Germline mutations in homologous recombination repair (HRR) pathway in a Chinese multi-cancer retrospective analysis

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Background

Germline mutations of HRR genes have been proven to be associated with familial cancers. Recently, FDA has approved olaparib for adult patients (pts) with deleterious germline or somatic HRR gene-mutated metastatic castration-resistant prostate cancer. Here, we reported an analysis of germline mutations of HRR genes in a multi-cancer cohort for pts who might benefit from PARP inhibitors in clinical development.

Methods

We retrospectively reviewed next-generation sequencing data of 49,895 pts with solid cancers in a Chinese cohort. The deleterious germline mutations in HRR genes (ATM, BARD1, BRCAl, BRCAl2, BRIP1, PALB2, RAD51C and RAD51D) were analyzed.

Results

A total of 110 (0.22%) pts with germline mutations in HRR pathway were detected in 12 types of cancer. The germline HRR mutation-positive rates were 6.52% (18/276) in ovarian cancer pts, 2.50% (1/40) in tongue cancer pts, 2.08% (3/144) in prostate cancer pts, 2.01% (12/596) in breast cancer pts and less than 1% in pts with other types of cancer.

The most common mutated HRR gene was BRCA1 (gBRCA1m, 50.00%), followed by BRCA2 (gBRCA2m, 29.09%) and BRIP1 (8.18%). For cancers (breast, ovary, pancreas and prostate) that the FDA has approved for treatment with PARP inhibitors, 35 of the 39 pts harbored gBRCA1/2m. Besides, there are another 52 pts with other cancers carrying gBRCA1/2m. Meanwhile, a total of 23 pts carried non-gBRCA1/2m. The germline HRR mutations mainly occurred on BRCA1/2, indicating the strong pathogenicity of gBRCA1/2m.

Conclusions

This study revealed the landscape of germline mutations in HRR pathway in Chinese cancer pts, which might result in more effective personalized diagnoses and therapies.

The authors declare no conflicts of interest.

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