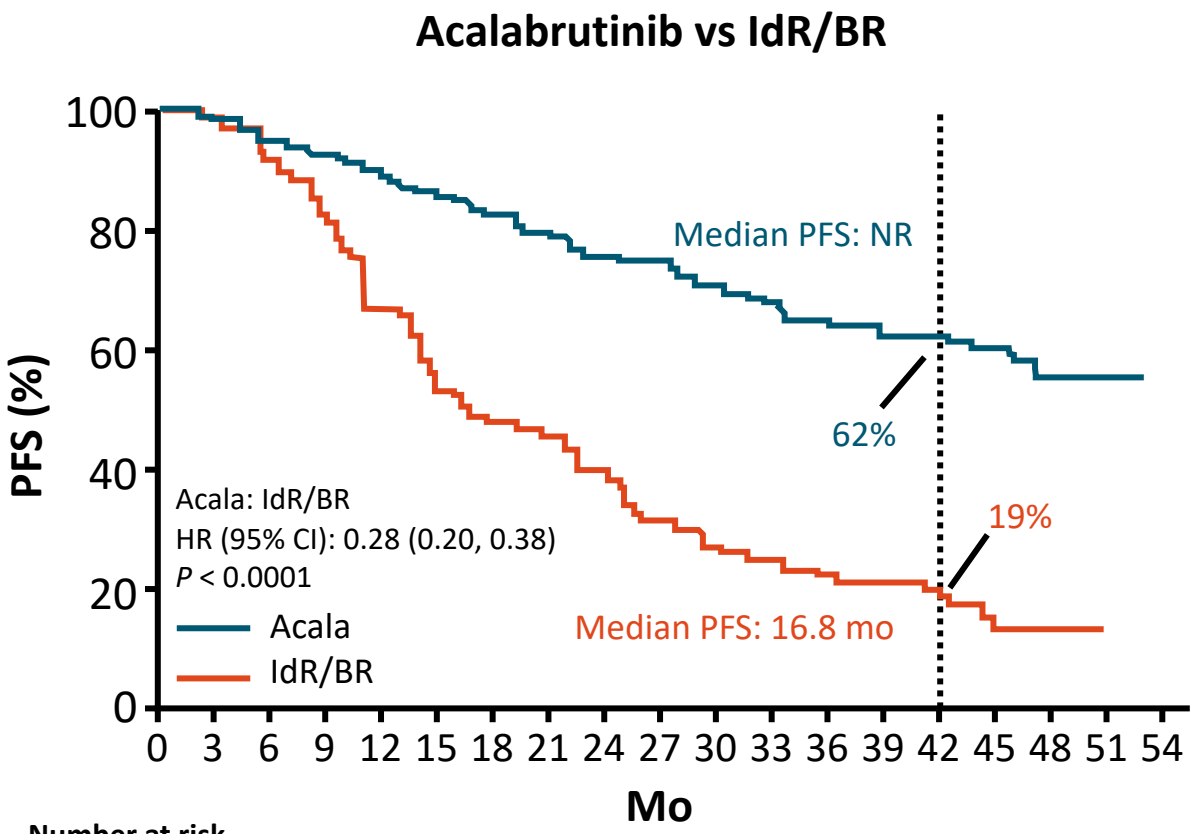
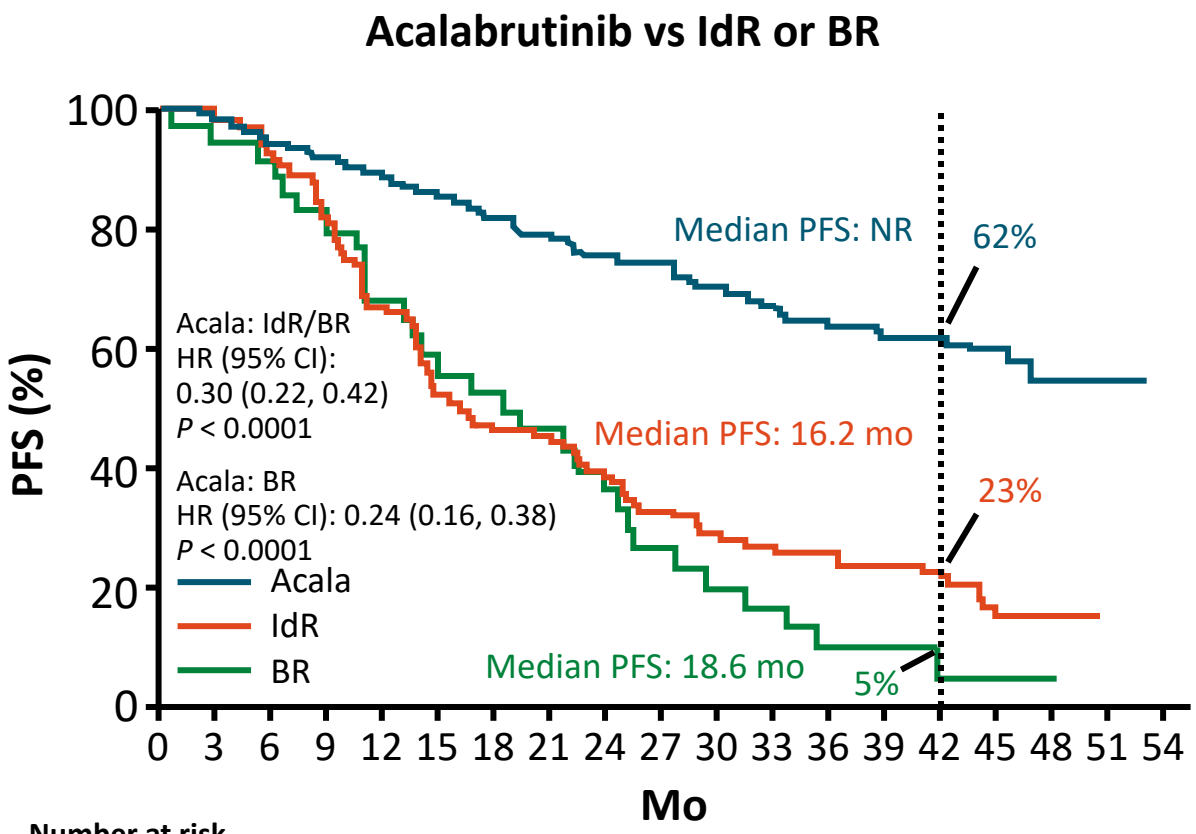
ASCEND 4-Yr Update: Investigator-Assessed PFS



Number at risk

Acala	155	151	143	139	133	128	121	117	111	110	100	94	85	80	79	52	21	4	0
IdR/BR	155	147	138	118	95	76	66	62	52	42	35	32	28	26	23	12	5	0	



Number at risk

Acala	155	151	143	139	133	128	121	117	111	110	100	94	85	80	79	52	21	4	0
IdR	119	114	106	90	73	57	49	48	40	34	29	27	25	23	22	11	4	0	
BR	36	33	32	28	22	19	17	14	12	8	6	5	3	3	1	1	1		

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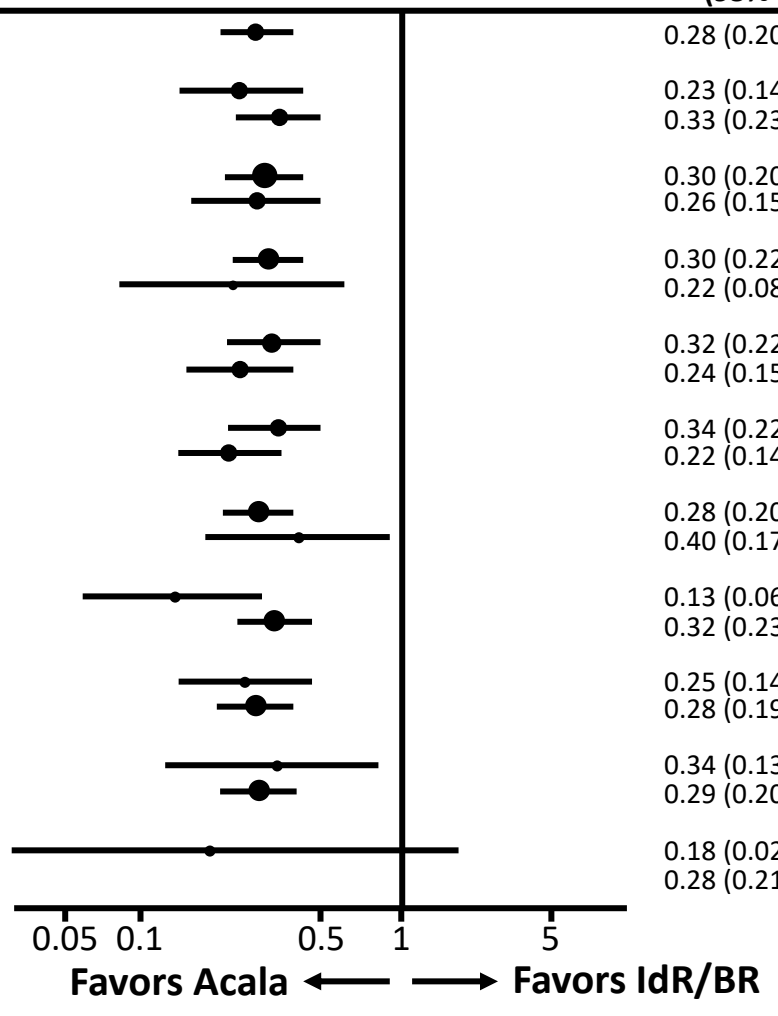
ASCEND 4-Yr Update: Investigator-Assessed PFS in Prespecified Patient Subgroups

Subgroup Analysis	Number of Events/Subjects: Acala	Number of Events/Subjects: IdR/BR	Hazard Ratio (95% CI)
Overall	62/155	119/155	0.28 (0.20, 0.38)
Age group			
< 65 years	21/58	46/57	0.23 (0.14, 0.39)
≥ 65 years	41/97	73/98	0.33 (0.23, 0.49)
Sex			
Male	45/108	80/100	0.30 (0.20, 0.43)
Female	17/47	39/55	0.26 (0.15, 0.47)
ECOG at randomization			
0,1	57/137	103/135	0.30 (0.22, 0.42)
2	5/18	60/20	0.22 (0.08, 0.61)
Rai Stage at screening			
Stage 0-II	37/90	67/90	0.32 (0.22, 0.49)
Stage III-IV	25/65	52/64	0.24 (0.15, 0.39)
Bulky disease			
<5 cm	30/79	56/80	0.34 (0.22, 0.53)
≥ 5 cm	32/76	63/75	0.22 (0.14, 0.35)
Number of prior therapies			
1-3	53/139	103/138	0.28 (0.20, 0.39)
≥ 4	9/16	16/17	0.40 (0.17, 0.92)
Presence of del (17p)			
Yes	12/28	22/26	0.13 (0.06. 0.29)
No	50/127	97/129	0.32 (0.23, 0.45)
***TP53* mutation**			
Yes	18/39	29/34	0.25 (0.14, 0.46)
No	43/113	90/119	0.28 (0.19, 0.41)
IGHV			
Mutated	6/21	11/17	0.34 (0.13, 0.93)
Unmutated	47/109	93/119	0.29 (0.20, 0.41)
Complex Karyotype			
Yes	2/3	3/3	0.18 (0.02, 1.84)
No	60/150	116/150	0.28 (0.21, 0.39)



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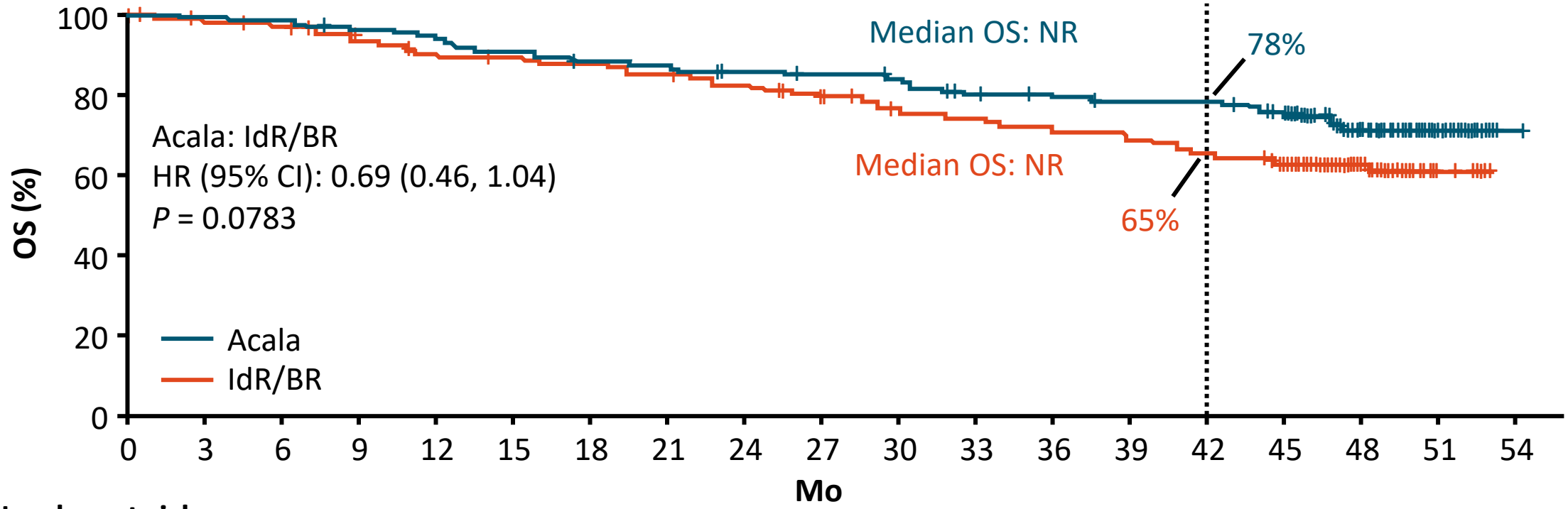
ASCEND 4-Yr Update: OS



Number at risk

Acala	155	153	151	147	144	139	133	132	127	125	122	115	112	110	109	100	52	15	1
IdR/BR	155	150	146	137	132	129	127	123	118	112	104	102	97	94	89	81	49	12	0

- 52% (80/155) of patients receiving IdR/BR crossed over to acalabrutinib

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ASCEND 4-Yr Update: Most Common AEs

Common AEs in ≥15% (Any Grade) or ≥5% (Grade ≥3) of Patients in Any Group, n (%)	Acalabrutinib (n = 154)		IdR (n = 118)		BR (n = 35)	
	Any	Grade ≥3	Any	Grade ≥3	Any	Grade ≥3
Neutropenia	37 (24)	29 (19)	55 (47)	47 (40)	12 (34)	11 (31)
Headache	36 (23)	1 (1)	7 (6)	0	0	0
Diarrhea	33 (21)	3 (2)	62 (53)	31 (26)	5 (14)	0
Upper respiratory tract infection	31 (20)	3 (2)	20 (17)	4 (3)	4 (11)	1 (3)
Pneumonia	30 (19)	15 (10)	17 (14)	12 (10)	2 (6)	1 (3)
Anemia	27 (18)	20 (13)	13 (11)	8 (7)	4 (11)	3 (9)
Cough	27 (18)	0	18 (15)	1 (1)	2 (6)	0
Pyrexia	25 (16)	5 (3)	23 (19)	8 (7)	6 (17)	1 (3)
Thrombocytopenia	20 (13)	6 (4)	19 (16)	10 (8)	5 (14)	1 (3)
Fatigue	19 (12)	2 (1)	10 (8)	1 (1)	8 (23)	1 (3)
Nausea	13 (8)	0	17 (14)	1 (1)	7 (20)	0
Hypertension	11 (7)	7 (5)	7 (6)	1 (1)	0	0
ALT increased	4 (3)	3 (2)	14 (12)	10 (8)	3 (9)	1 (3)
AST increased	4 (3)	2 (1)	11 (9)	6 (5)	2 (6)	1 (3)
Neutrophil count decreased	3 (2)	2 (1)	9 (8)	9 (8)	1 (3)	1 (3)
Infusion-related reaction	1 (1)	0	9 (8)	2 (2)	8 (23)	1 (3)
Transaminases increased	0	0	9 (8)	7 (6)	0	0

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ASCEND 4-Yr Update: Investigator Conclusions

- In patients with R/R CLL, prolonged PFS with acalabrutinib vs SoC regimens maintained after median 4-yr follow-up, regardless of high-risk features
  - PFS HR for acalabrutinib vs IdR/BR: 0.28 (95% CI: 0.20-0.38; *P* <.0001)
  - Median PFS not reached for acalabrutinib vs 16.8 mo for IdR/BR
- Median OS not reached in either arm; ORR comparable across arms
- Fewer patients discontinued treatment due to AEs with acalabrutinib vs IdR/BR
  - Acalabrutinib showed consistent tolerability profile and no new safety signals
- Investigators concluded that these data support long-term use of acalabrutinib in R/R CLL

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