Overall Survival, Duration of Treatment, and Reduction in Serum Tryptase Levels in Patients with Advanced Systemic Mastocytosis Treated with Avapritinib versus Best Available Therapy

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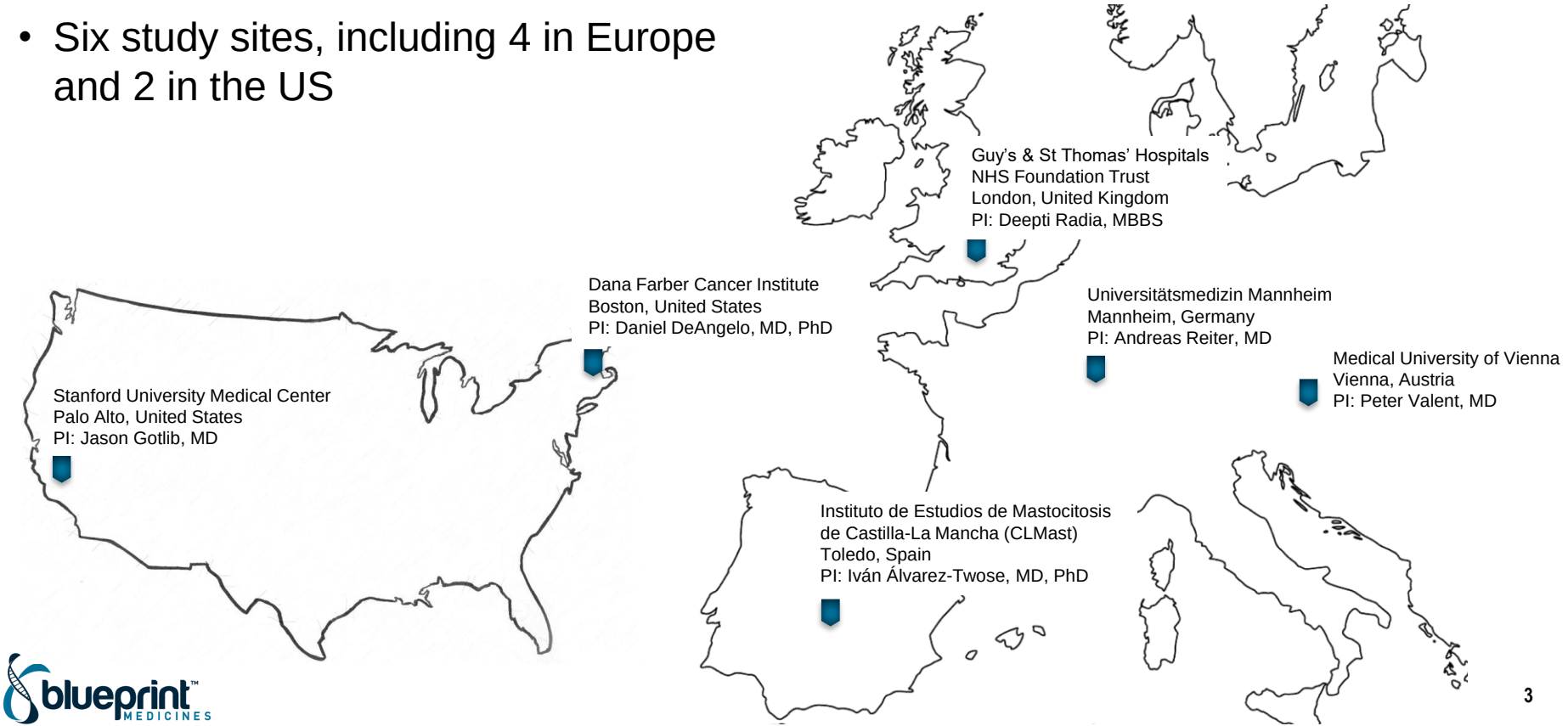
Background

- Advanced systemic mastocytosis (AdvSM) is a rare myeloproliferative neoplasm commonly distinguished by the accumulation of neoplastic mast cells in bone marrow and other tissues and organs[1,2]
- The majority (>90%) of patients with AdvSM harbor the *KIT* D816V mutation[3,4]
- Avapritinib, a selective *KIT* D816V inhibitor, was approved for the treatment of adults with AdvSM in the US,[5] and in Europe for treatment of patients with AdvSM in 2L+,[6] based on results from the Phase 1 EXPLORER (NCT02561988) and Phase 2 PATHFINDER (NCT03580655) studies[7,8]
- To date, no randomized controlled trial has compared the efficacy of avapritinib to alternative therapies for AdvSM
- This multi-center, observational and retrospective study was designed to
  - Generate real-world data on best available therapy (BAT) for patients with AdvSM
  - Conduct comparative analyses of clinical outcomes between patients treated with avapritinib in EXPLORER and PATHFINDER trials vs. BAT in standard clinical practice

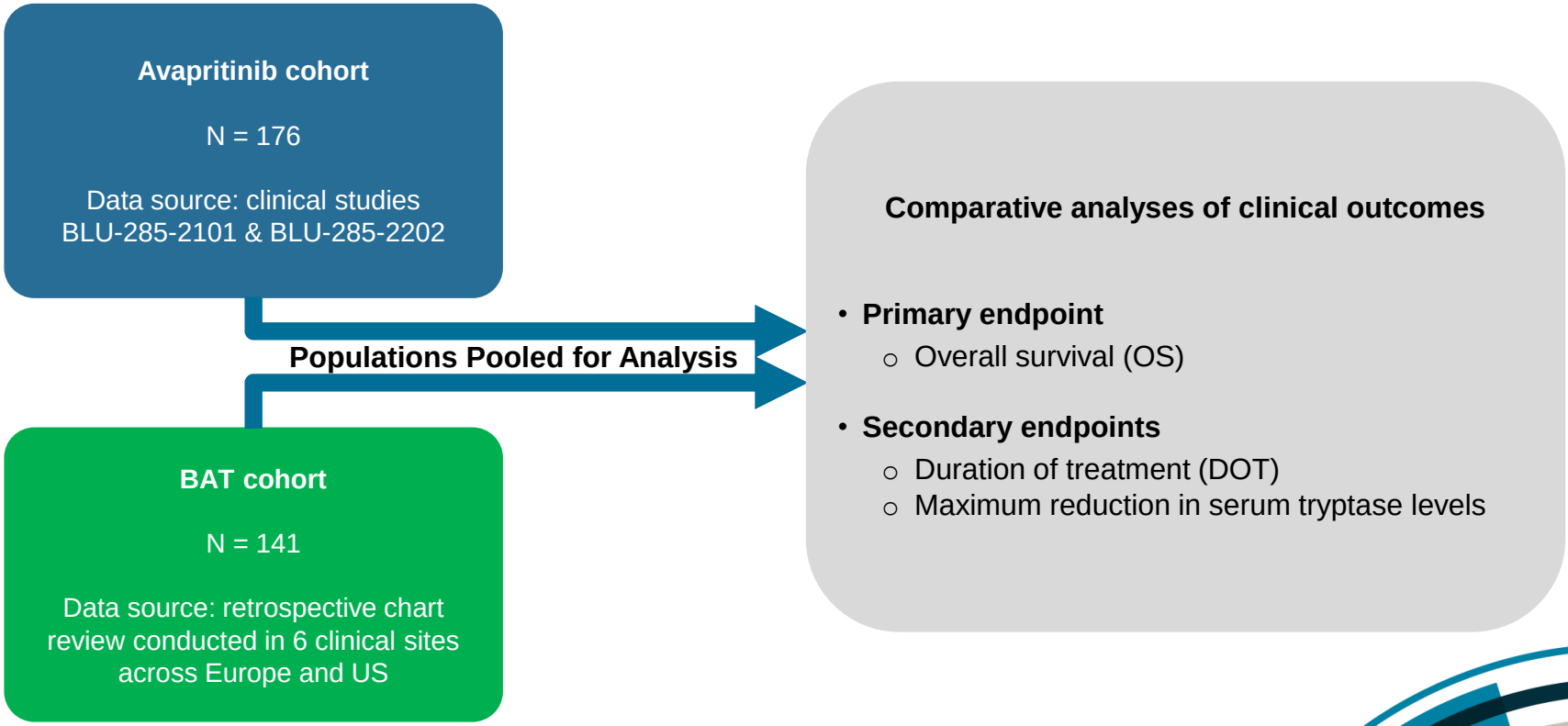
1. Valent, P. *Am J Cancer Res*. 2013;3(2):159-172.
2. Ustun, C., et al. *Haematologica*. 2016;101(10):1133-1143.
3. Kluin-Nelemans HC, et al. *Theranostics*. 2021;11(1):292.
4. Jawhar, M., et al. *J Clin Oncol*. 2019;37(31):2846-2856.
5. United States Food and Drug Administration. 2021. www.fda.gov.
6. Blueprint Medicines Corporation. 2022. ir.blueprintmedicines.com.
7. DeAngelo, DJ., et al. *Nat Med*. 2021;27:2183-2191.
8. Gotlib J., et al. *Nat Med*. 2021;27:2192-2199.

Leading institutions and experts in AdvSM research participated and contributed data on BAT

- Six study sites, including 4 in Europe and 2 in the US



Study design



Statistical analysis

- Descriptive analyses conducted to analyze baseline characteristics and treatments received
- Kaplan-Meier assessment of OS and DOT
- Comparative analyses of OS, DOT, and change in serum tryptase levels employed a two-step process:
  - Differences in key baseline covariates between cohorts were balanced using inverse propensity score (PS) weighting, i.e., inverse-probability-of-treatment-weighting (IPTW)
  - IPTW-weighted multivariable models were used,[1] with further adjustment for variables still unbalanced after weighting

[1] Cox proportional hazards models were used for OS and DOT and generalized estimating equation [GEE] linear models were used for serum tryptase. Robust variance estimation was used to account for inclusion of multiple lines of therapy from the same patient and for the use of weights.

Statistical analysis

Key covariates were selected *a priori* based on clinical input as well as validated prognostic scoring systems[1] for AdvSM:

- Age
- Sex
- Indicator for region
- ECOG score
- AdvSM subtype
- Skin involvement
- Serum tryptase level ≥125 ng/mL
- Leukocyte count of ≥16 × 10^9/L
- Anemia (hemoglobin <10 g/dL)
- Thrombocytopenia (platelet count <100 × 10^9/L)
- Presence and number of mutated genes within the *SRSF2/ASXL1/RUNX1* (*S/A/R*) panel
- Number of prior lines of therapy that were received
- Type(s) of prior therapy

[1] Prognostic variables included in the Mutation-Adjusted Risk Score (MARS) and the International Prognostic Scoring System in Mastocytosis (IPSM) were considered.

Results

Patient demographic and clinical characteristics

Unweighted sample	Avapritinib	BAT	*P* value
Number of unique patients	**N = 176**	**N = 141**	
Number of lines of therapy	**N = 176**	**N = 222**	
Demographic characteristics			
Age (years)			0.817
Mean (SD)	66.3 (10.7)	65.5 (11.8)	--
Median (min, max)	68.0 (31.0, 88.0)	67.8 (20.9, 87.5)	--
≥65 years, n (%)	109 (61.9%)	136 (61.3%)	
Sex, n (%)			
Female	73 (41.5%)	76 (34.2%)	0.168
Male	103 (58.5%)	146 (65.8%)	0.168
Region, n (%)			
North America	102 (58.0%)	34 (15.3%)	< 0.001*
Europe	74 (42.0%)	188 (84.7%)	< 0.001*
Medical history			
Performance status			
ECOG			0.093
n (%)	176 (100.0%)	222 (100.0%)	--
Mean (SD)	1.2 (0.8)	1.0 (0.7)	--
Median (min, max)	1.0 (0.0, 3.0)	1.0 (0.0, 3.0)	--
ECOG category, n (%)			
0	36 (20.5%)	50 (22.5%)	0.707
1	92 (52.3%)	129 (58.1%)	0.288
≥2	48 (27.3%)	43 (19.4%)	0.081
Anemia, n (%)	104 (59.1%)	125 (56.3%)	0.648
Thrombocytopenia, n (%)	67 (38.1%)	120 (54.1%)	< 0.01 *

**P<0.05.*

Abbreviations: *ECOG: Eastern Cooperative Oncology Group; max: maximum; min: minimum; SD: standard deviation.*

Note: Real-world patients with unknown ECOG score were excluded (N=20)

Results

Patient demographic and clinical characteristics

Unweighted sample	Avapritinib	BAT	*P* value
Disease characteristics, n (%)			
AdvSM subtype diagnosis			
SM-AHN	119 (67.6%)	121 (54.5%)	< 0.05 *
ASM	29 (16.5%)	68 (30.6%)	< 0.01 *
MCL	28 (15.9%)	33 (14.9%)	0.883
Any skin involvement	58 (33.0%)	71 (32.0%)	0.922
Leukocyte count ≥16 x 10^9/L	33 (18.8%)	54 (24.3%)	0.225
Serum tryptase ≥125 ng/mL	132 (75.0%)	144 (64.9%)	< 0.05 *
Patients tested for *KIT* mutation	170 (96.6%)	140 (99.3%)	0.137
KIT D816V positive	156 (91.8%)	128 (91.4%)	1.000
Patients tested for at least one mutation in the *S/A/R* mutation panel	176 (100.0%)	107 (75.9%)	<0.001 *
N mutated genes in *S/A/R panel*			
0	92 (52.3%)	41 (38.3%)	0.031*
1	54 (30.7%)	44 (41.1%)	0.097
≥2	30 (17.0%)	22 (20.6%)	0.560
Number of prior systemic therapy lines received, n (%)			
0	66 (37.5%)	118 (53.2%)	< 0.01 *
1	68 (38.6%)	69 (31.1%)	0.142
2	28 (15.9%)	24 (10.8%)	0.177
≥3	14 (8.0%)	11 (5.0%)	0.309

**P<0.05.*

Abbreviations: *AdvSM: advanced systemic mastocytosis; ASM: aggressive systemic mastocytosis; BAT: best available therapy; MCL: mast cell leukemia; S/A/R: SRSF2/ASXL1/RUNX1; SM-AHN: systemic mastocytosis with an associated hematologic neoplasm.*

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Results

Best available therapies in real world patients

	BAT
Number of unique patients	**N = 141**
Number of lines of therapy	**N = 222**
Agents used in each line of therapy,[1] n (%)	
TKI therapy	120 (54.1%)
Cytotoxic therapy	91 (41.0%)
Biologic therapy	25 (11.3%)
Agent-level information available[1]	**N = 196**
TKI	
Brentuximab vedotin	4 (2.0%)
Gemtuzumab ozogamicin	1 (0.5%)
Interferon-alpha	11 (5.6%)
Pegylated interferon	8 (4.1%)

Results for OS comparing patients treated with avapritinib in trials vs. midostaurin or cladribine in real-world clinical practice will be presented by poster at EHA 2022, June 9-12

Abstract title: Overall Survival in Patients with Advanced Systemic Mastocytosis Receiving Avapritinib versus Midostaurin or Cladribine

Abstract number: P1014

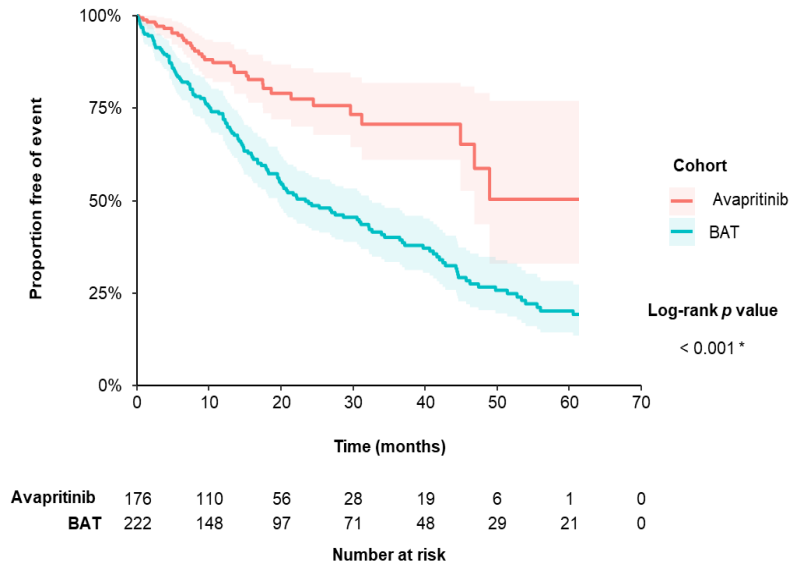
Abbreviations: *BAT: best available therapy; TKI: tyrosine-kinase inhibitor.*

Note: Agent-level information for prior treatments was reported among patients from all study sites except Medizinische Universität Wien (Vienna, Austria) (N=26 lines of therapy), where only treatment class information was collected per local regulations.

Results

Significantly longer OS among avapritinib patients compared to patients receiving BAT

Kaplan-Meier Curve for OS



Overall Survival (OS) Weighted by IPTW	Avapritinib	BAT
Number of unique patients	Effective N=172	Effective N=136
Number of lines of therapy	Effective N=172	Effective N=210
Mean follow-up time, months	17.9	25.7
Median OS, months (95% CI)	49.0 (46.9, NE)	26.8 (18.2, 39.7)
Adjusted HR (95% CI)	0.48 (0.29, 0.79)	
P value	0.004*	

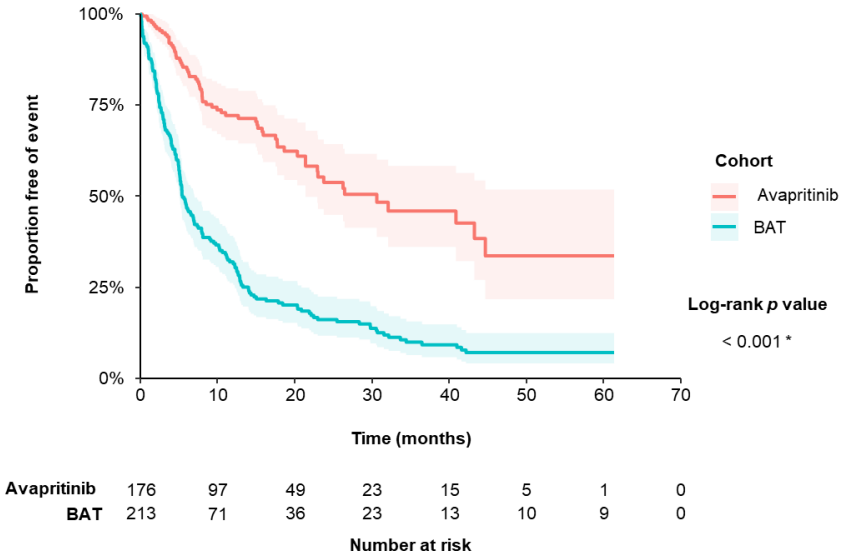
**P<0.05.*

Abbreviations: *CI: confidence interval; IPTW: inverse probability of treatment weighting; HR: hazard ratio; NE: not estimable.*

Results

Significantly longer DOT among avapritinib patients compared to patients receiving BAT

Kaplan-Meier Curve for DOT



Duration of Treatment (DOT) Weighted by IPTW	Avapritinib	BAT
Number of unique patients	Effective N=173	Effective N=131
Number of lines of therapy	Effective N=173	Effective N=201
Median DOT (months) (95% CI)	23.8 (20.3, 40.9)	5.4 (5.0, 7.5)
Adjusted HR (95% CI)	0.36 (0.26, 0.51)	
P value	<0.001*	

**P<0.05.*

Abbreviations: *CI: confidence interval; IPTW: inverse probability of treatment weighting; HR: hazard ratio.*

Results

Significantly greater reduction in serum tryptase levels observed among avapritinib vs. BAT patients

Maximum Reduction in Serum Tryptase Weighted by IPTW	Avapritinib	BAT
Number of unique patients	Effective N=173	Effective N=106
Number of lines of therapy	Effective N=173	Effective N=150
IPTW-weighted mean maximum percentage reduction in serum tryptase levels[1] (standard deviation)	-87.1 (17.2)	-18.0 (123.9)
Adjusted mean difference in percentage change (95% CI)[3]	-60.34 (-72.81, -47.86)	
P value	<0.001*	

*$P<0.05$.
Abbreviations: *BAT: best available therapy; CI: confidence interval; IPTW: inverse probability of treatment weighting; HR: hazard ratio.*

Notes:
[1] Mean maximum percentage change of serum tryptase was weighted by IPTW. Negative values indicated reduction in serum tryptase level.
[2] Mean time to maximum reduction after weighting was 8.5 months in the BAT cohort, and 8.8 months in the avapritinib cohort.
[3] Mean difference was obtained by a weighted regression model, with key variables that were disbalanced after weighting added as model covariates

Conclusions

- Given the lack of RCTs comparing avapritinib versus BAT, this real-world clinical practice data offers essential insights
- The results from this observational, retrospective study indicate that AdvSM patients treated with avapritinib in EXPLORER and PATHFINDER, compared to patients treated with BAT, experienced:
  - Significantly improved overall survival
  - Longer duration of treatment
  - Greater reductions in serum tryptase levels
- Results indicate superior efficacy of *KIT* D816V-targeting avapritinib compared to other available therapy

Acknowledgements

- The authors would like to thank the patients enrolled in the EXPLORER and PATHFINDER trials, and their families, and patients included in the external control study
- The authors would like to acknowledge the contributions of colleagues at Blueprint Medicines Corporation and Analysis Group, as well as research personnel at the study sites

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Thank you

Back-up slides

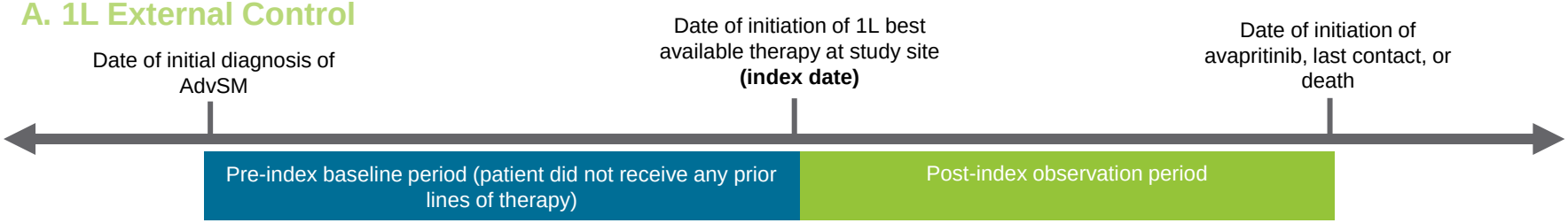
Inclusion and exclusion criteria

Real-world patients treated with BAT were identified based on inclusion and exclusion criteria similar to those from the EXPLORER and PATHFINDER single-arm trials such that patients included in the BAT cohort are comparable to trial patients

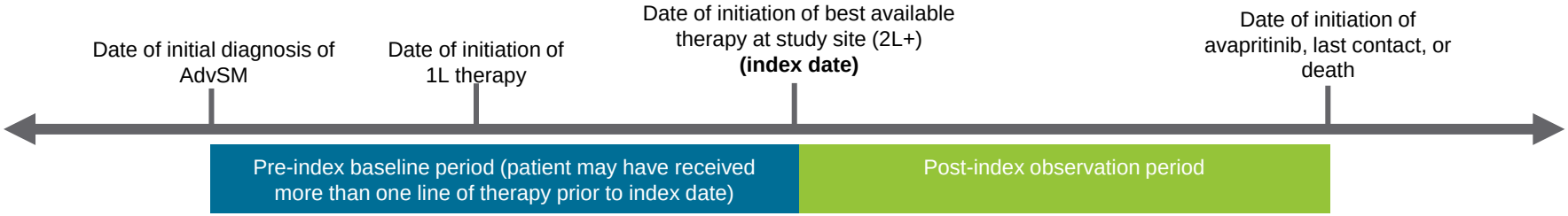
Inclusion	• Adults (aged ≥18 years) with a diagnosis of AdvSM and documented subtype in their chart (ASM, SM-AHN, or MCL) • Received ≥1 line of systemic therapy (not necessarily as first line) for AdvSM at a participating site on or after January 1, 2009 • The date of initiation of each line of therapy at the participating site was defined as the index date • Had an index date ≥3 months prior to the start of data collection, unless earlier death
Exclusion	• History of another primary malignancy that was diagnosed or required therapy within 3 years before the index date (excluding completely resected basal cell and squamous cell skin cancer, curatively treated localized prostate cancer, and completely resected carcinoma *in situ* in any site) • Received avapritinib as the first therapy for AdvSM at a participating site

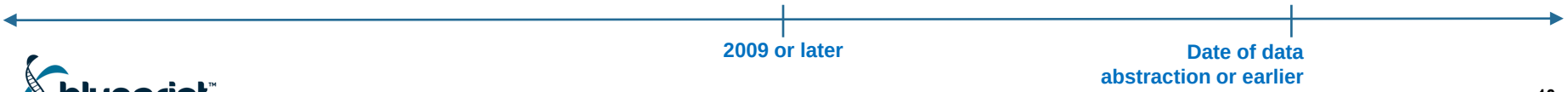
Study design

A. 1L External Control



B. 2L+ External Control





Statistical analysis

Inverse Probability of Treatment Weighting (IPTW)

- Adjusts the samples from trial data and real-world external control data using weighting by the inverse of the propensity score (i.e., propensity to receive avapritinib or BAT)
- This balances distribution of baseline covariates in the pooled sample of patients, and reduces impact of confounders[1]

1. Austin, PC and Stuart, EA. *Stat Med*. 2015;34(28):3661-3679.

Results

Treatments received by BAT cohort patients, by line of therapy

	Overall	First Line	Second Line	Third or Later Lines
Number of unique patients	N = 141	N = 118	N = 69	N = 35
Total number of lines of therapy included	N = 222	N = 118	N = 69	N = 35
Total number of lines of therapy contributed by patient				
Mean (SD)	1.6 (0.9)	--	--	--
Median (min, max)	1.0 (1.0, 7.0)	--	--	--
Number of lines of therapy contributed, n (%)				
1	86 (61.0%)	--	--	--
2	40 (28.4%)	--	--	--
≥3	15 (10.6%)	--	--	--
Agents used in each included line of therapy, n (%)				
TKI therapy	120 (54.1%)	71 (60.2%)	34 (49.3%)	15 (42.9%)
Cytoreductive therapy	91 (41.0%)	39 (33.1%)	33 (47.8%)	19 (54.3%)
Biologic therapy	25 (11.3%)	14 (11.9%)	8 (11.6%)	3 (8.6%)
Agent-level information available[b]	N = 196	N = 107	N = 59	N = 30
TKI				
Midostaurin	99 (50.5%)	58 (54.2%)	29 (49.2%)	12 (40.0%)
Ripretinib	4 (2.0%)	2 (1.9%)	0 (0.0%)	2 (6.7%)
Ibrutinib	3 (1.5%)	3 (2.8%)	0 (0.0%)	0 (0.0%)
Dasatinib	2 (1.0%)	1 (0.9%)	1 (1.7%)	0 (0.0%)
Imatinib	2 (1.0%)	1 (0.9%)	0 (0.0%)	1 (3.3%)
Cytoreductive therapy				
Cladribine	49 (25.0%)	20 (18.7%)	18 (30.5%)	11 (36.7%)
Hydroxyurea	17 (8.7%)	10 (9.3%)	5 (8.5%)	2 (6.7%)
Azacitidine	3 (1.5%)	0 (0.0%)	2 (3.4%)	1 (3.3%)
Biologic				
Interferon-alfa	11 (5.6%)	9 (8.4%)	2 (3.4%)	0 (0.0%)
Pegylated interferon	8 (4.1%)	3 (2.8%)	4 (6.8%)	1 (3.3%)
Brentuximab vedotin	4 (2.0%)	2 (1.9%)	2 (3.4%)	0 (0.0%)
Gemtuzumab ozogamicin	1 (0.5%)	0 (0.0%)	0 (0.0%)	1 (3.3%)

Results

Prior systemic therapy

Unweighted sample	Avapritinib	BAT	*P* value
Number of unique patients	**N = 176**	**N = 141**	
Number of lines of therapy	**N = 176**	**N = 222**	
Number with prior systemic therapy	110 (62.5%)	104 (46.8%)	< 0.01 *
Number of prior lines of systemic therapy received, n (%)			< 0.001 *
Mean (SD)	1.0 (1.1)	0.1 (0.3)	--
Median (min, max)	1.0 (0.0, 6.0)	0.0 (0.0, 2.0)	--
0	66 (37.5%)	118 (53.2%)	< 0.01 *
1	68 (38.6%)	69 (31.1%)	0.142
2	28 (15.9%)	24 (10.8%)	0.177
≥3	14 (8.0%)	11 (5.0%)	0.309
Prior treatments received, n (%)			
TKI therapy	92 (52.3%)	50 (22.5%)	< 0.001 *
Cytotoxic therapy	33 (18.8%)	61 (27.5%)	0.055
Biologic therapy	23 (13.1%)	30 (13.5%)	1.000

**P<0.05.*

Abbreviations: *BAT: best available therapy; max: maximum; min: minimum; SD: standard deviation; TKI: tyrosine kinase inhibitor.*

- Median (range) number of prior lines of systemic therapy received was 1 (0−6) in the avapritinib cohort and 0 (0−2) in the BAT cohort
- In the avapritinib cohort, patients were most frequently pretreated with tyrosine kinase inhibitors (TKI): 52.3%
- Patients in the BAT cohort were most frequently pretreated with cytotoxic therapies: 27.5%

Results

Two cohorts were more comparable with regards to key covariates after IPTW

	Unweighted sample			IPTW-weighted sample		
	Avapritinib	**BAT**	**Standardized Difference[1]**	**Avapritinib**	**BAT[2]**	**Standardized Difference[1]**
Number of unique patients	**176**	**141**		**Effective N = 172**	**Effective N = 134**	
Number of lines of therapy	**176**	**222**		**Effective N = 172**	**Effective N = 210**	
Age (years), mean (SD)	66.3 (10.7)	65.5 (11.8)	6.5%	66.4 (10.5)	65.3 (12.4)	9.2%
Male, n (%)	103 (58.5%)	146 (65.8%)	15.0%*	60.0%	62.6%	5.3%
Region, n (%)						12.3%*
North America	102 (58.0%)	34 (15.3%)		34.4%	28.6%	
Europe	74 (42.0%)	188 (84.7%)		65.6%	71.4%	
ECOG category, n (%)						
0	36 (20.5%)	50 (22.5%)	5.0%	16.3%	19.2%	7.4%
1	92 (52.3%)	129 (58.1%)	11.8%*	59.0%	56.2%	5.8%
≥2	48 (27.3%)	43 (19.4%)	18.8%*	24.6%	24.7%	0.1%
Anemia, n (%)	104 (59.1%)	125 (56.3%)	5.6%	55.4%	57.8%	5.0%
Thrombocytopenia, n (%)	67 (38.1%)	120 (54.1%)	32.5%*	38.9%	43.9%	10.2%*
AdvSM subtype diagnosis, n (%)						
SM-AHN	119 (67.6%)	121 (54.5%)	27.1%*	58.4%	58.2%	0.5%
ASM	29 (16.5%)	68 (30.6%)	33.8%*	26.5%	25.2%	3.0%
MCL	28 (15.9%)	33 (14.9%)	2.9%	15.1%	16.6%	4.3%
Any skin involvement, n (%)	58 (33.0%)	71 (32.0%)	2.1%	30.3%	32.5%	4.8%
Leukocyte count ≥16 × 10^9/L, n (%)	33 (18.8%)	54 (24.3%)	13.6%*	18.5%	19.8%	3.3%
Serum tryptase[10] ≥125 ng/mL, n (%)	132 (75.0%)	144 (64.9%)	22.2%*	72.5%	71.0%	3.2%

**Standardized difference >10%.*

Abbreviations: *ASM: aggressive mastocytosis; BAT: best available therapy; ECOG: Eastern Cooperative Oncology Group; IPTW: inverse probability of treatment weighting; MCL: mast cell leukemia; SD: standard deviation; SM-AHN: systemic mastocytosis with an associated hematologic neoplasm.*

Notes:

[1] A standardized difference of greater than 10% indicates meaningful imbalance between the two cohorts.

[2] Real-world patients with unknown ECOG score were excluded (N=20).

Results

Two cohorts were more comparable with regards to key covariates after IPTW

	Unweighted sample			IPTW-weighted sample		
	Avapritinib	**BAT**	**Standardized Difference[1]**	**Avapritinib**	**BAT[2]**	**Standardized Difference[1]**
Number of unique patients	**176**	**141**		**Effective N = 172**	**Effective N = 134**	
Number of lines of therapy	**176**	**222**		**Effective N = 172**	**Effective N = 210**	
Patients tested for at least one mutation in the *S/A/R* mutation panel	176 (100.0%)	169 (76.1%)		100.0%	70.8%	
N mutated genes in *S/A/R* panel						
0	92 (52.3%)	66 (29.7%)		55.3%	26.7%	
1	54 (30.7%)	68 (30.6%)	0.1%	28.7%	30.1%	3.1%
≥2	30 (17.0%)	35 (15.8%)	3.5%	16.0%	13.9%	5.8%
Number of prior lines of systemic therapy received						
0	66 (37.5%)	118 (53.2%)	31.8%*	47.2%	50.4%	6.4%
1	68 (38.6%)	69 (31.1%)	15.9%*	33.1%	32.4%	1.5%
2	28 (15.9%)	24 (10.8%)	15.0%*	14.6%	12.6%	5.6%
≥3	14 (8.0%)	11 (5.0%)	12.2%*	5.1%	4.6%	2.7%
Prior treatments received, n (%)						
TKI therapy	92 (52.3%)	50 (22.5%)	64.6%*	37.1%	29.9%	15.2%*
Cytotoxic therapy	33 (18.8%)	61 (27.5%)	20.8%*	20.1%	22.1%	4.8%
Biologic or other systemic therapy	23 (13.1%)	30 (13.5%)	1.3%	14.9%	15.2%	0.7%

**Standardized difference >10%.*

Abbreviations: *S/A/R: SRSF2/ASXL1/RUNX1; TKI: tyrosine-kinase inhibitor.*

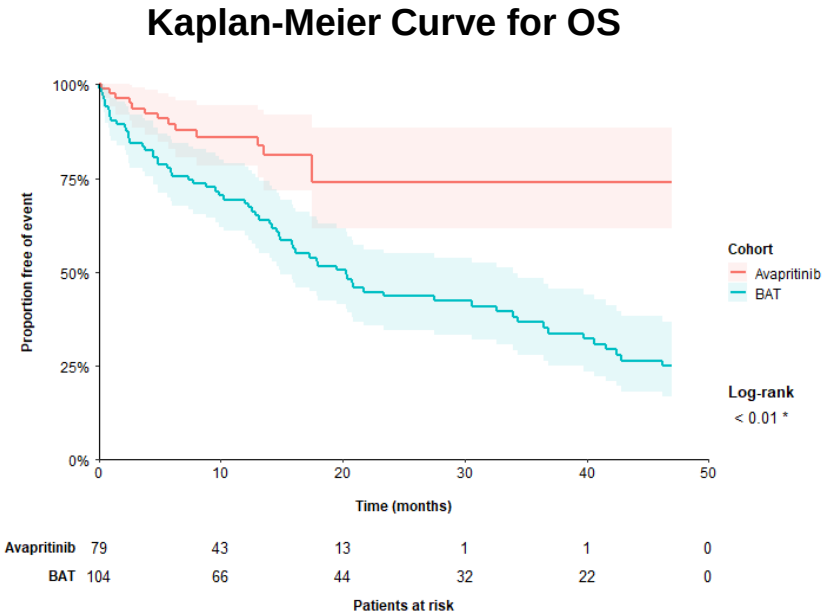
Notes:

[1] A standardized difference of greater than 10% indicates meaningful imbalance between the two cohorts.

[2] Real-world patients with unknown ECOG score were excluded (N=20).

Results

Significantly longer OS among pre-treated avapritinib (200mg) patients compared to pre-treated patients receiving BAT



- Among those with at least one prior LOT, patients treated with avapritinib 200mg had a 63% (*P*=0.006*) lower risk of death compared to BAT, after IPTW and multivariable adjustment
- The IPTW-weighted OS rates were higher for the avapritinib 200mg cohort versus the BAT cohort at all time points:
  - **6 months:** 93.3% vs. 81.6%
  - **12 months:** 91.0% vs. 72.8%
  - **24 months:** 71.6% vs. 42.2%
  - **36 months:** 71.6% vs. 36.7%
  - **48 months:** Not estimable vs. 24.2%

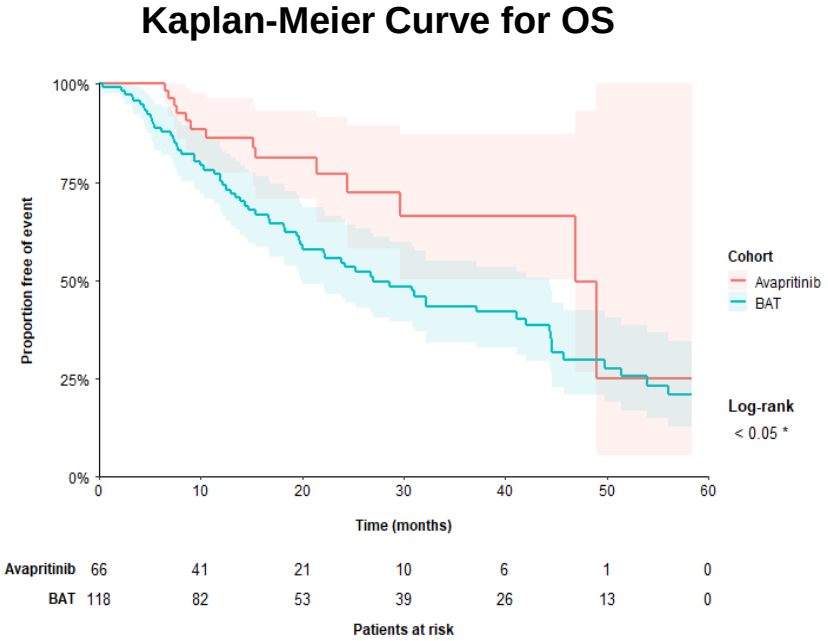
Overall Survival (OS) weighted by IPTW	Avapritinib	BAT
Number of unique patients	Effective N=77	Effective N=66
Number of lines of therapy	Effective N=77	Effective N=96
Mean follow-up time, months	12.6	25.2
Median OS, months (95% CI)	NR (NE, NE)	17.2 (14.6, 36.5)
Adjusted HR (95% CI)	0.37 (0.18, 0.75)	
P value	0.006*	

**P<0.05.*

Abbreviations: *CI: confidence interval; IPTW: inverse probability of treatment weighting; HR: hazard ratio; NE: not estimable.*

Results

Significantly longer OS among first-line (1L) avapritinib patients compared to patients receiving 1L BAT



- Among patients receiving first-line therapies, patients treated with avapritinib had a 60% (*P*=0.003*) lower risk of death compared to BAT, after IPTW and multivariable adjustment
- The IPTW-weighted OS rates were higher for the avapritinib cohort versus the BAT cohort at all time points:
  - **6 months:** 100.0% vs. 87.7%
  - **12 months:** 85.7% vs. 72.5%
  - **24 months:** 70.3% vs. 54.4%
  - **36 months:** 61.2% vs. 42.4%
  - **48 months:** 52.3% vs. 26.8%

Overall Survival (OS) weighted by IPTW	Avapritinib	BAT
Number of unique patients	Effective N=62	Effective N=115
Number of lines of therapy	Effective N=62	Effective N=115
Mean follow-up time, months	17.8	26.1
Median OS, months (95% CI)	49.0 (29.6, NE)	27.0 (19.7, 44.3)
Adjusted HR (95% CI)	0.40 (0.22, 0.74)	
P value	0.003*	

**P<0.05.*

Abbreviations: *CI: confidence interval; IPTW: inverse probability of treatment weighting; HR: hazard ratio; NE: not estimable.*

Limitations

- Due to the retrospective nature of data collection for patients treated with BAT, results may have been impacted by incomplete reporting for key characteristics, such as performance status, which informed prognostic score adjustment for the OS analysis
  - A sensitivity analysis assessing the impact of missing performance status indicated that this is not expected to impact results
- It is possible patients from the BAT cohort went on to receive avapritinib as part of the EXPLORER or PATHFINDER trials. Since no identifiable information was collected for real-world patients, these patients may have been included in the avapritinib trial cohort
  - These patients were included in the analysis, but were censored at avapritinib initiation to ensure their time on treatment was not counted in both the real-world and trial cohorts

Limitations

- AdvSM diagnoses for patients treated with BAT were based on local clinician-assessed evaluation using the 2016 revision to the WHO diagnostic criteria
  - Therefore, the correct subtype diagnoses may not have been made prior to the substantial increases in disease knowledge that have occurred over the last decade
- AdvSM diagnoses for trial patients treated with avapritinib were based on the same criteria, but adjudicated by the Response Assessment Committee
  - As such, misclassification of clinician-assessed AdvSM diagnosis for BAT patients may result in an underestimate of differences in OS
  - Since all participating centers hold expertise in AdvSM treatment, this concern is mitigated