

Efficacy outcomes by age from 5 observational or phase 4 studies of bevacizumab in mCRC

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Background

- Treatment selection for patients with mCRC should take into consideration age-associated comorbidities¹
- Limited data exist on bevacizumab treatment in elderly patients
 - Most patients in clinical trials evaluating antiangiogenic drugs are <65 yr¹
 - Yet ~2/3 of patients with newly-diagnosed CRC are ≥65 yr^{2,3}
- Therefore, data from 5 phase 4 or observational-cohort studies were pooled to obtain efficacy and safety outcomes according to age

Phase 4 or Observational-Cohort Studies

Study	n	Enrollment period	Median follow-up, mo	Location	Chemotherapy backbone
BRiTE ¹	1969	2004–2005	18.8	USA	No restrictions
BEAT ²	1916	2004–2006	20.5	Ex-USA	Fluoropyrimidine ± oxaliplatin or irinotecan
AWB ³	1777	2005–2008	15.7	Germany	No restrictions
ARIES ⁴	1550	2006–2008	21.0	USA	No restrictions
CONCERT ⁵	476	2008–2009	18.7	France	No restrictions

Methods

- The 5-yr age group was selected as the minimum age category providing sufficient patient numbers per group
- Descriptive statistics were used for patient baseline characteristics
- PFS and OS were estimated from Kaplan-Meier plots
- Serious adverse events estimates were provided for categories with >700 patients

Patient and Disease Characteristics at Baseline

Age, yr	n	Gender, % male	Race, % white	BMI, median (Q1, Q3), kg/m ²	ECOG PS ≤1, %	Site of primary tumor, %		Surgical resection, % yes
						Colon	Rectum	
20–<25	13	38.5	66.7	21.0 (18.9, 23.3)	92.3	63.6	18.2	72.7
25–<30	31	51.6	100	20.3 (17.6, 24.2)	96.8	53.6	35.7	75.0
30–<35	90	51.1	94.7	22.8 (21.0, 25.6)	96.6	74.7	24.1	81.0
35–<40	169	45.6	82.7	24.5 (20.9, 28.5)	94.0	64.3	28.6	76.0
40–<45	342	48.0	74.7	23.9 (21.2, 27.2)	95.8	67.8	26.3	79.9
45–<50	519	49.7	74.7	24.7 (22.1, 27.8)	94.1	68.9	25.5	82.8
50–<55	862	58.9	79.8	25.5 (22.6, 29.0)	93.4	68.6	27.1	82.8

Patient and Disease Characteristics at Baseline (cont'd)

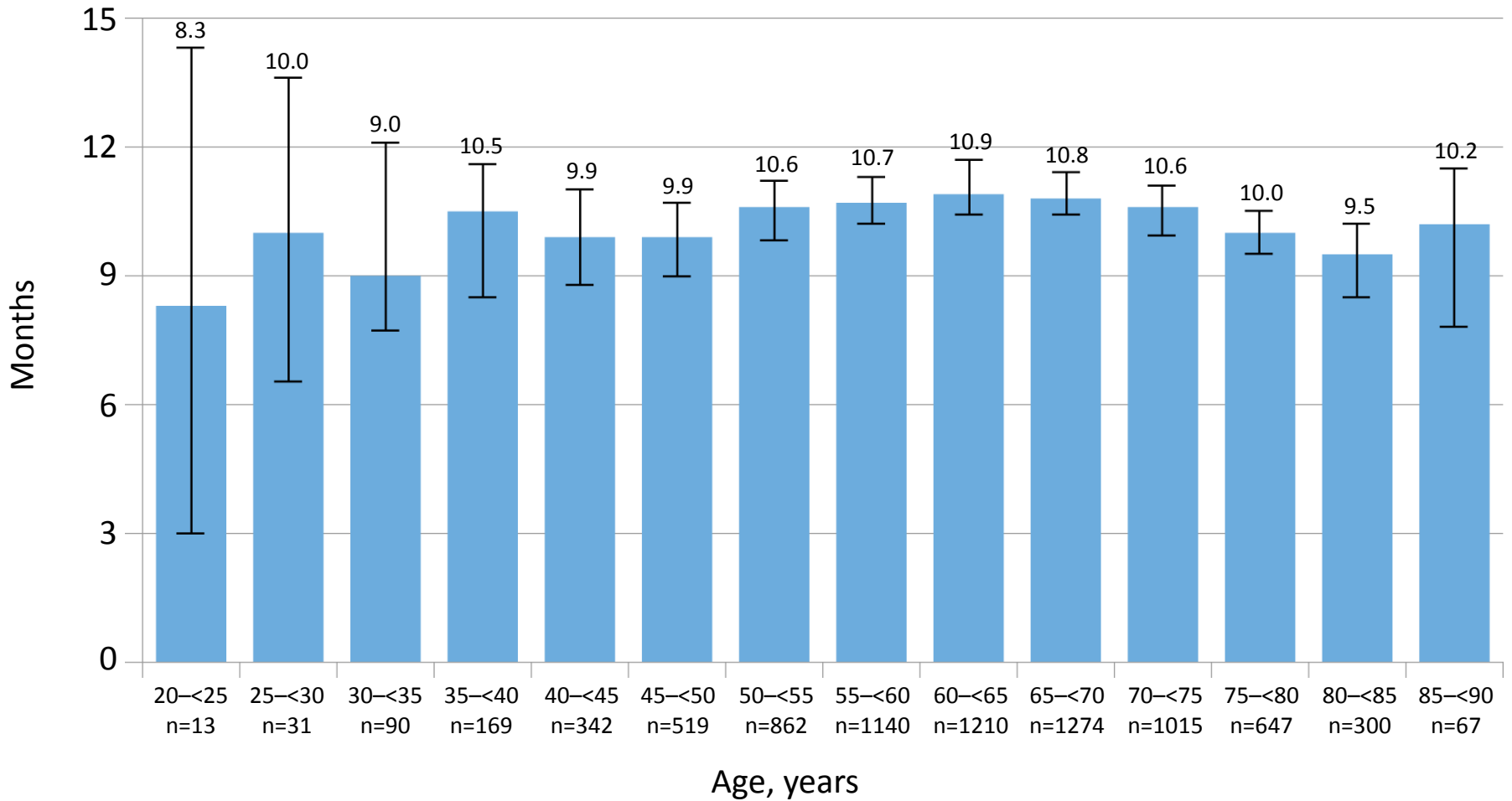
Age, yr	n	Gender, % male	Race, % white	BMI, median (Q1, Q3), kg/m ²	ECOG PS ≤1, %	Site of primary tumor, %		Surgical resection, % yes
						Colon	Rectum	
55–<60	1140	60.0	79.0	26.0 (22.8, 29.7)	92.9	69.2	26.0	83.8
60–<65	1210	61.4	81.0	25.8 (23.2, 29.1)	93.4	71.1	23.5	83.6
65–<70	1274	60.6	81.3	25.7 (23.0, 29.0)	91.8	71.6	22.9	84.2
70–<75	1015	59.3	84.1	25.5 (23.0, 28.9)	90.5	72.8	21.2	86.1
75–<80	647	59.5	85.0	25.3 (23.1, 28.4)	85.4	77.2	19.3	86.0
80–<85	300	56.5	84.1	24.8 (22.3, 27.6)	83.2	79.8	19.0	81.8
85–<90	67	50.7	89.1	24.2 (21.5, 27.0)	81.5	84.4	15.6	79.7

Progression-Free Survival

Age, yr	PFS, mo	
	n	Median (95% CI)
20–<25	13	8.3 (3.0; 14.3)
25–<30	31	10.0 (6.5; 13.6)
30–<35	90	9.0 (7.7; 12.1)
35–<40	169	10.5 (8.5; 11.6)
40–<45	342	9.9 (8.8; 11.0)
45–<50	519	9.9 (9.0; 10.7)
50–<55	862	10.6 (9.8; 11.2)

Age, yr	PFS, mo	
	n	Median (95% CI)
55–<60	1140	10.7 (10.2; 11.3)
60–<65	1210	10.9 (10.4; 11.7)
65–<70	1274	10.8 (10.4; 11.4)
70–<75	1015	10.6 (9.9; 11.1)
75–<80	647	10.0 (9.5; 10.5)
80–<85	300	9.5 (8.5; 10.2)
85–<90	67	10.2 (7.8; 11.5)

Progression-Free Survival

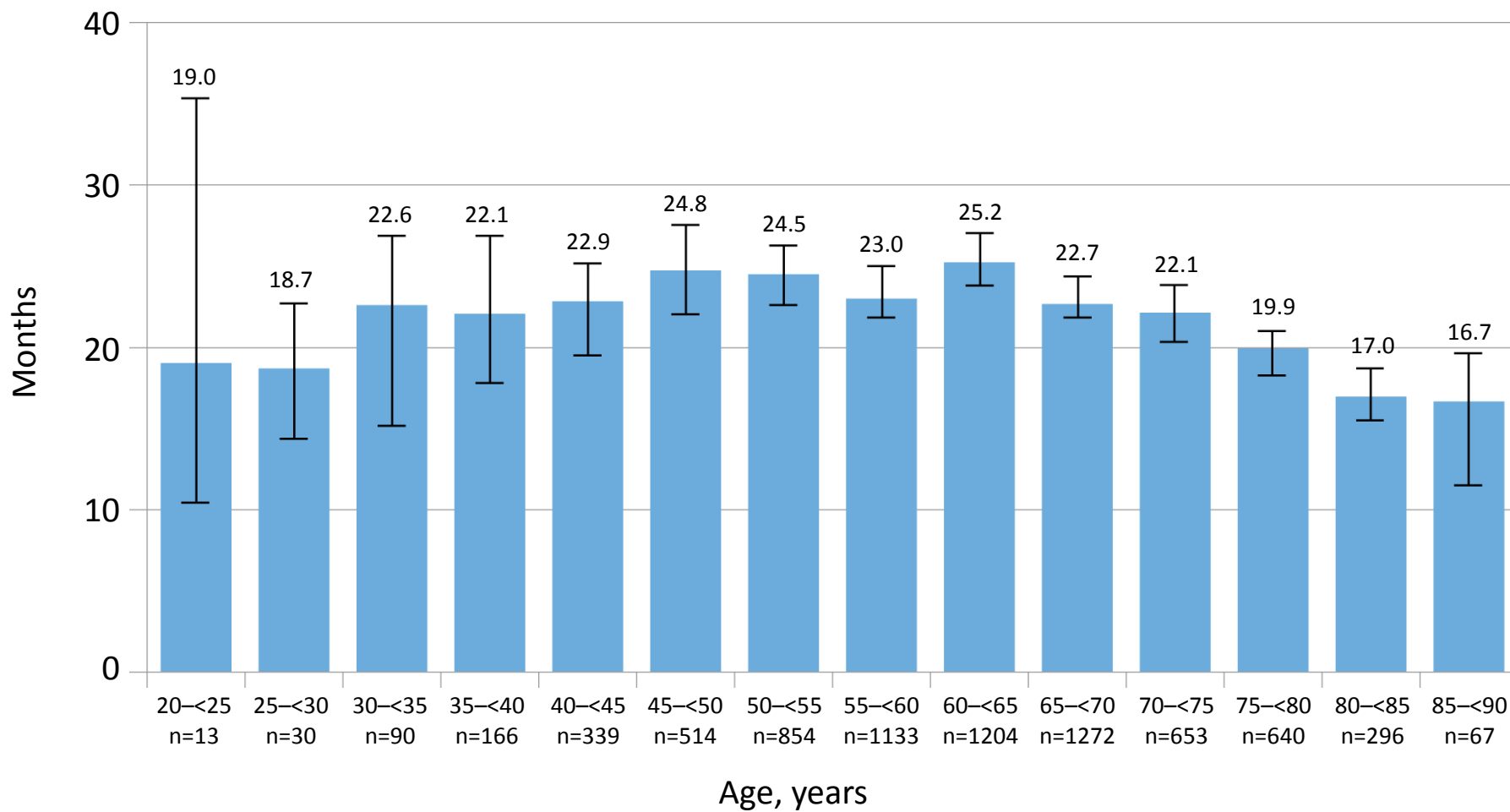


Overall Survival

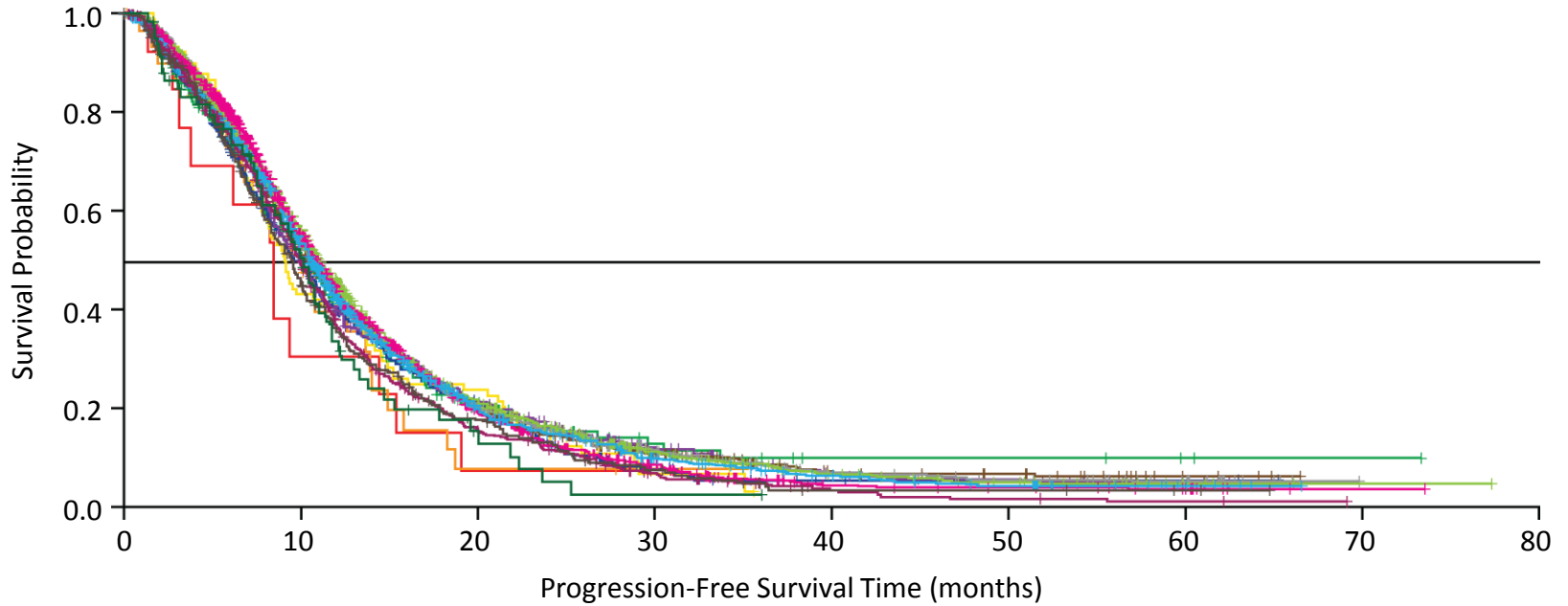
Age, yr	OS, mo	
	n	Median (95% CI)
20–<25	13	19.0 (10.4; 35.3)
25–<30	30	18.7 (14.4; 22.7)
30–<35	90	22.6 (15.2; 26.9)
35–<40	166	22.1 (17.7; 26.8)
40–<45	339	22.9 (19.2; 25.1)
45–<50	514	24.8 (21.9; 27.5)
50–<55	854	24.5 (22.6; 26.3)

Age, yr	OS, mo	
	n	Median (95% CI)
55–<60	1133	23.0 (21.8; 25.0)
60–<65	1204	25.2 (23.8; 27.0)
65–<70	1272	22.7 (21.8; 24.4)
70–<75	653	22.1 (20.3; 23.8)
75–<80	640	19.9 (18.2; 21.0)
80–<85	296	17.0 (15.5; 18.7)
85–<90	67	16.7 (11.5; 19.6)

Overall Survival

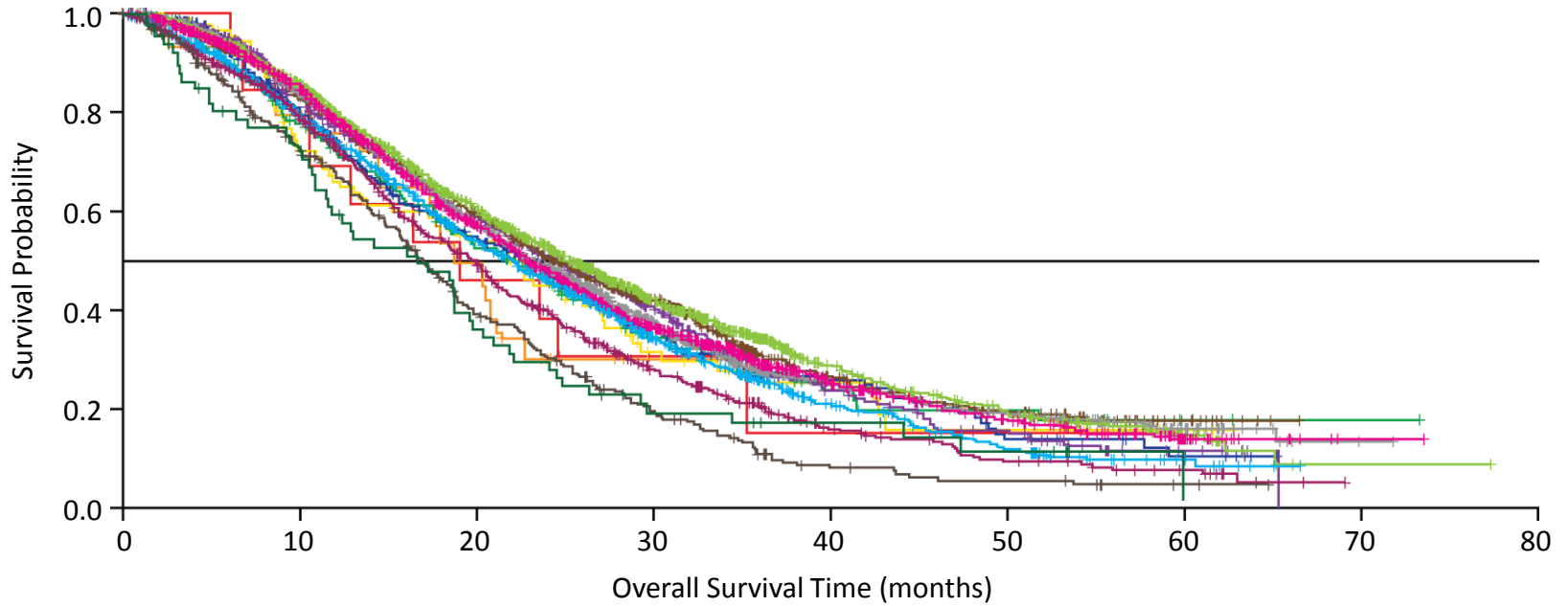


Progression-Free Survival Summary



Age Group	0-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80-90
20-<25	13	4	1	0					
25-<30	31	13	2	1	0				
30-<35	90	39	21	3	0				
35-<40	169	79	28	9	4	4	2	1	
40-<45	342	149	57	12	4	2	2	0	
45-<50	519	229	92	30	12	8	2	0	
50-<55	862	411	151	59	24	18	4	0	
55-<60	1140	554	187	81	34	24	13	0	
60-<65	1210	615	209	79	30	17	4	1	0
65-<70	1274	639	194	68	19	14	8	1	0
70-<75	1015	487	159	64	29	16	5	0	0
75-<80	647	286	83	28	8	4	2	0	
80-<85	300	120	40	15	4	4	2	0	
85-<90	67	28	6	1	0				

Overall Survival Summary



20-<25	13	11	6	2	1	1	0		
25-<30	30	23	13	1	0				
30-<35	90	61	43	17	8	5	2	0	
35-<40	166	116	70	33	13	10	3	1	0
40-<45	339	235	147	72	31	13	6	0	
45-<50	514	371	246	121	43	24	6	0	
50-<55	854	619	400	214	75	44	11	0	
55-<60	1133	844	522	260	104	71	24	1	0
60-<65	1204	921	575	297	121	65	17	1	0
65-<70	1272	964	582	294	125	70	19	1	0
70-<75	1006	707	428	212	77	34	9	0	
75-<80	640	446	256	114	41	21	10	0	
80-<85	296	195	98	45	14	9	2	0	
85-<90	67	45	22	10	7	4	0		

Serious Treatment-Related Adverse Events of Special Interest*

Related serious adverse events: Overall number of events, n (n per 100 PYE)	Patient age category (Total PYE for the category)						
	<50 (843.23)	≥50—<55 (630.77)	≥55—<60 (811.37)	≥60—<65 (793.14)	≥65—<70 (758.80)	≥70—<75 (646.30)	≥75 (627.26)
Venous thromboembolic event	26 (3.1)	18 (2.9)	37 (4.6)	36 (4.5)	25 (3.3)	27 (4.2)	27 (4.3)
Grade 3/4 bleeding	13 (1.5)	8 (1.3)	9 (1.1)	12 (1.5)	14 (1.8)	11 (1.7)	13 (2.1)
Gastrointestinal perforation	13 (1.5)	15 (2.4)	12 (1.5)	4 (0.5)	8 (1.1)	5 (0.8)	7 (1.1)
Arterial thromboembolic event	7 (0.8)	6 (1.0)	8 (1.0)	13 (1.6)	12 (1.6)	5 (0.8)	20 (3.2)
Wound healing complications	11 (1.3)	5 (0.8)	4 (0.5)	6 (0.8)	7 (0.9)	1 (0.2)	3 (0.5)
Hypertension	0	5 (0.8)	3 (0.4)	3 (0.4)	8 (1.1)	7 (1.1)	1 (0.2)

Serious Treatment-Related Adverse Events of Special Interest* (cont'd)

Related serious adverse events: Overall number of events, n (n per 100 PYE)	Patient age category (Total PYE for the category)			
	<65 (3078.50)	≥65 (2032.36)	<70 (3837.30)	≥70 (1273.56)
Venous thromboembolic event	117 (3.8)	79 (3.9)	142 (3.7)	54 (4.2)
Grade 3/4 bleeding	42 (1.4)	38 (1.9)	56 (1.5)	24 (1.9)
Gastrointestinal perforation	44 (1.4)	20 (1.0)	52 (1.4)	12 (0.9)
Arterial thromboembolic event	34 (1.1)	37 (1.8)	46 (1.2)	25 (2.0)
Wound healing complications	26 (0.8)	11 (0.5)	33 (0.9)	4 (0.3)
Hypertension	11 (0.4)	16 (0.8)	19 (0.5)	8 (0.6)

Conclusions

- PFS was consistent across all age groups
- OS was consistent among patients aged 30–<70 yr
 - A numerical decline was observed in age groups >80 yr, however other competing risks of death (other than mCRC) for the elderly could contribute to these findings
- Serious treatment-related adverse events of special interest were similar across age groups; however, the results should be interpreted with caution due to the limitations of this analysis
 - Low value and variability of related incidence estimates, the number of age categories, and the variability in which the safety data were collected in the different studies/registries
- Findings are consistent with other reports from pooled analyses of first- and second-line trials¹