

A Phase 1 study of SGR-1505, an oral, potent MALT1 inhibitor for relapsed/refractory (R/R) Waldenström macroglobulinemia (WM)

Authors:

Stephen Spurgeon¹, Adam Olszewski², Matthew McKinney³, Mengyang Di⁴, Erin Mulvey⁵, Vincent Ribrag⁶, Carlo Visco⁷, Michal Taszner⁸, Damian Cubillas Garcia de la Torre⁹, Eva Gonzalez-Barca¹⁰, Kenny Pham¹¹, Michele Corrado¹¹, Sen Zhang¹¹, Vipul K. Gupta¹¹, Brian Yoo¹¹, Kevin Y. Wu¹¹, Ahmed Hamdy¹¹, Oksana Karnabeda¹²

¹Oregon Health & Sciences University, Knight Cancer Institute, Portland, OR, United States, ²Brown University, Providence, RI, United States, ³Duke University Medical Center, Durham, NC, United States, ⁴Fred Hutchinson Cancer Research Center, Seattle, WA, United States, ⁵Weill Cornell Medicine, New York, NY, United States, ⁶Institute Gustave Roussy, Villejuif, France, ⁷University of Verona, Verona, Italy, ⁸Medical University of Gdansk, Gdansk, Poland, ⁹South Texas Accelerated Research Therapeutics (START) Madrid, Madrid, Spain, ¹⁰Institut Catala d'Oncologia - L'Hospitalet, Barcelona, Spain, ¹¹Schrödinger, New York, NY, United States, ¹²ARENSIA Research Clinic at the Institute of Oncology, Kyiv, Ukraine

Background: MALT1 is a central convergence node integrating BCR-BTK and TLR-MYD88 signaling—positioning it as a critical target for NF- κ B-driven B-cell malignancies, including WM. This occurs via destabilization of NF- κ B signaling by preventing A20/CYLD cleavage, preventing canonical NF- κ B activation by limiting RelB cleavage, suppressing IL-6 and IL-10 transcription via regnase-1/roquin cleavage, and blocking cell adhesion and microenvironmental interactions through increased BCL10 cleavage. SGR-1505 is a potent, selective inhibitor of MALT1 protease activity, while preserving scaffold function which mitigates off-target effects observed with complete pathway suppression. SGR-1505-101 (NCT05544019) is an ongoing Phase 1 study in patients (pts) with R/R B-cell malignancies who have received ≥ 2 prior therapies. For pts with WM, prior treatment must also include at least 1 BTK inhibitor. WM-specific efficacy (n=12 evaluable) and cumulative safety (N=79) are presented here.

Methods: Pts received oral SGR-1505 daily in 21-day cycles (once daily [QD] or twice daily [BID]) in a modified 3+3 dose escalation design. WM pts were enriched using a Bayesian two-stage design with randomized dose assignment (50 mg BID and 100 mg BID) to further characterize safety, tolerability, PK and preliminary efficacy.

Results: As of 01-Jun-2026, seventeen (17) WM pts were treated at 7 dose levels across two dosing schedules (50-200 mg QD, 50-150 mg BID). Median prior lines of therapy: 3 (range 2-10), with 100% BTKi exposure and 88% rituximab and/or rituximab-chemo exposure. Median time on SGR-1505 treatment: 119 days (28-1149+). Fourteen (14) (82%) pts remain on treatment, 1 discontinued due to pt withdrawal, and 2 discontinued due to herpes simplex reactivation (G3) and oral dysesthesia (G3).

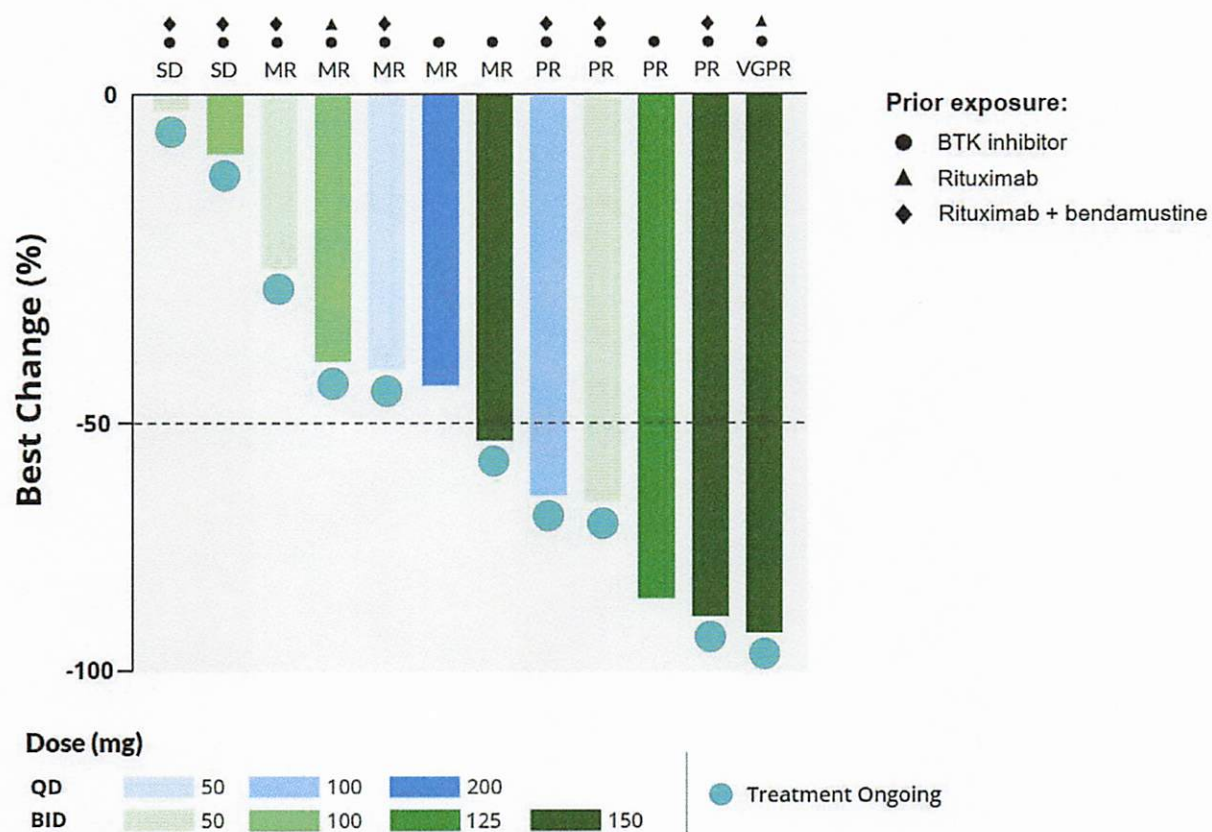
Twelve efficacy-evaluable WM pts demonstrated 83% objective response rate (ORR) and 42% major response rate (MRR). Major responses were achieved in 1 of 3 (33%) pts receiving QD dosing and 4 of 9 (44%) receiving BID dosing. Doses greater than 100 mg BID achieved 75% MRR. Median duration of response: 10.8 months (2.8 - 23.5+ months). Baseline prognostic, resistance markers and ctDNA analysis will be presented.

The incidence of treatment-emergent adverse events (TEAE) in the overall safety population (N=79) was 96%, ($\geq$ G3 61%); treatment-related adverse events (TRAE) was 63% ($\geq$ G3 41%). Common TEAEs ($\geq$ 10% pts) were rash (30%), neutropenia (22%), hyperbilirubinemia (20%), fatigue (14%), cough (10%), and thrombocytopenia (10%); common G3/4 TEAEs include neutropenia (22%) with no febrile neutropenia, hyperbilirubinemia (14%) and rash (10%). Common AEs were reversible and manageable. The WM cohort (n=17) demonstrated a similar safety profile compared to the overall safety population. No dose-limiting toxicities, AE-related deaths or Hy's law were observed across the overall safety population.

Conclusions: SGR-1505 monotherapy is well-tolerated, demonstrating a promising response rate and durability in R/R WM, including pts who progressed on SOC, including zanubrutinib, and those with negative prognostic markers. Dose optimization is ongoing for RP2D determination.

Best change in Immunoglobulin M levels and Best Overall Response (n=12)

The figure below includes 12 subjects previously exposed to a BTKi with ≥ 1 follow-up disease assessment with IgM assessment



Form record received

From International Workshop on Waldenstrom's Macroglobulinemia <pattersonkent@outlook.com>

Date Fri 31-Jul-26 4:11 PM

To Patterson, Christopher <Christopher_Patterson@DFCI.HARVARD.EDU>

External Email - Use Caution

Record saved to database with ID: 269

Form ID: 1

Form title: Abstract Submission

Form name: Abstract_Submission

Submitted at: 2026-07-31 16:10:28

Submitter IP: 71.233.185.181

User-ID: 0

Username: -

User full name: -

Submitter provider: Unknown

Submitter browser: Mozilla/5.0 (Windows NT 10.0; Win64; x64) AppleWebKit/537.36 (KHTML, like Gecko)

Chrome/150.0.0.0 Safari/537.36

Submitter operating system: win

First Name: Kenny

Last Name: Pham

Email: kenny.pham@schrodinger.com

Registration Type: Delegate

Abstract Title: A Phase 1 study of SGR-1505, an oral, potent MALT1 inhibitor for relapsed/refractory (R/R) Waldenström macroglobulinemia (WM)

Select abstract file to attach:

/home/dkwolfpk2016/public_html/waldenstromworkshop/media/breezingforms/uploads/sgr1505101iw
wm2026abstract.pdf

Conference: IWWM13