Effect of avapritinib on skin disease burden in patients with advanced systemic mastocytosis (AdvSM): A novel, artificial intelligence (AI)-based technology

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Karin Hartmann,[1,2] Marcus Maurer,[3,4] Frank Siebenhaar,[3,4] Andreas Reiter,[5] Daniel J. DeAngelo,[6] Deepti H. Radia,[7] Jason Gotlib,[8] Tracy I. George,[9] Tsewang Tashi,[10] Celalettin Ustun,[11] Iván Alvarez-Twose,[12] Kristen M. Pettit,[13] Brian D'Alessandro,[14] Mira Patel,[14] Hui-Min Lin,[15] Saša Dimitrijević,[16] Sigurd Broesby-Olsen[17]

[1]Division of Allergy, Department of Dermatology, University Hospital Basel and University of Basel, Basel, Switzerland; [2]Department of Biomedicine, University Hospital Basel and University of Basel, Basel, Switzerland; [3]Institute of Allergology, Charité –Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany; [4]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Allergology and Immunology, Berlin, Germany; [5]University Hospital Mannheim, Heidelberg University, Mannheim, Germany; [6]Dana-Farber Cancer Institute, Boston, MA, USA; [7]Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom; [8]Stanford Cancer Institute, Stanford University School of Medicine, Stanford, CA, USA; [9]ARUP Laboratories, Department of Pathology, University of Utah School of Medicine, Salt Lake City, UT, USA; [10]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; [11]Rush University Medical Center, Chicago, IL, USA; [12]Institute of Mastocytosis Studies of Castilla-La Mancha, Toledo, Spain; [13]Division of Hematology/Oncology, University of Michigan, Ann Arbor, MI, USA; [14]Canfield Scientific, Parsippany, NJ, USA;[15]Blueprint Medicines Corporation, Cambridge, MA, United States of America; [16]Blueprint Medicines Corporation, Zug, Switzerland; [17]Department of Dermatology and Allergy Centre, Odense University Hospital, Odense, Denmark

Introduction

- Advanced systemic mastocytosis (AdvSM), a rare hematologic neoplasm driven by the *KIT* D816V mutation in >90% of cases, is characterized by mast cell proliferation, hyperactivation, tissue and organ infiltration[1,2]
- ~50% of patients with AdvSM show maculopapular skin lesions, along with itching and flushing[3,4]
- Avapritinib, an oral, potent, selective inhibitor of KIT D816V, is approved in the United States and in the European Union based on results from the phase 1 EXPLORER (NCT02561988) and phase 2 PATHFINDER (NCT03580655) clinical studies[5,6]
- Avapritinib demonstrated a 75% overall response rate (defined as complete remission + complete remission with partial hematologic recovery + partial remission + clinical improvement) and improvements in patient reported outcomes (PROs) including skin symptoms[7]
- To evaluate avapritinib on maculopapular skin lesions, an analysis was conducted by an independent Skin Assessment Committee (SAC) using a novel, AI-based technology

Study design and patient characteristics

36 patients with AdvSM in PATHFINDER consented for skin evaluation

21 patients with baseline and ≥1 post-baseline skin assessments initiated avapritinib in 4-week cycles (200 mg QD n=20; 100 mg QD n=1)

AdvSM-SAF: used to capture patient reported skin symptoms (flushing, itching, and spots) and skin domain changes from baseline

Patient characteristics	All doses (n=21)
Median age, years (range)	66 (38–85)
Female, n (%)	6 (29)
AdvSM subtype per SRC, n (%)[a]	
ASM	4 (19)
SM-AHN	9 (43)
MCL	8 (38)
Prior therapy, n (%)	15 (71)

[a]Centrally adjudicated by SRC. ASM, aggressive systemic mastocytosis; MCL, mast cell leukemia; QD, once daily; SAF, Symptom Assessment Form; SM-AHN, systemic mastocytosis with an associated hematological neoplasm; SRC, Steering Review Committee.

Evaluation of avapritinib effect on skin lesions

High-resolution photographs were taken at screening and subsequent timepoints (C3D1, C7D1, C11D1, and C17D1) in a standardized manner (i.e., light, distance)

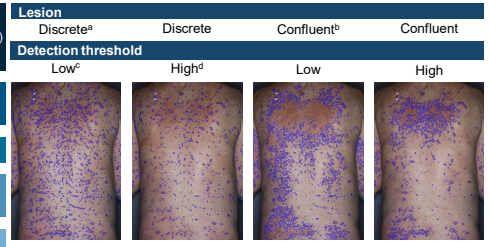
Areas of interest defined manually (front torso, back torso, front thigh, back thigh)

Lesions detected by four computer vision algorithms

Best algorithm for each patient selected by SAC at screening and used at all subsequent timepoints

Assessments: baseline most affected region, change in fraction of affected skin area, and change in skin color

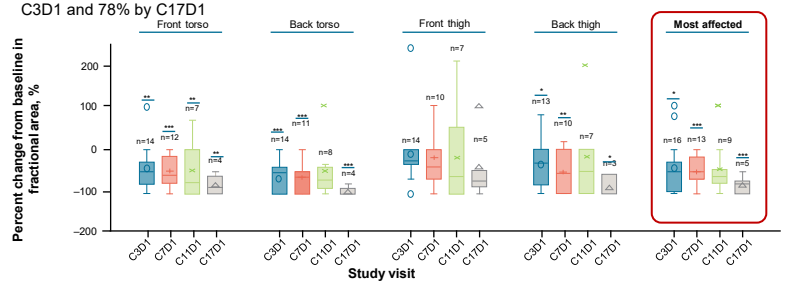
AdvSM-SAF (4-week treatment cycles) were also assessed at screening and subsequent timepoints



Note: All patients provided consent for use of their image in this presentation as part of a clinical trial. [a]The discrete lesion algorithms were tailored to find smaller, more discrete spots of mastocytosis; [b]The confluent lesion algorithms were tailored to find larger regions of the affected area that generally covered a significant portion of the skin; [c]The algorithms using a lower threshold detected more of the affected area; [d]The algorithms using a higher threshold detected less of the affected area. C3D1, Cycle 3 Day 1; C7D1, Cycle 7 Day 1; C11D1; Cycle 11 Day 1; C17D1, Cycle 17 Day 1.

Avapritinib reduced fractional skin lesion area

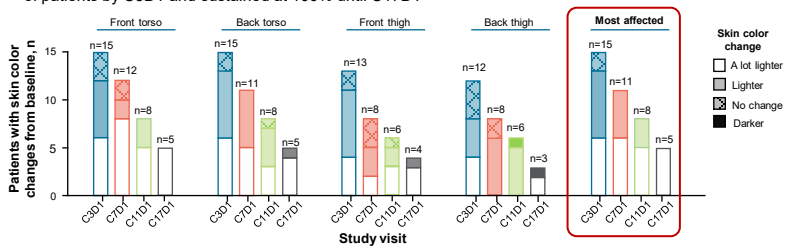
- Median reduction in fractional skin lesion area from baseline in the most affected body part reached 50% on C3D1 and 78% by C17D1



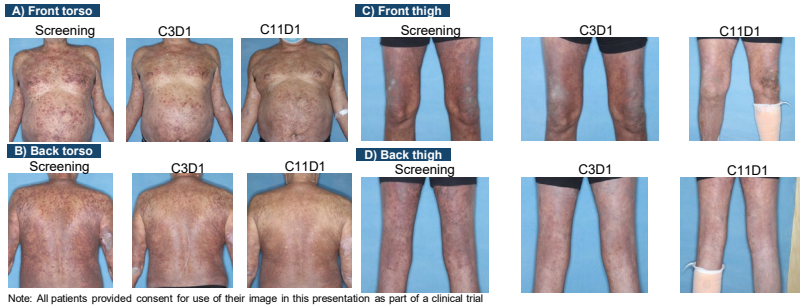
Note: For the boxplot, the 3 horizontal lines of the box represent 25th, 50th, and 75th percentile. The whiskers are drawn from the box to the most extreme point that is less than or equal to 1.5 times of the interquartile range (IQR = 75th – 25th). The dots beyond whisker represent observed outliers. *P<0.05; **P<0.01; ***P<0.001

Avapritinib improved skin lesion color

- Change in skin lesion color of the most affected body part was adjudicated as "lighter" or "a lot lighter" in 87% of patients by C3D1 and sustained at 100% until C17D1



Avapritinib reduced fractional skin lesion area and improved skin lesion color



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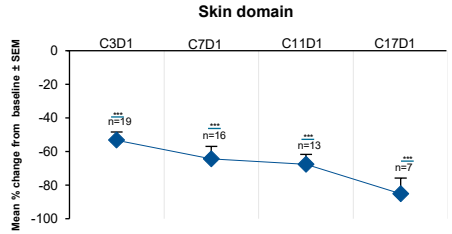
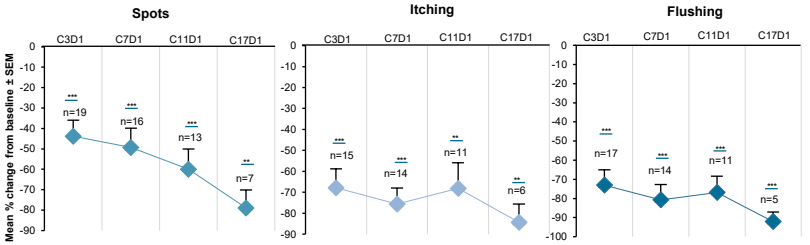
Avapritinib reduced skin symptoms (spots, itching, flushing) and skin domain changes from baseline based on AdvSM-SAF skin severity score[8]



- AdvSM-SAF skin severity score[a] was reduced by 53%, 64%, 68%, and 85% on C3D1, C7D1, C11D1, and C17D1, respectively

Data cut-off for skin domain SAF is April 20, 2021



[a]n=19 with baseline score. *P<0.05; **P<0.01; ***P<0.001. .

Avapritinib improved signs and symptoms of cutaneous manifestation in AdvSM

- First comprehensive evaluation of skin lesion improvement in AdvSM using a novel technology and methodology including AI
- Avapritinib resulted in:
  - Substantial, rapid (C3D1), and sustained (C17D1), reduction in skin lesion area
  - Major reduction of skin lesion color
  - Concomitant improvement in severity of patient-reported skin symptoms including spots, itching, and flushing

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