)	22,2 (26,5)	- (-)
Median (Q1; Q3)	16,7 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 83,3	-; -
Woche 145		
N ^c	20	0
Mittelwert (SD)	17,5 (23,2)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 149		
N ^c	18	0
Mittelwert (SD)	21,3 (28,5)	- (-)
Median (Q1; Q3)	8,3 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 153		
N ^c	17	0
Mittelwert (SD)	15,7 (22,4)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 157		
N ^c	12	0
Mittelwert (SD)	19,4 (22,3)	- (-)
Median (Q1; Q3)	16,7 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 161		
N ^c	11	0
Mittelwert (SD)	18,2 (22,9)	- (-)
Median (Q1; Q3)	0,0 (0,0; 50,0)	- (-; -)
Min, Max	0,0; 50,0	-; -
Woche 165		
N ^c	9	0
Mittelwert (SD)	14,8 (24,2)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 169		
N ^c	8	0
Mittelwert (SD)	16,7 (25,2)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 173		
N ^c	7	0
Mittelwert (SD)	14,3 (31,1)	- (-)
Median (Q1; Q3)	0,0 (0,0; 16,7)	- (-; -)
Min, Max	0,0; 83,3	-; -
Woche 177		
N ^c	6	0
Mittelwert (SD)	22,2 (32,8)	- (-)

EORTC QLQ-C30 Schmerzen	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	8,3 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 83,3	-; -
Woche 181		
N ^c	4	0
Mittelwert (SD)	8,3 (16,7)	- (-)
Median (Q1; Q3)	0,0 (0,0; 16,7)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 185		
N ^c	3	0
Mittelwert (SD)	38,9 (53,6)	- (-)
Median (Q1; Q3)	16,7 (0,0; 100,0)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 189		
N ^c	1	0
Mittelwert (SD)	33,3 (-)	- (-)
Median (Q1; Q3)	33,3 (33,3; 33,3)	- (-; -)
Min, Max	33,3; 33,3	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Items; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		



Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
 EORTC QLQ-C30 Pain

Abbildung 4G-3 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Schmerzen zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Symptomskala Dyspnoe

Tabelle 4G-9: Auswertung über den Studienverlauf der Symptomskala Dyspnoe des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Dyspnoe	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	178	164
Mittelwert (SD)	20,6 (24,6)	20,1 (25,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	159	145
Mittelwert (SD)	21,2 (25,8)	18,2 (24,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	152	156
Mittelwert (SD)	18,6 (23,3)	20,7 (27,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	147	142
Mittelwert (SD)	20,4 (25,1)	24,6 (26,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 13		
N ^c	130	116
Mittelwert (SD)	19,0 (21,5)	23,9 (25,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	92
Mittelwert (SD)	19,0 (22,6)	22,1 (23,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 21		
N ^c	106	78
Mittelwert (SD)	22,3 (25,1)	18,8 (25,0)
Median (Q1; Q3)	33,3 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 25		
N ^c	96	72
Mittelwert (SD)	19,4 (23,5)	17,1 (23,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	92	59
Mittelwert (SD)	14,9 (20,0)	14,1 (18,8)

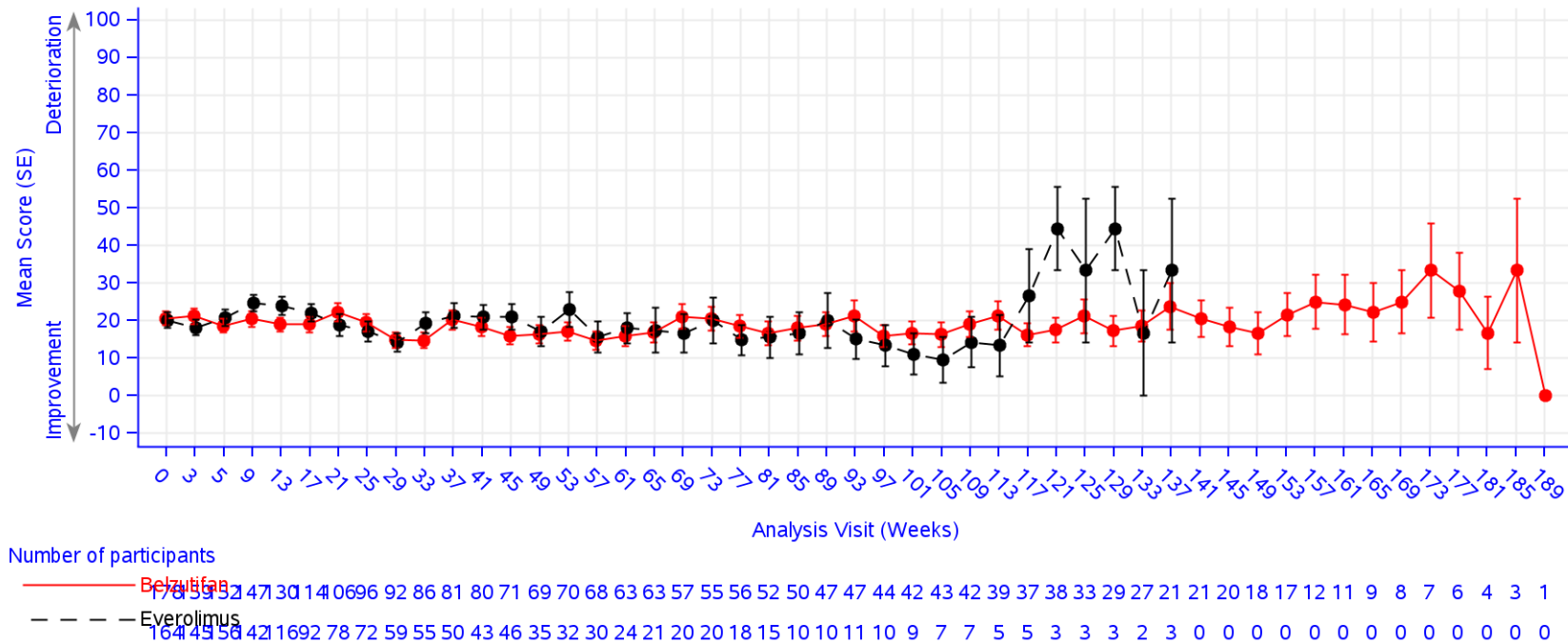
EORTC QLQ-C30 Dyspnoe	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 33		
N ^c	86	55
Mittelwert (SD)	14,7 (18,9)	19,4 (21,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 37		
N ^c	81	50
Mittelwert (SD)	20,2 (22,8)	21,3 (23,1)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 41		
N ^c	80	43
Mittelwert (SD)	18,3 (21,1)	20,9 (21,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 45		
N ^c	71	46
Mittelwert (SD)	16,0 (19,4)	21,0 (23,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 49		
N ^c	69	35
Mittelwert (SD)	16,4 (20,3)	17,1 (23,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 53		
N ^c	70	32
Mittelwert (SD)	17,1 (21,0)	22,9 (26,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 57		
N ^c	68	30
Mittelwert (SD)	14,7 (19,4)	15,6 (22,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 61		
N ^c	63	24
Mittelwert (SD)	15,9 (20,6)	18,1 (19,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 65		
N ^c	63	21
Mittelwert (SD)	16,9 (21,5)	17,5 (27,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)

EORTC QLQ-C30 Dyspnoe	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Min, Max	0,0; 66,7	0,0; 100,0
Woche 69		
N ^c	57	20
Mittelwert (SD)	21,1 (24,9)	16,7 (22,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 73		
N ^c	55	20
Mittelwert (SD)	20,6 (23,6)	20,0 (27,4)
Median (Q1; Q3)	33,3 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 77		
N ^c	56	18
Mittelwert (SD)	18,5 (21,9)	14,8 (17,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 81		
N ^c	52	15
Mittelwert (SD)	16,7 (23,3)	15,6 (21,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 85		
N ^c	50	10
Mittelwert (SD)	18,0 (23,5)	16,7 (17,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 89		
N ^c	47	10
Mittelwert (SD)	19,1 (21,7)	20,0 (23,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 93		
N ^c	47	11
Mittelwert (SD)	21,3 (29,0)	15,2 (17,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 97		
N ^c	44	10
Mittelwert (SD)	15,9 (19,7)	13,3 (17,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 101		
N ^c	42	9
Mittelwert (SD)	16,7 (19,8)	11,1 (16,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3

EORTC QLQ-C30 Dyspnoe	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Woche 105		
N ^c	43	7
Mittelwert (SD)	16,3 (21,0)	9,5 (16,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 109		
N ^c	42	7
Mittelwert (SD)	19,0 (22,3)	14,3 (17,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 113		
N ^c	39	5
Mittelwert (SD)	21,4 (23,6)	13,3 (18,3)
Median (Q1; Q3)	33,3 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 117		
N ^c	37	5
Mittelwert (SD)	16,2 (18,6)	26,7 (27,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 121		
N ^c	38	3
Mittelwert (SD)	17,5 (20,1)	44,4 (19,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (33,3; 66,7)
Min, Max	0,0; 66,7	33,3; 66,7
Woche 125		
N ^c	33	3
Mittelwert (SD)	21,2 (26,1)	33,3 (33,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 129		
N ^c	29	3
Mittelwert (SD)	17,2 (21,1)	44,4 (19,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (33,3; 66,7)
Min, Max	0,0; 66,7	33,3; 66,7
Woche 133		
N ^c	27	2
Mittelwert (SD)	18,5 (21,4)	16,7 (23,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 137		
N ^c	21	3
Mittelwert (SD)	23,8 (28,2)	33,3 (33,3)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 141		

EORTC QLQ-C30 Dyspnoe	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
N ^c	21	0
Mittelwert (SD)	20,6 (22,3)	- (-)
Median (Q1; Q3)	33,3 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 145		
N ^c	20	0
Mittelwert (SD)	18,3 (22,9)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 149		
N ^c	18	0
Mittelwert (SD)	16,7 (23,6)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 153		
N ^c	17	0
Mittelwert (SD)	21,6 (23,4)	- (-)
Median (Q1; Q3)	33,3 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 157		
N ^c	12	0
Mittelwert (SD)	25,0 (25,1)	- (-)
Median (Q1; Q3)	33,3 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 161		
N ^c	11	0
Mittelwert (SD)	24,2 (26,2)	- (-)
Median (Q1; Q3)	33,3 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 165		
N ^c	9	0
Mittelwert (SD)	22,2 (23,6)	- (-)
Median (Q1; Q3)	33,3 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 169		
N ^c	8	0
Mittelwert (SD)	25,0 (23,6)	- (-)
Median (Q1; Q3)	33,3 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 173		
N ^c	7	0
Mittelwert (SD)	33,3 (33,3)	- (-)
Median (Q1; Q3)	33,3 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 177		
N ^c	6	0
Mittelwert (SD)	27,8 (25,1)	- (-)

EORTC QLQ-C30 Dyspnoe	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	33,3 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 181		
N ^c	4	0
Mittelwert (SD)	16,7 (19,2)	- (-)
Median (Q1; Q3)	16,7 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 185		
N ^c	3	0
Mittelwert (SD)	33,3 (33,3)	- (-)
Median (Q1; Q3)	33,3 (0,0; 66,7)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 189		
N ^c	1	0
Mittelwert (SD)	0,0 (-)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 0,0	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Items; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		



Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
EORTC QLQ-C30 Dyspnea

Abbildung 4G-4 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Dyspnoe zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Symptomskala Schlaflosigkeit

Tabelle 4G-10: Auswertung über den Studienverlauf der Symptomskala Schlaflosigkeit des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Schlaflosigkeit	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	178	164
Mittelwert (SD)	26,2 (28,3)	24,2 (27,7)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	159	145
Mittelwert (SD)	23,5 (26,9)	21,1 (25,4)
Median (Q1; Q3)	33,3 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	152	156
Mittelwert (SD)	17,5 (24,2)	23,7 (26,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	147	142
Mittelwert (SD)	21,8 (27,2)	27,7 (29,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 13		
N ^c	130	116
Mittelwert (SD)	20,5 (23,6)	27,0 (28,8)
Median (Q1; Q3)	16,7 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	92
Mittelwert (SD)	20,5 (25,3)	25,7 (28,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 21		
N ^c	106	78
Mittelwert (SD)	18,2 (25,3)	27,4 (30,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 25		
N ^c	96	72
Mittelwert (SD)	14,9 (22,6)	22,7 (26,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	92	59
Mittelwert (SD)	16,3 (23,4)	24,9 (28,1)

EORTC QLQ-C30 Schlaflosigkeit	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 33		
N ^c	86	55
Mittelwert (SD)	14,0 (22,0)	23,0 (24,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 37		
N ^c	81	50
Mittelwert (SD)	14,8 (20,4)	24,7 (26,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 41		
N ^c	80	43
Mittelwert (SD)	17,5 (26,0)	26,4 (24,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 45		
N ^c	71	46
Mittelwert (SD)	16,9 (25,1)	26,8 (27,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 49		
N ^c	69	35
Mittelwert (SD)	18,4 (24,6)	23,8 (27,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 53		
N ^c	70	32
Mittelwert (SD)	17,1 (23,2)	22,9 (24,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 57		
N ^c	68	30
Mittelwert (SD)	20,6 (27,6)	23,3 (23,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 61		
N ^c	63	24
Mittelwert (SD)	15,9 (23,1)	22,2 (25,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 65		
N ^c	63	21
Mittelwert (SD)	21,2 (23,4)	23,8 (23,9)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 33,3)

EORTC QLQ-C30 Schlaflosigkeit	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Min, Max	0,0; 66,7	0,0; 66,7
Woche 69		
N ^c	57	20
Mittelwert (SD)	22,8 (26,1)	26,7 (27,8)
Median (Q1; Q3)	33,3 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 73		
N ^c	55	20
Mittelwert (SD)	20,6 (24,4)	31,7 (29,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 50,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 77		
N ^c	56	18
Mittelwert (SD)	21,4 (27,3)	20,4 (23,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 81		
N ^c	52	15
Mittelwert (SD)	19,2 (25,9)	24,4 (23,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 85		
N ^c	50	10
Mittelwert (SD)	19,3 (25,3)	26,7 (26,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 89		
N ^c	47	10
Mittelwert (SD)	22,0 (28,9)	30,0 (36,7)
Median (Q1; Q3)	0,0 (0,0; 33,3)	16,7 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 93		
N ^c	47	11
Mittelwert (SD)	19,9 (25,7)	15,2 (17,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 97		
N ^c	44	10
Mittelwert (SD)	16,7 (22,2)	13,3 (23,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 101		
N ^c	42	9
Mittelwert (SD)	17,5 (25,8)	18,5 (24,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7

EORTC QLQ-C30 Schlaflosigkeit	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Woche 105		
N ^c	43	7
Mittelwert (SD)	20,2 (27,4)	14,3 (26,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 109		
N ^c	42	7
Mittelwert (SD)	21,4 (28,3)	14,3 (26,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 113		
N ^c	39	5
Mittelwert (SD)	21,4 (28,1)	26,7 (27,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 117		
N ^c	37	5
Mittelwert (SD)	20,7 (29,8)	33,3 (23,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (33,3; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 121		
N ^c	38	3
Mittelwert (SD)	20,2 (27,4)	44,4 (19,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (33,3; 66,7)
Min, Max	0,0; 100,0	33,3; 66,7
Woche 125		
N ^c	33	3
Mittelwert (SD)	19,2 (26,4)	11,1 (19,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 129		
N ^c	29	3
Mittelwert (SD)	18,4 (26,1)	22,2 (19,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 133		
N ^c	27	2
Mittelwert (SD)	18,5 (29,7)	16,7 (23,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	16,7 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 137		
N ^c	21	3
Mittelwert (SD)	17,5 (27,1)	22,2 (19,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 141		

EORTC QLQ-C30 Schlaflosigkeit	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
N ^c	21	0
Mittelwert (SD)	19,0 (27,0)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 145		
N ^c	20	0
Mittelwert (SD)	15,0 (22,9)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 149		
N ^c	18	0
Mittelwert (SD)	16,7 (28,6)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 153		
N ^c	17	0
Mittelwert (SD)	15,7 (23,9)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 157		
N ^c	12	0
Mittelwert (SD)	19,4 (33,2)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 161		
N ^c	11	0
Mittelwert (SD)	15,2 (22,9)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 165		
N ^c	9	0
Mittelwert (SD)	11,1 (23,6)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 169		
N ^c	8	0
Mittelwert (SD)	12,5 (24,8)	- (-)
Median (Q1; Q3)	0,0 (0,0; 16,7)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 173		
N ^c	7	0
Mittelwert (SD)	14,3 (26,2)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 177		
N ^c	6	0
Mittelwert (SD)	16,7 (27,9)	- (-)

EORTC QLQ-C30 Schlaflosigkeit	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 181		
N ^c	4	0
Mittelwert (SD)	8,3 (16,7)	- (-)
Median (Q1; Q3)	0,0 (0,0; 16,7)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 185		
N ^c	3	0
Mittelwert (SD)	44,4 (50,9)	- (-)
Median (Q1; Q3)	33,3 (0,0; 100,0)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 189		
N ^c	1	0
Mittelwert (SD)	33,3 (-)	- (-)
Median (Q1; Q3)	33,3 (33,3; 33,3)	- (-; -)
Min, Max	33,3; 33,3	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Items; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		

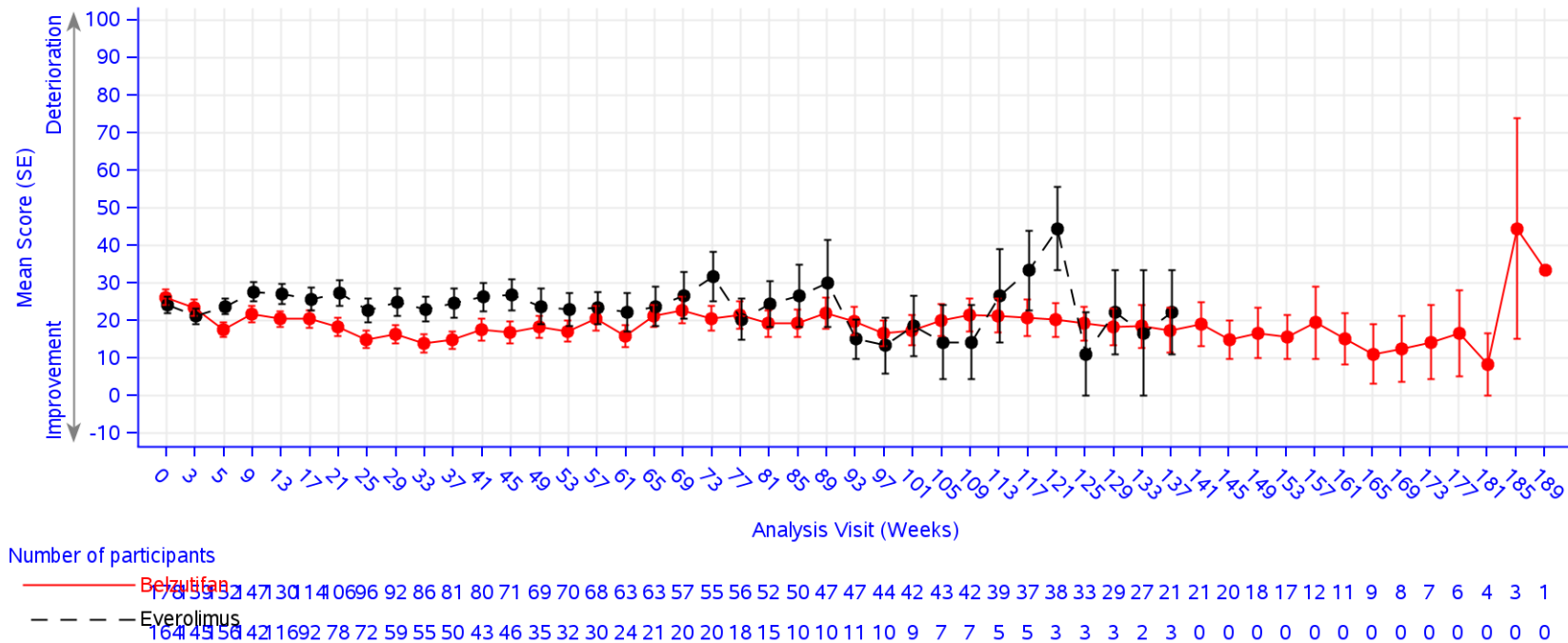


Abbildung 4G-5 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Schlaflosigkeit zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Symptomskala Appetitverlust

Tabelle 4G-11: Auswertung über den Studienverlauf der Symptomskala Appetitverlust des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Appetitverlust	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	178	164
Mittelwert (SD)	17,4 (26,8)	17,7 (27,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	159	145
Mittelwert (SD)	16,1 (25,9)	16,6 (24,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	152	156
Mittelwert (SD)	12,1 (23,2)	19,9 (27,2)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	147	142
Mittelwert (SD)	11,6 (23,0)	23,2 (26,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	33,3 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 13		
N ^c	130	116
Mittelwert (SD)	8,7 (20,1)	14,9 (23,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	92
Mittelwert (SD)	11,1 (22,5)	15,2 (19,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 21		
N ^c	106	78
Mittelwert (SD)	11,3 (23,9)	15,4 (26,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 25		
N ^c	96	72
Mittelwert (SD)	9,4 (21,5)	12,0 (20,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	92	59
Mittelwert (SD)	5,1 (14,8)	11,9 (23,8)

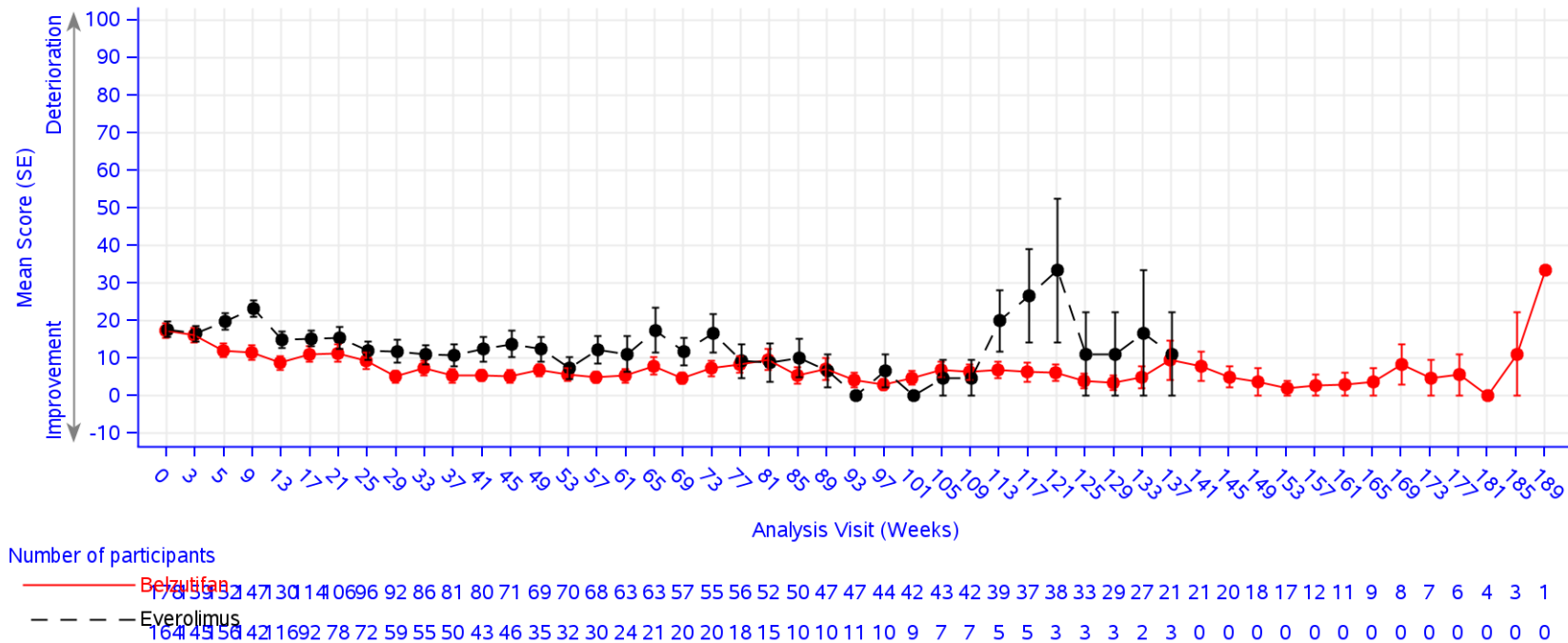
EORTC QLQ-C30 Appetitverlust	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 33		
N ^c	86	55
Mittelwert (SD)	7,4 (17,3)	10,9 (19,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 37		
N ^c	81	50
Mittelwert (SD)	5,3 (16,2)	10,7 (20,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 41		
N ^c	80	43
Mittelwert (SD)	5,4 (13,5)	12,4 (21,8)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 45		
N ^c	71	46
Mittelwert (SD)	5,2 (13,4)	13,8 (23,9)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 49		
N ^c	69	35
Mittelwert (SD)	6,8 (13,5)	12,4 (19,9)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 33,3	0,0; 66,7
Woche 53		
N ^c	70	32
Mittelwert (SD)	5,7 (13,9)	7,3 (16,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 57		
N ^c	68	30
Mittelwert (SD)	4,9 (11,9)	12,2 (20,5)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 33,3	0,0; 66,7
Woche 61		
N ^c	63	24
Mittelwert (SD)	5,3 (14,9)	11,1 (23,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 16,7)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 65		
N ^c	63	21
Mittelwert (SD)	7,9 (18,7)	17,5 (27,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)

EORTC QLQ-C30 Appetitverlust	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Min, Max	0,0; 100,0	0,0; 100,0
Woche 69		
N ^c	57	20
Mittelwert (SD)	4,7 (11,7)	11,7 (16,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 33,3	0,0; 33,3
Woche 73		
N ^c	55	20
Mittelwert (SD)	7,3 (15,3)	16,7 (22,9)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 77		
N ^c	56	18
Mittelwert (SD)	8,3 (15,9)	9,3 (19,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 81		
N ^c	52	15
Mittelwert (SD)	9,6 (20,2)	8,9 (19,8)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 85		
N ^c	50	10
Mittelwert (SD)	5,3 (15,6)	10,0 (16,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 89		
N ^c	47	10
Mittelwert (SD)	7,1 (19,6)	6,7 (14,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 93		
N ^c	47	11
Mittelwert (SD)	4,3 (13,2)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 0,0
Woche 97		
N ^c	44	10
Mittelwert (SD)	3,0 (9,7)	6,7 (14,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 33,3
Woche 101		
N ^c	42	9
Mittelwert (SD)	4,8 (11,8)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 0,0

EORTC QLQ-C30 Appetitverlust	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Woche 105		
N ^c	43	7
Mittelwert (SD)	7,0 (13,7)	4,8 (12,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 33,3
Woche 109		
N ^c	42	7
Mittelwert (SD)	6,3 (13,2)	4,8 (12,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 33,3	0,0; 33,3
Woche 113		
N ^c	39	5
Mittelwert (SD)	6,8 (13,6)	20,0 (18,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	33,3 (0,0; 33,3)
Min, Max	0,0; 33,3	0,0; 33,3
Woche 117		
N ^c	37	5
Mittelwert (SD)	6,3 (15,4)	26,7 (27,9)
Median (Q1; Q3)	0,0 (0,0; 0,0)	33,3 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 121		
N ^c	38	3
Mittelwert (SD)	6,1 (13,1)	33,3 (33,3)
Median (Q1; Q3)	0,0 (0,0; 0,0)	33,3 (0,0; 66,7)
Min, Max	0,0; 33,3	0,0; 66,7
Woche 125		
N ^c	33	3
Mittelwert (SD)	4,0 (11,0)	11,1 (19,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 33,3	0,0; 33,3
Woche 129		
N ^c	29	3
Mittelwert (SD)	3,4 (10,3)	11,1 (19,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 33,3	0,0; 33,3
Woche 133		
N ^c	27	2
Mittelwert (SD)	4,9 (15,2)	16,7 (23,6)
Median (Q1; Q3)	0,0 (0,0; 0,0)	16,7 (0,0; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 137		
N ^c	21	3
Mittelwert (SD)	9,5 (23,9)	11,1 (19,2)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 141		

EORTC QLQ-C30 Appetitverlust	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
N ^c	21	0
Mittelwert (SD)	7,9 (18,0)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 145		
N ^c	20	0
Mittelwert (SD)	5,0 (12,2)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 149		
N ^c	18	0
Mittelwert (SD)	3,7 (15,7)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 153		
N ^c	17	0
Mittelwert (SD)	2,0 (8,1)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 157		
N ^c	12	0
Mittelwert (SD)	2,8 (9,6)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 161		
N ^c	11	0
Mittelwert (SD)	3,0 (10,1)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 165		
N ^c	9	0
Mittelwert (SD)	3,7 (11,1)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 169		
N ^c	8	0
Mittelwert (SD)	8,3 (15,4)	- (-)
Median (Q1; Q3)	0,0 (0,0; 16,7)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 173		
N ^c	7	0
Mittelwert (SD)	4,8 (12,6)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 177		
N ^c	6	0
Mittelwert (SD)	5,6 (13,6)	- (-)

EORTC QLQ-C30 Appetitverlust	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 181		
N ^c	4	0
Mittelwert (SD)	0,0 (0,0)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 0,0	-; -
Woche 185		
N ^c	3	0
Mittelwert (SD)	11,1 (19,2)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 189		
N ^c	1	0
Mittelwert (SD)	33,3 (-)	- (-)
Median (Q1; Q3)	33,3 (33,3; 33,3)	- (-; -)
Min, Max	33,3; 33,3	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Items; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		



Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
EORTC QLQ-C30 Appetite Loss

Abbildung 4G-6 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Appetitverlust zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Symptomskala Verstopfung

Tabelle 4G-12: Auswertung über den Studienverlauf der Symptomskala Verstopfung des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Verstopfung	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	178	164
Mittelwert (SD)	14,2 (23,4)	16,5 (24,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	159	145
Mittelwert (SD)	14,7 (24,8)	11,7 (23,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	152	156
Mittelwert (SD)	12,1 (21,5)	12,6 (23,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	147	142
Mittelwert (SD)	12,9 (24,2)	12,4 (24,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 13		
N ^c	130	116
Mittelwert (SD)	13,6 (22,6)	10,6 (21,4)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	92
Mittelwert (SD)	14,9 (23,1)	10,5 (20,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 16,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 21		
N ^c	106	78
Mittelwert (SD)	14,2 (22,5)	9,0 (19,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 25		
N ^c	96	72
Mittelwert (SD)	10,8 (20,2)	6,9 (15,8)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 29		
N ^c	92	59
Mittelwert (SD)	12,0 (21,9)	4,5 (13,1)

EORTC QLQ-C30 Verstopfung	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 33		
N ^c	86	55
Mittelwert (SD)	10,5 (20,0)	6,1 (17,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 37		
N ^c	81	50
Mittelwert (SD)	14,0 (23,5)	10,0 (21,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 41		
N ^c	80	43
Mittelwert (SD)	13,3 (22,9)	7,0 (17,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 45		
N ^c	71	46
Mittelwert (SD)	13,6 (23,6)	8,0 (16,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 49		
N ^c	69	35
Mittelwert (SD)	10,6 (23,9)	8,6 (18,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 53		
N ^c	70	32
Mittelwert (SD)	8,6 (17,7)	7,3 (16,4)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 57		
N ^c	68	30
Mittelwert (SD)	14,2 (21,0)	12,2 (27,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 61		
N ^c	63	24
Mittelwert (SD)	9,5 (17,4)	4,2 (11,3)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 65		
N ^c	63	21
Mittelwert (SD)	9,5 (20,2)	6,3 (20,1)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 0,0)

EORTC QLQ-C30 Verstopfung	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Min, Max	0,0; 100,0	0,0; 66,7
Woche 69		
N ^c	57	20
Mittelwert (SD)	11,7 (24,0)	10,0 (15,7)
Median (Q1; Q3)	0,0 (0,0; 0,0)	0,0 (0,0; 33,3)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 73		
N ^c	55	20
Mittelwert (SD)	12,7 (20,8)	8,3 (23,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 77		
N ^c	56	18
Mittelwert (SD)	15,5 (25,4)	1,9 (7,9)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 81		
N ^c	52	15
Mittelwert (SD)	12,2 (18,7)	2,2 (8,6)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 85		
N ^c	50	10
Mittelwert (SD)	14,0 (21,4)	3,3 (10,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 89		
N ^c	47	10
Mittelwert (SD)	13,5 (22,7)	3,3 (10,5)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 93		
N ^c	47	11
Mittelwert (SD)	12,1 (18,9)	3,0 (10,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 97		
N ^c	44	10
Mittelwert (SD)	14,4 (20,8)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 0,0
Woche 101		
N ^c	42	9
Mittelwert (SD)	15,1 (24,6)	3,7 (11,1)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 33,3

EORTC QLQ-C30 Verstopfung	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Woche 105		
N ^c	43	7
Mittelwert (SD)	15,5 (23,4)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 0,0
Woche 109		
N ^c	42	7
Mittelwert (SD)	13,5 (20,9)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 0,0
Woche 113		
N ^c	39	5
Mittelwert (SD)	11,1 (17,7)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 0,0
Woche 117		
N ^c	37	5
Mittelwert (SD)	9,9 (17,3)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 0,0
Woche 121		
N ^c	38	3
Mittelwert (SD)	15,8 (27,7)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 0,0
Woche 125		
N ^c	33	3
Mittelwert (SD)	12,1 (21,8)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 0,0
Woche 129		
N ^c	29	3
Mittelwert (SD)	14,9 (22,9)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 0,0
Woche 133		
N ^c	27	2
Mittelwert (SD)	13,6 (23,1)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 100,0	0,0; 0,0
Woche 137		
N ^c	21	3
Mittelwert (SD)	15,9 (22,7)	0,0 (0,0)
Median (Q1; Q3)	0,0 (0,0; 33,3)	0,0 (0,0; 0,0)
Min, Max	0,0; 66,7	0,0; 0,0
Woche 141		

EORTC QLQ-C30 Verstopfung	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
N ^c	21	0
Mittelwert (SD)	12,7 (19,7)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 145		
N ^c	20	0
Mittelwert (SD)	11,7 (19,6)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 149		
N ^c	18	0
Mittelwert (SD)	9,3 (15,4)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 153		
N ^c	17	0
Mittelwert (SD)	9,8 (19,6)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 157		
N ^c	12	0
Mittelwert (SD)	8,3 (15,1)	- (-)
Median (Q1; Q3)	0,0 (0,0; 16,7)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 161		
N ^c	11	0
Mittelwert (SD)	12,1 (22,5)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 66,7	-; -
Woche 165		
N ^c	9	0
Mittelwert (SD)	7,4 (14,7)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 169		
N ^c	8	0
Mittelwert (SD)	0,0 (0,0)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 0,0	-; -
Woche 173		
N ^c	7	0
Mittelwert (SD)	4,8 (12,6)	- (-)
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 177		
N ^c	6	0
Mittelwert (SD)	0,0 (0,0)	- (-)

EORTC QLQ-C30 Verstopfung	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	0,0 (0,0; 0,0)	- (-; -)
Min, Max	0,0; 0,0	-; -
Woche 181		
N ^c	4	0
Mittelwert (SD)	8,3 (16,7)	- (-)
Median (Q1; Q3)	0,0 (0,0; 16,7)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 185		
N ^c	3	0
Mittelwert (SD)	11,1 (19,2)	- (-)
Median (Q1; Q3)	0,0 (0,0; 33,3)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 189		
N ^c	1	0
Mittelwert (SD)	33,3 (-)	- (-)
Median (Q1; Q3)	33,3 (33,3; 33,3)	- (-; -)
Min, Max	33,3; 33,3	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Items; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		

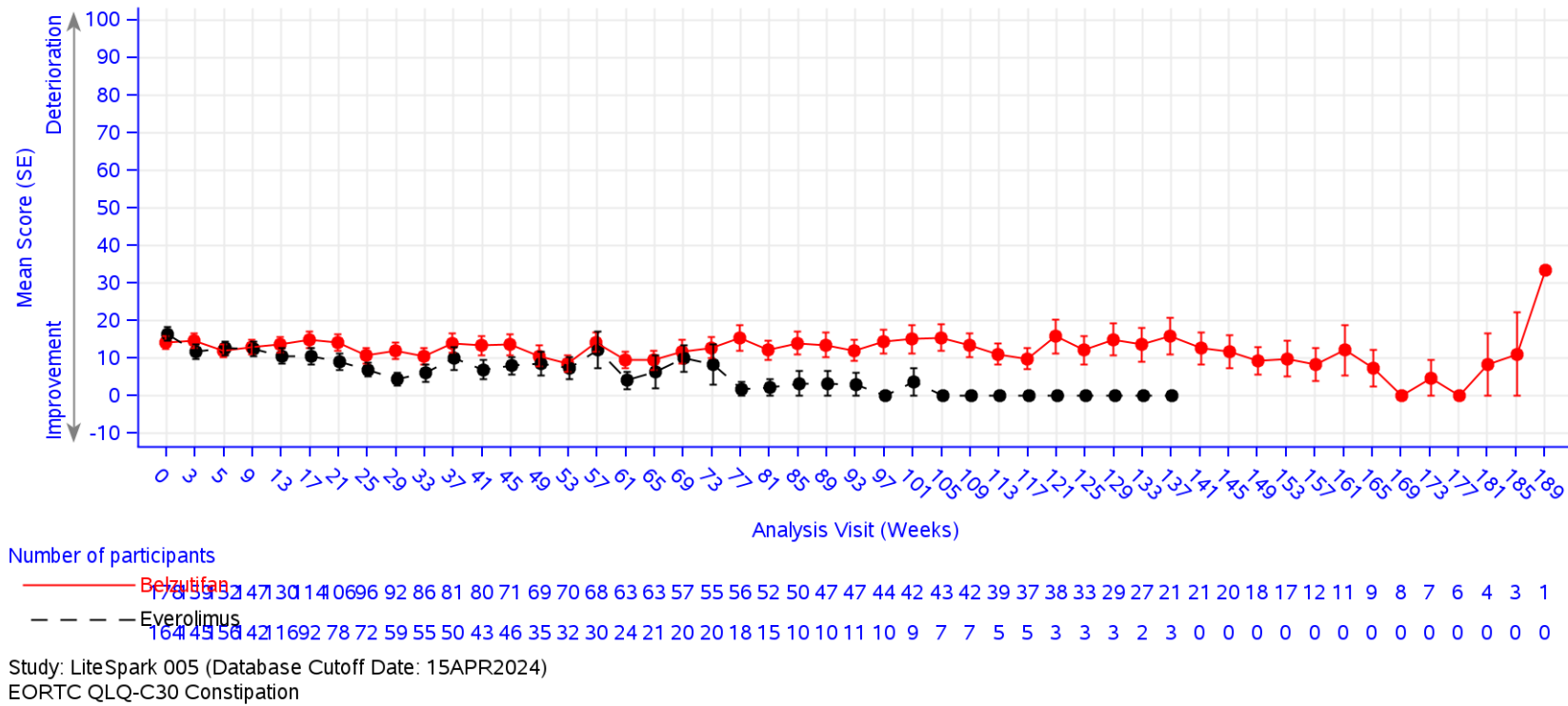


Abbildung 4G-7 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Verstopfung zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Symptomskala Diarrhö

Tabelle 4G-13: Auswertung über den Studienverlauf der Symptomskala Diarrhö des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Diarrhö	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	356	328
Mittelwert (SD)	4,7 (13,6)	5,5 (15,3)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	321	292
Mittelwert (SD)	2,8 (8,9)	6,5 (15,2)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 2,0)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 5		
N ^c	308	312
Mittelwert (SD)	2,7 (9,3)	6,4 (14,5)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 2,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 9		
N ^c	300	294
Mittelwert (SD)	3,1 (9,9)	6,2 (14,7)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 2,0)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 13		
N ^c	261	237
Mittelwert (SD)	3,3 (11,1)	5,7 (14,3)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 2,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	232	187
Mittelwert (SD)	3,6 (11,3)	4,6 (11,1)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 21		
N ^c	214	156
Mittelwert (SD)	4,5 (11,9)	6,2 (15,3)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 2,0)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 25		
N ^c	192	145
Mittelwert (SD)	3,2 (9,5)	4,8 (13,9)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 66,7	0,0; 100,0
Woche 29		
N ^c	185	118
Mittelwert (SD)	2,4 (8,2)	4,6 (12,3)

EORTC QLQ-C30 Diarrhö	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 33		
N ^c	175	113
Mittelwert (SD)	2,9 (9,0)	4,8 (10,8)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 37		
N ^c	166	102
Mittelwert (SD)	2,8 (10,4)	5,6 (11,6)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 2,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 41		
N ^c	163	88
Mittelwert (SD)	3,9 (10,4)	3,3 (8,9)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 45		
N ^c	142	95
Mittelwert (SD)	3,9 (12,6)	4,5 (10,5)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 49		
N ^c	139	70
Mittelwert (SD)	3,0 (11,7)	3,9 (9,9)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 53		
N ^c	140	66
Mittelwert (SD)	3,4 (9,2)	5,2 (11,3)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 2,0)
Min, Max	0,0; 33,3	0,0; 33,3
Woche 57		
N ^c	136	60
Mittelwert (SD)	2,8 (8,2)	2,8 (8,3)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 33,3	0,0; 33,3
Woche 61		
N ^c	127	49
Mittelwert (SD)	3,7 (10,5)	5,4 (13,4)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 65		
N ^c	128	42
Mittelwert (SD)	4,0 (10,8)	3,0 (8,6)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)

EORTC QLQ-C30 Diarrhö	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Min, Max	0,0; 66,7	0,0; 33,3
Woche 69		
N ^c	114	40
Mittelwert (SD)	2,9 (8,4)	6,5 (14,6)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 2,0)
Min, Max	0,0; 33,3	0,0; 66,7
Woche 73		
N ^c	111	41
Mittelwert (SD)	3,6 (12,2)	5,6 (11,7)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 2,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 77		
N ^c	113	37
Mittelwert (SD)	2,3 (7,4)	7,0 (15,1)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 2,0)
Min, Max	0,0; 33,3	0,0; 66,7
Woche 81		
N ^c	104	30
Mittelwert (SD)	2,5 (9,0)	7,4 (15,9)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 2,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 85		
N ^c	103	20
Mittelwert (SD)	3,8 (11,8)	5,7 (16,1)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 66,7	0,0; 66,7
Woche 89		
N ^c	94	20
Mittelwert (SD)	3,8 (10,9)	9,1 (14,4)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,5 (0,5; 17,7)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 93		
N ^c	94	22
Mittelwert (SD)	4,9 (14,7)	3,6 (9,6)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 97		
N ^c	88	20
Mittelwert (SD)	4,8 (12,0)	3,9 (10,1)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 101		
N ^c	85	18
Mittelwert (SD)	4,5 (13,8)	6,2 (12,5)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 2,0)
Min, Max	0,0; 100,0	0,0; 33,3

EORTC QLQ-C30 Diarrhö	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Woche 105		
N ^c	86	14
Mittelwert (SD)	4,9 (12,1)	3,0 (8,8)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 109		
N ^c	85	15
Mittelwert (SD)	3,7 (10,9)	2,8 (8,5)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 113		
N ^c	78	10
Mittelwert (SD)	4,9 (12,2)	7,4 (13,7)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 2,0)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 117		
N ^c	74	10
Mittelwert (SD)	3,3 (13,1)	3,9 (10,4)
Median (Q1; Q3)	1,0 (0,0; 1,0)	1,0 (0,0; 1,0)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 121		
N ^c	77	6
Mittelwert (SD)	4,5 (14,1)	11,9 (16,6)
Median (Q1; Q3)	1,0 (0,0; 1,0)	2,0 (1,0; 33,3)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 125		
N ^c	66	6
Mittelwert (SD)	3,6 (13,9)	11,9 (16,6)
Median (Q1; Q3)	1,0 (0,0; 1,0)	2,0 (1,0; 33,3)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 129		
N ^c	58	7
Mittelwert (SD)	4,1 (11,8)	10,5 (15,6)
Median (Q1; Q3)	1,0 (0,0; 1,0)	2,0 (1,0; 33,3)
Min, Max	0,0; 66,7	0,0; 33,3
Woche 133		
N ^c	55	4
Mittelwert (SD)	1,8 (6,2)	0,5 (0,6)
Median (Q1; Q3)	1,0 (0,0; 1,0)	0,5 (0,0; 1,0)
Min, Max	0,0; 33,3	0,0; 1,0
Woche 137		
N ^c	42	6
Mittelwert (SD)	5,4 (17,2)	11,9 (16,6)
Median (Q1; Q3)	1,0 (0,0; 1,0)	2,0 (1,0; 33,3)
Min, Max	0,0; 100,0	0,0; 33,3
Woche 141		

EORTC QLQ-C30 Diarrhö	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
N ^c	42	0
Mittelwert (SD)	3,0 (8,6)	- (-)
Median (Q1; Q3)	1,0 (0,0; 1,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 145		
N ^c	40	0
Mittelwert (SD)	1,4 (5,2)	- (-)
Median (Q1; Q3)	1,0 (0,0; 1,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 149		
N ^c	36	0
Mittelwert (SD)	4,3 (10,4)	- (-)
Median (Q1; Q3)	1,0 (0,0; 1,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 153		
N ^c	34	0
Mittelwert (SD)	3,5 (9,4)	- (-)
Median (Q1; Q3)	1,0 (0,0; 1,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 157		
N ^c	24	0
Mittelwert (SD)	3,4 (9,3)	- (-)
Median (Q1; Q3)	1,0 (0,0; 1,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 161		
N ^c	22	0
Mittelwert (SD)	6,7 (12,8)	- (-)
Median (Q1; Q3)	1,0 (0,0; 2,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 165		
N ^c	18	0
Mittelwert (SD)	0,5 (0,5)	- (-)
Median (Q1; Q3)	0,5 (0,0; 1,0)	- (-; -)
Min, Max	0,0; 1,0	-; -
Woche 169		
N ^c	16	0
Mittelwert (SD)	4,8 (11,2)	- (-)
Median (Q1; Q3)	1,0 (0,0; 1,5)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 173		
N ^c	14	0
Mittelwert (SD)	3,0 (8,8)	- (-)
Median (Q1; Q3)	1,0 (0,0; 1,0)	- (-; -)
Min, Max	0,0; 33,3	-; -
Woche 177		
N ^c	12	0
Mittelwert (SD)	0,5 (0,5)	- (-)

EORTC QLQ-C30 Diarrhö	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	0,5 (0,0; 1,0)	- (-; -)
Min, Max	0,0; 1,0	-; -
Woche 181		
N ^c	8	0
Mittelwert (SD)	0,5 (0,5)	- (-)
Median (Q1; Q3)	0,5 (0,0; 1,0)	- (-; -)
Min, Max	0,0; 1,0	-; -
Woche 185		
N ^c	6	0
Mittelwert (SD)	0,5 (0,5)	- (-)
Median (Q1; Q3)	0,5 (0,0; 1,0)	- (-; -)
Min, Max	0,0; 1,0	-; -
Woche 189		
N ^c	2	0
Mittelwert (SD)	0,5 (0,7)	- (-)
Median (Q1; Q3)	0,5 (0,0; 1,0)	- (-; -)
Min, Max	0,0; 1,0	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Items; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		

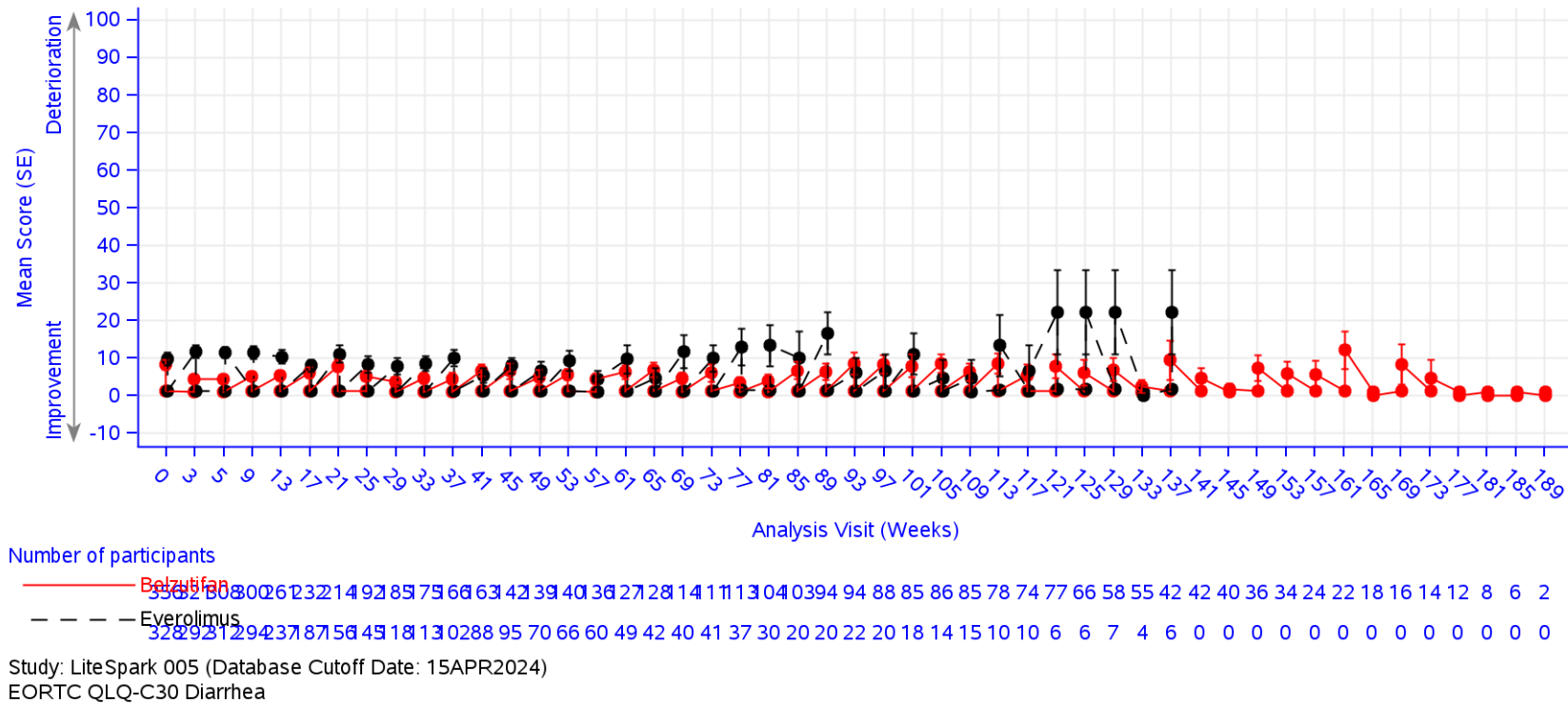


Abbildung 4G-8 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Symptomskala Diarrhö zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

FKSI-DRS: Gesamtscore

Tabelle 4G-14: Auswertung über den Studienverlauf des FKSO-DRS Gesamtscore aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

FKSI-DRS Score	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	179	165
Mittelwert (SD)	29,9 (4,8)	29,3 (4,9)
Median (Q1; Q3)	30,0 (27,0; 34,0)	30,0 (27,0; 33,0)
Min, Max	15,0; 36,0	14,0; 36,0
Woche 3		
N ^c	161	145
Mittelwert (SD)	29,8 (5,0)	29,6 (4,7)
Median (Q1; Q3)	31,0 (26,0; 34,0)	31,0 (28,0; 33,0)
Min, Max	13,0; 36,0	15,0; 36,0
Woche 5		
N ^c	154	156
Mittelwert (SD)	30,4 (4,8)	28,9 (5,3)
Median (Q1; Q3)	32,0 (27,0; 34,0)	30,0 (27,0; 33,0)
Min, Max	15,0; 36,0	11,0; 36,0
Woche 9		
N ^c	147	142
Mittelwert (SD)	30,1 (5,1)	28,2 (5,4)
Median (Q1; Q3)	31,0 (26,0; 34,0)	29,0 (24,0; 32,0)
Min, Max	13,0; 36,0	13,0; 36,0
Woche 13		
N ^c	130	117
Mittelwert (SD)	30,4 (4,6)	28,6 (5,0)
Median (Q1; Q3)	31,5 (28,0; 34,0)	30,0 (25,0; 32,0)
Min, Max	15,0; 36,0	14,0; 36,0
Woche 17		
N ^c	114	92
Mittelwert (SD)	30,8 (4,1)	28,9 (5,1)
Median (Q1; Q3)	32,0 (28,0; 34,0)	30,0 (26,0; 33,0)
Min, Max	20,0; 36,0	15,0; 36,0
Woche 21		
N ^c	106	80
Mittelwert (SD)	30,7 (4,7)	28,9 (6,2)
Median (Q1; Q3)	31,0 (28,0; 34,0)	31,0 (25,0; 33,0)
Min, Max	14,0; 36,0	6,0; 36,0
Woche 25		
N ^c	97	72
Mittelwert (SD)	31,0 (4,5)	29,9 (5,2)
Median (Q1; Q3)	32,0 (29,0; 34,0)	31,0 (26,0; 34,0)
Min, Max	13,0; 36,0	16,0; 36,0
Woche 29		
N ^c	92	59
Mittelwert (SD)	31,6 (4,3)	30,2 (5,2)

FKSI-DRS Score	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	33,0 (30,0; 35,0)	32,0 (29,0; 34,0)
Min, Max	15,0; 36,0	14,0; 36,0
Woche 33		
N ^c	86	56
Mittelwert (SD)	31,9 (3,5)	29,9 (4,5)
Median (Q1; Q3)	33,0 (30,0; 35,0)	31,0 (28,0; 33,0)
Min, Max	23,0; 36,0	16,0; 36,0
Woche 37		
N ^c	81	50
Mittelwert (SD)	31,7 (3,9)	29,6 (5,7)
Median (Q1; Q3)	32,0 (30,0; 35,0)	31,5 (28,0; 34,0)
Min, Max	18,0; 36,0	13,0; 36,0
Woche 41		
N ^c	80	44
Mittelwert (SD)	31,2 (4,1)	29,8 (4,5)
Median (Q1; Q3)	32,0 (29,0; 34,0)	30,5 (29,0; 33,0)
Min, Max	18,0; 36,0	16,0; 36,0
Woche 45		
N ^c	71	46
Mittelwert (SD)	31,7 (4,1)	29,2 (5,2)
Median (Q1; Q3)	32,0 (29,0; 35,0)	31,0 (25,0; 33,0)
Min, Max	19,0; 36,0	13,0; 36,0
Woche 49		
N ^c	69	35
Mittelwert (SD)	31,6 (3,5)	30,7 (3,8)
Median (Q1; Q3)	32,0 (30,0; 35,0)	31,0 (28,0; 34,0)
Min, Max	23,0; 36,0	22,0; 36,0
Woche 53		
N ^c	70	32
Mittelwert (SD)	31,7 (3,6)	31,1 (4,4)
Median (Q1; Q3)	32,0 (30,0; 35,0)	32,0 (29,0; 34,5)
Min, Max	23,0; 36,0	20,0; 36,0
Woche 57		
N ^c	68	30
Mittelwert (SD)	31,3 (4,2)	30,7 (4,6)
Median (Q1; Q3)	32,0 (29,5; 35,0)	31,0 (27,0; 35,0)
Min, Max	20,0; 36,0	20,0; 36,0
Woche 61		
N ^c	63	24
Mittelwert (SD)	31,9 (4,0)	31,6 (3,8)
Median (Q1; Q3)	33,0 (30,0; 35,0)	32,5 (30,0; 34,5)
Min, Max	21,0; 36,0	22,0; 36,0
Woche 65		
N ^c	63	21
Mittelwert (SD)	31,4 (3,9)	29,8 (5,7)
Median (Q1; Q3)	32,0 (29,0; 35,0)	31,0 (26,0; 34,0)

FKSI-DRS Score	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Min, Max	21,0; 36,0	15,0; 36,0
Woche 69		
N ^c	57	20
Mittelwert (SD)	31,5 (4,0)	29,4 (5,3)
Median (Q1; Q3)	33,0 (29,0; 34,0)	31,0 (25,0; 33,5)
Min, Max	21,0; 36,0	20,0; 36,0
Woche 73		
N ^c	55	20
Mittelwert (SD)	31,4 (4,2)	28,8 (6,3)
Median (Q1; Q3)	32,0 (30,0; 35,0)	30,5 (24,5; 33,5)
Min, Max	20,0; 36,0	10,0; 36,0
Woche 77		
N ^c	56	18
Mittelwert (SD)	31,0 (4,4)	31,6 (3,3)
Median (Q1; Q3)	32,0 (27,0; 34,0)	31,5 (29,0; 34,0)
Min, Max	18,0; 36,0	25,0; 36,0
Woche 81		
N ^c	52	15
Mittelwert (SD)	31,2 (4,0)	31,5 (4,4)
Median (Q1; Q3)	32,0 (30,0; 34,0)	33,0 (29,0; 35,0)
Min, Max	21,0; 36,0	20,0; 36,0
Woche 85		
N ^c	50	10
Mittelwert (SD)	31,6 (4,1)	32,1 (4,0)
Median (Q1; Q3)	32,5 (29,0; 34,0)	33,0 (30,0; 36,0)
Min, Max	21,0; 36,0	25,0; 36,0
Woche 89		
N ^c	47	10
Mittelwert (SD)	31,2 (4,6)	31,7 (4,4)
Median (Q1; Q3)	32,0 (29,0; 35,0)	32,5 (32,0; 34,0)
Min, Max	14,0; 36,0	20,0; 36,0
Woche 93		
N ^c	47	11
Mittelwert (SD)	30,8 (4,6)	32,4 (2,9)
Median (Q1; Q3)	32,0 (28,0; 34,0)	33,0 (32,0; 35,0)
Min, Max	19,0; 36,0	27,0; 35,0
Woche 97		
N ^c	44	10
Mittelwert (SD)	31,6 (4,0)	33,0 (2,3)
Median (Q1; Q3)	32,0 (29,5; 35,0)	33,5 (31,0; 35,0)
Min, Max	21,0; 36,0	29,0; 36,0
Woche 101		
N ^c	42	9
Mittelwert (SD)	31,5 (4,0)	32,1 (4,1)
Median (Q1; Q3)	32,0 (30,0; 34,0)	34,0 (28,0; 36,0)
Min, Max	18,0; 36,0	26,0; 36,0

FKSI-DRS Score	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Woche 105		
N ^c	43	7
Mittelwert (SD)	31,7 (3,7)	32,0 (3,4)
Median (Q1; Q3)	32,0 (29,0; 35,0)	31,0 (30,0; 35,0)
Min, Max	23,0; 36,0	27,0; 36,0
Woche 109		
N ^c	42	7
Mittelwert (SD)	31,1 (4,3)	32,1 (2,6)
Median (Q1; Q3)	31,5 (29,0; 35,0)	33,0 (31,0; 34,0)
Min, Max	19,0; 36,0	27,0; 35,0
Woche 113		
N ^c	39	5
Mittelwert (SD)	30,7 (5,1)	28,4 (3,6)
Median (Q1; Q3)	31,0 (29,0; 36,0)	28,0 (26,0; 31,0)
Min, Max	17,0; 36,0	24,0; 33,0
Woche 117		
N ^c	37	5
Mittelwert (SD)	31,8 (4,4)	27,6 (3,8)
Median (Q1; Q3)	33,0 (30,0; 36,0)	28,0 (25,0; 29,0)
Min, Max	16,0; 36,0	23,0; 33,0
Woche 121		
N ^c	38	3
Mittelwert (SD)	31,5 (4,6)	25,7 (6,5)
Median (Q1; Q3)	32,5 (29,0; 36,0)	26,0 (19,0; 32,0)
Min, Max	19,0; 36,0	19,0; 32,0
Woche 125		
N ^c	33	3
Mittelwert (SD)	31,6 (4,6)	29,0 (1,0)
Median (Q1; Q3)	33,0 (30,0; 36,0)	29,0 (28,0; 30,0)
Min, Max	20,0; 36,0	28,0; 30,0
Woche 129		
N ^c	29	3
Mittelwert (SD)	31,9 (4,3)	26,7 (2,3)
Median (Q1; Q3)	33,0 (31,0; 36,0)	28,0 (24,0; 28,0)
Min, Max	20,0; 36,0	24,0; 28,0
Woche 133		
N ^c	27	2
Mittelwert (SD)	31,7 (4,6)	27,0 (4,2)
Median (Q1; Q3)	32,0 (30,0; 36,0)	27,0 (24,0; 30,0)
Min, Max	20,0; 36,0	24,0; 30,0
Woche 137		
N ^c	21	3
Mittelwert (SD)	31,3 (5,3)	26,0 (4,4)
Median (Q1; Q3)	32,0 (30,0; 36,0)	24,0 (23,0; 31,0)
Min, Max	15,0; 36,0	23,0; 31,0
Woche 141		

FKSI-DRS Score	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
N ^c	21	0
Mittelwert (SD)	31,2 (4,4)	- (-)
Median (Q1; Q3)	32,0 (28,0; 36,0)	- (-; -)
Min, Max	22,0; 36,0	-; -
Woche 145		
N ^c	20	0
Mittelwert (SD)	32,0 (4,1)	- (-)
Median (Q1; Q3)	32,0 (29,5; 36,0)	- (-; -)
Min, Max	24,0; 36,0	-; -
Woche 149		
N ^c	18	0
Mittelwert (SD)	31,7 (4,8)	- (-)
Median (Q1; Q3)	32,0 (29,0; 36,0)	- (-; -)
Min, Max	21,0; 36,0	-; -
Woche 153		
N ^c	17	0
Mittelwert (SD)	31,8 (3,9)	- (-)
Median (Q1; Q3)	32,0 (29,0; 35,0)	- (-; -)
Min, Max	23,0; 36,0	-; -
Woche 157		
N ^c	12	0
Mittelwert (SD)	31,1 (4,5)	- (-)
Median (Q1; Q3)	31,5 (28,0; 35,5)	- (-; -)
Min, Max	22,0; 36,0	-; -
Woche 161		
N ^c	11	0
Mittelwert (SD)	31,4 (4,3)	- (-)
Median (Q1; Q3)	32,0 (29,0; 36,0)	- (-; -)
Min, Max	23,0; 36,0	-; -
Woche 165		
N ^c	9	0
Mittelwert (SD)	32,4 (3,9)	- (-)
Median (Q1; Q3)	32,0 (31,0; 36,0)	- (-; -)
Min, Max	24,0; 36,0	-; -
Woche 169		
N ^c	8	0
Mittelwert (SD)	31,5 (4,7)	- (-)
Median (Q1; Q3)	32,0 (29,5; 35,5)	- (-; -)
Min, Max	22,0; 36,0	-; -
Woche 173		
N ^c	7	0
Mittelwert (SD)	30,7 (4,9)	- (-)
Median (Q1; Q3)	32,0 (27,0; 35,0)	- (-; -)
Min, Max	22,0; 36,0	-; -
Woche 177		
N ^c	6	0
Mittelwert (SD)	31,8 (4,0)	- (-)

FKSI-DRS Score	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	32,5 (30,0; 35,0)	- (-; -)
Min, Max	25,0; 36,0	-; -
Woche 181		
N ^c	4	0
Mittelwert (SD)	33,3 (2,6)	- (-)
Median (Q1; Q3)	33,0 (31,0; 35,5)	- (-; -)
Min, Max	31,0; 36,0	-; -
Woche 185		
N ^c	3	0
Mittelwert (SD)	31,0 (4,6)	- (-)
Median (Q1; Q3)	32,0 (26,0; 35,0)	- (-; -)
Min, Max	26,0; 35,0	-; -
Woche 189		
N ^c	1	0
Mittelwert (SD)	29,0 (-)	- (-)
Median (Q1; Q3)	29,0 (29,0; 29,0)	- (-; -)
Min, Max	29,0; 29,0	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt FKSI-DRS: Functional Assessment of Cancer Therapy Kidney Cancer Symptom Index-Disease Related Symptoms; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		

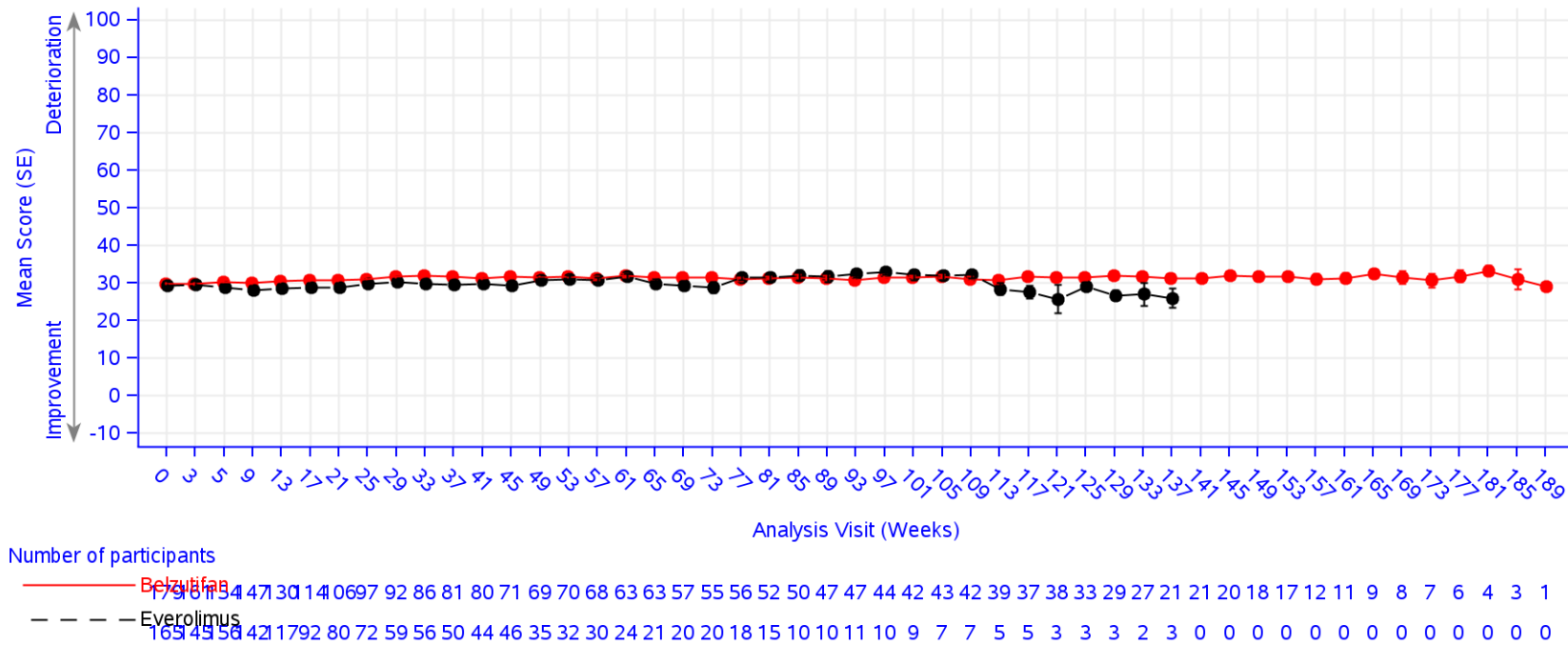


Abbildung 4G-9 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler zu den verschiedenen Erhebungszeitpunkten des FKSI-DRS Gesamtscore aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EQ-5D VAS

Tabelle 4G-15: Auswertung über den Studienverlauf der EQ-5D VAS aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EQ-5D VAS	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	179	164
Mittelwert (SD)	70,8 (18,5)	67,9 (20,8)
Median (Q1; Q3)	75,0 (60,0; 85,0)	70,5 (51,0; 85,0)
Min, Max	8,0; 100,0	18,0; 100,0
Woche 3		
N ^c	162	145
Mittelwert (SD)	71,1 (20,0)	70,8 (17,5)
Median (Q1; Q3)	75,0 (60,0; 86,0)	75,0 (60,0; 85,0)
Min, Max	9,0; 100,0	29,0; 100,0
Woche 5		
N ^c	156	154
Mittelwert (SD)	71,5 (18,7)	68,9 (19,2)
Median (Q1; Q3)	75,0 (59,0; 88,5)	70,0 (56,0; 84,0)
Min, Max	17,0; 100,0	0,0; 100,0
Woche 9		
N ^c	153	151
Mittelwert (SD)	71,5 (19,2)	65,4 (20,9)
Median (Q1; Q3)	75,0 (60,0; 87,0)	70,0 (50,0; 81,0)
Min, Max	10,0; 100,0	10,0; 100,0
Woche 13		
N ^c	131	121
Mittelwert (SD)	72,5 (19,8)	68,5 (20,2)
Median (Q1; Q3)	77,0 (60,0; 89,0)	70,0 (59,0; 83,0)
Min, Max	9,0; 100,0	0,0; 100,0
Woche 17		
N ^c	117	95
Mittelwert (SD)	72,7 (18,1)	68,9 (20,7)
Median (Q1; Q3)	79,0 (60,0; 88,0)	72,0 (53,0; 85,0)
Min, Max	20,0; 100,0	10,0; 99,0
Woche 21		
N ^c	108	78
Mittelwert (SD)	74,3 (18,1)	69,8 (20,4)
Median (Q1; Q3)	79,5 (63,5; 89,0)	75,0 (57,0; 85,0)
Min, Max	31,0; 100,0	10,0; 99,0
Woche 25		
N ^c	96	73
Mittelwert (SD)	74,9 (17,4)	70,6 (20,3)
Median (Q1; Q3)	77,5 (65,5; 90,0)	75,0 (60,0; 86,0)
Min, Max	21,0; 100,0	25,0; 98,0
Woche 29		
N ^c	92	59
Mittelwert (SD)	77,2 (16,5)	71,5 (21,0)

EQ-5D VAS	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	80,0 (68,0; 90,0)	80,0 (60,0; 89,0)
Min, Max	31,0; 99,0	19,0; 100,0
Woche 33		
N ^c	89	58
Mittelwert (SD)	76,2 (16,6)	70,7 (20,6)
Median (Q1; Q3)	80,0 (65,0; 90,0)	74,0 (60,0; 85,0)
Min, Max	29,0; 100,0	15,0; 98,0
Woche 37		
N ^c	85	51
Mittelwert (SD)	77,3 (15,3)	68,4 (21,5)
Median (Q1; Q3)	80,0 (69,0; 90,0)	70,0 (59,0; 85,0)
Min, Max	35,0; 100,0	17,0; 97,0
Woche 41		
N ^c	83	45
Mittelwert (SD)	74,7 (17,8)	68,8 (21,9)
Median (Q1; Q3)	79,0 (65,0; 87,0)	74,0 (60,0; 85,0)
Min, Max	20,0; 100,0	10,0; 97,0
Woche 45		
N ^c	71	49
Mittelwert (SD)	76,4 (17,6)	69,7 (21,5)
Median (Q1; Q3)	80,0 (70,0; 90,0)	75,0 (61,0; 85,0)
Min, Max	34,0; 100,0	9,0; 95,0
Woche 49		
N ^c	70	35
Mittelwert (SD)	75,2 (17,2)	75,4 (16,6)
Median (Q1; Q3)	80,0 (65,0; 88,0)	80,0 (65,0; 89,0)
Min, Max	31,0; 100,0	25,0; 97,0
Woche 53		
N ^c	69	34
Mittelwert (SD)	77,1 (16,0)	71,2 (17,4)
Median (Q1; Q3)	80,0 (70,0; 89,0)	72,5 (60,0; 83,0)
Min, Max	39,0; 100,0	14,0; 98,0
Woche 57		
N ^c	68	30
Mittelwert (SD)	75,8 (17,1)	71,2 (17,5)
Median (Q1; Q3)	80,0 (69,0; 89,0)	75,0 (60,0; 83,0)
Min, Max	30,0; 100,0	28,0; 95,0
Woche 61		
N ^c	64	25
Mittelwert (SD)	77,0 (15,6)	75,8 (17,2)
Median (Q1; Q3)	80,0 (69,0; 90,0)	83,0 (70,0; 85,0)
Min, Max	38,0; 99,0	30,0; 95,0
Woche 65		
N ^c	65	21
Mittelwert (SD)	76,7 (16,4)	71,3 (21,5)
Median (Q1; Q3)	80,0 (70,0; 88,0)	80,0 (58,0; 88,0)

EQ-5D VAS	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Min, Max	28,0; 100,0	20,0; 95,0
Woche 69		
N ^c	57	20
Mittelwert (SD)	77,3 (16,9)	70,4 (20,1)
Median (Q1; Q3)	81,0 (70,0; 90,0)	75,5 (58,5; 83,0)
Min, Max	31,0; 100,0	20,0; 95,0
Woche 73		
N ^c	56	21
Mittelwert (SD)	75,2 (19,5)	64,6 (24,0)
Median (Q1; Q3)	80,0 (70,0; 88,5)	70,0 (55,0; 80,0)
Min, Max	20,0; 100,0	9,0; 90,0
Woche 77		
N ^c	56	19
Mittelwert (SD)	73,8 (18,9)	74,5 (16,1)
Median (Q1; Q3)	79,0 (67,0; 87,0)	80,0 (61,0; 90,0)
Min, Max	19,0; 100,0	34,0; 94,0
Woche 81		
N ^c	52	15
Mittelwert (SD)	74,8 (19,9)	74,1 (20,3)
Median (Q1; Q3)	80,0 (67,5; 89,5)	80,0 (70,0; 88,0)
Min, Max	8,0; 100,0	30,0; 94,0
Woche 85		
N ^c	53	10
Mittelwert (SD)	76,1 (17,8)	72,4 (22,4)
Median (Q1; Q3)	80,0 (73,0; 89,0)	80,0 (70,0; 89,0)
Min, Max	30,0; 100,0	31,0; 90,0
Woche 89		
N ^c	47	10
Mittelwert (SD)	73,7 (18,4)	69,6 (23,8)
Median (Q1; Q3)	77,0 (69,0; 87,0)	77,5 (58,0; 89,0)
Min, Max	34,0; 100,0	25,0; 91,0
Woche 93		
N ^c	47	11
Mittelwert (SD)	75,4 (17,8)	77,7 (18,2)
Median (Q1; Q3)	80,0 (70,0; 89,0)	85,0 (70,0; 88,0)
Min, Max	20,0; 100,0	29,0; 96,0
Woche 97		
N ^c	44	10
Mittelwert (SD)	75,4 (17,9)	77,2 (16,1)
Median (Q1; Q3)	78,0 (69,5; 89,0)	85,0 (60,0; 90,0)
Min, Max	30,0; 100,0	47,0; 91,0
Woche 101		
N ^c	43	9
Mittelwert (SD)	75,1 (17,9)	74,4 (24,8)
Median (Q1; Q3)	77,0 (69,0; 89,0)	85,0 (80,0; 90,0)
Min, Max	28,0; 100,0	30,0; 93,0

EQ-5D VAS	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Woche 105		
N ^c	43	7
Mittelwert (SD)	75,2 (16,9)	83,0 (14,9)
Median (Q1; Q3)	79,0 (68,0; 88,0)	89,0 (84,0; 90,0)
Min, Max	32,0; 100,0	50,0; 93,0
Woche 109		
N ^c	43	8
Mittelwert (SD)	76,3 (15,5)	83,5 (17,2)
Median (Q1; Q3)	79,0 (66,0; 89,0)	88,5 (82,0; 94,5)
Min, Max	40,0; 100,0	43,0; 95,0
Woche 113		
N ^c	39	5
Mittelwert (SD)	74,8 (19,0)	68,0 (18,0)
Median (Q1; Q3)	76,0 (66,0; 91,0)	75,0 (75,0; 75,0)
Min, Max	30,0; 100,0	36,0; 79,0
Woche 117		
N ^c	37	4
Mittelwert (SD)	77,4 (17,2)	70,3 (22,9)
Median (Q1; Q3)	80,0 (70,0; 90,0)	77,5 (54,0; 86,5)
Min, Max	30,0; 100,0	38,0; 88,0
Woche 121		
N ^c	39	3
Mittelwert (SD)	76,4 (16,1)	58,3 (7,6)
Median (Q1; Q3)	80,0 (69,0; 89,0)	60,0 (50,0; 65,0)
Min, Max	36,0; 100,0	50,0; 65,0
Woche 125		
N ^c	33	3
Mittelwert (SD)	78,3 (17,2)	67,0 (22,1)
Median (Q1; Q3)	80,0 (73,0; 90,0)	65,0 (46,0; 90,0)
Min, Max	32,0; 100,0	46,0; 90,0
Woche 129		
N ^c	28	4
Mittelwert (SD)	79,9 (15,8)	68,0 (25,4)
Median (Q1; Q3)	80,5 (75,0; 92,0)	75,0 (51,0; 85,0)
Min, Max	40,0; 100,0	32,0; 90,0
Woche 133		
N ^c	28	2
Mittelwert (SD)	78,8 (16,6)	59,5 (43,1)
Median (Q1; Q3)	80,0 (74,5; 90,0)	59,5 (29,0; 90,0)
Min, Max	38,0; 100,0	29,0; 90,0
Woche 137		
N ^c	21	3
Mittelwert (SD)	75,6 (22,7)	57,3 (21,9)
Median (Q1; Q3)	80,0 (73,0; 89,0)	70,0 (32,0; 70,0)
Min, Max	1,0; 100,0	32,0; 70,0
Woche 141		

EQ-5D VAS	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
N ^c	21	0
Mittelwert (SD)	78,7 (14,9)	- (-)
Median (Q1; Q3)	80,0 (75,0; 89,0)	- (-; -)
Min, Max	36,0; 100,0	-; -
Woche 145		
N ^c	20	0
Mittelwert (SD)	78,5 (14,9)	- (-)
Median (Q1; Q3)	80,0 (69,0; 88,5)	- (-; -)
Min, Max	32,0; 100,0	-; -
Woche 149		
N ^c	18	0
Mittelwert (SD)	80,1 (12,0)	- (-)
Median (Q1; Q3)	79,5 (70,0; 88,0)	- (-; -)
Min, Max	60,0; 100,0	-; -
Woche 153		
N ^c	17	0
Mittelwert (SD)	79,8 (9,7)	- (-)
Median (Q1; Q3)	80,0 (74,0; 85,0)	- (-; -)
Min, Max	64,0; 100,0	-; -
Woche 157		
N ^c	12	0
Mittelwert (SD)	78,3 (10,9)	- (-)
Median (Q1; Q3)	76,5 (70,0; 87,0)	- (-; -)
Min, Max	64,0; 100,0	-; -
Woche 161		
N ^c	11	0
Mittelwert (SD)	79,6 (12,5)	- (-)
Median (Q1; Q3)	77,0 (70,0; 90,0)	- (-; -)
Min, Max	63,0; 100,0	-; -
Woche 165		
N ^c	9	0
Mittelwert (SD)	77,3 (13,4)	- (-)
Median (Q1; Q3)	78,0 (68,0; 84,0)	- (-; -)
Min, Max	55,0; 100,0	-; -
Woche 169		
N ^c	8	0
Mittelwert (SD)	70,8 (19,7)	- (-)
Median (Q1; Q3)	75,0 (62,5; 85,0)	- (-; -)
Min, Max	30,0; 91,0	-; -
Woche 173		
N ^c	7	0
Mittelwert (SD)	70,9 (12,6)	- (-)
Median (Q1; Q3)	77,0 (62,0; 80,0)	- (-; -)
Min, Max	50,0; 84,0	-; -
Woche 177		
N ^c	6	0
Mittelwert (SD)	75,8 (7,1)	- (-)

EQ-5D VAS	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	78,0 (70,0; 80,0)	- (-; -)
Min, Max	65,0; 84,0	-; -
Woche 181		
N ^c	4	0
Mittelwert (SD)	75,3 (10,4)	- (-)
Median (Q1; Q3)	79,0 (69,0; 81,5)	- (-; -)
Min, Max	60,0; 83,0	-; -
Woche 185		
N ^c	3	0
Mittelwert (SD)	66,3 (6,4)	- (-)
Median (Q1; Q3)	70,0 (59,0; 70,0)	- (-; -)
Min, Max	59,0; 70,0	-; -
Woche 189		
N ^c	1	0
Mittelwert (SD)	52,0 (-)	- (-)
Median (Q1; Q3)	52,0 (52,0; 52,0)	- (-; -)
Min, Max	52,0; 52,0	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt EQ-VAS: EuroQol Visual Analog Scale; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		

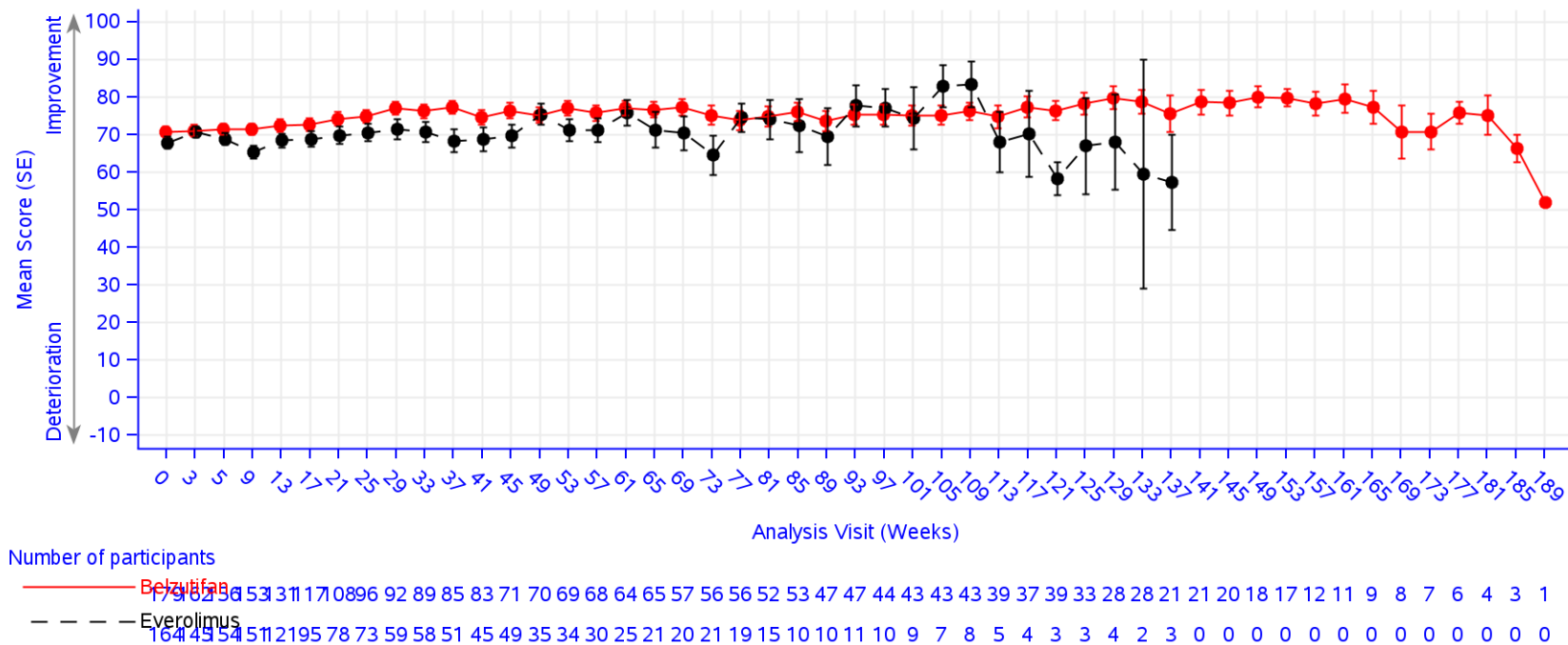


Abbildung 4G-10 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler zu den verschiedenen Erhebungszeitpunkten der EQ-5D VAS aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

Anhang 4-G4: Auswertung über den Studienverlauf: Gesundheitsbezogene Lebensqualität

EORTC QLQ-C30

EORTC QLQ-C30: Globaler Gesundheitsstatus

Tabelle 4G-16: Auswertung über den Studienverlauf des Globalen Gesundheitsstatus des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Globaler Gesundheitsstatus	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	178	164
Mittelwert (SD)	65,0 (20,1)	62,3 (21,3)
Median (Q1; Q3)	66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	159	145
Mittelwert (SD)	64,9 (22,1)	64,0 (19,1)
Median (Q1; Q3)	66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 5		
N ^c	152	156
Mittelwert (SD)	67,0 (21,6)	61,6 (20,9)
Median (Q1; Q3)	66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max	8,3; 100,0	0,0; 100,0
Woche 9		
N ^c	147	142
Mittelwert (SD)	66,1 (21,4)	58,0 (21,3)
Median (Q1; Q3)	66,7 (50,0; 83,3)	66,7 (41,7; 75,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 13		
N ^c	130	116
Mittelwert (SD)	66,9 (22,6)	61,5 (20,1)
Median (Q1; Q3)	66,7 (50,0; 83,3)	66,7 (50,0; 75,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	92
Mittelwert (SD)	68,1 (19,8)	62,8 (22,2)
Median (Q1; Q3)	66,7 (58,3; 83,3)	66,7 (50,0; 83,3)
Min, Max	8,3; 100,0	0,0; 100,0
Woche 21		
N ^c	106	78
Mittelwert (SD)	67,2 (23,5)	62,3 (23,8)
Median (Q1; Q3)	75,0 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max	8,3; 100,0	0,0; 100,0
Woche 25		
N ^c	96	72
Mittelwert (SD)	67,4 (21,2)	62,5 (23,2)

EORTC QLQ-C30 Globaler Gesundheitsstatus	Studie: LITESPARK 005 ^a	
	Belzutifan	Everolimus
	N ^b = 182	N ^b = 174
Median (Q1; Q3)	66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 29		
N ^c	92	59
Mittelwert (SD)	71,5 (18,6)	66,1 (20,6)
Median (Q1; Q3)	75,0 (66,7; 83,3)	66,7 (58,3; 83,3)
Min, Max	0,0; 100,0	8,3; 100,0
Woche 33		
N ^c	86	55
Mittelwert (SD)	70,0 (19,0)	61,7 (21,7)
Median (Q1; Q3)	66,7 (58,3; 83,3)	66,7 (50,0; 83,3)
Min, Max	25,0; 100,0	8,3; 100,0
Woche 37		
N ^c	81	50
Mittelwert (SD)	71,1 (18,5)	61,7 (21,5)
Median (Q1; Q3)	66,7 (58,3; 83,3)	66,7 (50,0; 75,0)
Min, Max	16,7; 100,0	8,3; 100,0
Woche 41		
N ^c	80	43
Mittelwert (SD)	69,8 (17,5)	58,5 (23,3)
Median (Q1; Q3)	66,7 (58,3; 83,3)	66,7 (50,0; 83,3)
Min, Max	25,0; 100,0	0,0; 100,0
Woche 45		
N ^c	71	46
Mittelwert (SD)	70,9 (20,0)	62,1 (19,5)
Median (Q1; Q3)	75,0 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max	25,0; 100,0	16,7; 83,3
Woche 49		
N ^c	69	35
Mittelwert (SD)	70,9 (19,5)	65,0 (13,7)
Median (Q1; Q3)	66,7 (66,7; 83,3)	66,7 (50,0; 83,3)
Min, Max	33,3; 100,0	50,0; 83,3
Woche 53		
N ^c	70	32
Mittelwert (SD)	71,2 (19,5)	59,6 (15,9)
Median (Q1; Q3)	66,7 (58,3; 83,3)	62,5 (50,0; 66,7)
Min, Max	8,3; 100,0	33,3; 83,3
Woche 57		
N ^c	68	30
Mittelwert (SD)	69,6 (19,0)	62,2 (17,1)
Median (Q1; Q3)	66,7 (62,5; 83,3)	66,7 (50,0; 83,3)
Min, Max	16,7; 100,0	33,3; 83,3
Woche 61		
N ^c	63	24
Mittelwert (SD)	72,8 (17,1)	63,2 (22,0)
Median (Q1; Q3)	75,0 (66,7; 83,3)	66,7 (50,0; 83,3)

EORTC QLQ-C30 Globaler Gesundheitsstatus	Studie: LITESPARK 005 ^a	
	Belzutifan	Everolimus
	N ^b = 182	N ^b = 174
Min, Max	25,0; 100,0	8,3; 100,0
Woche 65		
N ^c	63	21
Mittelwert (SD)	71,4 (18,2)	60,7 (19,7)
Median (Q1; Q3)	75,0 (58,3; 83,3)	66,7 (50,0; 75,0)
Min, Max	33,3; 100,0	16,7; 83,3
Woche 69		
N ^c	57	20
Mittelwert (SD)	71,2 (19,8)	59,6 (26,3)
Median (Q1; Q3)	75,0 (58,3; 83,3)	66,7 (45,8; 83,3)
Min, Max	16,7; 100,0	0,0; 83,3
Woche 73		
N ^c	55	20
Mittelwert (SD)	68,5 (21,0)	59,6 (20,1)
Median (Q1; Q3)	75,0 (50,0; 83,3)	66,7 (45,8; 70,8)
Min, Max	16,7; 100,0	16,7; 100,0
Woche 77		
N ^c	56	18
Mittelwert (SD)	69,0 (21,2)	64,4 (14,2)
Median (Q1; Q3)	66,7 (58,3; 83,3)	66,7 (50,0; 83,3)
Min, Max	0,0; 100,0	41,7; 83,3
Woche 81		
N ^c	52	15
Mittelwert (SD)	70,2 (19,6)	62,2 (19,4)
Median (Q1; Q3)	66,7 (54,2; 83,3)	66,7 (50,0; 75,0)
Min, Max	33,3; 100,0	16,7; 83,3
Woche 85		
N ^c	50	10
Mittelwert (SD)	69,8 (20,2)	62,5 (18,5)
Median (Q1; Q3)	66,7 (58,3; 83,3)	66,7 (50,0; 75,0)
Min, Max	16,7; 100,0	33,3; 83,3
Woche 89		
N ^c	47	10
Mittelwert (SD)	66,3 (21,8)	63,3 (21,6)
Median (Q1; Q3)	66,7 (50,0; 83,3)	66,7 (50,0; 83,3)
Min, Max	25,0; 100,0	16,7; 83,3
Woche 93		
N ^c	47	11
Mittelwert (SD)	68,3 (21,5)	68,2 (14,3)
Median (Q1; Q3)	66,7 (50,0; 83,3)	66,7 (66,7; 83,3)
Min, Max	0,0; 100,0	33,3; 83,3
Woche 97		
N ^c	44	10
Mittelwert (SD)	70,1 (21,1)	66,7 (16,2)
Median (Q1; Q3)	75,0 (62,5; 83,3)	66,7 (50,0; 83,3)
Min, Max	0,0; 100,0	41,7; 91,7

EORTC QLQ-C30 Globaler Gesundheitsstatus	Studie: LITESPARK 005 ^a	
	Belzutifan	Everolimus
	N ^b = 182	N ^b = 174
Woche 101		
N ^c	42	9
Mittelwert (SD)	68,5 (22,0)	64,8 (24,2)
Median (Q1; Q3)	70,8 (58,3; 83,3)	66,7 (66,7; 83,3)
Min, Max	0,0; 100,0	16,7; 83,3
Woche 105		
N ^c	43	7
Mittelwert (SD)	69,4 (18,1)	61,9 (25,4)
Median (Q1; Q3)	66,7 (50,0; 83,3)	66,7 (41,7; 83,3)
Min, Max	33,3; 100,0	16,7; 83,3
Woche 109		
N ^c	42	7
Mittelwert (SD)	70,2 (18,2)	72,6 (12,5)
Median (Q1; Q3)	70,8 (58,3; 83,3)	75,0 (66,7; 83,3)
Min, Max	33,3; 100,0	50,0; 83,3
Woche 113		
N ^c	39	5
Mittelwert (SD)	69,7 (21,7)	50,0 (5,9)
Median (Q1; Q3)	66,7 (50,0; 83,3)	50,0 (50,0; 50,0)
Min, Max	16,7; 100,0	41,7; 58,3
Woche 117		
N ^c	37	5
Mittelwert (SD)	72,7 (20,0)	61,7 (16,2)
Median (Q1; Q3)	75,0 (66,7; 83,3)	66,7 (50,0; 66,7)
Min, Max	16,7; 100,0	41,7; 83,3
Woche 121		
N ^c	38	3
Mittelwert (SD)	68,4 (20,9)	47,2 (12,7)
Median (Q1; Q3)	66,7 (58,3; 83,3)	50,0 (33,3; 58,3)
Min, Max	0,0; 100,0	33,3; 58,3
Woche 125		
N ^c	33	3
Mittelwert (SD)	66,9 (24,8)	52,8 (26,8)
Median (Q1; Q3)	66,7 (50,0; 83,3)	41,7 (33,3; 83,3)
Min, Max	0,0; 100,0	33,3; 83,3
Woche 129		
N ^c	29	3
Mittelwert (SD)	71,3 (17,5)	50,0 (16,7)
Median (Q1; Q3)	75,0 (66,7; 83,3)	50,0 (33,3; 66,7)
Min, Max	33,3; 100,0	33,3; 66,7
Woche 133		
N ^c	27	2
Mittelwert (SD)	71,6 (15,0)	58,3 (35,4)
Median (Q1; Q3)	66,7 (58,3; 83,3)	58,3 (33,3; 83,3)
Min, Max	50,0; 100,0	33,3; 83,3
Woche 137		

EORTC QLQ-C30 Globaler Gesundheitsstatus	Studie: LITESPARK 005 ^a	
	Belzutifan	Everolimus
	N ^b = 182	N ^b = 174
N ^c	21	3
Mittelwert (SD)	68,7 (22,0)	38,9 (9,6)
Median (Q1; Q3)	66,7 (58,3; 83,3)	33,3 (33,3; 50,0)
Min, Max	0,0; 100,0	33,3; 50,0
Woche 141		
N ^c	21	0
Mittelwert (SD)	69,0 (16,5)	- (-)
Median (Q1; Q3)	66,7 (58,3; 83,3)	- (-; -)
Min, Max	33,3; 100,0	-; -
Woche 145		
N ^c	20	0
Mittelwert (SD)	74,6 (18,2)	- (-)
Median (Q1; Q3)	70,8 (66,7; 83,3)	- (-; -)
Min, Max	33,3; 100,0	-; -
Woche 149		
N ^c	18	0
Mittelwert (SD)	72,2 (18,3)	- (-)
Median (Q1; Q3)	79,2 (58,3; 83,3)	- (-; -)
Min, Max	33,3; 100,0	-; -
Woche 153		
N ^c	17	0
Mittelwert (SD)	70,6 (14,2)	- (-)
Median (Q1; Q3)	66,7 (66,7; 83,3)	- (-; -)
Min, Max	50,0; 100,0	-; -
Woche 157		
N ^c	12	0
Mittelwert (SD)	70,1 (16,1)	- (-)
Median (Q1; Q3)	70,8 (54,2; 83,3)	- (-; -)
Min, Max	50,0; 100,0	-; -
Woche 161		
N ^c	11	0
Mittelwert (SD)	70,5 (18,0)	- (-)
Median (Q1; Q3)	66,7 (50,0; 83,3)	- (-; -)
Min, Max	50,0; 100,0	-; -
Woche 165		
N ^c	9	0
Mittelwert (SD)	71,3 (16,2)	- (-)
Median (Q1; Q3)	66,7 (66,7; 83,3)	- (-; -)
Min, Max	50,0; 100,0	-; -
Woche 169		
N ^c	8	0
Mittelwert (SD)	65,6 (20,6)	- (-)
Median (Q1; Q3)	70,8 (54,2; 83,3)	- (-; -)
Min, Max	25,0; 83,3	-; -
Woche 173		
N ^c	7	0

EORTC QLQ-C30 Globaler Gesundheitsstatus	Studie: LITESPARK 005 ^a	
	Belzutifan	Everolimus
	N ^b = 182	N ^b = 174
Mittelwert (SD)	59,5 (14,0)	- (-)
Median (Q1; Q3)	66,7 (50,0; 66,7)	- (-; -)
Min, Max	33,3; 75,0	-; -
Woche 177		
N ^c	6	0
Mittelwert (SD)	66,7 (11,8)	- (-)
Median (Q1; Q3)	66,7 (58,3; 75,0)	- (-; -)
Min, Max	50,0; 83,3	-; -
Woche 181		
N ^c	4	0
Mittelwert (SD)	62,5 (8,3)	- (-)
Median (Q1; Q3)	66,7 (58,3; 66,7)	- (-; -)
Min, Max	50,0; 66,7	-; -
Woche 185		
N ^c	3	0
Mittelwert (SD)	58,3 (8,3)	- (-)
Median (Q1; Q3)	58,3 (50,0; 66,7)	- (-; -)
Min, Max	50,0; 66,7	-; -
Woche 189		
N ^c	1	0
Mittelwert (SD)	50,0 (-)	- (-)
Median (Q1; Q3)	50,0 (50,0; 50,0)	- (-; -)
Min, Max	50,0; 50,0	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt QLQ-C30: Quality of Life Questionnaire-Core 30 Items; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartile; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		

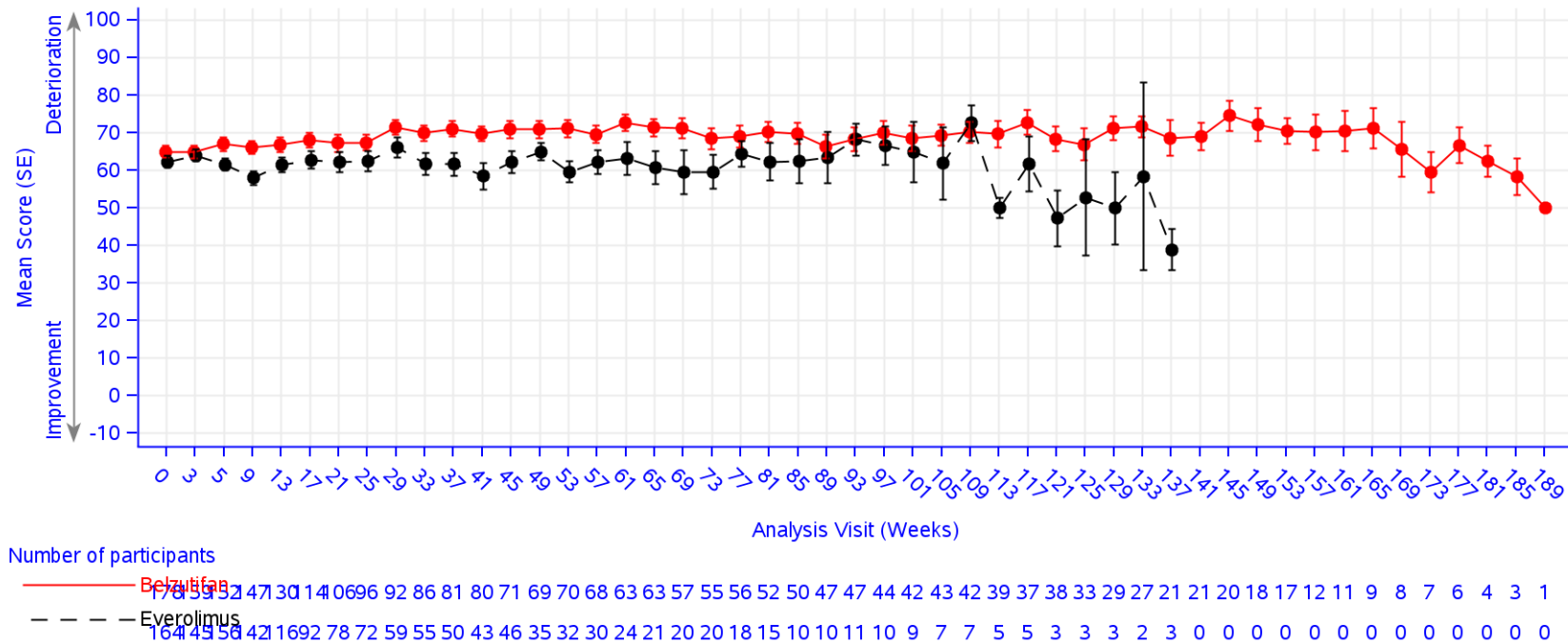


Abbildung 4G-11 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler des Globalen Gesundheitsstatus zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Funktionsskala Körperliche Funktion

Tabelle 4G-17: Auswertung über den Studienverlauf der Funktionsskala Körperliche Funktion des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Körperliche Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	178	164
Mittelwert (SD)	77,6 (21,2)	77,6 (18,8)
Median (Q1; Q3)	80,0 (66,7; 93,3)	80,0 (66,7; 93,3)
Min, Max	0,0; 100,0	20,0; 100,0
Woche 3		
N ^c	159	145
Mittelwert (SD)	76,4 (23,3)	77,1 (19,8)
Median (Q1; Q3)	86,7 (60,0; 93,3)	80,0 (60,0; 93,3)
Min, Max	6,7; 100,0	26,7; 100,0
Woche 5		
N ^c	152	156
Mittelwert (SD)	76,4 (23,8)	75,0 (22,5)
Median (Q1; Q3)	86,7 (60,0; 93,3)	80,0 (60,0; 93,3)
Min, Max	0,0; 100,0	6,7; 100,0
Woche 9		
N ^c	147	142
Mittelwert (SD)	76,6 (23,0)	71,8 (22,1)
Median (Q1; Q3)	86,7 (66,7; 93,3)	76,7 (60,0; 86,7)
Min, Max	0,0; 100,0	13,3; 100,0
Woche 13		
N ^c	130	116
Mittelwert (SD)	77,8 (21,7)	73,3 (21,4)
Median (Q1; Q3)	83,3 (66,7; 93,3)	80,0 (63,3; 86,7)
Min, Max	0,0; 100,0	13,3; 100,0
Woche 17		
N ^c	114	92
Mittelwert (SD)	77,3 (22,2)	74,6 (20,7)
Median (Q1; Q3)	86,7 (66,7; 93,3)	80,0 (63,3; 86,7)
Min, Max	0,0; 100,0	20,0; 100,0
Woche 21		
N ^c	106	78
Mittelwert (SD)	77,1 (23,5)	75,1 (23,8)
Median (Q1; Q3)	80,0 (66,7; 93,3)	80,0 (66,7; 93,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 25		
N ^c	96	72
Mittelwert (SD)	79,2 (21,4)	78,6 (18,8)
Median (Q1; Q3)	86,7 (70,0; 93,3)	86,7 (70,0; 93,3)
Min, Max	0,0; 100,0	20,0; 100,0
Woche 29		
N ^c	92	59

EORTC QLQ-C30 Körperliche Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Mittelwert (SD)	81,7 (20,4)	78,8 (19,4)
Median (Q1; Q3)	86,7 (73,3; 100,0)	80,0 (73,3; 93,3)
Min, Max	0,0; 100,0	13,3; 100,0
Woche 33		
N ^c	86	55
Mittelwert (SD)	82,9 (18,7)	76,4 (19,9)
Median (Q1; Q3)	86,7 (73,3; 100,0)	80,0 (66,7; 86,7)
Min, Max	6,7; 100,0	20,0; 100,0
Woche 37		
N ^c	81	50
Mittelwert (SD)	81,8 (19,1)	75,9 (21,2)
Median (Q1; Q3)	86,7 (80,0; 100,0)	80,0 (66,7; 93,3)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 41		
N ^c	80	43
Mittelwert (SD)	79,1 (21,7)	76,3 (20,6)
Median (Q1; Q3)	80,0 (66,7; 100,0)	80,0 (66,7; 86,7)
Min, Max	6,7; 100,0	0,0; 100,0
Woche 45		
N ^c	71	46
Mittelwert (SD)	80,2 (23,6)	75,4 (21,4)
Median (Q1; Q3)	86,7 (66,7; 100,0)	80,0 (66,7; 86,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 49		
N ^c	69	35
Mittelwert (SD)	80,3 (20,6)	81,1 (14,2)
Median (Q1; Q3)	86,7 (73,3; 93,3)	80,0 (73,3; 93,3)
Min, Max	0,0; 100,0	46,7; 100,0
Woche 53		
N ^c	70	32
Mittelwert (SD)	80,2 (21,3)	80,2 (15,7)
Median (Q1; Q3)	86,7 (73,3; 100,0)	86,7 (70,0; 93,3)
Min, Max	0,0; 100,0	46,7; 100,0
Woche 57		
N ^c	68	30
Mittelwert (SD)	79,0 (22,8)	79,6 (15,8)
Median (Q1; Q3)	83,3 (73,3; 100,0)	80,0 (66,7; 93,3)
Min, Max	0,0; 100,0	46,7; 100,0
Woche 61		
N ^c	63	24
Mittelwert (SD)	81,3 (20,4)	81,7 (16,9)
Median (Q1; Q3)	86,7 (73,3; 100,0)	86,7 (80,0; 93,3)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 65		
N ^c	63	21
Mittelwert (SD)	79,0 (22,0)	78,7 (15,7)
Median (Q1; Q3)	86,7 (66,7; 100,0)	80,0 (66,7; 86,7)

EORTC QLQ-C30 Körperliche Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Min, Max	0,0; 100,0	40,0; 100,0
Woche 69		
N ^c	57	20
Mittelwert (SD)	78,6 (21,5)	74,7 (16,7)
Median (Q1; Q3)	80,0 (73,3; 93,3)	73,3 (63,3; 86,7)
Min, Max	0,0; 100,0	46,7; 100,0
Woche 73		
N ^c	55	20
Mittelwert (SD)	77,2 (23,3)	72,7 (24,1)
Median (Q1; Q3)	80,0 (60,0; 100,0)	80,0 (70,0; 86,7)
Min, Max	6,7; 100,0	6,7; 100,0
Woche 77		
N ^c	56	18
Mittelwert (SD)	77,7 (20,6)	83,0 (13,2)
Median (Q1; Q3)	80,0 (66,7; 93,3)	86,7 (73,3; 93,3)
Min, Max	6,7; 100,0	60,0; 100,0
Woche 81		
N ^c	52	15
Mittelwert (SD)	78,3 (21,6)	80,9 (14,9)
Median (Q1; Q3)	80,0 (66,7; 93,3)	86,7 (73,3; 93,3)
Min, Max	13,3; 100,0	53,3; 100,0
Woche 85		
N ^c	50	10
Mittelwert (SD)	76,9 (23,2)	84,0 (14,8)
Median (Q1; Q3)	80,0 (66,7; 93,3)	86,7 (73,3; 100,0)
Min, Max	0,0; 100,0	60,0; 100,0
Woche 89		
N ^c	47	10
Mittelwert (SD)	75,7 (24,9)	77,3 (19,9)
Median (Q1; Q3)	80,0 (60,0; 100,0)	83,3 (66,7; 93,3)
Min, Max	6,7; 100,0	33,3; 100,0
Woche 93		
N ^c	47	11
Mittelwert (SD)	75,2 (25,9)	80,0 (14,6)
Median (Q1; Q3)	80,0 (60,0; 100,0)	86,7 (73,3; 93,3)
Min, Max	0,0; 100,0	53,3; 100,0
Woche 97		
N ^c	44	10
Mittelwert (SD)	77,9 (24,9)	80,7 (13,1)
Median (Q1; Q3)	80,0 (70,0; 100,0)	83,3 (73,3; 86,7)
Min, Max	0,0; 100,0	53,3; 100,0
Woche 101		
N ^c	42	9
Mittelwert (SD)	80,6 (20,0)	75,6 (20,8)
Median (Q1; Q3)	80,0 (73,3; 100,0)	80,0 (73,3; 86,7)
Min, Max	13,3; 100,0	33,3; 100,0

EORTC QLQ-C30 Körperliche Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Woche 105		
N ^c	43	7
Mittelwert (SD)	79,2 (23,3)	83,8 (14,8)
Median (Q1; Q3)	80,0 (73,3; 100,0)	86,7 (66,7; 100,0)
Min, Max	6,7; 100,0	66,7; 100,0
Woche 109		
N ^c	42	7
Mittelwert (SD)	75,7 (23,7)	81,9 (13,7)
Median (Q1; Q3)	80,0 (60,0; 100,0)	86,7 (73,3; 93,3)
Min, Max	6,7; 100,0	60,0; 100,0
Woche 113		
N ^c	39	5
Mittelwert (SD)	76,4 (25,0)	72,0 (9,9)
Median (Q1; Q3)	80,0 (60,0; 100,0)	73,3 (66,7; 73,3)
Min, Max	0,0; 100,0	60,0; 86,7
Woche 117		
N ^c	37	5
Mittelwert (SD)	82,3 (21,4)	73,3 (8,2)
Median (Q1; Q3)	86,7 (73,3; 100,0)	73,3 (66,7; 73,3)
Min, Max	20,0; 100,0	66,7; 86,7
Woche 121		
N ^c	38	3
Mittelwert (SD)	80,7 (22,5)	62,2 (16,8)
Median (Q1; Q3)	83,3 (73,3; 100,0)	60,0 (46,7; 80,0)
Min, Max	20,0; 100,0	46,7; 80,0
Woche 125		
N ^c	33	3
Mittelwert (SD)	81,0 (23,9)	66,7 (13,3)
Median (Q1; Q3)	86,7 (66,7; 100,0)	66,7 (53,3; 80,0)
Min, Max	6,7; 100,0	53,3; 80,0
Woche 129		
N ^c	29	3
Mittelwert (SD)	80,9 (24,9)	62,2 (21,4)
Median (Q1; Q3)	86,7 (73,3; 100,0)	53,3 (46,7; 86,7)
Min, Max	6,7; 100,0	46,7; 86,7
Woche 133		
N ^c	27	2
Mittelwert (SD)	79,8 (23,4)	53,3 (18,9)
Median (Q1; Q3)	80,0 (73,3; 100,0)	53,3 (40,0; 66,7)
Min, Max	6,7; 100,0	40,0; 66,7
Woche 137		
N ^c	21	3
Mittelwert (SD)	78,1 (28,9)	55,6 (3,8)
Median (Q1; Q3)	86,7 (73,3; 100,0)	53,3 (53,3; 60,0)
Min, Max	0,0; 100,0	53,3; 60,0
Woche 141		

EORTC QLQ-C30 Körperliche Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
N ^c	21	0
Mittelwert (SD)	79,7 (24,5)	- (-)
Median (Q1; Q3)	86,7 (73,3; 100,0)	- (-; -)
Min, Max	6,7; 100,0	-; -
Woche 145		
N ^c	20	0
Mittelwert (SD)	81,7 (23,4)	- (-)
Median (Q1; Q3)	86,7 (73,3; 100,0)	- (-; -)
Min, Max	6,7; 100,0	-; -
Woche 149		
N ^c	18	0
Mittelwert (SD)	81,9 (23,4)	- (-)
Median (Q1; Q3)	90,0 (66,7; 100,0)	- (-; -)
Min, Max	13,3; 100,0	-; -
Woche 153		
N ^c	17	0
Mittelwert (SD)	80,8 (24,3)	- (-)
Median (Q1; Q3)	86,7 (66,7; 100,0)	- (-; -)
Min, Max	6,7; 100,0	-; -
Woche 157		
N ^c	12	0
Mittelwert (SD)	78,9 (24,8)	- (-)
Median (Q1; Q3)	86,7 (66,7; 96,7)	- (-; -)
Min, Max	13,3; 100,0	-; -
Woche 161		
N ^c	11	0
Mittelwert (SD)	76,4 (27,5)	- (-)
Median (Q1; Q3)	80,0 (66,7; 100,0)	- (-; -)
Min, Max	6,7; 100,0	-; -
Woche 165		
N ^c	9	0
Mittelwert (SD)	78,5 (28,6)	- (-)
Median (Q1; Q3)	93,3 (66,7; 100,0)	- (-; -)
Min, Max	13,3; 100,0	-; -
Woche 169		
N ^c	8	0
Mittelwert (SD)	77,5 (30,2)	- (-)
Median (Q1; Q3)	90,0 (63,3; 100,0)	- (-; -)
Min, Max	13,3; 100,0	-; -
Woche 173		
N ^c	7	0
Mittelwert (SD)	67,6 (30,7)	- (-)
Median (Q1; Q3)	66,7 (60,0; 93,3)	- (-; -)
Min, Max	6,7; 100,0	-; -
Woche 177		
N ^c	6	0
Mittelwert (SD)	70,0 (31,2)	- (-)

EORTC QLQ-C30 Körperliche Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	76,7 (60,0; 93,3)	- (-; -)
Min, Max	13,3; 100,0	-; -
Woche 181		
N ^c	4	0
Mittelwert (SD)	80,0 (19,6)	- (-)
Median (Q1; Q3)	80,0 (63,3; 96,7)	- (-; -)
Min, Max	60,0; 100,0	-; -
Woche 185		
N ^c	3	0
Mittelwert (SD)	55,6 (40,2)	- (-)
Median (Q1; Q3)	60,0 (13,3; 93,3)	- (-; -)
Min, Max	13,3; 93,3	-; -
Woche 189		
N ^c	1	0
Mittelwert (SD)	60,0 (-)	- (-)
Median (Q1; Q3)	60,0 (60,0; 60,0)	- (-; -)
Min, Max	60,0; 60,0	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Items; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		

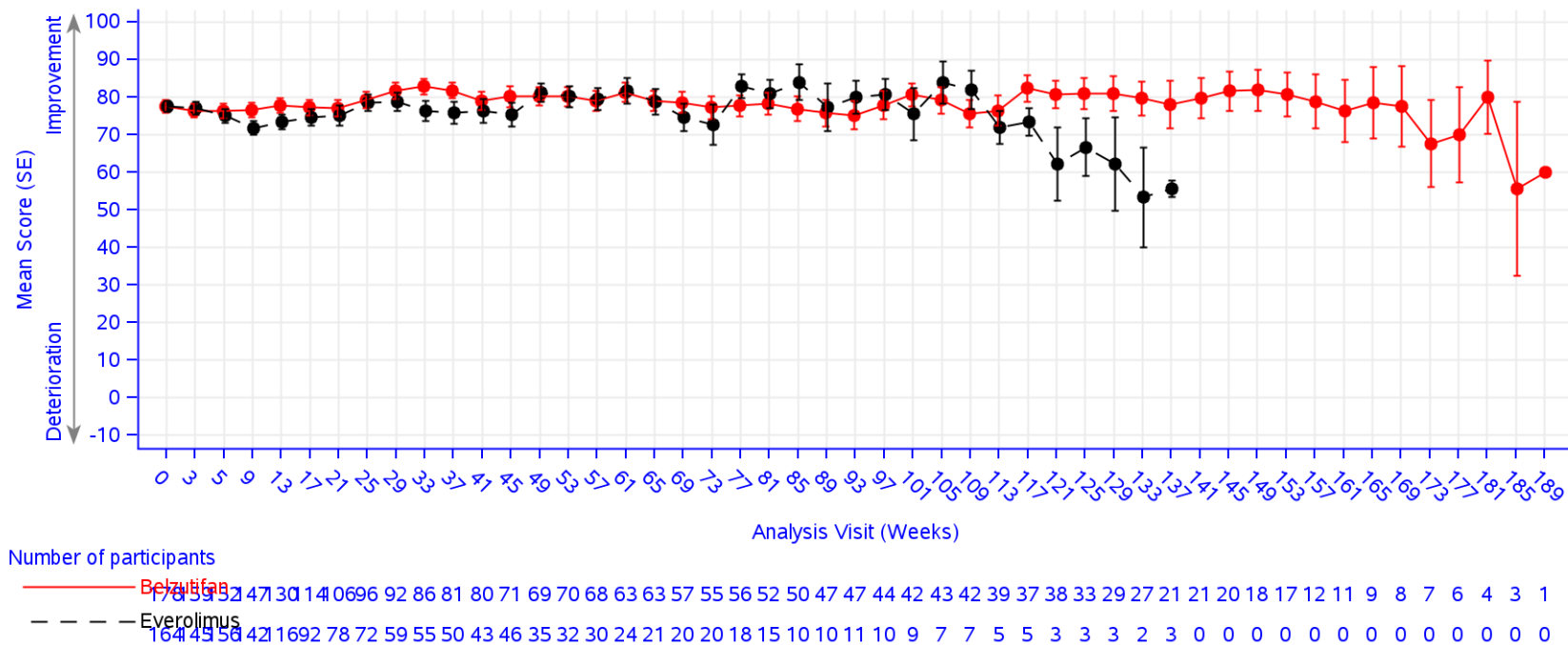


Abbildung 4G-12 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler des Funktionsskala Körperliche Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Funktionsskala Rollenfunktion

Tabelle 4G-18: Auswertung über den Studienverlauf der Funktionsskala Rollenfunktion des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Rollenfunktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	178	164
Mittelwert (SD)	75,4 (28,2)	75,5 (26,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	159	145
Mittelwert (SD)	71,9 (30,2)	72,1 (26,8)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	152	156
Mittelwert (SD)	73,0 (30,6)	71,7 (29,0)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 9		
N ^c	147	142
Mittelwert (SD)	71,8 (29,2)	67,3 (31,1)
Median (Q1; Q3)	66,7 (50,0; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 13		
N ^c	130	116
Mittelwert (SD)	74,5 (27,4)	66,7 (29,6)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (50,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	92
Mittelwert (SD)	74,7 (28,2)	72,6 (29,1)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 21		
N ^c	106	78
Mittelwert (SD)	75,6 (28,5)	72,9 (29,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 25		
N ^c	96	72
Mittelwert (SD)	76,6 (27,6)	76,2 (27,1)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 29		
N ^c	92	59

EORTC QLQ-C30 Rollenfunktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Mittelwert (SD)	79,7 (25,9)	75,7 (25,8)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 33		
N ^c	86	55
Mittelwert (SD)	81,0 (23,7)	73,3 (25,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 37		
N ^c	81	50
Mittelwert (SD)	79,4 (23,8)	71,7 (29,0)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 41		
N ^c	80	43
Mittelwert (SD)	79,4 (23,9)	70,9 (28,4)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 45		
N ^c	71	46
Mittelwert (SD)	79,3 (26,6)	70,3 (30,0)
Median (Q1; Q3)	100,0 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 49		
N ^c	69	35
Mittelwert (SD)	77,8 (25,8)	75,7 (23,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 53		
N ^c	70	32
Mittelwert (SD)	79,8 (23,7)	77,6 (25,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 57		
N ^c	68	30
Mittelwert (SD)	77,5 (26,4)	78,3 (23,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 61		
N ^c	63	24
Mittelwert (SD)	79,4 (25,3)	75,7 (20,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 65		
N ^c	63	21
Mittelwert (SD)	76,7 (24,8)	72,2 (31,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)

EORTC QLQ-C30 Rollenfunktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Min, Max	0,0; 100,0	0,0; 100,0
Woche 69		
N ^c	57	20
Mittelwert (SD)	74,3 (25,0)	70,0 (22,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (58,3; 91,7)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 73		
N ^c	55	20
Mittelwert (SD)	71,8 (30,9)	67,5 (28,9)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (58,3; 91,7)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 77		
N ^c	56	18
Mittelwert (SD)	74,4 (24,4)	77,8 (20,6)
Median (Q1; Q3)	66,7 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	33,3; 100,0	33,3; 100,0
Woche 81		
N ^c	52	15
Mittelwert (SD)	74,4 (23,9)	75,6 (27,4)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (50,0; 100,0)
Min, Max	16,7; 100,0	33,3; 100,0
Woche 85		
N ^c	50	10
Mittelwert (SD)	75,0 (26,1)	78,3 (22,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 89		
N ^c	47	10
Mittelwert (SD)	73,4 (27,7)	76,7 (27,4)
Median (Q1; Q3)	66,7 (50,0; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 93		
N ^c	47	11
Mittelwert (SD)	73,0 (28,1)	77,3 (22,7)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 97		
N ^c	44	10
Mittelwert (SD)	73,9 (30,4)	81,7 (20,0)
Median (Q1; Q3)	75,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	50,0; 100,0
Woche 101		
N ^c	42	9
Mittelwert (SD)	74,6 (29,5)	79,6 (26,1)
Median (Q1; Q3)	75,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0

EORTC QLQ-C30 Rollenfunktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Woche 105		
N ^c	43	7
Mittelwert (SD)	74,8 (28,0)	85,7 (20,2)
Median (Q1; Q3)	83,3 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	50,0; 100,0
Woche 109		
N ^c	42	7
Mittelwert (SD)	75,0 (28,8)	83,3 (25,5)
Median (Q1; Q3)	75,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 113		
N ^c	39	5
Mittelwert (SD)	73,1 (26,4)	66,7 (31,2)
Median (Q1; Q3)	66,7 (66,7; 100,0)	83,3 (33,3; 83,3)
Min, Max	16,7; 100,0	33,3; 100,0
Woche 117		
N ^c	37	5
Mittelwert (SD)	79,7 (24,6)	66,7 (23,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 66,7)
Min, Max	16,7; 100,0	33,3; 100,0
Woche 121		
N ^c	38	3
Mittelwert (SD)	75,4 (29,2)	33,3 (33,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	33,3 (0,0; 66,7)
Min, Max	0,0; 100,0	0,0; 66,7
Woche 125		
N ^c	33	3
Mittelwert (SD)	79,3 (27,0)	66,7 (33,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (33,3; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 129		
N ^c	29	3
Mittelwert (SD)	78,2 (28,2)	55,6 (38,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	33,3 (33,3; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 133		
N ^c	27	2
Mittelwert (SD)	74,7 (28,3)	66,7 (47,1)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (33,3; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 137		
N ^c	21	3
Mittelwert (SD)	75,4 (29,2)	55,6 (19,2)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (33,3; 66,7)
Min, Max	0,0; 100,0	33,3; 66,7
Woche 141		

EORTC QLQ-C30 Rollenfunktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
N ^c	21	0
Mittelwert (SD)	78,6 (23,7)	- (-)
Median (Q1; Q3)	83,3 (66,7; 100,0)	- (-; -)
Min, Max	16,7; 100,0	-; -
Woche 145		
N ^c	20	0
Mittelwert (SD)	78,3 (27,6)	- (-)
Median (Q1; Q3)	91,7 (66,7; 100,0)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 149		
N ^c	18	0
Mittelwert (SD)	83,3 (21,4)	- (-)
Median (Q1; Q3)	100,0 (66,7; 100,0)	- (-; -)
Min, Max	33,3; 100,0	-; -
Woche 153		
N ^c	17	0
Mittelwert (SD)	76,5 (26,4)	- (-)
Median (Q1; Q3)	66,7 (66,7; 100,0)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 157		
N ^c	12	0
Mittelwert (SD)	77,8 (30,4)	- (-)
Median (Q1; Q3)	91,7 (66,7; 100,0)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 161		
N ^c	11	0
Mittelwert (SD)	75,8 (30,2)	- (-)
Median (Q1; Q3)	66,7 (66,7; 100,0)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 165		
N ^c	9	0
Mittelwert (SD)	77,8 (33,3)	- (-)
Median (Q1; Q3)	100,0 (66,7; 100,0)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 169		
N ^c	8	0
Mittelwert (SD)	77,1 (29,5)	- (-)
Median (Q1; Q3)	83,3 (66,7; 100,0)	- (-; -)
Min, Max	16,7; 100,0	-; -
Woche 173		
N ^c	7	0
Mittelwert (SD)	66,7 (33,3)	- (-)
Median (Q1; Q3)	66,7 (66,7; 100,0)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 177		
N ^c	6	0
Mittelwert (SD)	66,7 (36,5)	- (-)

EORTC QLQ-C30 Rollenfunktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	66,7 (66,7; 100,0)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 181		
N ^c	4	0
Mittelwert (SD)	75,0 (16,7)	- (-)
Median (Q1; Q3)	66,7 (66,7; 83,3)	- (-; -)
Min, Max	66,7; 100,0	-; -
Woche 185		
N ^c	3	0
Mittelwert (SD)	61,1 (41,9)	- (-)
Median (Q1; Q3)	66,7 (16,7; 100,0)	- (-; -)
Min, Max	16,7; 100,0	-; -
Woche 189		
N ^c	1	0
Mittelwert (SD)	66,7 (-)	- (-)
Median (Q1; Q3)	66,7 (66,7; 66,7)	- (-; -)
Min, Max	66,7; 66,7	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Items; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		

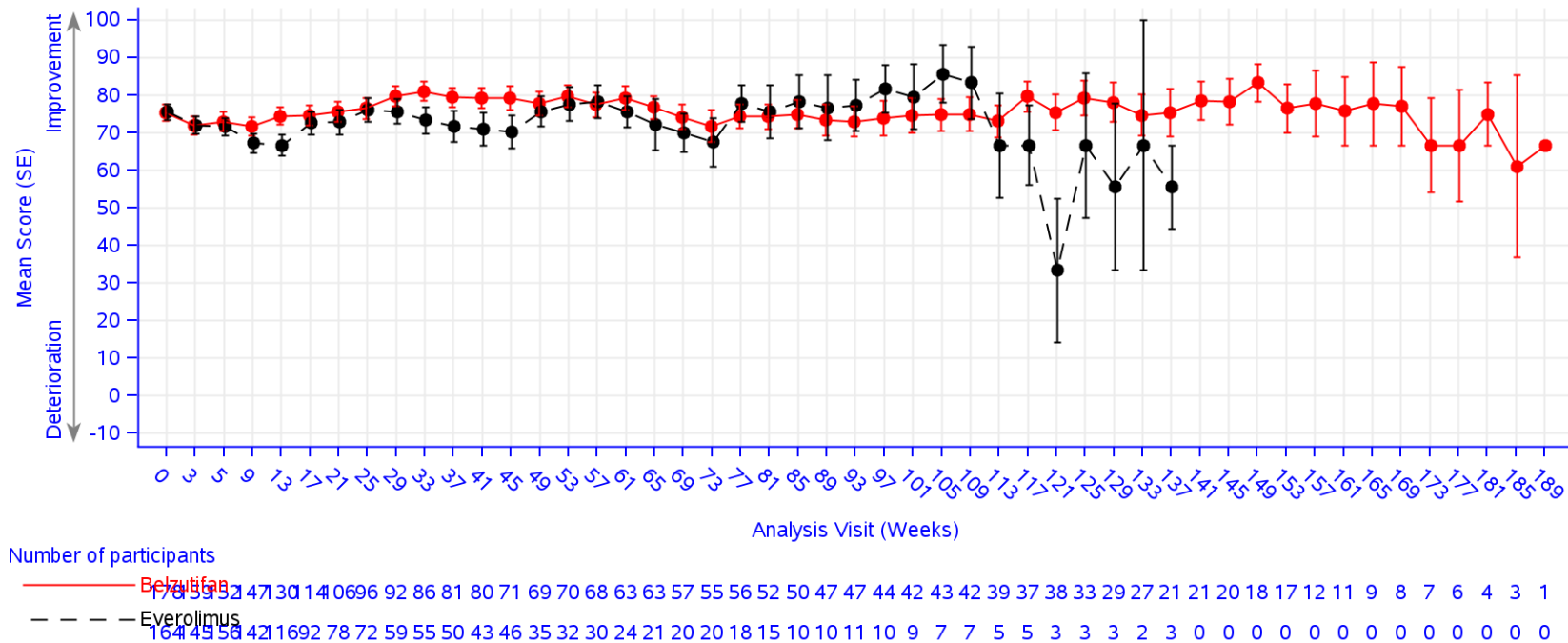


Abbildung 4G-13 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Rollenfunktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Funktionsskala Emotionale Funktion

Tabelle 4G-19: Auswertung über den Studienverlauf der Funktionsskala Emotionale Funktion des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Emotionale Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	178	164
Mittelwert (SD)	80,3 (19,4)	80,1 (19,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	8,3; 100,0
Woche 3		
N ^c	159	145
Mittelwert (SD)	81,0 (19,9)	81,8 (20,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (75,0; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 5		
N ^c	152	156
Mittelwert (SD)	79,9 (21,5)	81,3 (19,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 9		
N ^c	147	142
Mittelwert (SD)	80,3 (22,9)	78,6 (19,3)
Median (Q1; Q3)	91,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 13		
N ^c	130	116
Mittelwert (SD)	79,0 (22,4)	80,8 (20,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 17		
N ^c	114	92
Mittelwert (SD)	79,2 (21,5)	82,6 (18,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	87,5 (66,7; 100,0)
Min, Max	0,0; 100,0	25,0; 100,0
Woche 21		
N ^c	106	78
Mittelwert (SD)	78,9 (22,7)	81,1 (23,2)
Median (Q1; Q3)	83,3 (66,7; 100,0)	87,5 (66,7; 100,0)
Min, Max	8,3; 100,0	0,0; 100,0
Woche 25		
N ^c	96	72
Mittelwert (SD)	84,2 (18,8)	83,8 (18,0)
Median (Q1; Q3)	91,7 (75,0; 100,0)	91,7 (75,0; 100,0)
Min, Max	25,0; 100,0	33,3; 100,0
Woche 29		
N ^c	92	59

EORTC QLQ-C30 Emotionale Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Mittelwert (SD)	81,5 (21,1)	83,1 (18,2)
Median (Q1; Q3)	83,3 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	8,3; 100,0	33,3; 100,0
Woche 33		
N ^c	86	55
Mittelwert (SD)	83,6 (20,8)	81,2 (20,2)
Median (Q1; Q3)	91,7 (75,0; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	8,3; 100,0
Woche 37		
N ^c	81	50
Mittelwert (SD)	84,1 (16,9)	82,5 (19,1)
Median (Q1; Q3)	91,7 (75,0; 100,0)	87,5 (75,0; 100,0)
Min, Max	33,3; 100,0	0,0; 100,0
Woche 41		
N ^c	80	43
Mittelwert (SD)	81,1 (20,3)	84,9 (17,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	0,0; 100,0	25,0; 100,0
Woche 45		
N ^c	71	46
Mittelwert (SD)	82,3 (19,5)	79,2 (22,3)
Median (Q1; Q3)	91,7 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	25,0; 100,0	25,0; 100,0
Woche 49		
N ^c	69	35
Mittelwert (SD)	81,9 (17,8)	81,9 (18,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	25,0; 100,0	33,3; 100,0
Woche 53		
N ^c	70	32
Mittelwert (SD)	83,6 (18,9)	86,5 (15,2)
Median (Q1; Q3)	91,7 (66,7; 100,0)	91,7 (75,0; 100,0)
Min, Max	33,3; 100,0	50,0; 100,0
Woche 57		
N ^c	68	30
Mittelwert (SD)	83,2 (19,3)	85,3 (13,8)
Median (Q1; Q3)	91,7 (66,7; 100,0)	87,5 (75,0; 100,0)
Min, Max	25,0; 100,0	66,7; 100,0
Woche 61		
N ^c	63	24
Mittelwert (SD)	86,0 (17,3)	82,3 (18,3)
Median (Q1; Q3)	91,7 (75,0; 100,0)	83,3 (66,7; 100,0)
Min, Max	33,3; 100,0	33,3; 100,0
Woche 65		
N ^c	63	21
Mittelwert (SD)	82,9 (19,7)	80,6 (21,6)
Median (Q1; Q3)	91,7 (66,7; 100,0)	91,7 (66,7; 100,0)

EORTC QLQ-C30 Emotionale Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Min, Max	25,0; 100,0	33,3; 100,0
Woche 69		
N ^c	57	20
Mittelwert (SD)	83,3 (20,0)	76,3 (23,9)
Median (Q1; Q3)	91,7 (75,0; 100,0)	75,0 (62,5; 100,0)
Min, Max	33,3; 100,0	16,7; 100,0
Woche 73		
N ^c	55	20
Mittelwert (SD)	81,5 (21,6)	69,6 (31,0)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (62,5; 91,7)
Min, Max	8,3; 100,0	0,0; 100,0
Woche 77		
N ^c	56	18
Mittelwert (SD)	82,6 (17,7)	87,0 (15,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	95,8 (66,7; 100,0)
Min, Max	33,3; 100,0	58,3; 100,0
Woche 81		
N ^c	52	15
Mittelwert (SD)	83,7 (19,0)	78,9 (27,8)
Median (Q1; Q3)	91,7 (75,0; 100,0)	83,3 (66,7; 100,0)
Min, Max	25,0; 100,0	0,0; 100,0
Woche 85		
N ^c	50	10
Mittelwert (SD)	82,3 (21,5)	80,0 (27,3)
Median (Q1; Q3)	87,5 (66,7; 100,0)	95,8 (66,7; 100,0)
Min, Max	16,7; 100,0	33,3; 100,0
Woche 89		
N ^c	47	10
Mittelwert (SD)	80,3 (20,6)	79,2 (31,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	25,0; 100,0	0,0; 100,0
Woche 93		
N ^c	47	11
Mittelwert (SD)	81,9 (20,3)	82,6 (21,9)
Median (Q1; Q3)	83,3 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	8,3; 100,0	33,3; 100,0
Woche 97		
N ^c	44	10
Mittelwert (SD)	83,0 (18,5)	86,7 (17,2)
Median (Q1; Q3)	87,5 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	25,0; 100,0	66,7; 100,0
Woche 101		
N ^c	42	9
Mittelwert (SD)	81,7 (19,1)	87,0 (20,0)
Median (Q1; Q3)	83,3 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	25,0; 100,0	50,0; 100,0

EORTC QLQ-C30 Emotionale Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Woche 105		
N ^c	43	7
Mittelwert (SD)	81,8 (20,8)	94,0 (15,7)
Median (Q1; Q3)	83,3 (75,0; 100,0)	100,0 (100,0; 100,0)
Min, Max	0,0; 100,0	58,3; 100,0
Woche 109		
N ^c	42	7
Mittelwert (SD)	79,8 (22,4)	88,1 (20,9)
Median (Q1; Q3)	91,7 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	25,0; 100,0	50,0; 100,0
Woche 113		
N ^c	39	5
Mittelwert (SD)	80,6 (21,7)	76,7 (18,1)
Median (Q1; Q3)	83,3 (66,7; 100,0)	75,0 (75,0; 83,3)
Min, Max	25,0; 100,0	50,0; 100,0
Woche 117		
N ^c	37	5
Mittelwert (SD)	82,4 (23,1)	81,7 (13,7)
Median (Q1; Q3)	91,7 (66,7; 100,0)	75,0 (75,0; 91,7)
Min, Max	8,3; 100,0	66,7; 100,0
Woche 121		
N ^c	38	3
Mittelwert (SD)	80,9 (23,0)	80,6 (17,3)
Median (Q1; Q3)	87,5 (66,7; 100,0)	75,0 (66,7; 100,0)
Min, Max	8,3; 100,0	66,7; 100,0
Woche 125		
N ^c	33	3
Mittelwert (SD)	80,6 (24,2)	80,6 (21,0)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (58,3; 100,0)
Min, Max	0,0; 100,0	58,3; 100,0
Woche 129		
N ^c	29	3
Mittelwert (SD)	85,6 (19,3)	77,8 (21,0)
Median (Q1; Q3)	100,0 (75,0; 100,0)	75,0 (58,3; 100,0)
Min, Max	33,3; 100,0	58,3; 100,0
Woche 133		
N ^c	27	2
Mittelwert (SD)	82,7 (23,9)	75,0 (35,4)
Median (Q1; Q3)	91,7 (66,7; 100,0)	75,0 (50,0; 100,0)
Min, Max	0,0; 100,0	50,0; 100,0
Woche 137		
N ^c	21	3
Mittelwert (SD)	79,8 (28,7)	86,1 (17,3)
Median (Q1; Q3)	91,7 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	8,3; 100,0	66,7; 100,0
Woche 141		

EORTC QLQ-C30 Emotionale Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
N ^c	21	0
Mittelwert (SD)	84,1 (23,6)	- (-)
Median (Q1; Q3)	100,0 (75,0; 100,0)	- (-; -)
Min, Max	8,3; 100,0	-; -
Woche 145		
N ^c	20	0
Mittelwert (SD)	84,6 (22,7)	- (-)
Median (Q1; Q3)	100,0 (66,7; 100,0)	- (-; -)
Min, Max	33,3; 100,0	-; -
Woche 149		
N ^c	18	0
Mittelwert (SD)	84,3 (25,5)	- (-)
Median (Q1; Q3)	100,0 (75,0; 100,0)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 153		
N ^c	17	0
Mittelwert (SD)	86,3 (24,3)	- (-)
Median (Q1; Q3)	100,0 (75,0; 100,0)	- (-; -)
Min, Max	8,3; 100,0	-; -
Woche 157		
N ^c	12	0
Mittelwert (SD)	79,2 (26,7)	- (-)
Median (Q1; Q3)	91,7 (66,7; 100,0)	- (-; -)
Min, Max	16,7; 100,0	-; -
Woche 161		
N ^c	11	0
Mittelwert (SD)	80,3 (31,2)	- (-)
Median (Q1; Q3)	100,0 (66,7; 100,0)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 165		
N ^c	9	0
Mittelwert (SD)	85,2 (28,2)	- (-)
Median (Q1; Q3)	100,0 (83,3; 100,0)	- (-; -)
Min, Max	16,7; 100,0	-; -
Woche 169		
N ^c	8	0
Mittelwert (SD)	82,3 (35,2)	- (-)
Median (Q1; Q3)	100,0 (79,2; 100,0)	- (-; -)
Min, Max	0,0; 100,0	-; -
Woche 173		
N ^c	7	0
Mittelwert (SD)	84,5 (34,2)	- (-)
Median (Q1; Q3)	100,0 (83,3; 100,0)	- (-; -)
Min, Max	8,3; 100,0	-; -
Woche 177		
N ^c	6	0
Mittelwert (SD)	81,9 (33,5)	- (-)

EORTC QLQ-C30 Emotionale Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	100,0 (75,0; 100,0)	- (-; -)
Min, Max	16,7; 100,0	-; -
Woche 181		
N ^c	4	0
Mittelwert (SD)	91,7 (16,7)	- (-)
Median (Q1; Q3)	100,0 (83,3; 100,0)	- (-; -)
Min, Max	66,7; 100,0	-; -
Woche 185		
N ^c	3	0
Mittelwert (SD)	69,4 (52,9)	- (-)
Median (Q1; Q3)	100,0 (8,3; 100,0)	- (-; -)
Min, Max	8,3; 100,0	-; -
Woche 189		
N ^c	1	0
Mittelwert (SD)	100,0 (-)	- (-)
Median (Q1; Q3)	100,0 (100,0; 100,0)	- (-; -)
Min, Max	100,0; 100,0	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Items; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		

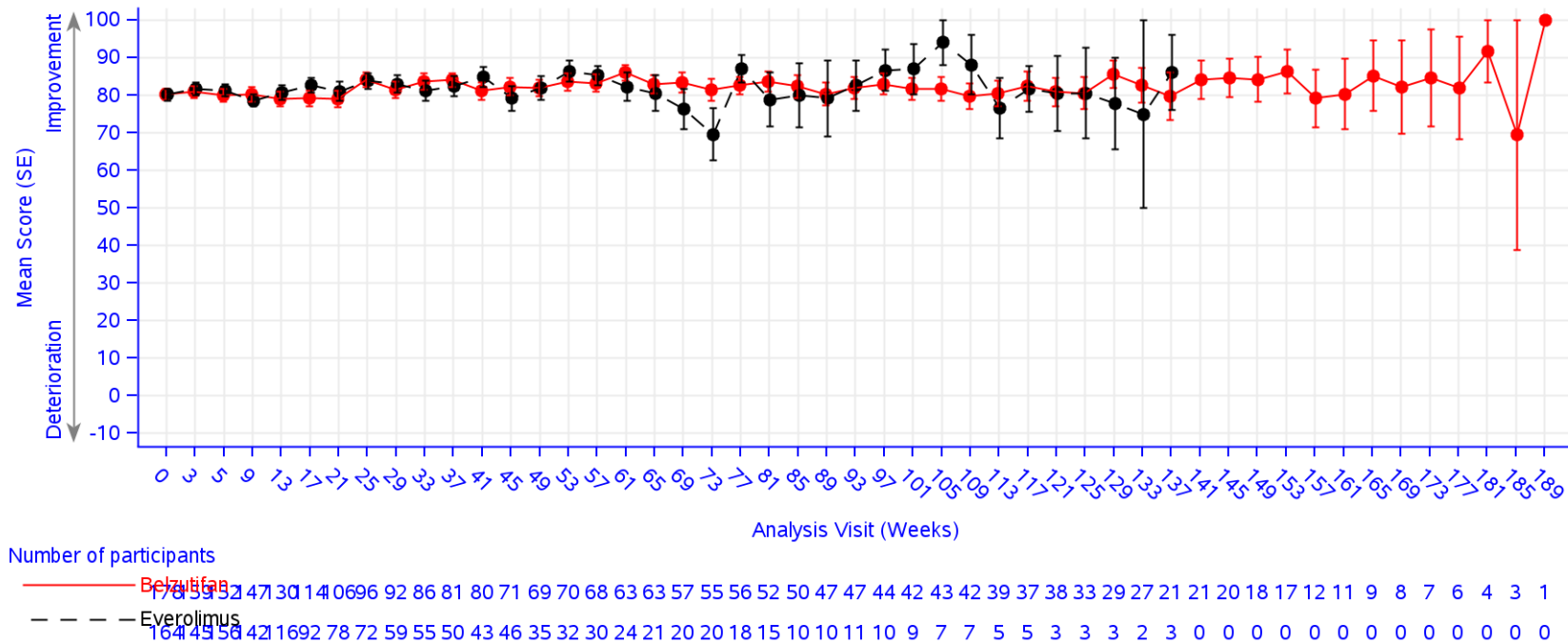


Abbildung 4G-14 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Emotionale Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Funktionsskala Kognitive Funktion

Tabelle 4G-20: Auswertung über den Studienverlauf der Funktionsskala Kognitive Funktion des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Kognitive Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	178	164
Mittelwert (SD)	88,3 (16,6)	87,9 (15,4)
Median (Q1; Q3)	100,0 (83,3; 100,0)	100,0 (83,3; 100,0)
Min, Max	16,7; 100,0	16,7; 100,0
Woche 3		
N ^c	159	145
Mittelwert (SD)	85,5 (20,2)	87,4 (15,1)
Median (Q1; Q3)	100,0 (83,3; 100,0)	83,3 (83,3; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 5		
N ^c	152	156
Mittelwert (SD)	83,8 (20,8)	85,9 (17,6)
Median (Q1; Q3)	91,7 (66,7; 100,0)	83,3 (83,3; 100,0)
Min, Max	16,7; 100,0	33,3; 100,0
Woche 9		
N ^c	147	142
Mittelwert (SD)	83,9 (22,4)	84,0 (19,1)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (83,3; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 13		
N ^c	130	116
Mittelwert (SD)	82,2 (20,9)	84,6 (16,9)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (83,3; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 17		
N ^c	114	92
Mittelwert (SD)	82,5 (19,8)	84,2 (20,0)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 21		
N ^c	106	78
Mittelwert (SD)	84,3 (20,3)	83,8 (21,3)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 25		
N ^c	96	72
Mittelwert (SD)	83,9 (19,9)	86,6 (16,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 29		
N ^c	92	59

EORTC QLQ-C30 Kognitive Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Mittelwert (SD)	84,2 (18,9)	88,1 (15,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	100,0 (83,3; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 33		
N ^c	86	55
Mittelwert (SD)	86,2 (20,2)	83,9 (17,0)
Median (Q1; Q3)	100,0 (83,3; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 37		
N ^c	81	50
Mittelwert (SD)	85,4 (21,1)	85,0 (16,6)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 41		
N ^c	80	43
Mittelwert (SD)	83,5 (21,0)	84,1 (19,2)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 45		
N ^c	71	46
Mittelwert (SD)	85,2 (20,6)	84,4 (17,0)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	50,0; 100,0
Woche 49		
N ^c	69	35
Mittelwert (SD)	84,5 (21,3)	86,2 (15,4)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 53		
N ^c	70	32
Mittelwert (SD)	86,0 (21,4)	84,9 (17,6)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	50,0; 100,0
Woche 57		
N ^c	68	30
Mittelwert (SD)	84,6 (20,0)	83,3 (17,0)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	33,3; 100,0	50,0; 100,0
Woche 61		
N ^c	63	24
Mittelwert (SD)	85,2 (22,0)	87,5 (14,1)
Median (Q1; Q3)	100,0 (66,7; 100,0)	91,7 (75,0; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 65		
N ^c	63	21
Mittelwert (SD)	84,4 (20,5)	80,2 (20,8)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)

EORTC QLQ-C30 Kognitive Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Min, Max	0,0; 100,0	33,3; 100,0
Woche 69		
N ^c	57	20
Mittelwert (SD)	86,5 (18,2)	81,7 (18,7)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	33,3; 100,0
Woche 73		
N ^c	55	20
Mittelwert (SD)	83,3 (20,0)	74,2 (23,2)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 83,3)
Min, Max	33,3; 100,0	0,0; 100,0
Woche 77		
N ^c	56	18
Mittelwert (SD)	85,4 (19,1)	88,0 (13,8)
Median (Q1; Q3)	100,0 (66,7; 100,0)	91,7 (83,3; 100,0)
Min, Max	16,7; 100,0	66,7; 100,0
Woche 81		
N ^c	52	15
Mittelwert (SD)	82,7 (21,1)	83,3 (15,4)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 85		
N ^c	50	10
Mittelwert (SD)	81,3 (24,4)	81,7 (16,6)
Median (Q1; Q3)	91,7 (66,7; 100,0)	75,0 (66,7; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 89		
N ^c	47	10
Mittelwert (SD)	82,3 (22,9)	80,0 (15,3)
Median (Q1; Q3)	100,0 (66,7; 100,0)	75,0 (66,7; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 93		
N ^c	47	11
Mittelwert (SD)	83,3 (21,7)	89,4 (13,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	100,0 (83,3; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 97		
N ^c	44	10
Mittelwert (SD)	82,6 (24,1)	86,7 (13,1)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (83,3; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 101		
N ^c	42	9
Mittelwert (SD)	80,2 (22,2)	83,3 (11,8)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (83,3; 83,3)
Min, Max	0,0; 100,0	66,7; 100,0

EORTC QLQ-C30 Kognitive Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Woche 105		
N ^c	43	7
Mittelwert (SD)	81,4 (22,2)	83,3 (13,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 109		
N ^c	42	7
Mittelwert (SD)	82,9 (24,0)	83,3 (16,7)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 113		
N ^c	39	5
Mittelwert (SD)	80,8 (23,4)	80,0 (13,9)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 83,3)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 117		
N ^c	37	5
Mittelwert (SD)	82,9 (24,1)	76,7 (14,9)
Median (Q1; Q3)	100,0 (66,7; 100,0)	66,7 (66,7; 83,3)
Min, Max	16,7; 100,0	66,7; 100,0
Woche 121		
N ^c	38	3
Mittelwert (SD)	79,4 (25,2)	83,3 (16,7)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	66,7; 100,0
Woche 125		
N ^c	33	3
Mittelwert (SD)	84,8 (21,4)	88,9 (19,2)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 129		
N ^c	29	3
Mittelwert (SD)	86,2 (20,9)	88,9 (19,2)
Median (Q1; Q3)	100,0 (83,3; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 133		
N ^c	27	2
Mittelwert (SD)	85,2 (25,0)	83,3 (23,6)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 137		
N ^c	21	3
Mittelwert (SD)	84,1 (28,1)	77,8 (19,2)
Median (Q1; Q3)	100,0 (83,3; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 141		

EORTC QLQ-C30 Kognitive Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
N ^c	21	0
Mittelwert (SD)	89,7 (17,1)	- (-)
Median (Q1; Q3)	100,0 (83,3; 100,0)	- (-; -)
Min, Max	50,0; 100,0	-; -
Woche 145		
N ^c	20	0
Mittelwert (SD)	90,0 (15,7)	- (-)
Median (Q1; Q3)	100,0 (83,3; 100,0)	- (-; -)
Min, Max	50,0; 100,0	-; -
Woche 149		
N ^c	18	0
Mittelwert (SD)	91,7 (13,1)	- (-)
Median (Q1; Q3)	100,0 (83,3; 100,0)	- (-; -)
Min, Max	66,7; 100,0	-; -
Woche 153		
N ^c	17	0
Mittelwert (SD)	91,2 (13,3)	- (-)
Median (Q1; Q3)	100,0 (83,3; 100,0)	- (-; -)
Min, Max	66,7; 100,0	-; -
Woche 157		
N ^c	12	0
Mittelwert (SD)	90,3 (13,2)	- (-)
Median (Q1; Q3)	100,0 (83,3; 100,0)	- (-; -)
Min, Max	66,7; 100,0	-; -
Woche 161		
N ^c	11	0
Mittelwert (SD)	86,4 (18,0)	- (-)
Median (Q1; Q3)	100,0 (66,7; 100,0)	- (-; -)
Min, Max	50,0; 100,0	-; -
Woche 165		
N ^c	9	0
Mittelwert (SD)	90,7 (14,7)	- (-)
Median (Q1; Q3)	100,0 (83,3; 100,0)	- (-; -)
Min, Max	66,7; 100,0	-; -
Woche 169		
N ^c	8	0
Mittelwert (SD)	85,4 (24,3)	- (-)
Median (Q1; Q3)	100,0 (75,0; 100,0)	- (-; -)
Min, Max	33,3; 100,0	-; -
Woche 173		
N ^c	7	0
Mittelwert (SD)	88,1 (24,9)	- (-)
Median (Q1; Q3)	100,0 (83,3; 100,0)	- (-; -)
Min, Max	33,3; 100,0	-; -
Woche 177		
N ^c	6	0
Mittelwert (SD)	88,9 (20,2)	- (-)

EORTC QLQ-C30 Kognitive Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	100,0 (83,3; 100,0)	- (-; -)
Min, Max	50,0; 100,0	-; -
Woche 181		
N ^c	4	0
Mittelwert (SD)	95,8 (8,3)	- (-)
Median (Q1; Q3)	100,0 (91,7; 100,0)	- (-; -)
Min, Max	83,3; 100,0	-; -
Woche 185		
N ^c	3	0
Mittelwert (SD)	77,8 (38,5)	- (-)
Median (Q1; Q3)	100,0 (33,3; 100,0)	- (-; -)
Min, Max	33,3; 100,0	-; -
Woche 189		
N ^c	1	0
Mittelwert (SD)	100,0 (-)	- (-)
Median (Q1; Q3)	100,0 (100,0; 100,0)	- (-; -)
Min, Max	100,0; 100,0	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Items; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		

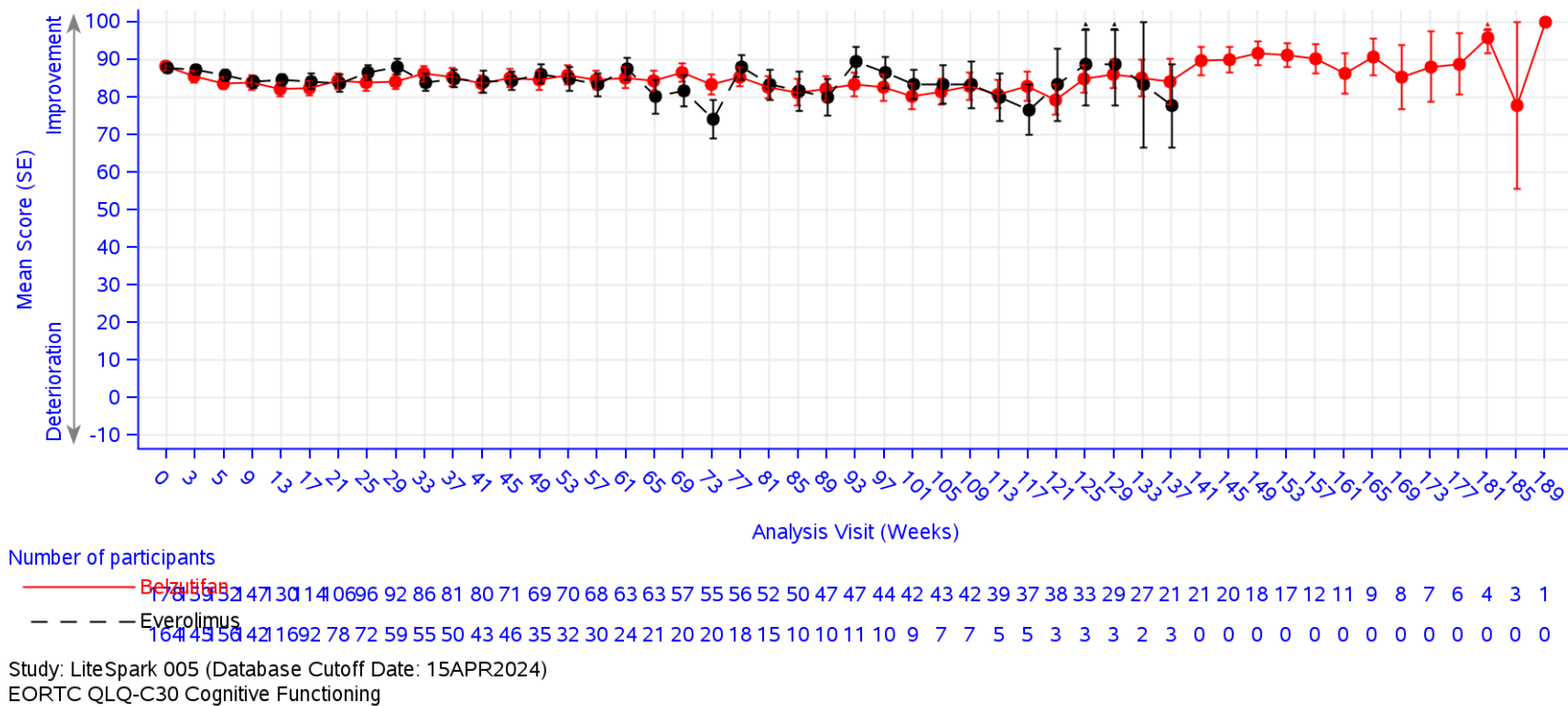


Abbildung 4G-15 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Kognitive Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30: Funktionsskala Soziale Funktion

Tabelle 4G-21: Auswertung über den Studienverlauf der Funktionsskala Soziale Funktion des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

EORTC QLQ-C30 Soziale Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Baseline		
N ^c	178	164
Mittelwert (SD)	80,5 (23,9)	79,3 (23,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 3		
N ^c	159	145
Mittelwert (SD)	80,2 (25,5)	81,1 (21,9)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 5		
N ^c	152	156
Mittelwert (SD)	79,9 (25,3)	78,7 (22,8)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 9		
N ^c	147	142
Mittelwert (SD)	81,4 (23,9)	74,5 (26,0)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 13		
N ^c	130	116
Mittelwert (SD)	80,9 (23,7)	76,0 (25,4)
Median (Q1; Q3)	83,3 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 17		
N ^c	114	92
Mittelwert (SD)	82,9 (22,4)	77,9 (26,0)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 21		
N ^c	106	78
Mittelwert (SD)	79,2 (26,8)	76,7 (27,8)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 25		
N ^c	96	72
Mittelwert (SD)	83,0 (22,4)	80,3 (24,3)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 29		
N ^c	92	59
Mittelwert (SD)	85,9 (20,8)	82,2 (22,1)

EORTC QLQ-C30 Soziale Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	16,7; 100,0	33,3; 100,0
Woche 33		
N ^c	86	55
Mittelwert (SD)	85,9 (20,4)	81,5 (23,5)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	33,3; 100,0	16,7; 100,0
Woche 37		
N ^c	81	50
Mittelwert (SD)	84,4 (20,0)	77,3 (24,9)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	33,3; 100,0	0,0; 100,0
Woche 41		
N ^c	80	43
Mittelwert (SD)	85,4 (21,8)	77,9 (26,4)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 45		
N ^c	71	46
Mittelwert (SD)	83,6 (23,1)	79,0 (25,4)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	16,7; 100,0
Woche 49		
N ^c	69	35
Mittelwert (SD)	84,5 (21,1)	81,4 (24,8)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	0,0; 100,0
Woche 53		
N ^c	70	32
Mittelwert (SD)	83,8 (21,0)	80,7 (21,2)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	33,3; 100,0	33,3; 100,0
Woche 57		
N ^c	68	30
Mittelwert (SD)	83,3 (21,5)	82,8 (22,5)
Median (Q1; Q3)	100,0 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	16,7; 100,0	0,0; 100,0
Woche 61		
N ^c	63	24
Mittelwert (SD)	86,2 (19,3)	81,3 (19,2)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	33,3; 100,0	33,3; 100,0
Woche 65		
N ^c	63	21
Mittelwert (SD)	82,3 (25,0)	81,7 (25,8)
Median (Q1; Q3)	100,0 (66,7; 100,0)	100,0 (66,7; 100,0)

EORTC QLQ-C30 Soziale Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Min, Max	0,0; 100,0	0,0; 100,0
Woche 69		
N ^c	57	20
Mittelwert (SD)	86,5 (18,8)	80,8 (21,8)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	16,7; 100,0	33,3; 100,0
Woche 73		
N ^c	55	20
Mittelwert (SD)	78,5 (27,2)	76,7 (23,8)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 77		
N ^c	56	18
Mittelwert (SD)	79,8 (21,5)	83,3 (22,9)
Median (Q1; Q3)	83,3 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	33,3; 100,0	33,3; 100,0
Woche 81		
N ^c	52	15
Mittelwert (SD)	82,1 (20,3)	82,2 (24,8)
Median (Q1; Q3)	83,3 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	33,3; 100,0	33,3; 100,0
Woche 85		
N ^c	50	10
Mittelwert (SD)	80,7 (27,6)	76,7 (23,8)
Median (Q1; Q3)	100,0 (66,7; 100,0)	75,0 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 89		
N ^c	47	10
Mittelwert (SD)	77,0 (26,6)	80,0 (24,6)
Median (Q1; Q3)	83,3 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 93		
N ^c	47	11
Mittelwert (SD)	81,6 (25,6)	83,3 (18,3)
Median (Q1; Q3)	100,0 (66,7; 100,0)	83,3 (66,7; 100,0)
Min, Max	0,0; 100,0	50,0; 100,0
Woche 97		
N ^c	44	10
Mittelwert (SD)	78,0 (28,3)	85,0 (16,6)
Median (Q1; Q3)	100,0 (66,7; 100,0)	91,7 (66,7; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 101		
N ^c	42	9
Mittelwert (SD)	81,3 (24,2)	90,7 (14,7)
Median (Q1; Q3)	91,7 (66,7; 100,0)	100,0 (83,3; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0

EORTC QLQ-C30 Soziale Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Woche 105		
N ^c	43	7
Mittelwert (SD)	80,2 (25,3)	90,5 (16,3)
Median (Q1; Q3)	83,3 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	66,7; 100,0
Woche 109		
N ^c	42	7
Mittelwert (SD)	77,4 (26,0)	83,3 (21,5)
Median (Q1; Q3)	83,3 (66,7; 100,0)	100,0 (66,7; 100,0)
Min, Max	0,0; 100,0	50,0; 100,0
Woche 113		
N ^c	39	5
Mittelwert (SD)	74,4 (28,3)	76,7 (22,4)
Median (Q1; Q3)	83,3 (66,7; 100,0)	66,7 (66,7; 100,0)
Min, Max	0,0; 100,0	50,0; 100,0
Woche 117		
N ^c	37	5
Mittelwert (SD)	82,0 (25,0)	70,0 (24,7)
Median (Q1; Q3)	100,0 (66,7; 100,0)	66,7 (66,7; 83,3)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 121		
N ^c	38	3
Mittelwert (SD)	81,1 (26,3)	38,9 (25,5)
Median (Q1; Q3)	100,0 (66,7; 100,0)	33,3 (16,7; 66,7)
Min, Max	33,3; 100,0	16,7; 66,7
Woche 125		
N ^c	33	3
Mittelwert (SD)	81,8 (27,4)	66,7 (33,3)
Median (Q1; Q3)	100,0 (66,7; 100,0)	66,7 (33,3; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 129		
N ^c	29	3
Mittelwert (SD)	84,5 (26,3)	55,6 (38,5)
Median (Q1; Q3)	100,0 (66,7; 100,0)	33,3 (33,3; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 133		
N ^c	27	2
Mittelwert (SD)	80,2 (27,4)	66,7 (47,1)
Median (Q1; Q3)	100,0 (66,7; 100,0)	66,7 (33,3; 100,0)
Min, Max	0,0; 100,0	33,3; 100,0
Woche 137		
N ^c	21	3
Mittelwert (SD)	83,3 (26,9)	50,0 (16,7)
Median (Q1; Q3)	100,0 (66,7; 100,0)	50,0 (33,3; 66,7)
Min, Max	0,0; 100,0	33,3; 66,7
Woche 141		

EORTC QLQ-C30 Soziale Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
N ^c	21	0
Mittelwert (SD)	84,1 (22,0)	- (-)
Median (Q1; Q3)	100,0 (66,7; 100,0)	- (-; -)
Min, Max	16,7; 100,0	-; -
Woche 145		
N ^c	20	0
Mittelwert (SD)	85,8 (19,7)	- (-)
Median (Q1; Q3)	100,0 (66,7; 100,0)	- (-; -)
Min, Max	33,3; 100,0	-; -
Woche 149		
N ^c	18	0
Mittelwert (SD)	84,3 (22,5)	- (-)
Median (Q1; Q3)	100,0 (66,7; 100,0)	- (-; -)
Min, Max	16,7; 100,0	-; -
Woche 153		
N ^c	17	0
Mittelwert (SD)	85,3 (23,5)	- (-)
Median (Q1; Q3)	100,0 (66,7; 100,0)	- (-; -)
Min, Max	16,7; 100,0	-; -
Woche 157		
N ^c	12	0
Mittelwert (SD)	83,3 (23,6)	- (-)
Median (Q1; Q3)	100,0 (66,7; 100,0)	- (-; -)
Min, Max	33,3; 100,0	-; -
Woche 161		
N ^c	11	0
Mittelwert (SD)	77,3 (26,1)	- (-)
Median (Q1; Q3)	66,7 (66,7; 100,0)	- (-; -)
Min, Max	16,7; 100,0	-; -
Woche 165		
N ^c	9	0
Mittelwert (SD)	79,6 (28,6)	- (-)
Median (Q1; Q3)	100,0 (66,7; 100,0)	- (-; -)
Min, Max	16,7; 100,0	-; -
Woche 169		
N ^c	8	0
Mittelwert (SD)	81,3 (30,1)	- (-)
Median (Q1; Q3)	100,0 (66,7; 100,0)	- (-; -)
Min, Max	16,7; 100,0	-; -
Woche 173		
N ^c	7	0
Mittelwert (SD)	76,2 (30,2)	- (-)
Median (Q1; Q3)	83,3 (66,7; 100,0)	- (-; -)
Min, Max	16,7; 100,0	-; -
Woche 177		
N ^c	6	0
Mittelwert (SD)	72,2 (25,1)	- (-)

EORTC QLQ-C30 Soziale Funktion	Studie: LITESPARK 005 ^a	
	Belzutifan N ^b = 182	Everolimus N ^b = 174
Median (Q1; Q3)	66,7 (66,7; 100,0)	- (-; -)
Min, Max	33,3; 100,0	-; -
Woche 181		
N ^c	4	0
Mittelwert (SD)	87,5 (16,0)	- (-)
Median (Q1; Q3)	91,7 (75,0; 100,0)	- (-; -)
Min, Max	66,7; 100,0	-; -
Woche 185		
N ^c	3	0
Mittelwert (SD)	72,2 (48,1)	- (-)
Median (Q1; Q3)	100,0 (16,7; 100,0)	- (-; -)
Min, Max	16,7; 100,0	-; -
Woche 189		
N ^c	1	0
Mittelwert (SD)	100,0 (-)	- (-)
Median (Q1; Q3)	100,0 (100,0; 100,0)	- (-; -)
Min, Max	100,0; 100,0	-; -
a: Database cutoff date: 15. April 2024 b: Anzahl der Patient:innen: Full-Analysis-Set Population mit zwei oder mehr vorherigen Therapielinien, darunter ein PD-(L)1-Inhibitor und mindestens zwei VEGF-gerichtete Therapien c: Anzahl der Beobachtungen zu jedem Zeitpunkt EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Items; Max: Maximum; Min: Minimum; Q1: Erstes Quartil; Q3: Drittes Quartil; SD: Standardabweichung PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death–Ligand 1; VEGF: Vascular Endothelial Growth Factor		

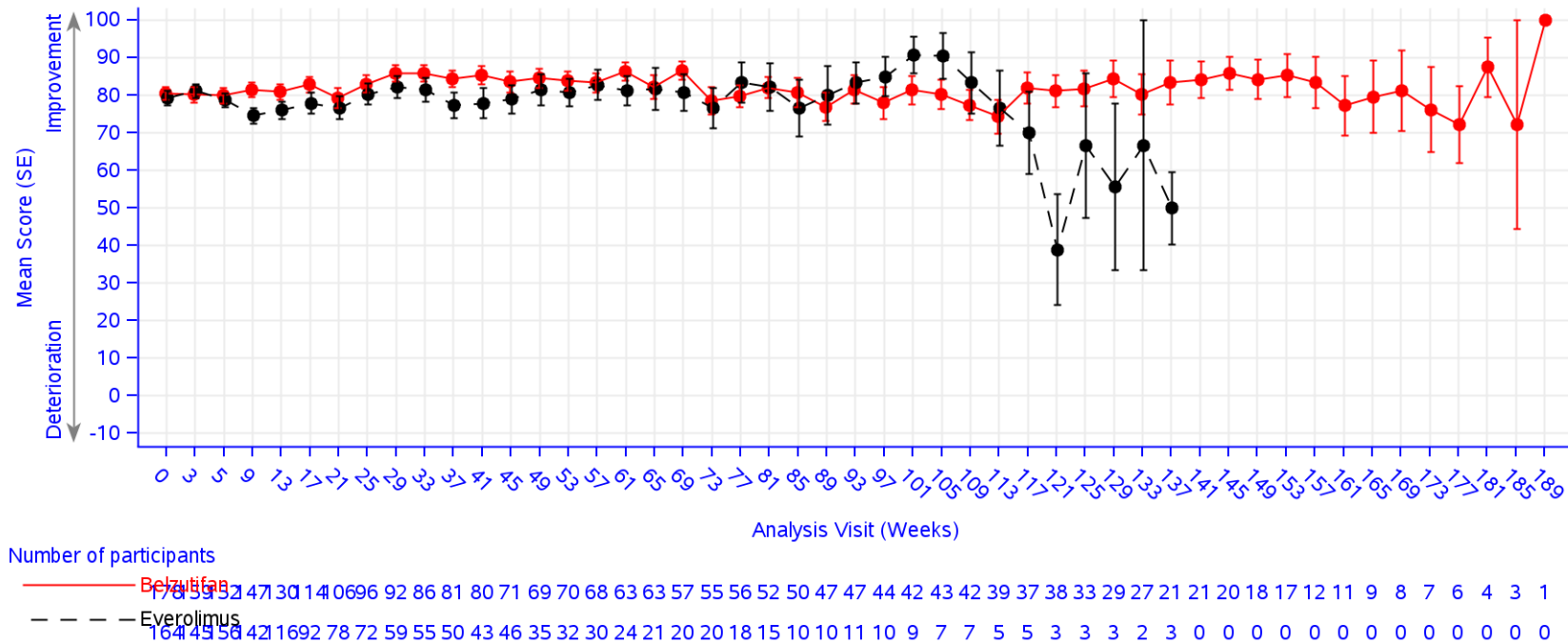
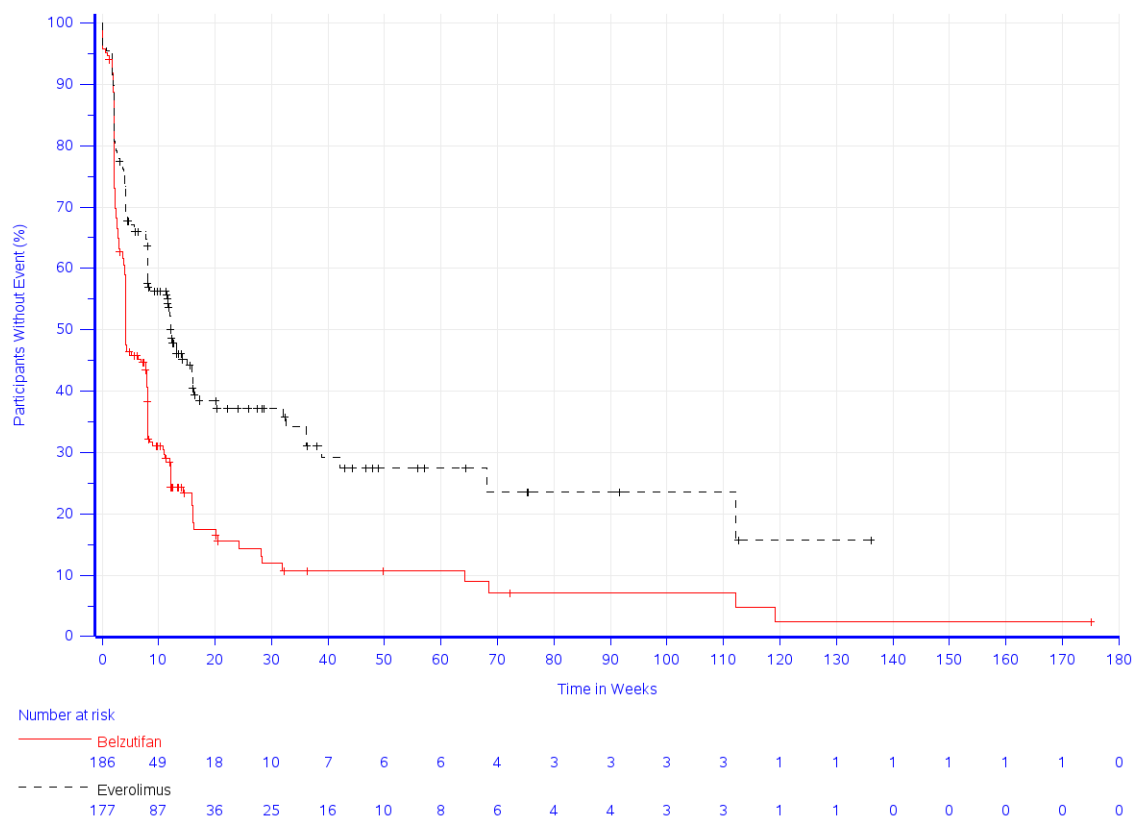


Abbildung 4G-16 Darstellung über den Studienverlauf: Mittelwert +/- Standardfehler der Funktionsskala Soziale Funktion zu den verschiedenen Erhebungszeitpunkten des EORTC QLQ-C30 aus der Studie LITESPARK 005 mit dem zu bewertenden Arzneimittel

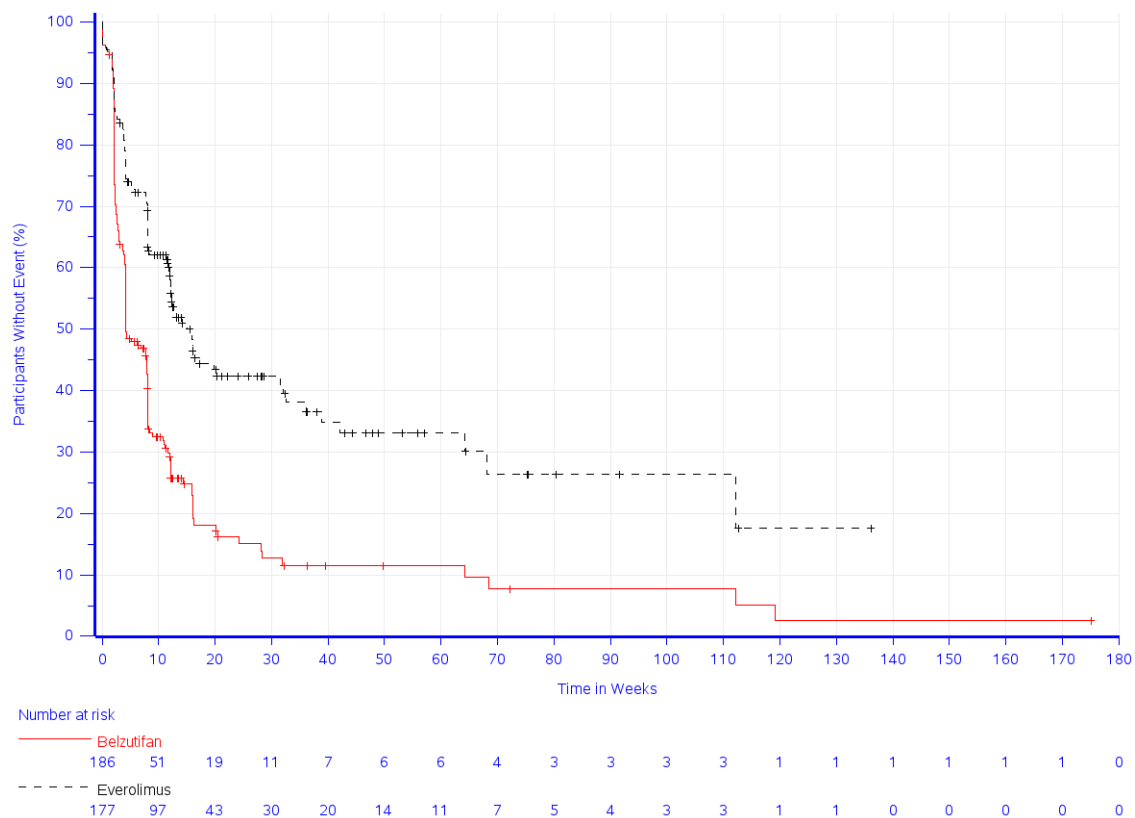
Anhang 4-G5: Kaplan-Meier-Kurven der signifikanten Unterschiede für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT)

Ergänzend zu Abschnitt 4.3.1.3.1.4.2 werden nachfolgend die Kaplan-Meier-Kurven der signifikanten Unterschiede dargestellt.



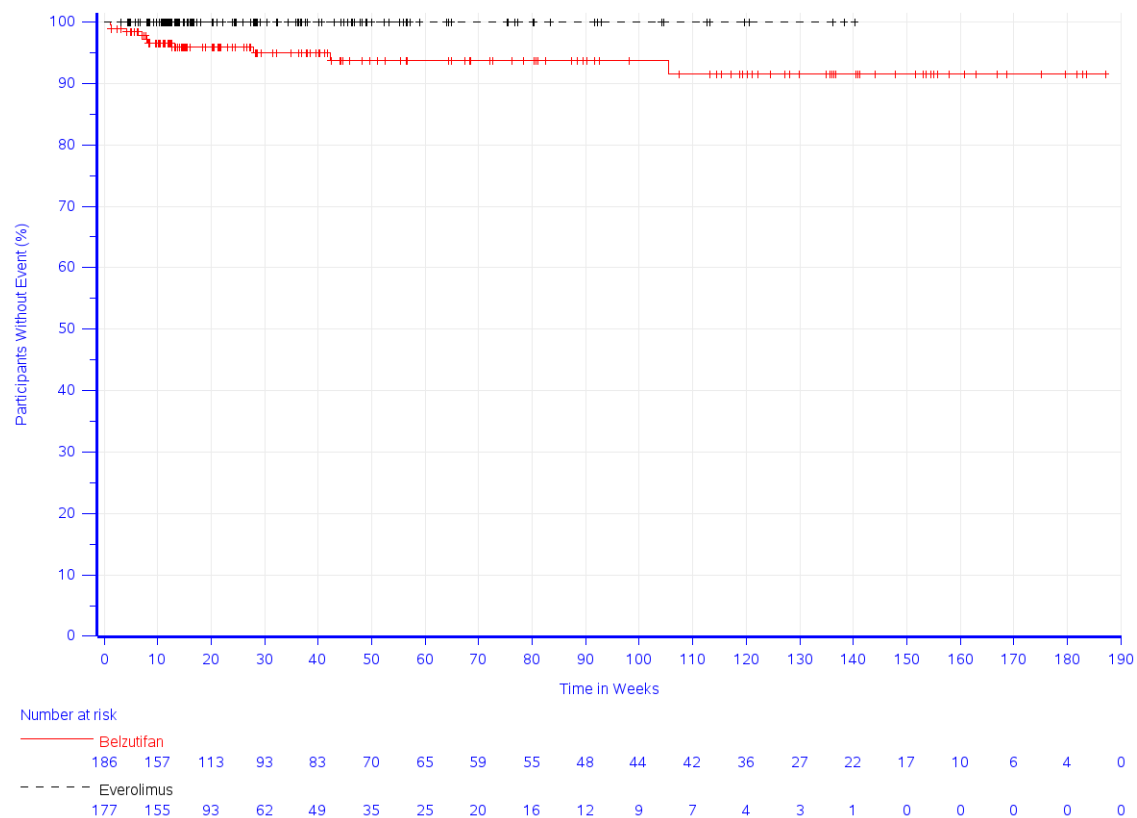
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
Adverse Event - System Organ Class: Blood and lymphatic system disorders

Abbildung 4G-17: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für die SOC Erkrankungen des Blutes und des Lymphsystems für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



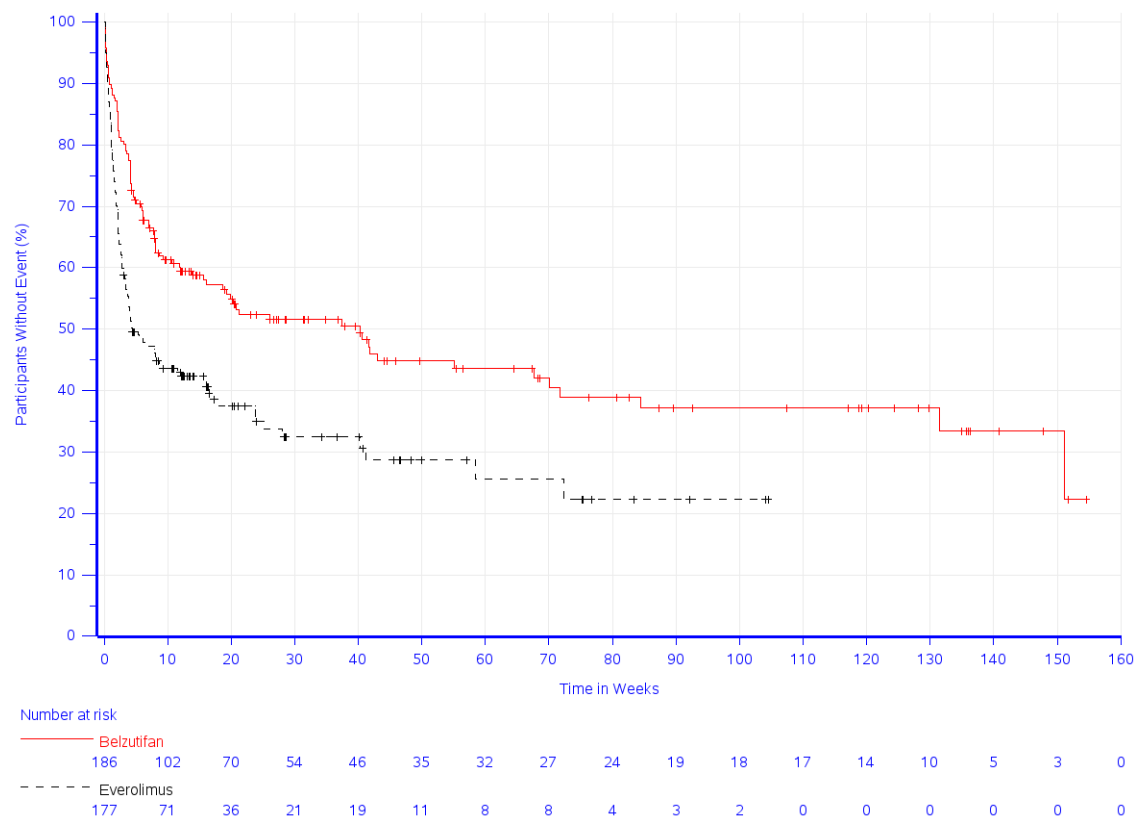
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
 Adverse Event - Preferred Term: Anaemia

Abbildung 4G-18: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Anaemie für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



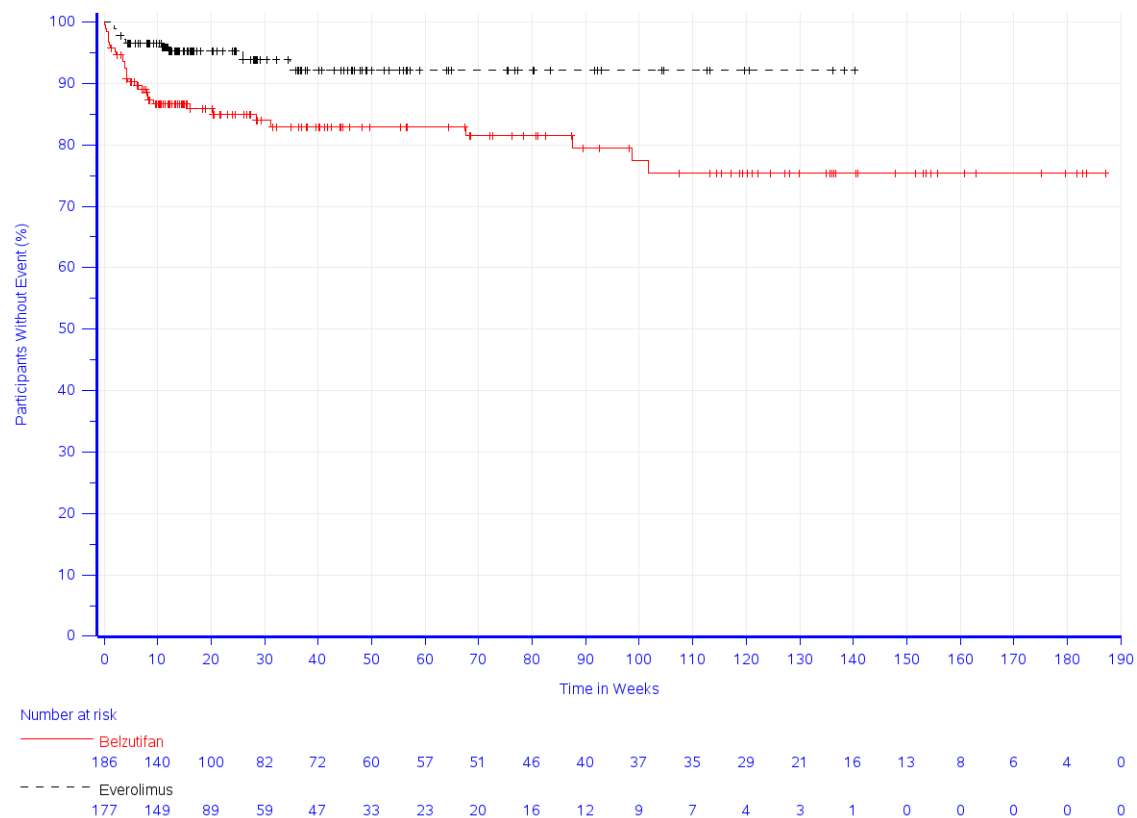
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
 Adverse Event - Preferred Term: Vision blurred

Abbildung 4G-19: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Sehen verschwommen für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



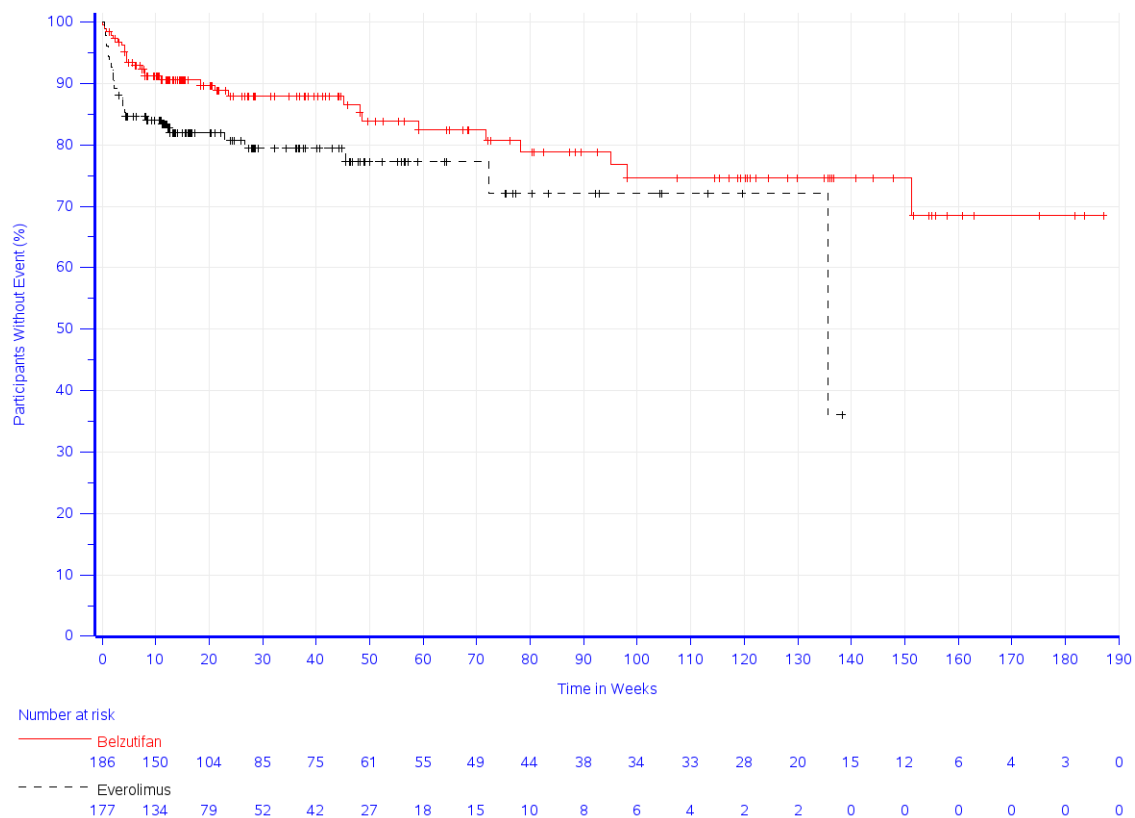
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
 Adverse Event - System Organ Class: Gastrointestinal disorders

Abbildung 4G-20: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für die SOC Erkrankungen des Gastrointestinaltrakts für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



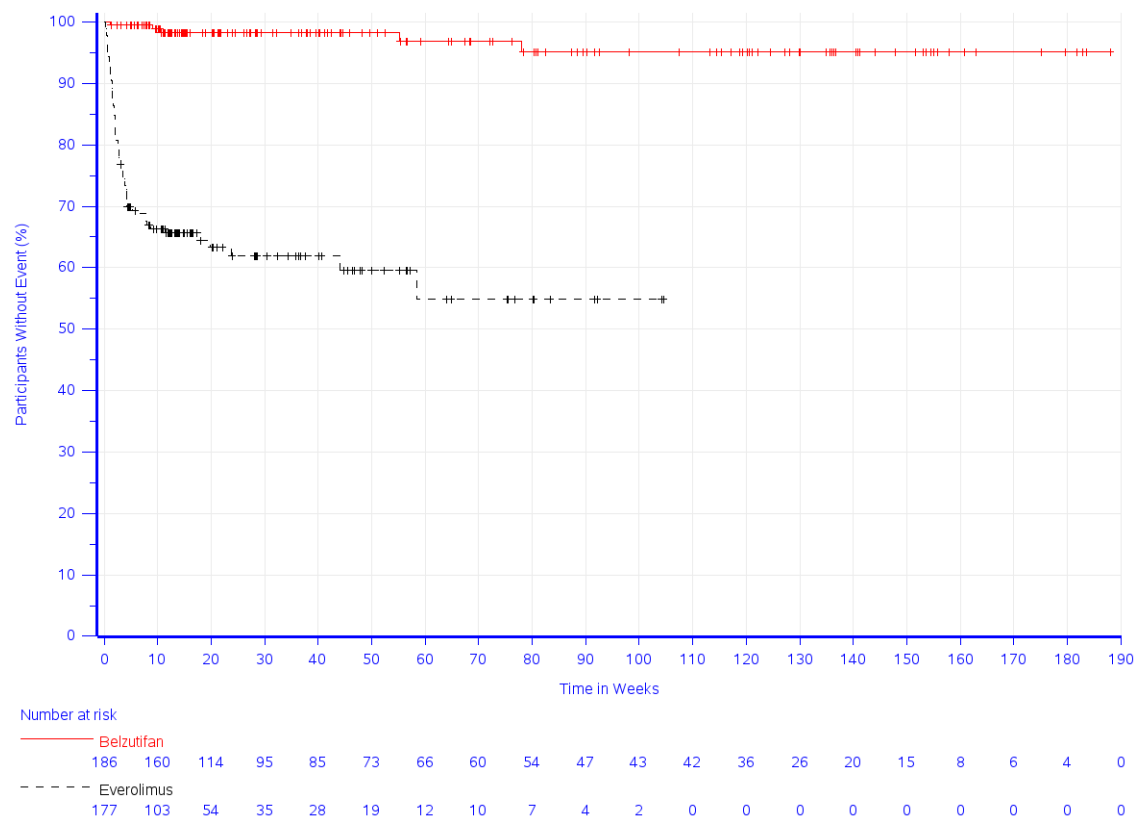
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
Adverse Event - Preferred Term: Constipation

Abbildung 4G-21: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Verstopfung für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



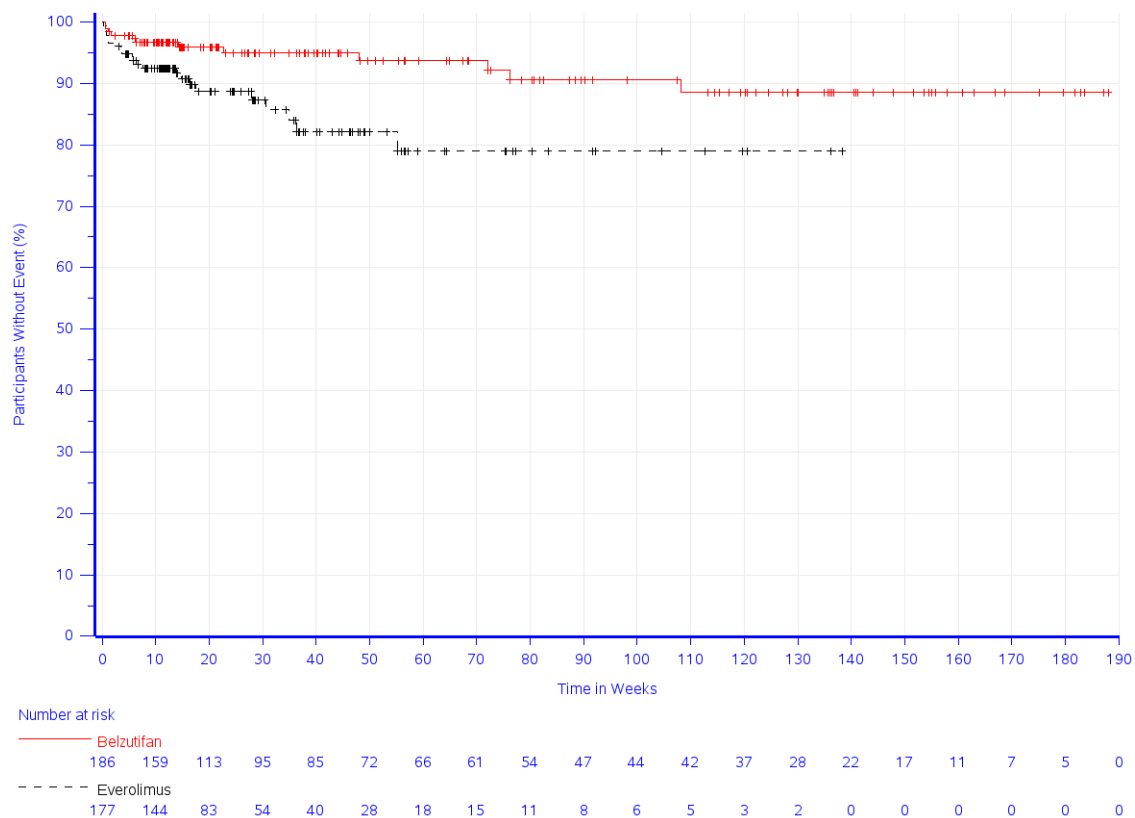
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
Adverse Event - Preferred Term: Diarrhoea

Abbildung 4G-22: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Diarrhoe für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



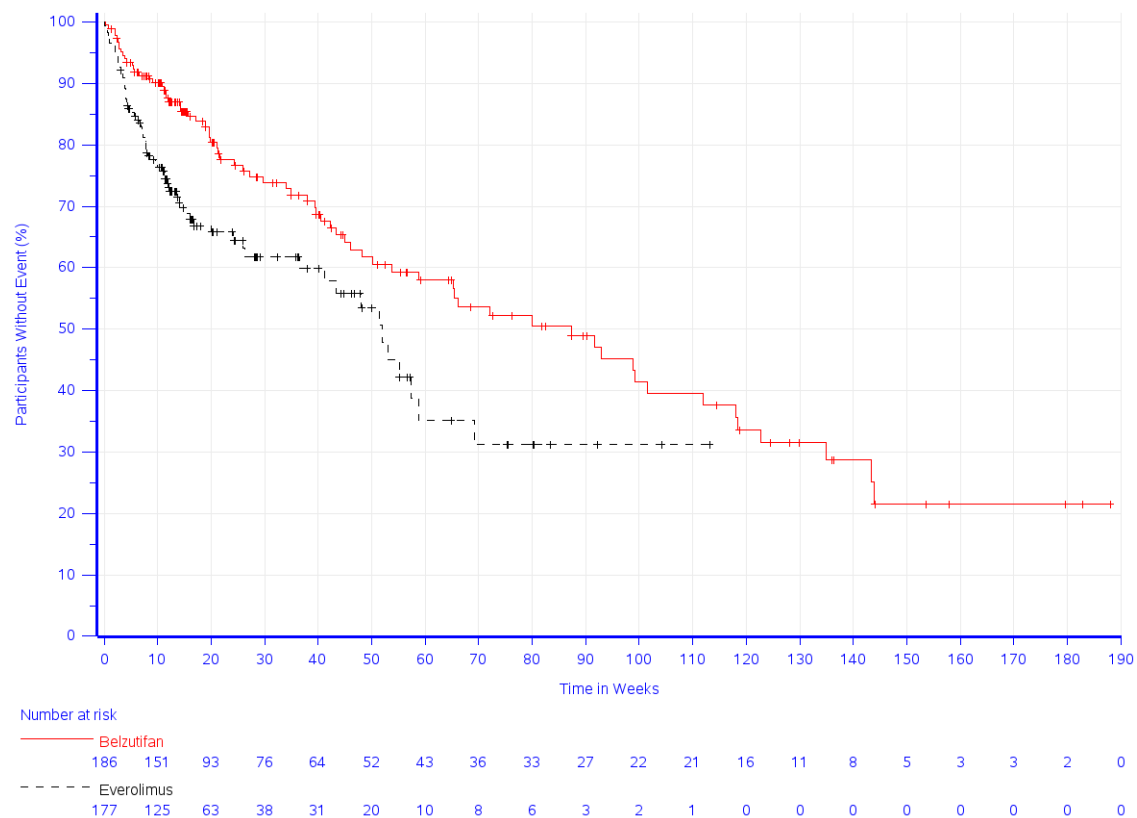
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
Adverse Event - Preferred Term: Stomatitis

Abbildung 4G-23: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Stomatitis für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
 Adverse Event - Preferred Term: Pyrexia

Abbildung 4G-24: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Fieber für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
 Adverse Event - System Organ Class: Infections and infestations

Abbildung 4G-25: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für die SOC Infektionen und parasitäre Erkrankungen für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005

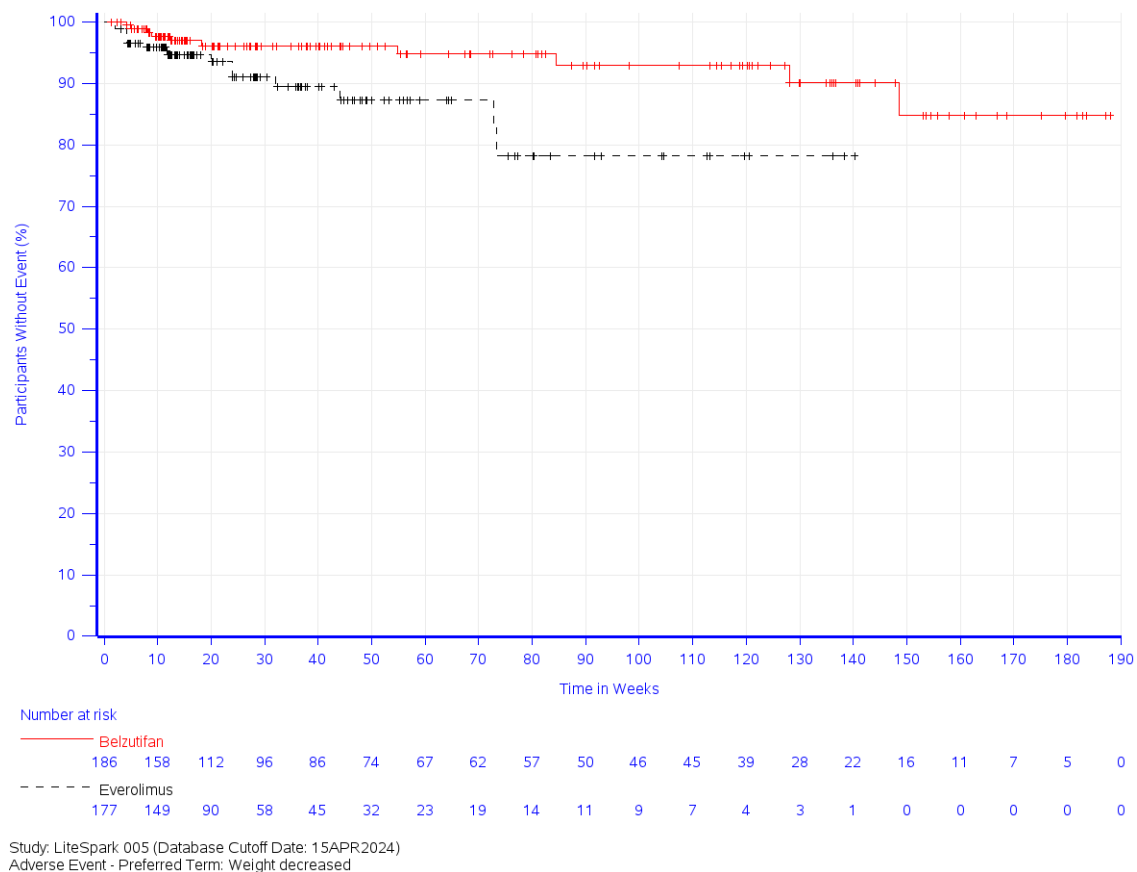
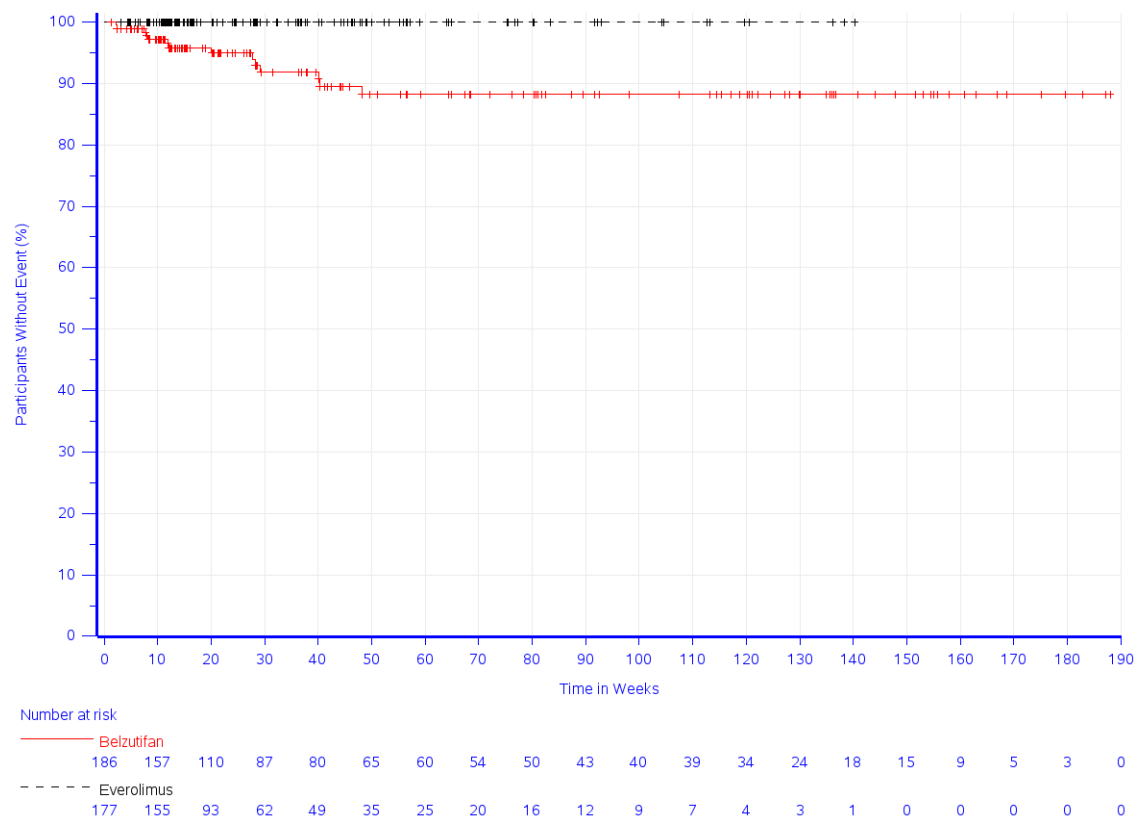
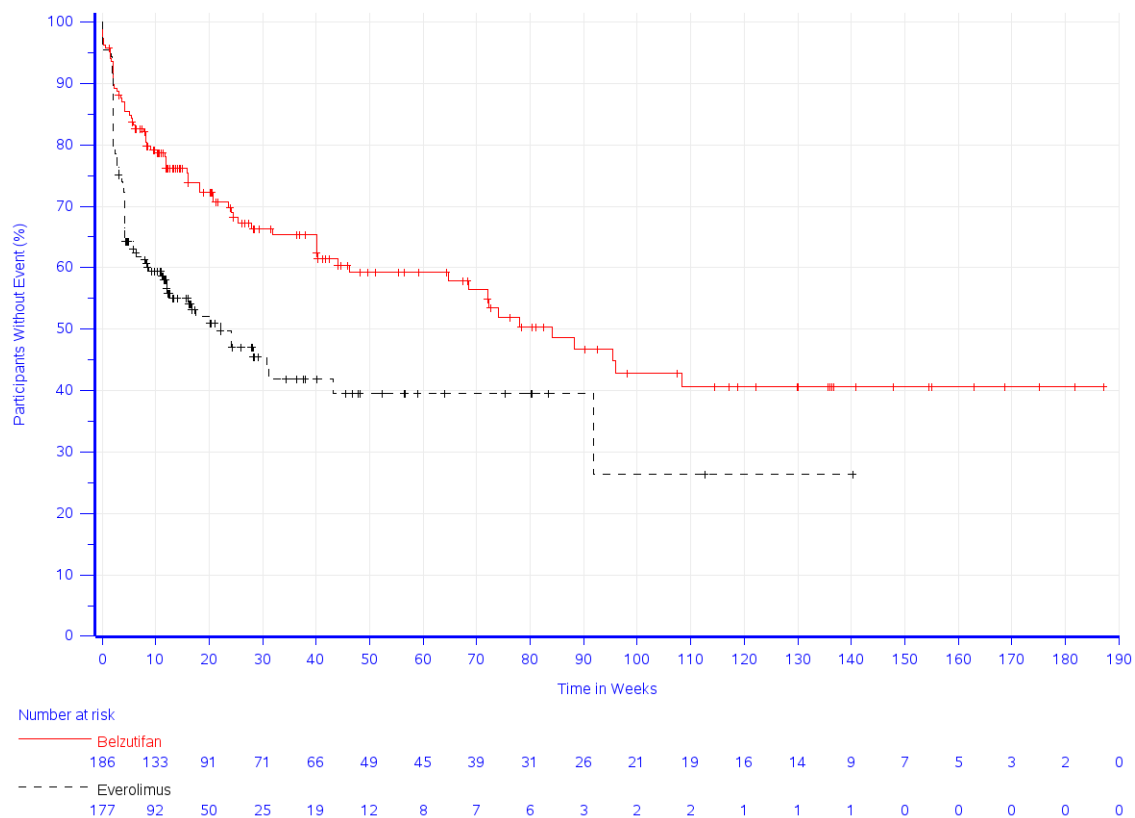


Abbildung 4G-26: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Gewicht erniedrigt für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



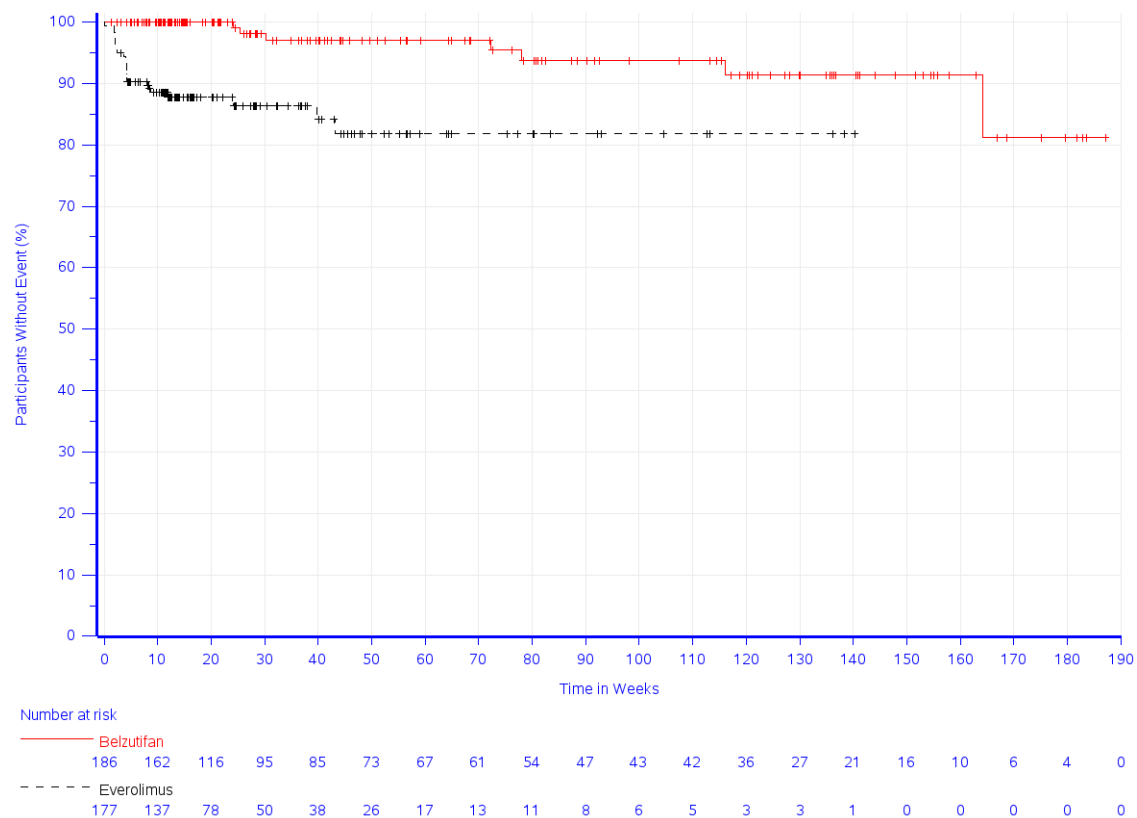
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
Adverse Event - Preferred Term: Weight increased

Abbildung 4G-27: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Gewicht erhöht für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



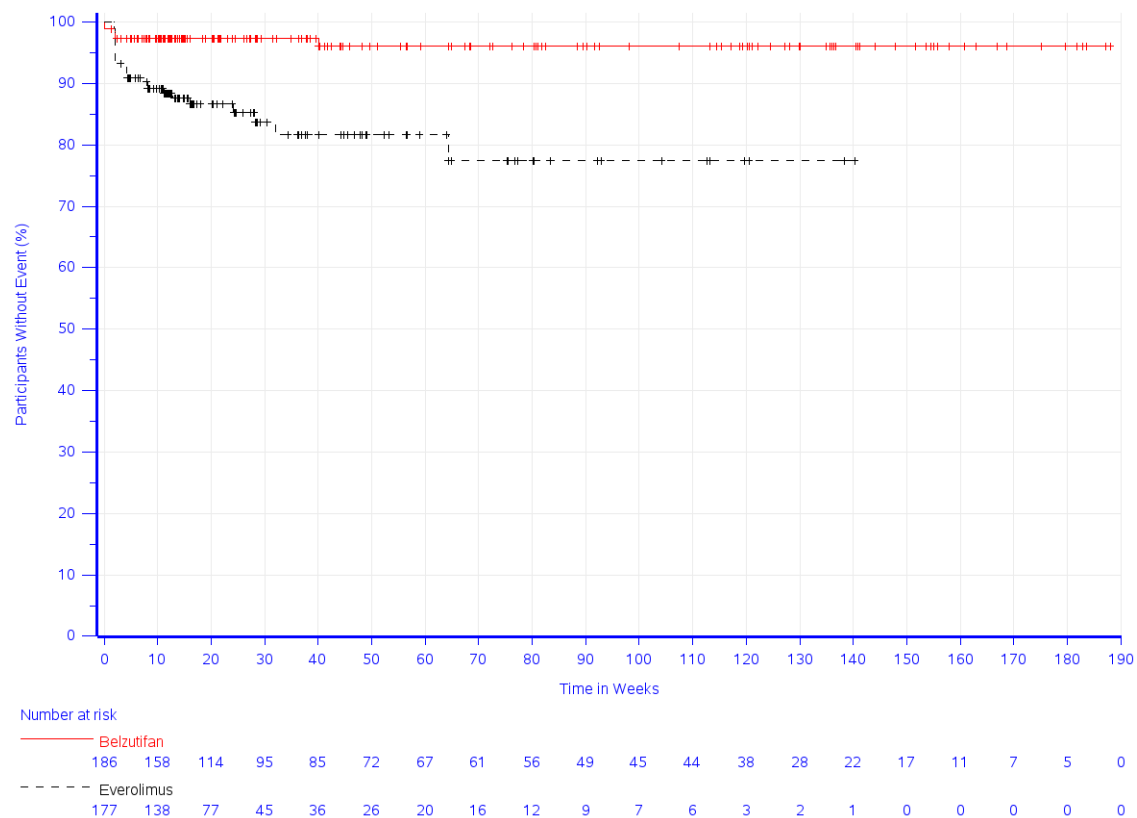
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
 Adverse Event - System Organ Class: Metabolism and nutrition disorders

Abbildung 4G-28: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für die SOC Stoffwechsel- und Ernährungsstörungen für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



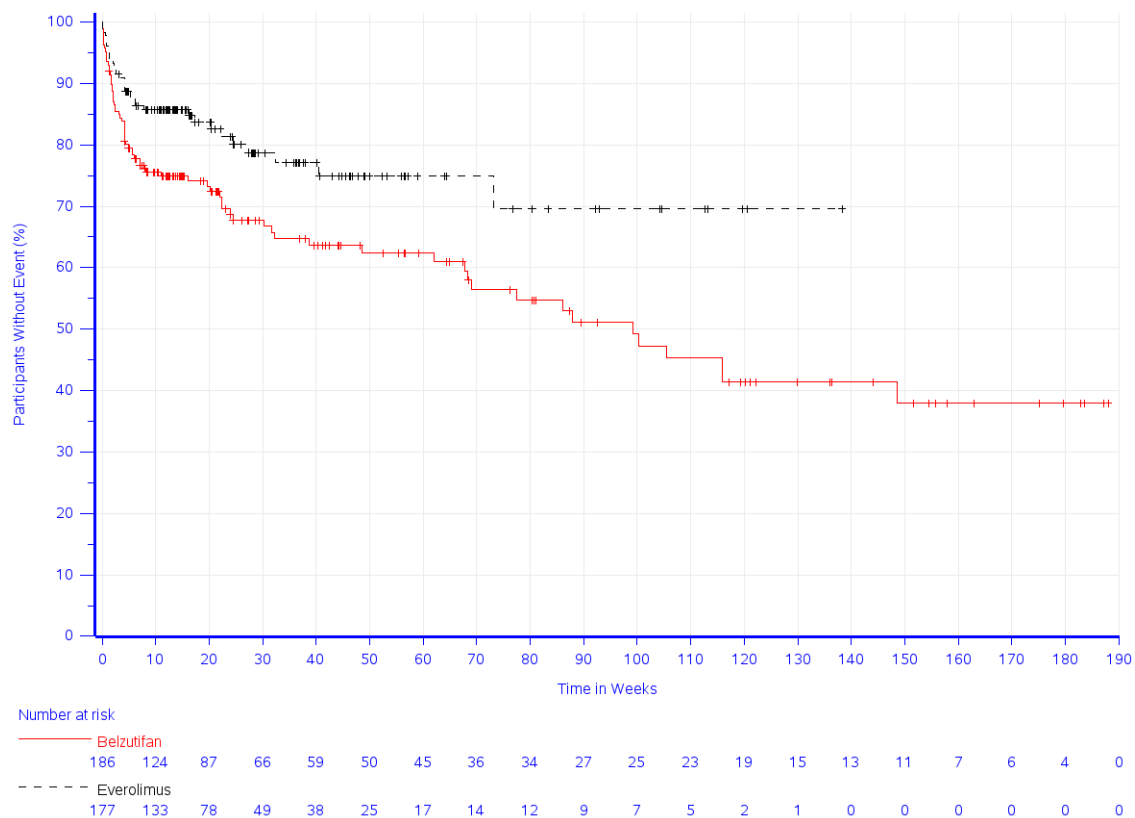
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
 Adverse Event - Preferred Term: Hyperglycaemia

Abbildung 4G-29: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Hyperglykaemie für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
 Adverse Event - Preferred Term: Hypertriglyceridaemia

Abbildung 4G-30: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Hypertriglyzeridaemie für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
 Adverse Event - System Organ Class: Nervous system disorders

Abbildung 4G-31: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für die SOC Erkrankungen des Nervensystems für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005

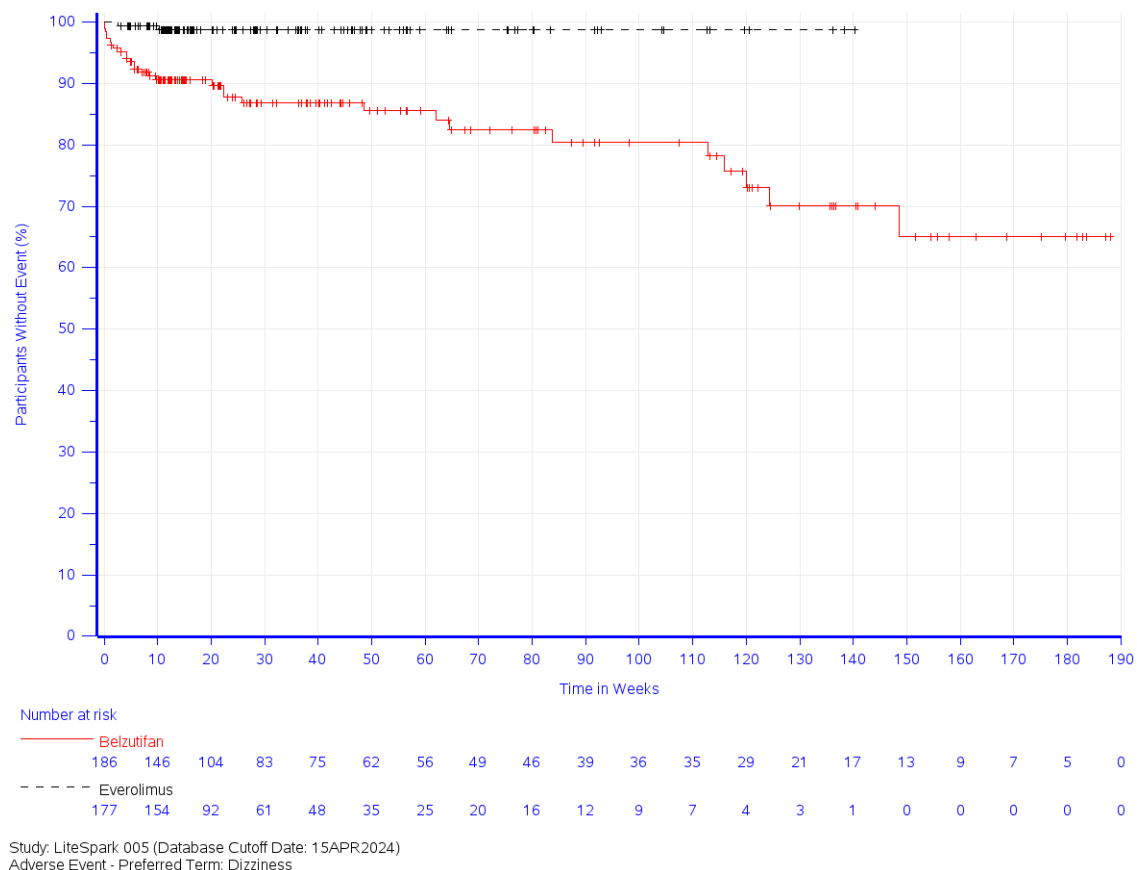
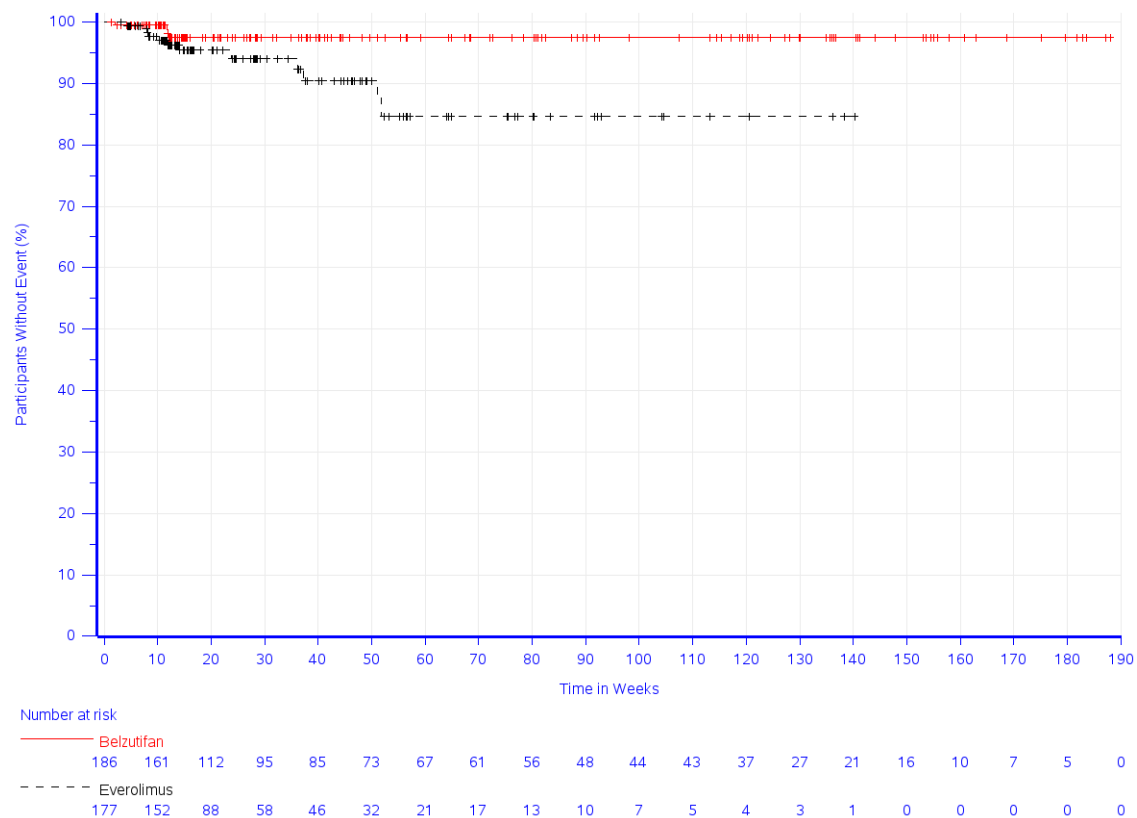
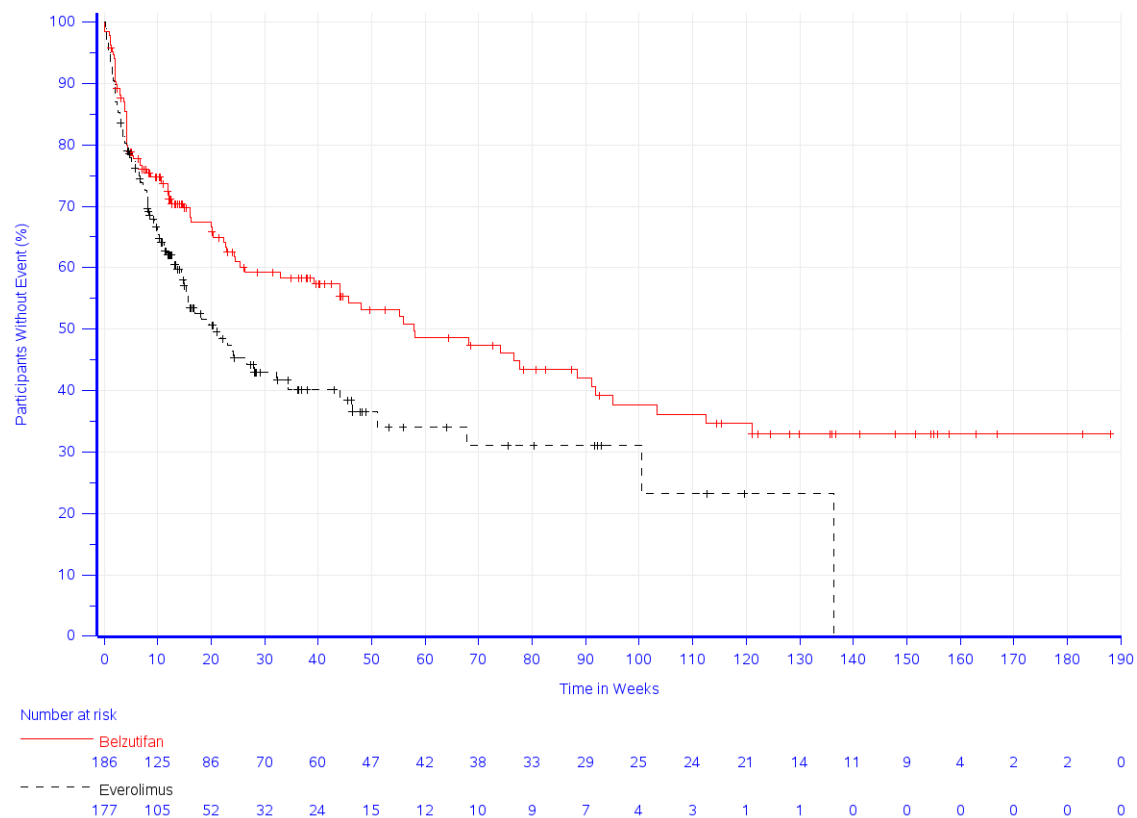


Abbildung 4G-32: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Schwindel für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



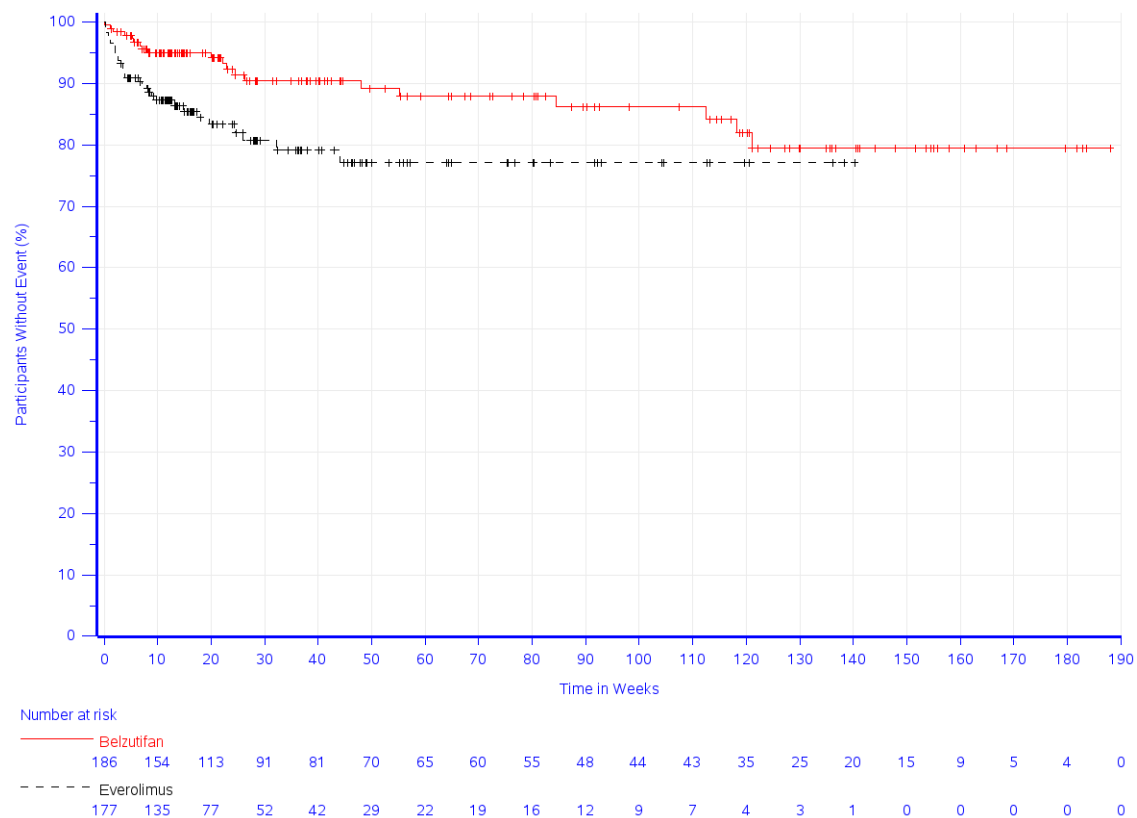
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
 Adverse Event - Preferred Term: Proteinuria

Abbildung 4G-33: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Proteinurie für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



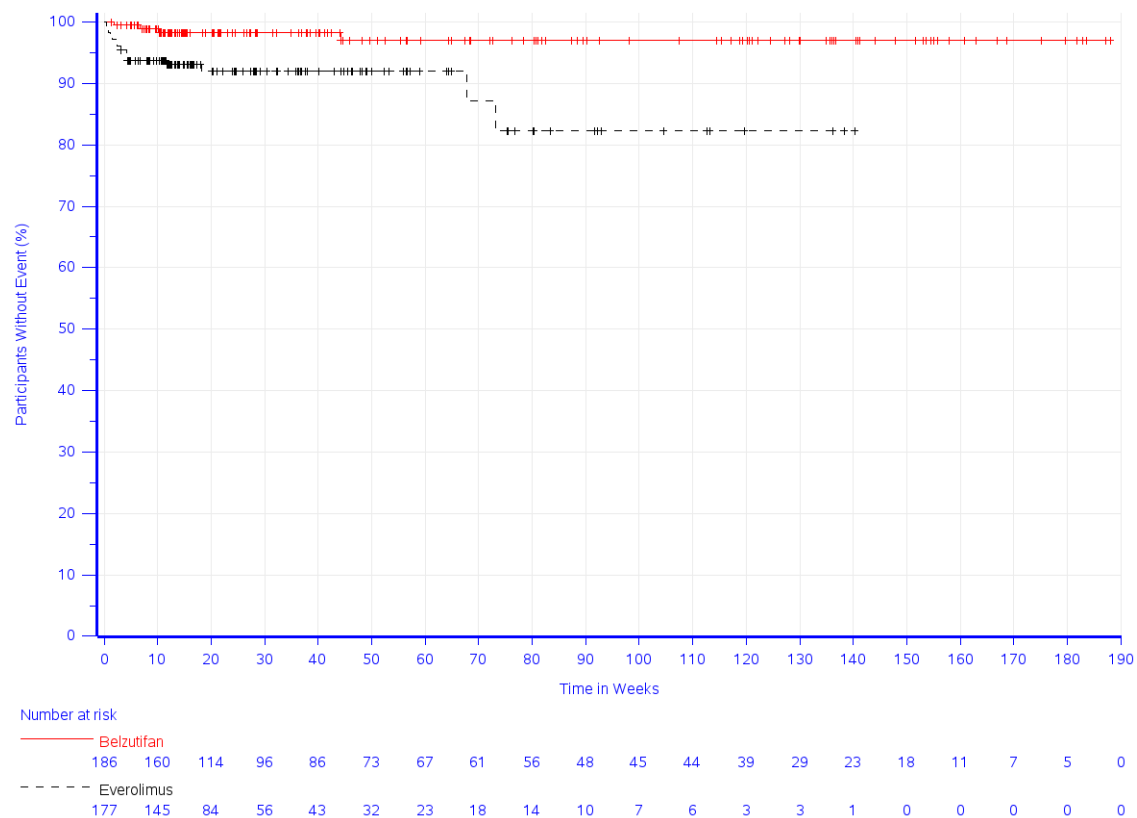
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
 Adverse Event - System Organ Class: Respiratory, thoracic and mediastinal disorders

Abbildung 4G-34: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für die SOC Erkrankungen der Atemwege, des Brustraums und Mediastinums für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



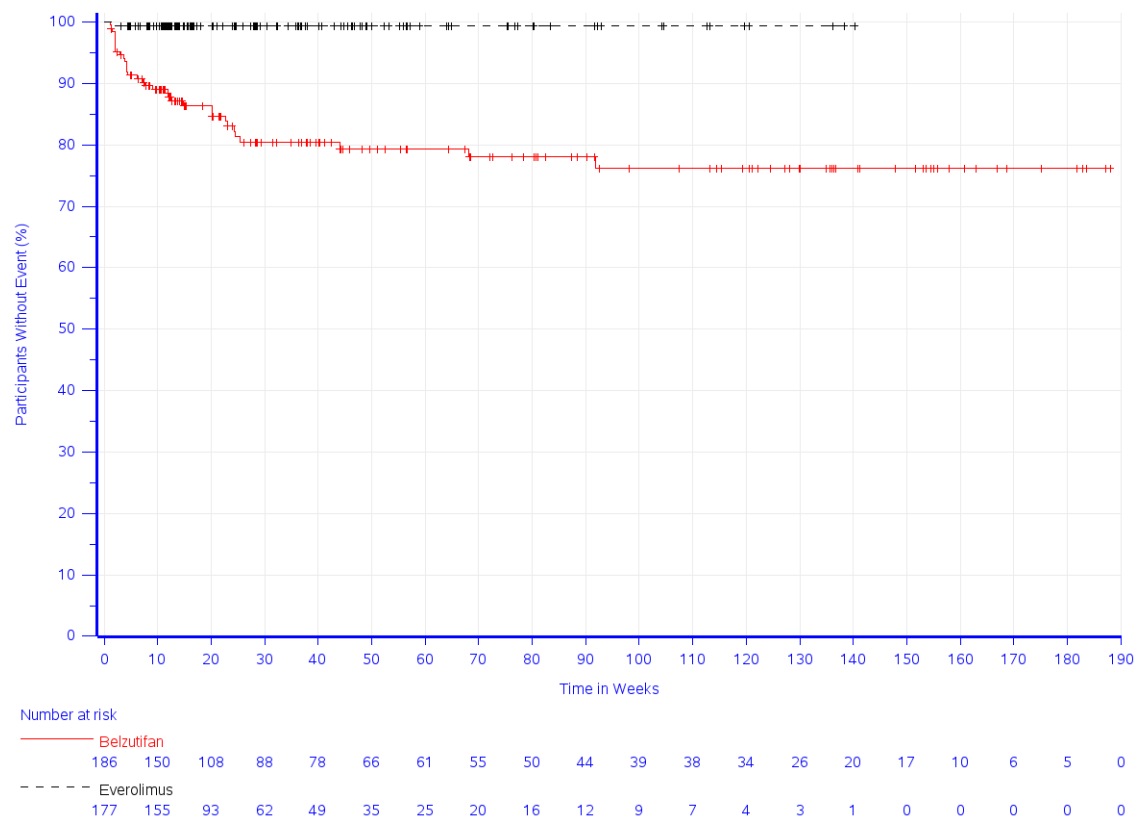
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
Adverse Event - Preferred Term: Cough

Abbildung 4G-35: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Husten für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



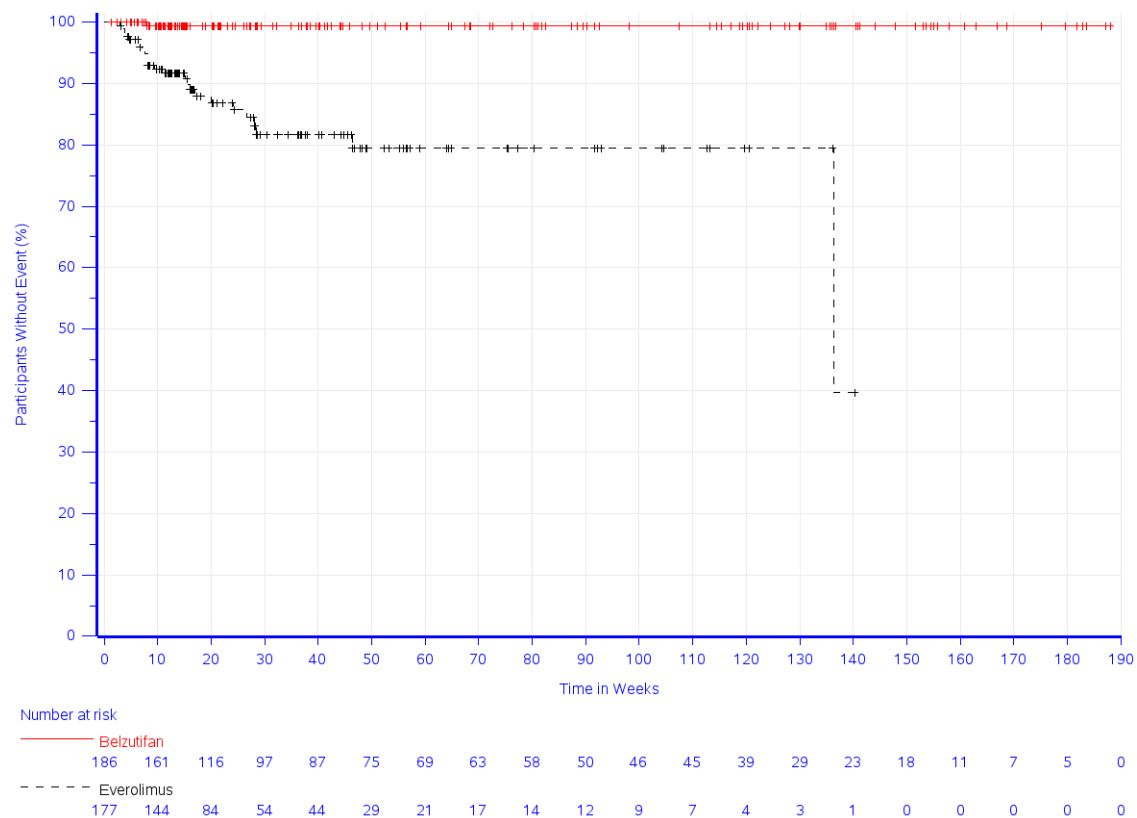
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
Adverse Event - Preferred Term: Epistaxis

Abbildung 4G-36: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Nasenbluten für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



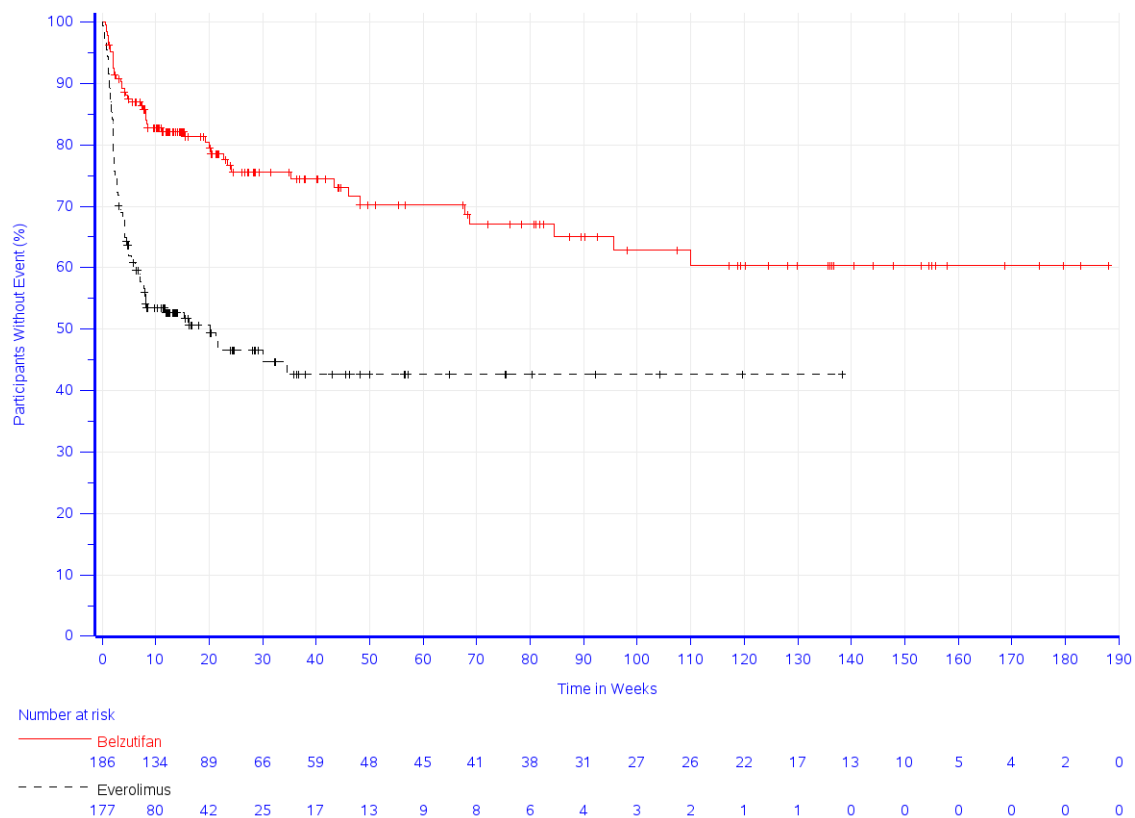
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
 Adverse Event - Preferred Term: Hypoxia

Abbildung 4G-37: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Hypoxie für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



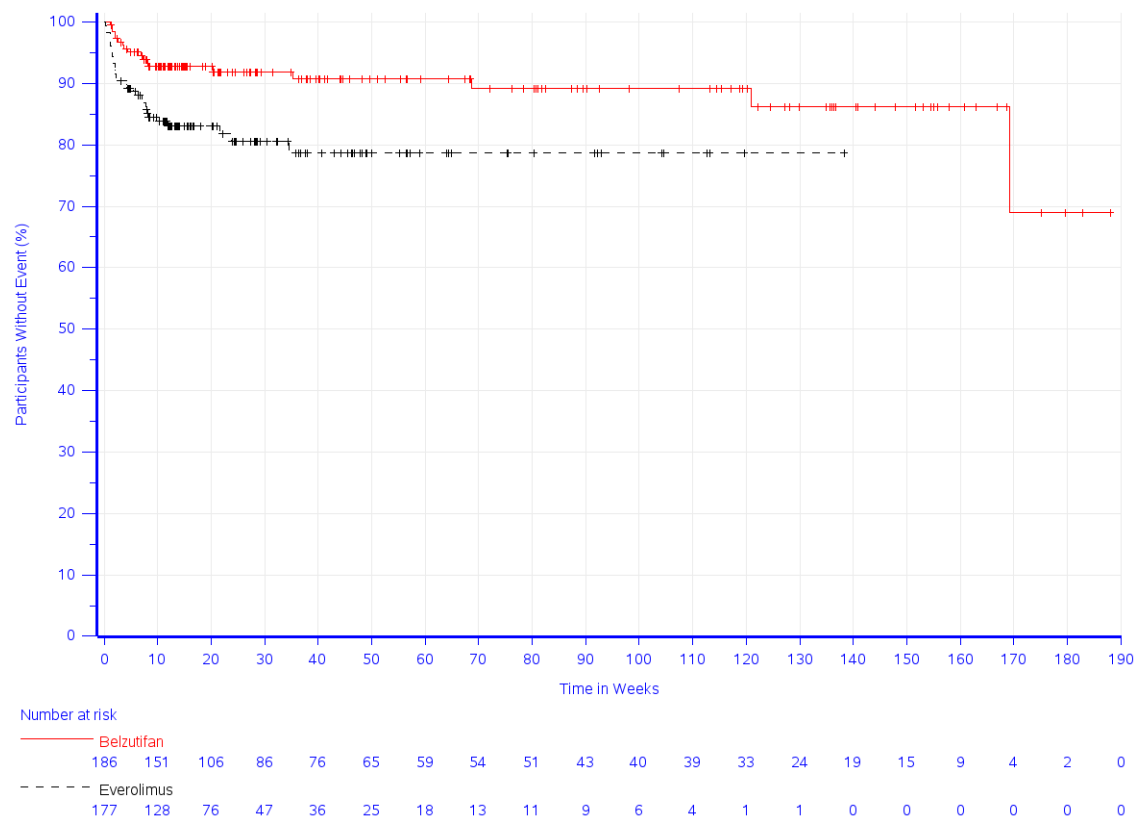
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
Adverse Event - Preferred Term: Pneumonitis

Abbildung 4G-38: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Pneumonitis für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



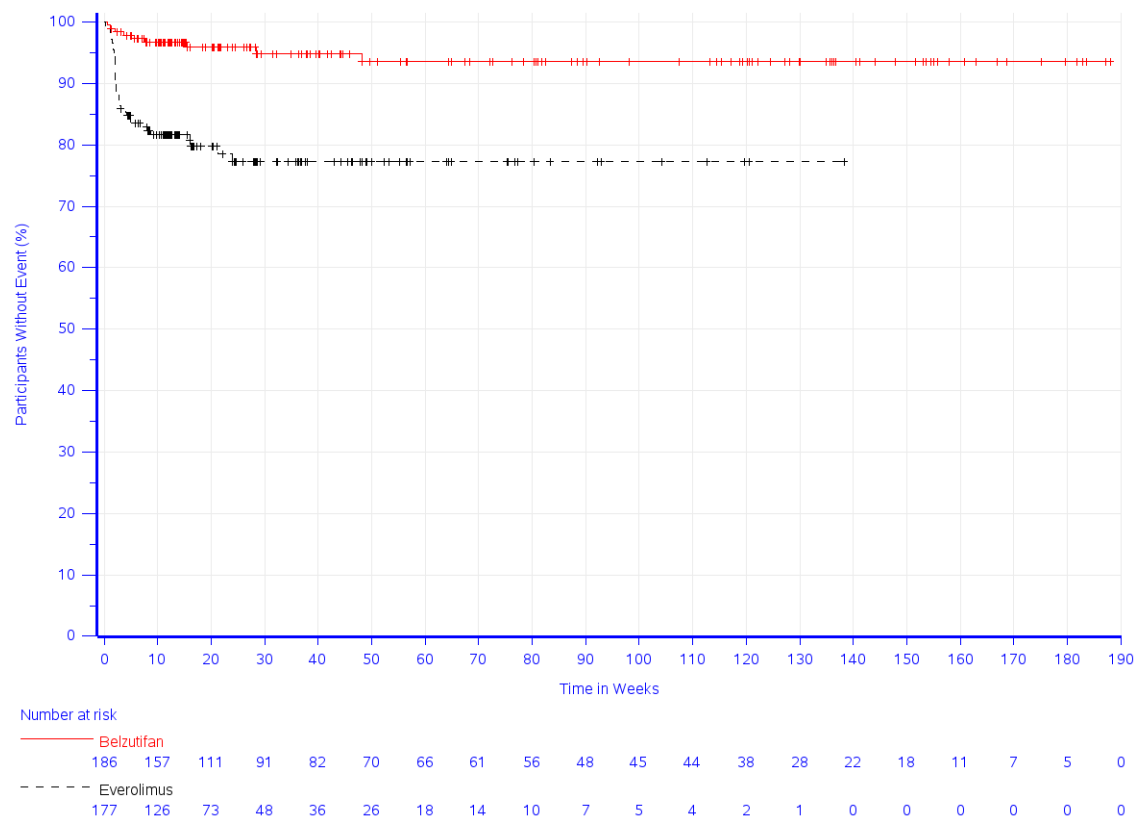
Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
Adverse Event - System Organ Class: Skin and subcutaneous tissue disorders

Abbildung 4G-39: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für die SOC Erkrankungen der Haut und des Unterhautgewebes für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
Adverse Event - Preferred Term: Pruritus

Abbildung 4G-40: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Juckreiz für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005



Study: LiteSpark 005 (Database Cutoff Date: 15APR2024)
 Adverse Event - Preferred Term: Rash

Abbildung 4G-41: Zeit bis zum ersten Auftreten eines Ereignisses: Kaplan-Meier-Kurve für den PT Ausschlag für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) der Studie LITESPARK 005

Anhang 4-G6: Kaplan-Meier-Kurven der Subgruppen mit signifikantem Interaktionstest ($p < 0,05$)

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.2.2 die Kaplan-Meier-Kurven der Subgruppenanalysen, für die ein signifikanter Interaktionstest ($p < 0,05$) vorliegt, dargestellt.

Anhang 4-G6.1: Morbidität

Krankheitssymptomatik und Gesundheitszustand

EORTC QLQ-C30: Symptomskala Schmerzen

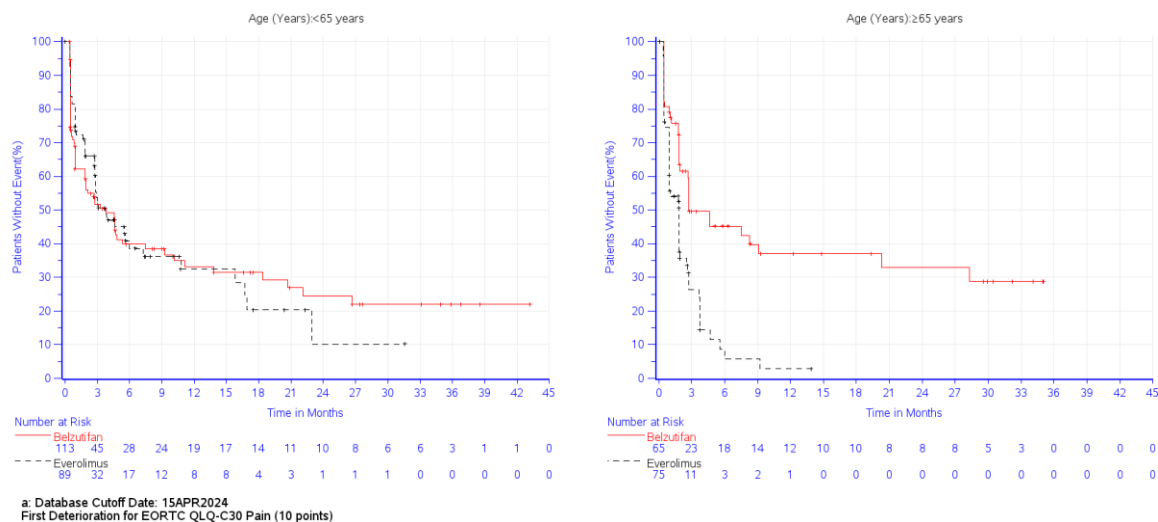
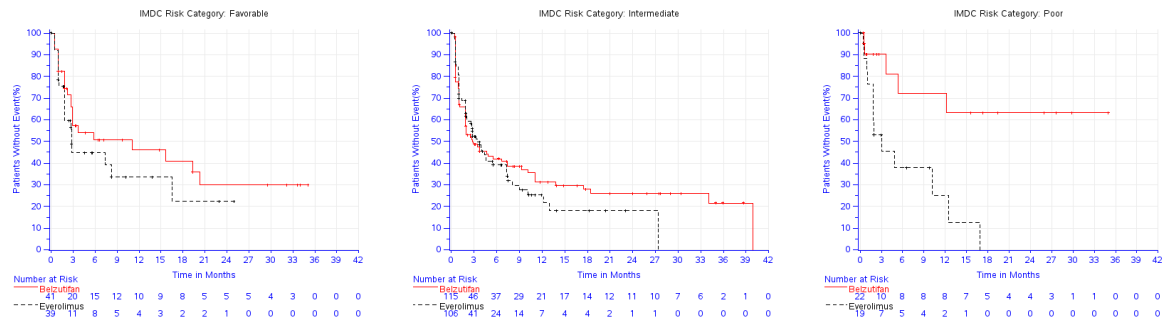


Abbildung 4G-1: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Alter für die Symptomskala Schmerzen des EORTC QLQ-C30 der Studie LITESPARK 005

Anhang 4-G6.2: Gesundheitsbezogene Lebensqualität

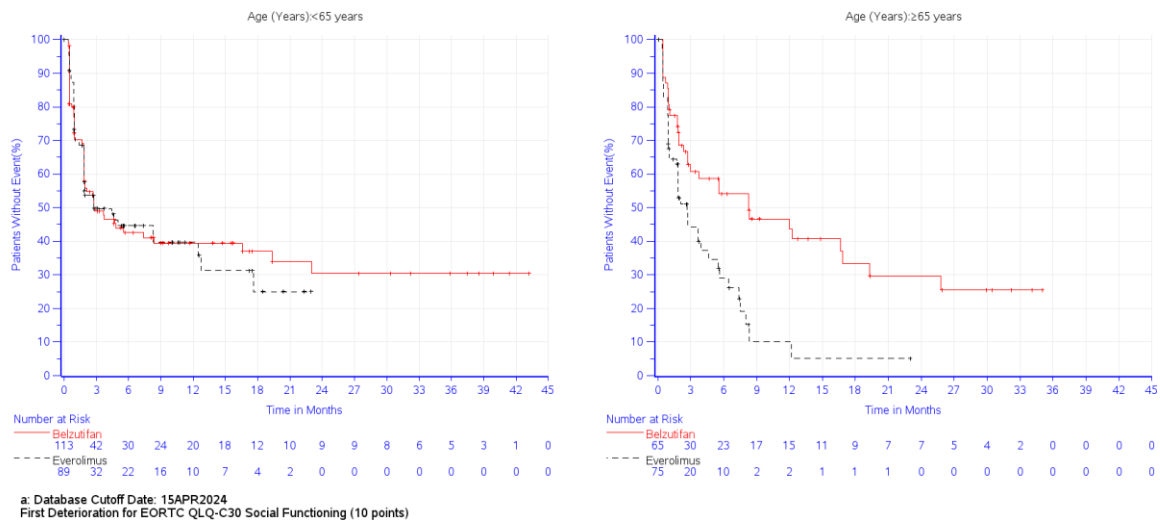
EORTC QLQ-C30: Funktionsskala Körperliche Funktion



a: Database Cutoff Date: 15APR2024
First Deterioration for EORTC QLQ-C30 Physical Functioning (10 points)

Abbildung 4G-2: Kaplan-Meier-Kurve für die Subgruppenanalyse nach IMDC-Risikokategorie für die Funktionsskala Körperliche Funktion des EORTC QLQ-C30 der Studie LITESPARK 005

EORTC QLQ-C30: Funktionsskala Soziale Funktion



a: Database Cutoff Date: 15APR2024
First Deterioration for EORTC QLQ-C30 Social Functioning (10 points)

Abbildung 4G-3: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Alter für die Funktionsskala Soziale Funktion des EORTC QLQ-C30 der Studie LITESPARK 005

Anhang 4-G6.3: Nebenwirkungen

Unerwünschte Ereignisse

Unerwünschte Ereignisse gesamt

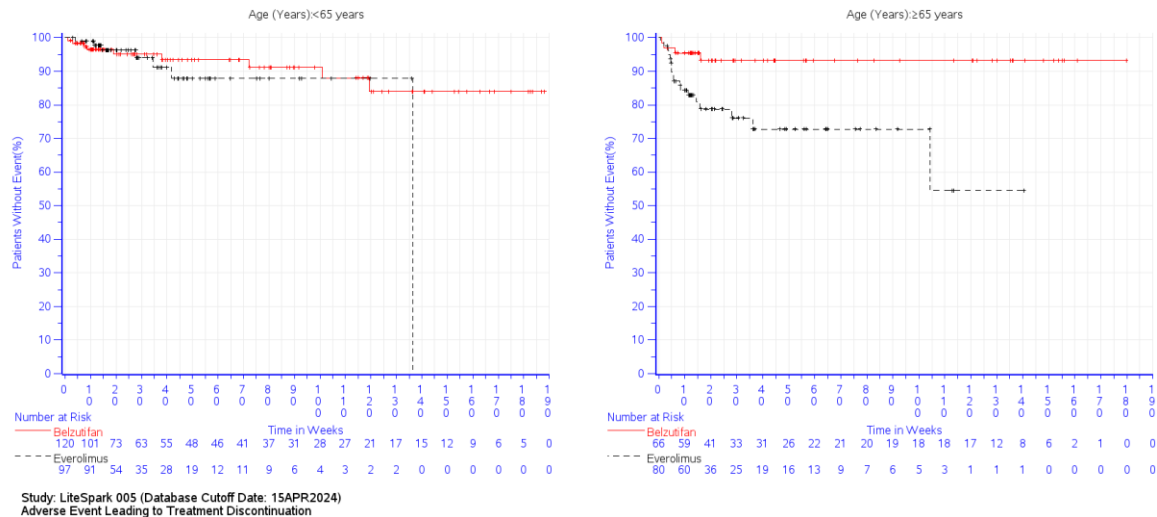


Abbildung 4G-4: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Alter für den Endpunkt Therapieabbruch aufgrund unerwünschter Ereignisse gesamt der Studie LITESPARK 005

Unerwünschte Ereignisse (gegliedert nach SOC und PT)

Unerwünschte Ereignisse gesamt (SOC und PT)

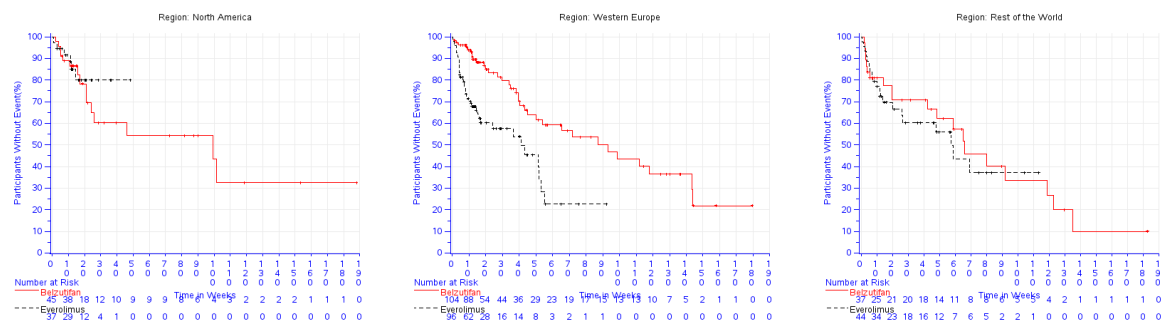


Abbildung 4G-5: Kaplan-Meier-Kurve für die Subgruppenanalyse nach Region für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für die SOC: Infektionen und parasitäre Erkrankungen der Studie LITESPARK 005

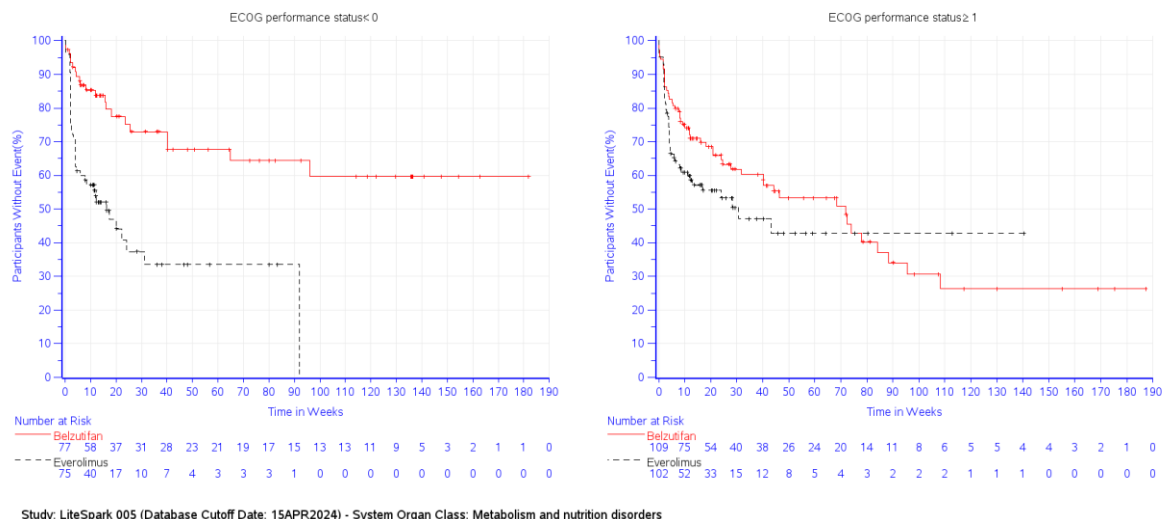


Abbildung 4G-6: Kaplan-Meier-Kurve für die Subgruppenanalyse nach ECOG-Leistungsstatus für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für die SOC: Stoffwechsel- und Ernährungsstörungen der Studie LITESPARK 005

Anhang 4-G7: Ergebnisse der Subgruppen mit nicht signifikantem Interaktionstest ($p \geq 0,05$)

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.2.2 die Ergebnisse der Subgruppenanalysen, für die ein nicht signifikanter Interaktionstest ($p \geq 0,05$) vorliegt, dargestellt.

Anhang 4-G7.1: Mortalität

Gesamtüberleben

Tabelle 4G-22: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Gesamtüberleben aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Overall Survival	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	149	99 (66.4)	22.2 [16.6; 26.1]	143	97 (67.8)	17.7 [13.9; 24.8]	0.94 [0.71; 1.24]	0.667	0.899
Female	39	29 (74.4)	20.8 [12.5; 31.6]	39	28 (71.8)	19.4 [9.2; 25.9]	0.95 [0.56; 1.60]	0.844	
Age (Years)									
< 65	121	86 (71.1)	21.5 [15.0; 25.1]	100	71 (71.0)	18.1 [14.1; 23.9]	0.97 [0.71; 1.33]	0.845	0.650
≥ 65	67	42 (62.7)	23.8 [12.2; 31.9]	82	54 (65.9)	19.3 [11.5; 25.9]	0.88 [0.58; 1.31]	0.518	
ECOG performance status									
0	77	50 (64.9)	23.0 [17.4; 26.3]	78	48 (61.5)	24.0 [15.6; 30.8]	1.05 [0.71; 1.57]	0.795	0.438
≥1	111	78 (70.3)	19.6 [14.6; 26.5]	104	77 (74.0)	15.2 [11.5; 19.9]	0.87 [0.63; 1.19]	0.379	
Region									
North America	46	31 (67.4)	25.0 [15.0; 31.9]	39	31 (79.5)	14.3 [9.2; 24.8]	0.62 [0.37; 1.02]	0.060	0.260
Western Europe	104	74 (71.2)	18.6 [12.0; 25.8]	99	70 (70.7)	17.2 [11.6; 23.3]	0.99 [0.72; 1.38]	0.971	
Rest of the World	38	23 (60.5)	22.6 [13.0; -]	44	24 (54.5)	29.7 [15.0; -]	1.17 [0.66; 2.07]	0.598	
IMDC Risk Category									
Favorable	42	25 (59.5)	25.6 [14.9; -]	42	21 (50.0)	29.1 [15.6; -]	1.22 [0.68; 2.18]	0.498	0.567
Intermediate	123	84 (68.3)	23.0 [17.8; 26.0]	120	86 (71.7)	17.4 [13.4; 24.6]	0.88 [0.65; 1.19]	0.399	
Poor	23	19 (82.6)	12.8 [5.3; 18.2]	20	18 (90.0)	8.1 [3.0; 18.2]	0.77 [0.40; 1.48]	0.429	
IMDC Risk Category 2									
Favorable	42	25 (59.5)	25.6 [14.9; -]	42	21 (50.0)	29.1 [15.6; -]	1.22 [0.68; 2.18]	0.498	0.322
Intermediate or Poor	146	103 (70.5)	19.1 [15.0; 25.4]	140	104 (74.3)	16.7 [12.5; 20.7]	0.88 [0.67; 1.15]	0.352	
Race									
White	148	104 (70.3)	19.4 [14.6; 25.4]	140	99 (70.7)	16.9 [12.0; 19.9]	0.92 [0.70; 1.22]	0.570	0.995

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Overall Survival	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
All Others	26	14 (53.8)	27.9 [17.2; -]	31	18 (58.1)	30.8 [15.0; -]	0.90 [0.45; 1.82]	0.772	
Number of prior lines of therapy									
2	28	16 (57.1)	29.1 [12.5; -]	36	23 (63.9)	17.1 [12.0; 33.4]	0.75 [0.40; 1.42]	0.380	0.420
3-4 ^g	160	112 (70.0)	19.4 [16.4; 25.1]	146	102 (69.9)	18.3 [13.9; 24.6]	0.98 [0.75; 1.28]	0.890	
a: Database Cutoff Date: 15APR2024 b: Number of participants in intention-to-treat population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies c: From product-limit (Kaplan-Meier) method for censored data d: Based on Cox regression model with treatment as a covariate using Wald confidence interval e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group) f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) g: Only two participants in the belzutifan arm and four participants in the everolimus arm received four prior lines of therapy CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; IMDC: International Metastatic RCC Database Consortium; PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death Ligand 1; RCC: Renal Cell Carcinoma; VEGF: Vascular Endothelial Growth Factor									

Anhang 4-G7.2: Morbidität

Progressionsfreies Überleben

Tabelle 4G-23: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Progressionsfreies Überleben aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Progression-Free Survival Based on BICR Assessment per RECIST 1.1	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	149	127 (85.2)	4.6 [2.5; 6.4]	143	109 (76.2)	5.4 [3.8; 6.6]	0.75 [0.57; 0.98]	0.033	0.653
Female	39	29 (74.4)	8.8 [2.1; 16.4]	39	28 (71.8)	3.9 [2.1; 7.4]	0.63 [0.37; 1.10]	0.102	
Age (Years)									
< 65	121	103 (85.1)	3.9 [2.0; 7.3]	100	75 (75.0)	4.8 [3.7; 5.7]	0.76 [0.55; 1.03]	0.081	0.733
≥ 65	67	53 (79.1)	5.7 [3.6; 9.3]	82	62 (75.6)	5.9 [3.7; 7.4]	0.65 [0.44; 0.96]	0.029	
ECOG performance status									
0	77	63 (81.8)	3.9 [1.9; 8.1]	78	57 (73.1)	5.6 [3.6; 7.4]	0.88 [0.61; 1.28]	0.504	0.224
≥1	111	93 (83.8)	5.4 [3.6; 9.2]	104	80 (76.9)	5.4 [3.7; 6.5]	0.61 [0.44; 0.84]	0.002	
Region									
North America	46	36 (78.3)	4.0 [2.0; 15.8]	39	26 (66.7)	4.4 [1.9; 6.6]	0.59 [0.34; 1.02]	0.058	0.277
Western Europe	104	94 (90.4)	4.6 [2.1; 8.1]	99	76 (76.8)	5.5 [3.7; 6.9]	0.80 [0.58; 1.09]	0.160	

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Progression-Free Survival Based on BICR Assessment per RECIST 1.1	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Rest of the World	38	26 (68.4)	5.4 [1.9; 16.6]	44	35 (79.5)	5.7 [3.7; 8.8]	0.65 [0.38; 1.11]	0.113	
IMDC Risk Category									
Favorable	42	32 (76.2)	3.8 [2.0; 10.9]	42	30 (71.4)	5.7 [3.7; 9.2]	0.96 [0.58; 1.60]	0.878	0.363
Intermediate	123	105 (85.4)	5.5 [3.5; 8.1]	120	91 (75.8)	5.4 [3.7; 6.9]	0.67 [0.50; 0.90]	0.009	
Poor	23	19 (82.6)	3.5 [1.9; 16.6]	20	16 (80.0)	3.4 [1.6; 5.5]	0.58 [0.28; 1.21]	0.147	
IMDC Risk Category 2									
Favorable	42	32 (76.2)	3.8 [2.0; 10.9]	42	30 (71.4)	5.7 [3.7; 9.2]	0.96 [0.58; 1.60]	0.878	0.221
Intermediate or Poor	146	124 (84.9)	5.4 [3.0; 7.5]	140	107 (76.4)	5.3 [3.7; 5.9]	0.66 [0.50; 0.87]	0.003	
Race									
White	148	123 (83.1)	4.4 [3.5; 7.3]	140	105 (75.0)	5.3 [3.7; 6.5]	0.71 [0.54; 0.93]	0.013	0.778
All Others	26	20 (76.9)	5.4 [1.9; 16.6]	31	23 (74.2)	5.6 [3.7; 7.6]	0.69 [0.37; 1.31]	0.258	
Number of prior lines of therapy									
2	28	20 (71.4)	2.0 [1.9; 19.5]	36	28 (77.8)	3.4 [1.9; 7.2]	0.57 [0.30; 1.10]	0.092	0.238
3-4 ^g	160	136 (85.0)	5.4 [3.6; 7.3]	146	109 (74.7)	5.6 [4.5; 6.8]	0.76 [0.59; 0.99]	0.039	
a: Database Cutoff Date: 15APR2024									
b: Number of participants in intention-to-treat population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
g: Only two participants in the belzutifan arm and four participants in the everolimus arm received four prior lines of therapy									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; IMDC: International Metastatic RCC Database Consortium; PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death Ligand 1; RCC: Renal Cell Carcinoma; VEGF: Vascular Endothelial Growth Factor									

Zeit bis zur ersten Folgetherapie (oder Tod)

Zeit bis zur ersten Folgetherapie oder Tod

Tabelle 4G-24: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Zeit bis zur ersten Folgetherapie oder Tod aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Time to Subsequent Oncologic Therapy or Death	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	149	120 (80.5)	9.3 [6.2; 13.3]	143	142 (99.3)	5.7 [4.7; 7.4]	0.56 [0.43; 0.72]	< 0.001	0.834
Female	39	35 (89.7)	7.1 [3.7; 17.8]	39	38 (97.4)	5.3 [3.4; 7.9]	0.56 [0.35; 0.92]	0.020	
Age (Years)									
< 65	121	104 (86.0)	8.4 [5.5; 14.0]	100	99 (99.0)	5.9 [4.7; 7.9]	0.61 [0.45; 0.81]	< 0.001	0.236
≥ 65	67	51 (76.1)	9.7 [5.6; 13.7]	82	81 (98.8)	5.3 [3.9; 6.8]	0.48 [0.34; 0.69]	< 0.001	
ECOG performance status									
0	77	62 (80.5)	6.5 [4.3; 12.3]	78	76 (97.4)	6.0 [3.4; 10.0]	0.63 [0.45; 0.89]	0.009	0.417
≥1	111	93 (83.8)	9.8 [6.4; 14.0]	104	104 (100.0)	5.4 [4.6; 6.6]	0.50 [0.37; 0.67]	< 0.001	
Region									
North America	46	40 (87.0)	6.5 [3.7; 15.4]	39	39 (100.0)	4.4 [2.9; 5.6]	0.42 [0.26; 0.69]	< 0.001	0.287
Western Europe	104	86 (82.7)	9.1 [5.6; 13.4]	99	98 (99.0)	5.7 [4.6; 7.9]	0.58 [0.43; 0.78]	< 0.001	
Rest of the World	38	29 (76.3)	10.7 [6.0; 17.3]	44	43 (97.7)	9.0 [5.2; 13.0]	0.60 [0.37; 0.98]	0.043	
IMDC Risk Category									
Favorable	42	32 (76.2)	6.0 [3.7; 15.7]	42	42 (100.0)	5.3 [3.8; 9.9]	0.58 [0.36; 0.93]	0.024	0.992
Intermediate	123	103 (83.7)	10.2 [7.1; 14.0]	120	118 (98.3)	6.1 [4.9; 7.9]	0.54 [0.41; 0.71]	< 0.001	
Poor	23	20 (87.0)	5.4 [2.5; 13.7]	20	20 (100.0)	3.4 [2.3; 10.7]	0.60 [0.32; 1.14]	0.121	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: intention-to-treat population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; RCC: Renal Cell Carcinoma; IMDC: International Metastatic RCC Database Consortium;									
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

Krankheitssymptomatik und Gesundheitszustand

EORTC QLQ-C30: Symptomskala Erschöpfung

Tabelle 4G-25: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Erschöpfung aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a		Belzutifan		Everolimus		Belzutifan vs. Everolimus		p-Value for Interaction Test ^f	
EORTC QLQ-C30 Fatigue	N ^b	Participants with Event	Median Time ^c in months	Participants with Event	Median Time ^c in months	Hazard Ratio	p-Value ^{d,e}		
		n (%)	[95 %-CI]	n (%)	[95 %-CI]	[95 %-CI] ^d			
Sex									
Male	143	100 (69.9)	1.87 [1.84; 2.79]	128	92 (71.9)	1.87 [0.99; 2.76]	0.79 [0.59; 1.06]	0.116	0.711
Female	35	26 (74.3)	0.89 [0.49; 2.76]	36	32 (88.9)	0.99 [0.66; 2.04]	0.93 [0.55; 1.58]	0.800	
Age (Years)									
< 65	113	81 (71.7)	1.87 [0.99; 2.69]	89	65 (73.0)	1.91 [0.95; 2.79]	0.95 [0.69; 1.32]	0.772	0.078
≥ 65	65	45 (69.2)	1.87 [1.05; 4.63]	75	59 (78.7)	1.84 [0.95; 1.87]	0.63 [0.42; 0.94]	0.023	
ECOG performance status									
0	73	49 (67.1)	1.87 [0.99; 2.69]	69	53 (76.8)	1.87 [0.95; 2.79]	0.83 [0.56; 1.22]	0.345	0.981
≥1	105	77 (73.3)	1.87 [0.95; 2.79]	95	71 (74.7)	1.87 [0.95; 2.04]	0.78 [0.56; 1.09]	0.144	
Region									
North America	43	30 (69.8)	1.87 [0.95; 2.86]	33	25 (75.8)	1.41 [0.89; 2.79]	0.75 [0.44; 1.28]	0.286	0.352
Western Europe	102	70 (68.6)	1.87 [0.99; 4.53]	89	70 (78.7)	1.87 [0.95; 2.04]	0.70 [0.50; 0.99]	0.043	
Rest of the World	33	26 (78.8)	1.87 [0.56; 2.79]	42	29 (69.0)	2.76 [0.95; 4.04]	1.16 [0.68; 1.98]	0.587	
IMDC Risk Category									
Favorable	41	27 (65.9)	1.91 [0.99; 3.61]	39	33 (84.6)	1.74 [0.95; 2.04]	0.57 [0.34; 0.96]	0.036	0.262
Intermediate	115	85 (73.9)	1.84 [0.99; 1.94]	106	80 (75.5)	1.87 [0.95; 2.79]	0.86 [0.63; 1.17]	0.344	
Poor	22	14 (63.6)	2.69 [0.53; 9.17]	19	11 (57.9)	1.87 [0.53; -]	0.99 [0.44; 2.20]	0.973	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core - 30 items; IMDC: International Metastatic RCC Database Consortium;									
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

EORTC QLQ-C30: Symptomskala Übelkeit und Erbrechen

Tabelle 4G-26: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Übelkeit und Erbrechen aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
EORTC QLQ-C30 Nausea and Vomiting	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	143	58 (40.6)	14.78 [8.31; -]	128	46 (35.9)	15.38 [3.71; -]	0.91 [0.61; 1.35]	0.634	0.632
Female	35	22 (62.9)	3.68 [2.69; 11.93]	36	20 (55.6)	3.75 [2.14; 12.71]	0.98 [0.53; 1.81]	0.949	
Age (Years)									
< 65	113	54 (47.8)	9.23 [4.83; 15.67]	89	37 (41.6)	12.71 [3.06; 18.60]	0.98 [0.64; 1.49]	0.910	0.365
≥ 65	65	26 (40.0)	19.32 [5.09; -]	75	29 (38.7)	9.96 [3.71; -]	0.74 [0.43; 1.27]	0.278	
ECOG performance status									
0	73	25 (34.2)	31.31 [9.30; -]	69	26 (37.7)	12.71 [3.71; 18.60]	0.71 [0.41; 1.25]	0.242	0.486
≥1	105	55 (52.4)	7.39 [3.68; 11.99]	95	40 (42.1)	3.94 [2.76; -]	0.98 [0.65; 1.49]	0.925	
Region									
North America	43	20 (46.5)	11.93 [2.86; 31.31]	33	8 (24.2)	Not reached [3.71; -]	1.30 [0.55; 3.07]	0.544	0.191
Western Europe	102	44 (43.1)	13.86 [6.44; -]	89	40 (44.9)	3.94 [2.79; 12.91]	0.70 [0.45; 1.08]	0.106	
Rest of the World	33	16 (48.5)	8.31 [2.79; -]	42	18 (42.9)	15.38 [3.65; -]	1.20 [0.61; 2.36]	0.589	
IMDC Risk Category									
Favorable	41	14 (34.1)	19.32 [7.39; -]	39	14 (35.9)	18.60 [3.71; -]	0.69 [0.32; 1.47]	0.337	0.781
Intermediate	115	56 (48.7)	8.28 [3.75; -]	106	44 (41.5)	8.38 [3.71; 12.91]	0.97 [0.65; 1.45]	0.891	
Poor	22	10 (45.5)	12.22 [2.69; -]	19	8 (42.1)	15.38 [1.02; -]	0.91 [0.35; 2.36]	0.841	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core - 30 items; IMDC: International Metastatic RCC Database Consortium;									
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

EORTC QLQ-C30: Symptomskala Schmerzen

Tabelle 4G-27: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Schmerzen aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a		Belzutifan		Everolimus		Belzutifan vs. Everolimus		p-Value for Interaction Test ^f		
EORTC Pain	QLQ-C30	Participants with Event	Median Time ^c in months	Participants with Event	Median Time ^c in months	Hazard Ratio				
		N ^b n (%)	[95 %-CI]	N ^b n (%)	[95 %-CI]	[95 %-CI] ^d	p-Value ^{d,e}			
Sex										
Male		143	79 (55.2)	4.63 [2.73; 10.15]	128	79 (61.7)	2.79 [1.87; 3.71]	0.71 [0.51; 0.97]	0.033	0.587
Female		35	26 (74.3)	1.87 [0.85; 2.79]	36	27 (75.0)	2.56 [0.95; 3.06]	0.81 [0.46; 1.41]	0.453	
ECOG performance status										
0		73	43 (58.9)	4.63 [1.94; 11.11]	69	50 (72.5)	2.76 [1.05; 2.99]	0.60 [0.40; 0.91]	0.017	0.411
≥1		105	62 (59.0)	2.76 [1.87; 4.70]	95	56 (58.9)	2.79 [1.87; 3.71]	0.84 [0.58; 1.21]	0.354	
Region										
North America		43	19 (44.2)	8.25 [1.94; -]	33	19 (57.6)	2.76 [1.81; 3.65]	0.55 [0.28; 1.08]	0.081	0.439
Western Europe		102	63 (61.8)	2.76 [1.87; 4.63]	89	57 (64.0)	2.56 [1.84; 3.06]	0.81 [0.57; 1.17]	0.263	
Rest of the World		33	23 (69.7)	4.63 [1.18; 10.15]	42	30 (71.4)	2.89 [0.99; 5.98]	0.71 [0.40; 1.25]	0.235	
IMDC Risk Category										
Favorable		41	23 (56.1)	3.29 [1.84; 28.32]	39	27 (69.2)	1.05 [0.95; 3.71]	0.54 [0.30; 0.97]	0.040	0.278
Intermediate		115	72 (62.6)	3.78 [1.87; 7.43]	106	67 (63.2)	2.76 [1.87; 3.65]	0.83 [0.59; 1.17]	0.286	
Poor		22	10 (45.5)	5.32 [1.87; -]	19	12 (63.2)	5.59 [0.95; 10.78]	0.64 [0.27; 1.49]	0.298	
a: Database Cutoff Date: 15APR2024										
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies										
c: From product-limit (Kaplan-Meier) method for censored data										
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval										
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)										
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)										
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core - 30 items; IMDC: International Metastatic RCC Database Consortium;										
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor										

EORTC QLQ-C30: Symptomskala Dyspnoe

Tabelle 4G-28: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Dyspnoe aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a		Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
EORTC QLQ-C30 Dyspnea	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Sex										
Male	143	68 (47.6)	8.31 [3.71; 21.13]	128	66 (51.6)	3.68 [2.79; 10.22]	0.73 [0.52; 1.03]	0.070	0.267	
Female	35	19 (54.3)	5.55 [1.77; 16.56]	36	18 (50.0)	3.71 [2.04; 11.07]	0.98 [0.50; 1.92]	0.962		
Age (Years)										
< 65	113	60 (53.1)	4.63 [3.68; 16.56]	89	46 (51.7)	3.71 [2.83; 11.07]	0.95 [0.65; 1.40]	0.805	0.065	
≥ 65	65	27 (41.5)	25.79 [5.55; -]	75	38 (50.7)	3.68 [1.87; 12.06]	0.54 [0.32; 0.90]	0.019		
ECOG performance status										
0	73	36 (49.3)	4.70 [3.68; 27.60]	69	31 (44.9)	7.43 [3.71; 16.56]	0.99 [0.61; 1.62]	0.982	0.121	
≥1	105	51 (48.6)	8.31 [4.63; 17.48]	95	53 (55.8)	2.79 [1.87; 3.71]	0.65 [0.44; 0.96]	0.032		
Region										
North America	43	24 (55.8)	3.75 [2.69; 10.09]	33	17 (51.5)	2.79 [1.68; -]	0.68 [0.36; 1.30]	0.240	0.797	
Western Europe	102	46 (45.1)	17.48 [3.98; 27.60]	89	44 (49.4)	3.68 [2.76; 10.22]	0.71 [0.46; 1.08]	0.108		
Rest of the World	33	17 (51.5)	5.32 [1.35; -]	42	23 (54.8)	7.43 [2.89; 16.56]	0.92 [0.49; 1.73]	0.794		
IMDC Risk Category										
Favorable	41	22 (53.7)	5.55 [2.96; 25.79]	39	22 (56.4)	3.71 [1.87; 11.07]	0.79 [0.43; 1.43]	0.431	0.678	
Intermediate	115	59 (51.3)	8.31 [3.68; 17.51]	106	55 (51.9)	3.68 [2.79; 10.22]	0.82 [0.56; 1.19]	0.292		
Poor	22	6 (27.3)	Not reached [3.71; -]	19	7 (36.8)	7.92 [0.66; -]	0.56 [0.19; 1.70]	0.309		
a: Database Cutoff Date: 15APR2024										
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies										
c: From product-limit (Kaplan-Meier) method for censored data										
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval										
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)										
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)										
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core - 30 items; IMDC: International Metastatic RCC Database Consortium;										
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor										

EORTC QLQ-C30: Symptomskala Schlaflosigkeit

Tabelle 4G-29: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Schlaflosigkeit aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a		Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
EORTC Insomnia	QLQ-C30	N ^b	Participants with Event	Median Time ^c in months	N ^b	Participants with Event	Median Time ^c in months	Hazard Ratio	p-Value ^{d,e}	
			n (%)	[95 %-CI]		n (%)	[95 %-CI]	[95 %-CI] ^d		
Sex										
Male		143	60 (42.0)	17.54 [9.20; -]	128	65 (50.8)	4.63 [2.79; 7.39]	0.59 [0.41; 0.84]	0.004	0.236
Female		35	21 (60.0)	2.86 [0.95; 10.09]	36	22 (61.1)	2.89 [1.05; 3.94]	0.89 [0.48; 1.64]	0.710	
Age (Years)										
< 65		113	50 (44.2)	16.59 [3.71; -]	89	50 (56.2)	2.89 [1.87; 5.55]	0.65 [0.44; 0.97]	0.035	0.714
≥ 65		65	31 (47.7)	11.07 [3.75; 24.84]	75	37 (49.3)	4.63 [2.83; 9.20]	0.58 [0.35; 0.96]	0.034	
ECOG performance status										
0		73	37 (50.7)	10.12 [2.76; -]	69	40 (58.0)	3.65 [1.87; 5.55]	0.66 [0.42; 1.04]	0.071	0.917
≥1		105	44 (41.9)	18.86 [5.52; -]	95	47 (49.5)	4.63 [2.79; 8.18]	0.63 [0.41; 0.96]	0.033	
Region										
North America		43	20 (46.5)	11.01 [3.71; 24.84]	33	20 (60.6)	2.79 [1.87; 5.49]	0.34 [0.17; 0.69]	0.003	0.647
Western Europe		102	46 (45.1)	11.07 [3.48; -]	89	45 (50.6)	4.63 [2.79; 7.39]	0.71 [0.47; 1.08]	0.110	
Rest of the World		33	15 (45.5)	8.25 [1.94; -]	42	22 (52.4)	2.89 [0.99; 16.56]	0.72 [0.37; 1.39]	0.327	
IMDC Risk Category										
Favorable		41	21 (51.2)	10.58 [2.76; 24.84]	39	22 (56.4)	2.79 [0.95; 9.20]	0.59 [0.32; 1.08]	0.086	0.877
Intermediate		115	52 (45.2)	16.59 [3.71; -]	106	55 (51.9)	3.88 [2.79; 6.47]	0.70 [0.47; 1.03]	0.068	
Poor		22	8 (36.4)	17.54 [9.20; -]	19	10 (52.6)	3.71 [0.99; -]	0.49 [0.18; 1.33]	0.161	
a: Database Cutoff Date: 15APR2024										
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies										
c: From product-limit (Kaplan-Meier) method for censored data										
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval										
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)										
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)										
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core - 30 items; IMDC: International Metastatic RCC Database Consortium;										
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor										

EORTC QLQ-C30: Symptomskala Appetitverlust

Tabelle 4G-30: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Appetitverlust aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a		Belzutifan		Everolimus		Belzutifan vs. Everolimus		p-Value for Interaction Test ^f	
EORTC QLQ-C30 Appetite loss	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	Hazard Ratio [95 %-CI] ^d p-Value ^{d,e}		
Sex									
Male	143	58 (40.6)	23.95 [9.33; 33.25]	128	68 (53.1)	3.68 [2.76; 4.70]	0.48 [0.33; 0.70]	< 0.001	0.312
Female	35	18 (51.4)	10.09 [2.92; 19.32]	36	20 (55.6)	3.78 [1.87; 11.07]	0.61 [0.31; 1.19]	0.149	
Age (Years)									
< 65	113	48 (42.5)	23.95 [5.52; -]	89	48 (53.9)	3.78 [2.79; 5.52]	0.54 [0.35; 0.81]	0.003	0.630
≥ 65	65	28 (43.1)	17.45 [9.33; -]	75	40 (53.3)	2.76 [1.87; 7.36]	0.45 [0.27; 0.75]	0.002	
ECOG performance status									
0	73	31 (42.5)	23.95 [3.75; -]	69	37 (53.6)	4.60 [2.76; 7.39]	0.62 [0.38; 1.02]	0.058	0.589
≥1	105	45 (42.9)	17.45 [9.33; 27.66]	95	51 (53.7)	3.06 [1.87; 5.52]	0.45 [0.29; 0.68]	< 0.001	
Region									
North America	43	16 (37.2)	20.21 [10.09; -]	33	13 (39.4)	4.57 [2.79; -]	0.45 [0.19; 1.04]	0.062	0.886
Western Europe	102	43 (42.2)	17.45 [7.36; -]	89	49 (55.1)	3.06 [1.97; 6.01]	0.49 [0.32; 0.76]	0.001	
Rest of the World	33	17 (51.5)	6.51 [3.71; -]	42	26 (61.9)	3.45 [0.99; 7.39]	0.62 [0.33; 1.17]	0.143	
IMDC Risk Category									
Favorable	41	14 (34.1)	27.60 [14.98; -]	39	19 (48.7)	4.53 [1.87; -]	0.48 [0.23; 0.99]	0.047	0.923
Intermediate	115	55 (47.8)	13.80 [5.55; 27.66]	106	61 (57.5)	3.45 [1.97; 5.52]	0.53 [0.36; 0.78]	0.001	
Poor	22	7 (31.8)	20.21 [3.65; -]	19	8 (42.1)	3.78 [1.02; -]	0.47 [0.16; 1.36]	0.161	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core - 30 items; IMDC: International Metastatic RCC Database Consortium;									
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

EORTC QLQ-C30: Symptomskala Verstopfung

Tabelle 4G-31: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Verstopfung aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a		Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
EORTC QLQ-C30 Constipation	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Sex										
Male	143	58 (40.6)	20.21 [8.31; 36.60]	128	43 (33.6)	15.70 [10.15; -]	1.07 [0.72; 1.60]	0.727	0.467	
Female	35	20 (57.1)	2.79 [1.87; 6.41]	36	16 (44.4)	7.39 [4.63; 12.71]	1.59 [0.82; 3.08]	0.165		
Age (Years)										
< 65	113	50 (44.2)	18.43 [4.83; 24.94]	89	38 (42.7)	12.71 [8.48; 16.89]	0.98 [0.64; 1.50]	0.937	0.393	
≥ 65	65	28 (43.1)	8.31 [2.79; -]	75	21 (28.0)	15.70 [7.39; -]	1.45 [0.82; 2.57]	0.203		
ECOG performance status										
0	73	28 (38.4)	23.03 [4.83; -]	69	22 (31.9)	15.70 [9.96; -]	1.17 [0.67; 2.05]	0.579	0.933	
≥1	105	50 (47.6)	12.09 [2.86; 23.46]	95	37 (38.9)	9.86 [4.90; 15.84]	1.11 [0.72; 1.71]	0.649		
Region										
North America	43	19 (44.2)	8.31 [1.94; -]	33	9 (27.3)	7.39 [3.65; -]	1.24 [0.55; 2.81]	0.600	0.964	
Western Europe	102	47 (46.1)	12.88 [3.58; 23.03]	89	34 (38.2)	9.96 [8.48; 21.13]	1.12 [0.72; 1.74]	0.626		
Rest of the World	33	12 (36.4)	Not reached [1.87; -]	42	16 (38.1)	15.70 [13.04; -]	1.02 [0.48; 2.16]	0.963		
IMDC Risk Category										
Favorable	41	16 (39.0)	6.74 [2.76; -]	39	13 (33.3)	15.70 [3.71; -]	1.07 [0.52; 2.23]	0.851	0.917	
Intermediate	115	54 (47.0)	12.88 [3.58; 28.78]	106	40 (37.7)	12.71 [8.51; 21.13]	1.20 [0.79; 1.82]	0.391		
Poor	22	8 (36.4)	24.94 [2.79; -]	19	6 (31.6)	15.84 [4.90; -]	0.84 [0.28; 2.54]	0.752		
a: Database Cutoff Date: 15APR2024										
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies										
c: From product-limit (Kaplan-Meier) method for censored data										
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval										
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)										
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)										
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core - 30 items; IMDC: International Metastatic RCC Database Consortium;										
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor										

EORTC QLQ-C30: Symptomskala Diarrhö

Tabelle 4G-32: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Diarrhö aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a		Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
EORTC QLQ-C30 Diarrhea	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
Sex										
Male	143	45 (31.5)	23.95 [9.23; -]	128	59 (46.1)	5.55 [3.68; 13.83]	0.47 [0.31; 0.69]	< 0.001	0.131	
Female	35	14 (40.0)	7.39 [3.71; -]	36	14 (38.9)	9.96 [2.40; -]	0.88 [0.42; 1.86]	0.746		
Age (Years)										
< 65	113	35 (31.0)	23.95 [7.39; -]	89	41 (46.1)	6.97 [3.06; 15.84]	0.48 [0.30; 0.77]	0.002	0.695	
≥ 65	65	24 (36.9)	15.21 [6.31; -]	75	32 (42.7)	5.59 [2.76; -]	0.61 [0.36; 1.04]	0.070		
ECOG performance status										
0	73	21 (28.8)	31.31 [7.39; -]	69	30 (43.5)	6.97 [2.83; -]	0.45 [0.25; 0.81]	0.007	0.600	
≥1	105	38 (36.2)	11.99 [7.39; -]	95	43 (45.3)	5.55 [2.79; 15.84]	0.59 [0.38; 0.91]	0.018		
Region										
North America	43	14 (32.6)	11.07 [4.86; -]	33	13 (39.4)	4.90 [1.87; -]	0.37 [0.17; 0.84]	0.017	0.598	
Western Europe	102	30 (29.4)	23.95 [9.23; -]	89	37 (41.6)	9.13 [3.06; -]	0.51 [0.31; 0.83]	0.007		
Rest of the World	33	15 (45.5)	7.39 [4.17; -]	42	23 (54.8)	5.59 [1.91; -]	0.70 [0.36; 1.36]	0.294		
IMDC Risk Category										
Favorable	41	13 (31.7)	15.21 [4.86; -]	39	16 (41.0)	5.59 [1.74; -]	0.50 [0.23; 1.06]	0.070	0.583	
Intermediate	115	41 (35.7)	21.62 [7.39; -]	106	48 (45.3)	6.97 [3.71; 13.83]	0.59 [0.38; 0.90]	0.014		
Poor	22	5 (22.7)	Not reached [4.57; -]	19	9 (47.4)	3.06 [1.12; -]	0.35 [0.11; 1.04]	0.059		
a: Database Cutoff Date: 15APR2024										
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies										
c: From product-limit (Kaplan-Meier) method for censored data										
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval										
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)										
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)										
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core - 30 items; IMDC: International Metastatic RCC Database Consortium;										
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor										

FKSI-DRS

Tabelle 4G-33: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den FKSI-DRS aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
FKSI-DRS Total	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	144	46 (31.9)	28.32 [18.40; -]	129	43 (33.3)	12.48 [8.18; -]	0.65 [0.42; 1.00]	0.052	0.965
Female	35	16 (45.7)	17.71 [2.76; -]	36	17 (47.2)	4.90 [2.56; -]	0.70 [0.34; 1.44]	0.328	
Age (Years)									
< 65	114	41 (36.0)	23.95 [14.75; -]	90	31 (34.4)	12.48 [7.39; 16.89]	0.82 [0.51; 1.33]	0.418	0.129
≥ 65	65	21 (32.3)	28.32 [17.71; -]	75	29 (38.7)	8.18 [3.94; -]	0.47 [0.26; 0.86]	0.014	
ECOG performance status									
0	74	29 (39.2)	23.95 [11.11; -]	69	26 (37.7)	9.43 [3.98; -]	0.81 [0.47; 1.40]	0.457	0.377
≥1	105	33 (31.4)	27.17 [17.71; -]	96	34 (35.4)	10.05 [6.51; 16.72]	0.55 [0.33; 0.90]	0.019	
Region									
North America	43	13 (30.2)	Not reached [15.74; -]	34	11 (32.4)	4.90 [2.83; -]	0.60 [0.25; 1.39]	0.232	0.376
Western Europe	103	33 (32.0)	27.60 [17.71; -]	89	32 (36.0)	10.05 [6.51; -]	0.58 [0.35; 0.96]	0.035	
Rest of the World	33	16 (48.5)	11.11 [3.19; -]	42	17 (40.5)	14.42 [5.55; -]	1.06 [0.53; 2.11]	0.872	
IMDC Risk Category									
Favorable	41	10 (24.4)	Not reached [28.32; -]	39	15 (38.5)	9.20 [2.76; -]	0.52 [0.23; 1.19]	0.123	0.346
Intermediate	116	49 (42.2)	20.67 [9.07; 27.60]	107	41 (38.3)	9.43 [6.51; 16.72]	0.75 [0.49; 1.16]	0.193	
Poor	22	3 (13.6)	Not reached [6.74; -]	19	4 (21.1)	16.89 [4.90; -]	0.37 [0.08; 1.74]	0.207	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; FKSI-DRS: Functional Assessment of Cancer Therapy Kidney Cancer Symptom Index-Disease Related Symptoms; IMDC: International Metastatic RCC Database Consortium;									
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

EQ-5D VAS

Tabelle 4G-34: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die EQ-5D VAS aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
EQ-5D VAS	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	144	62 (43.1)	19.81 [8.31; 35.98]	128	48 (37.5)	12.48 [5.49; -]	0.84 [0.57; 1.24]	0.383	0.351
Female	35	24 (68.6)	2.79 [1.68; 8.25]	36	19 (52.8)	7.59 [1.71; 11.07]	1.15 [0.62; 2.12]	0.660	
Age (Years)									
< 65	114	51 (44.7)	10.15 [6.37; 35.98]	89	30 (33.7)	12.48 [10.05; -]	1.15 [0.72; 1.82]	0.556	0.137
≥ 65	65	35 (53.8)	9.23 [2.89; 19.81]	75	37 (49.3)	4.53 [1.87; 20.53]	0.70 [0.44; 1.13]	0.148	
ECOG performance status									
0	74	37 (50.0)	7.43 [2.89; 20.27]	69	32 (46.4)	10.15 [3.94; 16.59]	0.90 [0.56; 1.46]	0.675	0.978
≥1	105	49 (46.7)	14.78 [7.36; 26.71]	95	35 (36.8)	12.48 [5.52; -]	0.91 [0.58; 1.42]	0.675	
Region									
North America	43	18 (41.9)	8.31 [4.86; -]	33	9 (27.3)	Not reached [2.76; -]	1.13 [0.49; 2.60]	0.767	0.304
Western Europe	103	50 (48.5)	11.99 [6.37; 21.29]	89	42 (47.2)	10.05 [1.87; 16.59]	0.73 [0.48; 1.11]	0.137	
Rest of the World	33	18 (54.5)	7.43 [1.87; -]	42	16 (38.1)	12.48 [5.03; -]	1.22 [0.61; 2.44]	0.565	
IMDC Risk Category									
Favorable	41	20 (48.8)	10.15 [4.86; -]	39	23 (59.0)	1.87 [0.99; 20.53]	0.60 [0.33; 1.10]	0.099	0.166
Intermediate	116	60 (51.7)	9.23 [3.78; 24.94]	106	39 (36.8)	10.15 [5.49; 17.58]	1.13 [0.74; 1.71]	0.571	
Poor	22	6 (27.3)	Not reached [5.32; -]	19	5 (26.3)	12.48 [1.87; -]	0.71 [0.21; 2.38]	0.576	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EQ-5D VAS: EuroQol - 5 Dimensions Visual Analog Scale; IMDC: International Metastatic RCC Database Consortium;									
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

Anhang 4-G7.3 Gesundheitsbezogene Lebensqualität

EORTC QLQ-C30: Globaler Gesundheitsstatus

Tabelle 4G-35: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den globalen Gesundheitsstatus aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a		Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
EORTC Global Status/QoL	QLQ-C30 Health	N ^b	Participants with Event	Median Time ^c in months	N ^b	Participants with Event	Median Time ^c in months	Hazard Ratio	p-Value ^{d,e}	
			n (%)	[95 %-CI]		n (%)	[95 %-CI]	[95 %-CI] ^d		
Sex										
Male		143	86 (60.1)	5.49 [3.75; 7.43]	128	70 (54.7)	4.40 [1.91; 5.55]	0.76 [0.55; 1.05]	0.095	0.763
Female		35	28 (80.0)	1.84 [0.56; 2.79]	36	29 (80.6)	1.05 [0.95; 1.87]	0.91 [0.54; 1.54]	0.727	
Age (Years)										
< 65		113	69 (61.1)	4.63 [2.92; 5.65]	89	51 (57.3)	4.57 [2.79; 10.05]	0.82 [0.57; 1.20]	0.310	0.481
≥ 65		65	45 (69.2)	2.76 [1.87; 7.36]	75	48 (64.0)	1.87 [1.05; 2.73]	0.72 [0.48; 1.10]	0.132	
ECOG performance status										
0		73	47 (64.4)	3.75 [1.94; 11.07]	69	40 (58.0)	3.94 [1.68; 5.59]	0.80 [0.52; 1.24]	0.318	0.851
≥1		105	67 (63.8)	4.57 [2.73; 5.78]	95	59 (62.1)	2.73 [1.87; 4.40]	0.77 [0.53; 1.10]	0.146	
Region										
North America		43	28 (65.1)	2.92 [1.84; 5.65]	33	18 (54.5)	2.73 [0.99; 4.60]	0.79 [0.42; 1.46]	0.443	0.998
Western Europe		102	64 (62.7)	5.45 [2.73; 8.35]	89	52 (58.4)	2.76 [1.87; 4.60]	0.77 [0.53; 1.12]	0.172	
Rest of the World		33	22 (66.7)	4.63 [1.91; 7.43]	42	29 (69.0)	2.79 [0.99; 5.59]	0.77 [0.44; 1.36]	0.375	
IMDC Risk Category										
Favorable		41	27 (65.9)	2.27 [1.84; 11.07]	39	31 (79.5)	1.68 [0.95; 1.87]	0.52 [0.30; 0.89]	0.018	0.156
Intermediate		115	76 (66.1)	3.78 [2.79; 5.59]	106	60 (56.6)	2.86 [1.91; 5.59]	0.91 [0.64; 1.28]	0.581	
Poor		22	11 (50.0)	7.39 [4.57; -]	19	8 (42.1)	12.48 [0.95; -]	0.77 [0.31; 1.95]	0.586	
a: Database Cutoff Date: 15APR2024										
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies										
c: From product-limit (Kaplan-Meier) method for censored data										
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval										
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)										
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)										
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core - 30 items; IMDC: International Metastatic RCC Database Consortium;										
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor										

EORTC QLQ-C30: Funktionsskala Körperliche Funktion

Tabelle 4G-36: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Körperliche Funktion aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
EORTC QLQ-C30 Physical Functioning	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	143	81 (56.6)	5.78 [2.92; 11.11]	128	73 (57.0)	4.60 [2.76; 8.05]	0.82 [0.59; 1.13]	0.216	0.307
Female	35	19 (54.3)	2.76 [0.95; -]	36	27 (75.0)	1.97 [1.05; 2.83]	0.64 [0.35; 1.17]	0.145	
Age (Years)									
< 65	113	61 (54.0)	5.32 [2.69; 13.83]	89	55 (61.8)	3.45 [2.69; 7.29]	0.75 [0.51; 1.09]	0.128	0.944
≥ 65	65	39 (60.0)	3.71 [2.27; 12.22]	75	45 (60.0)	2.79 [1.87; 7.43]	0.79 [0.51; 1.22]	0.288	
ECOG performance status									
0	73	42 (57.5)	7.39 [2.89; 15.67]	69	41 (59.4)	3.88 [2.76; 8.25]	0.80 [0.52; 1.24]	0.324	0.478
≥1	105	58 (55.2)	3.68 [1.87; 11.07]	95	59 (62.1)	2.79 [1.87; 4.60]	0.75 [0.52; 1.09]	0.128	
Region									
North America	43	23 (53.5)	3.71 [2.92; 34.07]	33	16 (48.5)	4.90 [1.87; 8.05]	0.64 [0.32; 1.24]	0.186	0.507
Western Europe	102	58 (56.9)	7.39 [1.91; 15.67]	89	57 (64.0)	2.73 [1.87; 4.40]	0.70 [0.48; 1.02]	0.063	
Rest of the World	33	19 (57.6)	4.83 [0.69; -]	42	27 (64.3)	7.43 [2.79; 12.48]	1.02 [0.56; 1.84]	0.950	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core - 30 items; VEGF: Vascular Endothelial Growth Factor;									
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

EORTC QLQ-C30: Funktionsskala Rollenfunktion

Tabelle 4G-37: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Rollenfunktion aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
EORTC QLQ-C30 Role Functioning	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	143	88 (61.5)	3.29 [1.87; 8.31]	128	81 (63.3)	2.73 [1.87; 3.25]	0.80 [0.59; 1.09]	0.162	0.948
Female	35	26 (74.3)	1.81 [0.53; 2.76]	36	29 (80.6)	1.05 [0.59; 1.87]	0.82 [0.48; 1.40]	0.470	
Age (Years)									
< 65	113	73 (64.6)	2.76 [1.02; 4.63]	89	56 (62.9)	2.73 [1.87; 6.47]	0.97 [0.68; 1.38]	0.863	0.073
≥ 65	65	41 (63.1)	2.76 [1.87; 10.22]	75	54 (72.0)	1.84 [0.95; 2.56]	0.61 [0.40; 0.92]	0.018	
ECOG performance status									
0	73	49 (67.1)	2.79 [1.87; 5.55]	69	47 (68.1)	2.56 [1.35; 3.94]	0.85 [0.57; 1.28]	0.438	0.522
≥1	105	65 (61.9)	2.76 [1.77; 6.67]	95	63 (66.3)	1.87 [0.99; 2.76]	0.76 [0.54; 1.08]	0.132	
Region									
North America	43	25 (58.1)	3.71 [1.81; 8.31]	33	24 (72.7)	0.95 [0.56; 2.73]	0.52 [0.29; 0.93]	0.029	0.240
Western Europe	102	67 (65.7)	1.91 [1.84; 6.47]	89	59 (66.3)	1.87 [1.84; 3.02]	0.85 [0.60; 1.22]	0.377	
Rest of the World	33	22 (66.7)	2.79 [0.56; 16.59]	42	27 (64.3)	1.91 [0.95; 12.48]	0.95 [0.54; 1.68]	0.852	
IMDC Risk Category									
Favorable	41	27 (65.9)	3.29 [2.27; 15.67]	39	27 (69.2)	1.87 [0.95; 2.76]	0.72 [0.42; 1.24]	0.239	0.397
Intermediate	115	77 (67.0)	1.87 [1.02; 4.63]	106	71 (67.0)	2.00 [1.84; 3.25]	0.89 [0.64; 1.24]	0.505	
Poor	22	10 (45.5)	12.22 [1.81; -]	19	12 (63.2)	1.02 [0.49; -]	0.47 [0.20; 1.14]	0.094	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core - 30 items; IMDC: International Metastatic RCC Database Consortium;									
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

EORTC QLQ-C30: Funktionsskala Emotionale Funktion

Tabelle 4G-38: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Emotionale Funktion aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
EORTC QLQ-C30 Emotional Functioning	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	143	68 (47.6)	11.01 [5.49; 18.40]	128	57 (44.5)	4.67 [3.25; -]	0.82 [0.57; 1.18]	0.295	0.599
Female	35	23 (65.7)	1.87 [0.95; 3.71]	36	23 (63.9)	2.56 [0.95; 7.33]	1.08 [0.61; 1.94]	0.784	
Age (Years)									
< 65	113	53 (46.9)	7.39 [3.71; 20.67]	89	44 (49.4)	4.53 [2.79; 10.15]	0.85 [0.57; 1.28]	0.447	0.791
≥ 65	65	38 (58.5)	5.78 [2.76; 14.78]	75	36 (48.0)	4.67 [1.91; 9.96]	0.87 [0.54; 1.39]	0.551	
ECOG performance status									
0	73	33 (45.2)	11.99 [3.71; 23.95]	69	37 (53.6)	4.63 [2.76; 9.96]	0.69 [0.42; 1.11]	0.124	0.299
≥1	105	58 (55.2)	5.52 [2.79; 14.78]	95	43 (45.3)	4.53 [2.79; 8.31]	1.01 [0.67; 1.51]	0.974	
Region									
North America	43	20 (46.5)	5.52 [3.71; 16.10]	33	10 (30.3)	Not reached [1.97; -]	0.98 [0.44; 2.18]	0.968	0.680
Western Europe	102	55 (53.9)	9.23 [2.76; 16.62]	89	47 (52.8)	3.25 [2.56; 8.31]	0.86 [0.58; 1.28]	0.464	
Rest of the World	33	16 (48.5)	7.39 [2.10; -]	42	23 (54.8)	4.63 [2.79; 10.15]	0.80 [0.42; 1.53]	0.505	
IMDC Risk Category									
Favorable	41	24 (58.5)	4.63 [2.27; 11.99]	39	20 (51.3)	2.79 [1.77; -]	0.91 [0.50; 1.65]	0.747	0.809
Intermediate	115	56 (48.7)	9.23 [3.68; 20.67]	106	52 (49.1)	4.63 [2.79; 8.31]	0.81 [0.55; 1.20]	0.301	
Poor	22	11 (50.0)	11.01 [0.69; -]	19	8 (42.1)	9.76 [1.02; -]	1.12 [0.45; 2.83]	0.803	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core - 30 items; IMDC: International Metastatic RCC Database Consortium;									
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

EORTC QLQ-C30: Funktionsskala Kognitive Funktion

Tabelle 4G-39: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Kognitive Funktion aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
EORTC QLQ-C30 Cognitive Functioning	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	143	91 (63.6)	3.71 [1.94; 6.41]	128	67 (52.3)	4.57 [2.79; 6.67]	1.04 [0.76; 1.43]	0.811	0.178
Female	35	30 (85.7)	1.68 [0.49; 1.87]	36	20 (55.6)	3.71 [1.87; 7.59]	1.65 [0.92; 2.93]	0.091	
Age (Years)									
< 65	113	78 (69.0)	2.92 [1.87; 5.55]	89	45 (50.6)	4.57 [2.79; 8.31]	1.33 [0.92; 1.92]	0.132	0.162
≥ 65	65	43 (66.2)	2.76 [1.84; 5.78]	75	42 (56.0)	3.68 [1.97; 4.63]	0.91 [0.59; 1.41]	0.676	
ECOG performance status									
0	73	49 (67.1)	3.65 [1.87; 7.39]	69	33 (47.8)	3.94 [3.65; 16.56]	1.32 [0.85; 2.06]	0.218	0.360
≥1	105	72 (68.6)	2.79 [1.84; 4.63]	95	54 (56.8)	2.86 [1.87; 5.52]	1.00 [0.70; 1.43]	0.994	
Region									
North America	43	27 (62.8)	5.49 [1.84; 8.31]	33	15 (45.5)	3.68 [1.81; -]	0.82 [0.42; 1.61]	0.560	0.472
Western Europe	102	73 (71.6)	2.76 [1.81; 3.68]	89	45 (50.6)	4.57 [2.86; 8.28]	1.31 [0.90; 1.91]	0.152	
Rest of the World	33	21 (63.6)	3.71 [0.95; 7.39]	42	27 (64.3)	2.83 [0.99; 7.39]	0.96 [0.54; 1.71]	0.893	
IMDC Risk Category									
Favorable	41	27 (65.9)	3.75 [1.87; 9.27]	39	20 (51.3)	3.65 [1.91; 8.28]	1.01 [0.57; 1.82]	0.964	0.926
Intermediate	115	81 (70.4)	2.76 [1.77; 4.17]	106	58 (54.7)	3.71 [2.79; 6.67]	1.18 [0.84; 1.66]	0.330	
Poor	22	13 (59.1)	3.71 [1.15; 10.19]	19	9 (47.4)	3.71 [1.02; -]	1.05 [0.44; 2.50]	0.912	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core - 30 items; IMDC: International Metastatic RCC Database Consortium;									
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

EORTC QLQ-C30: Funktionsskala Soziale Funktion

Tabelle 4G-40: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Soziale Funktion aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
EORTC QLQ-C30 Social Functioning	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in months [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
Sex									
Male	143	71 (49.7)	8.31 [2.96; 19.32]	128	75 (58.6)	2.79 [1.87; 5.62]	0.70 [0.51; 0.98]	0.037	0.309
Female	35	26 (74.3)	1.94 [0.95; 2.86]	36	23 (63.9)	1.87 [0.95; 8.31]	0.95 [0.54; 1.70]	0.871	
ECOG performance status									
0	73	43 (58.9)	3.75 [1.94; 11.99]	69	41 (59.4)	3.94 [1.87; 8.31]	0.82 [0.53; 1.26]	0.360	0.430
≥1	105	54 (51.4)	5.52 [1.94; 19.32]	95	57 (60.0)	2.07 [1.87; 4.40]	0.73 [0.50; 1.06]	0.098	
Region									
North America	43	20 (46.5)	5.52 [2.69; -]	33	19 (57.6)	2.76 [1.84; 8.05]	0.56 [0.29; 1.07]	0.078	0.475
Western Europe	102	57 (55.9)	5.55 [1.94; 16.59]	89	52 (58.4)	3.68 [1.87; 5.62]	0.74 [0.50; 1.09]	0.124	
Rest of the World	33	20 (60.6)	2.10 [0.95; -]	42	27 (64.3)	1.91 [1.02; 12.16]	1.00 [0.56; 1.79]	0.989	
IMDC Risk Category									
Favorable	41	23 (56.1)	8.35 [2.76; 16.85]	39	23 (59.0)	1.87 [0.99; 7.39]	0.51 [0.28; 0.93]	0.030	0.640
Intermediate	115	65 (56.5)	2.79 [1.87; 7.39]	106	67 (63.2)	2.76 [1.87; 5.03]	0.85 [0.61; 1.21]	0.371	
Poor	22	9 (40.9)	12.22 [1.81; -]	19	8 (42.1)	8.31 [0.95; -]	0.78 [0.30; 2.04]	0.618	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: full-analysis-set population with baseline with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core - 30 items; IMDC: International Metastatic RCC Database Consortium;									
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

Anhang 4-G7.4: Nebenwirkungen

Unerwünschte Ereignisse

Unerwünschte Ereignisse gesamt

Tabelle 4G-41: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Unerwünschte Ereignisse gesamt aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a		Belzutifan		Everolimus		Belzutifan vs. Everolimus		p-Value for Interaction Test ^f	
		Participants with Event	Median Time ^c in Weeks	Participants with Event	Median Time ^c in Weeks	Hazard Ratio ^d			
Adverse Events	N ^b	n (%)	[95 %-CI]	N ^b	n (%)	[95 %-CI]	[95 %-CI] p-Value ^{d,e}		
Sex									
Male	147	146 (99.3)	2.00 [1.57; 2.14]	139	137 (98.6)	1.71 [1.14; 1.86]	0.78 [0.61; 0.98]	0.037	0.148
Female	39	39 (100.0)	1.43 [1.00; 2.00]	38	38 (100.0)	1.14 [0.86; 1.86]	1.15 [0.73; 1.82]	0.550	
Age (Years)									
< 65	120	119 (99.2)	1.79 [1.14; 2.14]	97	97 (100.0)	1.43 [0.86; 2.00]	0.80 [0.61; 1.05]	0.102	0.589
≥ 65	66	66 (100.0)	2.00 [1.29; 2.14]	80	78 (97.5)	1.50 [1.14; 1.86]	0.86 [0.61; 1.19]	0.355	
ECOG performance status									
0	77	76 (98.7)	2.14 [1.71; 2.14]	75	73 (97.3)	1.57 [1.14; 2.00]	0.74 [0.53; 1.02]	0.067	0.370
≥1	109	109 (100.0)	1.57 [1.14; 2.00]	102	102 (100.0)	1.43 [1.14; 1.86]	0.91 [0.69; 1.20]	0.501	
Region									
North America	45	45 (100.0)	1.43 [1.00; 2.14]	37	36 (97.3)	1.43 [0.71; 2.00]	0.91 [0.59; 1.42]	0.691	0.539
Western Europe	104	103 (99.0)	2.00 [1.71; 2.14]	96	95 (99.0)	1.57 [1.14; 2.00]	0.74 [0.55; 0.98]	0.036	
Rest of the World	37	37 (100.0)	1.57 [1.00; 2.14]	44	44 (100.0)	1.50 [1.00; 2.14]	0.92 [0.59; 1.43]	0.708	
IMDC Risk Category									
Favorable	42	42 (100.0)	2.14 [1.14; 2.14]	42	42 (100.0)	1.57 [0.86; 2.14]	0.83 [0.54; 1.28]	0.396	0.968
Intermediate	122	122 (100.0)	1.79 [1.29; 2.14]	115	114 (99.1)	1.57 [1.14; 2.00]	0.82 [0.63; 1.06]	0.136	
Poor	22	21 (95.5)	1.50 [0.43; 2.14]	20	19 (95.0)	0.43 [0.14; 2.00]	0.83 [0.44; 1.55]	0.553	
a: Database Cutoff Date: 15APR2024									
b: Number of participants-as-treated population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; IMDC: International Metastatic RCC Database Consortium;									
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

Schwerwiegende unerwünschte Ereignisse

Tabelle 4G-42: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwerwiegende unerwünschte Ereignisse aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a		Belzutifan		Everolimus		Belzutifan vs. Everolimus		p-Value for Interaction Test ^f	
Serious Events	Adverse	Participants with Event	Median Time ^c in Weeks	Participants with Event	Median Time ^c in Weeks	Hazard Ratio ^d	p-Value ^{d,e}		
		N ^b n (%)	[95 %-CI]	N ^b n (%)	[95 %-CI]	[95 %-CI]			
Sex									
Male		147 64 (43.5)	98.86 [68.14; -]	139 52 (37.4)	69.29 [51.14; 122.57]	0.90 [0.61; 1.31]	0.568	0.939	
Female		39 19 (48.7)	149.14 [19.00; -]	38 17 (44.7)	119.43 [14.43; -]	1.05 [0.54; 2.06]	0.878		
Age (Years)									
< 65		120 54 (45.0)	98.86 [58.86; -]	97 36 (37.1)	119.43 [58.71; -]	0.99 [0.64; 1.53]	0.964	0.569	
≥ 65		66 29 (43.9)	108.29 [37.43; -]	80 33 (41.3)	57.43 [31.14; 88.00]	0.87 [0.52; 1.44]	0.580		
ECOG performance status									
0		77 28 (36.4)	149.14 [108.29; -]	75 23 (30.7)	88.00 [57.43; -]	0.96 [0.54; 1.70]	0.889	0.519	
≥1		109 55 (50.5)	72.14 [37.86; 143.86]	102 46 (45.1)	58.71 [24.43; -]	0.87 [0.58; 1.30]	0.500		
Region									
North America		45 21 (46.7)	72.14 [22.71; -]	37 12 (32.4)	Not reached [22.00; -]	1.13 [0.54; 2.37]	0.739	0.466	
Western Europe		104 47 (45.2)	95.43 [39.14; 143.86]	96 36 (37.5)	72.14 [36.14; -]	0.97 [0.62; 1.51]	0.896		
Rest of the World		37 15 (40.5)	Not reached [19.00; -]	44 21 (47.7)	58.71 [31.14; 119.43]	0.71 [0.35; 1.41]	0.322		
IMDC Risk Category									
Favorable		42 14 (33.3)	Not reached [39.00; -]	42 15 (35.7)	88.00 [62.57; -]	0.80 [0.38; 1.67]	0.549	0.934	
Intermediate		122 55 (45.1)	108.29 [38.29; -]	115 44 (38.3)	72.14 [38.86; -]	0.97 [0.64; 1.45]	0.871		
Poor		22 14 (63.6)	72.14 [4.29; 98.86]	20 10 (50.0)	24.43 [4.57; -]	0.89 [0.37; 2.09]	0.781		
a: Database Cutoff Date: 15APR2024									
b: Number of participants: all-participants-as-treated population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; IMDC: International Metastatic RCC Database Consortium;									
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5)

Tabelle 4G-43: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a		Belzutifan		Everolimus		Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Severe Events (CTCAE-Grade 3-5)	Adverse (CTCAE-Grade 3-5)	Participants with Event N ^b n (%)	Median Time ^c in Weeks [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
Sex								
Male		147 93 (63.3)	34.00 [16.29; 43.14]	139 79 (56.8)	23.00 [15.86; 36.14]	0.88 [0.65; 1.19]	0.409	0.966
Female		39 30 (76.9)	16.29 [6.00; 27.86]	38 26 (68.4)	11.86 [8.00; 26.86]	0.90 [0.52; 1.56]	0.715	
Age (Years)								
< 65		120 81 (67.5)	25.43 [15.86; 38.71]	97 56 (57.7)	23.00 [14.43; 50.29]	0.98 [0.69; 1.38]	0.891	0.320
≥ 65		66 42 (63.6)	27.86 [14.86; 43.14]	80 49 (61.3)	19.71 [10.71; 29.14]	0.78 [0.51; 1.18]	0.236	
ECOG performance status								
0		77 41 (53.2)	45.00 [25.43; 77.57]	75 36 (48.0)	51.29 [26.29; 69.29]	0.90 [0.57; 1.42]	0.650	0.497
≥1		109 82 (75.2)	20.29 [12.00; 27.86]	102 69 (67.6)	12.57 [10.71; 20.00]	0.82 [0.59; 1.14]	0.231	
Region								
North America		45 28 (62.2)	27.86 [14.00; 63.86]	37 16 (43.2)	23.86 [7.86; -]	0.83 [0.43; 1.61]	0.583	0.384
Western Europe		104 69 (66.3)	32.00 [16.14; 39.86]	96 64 (66.7)	16.14 [11.43; 23.86]	0.72 [0.51; 1.02]	0.067	
Rest of the World		37 26 (70.3)	12.14 [4.14; 72.14]	44 25 (56.8)	51.29 [15.86; 72.86]	1.22 [0.70; 2.15]	0.483	
IMDC Risk Category								
Favorable		42 21 (50.0)	63.86 [16.14; 125.57]	42 20 (47.6)	29.14 [14.43; 81.71]	0.82 [0.44; 1.55]	0.547	0.742
Intermediate		122 85 (69.7)	27.86 [15.43; 38.14]	115 68 (59.1)	23.00 [15.00; 38.71]	0.94 [0.68; 1.30]	0.706	
Poor		22 17 (77.3)	16.14 [4.29; 39.86]	20 17 (85.0)	9.43 [1.43; 16.14]	0.67 [0.34; 1.33]	0.257	
a: Database Cutoff Date: 15APR2024								
b: Number of participants: all-participants-as-treated population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies								
c: From product-limit (Kaplan-Meier) method for censored data								
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval								
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)								
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)								
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; CTCAE: Common Terminology Criteria for Adverse Events; IMDC: International Metastatic RCC Database Consortium;								
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor								

Therapieabbruch wegen unerwünschter Ereignisse

Tabelle 4G-44: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Therapieabbruch wegen unerwünschter Ereignisse aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a		Belzutifan		Everolimus		Belzutifan vs. Everolimus		p-Value for Interaction Test ^f	
Adverse Events to Leading Treatment Discontinuation	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}		
Sex									
Male	147	10 (6.8)	Not reached [-; -]	139	17 (12.2)	136.43 [104.29; -]	0.37 [0.16; 0.84]	0.017	0.579
Female	39	3 (7.7)	Not reached [-; -]	38	8 (21.1)	Not reached [34.43; -]	0.32 [0.08; 1.19]	0.089	
ECOG performance status									
0	77	4 (5.2)	Not reached [-; -]	75	10 (13.3)	136.43 [104.29; -]	0.29 [0.08; 0.98]	0.046	0.818
≥1	109	9 (8.3)	Not reached [-; -]	102	15 (14.7)	Not reached [-; -]	0.35 [0.15; 0.84]	0.019	
Region									
North America	45	3 (6.7)	Not reached [-; -]	37	6 (16.2)	Not reached [28.14; -]	0.21 [0.04; 1.06]	0.059	0.717
Western Europe	104	7 (6.7)	Not reached [-; -]	96	14 (14.6)	136.43 [136.43; -]	0.29 [0.11; 0.76]	0.011	
Rest of the World	37	3 (8.1)	Not reached [-; -]	44	5 (11.4)	Not reached [104.29; -]	0.65 [0.15; 2.79]	0.559	
IMDC Risk Category									
Favorable	42	4 (9.5)	Not reached [-; -]	42	7 (16.7)	Not reached [104.29; -]	0.50 [0.15; 1.74]	0.276	0.430
Intermediate	122	7 (5.7)	Not reached [-; -]	115	17 (14.8)	136.43 [-; -]	0.24 [0.09; 0.61]	0.003	
Poor	22	2 (9.1)	Not reached [72.14; -]	20	1 (5.0)	Not reached [-; -]	1.20 [0.10; 14.05]	0.884	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: all-participants-as-treated population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; IMDC: International Metastatic RCC Database Consortium;									
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

Unerwünschte Ereignisse (gegliedert nach SOC und PT)

Unerwünschte Ereignisse gesamt (SOC und PT)

Tabelle 4G-45: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Unerwünschte Ereignisse gesamt (SOC) aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f	
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}		
SOC ^g : Blood and lymphatic system disorders										
Sex										
Male	147	117 (79.6)	6.29 [4.14; 8.14]	139	81 (58.3)	13.14 [8.43; 16.29]	1.79 [1.34; 2.38]	< 0.001	0.352	
Female	39	35 (89.7)	3.71 [2.14; 4.14]	38	26 (68.4)	8.14 [4.14; 20.29]	2.46 [1.44; 4.23]	0.001		
Age (Years)										
< 65	120	95 (79.2)	6.86 [4.14; 8.14]	97	60 (61.9)	14.14 [8.29; 32.00]	1.71 [1.23; 2.37]	0.001	0.228	
≥ 65	66	57 (86.4)	4.14 [2.57; 4.14]	80	47 (58.8)	11.43 [8.14; 15.86]	2.28 [1.54; 3.37]	< 0.001		
ECOG performance status										
0	77	58 (75.3)	4.29 [4.00; 8.14]	75	38 (50.7)	17.29 [12.00; 68.14]	2.29 [1.51; 3.49]	< 0.001	0.157	
≥1	109	94 (86.2)	4.14 [3.86; 7.71]	102	69 (67.6)	8.29 [7.86; 13.14]	1.61 [1.18; 2.21]	0.003		
Region										
North America	45	38 (84.4)	4.14 [2.57; 7.86]	37	22 (59.5)	11.71 [4.14; -]	1.52 [0.89; 2.59]	0.126	0.112	
Western Europe	104	81 (77.9)	4.14 [4.00; 8.14]	96	60 (62.5)	12.29 [8.14; 16.00]	1.63 [1.17; 2.29]	0.004		
Rest of the World	37	33 (89.2)	4.14 [2.86; 8.14]	44	25 (56.8)	16.29 [8.14; 68.14]	3.37 [1.91; 5.97]	< 0.001		
IMDC Risk Category										
Favorable	42	32 (76.2)	4.14 [3.57; 8.14]	42	19 (45.2)	32.57 [11.43; -]	2.96 [1.61; 5.45]	< 0.001	0.117	
Intermediate	122	102 (83.6)	4.14 [4.14; 7.86]	115	72 (62.6)	12.14 [8.14; 15.86]	1.77 [1.31; 2.41]	< 0.001		
Poor	22	18 (81.8)	4.14 [2.14; 8.14]	20	16 (80.0)	6.21 [1.86; 12.43]	1.10 [0.56; 2.18]	0.775		
Sex										
Male	147	75 (51.0)	40.57 [18.71; 131.43]	139	89 (64.0)	4.43 [3.14; 16.57]	0.56 [0.41; 0.77]	< 0.001	0.570	
Female	39	22 (56.4)	15.57 [7.00; 70.14]	38	25 (65.8)	4.93 [2.29; 25.14]	0.67 [0.37; 1.19]	0.171		
Age (Years)										
< 65	120	64 (53.3)	26.00 [13.86; 67.71]	97	58 (59.8)	12.14 [3.86; 28.00]	0.71 [0.50; 1.02]	0.065	0.067	
≥ 65	66	33 (50.0)	40.57 [8.00; -]	80	56 (70.0)	3.43 [2.14; 7.00]	0.46 [0.29; 0.71]	< 0.001		

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
ECOG performance status									
0	77	31 (40.3)	71.71 [26.00; -]	75	46 (61.3)	8.29 [3.43; 25.14]	0.48 [0.30; 0.76]	0.002	0.178
≥1	109	66 (60.6)	18.71 [8.00; 40.57]	102	68 (66.7)	4.00 [2.57; 8.71]	0.65 [0.46; 0.92]	0.016	
Region									
North America	45	27 (60.0)	15.57 [4.14; 151.14]	37	28 (75.7)	4.00 [2.14; 8.14]	0.55 [0.32; 0.95]	0.031	0.555
Western Europe	104	49 (47.1)	41.71 [20.29; -]	96	59 (61.5)	6.14 [3.14; 28.00]	0.53 [0.36; 0.77]	0.001	
Rest of the World	37	21 (56.8)	19.29 [5.00; 55.14]	44	27 (61.4)	6.14 [1.86; -]	0.79 [0.45; 1.41]	0.431	
IMDC Risk Category									
Favorable	42	20 (47.6)	70.14 [9.29; -]	42	29 (69.0)	3.86 [2.14; 8.29]	0.44 [0.24; 0.78]	0.005	0.252
Intermediate	122	69 (56.6)	20.71 [8.14; 43.00]	115	72 (62.6)	8.00 [3.43; 23.86]	0.68 [0.48; 0.95]	0.022	
Poor	22	8 (36.4)	84.43 [2.00; -]	20	13 (65.0)	4.14 [0.57; -]	0.40 [0.16; 1.00]	0.050 ^h	
SOC ^g : Infections and infestations									
Sex									
Male	147	57 (38.8)	80.00 [48.14; 118.00]	139	54 (38.8)	52.00 [36.57; 58.71]	0.58 [0.39; 0.86]	0.006	0.956
Female	39	13 (33.3)	91.71 [29.71; -]	38	14 (36.8)	53.00 [24.14; -]	0.58 [0.26; 1.28]	0.177	
Age (Years)									
< 65	120	47 (39.2)	87.29 [48.14; 112.00]	97	36 (37.1)	53.00 [36.57; -]	0.59 [0.37; 0.94]	0.027	0.618
≥ 65	66	23 (34.8)	72.00 [42.29; -]	80	32 (40.0)	48.00 [24.14; 69.29]	0.56 [0.32; 0.97]	0.040	
ECOG performance status									
0	77	23 (29.9)	101.57 [66.14; -]	75	23 (30.7)	57.43 [48.00; -]	0.60 [0.32; 1.11]	0.103	0.470
≥1	109	47 (43.1)	58.86 [39.57; 99.29]	102	45 (44.1)	43.43 [16.71; 55.29]	0.52 [0.34; 0.81]	0.004	
IMDC Risk Category									
Favorable	42	12 (28.6)	101.57 [43.43; -]	42	15 (35.7)	55.29 [48.00; -]	0.63 [0.29; 1.37]	0.243	0.549
Intermediate	122	50 (41.0)	87.29 [50.14; 118.00]	115	48 (41.7)	43.43 [24.14; 58.71]	0.50 [0.33; 0.77]	0.002	
Poor	22	8 (36.4)	58.86 [19.00; -]	20	5 (25.0)	Not reached [26.00; -]	1.07 [0.34; 3.42]	0.903	
SOC ^g : Metabolism and nutrition disorders									
Sex									
Male	147	56 (38.1)	95.43 [68.43; -]	139	71 (51.1)	20.00 [11.57; 43.14]	0.49 [0.34; 0.71]	< 0.001	0.418

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
Female	39	17 (43.6)	64.71 [20.71; -]	38	18 (47.4)	22.14 [4.00; -]	0.64 [0.32; 1.27]	0.201	
Age (Years)									
< 65	120	49 (40.8)	72.00 [40.14; -]	97	46 (47.4)	28.29 [12.29; -]	0.60 [0.40; 0.91]	0.017	0.231
≥ 65	66	24 (36.4)	95.43 [74.00; -]	80	43 (53.8)	16.29 [4.14; 31.14]	0.44 [0.26; 0.74]	0.002	
Region									
North America	45	19 (42.2)	78.00 [16.14; -]	37	20 (54.1)	12.14 [3.71; -]	0.46 [0.23; 0.89]	0.021	0.718
Western Europe	104	38 (36.5)	88.29 [46.29; -]	96	47 (49.0)	28.29 [12.29; 91.86]	0.48 [0.31; 0.74]	< 0.001	
Rest of the World	37	16 (43.2)	64.71 [23.57; -]	44	22 (50.0)	17.43 [5.86; -]	0.72 [0.38; 1.38]	0.326	
IMDC Risk Category									
Favorable	42	13 (31.0)	Not reached [24.43; -]	42	15 (35.7)	Not reached [6.43; -]	0.68 [0.32; 1.44]	0.309	0.791
Intermediate	122	52 (42.6)	72.29 [40.14; -]	115	65 (56.5)	16.86 [6.29; 30.71]	0.46 [0.31; 0.68]	< 0.001	
Poor	22	8 (36.4)	108.43 [18.14; -]	20	9 (45.0)	17.43 [4.43; -]	0.50 [0.18; 1.36]	0.173	
SOC ^g : Nervous system disorders									
Sex									
Male	147	54 (36.7)	99.14 [68.29; -]	139	24 (17.3)	Not reached [-; -]	1.92 [1.18; 3.13]	0.008	0.546
Female	39	18 (46.2)	115.86 [22.00; -]	38	10 (26.3)	73.14 [40.43; -]	1.48 [0.67; 3.29]	0.335	
Age (Years)									
< 65	120	47 (39.2)	87.86 [67.71; -]	97	16 (16.5)	Not reached [-; -]	2.22 [1.25; 3.93]	0.007	0.326
≥ 65	66	25 (37.9)	115.86 [31.71; -]	80	18 (22.5)	Not reached [73.14; -]	1.35 [0.72; 2.51]	0.348	
ECOG performance status									
0	77	26 (33.8)	115.86 [69.00; -]	75	14 (18.7)	Not reached [-; -]	1.75 [0.91; 3.37]	0.092	0.841
≥1	109	46 (42.2)	77.43 [32.14; 148.57]	102	20 (19.6)	Not reached [73.14; -]	1.78 [1.04; 3.04]	0.036	
Region									
North America	45	23 (51.1)	62.00 [11.00; 100.29]	37	10 (27.0)	Not reached [27.43; -]	1.50 [0.69; 3.24]	0.304	0.894
Western Europe	104	39 (37.5)	87.86 [48.57; 148.57]	96	17 (17.7)	Not reached [73.14; -]	1.70 [0.95; 3.05]	0.074	
Rest of the World	37	10 (27.0)	Not reached [-; -]	44	7 (15.9)	Not reached [-; -]	1.80 [0.68; 4.74]	0.234	
IMDC Risk Category									
Favorable	42	14 (33.3)	148.57 [24.43; -]	42	9 (21.4)	Not reached [32.43; -]	1.34 [0.57; 3.15]	0.506	0.597
Intermediate	122	48	87.86	115	22	Not reached	1.82	0.022	

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
Poor	22	(39.3) 10 (45.5)	[62.00; -] 67.71 [1.71; -]	20	(19.1) 3 (15.0)	[73.14; -] Not reached [-; -]	[1.09; 3.04] 2.89 [0.78; 10.75]	0.114	
SOC^g: Respiratory, thoracic and mediastinal disorders									
Sex									
Male	147	67 (45.6)	68.14 [39.14; 103.29]	139	73 (52.5)	24.00 [14.43; 46.43]	0.66 [0.47; 0.92]	0.014	0.604
Female	39	21 (53.8)	22.86 [20.14; 95.14]	38	20 (52.6)	16.14 [11.43; 34.43]	0.63 [0.33; 1.21]	0.168	
Age (Years)									
< 65	120	56 (46.7)	57.86 [26.29; 95.14]	97	51 (52.6)	26.71 [14.71; 51.14]	0.69 [0.47; 1.01]	0.058	0.643
≥ 65	66	32 (48.5)	45.71 [16.14; -]	80	42 (52.5)	15.71 [10.29; 28.14]	0.66 [0.41; 1.06]	0.085	
ECOG performance status									
0	77	29 (37.7)	121.14 [25.43; -]	75	42 (56.0)	18.14 [10.14; 46.43]	0.52 [0.32; 0.85]	0.009	0.098
≥1	109	59 (54.1)	45.71 [22.86; 74.00]	102	51 (50.0)	21.86 [13.71; 44.14]	0.77 [0.52; 1.13]	0.186	
Region									
North America	45	31 (68.9)	16.14 [6.71; 22.71]	37	23 (62.2)	10.71 [4.43; 19.57]	0.81 [0.47; 1.42]	0.470	0.560
Western Europe	104	43 (41.3)	77.57 [44.14; 112.43]	96	49 (51.0)	21.14 [13.14; 100.43]	0.53 [0.34; 0.80]	0.003	
Rest of the World	37	14 (37.8)	Not reached [22.86; -]	44	21 (47.7)	46.43 [17.00; -]	0.71 [0.36; 1.41]	0.326	
IMDC Risk Category									
Favorable	42	17 (40.5)	Not reached [12.14; -]	42	25 (59.5)	14.43 [6.86; 67.71]	0.57 [0.30; 1.06]	0.074	0.535
Intermediate	122	61 (50.0)	56.00 [26.29; 91.14]	115	59 (51.3)	21.86 [15.43; 34.43]	0.71 [0.49; 1.03]	0.068	
Poor	22	10 (45.5)	45.71 [16.14; 103.29]	20	9 (45.0)	51.14 [5.86; -]	0.67 [0.26; 1.71]	0.403	
SOC^g: Skin and subcutaneous tissue disorders									
Sex									
Male	147	38 (25.9)	Not reached [110.00; -]	139	69 (49.6)	21.29 [8.00; -]	0.36 [0.24; 0.54]	< 0.001	0.824
Female	39	10 (25.6)	Not reached [68.71; -]	38	20 (52.6)	7.14 [4.14; -]	0.36 [0.16; 0.77]	0.009	
Age (Years)									
< 65	120	35 (29.2)	Not reached [95.57; -]	97	49 (50.5)	11.86 [6.29; -]	0.43 [0.28; 0.67]	< 0.001	0.162
≥ 65	66	13 (19.7)	Not reached [67.86; -]	80	40 (50.0)	20.14 [5.43; 34.57]	0.22 [0.12; 0.43]	< 0.001	

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
ECOG performance status									
0	77	18 (23.4)	Not reached [68.71; -]	75	40 (53.3)	16.29 [6.29; -]	0.31 [0.17; 0.54]	< 0.001	0.509
≥1	109	30 (27.5)	Not reached [110.00; -]	102	49 (48.0)	30.00 [5.71; -]	0.40 [0.25; 0.64]	< 0.001	
Region									
North America	45	11 (24.4)	Not reached [46.00; -]	37	15 (40.5)	Not reached [6.14; -]	0.46 [0.21; 1.02]	0.057	0.656
Western Europe	104	24 (23.1)	Not reached [110.00; -]	96	47 (49.0)	20.14 [5.43; -]	0.31 [0.18; 0.51]	< 0.001	
Rest of the World	37	13 (35.1)	Not reached [35.29; -]	44	27 (61.4)	7.43 [3.14; 34.57]	0.43 [0.22; 0.83]	0.012	
IMDC Risk Category									
Favorable	42	7 (16.7)	Not reached [46.00; -]	42	21 (50.0)	30.00 [4.14; -]	0.21 [0.09; 0.51]	< 0.001	0.406
Intermediate	122	37 (30.3)	Not reached [95.57; -]	115	61 (53.0)	8.29 [5.43; -]	0.41 [0.27; 0.63]	< 0.001	
Poor	22	4 (18.2)	Not reached [20.43; -]	20	7 (35.0)	Not reached [7.29; -]	0.32 [0.08; 1.22]	0.095	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: all-participants-as-treated population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
g: A system organ class appears on this report only if its incidence ≥10% or (incidence ≥1% and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is smaller than 0.05									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; IMDC: International Metastatic RCC Database Consortium; SOC: System Organ Class									
h: Unrounded p-value > 0.050									
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

Tabelle 4G-46: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Unerwünschte Ereignisse gesamt (PT) aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
		Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]		Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
Adverse Events	N ^b			N ^b					
SOC: Blood and lymphatic system disorders - PT ^g : Anaemia									
Sex									
Male	147	115 (78.2)	7.86 [4.14; 8.14]	139	75 (54.0)	16.00 [12.14; 38.86]	2.04 [1.52; 2.74]	< 0.001	0.368
Female	39	35 (89.7)	4.14 [2.14; 4.29]	38	24 (63.2)	12.14 [7.71; 32.00]	2.89 [1.66; 5.04]	< 0.001	
Age (Years)									
< 65	120	93 (77.5)	7.71 [4.14; 8.14]	97	57 (58.8)	16.00 [12.29; 32.57]	1.85 [1.33; 2.58]	< 0.001	0.122
≥ 65	66	57 (86.4)	4.14 [2.86; 7.71]	80	42 (52.5)	12.14 [8.43; 68.14]	2.79 [1.86; 4.19]	< 0.001	
ECOG performance status									
0	77	56 (72.7)	7.86 [4.14; 8.14]	75	33 (44.0)	64.14 [13.14; -]	2.75 [1.77; 4.28]	< 0.001	0.081
≥1	109	94 (86.2)	4.14 [4.00; 7.86]	102	66 (64.7)	12.14 [8.14; 15.86]	1.80 [1.31; 2.48]	< 0.001	
Region									
North America	45	37 (82.2)	6.29 [3.00; 8.14]	37	21 (56.8)	12.00 [5.86; -]	1.62 [0.94; 2.79]	0.082	0.222
Western Europe	104	81 (77.9)	4.14 [4.00; 8.14]	96	54 (56.3)	15.86 [8.43; 32.00]	2.01 [1.42; 2.85]	< 0.001	
Rest of the World	37	32 (86.5)	4.29 [2.86; 8.14]	44	24 (54.5)	17.29 [11.43; -]	3.59 [2.00; 6.43]	< 0.001	
IMDC Risk Category									
Favorable	42	32 (76.2)	5.93 [4.00; 10.86]	42	16 (38.1)	68.14 [16.29; -]	4.03 [2.09; 7.77]	< 0.001	0.051
Intermediate	122	100 (82.0)	4.29 [4.14; 8.00]	115	67 (58.3)	15.00 [11.86; 31.57]	2.03 [1.49; 2.78]	< 0.001	
Poor	22	18 (81.8)	4.14 [2.14; 8.14]	20	16 (80.0)	6.21 [1.86; 12.43]	1.10 [0.56; 2.18]	0.775	
SOC: Eye disorders - PT ^g : Vision blurred									
Sex									
Male	147	7 (4.8)	n.c.	139	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Female	39	3 (7.7)	n.c.	38	0 (0.0)	n.c.	n.c.	n.c.	
Age (Years)									
< 65	120	4 (3.3)	n.c.	97	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65	66	6 (9.1)	n.c.	80	0 (0.0)	n.c.	n.c.	n.c.	
ECOG performance status									
0	77	2 (2.6)	n.c.	75	0 (0.0)	n.c.	n.c.	n.c.	n.c.

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
≥1	109	8 (7.3)	n.c.	102	0 (0.0)	n.c.	n.c.	n.c.	
Region									
North America	45	5 (11.1)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Western Europe	104	4 (3.8)	n.c.	96	0 (0.0)	n.c.	n.c.	n.c.	
Rest of the World	37	1 (2.7)	n.c.	44	0 (0.0)	n.c.	n.c.	n.c.	
IMDC Risk Category									
Favorable	42	2 (4.8)	n.c.	42	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Intermediate	122	6 (4.9)	n.c.	115	0 (0.0)	n.c.	n.c.	n.c.	
Poor	22	2 (9.1)	n.c.	20	0 (0.0)	n.c.	n.c.	n.c.	
SOC: Gastrointestinal disorders - PT ^g : Constipation									
Sex									
Male	147	22 (15.0)	Not reached [-; -]	139	9 (6.5)	Not reached [-; -]	2.11 [0.97; 4.62]	0.061	0.108
Female	39	10 (25.6)	Not reached [98.57; -]	38	1 (2.6)	Not reached [-; -]	9.58 [1.22; 75.44]	0.032	
Age (Years)									
< 65	120	23 (19.2)	Not reached [-; -]	97	6 (6.2)	Not reached [-; -]	2.99 [1.21; 7.41]	0.018	0.797
≥ 65	66	9 (13.6)	Not reached [-; -]	80	4 (5.0)	Not reached [-; -]	2.42 [0.74; 7.91]	0.144	
ECOG performance status									
0	77	9 (11.7)	Not reached [-; -]	75	5 (6.7)	Not reached [-; -]	1.86 [0.62; 5.56]	0.265	0.269
≥1	109	23 (21.1)	Not reached [-; -]	102	5 (4.9)	Not reached [-; -]	3.66 [1.38; 9.74]	0.009	
Region									
North America	45	9 (20.0)	Not reached [-; -]	37	6 (16.2)	Not reached [25.86; -]	1.12 [0.39; 3.19]	0.829	0.064
Western Europe	104	18 (17.3)	Not reached [-; -]	96	2 (2.1)	Not reached [-; -]	6.92 [1.59; 30.13]	0.010	
Rest of the World	37	5 (13.5)	Not reached [-; -]	44	2 (4.5)	Not reached [-; -]	3.31 [0.64; 17.09]	0.154	
IMDC Risk Category									
Favorable	42	8 (19.0)	Not reached [98.57; -]	42	2 (4.8)	Not reached [-; -]	3.83 [0.81; 18.09]	0.090	0.387
Intermediate	122	21 (17.2)	Not reached [-; -]	115	8 (7.0)	Not reached [-; -]	2.44 [1.07; 5.52]	0.033	
Poor	22	3 (13.6)	Not reached [67.57; -]	20	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.282	
SOC: Gastrointestinal disorders - PT ^g : Diarrhoea									
Sex									
Male	147	21 (14.3)	Not reached [-; -]	139	31 (22.3)	135.71 [135.71; -]	0.50 [0.28; 0.89]	0.018	0.179

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
Female	39	8 (20.5)	98.14 [48.57; -]	38	5 (13.2)	Not reached [-; -]	0.77 [0.22; 2.70]	0.681	
Age (Years)									
< 65	120	17 (14.2)	Not reached [151.29; -]	97	18 (18.6)	Not reached [72.29; -]	0.61 [0.31; 1.21]	0.155	0.991
≥ 65	66	12 (18.2)	Not reached [98.14; -]	80	18 (22.5)	135.71 [-; -]	0.56 [0.26; 1.19]	0.131	
ECOG performance status									
0	77	7 (9.1)	Not reached [-; -]	75	13 (17.3)	Not reached [72.29; -]	0.44 [0.17; 1.12]	0.084	0.379
≥1	109	22 (20.2)	Not reached [151.29; -]	102	23 (22.5)	135.71 [-; -]	0.61 [0.33; 1.12]	0.112	
Region									
North America	45	10 (22.2)	Not reached [71.71; -]	37	10 (27.0)	45.43 [45.43; -]	0.46 [0.18; 1.20]	0.111	0.830
Western Europe	104	13 (12.5)	Not reached [151.29; -]	96	18 (18.8)	135.71 [72.29; -]	0.42 [0.19; 0.89]	0.025	
Rest of the World	37	6 (16.2)	Not reached [-; -]	44	8 (18.2)	Not reached [-; -]	0.90 [0.31; 2.60]	0.846	
IMDC Risk Category									
Favorable	42	7 (16.7)	Not reached [-; -]	42	11 (26.2)	135.71 [-; -]	0.46 [0.17; 1.23]	0.120	0.711
Intermediate	122	19 (15.6)	Not reached [151.29; -]	115	20 (17.4)	Not reached [-; -]	0.66 [0.34; 1.26]	0.205	
Poor	22	3 (13.6)	Not reached [59.14; -]	20	5 (25.0)	Not reached [11.29; -]	0.44 [0.10; 1.87]	0.268	
SOC: Gastrointestinal disorders - PT*: Stomatitis									
Sex									
Male	147	3 (2.0)	Not reached [-; -]	139	51 (36.7)	Not reached [44.00; -]	0.04 [0.01; 0.13]	< 0.001	0.364
Female	39	2 (5.1)	Not reached [-; -]	38	14 (36.8)	Not reached [8.00; -]	0.08 [0.02; 0.38]	0.001	
Age (Years)									
< 65	120	4 (3.3)	Not reached [-; -]	97	35 (36.1)	Not reached [44.00; -]	0.07 [0.02; 0.19]	< 0.001	0.362
≥ 65	66	1 (1.5)	Not reached [-; -]	80	30 (37.5)	Not reached [-; -]	0.03 [0.00; 0.21]	< 0.001	
ECOG performance status									
0	77	1 (1.3)	Not reached [-; -]	75	28 (37.3)	Not reached [-; -]	0.03 [0.00; 0.21]	< 0.001	0.312
≥1	109	4 (3.7)	Not reached [-; -]	102	37 (36.3)	58.43 [44.00; -]	0.06 [0.02; 0.17]	< 0.001	
Region									
North America	45	2 (4.4)	Not reached [-; -]	37	15 (40.5)	Not reached [4.00; -]	0.04 [0.01; 0.31]	0.002	0.898
Western Europe	104	2 (1.9)	Not reached [-; -]	96	30 (31.3)	Not reached [44.00; -]	0.05 [0.01; 0.19]	< 0.001	
Rest of the World	37	1 (2.7)	Not reached [-; -]	44	20 (45.5)	Not reached [3.57; -]	0.04 [0.01; 0.33]	0.002	

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
IMDC Risk Category									
Favorable	42	1 (2.4)	Not reached [-; -]	42	16 (38.1)	Not reached [7.86; -]	0.04 [0.01; 0.34]	0.003	0.502
Intermediate	122	4 (3.3)	Not reached [-; -]	115	41 (35.7)	Not reached [44.00; -]	0.07 [0.02; 0.19]	< 0.001	
Poor	22	0 (0.0)	Not reached [-; -]	20	8 (40.0)	23.86 [4.14; -]	n.a. [n.a.; n.a.]	< 0.001	
SOC: General disorders and administration site conditions - PT ^g : Pyrexia									
Sex									
Male	147	10 (6.8)	Not reached [-; -]	139	17 (12.2)	Not reached [-; -]	0.41 [0.18; 0.91]	0.028	0.639
Female	39	2 (5.1)	Not reached [-; -]	38	5 (13.2)	Not reached [-; -]	0.26 [0.05; 1.49]	0.132	
Age (Years)									
< 65	120	9 (7.5)	Not reached [-; -]	97	11 (11.3)	Not reached [-; -]	0.52 [0.21; 1.28]	0.156	0.288
≥ 65	66	3 (4.5)	Not reached [-; -]	80	11 (13.8)	Not reached [55.29; -]	0.21 [0.06; 0.78]	0.020	
ECOG performance status									
0	77	5 (6.5)	Not reached [-; -]	75	6 (8.0)	Not reached [-; -]	0.63 [0.19; 2.14]	0.459	0.247
≥1	109	7 (6.4)	Not reached [-; -]	102	16 (15.7)	Not reached [55.29; -]	0.28 [0.11; 0.70]	0.007	
Region									
North America	45	4 (8.9)	Not reached [108.14; -]	37	5 (13.5)	36.29 [28.00; -]	0.16 [0.03; 0.93]	0.041	0.472
Western Europe	104	3 (2.9)	Not reached [-; -]	96	9 (9.4)	Not reached [-; -]	0.22 [0.06; 0.86]	0.029	
Rest of the World	37	5 (13.5)	Not reached [-; -]	44	8 (18.2)	Not reached [-; -]	0.71 [0.23; 2.18]	0.551	
IMDC Risk Category									
Favorable	42	1 (2.4)	Not reached [-; -]	42	8 (19.0)	Not reached [55.29; -]	0.08 [0.01; 0.69]	0.021	0.111
Intermediate	122	11 (9.0)	Not reached [-; -]	115	13 (11.3)	Not reached [-; -]	0.59 [0.26; 1.36]	0.218	
Poor	22	0 (0.0)	Not reached [-; -]	20	1 (5.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.294	
SOC: Investigations - PT ^g : Weight decreased									
Sex									
Male	147	10 (6.8)	Not reached [-; -]	139	15 (10.8)	Not reached [-; -]	0.38 [0.16; 0.91]	0.029	0.333
Female	39	0 (0.0)	Not reached [-; -]	38	1 (2.6)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.311	
Age (Years)									
< 65	120	4 (3.3)	Not reached [-; -]	97	8 (8.2)	Not reached [73.43; -]	0.24 [0.07; 0.84]	0.026	0.396
≥ 65	66	6 (9.1)	Not reached [148.57; -]	80	8 (10.0)	Not reached [-; -]	0.54 [0.17; 1.73]	0.297	
ECOG performance status									
0	77	3 (3.9)	Not reached [-; -]	75	4 (5.3)	Not reached [-; -]	0.74 [0.17; 3.32]	0.696	0.533

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
≥1	109	7 (6.4)	Not reached [-; -]	102	12 (11.8)	Not reached [72.86; -]	0.23 [0.08; 0.66]	0.006	
Region									
North America	45	4 (8.9)	Not reached [128.14; -]	37	7 (18.9)	Not reached [32.00; -]	0.26 [0.07; 1.03]	0.054	0.627
Western Europe	104	4 (3.8)	Not reached [148.57; -]	96	5 (5.2)	Not reached [-; -]	0.34 [0.07; 1.52]	0.157	
Rest of the World	37	2 (5.4)	Not reached [-; -]	44	4 (9.1)	Not reached [73.43; -]	0.52 [0.09; 2.83]	0.446	
IMDC Risk Category									
Favorable	42	2 (4.8)	148.57 [128.14; -]	42	2 (4.8)	Not reached [-; -]	0.28 [0.02; 3.59]	0.328	0.507
Intermediate	122	7 (5.7)	Not reached [-; -]	115	10 (8.7)	Not reached [-; -]	0.55 [0.21; 1.46]	0.232	
Poor	22	1 (4.5)	Not reached [84.43; -]	20	4 (20.0)	72.86 [72.86; -]	n.a. [n.a.; n.a.]	0.997	
SOC: Investigations - PT ^g : Weight increased									
Sex									
Male	147	10 (6.8)	Not reached [-; -]	139	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	0.997
Female	39	4 (10.3)	Not reached [-; -]	38	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.085	
Age (Years)									
< 65	120	11 (9.2)	Not reached [-; -]	97	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004	0.997
≥ 65	66	3 (4.5)	Not reached [-; -]	80	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.079	
ECOG performance status									
0	77	6 (7.8)	n.c.	75	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥1	109	8 (7.3)	n.c.	102	0 (0.0)	n.c.	n.c.	n.c.	
Region									
North America	45	8 (17.8)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Western Europe	104	3 (2.9)	n.c.	96	0 (0.0)	n.c.	n.c.	n.c.	
Rest of the World	37	3 (8.1)	n.c.	44	0 (0.0)	n.c.	n.c.	n.c.	
IMDC Risk Category									
Favorable	42	3 (7.1)	n.c.	42	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Intermediate	122	9 (7.4)	n.c.	115	0 (0.0)	n.c.	n.c.	n.c.	
Poor	22	2 (9.1)	n.c.	20	0 (0.0)	n.c.	n.c.	n.c.	
SOC: Metabolism and nutrition disorders - PT ^g : Hyperglycaemia									
Sex									
Male	147	6 (4.1)	Not reached [164.29; -]	139	20 (14.4)	Not reached [-; -]	0.17 [0.06; 0.45]	< 0.001	0.900

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
Female	39	1 (2.6)	Not reached [116.14; -]	38	4 (10.5)	Not reached [-; -]	0.13 [0.01; 1.41]	0.093	
Age (Years)									
< 65	120	4 (3.3)	Not reached [164.29; -]	97	8 (8.2)	Not reached [-; -]	0.23 [0.06; 0.89]	0.033	0.498
≥ 65	66	3 (4.5)	Not reached [-; -]	80	16 (20.0)	Not reached [-; -]	0.12 [0.03; 0.47]	0.002	
ECOG performance status									
0	77	1 (1.3)	Not reached [-; -]	75	13 (17.3)	Not reached [-; -]	0.07 [0.01; 0.51]	0.009	0.073
≥1	109	6 (5.5)	Not reached [164.29; -]	102	11 (10.8)	Not reached [-; -]	0.21 [0.07; 0.67]	0.008	
Region									
North America	45	4 (8.9)	164.29 [78.00; -]	37	4 (10.8)	Not reached [-; -]	0.14 [0.01; 1.32]	0.086	0.240
Western Europe	104	2 (1.9)	Not reached [-; -]	96	13 (13.5)	Not reached [-; -]	0.09 [0.02; 0.43]	0.002	
Rest of the World	37	1 (2.7)	Not reached [-; -]	44	7 (15.9)	Not reached [-; -]	0.16 [0.02; 1.29]	0.085	
IMDC Risk Category									
Favorable	42	0 (0.0)	Not reached [-; -]	42	7 (16.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.005	0.117
Intermediate	122	6 (4.9)	Not reached [164.29; -]	115	16 (13.9)	Not reached [-; -]	0.16 [0.06; 0.49]	0.001	
Poor	22	1 (4.5)	Not reached [30.29; -]	20	1 (5.0)	Not reached [-; -]	0.61 [0.04; 10.13]	0.732	
SOC: Metabolism and nutrition disorders - PT ^g : Hypertriglyceridaemia									
Sex									
Male	147	4 (2.7)	Not reached [-; -]	139	21 (15.1)	Not reached [-; -]	0.15 [0.05; 0.43]	< 0.001	0.450
Female	39	2 (5.1)	Not reached [-; -]	38	5 (13.2)	Not reached [-; -]	0.38 [0.07; 1.98]	0.253	
Age (Years)									
< 65	120	4 (3.3)	Not reached [-; -]	97	16 (16.5)	Not reached [-; -]	0.18 [0.06; 0.55]	0.002	0.881
≥ 65	66	2 (3.0)	Not reached [-; -]	80	10 (12.5)	Not reached [-; -]	0.20 [0.04; 0.90]	0.036	
ECOG performance status									
0	77	3 (3.9)	Not reached [-; -]	75	14 (18.7)	Not reached [-; -]	0.19 [0.05; 0.67]	0.010	0.975
≥1	109	3 (2.8)	Not reached [-; -]	102	12 (11.8)	Not reached [-; -]	0.17 [0.05; 0.62]	0.007	
Region									
North America	45	2 (4.4)	Not reached [-; -]	37	4 (10.8)	Not reached [-; -]	0.40 [0.07; 2.21]	0.296	0.072
Western Europe	104	1 (1.0)	Not reached [-; -]	96	16 (16.7)	Not reached [-; -]	0.05 [0.01; 0.36]	0.003	
Rest of the World	37	3 (8.1)	Not reached [-; -]	44	6 (13.6)	Not reached [-; -]	0.58 [0.14; 2.33]	0.442	

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
		Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]		Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
Adverse Events	N ^b			N ^b					
IMDC Risk Category									
Favorable	42	2 (4.8)	Not reached [-; -]	42	3 (7.1)	Not reached [64.43; -]	0.57 [0.09; 3.51]	0.544	0.218
Intermediate	122	4 (3.3)	Not reached [-; -]	115	20 (17.4)	Not reached [-; -]	0.16 [0.05; 0.46]	< 0.001	
Poor	22	0 (0.0)	Not reached [-; -]	20	3 (15.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.064	
SOC: Nervous system disorders - PT ^g : Dizziness									
Sex									
Male	147	22 (15.0)	Not reached [-; -]	139	2 (1.4)	Not reached [-; -]	8.96 [2.09; 38.41]	0.003	0.271
Female	39	8 (20.5)	124.29 [115.86; -]	38	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.028	
Age (Years)									
< 65	120	18 (15.0)	Not reached [-; -]	97	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.099
≥ 65	66	12 (18.2)	Not reached [120.00; -]	80	2 (2.5)	Not reached [-; -]	5.33 [1.16; 24.50]	0.032	
ECOG performance status									
0	77	9 (11.7)	Not reached [-; -]	75	1 (1.3)	Not reached [-; -]	7.05 [0.87; 56.81]	0.067	0.608
≥1	109	21 (19.3)	Not reached [148.57; -]	102	1 (1.0)	Not reached [-; -]	15.28 [2.03; 114.88]	0.008	
Region									
North America	45	13 (28.9)	Not reached [62.00; -]	37	2 (5.4)	Not reached [-; -]	4.84 [1.08; 21.75]	0.040	0.160
Western Europe	104	13 (12.5)	Not reached [148.57; -]	96	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.007	
Rest of the World	37	4 (10.8)	Not reached [124.29; -]	44	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.061	
IMDC Risk Category									
Favorable	42	4 (9.5)	Not reached [148.57; -]	42	1 (2.4)	Not reached [-; -]	2.80 [0.29; 26.91]	0.373	0.398
Intermediate	122	21 (17.2)	Not reached [124.29; -]	115	1 (0.9)	Not reached [-; -]	14.31 [1.90; 107.77]	0.010	
Poor	22	5 (22.7)	Not reached [-; -]	20	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.026	
SOC: Renal and urinary disorders - PT ^g : Proteinuria									
Sex									
Male	147	3 (2.0)	Not reached [-; -]	139	12 (8.6)	Not reached [-; -]	0.19 [0.05; 0.67]	0.010	0.080
Female	39	1 (2.6)	Not reached [-; -]	38	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.333	
Age (Years)									
< 65	120	1 (0.8)	Not reached [-; -]	97	5 (5.2)	Not reached [-; -]	0.11 [0.01; 0.98]	0.048	0.435
≥ 65	66	3 (4.5)	Not reached [-; -]	80	7 (8.8)	Not reached [-; -]	0.41 [0.10; 1.57]	0.192	
ECOG performance status									
0	77	0 (0.0)	Not reached [-; -]	75	4 (5.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.034	0.140

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
≥1	109	4 (3.7)	Not reached [-; -]	102	8 (7.8)	Not reached [-; -]	0.34 [0.10; 1.15]	0.083	
Region									
North America	45	1 (2.2)	n.c.	37	4 (10.8)	n.c.	n.c.	n.c.	n.c.
Western Europe	104	3 (2.9)	n.c.	96	4 (4.2)	n.c.	n.c.	n.c.	
Rest of the World	37	0 (0.0)	n.c.	44	4 (9.1)	n.c.	n.c.	n.c.	
IMDC Risk Category									
Favorable	42	2 (4.8)	Not reached [-; -]	42	1 (2.4)	Not reached [-; -]	1.88 [0.17; 20.77]	0.605	0.149
Intermediate	122	2 (1.6)	Not reached [-; -]	115	10 (8.7)	Not reached [-; -]	0.16 [0.03; 0.73]	0.018	
Poor	22	0 (0.0)	Not reached [-; -]	20	1 (5.0)	Not reached [51.86; -]	n.a. [n.a.; n.a.]	0.102	
SOC: Respiratory, thoracic and mediastinal disorders - PT ^g : Cough									
Sex									
Male	147	15 (10.2)	Not reached [-; -]	139	27 (19.4)	Not reached [-; -]	0.40 [0.21; 0.76]	0.005	0.138
Female	39	5 (12.8)	Not reached [121.14; -]	38	3 (7.9)	Not reached [-; -]	1.15 [0.27; 5.01]	0.849	
Age (Years)									
< 65	120	15 (12.5)	Not reached [-; -]	97	13 (13.4)	Not reached [-; -]	0.67 [0.31; 1.45]	0.309	0.059
≥ 65	66	5 (7.6)	Not reached [-; -]	80	17 (21.3)	Not reached [-; -]	0.29 [0.10; 0.78]	0.014	
ECOG performance status									
0	77	6 (7.8)	Not reached [-; -]	75	14 (18.7)	Not reached [-; -]	0.35 [0.13; 0.94]	0.038	0.404
≥1	109	14 (12.8)	Not reached [-; -]	102	16 (15.7)	Not reached [-; -]	0.52 [0.24; 1.11]	0.090	
Region									
North America	45	8 (17.8)	Not reached [-; -]	37	11 (29.7)	26.00 [19.57; -]	0.40 [0.15; 1.05]	0.062	0.609
Western Europe	104	10 (9.6)	Not reached [-; -]	96	17 (17.7)	Not reached [-; -]	0.34 [0.15; 0.77]	0.010	
Rest of the World	37	2 (5.4)	Not reached [-; -]	44	2 (4.5)	Not reached [-; -]	1.18 [0.17; 8.46]	0.866	
IMDC Risk Category									
Favorable	42	4 (9.5)	Not reached [-; -]	42	3 (7.1)	Not reached [-; -]	1.32 [0.30; 5.91]	0.715	0.373
Intermediate	122	14 (11.5)	Not reached [-; -]	115	25 (21.7)	Not reached [-; -]	0.36 [0.18; 0.71]	0.003	
Poor	22	2 (9.1)	Not reached [24.43; -]	20	2 (10.0)	Not reached [-; -]	0.36 [0.03; 4.06]	0.410	
SOC: Respiratory, thoracic and mediastinal disorders - PT ^g : Epistaxis									
Sex									
Male	147	3 (2.0)	Not reached [-; -]	139	11 (7.9)	Not reached [-; -]	0.22 [0.06; 0.78]	0.020	0.987

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
Female	39	1 (2.6)	Not reached [-; -]	38	4 (10.5)	Not reached [73.14; -]	0.17 [0.02; 1.62]	0.124	
Age (Years)									
< 65	120	2 (1.7)	Not reached [-; -]	97	6 (6.2)	Not reached [-; -]	0.24 [0.05; 1.21]	0.084	0.958
≥ 65	66	2 (3.0)	Not reached [-; -]	80	9 (11.3)	Not reached [67.71; -]	0.19 [0.04; 0.92]	0.039	
ECOG performance status									
0	77	1 (1.3)	Not reached [-; -]	75	8 (10.7)	Not reached [-; -]	0.10 [0.01; 0.84]	0.034	0.353
≥1	109	3 (2.8)	Not reached [-; -]	102	7 (6.9)	Not reached [73.14; -]	0.30 [0.08; 1.22]	0.093	
Region									
North America	45	3 (6.7)	n.c.	37	4 (10.8)	n.c.	n.c.	n.c.	n.c.
Western Europe	104	1 (1.0)	n.c.	96	8 (8.3)	n.c.	n.c.	n.c.	
Rest of the World	37	0 (0.0)	n.c.	44	3 (6.8)	n.c.	n.c.	n.c.	
IMDC Risk Category									
Favorable	42	3 (7.1)	Not reached [-; -]	42	6 (14.3)	Not reached [67.71; -]	0.43 [0.11; 1.73]	0.235	0.414
Intermediate	122	1 (0.8)	Not reached [-; -]	115	9 (7.8)	Not reached [-; -]	0.08 [0.01; 0.63]	0.017	
Poor	22	0 (0.0)	Not reached [-; -]	20	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	
SOC: Respiratory, thoracic and mediastinal disorders - PT ^g : Hypoxia									
Sex									
Male	147	27 (18.4)	Not reached [-; -]	139	1 (0.7)	Not reached [-; -]	24.64 [3.34; 181.58]	0.002	0.498
Female	39	7 (17.9)	Not reached [-; -]	38	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.013	
Age (Years)									
< 65	120	21 (17.5)	Not reached [-; -]	97	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.218
≥ 65	66	13 (19.7)	Not reached [-; -]	80	1 (1.3)	Not reached [-; -]	14.42 [1.88; 110.68]	0.010	
ECOG performance status									
0	77	13 (16.9)	Not reached [-; -]	75	1 (1.3)	Not reached [-; -]	13.51 [1.77; 103.29]	0.012	0.195
≥1	109	21 (19.3)	Not reached [-; -]	102	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Region									
North America	45	10 (22.2)	Not reached [-; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.005	0.454
Western Europe	104	16 (15.4)	Not reached [-; -]	96	1 (1.0)	Not reached [-; -]	12.79 [1.69; 96.91]	0.014	
Rest of the World	37	8 (21.6)	Not reached [-; -]	44	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.002	

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
IMDC Risk Category									
Favorable	42	8 (19.0)	Not reached [-; -]	42	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004	0.663
Intermediate	122	23 (18.9)	Not reached [-; -]	115	1 (0.9)	Not reached [-; -]	20.64 [2.78; 153.22]	0.003	
Poor	22	3 (13.6)	Not reached [24.29; -]	20	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.128	
SOC: Respiratory, thoracic and mediastinal disorders - PT ^g : Pneumonitis									
Sex									
Male	147	1 (0.7)	Not reached [-; -]	139	17 (12.2)	136.43 [136.43; -]	0.04 [0.00; 0.29]	0.002	0.380
Female	39	0 (0.0)	Not reached [-; -]	38	8 (21.1)	Not reached [17.00; -]	n.a. [n.a.; n.a.]	0.002	
Age (Years)									
< 65	120	1 (0.8)	Not reached [-; -]	97	13 (13.4)	136.43 [-; -]	0.04 [0.00; 0.32]	0.003	0.313
≥ 65	66	0 (0.0)	Not reached [-; -]	80	12 (15.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
ECOG performance status									
0	77	0 (0.0)	Not reached [-; -]	75	14 (18.7)	136.43 [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.240
≥1	109	1 (0.9)	Not reached [-; -]	102	11 (10.8)	Not reached [-; -]	0.07 [0.01; 0.56]	0.012	
Region									
North America	45	1 (2.2)	Not reached [-; -]	37	4 (10.8)	Not reached [28.14; -]	0.14 [0.01; 1.29]	0.083	0.247
Western Europe	104	0 (0.0)	Not reached [-; -]	96	13 (13.5)	136.43 [136.43; -]	n.a. [n.a.; n.a.]	< 0.001	
Rest of the World	37	0 (0.0)	Not reached [-; -]	44	8 (18.2)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.008	
IMDC Risk Category									
Favorable	42	0 (0.0)	Not reached [-; -]	42	10 (23.8)	Not reached [46.43; -]	n.a. [n.a.; n.a.]	< 0.001	0.533
Intermediate	122	1 (0.8)	Not reached [-; -]	115	13 (11.3)	136.43 [-; -]	0.04 [0.00; 0.33]	0.003	
Poor	22	0 (0.0)	Not reached [-; -]	20	2 (10.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.124	
SOC: Skin and subcutaneous tissue disorders - PT ^g : Pruritus									
Sex									
Male	147	13 (8.8)	Not reached [169.14; -]	139	24 (17.3)	Not reached [-; -]	0.43 [0.21; 0.86]	0.017	0.762
Female	39	5 (12.8)	Not reached [120.86; -]	38	8 (21.1)	Not reached [-; -]	0.37 [0.11; 1.31]	0.124	
Age (Years)									
< 65	120	13 (10.8)	Not reached [169.14; -]	97	18 (18.6)	Not reached [-; -]	0.46 [0.22; 0.97]	0.041	0.566
≥ 65	66	5 (7.6)	Not reached [-; -]	80	14 (17.5)	Not reached [-; -]	0.36 [0.13; 1.02]	0.054	
ECOG performance status									
0	77	7 (9.1)	169.14 [169.14; -]	75	15 (20.0)	Not reached [-; -]	0.35 [0.14; 0.91]	0.031	0.774

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
≥1	109	11 (10.1)	Not reached [-; -]	102	17 (16.7)	Not reached [-; -]	0.50 [0.23; 1.10]	0.083	
Region									
North America	45	5 (11.1)	169.14 [169.14; -]	37	4 (10.8)	Not reached [23.86; -]	0.74 [0.18; 3.00]	0.679	0.569
Western Europe	104	7 (6.7)	Not reached [-; -]	96	15 (15.6)	Not reached [-; -]	0.40 [0.16; 0.98]	0.046	
Rest of the World	37	6 (16.2)	Not reached [120.86; -]	44	13 (29.5)	Not reached [-; -]	0.39 [0.14; 1.11]	0.077	
IMDC Risk Category									
Favorable	42	3 (7.1)	169.14 [-; -]	42	7 (16.7)	Not reached [34.57; -]	0.25 [0.05; 1.20]	0.083	0.922
Intermediate	122	13 (10.7)	Not reached [-; -]	115	22 (19.1)	Not reached [-; -]	0.46 [0.23; 0.94]	0.032	
Poor	22	2 (9.1)	Not reached [-; -]	20	3 (15.0)	Not reached [21.57; -]	0.52 [0.09; 3.09]	0.469	
SOC: Skin and subcutaneous tissue disorders - PT ^g : Rash									
Sex									
Male	147	7 (4.8)	Not reached [-; -]	139	25 (18.0)	Not reached [-; -]	0.23 [0.10; 0.54]	< 0.001	0.577
Female	39	2 (5.1)	Not reached [-; -]	38	11 (28.9)	Not reached [24.00; -]	0.15 [0.03; 0.67]	0.013	
Age (Years)									
< 65	120	8 (6.7)	Not reached [-; -]	97	21 (21.6)	Not reached [-; -]	0.28 [0.12; 0.62]	0.002	0.144
≥ 65	66	1 (1.5)	Not reached [-; -]	80	15 (18.8)	Not reached [-; -]	0.07 [0.01; 0.52]	0.010	
ECOG performance status									
0	77	2 (2.6)	Not reached [-; -]	75	17 (22.7)	Not reached [-; -]	0.10 [0.02; 0.43]	0.002	0.202
≥1	109	7 (6.4)	Not reached [-; -]	102	19 (18.6)	Not reached [-; -]	0.31 [0.13; 0.74]	0.008	
Region									
North America	45	0 (0.0)	Not reached [-; -]	37	4 (10.8)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.021	0.061
Western Europe	104	4 (3.8)	Not reached [-; -]	96	22 (22.9)	Not reached [-; -]	0.14 [0.05; 0.40]	< 0.001	
Rest of the World	37	5 (13.5)	Not reached [-; -]	44	10 (22.7)	Not reached [-; -]	0.58 [0.20; 1.70]	0.319	
IMDC Risk Category									
Favorable	42	1 (2.4)	Not reached [-; -]	42	13 (31.0)	Not reached [24.00; -]	0.06 [0.01; 0.48]	0.008	0.100
Intermediate	122	8 (6.6)	Not reached [-; -]	115	20 (17.4)	Not reached [-; -]	0.33 [0.15; 0.76]	0.009	
Poor	22	0 (0.0)	Not reached [-; -]	20	3 (15.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.064	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: all-participants-as-treated population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for									

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
interaction term)									
g: A system organ class appears on this report only if its incidence ≥10% or (incidence ≥1% and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is smaller than 0.05									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; IMDC: International Metastatic RCC Database Consortium; PT: Preferred Term ; SOC: System Organ Class									
n.a.: not applicable (when estimation not possible); n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

Schwerwiegende unerwünschte Ereignisse (SOC und PT)

Tabelle 4G-47: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwerwiegende unerwünschte Ereignisse (SOC) aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a		Belzutifan		Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f	
Serious Events	Adverse	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]		p-Value ^{d,e}
SOC ^g : Infections and infestations										
Sex										
Male		147	18 (12.2)	Not reached [-; -]	139	26 (18.7)	122.57 [69.29; -]	0.45 [0.24; 0.83]	0.011	0.536
Female		39	4 (10.3)	Not reached [-; -]	38	9 (23.7)	119.43 [37.00; -]	0.34 [0.10; 1.15]	0.082	
Age (Years)										
< 65		120	17 (14.2)	Not reached [-; -]	97	20 (20.6)	119.43 [119.43; -]	0.50 [0.25; 0.99]	0.047	0.272
≥ 65		66	5 (7.6)	Not reached [-; -]	80	15 (18.8)	Not reached [62.57; -]	0.28 [0.10; 0.77]	0.014	
ECOG performance status										
0		77	4 (5.2)	Not reached [-; -]	75	10 (13.3)	122.57 [119.43; -]	0.27 [0.08; 0.90]	0.034	0.637
≥1		109	18 (16.5)	Not reached [-; -]	102	25 (24.5)	Not reached [58.71; -]	0.45 [0.24; 0.84]	0.012	
Region										
North America		45	4 (8.9)	Not reached [-; -]	37	4 (10.8)	Not reached [36.29; -]	0.68 [0.17; 2.74]	0.584	0.721
Western Europe		104	13 (12.5)	Not reached [143.86; -]	96	17 (17.7)	122.57 [62.57; -]	0.46 [0.22; 0.97]	0.042	
Rest of the World		37	5 (13.5)	Not reached [-; -]	44	14 (31.8)	119.43 [58.71; -]	0.36 [0.13; 1.01]	0.052	
IMDC Risk Category										
Favorable		42	2 (4.8)	Not reached [-; -]	42	8 (19.0)	119.43 [62.57; -]	0.19 [0.04; 0.90]	0.036	0.376
Intermediate		122	16 (13.1)	Not reached [-; -]	115	24 (20.9)	122.57 [58.71; -]	0.44 [0.23; 0.86]	0.016	
Poor		22	4 (18.2)	98.86 [50.57; -]	20	3 (15.0)	Not reached [24.43; -]	0.57 [0.11; 2.99]	0.503	
a: Database Cutoff Date: 15APR2024										
b: Number of participants: all-participants-as-treated population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies										
c: From product-limit (Kaplan-Meier) method for censored data										
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval										
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)										
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)										
g: A system organ class appears on this report only if its incidence ≥5% or (incidence ≥1% and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is smaller than 0.05										
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; IMDC: International Metastatic RCC Database Consortium; SOC: System Organ Class										
PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor										

Tabelle 4G-48: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwerwiegende unerwünschte Ereignisse (PT) aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a		Belzutifan		Everolimus		Belzutifan vs. Everolimus		p-Value for Interaction Test ^f	
Serious Adverse Events	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]		p-Value ^{d,e}
SOC: Respiratory, thoracic and mediastinal disorders - PT ^g : Hypoxia									
Sex									
Male	147	15 (10.2)	Not reached [-; -]	139	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.998
Female	39	4 (10.3)	Not reached [-; -]	38	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.050 ^h	
Age (Years)									
< 65	120	12 (10.0)	Not reached [-; -]	97	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.002	0.998
≥ 65	66	7 (10.6)	Not reached [-; -]	80	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.004	
ECOG performance status									
0	77	9 (11.7)	Not reached [-; -]	75	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.002	0.998
≥1	109	10 (9.2)	Not reached [-; -]	102	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.003	
Region									
North America	45	5 (11.1)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Western Europe	104	8 (7.7)	n.c.	96	0 (0.0)	n.c.	n.c.	n.c.	
Rest of the World	37	6 (16.2)	n.c.	44	0 (0.0)	n.c.	n.c.	n.c.	
IMDC Risk Category									
Favorable	42	4 (9.5)	Not reached [-; -]	42	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.048	> 0.999
Intermediate	122	13 (10.7)	Not reached [-; -]	115	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Poor	22	2 (9.1)	Not reached [-; -]	20	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.198	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: all-participants-as-treated population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
g: A system organ class appears on this report only if its incidence ≥5% or (incidence ≥1% and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is smaller than 0.05									
CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; IMDC: International Metastatic RCC Database Consortium; PT: Preferred Term; SOC: System Organ Class									
h: Unrounded p-value < 0.050									
n.a.: not applicable (when estimation not possible); n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT)

Tabelle 4G-49: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC) aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f	
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}		
SOC ^g : Infections and infestations										
Sex										
Male	147	19 (12.9)	Not reached [-; -]	139	29 (20.9)	122.57 [58.71; -]	0.39 [0.21; 0.72]	0.002	0.754	
Female	39	4 (10.3)	Not reached [-; -]	38	8 (21.1)	119.43 [-; -]	0.37 [0.11; 1.31]	0.123		
Age (Years)										
< 65	120	17 (14.2)	Not reached [-; -]	97	21 (21.6)	119.43 [58.71; -]	0.46 [0.23; 0.90]	0.023	0.401	
≥ 65	66	6 (9.1)	Not reached [-; -]	80	16 (20.0)	Not reached [62.57; -]	0.30 [0.12; 0.77]	0.012		
ECOG performance status										
0	77	5 (6.5)	Not reached [-; -]	75	9 (12.0)	122.57 [119.43; -]	0.35 [0.11; 1.13]	0.080	0.777	
≥1	109	18 (16.5)	Not reached [144.57; -]	102	28 (27.5)	62.57 [36.57; -]	0.35 [0.19; 0.66]	0.001		
Region										
North America	45	5 (11.1)	Not reached [-; -]	37	4 (10.8)	Not reached [36.29; -]	0.64 [0.17; 2.44]	0.510	0.886	
Western Europe	104	12 (11.5)	Not reached [144.57; -]	96	19 (19.8)	122.57 [58.43; -]	0.33 [0.15; 0.71]	0.005		
Rest of the World	37	6 (16.2)	Not reached [-; -]	44	14 (31.8)	119.43 [57.43; -]	0.43 [0.16; 1.13]	0.087		
IMDC Risk Category										
Favorable	42	2 (4.8)	Not reached [-; -]	42	9 (21.4)	119.43 [62.57; -]	0.14 [0.03; 0.68]	0.015	0.434	
Intermediate	122	18 (14.8)	Not reached [-; -]	115	24 (20.9)	122.57 [58.43; -]	0.47 [0.25; 0.90]	0.022		
Poor	22	3 (13.6)	Not reached [50.57; -]	20	4 (20.0)	Not reached [25.29; -]	0.33 [0.06; 1.86]	0.210		
SOC ^g : Metabolism and nutrition disorders										
Sex										
Male	147	11 (7.5)	Not reached [-; -]	139	22 (15.8)	Not reached [-; -]	0.40 [0.19; 0.82]	0.013	0.821	
Female	39	3 (7.7)	Not reached [116.14; -]	38	5 (13.2)	Not reached [-; -]	0.37 [0.08; 1.68]	0.197		
Age (Years)										
< 65	120	10 (8.3)	Not reached [-; -]	97	12 (12.4)	Not reached [-; -]	0.62 [0.27; 1.45]	0.274	0.204	
≥ 65	66	4 (6.1)	Not reached [-; -]	80	15 (18.8)	Not reached [60.14; -]	0.19 [0.06; 0.61]	0.005		
ECOG performance status										
0	77	6 (7.8)	Not reached [-; -]	75	16 (21.3)	Not reached [60.14; -]	0.32 [0.13; 0.83]	0.019	0.484	

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio [95 %-CI] ^d	p-Value ^{d,e}	
≥1	109	8 (7.3)	Not reached [-; -]	102	11 (10.8)	Not reached [-; -]	0.49 [0.19; 1.27]	0.144	
Region									
North America	45	1 (2.2)	Not reached [-; -]	37	3 (8.1)	Not reached [-; -]	0.14 [0.01; 1.60]	0.113	0.544
Western Europe	104	8 (7.7)	Not reached [-; -]	96	16 (16.7)	Not reached [-; -]	0.35 [0.14; 0.83]	0.017	
Rest of the World	37	5 (13.5)	Not reached [-; -]	44	8 (18.2)	Not reached [-; -]	0.70 [0.23; 2.15]	0.532	
IMDC Risk Category									
Favorable	42	2 (4.8)	Not reached [-; -]	42	5 (11.9)	Not reached [-; -]	0.35 [0.07; 1.80]	0.208	0.110
Intermediate	122	10 (8.2)	Not reached [-; -]	115	22 (19.1)	Not reached [60.14; -]	0.32 [0.15; 0.69]	0.004	
Poor	22	2 (9.1)	Not reached [-; -]	20	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.178	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: all-participants-as-treated population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
g: A system organ class appears on this report only if its incidence ≥5% or (incidence ≥1% and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is smaller than 0.05									
CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; IMDC: International Metastatic RCC Database Consortium; SOC: System Organ Class									
n.a.: not applicable (when estimation not possible); PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor									

Tabelle 4G-50: Subgruppenanalysen mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (PT) aus RCT mit dem zu bewertenden Arzneimittel

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f	
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}		
SOC: General disorders and administration site conditions - PT*: Fatigue										
Sex										
Male	147	0 (0.0)	n.c.	139	8 (5.8)	n.c.	n.c.	n.c.	n.c.	
Female	39	1 (2.6)	n.c.	38	2 (5.3)	n.c.	n.c.	n.c.		
Age (Years)										
< 65	120	1 (0.8)	n.c.	97	5 (5.2)	n.c.	n.c.	n.c.	n.c.	
≥ 65	66	0 (0.0)	n.c.	80	5 (6.3)	n.c.	n.c.	n.c.		
ECOG performance status										
0	77	0 (0.0)	Not reached [-; -]	75	1 (1.3)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.285	0.701	
≥1	109	1 (0.9)	Not reached [-; -]	102	9 (8.8)	Not reached [70.14; -]	0.06 [0.01; 0.49]	0.009		
Region										
North America	45	0 (0.0)	n.c.	37	1 (2.7)	n.c.	n.c.	n.c.	n.c.	
Western Europe	104	0 (0.0)	n.c.	96	7 (7.3)	n.c.	n.c.	n.c.		
Rest of the World	37	1 (2.7)	n.c.	44	2 (4.5)	n.c.	n.c.	n.c.		
IMDC Risk Category										
Favorable	42	0 (0.0)	n.c.	42	2 (4.8)	n.c.	n.c.	n.c.	n.c.	
Intermediate	122	1 (0.8)	n.c.	115	6 (5.2)	n.c.	n.c.	n.c.		
Poor	22	0 (0.0)	n.c.	20	2 (10.0)	n.c.	n.c.	n.c.		
SOC: Metabolism and nutrition disorders - PT*: Hyperglycaemia										
Sex										
Male	147	2 (1.4)	Not reached [-; -]	139	10 (7.2)	Not reached [-; -]	0.15 [0.03; 0.68]	0.014	0.313	
Female	39	1 (2.6)	Not reached [116.14; -]	38	1 (2.6)	Not reached [-; -]	0.35 [0.02; 8.10]	0.512		
Age (Years)										
< 65	120	2 (1.7)	n.c.	97	4 (4.1)	n.c.	n.c.	n.c.	n.c.	
≥ 65	66	1 (1.5)	n.c.	80	7 (8.8)	n.c.	n.c.	n.c.		
ECOG performance status										
0	77	1 (1.3)	n.c.	75	6 (8.0)	n.c.	n.c.	n.c.	n.c.	
≥1	109	2 (1.8)	n.c.	102	5 (4.9)	n.c.	n.c.	n.c.		

Study: LiteSpark 005 ^a	Belzutifan			Everolimus			Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	N ^b	Participants with Event n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
Region									
North America	45	0 (0.0)	n.c.	37	2 (5.4)	n.c.	n.c.	n.c.	n.c.
Western Europe	104	2 (1.9)	n.c.	96	6 (6.3)	n.c.	n.c.	n.c.	
Rest of the World	37	1 (2.7)	n.c.	44	3 (6.8)	n.c.	n.c.	n.c.	
IMDC Risk Category									
Favorable	42	0 (0.0)	Not reached [-; -]	42	4 (9.5)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.035	0.352
Intermediate	122	3 (2.5)	Not reached [-; -]	115	7 (6.1)	Not reached [-; -]	0.23 [0.05; 0.99]	0.048	
Poor	22	0 (0.0)	Not reached [-; -]	20	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	n.a.	
SOC: Respiratory, thoracic and mediastinal disorders - PT ^g : Hypoxia									
Sex									
Male	147	20 (13.6)	Not reached [-; -]	139	1 (0.7)	Not reached [-; -]	17.35 [2.32; 129.70]	0.005	0.472
Female	39	6 (15.4)	Not reached [112.57; -]	38	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.028	
Age (Years)									
< 65	120	15 (12.5)	Not reached [-; -]	97	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	0.245
≥ 65	66	11 (16.7)	Not reached [-; -]	80	1 (1.3)	Not reached [-; -]	10.89 [1.39; 85.60]	0.023	
ECOG performance status									
0	77	9 (11.7)	Not reached [-; -]	75	1 (1.3)	Not reached [-; -]	8.25 [1.04; 65.75]	0.046	0.169
≥1	109	17 (15.6)	Not reached [-; -]	102	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	< 0.001	
Region									
North America	45	8 (17.8)	Not reached [121.29; -]	37	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.022	0.455
Western Europe	104	12 (11.5)	Not reached [-; -]	96	1 (1.0)	Not reached [-; -]	9.30 [1.20; 72.17]	0.033	
Rest of the World	37	6 (16.2)	Not reached [-; -]	44	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.007	
IMDC Risk Category									
Favorable	42	7 (16.7)	Not reached [121.29; -]	42	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.012	0.677
Intermediate	122	18 (14.8)	Not reached [-; -]	115	1 (0.9)	Not reached [-; -]	15.41 [2.05; 115.83]	0.008	
Poor	22	1 (4.5)	Not reached [24.29; -]	20	0 (0.0)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.403	
a: Database Cutoff Date: 15APR2024									
b: Number of participants: all-participants-as-treated population with two or more lines of therapy that included a PD-(L)1 inhibitor and at least two VEGF-targeted therapies									
c: From product-limit (Kaplan-Meier) method for censored data									
d: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
e: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)									
f: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)									
g: A system organ class appears on this report only if its incidence ≥5% or (incidence ≥1% and in at least 10 participants) in one or more treatment groups									

Study: LiteSpark 005 ^a	Belzutifan		Everolimus		Belzutifan vs. Everolimus		p-Value for Interaction Test ^f
Severe Adverse Event (CTCAE-Grade 3-5)	Participants with Event N ^b n (%)	Median Time ^c in Weeks [95 %-CI]	Participants with Event N ^b n (%)	Median Time ^c in Weeks [95 %-CI]	Hazard Ratio ^d [95 %-CI]	p-Value ^{d,e}	
groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is smaller than 0.05 CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; ECOG: Eastern Cooperative Oncology Group; IMDC: International Metastatic RCC Database Consortium; PT: Preferred Term; SOC: System Organ Class n.a.: not applicable (when estimation not possible); n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death 1 Ligand 1; VEGF: Vascular Endothelial Growth Factor							