Frontline Treatment of Sonrotoclax (BGB-11417) + Zanubrutinib for CLL/SLL Demonstrates High uMRD Rates With Favorable Tolerability: Updated Data From BGB-11417-101, An Ongoing Phase 1/1b Study

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CONCLUSIONS

- Sonrotoclax in combination with zanubrutinib was generally safe and well tolerated, with a median relative dose intensity of 99% across all dose levels
- No cases of laboratory or clinical tumor lysis syndrome occurred
- Majority of TEAEs were low grade; low rates of transient gastrointestinal TEAEs, predominantly grade 1, were observed
- The most common grade ≥3 TEAE was neutropenia, which was transient and did not lead to higher rates of grade ≥3 infections
- No fatal TEAEs, no complicated COVID-19 case or death
- Substantial efficacy was observed in this all-comer TN CLL/SLL population, including in patients with high-risk features
- Sonrotoclax + zanubrutinib demonstrated a high response rate, including 100% ORR across all dose levels
- With median follow-up of 30.7 months, no PFS events have been observed at the sonrotoclax RP2D of 320 mg
- High blood uMRD4 rates were achieved early, with a median time to uMRD of 7.2 months, that continued to deepen over time with a best uMRD rate of 98% at data cutoff in the 320-mg cohort
- No patient has progressed from uMRD4 to MRD4+ across both dose cohorts at data cutoff
- Sonrotoclax 320 mg in combination with zanubrutinib is currently being evaluated in patients with TN CLL in the phase 3 study, CELESTIAL-TNCLL (NCT06073821)

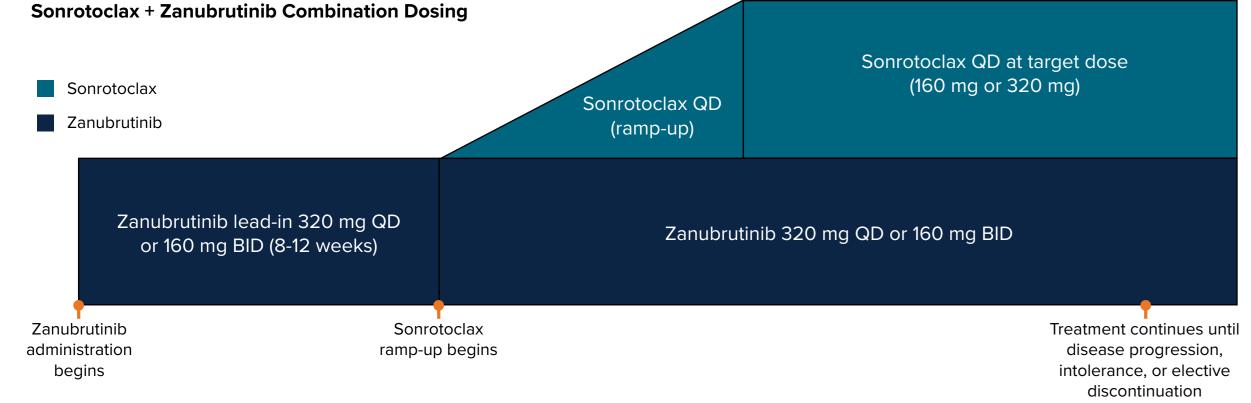
INTRODUCTION

- Frontline treatment of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) with a B-cell lymphoma 2 (BCL2) inhibitor and a Bruton tyrosine kinase (BTK) inhibitor has emerged as an important treatment option that can induce high rates of undetectable minimal residual disease (uMRD)
- A next-generation BCL2 inhibitor + BTK inhibitor combination is desired to improve the safety and efficacy of this treatment
- Sonrotoclax (BGB-11417), a next-generation BCL2 inhibitor, is a more selective and pharmacologically potent inhibitor of BCL2 than venetoclax, with a shorter half-life and no drug accumulation^{2,3}
- Zanubrutinib is highly effective in patients with treatment-naive (TN) and relapsed/refractory (R/R) CLL/SLL regardless of risk factors^{4,5}
- Zanubrutinib has shown superior progression-free survival (PFS) and favorable safety/tolerability compared with ibrutinib, including fewer cardiac adverse events (AEs), in patients with R/R CLL/SLL⁶
- Here, we report updated data from the BGB-11417-101 trial in patients with TN CLL/SLL treated with sonrotoclax in combination with zanubrutinib

METHODS

- BGB-11417-101 (NCT04277637) is a global phase 1/1b study evaluating sonrotoclax as monotherapy, or in combination with zanubrutinib and/or obinutuzumab in patients with B-cell malignancies (Figure 1)
- The study endpoints included safety and tolerability, recommended phase 2 dose, and overall response rate (ORR), defined as a partial response with lymphocytosis (PR-L) or better, and rate of MRD negativity as measured by ERIC-approved flow cytometry assay
- Treatment consisted of 8-12 weeks of zanubrutinib lead-in (320 mg once daily or 160 mg twice daily), then zanubrutinib + sonrotoclax until disease progression, intolerance, or elective discontinuation
- Patients who reach 96 weeks of combination treatment may elect to stop study drug treatment while remaining on study and entering long-term follow-up (protocol-defined elective discontinuation)

Figure 1. BGB-11417-101 Study Design

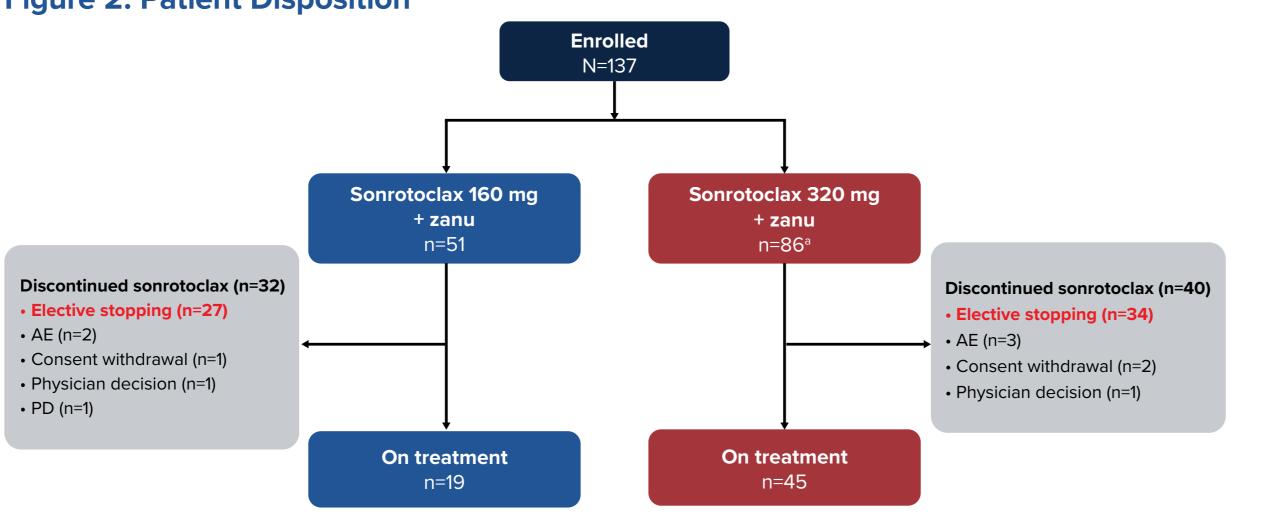


Abbreviations: BID, twice daily; C, cycle; D, day; QD, once daily.

RESULTS

- As of August 29, 2025, a total of 137 patients were enrolled in the sonrotoclax 160-mg (n=51) and 320-mg (n=86) cohorts (**Figure 2**)
- At the data cutoff date, 47% of patients (n=64) remained on treatment
- Most sonrotoclax discontinuations (85%; 61/72) were protocol-defined elective discontinuations after 96 weeks of sonrotoclax target dose
- Median study follow-up across cohorts was 30.7 months (range, 3.1-45.5 months)

Figure 2. Patient Disposition



^aOne patient received zanubrutinib but had not received sonrotoclax treatmen Abbreviations: AE, adverse event; PD, progressive disease; zanu, zanubrutinik

- Overall, median age was 62 years and 72% of patients were male (**Table 1**)
- At baseline, 29% (39/133) of tested patients had high tumor burden, 61% (82/135) had unmutated IGHV, and 14% (18/130) had *TP53* mutation or del(17p)

Sonro 160 mg + zanu Sonro 320 mg + zanu All patients

Table 1. Baseline Characteristics

Characteristics	(n=51)	(n=86)	(N=137)
Study follow-up, median (range), months	30.7 (17.5-45.5)	30.9 (3.1-41.9)	30.7 (3.1-45.5)
Age, median (range), years	63 (38-82)	61 (32-84)	62 (32-84)
≥65 years, n (%)	20 (39)	35 (41)	55 (40)
Male, n (%)	37 (73)	61 (71)	98 (72)
Disease type, n (%)			
CLL	48 (94)	82 (95)	130 (95)
SLL	3 (6)	4 (5)	7 (5)
Risk status, n/tested (%)			
del(17p)	6/46 (13)	8/83 (10)	14/129 (11)
TP53 mutation ^a	7/51 (14)	7/85 (8)	14/136 (10)
del(11q)	10/46 (22)	11/83 (13)	21/129 (16)
Unmutated IGHV, n/tested (%)	34/50 (68)	48/85 (56)	82/135 (61)
High tumor burden at baseline, n/tested (%) ^b	22/51 (43)	17/82 (21)	39/133 (29)

Abbreviations: ALC, absolute lymphocyte count; CLL, chronic lymphocytic leukemia; IGHV, immunoglobulin heavy chain variable region; LN, lymph node; SLL, small lymphocytic lymphoma; sonro, sonrotoclax;

• The majority of treatment-emergent adverse events (TEAEs) occured at grades 1 and 2, and no TEAE led to

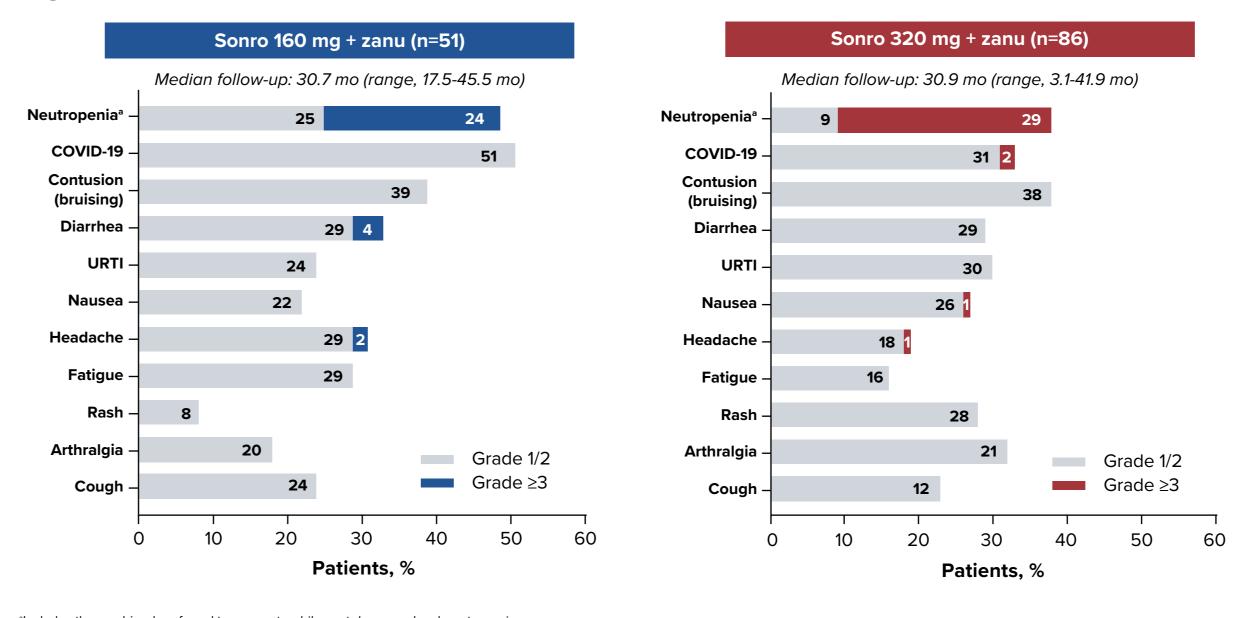
- death (**Table 2**) – The most common any-grade TEAEs were neutropenia (42%), COVID-19 (39%), contusion/bruising (39%), and diarrhea (31%) (**Figure 3**)
- The most common grade ≥3 TEAE was neutropenia (27%), which was transient and did not lead to higher rates of grade ≥3 infections
- Five patients (4%) discontinued sonrotoclax treatment due to TEAEs
- No clinical or laboratory tumor lysis syndrome occurred
- Rates of diarrhea were similar across dose cohorts, with no grade ≥3 events in the 320-mg cohort

Table 2. Overall Safety Summary

Patients, n (%)	Sonro 160 mg + zanu (n=51)	Sonro 320 mg + zanu (n=86)ª	All patients (N=137)
Any TEAEs	51 (100)	85 (99)	136 (99)
Grade ≥3	35 (69)	49 (57)	84 (61)
Serious TEAEs	19 (37)	26 (30)	45 (33)
Leading to death	0	0	0
Leading to discontinuation of zanu	2 (4)	6 (7)	8 (6)
Treated with sonro	51 (100)	85 (99)	136 (99)
Leading to discontinuation of sonro	2 (4)	3 (3)	5 (4)
Relative dose intensity of sonro, median, %	99	99	99
Duration of exposure, median (range), months	28.3 (5.8-45.5)	26.0 (0.8-41.9)	26.5 (0.8-45.5)

^aOne patient received zanubrutinib but had not received sonrotoclax treatment Abbreviations: sonro, sonrotoclax; TEAE, treatment-emergent adverse event; zanu, zanubrutinib.

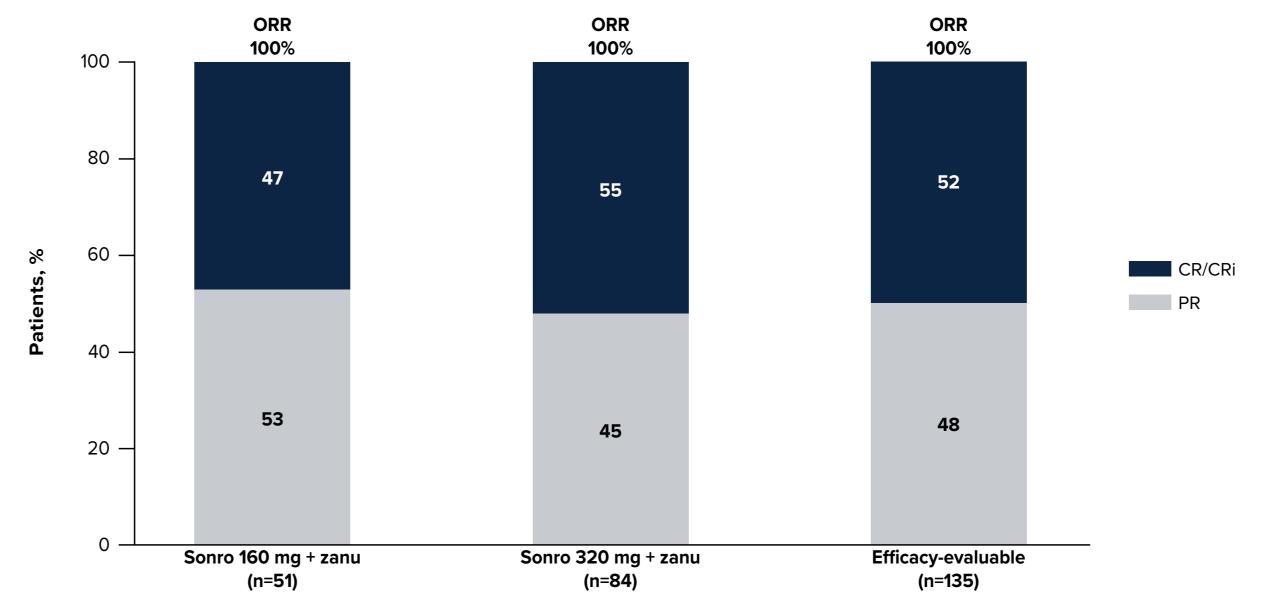
Figure 3. TEAEs in ≥15% of Patients



Abbreviations: mo, month; sonro, sonrotoclax; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection; zanu, zanubrutinib

• In 135 efficacy-evaluable patients, ORR was 100%, with complete response (CR)/CR with incomplete marrow recovery (CRi) in 47% and 55% of the 160- and 320-mg cohorts, respectively (**Figure 4**) - Median time to first response was 2.6 months (range, 1.5-10.8 months)

Figure 4. Overall Response Rates

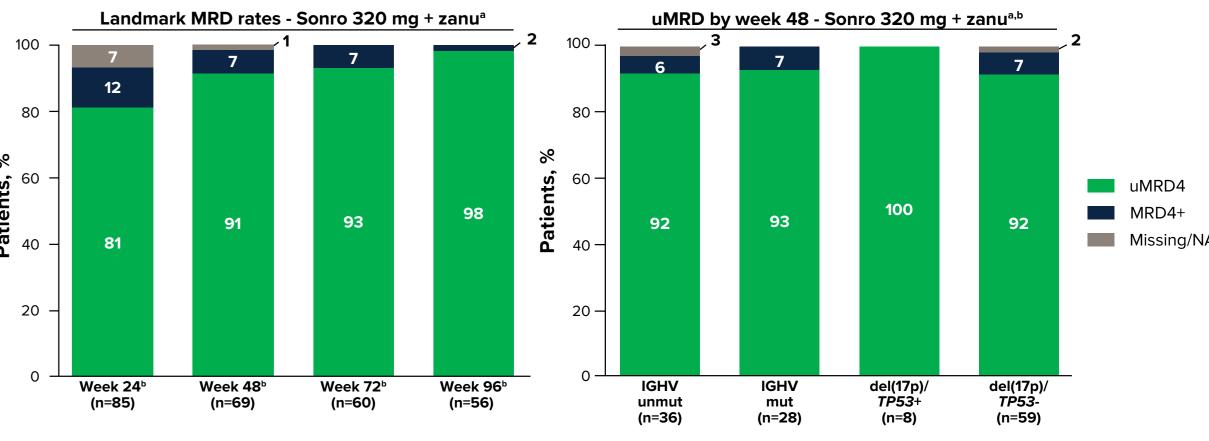


Abbreviations: CR, complete response; CRi, complete response with incomplete marrow recovery; ORR, overall response rate; PR partial response; sonro, sonrotoclax; zanu, zanubrutinib.

- At data cutoff, the uMRD4 rates for 160-mg and 320-mg cohorts at 48 weeks of combination treatment were 84% and 91%, respectively
- uMRD4 rates continue to increase over time with 98% (55/56) of patients in the 320-mg cohort achieving uMRD4 by 96 weeks

• High rates of uMRD4 were achieved regardless of risk factors; no patient with uMRD4 reverted to MRD4+ (Figure 5)

Figure 5. Landmark MRD Rates



^aAs measured by ERIC flow cytometry panel; uMRD4 = <1 CLL cell per 10,000 leukocytes (<10-4). Dumber of weeks at target dose, following zanu monotherapy and sonro ramp-up to target dose Abbreviations: IGHV, immunoglobulin heavy chain variable region; MRD, minimal residual disease; mut, mutated; NA, not assessable; sonro, sonrotoclax; uMRD, undetectable MRD; unmut, unmutated

• Time to uMRD4 was similar, regardless of IGHV mutation status (**Figure 6**)

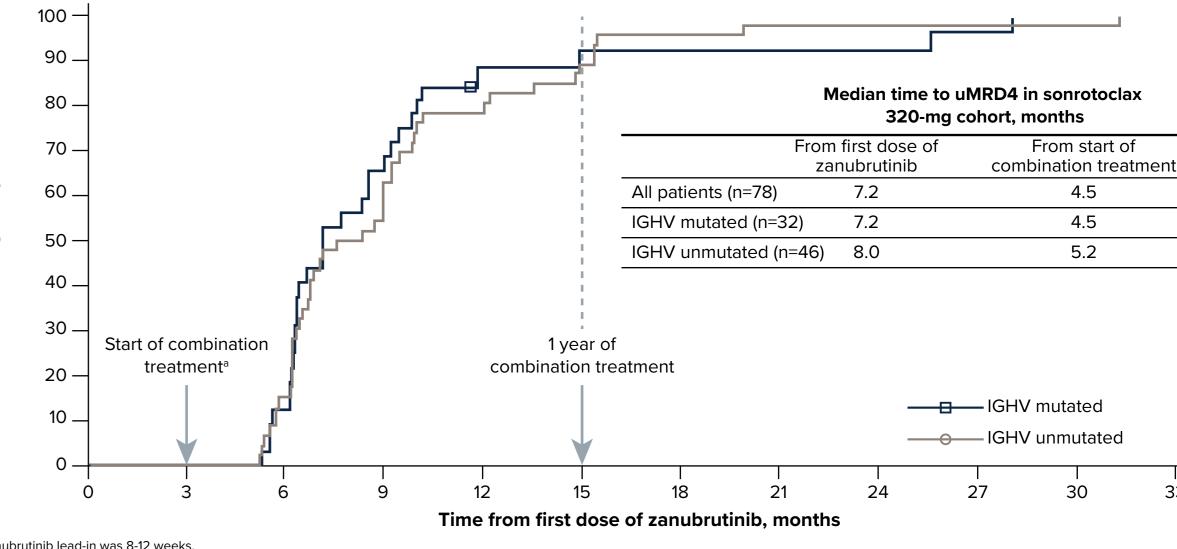
- Median time from first zanubrutinib dose to uMRD4 was 7.2 months in the 320-mg cohort

- Median time from start of combination treatment to uMRD4 was 4.5 months in the 320-mg cohort • In the 320-mg cohort, 34 patients (40%) electively discontinued treatment after at least 96 weeks of therapy

Median time off treatment was 7.0 months (range, 0.1-12.3 months)

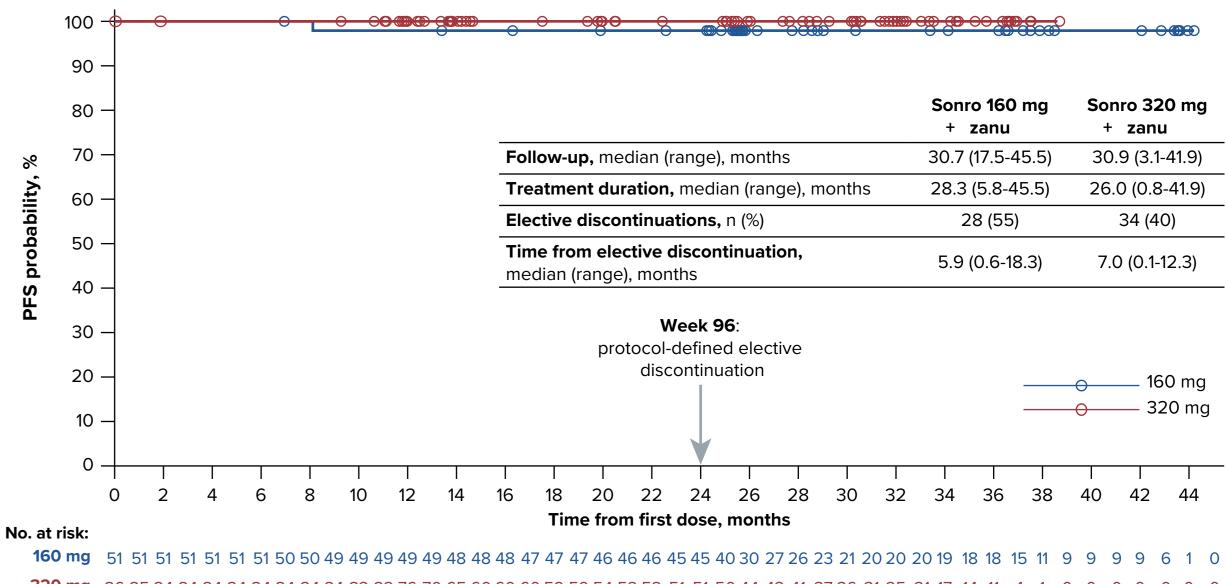
• With a median study follow up of 30.9 months, no progression was observed in the 320-mg cohort, including in those who have electively discontinued treatment (Figure 7)

Figure 6. Time to uMRD4 by IGHV Status, Sonrotoclax 320-mg Cohort



Abbreviations: IGHV, immunoglobulin heavy chain variable region; MRD, minimal residual disease; uMRD, undetectable minimal residual disease.

Figure 7. Progression-Free Survival



320 mg 86 85 84 84 84 84 84 84 84 84 83 82 76 70 65 60 60 60 59 59 54 52 52 51 51 50 44 43 41 37 36 31 25 21 17 14 11 4 1 0 0 0 0 0 0 Abbreviations: PFS, progression-free survival; sonro, sonrotoclax; zanu, zanubrutinib.

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