An Updated Analysis on Safety and Efficacy of Avapritinib in Patients With Advanced Systemic Mastocytosis From the EXPLORER Clinical Study: Long-term Efficacy and Safety

Daniel J. DoAngelo,1 Debipti H. Radia,1 Tracy I. George,1 William A. Robinson,1 Albert T. Quiery,2 Mark W. Drummond,3 Prithivraj Bose,3 Elizabeth O. Hoxier,4 Elliott Winton,1 Hans-Peter Horny,1 Michael T. Stassi,1 Ana Laura Munoz-Gonzalez1 and Michael W. Deininger4, Jason Golde5

1Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA; 2Guy’s & St Thomas’ NHS Foundation Trust, London, UK; 3ARUP Laboratories, University of Utah, Salt Lake City, UT; 4UC Denver, Denver, CO; 5University of Michigan, An Arbor, MI; 6Western Cancer Center, Dayton, OH; 7The University of Texas MD Anderson Cancer Center, Houston, TX; 8Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA; 9Department of Hematology and Medical Oncology Winship Cancer Institute, Emory University, Atlanta, GA; 10Institute of Pathology, Ludwig-Maximilians University, Munich, Germany; 11Novartis, Cambridge, MA; 12Blueprint Medicines Corporation, Zauber, Switzerland; 13Vessix Blood Research Institute, Worcestershire, WI; 14Stanford Cancer Institute, Stanford University School of Medicine, Stanford, CA

Background

- Advanced systemic mastocytosis (ASM) is a rare myeloid neoplasm driven by KIT D816V mutations in approximately 90% of patients.1
- Avapritinib includes three subtypes: aggressive SM (ASM), mast cell leukemia (MCL), and SM with an associated hematologic neoplasm (SM-AHN; most common).
- All subtypes of ASM are associated with poor quality of life and prognosis, and are extramedullary tumors from diagnostic ranging from 2 months for MCL to 3 years for SM-AHN and 3–4 years for ASM.2
- Avapritinib, an oral, highly potent and selective inhibitor of KIT D816V, is approved in the USA for the treatment of adult patients with SM-AHN and in the EU after a prior systemic therapy.2
- Avapritinib is not recommended for the treatment of patients with ASM with platelets of <150x10⁹/L.3
- The spectrum of treatment-related adverse events (TRAEs) is manageable, and the most frequent ≥30% treatment-related adverse events (TRAEs) were epistaxis, cognitive disorder, and fatigue in CENسود.4
- The most frequent (≥30%) treatment-related adverse events were epistaxis, cognitive disorder, and fatigue
- The majority of patients had observed reductions in objective measure of disease burden
- The majority of patients had showed a median duration of response of 11 months (95% CI: 20–30 months)
- The majority of patients had showed a median overall survival of 46 months (95% CI: 30–60 months)
- The majority of patients had showed a median progression-free survival of 26 months (95% CI: 10–40 months)

Methods

- Analyses included patients aged 18 years with centrally confirmed ASM who initiated avapritinib 30–400 mg once daily.
- Primary endpoints were MTD, RP2D, safety, and tolerability.
- Secondary endpoints included:
  - ORR per mIWG-MRT-ECNM criteria (67)
  - Progression-free survival (PFS) and overall survival (OS)
  - Diagnosis ■ ASM ■ SM-AHN ■ MCL

Results

- As of April 5, 2022, with a median follow-up of 45 months, 68% of patients (171/254) were enrolled in EXPLORER.
- The ORR per mIWG-MRT-ECNM criteria improved to 77% (n=135) vs. 67% (34–83) with ≥50% reduction from baseline (41/52).
- Eight events were associated with pre-existing severe TRAEs
- 80% (51/69) with ≥50% reduction from baseline 10 (14)
- 90% (41/46) with ≥50% reduction from baseline 23 (33)
- 83% (36/43) with ≥50% reduction from baseline in spleen volume (10)

Conclusions

- As of April 5, 2022, with a median follow-up of 45 months, 68% of patients (171/254) were enrolled in EXPLORER.
- The ORR per mIWG-MRT-ECNM criteria improved to 77% (n=135) vs. 67% (34–83) with ≥50% reduction from baseline (41/52).
- Eight events were associated with pre-existing severe TRAEs
- The majority of patients had observed reductions in objective measure of disease burden
- The median duration of response of 11 months (95% CI: 20–30 months)
- The median overall survival of 46 months (95% CI: 30–60 months)
- The median progression-free survival of 26 months (95% CI: 10–40 months)

References

- CRR per mIWG-MRT-ECNM response criteria were 77% in all patients (n=254) and 82% in patients with ASM (n=171).
- A median follow-up of 45 months, survival benefit was observed in patients with ASM, and median overall survival was 46 months (95% CI: 30–60 months).
- Among all patients treated with epistaxis, cognitive disorder, and fatigue, 75% of patients had ≥50% reduction from baseline in spleen volume (20–40 months).
- The majority of patients had observed reductions in objective measure of disease burden
- The majority of patients had showed a median duration of response of 11 months (95% CI: 20–30 months)
- The majority of patients had showed a median overall survival of 46 months (95% CI: 30–60 months)
- The majority of patients had showed a median progression-free survival of 26 months (95% CI: 10–40 months)

Disclosures

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