Supplemental Materials

Inclusion Criteria

- Age ≥18 years of age
- Written informed consent provided by patient
- ECOG performance status of 0-3
- Life expectancy >12 weeks
- Meeting the following laboratory values:
    - AST and ALT ≤2.5 x upper limit of normal (ULN)
        - If considered related to ASM or MCL: ≤5 x ULN
    - Serum direct bilirubin ≤1.5 x ULN
        - If considered related to ASM or MCL: ≤3 x ULN
    - Serum creatinine ≤2.0 mg/dL
    - Creatinine clearance (CrCl) ≥30 mL/min
- A diagnosis of SM per 2008 WHO criteria
- Neoplastic mast cells must express CD30 by immunohistochemistry or flow cytometry*.
- Patients with ASM and MCL with or without an AHNMD per 2008 WHO criteria must have at least 1 eligible organ damage finding per IWG-MRT-ECNM response criteria
- Both females of childbearing potential and males who have partners of childbearing potential must agree to use effective contraceptive methods during the study and for 30 days following the last dose of BV
- Females of childbearing potential must have negative serum or urine β-hCG pregnancy test result within 7 days prior to the first dose of BV
    - Exception for females who are >1 year post-menopausal or who have undergone bilateral tubal ligation or hysterectomy

Exclusion Criteria

- Patients unwilling or unable to comply with the study protocol
- Any other concurrent known severe and/or uncontrolled medical condition which could compromise study participation (eg. uncontrolled diabetes, active uncontrolled infection)
- History of another primary malignancy not in remission for ≥3 years
    - Exceptions to 3 year limit: non-melanoma skin cancer, fully excised melanoma in situ, curatively treated localized prostate cancer, cervical carcinoma in situ (colposcopy) or squamous intraepithelial lesion (Pap smear)
- History of cardiovascular disease including congestive heart failure (NYHA Grade 3 or 4), left ventricular ejection fraction <50%, myocardial infarction within the previous 6 months, or uncontrolled hypertension
- Females who are pregnant or lactating
- Patients with peripheral neuropathy of grade 2 or higher per CTCAE v4.03
- Patients with known hypersensitivity to any excipient contained in the drug formulation
- Patients with confirmed prior diagnosis of HIV infection or active viral hepatitis
- Patients presenting with an AHNMD requiring immediate cytoreductive therapy or targeted drugs (eg. AML)

- Patients who have received any investigational agent, chemotherapy, interferon-α, or cladribine (2-CdA) within 30 days prior to the first date of treatment with BV
- Patients who have received hematopoietic growth factor support (eg. G-CSF) within 14 days prior to the first date of treatment with BV
- Patient who have received prednisone >10 mg/day (or equivalent corticosteroid dose) for the treatment of SM; or those who have received any dose of prednisone for SM ≤28 days prior to the first date of treatment with BV
    - Exceptions for patient who are taking prednisone ≤10 mg/day (or equivalent corticosteroid dose) for medical conditions unrelated to SM, or those who started this dose for SM prior >28 days prior to the first date of treatment with BV
- Patients with known FIP1L1-PDGFRα fusion, even if resistant to imatinib therapy
- Patients who have received any treatment with BV prior to study entry
- Patient who have received any treatment with bleomycin
- Patients who have undergone a surgical procedure ≤14 days prior to the first date of treatment with BV
    - Exceptions for central venous catheter placements and other minor surgical procedures (eg. minimally invasive biopsies)

*Greater than 20% of MC expressing surface CD30 by flow cytometry (FCM) was used as a minimal threshold to consider a patient's advanced SM as CD30-positive.

Materials and Methods:

Bone Marrow Biopsy Processing

BM aspirate samples were obtained using EDTA-coated syringes. BM core biopsies were fixed in 10% neutral buffered formalin, with subsequent rapid decalcification performed in formic acid (MD Anderson) or RDO (Stanford; Apex Engineering, Plainfield, IL, USA). BM MC burden was assessed on aspirate and core biopsy samples using morphologic assessment in conjunction with multiparameter flow cytometry (FCM; CD25, CD2, CD117, CD45 and CD30) and immunohistochemistry (IHC; CD25, CD117, tryptase, and CD30).

CD30 Assessment

FCM quantification of MC surface CD30 expression was assessed on fresh anti-coagulated bone marrow aspirate samples using anti-BerH83 antibody [Becton Dickinson (BD) Biosciences, San Jose, CA, USA] via eight-parameter analysis on the FACSCanto instrument (BD Biosciences) with FACSDiva software (Version 8.0.1, BD Biosciences) for data analysis. A minimum of 100,000 events per tube was acquired per sample. CD30 expression was assessed on CD117-bright events (mast cells) over autofluorescence control and presented as a percentage of CD30 expression out of total CD117-positive mast cells. CD30 expression on the formalin-fixed, rapid decalcified BM core biopsy samples was assessed via IHC staining using an anti-BerH2 antibody (Dako, Glostrup, Denmark) with standard antigen retrieval on the Benchmark Ultra (Ventana, Tucson, AZ, USA); scoring was based on the percentage of CD30-positive mast cells out of total mast cells, using CD117 and tryptase as markers of mast cells.

Table S1: Patient characteristics and eligible organ damage findings at study entry

Patient	Sex / Age (y)	Diagnosis	IWG-MRT-ECNM Organ Damage Finding(s)
01	F / 84	ASM	▪ Symptomatic Splenomegaly
02	M / 73	SM-AHN (CMML-1)	▪ Alkaline Phosphatase Elevation [Grade 2]
03	F / 72	SM-AHN (MDS/MPN-U)	▪ Alkaline Phosphatase Elevation [Grade 2] ▪ Anemia (Transfusion Dependent) [Grade 3]
04	M / 78	SM-AHN (CEL, NOS)	▪ Symptomatic Splenomegaly ▪ Anemia (Transfusion Dependent) [Grade 3] ▪ Thrombocytopenia (Transfusion Independent) [Grade 3]
05	F / 79	ASM	▪ Anemia (Transfusion Independent) [Grade 2]
06	M / 41	MCL (CMML-1)	▪ Alkaline Phosphatase Elevation [Grade 2] ▪ Ascites
07	M / 82	SM-AHN (CMML-1)	▪ Alkaline Phosphatase Elevation [Grade 2] ▪ Neutropenia [Grade 3]
08	F / 65	SM-AHN (CMML-1)	▪ Anemia (Transfusion Independent) [Grade 2]
09	F / 40	MCL	▪ Alkaline Phosphatase Elevation [Grade 2]
10	F / 64	ASM	▪ Symptomatic Splenomegaly

Table S2: Patient-reported composite symptom burden indices

MPN-SAF TSS-10 --Each scored on a scale of 0-10 --Higher values indicate worse symptoms	Worst fatigue
	Concentration
	Early satiety
	Inactivity
	Night sweats
	Itching
	Bone or muscle pain
	Abdominal discomfort
	Weight loss
	Fever
MSAF --Each scored on a scale of 0-10 --Higher values indicate worse symptoms	Pruritus
	Dizziness
	Headache
	Worst fatigue
	Flushing
	Abdominal discomfort
	Diarrhea
	Bone or muscle pain
	Concentration
	Depression

Figure S1: Trial Scheme

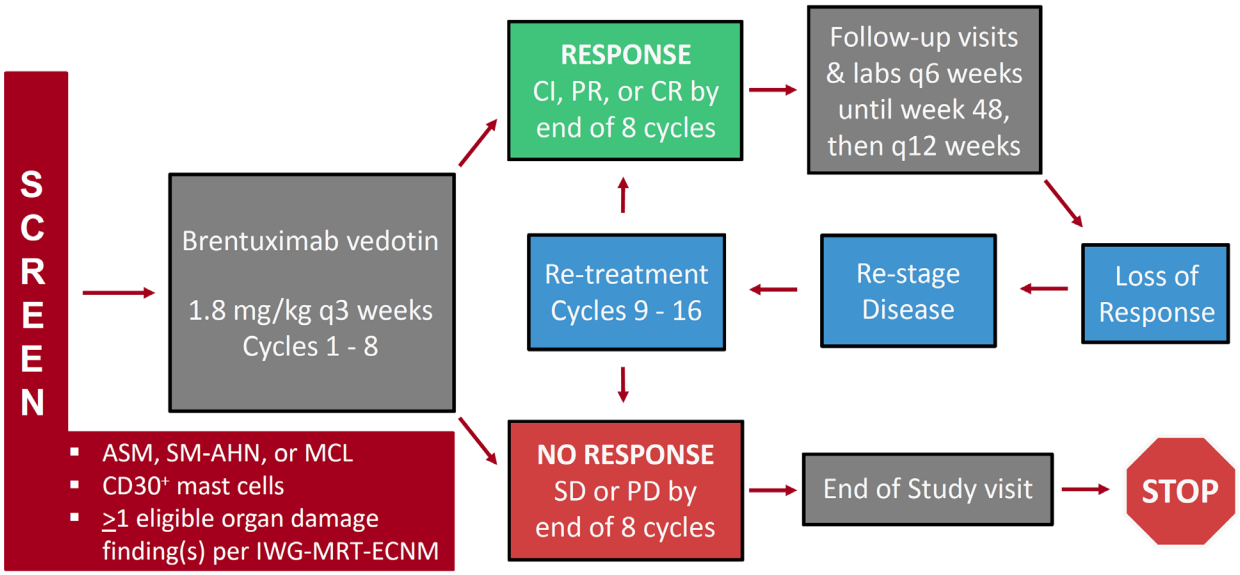
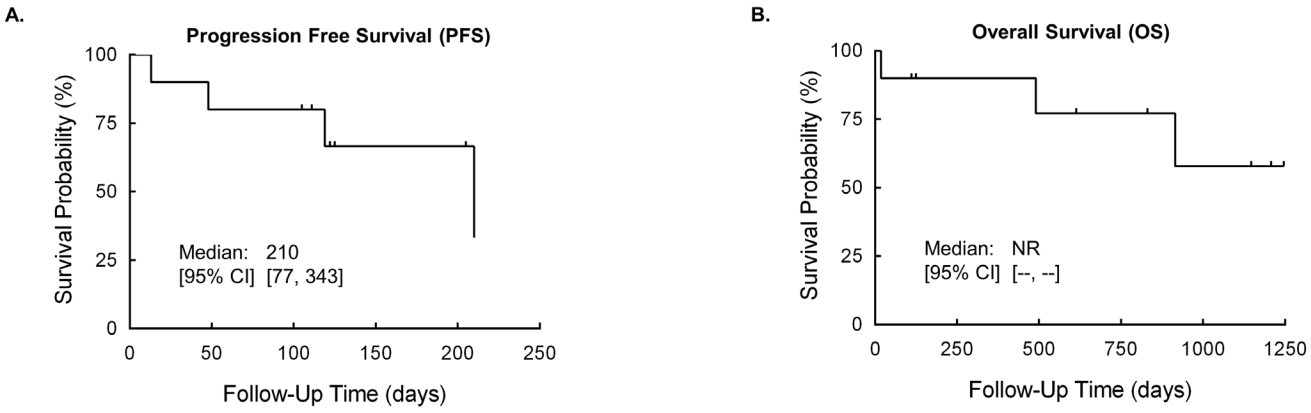


Figure S2: Progression-Free and Overall Survival

Kaplan-Meier survival curves showing progression free (A) and overall (B) survivals for the evaluable cohort.



PFS defined as the time from the start of treatment to the date of first confirmed PD, death, or institution of new therapy.
NR = not reached.