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BIOmarker driven trial of Vegf2 inhibitor in advanced or metastatic sarcoma (the BIOVAS trial): Results of the SNP positive cohort and the CSF1 high cohort

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Background

Tyrosine kinase inhibitor against VEGFR has been widely used in relapsed and refractory sarcoma. However, there is no biomarker(s) available to predict the efficacy and durability of response to date.

Methods

Since 2019 October, we started the BIOmarker-driven trial of Vegfr inhibitor in Advanced or metastatic Sarcoma (BIOVAS), a phase 2, biomarker-driven trial to assess the efficacy of VEGFR inhibitor in patients selected by single nuclear polymorphism(SNP) of VEGFR2 604A>G (1.SNP cohort), CSF1 amplification or upregulation (2.CSF1-high cohort), and chromosome 4q12 amplicon including KIT/KDR/PDGFRA (3. chr4q12-amp cohort). In each cohort, single-agent VEGFR inhibitor Apatinib is given until PD or unaccepted toxicities. The primary endpoint will be met if the 16-week progression-free rate (PFR) in biomarker-positive population is ≥ 70% (≥18 out of 28 pts), against the H0 of PFR ≤ 50% as in the general biomarker-unselected pts. Biomarker-negative pts are also treated as a non-comparative, non-randomized control. Here we report the outcome of the SNP cohort and CSF1-high cohort.

Results

In SNP cohort, a total of 29 A>G positive patients with advanced or metastatic sarcoma were included. The median age was 23 (Range 8-52) yrs with 15 females and 14 males. Histology types include 15 conventional OS, 2 conventional CS, 1 dedifferentiated OS , 1 Ewing, 1 FS, 1 radiation-associated sarcoma, 1 CIC-rearranged sarcoma, 2 SS, 1 malignant PEComa, etc. The primary endpoint was met, with 21 out of 29 being progression-free at 16 wks (16w-PFR =72.4%, mPFS=6.03 mo). In contrast, the 604A>G negative patients (n=22) have a 16w-PFR of 42.3% and an mPFS of 3.9 months, similar to historical control. In CSF1-high cohort, a total of 27 patients were recruited, including 13 COS,3 SS, 2 periosteal OS, 2 SRSC, etc. The primary endpoint was met, with 19 out of 27 being progression-free (16w-PFR =70.4%, mPFS= 6.7 mo). Patient with CSF1-low or unknown has a PFR of 42.5% with a mPFS of 4 months. RNAseq data between biomaker status will be presented in the congress.

Conclusions

Our trial supports the use of VEGFR inhibitor in a histology agnostic, biomarker-driven approach based on VEGFR 604A>G and CSF1-high status in sarcoma patients.

Clinical trial identification

NCT04072042.

Legal entity responsible for the study

Ruijin Hospital.

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Disclosure

All authors have declared no conflicts of interest.