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632.CHRONIC MYELOID LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL | NOVEMBER 5, 2021

PF-114 in Patients Failing Prior Tyrosine Kinase-Inhibitor Therapy Including *BCR::ABL1* ^{T315I}

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Abstract

Background: Not everyone with CML responds optimally to TKI-therapy, especially those with *BCR::ABL1* ^{T315I}. PF-114 is a 4 th-generation oral tyrosine kinase-inhibitor (TKI) active against wild-type and mutated *BCR::ABL1* isoforms including *BCR::ABL1* ^{T315I}. We present final results of a phase-1 study (NCT02885766).

Methods: 3+3 dose-escalation study to determine maximum tolerated dose (MTD) and dose-limiting toxicity (DLT). Secondary objectives included safety and efficacy based on haematological, cytogenetic and molecular response criteria. Adverse events (AEs) were graded using NCI-CTCAE v4.03.

Results: 51 subjects (5 with accelerated phase CML, 46 - with chronic CML), 23 males, were studied. Daily doses were 50-600 mg/d given once daily continuously. Median age was 50 y (range, 29-82 y). Median CML duration pre-study was 10 y (range, 0.3-23 y). 16 subjects had *BCR::ABL1* ^{T315I}. 25 subjects received ≥ 3 prior TKIs. Median follow-up was ≥ 31 mo and median exposure, 6 mo (range, 0.4-52). Therapy was ongoing in 7 subjects at study termination. Others discontinued because of progression (n = 20), AEs (n = 2), consent withdrawal (n = 5), entry into another study (n = 3) or other reasons (n = 14). The MTD was 600 mg with the grade-3 psoriasis-like skin AE as the DLT. There were no vascular occlusive events or deviations of ankle-brachial

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index. Complete haematologic response (CHR) was achieved in 14 of 30 subjects, major cytogenetic response (MCyR) in 15 of 44 subjects, complete cytogenetic response (CCyR) in 11 of 50 subjects and major molecular response (MMR) in 8 of 51 subjects. Median duration of CHR was 12 mo and has not been reached for MCyR, CCyR and MMR. The best safety/efficacy dose was 300 mg/d with 6 of 9 subjects achieving a MCyR, 5, a CCyR and 4, MMR. 5 of 16 subjects with *BCR::ABL1* ^{T315I} responded, including 4 achieving a MCyR, 2, a CCyR and 1, a MMR. 2 of 6 subjects failing ponatinib achieved a CHR.

Conclusion: PF-114 was safe and effective in subjects failing ≥ 2 TKIs and those with *BCR::ABL1* ^{T315I} including those failing ponatinib. The PF-114 dose for further study is 300 mg/d.

Disclosures

Turkina: *Bristol Myers Squibb:* Speakers Bureau; *Pfizer:* Speakers Bureau; *Pharmstandart:* Speakers Bureau; *Novartis Pharma:* Speakers Bureau. **Vinogradova:** *Bristol Myers Squibb:* Speakers Bureau; *Novartis Pharma:* Speakers Bureau; *Pfizer:* Speakers Bureau; *Pharmstandart:* Speakers Bureau. **Lomaia:** *Novartis:* Honoraria; *Pfizer:* Honoraria; *BMS:* Honoraria; *Pharmstandard:* Honoraria. **Chelysheva:** *Pfizer:* Speakers Bureau; *Novartis Pharma:* Speakers Bureau; *Bristol Myers Squibb:* Speakers Bureau; *Pharmstandart:* Speakers Bureau. **Petrova:** *Pfizer:* Speakers Bureau; *Novartis Pharma:* Speakers Bureau. **Cortes:** *Bio-Path Holdings, Inc.:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Sun Pharma:* Consultancy, Research Funding; *Takeda:* Consultancy, Research Funding; *Pfizer:* Consultancy, Research Funding; *Bristol Myers Squibb, Daiichi Sankyo, Jazz Pharmaceuticals, Astellas, Novartis, Pfizer, Takeda, BioPath Holdings, Incyte:* Consultancy, Research Funding; *Novartis:* Consultancy, Research Funding. **Baccarani:** *Novartis:* Consultancy, Membership on an entity's Board of Directors or advisory committees. **Ottmann:** *Fusion:* Honoraria; *Incyte:* Honoraria, Research Funding; *Amgen:* Honoraria, Research Funding; *Celgene/BMS:* Honoraria, Research Funding; *Novartis:* Honoraria. **Mikhailov:** *Fusion Pharma:* Current Employment. **Novikov:** *Fusion Pharma:* Current Employment. **Shulgina:** *Fusion Pharma:* Current Employment. **Chilov:** *Fusion Pharma:* Current Employment.

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