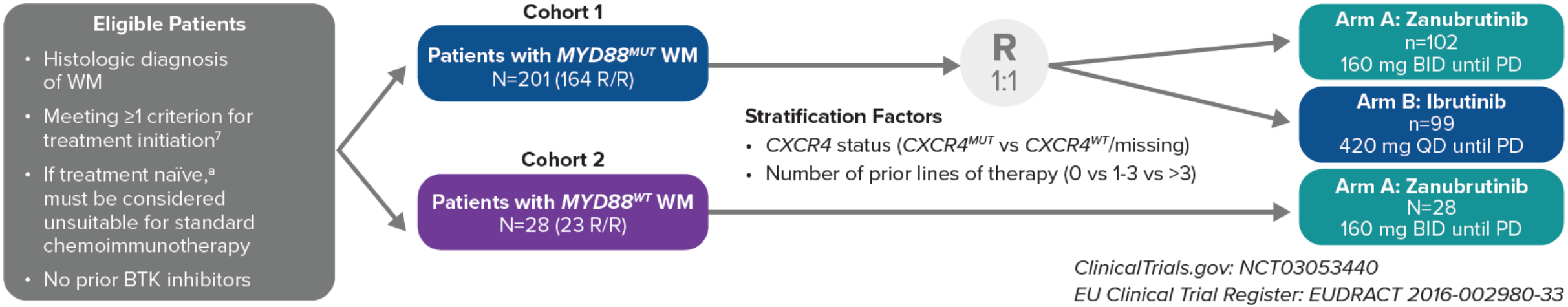
METHODS: ASPEN Study Design: Zanubrutinib vs Ibrutinib in WM[1,2]



Primary endpoint: CR+VGPR rate in cohort 1

Secondary endpoints: Efficacy, clinical benefit, antilymphoma effects, safety and tolerability of zanubrutinib vs ibrutinib

Exploratory endpoints: Efficacy and safety of zanubrutinib in cohort 2, and efficacy of zanubrutinib vs ibrutinib according to *CXCR4* status

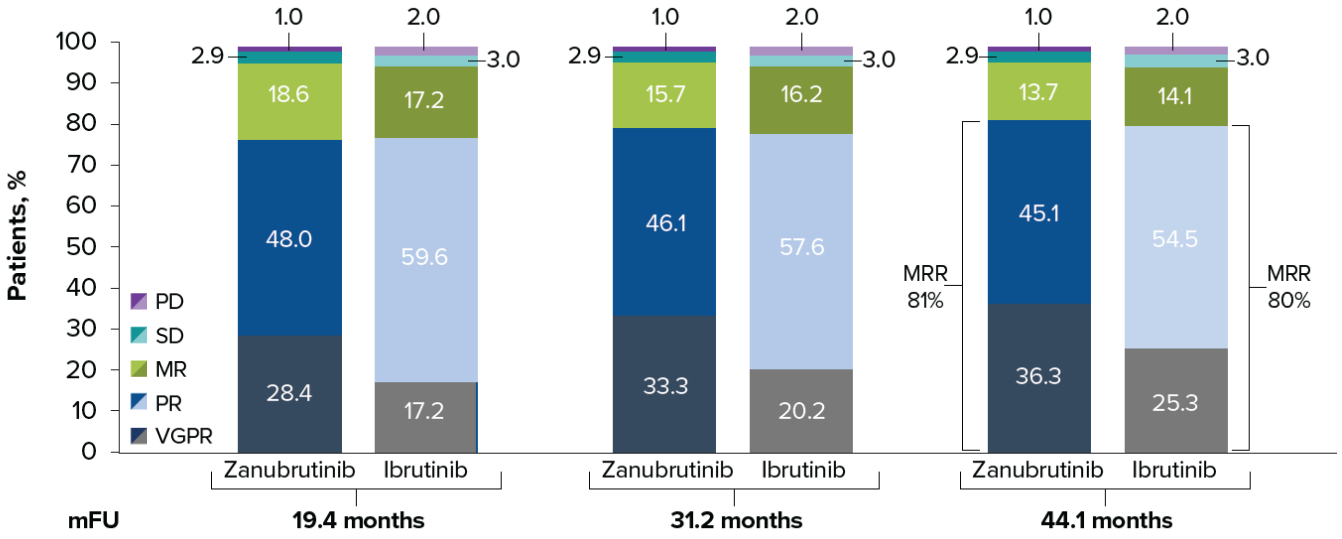
[a]Up to 20% of the overall population.

BID, twice daily; BTK, Bruton tyrosine kinase; CR, complete response; *CXCR4*, C-X-C chemokine receptor 4 gene; *MYD88*, myeloid differentiation primary response gene 88; MUT, mutant; PD, progressive disease; QD, daily; R, randomization; R/R, relapsed/refractory; VGPR, very good partial response; WM, Waldenström macroglobulinemia; WT, wild type.

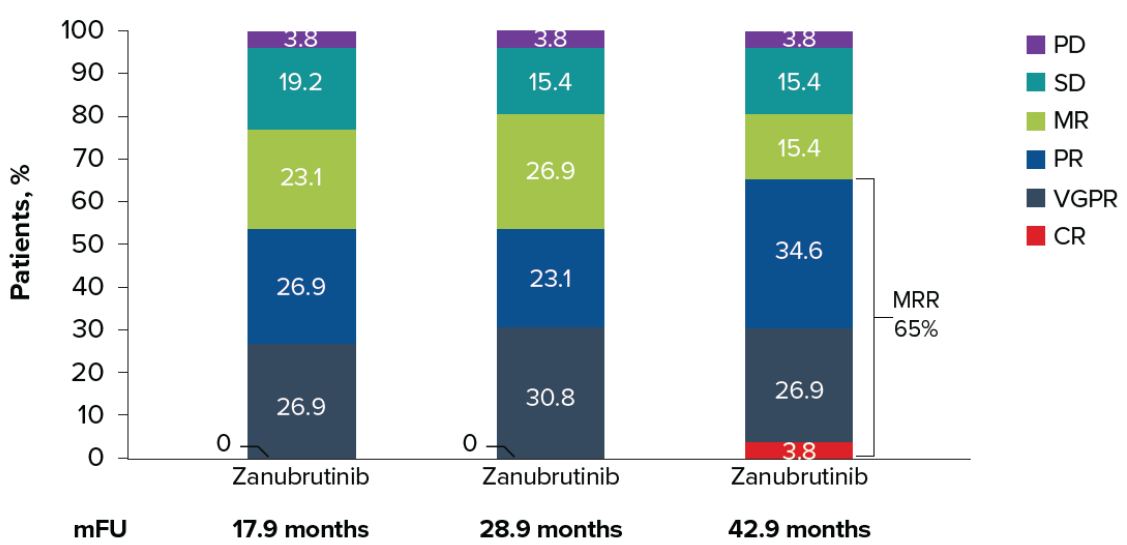
1. Tam et al. *Blood* 2020;136(18):2038-2050. 2. Dimopoulos et al. *Blood* 2014;124:1404-1411.

RESULTS: Best Overall Response by Investigator Over Time

Responses Over Time in Patients With *MYD88*^{MUT}



Responses Over Time Observed in *MYD88*^{WT}

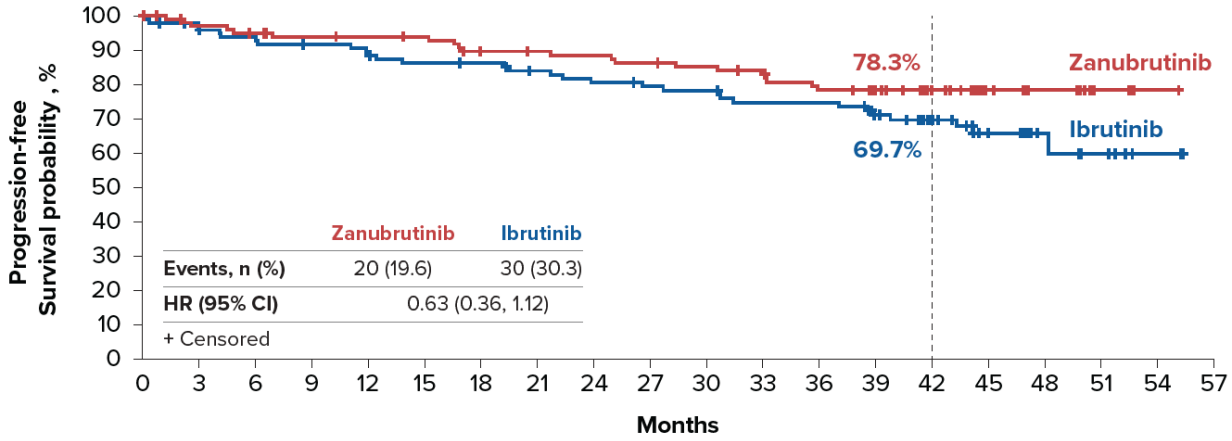


Data cutoff: October 31, 2021.

CR, complete response; mFU, median follow-up; MR, major response; MRR, major response rate; *MYD88*, myeloid differentiation primary response gene 88; MUT, mutant; PD, progressive disease; PR, partial response; SD, stable disease; VGPR, very good partial response; WT, wild type.

RESULTS: Progression-Free and Overall Survivals in ITT population

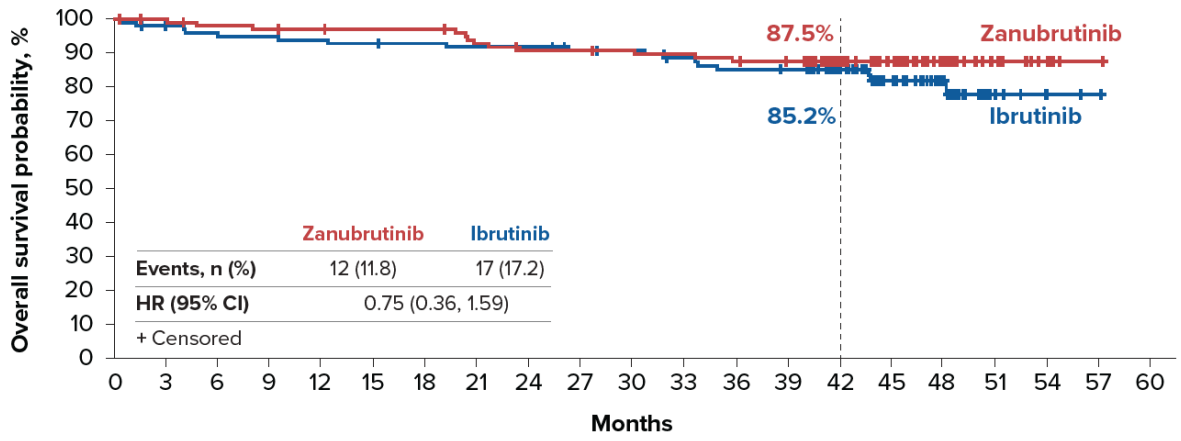
Progression-Free Survival[a]



No. of Patients at Risk:

Zanubrutinib	102	96	93	90	89	88	82	81	80	78	76	74	68	60	43	25	15	8	1	0
Ibrutinib	99	92	88	85	83	79	78	74	71	69	68	64	64	52	41	27	11	6	2	0

Overall Survival[a]



No. of Patients at Risk:

Zanubrutinib	102	100	97	96	95	94	94	89	86	86	85	84	82	80	65	49	27	13	5	1	0
Ibrutinib	99	96	93	92	91	90	89	88	88	85	84	80	77	76	62	43	21	7	3	1	0

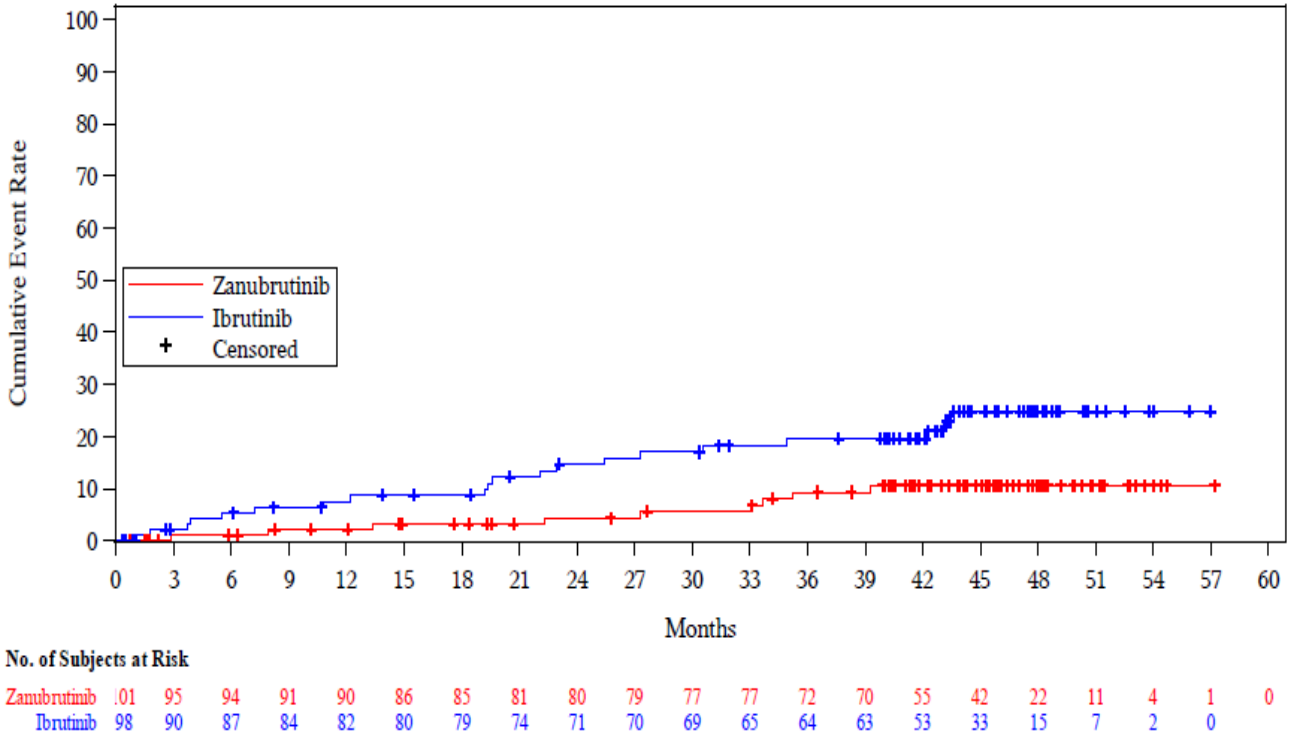
Data cutoff: October 31, 2021.
[a]By investigator assessment.
CI, confidence interval; HR, hazard ratio; ITT, intent to treat; OS, overall survival; PFS, progression-free survival.

RESULTS: Cumulative Event Rate and Treatment Discontinuations Due to AEs

Overall Safety Summary

Category, n (%)	Cohort 1 Ibrutinib (n=98)	Cohort 1 Zanubrutinib (n=101)	Cohort 2 Zanubrutinib (N=28)
Patients with ≥1 AE	98 (100.0)	100 (99.0)	26 (92.9)
Grade ≥3	71 (72.4)	75 (74.3)	20 (71.4)
Serious	49 (50.0)	57 (56.4)	14 (50.0)
AE leading to death	5 (5.1)[a]	3 (3.0)[b]	3 (10.7)[c]
AE leading to treatment discontinuation	20 (20.4)[d]	9 (8.9)[e]	6 (21.4)[f]
AE leading to dose reduction	26 (26.5)	16 (15.8)	2 (7.1)
AE leading to dose held	62 (63.3)	63 (62.4)	18 (64.3)
COVID-19–related AE	4 (4.1)	4 (4.0)	2 (7.1)

Time to Treatment Discontinuations Due to AEs

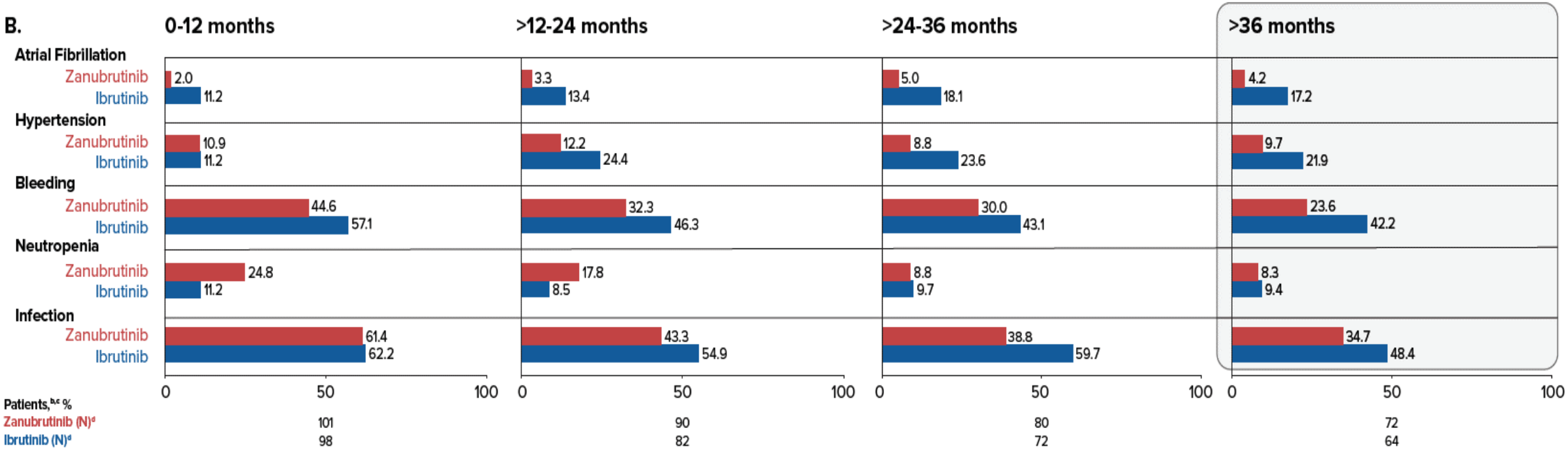


Data cutoff: October 31, 2021.

[a]Cardiac failure acute, death (unexplained), pneumonia, sepsis (n=2). [b]Cardiomegaly (cardiac arrest after plasmapheresis), metastatic malignant melanoma, subdural hematoma (after a fall). [c]Cardiac arrest, COVID-19 infection, lymphoma transformation. [d]Cardiac disorders (n=4, includes 2 due to atrial fibrillation), infection and infestations (n=4, pneumonia and sepsis, 2 each), respiratory, thoracic and mediastinal disorders (n=3), second malignancy (n=3), blood and lymphatic system disorders (n=2), renal and urinary disorders (n=1), death of unknown cause (n=1), drug induced liver injury (n=1), hepatitis (n=1). [e]Second malignancy (n=4, includes breast cancer, metastatic melanoma, multiple myeloma, and myelodysplastic syndrome, 1 each), cardiomegaly (n=1), drug-induced liver injury (n=1), neutropenia (n=1), subdural hemorrhage (n=1), worsening of chronic kidney disease (n=1). [f]Cardiac arrest, COVID-19 infection, diarrhea, hepatitis B infection, squamous cell carcinoma of lung, subdural hemorrhage (after a fall).

AE, adverse event.

RESULTS: Prevalence Analysis for AEs of Interest



Data cutoff: October 31, 2021.

[a]Descriptive purpose only, 2-sided P value. [b]Events of the same preferred term that occurred within 1 day of the previous event were combined as 1 event. Patients with ongoing or new events in the interval are counted. [c]Percentage is based on N. [d]N is the number of patients who are on treatment in each time interval or who discontinued treatment but the time from first dose date to the earliest date (last dose date +30 days, initiation of new anticancer therapy, end of study, death or cutoff date) is within the time interval.